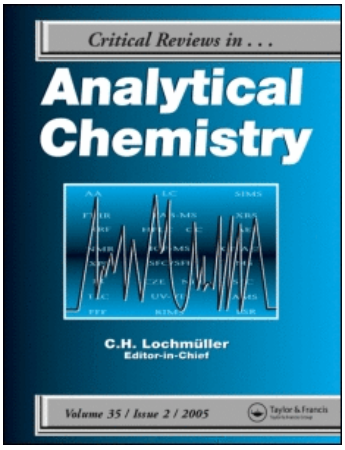

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Gas Diffusion/Permeation Flow Injection Analysis. Part I. Principles and Instrumentation

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Gas Diffusion/Permeation Flow Injection Analysis. Part I. Principles and Instrumentation

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ABSTRACT: Gas diffusion/permeation techniques involving different membrane interphases or an open fluid/fluid interface are presented as powerful tools for separation and/or preconcentration of a variety of classes of analytes, i.e., gases, gas-evolving species, volatile inorganic and organic substances, etc., from gaseous, aquatic, or organic sample matrices. Principles of the techniques and factors influencing transmembrane transport, such as acidity of the donor and the acceptor streams, their flow rates, membrane characteristics, temperature, pressure, etc., are described. Different configurations of FIA manifolds for stopped-flow, closed-loop, and continuous flow arrangements, designs of principal instrumental modules, characteristics of different semipermeable membranes, and special arrangements of detection systems are outlined.

KEY WORDS: flow injection analysis, membrane separation, preconcentration, instrumentation, gas diffusion, gas permeation.

I. INTRODUCTION

Among the classical preconcentration and separation techniques, the popularity of gas diffusion/permeation techniques, using either semipermeable membranes or an open fluid/fluid interface, has increased inasmuch as they offer a great potential for selectivity and/or sensitivity improvement for a number of areas. Gas diffusion/permeation techniques play more important roles in flow-injection analysis (FIA) than the other membrane-assisted techniques because they are well suited for adaptation into flow systems[1–7] and easy to automate. The continuous-flow versions are simple, fast, and reproducible, in contrast to equilibrium modes, which are normally time consuming and seldom appropriate for quantitative measurements. The flow versions can provide continuous- or stopped-flow measurement over an extended period of time. They do not require manual, time-consuming operations and eliminate most of the problems associated with other related preconcentration and separation techniques (e.g., liquid-liquid extraction, ion exchange, and precipitation). Furthermore, kinetic factors that are typical for flow-injection systems can enhance the selectivity of detection.[7]

II. PRINCIPLES

The concept of gas diffusion/permeation mass transport has been applied in continuous-flow systems with and without membrane-separation modules for many years, mainly in routine clinical laboratories. The use of gas diffusion/permeation in SCFA has been described by Skeggs.[8] A gas-permeation approach without air segmentation was first exploited in flow injection analysis (FIA) for the determination of carbon dioxide in blood.[9] Since that time, this progressive technique has been reviewed several times,[10–20] and numerous papers dealing with the technique have been published.[9–109] Despite these facts, the gas diffusion/permeation (GDP) FIA has not yet been exploited to its full potential mainly because it is thought to be a slow, insufficiently effective, and poorly defined process.

GDP FIA techniques are frequently used for separation and/or preconcentration of a wide

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variety of inorganic (gases, volatile compounds, and gas-evolving ions such as ammonium, carbonates, sulfides, etc.) and organic volatile analytes (phenols, aldehydes, ketones, alcohols, carboxylic acids, etc.) from aquatic or gaseous sample matrices into a stagnant, circulating, or continuously flowing receptor stream. The GDP FIA separation/preconcentration techniques can be used for

- Separation of an analyte from a matrix
- Separation of a matrix from an analyte
- Preconcentration (stagnant or continuously flowing acceptor stream at $Q_D > Q_A$)
- Dilution (continuously flowing acceptor stream at $Q_A > Q_D$)
- Speciation (different physicochemical forms of the analyte)
- Separation of two immiscible phases (including hydride techniques)
- Introduction of reagents and samples
- Preparation of standards
- Interfacing of hybrid techniques

The techniques are based on isolation of particular species from the original matrix by transmembrane transition through a semipermeable membrane into an appropriate receptor due to the differences in transport efficiencies across the membrane as a barrier or across an open gas/liquid interface. Mixtures of various chemical species are transported under a driving force of gradients in their chemical potentials across a restrictive interphase. The mass transport has been discussed with respect to several theoretical models,[21–26] general expressions for the membrane transport in a flow-through diffusion cell have been derived, and the theoretical predictions have been verified.[22] The separation efficiency of semipermeable membranes was optimized and the separation yield was determined by the fraction collection method.[27–32] Although mathematically consistent, the simplest models appear to be of limited value for optimization of the gas diffusion process because they assume perfect mixing in both channels (donor and acceptor), strictly laminar flows, and they do not explicitly contain all the factors affecting the transmembrane transport. More complex descriptions exceed the scope of this article and have been discussed elsewhere.[23–26]

In the simplest membrane-assisted GDP FIA version (Figure 1), untreated aqueous or gaseous samples are injected in definite volumes into either an inert carrier stream or a suitable modifier, both serving as the donor stream. Sample zones disperse into the inert carrier, or sample components react with the modifier in a mixing/reaction coil, to form species that are transportable through the membrane. The geometry of the coil is dictated by the rate of the mixing process, the dispersion, and the reaction rate. The presence of a modifier increases the efficiency and/or the selectivity of transmembrane transition of the species (Figure 1b) across the particular membrane converting the species of interest more or less quantitatively into their transportable forms or retarding the transport of unwanted species by their conversion to nontransportable species.

The donor stream enters the membrane device and all transportable species pass through the membrane from its donor side to the acceptor side where they are collected in a stagnant, circulating, or continuously flowing acceptor stream (liquid or gaseous). The acceptor fluid must have enough absorption capacity to quantitatively and rapidly collect all of the penetrated analytes. The degree of partition between the membrane matrix and both the donor and the acceptor streams depends on experimental factors such as sample contact time with the membrane, an active area of the membrane, composition of the donor, and the acceptor fluids and membrane properties. At given experimental conditions, the transfer efficiency for different species is related to Henry's constants, partial pressures, partition coefficients between the fluids and the membrane matrix, and diffusion coefficients through the membrane matrix.[21–26]

The penetrated analytes of interest can be detected directly based on their characteristic physicochemical properties. They can eventually be merged with a suitable organic analytical reagent to produce detectable products. The reagent can be present in either an acceptor stream or an additional reagent stream (see dotted line in Figure 2a). The resulting analytical signal has a typical FIA profile corresponding to the concentration profile of the original reaction zone. Peak heights or peak areas are commonly used for quantitation.

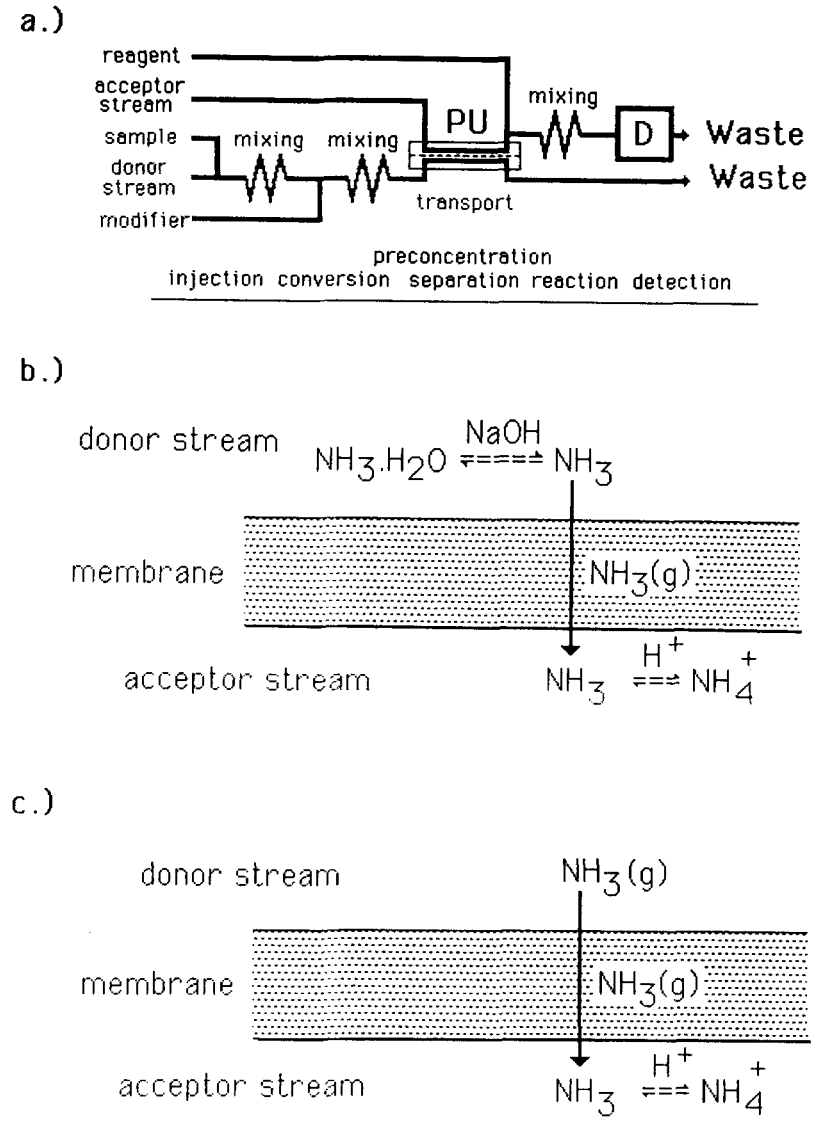

FIGURE 1. (a) A block scheme of DGP-FIA manifold (b) the principle of gas diffusion/permeation transmembrane transition of an analyte from a modified (c) an unmodified (gaseous) donor stream. PU, Membrane diffusion/permeation unit; D, detector.

The transmembrane transport can be realized from a gaseous,[33–35] liquid, aqueous,[36–68] or organic[69–72] donor stream (and also from solid samples in some special cases), in which the compounds of interest can eventually be chemically converted to a transportable species, into a suitable gaseous or liquid (organic solvent or aqueous) acceptor stream. Thus, different combinations can be realized depending on the character of the sample and of the analytical system (Table 1).

The techniques illustrated in Table 1 offer several features, the most striking being that they are particularly suitable for samples with a very complex matrix (e.g., those containing high concentrations of ionic species such as seawater[36,37]). This also applies because few compounds are effectively transported across the membranes at room temperature. Solids and particles, colloidal and colored matter, etc., which are often found in biological fluids,[8,9,38,39] wastewater,[40–47] process streams,[48,49] and related samples, also can be

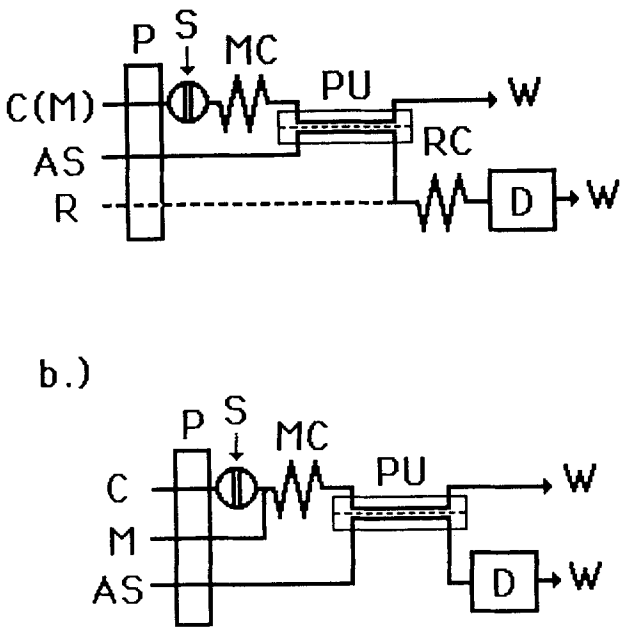

FIGURE 2. Manifolds for continuous-flow mode operations with a membrane separation unit showing injection of the sample into a carrier or a modifier stream (a) with (b) without chemical reaction prior to detection. C, Carrier; M, modifier; R, reagent; P, peristaltic pump; S, sample; AS, acceptor stream; MC, mixing coil; RC, reaction coil; W, waste; DS, donor stream.

III. INSTRUMENTATION

A. FIA Manifolds

Flow-injection apparatus (see Figures 2 through 16 for manifolds) are fabricated from parts commonly used in conventional FIA. A membrane device and an appropriate membrane are special parts of the manifolds that are detailed later; also, some unique arrangements of detectors developed in connection with the membrane device are addressed. The selection of particular instrumental modules can be made on the same basis as ordinary FIA manifolds.[1–7] No other requirements are usually needed for construction materials. Chemically inert materials (e.g., fluoroplastics such as Teflon and PVDF, stainless steel, and others), that do not interact either with the analyte or reagents are preferable. Optical, electrochemical, and other detectors, coupled either with a chart recorder or a computer, are commonly used for quantitation in a traditional way. Due to the high selectivity of transmembrane transport, the selectivity of detectors can be intrinsically enhanced.[50–56] Nonselective detectors, i.e., conductometric,[58–64] potentiometric, etc., also can be used to great advantage.

TABLE 1
Survey of Possible Combinations of Donor and Acceptor Media in Membrane Separation Techniques

Sample	Gas	Gas	Liquid[a]	Liquid[b]	Solid	Solid
Acceptor	Gas	Liquid[b]	Liquid[a]	Gas	Liquid[b]	Gas

[a] aq/aq, aq/org, aq/org/aq.
[b] Aqueous or organic.

physically separated from the detector (acceptor) stream, thereby greatly avoiding matrix effects. Furthermore, the composition of both the donor and the acceptor fluids might be chosen to enhance the selectivity of the determination in acid/base, redox, complexation, and other properties of analytes and/or interferents.[45–47] Needless to say, the modifier itself must not respond.

Several manifolds of different complexity have been utilized for determining gaseous, gas evolving, and volatile species using GDP FIA techniques. In common practice (Figure 2), definite volumes (from micro- to milliliters) of an aqueous or a gaseous sample can be introduced into a continuously flowing, inert carrier stream or into a suitable modifier by an injection or a

time-controlled introduction via an introductory device (Figure 2a). The sample zones eventually can be merged with an additional stream containing a modifier in the former case (Figure 2b). The acceptor stream continuously flowing through the membrane unit at Q_A–Q_D and containing a portion of the analyte penetrated across the membrane can optionally be merged with an analytical reagent (Figure 2a, dotted line) to form a detectable product.

The GDP unit obviously can serve as a means for the preconcentration of analytes from very dilute solutions or for the analyte dilution. Two modes of membrane operations can be used in the former case: the continuous flow mode (Figure 2) with the donor to acceptor flow rate ratio Q_D/Q_A » 1 and the stop-flow mode (Figure 3) with a small volume of an acceptor fluid enclosed inside a sample loop of the injection device[42,45–47] or continuously circulating in a closed loop (the typical enrichment factors being, respectively, 2 to 5 and 50 to 200). An untreated sample is fed continuously into the membrane device to be in direct contact with the semipermeable membrane for an extended time or it can be merged with the modifier in a continuous-flow mode before entering the membrane device in this particular case. The larger volume of the sample can be eventually injected into either a carrier stream or a suitable modifier forming the typical concentration FIA profile prior to entering the membrane device (Figure 2).

