Review

Automated, on-line membrane extraction

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Abstract

Over the last few years, membranes have been used to develop new approaches in analytical extraction, concentration and cleanup. An important advantage of membrane processes is that the sample and the extraction phase can be continuously brought into contact without physical mixing, and may be directly interfaced to an analytical instrument. This provides the basis for automated, real-time monitoring. Membrane extraction has been applied to a wide range of organic and inorganic analytes, and has been directly interfaced with chromatography, spectroscopy and mass spectrometry. Implementations of membrane extraction are diverse, encompassing different types of membranes, module designs and configurations. This review highlights some of these, and particularly the unique capabilities in automated, and on-line measurements.

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Keywords: Membrane extraction; Pervaporation; Automated sample preparation; LPME

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1. Introduction

The analysis of trace level analytes involves the discreet steps of extraction, concentration and clean up prior to detection by an instrument. Traditionally, extraction has been achieved by techniques such as head space analysis, purge and trap, solid-phase microextraction (SPME), liquid–liquid extraction (LLE) and solid-phase extraction (SPE) [1–5]. Rotary evaporation, gas purging and the Kuderna Danish method are usually used to concentrate the analytes, while the use of silica gel, gel permeation and Florisil™ columns are used to achieve cleanup [2]. These methods are often time consuming, use large amounts of sample and solvents, require extensive sample handling, and analysis cost per unit sample is high. Moreover, most of these processes cannot be carried out on-line in a continuous fashion.

Over the last few decades, membranes have found many applications in various separation processes, such as, desalination, dialysis, ultrafiltration, gas separation, dehumidification, osmosis, reverse osmosis and electrodialysis [6]. Thus, it is conceivable that they can be used to achieve extraction, concentration and cleanup in an analytical application. Being selective to a particular species, the membrane primarily functions as a separator of two bulk phases, and controls the mass transfer between them. This allows the enrichment of the species of interest and their removal from the sample matrix. The movement of the analytes of interest may be driven by a chemical, pressure or an electrical potential gradient [7,8].

In recent years, the use of membranes for sample preparation has in many instances become a preferred option. This is largely due to the fact that they facilitate extraction without the mixing of two phases, thus eliminating problems such as emulsion formation and high solvent usage. A very important advantage of the membrane processes is that the sample and the extractant can be continuously brought into contact, thus providing the basis for a continuous, real-time process leading to automation and on-line connection to instruments [9]. Consequently membrane techniques have advanced to solve numerous analytical problems. These techniques allow the simultaneous extraction and enrichment of analytes, and typically facilitate selective extraction at trace levels while consuming small amounts of solvents. Membrane extraction has been applied to a wide range of analytes including biological molecules [10–13], metals [14–19] and organic pollutants [20–22], and has been directly interfaced with gas chromatography (GC), liquid chromatography (LC), mass spectrometry (MS), ion chromatography (IC), atomic absorption spectroscopy (AAS), inductively coupled plasma atomic emission spectroscopy (ICP–AES) and capillary electrophoresis (CE) [23–31]. Moreover, there exist numerous other possibilities that are yet to be explored.

Membrane extractions are not limited to environmental media, such as water. They are becoming quite popular in biomedical applications with matrices, such as urine, blood and blood plasma, to analyze drugs and their metabolites. Jönsson et al. [10] were able to detect sub-ppb concentrations of an ester in urine flowing at rates as low as 50 µL/min. Such matrices are especially complex and usually require tedious and multiple sample preparation steps. Additionally, sample volumes needed for membrane processes, particularly liquid membranes, tend to be quite small.

Applications of membrane extraction are quite diverse, encompassing different types of membrane, their design as well as applications. As mentioned before, membranes offer the unique opportunity for bringing a sample and an extractant into contact in a continuous fashion. This review highlights this unique capability and focuses on automated analysis using membranes, with particular attention to on-line techniques for continuous analysis.

2. Principles

2.1. Permeation through membrane

A membrane is a selective barrier through which different gases, vapors and liquids move at varying rates. The membrane facilitates the two phases coming into contact with each other without direct mixing. Molecules move through membranes by the process of diffusion and are driven by a concentration (∆C), pressure (∆P) or electrical potential (∆E) gradient. The process is demonstrated in Fig. 1. The interesting aspect of this technique is that both the donor and acceptor can flow continuously leading to the development of real-time monitoring techniques.

This diffusion-based transport can be expressed by Fick’s first law of diffusion:

\[ J = -D \frac{dc}{dx} \]  

where \( J \) is the rate of transfer (or flux) (g/cm² s), \( D \) the diffusion coefficient (cm²/s) and \( dc/dx \) is the concentration gradient.

