Green Chemistry

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Do we need Green Analytical Chemistry?

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1. Introduction: The state of Analytical Chemistry

Analytical Chemistry is defined in Wikipedia as “the study of the separation, identification, and quantification of the chemical components of natural and artificial materials,” in which the target of qualitative analysis is to identify the chemical species in the sample, and that of quantitative analysis is to determine the amount of certain components in the substance. This aspect of Analytical Chemistry has been important and emphasised since the early days of chemistry, with regards to methods for determining which elements and chemicals are present in an object. However. Analytical Chemistry is broader and more complex than that, and the definition must reflect this. A more appropriate description of Analytical Chemistry is offered by R.W.Murray: “the science of inventing and applying the concepts, principles, and…strategies for measuring the characteristics of chemical systems”[1]. The following definition of Analytical Chemistry emphasises the importance of developing analytical methods [2]:

“The object of Analytical Chemistry is to obtain chemical information about materials concerning their qualitative and quantitative composition and structure. Analytical Chemistry investigates the type and the quantity of components and the structural relations between the constituents. Analytical investigations are directed to solve general problems and, for this purpose, to develop and to advance analytical methods including sampling, sample preparation, and evaluation, and to apply statistics and data analysis for the interpretation of analytical results”.

As mentioned above, Analytical Chemistry is the main means of obtaining chemical information on which decisions with regard to the quality and quantity of the material or processes will be made. Although it is true that alchemists attempted to obtain chemical information, most of the major developments in Analytical Chemistry have taken place since 1900, and instrumental analysis has become progressively dominant in the field. The entire history of chemistry is based on the invention and application of new principles and strategies for measuring the characteristics of chemical systems. Analytical Chemistry is not just a tool to be used in other areas of chemistry, but the engine driving the evolution of the whole discipline of chemistry. This underlines the possibility and need to include new principles and developments in chemistry into the Analytical Chemistry paradigm. The biggest step forward in philosophy of chemistry is the formulation of principles for Green Chemistry [3]. It is logical that these principles have been applied to the modification of existing analytical methods and the development of new ones.

The following are active opportunities for Analytical Chemistry to take part in societal developments:

- ✓ participation in the accumulation of knowledge and the formulation of theories;
- ✓ justification of the need for new laws and administrative prescriptions;
- ✓ development of standards and specifications;
- ✓ determination of the environmental benignancy of new methods, processes and products.

Analytical Chemistry performs the following functions:

- ✓ deals with qualitative and quantitative information about the nature, amount and identity of elements and molecules in our environment;
- ✓ provides sufficient information with the appropriate analytical sensitivity, selectivity and accuracy to make decisions and solve problems;
- ✓ provides specific information according to the requirements of the end-users of the chemical information.

Analytical labs and analysts are in a crucial position to solve various problems, and the demand for this kind of laboratories is growing, as is the number of analyses in different areas of activity. These labs produce large amounts of different kinds of information for further processing, for chemistry and other purposes. Monitoring and quality-control laboratories require a significant amount of chemicals and energy for the large number of runs. Their total waste production and energy consumption is substantial. Studies indicate that the cost of testing and quality-control measurement in Europe is close to 1% of GNP and exceeds EUR 90 billion annually [4]. The amount of waste produced and energy consumed by an analytical laboratory is comparable with that of the fine chemical or pharmaceutical industries. This makes it entirely reasonable to stipulate that environmentally benign processes be used in analytical laboratories and that methods be developed that employ a reduced amount of materials – analytes as well as supporting solvents, reagents and instruments – required to generate an analytical signal, and that produce a reduced amount of waste.

Undertaking this task was called for 20 years ago: “…. the efforts taken to reduce the undesirable side effects of the tools of the trade. Indeed, it is time to enhance the role of analytical chemistry to take a lead towards the preserving of our environment rather than to measure its deterioration” [5].

In essence, Analytical Chemistry provides information for making decisions and solving problems, as it is expressed with some exaggeration on Figure 1. However, questions arise: What kind of information is actually required — the precise number of molecules, or basic knowledge about the object? Does every molecule need to be counted for every analysis? The speed and cost of the analysis also becomes important in the case of a large number of analyses. In addition, the quality of the analytical data must be measured or assessed and presented. This means that Analytical Chemistry procedures with the requisite quality should target the specific requirements of end-users, while providing the analytical information in the most economical manner entailing the least possible expenditure of materials and energy, and generation of waste.