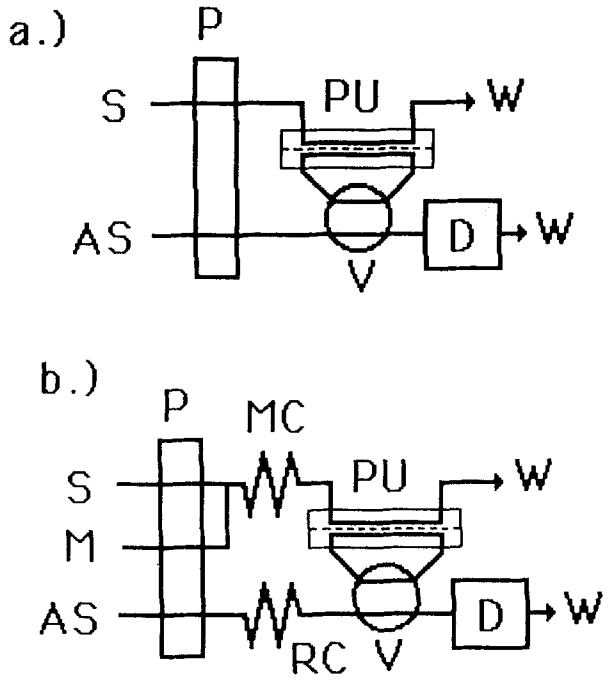

FIGURE 3. FIA manifolds for stop-flow preconcentration modes without (a) or with (b) modification of a continuously flowing donor stream. V, Four- or six-port injection valve.

Because of insufficient efficiency of transport through the membrane (typically from fractions of units to tens of percentages) when a continuously flowing acceptor stream is used, a considerable loss of sensitivity occurs even when the donor/acceptor stream flow rate ratio Q_D/Q_A is large. On the other hand, a considerable decrease of the analyte content can be achieved by applying the membrane technique with a high acceptor-to-donor flow ratio, Q_A » Q_D and/or a highly resistant (thick-wall) membrane. It should be mentioned in this context that by pumping the acceptor stream over the limited range n-times slower (faster) than the donor stream, the concentration in the acceptor stream will be approximately n-times higher (lower) than if both streams are pumped at the same flow rates; however, the signal increases exponentially at low flow rates of the acceptor stream (linearly proportional to the inverse value of Q_A) and vice versa. Thus, the analyte concentrations can be simply varied over a wide range.

The same FIA configurations also can be used for reducing interferences or even for separating transportable interferents (oxygen, carbon dioxide, etc.) from an analyte stream when an efficient transmembrane transition is used in combination with a membrane device of suitable length.

The extent of the preconcentration can be exploited to its fullest potential if the acceptor stream is stopped inside the injection loop while a large volume of sample is passed through the unit (Figure 3).[42,45–47] Because the sample can be pumped for any preset time period, the gas diffusion unit in this case not only serves to separate the analyte from matrix effectively, but also can be a tool for its preconcentration. A completely stationary acceptor solution in the acceptor channel produces a certain amount of preconcentration during the separation step, with the enrichment

factor being linearly dependent on the preconcentration period.

Another approach for the on-line preconcentration of gaseous and volatile analytes from fluid samples is the continuous transport into an acceptor liquid that is circulating in a closed loop.[65–68] The apparatus consists of an introductory part and an acceptor (closed-loop) part with a four-way switching valve and a circulating peristaltic pump. Both parts are separated from each other by a membrane device.

A fresh sample stream continuously enters the membrane device. The acceptor liquid is directed back repeatedly into the closed loop or to the waste by the four-way switching valve. This arrangement allows the acceptor liquid to be circulating in the loop while the sample stream flowing through the membrane device can be directed to the waste. The analyte is continuously separated and preconcentrated from a large volume of the sample into a small volume of the acceptor liquid circulating in the closed loop. The analytical signal is monitored either continuously by an on-tube detector situated on a closed-loop FIA manifold (Figure 4a) or after a preselected time period by a detector located outside of the loop. An enrichment factor depends on the loaded volume of the sample (time of sampling), the transfer efficiency, and the loop volume.

A similar approach for handling gaseous samples is based on the continuous transport of gases into an acceptor liquid across an open gas/liquid interface.[65–68] The loop is connected to a fresh sample stream, which continuously enters the closed loop system via a four-way valve and leaves the loop after separation in the phase separator (a membrane type or a simple debubbler). The apparatus consists of an introductory part with a four-way switching valve, a segmented (two-phase, gas/liquid) part, and an unsegmented part. The segmented part, in which alternate segments of a gaseous sample and an acceptor liquid are equilibrated, is separated from the unsegmented part by a gas/liquid separator. An on-loop photometric detector and a circulating peristaltic pump are located in the unsegmented part. The separated acceptor liquid is directed back repeatedly into the closed loop or to the waste by another four-way switching valve. The analytical signal is monitored continuously by an on-tube photometric detector situated on a closed loop FIA manifold (Figure 4b).

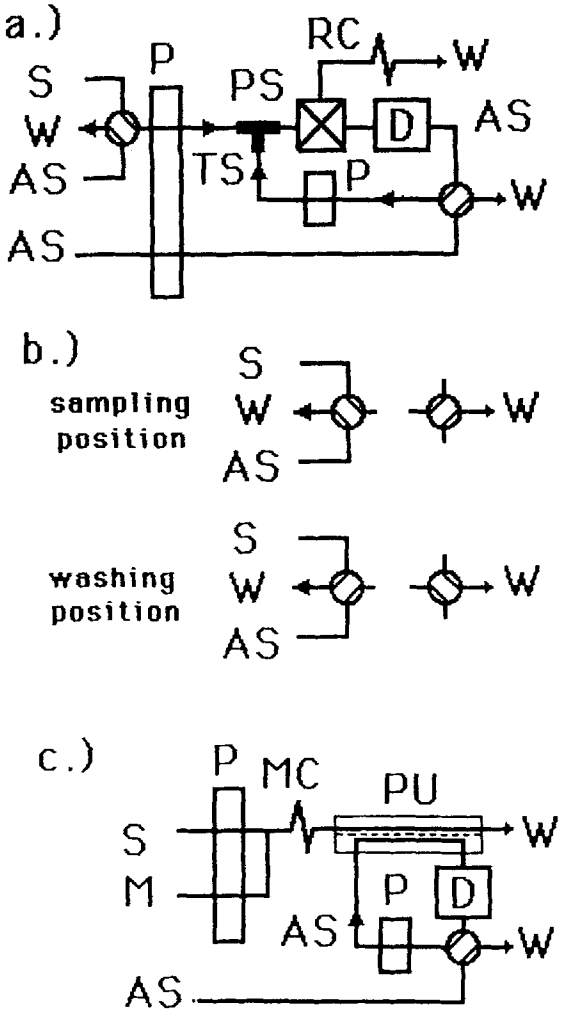

FIGURE 4. A closed-loop manifold for continuous introduction of a fresh gaseous sample into a continuously circulating acceptor stream (a) in a segmented mode (c) with a membrane diffusion/permeation device. Sampling and washing positions of the valves also are depicted (b). TS, T-piece segmenter; PS, debubbler or a membrane phase separator; RC, restriction coil.

Selectivity of the determination can be intrinsically improved by a two-stage membrane technique utilizing either a two-transmembrane mechanism or different discrimination chemistries.[35,45–47] Different configurations of the FIA manifold with two membrane units can be applied for the two-stage operation employing acid/base, complexation, or redox properties of the particular species for the discrimination of the transmembrane transition. A particular group of analytes can be preseparated from the major components of the

matrix in the first stage and subsequently selectively transported across the membrane in the second stage. A preconcentration step can eventually be performed in either the first or second stage (Figure 5a and b).

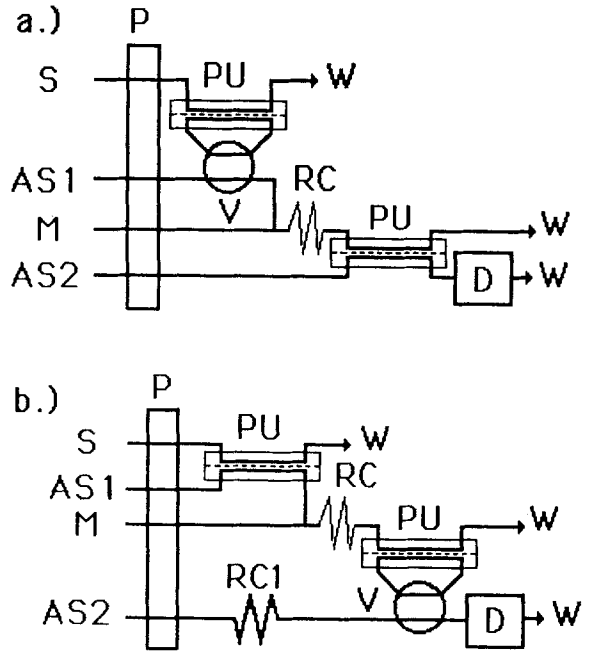

FIGURE 5. FIA manifolds for two-stage, membrane-assisted operation with the preconcentration stage in either the first (a) or second (b) step. AS1 and AS2, acceptor streams of different composition; RC1, restriction coil in front of detector to reduce pulsations.

A dual membrane device with either two identical or two different kinds of membranes can be used for the simultaneous determination of two particular analytes from a single donor stream by collecting them in two separate acceptor streams of different composition. Differences in transmembrane transport rates of the species also can be of practical interest (Figure 6). Manifolds with two membrane devices in series (one of them being connected to the alkaline acceptor stream and the other connected to the acidic acceptor stream, preferably absorbing acidic and alkaline analytes, respectively) have the same function (see Figure 7). The systems can, for example, be used for the simultaneous determination of acidic and alkaline gases with two detectors in parallel (Figures 6a and 7b) or with a single detector situated after the confluence point (Figures 6b

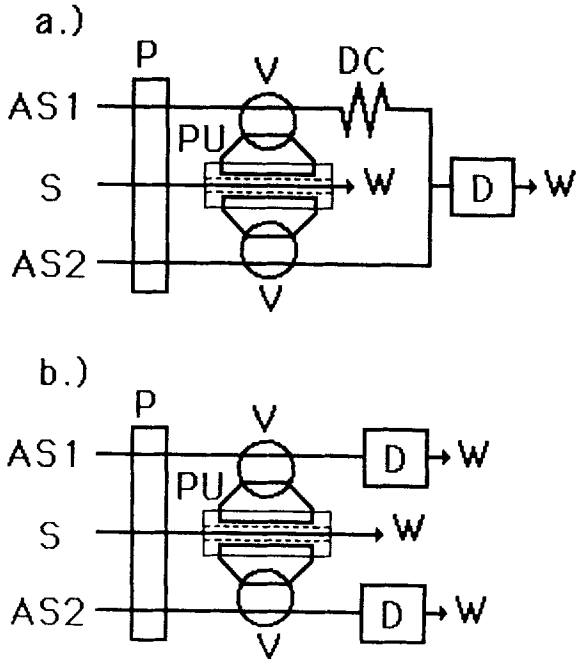

FIGURE 6. FIA manifolds with dual-membrane gas diffusion/permeation devices, with a single detector (a) or two detectors in parallel (b) and analytes preconcentration in both lines. DC, Delay coil.

and 7a). Two separated peaks are obtained using a delay coil of suitable length in one particular line in the latter case.

Speciation of a particular analyte can be provided using two membrane devices either in series or in parallel. An untreated sample can be fed continuously into the first membrane device to be in direct contact with the semipermeable membrane, with the analytical signal being related to the content of "free" species. The effluent is then mixed with a suitable modifier before it enters the second membrane unit. The analytical signal corresponds to the total or "available" content of the species in this particular case (Figure 5b). The sample also can be split or injected simultaneously into two separate channels passing two membrane units in a parallel configuration (Figure 8). One part of the donor stream passes through its particular membrane unit untreated, or it can be merged with an inert carrier while the second part of the donor stream is merged with an appropriate modifier to liberate all available forms of the analyte before entering its particular membrane device. Two detectors can be used to monitor the

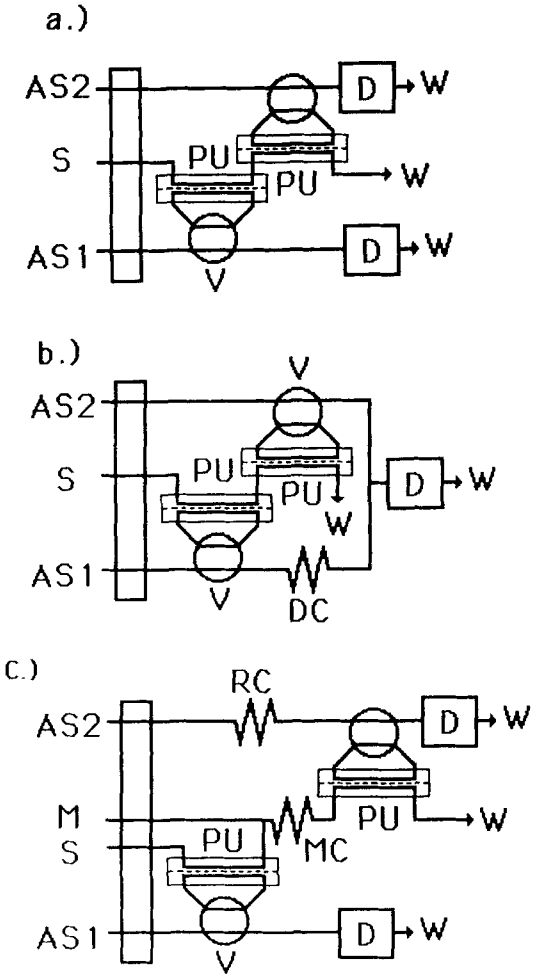

FIGURE 7. FIA manifolds with two membrane gas diffusion/permeation devices in series and with a single detector (b) or with two detectors in parallel (a and c) and with/without sample modification (a, b, and c, respectively). Preconcentration of analytes is applied in both lines.

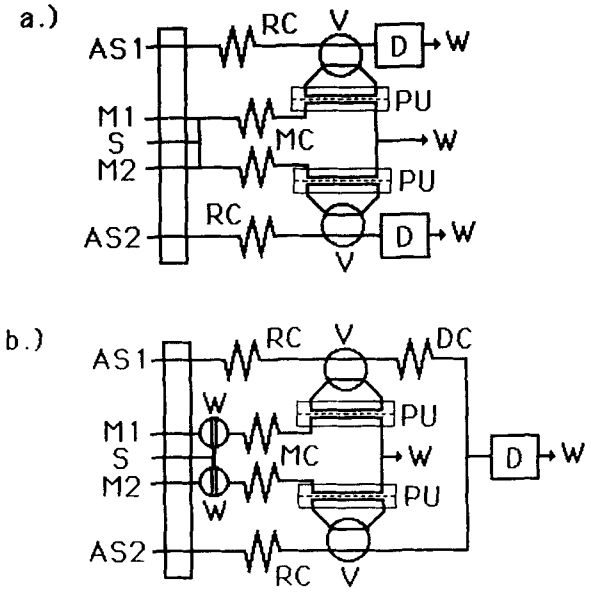

FIGURE 8. FIA manifolds for the simultaneous determination of two components or species applying a single detector (b) and two detectors in parallel (a), and the analyte preconcentration in both lines after splitting (a) or simultaneous injection (b) of the sample into two independent lines. M1 and M2, modifiers of different composition.

concentration of the "free" and the total (available) amount of the analyte (Figure 8a) or two separated peaks can be obtained using the delay coil of a suitable length in each particular line and a confluence point in front of a single detector (Figure 8b).

