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Particles Of Light, Webs Of Interaction: [Dr. Floyd Ratliff]

Fulvio Bardossi

Judith N. Schwartz

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THE ROCKEFELLER UNIVERSITY
RESEARCH PROFILES
WINTER 1981-82

Light brings us the news of the universe.
SIR WILLIAM BRAGG

Think often of the bond that unites all things, and their dependence upon one another.
MARCUS AURELIUS

Particles of Light, Webs of Interaction

Dr. Ratliff

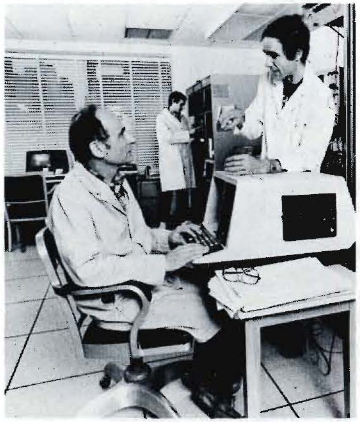
This issue of *Research Profiles* is about the work of Professor Floyd Ratliff. For you to read it, particles of light, reflected from the page, must spur the action of voltage-inducing molecules in the cells of your eyes to send electrical signals to your brain. Those signals, those "links between our consciousness and the external world," as Dr. Ratliff phrases it, are coded in the neural network of the retina.

"The most important thing to know about the retina," says Dr. Ratliff, "is that it is *not* a passive photosensitive device merely registering an image and sending it unaltered to the brain. Rather, the retina has a certain logic of its own. By means of interactions within and among neural networks, the retina selects and abstracts biologically useful features of the information in the ever-changing patterns of light and shade impinging on it, and then transmits this selectively filtered message to the brain. What we have been trying to discover is exactly how the retina performs the task of analyzing and reducing the apparent chaos of incoming data."

Dr. Ratliff is a physiological psychologist and biophysicist whose quest is a deeper understanding of perception and consciousness. Work in his laboratory has furnished information about molecular events elicited by single particles of light within individual nerve cells, and also has yielded the most complete analysis yet achieved in physiology of the interactions within an entire neural network. Recently, he and his colleagues have been applying their findings to a new method for diagnosing visual and other neurological disorders. Side-by-side with and related to his laboratory work, Dr. Ratliff has written extensively about the history of visual science and the visual arts. He came to The Rockefeller University in 1954 at the invitation of Professor H. Keffer Hartline, and the two worked together until Dr. Hartline's retirement some years ago.

Modern retinal electrophysiology began with Keffer Hart-

Limulus



In the computer room: Norman Milkman (seated), Ehud Kaplan (standing right), and Gary Schick (at rear). Progress of research is closely linked to development of right equipment.

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line. Fifty years ago, he and a colleague, Clarence Graham, were the first to record the activity of a single optic nerve cell. The nerve cells, which receive and transmit messages from the light-receiving cells in the retina, have fiberlike axons leading out of them; these axons bunch together like a cable to form the whole optic nerve, the pathway to the brain.

The isolation and recording of activity from individual nerve cells were the critical first steps toward understanding how the retina functions. While at the Marine Biological Laboratory at Woods Hole, Hartline and Graham chose as their experimental animal the invertebrate *Limulus* (the familiar "horseshoe crab," which is not really a crab at all). At that time they suspected that, in *Limulus,* a message from a single photoreceptor went to a single cell in a simple one-to-one pattern. Subsequently, Hartline was the first to record the activity of single optic-nerve fibers in more complex vertebrate retinas. But fortunately he never abandoned *Limulus.*

Dr. Hartline explored almost every aspect of vision. Among his discoveries, which won him the Nobel Prize in 1967, were those that led to the formulation of the basic principles of retinal processes. Briefly summarized, these are:

1) all impulses transmitted by an optic-nerve fiber are identical: information is coded only in the *rate* of the discharge of impulses;
2) the message transmitted by a single optic-nerve fiber is distilled from the activity generated by many photoreceptors converging on one neuron: the principle of the *receptive field;*
3) neurons joined in networks that form those receptive fields in the retina are *interdependent,* and may exert excitatory and inhibitory influences on one another.

