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JOSHUA FRANZOS

We don't see things as they are, we see them as we are.
—Anaïs Nin

Just months ago, I was hardly able to see without my glasses—my vision compromised by myopia since childhood and lately by cataracts. Now, after a surgeon replaced my inborn lenses with synthetic prescription lenses, using contemporary technology that I find amazing given the state of the art just a decade ago, I've gone from 20/200 vision to 20/15. It's been a transformative experience. There's clarity, resolution, and brilliance that I can barely describe. Colors appear as never before. Not only do I see better, I see differently. There is a poetry to this!

I have an inkling now for how Edwin Hubble might have felt in 1919, when he first pointed the enormous muzzle of the Hooker Telescope toward the heavens. At the time, the 100-inch lens was the largest in the world. The Hooker allowed Hubble to pick out stars in Andromeda and other spiral nebulae and gauge their distance from Earth. His work conclusively proved that the universe is larger than our own galaxy. Much larger, of course.

Edwin Hubble's heirs in physics and astronomy carry "the torch of science," as Alfred Noyes put it, to their own "deep-set boundary-mark in that immense darkness of Space and Time." In the life sciences, scientists carry that torch toward the infinitesimal.

We once thought that 200 nanometers—or about half a wavelength of light—was the limit at which we could see the cell's contents in visible light. An optical platform called STORM (stochastic optical reconstruction microscopy), developed by Xiaowei Zhuang of Harvard (who gave a Laureate Lecture here last June), gets around that by switching fluorescent probes on and off to capture overlapping molecules. This approach allows us to see life and the elements that comprise it at about 10 nanometers. The latest Nobel Prize in Chemistry was awarded to microscopists who first surpassed this perceived limit with similar "nanoscopy" systems. Using these platforms, researchers are seeing the most subtle of molecular interactions within cells. And they've discovered organelles that we didn't even know existed before.

Our own school boasts several talented scientists pushing microscopy forward. For instance, James Conway in our Department of Structural Biology studies viruses, including bacteriophages (viruses that infect bacteria—and some believe may be used one day to fight cholera and other pathogenic bacteria in humans), using cryo-electron microscopes. Cryo-EM microscopists preserve the structure of specimens by cooling them to liquid nitrogen temperatures before examining them in the vacuum of the electron microscope. James is now seeing pathogens at 4 angstroms—that's almost atomic resolution. He can even make out chains of amino acids. As he says in our story that begins on p. 30, "It's incredibly exciting . . . I can get a sample, put it in the microscope, and by this evening or tomorrow, I may be the first person to see what a particular virus looks like." And that is likely to translate to novel strategies for combating infectious disease.

Advances in technology pose new questions. (E.g., What is the function of the organelles that we are now seeing for the first time?) The answers are often incomplete and drive us to push the technology further. Research is iterative, and so is my newly enhanced view of the world!

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