

Bioprocessing of Commodity Chemicals

Research Directions for Government, Industry, and Academia

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ABSTRACT

The US chemical industry is facing maturing markets, variability in raw materials supply, and stiff competition from emerging chemical industries in other countries with abundant feedstock supplies. Bioprocessing could play a major role in the domestic industry's attempt to rejuvenate many of its mature segments. Potential advantages of bioprocessing include new products, improved process economics, reduced environmental hazard, and feedstock flexibility. However, socio-institutional factors and technical constraints must be resolved before routine commercial production of bulk chemicals by bioprocessing is possible. Important research directions include improvements in biocatalysts, design of innovative bioreactors, and developments in new separations technology. Both government and academic resources are available to assist the commodity chemicals industry in solving these research challenges.

Index Entries: Bioprocessing; research; ECUT; commodity chemicals.

INTRODUCTION

Bioprocessing of bulk chemical commodities may help the US chemical industry be more competitive in world trade. However, the new technology has unique and challenging problems that must be solved before it can rejuvenate at maturing industry. This paper discusses problems in

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the commodity chemicals industry; the prospects for bioprocessing of commodity chemicals; constraints on bioprocessing; and current research directions and strategies. It is the goal of this paper to promote a better understanding of the need for bioprocess research as well as the benefits of a collaborative strategy to overcome the institutional and technical difficulties that must be faced to make this technology a commercial reality.

PROBLEMS IN THE INDUSTRY: NEED FOR BIOPROCESSING

Currently, the commodity chemical business sells its products according to well defined specifications or physical properties. Examples include such basic petrochemical raw materials and intermediates as ethylene, propylene, and benzene. Success in this industry depends on the ability to manufacture and deliver a product of consistent quality at a lower price than competitors.

In the prior decade, the commodity chemicals industry was regarded as one of the strongest segments of US manufacturing in world trade. In 1985, however, US exports accounted for 12–15% of annual sales, down from 20% in 1982 (1). Several factors are contributing to the decline in the international competitiveness of this industry (1,2).

The market share for US companies in world trade has been weakened by the development of chemical industries in other countries. In oil and gas rich countries such as Saudi Arabia, Canada, Mexico, Indonesia, and Brazil, governments are subsidizing the building of facilities that manufacture commodities as well as value-added products. These facilities serve as outlets for a country's gas or oil resources, and also create a captive market for their commodities. With advantages such as government subsidies, raw materials availability, and captive markets; these countries can produce commodities and commodity-based products at a lower cost (2).

Production costs for the US chemicals industry are strongly dependent on petroleum prices, because most commodity chemicals are derived from fossil feedstocks and additional fossil resources are required to provide fuel for the process. The recent decline in the price of petroleum is allowing US companies to be competitive in world markets and still make some profit. However, past experience makes US companies reluctant to invest in an industry that is so vulnerable to fluctuations in raw materials costs. The OPEC oil price increases during the 1970s caused producer's costs for energy and petroleum feedstock to increase tenfold. The chemical industry was impacted severely by these price hikes, since it depended on OPEC for almost 80% of its raw materials (2). Should oil prices return to historic high levels, US commodity chemical plants would return to marginal operation (1).

Problems such as stiff competition and fluctuating raw materials costs are compounded by maturing markets. Annual growth rates for production of chemical products used by the agricultural sector are flat or dropping. Some new demand for commodities will result from the use of new plastics in automobiles and construction, but strong growth resulting from an emergence of new applications is unlikely in the near future. The growth phase for most commodities is expected to level out at around 2–3% per year. Most of the growth that does occur will result from increased demand from emerging third world countries (2).

As a result of these trends, the US manufacturing base for the commodity chemical industry is being eroded. US companies are not investing in building new manufacturing facilities, and aging facilities are not being refurbished. By 1995, the number of producers of each major commodity chemical is expected to decline from about 20 to 8. Many companies are shifting to specialty products where markets are growing more rapidly and feedstock advantages are less important (2).

Despite the problems facing the industry as a whole, there are many reasons for the US to promote a domestic industry. Even in a maturing marketplace, the world demand represents big tonnage with potential for significant sales revenue (2). In addition, chemicals are vital to US industry and the domestic standard of living. Excessive reliance on foreign sources of petroleum could be a threat to national security in the event of supply cutbacks or shortages.

This paper discusses the potential of bioprocessing of chemicals to rejuvenate the commodity chemical industry in the long term. Bioprocessing of chemicals includes any chemical process where at least one step makes use of complete living cells or their components to produce a desired change. The ability to develop and use bioprocesses for commodities would allow the chemical processing industry alternatives to the energy and capital intensive technologies that now exist for producing some of these chemicals.

