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Review

Contributions of theory to method development in solid-phase extraction

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Abstract

The kinetic and retention properties of solid-phase extraction devices are reviewed from the perspective of method development strategies. Models based on frontal analysis are used to correct retention properties of solid-phase extraction devices to account for the fact that too few theoretical plates are provided for retention to be independent of kinetic factors. The available pressure drop for the sampling device largely dictates the choice of useful particle sizes and maximum bed length. The use of octanol–water partition coefficients and extrapolated values of the retention factor obtained by liquid chromatography are poor empirical models for the estimation of breakthrough volumes with water as the sample solvent. The solvation parameter model provides an adequate description of sorbent retention for the estimation of breakthrough volumes, rinse solvent volume and composition, and elution solvent volume and composition. Combining the frontal analysis and solvation parameter models offers a comprehensive approach to computer-aided method development in solid-phase extraction. This is the first step in the development of a structure-driven approach to method development in solid-phase extraction that should be more reliable and less tedious than traditional trial and error approaches.

Keywords: Reviews; Breakthrough volume; Sorbent retention; Solid-phase extraction; Method development

Contents

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1. Introduction

Solid-phase extraction for liquid samples became a widely used laboratory technique following the introduction in the 1970s of disposable sorbent cartridges containing porous particles sized to allow sample processing by gentle suction [1–4]. A typical solid-phase extraction cartridge consists of a short column (generally an open syringe barrel) containing a sorbent with a nominal particle size of 50–60 μm, packed between porous metal or plastic frits. A large number of sorbents are in use today corresponding to the desire for general purpose, class-specific and even compound-specific extractions [5–7]. In addition, several approaches to automation of solid-phase extraction based on robotics, dedicated instruments using flow-processing, and on-line analyzers with direct coupling of the extraction column to a chromatographic instrument have gained acceptance and are used in many laboratories [1,8,9].

The early 1990s saw the development of alternative sampling formats based on disk technology that have prospered to challenge the supremacy of cartridge devices for off-line sample processing [10,11]. Disk technology was conceived to tackle several problems encountered in the use of cartridges. Namely, slow sample processing rates, low tolerance to blockage by particles, the inadequate and variable packing density of cartridges, to minimize non-specific matrix adsorption, and to miniaturize sampling devices for processing small sample volumes. At least three different disk devices are commercially available. The particle-loaded membranes consist of 8–10-μm sorbent particles suspended in a web of PTFE microfibrils. The membranes have a homogeneous structure containing about 80% (w/w) or more of sorbent particles formed into circular disks 0.5 mm thick with diameters from 4 to 96 mm. Particle-embedded glass fiber disks contain 10–30-μm sorbent particles woven into a glass-fiber matrix available in a wide range of sizes [12]. Speedisks™ consist of a thin sandwich of 10-μm sorbent particles held between two glass-fiber filters with a screen to hold the filters in place [1]. Disk technology has gained acceptance for processing large sample volumes and small diameter disks for processing small samples, but otherwise cartridge devices are still dominant.

Sample processing in solid-phase extraction consists of four distinct steps. Initially, the sorbent is conditioned with solvent to improve the reproducibility of analyte retention and to reduce the carry through of sorbent impurities at the elution stage [1–4,13]. The conditioning solvent is then replaced with the same solvent as the sample solvent and the sample passed through the sampling device at a controlled flow-rate. Optionally, after the sample has been processed, the sorbent is rinsed with a weak solvent to displace undesired matrix components from the sorbent without displacing the analytes. Finally, the analytes of interest are eluted from the sorbent in a small volume of strong solvent for subsequent determination. The conditioning step is critically important for processing aqueous samples using particle-loaded membranes but is less important for other sampling devices except as a general approach to minimize contamination of extracts by sorbent impurities. The high surface tension of water combined with the microporosity of the particle-loaded membranes results in slow and uneven flow through the membrane and low analyte recovery if the membranes are not first conditioned with an organic solvent. For large sample volumes a small amount of the same organic solvent is usually added to the sample to maintain a constant sample flow-rate. The drying step between processing aqueous samples and eluting the retained analyte with a water-miscible organic solvent is also important. The purpose of the drying step is to reduce the volume of water retained by the eluting solvent. Excess water may interfere in further concentration of the eluent by the gas-blow down method. Other practical considerations associated with sample processing by solid-phase extraction are summarized in Table 1.

The general approach to method development in solid-phase extraction has remained rather empirical based on experimental trial-and-error procedures. General guides for sorbent selection, such as Fig. 1, can provide a useful starting point given a minimum amount of sample information. Structured empirical rules then permit the method development process to be completed in an ordered if inexact fashion [1–4]. The outcome is a recipe, hopefully for success, at the expense of the human and physical laboratory resources consumed. In any event, it is a tedious and time-consuming process bringing little personal

Table 1
Experimental variables that affect analyte recovery by solid-phase extraction

Conditioning solvent (typically 3–5 holdup volumes)
(a) Ensures reproducible retention and flow. Critical step for particle-loaded membranes
(b) Helps to minimize contamination of extracts by sorbent impurities
(c) Replace by sample solvent before processing sample
Flow rates (typical range 0.2–1.5 mm/s)
(a) More critical for cartridges than disks due to their variable and heterogeneous packing density (channeling)
(b) More critical when the sample volume exceeds the breakthrough volume as typical sampling devices provide too few theoretical plates for flow independent retention
Sample properties
(a) Dilute viscous samples with a weak low viscosity solvent to reduce sample processing time
(b) Remove excessive particle matter by filtration or centrifugation to maintain a constant sample-processing rate
(c) Add small volume of organic solvent (1–3%, v/v) to large volume water samples to ensure sorbent remains solvated and to maintain a constant (fast) sample-processing rate. Important for particle-loaded membranes
(d) Adjust pH to reduce ionization of weak acids and bases for reversed-phase sampling
(e) Maintain approximately constant ionic strength for samples and standards when using reversed-phase sampling conditions. Ionic strength is a critical parameter for ion-exchange extraction
(f) Deproteination of biofluids may be required for acceptable recovery of low-molecular weight analytes for reversed-phase sampling
(g) Precipitation of inorganic acids (sulphate, phosphate, etc.) by barium hydroxide is sometimes required for acceptable recovery of organic acids from biofluids using ion-exchange extraction
Drying time (typically 1–5 min, but sometimes considerably longer)
(a) Sufficient to remove all sample solvent trapped in the sorbent pores
(b) Excessive drying may result in low recovery of analytes from evaporation or retention in poorly solvated regions of the sorbent
Rinse solvent (optional)
(a) Small volume of intermediate strength solvent to elute matrix components. Analytes remain immobilized on the sorbent
(b) Biological fluids, plant extracts and soil extracts often require a rinse step but surface waters may not
Eluting solvent (ideally 2–3 holdup volumes but often larger)
(a) Should be a strong solvent able to displace all analyte from the sorbent in a small volume
(b) Normally should be volatile and miscible with the sample solvent

gratification. Alternative approaches based on computer-aided strategies and simulation require an appropriate level of theory so that at decision steps in the method development process fast simulation or calculation procedures can be used in place of trial-and-error experiments. Solid-phase extraction seems to have had minimal appeal to the theoretician in spite of its obvious importance as a general sample preparation procedure. Real progress towards a theoretical framework for optimization of the design of solid-phase extraction devices and the development of structure-based, computer-aided approaches to method development has taken place over the last few years with promises that a more rational approach to solid-phase extraction will soon be available. These studies are the feature of this review. Other articles in this issue cover solid-phase microextration, ion-exchange and ion-pair extraction, automation, and gas-phase sorbent trapping, which are not discussed here. Although not entirely restricted to the sorbent extraction of neutral compounds from water, this has been the application area most extensively studied within the framework of our review, and provides the major portion of the work reported here.

2. Identification of critical parameters for modeling in solid-phase extraction

Most of the parameters that describe the sequence of processing steps in solid-phase extraction are amenable to measurement by liquid chromatography or estimation using theoretical principles derived from the theory of liquid chromatography [4,14–16]. Analyte concentrations are generally low and the type and amount of sorbent required to isolate sufficient analyte for its convenient determination is indicated by the breakthrough volume for the sampling device. Ultimately, the sample volume that must be processed depends on the analyte concentration and the operating characteristics of the

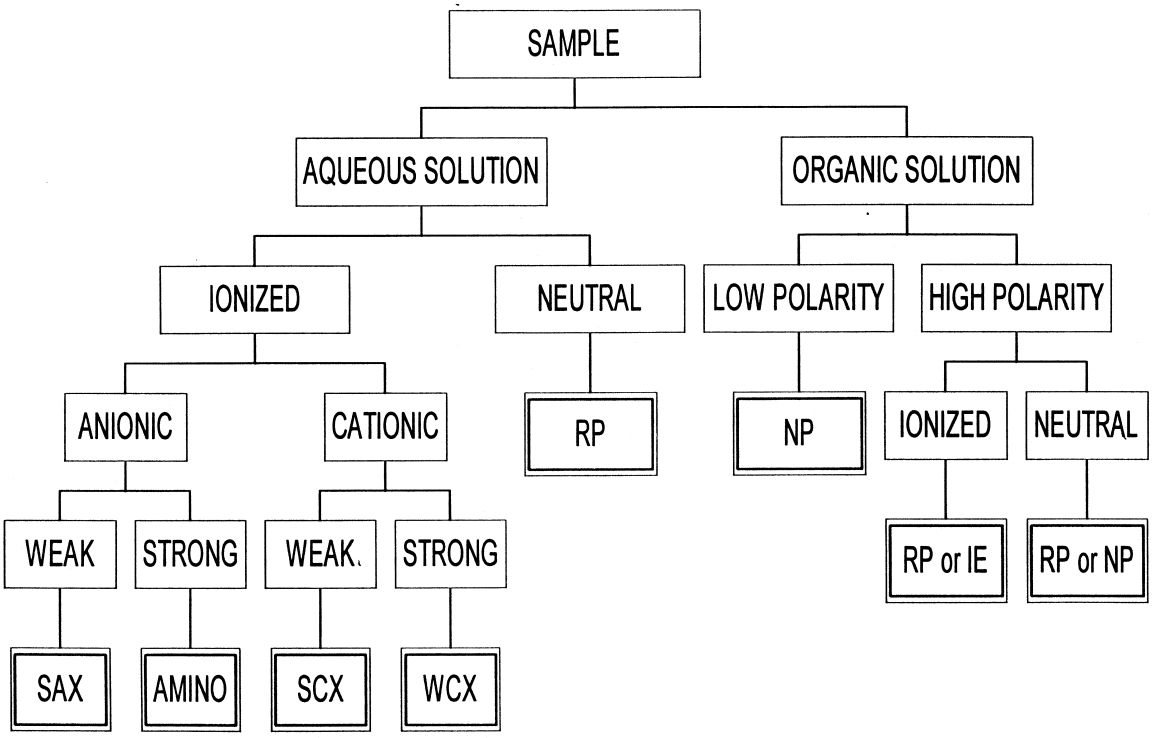

Fig. 1. Method selection guide for the isolation of organic compounds from solution. SAX, strong anion exchanger; SCX, strong cation exchanger; WCX, weak cation exchanger; RP, reversed-phase sampling conditions; NP, normal-phase sampling conditions; IE, ion-exchange sampling conditions.

instrument selected for the determination. The sampling device is required to accommodate this sample volume to deliver sufficient analyte for a secure determination. The analyte concentration is generally unknown, and this is the likely reason for analyzing the sample. Consequently, methods are generally established to ensure that if the sample contained more than a certain minimum analyte concentration then the analytical protocol would provide a secure method for its determination. Minimum analyte concentration limits may be set by regulatory authorities for monitoring purposes or are established from a knowledge of expected concentrations given the origin of the sample (e.g., a single dose of a drug given to an animal to study its clearance and excretion).

