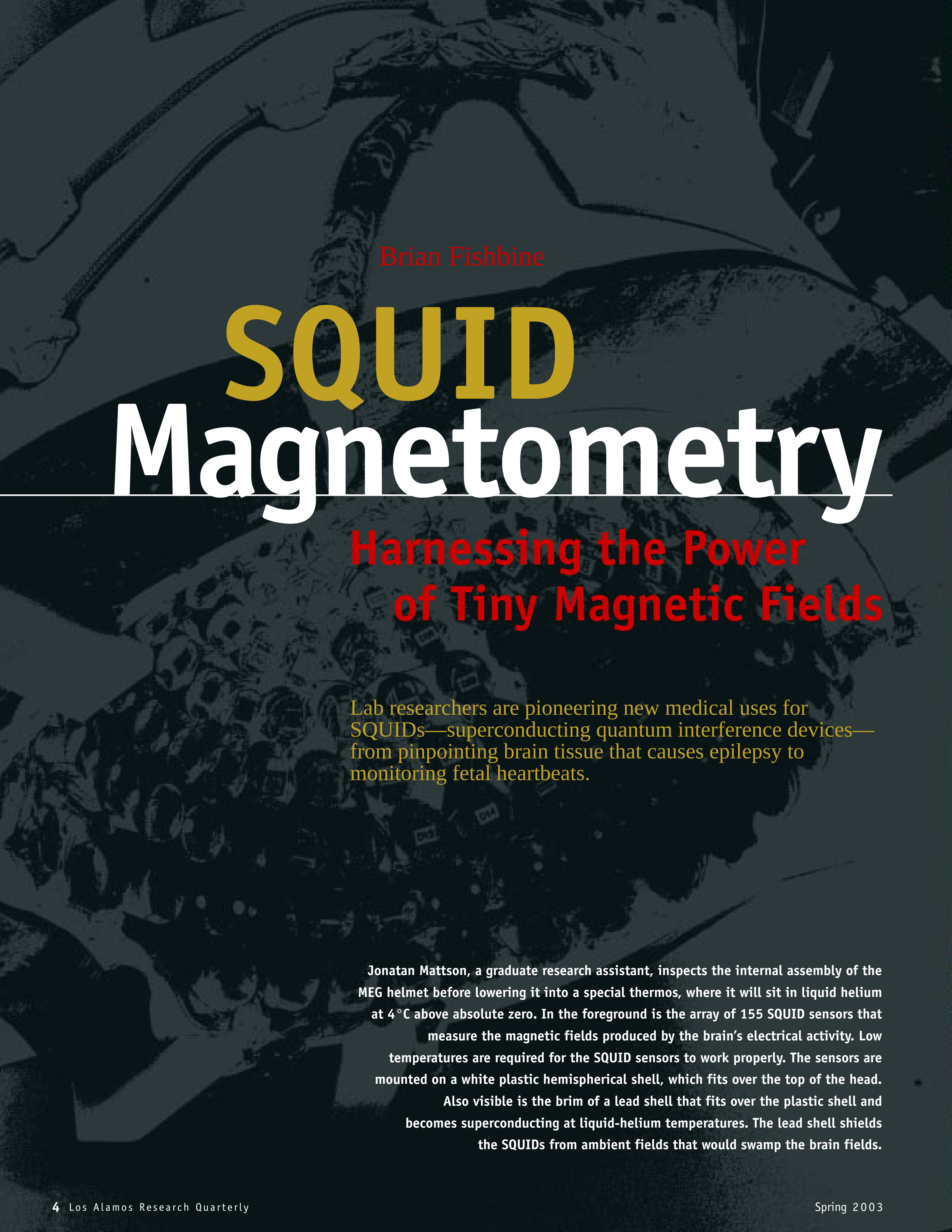


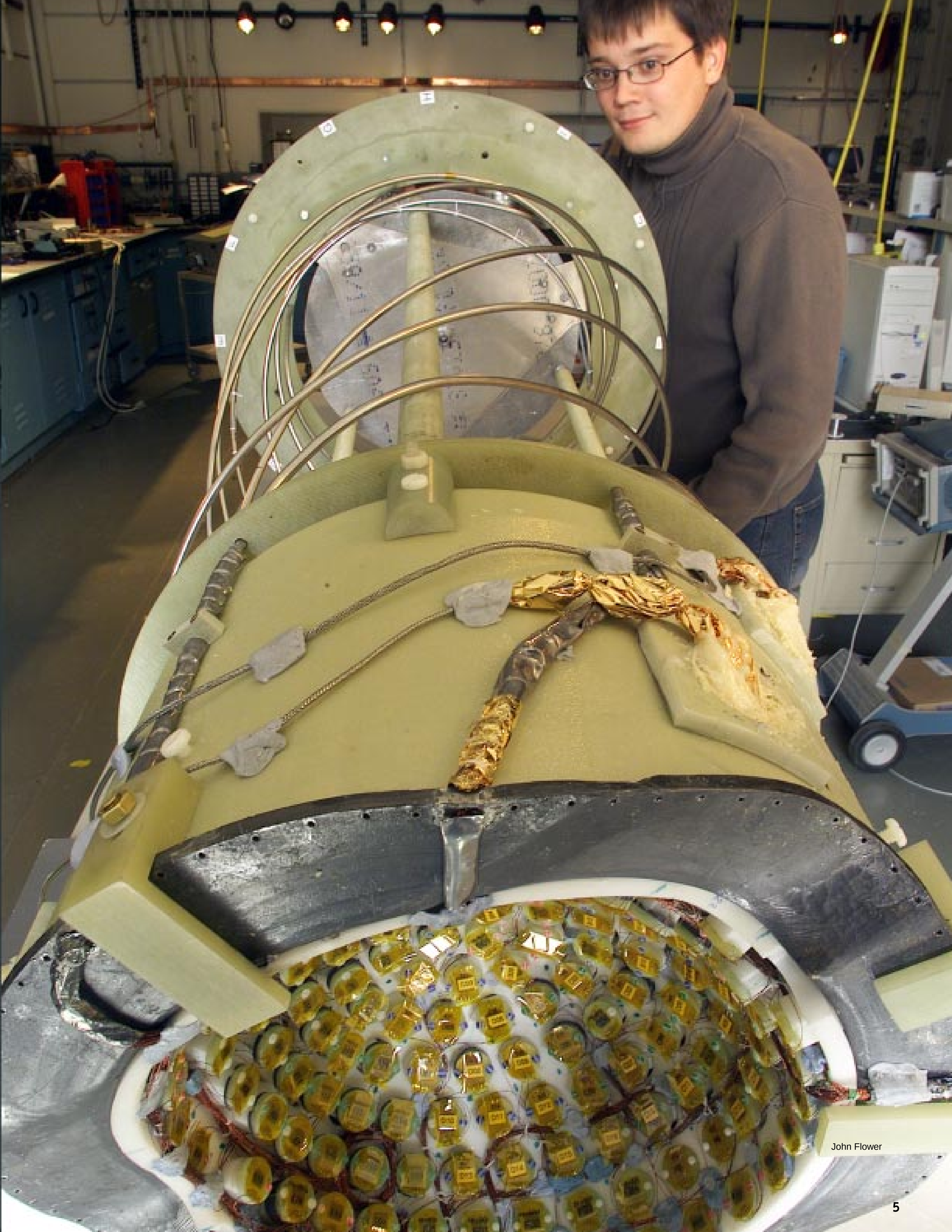
Brian Fishbine

SQUID Magnetometry

Harnessing the Power of Tiny Magnetic Fields

Lab researchers are pioneering new medical uses for SQUIDs—superconducting quantum interference devices—from pinpointing brain tissue that causes epilepsy to monitoring fetal heartbeats.

Jonatan Mattson, a graduate research assistant, inspects the internal assembly of the MEG helmet before lowering it into a special thermos, where it will sit in liquid helium at 4°C above absolute zero. In the foreground is the array of 155 SQUID sensors that measure the magnetic fields produced by the brain's electrical activity. Low temperatures are required for the SQUID sensors to work properly. The sensors are mounted on a white plastic hemispherical shell, which fits over the top of the head. Also visible is the brim of a lead shell that fits over the plastic shell and becomes superconducting at liquid-helium temperatures. The lead shell shields the SQUIDs from ambient fields that would swamp the brain fields.