Diffusion is a slow process and so it is necessary to control certain parameters to ensure that the flux is significant. Integration of Fick’s law gives:

\[ J = \frac{D(c_i - c_f)}{L} \]

Fig. 1. Permeation across a membrane. ∆C, ∆P, ∆E are the concentration, pressure and electrochemical gradients, respectively, down which analytes move.
where \( c_{im} \) is the concentration of \( i \) at outer membrane surface, \( c_{il} \) the concentration of \( i \) in the lumen and \( L \) is the membrane thickness.

It can be seen that reducing membrane thickness and creating large chemical potential gradients across the membrane will result in increased flux. It is important to note that the diffusion coefficient is a function of concentration. Thus, theoretical predictions in analytical applications are a difficult task, where concentration varies by orders of magnitude. The flux of analytes across the membrane is also affected by temperature because the diffusion coefficient depends upon it. For liquids, this can be best described by the Stokes–Einstein equation:

\[
D = \frac{kT}{6\pi \eta a}
\]  

(3)

where \( k \) is the Boltzmann’s constant, \( a \) the radius of solute and \( \eta \) is the solution viscosity.

So at increased temperatures, \( D \) increases leading to a higher flux. The other important factor, especially for non-porous membranes is the partition coefficient, \( K \), such that

\[
K = \frac{c_{im}}{c_{w}}
\]  

(4)

where \( c_{im} \) is the analyte concentration in the membrane and \( c_{w} \) is the analyte concentration in water (sample).

Permeation across non-porous dense membranes comprises several steps: (1) partitioning of the analyte in the membrane, (2) diffusion under a concentration gradient, and finally (3) partitioning into the extractant phase. There are also boundary layers present on the membrane surfaces that provide an additional barrier to mass transfer. These steps are illustrated in Fig. 2.

It is important to note that \( K \) decreases with temperature, while \( D \) increases under the same conditions. Consequently increasing temperature does not always increase flux, and an optimum temperature must be determined where the flux is greatest.

A key parameter that depends on both \( K \) and \( D \) is selectivity. After all, the purpose of extraction is the selective transport of analytes of interest. The selectivity, \( \alpha \), is measured as:

\[
\alpha = \frac{a_i/a_j}{d_i/d_j}
\]  

(5)

where \( a_i \) and \( a_j \) are the concentration of \( i \) and \( j \) in the acceptor and \( d_i \) and \( d_j \) are the concentration of \( i \) and \( j \) in the donor.

Therefore, the use of a particular “supported liquid” enhances the membrane selectivity by improving its ability to more readily transport the analytes of interest compared to other components [6].

2.2. Membrane classification

Synthetic membranes may be classified based on a number of properties including but not limited to geometry, function and morphology [32]. A basic classification is highlighted in Fig. 3.

2.2.1. Function

Membranes can be used in various separation functions as listed in Fig. 3. The method selected depends on the sample (e.g. aqueous, non-aqueous, biological, air, etc.) and also the properties of the analytes, such as, size and presence/absence of a charge. Dialysis refers to the process in which urea and other waste products are removed from blood by a saline solution flowing counter-current to the blood flowing in the membrane’s lumen. Cellulose membranes are most commonly used. Reverse osmosis (RO), ultrafiltration (UF) and microfiltration (MF) are all pressure driven water separation processes. They depend upon the pore size of the membranes used. Pore size in MF membranes ranges between 1000 Å and 10 μm, and these membranes are used to filter particles, such as, bacteria, salts and sugars. UF membrane pores range between 20 and 1000 Å and separate proteins and some dyes. RO is primarily used for desalination with pore size around 50 Å. Separation here is based on the solubility and mobility of ions. Gas separation separates gas mixtures, for example, nitrogen removal from air, and the separation of CO₂ from methane in the energy industry.

The membrane used in each function depends on its morphology, media and structure. For instance, polypropylene composite

![Fig. 2. Concentration profile in an extraction process, where \( C_w, C_m \) and \( C_s \) refer to analyte concentration in water, membrane and the extractant phases, respectively [59].](image-url)
membrane would be useful for pervaporation but not for ultrafiltration, where a porous membrane would be necessary. This paper will discuss select automated analysis techniques and not all methods mentioned above will be covered here.

2.2.2. Morphology and structure

Membrane morphology refers to the quantity, size and distribution of pores throughout the membrane structure. Membranes which have no pores in their structure are known as non-porous, while those which possess pores are referred to as porous. The size, shape and distribution of pores in a membrane are largely dependent on the processes by which they are made and play a significant role in their mode of separation. As the name suggests, porous membranes have openings through which select molecules pass. Movement through these membranes is therefore by size exclusion and the membranes are used in applications such as nanofiltration and dialysis. During extraction, two liquid phases meet at the pores and during pervaporation, the analytes vaporize at these sites. Non-porous membranes are solid (pore-free) structures and the molecules must move through them via diffusion, and therefore the compatibility with the analyte is critical.