A rinse solvent may be selected for matrix simplification. The type and amount of sorbent is fixed by the isolation step so the need here is to optimize solvent composition to displace matrix components from the sorbent while leaving the analytes of interest immobilized on the sorbent. This can often be restated as the identification of the strongest solvent that eliminates matrix components from the sorbent without loss of analyte. This is largely dictated by analyte retention factors. Optimum conditions can be established by selecting eluting conditions that preserve a certain minimum value for the retention factor of the least retained analyte of interest.

To accomplish a significant concentration of the analytes of interest with minimal further sample manipulation it is desirable to recover the analytes in a small solvent volume. For this purpose it is necessary to identify a solvent composition in which the analytes have minimal retention factors. Generally the minimum elution volume that can be safely employed, unless backflushing is used, is about 2–3 times the holdup volume for the sampling device. This corresponds to a retention factor <2. If a

solvent is chosen for analyte elution that leaves some matrix components immobilized on the sorbent then matrix simplification is also achieved.

To select and optimize the sample processing conditions for solid-phase extraction requires knowledge of the retention properties of the analytes on the sorbent under different mobile phase conditions corresponding to sample application, rinse (matrix simplification) and elution. In addition, the sorption mechanism for sample application occurs according to the characteristics of frontal analysis and the rinse and desorption step by elution. Typical solid-phase extraction devices contain short sorbent beds and cannot be expected to provide many theoretical plates. Therefore, the possibility that retention may be influenced by kinetic properties has to be considered. These features are discussed presently. For completeness, we note early work on the optimization of solid-phase extraction processing conditions using liquid chromatography by Weidolf and Henion [17] and Casas et al. [18]. Weidolf and Henion used columns packed with a solid-phase extraction sorbent and HPLC to predict the composition of rinse and elution solvents for the isolation of conjugated steroids from equine urine. The volume and composition of the rinse solvent for matrix simplification was determined from the retention factor of the peak front of the analytes and the composition for elution from the retention factors for the peak tails in appropriate mobile phases. Casas et al. [18] proposed a method to establish the relationships between the composition of the strongest binary solvent allowing complete sorption and the weakest binary solvent causing instantaneous elution for a series of structurally related standards on a sorbent cartridge and the retention factor for the same standards determined by HPLC. From these relationships a model was obtained to predict the most suitable rinse and elution solvents for other compounds with a family resemblance to the standards from their HPLC retention factors.

3. Breakthrough volumes

The breakthrough volume is the most important characteristic parameter to determine the suitability of a sampling device for isolating the analytes of interest. The breakthrough volume is established from a breakthrough curve, as indicated in Fig. 2. In the initial sampling phase a sample of fixed concentration, and usually at a constant velocity, enters the sampling device. The analytes are quantitatively retained during the initial sampling phase by the sorbent up to the point that the sample volume exceeds the retention capacity of the sorbent. Further sample entering the sorbent bed will not be quantitatively retained by the sorbent and eventually the concentration of analytes entering and exiting the sampling device become identical. The point on the curve at which some arbitrary amount of sample is detected at the outlet of the sampling device is the breakthrough volume (V_B). Different specifications of the ratio of the inlet to outlet concentration in the definition of the breakthrough volume result in different values. Typically 1, 5, or 10% are selected. From an experimental point of view the chosen definition reflects the measurement difficulty of determining small changes in the concentration of the analytes at the outlet of the sampling device. From the perspective of modeling the breakthrough

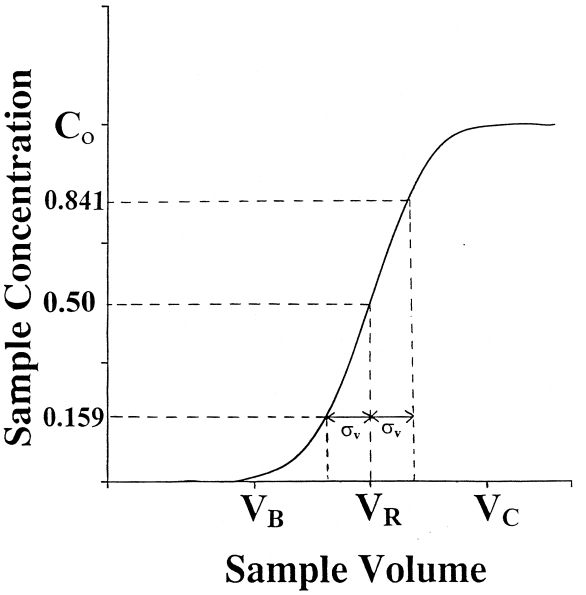

Fig. 2. Typical representation of a breakthrough curve. V_B is the breakthrough volume, V_R the chromatographic elution volume, V_C the sample volume corresponding to the isolation of the maximum amount of analyte, C_0 the concentration of analyte in the sample, and σ_V the standard deviation of the derivative curve for the plot.

process a value of 1% is generally chosen in keeping with the desire to define a maximum sample volume that can be processed with minimal (acceptable) loss of analyte.

The shape of the breakthrough curve is sigmoidal. A second point on the breakthrough curve, V_C, corresponds to the sample volume at which the retention capacity of the sorbent is saturated and the concentration of analyte exiting the sampling device is the same (actually 100−% used to define the breakthrough volume) as that entering the sampling device. It corresponds to the minimum volume of sample that will result in the isolation of the maximum amount of analyte by the sorbent. The point of inflection for the breakthrough curve corresponds to the chromatographic retention volume, V_R, since the first derivative of the breakthrough curve is a Gaussian distribution similar to the peak response observed during elution chromatography. This is true for typical columns used in HPLC but is not necessarily the case for sampling devices with low numbers of theoretical plates [19].

In general, there are two common causes of premature breakthrough in frontal chromatography. The retention capacity of the sorbent bed is overloaded due to a high concentration of either analyte or sorbed matrix components. This should not be a problem for trace analysis of environmental water samples where analyte concentrations are generally low and the matrix burden tolerable. Secondly, the sorbent bed may fail to adequately retain the analytes due to the provision of an insufficient number of theoretical plates for retention volumes to be independent of the plate count for the sampling device (Section 3.4).

3.1. Experimental determination of breakthrough volumes

Breakthrough volumes are typically determined in one of two ways [20,21]. The most straightforward is the direct method using either on-line or off-line detection. This is particularly convenient for precolumn sorbent traps used in on-line SPE-HPLC. A solution containing a constant concentration of analyte is pumped at a constant flow-rate through the precolumn, which is connected directly to the detector. The appearance of the analyte at the exit of the column bed is recorded producing a signal similar to that indicated in Fig. 2. The analyte concentration is selected such that it does not overload the sorbent while providing a reasonable detector response for ease of recording the breakthrough curve. Since the breakthrough volume may be flow-rate dependent the flow-rate used to record the breakthrough curve should be similar to the flow-rate used for sample application. In the absence of a suitable method for on-line detection the effluent from the sorbent bed can be collected by aliquots using a fraction collector and each aliquot analyzed separately to determine when breakthrough occurred [22].

For standard cartridge and disk devices off-line sample processing is commonly used. Samples are processed in aliquots and an off-line detection method used to determine the analyte concentration in the extracts recovered from each sample aliquot [13,23–25]. Aliquots are processed in the same way as regular samples. Each aliquot contains the same amount of analyte but in a different sample volume. Initially, an approximate value of the breakthrough volume is established by using decade changes in aliquot volumes, followed by a more systematic experimental design. For compounds with an estimated breakthrough volume between 0 and 50 ml, measurements are made at 2.5-ml volume increments, between 50 and 100 ml at 5-ml increments, 100 and 1000 ml at 10-ml increments, and >1000 ml at 100-ml increments. Plotting the observed recovery for the complete sampling process against the corresponding aliquot volumes generates the breakthrough curve. The breakthrough volume is estimated from the line representing the best fit through the experimental data.

A similar approach to the above has been used to determine the breakthrough volume of precolumn traps in on-line SPE-HPLC [26–29]. In this case the precolumn sorbent trap is connected to the analytical column through a selection valve that allows the sample to by-pass the analytical column during loading and the eluent for recovery to be switched to the analytical column for separation and determination. A small sample volume containing the analytes is pumped through the precolumn and the chromatogram obtained by on-line elution recorded. The initial sample volume is selected to be less than the breakthrough volume. Further sample volumes

are then prepared as multiples of the initial sample volume with each one spiked with a constant amount of analyte. Each sample is then processed as for the initial sample volume. Initially there will be no change in peak areas up to the breakthrough volume, then in each subsequent volume that exceeds the breakthrough volume there will be a decrease in peak areas in the chromatogram representing the loss of analyte from the precolumn due to its breakthrough. Plotting peak area for each analyte against the sample volume processed enables the breakthrough volume to be estimated from the breakthrough curve.

A mathematical model for estimating the breakthrough curve for precolumns used in SPE-HPLC was proposed by Ferrer et al. [30] based on the assumption that the continuous flow of a solution in frontal chromatography could be represented as the consecutive flow of many discrete volumes. Each volume injected gives a chromatographic peak separated from the next peak by the injection repetition rate. The sum of the individual peak areas measured at different mobile phase compositions simulates a breakthrough curve from which the breakthrough volume can be estimated.

