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Talanta 64 (2004) 1076–1083
Talanta
www.elsevier.com/locate/talanta

The impact of flow injection on modern chemical analysis: has it fulfilled our expectations? And where are we going?

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Received 3 February 2004; accepted 19 February 2004
Available online 19 July 2004

Abstract

Presenting a condensation of the opening lecture of the 12th ICFIA conference, this communication presents a view of the impact that flow injection analysis (FIA) has had on modern analytical chemistry, evaluated both within the academic community and outside it, i.e. in "industry". The ensuing developments of FIA, encompassing sequential injection analysis (SIA) and bead injection lab-on-valve (BI-LOV), are described and their individual features discussed. Finally, some recent results of the activities from the author's own research group are briefly mentioned.

Keywords: Flow injection; Sequential injection; Bead injection lab-on-valve; Impact of FIA; Determination of trace-levels of metals

1. Introduction

In the spring of 2002, that is, more than 1.5 years prior to the holding of the 12th ICFIA conference, this author was asked to submit a title and an abstract for the opening lecture. Since, it is very difficult to predict, especially about the future, I had at that time only a limited notion of what the next couple of years would bring in terms of scientific activity. As one of the early users of flow injection analysis (FIA), I therefore, concluded that it might be of interest, both to myself and to the participants, to take a retrospective view as to how FIA has fared in its almost 30 years of existence, or more precisely to address the questions posed in the title of my lecture.

This communication is a condensation of the lecture focusing initially on the impact of FIA in modern analytical chemistry. This is done by firstly looking at its role within "academia", because it is here that it has had its most profound effect and then in "industry", here defined as the world outside academia, taking in this context a look at how the commercial development of FIA has fared. The following section will then deal with the ensuing developments of the FIA-concept, leading to its next so-called two generations, that is, sequential injection analysis (SIA) and lab-on-valve (LOV). Finally, the ongoing research activities in the author's own group will be briefly mentioned, with emphasis on the results obtained after the organisers of the conference required the abstract submitted.

2. The impact of FIA within academia

There are a number of indicators that can be used to gauge the academic impact of a particular analytical chemical concept. Some very peculiar ones were promoted by Braun et al. in a couple of articles, where the first one [1] was entitled "The Epidemiology of Research on Flow-Injection Analysis: An Unconventional Approach", followed by a sequel in 1989 [2], where the authors maintained that the singular reasons of the success of FIA was due to two factors, namely, the "Invisible College" and the "Matthew Effect". Without boring the reader at this juncture with these strange, or indeed unconventional contentions, which have been dealt with in a previous paper [3], it is suggested to look at different options. Hence, one might look at how often that a specific concept has managed to capture the attention of the editors of the various analytical chemical periodicals to the extent, that they have opted to illustrate its applications or developments as a tantaliser on the front covers of their jour-

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doi:10.1016/j.talanta.2004.02.043

nals. And judged by that parameter, FIA has fared pretty well. Thus, it has managed to appear four times on the covers of both *Analytical Chemistry* and *The Analyst*, not to mention that there is a journal dedicated exclusively to FIA (*Journal of Flow Injection Analysis*), published by the Japanese Association of Flow Injection Analysis.

Another obvious parameter by which to measure the bearing of a given concept is to look at the number of scientific papers it has been able to generate, simply because, that in order to pass the scrutiny of peer reviews, the papers must inherently possess originality or innovative ideas. And here, FIA has by the end of 2003, most impressively, given rise to about 14,000 published articles in many different journals [4]. Primarily in English, but at an increasing rate in periodicals published in a multitude of languages, not the least in Chinese. In fact, the number of papers in that language is increasing at a higher relative rate than that in the English language periodicals. As seen in Fig. 1, the number of FIA-publications initially showed an exponential growth, but has in recent years found a level of around 1000–1100 papers per year. Yet, in this context it should also be pointed out that over the years several hundreds of FIA-Ph.D. theses and book chapters have appeared, not to mention a couple of dozens monographs (see Ref. [34–52]). Hence, it can be concluded that FIA has, indeed, been most successful within academia. The reasons for this is clearly that FIA has added a whole new dimension to analytical chemistry as compared to how analytical assays used to be done. Simply because it broke definitely with the concept of homogenisation that generations of analytical chemists had been indoctrinated to believe was the only sensible way to perform chemical analysis, that is, to rely on physical mixing and chemical equilibrium. In contrast, in FIA transient measurements are exploited, which, in turn, allow a number of entirely novel and unique possibilities to be used. Just to mention a few, one can point to examples, such as: (i) use of bio-and chem iluminescence for analytical purposes [5]. These very sensitive procedures were virtually non-existent as practical assays prior to the introduction of FIA, but have found extensive use ever since. (ii) Exploitation of kinetic discrimination schemes where, even subtle, differences in the reaction rates of occurring chemical reactions are judiciously utilised to favour the assay of the analyte species. As a good example may serve the elimination of interference due to the presence of transition metal ions, such as Cu(II), Ni(II) and Co(II), in hydride generation schemes [6]. (iii) Taking advantage of intermediary/metastable constituents of specific analytical characteristics for the analytical readout [7]. (iv) Drawing on enzymatic degradation procedures either for measurements of substrates or enzymatic activities (which traditionally have been very difficult to execute) [8], not the least via stopped-flow measurements [5,9]. Or (v) to perform appropriate on-line sample pre-treatments (separation and/or pre-concentration) procedures [10,11] (see Section 5, below).