Excitation and inhibition are the fundamental building blocks of the logic of the retina, as the collaborative research of Hartline and Ratliff was to demonstrate.

WHERE DOES THE TRAIN END AND WHERE DO I BEGIN?

About the time Hartline was first observing *Limulus,* Floyd Ratliff, growing up on a ranch on the Colorado prairie, was also making observations and asking questions.

"I would watch the freight train passing by on a branch of the Santa Fe Railroad a quarter of a mile or so away. I could see the steam from the whistle and then, later, I'd hear the whistle. I could feel the vibrations in the ground. These sensations were disjointed, and I would wonder where the train ended and I began, which part of the experience belonged to the train and which to me. I must have been around eight or ten when I started thinking about these things. I couldn't realize then, of course, that I was struggling with one of the most intractable problems in science and in philosophy—the delineation of the border between mind and matter and how the one interacts with the other. I'm still struggling.

"In the mid-30s, when severe drought resulted in short grass and overgrazing worsened matters, I learned first hand about the delicate balance of the ecosystem on the prairies. Without protective cover, top soil blew away in great dust storms or washed away, on the rare occasions when it did rain, and filled the ponds with silt. Waterfowl disappeared. The water table dropped and deeper wells lowered it still further. Brackish irrigation water salted and ruined the soil. That's when I began to understand that all things in nature are interdependent.

"Those two traits from my childhood, an insatiable curiosity about perception and a desire to understand the webs of interaction in nature, have stayed with me all my life."

Dr. Ratliff enjoys recounting that he was twice a high-school dropout. It is easy to imagine a youngster in love with nature and the out-of-doors feeling cooped up in a classroom. But intellectual curiosity won out. He completed high school and, in the depths of the Depression, alone among his seven brothers and one sister, he went on to college. It is harder to imagine the slender, soft-spoken man of today on a football scholarship. World War II ended his part-time career as a "running guard," interrupted his education for five years, and brought him face to face with the horrors of the Holocaust. As an artilleryman in the European theater, he helped to liberate a concentration camp. The experience, he remembers, led him to major in psychology when he returned after the war to Colorado College. "I felt I had to understand how human beings could do such things to one another." He soon discovered there were no ready answers—no science of "how to solve the world's problems." As it happened, the department at Colorado was strongly oriented toward sensory and physiological studies, which coincided with his interest in perception and biological systems, and he decided to study experimental and physiological psychology.

Dr. Ratliff attended graduate school at Brown University, working under Lorrin Riggs, one of the pioneers of modern vision research. His first project was an investigation of eye movement, specifically the tiny tremor—the so-called physiological nystagmus—that is continuous in the normal eye.

As he explains: "The eye is never completely still, even when one attempts to fixate steadily on a point. We wanted to find out why. What was the biological significance of the tremor? Utilizing an optical system that counteracted the effects of the tremor without actually immobilizing the eye, we discovered that almost the instant an image is stabilized on the retina, it disappears from view. It must be continuously moving across the retina by some small amount in order to remain visible. All that was very interesting to me because I knew that, in his early work, Hartline had observed that movement and change were the most significant stimuli to the retina. Our findings seemed to complement his, and I decided that I ought to go work with Hartline and get deeper into the physiology of the matter."

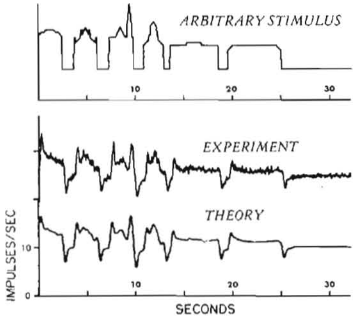
In 1950, when he completed his Ph.D., Dr. Ratliff applied for and received a National Research Council post-doctoral fellowship to join the Hartline Laboratory, then at The Johns Hopkins University.