Organic volatile compounds,[33,69–76] several gases, and ions can be determined by the membrane technique using supported liquid membranes consisting of a microporous (Teflon, PVDF, cellulose, etc.) membrane with either a permanently immobilized solvent[69] or continuously wetted with a suitable organic solvent (Figure 9a and b). A silicone rubber membrane surrounded by an organic solvent also can be used as a suitable barrier for separation of organic compounds.[70,71] The solvent may or may not contain an organic analytical reagent increasing selectivity and/or efficiency of the transmembrane transport of the species in interest. A device with a free gas/liquid interface can be applied for determination of gases or volatile substances in gaseous samples (Figure 9c).

Inherently, any membrane diffusion/permeation technique can be miniaturized and integrated into FIA microcircuits where an added advantage can be gained by combining the gas diffusion with the detection facilities offered by miniaturized optosensors or light-guided optical fiber detectors (see Section III.D).

B. Membrane Devices

A gas diffusion/permeation cell is used to transfer gaseous or volatile components from a donor stream to an acceptor fluid, with the streams usually being separated by a semipermeable membrane. Generally, the components are either formed

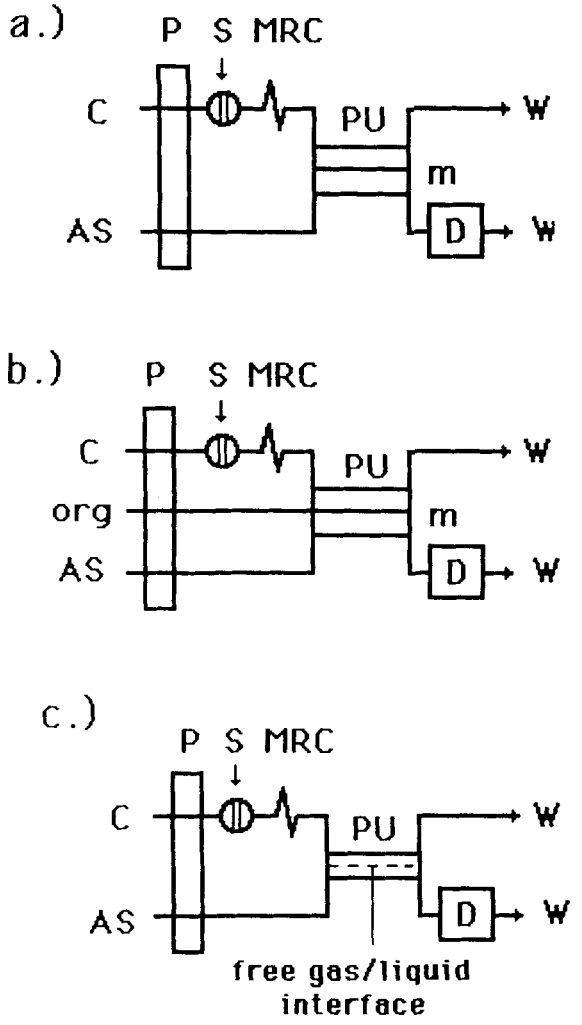

FIGURE 9. FIA manifolds with supported liquid-membrane devices with immobilized (a) or continuously wetted (b) microporous membranes, and with the open gas/liquid interface (c) org, organic phase; MRC, mixing and reaction coil; m, membrane.

in the system due to an induced chemical reaction or they are present as analytes of interest.

The membrane separation/preconcentration device is the most important part of the GDP FIA manifold. Its correct and highly efficient performance is one of the keys to successful development of any membrane separation process. The correct performance is critical for the good signal and baseline stability and signal-to-noise (S/N) ratio of the detector. Consequently, the membrane device has been the object of considerable study regarding its design and operational theory.[21–32] Several models have been designed with the aim of improving the transport efficiency but the appropriate selection of the membrane material and establishment of experimental conditions (discrimination chemistries) seem to be the more promising research areas for the near future.

Very few fundamental studies of cell designs and membrane properties have been published.[30–35] In order to design an efficient membrane device, the following factors should be considered: the membrane material, the area of the membrane exposed to the donor and acceptor streams, and the volume and the geometry of the grooves or the cavities on both sides of the membrane. The device has to continuously separate the analyte from the donor stream with the long-term stability of the transmembrane transition in order to work properly over a wide range of flow rates and flow rate ratios, to move the analyte at maximum transport efficiency (hopefully approaching 100%) and selectivity, to prevent any additional dispersion and unwanted dilution, to maintain the concentration profile of the analyte in the donor stream, to prevent deterioration of the original concentration profile, to handle the small volumes of the acceptor stream, and to handle different types of analytes. A well-defined concentration profile of the original sample plug and short contact time of the sample zone with the membrane will produce the sharper shape of the resulting analytical signal. This is important in order to construct the cell and to decide on the flow rate of the streams through the cell.

The membrane device must be made from a chemically inert material, e.g., fluoroplastics, Plexiglas, stainless steel, etc., to prevent any disruption with the sample, reagents, or modifiers. A transparent material is preferable to allow visual control of both channels because gas bubbles, particles, and other mechanical deposits must be removed carefully from the channels to assure proper function of the device. The long-term stability of the separation process should be adequate, and no adsorption should occur on the walls of the device, on the membrane surface, or even in the pores of the membrane matrix. Any changes in the active surface area can affect the transmembrane transport efficiency and the baseline parameters.

Depending on the configuration of the membrane (planar or tubular), a sandwich (groove)

cell with a rectangular or circular membrane or a coaxial diffusion cell with a tubular membrane are positioned in direct contact with the donor stream. The volume and geometry of the channels are fundamental parameters for the transport process. The volume should be as small as possible with the maximal contact area. Increasing the membrane area, which can be achieved either by making the grooves shallower and wider, or longer (or both), increases the transport efficiency, as does the use of multiple capillary membrane tubing. In nonsegmental systems, the unit can be made extremely small and the flow rates may be considerably reduced, thus retaining a wide range of flow rates and flow rate ratios.

A membrane support is useful when unbacked membranes are used in a grooved, and especially in a circular, sandwich device. Support structures, such as solid half-spheres protruding into the channels with slightly polished surfaces, glass or Teflon beds, or fibers, Teflon, nylon, or metallic net positioned from one or both sides, could be placed into both channels for flat support of the membrane (Figure 10). Better fluid mixing also should be expected if the support structures are placed in both channels for groove flatness distribution. They improve radial transport of a solute in channels (destroy the laminar flow and increase the radial diffusion), thus disrupting the laminar flow pattern. They reduce the thickness of diffusion layers and the total volume of the cavities. Agitation or ultrasonication of the membrane device has a negligible effect on the mass transfer efficiency.[35,77]

Radial diffusion in laminar flow is often the limiting factor that governs the efficiency of the transition. This phenomenon is preferable when a sample matrix contains solid particles; however, some turbulence can decrease the thickness of the diffusion layer in the liquid channels. Positioning the membrane horizontally with the donor side at the bottom increases the lifetime of the membrane because the separation process is governed by gravity forces.

The gas diffusion unit can be constructed so as to encompass an integral part of the injection valve system (Figure 3), i.e., the acceptor-part termini of the membrane device are connected either to a four- or a six-port injection valve to allow preconcentration by stopping the flow of the receptor liquid through the diffusion/permeation device in the stop-flow configuration. The device can be eventually a part of a closed loop, with the acceptor liquid continuously circulating in the loop.

1. Sandwich Membrane Device

Classical sandwich GDP modules with a rectangular or circular shaped membrane are the most frequently used designs (Figure 10). The devices consist of two pieces, each having a groove, measuring a few centimeters in length, facing the gas semipermeable membrane. Two identical grooves, or grooves of different volumes, with a constant cross-sectional area and rectangular, triangular, or circular profile are separated by the membrane. Straight, meandering, or concentric spiral grooves having several tenths of a millimeter depth and a 1- to 5-mm width are recommended. The inlet and outlet tubes at the ends of the grooves can be oriented either perpendicularly or at an angle to the main axis of the device. The membrane also can be sandwiched between two spacers (made of silicone rubber, Teflon, etc.) with straight grooves just fitting the inlet and outlet channels of the donor and acceptor bodies.[77] The components are pressed together using metallic plates and screws.

The device using circular membranes has the advantage of commercial membrane availability, higher area/volume ratio, and ease of handling. Supports (perforated Teflon, metallic screen, etc.) are necessary to prevent mechanical damage and to improve the durability and the long-term stability of the membrane because the active areas of the membrane exposed to the flow rates are usually larger than in the straight arrangements. The cells with the straight (Chemifold V) or spiral channels, separated by either the sheet (tape) or the circular membranes, have been adapted by some manufacturers and are commercially available (FIAtron, Tecator, etc.).

2. Dual Membrane Sandwich Device

The dual membrane device consists of two identical or different membranes (different material, porosity, etc.) positioned in two wells on either side of a sample (donor) channel of the central body. The body is sandwiched by two

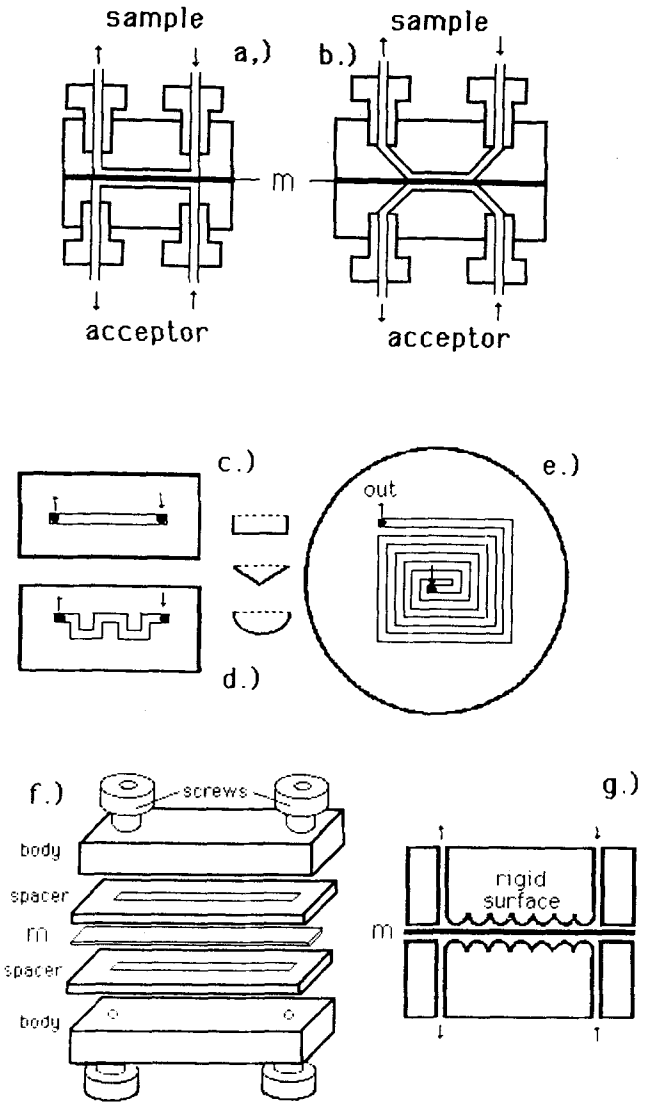

FIGURE 10. Sandwich membrane gas diffusion/permeation devices with rectangular (a to d and f) or circular (e) membranes sandwiched between two bodies (a to d) having straight (c), meander (d), or helical grooves (e) and a device with a membrane sandwiched between two planar bodies and two spacers each having a straight channel (f). A device with solid half-spheres protruding into the channels with slightly polished surfaces (g).

outer pieces, each having a groove just facing the membranes (Figure 11). The mirror-polished surfaces of the central and the outer parts of the device lying just behind the membranes are textured in a spoke-like pattern to facilitate the uniform flows of both acceptor streams around the membranes.

The donor stream flows through the central channel. The species of different properties pass across the particular membrane and are collected in suitable acceptor streams. The selectivity of the separation processes can be achieved by the differences in composition of the receptor streams (retarding absorption of particular species), experimental conditions in the donor stream, or differences in selectivities of transmembrane transport across the membranes of different character or different chemical and mechanical properties.

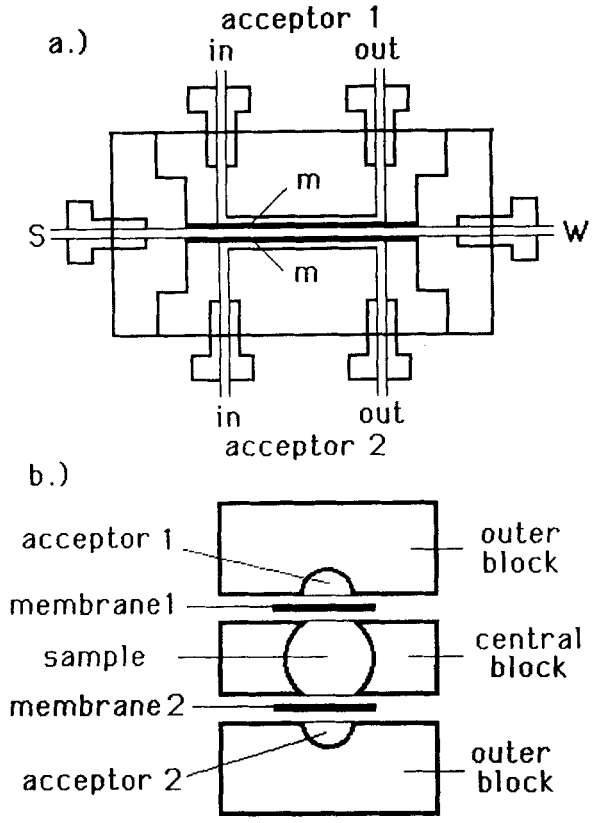

FIGURE 11. A dual-membrane device bearing two identical or different membranes. m_1 and m_2, membranes.

3. Coaxial Device

A coaxial membrane GDP module (Figure 12), a tube-in-shell device,[33,35,45–48,78,79] is made from membrane capillary tubing (from several tenths to several hundredths of millimeters wall thickness) with inlet and outlet tubing inserts (Teflon, stainless steel, etc.) at the termini for connections. Single or multiple membrane tubing is inserted into a larger tubing made of Teflon, glass, or other chemically inert material with T- or Y-joints (stainless steel, barbed polypropylene, glass, etc.) at each end for connection. The active length of the semipermeable tube can vary from several millimeters to several meters. Glass beads or other filling materials can be placed inside the membrane to reduce the internal volume of the acceptor part of the device. A fishing line also can be used for the same purpose or to make the spiral configuration of the membrane inside the large-diameter outer tube (shortening the total length of the device).[80] The precise, fixed positioning is important because the changes in an active area of the capillary membrane can cause a difference in transmembrane transport efficiency.

The donor stream flows in either the annular space or through the central membrane tube (see Figure 12 for different configurations). The former configuration has the advantage of minimizing analyte dispersion and preventing potential blockage by any particulate matter due to the larger volume. The configuration also is preferable when gaseous analytes must be separated selectively from the sample matrix containing the particles, solids, etc. because of the higher diffusion coefficients of gases compared to solids and liquids.

The coaxial modules have an advantage in their resistance to leakage of liquid and their ease of construction from the T- or Y-joints and tubing commonly used in FIA or low pressure high-performance liquid chromatography (HPLC). The higher area to volume of the device also is important. On the other hand, the device is not commercially available and the exact area of the active surface is less precisely defined and less reproducible in "homemade" constructions.