Figure 1.

2. Green developments

In order to satisfy society’s need for large amounts of information about the environment, products and processes, most research in Analytical Chemistry is directed towards highly automated instrumental methods, combining different methods for the treatment of samples and separation of components, or employing complex methods of detection. This kind of systems integration with high throughput and multiple tasks leads to savings of energy and materials, which is one of the principles of Green Chemistry; new materials (nanomaterials, microfilms, micro assays, etc.) allow the size of the sample needed for analysis and the amount of waste to be significantly reduced, which is the most important principle of green chemistry. In addition, the use of computing and communication technology in chemical data analysis, especially in sensor-related research and information/data handling, reduces the steps in chemical analysis and consumes less energy, in accord with another principle of green chemistry.

Despite these developments, Green Chemistry is very rarely mentioned in the literature related to Analytical Chemistry, and the purposeful incorporation of green chemistry principles into the selection of suitable methods of analysis for obtaining chemical information is haphazard. Several books and review papers on so called Green Analytical Chemistry were published last year, which leads one to expect an increase in the development and modification of analytical methods that conform to the principles of Green Chemistry [6, 7, 8].

The most frequently discussed areas of Analytical Chemistry related to Green Chemistry are separation science and sample preparation because these are the biggest consumers of solvents and other reagents [9]. For this reason, priority is given to the minimal use of solvents, the replacement of harmful ones, and recycling. It is called the “3R” approach – Reduction, Replacement, and Recycling [10], and has resulted in the wider introduction of alternative solvents and the re-design of instrumental methods. It also has a substantial economic impact in control labs with a large volume of analyses.

The following are some examples:

R1 – Reduction – Using elevated temperatures changes the properties of separation media and solid supports, increasing efficiency and reducing the use of solvents.[11] The disadvantages of this approach, in addition to the need for special temperature-resistant packing materials, include a potential risk of on-column degradation of thermally-labile compounds, and solubility problems with hydrophobic compounds. Using narrow-bore columns - which entail smaller particles - , higher pressures and shorter columns, substantially reduces solvent consumption and waste generation [12]. Additional economy is obtained with micro columns, which necessitate only a small fraction of the chromatographic stationary phase.

R2 – Replacement – Supercritical CO_2 is relatively widely used in preparative scale HPLC for the separation of biologically active compounds [13]. Intensive research is also being conducted to find a replacement for (environmentally harmful) acetonitrile, and reasonably good results are being obtained for ethanol [14]. There are some organic solvents such as the lactate esters obtained from biomass feedstock [15]. A disadvantage of the new eluents is the fact that many regulating agencies require the use of validated methods, which include acetonitrile as a mandatory component.

Ionic liquids, which are very fashionable solvents at the moment, could find a use in sample preparation methods – extraction – but they are not a likely medium in chromatographic methods [16]. However, one must be very careful in declaring these new solvents to be totally green. Ionic liquids are inert and not volatile, which are good properties for developing environmentally benign processes, but care must be taken because of possible toxicity some of them, and their environmental footprint is considerable because of the complex and multi-step synthesis.

R3 – Recycling – Whenever possible, the necessary equipment must be obtained and solvent recycling used in the lab to reduce the amount of waste generated. However, this is expensive, and the energy requirements unfortunately prevent it from being a truly green approach.

M. Koel and M. Kaljurand proposed a “4S” approach for Green Analytical Chemistry [17] in order to obtain the most environmentally benign and economical outcome:

S1 – Specific methods – The best example of employing different methods to solve similar problems is using capillary electrophoresis (CE) in place of HPLC. Capillary electrophoretic techniques are being considered because of their flexibility, high-efficiency separations, low consumption of solvents, and shorter analysis times relative to other techniques; in many applications, they are more effective than HPLC. CE features an unlimited selection of separation media (buffers), can be combined with chromatographic separation mechanisms, and used with different kinds of detectors. It is possible to use CE systems for sample collection.

One well-established tool to solve specific analytical problems is flow analysis, which has great potential to minimise reagent consumption and waste generation, and the ability to implement processes unreliable in batch [18].

