

of the national scientific effort, or of how it might interlock with national economic planning.

A lack of decisive action in this sphere is not too surprising. British national elections since the early 1960's have been won by narrow margins that hardly provided mandates for bold initiatives. The parties themselves have been divided internally on major political and social issues. And the soundest science advice based on the most irreproachable data may be ignored for countervailing political or economic reasons. For example, a recent cogent study by CPRS on the British motor industry laid out a case which the government found it politic to ignore in providing a major subsidy for Chrysler car-building operations in

Britain. The political realities of such things as unemployment may make unpalatable decisions unavoidable.

There has been a tendency in both Britain and the United States on the part of those interested in science policy to concentrate on the science-advisory and decision-making machinery in the upper echelons of government and to ponder—rather in the abstract—such questions as that of the proper balance between basic and applied research. The lessons of the last decade teach that this approach provides a one-dimensional view, that it is futile to consider science policy in isolation from the broad political and social context in which national decisions are made.

The new reorganization of the science

advisory machinery in Britain seems to reflect a recognition of how complex and formidable the economic and social problems facing Britain really are. When Wilson led his party to victory in the 1964 elections, he pledged an economic renewal forged in the “white heat of the technological revolution.” Today's Labour government is less flamboyant with its slogans and more modest and pragmatic with its science policy. The merging of the science advisory apparatus in the Cabinet Office into the CPRS can be seen as simply another logical step in the integration of science into the governmental process. This is a sensible thing to do if the grafting of science up and down the governmental tree in the past decade has really taken.—JOHN WALSH

RESEARCH NEWS

Liquid Membranes: New Techniques for Separation, Purification

Artificial membranes have been a topic of great interest in recent years because of their potential utility in applications ranging from desalination of water to timed release of drugs. One of the most intriguing classes of artificial membranes is liquid membranes, which were first discovered 10 years ago by Norman N. Li of Exxon Research & Engineering Company, Linden, New Jersey. Some of the many possible uses of liquid membranes were the subject of a special symposium at the recent Centennial Meeting of the American Chemical Society. Those uses include several medical applications, the removal of pollutants from waste waters, and the encapsulation of enzymes.

Liquid membranes consist, in simplest terms, of an emulsion suspended in a liquid that does not destroy the emulsion. In a typical application, small droplets of aqueous solution are encapsulated in a thin film of oil; this emulsion is then suspended in another aqueous solution. Alternatively, small droplets of oil can be emulsified with water and the emulsion suspended in oil. In the first case, the oil phase is the liquid membrane; in the second case, the water is the liquid membrane. A typical droplet might be about 100 micrometers in diameter. These coalesce into aggregates averaging about 1 millimeter in diameter. The thickness of the liquid membrane itself varies from roughly 1 to 10 micrometers. The

membrane is thus thinner by at least a factor of 10 than most other types of artificial membranes, and transport across the membrane is correspondingly faster.

The emulsions can be made very stable by the addition of surfactants (detergents) and other additives to the liquid membrane (LM) phase. The LM systems can easily be prepared with a shelf life of a year or longer, Li says. They can also be prepared so that the emulsion is degraded very rapidly for applications where the contents are to be released. Additives can also be mixed into the membrane phase to vary the membrane's permeability to various substances, to control the rate of diffusion through the membrane, and to control membrane absorption and adsorption.

Most applications of LM systems depend on the membrane's selective permeability to various substances. If a substance is soluble in the membrane and in the internal and external phases, for example, it can pass readily from phase to phase. But if it is not soluble in the membrane, it is effectively trapped in either the interior or the exterior phase. Li has demonstrated this effect by encapsulating lethal doses of sodium cyanide into LM systems and feeding it to rats. The rats are not harmed by this experience because the cyanide ions will not pass through the membrane.

If one component of a mixture is soluble in the membrane and the second is

less soluble or insoluble, the two can be separated. Li has shown that many surfactants provide differential permeability for hydrocarbons that are similar in molecular weight and boiling point. If, for instance, a mixture of benzene and hexane are encapsulated in an aqueous solution of saponin, and the emulsion is suspended in a hydrocarbon solvent, the benzene will permeate into the solvent much faster than the hexane. Similar results are obtained with other mixtures.

