Artificial Organs and Beyond

Computers, electronics and new materials still promise major impact on medical therapy

Abebe—the calf with an air-powered artificial heart—with researcher John Lawson.

BY JULIE ANN MILLER

Scientists on earth perform experiments on Mars. A wristwatch contains a miniaturized calculator. But where are the medical benefits of space-age technology, the fruits of a field called bioengineering? Researchers in universities across the country are applying computer, microcircuitry and new material techniques toward devices to improve human health. Yet the progress has been slower than many had expected due both to shortage of funds and to the complexities of the human body.

The University of Utah has supported an active bioengineering program for 13 years, concentrating biological, medical and engineering scientists. The research projects going on at that Salt Lake City facility reflect where science stands in the pursuit of the repairable and maintainable human.

In an attempt to address the real needs of people, many bioengineers follow ideas all the way from basic science to patient care. "If you lift problems out of the context of the total problem, you can end up with an elegant solution for a problem that doesn't exist," says Donald J. Lyman, whose own skills range from polymer chemistry to surgery.

As Lyman makes one of his frequent trips between the laboratory and a cooperating local hospital, a bare-legged, unhelmeted motorcyclist zooms around the car. Lyman comments that on such occasions he always counts up the body parts that surgeons may someday be able to replace. Researchers at Utah are designing, constructing and testing artificial arms, kidneys, hearts, blood vessels, livers, ears and eyes. Although progress is steady, none of the prosthetic devices so far is an adequate replacement for a natural organ.

In the last few years plastic hearts made of new materials have shown increased promise in animal tests. In 1970, animals with artificial hearts had survived only 50 hours (SN: 4/11/70, p. 375). Now Abebe, a Holstein calf that died May 12, holds the record by surviving 184 days. During that period its blood was pumped by a polyurethane heart connected to an external compressed-air power unit. In good health, Abebe gained more than 200 pounds and eventually outgrew the heart.

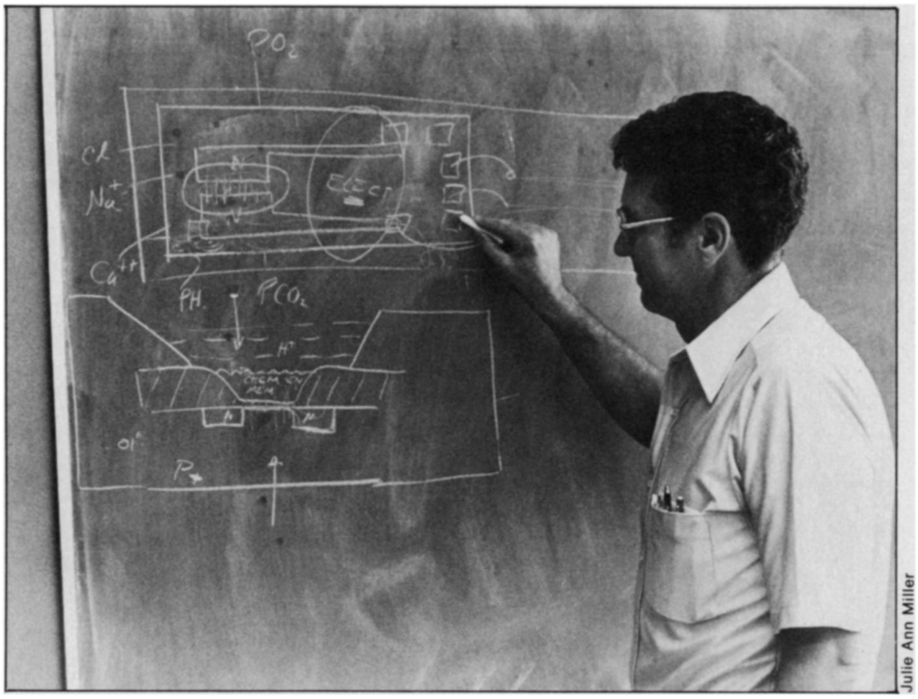
The next step in artificial heart development, the researchers say, is electrically driven hearts, which could someday be powered by nuclear capsules and be contained entirely within the body. The record survival on the first artificial hearts of this type, designed in Willem J. Kolff's research program, is 37 days by a calf named Charlie.

