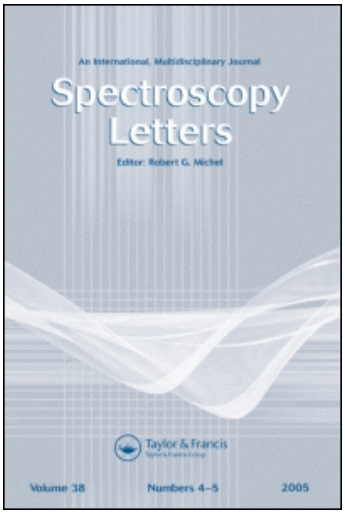

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Multipumping Flow Systems: An Alternative Approach to Sample Handling in Spectroscopy Measurements

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Multipumping Flow Systems: An Alternative Approach to Sample Handling in Spectroscopy Measurements

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Abstract: Multipumping flow systems (MPFSs) are one of the most recent developments in terms of flow-based analytical methodologies. They differ from conventional flow-based modalities such as flow injection analysis (FIA) and sequential injection analysis (SIA) in several aspects, including manifold components and configuration, operational mode, and flow hydrodynamics. This paper presents an overview of MPFSs and discusses their basic features, including methodological implementation, operational characteristics, analytical performance, potential, and limitations. Applications to different types of samples involving different detection techniques are discussed.

Keywords: Automation, multipumping flow systems, solenoid pumps, spectroscopy

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INTRODUCTION

During the past few decades, flow-based analyzers have played a relevant role in the implementation and automation of analytical procedures, especially in relation to wet chemical analysis. These analyzers have been intensively investigated and applied mainly to pharmaceutical, clinical, environmental, metallurgical, agricultural, and food analyses, as well as to industrial process control. The flow system is an excellent solution manager,[1] therefore the steps required for specific analytical application, such as sample conditioning, delivering, diluting, reagent addition, analyte separation/concentration, and reaction rate evaluation, are efficiently carried out under reproducible conditions inside a closed environment, leading to improved figures of merit such as accuracy, precision, sensitivity, and selectivity.

Miniaturization is currently a pronounced tendency in the field of analytical chemistry as it is often associated with high portability, low power demands, and a significant reduction of reagent consumption that leads to cost reduction and minimization of waste generation.[2] An important issue related to miniaturization refers to compactness and ruggedness, which should be envisioned as less components performing identical or increased number of tasks. More compact systems integrate fewer components thereby are more easily assembled and controlled. Moreover, reduction of the number of components leads to a less expensive unit and, simultaneously, to a lower probability of occurrence of operational malfunctions or errors.

Apart from miniaturization and compactness, the cost-effectiveness is also a relevant aspect to be taken into account when setting up an analytical procedure. In this context, reagent consumption, required time for analysis, operator intervention, and obviously the instrument cost and maintenance[3] should be taken into consideration. The recently proposed multipumping flow systems (MPFSs)[4] exhibited operational characteristics and analytical features suitable to meet the above-mentioned requirements.

Differently from the traditional flow-injection (FIA),[1] sequential injection (SIA),[5] and multicommuted (MCFS)[6] systems, which rely on the utilization of peristaltic or syringe pumps as propelling devices and of rotary, multiport or solenoid valves as sample insertion devices, MPFS relies exclusively on the utilization of multiple solenoid pumps. These pumps have been considered as an important and recent achievement in terms of solution propelling and can also be accountable for inserting sample and reagent solutions and for manifold commuting. In this way, specific insertion valves are not needed, and this feature makes the manifold easier to be designed. As the pumps are the only active elements of the analytical system, it is easily automated, operated, and controlled.

Solenoid pumps are low cost, robust, and reliable components able to produce a reproducible pulsed flowing stream, which is currently considered as an important advantage in contrast to the earlier consensus, "pulse establishment is a hindrance to be avoided."

Utilization of solenoid pumps as propelling devices was proposed by Weeks and Johnson.[7] However, in the original application, the pumps were used only as substitutes of a peristaltic pump in a typical two-channel FIA manifold. In MPFS, solenoid pumps are essential components of the flow manifold being accountable, as stated above, for sample insertion and propelling device, thus avoiding the need for a specific sample insertion unit.

Although MPFS is a recent flow approach, the results obtained in relation to different detection techniques (spectrophotometry, fluorimetry, chemiluminescence, etc.) have demonstrated that the operational and analytical features of MPFSs make them very attractive for the implementation of analytical methods. In fact, the pumps are able to perform multiple tasks, allowing the design of compact, accessible, and simple flow manifolds that are easily operated and controlled.

