Sample preparation for micro total analytical systems (μ-TASs)

Ángel Ríos, Mohammed Zougagh

The integration of sample treatment into a micro total analytical system (μ-TAS) represents one of the remaining hurdles towards achieving truly miniaturized systems. The challenge is made more complex by the enormous variation in samples to be analyzed. Moreover, the pretreatment technique has to be compatible with the analytical device to which it is coupled, in terms of time, reagent and power consumption, and sample volume.

This review, with more than 140 references, presents some recent advances and novel strategies for sample preparation in μ-TASs. We classify μ-TAS sample-preparation methods according to the mechanism that links the analyte(s) of interest to substrates: filtration, cell lysis, liquid-liquid extraction, solid-phase extraction, droplet membrane droplet, treatment by nanomaterials, stacking and isotachophoresis. We compare these techniques in terms of sample flexibility, arguing for these applications in some fields, such as biological and environmental. These discussions can help to determine the appropriate sample-preparation technique for generating a true μ-TAS. We provide a critical discussion and some key conclusions.

Keywords: Filtration; Integrated system; Isotachophoresis; Liquid-liquid extraction (LLE); Micro total analytical system (μ-TAS); Miniaturization; Nanomaterial; Sample preparation; Solid-phase extraction (SPE); Stacking

Ángel Ríos*
Department of Analytical Chemistry and Food Technology, University of Castilla-La Mancha, E-13004 Ciudad Real, Spain

Ángel Ríos, Mohammed Zougagh
Regional Institute for Applied Chemistry Research, IRICA, E-13004 Ciudad Real, Spain

Mohammed Zougagh
Albacete Science and Technology Park, E-02006 Albacete, Spain

*Corresponding author.
Tel.: +34 926295232;
Fax: +34 926295318;
E-mail: angel.rios@uclm.es

1. Introduction

The goal of analytical chemists over the years has been to make their jobs easier through automating as many of the steps of analytical process as possible. Three solutions have been proposed in order to satisfy this goal based on:

- selective chemical sensors [1] or micro-electromechanical sensors [2];
- the so-called total analysis system (TAS) approach [3]; and,
- the micro total analysis system (μ-TAS) [4].

Using these (micro)systems, (bio)chemical analysis is performed through a group of integrated steps and sub-steps connecting the sample with the corresponding results. Miniaturization can affect a single step, different sub-steps or the entire process. Fig. 1 illustrates these possibilities, taking the analytical process as central, and considering it the "analytical black box", which can be the basic subject of integrated analytical (micro)systems; or the specific sequence of three main steps: preliminary operations, analytical signal measurement and transduction, and data acquisition and processing. Hence, the upper part of Fig. 1 represents a (micro)system performing the whole process, whereas the lower part includes the different analytical standard operations involved in the process. This view allows description of the incidence of miniaturization in the analytical process:

(1) the partial miniaturization of step(s), devices or equipment; or,
(2) the miniaturization of the integrated systems performing the entire analytical process, in which miniaturization should be viewed in combination with automation and simplification of the process.

In all cases, for ideal analytical measurements, these (micro)systems can be characterized by:

(1) portability and self-operation, in order to avoid or to reduce the sampling step and allow the possibility of performing field tests;
(2) the non-invasive approach to the performance of in-line measurements, allowing minimum perturbation of the sample;
(3) facilities for the maintenance of the system and long lifetimes, or, alternatively, reusability at low price;
(4) self-calibration incorporated in the system; and,

 0165-9936/$ - see front matter © 2012 Elsevier Ltd. All rights reserved. doi:http://dx.doi.org/10.1016/j.trac.2012.12.009