POTENTIAL OF BIOPROCESSING OF COMMODITY CHEMICALS

Bioprocessing could be used by the commodity chemical industry in three ways. First, bioprocesses could provide an alternative to the use of petroleum feedstocks because industrially important chemicals could be produced based on biomass conversion. Biomass conversion involves changing the sugars present in biological materials such as agricultural wastes into organic chemicals. Second, bioprocessing routes could be developed to replace thermal and chemical routes to existing commodity chemicals via fossil feedstocks. Finally, biological routes (via fossil feedstocks or biomass) to chemicals with similar or improved functionality could be developed to replace existing products (3).

Using biological routes to commodity chemicals offers many potential advantages or alternatives not currently available to the industry. Some of these include new products, improved process economics, reduced environmental hazards, and feedstock flexibility. Each of these potential advantages is briefly summarized below.

New Products

Recent genetic engineering activities, particularly in the pharmaceutical and specialty chemicals areas, suggest that more function specific or completely new chemicals can be produced. Although most bioprocesses are currently unable to compete economically with conventional synthetic routes to commodity chemicals, a significant role for applied genetics may develop in the synthesizing of new chemicals where no other practical route to production is available (3).

Such an example from the food industry is the production of high fructose corn sweetener from corn starch using immobilized glucose isomerase enzyme. This sweetener has completely replaced cane sugar derived sucrose for certain applications (4).

Bioprocessing is also the route to the production of chiral (asymmetric) compounds. An important example, although not a commodity chemical, is the production of insect pheromones to be used as pesticides. For many insects, correct stereochemistry is critical. Only bioprocesses have the capability to produce the enantiomerically pure form of such chemicals (5). Although chirality is not an important feature for commodity chemicals of current interest, it is difficult to predict what properties might be desired for the products of the future.

Improved Process Economics

Biological synthesis may be less costly than chemical synthesis for several reasons. Biological systems typically require milder temperatures and pressures than most industrial chemical processes and exhibit high selectivity to the endproduct (6). Moreover, in biological systems, microorganisms often efficiently execute many sequential reactions in the same reaction vessel. As a result, bioprocessing may reduce the amount of process energy and capital equipment necessary for a conversion. An example is the possible use of the enzyme phenol hydroxylase to convert phenol to catechol. In this process, the enzyme that is secreted by bacteria causes the precise addition of an hydroxyl group to the phenol. This enzymatic sequence is potentially less expensive than the conventional production method (2).

Reduced Environmental Hazards

The use of enzymes or microorganisms as catalysts may result in improved chemical reaction selectivity. This leads to a reduction of undesirable byproducts, which may mean reduced environmental control

requirements. It should be noted, however, that bioprocesses can produce large amounts of wastes (mainly cell matter and residual nutrients) that may also have to be treated (6). Once treated, however, these wastes can be released to the environment. Many chemical wastes are sufficiently hazardous that they must be transported in drums to a disposal site.

In addition, hazardous materials used in many conventional reactions result in occupational risks. An example is the alkylation operation in petroleum refining where large quantities of acid must be utilized (7). Biological production methods offer minimal occupational risks.

Feedstock Flexibility

Bioprocessing would allow US chemical companies to use alternative resources, such as biomass, as feedstocks for the production of chemicals. Use of alternative resources would decrease US dependence on petroleum and natural gas. A scenario based on biomass is supported by the fact that many important industrial chemicals have been produced from biomass in the past through fermentation routes. These processes were displaced by what are now the conventional petrochemical processes that are a result of the emergence of cheap petroleum-based feedstocks (8).

NONTECHNICAL CONSTRAINTS TO BIOPROCESSING

Although any commodity chemical can, in principle, be produced biologically, many constraints need to be overcome in order to reap the potential advantages of bioprocessing for chemicals production. Besides technical challenges, socio-institutional factors influence the development of this technology. Some of the socio-institutional factors include government regulations and policies, as well as issues related to public perceptions, structure of the industry, and availability of trained manpower.

For example, there may be a regulatory need for liberalization of patent rights for inventions resulting from public-funded research. Modifications to patent procedures may give companies participating in government-sponsored research more incentive to commercialize new technology once it is developed (3).

Acceptance of bioprocessing by the chemical process industry (CPI) is impeded by the highly integrated nature of the industry (1). In the CPI, the byproduct of one reaction often forms the starting material for another. Manufacturers may be reluctant to displace conventional processes with new bioprocesses because of potential negative ramifications on overall process economics. These ramifications include shortages of byproducts no longer produced, oversupply of byproducts because they are no longer needed as feedstocks and idle process equipment from the resulting overcapacity, and the need to install new unit operations to accommodate feedstock supply changes.

Public perceptions of biotechnology also represent a social constraint that must be addressed. As a result of accidents such as the Bhopal tragedy, the public is increasingly calling for assurances that a technology (especially a new technology) is safe. It is highly desirable that the groups engaged in research be able to explain the benefits of a technology while simultaneously being honest about its negative attributes (9).

