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Solid-Phase Microextraction

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Introduction

Solid-phase microextraction (SPME) was introduced as a solvent-free sample preparation technique in 1990. The basic principle of this approach is to use a small amount of the extracting phase (usually less than 1 μL) compared to the sample matrix. Sample volume can be very large, when the investigated system, for example air or lake water, is sampled directly. The extracting phase can be either a high molecular weight polymeric liquid, similar in nature to chromatographic stationary phases, or it can be a solid sorbent, typically of a high porosity to increase the surface area available for adsorption.

To date the most practical geometric configuration of SPME utilizes a small fused silica fibre, usually coated with a thin film of polymeric phase. The fibre is mounted for protection in a syringe-like device (**Figure 1**A). The analytes are absorbed or adsorbed by the fibre coating (depending on the nature of the coating) until an equilibrium is reached in the system. The amount of an analyte extracted by the coating at equilibrium is determined by the magnitude of the partition coefficient (distribution ratio) of the analyte between the sample matrix and the coating material.

In SPME, analytes typically are not exhaustively extracted from the matrix. However, equilibrium methods are more selective because they take full advantage of the differences in extracting phase/matrix distribution constants to separate target analytes from interferences. Exhaustive extraction can be achieved in SPME when the distribution constants are large enough. This can be accomplished for most compounds by cooling the fibre coating. This concept was tested using a piece of microtubing coated on the outside instead of a solid rod and supplying liquid carbon dioxide into the tube to achieve an internally cooled fibre. In exhaustive extraction, selectivity is sacrificed to obtain quantitative transfer to target analytes into the extracting phase. One advantage of this approach is that, in principle, it does not require calibration, since all the analytes of interest are transferred to the extracting phase. On the other hand, the equilibrium approach usually requires calibration through the use of surrogates or standard addition to quantify the analytes and compensate for matrix-to-matrix variations and their effect on distribution constants.

Since equilibrium rather than exhaustive extraction occurs in microextraction methods, SPME is ideal for field monitoring. It is unnecessary to measure the volume of the extracted sample and therefore the SPME device can be exposed directly to the investigated system for quantitation of target analytes. Thin coatings of extracting phase result in fast separations. In addition, extracted analytes are introduced to the analytical instrument inlet system by simply placing the fibre in the desorption unit (Figure 1B and 1C). This convenient, solvent-free sample introduction process facilitates sharp injection bands and rapid separations. These features of SPME result in the integration of the first steps in the analytical process: sampling, sample preparation and introduction of extracted mixture to the analytical instrument. For example, total analysis time in field applications can be as low as a few minutes when portable instrumentation is used.

The equilibrium nature of the technique also facilitates speciation in natural systems since the presence of a minute fibre, which removes small amounts of target analytes, is not likely to disturb the system. Because of the small size, coated fibres can

