

Action in Chemistry

There's a lot going on in chemistry these days — and much of it is likely to have an impact on the world's long-term needs in energy, food, and materials

by HARRY GRAY

I BELIEVE THAT in the last quarter of this century chemists are going to occupy center stage in fundamental science because of one central problem—the need to learn how to take very small, very abundant molecules and make them into larger ones, which will be used for fuel, for the production of food, and for materials. Much of the fundamental work in this area is already in progress — some of it at Caltech — and if it is successful, it could have a major impact in slowing or even reversing the deterioration of the quality of life on this planet.

The battle has been joined in laboratories around the world in work on two molecules that are extremely recalcitrant and sluggish in their chemical reactions — nitrogen (N_2) and carbon monoxide (CO). These two molecules are, in fact, among the most inert chemical substances known to man. In most cases you have to

heat them to very high temperatures before they will react with other small molecules.

A particularly important chemical reaction is the reduction of atmospheric nitrogen by hydrogen (H_2) to give ammonia (NH_3). Ammonia production is of great interest, because this chemical substance is a key component in fertilizer. Not only must we improve the methods for ammonia synthesis from nitrogen (often called nitrogen fixation), we must also find ways to convert nitrogen directly to an energy-rich molecule called hydrazine, as well as to many organic nitrogen-containing compounds.

At present nitrogen is fixed industrially by the Haber-Bosch process, in which the sluggishness of the nitrogen-hydrogen reaction is partially overcome by utilizing an iron-containing catalyst and very high temperatures and pressures. But nature has found a better way, in which an enzyme called nitrogenase effects nitrogen reduction under extremely mild conditions — room temperature and atmospheric pressure. We chemists need to learn how to catalyze the reduction of nitrogen to ammonia for fertilizer as beautifully as nitrogenase does it biologically.

The reduction of carbon monoxide is of equal importance. In the famous Fischer-Tropsch process, again involving high temperatures and pressures, carbon monoxide is reduced by hydrogen to energy-rich hydrocarbons and alcohols. But we can no longer afford the extreme conditions and the lack of specificity of the Fischer-Tropsch process. We must learn to reduce carbon monoxide with the ease that biological systems convert nitrogen to ammonia.

Currently, chemists are attacking these problems both theoretically and experimentally. Bill Goddard of Caltech is a theoretician who has chosen to look carefully at one of the key steps in the reduction of carbon monoxide by hydrogen directly to the simplest of the

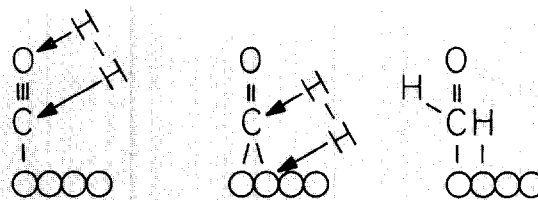


William A. Goddard, professor of theoretical chemistry: His studies are giving us some insight into the catalytic process.

energy-rich hydrocarbons, methane (CH_4). This reaction is known to be catalyzed very effectively by metallic nickel; or, to put it another way, the catalysis occurs at a surface comprised of nickel atoms. Goddard is calculating the energies of all the molecular species that could be involved as carbon monoxide and hydrogen come together on a nickel atom surface. He is using sophisticated chemical theory — and a large computer — to see which molecular species are reasonable and which are unreasonable, thereby giving us some insight into the catalytic process. As a result, eventually we may be able to design much better catalysts for the conversion.

Goddard has already shown quite convincingly that one of the old thoughts in this field — that carbon monoxide sits on the metallic nickel surface while one atom of hydrogen adds to the oxygen and one to the carbon — is a terribly unfavorable way to get to methane. It is so unfavorable energetically that there is no chance of it being the pathway that this system chooses in proceeding from reactants to products. Goddard's calculations show equally convincingly that what probably happens is that one atom of hydrogen adds to the carbon of the carbon monoxide and one to the nickel surface, giving both a CHO group and a hydrogen bound to nickel atoms (above right). From this point it is quite favorable for the system to continue on to methane.