THE LOGIC OF THE RETINA

Dr. Hartline had continued to study *Limulus,* and, contrary to his original belief, discovered that there were indeed interactions among its photoreceptors. In the retina, changing patterns of light and shade are transduced by the photoreceptors into patterns of neural activity. For a neural network to detect and to abstract this significant information, a comparison must be made between one part of the image and another. Such comparisons require interaction over space or time (or both) within the neural network. Inhibitory interactions are particularly critical. A receptor unit discharging impulses in response to light inhibits the discharge of its neighbor when that unit is illuminated. When Dr. Ratliff went to Hopkins the problem was on the shelf, ripe to be worked on, and that first year of collaboration resulted in a large body of descriptive data about how lateral inhibition depends on area, distance, and intensity.

At the year's end, Dr. Ratliff pondered a dilemma not uncommon to young scientists. Should he renew his fellowship and continue to live in a "state of indigence bordering on penury" in order to remain with Hartline or accept an appointment at Harvard? Having by now acquired a wife and baby, he chose Harvard. There, he and his first graduate student designed and executed behavioral studies of vision with pigeons. The experiments demonstrated that an animal could be trained to report on a "subjective" experience, in this case brightness contrast, where none actually is present. Since then, variations of the technique have been widely used in experiments on sensory processes in lower animals. After three years at Harvard, the opportunity to resume physiological experiments came with the invitation from The Rockefeller, to which Dr. Hartline had moved shortly before.

"The big step forward that we made at the very beginning, here at Rockefeller," Dr. Ratliff says, "was the introduction of applied mathematics to the study of interactions in neural networks. What was unique about our approach was the close relation between mathematical theory and physiological experiments. At times theory guided experiment, at other times experiment shaped theory. Once we had the proper mathematical tools in hand, we experienced no conflict between simultaneous analytic and organic points of view—seeing a cell acting alone and, at the same time, seeing it acting in concert with all the others. Conceptually, we could reassemble the retina's unitary cellular processes into a func-



As pattern (top) moves, it generates nerve impulses, which are recorded (as shown in middle). At bottom is a theoretical prediction, using mathematical methods, of how retina will respond to same pattern.

Relating mathematics to experiment: Bruce Knight and Lawrence Sirovich. (See page 5.)

tioning organ and predict patterns of activity in an entire neural system. Or, conversely, we could disassemble the whole system and predict functions of individual cells."

An enormous boon to that approach was the particular physiology of *Limulus,* which has made it, as Dr. Ratliff describes, "one of those ideal preparations nature occasionally gives biologists, like the fruitfly for genetics." The neural network of *Limulus* is linear. "It's like a high-fidelity tape recorder," he says. "Record a pure tone and the playback is a pure tone—no change in pitch and no overtones. Similarly, expose the *Limulus* eye to a pure sinusoidal wave pattern of light and the response is sinusoidal, without, for example, a doubling of frequency or a clipping of the sinusoid at the top or the bottom. This is so over a large enough range for us to feel comfortable with linear methods—at first a relatively simple pair of simultaneous linear equations.

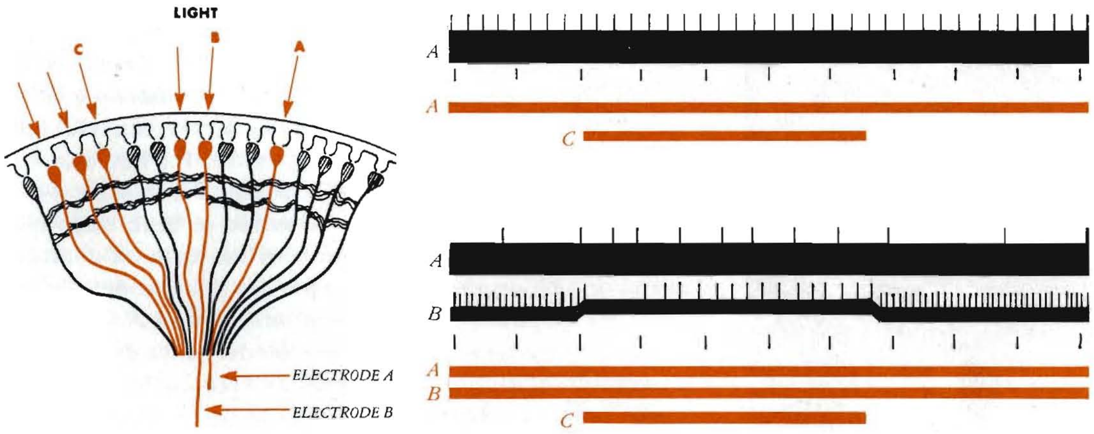
"Our first results enabled us to understand and to express in an exact mathematical form the interaction between two neurons in the retina. But we were frustrated because we were not able to deal with 20, or 200, interacting neurons in the same way. Such 'large' numbers seemed like an infinity. Much to our surprise, we found that we had only to go one step further: an understanding of how three neurons interacted was sufficient to treat an 'infinite' *Limulus* retina."

