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Review

Evolution of solid-phase microextraction technology

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Abstract

The main objective of this contribution is to describe the development of the concepts, techniques and devices associated with solid-phase microextraction, as a response to the evolution of understanding of the fundamental principles behind this technique. The discussion begins with an historical perspective on the very early work conduced almost a decade ago. As new fundamental understanding about the functioning of the technology developed, new ways of constructing and using the SPME devices evolved. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Reviews; Solid-phase microextraction

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1. Introduction

Solid phase microextraction was developed to address the need to facilitate rapid sample preparation both in the laboratory and on-site where the investigated system is located. In the technique a small amount of extracting phase dispersed on a solid support, is exposed to the sample for a well defined period of time. In one approach a partitioning equilibrium between the sample matrix and extraction phase is reached. In this case convection conditions do not affect the amount extracted. In a second approach utilizing short time pre-equilibrium extraction, if convection/agitation are constant, then the amount of analyte extracted is related to time. Quantification can then be performed based on timed accumulation of analytes in the coating. Fig. 1 illustrates several implementations of SPME which have been considered. They include mainly open bed extraction concepts such as coated fibres, vessels, agitation mechanism disks, but in-tube approaches are also considered. Some better address issues associated with agitation and others, ease of implementing sample introduction to the analytical instrument. It should be noted that solid-phase microextraction was originally named after the first experiment using an SPME device which involved extraction on solid fused-silica fibres, and later as such,

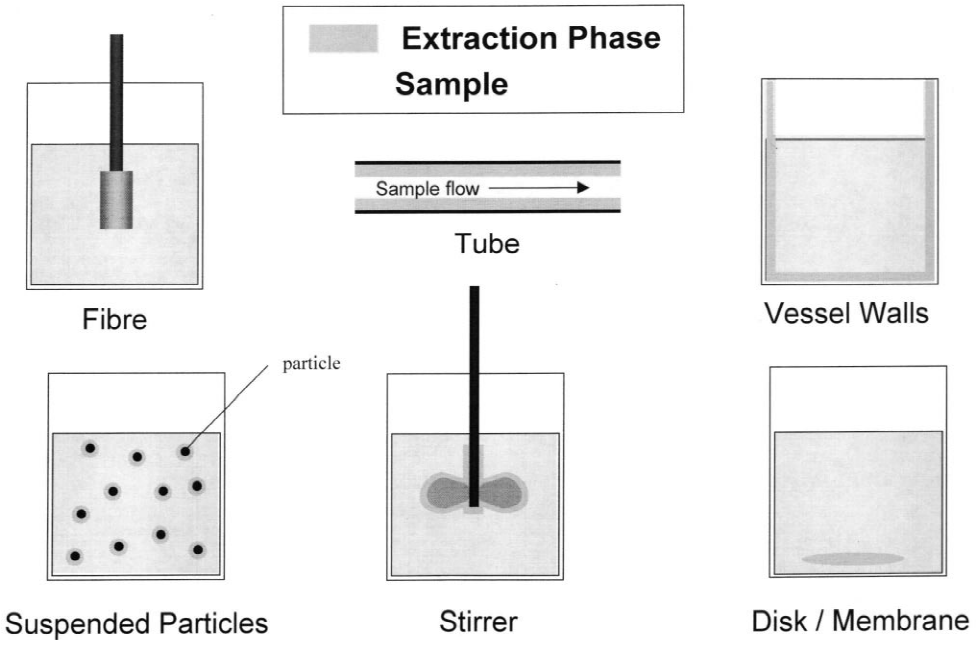

Fig. 1. Configurations of solid-phase microextraction.

as a reference to the appearance of the extracting phase, relative to a liquid or gaseous donor phase, even though it is recognized that the extraction phase is not always technically a solid.

In this review focus is placed on two primary implementations of the technique to date: Fibre and In-tube SPME. These have been explored theoretically and experimentally to a large extent. The first is based on externally coated fibers mounted in a syringe-like needle for protection, and the second on internally coated tubes or capillaries. General conclusions obtained in the studies involving these systems can be extended to other geometries.

2. Historical perspective on the evolution of SPME technology

The early work on laser desorption/gas chromatography conducted in our laboratory resulted in rapid separation times, even for very high molecular mass species [1]. However, the preparation of samples for this experiment took hours, which was over an order of magnitude longer than the separation times. In this experiment, optical fibers were used to transmit laser light energy to the GC instrument. The sample preparation process was analogous to standard solvent extraction procedures. The fiber tip was coated with the sample by dipping one end of the optical fiber in the solvent extract, coating the fiber and then removing volatile solvents through evaporation. The fiber tip, prepared in such a way, was inserted into the injector of a gas chromatograph, and analytes were volatilized onto the front of the GC column by means of a laser pulse. During that work, a need was recognized for rapid sample preparation techniques to retain the time efficiency advantages made possible by the use of the laser pulse and a high speed separation instrument. The challenge was addressed using fibers, since optical fibers could be purchased coated with several types of polymeric films. The original purpose of these coatings was simply to protect the fibers from breakage. Because of the thin films used (10–100 μm), the expected extraction times for these systems were very short. In addition, novel films could be prepared, since chromatographers have a good knowledge base on fused-silica coating methods gained from capillary columns manufacturing experience.

In the initial work on SPME, sections of fused-silica optical fibers, both uncoated and coated with liquid and solid polymeric phases, were dipped into an aqueous sample containing test analytes and then placed in a GC injector [2]. The process of introducing and removing the fibers required the opening of the injector which resulted in loss of head pressure at the column. Despite their basic nature, those early experiments provided very important preliminary data that confirmed the usefulness of this simple approach, since both polar and nonpolar chemical species were extracted rapidly and reproducibly, from aqueous samples.

The development of the technique accelerated rapidly with the implementation of coated fibers incorporated into a microsyringe, resulting in the first SPME device [3]. Fig. 2 shows an example of an SPME device based on the Hamilton® 7000 series microsyringe. The metal rod, which serves as the piston in a microsyringe, is replaced with stainless steel microtubing having an inside diameter (I.D.) slightly larger than the outside diameter (O.D.) of the fused-silica rod. Typically, the first 5 mm of the coating is removed from a 1.5 cm long fiber, which is then inserted into the microtubing. High temperature epoxy glue is used to permanently mount the fiber. Sample injection is then very much like standard syringe injection. Movement of the plunger allowed exposure of the fiber during extraction and desorption and its protection in the needle during storage and penetration of the septum. SPME devices do not need expensive syringes like the Hamilton® syringes. As Fig. 3a illustrates, a useful device can be built from a short piece of stainless steel microtubing (to hold the fiber), another piece of larger tubing (to work as a ''needle''), and a septum (to seal the connection between the microtubing and the ''needle''). The design from Fig. 3a is the basic building block of a commercial SPME device described later and illustated in Fig. 4. Another simple SPME construction is based on a piece of internally coated tubing [4]. This tubing can be mounted inside a needle or it can constitute the ''needle'' of a syringe itself [5]. Elimination of mechanical movement of a plunger of a syringe can be accomplished

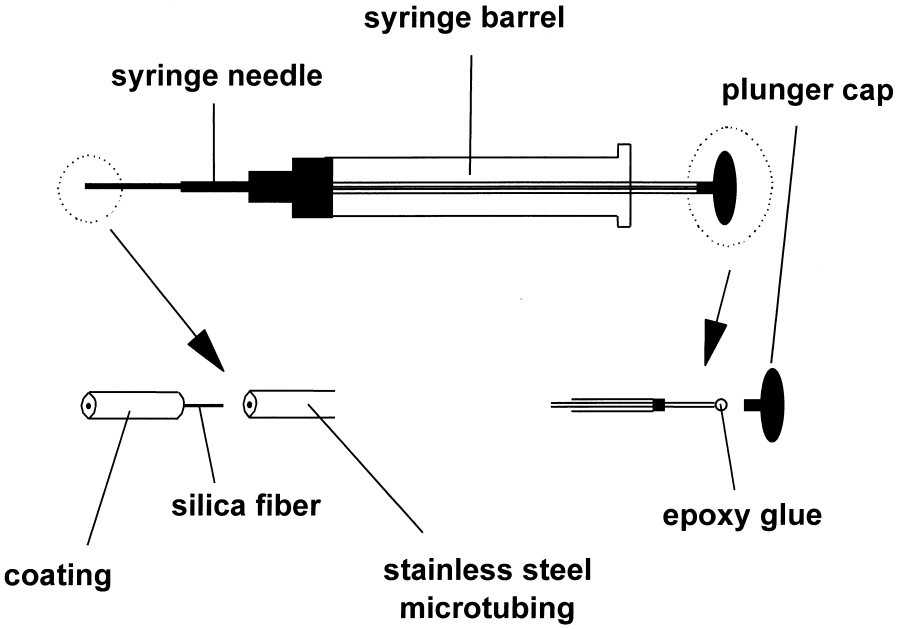

Fig. 2. The custom-made SPME device based on Hamilton 7000 series syringe.

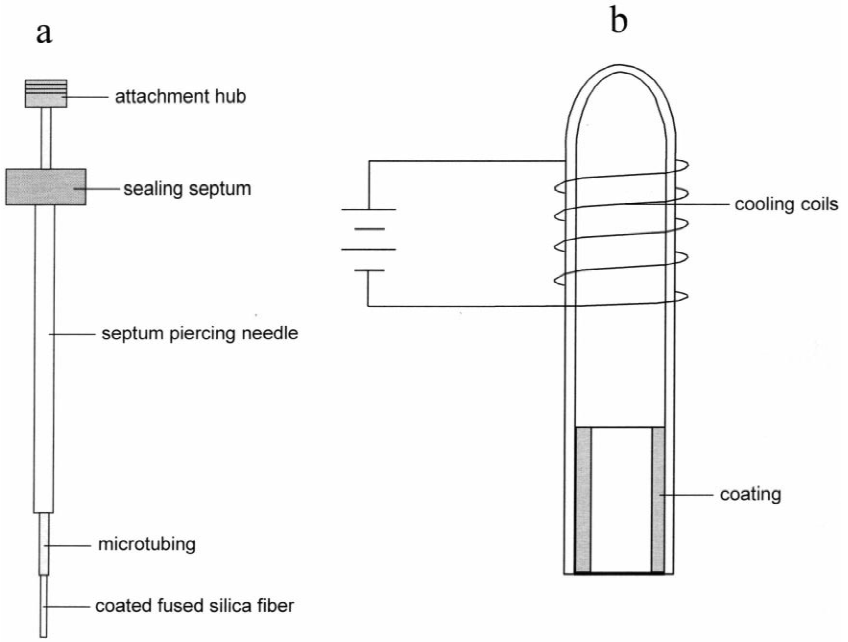

Fig. 3. Simple versions of the SPME device using coated fiber (a) and internally coated tubing (b).

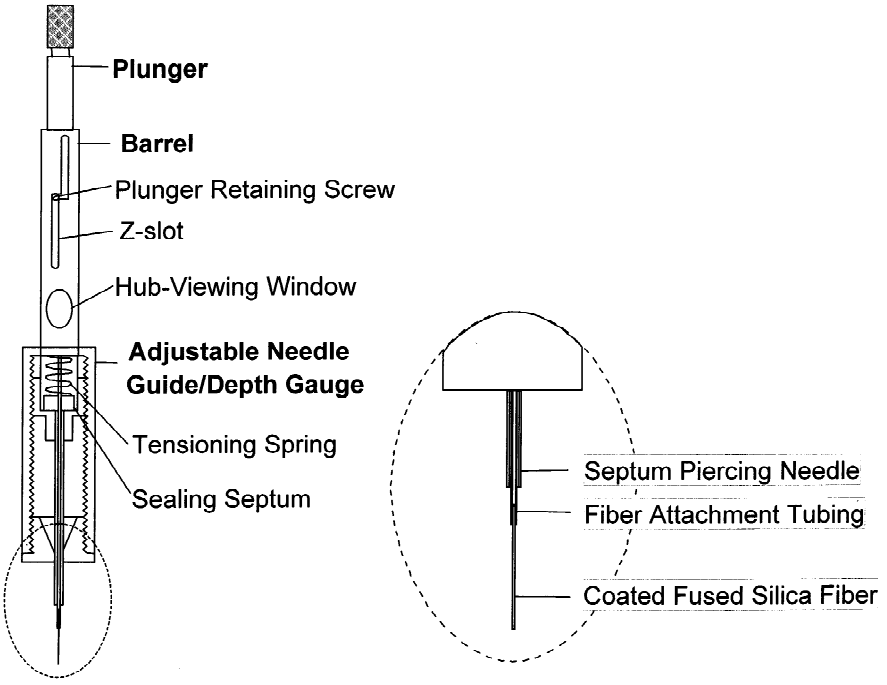

Fig. 4. Design of the first commercial SPME device made by Supelco.

by sealing the tubing at one end and installing a microheater as illustrated in Fig. 3b. Expansion of air caused by temperature increase allows removal of desorbed analytes from the extracting phase located inside the tubing. A coated tubing approach is useful in the design of passive sampling devices discussed later, since in this case, the extraction rate is limited by the diffusion of analytes into the needle [6]. In addition, active sampling is possible by heating and cooling of air contained in the upper part of the tubing, which causes movement of liquid or gaseaous samples into and out of the tubing, facilitating mass transport of analytes from the sample to the coating.

This in-tube concept has also been expanded to facilitate automation of sample preparation for HPLC. In that approach the sample componets are extracted by the coating located on the inner surface of the hollow tubing and after the extraction is completed the analytes are washed into the HPLC column using the mobile phase or solvent. Everything is easily automated using a conventinal autosampler (see Section 3.6). This concept is very similar to SPE (some researchers used packed tubes) [7], however the difference is associated with the principle of the process-total extraction vs. equilibrium-different selectivities, and taking full advantage of phase capacity.

The extraction coating has also been coated on other elements of the analytical system. Recently there have been reports of coating the interior of vessels [8], or the exterior of magnetic stirring bars [9]. Several of these implementations are shown in Fig. 1.

Although to date SPME devices have been used principally in laboratory applications, more current research has been directed toward remote monitoring, particularly for clinical, field environmental, and industrial hygiene applications. In their operating principles, such devices are analogous to the devices described above, but modifications are made for greater convenience in given applications. For example, as shown in Fig. 5a, adding a tube with a small opening to cover the needle of the SPME syringe results in a useful device for breath analysis in a non-invasive clinical application [10]. This design

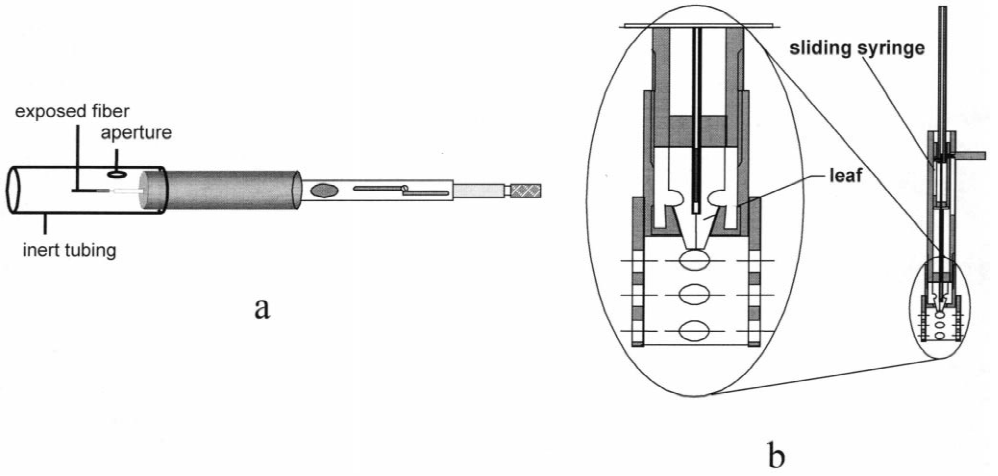

Fig. 5. SPME device modified for breath analysis (a) and for the field application (b).

can be further improved by adding a one-way valve mounted on the aperture, but the concept of operation remains the same.

