Medicine's New Magnetic Field

By DIETRICK E. THOMSEN

A magnetic field can be sensed at some distance from the place where it is generated. This can be true even if solid matter intervenes. In biological investigations that ability can mean noninvasive ways of studying structures and processes. Investigations can range from basic physiology — mapping which parts of the brain respond to particular sensory stimuli, for example — to medical diagnosis, for instance of certain malfunctions of iron metabolism.

The magnetism used may be naturally generated by electric currents in the body such as those involved in nerve impulses. It may be induced by an external magnetic field in magnetic substances naturally present in the body (iron in the liver) or in substances deliberately introduced to chart some function.

The magnetic fields detected are extremely weak. The ability to measure them depends on the development, over the past 10 or 15 years, of very sensitive magnetometers, usually ones based on the technology of superconductivity. Even when external magnetic fields are used, they are so weak as to be quite safe. One example is a technique for measuring iron stored in the liver. Writing about it in a recent NEW ENGLAND JOURNAL OF MEDICINE, a group of researchers from Cleveland Metropolitan General Hospital and Case Western Reserve University (Gary M. Brittenham, et al.) remark: "There are no known contraindications to or risks with magnetic-susceptibility measurement; the procedure is tantamount to placing a toy magnet over the liver."

Many things can be done even without the toy magnet. Ions moving inside cells constitute electric currents and so generate magnetic fields. It was a part of the heart that acts like a battery that attracted John Wikswo of Vanderbilt University in Nashville, Tenn., to the possibility of measuring such cellular magnetism, he said at the recent meeting in Baltimore of the American Physical Society. However, a lot of cells acting in concert is a bit too complicated for a beginning experiment. Wikswo and his collaborators decided to start with single, isolated cells.

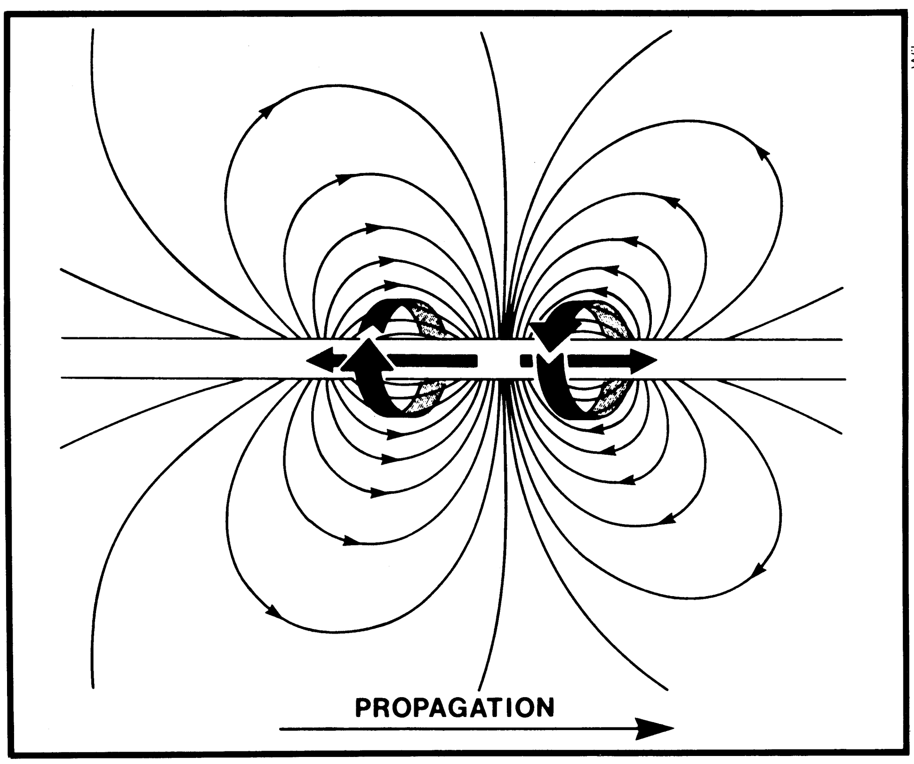
Nerve cells with their long threadlike extensions called axons were ideal for such a start. When a nerve cell "fires," ionic currents proceed in two directions along the axon. A few years ago Wikswo and co-workers succeeded in measuring the magnetic field produced by such firing in a frog axon (SN: 12/5/81, p. 362). It had a strength of about one nanotesla (10^{-9} tesla) just outside the fiber and a picotesla (10^{-12} tesla) a centimeter away. The earth's field is about 50,000 nanoteslas; a typical toy magnet would be about 200 times the earth's field or 10 million nanoteslas.

The nerve cell fields were first measured by a technique that involved a superconducting sensor. That required refrigeration of the sensing coil with liquid helium. More recently, an amplifying system that permits sensors at room temperature has been developed by Robin Gifford and Philip Sampson, so the cumbersome refrigeration technology is no longer necessary.

