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# Significant steps in the evolution of analytical chemistry—Is the today's analytical chemistry only chemistry?

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ABSTRACT

In this review the history of chemistry and specifically the history and the significant steps of the evolution of analytical chemistry are presented. In chronological time spans, covering the ancient world, the middle ages, the period of the 19th century, and the three evolutional periods, from the verge of the 19th century to contemporary times, it is given information for the progress of chemistry and analytical chemistry. During this period, analytical chemistry moved gradually from its pure empirical nature to more rational scientific activities, transforming itself to an autonomous branch of chemistry and a separate discipline. It is also shown that analytical chemistry moved gradually from the status of exclusive serving the chemical science, towards serving, the environment, health, law, almost all areas of science and technology, and the overall society. Some recommendations are also directed to analytical chemistry educators concerning the indispensable nature of knowledge of classical analytical chemistry and the associated laboratory exercises and to analysts, in general, why it is important to use the chemical knowledge to make measurements on problems of everyday life.

## 1. Introduction

Though modern chemistry, as we know it today, began with the Chemical Revolution of the 18th century, chemical analytical processes were in use long before that. Already from the epoch of Homer there are references in his poems Odyssey (Od.) and Iliad (Il.), to processes nowadays closely associated with chemistry, like fertilizing in agriculture (Od. $\rho$ 297), painting of ships (Od. $\lambda$ 124, Od. $\psi$ 271, Il. $\Delta$ 275, Il. $B$ 637), perfumery (Od. $\zeta$ 215, $\zeta$ 220, $\beta$ 339), disinfection (Od. $\chi$ 494), cheese-making (Od. $\delta$ 87, Il. $E$ 901, Od. $\iota$ 222, Od. $\rho$ 225) winery (Od. $\alpha$ 193, $\lambda$ 193) polishing of metals (Il. $\Pi$ 228), etc. [1]. The ceramic chemistry and technology as well as the painting and decoration (*Attic pottery coatings and black gloss*) of the Attic vases in ancient Greece ( Fig. 1), is today subject of studies and investigations by many analytical archaeometrists [2–4].

The roots of chemistry as a science are deep in Greece starting with pre-Socratic philosophers Embedocles of Sicily (493-433? BC) and Heraclitus of Ephesus (540-480? BC). Both philosophers established the concept of existence of the principal elements, named by Embedocles *roots*. These elements were: fire, air, water, and earth. Heraclitus suggested the possibility of changes and interconnections between each of these elements, through their opposing properties: hot-cold, wet-dry, i.e. fire is hot and dry, earth is dry and cold, water is cold and wet, air is wet and hot (Fig. 2). Leucippus (first half of 5th century BC) and his student, as well as his successor Demokritus of Abdera Thrace (460-370? BC) (Fig. 3) developed the theories of the nature of matter and atomism. They asserted that everything is composed of a variety of indestructible, unchangeable and indivisible elements called *atoms* and all substances are only different combinations of these atoms. Aristotle added the fifth element of æther, the material that fills the region of the universe above the terrestrial sphere, whereas Plato (424-348 BC) gave shapes to all atoms through his platonic solids (tetrahedron, cube, octahedron, dodecahedron and icosahedron) and used for the first time the word "στοιχειον" (stoicheion: element) to describe them.

During the Hellenistic era and up to the 4th century AD, a great number of philosophers and experimentalists appeared in the Hellenistic world and particularly in Hellenistic Egypt. They studied particular materials and processes (glasses, metals, sulphur, cinnabar, dyes, extraction, and distillations). The Arab conquerors of Egypt (639–642 AD) followed suit, made use of this ancient knowledge, they combined it with Persia, India and China knowledge and experience, and contributed greatly to the newborn science, the Alchemy, a term derived from the Arabic word "al kimiya", which most probably goes back to the Greek

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**Fig. 1.** Coatings and black gloss decoration of an Amphora by Exekias: Achilles and Ajax engaged in a board game, c.540-530 BC.

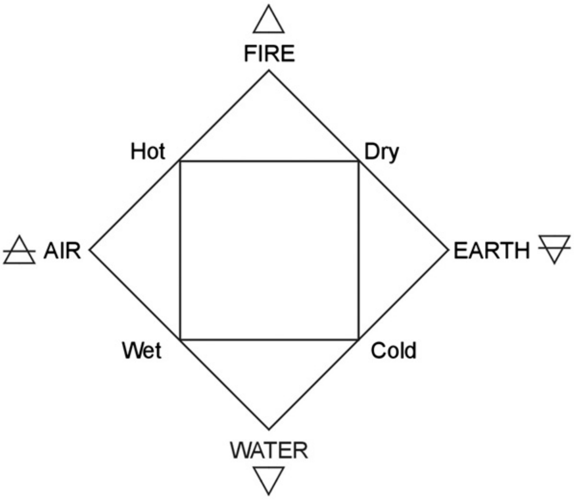

**Fig. 2.** The classic presentation of the four Embedocles roots: fire, earth, water, and air, at the corners of the outer square (the corresponding alchemical symbols are shown next to each root). Their interconnecting properties of these four elements, as suggested by Heraclitus, are shown in the inner square.

