Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(10):901-906

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

An approach of the historical aspects, the advantages and disadvantages of automated analyzers: Analysis in segmented flow (SFA) the Flow Analyzer - batch (FBA)

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ABSTRACT

Chemical analysis is indispensable in all areas of contemporary life and can be performed by quick, simple, accurate and robust procedures. Thus, automated analyzers are continually emerging and being employed successfully in the analysis of various substances in very diverse matrices. Therefore, this review discusses the historical aspect, the advantages and disadvantages of automated analyzers.

Keywords: Automated Analyzers, advantages, disadvantages. historical aspects

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INTRODUCTION

Conventional analytical methods are commonly developed and used in laboratories and research centers worldwide. However, analytical procedures that allow a lower consumption of reagents and samples, reduced waste generation, higher sensitivity, lower cost, higher sampling frequency, less risk analyst intoxication and, moreover, easy to perform, are still strongly required and applied in routine determinations, given the high demand analysis. Thus, in recent years, a great deal of analytical chemistry has been directed to the development of automatic systems and methods, and adaptations therefor [1].

The arguments for the use of automation are quite varied and are commonly employed to ensure greater security analyst in handling substances that could potentially pose risks to health, reduce costs due to their low consumption of reagents and samples, perform procedures in a smaller time interval, reducing the human effort, improving the accuracy of analysis, etc.

Automated analyzers can be classified into three groups: discrete automated analyzers or batch, robotic automated analyzers and automatic analyzers flow.

Discrete automated analyzers or batch, are mechanized versions of classic manual methods. They are generally characterized by using an individual container for each sample and for carrying the reaction mixture towards the detector through a mechanical system, usually in the form of the tray. Typically, measurements are carried out after

the establishment of chemical and physical equilibrium of the reaction under study, aiming to achieve maximum analytical sensitivity [2].

The robotic automatic analyzers are characterized by performing analytical operations with the aid of a mechanical arm controlled by computer, which mimics the procedures performed by an operator. The mechanical complexity and high cost make these systems have several limitations in performing automatic analyzes. However, they play an important role in preliminary stages of the analytical procedure, as in tasks involving handling of toxic or explosive material [2].

The analyzers have the flow characteristics of the sample processing reagent and streaming, or otherwise sectioned by air bubbles. In general, due to increasing amount of analyzers developed flow, the IUPAC (*International Union of Pure and Applied Chemistry*) has recommended a classification according to the processing of the sample and / or reagent (s) and the basic characteristic of its flow [3,4].

Despite the importance of discrete methods, and especially the robotic methods, implementation and automation of laboratory procedures, flow methods recorded a significant growth, both in terms of disclosure, such as application areas and even acceptability by the scientific community [1-5].

Since the development of the first automatic analyzer stream [6], in 1957, several analyzers have been proposed as can be seen in **Figure 1**. The different combinations of characteristics, such as the type of confluence, pumping / suction of samples and reagents, and its cleavage define the characteristics of each system.

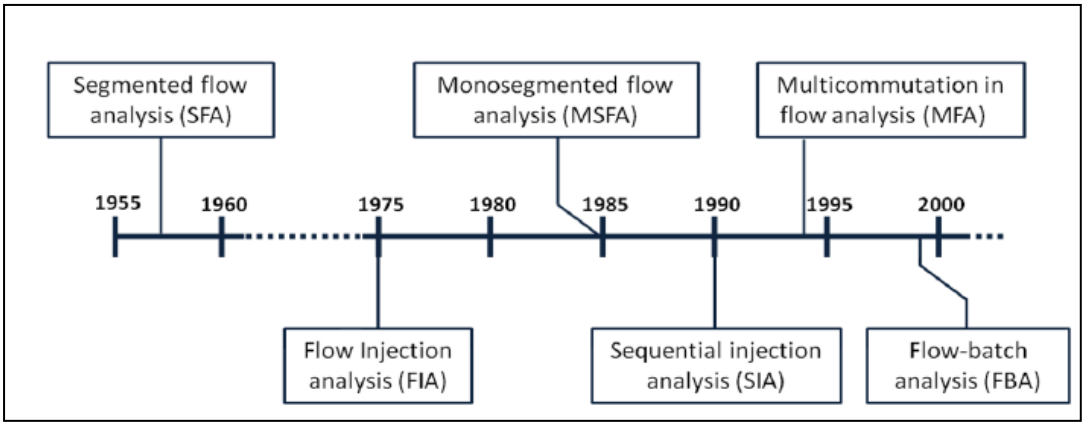

Figure 1 - Timeline with major automated analyzers in flux

Although each of these flow systems, presenting its own peculiarities, all of them show a general configuration in common. The propulsion fluid is usually performed by a peristaltic pump, although various other mechanisms may be used for this purpose, such as pumps piston. Adequate control of aliquots of reagents and samples added to the system is normally done by solenoid valves, rotary, or by proportional gun.

