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Foundations of Analytical Chemistry

A Teaching–Learning Approach

Springer

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Foreword

The new agreements concerning the European Space for Higher Education, and the need to harmonize university science programs throughout the world, have raised a pressing demand for a new approach to the disciplines in university curricula. In today's rapidly changing world, education in chemistry cannot absorb all recent developments in its area of knowledge. For this reason, the undergraduate and master programs to be taught by universities should be harmonized by critically and thoroughly reflecting on the foundations of each subject.

Principles of Analytical Chemistry, a previous book by Miguel Valcárcel published by Springer in 2000, was a useful tool for understanding the fundamentals of this chemical discipline. His recent book *Fundamentos de Química Analítica. Una aproximación docente–discente*, which is co-authored by Ángela I. López-Lorente and M^{a} Ángeles López Jiménez, and was released in Spanish by UCO Press early in 2017, provides an image-laden description of Analytical Chemistry and a highly interesting, attractive tool for teaching this discipline and its main concepts in the digital era. An English version of the book was thus highly desirable and needed.

This book is very original in that it introduces an innovative way of presenting university teaching material. Also, it is unusual because it follows a teacher–student approach: One of the co-authors is a student who learned the material recently in her chemistry studies. Approaching the subject from a student's point of view will certainly provide lecturers with highly valuable feedback and facilitate modulation of their teaching. In addition, the visual (slides) and written material (explanations, examples, and exercises) in the book can be of great help to plan lessons and seminars, and also to guide students' non-face-to-face work.

The book is very well structured. The initial chapters (Parts I and II) lay the foundations for analytical science and lead seamlessly to a highly innovative, contemporary view of the socioeconomic projection of Analytical Chemistry in Part III. Parts I and II provide the background needed to understand that Analytical Chemistry is the metrological discipline of chemistry and that it plays a key role in assuring quality in (bio)chemical information. Each chapter ends with a set of questions answered in Annex 2 for students to self-assess their learning. Also, the book includes a highly instructional glossary of terms in Annex 1. All topics are discussed in an orderly, clear manner.

To our minds, this book is a major contribution to a much needed shift from obsolete teaching practices to active, student-driven learning. Undergraduates not only in chemistry, but also in medicine, biology, pharmacy, and environmental science will surely benefit from its contents and structure, which convey a faithful image of Analytical Chemistry: a first-hand choice for solving a myriad of real-life problems with appropriate, fully validated methods.

With the current growing use of information and communication technologies at university, the image-based approach followed in the book makes it a convenient tool for teachers and students alike. We are certain that the English edition will be highly successful.

February 2017

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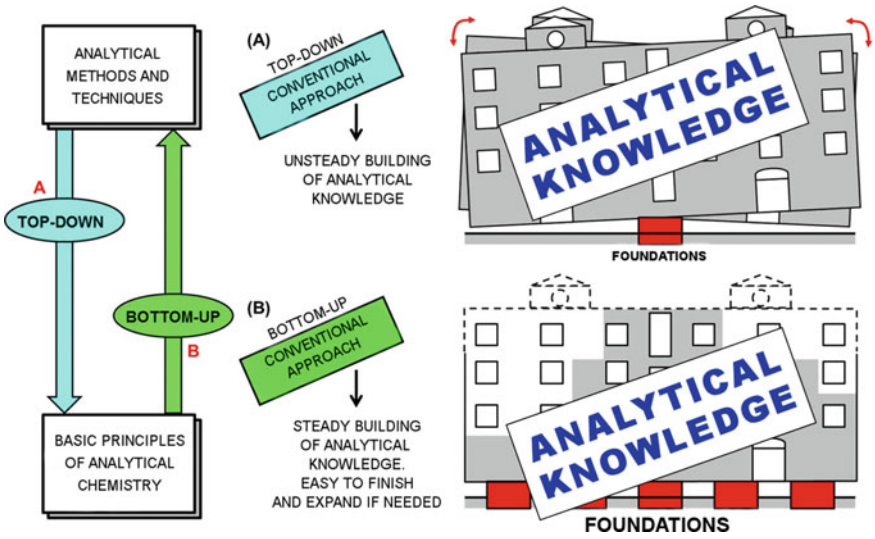
Preface

The authors were compelled to write this book by two main "drivers." One was their wish to further endorse the strategic significance of the true fundamentals of Analytical Chemistry in order to help students first approaching this discipline to understand them and to erect their "analytical chemical building" on solid foundations.



Two opposite approaches to the teaching and learning of Analytical Chemistry in undergraduate curricula. The traditional, top-down approach, which goes from descriptions to fundamentals, leads to an unsteady building and to abilities prevailing over attitudes. On the other hand, the bottom-up approach, which is used in this book, goes from fundamentals to the description of methods and techniques in order to construct a solid, steady building that can be completed with further analytical chemical subjects

The twofold primary aim of this book is to have students acquire a truthful image of Analytical Chemistry in order to develop abilities and attitudes that are consistent with the essence of the discipline, and to provide a firm background for addressing

other analytical chemical subjects (e.g., analytical separation systems, instrumental analysis).

Rather than to prepare the typical lectures for delivery in the classroom, this book requires teachers to contextualize concepts, emphasize especially relevant notions, support their messages with examples, and respond to students' questions. This novel teaching approach certainly calls for some changes in lecturers' traditional role.

The authors' second "driver" for writing this book was their commitment to teaching innovation in a subject that is initially difficult to understand. For this reason, the book contains a large collection of animated PowerPoint slides that are individually explained with text and illustrated with many examples testifying to the roles of Analytical Chemistry in today's world. This new teaching approach is expected to change the minds of those students who might initially be reluctant to be taught slide-driven lessons.

Because of its unusual teaching–learning standpoint, the preliminary sections of the book have been expanded with a technical introduction and a brief guideline for efficient use.

This book was previously released in Spanish by UCO Press (ISBN 978-84-9927-273-3) in January 2017. The authors are indebted to the publishing manager, Prof. Juan Pedro Monferrer Sala, for his support and help to have it released in English by Springer. Also, they wish to thank Antonio Losada, MSc, for his translation of the Spanish manuscript, and acknowledge the University of Córdoba for partial funding of the translation budget.

This book would never have been possible without the warm welcome and support of Dr. Steffen Pauly, Editorial Director of Springer.

Córdoba, Spain
April 2017

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Contents

Introduction

This section describes the most salient technical features of the book and provides suggestions for use by lecturers and students.

Technical Features

To the authors' minds, the unconventional teaching–learning approach to the *Foundations of Analytical Chemistry* used in this book may be easier to follow if it is previously summarized in terms of its most salient features.

Relative importance of slides and text in the book

1. The primary goal is to *facilitate teaching and learning* of the cornerstones of Analytical Chemistry as the discipline responsible for analysis, which is the third basic component of chemistry in addition to theory and synthesis.
2. The book is intended to be used by *undergraduates* on various programs (e.g., chemistry, pharmacy, food technology, biology, biochemistry) being *exposed to Analytical Chemistry for the first time* in their studies (that is, by young students with a limited scientific and technical background). To ease their first encounter with Analytical Chemistry, the authors have produced slides and accompanying text that are straightforward and easy to understand; also, they have strived to explain analytical chemical concepts with reference to a large number of real-life examples for even easier understanding. The fact that one

of the authors M.A. López-Jiménez is a chemistry undergraduate is expected to help convey the book's teaching message from a student's viewpoint.

3. One other major goal of the book is to *dismiss the wrong view of Analytical Chemistry* acquired by students who are directly introduced to concepts such as ionic equilibria, chemical calculations. Such is the case, for example, with the classic book *Analytical Chemistry*, by Gary Christian et al., now in its seventh edition (Wiley–VCH, USA, 2014). In fact, very few general analytical chemistry textbooks start with topics other than calculations or equilibria. Insisting on dealing with ionic equilibria as if they belonged in the *Foundations of Analytical Chemistry* in the twenty-first century is a gross error that seriously damages its image and should be avoided at any rate.
4. The book comprises *two distinct but mutually consistent elements*, namely a collection of more than three hundred, mostly animated, slides, which is its greatest strength, and explanatory text for each individual slide. In addition, it contains a glossary of terms and the answers to all questions posed in the nine chapters—240 in all.
5. The *book contents* are organized in three parts consisting of three chapters each. Part I is concerned with the principles of Analytical Chemistry, Parts II with the processes used to obtain (bio)chemical information from objects and systems, and Part III with the socioeconomic impact of the discipline.
6 *Each slide is unequivocally identified* by the number of the chapters where it appears, followed by that in the chapter sequence. Thus, Slide 2.5 is the fifth slide in Chap. 2. Also, the elements appearing in animated slides are identified by a further number according to their place in the animation sequence. Thus, the three paragraphs explaining the sequence of notions in Slide 2.5 are numbered 2.5.1, 2.5.2, and 2.5.3.
7. Each chapter contains the following sections:

    1. An introductory part including a Summary, a list of the chapter sections and subsections, and the teaching objectives to be fulfilled.
    2. Section X.1 (X being the chapter number) explains each individual slide. This section accounts for about 85% of the text in each chapter.
    3. Section X.2 provides students with suggested readings selected according to relevance and accessibility.
    4. Section X.3 is a list of questions on the chapter topic for students to answer. The questions are all answered in Annex 2 to facilitate self-assessment.
    5. Section X.4 is a proposal for shortening the chapter contents when delivered to undergraduates on programs other than chemistry.

8. *Internal consistency in the book contents* was permanently borne in mind in writing the text and is ensured by multiple cross-references to slides in other chapters. In this way, the chapters are not tight compartments bearing no mutual relationship; also, students are provided with an integral view of the discipline that is easier to understand.
9. The Glossary of Terms in Annex 1 briefly defines 250 keywords used in the book in order to acquaint students with *analytical chemical jargon*.

10. One other primary concern of the authors was to illustrate the book with appropriate examples of *required (bio)chemical information* and how to obtain it. The role of Analytical Chemistry is explained with real-life situations intended to arouse students' interest and to help them understand their implications.
11. Last but not least, Section X.4 in each chapter poses relevant questions and problems for students to review its contents and self-assess their learning. The questions are solved and problems worked out in Annex 2. In this way, continual evaluation is made possible.

Guidelines for Using the Book

Because this is an unusual book intended to facilitate the teaching–learning process, the authors wish to respectfully make some suggestions to students and lecturers in this respect.

Lecturers delivering a subject such as *Foundations of Analytical Chemistry* may feel that using a book that places the whole teaching material in students' hands will undermine their role as teachers. However, it is far from the authors' intention to replace the irreplaceable: the extremely high added value of taught lessons, personal teacher–student contact, doubt-solving sessions, online question posing, direct monitoring of students' progress, and continuous evaluation of their learning achievements.

Obviously, lecturing for students to simply take notes or merely going through slide contents in class is at the opposite end of the authors' proposal. What are lecturers expected to do then? Simply to be whole teachers, know their discipline in depth, use their own words to explain the slides—and connect their parts when needed—emphasize the relationships between concepts explained in other chapters, continuously interact with their students, help them with their doubts and the questions in each chapter, both in class and online, set up case-study seminars to solve specific analytical problems, and, especially, "conspire" to make students feel they are being permanently supported.

Students following the proposed teaching–learning approach will have to switch their mindsets if they are to improve their performance without resorting to the typical one-off efforts of traditional examinations. Because this book promotes and facilitates continuous evaluation of their progress, students should instead strive to (a) preview the slides for the topics to be dealt with in each lecture and read the accompanying text; (b) play an active role in lectures and seminars; (c) earn the lecturer's complicity, and (d) not learn contents by heart, but rather through dedicated, perseverant class and homework. The required switch in working method is almost certain to appeal to any student eager for change.

Part I
Introduction to Analytical Chemistry

Principles of Analytical Chemistry

1

Abstract

This chapter is an overview of the essentials of Analytical Chemistry intended to provide transversal support for all others. The first of its three parts discusses partial and complete definitions of Analytical Chemistry, and describes its aims and objectives, its essential references and the characteristics of (bio)chemical information (its primary "output"). The second part presents the most important key words of Analytical Chemistry in a hierarchical manner and complementary classifications of this scientific discipline. The third part introduces new paradigms in today's and tomorrow's Analytical Chemistry including scientific and technical research, and the transfer of analytical knowledge and technology.

Teaching objectives

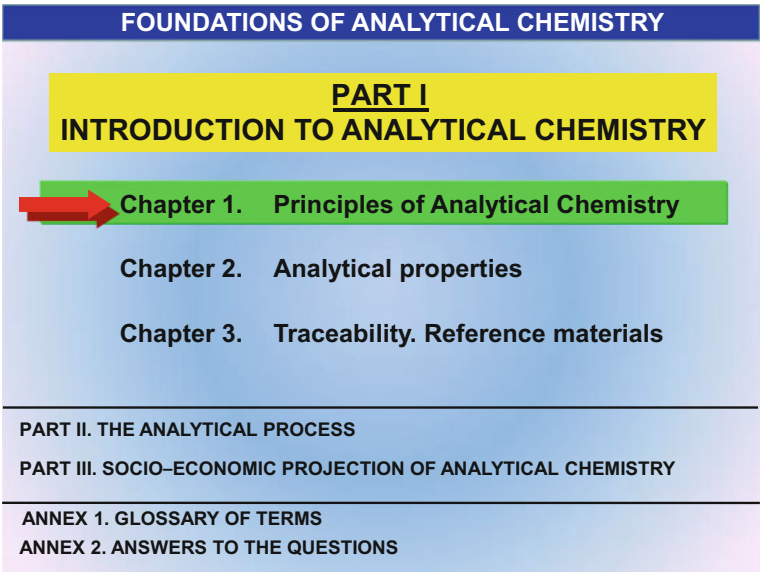
- To introduce students to Analysis, the third essential component of Chemistry in addition to Synthesis and Theory.
- To define Analytical Chemistry by highlighting its peculiarities with respect to other areas of Chemistry.
- To establish the landmarks that constitute its foundations.
- To state key definitions in a hierarchical manner and establish non-mutually exclusive classifications.
- To describe the new paradigms of Analytical Chemistry.
- To highlight the research and transfer connotations of Analytical Chemistry.

Electronic Supplementary Material The online version of this chapter (doi:10.1007/978-3-319-62872-1_1) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_1

1.1 Explanation of the Slides

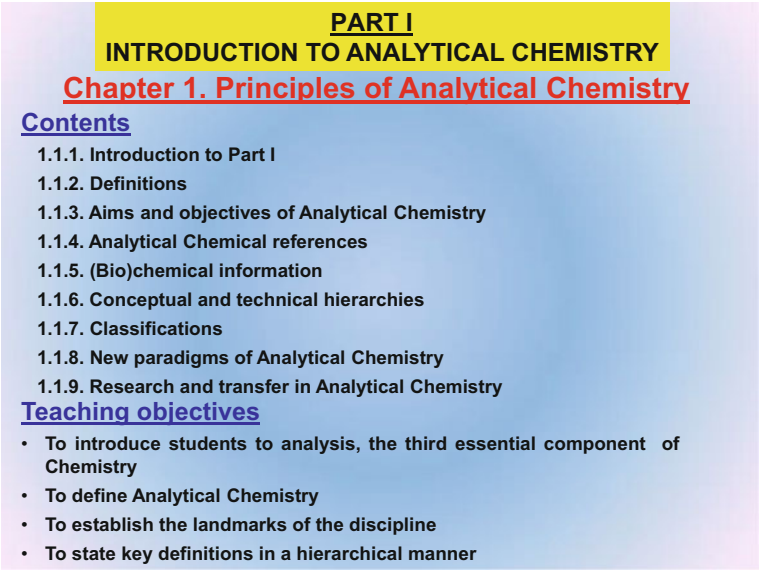
Slide 1.1



This slide places Chap. 1 in Part I of the book: Introduction to Analytical Chemistry. Also, it shows the other two parts and annexes.

This is an introductory chapter intended to serve as a general approach to Analytical Chemistry.

Slide 1.2

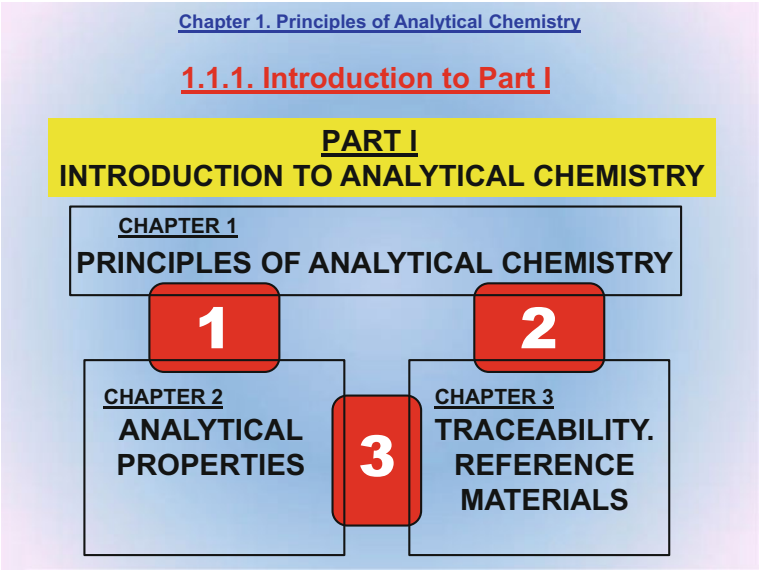


1.2.1. The nine sections of the chapter. After placing the chapter in the context of Part I, it provides a general description of Analytical Chemistry in the next four sections. Through conceptual and technical hierarchies and classifications, the contents of the discipline are established its essential key words identified.

1.2.2. The teaching aims to be fulfilled are defined: essentially, to provide an overview of Analytical Chemistry as the third basic component of Chemistry through its landmarks.

1.1.1 Introduction to Part I (1 Slide)

Slide 1.3



This is a schematic depiction of the relationships (boundaries 1–3) among the contents of the first three chapters, which together provide a general, harmonic overview of Analytical Chemistry.

Chapter 1 introduces the general principles of Analytical Chemistry and is connected with the other two as follows:

Boundary 1. Analytical Chemistry uses a series of indicators to assess analytical quality (Chap. 8) and its own social responsibility, that is, its internal and external impact on society and the environment (Chap. 9). The indicators are analytical properties, which are described in Chap. 2.

Boundary 2. Traceability, both internal and external, is essential with a view to acquiring an accurate image of Analytical Chemistry, which is the discipline of (bio)chemical[1] measurements: measuring requires comparing with standards (reference materials) and, inevitably, assuring traceability.

Boundary 3. This boundary relates Chaps. 2 and 3. The connection between quality-related analytical indicators and the analytical properties to be maximized (accuracy and representativeness) is closely related to the integral concept of traceability of analytical results (see Slide 3.25). Also, quality-related analytical

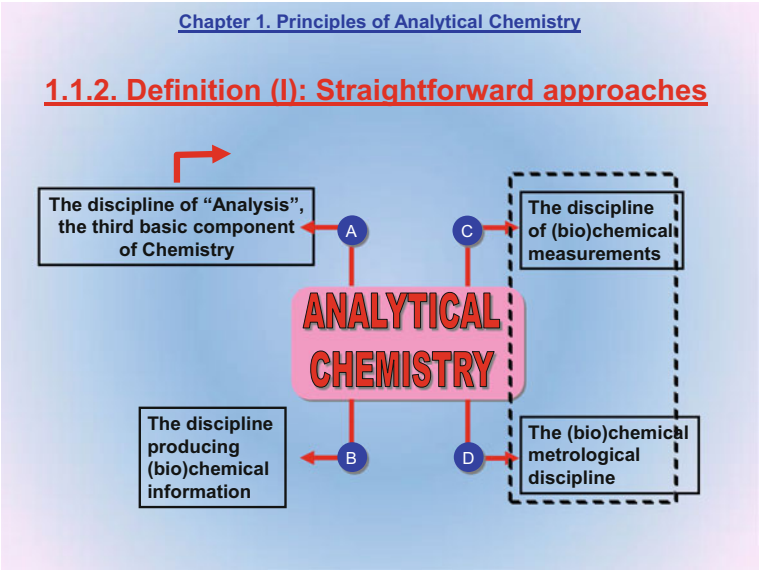
[1]The adjective "(bio)chemical" is intended to designate in a simple manner the type of information dealt with in Analytical Chemistry. It is a contraction of "chemical" and "biochemical", and applies indifferently to either type of information.

indicators rely critically on the reference materials used for (bio)chemical measurements.

1.1.2 Definitions of Analytical Chemistry (4 Slides)

The following slides provide various supplementary definitions of Analytical Chemistry intended to construct an identity of its own as an essential discipline of Chemistry.

Slide 1.4



1.4.1. This is a compilation of straightforward approaches to defining Analytical Chemistry.

First, Analytical Chemistry is defined as the discipline of "(Bio)chemical Analysis" and hence as the third essential element of Chemistry as shown in the next two slides.

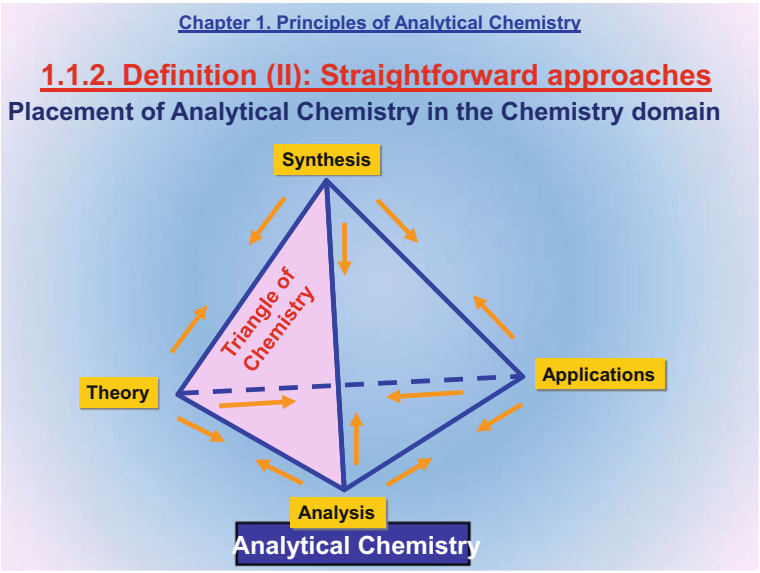
1.4.2. Analytical Chemistry is the discipline of Chemistry in charge of producing quality (bio)chemical information. This is the output of Analysis, the central element in the previous paragraph.

1.4.3. Analytical Chemistry is thus the discipline of (bio)chemical measurements.

1.4.4. And hence the (bio)chemical metrology discipline since Metrology is the science of measurements, whether physical (temperature), chemical (calcium concentration in milk), biochemical (enzyme activity in a biological fluid), microbiological (bacterial count in a culture) or otherwise.

As a result, the last two definitions are identical. In fact, they show where Metrology and Analytical Chemistry converge. As shown later on, however, their coincidences have synergistic connotations.

Slide 1.5



1.5.1. This slide places Analysis (Analytical Chemistry) in the context of Chemistry as an essential ingredient of its definition.

Thus, Analysis is an apex of the basic triangle defining Chemistry in addition to Theory and Synthesis.

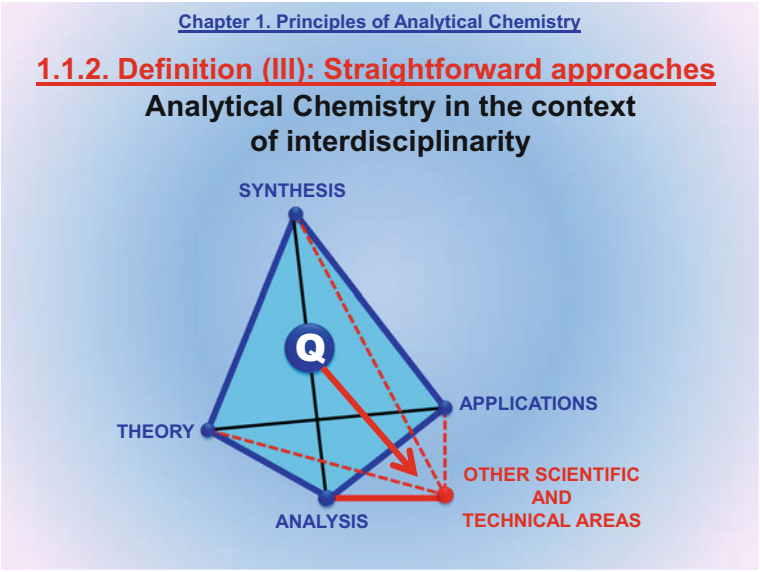
1.5.2. Applications are also essential for Chemistry. As a result, so the basic triangle of Chemistry becomes a tetrahedron.

1.5.3. The tetrahedron affords two- and three-way relationships among each component of Chemistry and those at the other apices. Thus, Synthesis provides the reagents needed for Analysis and Analysis is indispensable to characterize raw materials, intermediate products and end-products in a chemical synthesis process.

In addition, the tetrahedron distinguishes Analysis from Applications of Chemistry, which is essential in order to define Analytical Chemistry thoroughly.

1.5.4. Analysis definitely falls in the domain of Analytical Chemistry.

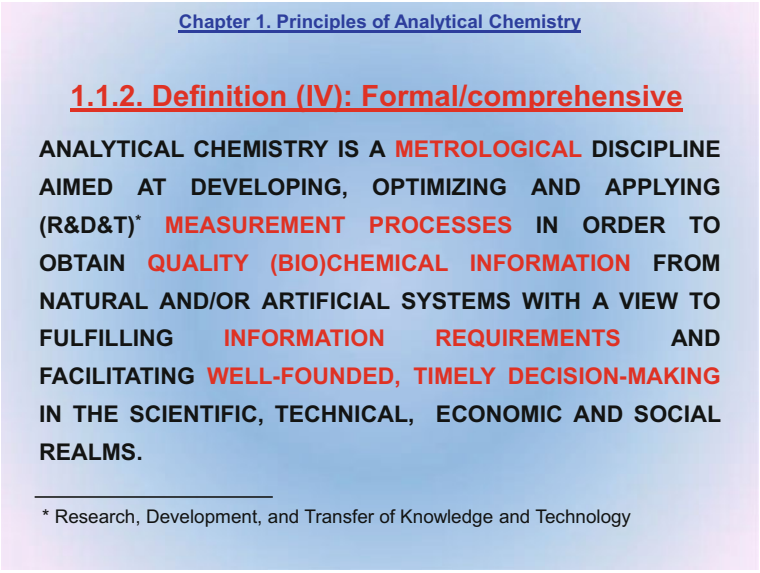
Slide 1.6



The tetrahedron in Slide 1.5 must be expanded to a pentahedron in order to accurately define Chemistry in the XXI century by adding another apex: boundaries to other scientific and technical areas.

It should be noted that Chemistry has evolved to relate to an increasing range of scientific and technical areas such as Physics, Engineering or Biology. Analytical Chemistry (Analysis) plays a central role in these cooperative relationships. In fact, having accurate (bio)chemical information is crucial with a view to making well-founded, timely decisions in such areas.

Slide 1.7

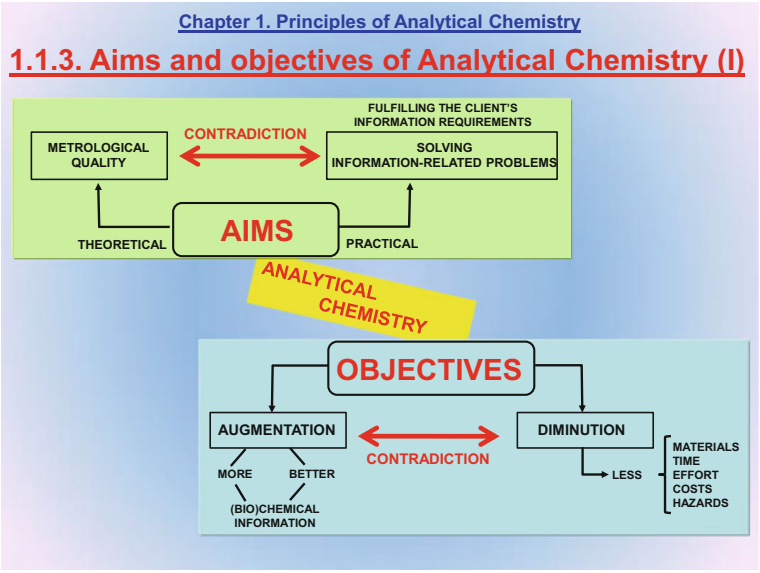


This slide provides a more comprehensive, almost formal definition of Analytical Chemistry. In fact, it is a compilation of the previous, simpler definitions that highlights the following notions:

- its metrological nature;
- research development (Research) and application (Transfer) of measurement tools and processes;
- (bio)chemical information about natural and artificial objects and systems;
- fulfilment of information needs; and
- well-grounded, timely decision-making in various domains.

1.1.3 Aims and Objectives of Analytical Chemistry (3 Slides)

Slide 1.8



1.8.1. The previous definitions are completed here by describing the aims and objectives of Analytical Chemistry.

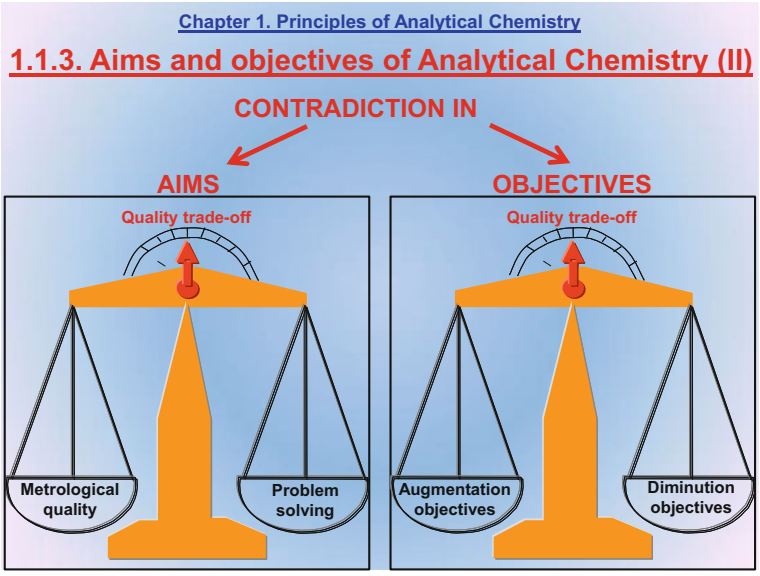
Analytical Chemistry has two primary aims. As a basic discipline, it aims at the highest possible metrological quality, that is, at producing highly accurate results or reports (Slides 2.14 and 2.15) with as low specific uncertainty as possible (Slides 2.7 and 2.29).

As an applied discipline, Analytical Chemistry aims at fulfilling needs for (bio)chemical information, that is, at solving so-called "analytical problems" (see Chap. 7). This requires optimizing not only the results, but also other factors such as response times, costs or available means.

1.8.2. Analytical Chemistry has two primary types of objectives. Augmentation objectives involve obtaining more (bio)chemical information of a greater quality. On the other hand, diminution objectives are to be fulfilled by using increasingly less material (sample, reagents, solvents, etc.) in analytical processes in order to produce results as expeditiously and with as little human involvement and low hazards to operators and the environment as possible.

1.8.3. As can be easily inferred, the two aims are mutually contradictory, and so are the two objectives as shown in the next slide.

Slide 1.9

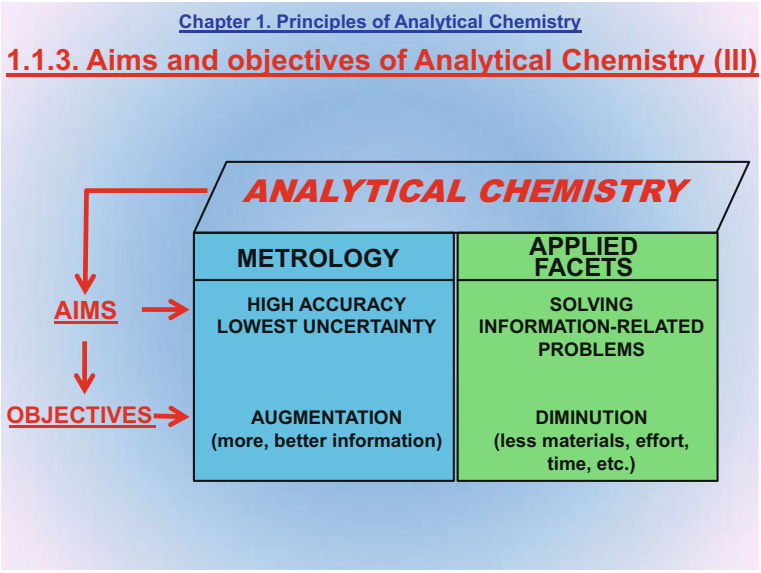


This slide exposes the contradiction between the aims of Analytical Chemistry on the one hand and its objectives on the other. To what extent either pan causes each balance to tip will depends on the "quality trade-offs" to be made, which should be accurately known before analyses are started.

When a high metrological quality is required or augmentation objectives are to be fulfilled, the corresponding balance should tip to the left. Similarly, when a practical end (solving a problem or fulfilling diminution objectives) is to be favoured, then the balance concerned should tip to the right.

It should be noted that trade-offs also arise from the contradictory relationships among analytical properties described in Slides 2.56–2.61.

Slide 1.10

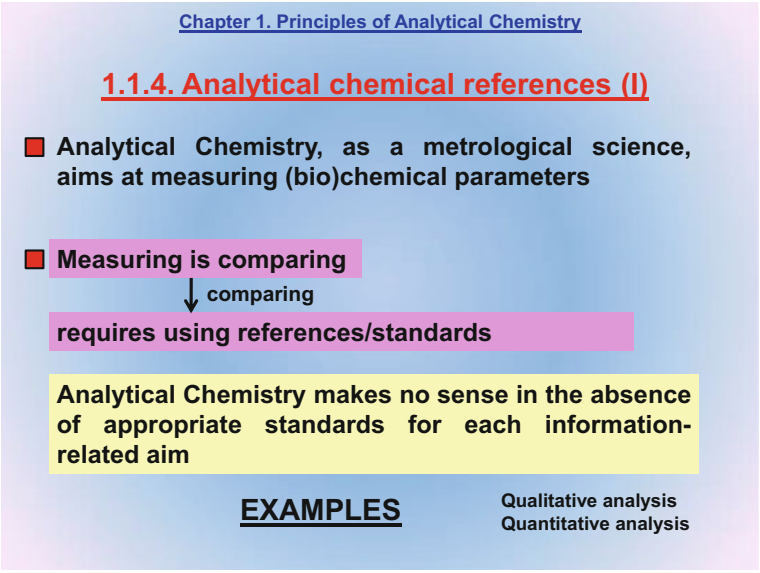


In addition to its basic metrological component, Analytical Chemistry has an essential applied component.

The two components encompass the aims and objectives described in Slide 1.8.

1.1.4 Analytical Chemical References (4 Slides)

Slide 1.11



As defined in Slide 1.4, Analytical Chemistry is the discipline of (bio)chemical measurements.

A tailor can hardly make a proper suit to measure if he uses an elastic tape to take the client's measures because each time he measures the sleeve he will get a different length.

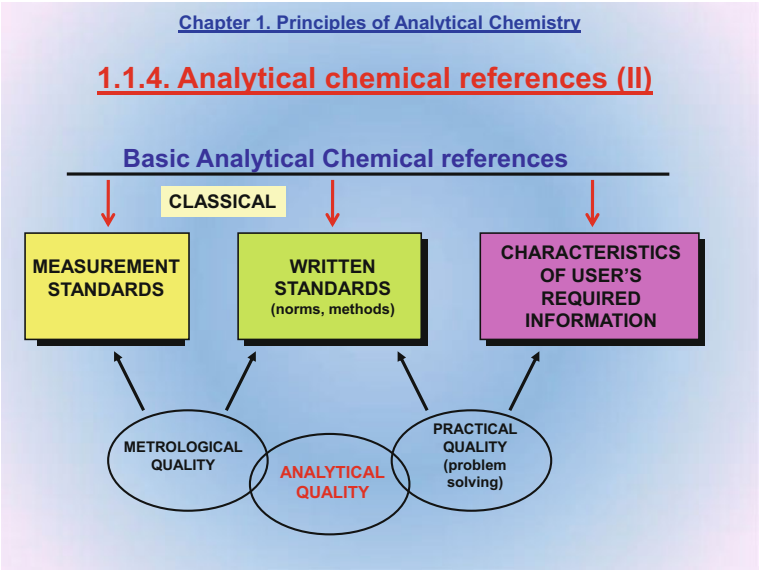
Measuring entails comparing with well-established, widely accepted references. The main references in the analytical fields are measurement standards, which are presented in Chap. 3. Analytical Chemistry makes no sense without tangible standards or references for each information-related purpose.

The references for Qualitative Analysis based on human senses are stored in the brain. Thus, one can "learn" the odour of acetic acid and tell whether a liquid is vinegar by smelling it.

In Quantitative Analysis, a standard of the target substance (e.g., copper present in trace amounts in spring water) produces an instrumental signal or a set of several standards of increasing concentration produce several signals that are plotted to construct a calibration curve (see Slide 2.36). The concentration of copper in the sample is determined by comparing the signal for the sample with those for the standards by interpolation into the calibration curve.

As shown in the following slide, however, in Analytical Chemistry the concept "standard" has wider implications.

Slide 1.12

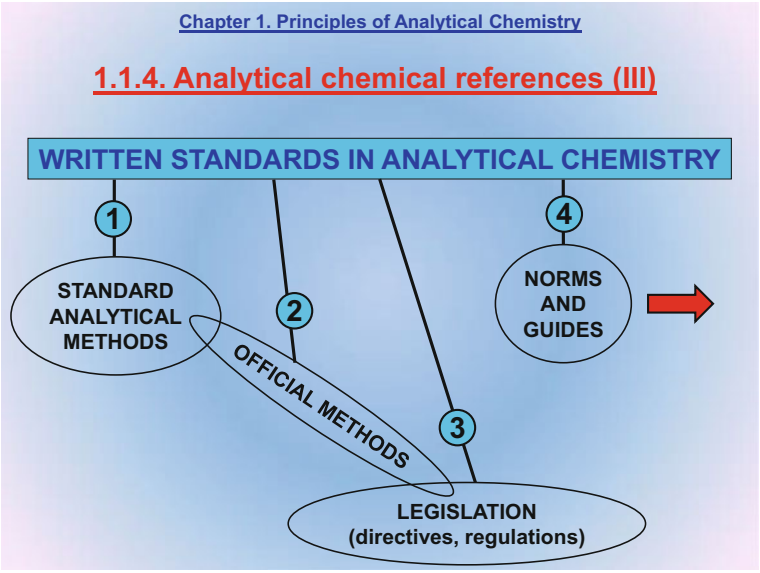


1.12.1. Analytical Chemistry uses two classical types of references. One is tangible measurement standards, which are those systematically used for comparisons in Metrology in Chemistry and described in Chap. 3. The other type is written (intangible) standards, which are especially relevant to Analytical Chemistry and described in Slide 1.13.

1.12.2. If the aims and objectives related to the non-metrological side of Analytical Chemistry are considered, then the (bio)chemical information required to make well-founded, timely decisions is its third basic reference. This atypical reference is crucial with a view to designing effective analytical processes (Chap. 4) and to properly solving analytical problems (Chap. 7) as it is their greatest influence: the aim of analysing a sample.

1.12.3. Classical standards are related to metrological quality just as the third basic reference of Analytical Chemistry is related to practical quality (solving information-related problems). These two types of quality must converge if integral analytical quality is to be achieved (see Chap. 8).

Slide 1.13



As can be seen, Analytical Chemistry uses four types of intangible (written) standards, namely:

1. *Standard methods*, each of which describes the process for detecting and/or quantifying one or more analytes in a given type of sample. These methods are endorsed by renowned non-government organizations such as AOAC in the USA and published in printed or electronic form for use by analysts.
2. *Official methods of analysis*, which are binding for government-dependent or accredited laboratories. These methods are published through official documents and fall in between standards 1 and 3.
3. *Legally binding documents* released through official publications (e.g., the Official Journal of the European Communities) and stating the highest tolerated limits of specific toxins in foods, for example. Such limits (C_{LL}) are essential with a view to validating an analytical method by comparison with its limits of detection (C_{LOD}) and quantification (C_{LOQ}), which are defined in Slides 2.40 and 2.41.
4. *Guides and standards* for specific purposes that are issued and periodically revised by international bodies. They provide the operational framework for some organizations and also for their evaluation (certification, accreditation).

A *written standard* is a consensus document endorsed by a competent, usually international, body stating the requirements to be fulfilled in addition to specific

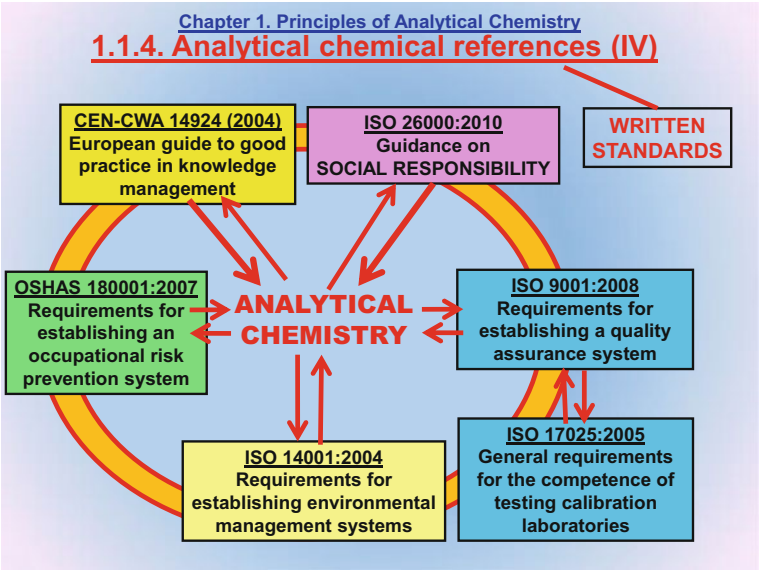
rules, guidelines and characteristics. Standards can apply to activities, products, processes and services. Their most salient purposes are as follows:

(a) providing guidance for designing specific activities; and
(b) establishing specific requirements to be fulfilled in order to ensure that an activity will be compliant with the standard concerned.

Standards are harmonized on an international scale by organisms such as the International Organization for Standardization (ISO). Some are pronounced legally binding by national governments or the European Union by conversion into type 3 standards.

Guides provide help to develop specific activities. They are not binding but can be very useful to assist organizations in matters such as emerging topics (see, for example, Social Responsibility in Chap. 9).

Slide 1.14



These are the most useful written standards for Analytical Chemistry, with which they bear a two-way relationship with this discipline.

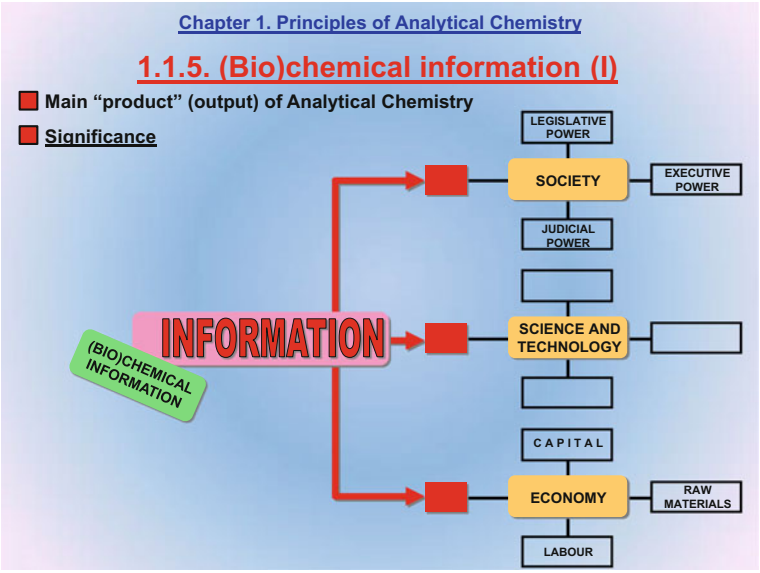
1. *Guide for implementing knowledge management systems*, which interprets information (qualitative and quantitative results) and places it in context. It is highly relevant to Social Responsibility in Analytical Chemistry (see Chap. 9).
2. *Guide for implementing Social Responsibility*, which, as shown in Chap. 9, can be easily adapted to Analytical Chemistry.

3. *Standards for implementing quality assurance systems.* The first standard is general in nature and states the requirements for establishing a quality assurance system (QAS). The second is specific to physical and chemical measurement laboratories, and states the managerial and technical requirements for laboratory accreditation. Its first part coincides with the general part. These standards, which are essential for laboratories aiming at accreditation, are described in detail in Chap. 8.
4. *Environmental management standards*, some of which pertain to air, water or soil analyses.
5. *Occupational risk management standards*, which establish a number of maximum tolerated levels for workers in contact with deleterious substances and compliance with which should be carefully checked from analytical information.

Each of the previous documents has a unique universal code shown in the slide.

1.1.5 (Bio)chemical Information (4 Slides)

Slide 1.15



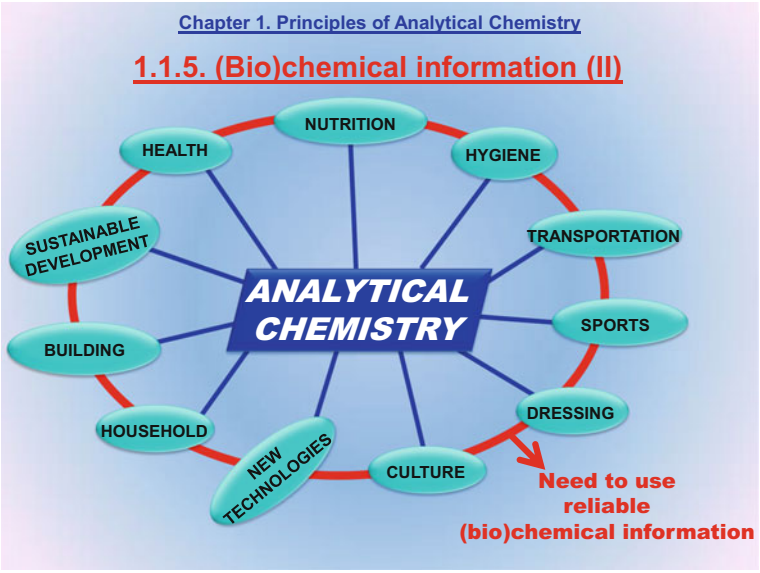
There is a tight relationship between Analytical Chemistry and (bio)chemical information extracted from analytical processes, which is their main output and can be improved by producing analytical knowledge (see the information hierarchy in Slide 1.20).

Information is a key element in many fields. In the social domain, information is the "fourth power" in addition to the legislative, executive and judiciary power (i.e., the classical powers).

There is a saying that "those who have the information have the power". Information is also an essential ingredient of scientific and technological development, which relies on effective communication of R&D centres with one another and with society. Information is also a crucial element of economy in addition to capital, labour and raw materials.

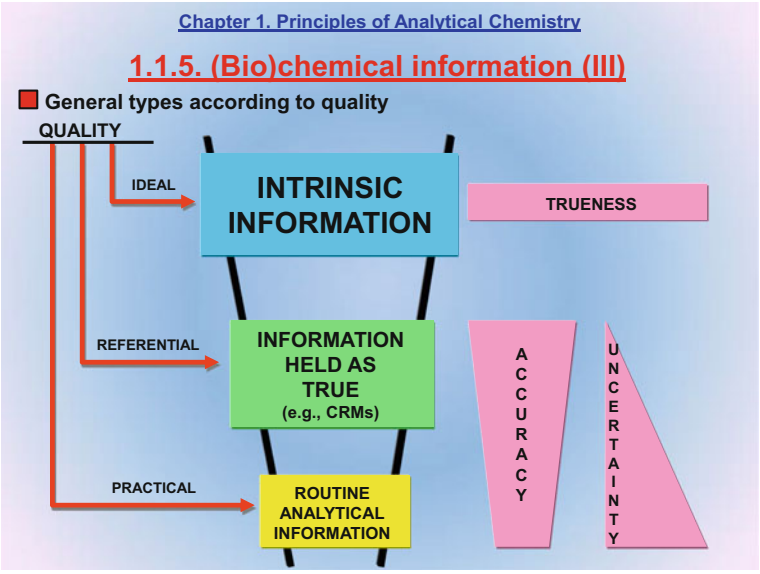
(Bio)chemical information is one part of information at large and hence also essential to society, science, technology and economy.

Slide 1.16



Based on the foregoing, Analytical Chemistry is essential for a wide range of human activities including healthcare, human and animal nutrition, hygiene, labour risk protection, transportation, sports, dressing, culture, new technologies, the household, building and sustainable development, among others, all of which require accurate (bio)chemical information to make well-grounded, timely decisions.

Slide 1.17



As shown in this hierarchy, there are three general types of (bio)chemical information according to quality.

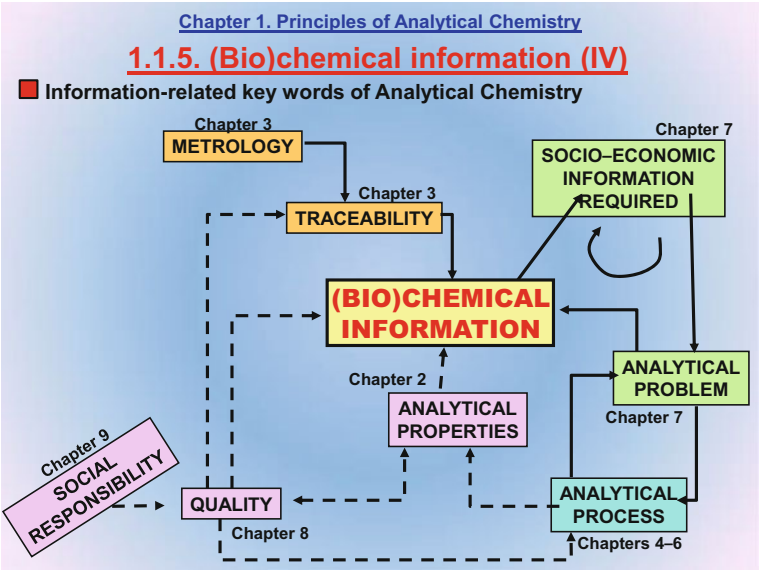
At the top is *ideal quality*, which pertains to the intrinsic (bio)chemical quality of objects and systems, and is unavailable to humans. Such is the case, for example, with the fat content of a food expressed with many decimals (e.g., 3.345237689… %) and hence subject to no uncertainty (see Slide 2.30). Ideal quality corresponds to the property "absolute trueness".

In the middle is *referential quality*, which can be accessed by humans but requires an unusually strong effort to achieve. Such is the case, for example, with a food fat content of $3.34 \pm 0.02\%$ certified via an inter-laboratory comparison exercise typically involving 5–25 laboratories analysing the same sample for the same analyte but with different methods. This special sample is a Certified Reference Material (CRM) and its certified value, with its estimated uncertainty, is the most accurate type of analytical chemical information that can be experimentally obtained—and hence the top reference for measurements (see Slide 3.17).

At the bottom is the *quality of routine (bio)chemical information* produced by laboratories analysing samples such as environmental matrices, foods, manufactured products, meteorites or lunar rocks. This type of information corresponds to true quality.

It should be noted that specific uncertainty does not affect ideal quality and that it increases from referential quality to true quality. On the other hand, accuracy increases from practical quality to referential quality and is maximal in trueness.

Slide 1.18



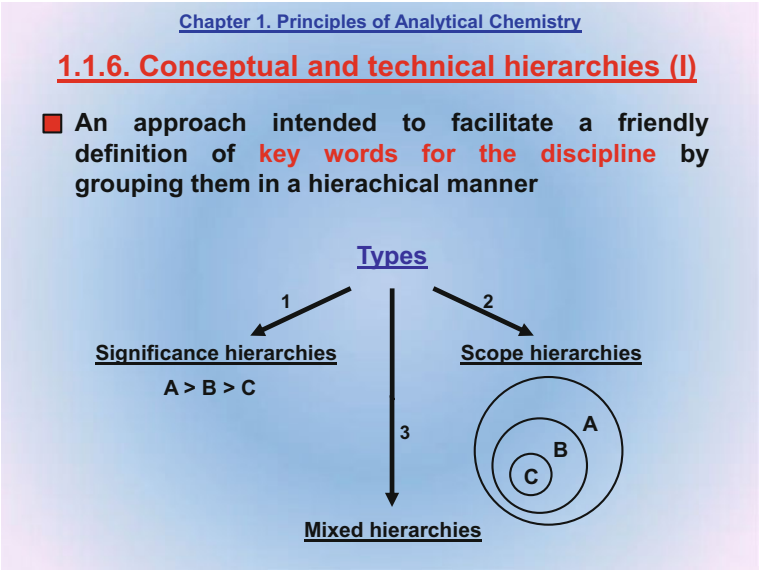
As can be seen, (bio)chemical information is connected with key aspects of Analytical Chemistry dealt with in this book. Around the discipline are its essential key words. The most salient connections are as follows:

- Chemical metrology relies on traceability, which provides the main support for information (see Chap. 3).
- (Bio)chemical information requirements about objects or systems constitute the socio–economic problem and lead to the definition of "analytical problem" (see Chap. 7). The most immediate response to the analytical problem is the development of an analytical method or procedure (Chap. 4) to obtain quantitative (Chap. 5) and/or qualitative information (Chap. 6). The resulting information is fed back as the solution to the analytical problem and also to the information requirement.
- Analytical quality (Chap. 8) is an essential element of Social Responsibility in Analytical Chemistry (Chap. 9). There are four main types of analytical quality:

  (a) *quality in the reference materials* in relation to traceability (Chap. 3);
  (b) *quality in the indicators* or *analytical properties* (Chap. 2), which is connected to both information and the analytical process;
  (c) as a result, *quality of the analytical process* (Chap. 4); and
  (d) *quality in the (bio)chemical information* (see Slides 1.15–1.17), which is the most important and influenced by all others (social responsibility included).

1.1.6 Conceptual and Technical Hierarchies (11 Slides)

Slide 1.19



This section aims at disseminating the key words of Analytical Chemistry and their meaning. Most often, the "jargon" of a discipline is disseminated through a glossary of terms (see Annex 1, which contains 250 terms and their definitions). Unfortunately, glossaries are usually unfriendly to students.

Rather than relying on a glossary, this book takes a new teaching–learning approach revolving about three major axes, namely:

- grouping key words by concept;
- ranking the words in hierarchies; and
- relating the hierarchies to one another.

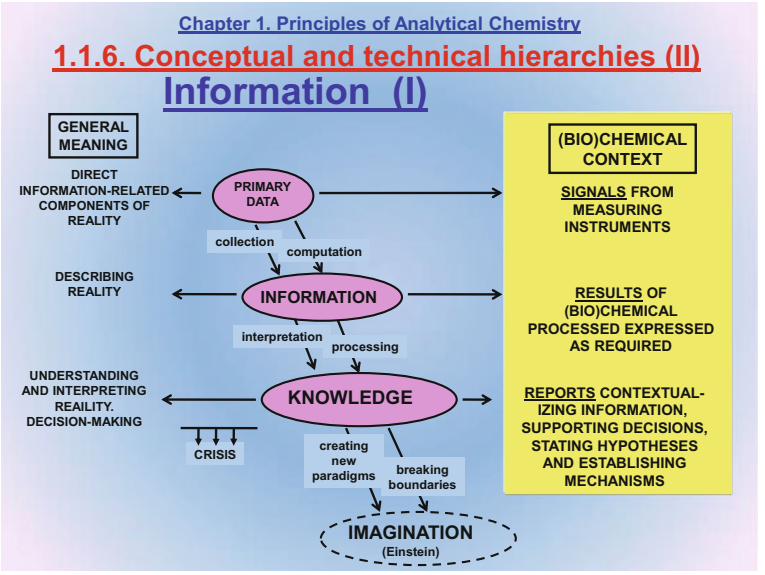
A hierarchy is an ordered sequence of things or persons. As can be seen in the slide, there are three basic types of hierarchies.

- *Significance hierarchies*, which are typical orderings of persons in an institution such as the Catholic Church (from priest to pope) or the Army (from private soldier to general).
- *Scope hierarchies*, which are commonly used in the geographic domain (e.g., America includes the USA, the USA includes Illinois and Illinois includes Chicago).

- *Mixed hierarchies* such as those used to classify living beings. Thus, the taxonomy is a significance–scope hierarchy of the terms, from top to bottom, kingdom, phylum, class, order, family, genus and species.

The following slides depict the hierarchies inherent in the key words of Analytical Chemistry for easier learning.

Slide 1.20



1.20.1. Here are three hierarchies of terms relating to information, which is an essential trait of Analytical Chemistry.

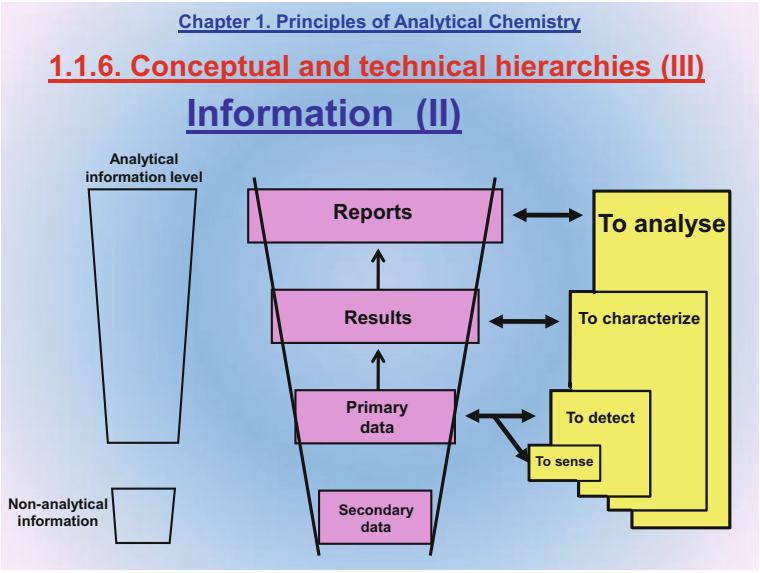
The first hierarchy depicted in this slide, considers information to be an intermediate stage in a ranking of increasing scope and significance from raw data to knowledge. *Raw data* are direct indicators of reality, and can be compiled and processed to obtain *information*, which is a depiction of reality. Processing and interpreting information leads to *knowledge*, which allows reality to be understood and provides the foundations for well-founded, timely decisions.

An additional step in the ranking is needed in critical times when knowledge does not suffice to solve social and economic problems: innovation driven by imagination, which was advocated by Einstein as early as almost one hundred years ago. Innovating entails creating new paradigms and breaking barriers by opting for interdisciplinarity (that is for merging different areas of knowledge).

1.20.2. In the (bio)chemical domain, raw data are provided by *signals* from a wide variety of measuring instruments (e.g., polarographs, spectrophotometers, spectrofluorimeters). *Information* here is equivalent to the results of analytical processes (see Chap. 4) as expressed in accordance with the particular requirements, while *analytical reports* are equivalent to knowledge.

For example, a spectrophotometer used in the second step of an analytical process to determine a food colouring in sauces (see Slide 1.22) provides measurements in absorbance units (AU) corresponding to an analyte content of (result), say, 0.03 ± 0.002 mg/kg. In the report to be issued, this content should be interpreted in relation to the maximum acceptable level, whether legally imposed (by, for example, a EU directive) or otherwise, for the food concerned to be deemed safe (that is, non-toxic): 0.01 mg/kg. The ensuing knowledge, contained in the report, will be that the food in question is safe for human consumption because the result fell below the accepted limit.

Slide 1.21



1.21.1. The second hierarchy of information-related words echoes that in the previous slide as it comprises reports, results and raw data at the top.

An additional step emerges at the bottom: *secondary data*, which are the parameter values (temperature, revolutions per minute) used to monitor[2] the operation of apparatuses such as furnaces, stoves or centrifuges involved in the analytical process. Secondary data help to check that apparatuses operate as they should[3] (see Slide 1.24) but are not analytical information.

[2] *To monitor* is to measure certain indicators or parameters.

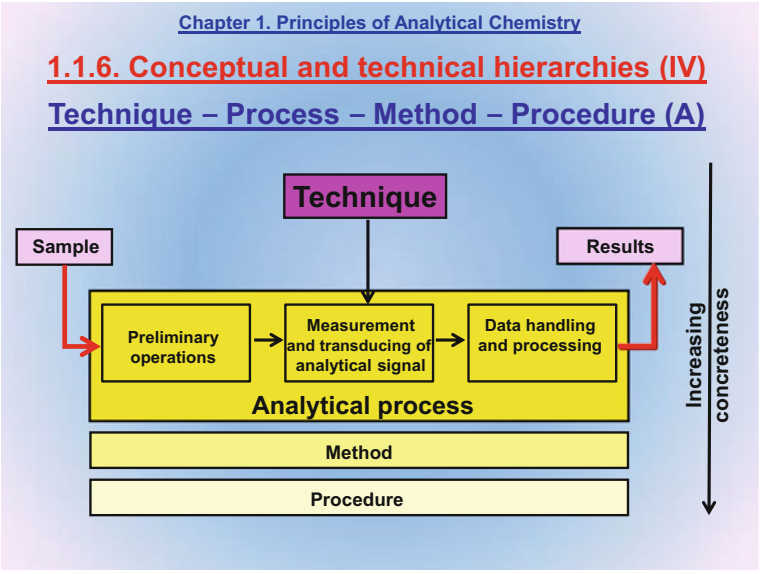
[3] *To control* has a twofold meaning: to monitor a system or process—and, if necessary, adjust it—in order to ensure that it operates as expected. Monitoring includes controlling. For example, if the temperature of a stove as measured with a thermocouple is 104 °C and the stove was programmed to operate at 110 °C, then it should be readjusted for consistency between the temperature as measured with the thermocouple and the actual temperature inside the stove. This process is known as "instrument calibration" and explained in Sect. 3.4.

1.21.2. Analytical information (results) is the information allowing reports to be produced and increases from raw data to results.

It should be noted that raw data, which contain the smallest possible amount of analytical information, are not the same as secondary data even though these are connected to analytical information. In fact, secondary data simply ensure that the analytical process is developing as it should—they provide no results by themselves.

1.21.3. The third hierarchy is rarely used because the words in it differ in meaning among languages. The words are connected with those in the other hierarchy in the slide. Thus, *to analyse* is connected with the production of reports, *to characterize* with that of analytical results, and *to detect/to sense* with that of raw data by measurement.

Slide 1.22

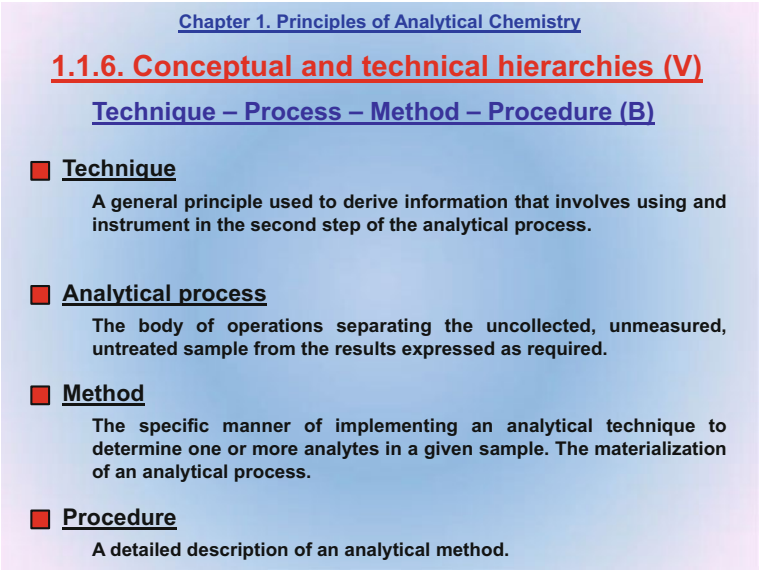


Understanding the differences between the terms "technique", "process", "method" and "procedure" is crucial with a view to avoiding confusion in the analytical chemical literature. This slide shows an atypical hierarchy of the four terms according to concreteness.

– At the top is *analytical technique*, which is the most abstract term and materializes in the use of an instrument (e.g., a gas chromatograph, a UV–vis spectrophotometer) in the second step of the analytical process.

– An *analytical process* is the general description of the three stages separating the sample from the results (preliminary operations, measurement and transducing of the analytical signal, and acquisition and processing of data).
– An *analytical method* is a more detailed description of an analytical process.
– An *analytical procedure* is an even more detailed description of an analytical process.

Slide 1.23



This slide provides the formal definitions of the analytical terms in the previous one. The following are typical examples of each term:

Technique: UV–visible absorption spectroscopy, where the instrument is a photometer.

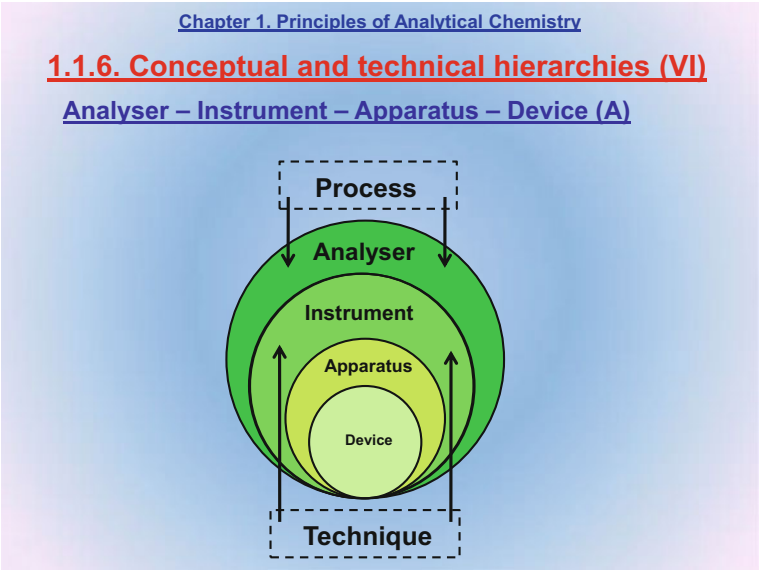
Analytical process: Photometric determination of a banned colouring in food.

Analytical method: An amount of 0.5 g of dry food is subjected to solid–liquid extraction with a benzene–ethanol mixture as solvent in a Soxhlet extractor. Then, an aliquot of solvent containing the colouring is used to measure the absorbance of the extract at 530 nm, which is then interpolated into a previously constructed calibration curve (see Slide 2.36) to determine the concentration of the banned substance in the target food.

Analytical procedure: This is a detailed description of the way samples are to be collected, preliminary operations (e.g., drying of the samples) performed, the extractor used, the solvent purity chosen and the calibration curve constructed, for example. Describing an analytical procedure typically takes 4–10 pages depending

on its complexity. Some organizations such as the American Society for Testing and Materials (ASTM) issue a number of procedure descriptions each year.

Slide 1.24

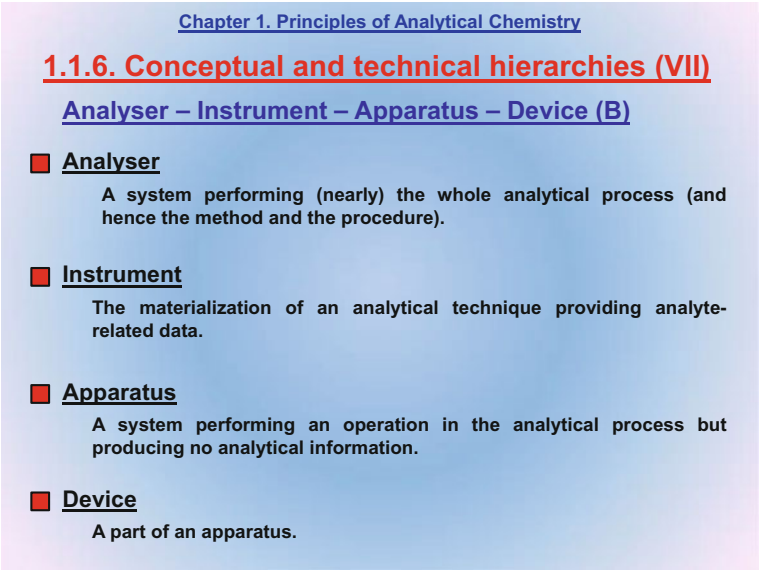


Similarly to the previous slide, this one distinguishes between four other key terms in Analytical Chemistry: analyser, instrument, apparatus and device.

Analyser falls at the top of the hierarchy and *device* at the bottom, with *instrument* and *apparatus* in between. The four terms are defined in the next slide.

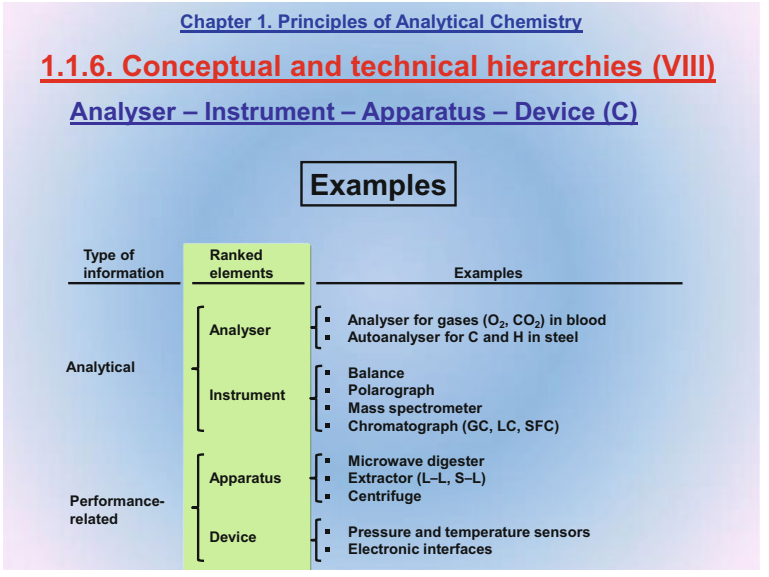
This hierarchy is connected to that in Slide 1.22. Thus, "analyser" is related to "analytical process", and so is "instrument" to "technique". Also, the outputs of an analyser and an instrument are related to "analytical information" (Slide 1.21), whereas the parameters used to monitor the operation of apparatuses and devices constitute "non-analytical information".

Slide 1.25



These are the definitions of the analytical terms in the previous hierarchy. As can be seen, the definitions are quite consistent with the positions of the terms in the hierarchy.

Slide 1.26



These examples illustrate the relationships of the terms in Slide 1.24 to analytical and non-analytical information.

The following are connected to analytical information:

(A) Analysers, which are automatic systems receiving samples and providing results in the required format, whether on screen or as printouts. Such is the case with sensors for the direct measurement of oxygen and carbon dioxide in blood from seriously ill patients in an Intensive Care Unit (ICU) or with a commercially available auto-analyser for carbon and hydrogen in steel, which receives the sample on a built-in balance pan and uses IR sensors to measure gases released upon heating in order to deliver the proportions of the two elements in the target steel through a printer.

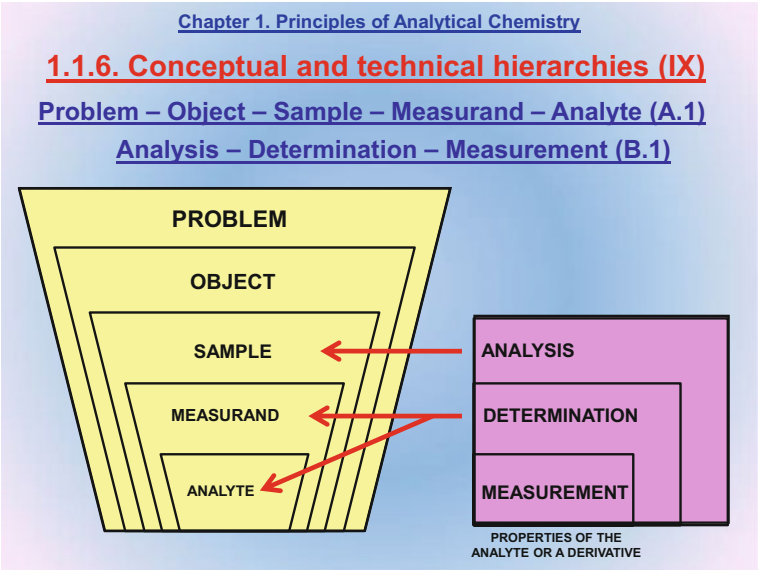
(B) The usual instruments involved in the second step of the analytical process (see Slide 1.22): a balance, a burette, a mass spectrometer, a UV–visible photometer, a fluorimeter, a gas or liquid chromatograph with an integrated detector.

The following produce no analytical information, but parameter values:

(1) Apparatuses equipped with controls allowing their operation to be checked and adjusted (e.g., centrifuges, extractors, microwave ovens, stoves, furnaces, refrigerators).

(2) Devices such as pressure, temperature or moisture sensors, and also electronic interfaces to instruments.

Slide 1.27

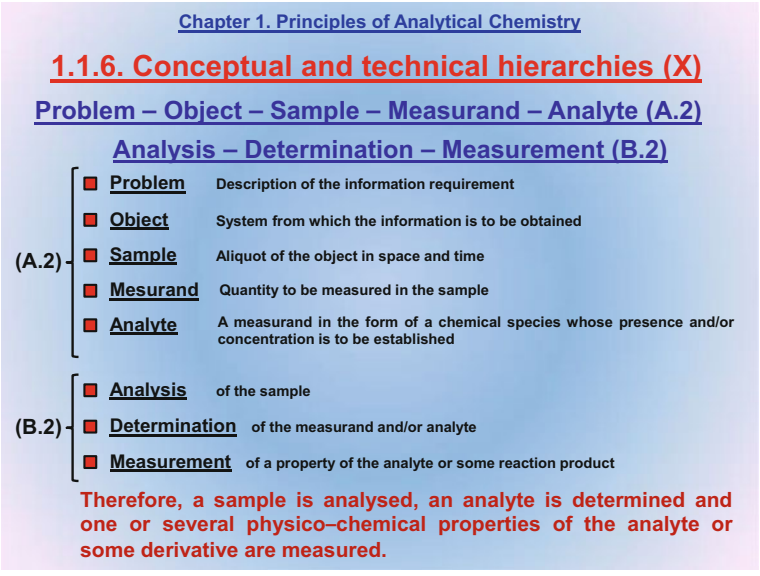


1.27.1. This scope and significance hierarchy of analytical terms (**A.1**) is related to the systematic use of the concept "traceability" in Analytical Chemistry (see Chap. 3). It relates *analytical problem* [that is, the (bio)chemical information required] to the *object* or *system* about which the information is required. A *sample* is an aliquot or representative portion taken from the object (see Item 4.5.2). At the bottom of the hierarchy are *measurand*, which is the parameter to be measured, and *analyte*, which is the chemical species to be detected or determined. Analytes are the most common types of measurands in Analytical Chemistry. These terms are formally defined in the next slide.

1.27.2. This is another, highly important significance and scope hierarchy for a metrological discipline such as Analytical Chemistry (**B.1**). *Analysis* includes *determination*, which in turn includes *measurement*. These terms are also defined in the next slide.

The relationship between these two hierarchies is very important. Thus, "analysis" refers to "sample", "determination" to "measurand" or "analyte", and "measurement" to a parameter or property of the analyte or its reaction product.

Slide 1.28



These are the formal definitions of the terms in hierarchies A.2 and B.2 in the previous slide. Many can be directly inferred from the hierarchies and their mutual relationships.

Hierarchy A.2 is discussed in relation to traceability in Chap. 3. Hierarchy B.2 is consistent with the following fundamental assessment in Analytical Chemistry:

A sample is analysed,

an analyte is detected or determined, and

one or several analyte properties are measured

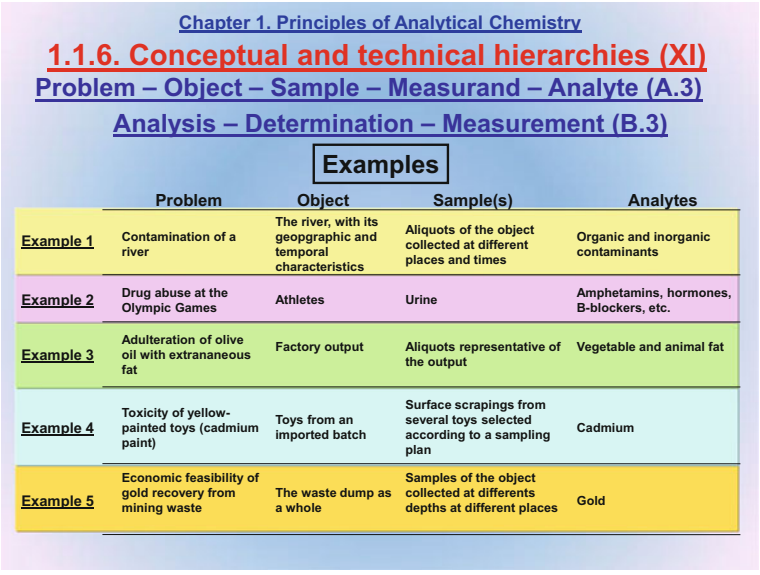
Therefore, the following phrases are wrong:

- Measurement of copper in lake water.
- Analysis of the sulphur content of petroleum crude.
- Analysis of drugs and/or their metabolites in urine from an athlete.

On the other hand, the following are right:

- Determination of copper (analyte) in lake water (object–sample).
- Determination of the content in sulphur (analyte) of petroleum crude (object–sample).
- Analysis of urine (sample) for banned drugs and/or their metabolites (analytes) in sports competitions.

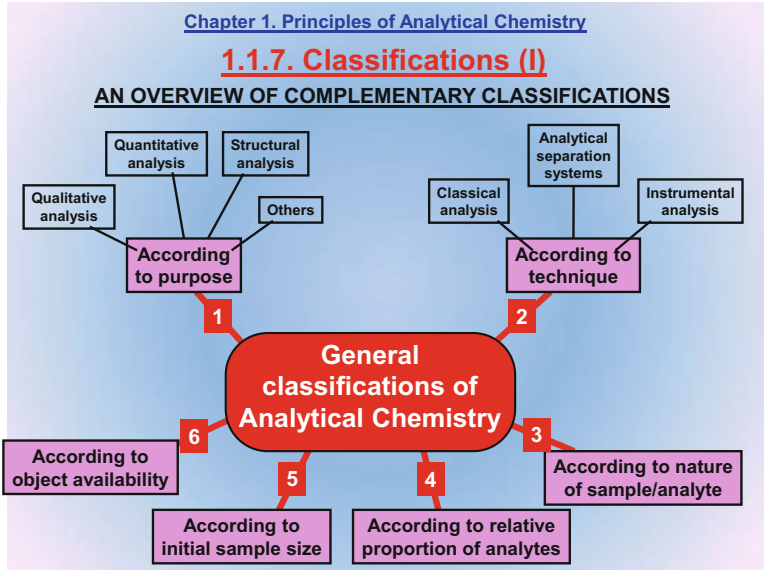
Slide 1.29



This slide clarifies the analytical terms in the hierarchies of Slide 1.27 with some examples. Each transversally described example states the problem (information required), object, sample(s) and analyte(s), so no further explanation is needed Supreess.

1.1.7 Classifications (10 Slides)

Slide 1.30



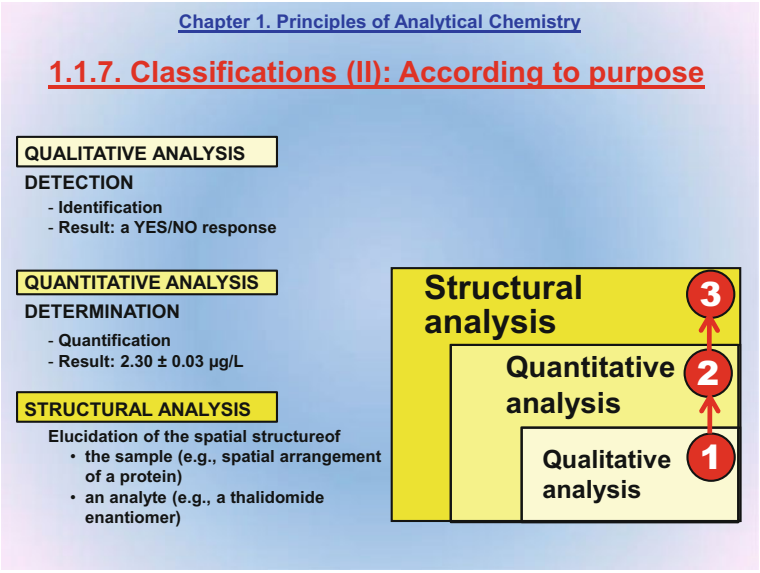
This slide starts Sect. 1.1.7, which establishes six hierarchies of especial usefulness to approach Analytical Chemistry conceptually and technically.

The six criteria behind the classifications are complementary rather than contradictory—in fact, the classifications are mutually related. The criteria are as follows:

(1) aim;
(2) technique;
(3) nature of the sample and analyte, and their combination;
(4) proportion of analyte in the sample;
(5) initial sample size; and
(6) object availability.

These classifications, which are depicted in Slides 1.31–1.39, include new analytical key words supplementing those in the hierarchies of Sect. 1.1.6.

Slide 1.31

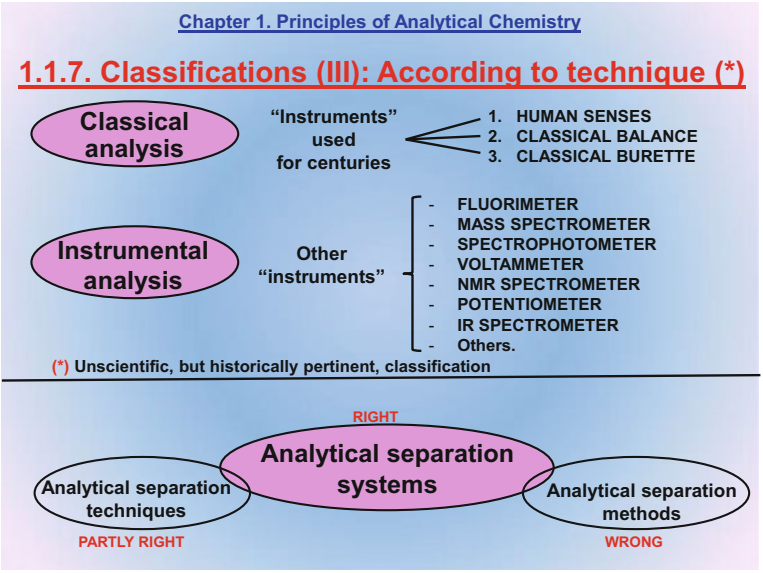


1.31.1. The aim of an analysis varies with the type of (bio)chemical information sought. There are three different types of analysis in this respect, namely:

- *Qualitative Analysis*, which is intended to provide binary (YES/NO) responses about the presence or absence of a particular analyte in a sample. Qualitative analysis is directly related to the word "detection" (e.g., detection of aflatoxins in dried fruits from a Middle East country via immunoassay) (see Chap. 6). Qualitative analysis is also related to the "identification" of species.
- *Quantitative Analysis*, which aims at providing responses in the form of absolute (e.g., 5.3 grams of boric acid in a shrimp box for export) or relative amounts of analyte (e.g., 3.23 micrograms of pesticide per kilogram of agricultural soil).
- *Structural Analysis*, which is intended to establish the structure of a sample or object (e.g., detection of cracks in airship fuselage), or that of an analyte (e.g., establishing the structural conformation of a protein).

1.31.2. As show here, the three types of Analysis can be ranked in a scope hierarchy. Thus, no quantitative determination or structural analysis is possible without previous quantitative knowledge. In fact, one cannot determine the concentration of mercury in seawater without knowing whether the water contains mercury traces. Similarly, one cannot accomplish speciation (that is, discriminating among mercury species) without knowing whether any mercury is present and, if so, if it is in a large enough amount to enable the determination.

Slide 1.32



1.32.1. This classification is based on the type of technique used and considers the three possibilities of Slide 1.30 (2), which provides a general view of classifications in Analytical Chemistry.

The first two distinguish on historical grounds, albeit unscientifically, between Classical Analysis and Instrumental Analysis.

Classical Analysis is that performed with the only "instruments" available until the first third of the XX century, namely:

- The human *senses* for Qualitative Analysis (e.g., identification of colours and precipitates) and for detecting titration end-points (by a colour change).
- Burettes to measure the volumes used in titrations.
- *Balances* for gravimetric weighing.

In any case, Qualitative and Quantitative Classical Analysis share some characteristics such as the use of acid–base, precipitation, chelation or redox reactions.

Instrumental Analysis uses an instrument different from the previous three (e.g., a photometer, a pH-meter, a mass spectrometer).

This classification should be avoided altogether but continues to be used at present. The weakness of the distinction is obvious, especially if one considers that the classical balance and burette have evolved dramatically over the last few decades by virtue of advances in automation, miniaturization and computerization.

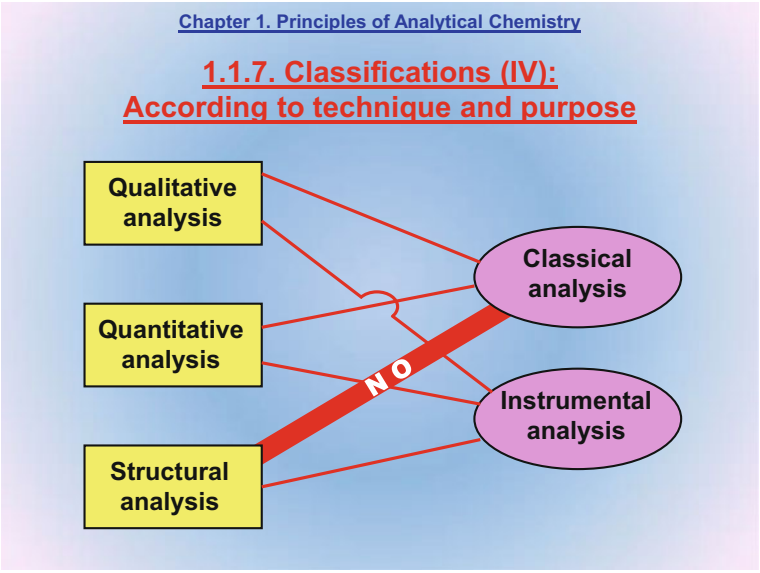
– Thus, the classical two-pan balance with weights handled by the user has given way to an autobalance with a single pan, and automatic taring and digital reading of the weights.
– Similarly, the classical glass burette made to volume by hand and read out visually at the endpoint of a titration has been replaced with a compact burette automatically performing all required operations and delivering measurements via an integrated mini-printer.

1.32.2. The third possibility of the classification criterion (analytical technique) poses a naming conflict with the general classifications of Analytical Chemistry in Sect. 1.30.2. Thus, chromatographic (e.g., gas chromatography) and non-chromatographic separations (e.g., liquid–liquid extraction) play an extremely important role in Analytical Chemistry today and deserve inclusion in the classification. The problem arises in labelling them.

- *Are they "techniques"?* Not in a strict sense if one considers the definition of "technique" in Slide 1.23. The name would only be accurate if it referred to a gas (GC) or liquid chromatograph (LC) having an integrated instrument (a detector). On the other hand, merely using a separation apparatus (e.g., a liquid–liquid extractor) does not imply that a technique is being applied.
- *Are they "methods"?* By no means. In fact, a method is a detailed description of the process connecting the sample to the results (see Slide 1.23).

However, both designations have been used in connection with separations, even in book titles (e.g., *Chemical Separation Methods,* by J.A. Dean, Van Nostrand Reinhold; New York, 1969) and subject names (e.g., Analytical Separation Techniques, AST). This book proposes for the first time the designation *ANALYTICAL SEPARATION SYSTEMS (ASS)*, which encompasses both chromatographic and non-chromatographic separations.

Slide 1.33



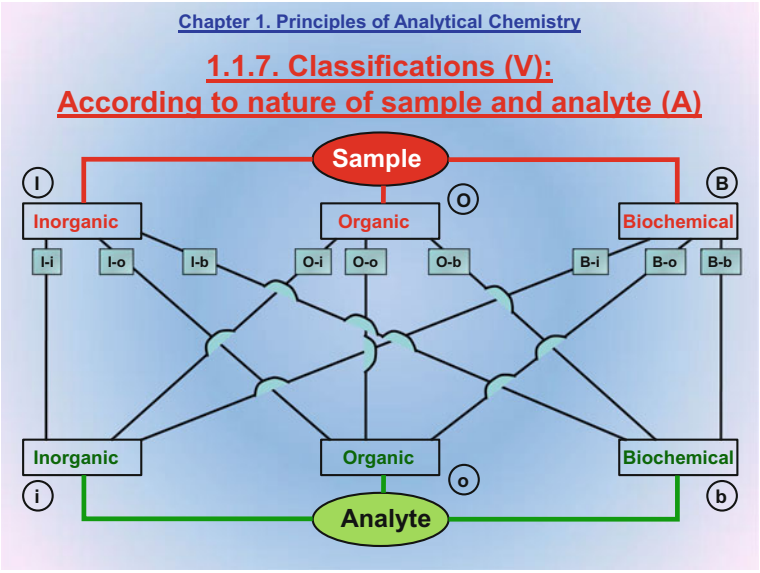
1.33.1. This slide combines the first two classifications in Slide 1.30 according to purpose and technique. According to technique, it distinguishes between Classical and Instrumental Analysis, which, as stated with regard to the previous slide, lacks scientific ground.

1.33.2. According to purpose, Analytical Chemistry comprises Qualitative, Quantitative and Structural Analysis (see Slide 1.31).

This slide also shows the connections between the two classifications. Thus, Qualitative Analysis can be performed with the human senses (Classical Qualitative Analysis) and also with other types of instruments (Instrumental Analysis). Likewise, Quantitative Analysis can be done with balances and burettes (Classical Quantitative Analysis) or with other instruments (Instrumental Quantitative Analysis). On the other hand, Structural Analysis is only possible with the more sophisticated instruments (Instrumental Analysis).

1.33.3. The only forbidden connection between the classifications is that shown in the slide: Structural Analysis cannot be done with classical analytical instruments.

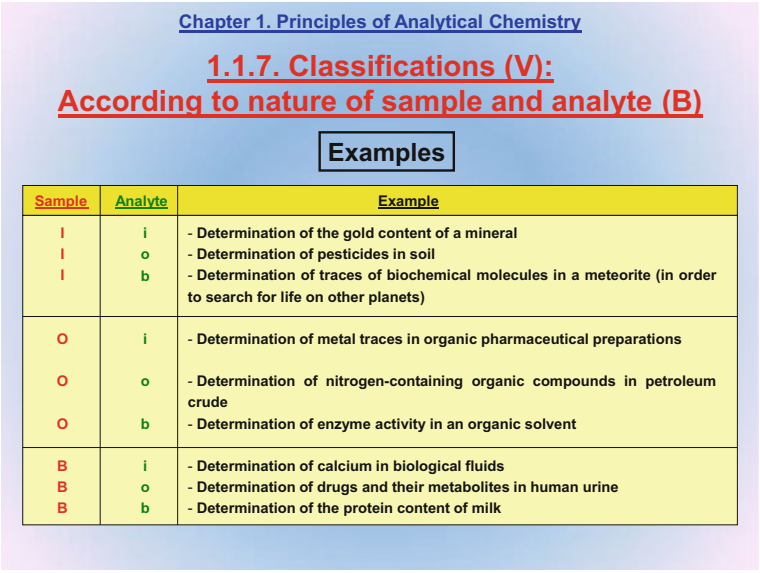
Slide 1.34



This slide shows the combinations of nature of the sample or object and analyte (viz., organic, inorganic or biochemical). Thus, the sample may have an inorganic (I), organic (O) or biochemical matrix[4] (B). Likewise, the analyte can be inorganic (i), organic (o) or biochemical (b) in nature. The following slide shows typical examples of each combination.

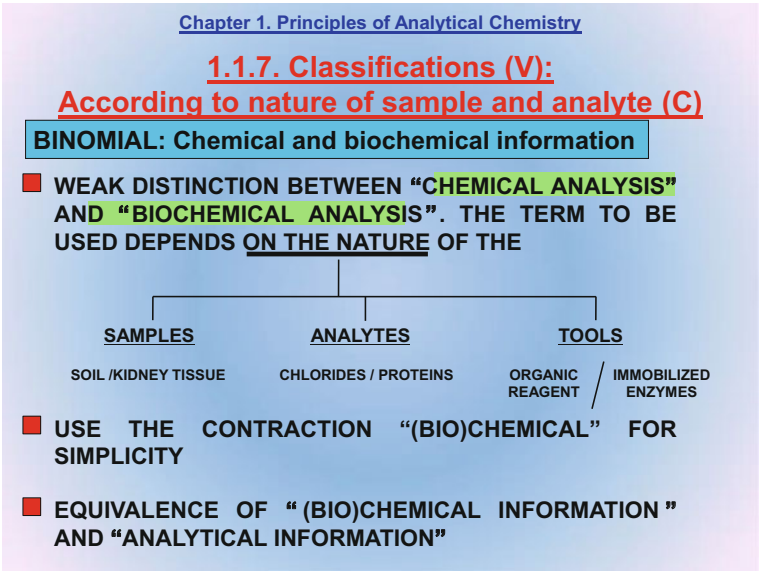
[4]In the analytical chemical domain, the word "matrix" refers to the characteristics of the sample extracted from the object. No other definition comes closer to this meaning.

Slide 1.35



Here are several example combinations of the nature of sample and analyte in real-life situations as classified according to the type of sample. Uppercase letters pertain to samples and lowercase letters to analytes.

Slide 1.36

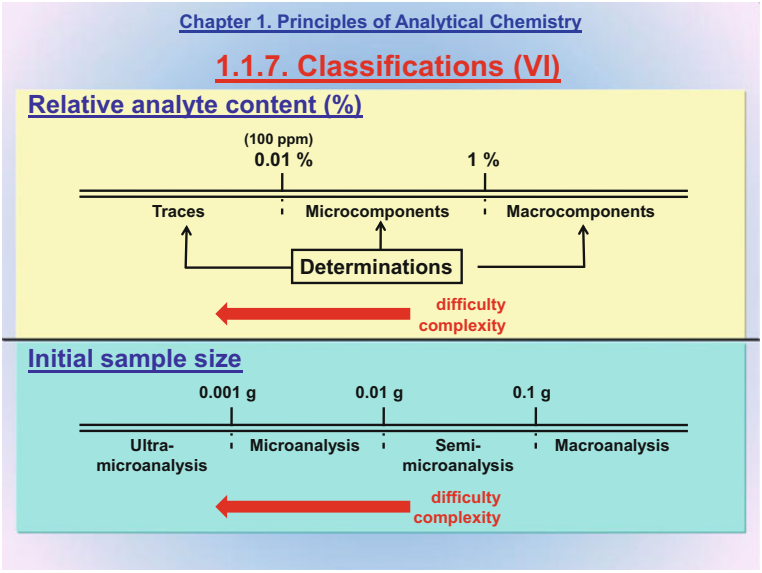


Classifying "analysis" according to the nature of the sample and analyte (Sect. 1.30.3) raises a naming problem. As can be seen, "chemical analysis" and "biochemical analysis" are virtually indistinguishable. The difference is in the chemical or biochemical nature of the sample and analyte, and in the analytical tools used. The examples are self-explanatory.

On these grounds, we use the contraction "(bio)chemical" as a qualifier of analysis, information and measurements.

As a rule, "(bio)chemical information" and "analytical information" are completely equivalent because Analytical Chemistry encompasses both Chemical Analysis and Biochemical Analysis.

Slide 1.37



1.37.1. The *relative proportion (percent mass) of analyte in the sample* is the fourth classification criterion in Slide 1.30.

Placing a landmark at 0.01% and another at 1% splits an increasing logarithmic scale into three zones according to the proportion of analyte in the sample, namely:

- *Determination of macrocomponents* when the proportion exceeds 1% (e.g., the percent content of chromium in steel).
- *Determination of microcomponents* if the proportion falls in the range 0.01–1% (e.g., the lactic acid content of fresh milk).

– *Determination of traces*[5] when the proportion is less than 0.01%, which is equivalent to 100 parts per million (ppm) (e.g., the determination of drugs or their metabolites in human hair).

Obviously, the difficulty and complexity of analyses increases with decreasing proportion of analyte in the sample (e.g., because the analytical process includes a preconcentration step).

1.37.2. *The initial sample size, in grams,* is the fifth classifying criterion in Slide 1.30.

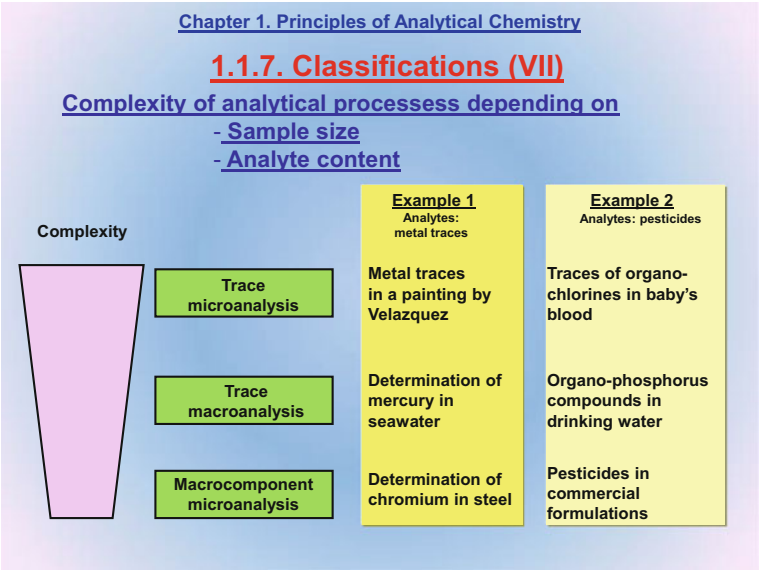
By placing three landmarks at 0.001, 0.01 and 0.1 g, an increasing logarithmic scale is split into four zones according to sample size and mass in which Analysis is named differently, namely:

- *Macroanalysis* when the initial sample size exceeds 0.1 g (e.g., the analysis of urine from a racehorse to detect anabolic steroids).
- *Semi-microanalysis* when the initial sample size falls in the range 0.1–0.001 g (e.g., the analysis of baby's urine to determine acetone traces). This intermediate designation is not accepted by the *International Union of Pure and Applied Chemistry* (IUPAC).
- *Microanalysis* when the initial sample size falls in the range from 0.1 or 0.01 to 0.001 g (e.g., the analysis of baby's blood to determine pesticide traces).
- *Ultra-microanalysis* when the initial sample size is smaller than 0.001 g (1 mg) (e.g., in the destructive analysis of a painting by Velazquez in order to determine the metal content of yellow paint in the picture).

The difficulty and complexity of the analysis increases with decreasing sample size.

[5]Although the term "determination of traces" is the most accurate in this context, it is scarcely used. In fact, "*Trace Analysis*" is much more common and acceptable even though it departs from the axiom that a sample is analysed and an analyte determined (see Slide 1.28). This is the exception that proves the rule and a "rebel" designation grounded on the fact that it refers to an atypical analytical process in that it requires exercising great care (e.g., using a clean chamber, gloves and hair covering, ultrapure reagents and solvents) to avoid unwanted contamination.

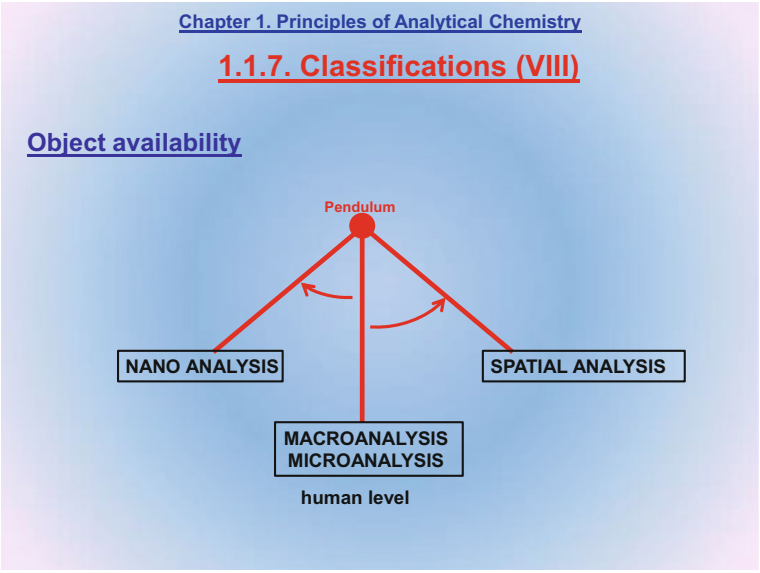
Slide 1.38



Here are two general examples illustrating how the complexity of the analytical process varies with the combination of sample size and proportion of analyte, namely: determinations of metals (1) and determinations of pesticides (2).

The greatest difficulty arises when very little sample is available (Microanalysis) and the proportions of the analytes are very low (Trace Analysis). On the other hand, the least difficult situation is that where a large amount of sample is available (Macroanalysis) to determine macrocomponents. Between these two extremes fall various situations of which Macroanalysis + Trace Analysis depicted in the slide.

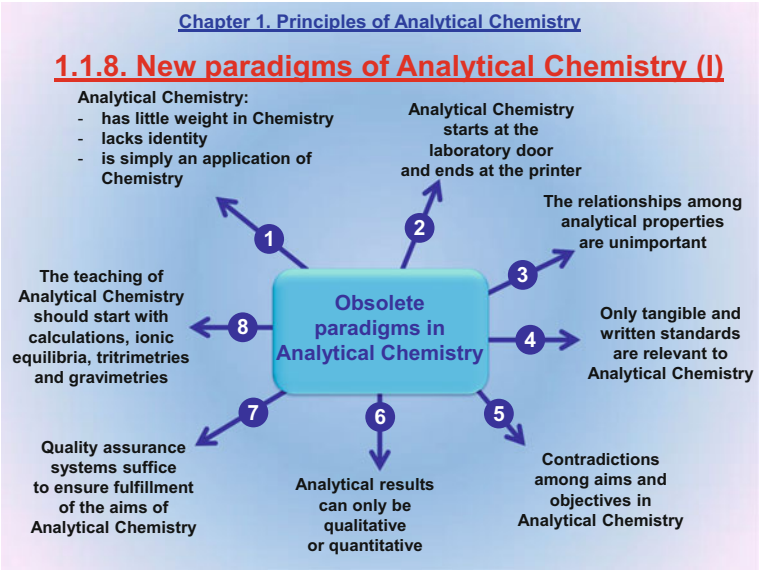
Slide 1.39



Object availability is the sixth classifying criterion in Slide 1.30. The resulting situations are shown as positions of a swinging pendulum in this slide: from Macroanalysis to Microanalysis of human samples to analysis of the Nanoworld—which provides essential support for Nanotechnology—at one end to spatial analysis (e.g., searching for water and life precursors on planets and asteroids) at the other. Obviously, the difficulty of the analytical process at both ends is much higher than it is in human-level analysis; also, the former requires strong innovation through interdisciplinarity (breaking traditional boundaries) and the creation of new paradigms (see Slide 1.20).

1.1.8 New Paradigms of Analytical Chemistry (3 Slides)

Slide 1.40



The word "*paradigms*"[6] is used to describe a series of essential, foundational, unarguable aspects that set the guidelines for some activity. Analytical paradigms are thus essential landmarks of Analytical Chemistry and, as such, change with time.

This slide shows analytical chemical paradigms which have become obsolete as a result of this discipline not developing in parallel with the almost frantic evolution of Science, Technology and Society. Its stagnation has propitiated the following:

1. A poor image of Analytical Chemistry among some chemists and other professionals as a result of ignorance or spurious interests.
2. Confining the analytical chemist's work to the laboratory without regard of the socio–economic projection of Analytical Chemistry, explained in Chaps. 7–9, the analytical chemist's role in assuring that samples are representative of the particular information requirements (Slide 1.26) and the fact that a substantial portion of all (bio)chemical information is produced outside the laboratory (e.g., with a glucose meter).

[6] A *paradigm* is a pattern, example or exemplar, but also a theory or body of theories whose central core is unquestionably accepted and provides the basis and a model for solving problems and advancing knowledge.

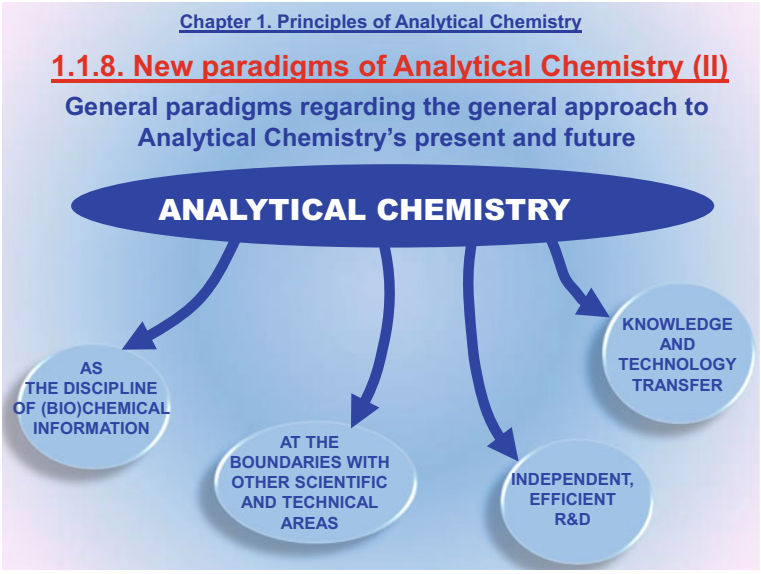
3. Approaching analytical properties (Chap. 2) in a non-holistic[7] manner. The complementary and contradictory relations between the characteristics of the results and the analytical process (see Items 2.56–2.61) are essential with a view to approaching the basic and applied sides of Analytical Chemistry in an integral manner.
4. Traditional analytical chemical standards are no longer sufficient. The importance of the (bio)chemical information required for decision-making purposes makes it the third basic standard of Analytical Chemistry today and tomorrow (see Slide 1.16).
5. Mutual distinctions between aims and objectives are essential as they require making quality trade-offs in order to harmonize the basic and applied facets of Analytical Chemistry (see Slide 1.9). This notion is closely related to that in item 3 above regarding the individual or joint relationships among analytical properties.
6. It is a gross error to believe that analytical results can only be qualitative or quantitative. There are two other possible types of results that are gaining increasing significance:

    - *Total indices*, which apply to compound families rather than individual analytes (e.g., total polyphenols in olive oil, dioxins in crematory ash, total hydrocarbons in water).
    - *Method-defined parameters* based on which analytes in a given sample can be measured in different manners to obtain also different types of data. Such is the case with the determination of available elements in serum: using different leaching solutions (i.e., liquid–solid extractants) depending on the particular standard method to be applied will lead to different types of results.

7. Quality assurance systems (Chap. 8) continue to be necessary but insufficient for Analytical Chemistry to reach excellence. Accomplishing integral quality additionally entails assuring Social Responsibility (Chap. 9).
8. The teaching of Analytical Chemistry should not start with ionic equilibria, calculations, titrations and gravimetries. Rather, students should be brought into first contact with the discipline through its principles and foundations as explained elsewhere in this book.

[7] "*Holistic*" means characterized by the belief that the parts of something are closely connected to one another so they can only be explained by reference to the whole.

Slide 1.41



The general paradigms of Analytical Chemistry shown in this slide constitute the very essence and foundations of an appropriate approach to this discipline.

The first key paradigm of Analytical Chemistry is systematically regarding it as the discipline of (bio)chemical information about natural and artificial objects and systems. This trait distinguishes it from all other disciplines of Chemistry (see Slide 1.5).

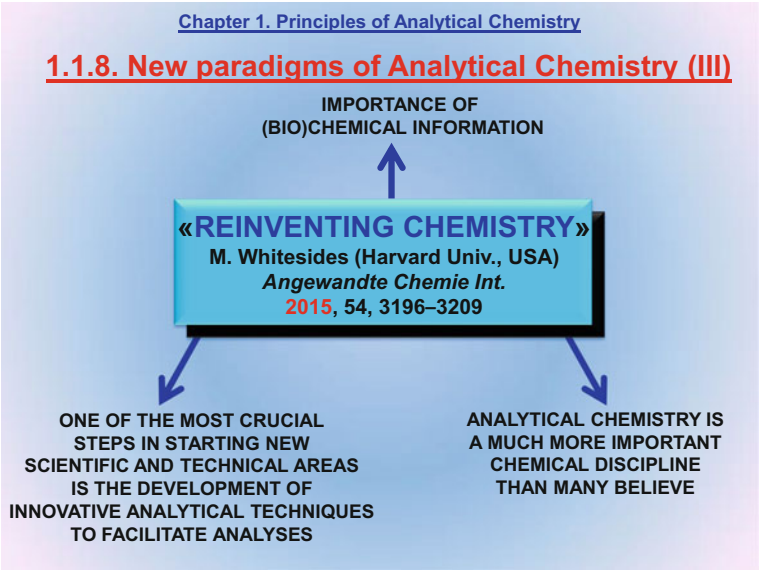
The second key paradigm of Analytical Chemistry is a multidisciplinary approach akin to Chemistry leading to fruitful connections with other scientific and technical areas in the future (see Slide 1.6).

The third key paradigm of Analytical Chemistry is possessing a research and development (R&D) system of its own (see Slide 1.43), one *consistent with its aims and objectives.*

The fourth general paradigm of Analytical Chemistry is having the transfer of analytical knowledge and technology among its essential activities (see Slide 1.44).

Only if the previous four paradigms converge will Analytical Chemistry play the scientific, technical and socio–economic roles it should today and tomorrow.

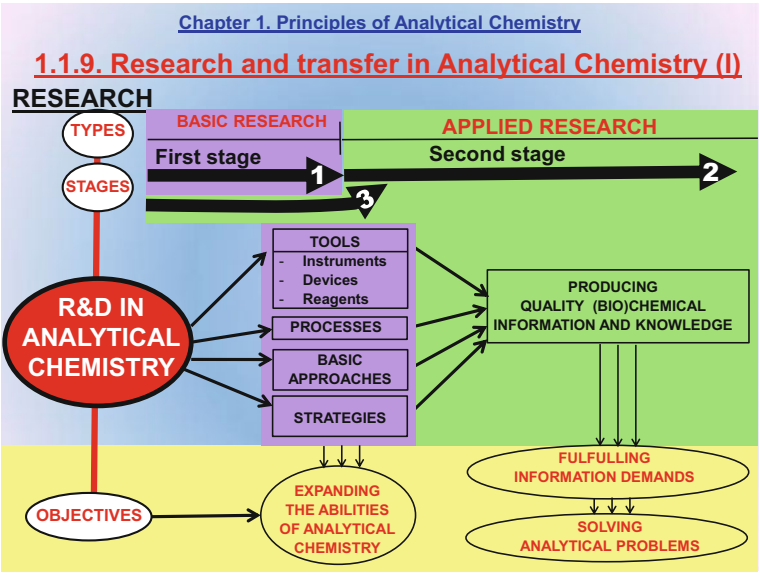
Slide 1.42



In his topical (2015), ground-breaking approach to Chemistry, Professor Whitesides of Harvard University, an organic chemistry, invites us to reinvent today's and tomorrow's Chemistry. In his formulation, he refers to Analytical Chemistry as the discipline of (bio)chemical information, which is more important than currently acknowledged. Also, he states that Analytical Chemistry is a bottleneck to innovative scientific and technological developments.

1.1.9 Research and Transfer in Analytical Chemistry (2 Slides)

Slide 1.43



1.43.1. As noted earlier, independent, efficient research and development (R&D) should be an essential paradigm of the new Analytical Chemistry (see Slide 1.41). This slide provides a brief description of the types, stages and objectives of R&D in this discipline.

1.43.2. The first type of R&D in Analytical Chemistry (no. 1 in the slide) is *basic research* (i.e., more R than D) and corresponds to the first stage. It is intended to increase the ability to extract (bio)chemical information in order to develop new analytical processes or improve existing ones.

Thus, basic research in Analytical Chemistry aims at developing new measuring instruments for multidisciplinary use, new reagents and solvents for implementing new analytical processes (methods), new chemometric tools and new approaches to analytical problems (See Chap. 7).

Basic research ends with the obtainment of these tangible or intangible "products". Obviously, it constitutes the support of applied research.

The significance of basic research in Analytical Chemistry can be easily inferred from the following example: the tennis player Maria Sharapova was charged with doping with mildronat (Meldonium) in March 2013. At the time, this substance was not on the banned drug list of the International Olympic Committee. However, in validating a new-generation mass spectrometer resulting from interdisciplinary basic research with hundreds of urine samples from athletes, an antidoping

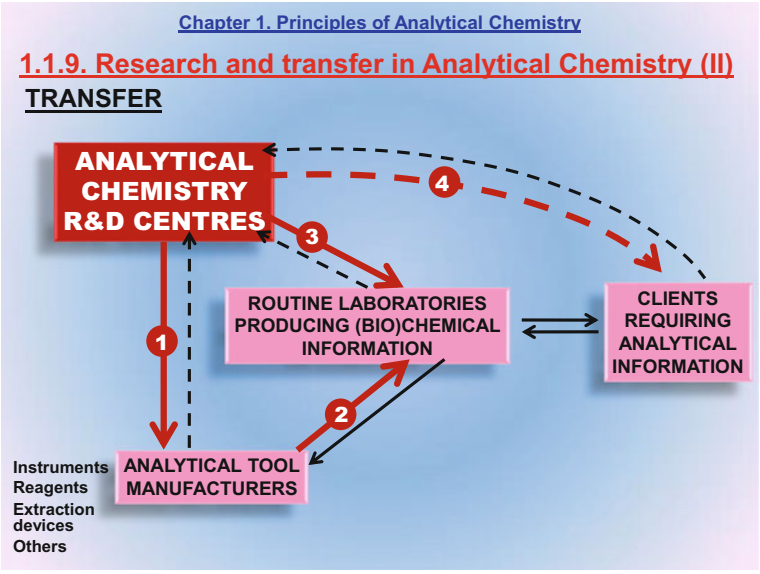
laboratory in Köln (Germany) encountered a previously unidentified peak corresponding to mildronat in a number of chromatograms in 2015. The laboratory found traces of this drug in Sharapova's urine and reported the finding to the sports authorities. In response, mildronat was included on the list in January 2016 and Sharapova banned from competition for two years for testing positive in the Australian Open.

1.43.3. The second type of R&D in Analytical Chemistry, *applied research*, involves more D than R. Its output is quality (bio)chemical information and knowledge, which it produces by using analytical processes to extract information from objects and systems.

The primary aim of applied research in Analytical Chemistry is fulfilling information requirements and hence solving analytical problems (see Chap. 7).

Applied research can follow two different pathways. One (no. 2 in the slide) uses tools, processes and approaches resulting from basic research to obtain (bio)-chemical information. The other (no. 3 in the slide) is needed when the "products" of basic research are inadequate to solve the analytical problem concerned, so the situation requires starting with basic research and then conducting applied research in accordance.

Slide 1.44



The transfer of analytical knowledge and technology is an essential general paradigm of Analytical Chemistry (see Slide 1.41), a relatively new but crucial approach.

Analytical knowledge and technology are transferred from analytical chemical R&D centres and departments.

(1) Transfers first reach industrial manufacturers of the "products" of basic research (instruments, apparatuses, reagents, solvents) (see Slide 1.43), which report their needs and claims to R&D centres (dotted line).
(2) "Analytical products" are also transferred from manufacturers and dealers to routine analytical laboratories.
(3) Some transfers directly connect R&D centres to clinical, agri-food, pharmaceutical or industrial laboratories routinely producing (bio)chemical information. Obviously, the laboratories require effective tangible or intangible tools to solve new problems. Routine analytical laboratories are the primary clients of analytical tool manufacturers.
(4) In special situations such as toxicological alarms, the clients requiring information and R&D laboratories can establish atypical transfer connections even though routine laboratories will still produce the information needed to make the final decision.

1.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry
M. Valcárcel
Springer–Verlag, Berlin, 2000.

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

The contents of Chap. 1 in Valcárcel's book, entitled "Introduction of Analytical Chemistry", overlap with those of this chapter. From experience gathered over 15 years of use as a textbook, we have simplified the text and expanded on those aspects best illustrating Analytical Chemistry's present and future. The book can be used to go deeper into the contents of this chapter.

PAPERS

Quo vadis, Analytical Chemistry?
M. Valcárcel
Analytical and Bioanalytical Chemistry, 408, 13–21 (2016).

This paper presents a new approach to today's and tomorrow's Analytical Chemistry. Some contents of this chapter (e.g., definitions, paradigms, research, transfer) are inspired by the paper. It makes recommended reading for students of Chemistry and also for any teachers and professionals holding a biased, wrong view of Analytical Chemistry.

Reinventing Chemistry
M. Whitesides
Angewandte Chemie Int., 54, 3196–3207 (2015).

A paper by a renowned professor of General and Organic Chemistry at Harvard University proposing a fresh, ground-breaking approach to Chemistry that places Analytical Chemistry in its proper place. This is compulsory reading for Chemistry students and lecturers.

1.3 Questions on the Topic (Answered in Annex 2)

1.1. Tick the type of determination corresponding to each of the following examples:

Examples	Determination of		
	Traces	Micro components	Macro components
Determination of pesticides in urine			
Determination of calcium in a milk sample			
Determination of proteins in beef			

1.2. Tick the correct statements among the following:

[ ] The word "analysis" refers to the analyte
[ ] Analysis of traces
[ ] Microanalysis of copper
[ ] Qualitative analysis comes before quantitative analysis

1.3. What type of information regarding quality can be assigned to the result for a certified reference material?
1.4. Explain the two types of quality trade-offs to be made in response to contradictions between aims or objectives in Analytical Chemistry.
1.5. What are the most salient differences between Analytical Chemistry and other disciplines of Chemistry?
1.6. When does analytical knowledge not suffice to solve problems? With what should it be replaced in those cases?
1.7. Why are the two classical standards of Analytical Chemistry insufficient? What is the third?
1.8. Explain with appropriate examples the importance of interdisciplinarity to Analytical Chemistry.
1.9. Explain and exemplify the most salient written standards for Analytical Chemistry.

1.10. What are the areas influenced by (bio)chemical information? Give an example for each area in Slide 1.26.
1.11. Relate two hierarchies of analytical terms.
1.12. Rank the following concepts according to representativeness:

Place	Concept: representativeness of
	The sample
	The information requirements
	The analytical problem
	The object

1.13. Illustrate the distinction between object availability and sample availability with several examples.
1.14. State the parts (items) of the paper by Whitesides mentioned in Slide 1.42 and recommended as reading. What aspect of Chemistry did you find the most surprising?
1.15. Give two real-life examples other than those depicted in Slide 1.29 and identify the information requirement, object, sample and analyte in each.
1.16. Justify the designation "Trace Analysis".
1.17. Give several examples of real-life situations where the sample and analyte differ in nature.
1.18. Is the designation "Analytical Separation Techniques" correct?
1.19. What are the differences between the following?

1. (Bio)chemical information and analytical information.
2. Chemical information and biochemical information.

1.20. How many pathways can applied research in Analytical Chemistry follow? Why?
1.21. When do analytical chemical R&D centres have to contact the clients requiring (bio)chemical information or vice versa? Give some examples.
1.22. What is the meaning of the four general paradigms of today's and tomorrow's Analytical Chemistry?

1.3.1 An Abridged Version of the Chapter

The contents of this chapter can be shortened for teaching Analytical Chemistry to students not majoring in Chemistry, albeit to a lesser extent than those of the other eight because of its transversal conception. The following 11 slides (one-fourth of all) can be omitted for this purpose:

- Section 1.1.1: Slide 1.3
- Section 1.1.2: Slide 1.6
- Section 1.1.3: Slide 1.10
- Section 1.1.4: Slide 1.14
- Section 1.1.5: Slide 1.15
- Section 1.1.6: Slide 1.20
- Section 1.1.8: Slides 1.40, 1.41 and 1.42
- Section 1.1.9: Slides 1.43 and 1.44

Analytical Properties

2

Abstract

This chapter uses definitions, descriptions and, especially, examples to highlight the importance of analytical properties with a view to ensuring quality in the analytical process and in quantitative results. Analytical properties allow one to compare methods in order to select the most appropriate choice for the analytical problem to be solved. In this chapter, analytical properties are classified according to a metrological hierarchy encompassing three levels, namely: capital properties, basic properties and productivity-related properties. The three types of properties and their associated parameters are described, and their computation explained with examples, in order to facilitate their understanding and mathematical calculation. The individual analytical properties are important, but their mutual relationships are even more so are. For this reason, Sect. 2.1.7 is exclusively devoted to such relationships, to the way each property depends on the others and to which are to be favoured depending on the particular analytical problem. The analytical properties pertaining to Qualitative Analysis (Chap. 6) are special and required adaptation to those dealt with in this chapter. The contents of this chapter are closely related to those of Chap. 7. In fact, analytical properties provide the ground on which effective problem-solving, and fulfilment of the client's information requirements. One other aim of this chapter is introducing students to numerical and statistical computations in Analytical Chemistry in context rather than in isolation as is usually the case.

Teaching Objectives

- To define analytical properties in a holistic manner.
- To assign analytical properties to specific facets of Analytical Chemistry.

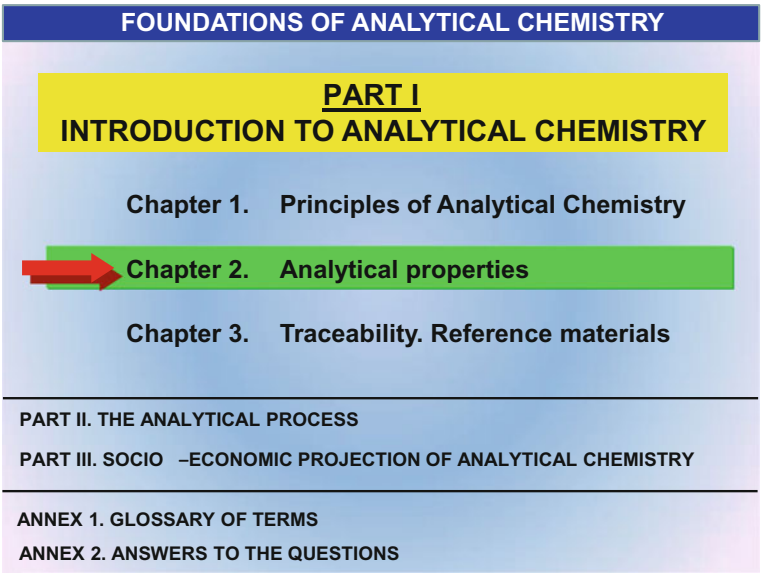
Electronic Supplementary Material The online version of this chapter (doi:10.1007/978-3-319-62872-1_2) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_2

- To establish mutual relationships among analytical properties.
- To relate analytical properties to analytical quality.
- To introduce students to numerical and statistical computations in Analytical Chemistry.