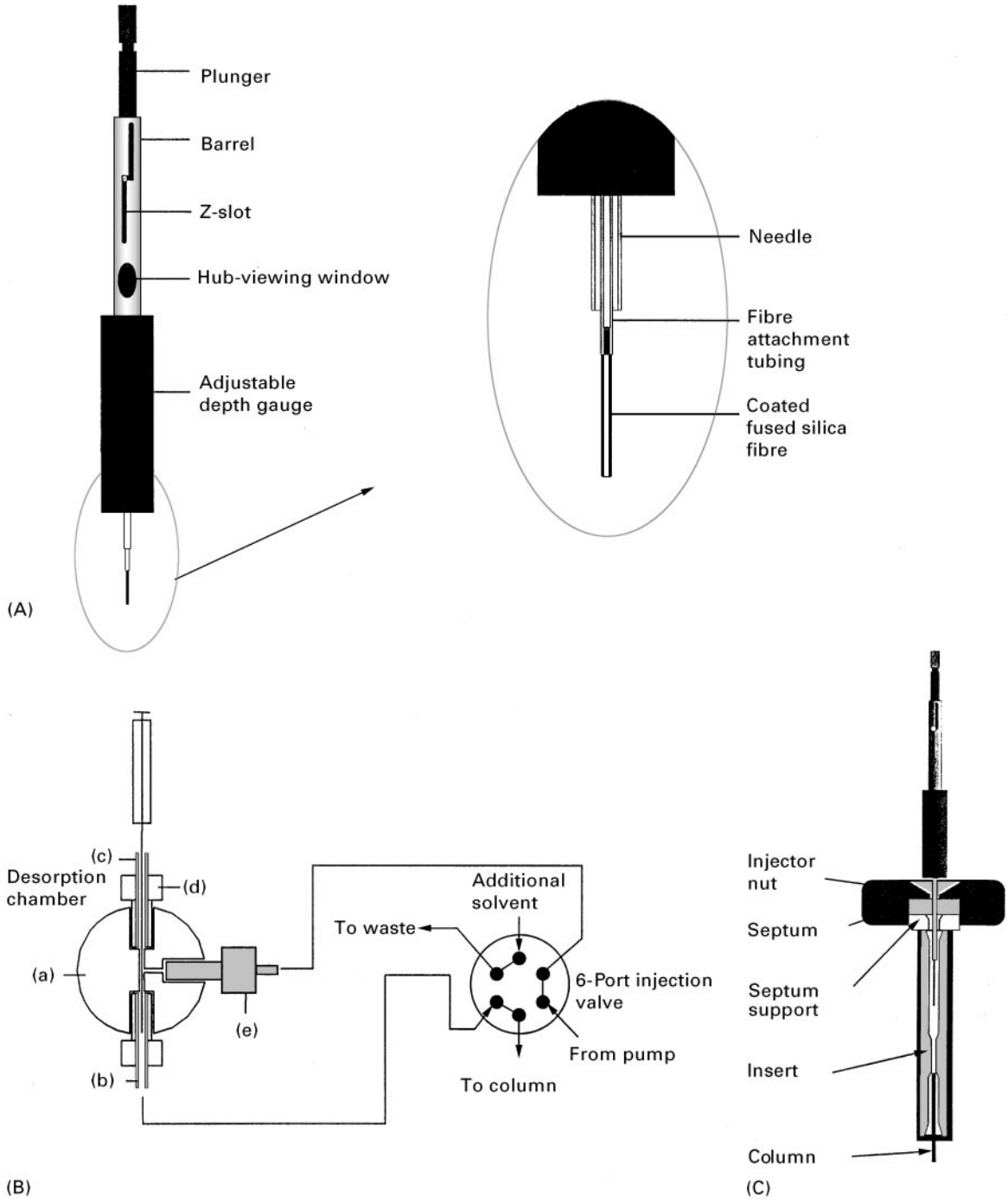

Figure 1 (A) Design of a commercial SPME device. (B) SPME–HPLC interface: (a) stainless steel (SS) 1/16″ tee; (b) 1/16″ SS tubing; (c) 1/16″ polyetheretherketone (PEEK) tubing (0.02″ i.d.); (d) two-piece finger-tight PEEK union; (e) PEEK tubing (0.005″ i.d.) with a one-piece PEEK union. (C) SPME–GC interface.

be used to extract analytes from very small samples. For example, SPME has been used to probe for substances emitted by a single flower bloom during its lifespan.

Figure 1A illustrates the commercial SPME device manufactured by Supelco, Inc. (Bellefonte, PA, USA). The fibre, glued into a piece of stainless steel tubing, is mounted in a special holder. The holder is equipped with an adjustable depth gauge, which makes it possible to control repeatably how far the needle of the device is allowed to penetrate the sample container (if any) or the injector. This is important, as the fibre can

be easily broken when it hits an obstacle. The movement of the plunger is limited by a small screw moving in the z-shaped slot of the device. For protection during storage or septum piercing, the fibre is withdrawn into the needle of the device, with the screw in the uppermost position. During extraction or desorption, the fibre is exposed by depressing the plunger, which can be locked in the lowered (middle) position by turning it clockwise (the position depicted in Figure 1A). The plunger is moved to its lowermost position only for replacement of the fibre assembly. Each type of fibre has a hub of a different colour. The hub-viewing window permits a quick check to be made of the type of fibre mounted in the device.

If the sample is placed in a vial, the septum of the vial is first pierced with the needle (with the fibre in the retracted position) and the plunger is lowered, which exposes the fibre to the sample. The analytes are allowed to partition into the coating for a predetermined time, and the fibre is then retracted back into the needle. When gas chromatography (GC) is used for analyte separation and quantitation, the fibre is inserted into a hot injector, where thermal desorption of the trapped analytes takes place (Figure 1C). All extracted compounds are introduced to the analytical instrument facilitating high sensitivity of determinations. The fibre desorption process can be automated by using an appropriately modified, commercially available syringe autosampler. For high performance liquid chromatography (HPLC) applications, a simple interface mounted in place of the injection loop can be used to re-extract analytes into the desorption solvent (Figure 1B). The extraction phase can also coat the inner wall of the capillary. This approach to microextraction can be automated using a number of commercially available autosamplers, but it is limited to extraction of relatively clean samples, which do not plug capillaries.