While artificial hearts for people remain some distance in the future, other research projects of the bioengineering department are already in clinical tests. A wearable artificial kidney frees patients from being confined to a hospital bed for hours while chemicals are filtered from their blood. Instead of the conventional complex of needles, pumps, clamps, timers, accumulators, dialyzers, bubble traps, tubes and tanks, Stephen Jacobsen and co-workers designed and built a 3.5-kilogram pack that is strapped to the patient. Blood flows from and returns to the patient through a single needle in the arm. The module must still be connected intermittently with a 20-liter tank. This artificial kidney is far less expensive than the conventional hospital models, and a patient can even take one on vacation.

The portable artificial kidney uses a newly developed type of pump and is powered by rechargeable batteries. When the machine turned out to need a new type of filter, workers in Jacobsen's laboratory, in their self-sufficient style, went ahead to design a machine to make the filters. "Ideas have to turn into things for people," Jacobsen explains. Two adjoining sections of his laboratory reflect the variety of activities—a room of laboratory equipment and machine-shop tools connects with a room lined with sophisticated computers. As well as designing the working parts of their devices, the research group makes the casings and other less essential parts. Jacobsen reports that companies are much more likely to show interest in manufacturing a device that is already in a finished state, rather than a laboratory composite of tubing and beakers. Among the courses Jacobsen teaches is one on entrepreneurship—to urge graduate students to pursue a project from concept to market.

The computers in Jacobsen's laboratory are used for programming the "Utah" arm, which is nearing its debut for clinical evaluation. This artificial limb can flex at the elbow, rotate at the wrist and open and close a hook that has several grips. Unlike previous artificial hands, this versatile hook can hold a fork, a pen-

Jacobsen makes filters for wearable kidney.



Julie Ann Miller

Complex circuitry for a tiny chip: Stanley D. Moss diagrams blood chemistry probe.

cil or a beer can.

The most interesting aspect of the arm is its control. Jacobsen and colleagues are using computers and volunteer amputees to link body signals with arm movements. Using a sensor they built that detects muscle contractions with electrodes placed against the skin, Jacobsen's team correlates the normal contraction pattern to the forces needed for each of thousands of possible movements of the artificial arm. "It can pick up and interpret body signals," Jacobsen explains. "This way we don't have to teach the man to use the arm. The arm already knows how to move."

Although prosthetics are the most obvious application of bioengineering, other scientists are developing instruments for monitoring the conditions of patients, such as the nonmetal thermometer (SN: 7/2/77, p. 7). Stanley D. Moss and his co-workers have accepted the challenge of replacing a hospital chemistry laboratory with a needle-tip sized integrated circuit chip. They envision a tiny "integrated data processing/data acquisition unit," which will be inserted into a patient's arm, continually reporting the concentrations of vital blood chemicals.

This futuristic monitoring device, referred to as "superprobe," is the offspring of two technologies. Large electrodes have already been developed for measuring specific ions in laboratory solutions. Moss is merging that ability with techniques of miniaturization that blossomed from the space program.

A practical method for immediate and continuous analysis of blood chemistry would initiate major changes in health care, according to Moss. For the patient just in for a checkup, it would mean not having blood drawn and not waiting several days for results. The device in a syringe-needle tip, hooked up to the doctor's desk-top computer, could give immediate read out. "No one has to come back," Moss says. The technique would also allow the physician to look for chemical warnings of disease that he would never detect with conventional blood samples, for example, comparisons of blood from a patient during exercise and at rest.

The technique would also have implications for hospital treatment. Data from continuously monitored patients could be stored in the hospital computer system, so that the physician could observe changes with time. The data might immediately indicate reactions to medication and changes after surgery.