3.2. Methods for estimating breakthrough volumes

The determination of breakthrough volumes, particularly by off-line methods, is time consuming and somewhat subjective. Consequently, methods that enable breakthrough volumes to be estimated from solute properties or calculated from models that require a minimal number of experimental measurements (Section 3.3) are useful. Early in the development of solid-phase extraction various relationships were sought between the breakthrough volume and the aqueous solubility of compounds [31–33]. These methods, although providing some rough agreement in a few cases, completely ignored the contribution of the sorbent to the retention process and are further limited by the availability and quality of solubility data, particularly for sparingly soluble compounds. Numerous methods exist for the estimation of aqueous solubility from structural parameters [34], which could fill the availability gap, but the lack of any quantitative fundamental relationship between solubility and the breakthrough volume diminishes the attraction of this approach.

Many regulatory agencies require the determination of the octanol–water partition coefficient ($\log P$ or $\log K_{OW}$) as a component of the approval process for the use of new chemical entities. The octanol–water partition coefficient has become a recognized parameter to estimate compound hydrophobicity of general importance for modeling numerous environmental and biological properties associated with the use and disposal of organic compounds [35,36]. Nakamura et al. [37] proposed a general guide for the selection of sample processing conditions for the isolation and recovery of agricultural chemicals from water based on estimated $\log K_{OW}$ values. A group of empirical rules were presented in the form of a decision tree and said to be useful for selecting reversed-phase sorbents and organic solvents to aid experimental trial-and-error approaches to method development. Hennion et al. [15] investigated the use of $\log K_{OW}$ to estimate $\log k_W$ (sorbent–water retention factor) for the purpose of modeling breakthrough volumes but concluded that it was of limited value. In Section 4.3 we will provide a fundamental argument for why $\log K_{OW}$ provides a poor surrogate model for the isolation of organic compounds from water.

3.3. Models for predicting breakthrough volumes

From the general theory of frontal chromatography it is possible to derive a relationship between the breakthrough volume and the sorption properties of solid-phase extraction devices [15,21,29,38–44]. At the 1% breakthrough level the breakthrough volume, V_B, is related to the retention volume, V_R, through Eq. (1):

$$V_B = V_R - 2.3\sigma_V \quad (1)$$

where σ_V is the standard deviation depending on the axial dispersion of the analyte along the sorbent bed (see Fig. 2) and is evaluated through Eq. (2):

$$\sigma_V = V_M(1 + k)/\sqrt{N} \quad (2)$$

where V_M is the interparticle volume of the sorbent bed (holdup volume), k the retention factor (capacity factor), and N the plate number for the sorbent bed calculated by Eq. (3):

$$N = V_R(V_R - \sigma_V)/\sigma_V^2 \quad (3)$$

In principle it should be possible to calculate V_B from Eqs. (1)–(3) by determining V_M and N for the sampling device and measuring V_R (or k) for the analytes of interest. N and V_M are easily determined for precolumn sorbent traps used in coupled SPE-HPLC by direct measurement since the on-line arrangement allows the recording of the breakthrough curves. There is no convenient way to make measurements of these parameters for off-line sampling conditions, and therefore estimates must be made from results obtained for the solid-phase extraction sorbent by HPLC [14,25,45]. Eqs. (1)–(3) are derived assuming that the conditions of linear chromatography apply and the plate count for the sorbent trap is reasonably large. Large sample amounts or strongly retained matrix components resulting in curved sorption isotherms [46] or sorbent beds with very low numbers of theoretical plates [19] may result in poor estimates of the breakthrough volume based on the above equations.

Lovkvist and Jonsson [19] proposed a model described by Eq. (4) to characterize the sampling properties of sorbent beds with a small number of theoretical plates that has been adopted by other groups [14,23,45,47–50] to calculate breakthrough volumes under solid-phase extraction conditions. The coefficients a_0, a_1, a_2 are characteristic of the breakthrough level and:

$$V_B = (a_0 + a_1/N + a_2/N^2)^{-1/2}(1 + k)V_M \quad (4)$$

are summarized in Table 2 [19]. Just as for Eqs. (1)–(3) the calculation of the breakthrough volume requires the determination of N and V_M for the sampling device and either a measurement or estimation of the retention factor. The influence of these parameters with respect to the performance of solid-phase extraction devices can now be discussed. The main requirements are the optimization of size (V_M and N), kinetic properties (N, particle size, flow-rate) and retention (N, k and V_M).

Table 2
Coefficients for the Lovkvist and Jonsson model, Eq. (4), for sorbent traps with small N values

Breakthrough level (%)	Coefficients		
	a_0	a_1	a_2
0.1	0.998	29.12	57.54
0.5	0.990	17.92	26.74
1.0	0.980	13.59	17.60
5.0	0.903	5.36	4.60
10.0	0.810	2.88	1.94

3.4. Optimization of physical properties for sampling devices

To maximize the breakthrough volume in the absence of any constraints Eqs. (1)–(4) indicate that the sampling device should have a large holdup volume (equivalent to stating that the sorbent bed should be large). The selected sorbent should provide a high retention of the analyte under the sampling conditions (large k) combined with a sufficiently large value for N that retention is largely independent of N. One could hope to maximize retention by sorbent selection but the other characteristic parameters of the sampling device will have to be arrived at through compromise.

For off-line or on-line sampling the sorbent bed cannot be too large because it is desirable to recover the analytes in a small solvent volume. In addition, in off-line sampling the pressure drop available to provide transport of the sample through the sampling device at an optimum or practical velocity is limited. The pressure drop per unit length of sorbent bed is given by Eq. (5) [51]:

$$\Delta P/L = u\eta\phi/d_P^2 \quad (5)$$

where ΔP is the pressure drop across a sorbent bed of length L, u the linear velocity of the sample solution through the sorbent bed, η the viscosity of the sample solution ($\approx 1\times10^{-3}$ N·s m^{-2} for an aqueous solution), ϕ the flow resistance parameter for the sorbent bed (typically 10^3 for cartridges and particle-loaded membranes [12,14,45,49,52]) and d_P the average particle size for the sorbent. A plot of $\Delta P/L$ against d_P is shown in Fig. 3 for different sample velocities corresponding to 0.11, 0.22, 0.43 and 1.08 mm/s. These values are equivalent to a sample flow-rate of 0.5, 1.0, 2.0 and 5.0, ml/min through a 1-cm diameter cartridge. For off-line sampling using cartridge devices the available pressure drop is limited to about 0.9 atm (as indicated in Fig. 3 for a 1-cm bed length). Although shorter and wider cartridges could be used to increase the sample

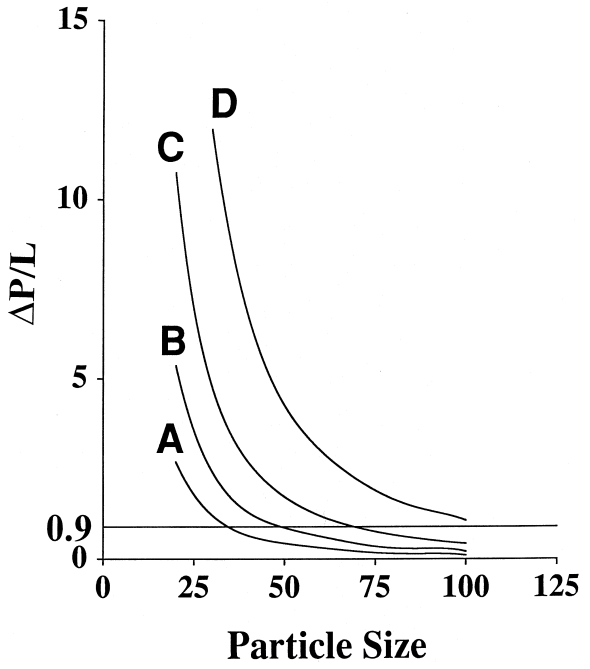

Fig. 3. Plot of ($\Delta P/L$) against the average particle size (d_p) for different linear velocities (u). $A=0.11$ mm/s, $B=0.22$ mm/s, $C=0.43$ mm/s and $D=1.08$ mm/s. The horizontal line represents the practical limit of 0.9 atm for a 1-cm bed length.

flow-rate the results shown in Fig. 3 are fairly typical of actual sampling conditions. In practice the available pressure drop limits cartridge sampling devices to particle sizes greater than about 40 μm with larger particles providing a wider and higher range of sample flow-rates. For a flow-rate of 1 ml/min and a sorbent bed of 1 cm diameter and 1 cm high the optimum particle size is ≈49 μm with a maximum pressure drop of 0.9 atm. Faster sample flow-rates require larger particles if the pressure drop cannot be increased. For on-line sampling using high-pressure pumps for sample application pressure is no longer the factor that dictates the particle size. In this case, particle sizes much smaller than those indicated for off-line sampling can be accommodated. These columns are also generally short to minimize sample desorption volumes. This results in conditions favorable for high sample processing rates. For off-line sampling the easiest solution to increase sample-processing rates is to increase the diameter of the sampling device at a constant bed height since the flow-rate is proportional to the diameter squared. This is conveniently achieved using particle-loaded membranes and particle-embedded glass fiber disks [12,49]. To operate with a low-pressure drop these materials are short (0.5 mm) and packed with small particles to provide reasonable efficiency. Membranes and disks with a 1-cm height and packed with cartridge-size sorbents would have an inconveniently large holdup volume requiring large solvent volumes for desorption. This represents a poor compromise and if large diameter devices are to be used they should be thin and packed with small diameter particles.