Another direction related to this approach could be using methods that allow for direct analysis of the probe with minimal sample preparation. Various laser-based and optical methods should be considered in this regard [19,20]. In addition, spectroscopic methods permit real-time process analysis/monitoring in situ/in vivo; and they can be implemented with simple and portable instrumentation while maintaining high selectivity and sensitivity [21].

S2 – Smaller dimensions – Performing measurements on a microchip platform in which functionalised microsystems integrate multiple sample-handling processes (pre-concentration/extraction, chemical/biochemical derivatisation) with the measurement (detection) step substantially reduces the amount of solvents and chemicals [22]. Electrophoretic separation of analytes can easily be included in these miniature systems.

The amount of sample available for analysis is often very small, as in bioscience and nanoscience where it is necessary to analyse individual cells or nanoparticles, sometimes even single molecules, and this is one reason to justify miniaturisation. Miniaturisation also results in energy savings. However, microchip systems have problems associated with connectivity, and a requirement for small-scale pumps, valves and reactors. To compensate for this, the Lab-on-a-Valve (LOV) concept is an interesting downscaled analytical tool for pressure-driven sampling at a low µL level. It can easily accommodate renewable micro-solid phase extraction, non-chromatographic speciation or chemical vapour generation using programmable flow, for optical and electrochemical detection on-chip including optosensing approaches [23].

Manipulation of droplets of liquid samples is also proposed to overcome interface problems in microfluidics. Individual droplets are like small sample vessels, which can be used as reactors, extraction vessels and transportation devices for later examination by other methods such as CE, in which it is used as the flexible input device. One example is where the resolved analytes in the CE capillary are sequentially fractionated into droplets and moved to the CE column, with separation completed in less than 15 min. [24]

S3 – Simpler methods – Sufficient information about chemicals can sometimes be obtained by methods in which sample pre-treatment is not necessary, or in which the whole process can be conducted with an instrument without any moving parts. Paper can be used as an inexpensive, biodegradable, renewable, flexible substrate for prototype “labs-on-a-chip”. It is a material that is universally available and compatible with many biological and chemical assays. The porous nature of the material eliminates the need for external pumps or energy. After use, this “device” can be easily disposed of [25, 26].

An increasing array of lateral flow devices is now available – porous material or membranes are combined with immunoassay testing, as in the common pregnancy test. Contemporary mobile phones can be used for sending pictures of reaction spots on paper to a personal computer via the internet for further processing (a calibration curve can be constructed and quantitative analysis completed using simple free software)[27]. This is a direction less studied but with great perspective – not to replace high performance laboratory instruments but get high quality analytical information on-the-site or point-of-care.

S4 – Statistics – Information relevant to the analyte signal could be generated from the data obtained by mathematical manipulation of the measurement results **–** meaning that a signal related to a particular analyte could be extracted mathematically from output data. In this case, chemical information is obtained by analysing chemical measurement data; this area of research is called Chemometrics (the chemical discipline that uses mathematical and statistical methods to design or select optimal measurement procedures and experiments) [28]. Chemometrics could be an alternative to chemical data processing, allowing for the use of much simpler measurement processes that usually avoid sample pre-treatment and entail a shorter analysis time. These are generally performed using multivariate statistical procedures.

Here is an example where Near-Infrared (NIR) Spectroscopy, in combination with chemometrics, was used as a rapid tool for determining if exposure to contamination from mine tailings had influenced the matrices of the specimens, compared to those from natural populations. It was possible in this case to establish how much the season of harvest, geographical origin, and level of soil contamination played a determining role in the chemical profiles of the individual specimens harvested from mine sites or natural populations[29].

Another example concerns the use of NIR system together with quantitative chemometrics to model hexahydro-1,3,5-trinitro-1,3,S-triazine (RDX) content in a propellant plant. A fibre-optic probe from the spectrometer was directly inserted into samples that were continuously stirred to record in situ spectra. Using the proposed NIR method eliminated the consumption of chemical reagent and the production of waste associated with the overall prediction procedure. The results show that the NIR system is inherently rapid, clean, capable of preventing hazardous residuals originating from the traditional analytical procedure, and has the potential for monitoring RDX content during solid propellant processing [30].

