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ADVENTURES IN SCIENCE

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Biomedical

This photomicrograph of a human fetal joint shows two cartilage surfaces close together. It was made using darkfield illumination, a method in which transparent structures appear white against a dark background.

by Kathiann M. Kowalski

Fluorescent — Glowing with the emission of electromagnetic radiation, especially visible light

Imaging

A CLOSE-UP LOOK AT LIFE

One image appears as an abstract group of glowing colors. Another resembles roots or tentacles. And a sequence of photos shows colored spheres pinching and dividing.

Beautiful, you think.

Then you learn that you're looking at an eye, brain cells, an embryo.

Welcome to the world of biomedical imaging. Close-up views of organs, tissues, and cells can make awesome art, but they also serve a purpose. Today's biomedical images often contain critical data. Or, they communicate important scientific concepts.

"This era of imaging, with its digital technology [and] the Internet, has given science a new voice," says Michael Peres, head of Rochester Institute of Technology's Biomedical Photographic Communications Department. Scientists can observe biological processes in amazing detail. Plus, they can share those images simultaneously around the world.

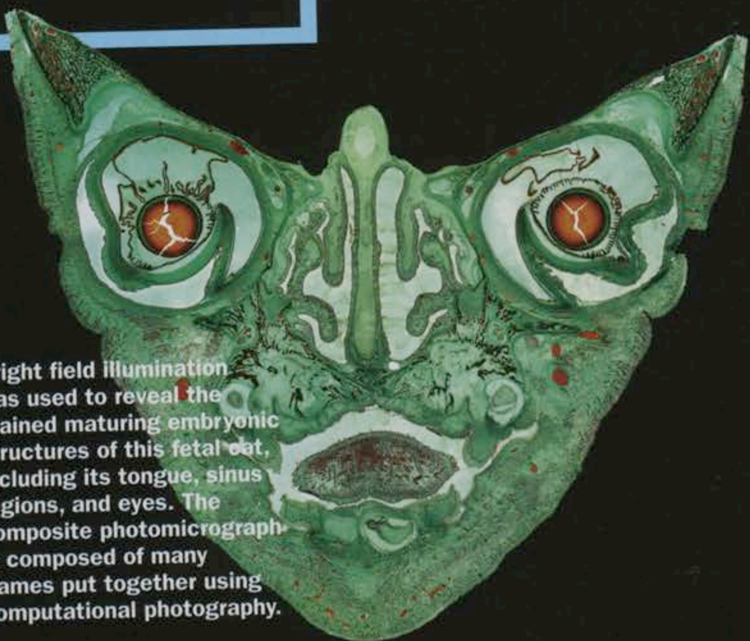
Technical Wonders

Imaging technologies have come a long way since electron microscopes first gave scientists black-and-white views of the details of dead cells in the 1930s. "Fluorescence has become one of the most powerful current tools used in the exploration of biological processes," notes Peres.

After scientists "tag" genes with *fluorescent* proteins, the proteins absorb energy. When exposed to certain wavelengths of light, the proteins release that energy by glowing different colors. Equipped with filters, microscopic imaging equipment can show what genes do in cells. Scientists can see how cells create and destroy proteins. They even observe cells signaling to each other "It really changes the way we can look at structures," says biologist Charles (Brad) Shuster at New Mexico State University.

Meanwhile, state-of-the-art microscopy has become "a combination of physics, math and computer science, and optics," says Jim McIlvain at Carl Zeiss Microscopy. "Fundamentally, we're pushing the limits of visualization." A new technique called *super resolution microscopy* can

Also made using darkfield illumination, this photomicrograph shows two swimming freshwater aquatic ciliated invertebrates called bursaria. Photographed using an electronic flash rather than a continuous light source, they are frozen in place and time. One can only guess what they are doing at that moment.



Bright field illumination was used to reveal the stained maturing embryonic structures of this fetal cat, including its tongue, sinus regions, and eyes. The composite photomicrograph is composed of many frames put together using computational photography.

photograph objects as small as 20 nanometers. Another technique, called *confocal microscopy*, uses laser light to photograph an object repeatedly at different *focal planes.* Computer software combines the photos into a continuous-focus image sharper than any single view through the microscope. Time-lapse filming, video, color stereo microscopy, new filters, and advanced lenses provide even more imaging tools.

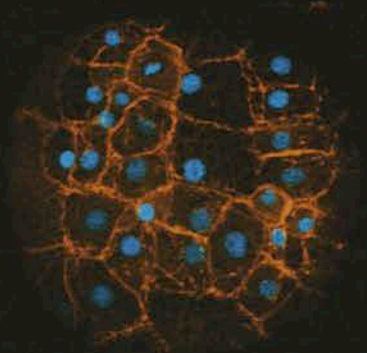
Nonetheless, creating effective images requires training and experience, plus an understanding of biology. "It's not point and shoot," stresses Peres. "The best photographers know their subjects as well as the camera."

Focal plane — The flat surface within a three-dimensional space on which a microscope focuses. Single microscope views focused on one focal plane leave areas above and below that plane out of focus.

Macular degeneration — A disease affecting the central part of the retina at the back of the eye

Ophthalmic — Related to the eye

Organelle — A structure within a cell



Embryos of crepidula, a type of sea snail photographed at the Marine Biological Laboratory at Woods Hole, Massachusetts

Images Are Data

Biomedical images have become crucial in healthcare. For example, America's overweight and aging population is especially susceptible to diabetes and *macular degeneration.* "Imaging plays a core role in the treatment and monitoring of the progression of those diseases," says Peres. *Ophthalmic* imaging can show tiny blood vessels and other details "that in a film world were just barely perceptible."

