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More Than Meets the Eye

Images of a Research Lab

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(Following is the text of the essay. To view the photos, please request a printed copy of the magazine from the Table of Contents page.)

If you depend only upon your eyes, you won't see what's really going on in a research lab—even in the Department of Ophthalmology and Visual Sciences, where the focus is on understanding vision.

"You don't really see with the eye," said Jennifer S. Lund, Ph.D., professor of ophthalmology at the University's John A. Moran Eye Center. "What we see is actually due to the activity of cells in the cerebral cortex, which are stacked like a three-dimensional mosaic with interplay via the feedforward and feedback relays between many cortical areas."

Light rays pass through the cornea and the pupil to the lens, which focuses the rays on the retina. There, light is transformed into electrical impulses, then sent through the optic nerve to the brain, where the image actually is recognized.

A laboratory can be just as complex. Everyone recognizes rooms lined with shelves of beakers and benches with microscopes. But to know the creativity and the drudgery, the loneliness as well as the exhilaration of "eureka" moments that make all of the effort worthwhile, you must piece together images and impressions.

"Each neuron in the retina sees a little bit of the outside world," said Lund, who is developing a wiring diagram to explain the visual functions of the cerebral cortex. "The neurons take these messages to the brain, first the thalamus, then the cerebral cortex, where there are millions of neurons elaborately wired together like a vast computer—better than anything man can build. We're quite a long way from understanding it all."

Lund's research, among the most basic science investigations at the medical school's comprehensive eye center, still is linked to vision problems for which patients are seen in the clinics one floor above her lab. "With some diseases, you fail to see motion, or you see only half of the visual scheme or no colors," said Lund. "That's because of defects in the cerebral cortex."

"We all work together toward one end," noted Jill Church-Kopish, a lab

specialist in the department's Cell and Molecular Biology Lab. "You work closer with people in a lab. It becomes like a family.

"It's not like I do the same thing every day," explained the Michigan native, who taught high school there and in Park City. "It keeps changing. I like being on the front edge of change, too."

She doesn't always like the pressure, though. "Deadlines," she said, shaking her head. "Researchers want experiments to get done right away-ASAP-so they won't get scooped. You have to roll with the pressure." Or, as Church-Kopish has done, resort to humor. Embroidered on her lab coat is a patch with Dexter, a Cartoon Network character who has a secret lab in his parents' house. Miniatures of Dexter and his spaceship sit atop her computer screen.

"You have to have a sense of humor," said Edward M. Levine, Ph.D., assistant professor of ophthalmology and visual sciences, whose lab is housed in the Eccles Institute of Human Genetics. "Things don't always work out on time and the way you plan. If you take everything seriously that goes wrong, you'll go crazy."

Appropriate attire—shorts, tee shirts, sandals, anything casual—also is important. "People have to be comfortable. This work isn't a list of assignments," said the researcher who studies the pathways of retinal development using transgenic and knockout mice. "It will stifle creativity if the lab's too structured."

Across the hall is the lab of Rajendra Kumar-Singh, Ph.D., where gene therapy for retinitis pigmentosa, one of the most common genetic causes of blindness in the United States, is being investigated. He is using cold viruses to deliver therapeutic DNA into diseased tissues. "The culture of a lab is very surreal. Everything happens in a test tube. As a scientist, you're like an enzyme in the tube," mused the assistant professor.

"Over here is a restriction enzyme in a little tube: a molecule that does wonderful things. But it's only theory. You can't see it, because it's at the molecular level. So you do your experiment in theory. It's a leap of faith. If it works out, then you see it.

"Scientists spend a lot of time in lonely environments," said Kumar-Singh. "But you could come in the lab and be the first one on the planet to see, to understand a concept. The first ever, ever, because you discovered it.

"Occasionally, there is drudgery," he acknowledged, "but there are different kinds." A 1994 graduate of the University of Dublin, Ireland, Kumar-Singh can recall vividly his student years in labs: "graduate students and postdocs are still paid buttons for the amount of work they do." Now the drudgery has evolved to writing grants for his own lab. The difference is in the amount of control he has.

