COMMENTARY

Separations Research Needs for the 21st Century

Figure 1 illustrates a basic separations unit operation with the various components.

The use of thermodynamic property relations is an important factor in the analysis of separations processes. For example, obtaining physical and thermodynamic property data for various types of proteins, small molecules, and bioproducts found in an aqueous fermentation broth is an important factor for bioseparations. When these data are available for standard proteins (bovine serum albumin, lysozyme, and lactalbumin), they do not represent products that are actually manufactured in industry. Because many of the products are difficult to obtain or would be considered proprietary, there is also a need to correlate the properties of model proteins to the ones being used in industry.

Separating agents are the key input to a separation process. It is useful to point out some general statements regarding the use of separating agents:

(i) Separation processes use mass and/or energy separating agents to perform the separation. Mass separating agents can be a solid, liquid, or gas. Heat is the most common energy separating agent used in distillation. External fields, such as magnetic and electric, are sometimes used as energy separating agents.

(ii) A different component distribution between two phases is obtained. This distribution change can be accomplished in two ways: (1) alteration of the original phase equilibrium (two phases are originally present, and the role of the separating agent is to change the composition in each phase relative to the initial values); (2) generation of a second phase with a different component distribution.

(iii) Separating agents employ four methods to generate selectivity: (1) modification of phase equilibrium; (2) geometry differences; (3) kinetics (rate of exchange) between phases; (4) rate of mass transfer within a phase.

Mass separating agents are generally characterized by their capacity to incorporate the desired solute (sometimes called loading) and their ability to discriminate between solutes (selectivity). Energy separating agents are usually described by the amount required to achieve a certain throughput (productivity) and selectivity for a given process. These values relate directly to the equipment size needed for a given separation.

Evolution of Separations Technology to the 21st Century

Separations technology evolved during the 20th century, driven primarily by advances in the petrochemical industry. Several technologies, such as distillation, extraction, and adsorption, have been known and used for quite some time, and other technologies, such as membranes, have evolved and are being used in new applications. Recent materials and other scientific and engineering advances provide the potential for expanded opportunities in almost all of the separations technologies.

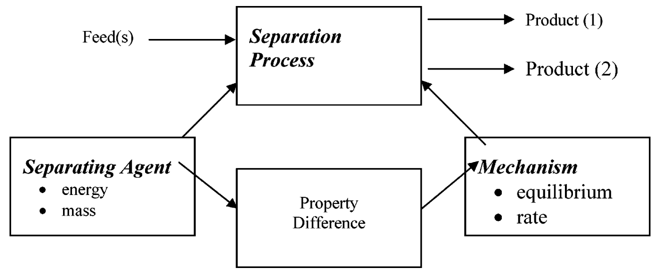

Figure 1. Generic unit operation for a separations process.

These separations technologies (and possibly others) will address the separations needs for the future. Future separations needs are related to the pharmaceutical, biomedical and other biotech industries, microelectronics, aerospace, and alternative fuels (i.e., hydrogen) segments of the economy. In addition, nanotechnology will impact separations in general with respect to scale and materials. Biotechnology provides additional opportunities to translate advances in this area to use in separations technology. Environmental concerns, such as CO_2 levels in the atmosphere, will continue to provide the impetus for improved separations technologies. These needs span a large range in scale, operating conditions, chemical environments, and lifetime requirements.

Key issues including the increased need for drinking water as well as recycling and reuse will be critically important in the future. Energy needs, in terms of both conventional sources such as oil, natural gas, and coal and the focus on the use of hydrogen and renewables, have economic and security issues for the foreseeable future. Advances in biotechnology will have a large impact on the life sciences where the separations needs will increase. Progress in nanotechnology and other materials-related research can translate into uses in a wide variety of separations processes. Underlying all industrial processing is the need to ensure that environmental concerns are addressed. There will also be general advances that can be implemented in several sectors of industrial usage.

