

# New Tools for Imaging the Brain

FEATURE

by Eric J. Lerner

Researchers are obtaining clues to the physical nature of consciousness

For nearly a generation, computer scientists and biochemists shaped the study of the human brain. Researchers from both disciplines sought to understand the mechanism of thought and brain function at the microlevel, emphasizing, as the most critical element, the interaction among individual neurons in a biochemical environment. But in recent years, new models have focused on how the brain functions as a whole, with millions or billions of neurons working in concert to produce such still-mysterious phenomena as intelligence and consciousness.

Increasingly, these new models have relied on ideas derived from physics, such as chaos theory and nonlinear dynamics. At the same time, the sophisticated use of physics has resulted in new tools to map the functioning brain in three dimensions, providing a growing flow of data to test and elaborate new models. In the process, researchers are obtaining clues to the physical nature of consciousness for the very first time.

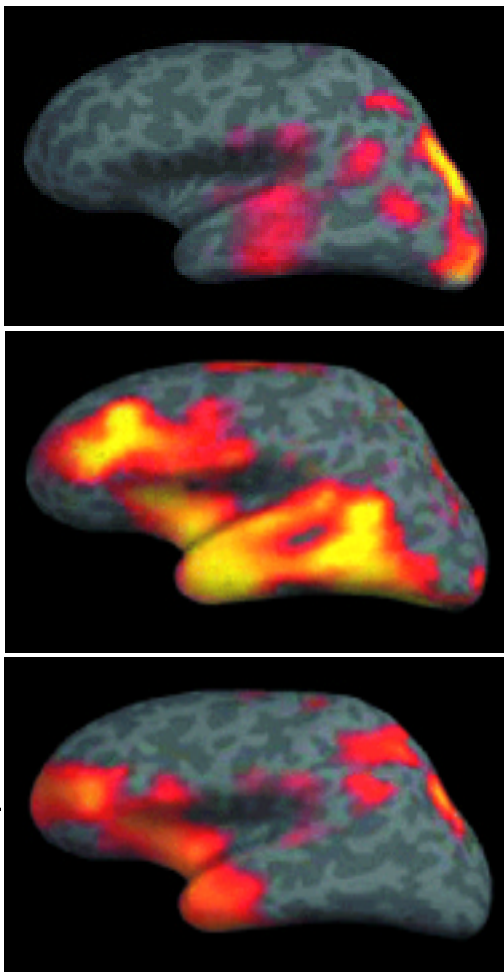
Until five years ago, the dominant model of the brain was hierarchical, focused on individual neurons, and patterned on the way digital computers work. In brief, the hypothesis held that single neurons operated by detecting features in the environment. At the base level, individual neurons in the optic region of the brain, for example, would detect simple features, such as lines and edges. At the next level, higher-order neurons integrated data from the hundreds of lower-order neurons to which each was linked to

detect more sophisticated features—a red ball, for example, or green squares. At the highest level, cardinal neurons would integrate sensations of higher-order neurons to recognize concepts such as “Grandmother’s face.”

The hypothesis had problems from the start. First, there was the “binding” problem: How could information obtained by different means be bound together into a single perception? How could the neuron that recognized Grandmother’s face, the neuron that recognized her voice, and the one that recognized the word “Grand-