Sorbent cartridges with short beds packed with course particles, or for that matter, very short beds packed with fine particles, cannot be expected to provide large plate numbers. Fig. 4 provides a plot of plate height against interparticle mobile phase velocity, the velocity of mobile phase passing through the interparticle space, for several cartridge sorbents

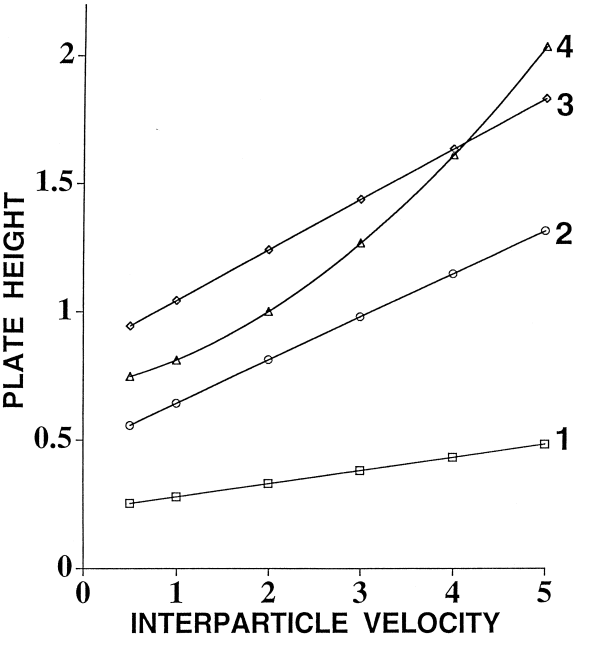

Fig. 4. Plot of the plate height (mm) against mobile phase interparticle velocity (mm/s) for silica-based cartridge sorbents. The test compound was anthracene and the mobile phase methanol–water (80:20, v/v). Identification: (1) octadecylsiloxane-bonded sorbent (light loading); (2) spacer-bonded propanediol sorbent; (3) cyanopropylsiloxane-bonded sorbent; and (4) butylsiloxane-bonded sorbent. (Reproduced with permission from Ref. [14]. Copyright Elsevier Science Publishers).

[14]. There is no observed minimum in the plots over the interparticle velocity range of 0.5–5.0 mm/s corresponding to a flow-rate of about 3–30 ml/min through a 1-cm diameter cartridge. The main contribution to the plate height arises from flow anisotropy in the packed bed and resistance to mass transfer. Over the velocity range indicated the various sorbents provide from five to 15 plates per centimeter of bed length for the butylsiloxane-bonded sorbent, six to 10 for the cyanopropylsiloxane-bonded sorbent, 10–20 for the spacer-bonded propanediol sorbent and 15–40 for the lightly loaded octadecylsiloxane-bonded sorbent [14,25,43,45,52–54]. If cartridges with a 1-cm diameter are operated at a low sample flow-rate of 1 ml/min they cannot be expected to provide more than about 20 plates per centimeter of bed length. At higher sample flow-rates only lower plate numbers are expected. Significant variation in the plate count as a function of the sample flow-rate is a likely cause of flow-rate dependence for breakthrough volumes (see later in this section). For sorbent beds with a low packing density even smaller plate numbers are to be anticipated. For example, it was shown that typical cartridges contain on average about 10–25% additional empty space compared to a stable consolidated sorbent bed [14]. The efficiency of these sorbent beds will be lower than indicated by Fig. 4 due, at least in part, to increased flow anisotropy and channeling.

The kinetic properties of particle-loaded membranes are different to those of cartridge sampling devices (Fig. 5) [49]. A minimum value for the plate height, corresponding to about seven particle diameters, is observed at an optimum interparticle velocity of about 0.19 mm/s. Fitting the data to the Knox equation indicates that the contribution of flow anisotropy is about three times greater and the contribution from resistance to mass transfer about an order of magnitude greater than predicted for a homogeneous consolidated bed. The heterogeneous structure of the membranes probably contributes unfavorably to their kinetic properties. Over the typical flow-rate range for a 47-mm diameter disk with a 38-mm active sampling area, 10–100 ml/min, the particle-loaded membrane will provide about four to nine theoretical plates, with the largest values in the region of the optimum flow-rate (about 13 ml/min).

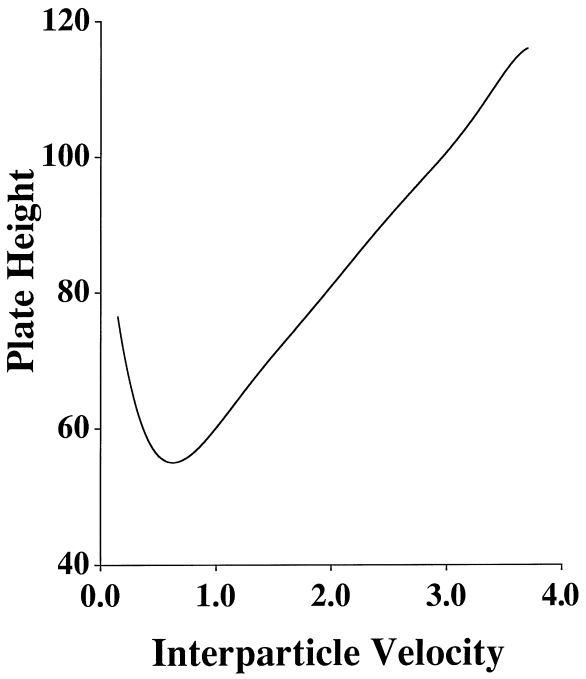

Fig. 5. Plot of the plate height (μm) against the interparticle mobile phase velocity (mm/s) for a particle-loaded membrane (velocity axis corresponds to a sample flow-rate of 0–100 ml/min for a disk with a 38-mm diameter active sampling area).

The influence of low plate numbers on breakthrough curves for solid-phase extraction devices can be calculated using Eq. (4). In Fig. 6, breakthrough curves are given for a sampling device with a holdup volume of 0.42 ml, a solute retention factor of 100, providing 5, 20 and 100 plates per cm bed length. Increasing plate numbers results in a sharper front boundary and a larger breakthrough volume (23 ml for $N = 5$, 34 ml for $N = 20$ and 40 ml for $N = 100$). Larger plate numbers are desirable for maximum sample retention but small values of N are capable of providing useful breakthrough volumes. In practice, typical sorbent cartridges and membrane devices used for off-line sampling provide values of N in the range of 5–30 where the breakthrough volume depends on the kinetic properties of the sampling device.

The flow-rate dependence of the breakthrough volume for cartridges arises because the plate height is (generally) linearly dependent on the mobile phase velocity for typical sample flow-rates. The break-

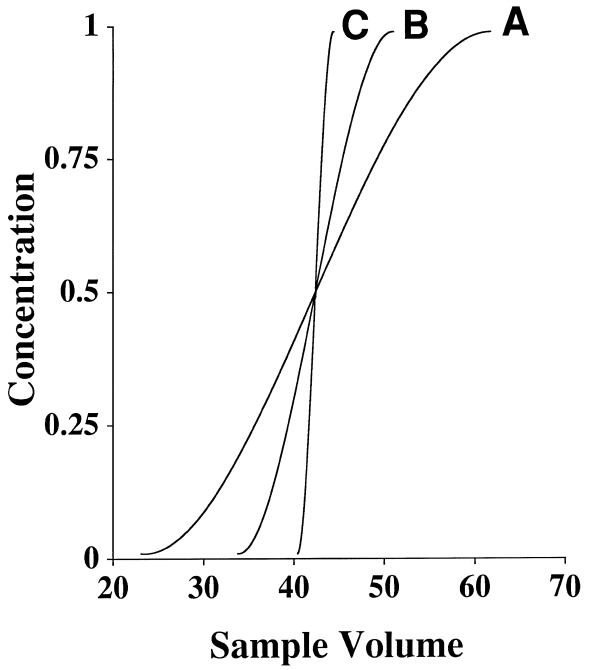

Fig. 6. Plot of the breakthrough curves for a sampling device with a holdup volume of 0.42 ml, retention factor 100, and five (A), 20 (B) and 100 (C) plates per cm of bed length.

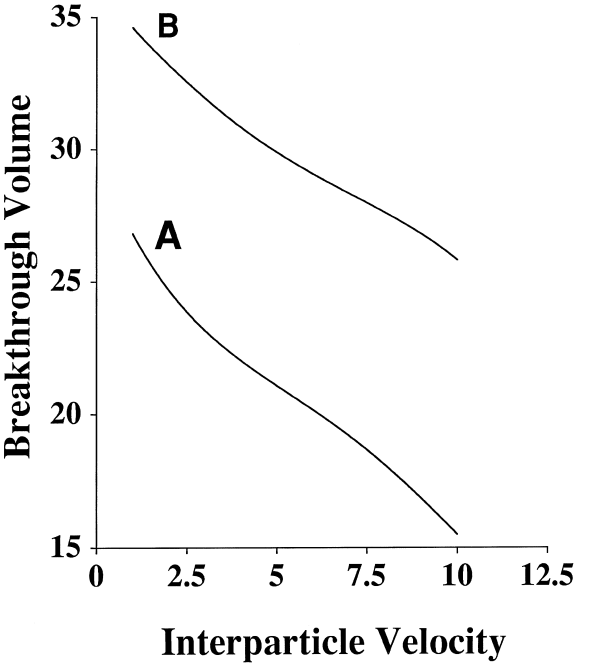

Fig. 7. Plot of the breakthrough volume against the mobile phase interparticle velocity for a cyanopropylsiloxane-bonded sorbent (A) and lightly loaded octadecylsiloxane-bonded sorbent (B). The data was modeled for a 1-cm diameter cartridge with a 1-cm bed length, holdup volume of 0.42 ml and a retention factor of 100. Plate height values were taken from Fig. 4.

through volume as a function of the mobile phase interparticle velocity (representing a flow-rate range of about 1–40 ml/min for a 1-cm diameter cartridge) for two sorbents is shown in Fig. 7. Curve A is for the cyanopropylsiloxane-bonded sorbent and curve B the lightly loaded octadecylsiloxane-bonded sorbent. In terms of kinetic performance they represent the extreme cases with the cyanopropylsiloxane-bonded sorbent providing from three to 10 plates over the velocity range illustrated and the octadecylsiloxane-bonded sorbent nine to 27 plates. There is a strong reduction in the breakthrough volume with increasing sample processing rates. There is no optimum value but the largest breakthrough volume is obtained at the lowest sample flow-rates. Similar effects are observed for particle-loaded membranes except in this case there is a maximum value for the breakthrough volume corresponding to the optimum sample flow-rate. Since the change in efficiency around the optimum value is shallow the breakthrough volume is not strongly affected by flow-rate in the range 10–30 ml/min assuming a 38-mm diameter active sampling area. At both higher and lower flow-rates a decrease in the breakthrough volume is observed.

When it comes to the recovery of analytes from the sorbent by elution in a small solvent volume it is necessary to consider the shape of the frontal elution curve as well as the retention capacity of the sorbent [42]. The required elution volume for 99% recovery of an analyte, V_E, on a sorbent trap with a low plate number is given by Eq. (6):

$$V_E = V_M[1 + k][1 + (2.3/\sqrt{N})] \quad (6)$$

The only practical way to minimize the volume of eluting solvent is to use a small sorbent bed (minimize V_M) and a strong solvent ($k < 3$ and ideally 0). Sorbent traps with relatively large values of N provide sharper desorption front profiles and require a smaller elution volume to quantitatively recover the analyte from the sorbent trap.