An important feature of a field device is the ability to preserve extracted analytes in the coating. The simplest practical way to accomplish this goal is to seal the end of the needle with a piece of septum. Additionally, cooling extends the storage time. Polymeric septum material, however, may cause losses of analytes from the fiber. Therefore, a more appropriate approach is to use metal to metal (or solid polymer) seals. Fig. 5b illustrates an example of a device construction based on a ''leaf'' closure. It is anticipated that future devices designed for field applications will be more rugged than the current laboratory versions and will look more like ''sticks'' or ''pens'' than syringes.

Recently, different configurations of field samplers were evaluted for the analysis of volatile compounds [11]. Percentage of compound retained in the coating was evaluated for the four devices, at different storage times and temperatures, and for different fiber coatings. The PDMS fiber demonstrated the lowest ability to retain these compounds. Carboxen-PDMS had the highest and PDMS-DVB was intermediate. The devices employed various sealing methods, to preserve the samples on the fiber, and to protect from external contamination. The Supelco field sampler seals by retracting the outer needle behind a silicone septum. Alternatively, a conventional manual sampler may be sealed by pressing the end of the needle into a piece of septum. Two prototype devices constructed were sealed by either a leaf system (Fig. 5b), which opens automatically when the outer needle is exposed, or by capping the outer needle after sampling, with a teflon cap.

Another promising technique uses a valve syringe, where the fiber is withdrawn into the barrel of the syringe, along with a sample of the air being analysed, by means of retracting the syringe plunger. The valve is then sealed until desorption into analytical instrument [12]. Initial data describing the new appraoches clearly demonstrate advantages of the new designs to seal the fibre in the needle, compared the the commercial devices, by eliminating the losses and contamination to the septa material of volatile components.

3. Principles of solid-phase microextraction

In SPME a small amount of extracting phase associated with a solid support is placed in contact with the sample matrix for a predetermined amount of time. If the time is long enough, a concentration equilibrium is established between the sample matrix and the extraction phase. When equilibrium conditions are reached, then exposing the fiber for a longer time does not accumulate more analytes. There are two different implementaions of the SPME

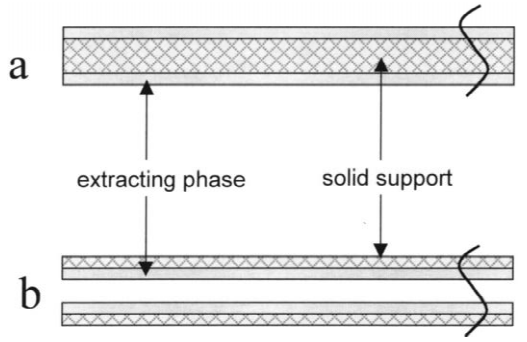

Fig. 6. Two different implementaions of the SPME technique. a, polymer coated on outer surface of fiber; b, polymer coated on internal surface of capillary tube.

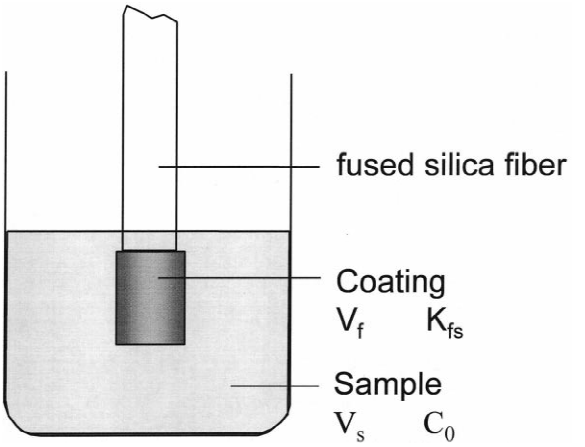

Fig. 7. Microextraction with SPME. V_f, volume of fiber coating; K_{fs}, fiber/sample partition coefficient; V_s, volume of sample; C_0, initial concentration of analyte in the sample.

technique explored extensively to date, which are shown in Fig. 6. One is associated with a tube design and the other with fiber design. The tube design can use very similar arrangements as SPE, however the primary difference, in addition to volume of the extracting phase, is that the objective of SPME is never an exhaustive extraction. This substantially simplifies the design of systems. For example, in-tube SPME for analysis of liquids uses 0.25 mm ID tubes and about 0.1 μl of extraction phase, because concern about breakthrough is not relevant since exhaustive extraction is not an objective. In fact the objective of the experiment is to produce full breakthrough as soon as possible, since this indicates equilibrium extraction has been reached.

A more traditional approach to SPME involves coated fibers. The transport of analytes from the matrix into the coating begins as soon as the coated fiber has been placed in contact with the sample (Fig. 7). Typically, SPME extraction is considered to be complete when the analyte concentraton has reached distribution equilibrium between the sample matrix and the fiber coating. In practice, this means that once equilibrium is reached, the extracted amount is constant within the limits of experimental error and it is independent of further increase of extraction time. The equilibrium conditions can be described as [13]:

$$n = \frac{K_{fs} V_f V_s C_0}{K_{fs} V_f + V_s} \quad (1)$$

where n is the number of moles extracted by the coating, K_{fs} is a fiber coating/sample matrix distribution constant, V_f is the fiber coating volume, V_s is the sample volume, and C_0 is the initial concentration of a given analyte in the sample.

Strictly speaking, this discussion is limited to partitioning equilibrium involving liquid polymeric phases such as poly(dimethylsiloxane). The method of analysis for solid sorbent coatings is analogous for low analyte concentration, since the total surface area available for adsorption is proportional to the coating volume if we assume constant porosity of the sorbent. For high analyte concentrations, saturation of the surface can occur, resulting in nonlinear isotherms as discussed later. Similarly high concentration of a competitive interference compound can displace the target analyte from the surface of the sorbent.

Eq. (1), which assumes that the sample matrix can be represented as a single homogeneous phase and that no headspace is present in the system, can be modified to account for the existence of other components in the matrix by considering the volumes of the individual phases and the appropriate distribution constants. The extraction can be interrupted and the fiber analyzed prior to equilibrium. To obtain reproducible data, however, constant convection conditions and careful timing of the extraction are necessary.

Simplicity and convenience of operation make SPME a superior alternative to more established

techniques in a number of applications. In some cases, the technique facilitates unique investigations. Eq. (1) indicates that, after equilibrium has been reached, there is a direct proportional relationship between sample concentration and the amount of analyte extracted. This is the basis for analyte quantification. The most visible advantages of SPME exist at the extremes of sample volumes. Because the setup is small and convenient, coated fibers can be used to extract analytes from very small samples. For example, SPME devices are used to probe for substances emitted by a single flower bulb during its life span; the use of sub-micrometer diameter fibers permits the investigation of single cells. Since SPME does not extract target analytes exhaustively, its presence in a living system should not result in significant disturbance. In addition, the technique facilitates speciation in natural systems, since the presence of a minute fiber, which removes small amounts of analyte, is not likely to disturb chemical equilibria in the system. It should be noted however, that the fraction of analyte extracted increases as the ratio of coating to sample volume increases. Complete extraction can be achieved for small sample volumes when distribution constants are reasonably high. This observation can be used to advantage if exhaustive extraction is required. It is very difficult to work with small sample volumes using conventional sample preparation techniques. Also, SPME allows rapid extraction and transfer to an analytical instrument. These features results in an additional adventage when investigating intermediates in the system. For example, SPME was used to study biodegradation pathways of industrial contaminants [14]. The other advantage is that this technique can be used for studies of the distribution of analytes in a complex multiphase system [15] and speciate diffferent forms of analytes in a sample [16].

In addition, when sample volume is very large, Eq. (1) can be simplified to:

$$n = K_{fs} V_f C_0 \quad (2)$$

which points to the usefulness of the technique for field applications. In this equation, the amount of extracted analyte is independent of the volume of the sample. In practice, there is no need to collect a defined sample prior to analysis as the fiber can be exposed directly to the ambient air, water, production stream, etc. The amount of extracted analyte will correspond directly to its concentration in the matrix, without being dependent on the sample volume. When the sampling step is eliminated, the whole analytical process can be accelerated, and errors associated with analyte losses through decomposition or adsorption on the sampling container walls will be prevented. This advantage of SPME could be enhanced practically, by developing portable field devices on a commercial scale.

3.1. Extraction modes with coated fiber

Three basic types of extractions can be performed using SPME: direct extraction, headspace configuration, and a membrane protection approach. Fig. 8 illustrates the differences among these modes. In the direct extraction mode (Fig. 8a), the coated fiber is inserted into the sample and the analytes are transported directly from the sample matrix to the extracting phase. To facilitate rapid extraction, some level of agitation is required to transport analytes from the bulk of the solution to the vicinity of the fiber. For gaseous samples, natural convection of air is sufficient to facilitate rapid equilibration. For aqueous matrices, more efficient agitation techniques, such as fast sample flow, rapid fiber or vial movement, stirring or sonication are required [6,17]. These conditions are necessary to reduce the effect caused by the ''depletion zone'' produced close to the fiber as a result of fluid shielding and slow diffusion coefficients of analytes in liquid matrices.

In the headspace mode, the analytes need to be transported through the barrier of air before they can reach the coating. This modification serves primarily to protect the fiber coating from damage by high molecular mass and other non-volatile interferences present in the sample matrix, such as humic materials or proteins. The headspace mode also allows modification of the matrix, such as a change of the pH, without damaging the fiber. Amounts of analyte extracted into the coating from the same vial at equilibrium using direct and headspace sampling are identical as long as sample and gaseous headspace volumes are the same. This is caused by the fact that the equilibrium concentration is independent of fiber location in the sample/headspace system. If the

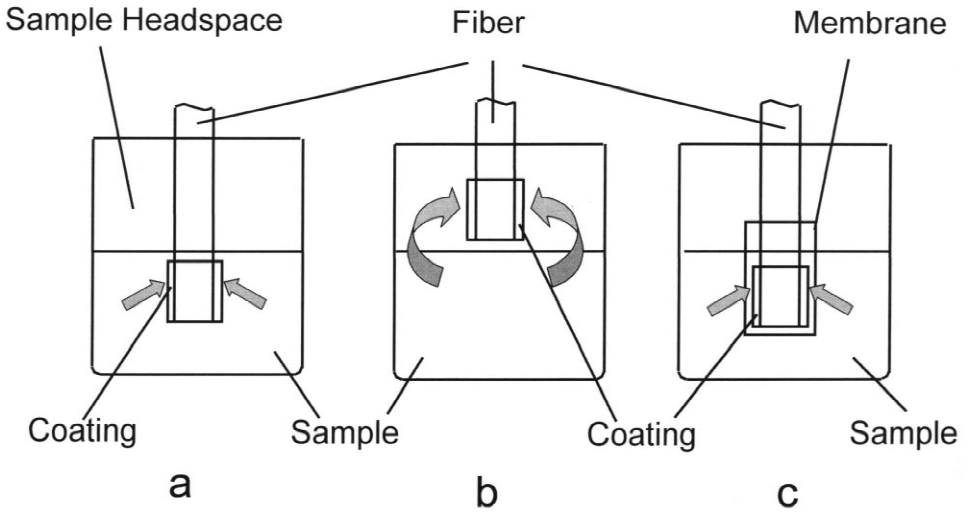

Fig. 8. Modes of SPME operation: (a) direct extraction, (b) headspace SPME, (c) membrane-protected SPME.

above condition is not satisfied, a significant sensitivity difference between the direct and headspace approaches exists only for very volatile analytes.

The choice of sampling mode has a very significant impact on extraction kinetics, however. When the fiber coating is in the headspace, the analytes are removed from the headspace first, followed by indirect extraction from the matrix as shown in Fig. 8b. Overall mass transfer to the fiber is typically limited by mass transfer rates from the sample to the headspace. Therefore, volatile analytes are extracted faster than semivolatiles since they are at a higher concentration in the headspace which contributes to faster mass transport rates through the headspace. Temperature has a significant effect on the kinetics of the process by determining the vapor pressure of analytes. In fact, the equilibration times for volatiles are shorter in the headspace SPME mode than for direct extraction under similar agitation conditions. This outcome is produced by two factors: that a substantial portion of the analyte is in the headspace prior to extraction, and that diffusion coefficients in the gaseous phase are typically four orders of magnitude larger than in liquid media. Since concentrations of semivolatiles in the gaseous phase at room temperature are typically small however, overall mass transfer rates are substantially lower and result in longer extraction times. They can be improved by using very efficient agitation or by increasing the extraction temperature [18].

Fig. 9a and b illustrate the effect of agitation on the extraction time profile obtained for polynuclear aromatic hydrocarbons (PAHs). As the rotational speed of the magnetic stirrer increases, the equilibration time of naphthalene and acenaphthene decreases from 8 min to 3 min and from 25 min to 10 min, respectively. For less volatile analytes, phenanthrene and chrysene, the equilibration is not reached during the experimental period in either case, but the amount of analyte extracted after 70 min extraction at low agitation (Fig. 9a) is about the same as after 45 min of more efficient stirring (Fig. 9b). Use of even more efficient agitation techniques, such as direct sonication, further cuts extraction time.

The effect of elevated sampling temperature is a lowering of fiber sample partition coefficients. This decreases the amount extracted at equilibrium but it may be acceptable if target limits of detection still can be reached. This effect is demonstrated dramatically with the analysis of amphetamines. As shown in Fig. 10, room temperature extraction produces a very long equilibrium extraction time, but ultimately the highest amount extracted. Conversely, the highest temperature tested (73°C) produces a very fast equilibrium time (ca. 5 min) but a significantly lower equilibrium amount extracted.

Fig. 9. Time extraction profile obtained for headspace solid-phase microextraction of several PAHs from aqueous samples at (a) 75% and (b) 100% stirring rates: A, naphthalene; B, acenaphthene; C, phenanthrene; D, chrysene. Source: Adopted with permission.