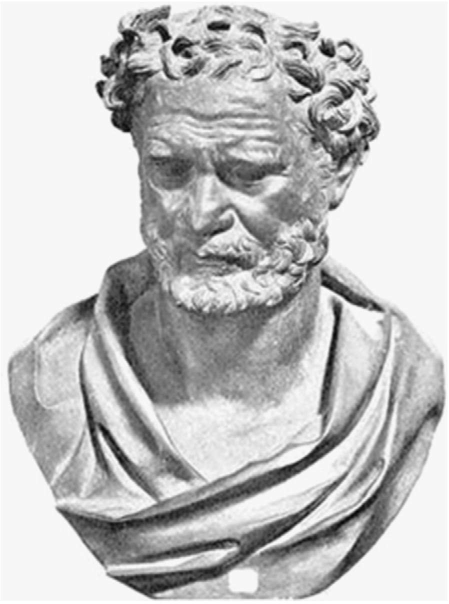

**Fig. 3.** Demokritus of Abdera, Thrace (460-370? BC).

**Fig. 4.** A section from the illumination of the Skylitzes Manuscript in the National Library of Spain, Madrid, showing the use of Greek fire.

word “χυμεια” (chymia) derivational from the verb “χεω” (cheo: to pour, to cast).

Thus, chemistry was served by those famous alchemists of the Arab world and later on by those of Medieval Europe; nevertheless little is known about the alchemists of the Eastern Roman Empire (the Byzantine Empire). For example, the unbeatable incendiary weapon of the Byzantines, the famous “υγρον πυρ” (hygron pyr: liquid fire), widely known as *Greek fire*, seems to be a chemical invention that kept invaders away for centuries, a weapon whose secrets were never revealed and eventually lost (Fig. 4).

In the middle ages the alchemists, known for their relentless pursuit of the *philosopher's stone* and a way to turn base metals into gold, are often associated with obscurity and fraud, but much of what they did was real science of their time.

## 2. The earlier analytical chemistry

Analytical chemistry is also an ancient art and its tools and basic applications date back to early recorded history [5]. The chemical balance and the weights, as stated in the earliest documents found, was supposed to be used only by the gods and chemical work dealt primarily with speculation and mystery. During the last 6000 years analytical chemistry and commerce would not have progressed beyond the barter system without the invention of a system of weights and measures. The grains and seeds of plants were chosen for their elegant uniformity as weights. Mustard seeds were used to weigh gold in India. The carob gave us carats, still used today to express weight and purity of gold and diamonds. “*A measure of the real civilization of a people, in any period of its history, may be obtained by studying the attention given to the invention and perfection of devices for weighing and measuring. For centuries the equal armed beam scale has figured as the supreme and traditional symbol of justice and truth*” [6].

During the middle ages (5th to 15th century), alchemists began to assemble scattered knowledge that later became chemistry and analytical chemistry, and this continued during the phlogiston era *The phlogiston theory*, was developed by J.J. Becher (1635–1682) late in the 17th century and was extended and popularized by G.E. Stahl (1659–1734) [7]. According to this theory all flammable materials contain phlogiston (derived noun form of the Greek *phlogistos*, meaning flammable) a substance without color, odor, taste, or weight, that is liberated in burning. Once burned, the “dephlogistated” substance was held to be in its “true” form, the *calx*.

Robert Boyle (1627–1691) introduced for the first time the term “analyst” in his 1661 book “*The Sceptical Chymist*”, Friedrich Hoffmann (1660–1742) invented *gravimetric analysis* in the 17th century, Joens Jakob Berzelius (1779–1848) introduced *stoichiometric concepts*, and Torben Bergman (1735–1784) founded the qualitative and quantitative analysis. Antoine Lavoisier (1743–1794) used balance to disprove the phlogiston theory and demonstrated the law of conservation of mass, which earned him the title "*father of quantitative analysis*". Priestley, Cavendish, Lavoisier, Scheele, in 18th century, and Bunsen in 19th century are known as the analytical chemists who established important gas analytical techniques. In 1843, Talbot and later Kirchhoff and Bunsen introduced spectroscopy as a powerful analytical tool and made significant spectroscopic investigations by studying the emission spectra of many elements in flames [8].

Titrimetric analysis was widely practiced by 1874, using natural dyes as indicators, much earlier than the modern acid–base indicators were introduced and defined by their p*K* values. Guy-Lussac (1778–1850) developed a titrimetric method for silver, which was accurate to better than 0.05%, and essentially unsurpassed since then. The only major advance in titrimetry in the 20th century was the introduction of complexometric techniques, which were based on the coordination theory presented in 1896 by Alfred Werner. Later on (1953), G. Schwarzenbach [9] developed the modern complexometric titrations based on EDTA and a variety of other chelating materials.

Up to the second half of the 19th century about 90 elements were discovered mainly by the support of analytical chemistry, while inorganic qualitative and quantitative analyses were developed and organized in systematic schemes. The chemists of this time had experienced a great progress in organic chemistry due to the elemental analysis of organic compounds, developed by Gay-Lussac, Liebig, Berzelius and Carius (19th century) for the determination of carbon, hydrogen, halogens and sulfur. Dumas developed the gasometric method, for the determination of nitrogen, using mainly Schiff's azotometer, much before the discovery in 1883 of the well known Kjeldahl method [10]. In 1876, W. Gibbs (1839–1903) published his famous paper "*On the Equilibrium of Heterogeneous Substances*", where such concepts, as *free energy*, *chemical potential*, *phase rule* and *chemical equilibria* were introduced and developed as cornerstones and fundamental principles for analytical chemistry. Jacobus H. van't Hoff (1852–1911, Nobel price 1901) (Fig. 5) worked on *osmotic laws*, *kinetic equilibria*, and discovered simultaneously with Le Bell the theory of the *asymmetric carbon atom-optical rotation*.

