Anal. Chem. **2006,** *78,* 3997

Modern Extraction Techniques

Douglas E. Raynie*

Department of Chemistry and Biochemistry, South Dakota State University, Brookings, South Dakota 57007

Review Contents

Extraction techniques play a unique role in analytical chemistry. In most laboratories, decades-old extraction procedures are still commonplace. Yet the development of instrumental analysis techniques has grown exorbitantly, especially since the development of enabling technologies, such as the transistor and microprocessor control, and still continues to grow. This is rightly so. Analytical chemistry and the fields it supports develop through the information, and the subsequent knowledge, gained through carefully executed analytical experiments. Chromatograms and spectra provide this information and advances in these techniques improve the quality of this information. On the other hand, extraction generally is relegated to a support role and it has just been within the past 15 years or so that the importance of extraction technology has been recognized for its role in the generation of quality analytical information.

Typically, extraction procedures fall into the realm of "sample preparation." That is, extraction serves to isolate analytes from potentially interfering sample components while getting these analytes into a form suitable for analysis. As a result, the primary literature contains both a wealth of peer-reviewed articles and a lack of fundamental studies focused on the development of extraction technologies when general search terms, like "extraction" or "sample preparation," are used. This review is based on articles published during the 2004 and 2005 calendar years. Articles cited tend to be those judged by this author that theoretically or experimentally advanced the development and understanding of analytical extraction techniques. Application articles generally were excluded, except where novel applications were reported with unique extraction-related developments.

In the previous review (*1*), it was noted that general trends in the development of modern extraction techniques centered on reduced-solvent methods, sorption-based methods, environmental applications, and both solid and liquid samples. During the current review period, the development membrane-based procedures, for example, using hollow-fiber membranes, were prominent; selectivity concerns, advanced through approaches such as molecularly imprinted polymers (MIPs) were addressed; and reduced-solvent methods, including supercritical fluid extraction (SFE), pressurized-liquid extraction (PLE), microwave-assisted extraction (MAE), solid-phase extraction (SPE), and solid-phase microextraction (SPME), grew in their maturity. Before embarking on this review, organized into sections based on the fundamental approach, general considerations are first presented.

GENERAL SAMPLE PREPARATION CONSIDERATIONS

When regulatory agencies or industry trade group endorse "standard methods", analytical consistency is achieved. Ong (*2*) discusses the opposite situation, that the need for standardization in less-regulated fields, like natural products and botanical and herbal preparations, exists. Procedures for the identification of marker compounds were proposed, and the effects of sample-to-sample variability were presented. Nyiredy (*3*) discussed the necessity of extraction methods to characterize both the volatile and nonvolatile components of these natural products. Similarly, the preparation of internal reference standards of soil and plant samples was proposed (*4*). Statistical methods to ensure sample homogeneity were investigated, and an interlaboratory validation was performed.

Obtaining an appropriate sample is an obvious first step in an analytical procedure. While sampling procedures and statistical considerations are established in the literature, state-of-the-art passive sampling techniques were recently reviewed (*5*). Strategies for sampler design and challenges in sampling aqueous field samples were presented. Another review (*6*) of passive sampling was extended to air, water, soil, and sediment samples and compared passive samplers and biomonitors.

Sample pretreatment prior to extraction often leads to the success of the analyte isolation procedure. Wickstrom et al (*7*) studied various combinations of sieving, milling, or grinding of humic or mineral samples before the determination of extractable elements. In nearly all cases, improved results were obtained with a combination of grinding and sieving. In a related area of general sample preparation, McIntyre and McRae (*8*) studied the effects of water content, temperature, time, and concentration on sample stability, the self-esterification of alcoholic humic extracts in this case. Hjorth (*9*) demonstrated that partitioning patterns between solutes may change with the freeze-drying of samples. Freeze-drying did not preserve the speciation pattern of major elements, trace metals, phosphorus, and sulfur in lake sediment samples. Similarly, others (*10*) reported the influence of solvent type, temperature, extraction time, and solvent volume on the mutagenicity of soil extracts.

10.1021/ac060641y CCC: $33.50
Published on Web 00/00/0000

Nearly all of the extraction techniques developed over the past 10−15 years has the feature of miniaturization. Ramos et al. (*11*) discussed the relationship of miniaturized extraction procedures for integrated at-line or on-line analytical systems.

When developing analytical protocols, a key step is the determination of the analyte recovery for the overall method and for each individual procedure. One study (*12*) presented the difference between recovery factor and apparent recovery. The dependence of the calibration recovery on sample analyte concentration and the constant or proportional matrix effect was discussed.

FLUID-PHASE PARTITIONING METHODS

Instrumental-based extraction methods, including SFE, PLE, and MAE, continue in their development. Meanwhile, other processes, such as single-drop microextraction, are joining more traditional liquid extraction procedures in a resurgence of interest. Ray (*13*) reviewed the 2003 literature for equilibrium-staged separation processes, including distillation, liquid−liquid extraction, and SFE. Lehotay et al. (*14*) developed a relatively simple procedure, which they termed "QUECHERS," for the quantitative determination of 229 pesticides in fruits and vegetables. The QUECHERS method compared favorably with traditional methods and is under consideration by regulatory bodies. Hildebrand solubility parameters were used to determine extraction solvents for organochlorine pesticides in soil and verified via Soxhlet extraction (*15*). Apps and Tock (*16*) demonstrated that magnetic stirring during liquid−liquid extraction minimized channeling effects, resulting in greater extraction efficiency. Paik et al. (*17*) demonstrated a low-volume modification to the traditional Soxhlet extraction with an approximately 90% solvent reduction and 67% time reduction compared with the Soxhlet method. An automated liquid−liquid extractor was presented (*18*) that used a peristaltic pump to effectively mix the aqueous and organic phases, while a specially designed leaching and microextraction column was developed for the extractive fractionation of environmental solid samples (*19*). Taylor and Wankat (*20*) reported a new recycle design for extractive distillation and developed simulations for energy use and column size for breaking azeotropes by the method. Kinetic modeling of steam distillation was compared with experimental data for essential oils (*21*). Vuorela et al. (*22*) compared aqueous methanol, aqueous ethanol, hot water, and enzymes for their effect on the antioxidant activity of extracted phenolics from rapeseed meal. Use of water or enzymes proved most suitable.