2.1 Explanation of the Slides

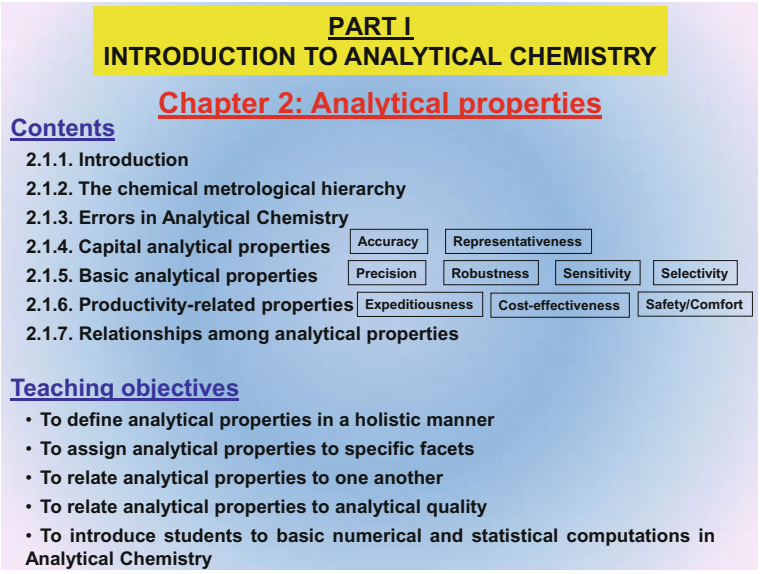
Slide 2.1



This slide places in Part I (Introduction to Analytical Chemistry) and shows the other two parts.

This chapter describes analytical properties, their calculation and the ways quantitative results can be expressed.

Slide 2.2

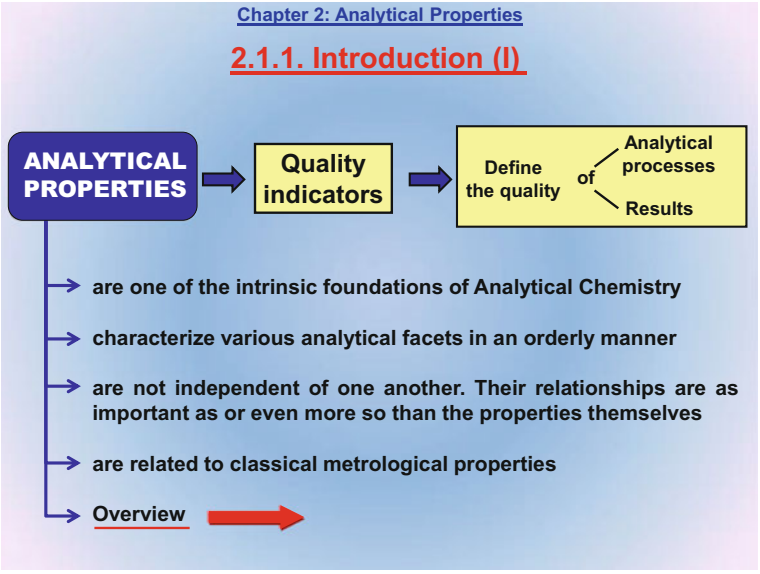


2.2.1. The contents of this chapter are organized in 8 sections dealing with analytical properties through hierarchies and examples. A preliminary section deals with errors in analytical measurements and the types of uncertainty in analytical results.

2.2.2. These are the teaching objectives to be fulfilled, namely: knowing analytical properties, relating them to one another and to analytical quality, and assigning and favouring some over others depending on the analytical problem to be solved.

2.1.1 Introduction (2 Slides)

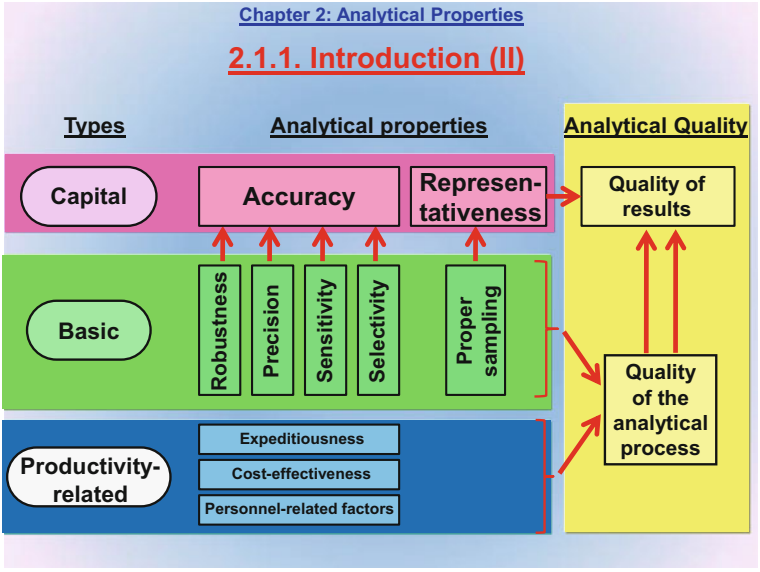
Slide 2.3



2.3.1. Analytical properties are the materialization of analytical quality. They are quality indicators for the analytical process and the results that facilitate their assessment and validation for solving specific analytical problems.

2.3.2. This slide shows the different facets and characteristics of analytical properties. Interestingly, the properties are not mutually independent; rather, they influence one another, whether directly or indirectly. A sound knowledge of the relationships among the properties is essential for analytical chemists to efficiently favour some over others depending on the analytical problem addressed (see Slides 2.56–2.61).

Slide 2.4



2.4.1. This is an overview of the three types of analytical properties (namely, capital, basic and productivity-related) in a top-to-bottom hierarchy.

Capital properties (accuracy and representativeness) only apply to results[1] and basic properties (robustness, precision, sensitivity, selectivity and proper sampling) only to the analytical process. The arrows in the scheme illustrate the dependence of capital properties on basic properties. Thus, robustness, precision, sensitivity and selectivity provide support for accuracy, and proper sampling is the basis for representativeness.

Like basic properties, productivity-related properties (expeditiousness, cost-effectiveness and personnel-related factors) also apply to the analytical process.

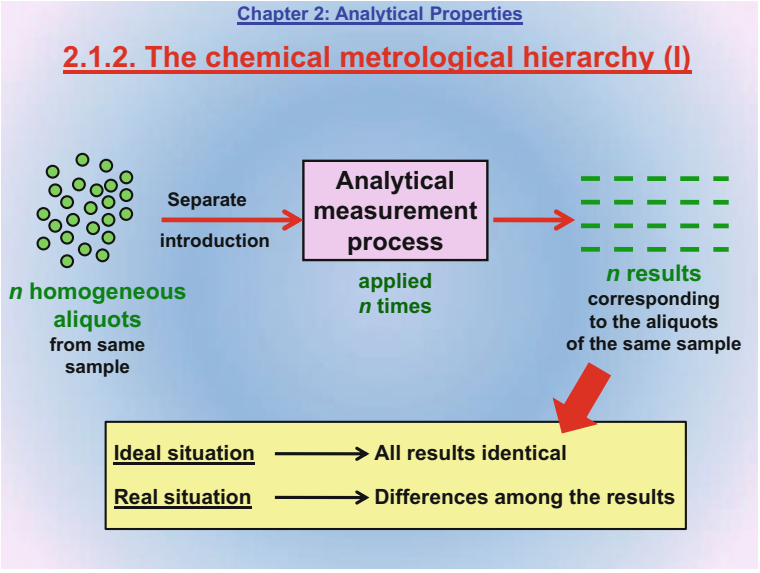
Each type of analytical property is dealt with individually in the following slides.

2.4.2. Capital analytical properties define the quality of results, whereas basic and productivity-related properties define the quality of the analytical process. As a whole, analytical properties are indicators of analytical quality.

[1]It is therefore incorrect to say an analytical process is accurate except unless it provides accurate results.

2.1.2 The Chemical Metrological Hierarchy (3 Slides)

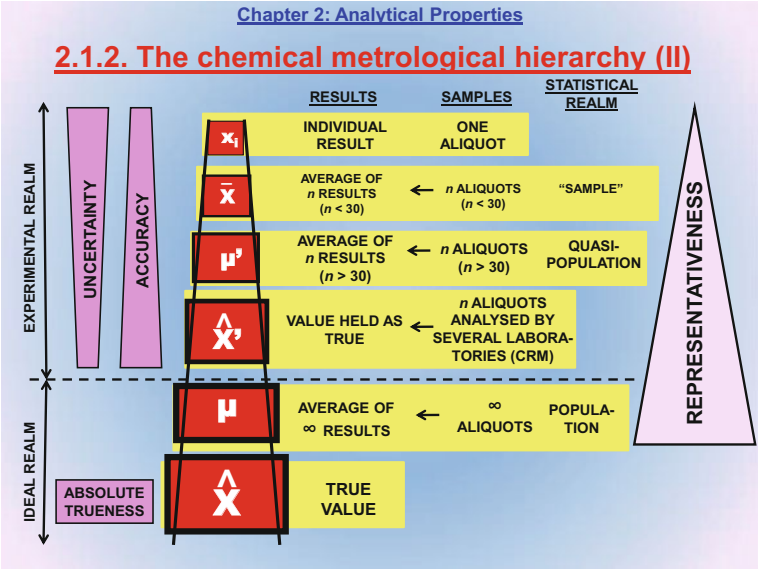
Slide 2.5



This is a simplified depiction of an analytical process starting with n aliquots of the same sample and leading to n results through a general chemical measurement process (CMP). The results can be

- Identical. This is the ideal situation, but highly unlikely in practice, where the results correspond to intrinsic information in the object and absolute trueness (see Slide 1.17).
- Different. This is usually the case in the laboratory because results tend to differ by effect of errors. This typical situation corresponds to analytical information (see Slide 1.17).

Slide 2.6



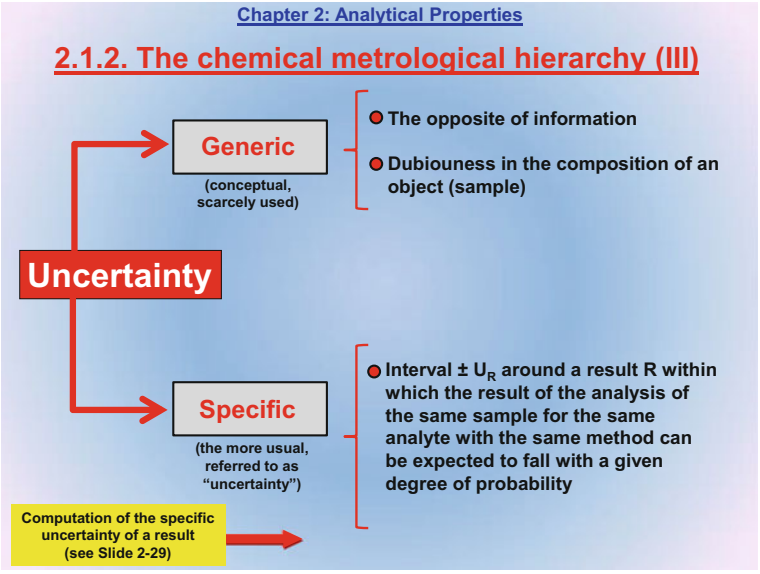
2.6.1. This is the metrological hierarchy of the results of a chemical measurement process, the sample (number of aliquots) from which they are obtained and the statistical designations assigned to some. The number of sample aliquots to be used in order to obtain the desired result increases from the top to the bottom. The results can be classified as follows:

- Individual results, averages and values held as true fall *in the experimental realm*. They can be determined in the laboratory and constitute analytical information accessible to the analytical chemist (see Slide 1.17).
- The average of infinite results and the true value fall *in the ideal realm*. They are inaccessible to the analytical chemist because it constitutes intrinsic information (see Slide 1.17).

2.6.2. Representativeness in the results increases with increasing number of aliquots analysed (that is, from the top to the bottom in the hierarchy). The average of an infinite number of results would correspond to the analysis of a whole population (that is, of all aliquots that can be extracted from a sample). Accuracy in the results also increases from top to bottom in the hierarchy (that is, as the results approach the reference value held as true). Uncertainty, decreases as the results approach the value held as true and also with increasing number of aliquots.

It should be noted that representativeness, accuracy and uncertainty do not apply to the true value because this represents absolute trueness.

Slide 2.7

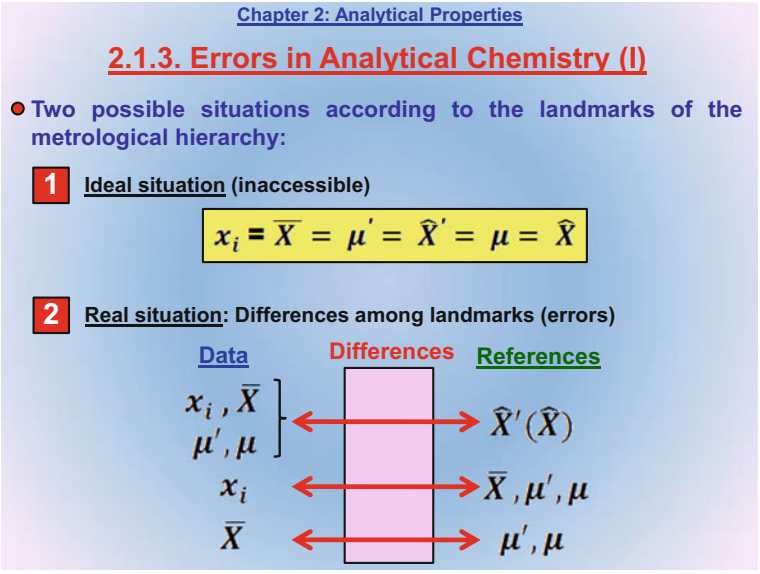


Uncertainty in a result is the lack of certainty about its trueness. Analytical results can be subject to the two types of uncertainty shown here. While *generic uncertainty* represents complete dubiousness (that is, nothing is known about the sample), *specific uncertainty* (U_R) restricts dubiousness to a given interval (that is, the lack of knowledge is confined to a specific range of values) around a fixed value.

The procedure used to calculate specific uncertainty is described in Slide 2.29.

2.1.3 Errors in Analytical Chemistry (5 Slides)

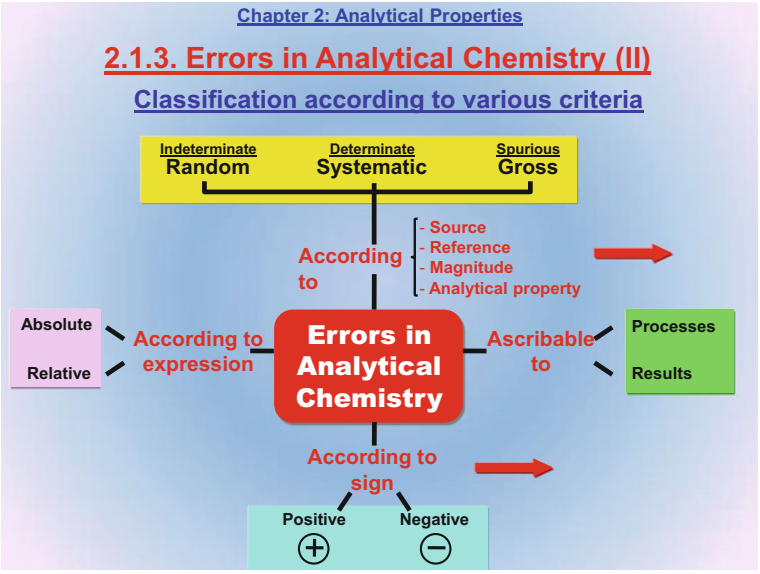
Slide 2.8



This slide shows two possible situations regarding results: the ideal situation and a real situation.

- In the ideal situation, all results are identical, so any result coincides with all others including the true value. This situation is inaccessible to the analytical chemist because chemical measurement processes (CMPs) are inevitably subject to errors (that is, differences between each individual result x_i and the true value, $\widehat{X}'$).
- In a real situation, which is typical of laboratories, the results are not identical and data differ from their reference values. Such differences, which can arise from various factors (Slide 2.9), are called "errors".

Slide 2.9



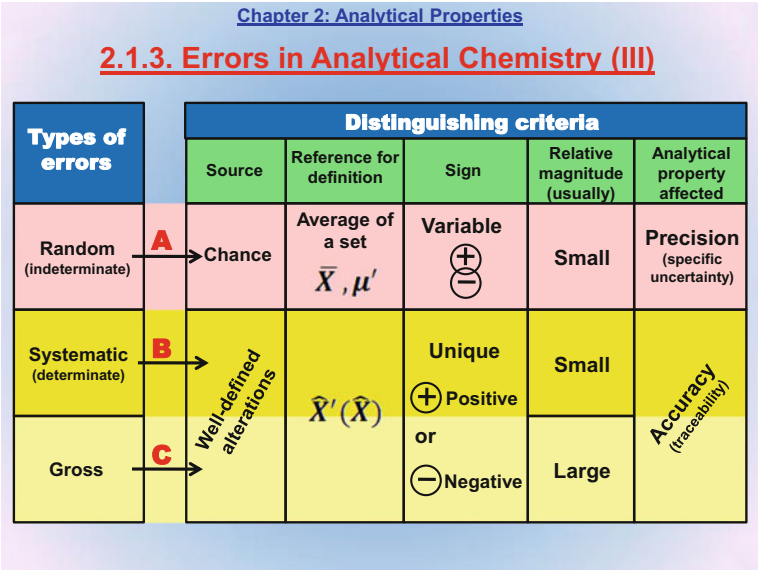
2.9.1. This slide classifies errors according to various criteria. Errors can be assigned to factors of the analytical process (e.g., the operator, instrument sensitivity, calibration) and to quantitative results.

2.9.2. Errors can be random, systematic or gross depending on the type of reference used, magnitude (large or small) and analytical property concerned (see Slide 2.10).

2.9.3. Also, errors can be positive or negative depending on the sign of the difference between the result and the reference value.

2.9.4. Finally, errors can be relative (that is, without a quantity, such as percentages, fractions of unity) or absolute (with a quantity).

Slide 2.10



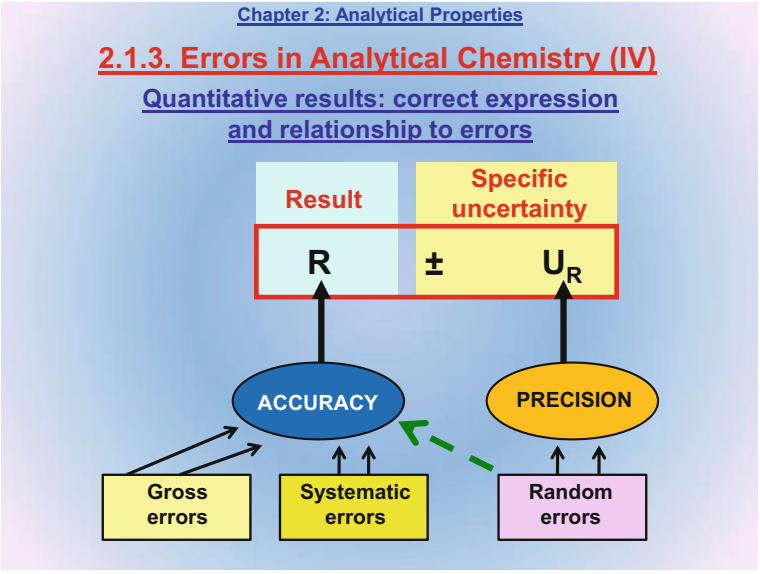
This slide depicts the three types of errors that can be made in making measurements and can affect the accuracy of a result. Their sources, the references used to express them and the analytical properties to which they are related, in addition to various other features, are stated.

A. *Random errors* are due to chance and hence indeterminate (that is, they cannot be known beforehand). Random errors are related to specific uncertainty, which influences the precision of the analytical process and establishes a confidence interval around the mean of the results (see Slides 2.7 and 2.29); hence, it has a variable sign (±).

B. *Systematic errors* are due to a well-defined alteration such as a failure in the analytical process (e.g., a poorly calibrated pipette) and are thus determinate (that is, they can be known). Systematic errors influence the accuracy of a result and are defined in terms of a reference value held as true (e.g., the value for a certified reference material) (see Slides 3.17 and 3.18). This type of error can be positive or negative.

C. *Gross errors* share some traits with systematic errors but are typically much larger (e.g., the error arising from spillage in transferring a liquid between vessels and ignoring it in computing the result).

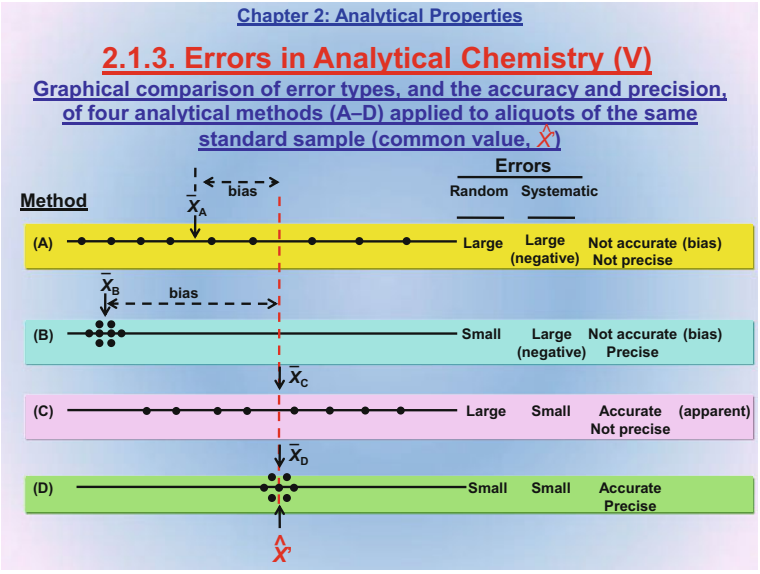
Slide 2.11



2.11.1. Any result R obtained from a series of measurements in an analytical process should be accompanied by its specific uncertainty, U_R, and expressed as shown in this slide. Accuracy is a property of a result that arises in comparing it with a reference value (e.g., a certified value). Precision is a property of the analytical process and is expressed in terms of the specific uncertainty accompanying the result.

2.11.2. As can be seen, errors influence the properties accuracy and precision, and hence results and their specific uncertainty. Systematic and gross errors have a direct impact on accuracy and cause results to depart in either direction from the reference value (see Slide 2.10). Random errors influence precision mainly and materialize in specific uncertainty. Because they are the source of differences among results for the same analytical process, they can also have an indirect impact on the accuracy of a result representing the average of a data series.

Slide 2.12

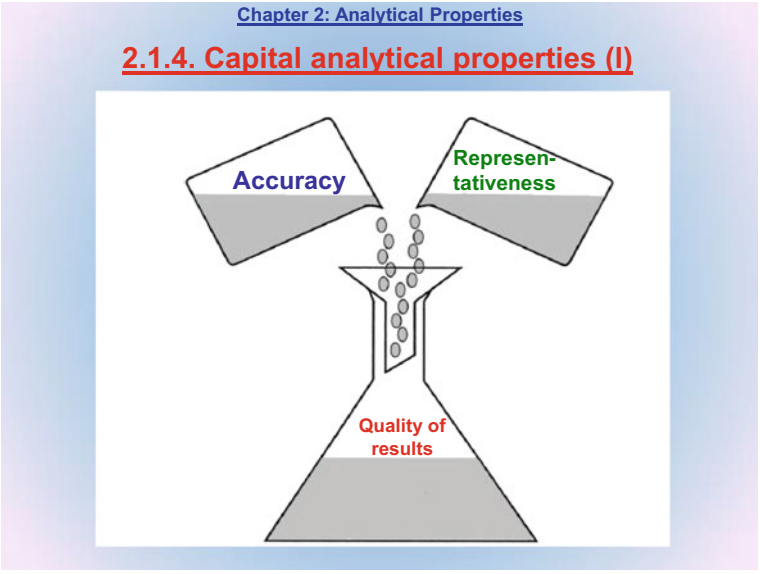


This slide compares and relates the three types of errors with accuracy and precision via four examples (methods A–D) where the same analyte was determined in identical aliquots of the same sample. The accuracy and precision are established from the errors made with each method. For this purpose, n aliquots of the same sample are independently subjected to each of the four methods and the results compared with the value held as true ($\widehat{X}'$, in red) as reference.

- *Method A* is precise but not accurate because the average result, $\bar{x}_A$, does not coincide with the reference value and the individual results, x_i, are highly disperse (that is, very distant from one another). Therefore, the method is subject to systematic and random errors.
- *Method B* is precise because the individual results, x_i, are tightly clustered; however, it is not accurate because the average result, $\bar{x}_B$, does not coincide with the reference value. The method is therefore subject to systematic errors that exceed random errors in magnitude.
- *Method C* is accurate because the average result, $\bar{x}_C$, coincides with the reference value; however, it is not precise because the individual results, x_i, are highly disperse. Therefore, random errors are larger than systematic errors. This is a coincidence but quite possible in practice.
- *Method D* is both accurate and precise. This is the ideal type of method for the analytical chemist because the overall result, $\bar{x}_D$, coincides with the reference value and the individual results, x_i, are tightly clustered, so systematic and random errors are very small.

2.1.4 Capital Analytical Properties (5 Slides)

Slide 2.13

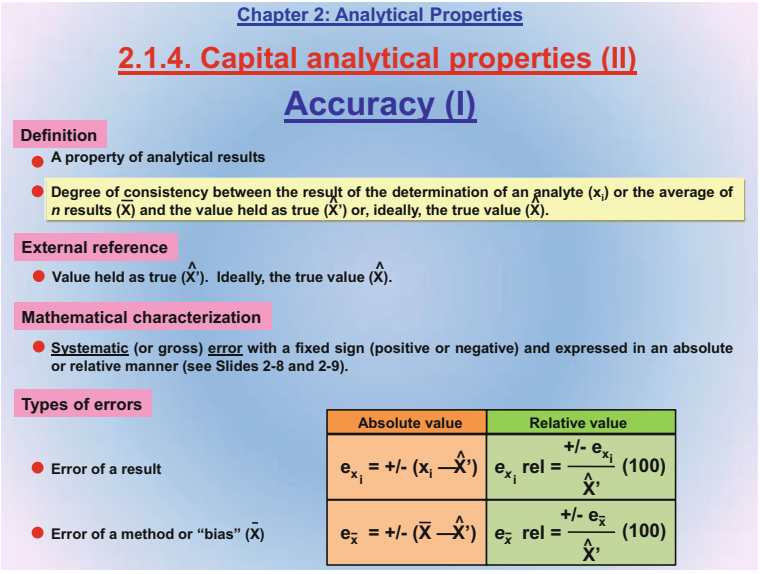


Capital analytical properties are at the top of the hierarchy in Slide 2.4 because they characterize the results and are directly connected to analytical information. The two capital properties are accuracy and precision; both are needed to ensure analytical quality in the results.

This slide illustrates the following notion: quality in the results is achieved when both "ingredients" (accuracy and representativeness) are accomplished simultaneously. A highly accurate result that is not representative of the sample is completely useless. In fact, such a result cannot describe the sample and is hence useless to solve the analytical problem concerned (Chap. 7).

Depending on the particular analytical problem addressed, however, some analytical properties can be favoured over others provided an acceptable minimum level of quality in all is ensured (see Slides 2.56–2.61).

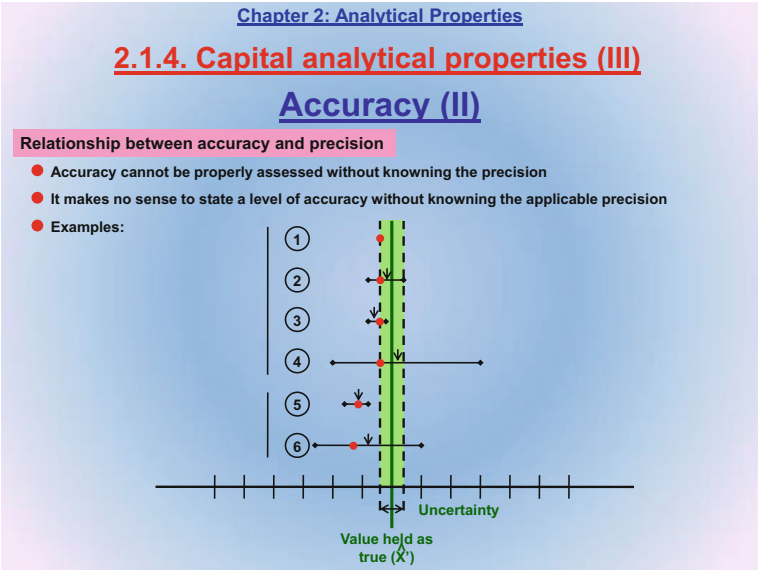
Slide 2.14



This slide defines accuracy and illustrates some of its features. Accuracy is a capital analytical property, a measure of consistency of results with the reference value. Accuracy can be applied to an individual result (x_i) or a body of n results. In the latter case, accuracy is used to characterize the method used to obtain the results.

The difference between a result and the reference value, $\widehat{X}'$, is the systematic error—or gross error if exceedingly large—and can be expressed in absolute or relative terms. The slide also shows the formulae typically used to calculate errors.

Slide 2.15



There can be no accuracy without precision. In fact, it makes no sense to refer to an individual result of an analytical process, x_i, without knowing the interval within which it can fall. The slide shows six examples relating accuracy to precision and quality of a result in relation to a reference value held as true.

In the first four examples (spots in red), the result is very close to the value held as true ($\widehat{X}'$).

Example 1. The result may seem accurate because it falls within the uncertainty interval for the reference value. However, the accuracy is indefinite because the precision of the method (that is, its specific uncertainty) is unknown. For this reason, the result may be due to chance, so it lacks analytical value.

Example 2. The result is accurate because it falls within the specific uncertainty interval for the reference value. Also, it has a well-defined precision spanning an interval highly similar to that of the reference value.

Example 3. The result is accurate because it falls within the specific uncertainty interval for the reference value. Also, it has a well-defined precision which, however, spans a range that is not so similar to that for the reference value as in the previous example.

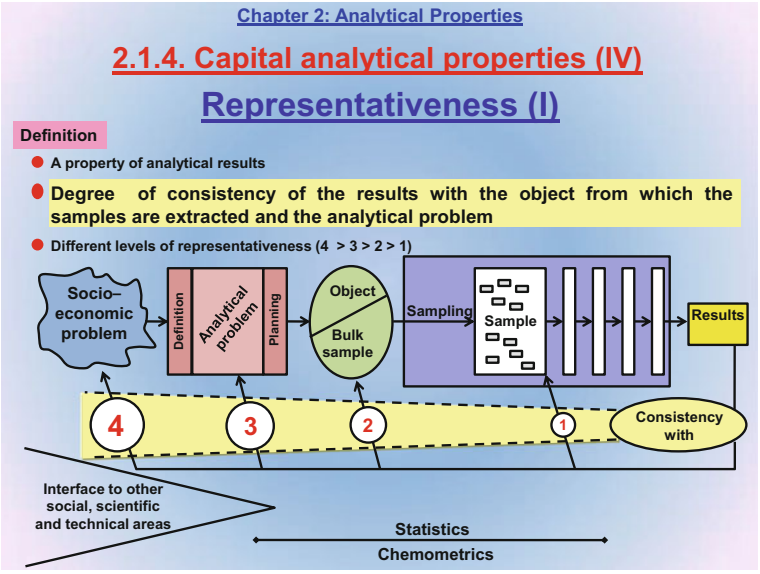
Example 4. The result cannot be deemed accurate because its specific uncertainty interval is rather broad and contains not only the values of the reference interval but also may other, widely different values.

In the last two examples, the result is identical but farther from the value held as true, $\widehat{X}'$, than in the first four.

Example 5. The result is not accurate because it does not fall in the specific uncertainty interval for the reference value. However, the method is highly precise because the uncertainty interval for the result is very narrow.
Example 6. The result is not accurate because it does not fall within the specific uncertainty interval for the reference value; also, it is not precise because the interval for the results is rather broad and contains highly disperse potential values.

It is therefore indispensable to know the precision of an analytical process in order to deem its results accurate.

Slide 2.16



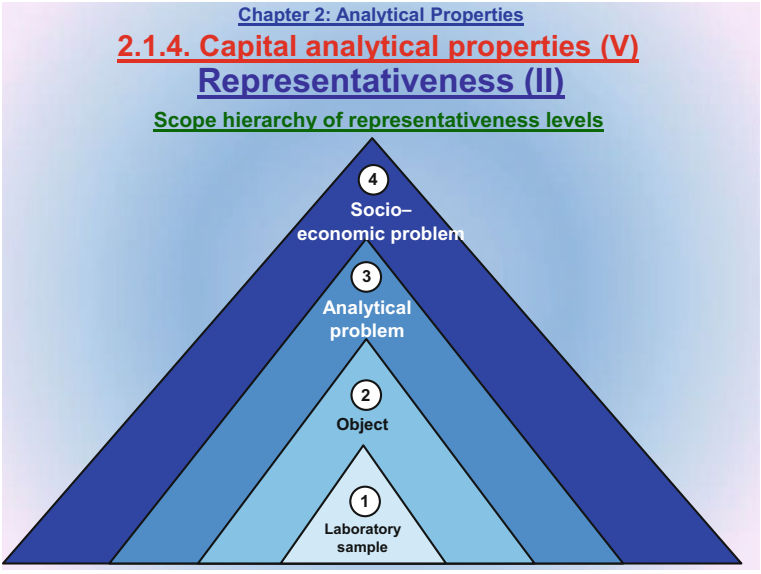
This slide defines representativeness and illustrates its importance. Representativeness increases from level 1 (lowest) to 4 (highest).

- Level 1. The results are consistent with the sample received and analysed by the laboratory; also, they provide a correct description of the sample. This level is essential because as it gives access to the others.
- Level 2. The results are consistent not only with the sample, but also with the object from which it was obtained. Representativeness is higher at this level than at the previous one because the results describe the target object in full rather than the sample alone.

– Level 3. The results should describe the object comprehensively enough to allow the analytical problem to be solved. This requires correctly interpreting the results at the previous levels.
– Level 4. At the top representativeness level, the solution to the analytical problem is applicable to the socio–economic problem from which the analysis ensued. This requires previously reaching Levels 1–3.

For the results to be representative, all links in chain (results, sample, object, analytical problem and socio–economic problem) should be traceable. Traceability is dealt with in Chap. 3, and the way the results are related to the analytical and socio–economic problem are illustrated in Slide 7.10.

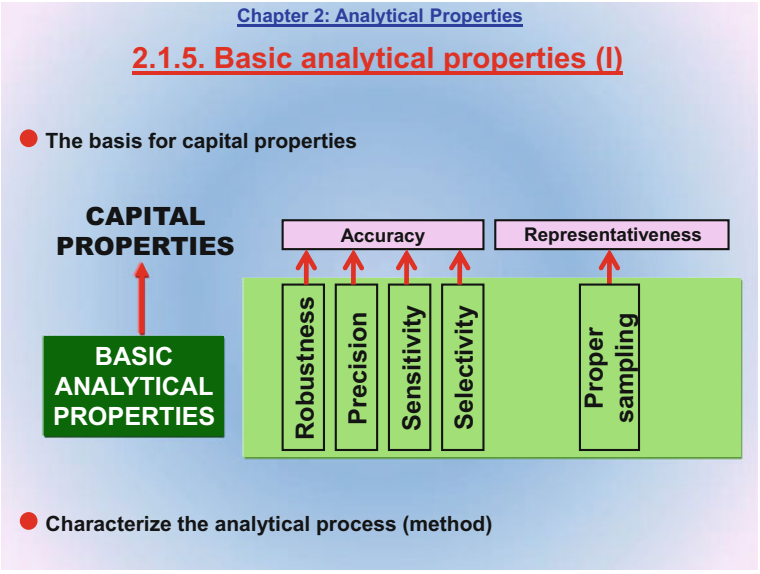
Slide 2.17



This slide ranks the different levels of representativeness described in Slide 2.16 in a scope hierarchy. Representativeness increases from level 1 to 4 here and accessing a higher level entails previously reaching the lower ones (that is, the top level includes all lower levels).

2.1.5 Basic Analytical Properties (1 Slide)

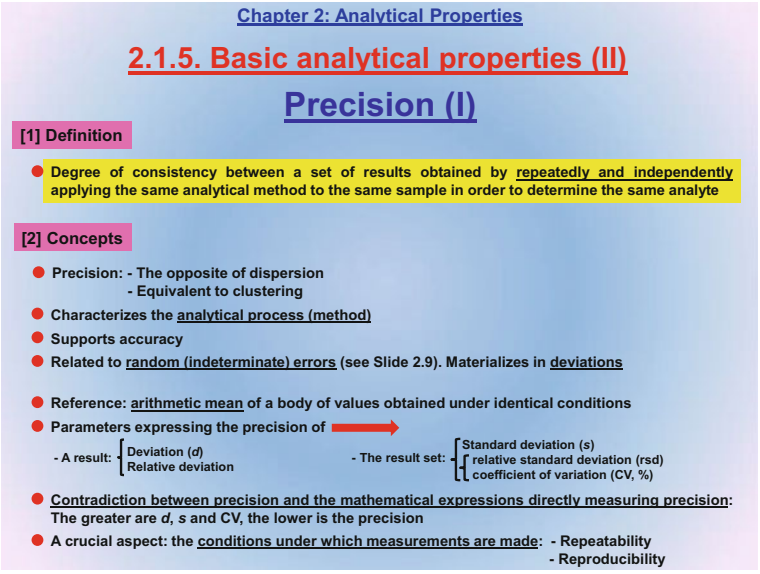
Slide 2.18



Basic analytical properties (namely, robustness, precision, sensitivity, selectivity and proper sampling) follow capital properties in the hierarchy of Slide 2.4. Proper sampling provides the basis for representativeness and the other three properties constitute the basis for accuracy (the two capital properties in Slide 2.13). All basic properties pertain to the analytical process.

2.1.5.1 Precision (13 Slides)

Slide 2.19

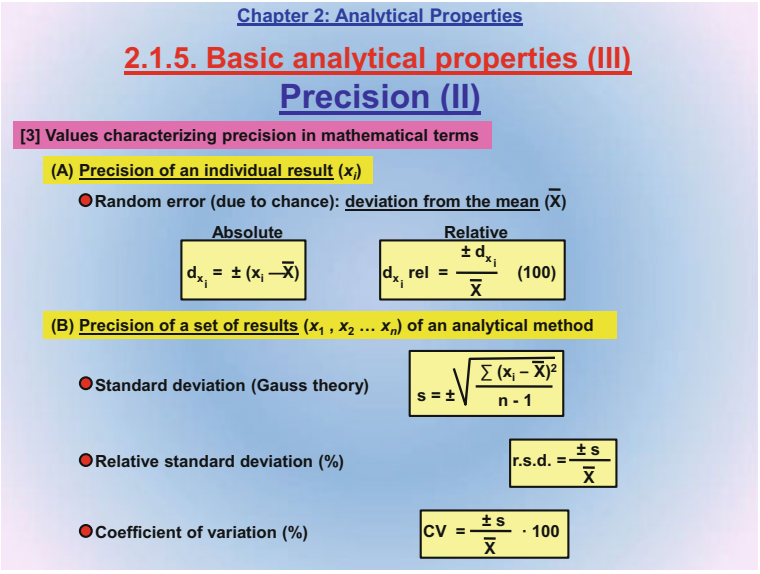


This slide defines precision and describes its most salient features. Precision is a basic property of the analytical process indicating how tightly clustered the body of independently obtained results of the analytical process is. Precision is essential to fully characterize accuracy as it confines the result within a well-defined confidence interval.

The parameters used to measure precision vary in the opposite direction to the property and are related to random errors. Thus, they measure dispersion or departure from a reference value (the average of the results): the greater the dispersion is, the lower will be the precision and vice versa.

Fully and properly characterizing the precision entails using well-defined experimental computation procedures (see Slides 2.21–2.23).

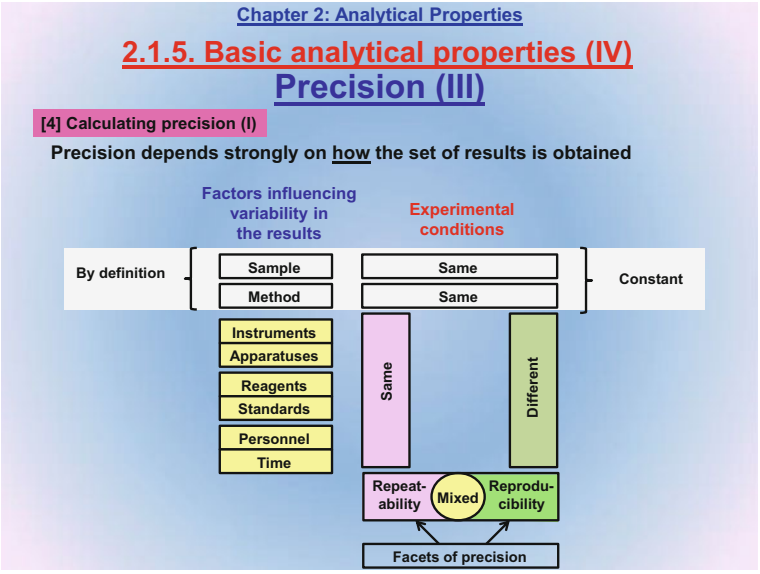
Slide 2.20



These are the two parameters typically used to express the degree of precision of an analytical process.

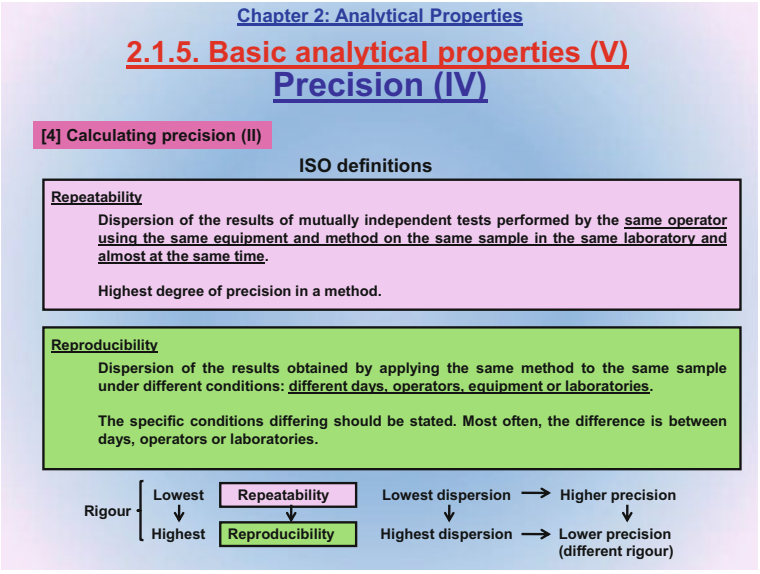
- The *precision of a result* is the individual deviation d_{xi} of the result from the arithmetic mean for the body of results, $\overline{X}$, and is expressed as an interval around the result.
- The *precision of a set of results* is its so-called "standard deviation", which represents an interval around the mean as calculated in the light of the theory of Gauss. The precision of a set of results can also be expressed as the "coefficient of variation", a parameter ranging from 0 to 1 and a relative measure of the standard deviation with respect to the mean that allows methods to be compared in order to identify the most precise (namely, that with the lowest coefficient of variation).

Slide 2.21



Because precision is a basic property of the analytical process, it depends on how the results are obtained. Although, by definition, the method, sample and experimental conditions are maintained throughout measurements, the instruments, apparatuses, reagents, standards, operators and time need not remain unchanged as well—whether they do depends on the capabilities of the laboratory and its personnel. Precision thus has two facets: repeatability and reproducibility, which are defined in the next slide.

Slide 2.22

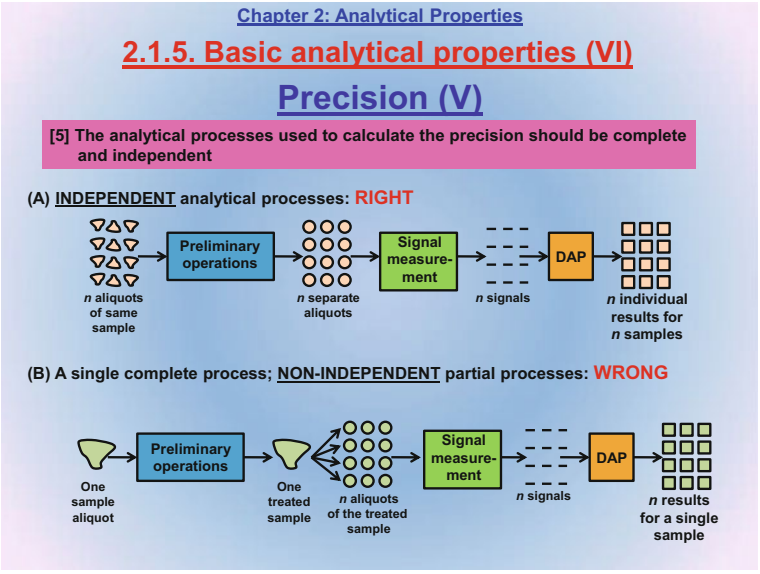


2.22.1. This slide defines the two facets of precision (repeatability and reproducibility) according to the International Organization for Standardization (ISO). Even if the instrument, time and operator differ, tests should be independently performed (that is, each sample aliquot should be individually subjected to the analytical process). The following slide exemplifies a properly conducted analytical process leading to a valid, significant precision value, as opposed to an incorrectly performed process leading to a spurious precision value.

2.22.2. The most salient difference between repeatability and reproducibility is their degree of rigour. Because repeatability is calculated with no change in the experimental conditions, it invariably leads to higher precision values (that is, to lower dispersion in the results) than does reproducibility, which is calculated with some change in the conditions. However, rigour decreases with increasing precision: although reproducibility is less precise than repeatability, it is much more rigorous because the results are reached through different pathways and hence confirmed under different experimental conditions.

In summary, precision cannot be expressed in quantitative terms without regard of the experimental conditions used to obtain the results.

Slide 2.23

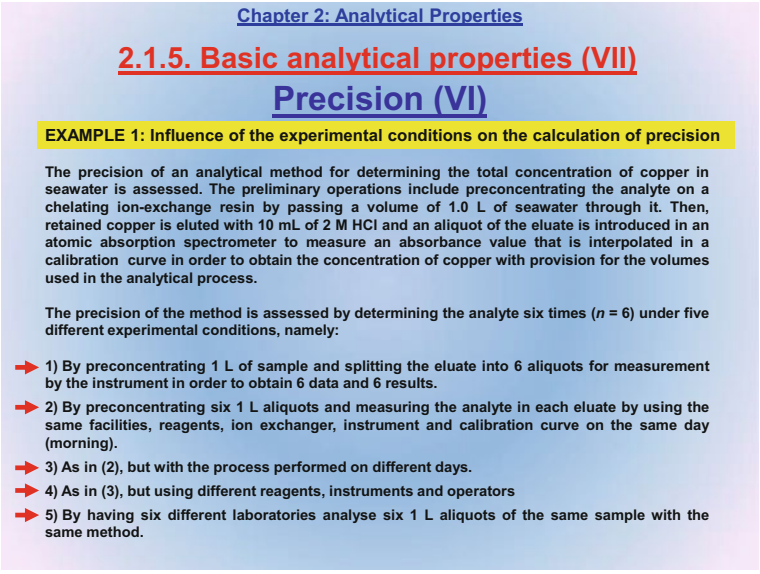


One of the essential requirements to be fulfilled in order to properly calculate the precision of an analytical process is that tests should be conducted independently on each sample aliquot. The two situations shown in this slide exemplify the assessment of precision in terms of independence of the tests.

- In *situation A*, each individual aliquot is separately subjected to the analytical process (that is, preliminary operations, measurement and transducing of the analytical signal, and data acquisition and processing) to obtain as many results as aliquots are processed. The way the analyses are conducted ensures that the results will be independent of one another and hence valid for calculating the precision of the method.
- In *situation B*, the whole sample is subjected to the preliminary operations and then split into aliquots for signal measurement, and data acquisition and processing. The output is mutually dependent results because the initial treatment was applied to the sample as a whole. For this reason, the results are useless to calculate the precision of the method because part of it (specifically, its preliminary operations) was applied, only once, to the whole sample rather than to each aliquot separately.

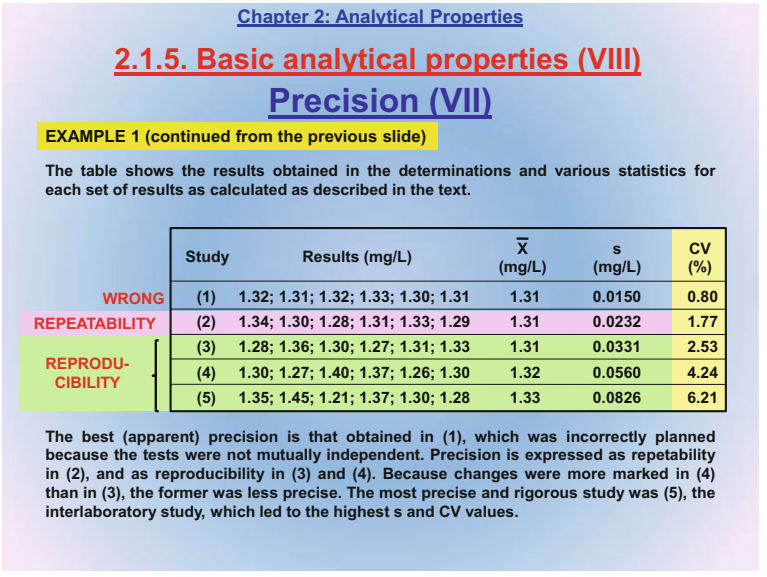
This "trick" is sometimes used to report good precision levels which are actually not so good.

Slide 2.24



This slide exemplifies the contents of the previous three with the calculation of precision under different experimental conditions (five different situations that are solved in the next slide).

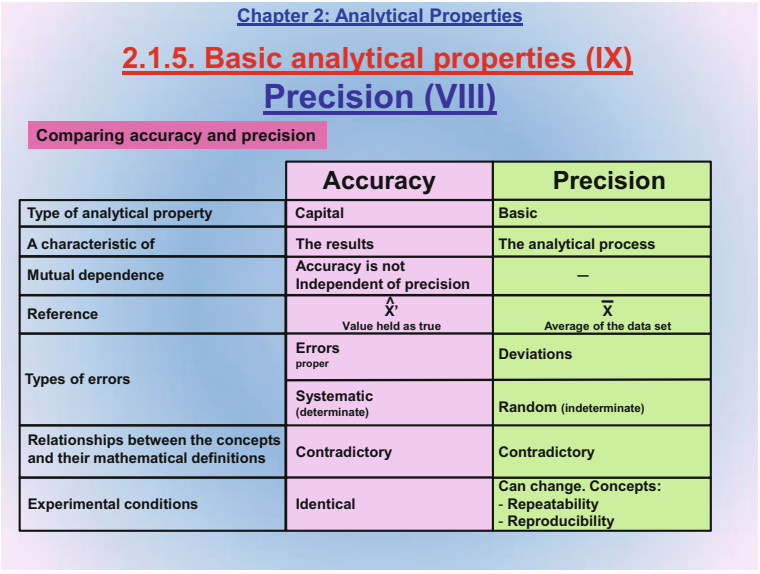
Slide 2.25



This slide completes the example of the previous one with a table of results for each of the five situations additionally showing the precision as standard deviation and coefficient of variation. The latter parameter allows one to compare conditions because it is a relative measure referred to the mean of the results.

The solution for each situation is shown in red. It should be noted that the experimental conditions for the first situation were wrong because aliquots were not analysed in separate tests; as a result, the precision was better but incorrect. Situation 2 has to do with repeatability, whereas situations 3–5 involve reproducibility at different levels of rigour.

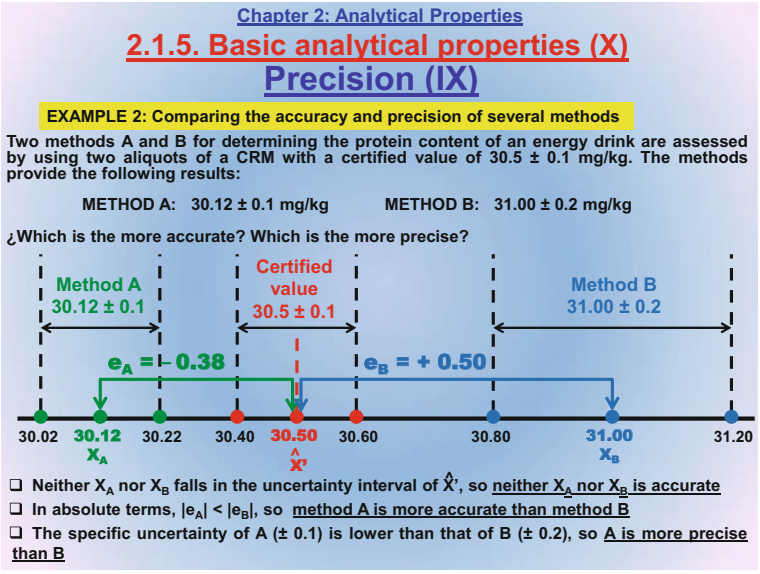
Slide 2.26



This slide compares the features of accuracy, a capital property, and precision, a basic property. Their greatest difference is that accuracy is a property of the results and hence directly related to analytical information. As a consequence, it can only be assessed under unchanged conditions. On the other hand, precision is a property of the analytical process and hence dependent on the particular conditions (repeatability and reproducibility).

The references used to calculate and express errors differ, and so do the relationships between the concepts and the parameters used to express them. Also, accuracy makes no sense without precision (that is, the former can never be meaningful without the latter) (see Slides 2.4 and 2.15).

Slide 2.27



2.27.1. This is the solution to an example problem: comparing the accuracy and precision of two methods A and B by using the value for a certified reference material (CRM) and its confidence interval as reference.

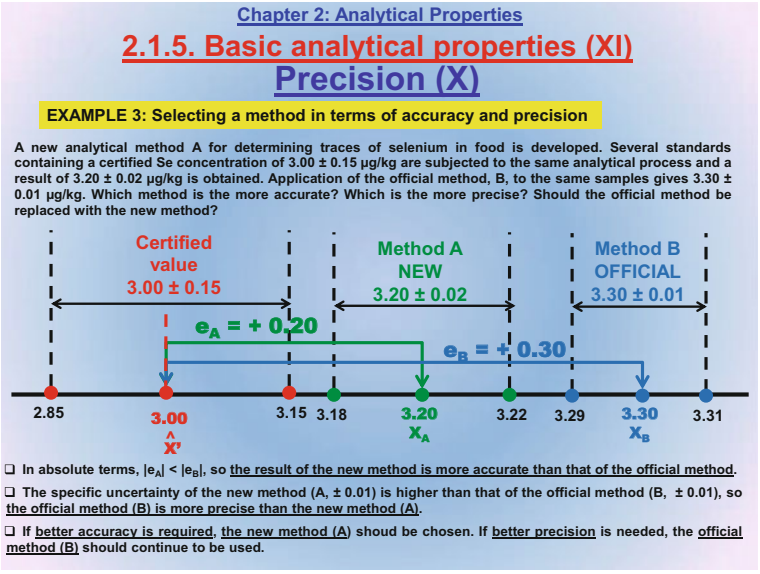
2.27.2. The first step involves placing the results of each method and the value for the CRM together with their confidence intervals in a graph. In order to find whether the results are accurate one must consider the confidence interval for the CRM and for the results of each method. If the results fall within the confidence interval for the CRM, then they will be accurate. If, on the contrary, none of the results falls within the confidence interval, then one must check if the confidence intervals for the methods share any region with that for the CRM. In the example, neither the result for method A (X_A) nor that for method B (X_B) or their respective confidence intervals fall within the confidence interval for the CRM. Therefore, as shown in the slide, neither result is accurate. As can also be seen, the result of method A is subject to a positive error and that of method B to a negative error.

2.27.3. Although neither result is accurate, the two can be compared in order to identify which is closer to the reference value. This entails calculating the absolute error e as the difference between the result of each method and the reference value. As can be seen from the graph, the result of method A is more accurate than that of method B because X_A is closer to the reference value than is X_B (0.3 vs. 0.5).

2.27.4. Identifying the more precise method entails comparing the width of the confidence intervals for the results. Since precision is inversely related to dispersion, the method exhibiting the broader interval (that is, the higher dispersion in its

results) will be the less precise. Because method A has a lower specific uncertainty than method B (0.1 vs. 0.2), the former is more precise than the latter.

Slide 2.28



2.28.1. This is the solution to a problem involving comparing a new analytical method A to an official method B in order to find whether the new method is more accurate and precise. All with regard to the value for a CRM held as reference and its confidence interval.

2.28.2. As in the previous example (Slide 2.27), the results and their confidence intervals are placed in a graph. As can be seen, both methods are subject to a positive error.

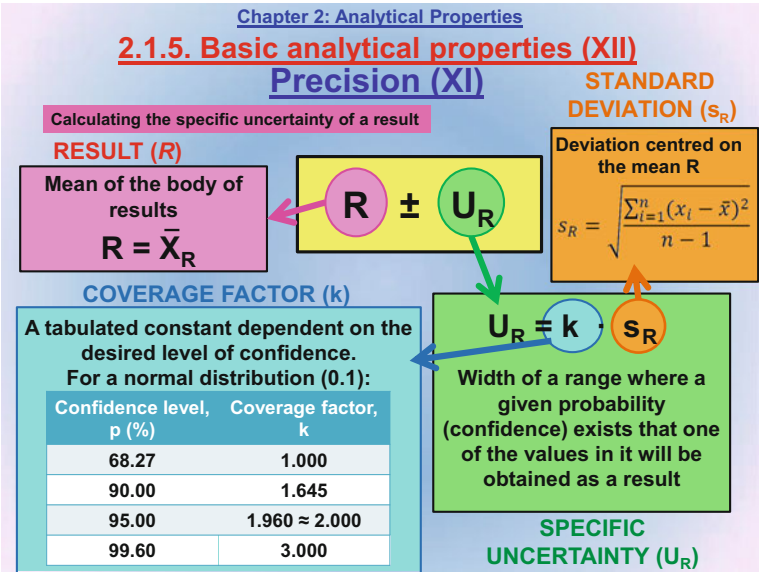
2.28.3. Identifying the method giving the most accurate results entails calculating the absolute error e as the difference between the result and the reference value. The two are compared in terms of absolute value: the result subject to the smaller error will be that falling closer to the reference value and hence the more accurate. Since $0.20 < 0.30$, the new method (A) is more accurate than the official method (B).

2.28.4. Identifying the more precise method entails comparing specific uncertainties. Since precision is inversely proportional to dispersion in the results, the method having the broader interval (that is, the higher dispersion) will be the less precise. The official method (B) is subject to less specific uncertainty than the new method (A) ($0.01 < 0.02$); therefore, the official method is more precise than the new method.

2.28.5. Which method is to be chosen depends on the preferences, conditions and aims in solving the particular analytical problem (Chap. 7). If the problem

requires more accuracy than precision, then the new method is that of choice. Conversely, if the problem requires more precision than accuracy, then the official method is to be preferred.

Slide 2.29



2.29.1. For a result to be correctly expressed, it must be accompanied by a confidence (or uncertainty) interval representing the likelihood of the result of repeating the analytical process falling in that interval with a given degree of confidence (e.g., 95%).

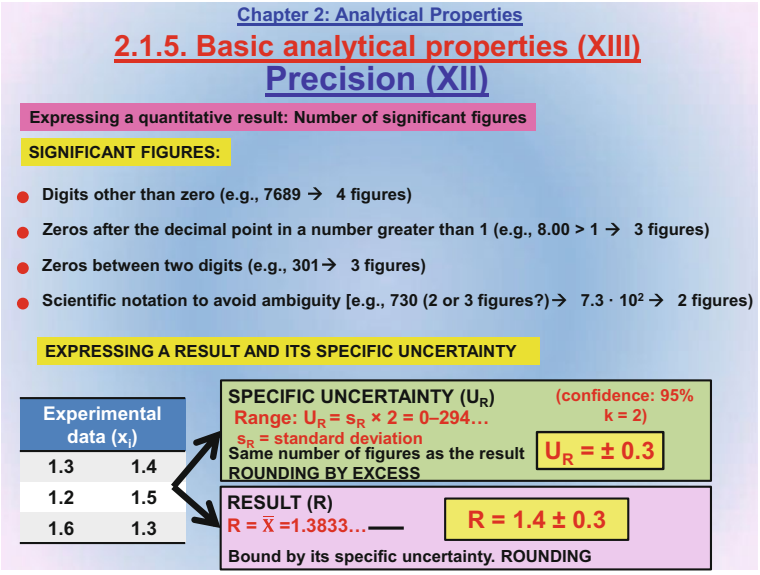
2.29.2. The result, R, should be the average of the n individual results x_i obtained by performing the analytical process n times on n independent aliquots.

2.29.3. The specific uncertainty, U_R, is the interval around the result where a given probability exists that of one of the values in the interval will be obtained when the analytical process is repeated. Mathematically, U_R is the product of a constant k dependent on the degree of confidence of the interval and the standard deviation s_R of a set of n results obtained from the analytical process.

2.29.4. The k values needed to calculate the specific uncertainty are tabulated. The slide shows those for a Gaussian distribution (0.1) and various levels of confidence. Obviously, k increases with increasing confidence level because increasing the probability of the results falling within the interval entails increasing its width. This is exemplified in Slide 2.31.

2.29.5. The standard deviation of the results, s_R, is calculated with the formulae of Slide 2.30; however, s_R, must be used in absolute rather than relative form in the expression for the specific uncertainty.

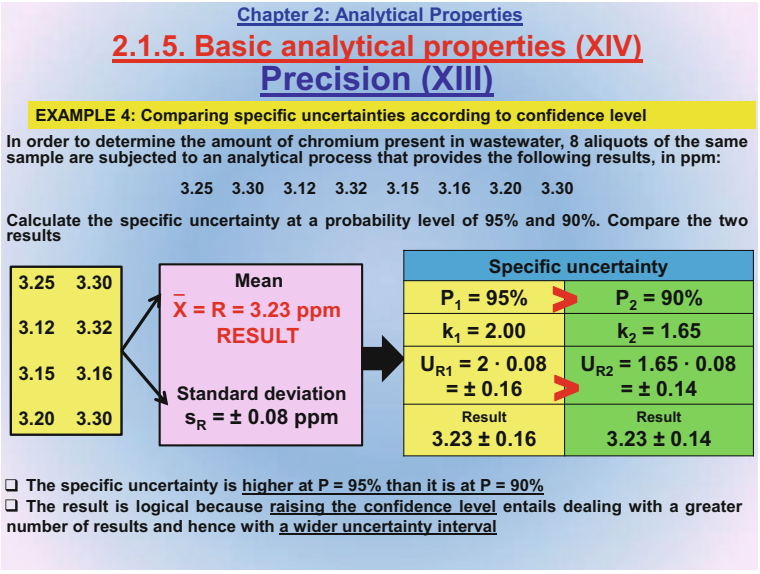
Slide 2.30



2.30.1. Properly expressing a result and its specific uncertainty entails using an appropriate number of significant figures. This slide shows the four rules to be obeyed in expressing an analytical result. As can be seen, scientific notation should be used when the results are multiples of a power of ten, whether positive or negative, in order to avoid ambiguity and facilitate interpretation.

2.30.2. In this example, a result and its specific uncertainty at the 95% confidence level are expressed in accordance with the four rules. The tabulated datum for k at the 95% confidence level in Slide 2.29, 2, is used to calculate the specific uncertainty, which is rounded by excess to the same number of significant figures as the tabulated data. The specific uncertainty is then used to calculate the mean of the results in the table, which is rounded to the same number of significant figures as the specific uncertainty ("*the specific uncertainty sets the bounds for the result*") by applying the usual rounding rules. Finally, the result is given together with is specific uncertainty as shown in the slide.

Slide 2.31



2.31.1. The slide shows how to solve an example problem involving calculating the specific uncertainty of a data series at two different confidence levels (95 and 90%).

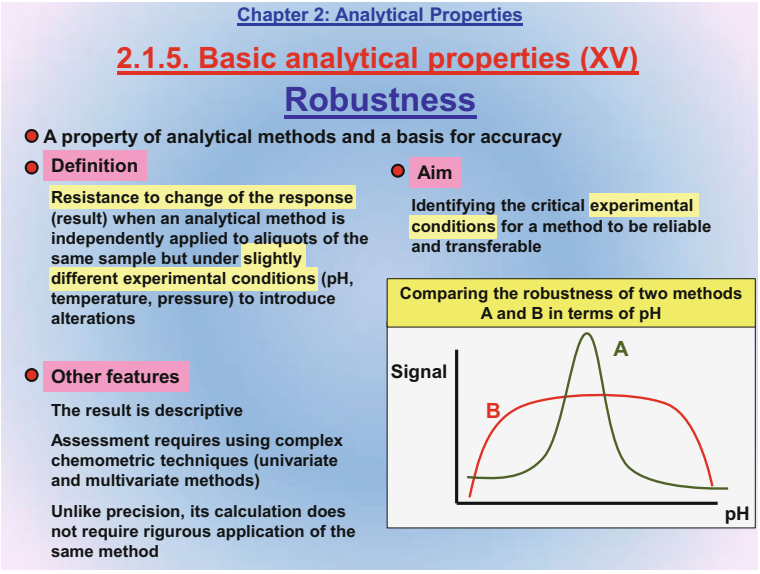
2.31.2. The data are used to calculate a mean and its standard deviation as expressed in Slide 2.29 and with the number of significant figures required (see Slide 2.30).

2.31.3. The specific uncertainty at each confidence level (95 or 90%) is calculated by using the corresponding k value in the table of Slide 2.29 and expressed with the required number of significant figures, which must coincide with that of the result (*R*).

2.31.4. As can be seen, the specific uncertainty at the 95% confidence level is higher than that at the 90% level because increasing the probability that the result of the analytical process will fall within the confidence interval entails widening it.

2.1.5.2 Robustness (1 Slide)

Slide 2.32



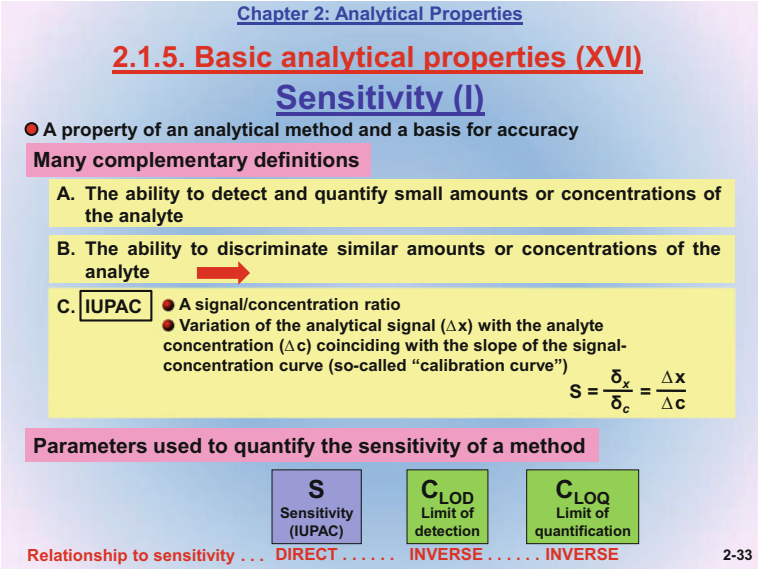
2.32.1. This slide defines robustness and describes its most salient features. Robustness is a basic property of the analytical process ensuring that a method will operate as expected and give quality results, even if the experimental conditions are changed slightly. Robustness provides support for accuracy.

Robustness is an atypical property in that it cannot be expressed quantitatively. Rather, it has to do with "reliability" (the resistance to change of the results by effect of changes in the experimental conditions, which is essential for a method to be reliable and transferable). Robustness is similar to precision but is calculated in a rather different manner.

2.32.2. The example in the box compares the final signals (results) obtained with method A or B depending on the pH at which the analytical process is performed. Note that, because method A is strongly dependent on pH, its results change abruptly with a change in this experimental variable; as a consequence, it is more sensitive to pH changes than method B. By contrast, method B is less markedly dependent on pH, so its results are very similar—virtually identical—even if the pH is altered; as a consequence, it is much more robust than method A.

2.1.5.3 Sensitivity (16 Slides)

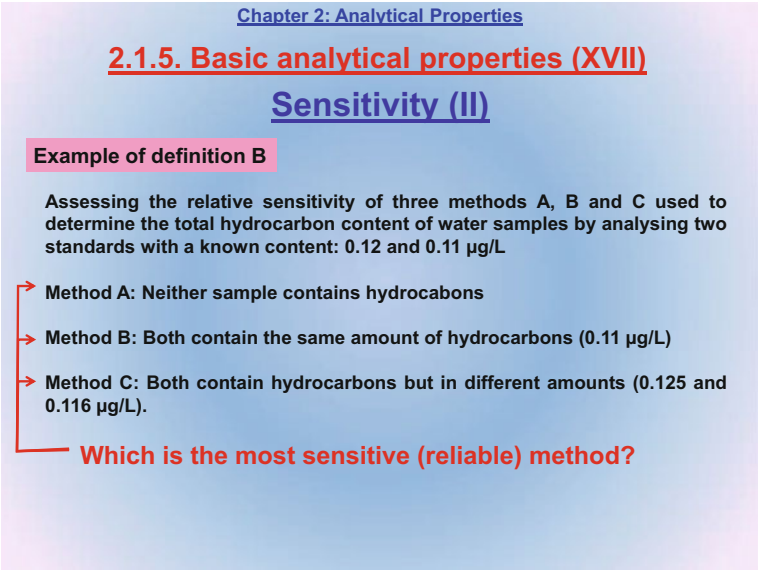
Slide 2.33



This slide shows three complementary definitions of the word "sensitivity". The first (A) is the most general and obvious; the second (B) is exemplified in the next slide; and the third (C) is IUPAC's definition, which is dealt with in detail in Slides 2.35–2.37 and in the Questions section.

Sensitivity is a basic analytical property also supporting accuracy and characterizing the analytical process. The sensitivity of a method can be expressed in three different ways, namely: as sensitivity proper (*S*), and as the limits of detection (LOD) and quantification (LOQ). The former is inversely related to the latter two: the lower is LOD or LOQ, the higher will be *S*. Only LOD can be used in Qualitative Analysis (Chap. 6), however.

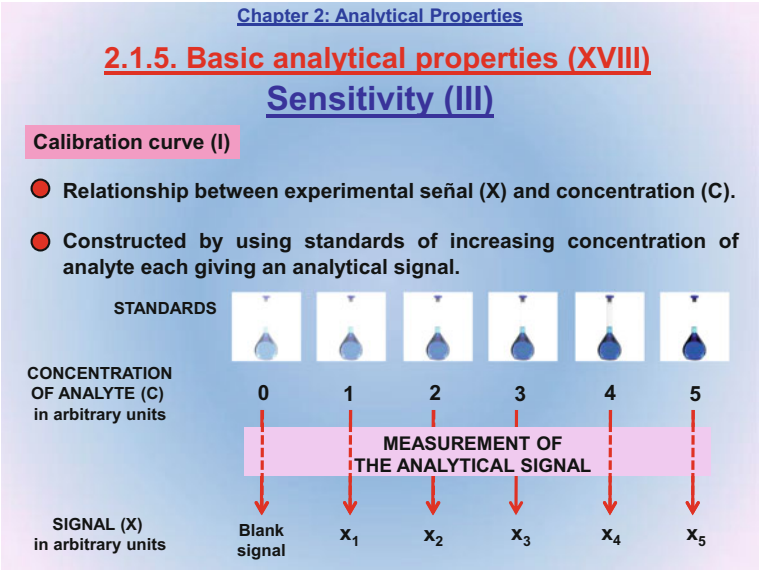
Slide 2.34



2.34.1. This is an example illustrating the second definition of sensitivity (B) in the previous slide. A sample of water containing hydrocarbons was analysed with three methods differing in sensitivity that gave different results in the separate determination of the analytes.

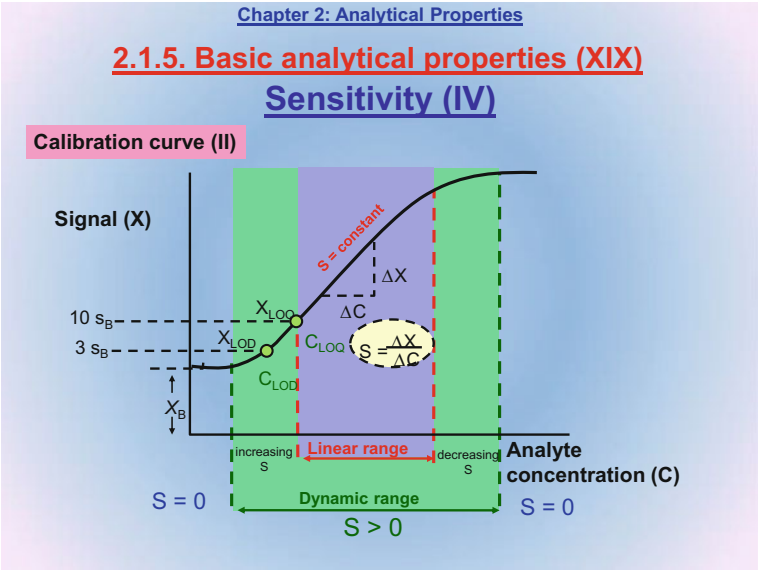
2.34.2. The most reliable method (that is, the most sensitive) will be that best discriminating hydrocarbons in the sample and most accurately quantifying them. Accordingly, method A is not sensitive enough for the intended purpose because it cannot detect the presence of the hydrocarbons. Method B is somewhat more sensitive than method B because it detects the hydrocarbons; however, it cannot discriminate them. Finally, method C is the most sensitive because it can both detect and discriminate (distinguish) them. This is one way of defining sensitivity: the ability of a method to discriminate analytes and determine their amounts (that is, to both detect and quantify the analytes).

Slide 2.35



As per IUPAC's definition, the sensitivity of a method (Slide 2.33) is the signal change per unit analyte concentration, that is, the slope of an analyte signal (X) versus concentration (C) graph. The graph is experimentally constructed by measuring the signals for a series of standards of known concentration including a blank (that is, a sample containing no analyte). The graph (Slide 2.36) exhibits various zones allowing not only the sensitivity, but also other detection-related parameters, to be quantified.

Slide 2.36



2.36.1. Plotting the signal for a standard against the analyte concentration gives a curve such as the one in this slide for the data shown in an arbitrary manner in the previous slide. The smallest possible signal (lower limit of the curve) is that produced by the instrument in response to a blank (a sample containing no analyte) and the outset, x_B, of the curve. The largest possible signal (upper limit of the curve) corresponds to the analyte saturation level, beyond which the instrument cannot detect any greater amounts.

2.36.2. The *dynamic range* is the concentration range where the signal departs from the blank signal (lower limit) and saturation signal (upper limit). The lower limit is called the "limit of detection" (x_{LOD}) because it coincides with the point beyond which the analyte can be distinguished from the blank. It is defined and calculated in Slides 2.40 and 2.42.

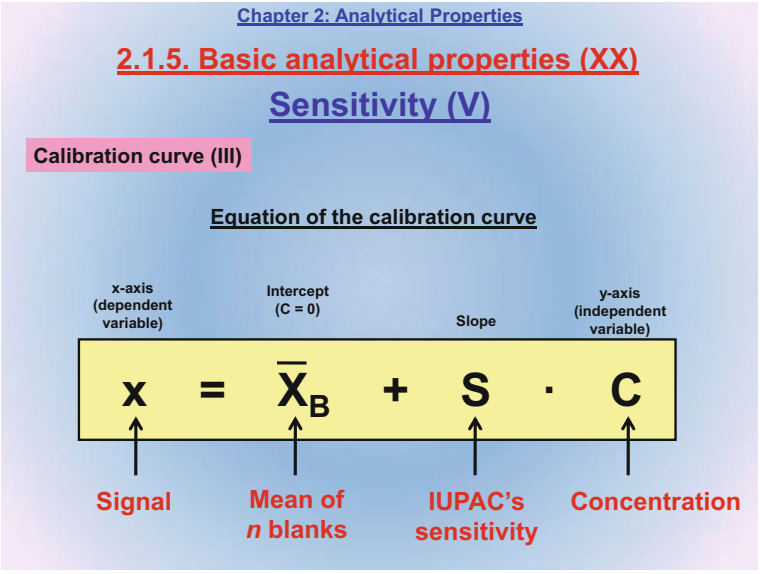
2.36.3. The *linear range* is the concentration range where the signal–concentration (X–C) graph is linear, that is, where the signal varies linearly with the concentration along a straight line—and hence in accordance with the first-order equation in Slide 2.37. The lower limit of this interval is called the "limit of quantification" (x_{LOQ}) because it is the point beyond which the amount of analyte in the sample can be determined from a simple signal–concentration relation. The limit of quantification is defined and calculated in Slides 2.41 and 24.2.

2.36.4. Based on IUPAC's definition (Slide 2.33), the sensitivity (S) can be calculated as the slope of the signal (X)–concentration (C) curve (Slide 2.33).

At analyte concentrations within the dynamic range, $S > 0$ because the instrument is capable of detecting and discriminating concentration differences, so the

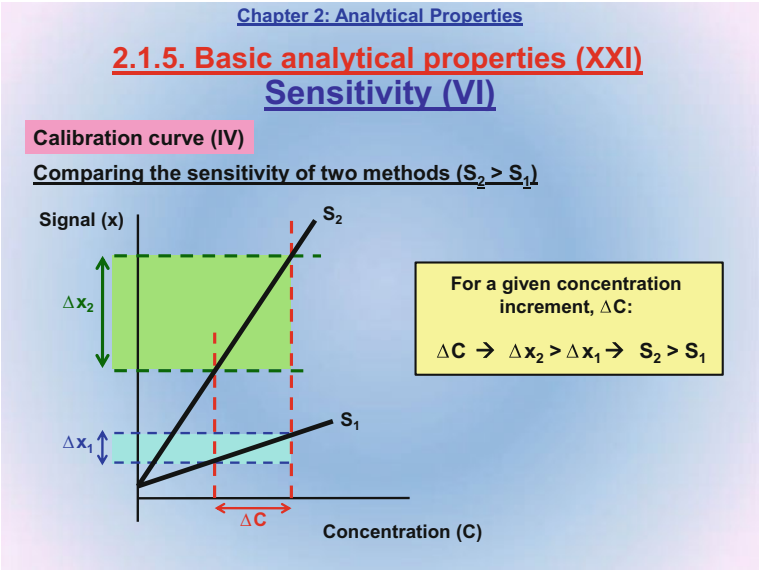
slope of the curve is invariably positive. Within the linear range, the signal changes slightly with the analytical concentration in accordance with a first-order law over the linear range (Slide 2.37); hence, the slope and the sensitivity are constant and equivalent. Finally, at concentrations outside the dynamic range—and hence also outside the linear range—the signal does not change with the analyte concentration because the instrument saturates in response to a sample with an exceedingly high concentration; as a result, the slope of the curve is constant and $S = 0$.

Slide 2.37



The calibration curve (Slide 2.36) is often a straight line conforming to a first-order equation as in this slide. Although at high dilutions the variation of the analytical signal with the analyte concentration is not a straight line, the curve can be approximated to one provided no concentrations near that of the blank are used. With this provision, the calibration curve can be defined in terms of a first-order equation where the intercept coincides with the blank signal (or the average signal if more than one blank is used) and the slope coincides with the sensitivity of the method as defined by IUPAC (Slide 2.33). This slide shows the general expression of the calibration curve and states the meaning of each parameter in it.

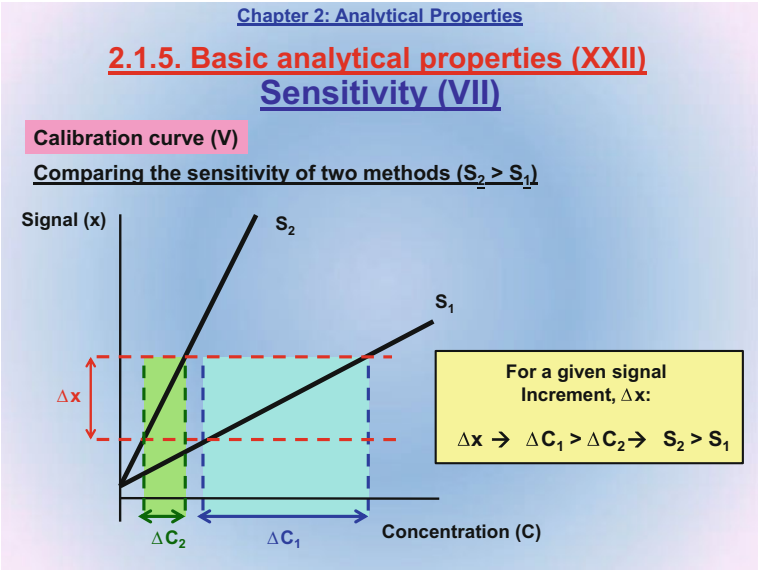
Slide 2.38



This slide and the next compare the sensitivity of two methods 1 and 2 according to two different criteria.

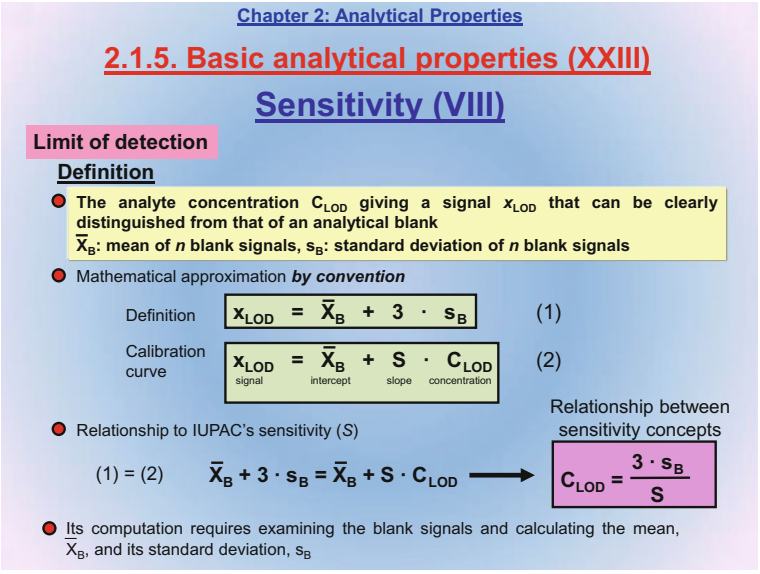
For an *identical concentration range*, the sensitivity increases with increasing change in the signal over the range because a given concentration range will lead to a more marked change in the signal. Because method 2 exhibits a greater signal change over the same concentration range, it is more sensitive than method 1. This is confirmed by IUPAC's definition of sensitivity (Slides 2.33 and 2.37): the calibration curve for method 2 has a higher slope than that for method 1.

Slide 2.39



In a given *signal range*, the sensitivity of a method will increase with decreasing concentration change over the range because a small change in analyte concentration will result in a more marked change in signal. In this example, method 2 is more sensitive because concentration changes are smaller than in method 1. The same conclusion is reached by comparing their sensitivity as defined by IUPAC (Slides 2.33 and 2.37): the slope of the calibration curve for method 2 is higher than that for method 1.

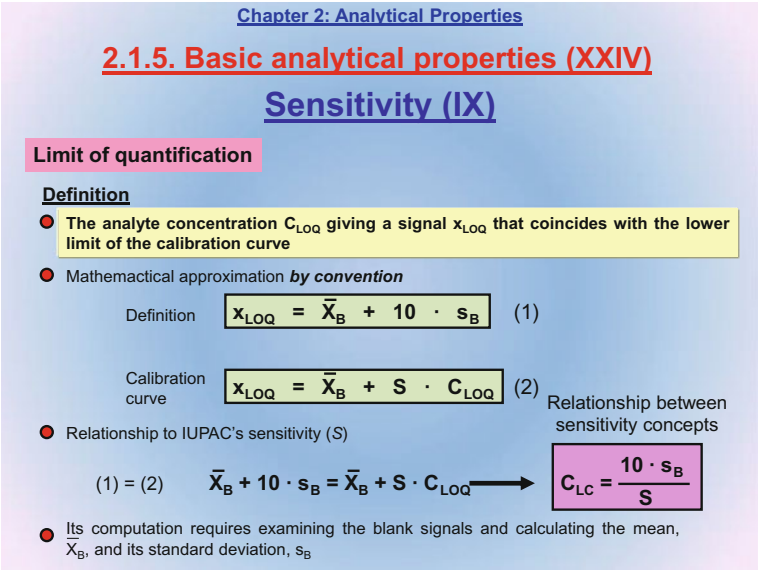
Slide 2.40



This slide defines *limit of detection* (LOD) and relates it to the calibration curve and to sensitivity as defined by IUPAC (Slide 2.33).

The limit of detection is the lower limit of the dynamic range (Slide 2.36), that is, the point where the sensitivity departs from zero to a positive value. Above LOD, the analyte can be discriminated from the blank (that is, the instrument becomes "sensitive" to the analyte). As can be seen, LOD is computed from the signal associated to the concentration in question and used to relate the analyte concentration to the sensitivity of the method via the equation of the calibration curve.

Slide 2.41

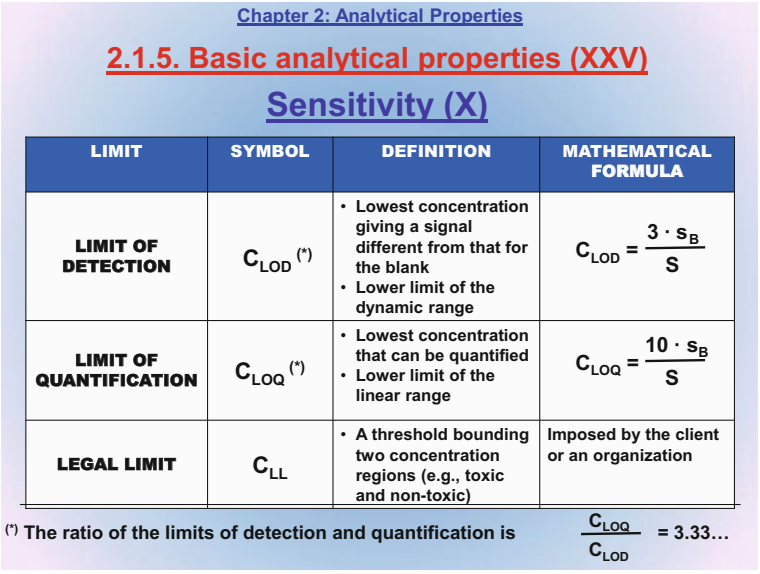


This slide defines *limit of quantification* (LOQ) and relates it to the calibration curve and to sensitivity as defined by IUPAC (Slide 2.33).

The limit of quantification is the lower limit of the linear range (Slide 2.36), that is, the point where the sensitivity becomes constant and the signal depends linearly on the concentration. Above LOQ, the instrument can discriminate between different amounts (concentrations) of analyte (or, in other words, the analyte is "visible" to the instrument and can be quantified with it). LOQ is computed from the signal associated to the concentration concerned and can be used to relate the analyte concentration to the sensitivity via the equation of the calibration curve.

It should be noted that the definition by convention of the limits of detection (x_{LOD}, Slide 2.40) and quantification (x_{LOQ}) requires the prior knowledge of the blank signal (the average) and its standard deviation (s_B) as the limits are assumed to be 3 and 10 times greater, respectively, than the blank signal (see the definition of Slide 2.40 and that in this slide above).

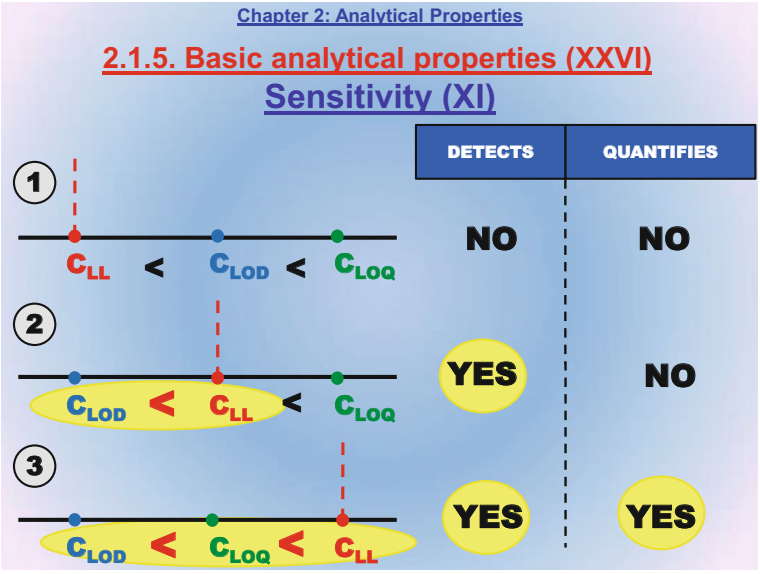
Slide 2.42



This slide summarizes the limits defined in the previous two and introduces a new concept: the legal limit (C_{LL}), which is a function of the particular analytical problem addressed and of the client or organization imposing it (see Slides 7.8 and 7.15). This is possibly the most important limit because it is used as a reference to validate analytical methods and confirm whether the limits of detection and quantification are adequate to solve the particular analytical problem.

The slide also shows the mathematical relation between the concentrations at the limits of detection (C_{LOD}) and quantification (C_{LOQ}).

Slide 2.43



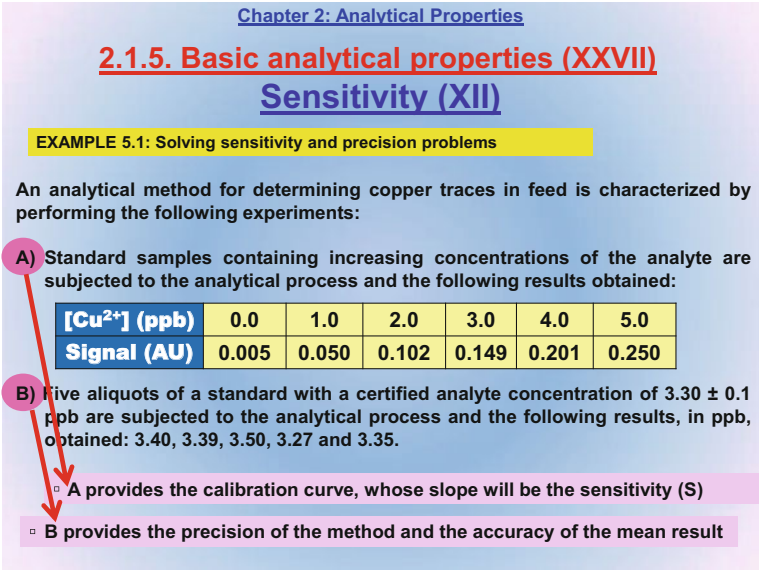
2.43.1. This slide illustrates three different situations regarding the limits defined in the previous one by comparing LOD and LOQ with the legal limit on a scale of increasing analyte concentrations in each.

2.43.2. In *situation 1*, LOD and LOQ are both greater than the legal limit. Because the instrument can only detect and quantify the analyte at concentrations above c_{LOD} and c_{LOQ}, respectively, the method is useful to neither detect nor quantify the analyte. In fact, the legal limit falls below both limits, so concentrations equal or similar to c_{LL} cannot be "seen" or quantified with the method in question.

2.43.3. In *situation 2*, the legal limit is higher than LOD but lower than LOQ. As a result, the method can only be used to detect the analyte ($c_{LOD} < c_{LL}$), that is, it allows the analyte to be identified but cannot be used to determine the amount present in the sample.

2.43.4. In *situation 3*, LOD and LOQ are both lower than the legal limit. As a result, the method can be used to both detect and quantify the analyte ($c_{LOD} < c_{LL}$ and $c_{LOQ} < c_{LL}$), that is, to identify it and to know the amount present in the sample.

Slide 2.44



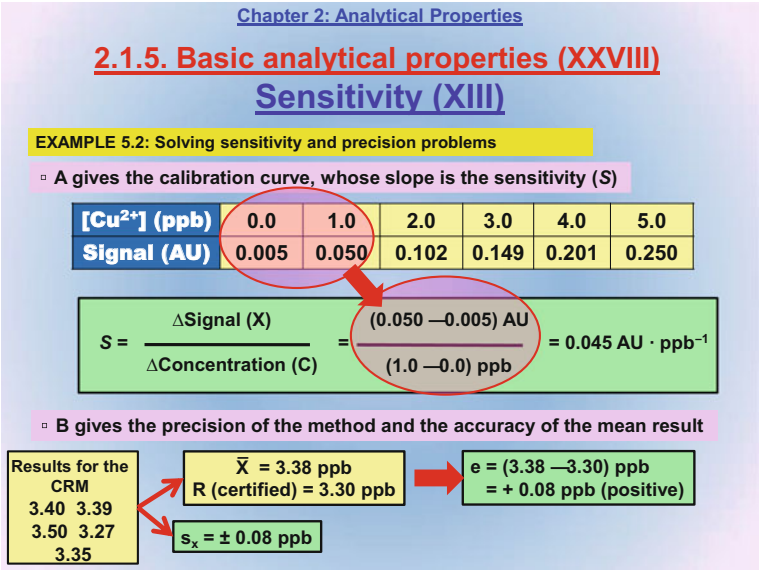
2.44.1. This problem illustrates the concepts behind the basic analytical properties precision (Slide 2.19) and sensitivity (Slide 2.33).

2.44.2. Section A shows the measured absorbance at the copper concentration in each standard, which can be used to construct a signal (AU) versus concentration (ppb) calibration curve in order to calculate the sensitivity of the method according to IUPAC's definition (Slide 2.33).

2.44.3. Section B shows the results obtained by subjecting a certified reference material five times to the analytical process, which can be used to assess the precision (from 5 results) and the accuracy of the result (by comparison with the certified value).

Slides 2.45–2.49 answer several questions arising from this example.

Slide 2.45



2.45.1. The data in the table of Section A in the previous slide can be used to calculate the sensitivity of the method according to IUPAC (Slide 2.33), that is, as the ratio of a signal change to a concentration change.

2.45.2. For example, the two data pairs highlighted in the table can be computed to calculate the sensitivity, S, in AU · ppb^{-1}. Using other data pairs leads to very similar results.

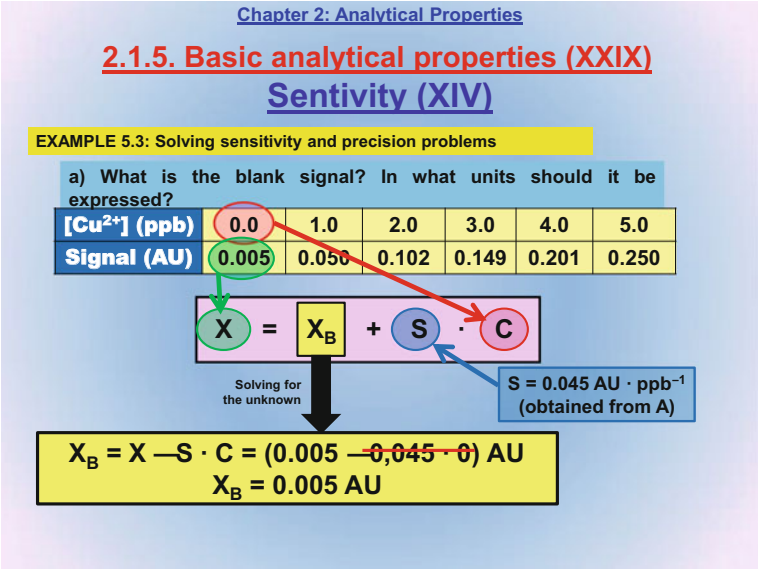
The most accurate way of calculating the sensitivity is by plotting the data in the table to construct a regression curve. Although this procedure is simple and provides an acceptable solution, it is advisable to use two or three more pairs in order to check that the differences are small enough.

2.45.3. The five results obtained by subjecting the certified reference material to the analytical process, and its certified value, can be used to calculate the precision of the method and the accuracy of the result.

Since no confidence level is stated, the specific uncertainty (Slides 2.7 and 2.29) is assumed to coincide with the standard deviation of the method, which is taken to be its precision

2.45.4. The standard deviation can be easily calculated from the equation in Slide 2.20 and the accuracy from the absolute error (see Slide 2.14). The results are expressed in accordance with rules for the number of significant figures in Slide 2.30.

Slide 2.46



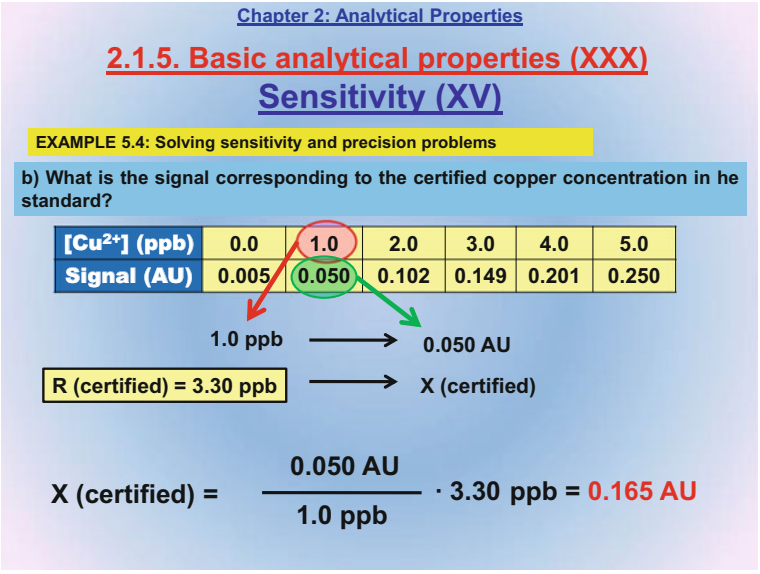
2.46.1. The sensitivity, precision and accuracy values calculated in the previous slide can be used to solve the different parts of the problem. Part (a) can be easily solved by using the equation for the calibration curve in Slide 2.37.

2.46.2. The calibration curve allows one to determine the sensitivity, *S*, which was calculated in the previous slide. The table gives the average of the blanks—a single value here because only one blank was analysed—and the blank concentration.

2.46.3. The data are substituted into the equation and the equation is solved for the unknown. By definition (Slide 2.35), the analyte concentration *C* in the blank is zero; therefore, the sensitivity, *S*, is also zero and the blank signal corresponds to the tabulated signal.

Again, the blank signal can be more accurately determined by constructing a regression curve from the tabulated data and calculating the intercept (that is, the signal at a zero concentration). However, the straightforward, approximate procedure used here suffices to obtain an acceptable value.

Slide 2.47

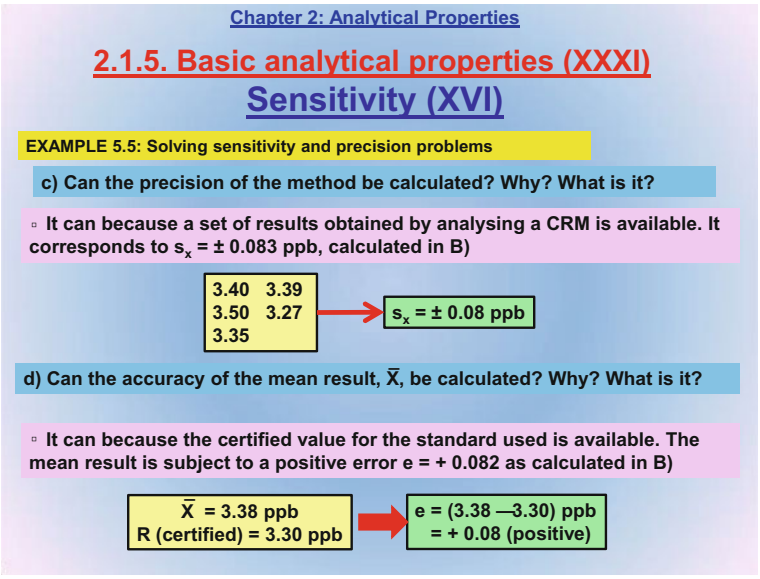


2.47.1. Part (b) of the problem requires determining the signal that would be produced by the certified concentration if the analytical process were applied to the CRM in order to measure the absorbance.

2.47.2. The signal, in AU, for the certified samples can be easily computed from the certified concentration and a couple of tabulated values.

Again, the result is only approximate and could be more accurately obtained by substituting the certified concentration in the equation of the regression curve, established from the slope (S) and intercept (blank average) of the curve.

Slide 2.48

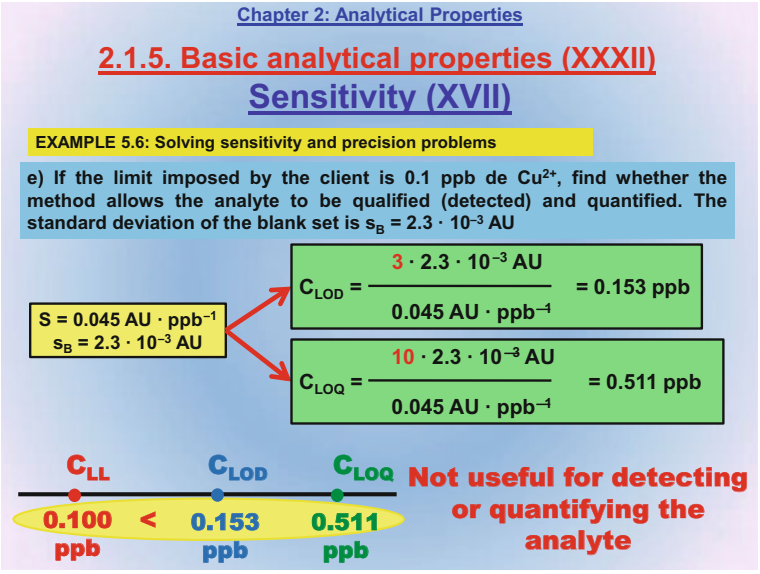


2.48.1. The solution to Part (c) of the problem is the precision of the method as calculated in Slide 2.45, B. Here, the precision is assumed to be identical with the standard deviation for the body of results obtained by analysing a certified reference material (CRM). Determining the specific uncertainty at a given confidence level requires using the procedures described in Slides 2.29 and 2.31.

It should be noted that the precision for the blanks cannot be extrapolated to the method but can be used as an approximation.

2.48.2. The solution to Part (d) of the problem is the absolute error as calculated in Slide 2.45, B.

Slide 2.49



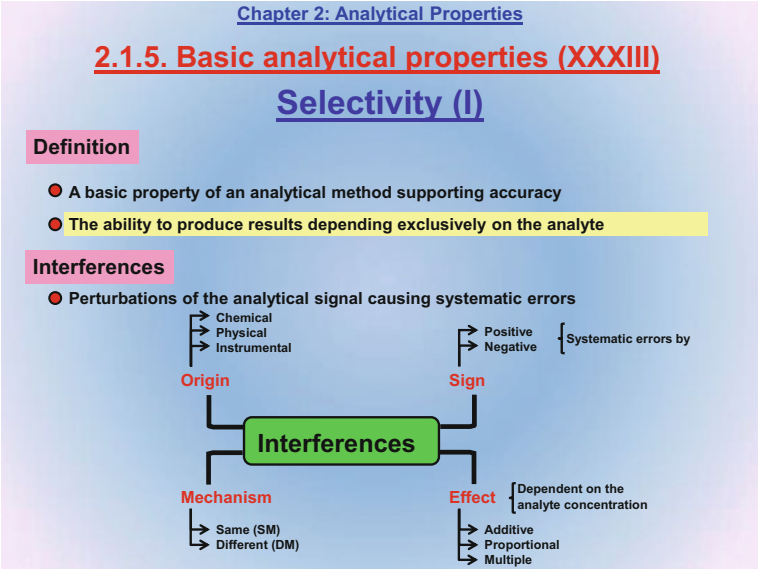
2.49.1. Part (e) of the problem involves validating the method for a given legal limit provided the sensitivity is known and the standard deviation for a set of blanks given.

2.49.2. Validating the method requires calculating the concentrations corresponding to the limits of detection and quantification from the equations in Slide 2.42.

2.49.3. Once calculated, the three limits are plotted on a scale of increasing concentrations of analyte. A comparison with the different cases illustrated in Slide 2.43 reveals that the method cannot be used detect or quantity the analyte, so it is useless for the analytical problem posed by the client's needs.

2.1.5.4 Selectivity (4 Slides)

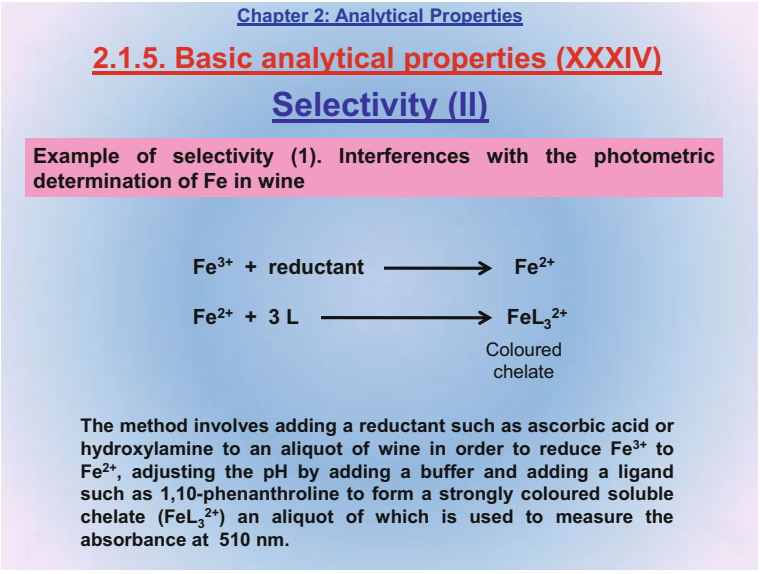
Slide 2.50



The slide defines another basic analytical property: selectivity. An analytical method is said to be selective when it gives signals and results exclusively dependent on the target analyte (that is, when it only responds to the presence of the analyte).

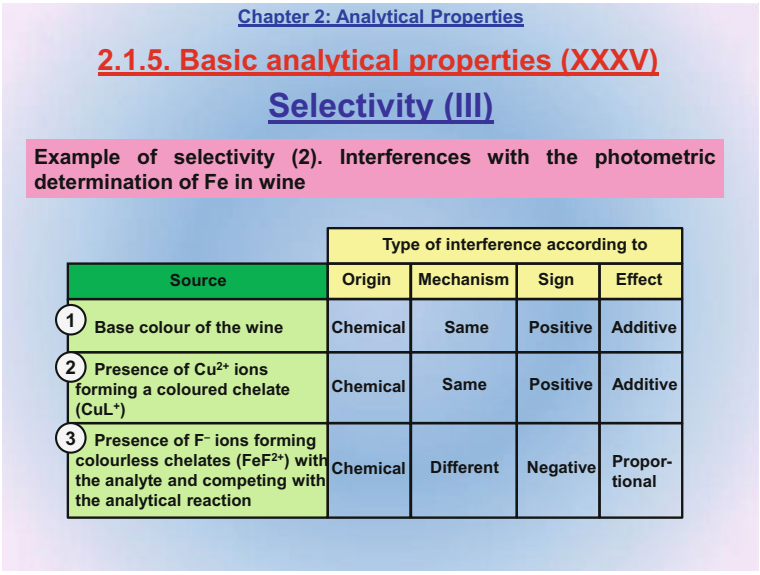
An ideal method is one that is unique for a specific analyte. In practice, however, this ideal situation is precluded by interferences. In this context, an interference is anything preventing a method from being exclusively selective for an analyte (that is, something altering the analyte signal and leading to systematic errors in the result). This slide depicts various types of interferences with analytical methods.

Slide 2.51



This colorimetric method for determining the amount of iron in wines involves a preliminary operation by which Fe^{3+} is reduced to Fe^{2+}; then, ferrous ion forms a coloured chelate L that is detected and quantified with a photometer.

Slide 2.52

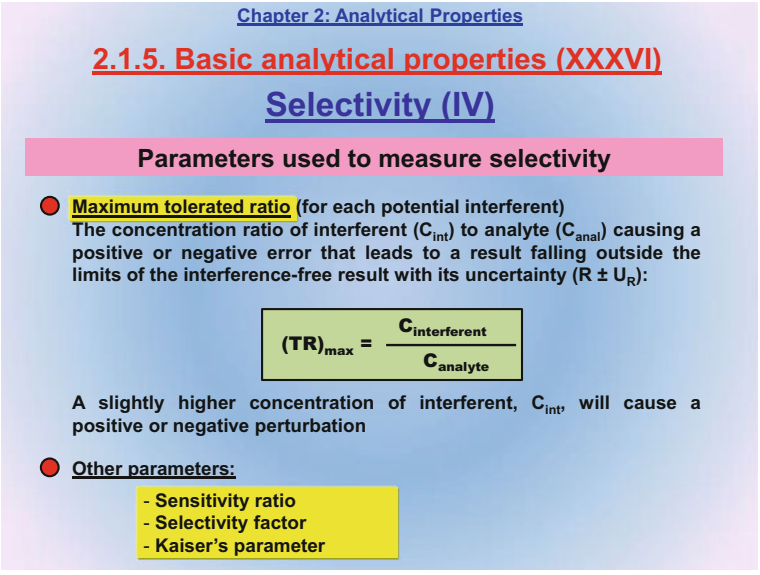


	Type of interference according to			
Source	Origin	Mechanism	Sign	Effect
1 Base colour of the wine	Chemical	Same	Positive	Additive
2 Presence of Cu^{2+} ions forming a coloured chelate (CuL^{+})	Chemical	Same	Positive	Additive
3 Presence of F^{-} ions forming colourless chelates (FeF^{2+}) with the analyte and competing with the analytical reaction	Chemical	Different	Negative	Proportional

The determination of Fe^{2+} in wine by formation of a coloured chelate (Slide 2.51) may be interfered with by three different factors:

(1) The typical colour of red wine, which may increase the absorbance readings of the photometer and lead to positive errors by effect of the instrument measuring a *colour excess* (e.g., one suggesting the presence of tannins in red wine). Although chemical in nature, this phenomenon arises from the presence of certain substances in the wine rather than from a chemical reaction (chelation) of Fe^{2+} or other ions in it (via a different mechanism).
(2) The formation of coloured chelates with Cu^{2+} resulting from an unwanted reaction of the ligand with Cu^{2+} ions in the wine may be a source of interference if the cuprous chelates are visible at the measured wavelength and lead to a positive error from a *colour excess*. This interference is of chemical nature and arises from the same mechanism used to determine Fe^{2+}: the formation of coloured chelates.
(3) The formation of colourless chelates of Fe^{2+} with fluoride ions prevents all ferrous ion from being chelated by the ligand (L) and becoming "visible" to the photometer. This leads to a negative error ("*a colour deficiency*"). This interference is also chemical in nature and arises from the same mechanism used to determine the analyte: the formation of coloured chelates.

Slide 2.53

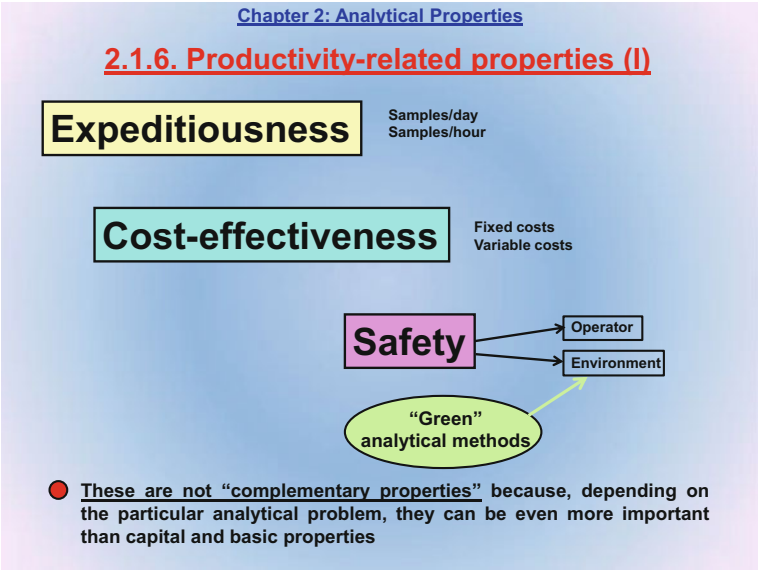


These are different ways of expressing the selectivity of an analytical process or method.

- The *maximum tolerated ratio* (TR_{max}) is the interferent-to-analyte concentration ratio giving a result coinciding with the lower or upper limit of the uncertainty interval for a result obtained in the absence of interferences. As a consequence, in the presence of the same amount of analyte, a greater amount of interferent will cause the results to depart markedly in either direction from the ideal result in the absence of interferences and to fall outside the uncertainty interval.
- The *sensitivity ratio* is the analyte-to-interferent sensitivity ratio. The more sensitive to the analyte an instrument is, the higher will be the ratio and the selectivity for the analyte.
- The *selectivity factor* is the TR_{max} ratio for two methods used to determine the same analyte in the presence of the same interferent. This factor is used to compare methods in terms of selectivity.
- *Kaiser's selectivity parameter* is defined in terms of a complex matrix containing the sensitivity for each analyte to be determined. This parameter is used with complex samples containing more than one target analyte.

2.1.6 Productivity-Related Analytical Properties (2 Slides)

Slide 2.54



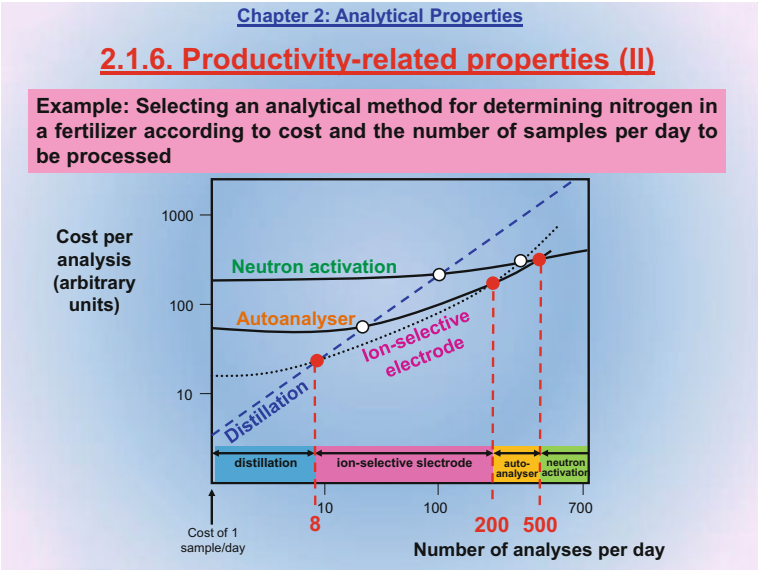
2.54.1. Productivity-related analytical properties are those relating to the development of the analytical process, and to the operators and laboratory

performing it. This slide shows the most salient of all: expeditiousness, cost-effectiveness and personnel-related factors. Expeditiousness, cost-effectiveness and personnel-related factors are related to sample analysis time, cost per analysis and safety (or risks) in the analytical process, respectively.

Although productivity-related properties are at the bottom of the hierarchy of analytical properties in Slide 2.4, they can be crucial with a view to properly solving an analytical problem and even more important than capital and basic properties. The next section of this chapter (2.1.7) is devoted to their integration with capital and basic properties, and to the need to favour some over others depending on the particular analytical problem.

2.54.2. At present, the productivity-related property "environmental safety" is being boosted by developing *green analytical methods*, that is, non-polluting methods causing no harm to the environment (see Slide 9.26).

Slide 2.55



2.55.1. This slide exemplifies the selection of an analytical method in terms of throughput and cost. Four different methods are represented on a log–log scale of cost versus number of analyses per day. Each method exhibits a different pattern of cost growth that is linear in the distillation method but curved to a different extent in those using the ion-selective electrode, autoanalyser or neutron activation instrument.

2.55.2. The most inexpensive method for a workload of less than 8 analysis per day is distillation. For more than 8, the curve for distillation intersects that for the ion-selective electrode, which becomes the more economical choice. Therefore,

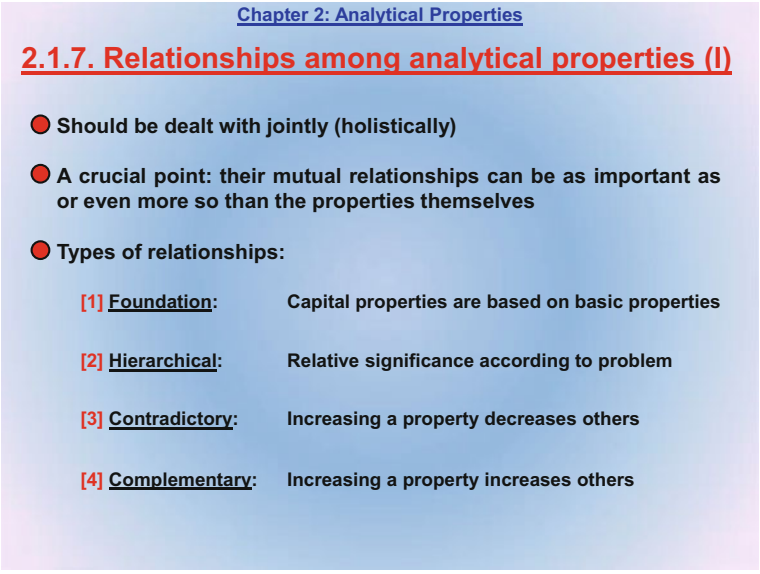
either method is cost-effective for 8 analyses per day but the electrode is to be preferred for a higher throughput.

2.55.3. The ion-selective electrode is the best choice for 8–200 analyses per day. At 200, however, its curve intersects that for the autoanalyser, which thus becomes more cost-effective.

2.55.4. The autoanalyser is to be preferred for a daily workload of 200–500 analyses. However, at 500 its curve intersects that of the neutron activation instrument. Consequently, the latter is the most cost-effective choice for more than 500 analyses per day.

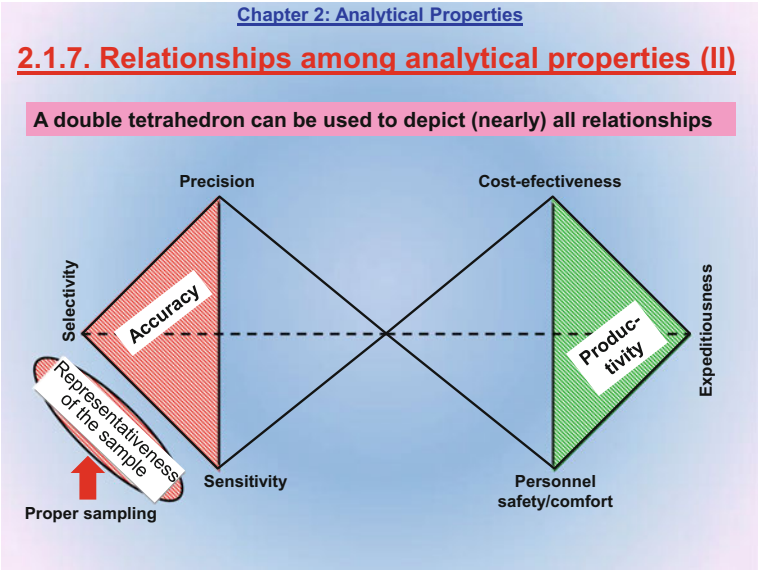
2.1.7 Relationships Among Analytical Properties (6 Slides)

Slide 2.56



The mutual dependence and relationships among analytical properties probably constitute one of the most important topics of this chapter. This slide shows various ways of associating and comparing the properties (namely, foundation, hierarchical, contradictory and complementary relationships). The relationships are illustrated in the next five slides.

Slide 2.57

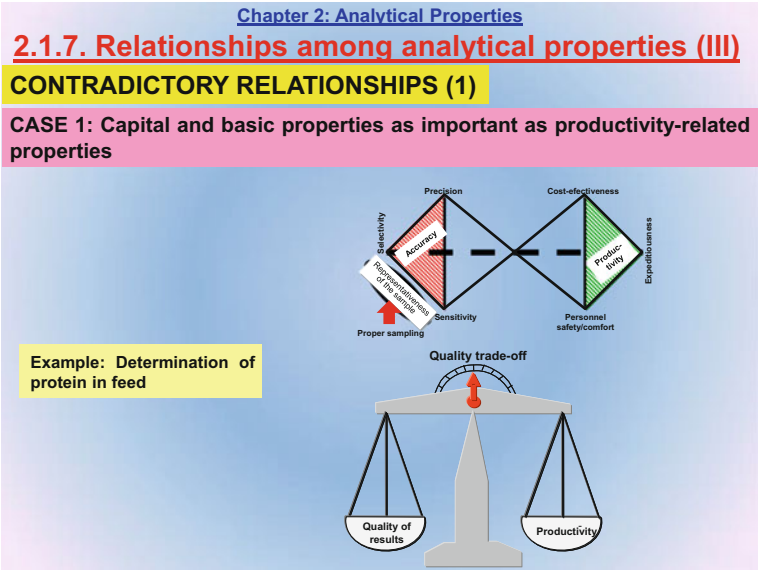


Virtually all possible relationships between the three types of analytical properties (capital, basic and productivity-related) can be depicted by connecting two tetrahedra via a common apex.

- The basic properties define and support the capital property accuracy in the tetrahedron on the left. Representativeness falls outside the tetrahedron because it supports proper sampling.
- The productivity-related properties define productivity and are in the tetrahedron on the right. "Personnel safety/comfort" is equivalent to "safety" in Slide 2.54.

Depicting analytical properties in tetrahedra facilitates relating sensitivity and selectivity or sensitivity and precision (Slide 2.61), for example. The apices in each tetrahedron can be connected to each of the apices in the other to establish a variety of relationships. Thus, accuracy can be related to expeditiousness (Slides 2.59 and 2.60), precision and accuracy to cost-effectiveness, and selectivity to safety, for example.