To enable the simultaneous analysis of very volatile substances (gases) and less volatile analytes, the headspace SPME technique can be combined with static headspace sampling by means of the gastight/SPME device illustrated in Fig. 11 [19]. A fused-silica fiber, coated with poly(dimethylsiloxane) (PDMS), is connected with 30 gauge stainless steel (SS) tubing. The empty end of this SS tubing/fiber assembly is then mounted to the plunger of a Hamilton 500 μl gastight syringe. When the fiber is withdrawn into the syringe needle, a certain volume of gas is also withdrawn into the gastight syringe

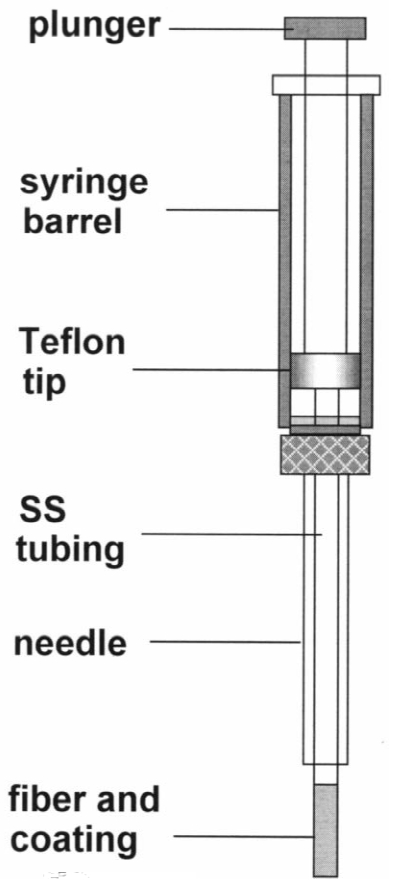

Fig. 10. Effect of extraction temperature on equilibrium time and amount extracted, for headspace methamphetamine analysis. Extraction conditions: PDMS 100 μm fiber, 0.5 *M* KOH, saturated NaCl, 2 ml sample in a 4 ml vial, extraction temperature as shown, extraction time 15 min., analysis by GC–FID, desorption time 15 min. Key: (u): 22°C; (s): 40°C; (j): 60°C; (d): 73°C.

Fig. 11. Gastight SPME device. Source: Adopted with permission.

passive or static, when the analytes are transferred into the sorbent using diffusion. In either of these approaches, the coating may be supported on a fused-silica rod, or coated on the inside of a tube or capillary. Below we briefly discuss the theoretical aspects of the extraction processes which use these geometric arrangements.

3.2.1. Dynamic in-tube SPME

In this system we assume the use of a piece of fused-silica capillary, internally coated with a thin film of extracting phase (a piece of open tubular capillary GC column), or that the capillary is packed with extracting phase dispersed on an inert supporting material (a piece of micro-LC capillary column). In these geometric arrangements, the concentration profile along the axis (x) of the tubing containing the extracting phase as a function of time (t) can be described by adopting the expression for dispersion of the concentration front [21].

The front of analyte migrates through the capillary with a speed proportional to the linear velocity of the sample, and inversely related to the partition ratio. For short capillaries with a small dispersion, the extraction time can be assumed to be similar to the time required for the centre of the band to reach the end of the capillary. The extraction time is proportional to the length of the capillary and inversely proportional to the linear flow-rate of the fluid. Extraction time also increases with an increase in the coating/sample distribution constant and with the thickness of the extracting phase but decreases with an increase in the void volume of the capillary. An increase in the coating/sample distribution constant produces an increase in absolute amount extracted. It has been observed that increases in amounts extracted can be achieved, in many cases, by preconditioning the capillary with methanol or some other appropriate solvent, prior to extraction. Enhancement has even been observed when a plug of methanol is aspirated into the capillary before the sample is drawn in, and follows the sample plug in the capillary during the extraction aspirate/dispense steps. This is analogous to the solvent pre-conditioning used in SPE to enhance extraction.

In practice, in-tube SPME is implemented by replacing a section of the tubing in a commercially available autosampler, and then programming the autosampler to pass sample in and out of the extraction capillary until equilibrium or a suitable extraction level has been reached. Several options for implementing in-tube SPME are summarized in Fig. 14.

It should be emphasized that the above discussion is valid only for direct extraction when the sample matrix passes through the capillary. This approach is limited to particulate-free gas and clean water samples. The headspace SPME approach can broaden the application of in-tube SPME. In that case, careful consideration to the mass transfer between sample and headspace should be given in order to describe the process properly. Also, if the flow-rate is very rapid producing turbulent behaviour and the coating/sample distribution constant is not very high, then perfect agitation conditions are met and Eq. (3) can be used to estimate equilibration times. In this case equilibration time, t_e, is assumed to be achieved when 95% of the equilibrium amount of analyte is extracted from the sample:

$$t_e = t_{95\%} \frac{(b-a)^2}{2D_f} \tag{3}$$

In this equation $b-a$ refers to the thickness of the sorbent material, and D_f refers to analyte diffusion in the sorbent.

Removal of analytes from a tube is an elution problem analogous to frontal chromatography and has been discussed in detail [22]. In general, if the desorption temperature of a GC is high and thin coatings are used, then all the analytes are in the gas phase as soon as the coating is placed in the injector, and the desorbtion time corresponds to the elution of two void volumes of the capillary. For liquid desorption (for example into a liquid chromatography system, Fig. 15), the desorbtion volume can be even smaller since the analytes can be focused at the front of the desorption solvent [23].

3.2.2. Static in-tube SPME time weighted average sampling

In addition to the analyte concentration measurement at a well defined place in space and time, obtained by using the approaches discussed above, an integrated sampling is possible with a simple SPME system. This is particularly important in field

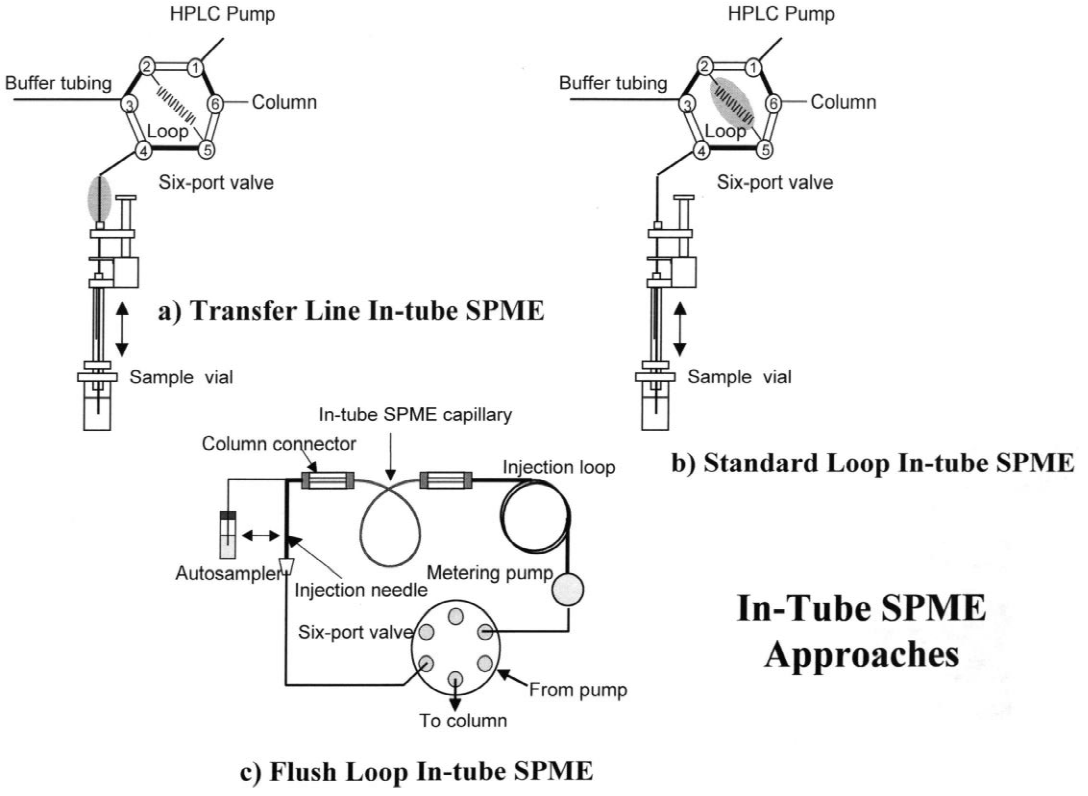

Fig. 14. Schematics of different implementations of in-tube SPME.

measurements when changes of analyte concentration over time and place variations, must often be taken into account.

When the extracting phase is not exposed directly to the sample, but is contained in a protective tubing (needle) without any flow of the sample through it (Fig. 13a), the extraction occurs through the static gas phase present in the needle. The integrated system can consist of extraction phase coating the interior of the tubing, or it can be an externally coated fiber withdrawn into the needle. These geometric arrangements represent a very powerful method able to generate a response proportional to the integral of the analyte concentration over time and space (when the needle is moved through the space) [24]. In these cases, the only mechanism of analyte transport to the extracting phase is diffusion through the gaseous phase contained in the tubing. During this process, a linear concentration profile (shown Fig. 16) is established in the tubing between the small needle opening, characterized by surface area A and the distance Z between the needle opening, and the position of the extracting phase. The amount of analyte extracted, dn, during time interval, dt, can be calculated by considering Fick's first law of diffusion [25]:

$$\mathrm{d}n = AD_{\mathrm{g}} \frac{\mathrm{d}c}{\mathrm{d}z}\,\mathrm{d}t = AD_{\mathrm{g}} \frac{\Delta C(t)}{Z}\,\mathrm{d}t \qquad (4)$$

where $\Delta C(t)/Z$ is a value of the gradient established in the needle between needle opening and the position of the extracting phase, Z; $\Delta C(t) = C(t) - C_{\mathrm{Z}}$, where $C(t)$ is a time dependent concentration of analyte in the sample in the vicinity of the needle opening, and C_{Z} is the concentration of the analyte in the gas phase in the vicinity of the coating. C_{Z} is close to zero for a high coating/gas distribution constant capacity, then: $\Delta C(t) = C(t)$. The concentration of analyte at the coating position in the needle, C_{Z}, will increase with integration time, but it

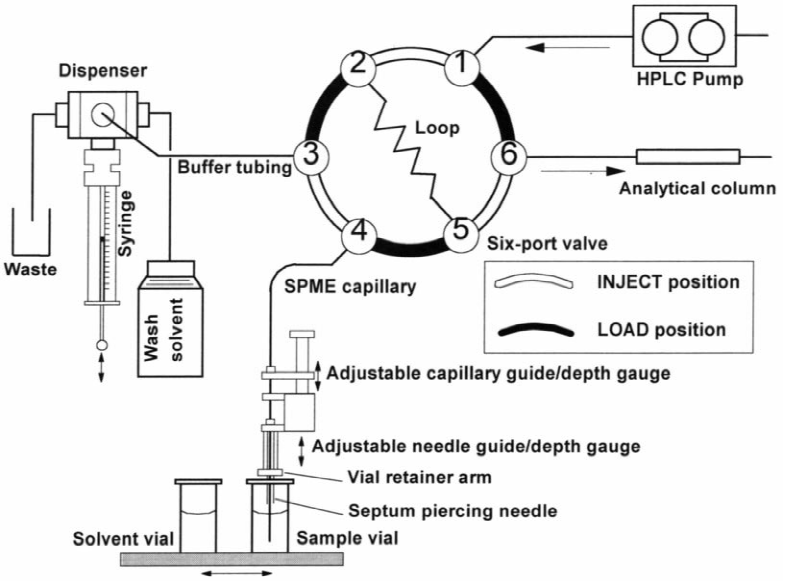

Fig. 15. SPME with modified needle to allow in-needle extraction and automated flow-through analysis of small samples (A) and automation of a coated tubing solid-phase microextractor using Spark Holland Autosampler (B).

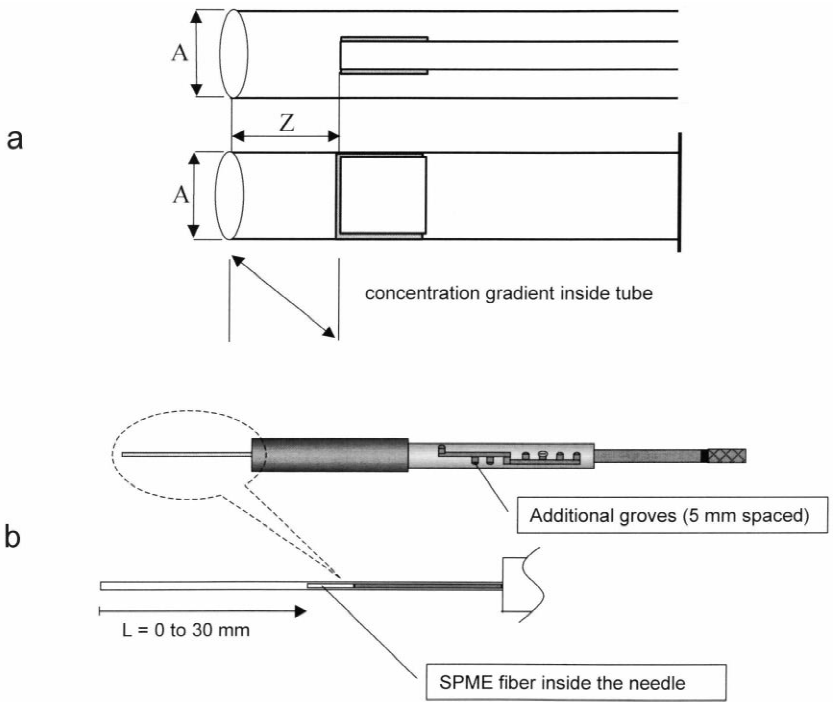

Fig. 16. Use of SPME for in-tube time weighted average sampling. (a) Schematic, (b) adaptation of commercial SPME manual extraction holder.

will be kept low compared to the sample concentration because of the presence of the sorbing coating. Therefore the accumulated amount over time can be calculated as:

$$n = D_g \frac{A}{Z} \int C(t)dt \quad (5)$$

As expected, the extracted amount of analyte is proportional to the integral of the sample concentration over time, the diffusion coefficient of analytes in gaseous phase, D_g, in the area of the needle opening, A, and inversely proportional to the distance of the coating position in respect of the needle opening, Z. It should be emphasized that Eq. (4) is valid only in a situation where the amount of analyte extracted onto the sorbent is a small fraction (below RSD of the measurement, typically 5%) of the equilibrium amount in respect to the lowest concentration in the sample. To extend integration times, the coating can be placed further into the needle (larger Z), the opening of the needle can be reduced by placing an additional orifice (smaller A), or a higher capacity sorbent can be used. The first two solutions will result in a low measurement sensitivity. An increase of sorbent capacity presents a more attractive opportunity. It can be achieved by either increasing the volume of the coating, or its affinity towards the analyte. An increase of the coating volume will require an increase of the device size. The optimum approach to increased integration time, is to use sorbents characterized by large coating/gas distribution constants.

The exploitation of restricted access to the absorbing medium allows the implementation of SPME for time-weighted average (TWA) sampling. Where diffusion to the sorbent surface is limited, the sorbent can act as a sort of ''zero sink'' such that extraction is very far from equilibrium under normal sampling conditions. In practice then, any analytes reaching the sorbent surface are absorbed, essentially exhaustively. The rate of diffusion however, is still dependent on the sample concentration, so the total amount absorbed by the coating is proportional to the average of analyte concentrations over time, hence time-weighted average sampling is achieved. This has been implemented to date with the conventional fiber assembly, by retracting the fiber a known distance inside the needle (Fig. 16b). The small size of the needle orifice limits diffusion to the sorbent surface, and the ultimate diffusion rate is also a function of the distance between the fiber tip and the end of the needle. Depending on the volatility and concentration of the analyte of interest, the fiber may be positioned either closer to or further from the end of the needle, to achieve the desired degree of non-equilibrium extraction and sensitivity. It would also be possible to implement this type of sampling with the sorbent coated on the interior wall of a capillary. To date however, the retractable needle implementation has gained the most attention, due to its ease of use and adjustability for the analyte and sample at hand.