The chemometric approach is very helpful in the case of hyphenated methods like LC-IR because of its user-friendly background correction that facilitates online multivariate curve resolution, provides improved signal-to-noise ratios, removes the remaining mobile phase and background signal contributions, and resolves overlapping chromatographic peaks, even in challenging situations when gradient conditions are employed and only poor chromatographic resolution is achieved [31]. Significant savings can also be obtained by making use of large data tables for analysis and visualisation; exploratory data analysis can assist in reaching conclusions without a detailed chemical analysis of every analyte. The measurement results obtained by spectroscopic, chromatographic, or electrophoretic techniques in this case, can be defined as a characteristic profile reflecting the complex chemical composition of the analysed sample – a fingerprint. By extending the information contained in the chemically complex sample over time, the individual compounds and their underlying information can be revealed. Fingerprint analyses are widely used as a methodology for the treatment of spectroscopic and chromatographic measurement data and have provided an efficient and powerful tool for the quality control and authentication of different herbs [32].

3. Instrumental analysis

Instrumental analysis is the core of chemical analysis at present, mainly because of its sensitivity, complexity and automation, as well as fast data processing and presentation. It is steadily replacing wet chemistry in analysis, and to some extent in sample preparation, but even in the latter case automated wet procedures are becoming an integrated part of the analyser. In many cases this allows for a substantial reduction in the use of chemicals and solvents in analysis.

There are a variety of analytical instruments ranging from stationary laboratory equipment to mobile sensors in use in chemical laboratories, which accommodate different instrumental methods; they can be presented in the form of a multi-level pyramid according to their complexity and analytical parameters (Fig.2).

At the top are high-performance instruments with maximum sensitivity, selectivity and precision, which require highly skilled personnel, and consume large amounts of chemicals, solvents and energy. These kinds of instruments are used mainly in research laboratories to develop new analytical methods, and in central test and control laboratories that provide validation of methods and final quality control of analytical information.

On the next level are instruments that perform reliable monitoring and testing methods with adequate specificity and accuracy, which require trained personnel and consume economical amounts of energy and materials. Most control laboratories in industry and the public sector use this type of instruments; they produce most of analytical information for process control and for the assessment of environmental conditions.

Despite the vast network of this kind of laboratories, there is a huge need for simple indicator-type sensors with sufficient specificity and accuracy, which do not require trained personnel, generate little or no waste, and consume minimal amounts of energy or none at all. This level forms the base of the pyramid, and these sensors are used to obtain chemical information from the point-of-care, including on-site process analysis for the widest use. The most important and exacting cases are analysed in a lab at the next level.

Figure 2.

Analytical instrumentation is the most expensive, energy- and materials-intensive part of Analytical Chemistry and also the most wasteful from a Green Chemistry perspective, especially when the footprint from the production of instruments is considered. Unfortunately it is difficult to confirm it with solid numbers; there are hardly papers available on life cycle analysis (LCA) on analytical instrumentation - only few examples on small-sized electronic products[[33]], on comparison of different methods [[34]] and solvents [[35]] were found.

It is clear, therefore, that high performance instrumental methods are not the only solution everywhere. It is often said that simple and robust analytical procedures produce low quality data, without mentioning that every method has its optimal area of application and that a variety of instruments is needed.

In the scientific literature there are many examples of environmentally benign and economical methods of analysis to which the word “green” can be applied, but introducing them into industrial practice has not been overly successful. Two main reasons can be given: the first is that it is difficult to validate and accredit new benign methods to obtain wide international recognition, which is especially important in areas related to food and health. The second reason has to do with the influence of the market economy on the development of new instruments. Consumerism encourages the acquisition of goods and services in ever-increasing amounts. New models usually have minor changes in performance and appearance, and revolutionary changes in instrumental methods are rare, which means that analyses could well be performed with older instruments that have been kept in good repair.

A solution in this regard can be found in the proposed principles of Green Engineering pertaining to instrument design, according to which the most important user requirements are the following: i) the instrument should be durable enough to withstand the necessary operating conditions for its expected lifetime; ii) the expenditure of underutilised and unnecessary materials and energy should be limited; iii) the use of different materials should be minimised; iv) the elements and parts of an instrument should have a commercial “afterlife” [36].

The environments in which analyses are performed – laboratories – have an influence on the greenness of Analytical Chemistry as well. Conserving energy and making the most economical use of equipment time must be considered in laboratory operations, and these optimised procedures are closely connected with good laboratory practices [37].