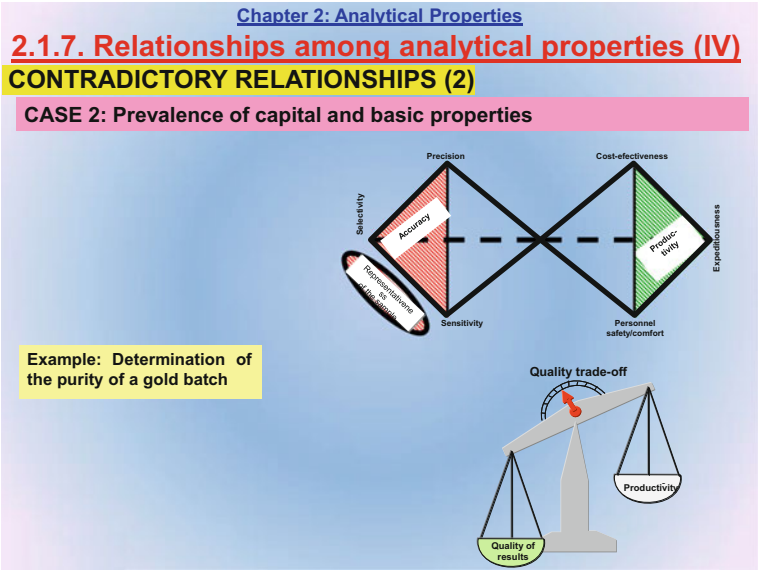
Slide 2.58



This slide and the next two illustrate contradictory relationships of capital and basic analytical properties to productivity-related properties. Which property in each pair is to be favoured depends on the particular information requirements and analytical process (see Chap. 7).

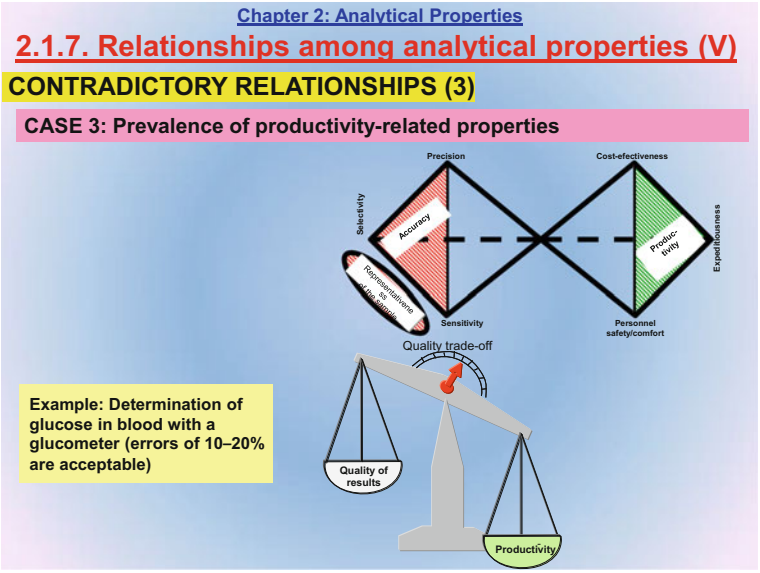
This slide depicts a situation where productivity-related properties are as important as basic and capital properties. The example involves the determination of protein in feed. This determination is subject to no time pressure because feed does not deteriorate easily with time. Also, its analysis is fairly inexpensive and hazard-free, and requires no specially high accuracy, precision or representativeness —rather, it is intended to provide information for rating the product in terms of quality. Therefore, all types of properties are similarly important here.

Slide 2.59



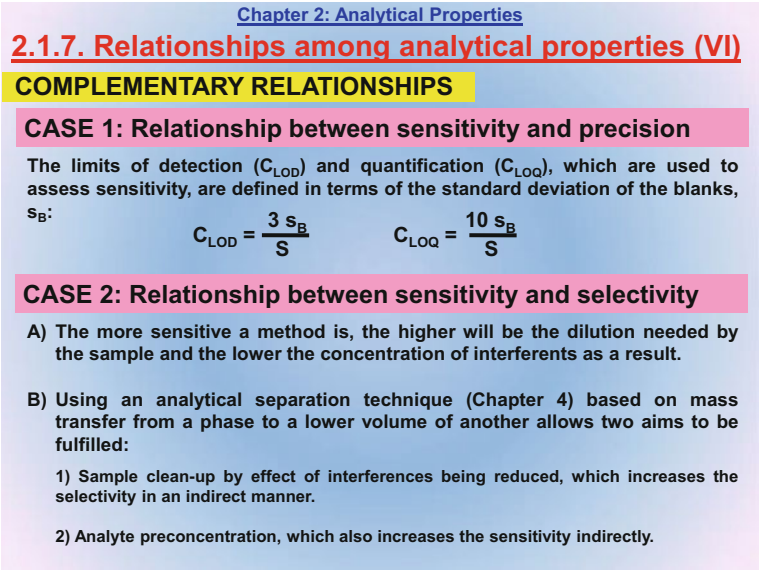
This slide illustrates the second type of contradictory relationship of capital and basic properties to productivity-related properties with a case where the former two must be favoured over the latter: increased accuracy and precision are sought even at the expense of slower, more expensive or even more complicated—and hazardous—analyses. The situation is illustrated with the determination of the purity of a gold batch. On the gold market, each decimal figure in the result counts because it can lead to substantial gains or losses of money. This calls for especially accurate and precise measurements even if making them requires investing more time or money. Therefore, capital and basic properties are favoured over productivity-related properties.

Slide 2.60



This slide presents the last example of a contradictory relationship of the capital and basic properties to productivity-related properties. In this case, the latter (expeditiousness, cost-effectiveness and personnel-related factors) are favoured over the former two (accuracy and precision). The example is the determination of glucose in blood with a portable meter. The portability and ease of operation of the meter, and the expeditiousness of the measurement method, allow the operator to know the patient's blood glucose level almost immediately and act as required in response. Even if the result is not accurate or precise, the result is quite acceptable because it is obtained very rapidly (that is, because productivity-related properties are favoured over capital and basic analytical properties).

Slide 2.61



The two cases illustrated in this slide exemplify complementary relationships among analytical properties.

- *Case 1*. The relationship between sensitivity and precision is given by the equations for the limits of detection and quantification used to calculate them (Slide 2.42). The precision of a method can be estimated from the standard deviation for a set of blanks. Because LOD and LOQ are related to the standard deviation of the blanks, the sensitivity is connected with the precision of the blanks. This relationship is complementary: the higher is the standard deviation of the blanks, the higher will be both limits, and the lower the precision and sensitivity as a result. Conversely, the lower is the standard deviation, the lower will be the limits, and the higher the precision and sensitivity.
- *Case 2*. The relationship between sensitivity and selectivity can be approached in two different ways.

In one (A), the sensitivity is related to the selectivity through the degree of dilution of the sample. The more sensitive the analytical method is, the smaller the amounts of analyte it will be able to detect; therefore, diluting the sample to an appropriate extent may even avoid saturation of the measuring instrument. In addition, dilution can reduce the effects of interferences and increases the selectivity of the analytical method for the target analyte.

In the other (B), the sensitivity is related to the selectivity through a preliminary operation: transfer of the analyte between two phases in an analytical separation

system (ASS, Slides 4.26–4.31) in order to remove interferents (for increased selectivity) and simultaneously preconcentrate the analyte (for increased sensitivity).

2.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

M. Valcárcel

Springer-Verlag, Berlin, 2000.

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means. This chapter is and abridged version of Chap. 2 in the book, entitled "Analytical Properties", which, however, has been expanded with new contents, and a number of examples and problems. Valcárcel's book can be used to go deeper into the contents of this chapter.

Statistics and Chemometrics for Analytical Chemistry

James N. Miller & Jane C. Miller

Pearson Education, 2010.

This is an elementary handbook of statistics whose contents are especially important and useful for analytical chemists. It is intended to facilitate calculation of analytical results and extraction of information from them.

Although this chapter is inspired by some of the book contents, we have strived to simplify the computation of the parameters used to quantify the analytical properties and illustrated it with examples intended to facilitate their mathematical and statistical understanding. The book can be used by students to both expand their knowledge of the parameters dealt with in this chapter and be introduced to others also used in Analytical Chemistry at present.

2.3 Questions on the Topic (Solved in Annex 2)

2.1. Tick the correct statements in relation to the dynamic range of a calibration curve obtained in the photometric determination of iron in wines:

[ ] The sensitivity remains constant

[ ] The lower limit coincides with the limit of detection

[ ] The sensitivity is always greater than zero

[ ] The lower limit coincides with the limit of quantification

2.2. To which analytical properties are the following concepts directly related?

TRACEABILITY	[ ] Precision	[ ] Accuracy	[ ] Sensitivity
ROBUSTNESS	[ ] Expeditiousness	[ ] Precision	[ ] Sensitivity
PRODUCTIVITY	[ ] Expeditiousness	[ ] Cost-effectiveness	[ ] Representativeness

2.3. Distinguish dynamic range from linear range in a calibration curve.
2.4. State whether the following statements are true (T) or false (F):

[ ] Precision decreases with increasing standard deviation
[ ] Accuracy decreases with decreasing relative error
[ ] Sensitivity increases with decreasing limit of detection and quantification
[ ] Selectivity increases with increasing interference

2.5. Define the analytical property robustness.
2.6. Define "bias" in relation to errors in Analytical Chemistry.
2.7. Tick the correct statements in the dynamic concentration range of the calibration curve for the photometric determination of calcium in milk:

[ ] The sensitivity remains constant
[ ] The sensitivity is always non-zero
[ ] The sensitivity is not always the same
[ ] The sensitivity decreases at the end of the range

2.8. Which datum is needed to assess the accuracy of an analytical result?

[ ] The mean of n results
[ ] The value held as true
[ ] The standard deviation

2.9. State whether the following statements are true (T) or false (F).

[ ] Selectivity increases with decreasing interference
[ ] Sensitivity increases with decreasing slope of the calibration curve
[ ] Accuracy increases with increasing precision
[ ] Precision increases with increasing standard deviation

2.10. Distinguish generic and specific uncertainty.
2.11. What are the differences between "repeatability" and "reproducibility"?
2.12. What kind of reference is used to calculate (a) the accuracy of the result for a sample and (b) the precision of a method?

2.13. State whether the following statements about accuracy and precision are true (T) or false (F).

[ ] Both analytical properties can be ascribed to results
[ ] The two are unrelated
[ ] Good precision can only be obtained with good accuracy
[ ] Good accuracy can only be obtained with good precision

2.14. Name the four types of relationships between analytical properties.
2.15. What are the similarities and differences between systematic and gross errors?
2.16. Two methods A and B are used to determine the same analyte in aliquots of a sample with a certified value of 1.23 ± 0.05 mg/L. The experimental result is 1.27 ± 0.03 mg/L with method A and 1.29 ± 0.01 mg/L with method B. Which method is the more accurate? Which is the more precise? Why?
2.17. Why stating the accuracy of a result is meaningless if its precision is unknown?
2.18. Can productivity-related properties be more important than capital and basic properties?
2.19. What is a "blank"? What is the "blank signal"?
2.20. Which are the references needed to define the following analytical properties in mathematical and conceptual terms? Tick the correct choices.

	Set of blanks	Value held as true	Mean of *n* results	Interferences from other systems
Accuracy				
Precision				
Limit of detection				
Selectivity				

2.21. State whether the following statements as regards accuracy and precision are true (T) or false (F).

[ ] Both analytical properties can be assigned to results
[ ] The two are mutually related
[ ] Good precision cannot be obtained without good accuracy
[ ] Good accuracy cannot be obtained without good precision

2.22. Why does accuracy rest on precision?
2.23. Tick the correct boxes in this comparison of precision and robustness.

	Same sample aliquot	Same method	Supports accuracy	Basic analytical property
Robustness				
Precision				

2.24. How are the facets of sensitivity related?
2.25. Two methods A and B for determining aflatoxins in milk are compared in terms of sensitivity by analysing two different certified reference materials with certified values of 0.25 ± 0.01 and 0.28 ± 0.01 ppb. Based on method A, both CRMs contain aflatoxins. Based on method B, both CRMs contain aflatoxins and the second CRM contains a slightly greater amount than the first. Which is the more sensitive method? Why?
2.26. What is the lower limit of the linear range of the calibration curve?
2.27. What is the "maximum tolerated ratio"? To which analytical property does it relate?
2.28. Give an example of analysis (state the sample and analyte) where accuracy is to be favoured over productivity-related properties?
2.29. Is it correct to assign accuracy to an analytical process? Why?
2.30. The sensitivity of a method is 1.02×10^{-3} UA mL ng^{-1}. What are the units for the following parameters?

Blank signal
Standard deviation of the blank
Limit of detection
Limit of quantification
Analyte concentration

2.31. Complete the following table comparing the analytical properties "accuracy" and "precision".

	Accuracy	Precision
Type of analytical property		
A typical property of		
Parameters used to measure it		
An indispensable numerical reference for calculating the parameters		
Mutually dependent		

2.32. (1) Discuss the ideal situation and (2) describe the real situation in independently subjecting n aliquots of sample to an analytical process in order to obtain n results.
2.33. Classify errors in Analytical Chemistry according to (1) form of expression; (2) direction; and (3) sources, references and magnitude.
2.34. A method provides accurate results. May it not be precise?
2.35. Define a parameter representing the analytical property "selectivity".
2.36. Solve the different parts of the following problems.

– *Problem A*

An analytical method for determining copper traces in feed is characterized as follows:

(1) Using the method to analyse standards of increasing concentrations of analytes provides the following results:

$[Cu^{2+}]$, ppb	0.0	1.0	2.0	3.0	4.0	5.0
Signal, AU	0.030	0.050	0.102	0.149	0.201	0.250

(2) Independently subjecting 5 aliquots of a reference standard with a certified concentration of 3.30 ± 0.10 ppb gives the following results, in ppb: 3.40, 3.39, 3.50, 3.27 and 3.35.

Questions:

(a) What is the blank signal? What are its units?
(b) What is the signal corresponding to the certified copper concentration in the standard?
(c) Can the precision of the method be calculated? Why? If it can, what is it?
(d) Can the accuracy of the result be calculated? Why? If it can, what is it?
(e) If the client's imposed limit is 0.1 ppb copper, is the method suitable for qualifying (detecting) and quantifying the analyte if the deviation of the blank signal is 2.3×10^{-3} AU?

– *Problem B*

An analytical process for determining pesticides (P) in water is applied through the following tests:

(1) Subjecting a total of 10 blanks to the process gives the following results in absorbance units (AU):

0.031	0.033	0.041	0.029	0.035	0.037	0.040	0.032	0.030	0.037

(2) A calibration curve is constructed from a set of standards of increasing hydrocarbon concentrations. The equation for the curve is

$$Signal(AU) = 0.035 + 1.07[P]$$

where $[P]$ is the pesticide concentration in ng/mL.

Questions:

(a) Can the precision of the method be calculated? Why? Explain your answer.
(b) Express the sensitivity of the method through three different parameters.
(c) If the legal limit for pesticides in water is 2 ng/mL, is the method useful for their detection and quantification?

– *Problem C*

The precision of an analytical process for determining copper traces in seawater is assessed in three tests involving different experimental conditions, namely:

(1) Processing a single aliquot of sample and introducing six portions of the treated aliquot into the measuring instrument.
(2) Independently processing six aliquots of the same sample and introducing them into the measuring instrument on the same day.
(3) As in (2), but having six different analysts perform the analytical process on different days.

The results obtained are as follows:

Test	Results (mg/L)					
1	1.32	1.31	1.32	1.33	1.30	1.31
2	1.28	1.36	1.30	1.27	1.31	1.33
3	1.35	1.45	1.21	1.37	1.30	1.28

Calculate the specific uncertainty at the 95% confidence level for each test and plot it. Use the uncertainty values to discuss the precision achieved in each case, and identify the facet that can be characterized with each test.

2.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened for teaching Analytical Chemistry to students not majoring in Chemistry, albeit to a lesser extent than those of others because of its transversal conception. The following 18 slides (30% of all) can be omitted for this purpose:

- Section 2.1.3: Slide 2.12
- Section 2.1.4: Slides 2.15 and 2.17
- Section 2.1.5: Slides 2.24, 2.25, 2.27, 2.28, 2.31, 2.34, 3.38, 2.39, 2.44, 2.45, 2.46, 2.47, 2.48, 2.49 and 2.53

Traceability: Reference Materials

3

Abstract

The primary purpose of this chapter is to explain the integral concept of traceability and illustrate its use in Analytical Chemistry. The most immediate impact of traceability on Analytical Chemistry is that on analytical chemical standards, which are key tools for a metrological discipline relying on measurements. The direct relationship of traceability to standards is used to describe in a systematic manner the different types of standards used in Analytical Chemistry and their practical implementation. This is followed by a discussion of the different meanings of traceability in relation to various analytical chemical concepts. The meanings are harmonically related to facilitate their seamless integration. The chapter ends by relating the different analytical meanings of traceability to capital analytical properties, which are dealt with at length in Chap. 2, in order to strengthen consistency among the essential principles of Analytical Chemistry explained in Part I.

Teaching Objectives

- To introduce students to the integral concept of traceability.
- To highlight the crucial role of standards in Analytical Chemistry.
- To describe the different types of standards relevant to Analytical Chemistry.
- To integrate the different meanings of traceability and relate them to specific facets of Analytical Chemistry.
- To relate traceability of a result to capital analytical properties.

Electronic supplementary material The online version of this chapter (doi:10.1007/978-3-319-62872-1_3) contains supplementary material, which is available to authorized users.

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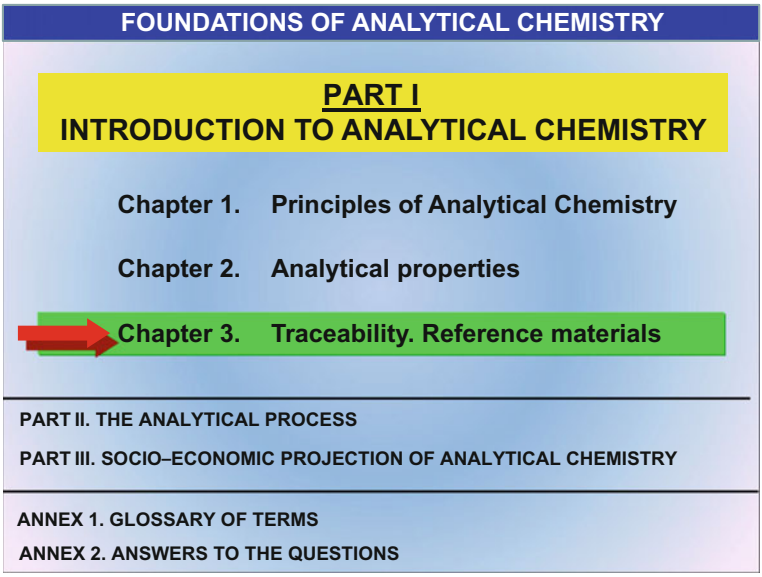
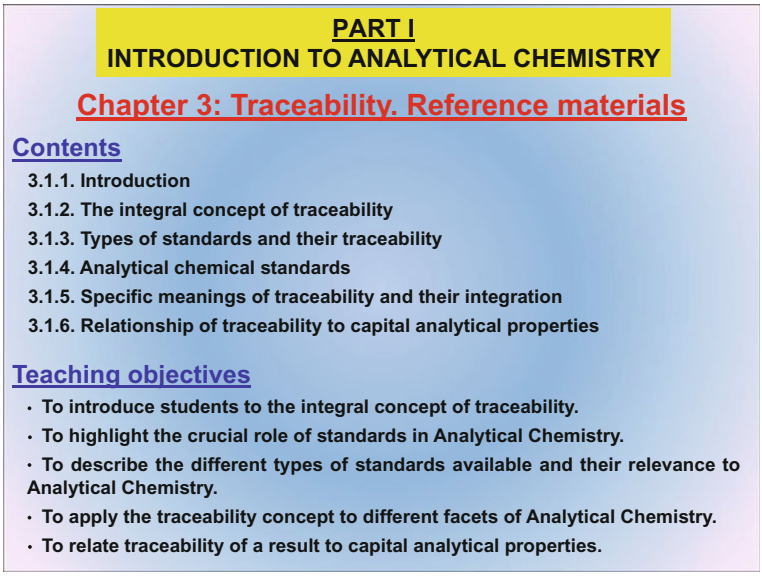
3.1 Explanation of the Slides

Slide 3.1



This slide places Chap. 3 in Part I (Introduction to Analytical Chemistry) and shows the other two parts. Chapter 3 is the third, last chapter presenting a basic approach to Analytical Chemistry.

Slide 3.2

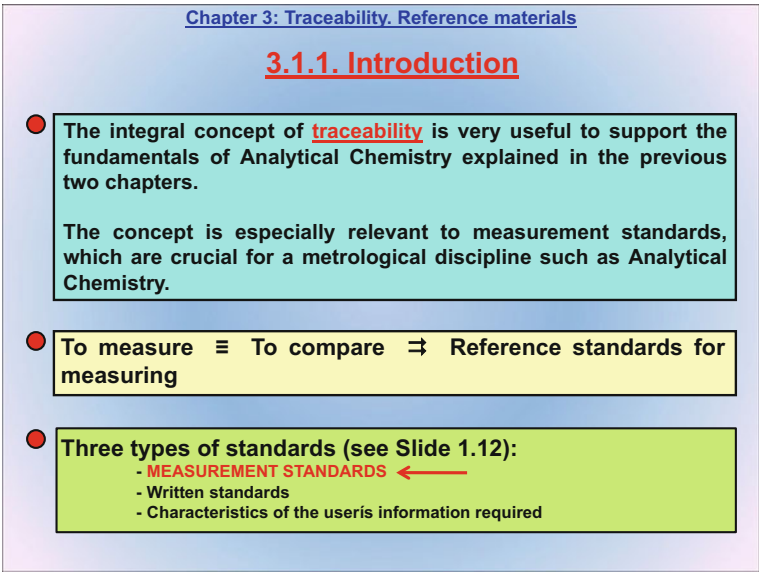


3.2.1. These are the six sections of this chapter.

3.2.2. The slide also shows the teaching objectives as regards traceability, its use in Analytical Chemistry and the key standards for this scientific discipline.

3.1.1 Introduction (1 Slide)

Slide 3.3

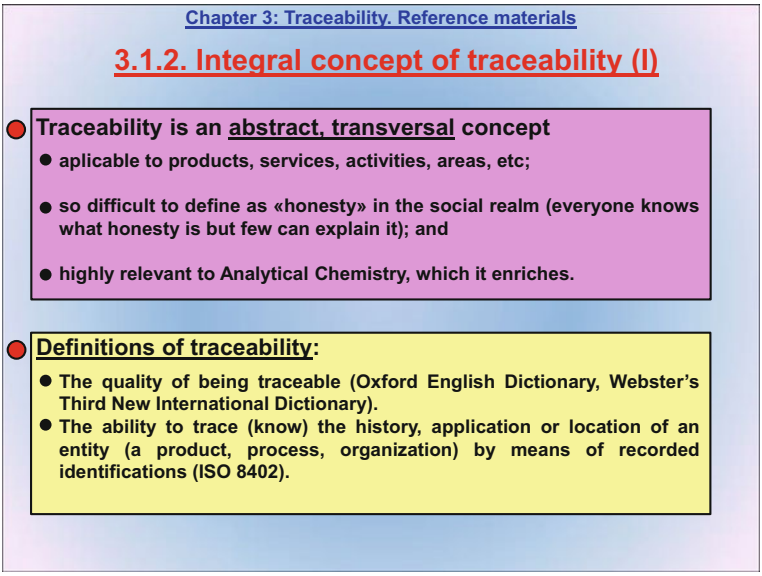


3.3.1. This is a general introduction to the chapter contents, which encompass traceability and analytical chemical standards. The aim is to summarize the relationship of Traceability to Analytical Chemistry (particularly to the tangible standards used for measurement).

3.3.2. Measurement standards play a crucial role in Analytical Chemistry, an essentially metrological discipline. Measurement standards constitute one of the three basic types of standards described in Sect. 1.3 (see Slide 1.12).

3.1.2 The Integral Concept of Traceability (4 Slides)

Slide 3.4

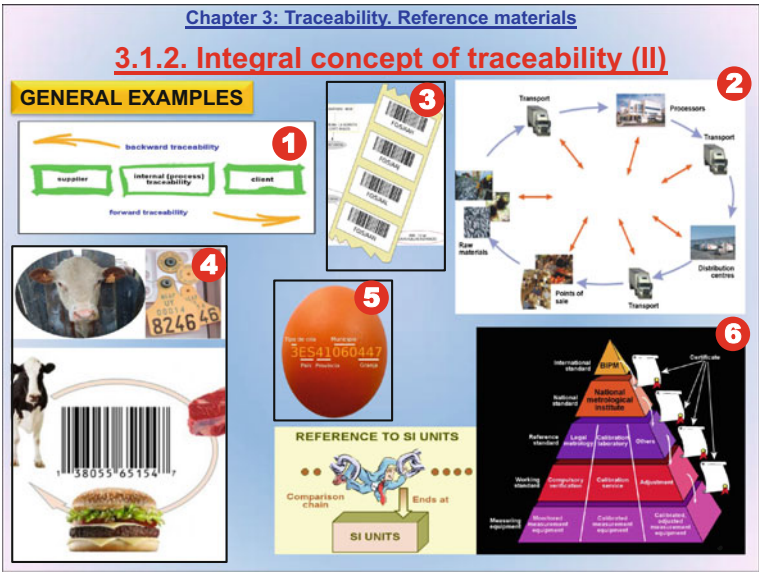


3.4.1. This slide introduces Sect. 3.2, which is concerned with the integral concept of traceability.

3.4.2. This is a generic description of "traceability", a transversally applicable abstract concept that is certainly difficult to define in a precise manner.

3.4.3. The definitions of "traceability" in dictionaries and written standards are far for friendly. Properly understanding what traceability is requires a more detailed description of its two main connotations ("reference" and "history"), which are used jointly in this chapter to build the integral concept of traceability.

Slide 3.5



These are selected graphical examples illustrating the integral concept of traceability.

1. Traceability in a production chain: the chain links the raw materials obtained from a supplier to the finished product received by the client. Traceability in this context can be classified in two different ways, namely:

   – *External and internal traceability*. The former applies to *inputs* and *outputs*, and the latter to processes of the production system.

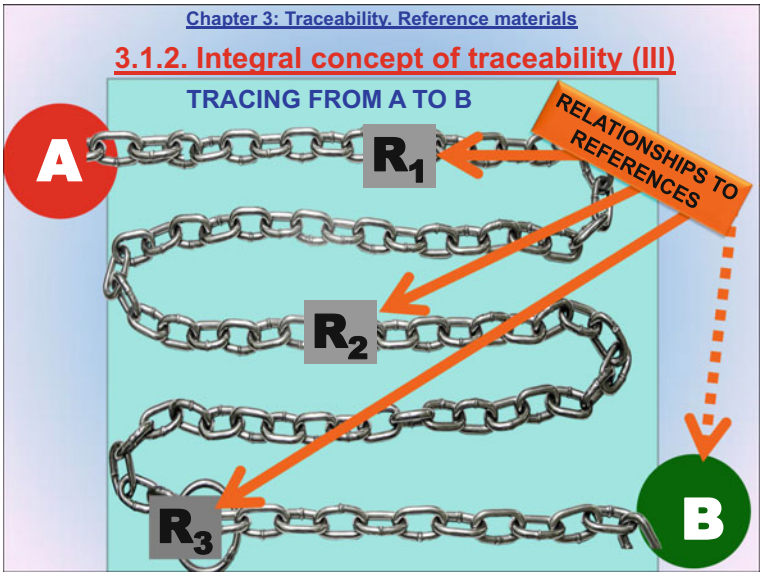
   – *Backward and forward traceability* around a circle connecting the raw materials to the product (forward) for quality-related purposes or the product to the raw materials (backward) for purposes such as dealing with clients' claims.

2. This is a more precise description of traceability of a product including transportation, distribution centres and points of sale, among others. The circular nature of traceability is clearer here. The arrows represent links in the traceability chain.
3. Bar coding is essential for proper monitoring—an unavoidable requirement with a view to ensuring traceability. Such is the case, for example, with blood or urine collection in the first step of clinical analyses at hospitals and outpatient clinics. The urine cup and blood collection tubes for each patient are identified with a unique bar code in order to start the sample custody chain. The samples

are sent to different laboratories and the analytical results compiled by appropriate software for delivery. In this way, traceability between patients and their results is assured.

4. Traceability in the agri-food industry is not only essential but also a legal requirement as per a European Union directive and the recommendations of the Food and Agriculture Organization of the United Nations (FAO). For example, a hamburger must be unequivocally traceable to the cow from which the meat came. Traceability here is established by using ear tags and bar codes.
5. A consumer-ready box of eggs on a supermarket shelf is labelled with a code identifying the type, country, place, farm and plant where the eggs were laid. In some countries, the eggs themselves have a printed bar code on the shell, but this identification system is less user-friendly.
6. The last example illustrates the typical traceability chain for measurements of physical parameters such as temperature, time or current intensity. Each step in the pyramid is connected to the next through a traceability link that should be certified. In this example, a measurement made with a given piece of equipment, and its calibration, are connected to an SI unit held as a top-quality international standard at the top of the pyramid. The links in the traceability chain, which should never be broken, include the standards prepared and used by the laboratory, which should be successively compared with commercially available reference standards. The commercial standards in turn are connected to national standards kept by a national organization. Unfortunately, no such well-defined hierarchy can be constructed for chemical measurements. In fact, the highly diverse nature of potential samples (industrial, clinical, environmental) would require having a number of national centres for chemical metrology in each country.

Slide 3.6

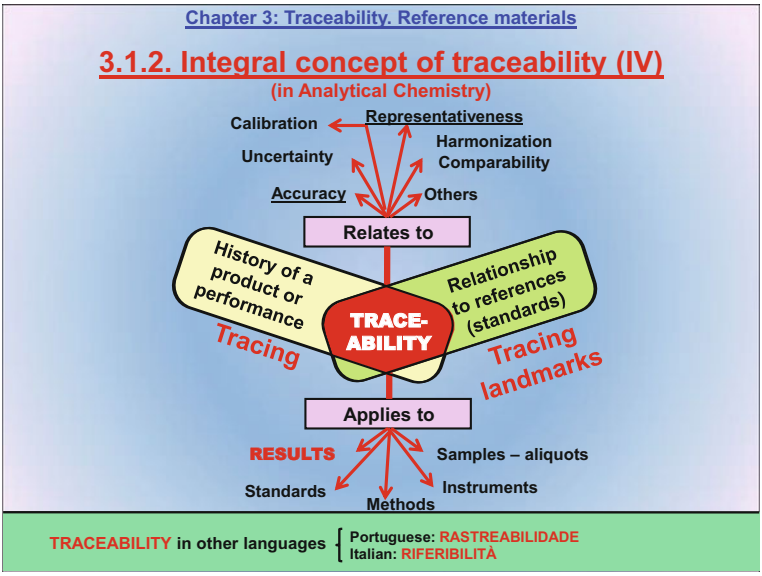


3.6.1. This is an imaginary traceability chain connecting A to B through an unbroken series of comparisons with three intermediate references (R_1, R_2 and R_3). Provided the chain is not broken, A and B can be said to be traceable to each other.

3.6.2. Tracing one end of the chain to the other requires using the "history" of the comparison made or relationship established at each individual link. Obviously, this is situation is unrealistic because traceability chains contain many fewer links in practice.

3.6.3. Connecting links to well-established references requires a sound knowledge of their nature and meaning. Frequently, end B is a reference itself (e.g., when an analytical result A is traced to a certified reference material B as described below).

Slide 3.7



3.7.1. From Slides 3.4 and 3.6 it clearly follows that defining traceability in an integral manner entails using its tracing and relational connotations jointly.

The tracing facet has to do with the documented history of (a) a production process from the raw materials or (b) the performance of an object or system. Such is the case, for example, with a laboratory instrument, for which there should be a detailed record of all actions including installation, servicing, calibration and measurements.

The other facet is the relationship to references, which are tracing landmarks (see Sect. 3.6.3) and, most often, standards of some type.

3.7.2. The unambiguous presence of the previous two facets in traceability is clearly apparent in its translations into some languages of Latin origin. Thus, the

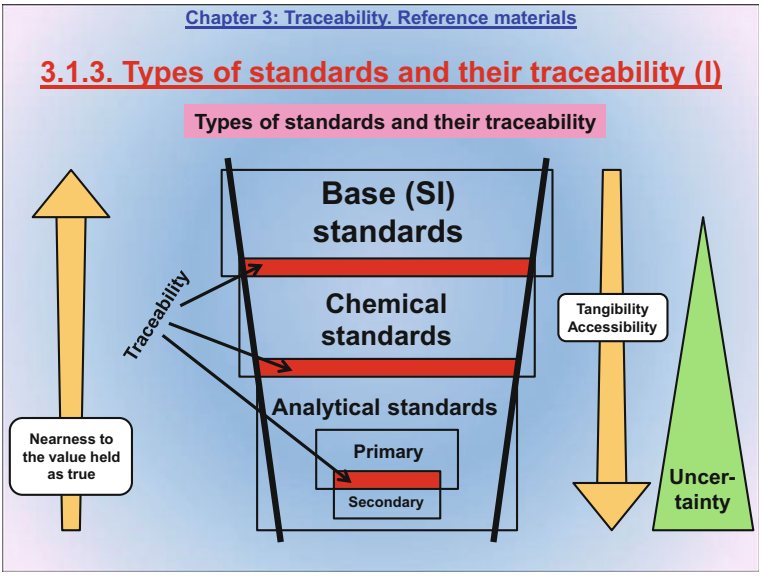
Portuguese word for "traceability" is *rastreabilidade* (tracing facet), whereas the Italian word is *riferibilità* (referential facet).

3.7.3. Traceability in Analytical Chemistry is related to such important concepts as accuracy, uncertainty, calibration, representativeness, and laboratory comparability and harmonization.

3.7.4. The integral concept of traceability is applicable to analytical chemical entities such as analytical results, standards, analytical methods, instruments and samples. The specific connotations of traceability are all discussed below.

3.1.3 Types of Standards and Their Traceability (4 Slides)

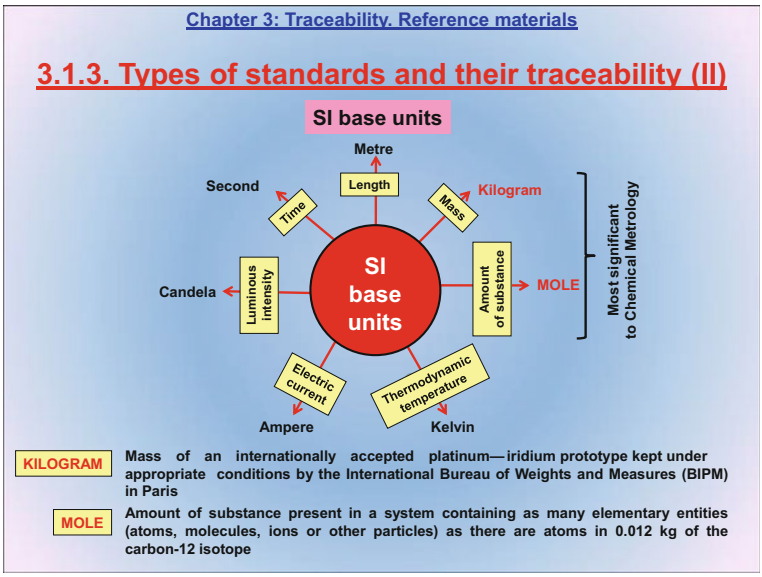
Slide 3.8



3.8.1. The pyramid of traceability in physical measurements (Example 6 in Slide 3.5) is not directly applicable to chemical measurements but can be replaced with a simpler traceability chain connecting analytical chemical standards (the tangible standards used in practice) to base standards (SI units) through so-called "chemical standards", which are intended to serve as traceability links. The two types of chemical standards (primary and secondary) can also be connected by a traceability chain.

3.8.2. In this simple ranking of traceability among standards in relation to chemical measurements, nearness to the true value for each type of standard increases from bottom (secondary chemical standards) to top (base standards). Consequently, specific uncertainty decreases in the same direction, and so do tangibility and accessibility.

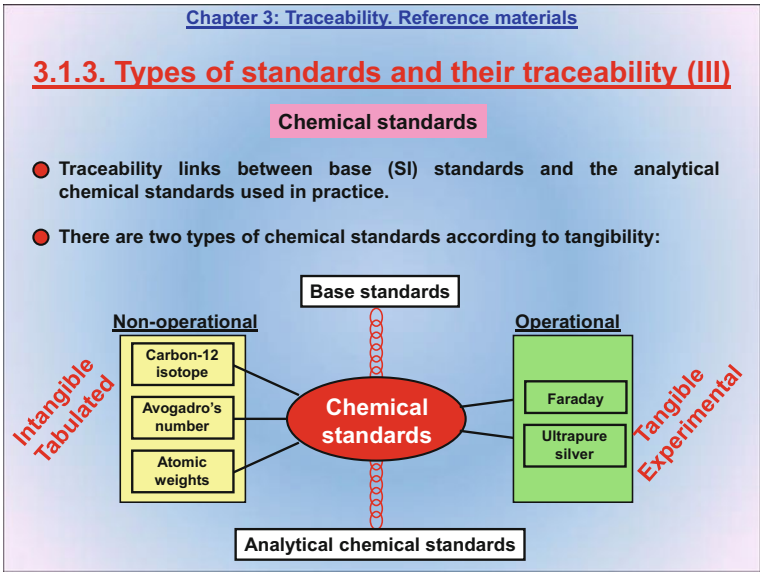
Slide 3.9



This slide shows the seven base units of the International System, namely: the metre for length, second for time, candela for luminous intensity, ampere for electric current, kelvin for thermodynamic temperature, mole for amount of substance and kilogram for mass.

The kilogram and the mole are the two most relevant to Metrology in Chemistry. The slide shows their classical definitions. Note that defining the mole requires mentioning the mass unit (the kilogram).

Slide 3.10

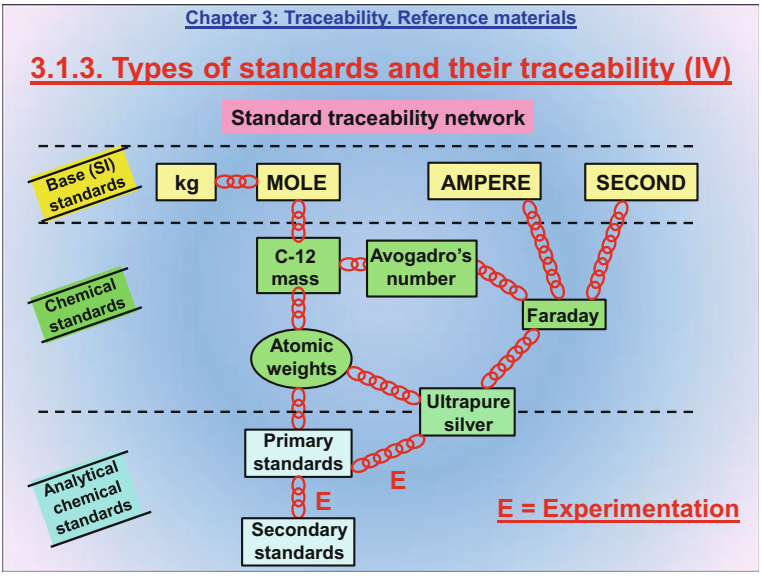


3.10.1. As stated in Slide 3.8, chemical standards are intended to serve as traceability links between base standards (SI units) and the analytical chemical standards used in the laboratory. Consequently, chemical standards play a crucial role in Analytical Chemistry because they determine the quality of laboratory standards.

3.10.2. There are two types of chemical standards according to tangibility:

- *Intangible standards*, also referred to as "non-operational standards", which are tabulated and include the mass of carbon-12, Avogadro's number and atomic weights.
- *Tangible standards*, also known as "operational standards", which require some experimentation prior to use. The most salient standards of this type are the faraday, which requires electrochemical equipment for verification, and ultrapure (>99.999% silver), also known as "five nine silver", which is extremely expensive.

Slide 3.11



This is an orderly depiction of the three types of standards relevant to Analytical Chemistry in a (traceability network) typical of chemical measurements. The mutual connections between standards are represented by red chains.

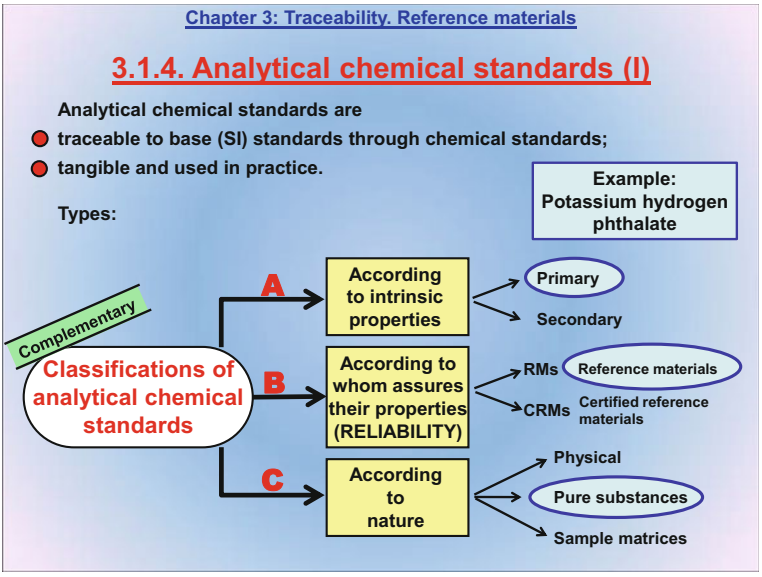
- As can be seen as regards SI standards, the mole cannot be defined without the kilogram.
- Base standards (SI units) are connected to chemical standards through three traceability chains, namely:

- one unequivocally linking the mole to the mass of carbon-12;
- another between the ampere and the faraday (1 C = 1 A × 1 s); and
- a third between the second and the faraday.

– Most traceability links occur in the realm of chemical standards. Thus, the mass of carbon-12 is related to the atomic weights used in chemical calculations and to Avogadro's number, which is in turn related to the faraday.
– Ultrapure silver is at the boundary between chemical standards and analytical chemical standards. In fact, it is so pure that it can be considered a chemical standard itself—one that is related to the chemical standards atomic weights and the faraday. Likewise, it can be exceptionally used in practice to standardize primary chemical standards by experimentation (E).
– Primary chemical standards can be traced to atomic weights and ultrapure silver. On the other hand, secondary standards can only be traced to primary standards (through experimentation). Primary and secondary standards are defined in the following section.

3.1.4 Analytical Chemical Standards and Their Integration (10 Slides)

Slide 3.12

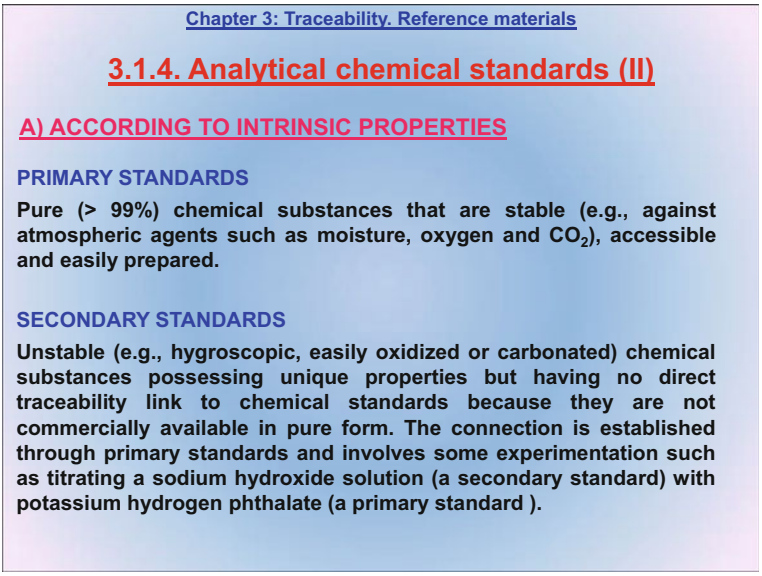


3.12.1. This slide defines and classifies analytical chemical standards. By definition (see Slide 3.8), they are at the bottom of the significance hierarchy of standards relevant to Metrology in Chemistry because their associated values are the farthest from the value held as true and also the most uncertain; by contrast, they are the most tangible and accessible, and hence the most commonly used in practice. Analytical chemical standards can be traced to SI units through chemical standards (see Slide 3.11).

Analytical chemical standards are confusingly or even contradictorily defined in the scientific literature. An integral approach to their characteristics enables their classification according to three different criteria, namely: (A) intrinsic properties, (B) reliability and (C) nature. Each classification is discussed in one of the next three slides.

3.12.2. For example, potassium hydrogen phthalate is a primary standard commonly used to standardize solutions of sodium hydroxide (classification A). Also, however, it can be considered a reference material (classification B) and a pure substance (classification C).

Slide 3.13



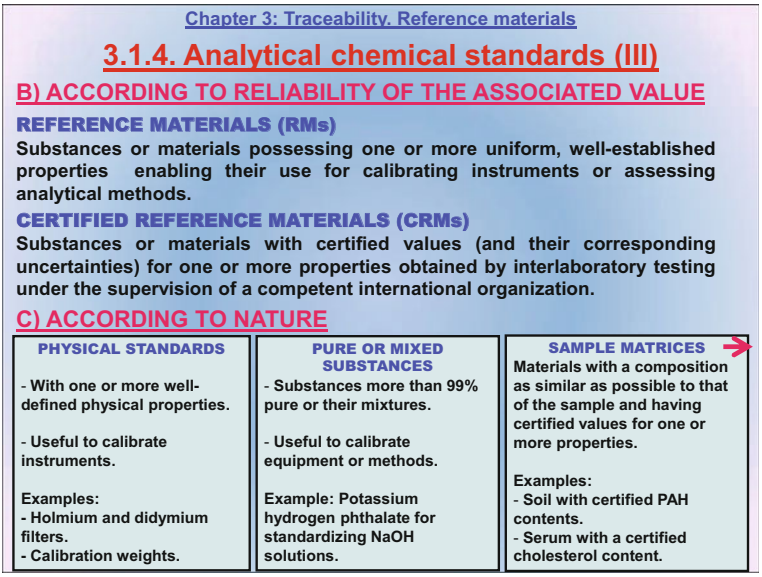
The analytical chemical standards used in the laboratory can be of two types according to their intrinsic properties, namely:

– *Primary standards*. These are chemical substances fulfilling two essential requirements:

1. a high purity (above 99 or 99.5%) that makes them traceable to atomic weights and ultrapure silver (Slide 3.11); and
2. stability against atmospheric agents (water, oxygen, carbon dioxide).

– *Secondary* standards. These are neither pure nor stable but can be useful for some purposes. However, they can only be made traceable by connection to a primary standard through experimentation (E in Slide 3.8).

Slide 3.14



There are two types of analytical chemical standards according to reliability or traceability to base standards (see classification B in Slide 3.13), namely: reference materials (RMs) and certified reference materials (CRMs). The former (RMs) are usually commercially available with a label stating their characteristics. The latter (CRMs) are produced by renowned international organisms that supply them with certificates stating with their associated values and their uncertainty. CRMs are usually of the sample matrix type.

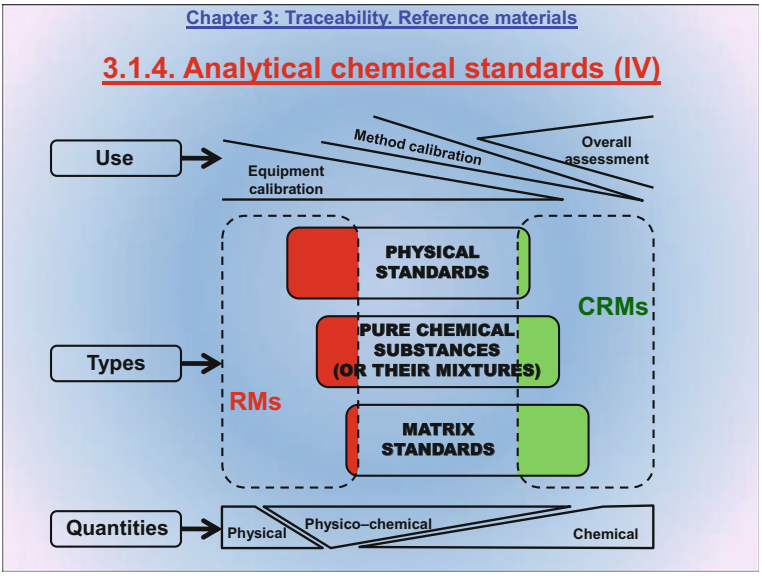
Analytical chemical standards can be of three types according to nature (classification C), namely:

– *Physical standards.* These are used as received for equipment verification (calibration). Thus, a UV–visible spectrophotometer can be checked with holmium and didymium filters for correct operation of its wavelength monochromator. Similarly, a balance is typically calibrated with so-called "transfer weights", which are traceable to the kilogram standard (an SI unit).
– *Pure substances or their mixtures.* These are analytical chemical standards (see Slide 3.13)—and hence, pure, stable substances—that can be used for both equipment and method calibration (e.g., with a calibration curve as in Slide 2.36).

Some are mixtures of pure substances (e.g., vials containing several C_3–C_6 hydrocarbons for calibrating gas chromatographs).

– *Sample (matrix) standards*. These are either certified reference materials (CRMs), which are described in Slide 3.17, or laboratory-made materials (working standards). Matrix standards are high-quality—and expensive—materials mimicking the composition of a sample and having the value of an associated quantity certified by a competent organization. Such is the case, for example, with a soil standard having certified contents and uncertainties in polycyclic aromatic hydrocarbons (PAHs), a milk standard with a certified aflatoxin content or a liophilized serum standard with a certified cholesterol content.

Slide 3.15

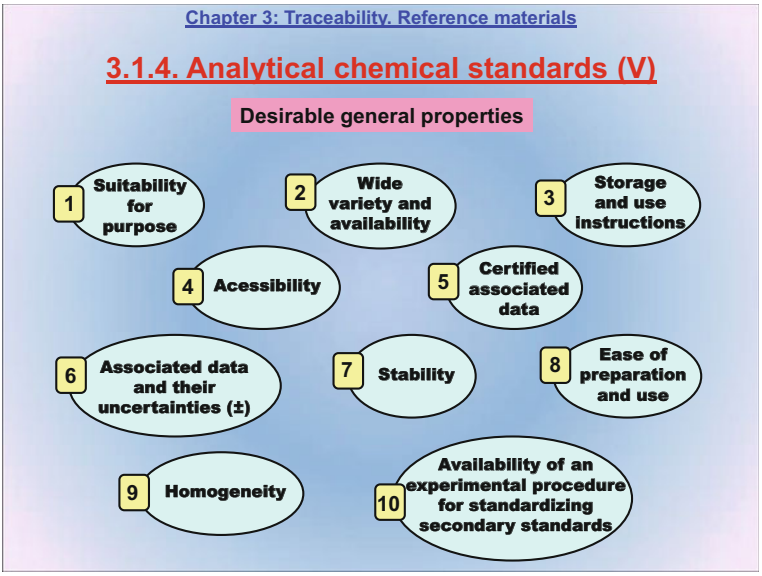


3.15.1. This scheme harmonizes the classifications of Slides 3.12 and 3.14 by classifying the three types of analytical chemical standards according to nature (classification C) in terms of reliability (classification B). Thus, physical standards are largely reference materials, whereas pure substances and their mixtures can be reference materials (RMs) or certified reference materials (CRMs), and matrix standards are mostly CRMs.

3.15.2. The use of each type of standard is described in detail below. In any case, RMs are used mainly for equipment and method calibration, whereas CRMs are typically used for the overall assessment of analytical methods.

3.15.3. The quantities involved can be physical (particularly with RMs), chemical (more commonly with CRMs) or, very often, physico–chemical.

Slide 3.16



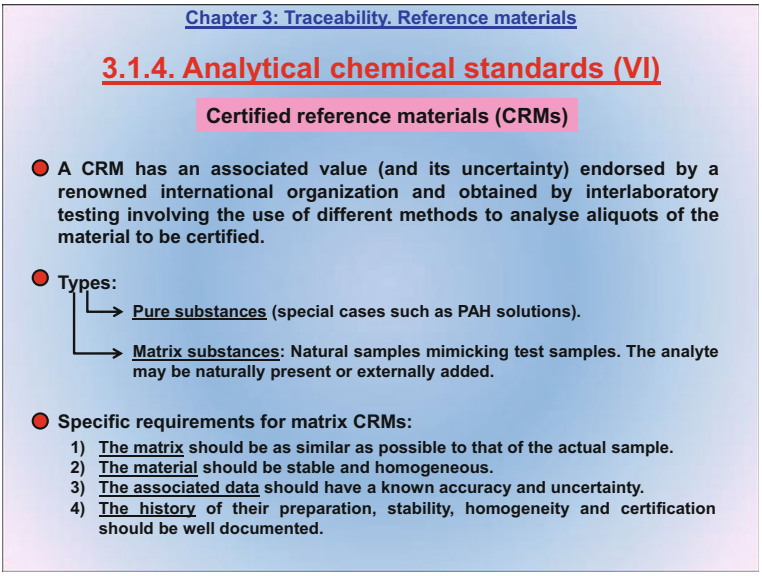
These are the ten desirable or indispensable properties for an analytical chemical standard.

The *indispensable* properties are as follows:

- Usefulness for the task concerned (that is, suitability for purpose) (1).
- Stability (7), homogeneity (8) and a well-defined uncertainty (6) for primary standards, in addition to certified values (5) for CRMs.
- Experimental traceability to primary standards (10) for secondary standards.
- Detailed storage and use instructions (3).
- Wide variety and availability (2).

The *desirable* properties include accessibility (4) and ease of preparation and use (8).

Slide 3.17

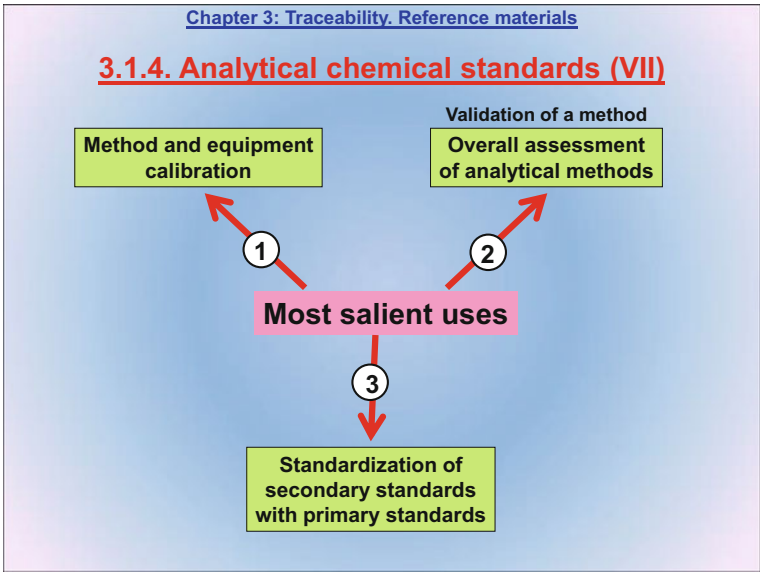


This is a brief description of *certified reference materials* (CRMs), which are standards having associated values and their uncertainties endorsed (certified) by a renowned non-profit international organization responsible for assuring that these atypical standards meet their requirements. They correspond to the so named "referential quality" (see Slide 1.17). The associated values and their uncertainties can only be established via interlaboratory exercises involving the use of different analytical processes. CRMs are usually expensive because they take long to prepare and can only be obtained in small amounts.

- Most CRMs are of the sample matrix type and mimic actual samples to be analysed by a laboratory. The analyte may be already present in the sample or externally added later. Some organisms also certify the purity of solutions containing substances such as dioxins or PAH.
- The slide shows the four requirements for a matrix-type CRM, which have to do with the sample matrix, homogeneity and stability in the material, the associated data and the history of the material from preparation to delivery.

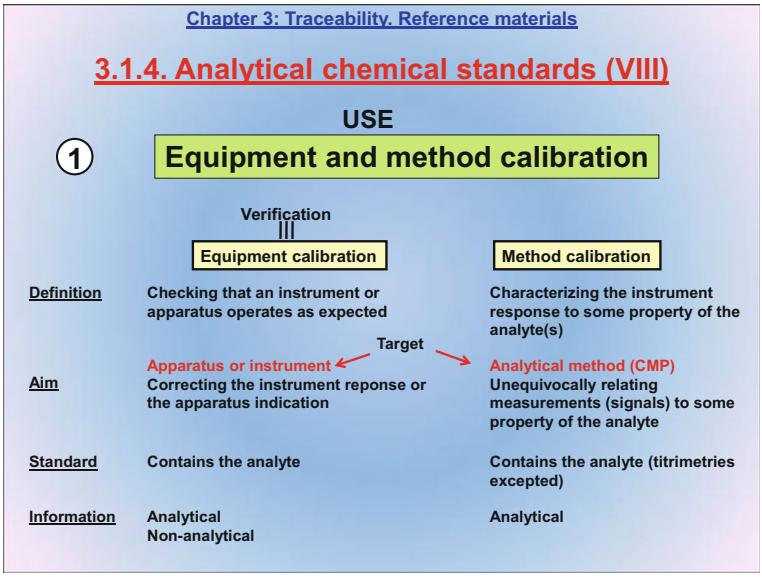
Interestingly, a CRM has several analytical connotations of traceability. Thus, the value for the associated quantity (e.g., the content, in ng/kg, in toxic dioxins of ash from an industrial incinerator) should be unequivocally connected to a chemical standard (referential facet): also, its characteristics and production should be accurately known (tracing facet).

Slide 3.18



These are the three main uses of analytical chemical standards in the laboratory. The first two are discussed in Slides 3.19–3.23. The third (Slide 3.23) is the use of primary standards such as potassium hydrogen phthalate to standardize secondary standards such as sodium hydroxide, which are those used in practice (delivered from a burette) to determine acids in samples by titration.

Slide 3.19



Analytical chemical standards are useful for both equipment and method calibration, which should be clearly distinguished by analytical chemists.

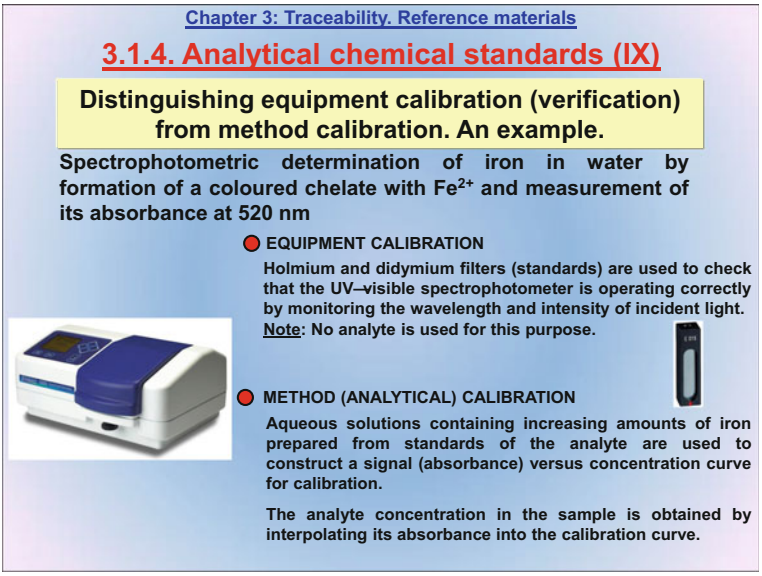
Thus, as implied by the designation, the target of *equipment calibration* or *verification* is an instrument or apparatus (the two are distinguished in Slide 1.25). The aim is to assure proper functioning of the instrument or apparatus concerned. For example, if the measurement delivered by an instrument in response to a standard (usually a physical reference material) departs from the value for the associated quantity, then the instrument should be adjusted to have the response coincide with that expected from the standard. An instrument delivers analytical information whereas an apparatus produces non-analytical information. There follows an example of each type of equipment.

- pH buffering solutions with a certified value including two decimal figures for calibrating pH-meters. If the experimental response does not coincide with the certified value, then the potentiometer of the instrument should be adjusted until it does.
- Calibrated thermocouples for monitoring the temperature inside stoves. If the temperature in the digital display of the apparatus departs from the reading of the thermocouple, then the stove should be adjusted to have the two temperatures coincide.

The target of method calibration is a *chemical method of analysis*. The aim is to characterize in an unequivocal manner the relationship between the instrument response and the presence and/or concentration of an analyte in the sample. This entails constructing a signal–concentration curve for calibration (see Slide 2.36 in relation to the analytical property "sensitivity"). This calibration procedure is not applicable to apparatuses because the information to be processed is purely analytical. The standard usually contains the analyte (unless, for example, a secondary standard such as a sodium hydroxide solution is to be standardized with a primary standard such as potassium hydrogen phthalate).

These two types of calibration are exemplified in the next slide.

Slide 3.20

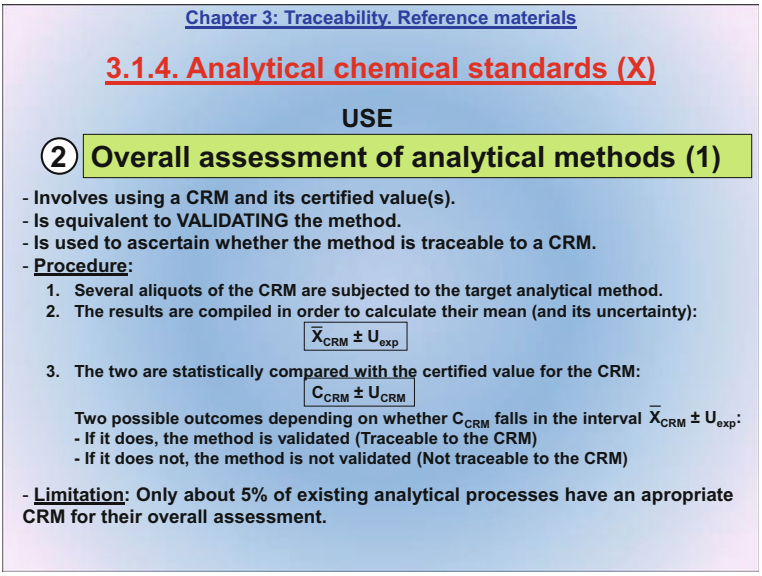


The following example distinguishes equipment calibration from method calibration with the spectrophotometric determination of iron in water by formation of a coloured chelate.

The target of *equipment calibration* here is the spectrophotometer and the calibration tools are physical standards rather than the analyte. A UV–visible absorption spectrum is obtained with a holmium filter (shown in the slide) in place for comparison with the spectrum associated to the standard. If the maxima in the two spectra fail to coincide, then the monochromator of the instrument is adjusted accordingly.

The purpose of *method calibration* in this example is finding the relationship between the absorbance and the concentration of iron by using a calibration curve constructed from standard solutions of the analyte. The iron concentration in the sample is determined by interpolating its absorbance into the curve.

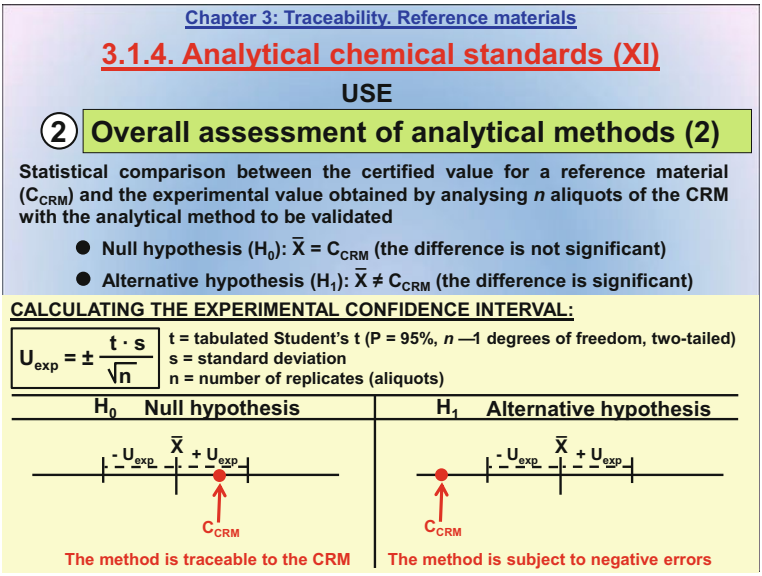
Slide 3.21



Another purpose of analytical chemical standards is the overall assessment of analytical processes by using standards (usually matrix-type certified materials) as references. As can be seen, the procedure involves comparing the result obtained from *n* aliquots of the CRM with its certified value, either qualitatively or statistically (see next slide). If the two values coincide, then the method in question is traceable to the CRM and has thus been "validated".

It should be noted that only a very low proportion of existing analytical processes can be assessed in this way. In most cases, an alternative solution must be found (see Slide 3.31).

Slide 3.22



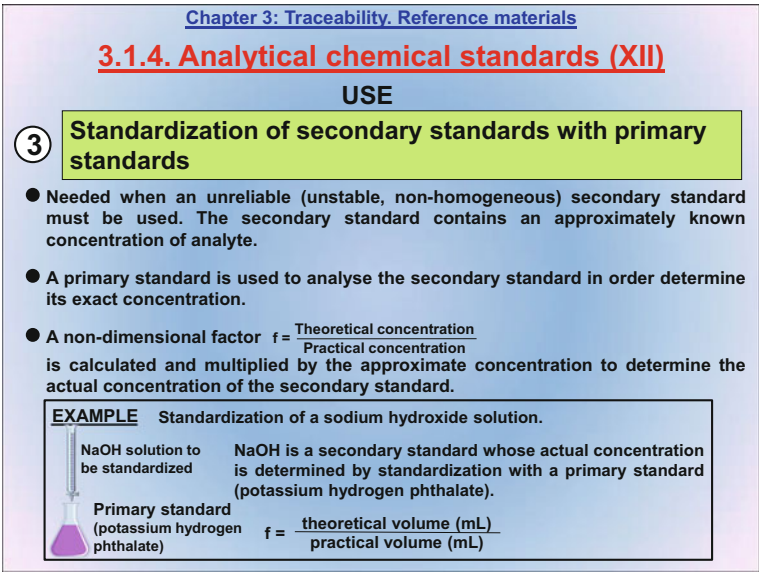
This slide compares in statistical terms the certified value of a reference material to the experimental value obtained by analysing *n* aliquots of the CRM with an analytical method for validation. The null hypothesis is that the two values will be identical and the alternative hypothesis that they will not.

A more rigorous comparison can be made by considering the specific uncertainty of the experimental value, using tabulated Student's *t*-values. The specific uncertainty is used to determine the uncertainty interval around the result at a given probability level (e.g., 95%).

The null hypothesis (H_0) and the alternative hypothesis (H_1) can be represented graphically for easier interpretation.

- If the value associated to the CRM (C_{CRM}) falls within the uncertainty interval, then the method (H_0) will be traceable to the CRM and hence validated.
- If the associated value falls outside the uncertainty interval (H_1), then the method will be subject to positive or, as shown in the slide, negative errors, so it cannot be validated.

Slide 3.23



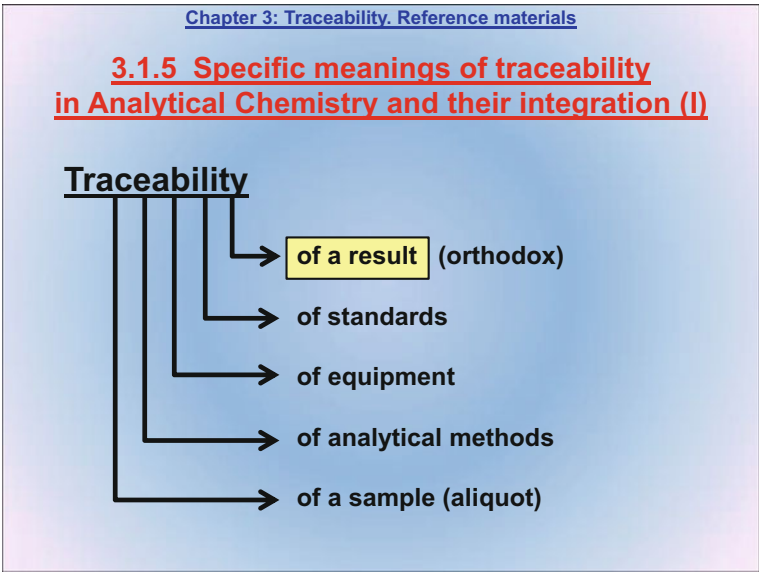
To standardize means to establish a (generally experimental) link from a standard to another of a higher rank (nearness to the true value) in the hierarchy. This is the third potential use of analytical chemical standards.

Standardizing is indispensable with a view to unequivocally connecting a secondary standard highly suitable for a given purpose (e.g., an NaOH, $KMnO_4$ or $Na_2S_2O_3$ solution) to a primary standard (potassium hydrogen phthalate, sodium oxalate and potassium iodate, respectively).

This procedure is also known as "factoring" because it involves calculating an experimental non-dimensional factor (below 1) by which the approximate concentration of the secondary standard is to be multiplied in order to determine the actual concentration. The slide shows an example of factoring: the standardization of an NaOH solution with potassium hydrogen phthalate.

3.1.5 Specific Meanings of Traceability in Analytical Chemistry and Their Integration (10 Slides)

Slide 3.24

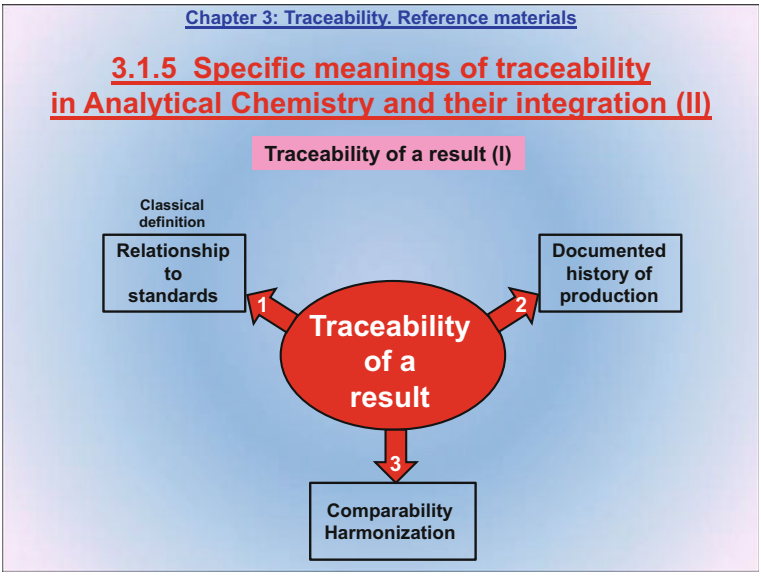


This slide illustrates different meanings of traceability in Analytical Chemistry.

Traceability of a result is the only possible, "orthodox" meaning in the realm of Metrology in general. The other uses of the word "traceability" in the slide are unorthodox because they are adapted to the specificities of Metrology in Chemistry. All are associated to the integral concept of traceability, which includes the tracing and referential facets—by exception, *traceability of a sample (aliquot)* only possesses the tracing facet and is thus the most unorthodox term.

These concepts are described in detail in Slides 3.25–3.33

Slide 3.25

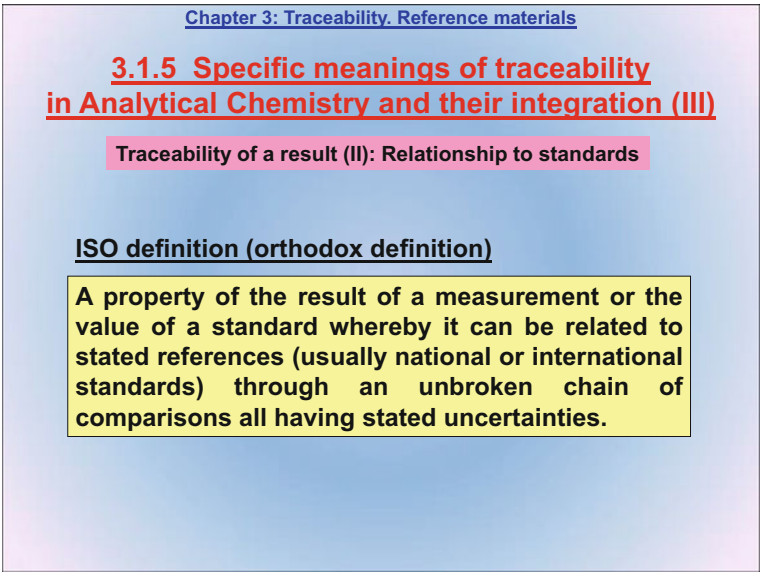


These are the three basic meanings of the integral concept of *traceability of a result*.

(1) A relationship to standards (referential facet), which is the classical, most orthodox definition.
(2) A documented history of the production of the result (the tracing facet), which directly influences its quality.
(3) Comparability and harmonization of laboratories (a practical consequence).

The integral concept of traceability can only be properly understood by considering all three meanings, which are discussed in detail in the following slides.

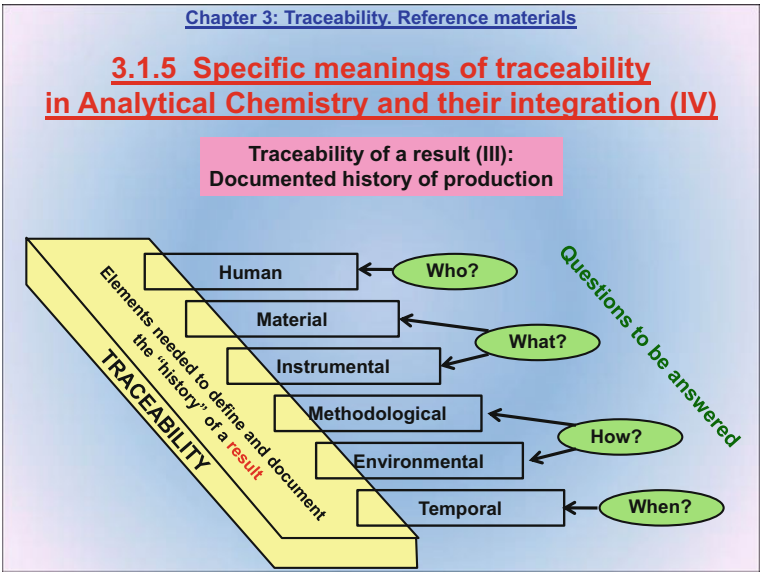
Slide 3.26



The most orthodox definition of *traceability of a result* is that based on its relationship to standards. In some cases, the relationship is established through intermediate landmarks (lower-rank standards). The description of this relationship constitutes the tracing facet. This is apparent from the ISO definition, shown in the slide, which holds quite well for physical measurements—in fact, it was issued specifically for them (see Example 6 in Slide 3.5).

As can be seen, the definition contains concepts extraneous to Metrology in Chemistry. What is a national (or international) standard? How distant is an analytical chemical laboratory from a base (SI) standard? Only with physical standards such as transfer weights for calibrating balances can the pyramid in Example 6 of Slide 3.5 be constructed.

Slide 3.27



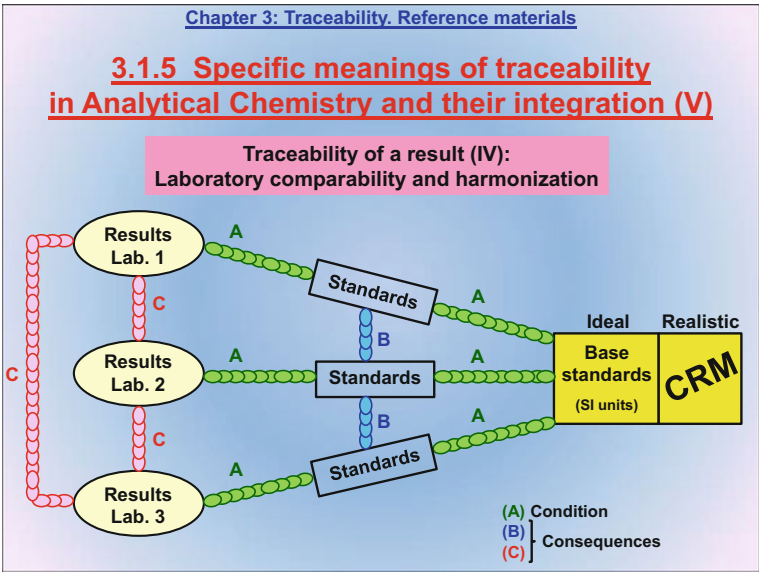
The second facet of traceability of a result is the documented history of its production. It is thus a tracing facet. The questions to be answered in this respect are as follows:

- Who performed the analytical process?
- What materials and equipment were used?
- When and how was the process performed?

Example: A laboratory determining a dioxin content of 0.1 ng/kg in a properly identified sample (e.g., code rd33245f-2012) of landfill ash analysed on February 4, 2012 should keep an accurate record of the persons taking part in the process of obtaining the result (who?); the materials (reagents, standards) and equipment used (what?); and the analytical method and environmental conditions in the laboratory (how?). Computers and, especially, bar codes, are indispensable for monitoring purposes in this context (that is, for the tracing facet of traceability).

Properly answering the previous questions is unavoidable with a view to fulfilling the requirements of laboratory accreditation in ISO 17025:2014 (see Chap. 8). Oddly, this standard imposes traceability in the results but does not refer specifically to the concept.

Slide 3.28



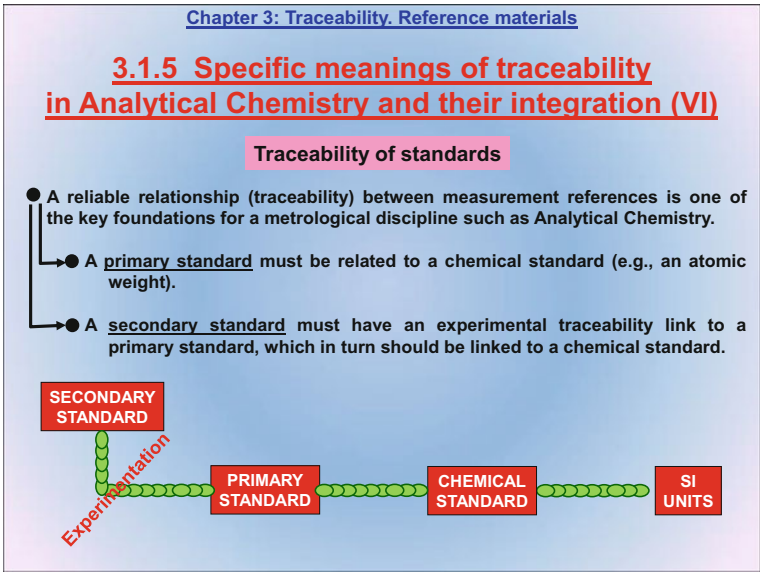
3.28.1. The practical consequence of *traceability of a result* is the ability to compare, harmonize and trace laboratories to one another.

For example, if three laboratories in Beijing, Barcelona and San Francisco (Labs 1–3 in the slide) are independently traceable through the unbroken green chains (A) in the determination of the same analyte in the same sample to an SI unit—only in theory—or the same CRM through different intermediate standards (e.g., standards obtained from national suppliers), then

3.28.2. The intermediate standards will be comparable and traceable to one another (blue chains, B); and

3.28.3. The results of the three laboratories for the same analysis or determination will be comparable and traceable to one another. Therefore, the three laboratories will be in harmony, which will make them highly competitive on the international market (the tree can be *mutually confident*). Thus, acceptance by a German dealer in alcoholic drinks of the results of an analysis for total tannins in wine conducted by the in-house laboratory of a producer in La Rioja (Spain) may lead to the dealer deciding to import the wine.

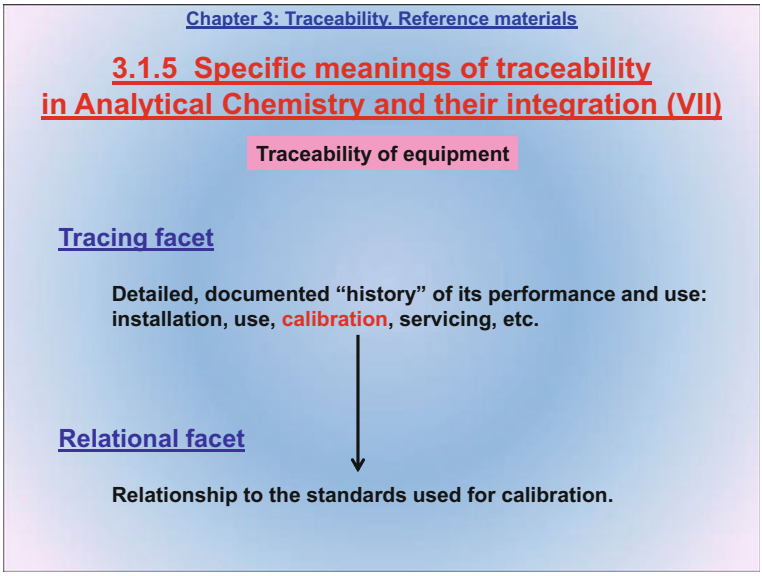
Slide 3.29



Traceability among standards is dealt with at length above (see, for example, Slide 3.8). This slide is simply a reminder of its significance to a metrological discipline such as Analytical Chemistry, where *traceability of a result* is also crucial.

The slide focuses on traceability in primary and secondary analytical chemical standards.

Slide 3.30

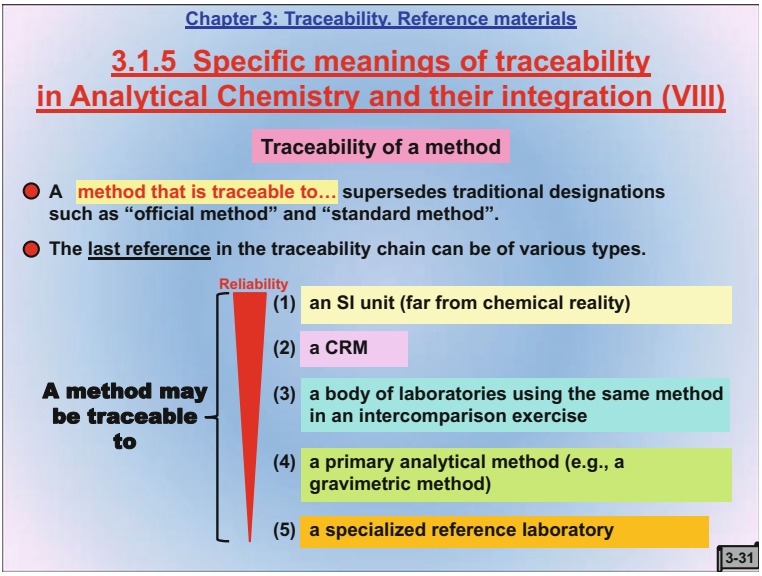


The *traceability of an instrument* delivering analytical chemical information provides an excellent example of the combination of the two basic facets of traceability.

– The *tracing facet* is inherent in the requirement set by ISO 17025:2004 for laboratory accreditation and involves recording the whole "history" of an instrument since it was installed.
– The *referential facet* focuses on the standards used to calibrate or verify the instrument (Slide 3.19).

The two facets are connected by calibration, which should be properly documented as well.

Slide 3.31



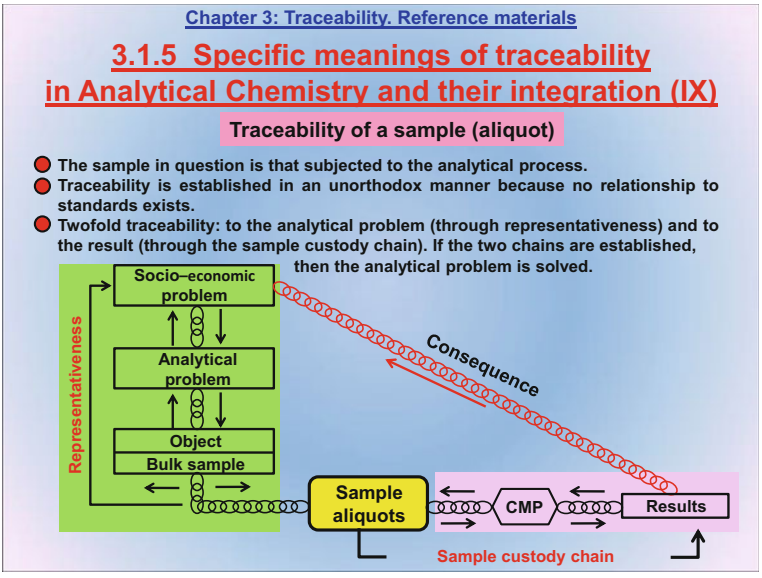
The terms "standard method" and "official method" formerly used to assure quality in analytical methods have been gradually replaced with "*a method traceable to…*" and led to the quality of a traceable method being judged by the particular reference at the end of the traceability chain.

(1) Ideally, the final reference should be an SI unit, but this virtually impossible in the chemical realm.
(2) The most realistic degree of quality is traceability to a certified reference material. However, the scarcity of CRMs makes it difficult to accomplish.
(3) A more affordable target is traceability to a body of laboratories using the same method to analyse aliquots of the same sample in an intercomparison exercise supervised by a widely acknowledged national or international competent organization.

(4) Next in the reliability ranking is traceability to a primary, absolute method using no analytical chemical standards (see Slide 5.12). Such is the case with gravimetric methods, for example. The problem arises when the same laboratory has to perform the target method and the primary method in the absence of external references.
(5) Traceability to a specialized international reference laboratory (a distinction issued by a competent international organization such as the European Union) is also limited in scope because most laboratories deal only with highly specific types of samples (e.g., bovine meat to be analysed for antibiotics or anabolic steroids).

As shown in the slide, reliability in the traceability chain decreases from 1 to 5.

Slide 3.32



3.32.1. The *traceability of the sample (aliquot)* subjected to an analytical process is very interesting for a number of reasons, namely:

(1) It is rather unorthodox in that it only encompasses the tracing facet of the integral concept of traceability.
(2) It represents traceability to two rather than one final reference: the information required and the results of two traceability chains, one corresponding to the capital property representativeness (Slide 7.10) and the other being the so-called "sample custody chain".
(3) It is cyclic: provided the partial traceability chains are not broken, the main goal of Analytical Chemistry (Slide 1.8) is reached. Such a goal is ensuring that the

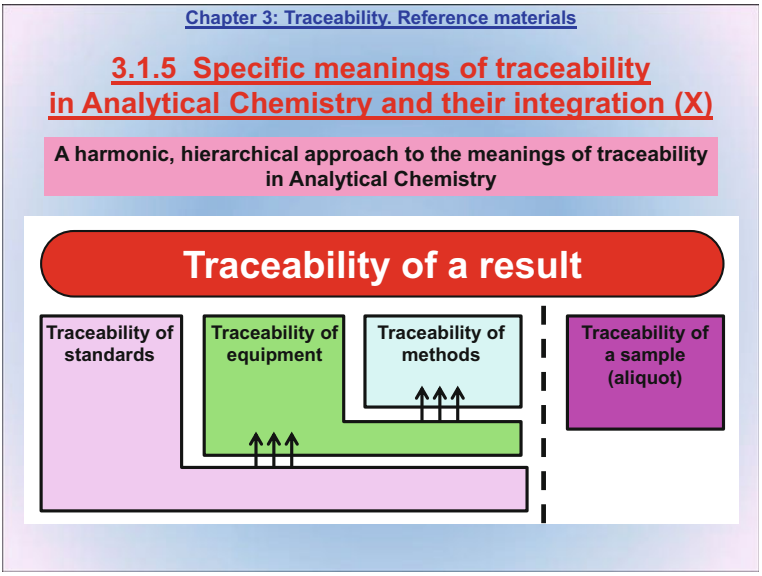
results fulfil the information demand because they are traceable to the specific socio–economic problem addressed (Slide 7.10).

3.32.2. Therefore, the sample aliquot that is subjected to the analytical process should be traceable to the information demand (the socio–economic problem) through unequivocal relationships to the bulk sample, the object and the analytical problem (see Chap. 7).

3.32.3. The second traceability chain starts at the aliquot, which should be unequivocally related to its results through the sample custody chain. The custody chain, which relies on the use of bar codes and computers, is essential for automated laboratories processing large numbers of samples each day. Thus, a clinical laboratory may lead to a healthy person being diagnosed with diabetic coma—or vice versa—if it does not ensure traceability of each sample (aliquot) to the patient from whom it was obtained.

3.32.4. The consequence of the two traceability chains that start at the sample aliquot not being broken is that the results are consistent with the information required and hence that the information demand is fulfilled. This is a permanent challenge for Analytical Chemistry (see Chap. 7, devoted to analytical problem-solving).

Slide 3.33



This hierarchical arrangement of the analytical meanings of traceability facilitates their integration.

At the top of the hierarchy is *traceability of a result*, which is the most orthodox concept and relies on the traceability of the standards, equipment and methods used to obtain it.

Traceability between tangible standards (analytical chemical standards) provides support for

- traceability of a result;
- traceability of equipment in its referential facet; and
- traceability of methods in its referential facet.

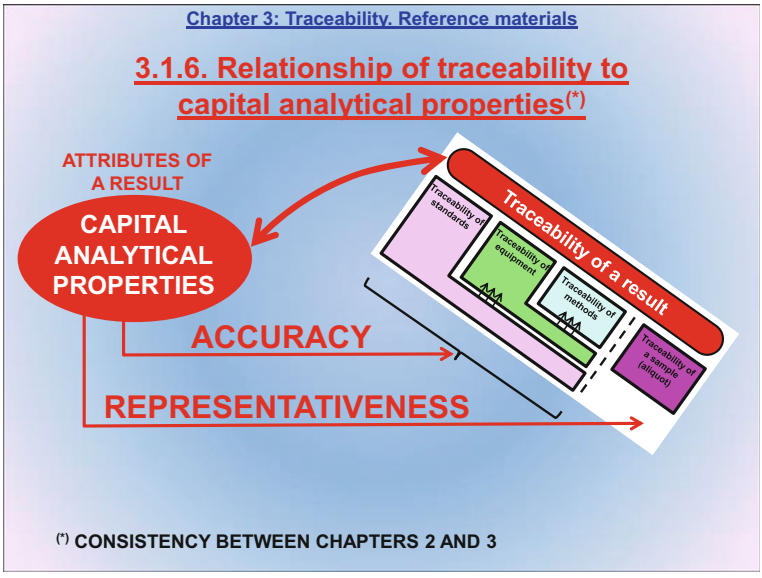
Traceability of equipment and methods relies on traceability of standards, which in turn rests on traceability of a result and traceability of a method.

Traceability of methods rests on traceability of standards and traceability of equipment, and provides support for traceability of a result.

This approach would be incomplete without an unequivocal relationship between the sample (aliquot) and the result in the context of *traceability of the sample aliquot*, which is an undeniable foundation of its traceability. It is separated from the previous types of traceability because it is a completely unorthodox concept—it lacks the typical referential facet of other meanings of traceability in Analytical Chemistry.

3.1.6 Traceability and Capital Analytical Properties (1 Slide)

Slide 3.34



This section harmonizes the contents of this chapter (Traceability. Reference materials) with those of the previous one (Analytical Properties).

3.34.1. Based on the general scheme of analytical properties in Slide 2.4, the capital properties (accuracy and representativeness) are attributes of the results.

3.34.2. Based on the integral view of the concepts behind *traceability of a result* (Slide 3.33), capital analytical properties are consistent with this form of traceability. Thus,

- *accuracy* is the first part of the support for traceability of a result, which relies on that of standards, equipment and methods; and
- *representativeness* corresponds to consistency of the sample aliquot with the information required and the results themselves.

Both properties are crucial (see Slide 2.13) with a view to assessing the quality of the results and building the integral concept of traceability.

3.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

M. Valcárcel

Springer-Verlag, Berlin, 2000.

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

This chapter overlaps to a great extent with Chap. 3 of Valcárcel's book, from which it borrows the title. This is a simplified version of that chapter, which, however, has been expanded in some respects to better illustrate abstracts concepts such as traceability, validation of analytical methods, and the relationship of traceability to analytical properties. Valcárcel's book can be used for direct consultation of the contents of this chapter.

Metrology in Chemistry and Biology: A practical approach

M. Valcárcel and 17 other authors.

O.O.P.E.C., UE (Luxemburg), 1999.

Scientists from 9 European countries led by Spain produced the first official publication on Metrology in Chemistry and Biology, which discusses coincidences with and differences from traditional Metrology (that is, Metrology in Physics). The most salient conclusion is the need to adapt general metrological principles to the specificities of chemical, biochemical and biological measurements. Some annexes to standards issued in the XXI century have echoed the recommendations. Many parts of this chapter are inspired by this document.

3.3 Questions on the Topic (Answered in Annex 2)

3.1. What are the main purposes of a sample matrix standard with a certified analyte content (a CRM)? Tick the correct answers.

[ ] Calibrating an instrument

[ ] Globally assessing an analytical process

[ ] Calibrating a method

[ ] Standardizing secondary analytical chemical standards

3.2. What is a matrix standard? What is its main use?

3.3. What are the essential requirements for establishing the traceability of an instrument?

3.4. Tick the type correct type of standard in each case.

	Standard			
	Basic	Chemical	Analytical chemical	
			Primary	Secondary
Carbon-12				
A 0.1 mol L^{-1} solution of $KMnO_4$				
Potassium hydrogen phthalate				
Ultrapure silver				
The faraday				

3.5. Describe the traceability network among standards relevant to Analytical Chemistry with emphasis on the connections between basic, chemical and analytical chemical standards.

3.6. How would you define "traceability of an analytical method (CMP)"?

3.7. The total free acid content of a wine sample is determined by acid–based titration with a sodium hydroxide solution previously standardized with potassium hydrogen phthalate. What standards are used in the process?

Chemical:
Primary analytical chemical:
Secondary analytical chemical:

3.8. Define "equipment calibration" and relate it to or distinguish it from "method calibration".

3.9. What are the purposes of equipment calibration (verification)? Tick the correct answer(s).

[ ] Constructing a calibration curve
[ ] Adjusting faulty equipment
[ ] Globally assessing an analytical method
[ ] Distinguishing error types in Analytical Chemistry

3.10. Connect each of the following standards to its type in the column on the right.

Standard	Type
A 0.1 mol HCl L^{-1} solution	Basic
The atomic weight of Ca	Chemical
Sodium carbonate	Analytical chemical (Primary)
The faraday	Analytical chemical (Secondary)
The second	

3.11. Rank the reliability of the following types of standards with a score from 1 (least reliable) to 4 (most reliable).

Standard	Reliability
Secondary analytical chemical standard	
Chemical standard	
CRM	
Primary analytical chemical standard	

3.12. What role do analytical chemical standards play in the traceability of a result?
3.13. What type of standard (basic, chemical or analytical chemical) has the greatest associated uncertainty? Why?
3.14. A sample of powdered milk with a protein content certified in a document issued by a renowned independent organization is

[ ] A primary standard
[ ] A certified reference material
[ ] A secondary standard
[ ] A reference material

3.15. Name the types of chemical standards, state their differences and give some examples.
3.16. Give an example of each complementary criterion used to classify analytical chemical standards.
3.17. Comment on the tracing facet of traceability of a result. What should it be consistent with?
3.18. Describe a procedure for assessing (validating) a new analytical method in terms of its relationship to matrix-type certified reference materials.
3.19. What is the main limitation of CRMs for establishing the traceability of methods?
3.20. What types of standards prevail among (a) reference materials (RMs) and (b) certified reference materials (CRMs)?

3.21. Which base standard is the most relevant to Chemical Metrology? Why?
3.22. Why are secondary standards used even though they have unsuitable properties (e.g., instability, impurity)?
3.23. What are the requirements for a matrix-type CRM?
3.24. What are the three most salient general uses of analytical chemical standards?
3.25. What are the three principal meanings of traceability of an analytical result?
3.26. How is an analytical method assessed to assure reliability?
3.27. What analytical properties are related to traceability? Explain your answer.
3.28. On what should mutual recognition of the results of two or more laboratories rest?
3.29. What feature and twofold meaning does traceability of the sample aliquot subjected to an analytical process have?

3.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened for teaching Analytical Chemistry to students not majoring in Chemistry, albeit to a lesser extent than those of others because of its transversal conception. The following 5 slides (15% of all) can be omitted for this purpose:

- Section 3.1.2: Slides 3.5 and 3.6
- Section 3.1.3: Slide 3.11
- Section 3.1.4: Slide 3.15
- Section 3.1.5: Slide 3.31

Part II
The Analytical Process

Generalities of the Analytical Process

4

Abstract

This chapter, which starts Part II, explains how to extract (bio)chemical information from objects and systems. It describes the generalities of the analytical process, which are dealt with in greater detail in Chaps. 5 and 6, devoted to quantitative and qualitative analytical processes, respectively. Following a brief placement in context of the topic, the concept "analytical problem" is defined and the three general steps of the analytical process are described in separate sections on preliminary operations (sample collection and treatment), measurement and transducing of the analytical signal, and signal acquisition and processing to produce results in the required format.

Teaching Objectives

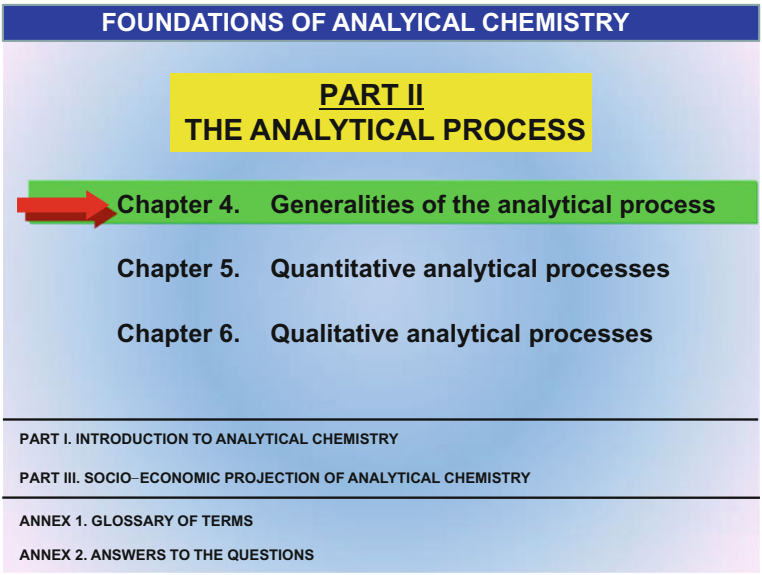
- To define the general features of analytical processes.
- To describe the preliminary operations (first step) of the analytical process.
- To describe sampling operations.
- To introduce students to analytical separations systems.
- To provide an overall description of measurement and transducing of the analytical signal.
- To describe manual and automatic systems for signal acquisition and data processing.

Electronic Supplementary Material The online version of this chapter (doi:10.1007/978-3-319-62872-1_4) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_4

4.1 Explanation of the Slides

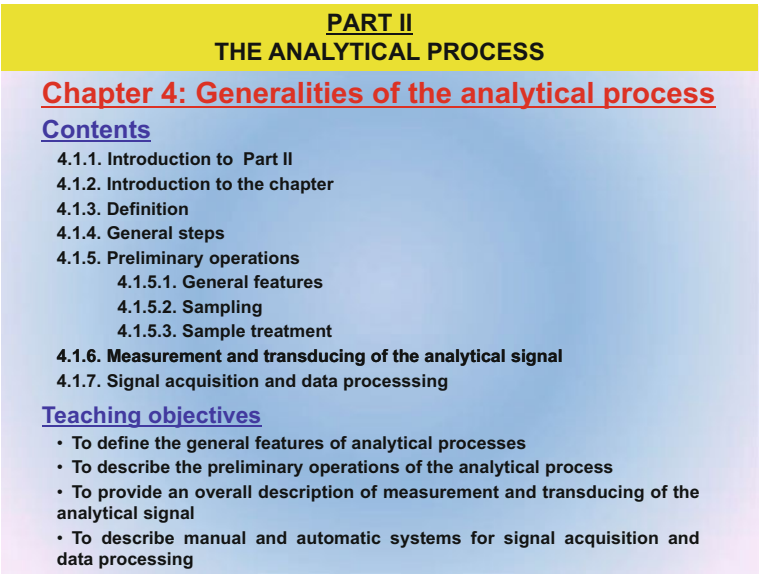
Slide 4.1



This slide places Part II (The Analytical Process) and shows the other two parts.

This is an introductory chapter approaching the generalities of the analytical measurement processes used to obtain (bio)chemical information (see Slide 1.4). Such processes can be quantitative (Chap. 5) or qualitative (Chap. 6) in nature.

Slide 4.2

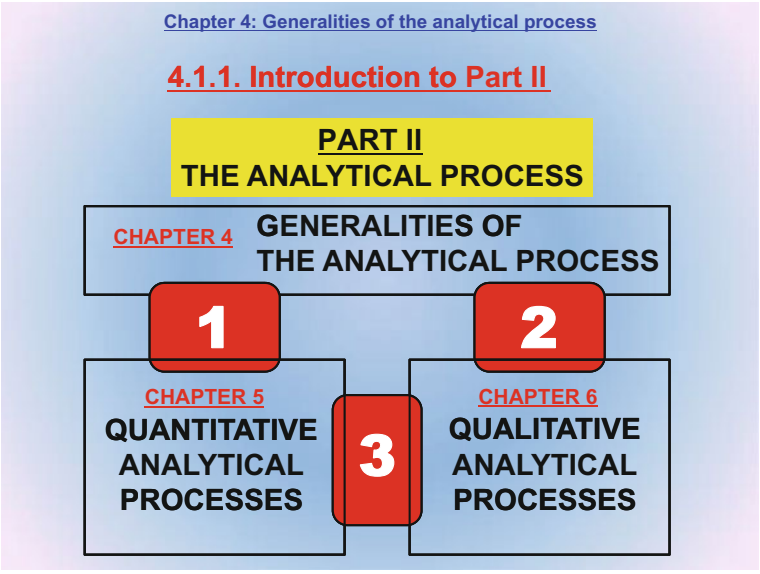


4.2.1. This slide shows the contents of this chapter, which span seven sections. The first section places the chapter in context within Part II and the next three provide an overview of analytical processes. The last three sections deal with the three main steps of the analytical process, namely: preliminary operations (4.5), measurement and transducing of the analytical signal (4.6), and data processing (4.7).

4.2.2. The slide also shows the main teaching objectives of the chapter, which can be summarized as follows: to provide an overview of analytical processes by describing their three general steps.

4.1.1 Introduction to Part II (1 Slide)

Slide 4.3



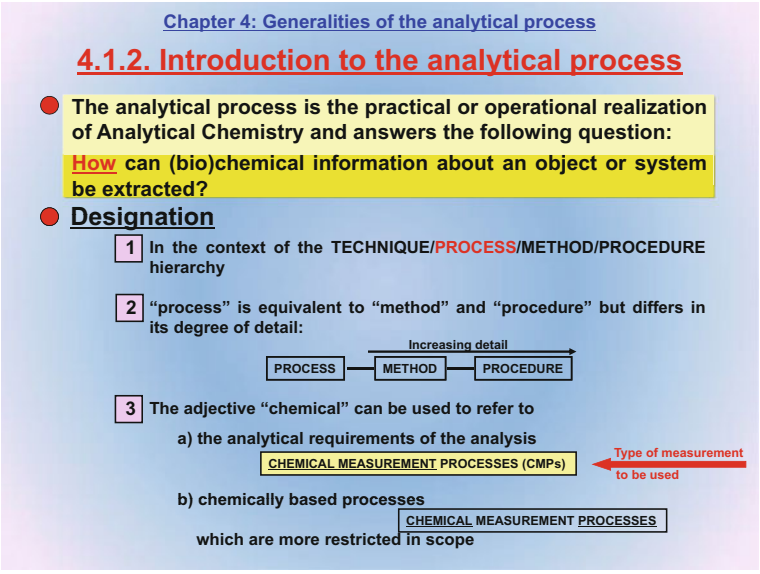
This slide depicts the relationships (interfaces 1–3) among the contents of this chapter and those of Chaps. 5, 6, which provide a general, harmonic answer to the following question: How can (bio)chemical information about an object or sample be extracted?

This chapter provides a framework for the generalities of the analytical process. The three chapters of Part II are related through the interfaces shown as follows:

- *Interfaces 1 and 2*. This chapter is general in scope and its contents pertain to both Quantitative Analysis (Chap. 5) and Qualitative Analysis (Chap. 6).
- *Interface 3*. The apparent difference between Quantitative Analysis (Chap. 5) and Qualitative Analysis is unrealistic. In fact, Qualitative Analysis frequently has quantitative connotations.

4.1.2 Introduction to the Analytical Process (1 Slide)

Slide 4.4



4.4.1. The analytical process is a set of operations separating a sample from its result (see Slide 1.22). It is the operational answer to the question "How can (bio)chemical information about an object (e.g., a lunar rock) or system (e.g., a river throughout the year) be obtained?" The object or system may be natural or artificial.

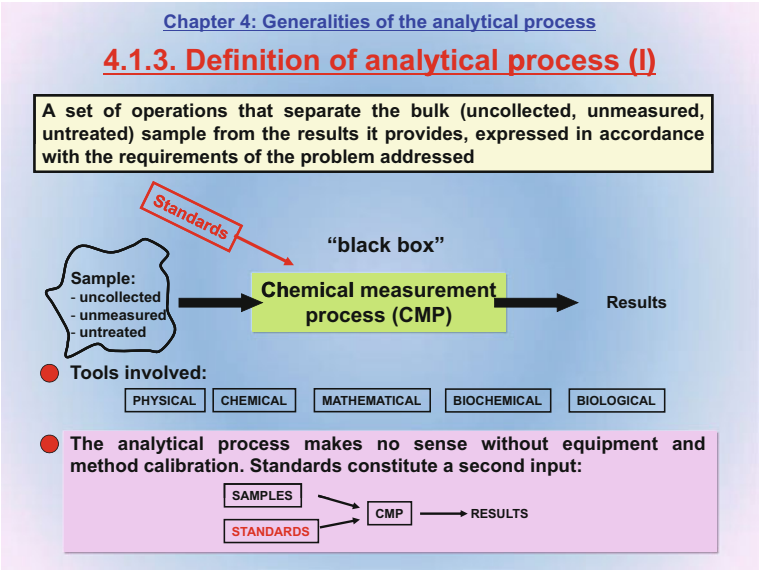
4.4.2. The designation "process" is intended to place Analytical Chemistry in the realm of Science and Technology. This designation is present in the hierarchy of Slide 1.22. The word "process" here represents how (bio)chemical information is obtained and materializes in increasingly detailed descriptions based on the words "method" and "procedure".

As can be seen, the adjective "chemical" is also troublesome because it can be applied indifferently to the information required and the tools needed to obtain it.

In this chapter, we use the designation *Chemical Measurements Processes* (CMPs), which are concerned with (bio)chemical information requirements even though they use chemical tools (reagents, solvents) to fulfil them.

4.1.3 Definition of Analytical Process (2 Slides)

Slide 4.5



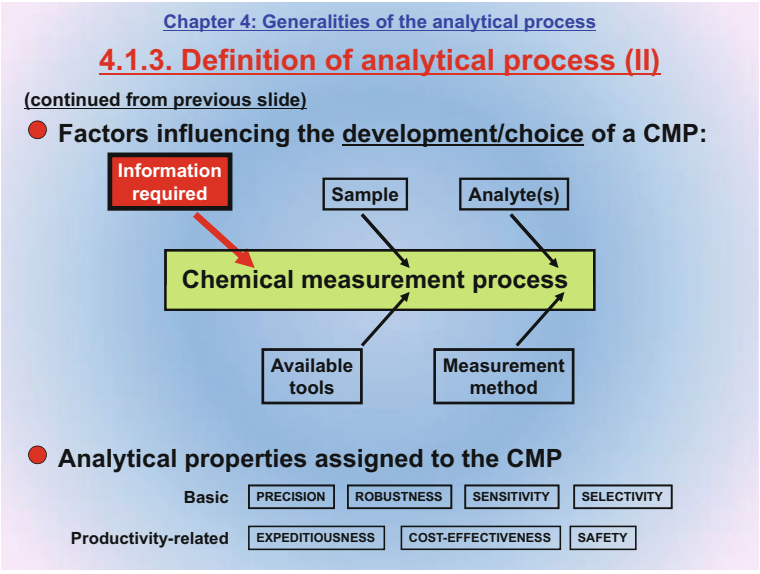
4.5.1. This slide provides a formal definition of "analytical process", which, as shown in the previous one, materializes in the acronym CMP.

As can be seen, a CMP is a sort of "black box" that receives samples as input and delivers results as output.

Depending on the characteristics of the analytical process, the "black box" can use *tools* of various types, namely: *physical* (e.g., apparatuses, instruments), *chemical* (e.g., reagents, solvents), *mathematical* [e.g., algorithms for converting raw data (signals) into results], *biochemical* (e.g., immobilized enzymes) and *biological* (e.g., tissue homogenate of banana peel to immobilize natural enzymes onto an electrode surface).

4.5.2. Since Analytical Chemistry is a metrological discipline (that is, one based on measurements), it requires using standards for comparison (see Slide 1.12). Measurement standards therefore constitute another input to the analytical process in addition to samples.

Slide 4.6



4.6.1. This slide completes the definition of "analytical process" by describing the factors governing its development or selection, and also the associated analytical properties (see Chap. 2).

An existing analytical process for determining a given analyte in a specific type of sample may be usable as such or require minimal adjustment. Such is the case with standard and official methods of analysis (see Slide 1.13). However, obtaining special information may require developing a new CMP from scratch. In any case, the development or selection of an analytical process should be guided by the following factors:

1. The specific *(bio)chemical information required* for well-grounded, timely decision-making, which, as shown in the slide, is crucial with a view to using the most suitable analytical process in each situation.

   The analytical process to be used for a given analyte will differ depending on whether the results are to be delivered expeditiously at the expense of accuracy or as accurately as possible at the expense of expeditiousness.

Two cases in point are the fast determination of the fat content of freshly harvested olives and that of moisture in an organic solvent. In the former case, the result should be delivered promptly because it will dictate the value of the olives. This can be accomplished by using a nuclear magnetic resonance (NMR) probe to measure the fat content with acceptable error (5–10%) virtually immediately. By contrast, moisture in an organic solvent must be determined with greater accuracy, which entails using a slower process such as Karl Fisher titrimetry with amperometric monitoring (a sluggish, expensive, labour-intensive process). These two examples illustrate how the type of information required and the expeditiousness with which it is to be delivered are two key factors in choosing or developing an analytical process for a given analytical purpose.

2. *Properties of the sample* such as state of aggregation (solid, liquid or gaseous), size (macroanalysis, microanalysis, etc., as shown in Slides 1.37 and 1.38) and availability (Slide 1.39), among others.
3. *Characteristics of the analyte(s)* such as nature (organic, inorganic, biochemical) (see Slide 1.34), number and concentration (macrocomponents to traces) (see Slide 1.37), among others.
4. *Available tools (apparatuses, instruments, reagents)*. Obviously, pesticides in soils can be more accurately and expeditiously determined with a gas chromatograph coupled to a mass spectrometer than with one equipped with a conventional detector. Thus, carcinogenic aflatoxins in milk can be more conveniently determined by direct immunoassay than with a liquid chromatograph coupled to a mass spectrometer—which requires labour-intensive sample treatment.
5. The *method of measurement*, which differs depending on whether qualitative or quantitative information is needed. For example, calculable methods (e.g., absolute methods) differ from relative methods in this respect (see Slides 5.11–5.14 and the sections that describe them).

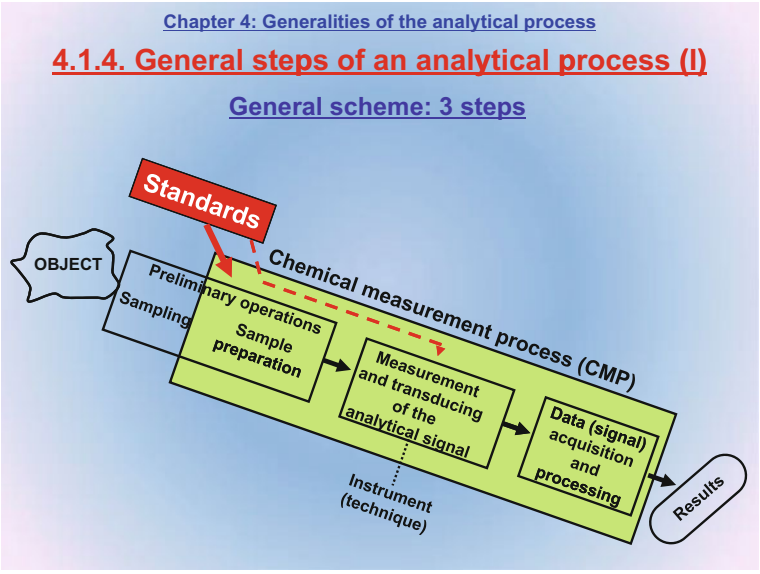
4.6.2. The analytical properties that dictate the quality of an analytical process depend on whether the process is of quantitative or qualitative kind.

Thus, Quantitative Analysis is linked to basic and productivity-related properties (Slide 2.4), and basic properties provide support for capital properties.

Because accuracy (a capital property) and precision do not apply to Qualitative Analysis, a new property called “reliability” is needed here (see Slides 6.14–6.16 and 6.21).

4.1.4 General Steps of an Analytical Process (2 Slides)

Slide 4.7

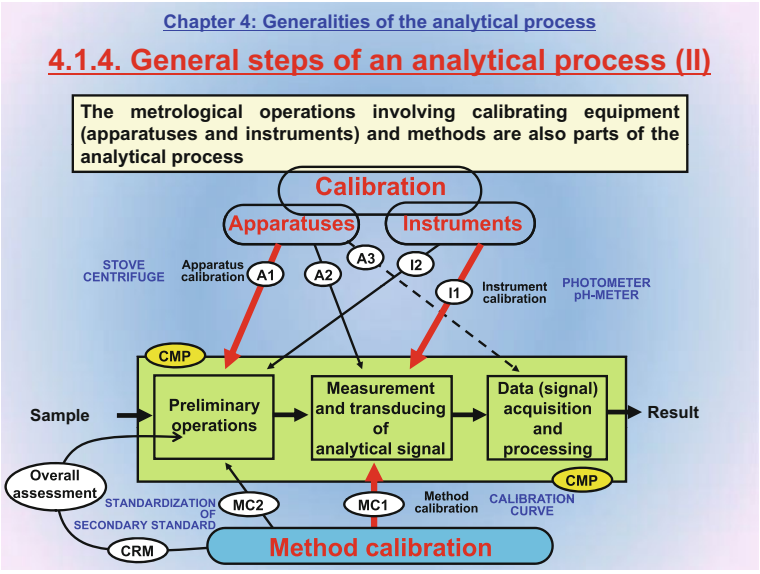


4.7.1. The definition of "analytical process" is completed in this section with a description of its main steps.

As shown in this slide, the analytical process comprises three steps separating the bulk sample from its results, namely: preliminary operations (sample collection and treatment), measurement of the analytical signal with an instrument, and acquisition and processing of raw signals to produce the results.

4.7.2. This slide emphasizes the crucial role of tangible measurement standards in the preliminary operations of the analytical process and in measurement of the analytical signal (see Chap. 3).

Slide 4.8



4.8.1. As noted in Chap. 3, a distinction should be made between equipment calibration, whose targets are apparatuses and instruments, and method calibration, where the target is the analytical process (see the example in Slide 3.19). Calibration is an essential part of the analytical process.

Equipment calibration can be aimed at two different types of targets, namely:

- Apparatuses (A.1) such as samplers, centrifuges, extractors, stoves or furnaces, which are typically used in the preliminary operations of the analytical process.
- Instruments (I.1) such as spectrophotometers, ammeters or chromatographs, which are normally used in the second step of the analytical process but may also be needed in the first (I.2) for purposes such as measuring volumes and weighing untreated or treated samples with labware (flasks, pipettes, burettes, balances) that requires calibration if accurate results are to be delivered.

Method calibration can be done for three main purposes (see Slides 3.19 and 3.20), namely:

- Establishing the signal–concentration relationship by constructing a calibration curve (see Slide 2.36) in the second step, where the instrument comes into play (CM1);
- Calibrating secondary standards by titration (CM2) with primary standards (see Slide 3.23).

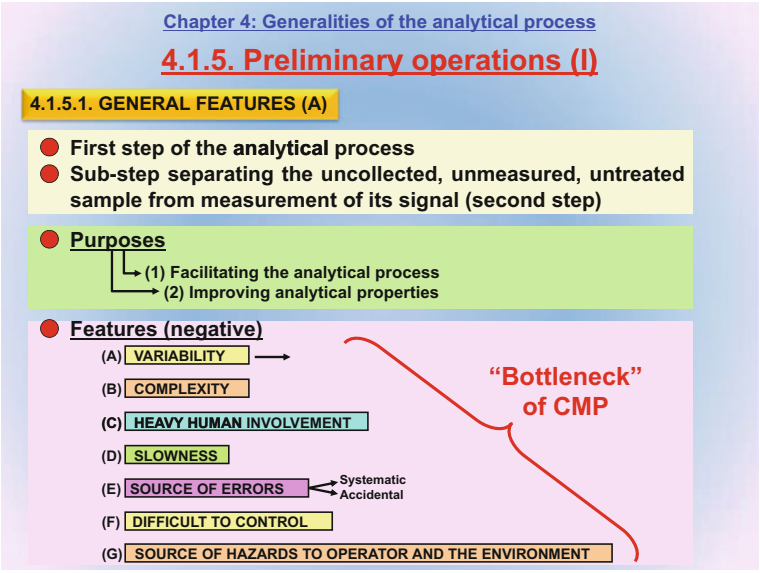
- Globally assessing analytical processes (see Slides 3.21 and 3.22) by application to a certified reference material (CRM) and statistical comparison of the results for the CRM and the samples.

4.8.2. These are selected examples of the two types of calibration in the analytical process.

4.1.5 Preliminary Operations of the Analytical Process (23 Slides)

4.1.5.1 General Features (4 Slides)

Slide 4.9



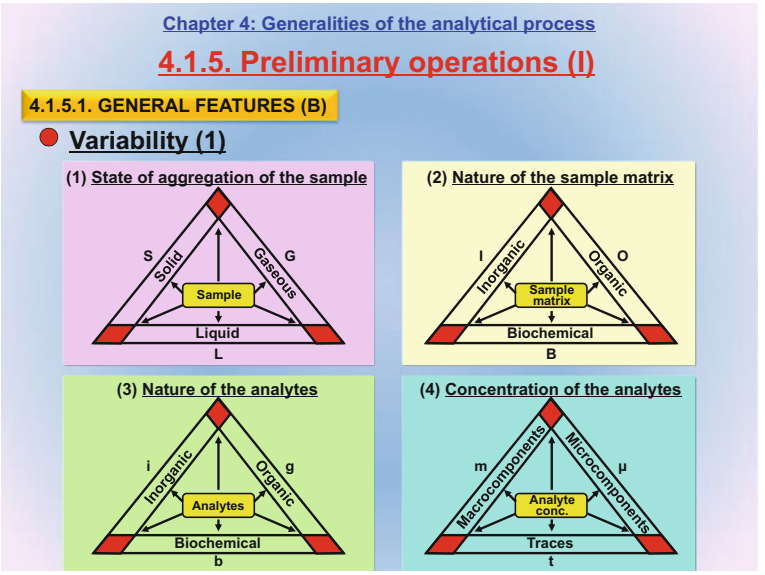
4.9.1. Slides 4.9–4.31 are concerned with the preliminary operations of the analytical process. The first four (4.9–4.12) explain its general features, the next eleven (4.13–4.23) sample collection and the last eight (4.24–4.31) sample treatment (with special emphasis on separation systems).

This slide defines "preliminary operations", which comprise sample collection and preparation (see Slide 4.7). Also, its describes their *general purposes* (namely, facilitating the analytical process and improving analytical properties) and their seven most salient features, which are as follows:

(A) Variability in the operations, which is a major hindrance. In fact, virtually each sample–analyte pair requires its own specific operation (see Slide 4.10), which precludes designing all-purpose equipment for this purpose.
(B) Preliminary operations are operationally complex as they typically involve transferring liquids, filtering, using analytical separation systems, measuring volumes, weighing, etc.
(C) As a result, they are labour-intensive and difficult to automate.
(D) Some operations (e.g., passing an eluent through a solid-phase extraction column, dissolving soil) are especially sluggish and take up 60–80% of the overall time spent in conducting an analytical process. This has made "direct methods of analysis" a priority goal to by-pass preliminary operations in the analytical process.
(E) One of the most negative features of preliminary operations is that they are the source of systematic and accidental errors. The former can arise from volume measurements with a poorly calibrated pipette, using inappropriate sampling equipment or not adhering to the recommended timing, for example. On the other hand, the latter are typically the result of human mistakes (e.g., distraction, poor readings, failing to distinguish colours). Properly performing preliminary operations is therefore very important because any errors made will propagate through the analytical process and have an adverse impact on the quality of the results.
(F) Preliminary operations are difficult to control because monitoring every single sub-step is nearly impossible. Calibrating apparatuses (e.g., extractors, stoves, centrifuges, thermometers) rarely suffices for this purpose. In fact, the best way to check that an analytical process is operating as expected is by assessing it—preliminary operations included—with a certified reference material (CRM). If the certified value and the result of the process are consistent, then the process can be validated and its preliminary operations assumed to be under control.
(G) Preliminary operations are the source of hazards for operators and the environment since they often use pressurized gas cylinders, toxic reagents and solvents, and high pressures and/or temperatures. Also, toxic waste from the operations can obviously affect analysts and the environment. So-called "green methods" are intended to minimize personal and environmental risks.