3. The use of FIA outside academia, i.e. in “industry”

When it comes to evaluate the use of FIA outside academia, this is much more difficult to gauge, because preciously little is traditionally published by public or private industrial sources. Either because they mainly make use of their equipment for routine applications and do not perform any development work as such, or because, if they indeed do it, they have no desire to publish it. However, it is known that FIA has found use in many laboratories in areas, such as environmental, clinical, pharmaceutical and food analysis. One of the most obvious and useful areas to employ FIA, namely, process control/monitoring, is almost a closed land, because the industrial companies generally are very secretive. Yet, it is a fact that within this area FIA offers great potentials for performing at-, in- or on-line analysis and for real-time data acquisition, which is indispensable for many operations. Besides, FIA entails a unique option,

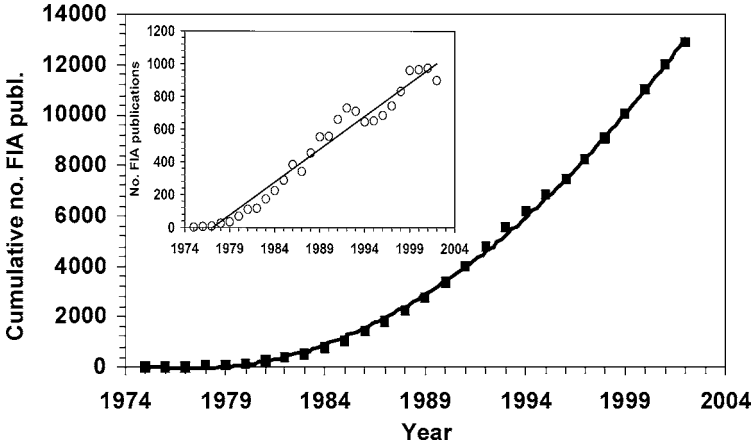

Fig. 1. The evolution in the cumulative numbers of FIA-publications as a function of time, as depicted in a semilogarithmic diagram. In the insert is shown the annual output of references.

namely, that it allows not only automatic control of the process itself, but also of the system/detection device used via the signal output.

The use of FIA outside academia, i.e. in "industry" is intimately a function of the accessibility to commercially available instruments. Already, when Jarda Ruzicka and this author in 1974/75 developed the first primitive FIA-manifolds, one of the foremost virtues of FIA was, in our estimation, the ease with which one readily might reconfigure a manifold to allow the implementation of a different chemistry or the assay of another analyte. But here we were proven entirely wrong, because: (1) commercial manufacturers want to sell dedicated instruments (optimally, one instrument per parameter). (2) People in "industry" are inherently reluctant to fiddle with their instrumentation. (3) The commercial manufacturers have most successfully exploited this reluctance to produce and sell dedicated instruments, or maybe and more correctly, to convince people in "industry" that this is the only feasible avenue to pursue. And then one is back to (1). However, to be fair, one should also look at from the angle of the manufacturers, that is, while scientists constantly are pre-occupied to develop rapid and highly sensitive and selective methods of analysis, the all important aspects for the manufacturers are the development of robust and rugged instruments, which flawlessly can perform routine analysis tasks over long periods of time without maintenance. In fact, as mentioned recently by Oguma [12], the issue in industry for determinations of major components is not so much sensitivity as it is reliability. Therefore, it is important that we as scientists have this dimension in mind when we develop methods that eventually might find their applications in routine analysis, for instance, as standard protocols within the Organisation of International Standards or the US Environmental Protection Agency, as several FIA-methods, in fact, already have managed to do.

The first commercially available FIA-instruments were introduced by the Swedish company Bifok, which was headed by Rune Lundin. Thus, in the late '70s came the model FIA-05 and later (early '80s) appeared the more advanced FIAstar 5020 instrument. With the help of Dr. Bo Karlberg, who later joined him at Bifok, Rune Lundin went to numerous meetings and conferences to promote FIA. Doing actually so well that he, within a few years, aroused the interest of one of the biggest chemical companies in Sweden, Perstorp AB, which bought him out. Some years later, it became a separate division of the Perstorp Corporation, called Tecator, which some years ago was acquired by the Danish company Foss Electric and was renamed Foss-Tecator. It was during the early years in the framework of Tecator, that an agreement was negotiated with Perkin–Elmer to allow this company to exploit FIA in conjunction with atomic absorption spectrometry (AAS). And as many readers know, this arrangement, which resulted in the units called FIAS-200 and FIAS-400, turned out to be highly beneficial, not the least for implementing procedures based on hydride generation schemes.