In 1862, the French chemist A.E. De Chancourtois and one year later the English physician and chemist John Newlands detected some periodicity patterns in characteristic properties of the 56 elements known at that time (spiraling around a cylinder and the *law of octaves* paralleling this periodicity to the musical scale) [11], but Dmitry Mendeleev in 1869 is credited as being the primary creator of the first version of the Periodic Table of elements. Mendeleev was also the first to predict the properties of elements yet to be discovered.

**Fig. 5.** Jacobus Henricus van't Hoff (1852–1911). Recipient of the 1901 Nobel Prize in Chemistry (first Nobel in Chemistry) "*in recognition of the extraordinary services he has rendered by the discovery of the laws of chemical dynamics and osmotic pressure in solutions*".

**Fig. 6.** Walther Hermann Nernst (1864–1941). Recipient of the 1920 Nobel Prize in Chemistry "*in recognition of his work in thermochemistry*".

**Fig. 7.** Wilhelm Ostwald (1853–1932). Recipient of the 1909 Nobel Prize in Chemistry "*in recognition of his work on catalysis and for his investigations into the fundamental principles governing chemical equilibria and rates of reaction*".

In 1834, Michael Faraday published a paper "*On Electrical Decomposition*", which popularized such common terms as *electrode*, *anode*, *cathode*, *anion*, and *cation*. He also concluded that the "*chemical decomposing action of a current is constant for a constant quantity of electricity*". In 1847, Faraday discovered the differences in optical properties of gold colloids from those of the corresponding bulk metal; therefore he is also considered as the first to report what later came to be called metallic nanoparticles.

In 1891, Walther Nernst (Fig. 6) published his famous equation, opening the way to potentiometry and potentiometric titrations, electroseparations, voltammetry, amperometric titrations and other techniques such as coulometry and polarography. Therefore he is considered as the father of modern electroanalytical chemistry.

## 3. The revolutionary steps of analytical chemistry

The year 1894 was very significant for analytical chemistry. Wilhelm Ostwald (Fig. 7) published an important and very influential text on the scientific fundamentals of analytical chemistry, entitled "*Die Wissenschaftichen Grundlagen der Analytischen Chemie*". He was the first chemist to recognize the role of analytical chemistry in the development of chemistry as a science, and he discussed for the first time theoretical explanations of analytical phenomena and processes, including equilibrium constants. He recognized the importance of analytical chemistry and using strong words stated that "*Analytical chemistry is doomed to continue occupying a position subordinate to other branches, if analytical chemists do not stop teaching and practicing analysis solely as an empirical technique and art, that requires skill and precision, and begin making use of the experimental and theoretical development of physical chemistry*". Much later I.M. Kolthoff expressed the same views about the importance of physical and biophysical chemistry for practicing analytical chemistry [12].

In the first quarter of the 20th century there were many important developments related to the theory of electrolytic solutions, which answered questions raised after the works of

Svante Arrhenius (1859–1927) on the dissociation of electrolytes in aqueous solutions [13]. Among them were the works of the physiological chemist Søren P.L. Sørensen (1868–1939), who in 1909 published his paper on the concept of pH [14] and at the same year the physical chemist N. Bjerrum published the paper on "*A new form for the electrolytic dissociation theory*" [15]. One year later A. Noyes and N. Bjerrum presented their work on "*The theory of indicators and applications to volumetric analysis and to acid base titrations in aqueous solutions*", which offered a theoretical background in titrimetry. Also, W.M. Clark, a physiological chemist, was the originator of a variety of oxidation–reduction indicators with standard potentials, which are mainly of physiological importance. In 1923, J.N. Br½?nsted introduced a new theory on acids and bases in his publication "*Some remarks on the concept of acids and bases*" [16]. At the same year appeared the Lewis theory on acids and bases, while Debye and Hückel improved the work of Arrhenius by giving explanations for the deviation of his theory on the behavior of the strong electrolytes in aqueous solutions [17].. Their work on the theory of electrolytes: "*Freezing point depression and related phenomena*" and the Debye–Hückel equation provided a way to obtain activity coefficients. Though, Nernst objected fanatically the Debye–Hückel theory of strong electrolytes. Even in 1924 in his talk, on the heat of dilution of lithium chloride, which was announced during the Deutsche Bunsengesellschaft meeting, Nernst concluded that this salt was not dissociated completely in aqueous solution, and he rejected the new theory. On the opposite, Arrhenius, who was present in the meeting, approached Hückel, and discussed with him his theory of strong electrolytes and asked to explain it to him in detail, fully welcoming it [18].

For many years after the so-called *Chemical Revolution*, which was initiated by the above scientists in the chemical science, analytical chemistry remained an established descriptive field of chemistry, based mainly on the skillfulness of the analysts. Even in the first quarter of the 20th century, the contributions made by van't Hoff, Gibbs, and Arrhenius, were only partially used in analytical chemistry. Until the beginning of the 1950s, analytical chemists applied methodologies, which were based mainly on simple and routine observations. They usually used knowledge, which was fed mainly from other branches of chemistry and worked meticulously on the development of analytical techniques, sometimes innovative and smart, but lacking rationality and theoretical base.