There is also an estimated shortage of bioprocess engineers (10), who could help solve the technical problems encountered when scaling up processes from the bench-scale to commercial reactor size. Scaleup problems are challenging, and academic scientists have had little experience with them (11). Educational institutions, government, and industry must recognize this and address remedial strategies to meet this need.

TECHNICAL CONSTRAINTS TO BIOPROCESSING

Such challenges are in addition to the technical constraints currently limiting the development of this technology. Some of the more prominent issues to be addressed in order for bioprocessing of commodity chemicals to become economically feasible include 1) reaction kinetics, 2) sterility requirements, 3) heat and mass transfer problems, and 4) high water requirements.

Reaction Kinetics

Bioprocessing for the production of commodity chemicals is plagued by low yields and low productivity. One reason for this is slow rates. Very high enzymatic reaction rates for biological reactions are often reported in the literature, and this is because of the very high specific activities exhibited by the individual biological catalysts *in vitro*. Currently, these rates are seldom encountered under large-scale conditions that would be needed for producing bulk chemicals (6).

Sterility Factors

Maintenance of sterile conditions with very large volumes of throughput will present difficulties and require substantial energy inputs. Sterile environments are usually required when whole cells are used as biocatalysts to ensure that reaction media is not consumed and undesirable by-products formed by contaminating organisms (12). Sterility becomes an even more important consideration when genetically engineered organisms are utilized, because the metabolic load from the inserted genetic coding may make them less able to compete against wild strains.

Heat and Mass Transfer Limitations

Removal of heat generated from mixing and as a result of cellular metabolism can be a problem for large-scale bioprocesses (12). Biological

reactions must usually be carried out at fairly low temperatures, because microorganisms usually exhibit optimal growth within limited temperature ranges.

Meeting the mass transfer requirements of large-scale bioreactors can also be difficult. These requirements include transfer of oxygen and nutrients to the microorganisms and transfer of the substances that would inhibit product synthesis from the microorganism to the bulk liquid (13). Meeting these problems becomes challenging when bioreactors are scaled-up from the laboratory or bench scale (liters in size) to the production levels required for industrial processes (thousands of liters in size).

High Water Requirements

A major obstacle in using microorganisms and enzymes as practical catalysts in bioprocessing is the need to carry out the catalyzed reactions in large volumes of water. Industrial-grade products are usually excreted by microorganisms and are present in the product stream in low concentrations. Energy-intensive industrial separations methods are currently required downstream of the bioreactor to recover the product (3). In addition, water is a poor medium for most industrial organic chemical processes because many substrates are insoluble in water (14).

RESEARCH NEEDS FOR OVERCOMING BIOPROCESS LIMITATIONS

A study by the National Academy of Sciences (3) identified several research directions that should allow researchers to overcome many of the technical challenges to developing large-scale bioprocesses for the production of commodity chemicals. These areas include development of improved biocatalysts, design of novel bioreactors, and development of low-energy separations technology.

Biocatalyst Development

Biocatalysts are substances produced by living cells that activate or accelerate a chemical change in a bioprocess. Biocatalysts can be employed either in the form of the producing microorganism or as the isolated enzyme. Use of isolated enzymes has at least two advantages: product concentrations in the reaction media can be higher, and there are no nutrient or oxygen requirements. If the transformation involves fairly complex reaction sequences, or if there is a requirement for cofactors, whole cells currently must be used as the biocatalyst. Whole cell biocatalysts have the advantage of lower costs to produce and the ability to provide through cellular metabolism, other substances that may be necessary for a reaction to proceed (15,16).

