# 13 Membrane Extraction in Preconcentration, Sampling, and Trace Analysis

Jan Åke Jönsson and Estelle Larsson

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13.1 INTRODUCTION

The use of membranes for extraction in analytical chemistry has been increasing during recent years. The main intention is to selectively extract and enrich compounds to be determined (analytes) from chemically more or less complex samples. In contrast to many technical uses of membranes, in analytical applications, it is imperative to recover as efficiently as possible the extracted analytes so they can be transferred to suitable analytical instruments for the final determination in a quantitative way. Another difference from technical uses is that the volume scale is small; extracts are seldom larger than a milliliter, often only several microliters.

Membrane techniques have a number of clear advantages over other extraction techniques used in analytical chemistry. These advantages especially concern selectivity, enrichment power, and automation potential but also economy and occupational health aspects.\textsuperscript{1–10}

13.1.1 SAMPLE PREPARATION FOR ANALYSIS AND SAMPLING

In most cases of chemical analysis, some kind of sample preparation is necessary. One intention could be to bring the sample into a physical form, which is suitable for the further application of an instrumental technique for the final determination. This could be made by, for example, grinding, dissolution, combustion, and filtration. In many cases, for example, as a preparation for gas chromatographic analysis, analytes need to be transferred from the original matrix (e.g., water) to a solution in an organic solvent, often even involving a chemical reaction (derivatization) to improve detectability and solubility. For the determination of analytes in very low concentrations (trace analysis), it will be necessary to enrich or preconcentrate the analyte, that is, increase its concentration to measurable levels. For analysis of complicated samples (e.g., biological or environmental origin), it is additionally crucial to perform cleanup procedures, whereby the concentrations of the analytes are increased relative to the matrix, that is, a selective enrichment of the analytes.\textsuperscript{11–14}

Several types of sampling tasks could involve various types of extraction at the sampling site. This would be the case in integrating sampling, where the mean concentration over a period of time or over an area is sought or when a speciation sampling is attempted, that is, where the aim is to determine not only total concentrations but also equilibria (dissolved–bound, different dissociation conditions, different redox conditions, etc.).

For many of these sample preparation tasks, various types of extraction (phase-transfer) procedures are used, such as classical liquid–liquid extraction (LLE)\textsuperscript{15–17} in different physical formats, solid-phase extraction (SPE),\textsuperscript{18–20} solid-phase microextraction (SPME),\textsuperscript{21,22} and others, when studying aqueous and other liquid samples. For solid samples, the classical technique is Soxhlet extraction, although techniques such as pressurized liquid extraction (PLE) and supercritical fluid extraction (SFE) are widely used today.\textsuperscript{23}

The conventional extraction techniques have a number of drawbacks. The most obvious one is that relatively large volumes of organic (often chlorinated) solvents are used. This aspect is easily illustrated by comparing the relevant U.S. Environmental Protection Agency (EPA) sample preparation protocols. For example, in a generic EPA SPE procedure (Method 3535),\textsuperscript{24} 85 mL of organic solvent is needed for the extraction of 1 L of water sample (30 mL for elution, 55 mL for washing and conditioning). Method 3510, which is the corresponding LLE method, is applicable to many more analytes. It requires 180 mL of organic solvent, which is more, but not dramatically so. In both these methods, the volume of the extract is reduced to 1–10 mL before analysis by evaporation. This applies to each sample, and an environmental laboratory handles thousands of samples. The use of large volumes of solvents leads to a significant expense, especially as high-purity solvents are demanded, and also to concerns for occupational safety and for general environmental pollution. These techniques are also quite labor intensive and difficult to automate why an important area of current research in analytical chemistry aims to the development of alternative extraction techniques meeting some of the disadvantages mentioned. These activities are somewhat moderated by the fact that the area of chemical analysis (especially regarding environmental and pharmaceutical applications, but also in other areas) is heavily regulated by various international and local rules, leading to that the acceptance of new technology is very slow and costly.

13.1.2 MEMBRANE EXTRACTION SYSTEMS

In all types of membrane extraction, the membrane separates the sample phase (often called donor or feed solution) from the acceptor or strip phase, and the analyte molecules pass through the membrane from the donor to the acceptor. This process is often called pertraction (Latin per-traho, by analogy with the derivation of the term extraction from ex-traho).\textsuperscript{25} The membrane extraction techniques can be divided into porous and nonporous membrane techniques. Another distinction is between one-, two-, and three-phase membrane extraction techniques. In Figure 13.1, schematic diagrams of the various phase arrangements are shown.

Typical examples of one-phase techniques are filtration and dialysis. The membrane is porous, so there is a liquid (or gas) contact through the pores between the donor and acceptor phases, which are of similar chemical composition (i.e., both of them are aqueous, organic, or gaseous). There is no phase boundary, and therefore no partition between phases so physical and not chemical properties govern the process. This review will not consider one-phase systems further. For information on dialysis, especially its analytically interesting version microdialysis, see the literature.\textsuperscript{26,27}

Nonporous membrane techniques involve two or three different phases separated by distinct phase boundaries. In three-phase membrane systems, a separate membrane phase is surrounded by two different liquid phases (donor and acceptor) forming a system with two-phase boundaries and
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thus two different extraction (partition) steps. These can be tailored to different types of chemical reactions, leading to a high degree of selectivity. The membrane phase can be a liquid, a polymer, or a gas, and the donor and acceptor phases can be either gas or liquid (aqueous or organic). Liquid membrane phases are often arranged in the pores of a porous hydrophobic membrane support material, which leads to a convenient experimental system, termed supported liquid membrane (SLM). There are several other ways to arrange a liquid membrane phase between two aqueous phases as will be described in the following.

In two-phase membrane systems, one of the surrounding phases is the same as the membrane phase, so there could be, for example, an organic solvent both in the membrane pores and in the acceptor, while the donor is aqueous or gaseous. There is only one phase boundary and, consequently, only one partition equilibrium. This technique is chemically analogous to LLE in separation funnels.

13.1.3 Membrane Devices for Sample Preparation

13.1.3.1 Flat-Sheet Devices

Classically, flat-sheet porous polytetrafluoroethene (PTFE) or polypropylene membranes are used as support for the membrane liquid and mounted in holders (cells, contactors) permitting one flow channel on each side of the membrane

![FIGURE 13.1 Schematic pictures of different membrane extraction phase systems. (a) One-phase membrane extraction (dialysis), (b) three-phase polymeric membrane extraction, (c) three-phase SLM extraction, and (d) two-phase SLM extraction system (MMLLE). (From Comprehensive Sampling and Sample Preparation, Jönsson, J.Å. (J. Pawliszyn and H. Lord, eds.), Membrane extraction: General overview and basic techniques, pp. 461–474, Copyright 2012, with permission from Elsevier.)](image1)

instruments, and thereby provide good possibilities for automated operation. Drawbacks of this type of devices are relatively large costs and limited availability, as well as some carry-over and memory problems since the membrane units are utilized many times, necessitating a cleaning between each extraction.

### 13.1.3.2 Hollow-Fiber Devices

In another type of membrane extraction devices, porous polypropylene hollow fibers are used, often in a disposable way, which minimizes carry-over problems and reduces costs. On the other hand, manual manipulations are needed, limiting the possibility for automation. With these devices, the extraction can be carried out in a static mode, either in large sample volumes, where the extraction is not intended to be complete, or in small volumes aiming for complete extraction. Usually stirring is applied to increase the speed of mass transfer. Some typical practical arrangements are shown in Figure 13.3. This type of SLM extraction is often called hollow-fiber liquid-phase microextraction (HF-LPME) or three-phase liquid-phase microextraction or two-phase liquid-phase microextraction, but the terminology in this active field of research has not settled. Also hollow fibers can be connected in flow systems.

