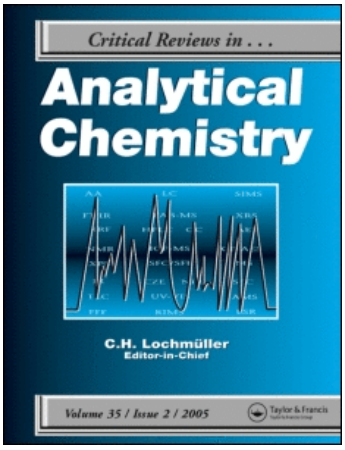

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An Overview of the Generations and Recent Versions of Flow Injection Techniques

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An Overview of the Generations and Recent Versions of Flow Injection Techniques

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The ever increasing demand for rapid, cost-effective, practically-safe, and environmentally-benign analytical methods has aroused researchers to develop automated, miniaturized, versatile, and inexpensive analytical techniques. Flow injection (FI) techniques were well-established to meet the requirements of modern chemical analysis. The family of FI techniques includes three generations, flow injection analysis (FIA), sequential injection analysis (SIA), and bead injection analysis (BIA). In addition, new versions of SIA, micro-SIA-lab-on-valve (μSIA-LOV), and sequential injection chromatography (SIC), have recently been developed for more downscaling analysis and broadening applications.
In the literature, we have not found a comprehensive and updated manuscript presenting all generations and recent versions of FI techniques. Therefore, the current manuscript briefly demonstrates the principles, developments, and applications of the FI techniques along with their consequent generations and recent versions.

Keywords flow injection analysis, sequential injection analysis, bead injection analysis, lab-on-valve, sequential injection chromatography

INTRODUCTION

The term "flow injection" (FI) describes a family of related techniques including, up-to-date, three generations and mainly two versions. Flow injection analysis (FIA), which was introduced in 1975 by Ruzicka and Hansen, is the first generation (1). In 1990, Ruzicka and Marshall introduced the second generation, which is called sequential injection analysis (SIA), with dramatic modifications and developments (2). Thereafter, Ruzicka et al. introduced bead injection analysis (BIA) in 1993, as the third generation, with special applications (3). Furthermore, in 2000, Ruzicka introduced a more miniaturized SIA version, which is termed micro-SIA-lab-on-valve (μSIA-LOV) (4). This development allows for more downscaling reagent and sample volumes. The most recent technique in the family of FI is sequential injection chromatography (SIC), which was developed by Satinsky et al. in 2003. SIC is another version of SIA enabling separation and multi-component determination (5).

This manuscript summarizes the principles, potentials, and limitations of the generations and recent versions of the FI techniques. The manuscript also briefly overviews the applications of FI techniques to such analytical fields as pharmaceutical, environmental, food, and biochemical. The applications of FI techniques to prior analysis including sample treatment and chemical reactions are also addressed.

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PRINCIPLES

Flow Injection Analysis

FIA is a simple and versatile analytical technology for partially automating wet chemical analysis. It is based on physical and chemical manipulations of a dispersed sample zone, which is formed from the injection of sample into a flowing carrier stream and detection downstream. During its transport through the manifold, the sample results in the creation of a concentration gradient corresponding to an innumerable number of sequential liquid segments representing all concentrations from zero to maxima. A FIA system includes basically the following devices (Fig. 1):

1. Pump, which it is usually a peristaltic pump (PP). It is used for transporting carrier (water or other solvents)
2. Two-position pump (TPV) used for introducing carrier and sample
3. Reaction coil (RC), in which reaction takes place
4. Detector. It could be a spectrophotometer, fluorometer, potentiometer, voltammeter, etc.

Sequential Injection Analysis

Unlike FIA, SIA applies a fully-automated bi-directional discontinuous precisely-choreographed flow. Sample and reagents

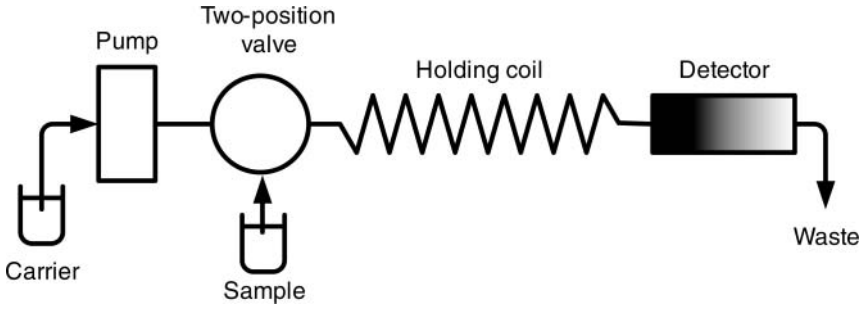

FIG. 1. Schematic diagram of basic devices of flow injection analysis manifold.

are introduced by sequential aspiration with no need for carrier. Only a liquid, which is usually water, is required for filling the syringe as well as pulling and pushing solutions. The mixture is propelled to a detector or, alternatively, before that delayed in a RC. The theoretical concepts of FIA and SIA techniques were thoroughly discussed in a number of informative publications (6–10). The basic devices of a SIA manifold are as follows (Fig. 2):

1 Pump, which is usually a syringe pump (SP), used for aspirating and dispensing solutions as well as mixing them
2 Holding coil (HC), in which reagents and sample are holed and mixed
3 Multi-position valve (MPV), which is connected with reagents and samples, allowing for programmable solution injection
4 RC — an alternative device usually used for kinetic reactions
5 Detector — all detectors coupled with FIA could also be coupled with SIA.