Cloud point extractions remain an alternative to traditional liquid−liquid extraction methods, and this method was shown (*23*) for the determination of aqueous lanthanides. Meanwhile, the differentiation of metallic species, oxidation states, and complexes was studied and a guide for optimizing cloud point extraction was presented (*24*).

A comparison (*25*) of a reactive extractant with pre-extraction analyte modification for the recovery of alcohols in aqueous samples demonstrated manipulations of analyte solubility to achieve quantitative extraction yields. Temperature effects during liquid extractions are well known. However, Canari and Eyal (*26*) showed that the temperature effect is strong in systems with ion pair interactions between protonated amines and anions of weak acids.

One intriguing, ongoing application of liquid extraction methods is the modeling and determination of the bioavailability of soil-bound pollutants. Barriuso et al. (*27*) demonstrated this approach for the environmental risk assessment of the pesticide atrazine in aged soils using aqueous methanol with and without added calcium chloride. Hickman and Reid (*28*) reported that a water-based cyclodextrin extracting phase was superior to carbon dioxide-equilibrated water for modeling the microbial mineralization of phenanthrene residues.

Ionic liquids are finding increasing use in analytical separations. These solvents possess negligible vapor pressure, thermal stability, and miscibility with both aqueous and organic solvents. Reviews (*29*, *30*) provided an overview of ionic liquids in analytical separations.

Single-Drop and Liquid Microextraction. Of the newly developed methods for liquid-based extractions that require minimal solvent amounts, the single-drop approach seems the most appealing due to the simplicity of the approach. A drop of immiscible extracting solvent, about 1−10 μL, is suspended from a syringe into the (liquid or gaseous) sample medium. Variations of this approach are seeing some development. Factors that affect traditional extractions, such as salting out, still come into play during the single-drop methods. For example, Zhang et al. (*31*) acidified an aqueous solution, added salt, and then used dilute sodium hydroxide in the single-drop microextraction of the resulting headspace. They achieved high enrichment factors for both volatile and semivolatile compounds in this organic solvent-free extraction. Derivatization of amino acids in solution was performed (*32*) prior to single-drop microextraction for the GC determination at nanogram levels. Headspace single-drop microextraction is becoming the one of the more popular approaches to the technique, and Nazarenko (*33*) provided an overview of this approach. Fakhari et al. (*34*) combined the single-drop approach to headspace sampling with continuous hydrodistillation and investigated the effects of solvent type, sample mass, drop volume, and time for the characterization of essential oils.

Li et al. (*35*) presented continuous-flow liquid microextraction for the determination of aqueous halohydrocarbons. Solvent type and volume, flow rates, sample volume, and salt concentration were all found to influence the extraction yields.

Supercritical and Pressurized Liquid Extraction. The liquid-based microextractions discussed above rely on the use of conventional liquids with extraction efficiency dependent on the geometry of the extracting system. Enhanced extraction methods are generally instrumental systems, and the enhanced efficiency of these methods comes from elevated solvent temperature. This temperature elevation leads to favorable kinetic, diffusion, solubility, and other parameters. Temperature increases lead to the improved extraction capabilities of more traditional techniques such as Soxhlet extraction. The new generation of enhanced extraction technologies is based on the use of temperatures above the atmospheric boiling point of the extracting solvent. In SFE and PLE, pressure is applied to the extraction system so that these high temperatures can be achieved. The fundamental difference between SFE and PLE is that SFE uses solvents near or above their critical point (generally carbon dioxide-based fluids), while PLE uses traditional aqueous and organic solvents. MAE, at least the closed-cell approach, is similar except that the heating is via microwave irradiation and the pressure is a consequence of

heating a closed system, as opposed to being directly applied. MAE will be discussed separately, since both closed- and open-vessel approaches are used and the instrumental configurations are somewhat different.

Analytical SFE has traditionally focused on carbon dioxide as the extracting solvent. CO_2 is a nonpolar solvent, so small amounts of alcohols or other polar organic solvents are added in an attempt to increase the fluid polarity. With the advent of PLE and other techniques, SFE applications appear to have reverted to CO_2-only extractions without the use of organic cosolvents. The current state of analytical SFE was critically reviewed (*36*), and no major chances in the technique have been observed since this publication. One area where CO_2 extraction has been prevalent is the isolation of essential oils and other natural products. Zizovic et al. (*37*) used scanning electron microscopy to examine the effect of CO_2 on the oil glands and developed a model for the SFE of essential oils in plants. Ozcan and Ozcan (*38*) similarly extracted the hydrocarbon components of an arid plant and compared the data to that obtained by Soxhlet extraction. A unique combination of ultrasonic energy to enhanced SFE was also investigated (*39*). By applying untrasound during the SFE of algal samples, extraction pressure, temperature, and time were reduced while the extraction yield was simultaneously improved. It is thought that the ultrasound aided in disrupting cell walls or the energy of interaction between the analyte and the algae matrix.

During the development of SFE to date, instrument quality has varied tremendously. One group (*40*) proposed a performance assessment protocol to ensure reproducible and traceable results between instruments. It is presumed that this performance assessment may be translated to other instrumental-based extraction techniques.