4. Sorbent retention

It is convenient to rearrange Eq. (4) into the general expression:

$$\log V = \log QV_M + \log(1 + k_S) \quad (7)$$

where V is either the breakthrough volume, volume of rinse solvent or elution volume, Q the contribution of kinetic factors to retention resulting from the small number of theoretical plates, V_M the holdup volume for the sorbent bed, and k_S the retention factor for the analyte with the sample solvent, rinse solvent or elution solvent as mobile phase. For a limited range of flow-rates and a specified sampling device, the product QV_M is approximately constant. Given the typical numerical values for QV_M it is easy for $\log(1+k_S)$ to become the dominant term in Eq. (7) and the most important factor determining the breakthrough volume. Changes in the holdup volume and plate number for the sorbent bed provide only an incremental change in $\log V$. On the other hand differences in the retention factor result in a selective change in $\log V$. Since the retention factor for a particular compound depends on its range of intermolecular interactions with the sorbent and sample solvent then sorbent selection should have a large influence on $\log V$ and the practical values for breakthrough, rinse and elution solvent volumes [25]. To maximize the breakthrough volume requires the selection of sample processing conditions that maximize the retention factor. The selection of a rinse solvent requires identification of experimental conditions that preserve a sufficiently large retention factor to avoid loss of analyte during the rinse step. The selection of the elution conditions requires identification of experimental conditions that minimize the retention factor. Methods that allow the measurement or estimation of retention factors for relevant sampling conditions are then of prime importance for method development in solid-phase extraction.

4.1. Experimental determination of retention factors

There are two general approaches for determining the retention factor of sorbents used for solid-phase extraction. The equilibrium method uses a fixed volume of sample solution with a known concentration of analyte that is continuously circulated by a mechanical pump through the sampling device and returned to the sample solution reservoir until a steady state is reached [43,44,55–58]. On-line monitoring of the analyte solution exiting the sampling device with a UV detector is one possible method to establish the time required to reach a steady state. Since mass transfer in liquids is slow this usually requires many hours. The sorbed amount of analyte for steady-state conditions is then determined by elution with a small volume of strong solvent using any suitable method for quantitation. Provided that the quantity of sorbed analyte does not exceed the linear portion of the sorption isotherm the retention factor can be calculated without resort to additional data other than the volume and concentration of the analyte in the sample solution, the holdup volume for the sorbent bed, and the amount of analyte taken up by the sorbent [43,58].

The alternative method of determining the retention factor is by direct measurement of retention in a typical chromatographic experiment [25,41,45,50,52,53,57,59,60] or forced-flow planar chromatography [12,49,61] in the case of particle-loaded and particle-embedded membranes. Columns are prepared by dry packing for sorbents typically used for off-line solid-phase extraction and by slurry packing for on-line precolumns. The choice between slurry packing and dry packing is based on the average particle size for the sorbent. Particles larger than about 20 μm being easily dry packed and smaller diameter particles requiring slurry packing [51]. Columns are usually 10–35 mm in length and of any convenient internal diameter. Larger diameter columns can be operated at higher flow-rates while minimizing extracolumn contributions to retention measurements. Compounds with retention factors up to about 10^4 can be determined in this way. It is possible to determine retention factors for more highly retained compounds but column residence times are inconveniently long. In practice, compounds with $k > 10^4$ are more than adequately retained for most likely sampling conditions and an accurate determination of their retention factor is rarely required. Of more general interest is the influence of sampling conditions and the choice of

sorbents in the $k < 10^3$ range, since this has a direct bearing on the suitability of a particular method.

4.2. Methods for estimating retention factors

There is nothing particularly difficult in determining retention factors using either the equilibrium method or the chromatographic method. Both methods are time consuming, however, and few experimental retention factors for conditions germane to solid-phase extraction are available in the literature compared to the number of sorbents in general use, even for compounds of broad interest. It has been more common to determine retention factors for the purpose of establishing the validity of general models for solid-phase extraction than to advocate their use as a general tool in method development. Methods that allow for the quick estimation of retention factors are then of interest to establish convenient approaches for method development in solid-phase extraction using models such as Eq. (7).

The general approach for estimating retention factors with sample solutions containing predominantly water is by extrapolation from retention factors determined at more convenient mobile phase compositions providing shorter separation times. Extrapolations are based on either linear, Eq. (8), or quadratic, Eq. (9), models:

$$\log k = \log k_W + S\phi_S \quad (8)$$

$$\log k = \log k_W + S_1\phi_S + S_2\phi_S^2 \quad (9)$$

where k_W can be considered as an equation intercept or identified as the retention factor for the analyte with water as the mobile phase, ϕ_S the volume fraction of organic solvent in a binary mixture of water and organic solvent, and the S coefficients are regression constants obtained by fitting the experimental data to the models. A comprehensive discussion of the validity of Eqs. (8) and (9) would be out of place here and only duplicate accounts provided elsewhere [4,15,36,57,62]. It is frequently assumed that $\log k_W$, the value of the retention factor required for the estimation of sampling conditions with water as a sample solvent, is independent of the mobile phase composition range and the relationship used for the extrapolation. This simple picture may conform to contemporary practice, but is far from adequate, and is difficult to justify.

Some typical plots of $\log k$ against mobile phase composition for an octadecylsiloxane-bonded silica sorbent with acetonitrile–water as mobile phase and a cyanopropylsiloxane-bonded silica sorbent with methanol–water as mobile phase are shown in Figs. 8 and 9, respectively. Most, but by no means all, $\log k$ against volume fraction of organic solvent plots are curved when volume fractions of organic solvent close to zero are included. A large contribution to this curvature is the change in phase ratio associated with significant changes in the composition and structure of the stationary phase in contact with predominantly aqueous mobile phases. For individual compounds linear, convex and concave plots are observed for the same sorbent and binary mobile phase. Different sorbents or mobile phases often produce different shaped plots for the same compound. Therefore, generalizations for individual solutes, sorbents, etc., cannot be made. For intermediate mobile phase compositions, an approximate linear

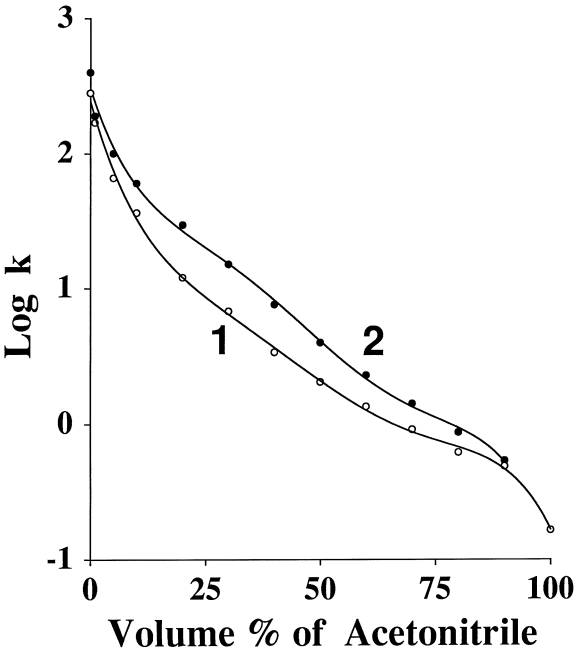

Fig. 8. Plot of the retention factor against percent volume fraction of acetonitrile in the mobile phase on a IST heavily loaded octadecylsiloxane-bonded silica sorbent for solid-phase extraction. Identification: (1) 2-phenylethanol and (2) benzonitrile.

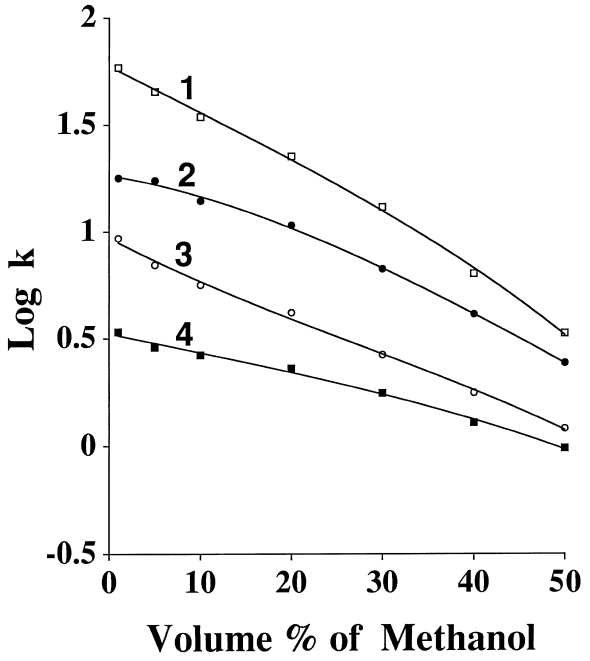

Fig. 9. Plot of the retention factor against the volume fraction of methanol in the mobile phase on a Bakerbond cyanopropylsiloxane-bonded silica sorbent for solid-phase extraction. Identification: (1) naphthalene, (2) bromobenzene; (3) acetophenone; and (4) 2-phenylethanol.

relationship between log k and the volume fraction of organic solvent can almost always be found. The intercept obtained by linear extrapolation, however, is generally different to the value obtained by curve fitting the experimental data when measurements at a low volume fraction of organic solvent are included. Also, quite different slopes, and therefore intercepts, are possible when different segments of the composition range are used for the linear extrapolation (see Figs. 8 and 9). When values for $\log k_W$ obtained by linear extrapolation, curve fitting, and experiment are compared there is often poor agreement between the results (Table 3) [15,36]. The agreement usually improves when results for low volume fractions of water are included in the extrapolation but this rather defeats the object of the extrapolation method since at low volume fractions of organic solvent separations times are long. In general, the linear extrapolation method provides a poor estimate of $\log k_W$ for most compounds. Curve fitting the experimental results for composition ranges including low organic solvent compositions provides better agreement but some significant differences still exist. Note that the curve fit results obtained using arbitrary functions providing the best statistical fit to the experimental data are superior to Eq. (9), which fails to provide a good fit to the data in a significant number of cases. It is unfortunate that no reliable method for determining $\log k_W$ by extrapolation exists, and the available approaches discussed above, result in both acceptable and poor estimates of $\log k_W$ without a method to distinguish into which category individual results fall. Because extrapolation methods provide unreliable estimates of $\log k_W$ with large errors likely in some cases, extrapolation methods cannot be used to estimate $\log k_W$ with any reasonable level of confidence.