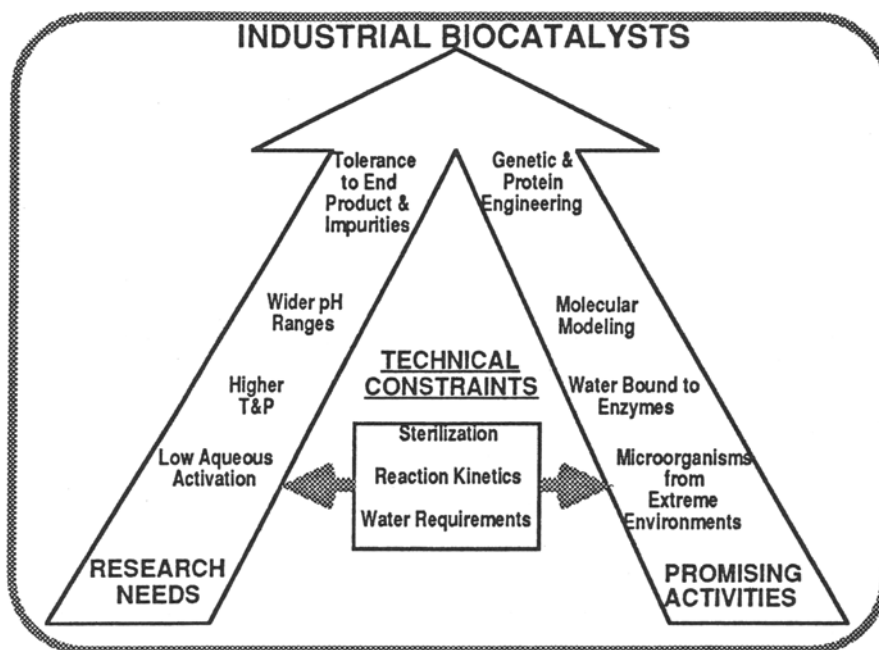


Fig. 1. Research needs and current activities for developing industrial biocatalysts.

In order to use biocatalysts in processes that produce commodity chemicals, the NAS recommends that microorganisms be developed with increased tolerance to substrates and endproducts, and microorganisms and isolated enzymes be developed capable of withstanding higher temperatures and pressures, wider pH ranges, and lower water conditions (see Fig. 1). Biocatalysts with these modifications should be more stable in the industrial environment, and, hence, demonstrate improved rates, yields, productivity, and selectivity in large-scale bioprocesses (3).

Developing microorganisms with increased stability in the industrial environment may be made possible by studying naturally-occurring microorganisms from extreme environments. There are thermophiles (reputed to be stable up to 250°C), acidophiles (to pH 1 in sulfuric acid), alkaliphiles (to pH 12 in ammonia), and barophiles (greater than 200 atm) (4). Investigating these microorganisms should allow identification of the genetic information and enzymatic features that impart this stability. Another advantage to incorporating these features into microorganisms and enzymes used as industrial biocatalysts is that there may be less requirements for sterilization (6).

Basic biological research has resulted in techniques to engineer improved biocatalysts such as recombination DNA (rDNA) technology and cell fusion. Recombinant DNA technology involves the joining of DNA

from different organisms, whereas cell fusion involves the formation of a single hybrid cell with nuclei and cytoplasm from different cells. These techniques were developed to understand the structure, organization, and function of genetic material and have been adopted by chemists, biochemists, and microbiologists to study the genetic code of microorganisms. In combination with instruments such as X-ray crystallography, they can be used to investigate and correlate structures and functions of proteins, particularly enzymes (6).

Developing improved biocatalysts may be possible by using the above techniques for genetic and protein engineering. With genetic engineering, improved microorganisms are possible by modifying their genetic information and causing their metabolism to produce new or greater quantities of desirable products. With protein engineering, it is possible to modify the nucleic acid sequence of genes to induce microorganisms to produce altered enzymes with desired properties. Development of special instruments such as DNA sequencers, protein synthesizers, and computer software systems for modelling proteins make the development of improved biocatalysts possible in the near term (6).

Developing biocatalysts with increased stability and the ability to function in low-aqueous environments might also be accomplished by binding water molecules to the enzyme (14). The rest of the water can be replaced by an organic substrate or solvent. This would allow biocatalysts to synthesize chemicals from water-insoluble organic substrates, and the product recovery problems from dilute aqueous solutions would be eliminated.

Recent developments in molecular modeling will also help researchers design improve enzymes for biocatalysts. Research at Cal Tech by Goddard and coworkers has resulted in the development of a model that calculated the structure of the native form of the enzyme, *thermolysin*, based on empirically and theoretically-derived descriptions of the atomic and molecular forces. The calculated structure of this thermophilic protease showed remarkable agreement with the crystallographically determined structure. This agreement is shown in Fig. 2 (17,18).

Innovative Bioreactor Design

Development of novel bioreactors will help overcome such problems as heat evolution and mass transfer limitations, low productivity, and high water requirements (*see* Fig. 3). It is expected that novel bioreactors for large-scale bioprocessing will possess one or more of the following characteristics.

Continuous Operation

Batch reactors are inefficient due to down time between batches, long startup time, end product inhibition, and substrate depletion (19). For



Fig. 2. Comparison of calculated (heavy line) and X-ray (light line) structures for thermolysin.