"Live cell imaging and its tools have become essential to how science is done today," says Boston College biologist David Burgess. How far did an *organelle* or protein move, and at what rate? Which genes "turn on" or get expressed within cells? How strong is a signal between cells? How do tumors grow and spread?

Modern imaging lets scientists observe such phenomena and measure them too. "It's gotten very, very quantitative," says Shuster. Various journals now require scientists to submit raw images and data in addition to JPEGs or another format for publication.

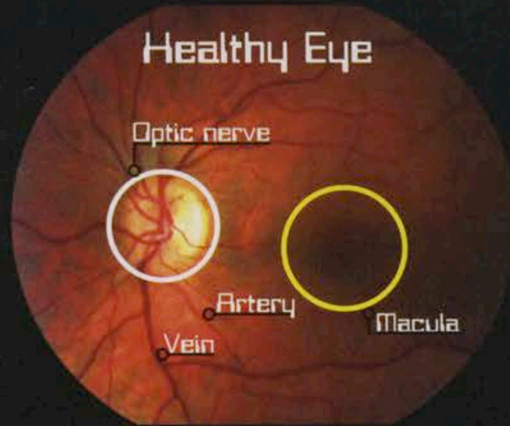
Unfortunately, Shuster notes, "Image data are very easily manipulated." Anything that is done should apply to the whole image evenly, he says.

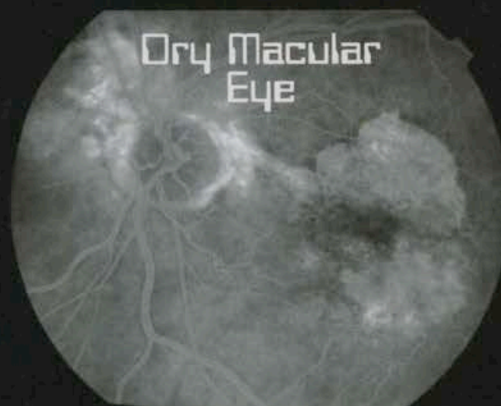
"You can't monkey with the images to selectively enhance" one thing or another, agrees Burgess. Doing so changes the data—and the results.

Glowing Reviews

Three scientists got glowing reviews when they shared the Nobel Prize in Chemistry in 2008. Back in 1962, Osamu Shimomura of the MBL in Massachusetts isolated green fluorescent protein (GFP) from a jellyfish. Afterward, Columbia University's Martin Chalfie showed how to use GFP as a glowing genetic tag. Then Roger Tsien at the Howard Hughes Medical Center developed different colors of fluorescent proteins. Their work made today's fluorescent biomedical imaging possible.

Students work in Professor Michael Peres's biomedical photography lab at Rochester Institute of Technology.





TOP: This photograph shows a healthy retina with no atypical anatomy or physiology present.

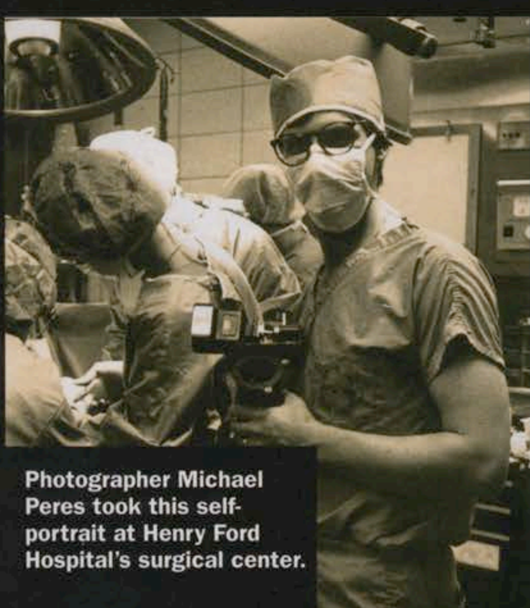
BOTTOM: This photograph shows a human retina revealing the effects of dry macular degeneration. The white regions show significant fiber/tissue growth in the region of central vision.

Adjusting contrast, brightness, color, or other factors to help people see better is generally acceptable as *clarification*. Manipulating or changing data is not. After all, says Peres, scientists who make biomedical images can't tell stories. "They have to record facts. They have to do it in a way that's standardized and repeatable so that other people in the field find it credible."

The Wow Factor

Biomedical images make biology beautiful too. "Many of these images are aesthetically spectacular," says Burgess.

Brainbow images are especially stunning. Harvard University researchers introduced the imaging technique in 2007. "Every neuron will be labeled a different color" with fluorescent proteins, explains Shuster. The technique lets scientists track individual nerve cells.



Photographer Michael Peres took this self-portrait at Henry Ford Hospital's surgical center.

Other awesome images show the wonder of life in action. It's one thing to know what an organ does; it's another to see it up close. It's one thing to listen to how embryos form; it's another to watch it happen. It's one thing to read about cellular functions; it's another to view them up close.

"Cells are way more exciting than we ever thought they were," notes Shuster Thanks to biomedical imaging, "Now we can see them in a totally different way."

Kathiann M. Kowalski was wowed by the biomedical images created as part of last year's Logan Science Journalism Program at the Marine Biological Laboratory (MBL) in Woods Hole, MA. She is the author of 22 books for young people and writes often for *ODYSSEY* and other Carus publications.

BRAINBOW:
http://cbs.fas.harvard.edu/science/connectome-project/brainbow