Micro-Sequential Injection Analysis-Lab-On-Valve

The principles of μSIA-LOV are the same of that of SIA. However, μSIA-LOV was developed for more downscaling reagent and sample volumes. With the exception of an integrated micro-conduit system, peripherals that are used in SIA are also used in μSIA-LOV (Fig. 3). The integrated micro-conduit system, which has been designed and meso-fabricated by computer aided design technology, is a transparent monolithic structure made of Perspex® (4).

It is worth noting that some researchers call μSIA-LOV the third generation of the FI techniques (11). Furthermore,

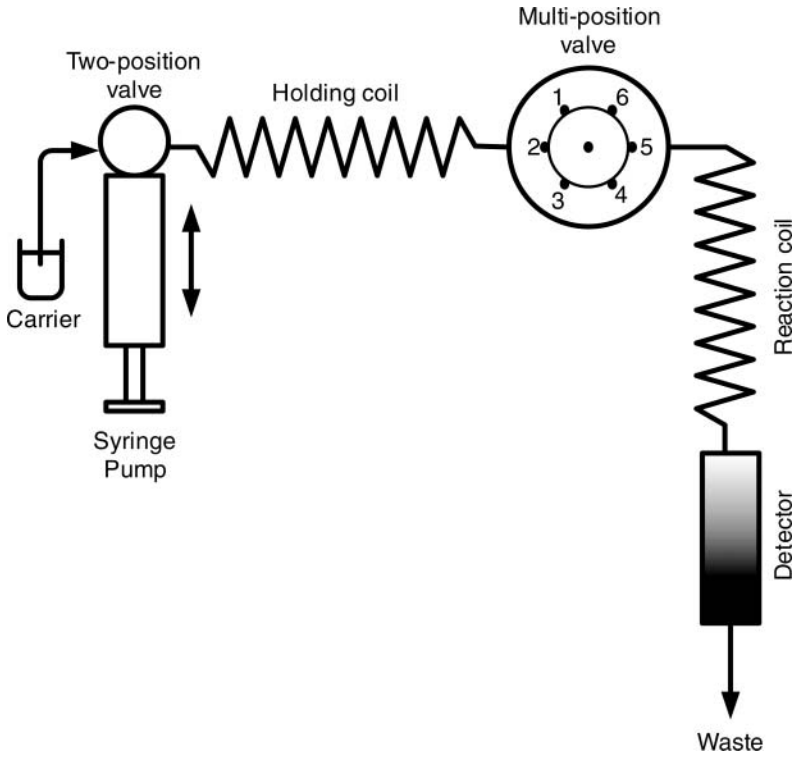

FIG. 2. Schematic diagram of basic devices of sequential injection analysis manifold.

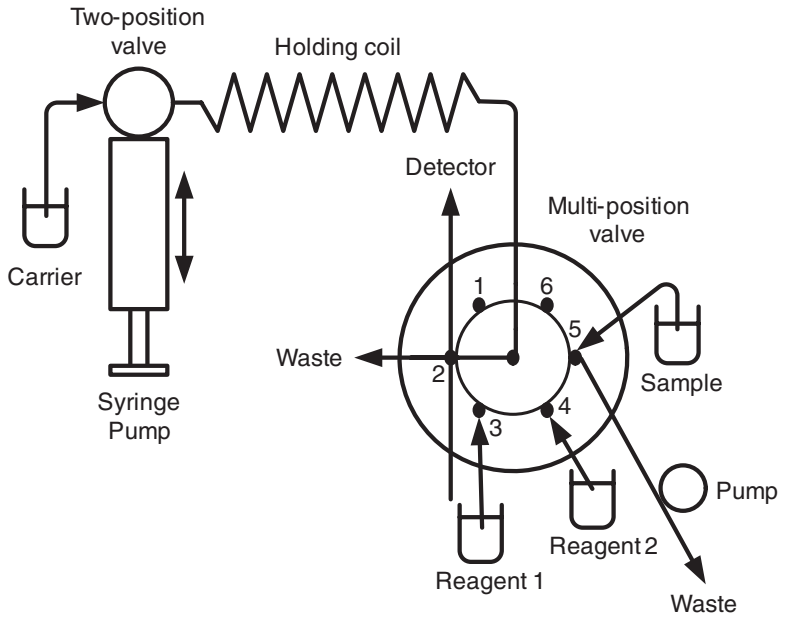

FIG. 3. Schematic diagram of basic devices of micro-sequential injection analysis-lab-on-valve manifold.

LOV-mesofluidic, as a new term, has recently appeared as a miniaturized version of μSIA-LOV (12).

Sequential Injection Chromatography

SIC is basically built on a typical SIA manifold, which includes, beside the basic devices of a SIA manifold, a monolithic column installed between MPV and detector (Fig. 4). SIC is based on the sequential injection of column conditioners, samples, and eluants, which are manipulated by a programmable flow.