The main objective of this paper is then to review the MPFS concept in order to permit a deep evaluation of the characteristics and potential of the related methodologies in order to motivate potential users and to encourage a more widespread use of this novel modality of flow analysis. Moreover, it aims at presenting an overview of proposed MPFS applications involving spectroscopy measurements and at demonstrating and discussing the scope and performance of this innovation.

SAMPLE (AND REAGENTS) INSERTION

The individual control of the pump assures a high flexibility in terms of sample and reagents addition thus in the establishment of the reaction zone. The insertion of a given solution is directly related to pump propulsion and is controlled in terms of time-based or pulse-counting routines. The sample volume could be easily defined by actuating the sample pump for a given number of pulses. In this sense, MPFS ensures a high versatility in the selection of the sample volume. Moreover, distinct sample strategies such as single sample volumes, binary sampling, merging zones, or even segmentation approaches could be straightforwardly exploited. Considering the simplest MPFS configuration (Fig. 1), the single sampling volume strategy (usually used in flow-based procedures) would be implemented by initially actuating the sample pump for a given number of pulses (inserting the required sample volume), which would be transported toward detection by the subsequent actuation of the carrier (reagent) pump. The binary sampling approach consists in intercalating small sample and reagent pulses, establishing not only two (as it happens with the single sample volume insertion) but multiple reaction interfaces, which permits a better homogenization of the reaction zone. To this end, sample and reagent pumps are alternately actuated for a given number of intercalation cycles and intercalation pulses, which defines the volume and pattern of the reaction zone. When using merging zones for sample insertion, the sample and reagent pumps are

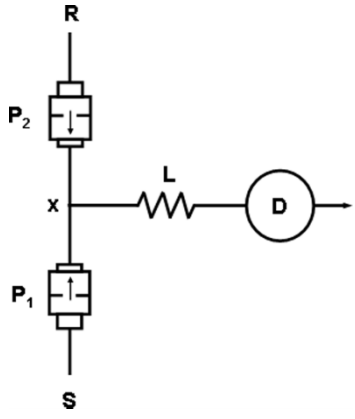

Figure 1. Flow diagram of MPFS involving insertion of two solutions. P_1 and P_2, solenoid pumps; S, sample solution; R, carrier reagent solution; x, confluence point; L, coiled reactor; D, detector. Extracted from Ref. 4.

simultaneously actuated and the number of pulses of both pumps determines the volume of the reaction zone.

Regarding sample and reagents insertion, the solution propulsion rates are determined by the pulse volume and the frequency of pump actuation (pulse frequency). Considering that each pump is characterized by an upper limiting operational frequency, a maximum flow rate is then established.

PULSED FLOW

Alternatively to the typical laminar regimen observed under constant flow conditions, the sudden pump diaphragm displacement produces a burst of solution at the solenoid pump outlet that generates a pulsed flowing stream characterized by a chaotic movement of the solutions in all directions. This is inherent to MPFS and a valuable feature of solenoid pumps. The disorganized sample/reagent solutions proximity in MPFS leads to improved mixing conditions thus efficient homogenization of the reaction zone. Consequently, length of the reaction coil could be reduced, minimizing sample dispersion. Better sensitivity in relation to laminar flow conditions for identical sample volumes is then usually attained. This aspect is even more evident under limited dispersion conditions. This characteristic makes MPFS particularly attractive for application in situations that required a faster sample/reagent mixing, as in relation to measurements of short-lived species yielding chemiluminescence emissions.[10] The advantageous aspects of the pulsed flow generated by solenoid pumps were recently confirmed in the development of an SIA system with fluorimetric detection, in which solenoid pumps replaced the conventional propeller units commonly used in this system.[11]

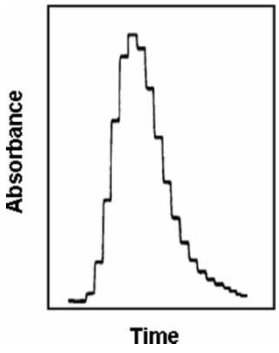

Figure 2. Typical stair-like shaped signal registered at high speed. The figure refers to the MPFS in Fig. 1. Extracted from Ref. 4.

Utilization of pulsed flows in flow analysis was recently reviewed,[12] and the recorded peak shape was emphasized. The pulsed nature of the flowing streams in a MPFS is evident in the stair-like shape of the recorded analytical signals (Fig. 2). It should be emphasized that the stair-like shape, although always present, is better noted when registered at high recording speed. The rippled fashion is dependent mainly on the pump volume and on the pulse frequency, length and internal diameter of the reactor, and the internal volume of the detector. The stepwise signal fluctuations are more pronounced in the portions of the flowing sample where the concentration gradients are more intense. Thus the effect becomes more apparent at the rising and falling portions of the recoded peak and decreases as the sample dispersion increases (Fig. 2).