PLE uses the same general technology as SFE, except that liquid solvents are used. The technique was initially developed for the characterization of environmental samples such as soils and sediment. The next logical extension is to the characterization of biota. A recent review (*41*) provided an overview of the use of PLE for food and biological samples. PLE was employed for the determination of linear alkylbenzenesulfonates in marine organisms following tissue homogenization (*42*). Other researchers (*43*) determined the free-radical scavenging activity of fractions obtained with a semicontinuous PLE approach and found that ethanol extracts maintained higher activity levels than hot water extracts. The isolation of additives from polymers has hisotrically been a very difficult area for SFE and PLE. Dawidowicz and Wianowska (*44*) found that performing a series of PLE extractions with decreasing sample amounts could more definitively estimate true analyte concentrations in plant material than a single multicycle PLE procedure. Garrido-Lopez and Tena (*45*) used a Plackett-Burman experimental design to screen extraction conditions and a central composite design to optimize PLE for the determination of additives in polyethylene. They found that a 2-propanol−cyclohexane solvent system at 105 °C provided the most efficient results.

Extractions using "hot water" are still finding their niche in the world of analytical sample preparation. The technique is commonly referred to as subcritical water extraction, since the practitioners of this approach come from an SFE background; other terms, like hot water extraction or superheated water extraction, are found in the literature. Regardless, the approach is identical to PLE—applied pressure allows the use of the solvent at temperatures above the atmospheric boiling point. The major difference is that water loses its "effective polarity" at these high temperatures, so both nonpolar and polar solutes may potentially be extracted with a single solvent at different temperatures. Again, the initial applications were in the environmental arena, but research is branching into other areas. Ozel and Kaymaz (*46*) demonstrated that in the range of 100−150 °C water was able to quantitatively extract essential oils more efficiently than steam distillation or Soxhlet extraction. Kasia and Ikehara (*47*) used the hot water technique in the stepwise extraction of proteins and carbohydrates from soybeans. Small- and medium-sized carbohydrates and proteins were extracted, but not those with higher molar mass. While hot water extractions have the advantage of the complete elimination of organic solvents, whether this technique finds increasing use in analytical laboratories will depend on the reluctance to use temperatures in the 150−250 °C range and the more lengthy solvent (water) evaporation times.

Microwave-Assisted Extraction. While MAE shares several similarities with SFE and PLE, there are also significant differences. MAE may use either an open- or closed-vessel approach. Of course, the open-vessel approach limits the upper temperature attainable. Additionally, MAE may allow the use of acids and bases, making, for example, acid digestions possible. MAE finds a diversity of applications, slanted more toward the food and biological areas than environmental uses. A nitric acid vapor extraction procedure was developed (*48*) to determine metals in biological samples. It was found that temperature was the most important parameter, followed by sample particle size in this microwave digestion. Ramon et al. (*49*) discovered that microwave power did not impact the mineralization and H_2O_2 oxidation of industrial wastewaters prior to the determination of Kjeldahl nitrogen. Time seemed to play the biggest factor in this chemical digestion. Chemat et al. (*50*) studied the kinetics of MAE for the extraction of monoterpenes from caraway seeds. They found that the microwaves aided in the disruption of cell walls, liberating the essential oils. Another approach to MAE is the use of focused-microwave irradiation during Soxhlet extraction, a method reviewed by Luque-Garcia and Luque De Castro (*51*).

Other Fluid-Phase Partitioning Methods. Liquid−liquid methods, cloud-point extractions, and other techniques have been mentioned. Foremost among other partitioning methods is the application of ultrasound energy to facilitate extraction. Priego-Capote and Luque De Castro (*52*) reviewed the principles and devices for the use of ultrasound in analytical sample preparation. A regulatory method (*53*) for the field-portable procedure to determine hexavalent chromium in air has been modified. Following sample collection, ultrasound extraction with a buffer system frees the Cr^{6+} for spectrophotometric determination. Others (*54*) used multivariate optimization when combining ultrasonic energy and moderate temperature for the acid−base extraction of humic substances from marine sediments. Temperature and replicate extractions were the most significant extraction parameters. Cautions are also needed when applying ultrasound. Castro and Korn (*55*) noted that when they applied ultrasound during the ammonium extraction of soils significant levels of ammonium were lost as N_2 and possibly converted to amines, nitrates, or nitrites.

A final partitioning method of note is magnetophoresis (*56*). By controlling a magnetic field gradient, a magnetic fractionation of ultrafine particles (for example, iron(III) oxide and copper(II) oxide in this paper) is achieved. A model was developed, a theory was proposed, and an experimental design was presented.

Comparisons of Fluid-Phase Extraction Methods. In the eyes of many researchers, new or novel extraction approaches will not gain acceptance until they "prove" themselves in comparison to other alternatives. Since analytical extractions are generally a preliminary step to the final method that produces the desired information, advantages of time, automation, reproducibility, or solvent use must be shown. Thus, as newer technologies are developed, they are often compared with other developing and/or existing techniques.

In the area of environmental concerns, Focant et al. (*57*) compared SFE, MAE, PLE, and SPE for the measurement of dioxins in biological samples. An integrated approach, with emphasis on parallel processing, was presented. In a more comprehensive comparison, Sporring et al. (*58*) investigated Soxhlet extraction, automated Soxhlet extraction, ultrasound extraction, SFE, MAE, and PLE for the determination of polychlorinated biphenyls in soil. The authors did not attempt to optimize any of the extractions, but used published methods. They concluded that each of these methods can provide successful results when care is taken in the choice of extraction conditions.

While food and biologicals have received significant attention in this review, the extraction of DNA from these materials has not. Smith et al. (*59*) compared eight methods for the isolation of DNA from potatoes and potato-derived products. The Kingfischer and CTAB methods recovered the highest levels of an important amplifiable gene, magnetic particle processors provided the highest quality extracts for fatty samples, and the Wizard method was the preferred method for potato-derived foods. Suenaga and Nakamura (*60*) compared three methods for extracting DNA from human hair prior to PCR experiments. The Chelex method was preferred based on simplicity and cost.