The scientific literature reports the active development of new analytical methods in university and research laboratories, but only a few of the environmentally benign and economical methods of analysis are put into practice. This directs to the necessity of advertising and emphasising the importance of the environmental aspects of analysis and especially of instrumental methods. However, certain conservatism on the part of authorities in accrediting and recognising new methods must be mentioned - the environmental aspects of the methods (saving chemicals and solvents, reducing energy use and generating less waste) are not at the top of the list in their assessments and recommendations for validation.

4. How to set priorities:

The main reason that Green Chemistry is rarely mentioned in the literature related to current trends in Analytical Chemistry is likely because of analytical requirements — sensitivity, selectivity, robustness, accuracy, and precision being the most essential factors in this regard; the time, cost (including purchase, operation, training, and space) and environmental benignity of the analytical procedure are secondary. However, judging from the number of publications on Green Analytical Chemistry, this situation is starting to change and more attention is being given to reducing solvents and chemicals used in analysis and saving energy. At the moment, "Web of Science" yields more than 1200 hits on the keywords "Green Analytical Chemistry".

As mentioned above, analytical measurements are important in many different areas, the main goals of which are to assess compliance with certain limits and to make decisions on the basis of the results. Different levels of decision making require different information, and this information can be successfully provided by different analytical methods/instruments. If a simple and robust paper-based assay can provide sufficient evidence of certain compounds in the environment, there is no need for gradient elution HPLC-ESI-MS/MS. Every analytical method has its optimal area of application due to its sensitivity, selectivity, robustness, accuracy, precision, and time required for and cost of the analytical procedure, which includes the cost of chemicals, solvents, energy and waste treatment.

One way to assess the environmental impact of analytical methods is to perform a life-cycle analysis of the components (chemicals, solvents, instrumentation, data processing equipment, etc.) used in the process and to calculate their carbon footprints. Analytical instrumentation is an essential part of the analysis process and a thorough life-cycle assessment of these instruments can indicate the greenness of the analytical method. But this is a laborious task and not easy to perform in many cases because of a lack of necessary information about the production of instruments and chemicals.

However, there is a great need to assess existing analytical methods, and a few examples can be cited. L.H.Keith, et al [38] have proposed four criteria for categorising existing methods and providing a basis for selecting environmentally safer methods, and establishing their greenness profiles: Persistent/Bioaccumulative/Toxic (PBT), Hazardous, Corrosive, and Waste. A fifth parameter — energy consumption — was later added [39]

A method is defined as less green if:

- ✓ PBT – A chemical used in the method is listed as persistent, bioaccumulative, and toxic (PBT), as defined by the EPA's Toxic Release Inventory (TRI);

- ✓ Hazardous – A chemical used in the method is listed on the TRI or on one of the RCRA’s D, F, P or U hazardous waste lists;
- ✓ Corrosive – the pH is less than 2 or greater than 12 during the analysis;
- ✓ Waste – The amount or waste generated is greater than 50 g;
- ✓ Energy-intensity – the energy consumption per sample is more than 1.5 kWh.

This approach identifies optimal and suboptimal methods for concerned users.

Because of the importance of assessing the amount of waste produced during the analysis (including any unused samples), it is crucial to include a waste-decontamination step in the analytical process [40]. For this purpose, the following (but not the only) steps are proposed: i) recycling, ii) degradation, and iii) passivation.

J.Namieśnik et al [41] have developed an “ecological scale” for evaluating analytical methods based on penalty points. According to this scale, a score of 100 corresponds to a completely eco-friendly methodology. This scale has recently been modified to weight the penalty points according to the volume of reagents consumed and waste generated [42].
Assessing analytical methods according to every scale is a multi-parameter process, and it is proposed that multidimensional statistical methods could be applied for assessing as well [43]. This could be a very serviceable tool for organisations that accredit and recommend analytical methods for regulated areas. Adding parameters for economic and environmentally significant aspects of methods would be very easy, and such statistical methods would give a more objective indication of the method’s position on a continuum of environmental benignity.
Widely available and easily applicable assessment techniques for analytical methods would constitute a major advance in greening Analytical Chemistry. Cooperation and coordination with national and international organisations responsible for accreditation and recognition of analytical methods would undoubtedly be necessary.

