

Advances in Flow Analysis

Edited by

Marek Trojanowicz



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Introduction

Chemical analysis is an indispensable element in all areas of contemporary life. Together with progress in science and technological development, and also with constantly increasing demand, one can observe progress in analytical chemistry as a scientific discipline, and methods and techniques of chemical analysis for practical application purposes. The increasing demand for analytical determinations results from the necessity to analyze an increasing number of different samples, as well as from the need to design analytical instruments and methods which can be employed directly by an end-user without the need for the services of specialized analytical laboratories. This increasing demand includes also the need for improvement of the quality of analytical determinations. Depending on the area of application, there may be a need to shorten the time of analysis, minimize the amount of sample needed for analysis, achieve lower limits of detection or better selectivity (resolution) in multi-component determinations, or obtain better precision and/or accuracy of the determination.

Progress in the development of analytical methods occurs in various ways and is a combination of various factors. There are as many factors affecting it as there are different parameters that affect the results of an analytical determination. There are factors resulting from progress in natural science, material science, electronics and informatics, as well as from progress in engineering of materials and devices, and their utilization in analytical procedures. Human inventiveness and the urge for discovery, which is a driving force for fundamental scientific research, is practically unlimited, hence no stage of the development of science or technology should be treated as definitive. This obviously also concerns progress in analytical chemistry and the methods and techniques of chemical analysis.

The carrying out of analytical determinations in flow conditions can, at first glance, be treated as a simplification of the conventional non-flow procedure by omitting a sampling step. Probably such measurements in the area recognized nowadays as process analysis were, in the 1930s or 1940s, the first examples of analytical measurements in flowing conditions, for example, conductivity measurements in process streams. Then, with the development of detection methods and progress in the construction of measuring instruments, measurements of redox potential, pH, turbidity, absorbance at a given wavelength, to mention just the most

common ones, were carried out in the same way in flow mode. These methods are commonly used in modern process analysis. This separate area of chemical analysis, very well developed in the last half century, with a large arsenal of specially designed measuring instruments, has numerous specific problems to cope with. There is a wide literature on this field of chemical analysis and this area of flow analysis will be not discussed in this book.

The area of chemical analysis that is covered by this book is laboratory flow analysis. It is associated with different environmental and technical conditions, and different scales of processes and devices. In this case it is much easier to identify a commonly recognized author and the background of the idea that analytical measurement can be carried out during sample flow through the detector. The background to this invention was the urgent demand from clinical analytical laboratories in large hospitals in the 1950s, which were overloaded with a huge amount of samples, to find a solution as to how to speed up analytical procedures. The inventor of the first laboratory flow analysis system was the American biochemist Leonard J. Skeggs Jr., known also as the co-inventor of the modern artificial kidney, from the hospital associated with Case Western Reserve University Medical School. He designed the first laboratory flow system for determination of blood urea nitrogen with photometric detection (L.T. Skeggs Jr, *Am. J. Clin. Pathol.*, 1957, 28, 311). Based on the intuition that such a concept of analytical measurements could significantly improve laboratory analysis, the author of this idea quickly patented the new instrument and, in three years, it was launched on the market by Technicon Co with great success. Already the first prototypes contained several breakthrough instrumental solutions, not only a flow-through photometer and strip-chart recorder for continuous signal recording, which determined the success of the concept. I will mention a few of them to illustrate the many inventions and pioneering solutions that were involved in the construction of this system. It was constructed for analysis of blood samples, hence it was necessary to design a rotary sampler for aspiration of samples from vials. The sample, aspirated into the tubing, could disperse during the flow, but the extent of this dispersion could be limited by segmentation of the liquid stream with air bubbles. The determination of urea required removal of proteins, hence it was necessary to design a flow-through membrane dialyzer. The continuous detection in a flowing stream was already known from liquid chromatography, which was being developed with various detections earlier. The developed air-segmented flow analyzing system allowed the mechanization of numerous operations (sample introduction, addition of reagents, incubation, dialysis), and this was the most essential breakthrough in laboratory analysis.

For about the next 20 years instruments based on this concept of mechanization of chemical laboratory analysis predominated in large (and rich) clinical laboratories, but then numerous other ideas of mechanization of analytical procedures became more and more competitive. They include centrifugal analyzers, devices employing solid-reagent strips and, especially, various designs of discrete analyzers, which in the last 20 years have completely replaced clinical flow analyzers. They were more efficient and versatile, designed to perform several tens of assays from one sample. The air-segmented flow analyzers are still quite widely used, however, in routine

analytical laboratories for environmental protection, agriculture analyses and food control.

A crucial new impulse was given to further development of laboratory flow analysis in the mid-1970s by the invention of flow measurements with injection of a small volume of sample into the stream of a flowing carrier or directly into a reagent flowing solution. Even some years earlier one can find in the literature reports on flow measurements with the introduction of a smaller sample volume than needed to achieve a steady-state equilibrium signal in the detector in air-segmented systems, with conclusions that the transient signal obtained in such systems can obviously also be used for analysis with the advantageous possibility of increasing the sampling rate. Based on the existing literature one can notice that the concept of flow injection measurements came simultaneously from different branches of analytical instrumentation. In one case it can be considered as an evolution of the earlier developed air-segmented systems by elimination of segmentation of the flowing stream and injection of a small volume of sample by an injection port instead of by continuous aspiration. This led to obtaining a transient signal and, with simultaneous reduction of the diameter of the tubings, such a system provided attractive fast analytical signals. Alternatively, the same concept of measurements originated from the application of commercial instrumentation for liquid column chromatography, and its utilization in flow measurements without a separation column. The selectivity of the determination of a particular analyte can be achieved by application of appropriate chemical conditions specific for the given analyte.