The SPME device is suitable for both spot and time-averaged sampling. As described above, for spot sampling, the fibre is exposed to a sample matrix until equilibrium is reached between the sample matrix and the coating material on the fibre. In the time-average approach, on the other hand, the fibre remains in the needle during the exposure of the SPME device to the sample. The coating works as a trap for analytes that diffuse into the needle, resulting in the integration of concentration over given time.

SPME sampling can be performed in three basic modes: direct extraction, headspace extraction and extraction with membrane protection. **Figure 2** illustrates the differences between these modes. In direct extraction mode (Figure 2A), the coated fibre 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 the analytes from the bulk of the sample to the vicinity of the fibre. For gaseous samples, natural flow (e.g. convection) is frequently sufficient to facilitate rapid equilibration, but for aqueous matrices, more efficient agitation techniques, such as fast sample flow, rapid fibre or vial movement, stirring or sonication are required to reduce the effect of the depletion zone produced close to the fibre as a result of slow diffusional analyte

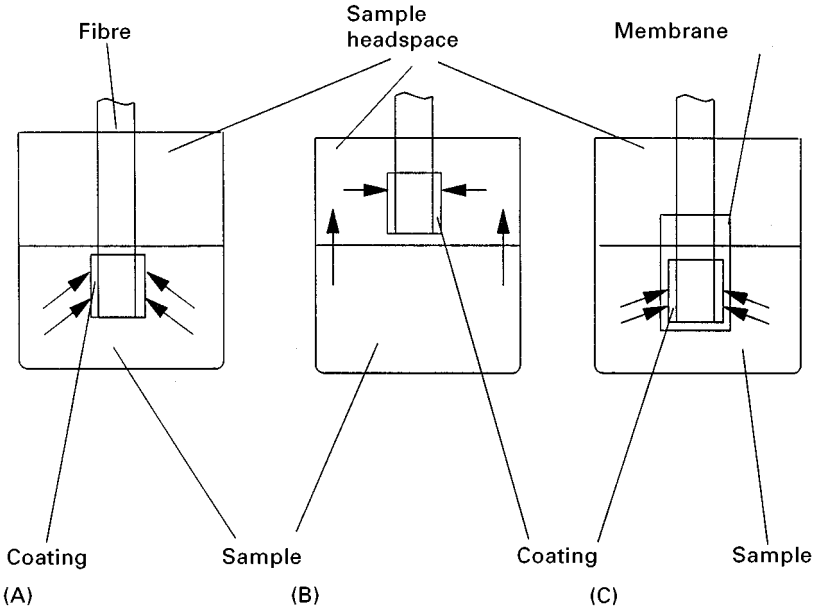

Figure 2 Modes of SPME operation: (A) direct extraction, (B) headspace extraction and (C) membrane-protected SPME.

transport through the otherwise static layer of liquid surrounding the fibre.

In the headspace mode (Figure 2B), the analytes are extracted from the gas phase equilibrated with the sample. The primary reason for this modification is to protect the fibre from adverse effects caused by non-volatile, high molecular weight substances present in the sample matrix (e.g. humic acids or proteins). The headspace mode also allows matrix modifications, including pH adjustment, without affecting the fibre. In a closed system consisting of a liquid sample and its headspace, the amount of an analyte extracted by the fibre coating does not depend on the location of the fibre, therefore the sensitivity of headspace sampling is the same as the sensitivity of direct sampling as long as the volumes of the two phases are the same in both sampling modes. Even when headspace is not used in direct extraction, a significant sensitivity difference between direct and headspace sampling can occur only for very volatile analytes. However, the choice of sampling mode has a significant impact on the extraction kinetics. When the fibre is in the headspace, the analytes are removed from the headspace first, followed by indirect extraction from the matrix. Therefore, volatile analytes are extracted faster than semivolatiles. Temperature has a significant effect on the kinetics of the process, since it determines the vapour pressure of analytes. In general, the equilibration times for volatile compounds are shorter for headspace SPME extraction than for direct extraction under similar agitation conditions, for the following reasons: (i) a substantial portion of the analytes is present in the headspace before the extraction process begins; (ii) there is typically a large interface between sample matrix and headspace; and (iii) the diffusion coefficients in the gas phase are typically higher by four orders of magnitude than in liquids. The concentration of semivolatile compounds in the gaseous phase at room temperature is small, consequently headspace extraction rates for those compounds are substantially lower. These rates can be improved by using efficient agitation or by increasing the extraction temperature.

In the third mode (SPME extraction with membrane protection, Figure 2C), the fibre is separated from the sample by a selective membrane, which lets the analytes through while blocking the interferences. The main purpose for the use of the membrane barrier is to protect the fibre against adverse effects caused by high molecular weight compounds when very dirty samples are analysed. While extraction from headspace serves the same purpose, membrane protection allows the analysis of less volatile compounds. The extraction process is substantially slower than direct extraction because the analytes have to diffuse through the membrane before they can reach the coating. Use of thin membranes and increase in extraction temperature, applied to analysis of polyaromatic hydrocarbons (PAHs) in matrices containing humic matter, result in shorter extraction times.