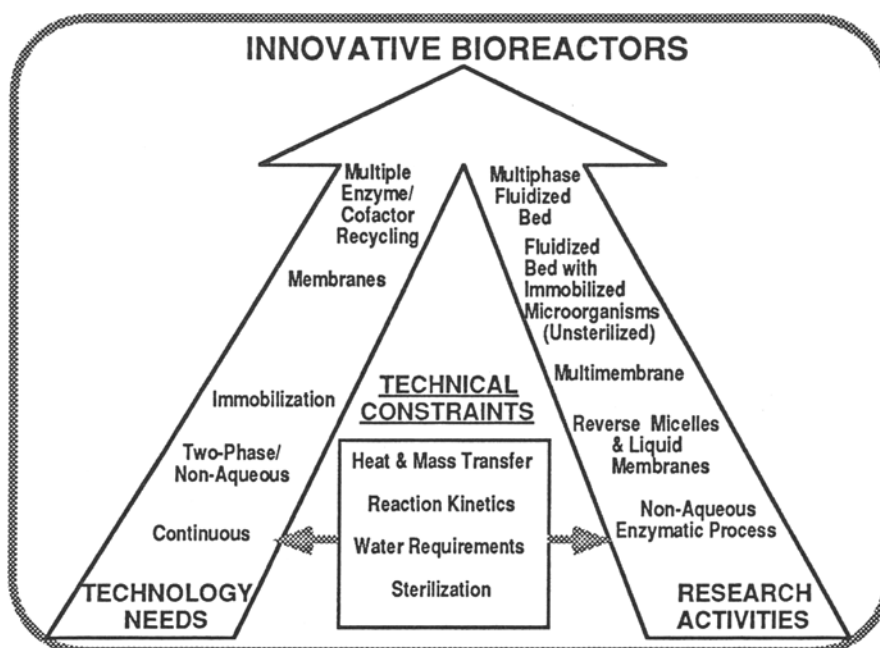


Fig. 3. Research needs and current activities for developing innovative bioreactors.

production of large quantities of material such as would be required for commodity chemicals, the focus has been on designing bioreactors that operate continuously. These high performance systems are expected to improve bioreactor productivity and yields by providing continuous removal of inhibitory end products, and eliminating downtime between batches.

Biocatalyst Immobilization

Success of a continuous process depends upon the ability to immobilize the biocatalyst without greatly decreasing its activity. An immobilized biocatalyst is one that is held in place for use by physical, chemical, or mechanical means. The primary reasons for immobilizing biocatalysts are economic ones. High cell densities are possible that result in improvements in bioreactor productivity. Biocatalysts can be expensive and if they can be reused, the cost of catalysis is reduced. In addition to this, when biocatalysts are immobilized, they can catalyze a continuous flow reaction (20).

Two Phase or Nonaqueous Systems

Recent developments in bioreactor systems includes completely organic systems or two phase enzymatic systems. These new systems allow the use of low solubility substrates, and have the potential to greatly reduce water requirements. Such systems also resolve some of the problems inherent to aqueous systems but, in particular, problems associated with product separation and recovery (14,15).

Membranes

Another new approach for large-volume operations is the use of membranes in bioreactors. Synthetic semipermeable membranes could be used to trap or confine the biological catalyst within the bioreactor, to continuously separate the biocatalyst from the reaction mixture so that it can be recycled back to the main vessel for further reaction, to allow continuous nutrient and cofactor supply, and to facilitate continuous removal of end-products. Use of membranes can also promote increased control of the reaction and the ability to regulate separations (19).

Several innovative bioreactor systems are under development that combine two or more of these features. Systems that have been studied under the auspices of the US Dept. of Energy's Energy Conversion and Utilization Technology (ECUT) division are discussed in the following paragraphs (17). Technical management for this research is provided to ECUT by staff at the Jet Propulsion Laboratory, Pasadena, CA.

A continuous biocatalytic system using immobilized whole cells is currently under development at the Oak Ridge National Laboratory. The laboratory scale fluidized bed bioreactor system involves immobilized

microorganisms. The system uses *Z. mobilis* immobilized on alginate beads to produce ethanol from a glucose feed. High ethanol productivities have been reported using unsterilized corn product (light steepwater) as a feedstock (17).

A. Klivanov and coworkers at the Massachusetts Institute of Technology have shown recently that enzymes can be both active and stable in the presence of a minimum of water by binding water to the enzyme (14). Further work is underway by Klivanov to develop a nonaqueous enzymatic process. The enzyme polyphenol oxidase is being used to catalyze hydroxylation of different substrates in organic solvents with the goal of developing new ways of using enzymes as catalysts in nonaqueous media (17).

H. Blanch of the University of California, Berkeley, is studying enzyme catalysis in two phase systems. His approach is based on the use of reverse micelles and liquid membranes. He uses a second organic liquid in which the substrate or product is much more soluble than in an aqueous system (17).

A multiphase fluidized bed bioreactor, under development at Battelle Memorial Institute, is a continuous system that combines the use of an immobilized biocatalyst with an *in situ* nonaqueous sorbant separation. The goal is to minimize end product inhibition, maximize productivity, and also increase product concentration. The biocatalyst is immobilized as dense particles (dense bed) and fluidized in a conventional manner using the fermentation media. An insoluble solvent phase is then circulated through the dense bed to entrain excreted product. The entrained phase enters a separation/desorption unit to allow product recovery and material regeneration for recycle (17).

