Research News

The Mind Revealed?

Some neuroscientists think that recently discovered oscillations of electrical potential at 40 hertz hold the key to how the brain assembles sense impressions into a single object

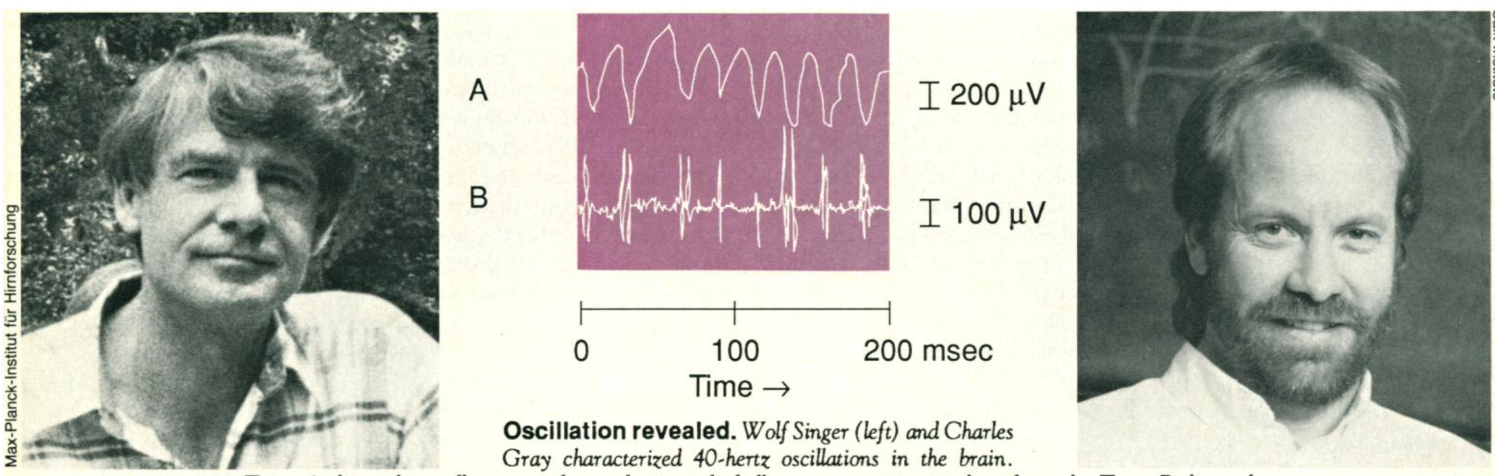
HAS WOLF SINGER UNCOVERED the cellular basis of consciousness? Some neuroscientists think he may have, although Singer himself stops short of such a bold claim.

Last year Singer's research team at the Max Planck Institute for Brain Research in Frankfurt, West Germany, published a dramatic finding.* While recording electrical signals from widely spaced neurons in the brains of cats, they found that the neurons tend to fire synchronous electrical impulses when responding to stimuli that appear to come from the same object. Presented with stimuli that clearly are unrelated, the neurons would also fire, but not in synchrony.

These provocative data have the neuroscience community humming with speculation. Only a few years ago, few neuroscientists would have believed that neurons in different parts of the brain could match their activity in such a way. But here was clear evidence of correlated firing, revealed by Singer's instruments as an oscillating wave of synchronous electrical activity with a frequency of roughly 40 hertz.

Singer and some others think the oscillations may provide the answer to a fundamental puzzle: how do distant neurons responding to a single visual object pool their information to create a coherent image? They may do it, Singer suggests, simply by firing in unison. A few bold theorists have pushed the notion further, claiming that, since visual awareness can be considered a model for consciousness in general, the 40-hertz oscillations may play a role in other forms of awareness as well.

Such grandiose theoretical leaps leave many experimental neuroscientists cold. Indeed, some suspect the oscillations are little more than an inconsequential side effect of neuronal activity. Yet the debate over Singer's findings has been sufficient to make 40-hertz oscillations one of the most talked-about topics in neuroscience this year.