Other additives can be used to facilitate the separation. Hexane and hexene, for example, diffuse through a surfactant membrane at about the same rate. But if cuprous ammonium sulfate is added to the membrane, it will form a weak complex with the double bond of hexene. This makes hexene more soluble in the membrane, so that it is transported faster. In a similar fashion, sulfuric acid facilitates the transport of aromatic hydrocarbons, strong bases facilitate that of mercaptans, and weak acids that of amines.

The LM systems have many potential medical applications. One use might be in the emergency treatment of drug overdoses. Poisoning by drugs and other chemicals is a major problem in the United States. There are more than 10,000 deaths and an estimated 1 million poisoning episodes in this country each year. Some 70 percent of the accidental poisonings involve children under the

age of 5. Many techniques currently used to treat poisoning are of limited effectiveness for many drugs, cannot be used at all in some cases, and often are extremely unpleasant for the patient. But many poisons can be trapped inside LM preparations for safe excretion from the body, according to John W. Frankenfeld of Exxon and Christopher T. Rhodes and George C. Fuller of the University of Rhode Island.

Aspirin is the most common drug found in child poisonings and barbiturates are the most common drugs used for suicides. Both drugs are organic acids that can be trapped, the investigators have found, by LM systems encapsulating strong bases. The bases ionize the acids so that they are no longer soluble in the membrane. Ionization also maintains the concentration gradient so that un-ionized drug continues to diffuse through the membrane. In laboratory studies, the investigators have found that such preparations can remove at least 95 percent of the two drugs within 5 minutes at a pH characteristic of the stomach. Drug absorption from the stomach and intestinal tract into the bloodstream is much slower than this.

Other agents that might be encapsulated include plasma proteins (which bind many types of drugs), specific drug antibodies that would bind certain drugs very strongly, and activated charcoal, which is an effective nonspecific adsorbant. Three or four such preparations, Frankenfeld says, might be sufficient to take care of most types of poisons, and more specific systems could be made up easily as they are required. The LM systems, furthermore, have the consistency of a milk shake and can be produced in many flavors. Administration of the preparations should thus not be a problem, even with children.

Other poisons that might be removed from the intestine are those, such as urea, that are produced when the kidney is injured or diseased. Removal of these toxins with LM systems might reduce the patient's dependence on dialysis or help him through a period of crisis. This possibility has been investigated by William J. Asher and his associates at Exxon, Kenneth C. Bovee and Phillip G. Holtzapfel of the University of Pennsylvania, and Robert W. Hamilton of the Bowman Gray School of Medicine.

Urea, which they have chosen as the first toxin to study, is not readily removed intact. The preferable method, they have found, is to degrade it first with the enzyme urease. Urease exists in the intestines, but not in high enough concentrations to remove the excess

urea associated with kidney problems. Li and Sheldon W. May of the Georgia Institute of Technology have demonstrated that urease from the jack bean retains its catalytic activity when it is encapsulated in an LM. Encapsulated urease can thus be used to supplement normal urease activity.

The primary problem, then, is the removal of carbon dioxide and ammonia, which are the products of urease activity. Carbon dioxide is readily expelled through the lungs, but the ammonia must be removed artificially. Asher and his associates accomplish this by encapsulating tartaric acid, which ionizes ammonia and traps it inside the membrane for excretion. Removal of urea in this fashion creates a concentration gradient that draws urea into the intestine from the blood.

Asher and his associates have passed LM preparations containing urease and tartaric acid through isolated dog intestines—which were, nevertheless, still attached via a bypass to the dogs' circulatory systems—and obtained results comparable to those of *in vitro* tests. But they found that the rate at which the system traps ammonia would not be adequate for humans. They are thus investigating ways to increase the trapping rate. They are also studying similar techniques to remove other, more important toxins, such as creatinine and uric acid.

Blood Oxygenation by LM Systems

A somewhat different type of LM system might be useful for oxygenating blood, according to Asher and Herbert W. Wallace and his associates at the University of Pennsylvania School of Medicine. In this case, the membrane is composed of liquid fluorochemicals and it encapsulates gaseous oxygen. An emulsion of oxygen in fluorochemicals is pumped through a specially constructed chamber where it comes in contact with blood that is pumped through at the same rate and in the same direction.

Fluorochemicals are very inert, but they can dissolve high concentrations of gases. Oxygen can thus easily be transferred from the emulsion to the blood, and waste carbon dioxide can be transferred in the opposite direction. Use of the LM system, Asher says, prevents the formation of blood-gas interfaces, which are known to cause damaging cellular and protein alterations. Asher and Wallace, in fact, observed no degradation of human blood that was pumped through the system for 24 hours.