On the experimental side there has been considerable progress, particularly in nitrogen fixation. Some of the



unfavorable

probable pathway

Bill Goddard's predicted pathway for the first step in the catalytic reduction of carbon monoxide ($\text{C}\equiv\text{O}$) on a nickel atom surface (0000) by hydrogen ($\text{H}-\text{H}$) involves the addition of one H atom to the carbon, and the second one to the nickel.

most exciting recent work has been done here at Caltech, as well as in England and in the Soviet Union. I've picked two examples to illustrate the progress that has been made. First, there's the work in Sussex, England, by Joseph Chatt's group. Chatt and his co-workers have been able to synthesize ammonia — under quite mild conditions — by simply adding acid to a compound in which atmospheric nitrogen is bound to atomic tungsten. Unfortunately, the reaction is not catalytic (that is, the atomic tungsten reagent is "used up" when one molecule of ammonia is made). But the fact that this reaction takes place at all under very mild conditions suggests strongly that we chemists should be able to design a catalytic nitrogen-reduction system that is just as good or better than the biological process.

Here at Caltech, John Bercaw and Juan Manriquez have prepared a zirconium compound that contains



Juan Manriquez, graduate student, and John Bercaw, assistant professor of chemistry: Their nitrogen-reduction system is a fundamental breakthrough in this field.

Fred Anson, professor of chemistry, and Robert Gagné, assistant professor: They are trying to reduce oxygen to water — directly.



three nitrogen molecules. This compound, when treated with acid under mild conditions, yields one molecule of hydrazine. Hydrazine is a very important substance. It has many chemical uses, and it is a good fuel. Again, the Bercaw-Manriquez nitrogen-reduction system is not catalytic; but the very demonstration that the reaction can be carried out under mild conditions is a terrific fundamental breakthrough in this field.

Devising better ways to make energy-rich molecules to be used as fuels is just part of the story. We still have much to learn about burning fuel. Strange as it may seem, reducing oxygen (from the air) to water is a major problem. Why do grown men worry about reducing oxygen to water when practically anybody and anything can do it? Why have such prominent men as Michel Boudart, James Collman, and Henry Taube at Stanford; Robert Gagné and Fred Anson at Caltech; and Howard Tennent of Hercules, Inc., banded together to try to figure out how to reduce oxygen to water? Well, nobody can reduce it directly — that is, reduce it without forming intermediates such as hydrogen peroxide, in an extremely rapid reaction. It's not enough to finally get to water; if you want to burn fuel really efficiently, you need to find out how to deliver four electrons to oxygen to form water in one burst, without being hung up in the usual way with all kinds of intermediates.

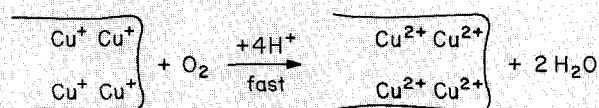
Although no chemist in the world has found a way to do a rapid-fire, four-electron reduction of oxygen to water, a few biological systems have, by using en-

zymes. One of the enzymes my group and I have been working with does the job. It is laccase, a beautiful blue copper-containing enzyme that can be extracted and purified from the Japanese lacquer tree. Each enzyme molecule contains four doubly positively charged copper ions, Cu^{2+} . When the four Cu^{2+} ions are reduced to Cu^+ , the enzyme rapidly reacts with oxygen, giving two water molecules and four Cu^{2+} ions again (as shown by the formula below).

Not surprisingly, we (and other people) have been trying to figure out exactly how laccase manages to do this amazing trick. Some questions of importance are: How are the four copper ions structured? And which of the four copper ions interacts with the oxygen initially?

