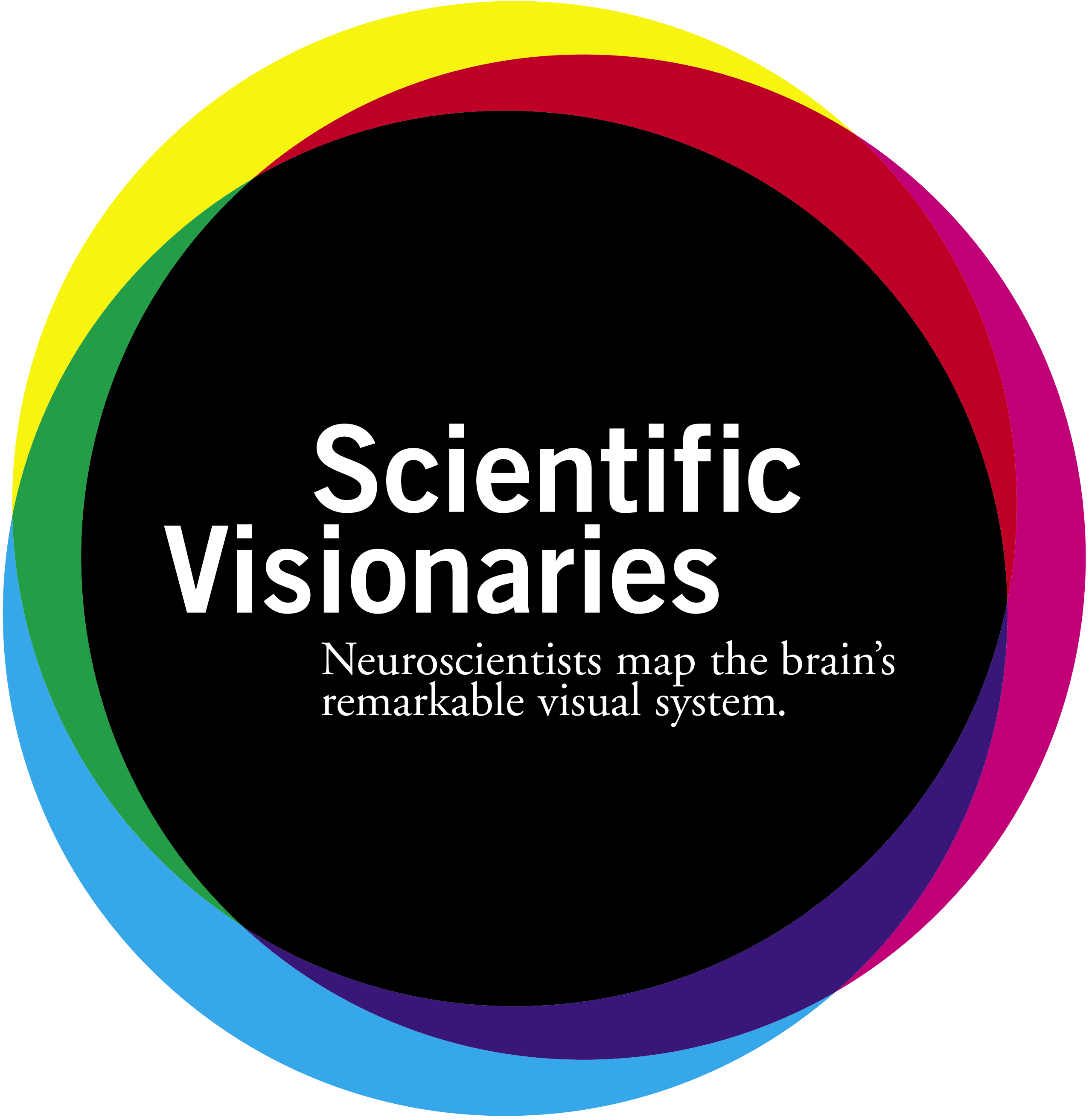

Scientific Visionaries

Neuroscientists map the brain's remarkable visual system.

