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.

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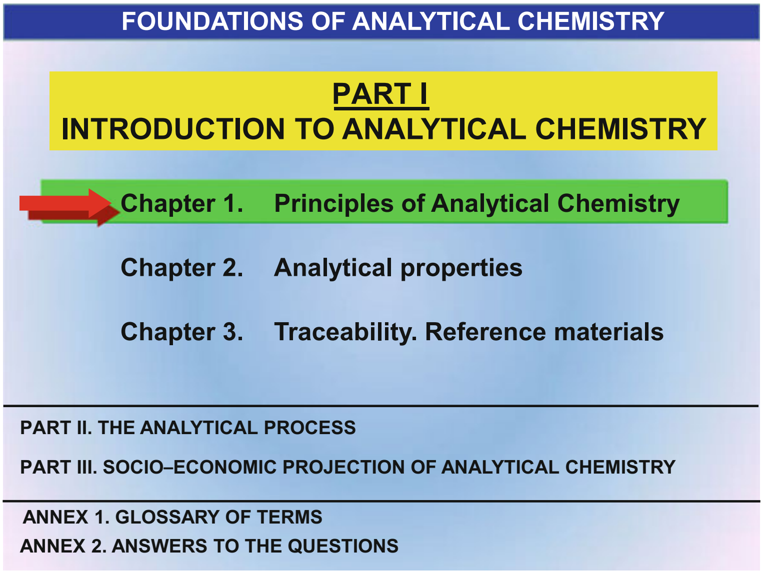
1.1 Explanation of the Slides

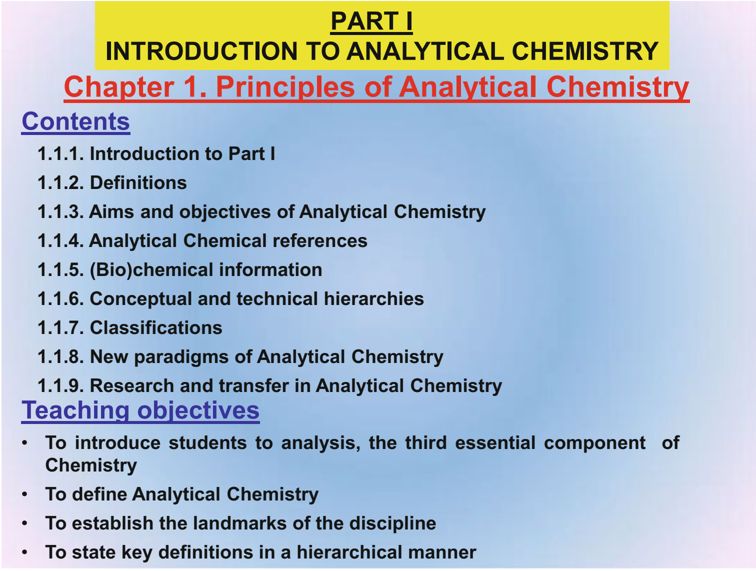
Slide 1.1



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

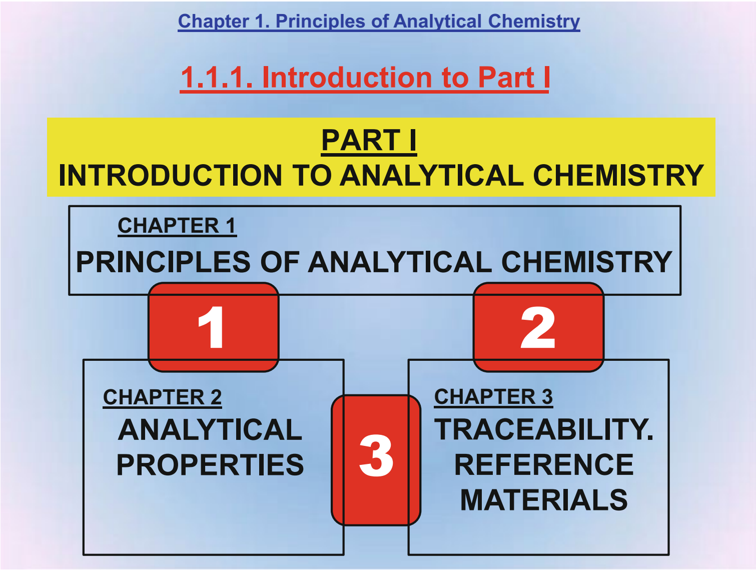


1.2.1. The nine sections of the chapter. After placing the chapter in the context of Part I, it provides a general description of Analytical Chemistry in the next four sections. Through conceptual and technical hierarchies and classifications, the contents of the discipline are established its essential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

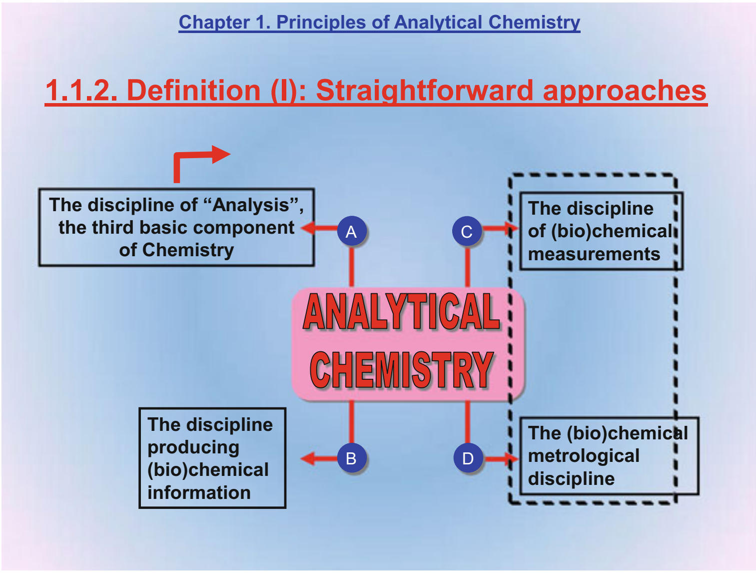
[1]The adjective "(bio)chemical" is intended to designate in a simple manner the type of information dealt with in Analytical Chemistry. It is a contraction of "chemical" and "biochemical", and applies indifferently to either type of information.

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.

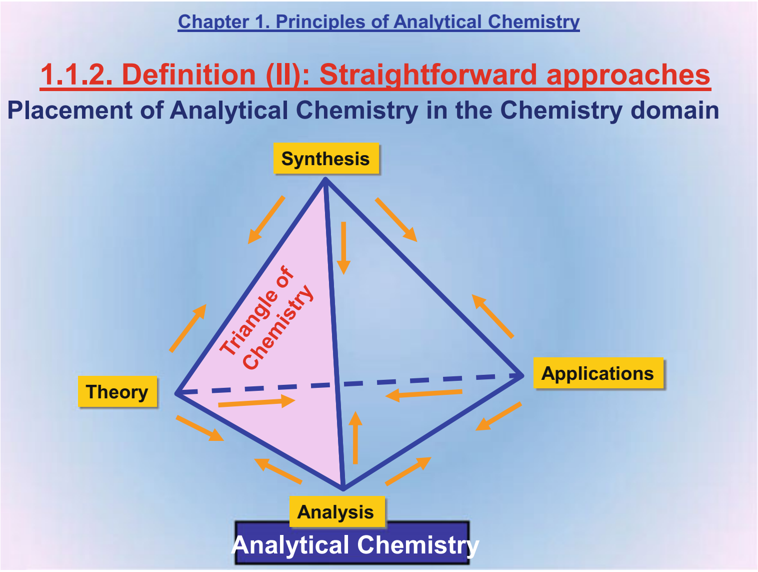
1.4.2. Analytical Chemistry is the discipline of Chemistry in charge of producing quality (bio)chemical information. This is the output of Analysis, the central element in the previous paragraph.

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.

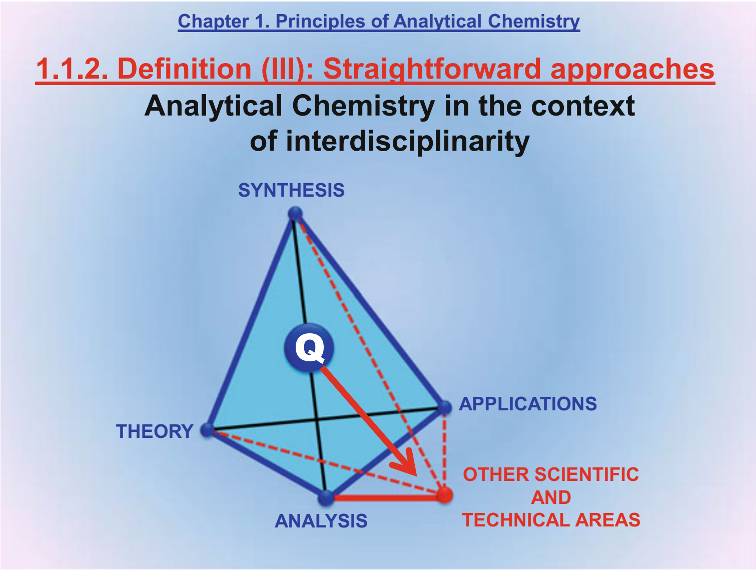
1.5.2. Applications are also essential for Chemistry. As a result, so the basic triangle of Chemistry becomes a tetrahedron.

