Scientists

Revealing potential

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Adam Cohen's development of optical tools to monitor neurons and other electrically active cells caught our attention. Curious to know more, *BioTechniques* contacted him to find out about the ambitions, character, and motivations that led to his success.

What led you to develop a method to monitor electrical activity in cells?

Neurons don't have any intrinsic contrast mechanisms to indicate when an action potential fires, so researchers have been trying since the late 1960s to develop optical tools for recording neuronal activity. Most efforts have focused on using fluorescent dyes and proteins that might convert the firing of a neuron into an optical signal. However, these indicators have been either toxic, too slow to respond to neuron firing, which lasts only about a millisecond, or lacked sensitivity, only increasing fluorescence by 1% to 10%, which was very hard to detect.

We took a different approach and started working with a transmembrane protein, archaerhodopsin, from an organism that lives in the Dead Sea. The protein absorbs sunlight and uses that energy to pump protons across the membrane of the cell. My idea was to run this protein in reverse: instead of light in and electricity out, we would put electricity in and get light out.

Was the native archaerhodopsin fluorescent?

That was one of the challenges. Although the protein was known to be slightly fluorescent, the fluorescence was so dim it was considered undetectable. We spent

considerable effort figuring out how to detect the signal until finally, in one of our experiments, we noticed a background signal that just wouldn't go away. This turned out to be the native fluorescence of the protein, which was indeed very dim, but also very stable and occurred in the end of the spectrum where there was little background, making it easy to detect. After overcoming some other challenges in getting the protein to traffic correctly, we had a membrane-bound protein with fluorescence that is very sensitive to voltage across the membrane. When these proteins are expressed in a neuron and an electrical action potential fires, we see a sharp momentary increase in fluorescence that can be recorded with microscopy.

I understand you were trained as a physicist. How did you transition into studying neurobiology?

This occurred only within the last two or three years when I became aware of the interesting problems in imaging neuronal activity. As I started to think about the question, and realized that we might have a good solution to it, I wanted to learn more about the needs in neuroscience so we could develop and apply our answers in the most useful way. Half of my lab is now dedicated to imaging voltage in neurons and cardiac cells.

What else are you working on?

The other half of the lab works on biophysics or basic physics projects. For example, one of my students recently built a machine that allows users to suppress the Brownian motion of a single molecule in solution. We are applying this to look at how the flexibility of short pieces of DNA is affected by modifications in the underlying sequence. This is a question that has not been answerable by conventional techniques.

Another project in the lab explores how birds and insects are able to navigate using the earth's magnetic fields. The fundamental transduction mechanism for this is unknown, so we are studying the physics of simple chemical reactions that are sensitive to small magnetic fields to look for applications in a biological context. And finally,

we are looking for forms of light that can preferentially excite chiral molecules of one handedness relative to their mirror image with greater selectivity than circularly polarized light, which is usually used in circular dichroism spectroscopy. I think we can find something better.

Outside of my laboratory science work, I work on improving science education and curriculum in Liberia. I think it's important to use science and technology to help people in situations where resources are scarce.

How did you get involved with education in Liberia?

I went to a public high school in New York City where one of my science teachers, Asumana Randolph, was from Liberia. While I was in high school, he was unable to travel home because of a civil war, which ended in 2003, but he constantly collected decommissioned school supplies to ship to Liberia. After the war ended, he started traveling to Liberia to rebuild some of the educational infrastructure that had been destroyed during the war. I heard about this and decided I wanted to help.

One of the big problems in Liberia is a lack of usable equipment because there's no electricity supply or running water. So we developed some exercises using things we could buy in the local marketplace and presented them in a two-week long workshop for faculty from several Liberian universities and technical schools. For example, we purified DNA using tomatoes, dish soap, and rubbing alcohol and we made batteries and talked about electricity. We presented a lot of math, statistics, and physics experiments, all performed with locally available materials. Our goal is to improve teaching and help re-establish curricula that include research and experimental components.

Interviewed by Kristie Nybo, Ph.D. Image courtesy of Martha Stewart.

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