Bead Injection Analysis

The BIA technique is the combination of the use of beads with a flowing stream of a solution into a FIA or SIA system. The flowing stream of solution is used to carry beads through a BIA manifold. Beads are utilized as solid surfaces to

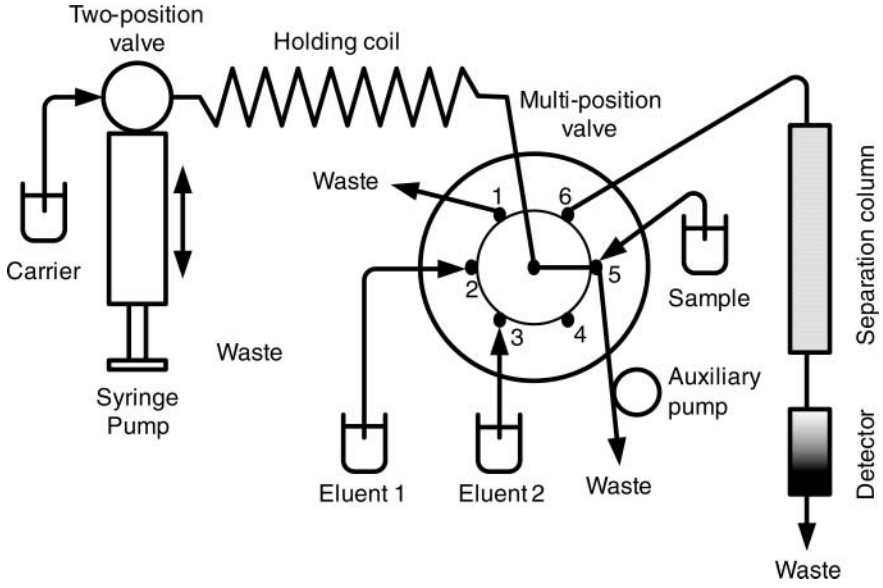

FIG. 4. Schematic diagram of basic devices of sequential injection chromatography manifold.

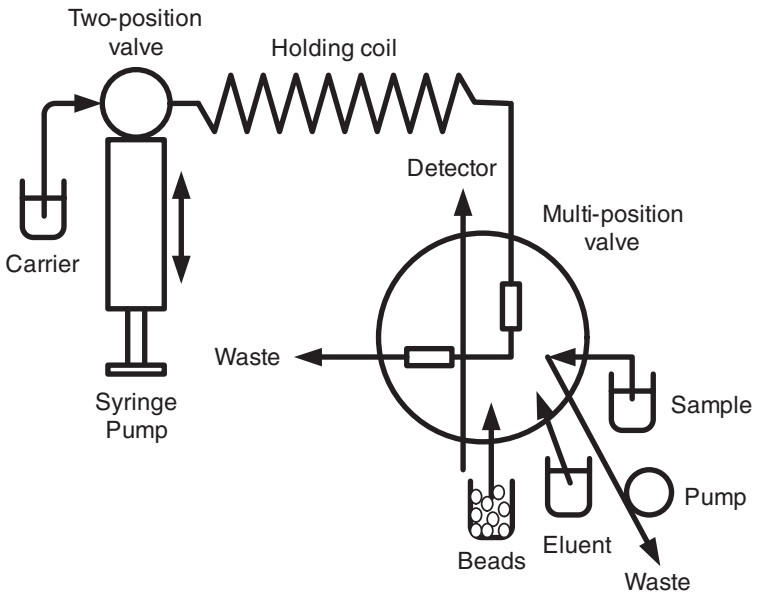

FIG. 5. Schematic diagram of basic devices of bead injection analysis manifold.

pre-concentrate or extract analytes and/or accommodate chemical reactions.

In its simplest form, the procedure of BIA is that (Fig. 5) microspheres are injected into a conduit, where they are trapped at a selected location. Next, a sample zone is injected and perfused through the beads. Then, the sample components react with the functional groups on the bead surfaces. Thereafter, retained analyte molecules are detected by spectroscopy in their native form, or subjected to chromogenic or fluorescence reaction. At the end of the procedure, beads are transported by flow reversals to different locations or discarded to waste (3, 9, 10).

POTENTIALS AND DEVELOPMENTS

General

In general, FI techniques enjoy outstanding features including automation, miniaturization, versatility, and inexpensiveness. Automation provides safety for handling reagents and samples. Automation also accelerates analysis as well as reduces effort and manpower. In addition, accuracy and precision could be enhanced by automation. On the other hand, miniaturization enhances rapidity and reduces the consumption of reagents and samples, which means better safety for the environment. In addition, miniaturization makes analytical techniques portable and hence enables on-site tests.

Due to their versatility, different analytical functions in a variety of ways are possibly automated and downscaled by FI techniques. This feature creates a broad range of FI methodologies. In this issue, various micro-analytical devices could be installed in FI systems allowing for conducting such online analytical processes as sample treatment, chemical reactions, and measurements. Furthermore, the versatility of FI techniques enables hyphenation to many analytical instruments as well as coupling various detectors. Many spectroscopic techniques (namely atomic absorption/emission spectrophotometry, mass spectrometry, and infrared spectrometry) as well as separation techniques (namely gas chromatography, high performance liquid chromatography, and capillary electrophoresis) were successfully hyphenated to FI systems. FI techniques in those hyphenations were usually applied for sample introduction, sample treatment, and conducting developing reactions. In addition, to improve selectivity and sensitivity, FI techniques proved successful coupling with various detectors including spectrophotometric, fluorescence, chemiluminescence, phosphorescence, potentiometric, voltammetric, and amperometric. Another advantage of FI techniques is that they work continuously so that virtually any number of additional lines with reagents can be added.

