

Vanguard-rearguard analytical strategies

M. Valcárcel, S. Cárdenas

The increasing demands for (bio)chemical information to contribute to solving environmental, health, food, industrial problems will promote important changes in analytical laboratories that should be supported by analytical research and development, and innovation (R&D&I). In this paper, we propose a new strategy: the sequential use of rapid, low-cost vanguard analytical systems and more accurate, rearguard analytical systems, including off-line, on-line and mixed on/off-line combinations. These strategies imply looking for synergies between metrology and problem solving to support the establishment of quality compromises as well as to emphasize the increasing importance of quality assurance principles and practices in modern (bio)chemical analyses.

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1. Introduction

Information is a key aspect of society, economy, science and technology. (Bio)chemical information from objects and systems can be considered a relevant part of the information required to make well-founded and timely decisions [1]. The demands of (bio)chemical information in a variety of fields, such as environmental, food, health, and industry, have increased dramatically in recent decades. Analytical laboratories receive and will receive a growing number of samples per day and the use of traditional analytical approaches will become obsolete in the next few years. New avenues to provide (bio)chemical information should be urgently addressed. The topic of this paper can be considered a new way of producing (bio)chemical information which is consistent with the increasing demands for such information.

The two principal aims of analytical chemistry are: achievement of a high metrological quality; and, correct solution of analytical problems based on clients' information needs. There are several sources of friction between them.

The first conflict arises from the contradictory relationships between classical analytical properties (e.g., traceability, accuracy, precision, sensitivity and selectivity) under the frame of metrology and productivity-related properties (e.g., expeditiousness, costs and risks) [2], which are substantial in problem solving [3].

The second source of conflict between metrology and problem solving is materialized in the two divergent sides of analytical excellence, namely the coincidence between delivered and required analytical information, the main goal of problem solving, and the coincidence between delivered and referential information, the main objective of metrology [4].

A third consideration is that sometimes the clients do not know exactly what information they want to obtain as they do not know the real problem to be solved. In these cases, the analytical chemist should teach and convince them, with clear reasons about that.

Undoubtedly, a permanent challenge of analytical sciences is to transform these conflicts between metrology and problem solving into synergies by defining the so-called quality compromises in each specific problem addressed, taking advantage of the main contribution of both sides, namely reliability of results from metrology and client satisfaction from problem solving. The vanguard-rearguard strategies described in this paper can be ascribed in this context and would be helpful to analytical chemists in establishing quality compromises in a practical way.

From a very broad, general point of view, the technical evolution of analytical sciences can be summarized by establishing three key milestones or inflexion points. After the use for centuries of so-called classical methods of analysis, the

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massive use of instruments (from simple photometers and potentiometers to chromatographs, X-ray techniques and mass spectrometers) can be considered the first technical inflexion point in the evolution of analytical sciences. Then, the use of computers, the second inflexion point, has supported specific trends, such as chemometrics, automation and, most recently, miniaturization. Simplification is the final turning point or key technical milestone. It is not fully integrated but will cause a dramatic change in routine analytical laboratories in the years ahead. It is based on the use of computers and in this way supported by automation, miniaturization and chemometrics. The topic of this paper can be ascribed to this technical milestone.

Required (bio)chemical information is a key general analytical reference in addition to the traditional ones, measurement and written standards. The most relevant trends in information requirements are as follows:

- predominance of simple, accurate information over useless over-information that is rather usual nowadays, 40–50% of which is not used for decision-making. This problem should be urgently addressed;
- the growing importance of qualitative analysis and binary responses it provides [5–7] in detriment of traditional quantitative information;
- increasing need for overall information (total indices) about a group of substances [8] at the expense of discrete information for each measurement;
- increasing importance of productivity-related properties (e.g., rapidity, costs and risks) instead of the exclusive predominance of the capital (accuracy and representativeness) and basic (precision, sensitivity and selectivity) ones; and,
- the urgent need to use more positive approaches in analytical reports instead of using negative connotations, as is usual. For example, the mandatory use of uncertainty intervals associated to analytical results can create serious misunderstandings in the analyst-client relationships (e.g., in courts of justice). The use of “reliability zone” or “confidence interval”, which have the same scientific and technical meaning, will be more appropriate in this context [9].