### 13.1.4 Equilibrium and Trapping

After an extraction system has been left for enough long time, equilibrium between the phases is reached and mass transfer of the extracted compounds from the donor to the acceptor has stopped. This is the natural end point for the extraction in many cases. In the majority of applications, however, the extraction is stopped well before equilibrium is attained, as this often results in procedures that are more efficient in terms...
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of time and convenience. In analytical chemistry, a usual aim of the sample preparation is to transfer (recover) as much of the analyte as possible from the donor to the acceptor in order to maximize sensitivity and minimize detection limits. This recovery can be improved in principally two ways: the acceptor can be continuously changed or continuously flow past the membrane, so extracted molecules are removed from the membrane surface by convection. This typically leads to a dilution of the analyte. Alternatively, and more efficiently, the analyte molecules can be trapped in a static acceptor by a chemical reaction (e.g., dissociation) or by exploiting a high distribution coefficient. This usually leads to enrichment, and with an efficient trapping reaction, there is a potential of obtaining very high enrichment factors.

To improve the mass transfer of the analyte that is extracted, a flowing donor is often used; that is, the sample is pumped past the donor side of the membrane in a dynamic flow system. Also static systems with a stagnant donor are common, often with convective mixing by stirring.

This chapter will mainly cover extraction systems with liquid membrane phases and trapping in the acceptor. Two- and three-phase systems are compared, as well as dynamic and static systems and flat versus hollow-fiber membrane materials. These types of systems have been successfully applied to a number of analyte and sample types and can be important alternatives to more older approaches to sample preparation.

13.2 VARIANTS OF MEMBRANE EXTRACTION

A number of nonporous membrane techniques with different phase systems have been suggested for sample preparation in analytical chemistry. The main versions are summarized in Table 13.1 and described in the following sections.

13.2.1 LIQUID MEMBRANE EXTRACTION TECHNIQUES

In all liquid membrane extraction techniques, the membrane is an organic liquid, which is in contact with the aqueous sample. Analytes are extracted either by simple partitioning of uncharged species into the organic phase or by the action of some extractant, a compound present in the membrane liquid that can form complexes with the analyte, thereby facilitating its transport into the membrane liquid. So far, this is in principle the same as classical LLE. The difference between the various liquid membrane extraction techniques refers mainly to the acceptor side of the membrane.

13.2.1.1 Three-Phase Liquid Membrane Extraction

With three-phase liquid membrane extraction techniques, there is a stagnant aqueous acceptor phase, constantly in contact with the liquid membrane, and the analytes are, after travelling through the membrane, transferred to the aqueous acceptor phase. The composition of the acceptor phase is such that the analyte molecules, after entering the acceptor phase, become nonextractable, for example, by pH changes (for acids or bases) or by a complexation reaction. This is referred to as trapping and it results in a transport of analyte molecules from the donor to the acceptor phase, which after the extraction can be transferred to an analytical instrument, either manually or online by a flow system. Trapping is crucial for the success of the three-phase liquid membrane extraction. By means of suitably selected acceptor conditions, it is possible to tune the mass transfer process and to obtain the desired selectivity and degree of enrichment for a number of useful applications.

13.2.1.1 Supported Liquid Membrane Extraction

In SLM extraction, the most widely applied type of three-phase membrane extraction, the membrane consists of an organic solvent, which is held by capillary forces in the pores of a hydrophobic porous membrane supporting the membrane liquid. Such membrane support can be either flat porous PTFE or polypropylene membrane sheets or porous polypropylene hollow fibers. Typical solvents are long-chained hydrocarbons like n-undecane or kerosene and more polar compounds like di-n-hexyl ether and di-octyl phosphate. Various additives can increase the efficiency of extraction considerably. The stability of the membrane depends on the

| TABLE 13.1 |
| Different Types of Membrane Extraction |

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Names Used</th>
<th>Abbreviation</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three-phase liquid membrane extraction</td>
<td>Supported liquid membrane extraction</td>
<td>SLM</td>
<td>[6,98]</td>
</tr>
<tr>
<td>Aq/org/aq</td>
<td>Three-phase liquid-phase microextraction</td>
<td>LPME3</td>
<td>[9,29,99]</td>
</tr>
<tr>
<td></td>
<td>Continuous flow liquid membrane extraction</td>
<td>CFLME</td>
<td>[91]</td>
</tr>
<tr>
<td>Two-phase liquid membrane extraction</td>
<td>Microporous membrane liquid–liquid extraction</td>
<td>MMLLE</td>
<td>[6,100]</td>
</tr>
<tr>
<td>Aq/org/org (org/org/aq)</td>
<td>Two-phase liquid-phase microextraction</td>
<td>LPME2</td>
<td></td>
</tr>
<tr>
<td>Three-phase solid membrane extraction</td>
<td>Polymeric membrane extraction</td>
<td>PME</td>
<td>[44]</td>
</tr>
<tr>
<td>Aq/polymer/aq or org/polymer/aq or aq/polymer/org</td>
<td>Membrane extraction with a sorbent interface</td>
<td>Mesi</td>
<td>[93,101]</td>
</tr>
</tbody>
</table>

* First ref. for analytical sample preparation, recent review.
solubility and volatility of the organic liquids, and it is generally possible to obtain membrane preparations that are stable up to several weeks.

13.2.1.2 Nonsupported Liquid Membrane Extraction

In addition to SLM, which is the most commonly used three-phase extraction principle, at least in analytical chemistry, other ways of placing an organic phase between two aqueous phases are known. In the classical bulk liquid membrane (BLM) setups, U-tubes or similar devices are used to confine bulk volumes of organic liquids between two aqueous phases. This type of devices is very little used for sample preparation in analytical chemistry, as the extraction process becomes slow and the enrichment factors possible are very limited.

Some devices, which permit the stacking of an aqueous acceptor phase above an organic liquid above an aqueous donor phase, have been described. Such systems are of course inherently physically unstable, especially when stirring, but some success with such principles has been shown.

A liquid membrane configuration that is frequently used for technical applications is the emulsion liquid membrane (ELM) systems where the acceptor phase is dispersed as a colloid phase, each colloid drop surrounded by a thin organic, surface active phase. This principle does not seem to have been used for analytical sample preparation, probably due to the difficulty of quantitatively recovering the disperse acceptor phase.

13.2.1.2 Two-Phase Liquid Membrane Extraction Systems

Two-phase liquid membrane extraction systems can be seen as a variant of SLM, where both the membrane (located in the pores of a hydrophobic porous membrane support) and the acceptor phases consist of an organic solvent. This is mainly suitable for hydrophobic analytes that are nondissociable and noncharged. These compounds are easily extracted from water to an organic solvent, but they cannot be back-extracted into a second aqueous phase as required by the SLM approach.

This is chemically the same principle as for conventional LLE but can be performed in a flow system, which permits easy automation and interfacing to analytical instruments. This technique is most easily interfaced to gas chromatography (GC) or to normal-phase high-performance liquid chromatography (NP-HPLC), as the extract ends up in an organic phase. In principle, the membrane could also be hydrophilic, which would lead to an aqueous phase in the membrane pores. This seems not yet to have been tried for analytical purposes.

LLE in a flow system (in the form of flow injection analysis) has been described many times as reviewed by Valcárcel and Luque de Castro, but then the organic and aqueous phases are mixed in the same flow channel and later separated. The practical problems with the phase separation seem to have prevented this technique to be widely used. Applying a membrane, the phases are never mixed and all mass transfers between the phases take place at the membrane surface.

As with three-phase membrane extraction, it is also here possible to work with flat membranes or with hollow-fiber membranes. In the first case, the technique is usually called microporous membrane liquid–liquid extraction (MMLLE), a name originating from Cussler et al. With hollow fibers, it can be called two-phase liquid-phase microextraction.