6. Efficiency – fitting the purpose

The main task of Analytical Chemistry in producing chemical information is to enable decisions to be made about the quality and quantity of the material or processes; in this regard, it would be useful to broaden the use of the term “fitness for purpose” (FFP). This could facilitate the selection of proper methods for collecting information. According to ISO/IEC Guide 2 [44], fitness for purpose is the ability of a product, process or service to serve a defined purpose under specific conditions. In the analytical sciences, this concept relates to the property of data produced by a measurement process that enables the user to make technically correct decisions for a stated purpose [45]. The dual purpose of Analytical Chemistry is thus becoming evident: on one hand it sets the limits and specifications for chemicals and compounds according to regulations, and on the other it ensures that measurement results are reliable and provide the means for making competent decisions. In practice, in order to obtain fitness for purpose results for established specification limits, one needs to know the probability of making conclusive correct decisions and the performance of the analytical system (Fig.3).

Figure 3.

A comparison of these functions indicates the fitness for purpose of a given condition of measurement [46]. Estimating the uncertainty of measurement results under rigorous statistical control is an important parameter for forming the basis for this comparison. This means that the quality of analytical results and procedures is associated with the concept of fitness for purpose [47]. The quality of measurements targeting the specific needs and demands of end users depends on instrumentation and procedures being used in their optimal area of application. It is not unfeasible that a decision can be made on the basis of sensor output without ultra-high performance laboratory instrument. The overall economy obtained from the selection of instruments and methods that meet the fitness of purpose in a given situation not only saves materials and energy but also reduces the use of chemicals and solvents.

7. Conclusions

There is strong opinion that Green Analytical Chemistry is needed beside so called common Analytical Chemistry. In this review it is made an attempt to convince people that there is no need for a separate branch of Analytical Chemistry.

Analytical Chemistry is defined as a means of obtaining chemical information about the nature, amount and identity of elements and molecules in our environment. This information is collected, classified, manipulated, stored and disseminated. The aim is to provide the required information about the amount of sample available at a level of analytical sensitivity, selectivity, accuracy and precision that meets the needs and demands of end-users of this information, and is provided within a reasonable time and at a reasonable cost. The science of Analytical Chemistry is developing new tools for solving problems, and providing high quality information to other specialists and to the public.

The methods of analysis used to obtain the necessary information must fit their purpose in order to minimise un-necessary information and the additional cost of chemicals, solvents and energy this entails.

Conducting research that optimises analytical processes in order to provide the required information in a manner that is inherently safe, non-toxic and environmentally benign, and with the least possible consumption of materials and energy and generation of waste, and which leads to the development of more environmentally safe and economical methods of chemical analysis; these are just changes in Analytical Chemistry according to new principles in chemistry to become environmentally benign, not the building of separate branch of Analytical Chemistry.