Flow Injection Analysis and Sequential Injection Analysis

Although FIA and SIA are both empowered with great potentials, the latter technique enjoys significant advantages over the frontal one. A simple comparison between SIA and FIA is useful for understanding the advantages of SIA over FIA and, at the same time, to deepen the concepts of both of them. The following points summarize the advantages of SIA over FIA (2, 6–10).

1. While SIA applies stopped-flow operation, FIA applies continuous-flow operation leading to excessive use of reagents.
2. FIA uses volumes of reagents and sample in milliliters while SIA uses those in microliters. This feature does not only means potential reduction in reagent and sample consumption, but also means, beside faster solution handling,

waste minimization and thus better safety for the environment.
3. Unlike FIA, SIA allows fo using widely different chemistries simply by changing the flow program rather than plumbing.
4. The replacement of a MPV in SIA instead of a TPV in FIA provides a means for selecting different sample streams and hence allows for conducting convenient automated calibration.
5. Unlike FIA, programmable flow rate in SIA makes analytical methods, especially kinetic ones, more accurate and precise.
6. Delaying a physical or a chemical process before detection, which takes place in a RC installed in SIA, usually enhances the detectability of analytical methods.
7. By the full-automation of SIA, one-shot on-line analytical procedures can be adopted.

Micro-Sequential Injection Analysis-Lab-On-Valve

The μSIA-LOV technique is basically developed for downscaling reagent-based assays to submicroliter levels. Typical sample and reagent volumes consumed in μSIA-LOV are between 5 and 25 μL per assay while those in SIA are between 25 and 200 μL. Besides the advantage of downscaling solution volumes, μSIA-LOV enjoys all the benefits of SIA. For the LOV-mesofluidic technique, volumes of reagents and samples applied are further downscaled, which are in the range of 0.1–10 μL per assay (12).

μSIA-LOV is the platform of not only reagent-based methodologies but also BIA and SIC methodologies. This feature empowers μSIA-LOV with applicability to numerous analytical methodologies. In addition, some sample treatment procedures such as dilution, pre-concentration, and developing reactions can be performed by μSIA-LOV.

Sequential Injection Chromatography

FI techniques had suffered from a major limitation until SIC was introduced. SIC provides a possibility for conducting simultaneous determinations with separation procedures. The heart and the most attractive device of SIC system is the monolithic columns. Due to their high porosity sorbent, monolithic columns permit high flow rates of mobile phase at low back pressures without losing efficiency. Monolithic columns consist of a single piece of a high-purity polymeric silica gel rod with a bimodal pore structure (macropores and mesopores—a porosity exceeding 80%). Macropores (average size 2 μm) dramatically reduce the column back-pressure and allow the use of higher flow rates. The fine porous structure of mesopores, with a 13-nm size average, creates a large uniform active surface. This feature enables high performance chromatographic separation. The monolithic rod demonstrates very high mechanical stability and long operative lifetimes, in most cases far exceeding the lifetime of particulate columns. Moreover, monolithic columns exhibit similar chromatographic properties with respect to retention and selectivity as particulate columns of the same specific surface area and pore diameter.

Comparing SIC with HPLC, the frontal technique enjoys advantages over the latter one, which could be summarized as follows:

1. Simplicity of instrumentation, which offers low cost, ease of use and friendly maintenance
2. Miniaturization of SIC provides instrumentation portability and possibility of conducting on-site tests
3. Reduction in volumes of column conditioners and eluants
4. Possibility of applying different separation mechanisms including reverse phase, ion-exchange, and affinity chromatography
5. Adaptability of installing different devices to perform on-line analysis including sample treatment, chemical reaction, separation, and detection.

Therefore, SIC is a promising separation technique and could be a competitor for HPLC if extensive research is conducted. It is proposed that future research will be more valuable if it focuses on coupling SIC with more selective and sensitive detectors than spectrophotometry, which is currently being used. Moreover, improving the pressure of pumps used in SIC will reduce back-pressure. Chocholous et al. has published a manuscript demonstrating the concepts of SIC in detail (13).

Bead Injection Analysis

Briefly, the following points address the potentials of BIA (3, 9, 10, 14–18):

1. Because beads are discarded and replaced by new ones, the risk of contamination, denaturation, and system fouling is drastically reduced.
2. Operation in a continuous flow system is possible in BIA because there is no need to regenerate beads.
3. BIA enjoys high precision of bead delivery as well as the absence of carryover.
4. BIA allows fast automated renewal of the reactive solid phase, which is delivered in a uniform composition throughout a series of measurements.
5. BIA can be carried out in either FIA or SIA format.

On the other hand, the major challenge confronting the development of BIA methodologies is that small amounts of beads must not only be moved reliably within the system, but also must be precisely metered and packed in a well-defined geometry within the optical path of a flow-cell (9, 10).