With two-phase liquid membrane extraction as with classical LLE, the extraction efficiency is limited by the partition coefficient. If this is very high, it is possible to work with a stagnant acceptor and still obtain a considerable enrichment into a small extract volume. With smaller partition coefficients, it might be necessary to arrange the acceptor phase to move with a slow flow rate in order to successively remove the extracted analyte and maintain the diffusion through the membrane. This will then lead to a lower degree of enrichment. The situation is similar to that for dialysis, and various focusing approaches can be applied to improve it, such as an SPE column or a retention gap.

13.2.2 Solid (Polymeric) Membrane Extraction Techniques

A number of applications with polymeric membranes have been described. The most commonly used membrane material is silicon rubber or polyethylene. The possibility for both aq/polymer/aq extraction (including trapping in the acceptor, very similar to SLM extraction) and also, for example, aq/polymer/organic extraction (similar to MMLLE) has been demonstrated.

Melcher et al. first described both these principles in cylindrical configurations, utilizing thin silicone tubes in flow systems. More recently, Hauser et al. introduced the principle of membrane-assisted solvent extraction (MASE), which comprises a polypropylene bag in an autosampler vial with an organic solvent inside the bag. This device is commercialized by Gerstel (Mülheim an der Ruhr, Germany).

In the aq/polymer/organic situation, the organic solvent typically penetrates the polymer causing it to swell considerably, and the situation is very similar to that of MMLLE. With a fixed composition of the membrane, the possibilities for chemical tuning (such as application of carriers) of the separation process are greatly reduced compared to SLM or MMLLE. Also, as diffusion coefficients in polymers are lower than in liquids, the mass transfer is slower, leading to slower extractions. On the other hand, as the membrane is virtually insoluble, any combination of aqueous and organic liquids can be used, and the entire system becomes very stable.

13.3 Theory and Principles of Membrane Extraction

13.3.1 Principles of SLM

An SLM extraction can be seen as a combination of extraction into an organic solvent followed by a back extraction into a second aqueous phase. However, as these two extraction
steps occur simultaneously, the mass transfer kinetics will be
different, and generally more efficient, compared to the situation
when the steps are performed in sequence in separation
funnels. The general mass transfer theory for SLM extraction
in flow systems has been described in detail,48 with some
additional aspects described more recently.49 A review on the
topic was recently published.10
The rate of mass transfer from donor to acceptor (in any
membrane extraction system) is proportional to the concentra-
tion difference, $\Delta C$, of the diffusing species over the mem-
brane, which can be written as follows:

$$\Delta C = C_D - \frac{1}{D} C_A$$

(13.1)

where

$C_D$ and $C_A$ are the total concentrations in the donor and
acceptor phases, respectively

$D$ is the equilibrium distribution constant between the
acceptor and the donor phases

In SLM, $D$ is given by the following expression:

$$D = \frac{C_A}{C_D} = \frac{\alpha_D K_D}{\alpha_A K_A}$$

(13.2)

where

$\alpha_D$ and $\alpha_A$ are the fractions of the analytes that are in
extractable (usually uncharged) form in the indicated
phase

$K_A$ and $K_D$ are the acceptor/membrane and donor/mem-
brane partition coefficients (i.e., pertaining to the
uncharged form only), respectively

Note that in many cases, it will be a good approximation that
$K_A = K_D$ as both the donor and acceptor phases are aqueous
and deviations from this equality will be mainly due to ionic
strength effects. Thus, the main influence in determining the
value of $D$ will be shown by the $\alpha$-values, which, for example,
for acids or bases, can easily be varied over many orders of
magnitude by selecting suitable pH values. Often, the extraction
conditions are set up so that $\alpha_D$ is close to 1 and $\alpha_A$ is a
very small value. $C_A$ is zero from the beginning of the extract-
ion and increases successively, usually to values well over
$C_D$. The maximum enrichment factor, which is reached when
there is a thermodynamic equilibrium between all phases, is
equal to $D$ as in Equation 13.2. In contrast to the conditions
for classical LLE and also MMLLE, high partition coeffi-
cients are not essential for high enrichment factors in SLM
extraction.

The rate at which the equilibrium conditions are approached
depends on many parameters, as detailed elsewhere48 for
the case of systems with flowing donor and stagnant accep-
tor. Briefly, two situations can be distinguished: membrane-
controlled extraction and donor-controlled extraction.

In the first case, the rate-limiting step is the diffusion of the
analyte compound through the membrane. The mass transfer
coefficient $k_M$ is then proportional to $K_D D_M h_M$, where $D_M$
is the diffusion coefficient in the membrane and $h_M$ is the thick-
ness of the membrane.

With donor-controlled conditions, typically a consider-
ably higher mass transfer rate can be obtained. It is then
limited by the diffusion in the donor phase and thus depends
on the diffusion coefficient in the donor phase, $D_D$, and on
the donor convection (flow, stirring, etc.) conditions. As a rule
of thumb, the donor-controlled extraction conditions prevail when $K_D$
is larger than about 10, while the mass transfer is mainly mem-
brane controlled when $K_D < 1$. It is found that the value of the partition coefficient has no large
influence on the efficiency of extraction or the enrichment
factors that can be obtained, as long as it is reasonably large.
On the other hand, the rate at which equilibrium is reached
will be influenced by the partition coefficients. Further,
there are observations that too large partition coefficients
are not favorable, as the transfer of analyte out of the mem-
brane into the acceptor phase in those cases may become
less efficient.

13.3.2 Chemistry of SLM Extraction

For SLM extraction, a number of chemical principles can be
used, which can be summarized according to Table 13.2 and
detailed as follows.

13.3.2.1 Simple Permeation: Acids and Bases

Many applications of SLM extraction in analytical chemis-
try concern the extraction of acids or bases. Here, the basic
principle is that uncharged species can be extracted from
an aqueous phase into an organic solvent phase, while the
charged species stay in the aqueous phase. This principle is
well known from classical LLE, where it is common prac-
tice to extract acids from acidic samples and back-extract
the acids into a second alkaline aqueous phase, using solvents
like n-hexane, diethyl ether, etc.

For an acidic analyte HA, the $\alpha$-factors mentioned earlier
will take the following form:

$$\alpha = \frac{[HA]}{[A^-][HA]} = \frac{1}{1 + 10^{(pK_a - pH)}}$$

(13.3)

and for a basic analyte B,

$$\alpha = \frac{[B]}{[BH^+][B]} = \frac{1}{1 + 10^{(pK_b - pH)}}$$

(13.4)

where

$pK_a$ is the acid dissociation constant (for a base for the
corresponding acid)

$pH$ refers to either the donor or acceptor phase
From Equations 13.2 through 13.4 follows the expression for the overall distribution constant at equilibrium for the extraction from the donor to the acceptor:

\[ D = \frac{C_A}{C_D} = \frac{\alpha_D K_D}{\alpha_A K_A} \left( \frac{1 + 10^{\alpha(pH_A-pK_a)}}{1 + 10^{\alpha(pH_D-pK_a)}} \right) \left( K_D \right) \]  

(13.5)

where \( s = 1 \) for acids and \( s = -1 \) for bases and, as the aforementioned, usually \( K_A \approx K_D \).

Knowing the pK\(_a\) of the compound to be extracted and the pH of the phases, it is easy to calculate the overall distribution constant and thus the maximum enrichment factor possible in the case of SLM extraction of acids or bases with simple permeation.

### 13.3.2.2 Carrier-Mediated Transport: Metal and Organic Ions

Ion-pairing or ion-chelating reagents can be added to the donor phase, which permits SLM extraction of various metal ions. Different carrier molecules or ions can be incorporated into the membrane phase to enhance selectivity and mass transfer. Various trapping reagents in the acceptor phase prevent analytes to be extracted back into the membrane. There are several reviews in this field.\(^{58-61}\)

As an analytical example of an addition of a reagent to the donor phase, extraction of metals from solutions containing a complex former as 8-hydroxyquinoline can be mentioned.

