1981 Nobel Prize for Physiology or Medicine

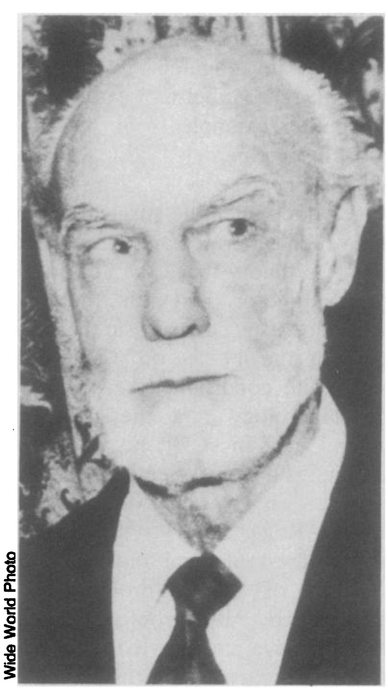
The 1981 Nobel Prize for Physiology or Medicine was awarded to three American-based scientists. Half of the prize went to Roger W. Sperry at the California Institute of Technology; the other half was awarded jointly to David H. Hubel and Torsten N. Wiesel at Harvard University.

Upon hearing the first news bulletin that Roger Wolcott Sperry, Ph.D., had been awarded the 1981 Nobel Prize for Physiology or Medicine, his colleagues and students could ask only the question, "Which aspect of his work was being rewarded?" Prior to actually knowing, there were at least three major areas of research that seemed deserving—developmental neurobiology, experimental psychobiology, and human split-brain studies. It was, of course, the final body of work that was honored, but disciples of the other studies remain convinced that the other approaches were just as deserving.

The Nobel award to Sperry, Professor of Psychobiology in the Division of Biology at the California Institute of Technology, serves as an inspiration to those who believe that understanding the human conscious process is the ultimate objective of neuroscience and that it can be studied with scientific rigor. It represents a grand appreciation of Roger W. Sperry for his relentless pursuit of an understanding of the conscious processes of the human brain, a pursuit he began with related but more fundamental studies over 40 years ago and has maintained with a singular excellence and passionate energy. In fact, it can be said that it is Roger Sperry's overall body of work that has served to conceptualize the objectives and questions pursued in much of current neuroscience.

The particular studies on the human brain cited in the Nobel award began in the early 1960's, and the application of the initial insight gained from these split-brain studies to subsequent brain research have all the earmarks of a Sperry enterprise. It all started in 1961 when Joseph E. Bogen, M.D., proposed split-brain surgery be carried out on a 48-year-old war veteran in an effort to control otherwise intractable epilepsy. Bogen was aware of Sperry's earlier work on severing the connections between the hemispheres in animals, and Sperry and Ronald E. Myers had already demonstrated striking disconnection effects, that is, that information learned by one half-brain did not transfer to the other. At the time of the human studies, the animal paradigm was already in pervasive use in experimental laboratories around the world (*1*).

In fact, the animal work done by Sperry stood in dramatic contrast to prior human work on callosum-sectioned patients that had been carried out in the early 1940's. These early reports suggested that cutting the forebrain commissures, as they are called, had no detectable effect on interhemispheric communication. It was these studies, in part, that discouraged the view that discrete pathways in the brain carried specific kinds of information. There was some question about the usefulness of the surgical technique as well for controlling epilepsy but Bogen, after a careful review of the medical cases, concluded there was a good chance the surgery should help. That proved correct. In this new light, the stage was also set for new experimental observations on split-brain humans—a task made possible over the years by the generous cooperation of the patients themselves.



Roger W. Sperry

No one was prepared for the riveting experience of observing a split-brain patient generating integrated activities with the mute right hemisphere that the language-dominant left hemisphere was unable to describe or comprehend. That was the sweetest afternoon. It was clear that the animal model held for humans, and, as a result, Sperry masterminded a program of human split-brain research that continues today. The implications of these findings for theories of consciousness and cerebral specialization, for cognitive science and clinical neurology, and even for thoughts about human values were all developed in Sperry's laboratory. He was exceedingly generous to a series of students who went through Caltech including Colwyn Trevarthen, Jerre Levy, Robert Nebes, Charles Hamilton, Eran Zaidel, and myself, all of whom assisted in developing the split-brain story. Yet, the overall achievement was Roger Sperry's. He is constitutionally only able to be interested in critical issues and he drove this herd of young scientists to consider nothing but the big questions.

