A Life-Size Human Brain

Each of the five senses activates a separate area of the cerebral cortex, the sheet of neurons that makes up the outer layer of the brain’s hemispheres. This brain, shown in actual size, is a computer reconstruction based on data from magnetic resonance imaging (MRI). Approximate locations of the primary sensory areas are shown in color. Most of the activity takes place within convolutions that cannot be seen from the surface of the brain.
We can recognize a friend instantly—full-face, in profile, or even by the back of his head. We can distinguish hundreds of colors and possibly as many as 10,000 smells. We can feel a feather as it brushes our skin, hear the faint rustle of a leaf. It all seems so effortless: we open our eyes or ears and let the world stream in.

Yet anything we see, hear, feel, smell, or taste requires billions of nerve cells to flash urgent messages along linked pathways and feedback loops in our brains, performing intricate calculations that scientists have only begun to decipher.

“You can think of sensory systems as little scientists that generate hypotheses about the world,” says Anthony Movshon, an HHMI investigator at New York University. Where did that sound come from? What color is this, really? The brain makes an educated guess, based on the information at hand and on some simple assumptions.
When you look at the illustration below, for instance, you see an X made of spheres surrounded by cavities. But if you turn the page upside down, all the cavities become spheres, and vice versa. In each case, the shapes seem real because “your brain assumes there is a single light source—and that this light comes from above,” says Vilayanur Ramachandran, a professor of neuroscience at the University of California, San Diego. As he points out, this is a good rule of thumb in our sunlit world.

To resolve ambiguities and make sense of the world, the brain also creates shapes from incomplete data, Ramachandran says. He likes to show an apparent triangle that was developed by the Italian psychologist Gaetano Kanizsa. If you hide part of this picture, depriving the brain of certain clues it uses to form conclusions, the large white triangle disappears.

We construct such images unconsciously and very rapidly. Our brains are just as fertile when we use our other senses. In moments of anxiety, for instance, we sometimes “hear things” that are not really there. But suppose a leopard approached, half-hidden in the jungle—then our ability to make patterns out of incomplete sights, sounds, or smells could save our lives.

Everything we know about the world comes to us through our senses. Traditionally, we were thought to have just five of them—vision, hearing, touch, smell, and taste. Scientists now recognize that we have several additional kinds of sensations, such as pain, pressure, temperature, joint position, muscle sense, and movement, but these are generally included under “touch.” (The brain areas involved are called the “somatosensory” areas.)

Although we pay little attention to them, each of these senses is precious and almost irreplaceable—as we discover, to our sorrow, if we lose one. People usually fear blindness above all other disabilities. Yet deafness can be an even more severe handicap, especially in early life, when children learn language. This is why Helen Keller’s achievements were so extraordinary. As a
result of an acute illness at the age of 19 months, she lost both vision and hearing and sank into a totally dark, silent universe. She was rescued from this terrible isolation by her teacher, Anne Sullivan, who managed to explain, by tapping signs into the little girl’s palm, that things have names, that letters make up words, and that these can be used to express wants or ideas. Helen Keller later grew into a writer (her autobiography, The Story of My Life, was published while she was still an undergraduate at Radcliffe College) and a well-known advocate for the handicapped. Her remarkable development owed a great deal to her determination, her teacher, and her family. But it also showed that when a sense (or two, in Helen Keller’s case) is missing, another sense (in her case, touch) may be trained to make up for the loss, at least in part.

What we perceive through our senses is quite different from the physical characteristics of the stimuli around us. We cannot see light in the ultraviolet range, though bees can, and we cannot detect light in the infrared range, though rattlesnakes can. Our nervous system reacts only to a selected range of wavelengths, vibrations, or other properties. It is limited by our genes, as well as our previous experience and our current state of attention.

What draws our attention, in many cases, is change. Our senses are finely attuned to change. Stationary or unchanging objects become part of the scenery and are mostly unseen. Customary sounds become background noise, mostly unheard. The feel of a sweater against our skin is soon ignored. Our touch receptors, “so alert at first, so hungry for novelty, after a while say the electrical equivalent of ‘Oh, that again,’ and begin to doze, so we can get on with life,” writes Diane Ackerman in A Natural History of the Senses.