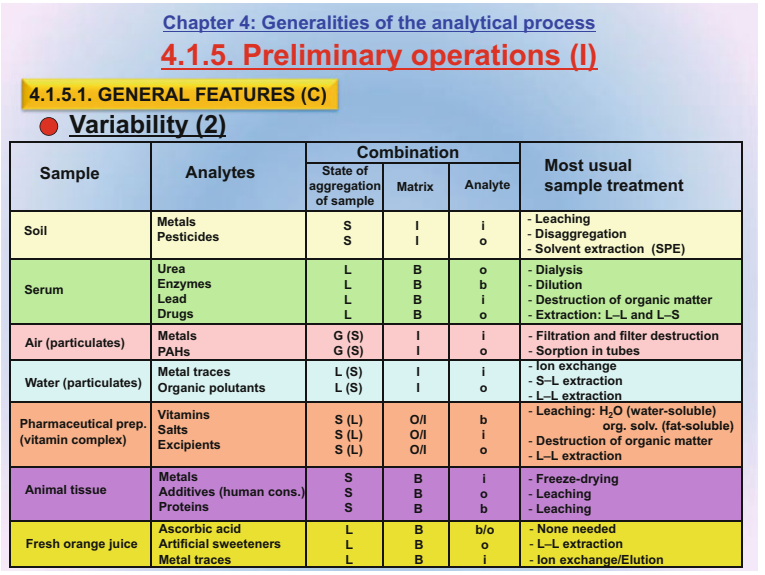
4.9.2. Based on the foregoing, the preliminary operations of the analytical process possess negative connotations although they are indispensable with a view to assuring integral quality in the analytical results.

Slide 4.10



This slide and the next illustrate the high variability of the preliminary operations of the analytical process (see also Slide 4.11) as regards state of aggregation of the sample (solid, liquid or gaseous), nature or the sample and analyte (organic, inorganic or biochemical), and concentration of the analyte (macrocomponents, microcomponents, traces). Also, the situation differs depending on whether one or more analytes are to be detected or determined in the same sample.

Slide 4.11



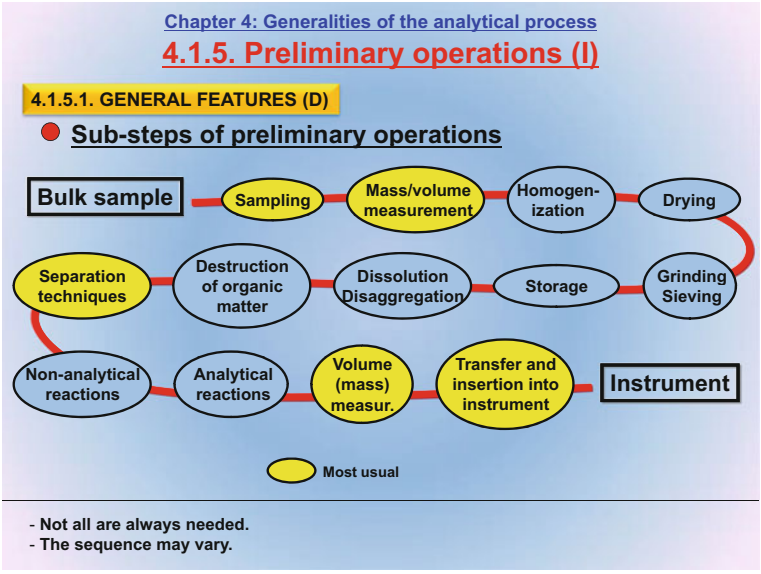
Sample	Analytes	Combination			Most usual sample treatment
		State of aggregation of sample	Matrix	Analyte	
Soil	Metals Pesticides	S S	I I	i o	- Leaching - Disaggregation - Solvent extraction (SPE)
Serum	Urea Enzymes Lead Drugs	L L L L	B B B B	o b i o	- Dialysis - Dilution - Destruction of organic matter - Extraction: L–L and L–S
Air (particulates)	Metals PAHs	G (S) G (S)	I I	i o	- Filtration and filter destruction - Sorption in tubes
Water (particulates)	Metal traces Organic polutants	L (S) L (S)	I I	i o	- Ion exchange - S–L extraction - L–L extraction
Pharmaceutical prep. (vitamin complex)	Vitamins Salts Excipients	S (L) S (L) S (L)	O/I O/I O/I	b i o	- Leaching: H_2O (water-soluble) org. solv. (fat-soluble) - Destruction of organic matter - L–L extraction
Animal tissue	Metals Additives (human cons.) Proteins	S S S	B B B	i o b	- Freeze-drying - Leaching - Leaching
Fresh orange juice	Ascorbic acid Artificial sweeteners Metal traces	L L L	B B B	b/o o i	- None needed - L–L extraction - Ion exchange/Elution

Each sample–analyte pair requires using a preliminary operation suited to the particular analytical purpose. This increases variability in the preliminary operations even further.

The examples in this slide show that the operations to be performed depend on the specific analyte to be detected or determined.

One example is the determination in animal or human serum of urea, enzymes, lead or drugs, which involves different types of preliminary operations such as dialysis, dilution, destruction of organic matter and solid–liquid extraction, respectively.

Slide 4.12



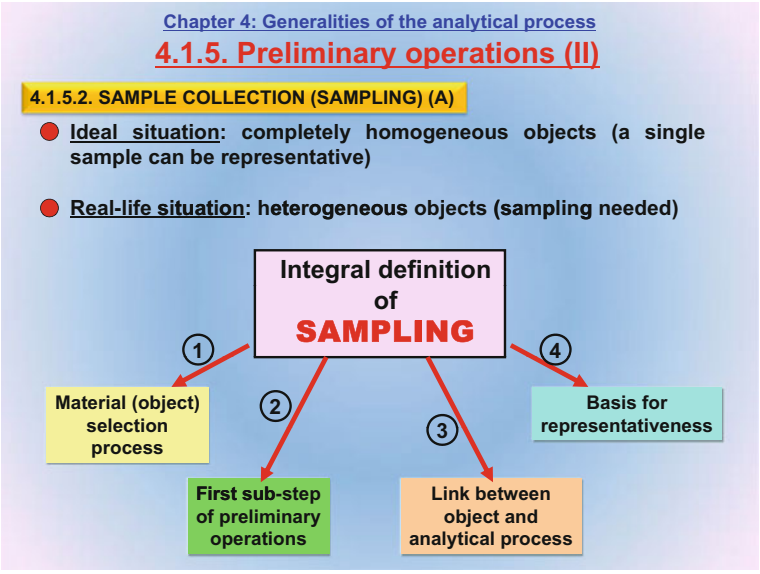
By definition, the preliminary operations of the analytical process separate the object (or bulk sample) from measurement with an instrument (second step of the process). This slide shows various types of operations for solid, liquid and gaseous samples. Those highlighted in yellow (namely, sampling, mass or volume measurement of the aliquot subjected to the analytical process, analytical separation, mass or volume measurement of the treated sample and insertion into the instrument) are the most usual.

In order to avoid misconceptions one should bear in mind that

(a) not every preliminary operation shown is always needed (e.g., no grinding or sieving is necessary with liquid samples); and
(b) the sequence of operations is not always as shown (e.g., non-analytical reactions may come before analytical separation in order to facilitate it).

4.1.5.2 Sample Collection (11 Slides)

Slide 4.13

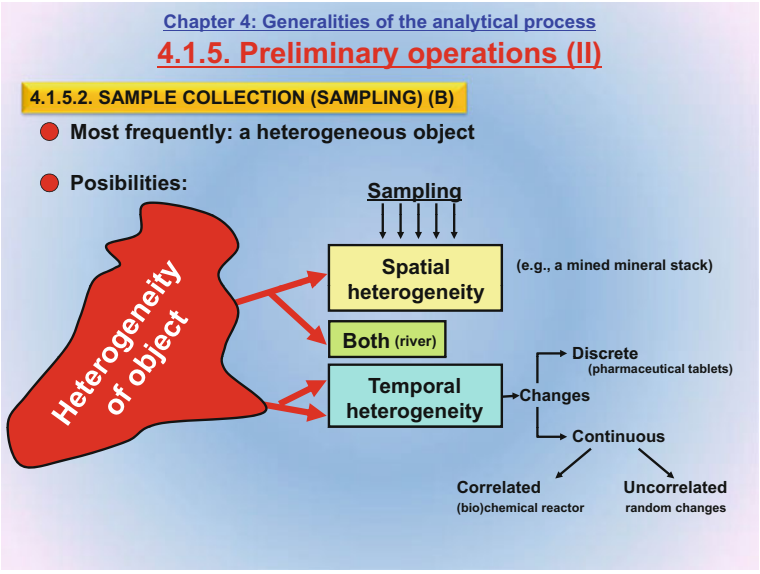


This slide starts the description of sample collection (sampling), which spans the next ten.

Sampling would be unimportant to the analytical process if the object were completely homogeneous since any sample withdrawn from it would be identical to and provide the same results as any other. This is an unrealistic scenario, however, because objects are nearly always heterogeneous, so any samples extracted from them will differ and lead to different results if subjected separately to the analytical process. As a consequence, the quality of the results depends critically on the quality of sampling, which is one of the most crucial preliminary operations.

This slide shows four complementary approaches to sample collection (sampling). The first defines sampling in technical terms, the second and third place it in context within the analytical process, and the last relate it to the capital property "representativeness",—which, together with accuracy, is an attribute of the results.

Slide 4.14

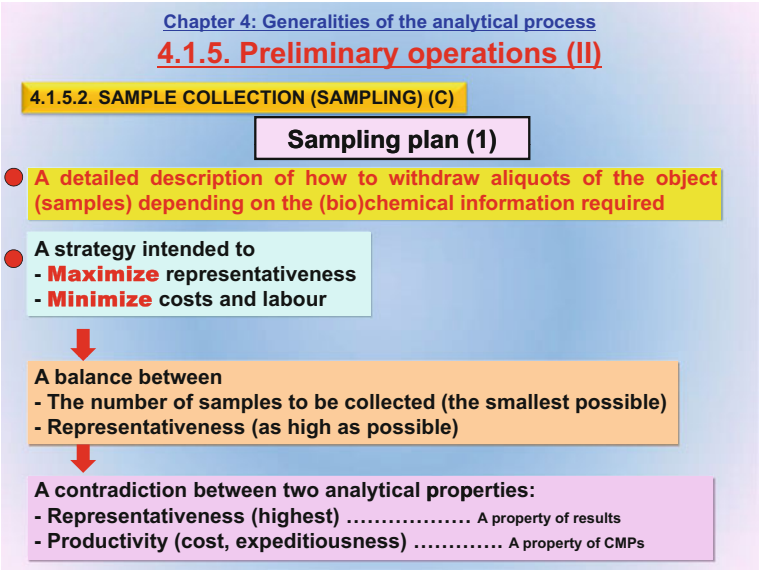


The degree of heterogeneity of the object (that is, its variability in space, time or both) dictates the sampling strategy to be used. There are three main types of object heterogeneity, namely:

(A) *Spatial heterogeneity* (e.g., differences in pesticide contents in the 10 cm deep layer of agricultural soil across a field of 1 ha).
(B) *Temporal heterogeneity* (that is, differences in object composition with time). The differences can be of two types:

- Discrete (e.g., those in the sweetener content of a non-alcoholic beverage among bottles).
- Continuous, whether predictable because changes in the object are mutually correlated (e.g., differences in the amount of glucose present in an enzymatic reactor used to produce it) or random in nature (i.e., following no well-defined pattern).
- *Spatial and temporal heterogeneity*, which is the most complex of the three (e.g., differences between heavy metal levels at different depths and in different seasons in a lake).

Slide 4.15



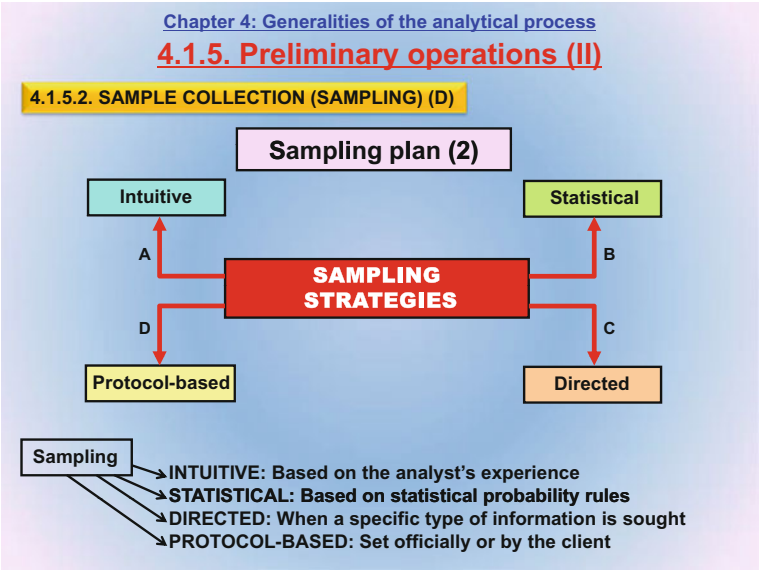
The so-called "sampling plan" or "sampling strategy" is a detailed description of the experimental procedure to be followed in order to collect samples, which differs depending on the particular information required. Thus, if contamination with organic matter by effect of vessel cleaning in a 1 ha beach strip is to be assessed, the sampling plan will differ depending on whether the target information is the average contaminant content of the whole beach, the shore or only tainted zones.

The sampling plan or strategy to be used in order to fulfil the information demand should afford *a balance* between

- representativeness (a capital analytical property as shown in Slide 2.4), which should be maximized, and
- productivity-related properties (namely, cost-effectiveness, and personnel and environmental safety).

The contradictory nature of these two aims is clearly apparent from Slide 2.60, which exposes the contradictions between analytical properties.

Slide 4.16



This slide defines the four most common types of sampling plans, which share some common traits despite their differences, and can be illustrated with the following examples:

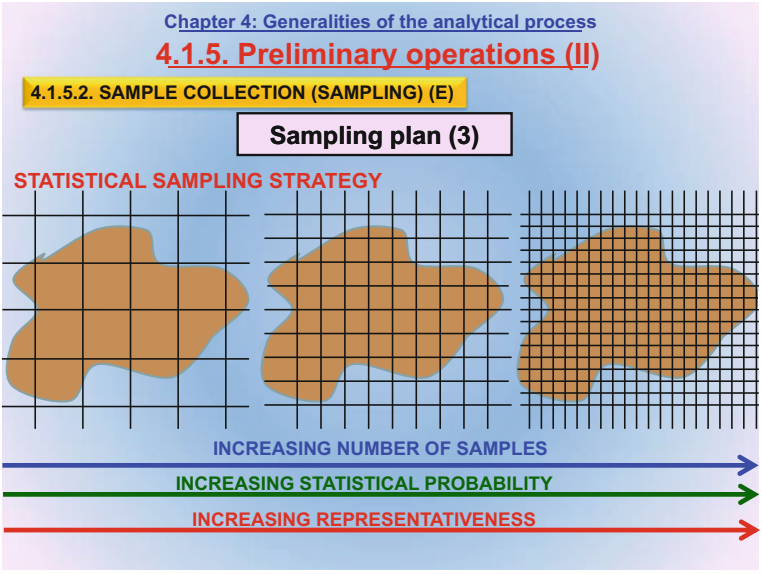
(A) *Intuitive sampling*. An expert collecting samples of mineral water from a spring will expand the collected set if any colour or odour change, or the presence of suspended matter, is observed.

(B) *Statistical sampling*. Representativeness of the samples is maximized according to a preset probability level. Thus, a field will be split into 200 squares for sampling if a high representativeness is sought but only 20 if moderate representativeness suffices.

(C) *Directed sampling*. This sampling strategy is used when very specific information such as the organic matter content of suspended particles in a water stream is needed—in which case samples will be collected by filtration.

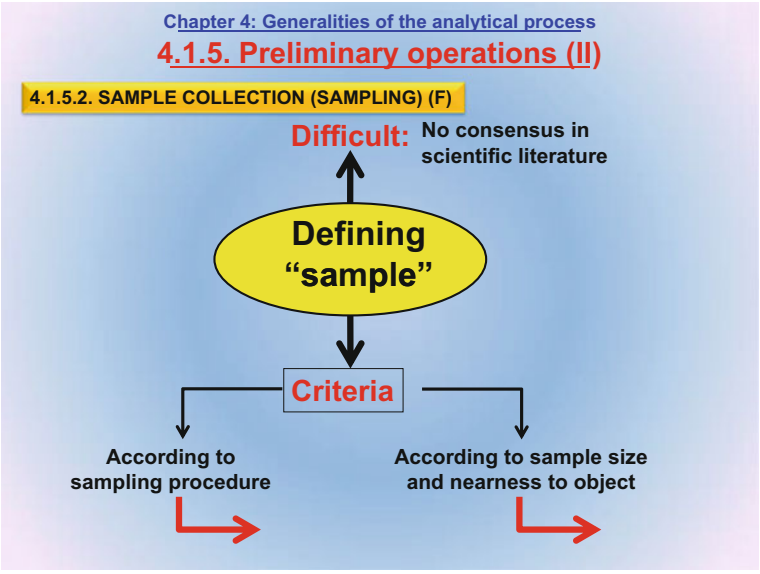
(D) *Protocol-based sampling*. This is the only choice when applicable regulations of the client require samples to be collected in a specific, carefully described manner. Such is the case, for example, with the determination of anabolic steroids in meat for human consumption, the sampling protocol for which is specified in an European Union directive.

Slide 4.17



This is an example of a statistical sampling plan. The aim is to determine available nitrogen in an agricultural field (the object). To this end, the field will be split into a variable number of imaginary squares depending on the desired level of representativeness. The probability of a sample being collected, and its representativeness, will increase with increasing number of squares. Samples will be collected from all squares or only from those previously selected in statistical terms.

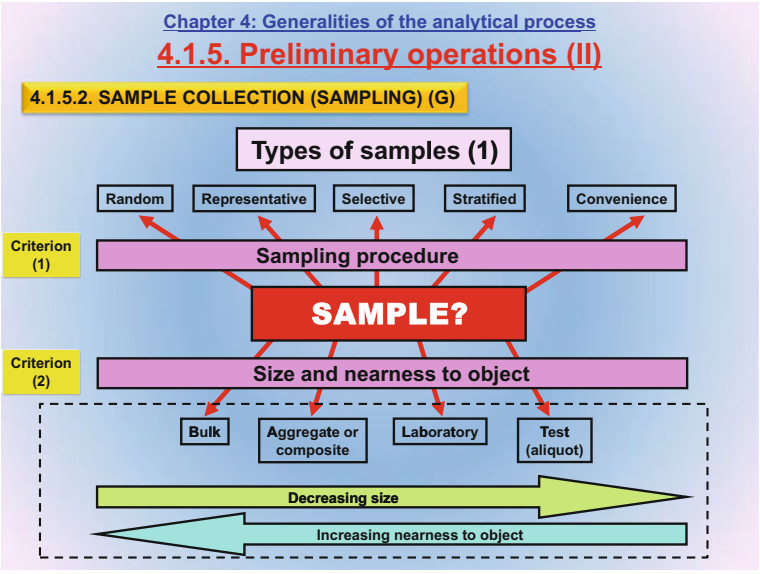
Slide 4.18



The word "sample" has been defined in a number of ways in the scientific and technical literature. This slide classifies sample designations according to two complementary criteria, namely: (1) sampling procedure, and (2) sample size and nearness to the object.

The two ensuing types of sample are shown in Slide 4.19 and defined in Slide 4.20.

Slide 4.19

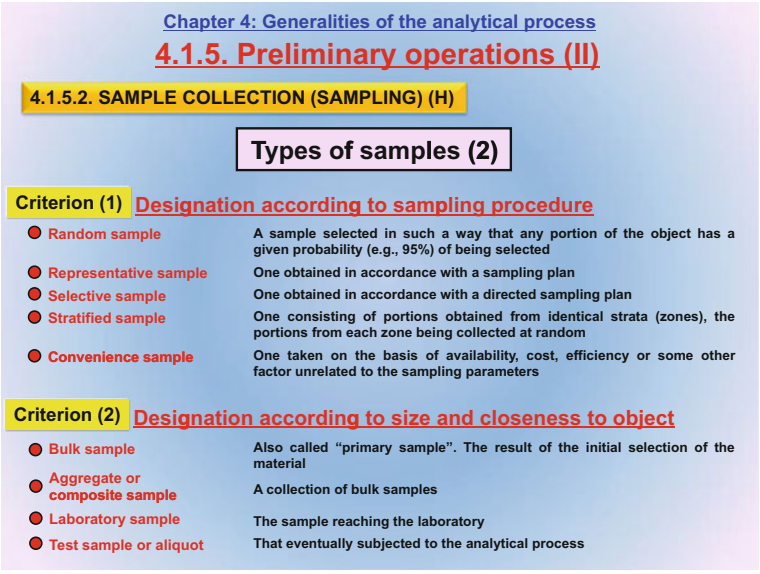


These are the different types of sample arising from the classification in the previous slide, based on the way samples are collected (Criterion 1), and their size and nearness to the object (Criterion 2).

These types of sample, designated by their qualifiers, are defined in the next slide.

Size decreases and nearness to the object increases from “bulk sample” to “test sample” among the sample types established according to Criterion 2.

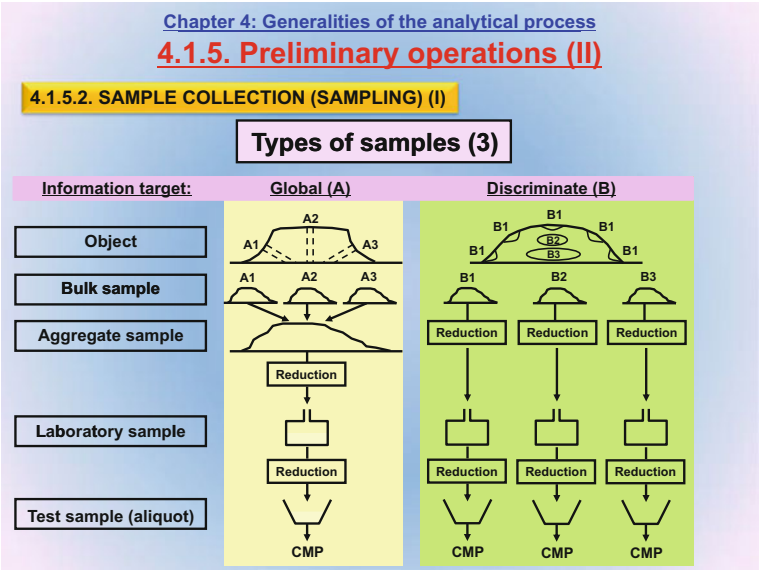
Slide 4.20



4.19.1. This slide defines the five types of samples established according to collection procedure (Criterion 1). The definitions are consistent with the sampling strategies in Slide 4.16.

4.19.2. The slide also defines the four types of samples according to size and nearness to the object (Criterion 2), which are illustrated in the next slide.

Slide 4.21



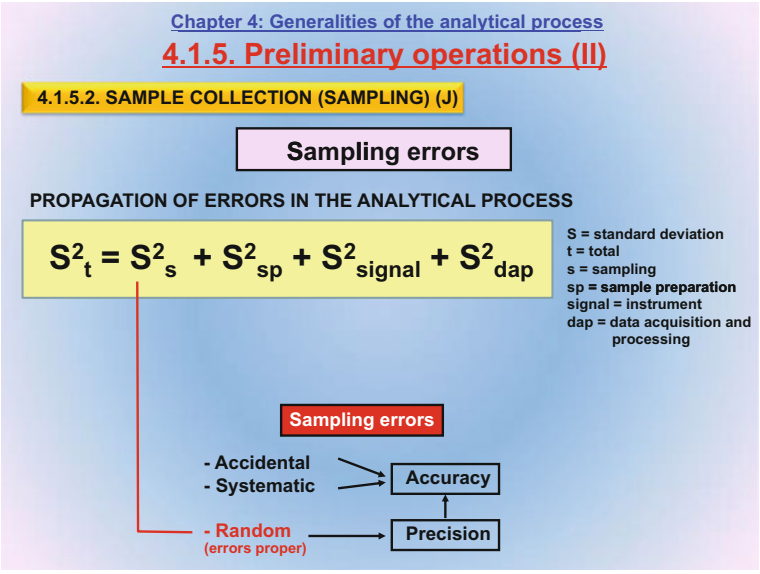
This slide illustrates the five types of samples established according to Criterion 2 in Slides 4.19 and 4.20 in relation to two different sampling strategies dictated by the type of information required, namely: (A) the mean content of the object (overall information) and (B) the contents of different parts of the object (discriminate information).

The example is the determination of the gold content in several tons of pyrite mining waste. The central and right-most columns show the object and the different types of samples that can be withdrawn from it.

If the aim is to know the concentration of gold (mg/kg) in the waste stack, and hence the total amount of gold that can be extracted from it, then the global sampling strategy should be used. For this purpose, a mechanically operated screw drill will be used to collect at least three samples (see Slide 4.23, solid sample) for mixing and homogenizing in order to obtain an aggregate or composite sample. The composite sample will be reduced in size for transfer to the laboratory, where it will be further reduced to a representative aliquot for direct application of the analytical process (CMP).

If the aim is to locate where the gold in the stack is, then bulk samples will be collected from the surface (B1), middle (B2) and bottom (B3) of the stock. Rather than being mixed, the three bulk samples will be reduced separately for delivery to the laboratory and independent processing with the CMP in order to obtain three different results that will reveal where gold in the stack is concentrated.

Slide 4.22



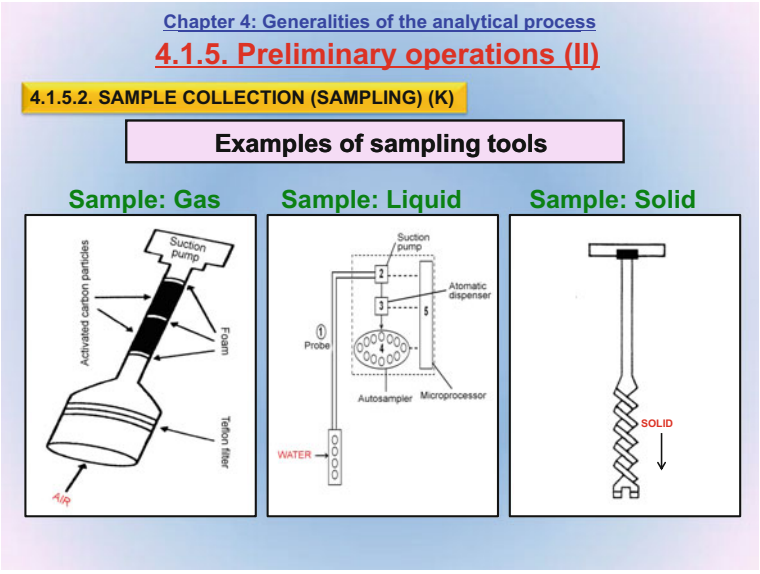
4.22.1. Based on the statistical theory of error propagation, the total error made in an analytical process is the combination of all errors made in its steps. Based on the principle of additivity of variances, the equation shows the approximate contribution of each step to the overall variance. As can clearly be seen, the preliminary operations of the analytical process (sampling and sample treatment) contribute especially markedly to its overall variance. Hence their strategic significance.

4.22.2. Similarly to the errors defined in Slides 2.9 and 2.10, sampling errors can be of the following types:

(1) *Accidental errors*, which occur in exceptional situations (e.g., operator distractions).
(2) *Systematic errors*, which will inevitable be present unless their source (e.g., poorly calibrated volume or mass measuring equipment) is eliminated.
(3) *Random errors*, which are due to chance in sampling and constitute "sampling errors" proper in statistical terms. They are denoted by S^2_S in the equation.

Accidental and systematic sampling errors have a direct impact on the accuracy of the results, whereas random errors affect precision—and hence accuracy (see Slide 2.10).

Slide 4.23



This slide exemplifies sampling systems for gaseous, liquid and solid samples. As can be seen, the sampling procedure of choice is again dictated by the type of information sought.

A gaseous object (e.g., air)

If the aim is to determine organic contaminants in the atmosphere near a chemical solvent factory, samples are obtained by using a portable suction pump with adjustable aspiration rate (e.g., in L/min) fitted with a nozzle. The pump includes a Teflon filter to retain air particulates and a sorption tube filled with foam containing activated carbon particles or carbon nanotubes. Organic molecules are retained on the filter as air circulates through the pump. When sampling is finished, the tube is transferred to the laboratory and the Teflon filter, which was previously tared, is weighed to determine the amount of particles present in the air. Then, retained contaminants are easily eluted with a volume of 2–5 mL of methanol.

A liquid object (e.g., lake water)

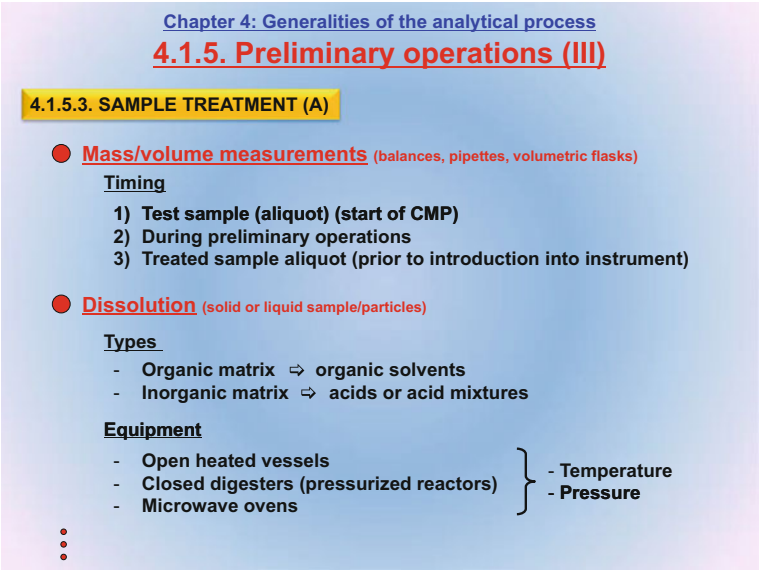
If the aim is to determine the concentration in mg/L of suspended particles at different depths in a mountain lake, then samples are obtained by using appropriate sampling equipment on board of a ship (see central image in the slide). The equipment comprises a sampling probe (1) that can be immersed to a variable depth; a suction pump (2) to aspirate water at a given flow-rate for a fixed time in order to collect samples at different depths; an automatic dispenser (3) to sequentially fill autosampler vials (4); and a microprocessor (5) to control the whole process. In this way, *n* discriminate samples are collected at different depths from the lake (the object).

A solid object (e.g., beach sand)

If the aim is to determine the concentration of organic contaminants at different depths in a beach sand under the potential influence of ship cleaning wastewater from a nearby port, then a screw drill such as that shown on the right picture is used. The operator will insert the drill in the ground with mechanical assistance and then draw it vertically in order to collect sand withdrawn at different depths from its thread.

4.1.5.3 Sample Treatment (8 Slides)

Slide 4.24



"Sample treatment" designates the body of operations performed to condition the bulk sample for insertion into the measuring instrument as depicted in Slide 4.12.

This slide and the next few provide a brief description of the most salient preliminary operations of the analytical process.

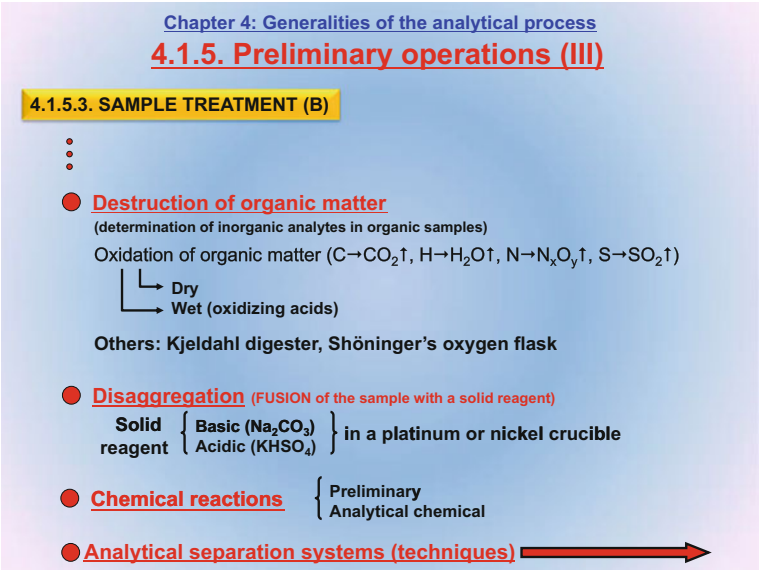
Mass and volume measurements, which are made with balances and volumetric ware (calibrated flasks, pipettes), respectively, constitute typical preliminary operations of the analytical process intended to establish the mass, in grams, or the volume, in millilitres, of test sample (aliquot) that is to be subjected to the CMP. Also, however, they are often made during the process or prior to inserting the sample portion to be measured into the instrument.

The preliminary operation *dissolution* (or *solubilization*) is only performed on samples containing solids. The "end-product" here is a transparent (colourless or otherwise) solution containing no suspended solids. The solvent to be used will depend on the nature of the sample matrix ("like dissolves like" is the rule of thumb here). Operationally, the solubilization procedure can vary widely. Thus, it may use

energy in the form of pressure or temperature, heated open tubes with or without a coolant, pressurized steel digesters, or microwave or ultrasound energy, for example. A detailed description of all possibilities is beyond the scope of this book, however.

The next slide describes additional types of sample preparation procedures.

Slide 4.25



This slide continues the description of sample treatment operations started in the previous one.

Destruction of organic matter is only used to determine inorganic analytes in organic samples (e.g., the total metal content of petroleum crude). Organic matter is "destroyed" by oxidizing carbon to carbon dioxide, hydrogen to water vapour, nitrogen to volatile oxides and sulphur to also volatile sulphur dioxide. These transformations can be accomplished simply by heating the sample until no further vapour is released—there may be losses through abrupt spillage—or by attack with an oxidant such as nitric acid. As a result, the sample first becomes brown, then black and eventually clear, leaving a residue of metal oxides.

Disaggregation can be considered an especially aggressive form of dissolution and is used when traditional solubilization procedures with acids or acid mixtures (e.g. *aqua regia*) fail to completely dissolve a sample—usually an inorganic sample. The procedure is usually as follows:

The solid sample to be dissolved is mixed with a fusion flux (e.g., a basic substance such as sodium carbonate) in a 1:10 ratio;

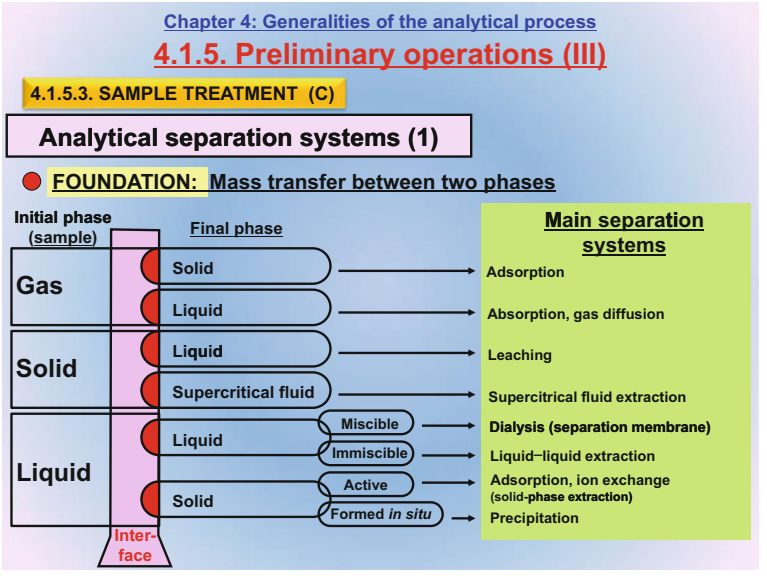
(1) the mixture is placed in a nickel or platinum crucible;
(2) the crucible is heated in a furnace at a high temperature until the mixture is completely melted;
(3) the crucible is allowed to cool down and
(4) the molten mass is dissolved at room temperature by immersion in the solvent to obtain a clear solution containing no suspended matter.

Preliminary chemical reactions are used to make the sample suitable for the intended purpose. One common preliminary reaction is that between a selective masking agent and the sample to form chelates with potentially interfering species present and improve the selectivity as a result (see Slide 6.29). Another common practice is to add a buffer in order to adjust the pH of the sample as required for its subsequent treatment. As a rule, preliminary chemical reactions involve the sample matrix rather than the analyte.

Unlike preliminary reactions, *analytical chemical reactions* involve the analyte to be detected or determined, which is "derivatized" (that is, converted into a suitable derivative for measurement in the second step of the analytical process). Thus, highly polar compounds must be subjected to a prior silylation reaction for determination by gas chromatography. Also, an analyte with inadequate photometric or fluorimetric properties must be derivatized for spectrophotometric or spectrofluorimetric determination, respectively, with adequate selectivity.

Analytical separation systems, which are the most relevant to sample preparation, are briefly described in Slides 4.26–4.31.

Slide 4.26



Analytical separation systems, often referred to as "analytical separation techniques" (ASTs) (see Slide 1.32), are extremely important in Analytical Chemistry because they help improve two essential properties: sensitivity and selectivity. Some authors have claimed that the history of Analytical Chemistry can be traced through progress in the development of separation systems.

Separation systems are operationally simple: a single or several analytes are partitioned between two phases on the assumption that they possess an increased affinity for either. Mass transfer between the two phases may also affect other components of the sample matrix—which should be removed in order to avoid interferences.

On the left of the slide are shown the phase types most usually involved in a separation process. The initial phase is that containing the sample and the final phase that added to the previous one or formed during the process. Mass transfer, which is the key to success in the separation, occurs at the interface between the two phases (red half-circles in the slide). Obviously, the interface should be as large as possible for easier transfer.

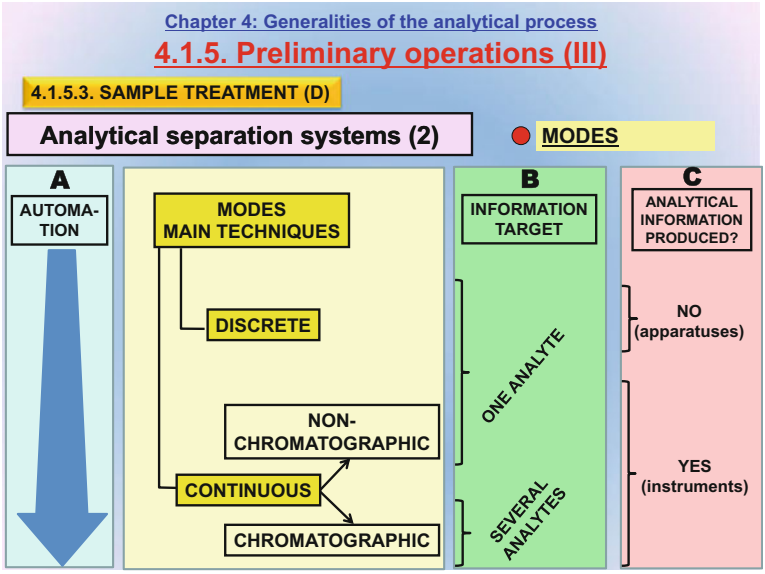
The phases involved are usually solids, liquids or gases, but can also be supercritical fluids. Combinations of the different types of phases have led to the development of a wide array of analytical separation systems for sample preparation the most salient of which are shown on the right of the slide.

If the sample (initial phase) is a *gas*, the phase to be added can be a solid for adsorption or a bubbling liquid for absorption (dissolution) or diffusion. Gas diffusion is a process by which the concentration gradient of a gas such as ammonia in a liquid causes dissolved volatile molecules to migrate to a porous membrane and pass through it into an acceptor stream (an acid stream for ammonia).

If the sample is a *solid*, the target component can be selectively dissolved with a suitable solvent (the final, liquid phase) for leaching or liquid–solid extraction (or supercritical fluid extraction if the final phase is supercritical CO_2, for example).

If the sample is a *liquid*, the final phase can be another liquid or a solid. The most common example of separation as a liquid phase—one that is formed in situ—is distillation, which is scarcely used for analytical purposes and not shown in the slide. If the liquid used as final phase is miscible with the liquid sample, the process is called "dialysis" and involves using a porous membrane for mass transfer (for example, a dialysis membrane to facilitate the passage of urea and uric acid from blood serum into an acceptor solution). On the other hand, if the final phase is not miscible with the sample, the process constitutes a typical liquid–liquid extraction. When the final phase is a surface-active solid, the transfer process involves absorption (as in solid-phase extraction, for example). Finally, a solid final phase can be formed in situ by precipitation from a liquid initial phase.

Slide 4.27



4.27.1. How are analytical separation systems implemented in the analytical process? This question is answered here by showing the most usual technical modes for this purpose.

- In *discrete separation systems*, contact between the two phases occurs in a single, unique manner, so only one separation equilibrium is established. Such is the case, for example, with liquid–liquid extraction in a separation funnel.
- In *continuous separation systems*, the so-called "mobile phase" is passed uninterruptedly through the so-called "stationary phase". In *non-chromatographic continuous separation systems*, the analyte partitions in a single thermodynamic equilibrium; in *chromatographic continuous separation systems*, however, it partitions in many different zones to give multiple analytes.

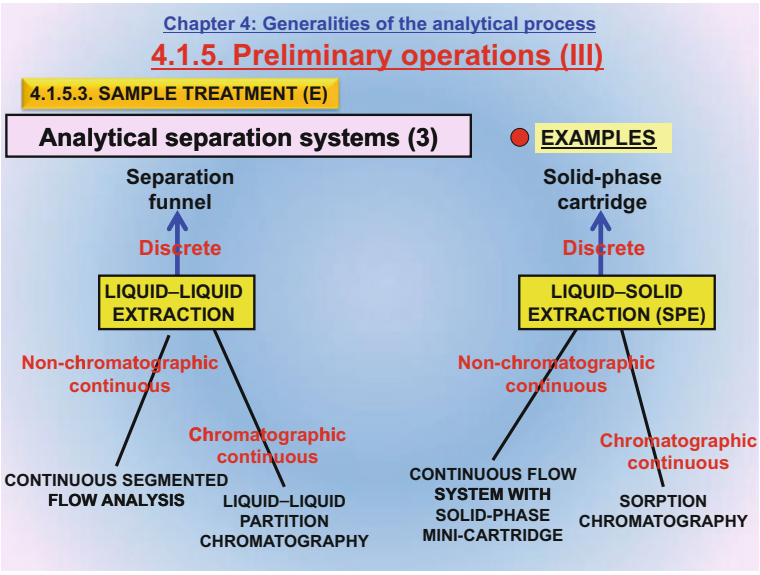
4.27.2. The ease of automation of analytical separation systems increases from discrete to continuous chromatographic systems by effect of commercial availability of separation equipment also increasing in that direction.

4.27.3. The information target(s) of analytical processes using separation systems can be (1) the presence or concentration of an analyte or analyte family with discrete and non-chromatographic continuous systems; and (2) the presence or concentration of individual analytes in a mixture with chromatographic continuous systems.

4.27.4. Discrete systems operate independently of analytical measuring equipment and are thus apparatuses because they produce no analytical information. On

the other hand, continuous separation systems, both chromatographic and non-chromatographic, invariably use a continuous detection system, whether destructive or non-destructive, and are thus instruments.

Slide 4.28

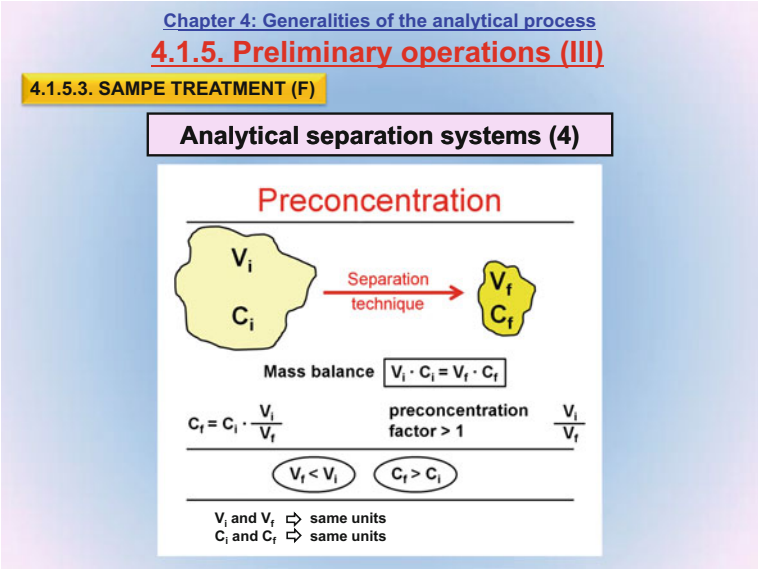


This slide exemplifies the separation modes explained in the previous one.

Liquid–liquid separation can be implemented in a discrete manner by using a separation funnel to mix appropriate volumes of the two phases. Also, it can be implemented by bringing the two phases into contact in a continuous segmented flow system for non-chromatographic continuous separation. Finally, it can be accomplished by having the analyte partition between a mobile liquid phase and a stationary solid phase (e.g., a chromatographic column) for chromatographic continuous separation.

Liquid–solid separation can be accomplished by inserting a solid-phase cartridge in a continuous-flow system (solid-phase extraction, SPE) or by having a liquid phase containing the analyte pass through a solid phase held in a column (sorption chromatography).

Slide 4.29



This slide illustrates one of the main purposes of separation systems, namely: preconcentrating analytes. If the analytes are highly diluted in the sample (that is, at very low concentrations, C_i, in a sample volume V_i), subjecting an aliquot to the analytical process will provide no measurable signal. However, reducing the sample volume (to V_f) can artificially increase the analyte concentrations to a high enough level C_f for a new sample aliquot to provide a measurable signal. Obviously, this procedure has a direct impact on the basic analytical property "sensitivity" (see Slide 2.33).

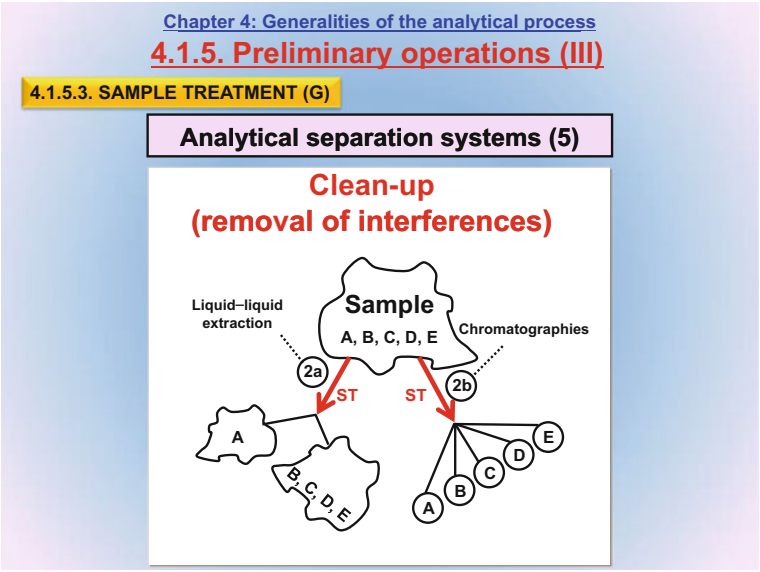
The final concentration of analyte, C_f, can be calculated from a mass balance (that is, from the amount of analyte present before and after reducing the sample volume, which will be identical).

The degree of preconcentration will increase with increasing preconcentration factor, which is the ratio of the initial to final sample volume: V_i/V_f.

For effective preconcentration, the final volume should obviously be smaller than the initial volume—and the final concentration higher than the initial concentration as a result.

The mass balance should be established by using volumes and concentrations in identical units.

Slide 4.30

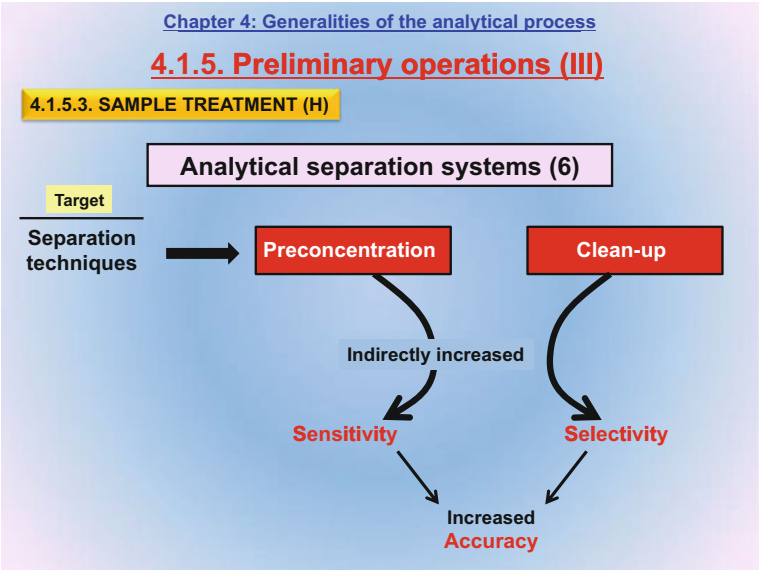


One other crucial purpose of analytical separation systems is the removal of interferences (so called "clean-up") to improve the basic analytical property "selectivity".

A sample can be cleaned up in two different ways with an analytical separation system depending on the nature of the information sought.

If the target information concerns a single analyte in the sample, the system to be used should allow the analyte to be physically isolated from all others in a separate phase. If a more ambitious goal such as determining the presence or concentration of more than one analyte is pursued, then each analyte should be isolated in its own, distinct zone by using a chromatographic separation system (see Slide 4.27).

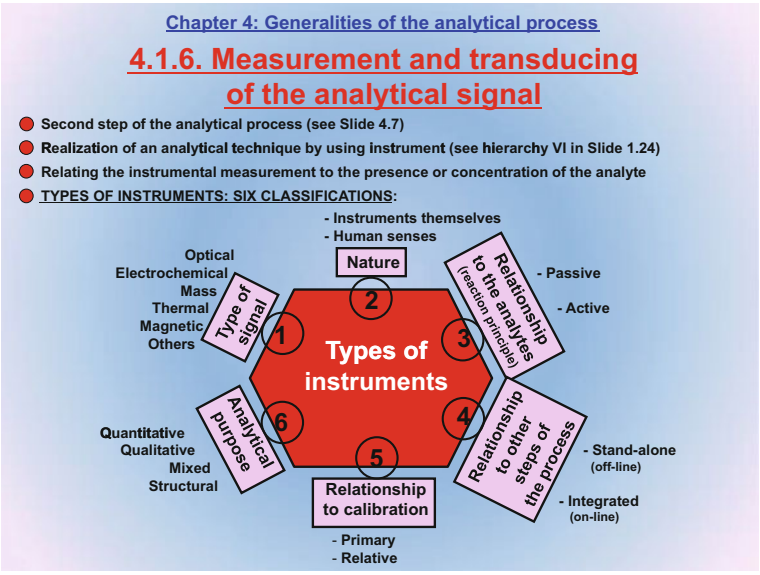
Slide 4.31



In summary, the primary purposes of using analytical separation systems for sample preparation in the second sub-step of the preliminary operations of the analytical process are preconcentration (Slide 4.29) and sample clean-up (Slide 4.30), which provide an indirect means for increasing sensitivity and selectivity, respectively, in addition to accuracy (see Slide 2.4).

4.1.6 Measurement and Transducing of the Analytical Signal (1 Slide)

Slide 4.32



The second step of the analytical process (see Slide 4.7) involves measuring and transducing[1] the analytical signal (primary data), which is processed to obtain the analytical results in the third. This operation requires using a measuring instrument (see the hierarchy in Slide 1.24).

A number of instruments for signal measurement and transducing based on a variety of principles have been made commercially available in the past fifty years that can be classified in a non-mutually exclusive manner as follows:

(1) According to the nature of the signals they measure, instruments can be of the *optical, electroanalytical, mass, thermal* or *magnetic* type, among others.
(2) According to their own nature, instruments can be the *human senses*, which are typically used in Classical Qualitative Analysis, or instruments proper (e.g., pH-meters, photometers, fluorimeters) (see Slide 6.27).
(3) According to their relationship to the analytes to be detected or quantified (or their reaction products with derivatizing agents), instruments can be *passive* (that is, simply receiving the analytical signal, as in mass weighed with a

[1]In this context, the word "transducing" designates the transformation of the signal originally produced by the instrument (usually in volts or millivolts) into the typical unit for the measured quantity (e.g., absorbance in UV-Visible absorption spectroscopy), which is that used in the third step of the analytical process.

balance), or *active* (that is, causing the analyte to emit a signal by applying it some form of energy such as light in photometry or fluorimetry).

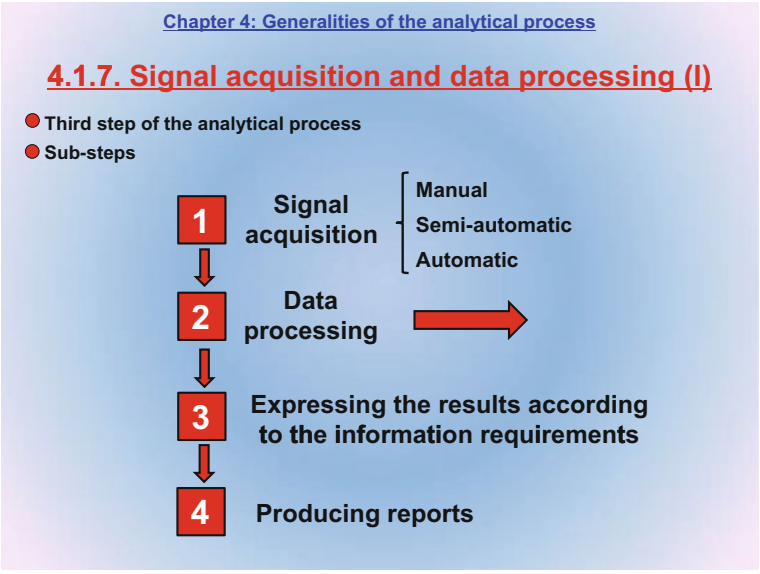
(4) According to their relationship to the first step of the analytical process, the instruments used in its second step can be of the *stand-alone* (*off-line*) type, to which samples are usually delivered by hand (e.g., by filling a cuvette for placement in a photometer); or of the *integrated* (*on-line*) type, which come with their own, automatic sample delivery system (e.g., the flame ionization detector in a gas chromatograph, which is used to continuously receive mobile phase from the column and detect passage of an analyte).

(5) Instruments require calibration to ensure proper functioning, and so do methods sometimes. Whereas calibrating a *relative method* is usually feasible (e.g., by constructing a calibration curve for a photometric determination), calibrating an *absolute method* such as a gravimetry is impossible (see Chap. 5).

(6) Finally, instruments can be classified as *qualitative*, *quantitative*, *mixed* and *structural* according to their analytical purpose. Most instruments are of the mixed type because they are flexible enough for adaptation to a variety of purposes; such is the case, for example, with mass spectrometers. Some, however, only have a single, specific purpose. Thus, a pH-meter can only be used for quantitative measurements; also, transmission infrared absorption spectrophotometers are basically used for identification (qualitative) purposes by routine analysis laboratories even though they also afford quantification.

4.1.7 Data Acquisition and Processing (2 Slides)

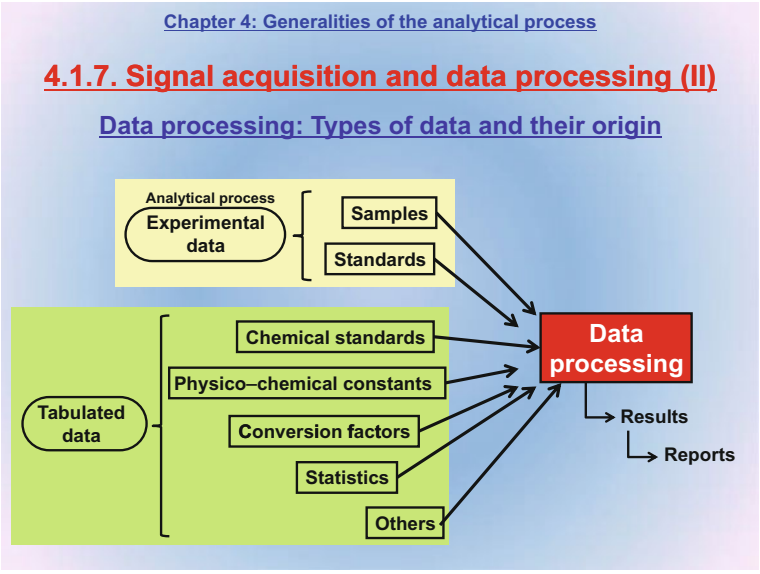
Slide 4.33



The third, last step of the CMP involves the acquisition of analytical signals and their processing to obtain the results needed. This step is commonly designated "data acquisition and processing" (DAP) and comprises the four sub-steps shown in this slide, which are closely related to the primary data—information—knowledge hierarchy of Slide 1.20.

(1) The first DAP sub-step is *signal acquisition*. Signals can be acquired manually (e.g., by reading a digital display and recording the readout on a laboratory notebook), semi-automatically (e.g., by measuring retention times, and peak heights and areas, in a chromatogram) or completely automatically.
(2) The next sub-step is *data processing*, which is dealt with in the next slide.
(3) The third step involves *expressing the results* (information), whether qualitative or quantitative, in accordance with legal requirements or the client's needs.
(4) The last step is *producing a report* (knowledge) based on the results for their placement in context and comparison with the information requirements and legal limits in order to, for example, facilitate well-grounded, timely decision-making.

Slide 4.34



This slide expands on the description of the second DAP sub-step given in the previous one, namely: *data processing*, which leads to obtainment of the results and production of a report.

The data to be processed can be of two different types:

- *Primary experimental data* obtained by analysing samples and tangible standards in the analytical process.
- *Tabulated data in printed or on-line form* for chemical standards (e.g., purity, hygroscopicity), physico-chemical constants (e.g., gravimetric factors, Slides 5.17 and 5.18), conversion factors (e.g., those for incomplete recoveries) or statistics (e.g., Student's *t*), among others.

4.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

M. Valcárcel

Springer-Verlag, Berlin, 2000

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

This chapter overlaps to a great extent with Chap. 4 in Valcárcel's book ("The measurement process in Chemistry") except that the text has been simplified in some parts and expanded in others to better illustrate the present and future of Analytical Chemistry 15 years later. Valcárcel's book can be used as a reference for direct consultation of the contents of this chapter.

Sampling for Analytical Purposes

Pierre Gy

Wiley, New York, 1999.

This is a short book (150 pages) exclusively devoted to the first operation of the analytical process. In addition to providing an integral, comprehensive definition, it summarizes all sampling choices dealt with in this chapter and a few others. The book is very useful for designing sampling processes and can help students expand their knowledge of specific sampling modes.

Non-chromatographic continuous separation techniques

M. Valcárcel & M.D. Luque de Castro

Royal Society of Chemistry (UK), Cambridge, 1991.

This was the first book to introduce the concept "non-chromatographic continuous separation systems", based on the principles of flow injection analysis. Such systems are used not for discriminate separation of analytes but rather to facilitate automation of sample preparation. The book deals with gas–liquid (diffusion, distillation), liquid–liquid (extraction) and solid–liquid systems (ion exchange, sorption).

4.3 Questions on the Topic (Answered in Annex 2)

4.1. What question does the development of an analytical process essentially answer regarding extraction of (bio)chemical information from an object: what, how, when or where?

4.2. Why do analytical processes invariably use measurement standards? How are they used?

4.3. A manufacturing process leads to an error in the quality-related parameters for the product that requires analytical control. What kind of sampling should be done in this situation?

[ ] Intuitive
[ ] Statistical
[ ] Directed
[ ] Protocol-based

Explain why.

4.4. What is the difference between "dissolution" and "disaggregation" of a solid sample?
4.5. Give four definitions of "sampling" or "sample collection".
4.6. How does the availability of materials and equipment (reagents, solvents, apparatuses, instruments, etc.) influence the choice of an analytical process for a specific sample–analyte pair? Use one or more examples.
4.7. What factors dictate the choice of an analytical method? What is usually the most important?
4.8. Tick the true statements about the preliminary operations of the analytical process:

[ ] They are equivalent to so-called "sample treatment"
[ ] They typically account for 50–70% of the length of a CMP
[ ] They come after measurement and transducing of the analytical signal
[ ] They have little impact on the quality of the final result

4.9. Why is sampling important in chemical measurement processes? Tick the correct answers.

[ ] Because it influences selectivity and sensitivity
[ ] Because it is essential to assure representativeness in the final result
[ ] Because it is a key to robustness in CMPs
[ ] Because it has a direct impact on the accuracy of the results of CMPs

4.10. Are equipment and method calibration part of a CMP? Why?
4.11. Name at least five features of the preliminary operations of CMPs. Is any of them positive?
4.12. What are the positive contributions of the preliminary operations of CMPs?
4.13. How are instruments classified according to the nature of the raw signals they provide?
4.14. What are the two information sources for the third step of the analytical process (data processing and result delivery)?
4.15. Name the five factors governing the development of an analytical measurement process.
4.16. What are the two main purposes of the preliminary operations of CMPs?
4.17. Why is variability a negative connotation of analytical processes?
4.18. How is automatability related to the preliminary operations of the analytical process?
4.19. What is the most sluggish, labour-intensive and error-prone step of an analytical process?

4.20. What should be balanced in designing a sampling plan?
4.21. What are the four types of sampling arising from the overall sampling plan?
4.22. What names are samples given according to size and nearness to the object?
4.23. Distinguish “object” and “sample”.
4.24. When and why must organic matter in a sample be destroyed in the preliminary operations of the analytical process?
4.25. What basic properties are favourably affected by separation techniques? What capital property is also favoured? What basic property can be adversely affected?
4.26. How are instruments classified according to the nature of the analytes to be determined?
4.27. How are sampling and representativeness related?
4.28. What are the main types of analytical separation systems?

4.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened by about 25% for teaching Analytical Chemistry to students not majoring in Chemistry. The following 8 slides can be omitted for this purpose:

- Section 4.1.1: Slide 4.3
- Section 4.1.2: Slide 4.4
- Section 4.1.4: Slide 4.8
- Section 4.1.5.1: Slide 4.10
- Section 4.1.5.2: Slides 4.16, 4.17, 4.23 and 4.27

Quantitative Analytical Processes

5

Abstract

This chapter is concerned with Quantitative Analysis and its classification. Once the presence of a given analyte is known, the former is used to obtain detailed information about the amount or concentration present in the sample. Quantitative Analysis is therefore indispensable with a view to solving analytical problems where the amount or concentration of the analyte (a numerical value) is a key datum. A brief introduction to the definition of "Quantitative Analysis" is followed by a discussion of the great difficulty involved in distinguishing the concept "instrument" in Classical Analysis and Instrumental Analysis. A subsequent section explains the different ways of expressing a quantitative result. However, the main focus of this chapter is methods for Quantitative Analysis, which are described and exemplified in Sects. 5.1.4 and 5.1.5. Some slides are exclusively devoted to gravimetry and titrimetry, which are typical of Classical Analysis.

Teaching Objectives

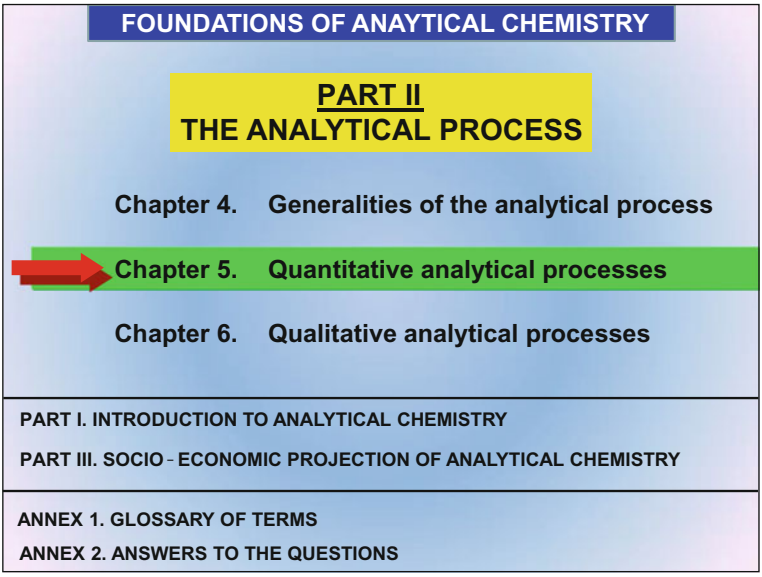
- To describe the most salient aspects of quantification processes in Analytical Chemistry.
- To characterize the quantitative response and its forms of expression.
- To explain the different manners of calibrating in Quantitative Analysis.
- To describe classical and instrumental quantification techniques.
- To exemplify the different types of analytical quantification methods.

Electronic supplementary material The online version of this chapter (doi:10.1007/978-3-319-62872-1_5) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_5

5.1 Explanation of the Slides

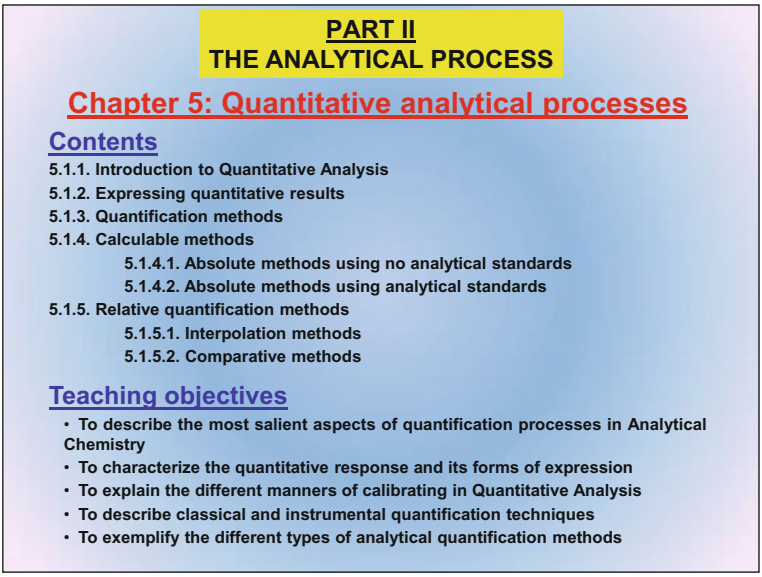
Slide 5.1



This slide places in context in Part II ("The Analytical Process") and shows the other two parts.

This chapter is the second in Part II and is concerned with analytical processes leading to the obtainment of quantitative results (that is, analytical information in the form of numerical values).

Slide 5.2

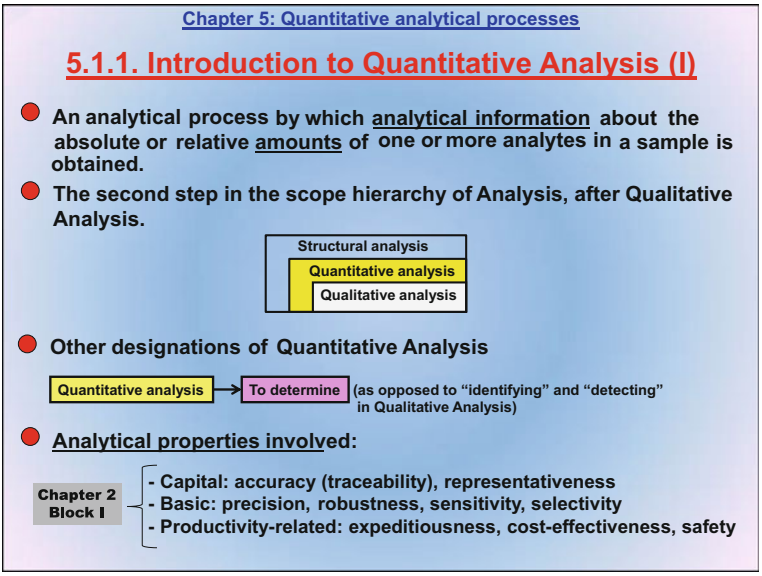


5.2.1. These are the five sections of the chapter. A brief introduction to the definition of Quantitative Analysis (5.1.1) is followed by a description of the forms of expression of quantitative results (5.1.2), and the description (5.1.3) and exemplification (5.1.4 and 5.1.5) of analytical quantification methods.

5.2.2. The slide also shows the teaching objectives to be fulfilled, which include introducing students to Quantitative Analysis, describing quantitative responses and their forms of expression, characterizing calibration, distinguishing classical and instrumental methods, and describing quantification methods.

5.1.1 Introduction to Quantitative Analysis (4 Slides)

Slide 5.3



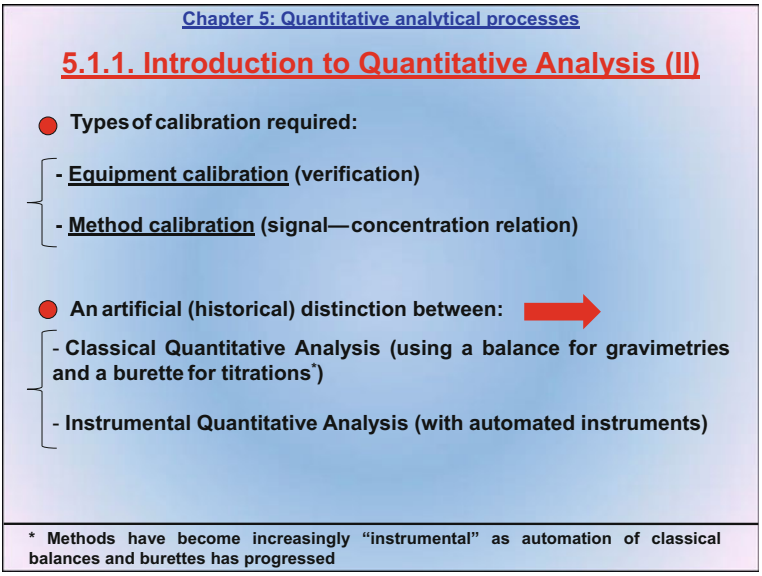
The term "Quantitative Analysis" designates those analytical processes leading to a numerical response (usually the amount or concentration of one or more analytes in a sample).

Based on the classification according to purpose of Slide 1.31, Quantitative Analysis is the second step in the analytical process and follows Qualitative Analysis (Chap. 6). In fact, it is pointless to perform a quantitative analytical process if the analyte to be quantified has not previously been found to be present in the sample.

Quantitative Analysis can be described in terms of the verbs *to determine* and *to quantify*, both of which involve finding a numerical value: the amount of analyte present in a sample. By contrast, Qualitative Analysis is concerned with the verbs *to identify* and *to detect*, which are related to the presence of the analyte in the sample.

Quantitative Analysis is linked to the three types of analytical properties described in Chap. 2, namely: capital, basic and productivity-related.

Slide 5.4



5.4.1. In Quantitative Analysis, traceability chains are sustained by equipment and method calibration.

- A quantitative result is incomplete unless the references used to obtain it are stated. Thus, an instrument must be subjected to *equipment calibration* against a well-established reference so that the results will be reliable and consistent with the analytical problem addressed (see Slide 7.10). In fact, a result should be traceable to the instrument that produced it (Slide 3.25) and hence to the standard used for calibration.
- Some analytical processes obtain the analytical result from a calibration curve (Slides 2.36 and 2.37) or by direct comparison (a rule of three) of signals and concentrations of references subjected to exactly the same analytical process as the sample (that is, by *method calibration*).

These concepts are defined in greater detail and exemplified in Slides 3.19 and 3.20.

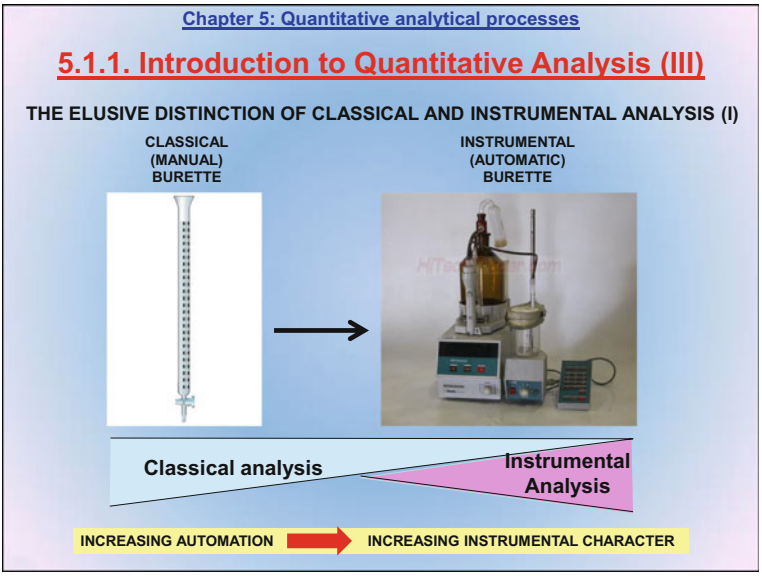
5.4.2. Recent advances in measuring instruments have rendered older ones obsolete for use in high-tech laboratories but not in more simple settings such as teaching laboratories. Quantitative Analysis can thus be classified as follows on historical grounds (specifically, in terms of advances in equipment over the years):

- *Classical* Quantitative Analysis, which encompasses those methods using traditional instruments such as conventional burettes and balances.

- *Instrumental* Quantitative Analysis, which uses more sophisticated (digital, automated, miniaturized) equipment such as UV–visible absorption spectrophotometers, potentiometers, mass spectrometers or liquid chromatographs.

Despite their clear-cut differences in concept, the two types of Quantitative Analysis are not so easy to distinguish in practice. Thus, as illustrated in the next two slides, sustained technical progress has increasingly blurred the boundary between classical and instrumental analysis.

Slide 5.5



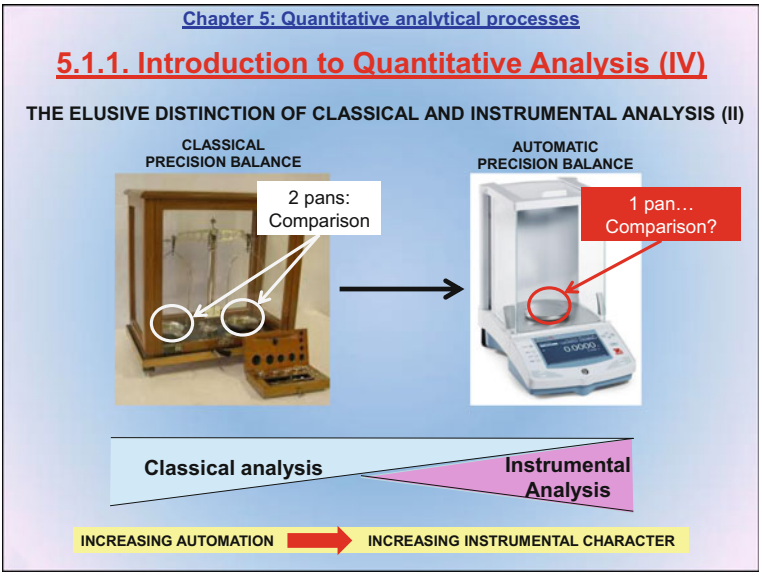
5.5.1. Whether burettes belong in classical or instrumental analysis is unclear. Thus, while manual burettes have been used in titrimetry for centuries, the classical burette has evolved to so great an extent that its automated, high-performance versions are more akin to Instrumental Analysis (see the examples in Slide 5.21).

Therefore, although a manually controlled burette could in theory be assigned to Instrumental Quantitative Analysis, it has become increasingly relevant to Classical Quantitative Analysis with time.

This slide exemplifies the difficulty in assigning instruments to either type of Quantitative Analysis.

5.5.2. Although the classification of Quantitative Analysis as classical or instrumental is based on historical grounds and somewhat artificial, the instrumental character of equipment increases with increasing automation (that is, decreasing operator involvement), and so does its closeness to Instrumental Quantitative Analysis.

Slide 5.6



5.6.1. Similarly to the previous slide, assigning a classical precision balance or an automated (analytical) balance to Classical or Instrumental Quantitative Analysis is complicated. Thus, the traditional two-pan balance is virtually obsolete now, so it can be associated to Classical Quantitative Analysis. On the other hand, the single-pan analytical balance is currently associated to Instrumental Quantitative Analysis. However, further technical progress in the future (e.g., automated weighing) may render the analytical balance obsolete and confine it to Classical Quantitative Analysis. Clearly, placing an instrument in either category of Quantitative Analysis can be rather difficult.

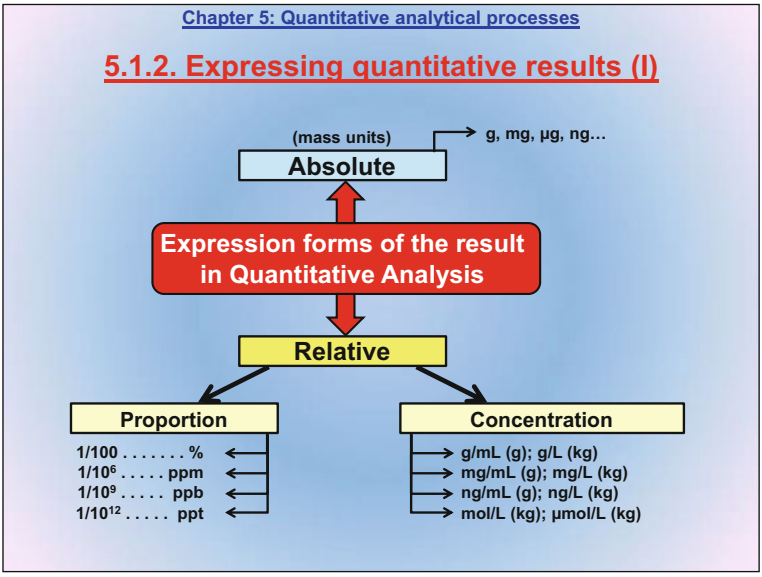
5.6.2. Although the boundary between Classical and Instrumental Analysis is blurry, whether an instrument is considered to pertain to Instrumental Analysis depends on its degree of automation (see Slide 5.5).

5.6.3. Interestingly, one of the greatest differences between classical and analytical balances is the number of pans they use. Thus, a classical balance has two pans: one for the sample to be weighed and the other for reference weights. As stated in Slide 3.3, measuring involves comparing. Clearly, in a classical balance the sample weight is compared with the combined weight of the reference weights placed on the other pan. Where, however, is the standard for an analytical balance, which uses a single pan (the sample pan)? Technical progress in the development of analytical balances has reduced operator involvement by avoiding the need to use reference weights—and hence led to increasing automation. The reference in an analytical balance is within the instrument: rather than weights, the balance uses magnets to measure the force needed to counter the sample weight (that is, the

atypical "standard" electromagnetic force). The measured force is automatically converted into mass units and shown on a display for reading by the operator.

5.1.2 Expressing Quantitative Results (4 Slides)

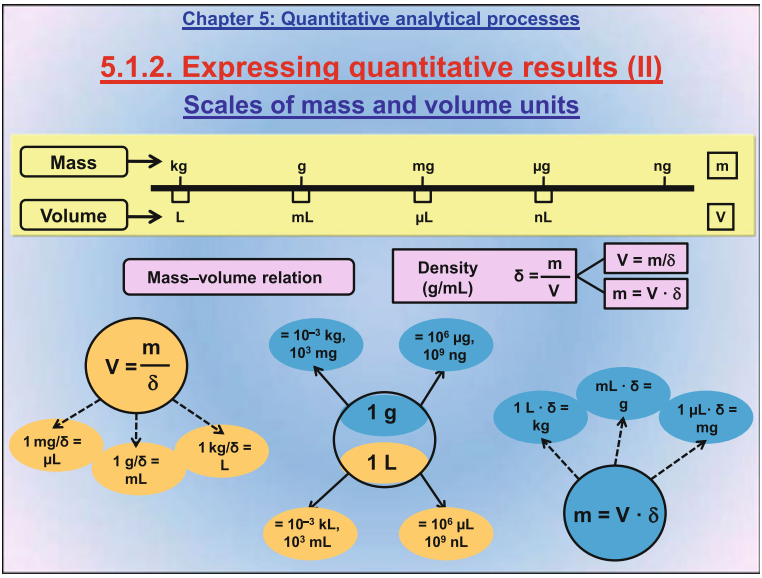
Slide 5.7



5.7.1. The results of quantitative analyses can be expressed in *absolute* form (namely, as the mass of analyte present in a given amount of sample) (see Slide 5.8). This slide shows some of the more commonly used mass units for this purpose.

5.7.2. Quantitative results can also be expressed in *relative* form (see Slide 5.8), whether as a proportion (e.g., the amount of analyte per unit, 10 units or 100 units of sample) or a concentration (the amount of analyte per—usually—sample mass or volume unit). The slide shows selected examples of the more common proportions and concentration units for expressing results.

Slide 5.8



5.8.1. This slide compares absolute forms of expression of mass and volume. Note that mass units are the references (the kilogram is an SI base standard), whereas volume units differ depending on density.

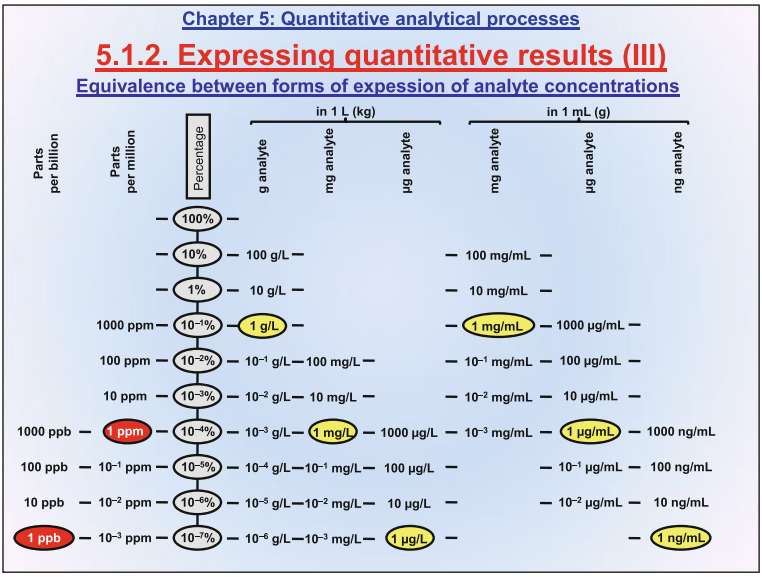
The slide also shows some mathematical equations for calculating mass and volume values at a given density—which relates the two quantities.

5.8.2. A volume of sample of 1 L can be expressed in different units and used to calculate the *sample volume* at a given density (in g/mL) for variable mass units. Thus, an amount of sample of 1 g corresponds to a volume in the millilitre (mL) range and 1 kg to a volume in the litre (L) range.

5.8.3. Similarly, a mass of sample of 1 g can be expressed in different units and used to calculate the *sample mass* at a given density (in g/mL) for variable volume units. Thus, a volume of sample of 1 L corresponds to a mass in the kilogram (kg) range and 1 µL to one in the milligram (mg) range.

National and international metrological bodies tend to avoid expressing results as volumes; rather, they convert them into masses through density. Thus, a concentration of 1.23 g/L in a liquid sample of unity density is usually reported as 1.23 g/kg.

Slide 5.9



This is an equivalence table relating ways of expressing the proportion or concentration of analyte in a sample. Percentages constitute the backbone of the comparisons and conversions are based on an assumed density of 1.00 g/mL.

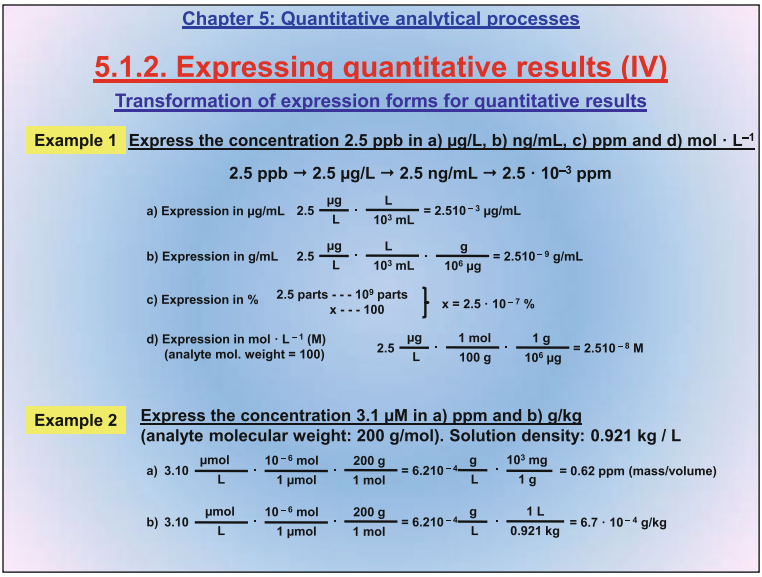
The more common concentration and proportion units are shown in yellow and red, respectively. The table can be useful to convert some units into others through specific factors (see Slide 5.10).

The terms "parts per million" (ppm) and "parts per billion" (ppb) are very frequently used to express analytical results.

- One *part per million* (ppm) is a proportion of one in a million in the same units (for example, a concentration of 1 mg/kg). Thus, 2 ppm is equivalent to 2 mg in 10^6 mg (or 2 mg in 1 kg).
- One *part per billion* (ppb) is a proportion of one in a billion in identical units (for example, a concentration of 10^{-3} mg/kg or 1 µg/kg) Thus, 5 ppb is equivalent to 5 mg in 10^{12} mg (or 5 µg in 1 kg).

Again, the relations of Slide 5.8 can be used in combination with density to relate ppm and ppb values to volumes. Thus, at a unity density, 1 ppm is equivalent to 1 mg/L and so is 1 ppb to 1 µg/L.

Slide 5.10

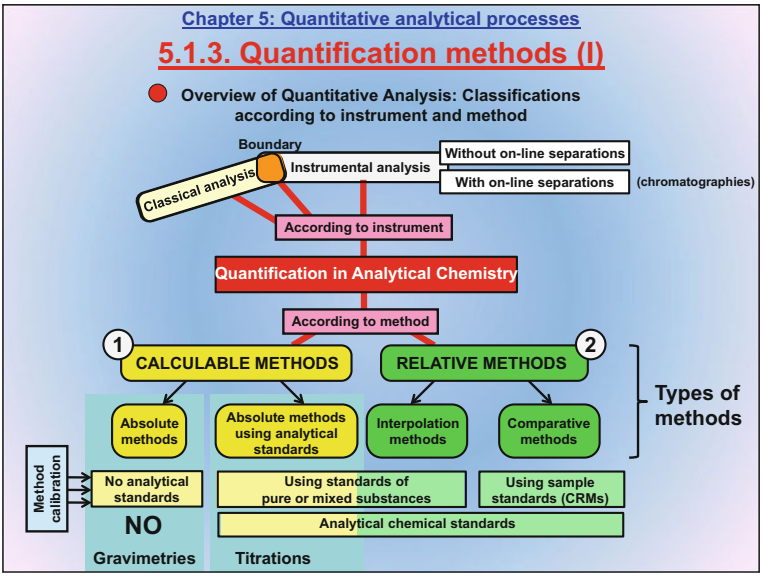


5.10.1. This is an example of unit conversion to express a quantitative result. The table in the previous slide was used to obtain conversion fractions for expressing concentrations in different units. As can be seen, the conversion in d) requires using the molecular weight of the analyte in order to relate its mass to the number of analyte moles and express its concentration in molar form (M).

5.10.2. Example 2 involves converting a micromolar concentration (µM). This requires using the molecular weight of the analyte to convert the number of moles into a mass. An appropriate conversion factor is used to convert the initial concentration into ppm. Then, the density of the sample solution is used to relate volume units to mass units (see Slide 5.8).

5.1.3 Quantification Methods (3 Slides)

Slide 5.11

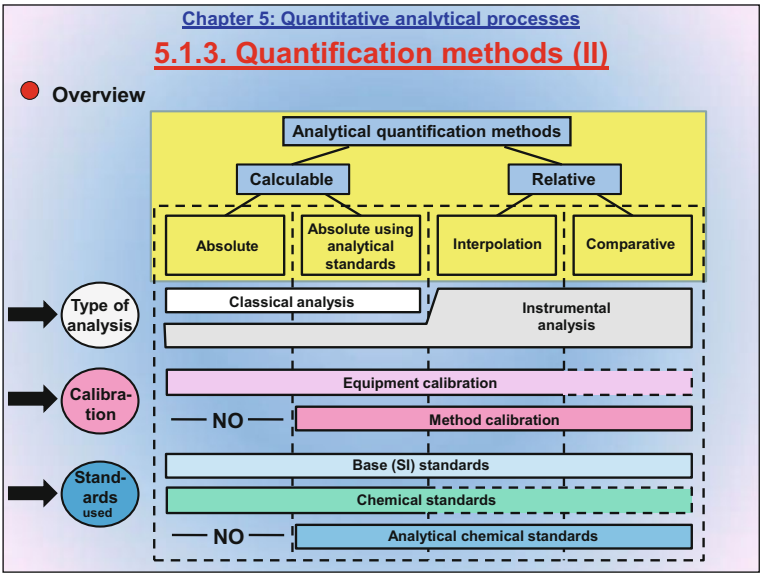


This slide classifies Quantitative Analysis in two non-mutually exclusive ways, namely: according to the instrument or method used.

- According to *instrument*, Quantitative Analysis can be classified as *Classical* or *Instrumental*. The latter may involve on-line separation as in liquid chromatography with UV–visible detection or no separation as in spectroscopic techniques. These two types of analysis are defined in Slides 5.5 and 5.6. Both *Classical* and *Instrumental* Quantitative Analysis require equipment calibration (that is, they use instruments requiring verification with a standard).
- According to *method*, Quantitative Analysis can be of the *Calculable* or *Relative* type.

  - *Calculable methods* are absolute methods that either (a) use no analytical standard and thus require no method calibration (e.g., gravimetry) or (b) use some analytical chemical standard and thus require method calibration (e.g., titrimetry).
  - *Relative methods* are either of the *Interpolation* or *Comparative* type. Both use analytical chemical standards for calibration but differ in the types of standards required (namely, pure substances or their mixtures in interpolation methods and certified reference materials in comparative methods).

Slide 5.12



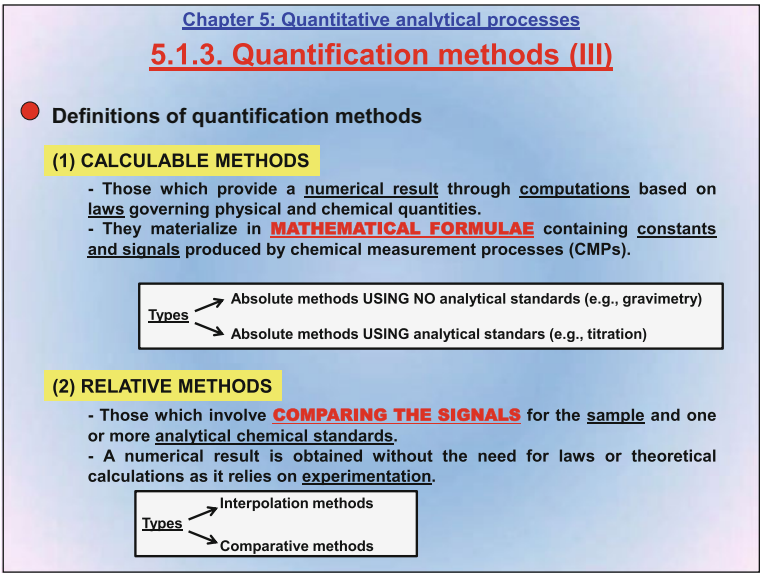
5.12.1. This slide expands on the characteristics of calculable and relative quantification methods briefly described in the previous one.

5.12.2. Analytical quantification methods can be further classified according to the characteristics of the measuring instrument used. Thus, automated instruments (Instrumental Analysis) are used in both calculable and relative quantification methods. On the other hand, classical instruments can only be used in calculable methods because relative methods rely on comparisons with signals produced by more sophisticated instruments.

5.12.3. Both types of analytical quantification methods use an instrument to obtain results and information, so they require equipment calibration (see Slide 5.4). However, not all quantification methods need method calibration; in fact, absolute methods using no analytical standard for comparison obviously require no calibration or verification.

5.12.4. Regarding references, all types of quantification methods use chemical standards (see Slide 3.10) to establish traceability links to base standards (SI units, Slide 3.9). The only exception is that of absolute methods using no analytical chemical standards, which require no method calibration; in fact, these methods produce results without the need for comparison with a standard. Also, chemical standards are useless for equipment calibration; thus, it is pointless to use a potassium dichromate solution to monitor the intensity of a spectrophotometer lamp. All other types of methods do use analytical chemical standards for verification and production of quantitative results.

Slide 5.13

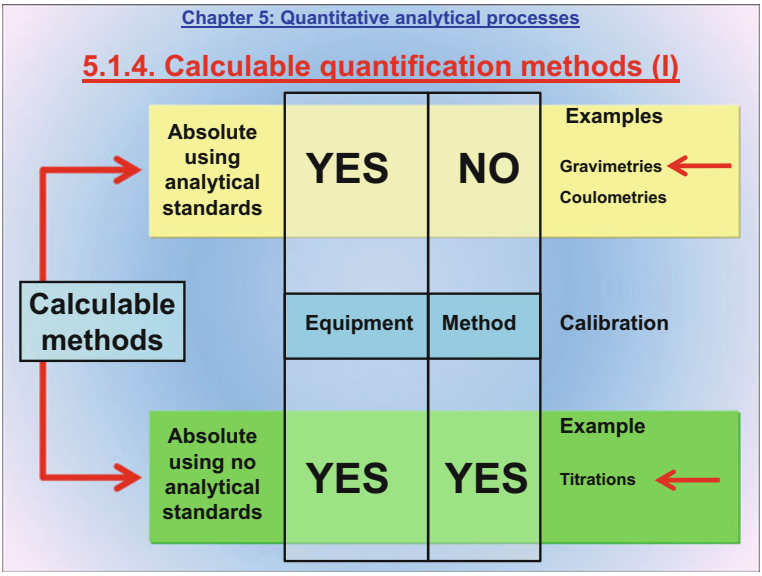


This slide defines each type of quantitative analytical method according to the criteria set in the previous two.

- *Calculable methods* are those which relate two numerical quantities, namely: the amount or concentration of analyte and the signal produced by the instrument in response to the sample. The relation is a *mathematical formula* allowing the analyte mass or concentration to be calculated in terms of known, tabulated constants and test results. Calculable methods are absolute methods that use some (Slides 5.15–5.18) or no analytical chemical standard (Slides 5.19–5.24).
- *Relative methods* are those which produce results by *comparing the sample signal with those for analytical chemical standards* subjected to the same analytical process (that is, through *experimental calculations*). Relative methods are of the *Interpolation* (Slide 5.26) or *Comparative* type (Slide 5.27).

5.1.4 Calculable Methods (1 Slide)

Slide 5.14



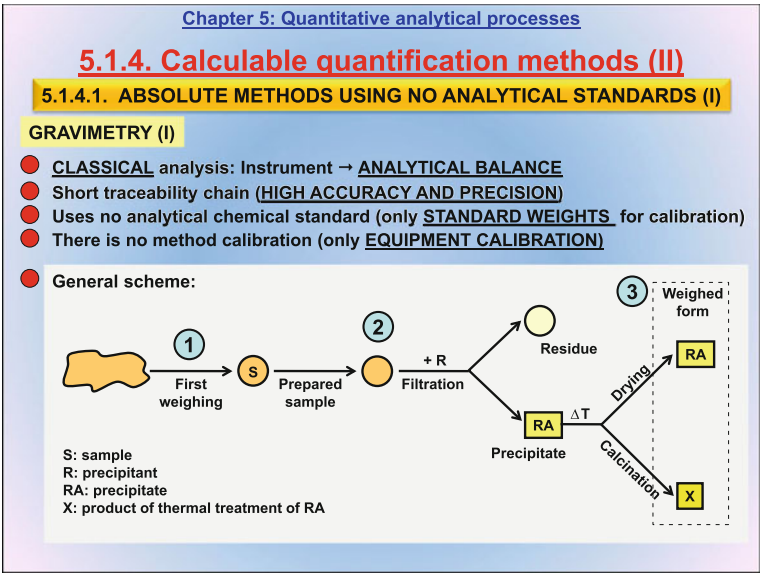
This slide highlights the most salient features of the two types of calculable methods.

Calculable methods using no analytical chemical standards only require equipment calibration. One case in point is that of gravimetry, which is explained in Slides 5.15–5.18.

On the other hand, calculable methods using analytical chemical standards (e.g., titrimetry, which is explained in Slides 5.19–5.24), require both equipment and method calibration.

5.1.4.1 Absolute Methods Using no Analytical Chemical Standards (4 Slides)

Slide 5.15



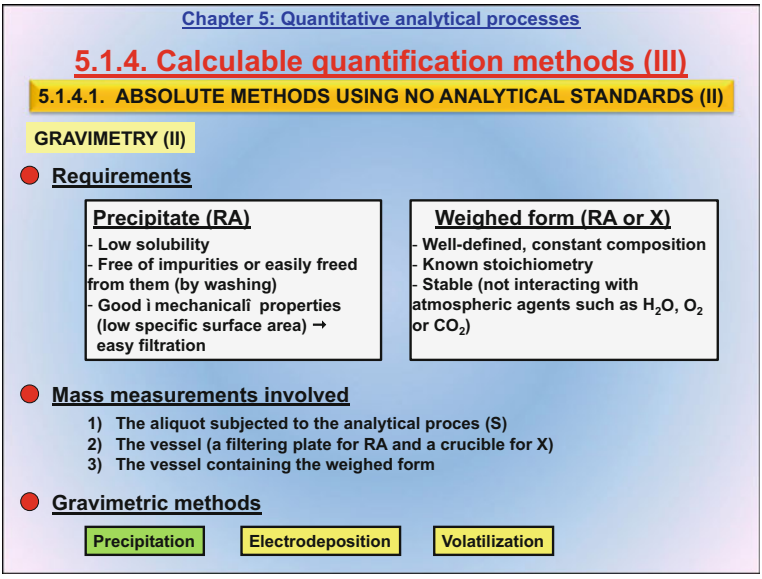
5.15.1. A gravimetry is a calculable method using no analytical chemical standards. Rather, it uses an analytical balance (that is, an instrument) to determine the mass of analyte contained in a sample from that of the weighed form—usually a dry precipitate. Therefore, a gravimetry only uses chemical standards to relate the mass of analyte, the weight of the weighed form and the equipment calibration standard. The result thus has a short traceability chain, so it is usually highly accurate and precise. No analytical chemical standard is normally used because no method calibration is usually required.

5.15.2. This slide provides an overall description of a gravimetric method in three steps.

(1) After the analytical balance is calibrated, it is used to weigh an aliquot of the bulk sample, the measured weight being subsequently used as a reference for comparison with the analyte weight.
(2) The sample is subjected to the preliminary operations needed to precipitate the analyte and isolate the precipitate by filtration.
(3) The precipitate containing the analyte is dried—or dried and calcined—and weighed to calculate the amount present in the sample, whether in absolute form (mass units) or in relation to the total sample weight measured in the first step (see the ways of expressing a quantitative result in Slides 5.7–5.9).

While these three steps constitute the minimum treatment required to obtain a solid form affording weighing of the analyte, the gravimetric process proper only involves the third step. Once the bulk sample and the precipitate have been weighed, the process is purely computational as it involves relating the precipitate weight to the analyte weight—hence the short traceability chain of gravimetries.

Slide 5.16

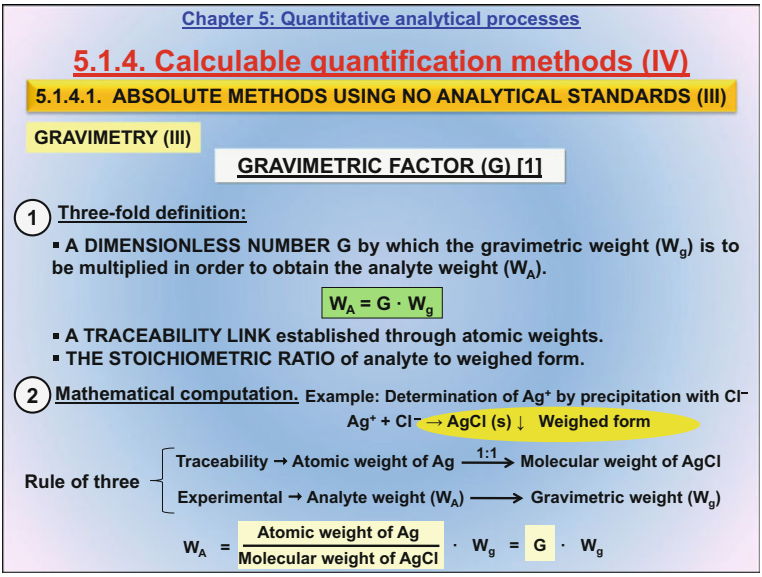


5.16.1. This slide shows the essential requirements for the precipitate and the weighed form with a view to assuring reliability in gravimetric results. As can be seen, the precipitate should be insoluble enough for the analyte to be readily withdrawn from the bulk solution; also, it should be easy to wash in order to remove any impurities. On the other hand, the weighed form should be stable and possess a well-defined composition and stoichiometry.

5.16.2. The slide also shows other features of gravimetric methods such as mass measurements and the three basic ways in which the weighed form can be obtained, namely: precipitation—the most usual—electrodeposition and volatilization.

The determination of sulphur as sulphate (for example, following oxidation of sulphur-containing organic matter via a wet reaction) involves precipitating the anion with barium chloride. The resulting precipitate, $BaSO_4$, is easily filtered, pure and stable against atmospheric agents. The precipitated form, once filtered and dried, constitutes the weighed form. The analyte (sulphur) and the precipitant (barium ion) bear a 1:1 stoichiometric relation.

Slide 5.17



This slide and the next are devoted to a key parameter in gravimetric determinations: the *gravimetric factor*, G, which can be defined in theoretical and mathematical terms as follows:

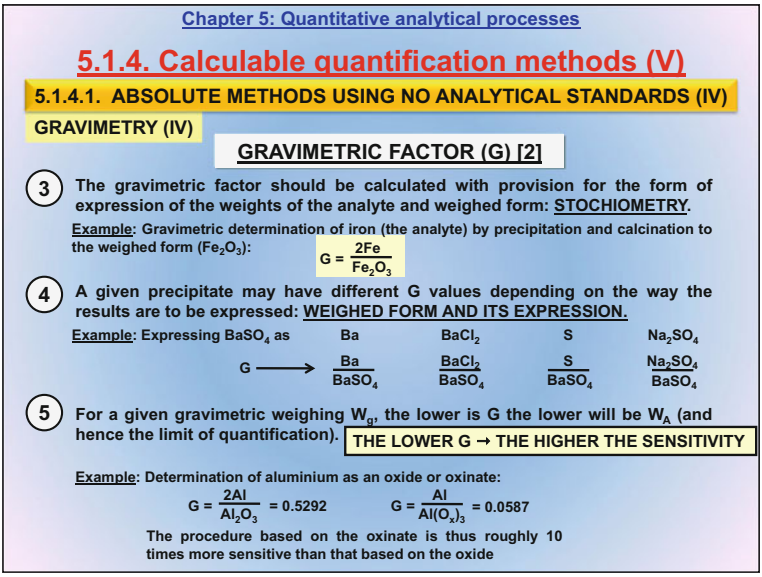
(1) The gravimetric factor is:

- a dimensionless quantity used as a proportionality constant between the analyte weight and the gravimetric weighing (see mathematical formula in the slide);
- a traceability link between atomic weights (chemical standards) and the weighed form (that is, a factor ensuring consistency between the result and chemical standards); and
- the stoichiometric ratio of the analyte to the weighed form.

(2) Mathematically, G is calculated as the ratio of the atomic weight of the analyte to the molecular weight of the weighed form.

The slide illustrates the calculation of G for the gravimetric determination of Ag^+ (the analyte) by precipitation as AgCl (a highly insoluble white solid). The stoichiometry of the reaction is 1:1. The weight of analyte (Ag^+) is related to that of precipitate (AgCl) by a constant G (the gravimetric factor).

Slide 5.18



This slide elaborates on the definitions of *gravimetric factor*, G, started in the previous one.

(3) G should be calculated with provision of the *stoichiometric relation* between the analyte and the weighed form. In the example shown, the amount of analyte (Fe^{3+}) is twice that of the weighed form (Fe_2O_3); therefore, calculating G entails multiplying the Fe^{3+}/Fe_2O_3 ratio by two.

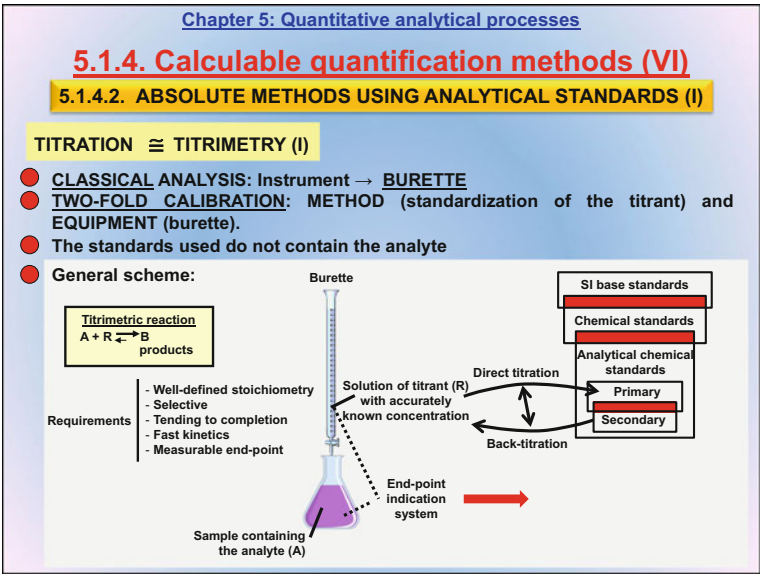
(4) The *weighed form* and the *form of expression of the result* are especially important here. Thus, the mass to be used in the denominator of the fraction for calculating G (Slide 5.17) depends on the way the analyte is obtained; similarly, the mass to be used in the numerator depends on the desired form of expression. Therefore, G differs with the specific weighed form and the way the analyte mass is expressed. In the example shown, a fixed mass of weighed form ($BaSO_4$) is used to express the result in terms of the masses of Ba, $BaCl_2$, S and Na_2SO_4. Each of these species has a different atomic or molecular mass and hence leads to a different gravimetric factor. It is therefore essential to specify the form of expression of the mass in order to produce accurate results.

(5) G is related to the *sensitivity* of the gravimetric method. In fact, the gravimetric factor is defined in Slide 5.17 as the molecular weight ratio of the analyte and to the weighed form. Therefore, the smaller is G, the smaller will be the amount of analyte per unit mass of weighed form that can be quantified (that is, the limit of quantification as defined in Slides 2.41 and 2.42) and the highest will be the sensitivity of the gravimetric method. In the example shown, the amount of

aluminium (Al) present in two aliquots of the same sample is determined by precipitation as an oxide or oxinate. Because the molecular weight of the oxinate is ten times greater than that of the oxide, the gravimetric factor for the former is ten times smaller. As a result, the amount of aluminium per mass unit of oxinate that can be quantified gravimetrically is much smaller and the method much more sensitive than that using the oxide as weighed form.

5.1.4.2 Absolute Methods Using Analytical Standards (6 Slides)

Slide 5.19



5.19.1. Although the word *titration* is widely used to refer to a variety of procedures for determining an amount of analyte by using a specific chemical reaction, it is usually associated to *titrimetries*. A titrimetry is a calculable method using a burette as an instrument to measure the amount of analyte present in a sample solution by adding known volumes of a reagent (R) to the sample in order to have it react with the analyte in a selective manner. A titrimetry uses analytical chemical standards not containing the analyte for equipment and method calibration in addition to chemical standards for reference to base (SI) standards.

Method calibration in titrimetries essentially involves determining the exact concentration of titrant used (standardization).

On the other hand, *equipment calibration*—of the burette—is intended to ensure that all volumes measured are accurate. This is a time-consuming process involving successive weighing of 2 mL portions delivered by the burette. Fortunately,

however, it is usually conducted by the manufacturer and burettes typically come with a calibration certificate.

5.19.2. This slide depicts a titrimetric method involving a generic reaction between an analyte (A) and its titrant (R). For the method to be quantitative, the titrimetric reaction should fulfil the following five requirements:

- Be *stoichiometric* so that the proportions in which the reactants interact can be easily established and used to relate the volume of titrant used to the amount of analyte present in the sample (see traceability chain in Slide 3.6).
- Be *selective* (see Slide 2.50) so that the titrant will react specifically with the analyte and only the amount strictly required for the analytical reaction to complete is used. In fact, parallel reactions with other sample components can lead to positive or negative errors (see Slides 2.9 and 2.10) detracting from the accuracy of the result.
- *Tend to completion* so that the equilibrium constant for the analytical reaction is very large and the reaction highly shifted to the product—and hence *quantitative*;
- Be *fast* so that the end-point can be immediately detected and adding excess titrant avoided—a slow reaction can never be a good titrimetric reaction—and
- Possess an effective *end-point indication system* allowing the operator to easily identify the end of the reaction between the analyte and titrant.

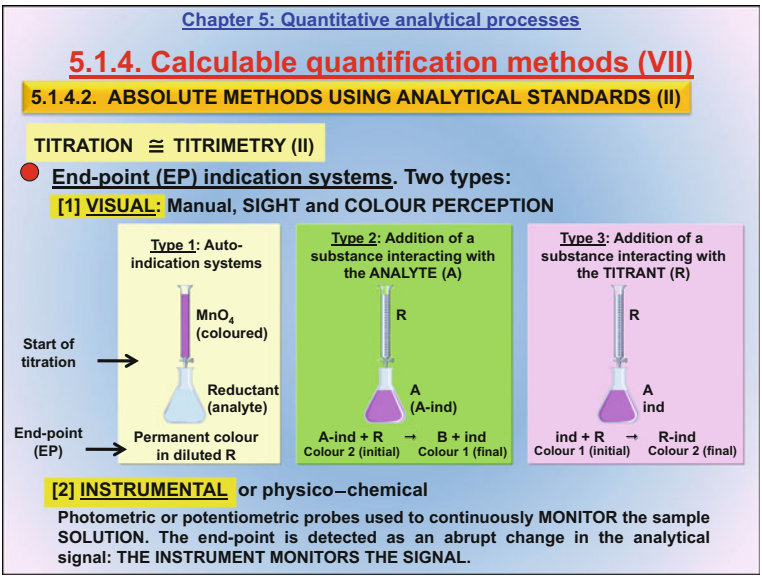
5.19.3. Classical titrimetries use a manual burette that is made to the mark with a solution of a reagent R (the titrant). The sample containing the analyte is held in an Erlenmeyer flask that is placed right under the burette tip. By turning the stopcock, the titrant is delivered to the flask for reaction with the analyte. When the indication system signals the end of the reaction, the stopcock is closed and the volume of titrant used is recorded in order to calculate the amount of analyte present in the sample with provision for the volume and concentration of titrant, and also for the stoichiometric relationship. The indication system can be the titrant itself (see next slide) or added to the flask together with the sample.

- The *end-point* of the titration is the practical status of the system when the titration is finished or, in other words, the volume of titrant added during the process (e.g., 32 mL in the example shown here).
- The *equivalence point* of the titration is the theoretical status of the system when the titration is finished, that is, the theoretical (stoichiometric) volume of titrant that should have been used to obtain an exact result subject to no uncertainty (31 mL in the example).

5.19.4. A titrimetric determination involves comparing the volume of titrant used and the amount of analyte that reacts with it. One essential requirement for this comparison is that the titrant concentration be accurately known. Such a concentration will be known if a primary standard such as highly pure potassium hydrogen phthalate is used as titrant; in fact, this standard can be used to prepare solutions of

accurately known concentration by precise weighing. However, primary standards are usually as pure as they are expensive; also, some may be incompatible with the analyte and the titrimetric reaction fail to fulfil the five above-described requirements. For these reasons, the usual practice is to use a secondary standard such as sodium thiosulphate previously standardized with a primary standard such as potassium iodate.

Slide 5.20



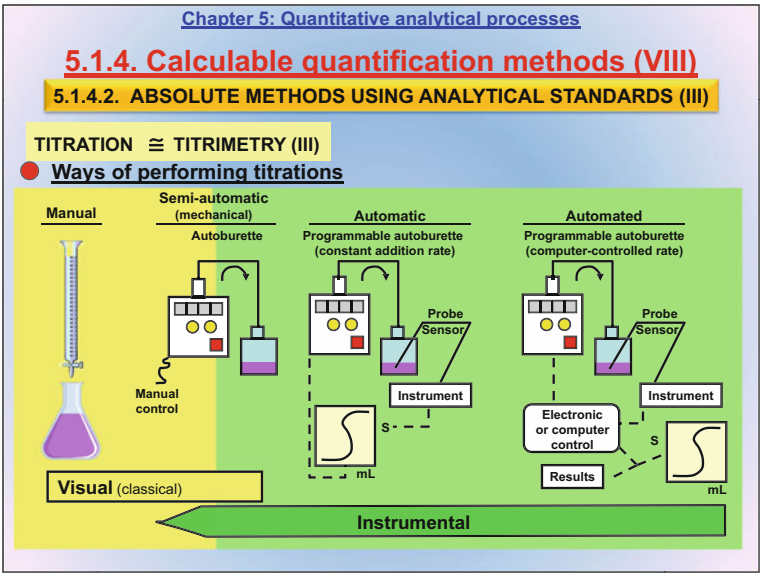
5.20.1. Manual titrimetric methods use a classical burette and rely on a colour change to detect the end-point of the titration. Because the change is identified visually, how accurately it is detected will depend on the operator's ability to distinguish colour differences. Although this detection system is subject to systematic and random errors (see Slide 2.10), the errors are usually acceptable (particularly in teaching laboratories, where it continues to be used). The slide shows three different types of visual indicators.

– In type 1 indicators, known as *auto-indicators*, the titrant or the analyte is coloured whereas the reaction product is colourless. The end-point occurs when the solution either acquires a colour by effect of the addition of excess coloured titrant (e.g., permanganate ion) or becomes colourless when the whole, coloured analyte (e.g., iron or cobalt ion) has reacted. Although auto-indication systems are rarely used, those based on a coloured titrant tend to be preferred because it is usually easier to visually detect the formation of a colour than its disappearance.

- In type 2 indicators, a substance (such as murexide) is added to the unknown solution in order to have it *react weakly with the analyte* (e.g., calcium ion). The substance in question should have a different colour in free form (e.g., free murexide is violet) and in complexed form (e.g., the calcium–murexide complex is pink). The titrant reacts with the analyte and removes the ligand from the solution, which acquires a mixed colour (e.g., pinkish violet) as a result. The end-point occurs when the whole analyte has reacted with the titrant and the ligand adopts the colour of the free form (violet for free murexide).
- In type 3 indicators, a substance (such as phenolphthalein) is used to *react with excess titrant* (e.g., sodium hydroxide) once the whole analyte (e.g., hydrochloric or acetic acid) has been neutralized. The substance to be used should have a different colour in unreacted form and after reacting with the titrant (e.g., phenolphthalein is colourless in an acid medium and pink in an alkaline medium). Also, the titrant–analyte reaction should be more favourable than the titrant–indicator reaction in order to avoid errors in detecting the end-point of the titration. Once the titrant has reacted with the analyte until depleting it, the addition of further (excess) titrant causes the indicator to react with it and change colour. Thus, excess sodium hydroxide added after all acetic acid has been neutralized causes phenolphthalein to change from colourless to pink.

5.20.2. Instrumental (automated) titrimetries use more sophisticated, automatic burettes that avoid operator handling errors. The burette operation is controlled by monitoring its response and recording it on a computer. The end-point is identified by an abrupt change in the analytical signal. The next slide shows various designs illustrating progress from the classical model and stressing the difficulty of classifying burettes as classical or instrumental equipment (see Slide 5.5).

Slide 5.21



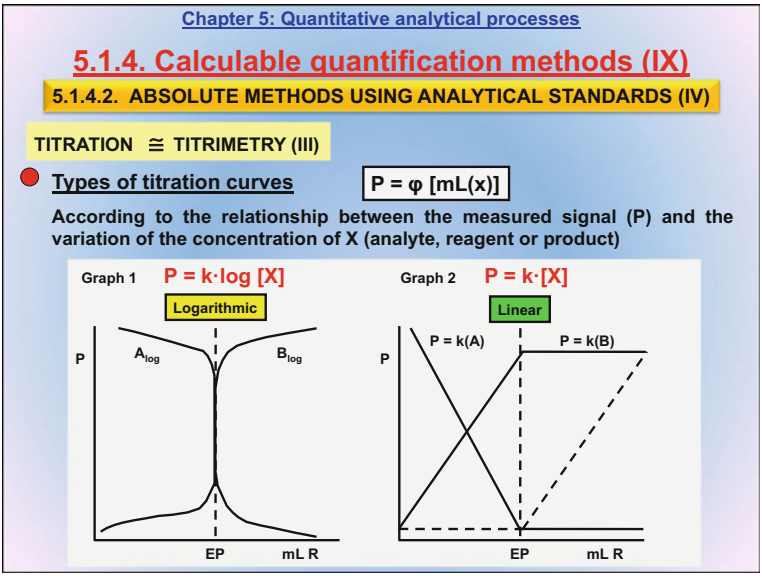
Automation has also reached titrations and titrimetries. In the process, formerly manual work has been rendered automatic. This slide compares three different types of autoburettes with a classical burette.

- *Semi-automatic (mechanical) burettes* operate similarly to a classical burette. The operator is responsible for detecting the colour change associated to the end-point of the titration; however, the titrant is delivered in a semi-automatic manner and the volume of titrant used is directly measured by the instrument. This operational procedure avoids volume measurement errors but is still subject to potential errors arising from the operator's inability to accurately identify the colour change.
- *Autoburettes* add a constant volume of a titrant at specific intervals and continuously monitor the response (e.g., by using a photometer to measure colour differences as the titrant is added). This avoids the need to have the operator add the titrant and read the response, and hence potential errors. The autoburette uses the responses it records to draw a titration curve (Slide 5.22) for the operator to interpret and identify the end-point. Autoburettes differ markedly from the classical burette; thus, the former operate automatically and the operator only needs to interpret the titration curve and calculate the result.
- *Automated burettes* allow one to set the volume of titrant to be delivered in each addition and monitor the response throughout the titration. As with autoburettes, they draw a titration curve as they acquire the response. However, in automated burettes the process is fully computer-controlled, which allows the titrant

addition rate to be decreased near the end-point; also, they calculate the result by themselves, so the operator only needs to interpret it.

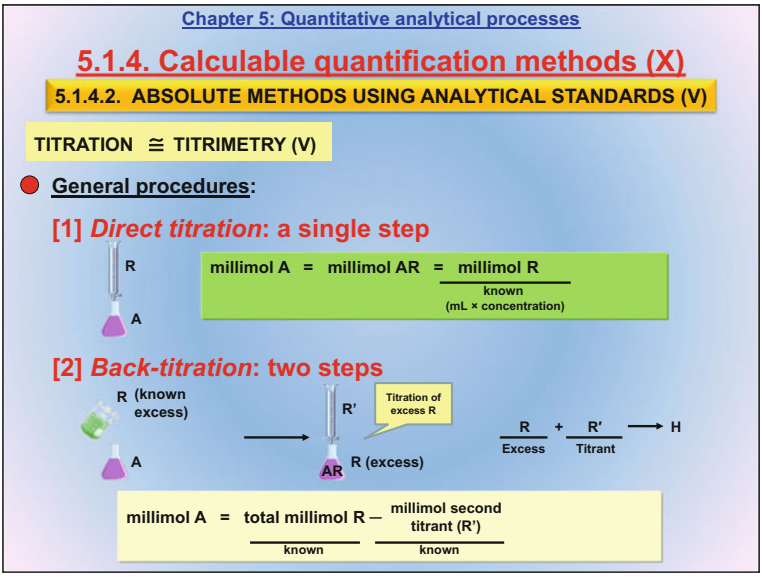
Placing each type of burette in Classical or Instrumental Analysis in not easy. Clearly, a manual burette can be deemed "classical" and an automated burette "instrumental", but a mechanical burette and an autoburette are more difficult to classify. This is a paradigmatic example of the difficulty in establishing the boundaries between Classical Analysis and Instrumental Analysis (see Slides 5.5 and 5.6).

Slide 5.22



A *titration curve* is constructed by plotting the analytical signal against the volume of titrant added. The signal can vary in a logarithmic (graph 1) or linear manner (graph 2) with the analyte concentration depending on whether the relationship between the instrument response and the concentration of the monitored species is of the proportional or logarithmic type.

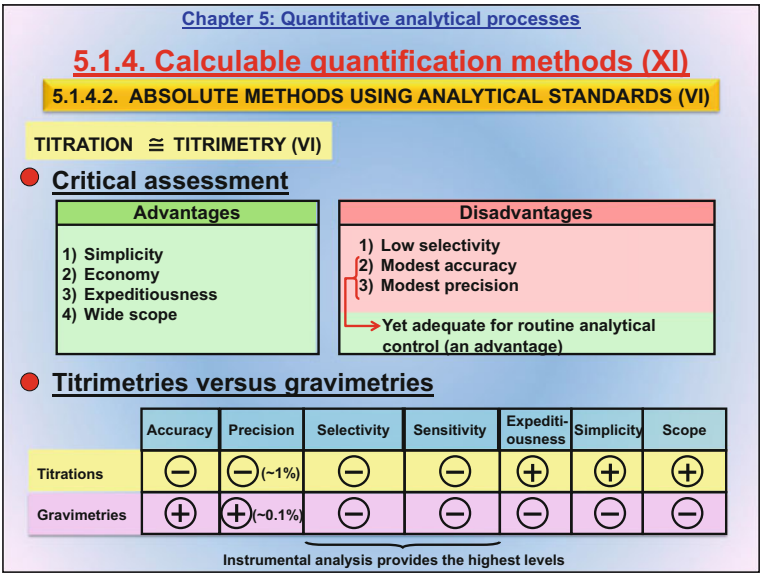
Slide 5.23



This slide depicts the most common ways of performing a titration.

– *Direct titrations* are done in a single step by adding titrant solution over the sample until the indication system signals the end-point. The amount of analyte in the sample is calculated directly from the volume of titrant used. One case in point is the determination of calcium and magnesium in water by titration with EDTA in the presence of Eriochrome Black T as indicator.
– *Back-titrations* involve two steps. In the first, a known excess volume of titrant is added in order to have all analyte present in the sample react with it. Excess titrant remaining in solution is then subject to direct titration with another reagent in the second step. The amount of analyte in the sample is calculated indirectly from the amount of titrant added in excess and that reacting with the analyte. Back-titrations are used when direct titration is impossible. For example, determining the chemical oxygen demand of wastewater involves using excess potassium dichromate and then titrating the residual amount of dichromate in solution with iron (II) in the presence of phenolphthalein as indicator.