A multimembrane bioreactor for chemical production is being developed by M. L. Schuler of Cornell University. This reactor involves the use of four layers. One layer involves cell entrapment, another substrate flow, another gas flow and the fourth, flow of an extractant that selectively removes a product (17,21).

Further research needs identified for bioreactors include the development of new reactor configurations to permit wider use of enzymes in large-scale bioprocessing. To accomplish this, development of systems for using multiple enzymes and solving the problem of using expensive cofactors are required (3). A cofactor is a substance associated with an enzyme and must be present for its activation. Cofactors currently must be regenerated and economics may prohibit carrying such reactions at an industrial level with isolated enzymes.

Low-Energy Separations Technology

In the bioproduction of relatively low-value products such as commodity chemicals, much of the product cost currently results from separations energy requirements. This is because such products have generally been produced as dilute aqueous solutions. Developments in separations technology are playing a key role in improving the economics of bioprocesses.

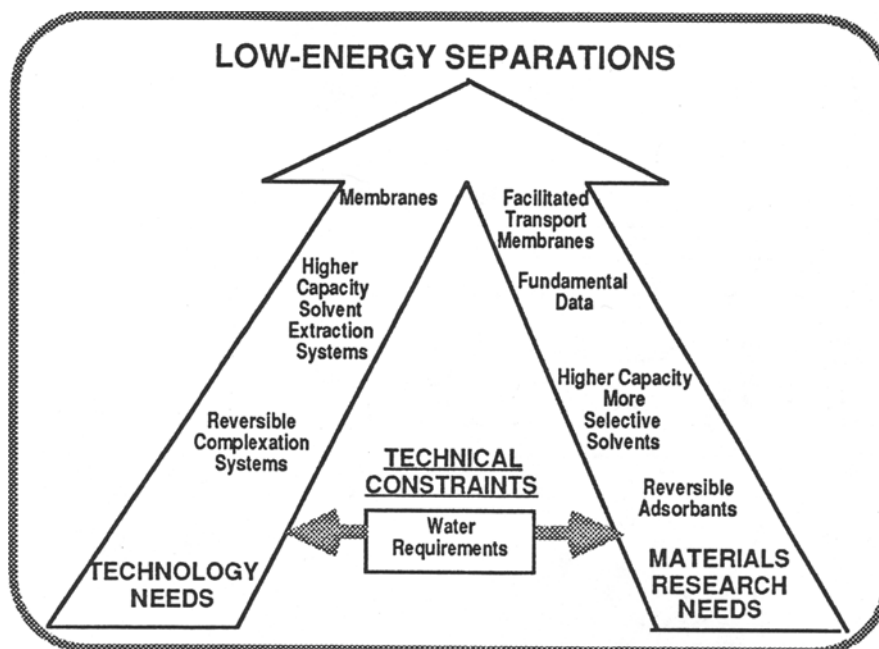


Fig. 4. Research needs for low-energy separations.

Two recent activities were conducted to identify research needs in separations. A study was conducted by the National Academy of Engineering on critical issues and needs in separations (22). In addition, the International Energy Agency (IEA) conducted a workshop hosted by the US Dept. of Energy on separation technologies (23).

Several promising research areas were identified for the recovery of products from dilute solutions (see Fig. 4). These include the development of more selective and higher capacity solvent extraction systems, and the development of reversible extraction systems that can swing with changes in pressure, temperature, and pH. Materials research needs include higher capacity and more selective reagents, and advances in affinity-based materials used to perform or promote reversible complexation reactions (21). There is also a need for fundamental data to better understand the kinetics, thermodynamics, and transport phenomena associated with these complex solvent systems (23).

Use of membranes also holds promise for low-energy separations in bioprocessing. Needs in membrane research identified in the IEA workshop (23) include development of new membrane materials, studies to understand transport phenomena especially in facilitated transport and liquid membrane systems, and better understanding of membrane degradation and fouling mechanisms. The problem of membrane sterilization was also identified.

It should be noted that many of the innovative bioreactor designs discussed earlier use complex solvent systems and membranes to increase