Although, most of the FIA-research work is done with laboratory-built setups, many of these prototypes have often been utilised for manufacturing routine commercial instrumentation and for its continuous improvement. As the years have passed, commercial companies have come to realise and appraise the advantages gained by FIA, including that it is fully computer-compatible and that automation does not imply that one necessarily has many samples to run, but that the strict control of the reaction conditions that FIA provides enables one to make use of novel measurement methodologies, which can justify the investment in even small series of samples. Furthermore, because sampling handling is so versatile, FIA can serve as a front end to practically all spectroscopic and electrochemical detectors and to various clinical, environmental and industrial assays.

Now-a-days, there are several manufacturers of FIA-instrumentation (between 15 and 20). A table with complete addresses is compiled in Trojanowics' recently published monograph [13]. Besides, useful information on commercial products and technologies can be obtained from two Product Review articles published in *Analytical Chemistry* in 1996 and 2002 [14,15], which each very meticulously list the features of selected commercial flow analysers, and an update on the methodology [16]. And, of course, by consulting the Internet. The problem here is that one easily gets flooded with an avalanche of hits.

4. Where are we going?

In the early 1990s, a variant of FIA was introduced, that is, SIA [17]. Termed the 2nd generation of FIA, it was at the end of that decade supplemented by the 3rd generation of FIA [18], also named the LOV. Both these approaches have, in their own right, proven to entail a number of specific advantages. Thus, for instance, miniaturisation of the manifolds, which, in turn, drastically reduces the consumption of sample and reagent solutions and hence leads to generation of minute amounts of waste. Or allowing complex sample manipulations to be facilitated in simple fashions. Or readily permitting the integration of sequential unit operations. These two analytical concepts are in the following compared to FIA and each individually briefly described.

In Fig. 2a, there is shown a traditional FIA-system. The advantage of FIA is that it works continuously, that virtually any number of additional lines with reagents can be added, that virtually any type of unit operation can be accommodated within the manifold and that practically any type of detector can be used. A disadvantage is that the continuous operation might lead to excessive use of reagents. While most FIA-procedures employ continuous, uni-directional pumping of carrier and reagent streams, SIA is based on using programmable, bi-directional discontinuous flow as precisely co-ordinated and controlled by a computer. A sketch of a typical SIA-manifold is reproduced in Fig. 2b.