John Flower

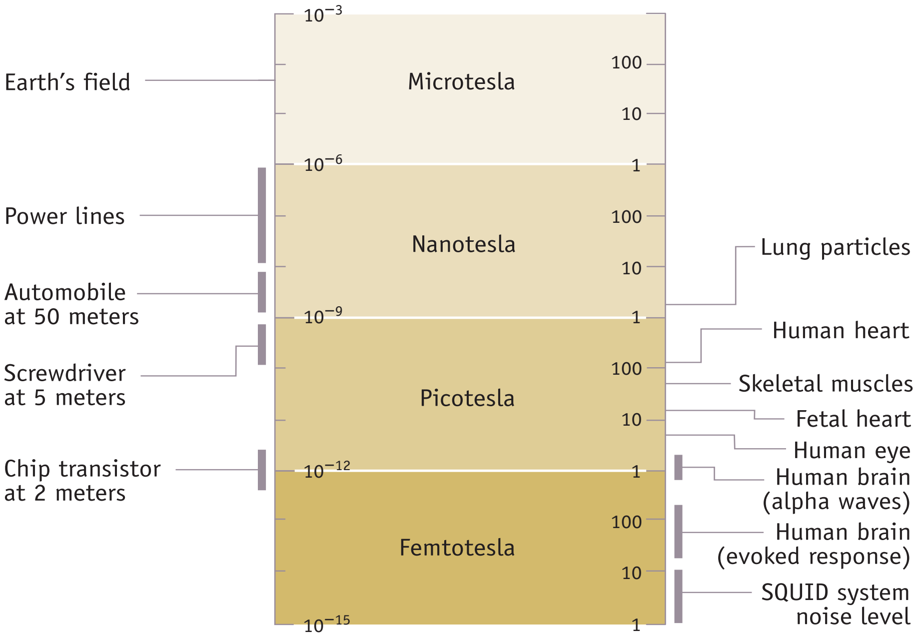
Measurements associated with the neural currents in the brain can be used to diagnose epilepsy, stroke, and mental illness, as well as to study brain function. One way to observe these tiny electrical currents is to measure the magnetic fields they produce outside the skull, a technique called magnetoencephalography, or MEG.

The traditional way to monitor the brain's electrical activity is with electroencephalography (EEG), which requires gluing as many as 150 electrodes to the scalp. MEG measures brain currents as precisely as EEG does but without physical contact, making it possible to screen large numbers of patients quickly and easily. MEG is also insensitive to the conductivities of the scalp, skull, and brain, which can affect EEG measurements.

Enter the SQUID

Measuring the brain's magnetic fields is not easy, however, because they are so weak. Just above the skull, they have strengths of 0.1 to 1 picotesla, less than a hundred-millionth of Earth's magnetic field. In fact, brain fields can be measured only with the most sensitive magnetic-field sensor known, the superconducting quantum interference device, or SQUID.

When cooled to very low temperatures, superconductors conduct electricity without resistance. This lack of resistance allows a SQUID to measure the interference of quantum-mechanical electron waves circulating in its superconducting loop as the magnetic flux enclosed by the loop changes. A SQUID can measure magnetic fields as small as 1 femtotesla.