4. Stationary Configuration

Tubular[81] or planar membranes also can be inserted into a high-volume reactor for studying transmembrane transport, chemical equilibria in solutions, and process streams (Figure 13). In these particular cases, the tubular membrane of appropriate length winds around a support construction (frame) or a specially constructed device holding the planar membrane in continuous contact with the reaction mixture. Although the cells may have a sample flow passing through, additional mixing is recommended to prevent a concentration depletion layer at the membrane/sample interface. In an unstirred device, the layer is formed rapidly around the membrane and response is controlled by diffusion through the layer. When intense stirring is applied, the response is controlled only by permeation/diffusion across the membrane wall.

Analytes should be collected in either a stationary (Figure 13b) or continuously flowing ac-

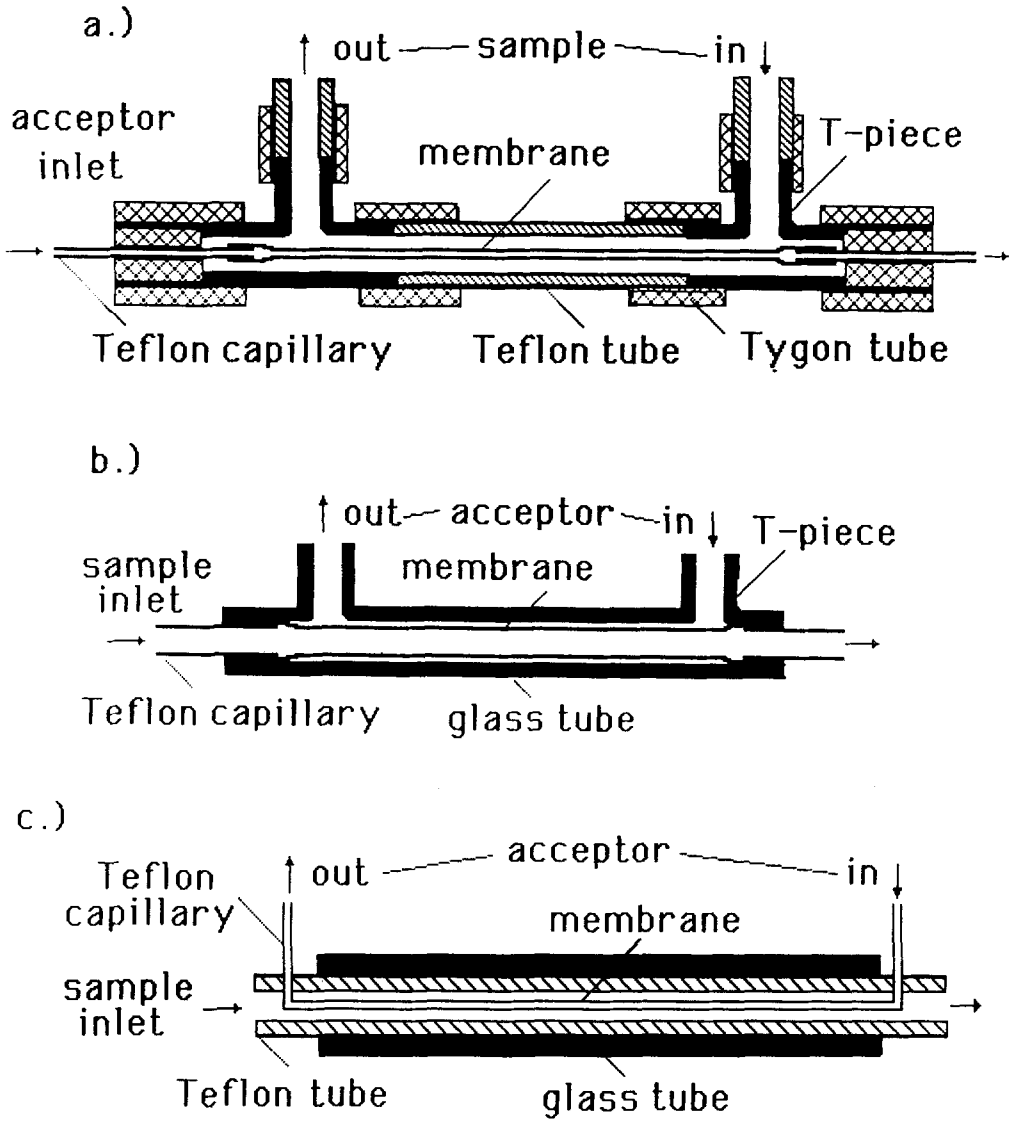

FIGURE 12. A coaxial (tube-in-shell) device constructed from barbed polypropylene T pieces (a), an all-glass device (b), and a straight diffusion scrubber device (c).

ceptor stream (Figure 13c). Among other factors, the amount of analyte in the acceptor stream is governed by experimental conditions on both sides of the membrane. The chemical reactions taking place in the reactor essentially influence the response, thus, the device is especially suitable for studying chemical equilibria in solution, dissolution processes, measurement of kinetics, etc. (Figure 13a).

Several commercially available GDP membrane devices can be used for monitoring technological[82] and biotechnological processes.[83,84] Two-step sampling operations are usually recommended because the matrix contains solids, particles, and colloidal matter. The species must be separated from the analytical system. Nonselective preseparation (filtration, dialysis, etc.) and/or dilution steps are often applied in the first stage. Homogeneous, skin-like, or double-layer membranes serve as the best barrier in the direct contact with the sample.

5. Devices With Open (g)/(l) Interfaces (Isothermal Distillation)

A gas diffusion device without a separation membrane[85] consists of a closed chamber holding

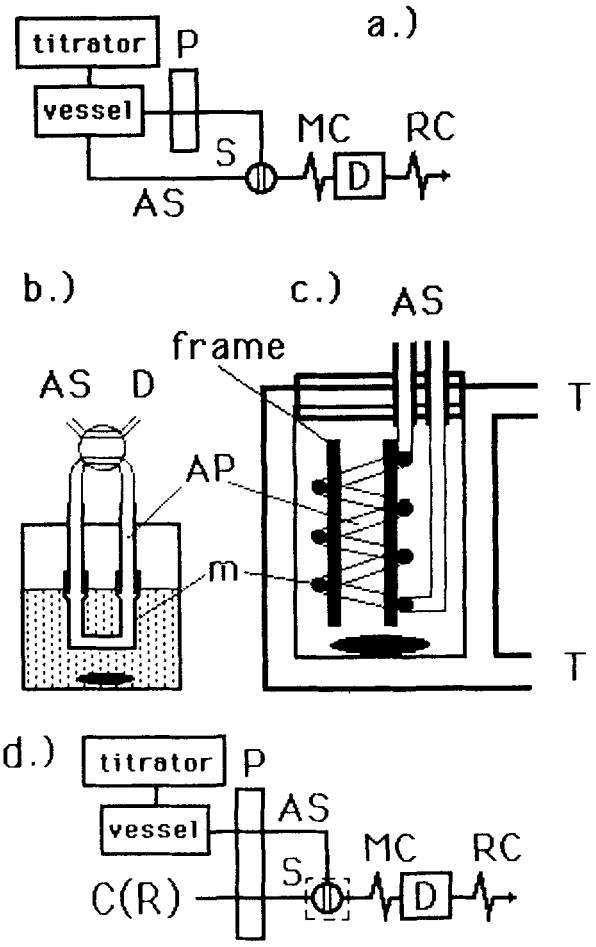

FIGURE 13. A manifold for equilibrium studies in a stationary mode (a) employing a diffusion/permeation device with the membrane inserted into the reaction vessels (b and c) with a stopped-flow (b) or a continuously flowing (c) acceptor liquid. AP, acceptor phase; T, water bath inlet/outlet for temperature control.

two silicone rubber sheets supported on parallel plates (Figure 14). The distance between the sheets can be adjusted by the screws and the spacers near the ends of the plates. The donor and acceptor streams enter the device and spread along the particular silicone rubber sheet producing thin films of the liquids on the surface of each membrane. The films, which are linked to the sheets by liquid-solid adhesion, pass the entire length of the device before going into the waste and the detector channels. The analyte liberated from the film of the donor liquid diffuses across the free gaseous interspace to the acceptor liquid where it is collected and then is sensed directly or through an analytical reagent. The system has been used to determine the total nitrogen in plant material by the potentiometric or photometric measurement of ammonia.[85] Its very complex design with the problematical long-term applicability has not found wider routine application.

C. Types of Membranes

Selection of a suitable membrane for the flow systems depends on many factors that may vary during experiments: the flow rates and the flow rate ratios; the physical and the chemical properties of the donor and the acceptor streams; the selectivity and the sensitivity requirements; the mechanical properties of the membrane material; the nature of the samples; the number of samples; the sample throughput; and the membrane separation cell design.

To serve its purpose successfully, the membrane should be semipermeable with good mechanical and chemical stability. It should allow the complete passage of certain chemical species while preventing or strongly retarding the permeation of other unwanted species. At the same time, transport rates for permeating species must be high enough so that reasonably fast and efficient separation can be achieved. In addition, the membrane material must avoid the transition of unwanted phases, solid or gaseous, to prevent contamination of the detector flow cell by solids or gas bubbles.

Several different types of semipermeable membranes can be applied in flow analysis for each particular membrane separation process. Most can be categorized into the following groups:

- Nonporous (silicone or natural rubber)
- Microporous (Teflon, PVDF, cellulose, etc.)
- Asymmetrical/skin
- Charged/ion exchange (catex, anex, mixed)
- Modified-supported liquid membranes (solvents, reagents, etc.)
- Liquid-surfactant
- Natural and biomembranes
- Others, e.g., ceramic, metallic, (poly)crystalline, etc.

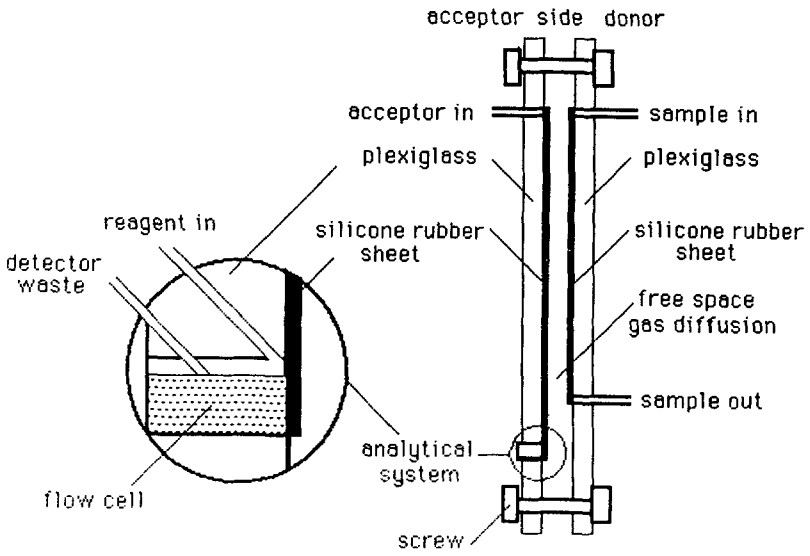

FIGURE 14. A gas diffusion device with open gas/liquid interfaces for isothermal distillation (right) and a flow-through cell (left).

The first two groups are most frequently used in GDP FIA, particularly for determination of gases, gas-evolving species, and highly volatile substances. The last three groups are less suitable for FIA purposes because of a lack of mechanical strength, availability in satisfactory dimensions, and reproducibility of preparation. They play an important role in separation of organic substances, biological materials, gases at elevated temperatures, and, mainly, ions, thus they are not discussed here in detail.

Most of the membranes are available in sheet and circular forms of different sizes (supported or unsupported) and a tubular (capillary) form in a variety of inner and outer diameters. Both types are manufactured with diverse porosity, pore size, and thickness. The mechanical support is sometimes necessary, especially when the thin planar membrane is used in a sandwich membrane device. Membranes incorporate polypropylene, nylon, or polytetrafluoroethylene (PTFE) web support for excellent durability, ease of handling, and to improve mechanical parameters of the planar membranes. Backing provides added strength and prevents blockage of channels by protruding into channels.

The lifetime of the membrane is dependent largely on the nature of the samples, character of the membrane, and other factors. Pure, natural water samples and atmospheric samples do not affect membranes at all and may permit daily analysis for several months without changing the membrane. For soils, waste waters, process streams, and related samples containing colloidal or solid particles, it may be necessary to change the porous membrane every day or even more frequently if the silicone rubber membrane is used for significantly longer periods.[45,46]

The membrane thickness is <0.5 mm in most cases. The membrane must not be stretched excessively when it is mounted because such handling will alter the diffusion properties and shorten the lifetime. In addition, sharp edges on the engraved channels, a rough surface, and overtightening may damage the membrane during the mounting procedure.

1. Homogeneous (Nonporous) Membranes

Volatile analytes can be easily transported across nonporous membranes. They have been found to be useful for preconcentration and/or separation of a wide range of compounds and for directly interfacing aqueous or gaseous samples to nonselective detectors or analytical instruments.[9,33,35,43,45–48,70,71]

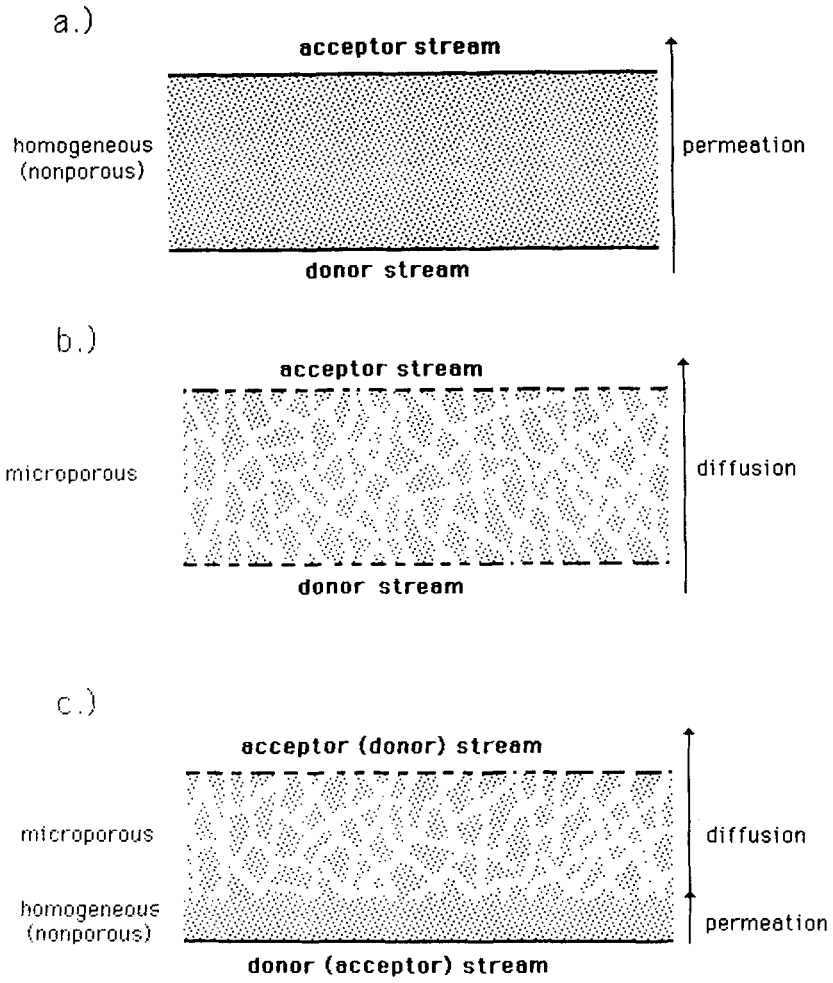

FIGURE 15. Structure of (a) homogeneous, (b) microporous, and (c) skin-like heterogeneous membranes.