If something in the environment changes, we need to take notice because it might mean danger—or opportunity. Suppose an insect lands on your leg. Instantly the touch receptors on the affected leg fire a message that travels through your spinal column and up to your brain. There it crosses into the opposite hemisphere (the right hemisphere of the brain receives signals from the left side of the body, and vice versa) to alert brain cells at a particular spot on a sensory map of the body.

This map extends vertically along a strip of cerebral cortex near the center of the skull. The cortex—a deeply wrinkled sheet of neurons, or nerve cells, that covers the two hemispheres of the brain—governs all our sensations, movements, and thoughts.

The sensory map in humans was originally charted by the Canadian neurosurgeon Wilder Penfield in the 1930s. Before operating on patients who suffered from epilepsy, Penfield stimulated different parts of their brains with electrodes to locate the cells that set off their attacks. He could do this while the patients were awake, since the brain does not feel what is happening to it. In this way, Penfield soon learned exactly where each part of the body that was touched or moved was represented in the brain, as he showed in his famous “homunculus” cartoons of the somatosensory

The black line in the back seems much longer than the one in the front because your brain assumes it is seeing the effects of perspective. Take a ruler to find out for yourself.
Brains of animals. In the 1930s and 1940s, scientists applied electrodes to the surface of the brain or placed them on the skull of humans to study “evoked responses,” the changing rhythms of electrical signals in the brain in response to specific stimuli such as light or sound. Unfortunately, these signals from billions of brain cells proved almost impossible to unscramble.

When extremely thin microelectrodes became available in the late 1950s, researchers implanted them into the brains of living animals to spy on the activity of individual cells. Sharp popping sounds could be heard as specific neurons fired, and the scientists tried to find out what provoked these electrical discharges.

Ever since humans have wondered about where their thoughts came from, they have tried to understand the senses. Much was learned from observing the results of head injuries and tumors, as well as by dissecting postmortem human brains and the brains of animals. In the 1930s and 1940s, scientists applied electrodes to the surface of the brain or placed them on the skull of humans to study “evoked responses,” the changing rhythms of electrical signals in the brain in response to specific stimuli such as light or sound. Unfortunately, these signals from billions of brain cells proved almost impossible to unscramble.

These famous maps by Wilder Penfield show that each part of the body is represented on two strips of the brain's cerebral cortex, the somatosensory cortex (left), which receives sensations of touch, and the motor cortex (right), which controls movements. Fingers, mouth, and other sensitive areas take up most space on both maps. Penfield called these cross sections the “sensory homunculus” and the “motor homunculus.”

and motor areas.

Surprisingly, these maps do not accurately reflect the size of body parts but rather, their sensitivity. Arms and legs take up very little space, despite their length. The face and hands, which have greater sensitivity, are given more space—especially the tips of the fingers. Nevertheless, the signal that a mosquito has landed on the back of your left leg comes through loud and clear. In a fraction of a second, through a decision process that is not yet understood, this signal leads you to swat the insect at just the right place.

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This is how David Hubel and Torsten Wiesel, who were then at Johns Hopkins University, began the groundbreaking
experiments on the visual cortex of cats and monkeys, for which they later won a Nobel prize. They discovered that one neuron in the primary visual cortex at the back of a cat’s brain might fire only when the animal’s eye was exposed to a line at a particular location and angle, while another next to it would fire only in response to a line at a slightly different angle. No one had suspected that these neurons would dissect a scene—and respond to particular elements of it—with such amazing specificity. Hubel and Wiesel’s success led to a general focus on the abilities of single neurons, especially in the visual system.

The past decade has seen an explosion of research on all the senses, partly because of the new tools supplied by molecular biology. Scientists can now analyze sensory neurons far more precisely, down to the level of specific genes and proteins within these neurons. This publication will describe some recent research on three of our senses—vision, hearing, and smell—in which there have been particularly interesting developments.

The visual system, which involves roughly a quarter of the human cerebral cortex, has attracted more research than all the other sensory systems combined. It is also the most accessible of our senses. The retina, a sheet of neurons at the back of the eye that any physician can see through an ophthalmoscope, is the only part of the brain that is visible from outside the skull. Research on the visual system has taught scientists much of what they know about the brain, and it remains at the forefront of progress in the neurosciences.