3.2.3. Time-weighted average samplers

The theory of TWA sampling using an SPME device, was evaluated both in the laboratory using a standard gas mixture of airborne hydrocarbons, and by comparison to standard methods for field sampling [26].

The U.S. Occupational Safety and Health Administration (OSHA) has developed standards to protect employees against harmful chemicals [27]. These standards are termed permissible exposure limits (PELs). The primary mechanism for calculating exposure limits is 8-h TWA sampling. The PEL-TWAs refer to airborne concentrations to which nearly all workers may be exposed for 8 h per day, 40 h per week, for a working lifetime without adverse effect.

There are two approaches for collecting integrated or TWA samples. The first way is by taking a large number of grab samples during the time period of interest and averaging the concentrations obtained. We would need forty-eight samples to obtain the time weighted average concentration of a compound over an 8 h period if a 10 min grab sampling time were used. Sometimes 5 min sampling intervals are needed for a more accurate description of the average concentration. Therefore obtaining a TWA concentration using this approach is impractical and expensive. The second way is achieved by collecting one sample over the time period of interest using one sampler. The analytes are mass loaded in direct proportion to their concentration in air. This approach is highly recommended due to its simplicity

and cost effectiveness because a lower number of samples is acquired [28].

Loading of an air sample can be carried out with either active sampling or diffusive (passive) sampling. The first approach utilizes pumps to draw air at a constant flow-rate through a bed of solid sorbent, liquid absorbent, or into other appropriate collection devices. The second approach relies on diffusion to move the analytes of interest to the sampling media. Diffusive sampling has been used since the 1950s for monitoring air pollutants, and is becoming increasingly popular due to the fact that air sampling pumps are usually expensive, noisy, and their potentially faulty batteries make them unreliable. Solid phase microextraction devices have been successfully used for diffusive TWA sampling of hydrocarbons with low to high vapor pressure. Air sampling with SPME provides significant advantages over traditional methods. It offers accuracy, precision, cost effectiveness, simplicity and the portability of its device makes SPME an ideal sample preparation technique for field analysis.

A 100 μm PDMS fiber was used in the device shown in Fig. 16b to determine mass uptake rates or sampling rates (SR). These values were determined for *Z* values of 0.3 cm, 1 cm, and 3 cm. The intercept value for the linear uptake rate equation represents the amount adsorbed on the stainless steel tubing. The higher the molecular mass of the compound, the higher is the intercept value. However, for a specific analyte, the SR value is proportional to the concentration of the gas analyte and the path-length *Z*. Therefore if these SR values are used to determine an unknown concentration without accounting for analyte adsorbed to the needle, a positive error will be introduced, which is the intercept value. This error becomes more significant as the volatility of the compound decreases [29].

Experimental values of uptake rates for the most volatile compounds like pentane and hexane were less than expected from the theory. These compounds have high vapor pressure and diffusion coefficients, which allows a fraction of them to leave the fiber coating before desorption in the GC. In addition, due to their low partition coefficients, these compounds reach equilibrium in a short time which makes it difficult to load less than 5% of the eqilibrium amount. These problems were solved by using an adsorptive coating like PDMS–DVB.

The problem of adsorption of the least volatile compounds on the stainless steel tubing is aggravated by retracting the fiber further into its housing needle (3 cm). The area of the adsorptive surface increases as we retract the fiber further into the needle. However, retracting the fiber further slows the equilibrium process and minimizes the loss of the most volatile compounds. It may be possible to use the PDMS–DVB fiber to minimize the loss of volatile compounds from the fiber coating.

3.2.4. Field TWA sampling using the modified SPME device

Indoor air samples were collected. Active TWA sampling through charcoal tubes was carried out following National Institute for Occupational Safety and Health (NIOSH) method 1550 for determination of hydrocarbons in air. A mass flow controlled air sampling pump was used to draw air through small charcoal tubes at a certain flow-rate, which was calibrated with a bubble flow meter.

The results obtained from the field study for the determination of TWA concentration of airborne styrene using the SPME device with PDMS coating, and charcoal tubes are summarized in Table 1.

In summary, the commercially available SPME fiber can be successfully used as a diffusive TWA sampler for volatile and semi-volatile compounds. The commercial SPME fiber should be modified for TWA sampling according to Fig. 16b. Deactivated stainless steel needles should be used when sampling compounds with very low vapor pressure such as pentadecane. There is a need for a new coating which has high capacity for volatile compounds. This coating should have a strong binding phase that can resist high temperatures. The main advantage of using an SPME device as a TWA sampler over other available techniques is the ability to change the

Table 1
Summary of data for analysis of styrene, obtained from field study using (A) TWA charcoal tubes, (B) TWA by SPME with 100 μm PDMS fiber (reacted 0.3 cm)

Sample type	SPME 100 μm PDMS	Charcoal tubes	Passive badge	PID
5 min sample ($\mu g\,l^{-1}$)	130	97	90	50–250
30 min TWA ($\mu g\,l^{-1}$)	56	54	72	N/A

distance between the coating and needle opening. This makes the technique very flexible for lower and higher concentrations and for different sampling times. TWA sampling by SPME requires no pumps and no polluting organic solvents, which significantly reduces sampling costs.

3.3. Fiber coatings

Eqs. (1) and (2) indicate that the efficiency of the extraction process is dependent on the distribution constant K_{fs}. This is a characteristic parameter that describes properties of a coating and its selectivity toward the analyte versus other matrix components. Specific coatings can be developed for a range of applications. Coating volume determines method sensitivity as well (see Eq. (1)), but thicker coatings result in longer extraction times (Eq. (3)). Therefore, it is important to use the appropriate coating for a given application. This is clearly demonstrated in Fig. 17, which compares the performance of two different coatings for analysis of polar and nonpolar compounds from an aqueous matrix. The distribution constant and the sensitivity of the method drop over two orders of magnitude for *o*-xylene, and increase by an order of magnitude for 2,4-dichlorophenol when the film is changed from nonpolar PDMS (Fig. 17a) to polar poly(acrylate) polymer (PA) (Fig. 17b) [30]. Coating selection and design can be based on chromatographic experience.

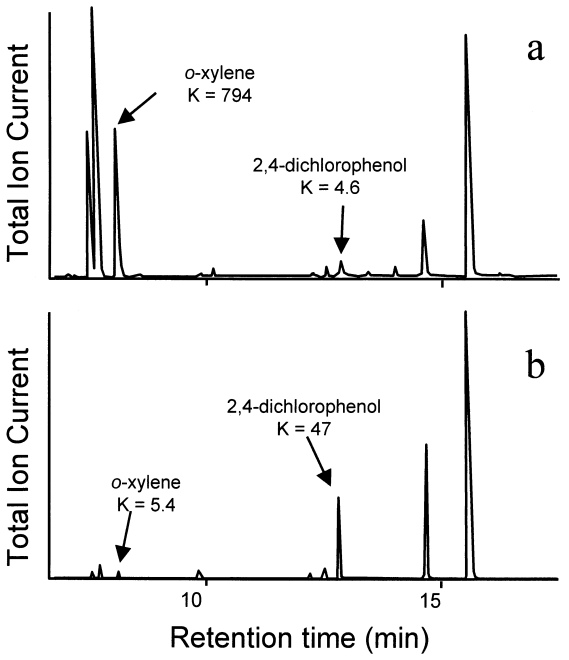

Fig. 17. Total ion current GC–MS chromatogram of benzene, toluene, ethylbenzene, and *o*, *m*, *p*-xylenes (BTEX) and phenol in water extracted with (a) a poly(dimethylsiloxane) coating and (b) a poly(acrylate) coating.

To date, several experimental coatings have been prepared and investigated for a range of applications. In addition to liquid polymeric coatings such as PDMS for general applications, other more specialized materials have been developed. For example, ion-exchange coatings were used to remove metal ions and proteins from aqueous solutions [31,32], liquid crystalline films to extract planar molecules and carbowax for polar analytes [2], metal rods to electorodeposit analytes [18,33] pencil ''leads'' to extract pesticides [34], and Nafion coatings to extract polar compounds from nonpolar matrices [35].

Polypyrole coatings have been recently developed to extract polar or even ionic analytes and possibly to explore the conductive polymer properties of the polymer [36]. This could involve applying a charge to the polymer during extraction in order to selectively extract analytes of interest, and then reversing the charge to facilitate desorption.

One of the main difficulties limiting the wide application of SPME/LC is the absence of a suitable stationary phase that not only has high extraction ability for the polar analytes but is also stable in solutions of various matrices. Polypyrole coatings have been investigated to fill this gap.

Conducting polymers are versatile materials in which molecular/analyte recognition can be achieved in different ways, including: (1) the incorporation of counter ions that introduce selective interactions, (2) utilizing the inherent and unusual multifunctionality (hydrophobic, base–acid and $\pi-\pi$ interactions, polar functional groups, ion-exchange, hydrogen bonding, electroactivity, and etc.) of the polymers, (3) the introduction of functional groups to the monomers, (4) the co-deposition of metals or other monomers within the polymer, and (5) the application of appropriate electrochemical potentials. Based on these properties, conducting polymers have found wide application in many fields including separation science [37], chemical sensors [38] and

electrochemical analysis [39]. So far, the widely used conducting polymers are based on polypyrrole, polythiophene and polyaniline. Of these three classes of materials, polypyrrole (PPY) and its derivatives have seen the most use and have been intensively studied in recent years, due to additional advantages: (1) they can be easily polymerized from organic or aqueous media at neutral pH by electrochemical or chemical methods, (2) they are relatively stable in air and solution, and (3) pyrrole monomer and some of its derivatives are available commercially.

Polypyrrole has been coated on the inner surface of a fused-silica GC capillary by the chemical polymerization method. This PPY coated capillary has been used successfully for automated in-tube SPME and determination of β-blockers in urine and serum samples when coupled with liquid chromatography/electrospray ionization mass spectrometry (LC/ESI–MS) [40]. Compared with the previous study using Omegawax 250 capillary for extraction of β-blockers [41], PPY coated capillary has shown better extraction ability for most of the compounds studied and therefore lower detection limits have been achieved. This method can be extended to other compounds such as amine containing drugs and anionic species due to the acid–base interaction and ion-exchange properties of polypyrrole coating.

A very pronounced difference in selectivity toward target analytes and interferences can be achieved by using surfaces common to affinity chromatography. Using the method of polymer imprinting [42], antibody mimics can be generated with specifities to an analyte of choice. Briefly, the desired affinity can be introduced by adding an amount of the compound of interest to the polymerization reaction. This ''pattern'' chemical may be removed after polymerization, leaving vacant sites of a specific size and shape, suitable for binding the same chemical again from an unknown sample. In this technique, we have observed that non-specific binding should be controlled for, but that enhancements in sensitivity are seen, particularly at low analyte concentrations.

There is a substantial difference in performance between the liquid and solid coatings (Fig. 18). In

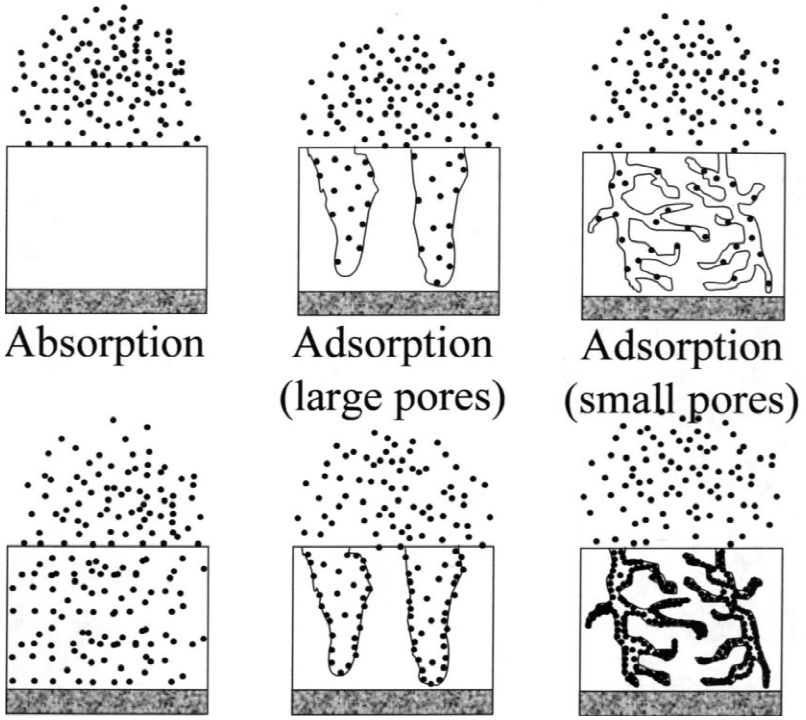

Fig. 18. Schematic representation of absorptive vs. adsorptive extraction, and adsorption in small vs. large pores.

the case of liquid coatings the analytes partition onto the extraction phase, where the molecules are solvated by the coating molecules. The diffusion coefficient in the liquid coating allows the molecules to penetrate the whole volume of the coating within a reasonable extraction time, if the coating is thin. In the case of solid sorbents the coating has a well defined crystaline structure, which if dense, substantially reduces the diffusion coefficients within the structure. Therefore within the experimental time the extraction occurs only on the surface of the coating. This can be demonstrated by considering extraction of proteins illustrated in Fig. 19. The original mixture contains three compounds: myoglobin, cytochrome and lysozyme. During fiber extraction with polyacrylic acid, compounds with weaker affinity are only observed at short extraction times. When extraction time is longer the displacement of analytes with lower affinities occurs. In this case, lysozyme with a stronger affinity for the coating, replaces the other two compounds during extraction. This effect is associated with the fact that there is only limited surface area available for adsorption. If this area is substentially occupied then the displacement effects occur [43,44] and the equilibrium amount extracted can vary with concentrations of both the target and other analytes. In extraction of analytes with liquid coatings on the other hand, partitioning between the sample matrix and extraction phase occurs. In this case, equilibrium extraction amounts vary only if the coating property is modified by the extracted components, which only occurs when the amount extracted is a substantial portion (a few percent) of the extraction phase. This is very rarely observed since SPME is typically used to determine trace contamination samples.