The membranes consist of a homogeneous film (Figure 15a) across which a mixture of chemical species is transported via molecular diffusion (permeation). Silicone rubber (poly[dimethylsiloxane]), the most commonly used material, is chemically and mechanically stable and has a high permeation rate for a large variety of analytes, particularly for acidic gases and inorganic and organic compounds. It cannot tolerate higher pressures when it is not backed and exposed to temperatures over 80°C. The other advantages are high resistance to fouling, mechanic and chemical resistance, differences in selectivity, and variable transport efficiency.

Transport across the membrane is based on a combination of solubility and molecular diffusion. The overall process is referred to as permeation. This involves dissolution of the analyte in the membrane, diffusing transport in the condensed phase across the membrane, and desorption (evaporation, diffusion) on the other side where it may be taken up by a suitable acceptor fluid. The silicone rubber membrane is a homogeneous plastic film through which the transporting species passes the material by dissolving in the membrane phase. Therefore, the selectivity is determined primarily by the solubility of the species (permeation), not the volatility, as is often stated. Separation is related to the transport rates within the interphase, which are determined by the diffusivities and concentrations of individual components in the membrane matrix. With homoge-

neous permeation-type membranes, particles of exactly the same size also may be separated when their concentrations (i.e., solubility in the membrane) differ significantly. Furthermore, due to the combination of solubility and diffusing transport through the membrane matrix, the membranes exhibit higher selectivity than microporous membranes.

The silicone rubber absorbs a considerable amount of water (4%), alcohols (8%), and other organic solvents (chloroform, benzene, hexane, etc.). Organic solvents digest the silicone rubber and can act as extractants for many organic substances.[70] The substances are then apparently soluble in the matrix and consequently produce higher responses. This allows the selective transport of certain types of organic compounds into organic solvents or aqueous scrubber solutions in an unsegmented FIA mode. The process can be viewed very much like a liquid-liquid extraction from a large volume of sample into a small volume of the organic solvent or into water in so-called unsegmented arrangement.[70] The high diffusion rates for most compounds result in a rapid response compared to the other polymeric materials (e.g., vinylacetate).

While permeating transport is typically much less efficient (typically one order of magnitude) than diffusion transport taking place in gas phase through pores in a microporous media, it also is far more resistant to membrane fouling[45,46] because the rate-determining element is the membrane matrix. Homogeneous and skin-like silicone rubber membranes, which are not easily fouled, also have been found useful for handling samples containing high concentrations of dissolved solids and particles often found in wastewater and process streams. With the membrane device, colored, oxidation, or degradation products from the donor stream do not permeate the membrane, permitting experiments with lower concentration than is possible with direct determination procedures. Under the operating conditions, no mass transport of ionic species is observed.

Response time is usually short enough for FIA application (typically from units to tens of seconds) for most analytes. It takes approximately 5 to 10 min when starting the experiment with nonequilibrated membranes. A longer time (up to 1 h) is needed to come to steady state when a dry membrane is first used in dry condition. Among the other factors, the time depends on the flow rate of the sample and the acceptor and their character, on the diffusion rate of the compound through the membrane, and on the wall thickness of the membrane.

2. Microporous Membranes

Volatile analytes are preferably isolated from the original matrix by diffusion through microporous membranes, which are typically highly hydrophobic Teflon membranes, into an appropriate receptor.[86–98] Many applications of planar or tubular fluoroplastic microporous membranes of different porosity, pore size, and mechanical properties from different suppliers (e.g., Enka, Germany; Sumimoto Electric Ind. Co., Japan; Millipore, USA; Celanese S.A., Belgium) have been proposed in order to improve the selectivity of analytical methods. They have proven to be a more versatile diffusion barrier because they can be used for a great variety of gases, volatile compounds, and other analytes. Transmembrane transition efficiencies are much higher compared to the other types of membranes (one or two orders of magnitude,[35] typically from 10 to 70%[30,32]); however, selectivity is typically poor and must be improved by the other experimental factors.

Microporous membranes with strictly heterogeneous structure are very similar to a traditional filter in structure and function (Figure 15b). They have a rigid, highly voided structure with randomly distributed interconnected pores (Figure 15b). The size of the pores is extremely small (0.01 to 1 μm) in comparison to the classical filters (>10 μm). In fact, the smaller the pore size and porosity, the higher the resistance to leakage of water across membranes due to much higher water permeable pressures (which determine the pressure limits over which the aqueous solution starts leaking across the membrane). The limit has to be high enough to ensure that no ionic species pass across the membrane during the gas diffusion/separation step.

The membranes are made of Teflon (PTFE), polyvinylidene difluoride (PVDF), polyvinyl chloride (PVC), isotactic polypropylene, cellulose esters (acetyl, nitro), and other materials. Polypropylene, nylon, vinyl/acrylic copolymer, and sometimes also hydrophobized paper represent economical alternatives to the more expensive PTFE and PVDF membranes, having an adequate chemical and mechanical resistance, low content of impurities, and high temperature resistance. Fluoroplastic porous membranes are more durable and more hydrophobic, while cellulose-based materials are much less hydrophobic and they also easily adsorb water on the surface and in their pores.

Originally, plumber's tapes, generally made of PTFE, were used; however, today, microporous membranes with a defined and uniform porosity and pore size are utilized. The porous structure of the lipophilic material repels water. Thus, the pores are preferably filled with gas, which forms the continuous gaseous layer. The species in the gas phase diffuse across the layer defined by the geometry of the pores. All molecules or particles larger than the largest pores are completely rejected by the membrane while all those smaller than the smallest pores pass through the membrane. All particles of intermediate size are partially rejected in correspondence to the pore-size distribution; thus, only partial separation of the species can be achieved.

Although the mechanism is based on physical properties, the membrane used adds some selectivity to the system.[18] The selectivity of the membrane is mostly governed by the volatility of the compound and the differences in diffusion coefficients in the gas phase. Selectivity is consistently poor, but the differences are typically less significant than for condensed phases (solid or liquid). Only particles that differ considerably in size and diffusivity can be separated directly. Different hydrophobic microporous membranes of different pore sizes and materials have been found to behave similarly in gas diffusion of different species. Higher transport efficiency has been found for hydrogen sulfide[30,99] (30 to 50%) compared to ammonia[30] (approximately 7 to 20%) for the PTFE membranes, and for HCN (14 to 25%) for PTFE microporous film.[32] Higher efficiency also has been found for gases like N_2, H_2S, and formic and acetic acids, but lower for larger molecules when using PVDF. The efficiency depends on the donor and acceptor fluid, geometry of the membrane, and the direction of the transport through the pores for HCN and HCNS. Nonhomogeneity of the pore size, porosity, and thickness of the membrane also produces the differences in transport efficiency.

In general, microporous membranes are susceptible to fouling with particulate matter by adsorption/desorption mechanisms on the surface or within the membrane or by irreversible changes in polarized diffusion layer close to membrane/liquid or membrane/gas interfaces. The walls of the pores are partly negatively charged; thus, hydrophobic cations can be absorbed on the surface. Any deposits on the walls of the pores change the lipophilic character of the material and can cause the leakage of water inside the membrane, forming aqueous channels that allow transport of ionic species. The membranes are sensitive to the presence of surface-active substances when used in aqueous streams. They cannot be used routinely as scrubber devices with solutions containing sufficient amounts of dissolved solids (salts) because evaporation of the solvent causes the solids to be deposited in the pores of the membrane when used with gaseous samples. In our experience, such membranes also do not tolerate samples containing suspended matter, oil, grease, etc.

The membranes also are sensitive to the high pressure applied either on the donor or the acceptor side, especially when the gaseous phase is used. Gases easily penetrate the pores, forming gaseous spheres protruding into the acceptor phase from the mouth of the pores.[35] The diffusion trajectories are thus seriously lengthened, decreasing the rate and increasing the efficiency of the transmembrane transport. In the worst case, the gases nonselectively pass through the membrane and cause bubble problems. Excessive pressure on the aqueous side can, on the other hand, create aqueous channels inside the lipophilic microporous structure (when it overcomes the limiting pressure) or even totally fill the pores, reducing the transport efficiency and permitting the solute transport. All these phenomena change the character

of the membrane barrier; thus, the microporous membrane allows some nonvolatile compounds to pass through the barrier, especially when larger pore size, porosity, and excessive pressure are applied. Also, the fact that some reagents pass through the microporous membrane indicates the ability of the membrane to pass the ionic species through the aqueous channels.

3. Ionomeric (Electrically Charged) Membranes

These membranes are used most frequently for separation of different ionic species and enhancement of selectivity[100] of detection, but they also can be used for separation and very effective collection of volatile analytes of a different nature[34,83] such as water, hydrogen peroxide, formaldehyde, or gases such as ammonia, sulfur dioxide, and others.

Ion-exchange (ionomeric) membranes are typically submicroporous in structure, with no macroscopic pores in the conventional sense. They carry fixed ionized groups, which may be positively (anion-exchange, alkylammonium groups) or negatively (cation-exchange, sulfonic, sulfate or carboxylic groups) charged. Membranes that consist of a mixture of negatively and positively charged macroscopic segments are referred to as *mosaic membranes*. Separation is achieved not only by the structure of the membrane matrix, but also by exclusion of co-ions (i.e., ions with the same charge as the fixed ones). The membranes exhibit good thermal, chemical, and ion transport properties. They also tolerate the use of solutions containing solids as a scrubber liquid for collecting gases.

A perfluorinated Nafion® ionomer membrane (a strong cation-exchange membrane with an active fluorosulfonic acid group), the most frequently used ionomer for GDP FIA, consists of two phases (domains)—ionic clusters and perfluorinated matrix (hydrophobic backbone structure similar to that in PVDF). Similarly, perfluorinated carboxylate membranes containing the –COOH group are rather strongly acidic in their H-forms (pK 1.9) because of the strong electron-withdrawing effect of the fluorine atoms. Cluster domains, containing mostly sulfonated groups and adsorbed water, form chambers (5 to 10 nm i.d.) connected to each other by interfacial narrow channels containing small amounts of water, a few sulfo groups, and pendant side chains. The unique structure is due to the molecular aggregation of hydrophilic and lipophilic segments of the polymer. It produces a more uniform exchange site environment and gives a dynamic nature to the cluster (large changes of water content for different forms of the material).

$$-(-CF_2-CF_2-)_m-(-CF_2CF-)_n-$$
$$[O-CF_2-CF(CF_3)-O-]_p-CF_2-CF_2-SO_3^- \text{ (or } -COO^-)$$

$m = 5\text{–}13.5, \quad n = 1000, \quad p = 1, 2, 3\ldots$

Its negatively charged sulfonate groups essentially inhibit anionic constituents from penetrating across the membrane either when dilute solutions or gaseous streams are on both sides of the membrane. On the other hand, acid gases, such as HCl, SO_2, and HNO_3, and aniline, cresols, etc., being fairly lipophilic compounds, are efficiently and relatively rapidly transmitted through the membrane when an aqueous stream is on one side. The mechanism of the transport behavior is unclear, but it probably takes place in un-ionized form in the superacid matrix. Transport of the species can eventually be realized through the aqueous channels by dissolution in water to form particular ions, inasmuch as Nafion® absorbs a high quantity of water, or through the lipophilic domains with a structure similar to PVDF.

4. Asymmetric (Skin)-Type Membranes

This structure consists of an extremely thin (0.1 to 1 μm) layer (skin) supported on a 0.1- to 1-mm thick microporous substructure (Figure 15c). The skin, which represents the actual discriminating element, may be a porous or homogeneous material and may be neutral (silicone rubber) or charged (ion exchanger). The microporous support (nylon, PTFE, PVDF, etc.) improves the mechanical strength of the membrane. Generally, it allows rapid transport of all species, relative to the skin, maintaining high diffusion rates for most of them.[33]

The double-layer structure combines the selectivities of the transmembrane mass transport of both materials. The selectivity is determined by the selectivity of the homogeneous part of the membrane and the transport phenomena are determined by the polymeric material. Due to the thinness of the homogeneous material, the rate of permeation is much higher than for single-layer homogeneous membranes. These properties favor using skin membranes for trace and ultratrace analysis.

5. Supported Liquid (Modified) Membranes

These membranes consist of microporous membranes (made of Teflon, PVDF, etc.), whose pores are saturated with a highly lipophilic organic solvent (e.g., isooctane, 1-hexadecane, 1-undecane, 1-decanol, petrolether, kerosene, etc.), eventually bearing an organic analytical reagent to improve the selectivity and/or efficiency of transport.[69,101] Selectivity is governed by the differences in solubility of the species of interest in the organic solvent, or by the combined selectivity of the appropriate chemical reaction between the analyte and the organic analytical reagents and the distribution coefficients of the transported species between the membrane solution and the phases on both sides of the membrane (similar to liquid-liquid extraction). Such membranes are useful for separating volatile and highly lipophilic substances. A difference in experimental conditions, i.e., acidity, composition, etc., between the two sides can then be used for trace enrichment of amines[69] and other analytes.

D. Detector Designs and Interfacing

Despite the high selectivity of the most up-to-date detection principles, serious interference from ionic, oxidizing, and reducing compounds has been reported in determinations of gases and volatile compounds, especially when using electrochemical detectors. Different solutions have been proposed to eliminate matrix effects, with GDP being the most promising one.

1. Detectors With Fiber Optics

The product formed, or the analyte itself, can be determined directly by an on-cell spectrophotometric (absorption or reflectance), fluorometric, luminescence, or electrochemical detector. In the first case, the optic fibers could be oriented axially to the main axis of the device, with the ends situated very close to the membrane inside the diffusion/permeation cell (Figure 16).[102–104] A support is usually needed to prevent protrusion of the membrane into the acceptor channel, which can eventually block the light passing into the coaxial arrangement.

Perpendicular orientation is preferred for the reflectance, fluorometric, and luminescence detectors. An optic fiber, bifurcated at the remote end to accept the incident light from an external light source and to accommodate a conventional detector to monitor the light reflected by the membrane (Figure 16b), is placed on the top of the transparent cover of the flow cell.[102] The PTFE membrane is nontransparent white and serves as an ideal reflecting opaque background on whose proximity the chemical reaction takes place.

Using an acceptor stream containing a single acid/base indicator (or a mixture of appropriately selected acid/base indicators) in its acid or base form, a simple photometric detection procedure can be used in which the incident light traverses the indicator solution twice. The indicator color changes depending on the acidity changes of the acceptor stream due to the respective absorption of basic or acidic species. A linear response can be obtained in the preselected concentration range changing the initial pH, the concentration of the indicator, and the concentration of the buffer solution. A sampling frequency of 10^2 can be achieved, with the analytical readout being available immediately after sample injection. The small portion of the acceptor solution eventually can be periodically renewed after each measuring cycle.