Theoretical Aspects of Solid-phase Microextraction Optimization and Calibration

Thermodynamics

SPME is a multiphase equilibration process. Frequently, the extraction system is complex, as in a sample consisting of an aqueous phase with suspended solid particles having various adsorption interactions with analytes, plus a gaseous headspace. In some cases specific factors have to be considered, such as analyte losses by biodegradation or adsorption on the walls of the sampling vessel. In the discussion below we will only consider three phases: the fibre coating, the gas phase or headspace, and a homogeneous matrix such as pure water or air. During extraction, analytes migrate between all three phases until equilibrium is reached. The following 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.

The mass of an analyte extracted by the polymeric coating is related to the overall equilibrium of the analyte in the three-phase system. Since the total mass of an analyte should remain constant during the extraction, we have:

$$C_0 V_s = C_f^\infty V_f + C_h^\infty V_h + C_s^\infty V_s \qquad [1]$$

where C_0 is the initial concentration of the analyte in the matrix: C_f^∞, C_h^∞ and C_s^∞ are the equilibrium concentrations of the analyte in the coating, the headspace and the matrix, respectively; V_f, V_h and V_s are the volumes of the coating, the headspace and the matrix, respectively. If we define the coating/gas distribution constant as $K_{fh} = C_f^\infty / C_h^\infty$, and the gas/sample matrix distribution constant as $K_{hs} = C_h^\infty / C_s^\infty$, the mass of the analyte absorbed by the coating, $n = C_f^\infty V_f$, can be expressed as:

$$n = \frac{K_{fh} K_{hs} V_f C_0 V_s}{K_{fh} K_{hs} V_f + K_{hs} V_h + V_s} \qquad [2]$$

Also:

$$K_{fs} = \frac{K_H}{K_F} = K_{fh}K_{hs} = K_{fg}K_{gs} \quad [3]$$

since the fibre/headspace distribution constant, K_{fh} can be approximated by the fibre/gas distribution constant K_{fg}, and the headspace/sample distribution constant, K_{hs}, by the gas/sample distribution constant, K_{gs}, if the effect of moisture in the gaseous headspace can be neglected. Thus, eqn [2] can be written as:

$$n = \frac{K_{fs}V_fC_0V_s}{K_{fs}V_f + K_{hs}V_h + V_s} \quad [4]$$

The equation states, as expected from the equilibrium conditions, that the amount of analyte extracted is independent of the location of the fibre in the system. It may be placed in the headspace or directly in the sample as long as the volumes of the fibre coating, headspace and sample are kept constant. There are three terms in the denominator of eqn [4] which give measures of the analyte capacity of each of the three phases: fibre ($K_{fs}V_f$), headspace ($K_{hs}V_h$) and the sample itself (V_s). If we assume that the vial containing the sample is completely filled (no headspace), the term $K_{hs}V_h$ in the denominator, which is related to the capacity ($C_h^{\infty}V_h$) of the headspace, can be eliminated, resulting in:

$$n = \frac{K_{fs}V_fC_0V_s}{K_{fs}V_f + V_s} \quad [5]$$

Equation [5] describes the mass absorbed by the polymeric coating after equilibrium has been reached in the system. In most determinations, K_{fs} is relatively small compared to the phase ratio of sample matrix to coating volume ($V_f \ll V_s$). In this situation the capacity of the sample is much larger compared to capacity of the fibre, resulting in a very simple relationship:

$$n = K_{fs}V_fC_0 \quad [6]$$

The above equation emphasizes the field-sampling capability of the SPME technique. It is not necessary to sample a well-defined volume of the matrix since the amount of analyte extracted is independent of V_s as long as $K_{fs}V_f \ll V_s$. The SPME device can be placed directly in contact with the investigated system to allow quantitation.