**TABLE 13.2**

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Donor</th>
<th>Membrane</th>
<th>Acceptor</th>
<th>Transported Species</th>
<th>Trapping</th>
<th>Refs.</th>
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</thead>
<tbody>
<tr>
<td>Simple permeation</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Acids</td>
<td>Acidic</td>
<td>Org (+TOPO)</td>
<td>Basic</td>
<td>Neutral</td>
<td>Anions</td>
<td>[6,102]</td>
</tr>
<tr>
<td>Bases</td>
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<td>Org</td>
<td>Acidic</td>
<td>Neutral</td>
<td>Cations</td>
<td>[6]</td>
</tr>
<tr>
<td>Carrier-mediated transport</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metal ions</td>
<td>8-Hydroxyquinoline</td>
<td>Org</td>
<td>DTPA</td>
<td>Complexes</td>
<td>Charged complexes</td>
<td>[53]</td>
</tr>
<tr>
<td>Metal ions, amino acids</td>
<td>Acidic, pH = 3</td>
<td>DEHPA</td>
<td>Acidic, chloride</td>
<td>Complexes</td>
<td>Cations</td>
<td>[60]</td>
</tr>
<tr>
<td>Amino acids: amino</td>
<td>Basic</td>
<td>Triocetylmethylammonium</td>
<td>Acridic, pH = 0</td>
<td>Ion pairs</td>
<td></td>
<td></td>
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<tr>
<td>phophonates</td>
<td></td>
<td></td>
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<td>Amino acids</td>
<td>Basic</td>
<td>Pd complex</td>
<td>Acid</td>
<td>Complexes</td>
<td>Cations</td>
<td>[106,107]</td>
</tr>
<tr>
<td>Sugars, diol-containing</td>
<td>Neutral</td>
<td>Boronic acid carrier</td>
<td>Acid</td>
<td>Covalently bound complexes</td>
<td>Protonation of carrier</td>
<td>[108,109]</td>
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<td>compounds</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Anionic surfactants</td>
<td>Acidic + amine</td>
<td>Org</td>
<td>Basic</td>
<td>Ion pairs</td>
<td>Deprotonation of amine carrier</td>
<td>[62]</td>
</tr>
<tr>
<td>Immunological trapping</td>
<td>Neutral</td>
<td>Org</td>
<td>Atrazine antibodies</td>
<td>Permeation</td>
<td>Immunological as antigen–antibody complex</td>
<td>[63]</td>
</tr>
</tbody>
</table>

**Abbreviations:** TOPO, trioctylphosphine oxide; DTPA, diethylenetriaminepentaacetic acid; DEHPA, diethylhexylphosphoric acid.

**FIGURE 13.4** Membrane extraction schemes for metal ions (Me). HQ = 8-hydroxyquinoline, DTPA\(^{3-}\) = diethylenetriaminepentaacetic acid anion, R\(_2\)N\(^+\) = methyltrioctylammonium cation, HD = DEHPA. For (a) through (c), see the text.
This reagent forms extractable complexes with many metals.\textsuperscript{53} See Figure 13.4a. The complex will be transported through the membrane, and the extracted analyte is trapped in the acceptor by another ligand, in this case diethylentriaminepentaacetic acid (DTPA), which forms a stronger complex that is charged and therefore nonextractable.

A carrier can be added to the membrane phase in several ways. A common compound is Aliquat-336 (methyltrioctylammonium chloride). This is a tertiary ammonium ion, which is permanently positively charged in ion pair with chloride and can thus be added to a suitable membrane solvent. After addition of thiocyanate ions to the donor, a negatively charged metal–thiocyanate complex is formed in the donor and can be extracted as ion pair with the Aliquat-336 cation. It was used for the extraction of Cu, Cd, Co, and Zn\textsuperscript{52} and for CrO\textsubscript{3}\textsuperscript{2−}.\textsuperscript{54} The metal ion is subsequently trapped in the acceptor using DTPA as described earlier and shown in Figure 13.4b.

Analogous principles have been used to extract also organic compounds, for example, amino acids\textsuperscript{65}\textsuperscript{−67} and peptides.\textsuperscript{66}\textsuperscript{,}\textsuperscript{67} In a basic donor, the extracted compounds are anionic and thus easily transported through the membrane by means of the cationic carrier to the acidic acceptor, where the analytes become cationic and thus nonextractable.

Another commonly used extraction reagent for metal ions is diethylhexyl phosphoric acid (DEHPA).\textsuperscript{58}\textsuperscript{,}\textsuperscript{59} See Figure 13.4c. In this case, a pH gradient must exist over the membrane, so the acceptor is kept more acidic than the donor (typically pH \(\approx 1\) and 3, respectively). Speciation of different chromium species (chromate and chromium ion) has been performed by the combination of two membrane extraction systems: one working with DEHPA for extraction of Cr\textsuperscript{3+} and the other with Aliquat-336 for extraction of the CrO\textsubscript{2}\textsuperscript{−} ions.\textsuperscript{54} Using the same principles, also organic compounds, such as amino acids\textsuperscript{60} and polyamines,\textsuperscript{61} can be extracted.

### 13.3 Analyte Trapping in SLM

In order to reach a concentration enrichment using SLM for the purpose of sample pretreatment for chemical analysis, the concept of trapping is imperative. It is necessary that the analyte that has reached the acceptor phase is in one way or the other prevented from diffusing back into the donor, so that a steady mass transfer of analyte, against a gradient of total analyte concentration, is maintained for sufficient time in order to permit a substantial concentration enrichment factor.

#### 13.3.3.1 Direct Trapping

The simplest principle for analyte trapping was described in Section 13.2.1.1. In order to perform enrichment of an acidic compound, the pH of the acceptor is held enough alkaline, so the main fraction of the acidic analyte becomes charged and thus nonextractable in the acceptor. This is analogous with the principle of back extraction in LLE, where an organic extract of an acidified sample is extracted with a second aqueous phase, in order to isolate acidic compounds.

The principle of this type of direct trapping is described by Equations 13.3 through 13.5, showing the influence of pH on the extractability of acidic (or basic) compounds. If the donor pH is selected less than or equal to the pK\textsubscript{a} and the acceptor pH > pK\textsubscript{a} + 3.3, the distribution coefficient between acceptor and donor at equilibrium (Equation 13.5) will be about 2000, promising potentially very high concentration enrichment factors. This is termed complete trapping.

Extracting an acid from an acidic donor to a basic acceptor brings about a cotransport of protons through the membrane, eventually neutralizing the pH gradient, the reason why it is imperative for good success that the buffer capacity of the acceptor is sufficient. Conversely, the extraction of a basic compound from a basic donor to an acidic acceptor will transport protons in the opposite direction.

Other variations of the principle to render the analyte nonextractable in the acceptor involve the use of complexing agents. These form charged complexes in the acceptor, preventing back extraction. The use of DTPA for trapping of metal ions, as described in Section 13.3.2.2, is a good example on this.

#### 13.3.3.2 Indirect Trapping

In systems employing carrier-mediated transport of the analyte through the membrane, the analyte trapping can be made in a somewhat different way, where the transporting properties of the carrier is influenced, so it can transport the analyte from the donor to the acceptor, but not the other way. An example is the use of DEHPA, for metal extraction, where the carrier is anionic at donor conditions, permitting transport to the strongly acidic acceptor where the carrier is neutralized, preventing back extraction of the analyte. Here is a countertransport of protons due to the pH gradient that drives the extraction, while the analyte is in the same form both in the donor and in the acceptor.

There are other versions of a similar principle. For the extraction of anionic surfactants,\textsuperscript{62} which are permanently charged, trihexyl amine was used as a carrier. The carrier is added to the sample in the donor. In the acidic donor, this amine is charged and can form an ion pair with the analytes, while in the alkaline acceptor, the amine is neutralized, thus killing the ion pair.