The designs decrease dispersion of the analyte in a manifold. The systems can be operated either in a continuous-flow or stopped-flow arrangement as the time-based collecting detectors, the advantage of the latter approach being that a small volume of an acceptor solution can be selected within the cell, enhancing the diffusion of the

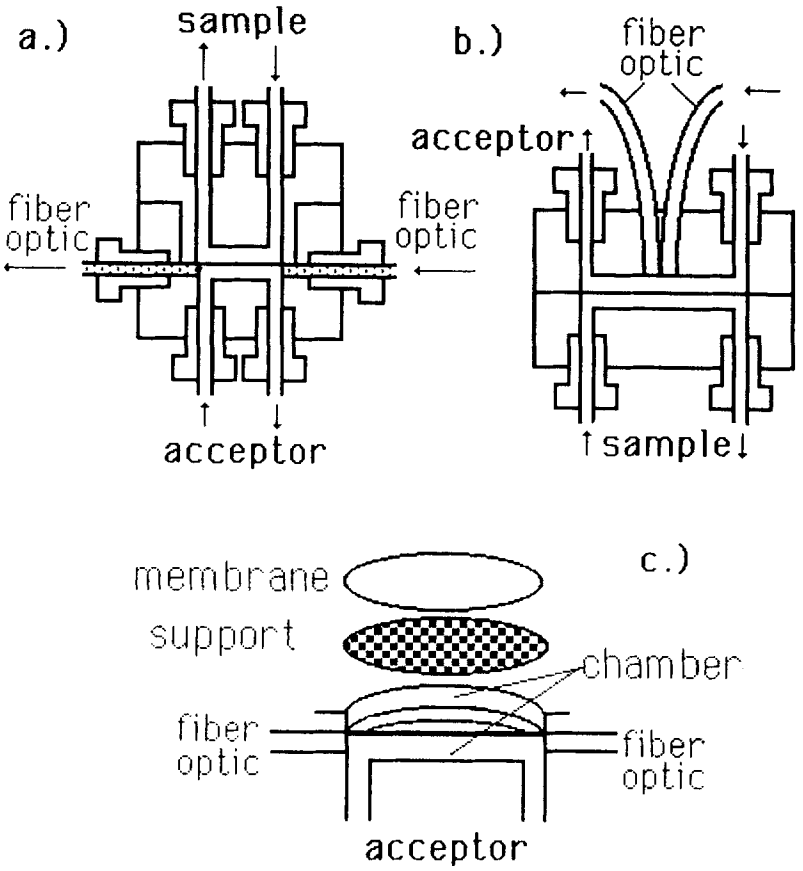

FIGURE 16. A diffusion/permeation device with an in-cell fiberoptic photometric (a) or a fluorometric or a reflectance photometric (b) detector, and a scheme of the cell (c) with the membrane supported by a screen.

species across the membrane. The sensitivity can be increased in this manner, with the length of the stopping period governing the degree of transfer of the analyte available within the entrapped segment of the sample zone.

A similar advantage can be gained by combining gas diffusion directly with the detection[105] facilities offered by atomic absorption spectrometry in the gas phase for determining mercury or using two detectors with different selectivity or different principles.[106]

2. Iterative Reversal System with an On-Loop Detector

Gas-diffusion operations also can be performed in a closed iterative reversal system without the characteristic membrane separation unit by inserting a single segment of a suitable acceptor liquid into a gaseous sample stream via a loop injector.[107] Two gas/liquid interfaces (menisci) are created together with a thin film of the acceptor liquid on the inner wall surface of the loop. The two phases are subjected to an iterative reversal movement in the closed loop. The gradual enrichment of the acceptor liquid with the volatile analyte can be monitored continuously using an on-loop situated detector that divides the loop into two uniform subloops.

A peristaltic pump controlled by an electronic timer allows the direction and the rate of drum rotation, the start of the reversal cycles, the number of cycles, and the cycle duration to be programmed. The sample loop is filled with the acceptor liquid in the filling position. The liquid is reverse transported by the gas stream until one of the menisci reaches the flow cell. At that moment,

the electronics reverse the flow direction until the other interface reaches the flow cell. Thus, at no time do any of the interfaces pass through the cell to produce parasitic signals due to the changes in the refractive index of the phases. This reversal process is repeated until a suitable enrichment factor is obtained by mass transport through the open gas/liquid interface (Figure 17).

- Type (selectivity) of membrane material
- Transport phenomena
- Rate of diffusion in the membrane material
- Geometry of the membrane unit
- Effective area-to-volume ratios
- Wall thickness
- Flow rates of both streams
- Composition of both streams

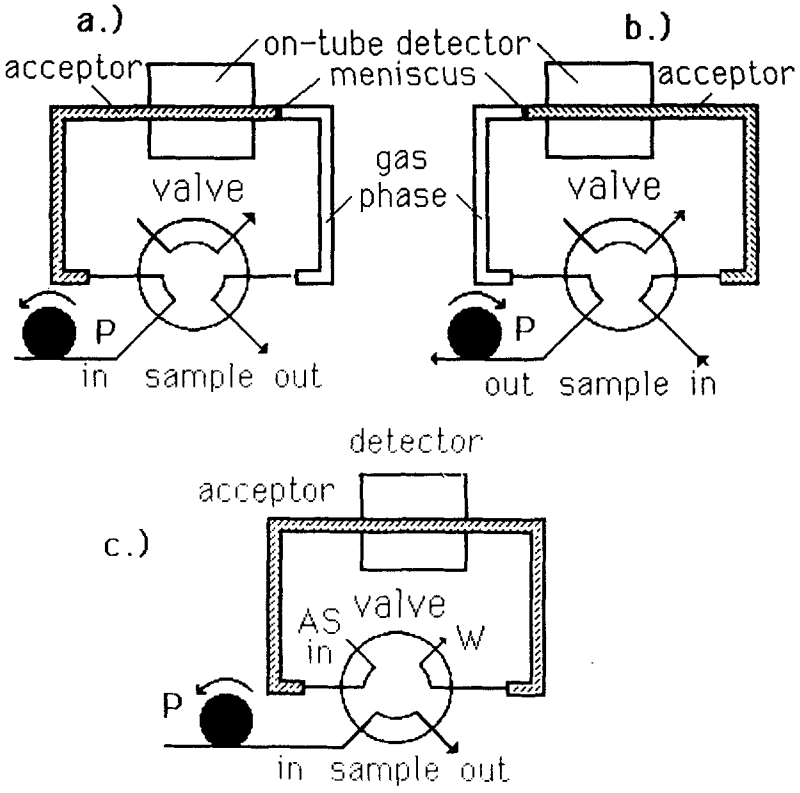

FIGURE 17. An iterative reversal system with free gas/liquid interface (meniscus) and an on-tube detector. An acceptor plug in both extreme positions (a and b) and in the filling position (c) are given.

IV. FACTORS INFLUENCING TRANSMEMBRANE MASS TRANSPORT

Some of the factors influencing transmembrane transport, and thus the selectivity and/or sensitivity of the determination, are unique for each type of membrane and were characterized in the previous sections. However, most are common for all transport processes and are examined here in detail. These factors are

- Time of exposure and sample volume
- Concentration gradient
- Experimental conditions on both sides, i.e., temperature and pressure.

All membrane-assisted techniques depend on the mass transfer resistance of the interphase (membrane, immobilized matter, etc.) and that of the donor and the acceptor channels of the membrane device on both sides of the membrane. The

efficiency of the permeation process and the concentration of each individual analyte transported through the membrane is primarily a function of the actual transportable form of the concentration gradient between the donor and the acceptor streams.

Generally, a linear relationship exists between the analytical signal and the concentration of the analyte, the volume of the acceptor solution inside of the donor channel (injector loop), the effective surface area of the membrane in direct contact with the sample, the permeability of the species, the temperature, etc. The sample and the acceptor flow rates, time of exposure of the membrane to the sample, the volume of the sample, the length, the diameter, and the wall thickness of the membrane, as well as the flow cell geometry, all affect the efficiency of the transmembrane transition. For any specified membrane material, temperature, analyte concentration, etc., the amount of analyte penetrating the membrane is constant.

The selectivity coefficient of the transport process can be expressed as a ratio of the normalized signals or the concentrations of the transportable forms and their permeabilities, which are related to their diffusion coefficients through solid/liquid interfaces and transport rates through the membrane material. The overall selectivity coefficient of each method is a product of the selectivity coefficients of the detection principle and that of the diffusion/permeation process.

The concentration profile also depends on the distribution coefficients of the species between a membrane and, respectively, a sample and an acceptor stream. Assuming fast transition through the membrane and rapid interfacial reactions, the concentration profile of the analyte in an acceptor stream and, of course, the resulting analytical signal follow the concentration profile of the sample zone in the donor stream.

A. Membrane Parameters

1. Type (Selectivity) of Membrane Material

Any transport mechanism involves three fundamental steps: (1) diffusion of the species from a bulk sample milieu across the diffusion layer close to a solid/fluid interface; (2) transport through the membrane matrix, including the adsorption/desorption process on both interfaces; and (3) the transport of the analytes into the acceptor fluid across the diffusion layer. The transition rate of any compound is a product of its diffusion rate in the membrane and, eventually, its solubility in the membrane matrix and diffusion through the two diffusion layers. In order to obtain good transmembrane transition efficiency, the compound must have high distribution coefficients from the sample into the membrane and from the membrane matrix into the acceptor fluid.

The response of the detector using microporous, ion-exchanger, and homogeneous membranes differs for different compounds.[48] The differences in enrichment factors reflect the difference in the transportability of the compounds through a membrane, solubility of the compounds in the donor and the acceptor fluid, and their form in both media. Response time is very short for microporous membranes compared to the other types of membranes (typically less than seconds) when switching between sample and blank and no memory effect is usually observed. These can be explained by the different mechanisms of mass transport through the membranes.

2. Distribution Coefficients

Transport efficiency depends on the distribution coefficients of the analytes between the membrane material and the donor and the acceptor fluids. The concentration (enrichment) factor is related to the distribution coefficients, $P = (x_m/V_m)/(x_a/V_a)$, where x_m and x_a are the concentrations of the compound in membrane and liquid phase (acceptor or donor), respectively, and V_m and V_a are volumes of membrane and liquid phase in a steady-state mode, respectively.[21–26,70]

A well-defined concentration profile of the original sample plug and a short contact time of the sample zone with the membrane will produce a sharper shape for the resulting analytical signal. The slope of the leading edge of the peak is governed mainly by the diffusion rate in the membrane material and the thickness of the membrane wall and partly by the shape of the original concentration profile. The analyte must diffuse rap-

idly through the membrane from one solid/fluid interface to the other. For silicone rubber, it takes seconds; for porous membranes, it is an immediate process. The parameters of the peak maximum depend on the sample concentration, the diffusion rate, and both distribution coefficients. The distribution coefficient between the membrane and the acceptor fluid governs the rapidity with which the analyte is removed from the membrane. This is the factor determining the slope of the trailing part of the signal and how rapidly the peak returns to baseline. A high value for the peak height/peak width ratio indicates that the analyte is removed efficiently from the membrane into the acceptor.

For transmembrane transition of different organic substances, such as phenols, carboxylic acids, etc., a good response can be obtained with the exception of compound that are either incompletely converted to the transportable species and less acidic (basic) or fully ionized and more nonpolar (i.e., the driving force is large and reduces the efficiency of the transport). Because the distribution coefficients of low polar substances are larger for organic solvents, their presence in the acceptor stream can improve the efficiency of the transmembrane transport.[70]

3. Geometry of the Membrane

Transport rates across membranes are nearly inversely proportional to the membrane thickness and proportional to the active surface area. The thinner wall membranes produce a better peak shape and a shorter response time. Smaller pore size is more effective in avoiding permeation of other species across the microporous membrane. To achieve high transport rates, it is desirable that the membranes be as thin as possible. Unfortunately, polymer film fabrication technology does not yet permit manufacture of defect-free films thinner than approximately 20 μm. Generally, stretched membranes are more sensitive; however, for tubular membranes, a more complex explanation is needed because of changes in thickness of the wall, reduction of the internal volume, and the surface area. The application of skin-like membranes with two layers of different parameters can enhance significantly the transport efficiency.

B. Experimental Conditions

The factors connected with the experimental conditions on both sides of the membrane are the most important factors from the point of view of sensitivity and/or selectivity of determination.

1. Flow Rates

Enrichment factors depend on total permeation through the membrane and the flow rate ratio of the donor and the acceptor streams in the continuous-flow mode. A high flow rate of the acceptor stream can be used as a dilution scheme, and a low flow rate or stop-flow mode can be used to concentrate trace samples. Inasmuch as a constant amount is collected in the acceptor flowing through the membrane device under given experimental conditions, the concentration can be controlled easily and is inversely proportional to the acceptor flow rate. The response decreases with the acceptor flow rate because transition efficiency does not increase proportionally with the flow rate and the preconcentration factor.

Although a very high concentration (a typical enrichment factor is from 3 to 10) can be obtained by using very low flow rates of the acceptor fluid, the stopped-flow mode is more suitable. In this particular case, the enrichment factor depends on the permeation rate per unit internal volume of the membrane device and the time of permeation. The analyte concentration (an enrichment factor up to the hundreds) can be controlled by time of the stopping period.

Gaseous sample flow rates over some limits (typically 0.1 l/min) were found to have relatively little influence on the response in both stopped-flow and continuous-flow regimes. This is understandable when it is recognized that under the most common operative conditions, only a certain percent (up to 5 to 10%) of the analyte is transferred to the acceptor stream and because of the high diffusion coefficients in the gas phase. However, if sufficient sample is available, a higher flow rate is beneficial in that residence time and carry-over effects are minimized.

When the acceptor solution is either static or flowing, the flow rate of the aqueous sample stream passing through the donor chamber is an impor-

tant parameter. Usually, the amount of species transported across the membrane increases with the flow rate, but the results show some decrease of the signal when contact time of the sample solution with the membrane is too short. The contact time is longer at lower flow rates and, thus, more species can pass across the membrane. The extent of transfer obviously increases with decreasing sample flow rates. Therefore, it is important to keep the optimized sample flow rate constant during experiments.

Sample flow rate (carrier with plug) and sample size have very similar effects because both control the contact time and hence the peak shape. Increasing the injected volume leads to a steady state and then broadens the peak. If the contact time is long enough, equilibrium is reached. Slowing the flow rate has an additional band-broadening effect because of dispersion of the sample plug in the manifold.

2. Time of Preconcentration

The amount of the analyte preconcentrated (enrichment factor) depends linearly on the sample volume passing through the donor chamber and, of course, mainly on the time of preconcentration at a constant-flow rate when sufficient absorption capacity of the receptor fluid is reached. A linear relationship exists between the signal corresponding to the amount of the analyte transported across the membrane, the product of the time of exposure of the membrane to the sampling environment, and the concentration of analyte in the sample, $m = K \cdot c \cdot t$, where m is the mass of the component collected (in micrograms), c is concentration (in micrograms per milliliters), t is the time of the exposure period (in minutes), and K is the calibration constant for each specie (milliliters per minute). This has been demonstrated many times both for aqueous[42,46,70] and air samples.[35]

Precise timing is thus critical when running in the stop-flow mode. Under any fixed preconcentration conditions, the system exhibits excellent response linearity and intercepts that are statistically indistinguishable from zero. The attainable detection limits are linearly dependent on the preconcentration times used. Based on the observed response behavior, long preconcentration times, of course, compromise the attainable throughput rates. Increasing the contact time leads to the steady state and then to broadening of the peak. Excessive washout times lead to peaks with a more or less expressed plateau at the trailing segment, which corresponds to the equilibrium transition in the continuous-flow arrangement.

3. Temperature

Temperature is another external factor affecting transport efficiency for both transport phenomena. An increase in temperature will increase the diffusion rates, diffusion coefficients, and also the solubility of the analyte in solution and in membrane material. Depending on the changes in distribution coefficients, this could result in either positive or negative change in the transition rate and the transport efficiency.

Generally, the permeation increases with increasing temperature, $m = c \cdot (K_0 + s \cdot T) \cdot t$, where K_0 is the permeation constant at 0°C, s is a slope of the temperature effect dK/dT, T is the average temperature of the sample over the sampling period t, and the other symbols have the same definition as described earlier. Usually, a positive influence is observed for an increase in temperature over a limited range (5 to 80°C) and no memory effect is observed for most compounds.[30,35,70] Transmembrane transport efficiency was increased, respectively, by factors of 1.2 and 1.8 for hydrogen sulfide and ammonia when temperature was elevated from 20 to 80°C. Similarly, respective increases over the range 0.8 to 5% and 1 to 3% per gradient for peak height and peak area were found for other gases (hydrogen cyanide, sulfur dioxide, etc.) when temperature increased up to 50°C. No effect is generally observed when the system is held at constant temperature and only the temperature of the injected sample is varied.