APPLICATIONS AND TRENDS

The MPFS is a recent strategy in terms of flow analysis, therefore the number of analytical applications is not so impressive.[13] The innovation was proposed[4] in relation to spectrophotometry. The authors established the general aspects of the approach, emphasizing that solenoid pumps are the only active elements of the flow manifold; injection valves are not needed; system control (and eventual reconfiguration) is simplified and fully automated; the discrete actuation of each pump enables the insertion of precisely selected solution volumes solution; the pumps generate a pulsed flowing stream with improved mixing conditions; analytical systems are compact, low cost, and reliable. An evident advantage of the proposed MPFS[4] is the operational versatility that enables the utilization of different approaches for sample insertion without changes in the manifold. In this way, variable sample volume, binary sampling, and merging zones could be exploited to manage formation and

development of the reaction zone. In the same work an MPFS flow system was designed for mimicking a conventional FIA system for the spectrophotometric determination of Cr(VI) exploiting the reaction with diphenylcarbazide. Under the same conditions, MPFS produced analytical signals three times higher relative to those obtained with the FIA system.

Further, an MPFS was proposed for the spectrophotometric determination of phytic acid in plant extracts,[14] which was able to run 150 samples per hour with low sample and reagent consumptions. Use of two sample volumes (20 and 50 sample pulses) provided two dynamic working ranges.

The possibility of delivering pulsed flows with syringe instead of solenoid pumps was investigated in relation to the spectrophotometric determination of isoniazid based on reaction with 1,2-naphthoquinone-4-sulfonate in alkaline medium.[15] Syringe pumps based on stepper motors provide pulses with fixed volumes. However, the stair-like peak characteristic of a pulsed flowing stream was observable only under extreme conditions (4-μL step syringe, 0.38-mm-i.d. tubing, and 7-μL flow cell)

Pharmaceuticals such as dypirone,[16] bromhexine,[17] and ambroxol[18] were relevant in the initial development of MPFS with spectrophotometric detection. The determination of dypirone involved reaction with *p*-dimethylaminobenzaldehyde in acidic medium. By employing a binary sampling approach, it was possible to overcome the problems related to the viscosity of the acidic solution, resulting in good mixing conditions that contributed to improve reaction development and analytical repeatability. The spectrophotometric determination of bromhexine involved a two-stage reaction with 3-methyl-2-benzothiazolinone and Ce(IV). The reaction was relatively slow, which required the establishment of a compromise between two essential aspects: the sample–reagents intermixing would have to be achieved promptly in order to ensure adequate reaction time prior to detection, and reaction zone homogenization would have to be, to a great extent, independent of the coil size as the utilization of long coils would restrain sensitivity due to the increased sample dispersion. The implemented binary sampling strategy made synchronization of addition of both reagents easier, leading a linear working range up to a bromhexine concentration of 400 mg mL^{-1} with a detection limit of 2 mg L^{-1}. The MPFS for spectrophotometric determination of buspirone involved reaction with Folin–Ciocalteu reagent.[19] The manifold was easily operated and controlled through the two parallel pathways, which allowed efficient carrying out of the "stopped-flow" approach. A fixed time kinetic procedure was attained. Moreover, measurements related to different residence times could be performed without affecting sample throughput.

The first MPFS application involving chemiluminometric detection was presented in 2005[10] and focused the catalytic chemiluminometric determination of metformin (Fig. 3). The beneficial features of MPFS for short-lived chemiluminescence emissions were confirmed. This aspect is due to the good mixing conditions between sample and reagents inside the flow

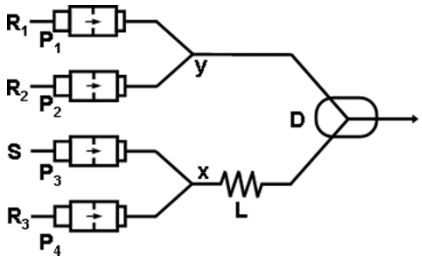

Figure 3. Flow diagram of MPFS for the catalytic chemiluminometric determination of metformin: P_1, P_2, P_3, and P_4, solenoid pumps; S, sample solution; R_1, luminol solution; R_2, H_2O_2 solution; R_3, copper (II) solution; x and y, confluence points; L, coiled reactor; D, detector.

cell, caused by the pulsed flow inherent to the solenoid pumps. The analytical procedure, involving three reagents, was straightforwardly implemented and automated, providing low reagent consumption, easy operation, and high sample throughput (95 hr^{-1}). Further, other chemiluminometric methods were implemented in MPFS. In this context, determination of carvedilol based on the hypochlorite scavenger effect in the luminol oxidation by hypochlorite[20] and the evaluation of the total antioxidant capacity of different chemicals[21] could be highlighted. Both applications provided enhanced sensitivity associated with low reagent consumption and reduced liquid wastes production.