By Richard Saltus

PHOTOGRAPH BY MOSHE KATVAN

Waiting for a friend

on a busy corner in New York City, you take in the towering buildings, flashing electronic signs, and rivers of pedestrians. Suddenly, you spot your friend's familiar face in the crowd and dart across the street—deftly avoiding many passing cars—to reach out and embrace her.

Our functioning in such a scenario seems routine—to us. But to neuroscientists it is filled with dazzling performances by the human visual system, truly a marvel of evolutionary bioengineering.

As you scan that New York street, your power of attention allows you to screen out irrelevant inputs and focus on small but important targets. The brain, a wondrous supercomputer, calculates the direction, speed, and acceleration of passing people and approaching cars based on inputs of various types of motion-detecting cells. Other cells encode the jumble of colors, shapes, and patterns in this visual field, which higher-brain resources then transform into meaningful perceptions of city street life.

When your friend comes into view, certain key features of her face strike a match with those encoded in your facial-memory bank—a positive identification! When you and she reach out in greeting, a frenzy of mental computations in 3-D space guide both sets of hands and arms along trajectories, with on-the-fly midcourse corrections, to join in an embrace.

No wonder that nearly one-third of our higher brain, the cerebral cortex, is dedicated to making sense of what we see. Strictly speaking, what registers on the eye's retina is essentially light and shadow; the brain constructs all the rest. The welter of reflected light from thousands of sources that constantly floods the retina has to be captured, filtered, and processed at diverse places along the visual pathways of your brain to construct a perception in your mind's eye of what you are looking at. And then there's the depth problem: A 3-D world is projected onto your 2-D retinas, but the brain has to transform it into three dimensions.

Vision has been studied for centuries, though in fits and starts. The initial tracing of nerves from the eye to certain brain regions came in the 1600s, for example, and theories of color vision were also first proposed in that century. But a quantum leap in vision research came in the 1960s when David Hubel and Torsten Wiesel carried out experiments that would eventually win them a Nobel prize. These pioneers showed that they could record electrical activity from individual neurons "and that they could describe what turns the neurons on and learn about the nature of sensory representation at early stages of the visual hierarchy," says David C. Van Essen, a veteran vision researcher at Washington University in St. Louis School of Medicine and a member of the HHMI Scientific Review Board, who was a postdoctoral fellow under Hubel and Wiesel.

Since then, Van Essen says, "we have certainly made progress." There have been numerous discoveries about the wiring of the brain areas that process visual signals, particularly information about motion, and we understand better how the eye/brain system uses viewers' memories and emotions to help interpret what they see. But it may take many more years to fully understand the neural processes of vision. Scientists are ardently working toward that goal, however, and among them four HHMI investigators in particular are making major contributions.

Perception to Decision

WILLIAM T. NEWSOME, an HHMI investigator at Stanford University School of Medicine and one of the acknowledged leaders in the field of visual neurosciences during the past few decades, has expanded on leads uncovered by Hubel and Wiesel—such as their discoveries of different types of brain cells specialized to respond to specific kinds of visual signals transmitted from the retina. Newsome credits recent progress to the field's move away from anesthetized laboratory animals to the more flexible and realistic system of humanely using alert, unsedated monkeys, whose brain activity can be recorded while they respond to visual cues and perform carefully designed tasks.

WILLIAM T. NEWSOME

➡ Recently, William Newsome has been interested in the processes that transform perceptual information into decisions for action. "Exactly where and how the sensory signals are evaluated to reach a categorical decision about an appropriate behavioral response is still quite mysterious," he says. Millions of neurons represent visual inputs in various parts of the brain, but only one or a limited number of actions can be taken.

TIMOTHY ARCHIBALD

When he explains his work to engineers, Newsome says, “I tell them we have monkeys looking at visual displays and ‘telling’ us what they see. Our goal, in turn, is to go into the brain with tiny microelectrodes and attempt to understand how the brain ‘sees’ by studying the electrical activity of single neurons one by one. It seems outrageous in principle—somewhat like taking the back off a Cray supercomputer and understanding how it works by measuring the activity of single resistors and capacitors one by one—but the amazing thing is that we can really make progress this way.”

