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Review

Designs and methods for interfacing SFC with MS

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A B S T R A C T

Hyphenating SFC with MS is now routinely performed in analytical laboratories. Major instrument providers supply commercial solutions for coupling SFC and MS, which has facilitated wider adoption of the technology. The current status, however, could be achieved based on the work done by many researchers over decades. Interfacing SFC with MS posed some unique challenges, compared to interfacing MS with LC or GC, demanding special solutions. Several interface designs were tried and tested over the years before suitable solutions could be detected. Additional measures, such as (a) mixing SFC mobile-phase with an additional liquid solvent at the column outlet, and (b) heating the interfacing device, had to be adopted to address some specific challenges. Although such modifications and measures look diverse, there is one factor that drove most of them - compressibility of SFC mobile-phase. There are two objectives of this review - (1) to compile various insights which were reported on describing and optimizing SFC-MS interfacing processes, and (2) to link these insights with the fundamental issue of solvent compressibility.

1. Introduction

Interest in SFC-MS has steadily increased over the last few years supported by commercial availability of more robust and reliable analytical SFC systems. Interfacing SFC with MS does not require special technical skills anymore as the solutions and guidance from major instrument providers sufficiently address most situations. During hyphenation, apart from the required SFC and MS-related method parameters, the only interface-specific parameters that need to be supplied are - the flowrate and the composition of a “make-up” solvent. Make-up solvent is the liquid organic solvent(s) added to SFC mobile-phase at the column exit, to improve MS detection. There is also a practice of heating the interface connector employing thermal sleeve(s). Empirical guidelines are available on selecting the make-up flowrates and compositions, and also on selecting connector heater temperatures, which are helpful most of the times. Sometimes, however, the situation can be baffling if the basic mechanisms that control the interfacing process are not properly understood. The purpose of this review is to provide some physical explanations behind the empirical guidelines.

Objectively, the only task of an *interfacing device* between chromatography and MS is to transfer the analyte molecules eluting from the column to the MS inlet, while ensuring that the separation achieved through chromatography is maintained. Such a device can be a simple connecting tube - like in GC-MS and LC-MS. For SFC-MS, however, the situation is not so simple. SFC requires to be conducted under highly pressurized conditions and because MS is a low-pressure detector, analytes eluting from SFC column must be depressurized before being supplied to the MS inlet. This depressurization must be done in a controlled way, otherwise it can destroy the resolution achieved by chromatography and also cause poor MS signals. This is the most complex problem related to SFC-MS interfacing and it exists because of the highly compressible nature of SFC mobile-phase. The other manifestation of the challenge of working with a compressible solvent is the requirement of employing an automated back-pressure regulator (ABPR), which is a control valve employed to maintain a set pressure inside the system while allowing the system to work with any flowrates. ABPRs are employed after the column for understandable reason and may come with voluminous designs that can add dispersion to analyte bands. To address this issue sometimes a part of the mobile-phase is diverted to the MS by splitting the main stream.

Most challenges related to SFC-MS interface design can be categorized under - (a) how to design a pressurized system where the pressure controlling device is not contributing significantly to system dispersion, and (b) how to manage solvent decompression properly so that chromatographic fidelity is not compromised. Solutions adopted to address SFC-MS interfacing problems inherently address either one or both the issues. Based on this insight the rest of the review is divided in two major parts, describing - (a) technological solutions developed to reduce the effect of additional system volume in form of ABPR (in Section 2), and (b) methods and designs developed to execute solvent decompression without losing chromatographic resolution (in