Several dogs have been connected to an LM oxygenation apparatus for as long as 4 hours with no ill effects. Blood

samples from these dogs showed no significant increase in the concentration of fluorine compounds. Asher and Wallace observed that LM oxygenation could supply the complete oxygen needs of large dogs, suggesting that the process might be useful in humans. Perhaps most important, they found that their technique does not produce the potentially dangerous blood-fluorochemical emulsions observed by other investigators studying artificial oxygenation. Further work with this technique, however, will require a better understanding of the long-term effects of exposure of humans to fluorochemicals.

Just as LM systems can remove substances from the body, so too can they add them. Sylvan G. Frank and his associates at Ohio State University are investigating their application for administration of naltrexone, a narcotic antagonist. The effects of this agent last only for a short time; hence it must be given either frequently or in some kind of timed-release form. Frank speculates that an LM system of the oil, water, oil type, which he prefers to call a multiple emulsion, will provide this timed release. He has found in test-tube studies that a multiple emulsion stabilized by liquid crystals and other additives will release naltrexone in effective amounts for at least 2 weeks and possibly for as long as a month. He plans to inject the preparations into animals this summer to try to confirm this result.

The most immediate application of LM systems might be in resource recovery and water purification. The membranes provide a unique, potentially low cost way to concentrate many materials that are difficult or much more expensive to concentrate by other techniques. One of the most thoroughly explored and simplest LM systems for water purification involves removal of phenols, aromatic alcohols that are generally found in waste waters from such operations as the production of metallurgical coke, the refining of petroleum, and the production of synthetic resins.

Dilute solutions of phenol—less than 200 parts per million (ppm)—can be cleaned up by biological oxidation at a cost of about \$1.60 to \$2.60 per 10,000 liters. These systems, however, are subject to expensive upsets if the concentration of phenol increases suddenly. Greater concentrations of phenol are frequently removed by solvent extraction at a cost of about \$5.20 per 10,000 liters.

Li and Robert P. Cahn of Exxon have shown that phenols in both concentration ranges can be removed by LM systems containing concentrated sodium hy-

dioxide. The base ionizes the phenol, just as in the trapping of aspirin, and prevents it from diffusing back into the water. Li and Cahn have demonstrated that such systems can reduce the phenol concentration in actual refinery waste

waters to well below 10 ppm at a projected cost of about \$1.60 per 10,000 liters. This cost includes the expense of incinerating the spent emulsion.

Similar techniques can be used for the removal of other pollutants. Toshio Kita-

gawa and Yuji Nishikawa of the Takuma Company in Osaka, Japan, have been experimenting with the removal of heavy metals. They have found that chromium(VI) ions can be almost completely removed by LM systems containing so-

Speaking of Science

Science and the Press: Communicating with the Public

Learning how to deal with the press is not a standard part of a scientific education. In fact, it is not an exaggeration to say that many scientists view science reporters with suspicion and a few with outright hostility. But faced with the reality that research funds will probably never again flow as freely as they did in the 1960's, a number of scientists are coming to grips with the fact that the press is a useful tool for educating the public about what is going on in scientific research and, they hope, for generating support for that research.

In the words of Neal Miller of the Rockefeller University, "To put it very bluntly, the public pays for our research; how intelligently they support it depends on how they are educated. The science writers are the chief source of education of the public, so we have a stake in trying to help them with their work." Miller made the comments while introducing a session on communicating the neurosciences to the general public at the first seminar for science writers sponsored by the Society for Neuroscience, held at Airlie House, Virginia, on 3 to 6 May. (The proliferation of this kind of seminar, in which scientists are more or less isolated with reporters in a setting that fosters both formal and informal discussions, is another indication of the seriousness with which the press is being courted these days.)

During the session, four journalists* who specialize in science reporting described the problems they face and the kind of help they need from scientists in order to do a good job, and the scientists in turn responded with some of the reservations they had about talking with the press. The ideas were exchanged in an atmosphere of amiability, if not of total agreement. And the participants generally thought that the session was worthwhile. At least one scientist (who will be unnamed for fear of causing him to revert to his former policy) said that in the past he had refused to talk with reporters but that in the future he would at least answer queries from those present at the seminar.