Research on hearing is also gathering momentum. One group of scientists recently discovered how receptor neurons in the ear—the so-called “hair cells”—respond to sounds. Another group explored how animals use sounds to compute an object’s location in space. This may be a model of similar operations in the auditory system of humans.

The olfactory system, which was almost a total mystery until a few years ago, has become the source of much excitement. The receptor proteins that make the first contact with odorant molecules appear to have been identified with the help of molecular genetics, and researchers are beginning to examine how information about smells is coded in the brain.

The use of molecular biology has enabled scientists to discover just how receptor neurons respond to light, to vibrations in the air, to odorant molecules, or to other stimuli. The receptor neurons in each sensory system deal with different kinds of energy—electromagnetic, mechanical, or chemical. The receptor cells look different from one another, and they exhibit different receptor proteins. But they all do the same job: converting a stimulus from the environment into an electrochemical nerve impulse, which is the common language of the brain (see p. 11). Recently, researchers have uncovered many of the genes and proteins involved in this process of sensory transduction.

From their understanding of this first step on the sensory pathway, researchers have edged up to analyzing how messages about a sensory stimulus travel through the brain to the cerebral cortex and how these messages are coded.

They know that nearly all sensory signals go first to a relay station in the thalamus, a central structure in the brain. The messages then travel to primary sensory areas in the cortex (a different area for each sense), where they are modified and sent on to “higher” regions of the brain. Somewhere along the way, the brain figures out what the messages mean.

Many factors enter into this interpretation, including what signals are coming in from other parts of the brain, prior learning, overall goals, and general state of arousal. Going in the opposite direction, signals from a sensory area may help other parts of the brain maintain arousal, form an image of where the body is in space, or regulate movement.

These interactions are so complex that focusing on the activity of single neurons—or even single pathways—is clearly not enough. Researchers are now asking what the central nervous system does with all the information it gets from its various pathways.

In more authoritarian times, scientists believed that the brain had a strictly hierarchical organization. Each relay station was supposed to send increasingly complex information to a higher level until it reached the very top, where everything would somehow be put together. But now “we are witnessing a
senses evolved “to help animals solve vital problems...”

paradigm shift,” says Terrence Sejnowski, an HHMI investigator who directs the Computational Neurobiology Laboratory at the Salk Institute in La Jolla, California. Instead of viewing the cortex as “a rigid machine,” scientists see it as “a dynamic pattern-processor and categorizer” that recognizes which categories go together with a particular stimulus, as best it can, every step of the way. “There is no ‘grandmother cell’ at the top that responds specifically to an image of Grandma,” Sejnowski emphasizes. “We recognize a face by how its features are put together in relation to one another.”

Sejnowski, a leader in the new field of computational neuroscience, studies neural networks in which the interaction of many neurons produces surprisingly complex behavior. He recently designed a computer model of how such a network might learn to “see” the three-dimensional shape of objects just from their shading, without any other information about where the light came from. After being “trained” by being shown many examples of shaded shapes, the network made its own generalizations and found a way to determine the objects’ curvature.

Vision and the other senses evolved “to help animals solve vital problems—for example, knowing where to flee,” says Sejnowski. Large populations of sensory neurons shift and work together in the brain to make this possible. They enable us to see the world in a unified way. They link up with the motor systems that control our actions. These neurons produce an output “that is more than the sum of its parts,” Sejnowski says. Just how they do it is a question for the next century.

Maya Pines, Editor

SPECIAL RECEPTOR CELLS FOR EACH OF THE SENSES

Rod and cone cells in the eye respond to electromagnetic radiation—light.
The ear’s receptor neurons are topped by hair bundles that move in response to vibrations—sound.
Olfactory neurons at the back of the nose respond—and bind—to odorant chemicals.

Taste receptor cells on the tongue and back of the mouth respond—and bind—to chemical substances.
Meissner corpuscles are specialized for rapid response to touch, while free nerve endings bring sensations of pain.