APPLICATIONS

The employment of the FI techniques in different fields of analysis is nowadays well-established. Using the database Scopus® with the key words "flow injection," "sequential injection," "bead injection" and "lab-on-valve," a literature survey revealed that the applications of FI techniques is accelerating.

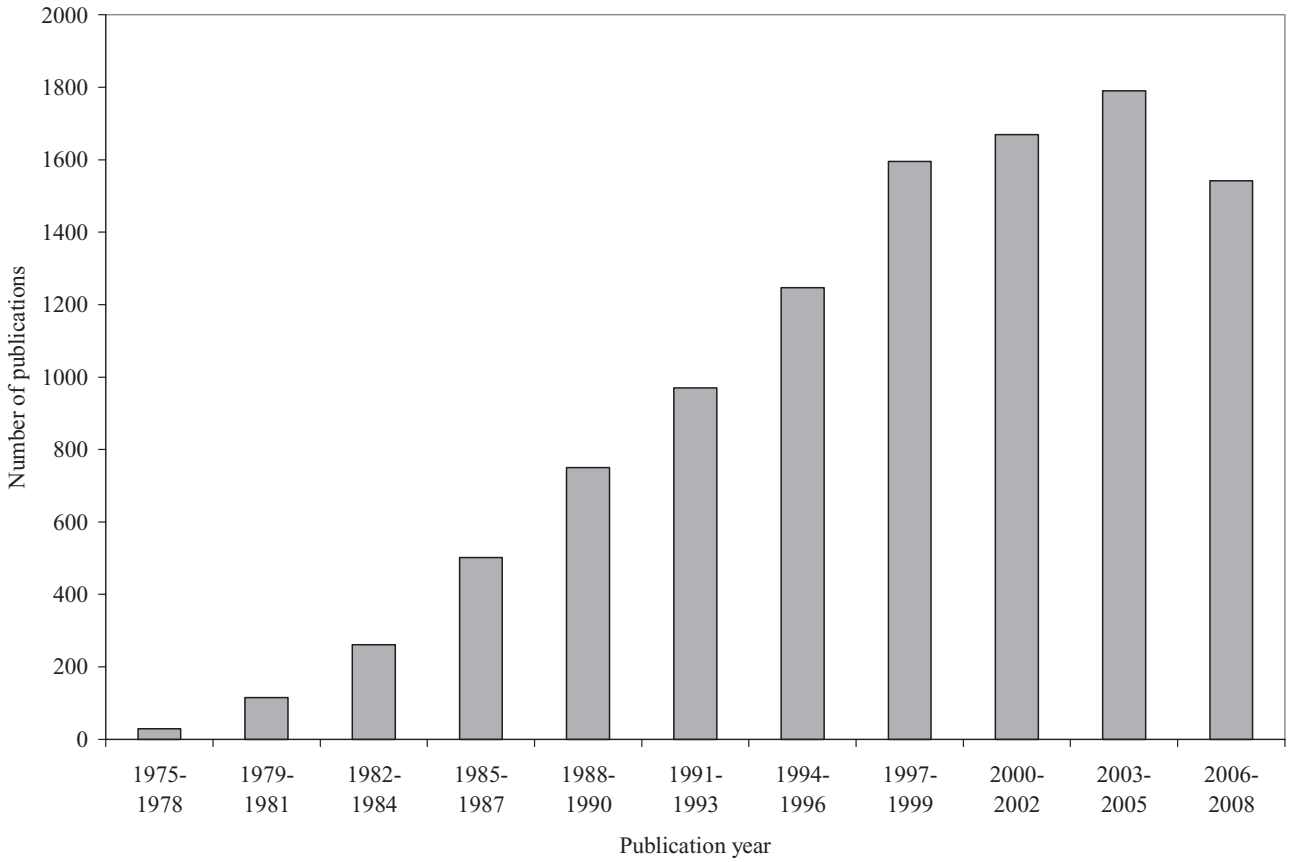

FIG. 6. Number of published manuscripts reporting the applications of FI techniques since their introduction in 1975 and up to 2008.

By the end of 2008, more than 8,500 scientific manuscripts reporting various applications can be retrieved. Figure 6 shows the number of manuscripts published since the introduction of the first generation of FI techniques. The following sections briefly demonstrate the applications of FI techniques to various fields of analyses.

FI techniques have gained special attention in pharmaceutical analysis. This could be attributed to the requirements of pharmaceutical laboratories with respect to high sample throughput, saving in reagent and sample consumption as well as minimization in both effort and manpower. FI techniques have been applied to pharmaceutical analysis for such purposes as serial assays, drug dissolution testing, and drug screening. Most pharmaceutical FI methods were validated based on either the International Union of Pure and Applied Chemistry (IUPAC) or the International Conference on Harmonisation (ICH) guidelines and realized by international pharmacopoeias. The applications of FI techniques to pharmaceutical analysis are well reviewed in some general manuscripts (6, 8, 19, 20) and other special ones (21–33).

FI techniques have also been exploited, but to a lesser extent, for environmental analysis. In this topic, several environmental samples (e.g., water, industrial effluent, soil, sediment, biological, etc.) were analyzed for many environmental parameters (e.g., heavy metals, radionuclides, anions, organic compounds, etc.). FI techniques not only provide direct determination of environmental parameters, but also provide speciation analysis, an issue which is of increasing concern in environmental analyses. Many previous environmental FI methods were realized either by using certified reference materials or by parallel analysis using standard methods. Some general manuscripts (6,8,19,20) and other special ones (34–40) reviewing the applications of the FI techniques to environmental analysis are available in the literature.

