Biomagnetism Attracts Diverse Crowd

Two decades after the first measurement of magnetic fields associated with biological processes, the discipline is opening new windows on the workings of the brain, heart, and other organs

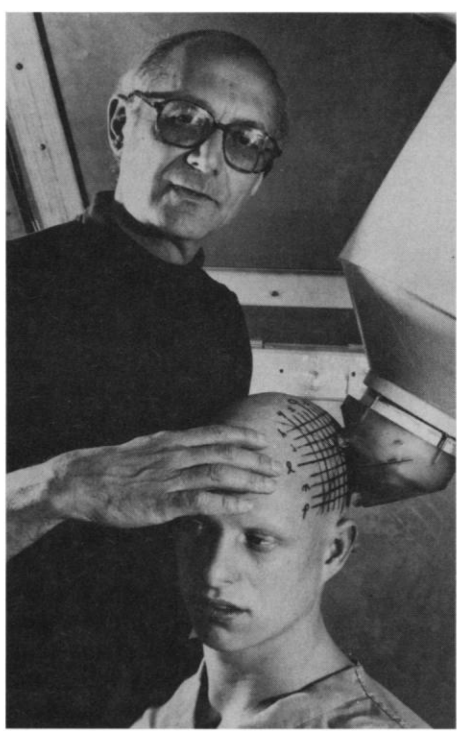
WHEN 40 SCIENTISTS GATHERED in 1976 at the First International Conference on Biomagnetism at the Massachusetts Institute of Technology, few would have predicted that 14 years later the biennial meetings would be drawing ten times that number. And fewer still would have imagined the variety of interests that would be reflected in the field. At the 7th International Conference on Biomagnetism held at New York University 14 to 18 August, for instance, attendees were treated to some 200 papers that included the following subjects:

- Magnetic contaminants in lung samples taken post mortem from asbestos miners, by a team that included physicists and epidemiologists.
- Ionic currents within developing chick eggs, by a physicist and a vision researcher.
- Spreading cortical depression in migraine patients, by a team that included neurologists and physicists.
- The different responses of the visual cortex when processing visual and linguistic tasks of comparable mental load, by a team of psychologists and physicists.
- Computer-graphic techniques of mapping brain activity, by a physicist and a computer scientist.

These strange interdisciplinary bedfellows clearly partook of the same field. Corridor conversations would begin with excited questions such as, "How many channels in your system?" "What's its noise level these days?" "How are you keeping track of head position?" and similar manifestations of the kind of shoptalk that indicates a genuine community. The field of biomagnetism—the study of magnetic fields associated with life functions—is expanding so rapidly, however, that some cognoscenti actually see signs that it will eventually fragment into a cascade of subdisciplines.

Biomagnetism is attracting researchers from a broad range of disciplines because it offers a powerful new tool for pinpointing electrical activity associated with the normal and abnormal functioning of the brain, heart, and other biological systems. Until recently, most quantifiable data about the electrical activity of the human brain and heart came from electrocardiograms (ECGs) and electroencephalograms (EEGs). But these have certain distinct limitations. EEGs see superimposed effects of electrical sources all throughout the brain, and there is no precise power-law relation between the strength of the source and its distance from the electrode. In contrast, magnetocardiograms (MCGs) and magnetoencephalograms (MEGs), which sample the magnetic field produced largely by the ionic current flow in the active cells themselves, allow much better localization of the source because there is a precise relationship between the strength of a field and the distance between sensor and source. "The beauty of it is that it's straight geometry," says conference cochairman Lloyd Kaufman. "You can ignore all the electrical properties of the head, which you can't do with EEGs."

MEGs also potentially offer another set of advantages over Positron Emission Tomography (PET), for the latter can be conducted for only short spells at a time and the information collected is averaged over a period of time measured at least in seconds.



Probing the brain. *Biomagnetism researcher David Cohen measuring the magnetic field around the head of a normal male subject.*

MEGs, however, provide a temporal resolution measured in milliseconds.

The study of biomagnetism is a mere 20 years old, and the vitality of the field testifies to the accelerated growth rate of modern scientific disciplines. It has three roots: quantum mechanics, superconductivity, and bioelectricity. Quantum mechanics, the study of the quantization of energy forms, has been shown to have implications for branches of science as diverse as metallurgy and vision research, but it wasn't until 1961 that two scientists at Stanford University—and, independently a short time later, a pair of West German scientists—experimentally detected the quantization of magnetic fields.

