Miniaturization of Analytical Systems: Principles, Designs and Applications

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Preface

Without question, the main drivers of modern analytical techniques are the simplification of procedures and the improvement of measurement quality. To reach these goals, modern analytical techniques try to reach lower detection limits, improve selectivity and sensitivity, and achieve faster analysis time, higher throughput and less expensive analysis systems with ever-decreasing sample volumes. These very ambitious goals are exacerbated by the need to reduce the overall size of the device and the instrumentation. These items are termed 'analytical miniaturization concepts'.

The miniaturization of analytical systems is a rapidly growing area. It is associated with performing the analytical process on a small scale (sometimes, a very small scale). Different terms have been used to represent this idea: 'miniaturized analytical systems', 'analytical micro(nano)systems' and, more ambitious, 'micro total analysis systems' (μTAS), also called 'lab-on-a-chip'.

Originally, microsystems came from the need to perform online control and monitoring of industrial processes. This mainly resulted in the development of (bio)chemical sensors. However, after this initial phase, society's needs increased and sensors became insufficient to respond to new specific problems, as they suffer from poor selectivity for many applications. As a consequence, the concept of the total analysis system appeared in analytical chemistry. The idea of such a system is to integrate all the steps of analytical process (sampling, sample treatment, separation of analytes and detection) in the same device. More recently, the interest in portable instruments, allowing field tests to be carried out with ease, has increased the practical usefulness of miniaturized analytical systems. Between sensors and lab-on-a-chip devices, a wide range of microsystems, which can affect either the entire analytical process or only a part of it, have been described.

This exciting challenge has guided our effort to offer a book with a general approach to miniaturization in analytical chemistry, including the principles, designs and applications of miniaturized systems. Through ten chapters, the different issues characterizing such systems are critically discussed.

The first two chapters include the basic concepts behinds miniaturization in analytical chemistry, as well as the mechanical and electronic tools needed for designing and fabricating these systems. It is very important to give an integrated classification of the systems and to define the different terms associated with miniaturization, in order to provide a systematic view of both the different levels of miniaturization and the main objectives of the downsizing developments.

Chapters 3 to 6 represent the solid core of the book. Taking as their basis the analytical process, these chapters deal with: the miniaturization of sample treatment (including the consequent automation), with sections devoted to the problems associated with sample introduction in micro(nano)systems; miniaturized systems for analyte separation, divided into two chapters according to the forces involved in moving the flow; and detection in micro-size environments. Through these chapters, practical aspects such as the representativeness of the portion of sample analysed, the analytical potential of micro- and nanochromatography, the advantages of miniaturized capillary electrophoresis with special attention to microchip format, and both well-established and new approaches to detection in miniaturized systems, are comprehensively studied.

Chapters 7 and 8 deal with the miniaturization of the entire process: from the sample introduction to the generation of the corresponding analytical results. Thus, when possible, Chapter 7 considers the use of sensors and biosensors in an online approach, or as micro(nano)probes, very useful for *in vivo* analyses. The objective of this chapter is not to give a wide report on the sensor field (different books address this topic), but to cover the integration of micro(nano)sensors in miniaturized technology. Chapter 8 covers the miniaturization of the entire analytical process under the philosophy of the μTAS approach. From a practical point of view, it is clear that μTAS entails many different challenges, but this trend in analytical chemistry is very attractive and will be the reality of future analytical work (both inside and outside the lab). Microfluidic concepts and lab-on-a-chip systems will make up the content of this chapter, in which a rich discussion of real samples is offered.

The last part of the book (Chapters 9 and 10) deals with two aspects directly connected to the usefulness of miniaturized analytical systems: the design of portable miniaturized systems (very interesting for the performance of field tests) and how to assure the practical reliability of micro(nano)systems (quality control tests, performance and validation activities, as well as the robustness of the miniaturized depicted systems). The ruggedness of micro(nano)systems is briefly discussed and related to the tools used for the design and fabrication described in the first chapters of the book.

Finally, the authors wish to thank the broad group of researchers who have contributed to analytical miniaturization developments over the past two decades. They have been cited throughout this book, where their works have been selected, studied and strategically related between them in order to give the reader a novel textbook on analytical miniaturization as a whole. The authors hope that the reader enjoys this book and finds it useful in their own teaching and research developments.

1

Miniaturization in Analytical Chemistry

1.1 Introduction

Miniaturization is rapidly growing, with novel ideas emerging in recent years. Like other fields, analytical systems have been affected by this new technology. Concretely, the capacity to carry out laboratory operations on a small scale using miniaturized devices is very appealing. *Micro total analysis systems* (μTAS), also called *lab-on-a-chip*, have renewed interest in scaling laws in the last 10–15 years. A small scale reduces the time required to synthesize and analyze a product, as greater control of molecular interactions is achieved at the microscale level. In addition, reagent cost and the amount of chemical waste can be very much reduced.

Now, at the beginning of the twenty-first century, it is clear that the lab-on-a-chip approach is starting to be considered as a potential analytical tool in many application fields. Nevertheless, additional efforts must be addressed to two main points: (i) the laws at nanometre scale must be established, as basic physical and chemical fundaments cannot be applied; and (ii) more applications demonstrating the real use of these systems must be developed, particularly in the area of complex samples analysis. There is no doubt that miniaturized chemical analysis systems have a tremendous potential. For instance, it is foreseeable that such devices will allow the study and analysis of complex cellular processes, facilitate the development of new diagnostic abilities that could revolutionize medicine, and have applications in environmental monitoring, food analysis and industry.

Some miniaturized analytical systems, such as capillary gas chromatography, microliquid chromatography and microcapillary electrophoresis – which can be

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