2. Vanguard-rearguard strategies

Fig. 1 depicts the principles of vanguard-rearguard analytical strategies. Samples from the objects are systematically subjected to a rapid, low-cost, vanguard analytical system, which allows one to select those samples with the target characteristics (e.g., toxicity

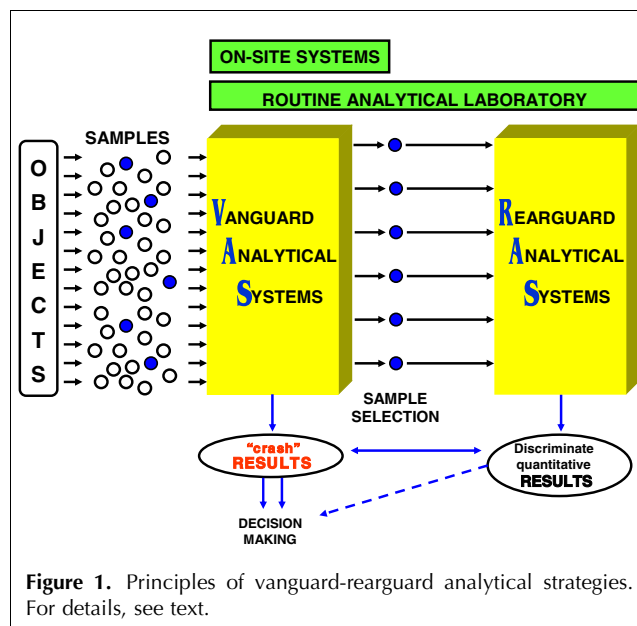


Figure 1. Principles of vanguard-rearguard analytical strategies. For details, see text.

index [10]). Only the selected samples are then subjected to conventional analytical systems that are more accurate and precise, but time consuming and involving expensive tools.

Vanguard analytical systems can work both inside and outside the analytical laboratory, whereas conventional systems are always located in the laboratory. In this analytical scenario, two types of results can be expected:

- those provided by vanguard systems (e.g., global indices and yes/no responses), which can be used for immediate decision making; and,
- conventional, discrete, quantitative results that can be used for three main purposes:
 - to confirm the results provided by vanguard systems;
 - to expand the binary and/or global information; and,
 - to control the quality of these rapid results.

In speciation studies implemented by environmental routine laboratories processing hundreds of samples per day, the following question arises from the bench level: “Is it necessary to analyze all the samples using thorough sample treatment and sophisticated expensive instrumentation (e.g., LC-ICP-MS)?” There are three main answers to this question, namely:

- The use of traditional analytical systems is time consuming and expensive, but they provide complete information about all the species of an element present in environmental samples. But, in many cases, no signals are obtained as a result. Analysts in charge often say: “It is quite depressing to get many baselines as a result of a working day”;

- (b) The use of a simple, fast method providing overall (total) information of the element (e.g., is or is not present) has practical advantages (simplicity, rapidity, and low cost) but they provide incomplete information; and,
- (c) The use of a sequential combination of these two previous approaches (first the rapid method and then the conventional method) is the best option because it has the advantages without the drawbacks of (a) or (b). This third option corresponds to a vanguard-rearguard analytical approach, as described in the speciation of lead in rainwater [11].

3. Vanguard analytical systems

Vanguard analytical systems provide analytical information in a simple, rapid way. They are designed and used when the number of samples per day is high in an immediate decision-making and/or an evolving system that needs to be monitored *in situ*. In them, productivity-related properties (e.g., speed, cost and risks) are of great relevance at the expense of the level of basic properties (e.g., precision, sensitivity and selectivity) and capital achieved (e.g., accuracy and representativeness). Usually, vanguard analytical systems are associated with a confirmatory method, which acts as a rearguard analytical system. They are applied both in and outside the analytical laboratory.