So far, the researchers have promising results with sensing hydrogen, calcium and potassium ions. The concentration of each of these ions in a solution alters the distribution of electrical charge on specific polymer membranes. On integrated circuit chips, tiny patches of an ion-sensitive membrane, 20 microns by 40 microns, are placed in contact with the input surface of a transistor. Eventually Moss hopes to combine many such patches, sensitive to different ions, on the same chip. The chip also contains a circuit, inscribed by a photolithographic process, that amplifies and processes the signals. The more the processing is done on the chip, as opposed to passing the signals out to laboratory equipment, the more accurate it can be, Moss says.

The sensors so far developed have given accurate measurements of ion concentrations in solutions of laboratory chemicals. "The next step is to take the probes into animal testing," Moss says. Within a few months he expects to make measurements of the ions in blood—first drawn from animals and later in the animals with the probe glued to the tip of a catheter. The researchers will compare their results with those of a standard medical laboratory to determine the efficacy of the technique.

Eventually Moss hopes to develop a superprobe that can monitor, in addition to ions, important organic molecules, disease organisms and the body's response to infection. For this the researchers plan to incorporate enzymes, antibodies and antigens into sensing membranes. Preliminary experiments by Jiri Janata demonstrate that the specific binding of a protein (conconavalin A) to a polysaccharide molecule does change the electrical charge at a membrane surface. A probe for broadly investigating a patient's immunochemical state could also be useful in monitoring signs of rejection in organ-transplant patients and effectiveness of immunotherapy in cancer treatment, Moss says.

The products of bioengineering must ultimately be suitable for safe use in people. While there is little potential danger in strapping on an artificial arm or in briefly inserting a probe-tipped catheter into the blood stream, procedures and devices that penetrate the body more deeply must be tested for efficacy. Such testing is difficult to do safely using people, and conventional measuring devices may change the characteristics of the system being studied. For these reasons, some researchers are relying on computers for detecting at least some of the potential problems of medical treatments and devices, as well as for analyzing causes of disease.

Harvey Greenfield is a long-time advocate of computers in medicine. His research has focused on fluid dynamics of blood, an area he says most medical people have ignored. His studies are relevant both to the improved design of heart valves and the study of one type of heart disease, atherosclerosis.

To study blood flow around an artificial heart valve or components of normal organs, Greenfield uses both a standard computer display screen and a three-dimensional, walk-through image that he and colleagues have devised. Greenfield stresses the importance of imaginative graphics to avoid being buried in the masses of unwieldly data that computers can spew. The computer, properly programmed with fluid dynamic equations and the shape of the heart and any implants, can indicate where blood turbulence will occur. On the display screen,

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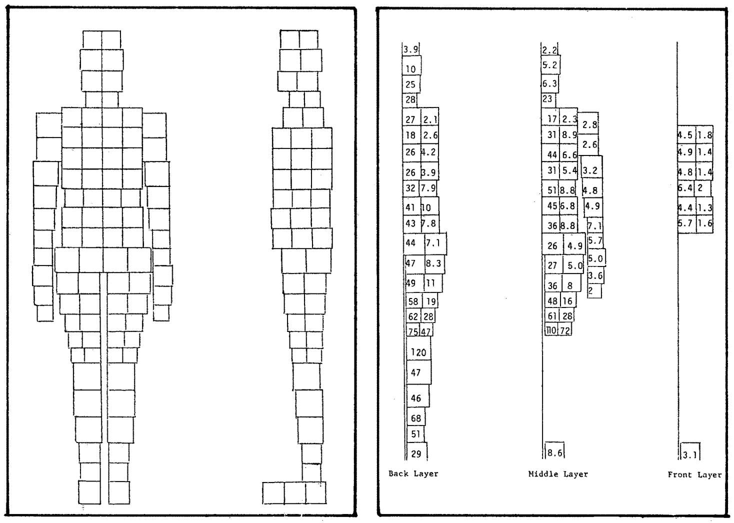
peaks on a graph find turbulence.