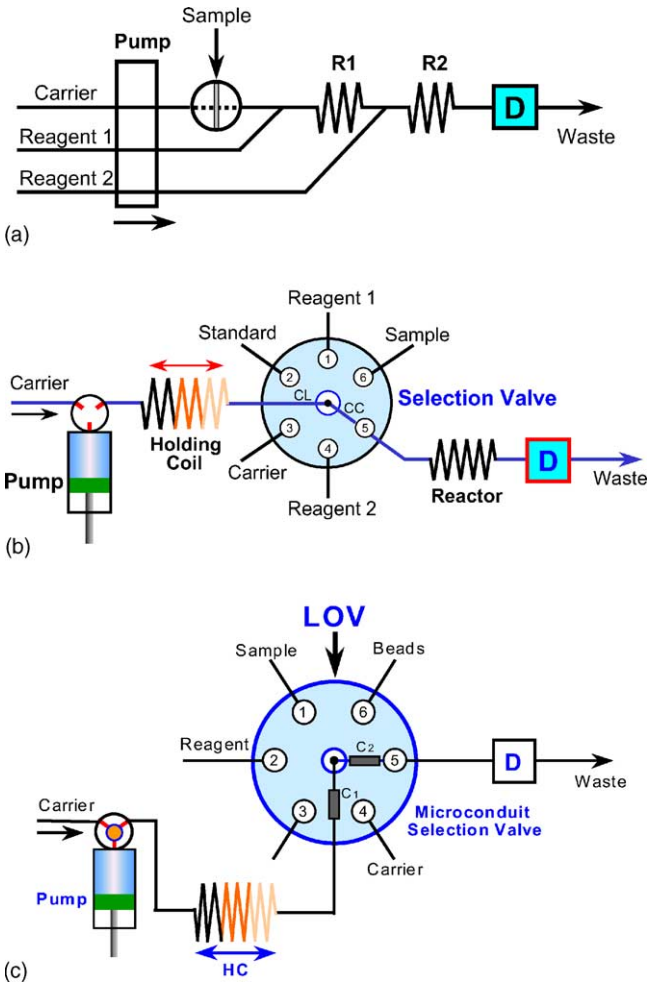

Fig. 2. The three generations of FIA, where (a) depicts a typical FIA-manifold, where a defined volume of sample is injected into a continuous flowing carrier stream, which subsequently is merged with two reagent streams. The ensuing transient generation of product is monitored by a suitable detector (D). (b) Typical sequential injection system, as based on using a selection valve and a bi-directional syringe pump. For operational details, see text. (c) Schematic drawing of a lab-on-valve (LOV) system, the concept of which is a microconduit placed atop a selection valve (as the one shown in (b)). The microconduit should ideally contain all means for executing the sample manipulations and chemistries required plus house a detection facility, i.e. act as a small laboratory. However, when large instrumental detector devices, e.g. ETAAS or ICPMS, are to be used, it is necessary to employ external detection (D) as shown in the figure. Besides aspirating liquids, it is also possible to handle small beads (furnished with active functional groups), that can be used to integrate small packed column reactors into the LOV.

The core of the system is a multiposition selection valve (here shown as a 6-port valve), furnished with a central communication channel (CC) that can be made to address each of the peripheral ports (1–6) and a central communication line (CL) which, via a holding coil (HC), is connected to a syringe pump. By directing the central CC to the individual ports, well-defined sample and reagent zones are initially time-based aspirated sequentially into the HC where they are stacked one after the other. Afterwards, the selection valve is switched to the outlet port (here position 5) and the segments are propelled forward towards the detector, undergoing on their way dispersion and, thereby, partial mixing with each other and hence promoting chemical reaction, the result of which is monitored by the detector. Notable advantages of SIA are in particular that it allows the exact metering of even small volumetric volumes (of the order of a few tenth of microlitres or even less) and that it, thanks to the use of a syringe pump, readily and reproducibly permits flow reversals.

Besides, it is extremely economical as to consumption of sample and reagents and hence in waste generation, which nowadays is an important parameter, since it is becoming increasingly expensive to dispose of chemical wastes. And since all manipulations are computer controlled, it is easy and simple to reprogram the system from one application to another one. However, it is generally difficult to accommodate (stack) more than two reagents along with the sample, although additional reagents might be added further downstream, i.e. by making an FIA/SIA-hybrid. And due to the use of a syringe pump, SIA has a somewhat limited operating capacity, although this in practice rarely is a constricting factor.

As outlined in Section 5, SIA has proven itself especially useful for various separation and pre-concentration schemes relying on, for instance, on-line liquid–liquid extraction, precipitation/coprecipitation in knotted reactors, or solid-phase extractions in column reactors with either hydrophilic or hydrophobic packing materials.

The LOV (Fig. 2c) encompasses many of the features of SIA. However, here an integrated microconduit is placed on top of the selection valve. The microconduit, which normally is fabricated by Perspex, is potentially designed to incorporate and handle all the necessary unit operations required for a given assay, that is, act as a small laboratory, hence the name LOV. Thus, it may contain facilities, such as mixing points for the analyte and reagents, appropriate column reactors packed for instance with immobilised enzymes, or small beads furnished with active groups, such as ion-exchangers, which in themselves might be manipulated within the LOV in exactly the same manner as liquids (the so-called bead injection lab-on-valve, or BI-LOV approach) and even detection facilities. For optical assays (e.g. UV–vis or fluorometry), this can readily be achieved by use of optical fibres, the ends of which, furthermore, can be used to define the optical path length to yield optimal measurement conditions [19]. Thus, one of the fibres is used to direct the light from a power source into the LOV, while the other one serves to guide the transmitted light to an appropriate detection device. For other detectors, such as AAS or inductively coupled plasma mass spectrometry (ICPMS), it is, of course, necessary to make use of external detection devices, as shown in the following section, in which instances the LOV can be used as an effective front-end means for introducing the analyte into the detector in an intelligent and optimal fashion. The same is true when employing the LOV in

connection with capillary electrophoresis, where the pre-treatment might encompass generation of a suitable complex. Both in SIA and LOV all flow programming is computer controlled, which implies that it is readily possible, via random access to reagents and appropriate manipulations, to devise different assay protocols in the microsystems.