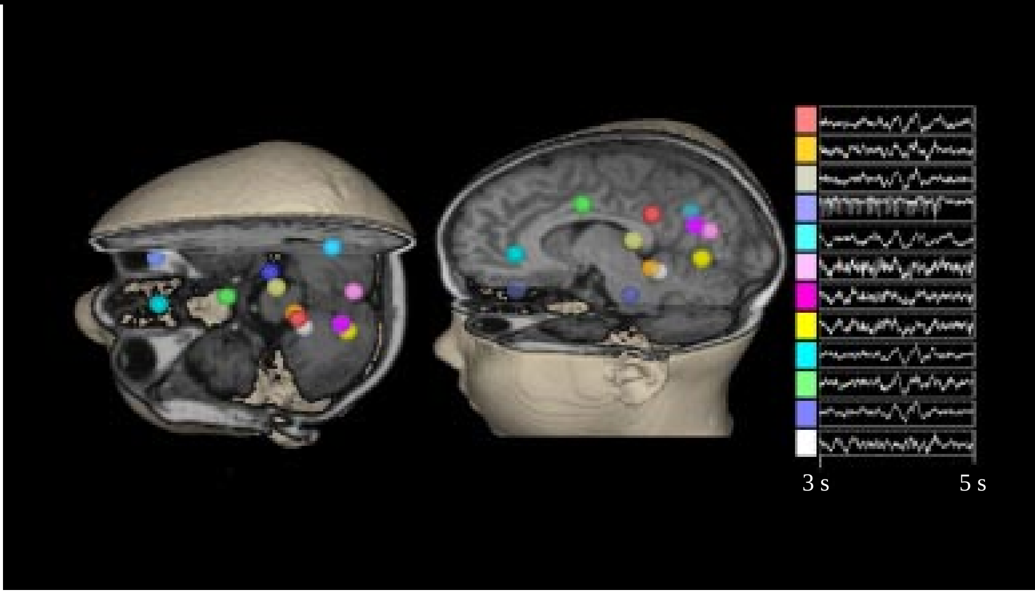
Just above the skull, the brain's magnetic fields can be as small as 10 femtoteslas. Measurable brain fields are produced by an "evoked response," that is, the electrical activity produced by the brain in response to stimuli such as sounds or light flashes. To measure brain fields, SQUIDs must be shielded from the ambient magnetic fields of Earth, power lines, and other sources, or the ambient fields must be canceled electronically or by computer programs. Even the steel in a car or a screwdriver has a magnetic effect. Also shown are the magnitudes of other biomagnetic fields. Note that the heart's magnetic fields above the chest are typically 100 to 1,000 times stronger than brain fields above the head. Thus, it is much easier to measure heart rhythms than it is to measure brain fields.

The MEG Helmet

Los Alamos physicists Bob Kraus, Michelle Espy, Andrei Matlachov, and Petr Volegov have built a MEG "helmet" that uses 155 SQUIDs to provide "whole head" brain-current images. The MEG helmet offers improved capabilities that could help make MEG more common in hospitals.

The SQUIDs become superconducting when immersed in liquid helium contained in a large thermos. The liquid helium cools the SQUIDs to 4°C above absolute zero. Resembling an oversized beauty-salon hair dryer, the helmet is positioned over a patient's head as he or she sits in a chair.

With sophisticated computer algorithms developed by Volegov, MEG data can be converted into current maps that give researchers an idea of where activity in the brain is occurring. Using specially designed current coils, the Los Alamos MEG system has achieved a spatial resolution of less than 0.25 millimeter. This resolution is at least four times better than that of any other MEG system, even though



A computer program converts the raw MEG data into maps of the brain's electrical activity as a function of time. These maps can be used to diagnose epilepsy, stroke, and mental disease and to study brain function.

other systems have up to twice as many SQUIDs.

But like other MEG systems, the Los Alamos system responds to brain-current changes in less than a thousandth of a second, adequate for most brain-current studies. The SQUIDs themselves respond in about a millionth of a second.

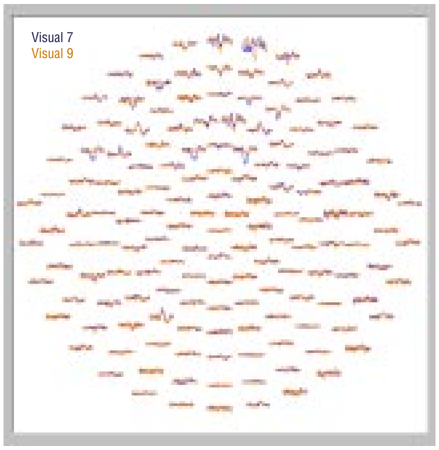
During a MEG measurement, the SQUIDs must be shielded from ambient magnetic fields, which tend to swamp the brain signals. Ambient fields are produced mainly by the power lines in a building, although Earth's magnetic field and even the steel in a passing car contribute. (Ferromagnetic materials like steel locally distort Earth's field.) At the frequencies of interest in brain studies—a few to several hundred hertz—the ambient fields must typically be reduced by a factor of 10,000 to 100,000.