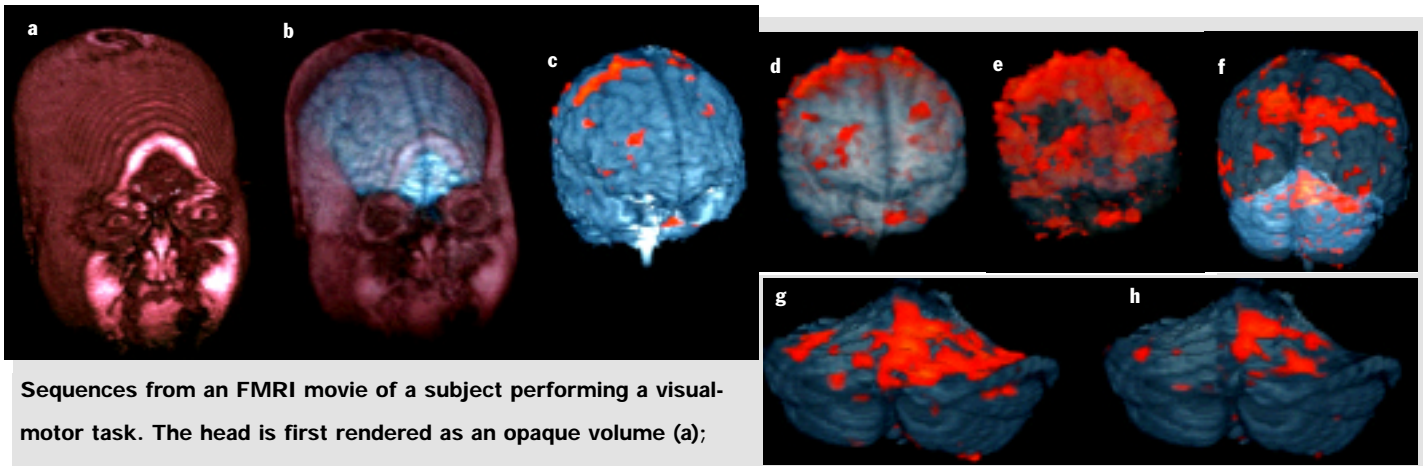
mother” all work together to create a single perception of Grandmother? Closely linked with these problems was the question of how billions of individual neurons could produce a single consciousness.

A competing model, one now becoming dominant, contends that the brain stores and processes information only when millions of neurons work together, with their electric potentials correlated or synchronized in patterns at various frequencies. Large-scale electric fields produced by the brain and recorded as electroencephalograms (EEGs) can only be produced by the cooperative actions of many neurons, the theory holds. These cell assemblies, as they are called, are not anatomical entities. Rather, they are temporary functional collections of neurons scattered across wide areas of the brain, whose firings are correlated or synchronized at a given frequency. “The brain works by harnessing together ever-shifting neuronal networks [assemblies of neurons], which work in a complex pattern of synchrony, like musicians in an orchestra,” says Rafael Yuste, professor of biology at Columbia University. In this view, the



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**FMRI is used to map the brain activity of a subject who reads a novel word from a monitor and must decide if the object or animal it represents is more than a foot long—70, 170, and 240 ms after stimulus onset.**



Sequences from an FMRI movie of a subject performing a visual-motor task. The head is first rendered as an opaque volume (a); the skull changes from translucent (b) to transparent to show activation on the cerebral cortex (c); from a posterior view, the cerebrum (d) fades out to leave only the cerebellum (f) performing a complex planning task (g) and a simple task (h).

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process of thought is the symphony produced by the brain as a whole.

Because this new model emphasizes the nonlinear interactions of many neurons through their electric and magnetic fields and accompanying electric currents, the tools and concepts of physics have emerged as central to understanding the functioning of the brain. In particular, scientists have turned to physics-derived concepts such as chaos theory to understand brain dynamics and to develop new ways of studying the brain.

In a many-body system that has nonlinear interactions, chaos theory can mathematically describe the system's behavior as it varies in a complex, unpredictable, but not random way. In particular, the EEG potential measured at a single point can be described by a certain number of chaotic dimensions—the more dimensions, the more complexly the EEG varies over time. Scientists have found that changes in the number of chaotic dimensions can be used as a highly sensitive measurement of brain activity.

For example, recent studies by Claude Tomberg of the University of Brussels showed that the number of dimensions increased from around 5.5 to around 6.8 in a specific region of the brain when subjects switched from resting to silent reading. Other studies at the California Institute of Technology and the Korea Advanced Institute of Science and Technology (Taejon, Korea) found that the number of chaotic dimensions decreased when people listened to music they perceived as pleasant, but rose for unpleasant music or noise.