Vanguard analytical systems are consistent with several key aspects of the modern approach to analytical chemistry, namely:

- client information needs (the frequently missed generic analytical reference) and client satisfaction (one of the principal aims of analytical sciences);
- the “reducing” objectives of analytical sciences, such as less material (samples, reagents or solvents), time, and human resources, with low costs and low risks;
- the quality compromises that should be established between metrology and problem solving;
- simplification, a technical trend in analytical R&D; and,
- several trends in analytical information required:
 - simple and useful;
 - importance of productivity-related properties;
 - yes/no binary responses [5]; and,
 - total indices [8].

A vanguard analytical system should be, reliable (precise), robust, sensitive, selective for one measurand or a group of measurands, and it should have a high level of the productivity-related properties (i.e., it should be simple, rapid, inexpensive (in terms of

purchasing and maintenance) and involve no risks). The results provided by vanguard analytical systems should be as representative and reliable as possible (i.e., accurate, traceable and with a narrow uncertainty interval).

Undoubtedly, a crucial practical objective in analytical sciences is to minimize or to avoid negative characteristics of the preliminary operations of analytical methodologies (e.g., complexity, variability and intensive human participation, which is tedious and time-consuming, prone to systematic and random errors, difficult to control and a source of risks) [12]. The establishment of a reliable by-pass to these negative characteristics is very relevant. Vanguard analytical systems can support this practical objective by efficiently contributing to increase the simplicity and the rapidity of the analytical processes as well as contributing to reduction in costs and hazards that are typical of conventional analytical processes.

Depending on where vanguard analytical systems are applied, they can be divided into two broad categories, namely:

- (a) out of the laboratory (i.e., on-site systems, that can be simple off-line, sample-screening systems and on-line monitoring of evolving systems); and,
- (b) in the laboratory, acting as sample-screening systems.

By definition, vanguard analytical systems should be based on rapid-response analytical tools (e.g., portable analytical instrumentation, (bio)chemical sensors, immunoassays, spot tests, test kits, analyzers, direct analytical tools and combinations of these). There are many examples of portable analytical instruments, ordinarily based on a simple or no sample treatment (e.g., portable nuclear magnetic resonance (NMR), gas chromatographs (GCs) [13] or mass spectrometers (MSs) [14] (with or without GC separation) as well as a variety of optical (mainly based on UV-Vis spectrometers) and electrochemical systems.

Analytical tools and systems that allow direct sample analysis play an important role in vanguard analytical systems. The special issue of this journal, *Trends in Analytical Chemistry*, devoted to rapid-response analytical tools [15], systematically discussed the suitability of laser ablation-atomic spectrometry (AS), ion mobility spectrometry (IMS), slurry-electrothermal vaporization-inductively coupled plasma-mass spectrometry (ETV-ICP-MS), near infrared (NIR) spectrometry and passive sampling for this purpose. Moreover, a critical discussion on the applicability of direct solid sampling-graphite furnace-based methodologies in those situations when speed is more important than great precision was published recently [16].

Vanguard analytical strategies have been used for many years in clinical, forensic and environmental areas. The following are representative examples.

Immunoassay has been extensively used for biomedical diagnosis [17]. The selectivity it provides in analyzing complex samples using relatively simple procedures and instrumentation has clearly advanced its popularity. However, many improvements have made available devices aimed at reducing the assay time and detection limits using miniaturized systems, which also require less sample volume, and clearly reduced non-specific absorption, thus contributing to reaching lower detection limits. In the clinical field, disposable enzyme electrode test strips for decentralized diagnosis (viz. personal blood meters) are commercially available and thus, widely used [18]. The success of such devices has fostered the development of new systems for multi-analyte determination (e.g., the i-STAT Portable Clinical Analyzer, which performs eight clinical tests using a rather low sample volume (60 μ l), the results being delivered in no more than 100 s [19]).