The “single most exhilarating moment” of his research career, says Newsome, came in 1989 when he and Daniel Salzmann, a Stanford medical student at the time, showed that they could do more than just locate the neurons responsive to incoming visual signals—they also could artificially stimulate them. The neurons in question were cells that respond exclusively to motion in a particular direction. When Newsome stimulated cells that respond to upward motion while the animal was watching a downward-moving target, the monkey’s reaction indicated that it “saw” the target moving in the opposite direction.

“This was proof of principle,” says Van Essen, “that you can go into a collection of neurons and with these moderately sized jolts of electricity actually produce subtle and precisely measurable changes in what the animal perceives.”

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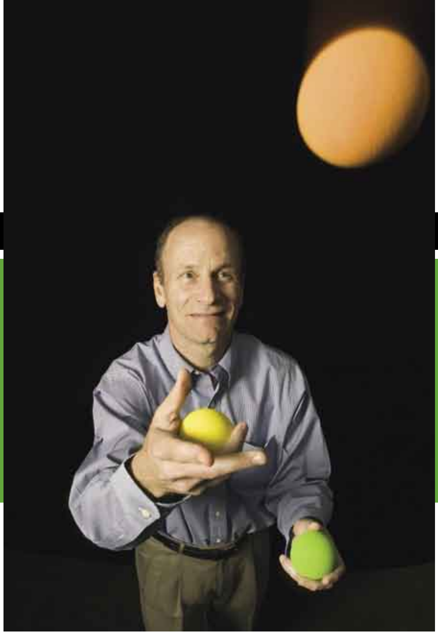
Moving from perception to decision is something like electing a nation’s president: Millions of voters have many different views of the candidates, but, when the votes are in, one bloc carries the day. Similarly, millions of neurons represent visual inputs in various parts of the brain, but only one or a limited number of actions can be taken.

For example, if a monkey is presented with visual targets moving in random directions but overall in a downward direction, how does the animal’s brain “pool,” or process, the cavalcade of information coming from different motion-detecting cells? “We realized there has to be some decision mechanism that takes the sensory evidence and reaches a judgment about whether the overall direction is up or down,” says Newsome. “The monkey has to put all of his eggs in one basket.”

Some of Newsome’s newest work incorporates research on the brain’s reward system—a field of study called “neuroeconomics.” This name reflects the fact that the expectation of a reward influences an individual’s decision about taking action—a fisherman, for example, throws a line into a part of the river that has produced catches before. “The question,” says Newsome, “is whether we can measure emotional arousal, manipulate those responses, show that they have effects on choice and behavior, and track the underlying neural signals.”



PAUL FETTERS

STEPHEN G. LISBERGER

➡ Stephen Lisberger has discovered that visual pursuit—tracking an object in motion—is not a reflexive action, but is actually a “complex voluntary behavior that comprises many components.” The eye and brain must choose which moving object to track, estimate the direction and speed of the target with respect to the moving eye, and command the eyeball to rotate along the object’s path at the correct speed.

Sensation to Action

STEPHEN G. LISBERGER, an HHMI investigator at the University of California, San Francisco, is investigating a complementary phenomenon. “I’m interested in how you take a visual sensory signal and convert it into a command for movement,” he says. For a window into this critical area, Lisberger has long studied the neuronal circuitry that enables monkeys to move their eyes smoothly while “pursuing”—that is, tracking—an object in motion.

Visual pursuit is a highly developed faculty in primates, and Lisberger likes to point out the virtuosity with which it performs in, for example, an outfielder turning and sprinting to the exact spot where a flying, curving baseball will come to earth. This feat depends on two separate faculties within the brain: keeping the eyes locked on the speeding ball, and compensating for the jerky, bouncing movements of the running fielder’s head.