Slide 5.24

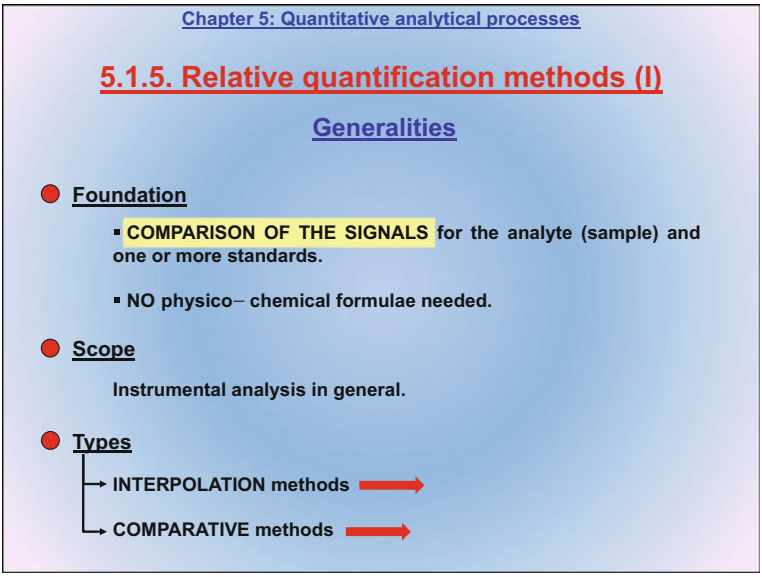


5.24.1. This slide highlights the advantages and disadvantages of titrimetry—and titrations in general. Titrations are inexpensive, expeditious and flexible—the titrimetric reaction can be an acid–base, redox, complex formation or even precipitation reaction—which make them widely applicable. Also, although they are not especially accurate, precise or selective, titrations are quite useful for routine laboratories and also to estimate the amount of analyte present in a sample.

5.24.2. The slide also compares the analytical properties and scope of gravimetry and titrimetry. As can be seen, titrations are simple, expeditious and flexible, whereas gravimetric determinations are highly accurate and precise, with errors of 0.1% versus 1% in titrations. Both, however, are scarcely selective and sensitive unless automated equipment (Instrumental Analysis) is used.

5.1.5 Relative Quantification Methods (1 Slide)

Slide 5.25

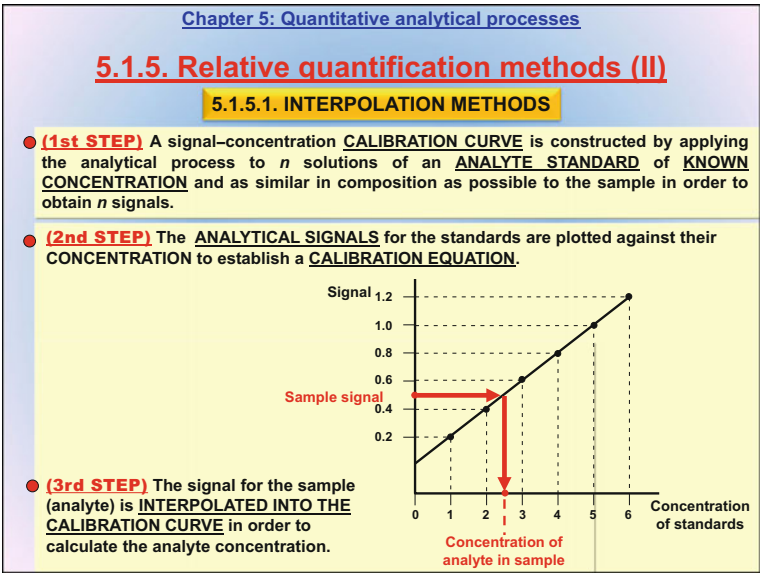


This is the essential foundation of *relative quantification methods*, which, unlike calculable methods (Slides 5.14–5.24), involve comparing the signal for a standard containing a known amount of analyte with that for the sample and using a mathematical relation to estimate the analyte concentration. The relation is established from a calibration curve in *interpolation methods* and from a rule of three in *comparative methods*. These two types of methods are described in the next two slides.

Relative quantification methods rely on Instrumental Analysis because they require high levels of sensitivity and selectivity.

5.1.5.1 Interpolation Methods (1 Slide)

Slide 5.26



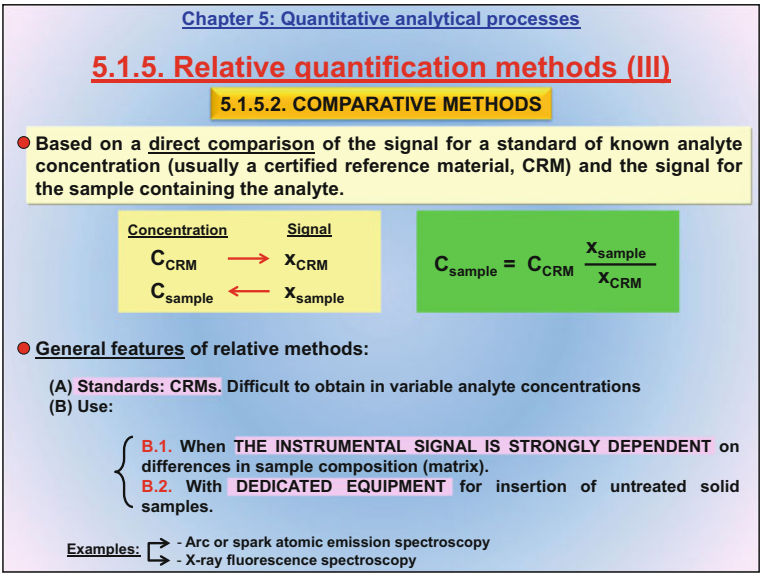
5.26.1. Relative interpolation methods use a calibration curve (Slides 2.36 and 2.37) as reference to determine the amount of analyte present in a sample. The curve is obtained by applying the analytical process to n standards containing known amounts of the analyte and plotting the instrument response to each standard against its concentration.

5.26.2. The ensuing plot is usually a point cloud requiring a regression treatment of the linear, polynomial or logarithmic type to derive the equation for the calibration curve: a *calibration function*.

5.26.3. Once the *calibration function* is established, it is used to substitute the measured sample signal in order and to calculate the corresponding analyte concentration. The interpolation and calculation procedures are represented by red arrows on the graph.

5.1.5.2 Comparative Methods (1 Slide)

Slide 5.27



5.27.1. *Comparative methods* directly compare the signal for a standard of known concentration to that for the sample via a rule of three or a conversion factor.

5.27.2. Comparative methods possess two salient features, namely:

(A) They typically use certified reference materials (CRMs, Slides 3.14 and 3.17) as standards. However, CRMs are often scant or expensive and can be replaced with laboratory-made standards prepared from known amounts of analyte.

(B) Because comparisons invariably involve a single standard and a single signal, the results will only be accurate if the signal is strongly dependent on the analyte concentration (that is, if the measuring instrument is highly sensitive and selective, B.1) or dedicated equipment (an instrument affording measurement of untreated samples, B.2) is used. Because they use only one standard to verify the results, comparative methods should only be used in these two situations.

Relative methods of the comparative type are typical of atomic emission and X-ray fluorescence spectroscopy. One case in point is the direct analysis of cylinders of steel standards and samples having an identical matrix. The two signals are compared via a rule of three in order to calculate the proportion of chromium (the analyte) present is stainless steel specimens on the basis of that of contained in the standard.

5.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

M. Valcárcel

Springer-Verlag, Berlin, 2000

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

Specifically, the contents of this chapter coincide to a great extent with those of Chapter 5 in Valcárcel's book ("Quantitative Aspects of Analytical Chemistry") except that the description of gravimetry and titrimetry has been shortened because these techniques are unrelated to the foundations proper. Rather, the two are used here to exemplify calculable methods. Also, this chapter contains new examples intended to facilitate understanding of the concept "Quantitative Analysis".

5.3 Questions on the Topic (Answered in Annex 2)

5.1. The determination of pyrethrins in a food sample gives a concentration of 10 μg/kg. Express it in ppb and as a percentage.

5.2 An amount of 0.231 mg of a compound of molecular weight 114 g/mol is added to a volume of 500 mL of water. Calculate the resulting concentration in (a) mol L^{-1}, (b) ppb and (c) μg/g water.

5.3. How do titrimetries differ from gravimetries? Tick the correct answers.

[ ] Titrimetries are not classical method of analysis
[ ] They are not quantitative methods
[ ] They use analytical chemical standards
[ ] They are not absolute methods
[ ] They use no atomic weights as chemical standards

5.4. Which features would you associate with titrimetries and gravimetries? Tick the correct answers.

Feature	Titrimetries	Gravimetries
Absolute methods using no analytical chemical standards		
Absolute methods using analytical chemical standards		
Relative quantification methods		
Only use atomic weights as standards		
Use analytical chemical standards		
Use base standards		
Have the shortest traceability chain		

5.5. Briefly describe the foundation of a back-titration.
5.6. Which of the following methods use no analytical chemical standards?

[ ] Titrimetries
[ ] Relative interpolation methods
[ ] Gravimetries

5.7. What are the key features of absolute analytical methods?
5.8. Convert the following concentrations into percentages:

Concentration	%
1 ppm	
1 ppb	
1 µg/L	
1 mg/L	
1 ng/L	

5.9. What are the differences between gravimetry and titrimetry in the following respects?

	Gravimetry	Titrimetry
Type of analytical method used		
Standards used		
Levels of analytical properties		

5.10. Explain the differences between "absolute" and "relative" quantification methods.

5.11. What analytical properties apply to Quantitative Analysis?

5.12. What are the instruments typically used in Classical Quantitative Analysis?

5.13. Name the two types of calculable methods and give an example (analytical process) of each.

	Calculable methods	Example
1		
2		

5.14. Describe several ways of expressing the results in Quantitative Analysis.

5.15. What type of quantitative analytical method requires no method calibration? Why? Give an example.

5.16. What is the gravimetric factor? Tick the correct answer.

[ ] A ratio of molecular or atomic weights.
[ ] A dimensionless number that is multiplied by the gravimetric weighing to calculate the mass of analyte
[ ] A number by which the atomic weight of the analyte is multiplied to express the result
[ ] A factor calculated from the molecular weight of the weighed form

5.17. What are the five requirements to be fulfilled by a chemical reaction to be useful for titrimetric purposes?

5.18. Name the three types of visual indication systems in titrimetry.

5.19. Is Classical Quantitative Analysis possible with a relative method? Why?

5.20. Why does sensitivity in gravimetries increase with decreasing gravimetric factor?

5.21. What is a titrimetry? Tick the correct answer.

[ ] A quantitative method for identifying analytes
[ ] A relative interpolation method
[ ] An absolute quantitative method using analytical standards
[ ] An absolute quantitative method using no analytical standards

5.22. Explain the relationship between gravimetric factor and sensitivity in gravimetry.

5.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened by about 30% for teaching Analytical Chemistry to students not majoring in Chemistry. The following 8 slides can be omitted for this purpose:

- Sect. 5.1.4: Slides 5.16–5.18 and 5.20–5.24.

Qualitative Analytical Processes

6

Abstract

This chapter is concerned with Qualitative Analysis, its description and its associated concepts, and also with analytical properties as adapted to the peculiarities of this branch of Analysis. The definition of Qualitative Analysis is followed by a description of screening systems for classifying samples. The YES/NO binary response, which is the output of qualitative analytical processes, is described and exemplified, particularly as regards its special analytical properties and its associated errors (false positives and false negatives). The main types of Qualitative Analysis possible according to the nature of the equipment used in the analytical process (namely, Classical and Instrumental Qualitative Analysis) are briefly discussed, and so is the high information potential of hybrid techniques.

Teaching Objectives

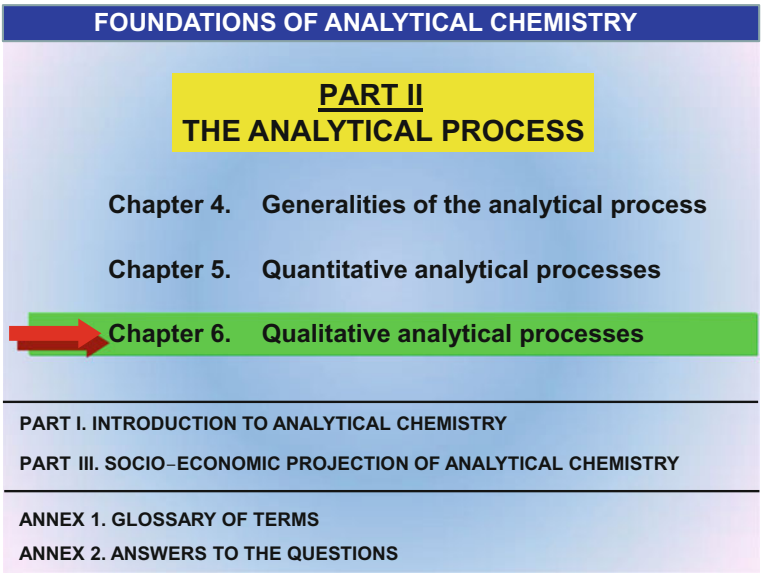
- To introduce students to Qualitative Analysis and underscore its present and future significance.
- To adapt classical analytical properties to the specificities of Qualitative Analysis.
- To define and characterize binary responses, and potential errors in them (false positives and false negatives).
- To describe the most salient classical and instrumental methods of qualitative analysis.

Electronic supplementary material The online version of this chapter (doi:10.1007/978-3-319-62872-1_6) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_6

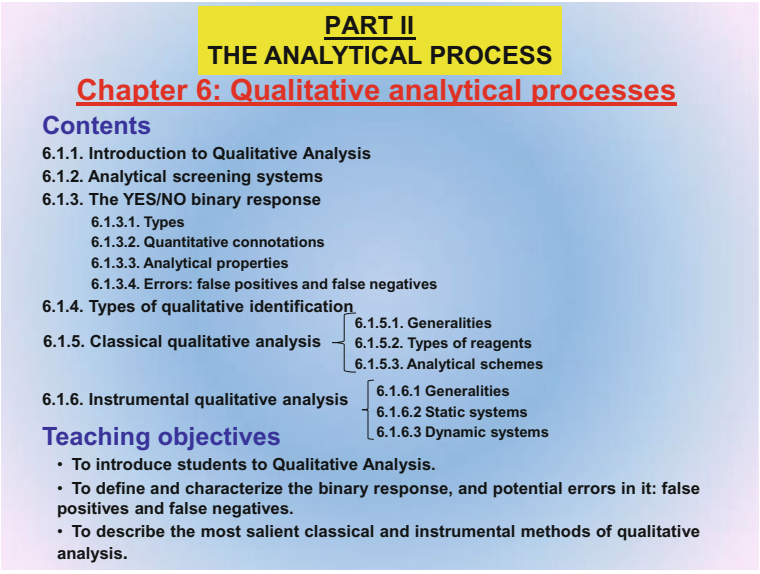
6.1 Explanation of the Slides

Slide 6.1



This slide places in Part II (The Analytical Process) and shows the other two parts. This is the third chapter in Part II and deals with analytical processes that produce qualitative results in the form of YES/NO binary responses.

Slide 6.2

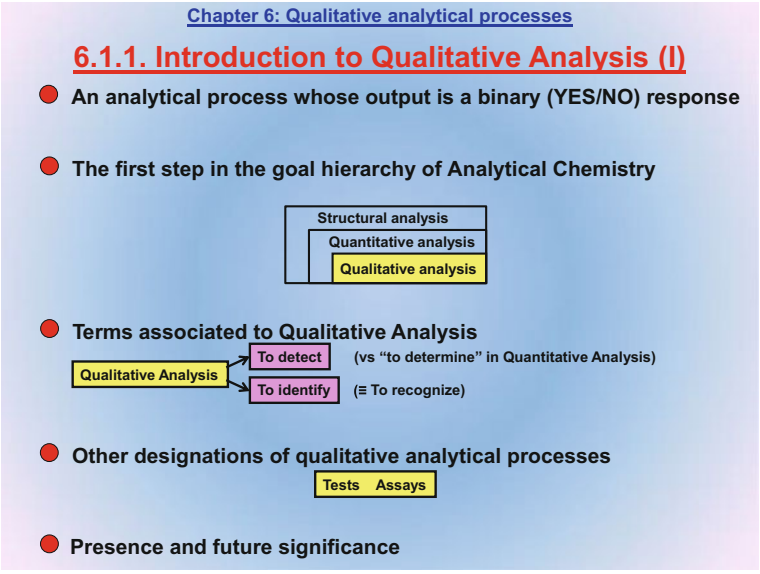


6.2.1. This is an outline of the contents of this chapter. The first section places Qualitative Analysis in context and is followed by a description of screening systems in the second. There follow the most salient features of the binary response in the third and various classifications of Qualitative Analysis in the fourth. The last two sections exemplify Classical and Instrumental Qualitative Analysis.

6.2.2. As can be seen, the primary teaching objectives of this chapter are to introduce students to Qualitative Analysis; and to describe the YES/NO binary response, its features and potential errors (false positives and false negatives) through examples of classical and instrumental qualitative methods.

6.1.1 Introduction to Qualitative Analysis (2 Slides)

Slide 6.3



Qualitative Analysis is the branch of analysis encompassing those analytical processes that yield a YES/NO binary response.

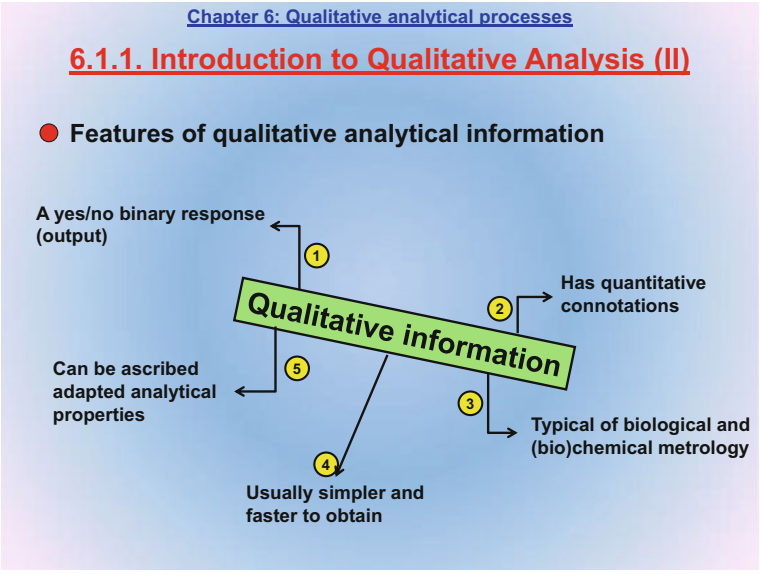
Qualitative Analysis is also the first step in the hierarchy of goals of Analytical Chemistry in Slide 1.9, where it is followed by Quantitative and Structural Analysis. It makes no sense to apply a quantitative analytical process to a sample before the sample is checked to contain the target analyte.

Qualitative Analysis can be described in terms of the verbs *to detect* (vs. "to determine" in Quantitative Analysis) and *to identify* (or, in other words, "to recognize"). Also, it is associated to the verb *to classify* (samples according to qualitative content).

Most qualitative chemical measurement processes (CMPs) are much simpler and faster than quantitative CMPs. As a result, the former are typically designated "tests" or "assays" rather than "methods".

Not long ago, Qualitative Analysis was considered to be the "lesser child" of Analytical Chemistry. As recently as the last quarter of the XX century, Qualitative Analysis was even used to undervalue the significance of this scientific discipline. At present, however, it is gaining increasing recognition as a means of fulfilling clients' information requirements—the ultimate goal as increasingly recognized by many. Very often, such requirements are in the form of binary information (see Slide 6.8) and fulfilled with an expanding array of commercially available qualitative analytical means such as screening systems, portable test kits and biosensors. Some (e.g., planar chromatography on paper) are semi-quantitative and afford estimating the concentration of an analyte in addition to identifying it.

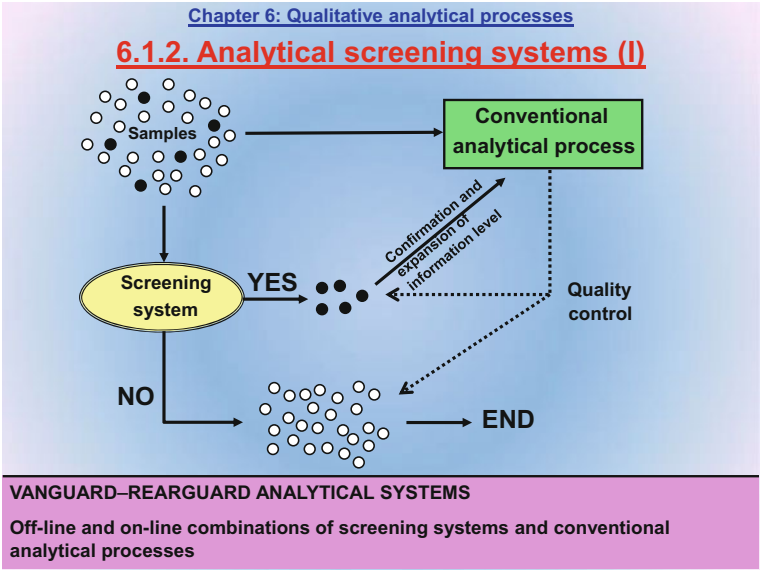
Slide 6.4



Qualitative analytical information therefore takes the form of a YES/NO binary response. As shown in Sect. 6.1.3.2, however, it almost invariably possesses some quantitative connotation. This type of information is rarely needed in Classical (Physical) Metrology; also, it is associated to special analytical properties and usually easier to obtain than other types of analytical information.

6.1.2 Analytical Screening Systems (3 Slides)

Slide 6.5



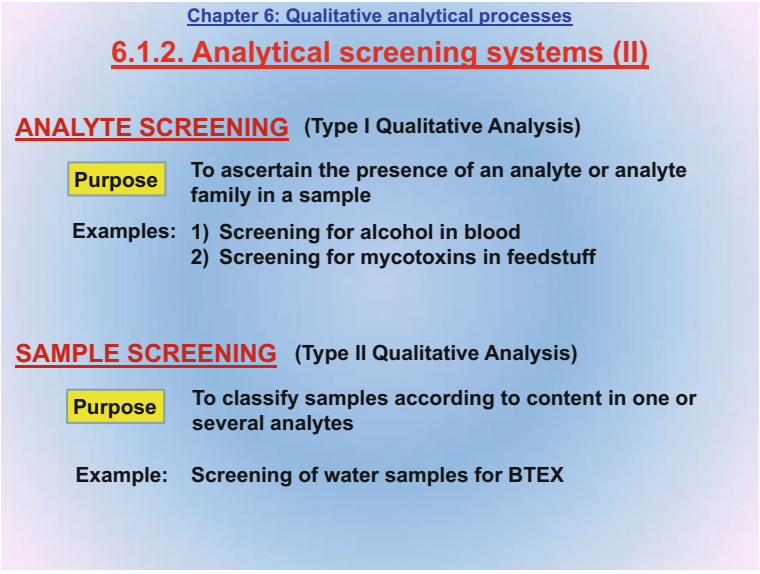
6.5.1. An analytical screening system is usually a simple analytical process used to classify samples into two groups according to whether they give a positive (YES) or negative (NO) response to the binary question posed.

This slide summarizes the operation of a screening system: each sample in a set is independently subjected to the screening process in order to rapidly classify it according to whether it gives a positive (black) or negative result (white).

6.5.2. The process is finished when the response is NO. On the other hand, a YES response requires confirmation with a conventional analytical process (e.g., sample treatment followed by gas or liquid chromatography). This process additionally allows the binary information initially obtained to be expanded. Thus, a sample of imported dried fruits testing positive for mycotoxins in an immunochemical test will be confirmed to contain them and assigned relative concentrations of the different toxins. Also, the results of screening analyses are frequently subjected to confirmation analyses for quality control purposes.

6.5.3. The combination of a screening system and a conventional analytical process constitutes a vanguard–rearguard analytical strategy. The two can be connected off-line (that is, operate independently) or on-line.

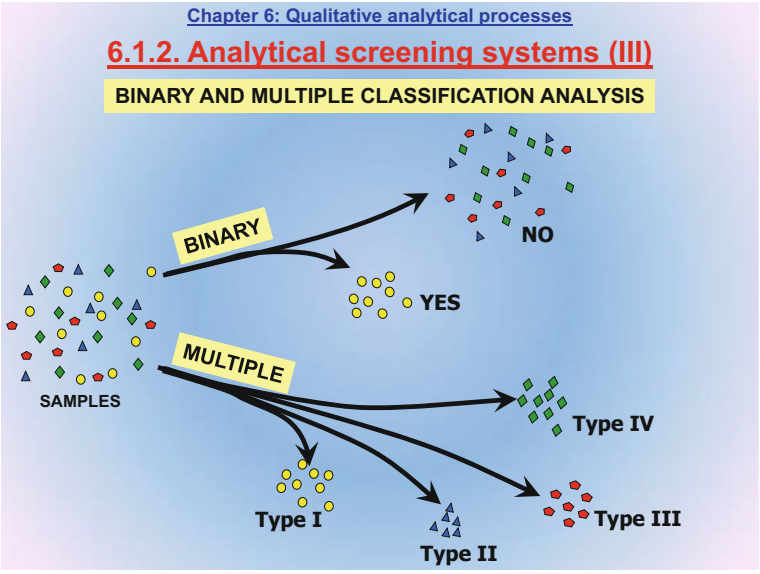
Slide 6.6



There are two types of screening in Qualitative Analysis, namely:

- *Analyte screening,* which is used *to identify* the presence of an analyte or analyte family in a sample and corresponds to Type I Qualitative Analysis in the next slide.
- *Sample screening,* which is used *to classify* samples according to the presence or absence of a particular analyte (e.g., benzene) or analyte family (e.g., BTEX, which comprises benzene, toluene, ethylbenzene and xylene organic molecules). This is the most common type of Qualitative Analysis (Type II in Slide 6.10).

Slide 6.7



It is not uncommon to refer to Qualitative Analysis as Classification Analysis (particularly in chemometric contexts).

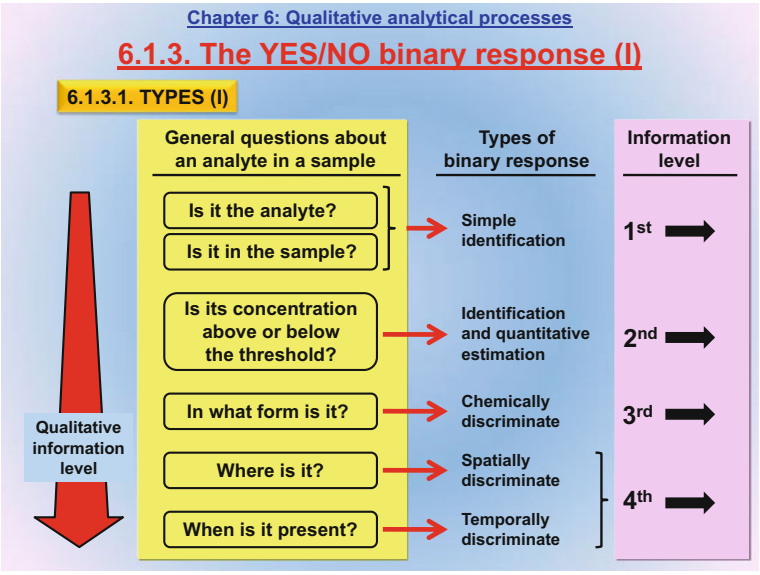
In *Binary Classification Analysis*, samples yielding a positive response (yellow circles) are separated from the rest (see Slide 6.5). One example is the classification of atmospheric samples into two groups depending on whether they contain acid rain gases (SO_x, N_xO_y) at levels exceeding the tolerated limits of the United States Environmental Protection Agency (US-EPA).

Multiple Classifying Analysis is more ambitious: it classifies samples into more than two groups, which usually requires using computers, chemometric software, sophisticated equipment and multiple information (e.g., the presence and concentration of several analytes) for each sample.

6.1.3 The YES/NO Binary Response (18 Slides)

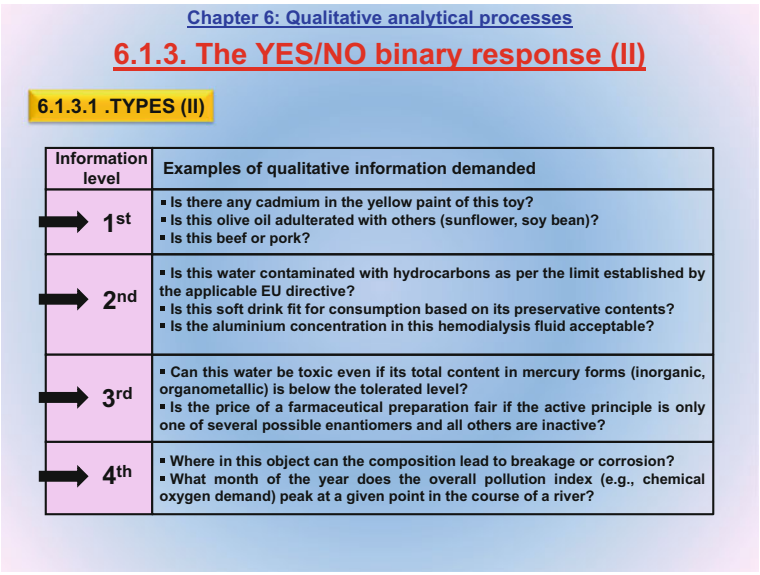
6.1.3.1 Types (4 Slides)

Slide 6.8



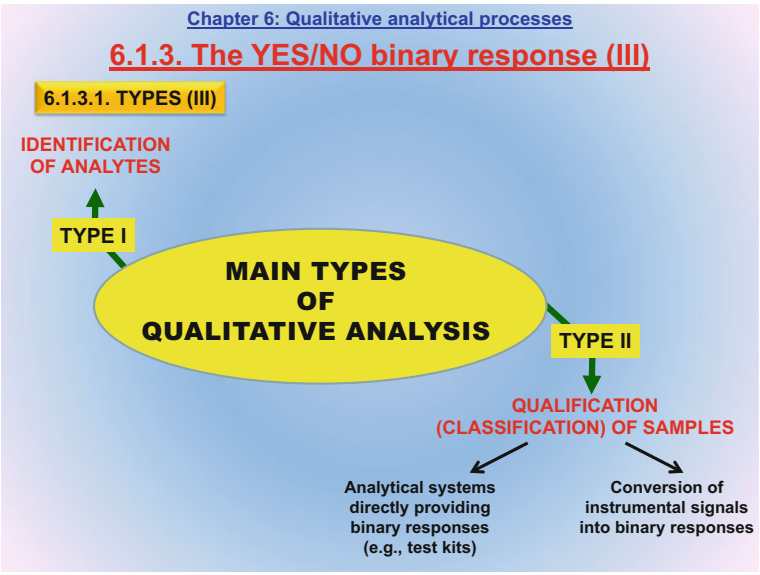
Qualitative Analysis can be classified in various ways. The classification in this slide is based on the type of information sought. The questions to be answered are shown here in increasing order of demand regarding the type of binary information involved. As can be seen, the types of response to be obtained range from simple identification (first level) through identification and quantitative estimation (second level), and chemically discriminate information (third level), to spatially and temporally discriminate information (fourth level).

Slide 6.9



These examples illustrate the four qualitative information levels in the previous slide. As noted earlier, these information requirements are becoming increasingly common, so Analytical Chemistry must gradually aim at their fulfilment.

Slide 6.10



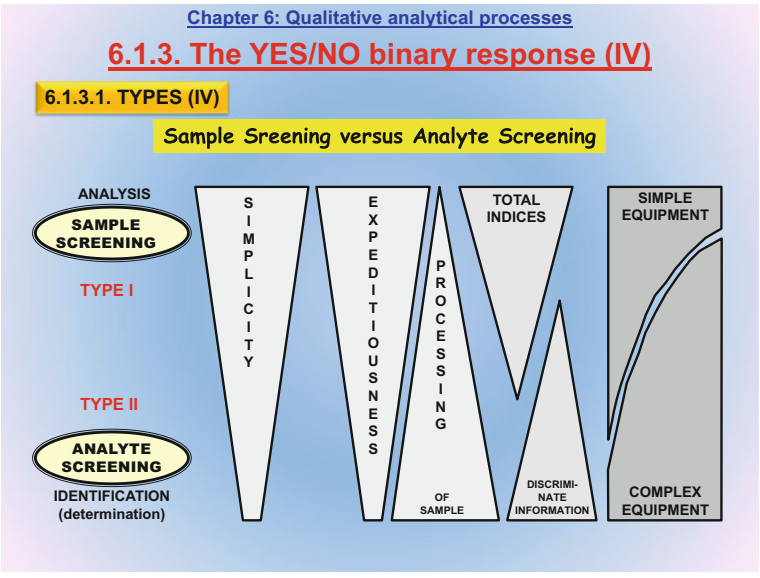
There are two major types of Qualitative Analysis according to primary purpose.

In *Type I* Qualitative Analysis the aim is to identify an analyte (e.g., phenol) or analyte family (several phenols including polyphenols).

In *Type II* Qualitative Analysis the target is the sample and the aim to qualify or classify it (e.g., to find whether it is edible on the basis of its toxin levels). Type II qualitative analyses can be performed in two ways.

- The simpler way involves using a straightforward, fast direct analysis system such as a reagent strip or test kit to obtain binary responses. One example is the pregnancy test kit for urine.
- Alternatively, a conventional analytical system such as a photometer, fluorimeter or chromatograph can be used to obtain instrumental signals for conversion into binary responses in accordance with a preset scheme. These modes of qualitative analysis is illustrated in the next slide.

Slide 6.11

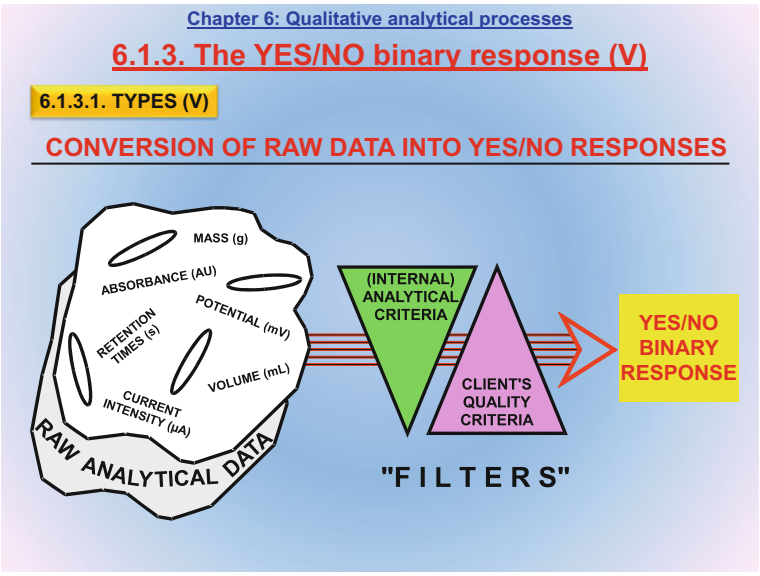


This slide highlights the differences between sample and analyte screening (that is, Type II and Type I Qualitative Analysis).

- Sample screening is more simple and expeditious than analyte screening—and so is the equipment needed by the former.
- Sample treatment is also more simple in sample screening than it is in analyte screening.

- Global information (e.g., total hydrocarbon levels in water) is more frequently managed in sample screening. On the other hand, specific information about individual analytes (that is, discriminate information such as hydrocarbon types in water) is more common in analyte screening.

Slide 6.12

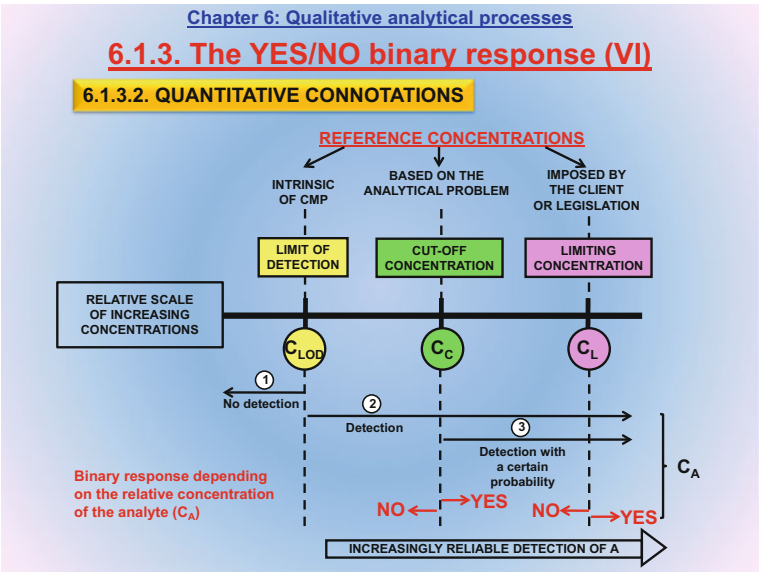


Converting primary instrumental data such as absorbances, fluorescence intensities, current intensities, volumes or potentials into binary responses is no easy task. In fact, it requires considering convergent and divergent criteria that are called "filters" here. The analytical criterion is intrinsic whereas the client's criterion, when applicable, is extrinsic.

In converting an absorbance datum for an analyte in a screened sample, the laboratory criterion materializes, for example, in constructing a calibration curve (see Slide 2.36) to derive a YES/NO binary response from the datum or using the limit of detection (LOD). The client's criterion, however, may differ depending on how strict the conversion is to be. Obviously, laboratory and client's criteria should always be reconciled when needed to solve an analytical problem (see Slides 7.8 and 7.23).

6.1.3.2 *Quantitative Connotations* (1 Slide)

Slide 6.13



6.13.1. As can be inferred from the previous slides, Qualitative Analysis frequently has quantitative connotations, especially when quantitative primary data are to be converted into binary responses (see Slide 6.12).

The conversion involves using a scale of absolute amounts (A) or concentrations (C_A) of analyte. The scale includes the *limit of detection* (C_{LOD}, Slide 2.40), which is typical of the analytical process, and the *limiting* or *threshold concentration* or amount imposed by legislation or the client (C_L). In some cases, the laboratory adopts a *cut-off concentration* C_C as a stricter limit than the threshold concentration for internal quality assurance—to avoid errors. Note that the limit of quantification (C_{LOQ}, Slide 2.41) has been excluded from the scale because it pertains to Quantitative Analysis.

6.13.2. The following two limits in the relative concentration scale define key zones in Qualitative Analysis.

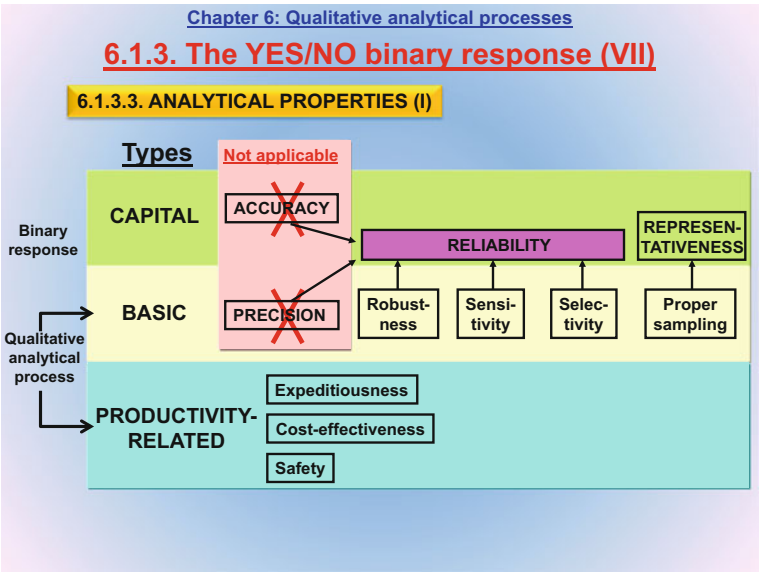
- The limit of detection sets the analyte concentration level above and below which the analyte is detected and not detected, respectively. This limit is inherent in the particular test or qualitative method.
- The cut-off concentration sets the level above which detection with a given probability will occur. This limit is self-imposed by the laboratory.

6.13.3. The cut-off and threshold concentrations also define the zones for the binary responses YES (right) and NO (left).

Interestingly, the proportion of errors in qualitative detection decreases with increasing analyte concentration. A new analytical property called "reliability" is defined in Slide 6.16.

6.1.3.3 Analytical Properties (7 Slides)

Slide 6.14

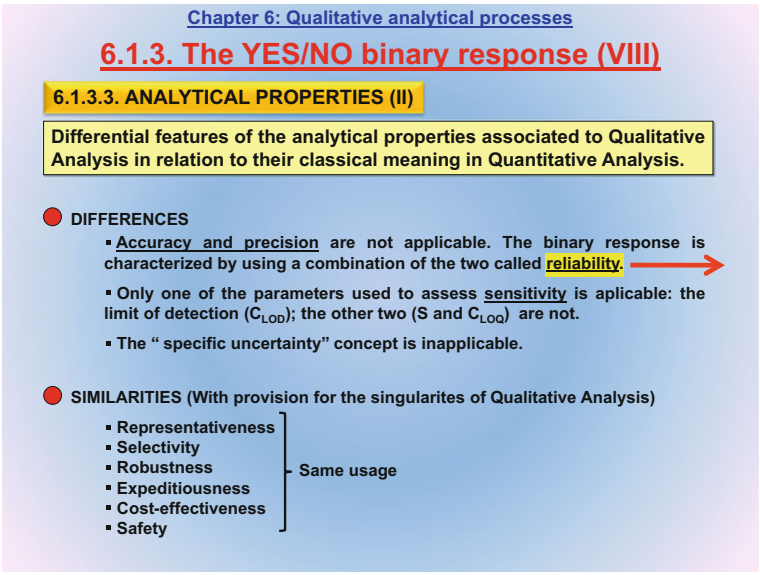


The overview of analytical properties in Slide 2.4 is directly applicable to Quantitative Analysis but requires some adaption for use in Qualitative Analysis. Although the three types of properties (namely, capital properties for the binary response, and basic and productivity-related properties for the analytical process) remain, they differ in two respects from those pertaining to Quantitative Analysis. Thus,

(1) accuracy and precision are not applicable to Qualitative Analysis; and
(2) a new capital property called *reliability*, which rests on the three basic properties (robustness, sensitivity and selectivity), is required.

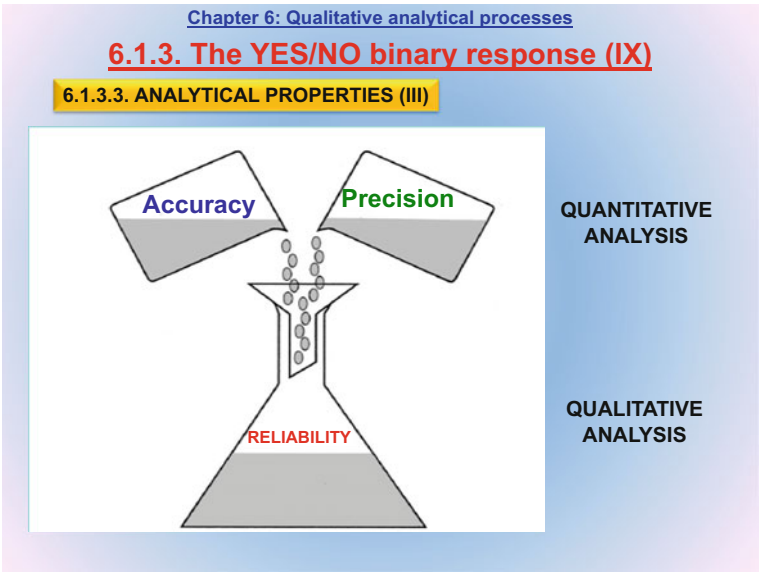
There next slide discusses other, more specific differences.

Slide 6.15



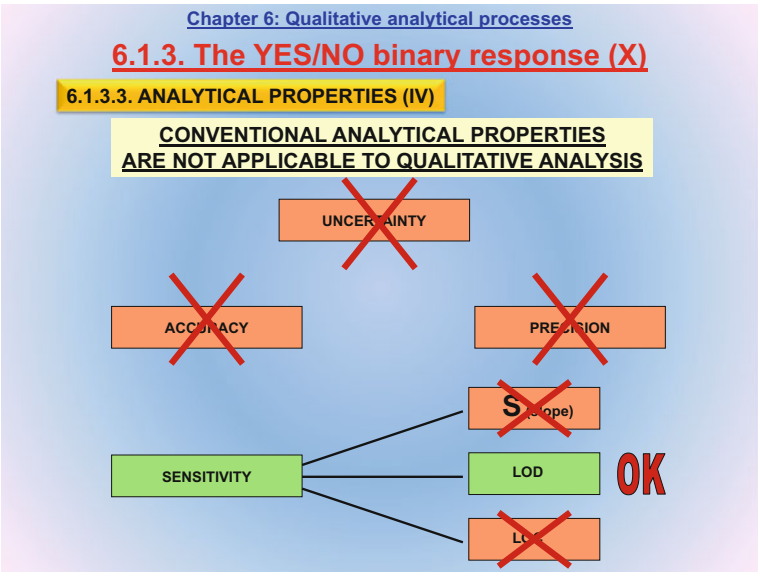
This slide summarizes again the similarities and differences between the analytical properties applicable to Quantitative and Qualitative Analysis. As can be seen, the limit of detection (LOD, Slide 2.40) is the only sensitivity-related parameter applicable to Qualitative Analysis.

Slide 6.16



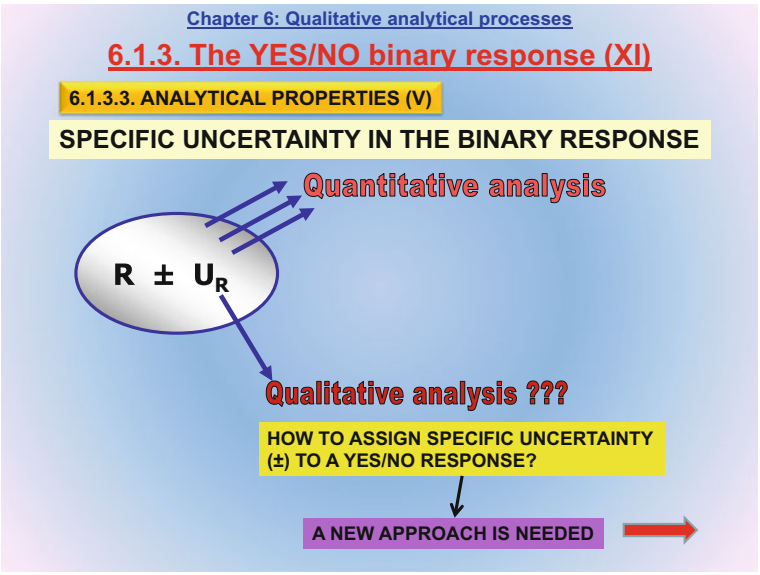
The capital property *reliability* pertains to Qualitative Analysis even though it is a combination of two classical properties pertaining to Quantitative Analysis, namely: accuracy and precision.

Slide 6.17



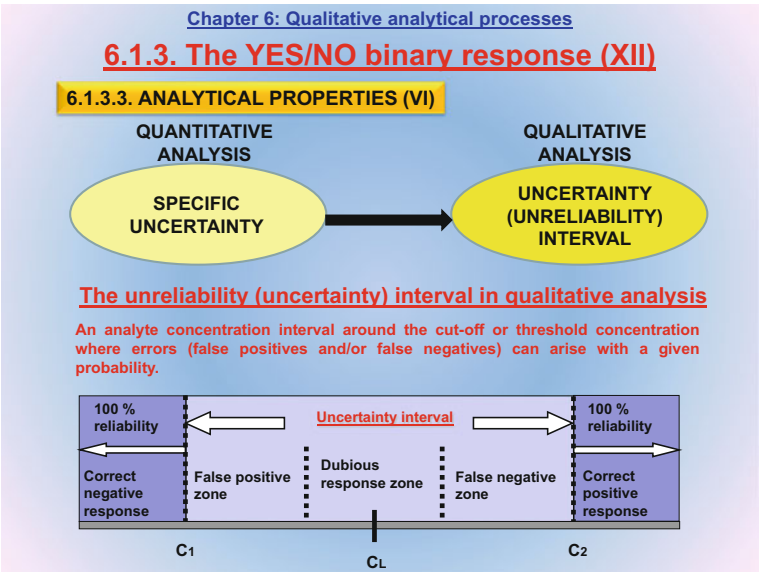
This is a brief summary of the capital (uncertainty and accuracy) and basic properties (precision and two sensitivity measures) not applicable to Qualitative Analysis.

Slide 6.18



The specific uncertainty of a numerical result R, U_R, which is described in detail in connection with Quantitative Analysis in Slides 2.29 and 2.31, cannot be used in Qualitative Analysis. How can a YES/NO binary response thus be assigned an uncertainty interval? By approaching uncertainty in a novel, unorthodox manner that is described in the next slide.

Slide 6.19



Specific uncertainty, which is typical of Quantitative Analysis (see Slide 2.29), should be converted into an *uncertainty* or *unreliability interval* in Qualitative Analysis.

The uncertainty or unreliability interval is defined as the —generally symmetric— range around the cut-off (C_C) or threshold concentration (C_L) where errors—whether false positives or false negatives—can be expected to occur at a given probability level (e.g., 95%). The interval is experimental established as follows:

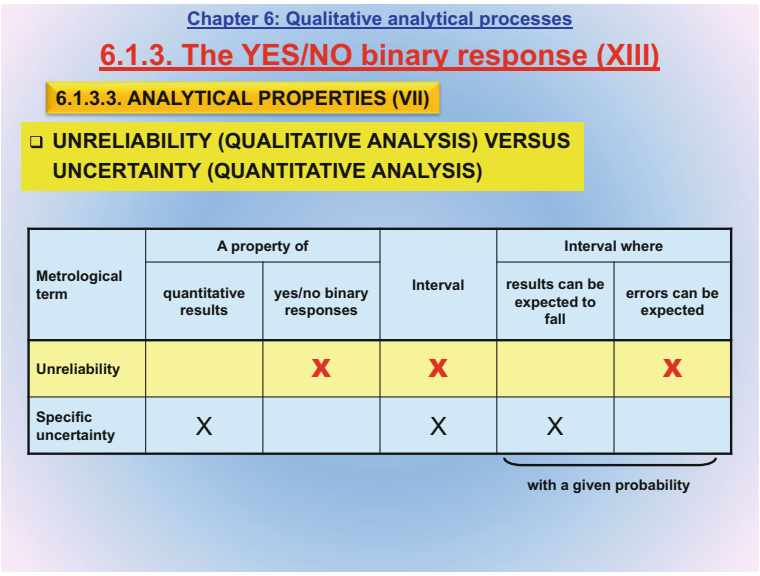
(1) A set of standard samples containing variable concentrations of analyte is prepared. Because the analyte concentration in each sample is known, the result (response) can directly be deemed correct or incorrect and a distinction between false positives and false negatives, which are explained in Slide 6.21, be made. Each sample in the set is subjected to the qualitative analytical process and the results recorded.

(2) The results are plotted on an analyte concentration scale including the threshold or limiting concentration. Around such a concentration is the uncertainty interval (C_1–C_2), which includes a zone of dubious responses, another of false positives at the low-concentration end (near C_1) and a third of false positives at the high-concentration end (near C_2). Outside the uncertainty interval are two zones where

– a negative response at low concentrations ($<C_1$) will be correct; and
– a positive response at high concentrations ($>C_2$) will also be correct.

Therefore, the width of the uncertainty interval determines the reliability or confidence of a qualitative result.

Slide 6.20



This slide compares unreliability in Qualitative Analysis to specific uncertainty in Quantitative Analysis. Both concepts represent a concentration interval which, however, differs between the two types of analysis. Thus,

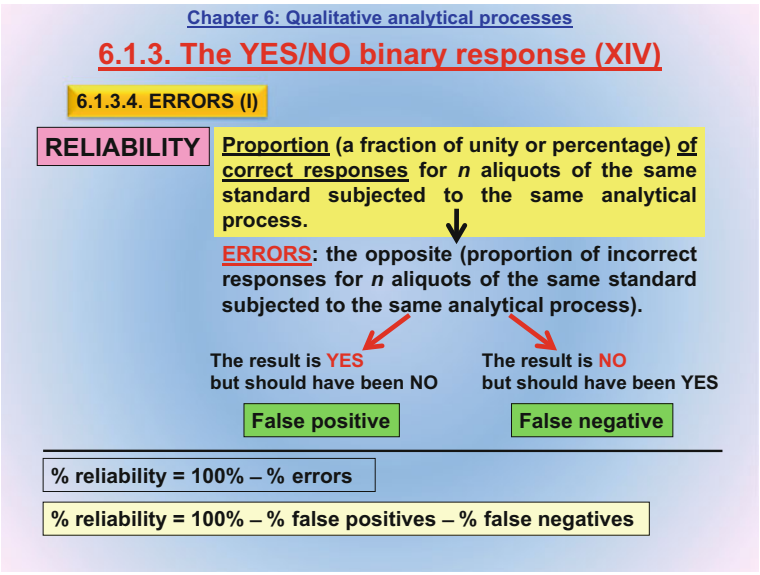
- in Qualitative Analysis, the unreliability interval is the zone where errors (false positives or false negatives) arise;
- in Quantitative Analysis, the specific uncertainty interval is the concentration range where the result for another aliquot of the same sample subjected to the same analytical process can be expected to fall (see Slide 2.7).

Both intervals share a common trait: their width depends on the selected probability level—albeit in a different manner. Thus, the unreliability interval is a range of values where the result is incorrect (that is, a range where trueness in a qualitative result cannot be assured). As a consequence, the higher is the statistical probability in Qualitative Analysis, the narrower will be interval. Conversely, the higher is the probability (confidence) in Quantitative Analysis, the higher will be the specific uncertainty and the wider the interval as a result (see Slides 2.29 and 2.31).

This difference arises from the way the intervals are conceived in Qualitative and Quantitative Analysis. Thus, the unreliability interval is a range of errors—an unwanted outcome—whereas the uncertainty interval is a range where the result can be expected to fall—a desirable outcome.

6.1.3.4 Errors: False Positives and False Negatives (3 Slides)

Slide 6.21



6.21.1. This slide defines "reliability", which appears in the overview of analytical properties applicable to Qualitative Analysis (see Slide 6.14).

Subjecting n aliquots of a standard sample with known binary responses to a qualitative test provides n binary responses the reliability of which will be given by the ratio of accurately identified aliquots to the total number of aliquots.

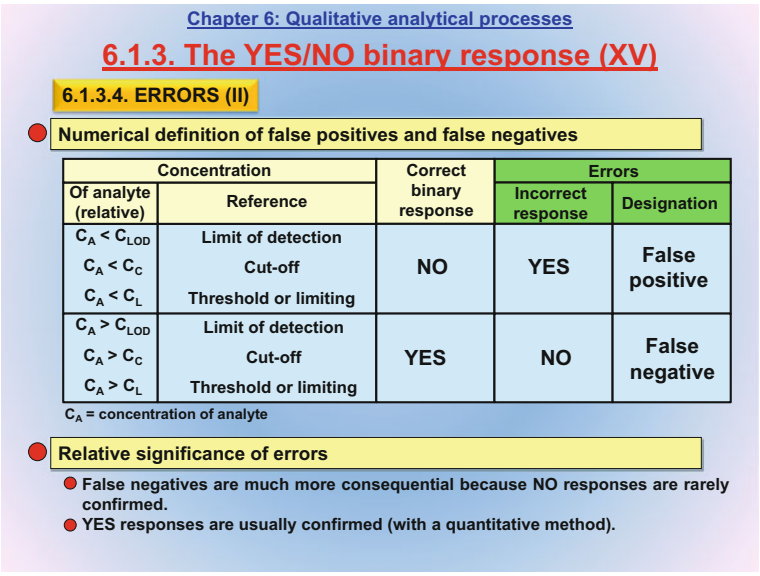
6.21.2. The opposite of "reliability" is "error", which is defined here as the proportion of incorrect responses. In Qualitative Analysis, errors can be of two types, namely:

- *False positives*, which occur when the result is YES but should have been NO and are especially likely at analyte concentrations slightly below the limiting concentration (C_L).
- *False negatives,* which arise when the result is NO but should have been YES and are therefore more likely to occur at concentrations slightly above C_L.

A sample containing an analyte concentration near C_L may give a *dubious result* (see Slide 6.19).

6.21.3. The percent reliability of a qualitative analysis is calculated by subtracting the proportion of errors (that is false positives and false negatives, which can be easily discriminated) from 100.

Slide 6.22



6.22.1. Whether a binary response is correct, a false positive or a false negative can be ascertained by relating the analyte concentration (C_A) to the limit of detection, cut-off concentration or threshold concentration.

- Thus, when C_A is lower than the previous limits, the correct binary response is NO, so YES is incorrect and constitutes a false positive.
- On the other hand, when C_A exceeds the previous limits, the correct response is YES, so NO is incorrect and a false negative.

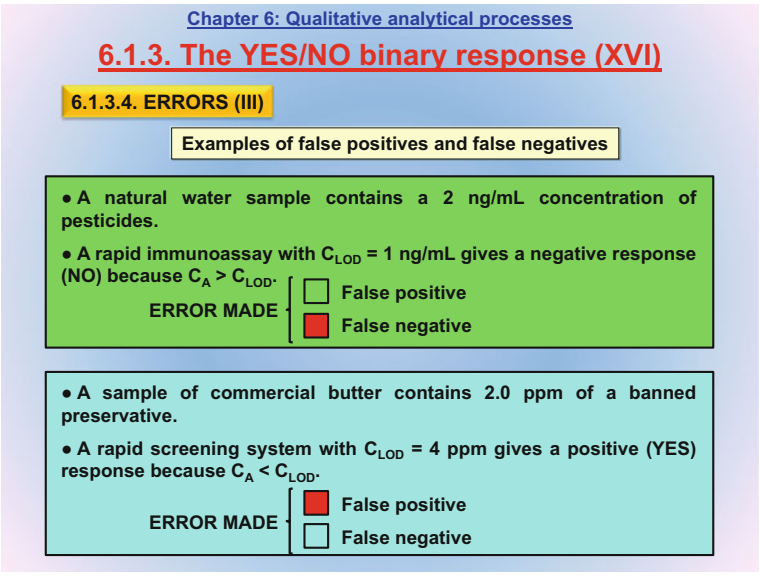
The table is highly illustrative. As can be seen, the concentration level to be used in order to classify a response as YES or NO depends on the particular limit chosen.

6.22.2. It is extremely important to understand that the two types of error in Qualitative Analysis differ strongly in their practical consequences. Thus, as can be seen in Slide 6.5, if the response of a screening system is NO, the analysis is finished; on the other hand, if the response is YES, the samples testing positive are almost invariably subjected to a confirmatory analysis with a conventional analytical process.

Consequently, false negatives should be avoided at any rate because they are not routinely confirmed. For example, a customs laboratory passing an imported batch of peanuts which has incorrectly tested negative for mycotoxins in a screening

analysis can have serious adverse consequences on consumers' health because mycotoxins are carcinogenic. The ensuing risk should be avoided by assuring the complete absence of false negatives in the analysis.

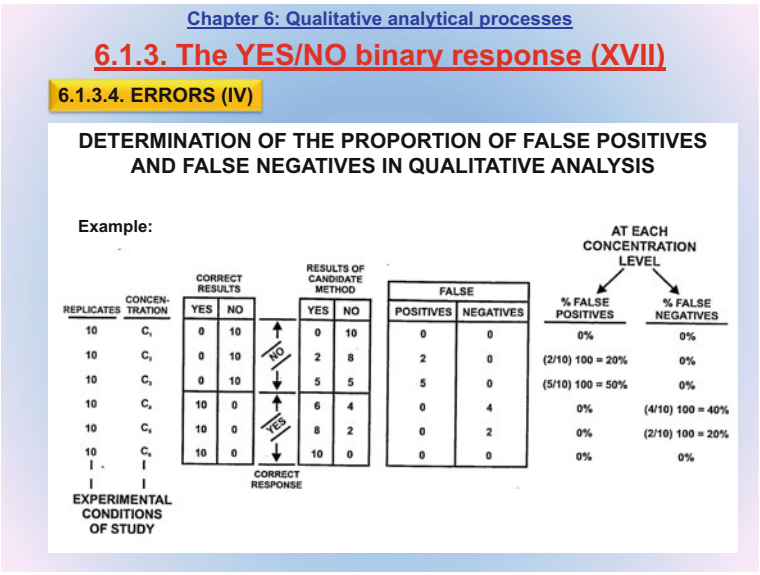
Slide 6.23



6.23.1. These are two examples of errors (false positives and false negatives) in Qualitative Analysis providing for the concepts explained in the previous slide.

6.23.2. The red boxes represent the correct way of labelling the ensuing errors.

Slide 6.24



The experimental procedure for calculating the proportion of false positives and false negatives, and the unreliability interval around the threshold concentration (C_L) for a screening system, is as follows:

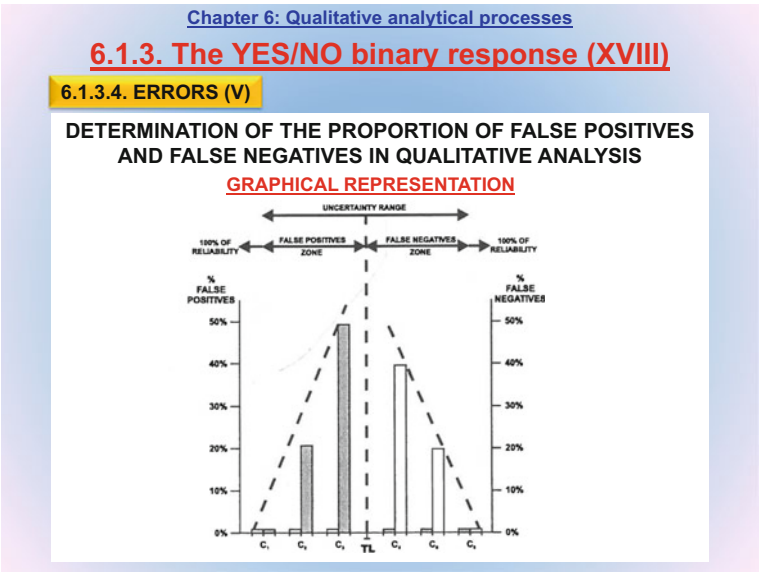
(1) A set of, for example, 60 standard samples containing 6 different analyte concentrations C_1–C_6 (that is, 10 replicates per concentration) is prepared. Three of the chosen concentrations (C_1–C_3) should be higher than the threshold concentration (C_L) and the other three (C_4–C_6) lower.
(2) The samples are subjected to the screening process in a random sequence and a binary response for each is obtained.
(3) Since the correct binary responses for the whose sample set are known, each sample can be classified as "correct", "false positive" or "false negative" by comparison with the actual (experimental) result.

The table shows the results for the 60 samples according to analyte concentration (C_1–C_6).

Although the 30 samples with $C_A < C_L$ should have yielded a NO response, not all did—particularly those containing the analyte at concentrations near the threshold (C_2 and C_3), which gave 2 (20%) and 5 (50%) false positives, respectively. Note that errors increased with increasing nearness of the analyte concentration to C_L.

Likewise, all 30 samples with $C_A > C_L$ should have tested positive (YES) for the analyte; however, 4 samples with C_4 and 2 with C_5 led to false negatives. Again, the number of errors increased with increasing nearness of the analyte concentration to C_L.

Slide 6.25

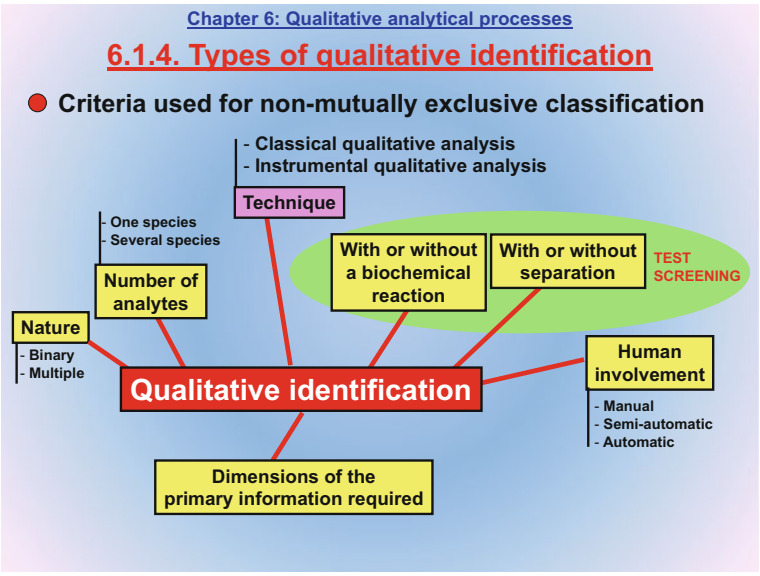


This graph shows the two types of errors in Qualitative Analysis (false positives and false negatives) on two *y*-axes as a function of the analyte concentration on the *x*-axis. The graph focuses on the zone around the threshold concentration, where the three concentrations below C_L and the three above it in the example of the previous slide are placed. As can be seen, the errors exhibit a Gaussian distribution on the analyte concentration scale, which encompasses the zones shown in that slide — that of dubious results excluded.

Both types of errors increase near the threshold concentration. At the two ends of the scale are the zones of total reliability, that is, of error-free classification of samples as YES (left end) or NO (right end).

6.1.4 Types of Qualitative Identification (1 Slide)

Slide 6.26



This is an overview of Qualitative Analysis in the form of non-mutually exclusive classifications according to various, complementary criteria, namely:

(1) *Nature of the response*, which can be binary (YES/NO) or multiple (see Slide 6.7).
(2) *Number of analytes*, which can be one (e.g., phenol) or several (e.g., an analyte family such as phenols).
(3) *Analytical technique*, which can be a classical or instrumental qualitative test or screening system. This criterion is used to describe Qualitative Analysis in Sects. 6.1.5 and 6.1.6.

(4) *Type of qualitative test* or *screening system* used, which can involve

- one or several *(bio)chemical reactions*; and
- With and without a chromatographic or non-chromatographic *analytical separation system.*

(5) Binary and multiple classification of samples entail using a given number of primary data (signals) obtained in a discriminate manner from a single or several instrumental parameters (that is, *specific information dimensions*).

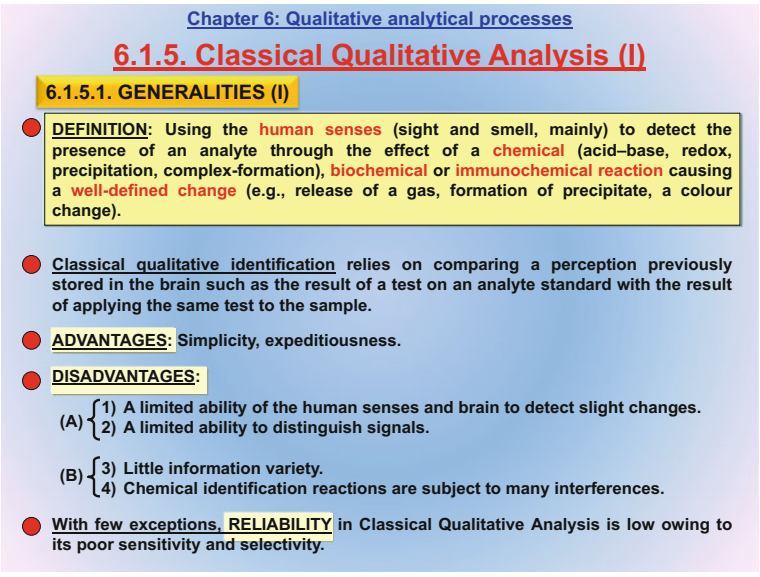
- Classical Instrumental Analysis generally uses a single "instrument" (e.g., human sight) to observe a single signal (e.g., formation of a precipitate).
- Identifying quinine in tonic water by its native fluorescence entails using two instrumental parameters (the excitation and emission wavelengths) to produce a signal (fluorescence intensity).
- Identifying a substance by infrared (IR) absorption spectroscopy requires using a whole IR spectrum, which entails acquiring a large number of absorbance signals at many different wavenumbers. Only in that way can the target substance be identified (see, for example, benzene in Slide 6.37).

In summary, Qualitative Analysis possesses a variety of nuances that substantially enrich it conceptually.

6.1.5 Classical Qualitative Analysis (8 Slides)

6.1.5.1 *Generalities* (2 Slides)

Slide 6.27



This brief description of *Classical Qualitative Analysis* is started with its definition, which comprises the use of

- human senses as "instruments" and the brain as a "computer"; and
- (bio)chemical or immunological reactions between the analyte and a reagent to obtain a product that can be easily seen or smelt.

Qualitative identification additionally involves *comparing* the signal for the analyte—or its absence—with that for a standard. The two are compared by the brain to produce a result: YES or NO. Thus, if an unknown liquid smells of acetic acid (the standard), the liquid can be identified as vinegar.

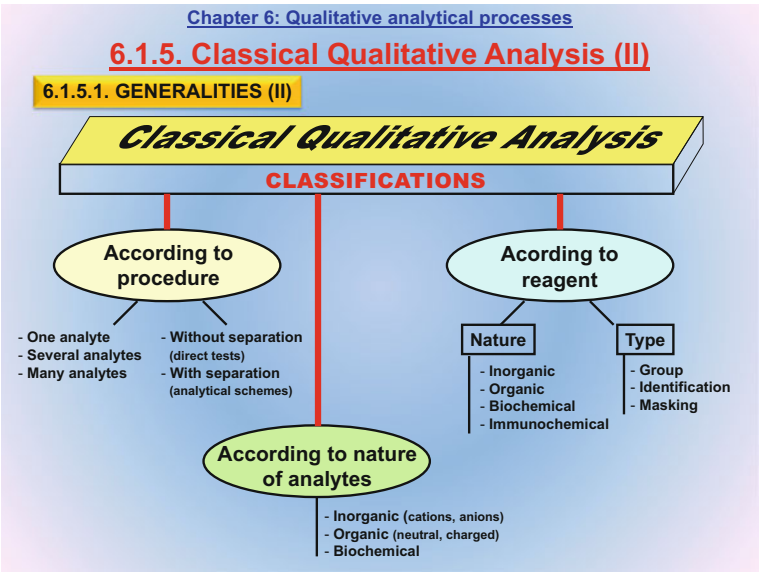
Although Qualitative Analysis possesses doubtless advantages (e.g. expeditiousness and simplicity), it also has major limitations such as the following:

- a low selectivity arising from little variety in the information that can be obtained and the fact that the reactions used—immunoassays excepted—are typically subject to many interferences; and
- an also low sensitivity resulting from the limited ability of human senses to detect small changes.

As a consequence, reliability in Classical Qualitative Analysis is usually modest because it rests on the basic properties sensitivity and selectivity (see Slide 6.14 for a general scheme of analytical properties in Quantitative Analysis).

The previous limitations preclude the use of Classical Qualitative Analysis for multiple classification and restrict it to binary (YES/NO) classification (see Slide 6.7).

Slide 6.28

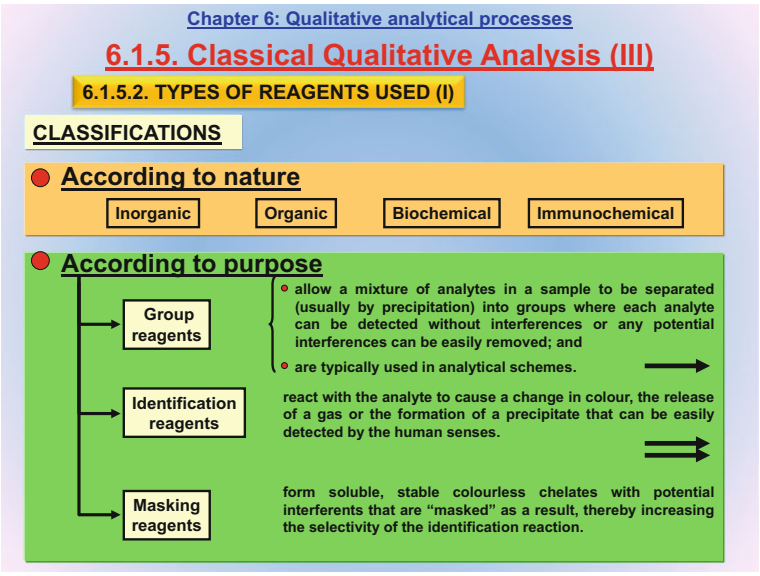


This slide classifies Classical Qualitative Analysis according to the following criteria:

(1) The *experimental procedure* used, which depends on whether one, several or many analytes are to be identified in the same sample. Sensitive, selective reagents, which are very scant, afford *direct analyses* (that is, analyses without separation); most often, however, some *analytical separation* into groups of species (that is, an analytical scheme) is needed to improve the sensitivity and selectivity of the identification.
(2) The *nature of the analytes*, which will require a different type of procedure depending on whether they are inorganic, organic or biochemical.
(3) The *nature and purpose of the reagents*, which is very important (see Slides 6.29 and 6.30).

6.1.5.2 Types of Reagents (3 Slides)

Slide 6.29



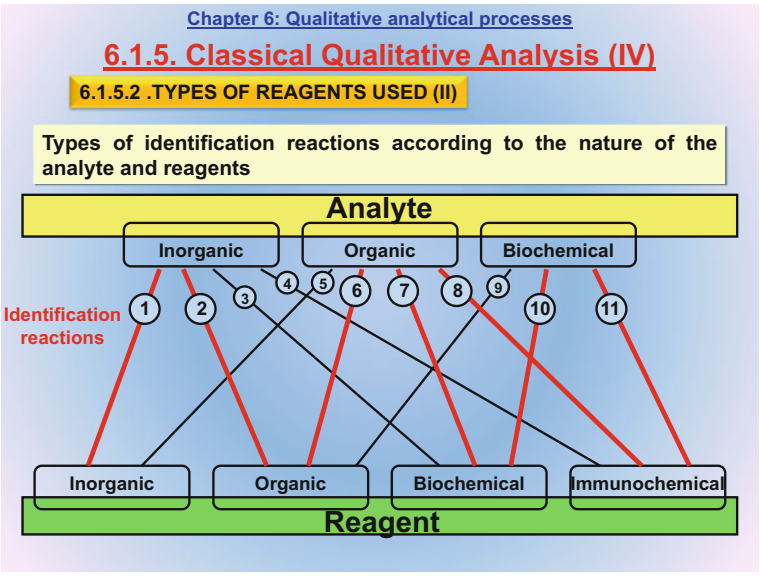
This slide expands on the classifications of Classical Qualitative Analysis according to the nature and purpose of the reagents used for identification.

The first classification, based on the *nature of the reagents*, distinguishes between biochemical and immunochemical reagents—the latter are especially useful by virtue of their high selectivity.

The second classification is based on the *function of the reagents*, namely: separating a group of analytes, identifying an analyte or masking it to facilitate the identification of others.

Both classifications are discussed in greater detail in the next two slides.

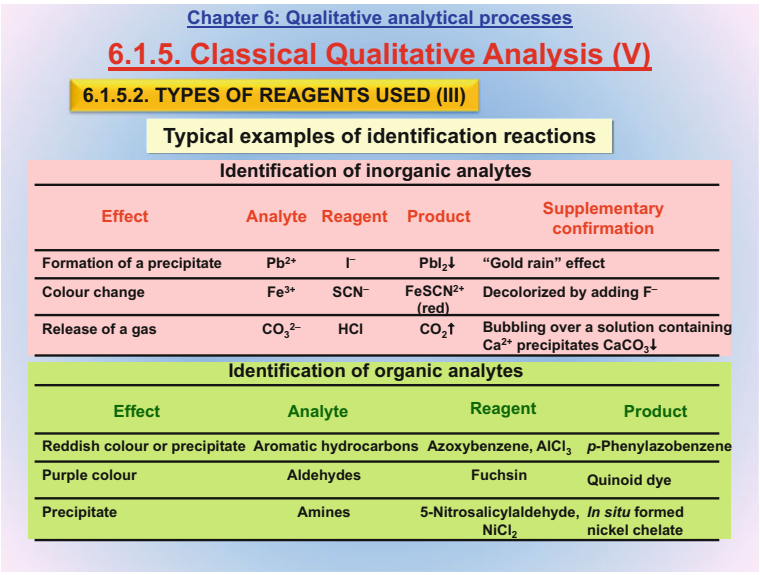
Slide 6.30



Based on their nature, analytes and reagents —largely identification reagents— can be related in eleven different ways for purposes the most common among which are as follows:

- detection of inorganic analytes with inorganic or organic reagents;
- detection of organic analytes with organic, biochemical or immunochemical reagents; and
- detection of biochemical analytes with biochemical or immunochemical reagents.

Slide 6.31

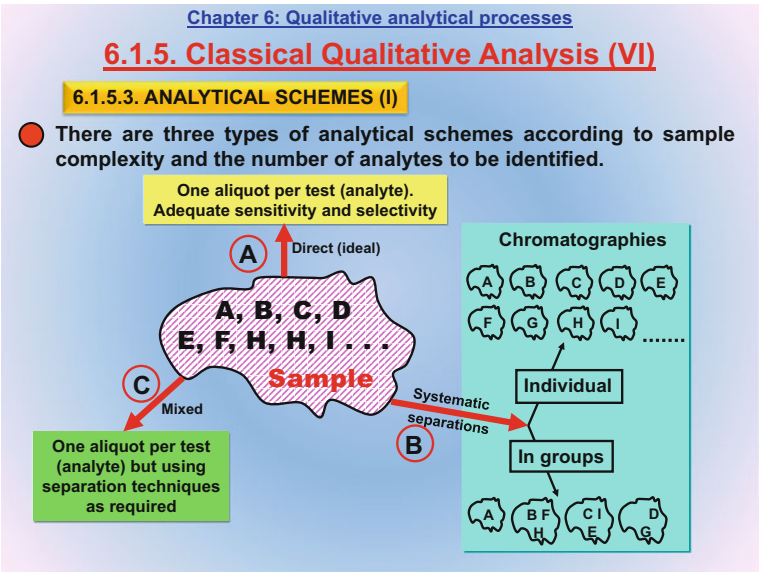


These are several examples of identification reactions.

- The first table exemplifies the detection of inorganic analytes according to the effect to be detected by the human senses (formation of precipitate, a colour change, bubbling of a gas). The analyte, the reagent and the substance producing the effect are stated, and so is the supplementary confirmation reaction to be used.
- The second table shows three examples of identification of organic species (or species families). The effect shown on the first column in each row is due to the product on the last.

6.1.5.3 Analytical Schemes (3 Slides)

Slide 6.32



Analytical schemes are classical qualitative analytical processes that are used to detect many analytes (A, B, C, D, E, F, etc.) in the same sample. There are three different types of systematic detection processes depending on the characteristics of the sample matrix and the number of analytes to be identified, namely:

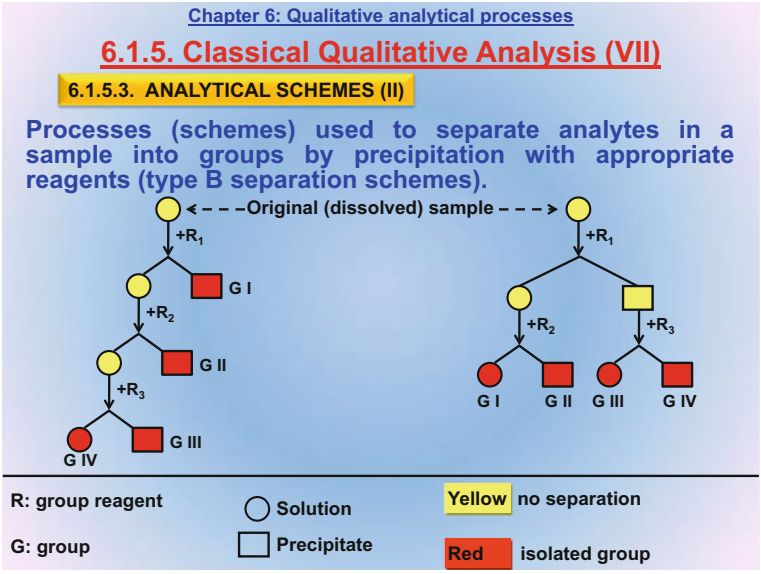
(A) *Direct detection processes*, which can only be used in ideal situations and involve subjecting *n* aliquots of sample to *n* direct, independent tests for each analyte. The low sensitivity and selectivity of Classical Qualitative Analysis make direct detection highly desirable but unfeasible unless only a few analytes contained in a simple sample matrix (e.g., water) are to be identified—which, however, usually requires using highly specific, expensive reagents.

(B) *Processes involving systematic separations* to isolate individual analytes or analyte groups in order to increase the sensitivity and selectivity of the detection tests. Analytes can be separated in two different ways, namely:

- *Chromatographically.* Each analyte is isolated in a given zone of the mobile phase to enable its interference-free detection.
- *By groups*. This requires using so-called "group reagents" (see Slide 6.29), which are usually precipitants, in systematic separations. *Analytical schemes with group separation* are described in Slides 6.33 and 6.34.

(C) *Mixed* processes. These are combinations of the previous two involving the sequential detection of each analyte in a sample aliquot with or without application of a separation system. These processes constitute *analytical schemes without group separation* (see Slide 6.34), a dubious designation because they do involve separations—to identify individual analytes rather that to separate them in groups, however.

Slide 6.33

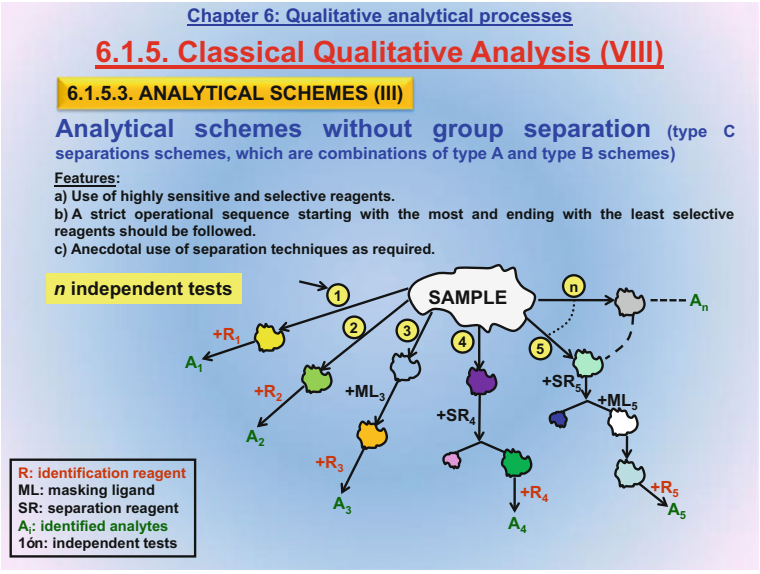


Analytes can be separated into different groups (G) by using precipitating reagents (R) in two different ways, namely:

(1) By sequentially adding the reagents (R_1–R_3 in the slide) to the sample solution in order to successively separate the analytes into groups (I–III), after which the sample will only contain a group of soluble analytes (IV) not reacting with the precipitants.
(2) By using a reagent R_1 to split the analytes in the sample into two large groups: soluble and insoluble analytes. In parallel, the two groups are treated separately with two other reagents R_2 and R_3 in order to eventually obtain two soluble groups (I and III) and another two insoluble groups of analytes (II and IV).

The symbols at the bottom of the slide make it easier to interpret the two types of schemes.

Slide 6.34



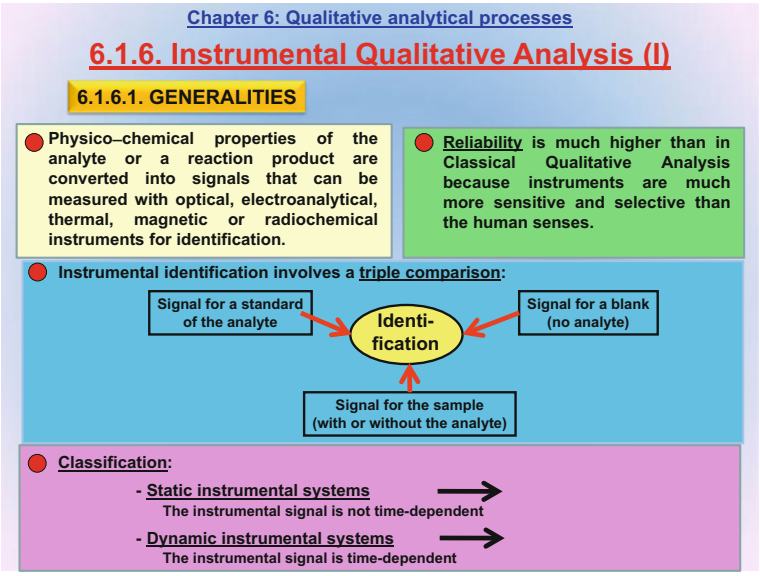
This slide explains analytical schemes without group separation for the identification of a set of analytes A_1–A_n in the same sample, which share several common features, namely:

- they involve performing *n* independents tests (one per analyte to be identified);
- they use highly sensitive and selective—and usually expensive—reagents;
- the identification tests must be conducted in a strictly controlled sequence—from the most sensitive or selective to the least;
- the qualitative information obtained in each test is used to adjust the next—hence the need to use highly sensitive and selective tests first;
- each test requires some separation, usually with a precipitating reagent or, less often, a masking (chelating) reagent (see Slide 6.29); and
- the complexity (number of steps) of the tests increases as the identification process develops.

6.1.6 Instrumental Qualitative Analysis (7 Slides)

6.1.6.1 Generalities (1 Slide)

Slide 6.35



6.35.1. *Instrumental Qualitative Analysis* uses instrumentally measured physico–chemical properties of analytes or their reaction products for identification.

6.35.2. Identification in Instrumental Qualitative Analysis relies on a *triple comparison* involving the measurements (signals) for a blank (the sample matrix containing no analyte), a standard of the analyte and the sample from which analytical information is to be extracted.

For example, the fluorescence intensity I_F at a given excitation and emission wavelength for the blank signal was 0.020; that for a sample standard containing an analyte concentration C_{AP} was 0.210; and that for the target sample 0.280. The signal (fluorescence intensity) corresponding to the analyte concentration is thus 0.260 and a simple proportion allows C_A to be easily calculated.

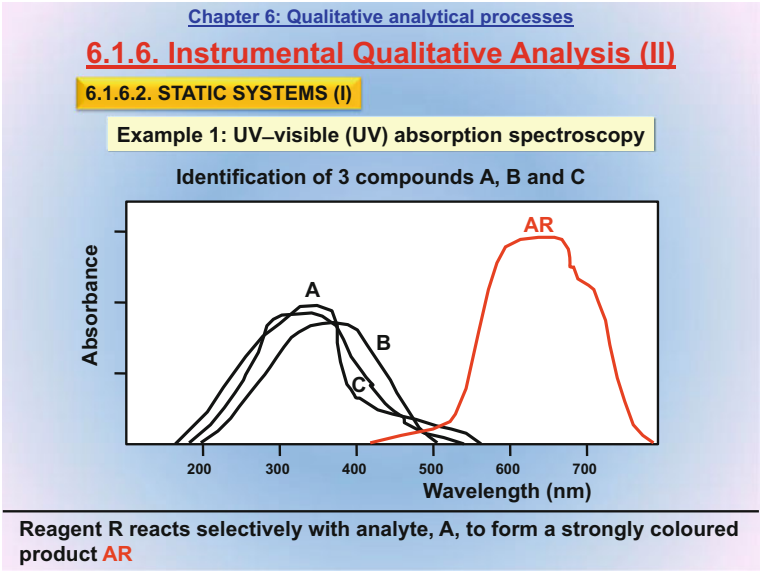
If the analyte concentration is equal to or greater than the limiting concentration ($C_A \geq C_L$), then the binary response will be YES; otherwise ($C_A < C_L$), the response will be NO.

6.35.3. Reliability is much greater in Instrumental Qualitative Analysis than it is in Classical Qualitative Analysis because instruments are much more sensitive and selective than the human senses.

6.35.4. Instrumental Qualitative Analysis can be classified in many different ways. The most immediate way is according to the type of signal (optical, electroanalytical, thermal, mass, radiochemical) used for identification. The following four slides describe an alternative classification based on the time-dependence of the signal, according to which instrumental qualitative analytical systems can be of the *static* or *dynamic* type.

6.1.6.2 Static Systems (2 Slides)

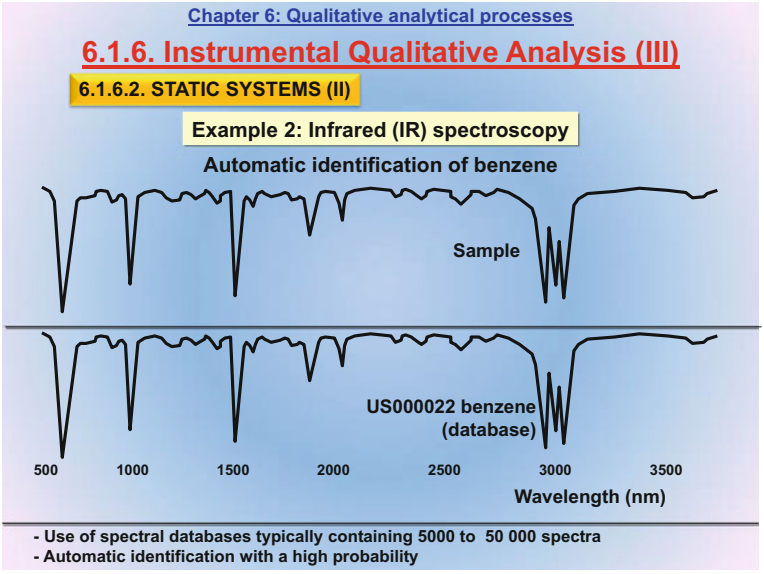
Slide 6.36



In *static systems*, the signal remains constant over time.

Not all measuring instruments are equally capable of discriminating signals for different sample components. Thus, UV–visible absorption spectroscopy has a low discrimination potential. As can be seen in the slide, identifying all three analytes (A, B, and C) in this example is impossible because their absorption spectra (absorbance vs wavelength recordings), in black, are very similar, so no wavelength zone exists where each analyte can be detected in the presence the other two. If no alternative detection equipment is available, the analytes must be discriminated chemically. For example, if a reagent R reacts selectively with only one of them (e.g., A) to form a bluish red chelate AR and the chelate absorbs at 600 nm without interference from the other two analytes, A can be reliably identified.

Slide 6.37



This slide illustrates the automatic identification of benzene by infrared (IR) absorption spectroscopy, which is a widely used technique for qualitative analytical purposes.

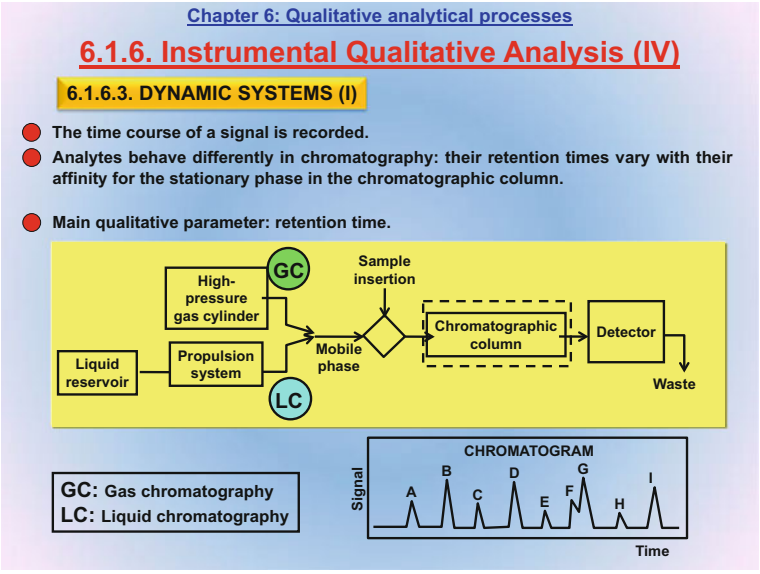
The signals for the sample and the standard (US000022) remain unchanged with time. Comparing a large number of instrumental (absorbance, wavenumber) data ensures a high reliability.

The first IR spectrum corresponds to the sample and the second to an analyte standard as recorded in a spectral database. A computer allows the sample spectrum to be compared to more than 50,000 spectra in a database and, if a coincidence is found, the analyte to be matched to a specific compound with a given level of reliability (98% in our case). Advances in miniaturization have allowed databases to be incorporated into measuring instruments and enormously empowered Instrumental Qualitative Analysis as a result.

A mass spectrometer (MS) is another instrument with a high analyte identification potential.

6.1.6.3 Dynamic Systems (4 Slides)

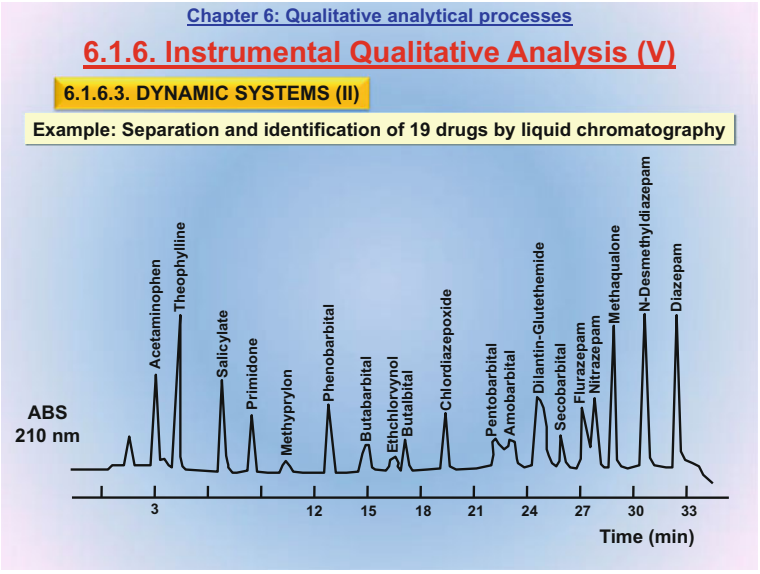
Slide 6.38



In *dynamic systems* for Instrumental Qualitative Analysis, the measured signal changes with time (it is time-dependent). These systems typically use a detector coupled to a GC or LC chromatographic column or electrophoretic capillary for detection after separation. Each analyte is identified in terms of a qualitative parameter called the "retention time". If the chromatogram exhibits a signal at the typical retention time for a given analyte, then the binary response for the presence of the analyte in the sample will be YES.

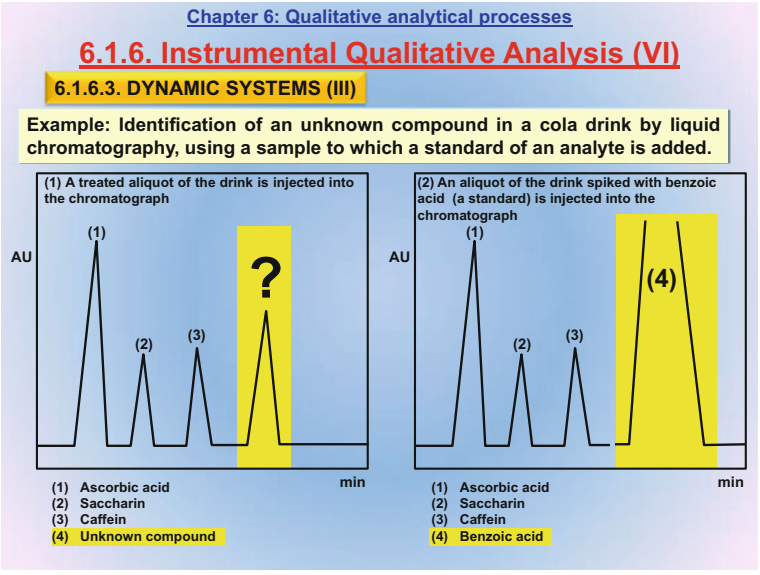
This slide depicts a gas chromatograph (GC) and a liquid chromatograph (LC), which differ in the way the chromatographic fluid is propelled and hence in the nature of the mobile phase. The two use a similar, but not identical, sample insertion (injection) system, column and continuous detector.

Slide 6.39



This slide illustrates the potential of liquid chromatography for multi-identification with the separation and identification of 19 drugs in human serum. Although some peaks in the chromatogram are overlapped, their retention times are different enough for qualitative identification purposes.

Slide 6.40

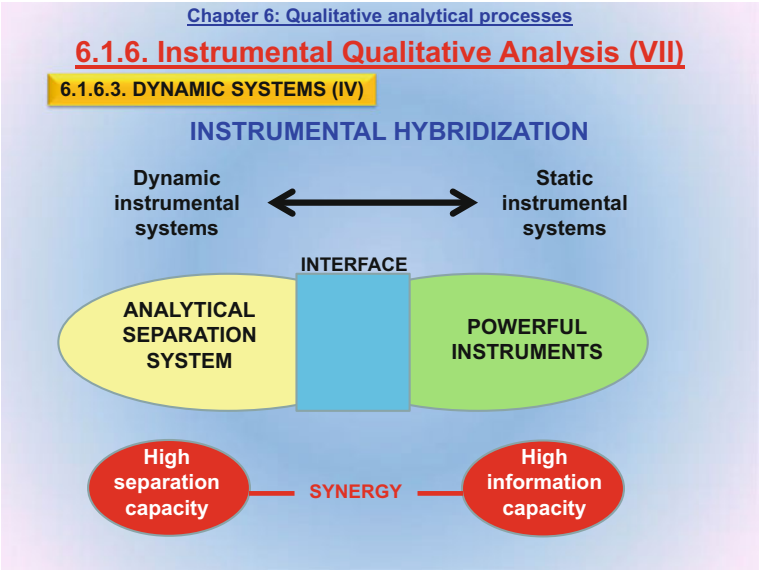


6.40.1. This is a real-life example: the identification by liquid chromatography of an unknown compound in a cola drink.

6.40.2. A sample of the drink gives a chromatograph including three identifiable (expected) peaks and a fourth corresponding to an unknown compound—possibly an acidulant.

6.40.3. Samples of the drink spiked with different preservatives are analysed in the same manner. The sample to which benzoic acid is added gives a peak coinciding with the fourth in the chromatogram for the initial sample, albeit much higher, which confirms that the peak in the original chromatogram corresponded to the acidulant benzoic acid.

Slide 6.41



So-called *instrumental hybridization* is the synergistic combination of two or more instrument systems in order to boost their individual qualitative and quantitative information potentials. The key to an effective connection here is finding an appropriate interface with a view to maximizing analyte separation and information production.

A large number of hybrid instrumental systems are commercially available at present. Especially interesting are those combining a dynamic system and a static system.

Most hybrid systems use a gas or liquid chromatograph, or a capillary electrophoresis system, in combination with a mass spectrometer. The detector coupled to the separation system should never be of the destructive type. Hybrid systems produce vast amounts of information that require computerized processing but afford extremely reliable qualitative identifications.

6.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

M. Valcárcel

Springer-Verlag, Berlin, 2000

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

The contents of this chapter coincide to a great extent with those of Chapter V in the book ("Qualitative Aspects of Analytical Chemistry"). Although this chapter is more synthetic, it contains more examples and elaborates on some topics to better illustrate the state of the art in Qualitative Analysis (particularly as regards screening systems and the adapted description of the "uncertainty" concept). The book provides a source for direct consultation. Few Analytical Chemistry textbooks deal with Modern Qualitative Analysis.

Metrology of Qualitative Chemical Analysis

M. Valcárcel et al.

European Commission, Brussels, 2002.

This 166-page document presents a systematic approach to basic and applied developments in Metrology in Qualitative Analysis. This chapter is based on it.

PAPERS

Qualitative Analysis

M. Valcárcel et al.

Encyclopaedia of Analytical Science, Elsevier (Amsterdam), 2005, 405–411.

This paper expands on the contents of the present chapter. The paper is structured similarly but contains additional figures that complete the message of this chapter.

Analytical Features of Qualitative Analysis

S. Cárdenas & M. Valcárcel

Trends in Analytical Chemistry, 2005, 24, 477–487.

This paper focuses on the singularities of analytical properties as applied to Qualitative Analysis. Thus, it provides firm support for the description of analytical properties and errors here. The paper additionally describes the validation of an analytical process for qualitative purposes.

6.3 Questions on the Topic (Answered in Annex 2)

6.1. Does the qualitative analysis of samples fit in Classification Analysis?

6.2. What name is usually given to qualitative analytical processes?

6.3. Tick the analytical properties that are not applicable to Qualitative Analysis.

[ ] Representativeness
[ ] Accuracy
[ ] Precision
[ ] Sensitivity

6.4. Two methods for the qualitative analysis of milk samples possibly contaminated with pesticides provide wrong information. Thus, method A gives false positives and method B false negatives. Which would you use? Why?

6.5. What are the main differences between Qualitative Analysis and Quantitative Analysis? Tick the correct answers.

[ ] The binary response
[ ] A classical method of analysis
[ ] The use of analytical chemical standards
[ ] The analytical property "reliability"
[ ] Selectivity

6.6. What are the differences between binary and multiple classification in Qualitative Analysis?

6.7. What are the factors dictating the following parameters?
(a) Limit of detection
(b) Cut-off concentration
(c) Threshold concentration

6.8. What is a false positive in Qualitative Analysis? Give an example.

6.9. What is a false negative in Qualitative Analysis? Give an example.

6.10. An immunochemical test (method A) and a chemical spot test (method B) are used to detect the same analyte in the same sample. The results of analysing 100 samples are as follows:

	Reliability (%)	False positives (%)	False negatives (%)
Method A	95	2	3
Method B	94	6	0

Which method provides the better results? Why?

6.11. What analytical properties are applicable to quantitative determinations but not to qualitative tests? Why?

6.12. What are "analytical systems with group separation" in Classical Qualitative Analysis?

6.13. What are the differences between group, identification and masking reagents in Classical Qualitative Analysis?

6.14. Name two identification (Qualitative Analysis) procedures used in dynamic instrumental systems (e.g., chromatography).

6.15. Tick the words directly connected with Qualitative Analysis:

[ ] Detection
[ ] Quantification
[ ] Identification
[ ] Qualification

6.16. How does a "white" sample differ from a "black" sample?

6.17. Is Qualitative Analysis important to modern Analytical Chemistry? Why?

6.18. What are the three quantitative landmarks for the binary response in Qualitative Analysis?

6.19. One brand of canned tuna fish contains 4 ppm tin. A qualitative test with C_{LOD} = 1 ppm for the metal gave a positive (YES) response. What type of error was made?

[ ] None
[ ] A false positive
[ ] A false negative

6.20. What type of error is the more crucial in Qualitative Analysis? Why? Give an example.

6.21. Is "specific uncertainty" applicable to Qualitative Analysis? Why?

6.22. What are the three most important limitations of Classical Qualitative Analysis in relation to Instrumental Qualitative Analysis?

6.23. What are the three types of reagents used in Qualitative Analysis? What is their purpose? Give an example of each.

	Name	Purpose	Example
Type 1			
Type 2			
Type 3			

6.24. What are the three main features of so-called "analytical schemes without group separation"?

6.25. What is the difference between a dynamic and a static instrumental system in Qualitative Analysis?

6.26. What analytical properties are applicable to Qualitative Analysis?

6.27. Are both types of calibration applicable to Qualitative Analysis?

Method calibration [ ] Yes [ ] No
Equipment calibration [ ] Yes [ ] No

6.28. What types of instruments does Classical Qualitative Analysis use?

6.29. What are masking reagents? In what context are they used?

6.30. Define "reliability" in Qualitative Analysis. To which classical analytical properties does it relate?

6.31. Instrumental Qualitative Analysis relies on a triple comparison of signals to be subjected to the analytical process. What do the three signals belong to?

6.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened by about 30% for teaching Analytical Chemistry to students not majoring in Chemistry. The following 12 slides can be omitted for this purpose:

- Section 6.1.2: Slides 6.5, 6.6 and 6.7.
- Section 6.1.3: Slides 6.11, 6.12, 6.17, 6.18, 6.19, 6.20, 6.24 and 6.25.
- Section 6.1.6: Slide 6.41.

Part III
Socio-economic Projection of Analytical Chemistry

Analytical Problem-Solving

7

Abstract

This chapter deals with the concept of "problem" in Analytical Chemistry, and is concerned with the impact and consequences, both internal and external, of solving analytical problems. The analytical problem as a target has invigorated Classical Analytical Chemistry with new challenges and goals beyond its chemical metrological role; also, it has led to analytical chemical knowledge crossing further traditional boundaries and reaching society at large to respond to the increasing needs for socio-economically useful answers. The ubiquity of the analytical problem in the analytical chemical and socio-economic realms has turned it into their interface and main link. So much so that solving analytical problems has become a priority goal in fulfilling the practical requirements of Analytical Chemistry; one that has required expanding the scope of representativeness to accommodate the results to the client's requirements. This chapter describes the steps involved in the analytical problem-solving process, and the potential coincidence or divergence between the information required by the client and that actually delivered by the analytical chemist. Also, it relates "quality", a general concept discussed at length in Chap. 8, to "analytical quality", which constitutes the central core of the topic: solving analytical problems.

Teaching Objectives

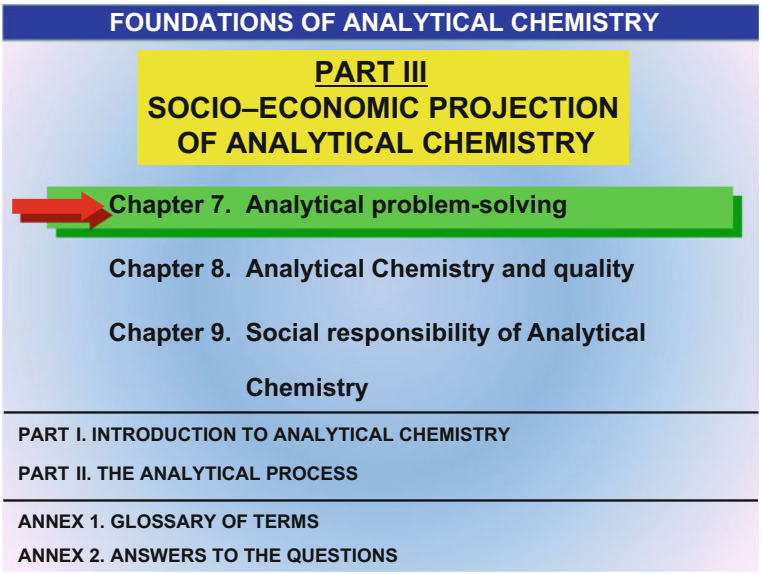
- To introduce students to "analytical problem" and describe its elements.
- To describe the general steps of the analytical problem-solving process.
- To compare "required information" and "delivered information".
- To emphasize the applied side of Analytical Chemistry.

Electronic Supplementary Material The online version of this chapter (doi:10.1007/978-3-319-62872-1_7) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_7

7.1 Explanation of the Slides

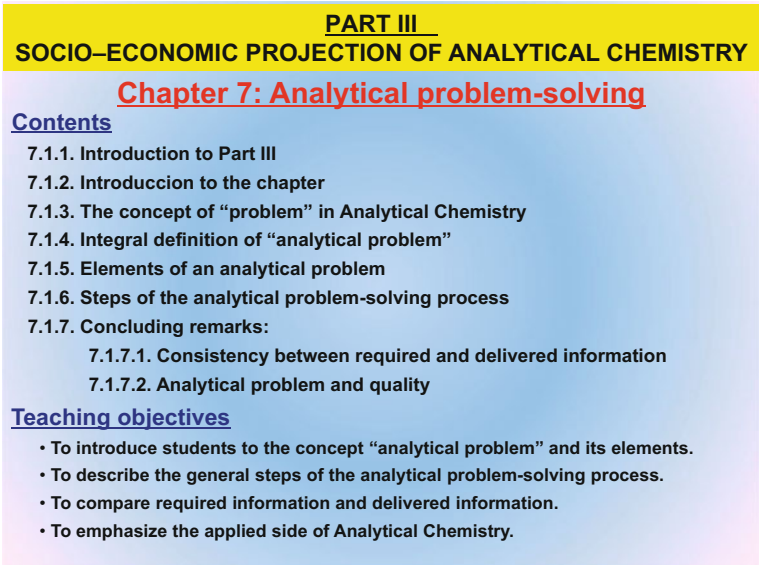
Slide 7.1



This slide places in Part III (Socio-economic Projection of Analytical Chemistry) and shows the other two parts of the book.

This chapter, which is the first discussing the socio-economic approach to Analytical Chemistry deployed across Part III, is concerned with solving analytical problems (that is, with fulfilling information requirements).

Slide 7.2



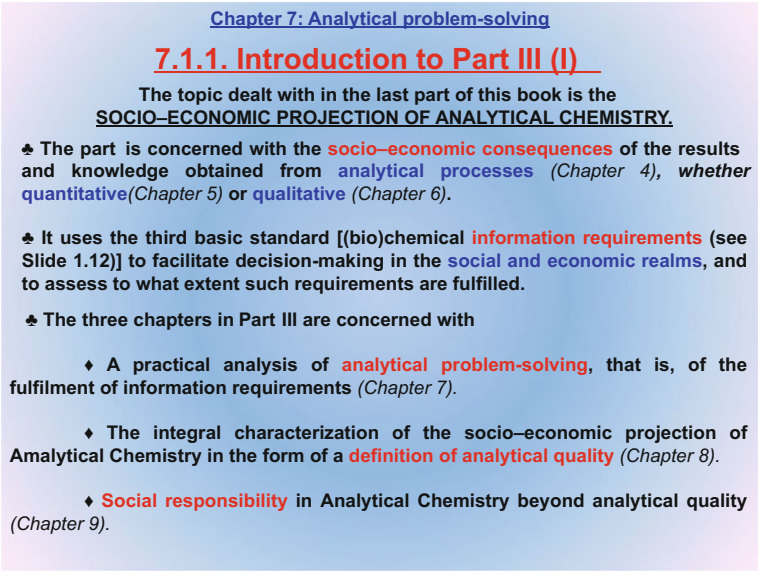
7.2.1. This slide outlines the contents of the chapter, which are explained in the seven sections shown. The last section comprises two sub-sections.

The chapter includes a preliminary introduction to Part III and several sections concerned with "analytical problem" and its elements. Also, it deals with the analytical problem-solving process, and relates "delivered information" to "required information". Finally, it places the analytical problem in the context of quality.

7.2.2. At the bottom of the slide are the objectives to be fulfilled in connection with the analytical problem, the problem-solving process, and the types of information involved (required and delivered). This chapter pertains to the applied side of Analytical Chemistry.

7.1.1 Introduction to Part III (2 Slides)

Slide 7.3



7.3.1. Part III is mainly concerned with the socio-economic inputs and outputs of Analytical Chemistry.

7.3.2. The part explores the impact and socio-economic consequences of the information (results and knowledge) derived from qualitative and quantitative analytical processes. The most salient features of the analytical process, Quantitative Analysis and Qualitative Analysis are explained in Chaps. 4, 5 and 6, respectively.

7.3.3. At the heart of the part is "required information", which constitutes the third basic standard of Analytical Chemistry. In fact, the information required by the client dictates how the analytical process is to be designed and decisions are to be made. Inevitably, such decisions have some socio-economic consequences—which also pertain to the thematic core of the part.

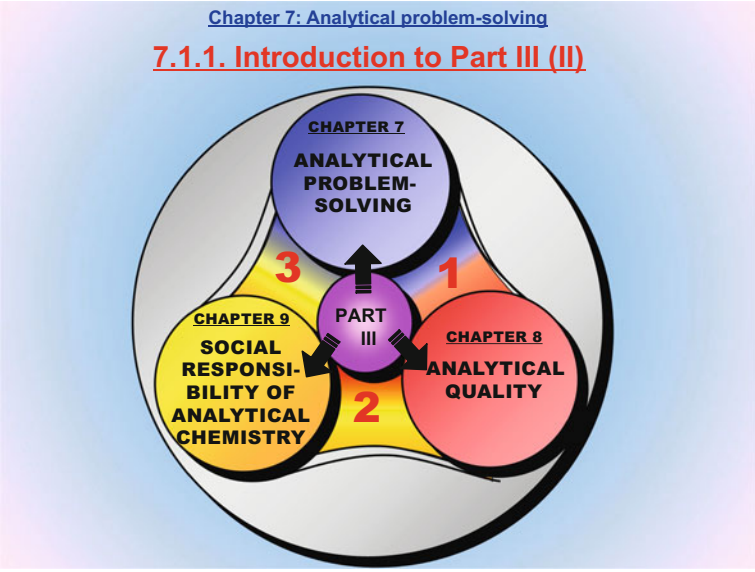
7.3.4. Part III comprises the following three chapters:

- This chapter, devoted to Analytical Problem-Solving;
- Chapter 8, concerned with Analytical Quality; and
- Chapter 9, devoted to Social Responsibility in Analytical Chemistry.

Although the socio-economic implications of Analytical Chemistry can be discussed in terms of Analytical Quality (Chap. 8), Social Responsibility (Chap. 9) constitutes the most comprehensive and faithful expression of its social and economic projection.

Despite their close relationships, the three facets are examined separately here for easier understanding.

Slide 7.4

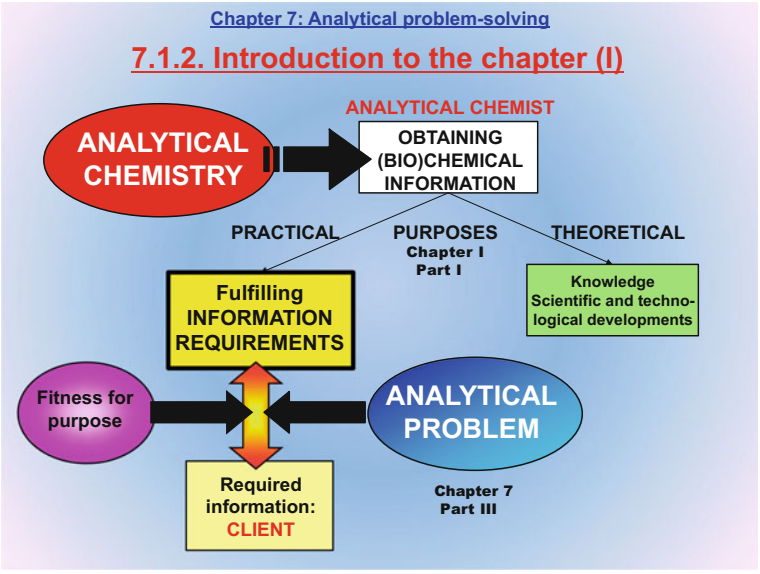


This slide connects the three chapters of Part III, which are concerned with the socio-economic projection of Analytical Chemistry. The triangle shows the three interfaces connecting the topics of this chapter and Chaps. 8, 9. As can be seen, each chapter is connected via two interfaces of the following types:

- *Interface 1*. Analytical Problem-Solving and analytical quality are related in Sect. 7.1.7.2. The basic side comprises properties or characteristics (indicators), whereas the applied side involves fulfilling information requirements (see Slide 7.28).
- *Interface 2*. Analytical Quality is only one element of Social Responsibility in Analytical Chemistry, which comprises more general social, economic and environmental implications. Even so, their internal and external connotations do not overlap in full.
- *Interface 3*. Providing a complete, honest response to specific information requirements (that is, solving the analytical problems) is the essential internal connotation of Social Responsibility in Analytical Chemistry.

7.1.2 Introduction to the Chapter (2 Slides)

Slide 7.5



7.5.1. This slide places the concept "analytical problem" in Analytical Chemistry.

As can be seen, one of the main goals of Analytical Chemistry is to obtain (bio)chemical information. The process is led and conducted by the analytical chemist.

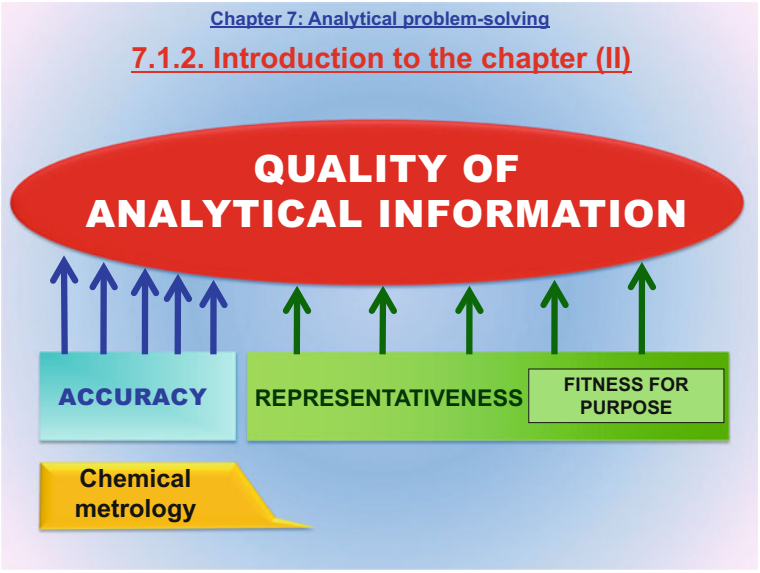
7.5.2. (Bio)chemical information can be sought for theoretical and/or practical purposes (see Slide 1.8). The practical purpose (fulfilling information requirements) is favoured over the theoretical purpose (deriving scientific and technological

knowledge, and development) here because this chapter pertains to the applied side of Analytical Chemistry.

7.5.3. The practical purpose is fulfilling a client's information requirements. Fluent communication between the client and the analytical chemist obviously requires the latter to supply the former with information that is fit for the intended purpose.

7.5.4. The analytical problem is depicted here as the interface between required information and its purpose. Fulfilling information requirements entails correctly planning and solving an analytical problem—and the problem, which is the subject matter of this chapter, connects the analytical chemist to the client.

Slide 7.6



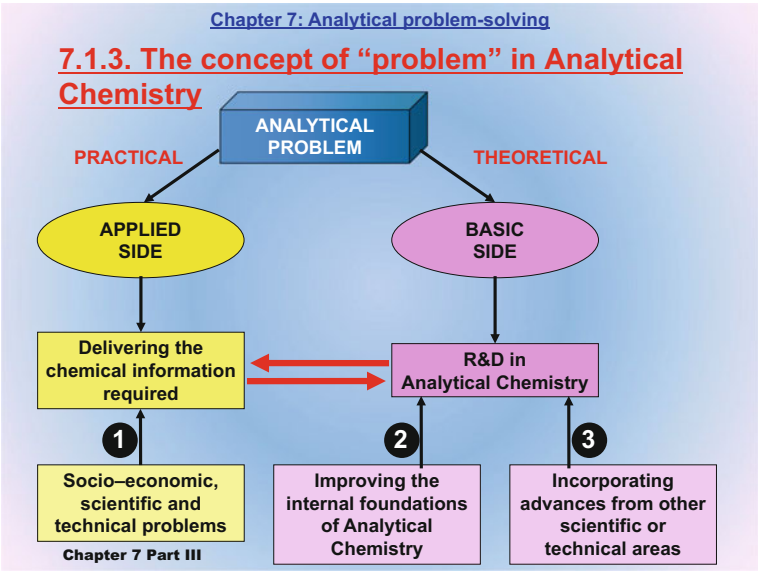
7.6.1. These are the essential ingredients of quality in analytical information, which include the capital analytical properties accuracy and representativeness (see Slides 2.4 and 2.13–2.17).

7.6.2. A third ingredient is also needed, however: fitness for purpose. This new ingredient is simply a new practical form of representativeness in Analytical Chemistry; in fact, in order to fulfil the client's information requirements (see Slide 7.5), the analytical chemist must deliver information that is fit for the intended purpose. Therefore, fitness for purpose is essential to Applied Analytical Chemistry, where it arises from the analytical problem and constitutes the third cornerstone of quality and representativeness in the results.

7.6.3. Chemical metrology is depicted here as a framework for accuracy. However, chemical metrology only includes the most orthodox notion of representativeness (namely, "internal representativeness", Slide 7.10), without provision for "fitness for purpose" and hence for analytical problem-solving as an integral element.

7.1.3 The Concept of "Problem" in Analytical Chemistry (1 Slide)

Slide 7.7



7.7.1. The concept "analytical problem" arises on both the applied (practical) and basic (theoretical) side of Analytical Chemistry. The two sides share the goal depicted in Slide 7.5: obtaining (bio)chemical information from objects and systems.

7.7.2. On the applied side, analytical information is obtained to fulfil information requirements (that is, for the practical purpose of Slide 7.5); on the basic side, information is obtained to further knowledge, research and innovation in Analytical Chemistry (that is, for the theoretical purpose of Slide 7.5).

7.7.3. The concept "analytical problem" is connected with the basic and applied sides at points 1–3 in the slide.

(1) On the *applied (practical) side* of Analytical Chemistry, the analytical problem arises from the need to solve social, economic, scientific and technical problems. Such problems constitute the starting point and unavoidable reference for correctly planning and solving the analytical problem. This is the facet of "analytical problem" dealt with in this chapter.

(2) On the *basic (theoretical) side*, the analytical problem arises as an element of the internal foundations of Analytical Chemistry. In addition, the analytical problem is an incentive for improvement. Thus, solving the problem entails relying on other foundations such as *analytical properties*, *proper planning* and

assurance of the traceability chain, which often calls for innovation and development through research.

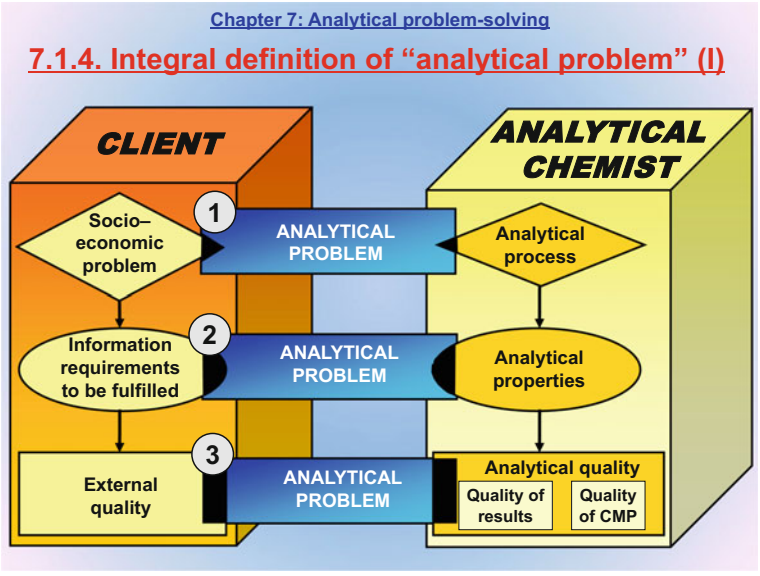
(3) On the basic side, the analytical problem also arises as a means of connecting scientific or technical areas (that is, as a link between the shared foundations of scientific disciplines). Because the knowledge used to address an analytical problem should be consistent with the particular information requirements, Analytical Chemistry must continuously acquire knowledge and incorporate advances from different branches of science.