A novel three-dimensional display allows the investigator to observe the operation of the heart as if he were standing within it. He peers into a head set, mounted on a shaft to the ceiling. From the two half-inch square cathode-ray tubes (similar to miniature television screens) inside the headset, the investigator perceives a real image several feet away. As he turns his head or walks around, the computer senses the movement and changes the picture to what the investigator would see if he were actually moving inside the heart. "The objects appear to be stationary, their apparent size and perspective changing as with real objects," Greenfield says. "It's like *The Fantastic Voyage*."

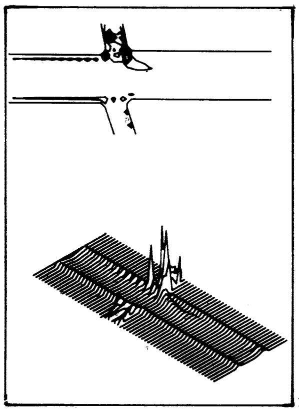
Greenfield believes that blood turbulence causes structural fatigue in arterial walls and damage to red blood cells. From the computer displays he makes recommendations to manufacturers of heart valves and designs new valves on the screen, remodeling the areas of highest stress. However, no valve designed on a computer has yet been produced.

The researchers are also using computers to try to understand the steps in formation of an atherosclerotic lesion. They start with a hypothetical small blockage of a blood vessel and observe changes in turbulence that result. Then they can predict what further obstruction will come from the damage. Finally, they compare the computer-generated lesions with those found in cadavers.



Mark J. Hagmann et al.

Cubist view allows estimates of how electromagnetic energy affects people. Numbers show different absorption of microwaves by body parts.



Harvey Greenfield

Spikes on a computer display show positions of turbulence that may lead to wall damage in renal arteries.

Greenfield hopes that computer modeling of the circulatory system will also aid in directing surgery rationally. For example, although by-pass operations are now popular for improving blood flow and relieving chest pain, Greenfield says there has been almost no serious analysis of the proper implantation positions for the replacement veins or arteries or of the subsequent blood flow.

Another computer project at Utah now takes a cubist view of the human body. The scientists started by depicting man as a spherical ball of muscle, then as a salt-water filled cigar. "Now it is more than 100 little blocks. This taxes the computer, but we're starting to get more realistic," explains Curtis C. Johnson, head of the bioengineering program. Mark J. Hagmann, Carl H. Durney and Om P. Gandhi are using their building-block person to evaluate possible harmful effects of microwave radiation. Besides setting standards for ovens, such data may be required for new medical procedures. Microwaves are being used to monitor water accumulation in patients' lungs, and preliminary clinical tests are evaluating selective destruction of cancer cells with the radiation. Utah researchers are also studying the potential of microwaves as a tool for diagnosing cancer and for making it more susceptible to drug and X-ray treatment.

The computer project comes in with the leap from safety tests in animals to the safety of people. Gandhi and his research team are studying the effect of low-level, long-term microwave radiation on rats. They will look for behaviorial as well as biochemical and physiological changes. But how much radiation is absorbed by an animal depends on its shape and body composition.

Hagmann and colleagues fit cubicle cells of various sizes to the shape biostatisticians have dubbed "the 50th percentile standard man." From published cross sections of human anatomy, the researchers determine what proportion of each block would be each of the ten types of tissue—bone, fat, skin, muscle, lung, heart, brain, kidney, liver and spleen—and air. The calculation then predicts how much microwave energy would be absorbed by each block. Johnson says eventually they hope to develop such models for different animals by altering the shape and composition. Then experimental data on rats and monkeys may be realistically extended to the human body.

The average person, not needing any replacement parts or extensive health monitoring, may still look forward to benefits from bioengineering. Besides quicker medical examinations and more accurate radiation standards, the research promises a painless, punctureless injection technique in the near future. To administer a local anesthetic for minor hand surgery, such as removal of warts, Jacobsen and colleagues strap a band holding two electrodes around the patient's wrist. Electric current moves the anesthetic across the skin. This treatment eliminates risks of tissue damage and infection, as well as the pain, that accompany needle injections.

So while satisfactory organ replacements remain far down the road, teamwork of physicians, scientists and engineers may soon send the threatening hypodermic needle the way of the leech. □