There were two main phases of the human work in Sperry's laboratory. The first task was to characterize the basic neurologic and psychologic consequences of split-brain surgery and to identify the individual psychological nature of each separated hemisphere. Results accumulated over a period of 6 years demonstrated that the cortical commissures were critical to the interhemispheric integration of perceptual and motor function. These studies also revealed that the mute right hemisphere was specialized for certain functions that dealt with nonverbal processes, while, not surprisingly, the left hemisphere was dominant for language. For the first time in the history of brain science the specialized functions of each hemisphere could be positively demonstrated as a function of which hemisphere was asked to respond. The important clinical observations of brain-damaged patients had only been able to show absence of function—not the concurrent but separate and lateralized coexistence of such functions. Finally, the implications for a theory of mind were abundantly clear after observing the patient's lack of awareness in one half-brain about the activities of the other (*2*).

The second phase of study empha-

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sized the different cognitive styles of the hemispheres and the special linguistic capacities of the right half-brain. These findings were pursued not only by Sperry but also by other researchers investigating the lateralization story, and have included observations of both neurologically damaged and normal populations. All of this has given rise to a wealth of possibilities concerning the nature of human brain organization. The issues raised are of great interest, and pursuit of hard answers to the questions raised by this work comprises much of the contemporary research in neuropsychology (*3*).

It has to be kept in mind that this body of work had been preceded by a series of studies by Roger Sperry that laid the groundwork for much of the present-day field of developmental neurobiology—the experiments of which probably consume about half of all activities of neuroscientists. It all began at the University of Chicago in the 1940's. The graduate student Sperry challenged the neurobiologic theory of his brilliant mentor, Paul Weiss, that "function precedes form," that is, that the central nervous system and its peripheral connections were not specified by genetic mechanisms. In a series of experiments that extended over 20 years, each more spectacular than the last, Sperry developed his theory of chemospecificity (*4*). His conception that chemical gradients are critical to the specification of cell to cell connections is still at the center of current neurobiological work, and every modern-day developmental neuroscientist is trying to find the loophole.

After Chicago, Sperry went to Yerkes Laboratory and spent some important time with Karl Lashley. Once again Sperry intuitively rejected the going model of cerebral function, and challenged Lashley's theories on equipotentiality and mass action. While carrying out new studies, which to some extent led to the animal discoveries in split-brain work, he also put to rest a few theories Gestalt psychologists had about brain mechanisms and perceptual processes. In the early 1950's, Sperry, already recognized as a world leader in brain research, was invited to be the Hixon Professor of Psychobiology at Caltech by Nobel Laureate George W. Beadle. It was a prime job in a glorious institution, and Sperry settled in and started his major systematic work with both animals and humans in split-brain research.

Life in science today is not as much fun as it used to be. It is full of time-consuming, boring administrative chores, of bureaucratic double-talk, of responding to endless mediocre demands for "programmatic applications" in scientific pursuits and grant writing, and all the rest. As the dollars allocated for science decrease in number as they have done for the last 15 years, the request for articulated trivia goes up, and some people are actually beginning to think that this is science. We all know this, and every time I have to deal with it, I think of Sperry. He is unable to be scientifically trivial. He scowled when people proposed an extensive series of experiments. He knows how science really works, how things just happen and that then the leads are actively pursued, and pursued with vigor. He never played the bureaucratic game; he never gave in to the forces of trivia, and I hope his steadfast ways with their now grand rewards will signal the larger community to set things straight once again. Those were happy days working in his lab, trying to keep up with the intellectual excitement and freedom he always so brilliantly engendered.