Getting enough space—or time, in the case of radio or television—is usually the biggest problem faced by reporters, according to the panel members. Thus, they want stories based on solid facts or conclusions, or on new concepts. Nevertheless, space limitations frequently mean that a story must be condensed and simplified while, at the same time, it is being translated from scientific jargon into English that the audience can understand. There is little room for ambiguity, which is hard to write about, or for historical perspective, although reporters for scientific audiences may have more leeway to include these.

The reporters conceded that all this increases the risk of introducing inaccuracy into a news account of a scientific development, despite the care taken by a good reporter. And it may mean that what the scientist perceives as "a little blip on a very long and slowly rising curve," in the words of Floyd Bloom of the Salk Institute, will appear as a major "breakthrough" to the nonscientist.

Since reporters have to cover a wide range of subjects—from space shots to quarks to flu vaccinations—they cannot be experts about all of them. Thus, the panel members emphasized, the reporters need to know scientists whose opinions they can trust and who are willing to advise them, off the record if necessary, as to whether or not a particular item is worth writing about. Moreover, reporters who have to meet deadlines tend to be in a hurry to get that guidance. In order to meet these needs, the Society for Neuroscience now plans to publish a directory of members who are willing to serve as such sources for the press.

The discussion following the panel's presentation made it clear that what one person considers information, another, in this case Edward Perl of the University of North Carolina School of Medicine, may consider "publicity." The problem is particularly acute for the clinician since a news story about a clinical advance can result in an influx of patients who will pay for his services.

Just about everyone at the seminar agreed that facts must be attributed to particular scientists if they are to have credibility; quoting a "source close to Mother Nature" would be preposterous, despite the example of political reporters. The scientists thought that reporters could avoid suggesting that a scientist had sought publicity by indicating that the reporter had gone to the scientist, and not the other way around. They thought that including the information that a particular treatment was available at more than one place would also help. The reporters replied that these were, or should be, standard journalistic practices.

Finally, several scientists expressed reservations about the mechanisms for correcting distortions or errors in news stories. They were concerned that letters to the editor or errata rarely had the prominence of the original report.

The discussions did not answer everyone's reservations about news coverage of research developments. But David Leff made a point that all scientists might ponder. He said that bad communication will drive out good communication just as bad money drives out good money. In other words, if reliable scientists do not communicate with competent journalists, then charlatans and more sensational media would fill the vacuum. The choice then is not whether to communicate, but what to communicate and to whom.—J.L.M.

*Harold Schmeck, Jr., *New York Times* (chairman of the session); Ira Flatow, National Public Radio; David N. Leff, *Medical World News*; and Patrick Young, *National Observer*.

dium hydroxide. Mercury(II) and copper(II) ions can be removed by systems containing sulfuric acid, and cadmium(II) ions by systems containing ethylenediaminetetraacetic acid.

Kitagawa and Nishikawa built a countercurrent, continuous-flow pilot plant in which waste waters from Takuma's factory are exposed to two LM treatment steps. The pilot plant, which has a maximum capacity of 20 liters per hour, has now been operated for 2 years. They find that most of the heavy metal ions are removed in the first step. Exposure of the waste water to a fresh LM emulsion in the second step then produces a final concentration of heavy metals well below 1 ppm.

On the basis of this work, Kitagawa estimates that treatment of the factory's waste water would cost about 15 cents per cubic meter in a facility with a capacity of 100 cubic meters per hour with an emulsion recycling system. This cost is higher than that of existing treatment facilities, but the LM system may provide the only way to meet stringent new Japanese pollution control laws for heavy metals. Before such a system can be installed, he adds, techniques for handling the emulsion must be refined and the company must find appropriate ways to recover or dispose of the acidic and basic reagents used in the purification.

Graham A. Davis and his associates at the University of Manchester in England have found that LM systems can be used to concentrate copper(II) ions in mine water and in waste water from large copper solvent extraction processes. The LM systems containing acids were shown to reduce copper concentrations to about 1.5 ppm. The trapped copper can then be recovered, so that the system not only prevents pollution but also reduces waste of a valuable resource.

Similarly, Edward L. Cussler and his colleagues at Carnegie-Mellon University have shown that nickel(II), copper(II), and chromium(VI) ions can be removed from waste water by LM systems containing ion-exchange resins in the membrane phase and acids or bases in the interior phase. Cussler, however, is somewhat pessimistic about applications of LM systems. He, and some other scientists, argue that incorporation of the ion-exchange components in a porous polymeric membrane might produce a more reliable system, even though the cost would be higher.