Tanamati et al. (*61*) were concerned with the use of chlorinated solvents for the study of total lipids in meat. They compared nine extraction methods covering a range of organic solvents. When toxicity concerns are removed, the Bligh−Dyer method and its modified version provide the highest yields. Other methods minimize solvent use and may be applicable regardless of the total lipid levels. In another food-related concern, PLE, Soxhlet, and ultrasound extractions were compared (*62*) for the analytical removal of terpenoids and sterols in tobacco. PLE was a good alternative to the conventional Soxhlet method, especially with large sample sizes, but Soxhlet gave high extraction efficiencies for sterols. SPME, SFE, steam distillation, and conventional solvent extraction were evaluated (*63*) for the analysis of volatile components in a Chinese fruit. Both SPME and SFE were found superior to the other methods, and SPME was preferred since it did not require specialized instrumentation. Presti et al. (*64*) did not use SPME, but compared steam distillation, SFE, solvent extraction, and microwave-assisted steam distillation for a similar determination, the isolation of essential oils from rosemary. They found the microwave-assisted method superior.

SORPTIVE AND MEMBRANE-BASED EXTRACTION METHODS

Extracting solutes from liquid or gaseous samples using sorptive phases has been described as "poor man's chromatography". That is, similar stationary phases are used, but the overall goal is the isolation of compound classes rather than the high resolution typically desired in analytical chromatography. This extraction mechanism likely started with conventional column chromatography cleanup and fractionation and developed into an extraction mode with what is now considered SPE. The cartridge format was quickly followed by the disk format as an attempt to accommodate larger sample volumes. These formats are now considered mature, though researchers may struggle with method development. The desire for even more selective phases, like restricted-access media (RAM) or MIPs, is the current driving force in SPE research. Newer sorptive extraction formats, such as SPME, are the most recent efforts in sorptive extraction. As SPME is widely used but still maturing, it will be addressed separately followed by other sorptive methods and phase developments.

Solid-Phase Microextraction. The idea of placing a stationary-phase coating onto an extraction fiber comes from gas chromatography. Hence, SPME phases tend to be similar to GC stationary phases, while SPE phases are more similar to liquid chromatography stationary phases. SPME is finding itself to be more versatile, since it can sample from air as well as liquid. However, SPME is a nonexhaustive technique. One type of newly developed SPME phases are sol−gels. Sol−gels of amphiphilic and hydrophilic oligomers were synthesized (*65*) and evaluated for a wide variety of nonpolar and polar analytes. The sol−gel phases gave comparable selectivity and detection limits as commercial SPME phases, but had a wider thermal range. Different fiber coatings were compared (*66*) for the extraction of volatile compounds in cured ham. Mixed commercial phases provided the optimal extraction results.

While selective phases are important to the SPME process, compounds with poor chromatographic performance, high reactivity, high volatility, or thermal instability often need derivatization during the sample preparation procedure. Stashenko and Martinez (*67*) reviewed derivatization for SPME and found it commonly used to increase the recovery of polar compounds.

In addition to the types of phases, SPME sampling methods have been the subject of research. Chen and Pawliszyn (*68*) developed a new SPME holder amenable to field sampling. The device was able to accommodate both time-weighted average and grab sampling and postextraction sample integrity was maintained. Silva et al. (*69*) constructed a device to allow SPME to be used during dynamic headspace spacing. With this approach, they obtained extraction yields six times higher than conventional headspace sampling. Cai et al. (*70*) reviewed the coupling of SPME with LC, an approach especially valuable for nonvolatile and thermally unstable compounds. Others (*71*) thoroughly reviewed the automation of SPME and discussed coupling with LC or GC, fiber and in-tube configurations, and recent developments.

More theoretically, Chen and Pawliszyn (*72*) investigated the desorption kinetics from SPME fibers and proposed a model for the dynamic desorption process. The model was based on steady-state analyte diffusion and was experimentally verified.

As with fluid-phase partitioning methods, environmental analysis drives the applications and developments of sorptive methods such as SPME. Aulakh et al. (*73*) reviewed the use of SPME in pesticide analysis, including alternative configurations such as the in-tube method. As with liquid extraction, SPME has been used to determine the bioavailability of environmental compounds in sediments and water (*74*). Unamended and carbon-amended soils were studied, and SPME was found to provide matrix-independent correlations with bioavailabilty. Darrouzes et al. (*75*) used a thermodynamic approach to study the effects of pressure and sample agitation on the SPME recoveries of organotin compounds in headspace samples. Quantitative structure−activity relationships were used to estimate partition coefficients, and shorter sampling times were achieved. Chia et al. (*76*) combined headspace cooling with sample heating and ultrasonication for the headspace-SPME of soil-bound polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans. Fast and efficient screening was achieved. Moeder and Schrader (*77*) evaluated different coatings, fiber lengths, and film thicknesses to enhance the extraction capacity and reduce noise in the SPME method. Using a custom-made poly(dimethylsiloxane) phase, they eliminated bisphenol A background, an interference in the analysis of endocrine-disrupting compounds.

Sorptive-Phase Developments. One of the attractive features of sorptive extraction techniques is the selectivity available from a variety of phases. This has been an active research area. Valuable research is continuing in the development of affinity media, including immunosorbents and MIPs. Haginaka (*78*) reviewed these developments. A similar review (*79*) focused specifically on immunoaffinity phases, especially for trace-level analysis of biological and pharmaceutical systems.

In addition to immunosorbents, MIPs are seeing increased use. Kandimalla and Ju (*80*) reviewed the developments and applications of MIP phases, while another review (*81*) summarized the literature and trends of the previous 10 years. Malaisamy and Ulbricht (*82*) blended MIP membranes from cellulose acetate and sulfonated polysulfone and investigated the resulting hydrophobicity of the phase. Hydrophobicity increased with increasing polysulfone content. Hydrophilic surface modification was combined with a conventional suspension polymerization in the approach developed by Haginaka (*83*). The molecularly imprinted sites remained unchanged after the surface modification.