The helmet's SQUIDs are partially shielded from ambient fields by a thick, hemispherical shell of lead, which becomes superconducting at liquid-helium temperatures. Because superconductors perfectly reflect magnetic fields, the shell reduces ambient fields to as little as one-thousandth of their initial strengths. The shielding is not perfect because the shell does not completely enclose the head. The SQUIDs near the shell's crown are better shielded than those near its brim. The shell also reflects the brain's magnetic fields back to the SQUID array, increasing the helmet's sensitivity.

Usually, ambient fields are reduced by taking MEG data in a room built with large sheets of aluminum and Mumetal (an alloy with high magnetic permeability), which magnetically shield the patient. The room reduces ambient fields by about a factor of 100 for frequencies near 0 hertz and by much larger factors for frequencies up to 1,000 hertz or more. The superconducting shell effectively blocks magnetic fields from zero to several thousand hertz. Thus, measurements made with the shell require only a "low-end" shielded room, which costs about $100,000, one-fifth the cost of conventional shielded rooms.

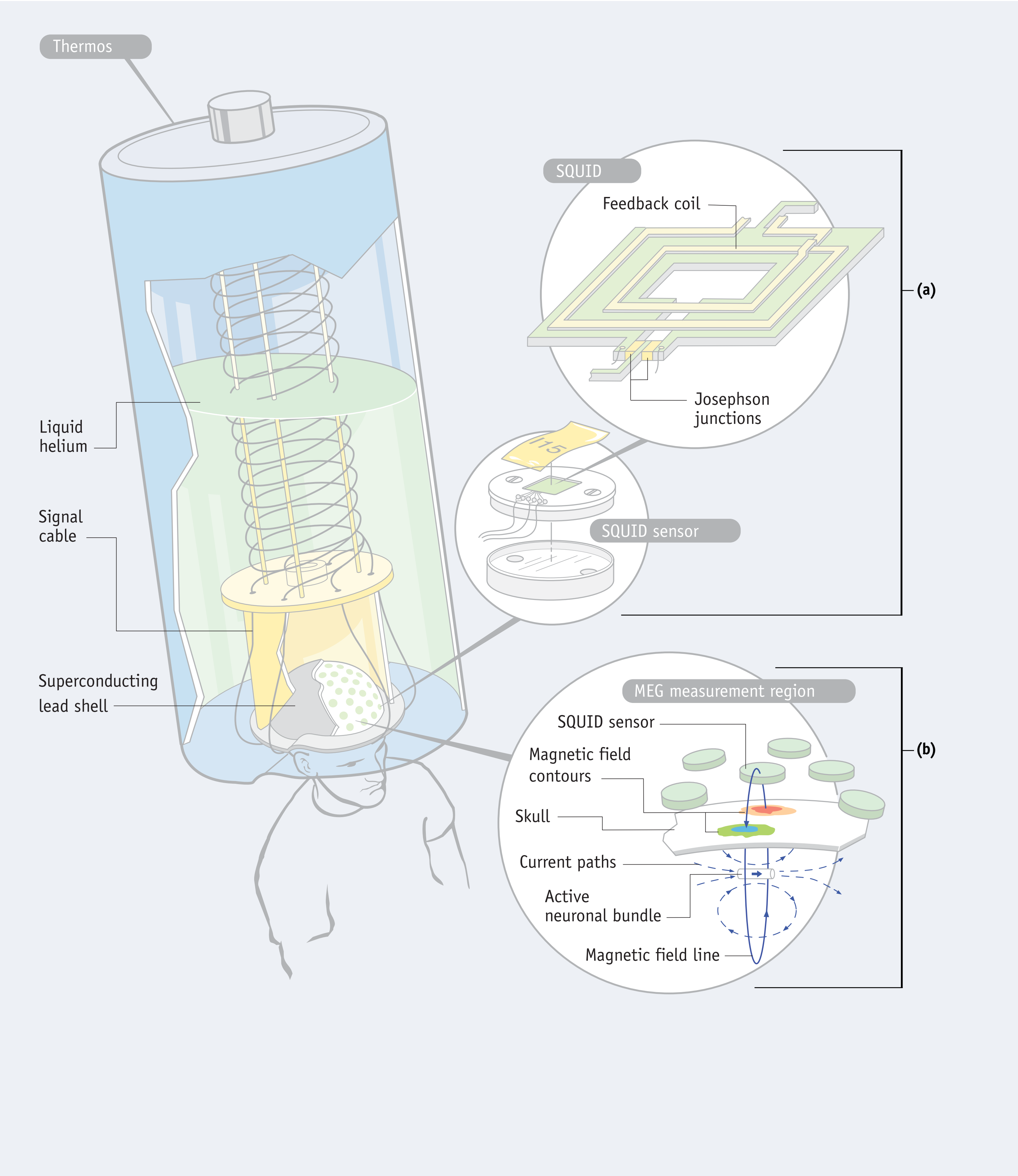
The team has recently added external SQUIDs to the helmet that further reduce the effects of ambient fields. The external SQUIDs measure these fields at several points just outside the superconducting shell, and a computer program then subtracts the fields from the brain-field data to reduce the ambient fields' effects by another factor of 1,000—at all frequencies. The computer correction is effective because the superconducting shell shields the external SQUIDs from brain fields in addition to shielding the SQUIDs in the array from ambient fields. Thus, the external SQUIDs measure *only* the ambient fields.