Some temperature dependence of transport efficiency can be controlled easily by thermostating. In applications where the temperature may vary significantly or differ from the calibration conditions, corrections for temperature changes also should be made by applying the temperature-related factor, by thermostating the whole apparatus, or by introducing

internal standards. Elevated temperatures can, on the other hand, be applied to improve efficiency of transmembrane transport and sensitivity of a procedure.

4. Pressure

The two different transport mechanisms for homogeneous and porous materials explain the differences in the influence of the gas pressure applied on the donor side of the membranes.[35] While an increase in the pressure increases the solubility of gases in silicone rubber and ion-exchange membranes, the pressure decreases the transport efficiency through the microporous membrane, probably widening the diffusion layer inside the membrane and making it protrude into the acceptor liquid. Some excess pressure on the donor side can be applied to improve the efficiency of the transmembrane transport and the sensitivity of a procedure using nonporous silicone rubber membranes.

C. Composition of Donor and/or Acceptor Streams

The actual composition of the fluids on both sides of the membrane is the most important factor affecting the selectivity of a determination. Appropriate chemical reactions, i.e., acid/base, complexation, oxidation, reduction, precipitation, etc., can improve the selectivity of the method significantly. Combining the different factors allows selectivity, and also sensitivity, to be simply changed over a wide range (several orders of magnitude).

1. Acidity

The acid/base properties of the analytes are the most important experimental factors influencing membrane separation processes. The pH discrimination of mass transport of molecular species through the microporous PVDF and the nonporous silicone rubber membranes was described as a tool for the separation and preconcentration of analytes from the aqueous and the gaseous samples.

Several assumptions are necessary to simplify the quantitative description of the separation techniques based on the acid/base nature of analytes. The transition and diffusion rates and the solubility of the species are constant in both phases. The constancy of the area of the active part of the membrane, the volume of the acceptor solution, the flow rates of both streams, the time of exposure to the sample, and other factors also are expected.

The amount of analyte transported through the uncharged membrane is related to the percentage of the compound in the nonionized form calculated from pK values[35,46,70] and vice versa. The exact transport behavior of any species across the membrane as a function of donor pH can therefore be expressed as the response under otherwise identical conditions vs. the donor pH using the following model: signal = const. $\times 10^{-pH}/(10^{-pK} + 10^{-pH})$.

For efficient transfer of the nonionized analytes through the membrane, the pH of the donor solution should be significantly below pK_{al} of the acidic species, such that they are present mostly in molecular forms. In contrast, the acceptor stream should have a pH significantly above pK_{al} such that the permeated species are immediately ionized. In general, if the pH is two units below the pK, optimum conditions are reached; if the pH is two units above the pK, the reverse is true.

Using this guideline, acidic gas-evolving species, such as carbonates, sulfides, etc., can be determined selectively in the presence of ammonium ions and other basic species in a single-stage arrangement with a nonselective detection. Acidic gases are liberated selectively by acidification of the sample solution while ammonium remains in the aqueous phase. Ammonium, in contrast, can be determined selectively in the presence of acidic gases in the same way after its evolution through an alkaline medium. Changes in the physicochemical properties of receptor liquids correspond to the content of the penetrating gases.

If desired, it may be possible to transport selectively weaker acidic species (like HCN or

H_2S) over stronger acids (like SO_2 or CO_2) by controlling the pH of the donor solution.[35] Similarly,[70] trace amounts of phenols with a pK > 7 (phenol, mono- and dichlorophenols) can be transported selectively from samples containing high concentrations of o-hydroxybenzoic acid, pentachlophenol, and 2,4-dichlorophenoxy acetic acid (pKs 3, 5, and 3.6, respectively), while 2,3,4,6- and 2,3,4,5-tetrachlorphenol (pK 5.2 and 7, respectively) are almost completely separated at pH 7.2.

Extending this guideline, acidic gases, such as carbon dioxide, hydrogen sulfide, etc., or the total content of acidic gases in the gaseous phase also can be determined selectively in the presence of ammonia and other basic species in a single-stage arrangement. Acidic gases are absorbed selectively in an alkaline solution (pH > 12) while ammonia remains in the gaseous phase. Ammonia, in contrast, can be absorbed selectively in a strongly acidic solution in the same way. This particular arrangement is, of course, less effective for species with similar pK_a values (like acidic gases) than that based on the control of the acidity of the donor stream.

2. Acceptor Stream Modifiers

The composition of the acceptor stream is important for quantitating the absorption of the analyte.[35] For acid/base analytes, the maximum concentration is limited to the amount of an absorption agent (acid or base) or by the absorption capacity of the acceptor. Once this is consumed, or equilibrium is reached, no further preconcentration takes place. Compounds that are not detected and/or other interferents also can limit the duration of the preconcentration period. Weaker acids also can be liberated easily when the acidity of the acceptor stream is drastically increased by the absorption of stronger acid components. A serious decrease in the efficiency of carbon dioxide collection in an acceptor fluid of low absorption capacity (water) can, for example, be expected when collected together with sulfur dioxide, nitrogen oxides, etc.

For neutral components, or a nonmodified acceptor liquid such as water, the enrichment factor is limited to the time it takes the sample/membrane/acceptor to reach equilibrium. Negative deviation from the linear dependence occurs when capacity is reached. The choice of receptor fluid is thus important because the distribution coefficient should be as good as possible (<10 and preferably <1 for good efficiency of neutral compounds).[70] Acids, bases, or buffer solutions are recommended as the acceptor media for ionizable species.

The organic solvents in the acceptor stream are more critical for the transport of neutral compounds such as benzene than for phenols[70] because they produce a suitable distribution coefficient (the compounds are quite soluble in the membrane). Sharper peaks with low trailing are obtained for neutral or low polar molecules when an organic solvent miscible with water is present. This may be related to the degree of membrane swelling, a change in distribution coefficients, or possibly the diffusion rates in the swollen membrane matrix. Methanol (>75%), acetonitrile, isopropanol (>50%), and hexane are recommended as receptors.[70]

3. Ionic Strength, Nonelectrolytes

The presence of inert electrolytes in the donor solution increases the response of the membrane techniques by a salting-out effect for the molecular species (it also is probably due to the variation of the Henry's constants with small values of ionic strength). This behavior has not yet been explained.[37,81] A critical concentration of electrolytes exists above which the response decreases; this can be explained by a change in the type of mass transfer across the membrane, above a given concentration, due to the changes in membrane properties. The transfer efficiency of ammonia increases[37] from 22 up to 54% when 2 *M* NaCl is added to a donor stream (0.1 *M* NaOH). The presence of a small amount of electrolytes in the acceptor stream can increase the solubility of ammonia in aquatic solutions and thus positively affect the efficiency of its transmembrane transition. An increase in the viscosity of the liquid due to the presence of nonelectrolytes increases the diffusion coefficients of the analytes and

hydrodynamic conditions in a donor channel and slows down their diffusion through the diffusion layer.

V. CONCLUSIONS

The GDP technique is simple; it does not require manual, time-consuming operations; and it also eliminates most of the problems associated with the other separation techniques due to the unique properties of the interfaces for rapid preferential permeability of gases and volatile substances. The continuously increasing number of publications every year indicates the growing interest in the technique in many areas of analytical chemistry due to the rapid development in membrane technology.

There are three main advantages from GDP FIA separation and/or preconcentration techniques: (1) **selectivity enhancement,** which can be adjusted for selection of various types of compounds while excluding others; (2) **concentration enhancement,** which can improve detection limits up to the parts per thousand to parts per billion levels (an enrichment factor of 10^2 or more can be obtained); and (3) depending on the mode and type of analyte, the GDP FIA membrane-assisted technique can be frequently used in **direct contact with the sample** stream without the need of manual sample pretreatment.

The differences in the selectivity of transmembrane transport of the species through particular membranes could obviously be used for the simultaneous determination of two or more analytes using two membrane devices in series or even a single membrane using differences in rates of transmembrane transition for the particular species through the membrane material.[18] The differences in response times for particular species are more markedly expressed for the homogeneous or electrically charged membranes than for the microporous ones. Thus, several schemes can be exploited for the simultaneous determination of a particular species, in the presence of the others, using the respective combination of high and low selectivity of different membranes.

The application of discrimination chemistries based on the differences in acid/base, redox, complexation, and other properties of a particular species on both sides of the membrane could be used to enhance the selectivity and/or sensitivity of the methods. The applicability of discrimination techniques will be discussed and demonstrated with some examples in the second part of the review.[108] Also, a combination of different separation and/or preconcentration techniques[109] with more sophisticated detectors could enhance the selectivity and sensitivity of the FIA methods.

Combining the gas diffusion unit with the sampling valve could be modified to produce an integrated microconduit or a compact separation/preconcentration and injection unit, or even "on-loop" detectors. These concepts open up new possibilities in the development of more sensitive and selective methods for FIA.

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REFERENCES

1. Růžička, J.; Hansen, E.H. *Flow Injection Analysis;* John Wiley: New York, 1988; Chapter 4.
2. Ueno, K.; Kina, K. *Introduction to Flow Injection Analysis;* Kodansha Scientific: Tokyo, 1983; Chapter 6.
3. Valcárcel, M.; Luque de Castro, M.D. *Flow Injection Analysis. Principles and Applications;* Ellis Horwood: Chichester, 1987; Chapter X.
4. Moeller, J. *Flow Injection Analysis*; Springer Verlag: Heidelberg, 1988; Chapter 3.
5. Karlberg, B.; Pacey, C.E. *Flow Injection Analysis. A Practical Guide;* Elsevier Science: Amsterdam, 1989; Chapter 6.
6. Burguera, J.L., Ed. *Flow Injection Atomic Spectrometry;* Marcel Dekker: New York, 1989; Chapter X.
7. Valcárcel, M.; Luque de Castro, M.D. *Non-Chromatographic Continuous Separation Techniques;* Royal Society of Chemistry: London, 1991; Chapter 2.
8. Skeggs, L. *Am. J. Clin. Pathol., Automatic method for the determination of carbon dioxide in blood plasma.* **1960,** *33,* 181.

9. Baadehuijsen, H.; Seuren-Jacobs, H.E.H. *Clin. Chem., Determination of total carbon dioxide in plasma by automated flow injection analysis.* **1979,** *25,* 443.
10. Valcárcel, M.; Luque de Castro, M.D. *J. Chromatogr., Continuous separation techniques in flow injection analysis: a review.* **1987,** *393,* 3.
11. Lazáro, F.; Luque de Castro, M.D. *Analysis, Gas diffusion/flow injection analysis. Applications and trends..* **1988,** *16,* 216.
12. Karlberg, B.; Twengstroem, S. *In Focus, Applications based on gas diffusion and flow injection analysis.* **1983,** *6,* 14.
13. Matschiner, H.; Sivers, P.; Ruettinger, H.H. *Wiss. Z. Martin-Luther Univ. Halle-Wittenberg, Math.-Naturwiss. Reihe B, Flow injection analysis — new method in wet analysis.* **1985,** *34,* 3 (in German).
14. Matschiner, H.; Sivers, P. *Wiss. Fortschr., Flow injection analysis — special solutions for general problems.* **1985,** *35,* 142 (in German).
15. Hansen, E.H. Flow Injection Analysis. Ph.D. dissertation. Polyteknisk Forlag, Copenhagen, DK, 1986.
16. Frenzel, W. *Fresenius Z. Anal. Chem., Membrane based gas sampling and analysis coupled to continuous flow systems.* **1992,** *342,* 817.
17. Fang, Z.; Zhu, Z.; Zhang, S.; Xu, S.; Guo, L.; Sun, L. *Anal. Chim. Acta, On-line separation and preconcentration in flow injection analysis.* **1988,** *214,* 41.
18. Pacey, G.E. *Anal. Chim. Acta, Selectivity enhancement obtained by using flow injection analysis.* **1986,** *180,* 36.
19. Moeller, J.; Winter, B. *Fresenius Z. Anal. Chem., Application of flow injection techniques for the analysis of inorganic anions.* **1985,** *320,* 451.
20. Luque de Castro, M.D.; Valcárcel, M. *Anal. Chim. Acta, Coupling of continuous separation techniques with unsegmented flow systems.* **1992,** *261,* 425.
21. van der Linden, W.E. *Anal. Chim. Acta, Membrane separation in flow injection analysis. Gas diffusion.* **1983,** *151,* 359.
22. van der Linden, W.E. *Anal. Chim. Acta, The optimum composition of pH sensitive acceptor solution for membrance separation in flow injection analysis.* **1983,** *155,* 273.
23. Kolev, D.S.; van der Linden, W.E. *Anal. Chim. Acta, Laminar dispersion in parallel plate section of flow systems used in analytical chemistry and analytical engineering.* **1991,** *247,* 51.
24. Kolev, S.D.; van der Linden, W.E. *Anal. Chim. Acta, Limits of mass transfer in parallel plate dialyzers.* **1992,** *256,* 301.
25. Kolev, S.D.; van der Linden, W.E. *Anal. Chim. Acta, Influence of the main parameters on a parallel plate dialyzers under laminar flow conditions.* **1992,** *257,* 317.
26. Kolev, S.D.; van der Linden, W.E. *Anal. Chim. Acta, Analysis of transient laminar mass transport in a parallel plate dialyzer.* **1992,** *257,* 331.
27. Risinger, L.; Johansson, G.; Torneman, T. *Anal. Chim. Acta, Optimization of flow-through cells for dialysis and other membrane separations in flow injection analysis using a laminar flow model.* **1989,** *224,* 13.
28. Risinger, L.; Johansson, G. *Anal. Chim. Acta, Effect of sample viscosity on the behavior of thin channel flow through dialyzers in flow injection analysis.* **1992,** *261,* 435.
29. Canham, J.S.; Gordon, G.; Pacey, G.E. *Anal. Chim. Acta, Optimization of parameters for gas diffusion flow injection systems.* **1988,** *209,* 157.
30. Schulze, G.; Brodowski, M.; Elsholz, O.; Thiele, A. *Fresenius Z. Anal. Chem., Dual detection for optimization of gas diffusion in flow injection analysis. Determination of ammonium and sulfide.* **1988,** *329,* 714.
31. Novič, M.; Zupančič-Kralj, L.; Pihlar, B. *Anal. Chim. Acta, Optimization of the two-phase separation process in flow injection analysis with an electron-capture detection system.* **1991,** *243,* 131.
32. Novič, M.; Pihlar, B. *Anal. Chim. Acta, Determination of the separation efficiency of semipermeable membranes using a two sample loop based flow injection system.* **1991,** *251,* 261.
33. van Nugteren-Osinga, L.C.; Bos, M.; van der Linden, W.E. *Anal. Chim. Acta, Hollow fiber membrane for sample introduction in flow injection system. Determination of carbon disulfide in air.* **1989,** *226,* 171.
34. Genfa, Z.; Dasgupta, P.K.; Dong, S. *Environ. Sci. Technol., Continuous measurement of atmospheric ammonia.* **1989,** *23,* 1467.
35. Kubáň, V.; Dasgupta, P.K. *Anal. Chem., Selective determination of gases by two-state membrane-differentiated flow injection analysis. Determination of trace hydrogen cyanide in the presence of large concentrations of hydrogen sulfide.* **1992,** *64,* 1106.
36. Johnson, K.S.; Petty, R.L.; Thomsen, J. *Adv. Chem. Ser., Flow injection analysis for seawater micronutrients.* **1985,** *209,* 7.
37. Willason, S.W.; Johnson, K.S. *Mar. Biol., A rapid, highly sensitive technique for the determination of ammonia in seawater.* **1986,** *91,* 285.
38. Svensson, G.; Anfält, T. *Clin. Chem. Acta, Rapid determination of ammonia in whole blood and plasma using flow injection analysis.* **1982,** *119,* 7.
39. Harrow, J.J.; Janata, J. *Anal. Chim. Acta, Heterogeneous samples in flow injection systems. Part 1. Whole blood.* **1985,** *174,* 115.
40. Pedersen, K.M.; Kummel, M.; Soeberg, H. *Anal. Chim. Acta, Monitoring and control of biological removal of phosphorus and nitrogen by flow injection analyzers in a municipal pilot scale waste water treatment plant.* **1990,** *238,* 191.
41. Nagashima, K.; Horie, H.; Suzuki, S. *Anal. Sci., Continuous determination of cyanide in waste water with ion selective electrode and gas-liquid separation.* **1986,** *2,* 271.
42. Zhu, Z.; Fang, Z. *Anal. Chim. Acta, Spectrophotometric determination of total cyanide in waste waters in*