Structure refers to the degree of uniformity of the pores as well as the membrane material. For instance, homogenous (isotropic) membranes are uniform throughout while asymmetric (anisotropic) and composite thin-films are not. It should be noted that so called uniform membranes have varying pore sizes, and the size quoted is usually an average. For some porous membranes, such as the Loeb–Sourirajan membrane, the variation throughout the membrane is quite significant with the sub-surface layer being as much as 10–15 times more porous than the top or skin layer. Isotropic membranes, shown in Fig. 4, include microporous, non-porous dense and electrically charged membranes. Separation in microporous membranes (pore size between $10^1$ and $10^4$ nm) is a function of particle and pore size distribution, and these membranes are used for processes such as microfiltration. In non-porous dense membranes, transport is via diffusion, and hence separation is influenced by partition coefficient as well as diffusivity of components in the membrane. These types of membranes are commonly used for extraction, reverse osmosis and pervaporation [33].

Anisotropic membranes refer to those in which the material, the porosity and pore size vary throughout the structure and include thin-film composites and Loeb–Sourirajan membranes [34]. The composite membrane, shown in Fig. 5, usually consists of different polymers where the surface layer determines selectivity, while the porous layer serves as a support.

Homogenous solid membranes, such as silicone, tend to provide lower fluxes but higher selectivity [33]. In a solid membrane, the analyte must first partition and then diffuse under a concentration gradient. In a porous membrane, as shown in Fig. 4, anything that can permeate through the pores migrates
across. As a result, the porous membranes provide higher flux but lower selectivity. Composite membranes are a compromise. The porous part provides for a high flux, while the solid layer on top provides selectivity. For example, a 1 μm silicone layer on top of a polypropylene composite provides high VOCs flux while preventing large amounts of water from permeating through. For thin-film composites, the thin surface layer represents a small percentage of the overall membrane but is responsible for much of the membrane’s selectivity. Scanning electron microscope (SEM) images of porous and composite membranes are shown in Fig. 6.

2.2.3. Geometry

In the context of membranes, geometry is synonymous with shape. The two main classes are flat and hollow fiber. The latter have a tubular geometry. Each shape has its advantages and disadvantages. The membrane module designs (shell and tube, flat sheet and microfluidic) are based on the membrane geometry. Typical hollow fibers are 100–500 μm in diameter and may be porous, solid or composite. They are often used in a shell and tube module as shown in Fig. 7. Multiple parallel fibers are encased in a large tubing to provide high packing density. For analytical purposes, the module may consist of a single fiber and the encasement may be made of glass, polyethylene or metal. The ends may be fitted with a tee and sealed. The sample enters the lumen and the extract is collected on the shell side. As a result the sample and extract do not mix. It is also used in pressure driven separations. These modules offer the advantage of being able to accommodate a much higher surface area per unit volume compared to their flat counterparts.

A simple flat sheet module, shown in Fig. 8a, could be comprised of a cell with a single flat sheet dividing the acceptor and donor. A more complicated structure is the one referred to as the plate and frame design. It essentially consists of flat sheets stacked on top of each other with an interspersed support material [35]. A generic design is shown in Fig. 8b. It is typically used in applications such as UF, MF and NF.

Microfluidics involves miniaturization with the eventual goal of developing lab-on-a-chip devices. Typically, the flow takes place in microchannels etched in silicon, glass or a polymer matrix as shown in Fig. 9. Their small size offers the advantages of a large surface to volume ratio, inexpensive mass production and low solvent usage. The channels are machined on each wafer and then the membrane is sandwiched between them to complete.

Fig. 5. Examples of anisotropic membranes. These membranes are heterogeneous in terms of pore size and pore distribution.

Fig. 6. SEM of thin-film composite (polyamide surface layer supported by polypropylene) and microporous polypropylene (courtesy of Center for Membrane Technology, NJIT).
Fig. 7. Shell and tube module. This module facilitates high membrane area in a relatively small space.

Fig. 8. (a) Simple flat sheet membrane module and (b) schematic of plate and frame design.

Fig. 9. A microfluidic membrane module using flat sheet membrane [36]. Channels can also be prepared by using lithography or laser ablation. Channel dimensions may be fine-tuned to facilitate optimal sample volumes and extraction efficiency.