As society became more sophisticated and dependent on advanced technology, it simultaneously became more dependent on chemical analysis. Samples, analytes and concentrations were no longer the discipline's primary targets, but the analytical problems and questions arising from society, economy and R&D. The questions *what is it*? and *how much is it*? were now linked not only with essential and critical questions and problems of other areas of sciences, but more and more with acute problems of the society as diverse as economy, trade, essential trace elements, nutrition, support of the research on vital phenomena, diagnosis of contamination of the environment and its remediation, medical diagnosis and treatment, scientific investigation of defense, quality assurance of medical supplies, improvement of the quality of foods, etc. Now, analytical chemistry should turn and interact to other scientific fields and mainly to physics, biology and mathematics, in order to tackle these tasks. From this time on, analytical chemistry started a struggle against the so-called *analytical error*, discussing now improvements in the *reliability* of existing techniques meeting the demands for better chemical measurements and focusing to the collection of larger numbers of data, which arose constantly in our society.

Analytical chemists performed research to discover completely new principles of measurements and were at the forefront of the utilization of major discoveries such as lasers and microchip devices for practical purposes as ion-selective electrodes (ISEs), chemical- and bio-sensors, etc. They made important contributions to many other fields, as diverse as *forensic chemistry*, *health*, *food safety*, *archeology*, *space science*, *ethics*, in servicing governments, and *environmental quality*. Even, analytical chemists are today philosophizing and they are using many new logical terms and concepts to describe population distributions at near zero concentrations, where the quantized nature of matter dominates. These new terms and concepts are needed to estimate the limits of detection, the limits of decision and the capability of detection of an analytical method, and link them with its sensitivity, selectivity and optimization (chemometrics) [19–21].

Very significant, for analytical chemistry, was also the evolution and development of separation techniques like distillation, extraction, paper and ion-exchange chromatography gas and liquid chromatography, electrophoresis, cloud point extraction, solid phase extraction, etc.

Now the Oswald's recommendations made in 1894 are followed and realised. The analytical chemists, starting already from the third decade of the 20th century, made significant use of the theoretical findings and achievements of sister areas of chemistry, in order to formulate a modern field and occupy a new position of equality among them. As Yuri Zolotov states: "*The opinion of some snobs in science that analytical chemistry is not an independent science and should only serve others*, *including* '*their*' *fields of science is worth I-don*'*t-know-what. These snobs*, *do not know the difference between analytical science and analytical service*, *as a system of analytical support of related and unrelated sciences*" [22]. From *kitchen maid*, analytical chemistry became a *lady of science* and could now conveniently move and compete with other areas of chemistry in scientific salons and fora [23]. This was achieved through consecutive revolutionary steps:

The *first revolution*, which happened in the years around the verge of the 19th and the beginning of the 20th century, was the start of introduction of scientific principles to what before had been more of an art or skill than a science [24].

The *second revolution*, which became obvious around the period of World War II, was the shift from the *classical* to *instrumental* methods of analysis. Before the beginning of the war, Heyrovský (Fig. 8) had already developed electrochemical techniques including polarography, which promoted many analytical applications. The 1959 Nobel Prize for Chemistry was awarded to Heyrovský for the invention of polarography. Very fast, appeared in the market spectrophotometers (1941), IR-instruments (1943), self-recording IR, direct-reading and self-recording emission spectrophotometers (1951), gas-chromatographs and nuclear magnetic resonance (NMR) spectrometers (1953) and so on [10,25]. In 1952, the Chemistry Nobel Prize was awarded to A.J.P. Martin and R.L.M. Synge for "*The invention of partition chromatography*" and the Physics Nobel Prize to F. Bloch and E.M. Purcell for their work on the "*developments of*

**Fig. 8.** Jaroslav Heyrovsky (1890–1967). Recipient of the 1959 Nobel Prize in Chemistry "*for his discovery and development of the polarographic methods of analysis*".

*new methods for nuclear magnetic precision measurements*". 1952 was also the year of the invention of the gas chromatography (GC), which met effectively the challenges presented and needed by petroleum analysis. Then, in the late 1960s high performance liquid chromatography (HPLC) came to meet biomedical challenges, for the which the linking of chromatography to mass spectrometry has been a very fruitful step for analyses of samples, analyses that were previously in the sphere of speculation and imagination.

Around 1960, atomic absorption spectroscopy (AAS) was developed and new spectral analytical methods were successively born. Mass spectrometry, which in its early stage contributed to the research of isotopes, was applied now to the organic analyses for the identification of organic compounds in combination with GC.