The only way to overcome this fundamental limitation of the porous coatings for high analyte concentration is, as the above figure suggests, to use an extraction time much less than the equilibrium time, so that the total amount of analytes accumulated onto the fiber is substantially below the saturation value. When performing such experiments, not only is it critical to precisely control extraction times, but also convection conditions must be monitored to ensure that they are constant or can be compensated for. One way of eliminating the need for compensation of convection is to normalize (use the same) aggitiation conditions. For example, the use of stirring means at well defined rotation rates in

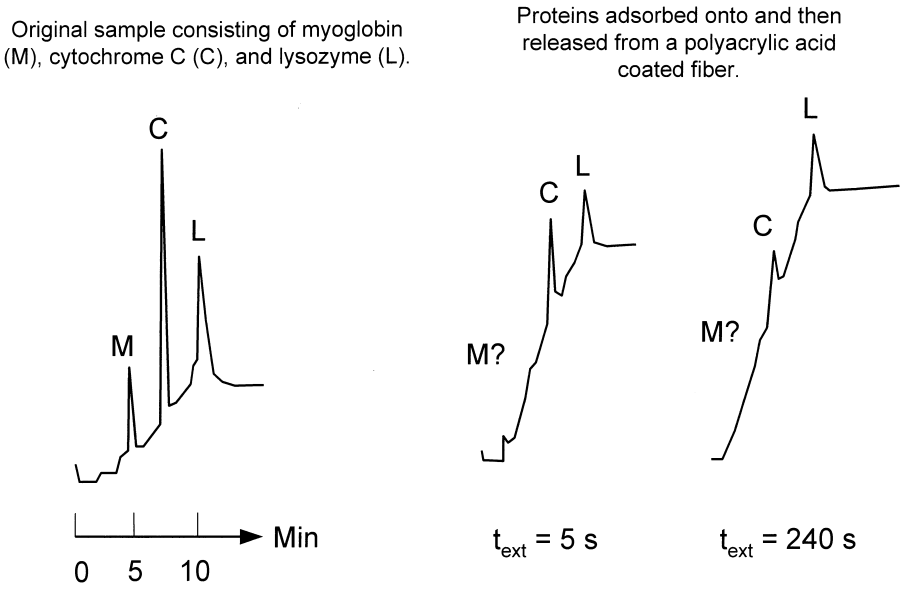

Fig. 19. Protein extraction using poly(acrylic) acid coated fiber. Demonstration of myoglobin and cytochrome C displacement by lysozyme with time.

the laboratory or fans for field air monitoring will ensure consistent convection.

The short time exposure SPME measurement described has an advantage associated with the fact that the rate of extraction is defined by diffusivity of analytes through the boundary layer of the sample matrix, and their corresponding diffusion coefficients, rather than distribution constants. This is demonstrated in Fig. 20.

A precise understanding of the definition and thickness of the boundary layer in this sense, is useful. The thickness of the boundary layer (δ) is determined by both rate of convection (agitation) in the sample and analyte diffusion. Thus in a single sample, the boundary layer thickness will be different for different analytes. Strictly speaking, the boundary layer is a region where analyte flux is progressively more dependent on analyte diffusion and less on convection, as the extraction phase is approached. For convenience however, analyte flux in the bulk of the sample (outside of the boundary layer) is assumed to be controlled by convection, whereas analyte flux within the boundary layer is assumed to be controlled by diffusion. δ is defined as the position where this transition occurs, or the point at which convection in is equal to diffusion away. At this point, analyte flux from δ towards the extraction phase (diffusion controlled) is equal to the analyte flux from the bulk of the sample towards δ, controlled by convection.

The differences in diffusion coefficients between compounds are small compared to the differences in distribution constants. This makes it easier to calibrate the system. Because of the large differences in distribution constants between analytes, the resulting chromatograms are characterized by small peak areas for compounds with small distribution constants, and large areas for those with large constants. With uptake dependent on diffusion coefficients, all compounds in a chromatogram with similar molecular masses will have similar peak areas, given similar detector responses. Also, it is relatively simple to calculate the diffusion coefficients for given analyte and therefore correct for the small differences in it. It must be understood that this system is only suitable for trace analysis. When sample concentrations become too high, saturation occurs, and uptake rates are no longer linear. Shorter exposure times, where smaller amounts are extracted, can solve this problem. Also, at these higher concentrations, samples are easily extracted and analyzed with PDMS fiber, using conventional SPME extraction methods. Results of extraction by the diffusion type of approach are shown in Fig. 21. Accumulation of volatile components on the solid coating in 10 s is much larger compared to the 10 min equilibrium extraction

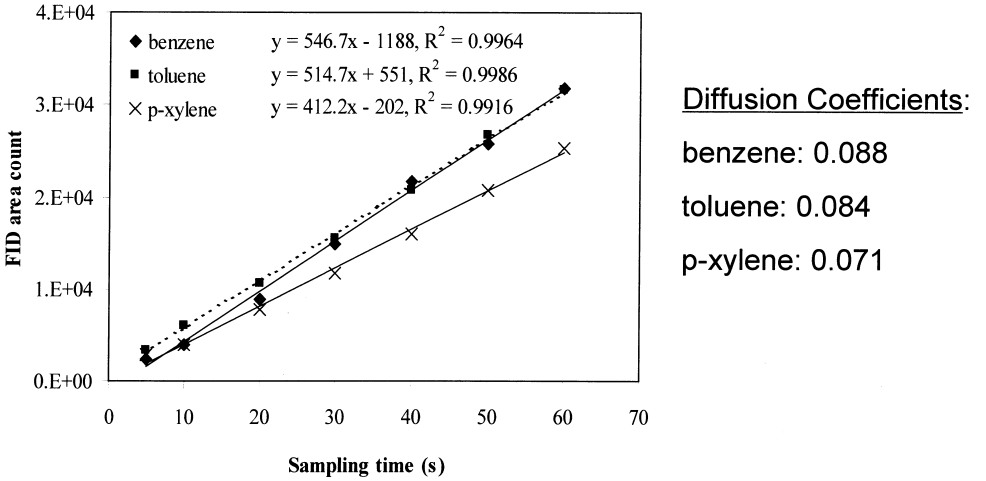

Fig. 20. Correlation of uptake rate with diffusion coefficient, for short sampling time (non-equilibrium) extraction of VOCs by PDMS–DVB fiber.

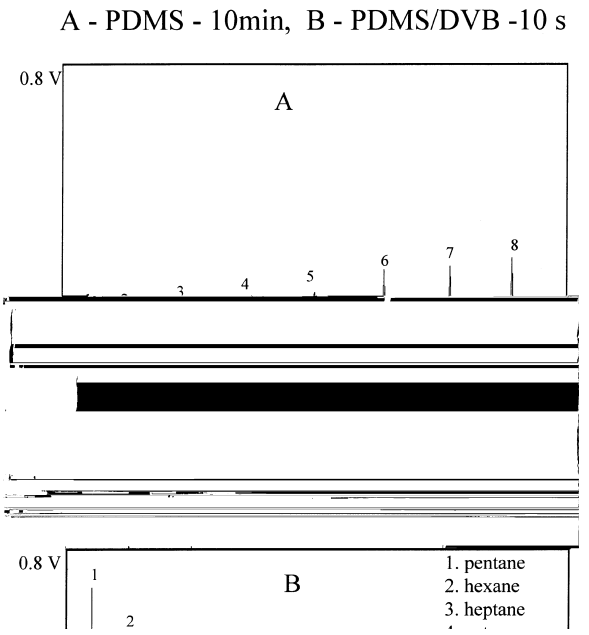

Fig. 21. Comparison of VOC mass loading between PDMS and PDMS/DVB.

on PDMS. This approach to extraction is not limited to devices using the fibre geometry, but is generally applicable.

3.3.1. Fiber preparation

There are several different methods of depositing coatings onto fibers. The dipping technique typically consists of placing a fiber in a concentrated organic solvent solution of the material to be deposited for a short time. After removal of the fiber from the solution, the solvent is evaporated by drying and the deposited material can be crosslinked [2]. An extension of this method is electrodeposition, which can be used to deposit selective coatings on the surface of metallic rods [30]. The limitation of this approach is coating thickness variance from fiber to fiber. Therefore, the preparation of films for commercial devices is carried out simultaneously during the drawing of the fused-silica rod. While this process requires dedicated and very expensive equipment, reproducibility of the coating thickness is excellent. This process is identical to the preparation of optical fibers [45], and so the required equipment is commercially available. Similar results can be obtained using a piece of hollow fiber membrane (small I.D. tubing), made from the desired extraction material. Preparation consists of swelling the membrane by means of an appropriate volatile solvent, placing the enlarged membrane onto the tip of the fiber, and evaporating the solvent. The thickness of the coating is determined by the membrane thickness. Therefore the volume of the coating can be large, reaching up to 3 μl for a 300 μm thick PDMS hollow fibre membrane. A porous hollow fiber membrane can also be used for adsorption of target analytes, or its pores can be filled with organic solvent to allow for solvent microextraction [46].

3.4. Experimental parameters affecting extraction efficiency

A better understanding of SPME theory has allowed us to more rationally optimize extraction conditions [47]. This is particularly important for equilibrium dynamic method.

When performing extraction from gaseous samples at short sampling times (pre-equilibrium) it has been observed that increasing windspeed, up to about 5 cm s^{-1} (10 ft min^{-1}), enhances extraction. Fig. 22 shows the effect of wind speed on the adsorption of benzene, *p*-xylene ethylbenzene and toluene from air samples on a carboxen/PDMS fiber. The curves indicate that the wind speed or air bulk movement

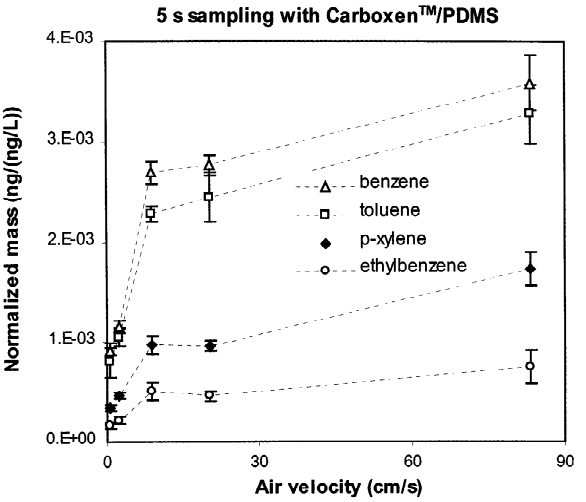

Fig. 22. Effect of wind speed on non-equilibrium extraction of VOCs (exposed fiber).

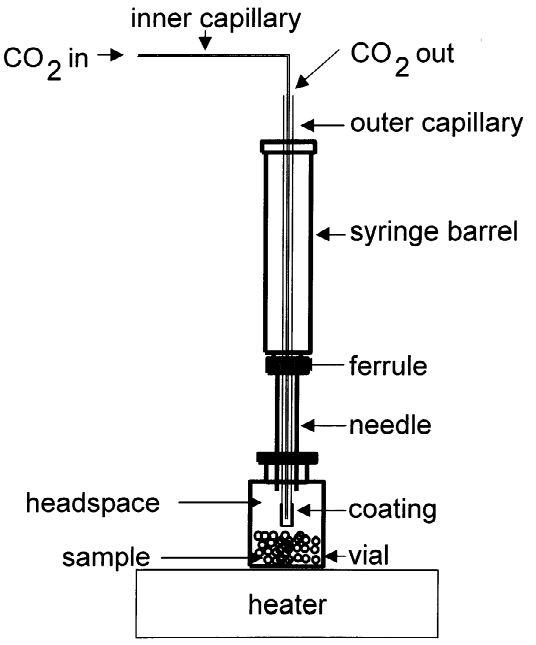

Fig. 24. Design of internally cooled SPME device.

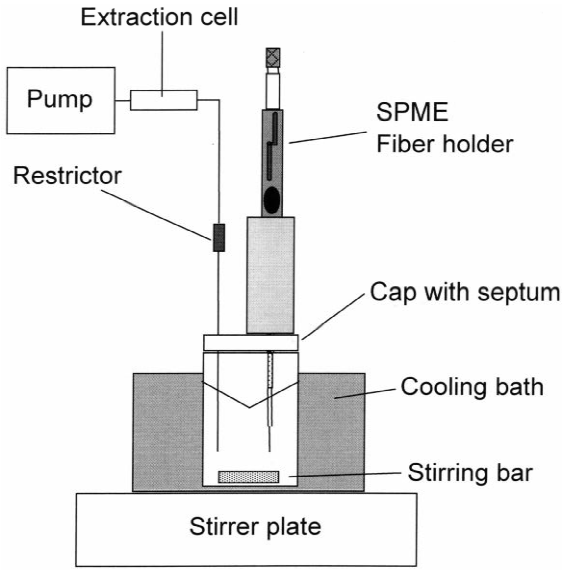

Fig. 25. Hot water dynamic extraction system combined with SPME for analysis of solid samples.

possible with the internal cooling approach, even for volatile organic compounds such as substituted benzene, in a range of matrices. This approach can be used effectively to increase the sensitivity of the SPME methods without changing the chemical nature of the fiber. One significant drawback of increased fiber capacity is loss of selectivity, since in this case not only the analytes but also most of the interferences are extracted exhaustively into the coating.

Water has proven to be a very effective additive to facilitate the release of analytes from the matrix and it is often used to accelerate extraction [48]. It can also be used in combination with high temperature extractions to remove and dissolve even very nonpolar analytes such as PAHs. This is possible because the dielectric constant of water decreases rapidly with temperature increase [49]. This property can also be used in the solid-phase microextraction of solids. Fig. 25 shows the dynamic hot water extraction system. The solid sample is placed into the extraction vessel which is in the form of a piece of thick-walled tubing. This is important to facilitate efficient removal of the extracted components from the extraction cell [22]. The vessel is then fitted into a high pressure system consisting of a pump delivering water, a heater to control extraction temperature, and a restrictor to maintain the extraction pressure. Water with extracted analytes is collected in a cooled vial supplied with agitation and an SPME device (see Fig. 25). The analytes are extracted into the fiber

Table 2
Quantitative extraction of BTEX from different matrices

Analytes	% Extracted			
	Water (80°C)	Soil, 15% water (120°C)	Sand (110°C)	Clay, 5% water (170°C)
Benzene	50	48	84	64
Xoluene	65	101	105	84
Ethylbenzene	85	96	106	91
m,p-Xylene	90	99	102	95
o-Xylene	100	104	100	100

coating from the water immediately upon delivery to the vial. Good quantitation has been obtained for extraction of PAHs from contaminated soil when the collection vial is cooled and the SPME fiber is immersed in water continuously during the extraction [50].

Fig. 26 shows how the extraction system can be made simpler and less expensive: when a static extraction technique is performed in a high pressure vessel, the need for a high pressure pump is eliminated. The procedure consists of adding the sample and water to the vial, inserting the fiber, and sealing it. The extraction can be performed in either direct, headspace, or membrane protection mode (see Fig. 8). The vial is heated to facilitate the release of analytes to water. After a cooling period to ensure good partitioning onto the fiber, the extracted analytes are desorbed into the analytical instrument and typically quantified, based on an isotopically labeled standard spike (introduced to the sample prior to extraction).

3.5. Derivatization

The main challenge in organic analysis is polar compounds. These are difficult to extract from environmental and biological matrices and difficult to separate on the chromatographic column. Derivatization approaches are frequently used to address this challenge. Fig. 27 summarizes various derivatization techniques that can be implemented in combination with SPME [51]. Some of the techniques, such as direct derivatization in the sample matrix, are analogous to well-established approaches used in solvent extraction. In the direct technique, the derivatizing agent is first added to the vial containing the sample. The derivatives are then extracted by SPME and introduced into the analytical instrument (Fig. 28). For example, this approach has been applied to extract and separate phenols from aqueous samples by first converting the target analytes to their acetate derivatives [52].