Test systems are also useful for environmental monitoring; the majority of them provide global indices in order to assess water or air quality, such as total heavy metals, chemical oxygen demand and petroleum hydrocarbons [20] or total organic carbons [21].

Field screening of explosives, pyrolysis of materials and even chemical and biological agents is of great importance at security checkpoints. Fast responses can be obtained using miniaturized ion mobility analyzers [22,23]. The intrinsic toxicity of the above-mentioned compounds can be addressed as a health hazard and a general environmental problem. In addition to conventional analytical processes, immunochemical methods, such as the use of enzyme-linked immunosorbent assay (ELISA) for the rapid screening of soils and waters for TNT and other nitrocompounds has been proposed [24]. These compounds can also be monitored using either a fiber-optic biosensor [25] or electrochemical sensors [26].

There are many examples of dedicated analyzers, which allow direct, untreated sample processing (except the initial mass/volume-measurement step) because, if any sample treatment is required, it is automatically implemented by the analyzer. Some of these analyzers are tailored to the analyte (e.g., the Milestone DMA-80 direct mercury analyzer, which allows the direct introduction of both solid and liquid samples and provides a total index as a result: total mercury concentration). Another group is tailored to the type of sample (e.g., steel analyzers for carbon determination, some clinical analyzers (from portable glucosimeters to fast multiparameter systems), wine analyzers based on NIR spectrometry, food analyzers for the determination of total antioxidant activity, and water analyzers for determination of the total toxicity index).

Sample-screening systems [27] are also involved in vanguard analytical strategies intended to classify samples into two groups (positive or negative) in a fast,

reliable way. If a negative response is obtained, no further sample processing is needed. Positive samples are then subjected to a rearguard conventional analytical process to confirm the response and to expand the information level (discrimination and quantitation). Additionally, the rearguard analytical system is used to control the quality of both positive and negative responses.

The three primary objectives of sample-screening systems can be summarized as follows:

- (a) to provide a rapid, reliable response about a specific characteristic of an object/system for immediate decision making;
- (b) to minimize or avoid the preliminary operations of conventional analytical processes; and,
- (c) to reduce the permanent use of high cost, high maintenance instruments in routine analysis. Books by Zolotov [28] and Alegret [29] also propose the use of a variety of screening methods in different application fields.

Sample-screening systems can be ordered using different criteria. The most relevant classification from a practical point of view is based on the sample treatment required. There are direct screening systems, which involve no sample treatment. Undoubtedly, they are the best option. Others are applied after a simple, smooth sample treatment (e.g., a single step). In some special cases, screening systems are applied after a full sample treatment; its use is justified if the equipment involved in the rearguard analytical system is expensive to maintain.

An example of the most favorable situation is the direct screening of soils for a variety of pollutants, such as polychlorinated biphenyls (PCBs), polyaromatic hydrocarbons (PAHs) and chlorinated pesticides, can be accomplished using a portable MS to which a thermal desorption sample probe is connected [30]. Sample is simply mixed with an internal standard in an aluminum foil-covered Petri dish. The analytes are thermally desorbed and transferred to the detector through a fused silica capillary. A silicon membrane is located between the sample probe and the electron impact ionization chamber to prevent oxygen from reaching the detector. In this way, it is possible to know in a few minutes the degree of contamination of a soil.

In an alternative, a rapid, non-exhaustive sample treatment is very convenient in order to minimize the complete sample-treatment (e.g., screening of meat for clenbuterol and other β -agonists by using an ELISA test). The sample-preparation procedure is quite simple and involves acid extraction, filtration and neutralization of the extract, which is further applied to the ELISA test. If a positive response is obtained, then another sample aliquot is subjected to the conventional method based on GC-MS, for which several, complex sample-preparation steps are required (centrifugation,

solid phase extraction, dissolution and derivatization prior injection in the instrument) in addition to that of the vanguard system.