Oscillation revealed. *Wolf Singer (left) and Charles Gray characterized 40-hertz oscillations in the brain. Trace A shows the oscillations in electrical potential of all neurons near a recording electrode. Trace B shows the firing pattern of a pair of neurons near the electrode; the neurons tend to fire when the potential is at a low.*

The central issue from which all the theoretical hubbub derives is one neuroscientists have been tossing around for years. To be aware of a specific object—a pen, say, lying in the nest of papers on your desk—your brain must be able to separate the bits of information relating to the pen from all the other visual cues you are taking in. But that is not a trivial task, since the bits relevant to the pen are collected by nerve cells scattered among the visual areas of the brain. Some cells respond to the orientation of the pen's edges; cells in other areas record its color, movement, and so on. But somehow the widely spaced regions manage to coordinate their bits of information into one coherent image. How that process (known as "visual binding") occurs has remained a mystery.

In 1981, Christoph von der Malsburg of the University of Southern California offered an intriguing solution to the problem of visual binding. He said that the neurons involved might bind by briefly synchronizing their patterns of activity. But how could a researcher know where to look for that synchronous activity among all the other neural commotion in the brain? "For a while I was rather depressed about the possibility of finding it," von der Malsburg told *Science*. "I thought sets of cells that would be correlated would be scattered all over the brain—there would be no way to pick them out. The mind would be invisible."

For a while von der Malsburg's depression was justified—there was no experimental support for his idea. Then, in 1986, Singer and postdoc Laurence Mioche were conducting experiments on a part of the visual system called the primary visual cortex, where nerve cells are segregated into columns about 100 micrometers in diameter. Each cluster of columns surveys a particular patch of visual space, and individual columns respond to edges of objects with a certain orientation. Some are sensitive to horizontal edges; others to vertical edges; still others to edges with orientations in between. In response to an edge that has the orientation for which they are tuned, the cells of a column fire off electrical impulses, called action potentials, in periodic bursts.

Neither Singer nor Mioche was thinking about von der Malsburg's theory. Mioche

* C. M. Gray, P. Konig, A. K. Engel, W. Singer, "Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties." *Nature* **338**, 334 (1989).

was recording from electrodes chronically implanted in the orientation columns of kittens, as a means of studying brain development. By using filters to remove background noise generated by neighboring neurons, she could detect the action potentials of individual neurons. As part of a routine equipment check, she removed the filter, providing a record of the field potential, or average electrical activity of all the neurons near the electrode.

It was in this recording that Singer noticed that, for short periods of less than half a second, the field potential was oscillating—alternately rising and dipping—with a frequency of 40 hertz. Those oscillations reflected a synchronous, repeating pattern of current flow into the neurons in the vicinity of the electrode. And since such an ion flow often triggers an action potential, that meant that many of those neurons must be firing action potentials together, in brief phase-locked synchrony.

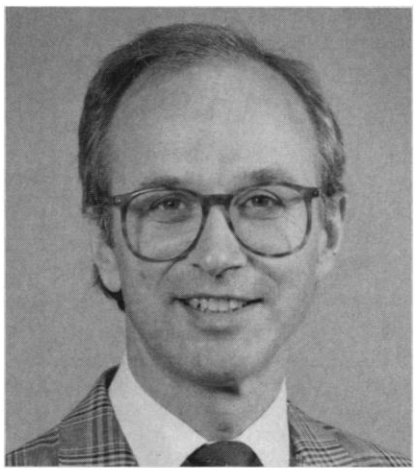
The oscillations reminded Singer of electrical oscillations that have been seen in the olfactory cortex. University of California neurobiologist Walter Freeman has studied olfactory oscillations for decades and shown that they seem to be involved in discriminating between different odors. In homage to Freeman, Singer dubbed his new finding "the visual sniff." And then he made the next intellectual leap.

If Singer hadn't been familiar with Freeman's and von der Malsburg's work, he says, he might have thought of the 40-hertz oscillations as nothing more than a curiosity. But instead he realized they may be something much more important: the synchronous activity von der Malsburg had postulated. So he and postdoc Charles Gray (who had recently finished graduate work in which he collaborated with Freeman on the olfactory oscillations) set out to see what the synchronized visual neurons were responding to. By positioning electrodes in the brains of anesthetized cats, and flashing light images on the cats' eyes, Gray (who was later joined in the work by postdocs Peter König and Andreas Engel) found that the oscillations occurred not only within orientation columns but between separate columns as well.

In the most telling experiment, the group found that cells in columns separated by as much as 7 millimeters would oscillate in synchrony if presented with light bars of the same orientation moving in the same direction—that is, as if they were parts of a single object. If the bars moved in different directions, the cells in both columns would fire, but not in synchrony.