Food analyses have also been successfully employed FI techniques. Various food and beverage samples were analyzed for such ingredients as fatty acids, amino acids, vitamins, carbohydrates, fertilizers, metals, nonmetals, etc. Gao et al. reviewed the applications of the FI techniques to food analysis (41). In addition, Moreno-Cid et al. reviewed FI determinations of citric acid in various food and drink samples (42).

FI techniques have also proved to be powerful for the automation and miniaturization of bioanalysis. In particular, μSIA-LOV has been found to be a more efficient technique for

cell-culture and antibody studies, which were applied for assessing the metabolic regime of living cells. The μSIA-LOV technique was also exploited for detecting single-stranded nucleic acid sequences in DNA assays. Therefore, μSIA-LOV is a promising technique for in-valve biochemical steps when it is coupled with various units, e.g., dialyzers, gas diffusers, pervaporators, liquid-liquid extractors, etc. Those couples facilitate automated interference removal and pre-concentration of analytes at trace levels in complex matrices. A number of review manuscripts reporting the applications of FI techniques to bioanalysis are published elsewhere (43–49).

Basically, FI techniques are designed to perform solution chemistry. However, their great potentials can perform more complicated on-line sample manipulation processes before measurement such as sample treatment and developing reactions. Recently, liquid/liquid extraction, gas/liquid extraction, and SPE were successfully performed for sample treatment using SIA. Of particular interest is the assay methods based on the SPE approach because it offers a great range of versatility. Various SPE approaches, including ion-exchange, chelation, or hydrophobic interactions, hydride generation, precipitation/co-precipitation, and sorption of neutral complexes in PTFE knotted reactors were miniaturized and adapted to FI techniques. In addition, other sample pre-treatment processes such as filtration, dilution, dialysis, and gas diffusion were successfully automated and downscaled by SIA (50). Besides rapidity, the unique benefits of employing FI techniques for sample treatment are the significant reduction of solvent and sample volumes as well as high secure handling solution.

On the other hand, many developing reactions such as chromogenic, fluorescent, phosphorescent, and chemi/bioluminescence were successfully conducted by FI techniques. Developing reactions are always applied to improve sensitivity and selectivity. It is worth noting that some analytical methods based on reactions such as chemiluminescence are difficult to be satisfactorily conducted without using FI techniques. (51). Review manuscripts reporting the use of FI techniques for sample treatment and developing reactions are available in the literature (49, 51–54).

CONCLUSIONS AND FUTURE PERSPECTIVES

From the current overview manuscript, the following conclusions and future perspectives can be made:

- The potentials of FI techniques could practically provide endless possibilities for automating and miniaturizing analytical procedures dedicated to almost all analytical fields.
- Automation and miniaturization of FI techniques work hand in hand to offer potential reduction of reagent/sample volumes, high sample frequency, high-secure reagent/sample handling, excellent reproducibility, and better safety for the environment.
- The compatibility of FI techniques with various types of detectors always provides satisfactory detectability of trace and ultra trace levels of such analytes in various matrices.
- The μSIA-LOV technique is highly recommended for chemical analysis involving rare samples and expensive reagents.
- SIC is a promising separation technique and it could be a competitor for HPLC in the future.
- The BIA technique is especially useful for accommodating such prior analytical procedures as developing reactions, pre-concentration, separation, etc.

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ABBREVIATIONS

BIA	Bead injection analysis
FI	Flow injection
FIA	Flow injection analysis
HC	Holding coil
μSIA-LOV	Micro-sequential injection analysis-lab-on-valve
MPV	Multi-position valve
PP	Peristaltic pump
RC	Reaction coil
SIA	Sequential injection analysis
SIC	Sequential injection chromatography
SP	Syringe pump
SPE	Solid-phase extraction
TPV	Two-position valve

REFERENCES

1. J. Ruzicka, and E.H. Hansen, Flow injection analysis: Part I. A new concept of fast continuous flow analysis. *Analytica Chimica Acta* 78 (1975):145–157.
2. J. Ruzicka, and G.D. Marshall, Sequential injection: A new concept for chemical sensors, process analysis and laboratory assays. *Analytica Chimica Acta* 237 (1990):329–343.
3. J. Ruzicka, C.H. Pollema, and K.M. Scudder, Jet ring cell: A tool for flow injection spectroscopy and microscopy on a renewable solid support. *Analytical Chemistry* 65 (1993):3566–3570.
4. J. Ruzicka, Lab-on-valve: Universal microflow analyzer based on sequential and bead injection. *Analyst* 125 (2000):1053–1060.
5. D. Satinsky, P. Solich, P. Chocholous, and R. Karlicek, Monolithic columns — A new concept of separation in the sequential injection technique. *Analytica Chimica Acta* 499 (2003):205–214.
6. N.W. Barnett, C.E. Lenehan, and S.W. Lewis, Sequential injection analysis: An alternative approach to process analytical chemistry. *Trends in Analytical Chemistry* 18 (1999):346–352.
7. J.H. Aldstadt, D.C. Olson, D.K. Wolcott, G.D. Marshal, and S.W. Steig, *Flow and sequential injection analysis techniques in process analysis*. In R.A. Meyers, R.A. Meyers, *Encyclopedia of Analytical*