Microfluidic modules using a flat sheet have also been fabricated [36]. Although analytical operations, such as electrophoresis, have been quite successful, extraction on a microfluidic device has been a challenge. Membrane extraction offers a plausible solution [36] as shown in Fig. 10. The system essentially consisting of microsyringe pumps can be interfaced to other microfluidic or conventional devices.

2.2.4. Membrane material

The material from which the membrane is made is referred to as the membrane material. Typical polymeric hollow fiber membranes used in analytical chemistry are polypropylene, silicone, polytetrafluoroethylene (PTFE), polyvinylidene fluoride (PVDF) and polysulfone (PS) which are resistant to most acids, bases and other chemicals, are thermally stable and are hydrophobic. Membranes can also be made of metal. Common examples are Pd alloys [37,38], which have a high hydrogen flux, are chemically resistant and are typically used in hydrogen purification. Ceramic membranes are usually tubu-
lar and are resistant to high temperature/pressure, corrosion and abrasion. They have been used in the food/beverage, pharmaceutical and biotechnology industries [39]. Lobo et al. [40] recently reported on the use of Carbosip (active layer of ZrO2/TiO2 on carbon) to remove contaminants, such as oil, from metal working fluids before disposal. Other ceramic membranes include Anodisc (γ-Al2O3 with a polypropylene support) and La1−xSrxCoyFe3−yO6−α (LSCF) [41].

2.3. Membrane extraction

Although many types of extractions have been carried out using membranes, the two most common approaches in analytical separations are: (1) supported liquid membrane extraction (SLME) and (2) liquid–liquid membrane extraction (LLME). These are used for the analysis of SVOCs, ionic compounds and metals. The third type of membrane extraction, pervaporation, differs from the above. Here, the permeate is extracted into a gas, and this method is mainly used for the analysis of VOCs, and for sample preconcentration. The enrichment factor (EF) and extraction efficiency (EE) are the two major parameters used to evaluate the effectiveness of a particular extraction. The EF may be defined as the ratio of analyte concentration in the extract to that in the initial donor:

\[ EF = \frac{C_a}{C_d} \]  

where \( C_a \) and \( C_d \) represent the analyte concentration in the acceptor after extraction and in the initial donor. The EE refers to the fraction of analyte that is extracted into the acceptor such that:

\[ EE = \frac{m_a}{m_d} = \frac{C_a \times V_a}{C_d \times V_d} = EF \frac{V_a}{V_d} \]

where \( m_a \) and \( m_d \) represent the total mass of the analyte in the acceptor and donor, respectively, and \( V_d \) and \( V_a \) are the volumes of the donor and extract.

2.3.1. Liquid–liquid membrane extraction

In LLME, the analyte is typically extracted from an aqueous solution into an organic one and hence it is a two-phase organic-aqueous system as shown in Fig. 11. It is essentially liquid–liquid extraction with the phases physically separated by a membrane, and in contact only at the membrane pores. It is easily interfaced with normal phase HPLC and GC. The efficiency of this system will therefore be largely dependent on partition coefficient, \( K_p \) such that:

\[ K_p = \frac{C_o}{C_w} \]

where \( C_o \) and \( C_w \) represent the equilibrium analyte concentration in the organic and aqueous phases, respectively.

The extractant should have low solubility in the aqueous phase and low volatility. The enrichment factor for non-polar organic compounds is usually higher than polar and charged compounds. This is mainly because the solubility of these compounds tends to be higher in the aqueous phase. The enrichment is driven by the concentration gradient of the analyte and is limited by its partition coefficient. This means that in the case where the acceptor is stagnant, the greater hydrophobicity of any analyte translates into increased efficiency because of the driving force to reach equilibrium. Consequently having a mobile acceptor tends to increase the enrichment and EE.

2.3.2. Supported liquid membrane extraction

When a liquid is immobilized in the pores of a porous material, via capillary action, that liquid can serve as the membrane, and the latter functions solely as a support as shown in Fig. 12 [6,42]. This is referred to as supported liquid membrane and
can be prepared simply by immersing a porous membrane in the supporting solvent.

To enhance the selectivity of the liquid membrane, a carrier molecule with a high affinity for the analyte is used. A carrier mediated transport that involves the reversible complex formation between the carrier and the analyte may also be used. SLME is suitable for polar and ionic compounds such as organic acids, bases and metals. As shown in Fig. 13, it is a three-phase system in which an organic phase is sandwiched between two aqueous phases. For instance, in the analysis of acids, the pH of the donor solution must be such that the compounds are in their neutral or uncharged forms, thus allowing them to enter the membrane. The pH of the acceptor is maintained such that once in the membrane, the analytes are extracted into the acceptor in a charged form and cannot be back-extracted into the donor. The pH gradient therefore provides the driving force. This technique usually results in high enrichment factors (thousands) and is compatible with reversed phase HPLC. Consequently, SLME offers distinct advantages such as high selectivity, donor/acceptor ratio and extraction efficiency when compared to LLME.