A substantial body of work exists on the estimation of $\log k_W$ values from octanol–water partition coefficients [15,36,63–67]. Since these correlation models have been formulated most commonly on $\log k_W$ values obtained by the linear extrapolation method they possess all the deficiencies discussed above for extrapolation methods combined with the added uncertainty that arises from the quality of the fit of the correlation models. Individual models are needed for compounds lacking a family resemblance suggesting that these models are not rigorous chemical models. Literature values for the octanol–water partition coefficient vary widely with the method of measurement or calculation adding to the uncertainty when they are used to estimate values of $\log k_W$ [35,68]. Hennion et al. [15] concluded that $\log K_{OW}$ is of limited utility for the prediction of sample processing conditions for herbicides. Baltussen and co-workers [47,48] used $\log K_{OW}$ to represent the unknown partition coefficient for pesticides and polycyclic aromatic hydrocarbons between solid poly(dimethylsiloxane) particles and water. Eq. (4) provided the model for the breakthrough volume. Acceptable agreement between experimental and model predicted values for the breakthrough volumes was taken as confirmation that $\log K_{OW}$ provided a reasonable estimate of the poly(dimethylsiloxane)–water partition coefficient.

4.3. Solvation parameter model

The solvation parameter model provides a bridge

Table 3
Comparison of measured and extrapolated values for log k_w for an octadecylsiloxane-bonded silica sorbent

Compound	Log k_w Linear Eq. (8)[a]	Quadratic Eq. (9)[b]	Best fit[c]	Experimental
Methanol–water:				
2-Phenylethanol	2.00	2.36	2.36	2.45
4-Chlorophenol	2.52	2.50	2.45	2.73
4-Nitrobenzyl alcohol	1.58	2.15	2.43	2.40
Acetanilide	1.60	2.19	2.27	2.52
Acetophenone	2.26	2.81	2.89	3.01
Benzaldehyde	1.87	2.43	2.51	2.56
Hexan-2-one	1.91	2.49	2.57	2.62
Acetonitrile–water:				
2-Phenylethanol	1.27	2.05	2.23	2.45
4-Chlorophenol	1.81	2.35	2.35	2.73
4-Nitrobenzyl alcohol	1.21	1.89	1.98	2.40
Acetanilide	1.03	1.92	2.12	2.52
Acetophenone	1.71	2.33	2.63	3.01
Benzaldehyde	1.66	1.94	2.41	2.56
Hexan-2-one	1.74	2.31	2.50	2.62
Tetrahdrofuran–water:				
2-Phenylethanol	1.32	1.65	1.89	2.45
4-Chlorophenol	2.69	2.46	2.40	2.73
4-Nitrobenzyl alcohol	1.63	1.56	1.78	2.40
Acetanilide	1.04	1.39	1.60	2.52
Acetophenone	1.59	1.99	2.13	3.01
Benzaldehyde	1.56	1.74	1.77	2.56

[a] From 40 to 70% (v/v) methanol and acetonitrile and 30 to 60% (v/v) tetrahydrofuran.
[b] For the full data range from 1 to 100% (v/v) methanol and acetonitrile and 1 to 70% (v/v) tetrahydrofuran.
[c] Arbitrary mathematical functions were used that gave the best statistical fit to the full range of data from 1 to 100% (v/v) methanol and acetonitrile and 1 to 70% (v/v) tetrahydrofuran.

between compound structure and retention and can be used to estimate retention factors or distribution constants in chromatography and other two-phase distribution systems [36,69–78]. In solid-phase extraction it has been used to estimate breakthrough, rinse and elution volumes [12,14,23–25,45,50,52,53,59–61,79,80]. The appropriate form of the model for solid-phase extraction from a liquid phase is given by Eq. (10):

$$\log \mathrm{SP} = c + mV_X + rR_2 + s\pi_2^H + a\Sigma\alpha_2^H + b\Sigma\beta_2^H \quad (10)$$

The model equation is made up of product terms representing solute properties (descriptors) and system properties characteristic of the sampling system. Each product term represents the contribution of a defined intermolecular interaction to the correlated solute property (SP), in this case either the retention factor ($\log k$) or breakthrough, rinse and elution volumes ($\log V$) when $\log QV_M$ in Eq. (7) is approximately constant.

The solute descriptors in Eq. (10) are McGowan's characteristic volume V_X (in $\mathrm{cm^3\ mol^{-1}}/100$), excess molar refraction R_2 (in $\mathrm{cm^3}/10$), the solute's dipolarity/polarizability π_2^H, and the solute's effective hydrogen-bond acidity and hydrogen-bond basicity, $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$, respectively. McGowan's characteristic volume is an additive property and is easily calculated for any solute by summing the atomic volumes for all atoms and subtracting a constant amount for each bond [69,81]. The solute's excess molar refraction is calculated from its refractive index and characteristic volume as the difference in molar refraction of the solute and an *n*-alkane of identical volume [82]. The refractive index is almost

an additive property, and is easily estimated for any compound of interest from fragmental constants. The solute dipolarity/polarizability parameter can be obtained experimentally from gas–liquid chromatographic data or water-solvent distribution constants [71,83,84]. The solute's effective hydrogen-bond acidity and effective hydrogen-bond basicity were originally obtained directly from hydrogen-bond complexation constants in an inert solvent [85,86], but now that these scales are established, further values can be obtained by gas–liquid chromatography or through the use of water–solvent distribution constants [71,84]. For distribution systems containing water, some solutes (e.g., anilines, pyridines, and sulfoxides) exhibit variable hydrogen-bond basicity. For these solutes two different descriptors, $\Sigma\beta_2^H$ and $\Sigma\beta_2^0$, are used, with selection of the most appropriate descriptor based on the intended application. For aqueous samples $\Sigma\beta_2^0$ is the solute descriptor usually chosen while $\Sigma\beta_2^H$ is more appropriate for non-aqueous samples. Solute descriptors are available for about 4000 compounds [72] with others available through parameter estimates and by computational approaches [69–71,87,88].

The system constants in Eq. (10) are defined by their complementary interactions with the solute descriptors. The *r* constant determines the difference in capacity of the sorbent and sample solution to interact with solute *n*- or π-electrons; the *s* constant to the difference in capacity of the sorbent and sample solution to take part in dipole–dipole and dipole-induced dipole interactions; the *a* constant is a measure of the difference in hydrogen-bond basicity of the sorbent and the sample solution; the *b* constant is a measure of the difference in hydrogen-bond acidity of the sorbent and sample solution; and the *m* constant is a measure of the relative ease of cavity formation for the solute in the solvated sorbent and sample solution together with contributions from dispersion interactions that fail to cancel when the solute is transferred between phases. For any sampling system, the system constants can be obtained by multiple linear regression analysis of experimental retention properties acquired for a group of varied solutes with known descriptors.

The main criteria for solute selection to characterize a sampling system are that the solutes should be of sufficient number and variety to establish the statistical and chemical validity of the model; cross-correlation between individual descriptor values should be absent ($R^2 < 0.8$); and clustering of individual descriptor values should be avoided [78]. For statistical soundness three varied values for each solute descriptor and the intercept are a reasonable minimum number of data points to fit Eq. (10). However, since each solute expresses several interactions simultaneously, the minimum number of solutes required could be reduced from 18 to nine. Such small data sets rarely provide valid models, however, because of the lack of compensation for the uneven distribution of experimental error. It is, therefore, both sensible and prudent to seek an exhaustive fit. That is, a fit that shows little variation in the system constants as small groups of randomly selected solutes are sequentially removed from the model. This can usually be achieved using 20–30 varied solutes.

A plot of the system constants as a function of solvent composition provides a system map. System maps are the most useful approach for method development. A typical system map is shown in Fig. 10. The individual system constants usually change smoothly with composition and can be fit to simple linear or polynomial functions for computer-aided calculation of sampling properties. Once generated the system maps are permanent and can be used to estimate sample-processing conditions using Eqs. (7) and (10) for any analyte whose solute descriptors are known or can be reasonably estimated.

In general terms there are three regions of the system map of interest for method development in solid-phase extraction. The left-hand side of the map, corresponding to low organic solvent, is the region of interest for establishing a safe sampling volume. From system maps for different sorbents the preferred sorbent for the isolation step can be identified. The intermediate region of the system map is of interest for selection of the rinse solvent. The right-hand side of the system map is the region of interest for selecting solvent compositions for elution of the analytes from the sorbent by identifying conditions that minimize retention so that the sample can be recovered in a small volume of solvent. System maps for a heavy (A.D. Gunatilleka, C.F. Poole, unpublished results) and light loaded [25] octadecylsiloxane-bonded silica sorbent, for a butylsilox-

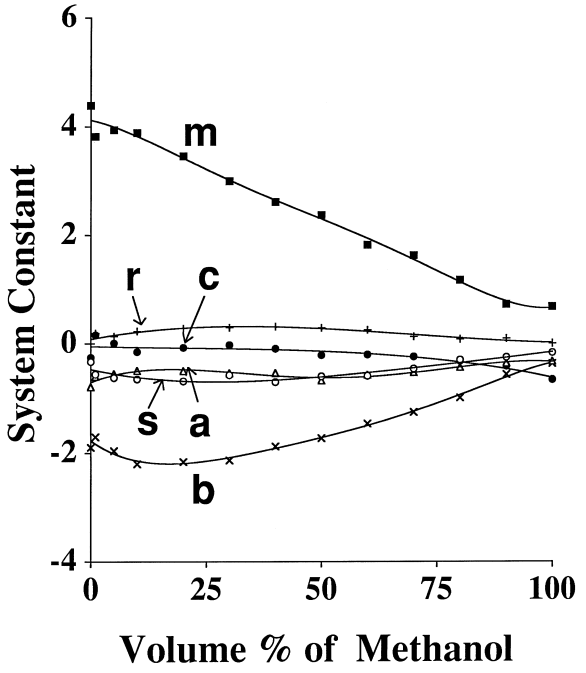

Fig. 10. System map for a heavily loaded octadecylsiloxane-bonded silica sorbent with methanol–water as the sample solvent.

ane-bonded [60], cyanopropylsiloxane-bonded [59], and spacer-bonded propanediol [53] silica sorbents, and for a macroreticular porous polymer [50] are available for several aqueous–organic solvent mixtures. Limited data are available for other sorbent types, generally restricted to predominantly aqueous organic solvents or water as the sample solvent.