Then, in 1963, a chance observation at the Ford Motor Company lab in Dearborn, Michigan, brought superconductivity firmly into the picture when researchers there noticed that strange quantum interference effects occur when a nonsuperconducting boundary is present in a superconducting loop. These effects are extremely sensitive to the amount of magnetic flux passing at right angles through the loop. This, of course, was a manifestation of the Josephson effect, which had been predicted and discovered the previous year, but initially none of the Ford scientists were aware of the connection. Ford scientist James Zimmerman utilized the phenomenon to build a device that could detect extremely tiny magnetic fields. He called it a SQUID, or Superconducting QUantum Interference Device, but he couldn't figure out an important use for it. Not that that made him lose interest in the novel toy; on the contrary, he spent the next few years improving it. And meanwhile, the device proved to be a source of amusement for his fellow Ford researchers. As Zimmerman recalled during the NYU meeting, his colleagues developed the popular pastime of watching the SQUID signal change as he moved the lab's metal chairs back and forth. "It was obvious," he said, "that we had an extremely sensitive detector of lab chairs."

The device would soon become a godsend to University of Illinois physicist David Cohen, who had left high energy physics to study bioelectricity. In the mid-1960s, that field had principally been studied with the aid of ECGs and EEGs. In 1967, however, Cohen used a magnetic induction coil inside a magnetically shielded room to measure the field of the human heart (*Science*, 5 May 1967, p. 652). The following year, he made the first measurement of the magnetic field of the brain, some 500 times weaker than that of the heart (*Science*, 23 August 1968, p. 784).

Early in 1969, Cohen moved his renovated shielded room to MIT's Francis Bitter National Magnetic Laboratory, where he continued his work. Still, his induction coil device was cumbersome and slow. "It was like trying to explore a new continent for the first time using a rowboat," he says.

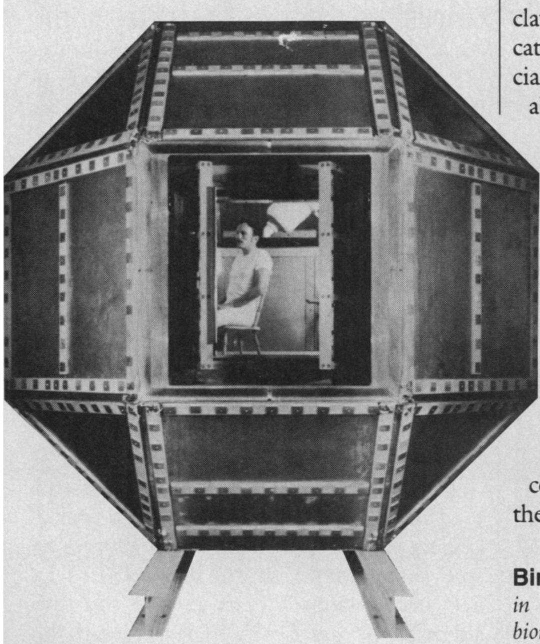
Then Edgar Edelsack, an Office of Naval Research official who was funding both Zimmerman and Cohen, had a brainstorm—why not get Zimmerman with his ultrasensitive lab chair detector together with Cohen with his shielded room and biomagnetic projects? Shortly after Christmas of 1969, Zimmerman brought his SQUID to MIT, and he and Cohen spent a few days setting it up. "Now I had a powerboat instead of a rowboat," says Cohen. On New Year's Eve, Edelsack watched as Zimmerman, clad only in undershorts, clambered up the wooden staircase into the shielded room while Cohen adjusted the dials; the magnetic field of Zimmerman's heart came through clearly.

"Oh, we had a great time that evening," Cohen recalls. The three collaborated on a paper, "Magnetocardiograms taken inside a shielded room with a superconducting point-contact magnetometer," published in the 1 April 1970 issue of the *Journal of Applied Physics*; the final sentence of the abstract, "These results suggest new medical uses for this magnetometer," amounted to the Magna Carta of a new field: biomagnetism.

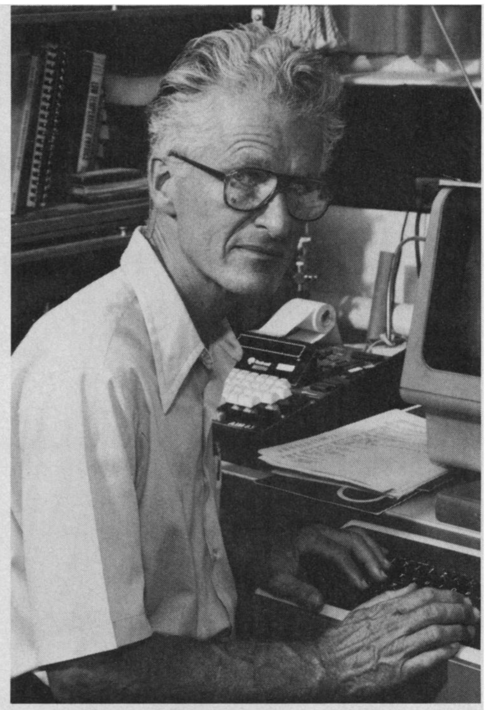
What emerged from that room that New Year's Eve was more than a quirky tool for biological research. MEGs and MCGs proved able to complement EEGs and ECGs, and the MIT group showed, for instance, that contamination in the lungs can be detected magnetically with magnetopneumograms (MPGs), which may prove important for occupational health and safety (*Science*, 18 May 1973, p. 745). Another potential clinical application is in the treatment of epilepsy. Epilepsy can sometimes be cured by the removal of tissue at an epileptic focus. Pinpointing that focus thus becomes all-important. At present, EEGs can localize foci only to general areas. MEGs may be able to localize foci faster, more accurately, and using simpler, noninvasive techniques.