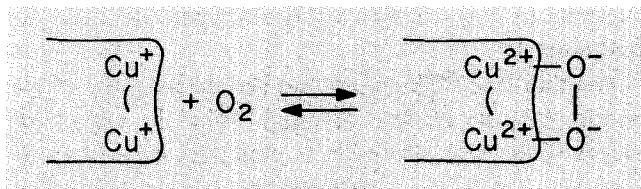
If we could answer those questions, we could provide some real help to Fred Anson and his co-workers, who are now struggling to design a catalytic oxygen electrode, which in turn could be used to fabricate an efficient fuel cell. One of the answers may come from study of another copper-containing protein,

laccase, a blue enzyme



Laccase is an enzyme containing four coppers, whose function is to reduce oxygen to water.

hemocyanin, a blue blood protein



Hemocyanin is a copper-containing protein that picks up and releases atmospheric oxygen (O_2).

hemocyanin (above). This is a blue blood protein that is found in octopi, squid, lobsters, and snails, not to mention Caltech trustees! All these creatures have blue copper-protein blood.

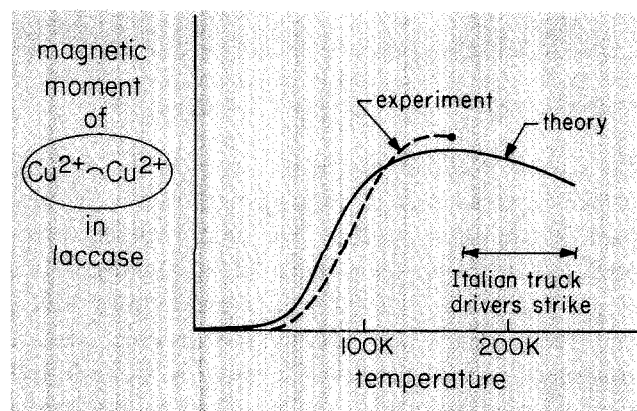
What my group and several other groups around the world have found is that in blue blood two Cu^+ ions are needed to hold each oxygen molecule from the air. These two Cu^+ ions interact with the oxygen to give some type of complex species involving Cu^{2+} ions and peroxide (O_2^{2-}); this species is believed to be responsible for the blue color of the copper blood protein. We suspect from the results of these blue blood experiments that two of the four Cu^+ ions in a reduced sample of laccase are responsible for attaching oxygen in the first quick step. The other two coppers must be close by to shoot additional electrons into the oxygen once it is attached. The key to obtaining more information relating to this hypothesis is an experiment in magnetism.

If two of the Cu^+ ions in reduced laccase must be near neighbors, it is likely that they are in the normal (Cu^{2+}) form of the enzyme also. Now in molecules in which Cu^{2+} ions are neighbors, the magnetism has a very peculiar, distinctive temperature dependence. If we could measure the magnetism of the laccase enzyme, we could tell you whether or not it possesses two Cu^{2+} ions that are neighbors. Since this is such a key problem in the overall area of oxygen reduction, we've devoted a good bit of time to its solution. It is by no means an easy problem, unfortunately, owing to the fact that the magnetic effects we are looking for are so tiny in relationship to the enormous size of the laccase enzyme itself.

We thought we had the problem knocked several years ago, when two physicists at Caltech, Jim Mercereau and Han Wang, built a marvelous magnetometer in the low-temperature laboratory in Sloan. The magnetometer was so sensitive that we believed we could use it to find the peculiar and distinctive temperature dependence of the magnetism that was predicted for the laccase enzyme. Two of my co-workers, Bob Holwerda and Barry Dohner, carefully purified 10 milligrams of laccase, took the sample over to Han, and

he inserted it into the magnetometer. Unfortunately, the magnetometer operated in too low a temperature range to see the effect that we were looking for, and, to make matters worse, our sample was too small.