Prediction of distribution constants In many cases, the distribution constants present in eqns [2]–[6] which determine the sensitivity of SPME extraction can be estimated from physicochemical data and chromatographic parameters. For example, distribution constants between a fibre coating and gaseous matrix (e.g. air) can be estimated from isothermal GC retention times on a column with a stationary phase identical to the fibre-coating material. This is possible because the partitioning process in gas chromatography is similar to the partitioning process in SPME, and there is a well-defined relationship between the distribution constant and the retention time. The nature of the gaseous phase does not affect the distribution constant, unless the components of the gas, such as moisture, swell the polymer, thus changing its properties. A most useful method for determining coating-to-gas distribution constants uses the linear temperature programmed retention index (LTPRI) system, which relates retention times relative to the retention times of *n*-alkanes. The logarithm of the coating-to-air distribution constants of *n*-alkanes can be expressed as a linear function of their LTPRI values. For poly(dimethylsiloxane) (PDMS), this relationship is $\log K_{fg} = 0.00415 * \text{LTPRI} - 0.188$. Thus, the LTPRI system permits interpolation of the K_{fg} values from the plot of $\log K_{fg}$ versus retention index. The LTPRI values for many compounds are available in the literature, hence this method allows estimation of K_{fg} values without experimentation. If the LTPRI value for a compound is not available from published sources, it can be determined from a GC run using a GC column coated with the same material as the fibre.

Estimation of the coating/water distribution constant can be performed using eqn [5]. The appropriate coating/gas distribution constant can be found by applying techniques discussed above, and the gas/water distribution constant (Henry's constant) can be obtained from physicochemical tables or can be estimated by the structural unit contribution method.

Some correlations can be used to anticipate trends in SPME coating/water distribution constants for analytes. For example, a number of investigators have reported correlation between the octanol/water distribution constant, K_{ow}, and K_{fw}. This is to be expected, since K_{ow} is a general measure of the affinity of compounds for the organic phase. It should be remembered, however, that the trends are valid only for compounds within homologous series, such as aliphatic hydrocarbons, aromatic hydrocarbons or phenols; they should not be used to make comparisons between different classes of compounds, because of different analyte activity coefficients in the polymer.

Effect of extraction parameters Thermodynamic theory predicts the effects of modifying certain

extraction conditions on partitioning and indicates parameters to be controlled for reproducibility. The theory can be used to optimize the extraction conditions with a minimum number of experiments and to correct for variations in extraction conditions, without the need to repeat calibration tests under the new conditions. For example, SPME analysis of outdoor air may be done at ambient temperatures that can vary significantly. A relationship that predicts the effect of temperature on the amount of analyte extracted allows calibration without the need for extensive experimentation. Extraction conditions that affect K_{fs} include temperature, inorganic salt concentration, pH and organic solvent content of the water.

Kinetics

The kinetic theory is useful to optimize the extraction conditions by identifying 'bottlenecks' in SPME and indicating strategies to increase extraction speed. In the discussion below we will limit our consideration to direct extraction (**Figure 3**).

Perfect agitation Let us first consider the case where the liquid or gaseous sample is well agitated. In other words, the sample phase moves rapidly with respect to the fibre, so that all the analytes present in the sample have access to the fibre coating. In this case, the equilibration time, defined as the time required to extract 95% of the equilibrium amount (**Figure 4**) of an analyte from the sample, corresponds to:

$$t_e = t_{95\%} = \frac{2(b-a)^2}{D_f} \qquad [7]$$

Using this equation one can estimate the shortest equilibration time possible for a practical system by substituting appropriate data for the diffusion coefficient of an analyte in the coating (D_f) and the fibre-coating thickness ($b - a$). For example, the equilibration time for the extraction of benzene from a highly agitated aqueous solution with a 100 μm PDMS film is expected to be about 20 s assuming diffusion coefficient of 10^{-5} cm^2 s^{-1} in PDMS. Equilibration times close to those predicted for agitated samples have