VISION
HEARING
SMELL
TASTE
TOUCH

Rod Cone

Free Nerve Ending

Meissner Corpuscle
For centuries, scientists dreamed of being able to peer into a human brain as it performs various activities—for example, while a person is seeing, hearing, smelling, tasting, or touching something. Now several imaging techniques such as PET (positron emission tomography) and the newer fMRI (functional magnetic resonance imaging) make it possible to observe human brains at work.

The PET scan on the left shows two areas of the brain (red and yellow) that become particularly active when volunteers read words on a video screen: the primary visual cortex and an additional part of the visual system, both in the left hemisphere.

Other brain regions become especially active when subjects hear words through earphones, as seen in the PET scan on the right.

To create these images, researchers gave volunteers injections of radioactive water and then placed them, head first, into a doughnut-shaped PET scanner. Since brain activity involves an increase in blood flow, more blood—and radioactive water—streamed into the areas of the volunteers’ brains that were most active while they saw or heard words. The radiation counts on the PET scanner went up accordingly. This enabled the scientists to build electronic images of brain activity along any desired “slice” of the subjects’ brains. The images below were produced by averaging the results of tests on nine different volunteers.
Much excitement surrounds a newer technique, fMRI, that needs no radioactive materials and produces images at a higher resolution than PET. In this system, a giant magnet surrounds the subject’s head. Changes in the direction of the magnetic field induce hydrogen atoms in the brain to emit radio signals. These signals increase when the level of blood oxygen goes up, indicating which parts of the brain are most active.

Since the method is non-invasive, researchers can do hundreds of scans on the same person and obtain very detailed information about a particular brain’s activity, as well as its structure. They no longer need to average the results from tests on different subjects, whose brains are as individual as fingerprints.

The volunteer’s brain is particularly active in an area of her right hemisphere called the fusiform gyrus (arrow) as she matches one of the two faces at the bottom of the display with the face at the top. This “slice” of her brain is seen as though looking through her face.

**A GIANT MAGNET REVEALS THE BRAIN’S ACTIVITY**

Much excitement surrounds a newer technique, fMRI, that needs no radioactive materials and produces images at a higher resolution than PET. In this system, a giant magnet surrounds the subject’s head. Changes in the direction of the magnetic field induce hydrogen atoms in the brain to emit radio signals. These signals increase when the level of blood oxygen goes up, indicating which parts of the brain are most active.

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*Here a normal volunteer prepares for a fMRI study of face recognition. She will have to match one of the two faces at the bottom of the display with the face at the top. James Haxby, chief of the section on functional brain imaging at the National Institute of Mental Health in Bethesda, Maryland, adjusts the mirror that will allow her to see the display from inside the magnet.*
David Corey and James Hudspeth, who played major roles in discovering how the ear's hair cells respond to sound, discuss the cells' conversion of vibrations into nerve signals. In the background, a slide shows hair cells in the inner ear.
Locating a Mouse by Its Sound

by Jeff Goldberg
While some scientists investigate the mystery of how we hear from the bottom up, beginning with the ear’s sound receptors, others search for answers from the top down, mapping networks of auditory neurons in the brain in an effort to understand how the brain processes sounds.

At Caltech in the mid-1970s, Masakazu (“Mark”) Konishi began studying the auditory system of barn owls in an effort to resolve a seemingly simple question: Why do we have two ears?

While most sounds can be distinguished quite well with one ear alone, the task of pinpointing where sounds are coming from in space requires a complex process called binaural fusion, in which the brain must compare information received from each ear, then translate subtle differences into a unified perception of a single sound—say a dog’s bark—coming from a particular location.

Konishi, a zoologist and expert on the nervous system of birds, chose to study this process in owls. The ability to identify where sounds are coming from based on auditory cues alone is common to all hearing creatures, but owls—especially barn owls—excel at the task. These birds exhibit such extraordinary sound localization abilities that they are able to hunt in total darkness.

In total darkness, a barn owl swoops down on a mouse.
Working with Eric Knudsen, who is now conducting his own research on owls at Stanford University, Konishi undertook a series of experiments on owls in 1977 to identify networks of neurons that could distinguish sounds coming from different locations. He used a technique pioneered by vision researchers, probing the brains of anesthetized owls with fine electrodes. With the electrodes in place, a remote-controlled sound speaker was moved to different locations around the owl’s head along an imaginary sphere. As the speaker moved, imitating sounds the owl would hear in the wild, the investigators recorded the firing of neurons in the vicinity of the electrodes.