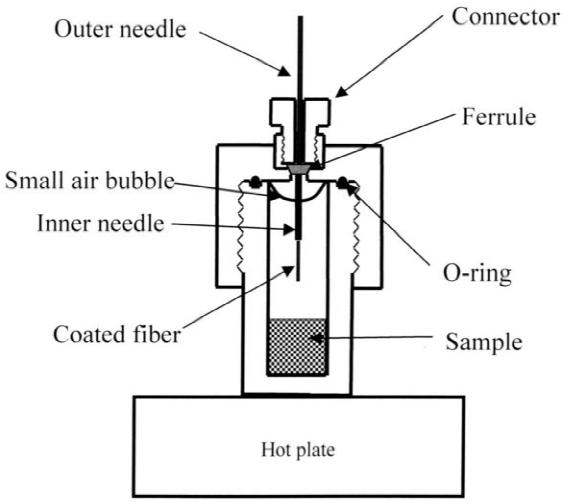

Fig. 26. Static hot water-SPME system.

Because of the availability of polar coatings, extraction efficiency for polar underivatized compounds is frequently sufficient to reach the sensitivity required. Occasionally, however, there are problems associated with the separation of these analytes. Good chromatographic performance and detection can be facilitated by in-coating derivatization following extraction. This has been shown with high molecular mass carboxylic acids. After exposing an SPME coating containing extracted analytes to diazomethane, the resulting ester derivatives can be separated as narrow bands on a GC column (see Fig. 29). In addition, selective derivatization to analogues containing high detector response groups will result in enhancement in sensitivity and selectivity of detection. Derivatization in the GC injector is an analogous approach, but it is performed at high injection port temperatures. For example, long chain carboxylic acids can be extracted onto the coating as ion pairs when tetramethylammonium hydrogen sulfite is added to the sample. During volatilization, analytes are converted to methyl esters [53].

The most interesting and potentially very useful technique is simultaneous derivatization and extraction, performed directly in the coating. This approach allows high efficiencies and can be used in remote field applications. The simplest way to execute the process is to dope the fiber with a derivatization reagent and subsequently expose it to the sample. Then the analytes are extracted and simultaneously converted to analogues having high affinity for the coating. This is no longer an equilibrium process as derivatized analytes are collected in the coating as long as extraction continues (see Fig. 30). This approach, which is used for low molecular mass

Fig. 27. SPME derivatization techniques.

carboxylic acids, results in exhaustive extraction of gaseous samples [54]. When 1-pyrenyldiazomethane is used as the derivatization reagent, it is introduced into the coating by first dissolving the reagent in a volatile solvent. The fiber is then immersed in the solution. The fiber coating swells and is doped with the reagent. After evaporation of the solvent, the fiber is ready to perform extraction. The reagent, having low vapor pressure and high affinity toward the coating, remains on the fiber during its exposure to the sample. Volatilities of the pyrenylmethyl esters formed during the reaction also are low, resulting in the accumulation of the product onto the fiber until analyte or reagent is exhausted or decomposed. At a

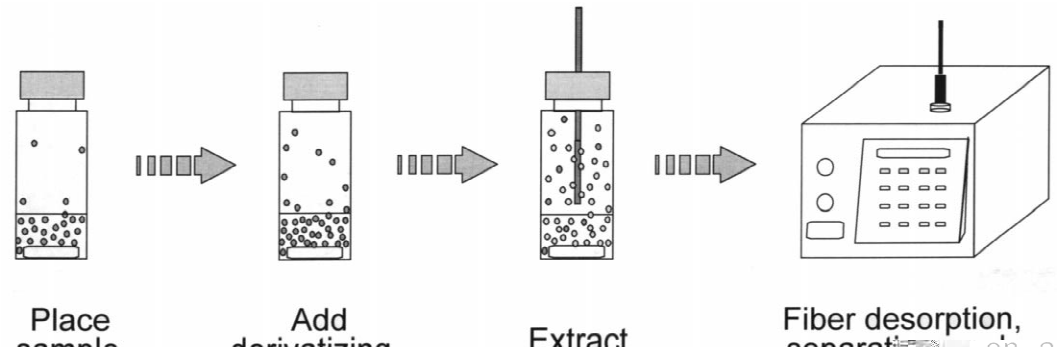

Fig. 28. In-sample matrix direct derivatization SPME technique.

xylene using porous coatings, described earlier (Fig. 20). The derivatizing agent, *o*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine is first doped onto the fiber by room temperature headspace extraction from an aqeuous solution. Formaldehyde is subsequently extracted from an unknown sample, and converted to the oxime derivative in the fiber. In this case the kinetics of the derivatizing reaction are fast, and uptake is controlled by mass transport. If reaction kinetics were slow, uptake may be controlled by both the distribution constant and the reaction kinetics [47]. With fast derivatization reaction kinetics, the process is similar to the mass transport controlled extraction described above for VOCs analysis from air, where uptake rates for short sampling times are proportional to diffusion coefficients. The significant difference between the two approaches is that the formaldehyde analysis approach has a much higher capacity.

This simple, but powerful procedure as described above for this analysis, is limited to low volatility reagents. The approach can be made more general by chemically attaching the reagent directly to the coating. The chemically bound product can than be released from the coating either by high temperature in the injector, light illumination or change of an applied potential etc. The feasibilty of this approach was recently demonstrated by synthetizing standards bonded to silica gel, which were released during heating. This approach allowed solvent-free calibration of the instrument [56]. The other interesting option is to use an SPME device similar to the one shown in Fig. 24, but with the derivatization reagent, instead of carbon dioxide, delivered to the coating.

In addition to using a chemical reagent, electrons can be supplied to produce redox processes in the coating and convert analytes to more favorable derivatives. In this application, the rod as well as the polymeric film must have good electrical conductivity. Fig. 31 shows the schematic of the three-electrode cell used to deposit mercury species onto a gold-coated metallic fiber [30,33]. A similar principle has been used to extract amines onto a pencil ''lead'' electrode [57]. In addition the SPME approach can be used to study the properties of electrochemical processes occuring on the electrode surface. The use of conductive polymers, such as polypyrole will introduce additional selectivity of the electrochemical processes assiociated with coating properties.

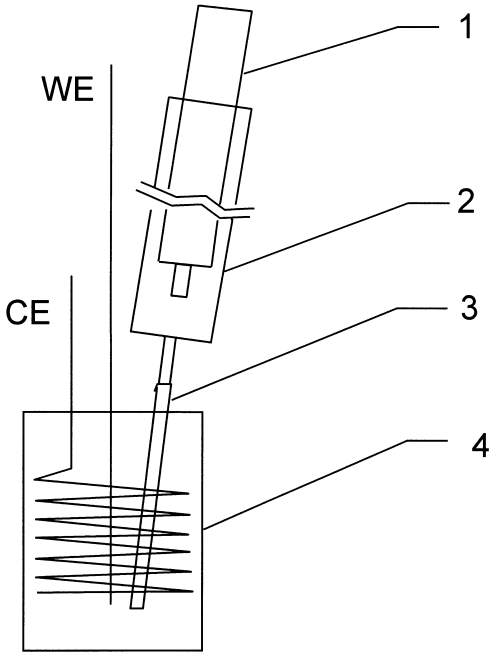

Fig. 31. SPME-electrochemistry minicell: 1, reference electrode; 2, 100 ml plastic syringe; 3, Teflon capillary; 4, 8 ml Teflon vial; 5, SPME fiber working electrode (WE); 6, platinum wire counter electrode (CE).

3.6. Interfaces to analytical instrumentation

Because of its solvent-free nature, SPME can be interfaced conveniently to analytical instruments of various types. Only extracted analytes are introduced into the instrument, since the extracting phase is non-volatile. Thus there is no need for complex injectors designed to deal with large amounts of solvent vapor, and these components can be simplified for use with SPME. The sensitivity of determinations using the SPME technique is very high, facilitating trace analysis. Although in most cases the entire complement of analytes is not extracted from the sample, all material that is extracted is transferred to the analytical instrument, resulting in good performance. Also, the solvent-free process results in narrow bands reaching the instrument, giving taller, narrower peaks and better quantification.

3.6.1. SPME–GC Interface

The analytical instrument used most frequently with SPME has been the gas chromatograph. Standard GC injectors, such as split/splitless can be applied to SPME as long as a narrow insert with an inside diameter close to the outside diameter of the needle is used. The narrow inserts are required to increase the linear flow around the fiber, resulting in efficient removal of desorbed analytes. The split should be turned off during SPME injection. Under these conditions, the desorption of analytes from the fiber is very rapid, not only because the coatings are thin but because the high injector temperatures produce a dramatic decrease in the coating/gas distribution constant and an increase in the diffusion coefficients. The speed of desorption in many cases is limited by the time required to introduce the fiber into the heated zone.

One way to facilitate sharper injection zones and faster separation times is to use rapid injection autosampling devices. An alternative solution is to use a dedicated injector, which should be cold during needle introduction, but which heats up very rapidly after exposure of the fiber to the carrier gas stream. A schematic diagram of such an injector is presented in Fig. 32. During desorption, the fiber is located inside the heated part of the fused-silica capillary, its end being close to the bottom of the heated zone. The distance between the fiber and the capillary wall is approximately 0.15 mm. A close match between

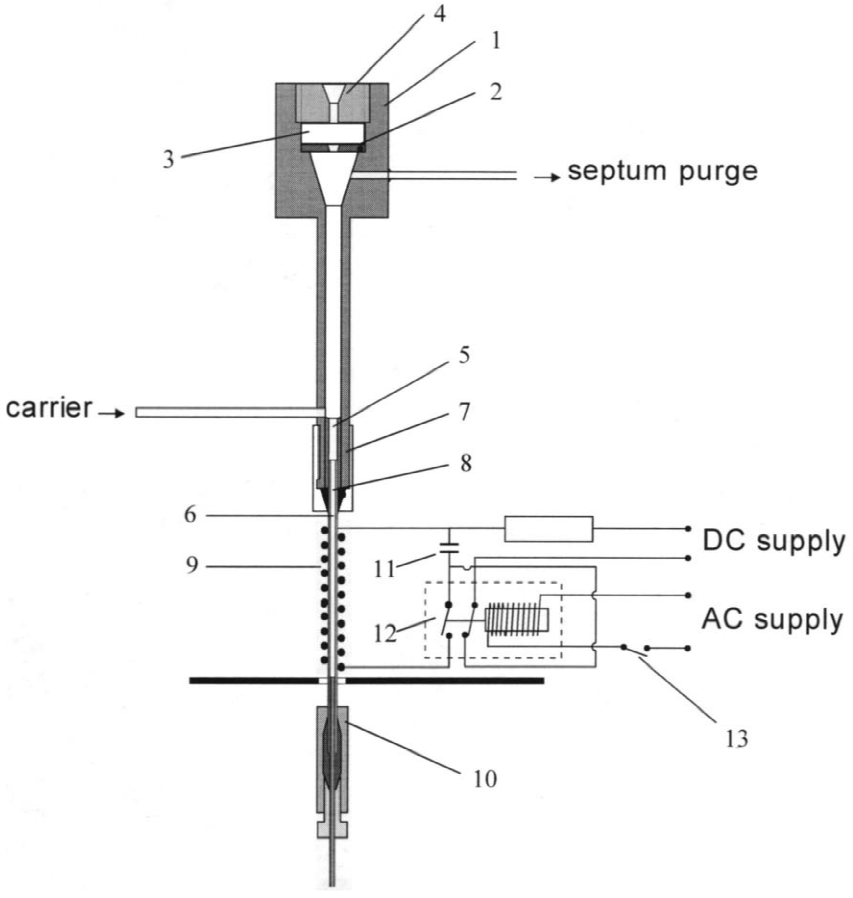

Fig. 32. Schematic diagram of the flash SPME injector: 1, injector body; 2, washer; 3, septum; 4, nut; 5, needle guide; 6, 0.53 mm I.D. fused-silica capillary; 7, nut; 8, ferrule; 9, heater; 10, butt connector; 11, relay; 12, capacitor; 13, switch. Source: Adopted with permission from Ref. [32].

inner diameter of the capillary and the outer diameter of the fiber assures effective heat transfer from the heater to the fiber, and a high linear flow-rate of the carrier gas along the fiber. The injector is rapidly heated via a capacitive discharge. Heating rates of 1000°C s^{-1} have been determined experimentally [58].

The injector just described has achieved separation of BTEX (benzene, toluene, ethylbenzene, xylenes) in 9 seconds (see Fig. 33). Separation of the 28 volatile organic compounds listed in U.S. EPA method 624 has been accomplished in 150 seconds with reproducibility better than 5% RSD for most analytes [59]. The fiber can be also be designed to contain the heating element, as shown in Fig. 34. In this case, no injector is necessary. The modified fiber can be introduced directly into the front of the column, and analytes can be desorbed rapidly by heating with a capacitive discharge current after the fiber has been exposed from the needle.

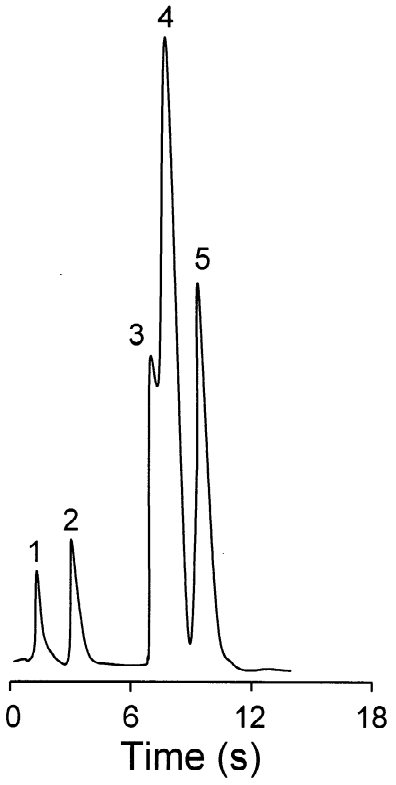

Fig. 33. Rapid analysis of BTEX in water by SPME–flash injector-GC: 1, benzene; 2, toluene; 3, ethylbenzene; 4, *m*, *p*-xylenes; 5, *o*-xylenes.

Flash desorption injectors can be alternatively designed by passing a current directly through the fiber. This is possible if the rod is made of conductive material, as it is in the case of the electrochemical SPME devices already mentioned. Fig. 35 illustrates such an interface [30]. When the electrical connection is made at the bottom of the interface, the fiber is rapidly heated by the discharging current. The other option is to use laser energy to desorb analytes from the surface of fused-silica optical fiber, as discussed previously.

Flash desorption injectors can be applied to directly interface SPME to a range of detection devices such as mass spectrometers and atomic emission devices. The sharp bands obtained during the desorption process result in very sensitive detection. For example, Fig. 36 shows a sharp peak corresponding to the toluene band desorbed from the SPME fiber and directly detected by the mass spectrometer. The limit of detection is about two orders of magnitude lower than is obtainable with conventional GC–MS techniques, because of a much sharper band. To facilitate proper quantification, the extract needs to be very clean, which puts an additional demand on the coating selectivity. Some help in proper quantification can be obtained if the apparatus for tandem mass spectrometry (MS–MS) is available.