8. References

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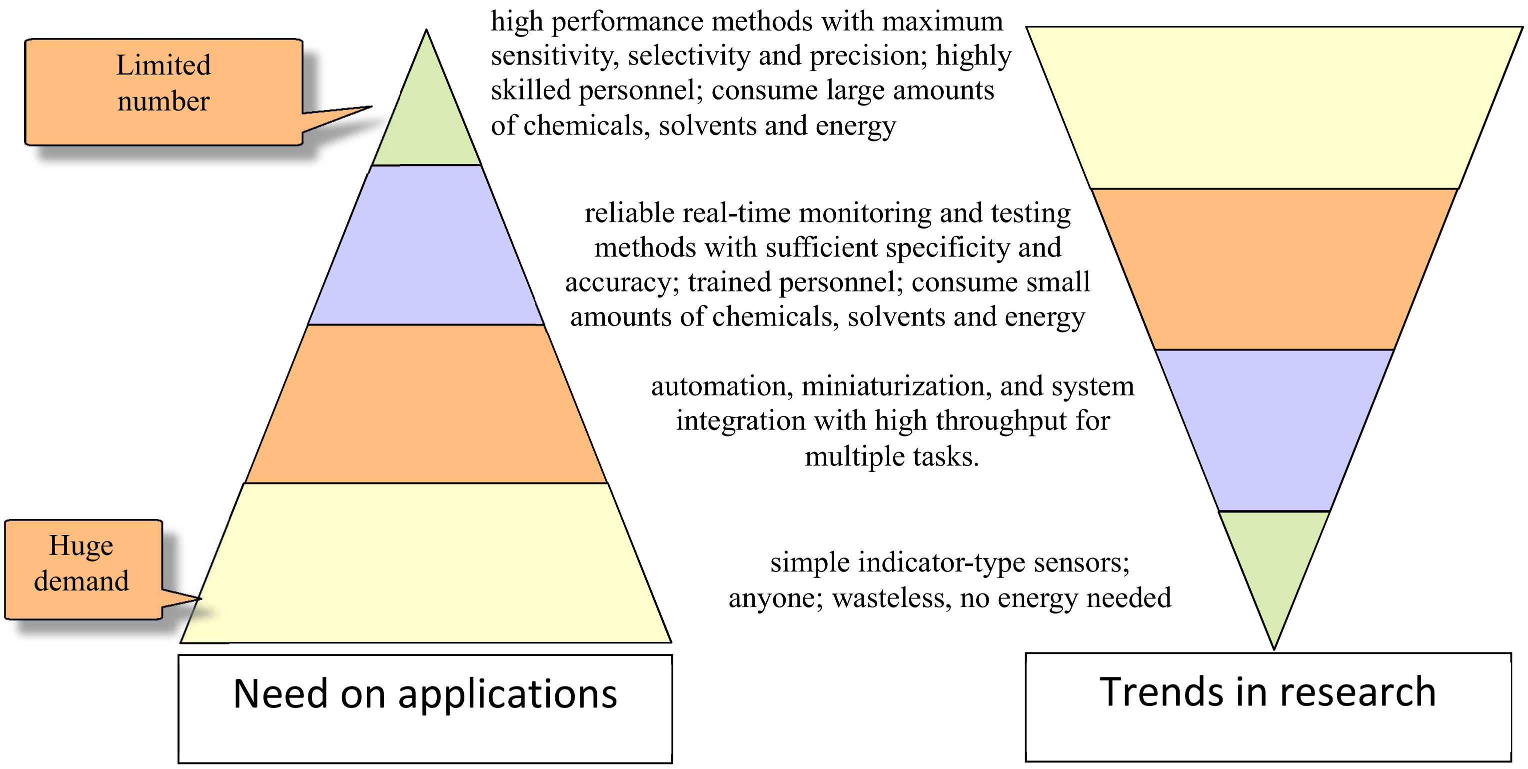
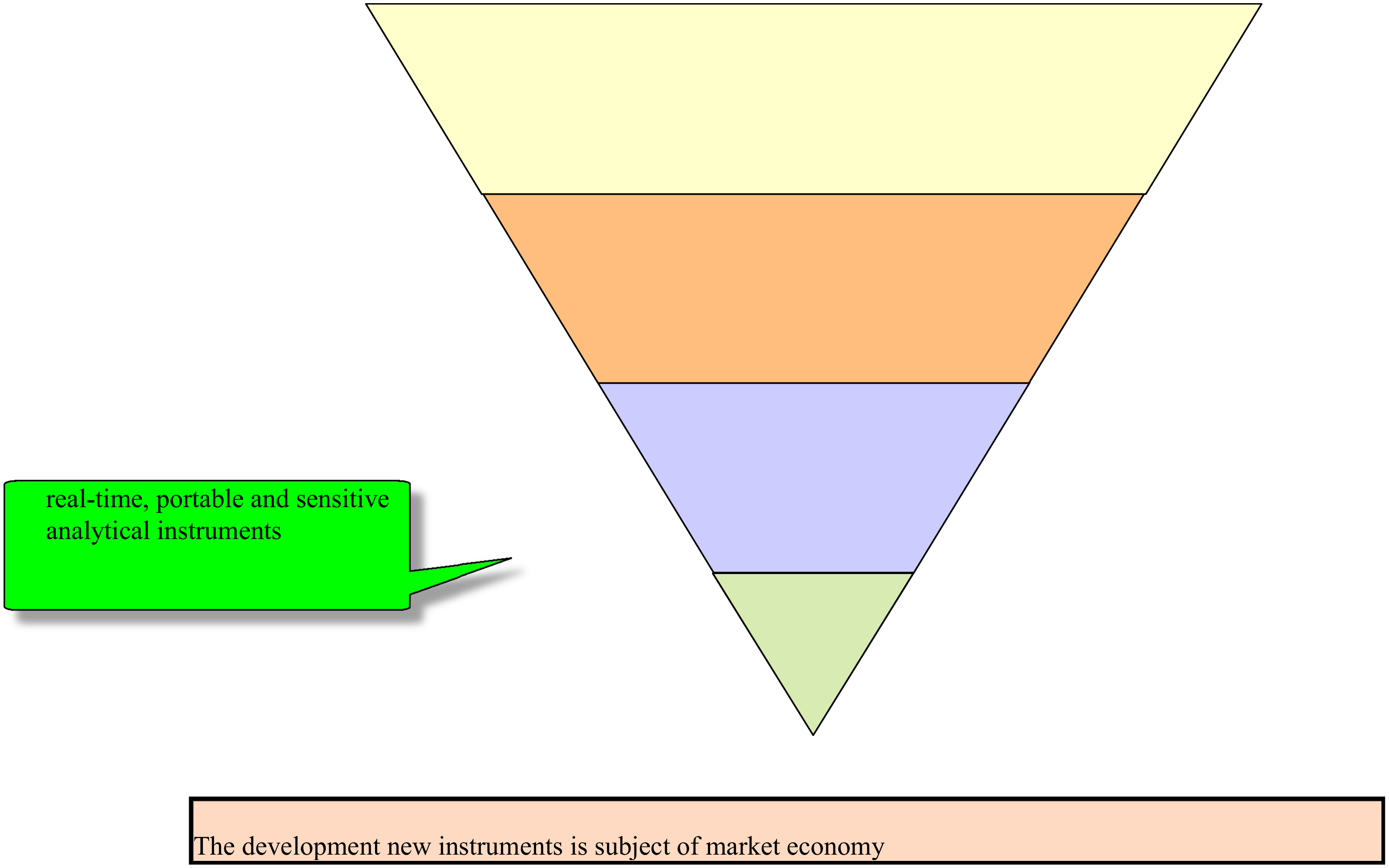