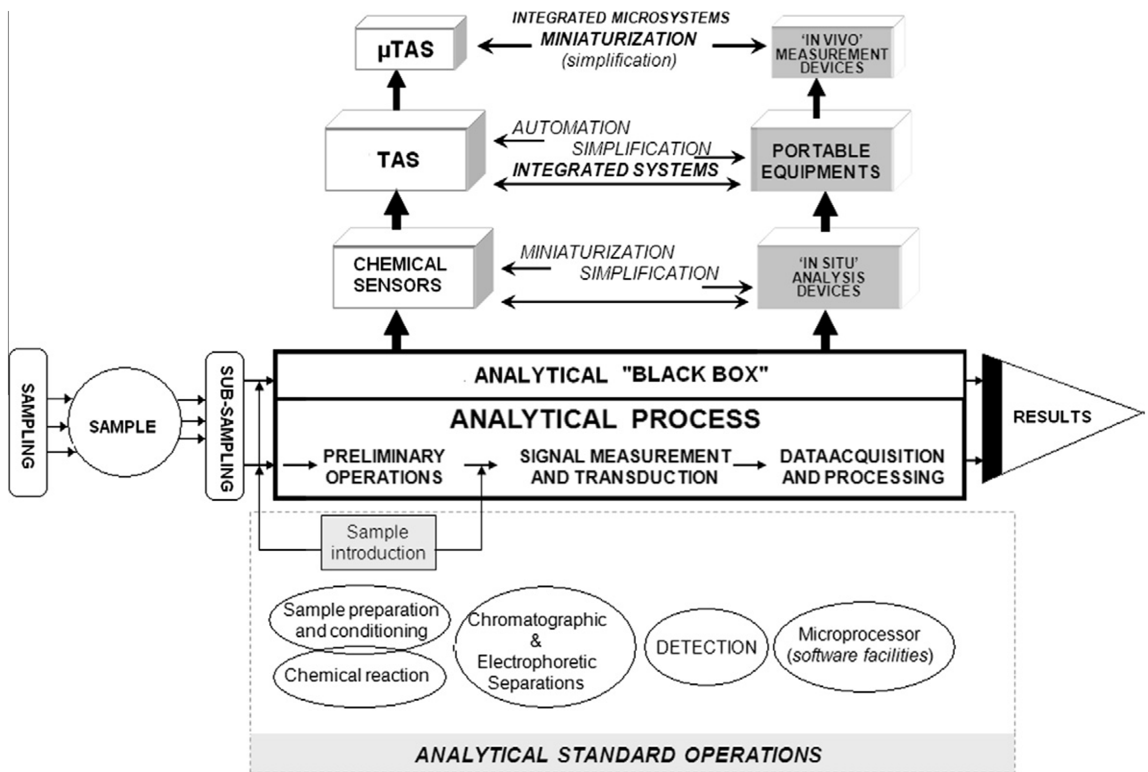

Fig. 1. Incidence of miniaturization in the whole analytical process and main achievements.

(5) the possibility of the incorporating quality-control activities, in order to assure a reliable response.

Although sensors have the advantages of *in situ* analysis and fast response, the main limitations are the high sensitivity and selectivity required for the detection of tiny amounts of analytes in complex sample mixtures. Ideally, a TAS performs all the component stages of a complete analysis in an integrated, automated fashion. These stages can include sampling, sample pre-treatment, chemical reactions, analytical separations, analyte detection, product isolation and data analysis. The philosophy of TAS has enabled enhancements in on-line chemical analyses, but significant drawbacks still exist, including slow sample transport, high reagent consumption, poor separation efficiencies and the need to fabricate interfaces between distinct components.

In 1990, Manz et al. proposed the μ-TAS concept, opening a new era in the field of analytical chemistry [4]. The μ-TAS is a smaller, faster version of TAS, with analyses taking place in flow systems having μL and even sub-μL volumes, to achieve analysis times of the order of seconds rather than many minutes. The devices used are small and monolithic in nature, with cross-sectional dimensions of the order of tens of μm.

Sample processing and pre-treatment can take a number of forms, depending on the nature of the system to be sampled. Often, an analyte of interest is accommodated within an extremely complex matrix. Thus, isolation and ''clean-up'' of a particular analyte or set of analytes is desirable under most circumstances. Typical processes may include sample filtration, centrifugation, distillation, dilution, target amplification and extraction. Successful execution of these processes is required to ensure that the analyte is present in a form compatible with the analytical principle. In addition, small volumes of sample and reagent (pL–nL) are a characteristic of most miniaturized systems, which has clear advantages associated with cost and analytical throughput, but poses constraints on appropriate or available detection methods. Consequently, much research has focused on the development of miniaturized, sensitive detection techniques. Another approach to increasing the sensitivity of analyte-detection methods is to preconcentrate the sample prior to analysis, thus indirectly yielding superior limits of detection (LODs).

The field of μ-TAS has extended its usefulness into many new fields and disciplines, spanning basic research to commercial applications [5]. The importance of μ-TAS is reflected in both the growing number and the improved quality of published articles. μ-TAS has expanded into a diverse number of analytical chemistry applications and a wide spectrum of fields {e.g., food [6,7], environmental [8,9] and biological [10,11]}. In this sense, μ-TAS is highly interdisciplinary and has served