3.6.2. SPME–HPLC Interface

Research effort has also been focused on designing interfaces for liquid phase separation techniques to address the need for analysis of nonvolatile and thermally labile analytes. The interface to high-performance liquid chromatography (HPLC) can be a straightforward analogue of the traditional loop injection system. A typical SPME–HPLC interface consists of a custom-made desorption chamber and a six-port injection valve (Fig. 37) [60]. The upper part of the PEEK tubing, (c), fitted into a tee-union, is enlarged to fit the needle of the syringe. The internal tubing of the SPME device, which holds the fiber, can be sealed by the PEEK tubing and the tee-union tightly enough to withstand solvent pressures as high as 4500 p.s.i.. The desorption chamber is placed in the position at which the injection loop normally resides on the injection

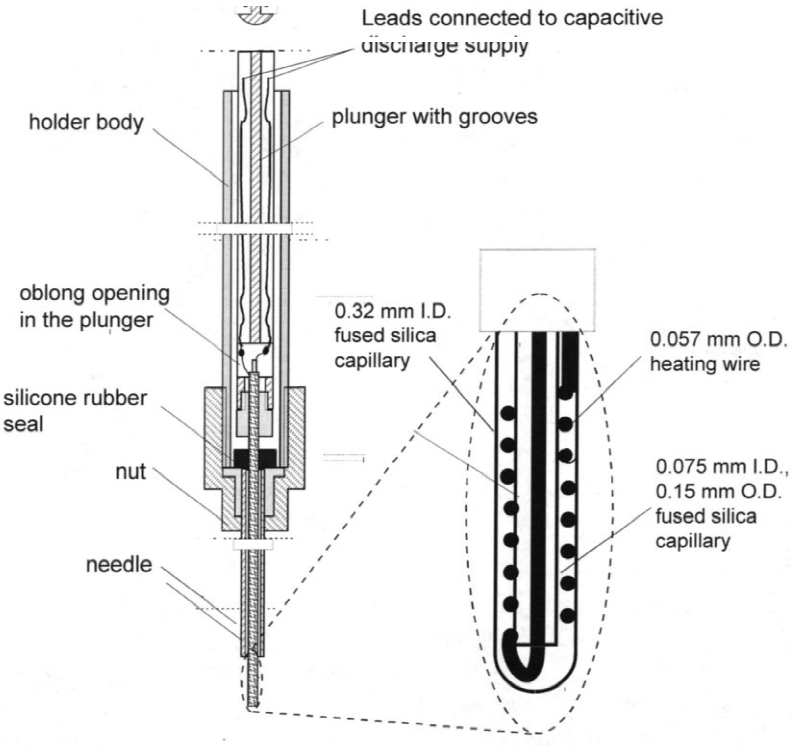

Fig. 34. Internally heated SPME device. Source: Adopted with permission.

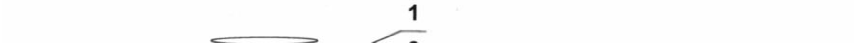

Fig. 35. Direct capacitive discharge desorption system: 1, SPME syringe; 2, electric connection I; 3, injector body; 4, steel wire; 5, gold coating; 6, electric connection II; 7, transfer line; 8, capacitor; 9, relay; 10, butt connector.

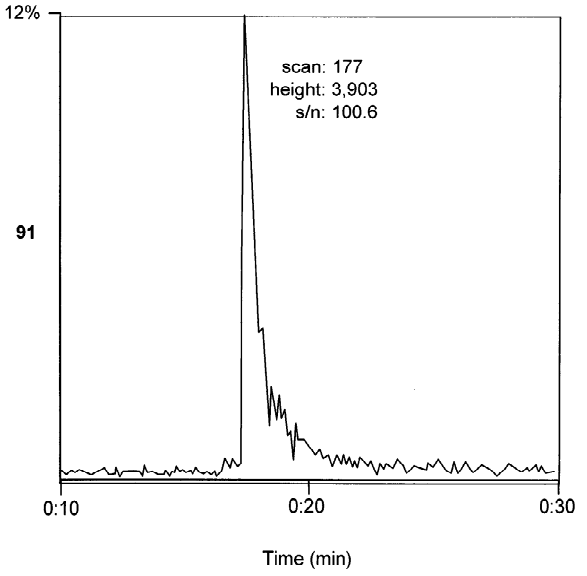

Fig. 36. High sensitivity of toluene detection by directly hyphenating SPME device to an ion trap mass spectrometer.

valve. When the injection valve is in the ''load'' position, it allows the fiber to be introduced into the desorption chamber under ambient pressure. It also allows for the introduction of a desorption solvent if different from the mobile phase. The valve is then switched to ''inject'' to transfer the desorbed analytes to the column. A heater can be installed in the device to facilitate the desorption process. The interface performs well, and its desorption volume is similar to the volume of the typical injection loop. The use of small-volume desorption chambers results in very efficient supercritical fluid chromatography separation (see Fig. 38) with very narrow bore capillary columns [61].

3.6.3. In-tube SPME–HPLC

There is a significant need to automate SPME–HPLC analyses, and this is addressed conveniently through the development of in-tube SPME using internally coated tubing [62] (Fig. 14). In one embodiment of this approach, a section of coated fused-silica GC capillary is placed between the needle of an HPLC autosampler and the injection valve. The capillary sections selected have coatings similar to common commercially available SPME fibers. Fig. 15 illustrates the system based on a modified Spark Holland micro LC autosampler [63]. In this system the analytes are extracted first into the coating by passing sample through the tubing, followed by desorption of the compounds using a small volume of solvent or mobile phase. These approaches, which are suitable for analysis of very small samples, also offer convenient interfacing to micro HPLC instrumentation.

The theory of extraction and desorption by this method was investigated and validated with the automated analysis of six phenylurea pesticides. For extraction, sample is aspirated and dispensed from the capillary a number of times, preferably until an equilibrium is nearly achieved. It was expected that the number of aspirate/dispense steps required to reach equilibrium would increases with the K-values of the analytes. Experimentally, equilibrium extraction was not obtained for any of the analytes. It was reasoned that during each dispense step, analyte would at least partially desorb into the mobile phase that follows the sample in the capillary, thus complicating the extraction. One significant difference between in-tube SPME and manual fiber-based SPME–HPLC is the decoupling of desorption and injection possible with the in-tube method. In the fiber-based method, analytes are desorbed during injection, as the mobile phase passes over the fiber. With in-tube SPME, analyte are desorbed either by mobile phase flow or by aspirating a desorption solvent of choice from a second vial, and then later transferring the solvent with desorbed analytes to the injection loop for injection onto the column. While fiber-based HPLC has the advantage of eliminating the need to filter cloudy samples, the method does suffer peak broadening in applications where analytes are slow to desorb from the fiber to the mobile phase due to the coating thickness. With in-tube SPME, analytes are completely desorbed prior to injection, so peak broadening is less of a factor. The coating thickness is only a fraction of a micron, so desorption is fast. If analytes are sufficiently solvated by the mobile phase, there is no need to use additional solvent for desorption. For the analysis of phenylurea pesticides, a 60 cm section of carbowax GC capillary (0.25 mm ID, 0.25 μm film thickness) was used for extraction, with a total of 10 sample aspirate/dispense steps, with subsequent desorption into 38 μl methanol. An aspirate/dispense rate of 50

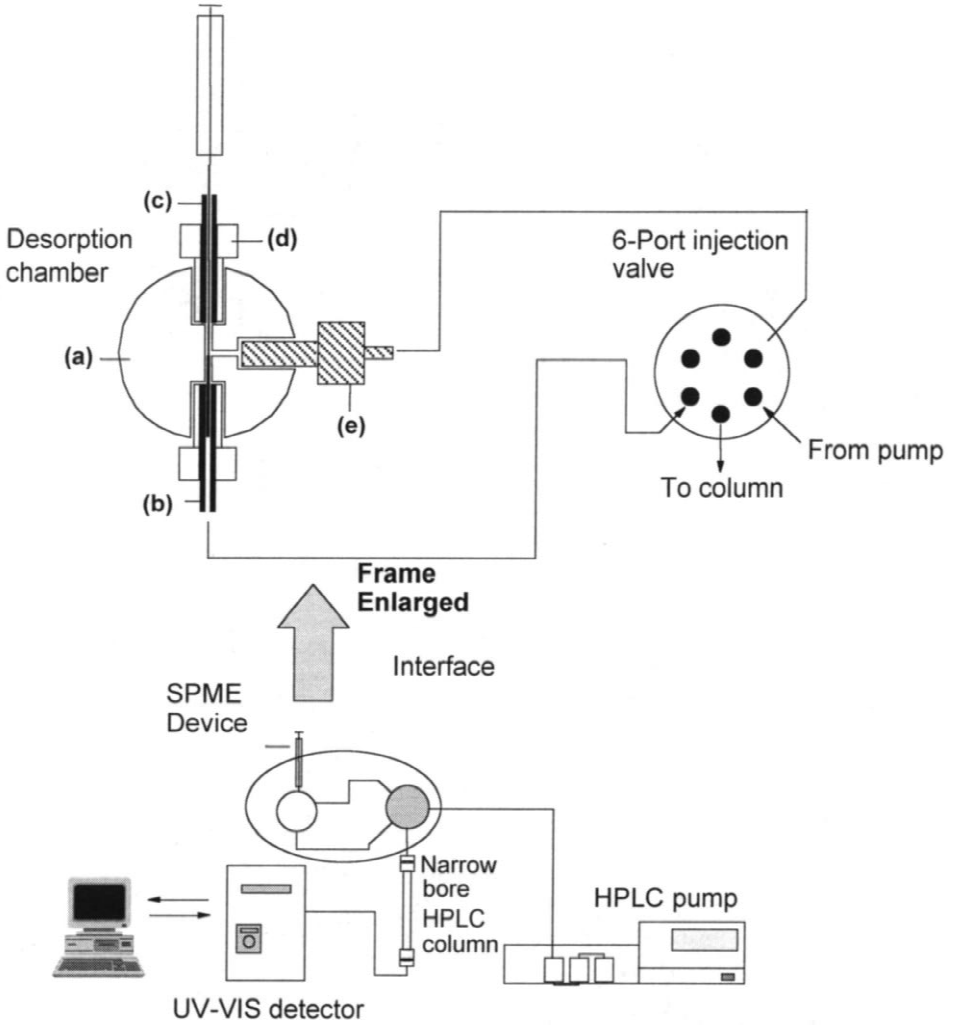

Fig. 37. SPME–HPLC interface: (a) stainless steel (SS) 1/16 in. tee, (b) 1/16 in. SS tubing, (c) 1/16 in. PEEK tubing (0.02 in. I.D.), (d) two-piece, finger-tight PEEK union, (e) PEEK tubing (0.005 in. I.D.) with a one-piece PEEK union.

to 100 $\mu l\,min^{-1}$ was found optimal for extraction and desorption. Below this level, aspiration and desorption require an inconveniently long time, and above this level, bubbles formed on the inside of the capillary, reducing extraction/desorption efficiency. Method precision was found to vary between 1.6 and 5.6%RSD, and linearity of the method was observed over the range of 10 to 10,000 $\mu g\,l^{-1}$. The limit of detection achieved was below 5 $\mu g\,l^{-1}$.

This technique was applied to the analysis of the thermally labile carbamate pesticides, using both the FAMOS autosampler from LC Packings and the Hewlett–Packard (HP) 1100 autosampler, in both cases without modification of the autosampler itself [64]. Extraction, desorption, separation and MS detection parameters were optimized, including capillary selection, desorption conditions, gradient composition, and MS fragmentor voltage. Both standard and capillary LC formats were employed. For capillary LC detection limits were reduced by a factor of 10. The effect of sample alcohol content was determined, and the method was applied to the

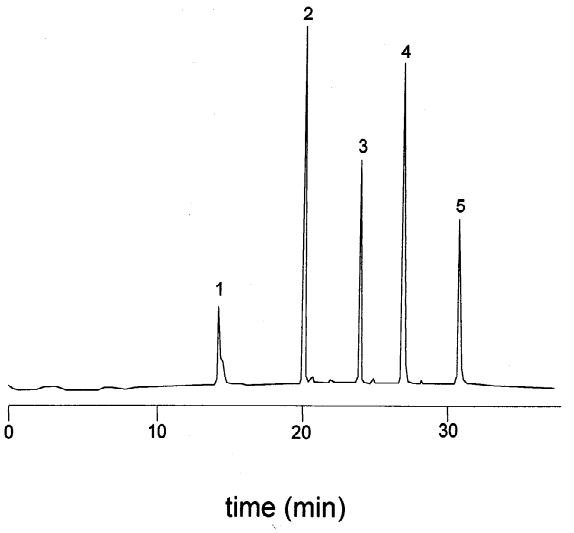

Fig. 38. Separation of PAHs on a 50 micrometer ID capillary using the SPME device as a sample introduction technique: naphthalene (1), acenaphthene (2), phenanthrene (3), fluoranthene (4) and benz[a]anthracene (5). Source: Adopted with permission.

analysis of spiked water (12% ethanol) and wine samples.

Automated in-tube solid-phase microextraction (SPME) coupled with liquid chromatography/electrospray ionization mass spectrometry (LC–ESI–MS) using the HP1100 system, was evaluated for the analysis of β-blockers [41], ranitidine [65] and amphetamines [66] in biological and pharmaceutical samples. Extractions required 10–15 min per sample. For quantification, LC–MS analyses were initially performed by liquid injection onto the LC column with analysis in selected ion mode. Several in-tube SPME parameters were optimized. These included capillary column stationary phase selection, sample pH, extraction flow-rate and number and volume of aspirate/dispense steps. The compounds extracted by the capillary column were easily desorbed by either mobile phase flow or a small quantity of methanol. Carryover was not observed.

A serum sample from a patient administrated propranolol was analyzed using this method and both propranolol and its metabolites were detected. This was a significant finding as metabolites are typically more challenging to analyse, due to their higher polarity. For ranitidine analysis both tablet and urine samples were analyzed with a detection limit at $S/N=3$ of 1.4 ng ml^{-1}. and within-day and between-day variations in ranitidine analysis were 2.5 and 6.2% ($n=5$), respectively. For the analysis of amphetamine, methamphetamine, and their 3,4-methylenedioxy derivatives in urine samples detection limits ($S/N=3$) of 0.38–0.82 ng ml^{-1} were observed.

Mutagenic heterocyclic amines were also analysed by this technique [67]. The amines extracted by the capillary column were desorbed by aspiration of 30 μl of methanol prior to injection, and carryover of heterocyclic amine was not observed. The detection limits ($S/N=3$) were 0.2–3.1 ng ml^{-1} and IQ, MeIQx and PhIP concentrations in grilled beefsteak were determined.

3.6.4. Other interfaces

Smaller injection volumes for applications of SPME to micro-HPLC and capillary electrophoresis can be accomplished by modifying microinjector designs; the sliding injector developed for capillary isotachophoresis is one example [68]. The other approach is to design an appropriate sample introduction system based on guides, to introduce the fibre with the extracted components directly into the capillary (see Fig. 39). Using this method very efficient separation was achieved (Fig. 40) [69].