Sperry's dazzling career had its origins in a time when brain scientists, then not so chic, studied the brain because they were interested in how its workings explained behavior. In some sense they were not interested in the brain per se, as are so many current-day neuroscientists. Their experiments constantly focused on discerning something about how the biologic system worked to support behavior, and ultimately the generation of conscious awareness. Roger W. Sperry, even while studying individual neurospecificity, saw and talked about its implications for the broader problems of nature versus nurture, a theme also so eloquently investigated by co-award winners David Hubel and Torsten Weisel. Another example of his functional approach was Sperry's brilliant paper on how certain aspects of fish behavior changed after selective surgical manipulation which generated an "efferent copy theory," a theory that is central in most perceptual-motor research today (*5*). There were also those classic theoretical papers of the 1950's on "The neural basis of the conditioned response" (*6*) and "Neurology and the mind-brain problem" (*7*). In short, he always was and remains a neuroscientist who is perfectly clear on why he chose to study the brain (*8*). Roger Sperry worked to help elucidate the biological and psychological nature of man, a problem by no means solved, but a problem he helped define and advance knowledge about like no other scientist in the history of the world.—MICHAEL S. GAZZANIGA

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"Filling out the Forms"
An Appreciation of Hubel and Wiesel

Philosophers rightly stress the inaccessibility of percepts. Nevertheless, it can also be held that whatever percepts are, they are had in part by process on sense data, not by revelation. That is what Leibnitz meant by "innate ideas"—those pre-given ways by which experience is formed from affection of the senses. Physiology of brain is concerned with process insofar as it can be guessed from the action of the mechanism. It is possible to develop a theory of image handling that does not address the vexed question of perception except in an important negative way. On the principle that one cannot use information which is excluded by processing, a strategy for seeing can be inferred from experiment that reveals the information discarded. This modern approach through shaped filters is in accord with the general treatment of complex machines that has burgeoned since World War II, and the Nobel Prize in Medicine this year properly honors it.

Two main notions lie at the foundation of the work by Hubel and Wiesel. First, physiological psychology teaches that the sense elements adapt to light. This adaptation is a function not only of the rods and cones themselves but of the first layer of neurons to which they connect. Adaptation, in more general terms, means the following: A single rod or cone adjusts its sensitivity according to the steady flux on it and on its neighbors. Any change it reports is normalized to the temporal and spatial averages of the light in the neighborhood. Such an automatic gain control ensures that, for the most part, only representations of change are available for later processing. (In a word, we are blind if nothing alters in the retinal image—as Helmholtz remarked.)

The second notion comes from anatomy. As with any other sensory system, the sheet of sensors is the first of layer after layer of neurons from rods and cones to cortex. Each rod or cone is connected to several local neurons of the second layer, and each second-layer neuron is fed by several local rods and cones. This many/many relation holds between successive layers in the system so that continuous mapping is preserved between sensory surface and furthermost nervous layers. From this connectivity, one infers that sequential visual processing, while hierarchical, is always local around every point in the field of vision—a principle stated for all sensory systems by Mountcastle.

It can then be adduced that spatial processing of change in the image begins immediately behind the rods and cones and progesses with each layer until the information is in such a form as to permit broader combinations. That area of many sensors within which a neuron of any succeeding layer processes information is the "receptive field" of that neuron.

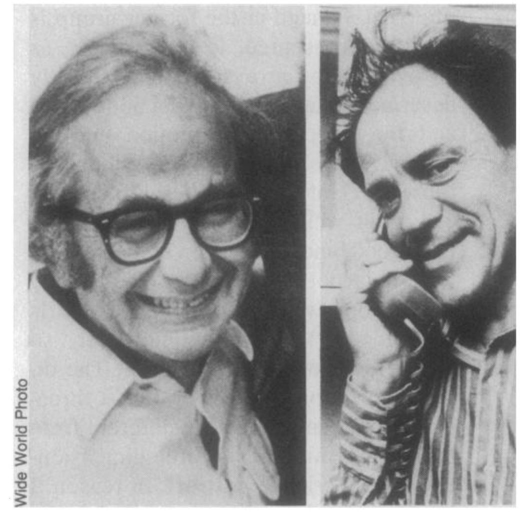
In the 1930's, the areal processing of images was first sought in frog's optic nerve by Hartline and, then, more explicitly, by Barlow, who, in searching for image processors, described a kind of differencing operation on flux that was also found by Kuffler in the cat. The receptive fields found by Hartline are large and uniform in that some fibers respond to an increase in illumination anywhere within the field, some to a decrease—the "on" and "off" elements. The receptive fields found additionally by Barlow are also large but have an annular form, a center and a surround. Response occurs only if the difference in lighting between center and surround increases. In Kuffler's neurons, the difference had to have a sign—for example, darkening in the center and/or brightening in the surround, but not the other way round—that would describe another neighboring neuron.