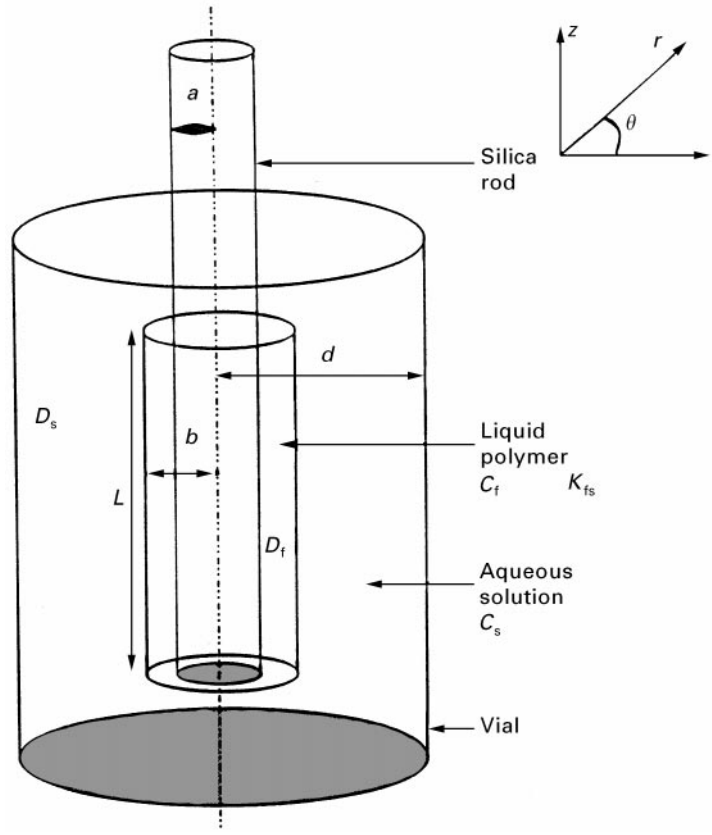

Figure 3 Graphic representation of the SPME/sample system configuration, with dimensions and parameters labelled as follows: *a*, fibre coating inner radius; *b*, fibre coating outer radius; *L*, fibre coating length; *d*, vial inner radius; C_f, analyte concentration in the fibre coating; D_f, analyte diffusion coefficient in the fibre coating; C_s, analyte concentration in the sample; D_s, analyte diffusion coefficient in the sample; K_{fs}, analyte distribution coefficient between fibre coating and sample; $K_{fs} = C_f/C_s$. (With permission from Louch *et al.* (1992) *Analytical Chemistry* 64: 1187.)

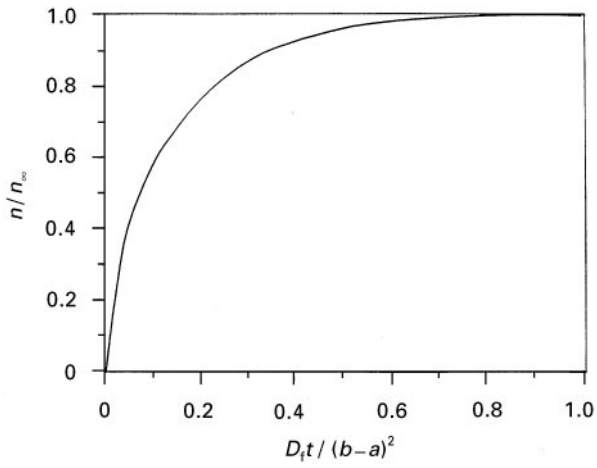

Figure 4 Mass absorbed versus time for a well-agitated solution of infinite volume. (With permission from Louch *et al.* (1992) *Analytical Chemistry* 64: 1187.)

been obtained experimentally for extraction of analytes from air samples (because of high diffusion coefficients in gases) or when high sonication power is used to facilitate mass transfer in aqueous samples. However, in practice there is always a layer of unstirred water around the fibre, although a high stirring rate will reduce its thickness.

Practical agitation Independently of the level of agitation, fluid contacting the fibre surface is always stationary, and as the distance from the surface increases, the fluid movement gradually increases until it corresponds to the bulk flow in the sample. To model mass transport, the gradation in fluid motion and convection of molecules in the space surrounding the fibre surface can be simplified by a zone of a defined thickness in which no convection occurs, and perfect agitation in the bulk of the fluid everywhere else. This static layer zone is called the Prandtl boundary layer (**Figure 5**). Its thickness is determined by the agitation conditions and the viscosity of the fluid.

The equilibration time can be estimated for practical cases from the equation below:

$$t_e = t_{95\%} = 3\,\frac{\delta K_{fs}(b-a)}{D_s} \qquad [8]$$

where $(b-a)$ is the coating thickness on the fibre, D_s is the diffusion coefficient of the analyte in the sample fluid, K_{fs} is the distribution constant of the analyte between the fibre and the sample and δ is a boundary layer thickness. This equation can be used to predict equilibration times when the extraction rate is controlled by the diffusion in the boundary layer. The extraction time calculated using eqn [8] must be longer than the corresponding time predicted by eqn [7].

Conclusion

SPME is gaining acceptance principally because of its simplicity, speed and low cost of operation. The detection limits are comparable to a total extraction technique since all extracted analytes are introduced to the analytical instrument in SPME versus only a fraction for a total extraction techniques. Selectivity