a flow injection system with gas-diffusion separation and preconcentration. **1987,** *198,* 25.
43. Sonne, K.; Dasgupta, P.K. *Anal. Chem., Simultaneous photometric flow injection determination of sulfide, polysulfide, sulfite, thiosulfate and sulfate.* **1991,** *63,* 427.
44. Luedi, H.; Garn, M.; Ghisalba, O.; Schaer, H.P. *Int. J. Environ. Anal. Chem., Enzymatic determination of dimethylformamide in waste water using flow injection analysis.* **1988,** *33,* 131.
45. Kubáň, V. *Anal. Chim. Acta, Gas permeation/preconcentration flow injection determination of cyanide in waste water.* **1992,** *260,* 45.
46. Kubáň, V.; Dasgupta, P.K.; Marx, J.N. *Anal. Chem., Nitroprusside and methylene blue methods for silicone membrane differentiated flow injection determination of sulfide in water and wastewater.* **1992,** *64,* 36.
47. Kubáň, V.; Dasgupta, P.K. *Mikrochim. Acta, Comparison of photometry and conductometry for the determination of carbon dioxide.* Submitted.
48. Kubáň, V.; Dasgupta, P.K. *Determination of ammonia in process streams.* To be published.
49. van der Linden, W.E. *Anal. Chim. Acta, Flow injection analysis in on-line process control.* **1986,** *179,* 91.
50. Alegret, S.; Alonso, J.; Bartolli, J.; Martinez Fabregas, E. *Analyst, Flow injection system for on-line potentiometric monitoring of anions in freshwater streams.* **1989,** *114,* 1443.
51. Frenzel, W. *Fresenius Z. Anal. Chem., Gas-diffusion separation and flow injection potentiometry. A fruitful alliance of analytical methods.* **1990,** *336,* 21.
52. Alegret, S.; Alonso, J.; Bartolli, J.; Del Valle, M.; Jafferezic-Renault, N.; Duvault Herrera, Y. *Anal. Chim. Acta, Flow through pH-IS FET as a detector in the determination of ammonia.* **1990,** *231,* 53.
53. Hansen, E.H. *Anal. Proc., Flow injection analysis. New analytical methods based on the use of potentiometric and spectrophotometric flow-through detectors.* **1981,** *18,* 261.
54. Martin, G.D.; Meyerhoff, M.E. *Anal. Chim. Acta, Membrane dialyzer injection loop for enhancing the selectivity of anion-response liquid-membrane electrodes in flow systems. I. A sensing system for nitrogen oxide and nitrite.* **1986,** *186,* 71.
55. Hara, H.; Motoike, A.; Okazaki, S. *Analyst, Continuous flow determination of low concentrations of ammonium ions using a gas dialysis concentrator and gas electrode detector system.* **1988,** *113,* 113.
56. Chang, O.; Meyerhoff, M.E. *Anal. Chim. Acta, Membrane dialyzer injection loop for enhancing the selectivity of anion-response liquid-membrane electrodes in flow systems. II. A selective sensing system for salicylate.* **1986,** *186,* 81.
57. Blet, V.; Pons, M.N.; Greffe, J.L. *Anal. Chim. Acta, Separation of ammonia with a gas permeable tubular membrane.* **1989,** *219,* 309.
58. Frenzel, W.; Liu, C.Y. *Fresenius Z. Anal. Chem., Potentiometric and conductometric determination of ammonium, by gas diffusion flow injection analysis.* **1992,** *342,* 276.
59. Schulze, G.; Liu, C.Y.; Brodowski, M.; Elsholz, O.; Frenzel, W.; Moller, J. *Anal. Chim. Acta, Different approaches to the determination of ammonium ions at low levels by flow injection analysis.* **1988,** *214,* 121.
60. Pasquini, C.; Cardoso de Faria, F.L. *Anal. Chim. Acta, Flow injection determination of ammonia in Kjehldahl digests by gas diffusion and conductometry.* **1987,** *193,* 19.
61. Rohwedder, J.J.R.; Pasquini, C. *Analyst, Differential conductimetry in flow injection determination of ammonia in Kjehldahl digests.* **1991,** *116,* 841.
62. Cardoso de Faria, L.; Pasquini, C. *Anal. Chim. Acta, Flow injection determination of inorganic forms of nitrogen by gas diffusion and conductometry.* **1991,** *245,* 183.
63. Barros, G.F.; Tubino, M. *Analyst, Conductimetric and spectrophotometric determination of the volatile acidity of wines by flow injection analysis.* **1992,** *117,* 917.
64. Tubino, M.; Barros, F.G. *J. Assoc. Off. Anal. Chem., Conductometric and spectrophotometric determination of the volatile acidity of winegars.* **1991,** *74,* 346.
65. Ramasamy, S.M.; Mottola, H. *Anal. Chem., Repetitive determination of sulfur dioxide gas in air samples by flow injection and chemical reaction at a gas-liquid interface.* **1982,** *54,* 283.
66. Nyasulu, F.W.; Mottola, H.A. *J. Autom. Chem., Amperometric determination of nitrogen dioxide in air samples by flow injection and reaction at a gas liquid interface.* **1987,** *9,* 46.
67. Rios, A.; Luque de Castro, M.D.; Valcárcel, M.; Mottola, H. *Anal. Chem., Electrochemical determination of sulfur dioxide in air samples in a closed loop flow injection system.* **1987,** *59,* 666.
68. Milosavljevič, E.B.; Solujič, L.; Hendrix, J.L.; Nelson, J.A. *Anal. Chem., Flow injection gas diffusion method for preconcentration and determination of trace sulfide.* **1988,** *60,* 2791.
69. Audunsson, G. *Anal. Chem., Aqueous/aqueous extraction by means of a liquid membrane for sample cleanup and preconcentration of amines in a flow system.* **1986,** *58,* 2714.
70. Melcher, R.G. *Anal. Chim. Acta, Flow injection determination of membrane selected organic compounds.* **1988,** *214,* 299.
71. Gonzalo, E.R.; Pavon, J.L.P.; Růžička, J.; Christian, G.D. *Anal. Chim. Acta, Flow-injection analysis determination of phenols in kerosene and naphtha by membrane extraction-preconcentration.* **1992,** *259,* 37.
72. Kwade, C.; Salvador, A.; De la Guardia, M. *Fresenius Z. Anal. Chem., On-line sample preconcentration and determination of phenols with a flow injection analysis method.* **1992,** *342,* 426.
73. Okura, H.; Imato, T.; Asano, Y.; Yamasaki, S.; Ishibashi, N. *Anal. Sci., Potentiometric determination of ethanol in alcoholic beverages using FIA system*

equipped with gas diffusion unit with a microporous PTFE membrane. **1990,** *6,* 541.
74. Kuennecke, W.; Schmid, R.D. *J. Biotechnol., Development of a gas diffusion flow injection analysis system for on-line monitoring of ethanol.* **1990,** *14,* 127.
75. Marstorp, P.; Anfält, T.; Andersson, L. *Anal. Chim. Acta, Determination of oxidized ketone bodies in milk by flow injection analysis.* **1983,** *149,* 281.
76. Malasolti, N.L. *Dis. Abstr. Int. B., Chemiluminescent determination of clinical analytes using microporous membrane flow cells.* **1987,** *47,* 2874.
77. Nakata, R.; Kawamura, T.; Sakashita, H.; Nitta, A. *Anal. Chim. Acta, Determination of ammonium ion in a flow injection system with a gas diffusion membrane. Selection of optimal conditions for the pH indicator.* **1988,** *208,* 81.
78. Motomizu, S.; Toei, K.; Kuwaki, T.; Oshima, M. *Anal. Chem., Gas diffusion unit with tubular microporous poly(tetrafloroethylene) membrane for flow injection determination of carbon dioxide.* **1987,** *59,* 2930.
79. Tanaka, A.; Mashiba, K.; Deguchi, T. *Anal. Chim. Acta, Simultaneous determination of cyanide and thiocyanate by the pyridine/barbituric acid method after diffusion through a microporous membrane.* **1988,** *214,* 259.
80. Dasgupta, P.K.; Bligh, R.Q.; Mercurio, M.A. *Anal. Chem., Dual membrane suppressor in ion chromatography.* **1985,** *57,* 484.
81. Marion, P.; Rouillier, M.C.; Blet, V.; Pons, M.N. *Anal. Chim. Acta, On-line monitoring of cyanide concentration via a gas membrane system in extractive metallurgical processes.* **1990,** *238,* 117.
82. Christensen, L.H.; Nielsen, J.; Villadsen, J. *Anal. Chim. Acta, Monitoring of substrates and products during fed-batch penicillin fermentations in complex media.* **1991,** *249,* 123.
83. Kubáň, V.; Dasgupta, P.K.; Olson, D.C.; Bysouth, S.R. *Hydrogen cyanide process analyzer.* To be published.
84. Parker, C.P.; Gardell, M.G.; Biasio, D.D. *Int. Biotech. Lab., A complete system for fermentation monitoring.* **1986,** *4(2),* 33.
85. Zagato, E.A.G.; Reis, B.F.; Bergamin, F.H.; Krug, F.J. *Anal. Chim. Acta, Isothermal distillation in flow injection analysis. Determination of total nitrogen in plant material.* **1979,** *109,* 45.
86. van Son, M.; Schothorst, R.C.; den Boef, G. *Anal. Chim. Acta, Determination of total ammoniacal nitrogen in water by flow injection analysis and a gas diffusion membrane.* **1983,** *153,* 271.
87. Clinch, J.R.; Worsfold, P.J.; Sweeting, F.W. *Anal. Chim. Acta, An automated spectrophotometric field monitor for water quality parameters. Determination of ammonia.* **1988,** *214,* 401.
88. Hauser, P.C.; Tan, S.S.; Cardwell, T.J.; Cattrall, R.W.; Hamilton, I.C. *Analyst, Versatile manifold for the simultaneous determination of ions in flow injection analysis,* **1988,** *113,* 1551.
89. Aoki, T., *J. Flow Injection Anal., Flow injection analysis of ammonia in water with membrane separation and UV detection.* **1988,** *5,* 95.
90. Meyerhoff, M.E.; Fraticelli, Y.M. *Anal. Lett., Flow injection determination of ammonia–N using polymer membrane electrode based gas sensing system.* **1981,** *14,* 415.
91. Hollowell, D.A.; Pacey, G.E.; Gordon, G. *Anal. Chem., Selective determination of chlorine dioxide using gas diffusion flow injection analysis.* **1985,** *57,* 2851.
92. Hollowell, D.A.; Gord, J.R.; Gordon, G.; Pacey, G.E. *Anal. Chem., Selective chlorine dioxide determination using gas diffusion flow injection analysis with chemiluminescence detection.* **1986,** *58,* 1524.
93. Gord, J.R.; Gordon, G.; Pacey, G.E. *Anal. Chem., Selective chlorine determination by gas diffusion flow injection analysis with chemiluminescence detection.* **1980,** *60,* 2.
94. Pacey, G.E.; Hollowell, D.A.; Miller, K.G.; Straka, M.R.; Gordon, G. *Anal. Chim. Acta, Selectivity enhancement by flow injection analysis.* **1986,** *179,* 259.
95. Nikolič, S.D.; Molosavljevič, E.B.; Hendrix, J.L.; Nelson, J.H. *Analyst, Indirect determination of chloride by gas diffusion flow injection with amperometric detection.* **1991,** *116,* 49.
96. Motomizu, S.; Yoden, T. *Anal. Chim. Acta, Porous membrane permeation of halogens and the application to the determination of halide ions and residual chlorine by flow injection analysis.* **1992,** *261,* 461.
97. Straka, M.R.; Gordon, G.; Pacey, G.E. *Anal. Chem., Residual aqueous ozone determination by gas diffusion flow injection analysis.* **1985,** *57,* 1799.
98. Nikolič, S.D.; Jankovič, T.D.; Milosavljevič, E.B.; Hendrix, J.L.; Nelson, J.H. *Fresenius Z. Anal. Chem., Indirect determination of bromide by diffusion flow injection analysis with amperometric detection.* **1992,** *342,* 98.
99. Brunt, K. *Anal. Chim. Acta, Rapid determination of sulfide in waste waters by continuous flow analysis and gas diffusion and a potentiometric detector.* **1984,** *163,* 293.
100. Rosario, S.A.; Cha, G.S.; Meyerhoff, M.E.; Trojanowicz, M. *Anal. Chem., Use of ionomer membranes to enhance the selectivity of electrode based biosensors in flow injection analysis.* **1990,** *62,* 2416.
101. Barnes, D.E.; van Staden, J.F. *Anal. Chim. Acta, Flow injection analysis in the evaluation of supported liquid membranes.* **1992,** *261,* 441.
102. Růžička, J.; Hansen, E.H. *Anal. Chim. Acta, Optosensing on active surfaces — a new detection principle in flow injection analysis.* **1985,** *173,* 3.
103. Růžička, J.; Hansen, E.H. *Anal. Chim. Acta, Integrated microconduits for flow injection analysis.* **1984,** *161,* 1.
104. Pavon, J.L.P.; Gonzalo, E.R.; Christian, G.D.; Růžička, J. *Anal. Chem., Universal sandwich membrane cell and detector for optical flow injection analysis.* **1992,** *64,* 923.

105. Andrade, J.C.; Pasquini, C.; Baccan, N.; van Loon, J.C. *Spectrochim. Acta, Cold vapor atomic absorption determination of mercury by flow injection analysis using a teflon membrane phase separator coupled to the absorption cell.* **1983,** *38,* 1329.
106. Liná res, P.; Luque de Castro, M.D.; Valcárcel, M. *Anal. Chim. Acta, Simultaneous determination of carbon dioxide and sulfur dioxide in wine by gas diffusion flow injection analysis.* **1989,** *225,* 443.
107. Canete, F.; Rios, A.; Luque de Castro, M.D.; Valcárcel, M. *Anal. Chim. Acta, Analysis of gaseous samples by flow injection.* **1989,** *224,* 127.
108. Kubáˇn, V. *Crit. Rev. Anal. Chem., Gas diffusion/permeation in flow injection analysis. Part II. Applications and trends.* To be published.
109. van Staden, J.F. *Anal. Chim. Acta, Simultaneous flow injection analysis for two components with on-line dialysis and gas diffusion in series. Determination of chloride and ammonia nitrogen in industrial effluent water.* **1992,** *261,* 453.