Sorbent selection is based on identifying an appropriate sorbent that provides an adequate breakthrough volume for the analytes of interest in the solution to be processed. The required sample volume is established by the characteristics of the determination step. The breakthrough volume should be greater than the sample volume required to isolate sufficient analyte for convenient detection, identification and quantitation. The breakthrough volume can be calculated from Eq. (7) when the parameters for $\log QV_M$ are known or confidently estimated, as is generally the case, and only the retention factor need be calculated using Eq. (10) [25]. The system constants for a wide variety of sorbents used for solid-phase extraction with water or water containing 1% (v/v) methanol as the sample solvent are summarized in Table 4. Given that only system constants with a positive sign contribute favorably to sorbent retention we can obtain some general insight into the factors responsible for retention under reversed-phase sampling conditions. For all sorbents the cavity/dispersion term (*m* coefficient) is most important for promoting retention. All sorbents are at least as competitive as water for lone-pair electron interactions ($r=0$) and in some cases these interac-

Table 4
System constants for the estimation of solute retention in solid-phase extraction for aqueous samples (water or 1%, v/v, methanol in water)

Sorbent[a]	System constants						Refs.
	m	*r*	*s*	*a*	*b*	*c*	
IST C_{18} (HL)	4.39	0	0	−0.79	−1.90	−0.27	–[b]
JTB C_{18} (LL)	3.92	0	−0.11	−0.54	−1.53	−0.90	[25]
IST C_8	4.91	0	−0.84	−1.43	−2.27	−0.54	–[b]
IST CHX	3.94	0	−0.32	−0.83	−1.98	−0.31	–[b]
IST CH	3.22	0.35	0	−0.92	−1.61	−0.37	–[b]
JTB C_4	3.36	0	0	−0.46	−1.53	−1.38	[60]
JTB CN	2.06	0.53	0	−0.51	−1.45	−0.88	[59]
JTB DIOL	1.57	0.61	0	−0.45	−0.80	−1.05	[53]
PLRP-S	5.22	0.84	−0.49	−1.39	−4.01	−0.18	[50]
PGC	5.62	0	1.35	0	−3.54	−2.78	–[c]
AC	3.81	0	0.59	0	−3.06	−1.83	[80]

[a] IST, International Sorbent Technology; JTB, J.T. Baker; PLRP-S, Polymer Laboratories (styrene–divinylbenzene porous polymer); PGC, hypersil porous graphitic carbon; AC, activated charcoal; HL, high loading; LL, light loading; CHX, cyclohexanesiloxane-bonded; CH, phenylsiloxane-bonded; CN, cyanopropylsiloxane-bonded; and DIOL, spacer-bonded propane diol.

[b] A.D. Gunatilleka, C.F. Poole, unpublished results.

[c] R. Sethuraman, C.F. Poole, unpublished results.

tions contribute favorably to retention (r is positive), if only in a minor way compared to the cavity/dispersion term. In general, polar interactions favor transport in the sample solution and result in smaller breakthrough volumes. The exception is the carbon-based materials which have a significantly larger capacity for dipole-type interactions than water (s is positive). This is the distinguishing feature of carbon-based sorbents compared to porous polymer and chemically bonded silica sorbents and combined with a favorable cavity/dispersion term is the root of their high retention and different selectivity to the other sorbents. For the chemically bonded sorbents dipole-type interactions are of limited importance (s is either zero or small and negative). This is perhaps surprising for the cyanopropylsiloxane-bonded sorbents but is probably due to either selective solvation of the cyano group by water molecules or strong intermolecular interactions between neighboring cyano groups diminishing their availability for interactions with analyte molecules. The cyanopropylsiloxane-bonded and spacer-bonded propanediol sorbents have small values for the cavity/dispersion term compared to other chemically bonded sorbents indicating greater cohesion and a lower retention capacity. The greater cohesion of these sorbents easily eclipses their capacity for selective polar interactions with the result that they are less effective for the isolation of polar analytes from water than the alkylsiloxane-bonded sorbents. None of the sorbents are competitive with water for hydrogen-bond interactions except for carbon-based sorbents which are similar in their hydrogen-bond basicity ($a=0$). The general difficulty in isolating hydrogen-bond acid solutes arises because the b constant for all sorbents is numerically quite large and negative. The system properties most important for controlling retention are the high cohesive energy and hydrogen-bond acidity of water for which the solvated sorbents compete to varying extents but fail to dominate. Ironically, these properties are in opposition with respect to sorbent retention. The high cohesive energy of water promotes retention while the hydrogen-bond acidity of water is the principle reason for low retention of hydrogen-bond bases. The equation constant (c term) is not related to fundamental properties of the analytes but is clearly important in establishing retention. It is a complex combination of factors, one of which is the phase ratio for the sampling system when the retention factor or breakthrough volume is used as the dependent variable in Eq. (10).

To illustrate the role of sorbent selection on retention for aqueous samples a few representative calculations are summarized in Table 5. The importance of the cavity/dispersion contribution (mV_X), solvent hydrogen-bond acidity and solute hydrogen-bond basicity $(b\Sigma\beta)_2^H$ and the model constant term (c) to retention when water is the sample solvent is clearly indicated. In terms of maximizing retention the octadecylsiloxane-bonded silica sorbent (IST C_{18} HL), the porous polymer (PLRP-S) and the porous graphitic carbon (PGC) are superior to the other sorbents. Short-chain alkanesiloxane-bonded sorbents and chemically bonded sorbents with polar functional groups are not as retentive as the three sorbents identified above for sampling aqueous solutions. In terms of selectivity the porous polymer and porous graphitic carbon sorbent are preferred for solutes with low hydrogen-bond basicity. Porous graphitic carbon is particularly useful for the isolation of large solutes and solutes with significant dipolar character and low hydrogen-bond basicity (e.g., polycyclic aromatic compounds, steroids, etc.) Porous graphitic carbon is limited for the isolation of small molecules, unless they are considerably dipolar, such as acetanilide, because it has an unfavorable model constant (c term) which opposes the favorable cavity/dispersion contribution to retention. Thus porous graphitic carbon would be a good choice for the isolation of acetanilide but not the best choice for the isolation of phenol. In fact, none of the sorbents in Table 5 are particularly useful for the isolation of phenol due to its small size and capacity for hydrogen-bond interactions.

The above discussion has been limited to the isolation of solutes from water by solid-phase extraction. There are several additional factors to note. The solvation parameter model is strictly applicable to neutral compounds and ionizable compounds in their neutral form. Ionization tends to reduce retention compared to the neutral form of the solute in solid-phase extraction from aqueous solution. Recently, the solvation parameter model has been extended to the prediction of the retention of phenols in various states of ionization in liquid chromatog-

Table 5
Contribution of intermolecular interactions to retention of some varied solutes in solid-phase extraction with water (or water containing 1%, v/v, methanol) as the sample solvent

Compound	Sorbent	Contribution to log k_w						Predicted log k_w
		mV_X	rR_2	$s\pi_2^H$	$a\Sigma\alpha_2^H$	$b\Sigma\beta_2^H$	c	
n-Propylbenzene	IST C_{18} (HL)	5.00				−0.29	−0.27	4.40
	JTB C_{18} (LL)	4.46		−0.06		−0.23	−0.90	3.27
	IST C_8	5.59		−0.42		−0.34	−0.54	4.29
	IST CHX	4.49		−0.16		−0.30	−0.31	3.72
	IST CH	3.67	0.21			−0.24	−0.37	3.27
	JTB C_4	3.82				−0.23	−1.38	2.22
	JTB CN	2.20	0.33			−0.22	−0.88	1.44
	JTB DIOL	1.79	0.37			−0.12	−1.05	0.99
	PLRP-S	5.95	0.51		−0.25	−0.60	−0.18	5.43
	PGC	6.40			0.68	−0.53	−2.78	3.77
	AC	4.34			0.30	−0.46	−1.83	2.35
Benzonitrile	IST C_{18} (HL)	3.82				−0.63	−0.27	2.92
	JTB C_{18} (LL)	3.41		−0.12		−0.50	−0.90	1.89
	IST C_8	4.27		−0.93		−0.75	−0.54	2.05
	IST CHX	3.43		−0.36		−0.65	−0.31	2.11
	IST CH	2.80	0.26			−0.53	−0.37	2.16
	JTB C_4	2.93				−0.51	−1.38	1.04
	JTB CN	1.68	0.40			−0.49	−0.88	0.71
	JTB DIOL	1.37	0.45			−0.26	−1.05	0.51
	PLRP-S	4.55	0.62	−0.54		−1.32	−0.18	3.13
	PGC	4.90		1.50		−1.17	−2.78	2.45
	AC	3.32		0.65		−1.10	−1.83	1.04
Acetophenone	IST C_{18} (HL)	4.45				−0.91	−0.27	3.27
	JTB C_{18} (LL)	3.97		−0.11		−0.73	−0.90	2.23
	IST C_8	4.98		−0.85		−1.09	−0.54	2.50
	IST CHX	4.00		−0.32		−0.95	−0.31	2.42
	IST CH	3.27	0.29			−0.77	−0.37	2.42
	JTB C_4	3.41				−0.73	−1.38	1.30
	JTB CN	2.09	0.43			−0.70	−0.88	0.94
	JTB DIOL	1.59	0.50			−0.38	−1.05	0.66
	PLRP-S	5.29	0.69	−0.49		−1.92	−0.18	3.39
	PGC	5.70		1.36		−1.70	−2.78	2.58
	AC	3.86		0.60		−0.88	−1.83	1.75
Acetanilide	IST C_{18} (HL)	4.89			−0.40	−1.27	−0.27	2.95
	JTB C_{18} (LL)	4.37		−0.15	−0.27	−1.03	−0.90	2.02
	IST C_8	5.46		−1.17	−0.71	−1.52	−0.54	1.52
	IST CHX	4.39		−0.45	−0.42	−1.33	−0.31	1.88
	IST CH	3.58	0.30		−0.46	−1.08	−0.37	1.97
	JTB C_4	3.74			−0.23	−1.03	−1.38	1.11
	JTB CN	2.15	0.47		−0.26	−0.98	−0.88	0.50
	JTB DIOL	1.75	0.53		−0.23	−0.54	−1.05	0.47
	PLRP-S	5.81	0.73	−0.69	−0.70	−2.69	−0.18	2.28
	PGC	6.26		1.89		−2.37	−2.78	3.00
	AC	4.24		0.83		−2.05	−1.83	1.19
Phenol	IST C_{18} (HL)	3.40			−0.47	−0.57	−0.27	2.09
	JTB C_{18} (LL)	3.04		−0.10	−0.32	−0.47	−0.90	1.25
	IST C_8	3.80		−0.74	−0.86	−0.68	−0.54	0.98
	IST CHX	3.05		−0.28	−0.50	−0.59	−0.31	1.37
	IST CH	2.50		0.28	−0.55	−0.48	−0.37	1.38
	JTB C_4	2.60	−0.28			−0.47	−1.38	0.47
	JTB CN	1.49	0.43		−0.31	−0.44	−0.88	0.29
	JTB DIOL	1.22	0.49		−0.27	−0.24	−1.05	0.15
	PLRP-S	4.05	0.68	−0.44	−0.83	−1.24	−0.18	2.04
	PGC	4.36		1.20		−1.06	−2.78	1.72
	AC	2.95		0.53		−0.92	−1.83	0.73