This understanding was achieved, in large part, by the discovery of what Dr. Ratliff called disinhibition. That is, if two units are interacting, with inhibition in progress, and a third unit is illuminated at a distance where it can interact with only one of the first two units, its inhibition of that unit will reduce the inhibition of the other. The phenomenon of disinhibition confirmed directly what their mathematical analyses had led them to suspect and showed them that they were dealing with the interaction among "networks of networks" that extended over virtually the entire retina, rather than within a small, circumscribed region. At first, disinhibition was thought to be unique to the *Limulus* retina, but it has turned out to be a basic principle of neural organization, widespread in other species and other systems.

"A significant aspect of our work on disinhibition," says Dr. Ratliff, "was that it showed very early the necessity for and importance of recording separately and simultaneously from several interacting units in a neural network.

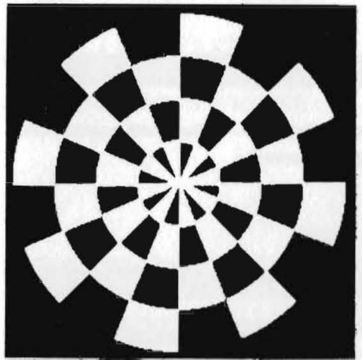
"Hartline and I were delighted by the quick and widespread interest in the principles of neural organization that we had elucidated. There were several reasons for this. In the first place, although there was much speculation then, as now, about the functions of neural networks, there was practically no theoretical work dealing with real nervous systems. Second, the principles and concepts we advanced were simple and straightforward, but at the same time sufficiently complex to yield interesting and significant results. Finally, although no comparable theoretical work was being done then on the vertebrate retina, our studies could be related by analogy to human experience—simultaneous brightness contrast, border contrast, color contrast, and the like. Furthermore, we were dealing with general principles. Negative-feedback systems of this type are very common, both in nature and in man-made devices. It is most rewarding to meet people, even those working in other fields, and have them tell me how much their ideas were influenced by our early studies."

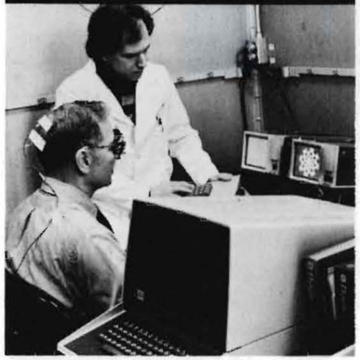
The first Hartline-Ratliff equations described the integra-



Disinhibition of a receptor in Limulus *retina (drawing at left) is demonstrated by records, at right, obtained by connecting nerve fibers from receptors to electrodes from an amplifier and a recorder. Upper record shows discharge of nerve impulses generated by shining light on receptor A. When receptors at C are also illuminated, there is no change in A's rate of discharge. They are too far from A to affect it. First part of lower record shows that when A and receptors at B are illuminated simultaneously, A's rate of discharge is inhibited (slowed down). Later when C also is illuminated, B's rate of discharge is inhibited. This releases A from inhibition by B. A then returns to a higher rate of activity. When illumination of C stops, B's discharge rate increases and its inhibition of A resumes.*