Commonly, flow analysis require accessories to promote mixtures, digests or separations. These steps are promoted by a reaction coil that can be modified according to the required reaction. Detection (s) of the analyte (s) in a flow analyzer can be accomplished in many different ways.

Because of that, this review discusses the historical aspects, the evolution, the advantages and disadvantages of automated analyzers.

Analysis in segmented flow (SFA)

He development of the first flow analysis system occurred in 1957 by Leonard Skeggs [6], a clinical laboratory researcher. This system, which was initially called continuous flow analysis (English: continuous flow analysis - CFA) and that shortly thereafter had its terminology changed to analysis segmented flow (English: segmented flow analysis - SFA), is first segmentation of the sample by air bubbles.

In this system, the sample is pumped continually occurring cleavage by air bubbles and then immediately adding the reagent. Thus, the mixing and subsequent reaction occur while the sample / reagent segments follow toward the detector, thereby allowing the chemical equilibrium of the reaction and a high sampling rate. With its features the SFA allows for an array of chemical analysis with a relatively simple analytical technique.

This concept has achieved widespread acceptance, especially in the field of clinical analysis, through the development and marketing of Technicon Auto Analyzer. Its use in clinical laboratories has decreased due to a move toward more highly automated systems that require less operator involvement and lower consumption of reagent and sample important factor in enzymatic reactions. The SFA is still dominant in large laboratories, especially for determinations using extensive or complex procedures [7].

Flow injection analysis (FIA)

In 1975, Ruzicka and Hansen [8] introduced the concept analysis system in flux, which became known internationally by the acronym FIA (English: flow injection analysis). This process of chemical analysis, which was initially developed in Brazil during the advice of the then expert of the International Atomic Energy Agency Dr. Jaromir Ruzicka the Analytical Chemistry Laboratory installation of Center for Nuclear Energy in Agriculture University of São Paulo (SCENE / USP) has become a well-known tool for automation of analytical procedures worldwide [9].

In the process of chemical analysis by flow injection, in contrast to SFA, a reproducible sample volume is inserted, in a short period of time, not sectioned in a fluid carrier, where the reaction occurs until the sample reaches the detector.

FIA systems have several advantages, such as possibility of conducting kinetics studies, low sample consumption, high speed and a simple analytical instrumentation.

However, these systems as targeting no air bubbles, the sample inevitably suffers scattering during transport to the detector and the physical and chemical equilibrium can often not be achieved. Consequently, the sensitivity of the method may be lower than that obtained by other analyzers. The decrease in assay sensitivity can be further compounded by mixing often inefficient between sample and reagents.

Another disadvantage of the FIA system, when compared to other analyzers, is its low flexibility, because if a change is necessary, there is need to study the numerous parameters again (flow, level of dispersion, etc.) or even prepare a new configuration to the analyzer.

The FIA was the system flow that caused the greatest impact [1], generating dozens of works on the subject to the present day. These works include books, manuals and practical guides on the principles, instrumentation and applications. In addition, thousands of scientific papers have been published concerning the flow analysis technique to various analytical methodologies.

Analysis monosegmented flow (MSFA)

The first genuinely brazilian system was developed by Celio Pasquini in his thesis work at the Chemistry Institute of the University of Campinas [10], being circulated to the international scientific community in 1985 [11].

The system monosegmented flow was proposed as an SFA hybrid with the FIA, adding important aspects of both systems [5]. As in the SFA, due to the presence of bubbles, the longitudinal dispersion is minimal, enabling, if necessary, the remaining segment of the reaction path for long periods of time without the risk of contamination between respective samples. Have the FIA brings low consumption of reagents and samples and high precision of the analysis.

As in the SFA, the MSFA bringing the sample and reagents from air bubbles, allows the realization of measurements in which the sensitivity is kinetically connected. Thus, the sensitivity of the method is not impaired even in determinations involving slow reaction kinetics.

To achieve greater frequency rate, simply enter sequentially samples, lining up the various segments in the analytical course. Prior to detection, the air bubbles are removed and the resulting stream, now solid, is transported to immediately flow cell, where the readings are made of the analytic signal. It is worth mentioning that with the advancement of instrumentation, this removal of bubbles is not a sine qua non for signal capture, as this process can be performed continuously.

Various analytical procedures have been developed by exploiting the MSFA system characteristics such as, for example, titration [10] Gas analysis [12,13], and extraction [14,15].