7.7.4. The purposes of the two sides are obviously and necessarily related by the analytical problem. Obtaining appropriate information to solve an analytical problem requires using theoretical knowledge produced by research. Also, scientific and technical research and development rest on information obtained by solving analytical problems in order to improve the theoretical knowledge base of Analytical Chemistry and propagate it to other scientific areas.

7.1.4 An Integral Definition of "Analytical Problem" (5 Slides)

The concept "analytical problem" is briefly defined and exemplified in Slides 1.28 and 1.29, respectively. This section provides a more comprehensive definition that considers its socio-economic connotations (client–chemist communication), its place in analytical concept hierarchies; its innovative, ground-breaking nature; and its traceability chains.

Slide 7.8



7.8.1. This slide deals with "analytical problem" from a socio-economic perspective (specifically, as the link between the client requiring information and the analytical chemist producing it).

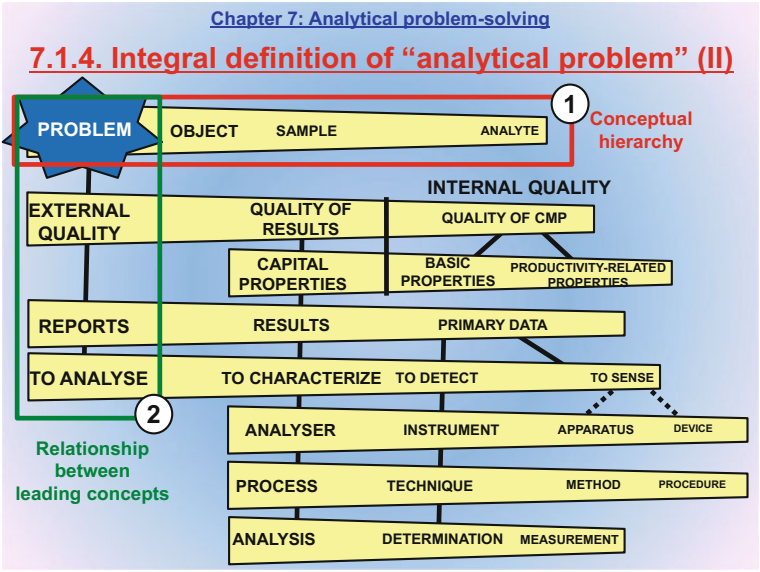
In the client's realm fall the socio-economic problem to be solved by fulfilling specific information requirements and the external quality imposed by the client.

In the analytical chemist's realm falls the analytical process. Depending on how effectively the process is planned and implemented, the ensuing levels of analytical properties will lead to a given degree of analytical (internal) quality (a combination of quality in the results and quality in the CMP).

7.8.2. The analytical problem arises as the interface connecting the client to the analytical chemist in three different ways.

(1) *First*, the analytical problem is the link between the socio-economic problem on the client's side and the analytical process on the analytical chemist's side. Correctly planning an analytical problem in accordance with the client's socio-economic problem entails designing a valid, assessed analytical process adjusted to the client's information needs.
(2) *Second*, the analytical problem connects the information requirements to be fulfilled on the client's side to analytical properties on the analytical chemist's side. The analytical chemist should be able to assure the levels of analytical properties required by the client; this in turn will require that the analytical problem contain any information needed to express, discard and validate the analytical properties of the associated analytical process.
(3) *Third*, the analytical problem relates external quality on the client's side to analytical quality on the analytical chemist's side—a product of quality in the results and in the Chemical Measurement Process (CMP). The analytical quality arising from implementation of an analytical process should fulfil the client's quality requirements. The analytical problem should translate external quality requirements into analytical quality goals to be reached through analytical properties of the results and the CMP.

Slide 7.9

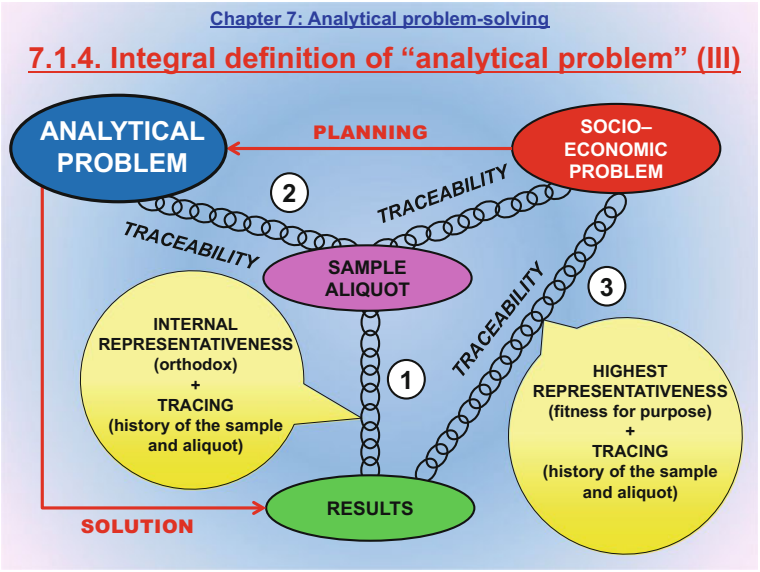


7.9.1. This slide is a conceptual and technical depiction of the hierarchies in Slides 1.21, 1.24 and 1.27. Below are discussed it most salient implications (1 and 2).

7.9.2. The analytical problem is at the top of the hierarchy and followed by "object", "sample" and "analyte". This ranking is further discussed in Slide 7.13.

7.9.3. The analytical problem can be related to the top concepts in other hierarchies (e.g., "external quality", "reports" and "to analyse"). Thus, solving an analytical problem entails producing a report to compiled the information gathered and knowledge derived from results obtained by analysing. The report, which is the solution to the analytical problem, should possess internal quality (quality in analytical properties) but also external quality (the ability to solve the socio-economic problem addressed).

Slide 7.10



7.10.1. This slide shows the traceability (consistency) chains and links to be established in solving an analytical problem.

7.10.2. Link 1 is a relationship of consistency between the results and the sample aliquot—which in turn should be consistent with the sample. Assuring traceability between these two components requires that the results be representative of the assayed aliquot and the sample (internal representativeness), but also the documented history of the obtainment, processing and storage of the sample and aliquot.

7.10.3. The sample aliquot is directly connected to the socio-economic problem. It is essential that any samples collected from the object be consistent with the socio-economic problem addressed if the problem is to be correctly solved.

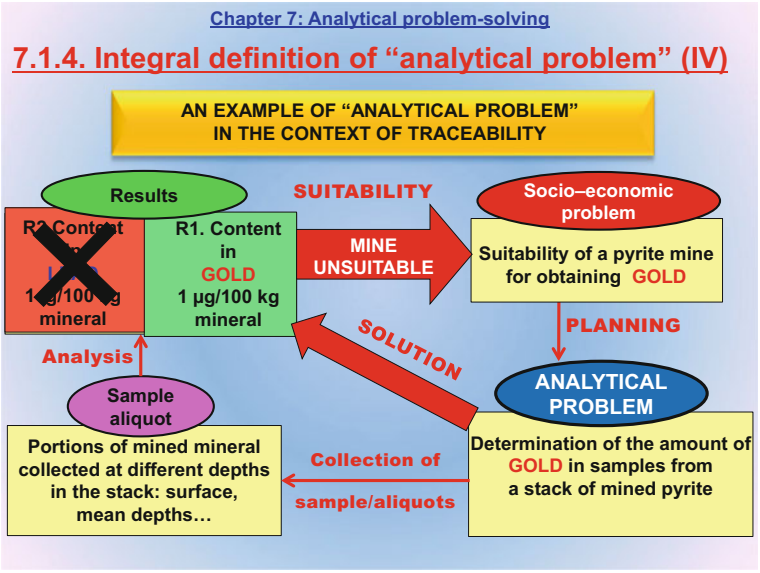
7.10.4. The analytical problem arises in adapting the socio-economic problem to the analytical chemist's realm by adhering to the client's information requirements. Since the analytical problem arises from the socio-economic problem, the former can be traced to the sample aliquot (2) and the chain fulfils the same representativeness and consistency conditions than that connecting the sample and its aliquot to the socio-economic problem.

7.10.5. Correctly solving the analytical problem leads to the obtainment of results that will be consistent with the socio-economic process (3). For this traceability chain to be established, the results should be accompanied by the documented history of the sample collection, processing and storage to maximize representativeness. In addition to assuring orthodox representativeness (namely, relating the results to the sample and its aliquot), maximizing representativeness

requires that the results be consistent with the information required to solve the socio-economic problem (the new ingredient of representativeness in Slide 7.6).

"Internal (orthodox) representativeness" and "maximum representativeness" (fitness for purpose) differ in that they are two facets of representativeness arising from each traceability chain. Thus, the results—sample—aliquot chain is akin to basic representativeness (a chemical metrological notion affording statistical calculation). On the other hand, the results—socio-economic problem chain rests not only on statistical representativeness but also on consistency of the results with the information requirements (that is, on fitness for purpose).

Slide 7.11



7.11.1. This slide exemplifies the traceability chains in the previous one.

The socio-economic problem addressed in the example is finding whether a stack of mined pyrite can be profitably exploited to extract gold. Pyrite is a mineral with a shiny appearance resembling that of gold.

7.11.2. The socio-economic problem here is the source of the analytical problem: assessing previously mined mineral for profitable extraction of gold. The analytical problem therefore involves quantifying the amount of gold present in a mined pyrite stack in order to find whether exploiting the stack to extract the gold would be profitable. The analytical problem is consistent with the socio-economic problem because it is its realization in the analytical chemical realm.

7.11.3. The assessment process starts with sample collection. Collected samples will be representative of the object provided they are obtained at different depths in the mineral stack in order to locate the part containing the highest concentrations of gold. Also, they will be consistent with the analytical problem and the

socio-economic problem if they are collected in accordance with the type of information to be obtained (see sampling strategies in Slide 4.16).

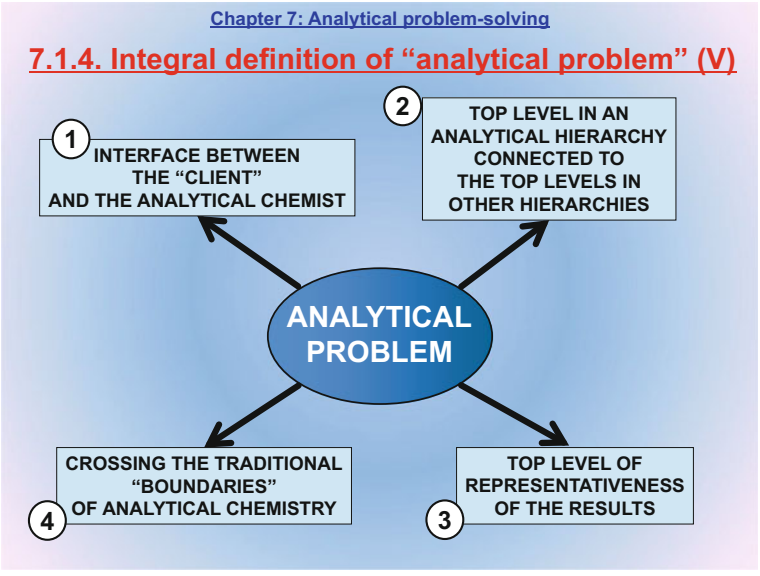
7.11.4. The analysis of each sample yields two results (outputs): the amount of gold (R1) and that of lead (R2) present in the mineral stack.

7.11.5. Only the amount of gold (R1), however, is the solution to the analytical problem here. Therefore, the other result (R2, the amount of lead) is discarded and the amount of gold (R1) is related to the analytical problem as shown in the slide.

7.11.6. After the analytical problem is solved, the true result (R1) is interpreted in order to solve the socio-economic problem. Since the amount of gold present in 100 kg of mined mineral is too small (barely 1 μg), exploiting the mine for gold would obviously be unprofitable. This information is therefore fit for the purpose and the result (the amount of gold present, R1, which is the solution to the analytical problem) is directly connected to the socio-economic problem.

A chain of three links (namely, the socio-economic problem, the analytical problem and the results) is thus established where correctly solving the analytical problem produces results that are "traceable" to the socio-economic problem.

Slide 7.12



This slide summarizes the four essential notions behind the definition of "analytical problem".

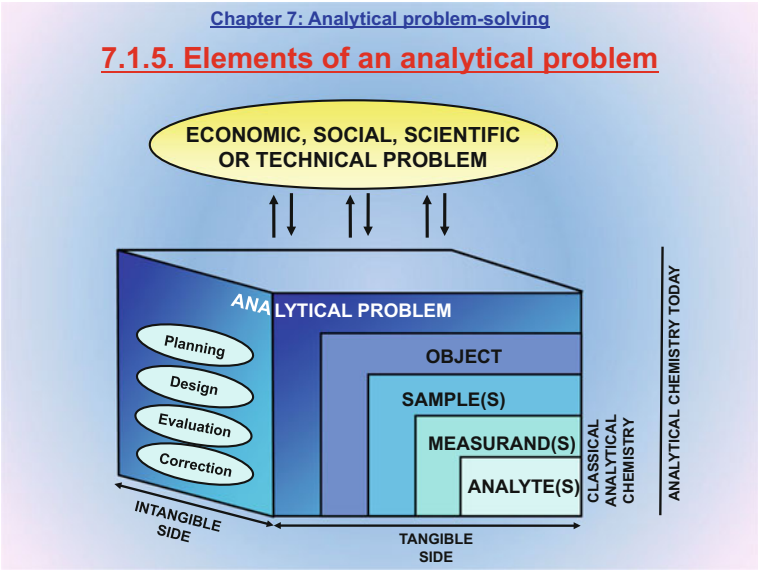
(1) The analytical problem is the interface or link between the client and the analytical chemist (see Slide 7.8).
(2) Also, it is the top level in an analytical hierarchy and connected to the top levels of others (see Slide 7.9).

(3) Correctly solving the analytical problem entails maximizing representativeness in the results (that is, consistency of the results with their purpose). The concept of "maximum representativeness" in Applied Chemistry is illustrated in Slide 7.10 together with the traceability chains involving the analytical problem.
(4) The analytical problem crosses the traditional "boundaries" of Analytical Chemistry and projects it outside the laboratory. The analytical problem as a link between the client and the analytical chemist sets a socio-economic goal for laboratory work. In this way, Analytical Chemistry acquires a new dimension in addition to its traditional function as a chemical metrological science and adopts a socially active role.

The four definitions in this slide are mutually related. Thus, the analytical problem as the interface between the client and the analytical chemist requires maximizing representativeness in order to fulfil the particular information requirements. The client–analytical chemist relation is an element of the new dimension of Analytical Chemistry (crossing traditional borders); also, it falls at the top of a hierarchy.

7.1.5 Elements of an Analytical Problem (1 Slide)

Slide 7.13



7.13.1. This slide depicts the analytical problem as a cube containing the specific information requirements of the particular social, economic, scientific or technical problem addressed. The elements of the problem are shown on two sides of the cube.

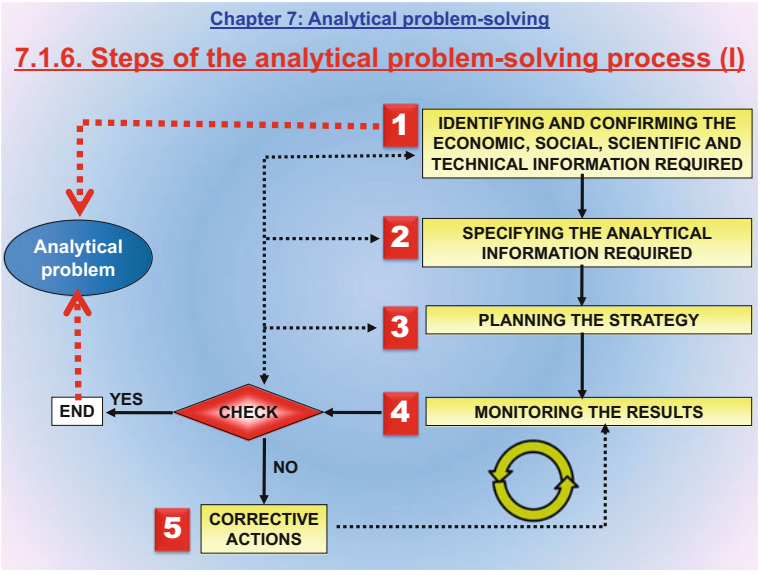
7.13.2. On the tangible side of the cube is a scope hierarchy with the analytical problem at the top. The elements of the hierarchy are defined in Slide 1.28. The object should be consistent with the analytical problem and accurately described by the results. Also, the sample should be collected in accordance with the type of information required, and the measurands and analytes should be carefully selected in order to ensure that the results can be correctly interpreted to solve the analytical problem.

7.13.3. On the intangible side of the cube are the terms "planning", "design", "evaluation" and "correction", which are key actions towards solving the analytical problem. These actions are dealt with in Sect. 7.1.6.

7.13.4. The slide also illustrates the notion of "border crossing" (see Slide 7.12). Thus, incorporating the analytical problem as the realization of an actual social, economic, scientific or technical problem makes Analytical Chemistry a modern science consistent with its new goals. The analytical problem has expanded Classical Analytical Chemistry and facilitated its adjustment to the new information requirements that have emerged in recent years.

7.1.6 Steps of the Analytical Problem-Solving Process (9 Slides)

Slide 7.14



7.14.1. These are the steps to be followed in order to properly solve an analytical problem. Each individual step is described and exemplified in Slides 7.15–7.22 and briefly discussed here.

7.14.2. *First step:* identifying and confirming the information requirements. This entails the exchange of information between the client and the analytical chemist so that the latter can correctly plan the analytical problem to be solved in order to fulfil the information requirements of the former. This step is occasionally difficult to overcome.

7.14.3. *Second step*: identifying the analytical by "translating" the client's information requirements into analytical chemical terms.

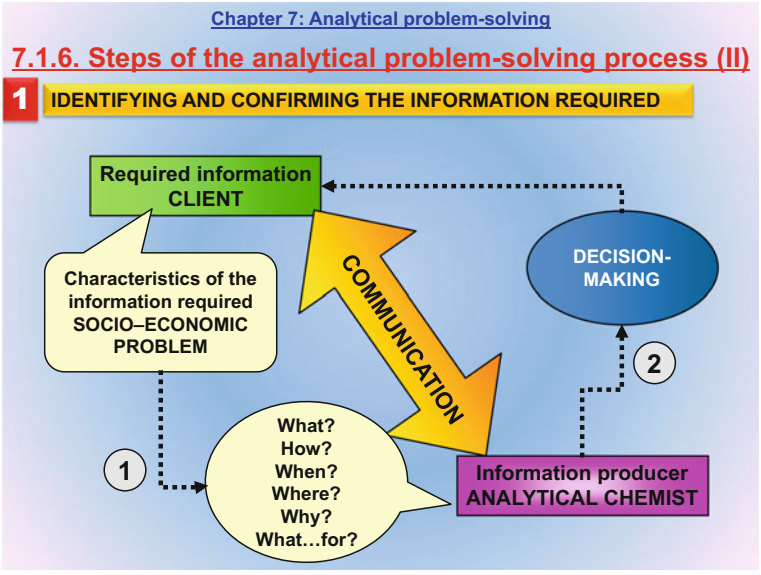
7.14.4. *Third step*: planning the strategy to be followed in order to obtain the information required, which roughly involves developing an appropriate Chemical Measurement Process (CMP) or choosing an existing one for the intended purpose.

7.14.5. *Fourth step*: monitoring the results by comparison with internal references (the analytical information required) and external references (the client's information requirements).

7.14.6. If the results compare well with the references and are consistent with the information requirements, the analytical problem is deemed solved. Otherwise, a fifth, corrective step (7.14.7) is required.

7.14.7. *Fifth step*: corrective actions. Previous steps are checked in order to identify the error preventing the analytical problem from being correctly solved. Once all errors are corrected, the process returns to the fourth step (7.14.5) and the results are re-checked in order to decide whether new corrections (a new fifth stage) are needed. If none is required, the cycle is closed and the process ended.

Slide 7.15



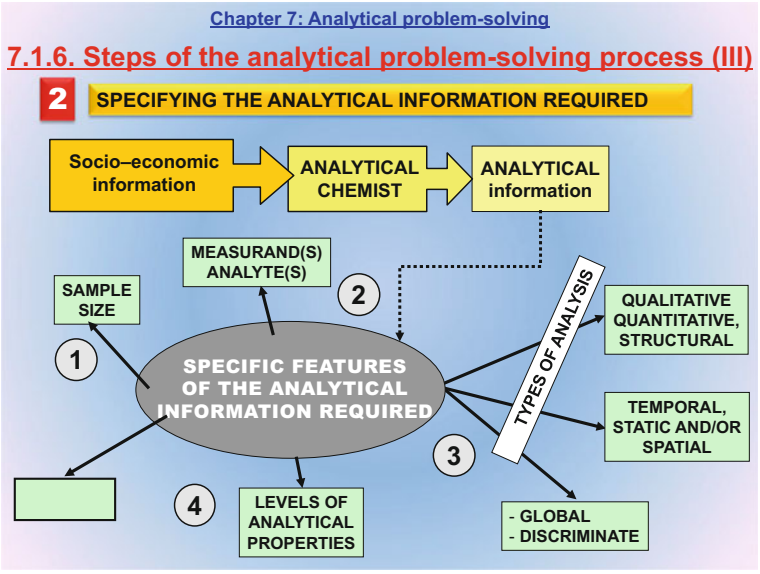
7.15.1. This slide depicts the first step of the analytical problem-solving process: identifying and confirming the information requirements.

7.15.2. Properly planning and solving an analytical problem rests heavily on accurate communication between the client and the analytical chemist so that client's socio-economic problem can be made consistent with the analytical problem to be planned and solved by the analytical chemist (that is, on assuring the traceability chain of Slide 7.10). Communication between the client and the analytical chemist should proceed via two different routes (1 and 2 in the slide).

7.15.3. *Route 1*. Properly planning the analytical problem requires the analytical chemist to obtain as much information about the client's socio-economic problem as possible by asking key questions such as what?, how?, when?, where?, why? or what… for?

7.15.4. *Route 2*. The strategy to be followed in order to solve the analytical problem depends on the particular requirements identified in this step. Such requirements provide useful clues with a view to obtaining the required information and hence facilitating decision-making by the analytical chemist. The chemist's decisions will clearly determine whether the client's socio-economic problem can be solved correctly and timely.

Slide 7.16



7.16.1. The second step in the analytical problem-solving process involves specifying the analytical information required.

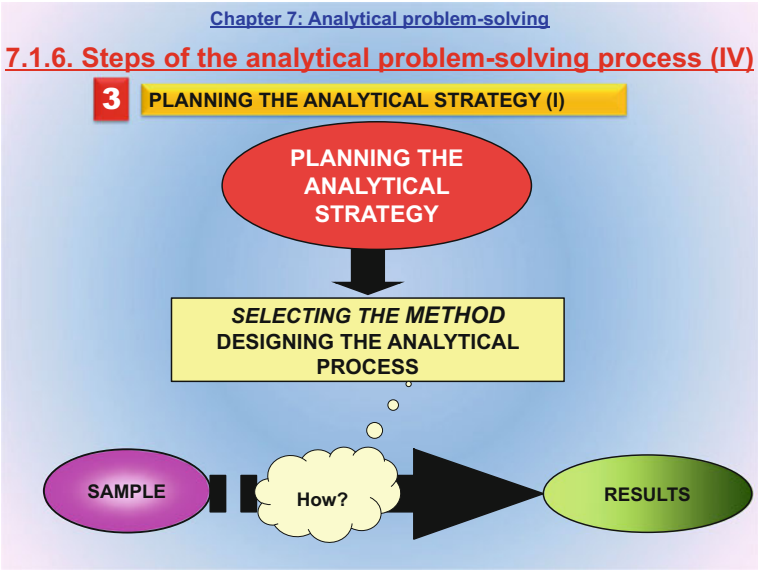
7.16.2. The client provides the analytical chemist with socio-economic information that must be translated into analytical information of use to solve the analytical problem. This is the sole responsibility of the analytical chemist, who must

establish the analytical requirements in accordance with the specific problem posed by the client.

7.16.3. The analytical information required should be carefully stated in terms such as the four depicted in the slide.

(1) The first elements to be established are the sampling plan and the object (see sampling strategies in Slide 4.16).
(2) Then come the measurand(s) and/or analyte(s) to be sought (that is, those to be determined in the analytical process).
(3) Which type of analysis is to be performed comes then. The analytical chemist must choose among quantitative (Chap. 5), qualitative (Chap. 6) or structural analysis; static, temporal or spatial analysis; and global (total) or discriminate (single species) analysis.
(4) Finally, the levels of analytical properties to be reached are established. This requires a sound knowledge of capital and basic properties in order to correctly express the results and assure the required level of confidence in them, and also of productivity-related properties in order to be able to deliver the required information in a timely manner to facilitate decision-making by the client.

Slide 7.17

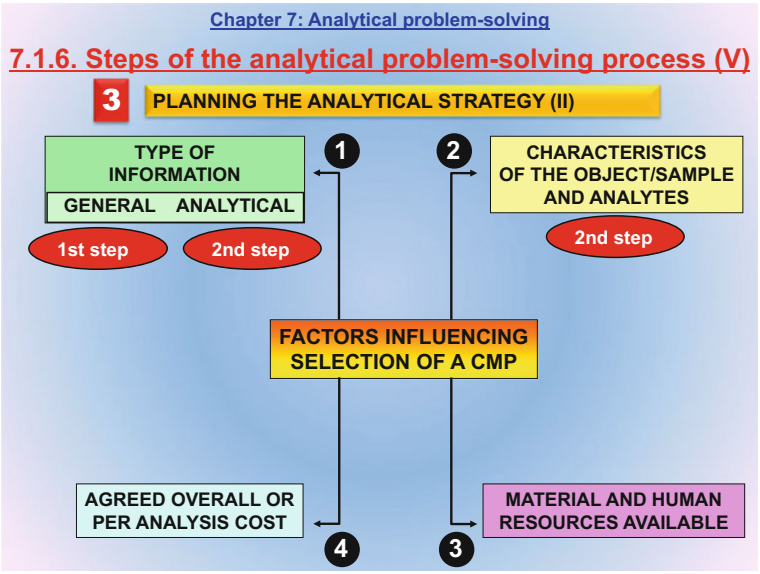


7.17.1. This is the third step in the analytical problem-solving process: planning the analytical strategy.

Planning the strategy basically entails selecting an analytical process or developing a new one for the intended purpose.

7.17.2. The aim is to answer the question "*how can the information required (results) be obtained from the sample*?" by designing an effective experimental plan.

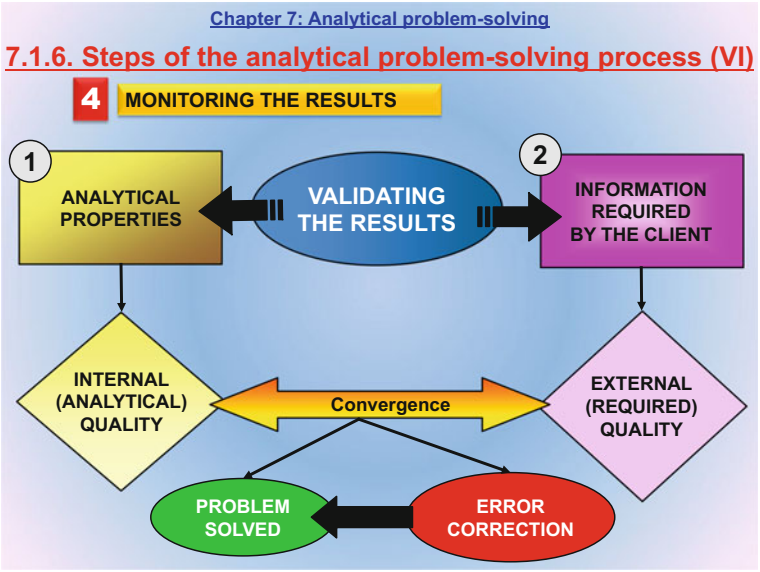
Slide 7.18



This slide shows the factors influencing selection or development of a Chemical Measurement Process (CMP) in the third step of the analytical problem-solving process.

(1) The first factor is the type of information to be obtained (general in the first step of the process and analytical in the second). The CMP should be planned with provision for the analytical properties and type of analysis required in order to ensure that the results will be appropriate and consistent with the information requirements.
(2) The second factor is the characteristics of the object, the sample to be analysed and the analyte to be sought or quantified. The nature of the object, sample and analyte will dictate the sampling plan, the preliminary operations to be conducted and the specific method to be used to determine the analyte. These factors are all parts of the analytical process and should therefore be considered in its development.
(3) The third factor is the material and human resources available to the analytical chemist. Such resources include laboratory staff and equipment, which can restrict or expand the range of available analytical methods.
(4) The last factor is the overall or individual cost agreed with the client, depending on which the range of choices may also be wider or narrower.

Slide 7.19



7.19.1. This is the fourth step in the analytical problem-solving process: monitoring the results by comparison with established references, which is known as "validation of the results".

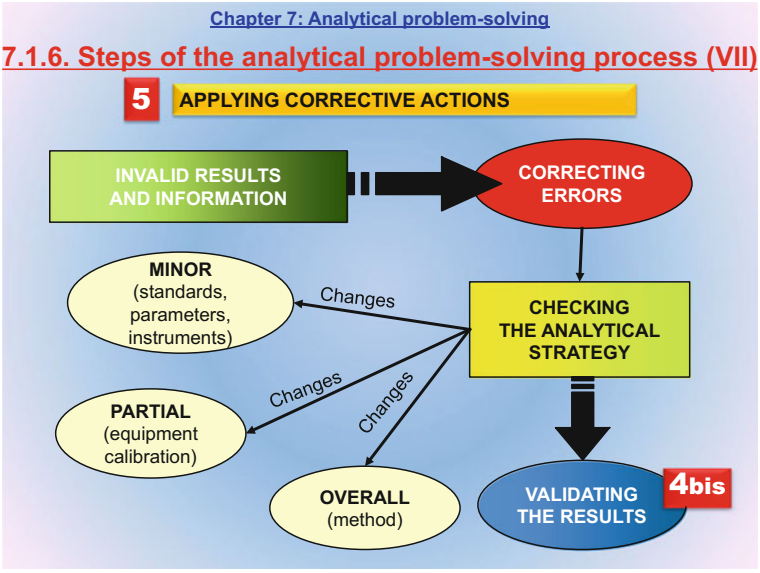
7.19.2. The process involves validating analytical properties and information as follows:

(1) Validating the levels of analytical properties involves checking that they conform to the requirements of the laboratory (legal limit and cut-off concentration, Slide 6.13) and the client. This is the entire responsibility of the analytical chemist and assures analytical (internal) quality, which pertains exclusively to the analytical chemical realm.

(2) Validating the information obtained against that required by the client involves checking that the results fulfil the client's needs (i.e., that interpreting the results allows the socio-economic problem to be solved and representativeness—Slide 7.10—to be maximal as a result). At this point, the client and the analytical chemist must engage in communication as they did in the first step of the analytical problem-solving process (see Slide 7.15).

7.19.3. Validation against the two types of references allows internal and external quality to be assured. If both are adequate, their combination ensures that the analytical problem has been correctly solved. Otherwise, some error has been made in the process that will require correction so that the analytical and the socio-economic problem can be eventually solved (see Slide 7.20).

Slide 7.20



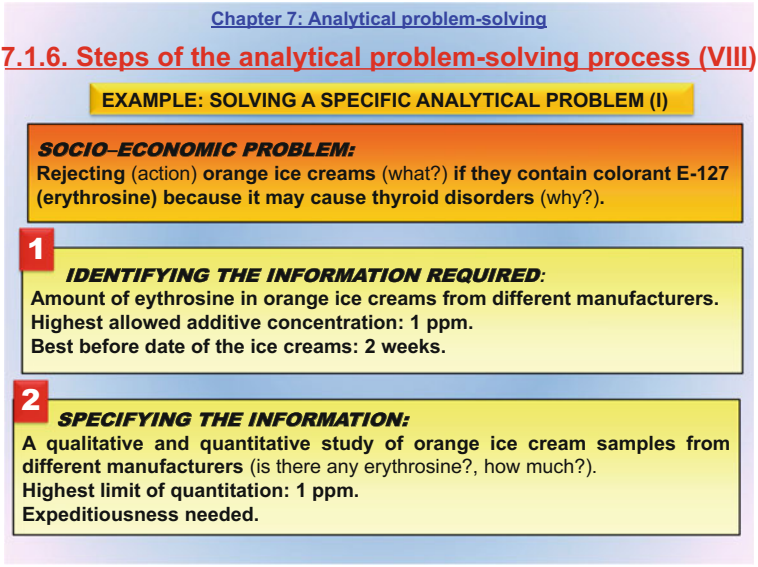
7.20.1. This is the fifth step in the analytical problem-solving process: applying corrective actions. This step is only needed when the results and information produced by the analytical chemist do not allow the analytical problem and the originating socio-economic problem to be solved. The aim is to correct errors in the process, which usually arise in the analytical strategy followed in the third step.

7.20.2. Corrective actions are performed by checking the procedures used in the process and making appropriate changes. The changes needed can be of one of the following three types:

- *Minor*. The error is easily identified and arose from a standard or an individual parameter, for example.
- *Partial*. The error is more substantial because it involves a whole instrument or its calibration, for example.
- *Overall*. The error lies in the way the procedures were developed and can only be corrected by using an alternative approach.

7.20.3. The results obtained upon correction should be validated against the references of Slide 7.19. If the new results are valid, the analytical and socio-economic problem can be deemed solved; otherwise, new corrections will be needed. The cyclic nature of the process as shown in Slide 7.14 emerges here as well: "4bis" denotes repetition of the fourth step and connects corrective actions to monitoring of the results.

Slide 7.21



7.21.1. This slide and the next exemplify the process used to solve a socio-economic problem by solving an analytical problem as described in Slides 7.14–7.20.

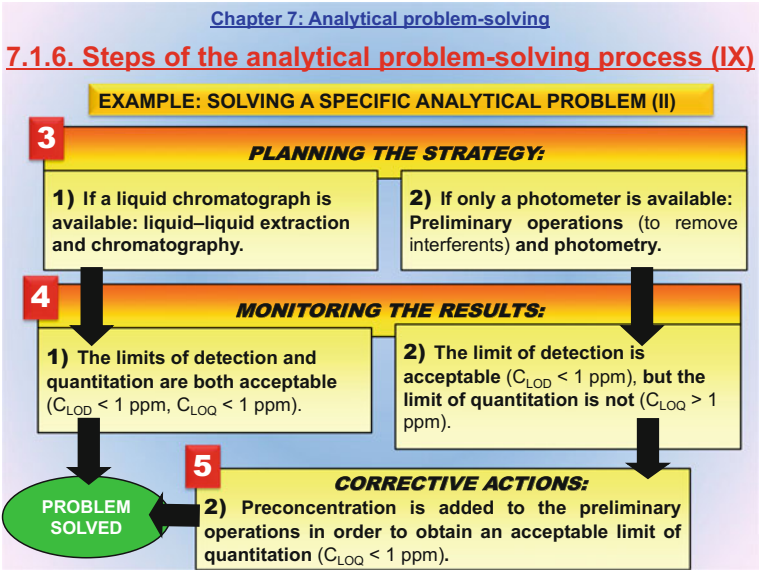
The problem in question is rejecting ice creams potentially containing a deleterious additive: the food colorant erythrosine. The information gathered from the statement of the socio-economic problems is the answer to the questions what? and why?, namely: rejecting, orange ice creams and the presence of additive E-127 (erythrosine), respectively.

7.21.2. The first step in the process involves identifying the client's information requirements. Communication between the client and the analytical chemist allows the information in box 1 to be gathered.

7.21.3. The second step involves translating the information obtained from the client into analytical information. Determining the amount of erythrosine (the client's requirement) entails previously checking that the ice creams contain it (that is, a qualitative study) and, if they do, measuring the amount present (that is, a quantitative study). Also, if the legal limit for the substance is known, the laboratory can establish a cut-off concentration such that the accepted limit of quantification will coincide with the legal limit (1 ppm). Because the ice creams have a best before date of only 2 weeks, the analytical property "expeditiousness" comes into play.

The problem-solving process is continued in the next slide.

Slide 7.22



7.22.1. The third step of the problem-solving process is approached in two different ways here, namely:

- *Strategy 1*. If a liquid chromatograph is available, the procedure of choice is liquid–liquid extraction of the additive (erythrosine) and direct determination on the chromatograph.
- *Strategy 2*. If only a photometer is available, the procedure requires some preliminary operations prior to determining the analyte photometrically.

7.22.2. The quality of the results will depend on whether strategy 1 or 2 is used.

- *Strategy 1*. The limits of detection and quantification of the chromatograph are both lower than the legal limit. As a consequence, the determination method provides acceptable levels of analytical properties and the results allow the analytical problem and the socio-economic problem to be correctly solved.
- *Strategy 2*. The limit of detection of the photometer is lower than the legal limit and hence acceptable; however, its limit of quantification is higher than the legal limit and hence useless. This entails performing some corrective action to enable the photometric determination of the colorant without interference.

7.22.3. Because the chromatograph provides valid results, the problem is solved. Thus, fifth step (corrective actions) is only needed with the photometer.

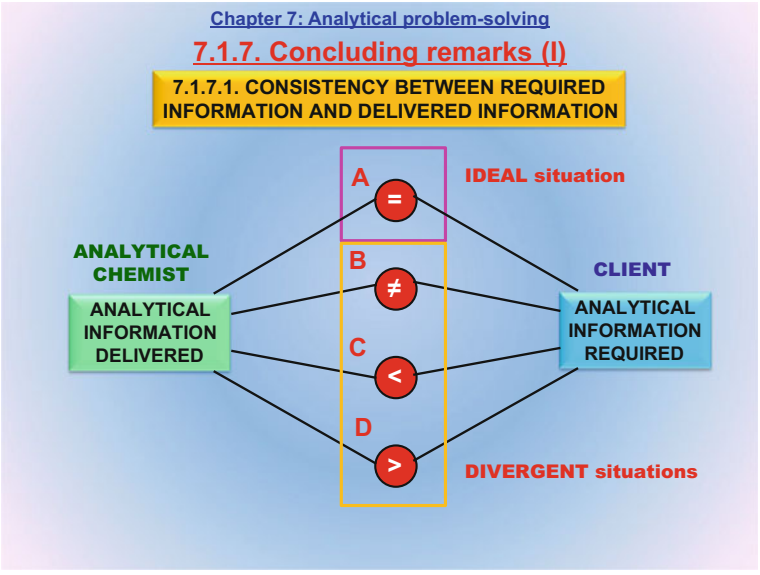
7.22.4. In *Strategy 2*, the limit of quantification of the photometric determination is improved by expanding the preliminary operations of the analytical process with a preconcentration step. This allows the analytical problem, and hence the originating socio-economic problem, to be solved.

7.1.7 Concluding Remarks (6 Slides)

7.1.7.1 Consistency Between Required Information and Delivered Information (5 Slides)

Correctly solving the analytical and socio-economic problems entails assuring that the information supplied by the analytical chemist is consistent with that required by the client. This section discusses and exemplifies various potential outcomes in comparing the information required and that actually delivered.

Slide 7.23



7.23.1. This slide depicts the four possible outcomes in comparing the information supplied by the analytical chemist and that required by the client.

7.23.2. Ideally (*situation A*), the information supplied by the analytical chemist is consistent with that required by the client (hence the = sign).

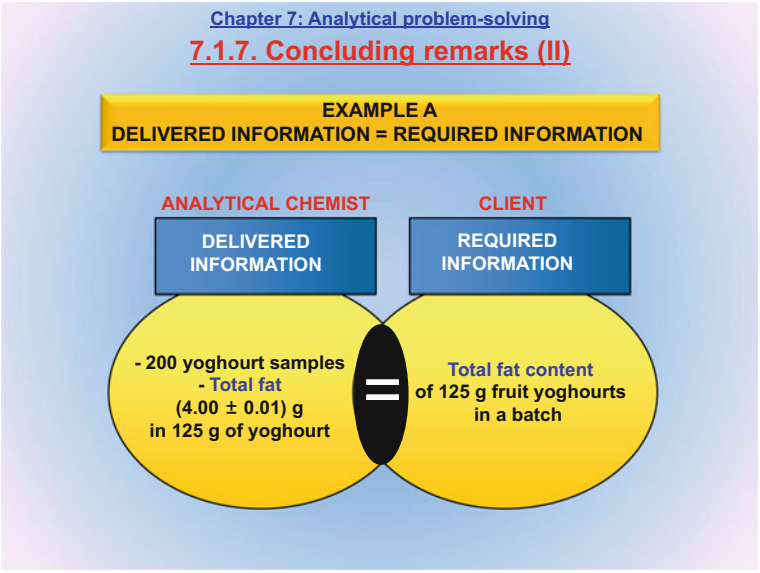
7.23.3. This is not the case with the three divergent situations denoted by letters B, C and D, and the signs $\neq$ (different from), $<$ (less than) and $>$ (greater than), respectively. These situations arise when the analytical chemist fails to solve the client's problem owing to miscommunication or to some uncorrected error in the way the analytical problem was addressed.

– In *situation B*, the information supplied by the analytical chemist is completely different from that needed by the client to solve the socio-economic problem, so the delivered information is different from the required information.
– In *situation C*, the information supplied by the analytical chemist is inadequate to entirely fulfil the client's requirements. As a result, the delivered information is less than the required information.
– In *situation D*, the information supplied by the analytical chemist exceeds the client's requirements and answers additional questions not raised by the client. Therefore, the client is supplied with excess information and the delivered information is greater than the required information.

Fluent two-way communication between the client and the analytical chemist is paramount to ensure proper mutual understanding. In situations B and C, the client's requirements are not properly fulfilled; as a result, and the originating socio-economic problem cannot be solved. By contrast, the excess information produced in situation D does allow the problem to be solved but is obtained by incurring unnecessary expenses.

Slides 7.24–7.27 exemplify situations A–D.

Slide 7.24

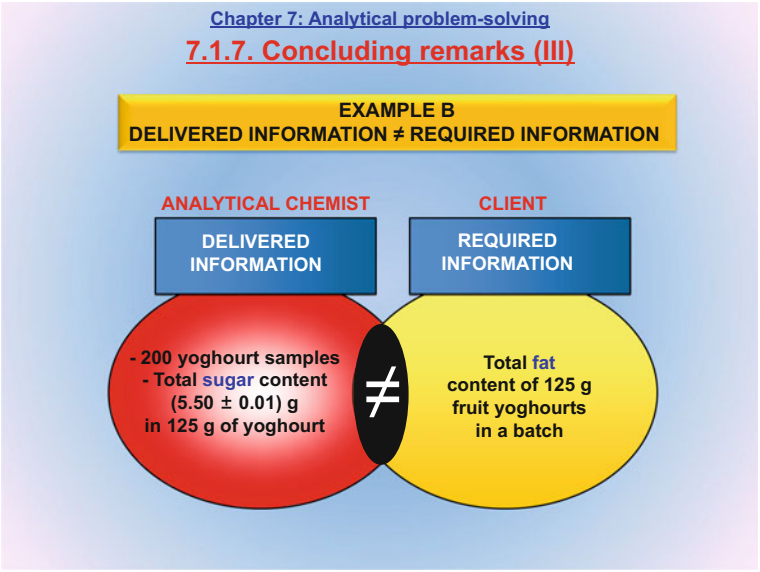


7.24.1. This slide illustrates situation A in Slide 7.23. The specific information required and that delivered are as follows:

– *Required information*. The client needs to know the overall fat content of 125 g fruit yoghourts in order to check that it meets the specifications prior to marketing.
– *Delivered information*. The analytical chemist supplies the total amount of fat in each of 200 yoghourt samples. The result is (4.00 ± 0.01) g.

7.24.2. In this situation, the information supplied by the chemist coincides (hence the = sign) with that required by the client. Communication between the client and chemist was perfect and the information requirements of the former were successfully fulfilled.

Slide 7.25



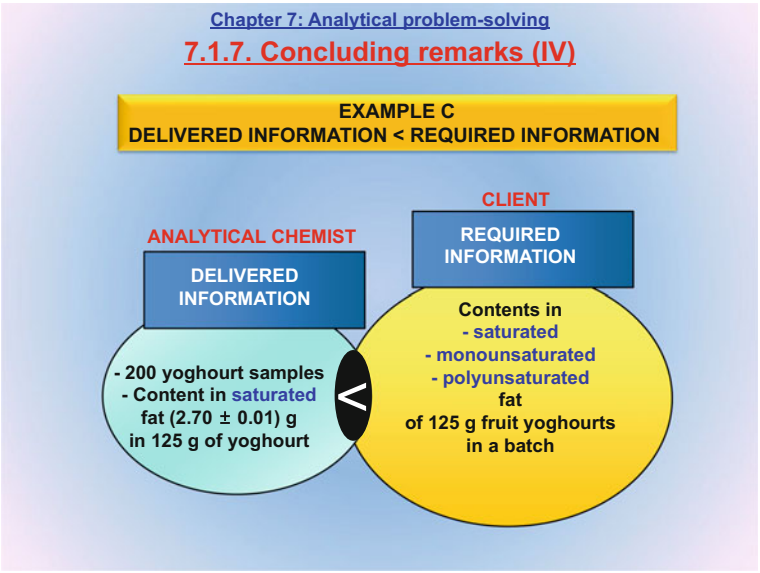
7.25.1. This slide illustrates situation B in Slide 7.23.

– *Required information*. As in situation A (Slide 7.24), the client needs to know the overall fat content of 125 g fruit yoghourts in order to check that it meets the specifications prior to marketing.
– *Delivered information*. The analytical chemist supplies the client with the total sugar content in the yoghourt as determined by analysing 200 samples. The result is (5.50 ± 0.01) g.

7.25.2. In this situation, the information supplied by the chemist is completely different (hence the ≠ sign) from that required by the client, which was the fat content of the yoghourts rather than their sugar content. Communication between

the analytical chemist and the client probably failed and prevented the originating socio-economic problem from being solved.

Slide 7.26

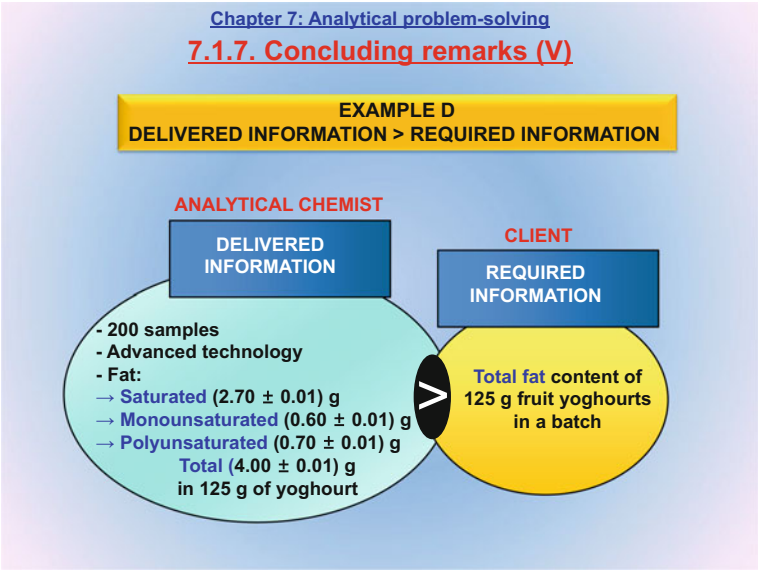


7.26.1. This slide illustrates situation C in Slide 7.23.

- *Required information*. The client needs to know the individual contents in saturated, monounsaturated and polyunsaturated fat of 125 g yoghourts in order to check that they meet the specifications prior to marketing.
- *Delivered information*. The analytical chemist supplies the amount of saturated fat in the yoghourts as determined by analysing 200 samples. The result is (2.70 ± 0.01) g.

7.26.2. The information supplied by the analytical chemist was only part (hence the < sign) of that required by the client. Communication between the two parties was probably ineffective and the client's requirements were incompletely fulfilled as a result.

Slide 7.27



7.27.1. This slide illustrates situation D in Slide 7.23.

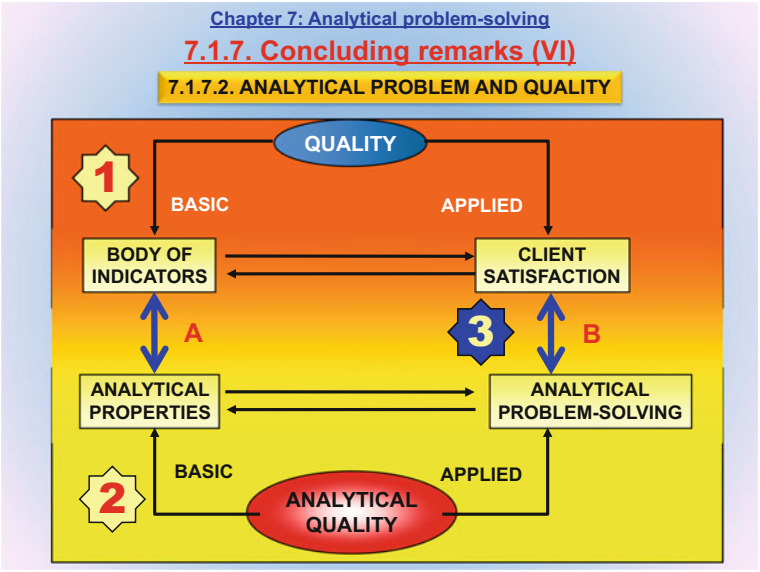
- *Required information*. As in situations A and B (Slide 7.24 and 7.25, respectively), the client needs to know the overall fat content of 125 g fruit yoghourts in order to check that it meets the specifications prior to marketing.
- *Delivered information*. The analytical chemist supplies the client with the amounts of saturated, monounsaturated and polyunsaturated fat present in the yoghourts as determined in 200 samples. The result is (2.70 ± 0.01) g for saturated fat, (0.60 ± 0.01) g for monounsaturated fat and (4.00 ± 0.01) g for polyunsaturated fat.

7.27.2. The information supplied by the analytical chemist exceeds that required by the client (hence the sign >). Communication between the two parties was successful in part. In fact, the client's information requirement was fulfilled by the analytical chemist, albeit at the expense of added costs in the additional, unnecessary determinations.

7.1.7.2 Analytical Problem and Quality (1 Slide)

Quality is the core topic in Chap. 8, which provides an integral definition of the concept (see Slide 8.5). This section deals with the concept "analytical problem" as relating to quality.

Slide 7.28



7.28.1. External (general) quality (Part 1 in the slide) can be viewed as a body of indicators (intrinsic properties inherent in external quality) and also, in practical terms, as the result of client's satisfaction. These two views are obviously related: the body of quality indicators provides the foundation and an authoritative basis to fulfil the client's requirements; however, satisfying the client validates the goodness (quality) of the information delivered.

7.28.2. Analytical (internal) quality (Part 2 in the slide) can be viewed as the body of capital, basic and productivity-related analytical properties (Slide 2.4), and also as the result of solving analytical problems. These two views are related as follows:

- Correctly solving an analytical problem entails assuring adequate levels of specific analytic properties in each case.
- The information and techniques used to solve an analytical problem can be incorporated into analytical chemical knowledge in order to improve analytical properties (see the relationship between intrinsic foundations in Slide 7.7).

7.28.3. Part 3 in the slide relates the general concept "quality" to the specific concept "analytical quality". The two are related as follows:

A. Analytical properties (Chap. 2), which are the cornerstones of analytical quality, can be used as indicators of general (external) quality. This is the

chemical metrological notion: external quality is the result of internal representativeness only (see Slides 7.6 and 7.10).

B. As shown throughout this chapter, the analytical problem-solving process is unequivocally related to client's satisfaction. Analytical quality in the solution to an analytical problem has a direct impact on external quality because it allows a real-life socio-economic problem to be solved.

"Quality" can be defined in countless ways, but the saying "no quality is possible without a clear definition of the given task" is especially enlightening: achieving external quality from analytical quality entails solving analytical problems.

7.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry

Miguel Valcárcel

Springer-Verlag, Berlin, 2000.

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

This chapter coincides largely with Chap. 7 in the book ("The Analytical Problem"). Some text in the book has been replaced with explanatory slides, however. Also, a graph depicting the traceability chains including the analytical problem has been added, and a few examples are used to illustrate traceability, the steps of the analytical problem-solving process, and consistency in the analytical chemist–client relationship.

PAPERS

The analytical problem

Miguel Valcárcel, Ángel Ríos

Trends in Analytical Chemistry, 1997, vol. 16, no. 7, 385–393.

This paper summarizes the most salient aspects of this chapter. It discusses the relationship between the analytical chemist and the client, their understanding, and the planning of analytical problem-solving processes based on their communication. Some of the slides used in this chapter originally appeared in the paper.

7.3 Questions on the Topic (Answered in Annex 2)

7.1. Identify the binary interfaces between Analytical Problem-Solving, Analytical Quality and Social Responsibility.

	Analytical problem-solving	Analytical quality	Social responsibility
Analytical problem-solving	×		
Analytical quality		×	
Social responsibility			×

7.2. What is the third basic standard in Analytical Chemistry? How is it related to the analytical problem?
7.3. How would you define "fitness for purpose"? To which facet of representativeness is it related? Is it related to chemical metrology?
7.4. Describe the roles of the analytical problem in the basic and applied sides of Analytical Chemistry.
7.5. How does the analytical problem relate the analytical chemist to the client?
7.6. What are the components of the concept hierarchy containing the analytical problem? What place does the analytical problem take in it?
7.7. How would you relate the analytical problem to the leading concepts "reports", "external quality" and "to analyse" in other hierarchies?
7.8. Distinguish "orthodox" representativeness from "maximum" representativeness. Which traceability chain does each belong to?

7.9. A river is suspected to be polluted with toxic organic waste that may be having adverse effects on the nearby population. This hypothesis is verified by collecting 200 samples of water at different depths along the river for analysis. The method used has a limit of detection of 0.7 ppm and a limit of quantification of 2.1 ppm. The effects of the organic waste are felt at concentrations above 3 ppm. The concentration of waste obtained with the chosen method is 2.7 ppm. Complete the following table. Can the socio-economic problem addressed be correctly solved? Does the analytical method require any corrective actions?

Socio-economic problem	
Analytical problem	
Object	
Sample/aliquot	
Analyte(s)	
Limit of detection (C_{LOD})	
Limit of quantification (C_{LOQ})	
Legal limit (C_{LL})	
Result ($C_{obtained}$)	

7.10. What are the intangible elements of an analytical problem? How do they relate to the steps of the analytical problem-solving process?

7.11. Define and briefly describe the five steps of the analytical problem-solving process. Give an example of socio-economic problem and describe the steps needed to solve it.

7.12. Why is fluent communication between the analytical chemist and the client important in the first step of the analytical problem-solving process?

7.13. Name three essential items of information needed to identify the analytical information required in the second step of the analytical problem-solving process.

7.14. What is the purpose of the third step of the analytical problem-solving process? What are the factors influencing selection and design of a CMP?

7.15. What are the references used to assess the results in the fourth step of the analytical problem-solving process? How are they related to quality?

7.16. When is the fifth step of the analytical problem-solving process needed? Why?

7.17. How can delivered information be in relation to required information? Give an example of each situation.

7.18. In order to decide whether a person should be pronounced guilty of murder, a laboratory is asked to perform a comparative analysis of a blood sample from the defendant and one containing a mixture of blood from the defendant and the victim blood found in the crime scene. The analysis involves determining the DNA sequence of the defendant, the victim and the mixed blood sample. Please complete the following table by identifying the different elements.

Socio-economic problem	
Analytical problem (1st step)	
Analytical information (2nd step)	
CMP to be used (3rd step)	
Verification of the results (4th step)	

7.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened for teaching Analytical Chemistry to students not majoring in Chemistry, albeit to a lesser extent than those of others because of its transversal conception. The following 7 slides (25% of all) can be omitted for this purpose:

- Section 7.1.4: Slides 7.9 and 7.13.
- Section 7.1.6: Slide 7.18.
- Section 7.1.7: Slides 7.24–7.27.

Analytical Chemistry and Quality

8

Abstract

The main aims of this chapter are to provide students with an integral view of quality in the realm of Analytical Chemistry and to relate its elements. Although quality is dealt with in various respects in previous chapters, this one focuses on general aspects of quality in Analytical Chemistry by discussing the relationship of quality to analytical properties and the analytical problem. Also, it provides an overview of the standards and factors governing quality in analytical laboratories, discusses analytical quality control and assessment systems, and describes their supports. The chapter ends with a few concluding remarks.

Teaching Objectives

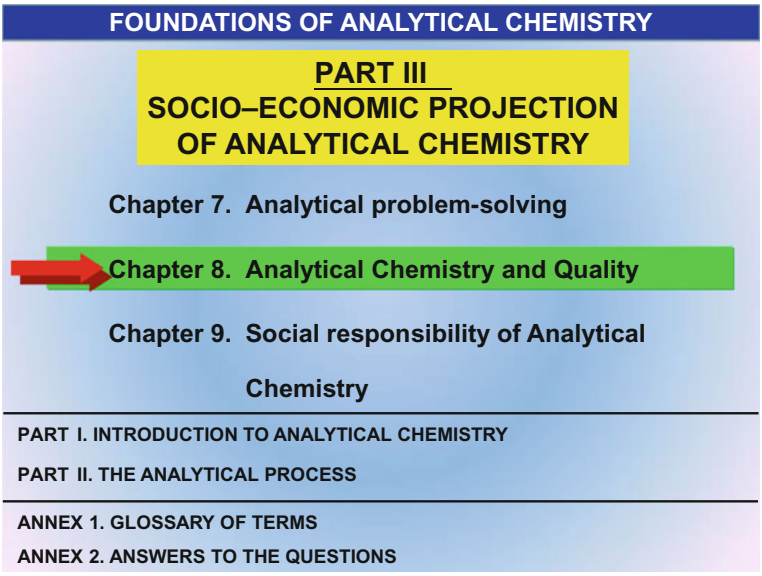
- To define "Quality".
- To relate quality to the general and specific goals of Analytical Chemistry.
- To introduce students to the planning and development of Quality Systems in analytical laboratories.
- To describe the methodological tools needed to implement control and assessment activities in analytical laboratories.

Electronic supplementary material The online version of this chapter (doi:10.1007/978-3-319-62872-1_8) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_8

8.1 Explanation of the Slides

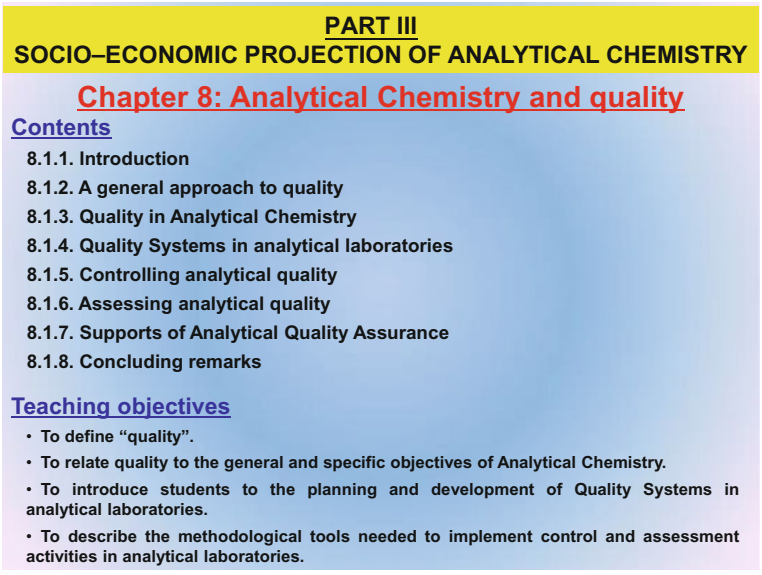
Slide 8.1



This slide places in the context of Part III (Socio-economic Projection of Analytical Chemistry) and shows the other two parts of the book.

This is the second of three chapters explaining how Analytical Chemistry relates to society.

Slide 8.2

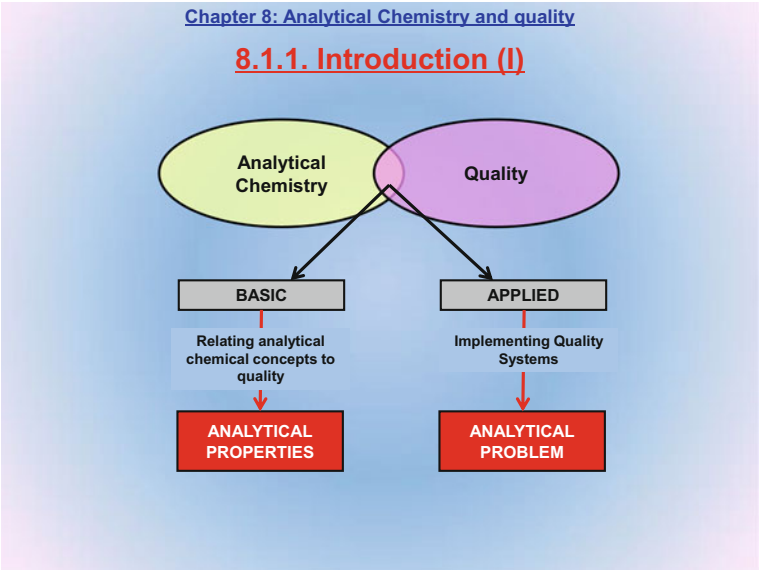


8.2.1. As can be seen in this slide, the contents of this chapter are distributed in eight sections. The Introduction (Sect. 8.1.1) is followed by a general approach to quality (8.1.2), and a definition of the concept in the context of Analytical Chemistry and its relationship to the term in its broadest sense (8.1.3). Section 8.1.4 describes Quality Systems in the analytical laboratory, and Sects. 8.1.5 and 8.1.6 are concerned with two of their most salient elements (Quality Control and Quality Assessment). Finally, Sect. 8.1.7 deals with Analytical Quality Assurance and is followed by some concluding remarks in Sect. 8.1.8.

8.2.2. The slide also shows the teaching objectives of the chapter as regards quality, its relationship to Analytical Chemistry, and the quality-related standards and Quality Systems applicable to analytical laboratories.

8.1.1 Introduction (2 Slides)

Slide 8.3



8.3.1. This slide introduces the contents of this chapter, which is concerned with the Analytical Chemistry–Quality pair as viewed from a basic and an applied side.

8.3.2. (1) The basic side encompasses most of the analytical chemical elements (for example, analytical properties).

8.3.3. (2) The applied side contains the implementation of Quality Systems in analytical laboratories, which bears a relation to the analytical problem.

Slide 8.4

Chapter 8: Analytical Chemistry and quality

8.1.1. Introduction (II)

EXAMPLE OF THE NEED FOR LABORATORIES TO USE QUALITY SYSTEMS: several laboratories obtained rather different results in the determination of various elements in a sample of lichen.

ELEMENT	Lowest value (µg/g)	Highest value (µg/g)	Ratio
Calcium	200 (FRX)	3155 (FRX)	15
Copper	0.80 (FAAS)	38.8 (ICP-AES)	48
Mercury	0.008 (CVAAS)	0.551 (CVAAS)	110
Molybdenum	0.056 (ICR-MS)	2.072 (ICP-AES)	37
Zinc	9.7 (FAAS)	282.5 (ICP-AES)	29

This slide explains why quality systems are needed in analytical laboratories by illustrating the varying consistency among the results of the determination of metal traces in a lichen sample analysed by fourteen expert laboratories from different European countries. The analytical techniques used for the determination, which are shown in brackets, included X-ray fluorescence spectroscopy (XRF), flame atomic absorption spectroscopy (FAAS), inductively coupled plasma atomic emission spectroscopy (ICP-AES), cold-vapour atomic absorption spectroscopy (CVAAS) and ion cyclotron resonance mass spectrometry (ICR-MS).

As can be seen, there were large differences among the results. Such differences testify to the pressing need for some laboratories to implement Quality Systems involving control, assessment and correction actions (Slide 8.14) and to participate in interlaboratory exercises (Slide 8.26).

8.1.2 A General Approach to Quality (5 Slides)

Slide 8.5

This slide provides an integral definition of "quality" from two sides. On the basic side, "quality" can be defined as "the body of characteristics, properties, attributes or abilities of an entity that make it better, worse than, or equal to, other entities of the same type". Therefore, quality can only be assessed by comparison.

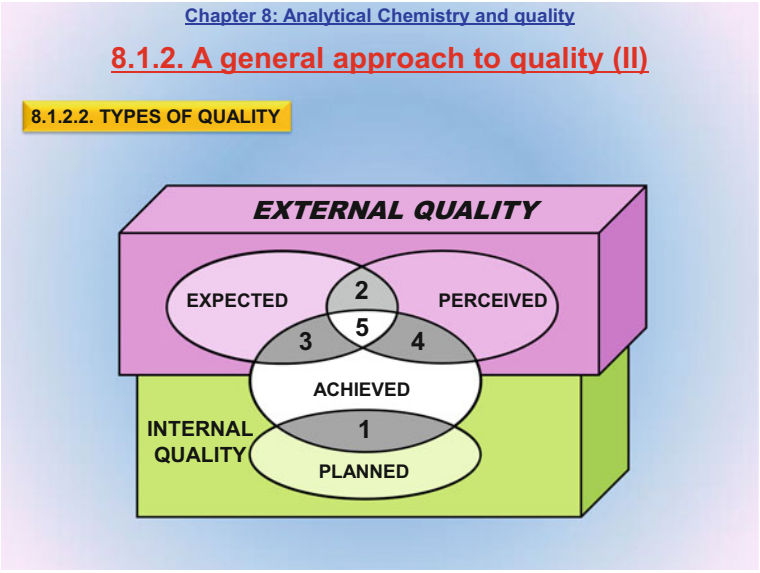
On the applied side, quality in a body comprises usefulness, fulfilling requirements, satisfying needs, following clients' directions and complying with regulations.

The comparisons involved in assessing quality should use appropriate indicators of the quantitative (numerical data), qualitative (e.g., opinions) and integral (qualitative and quantitative) types.

The three facets of quality are mutually related. Thus, the characteristics, attributes or properties of a body materialize in indicators reflecting its usefulness, abilities, etc. The comparative facet is always present; in fact, to assess its quality, the body must compare its characteristics to its needs, whether intrinsic or regulated.

Quality materializes in so-called *Quality Systems*, which are discussed in Slides 8.14–8.20.

Slide 8.6

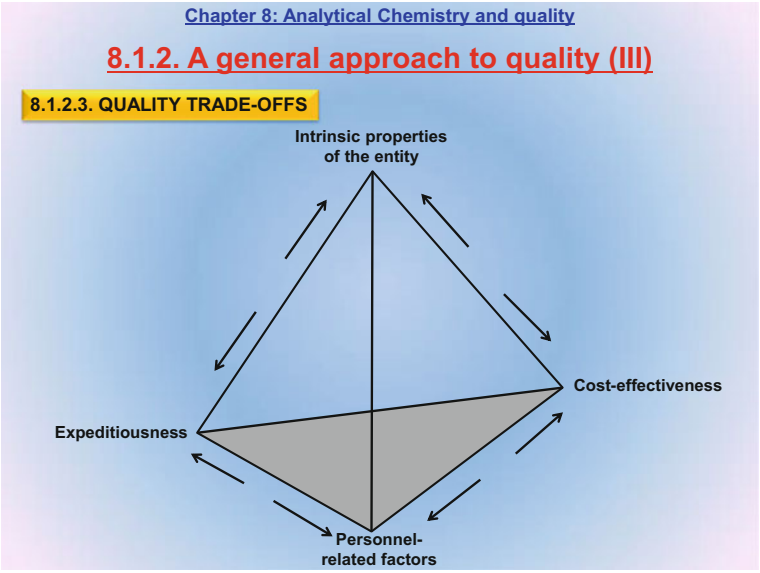


Quality can be classified according to various criteria. In broad terms, quality can be internal or external. Internal quality pertains entities delivering products or services, and external quality to clients receiving them.

Quality can also be classified in terms of its characteristics and of who defines such characteristics. Thus, quality can be (a) *planned* (designed) or (b) *achieved*, both of which are associated to a body or organization and define internal quality. In addition, quality can be (c) *required* and *expected* or (d) perceived as regards the client and hence related to external quality. Ideally, expected and required quality should coincide.

Achieved quality is at the boundary of external and internal quality. Thus, internal quality is accomplished when designed and achieved quality coincide (1). By contrast, external quality is reached when perceived quality exceeds expected quality in the eyes of the client (2). The most critical comparisons are those of achieved quality with expected quality (3) and perceived quality (4). Ideally, achieved, expected and perceived quality should be identical.

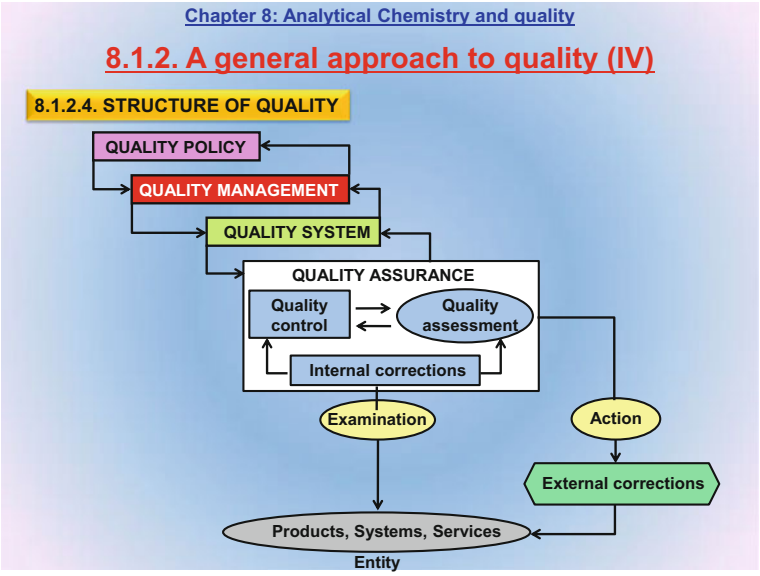
Slide 8.7



Quality should always be approached realistically. A body will obviously aim at achieve high levels of its intrinsic properties, albeit in a cost-effective, expeditious manner while ensuring personnel safety (that is, by ensuring acceptable levels of productivity-related properties). In real life, however, the previous characteristics are mutually contradictory. Thus, each characteristic at a tetrahedron vertex in the slide can only be enhanced at the expense of the others (that is, of distorting the tetrahedron). As with analytical properties (Slides 2.58–2.61), a *quality trade-off* must thus often be accepted.

For example, maximizing intrinsic properties will raise costs, delay processes and make them more labour-intensive. On the other hand, expediting measurements will also raise costs and call for greater staff involvement. Therefore, enhancing two characteristics causes the tetrahedron side that contains them to expand.

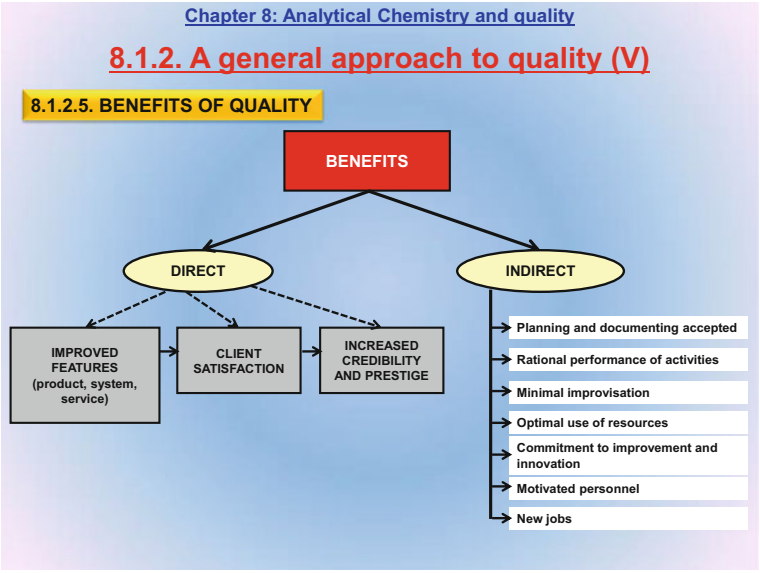
Slide 8.8



A body aiming at quality must adopt a stepwise structure called a "quality cascade". First, the body should develop a *quality policy* materializing in a document sanctioned by its top decision-making organ. The quality policy comprises elements of *Quality Management*, *Quality Systems* and operating procedures of *Quality Assurance*, which encompasses all activities needed to ensure that the body accomplishes its intended level of quality.

Quality Assurance involves three different types of activities, namely: *Quality Control* which is done by direct examination of the body in terms of essentially quantitative indicators; *Quality Assessment*, which entails examining both the body and its activities; and *Internal Corrections* derived from the previous two activities. In summary, Quality Assurance involves examining the products, systems and/or services of a body, and also applying external corrections when necessary according to the outcome of the assessment activities.

Slide 8.9



8.9.1. Achieving quality has a number of benefits, both direct and indirect.

8.9.2. The direct benefits of quality arise from improved characteristics (products, systems or services) leading to client satisfaction, and increased credibility and prestige—which are bound to have a favourable impact on the socio-economic potential of the body concerned.

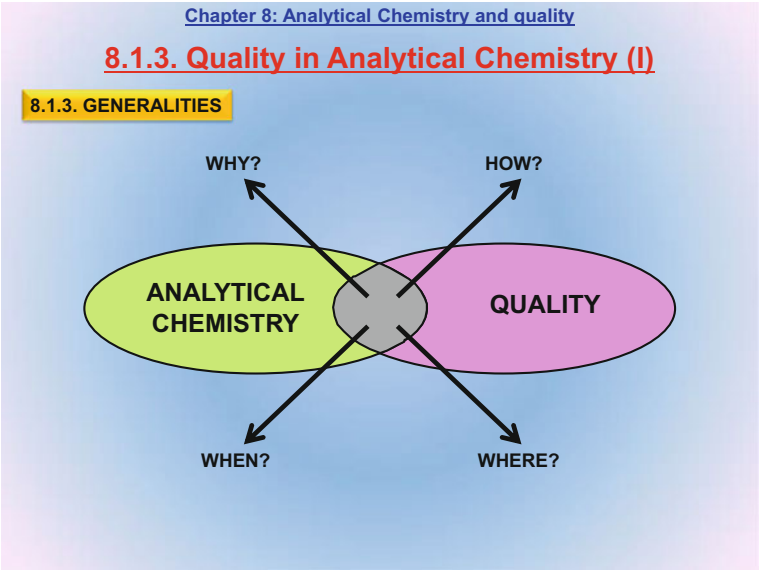
8.9.3. Implementing a quality system can also provide indirect benefits such as the following:

- Acceptance of the need to plan and document all activities, and, as a result, the ensuing advantages that follow.
- Rational performance of all activities.
- Minimal improvisation.
- Optimization of human and material resources.
- Commitment to continuous improvement and innovation, which can result in increased personnel motivation and in new employment opportunities.

These substantial improvements can be expected to have a favourable impact on the bodies adopting a quality system.

8.1.3 Quality in Analytical Chemistry (4 Slides)

Slide 8.10

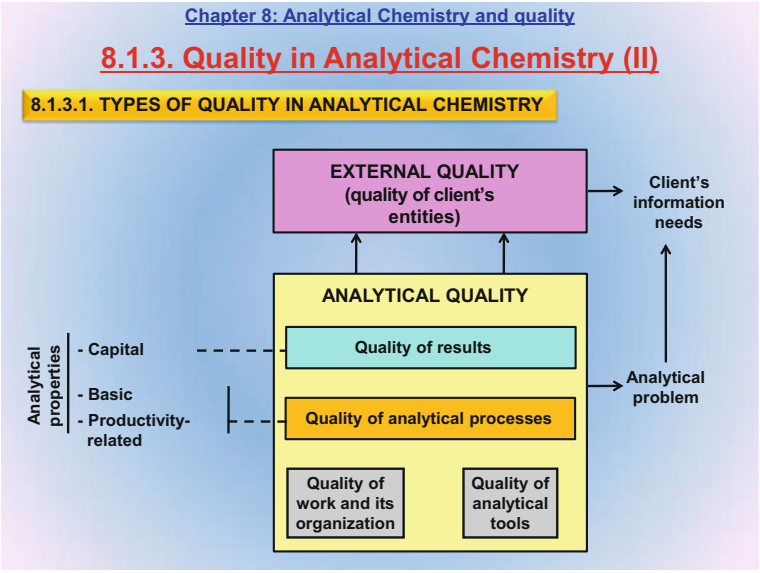


This section discusses general notions of quality in Analytical Chemistry and examines the relationship between quality and this chemical discipline by answering the following questions:

- Why are Quality Systems needed in Analytical Chemistry?
- How should Quality Systems be implemented?
- Where should they be implemented?
- When should they be developed?

The final aim is to implement quality in a systematic manner in the analytical chemical realm.

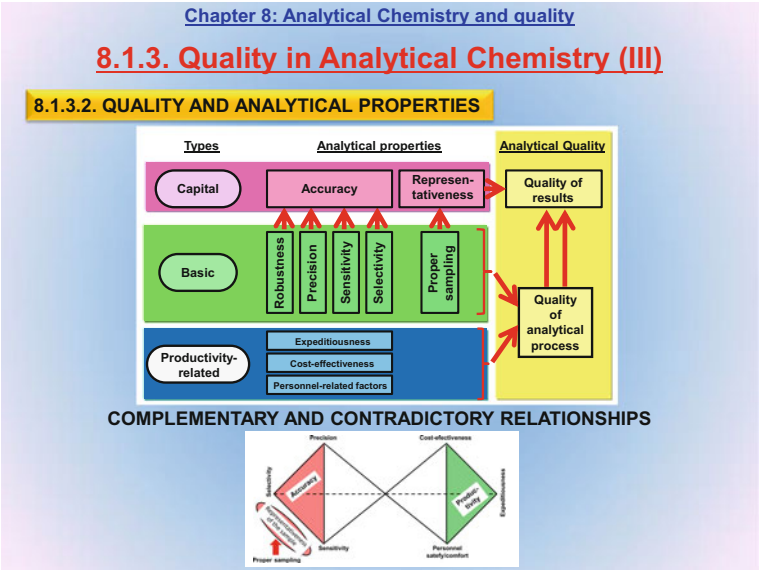
Slide 8.11



This slide depicts the different facets of quality in Analytical Chemistry. As can be seen, there is (a) *external quality* (the quality of a client's or body's entities), which is related to the client's information requirements, and (b) *analytical quality*.

Analytical quality comprises several elements. One is *quality of results*, which rests on quality of chemical measurements processes (CMPs) and is directly related to the analytical problem and to analytical properties (capital, basic and productivity-related). Quality of CMPs in turn depends on *quality of work* and its organization, and also on *quality of analytical tools*, both methodological (e.g., calibration) and material (e.g., instruments, apparatuses, reagents, standards, etc.).

Slide 8.12

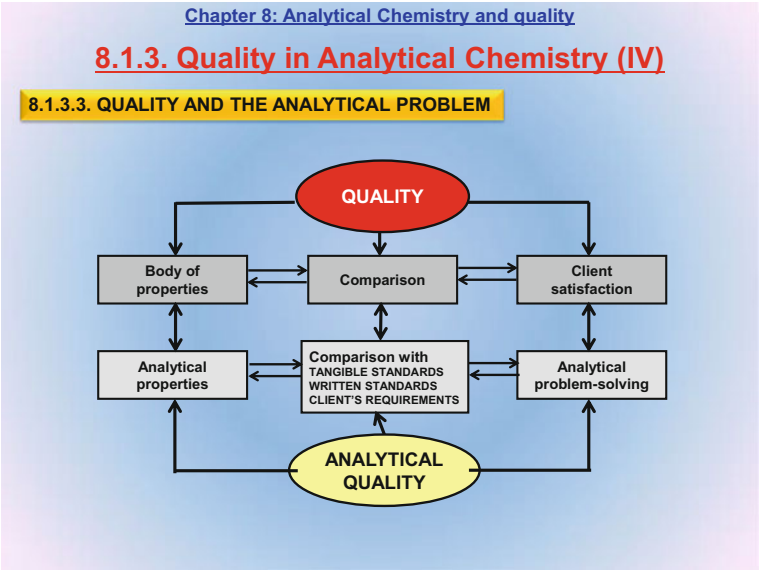


8.12.1. This slide relates analytical quality to analytical properties as described in Chap. 2. Thus, *quality of analytical results* is related to the capital analytical properties accuracy and representativeness.

Also, basic and productivity-related analytical properties are attributes of *quality of analytical processes*. In fact, basic properties (robustness, precision, sensitivity, selectivity and proper sampling) support capital properties, whereas productivity-related properties (expeditiousness, cost-effectiveness and personnel-related factors such as safety) are associated to laboratory productivity.

8.12.2. As noted earlier and discussed in greater detail in Chap. 2, analytical properties can bear different types of relationships (hierarchical, complementary and contradictory). Especially important in this context are contradictory relationships, which lead to quality trade-offs (Slide 8.9) in solving the analytical problem. As can be seen, the two tetrahedra share a common vertex. Enhancing the quality of the results will detract from productivity-related properties (for example, the analytical process will be less expeditious and cost-effective). Also, if a rapid response to the analytical problem is needed, the quality of the results may be adversely affected (see Slides 2.58–2.61).

Slide 8.13

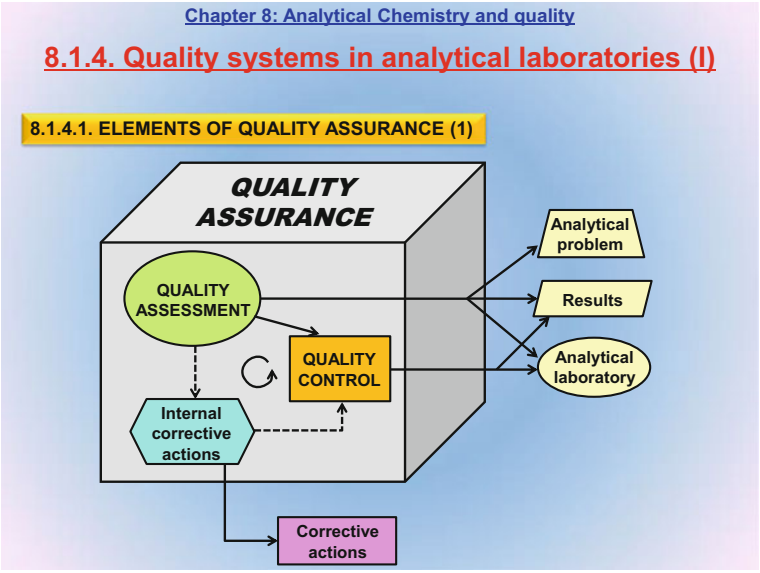


8.13.1. As stated above, the term "quality" can be defined as a body of characteristics or properties that are assessed by comparison and intended to satisfy the client mainly.

8.13.2. As shown in the previous slide, analytical quality is related to quality through analytical properties, which are essential with a view to specifying the characteristics of the analytical information required and constitute a very important reference for assessing the results. Also, properly solving the analytical problem (Slides 7.24–7.27) entails fulfilling the client's information needs and assuring consistency between the analytical information delivered and that required in order to achieve the analytical quality required to support external quality (see Slide 8.11). Finally, analytical quality is established by comparison with standards and the client's information needs.

8.1.4 Quality Systems in Analytical Laboratories (7 Slides)

Slide 8.14

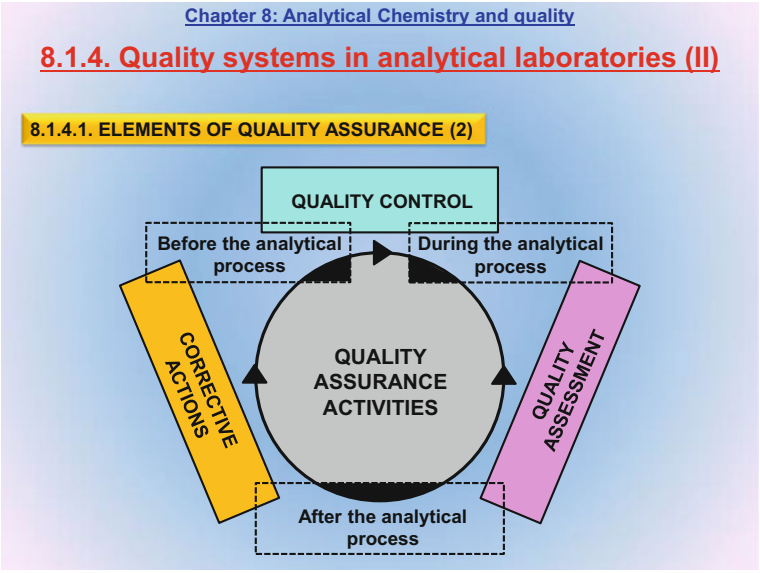


As shown in Slide 8.8, Quality Assurance in analytical chemistry comprises Quality Control, Quality Assessment and internal correction activities, the three being mutually connected by a cyclic chain.

Thus, Quality Control involves examining the analytical laboratory and its output (results), whereas Quality Assessment involves examining quality control procedures, the laboratory, the results it produces and their relationship to the analytical problem.

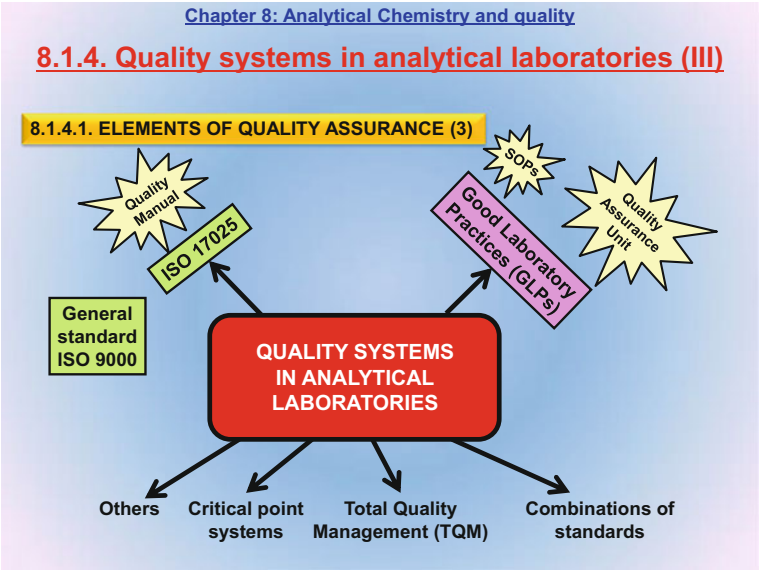
If quality is negatively assessed, internal correction actions will be required within the framework of Quality Assurance. Such actions will largely focus on performance of the analytical laboratory (specifically, on the quality of analytical processes in terms of work organization and analytical tools) with the aim of improving the analytical results and the laboratory as a whole. Any improvements thus made will become apparent in the next quality control. As can be seen, this is a *cyclic process* where each element comes into play at a specific point in time.

Slide 8.15



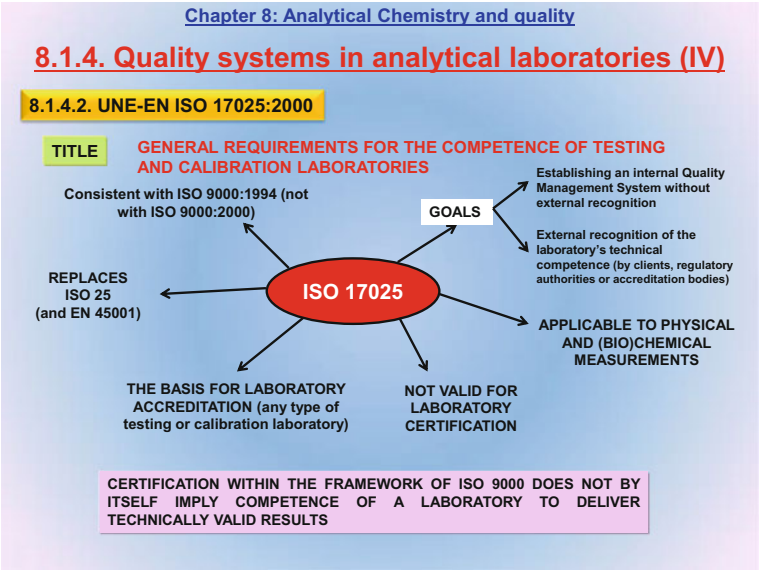
As noted in describing the previous slide, quality assurance activities are cyclic and applied before, during and after the analytical process. Thus, Quality Control takes place before and during the analytical process—in parallel with production of the results. On the other hand, Quality Assessment takes place during and after the analytical process. Finally, corrective actions are usually applied after the analytical process if deemed necessary according to the outcome of Quality Assessment—they are thus performed before the next Quality Control—and dictate whether the analytical process is to be modified in any way. These activities must all be planned and designed beforehand, and also documented and archived after the process. As can be seen, each element of Quality Assurance is involved in two different stages of the analytical process.

Slide 8.16



Quality Systems in analytical laboratories should comply with general international standards on quality management (e.g., ISO 9000), laboratory-specific standards (ISO 17025) and applicable regulations. This slide depicts the main frameworks of standards for quality systems in analytical laboratories. Because of their especial relevance to Quality Systems, ISO standards and Good Laboratory Practices (GLPs) are described in greater detail in Slide 8.17 and 8.18, respectively. There are various alternatives such as combinations of major standards, so-called "total quality systems" and critical point systems, a detailed description of which is beyond the scope of this book.

Slide 8.17



8.17.1. ISO/IEC 17025 ("General requirements for the competence of testing and calibration laboratories"), developed by the International Organization for Standardization (ISO), is the primary standard for Quality Systems in analytical laboratories.

8.17.2. As clearly stated in its "Object and scope" section, the targets of the standard are all types of testing and calibration laboratories (e.g., laboratories whose results are used for product inspection or certification, and laboratories using standard, non-standard or self-developed methods). Therefore, the standard applies to both physical and (bio)chemical measurements.

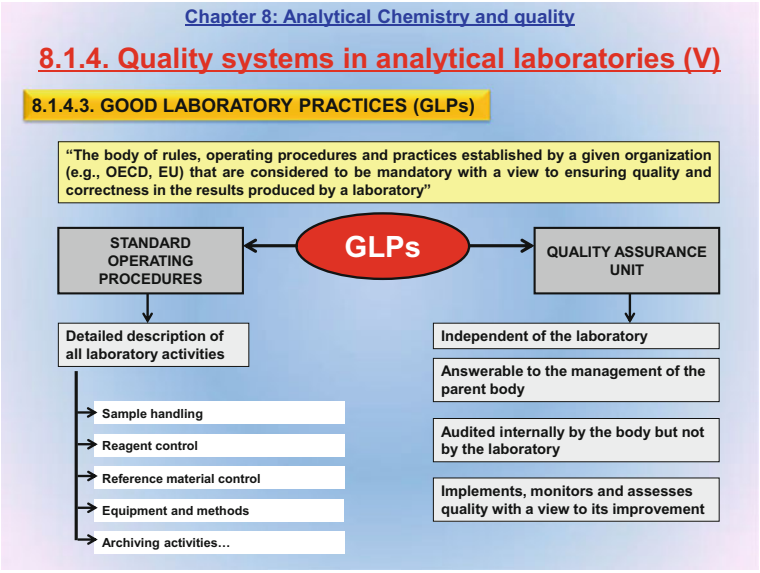
8.17.3. The main goals of this standard are (a) establishing a quality management system that will require no external recognition and (b) gaining external recognition of technical competence by clients, regulatory authorities or accreditation bodies.

8.17.4. ISO/IEC 17025 is based on two previous standards, namely: ISO Guide 25, which formerly held worldwide, and EN 45001, which was used in Europe until 2001 to assess the technical competence of testing and calibration laboratories. These two standards have been superseded by ISO 17025. ISO/IEC 17025 is consistent with the ISO 9000:1994 series (specifically, with ISO 9001 and 9002, issued in 1994).

8.17.5. ISO 17025 is concerned with the accreditation of all types of testing and calibration laboratories. Although it includes two sections on management requirements and technical requirements, accreditation under this standard does not imply direct accreditation under ISO 9001 or 9002.

Certification in the framework of ISO 9000 does not by itself imply that a certified laboratory is competent to produce technically valid results. In fact, it only provides for part of ISO 17205, which certifies Quality Management but not technical competence.

Slide 8.18

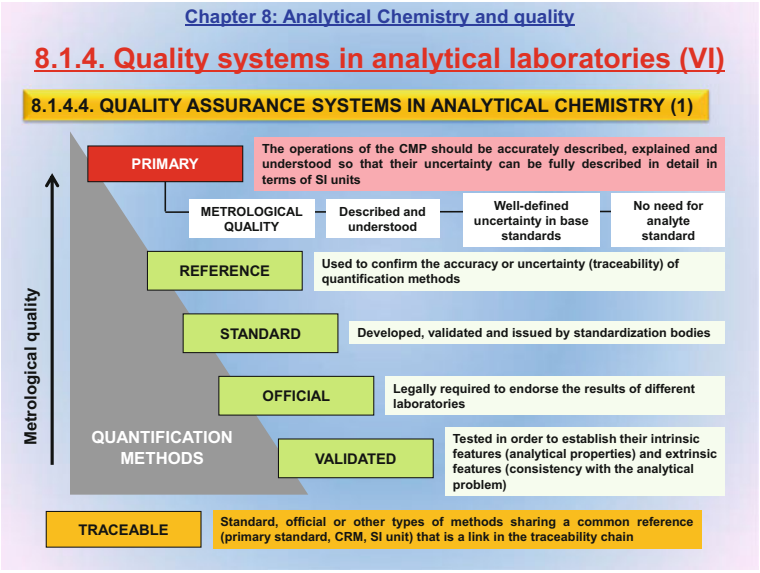


8.18.1. *Good laboratory practices* (GLPs) constitute an alternative to quality-related ISO standards. GLPs are a body of rules, operating procedures and practices established by a given institution such as the European Union or an organization such as the OECD (the Organization for Economic Cooperation and Development) for compulsory adoption worldwide in order to ensure quality and correctness in the results of laboratories performing analysis of substances with a potential social or environmental impact (e.g., drugs, cosmetics, foods, wastewater).

8.18.2. Good laboratory practices encompass so-called *Standard Operating Procedures* (SOPs), which are detailed descriptions of the way laboratory activities should be performed. Each individual laboratory activity (e.g., control of reference materials, use of equipment, archiving) should be assigned an SOP. SOPs typically contain detailed instructions to act in each case and should be followed to the letter. Any modification needed because of failure or changes in the procedure should materialize in a separate SOP for the modification itself. Also, anything pertaining to a Quality System should be recorded in writing. SOPs are equivalent to "procedures" in the Quality Manual.

8.18.3. Good laboratory practices also include the *Quality Assurance Unit* (QAU), which should be independent of the laboratory and answerable to the management only (that is, the QAU should be external to the laboratory but pertain to the body to which it is answerable). The main duties of the QAU are to institute, control and assess quality, and to propose improvement actions. It should consist of personnel exclusively concerned with quality matters—which is often impossible for economic reasons—in order to preserve its greatest asset: independence.

Slide 8.19



8.19.1. The quantification methods used by analytical laboratories can be ranked according to accuracy, precision and who imposes their use. In any case, using a quality method does not necessarily ensure quality in the results unless the method is performed in a correct, verified manner.

Primary quantification methods are those at the top of the metrological quality ranking. According to the Consultative Committee for the Amount of Substance (CCQM), "a primary method of measurement is a method having the highest metrological qualities, whose operations can be completely described and understood, for which a complete uncertainty statement can be written down in terms of S.I. units and whose results are, therefore, accepted without reference to a standard of the quantity being measured".

A primary method thus has four distinct traits, namely:

(1) a high metrological quality;
(2) a complete, understandable description;
(3) an uncertainty defined in terms of SI (base) standards; and
(4) the need for no analyte standard.

Also, a primary method is specific for an analyte/sample pair and the parameters depending on other species or the sample matrix should be known or easy to calculate. Primary methods are assumed to be traceable methods. They should be validated internationally through intercomparison exercises involving laboratories of excellence (reference laboratories). Gravimetric, titrimetric, coulometric and isotopic dilution–mass spectrometry methods are all primary methods.

8.19.2. On a lower level in the metrological quality ranking are **reference methods**, which are those used to check the accuracy or uncertainty (traceability) of quantification methods. Reference methods can be used for quality control purposes by routine laboratories or by external national or internal laboratories.

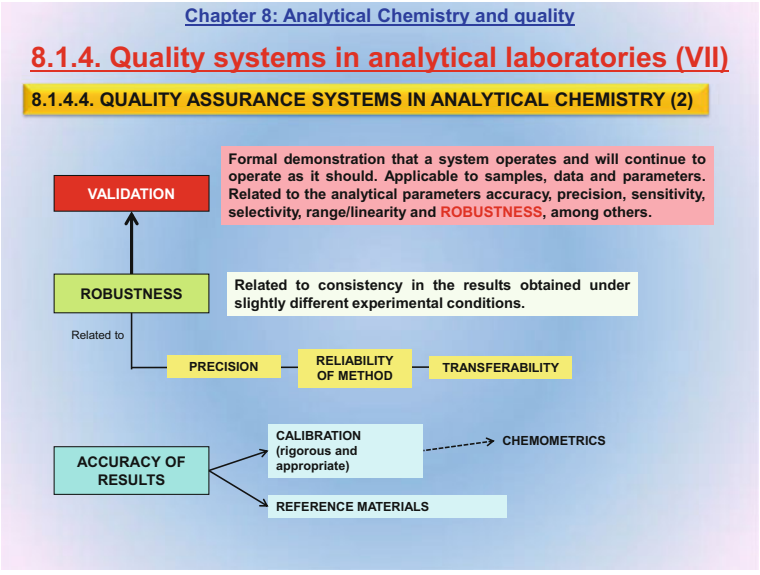
8.19.3. **Standard methods** are developed, validated and issued by standardization bodies such as the International Organization of Standardization (ISO) or the European Committee for Standardization (CEN), and also by associations in support of Analytical Chemistry such as the Association of Official Analytical Chemists (AOAC).

8.19.4. An **official method** is a quantification method described in detail and issued by a government body such as the US Environmental Protection Agency (EPA) for legal adoption with a view to sanctioning the results of laboratories. Some official methods can be used as reference methods, however.

8.19.5. A **validated method** is a method that is described in detail and subjected to a twofold study in order to establish its intrinsic (analytical properties) and extrinsic features (consistency with the analytical problem).

8.19.6. Finally, a **traceable method** is an official or standard method that is unequivocally associated to a reference such as a reference method, a CRM or an SI unit and constitutes the last link in a traceability chain.

Slide 8.20



8.20.1. At this point, it is worth reviewing some important concepts. One is *validation*, which can be defined as the formal demonstration that a system operates and will continue to operate as it should. Validation is applicable to samples, data and methods. Validating a method entails demonstrating that it possesses appropriate levels of some analytical parameters such as accuracy, precision, sensitivity, selectivity, range (linearity), expeditiousness and robustness, among others.

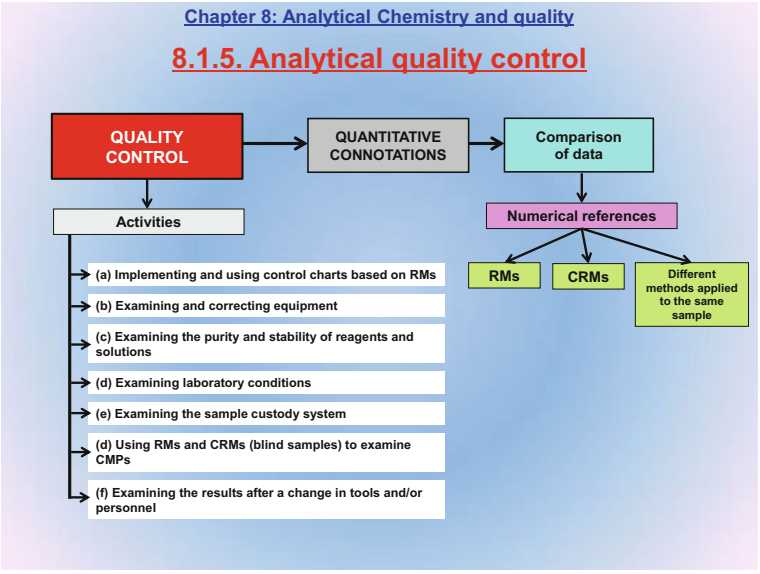
8.20.2. As can be seen in Slide 2.32, the *robustness* of an analytical method is dependent on the degree of constancy of its results in response to a slight change in the experimental conditions. Thus, a method will be robust if its results remain essentially constant over a given range of each operational variable (e.g., pH, temperature). For example a method will be robust in terms of temperature if it invariably produces identical results when performed by a laboratory with no air conditioning in the coldest winter months or the hottest summer months. By contrast, a method whose results are considerably altered by a change of only 0.2 pH units, for example, will be scarcely robust and require strict control of this operational variable.

Robustness is therefore related to two potential attributes of analytical methods, namely: precision and transferability. The precision (reliability) of an analytical method can be defined as the resistance to alteration of the results by slight changes in the operating conditions, and its transferability as its amenability to implementation at different times of year by different operators or laboratories with identical results.

8.20.3. Accuracy in the results rests on two cornerstones, namely: (a) calibration, which should be rigorous and appropriate—chemometrics is of great help for this purpose; and (b) certified reference materials (CRMs), which are described in Chap. 3.

8.1.5 Analytical Quality Control (1 Slide)

Slide 8.21



8.21.1. As stated in explaining Slides 8.14 and 8.15, Quality Control is an essential ingredient and support of Quality Assurance. Quality Control can be defined as a body of planned, documented actions performed by laboratory staff and involving direct examination of how laboratory work is organized, what analytical tools are used and what results are obtained, all with a view to proposing any corrective actions needed—which should also be documented.

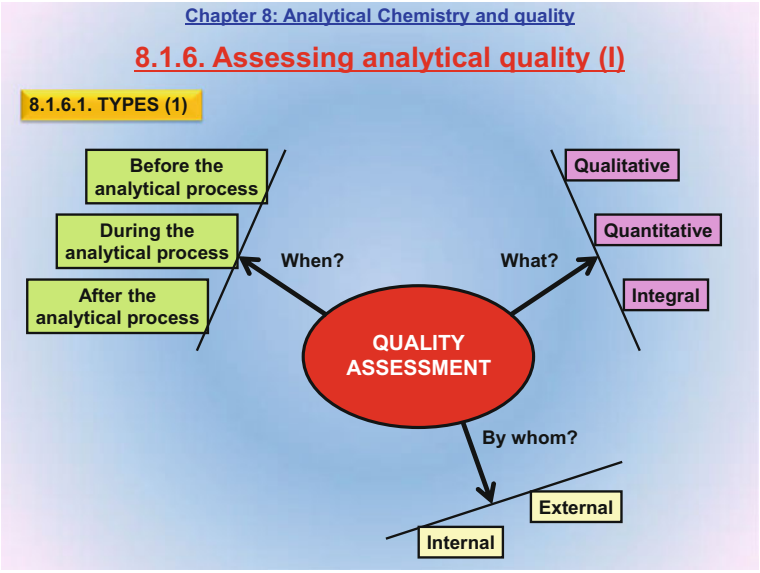
8.21.2. Quality Control is basically quantitative in nature. In fact, it involves comparing data, whether statistically or chemometrically. Comparing data obviously requires using numerical references such as RMs or CRMs, and also results produced by alternative methods, for example.

8.21.3. These are some activities involved in quality control.

(a) Implementation and use of control charts based on reference materials.
(b) Examination and correction of instruments and apparatuses to ensure that they operate as they should. In fact, equipment calibration with reference materials not containing the analyte to establish their traceability (Chap. 3) is one of the most important actions in this context.
(c) Examination of the purity and stability of the reagents and solutions used in CMPs. It is important to store reagents under appropriate conditions (e.g., refrigerated, in the dark), and also to check that solutions have not deteriorated or lost some property in order to avoid errors in the results of the analytical process.
(d) Examination of environmental conditions such as temperature, relative humidity, presence of contaminants or cleanliness in the laboratory. Cleanliness is especially important in so-called "clean rooms" or "white rooms", access to which should be strictly controlled and restricted to staff wearing appropriate clothing by instituting effective control measures such as using air jets or pressure differences (for example, to ensure that trace analyses or microfabrication processes do not fail).
(e) Examination of the sample custody chain in order to ensure correlation between samples and results—a traceability-related feature of sample aliquots. For example, clinical laboratories frequently use bar-coded samples in order to facilitate correct assignation of their results.
(f) Use of RMs and CRMs to examine CMPs at specific points. Frequently, this involves introducing a "blind sample" unknown to the operator among the client's samples in order to more accurately control CMP results.
(g) Examination of any changes in the results arising from use of a CMP to determine specific analytes in a given sample by different staff or with a different instrument. The less the results differ, the more robust will be the CMP.

8.1.6 Assessing Analytical Quality (6 Slides)

Slide 8.22



8.22.1. Together with Quality Control, described in the previous slide, Quality Assessment provides firm support for Quality Assurance—which, as shown in Slide 8.14, is related to Quality Control and leads to internal correction actions if required. Assessing quality entails directly examining not only the results of a laboratory, but also its quality control and routine activities.

8.22.2. Quality assessment activities can be classified according to various criteria. One is the point in time they are performed (namely, before, during or after the analytical process). As shown in Slide 8.15, quality assessment in the analytical laboratory takes place mainly during and after the process.

8.22.3. According to target object and examination procedure, Quality Assessment Systems can be of the qualitative, quantitative or integral type. Qualitative assessment involves the visual and documental inspection of the laboratory, its analytical processes and its quality control systems. This usually entails on-site

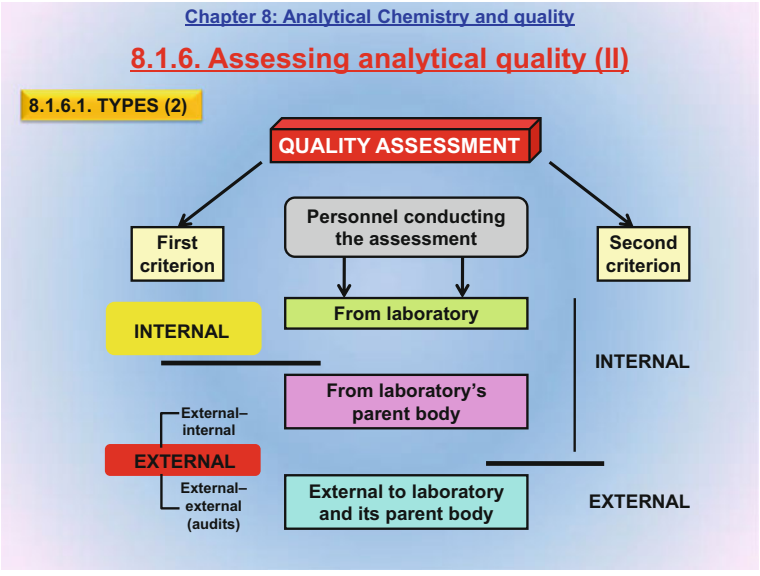
inspection of laboratory work, the way it is organized, and its documentation (e.g., laboratory notebooks, SOPs, primary data, reports, etc.) and archiving procedures. Also, the results delivered by the laboratory should be compared for consistency with the analytical problem, the client's requirements and the reports issued.

On the other hand, quantitative assessment involves examining the metrological quality of the results obtained by subjecting certified reference materials to the analytical process in order to compare the certified values and their uncertainty with those of the laboratory results.

Finally, integral assessment involves qualitative and quantitative examination. It is thus the most categorical because it assures quality in the results and allows any future deficiencies potentially detracting from quality to be timely corrected.

8.22.4. Quality assessment can be internal or external depending on who performs it. As shown in the next slide, the two may not be easy to distinguish depending on the particular reference used. One typical example of external assessment by the client is requiring a laboratory to analyse a sample with previously determined results for comparison.

Slide 8.23



8.23.1. As shown in the previous slide, it is not always easy to deem Quality Assessment internal or external according to the assessor. Thus, quality can be assessed by laboratory staff, personnel from the laboratory's parent body not working in the laboratory (e.g., members of the Quality Assurance Unit for Good Laboratory Practices, personnel from other departments) or even personnel pertaining to neither the laboratory nor its parent body.

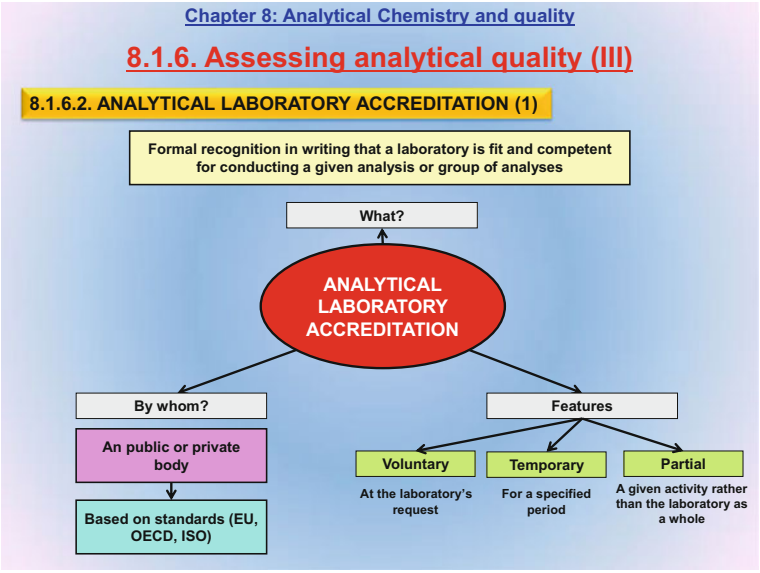
8.23.2. The most immediate classification criterion is thus whether the assessors are laboratory staff. An alternatively, less commonplace criterion is whether the assessors pertain to the body concerned (e.g., a company). Let us focus on the former criterion, which is the more widely used.

8.23.3. *Internal quality assessment* is done by laboratory staff either exclusively concerned with quality-related matters or having additional duties. Discriminating between internal quality assessment and quality control is difficult because the two are done by the same personnel; however, the former includes additional connotations (e.g., qualitative or global determinations).

8.23.4. *External quality assessment* is in theory more rational and objective than internal assessment because assessment activities are performed by personnel not pertaining to the laboratory, but rather to another department of the body or institution (external–internal assessment) or even to a different body or institution (external–external assessment).

- *External–internal quality assessment* is in fact conducted by personnel of the organization or institution concerned other than its laboratory staff. Thus, the assessors may be members of the Quality Assurance Unit in charge of GLPs or of a group pertaining to the quality department. In any case, the assessors should guide, direct and survey quality control systems and the laboratory as a whole by using appropriate protocols or SOPs, or the Quality Manual.
- *External–external quality assessment* is done by expert personnel from other bodies or organizations and is thus doubly external to the laboratory. Their activities are commonly known as *audits* and may comprise systems (qualitative, visual and documental examination), performance (with quantitative connotations) or both (integral assessment). In the analytical realm, audits can be of two types, namely: (a) direct, which lead to accreditation of a laboratory (see Slides 8.24 and 8.25); and (b) indirect (e.g., proficiency testing) (Slides 8.26 and 8.27).

Slide 8.24



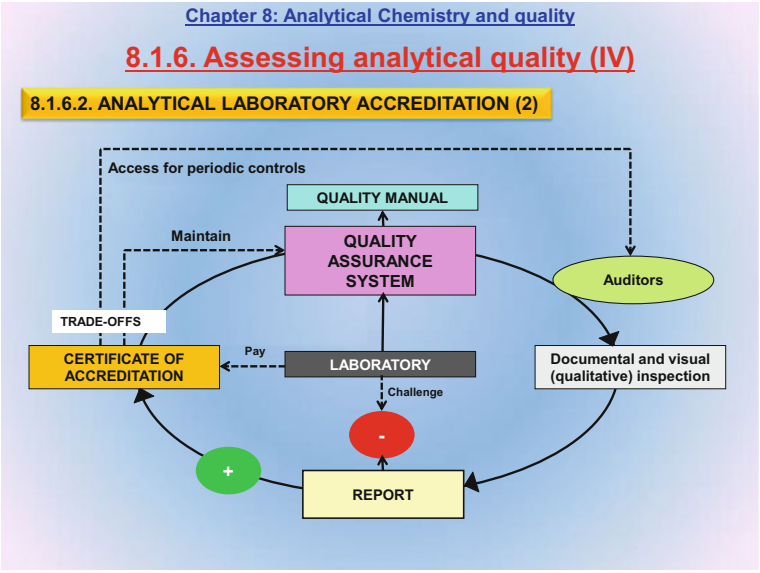
8.24.1. As shown in the previous slide, direct audits, which pertain to external–external quality assessment, lead to *laboratory accreditation*. In this context, accreditation is defined as "*the formal recognition, in writing, that a laboratory is fit and competent to perform a given analysis or specific groups of analyses*."

8.24.2. Laboratories are accredited by a public or private body from their country using internationally applicable standards such as those from EU, OECD or ISO.

8.24.3. The accreditation of analytical laboratories is (a) *voluntary*[1] because it is done at their request; (b) *temporary* because it holds for a specified length of time only; and (c) *partial* because it applies to specific activities or groups of activities rather than to the laboratory as a whole.

[1]Very often, voluntariness is only theoretical because public and private clients are increasingly demanding accreditation in order to award contracts for the conduct of specific analyses through public auction.

Slide 8.25



8.25.1. For a laboratory to be accredited, it must possess a Quality System accurately described in its Quality Manual.

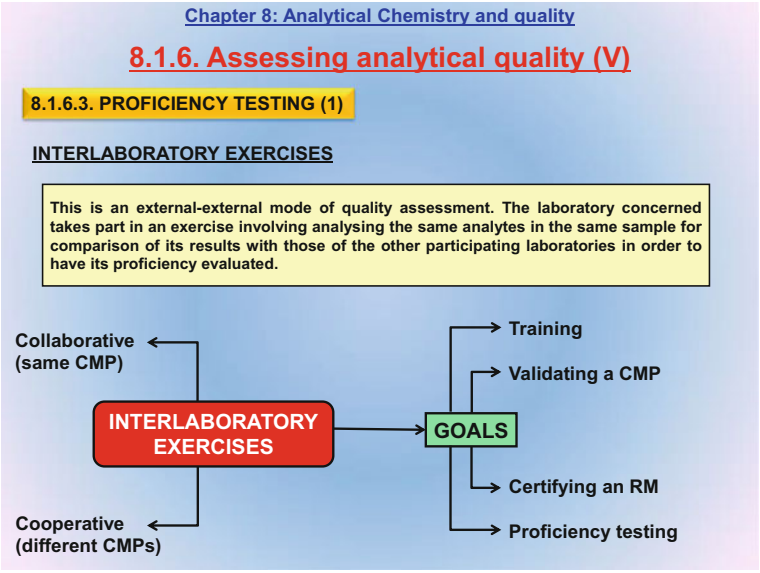
8.25.2. The accreditation process starts with a visual (qualitative) and document inspection by the auditors.

8.25.3. Based on the inspection, the auditors issue a report. If the report is unfavourable, the laboratory can challenge its conclusions.

8.25.4. On the other hand, if the report is favourable, the laboratory is awarded a Certificate of Accreditation. The certificate, which must be paid by the laboratory, carries the twofold commitment of maintaining the existing quality systems and allowing the auditors free access to perform periodic controls during the period of validity. As noted earlier, accreditation is only temporary, so it must be renewed after the validity period has expired or if the laboratory undergoes any substantial changes in the meantime. Renewal involves repeating the whole accreditation process, a task which, however, is made easier by the auditors' prior knowledge of the laboratory to be re-accredited. The specific aspects to be considered in the accreditation process are similar to those described in the Quality Manual.

Although some accreditation systems remain purely qualitative, there is a growing trend to integral accreditation, which additionally involves quantitative assessment by use of CRMs or the results of proficiency testing (see Slide 8.26).

Slide 8.26



8.26.1. Proficiency testing is one way of performing external–external quality assessment. The interested laboratory takes part in an interlaboratory exercise involving the analysis of a given sample for specific analytes, its results being compared with those of the other laboratories for quantitative assessment. The next slide shows an example of interlaboratory exercise.

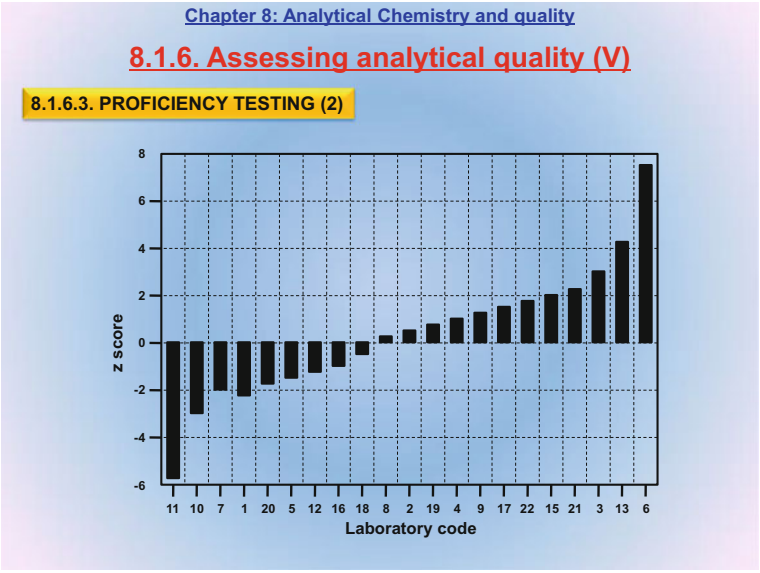
8.26.2. An interlaboratory exercise is a body of analytical processes performed independently by several laboratories on aliquots of the same sample to determine the same analytes in order to compare the results and their uncertainties. For the ensuing conclusions to hold, the exercise should be designed, planned and managed by a prestigious independent national or international body.

Interlaboratory exercises can be collaboratory or cooperative depending on whether the participating laboratories use the same or different chemical measurement processes.

8.26.3. Interlaboratory exercises may be conducted for various purposes including (a) allowing non-expert laboratories to learn how to conduct a given CMP; (b) validating a CMP developed in response to a new information requirement (see Chap. 4); (c) certifying the values and uncertainties for a CRM (see Chap. 3); and (d) assessing the quality of the results produced by the participating laboratories.

Participation in interlaboratory exercises is usually voluntary unless it is prescribed by the Quality Manual or the accreditation system. In any case, it generates a number of benefits such as allowing the laboratories to engage in a useful network to exchange experience or leading to substantially improved results after successive exercises. In Europe, the *Community Bureau of Reference* (BCR) plans and manages a number of interlaboratory exercises each year.

Slide 8.27



8.27.1. This slide illustrates the concept of *proficiency testing* with an example: an international body organizes an exercise where several laboratories are to analyse seawater samples for cadmium traces. For this purpose, it prepares uniform aliquots of an RM or CRM previously found to be stable and contain a concentration of analyte $\widehat{X}'$.

The interested laboratories agree to comply with the regulations of the exercise and receive a sample aliquot that they are to analyse n times in order to obtain a mean result $\bar{x}_l$ that is to be reported to the organizing body by a specified deadline.

Each laboratory is given a z score that is calculated by subtracting the value held as true for the sample, $\widehat{X}'$, from the reported mean value, x_i, and dividing into the standard deviation for $\widehat{X}'$ (σ):

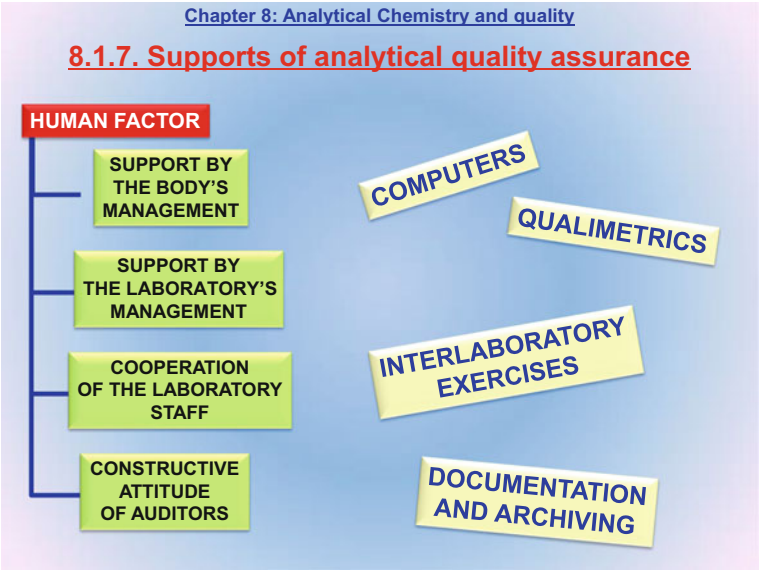
$$z = \frac{\bar{x}_l - \widehat{X}'}{\sigma}$$

where z can be positive or negative and is used to construct a quality graph for the participating laboratories. Usually, a z score of ± 2 is deemed acceptable, one greater than ± 2 but smaller than ± 3 dubious and one greater than ± 3 out of control.

Some authors identify global assessment based on a CRM with participation in proficiency tests because the result and its uncertainty are compared with certified values obtained in interlaboratory exercises.

8.1.7 Supports of Analytical Quality Assurance (1 Slide)

Slide 8.28



8.28.1. It makes no sense to refer to Quality Assurance in the analytical laboratory without considering the human factor. Thus, Quality Assurance should be supported by the laboratory and body management. Also, it should be willingly accepted by the laboratory staff concerned, who should view a Quality System as the opportunity to develop and foster excellence rather than as stricter control of their personal work. Also, auditors should adopt a constructive attitude to their duties and aim at sustained improvement of the laboratory.