Conventional phase technology has not been ignored during this review period. Both polymeric and monolithic phases were reviewed by Fontanals et al. (*84*), with an emphasis on the recovery of polar compounds. Silica and polymer phases were compared (*85*) for the recovery of pharmaceuticals from bovine serum. Ponde (*86*) found that a hydrophilic−lipophilic balanced polymer-based phase had a wide pH stability and good reproducibility with high analyte recoveries. Polymeric phases were also preferred in a comparison (*87*) of SFE phases for the determination of phenoxyacetic acid herbicides, though low-flow rates were required.

Other Sorptive Techniques. The major disadvantage of SPME is the amount of available phase, which limits the mass of analyte that can be extracted. The in-tube configuration of SPME is one attempt to address this issue. Other techniques, notably stir bar sorptive extraction (SBSE), are being developed to deliver more sorptive-phase mass and surface area. In this technique, the phase, similar to GC stationary phases, is coated and bonded onto a magnetic stir bar. The stir bar is then immersed into the liquid sample for extraction. Lambert et al. (*88*) developed an alkyl−diol−silica RAM coating for the SBSE of caffeine and metabolites in biological fluids. They found that fouling of the sorptive coating was minimized with the RAM. Cation-exchange RAM was integrated (*89*) with LC for the on-line determination of atropine in human plasma.

An approach more similar to the traditional SPE is microextraction in a packed syringe (MEPS). The MEPS technique uses conventional SPE material packed into the tip of a disposal-tip pipet or syringe. The technology is compatible with repeating pipets or automated liquid-handling systems. This approach was validated (*90*−*92*) for the determination of anesthetics and related compounds in human serum prior to LC−MS/MS. MEPS was claimed to be easily used for pharmacokinetic and pharmacodynamic studies.

Several other formats of sorptive extraction also exist. An attractive alternative format for conventional SPE is a configuration compatible with the 96-well plates used in pharmaceutical and biotechnology applications. A brief history of 96-well SPE plates was presented (*93*). Extraction efficiency for on-line microcolumn LC was significantly improved (*94*) by packing polymer-coated fibers longitudinally into a short PEEK capillary. The effect of the polymeric coating was studied and nanogram per milliliter detection limits were obtained.

Hollow-Fiber Membrane Extractions. Membrane extractions take on many of the same configurations as sorptive extractions. One common approach is to use partitioning through immobilized solvents as the selectivity procedure, such as in hollow-fiber membranes. Pedersen-Bjergaard and Rasmussen (*95*) used fatty oils and essential oils as the immobilized organic phase for the removal of basic drugs from aqueous solution. The oily phase eliminated the need for hazardous organic solvents. This group (*96*) later studied ion pairing for this carrier-mediated transport approach for sample preparation. Others (*97*) investigated the hollow-fiber approach for the determination of acidic drugs in waters. They called for the development of commercial phases and fibers to improve method repeatability. Basheer et al. (*98*) found reproducibility and nanogram per liter detection limits for the determination of estrogens in water with a new hollow-fiber membrane coating, dihydroxylate poly(methyl methacrylate). Yazdi and Es'haghi (*99*) demonstrated the use of a hydrophobic porous polypropylene membrane as the interface between the donor and acceptor phases. With this membrane, enrichment factors of 60 were obtained for the determination of aromatic amines in water. A thorough examination of parameters such as agitation, organic solvent, sample volume, exposure time, salt additives, and pH was presented (*100*) for the investigation of aqueous insecticide samples. A resistance-in-series model for hollow-fiber membrane extractions was developed (*101*) and tested with the extraction of aqueous ethanol or acetone with supercritical carbon dioxide or propane. Optimal values of feed and solvent velocities were obtained.

A unique variation of the hollow-fiber approach is solvent bar microextraction (SBME). Typically, membrane extractions require that the donor or the acceptor phase flow across the membrane. In SBME, Jiang and Lee (*102*) sealed an organic solvent within a short length of hollow-fiber membrane and then extracted from

a stirred aqueous solution. Comparisons to single-drop microextractrion, static hollow-fiber membranes, and SPME were shown. Another unique variation is a dynamic hollow-fiber supported headspace extraction. Jiang et al. (*103*) reported affixing the hollow-fiber membrane to a syringe needle to sample the gaseous headspace for polycyclic aromatic hydrocarbons in soil. They reported the effects of sampling temperature, water, salt, and dwell time.

Other Membrane Extraction Techniques. A recent review (*104*) presented the theory, principles, and applications of membrane extractions in analytical chemistry. Miro and Frenzel (*105*) reviewed dialysis, gas diffusion, pervaporation, and related techniques. A number of these approaches besides the hollow-fiber membranes, often borrowed from processing technology, are developing. Key among these is supported-liquid membrane (SLM) extraction. Msagati and Nindi (*106*) examined the role of acceptor and donor pH and enrichment time for the determination of macrolide antibiotics in milk and tissue samples. SLM without sample derivatization was used (*107*) for the enrichment of haloacetic acids in water with a miniaturized device.

Pervaporation consists of the selective movement of volatile compounds across a membrane into a gaseous stream. Bishop and Mitra (*108*) recently investigated this approach for the on-line concentration and monitoring of trace analytes in a pharmaceutical stream. Residence time and temperature were important factors in this method. Microdialysis methods have traditionally been the realm of biological studies, but Miro and Frenzel (*109*) presented the method for sample processing in environmental research. In the engineering realm, an experimental phase-free membrane extraction process using a ceramic microfiltration tube membrane dispersion extractor was developed (*110*). A variety of influences were studied, and high efficiency was observed. It is conceivable that as the engineering developments continue, this approach could move into the analytical world.

CONCLUSIONS

During this review period, significant advances were made in the areas of sorptive membrane-based extraction. Fluid-phase partitioning methods primarily grew on an application-driven basis. Future developments in all areas of analytical sample preparation are expected to continue to be application-driven in a quest for improved recoveries, higher sample throughput, and less organic solvent consumption.