Scientists used to think that smooth pursuit was a straightforward reflexive action. But over the past several years, Lisberger has discovered that pursuit is actually a “complex voluntary behavior that comprises many components.” The eye and brain must choose which moving object to track, estimate the direction and speed of the target with respect to the moving eye, and command the eyeball to rotate along the object’s path at the correct speed.

One of the most interesting components Lisberger discovered is an “online volume control” that selectively dials up or down the strength of visual inputs to the motor system. Analogous to Newsome's experiments, where stimulation in the brain area labeled "MT" changed what the monkey reported he "saw" for a given moving stimulus, Lisberger's laboratory demonstrated that stimulation in a part of the frontal motor cortex can change how the monkey's pursuit system responds to a given visual stimulus. The effect of stimulation seems to be mediated by altering the setting of the volume control.

Another longtime interest of Lisberger's is how the proverbial outfielder, despite running along and turning his gaze rapidly from place to place, manages to perceive the world as stable. It's due to the vestibulo-ocular reflex, or VOR, which occurs when, for instance, in watching someone pass by, you turn your head to the right: This action produces a smooth eye rotation to the left. Remarkably, even though the VOR is a simple reflex, it is capable of learning, so that any errors in stabilizing the world are quickly eliminated. Lisberger's lab has pinpointed the neural loci of learning to two places in the cerebellum and has begun to explain how learning at specific loci in the brain can be converted into organized changes in motor output.

JOHN H.R. MAUNSELL

➡ Visual inputs flow from the retina through a series of processing centers in the brain, climbing a ladder of increasingly higher-level stages until the image is in a "finished" form that, John H.R. Maunsell says, has been "edited to suit the immediate goals of the viewer." Maunsell's aim is to understand how changes in attention alter the responses of visual nerves involved in this editing process.

PAUL FETTERS

Attention Improves Perception

VISUAL INFORMATION from the outside world falls on our retinas in an overwhelming jumble of stimuli, like the incoherent babble of voices at a cocktail party. Fortunately, the brain is equipped to focus on small, important parts of a scene while screening out what is irrelevant. Attention, as this filtering process is called, sharpens our perception of the target and enables the brain to make better-informed decisions about responding.

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Maunsell and his colleagues at Baylor College of Medicine have worked with monkeys trained to fix their gaze on a central spot on a computer screen and then—without moving their eyes—shift attention to other targets. Meanwhile, a computer-aided sensing system records the electrical activity of the neurons in the brain that are receiving stimuli from the retinal cells that capture the object of the animal's attention.

This research has shown that when monkeys thus shift their attention, a surge of electrical activity occurs in those neurons. The investigators have demonstrated such an effect in many areas of the brain, in nerve cells specialized for different features such as detecting edges and motion as well as recognizing patterns.

More recently, the researchers changed the test conditions. The monkeys were trained to concentrate on a single dot. When dedicated neurons detected the target dot, their electrical activity spiked to twice the normal firing rate, and the same cells "turned down" their response when they encountered a similarly moving dot that wasn't the one on which they were trained to focus.

"The behavioral result is that you get improved perception or faster reaction times when the monkeys detect a small change or respond to it," Maunsell says. "What attention is doing is just altering the sensory representation the animal will use to make his decisions."

Maunsell emphasizes, however, that the allocation of attention is a dynamic, constantly changing process, and the strength of responses in the brain cells "can fluctuate over a fraction of a second as the animal directs more or less attention to different parts of the visual scene."

Maunsell is currently conducting experiments to discover how the brain translates a visual image's information into a motor response. So far, it looks as if this process is based on information from a limited voting body, so to speak, rather than a large population. A relatively small number of neurons—

hundreds, perhaps—are involved in different areas of the cortex.

This kind of research, Maunsell says, reflects a new stage in the daunting journey to understanding the workings of the brain. “I view the last 30 years as coming to grips with how things are laid out in the brain and where visual images are represented,” he says. “We have a decent first draft.”

Now, he says, researchers are delving into the still-mysterious processes “by which, using the 1.2 billion neurons in the visual cortex, the important bits of information are extracted and an appropriate motor response is determined.”