One of the fellows who was working with Jim and Han at the time was an Italian by the name of Massimo Cerdonio. Massimo went back to Rome and built a second magnetometer, one that would operate in the temperature region that was so critical for our experiment. By the time the second magnetometer had been completed, I had attracted to my group two bright young men — Ed Solomon and Dave Dooley. Dave prepared a nice sample of laccase, which he gave to Ed to take to Rome. Ed arrived in Rome, after some delays, and put the sample into the magnetometer. Up to a point, the experiment gave results that were predicted for the model in which two Cu^{2+} ions were near

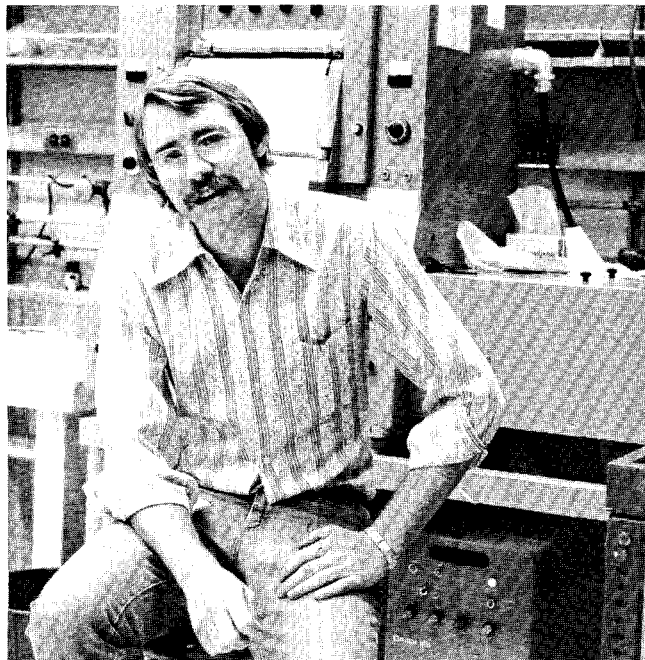


Results of the Gray-Solomon-Dooley-Cerdonio experiment on the magnetism of laccase. The experiment demonstrated for the first time that two of the four Cu^{2+} ions in the enzyme are close to each other. These two coppers are believed to be the site of oxygen attachment.

neighbors; but, before he could collect the final few data points he needed to settle the matter, Ed ran out of liquid helium, which is required for the operation of the damned machine. He and Massimo frantically called all over Rome for more liquid helium, but — you guessed it — the Italian truck drivers had just gone on strike and wouldn't deliver any. Dave Dooley is now preparing (in the sixth year of this experiment) still another sample of laccase, which he will soon take to Rome. If all goes well,* we should be able to finish this experiment before I start collecting my TIAA-CREF.

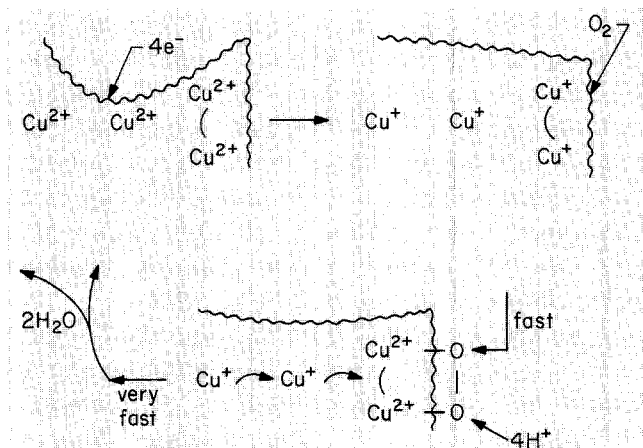
Although we need a few more data points, we're pretty sure that two of the Cu^{2+} ions in laccase are very close to one another. We believe the environment of these Cu^{2+} ions is very similar to that of the two coppers in blue blood protein, and further that in the reduced

*It didn't! This time someone soaked the magnetometer in pump oil. It now looks as if we're out of business for at least six more months.



David Dooley, graduate student: He is now preparing still another sample of laccase — in the sixth year of this experiment.