These examples represent what might be termed a passive approach to pollution control, since the pollutants are merely collected in the system. The LM systems can also be adapted actively so

that the pollutants are chemically converted into less harmful species. Li and Raam R. Mohan of Exxon have used this approach to reduce nitrate (NO_3^-) and nitrite (NO_2^-) ions to elemental nitrogen.

They use enzymes from the bacterium *Micrococcus denitrificans*, which performs that reduction in vivo. They found that they could isolate from the bacteria a complex of enzymes and cofactors that perform the reduction in a test tube. This complex can be encapsulated in LM's with only a slight loss of activity, and has been shown to reduce nitrate and nitrite ions in waste water effectively. The particular advantage of encapsulation by LM's, Li says, is that all the necessary enzymes and cofactors remain in close proximity—a feat that is difficult to accomplish with other forms of enzyme immobilization.

Encapsulation of Bacterial Cells

Mohan and Li carried this idea one step further and encapsulated whole cells of the same bacterium. They found that the encapsulated cells reduce nitrate and nitrite ions almost as effectively as free cells—if a secondary amine of high molecular weight is incorporated into the liquid membrane to facilitate transport of the ions. They also observed little deterioration of reductase capacity or cell viability, even after the LM system had been functioning for a week in a constantly stirred reactor. Free cells under the same conditions die within about 16 hours.

The encapsulated cells exhibit two further major advantages compared to free cells. The encapsulated cells can function in waste waters over a broad range of pH's, whereas the free cells can function only in a very narrow pH range. And the membranes protect the cells from toxic substances in the waste water. The encapsulated cells show no deterioration, for example, in the presence of concentrations of mercuric chloride that are lethal to free cells. Li suggests that if appropriate nutrients were encapsulated with the cells, the bacteria might have a very long lifetime in a water treatment facility.

The LM-encapsulated enzymes have many potential uses beyond water purification. They can, in fact, be adapted for virtually any use requiring immobilized enzymes. But encapsulation offers several advantages over other methods of immobilization. One of the most important is the incorporation of cofactors into the system without resort to techniques, such as attachment to macromolecular carriers, that always lower the activity of the cofactor. One example of such a

system is the nitrate reductase complex of Li and Mohan. Another is offered by May and Laura M. Landgraff of Georgia Institute of Technology.

May and Landgraff studied yeast alcohol dehydrogenase, the enzyme which, in the presence of the cofactor nicotinamide adenine dinucleotide (NAD^+), converts ethanol to acetaldehyde. In the process, NAD^+ is converted to its reduced form, NADH, and the reaction can continue only if the NAD^+ is replenished. Spent NADH can be reoxidized to NAD^+ by another enzyme, diaphorase, in the presence of the electron acceptor potassium ferricyanide. The two investigators combined both enzymes, potassium ferricyanide, and a small amount of NAD^+ in an LM system and observed that it could convert large quantities of ethanol to acetaldehyde.

This finding indicates not only that all the components are being retained within the LM capsule, but also that the cofactor is, indeed, being recycled. In a sense, the LM creates a kind of artificial cell that provides a framework for all the components of the system without interfering with their activity. May speculates that a similar efficiency could not be achieved with any other immobilization system.

The LM systems have the additional advantage, May says, that the emulsion can be broken and the enzymes recovered at the end of the process. His experiments with another enzyme, trypsin, indicate that less than 10 percent of the enzyme is denatured during the recovery process. Another benefit, he adds, is that the enzyme can be put into the membrane itself to simulate the hydrophobic environment characteristic of some enzymes in the cell. Such enzymes might thus exhibit enhanced physical stability or radically altered reactivity in LM systems. May is currently looking at other enzymes to see if this is the case.

Liquid membranes may not be the best solution for all systems. Some investigators, such as Cussler, report that they have had problems finding reliable recipes for preparing membranes for certain applications. Li argues, however, that some of the most reliable recipes are trade secrets of Exxon or are the subjects of patent applications. Maintenance of the emulsions in a commercial application might also require the attention of a skilled engineer, Cussler argues, whereas polymeric membranes could probably be maintained by semiskilled laborers. But the LM systems do provide some unique capabilities that will undoubtedly be the subject of a great deal more research.—THOMAS H. MAUGH II