Dr. Douglas Raynie *is a Research Assistant Professor in the Department of Chemistry and Biochemistry at South Dakota State University. Prior to joining SDSU, he was employed for eleven years as a Senior Scientist at Procter and Gamble's Corporate Research Division. At P&G, he introduced PLE to industry as one of the world's first practitioners of the technique. He earned his Ph.D. at Brigham Young University under the direction of Dr. Milton Lee. His undergraduate degree is from Augustana (South Dakota) College, with majors in chemistry and biology. Dr. Raynie's research program focuses on analytical chemistry and bioprocessing. His analytical research interests include high-resolution chromatography, chromatographic sample preparation (using PLE, SFE, SPME, and SPE), chromatography theory, and problem-based learning. In the bioprocessing area, he is applying sustainable and green chemistry approaches using near- and supercritical carbon dioxide and water to the processing of biomass for energy and materials production.*

LITERATURE CITED

(1) Raynie, D. E. *Anal. Chem.* **2004**, *76*, 4659−4664.
(2) Ong, E. S. *J. Chromatogr., B* **2004**, *812*, 23−33.
(3) Nyiredy, S. *J. Chromatogr., B* **2004**, *812*, 35−51.
(4) Lopez-Romero, R. Ma.; Etchevers, J. D.; Humberto Vaguera, H. *Commun. Soil Sci. Plant Anal.* **2005**, *36*, 431−438.
(5) Vrana, B.; Allan, I. J.; Greenwood, R.; Mills, G. A.; Dominiak, E.; Svensson, K.; Knutsson, J.; Morrison, G. *Trends Anal. Chem.* **2005**, *24*, 845−868.
(6) Namiesnik, J.; Zabiegala, B.; Kot-Wasik, A.; Partyka, M.; Wasik, A. *Anal. Bioanal. Chem.* **2005**, *381*, 279−301.
(7) Wickstrom, T.; Ogner, G.; Remedios, G. *Commun. Soil Sci. Plant Anal.* **2004**, *35*, 369−384.
(8) McIntyre, C.; McRae, C. *Org. Geochem.* **2005**, *36*, 543−553.
(9) Hjorth, T. *Anal. Chim. Acta* **2004**, *526*, 95−102.
(10) Courty, B.; Curieux, F. L.; Milon, V.; Marzin, D. *Mutat. Res.: Genet. Toxicol, Environ. Mutat.* **2004**, *565*, 23−34.
(11) Ramos, L.; Ramos, J. J.; Brinkman, U. A. Th. *Anal. Bioanal. Chem.* **2005**, *381*, 119−140.
(12) Cuadros-Rodriguez, L.; Almansa-Lopez, E. M.; Garcia-Campana, A. M.; Gonzalez-Casado, A.; Garrido-Frenich, F. J.; Martinez-Vidal, J. L. *Talanta* **2005**, *66*, 1063−1072.
(13) Ray, M. S. *Sep. Sci. Technol.* **2005**, *40*, 1145−1168.
(14) Lehotay, S. J.; DeKok, A.; Hiemstra, M.; Van Bodegraven, P. *J. AOAC Int.* **2005**, *88*, 595−614.
(15) Lang, Y. H.; Cao, Z. M.; Jiang, X. *Talanta* **2005**, *66*, 249−252.
(16) Apps, P.; Tock, M. L. A. *J. Chromatogr., A* **2005**, *1083*, 215−218.
(17) Paik, M. J.; Park, J. E.; Koo, W. H.; Chung, G. H.; Kim, J. H.; Kim, K. R. *Chromatographia* **2004**, *60*, 693−698.
(18) Diniz, M. C. T.; Filho, O. F.; Rohwedder, J. J. R. *Anal. Chim. Acta* **2004**, *525*, 218−287.
(19) Chomchoei, R.; Miro, M.; Hansen, E. H.; Shiowatana, J. *Anal. Chim. Acta* **2005**, *536*, 183−190.
(20) Taylor, M.; Wankat, P. C. *Sep. Sci. Technol.* **2004**, *39*, 1−17.
(21) Romdhane, M.; Tizaoui, C. *J. Chem. Technol. Biotechnol.* **2005**, *80*, 759−766.
(22) Vuorela, S.; Meyer, A. S.; Heinonen, M. *J. Agric. Food Chem.* **2004**, *52*, 8202−8207.