Chemistry, volume 15: *Applications, Theory and Instrumentation*, John Wiley & Sons Inc (2000).
8. C.E. Lenehan, N.W. Barnett, and S.W. Lewis, Sequential injection analysis. *Analyst* 127 (2002):997–1220.
9. E.H. Hansen, and J. Wang, The three generations of flow injection analysis. *Analytical Letters* 37 (2004):345–359.
10. J. Ruzicka, *Flow Injection Analysis*, 4th ed. on CD. FiaLab® (2009).
11. J. Wang, and E.H. Hansen, Coupling on-line preconcentration by ion-exchange with ETAAS: A novel flow injection approach based on the use of a renewable microcolumn as demonstrated for the determination of nickel in environmental and biological samples. *Analytica Chimica Acta* 424 (2000): 223–232.
12. J. Wang, Lab-on-valve mesofluidic analytical system and its perspectives as a "world-to-chip" front-end. *Analytical and Bioanalytical Chemistry* 381 (2005):809–811.
13. P. Chocholous, P. Solich, and D. Satinsky, An overview of sequential injection chromatography. *Analytica Chimica Acta* 600 (2007):129–135.
14. J. Ruzicka, and L. Scampavia, Flow injection to bead injection. *Analytical Chemistry* 71 (1999):257A–263A.
15. M.J.A. Canada, A.R. Medina, J. Frank, and B. Lendl, Bead injection for surface enhanced Raman spectroscopy: Automated on-line monitoring of substrate generation and application in quantitative analysis. *Analyst* 127 (2002):1365–1369.
16. S.K. Hartwell, G.D. Christian, and K. Grudpan, Bead injection with a simple flow-injection system: An economical alternative for trace analysis. *Trends in Analytical Chemistry* 23 (2004):619–623.
17. M.J. Ruedas-Rama, A. Ruiz-Medina, and A. Molina-Díaz, Resolution of biparametric mixtures using bead injection spectroscopic flow-through renewable surface sensors. *Analytical Science* 21 (2005):1079–1084.
18. J.B. Quintana, M. Miro, J.M. Estela, and V. Cerda, Automated on-line renewable solid-phase extraction-liquid chromatography exploiting multisyringe flow injection-bead injection lab-on-valve analysis. *Analytical Chemistry* 78 (2006):2832–2840.
19. P. Fletcher, K.N. Andrew, A.C. Calokerinos, S. Fobes, and P.J. Worsfold, Analytical applications of flow injection with chemiluminescence detection. *Luminescence* 16 (2001):1–23.
20. M. Miro, J.M., Estela, and V. Cerda, Potentials of multisyringe flow injection analysis for chemiluminescence detection, *Analytica Chimica Acta* 541 (2005):57–68.
21. A. Rios, M.D.L. de Castro, and M. Valcarcel, Flow injection analysis: A new approach to pharmaceutical determinations. *Journal of Pharmaceutical and Biomedical Analysis* 3 (1985):105–112.
22. M.D.L. de Castro, and M. Valcarcel, Automation of pharmaceutical dissolution testing by flow injection analysis, *Journal of Pharmaceutical and Biomedical Analysis* 8 (1990):329–336.
23. J.M. Calatayud, *Flow Injection Analysis of Pharmaceuticals. Automation in the Laboratory*, Taylor & Francis, London (1996).
24. P. Solich, H. Sklenarova, M. Polasek, and R. Larlicek, Application of flow injection technique in pharmaceutical analysis. Part I: Spectrophotometric and chemiluminescence detection. *Journal of Flow Injection Analysis* 18 (2001):1–13.
25. P. Solich, H. Sklenarova, M. Polasek, and R. Larlicek, Application of flow injection technique in pharmaceutical analysis. Part II: Other spectroscopic methods and electroanalytical detection. *Journal of Flow Injection Analysis* 18 (2001):118–132.
26. P. Pavlina, and M. Polasek, Improvement of amperometric detection (AD) by determination of drugs by flow injection methods-flow injection analysis (FIA) and sequential injection analysis (SIA). *Ceska Slovenska Farmacie* 50 (2001):107–112.
27. M.I. Evgenev, S.Yu. Garmonov, and L.Sh. Shakirova, Flow-injection analysis of pharmaceuticals. *Journal of Analytical Chemistry* 56 (2001):313–332.
28. J.M. Bosque-Sendra, L. Gamiz-Gracia, and A.M. Garcìa-CampanÞa, An overview of qualimetric strategies for optimisation and calibration in pharmaceutical analysis using flow injection techniques. *Analytical and Bioanalytical Chemistry* 377 (2003):863–874.
29. P. Solich, M. Polasek, J. Klimundova, and J. Ruzicka, Sequential injection technique applied to pharmaceutical analysis. *Trends in Analytical Chemistry* 23 (2004):116–126.
30. L. Hlabangana, S. Hernández-Cassou, and J. Saurina, Multicomponent determination of drug using flow-injection analysis. *Current Pharmaceutical Analysis* 2 (2006):127–140.
31. A.M. Pimenta, M.C.B.S.M. Montenegro, A.N. Araujo, and J.M. Calatayud, Application of sequential injection analysis to pharmaceutical analysis. *Journal of Pharmaceuticals and Biomedical Analysis* 40 (2006):16–34.
32. K. Mervartova, M. Polasek, and J.M. Calatayud, Recent applications of flow-injection and sequential-injection analysis techniques to chemiluminescence determination of pharmaceuticals. *Journal of Pharmaceutical and Biomedical Analysis* 45 (2007):367–381.
33. P.D. Tzanavaras, and D.G. Themelis, Review of recent applications of flow injection spectrophotometry to pharmaceutical analysis. *Analytica Chimica Acta* 588 (2007):1–9.
34. V. Cerda, A. Cerda, A. Cladera, M.T. Oms, F. Mas, E. Gomez, F. Bauza, M. Miro, R. Forteza, and J. M. Estela, Monitoring of environmental parameters by sequential injection analysis. *Trends in Analytical Chemistry* 20 (2001):407–418.
35. M. Miro, and W. Frenzel, What flow injection has to offer in the environmental analytical field. *Microchimica Acta* 148 (2004):1–20.
36. M. Miro, J.M. Estela, and V. Cerda, Application of flowing stream techniques to water analysis: Part III. Metal ions: Alkaline and alkaline-earth metals, elemental and harmful transition metals, and multielemental analysis. *Talanta* 63 (2004):201–223.
37. W. Xu, R.C. Sandford, P. Worsfold, A. Carlton, and G. Hanrahan, Flow injection techniques in aquatic environmental analysis: Recent applications and technological advances, *Critical Reviews in Analytical Chemistry* 35 (2005):237–246.
38. M. Miro, E.H. Hansen, R. Chomchoei, and W. Frenzel, Dynamic flow-through approaches for metal fractionation in environmentally relevant solid samples. *Trends in Analytical Chemistry* 24 (2005):759–771.
39. M. Miro, and E.H. Hansen, Solid reactors in sequential injection analysis: Recent trends in the environmental field. *Trends in Analytical Chemistry* 25 (2006):267–281.
40. J.W. Grate, O.B. Egorov, M.J., O'Hara, and T.A. DeVol, Radionuclide sensors for environmental monitoring: From flow injection solid-phase absorptiometry to equilibrium-based preconcentrating minicolumn sensors with radiometric detection. *Chemical Reviews in Analytical Chemistry* 108 (2008):543–562.
41. Z Z. Gao, X. Jin, Y. Fang, and W.S.Y. Jiu, Flow injection analysis technique and its application in food analysis. *Journal of Hygiene Research* 32 (2003):78–80.