After recent side-by-side comparisons with a commercial MEG system at the Veteran's Administration (VA) Hospital in Albuquerque, New Mexico, the helmet is back at Los Alamos for further development. The VA's commercial system has been used to



The raw data obtained from the 155 SQUID sensors in the MEG helmet. The red waveforms (Visual 9) were obtained with the patient's eyes closed. The blue waveforms (Visual 7) were obtained as the patient observed a flashing light.

MEG Helmet and Measurements



The MEG helmet's array of SQUID sensors and the superconducting lead shell are cooled by immersion in liquid helium. Each SQUID sensor contains a coil of superconducting wire that receives the brain fields and is magnetically coupled to the SQUID, which produces a voltage proportional to the magnetic field received by the coil. A computer program converts the SQUID data into maps of the currents flowing throughout the brain as a function of time.

(a) The magnetic field lines that pass through the square hole at the SQUID's center determine the phases of electron waves circulating in the SQUID's superconducting region (green): the waves' interference is proportional to the magnetic flux over the hole. Since superconductors have no electrical resistance, the interference can be measured only by interrupting the superconductor with small regions that have electrical resistance—the two Josephson junctions—so that voltage drops will develop across them. The voltage measured across the junctions is proportional to the magnetic flux over the SQUID's square hole. The feedback coil magnetically couples the SQUID to the pickup coil in the SQUID sensor. A SQUID is typically 10 to 100 micrometers on a side.

(b) The colored contours show how the magnetic field produced by neural brain currents (dashed arrows) changes intensity and polarity over the skull's surface. In the red region, the field is most intense in a direction pointing out of the skull. In the blue region, the field is most intense in a direction pointing into the skull.

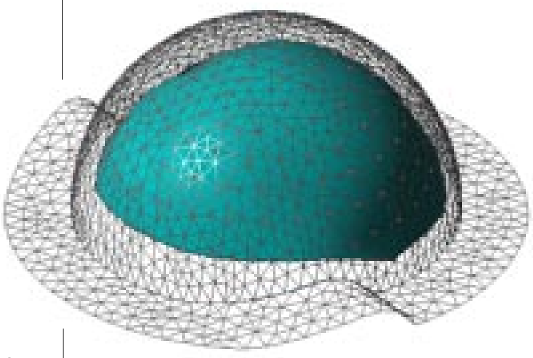
study stroke, epilepsy, schizophrenia, and brain function. Eventually, Espy says, the MEG helmet could find a home in a future Los Alamos brain-imaging facility along with EEG, magnetic resonance imaging (MRI), and other brain-imaging tools. In developing this and other medical applications for SQUIDs—such as detecting tumors and screening for disease—the team has collaborated with researchers at the Universities of New Mexico, Nebraska, and Oregon and the University of California at San Francisco.