raphy by use of an additional solute descriptor in Eq. (10) [89,90]. This approach has not been applied to solid-phase extraction but there is no reason to believe that it would not be equally applicable. Silica-based sorbents contain a low concentration of silanol groups with sufficient ion-exchange capacity to adsorb basic solutes [91–94]. The properties of these sites are not included in the solvation parameter model and are a potential source of disagreement between experiment and model predictions for easily protonated solutes. A general cause of low recovery of these compounds is not premature breakthrough but strong retention that prevents high recovery of the solutes by elution with an organic solvent. This problem can sometimes be circumvented by addition of a competing base to the elution solvent. It is common practice to use binary solvent mixtures for method development in solid-phase extraction. Retention in ternary solvent mixtures can be predicted using the solvation parameter model and a mixture design approach to define the system surfaces obtained [77,95].

System maps with methanol–water mixtures are available for particle-loaded membranes [14,61] and particle-embedded glass fiber discs [12,14] containing octadecylsiloxane-bonded silica sorbents. Particle-loaded membranes containing porous polymer sorbent particles are more retentive for most solutes than those containing octadecylsiloxane-bonded sorbent particles [61]. Solvent effects are very significant for the porous polymer containing membranes, which are capable of absorbing organic solvent from the sample solution changing their selectivity and phase ratio [24]. One percent organic solvent is used to increase the sample processing rate with particle-loaded membranes and the selective uptake of the organic solvent by the porous polymer particles resulted in differences in breakthrough volumes exceeding an order of magnitude depending on the identity of the solute and organic solvent. The solvation parameter model provided the necessary theoretical framework to enable the most favored sample processing solvent to be identified for a particular application.

As a demonstration experiment Seibert and Poole [25] used Eq. (7) and the solvation parameter model, Eq. (10), to predict the sample processing conditions for the isolation of estrogens from urine. System maps were used to determine breakthrough volumes for sample processing, the composition and volume of rinse solvents for matrix simplification, and the composition and volume of elution solvents. The plot of sample solvent composition against log V for three estrogens on an octadecylsiloxane-bonded silica sorbent is shown in Fig. 11. A sample volume of 45 ml of urine was required to provide a sufficient amount of estrogens for analysis. Consequently, a minimum breakthrough volume for estriol of 45 ml, the least retained of the estrogens, is required of the sampling device. As shown in Fig. 11 this can be achieved at any sample solvent composition containing less than 25% (v/v) methanol in water. A rinse solvent volume of 6 ml was selected for matrix simplification. From Fig. 11 a rinse solvent containing up to 40% (v/v) methanol can be used without breakthrough of estriol. The most retained of the estrogens is estrone and the solvent composition required for elution of all estrogens can be predicted from the retention properties of this compound. Pure methanol

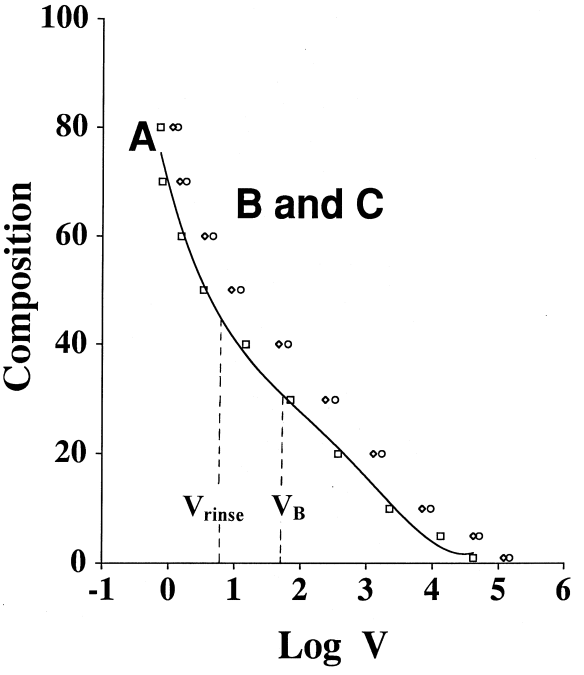

Fig. 11. A plot of methanol–water composition against log V (Eq. 7) for estriol (A), 17β-estradiol (B), and estrone (C) on an octadecylsiloxane-bonded silica sorbent. V_B indicates the required breakthrough volume and V_{rinse} the composition of the rinse solvent for matrix simplification.

was selected as the elution solvent to minimize water contamination of the extract, which interfered in the derivatization step required for gas chromatography. It was estimated that about 4 column void volumes were required for quantitative recovery of estrone. The good agreement between model predictions and experiment was taken as confirmation of the success of the approach. The authors note that the simple theoretical framework provides a significant step forward towards computer-aided method development in solid-phase extraction.

The solvation parameter model provides a general framework to explain why the octanol–water distribution constant provides a poor tool for the prediction of sample processing conditions in solid-phase extraction of aqueous samples. The system constants for the octanol–water partition coefficient ($\log K_{OW}$) are well established [36,71]. To construct a correlation model so that $\log K_{OW}$ can be used to estimate $\log V$ or $\log k$ the minimum requirement is that the ratio of the system constants for the systems to be correlated are (nearly) identical. The system constant ratios for the octanol–water partition coefficient and sorbents for solid-phase extraction are summarized in Table 6. For all 11 sorbents there is only a poor match between the solvation properties of wet octanol and the sorption properties of the solvated sorbents. The only likely correlation is for solutes with minimum polarity since all solutes with a significant capacity for dipole-type and hydrogen-bond interactions are expected to exhibit different solvation properties towards wet octanol and the sorbents indicated in Table 6. The general case is that $\log K_{OW}$ is not expected to provide a reasonable model for the estimation of sampling conditions for the common sorbents used in solid-phase extraction.

Table 6
System constant ratios for the octanol–water partition coefficient and solid-phase extraction sorbents with water or 1% (v/v) methanol in water as the sample solvent

System	System constant ratios (solvation parameter model)			
	r/m	s/m	a/m	b/m
Octanol–water	0.147	−0.276	0.08	−0.908
IST C_{18} (HL)	0	0	−0.18	−0.43
JTB C_{18} (LL)	0	−0.03	−0.14	−0.39
IST C_8	0	−0.17	−0.29	−0.46
IST CHX	0	−0.08	−0.21	−0.50
IST CH	0.11	0	−0.29	−0.50
JTB C_4	0	0	−0.14	−0.46
JTB CN	0.26	0	−0.25	−0.70
JTB DIOL	0.39	0	−0.29	−0.51
PLRP-S	0.16	−0.09	−0.27	−0.77
PGC	0	0.24	0	−0.63
AC	0	0.15	0	−0.80

System maps and single solvent composition models for normal-phase sampling conditions are few in number [53,79,96–98]. The driving force for retention under normal-phase conditions is the capacity of the solvated sorbent for polar interactions; in contrast to extraction from water the cavity/dispersion term (m constant) is generally unimportant or negative. As would be expected, the main contribution to retention on aminopropylsiloxane-bonded phases is the high basicity of the solvated sorbent (a constant). For the cyanopropylsiloxane-bonded sorbent it is the capacity of the solvated sorbent for dipole-type interactions (s constant). For the spacer-bonded propanediol sorbent it is the capacity for hydrogen-bond interactions, particularly as a hydrogen-bond acid (b constant), combined with a significant capacity for dipole-type interactions (s constant) that are important. In effect, the reasons for choosing a particular sorbent for extraction from an organic solvent are completely different to those for water with most of this difference attributed to the unique properties of water. Although the solvation parameter model can model retention on chemically bonded sorbents using organic solvents it is possible that the model does not correctly account for differences in solute size and sorbent site-specific interactions when silica gel is the sorbent [96].

5. Other approaches

Hughes and Gunton [99] proposed a graphical method to estimate the volume and solvent strength of rinse and elution solvents in solid-phase extraction based on an extension of the classical theory of liquid–liquid extraction. This leads to the equation:

$$\ln(1 - R_T) = n \ln(1 - R_0) + \ln R_{RET} \quad (11)$$

where R_T is the total extraction recovery, n the number of extractions, R_0 the extraction efficiency,

and R_{RET} the limiting extraction recovery used to account for irreversible solute retention by the sorbent. A plot of $-\ln(1-R_T)$ against n (or the equivalent volume of rinse or elution solvent) yields a straight line from which the extraction efficiency and the R_{RET} factor are calculated from the slope and intercept, respectively. Within this model favorable conditions for matrix simplification are recognized as those in which the extraction efficiency (slope of the plot) is low for the analytes and high for the matrix in the rinse step and high for the analytes in the elution step. In practice the plots are often non-linear but this does not prevent a qualitative assessment of the recovery and matrix simplification procedure being graphically evaluated from the experimentally derived curves.

6. Conclusions

Steady progress has been made towards the development of computer-aided method development strategies for solid-phase extraction as a replacement for traditional trial and error approaches. Contemporary models based on frontal analysis to accommodate the contribution of kinetic factors to retention resulting from the small number of theoretical plates provided by sorbent sampling devices and the solvation parameter model for the prediction of sorbent retention are the most promising. Current evolutionary development of the solvation parameter model towards computational approaches to the estimation of solute descriptors from compound structure would further enhance its use in method development for solid-phase extraction. At the same time estimation methods based on octanol–water partition coefficient and extrapolated retention factors ($\log k_W$) have to be considered more circumspect as lacking a sound theoretical basis as well as associated experimental uncertainties.

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