Wikswo says he and his colleagues now understand as much as they need to know about single cells and are going to study two cells electrically joined together as in earthworm nerves. There is a barrier in the earthworm nerve that may be similar to the junction between two cardiac cells. Eventually the researchers intend to work up to the cardiac case and study how the magnetic fields of the heart relate to its electric fields.

Meanwhile the technique they have developed could find applications in neurosurgery. Wikswo says that 30 percent of all accidents involve injury to a limb, and half of those (15 percent of the total) involve injury to a nerve. Axons below the injury die; after about six months, axons above the injury start to regrow down the limb. Sometimes, however, instead of proceeding properly to replace the dead axons, the regenerating axons get tangled into a knot called a neuroma.

The usual way to test for a neuroma is to expose the nerve surgically, insert electrodes into it above and below the injury and see how well it conducts across the injury. Wikswo says his group is beginning to study whether it is possible to use magnetic-field measurements above and



Wikswo

How a nerve makes a magnetic field. The thick straight arrows represent ionic currents flowing in two directions inside the nerve. The thin curved lines are also electric currents, outside the nerve. The thick curved arrows looping around the nerve represent the magnetic field.

Magnetic techniques are finding growing use in biological investigations. Some have clinical applications.

below the injury to make this determination. The magnetic method would not require sticking the nerve with electrodes. Also, it could be done with the nerve and its surrounding tissue lying in normal saline solution. The electric method requires lifting the nerve into the air with hooks and letting it dry.

Specialists in neurology, psychology, psychiatry, etc., have long wanted to know which cells in the brain fire in response to which stimuli. Much work in the past has used surgically implanted electrodes. Lloyd Kaufman of New York University told the Baltimore APS meeting about experiments with magnetic methods as a substitute. Magnetic methods avoid the inconveniences and risks involved with electrodes. Furthermore, the skull and fluids do not affect magnetic fields; they do affect electrodes.

As mentioned above, the strength of the magnetic field declines with increasing distance from the source. Thus the strength of the field as measured on the scalp will tell how deep the neuron that produces it lies. Kaufman says the method has detected activity as much as 5 centimeters below the scalp. "Above 4 cm you get most of the brain," he says. Two to three millimeters is the resolution, the minimum distance between sources that can be distinguished from one another.

Fields as weak as a billionth of the earth's field have to be measured, he says. This is not done in a magnetically shielded room, but in an ordinary laboratory environment. It uses a SQUID (Superconducting QUantum Interference Device) magnetometer, in which the sensing coils are kept at liquid helium temperature, 4 kelvins. (These coils are under thermal shielding, of course; nothing that cold touches the subjects.)

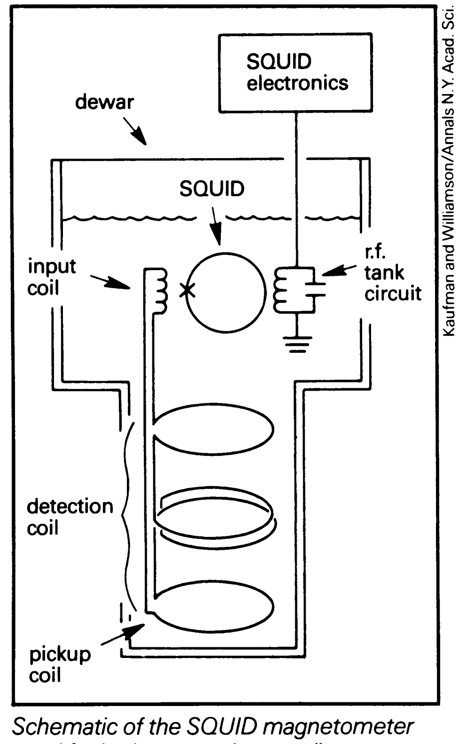
Earlier Kaufman and colleagues had reported that they were able to distinguish different locations in the auditory cortex of the brain that responded to different frequencies of sound, a kind of mapping of the cochlea of the ear onto the brain (SN: 6/26/82, p. 421). The work has now been extended in a number of ways. Tactile stimulation of the thumb, index finger, little finger or ankle have been found to evoke magnetic fields originating in different locations of the brain. In a similar fashion the investigators presented to subjects' view grating patterns designed to stimulate different parts of the visual field, and determined that magnetic fields were evoked in different parts of the optical cortex.

The work has also been extended to brain activity accompanying voluntary motion, the lifting of a finger in response to a signal. The researchers have found magnetic activity in the motor cortex just prior to the action. However, if the finger, instead of moving itself, is passively lifted by the other hand (which is controlled by the opposite hemisphere of the brain) the previously observed magnetic activity does not appear. They believe they will be able to resolve the location of these active cells with the same accuracy as they have done those involved with sensory stimuli. Eventually, Kaufman says, they hope to go on to cognitive activities, such as disappointed expectations.