Recently, the double use of a triple quadrupole time-of-flight MS (Q-ToF MS) for screening and confirmation of pharmaceutical residues in water has been proposed [31]. The screening step is based on monitoring one specific MS-MS ion of the target compounds. Confirmation of the identity of pharmaceuticals was based on the monitoring of two specific MS-MS ions or the exact mass for a molecular ion using liquid chromatography (LC)-Q-ToF-MS. The accuracy and reliability of the vanguard strategy compensated for its high cost and reduced the use of the rearguard system.

As with conventional analytical procedures, the representativeness of the sample being processed using either vanguard or rearguard analytical strategies is crucial to ensure the reliability and the quality of the analytical information delivered. If one of the main objectives of a vanguard strategy is to decide absence/presence of a target characteristic (e.g., measurement of a binary response, such as the presence of a pollutant in an environmental matrix), composite sampling usually reduces the number of required tests and then minimizes the cost and the time required to obtain analytical information. Extensive reviews on this topic can be found in the literature [32].

However, this sampling strategy can magnify the false negative rate as the likely result of diluting contaminated individual samples with clean ones when forming composites. There should be an exhaustive retesting protocol for negative results in order to reduce the percentage of false negatives [33].

4. Rearguard analytical systems

Rearguard analytical systems are conventional methods that usually involve complete sample pre-treatment, chromatographic and capillary electrophoretic (CE) separations and powerful spectrometric instruments (e.g., MS, Fourier transform infrared (FTIR), NMR, inductively coupled plasma (ICP) as well as hybridizations (e.g., GC-MS, LC-MS, CE-MS, ICP-MS, GC-MS-FTIR, LC-ICP-MS, LC-ToF and LC-MS/MS). They should be very precise, selective and sensitive and the results that they provide should have a high level of metrological features (viz. high traceability (accuracy) with low uncertainty), the productivity-related properties (expeditiousness, costs and risks) being of less significance as regards vanguard analytical systems. Ordinarily, they are used in the laboratory.

Rearguard analytical systems have three main objectives. The first one is to confirm the summarized information (yes/no binary responses and total indices)

provided by vanguard analytical systems (Fig. 2). Rearguard analytical systems are systematically applied in qualitative analysis when a positive or an inconclusive binary response is obtained or the total index is open to doubt, so they should offer higher sensitivity. It is worth noting that the rearguard systems are not regularly applied to confirm "no response", so reducing the rate of false negatives in a vanguard analytical strategy is crucial. In other words, the false negative rate is one of the most definitive quality indicators of a qualitative method. The determination of chlorophenoxy acid pesticides in waters [34] is representative of this objective. The vanguard system is based on direct analysis using ELISA, whereas the rearguard system involved full sample treatment and GC-MS. Both detection limits are below the corresponding threshold limits, so they can properly solve the analytical problem raised. After the analysis of 100 blank samples spiked with 0.1 ng/ml (the threshold-limit concentration), the vanguard system provides 90% of true positives and 10% of false negatives, which are detected by the rearguard system. The rates of both errors diminish dramatically when increasing the concentration of the analyte. In the analysis of 100 real water samples, all positive and negative responses provided by vanguard systems were confirmed; the two inconclusive responses were found to be one positive and the other negative.