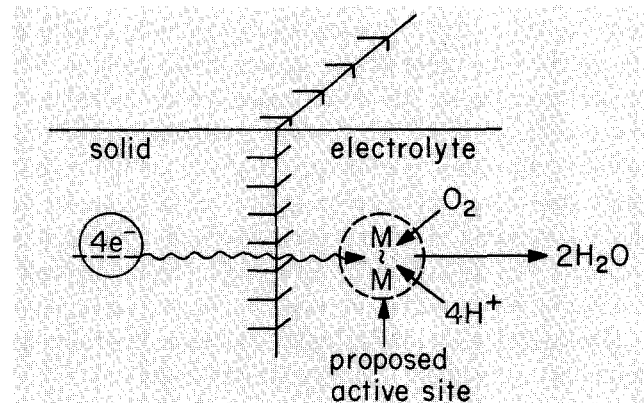
(Cu^+) form, the pair provides a site on the enzyme surface for attachment of an oxygen molecule. We also know that the other two Cu^{2+} ions are differently structured, and are biding their time until they are needed for oxygen reduction. In a few words (and below), here's how the enzyme works: Four electrons enter laccase and reduce each of the four Cu^{2+} ions to Cu^+ . At this point oxygen becomes attached to the two near-neighbor Cu^+ ions, just as it does in blue blood protein. But the oxygen in laccase is not allowed to escape as it does in blue blood. As soon as it attaches, the two other Cu^+ ions fire two extra electrons (one each) into the oxygen, thereby reducing it to water. (This mechanism



The proposed pathway of the reduction of oxygen by laccase. After initial attachment of O_2 at the near-neighbor Cu^+ ions, electrons are delivered to the site rapidly from the other two Cu^+ 's, which produces two molecules of water ($2\text{H}_2\text{O}$).

— below — has influenced Gagné and Anson in their attempts to construct a catalytic oxygen electrode for fuel cells.)

Another line of research that should have an impact on the general problem of small-molecule conversion involves the use of light to generate new types of catalysts. This is a research area that George Hammond (former chairman of Caltech's division of chemistry and chemical engineering and currently at UC, Santa Cruz) and I have been exploring in collaboration with a number of scientists at JPL — Alan Rembaum, Ami Gupta, Willie Volksen, and others. Here's our idea. You make a new kind of catalyst by taking a rather inactive cluster of metal atoms and irradiating it with ultraviolet or, in some cases, visible light. You have to do a lot of fundamental work to find out what wavelength to use to split the metal-atom cluster into fragments — if possible, all the way to fragments

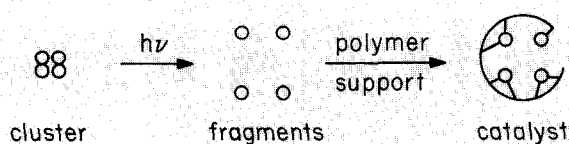


The Gagné-Anson-Taube-Tennet (or GATT) design of an electrode for the catalytic reduction of oxygen to water. One key component is the proposed active site, which features two near-neighbor metal (M) ions (as in the enzyme laccase). If such an electrode can be made to work as well as the enzyme, it could be used to fabricate an efficient fuel cell.

containing individual metal atoms. These single-atom fragments are terrific catalysts; they're fantastically active for the conversion of small molecules to bigger and better ones. But if we left the fragments alone, they would be so active the single atoms would recombine to give back the old inactive cluster of atoms. And so we not only have to generate the active fragments, but we have to trap them and keep them apart. We do this by attaching them to a polymer through chemical bonds. We call these new materials "photocatalysts," because they are generated using light, and we hope ultimately to make them as active as nature's enzyme catalysts are.

We've been successful in this work thus far. Alan, Ami, and Claude Frazier, a former Gray-Hammond student, showed a year ago that you could irradiate a "dicobalt" system (two cobalt atoms bound to eight

"Photocatalyst" Preparation



A new type of catalyst can be made by shining light ($h\nu$) on a cluster of metal atoms in the presence of a polymer. The light splits the cluster into atomic fragments, which are trapped by the polymer. The trapped fragments are the active sites of the "photocatalyst."

carbon monoxide molecules) with ultraviolet light, in the presence of a large polymer called polyvinylpyridine, and trap individual cobalt-atom fragments.