Such synchrony—between columns separated by 7 millimeters—would once have been regarded as heresy, since neuroanatomists believed there were few (if any) long-distance connections linking such columns. But Charles Gilbert, Torsten Wiesel, and Daniel Ts'o, at Rockefeller University, have recently shown that connections do exist between columns of like orientation preference. And those connections probably carry signals that initiate the synchrony.

That much is fairly clear, because it is grounded in data. But those data are open to many widely differing interpretations. Because the columns oscillate synchronously when they are stimulated by bars that act like part of the same object, the synchrony is a good candidate for some role in visual binding. But how much binding could such a system actually do? The primary visual cortex is only at the very early stages of visual processing, von der Malsburg notes, and may be binding only on the most basic level. "It discovers short segments of lines which are colinear—maybe that's all it does," he suggests. To account for other types of binding, he says, one may need to look elsewhere.



In sync. *Christoph von der Malsburg proposed that the brain "binds" sense impressions by synchronous activity patterns of neurons.*

And that's exactly what Singer and others are doing. There is already preliminary evidence for phase-locked oscillations between different visual areas. Reinhard Eckhorn and his colleagues at the Philipps Universität in Marburg, West Germany, have found synchronous oscillations between the primary visual cortex and an adjacent visual area known as area 18, and Singer's group has found them between the primary visual cortex and more distant visual areas that detect motion.

In applying the idea of 40-hertz oscillations to visual binding, Singer and his colleagues are sticking fairly close to the empirical findings. But others want to go much further. "This could be the neuronal expression of attention," Christof Koch, a computational neuroscientist at the California Institute of Technology, recalls thinking when he first heard of Singer's data. With that proposal, Koch has expanded the visual binding problem to ask whether the brain may use a similar mechanism to focus attention on objects which may not only be seen, but felt, heard, or smelled as well—a process that may require binding between different sensory areas of the brain.

And Koch, along with Francis Crick of the Salk Institute, has gone further yet, asking whether the mechanisms that carry out these tasks could also link the brain cells responsible for ideas and thoughts that may not even originate in the senses. Koch and Crick developed a loosely sketched "neurobiological theory of consciousness," based on Singer's data, suggesting that the brain could use such synchronous firing not only as a means of focusing attention, but as a general mechanism for establishing consciousness.

Koch and Crick are quick to admit that their theory cannot be established solely by Singer's data. Furthermore, they admit, it's little more than a first approximation: "Ultimately, [the theory] is bound to be very oversimplified, and probably wrong," Koch says. The purpose of publicizing it, according to Crick and Koch, was not to make grand claims that the problem is solved, but to stimulate research into the subject of visual awareness, an area which they feel is experimentally approachable—and one that could provide an important stepping stone toward the bigger challenge of understanding consciousness.

"We think of consciousness as occurring in different ways," Crick says. "You can be conscious of pain; you can be self-conscious; you can be conscious of hearing, seeing, even of making plans. Our hypothesis is that all of these may have something in common, and therefore why not study the easiest one? We think the easiest one is visual awareness."

One of the features that makes the 40-hertz oscillations attractive as a mediator of visual awareness, Koch says, is that their time scale corresponds with that of attention flitting from one object to another. The neurons typically stay phase-locked for several hundred milliseconds, which would allow them to make and break their liaisons in roughly the same period that a person's attention moves from one subject to the next. As different subjects compete for attention, different sets of neurons may set up oscillations, Koch proposes. One wins momentarily, and attention is briefly focused. Then that oscillation fatigues and attention is directed elsewhere. "It's a very beautiful picture," he enthuses.

Despite the appeal of this picture to theorists, experimentalists remain skeptical about the importance of the oscillations—even for visual binding. "I think it's an ingenious idea, but I'm not completely sold on it," says Harvard neurobiologist David Hubel. "And what I don't find so great is the philosophical tangents . . . equating it with consciousness and every other thing." Rockefeller's Gilbert describes his position as agnostic. "I would like to be open minded," he says, "but it requires a lot more backup information to know what the significance [of the oscillations] is, and whether it's not just something artifactual that is not used by the brain."