Recently, an MPFS with spectrophotometric detection for determination of anionic surfactants in water was proposed.[22] This flow system was very simple and provided better detection limit, sampling rate, sample/reagent consumption, and waste generation relative to the analogous FIA procedure.

The above-mentioned flow systems were very similar to each other and presented favorable characteristics of simplicity, versatility and potentiality in relation to application to different analytical situations, involving distinct reactional process, without requiring significant modifications in the manifold.

Nevertheless, more complex manifolds with higher automation level could be implemented, still keeping the operating simplicity. Figure 4 illustrates the MPFS for spectrophotometric determination of glucose and fructose in syrups exploiting an improved sampling strategy.[23] The flow system comprised nine solenoid pumps, but, despite its complexity, it was very stable and enabled the analysis of 50 samples per hour, with an efficient sample treatment, low reagent consumption, and minimal chemical waste generation.

An MPFS with a complex configuration was also designed for the solid-phase extraction/speciation analysis and spectrophotometric determination of iron at two wavelengths.[24] The flow system proved to be suitable for solid-phase extraction with evident advantages relative to ordinary FIA systems, as it did not require time-consuming steps such as replacement of the injection

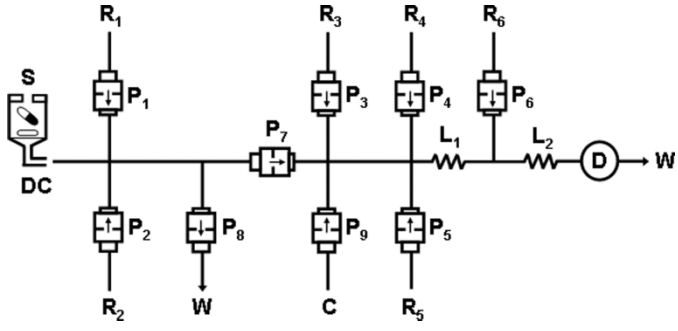

Figure 4. Flow diagram of MPFS for spectrophotometric determination of glucose and fructose in syrups. P_1 to P_9, solenoid pumps; S, sample solution; C, carrier stream; R_1, diluted aqua regia; R_2, water; R_3, periodate reagent; R_4, buffer solution (pH = 9); R_5, buffer solution (pH = 6); R_6, iodide reagent (pH = 6.8); L_1 and L_2, coiled reactors; D, detector; W, waste; DC, dilution chamber.

coil or periodical unloading of the liquid-drive. Moreover, the reagent consumption was reduced. Very recently, an MPFS was proposed for sequential determination of copper in serum and urine samples by flame atomic absorption spectrometry.[25] This was the first coupling of solenoid pumps to atomic absorption spectrometer, being noteworthy, for instance, in terms of evaluating the performance of the pumps in feeding the spectrometer nebulizer (under the influence of the spectrometer's own aspiration) or the effect of the pulsed stream in the analytical signal. The flow system included a solid-phase extraction minicolumn for copper concentration, which was fed by means of a 25-μL pump. In relation to the solid-phase extraction in flow analysis, a very recent work[26] confirmed the potential of the pulsed flows inherent to MPFS. Effectively, the pulsed flow enables solid particles to be maintained in constant floating, reflux, and circulation inside the columns, allowing the minimization of the common drawbacks of solid-phase packed columns such as backpressure, preferential pathways, and swelling.

MPFSs are considered a recent strategy, only 3 years old, still in the early stage of evolution seeking recognition from the community of analytical chemists. Anyhow, the results already obtained with spectrophotometric, fluorimetric, chemiluminometric, and FAAS detectors permits one to predict that these systems could be advantageous alternatives to implement determinations already carried out by other modalities of flow analyzers. This aspect is supported by the simplicity and flexibility of the pumps' operational adjustment, which allow us to anticipate that MPFS might be an excellent tool for implementation of automated analytical systems with feedback control, thus able to adapt system operation to the desirable performance or the sample characteristics.

An interesting feature of MPFS pulsed flow is that the flowing stream can be considered as a continuous sequence of very small segments,

corresponding with each moving pulse, which could then be subjected to an individual monitoring. Thus, if the internal volume of the flow manifold is known, it is possible to predict the positioning of the sample zone in the flowing stream and to estimate the extent of dispersion related to any specific pulse of the reaction zone. This might be useful, for instance, in the establishment of continuous flow titrations. The authors believe[15] that use of mechanical action of pulsed flows caused by the pumps could be used to establish an ascending turbulent flow through a fluidized bed reactor with an exchange resin, which is then suspended magnifying the chemical processes that occur between phases, as confirmed in a recent work whose publication is under preparation.

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