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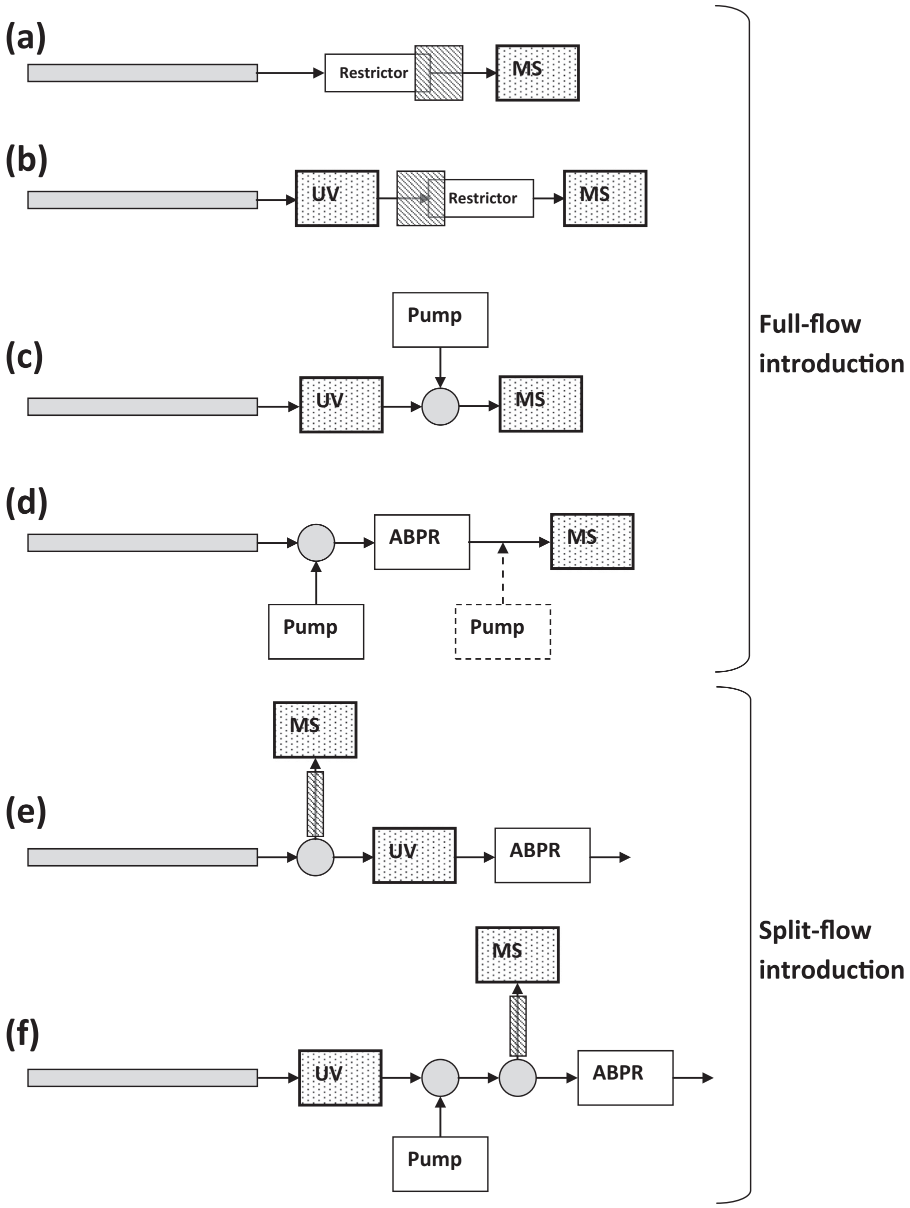

Fig. 1. Schematic representations of various SFC-MS interfacing configurations. (a) A chromatographic column is connected directly to an MS through a pressure restrictor where the end of the restrictor is subjected to heating, (b) same as in (a) but here the restrictor is subjected to heating at the beginning of the restrictor, (c) here flow from the column is first passed through a UV detector, which is then mixed with a fixed-pressure pump flow, before being expanded to MS through a restrictor, (d) here flow from the column is passed through an automated back-pressure regulator (ABPR) before the MS and the flow is mixed with a make-up pump flow, either before or after the ABPR, (e) here a part of the outlet from the column is directed towards an MS whereas the other part is taken to an ABPR passing through a UV detector, (f) in this configuration, flow from the column is first passed through a UV detector, which is then mixed with a make-up pump flow. A part of the mixed stream is then taken to the MS and the other part to an ABPR. Detailed description of these configurations are provided in Section 2.

Section 3). Note that both components are critical to successfully couple SFC with MS.

2. SFC-MS coupling strategies

One of the main issues that influenced strategies to fluidically couple SFC with MS was of maintaining a set pressure inside SFC system while *not* adding a significant volume by placing a bulky pressure-controlling device before MS. Excellent reviews on this topic has been published before [1, 2]. The design approaches taken to accomplish this task can be divided in two broad categories - (a) full-flow introduction, and (b) split-flow introduction. Schematic diagrams representing the two approaches are presented in Fig. 1 and a review from different reports that applied these designs are presented in the rest of this section.

2.1. Full-flow introduction

Directing the full flow from SFC to MS was the earliest design adaptation for SFC-MS interfacing, reported by Randall and Wahrhaftig [3]. Referring the design as dense gas-chromatography/mass-spectrometer interface, the authors expanded the dense gas in a nozzle-skimmer-collimator system. The advantage of full-flow is the ability to introduce all or most of the analyte molecules for detection - potentially increasing sensitivity for mass-flow sensitive ionization methods e.g. APCI (atmospheric pressure chemical ionization). The challenge, however, is to design an interface which is low-volume, robust and does not put any constraint on SFC method design. Based on the reported design alternatives, full-flow is achieved through - (1) employing a capillary restrictor, (2) employing a liquid pump to control SFC system pressure, and (c) employing low-volume ABPR.

2.1.1. Full-flow through capillary restrictor

Directing full-flow through a capillary restrictor, which acts as a passive pressure regulator, was first introduced by Smith et al. [4] in 1982. The process was called direct fluid introduction (DFI). The authors reported coupling an open-tubular capillary SFC with a chemical-ionization MS by employing a short restrictor with a carefully designed pinched-end. Smith and co-workers reported a series of pioneering work in SFC-MS interfacing [4-6]. The group designed and tested various restrictor geometries to optimize MS performance [6]. More detailed discussion on these designs is presented in Section 3.2.