The SI-LOV renewable column approach with bead injection (BI) has proven to be a very attractive methodology in many contexts. Thus, immunoassays can take advantage of the fact that, since, the beads upon completion of measurement are discarded, no restrictions are placed on the binding characteristics between antibody and antigen [20]. In the so-called μSI-BI-LOV mode [21], the flow cell is configured into the jet-ring-cell approach, or more precisely the renewable column concept is adapted (see below), in order to perform bioligand interactions assays. In this case, an appropriate suspension of beads is injected into and entrapped within the flow cell, whereupon the beads are perfused with analyte solution. Afterwards, the loaded beads are exposed to various stimuli and the (bio)chemical reactions taking place on the bead surface are recorded in real-time. This methodology has been demonstrated for both bioligand interactions assays of immunoglobulin (IgG) on protein G immobilised Sepharose beads and for enzymatic assays [18]. Very recently, the μSI-LOV system has been interfaced to capillary electrophoresis for anion separation. In this case, the multi-purpose flow cell was reconfigured to act as a front end between the μSI-LOV and the CE system [22]. The micro-fluidic property of the μSI-LOV did not only provide an efficient sample delivery conduit for the CE system with various sample injection modes, including electrokinetic, hydrodynamic and head column field amplification sample stacking, but at the same time served as a versatile means of sample pre-treatment to facilitate the ensuing CE separation.

Commercial instruments for SIA and LOV are produced by the American company FIA-lab Instruments and they are characterised by an unusual user-friendly software, which readily and transparently allows the reconfiguration of all necessary operations [23].

5. And where are *we* going?

In this final section will be given a few examples of the research activities that this research group is focused on, that is, use of the SI-LOV concept for determination of trace-level concentrations of metal ions in complex matrices by electrothermal AAS (ETAAS) and ICPMS via integrated sample pre-preparations schemes comprising separation and pre-concentration procedures [24,25]. What one generally wants of any analytical chemical procedure, is to obtain the optimal sensitivity and the optimal selectivity, yet although, both ETAAS and ICPMS are some of the most sensitive detection devices available, they are both prone to interferences (spectroscopic and/or non-spectroscopic)—especially if the matrix contains high levels of salts. And such interferences must necessarily be overcome in order to obtain correct analytical results.

Various schemes have been suggested to alleviate the interfering effects and facilitate reliable analyses, such protocols ranging from instrument modifications (e.g. background correction or use of a dynamic reaction cell) to experimental designs (e.g. standard addition or internal standardisation). However, instead of doing all this kind of propositions, there is a much simpler and effective solution to the problem, namely, to subject the sample to appropriate pre-treatments before it is presented to the detector, that is, separating the analyte from the matrix and then at the same time accomplishing analyte pre-concentration - which might, indeed, be advantageous/necessary if very low concentrations are to be measured.

As mentioned above, a variety of separation and pre-concentration schemes are feasible by FI or SI, such as: liquid–liquid solvent extraction–back extraction [26], hydride generation (HG)–vapour generation (VG) [27,28], precipitation–(co)precipitation [6,29]. This group has used all of them, but here the focus will be on solid phase extraction, that can be subdivided into ion exchange (where column reactors packed with hydrophilic materials are used) and adsorption (which mostly rely on the use of hydrophobic materials).

In practice, the incorporation of packed columns reactors in flow system might give rise to some difficulties, including flow resistance or back pressure as caused by progressively tighter packing of the sorbent material (this can however, to a large extent, be circumvented by loading in one direction and eluting in the opposite direction). More serious are malfunctions of the sorbent surfaces related to surface contamination or deactivation due to repetitive operation and loss of functional groups or active sites. However, these problems can be eliminated by using the so-called renewable surface scheme, that is, a scheme where one simply generates a new packed reactor for each assay. This is readily facilitated by the BI-LOV concept (Fig. 3). Here, the sample can be aspirated, columns can be generated by aspirating beads with special surface characteristics and the beads can even be manipulated between different column positions within the LOV. Appropriate eluents can be aspirated and the eluate propelled to an external detection device (via port 4, or possibly port 3, in Fig. 3). After the assay, the beads can be reused or they can be discarded and new ones aspirated, depending on the circumstances. Now-a-days, a wide variety of bead materials can be bought with various surface groups/properties, possessing either hydrophilic (e.g. ion-exchange entities) or hydrophobic characteristics.

Whatever the bead material applied, the concept or principle of the pre-concentration/separation renewable surface scheme is as shown in Fig. 4: (i) firstly the column is packed with an appropriate column material, which for the

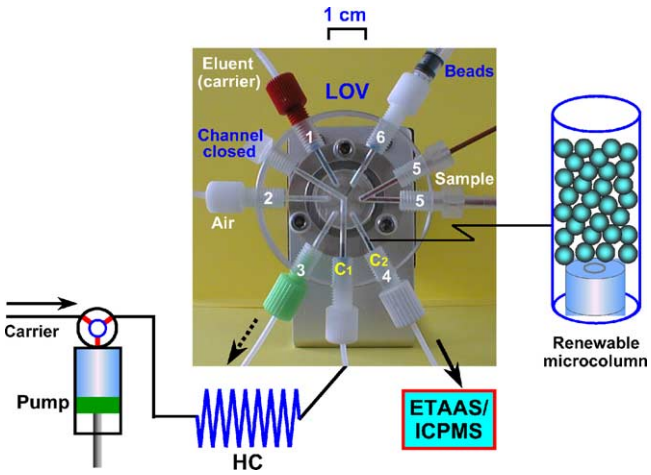

Fig. 3. Diagram of a LOV system for bead injection (BI) incorporating two microcolumn positions (C_1 and C_2), along with a close-up of a packed renewable microcolumn. In order to withhold the aspirated beads within the column positions, they are each furnished with small PEEK rods, which allow solutions freely to flow, either along the walls or through the hole in the middle, but effectively retain the beads (from Ref. [24], courtesy Elsevier Science Publishers).