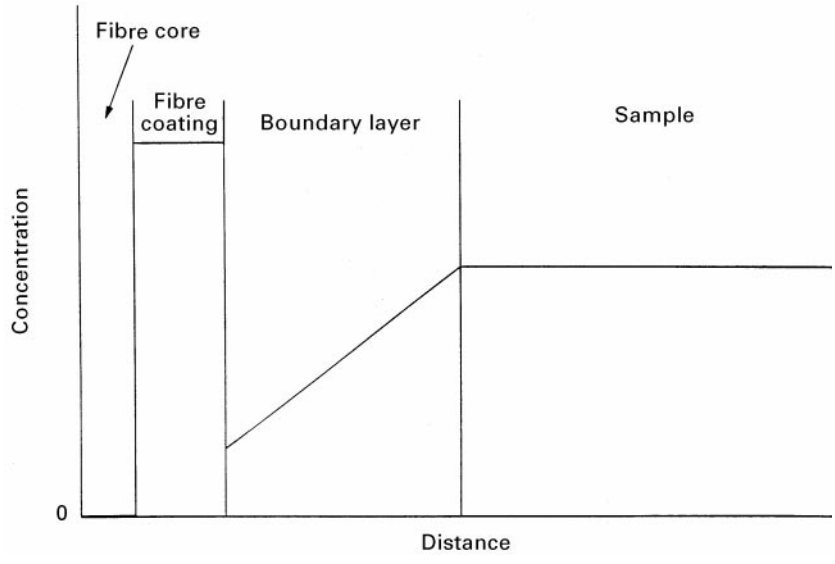

Figure 5 Boundary layer model configuration showing the different regions considered and the assumed concentration versus radius profile for the case when the boundary layer determines the extraction rate.

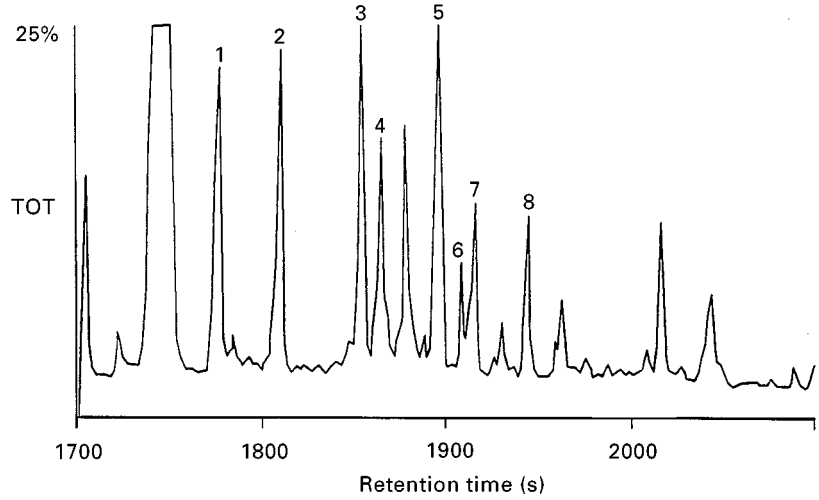

Figure 6 Reconstructed GC-MS chromatogram indicating short chain fatty acids in a sewage sample. Peak assignment: 1, acetic; 2, propionic; 3, isobutyric; 4, butyric; 5, pivalic; 6, isovaleric; 7, valeric; 8, hexanoic acids. The peaks correspond to pyrenylmethyl esters of these acids.

of the technique is controlled by chemical properties of the coating and it is determined by the appropriate distribution constants. Selecting the appropriate fibre allows discrimination against interferences and therefore a separate clean-up step is not necessary. In addition, the coating can contain derivatization reagent, which can specifically bind target analytes, resulting in high specificity and sensitivity of the process. **Figure 6** shows a chromatogram obtained after selective headspace SPME extraction of low molecular weight carboxylic acids from a sewage sample by poly(acrylate)-coated fibre containing 1-pyrenyldiazomethane which selectively reacts with the target analytes. New coatings and reagents will allow expansion of SPME applications to new areas such as inorganic analysis and analysis of biomolecules.