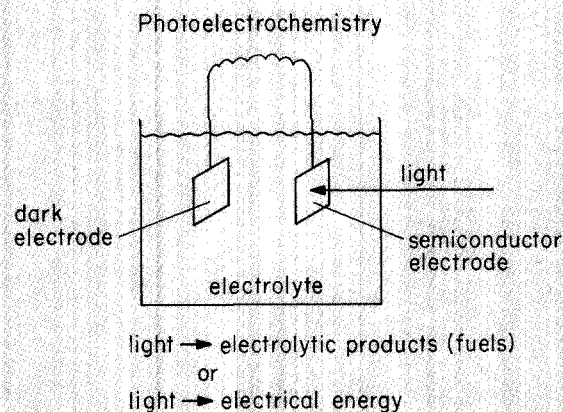
This cobalt-polyvinylpyridine system does some very interesting catalytic feats. One is the catalysis of the addition of carbon monoxide and hydrogen to organic olefins, giving organic aldehydes. This process, which is called "hydroformylation," is of great importance industrially — in fact, several billion dollars worth of chemicals per year are made by reactions of this type. At present hydroformylation and many other industrial chemical processes are operating under conditions that consume enormous amounts of energy. It is critically important to develop better ways to run these reactions, such as may be possible with the new photocatalysts, in order to cut down the energy-consumption requirements.

I've mentioned hydrogen a number of times. It is used to reduce nitrogen to ammonia, to reduce carbon monoxide to methane, and it's also a good fuel by itself. Clearly, we need to make more and more hydrogen at less and less cost. One way to do this is to combine photochemistry and electrochemistry. There are a lot of screwball schemes for doing this, but here is one that will work; it doesn't violate any of the laws of thermodynamics. You take semiconductor electrodes, immerse them in water solution, and allow one of them to be irradiated with light, preferably with sunlight. Upon irradiation, electrons in this semiconductor electrode system are stimulated to travel to the so-called dark electrode. Along the way these electrons can either be pulled off directly as electricity, or they can be used at the dark electrode to reduce the water in the system to hydrogen. If all goes well, other water molecules around the irradiated electrode are oxidized to oxygen. Thus, in this experiment, light is used to produce both hydrogen and oxygen from water, which is a very abundant starting material.

There are a large number of fundamental problems that must be solved before "water splitting" by sunlight will be a common means of storing energy. One of

the biggest problems in the field has to do with the fact that semiconductor electrodes that are sensitive to sunlight fall apart rather quickly when they are irradiated. Neither water splitting nor direct electrical energy production from sunlight can ever be efficient as long as this problem remains unsolved. Recent progress in this area has been made at MIT, where Mark Wrighton, who was a joint Gray-Hammond student at Caltech a few years ago, directs a group of very active inorganic photochemists. Mark and his co-workers have immersed cadmium sulfide and cadmium selenide electrodes in polysulfide solutions, and in such media sustained conversion of visible light to electricity has been achieved. This experiment, which demonstrates that the "electrode instability problem" can be overcome, represents a major breakthrough in the field. The experiment also gives us real hope that similarly stable, sunlight-sensitive semiconductor electrodes can be fabricated for water splitting.

I hope that by now I have convinced you that there's a lot going on in chemistry these days. And an increasingly large fraction of what's going on is likely to have an important positive impact on the world's long-term needs in energy, food, and materials. I'd like to leave you with a few predictions: I am confident that within 30 years we will make hydrogen from water using solar energy. We will produce synthetic fuels by reduction of carbon monoxide and carbon dioxide. And we will catalytically convert nitrogen under mild conditions to ammonia, hydrazine, and new materials. For these reasons, and many others, it's a fantastically exciting time to be working in chemistry. □



A promising scheme for the conversion of light to energy-rich molecules or directly to electricity involves irradiation of a semiconductor electrode immersed in solution. It is possible that research now in progress will lead to the development of a photoelectrochemical cell in which sunlight can be used to split water to hydrogen (at the dark electrode) and oxygen with reasonable efficiency.