determination of metal ions can be beads with ion-exchange surface groups, or a hydrophobic bead material if the sample metal ions initially are complexed with an appropriate ligand and to form a non-charged compound. Then (ii), the packed column is loaded with sample, the analyte/analyte complex being retained on the column while the matrix goes to waste. Thereafter (iii), the retained analyte is eluted by a small, well defined volume of an appropriate eluent, which subsequently is transferred to the detector, as sandwiched by air bubbles for ETAAS, or by liquid segmentation for ICPMS, in order to preserve the identity of the eluate zone. And finally (iv), the beads are discarded and new beads are aspirated for the next cycle. In fact, beads might be used once, twice or several times, as experience dictates, but the beads can, in principle, be wasted after each cycle. If cation-exchange beads are used and detection is done by ETAAS there is, in addition to elution [30], an alternative approach that has been exploited, namely, to load the cation-exchange beads with the analyte metal ions and then transport the loaded beads directly into the graphite tube of the ETAAS, where the bead material (which is organic) is pyrolized and the metals detected [31].

The use of hydrophobic beads as a means for separation/pre-concentration of metal ions requires, of course, that the metal analyte ions are reacted with appropriate ligands to form neutrally charged chelates, which can be retained on hydrophobic surfaces. However, this approach entails some specific advantages, because one can via intelligent choice of chelating reagent obtain increased selectivity and one can, again by playing on good chemistry, obtain higher tolerance for potentially interfering ions, plus eliminate inert ions in samples of high salt contents. In the author's research group a number of hydrophobic bead materials have been used, including chemically modified poly(styrenedivinylbenzene) (C-18 polysorb) and PTFE (Teflon) [32]. As an example is in Fig. 5 shown the LOV-manifold used when applying

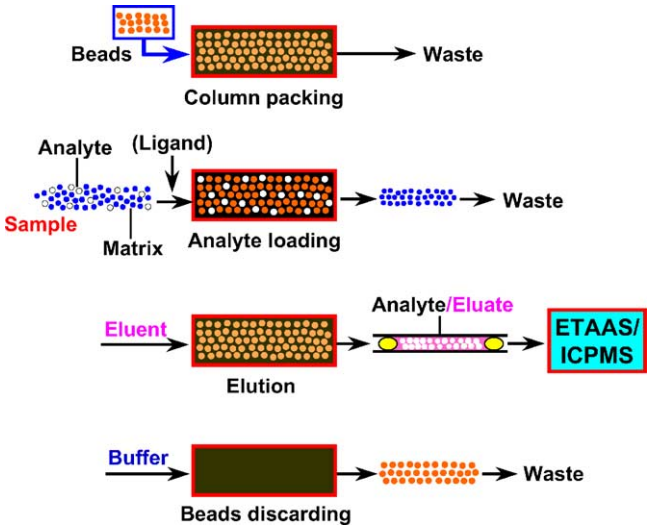

Fig. 4. The principle of sample pre-treatment (pre-concentration and separation) in the LOV approach via use of packed column reactors for determinations of metal ions. Firstly, the packed column is prepared and then the sample solution is passed through the column. If a cation-exchanger is used, the metal ions are retained directly on the column, while if a hydrophobic column material is employed, the metal ions are initially reacted with a suitable ligand to form non-charged complexes, while the matrix goes to waste. Afterwards, the retained material is eluted by an appropriate eluent and transferred to the detector, sandwiched by air segments for ETAAS or liquid-segments for ICPMS.