One reason Gilbert and others remain lukewarm is that they suspect the oscillations are merely a side effect of neuronal activity, rather than a key element in brain function. In experiments in which he has recorded from the same brain regions as Singer, Gilbert says he only occasionally has seen synchronous oscillations. "We tended to interpret it as a funny state the cortex had gotten into," he says.

That "funny state" could be an epiphenomenon, or nonfunctional by-product, of the firing of neurons linked together in a network. Computer simulations by several groups have shown that oscillations can easily arise in active neural networks, a fact that Singer readily acknowledges. "I am entirely open to the possibility that it is an epiphenomenon," he says. "We have to go on and collect more evidence which suggests that the brain may actually be using it."

Gathering that evidence will require experiments on waking monkeys. Both Andreas Kreiter in Singer's lab and Singer's former postdoc Gray (now working independently at the Salk Institute) have observed the oscillations in monkeys, although they are more transient and harder to detect. Next, both labs plan to devise images that can be altered to appear as one object or two, show them to monkeys and test whether the oscillations between columns go in and out of phase-lock depending on whether the monkey perceives specific features to be part of the same object or not.

These experiments will address not only the binding issue, but also a major charge that has been leveled against Koch and Crick's consciousness theory: that it is based on data taken largely from anesthetized (that is, unconscious) animals. How, the critics ask, can a theory of consciousness be based on observations of animals that are not conscious? Though Singer and Gray have observed the oscillations in waking cats, most of their characterization has been done with anesthetized cats, because it is technically easier. And they agree that if the oscillations are contributing to any conscious process, whether it be simple binding or something grander, they must be confirmed to not only exist but to play a role in alert animals.

As the experimentalists pursue the oscillations in their biological context, the theorists are cheering from the sidelines. Von der Malsburg, for one, is eagerly awaiting the next round of results. "Wolf Singer and the others are onto something extremely important," he says. "If this experimental-theoretical story materializes even further, it will open the door to a completely new era."

■ Marcia Barinaga

ADDITIONAL READING

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A New Wave in Applied Mathematics

A technique called wavelets may upstage Fourier analysis in a multitude of applications—from CAT scanning to locating subs

Wavelets are making a big splash in mathematics. Despite the diminutive name, wavelet theory is something of a tidal wave breaking over a venerable technique that has been king of the hill for a century and a half: Fourier analysis. Almost since the day in 1822 when French mathematician Joseph Fourier first published a treatise on the theory of heat, the technique he introduced in that treatise revolutionized mathematical physics. The technique—Fourier analysis—rapidly came to dominate the analytic approach to scientific problems from acoustics to quantum mechanics to climatology to crystallography.

Now a new theory—wavelets—has appeared, one its enthusiasts see as a significant advance over Fourier analysis. They believe it will help solve pressing problems in many branches of engineering and physics. Among possible applications: data compression for storing and transmitting digitized images; music and speech synthesis; seismic exploration; detecting engine problems or submarines gliding through deep waters; analyzing the dangerous downdrafts known as microbursts that are associated with thunderstorms; and improvements in medical imaging from CAT scans and nuclear magnetic resonance.

"Never before in anything on which I've worked have I had contacts with people from so many different fields," says Ingrid Daubechies, a leading wavelet theorist at Bell Laboratories. "Because you have everybody interested and everybody has a different way of looking at it, you have all these ideas brewing together, and it's very fertile for everybody concerned."

This ubiquitous appeal arises from wavelet theory's way of rearranging data to reveal key features of a physical or mathematical system—features that might otherwise be hidden. Fourier analysis shares that essence, but the big difference between the two methods is in how they tackle the data.

Fourier analysis assumes the world is made of sine and cosine curves—the simple, undulating functions of high-school trigonometry. This might seem to limit the method to studying smooth, periodic phenomena, but in fact it works in many settings. That was the nub of Fourier's innovation and the reason Fourier analysis has occupied center stage for so long.

Starting with an arbitrarily complicated function, the Fourier analyst looks for a collection of sines and cosines of varying frequencies and amplitudes that, when added together (or more precisely, integrated), reproduce the original curve. The assignment of an amplitude to each frequency is a function in its own right; mathematicians call it the Fourier transform of the original function.

A large amplitude at a particular frequency indicates something important is happening there. For example, a Fourier transform of weather data—the temperature in Detroit as a function of time, say—is likely to have a