2.3.3. Pervaporation

While LLME and SLME deal with the extraction of analytes from one liquid into another, volatile organics are better separated by extracting into a gas phase. Pervaporation refers to the separation of a liquid mixture by partial vaporization through a porous, or a non-porous membrane. The sample flows on one side of the membrane, and the volatile species permeate as a gas to the other side, which is maintained under low pressure, or just purged with a stream of carrier gas. Theoretically, pervaporation can be viewed as a three-step process comprising of partitioning from the donor to the membrane, diffusion through the membrane followed by evaporation into the gas phase [43]. Separation is due to the differences in the partitioning coefficient and vaporization of the donor components. Flux through a pervaporation membrane can be expressed in terms of the partial vapor pressure on either sides of the membrane such that:

\[
J_a = \frac{P_G a \cdot (P_{ao} - P_{al})}{L}
\]

where \(J_a\) is the flux, \(L\) the membrane thickness, \(P_G a\) the gas separation permeability coefficient, \(P_{ao}\) the partial vapor pressure of donor and \(P_{al}\) is the partial vapor pressure in acceptor.

Apart from factors, such as chemical potential gradients and membrane thickness, another important consideration is the permeation through the boundary layer. Typically, there is poor mixing at the membrane/aqueous phase interface. Consequently, a stagnant aqueous boundary layer is formed on the membrane surface that impedes permeation. For continuous monitoring, permeation must be complete before another injection can be made. Much effort has gone into reducing the boundary layer to facilitate faster permeation and instrument response time.

3. Automated, on-line analysis of volatile organic compounds (VOCs)

Characterized by their low boiling points, high vapor pressure and low molecular weights, VOCs are usually extracted and concentrated using techniques such as head space analysis, purge and trap and solid-phase microextraction. These techniques are discrete processes that do not readily facilitate on-line analysis or automation. Additionally, some are not very reproducible and do not exhibit low detection limits. In general, on-line methods reduce sample handling and hence the probability of analytical errors and sample loss. The following sections will look at the progressive development in membrane extraction of VOCs.

Membrane separation has also been interfaced with mass spectrometers in a technique referred to as membrane introduction mass spectrometry (MIMS). In this configuration, shown in Fig. 14, the sample is constantly introduced to the membrane and the permeate is pulled by vacuum into the ion source. Membrane media such as latex, polyethylene, Teflon, polyimide and nitrile have been investigated for use in environmental analyses [44,45]. Recently, Thompson et al. [46] used polydimethlysilox-
ane (PDMS) hollow fiber membranes in a MIMS configuration to determine VOCs and SVOCs in air at ppt levels. MIMS allows for direct analysis of VOCs in air and water and has been used on compounds such as dichloromethane, chlorobenzene, 1,1-
chloroethene and acetone [47]. This technique has also been used in the food industry for real-time monitoring of bioreductions by bakers yeast [48], and for concentrating o-nitrotoluene and methyl salicylate in air [49].

GC interfacing of membrane extraction, shown in Fig. 15, is more complicated, because a positive pressure is maintained on the permeate side to facilitate the flow of gas.

Pervaporation can be used for VOC analysis and may be designed to operate in an automated fashion. It has been implemented in several different ways and may be classified as follows [50]: (1) membrane in sample (MIS) and (2) sample in membrane (SIM). These are shown in Fig. 16.

In the first case, a hollow fiber is dipped into the water containing the VOCs. A gas flowing through the membrane picks up the VOCs. SIM uses a shell and tube module. The aqueous sample is passed through a hollow fiber membrane. The VOCs selectively migrate across the membrane into an inert gas stream. In either case, the organics are concentrated in a sorbent before analysis by GC for fast on-line analysis.

As mentioned before, because of the boundary layer effects, permeation may take a relatively long time to reach steady state, and any measurement during the transitional period provides erroneous results. The time taken to complete the permeation process can be the limiting factor in analysis. Consequently it was realized that the best approach may be a non-steady state one. A pulse introduction process using a flow-injection type sample introduction was developed thus eliminating the need for the system to equilibrate. This led to a significantly quicker instrument response [51].