Indeed, MEGs can locate clinically important features that have not been detected with EEGs. The first universally acclaimed instance of this was announced at the NYU meeting. A team from the University of Münster in the Federal Republic of Germany, in one of the most talked-about papers of the conference, announced that its MEG researchers had discovered that tinnitus, or ringing in the ear, is characterized by the absence of one of the components of a brain wave, presumably related to a defect somewhere in the auditory cortex. Until now, all attempts to detect a difference using EEGs have failed. This work provides the first objective measure of tinnitus—which seriously affects the ability to lead a normal life of between 0.5 and 1% of the population.

Another hot topic at the New York conclave was the development of more sophisticated biomagnetic instrumentation, especially the appearance of commercially available multichannel SQUIDs, or SQUIDs with arrays of several detectors in each cryostat ("fleets of powerboats," to use Cohen's analogy). In NYU's Greenberg lounge, several companies set up booths to market the multichannel devices. Biomagnetic Technologies promised a 37-channel system at a price yet to be determined. Siemens said it had a 37-channel system operating since January that costs approximately $2.5 million. A CTF Systems Inc. representative said his company targets a 60-channel system in the next year or so.



Birthplace of biomagnetism. *Experiments in this shielded room at MIT led to the first biomagnetism publications.*



SQUID developer. *James Zimmerman's detectors provided the key to biomagnetism.*

Yet another topic of avid discussion was the possibility of high-temperature superconducting SQUIDs. Roger Koch of IBM Yorktown Heights likened their advantage with respect to existing SQUIDs to that of portable computers to mainframes. While high-temperature superconducting SQUID "chips" could never be as sensitive as larger, low-temperature devices, their small size and great flexibility could lead to new applications.

MEGs and MCGs, for instance, might be used to monitor brain or heart activity during delicate operations; if so, it would be extremely useful to have portable high-temperature superconducting versions that could be brought directly into an operating room. Moreover, such SQUIDs would be attachable directly to the skull—like EEGs and unlike conventional SQUIDs, which must be bathed inside liquid helium inside a dewar, at least a centimeter removed from the subject's head. This would avoid the problems that arise when the subject's head moves. Koch estimated that laboratory-grade high-temperature SQUIDs would be available in about 2 to 3 years.

But the field of biomagnetism, for all its recent progress, is hampered by the cost of its large-array devices, which has put them beyond the reach of hospitals, small laboratories, and even large facilities. The timetable for the development of such arrays may depend on their clinical effectiveness, which is still uncertain. "It's not clear yet," says Cohen, "how useful MEGs are going to be. It *is* clear that you can get some new information with them that you can't get with an EEG. But whether that's going to justify the enormous expense to a hospital, say, of laying out $2 million on something that complements a $20,000 EEG system is another question. Quite crudely, it will depend on how many lives you can save. And whether you can save any lives or not isn't clear right now." Indeed, some of the commercial companies seem to be waiting for successful clinical applications before committing themselves to full-scale production of the large arrays.

As a research tool, however, biomagnetism unquestionably has enormous significance. The study of high brain functions such as mental imaging, language production, and memorization, for instance, up to now has had to rely primarily on case studies of individuals who have suffered various forms of brain damage, often incurred during wartime. Moreover, conventional EEG and positron emission tomography techniques look only for point sources of current. To understand higher brain functions, however, one has to look at a sequence of activity—how each area communicates with several others over time—and MEGs may allow you to do that. New York University is an important center for such research, and an NYU team announced at the conference results in which differences between how the brain processes visual and linguistic tasks had been detected. Another breakthrough was announced by a team of British scientists at the Open University who had developed computer methods of graphically presenting in three dimensions and in real time brain current densities picked up by MEGs.