8.28.2. In addition to the human factor, successfully implementing a Quality System in a laboratory entails providing the technical means required and re-training its staff. The main supports for laboratory quality include computers, qualimetrics, interlaboratory exercises, and documentation and archiving activities.

No Quality System can operate reliably today without the aid of *computers*, which play a central role in Quality Assurance. In fact, some software packages enormously facilitate control of analytical equipment or quality activities.

The word *qualimetrics* is at the threefold interface among computers, chemometrics and quality. Essentially, qualimetrics is concerned with the used of chemometrics to establish Quality Assurance with the help of computers. As such, qualimetrics affects analytical information, and the optimization of analytical processes and quality systems.

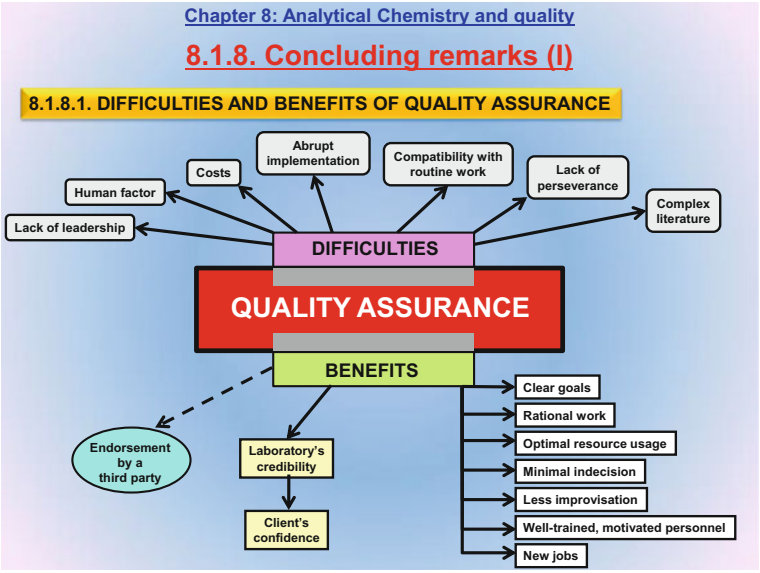
- One use of chemometrics in this context is for the computer-assisted validation of analytical methods in terms of accuracy, precision, sensitivity, selectivity, linear concentration range, robustness, etc.
- Chemometrics enables the validation of primary data. As noted earlier, proper calibration is the basis for traceability of results.
- One other interesting use of chemometrics relating to analytical quality is for comparing results, which is the basis for quality control and assessment systems.
- Chemometrics affords rigorous, reliable comparison of results—and also, in many cases, identifying the sources of inconsistencies. In addition, it plays a major role in the comparison of results through interlaboratory exercises or the use of reference materials.

Interlaboratory exercises, which are described in Slide 8.28, facilitate assessment of laboratory proficiency.

Finally, *documentation and archiving activities* are usually the greatest hindrance to the implementation and monitoring of Quality Systems in analytical laboratories, and also the main source of staff resistance because they are usually labour-intensive and time-consuming. Properly maintaining a quality system entails recording and archiving every activity, and also establishing an SOP for each. Also unavoidable is keeping a written record of the sample custody chain, the performance of instruments (e.g., chromatographs, electrophoretic systems) and apparatuses (e.g., balances, refrigerators) immediately after installation, the monitoring of other materials, SOPs, primary data, results, reports and documenting activities themselves. As a result, documentation activities demand high involvement and are usually the bottleneck of quality assurance programmes. Obviously, all documents should be effectively protected against loss, theft or tampering with. The documentation facet of quality is consistent with the integral concept of traceability explained in Chap. 3.

8.1.8 Concluding Remarks (2 Slides)

Slide 8.29



8.29.1. This slide summarizes the cost and benefits of implementing a quality system in an analytical laboratory.

8.29.2. Although the goal is to improve the laboratory and derive specific benefits, starting and maintaining a Quality Systems may involve some problems or dangers that should be known in order to take effective measures. Some of the more common potential problems are as follows:

- *Lack of leadership*. For a quality system to be viable, the body to which the laboratory is answerable must have unequivocally defined goals set by a leading organ and accept unavoidable quality trade-off in some cases. Also, Quality Assurance must rest on an appropriate quality policy. A laboratory instituting a Quality System simply to maintain accreditation or exhibit a certificate can hardly have a functional, rigorous system.
- *The human factor*. This is one of the basic supports for implementing and properly maintaining a Quality System. Staff should be motivated to accept performing the occasionally tedious tasks involved because any imposed duties will most certainly fail unless they are persuaded of the importance of quality.
- *Costs*. Quality Systems require starting and maintenance investments to be considered in their implementation.
- *Abrupt implementation*. Abruptly starting a Quality System can elicit outright rejection by staff. Rather, the system should be developed in a gradual manner,

starting with specific tasks such as establishing the sample custody chain, developing SOPs or validating charts and progress to the Quality Manual and auditing, both internal (by the Quality Assurance Unit for GLPs) and external (by participation in interlaboratory exercises and proficiency tests).

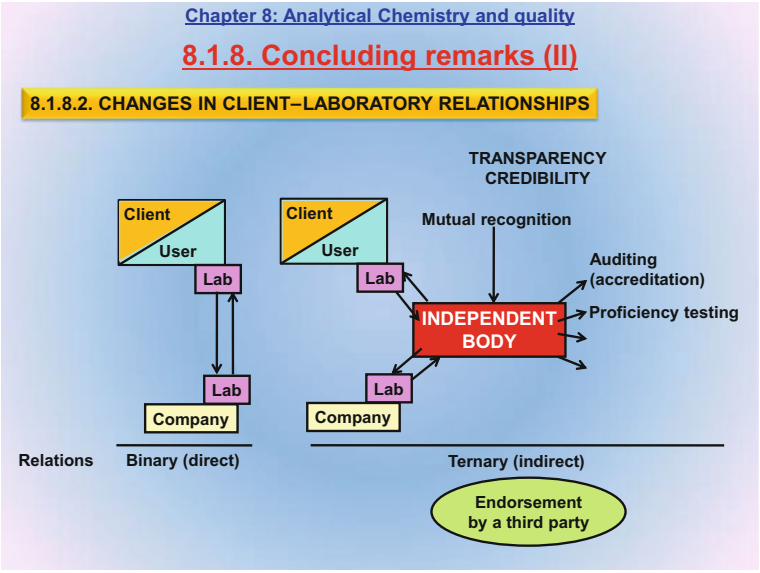
- *Compatibility with routine tasks*. The tasks involved in implementing a Quality System should be compatible with the basic goal of analytical laboratories, namely: producing quality analytical information in a timely manner and at the agreed cost.
- *Lack of constancy*. The implementation of a quality system is a long-distance race. Therefore, those involved in the process should not expend their whole energy at the start if they are to retain their involvement and stamina for the more labour-intensive tasks (e.g., documenting and archiving). Internal and external audits may help to sustain motivation.
- *Complex literature*. The literature on quality is atypical or even contradictory, and full of abbreviations and laws that raise an initial barrier which is sometimes difficult to overcome.

8.29.3. In any case, the benefits of Quality Systems, outlined in Slide 8.9, clearly surpass their potential costs. The most immediate and direct benefit of Quality Assurance is that it provides a well-grounded guarantee of the reliability in the information produced by a laboratory and hence can boost the confidence of their clients. As shown in the next slide, endorsement by a third party such as an independent body can increase the transparency and credibility of laboratories.

Quality Assurance also has additional benefits such as the following:

- *Better defined goals.* The large amount of documentation produced in the process can facilitate decision-making in terms of internal organization of work and help fulfil the goals of the body to which the laboratory is answerable.
- *More rational organization of work* as a result of avoiding unnecessary, repetitive operations by carefully planning laboratory activities in developing the Quality Manual.
- *Optimal use of resources*.
- *Minimal indecision*.
- *Less improvisation* as a result of all laboratory procedures—documentation and archiving included—being described in SOPs.
- *Better trained, more motivated personnel*. This is especially important because it helps to maintain the Quality System and enjoy its benefits.
- *Creation of jobs* such as those of the members of the Quality Assurance Unit.

Slide 8.30



8.30.1. As shown in the previous slide, the most immediate benefit of Quality Assurance is that it provides firm support for reliability in the information produced by a laboratory. This scheme shows the transparency and credibility gained by companies relying on an independent body to relate to others through the results of their respective laboratories. The body concerned will be responsible for external audits (accreditation) and proficiency testing or intercomparison exercises.

8.30.2. Indirect (ternary) relations, referred to as "*endorsement by a third party*", imply mutual recognition and boost trading in relation to direct (binary) relations. This is how the external and internal (within-body) image of the laboratory's parent body is promoted and the client's or user's confidence increased.

8.2 Annotated Suggested Readings

BOOKS

Principles of Analytical Chemistry
M. Valcárcel
Springer-Verlag, Berlin, 2000.

This was the first book to start the teaching of Analytical Chemistry with its foundations before dealing with methods and techniques in order to provide students with an accurate notion of what Analytical Chemistry is and means.

This chapter coincides to a great extent with Chap. 8 in the book ("Analytical Chemistry and quality"). Some sections have been abridged, whereas others have been expanded to better illustrate the state of the art and future of Analytical Chemistry fifteen years later. The book can be used for direct consultation of the contents of this chapter.

Quality Assurance in Analytical Chemistry, 2nd edition

B.W. Wenclawiak, M. Koch, E Costas (Eds.)

Springer Verlag, Heidelberg (Germany), 2010.

This books uses a similar format (slides and text) to deal with the most salient aspects of Quality in Analytical Chemistry, namely: Quality Management Systems based on ISO/ITEC 2000, accreditation based on ISO/ITEC 17025, Good Laboratory Practices, the Quality Manual, Basic Statistics, Validation, Measurement Uncertainty, Control Charts, Certified Reference Materials and Interlaboratory tests. Most of these concepts are discussed in Chap. 7, so the book by Wenclawiak et al. is probably the best source for expanding on its contents as regards notions and approaches to analytical quality.

STANDARDS

ISO 9000:2005. Quality management systems: Fundamentals and vocabulary

International Organization for Standardization (ISO), Geneva (Switzerland), 2005.

ISO 9000 was developed by Subcommittee SC1 (Concepts and Terminology) of Technical Committee ISO/TC 176 on Quality Management and Assurance. This is the third edition of the standard, which supersedes the second (ISO 9000:2000) and includes the changes accepted in draft ISO/DAM 9000:2004. In addition to a foreword, an annex describing the procedure used to develop the vocabulary and a reference list, the standard includes the following sections: Introduction, Object and scope, Fundamentals of quality management, and Terms and definitions

EN ISO/IEC 17025. General requirements for the competence of testing and calibration laboratories

This standard, issued in May 2015, is the adapted version for Europe of the original international standard: ISO/IEC 17025:2005. ISO/IEC 17025 was developed by the ISO Committee for Conformity Assessment and comprises the following sections: Foreword, Introduction, Object and scope, Normative references, Terms and definitions, Managerial requirements, Technical requirements, Annex A (Nominal cross-references to ISO 9001:2000), Annex B (Guidelines for establishing applications for specific fields) and Bibliography.

8.3 Questions on the Topic (Answered in Annex 2)

8.1. To what analytical chemical concepts do the basic and applied sides of quality relate?
8.2. What types of indicators are used to assess quality?
8.3. How are the quality expected and that perceived by the "client" related to the quality planned and designed a body or organization?
8.4. Distinguish external and internal quality, and relate the two, through two examples: (a) a government environmental agency and (b) analytical laboratory.
8.5. What are quality trade-offs? Give some examples in various fields.
8.6. What are the structural landmarks in the quality of a body or organization?
8.7. Explain some direct or indirect benefits of implementing a Quality System.
8.8. In what way is Analytical Quality related to analytical properties? To which properties are (a) quality of results and (b) quality of the analytical process related?
8.9. What is the relationship of quality to analytical quality?
8.10. Distinguish external and internal corrective actions in the framework of Quality Assurance.
8.11. What Quality Assurance elements examine an analytical laboratory?
8.12. Comment on the cyclic nature of Quality Assurance activities in the analytical chemical realm.
8.13. On what standards and elements do Quality Systems applied to analytical laboratories rest?
8.14. What are the goals of ISO 17025?
8.15. What are Good Laboratory Practices?
8.16. What are Standard Operating Procedures? Where are they used?
8.17. What is the Quality Assurance Unit?
8.18. What is a primary method? How does it affect analytical quality?
8.19. What is the difference between an official method and a standard method?
8.20. What activities does quality control involve?
8.21. Why is labelling quality assessment activities as external or internal confusing?
8.22. What are the goals of interlaboratory exercises? Where do they fall in the analytical quality realm?
8.23. Why are documentation and archiving activities the bottleneck in implementing quality in a laboratory?
8.24. What is external–external assessment? Give some examples and distinguish it from external–internal assessment.
8.25. Who accredits analytical laboratories? What is laboratory accreditation it based on?
8.26. Define "accreditation". What are the main features of analytical laboratory accreditation?
8.27. What does the process of accrediting a laboratory involve?
8.28. What does analytical quality assurance rest on?

8.29. Comment on the problems potentially arising in implementing quality assurance in analytical laboratories.

8.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened by about one-sixth for teaching Analytical Chemistry to students not majoring in Chemistry. The following five slides can be omitted for this purpose:

- Section 8.1.2: Slide 8.9
- Section 8.1.3: Slide 8.12
- Section 8.1.4: Slide 8.20
- Section 8.1.5: Slide 8.21
- Section 8.1.6: Slide 8.25

Social Responsibility in Analytical Chemistry

9

Abstract

Social Responsibility (SR) in Analytical Chemistry, the central topic of this chapter, constitutes the synergistic combination of the concepts contained of the previous two chapters of Part III: "Analytical problem-solving" and "Analytical Quality". The part is concerned with the socio–economic projection of Analytical Chemistry. The initial sections of this chapter provide a brief description of the key notions underlying the Social Responsibility inherent in individuals, organizations, and scientific and technical areas, which is essential for life today. The remainder of the chapter discusses the internal and external connotations of Social Responsibility in the analytical chemical realm. The notions associated to these two facets are illustrated with a number of real-life examples.

Teaching Objectives

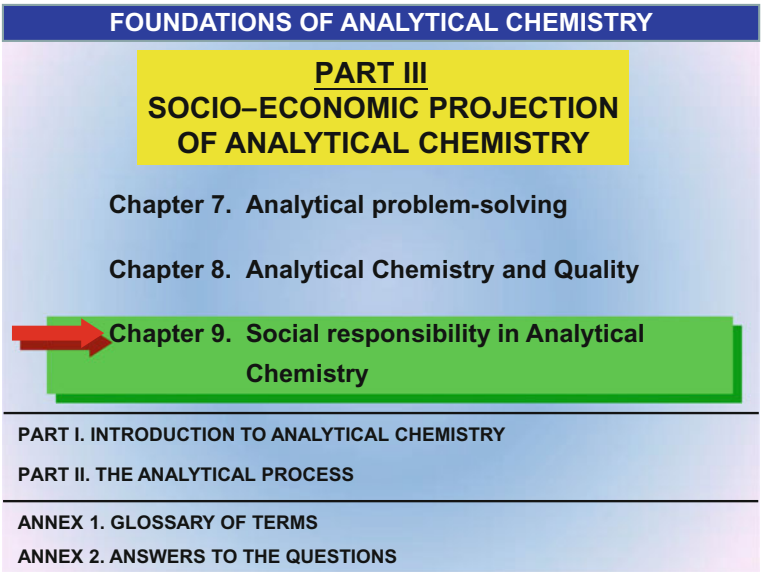
- To introduce students to the concept of "Social Responsibility".
- To highlight the crucial role of SR in Science and Technology.
- To describe SR in Analytical Chemistry and define SR in (bio)chemical information.
- To apply the traceability concept to various facets of Analytical Chemistry and their integration.
- To distinguish the internal and external connotations of SR in Analytical Chemistry using a variety of real-life examples.

Electronic supplementary material The online version of this chapter (doi:10.1007/978-3-319-62872-1_9) contains supplementary material, which is available to authorized users.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1_9

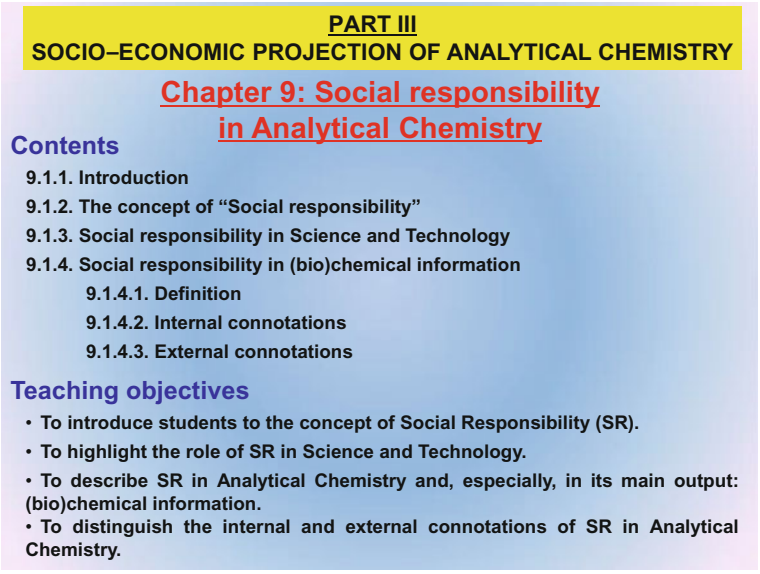
9.1 Explanation of the Slides

Slide 9.1



This slide places Social Responsibility (SR) in Analytical Chemistry in the context of Part III ("Socio–economic Projection of Analytical Chemistry") and depicts the other two parts, which, as shown in Slide 7.4, are mutually related. This is the third, last chapter in the part and completes the description of the relationships of Analytical Chemistry to society, industry and the economy, for which information continues to be a key element.

Slide 9.2

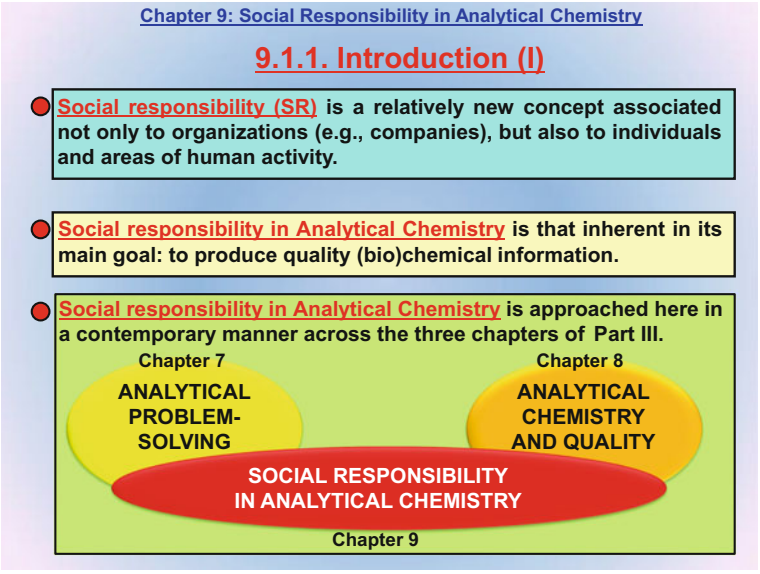


9.2.1. The contents of this chapter are organized in four sections including an Introduction and three others describing the general meaning of SR and its particular meaning in connection to Science and Technology. The chapter then focuses on SR in Analytical Chemistry, which is defined in equivalent terms, and on its internal and external connotations.

9.2.2. The slide also shows the teaching objectives of the chapter as regards SR in general and SR in Analytical Chemistry in particular.

9.1.1 Introduction (2 Slides)

Slide 9.3

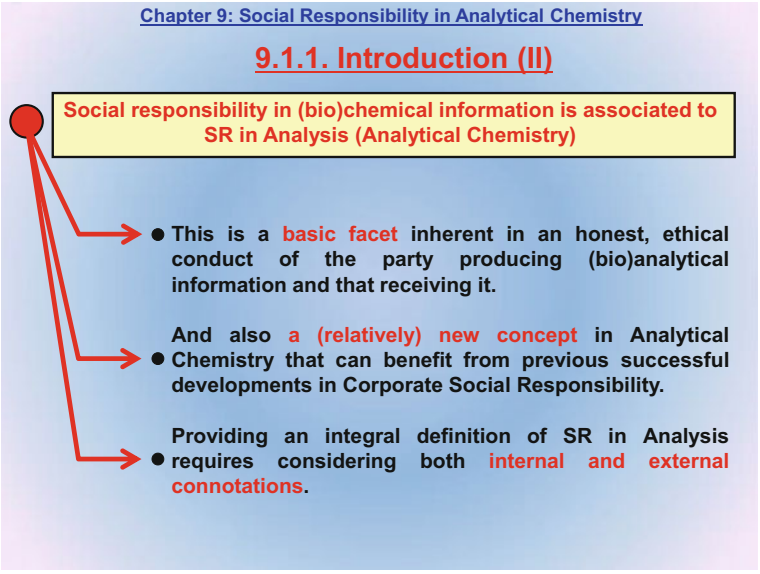


9.3.1. This slide introduces the contents of the chapter, which is essentially concerned with Social Responsibility and its adaptation to Analytical Chemistry.

The SR concept arose with great strength as a complement to "quality"—a vogue word in the last quarter of the XX century—early in the next. The concept is transversal in nature and is currently applied not only to organizations and businesses, but also to industrial, scientific and technical areas, for example.

9.3.2. This chapter deals with SR in a modern manner that connects to, and integrates, the other chapters dealing with the socio–economic projection of Analytical Chemistry.

Slide 9.4



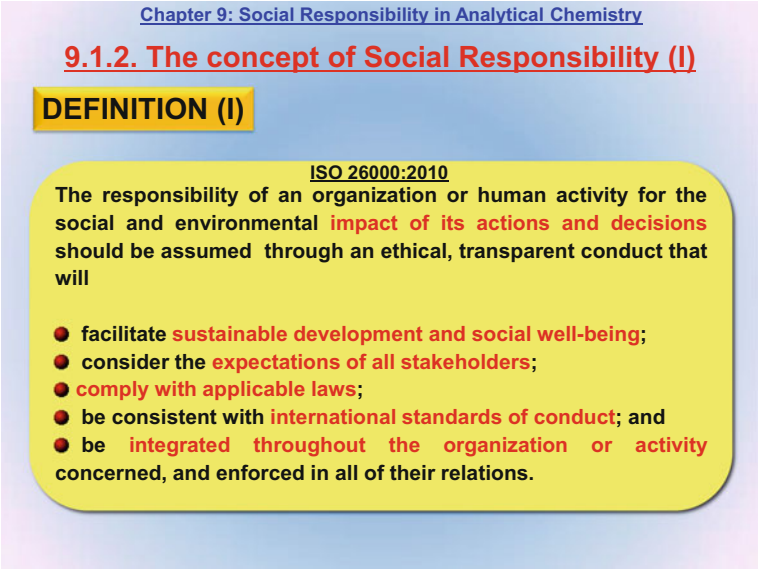
9.4.1. Social Responsibility in Analytical Chemistry is fully consistent with SR (bio)chemical information. In fact, the (bio)chemical information required by clients and delivered by analytical chemical laboratories should be communicated honestly and ethically between the two parties. Information constitutes a major social power today (see Slides 1.15 and 1.16).

9.4.2. Social Responsibility is a fairly new concept which, however, has always underlain Analytical Chemistry. Some of the great developments in Corporate SR from the 50s can be easily extrapolated or adapted to scientific and technical areas such as Analytical Chemistry.

9.4.3. The nature and impact of SR in Analytical Chemistry are best understood by considering its internal and external connotations as done in this chapter.

9.1.2 The Concept of "Social Responsibility (9 Slides)

Slide 9.5



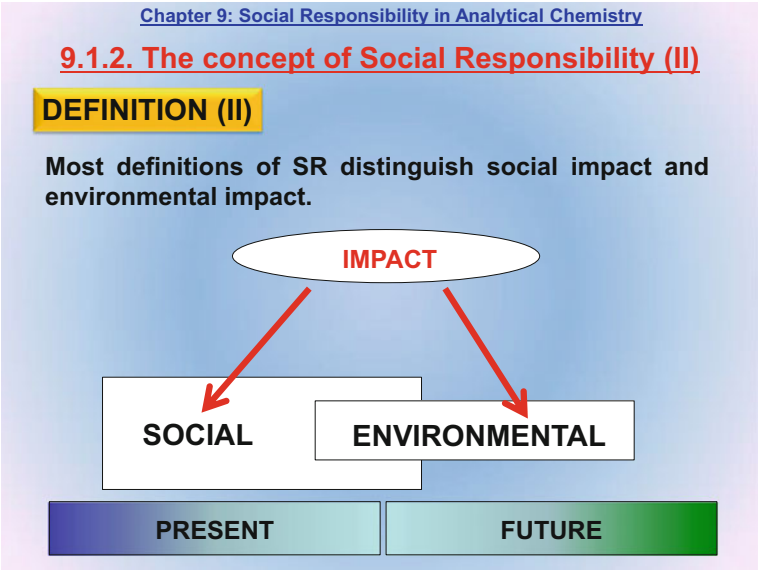
Social Responsibility has been defined in a number of ways in the corporate realm. Each definition emphasizes some specific aspect. Thus, the most frequently underscored notions in forty definitions found in the literature are as follows:

- stakeholders (88% of definitions) (see Slide 9.8),
- social impact (88%),
- economic impact (86%),
- voluntariness (80%), and
- environmental impact and sustainability (59%).

This slide shows one of the "official" definitions: that in the written standard ISO 26000:2010 for SR in human organizations and activities (see Slide 1.14). Interestingly, the definitions in ISO standards contain the defined term ("responsibility") when an alternative word such as "awareness" would probably be more appropriate.

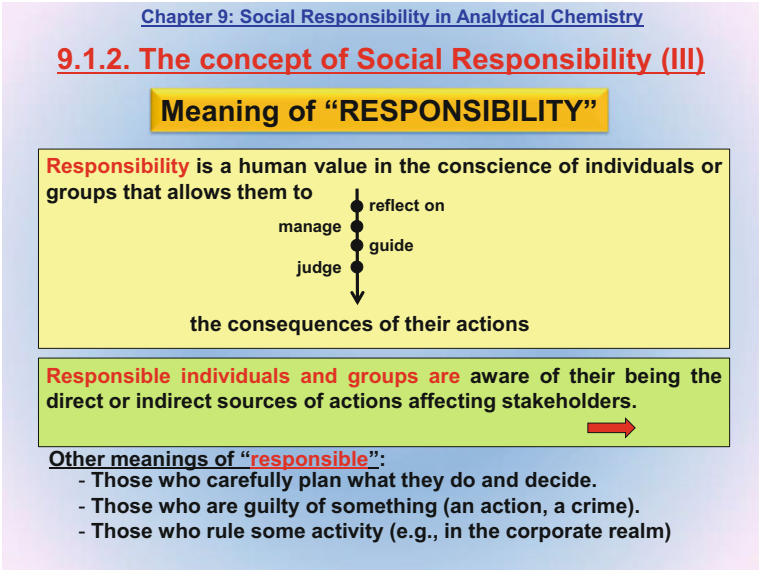
The terms *impact* (social and environmental), *ethics* and *transparency and compliance with laws and norms* are essential to fulfil SR. Although these notions are described in detail in discussing the SR principles contained in the standard (see Slide 9.12), some relatively unusual terms in it merit clarification in the following slides.

Slide 9.6



This slide illustrates the basic meaning of SR, namely: the impact on society (with provision for the present) and on the environment (looking into the future). However, dissociating the impact on society and the environment is completely unwarranted (as can be seen, the two are clearly overlapped).

Slide 9.7



This slide summarizes the meaning of "responsibility", which is an ethical value of individuals or groups allowing them to reflect on, manage, guide and judge the consequences of their actions.

Awareness and acceptance of the direct and indirect consequences of such actions on stakeholders are key elements of responsibility (see Slide 9.8).

The word "responsibility" can have other meanings depending on the particular context. The slide shows some.

Slide 9.8

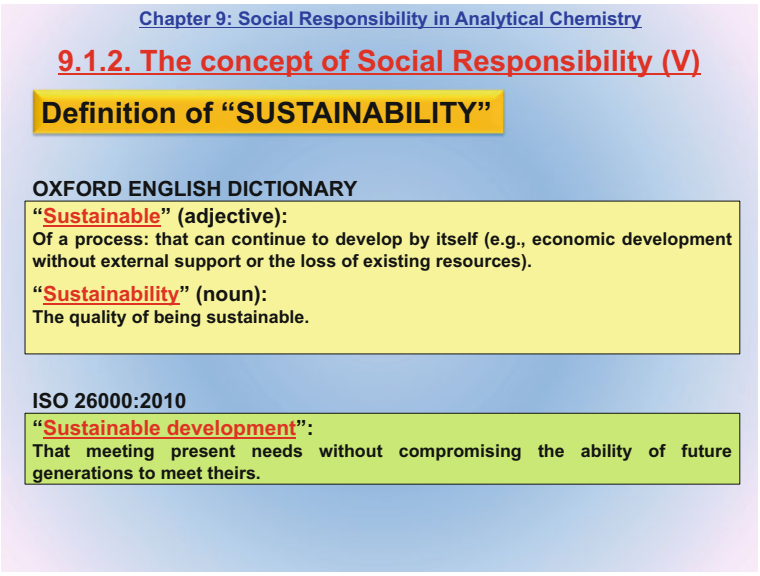
9.8.1. Stakeholders are individuals or groups receiving outputs (e.g., products, environmental pollution) from some organization (e.g., a company, a scientific or technical area). Also, they can influence the organization in some way (e.g., by compelling it to improve its products, lower its prices and/or reduce pollution).

Therefore, the activities of an individual, an organization, or a scientific or technical area have an impact on stakeholders, and stakeholders can cause such activities to be remodelled. Closing this cycle is a key to practicing Social Responsibility.

9.8.2. There are two main types of corporate stakeholders, namely:

(a) *classic* (clients, shareholders, investors, employees, financial institutions, sub-contractors); and
(b) *new* (think-tanks, social communities, partnerships, NGOs).

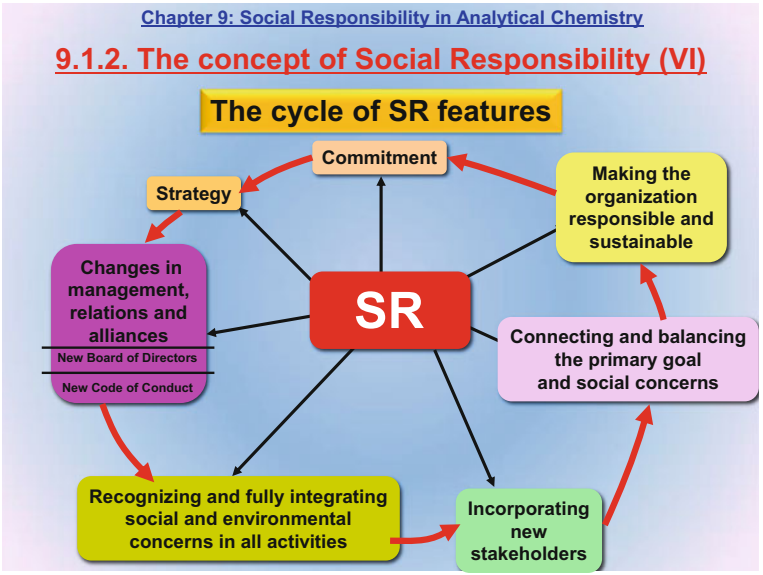
Slide 9.9



The environmental impact of SR is closely related to "sustainability", the concept illustrated in this slide.

Broadly speaking, a process is deemed sustainable if it can continue to develop by itself.

ISO standards on SR establish a direct link between sustainability and the environment.



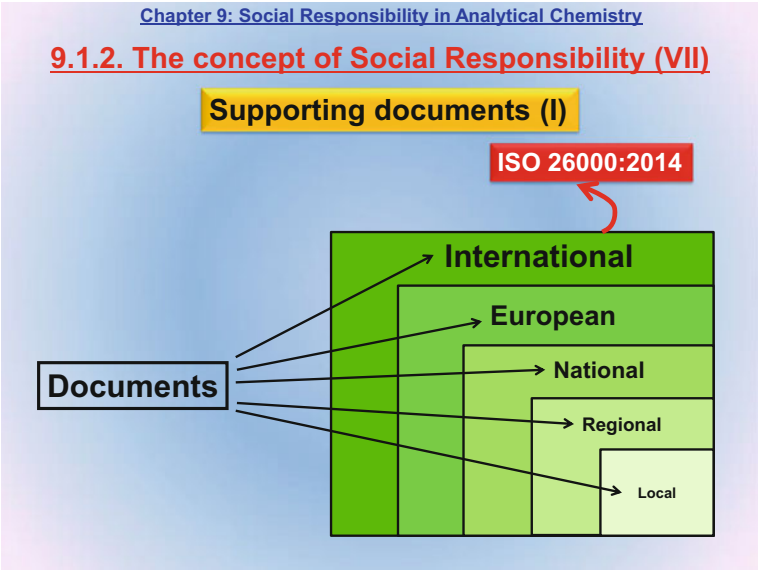
The concept cycle defining SR in an integral manner is a succession of complementary facets.

First, SR entails an explicit, written commitment to adopt a new strategy leading to substantial managerial changes in organizations or activity areas that will materialize in a new code of conduct.

Because the target activities should respond to social and environmental concerns, classic stakeholders usually need to be expanded with new stakeholders.

For an organization or activity area to be responsible and sustainable, Social Responsibility should be the link and balancing factor for its main goals, and its social and environmental concerns. This obviously requires a strong commitment that closes the SR cycle.

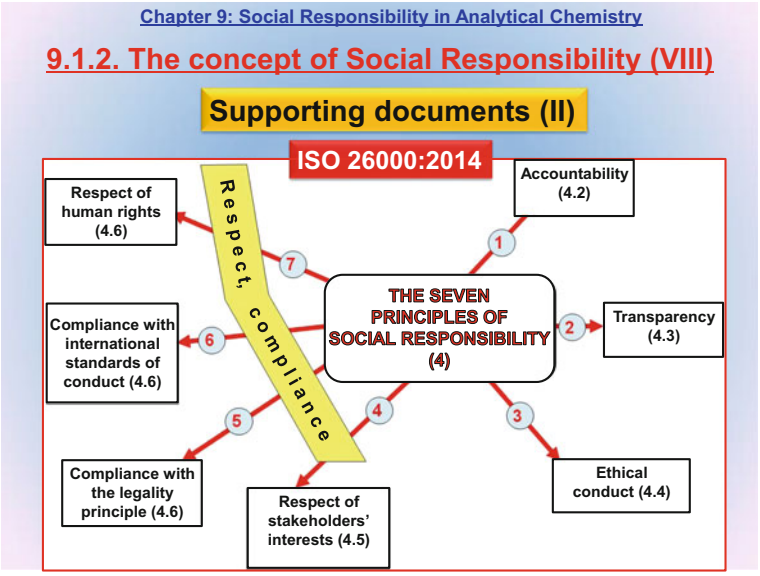
Slide 9.11



Social Responsibility has been the subject of a myriad of documents issued by local or regional councils, countries and international institutions since the turn of the century. As shown in this slide, they feed back in the opposite direction. The most widely accepted and used SR documents include ISO Guide 26000:2014 on the establishment of Social Responsibility in organizations. These documents can be considered a written standard (see Slide 1.15).

Such a vast amount of documents has no doubt facilitated adoption of SR and its practical development.

Slide 9.12



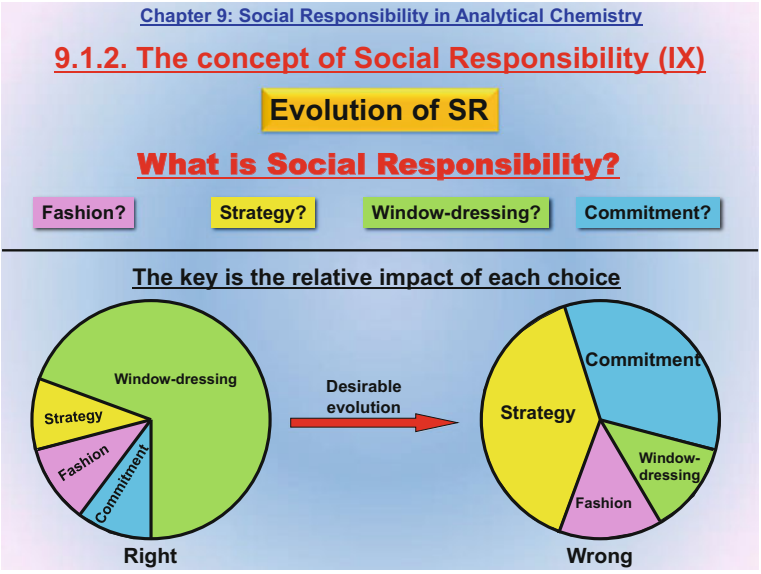
Item 4 in ISO Guide 26000:2010 lists the seven cornerstones or principles underlying Social Responsibility, which are essential in order to understand and assume the concept.

The first three principles are *accountability*, *transparency* and *ethical conduct*. Social Responsibility thus includes ethical conduct despite the reluctance of classic stakeholders to admit it. These principles are essential and go beyond the bounds of quality.

The other four principles can be merged into a single one. In fact, all share the notions respect and compliance with specific values; three such values (human rights, international standards of conduct and law) are general in scope whereas the fourth (stakeholders' interests) is specific.

Especially prominent among the seven principles is *stakeholders' integral satisfaction*, where all others converge.

Slide 9.13



9.13.1. Social Responsibility emerged momentously early in this century. Since then, advocates and critics have deemed SR a short-lived fashion;

9.13.2. a genuine strategy for improvement;

9.13.3. self-interested window-dressing; and

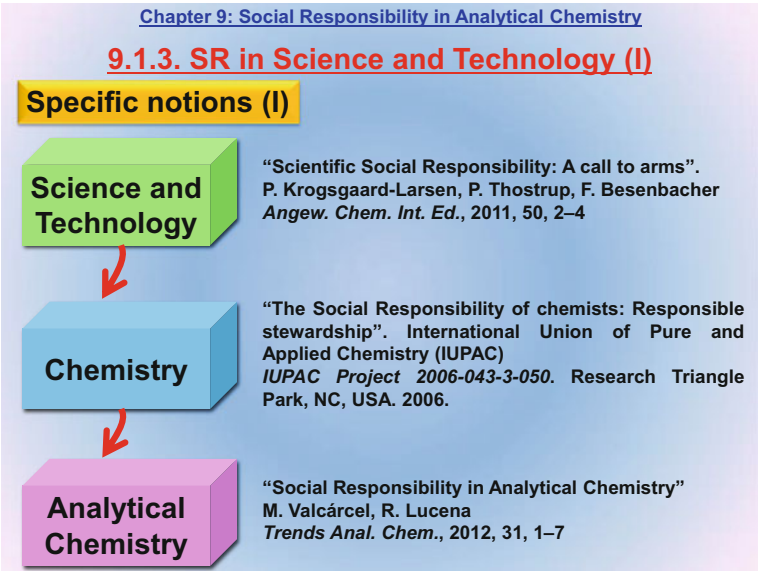
9.13.4. a commitment to society and the environment.

9.13.5. The current scenario may be distorted in the wrong direction (e.g., window-dressing and a prevalence of self-interest).

9.13.6. This situation should evolve to a prevalence of the genuine facets of SR (strategy and commitment) at the expense of "marketing" (fashion, window-dressing)—which can be a legitimate additional aim provided priority is given to strategy and commitment.

9.1.3 Social Responsibility in Science and Technology (2 Slides)

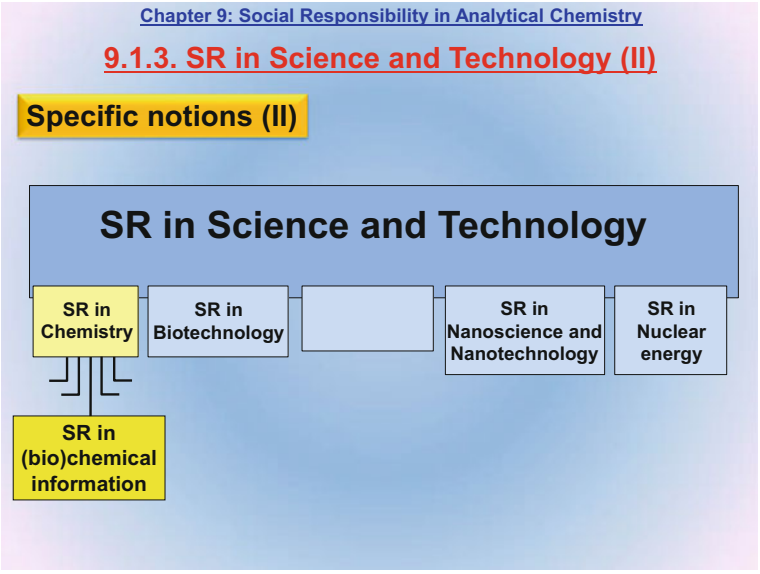
Slide 9.14



Like any human activity, scientific and technological progress through research, development and transfer (R&D&T) should not evade its Social Responsibility.

This slide shows several pieces of scientific literature showing that each step in the Science and Technology–Chemistry–Analytical Chemistry hierarchy is amenable to application of the SR concept.

Slide 9.15



The notions of slide in 9.14 are depicted schematically here. As can be seen,

9.15.1. Social Responsibility in Science and Technology…

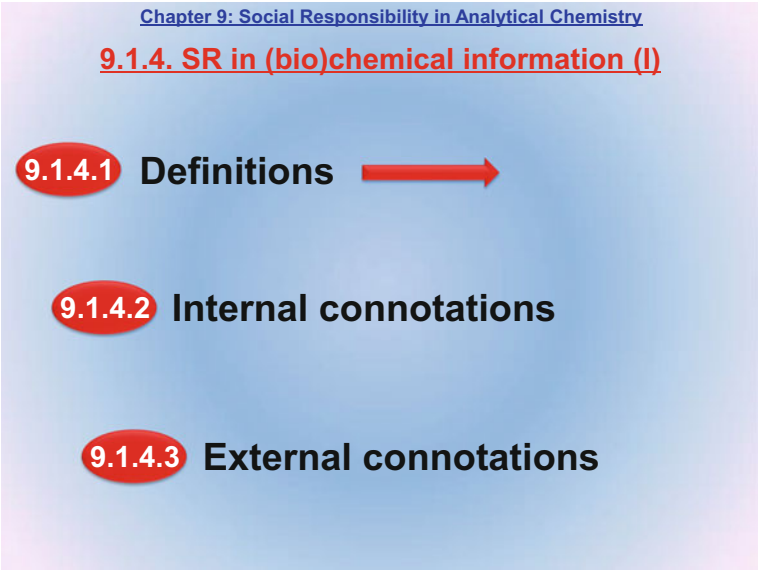
9.15.2. …comprises SR in Chemistry, Biology, Biotechnology, Nanotechnology, and many other scientific and technical areas.

9.15.3. In turn, Social Responsibility in Chemistry encompasses its various disciplines including Analytical Chemistry, where SR reaches (bio)chemical information.

9.1.4 Social Responsibility in (Bio)Chemical Information (36 Slides)

9.1.4.1 Definition and Contextualization (8 Slides)

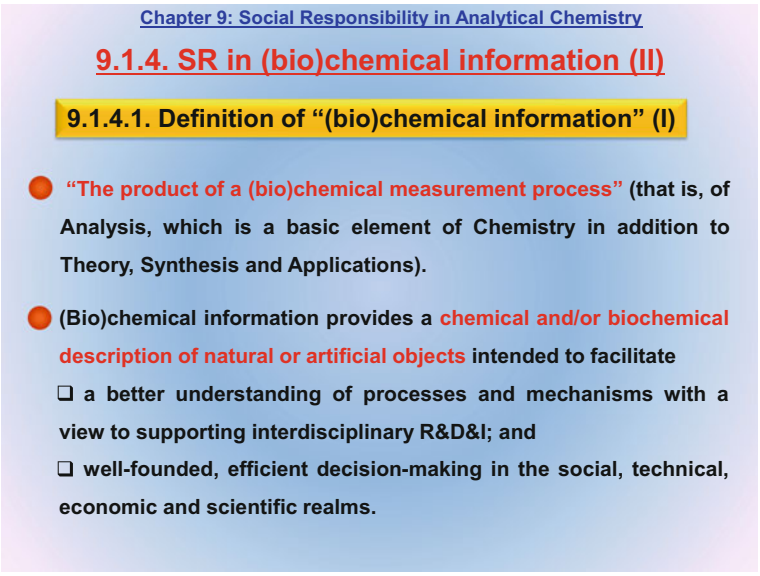
Slide 9.16



The fourth, last section of this chapter describes Social Responsibility in (bio)chemical information, which is the main output of Analytical Chemistry. Consequently, SR in (bio)chemical information is equivalent to SR in Analytical Chemistry.

The definition of (bio)chemical information and its Social Responsibility in Sect. 9.1.4 is followed by a description of its internal and external connotations (Sects. 9.1.4.1 and 9.1.4.2, respectively), which are indispensable with a view to approaching SR in Analytical Chemistry in an integral manner.

Slide 9.17



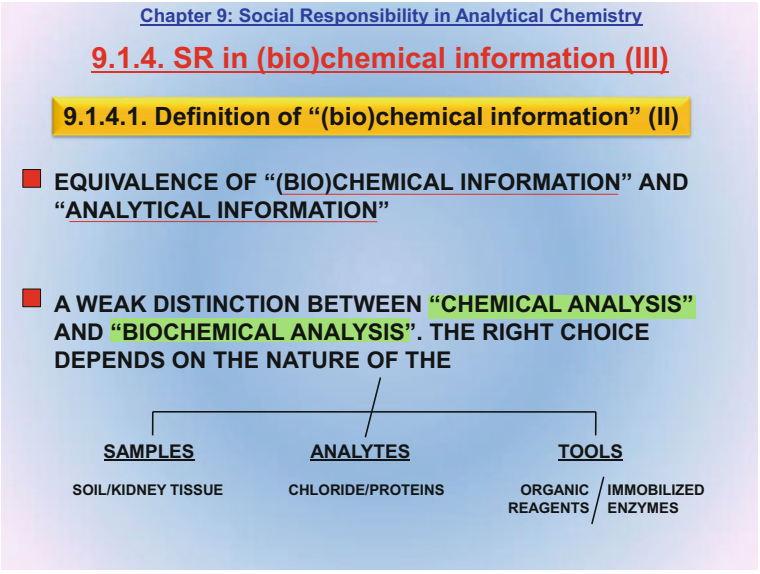
9.17.1. The concept of (bio)chemical information is explained broadly in Chap. 1. This is the third basic component of Chemistry and the "output" of (bio)chemical measurement processes (that is, of the "Analysis" of objects and systems).

9.17.2. (Bio)chemical information constitutes the chemical or biochemical description of natural or artificial objects or systems for two general purposes, namely:

- acquiring a better understanding of the processes and mechanisms, whether chemical or otherwise, involved in research, development and transfer activities; or
- making well-grounded, timely decisions in the social, technical, economic or scientific realm.

This definition is enriched with enlightening nuances in the following two slides.

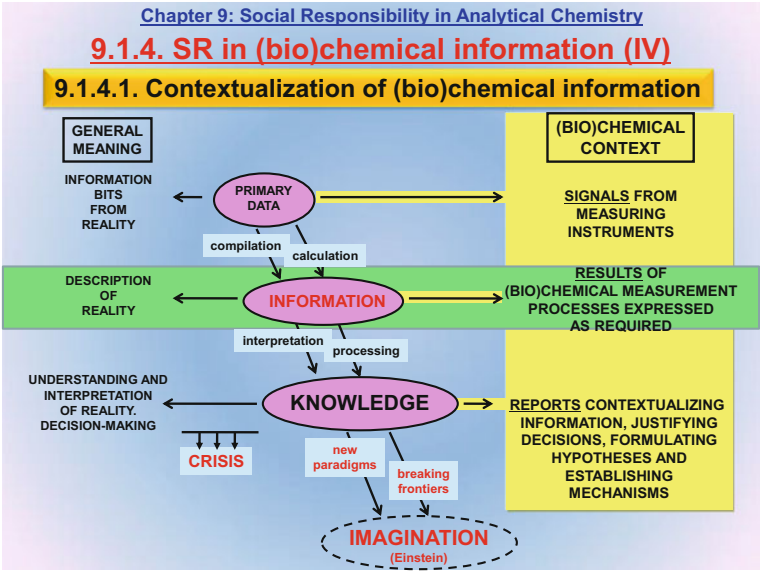
Slide 9.18



"(Bio)chemical information" and "analytical information" are two equivalent terms. In this book, *(bio)chemical information* is used for simplicity to refer to both chemical information (e.g., the concentration of a banned adulterant in a soft drink) and biochemical information (e.g., the total protein content of blood serum).

The difference between "chemical analysis" and "biochemical analysis" is not categorical either. Thus, the designation of choice in each case depends on the nature of the samples (e.g., waste water, spinal marrow), analytes (e.g., iron, an enzyme) and analytical tools (e.g., inorganic reagents, immobilized enzymes).

Slide 9.19



9.19.1. Dealing with "information" in isolation in this hierarchy, which is also shown in Slide 1.20, makes no sense. In fact, information (a description of reality) is obtained by compiling raw (primary) data (that is, information components of reality).

Processing and interpreting information produces "knowledge" (an understanding and interpretation of reality that facilitates decision-making).

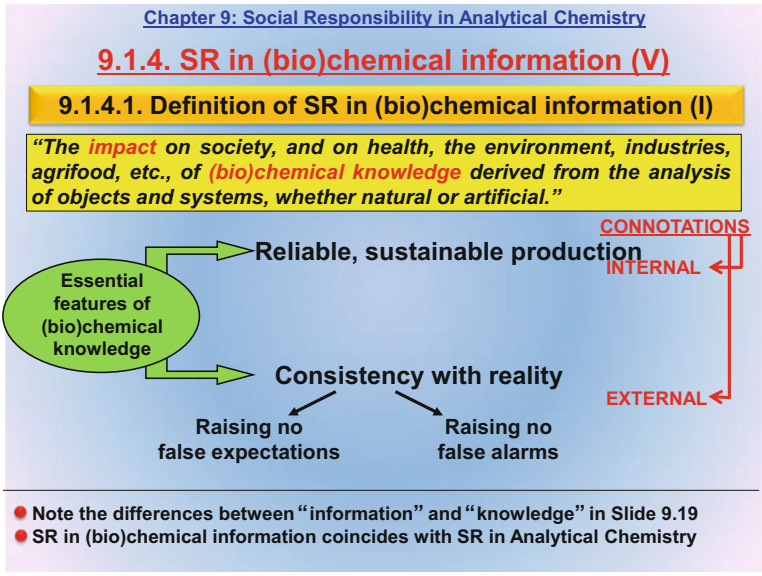
According to Einstein, in critical times where knowledge does not suffice, humans must create new paradigms and cross boundaries between scientific and technical areas (interdisciplinarity) to reach "imagination" (or its etymological equivalent, "innovation").

9.19.2. This ranking is easily adapted to the (bio)chemical context. Thus,

- "signals" from measuring instruments are "primary data";
- "results" of measurement processes, expressed as required by the clients, constitute "information"; and
- "reports", equivalent to "knowledge", help to contextualize information, make decisions, formulate hypotheses and elucidate mechanisms.

Analytical Chemistry is not impervious to crises arising from a variety of situations such as new information requirements in unusual settings. One case in point is information from the Nanoworld, extraction of which poses a great challenge that can only be met by leaving traditional physico–chemical concepts behind and approaching problems in a multidisciplinary manner.

Slide 9.20



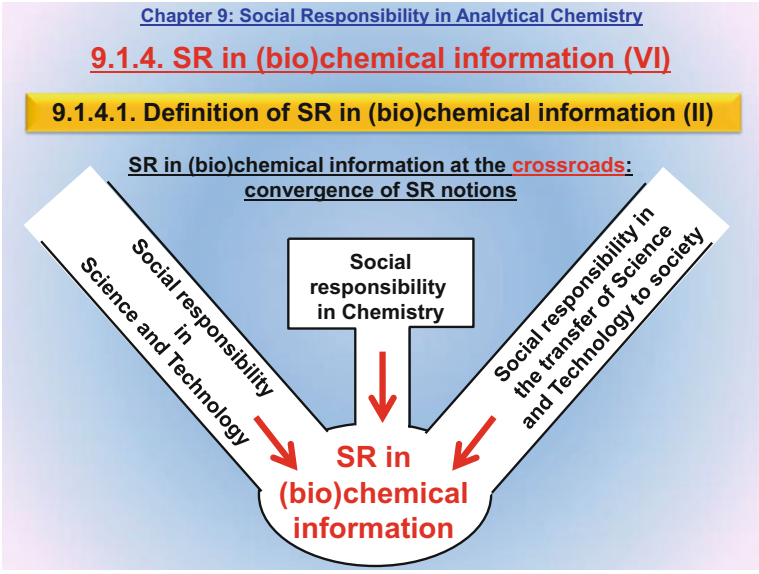
9.20.1. Social Responsibility (SR) in (bio)chemical information, which is equivalent to SR in Analytical Chemistry, is defined here as the social and environmental impact of (bio)chemical knowledge derived from the information (output) provided by analytical processes applied to natural or artificial objects and systems.

One should bear in mind here the differences between "information" (results) and "knowledge" (reports) established in the previous slide.

9.20.2. The Social Responsibility of Analytical Chemistry comprises

- internal connotations (the reliable, sustainable production of knowledge); and
- external connotations (ensuring that delivered knowledge is fully consistent with reality).

Slide 9.21



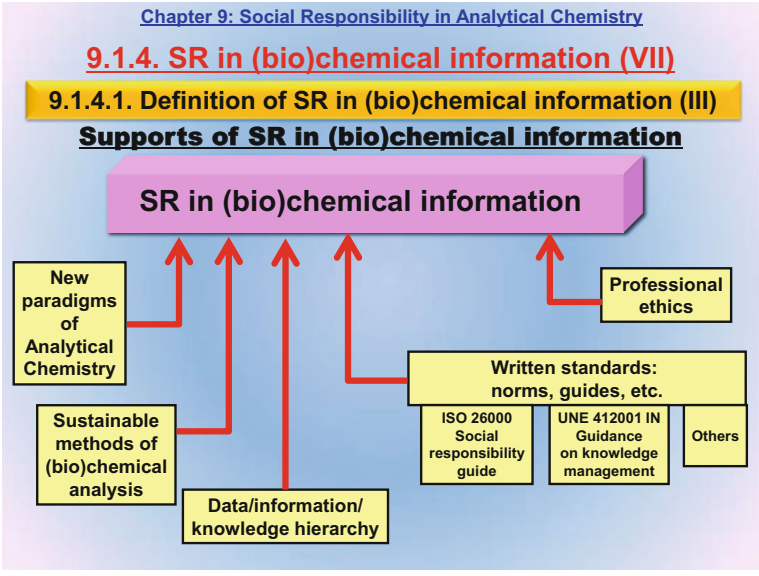
9.21.1. Social Responsibility in (bio)chemical information is at the crossroads of three converging concepts, namely:

9.21.2. SR in Science and Technology;

9.21.3. SR in Chemistry; and

9.21.4. SR in the transfer of scientific and technological outputs to society.

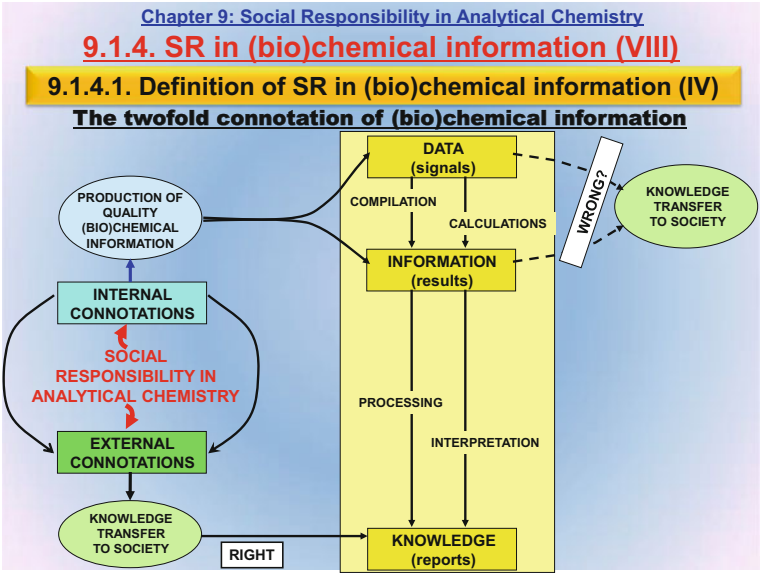
Slide 9.22



Social Responsibility in (bio)chemical information rests on the following five cornerstones:

- a contemporary view of Analytical Chemistry and its new paradigms that has inspired the contents of this book;
- sustainable (green) methods of (bio)chemical analysis (see Slide 9.26);
- the data–information–knowledge–imagination hierarchy explained in Slide 9.19;
- written standards such as the ISO Guide to Social Responsibility and Knowledge Management, among others; and
- professional ethics in the information producer and receiver.

Slide 9.23



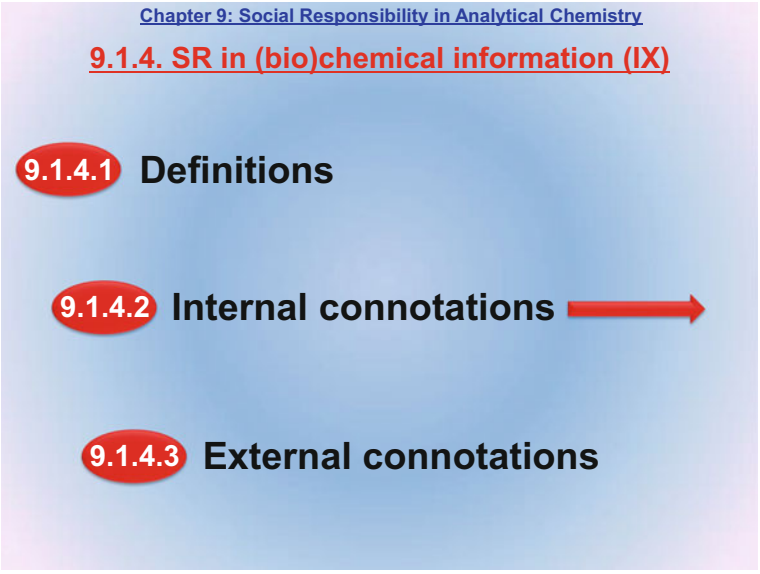
9.23.1. This slide illustrates the twofold connotation of Social Responsibility in (bio)chemical information with the data–information–knowledge hierarchy (see Slide 9.19).

9.23.2. Social Responsibility in Analytical Chemistry, and hence SR in (bio)-chemical information, has internal and external connotations.

9.23.3. The internal connotations materialize in the production of data and information, which, as shown below, can be correctly or incorrectly transferred to society.

9.23.4. The external connotations revolve around the transfer of knowledge in the form of reports contextualizing and interpreting the information produced by a laboratory to be delivered to society.

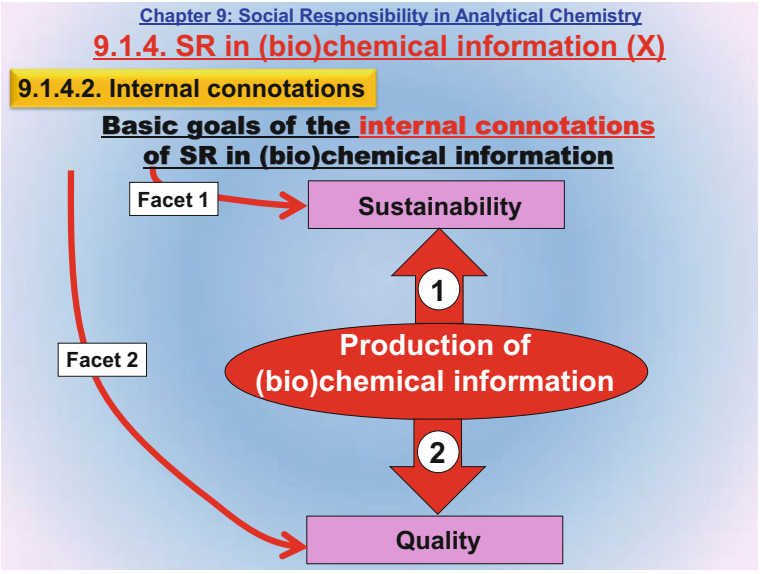
Slide 9.24



The following five slides discuss the internal connotations of Social Responsibility in (bio)chemical information derived by compiling data produced by a laboratory (e.g., instrument measurements) or processing data obtained on-site (e.g., by monitoring water in a river with a remote pH sensor continuously sending readings to the laboratory).

9.1.4.2 Internal Connotations (6 Slides)

Slide 9.25

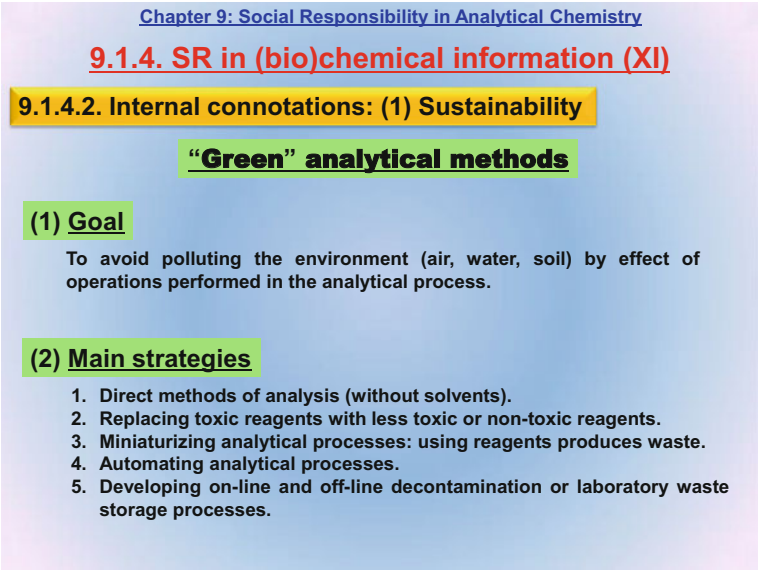


9.25.1. The internal connotations of Social Responsibility in (bio)chemical information are related to its production and materialize in reaching two different goals.

9.25.2. One goal (Facet 1) is the sustainable production of (bio)chemical information, which entails avoiding personnel hazards and environmental pollution (e.g., from laboratory waste).

9.25.3. The other goal (Facet 2) is to ensure quality in the (bio)chemical information produced, which requires ensuring that it is consistent with the (bio)-chemical reality to be described and fulfilling the client's needs (e.g., expeditious delivery).

Slide 9.26



Sustainability in the production of (bio)chemical information has been sought by developing so-called *green analytical methods*, which have been the result of much analytical chemical research.

Green methods are intended to reduce air, water, soil and animal pollution by effect of analytical processes.

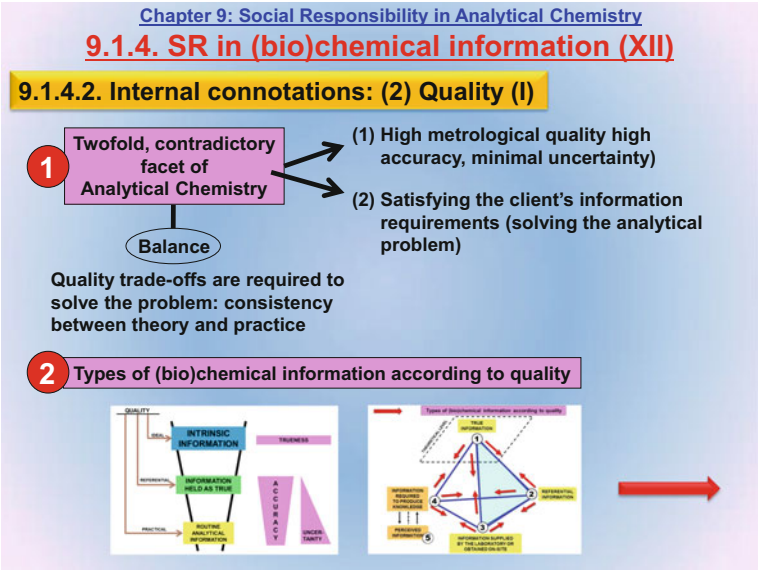
The following are obvious poor laboratory practices:

- Directly releasing organic or inorganic volatiles formed during an analytical process to the atmosphere or simply not avoiding exposure of laboratory staff to their vapours as a result of not complying with occupational risk prevention regulations.
- Disposing of organic or inorganic solvents or reagents such as sulphuric, nitric or hydrochloric acid through laboratory sinks, thus severely contaminating urban waste water. The applicable Good Laboratory Practice in developed countries compels that hazardous waste should be properly stored in the laboratory for periodic collection by waste handling companies.

Green methods can be implemented in various ways with a view to minimizing the negative impact of analytical processes on staff health and the environment the most salient of which are as follows:

- Simplifying the analytical process by using direct analyses involving no intermediate operations in order to considerably reduce or even completely dispense with the use of potentially polluting solvents and reagents.
- Replacing traditional toxic reagents (e.g., mercury-based compounds) with safer alternatives.
- Downscaling (miniaturizing) the analytical process to minimize use of potentially hazardous solvents and reagents.
- Partially or completely automating the analytical process in order to decrease staff risks by reducing human involvement.
- Developing effective laboratory decontamination procedures to be performed on-line (as part of the analytical process) or off.

Slide 9.27



The second internal facet of SR in (bio)analytical information has to do with analytical quality (Chap. 8).

One should bear in mind the contradictory relationship between the two main goals of Analytical Chemistry (see Chap. 1, Slides 1.8 and 1.9), namely:

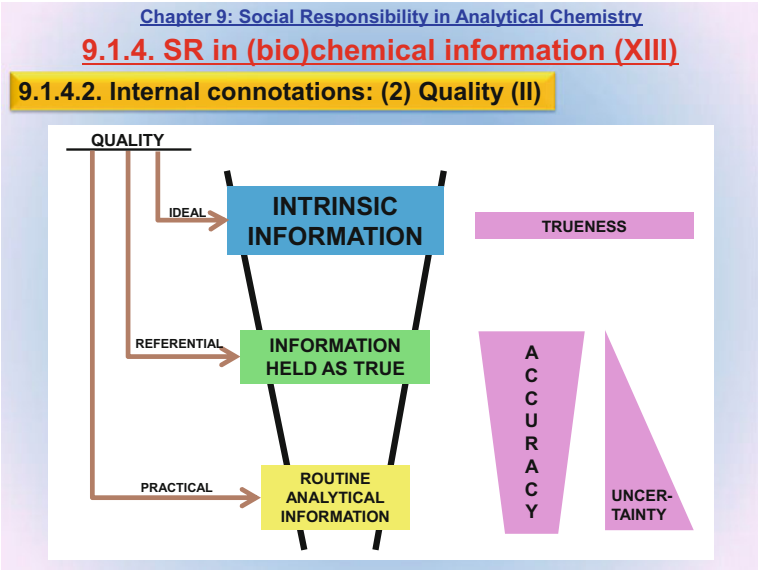
(1) to maximize the accuracy and minimize the specific uncertainty of results; and
(2) to fulfil information requirements (that is, to solve analytical problems) (Chap. 7).

Both goals are discussed in Slide 1.9.

In some cases, information requirements must be met within a short time or at a low cost and hence in contradiction with the first goal. As a result, analytical chemists are permanently confronted with the need to adopt "quality trade-offs".

(Bio)chemical information can be classified in the two ways explained in Slides 9.28 and 9.29.

Slide 9.28

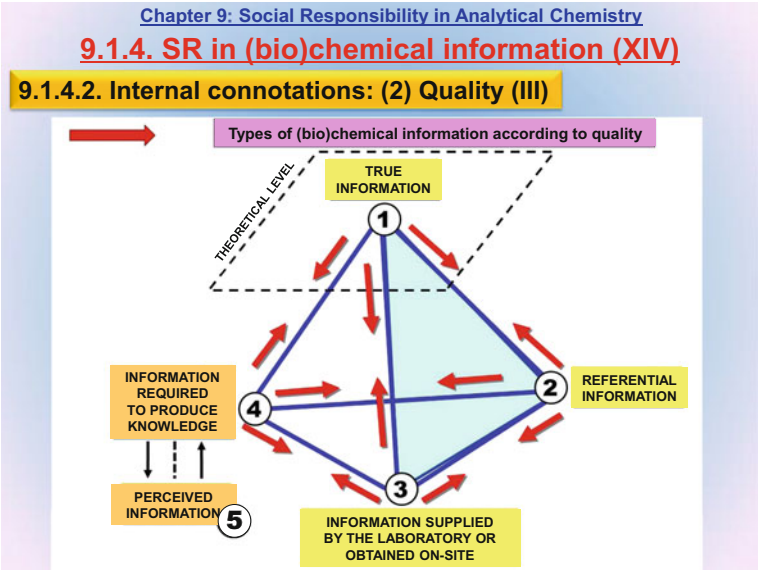


There are three different types of (bio)chemical information according to quality, namely: ideal, referential and practical, which correspond to true (intrinsic) information, information held as true and routine information. This scheme is also present in Slide 1.17.

The ideal notion of trueness corresponds to true or intrinsic information about objects or systems. On the other hand, information held as true is associated to a certified reference material (CRM) and routine information is laboratory-produced information.

In this hierarchy, accuracy decreases with decreasing quality from intrinsic information (absolute accuracy). Conversely, uncertainty increases with decreasing information quality and is lowest in intrinsic information (zero uncertainty).

Slide 9.29



This quality ranking of analytical information supplements that in the previous slide and introduces two additional quality-related concepts. One can therefore define five different quality concepts (1–5), namely:

(1) True (ideal) information about analysed objects and systems, which is purely theoretical because it is inaccessible to humans.
(2) Referential information, which is that usable in practice. This is the type of information extracted from CRMs. Unfortunately, referential information is not easy to obtain owing to the high cost of CRMs and their scarcity (only about 5% of current needs in this respect are estimated to be fulfilled).
(3) Information derived from laboratory (e.g., instrument signals) or on-site acquired data.

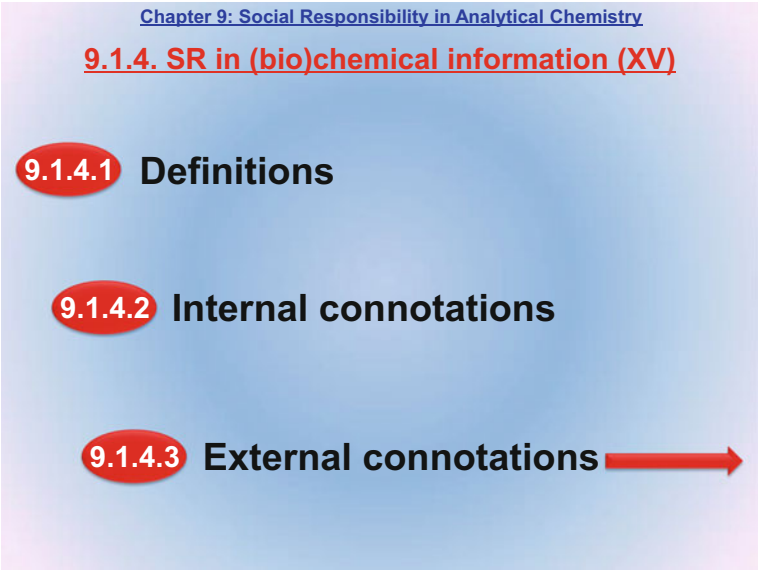
These three notions of quality in (bio)chemical information can be placed at the vertices of the triangle shown in the previous slide.

(4) The information to be delivered so that clients can obtain the knowledge needed to meet their information requirements is another quality concept. Although it falls outside the scope of the laboratory, analytical chemists remain responsible for cooperating with clients in order to properly understand what they need from the laboratory.
(5) Finally, the client's perceived quality in the information received is very important but rarely considered. Although the relationship of perceived

information to required information is especially important, it is beyond the scope of this book.

The tetrahedron outlines the contradictory and complementary binary and ternary relationships between the four basic types of (bio)chemical information. A detailed discussion of such relationships is also beyond the scope of this book, however.

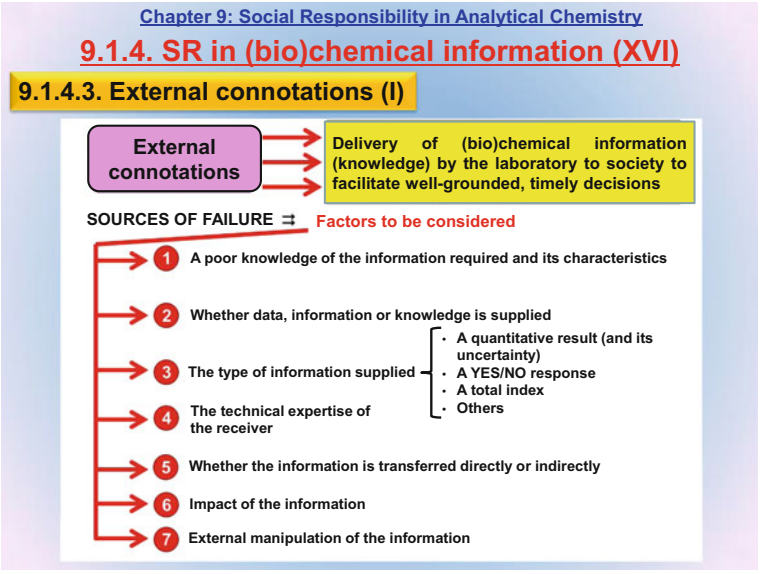
Slide 9.30



Slides 9.31 to 9.44 describe the relevant external connotations of Social Responsibility in (bio)chemical information.

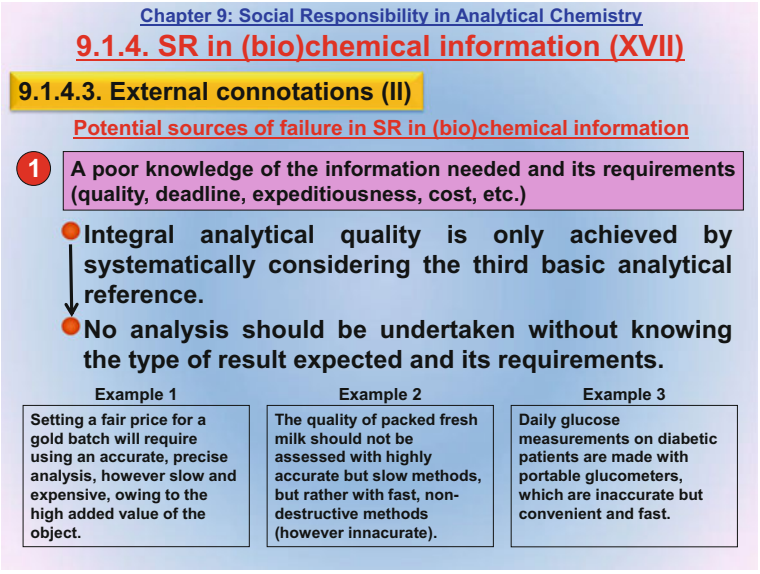
9.1.4.3 External Connotations (15 Slides)

Slide 9.31



The external connotations of SR in (bio)chemical information materialize in its correct transfer to society in order to facilitate well-grounded, timely, cost-effective decisions. Unfortunately, the transfer can fail for a number of reasons. Seven of the most common are depicted in this slide and described in detail in the next few.

Slide 9.32



The most common sources of failure in the transfer of (bio)chemical information from the laboratory to society include the following:

(1) poor communication with the client;
(2) an inordinate interest in achieving analytical quality, which is incompatible with laziness or carelessness in either party; and
(3) adhering to a strict protocol which does not cater for the specific needs of the client.

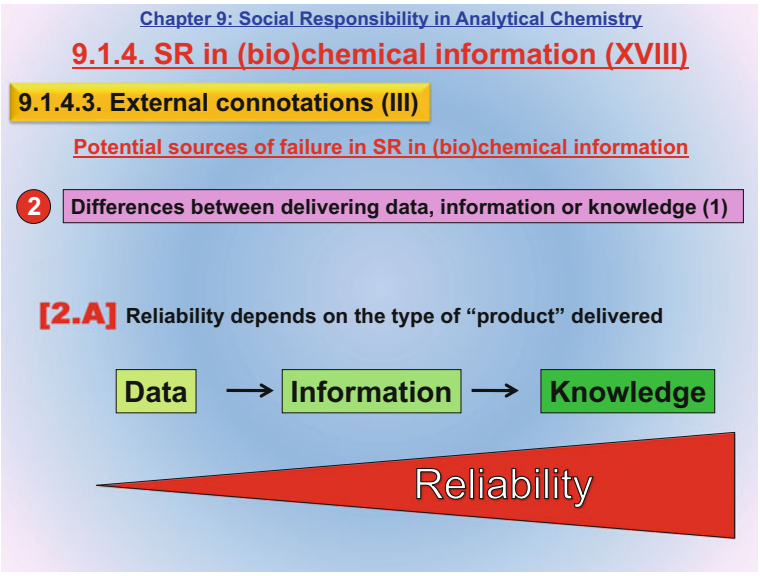
As shown in Slide 1.12, integral analytical quality rests on unconditional acceptance of the basic standard (information requirements) in addition to classic tangible (e.g., potassium hydrogen phthalate) and intangible standards (e.g., official methods, ISO norms).

In summary, the analytical process should be designed in such a way as to ensure obtainment of the (bio)chemical information required, albeit with provision for additional but also important factors (see Slide 4.6).

This slide uses three examples to illustrate how the choice of the analytical process is dictated by the characteristics of the particular (bio)chemical information to be derived (e.g., the gold content of a batch, the quality of packaged milk and the glucose concentration of blood from a diabetic patient).

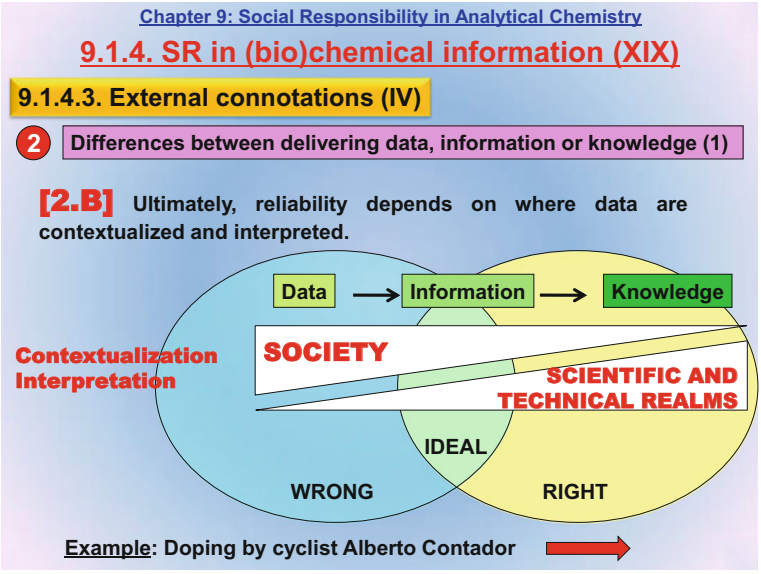
Example 1 requires maximizing accuracy, whereas Examples 2 and 3 require favouring the productivity-related analytical property expeditiousness at the expense of accuracy (see Slide 2.57 in Chap. 2).

Slide 9.33



The second major source of error in transferring (bio)chemical information to society arises from what the laboratory actually delivers (2A). In fact, supplying signals (data), results (information) or reports containing contextualized information (knowledge) is not the same. As shown here and in Slide 9.19, reliability increases from data to knowledge.

Slide 9.34



9.34.1. One additional, consequential source of distortion in the transfer of (bio)chemical information (2B) is where the information is contextualized and interpreted: society, or a scientific and/or technical area.

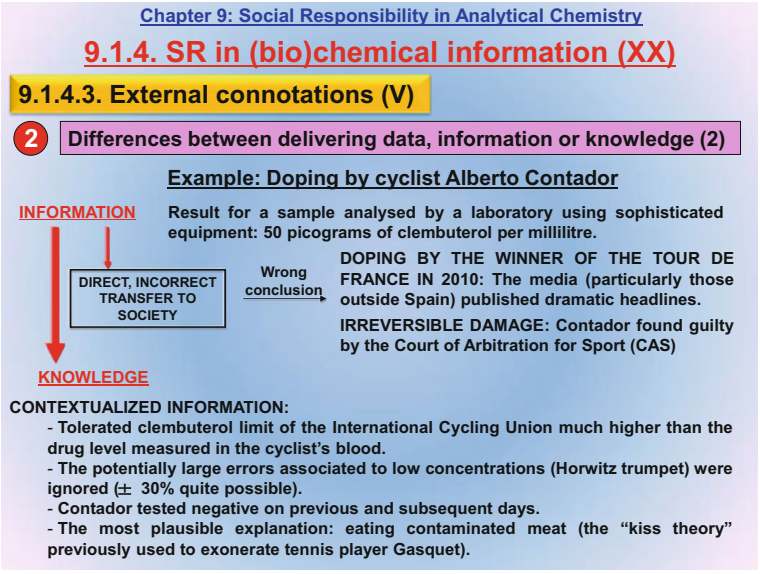
9.34.2. It is utterly wrong to directly deliver uninterpreted data (instrument signals) to society because most individuals lack the knowledge and training required to interpret them in a correct manner.

9.34.3. (Bio)chemical information should therefore be interpreted and knowledge in the analytical chemical realm produced by cooperating with other scientific and technical stakeholders.

Ideally, information should be contextualized and interpreted by scientists in collaboration with society.

9.34.4. The next slide illustrates the significance of who or where (bio)chemical information is converted into knowledge with the paradigmatic case of the alleged doping by cyclist Alberto Contador during the *Tour de France* in 2010.

Slide 9.35

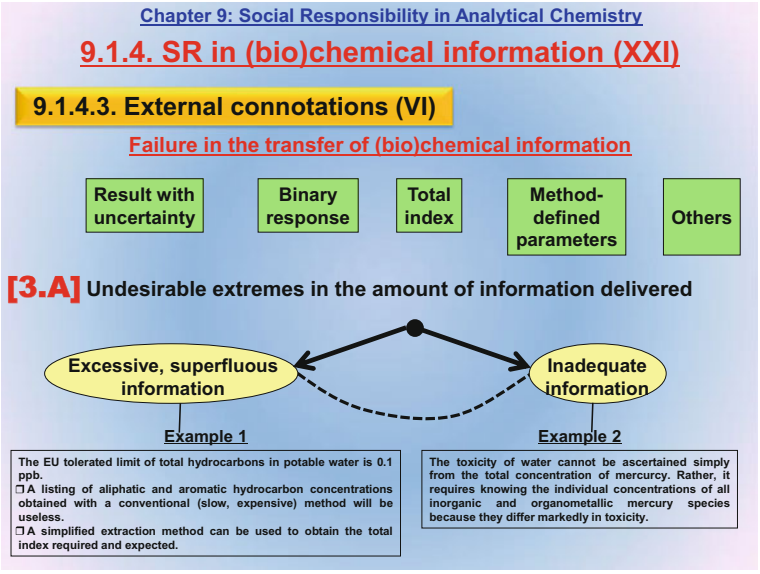


9.35.1. While taking part in the Tour de France 2010, Alberto Contador was charged with drug abuse because his blood was found to contain a very small amount of clembuterol as determined with sophisticated equipment only affordable by a few elite laboratories in the world at the time.

Directly transferring the result (information) to society led to the following unanimous interpretation outside Spain: Contador took drugs on a resting day during the race. The media published abusive headlines that inflicted serious moral damage on the cyclist and "compelled" the Court of Arbitration for Sport (CAS), based in Switzerland and also known as the "Tribunal Arbitral du Sport" (TAS) in French, to declare him guilty of doping. Directly delivering analytical information to society can thus have disastrous consequences (see Slide 9.23); in fact, the interpretation of an analytical result cannot be left to society at large or the media.

9.35.2. Had the analytical information been properly contextualized and interpreted in a report—which is what society should in fact have been delivered—society would have known that the clembuterol concentration found in Contador's blood was below the International Cycling Union's tolerated limit, that very low concentrations are typically subject to very large errors, that the analysis was not replicated and that Contador tested negative for drugs on the previous and subsequent days. Most probably, the presence of clembuterol was the result of the cyclist eating meat contaminated with this anabolic steroid (the analyte). Previously, French tennis player Richard Gasquet was exonerated of doping charges because he pleaded that the cocaine found in his blood was due to his kissing her partner, who was an addict at the time.

Slide 9.36



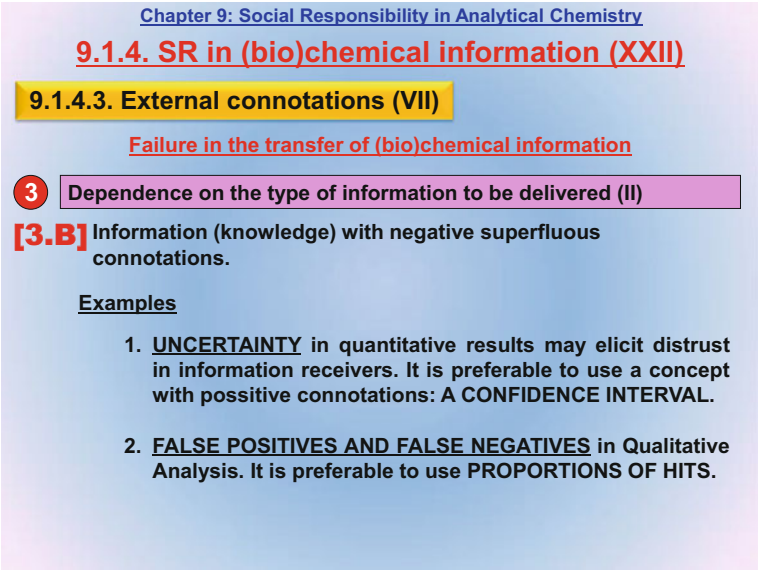
9.36.1. The third major source of failure in transferring information to society has to do with the type of result (information) transferred, which may be a quantitative datum with its associated specific uncertainty (Chap. 2), a YES/NO qualitative response (Chap. 6) or a special form of information not dealt with in this book such as a global index for the total amount of members of an analyte family (e.g., total polyphenols in wine, total dioxins in ash) or a parameter (result) associated to the particular method used (e.g., soil extraction, where the specific ions extracted will depend critically on the leaching solution used).

There follow three different frequent situations that can be easily avoided.

9.36.2. The first (3.A) occurs when the information delivered is either excessive or deficient.

Delivering too much information (e.g., individual hydrocarbon concentrations when a total index would have sufficed) makes the process unduly costly and time-consuming; also, it can lead to the actual question (e.g., whether the total concentration sought complies with applicable legal limits) remaining unanswered. Similarly, delivering inadequate information (e.g., the total concentration of mercury in polluted water) may also leave the primary question (e.g., whether a river has been contaminated by mercury spillage) unanswered as a result of the actually required information (the presence and concentration of various mercury species differing markedly in toxicity such as Hg^{2+}, methyl-mercury and phenyl-mercury, for example) not being supplied.

Slide 9.37

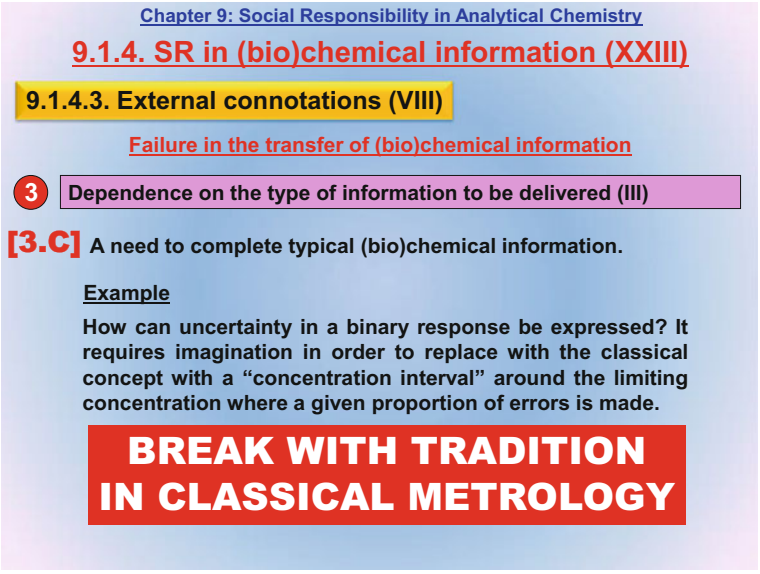


The second situation (3.B) occurs when the information delivered possesses unnecessary negative connotations that may lead a receiver with inadequate scientific and technical knowledge to spurious conclusions (see Slider 9.39).

Thus, the *specific uncertainty* that should accompany a quantitative result can be taken to be the laboratory's degree of distrust in the information it is delivering. In the realm of Chemical Metrology, specific uncertainty can be replaced with a *confidence interval*; technically, the interval has the same meaning but is much easier to interpret by non-experts.

This is also the case with Qualitative Analysis (Chap. 6), where expressing reliability (a combination of accuracy and precision) in the form of false positives and false negatives can leave a bad impression on the information receiver. Why not replace them with the "proportion of hits" in the YES/NO binary response, which is one other way of defining reliability? Providing they retain some scientific and technical rigour, the results should be expressed in forms bearing positive connotations in order to boost the client's confidence in the delivering laboratory.

Slide 9.38

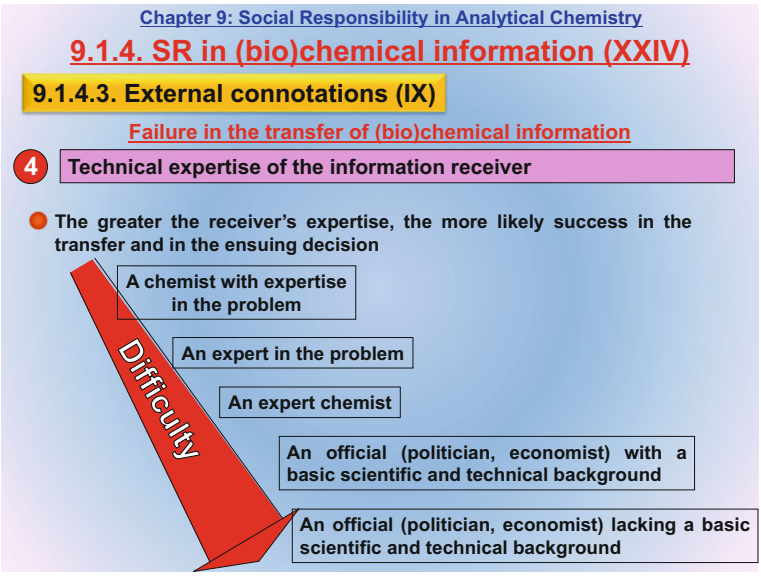


9.38.1. In the third situation (3.C), the information transferred is inadequate and should be completed.

Such is the case with uncertainty in the YES/NO binary response in Qualitative Analysis. How can an interval around a YES/NO response be expressed in familiar terms? This obviously entails replacing established knowledge with imagination (see Slide 9.9) to conceive new concepts such as the concentration range around a limiting concentration at which an acceptable proportion of errors in terms of a statistical probability level can be expected.

9.38.2. This example illustrates the need to break with tradition in Classical Metrology whenever required to solve a specific analytical problem (see Slide 7.12, Sect. 7.4).

Slide 9.39

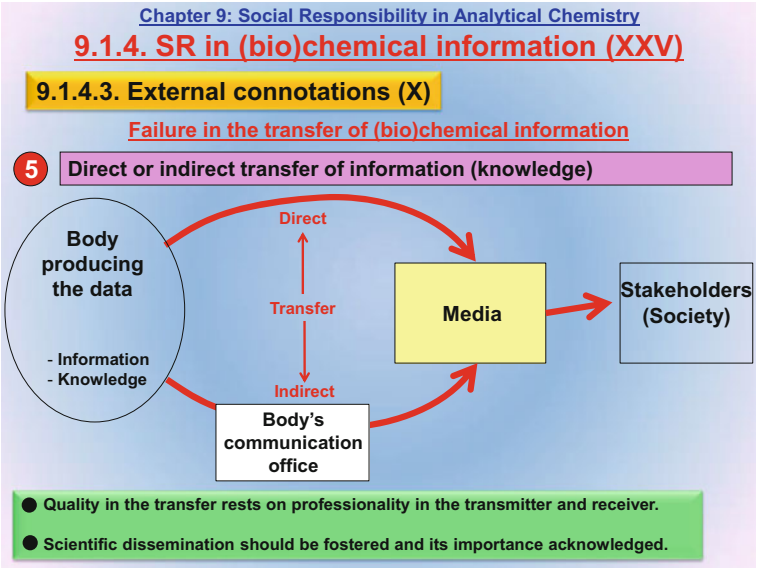


The nature of the receiver is crucial for correct transfer and interpretation of (bio)chemical information from a laboratory. The greater the receiver's experience is the more likely will be correctly understanding the information delivered.

The difficulty increases from a receiver being a scientist (e.g., an analytical chemist) with experience in the type of problem addressed to a judge, politician or corporate executive with no scientific or technical background. The slide shows various situations in between these two extremes.

As the difficulty grows, the results (information) should be converted into increasingly well documented reports.

Slide 9.40



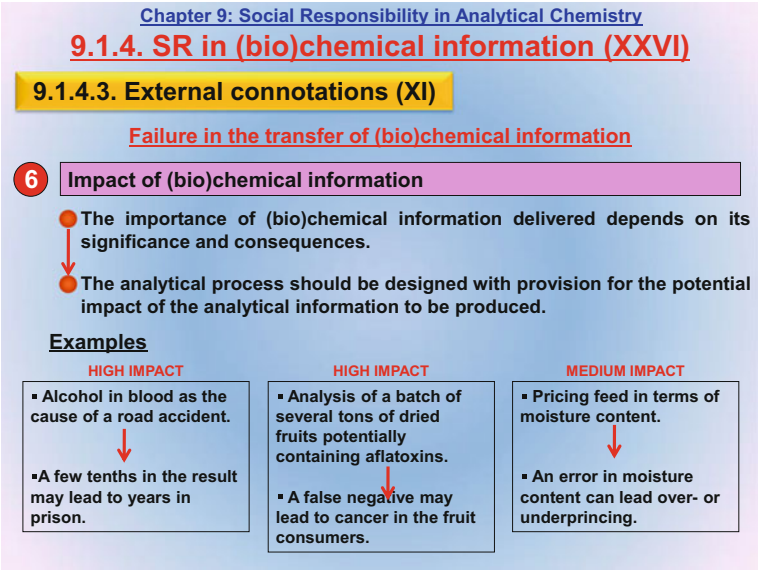
9.40.1. The fifth source of distortion in the transfer of (bio)chemical information is its direct or indirect nature.

In direct transfers, the laboratory's parent body—or the laboratory itself if entitled—issues not only results, but also reports for the media to be conveyed to society. Obviously, the media should disseminate the information they receive with Social Responsibility (for example, with alarming or appealing rather than factual headlines).

9.40.2. Indirect transfer can be done through the communication office of the laboratory's parent body, which should obviously act socially responsibly in order to avoid distortion of the (bio)chemical knowledge it transfers.

9.40.3. Proper transfer rests on ethical conduct in both the organs conveying the information (that is, information producers) and those receiving it (information receivers and disseminators). Also, scientific dissemination should be strongly boosted through appropriate training and recognition.

Slide 9.41



9.41.1. The potential importance and impact of (bio)chemical information transfer should always be considered.

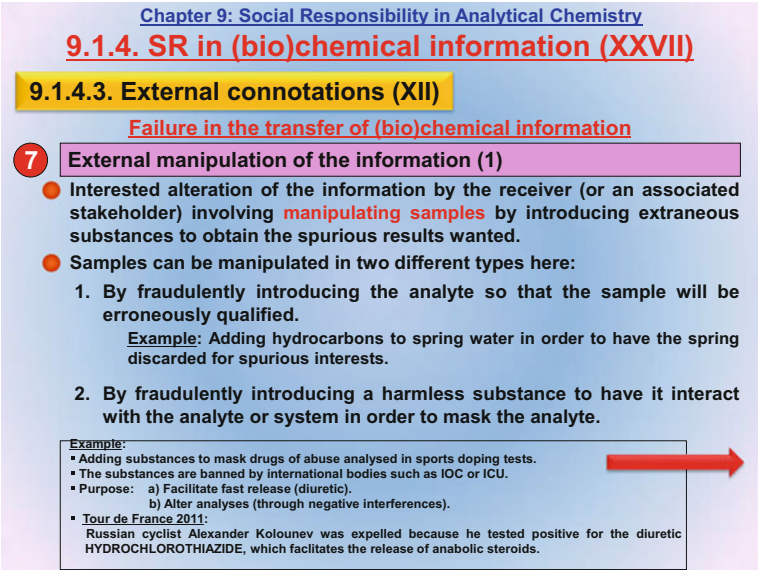
9.41.2. Thus, the analytical process should be suited to the strength of the predicted impact. This slide exemplifies three different situations.

(1) One case where (bio)chemical information can have a strong impact is the determination of alcohol in blood from individuals involved in a road or work accident. A few tenths in a result can lead to several years in prison. Also strong can be the impact of the results of a screening (qualitative) analysis of a batch of imported dried fruits potentially containing aflatoxins. A false negative (Slide 6.22) may lead to carcinogenic effects on consumers. In this situation, it is crucial to analyse the fruits with a proven, validated method.

(2) A lesser impact of (bio)chemical information is to be expected from inaccurate measurements of feed moisture; in fact, a positive or negative error can lead to the feed being under- or overpriced, respectively, but not to deleterious effects on cattle. Therefore, direct, non-destructive analysis with, for example, a near-infrared (NIR) probe can suffice to set a fair price despite the likely errors in the measurements.

(3) Finally, using an analytical method with a limit of detection well below the critical concentration (e.g., toxic level) of an analyte in a given type of sample can have little unfavourable impact on the (bio)chemical information derived.

Slide 9.42



The last source of failure in transferring (bio)chemical information is fraudulent manipulation of the target sample or system under study by the receiver prior to submission to the laboratory.

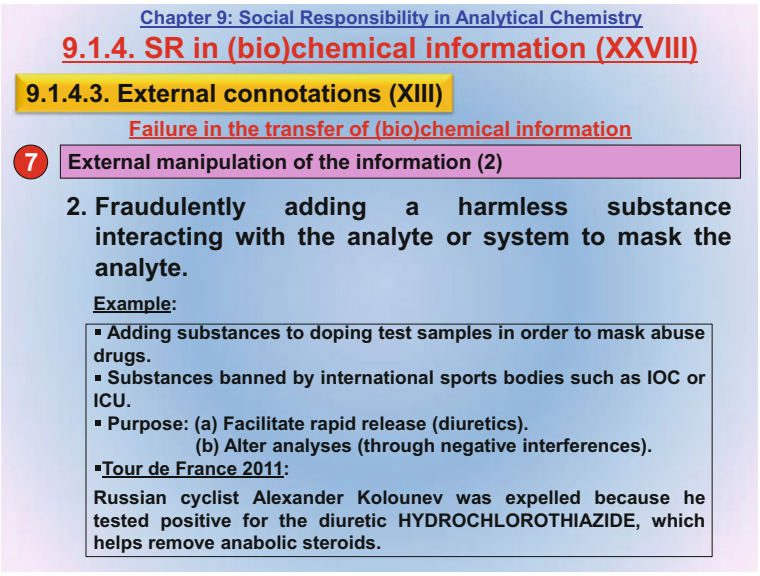
The source of error in this case is the deliberate addition of one or more substances to alter the original sample for spurious purposes—usually increasing the value of a commercial product. Obviously, the information received from the laboratory will be erroneous.

The target analyte can be added to the sample for two different purposes, namely:

1. To have its concentration exceed legally tolerated limits and the sample be incorrectly deemed toxic (e.g., deliberately adding hydrocarbons to spring water to have it discarded for spurious reasons).
2. To have an added substance interact with the analyte or its moiety in order to reduce its concentration to undetectable levels (a fraud). The slide shows a typical example of drug abuse in sports. Some bodies such as the International Olympic Committee (IOC) and the International Cycling Union (ICU) have their own lists of banned susbstances that they are not drugs.

The next slide elaborates on the second example.

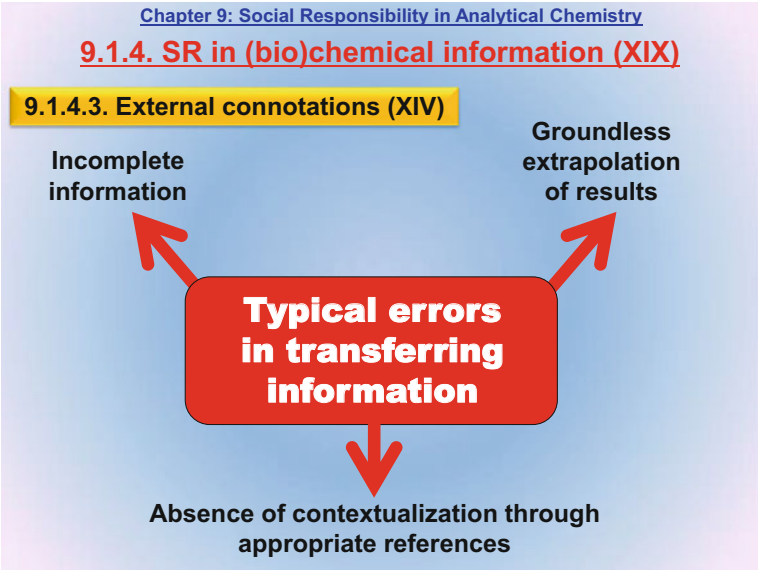
Slide 9.43



As can be seen, spuriously added substances (second example in Slide 9.42) can act in two different ways, namely:

(a) By facilitating the fast release of drugs (for example, with diuretics), as in the case of doping in the Tour de France.
(b) By introducing a negative interference with the analytical process to, for example, facilitate retention of a drug (the analyte) on a sorbent in order to avoid its detection—and potential consequences—as a result.

Slide 9.44



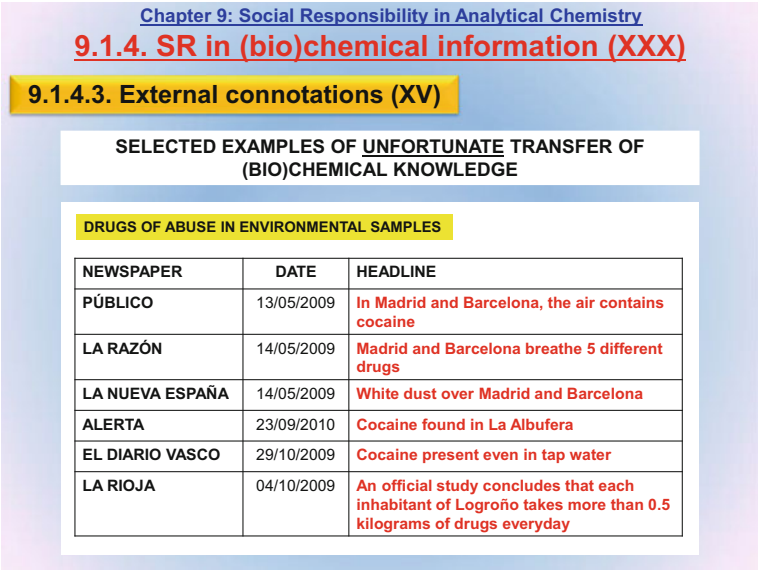
This is a brief summary of the three commonest errors in transferring (bio)-chemical information.

9.44.1. Delivering incomplete information that will lead to a wrong decision.

9.44.2. Misinterpreting results—and extrapolating them wrongly, for example.

9.44.3. Using no appropriate references to contextualize information in reports. It is knowledge rather than information or results that should be transferred.

Slide 9.45



This slide shows sensationalistic headlines published by various Spanish media that misinterpreted anecdotal results of drug determinations in air and water.

The most serious problem with the resulting alarmism was that it was caused by the communication offices of public or private bodies seeking popularity. Such offices were directly responsible for the analyses and hence for avoiding these relatively common errors in transferring (bio)chemical information given the—presumed—scientific and technical background of their members.

9.2 Annotated Suggested Readings

PAPERS

Scientific social responsibility: A call to arms

P. Krogsgaard-Larsen, P. Thostrup and F. Besenbacher

Angewandte Chemie Int., 2011, 50, 2–4.

This is a short, brave, somewhat provocative but realistic paper written by three highly renowned European scientists that emphasizes the significance of Social Responsibility in Science and Technology in the XXI century.

Social responsibility in Analytical Chemistry

M. Valcárcel and R. Lucena

Trends Anal. Chem., 2012, 31, 1–7.

This paper constitutes the backbone for the present chapter and deals with virtually all of its contents.

Teaching social responsibility in Analytical Chemistry
M. Valcárcel, G.D. Christian and R. Lucena
Analytical Chemistry, 2013, 85, 6152–6161.
This paper describes strategies for teaching Social Responsibility in Analytical Chemistry. Its contents overlap with those of this chapter.

BOOKS

Handbook of Green Analytical Chemistry
M. Guardia and S. Garrigues (Eds)
Wiley, New York, 2012.
This book discusses the first facet of the internal connotations of SR in Analytical Chemistry and available choices for making analytical laboratories sustainable.

9.3 Questions on the Topic (Answered in Annex 2)

9.1. Relate SR in Analytical Chemistry to

– analytical quality (Chap. 8); and
– analytical problem-solving (Chap. 7).

9.2. What are the keywords defining Social Responsibility? Which are especially significant because they are shared by many definitions of SR?
9.3. Define "stakeholders" in the context of SR, and of ISO guides and norms.
9.4. Describe the cycle of concepts that provides an integral definition of SR in an individual, an organization and a scientific or technical area.
9.5. Highlight four of the five principles governing SR. Which is the most important? Why?
9.6. Can marketing SR be

(a) positive?
(b) negative?
(c) neither positive nor negative?

Justify your answer.
9.7. What is the most important link in the cyclic succession of SR concepts? Why is it more important than the others?
9.8. Are the following statements true or false?

(a) Ethical principles encompass SR.
(b) Implementing SR in a scientific or technical area encompasses quality systems.
(c) For many organizations and businesses, SR is merely a window-dressing opportunity.

Justify your answers.

9.9. Why are SR in Analytical Chemistry and SR in (bio)chemical information equivalent?

9.10. What are the internal and external connotations of SR in (bio)chemical information? Are they related in any way? How?

9.11. Explain the differences between the transfer of data (signals), results (information) and reports (knowledge) to society.

9.12. Which of the three sources of distortion in the transfer of (bio)chemical information is the most important? Rank them according to significance.

9.13. Are the two internal connotations of SR in Analytical Chemistry related? Which is the more important? Why?

9.14. What is the difference between the two models of quality in (bio)chemical information (the second facet of external connotations of SR in Analytical Chemistry)?

9.15. Why can the type of information delivered be important with a view to facilitating effective communication between analytical laboratories and clients requiring information?

9.16. Can using a communication office to deliver information from a laboratory have a positive effect on the parent body? Why?

9.17. How is the choice of an analytical process dictated by the potential impact of the (bio)chemical information to be delivered?

9.18. Explain the sentence "quality in information transfer depends on both the producer and the receiver of the information". Discuss the significance of the information required by the receiver.

9.19. How important can experience in the dissemination of science be to transfer (bio)chemical information? Why?

9.20. How can SR in Analytical Chemistry be assured?

9.21. Explain the "transparency principle" supporting SR in Analytical Chemistry.

9.22. Describe the two main ways in which a sample can be tampered with in order to have it give spurious results for fraudulent purposes.

9.4 An Abridged Version of the Chapter

The contents of this chapter can be shortened by about one-half for teaching Analytical Chemistry to students not majoring in Chemistry. The slides to be omitted for this purpose are as follows:

- Section 9.1: Slide 9.3.
- Section 9.2: Slides 9.6–9.9 and 9.13.
- Section 9.3: Slides 9.14 and 9.15.
- Section 9.4: Slides 9.18, 9.19, 9.21–9.23, 9.28, 9.29, 9.44 and 9.45.

Annex 1: Glossary of Terms

Accreditation Formal written acknowledgement that a laboratory is fit and competent to perform one or more given types of analysis. Obtained by subjecting the laboratory to an audit (accreditation process) conducted by personnel external to the laboratory and its parent body.

Absolute error The difference between the value to be qualified and its reference.

Absolute method A type of calculable quantification method that uses no analytical standard.

Absolute method with analytical standards. A calculable method that uses one or more tangible analytical chemical standards.

Absolute trueness An ideal analytical feature and an attribute of chemical information inherent in the target object or sample. Corresponds to the true value

Accuracy – An ideal analytical feature and an attribute of chemical information inherent in the target object or sample. Corresponds to the true value– A capital analytical property of a result or a CMP (the opposite of bias).

Aliquot A well-defined portion (mass, volume) of a sample.

Amount An attribute of an object that can be qualitatively distinguished and quantitatively determined. Amount encompasses "measurand" and "analyte".

Analyse, to – To subject a sample to an analytical process in order to extract information about measurands or analytes.
– To interpret analytical results with a view to producing a report.

Analyser An integrated system consisting of instruments, apparatuses and devices that performs virtually the whole analytical process (CMP).

Analysis In a general sense, "analysis" involves examination, study, acquisition of knowledge to provide information about objects, facts, systems, performance and attitudes. In the chemical realm, "analysis" involves subjecting a sample to an analytical process in order to extract (bio)chemical information about it.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1

Analyte A chemical or biochemical species in a sample about which qualitative or quantitative information is required.

Analytical blank A usually artificial sample containing no analyte. In theory, a blank should give no signal if it does it is called the "blank signal".

Analytical Chemistry A metrological science that develops, optimizes and uses measurement processes intended to derive quality (bio)chemical information about natural or artificial objects or systems with a view to solving analytical problems.

Analytical error Broadly speaking, an alteration in analytical information. Analytical errors can be of the random, systematic or gross type.

Analytical fundamentals The cornerstones on which the theoretical and practical sides of Analytical Chemistry stand. Intrinsic to Analytical Chemistry or shared with other scientific and technical areas

Analytical information – Chemical characteristics of an object or system, usually ascribed to its components (analytes) or to the entity as a whole.
– The opposite of "generic uncertainty" and the primary goal of Analytical Chemistry.
Information held as true. That obtained through special testing (e.g., an interlaboratory exercise) or possessed by a CRM. Corresponds to referential quality.
Intrinsic information. That possessed by the object or system to be analysed. Corresponds to ideal quality.
Routine information. That ordinarily produced by laboratories. Corresponds to real quality.

Analytical knowledge Analytical results (information) that are discussed, compared with references, contextualized and accompanied by decision-making proposals. Analytical knowledge materializes in "analytical reports" and is thus at the highest step in the data–information–knowledge ranking.

Analytical method The body of specific operations used in the qualitative or quantitative characterization of an analyte (or analyte family) in a given sample. Entails using a technique (instrument) and is the materialization of a CMP.

Analytical problem An approach to solving the client's information needs by designing and planning a CMP, and interpreting the ensuing results.

Analytical properties Attributes ascribed to results and/or a chemical measurement process (CMP). The quality indicators of Analytical Chemistry.
Basic properties. Those that can be ascribed to a CMP and support capital properties.
Capital properties. Those that can be ascribed to results.

Productivity-related properties. Those that can be ascribed to a CMP and define laboratory productivity.

Analytical quality The degree of excellence in the chemical information supplied with a view to solving an analytical problem. Comprises four components: quality of results, quality of CMPs, quality of analytical tools and quality of work and its organization.

Analytical references Landmarks used in the comparisons inherent in analytical measurements. Can be materials (standards) or methods.

Analytical reports – The body of analytical results (data) and their interpretation in the light of the analytical problem addressed.
– The top level in the information hierarchy.

Analytical results Qualitative and/or quantitative data obtained by mathematical (chemometric) treatment of primary data produced by an instrument in the analytical process.

Analytical schemes Sequential, orderly processes that use separation methods (e.g., precipitation) in Classical Qualitative Analysis to classify species into groups where each analyte can be reliably identified.

Analytical tools Material, strategic and methodological means of varied nature on which chemical measurement processes (CMPs) rely.

Apparatus A system consisting of devices that serves a specific function in a CMP but provides no analytical information. An apparatus produces secondary data.

Applied research in Analytical Chemistry Development of analytical methods based on the "products" of basic research to extract (bio)chemical information with a view to fulfilling information demands. If no effective tool for the intended purpose exists, it must be produced through new basic research.

Audit An instance of external–external assessment conducted by specialists external to the laboratory and its parent body.

Automation Partial or total reduction of human participation in a CMP.

Avogadro's number A chemical standard defined as the number (6.023×10^{23}) of atoms or molecules contained in one mole of any chemical substance.

Balance An instrumental tool primarily used to measure the initial mass of the test sample to be subjected to a CMP or that of the weighed form in gravimetries.

Basic research in Analytical Chemistry Development of new analytical tools (e.g., reagents, solvents, equipment, sensors) and approaches for no specific purpose other than advancement of the discipline

Bias A systematic or determinate error equal to the positive or negative difference between the mean of n results and the value held as true, $\overline{X} - \widehat{X}'$, that can be ascribed to an analytical method and is related to its accuracy.

Binary response – The result (YES or NO) of a qualitative analysis.
– The answer to various questions the most crucial of which are "is it the analyte?" and "is it in the sample?"

Black sample A sample whose composition is completely unknown before analysis.

Blank signal The signal produced by a blank sample.

Blind sample A sample of well-defined composition that is interspersed for quality control purposes with those to be routinely analysed by a laboratory.

Burette An instrumental tool used to measure the volume of titrant solution used in titrations. Burettes can be manual or automatic in operation.

Calculable method One that provides results based on mathematical calculations involving both tabulated data and measurements made during the CMP. May use some or no analytical standard.

Calibration curve A two-dimensional graphical plot showing the variation of the analytical signal with the amount or concentration of analyte (standard). See also "Linear calibration graph".

Capillary electrophoresis A separation process occurring within a capillary under a high electric field. Because the system is equipped with a detector, it can be considered an instrument.

Certified reference material (CRM) A reference material with certified values (specific uncertainties included) for one or more of its properties that are obtained by special procedures (e.g., interlaboratory exercises) under the supervision of a competent, independent body. A CRM should be accompanied by comprehensive documentation.

Characterize, to To identify distinct features in an object or system from analytical results.

Chemical analysis A process by which chemical measurement processes (CMPs) are used to extract information from objects or systems.

Chemical measurement process (CMP) See "Analytical process".

Chemical metrology The science of (bio)chemical measurements.

Chromatograph An analytical system that performs chromatographic separations in a column (gas or liquid chromatography) and includes an on-line detector for continuous monitoring of the fluid emerging from the separation column. Because it provides analytical information, a chromatograph is an instrument.

Chromatography A word that describes a broad range of highly efficient analytical separation techniques based on multiple mass transfer between a mobile phase and a stationary phase.

Gas chromatography. A chromatographic technique where the mobile phase is a gas (into which the sample aliquot is inserted) and the stationary phase is a solid or a liquid supported on an inert solid that is placed in a column.

Liquid chromatography. A chromatographic technique where the mobile phase is a liquid (into which the sample aliquot is inserted) and the stationary phase is a solid or a liquid that is either supported on an inert solid for placement in a column or spread onto a thin layer of a support (in Thin Layer Chromatography).

Classical analysis A type of qualitative or quantitative analysis based on chemical reactions in solution and involving the use of human senses for identification and a balance or burette for quantification.

Classification analysis Classification of samples of similar composition into groups (clusters) that can be distinguished by analysis. Samples can be classified into two groups (e.g., positive and negative samples) by qualitative analysis or into more than two by multiple classification analysis.

Clean-up The process by which interferents in a sample are removed using a separation technique to indirectly enhance selectivity.

Client A general designation applied to an individual or body requiring (bio)chemical information with a view to solving a socio-economic problem.

Coefficient of variation The relative standard deviation in percent form.

Comparative method A type of relative quantification method in which the final result is obtained by comparing the sample signal with that for a sample standard.

Concentration An form of expressing a relative quantitative result: the amount of analyte contained in a given volume or mass of sample.

Cut-off concentration. The concentration chosen by the analyst in establishing a given probability level that a binary response will be correct.

Limiting concentration or **threshold concentration**. Highest or lowest level, established by the client or legislation, to be used in deciding whether a sample or object warrants assignation of a given attribute (e.g., toxic or non-toxic).

Confidence interval A value (concentration) range within which the result of an analytical process can be expected to fall with a given level of confidence. Related to specific uncertainty in the context of precision of a method.

Data processing The body of mathematical calculations leading to the expression of the analytical result from tabulated data (chemical standards, constants, conversion factors) and experimental data produced by a CMP applied to the sample and standards.

Detect, to Of an instrument: To produce a signal and transduce it into an easily measured physical quantity (a primary datum).

Detection The action of detecting. The process of measuring for qualitative purposes.

Determinate error See "Systematic error".

Determination The process by which the amount or concentration of an analyte (or analyte family) in a sample is established.

Deviation The difference between an individual result (x_i) in a set and the mean for the set ($\bar{X}$, the random error).

Device A part of an apparatus, instrument or analyser that can serve one or more of a wide variety of possible functions.

Dialysis The process by which mass transfer between two miscible liquid phases separated by a membrane permeable to the analytes or their interferents takes place.

Disaggregation A substep of the preliminary operations of a CMP involving the fusion of an insoluble solid sample mixed with an acid or alkaline solid reagent.

Dissolution A substep of the preliminary operations of a CMP where a solid (or semi-solid) sample is completely dissolved by treatment with a solvent.

Electrodeposition A gravimetric method performed by an electrochemical device in order to deposit the analyte quantitatively onto one electrode (usually the cathode) that is weighed before and after the process.

End-point In a titration, the volume of titrant added to the solution containing the analyte or standard by the time the indicator system produces a signal in response to which the titration should be stopped.

End-point indicator A system of the visual or instrumental type that exposes the end-point of a titration.

Equipment calibration The process by which a standard containing no analyte is used to check that an instrument (or apparatus) operates as expected. Otherwise, corrections are introduced until the instrument response (or the indication of an apparatus) reaches the value held as true for the standard used.

Equipment verification Equivalent to "Equipment calibration".

Equivalence point In a titration, the theoretical volume of titrant required to react in a quantitative, stoichiometric manner with the analyte or a standard

Error accumulation In a multi-stage process (e.g., the analytical process), the overall error is the arithmetic sum of the variances (standard deviations squared) arising at each stage (sub-process).

Errors in qualitative analysis Deviations from true YES/NO responses. See "False positive" and "False negative".

External manipulation of (bio)chemical information In the context of Social Responsibility in Analytical Chemistry, fraudulent alteration of the composition of a sample in order to obtain spurious results for unethical purposes (e.g., by directly adding a harmless substance to "conceal" the analyte in order to alter a sample and/or an analytical process).

Extraction The process by which one or several substances are separated from a solid or liquid sample.

Liquid–liquid extraction. Treatment of a liquid sample with an immiscible solvent intended to separate the analytes or their interferents.

Liquid–solid extraction. Use of a solid sorbent to retain the analytes or interferents in a liquid sample. Usually called *Solid-phase extraction* (SPE).

Solid–liquid extraction. Treatment of a solid sample with a suitable solvent to dissolve the target analytes. Also called *leaching*.

Supercritical fluid extraction. Treatment of a solid sample with a supercritical fluid to separate the soluble fraction.

False negative An error in Qualitative Analysis that results when a NO response is obtained from a sample that should have yielded a YES response.

False positive An error in Qualitative Analysis that results when a YES response is obtained from a sample that should have yielded a NO response.

Faraday A chemical standard defined as the amount of electricity (96 487.3 C) needed for one equivalent of a redox substance to be electrochemically converted at an electrode.

Generic uncertainty Dubiousness in the chemical composition of an object or sample, that is named "black sample". The opposite of "information".

Good Laboratory Practices (GLPs) The body of rules and procedures that are held as mandatory with a view to assuring quality and correctness in the results produced by laboratories engaged in the analysis and evaluation of substances with direct social implications and as such necessitating regulation.

Gravimetric factor – The ratio of the formula weight of the analyte to the molecular weight of the weighed form in gravimetry (a dimensionless number by which the result of a gravimetric weighing is multiplied in order to determine the analyte weight).
– A combination of chemical standards (atomic weights).

Gravimetry A type of calculable analytical quantification method that uses no analytical standards and is based on measurements of the mass of an analyte or a chemical derivative of the analyte.

Green analytical methods Ecological, environmentally friendly methods of analysis intended to avoid contaminating air, water, soil, etc., by effect of operations of the analytical process.

Grey sample A sample whose composition is known only approximately.

Gross error A large systematic error.

Heterogeneity A property of an object or sample in space or time that poses a problem which must be solved during sample collection if the results produced by the ensuing CMP are to be representative.

Hyphenated techniques Those using a powerful dynamic analytical separation system (e.g., a gas or liquid chromatograph) in combination with an instrument possessing a high information capacity (e.g., a mass spectrometer).

Identification A qualitative analytical process by which the presence of an analyte is ascertained on the basis of chemical or physico–chemical properties of the analyte or a reaction product of the analyte.

Indeterminate error See"Random error".

Information consistency In regard to "analytical problem", suitability of data and results to the client's information requirements.

Instrument
- A measuring system that produces raw (primary) data that can be processed in order to be related to the presence or concentration of one or more analytes in a sample.
- The materialization of an analytical technique.

Instrumental analysis A type of qualitative, quantitative and structural analysis based on the use of instruments other than the balance, burette and human senses.

Interferences Chemical or physical perturbations of various types that systematically alter one or more steps of a CMP and hence the analytical result in terms of selectivity.

Interlaboratory exercise A series of CMPs performed by different laboratories under the supervision of a competent body to analyse aliquots of the same sample for the same analytes. Used to check the results (and their uncertainties) for a variety of purposes (e.g., preparing a CRM).

Internal representativeness In regard to the analytical problem, degree of consistency between the results obtained in the analytical process and the analysed sample, the object from which the sample was taken and the analytical problem addressed by the analytical chemist.

Ion exchange A process by which dissolved ionic species are separated by using an active solid called an "ion-exchange resin".

ISO 17025 A 2005 standard specific to testing laboratories that is entitled "General requirements for the competence of testing and calibration laboratories".