A unique and critical aspect of separations technology is the fact that it is pervasive in U.S. industry. Separations are a key component in the production cycle of many important industries including those listed above. As such, there are two overriding issues that must be considered in any overall plan in this technology area. The first relates to the overall cost of the separations technology. The capital cost of installation as well as the operating cost, which includes energy utilization, must be considered. For commodity chemicals, the separations component is often the major factor in the final product cost. The efficiency of this step is therefore critical to maintaining a competitive position for a given product. For high-value-added products, the need for high yield and purities cannot often be met by conventional separations processes. “Brute force” methods, such as scale-up of an analytical-scale apparatus, are often used.

10.1021/ie0501475 CCC: $30.25
Published on Web 03/16/2005

Cost cannot be a primary issue when evaluating basic research but will become more relevant as applied research is moved toward commercial development.

The development of economical and reliable technologies requires a strategy that encompasses the entire spectrum from basic research to industrial implementation. The need for basic and applied research with industrial relevance is the second issue to be considered. Separations technology is truly an interdisciplinary topic. Researches in chemistry, materials science, chemical and mechanical engineering, as well as others can all contribute to advances in this area in academic, national laboratory, and industrial settings. Generic research frontiers that provide advancements in basic knowledge can find a path to industrial usage if the proper linkages and communication mechanisms can be put in place.

The National Research Council published a report in 1987 entitled "Separation & Purification: Critical Needs and Opportunities". This report stated six high-priority research needs and opportunities. They are (i) generating improved selectivity among solutes in separations, (ii) concentrating solutes from dilute solutions, (iii) understanding and controlling interfacial phenomena, (iv) increasing the rate and capacity of separations, (v) developing improved process configurations for separations equipment, (vi) improving energy efficiency in separations systems. The Workshop participants clearly recognized that these opportunities are still valid. Improvements in any of these areas will continue to be beneficial. These items are included in the recommendations below in a slightly different form.

Recommendations

I. Critical Research Needs and Opportunities. There are several topics that were identified as critical research needs and opportunities:

I.1. Process Intensification (PI). PI can have several facets. The overriding consideration is to provide an additional benefit that is not currently attainable. While improved processing would be one obvious facet, there are several others that come under this classification. A Topical Conference on Process Intensification was held at the AIChE meeting in New Orleans, LA, Apr 1–3, 2003. The conference report identified the advantages of PI, and some are listed as follows.

1. Novel or enhanced products: The strongest driver for PI may well be the possibility of producing novel products that cannot safely or successfully be produced by any other means because the reaction rates are too high, the reactions are too exothermic, or the reactants are too hazardous.

2. Improved chemistry: Some novel PI reactors offer control of the reaction environment in a precise way, leading to improvements in chemical yields and conversions and product purity. Such improvements in chemistry may offer some or all of the following advantages: reduced raw materials losses, reduced energy consumption, and reduced purification and waste disposal costs.

3. Enhanced safety: PI may improve safety both by reducing the total volume of potentially hazardous materials and by possibly improving control of a very fast and/or dangerous reaction. Safety can be a strong driver for PI in cases where there is a strong desire to reduce the in-process inventory of dangerous materials, particularly for plants that are close to residential areas.

4. Improved processing: It has been suggested that industries based on batch processing, such as pharmaceuticals and fine chemicals, should be a major opportunity for the use of PI. The reaction time in batch processes is much shorter than the overall cycle time, making them a good candidate for PI if the process innovation results in lower in-process inventories and more readily cleanable equipment.

5. Energy and environmental benefits: Some applications of PI may offer opportunities for energy savings and environmental benefits. Energy savings by process modification must pass the high return on investment (ROI) hurdle rate for new technologies; there is little incentive to invest in energy savings that do not meet ROI criteria. A similar argument may be made for process modifications for environmental benefits.

6. Capital cost reduction: While it is true that PI can offer capital cost reduction if it replaces conventional process steps in a new plant, the savings must be balanced against the risks involved in being the first to use novel technology. Unless the potential capital cost reduction is very substantial and/or unless there are other desirable benefits that come from the use of PI, it is unlikely that capital savings alone can be a strong driver for PI.

7. Low inventory advantage: Some applications of PI may offer lower inventory, which is important particularly for hazardous materials. The thrust for "inherently safe" process plants will encourage new applications for PI.