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.

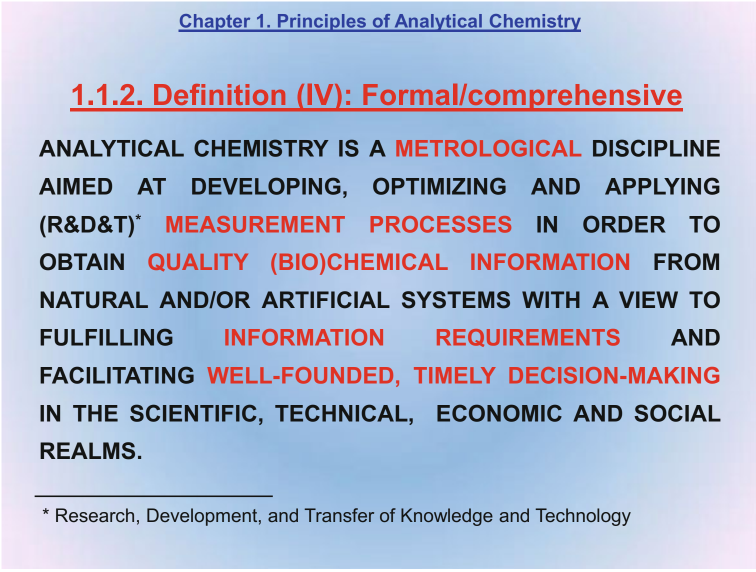
Slide 1.6



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

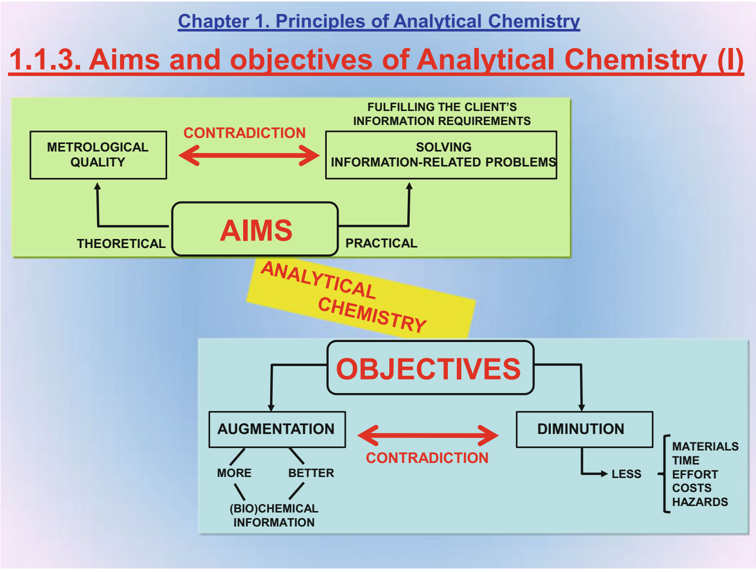


This slide provides a more comprehensive, almost formal definition of Analytical Chemistry. In fact, it is a compilation of the previous, simpler definitions that highlights the following notions:

- 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.

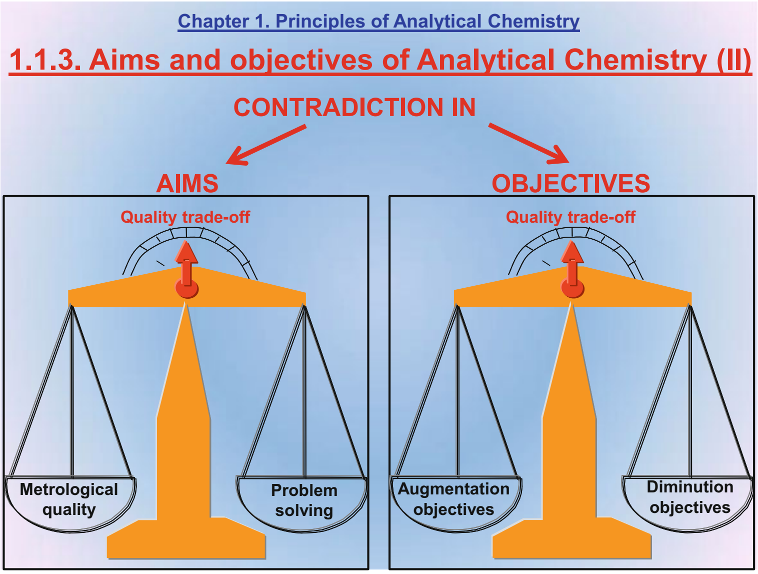
Analytical Chemistry has two primary aims. As a basic discipline, it aims at the highest possible metrological quality, that is, at producing highly accurate results or reports (Slides 2.14 and 2.15) with as low specific uncertainty as possible (Slides 2.7 and 2.29).

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

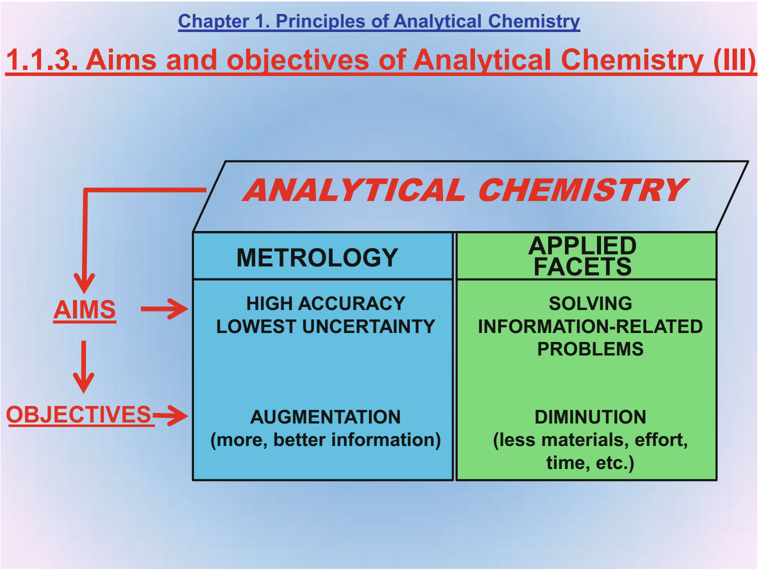


This slide exposes the contradiction between the aims of Analytical Chemistry on the one hand and its objectives on the other. To what extent either pan causes each balance to tip will depends on the "quality trade-offs" to be made, which should be accurately known before analyses are started.

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

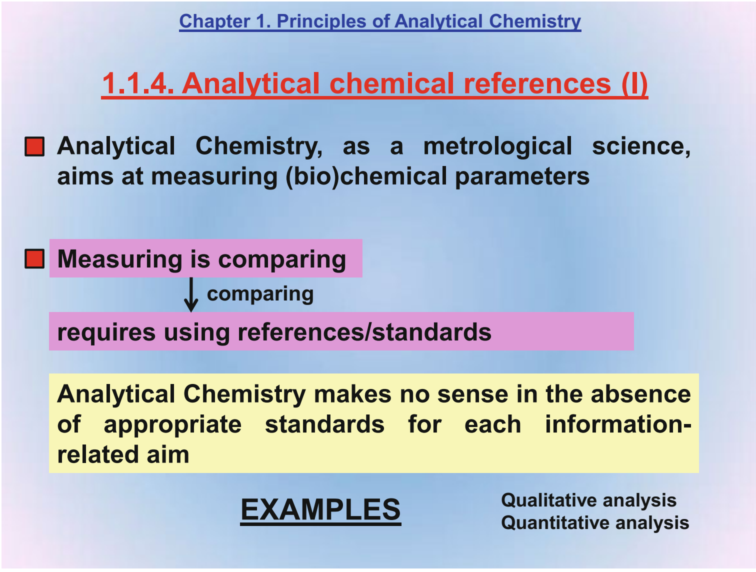


In addition to its basic metrological component, Analytical Chemistry has an essential applied component.

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.

