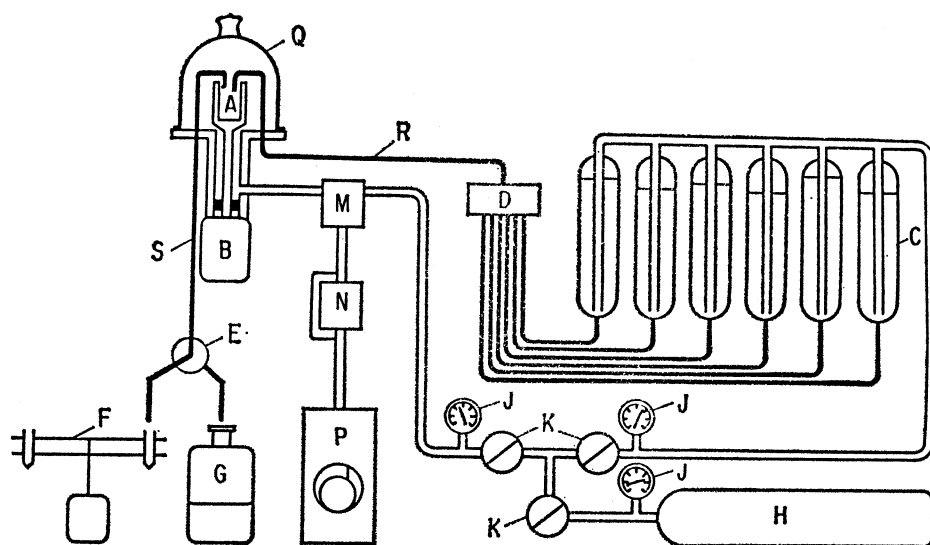


# Protein Structure in Days



Dr. Edman's sequenator: proteins go in (A); amino acids come out (F).

## A 20-year effort to automate protein analysis promises to cut decades of tedious biochemistry

In slow but persistent pursuit of the key to life, scientists in laboratories all over the world spend their days taking proteins apart piece by piece to learn how they're made, and therein, how they work.

A protein is a string of amino acid molecules—anywhere from 51 to several thousands—hooked together like a rope of colored beads; the total effect depends on the particular sequence of colors.

Scientists want to know precisely what that sequence is and, if they have patience enough—about 10 years' worth—they can find out.

The amino acid sequence of most proteins is today unknown. But the situation is going to change radically in the next three or four years because of a new machine that does automatically in a matter of days what chemists need a decade to do by hand; it splits proteins apart and pulls amino acid beads off the rope one by one, in the proper order.

Scientists call the new robot chemist "spectacular," "amazing," "fantastic," and "a very significant step forward."

"This is one of the biggest things that's happened in protein work," says Dr. Michael Naughton of Johns Hop-

kins University Medical School. "It's going to bring automation in with a vengeance."

According to Rockefeller University's Dr. Stanford Moore, who devoted 10 years to working out the sequence of the 124 amino acid molecules in ribonuclease, a protein-enzyme that deactivates RNA, automation will hasten the eventual synthesis of proteins by years.

The machine, designed by Dr. Par Edman and co-workers at St. Vincent's School of Medical Research, Melbourne, Australia, is called a protein sequenator. Dr. Edman, for political reasons, has been made to feel unwelcome in the U.S.

Essentially the sequenator is programmed to carry out a repetitive series of chemical reactions according to the hand method Edman himself refined and others have been using for years.

About five milligrams or 175 millionths of an ounce of protein are put into a continuously spinning glass cup atop the sequenator. Reagents and solvents are fed into the cup to split the intact protein and separate the amino acid molecules.

The sequenator is controlled by an electronic timer with 30 channels, each one set to time a single stage in the

breakdown. The channels, like amino acids, are arranged in sequence so that each sets the next working.

Once the cycle is complete, an isolated amino acid is deposited in one of 50 individual receptors.

One breakdown cycle takes 93.6 minutes, allowing 15.4 cycles to run every 24 hours. By contrast, scientists working by hand, adding each chemical reagent by pipette as it is needed, can work out the order of only two or three amino acids in a day.

So far, Dr. Edman's sequenator can run through 50 cycles unattended, but he expects the number to grow as some of the technical defects in the infant automaton are ironed out.

Dr. Edman conducted his initial studies on myoglobin, an oxygen-storing muscle protein that makes meat red. He used myoglobin from the humpback whale and then compared it to myoglobin from the sperm whale.

Sperm whale myoglobin was the first protein to be fully described in terms of its amino acid sequence and its three-dimensional structure. For this, Britain's Dr. John C. Kendrew won a Nobel Prize.

The protein sequenator, in four days, unraveled the sequence of myoglobin's first 60 amino acids.

Comparing the whale species, Dr. Edman found variations in the fourth, fifth, twelfth, thirteenth, thirty-fifth and forty-fifth amino acid molecules.

Dr. Par Edman is a Swede with Australian citizenship. Just after World War II he spent three years in the United States as a fellow of the Rockefeller Institute for Medical Research, then in Princeton, N.J. When his fel-

lowship was over, he moved on to Australia.

In the late 1950s he failed to arrive at a New York Academy of Sciences meeting where he was slated to present a paper; his visa request had been denied by the U.S. Government.

"Edman, like most young Europeans, had some leftist leanings during his school days in Sweden," says one U.S. scientist. "When McCarthyism came in, such Europeans stayed out."