#### 13.3.3.3 Immunological Trapping

To utilize the high degree of selectivity possible with biological recognition in sample preparation, SLM extraction was combined with immunologic recognition, both by using antibodies as trapping reagent in the acceptor and by exploiting the antibody–antigen complex in a flow immunoassay, for successful determination of both p-nitrophenol\textsuperscript{63} and atrazine.\textsuperscript{64} In a recent development utilizing magnetic beads with antibodies, simazine was determined in low concentrations.\textsuperscript{65}

#### 13.3.4 Mass Transfer in MMLLE

For two-phase liquid membrane extraction, MMLLE, the basic principles are more simple than those for SLM, as there is only one phase boundary involved in the extraction, usually
from an aqueous to an organic phase, which is chemically equivalent to LLE in a separatory funnel. The extraction is driven by the difference in chemical potential of the analytes in organic solvent and in aqueous solution, which is described as a partition coefficient. In many cases, the octanol–water partition coefficient (log $K_{ow}$) is considered as an estimate for the partition coefficient in MMLLE and LLE, even if the organic solvents used usually are other than octanol. The techniques work best for relatively nonpolar compounds, having values of log $K_{ow} > 3$.

With obvious modifications, Equation 13.1 is valid also for MMLLE. The definition of the relevant distribution coefficient is different. For MMLLE, it is

$$D = \frac{C_A}{C_D} = \alpha_D \cdot K_D$$  \hspace{1cm} (13.6)

Here, $K_D$ is the partition coefficient between the organic acceptor phase and the aqueous donor (sample) phase. For acidic or basic compounds, $\alpha_D$ is given by Equation 13.3 or 13.4, while for nonchargeable compounds, $\alpha_D = 1$. Thus, in MMLLE, the organic/aqueous partition coefficient directly governs the extraction.

### 13.3.5 Differences between MMLLE and SLM

The MMLLE technique can be seen as a complement to the SLM extraction, permitting membrane-based extraction to be extended to further classes of compounds. Compared with SLM, MMLLE has the following characteristics:

- It is applicable to hydrophobic, preferably uncharged compounds, that is, those that cannot be extracted with SLM.
- The maximum concentration enrichment possible is limited by the partition coefficient (Equation 13.6), whereas in SLM, it is dependent on the degree of trapping (Equation 13.2), which can be influenced by controlling the pH of the different phases. Therefore, SLM provides more degrees of freedom by which the conditions of extraction can be tuned.
- The extract ends up in the organic solvent, not in water. Thus, MMLLE is more easily interfaced to GC and NP-HPLC than is SLM, which is most compatible with reversed phase HPLC.
- The hardware is identical or similar, so the possibilities for automation should be similar, considering the aforementioned point.

### 13.3.6 Concentration Enrichment

One of the main purposes of membrane extraction in sample preparation is to enrich the analyte, that is, to increase the concentration of the analyte in order to permit determination of low concentrations. Plotting the concentration of analyte in the acceptor ($C_A$) either directly as determined by analysis of the acceptor phase or as a concentration enrichment factor $Ee$

\[
Ee = \frac{C_A}{C_S} = \frac{1}{((V_A/V_S)+(1/D))} \left[ 1 - \exp \left( -k \cdot \left( \frac{V_A}{V_S} + \frac{1}{D} \right) \right) \right] \cdot t \hspace{1cm} (13.8)
\]

(C$_A$/C$_S$—where C$_S$ is the initial concentration in the sample) versus time will typically produce a curve, which initially raises approximately linearly and asymptotically eventually reaches a steady equilibrium value. See Figure 13.5.49

Assuming that the rate of mass transfer is proportional to the concentration difference over the membrane according to Equation 13.1 and noting that in static extraction, the concentration in the donor phase $C_D$ decreases as analyte is transferred over the membrane, we get the following differential equation:

\[
\frac{dC_A}{dt} = k \cdot \left( C_S - \left( \frac{V_A}{V_S} + \frac{1}{D} \right) \cdot C_A \right) \hspace{1cm} (13.7)
\]

where

- $V_A$ and $V_S$ are the volumes of the acceptor (strip) phase and the extracted sample, respectively
- $C_S$ is the initial concentration in the sample ($C_SA = C_DA + C_AV_A$)
- $D$ is the equilibrium distribution coefficient (see Equations 13.2, 13.5, and 13.6)
- $k$ is a rate constant

The general solution expressed as a concentration enrichment factor $Ee$ is

\[
Ee = \frac{C_A}{C_S} = \frac{1}{((V_A/V_S)+(1/D))} \left[ 1 - \exp \left( -k \cdot \left( \frac{V_A}{V_S} + \frac{1}{D} \right) \right) \right] \cdot t
\]
The rate of mass transfer through the membrane is proportional to the gradient of this curve and thus decreases from an initial value to practically zero. The concentration enrichment factor value at equilibrium will be

\[ E_{eq} = \frac{1}{((V_A/V_S)+(1/D))} \]  

(13.9)

Equations 13.7 through 13.9 are basically valid for static extraction. In the case of extraction in a flow system with flowing donor and stagnant acceptor, the phase ratio \( (V_d/V_a) \) is zero, as depletion of the sample is not possible.

There are several limiting cases for Equations 13.8 and 13.9:

1. With a large equilibrium distribution coefficient \( D \) (complete trapping) and a large phase ratio, \( E \) will increase linearly up to large values. In Figure 13.5, which refers to an SLM flow system experiment, \( D \) in curve 1 is approximately 40,000 and the enrichment factor is linear at least up to at least 6,000 times. In many cases, especially in flow systems, the extraction is not allowed to go to equilibrium, and an extraction efficiency \( E \) is defined as the fraction of the total amount of analyte that is transferred to the acceptor. Thus,

\[ E = \frac{C_A}{C_S} \cdot \frac{V_A}{V_S}; \quad Ee = E \cdot \frac{V_S}{V_A} \]  

(13.10)

The extraction efficiency is related to the slope of the extraction curve, so if the extraction is linear, \( E \) is constant and <100%. By careful calibration and keeping the experimental parameters constant so the system is kinetically stable, repeatable values for \( Ee \) and \( E \) can be obtained. This will give reproducible quantitative results and most of the applications of membrane extraction to practical analyses are in fact based on this principle.

2. With a finite sample volume in static extraction mode under complete trapping conditions, the sample will eventually be depleted with regard to analyte, so a decrease of mass transfer is due to the decrease of analyte concentration, and the equilibrium occurs after virtually all analyte has been transferred to the acceptor. Equation 13.9 then leads to

\[ Ee_{eq} = \frac{V_S}{V_A}; \quad C_A = C_S \cdot \frac{V_S}{V_A} \]  

(13.11)

that is, the enrichment factor is determined by the phase ratio.

Thus, if the extraction is continued until equilbrium so that the sample is totally depleted with analyte, very simple and straightforward calculations of the enrichment factor are possible, according to Equation 13.11, which contains no other parameters than the phase volumes. This can be the basis for accurate quantitative determinations.

3. The third limiting case of Equation 13.9 is the situation where equilibrium is attained without depletion of the analyte in the sample. It is treated in Section 13.3.8.

### 13.3.7 Selectivity

To obtain a high selectivity, that is, discrimination between the analytes and various unwanted matrix compounds, membrane extraction has a clear advantage over other sample preparation techniques, as all compounds that reach the analytical instrument must travel through the membrane. There is no direct connection and possibility for transferring compounds into the analytical instrument in other ways. This is not the case with other extraction techniques. With SPE, SPME, etc., there is a definite possibility that matrix components are absorbed on the sorbing phase and subsequently being eluted into the extract. With LLE, such transfer is less probable and it is generally considered that extracts after LLE are cleaner than after SPE. The possible and common problem of the formation of emulsions at the phase interface with LLE, which is avoided with all types of membrane extraction, is a source of contamination across the phase border.

Further, with SLM extraction, the pH of the donor solution and the acceptor phase can easily be fine-tuned to obtain extraction that is selective for certain groups of compounds, as described earlier. Alternatively, a carrier can be added in the membrane to increase the selectivity and/or mass transfer of the compounds of interest. When the primary aim of adding a carrier is to increase the mass transfer of the analytes by analyte–carrier interactions in the membrane, it is important to choose other conditions carefully so that selectivity is still retained.

