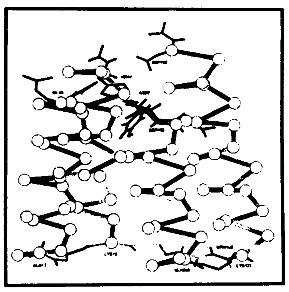
SCIENCE NEWS of the week

New Enzyme Synthesized From Scratch

Biological cells no longer hold a monopoly on enzyme design. After striving for years to break into this exclusive catalyst-creating territory, scientists seem finally to have made it. The achievement, they say, could lead to "designer enzymes" for specific medical, industrial or research uses.



Stewart et al.

Computer image of CHZ-1, a synthetic protein made of 73 amino acids. The catalytic triad appears at the top of four linked, helical columns.

In a biochemical *tour de force,* three Denver researchers designed and drew up blueprints for a hypothetical protein they predicted would act somewhat like the pancreatic digestive enzyme chymotrypsin. Then they chemically assembled their brainchild in the lab, and found that the synthetic molecule shows the predicted enzyme-like behavior.

Although others have assembled noncatalytic proteins with specific shapes (SN: 9/28/85, p.204) or commandeered biological cells to manufacture catalytic proteins, or enzymes (SN: 9/2/89, p.152), Stewart says his group is the first to both design and chemically synthesize an artificial enzyme from scratch.

"For the first time, we have shown that you can put together amino acids [the building blocks of proteins] in a designed structure and get a molecule with catalytic activity having the characteristics of an established enzyme," asserts biochemist John M. Stewart of the University of Colorado Medical School. Stewart, Karl W. Hahn and Wieslaw A. Klis detail the work in the June 23 SCIENCE.

Their synthetic enzyme, called chymohelizyme-1 (CHZ-1), began as a few lines on a computer screen. These represent the precise spatial arrangement of three pivotal amino acids in chymotrypsin's molecular structure that give the natural protein its catalytic powers.

Like archaeologists reconstructing entire skulls from a jawbone, the researchers built the entire 73-amino-acid protein around the catalytic fragment of chymotrypsin. Hahn spent two years designing CHZ-1 — amino acid by amino acid — with guidance from computer programs that use fundamental biochemical and thermodynamic theories to assess the physical viability of each new assembly proposed.

This modeling effort yielded a molecular blueprint comprising four parallel helical columns chemically tied together on one end. The other end of the columns hosts the catalytic triad of amino acids and an oily binding pocket for holding the synthetic protein's target molecules in place. It took Klis only one attempt, lasting about two months, to assemble molecules of CHZ-1 using techniques and machinery developed by Stewart and others. The team already has drawn up blueprints for other enzymes.

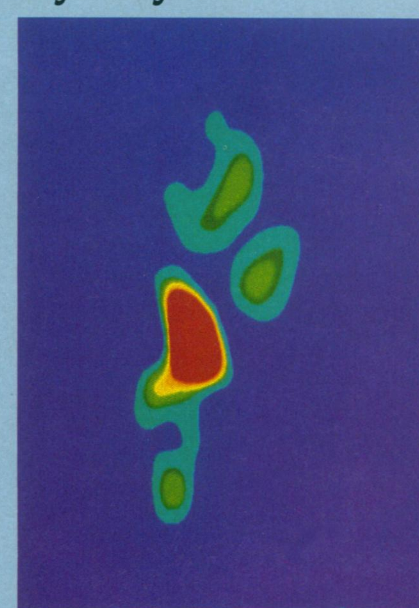
Biochemical studies indicate that CHZ-1 binds some target molecules as readily as chymotrypsin. Solutions containing CHZ-1 snip apart some targets about 100,000 times faster than catalyst-free solutions, though only about one-thousandth as fast as chymotrypsin solutions. CHZ-1 gets inhibited by the same agents that inhibit its natural counterpart, and it does not act on targets of related enzymes such as trypsin. In short, the humanly created protein behaves like a *bona fide* enzyme.

"It's the first clear-cut example of a *de novo* synthesis of a protein with catalytic activity," says protein chemist William F. DeGrado of Du Pont in Wilmington, Del.

Adds biochemist Bruce Merrifield of Rockefeller University in New York City, who won a 1984 Nobel prize for his work on protein synthesis, "If others can reproduce and expand on this work, it will be one of the most important achievements in biology or chemistry." — *I. Amato*

Radio blobs at the Milky Way's center

The most detailed portrait yet of the Milky Way's core reveals an array of huge plasma blobs just a fraction of a light-year away from an intense, compact source of radio waves. The location and orientation of these blobs of hot, ionized gas suggest they may have been expelled in opposite directions from a turbulent sea of material surrounding a massive, unseen black hole.



National Radio Astronomy Observatory

In this radio-wave map of the Milky Way's center, the red spot marks an intense radio-wave source. Surrounding blobs may represent ejected material.

The newly discovered array of plasma blobs represents just one of several previously unrecognized features now apparent in the vicinity of the Milky Way's center, says Farhad Yusef-Zadeh of Northwestern University in Evanston, Ill., who described the discoveries at last week's American Astronomical Society meeting in Albuquerque, N.M. The findings support the notion that the radio source Sgr A*, which presumably envelops a black hole, marks the position of the Milky Way's active nucleus.

The galactic center lies about 25,000 light-years away from Earth in the direction of the constellation Sagittarius. To map it, Yusef-Zadeh and his collaborators used the Very Large Array radiotelescope near Socorro, N.M., measuring the intensity of radio emissions at a wavelength of 2 centimeters.

The most detailed maps show a pattern of radio-emitting plasma blobs less than 0.2 light-year from the central radio source. Farther out, the astronomers detected more blobs and a cavity about 0.3 light-years across, perhaps swept out by strong particle and radiation "winds" emanating from the center.

They also see evidence for a trail of hot, ionized gas apparently streaming from a red, supergiant star less than 1 light-year from Sgr A*. This flow, possibly driven by a powerful wind of charged particles or by intense ultraviolet radiation from the galactic center, appears as a tail pointing directly away from the central radio source.

Whereas the Milky Way's nucleus is a relatively calm place compared with the centers of some other galaxies, the kinds of activity witnessed there may be similar to those powering even the most energetic quasars and radio galaxies, Yusef-Zadeh says. "In no other nucleus do we get such a good view of what is taking place." — *I. Peterson*