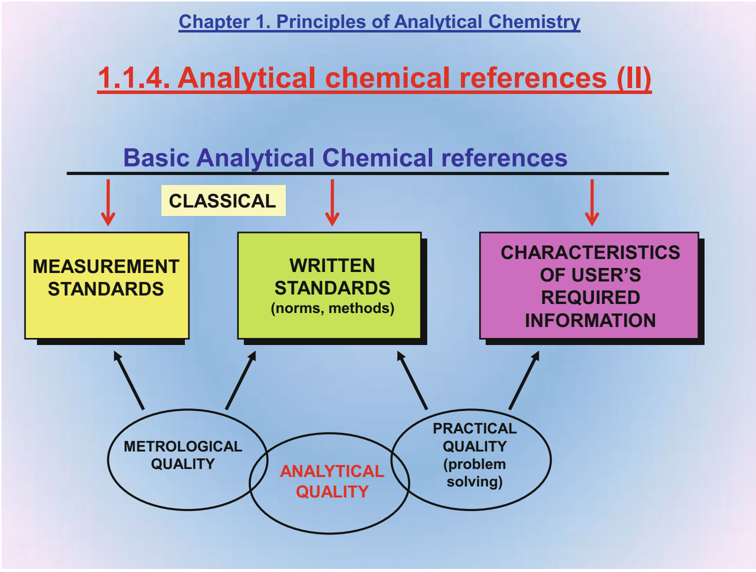
Measuring entails comparing with well-established, widely accepted references. The main references in the analytical fields are measurement standards, which are presented in Chap. 3. Analytical Chemistry makes no sense without tangible standards or references for each information-related purpose.

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

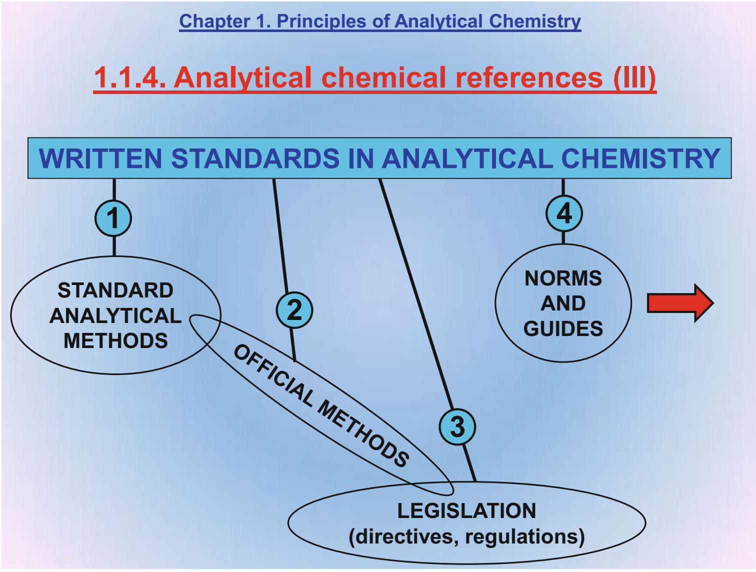


1.12.1. Analytical Chemistry uses two classical types of references. One is tangible measurement standards, which are those systematically used for comparisons in Metrology in Chemistry and described in Chap. 3. The other type is written (intangible) standards, which are especially relevant to Analytical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

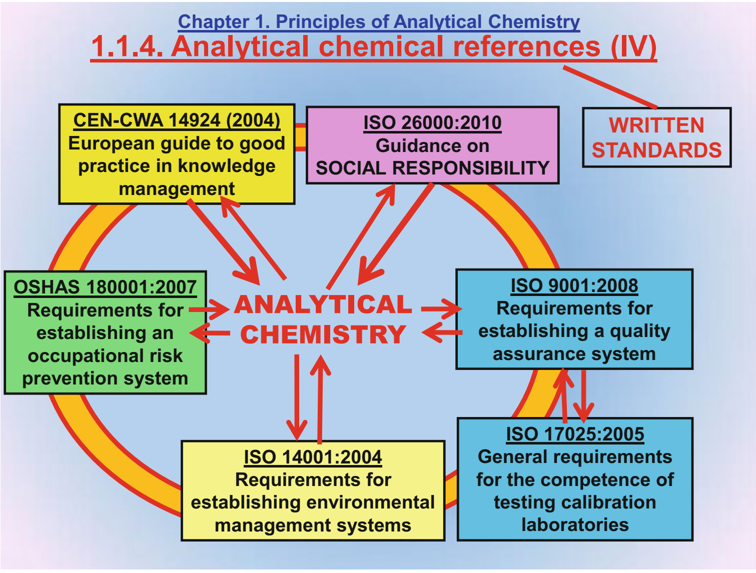
A *written standard* is a consensus document endorsed by a competent, usually international, body stating the requirements to be fulfilled in addition to specific rules, guidelines and characteristics. Standards can apply to activities, products, processes and services. Their most salient purposes are 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.

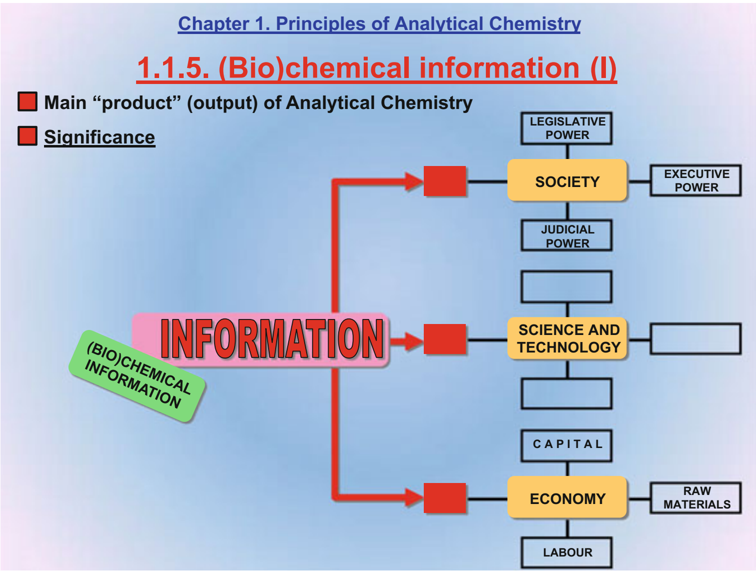
1. *Guide for implementing knowledge management systems*, which interprets information (qualitative and quantitative results) and places it in context. It is highly relevant to Social Responsibility in Analytical Chemistry (see Chap. 9).
2. *Guide for implementing Social Responsibility*, which, as shown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



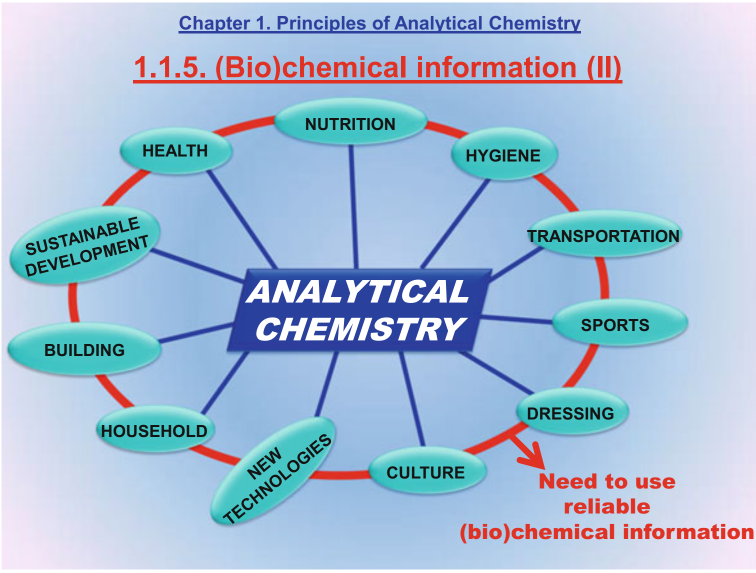
There is a tight relationship between Analytical Chemistry and (bio)chemical information extracted from analytical processes, which is their main output and can be improved by producing analytical knowledge (see the information hierarchy in Slide 1.20).

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.

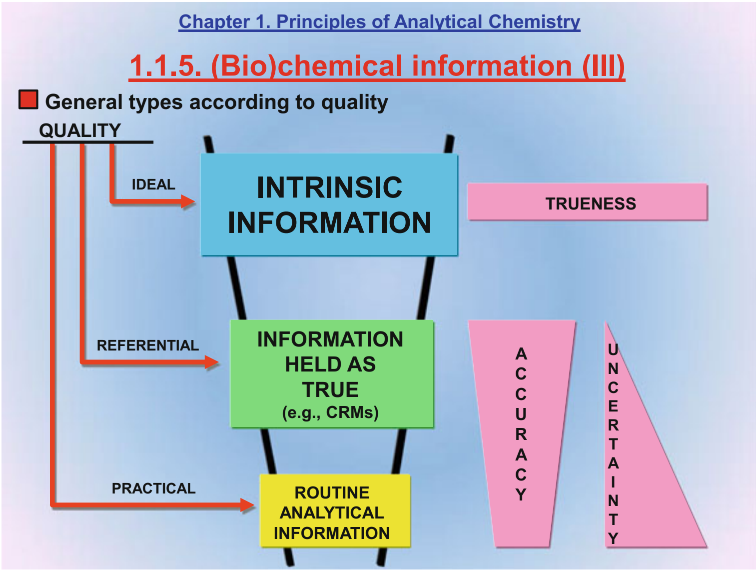
(Bio)chemical information is one part of information at large and hence also essential to society, science, technology and economy.