Such studies contribute powerful evidence to support the new model of collective nonlinear action of the brain, because uncoordinated action of neurons would produce an EEG with random noise or simple periodicity—as a digital computer does—not a changing chaotic signal. Thus, the EEG is not just background noise but a com-

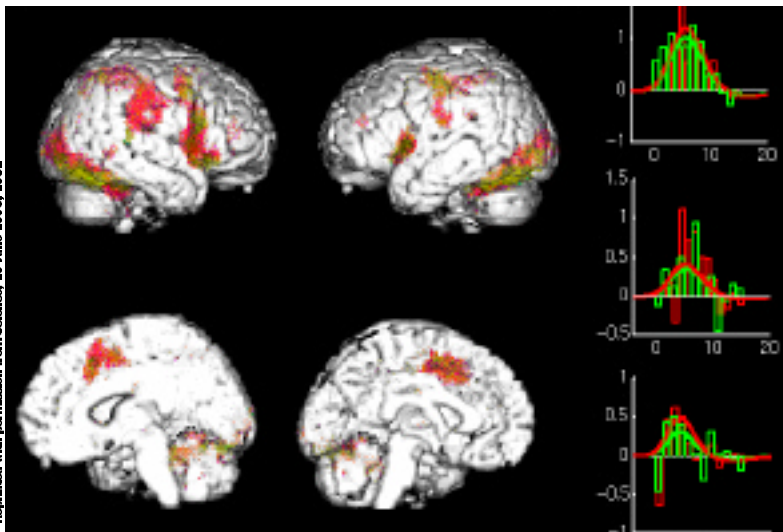
plex signal that links the collective activity of the neurons into a coherent whole.

Because the electric fields measured by EEGs are crucial to understanding brain function, researchers have recently attempted to achieve high spatial resolution with EEGs and especially to use the two-dimensional EEG recorded on the scalp to determine the three-dimensional fields in the brain. At the simplest level, this has meant replacing the traditional one or two dozen electrodes with 100-electrode sets, which reduces the spacing on the scalp between electrodes to about 2.5 cm. Nevertheless, the brain's electric fields are severely distorted and blurred as they pass through the skull.

Recently, biophysicists have developed what is called finite-element deblurring to address this problem. In this technique, a conventional magnetic resonance image (MRI) is made of a person's scalp, skull, and brain. This image is then used to construct a model—consisting of many small tetrahedral units—of the head's electrical characteristics. Assigning a conductivity value to each type of tissue yields a conductivity map that is used to derive the electric potential in the brain from that measured on the scalp.

Unfortunately, this technique still gives only the potential at the surface of the brain, and these potentials provide no unique solution that identifies the locations of charge and current within the brain. In the past, researchers used simplifying assumptions to derive three-dimensional locations of current, such as the assumption that the sources were simple dipoles oscillating at a given frequency. However, these hypotheses tended to be arbitrary and produced too simple a picture of the brain's actual functioning.

To resolve the ambiguity in three-dimensional mapping, additional data are needed. One new approach is to simultaneously record functional MRI (fMRI) data—which measures the flow rate of blood in the brain and thus the activity of neurons—and EEG data. The fMRI data give direct three-dimensional locations of the most active



**When different images are presented to our two eyes, they compete for perceptual dominance so that each image is visible in turn for a few seconds while the other is suppressed. FMRI can indicate which areas of the brain are associated with the two conditions (red and green).**

regions of the brain, but without the high time resolution of the EEG. Constraining the EEG sources to the boundaries shown by the FMRI gives a more detailed picture in both time and space (see figures).

It is not enough, however, to simply map locations where the brain is active at any given time. Most of the brain's function requires the involvement of more than one region, and it is important to know how and in what way the various regions act together. One relatively new and powerful technique for doing this is evoked potential covariance (EPC).

In this approach, the reaction of a human or animal to a specific stimulus is recorded with multi-electrode arrays, and the correlation or covariance between each pair of electrodes is calculated. Researchers have learned that when two separate populations of neurons interact, their electric potentials come into phase, at least at some frequencies. By mapping which sets of neurons are correlated with other sets, EPC can identify momentary long-distance connections within the brain.

Such correlation maps can detect subtle change in brain function. For example, recent experiments at EEG Systems Laboratory, a San Francisco, California-based company, have shown that far more extensive correlations occur when people are prepared to give the "correct" response to a stimulus than when they realize that the response they anticipate giving is "wrong" and quickly have to change it. Such research will help illuminate how conscious intention is transformed into action. "We are currently applying the same technology to studying the onset of epileptic seizures," says Alan Gevins of EEG Systems. "So far, the results look very promising."

## The magnetic brain

Although an infinite number of current and charge arrangements can produce a given pattern of potentials at the surface of the brain, this ambiguity does not apply when the magnetic field vector is measured at many points on the brain's surface. The three-dimensional

information provided by the magnetic field vectors as they vary in time can, in principle, provide a unique solution.