(23) Favre-Regullion, A.; Draye, M.; Lebuzit, G.; Thomas, S.; Foos, J.; Cote, G.; Guy, A. *Talanta* **2004**, *63*, 803−806.
(24) Paleologos, E. K.; Giokas, D. L.; Karayannis, M. I. *Trends Anal. Chem.* **2005**, *24*, 426−436.
(25) Kuzmanovic, B.; Kuipers, N. J. M.; DeHaan, A. B.; Kwant, G. *Ind. Eng. Chem. Res.* **2004**, *43*, 7572−7580.
(26) Canari, R.; Eyal, A. M. *Ind. Eng. Chem. Res.* **2004**, *43*, 7608−7617.
(27) Barriuso, E.; Koskinen, W. C.; Sadowsky, M. J. *J. Agric. Food Chem.* **2004**, *52*, 6552−6556.
(28) Hickman, Z. A.; Reid, B. J. *Environ. Pollut.* **2005**, *138*, 299−306.
(29) Liu, J.-F.; Jiang, G.-B.; Jonsson, J. A. *Trends Anal. Chem.* **2005**, *24*, 20−27.
(30) Zhao, H.; Xia, S.; Ma, P. *J. Chem. Technol. Biotechnol.* **2005**, *80*, 1089−1096.
(31) Zhang, J.; Su, T.; Hian, K. L. *Anal. Chem.* **2005**, *77*, 1988−1992.
(32) Fiamegos, Y. C.; Nanos, C. G.; Stalikas, C. D. *Anal. Chem.* **2004**, *813*, 89−94.
(33) Nazarenko, A. Y. *Am. Lab.* **2004**, *36* (16), 30−33.
(34) Fakhari, A. R.; Salehi, P.; Heydari, R.; Ebrahimi, S. N.; Haddad, P. R. *J. Chromatogr., A* **2005**, *1098*, 14−18.
(35) Li, Y.; Zhang, T.; Liang, P. *Anal. Chim. Acta* **2005**, *536*, 245−249.
(36) Zougagh, M.; Valcarcel, M.; Rios, A. *Trends Anal. Chem.* **2004**, *23*, 399−405.
(37) Zizovic, I.; Stamenic, M.; Orlovic, A.; Skala, D. *Chem. Eng. Sci.* **2005**, *60*, 6747−6756.
(38) Ozcan, A.; Ozcan, A. S. *Talanta* **2004**, *64*, 491−495.
(39) Hu, A.-J.; Zheng, J.; Qiu, T.-Q. *Xiandai Huagong* (*Mod. Chem. Ind.*) **2004**, *24*, 141−143.
(40) Palenzuela, B.; Manganiello, L.; Bauza, R.; Rios, A.; Valcarcel, M. *Accredit. Qual. Assur.* **2005**, *10*, 219−288.
(41) Carabias-Martinex, R.; Rodriguez-Gonzalo, E.; Revilla-Ruiz, P.; Hernandez-Mendez, J. *J. Chromatogr., A* **2005**, *1089*, 1−17.
(42) Alvarez-Munoz, D.; Saez, M.; Lara-Martin, P. A.; Gomez-Parra, A.; Mazo-Gonzalez, E. *J. Chromatogr., A* **2004**, *1052*, 33−38.
(43) Chen, P.-Y.; Tu, Y.-X.; Wu, C.-T.; Jong, T.-T.; Chang, C.-M. J. *J. Agric. Food Chem.* **2004**, *52*, 1945−1949.
(44) Dawidowicz, A. L.; Wianowska, D. *J. Pharm. Biomed. Anal.* **2005**, *37*, 1161−1165.
(45) Garrido-Lopez, A.; Tena, M. T. *J. Chromatogr., A* **2005**, *1099*, 75−83.
(46) Ozel, M. Z.; Kaymaz, H. *Anal. Bioanal. Chem.* **2004**, *379*, 1127−1133.
(47) Kasai, N.; Ikehara, H. *J. Agric. Food Chem.* **2005**, *53*, 4245−4254.
(48) Araujo, C. G. L.; Nogueira, A. R. A.; Nobrega, J. A. *Microchim. Acta* **2004**, *144*, 81−85.
(49) Ramon, R.; Del Valle, M.; Valero, F. *Anal. Lett.* **2005**, *38*, 2415−2430.
(50) Chemat, S.; Ait-Amar, H.; Lagha, A.; Esveld, D. C. *Chem. Eng. Process.* **2005**, *44*, 1320−1326.
(51) Luque-Garcia, J. L.; Luque De Castro, M. D. *Talanta* **2004**, *64*, 571−577.
(52) Priego-Capote, F.; Luque De Castro, M. D. *Trends Anal. Chem.* **2004**, *23*, 644−653.
(53) Hazelwood, K. J.; Drake, P. L.; Ashley, K.; Marcy, D. *J. Occup. Environ. Hygiene* **2004**, *1*, 613−619.
(54) Moreda-Pineiro, A.; Beermejo-Barrera, A.; Bermejo-Barrera, P. *Anal. Chim. Acta* **2004**, *524*, 97−107.