In 1959, Maturana and I showed that Barlow and Hartline were recording from only the large myelinated fibers in the frog's optic nerve. These are 3 percent of the population. The remaining fibers are unmyelinated and have receptive fields ranging from 3° to 7° in visual angle. They are insensitive to average illumination, are only secondarily affected by changes in the average. There are two types. One type is sensitive to any boundary between dark and light produced in the field, however shaped or moved, providing the boundary is sharp. The other is sensitive to specific shapes and movements as well as to the sharpness of boundaries between dark and light. Such neurons are image-parsers—they are the elements underlying form perception for the frog.

But mammals are not frogs. Kuffler's exhaustive work showed that none of the ganglion cells of the cat (those whence the optic nerve springs) give the detailed boundary information to be found in frog. Instead, they are almost all of the differencing character described above, but vary greatly in size of center versus size of surround, and in total size of receptive field. All are fairly indifferent to the level of illumination and only secondarily dependent on change of level. The smaller ones occur mainly toward the center of the retina; the larger ones are mainly peripheral, but a wide spectrum of size is generally the case everywhere.

From Kuffler's work it was necessary to look higher in the hierarchy of the visual system in order to find such spatial or extensional processing as would seem to qualify as the basic elements of visual form for cats. That is where Hubel and Wiesel began.

Their first accounts of the image processing by single cells in the visual cortex of cat issued in 1959 and gave what were later called the "simple" and the "complex" cells. It would dilute this tribute to try abridging those accounts. They can be had from many current textbooks, and the details are important, as in any other description of receptive fields. Suffice it to say that each cell in the "primary visual cortex" (area 17) has one of two types of receptive field, simple or complex. A third type, "hypercomplex," was found later in another region (area 18). All the neurons are indifferent to the amount of illumination so long as the objects to be seen are clearly visible, and are relatively insensitive to changes in average illumination. All three types are also insensitive to unchanging images on the retina. But they are affected greatly by changes in the distribution of light at the time of the change and for a short period thereafter. In particular they are most sensitive to boundaries between dark and light. If these boundaries are straight edges and referred to the dark phase, the angle that the boundary makes to the meridian of the eye is critical, for the preferred angle



David H. Hubel and Torsten N. Wiesel

changes from cell to cell of the same type. For some simple cells, the most effective stimulus is not a protracted straight boundary, but a band. For some hypercomplex cells, the most effective boundary shape is a corner, for others a tongue. These optimal stimuli have a defined locus on the retina, a defined size in terms of visual angle, and often a preferred direction of movement. The complex cells are sensitive to the angle of a straight boundary but relatively insensitive to where in the receptive field the boundary is produced, and the field can be quite wide. Frequently, there will be a preferred direction of translation of this boundary. Any point in the visual field lies within the receptive fields of many such cortical cells that vary in a preferred angle of boundary, the necessary kind of motion, and the shape of optimal stimulus.

Each patch of primary visual cortex is supplied by both retinas. Some cells respond to one eye, some to the other. But in some, the processing in the receptive field depends on local detail in corresponding parts of both retinas, so that registration of the eyes with respect to the visual field can be told from the cell's response. Thus Hubel and Wiesell uncovered a subtler notion than that of simple spatial processing which was already in their heritage. And that is why so much of their work is concerned with binocular interaction in cortex.

The difficulty of imagining how a binocular system can work is well described by Helmholtz in his terminal essay for the *Physiological Optics*. If one contrasts other vertebrates, say frogs, birds, and even rabbits, with cats, monkeys, and man, the most salient difference is that the latter group defers any boundary processing from the retina through the lateral geniculate nucleus to the cortex.