Here it is necessary to mention a discussion about the naming confusion raised by Celio Pasquini, in the article "Why is it Called Analysis in Flow monosegmented" [16]. In this work, the author recalls that the MSFA system was originally named MCFA (English: monosegmented continuous flow analysis) and this nomenclature remained in use until the IUPAC recommendations on the classification and definition of analytical methods in flow were published [3,4]. Since then, many researchers have recognized that the word "continuous" does not contribute significantly to the description of the process that occurs in this flow system, and welcomed the name recommended by the IUPAC, monosegmented flow analysis, but others remain in the misconception calling such a system yet for MCFA giving term or other classifications such as SFIA [32].

Sequential injection analysis (SIA)

Analysis by sequential injection (SIA) has been devised by Ruzicka and Marshall in 1990 [33] in order to mechanically simplify FIA systems and overcome certain drawbacks of this technique, the need for fluid continuous loader and the need for a new physical configuration for separate determinations.

Thus, the SIA came in order to facilitate the implementation of the methods in flux in the online monitoring of industrial processes, where robustness and automatic calibration are required [33].

In SIA systems volumes of sample and reagents are aspirated sequentially, using a peristaltic pump, or as is more common for a piston pump. A selector valve (SIA valve) with several inlet channels (six to ten) and one output only, is used for directing predetermined amounts of reagents and sample into the collector where it could cause homogenization, separating and mixing the solutions. Then, the flow direction is reversed and the reaction mixture is directed to the detector.

The simplicity and versatility combined with the robustness generates an exponential growth in analytical applications SIA systems [1]. Other qualities, for this upward, could be mentioned as the low sample consumption, and reducing the amount of waste analysis.

However, it is important to note that the SIA due to the operational characteristics of the injection device used, has the disadvantage of performing the analysis with a low frequency rate, when compared to other analyzers, as the aspirations of the solutions are carried out sequentially.

Flow analysis with multicommutation (MFA)

In the mid 90s, another Brazilian researcher, has proposed an automatic analytical methodology based on multicommutation flow systems. This system was called in multicommutation flow analysis (MFA) [19].

The main feature of the system developed by Reis Bonaventure is inserting small aliquots of sample and consecutively and alternately reagent, yielding a binary sampling. This formation reaction zone favors the homogenization process between the sample and the reagent does not influence the analytical speed [20].

Work [20] show a series of job advantages of the binary sample on a flow analysis systems and among these we highlight the increased precision and analytical sensitivity, besides decreasing the reagent volume for analysis, resulting, with a consequent reduction the amount of waste generated.

Despite the qualities provided by the analysis in multicommutation flow, MFA has not found by the scientific community to the desired acceptance, perhaps because of its novelty, as this system keeps great similarities with systems already commercially established, as the FIA [21] . This lack of responsiveness was reviewed by Santos [21], which attributes this lack of robustness to solenoid valves commercially available and the difficulty in finding commercial electronic circuits for driving the valve, which forces its confection.

Anyway, the multicommutation has gained its space between the flow analysis methodologies, in a flowing already recognized by the IUPAC technique.

Analyzer flow-batch (FBA)

In 1999, Honorato et al. [22] proposed an automated system to enable the execution of titrations, using the Fibonacci method to detect the end point. At the time, he studied the acidity in white wines by titration with NaOH using metacresol purple indicator. This system was called analyzer flow-batch (English: *flow-batch analyzer - FBA*), since it incorporates the main features of analyzers flow, for example, the transport of reagents and samples and monitoring signal analytical with batch analyzers, since the processing of the sample is performed in a chamber before being subjected to the detection.

As can be seen in the schematic illustration shown in **Figure 2**, the FBA is basically composed of the following parts:

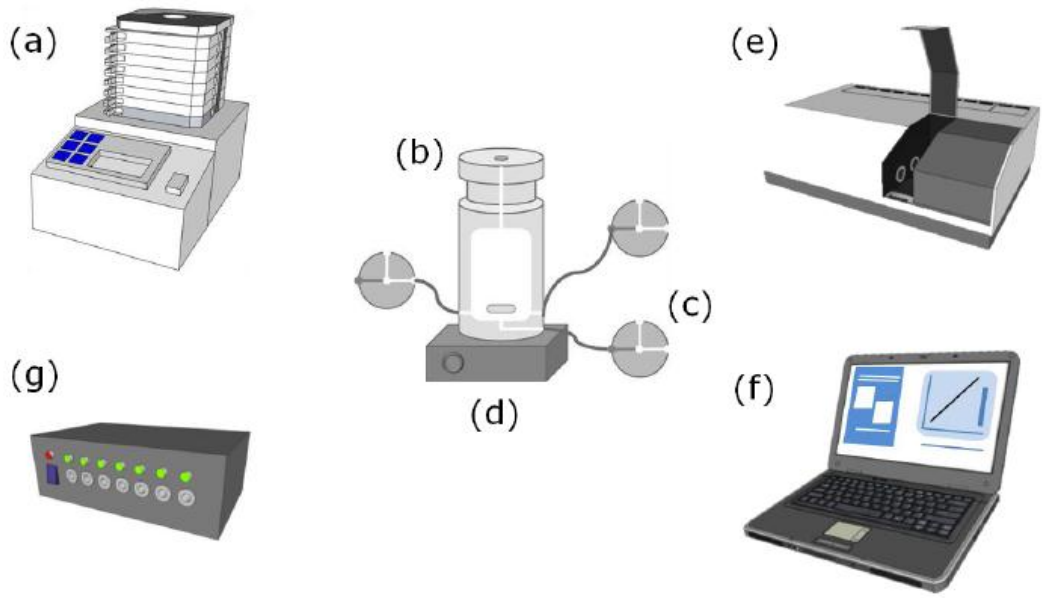

Figure 2. Diagram illustrating the main components of FBA. (a) peristaltic pump, (b) mixing chamber, (c) solenoid valves, (d) magnetic stirrer (e) detection system, (f) computer and (g) valve actuator. (Adapted from [23])

Propulsion system: to effect the propulsion of the fluid in the FBA, is generally used a peristaltic pump (Figure 2(a)), due to its ability to boost the liquids by several channels simultaneously, maintaining constant flow rate.

System addition of the fluids: in FBA predefined and precise volumes of reagents and samples added and aspirated from the mixing chamber are controlled by solenoid valves (figure 2(c)). Other switching schemes may be employed as a clamp valve, SIA valves, micropumps (which perform the function of the valve and the propulsion system).

Mixing chamber: a mixing chamber or reaction chamber (Figure 2 (b)) is one of the main features of the FBA. It consists of a small cylindrical part generally Teflon® or acrylic, with variable internal volume from 0.5 to 2.0 ml. In this mixing chamber occurs most analytical procedures, such as addition, homogenisation, pre-treatment reactions packaging of fluids, preparing calibration solutions, analyte detection, etc. Efficient mixing of fluids can be achieved by using a small magnetic bar inside the chamber, the movement of the driven bar magnet field generated by a magnetic drive stirrer (Figure 2 (d));

Detection System: the device used for detection (Figure 2(e)) will depend on the method used in analysis and may even, if necessary, attach the sensor to the camera;

Control system: full control of the system is carried out with computer assistance (Figure 2(f)), ensuring speed and accuracy in analysis. For valve control is used a valve actuator (figure 2(g)).

The combination of these accessories ensures intrinsic characteristics of flow analyzers (high sample throughput, low consumption of sample and reagents, low cost of installation and ease of automation) and the analyzers batch (universal applications, robustness and versatility) providing the flow batch analyzer , figures of merit such as high precision and analytical throughput, low cost per analysis, low consumption, handling and contamination of reagents and samples and generating little waste to the environment.

Despite the FBA have been originally designed to perform titrations time demonstrated that this system has a very different purpose and that of the previously proposed this analytical approach could be applied to other analytical processes.

Several analytical methodologies have been addressed in the last 12 years [24], exploring the characteristics of FBA. Strategies pretreatment of samples, such as liquid-liquid extraction [25] and digestion [26], screening [27] analysis, titration [28] standard addition [29] and approaches exploiting chemiluminescence [30], fluorescence [25]

turbidimetry [31] nephelometry and [32] have been developed. Several forms of detection may also be integrated into the mixing chamber, for example, recently, Andrade et al. They suggested using the webcam as a way to detect the FBA [23].
Despite the FBA be a relatively new technique, compared to other analyzers in flux, its capabilities have already been recognized in the scientific community, including being mentioned in textbooks Area [1,5]. Iñón and Tubino [33] reaches the rank FBA with the other analyzers, discussed in the previous sections, as recognized by IUPAC.

CONCLUSION

Given the above, it is observed that the evolution of automated analyzers is the sample injection system and reagents. In FIA, the injection was given initially via syringe, and was replaced by acrylic nozzles. In SIA injection is given through the rotary valves already in MFA through Solenoids valves and finally the FBA allied MFA the advantages of the system with the introduction of a Teflon mixing chamber.

Even with these developments described analyzers have advantages and disadvantages, but nothing that prevents them from being used in chemical analysis. So fitting by the analyst find what (s) could (am) better suit your needs.

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