According to some leaders in the field, the science of analytical chemistry is already in its *third revolution* since 10–20 years. This revolution stems from the accomplishments brought about by the first and second revolutions. Those made it possible for analytical chemistry to give very good and more detailed answers to its fundamental questions *what* and *how much* and to some new added to them like *how accurate*, *how precise*, *how convenient* or *how prompt and how economic* [26]. Now, in addition to composition and concentration, the analytical chemist is called upon to furnish a lot more detailed information about properties of material being analyzed: *Oxidation states*, *speciation of the analytes*, *crystalline structures*, *surface and spatial distribution of an analyte*, *life times of unstable species*, etc. Using basic principles, concepts, findings in physics, mathematics, electronics and those in sister areas of organic, physical and inorganic chemistry, analytical chemistry succeeded to achieve: (1) High speeds of collection of analytical data and development of competence to study fast phenomena, (2) objectiveness in measurements, (3) automation, (4) more efficient processing, evaluation and interpretation of analytical data, and (5) more rational design of experiments in order to achieve more reliable analytical data (optimization). The users of analytical instruments measure now all kinds of phenomena ranging across molecular and supramolecular structure in bulk and at surfaces, homogeneous and heterogeneous chemical reaction rates, excited-state lifetimes, transport rates in solids and membranes, molecular weight distributions, and receptor site specificities.

All these evolutionary developments of analytical chemistry in the last six decades are concentrated in its last formal definition, which was decided during the 8th Euroanalysis Conference in Edinburgh in 1993. This definition also shows the considerable distance between the classical and the contemporary analytical chemistry: "*Analytical Chemistry is a scientific discipline which develops and applies methods*, *instruments and strategies to obtain information on the composition and nature of matter in space and time*" [27–30].

In the last 60 years analytical chemists succeeded to introduce many improvements in their work as well as cost and time saving procedures: (1) Gravimetric and titrimetric analyses, which produce only one dimensional information, are now in most cases replaced by instrumental techniques producing *two- and multi-dimensional* information. The massive use of equilibrium approaches, for development of analytical applications in the past, is now on a par with *chemical kinetic methods*, which allow the determination of analytes in organic and biochemical as frequently as in inorganic samples. (2) With the aid of the new technologies, there were also many new approaches in gaining the *true analytical result*: Former applications affording the determination of a *single* or at most *two* analytes have been improved or replaced by others allowing *dozens* of analytes to be assayed simultaneously at quantities of a few *nanograms*, *picograms* or even *femtograms*, as compared to former limits of detection of a few milligrams or micrograms. We are approaching the detection of single molecules and atoms as well as the analysis of matter at the very fringes of our universe. (3) Early determinations of overall contents have been displaced by *speciation analysis* and the determination of *space and time distribution* of chemical species. Finally, analyses are no longer limited to be performed on the laboratory *bench* but, in an increasing rate, various portable instruments are used in *field-work*. (4) Thinking and acting machines and robotics that include an incredible complexity and density of electronic elements, are also available in the market as indispensable tools of experimental analytical chemists.

Forty years ago, most analytical instruments were isolated units, now we have hyphenated systems as a rule, seeking to take advantage of the selectivity of one technique and the sensitivity and identifying power of another. The title of a recent research article in Analytical Chemistry shows how far we have come: '*Reversed-phase high-performance liquid chromatography combined with on-line ultraviolet diode array*, *Fourier transform infrared*, *and proton NMR spectroscopy and time-of-flight mass spectrometry*: *application to a mixture of nonsteroidal anti-inflammatory drugs* [31].

Nanotechnology is today an area, which gives new dimensions to analytical chemistry in developing instrumentation for on-line process analysis, environmental monitoring, field portable instruments and microfluidic devices. In nanotechnology we are working today with nanoparticles, particularly carbon nanotubes, as adsorbents in chromatographic stationary phases, in functionalization or as polymer composites. An obvious example is nanobioelectronics in which nanomaterials are applied to the determination of biomolecules. Nanobioelectronics is a rapidly developing field aimed at integrating nano- and bio-materials with electronic transducers. These include the so called lab-on-a-chip microfluidic devices, nanoparticle-based bioassays, the bioelectronic detection of biomolecules, such as nucleic acids and proteins, electrochemical sensing devices for clinical and environmental monitoring, in-vivo biospecies, biosensors, etc. These developments will clearly aid analytical chemistry in the search for solutions to new problems [32,33]. Other, very promising areas are:

*Photoacoustic spectroscopy*. In 1880–1881, Alexander Graham Bell found that, when a thin disk was exposed to mechanically chopped sunlight, sound was emitted. In addition, he noted a similar effect when infrared or ultraviolet light was used [34]. The method has great advantages, because it does not require anything special in the way of sample preparation and is therefore especially suitable for turbid or opaque samples. Photoacoustic spectroscopy can be also applied to measure pollutants such as $NO_x$ or soot in the atmosphere or in automobile exhaust. Haisch and Niessner also list the analysis of textile dyes as another practical application of photoacoustic spectroscopy [35].

*Mass spectroscopy*. The combination of newer ionization methods (laser desorption, plasma desorption and secondary ionization) with super strong magnets or with improved time-of-flight (TOF) spectrometers has extended the useful range of mass spectrometry to the point that ions with masses as high as 10 kDa can be detected with unit mass resolution. For sorting out very complex mixtures sophisticated instruments are now used in routine (LC–MS, LC–MS/MS, LC–TOF). Libraries of mass spectra have made the identification of components of complex mixtures a trivial task.

*Inductively coupled plasma-mass spectrometry (ICP-MS)*. ICP-MS, is undoubtedly the fastest growing trace element technique available today. Since its commercialization in 1983, because of its ability to carry out rapid multielement determinations at the ultra-trace level, it covers a diverse range of application areas including environmental, geochemical, semiconductor, clinical, nuclear, chemical, and metallurgical. ICP-MS has clear advantages in its multielement characteristics, such as speed of analysis, detection limits, and isotopic discrimination capabilities. The method will eventually replace older relevant techniques, like flame atomic absorption (FAA), graphite furnace atomic absorption (GFAA), and inductively coupled plasma-optical emission spectrometry (ICP-OES) [36,37].