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.

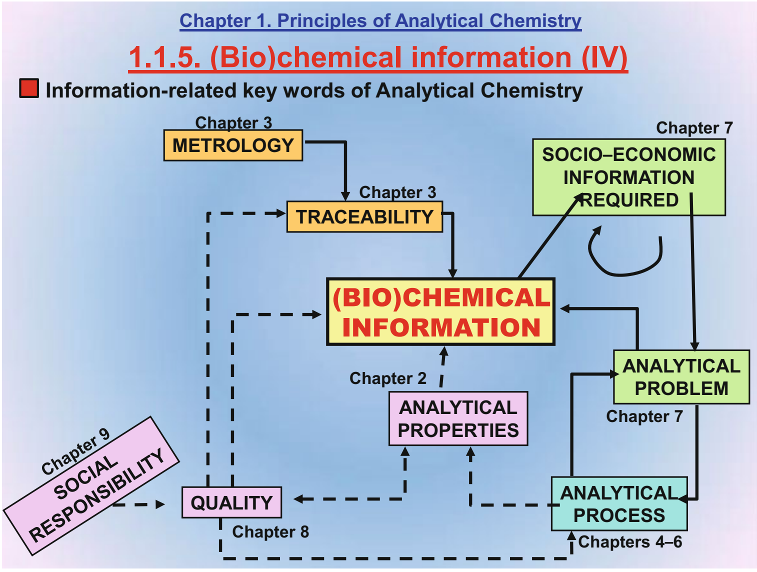
At the top is *ideal quality*, which pertains to the intrinsic (bio)chemical quality of objects and systems, and is unavailable to humans. Such is the case, for example, with the fat content of a food expressed with many decimals (e.g., 3.345237689…%) and hence subject to no uncertainty (see Slide 2.30).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



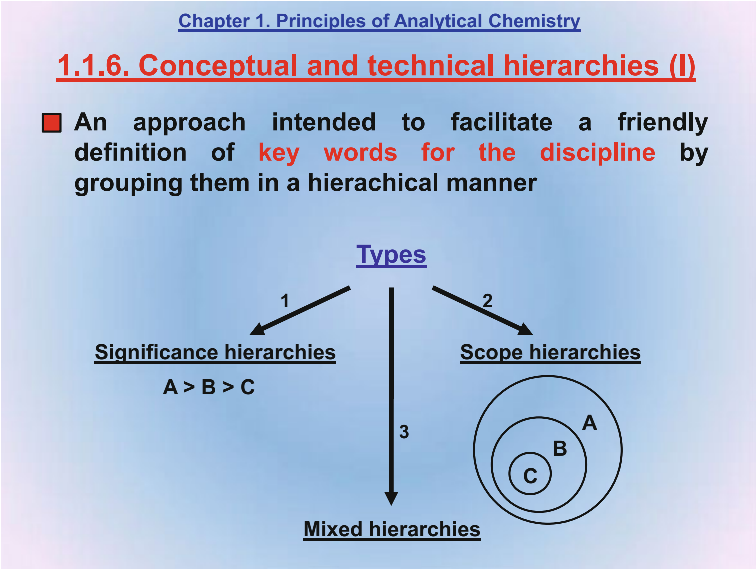
As can be seen, (bio)chemical information is connected with key aspects of Analytical Chemistry dealt with in this book. Around the discipline are its essential key words. The most salient connections are as follows:

- 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.

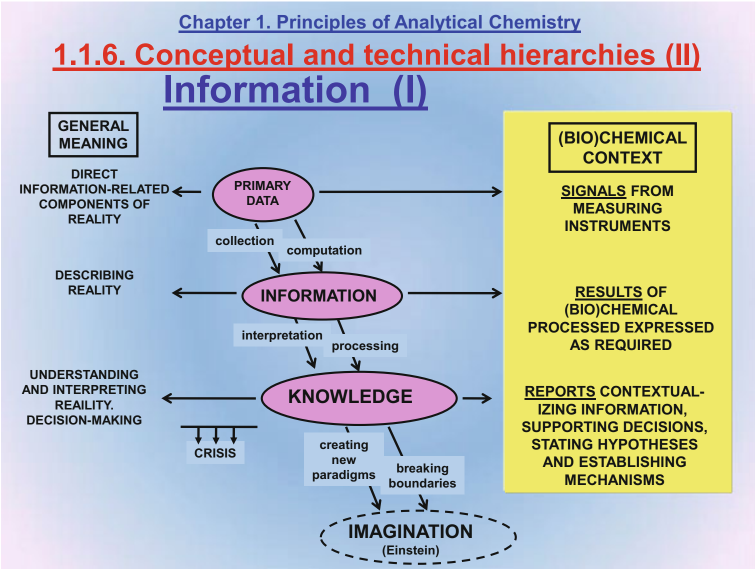
A hierarchy is an ordered sequence of things or persons. As can be seen in the slide, there are three basic types of hierarchies.

- *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.

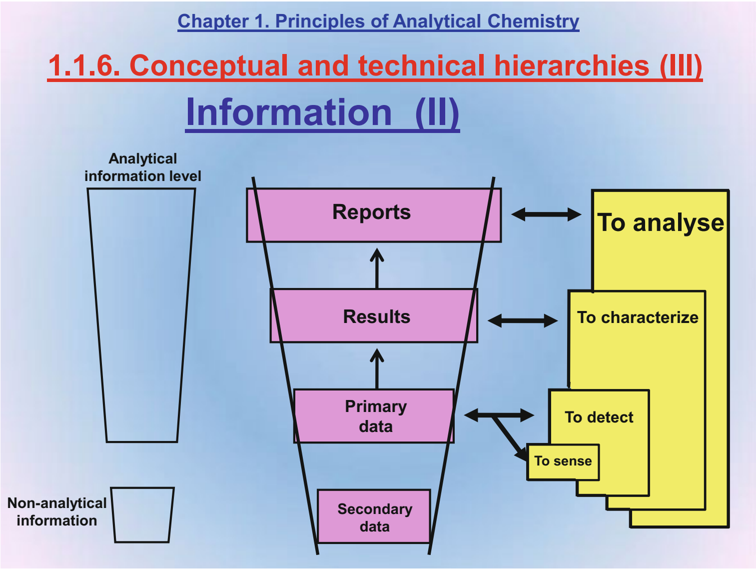
The first hierarchy depicted in this slide, considers information to be an intermediate stage in a ranking of increasing scope and significance from raw data to knowledge. *Raw data* are direct indicators of reality, and can be compiled and processed to obtain *information*, which is a depiction of reality. 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.

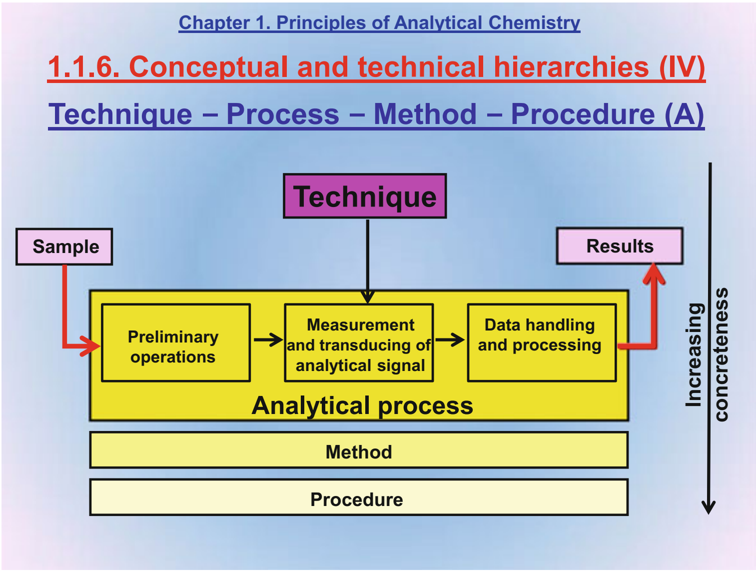
[3] *To control* has a twofold meaning: to monitor a system or process—and, if necessary, adjust it—in order to ensure that it operates as expected. Monitoring includes controlling. For example, if the temperature of a stove as measured with a thermocouple is 104 °C and the stove was programmed to operate 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