Controlling Seizures

In the last five to ten years, whole-head MEG systems have dramatically improved the treatment of epilepsy. For 20 percent of epilepsy patients, drugs cannot adequately control seizures, and surgically removing the brain tissue where the seizures originate—the epileptigenic tissue—is the only option. But the surgeon must know precisely where the aberrant tissue is to avoid removing nearby tissue required for motor control, sense perception, language, and memory.

A brain scan can precisely locate the epileptigenic tissue if the imaging method has high spatial resolution and is fast enough to detect the seizure discharge or the electrical activity that precedes a seizure, which also originates in the epileptigenic tissue. Although seizures occur sporadically, the electrical activity associated with them occurs continually. Thus, locating the source of these precursors can isolate the epileptigenic tissue.

Both EEG and MEG have high spatial resolution and are fast enough to detect seizure-related electrical activity,



The superconducting lead shell. The gray mesh defines the shell's contour. SQUID sensors are attached to the blue surface. At liquid-helium temperatures, the lead shell becomes superconducting and therefore an excellent magnetic shield. Because a superconductor perfectly reflects magnetic fields at all frequencies, the shell helps shield the underlying SQUID array from ambient magnetic fields. The shell also shields SQUIDs placed outside the shell from the brain's magnetic fields. These external SQUIDs provide data used to help cancel the effects of ambient fields. The superconducting shell and field cancellation method greatly reduce the cost of the magnetically shielded room required for MEG measurements, making them more affordable.

John Flower

Los Alamos researcher Michelle Espy adjusts the MEG helmet on Michelle Martinez. Shown is the exterior wall of the helmet's thermos, which maintains the liquid helium at cryogenic temperatures. Even though the top of the patient's skull is just centimeters from a pool of liquid helium at nearly absolute zero, the thermos material insulates so well that the patient feels no discomfort.

but sometimes the position or orientation of the electrical activity is such that MEG can locate the epileptigenic tissue while EEG cannot. In addition, by pinpointing how the brain responds to visual, auditory, tactile, or other stimuli, MEG can help assess the effects of possible collateral damage during surgery. Along with other brain-imaging techniques, MEG is also being used to diagnose schizophrenia and stroke.

Peering into Brain Columns

The SQUID team has also developed MicroMEG—a centimeter-long linear array of SQUIDs with a potential spatial resolution of tens of micrometers. Made of high-temperature superconductors, the array's twelve SQUIDs are cooled by liquid nitrogen instead of liquid helium. At atmospheric pressure, the temperature at which nitrogen liquefies is about 70°C higher than that at which helium liquefies. Thus, the MicroMEG array requires less thermal insulation than arrays cooled with liquid helium. As a result, the MicroMEG SQUIDs can be brought within half a millimeter of the tissue under study, allowing extremely high-resolution measurements.

MicroMEG has been used to study how impulses travel along a single nerve, such as a frog's sciatic nerve. Eventually, MicroMEG will be used to probe the electrical activity of as few as 100 to 1,000 neurons in one of the brain's cortical columns. The columns are believed to operate in parallel, like the hundreds of microprocessors in a supercomputer that work in parallel to achieve high overall speed. Such studies will improve our understanding of brain function.

The team has also used the MicroMEG array in a highly sensitive SQUID microscope that detects flaws or defective welds in metallic nuclear-weapon parts. The SQUID microscope can detect defects invisible to ultrasound, x-rays, or traditional eddy-current methods. The metal parts are inspected to ensure that the weapons will perform as expected.

Measuring a Baby's Heartbeats

A variant of MEG called fetal magnetocardiography, or FMCG, can be used to diagnose and treat fetal heart conditions. In fact, FMCG is the only way to measure the electrical signals produced by the heartbeat of a baby in the womb. And only the heart's electrical signals contain the detailed timing information required to diagnose and treat fetal arrhythmias.