In another version, a gas was used to inject a liquid sample. The system referred to as gas injection membrane extraction (GIME) is shown in Fig. 17. GIME involves the introduction of an aqueous sample by a N2 stream which injects the sample into the membrane. The membrane serves as a selective barrier through which organic analytes permeate. On the permeate side, a counter-current gas stream strips the organics and transports them to a microtrap. The VOCs are trapped and concentrated by a microtrap in front of the GC column. The retained VOCs are desorbed from the microtrap by an electrically generated temperature pulse. Rapid heating generates a concentration pulse which serves as an injection for chromatographic separation [52]. Con-
continuous monitoring is achieved by making a series of pulses (or injections) and corresponding to each pulse a chromatogram is obtained [53,54]. The system shown below in Fig. 17 can be used for the analysis of individual samples by discrete injections, as shown in the chromatogram in Fig. 18, or for continuous on-line monitoring by sequentially injecting a series of samples.

The advantage of gas injection is that the gas cleans the membrane and destroys the boundary layer on its surface. The response time decreased dramatically and tailing in permeation profiles was eliminated. The overall membrane extraction of benzene was found to be completed in 2 min by gas injection compared to 8 min by liquid. This method is also simpler in terms of instrumentation and operational procedures. The process, illustrated by Kou et al. [55] used a composite membrane, and the detection limits were at low ppb (µg/L) levels.

4. Automated analysis of semi volatile organic compounds (SVOCs)

SVOCs refer to compounds that are not readily volatilized and include compounds such as PAHs, PCBs, biomolecules, acids, phenols and pesticides. Both SLME and LLME techniques can be applied to these compounds [56–58]. Methods that have been successfully developed integrating these tech-

4.1. On-line LLME

This is essentially, automated liquid–liquid extraction across a membrane, which allows faster sample throughput, less sample handling and continuous monitoring of non-polar analytes. Regardless of the analyte, the basic set-up is as illustrated in Fig. 19.

The use of both polymeric hollow fibers [59] and flat sheet [60] has been reported. On-line LLME has been demonstrated to effectively monitor the concentration of different SVOCs in water with the time between injections limited by the separation time. Fig. 20 illustrates the results obtained from a sequence of injections, with enrichment factors as high as 62 and ppb level detection limits [59].

In on-line LLME, the extractant may be static or flowing [16,61]. Highest EFs are typically obtained when the acceptor phase is mobile. Sandahl et al. [60] used on-line LLME for moni-
Fig. 21. Simultaneous extraction and concentration [64]. The analyte is selectively enriched while the solvent is selectively removed.

4.2. On-line membrane concentration

For trace analysis, once the analytes have been extracted into a solvent, often a concentration step is necessary. Traditionally, this is carried out off-line using a rotary evaporator, gas purging and Kuderna Danish apparatus. These methods are time consuming, cumbersome and do not allow for automation. While there has been much attention placed on on-line extraction techniques, a concurrent development in concentration procedures has not occurred. With the push to develop totally automated systems, concentration procedures must be integrated.

A membrane based, on-line concentration technique has been reported by Bishop and Mitra and is shown in Fig. 22 [65]. This is based on the principle of pervaporation. Instead of the selective permeation of the solute (as mentioned before), selective solvent permeation leads to analyte preconcentration. The dilute solution is injected into a shell and tube module, and an inert gas such as nitrogen flows on the permeate side. The membrane preferentially allows migration of the solvent across it and a concentrated solution results in the lumen. The process was demonstrated using both polar and non-polar membranes for analytes such as, atrazine, pentachlorophenol, naphthalene and biphenyl. The process is illustrated below. The instrumentation
is simple and can be automated to concentrate either multiple samples or interfaced with chromatography.

The solvents tested were hexane (non-polar) and methanol (polar). The choice of membrane depended on the solvent. The combination of hexane and a non-polar composite membrane (polypropylene with a thin layer of siloxane) provide enrichment factors close to 20 in less than 30 s. Equivalent concentration in a rotary evaporator would take hours. A Nafion™ membrane was used for polar solvents, such as methanol, and the concentration time was same as above. This is clearly a significant development in an on-line concentration procedure.

In addition, on-line coupling of pervaporation and HPLC was applied to the continuous monitoring of trace pharmaceuticals in a process stream [66]. A Nafion hollow fiber membrane module was used for monitoring 2,6-dichlorophenylacetic acid (D CPA), naphthylacetonitrile (NA), 4-chloro-3-nitrobenzophenone (CNBP), 1,2-diphenylhydrazine (DPh) and 2-chloro-3,4-dihydroxyacetophenone (CDHAP) in methanol. Analysis and detection was via HPLC-UV and enrichment factors as high as 7.9 with 91% solvent reduction were observed. On the whole, the advantage of this approach is that it can provide fast (30–60 s) preconcentration of discrete samples for off-line analysis, and can also be performed on-line for continuous monitoring.