"Dartboard" stimulus





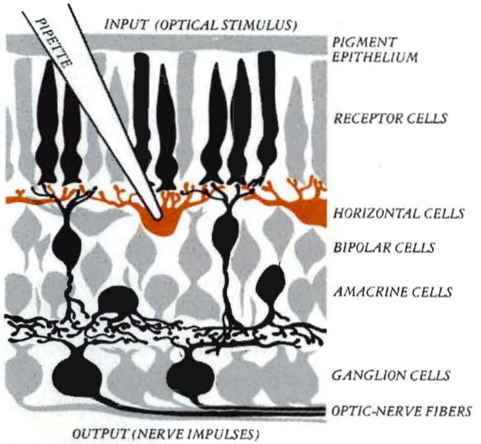
Vance Zemon (standing) and Dr. Ratliff test microcomputer-based visual stimulator and data analyzer for study of VEPs, changes in brain waves evoked by visual stimuli. Response of visual cortex to "dartboard" stimulus, on screen, is recorded through electrodes on scalp. In one type of epileptic patient, the normal response to borders in the dartboard pattern was found to be missing. No abnormality was indicated by an encephalogram, VEPs generated by conventional stimuli, or a CAT-scan of the patient's brain.

tion of the opposed influences of excitation and inhibition in the steady state. Attempts to extend the analysis to dynamic conditions yielded limited results until Bruce Knight, who came to The Rockefeller in 1961, introduced more sophisticated mathematical means of analysis and synthesis. For instance, Fourier methods made it possible for him and his colleagues, Fred Dodge and Jun-ichi Toyoda, to treat what happened when stimulus patterns varied in both time and space as they do in nature. From this has come a detailed description of how the retina suppresses unimportant information and amplifies key features of motion and contour.

In recent years, the mathematical models have drawn substantially on the advanced methods created by Norbert Wiener. For example, the so-called Wiener-Hopf technique, which was designed to evaluate certain boundary problems in physics, has been successfully applied by Knight, Lawrence Sirovich, and Scott Brodie to the analysis of the effects that occur at the edge of the *Limulus* eye, where the neural networks terminate.

The progress of the laboratory's research has been closely linked to the development of the right equipment. When the work began, the equipment was largely homemade and, by today's standards, very simple. "As we progressed," says Dr. Ratliff, "the support of the University's instrument makers became invaluable in the design and construction of special manipulators and high-speed shutters and, with the continuing advances in electronic technology, we have become more and more dependent on the University's electronics engineers and computer specialists." For example, the rate of discharge from *Limulus* averages 20 to 30 impulses a second with a maximum of perhaps 100. In the vertebrate retina, the rate may be as high as several hundred impulses per second. Computers have made it possible for huge volumes of information, transmitted at a very high rate, to be recorded, stored, and interpreted. The Hartline-Ratliff laboratory had the first and, for many years, the only computer in the University. Its now defunct "heart"—the core memory—sits in a place of honor on Dr. Ratliff's desk.

Gradually, techniques of stimulus control and data analysis derived from the study of *Limulus* have been applied to the more complex nonlinear systems of vertebrates. The results of the first of these studies on the mammalian retina, by Robert Shapley and Shaul Hochstein, have changed previously held assumptions about its functional organization. Among other things, it was believed that the influences converging on a nerve cell combined linearly and were arranged in a simple concentric form, a small central excitatory zone with a larger inhibitory surround (or vice versa). Instead, they found that some types of cells have small, nonlinear subunits across the entire receptive field, superimposed on the conventional linear center and surround. In addition, a new and much simpler generalization of the classical Wiener method of nonlinear



At left, Robert Shapley prepares turtle retina for recording electrical activity of single cell. Above, drawing of retinal structure shows micropipette inserted in a horizontal cell. This type is activated by many photoreceptor cells and is the first stage where lateral interactions can take place. Amacrine cells provide a second such stage. Receptor, bipolar, and ganglion cells constitute a vertical input-output pathway.

analysis, developed by Knight, Jonathan Victor, and Shapley, has shown that one of these cells with a nonlinear receptive field can exert a strong influence on the "gain" or amplification of a neighboring cell with a simple linear receptive field. Thus, even at the retinal level, there is interaction among different types of parallel channels in the visual system—interaction between, and within, networks.