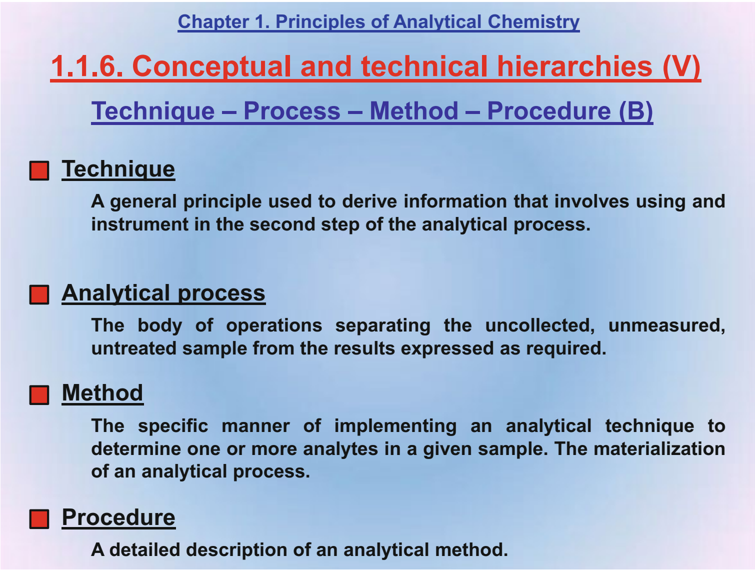


Understanding the differences between the terms “technique”, “process”, “method” and “procedure” is crucial with a view to avoiding confusion in the analytical chemical literature. This slide shows an atypical hierarchy of the four terms according to concreteness.

– 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:

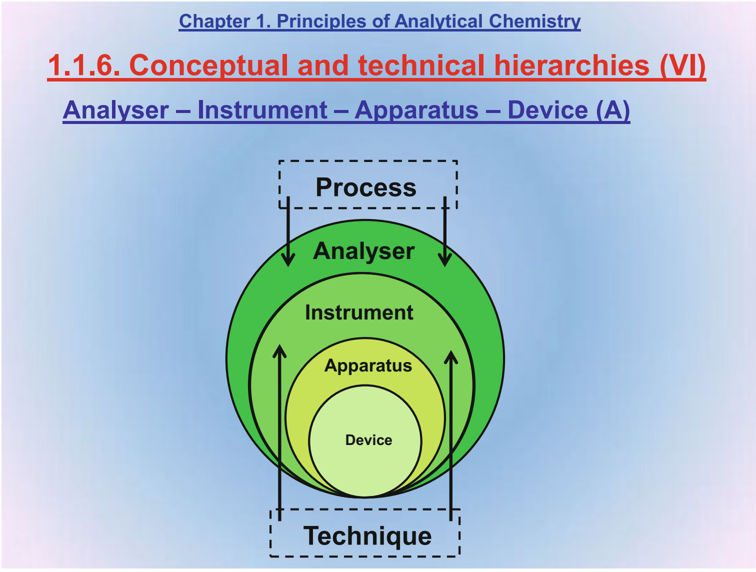
Technique: UV–visible absorption spectroscopy, where the instrument is a photometer.

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

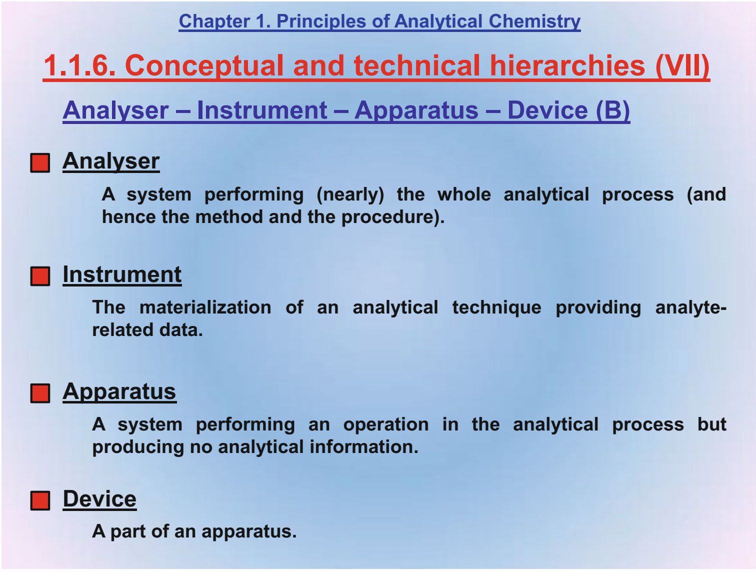


Similarly to the previous slide, this one distinguishes between four other key terms in Analytical Chemistry: analyser, instrument, apparatus and device.

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.

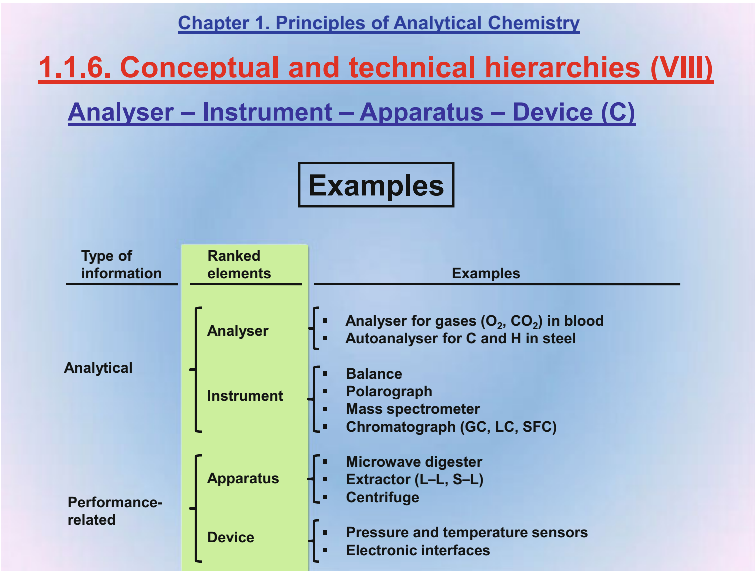
This hierarchy is connected to that in Slide 1.22. Thus, “analyser” is related to “analytical process”, and so is “instrument” to “technique”. Also, the outputs of an analyser and an instrument are related to “analytical information” (Slide 1.21), whereas the parameters used to monitor the operation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

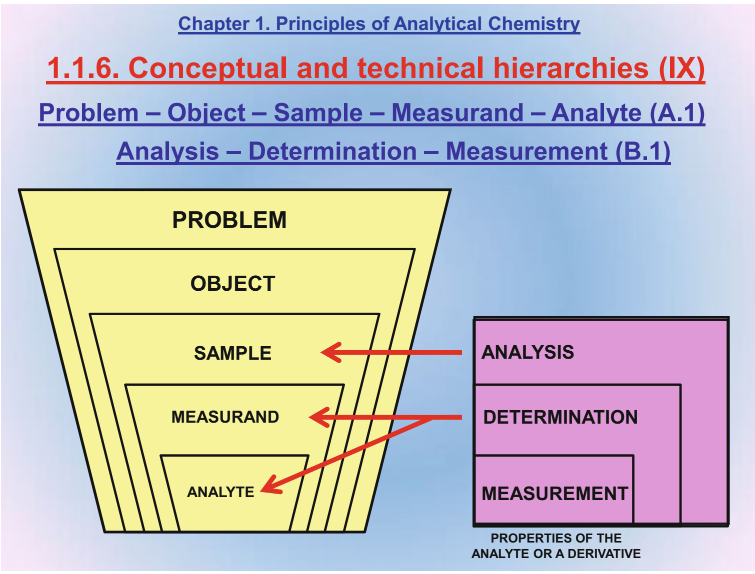
(B) The usual instruments involved in the second step of the analytical process (see Slide 1.22): a balance, a burette, a mass spectrometer, a UV–visible photometer, a fluorimeter, a gas or liquid chromatograph with an integrated detector.