SPME can be directly combined to optical detection, based on reflectometric interference spectrometry [70–72]. A light beam, passing through an optically transparent fiber coated with transparent sorbing material interacts with absorbed substances through internal reflection. Therefore, if any of the extracted analytes strongly absorb the transmitted light, there is a loss in intensity that can be detected with a simple optical sensor. These devices demonstrate poor sensitivity primarily because it is difficult to find light wavelengths that are specifically adsorbed by the analytes and not by the coating or interferences. In an alternative design, the light can pass directly through the absorbing polymer which is then cooled to facilitate high sensitivity of determination [73]. Fluorescence can be used to detect analytes in the coating. The selectivity of the extraction process and spectroscopy can be combined with selectivity of the electrochemical process resulting in a spectorelectrochemical sensor [74].

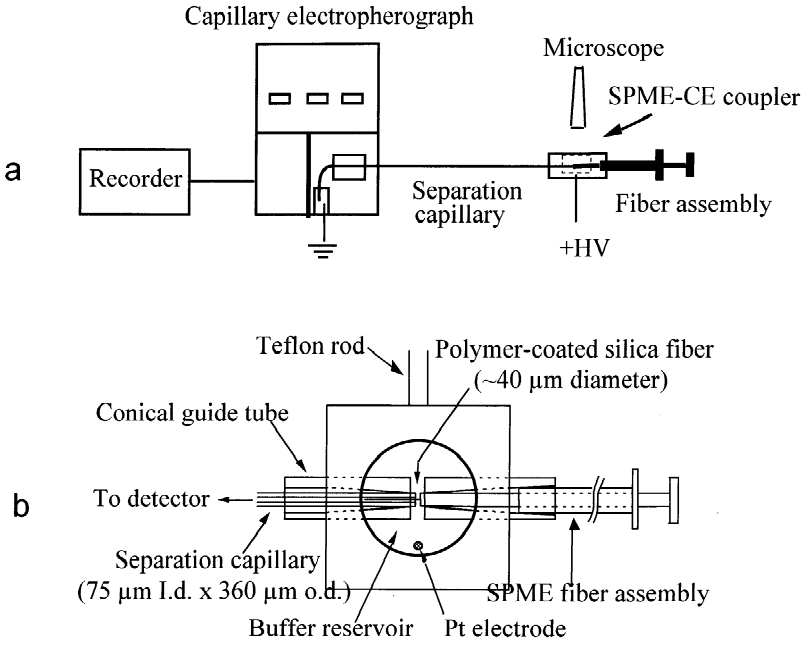

Fig. 39. Schematic of the SPME–CE system (a) and interface (b).

4. Commercial devices

4.1. Fiber assemblies

The first commercial version of the laboratory SPME device was introduced by Supelco in 1993 (see Fig. 4). The device is similar in operation principle to the custom-made device shown in Figs. 2 and 3a. Some additional improvements include the adjustment for depth of the fiber with respect to the end of the needle, which allows control of the exposure depth in the injector and extraction vessel. The device incorporates such useful features as color marking of the fiber assemblies to distinguish among various coating types. In addition to standard PDMS coatings of various thickness and polyacrylate (PA), Supelco developed new mixed phases based on solid/liquid sorption, such as Carbowax–DVB and PDMS–DVB. Supelco also introduced an HPLC interface (Fig. 41) that integrates the original concept with the injection valve (Fig. 37).

4.2. Autosamplers for GC

Varian has developed an SPME autosampler based on their 8000 GC autosampler system, taking advantage of the fact of the SPME device is analogous to a syringe in its operation and that after desorbtion the coating is cleaned and ready for re-use [75]. The major challenge is to incorporate agitation and temperature control as well as other enhancements, such as fiber internal cooling or dedicated injectors. One improvement is an SPME system that incorporates an agitation mechanism consisting of a small motor and a cam to vibrate the needle. The fibre in this design works as a stirrer. The vibration causes the vial to shake and the fiber to move with respect to the solution; the result is a substantial decrease of equilibration times compared to a static system. This mode of agitation simplifies fiber handling because it does not require the introduction of foreign objects into the sample prior to extraction.

Recently, Varian has reached an agreement with CTC Analytics of Switzerland, to incorporate SPME sampling on their CombiPalE autosampler. This is a robotic system with a great deal of flexibility for programming SPME analyses. Samples are loaded onto trays accomodating five vial sizes, and samples are heated and agitated during extraction, using a separate sample preparation chamber. To facilitate

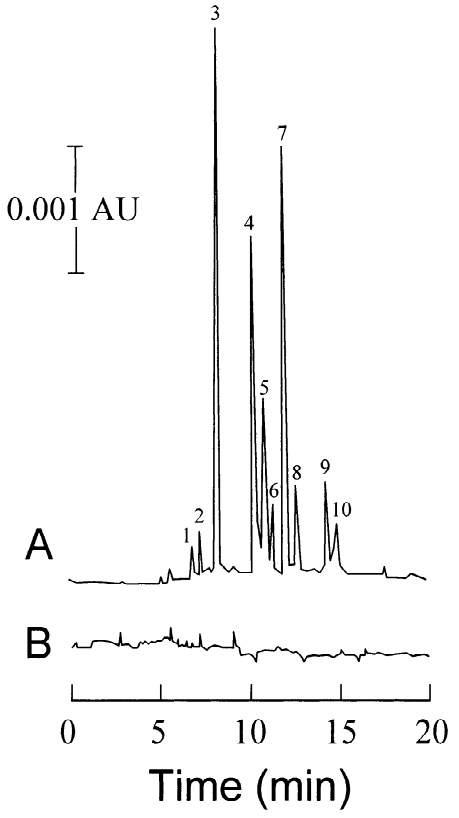

Fig. 40. Electropherogram of ten phenolic compounds obtained by SPME–CE using, A, a 40 μm O.D. PA-coated silica fiber and B, a 40 μm O.D. bare silica fiber. Peak identities: 1: 2,4-dimethylphenol, 2: phenol, 3: 4-chloro-3-methylphenol, 4: pentachlorophenol, 5: 2,4,6-trichlorophenol, 6: 2-methyl-4,6-dinitrophenol, 7: 2,4-dichlorophenol, 8: 2-chlorophenol, 9: 4-nitrophenol, 10: 2-nitrophenol.

agitation, the extraction chamber is rotated at a programmable rotation speed during extraction. Additional vials/stations are present to accommodate wash solutions, derivatizing agents, temperature control, derivatization and fibre conditioning, to facilitate operation of SPME at optimal conditions. While the built-in software can be used to perform basic SPME analyses, extra programming flexibility is provided by the Cycle Composer™ software, available as an accessory. We expect this new instrument with its greatly enhanced flexibility, will significantly expand the range of SPME methods amenable to automation. New coatings and devices are expected to follow, as interest in SPME grows along with the unprecedented numbers of new applications appearing in the literature.

4.3. Field Portable SPME–FastGC

Solid Phase Microextraction coupled to high speed gas-chromatography is a good combination to perform rapid and cost-effective investigations in the field, even of complex organic samples. As discussed above, SPME is particularly suited for fast GC, as it is solvent-free, and the thin coatings can provide very fast desorption of analytes at high temperatures. Some instrumental modifications were performed recently in order to achieve successful fast separations [58].

A portable system was optimized for SPME–fast GC field investigations and was commercialized by SRI Instruments (model 8610C, SRI Instruments, Torrance, CA). The instrument was tested in combination with a flame ionization detector (FID), a photoionization detector (PID), and a dry electrolytic conductivity detector (DELCD). A dedicated injector, presented in Fig. 42, was mounted on the portable system in order to use SPME for high-speed separation. The injector guarantees very fast thermal desorption of the analytes from the SPME fiber [76].

The injector for high-speed GC should produce as narrow an injection band as possible. Internal volumes of regular injector ports are too large (e.g.: split/splitless injector), since they have been designed to accommodate large volumes of gaseous samples or vapors produced by solvent injection. Thermal focusing for separation improvement is not convenient for fast separations, since temperature programming is impractical for high-speed GC. Hence, an injector port with a small internal volume was required for this application. Also, very fast thermal desorption from the SPME fiber was required to produce a narrow injection band and achieve effective separation. In the dedicated injector for SPME–fast GC, the injector port was maintained cold during needle introduction and was rapidly heated only when the fiber was exposed to the carrier gas stream. The desorption area of the injector was heated by capacitive discharge that allowed heating rates as fast as $4000^{\circ}C\,s^{-1}$, and very narrow injection bands were observed, as required by fast GC.

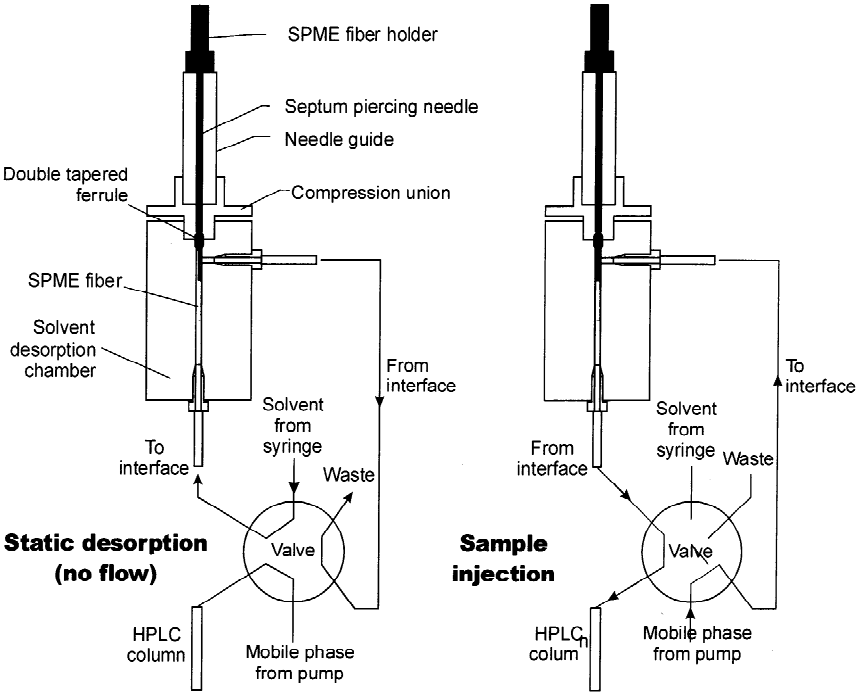

Fig. 41. Schematic diagram of the Supelco SPME–HPLC interface.

4.4. Fiber conditioners

SRI has also has a dedicated fiber injector available for their systems, and CTC Analytics has introduced a fiber cleaning station for their SPME autosampler. New SPME fibers require initial conditioning at manufacturer-recommended temperatures ranging from 210°C to 320°C, for time periods ranging from 0.5 to 4 h. Conditioning is also recommended at the beginning of the work day, and between runs in the case where analyte carry-over is a possibility. In addition, many SPME–fast GC

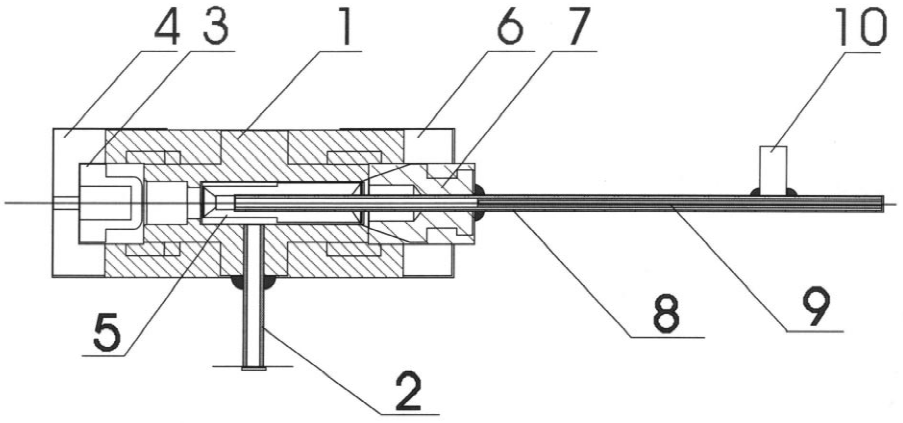

Fig. 42. Design of dedicated injector. 1, modified Swagelok fitting; 2, stainless steel tubing; 3, molded septum; 4, nut; 5, needle guide; 6, nut; 7, blind ferrule; 8, stainless steel tubing; 9, 0.53 mm I.D. fused-silica capillary, 10, contact.

applications, such as field sampling, require additional fiber cleaning in order to reduce desorption time in the GC injector and eliminate carry-over of non-target analytes [77].

Typically, fiber conditioning is performed by desorption in a temperature-controlled GC injector for the recommended conditioning time. However, this procedure reduces available GC time by occupying an injector and in many cases prevents analytical work from being performed on the instrument. It may also load a GC column with unwanted products of desorption, which in turn may require additional column conditioning and column ''blank'' determinations.

To address the aforementioned concerns, we have studied the process of fiber conditioning, and designed, built and tested a stand-alone SPME fiber conditioner [78]. This new device allows for fast conditioning of SPME fibers, using high temperature and gas flow for the desorption and subsequent purging of fiber contaminants. This device, intended for laboratory and field sampling applications, was based on a modified commercial syringe cleaner. The performance of the new fiber conditioner was tested for several types of commercially-available SPME fibers and compared with the traditional, GC-injector fiber conditioning method. The new device performed equal to, or better than GC injectors for both new fiber conditioning and the desorption of *n*-alkanes representing a wide range of boiling points, in addition to being significantly less expensive.

4.5. Additional applications

Small custom modifications of the commercial devices can lead to new possibilities. For example, the addition of input and output connections to the autosampler vial allows the system to be used to continuously monitor flowing streams, as shown in Fig. 43. The flow-through design facilitates agitation of the sample [79]. Alternatively, when a connection is added directly to the needle of the autosampler syringe, as in Fig. 13b, the system can analyze samples present in the vial without the need to expose the fiber [4]. Then the fiber containing the extracted analytes in its coating is introduced to the instrument for desorption.

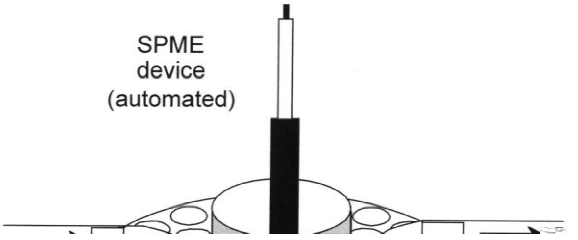

Fig. 43. On line monitoring of flowing streams by Varian autosampler using the modified vial design. Source: Adopted with permission.

5. Conclusions

5.1. Comparison of SPME and SPE

Solid phase microextraction is often considered as another form of solid-phase extraction or micro-SPE. There are significant differences between the methods however. Solid phase extraction is essentially a three-step process. A sample is initially passed through the sorbent bed, and analytes present in the sample are exhaustively extracted from the sample matrix to the solid sorbent. In a second step, unwanted analytes are selectively desorbed from the solid sorbent by washing with a solution capable of desorbing unwanted analytes, but leaving desired analytes retained on the sorbent. In the final step the wash solution is changed for one able to desorb analytes of interest. The resulting eluent may then be concentrated by evaporation, to the desired volume. Solid phase microextraction however takes advantage of equilibrium extraction and selective sorption from the matrix onto the coating. In the first step, the fiber coating is exposed to the sample and analytes with a high affinity for the sorbent are selectively extracted. In the second step, everything extracted by the fiber is desorbed into the analytical instrument. No intermediate clean-up step is normally implemented. Micro-SPE is more related to SPE as it is