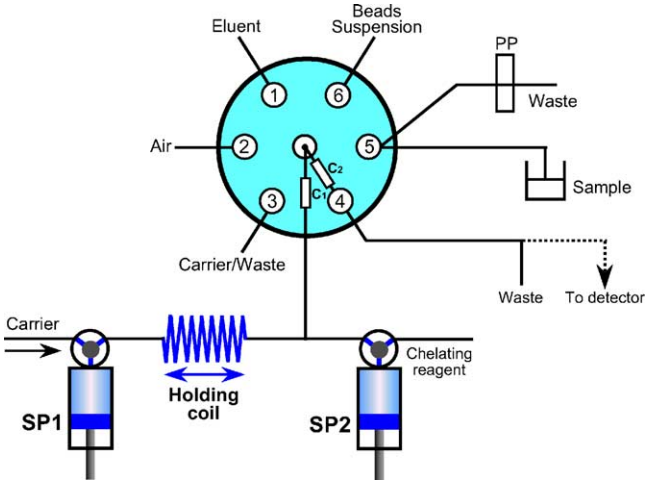

Fig. 5. Manifold for the SI-BI-LOV on-line renewable column pre-concentration system. The analyte-loaded beads are eluted and the eluate is transported to the graphite tube of the ETAAS-detector for quantification. SP_1, SP_2: syringe pumps; PP: peristaltic pump. Preconcentration takes place in column C_2 connected to port 4. The scheme is, in principle, applicable for handling both hydrophilic beads and hydrophobic beads (for details, see text. From Ref. [32], courtesy Elsevier Science Publishers).

Table 1
Performance data for pre-concentration of Cd(II) in the SI-BI-LOV system with detection by ETAAS by using renewable columns packed with PTFE or C_{18}-PS/DVB beads

	PTFE	C_{18}-PS/DVB
Reproducibility (%)[a]	4.3	3.4
Repeatability (%)[b]	3.0	3.1
LOD (3σ, $ng\,l^{-1}$)	15	126
Linear range ($\mu g l^{-1}$)	0.05–1.0	0.2–1.5
Enrichment factor	17.2	7.4
Retention efficiency (%)	74	28

All the results were obtained by elution procedures [33]. Sample loading volume: 1.25 ml.
[a] Seven measurements on the same column ($C_{Cd} = 0.5\,\mu g\,l^{-1}$).
[b] Measurements on six individual columns ($C_{Cd} = 0.5\,\mu g\,l^{-1}$).

the C18-Polysorb bead material. Following the scheme outlined in Fig. 4 and used for the determination of Cd(II) via complexation with diethyldithiophosphate (DDPA), it gave very satisfactory results. Yet, the Teflon beads, which, however, turned out to be somewhat more difficult to manipulate because of their non-spherical size, morphology and uneven size distribution yielded, as shown in Table 1, much better results. Details of these investigations are given in already published articles [24,25,32,33] and the reader is referred to these for experimental particulars. But as seen in Table 1, it is obvious that Teflon presents itself as an ideal column packing material, provided, of course, that it is feasible to obtain it as uniform, spherical beads. So far, it has not been feasible to identify a supplier of this material, yet if anybody reading this article should possess such knowledge, we should appreciate very much to be informed.

Acknowledgements

The author wishes to extend his sincere appreciation to the organisers of the 12th ICFIA conference, Professors José Luis Burguera and Marcela Burguera from Venezuela and Jacobus (Koos) von Staden of South Africa, for the invitation to the meeting. Thanks are also due to Jianhua Wang and Manuel Miró for their extensive contributions to the experimental work cited from the author's research group. Special thanks go to Jianhua Wang for his graphical assistance in preparing several of the illustrations for the lecture.