Stethoscopes and ultrasound cannot provide this information because they use sound. Nor is electrocardiography (ECG) useful, because it directly measures the electricity produced by the heart through electrodes taped to the body. However, the baby is electrically insulated from the mother.

Around the twentieth week, Espy says, the baby's sebaceous glands secrete a waxy, white substance called *vernix caseosa*, which covers the baby's skin to protect it from amniotic fluid in the womb. Because the *vernix* is electrically insulating, electrical signals from the baby's heartbeat cannot pass into the mother's body for measurement on her skin. However, the magnetic fields produced by the baby's heartbeat pass easily through the *vernix* and can be measured with FMCG. Although in principle ECG could be used before the *vernix* forms, the fetal heart is then too small to produce a detectable electrical signal.

Espy says that fetal heart conditions detected with FMCG can often be treated before the baby is born, or if surgery is required, the necessary equipment and specialists can be on hand at birth. And unlike other medical diagnostic techniques, FMCG poses no risk to the unborn baby or the mother. X-rays can harm even adults, and amniocentesis is invasive, with potential risk to the fetus. FMCG, however, merely receives the magnetic signals sent out by the baby's heart. FMCG is passive, noninvasive, and harmless.

The team acquired some of its MCG expertise while developing a hand-held battlefield MCG monitor. The device will allow a medic to monitor the heart rhythms of wounded soldiers without moving them or removing their clothing. The monitor can be portable because the heart's magnetic fields above the chest are about 100 to 1,000 times stronger than the brain's magnetic fields above the skull. Using advanced SQUID-sensor designs and ambient-field cancellation techniques, the team has built a hand-held MCG monitor that needs no shielding at all. The SQUID can be cooled by liquid nitrogen or an electric cryocooler. The same technology could also be incorporated in a small monitor for clinical use in a doctor's office.

From measuring brain currents and heartbeats to inspecting welds in nuclear weapons, the Los Alamos SQUID team is exploring the potential of tiny magnetic fields to solve a host of medical and defense problems. ■

SQUID Team's Unusual Origins

Research on SQUID magnetometry at Los Alamos has its roots in personal frustration. In the mid-1980s, the wife of Lab physicist Ed Flynn suffered a heart attack that left her in a coma, and she died eighteen months later. Frustrated that doctors could not determine the condition of her brain during that time, Flynn sought and received support from John Browne—then the Physics Division Leader—to investigate the use of SQUIDs for imaging brain function. Gathering experts in cryogenics and the life sciences from around the Laboratory, Flynn formed a neuromagnetism group for this purpose. Initial measurements with a single SQUID were followed by increasingly sophisticated multi-SQUID systems. A major breakthrough was the group's development of the superconducting-shell concept.

In time, Flynn's group expanded, eventually becoming the Biological and Quantum Physics Group—the SQUID team's current home. Headed by Bob Kraus, the team consists of Michelle Espy, Andrei Matlachov, Petr Volegov, Carl Kumaradas, Chris Carr, Val Armijo, Shaun Newman, Walter Roybal, and Jonatan Mattson. The team is using SQUIDs for a wide range of applications. Most recently, it has begun designing experiments to use a SQUID to measure the neutron's electric dipole moment, measurements that could have a major impact on theories of elementary particles and cosmology. The research Flynn began has made lasting contributions not only to neuroscience and other areas of biophysics but also to defense science and basic physics.

The Researchers

Bob Kraus has a Ph.D. in nuclear chemistry from Oregon State University. He first came to Los Alamos as a postdoctoral research fellow in 1984, becoming a technical staff member in 1986 and joining the biophysics group in 1994. Kraus is currently the SQUID team leader and the principal investigator for the MEG project.

Michelle Espy first came to Los Alamos as a graduate student in 1991. After completing a Ph.D. in nuclear physics at the University of Minnesota, she began postdoctoral research in the Los Alamos biophysics group in 1996 and became a technical staff member in 1999.

John Flower