Fig. 3 reflects the second objective of rearguard analytical systems: the systematic quality control of all results provided. Aliquots of measurement standards, such as a reference material (RM) or a certified reference material (CRM), blank samples and previously analyzed samples are not subjected to rearguard systems because the information associated with them can be used as reference in a direct way by subjecting them to the vanguard system. The rest of the samples, despite the binary responses provided (no, yes and inconclusive) and total indices (inconclusive and well-defined), should also be subject to confirmatory methods (rearguard analytical systems) in a systematic way, according to a previously established quality plan. The application of

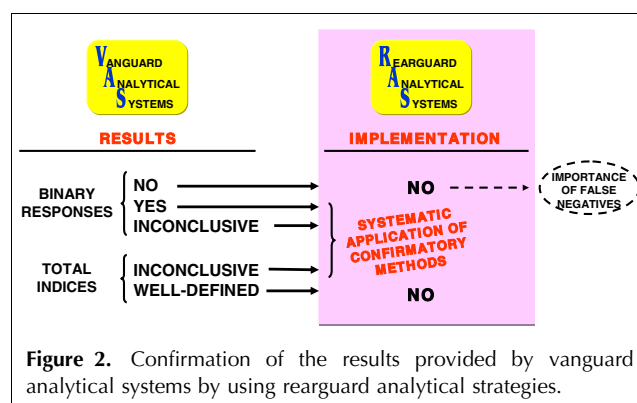
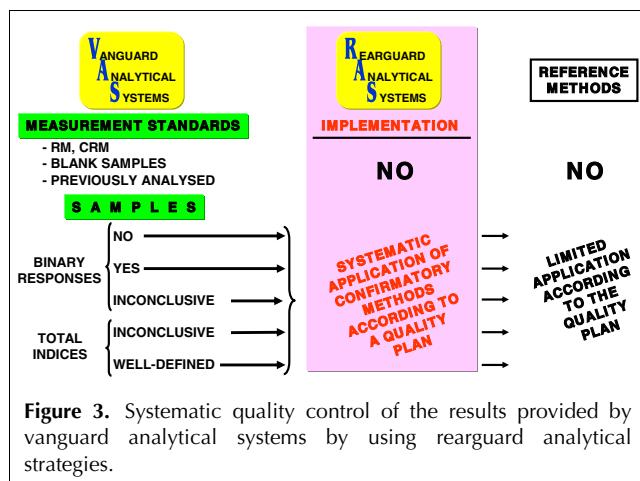


Figure 2. Confirmation of the results provided by vanguard analytical systems by using rearguard analytical strategies.



reference or primary methods of higher metrological quality is only justified in special cases.

The determination of cocaine in hair [35] constitutes an example of the second main function of vanguard analytical systems. The vanguard analytical system involves the use of radioimmunoassay after a simple sample treatment, whereas the rearguard system implies full sample treatment and determination by GC-MS. Again, the detection limit is lower in the rearguard system. The analysis of 100 blank and spiked blank samples by using both, vanguard and rearguard systems allows one to conclude that:

- the vanguard analytical systems provide no false positives and 6% false negatives at a concentration level of 0.5 ng/mg of hair, which are confirmed by using the rearguard system; and,
- the correct responses of the vanguard system (42% true positives and 52% true negatives) were confirmed by the rearguard system. The fact that the method provides 6% false negatives reduces its practical application. Special attention should be paid to false negatives, which should be avoided and guaranteed as these samples are no longer analyzed so the information they contain will be lost.

The third main function of rearguard analytical systems (Fig. 4) comprises the expansion of the summarized information provided by vanguard analytical systems. In this way, qualitative information is converted into quantitative data and total indices are transformed into discrete information about each of the species belonging to the group of compounds. The determination of bile acids in blood is representative of the two information levels provided by vanguard and rearguard systems. The vanguard system involves a simple sample treatment and a single-channel flow-injection manifold furnished with a fluorimetric detector. The rearguard analytical system is based on full sample treatment and LC separation with a post-column reactor

prior to fluorimetric detection. The vanguard analytical system provides information about the total concentration of bile acids and, thus, a global diagnosis of the hepatic function. The rearguard analytical system provides information about the presence and relative concentration of 4–6 bile acids, which allows us to diagnosis specific liver disease, such as hepatitis or cirrhosis. In a big hospital, hundreds of samples every day can be subjected to the vanguard system. Just those samples with a total concentration of bile acids higher than a previously established threshold or alarm limit should be analyzed by the rearguard analytical system.