Clearly, all six specific research needs and opportunities referred to in the 1987 NRC report can be included in this one topic.

I.2. Process Synthesis. Process synthesis is a technique for synthesizing a chemical process from concept to flowsheet. It encompasses the experimental program, the modeling of the experimental results, the choice of processing units, how they are interconnected, and the optimization of the proposed plant.

Traditionally, new processes have been developed in a sequential way. First an opportunity is identified, the process chemistry is investigated, and finally the information is handed over to the engineers in order to design a process flowsheet. This approach has intrinsic shortcomings.

To overcome the shortcomings of sequential process design, the process synthesis approach requires interaction between the various aspects of process development and design and is therefore iterative in nature rather than sequential. Process synthesis is thus a process design technique that also incorporates the experimental aspects of process development and design.

The advantages of this approach are as follows:

(i) Separation processes can be developed more rapidly, with less time and money spent on irrelevant experiments or ones with inappropriate accuracy.

(ii) The resultant process flowsheet is more optimal especially in separations tasks because process conditions are not arbitrarily set early on in the development of the process, before the necessary information is available. The iterative nature provides early process feedback in the experimental data collection/development.

I.3. Enabling Technologies. Enabling technology can be defined as a fundamental or basic capability in one area that allows significant progress to be made in another area (and sometimes many other areas). Two specific technologies that were identified are nanotechnology and biotechnology. There can be others, as shown in the following examples. It may be a very specific need (like a new chemistry or a catalyst tolerant of some specific feed contaminant), or it may be very broad (like

Feed	Solid	Liquid	Gas
Solid		Leaching	Steam Stripping
Liquid	Ion Exchange	Solvent Extraction	Stripping
Gas	Adsorption	Absorption	

Figure 2. Examples of separations processes using mass separating agents.

amino acid sequencing, high throughput experimentation, atomic force microscopy, computer-assisted tomography, etc.). For example, in process synthesis, probably the most significant recent enabling technology is the ability to formulate and solve large-scale mixed-integer nonlinear optimization problems. Such a capability has enabled advances in obvious applications such as model predictive control, the improved operation of existing plants, and the synthesis and development of superior new designs. However, it has also enabled solution of phase equilibria, quantum mechanical calculations, prediction of the shape of proteins, design of superior compositions of matter, location of production and distributing centers, data reconciliation, location of distillation feed, reflux, and side streams, and on and on. In many instances, this technology has been even more important than the ability to formulate mathematical descriptions of physical phenomena in the first place.

I.4. Ultrapurification. This topic was specifically addressed in the 1987 NRC report. Many evolving industries such as electronics, fiber optics, and other materials-related thrusts such as nanotechnology as well as pharmaceuticals and food processing have increasing requirements for extremely high purity. Parts per million levels in impurities are now common, and the need for parts per billion or less concentrations is becoming more frequent.

The need for analytical tools that can provide measurements at these low concentration ranges is critical to any implementation in this area. Quality control, increased testing reliability, and process monitoring are areas where improvements will be beneficial.

I.5. New Materials. A mass separating agent is key to many separations processes, as shown in Figure 1. Figure 2 illustrates the fact that solid-, liquid-, and gas-phase separating agents can be used. Thus, advances in new materials have the potential to be translated into mass separating agents with properties superior to those presently used. These properties can include higher loading capacities, better selectivity, improved temperature and pressure ranges of operation, and the ability to tolerate a wide range of chemical environments. In addition, improvements in mechanical properties and chemical resistance can be extremely useful in the construction and operation of separations devices.

I.6. Materials Processing/Devices/Rapid Prototypes. As stated earlier, the total cost of a separations process is critical to its implementation. The use of new materials in separations devices, while dependent on the material properties for implementation, is also dependent on the ability to process the material in a timely and cost-effective manner to produce rapid prototypes for testing and, eventually, the separations device itself.