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

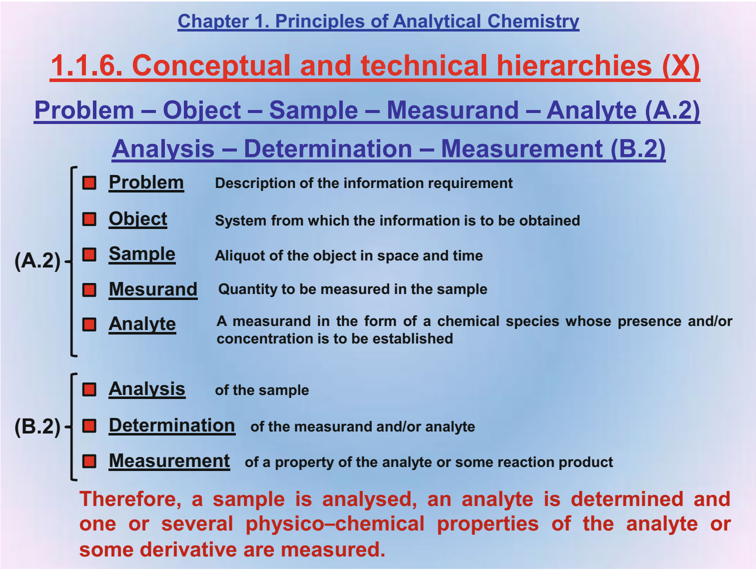


1.27.1. This scope and significance hierarchy of analytical terms (**A.1**) is related to the systematic use of the concept "traceability" in Analytical Chemistry (see Chap. 3). It relates *analytical problem* [that is, the (bio)chemical information required] to the *object* or *system* about which the 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

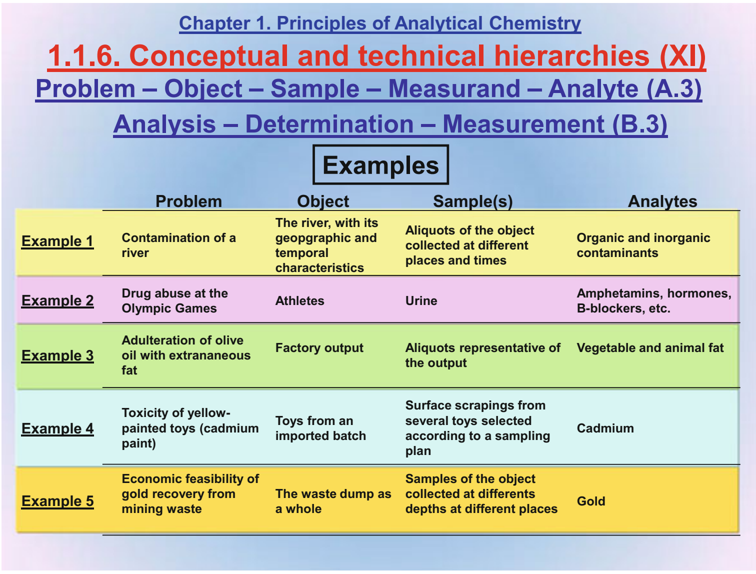
Therefore, the following phrases are wrong:

- 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

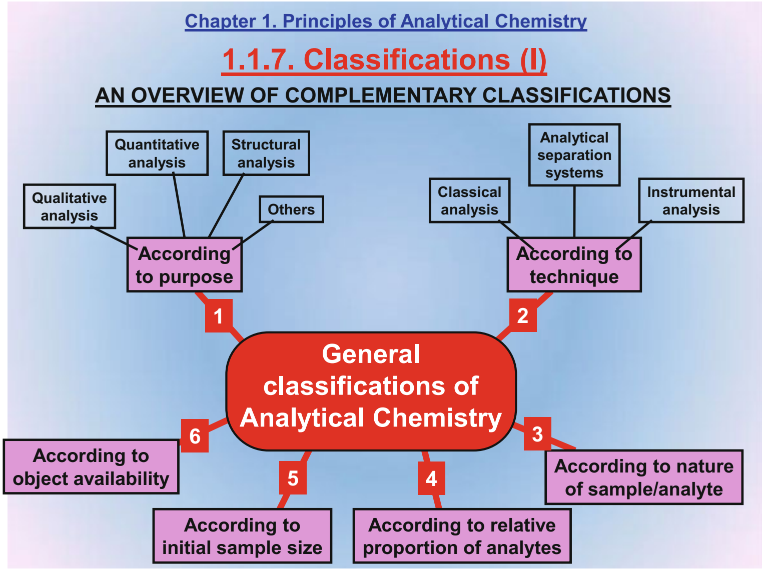


	Problem	Object	Sample(s)	Analytes
Example 1	Contamination of a river	The river, with its geopgraphic and temporal characteristics	Aliquots of the object collected at different places and times	Organic and inorganic contaminants
Example 2	Drug abuse at the Olympic Games	Athletes	Urine	Amphetamins, hormones, B-blockers, etc.
Example 3	Adulteration of olive oil with extrananeous fat	Factory output	Aliquots representative of the output	Vegetable and animal fat
Example 4	Toxicity of yellow-painted toys (cadmium paint)	Toys from an imported batch	Surface scrapings from several toys selected according to a sampling plan	Cadmium
Example 5	Economic feasibility of gold recovery from mining waste	The waste dump as a whole	Samples of the object collected at differents depths at different places	Gold

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



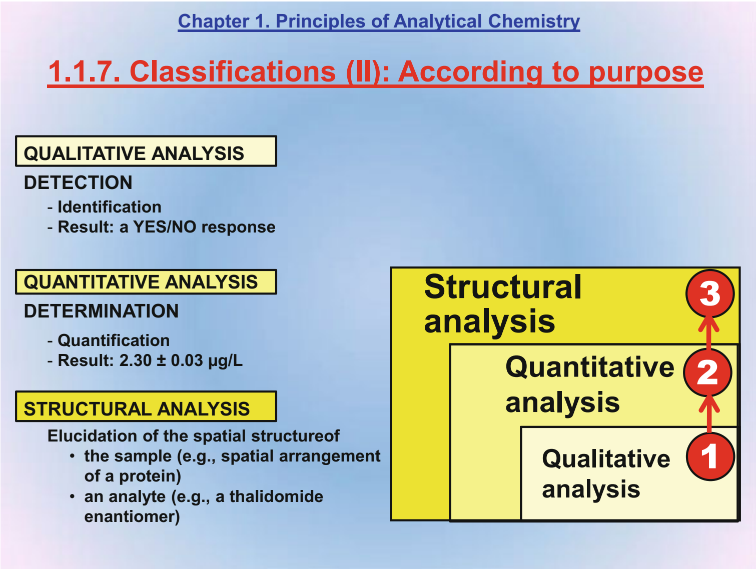
This slide starts Sect. 1.1.7, which establishes six hierarchies of especial usefulness to approach Analytical Chemistry conceptually and technically.

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

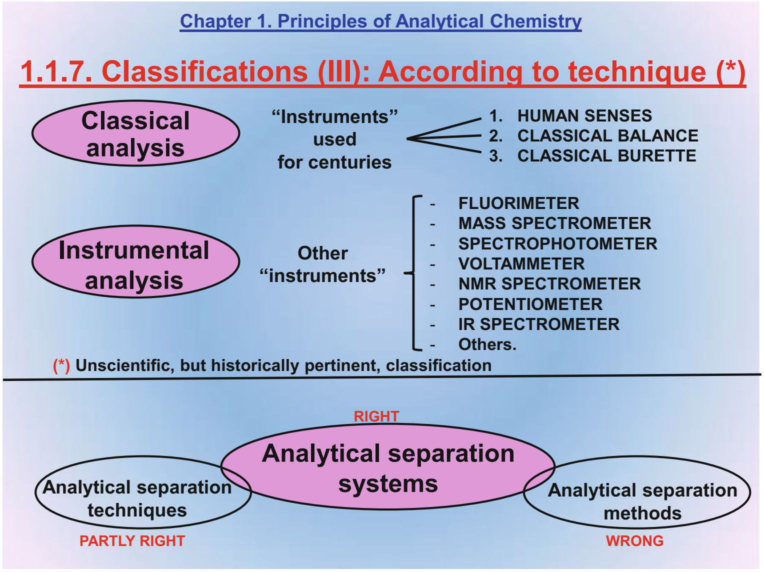


1.31.1. The aim of an analysis varies with the type of (bio)chemical information sought. There are three different types of analysis in this respect, namely:

– *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.