42. A. Moreno-Cid, M.C. Yebra, and X. Santos, Flow injection determinations of citric acid: A review. *Talanta* 63 (2004): 509–514.
43. B. Rocks, and C. Riley, Flow injection analysis: A new approach to quantitative measurements in clinical chemistry. *Clinical Chemistry* 28 (1982):409–421.
44. A.L. Reed, Flow injection analysis in bioprocess control. *Bioprocess technology* 6 (1990):221–241.
45. L.D. Scampavia, and J. Ruzicka, Micro-sequential injection: A multipurpose lab-on-valve for the advancement of bioanalytical assays. *Analytical Sciences* 17 (2001):i429–i430.
46. A.D. Carroll, L. Scampavia, and J. Ruzicka, Label dilution method: A novel tool for bioligand interaction studies using bead injection in the lab-on-valve format. *Analyst* 127 (2002):1228–1232.
47. Y. Gutzman, A.D. Carroll, and J. Ruzicka, Bead injection for biomolecular assays: Affinity chromatography enhanced by bead injection spectroscopy. *Analyst* 131 (2006):809–815.
48. X. Chen, and J. Wang, The miniaturization of bioanalytical assays and sample pretreatments by exploiting meso-fluidic lab-on-valve configurations: A review. *Analytica Chimica Acta* 602 (2007):173–180.
49. M.D.L. deCastro, J. Ruiz-Jimenez, and J.A. Perez-Serradilla, Lab-on-valve: a useful tool in biochemical analysis. *Trends in Analytical Chemistry* 27 (2008):118–126.
50. J. F. van Staden, H. du Plessis, and R.E. Taljaard, Determination of reaction stoichiometries by using the sequential injection analysis technique*, Instrumentation Science and Technology* 27 (1999):1–11.
51. Z.L. Fang, Trends of flow injection sample pretreatment approaching the new millennium. *Analytica Chimica Acta* 400 (1999):233–247.
52. V. Grassi, A.C.B. Dias, and E.A.G. Zagatto, Flow manifolds exploiting in-line prior assays. *Talanta* 64 (2004):1114–1118.
53. A. Economou, Sequential-injection analysis (SIA): A useful tool for on-line sample handling and pre-treatment. *Trends in Analytical Chemistry* 24 (2005):416–425.
54. M. Miro, S.K. Hartwell, J. Jakmunee, K. Grudpan, and E.H. Hansen, Recent developments in automatic solid-phase extraction with renewable surfaces exploiting flow-based approaches. *Trends in Analytical Chemistry* 27 (2008):749–761.