*Light detection and ranging (LIDAR or LADAR)*. This is an optical remote sensing technology, which apart of other surveying applications (geology, seismology, archeology, etc.), today is also applied for the detection and determination of chemical compounds in aerosols, clouds and even single molecules.

*Kinetic methods of analysis*. During the years of domination of gravimetric and volumetric methods in analytical chemistry, kinetics was considered responsible for the sluggishness of some end points in titrimetry or the appearance of muddy precipitates. Though, in those early times, there were also positive aspects of kinetics as for example the kinetics of crystal growth greatly influences the crystal size, their purity and finally the filterability of the precipitates. Sixty years ago, undergraduate students, or even graduate students were persistently taught to mix all solutions thoroughly and homogeneously and wait for equilibrium to be established, before any rational measurement and assay could be made. Nobody disputed this approach. However, later these kinetic phenomena were exploited and adopted in kinetic schemes of quantitative analysis [38,39]. Reaction-rate methods are characterized by two inherent advantages, the *scarcity of parasitic blank signals and the possibility to make kinetic discriminations*. Therefore kinetic methods are of great relevance to all procedures intended to increase the selectivity of an analytical method. This was materialized in the differences of the reaction rate (kinetic based determinations), in differences in mobility (chromatography or electrophoresis), or in the evolution of the response of the analytes over time, when they are kinetically excited by instrumental parameters (time-resolved fluorimetry and electrode kinetics in some electroanalytical techniques). Undoubtely the introduction of time as a measured parameter or as discriminating factor/parameter gave a new dimension in analytical chemistry. Many analytical techniques or approaches, like Chromatographic separations, fluorescence and chemiluminescence measurements, electrothermal atomic absorption, electrode reactions, and others, closely examined, include their kinetic nature or are characterized by key kinetic parameters [40].

*Flow analysis methods*. The outstanding example of the mid 1970s through the 1980s, and perhaps one of the highlights of the impact of kinetics in analytical methodology, is the dynamic characteristic of signal acquisition in continuous-flow sample processing. The stopped-flow techniques and especially the *flow-injection analysis* (FIA) are the most important representatives of this area. With the stopped-flow instruments very fast reactions were possible to be studied and applied for the development of reaction rate methods.

We will stay for a little in the FIA, which from 1974, after its discovery by Hansen and Ruzicka, was developed in one of the most powerful analytical techniques [41]. FIA is based on creating a reproducible concentration gradient of an injected sample within a carrier stream (of reagents), instead of mixing the sample and reagent homogeneously. Doing so, any point of the reaction on the approach to chemical equilibrium is inherently as good a measure of the steady-state as the steady-state itself. That is possible in FIA, due to its *reliance of sample injection*, *reproducible timing and controllable dispersion*. Therefore FIA has become a vehicle for speeding up analysis because: (1) it allowed transient/metastable products to be ascertained and thereby used for quantifying analytes, thus it made possible the use of very sensitive and selective reagents, but totally unusable to be used for equilibrium measurements, because of the instability of products; (2) it facilitated delicate procedures such as chemi- and bio-luminescence, which before were laborious or impossible to be administered; (3) it aided and augmented the applications of chemical sensors and biosensors; (4) it permitted new concepts such as pre-concentrations of trace constituents; (5) it facilitated enzyme amplification schemes; and (6) it yielded possibilities for enhanced selectivity by exploiting kinetic discriminations [42,43]. As a result the number of publications in the area of FIA has really exploded exponentially from 1974 till today. The FIA technique was further improved and fully automated in the Sequential Injection Analysis (SIA), where the single injection valve was replaced with a multiport selection valve and the solutions were sequentially aspirated, under computer control, in the reaction coil, reducing further the consumption of reagents. FIA and SIA revived long forgotten and analytically abandoned chemical reactions schemes [44,45].

*Biosensors*. The appearance, fabrication and application of biosensors was a follow up of the development of various types of chemical sensors (Ion Selective Electrodes, ISE), which were in use already in the verge of the 5th decade of the twentieth century [46,47]. In 1956, Leland Clark Jr. (1918–2005) published his definitive paper on the oxygen electrode. The burgeoning field of biosensors began with Clark's paper on the enzyme electrode, announced in the New York Academy of Sciences in 1962. Based on this experience and addressing his desire to expand the range of analytes that could be measured in the body, he made a landmark address, in which he described how "*to make electrochemical sensors*, *pH*, *polarographic*, *potentiometric or conductometric*, *more intelligent*", by adding "enzyme transducers as membrane enclosed sandwiches". A pivotal patent on an oxidase electrode resulted, for one thing, in the first commercially successful glucose electrode marketed. The patent also covered alcohol, galactose, oxalate, cholesterol, lactate, amino acids, and many other peroxide-generating substrates. Scientific journals now contain descriptions of a wide variety of devices exploiting enzymes, nucleic acids, cell receptors, antibodies and intact cells, in combination with electrochemical, optical, piezoelectric, impedimetric and thermometric transducers. Each approach can be applied to numerous analytical problems in health care, food and drink, the process industries, environmental monitoring, agriculture, defense and security. The design of integrated systems approaches to patterning sensitive elements and methods to improve the sensitivity, stability, cost and selectivity of biosensors, are today key areas in analytical chemistry [48,49].