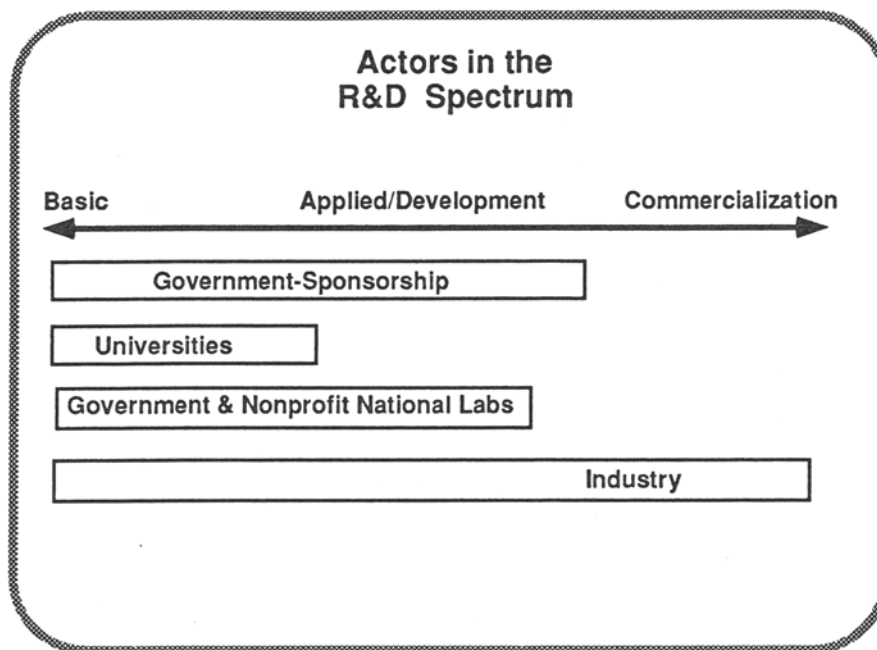


Fig. 5. Actors in the R&D spectrum.

the concentration of the product. Developments in separations technology would promote advances in innovative bioreactor technology as well.

RESEARCH STRATEGIES FOR THE FUTURE

In order to solve the problems associated with bioprocessing, a focused research approach is needed (3). Research and development (R&D) activities can be conducted in the industrial sector, in universities, and under government sponsorship (24). Where these activities can be conducted and who sponsors them is diagrammed in Fig. 5. Much of the basic, applied, and exploratory development activities related to the bioprocessing of lower-value chemicals and fuels is taking place under government sponsorship because of the long-term, high risk nature of these phases of R&D. Government relies on industry to commercialize developed technologies for the private sector.

The US Dept. of Energy (DOE) is a mission-oriented federal agency which conducts bioprocess-related research as a part of its mission to improving national energy security, and stability, and its commitment to improving the competitiveness of US industry in world trade (25). Technological accomplishments are realized from DOE-sponsored research not only in areas related to energy consumption, but "spinoffs" into other areas often result from the associated knowledge base.

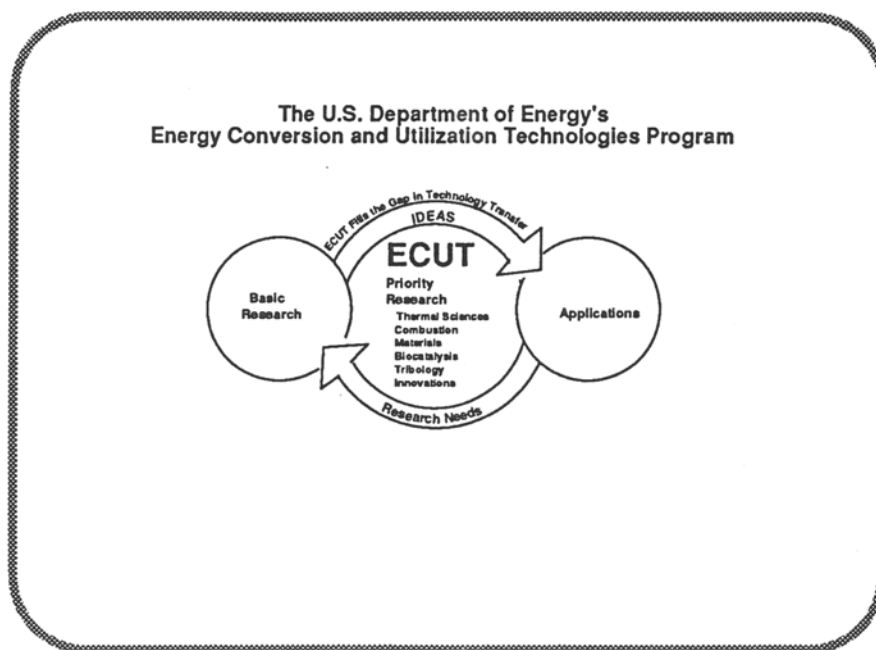


Fig. 6. The US Department of Energy's Energy Conversion and Utilization Program.

DOE through its Energy Conversion and Utilization Technologies (ECUT) Division is specifically investigating the potential of bioprocessing for the production of bulk chemicals (17). The goal of this program is to contribute to the development of the enabling technology base that will permit private industry to biologically produce large volume chemicals in an energy-efficient and economically competitive manner. ECUT seeks to span the gap between basic scientific disciplines and engineering development (*see* Fig. 6).

Industry may seek to use this knowledge or technology base developed under government sponsorship to address technical problems (e.g., waste management) or business needs. Most major chemical companies in this country have already committed significant research funds to applying biotechnology in the area of specialty products, such as, amino acids and enzymes. Chemical companies are also focusing on agricultural and health-care related biotechnological opportunities (6). The existence of overcapacity, low commodity prices, and other problems, however, have made companies reluctant to invest in bioprocess research for the purpose of producing high-volume or commodity chemicals (1,26).