Finally, it is interesting to address the question: “Will conventional tools and methods become obsolete?” The definitive answer is no, but they should evolve to play new roles in the analytical laboratory such as:

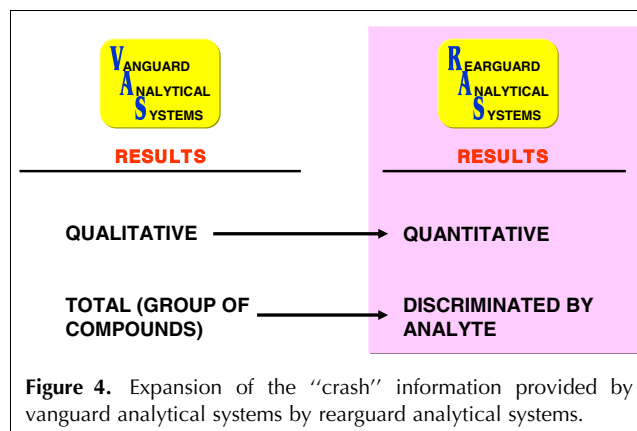
- application to analytical problems requiring results with a high level of metrological features and,
- application as rearguard analytical systems in connection with the use of vanguard analytical systems.

5. Combining vanguard and rearguard analytical systems

Vanguard and rearguard analytical systems can be combined in two principal modes, as shown in Fig. 5.

In the first, different sample aliquots are independently introduced into each system. The possible alternatives under this option are off-line and mixed on/off-line configurations. In the on-line combination, the same sample aliquot is introduced first into a non-destructive vanguard system and then, sequentially, into a rearguard system.

The most frequent situation is when vanguard and rearguard analytical systems are connected off-line. Samples are first analyzed by the vanguard system for sample qualification/classification. The aliquots of the



selected samples are then independently analyzed by a rearguard system (e.g., the on-site vanguard system is used for in-line monitoring of evolving systems by using chemical or biochemical sensors). Unexpected evolution detected by the vanguard system should be checked by transferring samples to the laboratory where they are analyzed using the rearguard methodology.

Also representative is the use of an NIR instrument as a vanguard system that allows one to determine humidity, total protein and total fat in animal feed. The rearguard systems (Karl Fischer for humidity, titrimetry for total protein and Soxhlet-GC for total fat) are used when the results fall outside the tolerated intervals (and for quality-control purposes).

The EPA method for characterizing the toxicity of liquid, solid and multiphase wastes also combines vanguard/rearguard strategies [36]. First, a total analysis of the waste is carried out and, if it is demonstrated that the target pollutants are not present or that they are present but at a concentration lower than the appropriate regulatory levels, the whole method need not be run. Otherwise, the whole process should be followed and the individual contaminant identified.

The mixed off/on-line approach in the combination of vanguard and rearguard analytical systems involves the same two steps as the off-line approach but an auto-sampler establishes a unique combination (e.g., the dual use of a flow-injection system as a vanguard system and as a post-column reactor–detector, which is an integral part of a rearguard system). In the first step, samples are introduced into the flow-injection manifold, which acts as screening (vanguard) system by selecting those samples that provide a global response higher than the previously established limit. In the second step, the selected samples are injected into the LC that uses the flow system as post-column reactor–detector. In this way, the use of the LC is minimized and that is of great interest in routine laboratories dealing with a large number of

samples (e.g., in determining nine transition metal ions in water [37] and aflatoxins in peanuts [38]). In addition, continuous configurations based on solid-phase extraction can be used either for screening purposes (vanguard system) for enrichment and clean-up of the analytes from the sample or as an introduction system for the chromatograph or electrophoretic instrument (rearguard system) for analyte separation and individual identification in those samples providing a global response outside the previously established cut-off limit (e.g., the screening of biological fluids for bile acids using an evaporative light scattering detector [39] or the piezoelectric screening unit coupled on-line to capillary electrophoresis for detection and speciation of mercury in waters [40]).