high performance methods with maximum sensitivity, selectivity and precision; highly skilled personnel; consume large amounts of chemicals, solvents and energy

reliable real-time monitoring and testing methods with sufficient specificity and accuracy; trained personnel; consume small amounts of chemicals, solvents and energy

automation, miniaturization, and system integration with high throughput for multiple tasks.

simple indicator-type sensors; anyone; wasteless, no energy needed


real-time, portable and sensitive analytical instruments
The development new instruments is subject of market economy

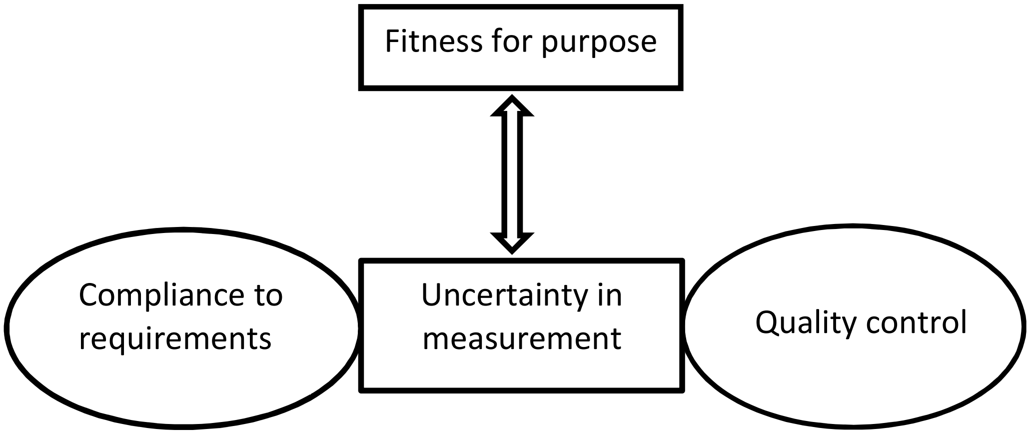

Fitness for purpose
Compliance to requirements
Uncertainty in measurement
Quality control

Figure captions.

Figure 1. Means to target the object.

Figure 2. Pyramids on instrumental methods.

Figure 3. Fitness for purpose relation with uncertainties in measurement