David R. Clair, President of Exxon Research and Engineering Co., has indicated that a critical issue in mature industries is the need to appreciate basic research and the way that rapidly emerging tools of science are revealing much about even mature processes and products. What is re-

quired, according to Clair, is a collaboration between basic research and applied research in a company so that the prospects and limits for current technologies can be clearly understood (27). These comments, though aimed at the particular problems faced by the petroleum refining and petrochemicals companies, it also supports the need for industry to take advantage of basic and applied research conducted under government-sponsorship.

As illustrated in Fig. 5, it is the joint responsibility of government and industry to perform the development activities required to bring bioprocessing to commercialization stages. Collaborative research endeavors are strongly encouraged (3). One benefit of collaborative research endeavors is the technology transfer that will occur across organizations and disciplines. It is unrealistic to rely on the individual researcher to explore the base of scientific knowledge in all disciplines, and then familiarize himself with market-based needs. This results in duplication of efforts, lost time, and lost opportunities (24). A more productive strategy may be to encourage the formation of multi-disciplinary teams conducting research to meet cross-organizational objectives. For bioprocessing of commodity chemicals, the end result may be a more competitive domestic industry.

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REFERENCES

1. US Dept. of Commerce (1986), *A Competitive Assessment of the US Ethylene Industry* International Trade Administration, Washington, DC.
2. DeYoung, H. G. (1987), *High Technology* 7(4), 28-37.
3. National Research Council. (1986), NMAB-28, National Academy Press, Washington, DC.
4. Stiefel, E. I. (1987), *Chemical Engineering Progress* 83(10), 21-33.
5. Sonnet, P. E. (1988), *ChemTech* 18(2), 94-98.
6. Office of Technology Assessment (OTA): US Congress (1984), *Commercial Biotechnology: An International Analysis* US Government Printing Office, Washington, DC.

7. Gary, J. H. and Handwerk, G. E. *Petroleum Refining Technology and Economics*, Marcell-Dekker, New York, NY.
8. Goldstein, I. S. (1981), *Organic Chemicals from Biomass*, CRC Press, Boca Raton, FL.
9. Young, J. K. and Griffin, E. A. (1987), Ninth Symposium on Biotechnology for Fuels and Chemicals, Boulder, CO.
10. National Academy of Sciences. (1984), *Research Briefings 1984 Report of the Research Briefing Panel on Chemical and Process Engineering for Biotechnology*, National Academy Press, Washington, DC.
11. Dubinskas, F. A. (1988), *Technol. Rev.* **88**(4), 24-30.
12. Bjurstrom, E. (1985), *Chem. Eng.* **92**(2), 126-158.
13. Brown, D. E. (1983), *ChemTech* **13**(13), 164-167.
14. Klibanov, A. M. (1986), *ChemTech* **16**(6), 354-359.
15. Cooney, C. L. (1983), *Science* **219**, 728-731.
16. Klibanov, A. M. (1983), *Science* **219**, 722-727.
17. Department of Energy (1986), *ECUT Program Bulletin*. DOE/ECU-86/1, Office of Scientific and Technical Information, DOE, Oak Ridge, TN.
18. Goddard III, W. A. (1985), *Science* 917-923.
19. Cheryan, M. and Mehaia, M. (1986), *ChemTech* **16**(11), 676-681.
20. Quелlette, R. P. and Cheremisinoff, P. (1985), *Essentials of Biotechnology*, Technomic Publishing, Inc., Lancaster, PA.
21. Shuler, M. L. and Cho, T. (1986), *Biotechnol. Prog.* **2**, 53-60.
22. National Research Council. (1987), *Separation and Purification: Critical Needs and Opportunities*. National Academy Press, Washington, DC.
23. Proceedings of the IEA Workshop on Separating Technologies, Sponsored by the International Energy Agency (IEA) (1988), Coral Gables, FL. Draft available from Pacific Northwest Laboratory, Battelle Washington Office, Washington, DC, in press.
24. Mohler, B. L., Harrer, B. J., and Garret, B. A. (1988), *The Federal Laboratories: What Kind of Economic Impact Can the Region Expect?* Presented at the 22nd Annual Pacific Northwest Economic Conference, Boise, ID. Available from Pacific Northwest Laboratory, Richland, WA.
25. US Dept. of Energy. (1987), *Multi-Year Plan FY 1989-93*, Office of Conservation, Washington, DC.
26. Shamel, R. E. (1986), *Chem. Eng. Prog.* **82**(8), 8-12.
27. Caruana, C. M. (1986), *Chem. Eng. Prog.* **83**(4), 66-69.