Measuring the brain's magnetic field with magnetoencephalography (MEG) became common with the introduction of Josephson junction detectors. In general, however, only a single component of the field was measured, which left the same ambiguities as with the EEG. But in work performed in 1999 at Kyoto Prefecture University of Medicine (Kyoto, Japan), researchers used 43 sets of three-dimensional magnetometers, each with three perpendicular coils, to measure the magnetic vectors over the entire skull. They demonstrated—in laboratory simulations in which the source of the current was known—that the magnetometer array could locate multiple current sources with an accuracy of 0.5 mm. Such precision is much better than that obtainable with conventional single-component MEG. The Kyoto team used a mathematical technique called spatial filters to convert the magnetometer data to current-source locations.

When the three-dimensional MEG technique was applied to humans in simple visual response experiments, it produced complete, detailed maps of current flow within the brain with high spatial resolution and a time resolution of just milliseconds. Such simultaneous three-dimensional images of high spatial and time resolution can give brain researchers a powerful new tool for understanding brain dynamics.

## Brain microscopy

The highest spatial resolutions in brain mapping are now being obtained with FMRI, which can map changes in blood flow to active regions of the brain. Although these changes take a few seconds to occur, and so do not yield the higher time resolution of EEG and MEG, FMRI allows researchers not just to observe current flow but to locate the portions of the brain that generate the oscillating currents.

The FMRI technique works by measuring the relaxation times of the spins of atomic nuclei—the time it takes nuclei, whose spins are flipped by radio-frequency pulses, to relax back to a random orientation. One of the more sensitive FMRI techniques, flow-sensitive inversion recovery, measures relaxation times in flowing blood. These times are faster when flow is increased because of greater turbulence in the blood. At high magnetic fields (up to 4 T), this technique can deliver spatial resolution of less than 1 mm in three dimensions. As in all MRI imaging, the locations in three-dimensional space are quite unambiguous.

In one recent human study at the University of Minnesota, neuroscientists observed the separate, millime-

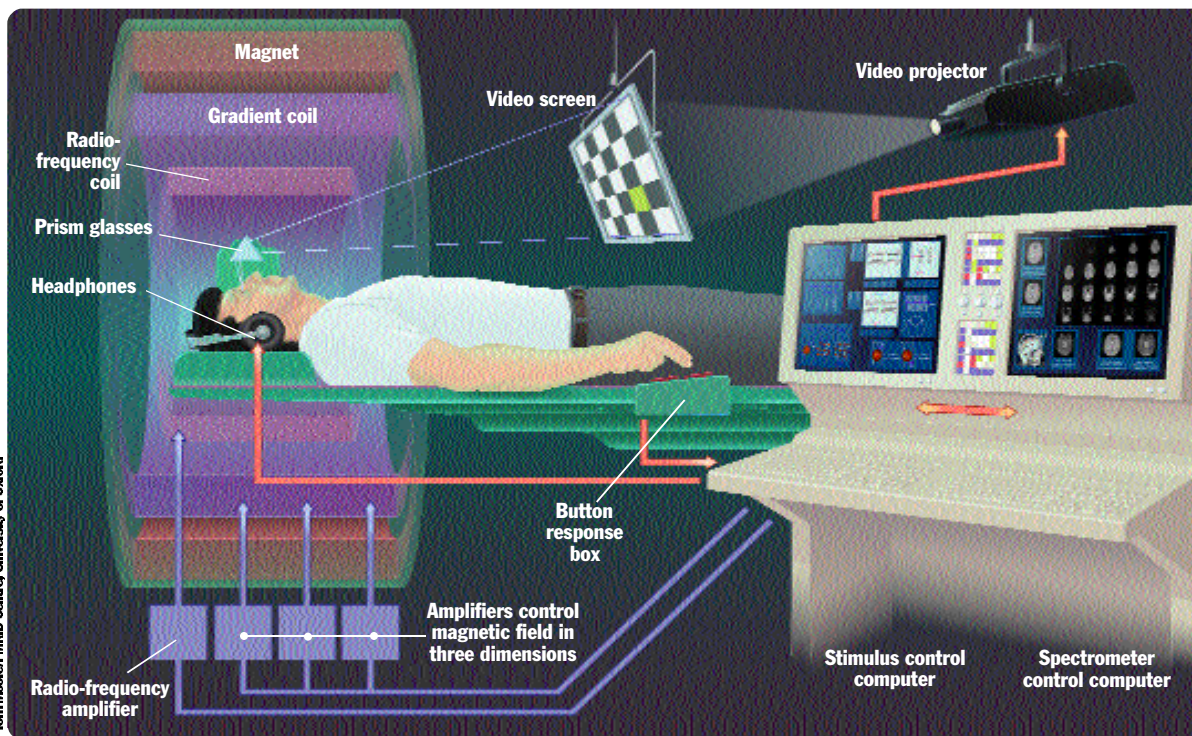
ter-wide ocular dominance columns in the visual cortex as they processed alternating inputs from the left and right eye. This fine degree of resolution opens up the possibility of mapping brain responses at the millimeter scale, where scientists believe that neuron assemblies operate almost as single units.