Context: “The Brain’s Best Guess”

WE’VE ALL SEEN puzzling photos of objects that are unrecognizable until we’re told or eventually figure out that they are small parts of something larger—an architectural detail, perhaps, of a familiar building. What was initially lacking was a context for the otherwise meaningless shape we were looking at. As soon as the context became apparent, recognition was a snap.

In one area of his wide-ranging vision research, Thomas D. Albright, an HHMI investigator at the Salk Institute for Biological Studies, in La Jolla, California, has been studying the crucial importance of contextual clues to visual perception. Context can mean many things, from the physical features of a visual target’s environment to memories stored in the brain that are associated with the object. Context, says Albright, helps us “recover” information that’s missing from the original image captured on our light-sensitive retinas.

At the first of several stages of increasingly sophisticated processing and interpretation, the retina senses mainly a patchwork of light, dark, and color—contrasts without recognizable shape or significance. In the next round of processing, Albright explains, brain cells that respond exclusively to certain features of an image begin providing rough interpretations of the visual scene. Some specialized cells are activated when they sense an edge or a contour, others when they detect motion in a specific direction, and still others when certain colors or brightness levels are present.

Next, these growing sensory impressions, not yet full-fledged perceptions, are fleshed out at the highest level—cognitive processing that integrates context in the form of memories, emotional responses, anticipated rewards, and the “mental set” of the viewer.

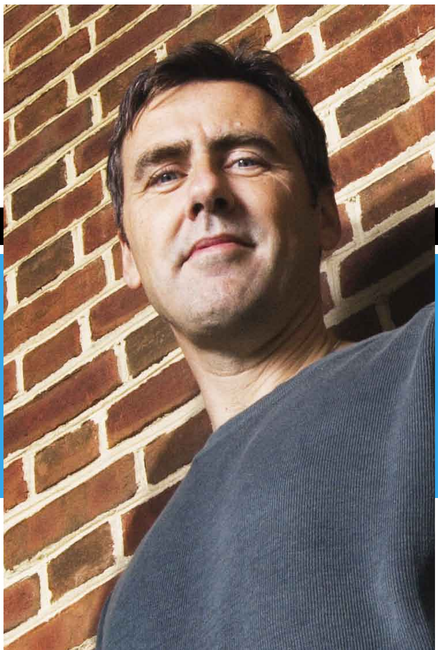
Up to this point, says Albright, context is supplied mainly by hard-wired rules of interpretation, so that most people’s perceptions of a scene are in agreement—we all pretty much see the same objective reality. But in the cognitive stages, the perception takes on more personal guises, with greater variation among viewers.

“People who’ve been deprived of many sensory experiences may have a very limited interpretation,” says Albright. “On the other hand, an artist like J.M.W. Turner, the English pre-Impressionist painter, may have a radically different view of the world.” Turner, whose landscapes and sunsets often were rendered in multihued, brilliant colors that were far from straight realism, once was told by a viewer, “I’ve never seen a sunset that looked like that,” recounts Albright. The artist responded, “Don’t you wish you could!”

Another form of contextual influence that Albright studies involves the visual system’s ability to “fill in” gaps in the eye’s image caused by events that obscure part of the scene. One omnipresent gap, for instance, is a “hole” in the retina’s image caused by the lack of light-detecting cells in a small circular area where the bundle of neurons forming the optic nerve leave the back of the eye and connect to the visual centers at the rear of the cortex. “The visual system has to have a mechanism to keep you from seeing a blind spot,” Albright explains.

How does it compensate? By sampling the image surrounding the exit hole in the retina so that we see “the brain’s best guess as to what’s there,” he says. “The brain will fill that space with the representation of the space around it,” Albright says. “And the remarkable thing is that it happens so fast.”

Or, as David Van Essen characterizes the overall context-establishing process, “The brain doesn’t have access to truths but to evidence, which is always incomplete. So what the brain has to do is make inferences.” ■



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