ISO 9000 A general standard for quality entitled "Quality management systems—Fundamentals and vocabulary".

Leaching See "Solid–liquid extraction" under "Extraction".

Limit of detection The analyte concentration yielding an analytical signal that can be statistically distinguished from an analytical blank.

Limit of quantification The analyte concentration yielding a signal that is taken to be the lower limit of the linear range of the calibration curve.

Linear calibration graph A linear (first-order) mathematical function relating the signal with the concentration of standards containing a known analyte concentration that are subjected to the analytical process. It allows the sample signal to be related to the signals for standards in order to calculate the analyte concentration by extrapolation.

Linear range The linear portion of the calibration curve where the sensitivity (slope) remains constant.

Macroanalysis A type of chemical analysis where the initial size of the sample aliquot subjected to the CMP is greater than 100 mg.

Macrocomponents Analytes whose proportions in the sample exceed 1% of their masses.

Masking The use of a reagent to interact chemically in solution with interfering species in a sample in order to avoid their perturbation without the need to physically separate the reaction products from the medium (*pseudo*-separation).

Maximum representativeness In regard to the analytical problem, highest degree of consistency between the results obtained in the analytical process, which is reached when the results are significant both internally (that is, consistent with the sample, object and analytical problem) and with the client's socio-economic problem

Maximum tolerated ratio A parameter that describes the influence of an interfering species in the context of selectivity. The highest interferent-to-analyte concentration ratio that results in no perturbation to a CMP.

Measurand The quantity measured in a CMP, which may be the analyte or some quantity such as pH.

Measurement The process by which a signal yielded by the analyte or a reaction product of the analyte is compared with one produced by a standard.

Method calibration The process by which an analytical standard is used to characterize the response of an instrument in terms of the properties of an analyte or analyte family. Method calibration entails unequivocally relating the signal to the presence or concentration of the analyte.

Method-defined parameter An analytical result that can only be obtained by using a well-defined protocol that constitutes a reference established by law or custom because using another method leads to a different result.

Metrology The science of physical, chemical, biochemical and biological measurements. See "Chemical metrology".

Microanalysis A type of chemical analysis where the initial size of the sample aliquot subjected to the CMP ranges from 10 to 1 mg.

Microcomponents Analytes whose proportions in the sample range from 0.01 to 0.1% of their masses.

Miniaturization A term defining a technological trend to considerably reducing the size of analytical tools, integrating modules of a CMP or both.

Mole A base standard and a base unit of the International System (SI) defined as the amount of substance containing as many elemental units (atoms, molecules, ions, electrons or other individual particles or particle groups) as are in 0.012 kg of the isotope carbon-12.

Nanoanalysis See "Nanoworld analysis".

Nanoworld analysis Extraction of (bio)chemical information (identity, differences, concentration, structure) from objects of nanometric size (1–100 nm).

Negative error A negative difference between the value to be qualified and the reference used to establish it.

Object A system from which chemical information is required and samples are collected for analysis.

Official method A method endorsed and issued by an official body that is to be strictly adhered to.

Outlier A datum not belonging to a set obtained under reproducible or repeatable conditions that exhibits a significantly greater or smaller difference from the mean of the set than do the other data in the set.

Paradigm A body of essential, crucial, unarguable notions that set the guidelines for some activity. Analytical chemical paradigms are thus essential landmarks of Analytical Chemistry and, as such, change with time.

Positive error A positive difference between the value to be qualified and the reference used to establish it.

Precision The degree of mutual agreement of a set of results. The opposite of dispersion of the results around their mean, which is the reference used to calculate individual deviations (random errors).

Preconcentration A process by which sensitivity is indirectly enhanced through a separation. Involves reducing the original volume of a sample containing the analytes at low concentrations.

Preconcentration factor A dimensionless number greater than unity that is obtained by dividing the original volume into the reduced volume obtained upon application of an analytical separation technique to a sample. Multiplying by the original analyte concentration gives the final concentration of the aliquot subjected to the second step of the CMP.

Preliminary operations
- The body of actions performed in the first step of an analytical process (CMP).
- The link between the uncollected, unmeasured, untreated sample and the principal measuring instrument.
- The first step in a CMP.

Primary data
- Those produced by instruments in measurement processes.
- The most elementary form of information and the foundation of the results.
- The third step in the analytical information hierarchy.
- The results of detecting and sensing.

Primary method The type of method with the highest metrological quality.

Procedure A detailed specification of an analytical method.

Productivity A characteristic of a laboratory defined as the combination of its productivity-related analytical properties (expeditiousness, cost-effectiveness, and personnel safety and comfort).

Proficiency testing A form of external assessment of quality in the results of an analytical laboratory that involves participation in a specially designed interlaboratory exercise in order to compare its results with those of the other participating laboratories.

Qualimetrics The triple interface where Computers, Chemometrics and Quality in the laboratory converge.

Qualitative analysis
- A type of chemical analysis by which the analyte or analytes in a sample are identified.
- The result is a YES/NO binary response.

Quality The body of characteristics or abilities of an entity that make it better, equal to or worse than others of the same kind. In practice, quality is identified with client satisfaction.

Quality assessment Specific activities (audits) carried out by personnel from outside a laboratory to examine both the results produced and the laboratory as such and in regard to its quality control systems.

Quality assurance The body of activities performed in order to assure quality in the results produced by an analytical laboratory. Involves specific control, assessment and correction activities.

Quality assurance unit (QAU) A unit associated to GLPs that is independent of the laboratory, answerable to the president or manager of the parent body, and responsible for implementing, controlling and assessing quality in addition to proposing improvement actions.

Quality control The body of specific activities carried out by laboratory personnel in order to—basically—examine, in a direct manner, the results obtained and tools used by the laboratory.

Quality indicator A qualitative and quantitative aspect into which some characteristic or ability of an entity meeting a client's requirements materializes.

Quality manual A detailed written description of a laboratory and its activities (particularly quality control and assessment).

Quality system A series of coordinated activities performed on various elements (procedures, documents, structures) in order to assure quality in the products or services delivered by a given organization.

Quantitative analysis A type of chemical analysis by which the proportion (concentration) or amount of each analyte in a sample is determined. The result is a numerical response.

R&D&T in Analytical Chemistry Research, development and transference of analytical knowledge and technology.

Random error
- An error that can be ascribed to positive or negative (random) fluctuations typical of experimental operations.
- The basis on which precision and specific uncertainty are established.
- Also called "indeterminate error".

Reagent A chemical species that is added to a sample or standard in order to yield a reaction product with the analyte(s).

Group reagent. One that separates a small number of analytes from those present in the sample. Used in the framework of analytical schemes in Classical Qualitative Analysis.

Identification reagent. One that reacts with the analyte to produce an external effect that can be readily identified by the human senses (e.g., in Classical Qualitative Analysis) or detected by an instrument.

Masking reagent. One that reacts in solution with species accompanying the analyte in the sample in order to cancel their interferences.

Reference material A material or substance one or more properties of which are sufficiently uniform and well known for use to calibrate an instrument or apparatus, assign values to materials and systems or assess CMPs.

Reference method A method that is used to compare the accuracy and uncertainty of routine methods.

Relative error The ratio of an absolute error to the reference value used to calculate it. Multiplying a relative error by 100 gives a percent error.

Relative interpolation and extrapolation methods Relative quantification methods based on a signal–concentration relation (a calibration curve).

Relative method In Quantitative Analysis, a method based on comparisons between measurements of the sample and of one or a set of analytical standards. The output of such comparisons is the result.

Relative standard deviation An expression of the standard deviation in relative terms (as a fraction of unity with respect to the mean for the set of results).

Reliability
- A characteristic of a method (CMP) defined as its ability to retain its accuracy and precision over time. Related to robustness and transferability.
- The proportion of correct identifications in individual qualitative tests performed on aliquots of the same sample.
- A capital property in Qualitative Analysis that combines accuracy and precision, and is assigned to binary responses.

Repeatability A manner of expressing precision. Defined as the dispersion of the results of mutually independent tests using the same method as applied to aliquots of the same sample, at the same laboratory, by the same operator, using the same equipment over a short interval of time.

Representativeness A capital analytical property related to consistency between the results, the samples received, the object, the analytical problem and the socio-economic problem addressed.

Reproducibility A manner of expressing precision. Defined as the dispersion of the results for mutually independent tests performed by applying the same method to aliquots of the same sample under different conditions: different operators, equipment, days or laboratories.

Robustness An analytical property of a CMP that reflects its resistance to slight changes in the experimental conditions under which it is performed.

Safety An attribute of a laboratory or CMP related to the absence of hazards to human health and/or the environment.

Sample A part (aliquot) of an object potentially containing the analyte.
Bulk sample or **primary sample**. The result of the first selection from the object. Usually of a large size.

Composite sample. The result of combining several portions of a bulk sample.
Convenience sample. One selected in terms of availability, cost-effectiveness, efficiency, etc.
Laboratory sample. A portion of the object that is submitted, in an appropriate container, to the laboratory for analysis.
Random sample. One selected in such a way that any portion of the object will have a specified probability (e.g,. 95%) of being withdrawn.
Representative sample. A portion of the object that is selected by applying a sampling plan consistent with the analytical problem addressed.
Selective sample. A sample that is collected by following a guided sampling procedure.
Stratified sample. One withdrawn from a stratum or well-defined zone of the object.
Test sample or **aliquot**. The object portion that is eventually subjected to the analytical process.

Sample collection See "Sampling".

Sample custody chain The action or series of actions that ensures an unequivocal relationship between the sample aliquot subjected to a CMP and the result it produces (sample traceability).

Sample matrix Structure and chemical composition of the sample to be analysed. Includes the analytes and all other components.

Sample throughput A measure of expeditiousness of CMPs. The number of samples that can be processed per unit time (e.g., hour, day).

Sample treatment A general term used to refer to the substeps of the preliminary operations of the CMP performed in order to prepare the test sample or aliquot for measurement of the analytical signal (second step of the CMP).

Sampling An operation by which one or more portions (aliquots) of an object are chosen for individual or joint subjection (following size reduction) to a CMP. Sampling can be of the intuitive, statistical, directed or protocol-based type.

Sampling error A deviation in the representativeness of the collected sample. Sampling errors can be accidental, systematic or random in nature

Sampling plan The strategy to be used in order to ensure that the analytical results will be representative of the analytical problem addressed.

Screening of analytes A process used to systematically identify analytes or analyte families in samples.

Screening of samples Classifying a set of samples into two groups according to (bio)chemical composition.

Secondary data – Items of non-analytical information that characterize the performance of apparatuses and instruments in the analytical process.
– The lowest level in the information hierarchy.

Selectivity A basic analytical property of an analytical method that is defined as the ability of the method to produce results exclusively dependent on the analyte for its identification or quantification in the sample.

Selectivity factor A parameter describing the selectivity of a method with respect to another. Defined as the quotient of the tolerated interferent-to-analyte ratios obtained by using the two methods to determine the same analyte in the same sample.

Semi-microanalysis A type of chemical analysis where the initial size of the sample aliquot subjected to the CMP ranges from 100 to 10 mg.

Sense, to To use a device responding to the presence or concentration of an analyte in a sample. Entails interacting with an instrument proper.

Sensitivity – A basic analytical property defined as the ability of a method (CMP) to detect (qualify) and determine (quantify) small amounts of analyte in a sample.
– The ability of a CMP to distinguish between similar concentrations (amounts) of analyte.

Sensor A portable, easy to use miniature device or instrument that responds to the presence or concentration of an analyte (or analyte family) in a sample. Usually connected to or integrated in an instrument.

Separation An operation involving mass transfer between two phases. A crucial element of the preliminary operations of a CMP. Discrete or continuous in nature.

Chromatographic separation. One where distribution between phases reaches equilibrium many times (e.g., in a column, thus significantly enhancing the separation efficiency.
Non-chromatographic separation. One where mass transfer between phases reaches equilibrium only once or a small number of times.

Simplification A technological trend to reducing the number of steps traditionally involved in CMPs in order to increase expeditiousness and decrease costs.

Social responsibility (SR) – Awareness of organizations (e.g, private and public bodies) and individuals of the impact (consequences) of their actions and decisions, which may directly or indirectly affect stakeholders—who can in turn influence such actions and decisions or those who make them.
– The next step to ultimate Quality: a perfect mankind.

Social responsibility in Analytical Chemistry The impact of (bio)chemical knowledge resulting from the analysis of objects and systems on society at large, and on human and animal health, the environment, nutrition, industry, etc.

Social responsibility principles Cornerstones of Social Responsibility: answerability, transparency, ethical conduct, meeting stakeholders' expectations, and complying with national and international laws and norms.

Socio-economic problem – A question posed by the client that is to be answered by delivering appropriate information.
– The origin of the analytical problem.

Spatial analysis Extraction of (bio)chemical information from different zones of an object or system or from objects and systems in outer space.

Speciation A type of analysis that provides qualitative and quantitative information about the different forms in which an analyte may occur in a (usually environmental) sample.

Specific uncertainty The range of values where a result, a mean of such values and the value held as true may fall with a given probability. Similar to, but not the same, as precision. Can be absolute, partial or zero.

Stakeholders In the context of Social Responsibility (applicable ISO norms), the individuals, groups, NGOs, etc., potentially affected by the decisions and actions of a body, in which they can participate through ordinary procedures.

Standard A tangible or intangible reference used to support or perform analytical chemical measurements.

Base standard. A standard that coincides with one of the seven SI base units. Only the kilogram prototype is of the tangible type, however.
Chemical standard. A standard that can acts as a traceability link between base (SI) standards and analytical chemical standards.
Analytical chemical standard. Any of the standards used in ordinary analytical practice. Of the primary or secondary type.

Standard deviation A statistical parameter that reflects the precision of a set of results according to the theory of Gauss.

Standard method A method that is developed, validated and specified in detail by a competent body.

Standard operating procedure (SOP) A detailed description of how each individual laboratory activity should be conducted. Each activity should have an associated SOP. SOPs are related to Good Laboratory Practices (GLP).

Standard sample An artificial, naturally occurring or modified natural material intended to simulate as closely as possible an actual sample that possesses the properties of a reference material or certified reference material.

Structural analysis A type of chemical analysis by which the structure of a sample (viz., the spatial distribution of its constituents) or a pure analyte is established

Sustainable development That meeting current needs without compromising the ability of future generations to fulfil their own.

Systematic error An error ascribed to well-defined operational alterations in a CMP that has the true value or the value held as true as reference. Consistently positive or negative in sign. Can be assigned to a result or a CMP.

Technique A scientific principle used to obtain analytical information by using an instrument.

Titrant A reagent solution containing a referential concentration (that is, one prepared from primary and analytical standards) which is used in a titrimetry.

Titration See "Titrimetry".

Titration curve A logarithmic or linear plot of the monitored signal as a function of the titrant volume used in a titration.

Titrimetry A classical quantification technique involving an absolute method based on the use of analytical standards that relies on accurate measurements of the volume of titrant solution required to react, in a quantitative manner, with the analyte present in a sample. Can be of the direct or indirect type and performed in a manual, semi-automatic, automatic or automated manner.

Total index A measurand describing the presence and/or concentration of a family of analytes (e.g., total polyphenols in tomatoes).

Trace analysis An analytical process especially suitable for the identification or quantification of analytes present in proportions lower than 0.01% (100 ppm) in the sample.

Traceability An attribute that characterizes various analytical concepts. An abstract concept that integrates two notions: tracing (the history of production or performance) and relationship to standards.

> **Traceability of an aliquot**. An unequivocal relationship of a sample aliquot subjected to a CMP to both the socio-economic problem (representativeness) and the result (sample custody chain) which thus assures consistency between the problem and the result (cyclic traceability).
>
> **Traceability of an instrument**. The documented history of the performance of an instrument (installation, malfunctioning, repairs, servicing, calibration, correction, hours of use, samples processed, etc.). Through calibration, the relationship to standards implicit in traceability is established.
>
> **Traceability of a result**. A property of a result or of the value of standard through which the result or value is related to well-established national or international references via an unbroken chain of comparisons characterized by their respective uncertainties.

Traceable method A method whose results (and uncertainties) are linked to a well-known standard (e.g., a CRM).

Traces A word used to designate analytes present in proportions lower than 0.01% (100 ppm) in the sample.

Transducing The process by which a raw signal produced by an instrument is transformed into a (usually electrical) measurable signal.

Transfer in Analytical Chemistry The process by which basic and applied knowledge and technology developed at Analytical Chemistry R&D centres is supplied to routine analytical laboratories.

Transfer weights Objects of fixed mass used to calibrate balances. Available in various classes dependent on their uncertainty and issuer.

Transferability An attribute of a CMP that reflects its ability to provide consistent results on application to the same samples in different laboratories. Related to robustness and reliability.

True value The value corresponding to absolute trueness: the analyte concentration in a sample with zero uncertainty. Corresponds to ideal quality.

Ultra-microanalysis A type of chemical analysis where the initial size of the sample aliquot subjected to the CMP is less than 1 mg.

Uncertainty range A concept used in Qualitative Analysis instead of specific uncertainty (Quantitative Analysis) even though it has a different meaning. A feature of binary responses defined as the concentration range around the threshold value where errors (false positives and negatives) are made.

Validated method A method whose properties have been thoroughly studied and specified

Validation
- The experimental, documented demonstration that an overall process (CMP) or a particular step (e.g., sampling, data processing) has developed and will continue to develop as expected.
- The experimental, documented demonstration that an object (e.g., an apparatus, an instrument) possesses and will continue to possess specific properties.

Value held as true A datum (accompanied by its uncertainty) derived by chemometric treatment of the results obtained by having many different laboratories process aliquots of the same sample (a CRM) to determine the same analyte. Corresponds to referential quality.

Volatilization A separation technique occasionally used for gravimetric purposes that relies on the mass difference of the sample prior to and after controlled heating in the presence or absence of a reagent.

Volumetric factor A dimensionless number by which the approximate concentration of a titrant solution prepared from a secondary standard is to be multiplied in order to calculate the actual concentration. Obtained by experimentation and computation.

White sample A sample with well-defined properties which, with few exceptions, remain virtually constant on the whole.

Annex 2: Answers to the Questions

Chapter 1. Principles of Analytical Chemistry

1.1. Tick the type of determination corresponding to each of the following examples:

Answer:

Examples	Determination of		
	Traces	Micro components	Macro components
Determination of pesticides in urine	X		
Determination of calcium in a milk sample		X	
Determination of proteins in beef			X

1.2. Tick the correct statements among the following:

Answer:

[ ] The word "analysis" refers to the analyte
[X] Analysis of traces. ***Accepted, but incorrect***
[ ] Microanalysis of copper
[X] Qualitative analysis comes before quantitative analysis

1.3. What type of information regarding quality can be assigned to the result for a certified reference material?

Answer:

Information held as true or referential information, which possesses the highest level of quality that can be reached with special experimentation: certification of the analyte content of a sample (a certified reference material, CRM) through an interlaboratory exercise.

M. Valcárcel Cases et al., *Foundations of Analytical Chemistry*,
DOI 10.1007/978-3-319-62872-1

1.4. Explain the two types of quality trade-offs to be made in response to contradictions between aims or objectives in Analytical Chemistry.

Answer:

One should distinguish between aims and objectives here.

Aims: A decision must be made if a high metrological quality, in the form of high accuracy and low specific uncertainty, is to prevail over fulfilment of the information requirements or vice versa.

Objectives: The decision here is whether to maximize the amount of information and its quality or minimize the use of sample and reagents, time, effort and risks.

The laboratory and the client should share some quality trade-offs.

1.5. What are the most salient differences between Analytical Chemistry and other disciplines of Chemistry?

Answer:

Analytical Chemistry is responsible for producing reliable (bio)chemical information about natural and artificial objects and systems. It lies at the third apex of the basic triangle of Chemistry, which includes Synthesis and Theory.

1.6. When does analytical knowledge not suffice to solve problems? With what should it be replaced in those cases?

Answer:

A need exists to push boundaries towards interdisciplinarity and to create new paradigms in order to address the new problems to be faced by today's world (e.g., exploring the Nanoworld).

1.7. Why are the two classical standards of Analytical Chemistry insufficient? What is the third?

Answer:

Because one of the goals of Analytical Chemistry is to fulfil (bio)chemical information requirements. This obviously entails knowing the type and characteristics of the information to be delivered. Hence, the information required is the third basic standard of Analytical Chemistry in addition to the classical (tangible and written) standards.

1.8. Explain with appropriate examples the importance of interdisciplinarity to Analytical Chemistry.

Answer:

The future of Chemistry lies in an interdisciplinary approach linking it to Biology, Medicine, Physics, Engineering and other scientific and technical areas at the boundaries of which major innovations can be expected to arise.

Analytical Chemistry cannot evade this trend. In order to reach its goals and objectives, it must connect to other areas of knowledge.

Thus, analysing the Nanoworld requires cooperating with physicists capable of designing the analytical instruments needed for this purpose (e.g., transmission electron microscopes).

Also, there is a growing trend to using immunoreagents to detect or determine traces of analytes on the grounds of their high sensitivity and selectivity. These reagents are synthesized in close cooperation with biochemists.

1.9. Explain and exemplify the most salient written standards for Analytical Chemistry.

Answer:

Analytical Chemistry uses two major types of written standards, namely:

- ***Official, standard methods issued by government agencies or by prestigious national or international bodies (e.g., AOAC, EU, OECD)***.
- ***Norms and guides issued by international organizations (e.g., ISO) that are adapted by a competent national body for application in each country. These standards provide the framework for managing analytical quality (e.g., ISO 17025:2010) or implementing Social Responsibility in Analytical Chemistry (ISO 26000:2010)***.

1.10. What are the areas influenced by (bio)chemical information? Give an example for each area in Slide 1.26.

Answer:

HEALTH. Enzymatic determination of creatinine in blood serum to monitor patients with chronic renal disease.

NUTRITION. Analysis by a customs laboratory of a batch of bottled Russian liquor in order to quantify its content in methanol, which is a toxic substance.

HYGIENE. Determination of the concentration of hydrochloric acid in harsh cleaning products.

TRANSPORTATION. Analysis of aviation fuel for banned polluting additives.

DRESSING. Determination of a marker such as lithium deliberately added during the production of branded sportswear in order to fight the growing fraud of counterfeiting.

SPORTS. Analysis of athletes' urine to determine substances banned by the International Olympic Committee.

CULTURE. Dating of works of art by C-14 radiometry.

NEW TECHNOLOGIES. Determination of the exact purity of ultrapure silica used in wafers for TIC equipment.

HOUSEHOLD. Analysis of sofa and carpet stain removers to ensure that they contain no banned toxic solvents. Unbranded removers are not guaranteed to be completely safe.

BUILDING. Determination of the titanium dioxide content of dirt-repelling nanomodified concrete for use outdoors.

SUSTAINABLE DEVELOPMENT. Determination of the components of acid rain (sulphur and nitrogen oxides) in air from thermal power stations. The analytes react with water vapour in the atmosphere to form nitric and sulphuric acid, which destroy plants, erode monuments and damage animals' lungs.

1.11. Relate two hierarchies of analytical terms.

Answer:

In the analyser–instrument–apparatus–device hierarchy, the analyser is associated to the process and the instrument to the technique.

In the data–information–knowledge hierarchy, instrument signals are data, results constitute information and reports convey knowledge.

1.12. Rank the following concepts according to representativeness:

Answer:

The particular information requirements lead to the choice of an analytical process that is applied to a well-defined object in a specific sample.

Place	Concept: representativeness of
4	The sample
1	The information requirements
2	The analytical problem
3	The object

1.13. Illustrate the distinction between object availability and sample availability with several examples.

Answer:

A readily available object is a macro- or microscopically sized entity (e.g., a river) from which samples are withdrawn for analysis. Objects such as the Nanoworld and the earth's outer space are much more difficult to analyse.

A readily available sample is one that can be easily withdrawn from a macro- or micro-sized object. Thus, baby's blood is less easily available than horse urine. Also, it is more difficult to date a piece of artwork from Roman times than a painting from the XV century.

1.14. State the parts (items) of the paper by Whitesides mentioned in Slide 1.42 and recommended as reading. What aspect of Chemistry did you find the most surprising?

Answer:

The paper emphasizes the importance of (bio)chemical information. Also, it underlines the significance of Analytical Chemistry in the chemical realm and deems it a bottleneck for major scientific and technical developments.

1.15. Give two real-life examples other than those depicted in Slide 1.29 and identify the information requirement, object, sample and analyte in each.

Answer:

Example 1:

- ***Information required: The pesticide concentration, in ppb, of a tomato batch from Almeria, Spain. If the concentration is lower than the maximum tolerated level in the applicable EU Directive, the batch will be fit for export***.
- ***Object: A tomato batch ready for export***.
- ***Samples: Aliquots (tomatoes) withdrawn from boxes according to a specific sampling plan***.
- ***Analytes: The pesticides concerned***.

Example 2:

- ***Information required: The point in time a bioreactor should be stopped because more than 95% of the target product (glucose) will have by then been produced***.
- ***Object: The bioreactor and its contents***.
- ***Samples: Aliquots of the reactor contents taken at preset intervals***.
- ***Analyte: Glucose***.

1.16. Justify the designation "Trace Analysis".

Answer:

Technically, the definition is not strictly correct because the analytes (traces) are not "analysed" but rather "determined".

However, the designation "Trace Analysis" remains widely used, so, for historical reasons, it can be retained. The term designates special analytical processes for preventing contamination that are conducted in clean rooms by operators wearing appropriate apparel (caps, gloves, masks) and using ultra-pure reagents. Organic and inorganic traces are analysed with rather different methods.

1.17. Give several examples of real-life situations where the sample and analyte differ in nature.

Answer:

- ***Analysis of soils to determine pesticides.***
- ***Determination of calcium in milk.***
- ***Analysis of oil crude to determine vanadium.***
- ***Determination of traces of organic compounds in atmospheric air.***
- ***Analysis of blood to determine iron.***

1.18. Is the designation "Analytical Separation Techniques" correct?

Answer:

Strictly, this designation is incorrect because a technique uses a measuring instrument. Thus, liquid–solid extraction and filtration are not "techniques" because they use no measuring instrument.

Two correct designations for analytical separations as a whole are "Analytical Separation Systems" and "Analytical Separation Processes".

"Analytical Separation Techniques" is correct when a detector is coupled to a gas chromatograph, liquid chromatograph or capillary electrophoresis system, for example.

1.19. What are the differences between the following?

1. (Bio)chemical information and analytical information.
2. Chemical information and biochemical information.

Answer:

1. ***The two terms are completely equivalent. There is no difference.***
2. ***Differences can arise from the nature of the sample (e.g., a lunar rock and plant tissue) or the analyte (e.g., iron and an enzyme).***

1.20. How many pathways can applied research in Analytical Chemistry follow? Why?

Answer:
Basically, two.

- ***The more simple pathway involves using the body of processes, techniques and strategies supplied by basic research as adapted to the sample–analyte pair concerned***.
- ***The more complex pathway must be followed when an unusual analytical problem that cannot be solved with the means of basic research is addressed and directed, more specific research is required instead***.

1.21. When do analytical chemical R&D centres have to contact the clients requiring (bio)chemical information or vice versa? Give some examples.

Answer:
In principle, clients requiring some (bio)chemical information use routine analytical laboratories to monitor raw materials, intermediates and end-products. Only rarely (e.g., when diversifying production) do new information requirements arise that can only be fulfilled by developing new analytical processes for use by routine laboratories. In these situations, a direct connection between clients and research centres may be advisable.

1.22. What is the meaning of the four general paradigms of today's and tomorrow's Analytical Chemistry?

Answer:
The paradigms define the correct way of approaching Analytical Chemistry today and in the future. In their light, Analytical Chemistry is defined as the discipline of (bio)chemical information; one that seeks interdisciplinarity with other scientific and technical areas, and that possesses R&D&I of its own where analytical knowledge and technology transfer plays a prominent role.

Chapter 2. Analytical Properties

2.1. Tick the correct statements in relation to the dynamic range of a calibration curve obtained in the photometric determination of iron in wines:

Answer:

[ ] The sensitivity remains constant
[X] The lower limit coincides with the limit of detection
[X] The sensitivity is always greater than zero
[ ] The lower limit coincides with the limit of quantification

2.2. To which analytical properties are the following concepts directly related?

Answer:

TRACEABILITY	[ ] Precision	[X] Accuracy	[ ] Sensitivity
ROBUSTNESS	[ ] Expeditiousness	[X] Precision	[ ] Sensitivity
PRODUCTIVITY	[X] Expeditiousness	[X] Cost-effectiveness	[ ] Representativeness

2.3. Distinguish dynamic range from linear range in a calibration curve.

Answer:

Sensitivity as defined according to IUPAC's criteria is greater than zero throughout the dynamic range; however, it differs among zones in the range. In the linear portion of the dynamic range, the sensitivity is also greater than zero, but it is a constant value, so the analytical signal (X) is linearly related to the concentration and the calibration curve is linear as a result.

2.4. State whether the following statements are true (T) or false (F).

Answer:

[T] Precision decreases with increasing standard deviation
[F] Accuracy decreases with decreasing relative error
[T] Sensitivity increases with decreasing limit of detection and quantification
[F] Selectivity increases with increasing interference

2.5. Define the analytical property robustness.

Answer:

Robustness is the resistance of a method to its results changing by effect of slight changes in the experimental conditions.

2.6. Define "bias" in relation to errors in Analytical Chemistry.

Answer:

In the context of accuracy, bias is the deviation of the mean result of a method from the value held as true $(\widehat{X}')$***. The deviation is a positive or negative error depending on whether the mean is greater or smaller, respectively, than*** $\widehat{X}'$.

2.7. Tick the correct statements in the dynamic concentration range of the calibration curve for the photometric determination of calcium in milk:

Answer:

[ ] The sensitivity remains constant
[X] The sensitivity is always non-zero
[X] The sensitivity is not always the same
[X] The sensitivity decreases at the end of the range

2.8. Which datum is needed to assess the accuracy of an analytical result?

Answer:

[ ] The mean of n results
[X] The value held as true
[ ] The standard deviation

2.9. State whether the following statements are true (T) or false (F).

Answer:

[T] Selectivity increases with decreasing interference
[F] Sensitivity increases with decreasing slope of the calibration curve
[T] Accuracy increases with increasing precision
[F] Precision increases with increasing standard deviation

2.10. Distinguish generic and specific uncertainty.

Answer:

Generic uncertainty is the overall dubiousness in the composition of a sample or object and arises from a complete lack of knowledge about it. On the other hand, specific uncertainty restricts the dubiousness to a specific range where the result obtained by repeating the analytical process will fall with a given probability.

2.11. What are the differences between "repeatability" and "reproducibility"?

Answer:

These are two ways of calculating precision experimentally. Repeatability is assessed by using the same experimental conditions (time, instrument, operator, laboratory, etc.) each time the analytical process is performed. On the other hand, reproducibility is assessed by changing some experimental condition between replications of the process. Obviously, reproducibility is a more rigorous statistical concept than is repeatability.

2.12. What kind of reference is used to calculate (a) the accuracy of the result for a sample and (b) the precision of a method?

Answer:

(a) ***The value held as true*** $(\widehat{X}')$.
(b) ***The mean of a set of results*** $(\overline{X})$.

2.13. State whether the following statements about accuracy and precision are true (T) or false (F).

Answer:

[F] Both analytical properties can be ascribed to results
[F] The two are unrelated
[F] Good precision can only be obtained with good accuracy
[T] Good accuracy can only be obtained with good precision

2.14. Name the four types of relationships between analytical properties.

Answer:

1. ***Hierarchical***.
2. ***Foundation***.
3. ***Contradictory***.
4. ***Complementary***.

2.15. What are the similarities and differences between systematic errors and gross errors?

Answer:

– ***Similarities***:

1. ***Both are associated to accuracy***.
2. ***Both can be positive or negative***.
3. ***Both arise from well-defined changes during the analytical process***.

– ***Differences***:
In magnitude: systematic errors are typically much smaller than gross errors.

2.16. Two methods A and B are used to determine the same analyte in aliquots of a sample with a certified value of 1.23 ± 0.05 mg/L. The experimental result is 1.27 ± 0.03 mg/L with method A and 1.29 ± 0.01 mg/L with method B. Which method is the more accurate? Which is the more precise? Why?

Answer:
Method A is the more accurate because its result is closer to the value held as true, $\widehat{X}'$. Thus, $e_A = 0.04 < 0.06 = e_B$. On the other hand, method B is the more precise because its uncertainty range is narrower: 0.01 < 0.03.

2.17. Why stating the accuracy of a result is meaningless if its precision is unknown?

Answer:
If the precision is inadequate (too low), the probability of obtaining the same result when the analytical process is repeated will also be very low.

2.18. Can productivity-related properties be more important than capital and basic properties?

Answer:
Yes. In fact, the importance of analytical properties depends on the particular analytical problem. If the problem requires prioritizing cost-effectiveness, expeditiousness and safety, it will be at the expense of accuracy and the basic analytical properties (e.g., precision, sensitivity and selectivity).

2.19. What is a "blank"? What is the "blank signal"?

Answer:
A "blank" is a sample not containing the target analyte. The "blank signal is the signal produced by a blank subjected to the analytical process.

2.20. Which are the references needed to define the following analytical properties in mathematical and conceptual terms? Tick the correct choices.

Answer:

	Set of blanks	Value held as true	Mean of *n* results	Interferences from other systems
Accuracy		X		
Precision			X	
Limit of detection	X			
Selectivity				X

2.21. State whether the following statements as regards accuracy and precision are true (T) or false (F).

Answer:

[F] Both analytical properties can be assigned to results
[T] The two are mutually related
[T] Good precision cannot be obtained without good accuracy
[T] Good accuracy cannot be obtained without good precision

2.22. Why does accuracy rest on precision?

Answer:
There can be no accuracy without good precision. Otherwise, the probability of obtaining identical or similar results when the analytical process is repeated will be low.

2.23. Tick the correct boxes in this comparison of precision and robustness.

Answer:

	Same sample aliquot	Same method	Supports accuracy	Basic analytical property
Robustness	X		X	X
Precision	X	X	X	X

2.24. How are the facets of sensitivity related?

Answer:

The lower are the limits of detection (C_{LOD}) and quantification (C_{LOQ}), the higher is the sensitivity (S, IUPAC) and the greater is the ability of a method to discriminate between similar analyte concentrations.

2.25. Two methods A and B for determining aflatoxins in milk are compared in terms of sensitivity by analysing two different certified reference materials with certified values of 0.25 ± 0.01 and 0.28 ± 0.01 ppb. Based on method A, both CRMs contain aflatoxins. Based on method B, both CRMs contain aflatoxins and the second CRM contains a slightly greater amount than the first. Which is the more sensitive method? Why?

Answer:

Method B is the more sensitive because it can discriminate between samples with similar concentrations of the analyte.

2.26. What is the lower limit of the linear range of the calibration curve?

Answer:

The limit of quantification (C_{LOQ}).

2.27. What is the "maximum tolerated ratio"? To which analytical property does it relate?

Answer:

The maximum tolerated ratio (MTR) is the highest interferent-to-analyte concentration ratio not altering a result. MTR is associated to the basic analytical property selectivity.

2.28. Give an example of analysis (state the sample and analyte) where accuracy is to be favoured over productivity-related properties?

Answer:

The determination of the purity of a gold batch directly imported from a mining company. Gold is the analyte and the mined batch is the sample.

2.29. Is it correct to assign accuracy to an analytical process? Why?

Answer:

It is not because accuracy is a capital analytical property that characterizes results.

2.30. The sensitivity of a method is 1.02×10^{-3} AU mL ng^{-1}. What are the units for the following parameters?

Answers:

Blank signal: ***AU***
Standard deviation of the blank: ***AU***
Limit of detection: ***ng/mL***
Limit of quantification: ***ng/mL***
Analyte concentration: ***ng/mL***

2.31. Complete the following table comparing the analytical properties "accuracy" and "precision".

Answer:

	Accuracy	Precision
Type of analytical property	***Capital***	***Basic***
A typical property of	***Results***	***The analytical process***
Parameters used to measure it	***Errors***	***Standard deviation***
An indispensable numerical reference for calculating the parameters	***The value held as true*** $(\widehat{X}')$	***The mean of a set of results*** $(\overline{X})$
Mutually dependent	***Depends on precision***	***Does not depend on accuracy***

2.32. (1) Discuss the ideal situation and (2) describe the real situation in independently subjecting n aliquots of sample to an analytical process in order to obtain n results.

Answer:

(1) ***The individual results*** (x_i) ***are identical with one another, with the mean and with the value held as true*** $\left(x_i = \overline{X} = \widehat{X}'\right)$.

(2) ***The individual results*** (x_i) ***are different from one another, from the mean and from the value held as true*** $\left(x_i \neq \overline{X} \neq \widehat{X}'\right)$.

2.33. Classify errors in Analytical Chemistry according to (1) form of expression; (2) direction; and (3) sources, references and magnitude.

Answer:

1. ***Absolute and relative***
2. ***Positive and negative***
3. ***Random, systematic and gross***.

2.34. A method provides accurate results. May it not be precise?

Answer:

No. Properly defining the accuracy of a method requires knowing its precision. If the precision is poor, the results can only be accurate by chance.

2.35. Define a parameter representing the analytical property "selectivity".

Answer:

Selectivity can be assessed in terms of the highest tolerated interferent-to-analyte ratio not leading to error:

$$S = (TR)_{max} = \frac{C_{int}}{C_{an}}$$

2.36. Solve the different parts of the following problems.

Problem A

An analytical method for determining copper traces in feed is characterized as follows:

(1) Using the method to analyse standards of increasing concentrations of analytes provides the following results:

$[Cu^{2+}]$, ppb	0.0	1.0	2.0	3.0	4.0	5.0
Signal, AU	0.030	0.050	0.102	0.149	0.201	0.250

(2) Independently subjecting 5 aliquots of a reference standard with a certified concentration of 3.30 ± 0.10 ppb gives the following results, in ppb: 3.40, 3.39, 3.50, 3.27 and 3.35.

Questions:

(a) What is the blank signal? What are its units?

Answer:

The blank signal must be expressed in the same units as the instrument signal. Since the instrument was used to measure absorbance, the blank signal should be expressed in absorbance units (AU).

Based on the definition of "blank", the blank signal will be that corresponding to a copper concentration [Cu^{2+}] = 0 ppb. This datum is contained in the table. Therefore, the blank signal will be

$$Signal\left(\left[Cu^{2+}\right] = \mathbf{0\,ppb}\right) = \mathbf{0.030\ AU}$$

(b) What is the signal corresponding to the certified copper concentration in the standard?

Answer:

Calculating the signal corresponding to the analyte concentration of the CRM entails constructing a calibration curve and using it to calculate the following parameters:

1. ***The sensitivity of the method, which will coincide with the slope of the curve. A few data pairs from the table are applied the IUPAC criterion to calculate the corresponding S values. The mean of the more similar values is taken to be the slope of the calibration curve***:

$$S = \frac{\Delta X}{\Delta C}$$

$$S_1 = \frac{(\mathbf{0.050} - \mathbf{0.030})\ \mathbf{AU}}{(\mathbf{1.0} - \mathbf{0.0})\ \mathbf{ppb}} = \mathbf{0.020\ AU/ppb}$$

$$S_2 = \frac{(\mathbf{0.149} - \mathbf{0.102})\ \mathbf{AU}}{(\mathbf{3.0} - \mathbf{2.0})\ \mathbf{ppb}} = \mathbf{0.047\ AU/ppb}$$

$$S_3 = \frac{(\mathbf{0.201} - \mathbf{0.250})\ \mathbf{AU}}{(\mathbf{5.0} - \mathbf{4.0})\ \mathbf{ppb}} = \mathbf{0.049\ AU/ppb}$$

Using S_2 and S_3, which are the more similar values, allow one to calculate the sensitivity of the method as their mean:

$$S = \frac{(\mathbf{0.047} + \mathbf{0.049})\ \mathbf{AU/ppb}}{\mathbf{2}} = \mathbf{0.048\ AU/ppb}$$

2. ***The equation of the calibration curve, which is established from the blank signal and the previously calculated sensitivity, is***

$$\mathbf{Signal}(\mathbf{AU}) = \mathbf{0.030} + \mathbf{0.049} \cdot \left[\mathbf{Cu}^{\mathbf{2}+}\right]$$

The signal corresponding to the CRM can now be calculated by substituting the certified copper concentration into the previous equation:

$$\mathbf{Signal}(\mathbf{CRM}) = (\mathbf{0.030} + \mathbf{0.049} \cdot \mathbf{3.30})\ \mathbf{AU} = \mathbf{0.193\ AU}$$

(c) Can the precision of the method be calculated? Why? If it can, what is it?

Answer:

In fact, the precision of the method can be calculated from the set of results obtained by applying the analytical process to aliquots of a CRM sample. Since no confidence level was provided, the precision is assessed in terms of the standard deviation of the results:

$$s_c = \pm\sqrt{\frac{\sum\left(c_i - \overline{C}\right)^2}{n-1}}$$

The precision of the method is thus $s_c = \pm\ \mathbf{0.09\ ppb}$.

(d) Can the accuracy of the result be calculated? Why? If it can, what is it?

Answer:

The accuracy of the result can also be calculated because a certified value that can be taken to be the value held as true is known. Thus, the accuracy can be defined in terms of the error of the method, which can be calculated as the difference between the mean of the results and the certified value:

$$e = \overline{X} - \widehat{X}' = (\mathbf{3.38} - \mathbf{3.30})\ \mathbf{ppb} = +\mathbf{0.08\ ppb}$$

$$e(\%) = \frac{\overline{X} - \widehat{X}'}{\widehat{X}'} \cdot \mathbf{100} = \frac{(\mathbf{3.38} - \mathbf{3.30})\ \mathbf{ppb}}{\mathbf{3.30\ ppb}} \cdot \mathbf{100} = +\mathbf{2.43\%}$$

The error of the method is thus positive and equal to 2.43%.

(e) If the client's imposed limit is 0.1 ppb copper, is the method suitable for qualifying (detecting) and quantifying the analyte if the deviation of the blank signal is 2.3×10^{-3} AU?

Answer:

The sensitivity and deviation of the blanks can now be used to calculate the limits of detection and quantification:

$$C_{LOD} = \frac{3 \cdot s_B}{S} = \frac{3 \cdot 2.3 \times 10^{-3}\ \text{AU}}{0.049 \cdot \text{AU/ppb}} = 0.14\ \text{ppb}$$

$$C_{LOQ} = \frac{10 \cdot s_B}{S} = \frac{10 \cdot 2.3 \times 10^{-3}\ \text{AU}}{0.049\ \text{AU/ppb}} = 0.46\ \text{ppb}$$

Graphically comparing C_{LOD} and C_{LOQ} with the stated legal limit, C_{LL}, reveals that both exceed the stated legal limit. Therefore, the method is not valid for detecting or quantifying the analyte.

– *Problem B*

An analytical process for determining pesticides (P) in water is applied through the following tests:

(1) Subjecting a total of 10 blanks to the process gives the following results in absorbance units (AU):

0.031	0.033	0.041	0.029	0.035	0.037	0.040	0.032	0.030	0.037

(2) A calibration curve is constructed from a set of standards of increasing hydrocarbon concentrations. The equation for the curve is

$$Signal(AU) = 0.035 + 1.07[P]$$

where $[P]$ is the pesticide concentration in ng/mL.

Questions:

(a) Can the precision of the method be calculated? Why? Explain your answer.

Answer:

The precision of this method cannot be calculated because no set of results allowing calculation of its precision is available. Although the results of the analysis of blanks cannot be used to assess precision, their standard deviation allows the actual precision to be estimated.

(b) Express the sensitivity of the method through three different parameters.

Answer:

The sensitivity of a method can be expressed in the form of IUPAC's parameter (S), and also as the limit of detection (C_{LOD}) and the limit of quantification (C_{LOQ}). The sensitivity is directly proportional to the former parameter and inversely proportional to the latter two.

The IUPAC sensitivity (S) can be directly extracted from the statement of the problem as it coincides with the slope of the calibration curve:

$$S = 1.07\ \text{AU mL/ng}$$

The limits of detection and quantification can be calculated from the standard deviation of the blank signals:

$$s_B = \pm\sqrt{\frac{\sum\left(X_{i,B} - \overline{X}_{i,B}\right)^2}{n-1}} = \pm 0.004\ \text{AU}$$

$$C_{LOD} = \frac{3 \cdot s_B}{S} = \frac{3 \cdot 0.004\ \text{AU}}{1.07\ \text{AU mL/ng}} = 0.011\ \text{ng/mL}$$

$$C_{LOQ} = \frac{10 \cdot s_B}{S} = \frac{10 \cdot 0.004\ \text{AU}}{1.07\ \text{AU mL/ng}} = 0.037\ \text{ng/mL}$$

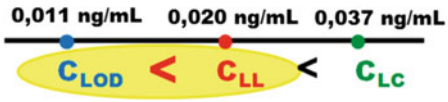
In summary, the sensitivity of the method can be expressed in the following three forms:

$$\begin{aligned} S &= 1.07\ \text{AU mL/ng} \\ C_{LOD} &= 0.011\ \text{ng/mL} \\ C_{LC} &= 0.037\ \text{ng/mL} \end{aligned}$$

(c) If the legal limit for pesticides in water is 2 ng/mL, is the method useful for their detection and quantification?

Answer:

Graphically comparing the previously calculated limits of detection and quantification with the legal limit,



allows one to conclude that the method is valid for detecting the analyte but not for quantifying it because the limit of quantification exceeds the legally tolerated limit.

– *Problem C*

The precision of an analytical process for determining copper traces in seawater is assessed in three tests involving different experimental conditions, namely:

(1) Processing a single aliquot of sample and introducing six portions of the treated aliquot into the measuring instrument.
(2) Independently processing six aliquots of the same sample and introducing them into the measuring instrument on the same day.
(3) As in (2), but having six different analysts perform the analytical process on different days.
(4) The results obtained are as follows:

Test	Results (mg/L)					
1	1.32	1.31	1.32	1.33	1.30	1.31
2	1.28	1.36	1.30	1.27	1.31	1.33
3	1.35	1.45	1.21	1.37	1.30	1.28

Calculate the specific uncertainty at the 95% confidence level for each test and plot it. Use the uncertainty values to discuss the precision achieved in each case, and identify the facet that can be characterized with each test.

Answer:

The specific uncertainty at the 95% confidence level is

$$U_R = k \cdot s_R, \quad \textit{where} \quad k(95\%) = 2$$

Since the standard deviation is given by

$$s_R = \pm\sqrt{\frac{\sum\left(X_R - \overline{X}_R\right)^2}{n-1}}$$

the respective specific uncertainties are as follows:

$$U_A = k \cdot s_A = \pm 2 \cdot 0.02\,\mathrm{mg/L} = \pm 0.04\,\mathrm{mg/L}$$
$$U_B = k \cdot s_B = \pm 2 \cdot 0.04\,\mathrm{mg/L} = \pm 0.08\,\mathrm{mg/L}$$
$$U_C = k \cdot s_C = \pm 2 \cdot 0.09\,\mathrm{mg/L} = \pm 0.18\,\mathrm{mg/L}$$

If the results are expressed in the form

$$R \pm U_R \quad \textit{where} \quad R = \overline{X}_R,$$

then:

$$\textit{Method A} : 1.32 \pm 0.04\,\mathrm{mg/L}$$
$$\textit{Method B} : 1.31 \pm 0.08\,\mathrm{mg/L}$$
$$\textit{Method C} : 1.33 \pm 0.18\,\mathrm{mg/L}$$

Method A is therefore seemingly the most precise. However, it was used incorrectly because it was applied to the whole sample rather than to aliquots. Therefore, the calculated precision is spurious and should be discarded.

Method B is the most precise after A. The analytical process was performed correctly, so the calculated precision can be deemed valid. However, the precision corresponds to repeatability and is thus scarcely rigorous.

Method C is the least precise. The analytical process was performed correctly, so its calculated precision can be deemed valid. Also, it corresponds to reproducibility and is therefore more rigorous than that of Method B.

In summary, Method B, which was performed under repeatable conditions, is the most precise. Method C is less precise than B but more rigorous because it was performed under reproducible conditions. Finally, Method A was performed under neither repeatable nor reproducible conditions, so its results can hardly be valid.

Chapter 3. Reference Materials

3.1. What are the main purposes of a sample matrix standard with a certified analyte content (a CRM)? Tick the correct answers.

Answer:

[ ] Calibrating an instrument
[X] Globally assessing an analytical process
[ ] Calibrating a method
[ ] Standardizing secondary analytical chemical standards

A CRM can also be used to calibrate a special instrument such as an X-ray spectrometer.

3.2. What is a matrix standard? What is its main use?

Answer:

A matrix standard is a high-quality material mimicking the composition of a sample and having the value of an associated quantity certified by a competent body. Matrix standards are certified reference materials (CRMs) that are typically used to globally assess analytical methods but can also be useful to calibrate special instruments.

3.3. What are the essential requirements for establishing the traceability of an instrument?

Answer:

The two basic requirements for establishing traceability in an instrument coincide with the notions inherent in traceability, namely:

- ***Linking the instrument to its calibration standards, which in turn must be connected to standards of a higher quality (e.g., certified reference materials)***.
- ***Tracing the "history" of the instrument by recording the time it was installed, its usage and users, its routine calibrations, any servicing or repairs, etc. This facet is closely related to analytical quality***.
- ***The two are related by the history of the instrument's calibration***.

3.4. Tick the type correct type of standard in each case.

Answer:

	Standard			
	Basic	Chemical	Analytical chemical	
			Primary	Secondary
Carbon-12		X		
A 0.1 mol L^{-1} solution of $KMnO_4$				X
Potassium hydrogen phthalate			X	
Ultrapure silver	X	X		
The faraday		X		

3.5. Describe the traceability network among standards relevant to Analytical Chemistry with emphasis on the connections between basic, chemical and analytical chemical standards.

Answer:

This traceability network comprises linear and branching links among base (SI) standards, chemical standards and the analytical chemical standards used in practice.

There is a linear traceability chain connecting the mole (a base standard), the mass of carbon-12, atomic weights (chemical standards), and primary and secondary analytical chemical standards.

The linear link backbone branches as follows:

(1) ***The mole is defined in terms of the kilogram, a base (SI) standard***.
(2) ***The faraday (an operational chemical standard) is related to the mass of carbon-12 through Avogradro's number (N), and also to the ampere and the second (two base standards)***.

3.6. How would you define "traceability of an analytical method (CMP)"?

Answer:

An analytical method or (bio)chemical measurement process (CMP) is traceable if it can be linked to a reliable reference. Such is the case, for example, with

- ***a certified reference material (CRM) if the results of subjecting it to the CMP coincide with the certified value; and***
- ***the result of an intercomparison exercise—one managed by a prestigious national or international organization—if the result of the laboratory concerned does not differ substantially from the mean for the body of participating laboratories and its uncertainty***.

Proven traceability in the results of a method can be included in a laboratory's reports in order to persuade clients of the quality of the method.

3.7. The total free acid content of a wine sample is determined by acid–based titration with a sodium hydroxide solution previously standardized with potassium hydrogen phthalate. What standards are used in the process?

Answer:

Chemical: ***Atomic weights used in calculations***
Primary analytical chemical: ***Potassium hydrogen phthalate***
Secondary analytical chemical: ***Sodium hydroxide***

3.8. Define "equipment calibration" and relate it to or distinguish it from "method calibration".

Answer:

Equipment calibration is intended to assure proper performance of an instrument or apparatus used in the second step of the analytical process. Equipment is calibrated by using reference materials not containing the analyte to record their signals. If the signals depart from the expected values, the instrument is adjusted as required (e.g., by replacing the lamp in a spectrophotometer).

Method calibration differs from equipment calibration in the following respects:

(a) ***The target is an analytical method rather than an instrument or apparatus***.
(b) ***A signal is related to the presence or concentration of the analyte through a calibration curve***.
(c) ***A standard containing the analyte is used***.
(d) ***It is performed after equipment calibration***.

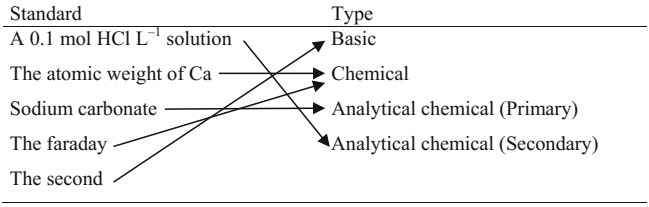
3.9. What are the purposes of equipment calibration (verification)? Tick the correct answer(s).

Answer:

[ ] Constructing a calibration curve
[X] Adjusting faulty equipment
[ ] Globally assessing an analytical method
[ ] Distinguishing error types in Analytical Chemistry

3.10. Connect each of the following standards to its type in the column on the right.

Answer:



3.11. Rank the reliability of the following types of standards with a score from 1 (least reliable) to 4 (most reliable).

Answer:

Standard	Reliability
Secondary analytical chemical standard	***4***
Chemical standard	***1***
CRM	***2***
Primary analytical chemical standard	***3***

3.12. What role do analytical chemical standards play in the traceability of a result?

Answer:

Traceability of results cannot be assured without analytical chemical standards, which play two crucial roles, namely:

(a) ***Certified reference materials (CRMs) are the ultimate references***.
(b) ***Primary standards are intermediate links in the traceability chain connecting a result to a CRM***.

3.13. What type of standard (basic, chemical or analytical chemical) has the greatest associated uncertainty? Why?

Answer:

Uncertainty is greatest in analytical chemical standards because they constitute the last link in the traceability (comparison) chain among the standards that are relevant to Analytical Chemistry.

3.14. A sample of powdered milk with a protein content certified in a document issued by a renowned independent organization is

Answer:

[ ] A primary standard
[X] A certified reference material
[ ] A secondary standard
[ ] A reference material

3.15. Name the types of chemical standards, state their differences and give some examples.

Answer: There are two main types of chemical standards:

- ***Non-operational (tabulated) standards such as the mass of Carbon-12, atomic weights, among others***.
- ***Operational standards (e.g., the Faraday), which are established through experimentation***.

3.16. Give an example of each complementary criterion used to classify analytical chemical standards.

Answer:

The standards used in chemical processes can be classified in a non-excluding manner according to nature (physical, chemical), stability and/or purity (primary, secondary), and the certifying authority (reference materials and certified reference materials).

3.17. Comment on the tracing facet of traceability of a result. What should it be consistent with?

Answer:

The tracing facet of an analytical result, which is complementary to the relation to references, requires that a laboratory result be invariably accompanied by information allowing questions such as the following to be answered: Who performed the analysis? When was it performed? How? What tools were used? Under which environmental circumstances was it conducted? etc.

This facet is fully consistent with the quality systems to be implemented in analytical laboratories. One essential aspect of quality systems is the production of documents facilitating characterization of past results—in order, for example, to meet auditors' requests.

3.18. Describe a procedure for assessing (validating) a new analytical method in terms of its relationship to matrix-type certified reference materials.

Answer:

Ideally, new analytical methods should be validated with a certified reference material (CRM) whose matrix is identical with that of the sample to be analysed and comes with a certified analyte concentration and its uncertainty.

A total of* n *aliquots of the CRM are subjected to the analytical process to be validated, and the ensuing result and its specific uncertainty are compared with those of the CRM. The following conclusions can be made if they coincide statistically:

- ***the method is validated (that is, deemed valid for the intended purpose); and***
- ***the method is traceable to the CRM used.***

3.19. What is the main limitation of CRMs for establishing the traceability of methods?

Answer:

The greatest constraint of CRMs is their scarcity in commercial form (only 5–10% of the CRMs required by analytical laboratories are commercially available). This entails using alternative procedures to assure traceability in analytical methods (e.g., participating in intercomparison exercises involving a large number of laboratories).

3.20. What types of standards prevail among (a) reference materials (RMs) and (b) certified reference materials (CRMs)?

Answer:

Most RMs are physical or chemical (e.g., pure or mixed substances), whereas most CRMs are chemical and of the sample matrix type.

3.21. Which base standard is the most relevant to Chemical Metrology? Why?

Answer:

The ultimate base (SI) chemical standard is the mole, which is defined in terms of the kilogram. Several other base standards are also relevant to Metrology in Chemistry, however. The importance of the mole arises from the fact that it is related to the mass of carbon-12, to atomic weights and to primary and secondary standards, through a traceability chain.

3.22. Why are secondary standards used even though they have unsuitable properties (e.g., instability, impurity)?

Answer:

Because they possess unique chemical properties. Such is the case with sodium hydroxide, a very strong base that is highly suitable for titrating both strong and weak acids.

3.23. What are the requirements for a matrix-type CRM?

Answer:

- ***The material should be homogeneous and stable***.
- ***It should be very similar to the target sample in composition***.
- ***It should come with a certified value and its uncertainty or be assigned the two in an interlaboratory exercise (the relational facet of traceability)***.
- ***The material should come with a detailed history of its origin (natural or artificial), stability and homogeneity, and information about the certifying campaign including the results of all participating laboratories (the tracing facet of traceability)***.

3.24. What are the three most salient general uses of analytical chemical standards?

Answer:

1. ***Equipment and method calibration***.
2. ***Overall assessment (validation) of chemical measurement processes (CMPs)***.
3. ***Standardization of secondary standards with primary standards***.

3.25. What are the three principal meanings of traceability of an analytical result?

Answer:

1. ***Relationship to references (standards)—the most orthodox***.
2. ***Tracing facet: documented history of production***.
3. ***Practical facet: Comparison and harmonization of analytical laboratories***.

3.26. How is an analytical method assessed to assure reliability?

Answer:

By subjecting n aliquots of a certified reference material (CRM) to the method (analytical process) and comparing the result and its uncertainty with the certified values. If they coincide, the method can be reliably used for the intended purpose.

In the absence of an appropriate CRM, the best choice is to take part in an intercomparison exercise. If the result obtained by the laboratory concerned is consistent with the mean for the body of participating laboratories, the method can be deemed reliable.

3.27. What analytical properties are related to traceability? Explain your answer.

Answer:

Traceability is related to the capital properties (accuracy and representativeness).

Accuracy is associated to the relationship to traceability references and representativeness is associated to the traceability of the sample aliquot subjected to the analytical process.

3.28. On what should mutual recognition of the results of two or more laboratories rest?

Answer:

On the comparability of the results obtained by analysing the same CRM and/or on consistency of their results with the mean of an intercomparison exercise where the two have participated.

3.29. What feature and twofold meaning does traceability of the sample aliquot subjected to an analytical process have?

Answer:

Traceability to samples is an unorthodox concept because it includes the tracing facet but excludes the relational facet (that is, the linkage to references).

Because of the dual nature of traceability, the sample aliquot should be related to both the information required and the result of an analytical process.

Chapter 4. Generalities of the Analytical Process

4.1. What question does the development of an analytical process essentially answer regarding extraction of (bio)chemical information from an object: what, how, when or where?

Answer:

Essentially, it answers the following question: How is the information extracted?

The other questions are intended to identify the analyte (what?), and the place (where?) and time (when?) the sample is obtained.

4.2. Why do analytical processes invariably use measurement standards? How are they used?

Answer:

Analytical Chemistry is the chemical and biochemical metrological science. In other words, it is the science of (bio)chemical measurements. Measuring involves comparing and comparing requires using a reference (e.g., a standard). The analytical process is therefore meaningless unless appropriate standards are used for equipment and method calibration.

4.3. A manufacturing process leads to an error in the quality-related parameters for the product that requires analytical control. What kind of sampling should be done in this situation?

[ ] Intuitive
[ ] Statistical
[X] Directed
[ ] Protocol-based

Explain why.

Answer:

After the error is identified, only the samples leading to the error are resampled. Hence the sampling is of the directed type.

4.4. What is the difference between "dissolution" and "disaggregation" of a solid sample?

Answer:

Both operations are related to the preparation of solid samples.

Dissolution uses a solvent (e.g., an acid) to solubilize a solid solute (e.g., a calcareous rock) until none remains suspended or in the bottom of the vessel. Leaching (solid–liquid extraction) is used to selectively dissolve a given component of a solid sample.

Disaggregation is a drastic dissolution operation used when attack with a solvent proves ineffective. The sample is mixed with an acid flux such as $KHSO_4$ or an alkaline one such as Na_2CO_3 and melted at a high temperature in a platinum or nickel crucible. Then, the molten mass is allowed to cool for easy dissolution in an appropriate solvent.

4.5. Give four definitions of "sampling" or "sample collection".

Answer:

(1) ***The body of operations used to select a portion (aliquot) of the object from which (bio)chemical information is to be extracted***.
(2) ***The first substep in the preliminary operations of the analytical process***.
(3) ***The link between the object and the analytical process***.
(4) ***The foundation of the capital analytical property "representativeness", which, together with "accuracy", characterizes the quality of analytical results***.

4.6. How does the availability of materials and equipment (reagents, solvents, apparatuses, instruments, etc.) influence the choice of an analytical process for a specific sample–analyte pair? Use one or more examples.

Answer:

In the following example, the information required is the content, in ppb, of aflatoxins of whole milk from cows fed with contaminated feed.

The analytical process will be very simple, expeditious and reliable—but also very expensive—if a specific immunoassay is used; also, the sample will require little processing. In the absence of a direct test, the sample treatment will be a complex, time-consuming process using a liquid chromatograph interfaced to a mass spectrometer. This equipment is unaffordable for many laboratories. In fact, a modest peripheral laboratory at a dairy cooperative will hardly be able to obtain the information needed to confirm whether its milk is contaminated with aflatoxins.

4.7. What factors dictate the choice of an analytical method? What is usually the most important?

Answer:

The most important factor is the analytical information required (and its characteristics). Thus, the method of choice will differ depending on whether

- ***overall or discriminate, individual information about a mixture of analytes from the same family (e.g., polyphenols in food) is needed;***
- ***a high accuracy is indispensable (e.g., in the determination of the purity of an imported gold batch);***
- ***the results are to be obtained within a short time (e.g., determining the fat content of an olive batch in order to establish the price to be paid to members of an agricultural cooperative)***.

4.8. Tick the true statements about the preliminary operations of the analytical process:

Answer:

[X] They are equivalent to so-called "sample treatment"
[X] They typically account for 50–70% of the length of a CMP
[ ] They come after measurement and transducing of the analytical signal
[ ] They have little impact on the quality of the final result

4.9. Why is sampling important in chemical measurement processes? Tick the correct answers.

Answer:

[ ] Because it influences selectivity and sensitivity
[X] Because it is essential to assure representativeness in the final result
[ ] Because it is a key to robustness in CMPs
[ ] Because it has a direct impact on the accuracy of the results of CMPs

4.10. Are equipment and method calibration part of a CMP? Why?

Answer:

Both are in fact essential components of CMPs. Thus, it is crucial to ensure proper functioning of the instruments and apparatuses used (equipment calibration) and to unequivocally relate the presence and/or concentration of the analyte to an instrumental signal through, for example, a calibration curve (method calibration).

4.11. Name at least five features of the preliminary operations of CMPs. Is any of them positive?

Answer:

- ***Variable***
- ***Complex***
- ***Difficult to automate and control***
- ***Sources of error***
- ***Sources of hazards to operators and the environment***
- ***Slow***

In principle, none of these features is positive.

4.12. What are the positive contributions of the preliminary operations of CMPs?

Answer:

They allow samples to be prepared for measurement. In fact, most samples cannot be analysed directly—the ideal situation in Analytical Chemistry as it would allow the adverse effects of preliminary operations to be circumvented.

4.13. How are instruments classified according to the nature of the raw signals they provide?

Answer:

Instruments can be

- ***Optical (e.g., atomic or molecular absorption or emission spectrophotometers)***.
- ***Electrochemical (e.g., potentiometers, voltammeters)***.
- ***Thermal (e.g., thermogravimeters, differential thermal analysers)***.
- ***Mass (e.g., balances, mass spectrometers)***.
- ***Magnetic (e.g., nuclear magnetic resonance spectrometers)***.

Various other types of instruments are also used, albeit less commonly, in Analytical Chemistry.

4.14. What are the two information sources for the third step of the analytical process (data processing and result delivery)?

Answer:

(1) ***Experimental data obtained by subjecting samples, standards and blanks to an analytical process***.
(2) ***Tabulated, non-experimental data required for computations (e.g., atomic weights, statistical factors)***.

4.15. Name the five factors governing the development of an analytical measurement process.

Answer:

The choice of an existing CMP—and the development of a new one, if needed—essentially depends on the type of (bio)chemical information to be obtained from the target object or sample. The choice may also be influenced by factors associated to the sample (e.g., availability, nature, state of aggregation), the analyte (e.g., nature, concentration) and whether absolute or relative measurements are to be made.

4.16. What are the two main purposes of the preliminary operations of CMPs?

Answer:

1. ***To facilitate the analytical process (by making the sample ready for measurement)***.
2. ***To improve analytical properties (sensitivity and selectivity, mainly)***.

4.17. Why is variability a negative connotation of analytical processes?

Answer:

Because each sample–analyte combination requires a specific sample treatment. This precludes generalization, so

- ***it entails developing an analytical process and sample treatment suited to each situation; and***
- ***it precludes the development of affordable all-purpose commercial equipment except for widespread determinations such as that of Kjeldahl nitrogen***.

4.18. How is automatability related to the preliminary operations of the analytical process?

Answer:

The mechanical complexity of some preliminary operations of sample treatment (e.g., precipitation, disaggregation, extraction) precludes their automation—which would provide highly interesting advantages such as reduced human involvement and operator risks. Some techniques such as solid-phase extraction (SPE) have benefited from the development of multi-extraction equipment that is highly appreciated by routine laboratories receiving large numbers of samples each day.

4.19. What is the most sluggish, labour-intensive and error-prone step of an analytical process?

Answer:

That of preliminary operations (sample collection and treatment here). According to some authors, sampling does not belong in the analytical process.

4.20. What should be balanced in designing a sampling plan?

Answer:

The number of samples to be collected from the object, which should be as small as possible in order to maximize productivity-related analytical properties, and representativeness (a capital analytical property), which should be as high as possible.

4.21. What are the four types of sampling arising from the overall sampling plan?

Answer:

- ***Intuitive sampling (designed by an experienced analyst)***
- ***Statistical sampling (based on statistical probability rules)***
- ***Directed sampling (when a specific type of information is sought)***
- ***Protocol-based sampling (established by the client or official regulations)***

4.22. What names are samples given according to size and nearness to the object?

Answer:

Bulk sample, aggregate (composite) sample, laboratory sample and test sample (aliquot).

4.23. Distinguish "object" and "sample".

Answer:

The object is the entity about which (bio)chemical information is required (e.g., a river, a mine, an agricultural field).

The sample is an aliquot of the object that is collected according to a specific sampling plan.

4.24. When and why must organic matter in a sample be destroyed in the preliminary operations of the analytical process?

Answer:

Organic matter is destroyed by using an appropriate wet or dry procedure in order to prevent it from interfering with the determination of inorganic analytes.

4.25. What basic properties are favourably affected by separation techniques? What capital property is also favoured? What basic property can be adversely affected?

Answer:

(a) ***Sensitivity (through preconcentration) and selectivity (through interference removal)***.
(b) ***Accuracy, which rests on sensitivity and selectivity***.
(c) ***Precision (random errors increase as more preliminary operations are needed)***.

4.26. How are instruments classified according to the nature of the analytes to be determined?

Answer:

There are two types of instruments according to analyte nature, namely:

Active instruments, which interact with the analyte to have it respond in some form (e.g., by producing fluorescence).

Passive instruments (e.g., a potentiometer), which receive a response from the analyte without the need to previously excite it.

4.27. How are sampling and representativeness related?

Answer:

The capital analytical property "representativeness" rests on the atypical basic property "proper sampling".

4.28. What are the main types of analytical separation systems?

Answer:

There are two types of systems, namely:

- ***Batch systems***.
- ***Continuous systems, which can be chromatographic or non-chromatographic***.

Chapter 5. Quantitative Analytical Processes

5.1. The determination of pyrethrins in a food sample gives a concentration of 10 μg/kg. Express it in ppb and as a percentage.

Answer:

Expressing the stated concentration in ppb entails using a conversion factor. Since 1 ppb is equivalent to 1 μg/kg, then

$$10\,\frac{\mu g}{kg}\cdot\frac{1\ ppb}{1\,\frac{\mu g}{kg}}=10\ ppb$$

Expressing the concentration as a percentage requires using the definition of "ppb" (one part per billion) in order to establish a proportion (a fraction of unity that is then multiplying by 100 to obtain the percentage):

$$10\ ppb\equiv\frac{10\,parts}{10^9\,parts}\rightarrow\frac{10\,parts}{10^9\,parts}\times 100=10^{-6}\%$$

5.2. An amount of 0.231 mg of a compound of molecular weight 114 g/mol is added to a volume of 500 mL of water. Calculate the resulting concentration in (a) mol L^{-1}, (b) ppb and (c) μg/g water.

(a) mol L^{-1}

Answer:

The mass is divided into the molecular weight to obtain an amount of substance (mol) and then by the volume of water used to dissolve it because the resulting solution volume is assumed to be very similar to the volume of water used to prepare the solution:

$$0.231\times10^{-3}\ g\cdot\frac{1\ mol}{114\ g}=2.03\times10^{-6}\ mol$$

$$Concentration\left(mol\ L^{-1}\right)=\frac{2.03\times10^{-6}\ mol}{0.5\ L}=4.06\times10^{-6}\ mol\ L^{-1}$$

(b) ppb

Answer:

Since* 1 ppb *is equivalent to* 1 μg/kg *and, on the assumption that the solution will be so highly dilute that is density will virtually coincide with that of water* (1 g/mL), *then

$$\mathbf{0.231\,mg \equiv 231\,\mu g}$$
$$\mathbf{500\,mL \equiv 500\,g \equiv 0.5\,kg}$$
$$\textit{Concentration}(\mathbf{ppb}) = \frac{\mathbf{231\,\mu g}}{\mathbf{0.5\,kg}} = \mathbf{461\,ppb}$$

(c) μg/g

Answer:

The concentration in ppb obtained in (b) is multiplied by an appropriate conversion factor:

$$\mathbf{461\,ppb} = \frac{\mathbf{461\,\mu g}}{\mathbf{1\,kg}} \cdot \frac{\mathbf{1\,kg}}{\mathbf{1000\,g}} = \mathbf{0.461}\ \frac{\mu g}{g}$$

5.3. How do titrimetries differ from gravimetries? Tick the correct answers.

Answer:

[ ] Titrimetries are not classical method of analysis
[ ] They are not quantitative methods
[X] They use analytical chemical standards ***(only titrimetries do)***
[ ] They are not absolute methods
[ ] They use no atomic weights as chemical standards

5.4. Which features would you associate with titrimetries and gravimetries? Tick the correct answers.

Answer:

Feature	Titrimetries	Gravimetries
Absolute methods using no analytical chemical standards		X
Absolute methods using analytical chemical standards	X	
Relative quantification methods		
Only use atomic weights as standards		X
Use analytical chemical standards	X	
Use base standards	X	X
Have the shortest traceability chain		X

5.5. Briefly describe the foundation of a back-titration.

Answer:

A back-titration must be performed when no direct titration is possible. Essentially, it involves adding excess titrant in order to ensure that the whole amount of analyte present will react and then titrating unreacted titrant with an appropriate reagent.

5.6. Which of the following methods use no analytical chemical standards?

Answer:

[ ] Titrimetries
[ ] Relative interpolation methods
[X] Gravimetries

5.7. What are the key features of absolute analytical methods?

Answer:

Absolute analytical methods possess two main features, namely:

- ***They use base and chemical standards—and also analytical chemical standards in some cases***.
- ***They are used in both Classical and Instrumental Analysis***.

5.8. Convert the following concentrations into percentages:

Answer:

Concentration	%
1 ppm	10^{-4}
1 ppb	10^{-7}
1 µg/L	10^{-7}
1 mg/L	10^{-4}
1 ng/L	10^{-10}

5.9. What are the differences between gravimetry and titrimetry in the following respects?

Answer:

	Gravimetry	Titrimetry
Type of analytical method used	***Absolute calculable***	***Absolute calculable***
Standards used	***Base, chemical***	***Base, chemical, analytical chemical***
Analytical properties	***High accuracy, short traceability chain***	***Low accuracy, high simplicity, high expeditiousness***

5.10. Explain the differences between "absolute" and "relative" quantification methods.

Answer:

Absolute methods use a mathematical law in combination with a tabulated constant to calculate the amount of analyte present in a sample.

On the other hand, relative methods compare experimental signals for standards with that for the analyte in order to calculate the amount of analyte.

5.11. What analytical properties apply to Quantitative Analysis?

Answer:

The three types discussed in Chap. 2***, namely***:

- ***Capital properties: accuracy and representativeness***.
- ***Basic properties: precision, sensitivity, selectivity, robustness and proper sampling***.
- ***Productivity-related properties: expeditiousness, safety and cost-effectiveness***.

5.12. What are the instruments typically used in Classical Quantitative Analysis?

Answer:

Basically, the classical burette in titrimetries and the two-pan balance in gravimetries.

5.13. Name the two types of calculable methods and give an example (analytical process) of each.

Answer:

	Calculable methods	Example
1	***Absolute methods using no analytical standards***	***Gravimetry***
2	***Absolute methods using analytical standards***	***Titrimetry***

5.14. Describe several ways of expressing the results in Quantitative Analysis.

Answer:
A quantitative result can be expressed in two different forms, namely:

- ***Absolute (as a mass)***.
- ***Relative: as a proportion (e.g., %, ppm, ppb), a mass–volume ratio (e.g., g/L) or as a mass–mass ratio (e.g., g/kg)***.

5.15. What type of quantitative analytical method requires no method calibration? Why? Give an example.

Answer:
Method calibration is unnecessary in absolute methods using no analytical standards (e.g., gravimetries) because they have a very short traceability chain and their results can be directly related to base and chemical standards.

5.16. What is the gravimetric factor? Tick the correct answer.

Answer:

[X] A ratio of molecular or atomic weights.
[X] A dimensionless number that is multiplied by the gravimetric weighing to calculate the mass of analyte
[ ] A number by which the atomic weight of the analyte is multiplied to express the result
[X] A factor calculated from the molecular weight of the weighed form

5.17. What are the five requirements to be fulfilled by a chemical reaction to be useful for titrimetric purposes?

Answer:

(1) ***A well-defined stoichiometry***.
(2) ***Developing to completion (that is, having a large product formation constant)***.
(3) ***Being fast***.
(4) ***Being selective***.
(5) ***Having an appropriate end-point indicator***.

5.18. Name the three types of visual indication systems in titrimetry.

Answer:

(1) ***Auto-indicators***.
(2) ***Chemical substances interacting with the analyte***.
(3) ***Chemical substances interacting with the titrant***.

5.19. Is Classical Quantitative Analysis possible with a relative method? Why?

Answer:
No. The instruments used in Classical Analysis produce no signals. Therefore, they do not allow the use of a relative method to compare the signal for the sample with that for a standard.

5.20. Why does sensitivity in gravimetries increase with decreasing gravimetric factor?

Answer:
Because the smaller the gravimetric factor is, the greater is the molecular weight of the weighted form relative to the analyte—and hence the smaller is the amount of analyte that can be detected in a given gravimetric weighing.

5.21. What is a titrimetry? Tick the correct answer.

Answer:

[ ] A quantitative method for identifying analytes
[ ] A relative interpolation method
[X] An absolute quantitative method using analytical standards
[ ] An absolute quantitative method using no analytical standards

5.22. Explain the relationship between gravimetric factor and sensitivity in gravimetry.

Answer:

$$P_A = G \cdot P_g$$

The smaller the gravimetric factor (G) is, the higher is the sensitivity of a method (that is, the smaller is the amount of analyte it can detect with a gravimetric weighing).

Chapter 6. Qualitative Analytical Processes

6.1. Does the qualitative analysis of samples fit in Classification Analysis?

Answer:

Yes. This is the simplest form of classification analysis. Samples are classified into two groups depending on whether they give a YES response or a NO response. Dubious samples may be included in a third group.

6.2. What name is usually given to qualitative analytical processes?

Answer:

Test (or assay).

6.3. Tick the analytical properties that are not applicable to Qualitative Analysis.

Answer:

[ ] Representativeness
[X] Accuracy
[X] Precision
[ ] Sensitivity ***(only the limit of detection can be used)***

6.4. Two methods for the qualitative analysis of milk samples possibly contaminated with pesticides provide wrong information. Thus, method A gives false positives and method B false negatives. Which would you use? Why?

Answer:

Method A because

(a) ***it gives no false negatives; and***
(b) ***any false positives it provides can be ascertained by using an appropriate confirmation technique***.

6.5. What are the main differences between Qualitative Analysis and Quantitative Analysis? Tick the correct answers.

Answer:

[X] The binary response
[ ] A classical method of analysis
[ ] The use of analytical chemical standards
[X] The analytical property "reliability"
[ ] Selectivity

6.6. What are the differences between binary and multiple classification in Qualitative Analysis?

Answer:

Binary classification splits the body of samples into two groups only according to whether they give a YES response or a NO response. On the other hand, multiple classification provides more than two groups according to various criteria (e.g., the origin of wine samples).

6.7. What are the factors dictating the following parameters?

Answer:

(a) Limit of detection ***(The analytical process, CMP)***
(b) Cut-off concentration ***(The laboratory)***
(c) Threshold concentration ***(Applicable legislation and the client)***

6.8. What is a false positive in Qualitative Analysis? Give an example.

Answer:

A YES response which should have been NO.

Example: A YES response to an analyte concentration of 1.5 ppb by a method with C_{LOD} = 2 ppb is a false positive.

6.9. What is a false negative in Qualitative Analysis? Give an example.

Answer:

A NO response which should have been YES.

Example: A NO response to an analyte concentration of 2.5 ppb by a method with C_{LOD} = 2 ppb is a false negative.

6.10. An immunochemical test (method A) and a chemical spot test (method B) are used to detect the same analyte in the same sample. The results of analysing 100 samples are as follows:

	Reliability (%)	False positives (%)	False negatives (%)
Method A	95	2	3
Method B	94	6	0

Which method provides the better results? Why?

Answer:

Method B. Although it is less reliable, its proportion of false negatives is 0%, which makes it highly reliable. Also, any false positives it provides can be ascertained by using a confirmation technique.

6.11. What analytical properties are applicable to quantitative determinations but not to qualitative tests? Why?

Answer:

Accuracy, precision and two sensitivity-related parameters (IUPAC's S and the limit of quantification, C_{LOQ}).

6.12. What are "analytical systems with group separation" in Classical Qualitative Analysis?

Answer:

Analytical schemes that are used to classify analytes experimentally (e.g., by chemical precipitation). The resulting groups allow the analytes in them to be determined individually (that is, without interference from the others in the group).

6.13. What are the differences between group, identification and masking reagents in Classical Qualitative Analysis?

Answer:

Group reagents ***allow a mixture of analytes to be separated into groups where each individual analyte can be reliable detected***.

Identification reagents ***react with the analyte to produce an external effect (e.g., a colour change, formation of a gas or precipitate) that can be identified by the human senses***.

Masking reagents ***form stable, soluble, colourless chelates with interfering species***.

6.14. Name two identification (Qualitative Analysis) procedures used in dynamic instrumental systems (e.g., chromatography).

Answer:

- ***Use of an internal standard to make standardized measurements***.
- ***Addition of a standard of the analyte to the sample***.

6.15. Tick the words directly connected with Qualitative Analysis:

Answer:

[X] Detection
[ ] Quantification
[X] Identification
[X] Qualification

6.16. How does a "white" sample differ from a "black" sample?

Answer:

A white sample is a sample whose properties are quite well-known or predictable (e.g., water from a spring). On the other hand, a black sample is one whose properties are completely unknown (e.g., a previously never analysed lunar rock).

6.17. Is Qualitative Analysis important to modern Analytical Chemistry? Why?

Answer:

Qualitative Analysis in its classical and instrumental forms continues to be in wide use today because most of the analytical information required is of the binary type.

6.18. What are the three quantitative landmarks for the binary response in Qualitative Analysis?

Answer:

The limit of detection (C_{LOD}), the cut-off concentration (C_C) and the threshold concentration (C_L).

6.19. One brand of canned tuna fish contains 4 ppm tin. A qualitative test with $C_{LOD} = 1$ ppm for the metal gave a positive (YES) response. What type of error was made?

Answer:

[X] None
[ ] A false positive
[ ] A false negative

6.20. What type of error is the more crucial in Qualitative Analysis? Why? Give an example.

Answer:
A false negative because a NO response terminates the process whereas a YES response requires confirmation.

6.21. Is "specific uncertainty" applicable to Qualitative Analysis? Why?

Answer:
No. It must be adapted to the singularities of Qualitative Analysis in the form of an unreliable range around the threshold or cut-off concentration within which errors (false positives and false negatives) occur.

6.22. What are the three most important limitations of Classical Qualitative Analysis in relation to Instrumental Qualitative Analysis?

Answer:

- ***A low sensitivity***
- ***A low selectivity***
- ***A narrower scope***

6.23. What are the three types of reagents used in Qualitative Analysis? What is their purpose? Give an example of each.

Answer:

	Name	Purpose	Example
Type 1	***Identification***	***Recognition***	***Detection of Pb^{2+} with I^-***
Type 2	***Group***	***Grouping species to avoid interferences***	***Separation of Ag^+, Pb^{2+} and Hg_2^{2+} with Cl^-***
Type 3	***Masking***	***Avoiding interferences***	***CN^- to detect Cd^{2+}***

6.24. What are the three main features of so-called "analytical schemes without group separation"?

Answer:

- ***They use highly sensitive and selective reagents***
- ***Their operational sequence must be strictly followed***
- ***They occasionally require using a separation technique***

6.25. What is the difference between a dynamic and a static instrumental system in Qualitative Analysis?

Answer:
In a dynamic system, the instrumental signal is time-dependent; in a static system, it does not change with time.

6.26. What analytical properties are applicable to Qualitative Analysis?

Answer:

- ***Capital (accuracy and representativeness)***.
- ***Basic (sensitivity, selectivity, precision and robustness)***.
- ***Productivity-related (expeditiousness, cost-effectiveness and safety)***.

6.27. Are both types of calibration applicable to Qualitative Analysis?

Answer:

Method calibration [X] Yes [ ] No
Equipment calibration [X] Yes [ ] No

6.28. What types of instruments does Classical Qualitative Analysis use?

Answer:
It uses the human senses (sight and smell, mainly) as instruments.

6.29. What are masking reagents? In what context are they used?

Answer:
Masking reagents are substances forming stable, soluble, colourless chelates with interfering substances which enable the reliable identification of a species in a group or a sample without the need for separation. They are typically used in Classical Qualitative Analysis.

6.30. Define "reliability" in Qualitative Analysis. To which classical analytical properties does it relate?

Answer:

- ***The proportion of correct YES/NO answers obtained by subjecting a large number of aliquots from a standard sample to a qualitative process (a test)***.
- ***A combination of the properties "accuracy" and "precision", which are used in Quantitative Analysis***.

6.31. Instrumental Qualitative Analysis relies on a triple comparison of signals to be subjected to the analytical process. What do the three signals belong to?

Answer:

- ***A sample standard containing the analyte***.
- ***A blank (that is, a sample not containing the analyte)***.
- ***A sample***.

Chapter 7. Analytical Problem-Solving

7.1. Identify the binary interfaces between Analytical Problem-Solving, Analytical Quality and Social Responsibility.

Answer:

	Analytical Problem-Solving	Analytical Quality	Social Responsibility
Analytical problem-solving	×	***Analytical properties as indicators Satisfying information requirements***	***Satisfying information requirements as an internal connotation of Social Responsibility***
Analytical quality	***Analytical properties as indicators Satisfying information requirements***	×	***Quality as a general approach to Social Responsibility***
Social responsibility	***Satisfying information requirements as an internal connotation of Social Responsibility***	***Quality as a general approach to Social Responsibility***	×

7.2. What is the third basic standard in Analytical Chemistry? How is it related to the analytical problem?

Answer:

The third basic Standard of Analytical Chemistry is "required information", which constitutes the foundation, core and goal to be fulfilled in order to solve the analytical problem: the analytical problem delivers the required information.

7.3. How would you define "fitness for purpose"? To which facet of representativeness is it related? Is it related to chemical metrology?

Answer:

"Fitness for purpose" is the suitability of the information or results delivered for the intended purpose and is related to the highest level of representativeness in the results, which arises in the socio-economic (external) realm. However, it is completely unrelated to chemical metrology, where representativeness bears an orthodox, internal meaning, namely: consistency of the relationship of the results with the sample or aliquot used to obtain them.

7.4. Describe the roles of the analytical problem in the basic and applied sides of Analytical Chemistry.

Answer:

On the basic side, the analytical problem operates as a support and as an incentive to improve the intrinsic foundations of Analytical Chemistry (analytical properties, sampling). Also, it facilitates harmonization and communication among the different branches of Science for effective transfer of information and mutual recognition of their results.

On the applied side, the analytical problem is a means for fulfilling clients' information needs. In fact, correctly solving the analytical problem provides a solution to a real-life socio-economic problem.

7.5. How does the analytical problem relate the analytical chemist to the client?

Answer:

The analytical problem is the communication interface between clients and analytical chemists, and the link between the following pairs of elements:

(1) ***The socio-economic problem and the analytical process. The analytical process is designed in accordance with the specificities of the analytical problem, which in turn is conceived with the requirements of the particular socio-economic problem to be solved in mind***.
(2) ***The information needs and analytical properties. The information required by clients is converted into objectives to be fulfilled in order to solve the analytical problem—and the objectives contain the analytical properties needed to solve it***.
(3) ***External quality and internal (analytical) quality. Internal quality reflects quality in the results and in the analytical process with a view to solving the analytical problem. It should match external quality, which is required by the client to solve the originating socio-economic problem***.

7.6. What are the components of the concept hierarchy containing the analytical problem? What place does the analytical problem take in it?

Answer:

The analytical problem is at the top of the scope hierarchy:
Analytical problem > Object > Sample/Aliquot > Analyte.

7.7. How would you relate the analytical problem to the leading concepts "reports", "external quality" and "to analyse" in other hierarchies?

Answer:

The analytical problem requires a solution that is provided by results that are obtained by analysing and contained in a report. The quality of the results should match the external quality needed for the socio-economic problem to be properly solved.

7.8. Distinguish "orthodox" representativeness from "maximum" representativeness. Which traceability chain does each belong to?

Answer:

"Orthodox representativeness", which is that implicit in chemical metrology, is the consistency between the results and the sample or aliquot analysed to obtain them. Therefore, it applies to traceability of the results to the sample or aliquot.

"Maximum representativeness" comprises consistency between the results and the sample or aliquot used to obtain them, and also between the analytical problem and the socio-economic problem. The concept includes fitness for purpose, which pertains to the applied, socio-economic side of Analytical Chemistry only. Therefore, maximum representativeness is associated to the traceability chain results–sample (aliquot)–analytical problem–socio-economic problem; also, it is the result of a mixed (orthodox–heterodox) approach to traceability of the sample (aliquot).

7.9. A river is suspected to be polluted with toxic organic waste that may be having adverse effects on the nearby population. This hypothesis is verified by collecting 200 samples of water at different depths along the river for analysis. The method used has a limit of detection of 0.7 ppm and a limit of quantification of 2.1 ppm. The effects of the organic waste are felt at concentrations above 3 ppm. The concentration of waste obtained with the chosen method as the average of 200 individual values is 2.7 ppm.

(a) Complete the following table.
(b) Can the socio-economic problem addressed be correctly solved?
(c) Does the analytical method require any corrective actions?

Answer:

(a)

Socio-economic problem	***Checking whether the river is contaminated with toxic organic waste***
Analytical problem	***Detecting and determining organic compounds with potentially detrimental effects on the population***
Object	***The river***
Sample/aliquot	***Water from the river as collected at a variable depth at different points along its course***
Analyte(s)	***Toxic organic compounds***
Limit of detection (C_{LOD})	**0.7 ppm**
Limit of quantification (C_{LOQ})	**2.1 ppm**
Legal limit (C_{LL})	**3 ppm**
Result ($C_{obtained}$)	**(2.7 ± 0.1) ppm**

(b)

Yes. The socio-economic problem can be solved because the analytical process allows the presence of toxic organic compounds to be confirmed and their concentration, which is close to the legally accepted limit, determined.

(c)

No corrective actions are needed because the limits of detection (C_{LOD}) and quantification (C_{LOQ}) are valid for detecting and quantifying the analytes—both are lower than the legal limit (C_{LL}).

7.10. What are the intangible elements of an analytical problem? How do they relate to the steps of the analytical problem-solving process?

Answer:

Intangible elements: planning, design, evaluation and correction, which are connected to the steps of the analytical problem-solving process as follows:

1. ***"planning" to the first and second step (identification, confirmation and definition of the information requirements);***
2. ***"design" to the third step (planning of the analytical strategy);***
3. ***"evaluation" to the fourth step (monitoring and validation of the results); and***
4. ***"correction" to the fifth step (corrective actions)***.

7.11. Define and briefly describe the five steps of the analytical problem-solving process. Give an example of socio-economic problem and describe the steps needed to solve it.

Answer:

First step: Identification of the information requirements, which rests on effective communication between the client and the analytical chemist in order to define the characteristics of the information needed. Example: the client asks the analytical chemist to determine whether a salmon batch is fit for marketing based on its pinkish colour.

Second step: Specifying the analytical information required. Conversion of the socio-economic information requested in the first step into analytical information. Example: the analytical chemist associates the pinkish colour of salmon to the concentration of astaxanthin.

Third step: Planning the analytical strategy. Development of the methodology to be applied (an appropriate analytical process). Example: The analytical chemist develops a method by which samples are subjected to solid–liquid extraction, elution with acetone and liquid–liquid extraction with hexane in order to isolate astaxanthin free of interferences from other substances. The pinkish colour is determined by using a photometer to measure the absorbance at 470 nm of the hexane extract.

Fourth step: Monitoring the results, which involves assessing them against internal and external references. If the results are correct, the analytical process will have been solved; otherwise, a fifth step will be needed. Example: The experimental result is compared with a tabulated reference and the analyte percent recovery as determined by adding a known amount of astaxanthin as internal standard to a sample.

Fifth step: Corrective actions. Identifying errors in the previous steps and correcting them. After each corrective action, the process returns to step 4 until the analytical problem is solved. Example: if the results are not acceptable, the solvent used in either or both extractions may have to be changed with a similar one where astaxanthin is more readily soluble.

7.12. Why is fluent communication between the analytical chemist and the client important in the first step of the analytical problem-solving process?

Answer:

Because it is the origin of the integral definition of "required information" and hence the only way in which the analytical chemist can know what the client needs and how to supply it.

7.13. Name three essential items of information needed to identify the analytical information required in the second step of the analytical problem-solving process.

Answer:

- ***The characteristics of the sample (sampling + sample size)***.
- ***The type of analyte or measurand sought, and the type of analysis to be performed***.
- ***The required levels of analytical properties***.

7.14. What is the purpose of the third step of the analytical problem-solving process? What are the factors influencing selection and design of a CMP?

Answer:

The third step involves designing and developing an analytical process suited to the client's information needed in order to obtain useful results for the intended purpose.

The factors influencing the choice of an existing process or the development of a new one include

- ***the type of information required (general or analytical);***
- ***the specific analyte or measurand;***
- ***the laboratory's human, technical and economic resources; and***
- ***the agreed cost (overall or per analysis)***.

7.15. What are the references used to assess the results in the fourth step of the analytical problem-solving process? How are they related to quality?

Answer:

Results are assessed with respect to two main references, namely:

(1) ***The minimum levels of analytical properties required by the client, which may or may not be fulfilled by the laboratory. This reference is associated to internal (analytical) quality in the results because it pertains to the analytical realm***.

(2) ***The information required by the client (the intended purpose). The results must be validated and properly interpreted in order to solve the originating socio-economic problem. This reference is associated to external quality in the results because it falls outside the scope of the analytical laboratory: the analytical information delivered must be interpreted by the client or expert professionals in order to solve the socio-economic problem***.

7.16. When is the fifth step of the analytical problem-solving process needed? Why?

Answer:

The fifth step (corrective actions) is needed when the results of a CMP are not valid (that is, when they do not meet the required levels of quality and analytical properties or do not allow the socio-economic problem to be solved).

This step is intended to correct errors made in the previous ones. Such errors may arise from poor communication between the client and the analytical chemist, misidentification of the analytical information needed or use of a CMP whose results do not allow the socio-economic problem to be solved.

7.17. How can delivered information be in relation to required information? Give an example of each situation.

Answer:

The following situations are possible:

(1) ***Delivered information = Required information. The two are completely identical. Example: A client requires the content in vitamin C of a given fruit juice and the analytical chemist provides the amount of ascorbic acid (that is, vitamin C) present.***

(2) ***Delivered information $\neq$ Required information. The two are completely different: what is delivered is not what was expected. Example: A client requires the content of vitamin C in a fruit juice and the analytical chemist provides the amount of retinol (vitamin A) in it.***

(3) ***Delivered information < Required information. The client is supplied with inadequate information. Example: A client needs the amounts of vitamins A and C in a juice but the analytical chemist only provides the amount of retinol (vitamin A) present.***

4) ***Delivered information > Required information. The client receives more information than is needed for the intended purpose. Example: A client needs the amount of vitamin C but the analytical chemist additionally supplies those of retinol (vitamin A) and cyannocobalamin (vitamin B12), both of which are superfluous for the intended purpose.***

7.18. In order to decide whether a person should be pronounced guilty of murder, a laboratory is asked to perform a comparative analysis of a blood sample from the defendant and one containing a mixture of blood from the defendant and the victim blood found in the crime scene. The analysis involves determining the DNA sequence of the defendant, the victim and the mixed blood sample. Please complete the following table by identifying the different elements.

Answer:

Socio-economic problem	***Whether the defendant is guilty or not guilty***
Analytical problem (1st step)	***A comparative analysis of blood from the victim and the defendant with that found in the crime scene***
Analytical information (2nd step)	***A qualitative (comparative) characterization of the blood samples for DNA***
CMP to be used (3rd step)	***– Individual analyses of blood from the victim and the defendant*** ***– Analysis of the mixed blood sample found in the crime scene and of an artificial mixture containing blood from the victim and the defendant*** ***– Separation of the two types of blood contained in the mixture for individual analysis***
Verification of the results (4th step)	***Comparison of the results for the victim-defendant mixed blood sample and the crime scene sample*** ***Comparison of the DNA profile for the defendant with that for the mixed sample not containing blood from the victim***

Chapter 8. Analytical Chemistry and Quality

8.1. To what analytical chemical concepts do the basic and applied sides of quality relate?

Answer:

The relationship between Analytical Chemistry and Quality has two sides: a basic side and an applied side. On the basic side, Quality is defined as the body of characteristics, properties, attributes or abilities of an entity that make it better, worse than or equal to, other entities of the same type. Consequently, the basic side relates the major analytical chemical concepts (analytical properties) with Quality in its broadest sense.

On the applied side, Quality is understood as the body of characteristics of an entity that allow it to fulfil specific or implicit requirements of clients or legislation. This side has to do with the implementation of Quality Systems in analytical laboratories and is therefore related to the analytical problem.

8.2. What types of indicators are used to assess quality?

Answer:

The comparisons inherent in the very notion of Quality can be made by using various types of indicators. Thus, there are quantitative (numerical data), qualitative (e.g., opinions) and integral indicators (combinations of the previous two). Obviously, the last are the most comprehensive. For example, properly characterizing a natural environment involves more than simply checking that the typical parameters (e.g., temperature, pollutant concentrations in air, water and soil) fall within acceptable or legally set ranges. The human perception of well-being is different in technical "clean", appropriate places. Also, a given type of agri-food may fulfil all applicable regulations and yet lack the quality needed for marketing owing to an unappealing appearance, colour or flavour.

8.3. How are the quality expected and that perceived by the "client" related to the quality planned and designed a body or organization?

Answer:

Achieved quality falls at the boundary between external and internal quality. The primary aim of an entity is to have achieved quality fully coincide with designed quality. On the other hand, clients expect perceived quality to surpass or at least match expected quality—the former may increase expenses for the entity concerned. The most critical comparison is that of expected and perceived quality. Ideally (total quality), the three types of quality should coincide.

8.4. Distinguish external and internal quality, and relate the two, through two examples: (*a*) a government environmental agency and (*b*) analytical laboratory.

Answer:

Quality can be classified in various ways. One divides quality into internal and external. Internal quality is quality in the entity delivering products or services, whereas external quality is that in the client receiving them.

Example (a)

In an environmental agency, internal quality refers to quality of the agency itself, which influences its management and staff, whereas external quality refers to client satisfaction. For example, the clients of an environmental certification agency may be firms seeking certification of their environmental management and quality, professionals attending training courses taught by the agency, individuals or firms commissioning environmental studies, etc.

Example (b)

In an analytical laboratory, external quality refers to quality of the client or user (e.g., a farmer needing to have his irrigation water analysed, members of a residents' community wishing to have the quality of their pool water assessed). On the other hand, internal quality coincides with analytical quality, which is that leading to external quality by fulfilling information requirements. Internal quality rests on quality in the results, analytical processes, work and its organization, and the analytical tools used.

8.5. What are quality trade-offs? Give some examples in various fields.

Answer:

Quality is not utopic. Ideally, a body should reach a high level of internal properties in an expeditious, economical and safe manner. In practice, however, internal, economic, and time- and safety-related features are frequently contradictory and require adopting some trade-off. Thus, if quality is to be achieved by maximizing intrinsic properties, costs can be expected to rise, processes to be slower and staff involvement to increase.

One clear example in the field of clinical analysis is that of a patient admitted to the emergency department of a hospital. The patient will have to be correctly diagnosed (e.g., with a blood analysis for various parameters) in order to be properly treated. This situation will require expeditiousness at the expense of other analytical properties and also greater staff involvement.

One other example is that of the determination of inorganic nitrogen in a fertilizer. If a very large number of samples is to be analysed each day, the laboratory may seek to minimize costs by using an appropriate tool from a wide range of choices from a straightforward burette to a sophisticated neutron activation analyser, for example. The particular tool or technique of choice will also depend on the intrinsic properties the results are to have, the availability of staff to implement it and the time taken by each individual analysis.

Finally, the determination of the gold content of a jewel in order to assess its purity should prioritize accuracy because the jewel price will depend considerably on it. This will entail maximizing intrinsic properties at the expense of increased costs—the increase may be offset by rising the jewel price as well, however—longer analysis times and greater staff involvement.

8.6. What are the structural landmarks in the quality of a body or organization?

Answer:

First, the body or organization should have a Quality Policy in the form of a document endorsed by the top decision organ. The Policy materializes in Quality Management elements and operational systems that are realized in Quality Assurance, which encompasses all activities performed in order to assure quality in the body or organization concerned. Such activities include Quality Control, which involves direct assessment of the body or organization in terms of quantitative indicators mainly; Quality Assessment, which involves examining both the body or organization and its activities; and internal corrections deriving from the previous two types of activities.

8.7. Explain some direct or indirect benefits of implementing a Quality System.

Answer:

The direct benefits of a Quality System are improved characteristics of the product, system or service. The improvements can be expected to increase client satisfaction, and also the supplier's credibility and prestige. For example, satisfied clients are bound to recommend the services of laboratories they trust to their acquaintances and their positive opinions are bound to increase the prestige of the recommended laboratories as a result.

As regards indirect benefits, implementing a Quality System can lead to new jobs (e.g., staff for the Quality Assurance Unity of Good Laboratory Practices). One other potential benefit is more rational work avoiding superfluous repetitive tasks by careful planning of laboratory activities in developing the Quality Manual. Any deficiencies and mistakes arising during operation will thus be clearly exposed. Also, using a Quality System makes it easier to establish and clarify goals, helps reduce indecision and facilitates fluent communication.

8.8. In what way is Analytical Quality related to analytical properties? To which properties are (*a*) quality of results and (*b*) quality of the analytical process related?

Answer:

In its basic definition, Quality is a body of characteristics or properties. As a result, analytical properties are directly related to analytical quality and allow its different facets to materialize. Thus, the quality of analytical results is related to the capital analytical properties (accuracy and representativeness), integration of which is indispensable.

Also, basic and productivity-related analytical properties are attributes of the analytical process. Thus, the basic properties (robustness, precision, sensitivity, selectivity and proper sampling) provide support for the capital properties, whereas the productivity-related properties (expeditiousness, cost-effectiveness and safety) characterize laboratory productivity.

8.9. What is the relationship of quality to analytical quality?

Answer:

Quality can be defined as a body of properties and is thus related to analytical quality through analytical properties. Analytical properties play a central role in the materialization of the characteristics of required analytical information—a crucial reference for assessing results.

Also, properly solving an analytical problem entails fulfilling the client's information needs and ensuring consistency between required analytical information and laboratory-delivered information (that is, ensuring the degree of analytical quality required to achieve external quality). In the analytical chemical realm, this entails comparing with standards, whether written or otherwise, and also with the client's information needs.

8.10. Distinguish external and internal corrective actions in the framework of Quality Assurance.

Answer:

Quality Assurance comprises Quality Assessment, Quality Control and, if needed in view of the quality of the results, Internal Corrective Actions. Such actions may lead to partial or total changes in control activities. Quality Assurance activities of the three types frequently raise the need for corrective (external) actions initially involving the laboratory. Such actions must assure quality in the analytical processes performed by the laboratory through properly organized and conducted work, and the use of effective analytical tools. In any case, corrective actions should lead to improved quality in the laboratory's analytical results and ability to solve analytical problems.

8.11. What Quality Assurance elements examine an analytical laboratory?

Answer:

Quality Assurance involves examining both Quality Control activities and the analytical laboratory—in addition to the results it produces and its ability to solve specific analytical problems. Quality Control essentially involves examining the laboratory and its results.

8.12. Comment on the cyclic nature of Quality Assurance activities in the analytical chemical realm.

Answer:

The activities inherent in the three elements of Quality Assurance are in fact cyclic in nature. Thus, Quality Control, which comes into play before and during the analytical process, involves examining the analytical laboratory and the results it produces. By contrast, Quality Assessment takes place during and after the analytical process. Finally, Corrective Actions are usually performed after the analytical processes if judged necessary from the outcome of the assessment and can lead to changes in control activities or the adoption of new ones the next time the analytical process is conducted.

8.13. On what standards and elements do Quality Systems applied to analytical laboratories rest?

Answer:

The main frameworks for developing quality systems in analytical laboratories are as follows:

- ***The general standard ISO 9000 (Quality Management Systems. Fundamentals and Vocabulary)***.
- ***The specific standard 17025 ("General Requirements for the Competence of Testing and Calibration Laboratories), which, as implied by its title, applies to testing and calibration laboratories only***.
- ***Good Laboratory Practices (GLPs), which comprise Standard Operating Procedures (SOPs) and the Quality Assurance Unit (QAU)***.

Quality systems can also be developed from combinations of major standards, Total Quality Systems and Critical Point Systems, among others.

8.14. What are the goals of ISO 17025?

Answer:

The main goals of ISO 17025 are as follows:

(a) ***To establish a Quality Management System requiring no external recognition***.

(b) ***To have technical competence recognized by clients, regulation authorities or accreditation bodies***.

8.15. What are Good Laboratory Practices?

Answer:

Good Laboratory Practices (GLPs) are bodies of rules, operational procedures and practices established by a given institution such as the Organization for Economic Cooperation and Development (OECD) or the European Union (EU) that are deemed compulsory with a view to assuring quality and correctness in laboratory results.

GLPs are issued by international bodies and adopted by national governments through publication in their official state gazettes and are typically binding for laboratories performing socially influential analyses such as those of pharmaceuticals, cosmetics, foodstuffs and products with a potential environmental impact.

8.16. What are Standard Operating Procedures? Where are they used?

Answer:

A Standard Operating Procedure (SOP) is a detailed description of each individual activity to be performed by a laboratory (e.g., sample handling; control of reagents, reference materials, equipment and methods; archiving).

8.17. What is the Quality Assurance Unit?

Answer:

The Quality Assurance Unit (QAU) is an essential element of Good Laboratory Practices. The Unit consists of staff belonging to the laboratory's parent body but not to the laboratory itself and is answerable to the body's management only. The QAU's roles include implementing, controlling and assessing quality with a view to proposing improvement actions.

8.18. What is a primary method? How does it affect analytical quality?

Answer:

Primary quantification methods are at the top of the metrological quality ranking. According to the Consultative Committee for the Amount of Substance (CCQM), a primary method is "a method having the highest metrological qualities, whose operations can be completely described and understood, for which a complete uncertainty statement can be written down in terms of SI units and whose results are, therefore, accepted without reference to a standard of the quantity being measured".

In summary, a primary method possesses a high metrological quality, is completely described and understood, is subject to well-defined uncertainty in terms of SI base standards and requires no analyte standard.

8.19. What is the difference between an official method and a standard method?

Answer:

An official method is a quantification method described in detail and issued by a government body such as the US Environmental Protection Agency (EPA) for legal adoption with a view to sanctioning the results of laboratories. Some official methods are used as reference methods, however.

On the other hand, a standard method is a method developed, validated and issued by a standardization body (ISO, CEN) or an association supporting Analytical Chemistry (e.g., the AOAC).

8.20. What activities does quality control involve?

Answer:

Quality Control is a body of planned, documented actions to be performed by laboratory staff in order to directly examine the laboratory's work, the tools it uses and the results it produces. Such activities typically include the following:

(a) ***Implementing and using control charts based on reference materials***.
(b) ***Examining and correcting instruments and apparatuses to ensure that they operate as they should***.
(c) ***Examining the purity and stability of the reagents and solutions used in CMPs***.
(d) ***Examining experimental laboratory conditions such as temperature, relative humidity, cleanliness and presence of contaminants***.
(e) ***Examining the sample custody system in order to ensure correlation between samples and results***.
(f) ***Using RMs and CRMs to examine CMPs at specific points***.
(g) ***Examining any changes in the results arising from the use of a CMP to determine specific analytes in a given sample by different staff or with different analytical tools***.

8.21. Why is labelling quality assessment activities as external or internal confusing?

Answer:

Depending on the assessor (that is, on the human factor), Quality Assessment is classified as internal or external. This classification, however, can be confusing because it rests on at least two different criteria. Thus, assessors may members of the laboratory staff, its parent body or an external entity. It is therefore preferable to classify Quality Assessment according to the following two alternative criteria:

- ***Whether the assessors belong to the laboratory. Their assessment will be of the internal type if they do and of the external type if they do not. In the latter case, Quality Assessment will be external–internal if the assessors are members of the parent body but not of the assessed laboratory and external–external if they belong to another body***.
- ***Whether the assessors belong to the assessed body. Their assessment will be internal if it is conducted by staff from the laboratory or its parent body, and external if performed by staff from another body***.

8.22. What are the goals of interlaboratory exercises? Where do they fall in the analytical quality realm?

Answer:

Interlaboratory exercises constitute a mode of external–external quality assessment. Each participating laboratory analyses the same sample to determine the same analyte(s) in order to have its results quantitatively assessed by comparison with those of the other laboratories.

The main goal of an interlaboratory exercise is to compare results and their uncertainty, and its primary objectives are (a) to have inexperienced laboratories learn to conduct specific CMPs; (b) to validate CMPs developed in response to new information needs; (c) to have the values and uncertainties for a given CRM certified; and (d) to have the quality of the results produced by the participating laboratories assessed.

8.23. Why are documentation and archiving activities the bottleneck in implementing quality in a laboratory?

Answer:

Documentation and archiving activities are in fact the bottleneck of Quality Assurance programmes and the greatest hindrance to implementing and monitoring Quality Systems in analytical laboratories. Thus, documentation and archiving are two time-consuming activities that frequently make laboratory staff reluctant to adopt a Quality System.

A laboratory having a Quality System must document and archive everything as stated in a Standard Operating Procedure (SOP) describing how each

laboratory operation is to be performed. Also, the laboratory must record sample custody chains and how its equipment performs after it is installed; also, it must monitor materials, SOPs, primary data, results, reports and documentation activities themselves, all of which demand a strong commitment.

8.24. What is external–external assessment? Give some examples and distinguish it from external–internal assessment.

Answer:

External–external assessment is performed by experts from a body other than that being assessed and hence doubly external to the laboratory. The activities to be performed for this purpose are known as "audits" in the realm of Quality. Audits can be conducted on systems (qualitative, visual and documental examination), performance (quantitative) or both (integral audits). In the analytical realm, audits can be of two main types, namely: (a) direct, which lead to accreditation of laboratories; and (b) indirect (e.g., proficiency testing).

One example of external–external assessment is that of a laboratory wishing to be accredited for performing a given type of clinical analysis. The auditors should belong neither to the candidate laboratory nor to its parent; rather, they should pertain to a certified national auditing body, whether public or private.

One other example is that of a laboratory wishing to assess a method it is using to determine benzene by participating in an interlaboratory exercise in order to compare its results with those of other laboratories analysing the same sample for the analyte. Usually, the body coordinating the exercise will be independent of the interested laboratory's parent body. Therefore, the laboratory will be subjected to external–external assessment of its results.

In external–internal assessment, the assessors are staff members of the interested body but not of its laboratory. One example is that of an agri-food multinational firm having several factories each with its own quality control laboratory in the same country. The body's headquarters may set up an intercomparison exercise involving the different quality control laboratories, whose results will be assessed by staff from the body but not from any of the laboratories.

8.25. Who accredits analytical laboratories? What is laboratory accreditation based on?

Answer:

Laboratories are accredited by a public or private body from their country using internationally accepted standards issued by EU, OECD or ISO, for example.

8.26. Define "accreditation". What are the main features of analytical laboratory accreditation?

Answer:

In the quality realm, "accreditation" is defined as "the formal recognition in writing that a laboratory is fit and competent to perform a given analysis or specific group of analyses".

The accreditation of analytical laboratories is (a) voluntary (done at their request), (b) temporary (it holds for a specified length of time only) and (c) partial (it applies to specific activities or groups of activities rather than to the laboratory as a whole).

8.27. What does the process of accrediting a laboratory involve?

Answer:

A laboratory can be accredited if it has a Quality System that has materialized in a Quality Manual. The accreditation process is started by the auditors conducting a documental and visual (qualitative) inspection and producing a report. If the report is unfavourable, the laboratory can challenge it; if it is favourable, the laboratory will be awarded a Certificate of Accreditation to be paid at its own expense.

The Certificate carries the twofold commitment of maintaining the existing quality systems and allowing the auditors free access to perform periodic controls during its validity period. Because accreditation is temporary, it must be renewed after the validity period has expired or if the laboratory undergoes any substantial changes in the meantime. Renewing accreditation involves repeating the whole accreditation process; however, the new audit may be made easier by the auditors' prior knowledge of the laboratory to be re-accredited.

8.28. What does analytical quality assurance rest on?

Answer:

First of all, Quality Assurance (QA) in an analytical laboratory is impossible without human contribution. In fact, QA requires support from the management of the laboratory's parent body and willing acceptance by the laboratory staff. Also, auditors must have a constructive attitude in their work to facilitate sustained improvement in the laboratory.

Successfully implementing a Quality System in a laboratory entails providing it with the required technical means and training its staff in the new way of working. The supports for QA in a laboratory include computers, participation in interlaboratory exercises, and documentation and archiving activities.

Computer hardware and software play a crucial role in implementing Quality Assurance. Quality control and analytical equipment control software can be highly useful for this purpose. At the boundary of Computers, Chemometrics and Quality is Qualimetrics, which influences analytical information, and the

optimization of analytical processes and Quality Systems. Chemometrics enables validation of primary data and comparison of results—which is the basis for Quality Control and Quality Assessment systems—whereas interlaboratory exercises facilitate assessment of laboratory proficiency.

Finally, documenting and archiving all activities, and having a standard operating procedure (SOP) for each, is crucial for proper performance in a laboratory possessing a Quality System. The laboratory should also keep a record of sample custody chains, equipment performance from installation, monitoring of other materials, SOPs, primary data, results, reports and documenting activities themselves.

8.29. Comment on the problems potentially arising in implementing quality assurance in analytical laboratories.

Answer:

Successfully establishing and maintaining Quality Assurance may require solving various problems such as the following:

- *Lack of leadership. The laboratory's parent body should have clear-cut goals (leadership). Also, the laboratory should be committed to quality and the inspiring Quality Assurance principles be supported by a Quality Policy. The body's management should encourage and support quality-related activities*.
- *The human factor. This is one of the cornerstones of effective laboratory quality systems. Motivating laboratory staff is in fact essential to have them accept the burden of some labour-intensive tasks involved in keeping the system working. Although some duties may initially be imposed by management, the system will fail in the long term in the absence of an awareness of the significance of Quality*.
- *Costs. Implementing a Quality System requires starting and maintenance investments that should be carefully considered before its establishment is addressed*.
- *Abrupt implementation. Abruptly adopting a Quality System may elicit outright rejection from by the staff concerned. Rather, the system should be implemented in a gradual manner in order to give the staff the opportunity to get acquainted with specific activities (e.g., keeping sample custody chains, developing and adhering to SOPs, validating charts) before development of the Quality Manual and subjection to internal audits (creation of the Quality Assurance Unit for Good Laboratory Practices) and external audits (accreditation and intercomparison exercises) are undertaken in a second step*.
- *Compatibility with routine work. The tasks involved in implementing a Quality System should be compatible with the laboratory's primary goal, namely: to produce quality analytical information within the applicable deadline and at the agreed cost*.
- *Lack of constancy. Implementing a Quality System is a long-distance race in which the staff should not exhaust their energy at the start if they are to retain*

their willingness to perform the more labour-intensive tasks (e.g., documentation and archiving). The outcome of internal and external audits can help preserve staff motivation.

– ***Complex literature. The literature on Quality is atypical, contradictory, and occasionally plagued with acronyms and rules that may raise a high initial barrier for staff to overcome***.

Chapter 9. Social Responsibility in Analytical Chemistry

9.1. Relate SR in Analytical Chemistry to

- analytical quality (Chap. 8); and
- analytical problem-solving (Chap. 7).

Answer:

Social Responsibility in Analytical Chemistry is related to analytical quality because the latter is essential with a view to the sustainable production of truthful information.

Social Responsibility in Analytical Chemistry is also related to analytical problem-solving because both involve supplying (bio)chemical information to make grounded, timely decisions.

In other words, SR is the materialization of the social and environmental connotations of analytical problem-solving and quality.

9.2. What are the keywords defining Social Responsibility? Which are especially significant because they are shared by many definitions of SR?

Answer:

The keywords for SR are "responsibility", "stakeholders", "quality of life" and "sustainability", and its most common dimensions "stakeholders" and "social".

9.3. Define "stakeholders" in the context of SR, and of ISO guides and norms.

Answer:

Stakeholders are individuals or groups of individuals that may be affected by the activities or decisions of a body or area of knowledge but may also influence or take part in such activities or decisions. Stakeholders constitute a key element of Social Responsibility.

9.4. Describe the cycle of concepts that provides an integral definition of SR in an individual, an organization and a scientific or technical area.

Answer:

The cycle of Social Responsibility concepts is a series of mutually connected actions that start and end at the binding "commitment" of an entity to systematically support SR.

The commitment comprises the following sequence of actions:

- ***designing and developing an SR implementation strategy;***
- ***managerial changes;***
- ***recognizing social and environmental concerns;***

- ***expanding classic stakeholders with new stakeholders such as NGOs;***
- ***objectively balancing SR support and the goals of the entity or area of knowledge concerned so that their fulfilment is not hindered by the adoption SR; and***
- ***ensuring responsibility and sustainability in the entity or area concerned***.

9.5. Highlight four of the five principles governing SR. Which is the most important? Why?

Answer:

The most salient principles of SR are accountability, transparency, ethical conduct and respect for stakeholders' interests, the last of which is the most important because it ensures fulfilment of SR.

9.6. Can marketing SR be

(a) positive?
(b) negative?
(c) neither positive nor negative?

Justify your answer.

Answer:

(a) ***Yes. Example: integral SR is systematically publicized by the entity or area of knowledge concerned***.
(b) ***Yes. Example: SR is only publicized with anecdotal actions such as stating that each consumer buying a given brand of yoghourt will be thus supporting a humanitarian cause***.
(c) ***Yes. Example: when support of SR is not systematically publicized***.

9.7. What is the most important element of the cyclic succession of SR concepts? Why is it more important than the others?

Answer:

The commitment that starts and ends the cyclic succession of concepts leading to the establishment of SR in a body or area of knowledge. It is more important than the other elements because no integral SR system can be successfully established without the commitment of those involved.

9.8. Are the following statements true or false?

(a) Ethical principles encompass SR.
(b) Implementing SR in a scientific or technical area encompasses quality systems.
(c) For many organizations and businesses, SR is merely a window-dressing opportunity.

Justify your answers.

Answer:

(a) ***False. SR rests largely on ethical conduct—it encompasses ethical principles***.
(b) ***True. SR can be considered an extension of Quality Systems***.
(c) ***Unfortunately true. Some organizations and businesses market SR without supporting it systematically and wholeheartedly***.

9.9. Why are SR in Analytical Chemistry and SR in (bio)chemical information equivalent?

Answer:

Because the main output of Analytical Chemistry is (bio)chemical information on objects and systems. If Analytical Chemistry is socially responsible and sustainable, so will be the production and dissemination of (bio)chemical information.

9.10. What are the internal and external connotations of SR in (bio)chemical information? Are they related in any way? How?

Answer:

The internal connotations are the sustainable production of quality (bio)chemical information (that is, of information that is consistent with reality).

The external connotations can be the summarized as the correct dissemination of such information to society through reports in order to derive knowledge.

There is an obvious relationship between the two: the external connotations can never be fulfilled unless the internal connotations are satisfied. For example, no reliable knowledge can be produced without quality (bio)chemical information.

9.11. Explain the differences between the transfer of data (signals), results (information) and reports (knowledge) to society.

Answer:

They key is who interprets them. Thus, if transferred data and results are interpreted by society or the media, they may be misinterpreted—and reality distorted as a consequence—through poor knowledge or disinterest. On the other hand, the facts behind contextualized transferred knowledge are bound to be correctly interpreted by society and to help decision-making.

9.12. Which of the three sources of distortion in the transfer of (bio)chemical information is the most important? Rank them according to significance.

Answer:

Although the significance of each potential source of distortion differs depending on the particular situation, the following three are usually the most important:

(a) ***Malicious external manipulation of the object or sample***.
(b) ***The type of information required***.
(c) ***A poor knowledge of the required information and its features***.

The latter two sometimes exchange their place in the significance ranking.

9.13. Are the two internal connotations of SR in Analytical Chemistry related? Which is the more important? Why?

Answer:

The internal connotations of SR in Analytical Chemistry are the reliable, sustainable production of quality (bio)chemical information. In principle, they are unrelated. SR provides a relational framework for the two.

9.14. What is the difference between the two models of quality in (bio)chemical information (the second facet of external connotations of SR in Analytical Chemistry)?

Answer:

The model comprising three facets of quality (namely, intrinsic, referential or held as true and routine) is more simple. Also, it constitutes one side of the tetrahedron including required information (the third basic standard for Analytical Chemistry) as a fourth facet in addition to perceived quality as a fifth.

The most salient difference between the two models is that the latter is much more comprehensive than the former.

9.15. Why can the type of information delivered be important with a view to facilitating effective communication between analytical laboratories and clients requiring information?

Answer:

Because it is not the same to deliver primary data, results (information) or knowledge (contextualized, interpreted data). The probability of clients properly understanding what they receive from laboratories grows from primary data to results to knowledge. Therefore, it is more reliable to transfer knowledge than results.

9.16. Can using a communication office to deliver information from a laboratory have a positive effect on the parent body? Why?

Answer:

The main function of the communication office of the laboratory's parent body is to facilitate communication by delivering a message that can be easily interpreted by society. The office should therefore avoid triggering false alarms and raising false expectations. Ultimately, the communication office is concerned with the tough task of disseminating analytical science and technology.

9.17. How is the choice of an analytical process dictated by the potential impact of the (bio)chemical information to be delivered?

Answer:

One essential requirement for performing a given analysis is knowing the potential consequences of the information or knowledge to be produced, which influence the choice of the analytical process. In choosing, one should be aware that specific uncertainty may be highly consequential. For example, a few tenths in the purity of a 500-kg gold batch can be more consequential on price than a few units in the percent moisture content of animal feed.

9.18. Explain the sentence "quality in information transfer depends on both the producer and the receiver of the information". Discuss the significance of the information required by the receiver.

Answer:

Honesty and professionalism in the transfer of (bio)chemical information rests both on the producer (the analytical chemist) and the receiver (the client)—which may or may not coincide with the requester. This is especially important when interpreting the information with a view to proposing or making decisions.

The difference between the information required and that received falls outside the analytical chemical realm but is extremely important. The two can be intentionally mismatched for dishonest purposes. Thus, a firm may be informed that its vegetable produce contains small amounts of a pesticide and yet ignore the analytical information and give its produce the green light for export. This misconduct is not be expected if effective administrative controls (e.g., certification by an accredited laboratory) are established.

9.19. How important can experience in the dissemination of science be to transfer (bio)chemical information? Why?

Answer:

It is crucial with a view to avoiding errors in transferring (bio)chemical information that might lead to false alarms or expectations. The only limitation arises from the communication office being pressed to produce information simply highlighting the importance of its parent body.

9.20. How can SR in Analytical Chemistry be assured?

Answer:

Through the commitment of laboratories and their parent bodies. Social Responsibility is a voluntary prior commitment which, however, is indirectly required by public administrations and society (e.g., NGOs).

9.21. Explain the "transparency principle" supporting SR in Analytical Chemistry.

Answer:

As per ISO Guide 26000:2010, transparency is one the principles of SR. Transparency in the conduct of an analytical chemist or laboratory implies the following:

- ***as regards the external connotations of SR in Analytical Chemistry, establishing a Quality System, and ensuring that all activities are sustainable, recorded and easily accessed by auditors;***
- ***in regard to the internal connotations, ensuring that results and reports are based on objective, easily assessed data***.

9.22. Describe the two main ways in which a sample can be tampered with in order to have it give spurious results for fraudulent purposes.

Answer:

(1) ***An extraneous analyte may be deliberately added to the sample so that the object from which it is extracted is spuriously deemed "contaminated". One example is pollution of a bay with mercury. If mercury is deliberately added to the water from a ship, the coastal environment may be declared polluted and unsafe for bathing and/or fishing. This may boost tourism and fishing in an unpolluted competing area***.

(2) ***A harmless substance may be added to the sample in order to conceal the presence of the analyte in either of two ways***:

- ***By having it interact with the analyte (e.g., to form a compound that will be retained during the preliminary operations and prevented from reaching the measuring instrument)***.
- ***By having it interact with the object in order to eliminate the analyte (e.g., using a diuretic to remove any traces of anabolic steroids or drugs of abuse taken by an athlete)***.