The visual image in the former group is already represented, in optic nerve, as an overlapping array of patches locally described in terms of moving boundaries and the directions of motion and, in general, with properties very similar to those of Hubel and Wiesel's cortical cells. But while these animals certainly have good binocular vision by behavioral test, it is not obvious that they enjoy stereoscopic vision in the sense that is stressed by Helmholtz and, later, so clearly developed by B. Julesz. The direct perception of the world as a three-dimensional image is very different from the apperception of its three-dimensionality by experience, instinct, or reason. I have no idea of how to put numbers to the matter, but it seems to me that processing two flat images to a single solid image, when the flat images are given in terms of boundaries, requires far too much operation, every patch seen in the light of all the others. The cyclopean eye (the stereo view of a single world) that Helmholtz and Julesz treat, is one in which the processing itself, patch by patch over the visual field, determines depth as well as extension along the image plane before the form is construed, even before edges are definitively taken. And this requires, I think, that as Kuffler found, the ganglion cells of animals blessed with stereoscopy take a kind of textural context around a central region of the receptive field rather than any more explicit operation on continuous boundaries. It also requires that the cortical operation can be done under conditions of disparity in the two representations offered (particularly along the interocular axis) so as to free the system from the impossible job of registering, point by point, two different views of the same scene. And all this must be done without loss of resolution.

That processing for depth occurs independently of clearly bounded form was proven by the ingenious experiments of Julesz. Accordingly, the objects of perception and the space in which they seem to lie are not abstracted by a rigid metric but a far looser one than any philosopher ever proposed or any psychologist dreamed. And precisely here the mammalian cortex, in the hands of Hubel and Wiesel, poses one of the most fascinating and complex problems in contemporary brain science. By their descriptions, the problem has assumed its proper status, that of a remarkably clever program of processing to which very specific kinds of image dissection are necessary. They have, thereby, opened a new field in the physiology of vision.

On the practical side, the treatment in pediatric ophthalmology is indebted to them. For in a collateral branch of their research, they did a tour de force of some consequence. As they showed, a newborn kitten has a visual cortex capable of handling the disparate images of the binocular animals. Between the third and fifth postnatal weeks there is a critical period in this sense: Let one eye be deprived of form, but not of light, as with a diffuser, or be caused to squint so that the image represented to the cortex is much displaced out of tolerable disparity. Then the central connections of that eye change functionally, and the ill-seeing eye is suppressed from the cortical processing. Its nerve fibers still report to the geniculate body, and the geniculate still reports to cortex, but the reports are mainly discounted. And this functional blindness persists thereafter even though normal imaging and registration in that eye is restored.

This study gives the lie to the notion that children born with a squint can grow out of it several years later and have normal stereoscopic vision, or even normal equivalent use of the strabismic eye. The same experiment that showed for the first time in higher animals how experience changes connectivity of the brain, showed also the folly of not intervening as soon as possible before the critical period. For whenever that period occurs in children, and it occurs early by all indications, it so reconnects the system functionally that no cosmesis, however attained later, can rectify the trouble. Reflect that this same principle may hold true for many other systems, including the higher functions, that critical periods occur all through a child's growth, and be properly awed by the new view of pedagogy that emerges. On this one major step, were this the only thing they had done, Hubel and Wiesel eminently deserve the honor accorded them.

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1981 Nobel Prize in Economics

When Albert Einstein's first marriage broke up, he promised his wife as alimony the proceeds he would be getting from the Nobel Prize. So certain was he to get it that this was like money in the bank. The only wonder was that it was so late in coming, and that the Royal Swedish Academy of Sciences went out of its way to make clear that the award had not been given for Einstein's work in relativity. (In rebuke, Einstein devoted his Nobel Lecture to the subject of relativity.)

It was just as certain that James Tobin would receive the Nobel Prize in Economics. It was never a question of whether, only of when. The breadth of Tobin's work in empirical macroeconomics and the depth of his many analytical innovations make this a popular award in a field of not-so-hard science, where not all awards are greeted with unmixed enthusiasm.

I shall try to give a sample of Tobin's researches. But first it is worth examining the scholar as a person. For James Tobin is the archetype of a late 20th-century American scholar.

Son of the Middle Border

Tobin had to win the Nobel Prize because he can't help winning any prize that's out there. This began at nursery school in Champaign, Illinois, that oasis of culture and incubator for Nobel Laureates in diverse fields. Michael Tobin, his father, was publicity director for athletics at the University of Illinois, and his eruptions at the conservatism of Colonel McCormick's *Chicago Tribune* recruited Jim early into the camp of liberalism.

Prior to 1935 Harvard College was still a finishing school for Grottlesex gradu-