I.7. Composite Separation Systems. The idea of a composite separations system is to combine two or more separating agents into one process. One such approach is to use the properties of two mass separating agents in a synergistic fashion to obtain separations capabilities that are not available through the use of a single separating agent. As an example, zeolites or other molecular sieves can be incorporated into a polymer membrane to form a new class of membranes called “mixed matrix membranes”. The solid phase enhances or alters the polymer membrane selectivity. This concept of composite separation can be applied to other separations systems such as distillation; one can use a mass separating agent or active material (instead of inert silica or metal) to fabricate the packing. The added mass separating agent may potentially enhance the separation of the conventional packing column.

Specific research items that encompass these topics in areas of importance for present and future separations needs were then discussed and prioritized. These areas are water, energy, hazardous materials/operating conditions, life sciences, food, environmental, and general (generic issues).

Some key recommendations are listed below. The first set of recommendations below is related to specific applications.

(i) There is a clear need for water purification methods and processing and delivery systems for drinking water as well as reuse. While there are current methods available, methods that can provide attributes such as portability, low-cost, less byproduct waste, and economies of scale for various production rates are important targets.

(ii) Hydrogen purification processes have been and will continue to be critical for the drive toward a hydrogen-based economy.

(iii) Separation and purification of high-value-added pharmaceutical products from complex feed mixtures, including very similar (i.e., chiral) compounds, are necessary. Sensing applications are also needed.

(iv) Separations associated with carbon dioxide emission in air continue to be a critical environmental- and energy-related issue.

The next set of key recommendations below is related to various technologies.

(i) Terrorism concerns remain an important topic, where the ability to provide sensing capability and separations methods to clean large areas contaminated by chemical, biological, or radiological materials is a key issue.

(ii) The implementation of nanotechnology to prepare very thin and uniform layers on robust layers for membrane applications is a key general need that can be used in a multitude of applications.

(iii) Sorbents that use improved materials can have a wide application in various segments of the chemical processing industry.

(iv) Hybrid processes that provide synergistic improvements for reaction/separations processes are an important example of PI.

(v) Also, the development of devices that can perform multiple separations and reduce the processing time and energy will be attractive.

The complete listing is provided in the Appendix.

Acknowledgment

The authors acknowledge the support of the National Science Foundation Grant CTS 0434437. The following individuals participated in the Workshop and provided valuable input: Kumar Abhinava, Ron Chance, Ned Corcoran, Saied Delagad, Gordon Jarvinen, Bill Koros, Santi Kulprathipanja, Mike Ladisch, Frank Leitz, Mike Lockett, John Pellegrino, James Ritter, Thatcher Root, Paul Scovazzo, David Sholl, Jeff Siirola, Kamelesh Sirkar, Doug Way, and Ralph Yang. The authors also acknowledge the contributions of the following individuals that provided additional input: Ed Cussler, Liese Dallbaumann, Babak Fayyaz, Mahnaz Firousi, Karl Gerdes, Jimmy Humphrey, John Kunesh, Zarko Olyjic, Sharon Robinson, Costas Tsouris, Francis Via, Vince VanBrunt, and Andrew Zydney.

Appendix

See Table 1.