"As a research scientist, you can explore more things. You can follow the clues in the way you want to. You know Robert Frost's poem 'The Road Not Taken'? You can take that road. In how many jobs can you do that? It's a wonderful job."

"It was a lot of fun in the lab," agreed Wolfgang Baehr, Ph.D., professor and director of the department's Wynn Center for the Study of Retinal Degeneration, who started out as an organic chemist in Germany. "I did it for 30 years. That's enough. I still do analyzing and sequencing gels, but I hire people to do pipetting.

"Since I'm a senior guy, I do fundraising. Writing papers is my major occupation," noted Baehr, whose lab is working to identify genes that cause retinal degeneration and understand how gene mutations produce disease. "If you don't publish papers, you don't get funded. If you don't get funded, you're out of business-no matter how smart you are."

The author of more than 400 publications, Raymond D. Lund, Ph.D., is intimately familiar with administrative responsibilities. He served as a department chair for 15 years-including three at Cambridge University in England-before joining Utah's medical school as a researcher last fall. "The problem is administration has become a full-time job these days," said Lund. "I sidestepped back into science.

"I thought why not? It's like being a kid again," he said with a characteristic laugh. But he had another reason, too. "It's really corny. I'm the vice chair of the scientific committee of the Foundation Fighting Blindness. I kept going to these meetings and seeing people going blind, and I thought: what am I doing in administration?"

Lund is studying retinal cell transplantation that, someday, may prevent deterioration caused by retinitis pigmentosa, macular degeneration and other retinal diseases, which lead to blindness. He's devised ways to map the visual field by exposing rats-in which retinitis pigmentosa was first discovered-to light signals, then recording the electrical activity in their brains before and after receiving retinal transplants. The tests, which mimic those of human patients, are helping researchers determine how disease is distributed across the retina before transplantation and evaluate the effectiveness of treatment.

"We pick up what other researchers like Ed and Rajendra are doing, and apply it to animal models to see how it can help people. There's a kind of synergy in putting all these parts together," said Lund.

"When we started studying how the brain is put together and what happens when it's damaged, we had no linkage to anything conceivably clinical. But the culture of the lab has changed from basic research-trying to do experiments that provide scientific solutions-to experiments that provide clinical outcomes. We're trying to bridge that gap.

"It's a major change in the way we do business," noted the British investigator. "It's quite interesting."

Even the department's most futuristic project, an artificial vision system being developed by Richard A. Normann, Ph.D., has a clinical application in sight. "Eventually, we'll implant six to seven microelectrode arrays in the visual

cortex of a blind person," said Normann, professor of ophthalmology and bioengineering who directs the Moran Laboratories for Applied Vision and Neural Sciences.

Each silicon array measures four millimeters by four millimeters and contains 100 electrodes. The patient will wear glasses embedded with a miniature television camera in the nosepiece, which will pick up video signals. These will be changed by a signal processor into a set of stimulus signals, which will be sent to the electrode arrays implanted in the brain. The electrodes will thereby excite specific neurons.

"We will remap visual space into an appropriate two-dimensional array of electrical signals," said Normann. "It's got a way to go. We're working on other parts of the puzzle. For instance, how close can the electrodes be and still produce two distinct points of light?"

Normann's lab has a synergy of its own with ideas coming from bioengineering, materials science, electrical and mechanical engineering, and applied neuroscience. Yet the researcher sees this creativity distinct from the physical space.

"I think of the lab more as a work environment. There is no special environment where you go to create ideas. They come when you're driving, when you're in the shower. You're not going to have those ideas unless you work hard and immerse yourself in your problem.

"One of the great things about academic labs is you get to work with students," added Normann. "Trying to explain yourself to students makes you think why you're doing something and how you could do it better."

When the subject is artificial vision, the researcher frequently has to explain how real science differs from Hollywood's version. In the movie *The Matrix*, for instance, people received computer brain transplants and were plugged into a virtual world. "A lot of the students who come into the lab have fantasies of doing that. We try to channel their actions into real-world problems."

But not the fascination and curiosity that are essential to any successful lab. "Curiosity," said Normann, leaning back in his chair, "is the motivation for what goes on here."

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