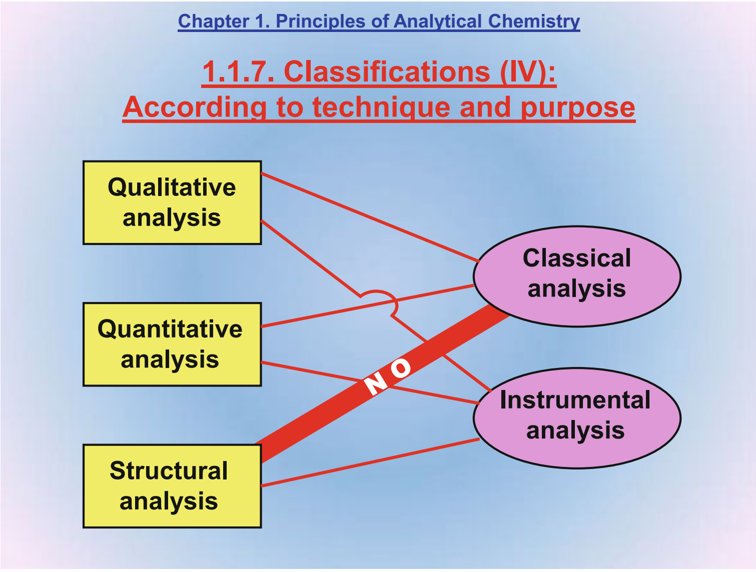
– Thus, the classical two-pan balance with weights handled by the user has given way to an autobalance with a single pan, and automatic taring and digital reading of the weights.
– Similarly, the classical glass burette made to volume by hand and read out visually at the endpoint of a titration has been 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



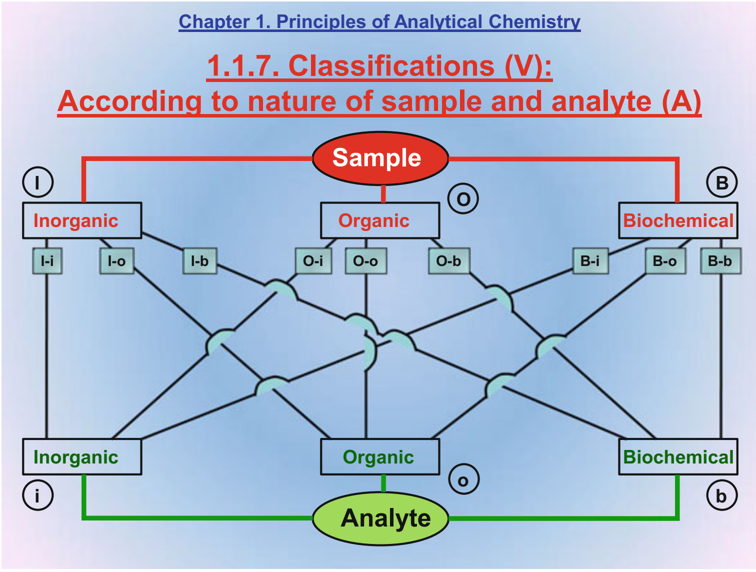
1.33.1. This slide combines the first two classifications in Slide 1.30 according to purpose and technique. According to technique, it distinguishes between Classical and Instrumental Analysis, which, as stated with regard to the previous slide, lacks scientific ground.

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.

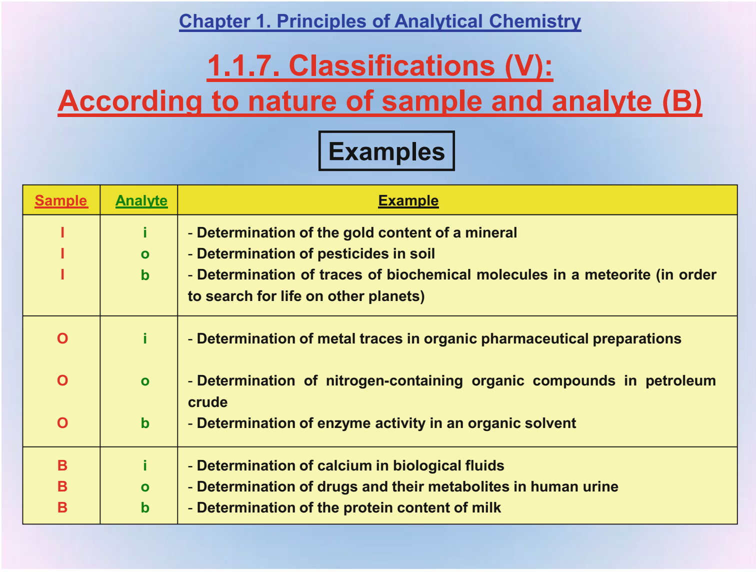
Slide 1.34



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.

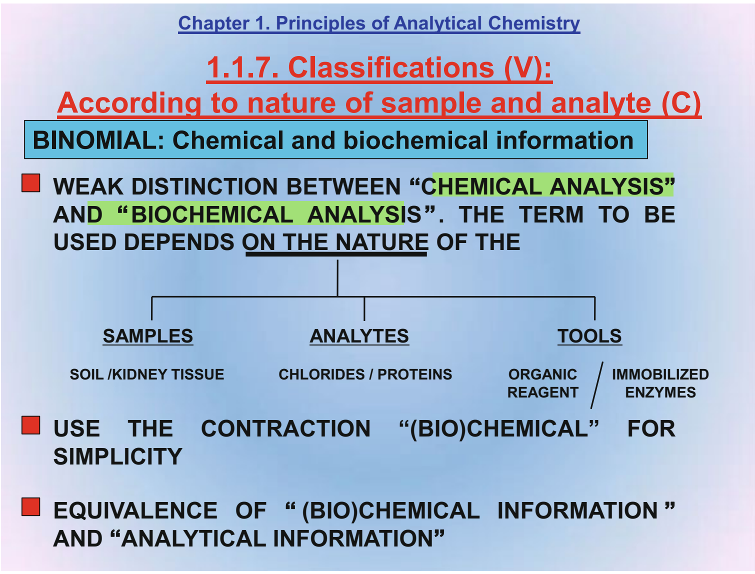
[4]In the analytical chemical domain, the word "matrix" refers to the characteristics of the sample extracted from the object. No other definition comes closer to this meaning.

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

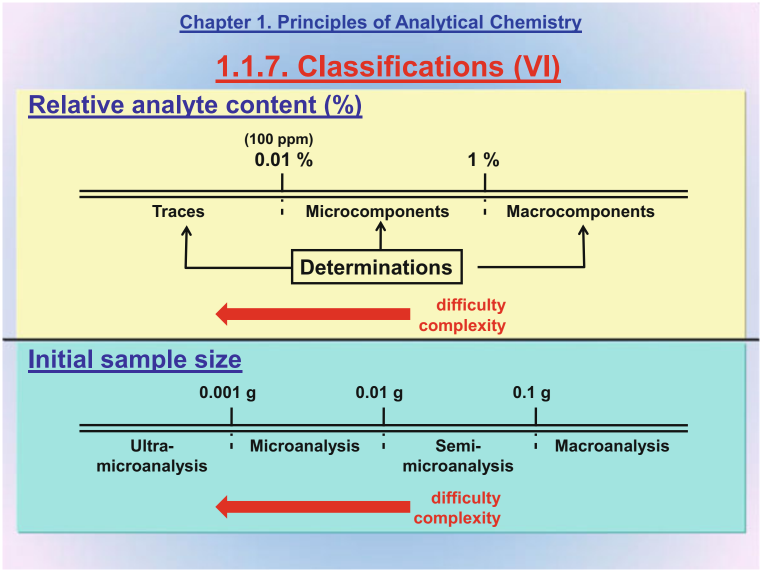


Classifying "analysis" according to the nature of the sample and analyte (Sect. 1.30.3) raises a naming problem. As can be seen, "chemical analysis" and "biochemical analysis" are virtually indistinguishable. The difference is in the chemical or biochemical nature of the sample and analyte, and in the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

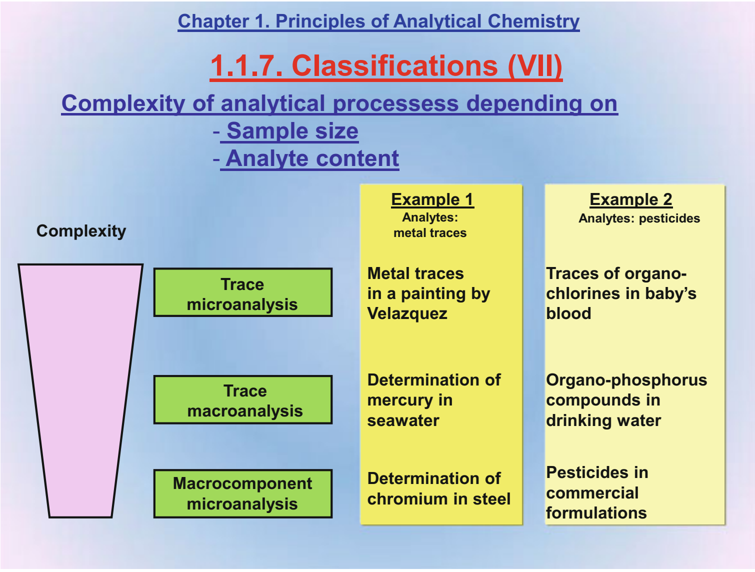
By placing three landmarks at 0.001, 0.01 and 0.1 g, an increasing logarithmic scale is split into four zones according to sample size and mass in which Analysis is named differently, namely:

- *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.