The rapid increase in interest in this methodology of analytical measurements in the next years (almost exponential, if it is measured by the number of published papers in analytical journals) has to be assigned, to a great extent, to a tandem of authors J. Ruzicka and E.H. Hansen, and their research group in the Technical University of Denmark, who in numerous pioneering publications demonstrated that, for academic laboratory research, flow injection measuring systems can be built easily with low-cost, simple components in almost every analytical laboratory, without big instrumental investment. This can be a way to realize various ideas of technical design, to carry out in such systems various chemical reactions and sample treatment operations, and to employ various detection methods. It is then a very attractive way of mechanization of analytical procedures in flow systems, but it has to be admitted that this is not a way to the automation of measurements, as this term is very commonly misused. Performing analytical measurement in flow conditions does not mean automation of measurements as, according to automation theory, and also following the IUPAC terminology recommendations, the automated system has to be equipped with an intelligent control system which, with the use of a feed-back loop mechanism, can control and regulate conditions of measurements without the participation of a human operator.

The flow injection methodology of analytical determinations, being developed since the 1970s, has gained already very many technical modifications such as the most commonly known flow systems: with sequential injection of sample and reagents into a single line system (called *sequential injection analysis* – SIA), flow

measurements in tubeless systems with direct injection to the detector sensing surface (called *batch injection analysis* – BIA), or application in flow injection systems with moveable solid particles, called *bead-injection analysis*, with the same abbreviation BIA. Another aspect of the evolution of flow injection measuring systems is the rapidly progressing miniaturization of particular modules of the flow system, as well as their integration, for example, by incorporation of some modules into the injection valve (named generally as the *lab-on-valve* concept), or their miniaturization down to microfluidic format.

Generally, it seems that flow analytical systems can be described as analytical measuring devices in which all operations of sample pretreatment and detection of analyte are carried out in flowing streams. This seems to be a very common understanding of flow analysis, but at the same time one can find several inaccuracies or problems with such a description. Can one include as flow analysis simple AAS measurements with flame atomization, where the sample is aspirated, nebulized and then transported to the flame for optical detection? Can we talk about flow analysis in the case of mass spectrometry measurements with direct sample injection, where the injected liquid sample is evaporated, the analytes are ionized (and also can be fragmented), separated and then transported to the detector? And the most difficult problem to solve, namely the differentiation of liquid column chromatography and flow analysis. In column chromatography analytes present in an injected sample are separated on the column, then they can also sometimes be derivatized and then transported to a flow-through detector. A similar situation arises with capillary electrophoresis. From the point of view of tradition and history of development, and also, much more importantly, the role in analytical chemistry, it does not seem to be appropriate to include column chromatography in flow analysis. On the other hand, in typical flow systems of any kind (air-segmented continuous systems, flow injection systems etc.), packed reactors are very commonly used for sample clean-up, or preconcentration, and the operations carried out are chromatographic ones if we follow the common mechanism of chromatography. So, where to draw the line? For the sake of a framework for the subject of this book, as flow analysis is meant analysis in measuring systems where all operations of sample treatment and detection are carried out in flowing solutions but without multi-component chromatographic or electrophoretic separation. Most often it is a single component method with mechanized sample pretreatment, while multicomponent analysis in flow systems is carried out in a system with more complex manifolds or by employing detectors that are multicomponent in the mechanism of their sensing. The dynamic properties of flow measurements are widely employed in sample processing, in many cases for improvement of the parameters of some detection methods, however, still very little is done on the design of multicomponent determinations.

The principal intention in the preparation of this joint work was to present the achievements of flow analysis in recent years that may be helpful in the determination of its position in modern chemical analysis. In spite of many thousands of papers published during the 60 years since the pioneering invention of Skeggs, this methodology of analytical measurements seems to be underestimated in various

fields of routine chemical analysis. Certainly, the spectacular success in the 1960s and 1970s was the application of commercial flow analyzers with air-segmentation in clinical laboratories. Long years of development, numerous published papers, some commercial instruments for flow injection methods, have not introduced flow injection methods sufficiently into routine analytical laboratories. Nowadays, if some flow analyzers are used in routine analytical laboratories, they are mostly continuous flow analyzers with air-segmented flow and recording of a steady-state equilibrium signal.

The selection of subjects for all chapters was my subjective choice, as I am convinced that in these areas of flow analysis the largest progress has been made in recent years. I express thanks to our Publisher for acceptance of my choice. My special thanks I address to all the authors who accepted my invitation to contribute to this joint work. I am convinced they all share my hope that this book will be fruitful for the further development of flow analysis and the promotion of these methods of chemical analysis.

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