References

[1] T. Braun, W.S. Lyon, Fresenius Z. Anal. Chem. 319 (1984) 74.
[2] T. Braun, W. Glänzel, A. Schubert, Trends Anal. Chem. 8 (1989) 281.
[3] E.H. Hansen, Anal. Chim. Acta 308 (1995) 3–13.
[4] E.H. Hansen, Flow Injection Bibliography, 2003, http://www.flowinjection.com/
[5] J. Ruzicka, E.H. Hansen, Flow Injection Analysis, second ed., Wiley, New York, USA, 1988.
[6] Z.L. Fang, Flow Injection Separation and Preconcentration, VCH, Weinheim, 1993 (Chapter 5), pp. 121–156.
[7] A.B. Bendtsen, E.H. Hansen, Analyst 116 (1991) 647.
[8] E.H. Hansen, Talanta 41 (1994) 939.
[9] E.H. Hansen, Fresenius Z. Anal. Chem. 329 (1988) 656.
[10] Z.L. Fang, Analytical methods and techniques, in: J.L. Burguera (Ed.), Flow Injection Atomic Spectroscopy, Practical Spectroscopy Series, vol. 7, Marcel Dekker Inc., New York, 1989 (Chapter 4), pp. 103–156.
[11] Z.L Fang, Flow Injection Atomic Spectrometry, Wiley, New York, 1995 (Chapters 8 and 9), pp. 143–202.
[12] K. Oguma, J. Flow Injection Anal. 20 (2003) 145.
[13] M. Trojanowicz, Flow Injection Analysis, Instrumentation and Applications, World Scientific Ltd., Singapore, 2000 (Chapter 10), p. 464.
[14] A. Newman, Anal. Chem. 68 (1996) 203A.
[15] J.P. Smith, V. Hinson-Smith, Anal. Chem. 74 (2000) 385A.
[16] J. Ruzicka, E.H. Hansen, Anal. Chem. 72 (2000) 212A.
[17] J. Ruzicka, G.D. Marshall, Anal. Chim. Acta 237 (1990) 329.
[18] J. Ruzicka, Analyst 125 (2000) 1053.
[19] C.H. Wu, L. Scampavia, J. Ruzicka, B. Zamost, Analyst 126 (2001) 291.
[20] P.S. Hodder, C. Beeson, J. Ruzicka, Anal. Chem. 72 (2000) 3109.
[21] J. Ruzicka, L. Scampavia, Anal. Chem. 71 (1999) 257A.
[22] C.-H. Wu, L. Scampavia, J. Ruzicka, Analyst 127 (2002) 898.
[23] http://www.flowinjection.com/
[24] J.-H. Wang, E.H. Hansen, Trends Anal. Chem. 22 (2003) 225.
[25] J.-H. Wang, E.H. Hansen, Trends Anal. Chem. 22 (2003) 836.
[26] J.-H. Wang, E.H. Hansen, J. Anal. At. Spectrom. 17 (2002) 1284.
[27] D.L. Tsalev, M. Sperling, B. Welz, Talanta 51 (2000) 1059.
[28] S. Nielsen, J.J. Sloth, E.H. Hansen, Analyst 121 (1996) 31.
[29] K. Benkhedda, H.G. Infante, E. Ivanova, F. Adams, J. Anal. At. Spectrom. 15 (2000) 1349.
[30] J.-H. Wang, E.H. Hansen, Anal. Chim. Acta 424 (2000) 223.
[31] J.-H. Wang, E.H. Hansen, Anal. Chim. Acta 435 (2001) 331.
[32] J.-H. Wang, E.H. Hansen, M. Miró, Anal. Chim. Acta 499 (2003) 139.
[33] M. Miró, S. Jónczyk, J.-H. Wang, E.H. Hansen, J. Anal. At. Spectrom. 18 (2003) 89.
[34] J. Ruzicka, E.H. Hansen, Flow Injection Analysis, Wiley, New York, 1981.
[35] J. Ruzicka, E.H. Hansen, Flow Injection Analysis (N. Ishibashi, N. Yoza, Trans.) Kagakudonin, Kyoto, 1983 (in Japanese).
[36] K. Ueno, K. Kina, Introduction to Flow Injection Analysis, Experiments and Applications Kodansha Scientific, Tokyo, 1983 (in Japanese).
[37] M. Valcarcel, M.D. Luque de Castro, Flow-Injection Analysis Imprenta San Pablo, Cordoba, 1984 (in Spanish).
[38] E.H. Hansen, Flow Injection Analysis, Polyteknisk Forlag, Copenhagen, 1986.
[39] J. Ruzicka, E.H. Hansen, Flow Injection Analysis (Z.-L. Fang, Trans.) Science Press, Beijing, 1986 (in Chinese).
[40] M. Valcarcel, M.D. Luque de Castro, Flow-Injection Analysis, Principles and Applications, Ellis Horwood Ltd., Chichester, 1987.
[41] J. Ruzicka, E.H. Hansen, Flow Injection Analysis, second ed., Wiley, New York, 1988.
[42] J.L. Burguera (Ed.) Flow Injection Atomic Spectroscopy, Marcel Dekker, New York, 1989.
[43] B. Karlberg, G.E. Pacey, Flow Injection Analysis, A Practical Guide, Elsevier, Amsterdam, 1989.
[44] J. Ruzicka, E.H. Hansen, Flow Injection Analysis, second ed.(Z.-L. Fang, Trans.) Beijing University Press, Beijing, 1991 (in Chinese).
[45] Z.-L. Fang, Flow-Injection Separation and Preconcentration, VCH Verlagsgesellschaft mbh, Weinheim, 1993.
[46] W. Frenzel, Flow Injection Analysis. Principles, Techniques and Applications, Technical Univ. Berlin, Berlin, 1993.

[47] M. Valcarcel, M.D. Luque de Castro, Flow-Through (Bio)Chemical Sensors, Elsevier, Amsterdam, 1994.
[48] Z.-L. Fang, Flow Injection Atomic Spectrometry, Wiley, Chichester, 1995.
[49] J.M. Calatayud (Ed.), Flow Injection Analysis of Pharmaceuticals, Automation in the Laboratory, Taylor & Francis, London, 1997.
[50] A. Sanz-Medel (Ed.), Flow Analysis with Atomic Spectrometric Detectors, Elsevier, Amsterdam, 1999.
[51] Z.-L. Fang (Ed.), Flow Injection Analysis, Science Press, Beijing, 1999 (in Chinese).
[52] M. Trojanowicz, Flow Injection Analysis, Instrumentation and Applications, World Scientific Ltd., Singapore, 2000.