Other groups that have been doing this kind of work, those associated with Giovanni Ricci in Rome and Jackson Beatty at the University of California in Los Angeles, have been studying epileptics, Kaufman notes, hoping to find areas of the brain that are active during seizures. Sometimes epilepsy is caused by a tumor, and, according to Kaufman, in the course of this work the Rome group has found epileptic tumors that failed to show up in electroencephalograms and CAT scans.

In addition to electric currents in the body, magnetic materials present in the body can be the source of magnetic fields. This usually requires the stimulus of an external field.

Iron is one of the elements necessary to life. The body stores it in the liver. Either too much or too little storage can be a sign of disease. David E. Farrell of Case Western Reserve University in Cleveland reported recent progress on work by Brittenham, himself and several others on the use of magnetic susceptibility of the compounds in which iron is stored to detect iron overload (SN: 9/5/81, p. 155). In the method a magnet is placed over the subject's liver to provoke a magnetic response in the compounds that carry the iron. The magnetic elements in them line up and produce their own field. A ferromagnetic material such as an iron bar frequently generates a field of its own that is stronger than the external one. No substance naturally in the body is ferromagnetic, but the iron-containing compounds in the liver, ferritin and hemosiderin, do give a paramagnetic response — that is, they contribute a very weak field of their own. This field is picked up by a SQUID magnetometer.



Schematic of the SQUID magnetometer used for brain magnetism studies.

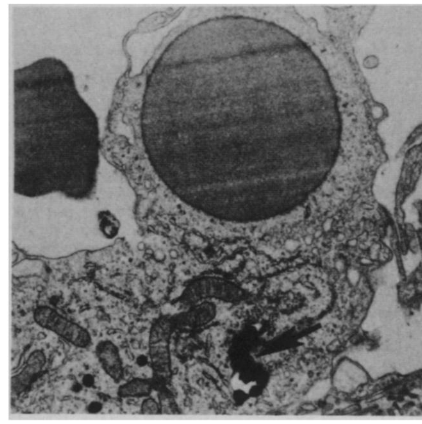
At the Baltimore meeting Farrell noted that 130 individual determinations that they have done correlated well with the patients' clinical condition as determined by other means. Furthermore in 19 of these cases biopsies were necessary for one reason or another, and the biopsies gave a direct confirmation of the magnetic measurements. Farrell sees the technique as a safe and easy method for routine scanning for iron overload.

To quote the group's paper in the New England Journal: "Unlike diagnostic procedures that transfer energy into the body (e.g. x-rays, ultrasound or radionuclide studies), this technique relies on a constant magnetic field, in which no energy is absorbed by the body.... [T]here is no known mechanism that could lead to adverse effects." The group is working on extending the method to iron-deficiency measurements.

Iron can also be introduced into the body for magnetic susceptibility studies. It is, of course, magnetic, and it happens also to be relatively nontoxic, says Joseph D. Brain of the Harvard University School of Public Health. Much of his work so far has to do with the lungs.

As Brain points out, many people have to live and work in environments where they inhale various kinds of dust. The lungs have a method of handling this contamination. Cells called alveolar macrophages engulf the invading particles and carry them out of the lungs.

Subjects who have inhaled iron dust either as part of their environment or as part of the experiment stand in a magnetic field of 1,000 gauss (a tenth of a tesla). This field aligns the iron particles inside the subject's body and gets them to produce a



A hepatic macrophage that has ingested iron oxide particles (arrow).

field of their own that persists for some time after the subject is removed from the external field.

Studying how the remanent field relaxes — that is, how the alignment of the particles gradually breaks down — is a way of following how the macrophages engulf the iron particles, what they do to the particles inside themselves and how they flush them out of the lungs, Brain and coworkers say. One of the results that came out of this kind of a study by David Cohen of welders' lungs is that smokers' lungs clear more slowly than those of nonsmokers, Brain says.

This work has now been extended to the liver, which has macrophages of its own. The iron is introduced to the liver by injection into the blood. The subjects have been hamsters and New Zealand white rabbits, which lived on a diet that must have been gourmet food to them — nothing but fresh vegetables. (Commercial rabbit food was found to contain magnetic particles. The rabbits were kept in nonferrous cages, too.) The finding that magnetic relaxation occurs in the livers of the rabbits was published by Peter Gehr, Brain, Steven B. Bloom and Peter A. Valberg in the March 24 NATURE. It is the first demonstration of relaxation in an organ other than the lung, they say, and it thereby settles an important question, whether the relaxation is the work of the macrophages or whether gross organic motion, such as respiration, is necessary. Gross organic motion is not necessary; organelles within the macrophages do the disaligning, these researchers conclude. As a result, Brain says, the method can be useful for studying intracellular motion in other parts of the body.

As equipment of the requisite sensitivity becomes more widespread, biomagnetic investigations of these varieties are likely to become more common. Some of them will lead to clinical applications. Farrell mentions that a company is working under a small business grant to develop a commercial version of the liver-survey apparatus that could be sold to hospitals and used for routine scanning. Other such developments could follow. □