Membrane extraction is especially effective in discriminating toward macromolecules. In environmental analysis, macromolecular humic acids are ubiquitous and usually very efficiently removed. Megersa et al. compared SLM and SPE extraction of some triazine herbicides spiked in river water. As is seen from Figure 13.6, the difference is dramatic. Also, there are a number of examples of how various drugs can be determined in blood plasma and also urine without matrix interferences.

### 13.3.8 Equilibrium Extraction

A somewhat different approach to analytical extraction involves selection of a relatively low value of \( D \) and a virtually infinite phase ratio \( (V_S \gg V_A) \). With these conditions, Equation 13.9 reduces to

\[ Ee = D \]  

(13.12)
This is essentially the same as Equation 13.2. Curves 3 and 4 (and to some extent curve 2) in Figure 13.5 are illustrations to this. Experimentally, enrichment factors at equilibrium agree reasonably with calculated (Equation 13.5) values of $D$. The concentration of analyte in the sample will not be influenced by the extraction, and this permits extraction and sampling without influencing speciation conditions in the sample. This is the basis for a novel sampling technique, called equilibrium sampling through membranes (ESTMs), which is currently developed for the measurement of freely dissolved fractions of environmental pollutants (as distinguished from total concentrations). This parameter is of environmental interest, as it describes transport processes and bioavailability better than total concentrations. The ESTM principle is especially suitable for polar compounds and metals, in contrast to SPME-based methods, which are more suitable for nonpolar compounds. ESTM has been evaluated with both phenolic pollutants and metal ions. An analogous problem in pharmacology is the measurement of drug–protein binding, to which ESTM has been successfully applied.

### FIGURE 13.5

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### FIGURE 13.6

Chromatograms (LC–UV) of methoxy-s-triazine herbicides (simetone, atratone, secbumetone, terbumetone): (a) SPE of spiked river water (1.0 mg/L of each analyte in 1 L). (b) SLM extraction of spiked river water (0.5 mg/L of each analyte). (From J. Chromatogr. A, 830, Megersa, N., Solomon, T., and Jönsson, J.Å., Supported liquid membrane extraction for sample workup and preconcentration of methoxy-s-triazine herbicides in a flow system, 203–210, Copyright 1999, with permission from Elsevier.)

### 13.4 DEVICES FOR MEMBRANE EXTRACTION

#### 13.4.1 Static Extraction

##### 13.4.1.1 Aqueous Matrices

In analytical sample preparation, static extraction, that is, extraction from the donor, into a stagnant acceptor held in the lumen of a hollow fiber is superior in terms of enrichment as well as simplicity. The small acceptor volume (typically a 20 cm of a hollow fiber with i.d. of 0.3 mm holds approximately 10 μL in the lumen) leads to very high enrichment, usually several thousands of times and thereby low detection limits if combined with a sensitive detection technique such as mass spectrometry. Enrichment factors as high as 27,000–28,000 times have been reported for pinonic and pinic acid from aqueous aerosol extracts as well as antidepressants from water samples leading to method detection limits down to pg/L.

These extraction systems also entail very simple and low-cost equipment (principally syringes, hollow fibers, magnetic stirrers, and bottles/flasks). The preparation of the fibers and collection of extracts only take a few minutes per sample, and the samples can be left unattended during the extraction. The low cost and the simple setup allows for disposal of the fibers after extraction, thus eliminating memory and carry-over effects. The main disadvantage with this setup is the lack of automation possibilities, that is, each sample has to be prepared manually.

In static extraction systems, the hollow fiber is sealed in both ends and immersed into the donor/sample placed inside a beaker, bottle, or flask. To increase mass transfer, the sample is stirred during the extraction. Due to its low weight and hydrophobic character, polypropylene hollow fibers will float on the surface of the aqueous sample and hence need to be stabilized. There are several principal setups, of which some are depicted in Figure 13.3. In the Liu et al. setup (Figure 13.3a), employing fibers with an i.d. of 0.3 mm for extraction of organic compounds, the fiber is sealed in both ends either by heat or aluminum foil, and a piece of copper wire can be coiled around it to act as a weight. For very basic donor solutions, aluminum foil as well as copper can be attacked by hydroxide ions, and PTFE tape combined with a vial glass insert has been successfully applied instead. The same setup can also be used for extraction of metals where any metallic material should be avoided. In the Zhao and Lee setup (Figure 13.3c), the fiber is only sealed in one end and the acceptor immersed via a syringe, which is then left in the fiber and secured above the sample using a clamp, ensuring that the fiber is totally immersed into the sample.

For three-phase HF-LPME, the fiber is first filled with the aqueous acceptor solution via a syringe, and the porous wall is then impregnated by dipping the fiber into an organic solvent for ~1 min. Sealing of the fiber can be performed either before or after impregnation depending on the sealing technique employed.

For two-phase HF-LPME, the lumen, as well as the porous wall of the fiber, is filled with the organic solvent. Since the fibers are hydrophobic, organic solvents easily diffuse through the wall; hence, the most convenient way to fill the fibers is to seal them in both ends by heat and place...
them in a bottle holding the solvent and sonicate. As long as the solvent used has a higher density than water, the fibers can then be placed in aqueous samples without any kind of support. Of course, the Lee or Liu setup can also be used for two-phase systems, using a syringe to fill the lumen as well as the pores with solvent. Simply, in two- and three-phase extraction, any kind of sealing and support technique can be used. However, plastic materials should be avoided in extraction of organic compounds and metallic material in extraction of metals. After the extraction, the fiber is cut open in the end/ends and the acceptor either aspirated into a syringe and then transferred to a vial or pushed directly into a vial by attaching an air-filled syringe to the fiber. Usually the extract is then ready for direct injection into HPLC or GC for organic compounds or a graphite furnace atomic absorption instrument for metals. If flame atomic absorption or inductively coupled plasma atomic emission/mass spectrometry is employed, larger injection volumes are needed and dilution of the extract is required. Low-volume spectrophotometers such as NanoDrop 2000 from Thermo Scientific (Waltham, MA), which can handle volumes down to 0.5 μL, allow direct spectrophotometric detection in HF-LPME extracts.

### 13.4.1.2 Solid Matrices

A recent development within membrane extraction for analytical purposes is its extension to also include solid samples. This provides a more simple way to work up such samples compared to currently prevailing techniques such as PLE. It also greatly simplifies measurements in semisolid samples (such as nondigested sewage sludge), which cannot be extracted with techniques for aqueous samples due to their large content of particulate matter but, on the other hand, require extensive dewatering by, for example, lyophilization if extracted by techniques for solid samples.

The basic principle is that the solid or semisolid sample is suspended in an aqueous solution and left under stirring to reach equilibrium of the analyte between the solid particles and water. In some methods, the solid phase is then removed by centrifugation, while in others, it is kept in the sample during the extraction.

In the latter case, as the analyte is extracted into the fiber, a simultaneous release from the solid matrix will take place (see Figure 13.7), thus allowing measurements of total concentrations after quantification using a modified standard addition technique described in detail by Sagrista et al. It could be valuable to homogenize the samples prior to the extraction since when working with very heterogeneous samples containing large particles, the composition of replicates may otherwise differ leading to decreased precision.

The application of HF-LPME on suspensions of solid samples is a rather new and developing research area. However, the technique has been successfully applied onto extractions of anti-inflammatory drugs from digested sewage sludge as well as a wide range of sludge and water samples collected from inside the sewage treatment plant and triazine herbicides in digested sewage sludge, methylmercury in human hair and sewage sludge, as well as bile acids in rat cecum samples.