(55) Castro, J. T.; Korn, M. *Microchem. J.* **2004**, *78*, 41−45.
(56) Ying, T.-Y.; Prenger, F. C.; Worl, L. A.; Johnson, M. D.; Waynert, J. A.; Wingo, R. M. *Sep. Sci. Technol.* **2004**, *39*, 2915−2930.
(57) Focant, J.-F.; Pirard, C.; DePauw, E. *Talanta* **2004**, *63*, 1101−1113.
(58) Sporring, S.; Bowadt, S.; Swensmark, B.; Bjorklund, E. *J. Chromatogr., A* **2005**, *1090*, 1−9.
(59) Smith, D. S.; Maxwell, P. W.; DeBoer, S. H. *J. Agric. Food Chem.* **2005**, *53*, 9848−9859.
(60) Suenaga, E.; Nakamura, H. *J. Chromatogr., B* **2005**, *820*, 137−141.
(61) Tanamati, A.; Oliveira, C. C.; Visentainer, J. V.; Matsushita, M.; De Souza, N. E. *J. Am. Oil Chem. Soc.* **2005**, *82*, 393−397.
(62) Shen, J.; Shao, X. *Anal. Bioanal. Chem.* **2005**, *383*, 1003−1008.
(63) Shen, S.; Sha, Y.; Deng, C.; Fu, D.; Chen, J.; Zhang, X. *J. AOAC Int.* **2005**, *88*, 418−423.
(64) Presti, M. L.; Ragusa, S.; Trozzi, A.; Dugo, P.; Visinoni, F.; Fazio, A.; Dugo, G.; Mondello, L. *J. Sep. Sci.* **2005**, *28*, 273−280.
(65) Basheer, C.; Jegadesan, S.; Valiyaveetil, S.; Hian, K. L. *J. Chromatogr., A* **2005**, *1087*, 252−258.
(66) Garcia-Esteban, M.; Ansorena, D.; Astiasaran, I.; Ruiz, J. *Talanta* **2004**, *64*, 458−466.
(67) Stashenko, E. E.; Martinez, J. R. *Trends Anal. Chem.* **2004**, *23*, 553−561.
(68) Chen, Y.; Pawliszyn, J. *Anal. Chem.* **2004**, *76*, 6823−6828.
(69) Silva, R. C.; Aguiar, P. M. S.; Augusto, F. *Chromatographia* **2004**, *60*, 687−691.
(70) Cai, Y.; Liu, J.; Jiang, G. *Prog. Chem.* **2004**, *16*, 708−716.
(71) O'Reilly, J.; Wang, Q.; Setkova, L.; Hutchinson, J. P.; Chen, Y.; Lord, H. L.; Linton, C. M.; Pawliszyn, J. *J. Sep. Sci.* **2005**, *28*, 2010−2022.
(72) Chen, Y.; Pawliszyn, J. *Anal. Chem.* **2004**, *76*, 5807−5815.
(73) Aulakh, J. S.; Malik, A. K.; Kaur, V.; Schmitt-Kopplin, P. *Crit. Rev. Anal. Chem.* **2005**, *35*, 71−85.
(74) Conder, J. M.; La Point, T. W. *Environ. Toxicol. Chem.* **2005**, *24*, 1059−1066.
(75) Darrouzes, J.; Bueno, M.; Pecheyran, C.; Holeman, M.; Potin-Gautier, M. *J. Chromatogr., A* **2005**, *1072*, 19−27.
(76) Chia, K.-J.; Lee, T.-Y.; Huang, S.-D. *Anal. Chim. Acta* **2004**, *527*, 157−162.
(77) Moeder, M.; Schrader, S. *J. Sep. Sci.* **2004**, *27*, 1517−1523.
(78) Haginaka, J. *Trends Anal. Chem.* **2005**, *24*, 407−415.
(79) Delaunay-Bertoncini, N.; Hennion, M.-C. *J. Pharm. Biomed. Anal.* **2004**, *34*, 717−736.
(80) Kandimalla, V. B.; Ju, H. *Anal. Bioanal. Chem.* **2004**, *380*, 587−605.
(81) Hu, S.; Li, L.; He, X. *Prog. Chem.* **2005**, *17*, 531−543.
(82) Malaisamy, R.; Ulbricht, M. *Sep. Pur. Technol.* **2004**, *39*, 211−219.
(83) Haginaka, J. *Anal. Bioanal. Chem.* **2004**, *379*, 332−334.
(84) Fontanals, N.; Marce, R. M.; Borrull, F. *Trends Anal. Chem.* **2005**, *24*, 394−406.
(85) Motyka, R. J.; Sadjadi, S.; Gerhards, P. *LC-GC* **2005**, *23*, 66.
(86) Ponde, D. E. *Aust. J. Chem.* **2005**, *58*, 375.
(87) Moret, S.; Sanchez, J. M.; Salvado, V.; Hidalgo, M. *J. Chromatogr., A* **2005**, *1099*, 55−63.
(88) Lambert, J.-P.; Mullet, W. M.; Kwong, E.; Lubda, D. *J. Chromatogr., A* **2005**, *1075*, 43−49.
(89) Rbeida, O.; Christiaens, B.; Hubert, Ph.; Lubda, D.; Boos, K.-S.; Crommen, J.; Chiap, P. *J. Pharm. Biomed. Anal.* **2005**, *36*, 947−954.
(90) Abdel-Rehim, M.; Altun, Z.; Blomberg, L. *J. Mass Spectrom.* **2004**, *39*, 1488−1493.
(91) Altun, Z.; Abdel-Rehim, M.; Blomberg, L. G. *J. Chromatogr., B* **2004**, *817*, 129−135.
(92) Abdel-Rehim, M.; Skansen, P.; Vita, M.; Hassan, Z.; Blomberg, L.; Hassan, M. *Anal. Chim. Acta* **2005**, *539*, 35−39.
(93) Venn, R. F.; Merson, J.; Cole, S.; Macrae, P. *J. Chromatogr., B* **2005**, *817*, 77−80.
(94) Imaizumi, M.; Saito, Y.; Ban, K.; Wada, H.; Hayashida, M.; Jinno, K. *Chromatographia* **2004**, *60*, 619−623.
(95) Pedersen-Bjergaard, S.; Rasmussen, K. E. *J. Sep. Sci.* **2004**, *27*, 1511−1516.
(96) Ho, T. S.; Reubsaet, J. L. E.; Anthonsen, H. S.; Pedersen-Bjergaard, S.; Rasmussen, K. E. *J. Chromatogr., A* **2005**, *1072*, 29−36.
(97) Quintana, J. B.; Rodil, R.; Reemtsma, T. *J. Chromatogr., A* **2004**, *1061*, 19−26.
(98) Basheer, C.; Jayaraman, A.; Lee, M. K.; Valiyaveettil, S.; Lee, H. K. *J. Chromatogr., A* **2005**, *1100*, 137−143.
(99) Yazdi, A. S.; Es'haghi, Z. *J. Chromatogr., A* **2005**, *1082*, 136−142.
(100) Lambropoulou, D. A.; Albanis, T. A. *J. Chromatogr., A* **2005**, *1072*, 55−62.
(101) Bocquet, S.; Torres, A.; Sanchez, J.; Rios, G. M.; Romero, J. *AIChE J.* **2005**, *51*, 1067−1079.
(102) Jiang, X.; Lee, H. K. *Anal. Chem.* **2004**, *76*, 5591−5596.
(103) Jiang, X.; Brasheer, C.; Zhang, J.; Hian, K. L. *J. Chromatogr., A* **2005**, *1087*, 289−294.
(104) Jakubowska, N.; Polkowska, Z.; Namiesnik, J.; Przyjazny, A. *Crit. Rev. Anal. Chem.* **2005**, *35*, 217−235.
(105) Miro, M.; Frenzel, W. *Trends Anal. Chem.* **2004**, *23*, 624−636.
(106) Msagati, T. A. M.; Nindi, M. M. *Microchim. Acta* **2004**, *148*, 199−214.
(107) Wang, X.; Saridara, C.; Mitra, S. *Anal. Chim. Acta* **2005**, *543*, 92−98.
(108) Bishop, E. J.; Mitra, S. *J. Pharm. Biomed. Anal.* **2005**, *37*, 81−86.
(109) Miro, M.; Frenzel, W. *Trends Anal. Chem.* **2005**, *24*, 324−333.
(110) Chen, G. G.; Luo, G. S.; Sun, Y.; Xu, J. H.; Wang, J. D. *AIChE J.* **2004**, *50*, 382−387.

AC060641Y