Meanwhile, research is shooting out in so many directions that biomagnetism may not be a unified discipline much longer; indeed, researchers sometimes liken its probable fate to that of the discipline once spawned by the Mössbauer effect, the phenomenon of recoilless emission and absorption of gamma rays by certain nuclei which is widely used in many fields. "Of itself," Cohen says, "the Mössbauer effect isn't all that interesting anymore, but it does have applications. You don't see Mössbauer conferences like you used to, but you do see Mössbauer people using it in different fields. The same may happen to biomagnetism." Indeed, MPG researchers were less prominent at the NYU conference than in previous years, suggesting that they have gone elsewhere and that the process of fragmentation has already begun. ■ ROBERT CREASE

Robert Crease is a science writer who teaches philosophy of science at the State University of New York, Stony Brook, and is a historian at Brookhaven National Laboratory.

The (Liquid) Breath of Life

Fluid in the lungs is a bad sign—unless the fluid is perfluorocarbon, which could save many premature infants and lung-damaged adults

AFTER 2 WEEKS it was clear that nothing more was going to help: the infant girl, born prematurely at 28 weeks and under intensive care at Saint Christopher's Hospital for Children in Philadelphia, had failed to respond to any of the conventional therapies. Indeed, the high-pressure oxygen that made it possible for her to breathe at all had slowly ruptured the membranes of her lungs beyond healing.

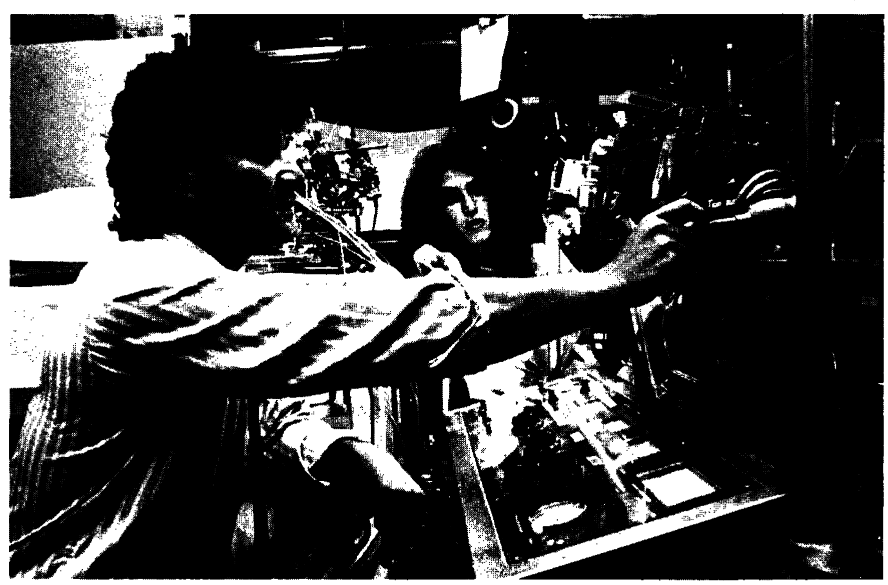
And so on 10 May, when the doctors agreed that the end was probably minutes away, the parents gave their permission for the first human test of a treatment as radical as it was bizarre. Through a thin plastic tube, researchers flooded the girl's damaged lungs with the kind of "perfluorocarbon" fluid that is widely used to cool electronics gear—and that just happens to be capable of carrying more oxygen than air itself.

Within minutes, her condition improved markedly, and she lived for another 19 hours.

"Just seeing that fluid go into a human lung was a very intense experience emotionally," says team leader Thomas H. Shaffer, who has spent the past decade and a half testing the procedure on animals. "We were very nervous. A baby this sick could die just from having you walk up to it."

Nervous or not, Shaffer has become something of a hero in the tiny community of liquid breathing researchers. "So many things in medicine require a psychological breakthrough," says Leland C. Clark of the Children's Hospital Medical Center in Cincinnati, the chemist who first discovered perfluorocarbons' application for liquid breathing. There have been abundant animal tests demonstrating the technique's potential for saving many premature babies who would otherwise die—and for treating adults suffering from smoke inhalation and other types of lung damage. "[But] Shaffer deserves a lot of credit for breaking through that barrier and trying it on humans."

Shaffer has been working his way to this point since the early 1970s, when he was an undergraduate engineering student at Drexel University. Clark had demonstrated perfluorocarbon breathing only a few years before, in 1966, and the concept was still enjoying something of a vogue. Not only were perfluorocarbons known to be extremely stable and generally nontoxic—the name denotes an organic molecule in which



Temple University

Perfluorocarbon pioneers. *After 15 years of experiments with animals, engineer-cum-physiologist Thomas Shaffer and colleague Marla Wolfson conducted the first human test of liquid breathing.*