Over the course of several months, Konishi and Knudsen were able to identify an area in the midbrain of the birds containing cells called space-specific neurons—about 10,000 in all—which would fire only when sounds were presented in a particular location. Astonishingly, the cells were organized in a precise topographic array, similar to maps of cells in the visual cortex of the brain. Aggregates of space-specific neurons, corresponding to the precise vertical and horizontal coordinates of the speaker, fired when a tone was played at that location.

“Regardless of the level of the sound or the content of the sound, these cells always responded to the sources at the same place in space. Each group of cells across the circuit was sensitive to sound coming from a different place in space, so when the sound moved, the pattern of firing shifted across the map of cells,” Knudsen recalls.

The discovery of auditory brain cells that could identify the location of sounds in space quickly produced a new mystery. “The
lens of the eye projects visual space onto receptors on a 2-dimensional sheet, the retina, and the optic nerve fibers project the same spatial relationships to the brain,” says Konishi. “But in the auditory system, only the frequency of sound waves is mapped on the receptor layer, and the auditory nerve fibers project this map of frequency to the brain. How can the brain create a map of auditory space, based only on frequency cues?”

The answer, Konishi believes, may shed light on how the brain and the auditory system process all sounds.

To enable the brain to process efficiently the rapid stream of impulses emanating from the hair cells in the ear, the auditory system must first filter out simple, discrete aspects of complex sounds. Information about how high- or low-pitched a sound is, how loud it is, and how often it is heard is then channeled along separate nerve pathways to higher-order processing centers in the brain, where millions of auditory neurons can compute the raw data into a recognizable sound pattern.

This filtering process begins with the hair cells, which respond to different frequencies at different locations along the basilar membrane. Hair cells at the bottom of the basilar membrane respond more readily when they detect high-frequency sound waves, while those at the top are more sensitive to low-frequency sounds. David Corey compares the arrangement to the strings of a grand piano, with the high notes at the base of the cochlea, where the basilar membrane is narrow and stiff, and the bass notes at the apex, where the membrane is wider and more flexible.

Hair cells also convey basic information about the intensity and duration of sounds. The louder a sound is at any particular frequency, the more vigorously hair cells tuned to that frequency respond, while their signaling pattern provides information about the timing and rhythm of a sound.

Konishi hypothesized that such timing and intensity information was vital for sound localization. So he placed microphones in the ears of owls to measure precisely what they were hearing as the portable loudspeaker rotated around their head. He then recorded the differences in time and intensity as sounds reached each of the owl’s ears. The differences are very slight. A sound that originates at the extreme left of the animal will arrive at the left ear about 200 microseconds (millionths of a second) before it reaches the right ear. (In humans, whose sound localization abilities are keen but not on a par with those of owls, the difference between a similar sound’s time of arrival in each ear would be about three times greater.)

As the sound source was moved toward the center of the owl’s head, these interaural time differences diminished, Konishi observed. Differences in the intensity of sounds entering the two ears occurred as the speaker was moved up and down, mostly because the owl’s ears are asymmetrical—the left ear is higher than eye level and points downward, while the right ear is lower and points upward.

Based on his findings, Konishi delivered signals separated by various time intervals and volume differences through tiny earphones inserted into the owls’ ear canals. Then he observed how the animals responded. Because owls’ eyes are fixed in their sockets and cannot rotate, the animals turn quickly in the direction of a sound, a characteristic movement. By electronically monitoring these head-turning...
movements, Konishi and his assistants showed that the owls would turn toward a precise location in space corresponding to the interaural time and intensity differences in the signals. This suggested that owls fuse the two sounds that are delivered to their two ears into an image of a single source—in this case, a phantom source.

“When the sound in one ear preceded that in the other ear, the head turned in the direction of the leading ear. The longer we delayed delivering the sound to the second ear, the further the head turned,” Konishi recalls.