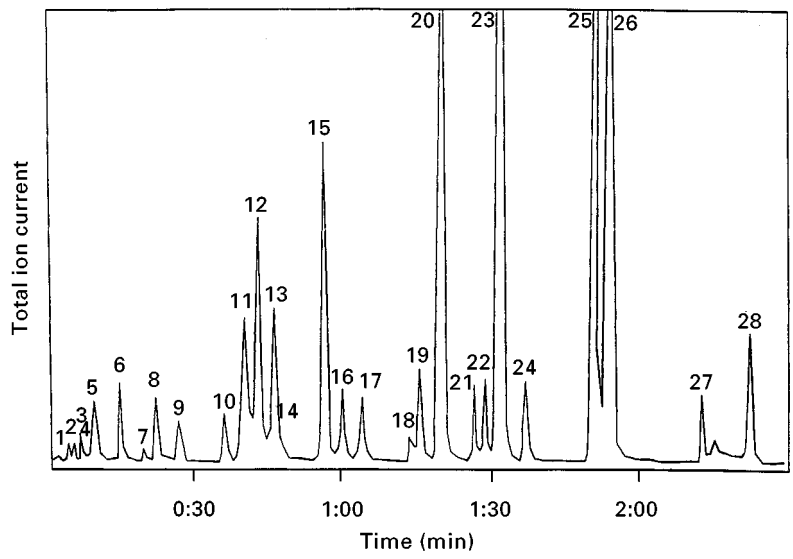

Figure 7 Separation of purgeables A, B and C on a Vocol column. Conditions: 0°–30°C min^{-1} 70°; 2.1 atm, dedicated injector, capacitor voltage 24 V, MS detector, mass range 45–250. Peak assignment: 1, chloromethane; 2, vinyl chloride; 3, bromomethane; 4, chloroethane; 5, trichlorofluoromethane; 6, 1,1-dichloroethene; 7, dichloromethane; 8, 1,2-dichloroethene; 9, 1,1-dichloroethane; 10, trichloromethane; 11, 1,1,1-trichloroethene; 12, tetrachloromethane; 13, benzene; 14, 1,2-dichloroethane; 15, trichloroethene; 16, 1,2-dichloropropane; 17, bromodichloromethane; 18, 2-chloroethyl vinyl ether; 19, *cis*-1,3-dichloropropene; 20, toluene; 21, *trans*-1,3-dichloropropene; 22, 1,1,2-trichloroethane; 23, tetrachloroethylene; 24, dibromochloromethane; 25, chlorobenzene; 26, ethylbenzene; 27, tribromomethane; 28, 1,1,2,2-tetrachloroethane.

In addition to solvent-free sample extraction, SPME is also a solvent-free sample introduction technique which facilitates design of a simple, low volume injection system. The net result is rapid desorption and good chromatographic separation, especially when flash-heated injectors are used. **Figure 7** illustrates 2.5 min extraction and separation of 28 Environmental Protection Agency volatile priority pollutants, which is over an order of magnitude faster than the standard purge and trap technique. This approach is particularly useful in combination with online SPME extraction. As eqn [6] indicates, it is possible to integrate sampling with a sample preparation step. This not only results in elimination of analyte losses to container walls and degradation during the transport, but also saves time and transport costs. This is particularly true when online SPME extraction is combined with field portable GCs.

Another interesting feature of SPME which is currently being explored includes speciation of analytes in complex matrices. The small amount of extracting phase does not disturb the equilibrium existing in the natural system and therefore allows quantitation of individual species or the determination of distribution constants in a multiphase system. In addition, the fibre can be made very specific, so separation using chromatographic systems may not be necessary. Therefore development of coupling between SPME with other analytical instrumentation, such as mass spectrometry and inductively coupled plasma–mass spectrometry will facilitate high sensitivity and a large throughput.

See also: **II/Extraction:** Solid-Phase Extraction; Solvent Based Separation. **III/Environmental Applications:** Solid-Phase Microextraction; **Solid-Phase Microextraction:** Overview.

Further Reading

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Solvent Based Separation

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Introduction

Separation involves removal of one or more of the constituent parts from a mixture. A solvent is that constituent of a solution that is liquid in the pure state, is usually present in the larger amount, and has dissolved the other constituent (a solute) of the solution. The solute may be a solid, a liquid or a gas. The solvent may be a single compound or a mixture of compounds. Solvent-based separation techniques become necessary when separation or removal of a solute(s) from a mixture become difficult or infeasible by conventional separation techniques such as distillation. If the addition of a solvent causes a totally miscible liquid to split into two liquid phases and produce the necessary property difference, the solvent-based separation technique is commonly known as liquid–liquid extraction. If the addition of a solvent causes the coexisting vapour and liquid phases to have different properties, the solvent-based separation technique is called extractive distillation. **Figure 1**A and 1B highlight the change of the mixture properties as a result of the addition of a solvent. In Figure 1A, the difference between the properties of the liquid and vapour for the binary azeotropic mixture of ethanol–water with and without the addition of solvents is highlighted. It is clear from Figure 1A that addition of a solvent removes the barrier of the azeotropic condition. Figure 1B highlights through a ternary diagram that addition of the solvent causes the totally miscible binary liquid mixture (components 1 and 2) to split into two liquid phases, a solvent-rich phase and a solute-rich (1 or 2) phase.

Examples of industrial processes employing solvent-based separation techniques are numerous. Almost all chemical, petrochemical, biochemical and pharmaceutical processes employ one or more solvent-based separation techniques. In chemical and petrochemical processes, solvents are used mainly to separate components from liquid and/or gaseous mixtures, while in biochemical and pharmaceutical processes, solvents are typically employed for dissolving or removing solids. Use of a solvent to extract aromatic compounds from a petroleum by-product