### 13.4.2 Stand-Alone Equipment

Simple and cheap membrane extraction flow systems for relatively large sample volumes can be built up around a peristaltic pump. An example of such a system is seen in Figure 13.8a. Here, the sample is pumped through the donor channel and the acceptor phase is manually removed by the use of a syringe after each extraction. Such systems have been used both for laboratory work and for sampling in natural waters. A tutorial for the operation of this type of devices has been published.

Hollow-fiber devices, working in flow systems, are also known. In those cases, either single fibers or bundles of fibers, perhaps in commercial cartridges, are employed and used in flow system configurations.

### 13.4.3 Online Connection to Chromatography

For online connection to HPLC, SLM is the preferred extraction technique, as the extract obtained is aqueous and therefore in principle compatible with HPLC. With large membrane units (channel volumes around 1 mL), direct transfer of the entire volume of the acceptor phase to an HPLC can be arranged by means of a precolumn in order to inject as much as possible of the extracted analyte. See Figure 13.8b.

**FIGURE 13.7** Setup for LPME of semisolid samples. The solid matrix is suspended in water; the analytes will equilibrate between the solid particles and the aqueous phase, thus driving the equilibrium between the solid particles and the donor solution toward desorption.
Such systems can be automated with pneumatically or electrically actuated valves controlled by timers or by computer systems. Smaller membrane channels can also be used. Then a heart cut that contains a major part of the extract can be accommodated in the injection loop for direct injection into the HPLC column without a precolumn.

For small samples (<1 mL) and small channel volumes, the liquid delivery precision of peristaltic pumps is not adequate and membrane extraction equipment based on syringe pumps connected to robotic liquid handlers can be applied. A typical example is shown in Figure 13.8c. Here, a robotic needle connected to a syringe pump submits reagent to adjust the pH of samples in the vials, picks up an aliquot, and passes it through the donor channel of a small membrane unit (channel volume around 10 μL). The entire extract collected in the acceptor channel is then transferred to an injection loop injector connected to the HPLC system in the usual manner. Thus, the entire extract from, for example, 1 mL sample ends up in one chromatographic injection. Typically, while one sample is chromatographed, the next sample is extracted, so the cycle time of the system is determined by the chromatogram time.

For GC, the most suitable membrane extraction technique is MMLLE. The organic acceptor is better compatible with GC than with HPLC, as are the analytes that are best extracted in such a system, that is, relatively hydrophobic compounds. In the ESy instrument (ESyTech AB, Lund, Sweden), an MMLLE extraction in microscale (1 mL extracted into a volume ca. 1 μL) is automatically performed, and the organic extract is directly injected into the GC by means of an injection needle, directly connected to the extraction cell. See Figure 13.9.
Membrane Extraction in Preconcentration, Sampling, and Trace Analysis

13.4.4 Continuous flow liquid membrane extraction

By combining continuous flow LLE and SLM extraction, a novel aqueous–aqueous extraction technique termed continuous flow liquid membrane extraction (CFLME) was developed for trace enrichment. The setup is shown in Figure 13.10. The aqueous sample is mixed with an organic solvent in a flow system, and the analyte is extracted into the organic phase. This is then transported to the liquid membrane formed in the microporous membrane of the SLM equipment. Finally, it is transferred through the liquid membrane and is trapped by the acceptor. Chemically, this is a three-phase extraction system, analogous to SLM, but it overcomes a disadvantage of SLM, as it is possible to use also relatively volatile and also polar solvents with this principle. On the other hand, it involves a more technically complex arrangement, and it typically requires more solvent (although still very little) than SLM.

13.4.5 Membrane Extraction with a Sorbent Interface

The techniques mentioned earlier are all characterized by liquid donor and acceptor phases. However, a gaseous acceptor phase is also possible, and that would be the most convenient and compatible arrangement for direct connection with GC. This is realized with the membrane extraction with a sorbent interface (MESI) technique. MESI can be used for either gaseous or aqueous samples, and the equipment employs a membrane module with a (usually) silicone rubber hollow fiber, into which the analytes are extracted from the surrounding liquid or gaseous sample. The carrier gas of a gas chromatograph flows inside the fiber and transports the analyte molecules as they are extracted from the membrane into a cooled sorbent trap where they are trapped. The analytes are subsequently desorbed from the sorbent trap by heating and are transferred to GC analysis.

In Figure 13.11, a typical MESI setup is shown. Sampling can also be made off-line with the extraction module and sorbent trap.
in, for example, field sampling, and the sorbent trap can later be connected to the GC and desorbed in a separate step. Matz et al. recently presented and compared this and a few other variants.

### 13.4.6 Field Sampling Apparatus

Simple flow systems comprising flat membrane devices and a peristaltic pump were used for field sampling in natural waters and also for sampling of nutrient solutions for soil-free (hydroponic) growing in greenhouses.

A portable sampler (Figure 13.8d), based on syringe pumps and powered by batteries and solar power, was recently constructed and used for sampling of triazine herbicides in Ethiopian lakes.

### 13.5 Applications

Over the last decades, a large number of applications to membrane extraction have been presented. In Tables 13.3 through 13.5, some examples of such applications

#### TABLE 13.3

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Matrices</th>
<th>Membrane Technique</th>
<th>Analytical Technique</th>
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<td>GC</td>
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<tr>
<td>PCB</td>
<td>Water</td>
<td>MMLLE (ESy)</td>
<td>GC</td>
<td>[89]</td>
</tr>
<tr>
<td>Amines</td>
<td>Water</td>
<td>MMLLE</td>
<td>CE</td>
<td>[146]</td>
</tr>
<tr>
<td>Nonylphenol</td>
<td>Water</td>
<td>MMLLE</td>
<td>HPLC</td>
<td>[147]</td>
</tr>
<tr>
<td>Triazine herbicides</td>
<td>Water</td>
<td>MMLLE</td>
<td>FIA</td>
<td>[148]</td>
</tr>
<tr>
<td>Cationic surfactants</td>
<td>Water</td>
<td>MMLLE</td>
<td>HPLC</td>
<td>[149]</td>
</tr>
<tr>
<td>Organophosphorus pesticides</td>
<td>Water</td>
<td>MMLLE, LPME2</td>
<td>GC</td>
<td>[150–152]</td>
</tr>
<tr>
<td>Organochlorine pesticides</td>
<td>Water</td>
<td>LPME2, MMLLE</td>
<td>GC</td>
<td>[90, 153, 154]</td>
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<tr>
<td>Semivolatile organics</td>
<td>Water</td>
<td>PME</td>
<td>HPLC</td>
<td>[45, 155–157]</td>
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<tr>
<td>Organics</td>
<td>Water</td>
<td>PME (MASE)</td>
<td>GC/MS</td>
<td>[47, 158–161]</td>
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<td>Volatile organics</td>
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<td>MESI</td>
<td>GC</td>
<td>[94, 162–166]</td>
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<td>Phenols, sulfonylureas</td>
<td>Water</td>
<td>CFLME</td>
<td>HPLC, CE</td>
<td>[167–172]</td>
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<td>Water</td>
<td>LPME3</td>
<td>HPLC</td>
<td>[173]</td>
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<td>Drugs</td>
<td>Water</td>
<td>LPME3</td>
<td>CE, LC/MS</td>
<td>[74, 177, 174–185]</td>
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<td>Sewage sludge</td>
<td>LPME3</td>
<td>HPLC</td>
<td>[186]</td>
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<td>Triazine herbicides</td>
<td>Water</td>
<td>LPME2</td>
<td>GC/MS</td>
<td>[187]</td>
</tr>
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<td>Phthalate esters</td>
<td>Water</td>
<td>LPME2</td>
<td>GC/MS</td>
<td>[188]</td>
</tr>
<tr>
<td>Pesticides</td>
<td>Water</td>
<td>LPME2</td>
<td>GC/MS</td>
<td>[189–191]</td>
</tr>
<tr>
<td>Drugs</td>
<td>Water</td>
<td>LPME2</td>
<td>GC/MS</td>
<td>[192]</td>
</tr>
<tr>
<td>Vinclozolin</td>
<td>Water, soil</td>
<td>LPME2</td>
<td>GC</td>
<td>[193]</td>
</tr>
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<td>PAH</td>
<td>Soil</td>
<td>LPME2</td>
<td>GC</td>
<td>[194]</td>
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<td>Explosives</td>
<td>Water</td>
<td>LPME2</td>
<td>GC</td>
<td>[195]</td>
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</table>