## Consciousness

With these newly developed tools, brain researchers are turning their attention to the central mysteries that have long resisted scientific understanding, such as the nature and mechanisms of conscious experience. One problem is distinguishing phenomena associated with states of consciousness, such as changes in EEG or blood flow, from those associated just with sensory inputs or motor outputs. But using fMRI techniques, Erik Lumer and Geraint Rees at University College London took steps to doing just that (see figure p. 20). They had people view a grating with one eye and a face with the other. The researchers could thereby induce binocular rivalry, a condition in which the image that was consciously perceived switched back and forth on a time scale of several seconds, even though the sensory input presented to the brain remained unchanged. That is, the subject's brain first perceived the grating, then the face, then the grating again, and so on.

The researchers then examined the fMRI images of participants' brains. They looked to see which areas alternated their activity in unison—as they would be expected to do if they were dealing with a changing conscious perception—and which areas were relatively constant, as they would be in dealing with stable sensory input. They found that the prefrontal regions of the brain and a few central areas alternated in step with large areas of the visual cortex near the back of the brain. This indicated that conscious experience requires cooperation and synchronous action among these regions. The nonvisual regions are known from other studies to be critical in short-term memory. Thus, the research implies that the use of such memory to integrate visual events into a larger context is an integral part of producing conscious experience.

Tom Hones/FMRIB Centre, University of Oxford



## Functional Magnetic Resonance Imaging (fMRI)

**F**MRI is a technique for determining which parts of the brain are activated by different types of physical sensation or activity, such as sight, sound, or the movement of a subject's fingers. This "brain mapping" is achieved by setting up an advanced magnetic resonance imaging (MRI) scanner in a special way so that increased blood flow to the activated areas of the brain shows up on functional MRI scans.

In a typical experiment, the subject lies within the magnetic field, and a particular form of stimulation is set up. Then, a series of MRI images of the subject's brain is taken over time. For some of these scans, the stimulus is present, and for others, it is absent. The images can be compared in the two cases to see which parts of the brain were activated by the stimulus.

After the experiment is finished, the images are analyzed. First, they are mathematically transformed to reconstruct them into "real space," so that they look like brains. A series of tools make other corrections. In the final image, those parts of the brain that were activated by the experiment are bright. This activation image can be rendered in color and three dimensions, and the rendering calculated from any angle.

The principles of MRI were explained in *The Industrial Physicist* (March 1996, p. 23) and are demonstrated in the figure above. MRI generates cross-sectional images of the body by using nuclear magnetic resonance (NMR). The body is positioned in a strong magnetic field, which polarizes the magnetic moments of protons in water by forcing their spins into one of two possible orientations. A radio-frequency field forces spin transitions that create signals, which are detected by a receiving coil. This procedure can be adjusted to examine only a thin, predetermined slice of the body. The process creates a data matrix in which each element represents an NMR signal from a single, localized volume element. A two-dimensional display of this matrix creates a human-readable image of the selected slice.

The figure shows some of the items that typically are added in an fMRI experiment. The subject wears headphones and prism glasses to receive audio and visual stimuli and has a button response box.

Such high-resolution tools for studying the brain as a biophysical system are just starting to emerge, and researchers are beginning to learn how to use them and link their results. So the next several years will likely see rapid growth in the understanding of how the human brain functions. 