*Chemometrics*. Chemometrics is defined as the branch of analytical chemistry, which applies mathematical and statistical methods in the chemical analysis. We would add that these techniques, in many cases, include also logical and philosophical concepts, specifically when they are referred and applied in the vicinity of trace concentrations of the analyte, where the distribution of populations are not Gaussian. Also, the consideration of *noises and interferences* of the analytical signal, the strategies of their removal as well as the concepts of *sensitivity*, *limit of detection* (*LOD*), *limit of decision*, *response time*, *resolution*, of an analytical device or method, are treated in some cases by applying also logical or/and philosophical ideas. *Cluster analysis* and *pattern recognition* techniques are handling very large volumes of analytical data using appropriate software to sort them out in groups revealing internal structures and similarities between the members of each group. *Optimization methods* applied in a wide extend in chemical analysis to improve its performance, in dependence of various parameters, is the procedure by which the analytical chemist makes adjustment of the values of these parameters in order to get the best results. The *Simplex optimization* is one of many existing approaches to reach this task [50,51]. Today specialized statistical and software packages, applying chemometric concepts, are ubiquitous in analytical laboratories for the treatment of large amounts of analytical data. Though, the teaching of these concepts to the analytical chemistry students is necessary in order to make the proper use during their work.

## 4. Education and ethics in analytical chemistry

*Education in analytical chemistry*. Teaching of analytical chemistry requires good background knowledge of the student on mathematics, general chemistry, and physics. At the college level, parallel to the traditional chemistry curriculum, the students should also take courses in statistics, electronics and computer science [52,53].

Fifty to sixty years ago, teaching of analytical chemistry was almost exclusively confined to qualitative and quantitative inorganic classical analysis. Some titrimetric methods, and to a lesser extent gravimetric methods, are still included in the curricula, but the corresponding laboratory exercises have been significantly reduced giving place to instrumental ones. However, the "wet chemistry" on which most earlier analytical methods were based, is still of fundamental importance. The complete abolition of classic qualitative analysis from many university curricula has been the subject of criticisms. The Priestley Medalist Henry Taube, a specialist in coordination chemistry, interested in reactivity of ions, states: "*I think a major mistake was made when qualitative analysis disappeared from the curriculum. It was a way of introducing descriptive chemistry which, if you look at it deeply, can interest students in reactions. I consider reactions to be the heart of chemistry. Spectra, for example, are important not only in themselves, but because they reveal important features of electronic structure which, in turn, affects reactivity*" [54]. The same is true for classic quantitative analysis, such as gravimetry and titrimetry, which are fundamental in the basic education in analytical chemistry, because they are *absolute* analytical methods [55].

Instrumental analysis is essentially based on the comparison of the signal from a sample with that from a standard. Although standard solutions for instrumental analysis are easily available in the market, it is the basic analytical chemistry that will teach students, how to obtain an accurate amount of a standard or of a sample, by weighing, or by obtaining an aliquot of their standard solutions.

A lot of effort is put today in shrinking the analysis steps (sampling, sample transport, filtration, dilution, chemical reactions, separation and detection) to chip size, the so-called Total Analysis System (TAS). A TAS, describes a device that automates and includes all necessary steps for chemical analysis of a sample, e.g. sampling, sample transport, filtration, dilution, chemical reactions, separation and detection. Although there are only few examples of such systems competitive with traditional analysis techniques, their potential advantages include size/portability, speed, and cost.

The contemporary trend of expanding the teaching of instrumental methods in the university courses necessitates the teaching of the associated physical and chemical theories, quite often accompanied with some practical aspects on electronics and informatics. Thirty or forty years ago a giant step in instrumental analysis occurred. This was the introduction of microcomputer control on almost all analytical instruments. Hence, nowadays, almost all instrumental analysis textbooks include material on electronics, on data acquisition and processing (i.e. operational amplifiers, digital electronics, D/A and A/D converters, microcomputers, noise measures and reduction, signal sampling and signal smoothing techniques). Elective courses on instrumentation (Chemical Instrumentation), dealing in more details with topics like these, are offered to chemistry students and are published in many textbooks [56].

Analytical chemistry teachers have the responsibility to use and teach the correct terminology. In many cases terms like *analytical process*, *analytical technique*, *analytical method*, *analytical procedure*, as well as terms like *analysis of* …, *determination of* …, *measurement of* …, and so on, are used indiscriminately in analytical chemistry publications or oral presentations. For example, we are *analyzing a sample* (not an analyte), we are *determining an analyte in a sample* (not the sample or its absorbance) or *we are measuring a property associated with an analyte* (not of the sample).