**Abbreviations:** SLM, supported liquid membrane extraction (aq/org/aq); MMLLE, microporous membrane liquid–liquid extraction (aq/org); PME, polymer membrane extraction (aq/polymer/org); MESI, membrane extraction with sorbent interface (aq [or gas]/polymer/gas/sorbent); CFLME, continuous flow liquid membrane extraction (aq/org [in flow]/aq); LPME2, two-phase liquid-phase microextraction in hollow fibers (aq/org); LPME3, three-phase liquid-phase microextraction in hollow fibers (aq/org/aq).
### TABLE 13.4
Applications of Membrane Extraction to Biological Samples

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Matrices</th>
<th>Membrane Technique</th>
<th>Analytical Technique</th>
<th>Refs.</th>
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<tbody>
<tr>
<td>Aliphatic amines</td>
<td>Urine</td>
<td>SLM</td>
<td>GC</td>
<td>[196]</td>
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<tr>
<td>Aliphatic acids</td>
<td>Manure</td>
<td>SLM</td>
<td>GC</td>
<td>[197]</td>
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<td>Aliphatic amines</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>GC</td>
<td>[198]</td>
</tr>
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<td>Amperozide</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>HPLC</td>
<td>[28]</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Blood plasma</td>
<td>LPME3</td>
<td>HPLC</td>
<td>[199]</td>
</tr>
<tr>
<td>Bambuterol</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>CE</td>
<td>[200–202]</td>
</tr>
<tr>
<td>Bambuterol</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>LC–CE</td>
<td>[203]</td>
</tr>
<tr>
<td>Diprivan (propofol)</td>
<td>Urine</td>
<td>SLM</td>
<td>HPLC</td>
<td>[204]</td>
</tr>
<tr>
<td>Phenols</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>HPLC–biosensor</td>
<td>[205]</td>
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<td>Peptides</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>HPLC</td>
<td>[57]</td>
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<td>Drugs</td>
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<td>SLM (ESTM)</td>
<td>HPLC</td>
<td>[36,71]</td>
</tr>
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<td></td>
<td></td>
<td>LPME3 (ESTM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various drugs</td>
<td>Urine</td>
<td>LPME3</td>
<td>MS</td>
<td>[206]</td>
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<td>Lead</td>
<td>Urine</td>
<td>SLM</td>
<td>AAS</td>
<td>[59]</td>
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<tr>
<td>Lead</td>
<td>Urine</td>
<td>SLM</td>
<td>PSA</td>
<td>[207]</td>
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<td>Local anesthetics</td>
<td>Blood plasma</td>
<td>SLM</td>
<td>GC</td>
<td>[100]</td>
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<td>Local anesthetics</td>
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<td>SLM</td>
<td>GC</td>
<td>[208]</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Blood plasma, urine</td>
<td>LPME3 (LLLME)</td>
<td>CE</td>
<td>[29]</td>
</tr>
<tr>
<td>Amphetamine, benzodiazepines, naproxen, ketoprofen</td>
<td>Blood plasma, urine</td>
<td>LPME2, LPME3</td>
<td>HPLC, GC, CE</td>
<td>[209]</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Blood plasma, urine</td>
<td>LPME2</td>
<td>GC</td>
<td>[210]</td>
</tr>
<tr>
<td>Ibuprofen, naproxen, ketoprofen</td>
<td>Urine</td>
<td>LPME3</td>
<td>CE</td>
<td>[211]</td>
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<tr>
<td>Metabolites of ropivacaine</td>
<td>Urine</td>
<td>SLM</td>
<td>HPLC</td>
<td>[67]</td>
</tr>
<tr>
<td>Citalopram and metabolites</td>
<td>Blood plasma</td>
<td>LPME3</td>
<td>CE</td>
<td>[212]</td>
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<td>Amphetamines</td>
<td>Blood, urine</td>
<td>LPME3</td>
<td>FIA–MS/MS</td>
<td>[30]</td>
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<td>Trime thazine</td>
<td>Blood plasma</td>
<td>LPME3</td>
<td>HPLC</td>
<td>[213]</td>
</tr>
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<td>Osthol</td>
<td>Blood plasma</td>
<td>LPME3</td>
<td>HPLC</td>
<td>[214]</td>
</tr>
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<td>Organophosphate esters</td>
<td>Blood plasma</td>
<td>MMLLE</td>
<td>GC–MS</td>
<td>[215]</td>
</tr>
<tr>
<td>Sulfonurea drugs</td>
<td>Blood plasma</td>
<td>PME (off-line)</td>
<td>LC–MS/MS</td>
<td>[216]</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Urine</td>
<td>SLM</td>
<td>HPLC</td>
<td>[217]</td>
</tr>
<tr>
<td>Methimazole</td>
<td>Various biol. samples</td>
<td>HPLC</td>
<td>LPME3 (ion pair)</td>
<td>[218]</td>
</tr>
<tr>
<td>Benzimidazole anthelmintics</td>
<td>Urine, tissue, milk</td>
<td>SLM</td>
<td>HPLC, LC–MS</td>
<td>[219]</td>
</tr>
</tbody>
</table>

**Note:** Abbreviations as in Table 13.3.
are presented, divided into environmental, biomedical, and other (mainly industrial) applications. The wide variety of analytes and sample types shows that membrane extraction is very versatile and a useful tool for the analytical chemist. A thorough review of the use of membrane extraction in environmental applications was recently published.

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During recent years, the membrane extraction work at Lund University was supported by grants from the Swedish Science Research Council (VR), the Foundation for Strategic Environmental Research (MISTRA), the Swedish Institute (SI), the Swedish International Development Co-operation Agency (SIDA), the Crafoord Foundation and the Wennergren Foundation, the Skåne Regional Council, and the Research School Receto. The work would not have been possible without a number of colleagues, graduate and undergraduate students as well as postdoc fellows and other guest researchers.

REFERENCES


### TABLE 13.5

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<tr>
<th>Analytes</th>
<th>Matrices</th>
<th>Membrane Techniques</th>
<th>Analytical Techniques</th>
<th>References</th>
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<tr>
<td>Cr(VI)</td>
<td>Waste water</td>
<td>LPME3</td>
<td>AAS</td>
<td>[220]</td>
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<tr>
<td>Phenols</td>
<td>Kerosene, naphtha</td>
<td>PME</td>
<td>FIA</td>
<td>[221]</td>
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<td>Triazines</td>
<td>Cooking oil</td>
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<td>FIA, HPLC</td>
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<td>Herbicides</td>
<td>Crude oil</td>
<td>PME</td>
<td>HPLC</td>
<td>[223]</td>
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<td>Gasoline, kerosene</td>
<td>PME</td>
<td>HPLC</td>
<td>[224]</td>
</tr>
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<td>Crude oil, fuels</td>
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<td>HPLC</td>
<td>[225]</td>
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<td>Vitamin E</td>
<td>Butter</td>
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<td>HPLC</td>
<td>[87]</td>
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<td>Snuff</td>
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<td>UV</td>
<td>[226]</td>
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<td>UV</td>
<td>[227]</td>
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<td>Eggs</td>
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<td>HPLC</td>
<td>[228]</td>
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<td>LC–MS/MS</td>
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<td>HPLC</td>
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<td>LC–MS/MS</td>
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<td>FIA</td>
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<td>LC–LC</td>
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<td>HPLC</td>
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</table>

Note: Abbreviations as in Table 13.3.


Membrane Extraction in Preconcentration, Sampling, and Trace Analysis