Table 1

problem to be addressed	importance	separations issue
	Water	
increased need for drinking water	increases in population, including areas with few natural resources, generating increased demand	treatment technology inprovements including reverse osmosis, nanofiltration, flash evaporation, and solar stills
arsenic, selenium, manganese, antimony, and other heavy-metal removal	water purity	
drinking water for small communities that are off the grid		lower cost and fewer maintenance issues
total organics/pathogen separation from water	low concentrations (5 ppb to 50 ppm) of organics becoming an increasing problem; also, many alcohol/ water streams	method to remove or destroy the organics at low cost needed; need high selectivity for water or organic, e.g., oestrogen removal
sensing in mixtures	implementing nanotechnology advances	removing interferences
soluble ions	large quantities of water are now treated to neutralize and then discharged with large amounts of soluble ions	need alternative to neutralization and discharge; electrochemical membrane, adjust pH without adding salts, acids, or bases
production of ultrapure water	semiconductor applications, life sciences	reduce 15−20 steps to 2−3 steps
removal of divalent ions that cause precipitation on membrane surfaces	need to address this problem for high recovery in reverse osmosis processing	treatment methods for high ionic strength solutions needed to allow reverse osmosis to operate at high efficiency
recovery of clean/potable/usable water in military and/or space applications	portable units	
water cycle management	treatment and recycling from all phases for advanced life support applications	reduce sensible heat cost of dehumidification; reduce energy and space demands on purifiers
trace methyl *tert*-butyl ether/water separation		
	Energy	
adsorption chemistry: gas and liquid phases	large-scale usage in the chemical process industry with large energy usage; extension to the liquid phase	can nanostructured materials developed for other purposes have value here? molecular tailoring of separating agents; bulk liquid separation with adsorption difficult
generation of power without CO_2 emissions	water gas shift reaction; increase alternative fuel production; CO_2 capture and conversion	
hydrogen production/purification	need to process large and small volumes at a range of pressures	separation from streams containing a multitude of impurities, including H_2S, H_2O, and NH_3; keep H_2 at feed pressure
desulfurization of fuels (sulfur removal)	worldwide environmental mandates requiring drastic reductions of sulfur in transportation fuels	new purification methods needed for both liquid and gaseous fuels
CO_2/CH_4 separation; treatment of substandard natural gas including N_2/CH_4 separation	natural gas production in high CO_2 content gas fields; natural gas recovery and enhanced oil recovery	need high-pressure operation; membrane or sorption systems that are robust to foulants and are economical, have a good "footprint", and avoid recompression; difficulty in finding suitable sorbent or membrane
energy efficiency in refineries and chemical plants; system performance and availibility of low-cost techologies are key impediments	increased throughput at low investment, improved purities, and more efficient operation	selective, low-energy processes that can replace or augment high-energy, capital-intensive units
separations of close boiling compounds such as olefin/paraffin mixtures	present separations are most energy-intensive distillations in the chemical and petrochemical industries	less energy-intensive separation techniques needed, particularly for small-scale applications
separations of large-scale commodity chemicals and water	associated energy needs; security and environmental aspects also	improved efficiencies because separations cost can approach the product value

Table 1 (Continued)

problem to be addressed	importance	separations issue
	Energy	
separations involved in portable power applications		fuel cell related separations
improved efficiency for distillation, cleaner distillation systems, distillation foaming, batch distillation, and distillation with some nonvolatile species	huge consumer of energy, limited to certain separations; competetive advantage, present offshore loss of industry, and destroys efficiency; use for specialties; concentrating bioproducts	methods to improve the efficiency: structured packings, active packing (active material), and high capital cost; reduce emissions, integrate processes, and increase efficiency; rapid change of operating conditions
azeotropic mixture separations	large volume separation such as ethanol/water	need to break the azeotrope with low-energy usage
	Food	
sensing in complex mixtures	bring nanotechnology advances to application	cleaning up complex food, soil, etc., sample for sensing desired analytical properties
dewatering high-viscosity fluids and high solids processing	energy efficiency	avoid evaporation
continuous chromatography		new process improvement
barrier packaging and materials	needed for light-emitting-diode displays and medical implantation, as well as food applications	rigorous material (and optical properties) with barrier objectives toward O_2 and H_2O
nanofiltration (beverages)	alternative to pasteurization	
flavor and aroma capture		
cheaper production of high-fructose corn syrup		low selectivity; better adsorbents and better process concepts beyond simulated moving beds required
	Life Sciences	
understanding chemistry and nanostructure of sorbents, chromatography phases, and membranes	purification of proteins, peptides, and extracellular fermentation products	basic component for understanding interactions between solutes and the surfaces of separations materials
separation of chiral compounds	many pharmaceutical compounds are chiral in nature, where one is active and one is potentially hazardous	adaptable technologies
separate protein glycoforms, variants, and monomers from dimers and other aggregates	development of more reliable, effective, and economical biopharmaceuticals	jigh resolution and efficient separation
separation of biosynthesized pharmaceuticals; effective and reliable cell and cell debris removal; virus removal	process simplification	minimize opportunities for proteolysis, oxidation, deamidation, and other degradation pathways; effective and demonstratable technology needed; solvent-stable nanofiltration membranes needed
alternatives to protein A affinity systems used for antibody purification	present systems have a major bottleneck that limits availibility	new technologies and/or approaches needed (adsorbent materials)
separation of organic chemistry synthesized pharmaceuticals; concentration of active pharmaceutical intermediates containing waste streams; separation of a wide variety of solvent/solvent and solvent/water mixtures; calrification, impurity removal, and virus reduction in the clarification step	process simplification	solvent-stable nanofiltration or reverse osmosis membranes needed; pervaporation membranes needed; nontoxic flocculating agent needed
dramatic increases in the scale of antibody bioprocessing	present systems have a major bottleneck that limits availibility	"scalable" unit operations (adsorbent materials)
transport mechanisms between flowing fluids and surfaces	purification of proteins, peptides, and extracellular fermentation products	fundamental understanding of mass-transfer phenomena over many length scales
plasmid DNA separation for gene therapy applications	development of more reliable, effective, and economical biopharmaceuticals	new technologies needed
more efficient multidimensional separations for proteomics applications	impact on fundamental understanding and significant potential diagnostic and therapeutic applications	address the significant dynamic concentration ranges under a wide variety of conditions
high-resolution chromatography without flammable solvents	process simplification	high-performance liquid chromatography with nonflammable solvents