4.3. Development of total analytical system based on membrane separation

The concept of a total analytical system (TAS) refers to the coupling of different sample preparation and analytical steps into one integrated system. Membrane based extraction and concentration techniques presented so far can be coupled to form a TAS. Fig. 23 shows the coupling of two membrane modules. In the first, the analytes are extracted by LLME, and in the second they are concentrated via pervaporation, which is followed by on-line HPLC detection. This was demonstrated by Wang and Mitra [67] for naphthalene and biphenyl, where EF was as high as 192, and ppt level detection limits were obtained. Conceptually, this idea serves as the basis for developing other integrated systems.

4.4. Automated SLME

SLME has been used extensively in a variety of laboratory based off-line extraction techniques [68–71]. These are not discussed here because this article mainly focuses on automated analysis. An important application of automated SLME analysis reported recently, is for monitoring haloacetic acids (HAAs) in water. Conventional methods for HAA analysis involves, off-line extraction and derivatization followed by GC-ECD. On-line monitoring of HAA was tried using both LLME and SLME. In the SLME mode, the HFM was soaked in supporting liquid comprising 5% trioctylphosphine oxide (TOPO) in dihexyl ether which was held in the pores of the hydrophobic membranes by capillary forces. The pH of the sample solution was kept low so that the HAAs were in their uncharged form. The HAAs were then extracted by a high pH acceptor and analyzed by on-line HPLC. The set-up was like the one shown in Fig. 18. A typical series of chromatograms of the HAAs generated by on-line analysis is shown in Fig. 24. EFs were as high as 500 and EE reached 54%. Automated LLME using MTBE as the extraction solvent showed an EF of 50 and EE of around 50% [72]. The SLM had a fairly long lifetime and can be re-supported on-line.

Automated SLME has also been used for the determination of triazines in oil [73], thiophanate methyl and its metabolites [74]
and Ropivacaine metabolites in urine [75] and for the enrichment of triazine herbicides in both urine and surface water [76]. Ropivacaine was analyzed using a microfluidic membrane module in tandem with ion-pair chromatography [75] while the triazine studies involved a flat sheet block module coupled to either a diode array spectrophotometer or to HPLC [73]. Since thiophanate methyl, is non-polar and its metabolites are polar, Sandahl et al. [74] developed an on-line sample preparation system that used parallel SLME and LLME. The system, shown in Fig. 25, consisted of flat porous PTFE membrane enclosed between blocks of microchannels, syringe pumps and multiport injection valves which allowed interface of the membrane unit and HPLC-UV.

4.5. Automated hollow fiber based microextraction

This technique has also been called hollow fiber liquid phase microextraction (HF-LPME). It refers to the use of a single hollow fiber strand filled with a few microliters of an extractant. It is placed in an aqueous sample and extraction is carried out over 20–40 min. It can be used in the LLME or SLME mode depending on the analyte being investigated. It has been used for a wide range of organics including PAHs, drugs and pesticides [77–79].

Hollow fiber liquid phase microextraction (HF-LPME) may be carried out in two modes: (1) static HF-LPME and (2) dynamic HF-LPME. In static mode, the acceptor solution remains in the lumen throughout the entire extraction. In dynamic mode however, the acceptor is repeatedly introduced and withdrawn from the lumen. In 2002, Zhao and Lee [80] reported a semi-automated technique for PAHs which exhibited EF of approximately 35 and 70 for static and dynamic HF-LPME, respectively. Other studies [77,78,81] have also shown that dynamic HF-LPME typically gives higher enrichment factors. HF-LPME is capable of achieving high EE and EF within 15–45 min and is compatible with matrices such as plasma, urine, saliva, breast milk, pond water, seawater and soil slurries [61]. Basheer et al. [81,82] used LPME in conjunction with GC–MS and reported EF up to 100 for organochlorine pesticides (OCPs) and PAHs in rainwater and detection limits comparable to EPA method 508 for OCPs in seawater. Hou et al. [77] in 2003 developed an automated HF dynamic LPME for organochlorine pesticides. A programmable syringe pump was attached to the syringe, as shown in Fig. 26, and parameters such as refill speed and sample volume could be automatically controlled.

Following extraction, the extract filled syringe was injected directly into a GC–MS. This technique provided enrichment factors of 480 and upper RSDs of 9.8% compared to 11.3% [83] and 14% [82] for HF-LPME non-automated. In 2005, Wu et. al. reported another automated LPME called automated dynamic liquid–liquid–liquid microextraction (D-LLLME) coupled with HPLC-UV. This was a three-phase system in which chlorophenoxy herbicides were extracted with enrichment factors up to 490 and RSDs below 7.5% [84]. While this technique provided high enrichment factors it is not a continuous or on-line process, and is automated by a series of batch operations.