Although scientists believe Edman would no longer be barred from the U.S., red tape apparently lies behind his refusal of frequent invitations to come here.

"Our country has some strange laws," one man explained. "In order for Edman to get in, he'd have to go through both the Swedish and Australian governments before tackling the State Department. He just doesn't think coming here is worth all that."

Currently, Dr. Edman is working on the structure of Bence-Jones proteins that come from cancer patients. Immunologists hope to find out how these proteins differ structurally from normal proteins and how they manage to bypass the body's immune system.

Eventually, scientists hope to move from structure analysis to protein synthesis with implications for correcting genetic defects, eliminating some forms of cancer and designing new drugs far more selective in their action than today's products. But with the exception of insulin, a short 51 amino acid compound, proteins have not been synthesized.

Insulin synthesis was first reported by Red Chinese scientists in November 1965. Since then, German and American scientists have duplicated their results, but synthetic insulin still is not available commercially.

Dr. Moore predicts another protein, ribonuclease, will be synthesized within the year, but its full structure is already known. Edman's sequenator will lead to more.

Czechoslovakian scientists are the only ones who have built a replica of the protein machine, Dr. Moore says. But researchers in Baltimore, Boston, Chicago, Washington and New York are working on it. "I think there are some ways to simplify the sequenator," Dr. Moore says.

The protein sequenator, mass-produced, would cost about \$15,000. ♦

#### RACIAL DISORDERS

### Negro Militancy: A Complicating Dimension

Two years ago, Negro grievances seemed the cause when violence flared in Watts, Los Angeles' Negro ghetto. This year, as city after city boils, sociologists are no longer certain. The grievances still exist, but there is another factor.

Negro militancy has grown considerably stronger in the past two years, not necessarily in numbers of militants, but certainly in influence, according to reports from sociologists in the West, Midwest and East. The new dimension makes the task of forestalling violence in American cities immeasurably more difficult, and the social scientists seeking cause and cure are feeling more and more pessimistic.

**American cities** do not erupt purely out of a militant spirit. The ghetto grievances are real—lack of jobs, segregated housing and schools, squalid slums, insensitive city administrations, insulting police officers and the rest. And no sociologist is willing to declare a city free of those conditions, whether it's Detroit, Newark, Cleveland or San Francisco. Professor of Sociology Theodore Hadwen at the University of Southern California puts it, "A lot of us have nothing very new to say. Most of us feel we have said our piece. The problems remain."

"The only new thing," says Dr. Hadwen, whose familiarity with Watts antedates the riot there, "is the role of black militants."

The question now facing the nation is: With rising black militancy will a city erupt no matter what its level of grievance and no matter what steps officials take to sooth resentment?

"That's possible," says Dr. John P. Spiegel, director of the Lemberg Center for the Study of Violence at Brandeis University. "I tend to think it might be the case."

Measures, from Presidential commissions like the one President Johnson formed after Detroit exploded to municipal efforts like one undertaken in Washington, D.C., to forestall trouble, may be ineffective, even if they accomplish everything they set out to do in terms of eliminating grievances.

Dr. Raymond J. Murphy, professor of sociology at the University of California, Los Angeles, expresses similar gloom. "I'm pessimistic," he says. "It may well be a case of too little and too late."

**Dr. Murphy** and Dr. James M. Watson, also of UCLA, recently concluded a study of 600 ghetto residents in Los Angeles and found that rioting is not a simple reflection of economic distress.

A significant number of even the more successful Negroes—those with white collar jobs and at least a high school education—are "emotionally prepared for violence as a strategy to end the problems of segregation, exploitation and subordination," says Dr. Murphy.

Adding to the difficulty is the problem of double backlash. Black nationalists, for all their implacable stance, remain a minority among ghetto residents. But whites are generalizing militancy to all Negroes, and people in the ghetto resent it, and resent the whites for it, says Dr. Hadwen.

**He believes** as well that "we are seeing a white reaction that is very bad." After Watts, many Los Angeles whites were able to maintain an understanding view. But that ability is cracking too.

As one Los Angeles woman said, "If this riot starts to happen again, we should give one warning and then drop a bomb."

In Dr. Hadwen's view, it is not likely to happen again in Watts. The area is depressed, psychologically and economically, he says. Much destruction was never repaired and in many areas more than half the businesses are closed.

"Watts people are aware of how much damage the riot did," he says. "Only the young men are at all interested in starting another."

Despite their pessimism, however, sociologists do have advice to offer cities.

Dr. Spiegel's group studied six—Cleveland, Dayton, San Francisco, Pittsburgh, Akron and Boston, 6,000 people in all—and found that the ghetto attitude toward local government was a most important, if not the most important, measure of grievance.

"The evidence indicates that Negroes are not responding purely and simply to the actual steps a city is taking, but rather to the emotional attitude of the local administration," he says.

**Either a city** takes a get-tough attitude, or it says more complacently, in effect, "Look at all we are doing for you." Neither attitude is any good, comments Dr. Spiegel.

Ghetto residents know that problems are difficult and long range, he says. If an administration is frank, gets down to the ghetto and keeps informed, the anger is less. Dr. Spiegel took Detroit to task on this score. Much of the talk to the effect that Detroit had few grievances was simply propaganda, he says, and Negroes perceived the insincerity.

After city attitudes come the multitude of other problems—employment, education, etc.—that vary in seriousness from city to city. Each has its specific source of trouble, says Dr. Spiegel. In San Francisco, it was lack of jobs; in Boston, it was segregated schools.