Next, Konishi tried the same experiment on anesthetized owls to learn how their brains carry out binaural fusion. Years earlier, he and Knudsen had identified space-specific neurons in the auditory area of the owl’s midbrain that fire only in response to sounds coming from specific areas in space. Now Konishi and his associates found that these space-specific neurons react to specific combinations of signals, corresponding to the exact direction in which the animal turned its head when phantom sounds were played. “Each neuron was set to a particular combination of interaural time and intensity difference,” Konishi recalls.

Konishi then decided to trace the pathways of neurons that carry successively more refined information about the timing and intensity of sounds to the owl’s midbrain. Such information is first processed in the cochlear nuclei, two bundles of neurons projecting from the inner ear. Working with Terry Takahashi, who is now at the University of Oregon, Konishi showed that one of the nuclei in this first way station signals only the timing of each frequency band, while the other records intensity. The signals are then transmitted to two higher-order processing stations before reaching the space-specific neurons in the owl’s midbrain.

One more experiment proved conclusively that the timing and intensity of sounds are processed along separate pathways. When the researchers injected a minute amount of local anesthetic into one of the

CAN FUNCTIONAL MRI TELL WHETHER A PERSON IS HEARING MUSIC OR JUST MEANINGLESS CLICKS?

Parts of a volunteer’s brain were activated (white box on left of first picture) when he heard a series of sharp but meaningless clicks while inside a fMRI magnet at Massachusetts General Hospital. Some of the same areas became much more active and several new areas were activated as well (square box on right of second picture) when he listened to instrumental music, reflecting the richer meaning of the sounds.
cochlear nuclei (the magnocellular nucleus), the space-specific neurons higher in the brain stopped responding to differences in interaural time, though their response to differences in intensity was unchanged. The converse occurred when neurons carrying intensity information were blocked.

“I think we are dealing with basic principles of how an auditory stimulus is processed and analyzed in the brain. Different features are processed along parallel, almost independent pathways to higher stations, which create more and more refined neural codes for the stimulus,” says Konishi. “Our knowledge is not complete, but we know a great deal. We are very lucky. The problem with taking a top-down approach is that often you find nothing.”

Konishi has been able to express the mechanical principles of the owl’s sound localization process as a step-by-step sequence. He has collaborated with computer scientists at Caltech in developing an “owl chip” that harnesses the speed and accuracy of the owl’s neural networks for possible use in computers.

At Stanford University, Eric Knudsen has recently been conducting experiments on owls fitted with prism spectacles to determine whether distortions in their vision affect their sound localization abilities. Despite their exceptionally acute hearing, he has found, the owls trust their vision even more. When they wear distorting prisms, their hunting skills deteriorate over a period of weeks as their auditory systems try to adapt to the optical displacement of the prisms. “The visual system has ultimate control and basically dictates how the brain will interpret auditory localization cues,” Knudsen says.

He is also examining a particular network of neurons in the animals’ brains where he believes auditory and visual system signals converge. “This network makes it possible for the owls to direct their eyes and attention to a sound once it’s heard,” Knudsen explains. His research is part of a new wave of studies that focus not just on single sensory pathways, but on how the brain combines information it receives from many different sources.

### Help from a Bat

Perhaps the finest achievement in sound processing is the ability to understand speech. Since this is a uniquely human trait, it would seem difficult to study in animals. Yet a researcher at Washington University in St. Louis believes it can be examined—by working with bats.

Bats navigate and locate prey by echolocation, a form of sonar in which they emit sound signals of their own and then analyze the reflected sounds. Nobuo Suga, who has spent nearly 20 years investigating the neural mechanisms used by bats to process the reflected signals, is convinced that such research can shed light on the understanding of human speech.

When Suga slowed down recordings of the high-frequency, short-duration sounds that bats hear, he found that the sounds’ acoustic components were surprisingly similar to those of mammalian communication, including human speech. There were some constant frequencies and noise bursts, not unlike vowel and consonant sounds, as well as frequency-modulated components that were similar to those in combinations of phonemes such as “papa.”

Each of these acoustic elements is processed along a distinct pathway to higher-order neurons, which combine and refine different aspects of the sonar pattern in much the same way that space-specific neurons combine the timing and intensity cues of sound signals.

Suga also identified maps of neurons in the bats’ auditory cortex which register slight variations in these components of sound. Humans may use similar maps to process the basic acoustic patterns of speech, though speech requires additional, higher-level mechanisms, he points out.