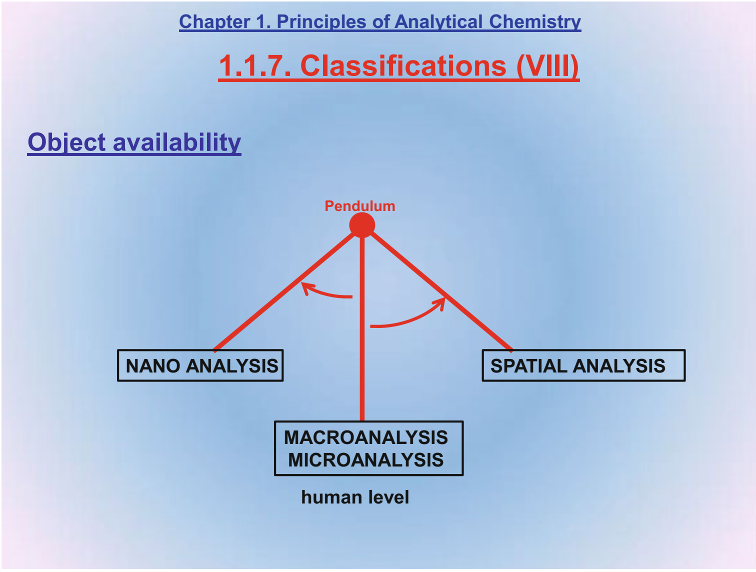
Slide 1.38



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.

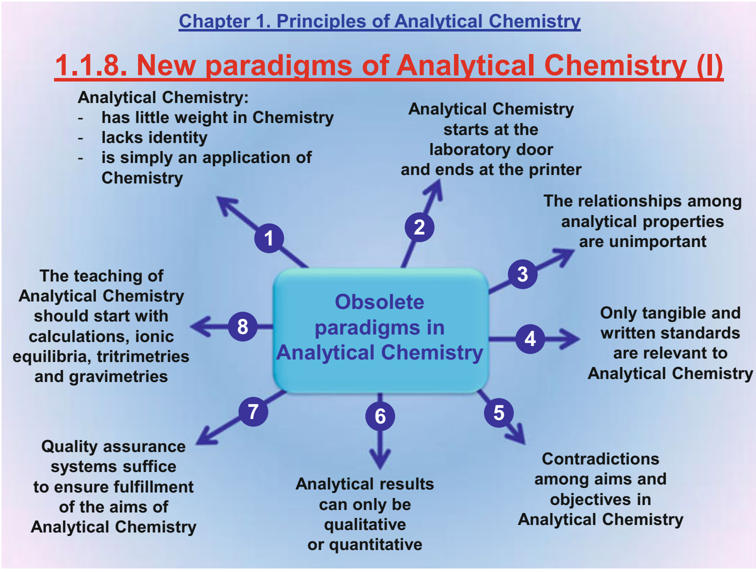
Slide 1.39



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.

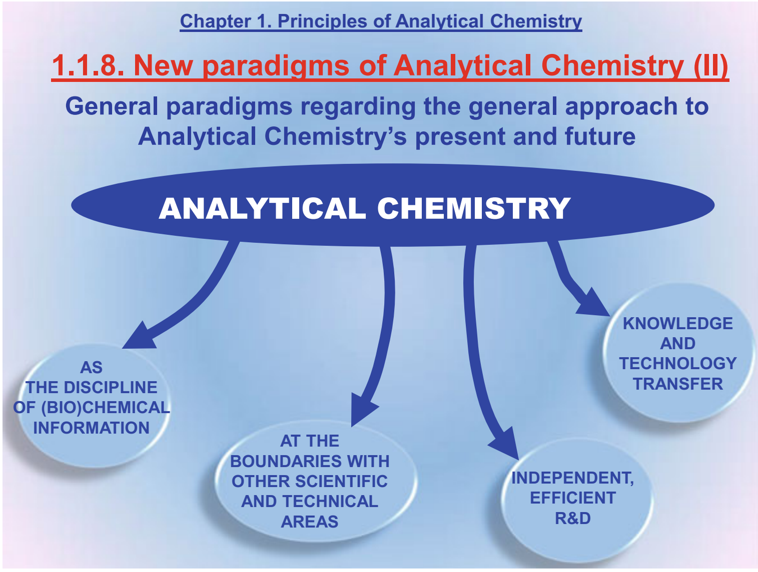
3. Approaching analytical properties (Chap. 2) in a non-holistic[7] manner. The complementary and contradictory relations between the characteristics of the results and the analytical process (see Items 2.56–2.61) are essential with a view to approaching the basic and applied sides of Analytical Chemistry 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).

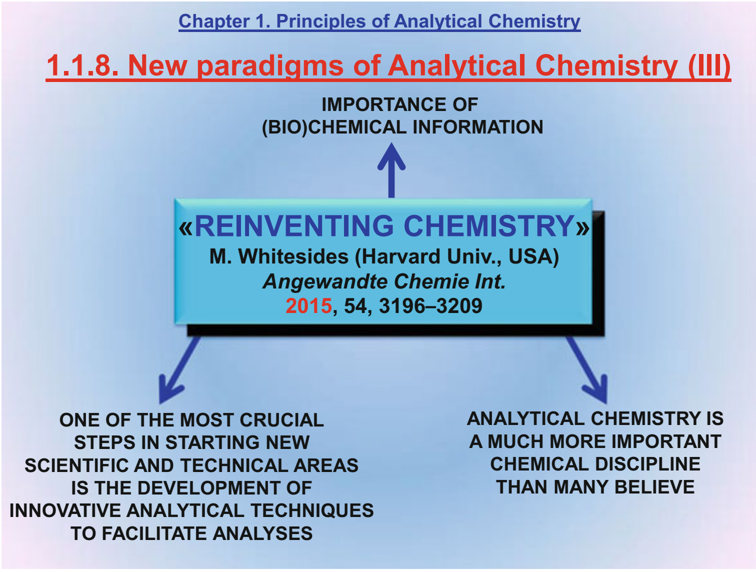
The second key paradigm of Analytical Chemistry is a multidisciplinary approach akin to Chemistry leading to fruitful connections with other scientific and technical areas in the future (see Slide 1.6).

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.

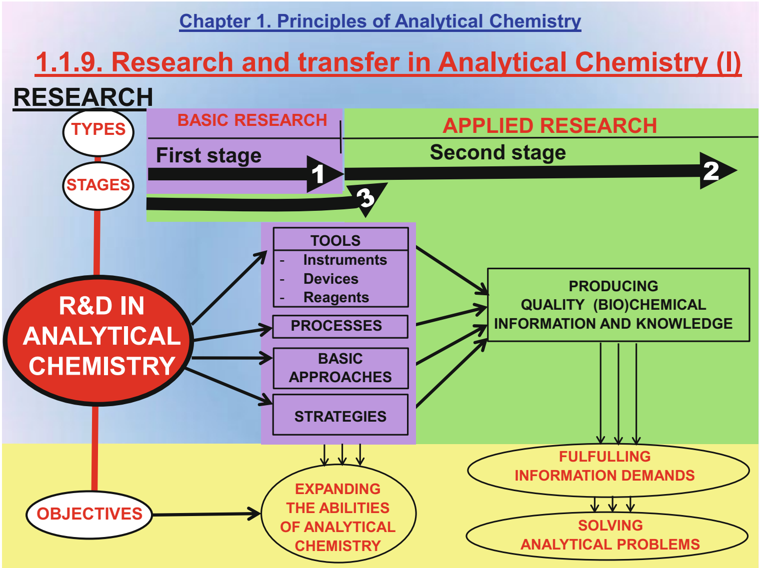
Slide 1.42



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.

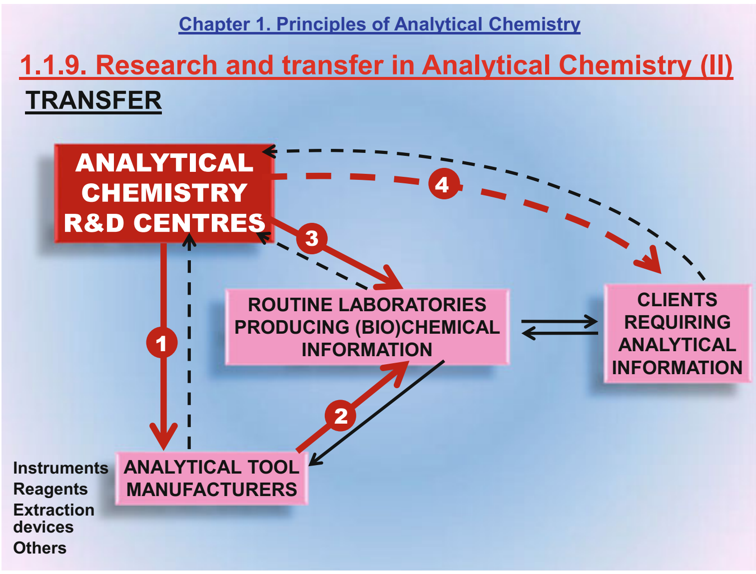
The significance of basic research in Analytical Chemistry can be easily inferred from the following example: the tennis player Maria Sharapova was charged with doping with mildronat (Meldonium) in March 2013. At the time, this substance was not on the banned drug list of the International Olympic Committee. 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