Table 1 (Continued)

problem to be addressed	importance	separations issue
	Hazardous Materials/Operating Conditions	
deliberate contamination of urban areas with chemical, biological, or radiological materials	response to terrorist attacks	need sensors and separation methods for removal of hazardous materials from surfaces and water
processing of spent nuclear fuel	needed for advanced nuclear power cycle systems	radioactive environment and need to operate and maintain equipment remotely
CO_2 separation from air oxygen/air separation revitalization (production)	advanced life support including space exploration	high selectivity, low energy, and weight requirements
	Environment	
CO_2 capture, improve existing CO_2 recovery technologies	large volume production and discharge to the environment; high CO_2 concentrations needed for all CO_2 storage and reuse options, e.g., supercritical processing; CO_2 dry cleaning; many submarginal applications	need new adsorbent materials and separation strategies for CO_2 capture and sequestration in power generation; need cost-effective technologies for CO_2 capture and concentration; ability to regenerate and reuse; improve affinity; upgrade capabilities; expand operating ranges; high temperature and O_2 stability
NOx	combustion processes	cyclic adsorber operation
toxic metals and radioactive contaminants	nuclear wastes	reaction or separation, reactive barriers, concentration
SOx	power plants and mobil sources	remove from fuel or emissions, sorbent regeneration, and lower temperature adsorbents
Hg	coal plant emissions in lakes rivers	remove from fuel or emissions, other companion species
nanoparticle release	consequence of nano uses, water, solvents, or air	study mobility, migration, and control of new emissions
polychlorinated biphenyls and other refractory organics	waterway accumulation	sludge processing, adsorbents
sensing/sampling technology	air pathogens	sample concentrations to detect low level virus and chemical species
leaching	environmental remediation	separating contamination from the soil matrix
VOC removal		
oil/water separations		
	General	
combine reaction and separation	achieve high throughput product, improve catalyst life, lower energy comsumption, and enhance selectivity	develop viable technologies such as hybrid processes
preparation of very uniform and thin porous layers on robust supports for either organic or inorganic membranes	wide range of applications for high selectivity materials	use of advances in nanofabrication methods
active transport membranes	fuel cells, hydrogen transport, CO_2 recovery	greater stability, selectivity, and flux
alternatives for distillation	replace robust, widespread default technique	identify new technologies for technology jumps
fractionation of nanosized particles	electronically active emitter could be used like ink jet dyes; very large market	separation of quantum dots and semiconductor spheres into fixed size distributions
sorption technique selection	competing technologies	develop systematic method for comparison
multicomponent distillation in packed columns	most separations use mixtures	need for simple models (alternative to rate-based model)

Richard D. Noble*

Chemical & Biological Engineering Department
University of Colorado
Boulder, Colorado 80309-0424

Rakesh Agrawal

School of Chemical Engineering
Purdue University
West Lafayette, Indiana 47907

IE0501475