On-line combination of vanguard and rearguard analytical systems is the best option, but the basic requirements for this coupling are rather difficult to fulfill. Samples are first analyzed with a non-destructive vanguard system for sample qualification or classification and the same sample aliquots are then analyzed by the rearguard system. The direct determination of PAHs in soil samples [41] is accomplished using a combination of a vanguard system (based on the continuous fluorimetric monitoring of the supercritical fluid phase after the extraction cell of a supercritical fluid extractor) and a rearguard system that is an LC. Samples containing PAHs are qualified by the vanguard system and collected in a sampler of an LC. The other samples are sent to waste.

6. Final remarks

Although vanguard-rearguard analytical strategies are increasingly applied in routine laboratories and these strategies have been applied for a long time (viz. the use of ELISA as vanguard system and confirmation of results by GC-MS), they have not previously been presented systematically and the name proposed could help in their description.

They can be attributed to simplification, the next turning point in the technical evolution of analytical sciences, and they will induce a new profile in routine analytical laboratories, just as computers did 20 years ago.

These strategies are consistent with the increasing (bio)chemical information demands posed by a variety of clients and imply the establishment of a well-founded, flexible balance between metrology and problem solving realized in well-stated quality compromises. Although several analytical approaches have already been described in this context, it is necessary to develop a sound basic, practical framework to support them; this implies new challenge for R&D&I in analytical sciences.

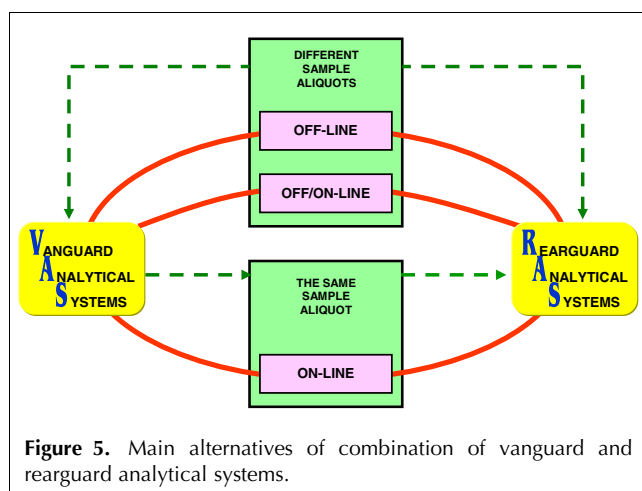


Figure 5. Main alternatives of combination of vanguard and rearguard analytical systems.

It is a great mistake to concentrate all efforts in developing new instruments and their combinations, new chemometric approaches, new stationary phases, new certified reference materials, new immunoreagents, and so on, while forgetting that intangible R&D&I products, such as new basic developments and new strategies, are also very relevant.

A bottleneck of vanguard-rearguard strategies is the routine use of vanguard systems. Many are described in the literature, but they need to overcome three sequential barriers, namely:

- reliability (e.g., instability of biochemical/biological tools, false negative rate provided);
- classical metrology, because of the existing black hole in norms and guides as regards binary responses and total indices, which could be a serious problem in laboratory-accreditation processes; and,
- commercialization by prestigious companies, which is the best way to disseminate their use.

Efforts should aim to test available devices at a laboratory scale and, after establishing collaboration between scientists and engineers, develop really useful instruments and test them in the field.

Finally, it is interesting to emphasize the crucial importance of quality-assurance principles and practices in vanguard-rearguard strategies in ensuring the reliability of vanguard analytical strategies. This implies that traditional quality control and assessment activities in routine laboratories will be increased by a factor of 2–3 and that they need to be planned differently.

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