Fig. 25. Simplified schematic of simultaneous SLME and LLME. The membrane module was fabricated on PTFE or titanium blocks [74].

Fig. 26. Automated dynamic HF-LPME. A programmable pump continuously injects the organic solvent into, and then withdraws it from the lumen.
5. Automated metal analysis

The most common sample preparation technique for metals in water is organic extraction via chelation. A chelating agent such as 8-hydroxyquinoline, dithizone or cupferron along with an organic solvent (such as methyl isobutyl ketone) is added to the sample and shaken in a separatory funnel [1]. In 1980, Babcock et al. reported the use of hollow fiber membrane in SLM [85], and in 1984, Danesi described a simplified model for the carrier-facilitated transport of metal ions through hollow fiber supported liquid membranes [86]. By the late nineties, membrane extraction of metals became an acceptable technology for

Table 1
Overview of automated, on-line membrane extraction

<table>
<thead>
<tr>
<th>Technique</th>
<th>Membrane used</th>
<th>Interface</th>
<th>Compounds extracted</th>
<th>Reference</th>
</tr>
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</table>
| Automated VOC analysis | ● Composite silicone (homogenous siloxane supported on microporous polypropylene)  
● Polydimethylsiloxane  
● Polyethylene | MS, GC, GC/MS                      | Polar and non-polar VOCs, e.g. benzene, toluene, chlorobenzene, methanol, acetone, methylene chloride, o-nitrotoluene | [46,49,51,52,94,95] |
| Automated SVOC analysis  | ● LLME: microporous polypropylene filled with n-hexane, flat sheet microporous polypropylene and isoctane as extractant  
● SLME: n-decane with microporous polypropylene support, dihexyl ether or 6-undecanone, immobilized in microporous polypropylene | GC-ECD, GC-NPD  
HPLC-UV, LC/ESI-MS, CE-UV | Polar and non-polar SVOCs, e.g. PAHs, acids, PCBs, pesticides, drugs and their metabolites, anesthetics | [60,62] |
| Automated concentration  | ● Microporous hydrophobic polypropylene coated homogenous siloxane  
● Nafion [co-polymer of tetrafluoroethylene (Teflon) and perfluoro-3,6-dioxo-4-methyl-7-octene-sulfonic acid]  
● Flat sheet P84[co-polyimide of 3,3-4, 4-benzophenone tetracarboxylic dianhydride and 80% methylphenylene-diamine + 20% methylene diamine) | HPLC-UV | Naphthalene, atrazine, pentachlorophenol, isopropanol, 2,6-dichlorophenylacetic acid | [65,66] |
| Automated metal extraction | ● Porous PTFE with di-2-ethylhexyl phosphoric acid as membrane liquid  
● Polypropylene HFM with Cyanex 471 and Aliquat 336 as extractant | ETAAS, FAAS, ICP-MS  | Co, Zn, Cd, Pd, Pt, Rh | [71,73,89] |
the recovery of metals from waste streams [87–91]. Its use in analytical sample preparation has been rather limited.

The use of HF-SLME in the cleanup, extraction and enrichment of numerous metals including Pb, Cu, Cr, La, Ce, Zn and Co has been reported [14,92,93]. This method has usually been interfaced with atomic absorption spectroscopy (AAS) or inductively coupled plasma mass spectrometry (ICP-MS) as shown in Fig. 27, although Ndungu et al. [14] reported an interface with ion pair chromatography for Zn, Ni, Co, Mn and Cd. Typical extractants include di-hexylether or kerosene diluted di-(2-ethylhexyl) phosphoric acid (DEHPA), Aliquat 336, LIX 860-I, Cyanex 302 and tri-n-butyl phosphate (TBP). Extraction efficiencies and enrichment factors up to 95% and 200, respectively, have been reported [92].

6. Conclusion

Non-porous and microporous membranes are versatile structures that can be used for the extraction and concentration of a wide range of compounds, such as, VOCs, SVOCs, organic acids, ions and metals. Different processes have been developed to facilitate automation and direct interfacing with analytical instrumentation like GC, HPLC, MS and AA. Table 1 summarizes the extraction techniques discussed in this paper. Moreover, there exist numerous other possibilities that are yet to be explored. On the whole membrane extraction and concentration offers some unique possibilities beyond the capabilities of conventional means, particularly in the field of automated analysis. The challenge in the future lies in enhancing selectivity, testing diverse analytes and incorporation in lab-on-a-chip devices.

References