"Since Hartline's original work on the vertebrate retina in the mid-1930s, a large number of very important findings about the retina and higher visual pathways have been made in laboratories throughout the world," says Dr. Ratliff. "But to a large extent, these findings remain in bits and pieces. The real importance of our combined mathematical and physiological approach is that it has the power to fit these bits and pieces together into an integrated whole. Since the techniques are general-purpose, as well as comprehensive, they are ideal for comparative studies on whatever species may provide the best access to a particular problem. Furthermore, they are well-suited for following the flow of information from single photoreceptors in the retina to networks in the visual cortex; essentially the same methods can be applied at every level in the visual pathway from eye to brain."

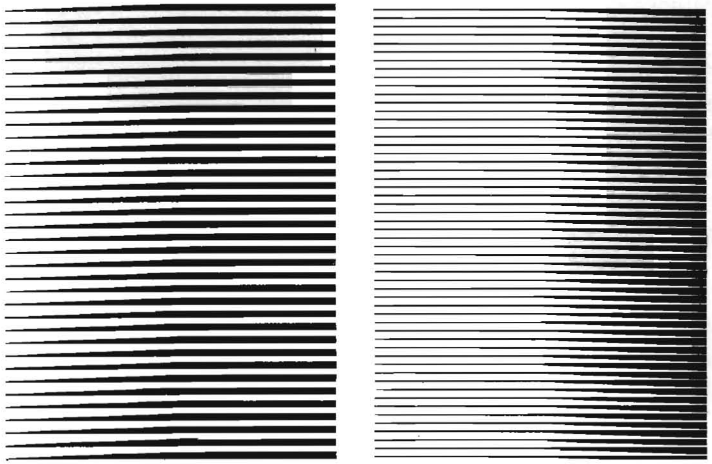
As an outgrowth of their more fundamental research, some members of the Ratliff laboratory have designed a microcomputer-based visual stimulator and data analyzer for the study of so-called VEPs, the visual evoked potentials in the human visual cortex. VEPs are changes in the brain waves elicited by visual stimuli and are now used to pinpoint anomalies along the visual pathways. It is hoped, with good expectation, that the new test will help diagnose visual and other neurological disorders at an earlier stage than previously possible, before damage has become widespread or irreversible.

"THERE IS NOTHING SO AWE-INSPIRING AS A BORDER"

One kind of change of enormous importance to life is the point at which one object ends and another begins. At Harvard, the noted biophysicist Georg von Békésy had pointed out to Dr. Ratliff the relation between his research with Hartline and some of the theories of the 19th-century physicist Ernst Mach. In 1865, Mach had proposed that the subjective visual phenomenon now called Mach bands—a heightened experience of border delineation—had to do with excitation and inhibition in the neural network; the retina, in effect, overreacting to stimulus. The bands are an illusion of the actual pattern of illumination; but they can be so striking and pronounced it is difficult to believe they are subjective. Indeed, when X-rays were first discovered, Mach bands were mistaken for an X-ray diffraction pattern, and the wave length of X-rays incorrectly deduced from them.

Mach's extraordinary theoretical insights, in this and so many other fields of inquiry, greatly stimulated Dr. Ratliff's long fascination with the history of the science of perception. He began a major study that resulted in the book *Mach Bands: Quantitative Studies on Neural Networks in the Retina*, published in 1965. He went on to relate this area to his interest in art, and he has found enormous pleasure in exploring and explaining the mechanisms by which artists over the centuries, particularly Chinese potters and artists of the Sung Dynasty and the French Neo-Impressionists, intuitively intensified contour and manipulated contrast illusions. He quotes from the Japanese novelist Yukio Mishima: "Be it the edge of time or space, there is nothing so awe-inspiring as a border."

The moon's disk in the advertisement above appears much brighter than the surrounding white space. Actually, both areas are the same shade of white. The effect of enhanced brightness results from the graded stippling (contour) outlining the moon. This same "trick" of technique was used by Chinese potters a thousand years ago for subtle contrast effects.



Mach bands: When viewed at arm's length (or more), a dark vertical band is seen in the middle of the frame at far left; a bright vertical band is seen in the middle of the other frame. Actually, the bands are an illusion. Similar bright and dark bands are seen at the edges of shadows.