“The ability to recognize variations in sound is what enables us to understand each other. No two people pronounce vowels and consonants in exactly the same way, but we are able to recognize the similarities,” says Suga. He believes that neuronal maps may also play a role in human voice recognition—the ability to recognize who is speaking as well as what is being said.
Messages from the senses travel so swiftly through the brain that imaging machines such as PET and fMRI cannot keep up with them. To track these messages in real time, scientists now use faster methods—electrical recording techniques such as MEG (magnetoencephalography) or EEG (electroencephalography). These techniques rely on large arrays of sensors or electrodes that are placed harmlessly on the scalp to record the firing of brain cells almost instantaneously. Their data are then combined with anatomical information obtained by structural MRI scans.

One of the first experiments in which structural MRI was used jointly with MEG produced a three-dimensional map of the areas of the brain that are activated by touching the five fingers of one hand (below). A New York University research team headed by Rodolfo Llinás found this map to be distorted in the brain of a patient who had two webbed fingers since birth. A few weeks after the man’s fingers were separated by surgery, however, parts of his brain reorganized and the map became almost normal.

Each of the color-coded areas in this combined MRI/MEG image of the brain responds to the touch of a different finger of the right hand.
The rapidly-shifting patterns of activity in the six images below reflect what goes on in the brain of a woman who is looking at a letter on a screen during a test at the EEG Systems Laboratory, a private research center directed by Alan Gevins in San Francisco. The woman’s task is to decide whether the letter is located in the same place as a letter she has seen before.

In the “low load” test she compares the new letter’s location to a previous one. In the “high load” test she compares the new location to three previous ones, and the brighter colors reflect a higher degree of brain activation.

The images are based on data from 124 recording electrodes positioned in a soft helmet that covered the woman’s head. The scientists used an MRI-derived model of the head to place the recording electrodes.

**MATCHING A LOCATION**

Comparing (High load)  Comparing (Low load)  Updating (High load)

These computer-generated images recreate the electrical signals that flash across the brain of a volunteer during the matching test. A strong electrical signal (first image) sweeps across the frontal cortex of her right hemisphere 320 milliseconds after a new letter has appeared on the screen, as she compares the letter’s location to three locations that she has seen before. The same areas of her brain are activated—but less intensively—in the second image, as she compares a new letter’s location to only one location that she has seen before.

Only 140 milliseconds later, a different set of electrical signals is recorded from the volunteer’s brain and recreated in these images. This time the frontal cortex of her left
of her head to correct for any distortions in electrical transmission that might be caused by variations in the thickness of her skull.

The resulting images clearly show that various areas of the woman’s brain are activated in turn. However, these images are limited to the brain’s surface.

The next generation of imaging technology will use functional MRI in various combinations with MEG and EEG, predicts John Belliveau, director of cognitive neuroimaging at the Massachusetts General Hospital in Cambridge. Functional MRI shows activity deep in the brain with high spatial resolution, but is relatively slow since it is based on the blood-flow response, which takes about 450 milliseconds. “If you do a visual stimulation experiment, four to five different areas may have turned on within that time,” Belliveau says. “We know where those areas are, but we don’t know which one turned on first.” By contrast, EEG’s spatial resolution is relatively poor, but because of its speed it may reveal the sequence of events. His group has already done some EEG recordings right inside the magnet of an fMRI machine, to get simultaneous measurements.

Together, such techniques will offer scientists a glimpse of how information from the senses is processed in different parts of the brain. Building on the studies shown here, the new hybrids may then begin to tackle neural networks. They may help researchers examine how various parts of the brain exchange information and—most intriguing—how sensory information leads to thought.

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**Updating** *(Low load)*

**Rehearsing** *(High load)*

**Rehearsing** *(Low load)*

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hémisphere is activated as she enters the location of the new letter into her working memory. The signals are more intense in the high load than in the low load condition.

After the screen goes blank, the volunteer rehearses the new memory. As the next two images show, this activity produces yet another electrical signal over her right hemisphere. The signal is stronger in the high load than in the low load condition, but in both cases it is maintained until a new letter appears on the screen.