

The molecules leave in two steps, the Illinois chemists and biochemist Quentin H. Gibson of Cornell University reported this week at an American Chemical Society meeting in Washington, D.C. First a carbon monoxide must push aside and move around a six-atom ring belonging to one of the protein's amino acids, a phenylalanine. That ring traps the carbon monoxide in an iron-rich cavity, called the heme pocket.

Then the carbon monoxide waits until the protein's ever-shifting backbone untwists. "[The protein] needs to change its shape very drastically," Elber told *SCIENCE NEWS*. "Hundreds of atoms move to the side." When the backbone's two helices nearest the heme pocket split apart, the small molecule can drift out.

Elber thinks molecules move into the protein along this same path.

"[The new work] is helping to clarify the mechanism of operation of this class of proteins," comments J. Andrew McCammon of the University of Houston.

In the past, scientists tended to simulate small molecules or much-simplified replicas of larger ones because computers lacked the computational power to keep track of all the atoms in a larger molecule. To complicate matters more, realistic simulations should deal with many molecules, each oriented differently in relation to the molecules with which they interact, Elber says.

"But with the steady increase in computing power and the development of more theoretical methods, people are beginning to look at very realistic biological molecules," says McCammon. "People are beginning to learn how these molecules actually work."

While at Harvard, Elber developed one method for avoiding the computational nightmare created by large molecules. Because the leghemoglobin dwarfs carbon monoxide, Elber's new program models just one leghemoglobin as hundreds of carbon monoxide molecules try to move around and through it.

These molecular pinballs then must maneuver through the protein pinball-machine. "The protein can move in so many different ways that there are going to be many ways that a [molecule] could go in," notes Elber. But only a few low-energy pathways exist, and his technique represents a promising way to determine those routes for carbon monoxide and other molecules, he adds.

"The molecular dynamics simulations offer a way of relating what is seen [in experiments] to the actual structure of the protein," says Gibson. "You can explain what is happening in terms of atoms." He and the Illinois duo have recently sought to harness simulations for designing new proteins.

As part of his research developing blood substitutes and understanding

oxygen transport by heme proteins, biochemist John S. Olson at Rice University in Houston uses genetic engineering to make mutant forms of myoglobin. When Gibson used the Illinois model to study the dynamics of one mutant, the simulation indicated that the change would slow the movement of small molecules, which it did. This effort has prompted Elber to refine the model to make it more useful for biochemists seeking to redesign proteins, Olson says.

Another research group has already demonstrated the potential of this synergy between computational chemistry and molecular biology by making an enzyme that scavenges oxygen free radicals better than the natural version of that enzyme.

These enzymes work by attracting the negatively charged free radicals with a positively charged region.

To design the enzymes, researchers led by Elizabeth D. Getzoff, a structural biologist at the Scripps Research Institute in La Jolla, Calif., used computer modeling to examine how slight changes in the natural enzyme's amino acid sequence might alter the rate at which the free radicals enter the enzyme. The simulations suggested a change that focused the positive force field and guided free radicals more directly to binding sites in the enzyme, the group reports in the July 23 *NATURE*.  
— E. Pennisi

## Old idea may solve climate conundrum

If the past is truly the key to the future, then researchers interested in forecasting the expected greenhouse warming must understand how carbon dioxide gas participated in the geologically recent ice ages.

Climate experts have known for more than a decade that atmospheric concentrations of this heat-trapping gas fluctuated wildly from warm periods to cold ones. But scientists still lack a satisfactory theory to explain how levels of carbon dioxide could vary so drastically as the ice sheets waxed and waned. Two researchers are now dusting off a previously discarded idea that they say may solve this problem.

In 1980, bubbles of ancient air recovered from glacial ice taught scientists that the atmospheric concentration of carbon dioxide sank to 200 parts per million during the last ice age and then rose to roughly 280 parts per million after the ice age. The swings in the greenhouse gas are important because they help keep Earth in a deep freeze during glacial periods and help warm the climate between ice ages.

Bradley N. Opdyke and James C. G. Walker of the University of Michigan in Ann Arbor are now reviving a 10-year-old theory to explain the variations in

carbon dioxide concentrations. This scenario focuses on the interplay between changing sea levels and the growth of calcium carbonate coral reefs on the continental shelves.

During glacial periods, the expansion of massive ice sheets on the continents pulled water from the ocean, lowering the global sea level. This process exposed carbonate reefs, causing them to erode through a chemical process that pulls carbon dioxide from the atmosphere and deposits it in the deep sea, according to the theory.

When the ice sheets melted at the end of the glacial period, sea levels rose and coral reefs regrew on the continental shelves. The growth of reefs released carbon dioxide into the sea water. From there, the gas escaped into the air.

Wolfgang H. Berger of the Scripps Institution of Oceanography in La Jolla, Calif., originally proposed the reef hypothesis in 1982. Yet he and other scientists thought this process could account for only a small fraction of the carbon dioxide changes between glacial and interglacial times.

In the August *GEOLOGY*, Opdyke and Walker suggest that reefs may play a much greater role than anyone realized. "What we're arguing is that this may be

the dominant, first-order effect in terms of the historic carbon dioxide changes that we see over the last 100,000 years," says Opdyke.

Previous analyses missed the importance of the reef hypothesis because they underestimated the amount of carbonate currently being deposited on the continental shelves by coral, says Opdyke. He and Walker present evidence that reef growth is depositing double what others had assumed.

Plugging the new numbers into a simple model of the global carbon cycle, they found that reefs could raise and lower atmospheric concentrations of carbon dioxide by almost 80 parts per million — roughly the same spread as that seen in the air bubble record.

Berger says the reef hypothesis will probably not explain the full carbon dioxide changes. "There is a tendency to look for a silver bullet," he says. "We would all like to find one factor that does more than two-thirds of the job so that we don't have to worry about five factors. . . . My feeling is that it's not going to turn out to be one mechanism that explains it."

Other factors proposed to explain the carbon dioxide swings are increased growth of photosynthetic ocean plants and a reorganization of ocean currents.

— R. Monastersky