It is of utmost importance for the students of analytical chemistry to realize that, instrumental analysis provides only the final and usually the easier step of an analytical protocol, that is the measurement of a property associated with the amount or concentration of the sought for analyte. Before that, a chain of more tedious steps is usually needed. Therefore it is imperative for the teacher to teach how various real samples must be obtained and treated before the measurement step. Hence, emphasis must be given on sampling theory, sample decomposition methods, separation techniques from interfering matrices, preconcentration of analytes, etc. Here is where knowledge provided by classic analytical techniques is indispensable

Even the measurement step is not the final one. In order to understand how to assess the analytical data, chemistry students have to know the meanings of accuracy and precision and familiarize themselves with aspects like propagation of error and error distributions (Gaussian, Poisson, binomial, etc.). New metrological terms of fundamental importance such as uncertainty and traceability have been relatively recently introduced, therefore students must be exposed and get accustomed with them as early as possible. It is very important for them to learn to express their analytical results in a reasonable manner reflecting the overall precision of the method used. Later, in the real world, they will try to minimize the overall error and choose the most appropriate analytical techniques for the analysis of a particular sample after making the necessary trade-offs between sensitivity, precision, and cost of analysis.

The wide diversity of demands by society on analytical chemistry combined with the astonishing scientific developments in the field, as previously described, made necessary the specialization of the majority of analytical chemists on specific techniques and/or particular type of samples. Today, most postgraduate chemistry students specialize in fields other than analytical chemistry. However, regardless of their actual specialization, it is highly probable to present results heavily based on analytical data.

Finally, we would like to point out that the basic education in analytical chemistry, for future generations of chemists, is to teach how to get the accurate analytical data by exploring new ideas and by avoiding to stay on routine analytical methods "*The object of teaching chemistry in college or university is not to turn out mere routine analytical chemists*" [57,58]. An analytical chemistry student must learn to consider innovative ideas and new concepts not as threats or something tremendously difficult, but as a challenge. The teachers, among the readers of this article, will certainly agree that sometimes it is difficult for them to reconsider and reform the content of their lectures and renounce obsolete concepts. On the contrary, their students can easily grasp new theories and explore fresh ideas (see the example of Nernst, mentioned before, who denied accepting the theory of Debye-Hückel).

*Ethics in analytical chemistry*. Teaching analytical chemistry, we must keep in mind the following principles and questions:

(1) Do analytical chemists as research scientists have specific kinds of philosophically founded responsibility and duties to

the international society, because of their knowledge, skills, or practice?

(2) What lessons can we learn from case studies of chemical research with negative effects on living beings, e.g. weapon research, drug design, animal experiments, etc.?

(3) In which way does chemistry contribute to non-economic developments of society (e.g. moral, political, intellectual, esthetic, etc.)?

(4) What can we learn about the ethics of science in general and analytical chemistry in particular from historical cases of the involvement of scientists in public affairs, such as the use of DDT, the Minimata case, the Bhopal incident, etc.?

## 5. Conclusions

Modern analytical chemistry is definitely no longer in the margin of any other field of chemistry but the "*interdisciplinary science of the generation of information about the composition and the structure of matter*". Furthermore analytical chemistry is the "*key to solve problems related to material systems and to society*".

The efforts that Boyle, Berzelius, Lavoisier, Ostwald, van't Hoff, Faraday, Nernst, and others started, by making the chemical world quantitative, are not yet finished. The ground work that the chemist made during the 19th, the 20th century and the analytical chemist of the 20th century Pregl, Kolthoff, Lingane, Laitinen, Reilly, Rogers, Popoff, Malissa, Belcher, Thomas, Ewing, Pungor, Malmstadt, Zolotov and others laid by their innovative leadership, has certainly paid off. Analytical chemistry is today stronger than ever. However, it is still far from established since, some of the academic chemical community opposes the acceptance of analytical chemistry as autonomous branch of chemistry [22,59]. Nevertheless, after the impressive progress made in the last 50 years, its influential and successful involvement to answer acute questions of the society, in many areas of science and its contribution in the development of the technology, analytical chemistry gained high reputation and was recognized as an autonomous field of chemistry in academia.

Much effort is also put today into studying and analyzing biological systems. Examples of rapidly expanding fields in this area are: the large-scale study of proteins, particularly their structures and functions (*proteomics*), the scientific study of chemical processes involving metabolites (*metabolomics*), and the study of metal and metalloid species within a cell or tissue (*metallomics*), the later dealing with metal binding to proteins and other molecules.

Twenty years ago we were considering ourselves as being in the doorstep (eve) of an era of large development in biological sciences, today we are already in the core of this age. We can predict that the science of analytical chemistry will become more attractive and fascinating in the next 20 years. New diseases, new materials, new-sophisticated methods in crime, and the questions alerted by mankind (terrorism), all create new challenges. World population has quadrupled during the twentieth century, and the problems have been magnified several times over as the increased population strives to enhance standards of living. Analytical chemistry can monitor and provide solutions. In teaching, students need to be shown, as early as possible, a true picture of analytical chemistry research, that is beyond instrument architecture and performance, and they must be directed at making measurements on problems relevant to everyday life.

Though, it must be pointed out, that because of the interdisciplinary nature and approaches in analytical applications, the limits between the scientific areas tend to be obscure and diffuse. Nevertheless, it is believed that the science of chemical measurements, which is the basis of analytical chemistry, continues to have self-existing hypostasis. Analytical chemistry is a field of chemistry, as always was, but today it is also a scientific tool to serve the society, the environment the humanistic sciences and the democracy, using continuously knowledge from almost all fields, in order to reach its tasks. "*The analytical chemist is still engaged in a never ending campaign to which there can be no ultimate victory*, *although there will be many outstanding successes and triumphs along the way*" [10].

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