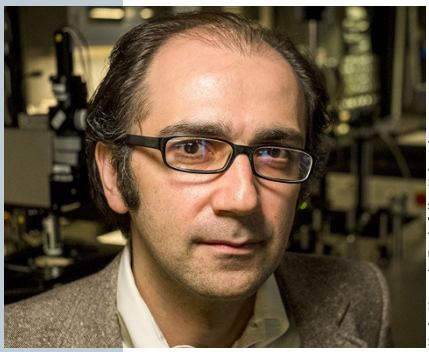
THE AUTHOR FILE

Alipasha Vaziri

A physicist handy with charcoal and ink uses sculpted light to image the brain.

His lab group meetings are video conferences. Physicist Alipasha Vaziri's neuroscience-related research is at Rockefeller University, and he has another team at the Research Institute for Molecular Pathology (IMP) in Vienna that has worked on super-resolution microscopy and has been applying single-molecule optical methods to cell biology questions. Most of Vaziri's group is in New York, but every few months he is in Vienna. He bridges the distance between visits with electronic tools that help with interaction and data sharing.



Mario Morgado/Rockefeller University

Alipasha Vaziri

Vaziri's latest development addresses neuroscientists' desire to image activity of many neurons in a behaving animal's brain and observe how these neurons interact. Electrophysiological recordings that capture data from a handful of neurons don't offer enough context for interpreting behavior. "It's as if you would be trying to guess the content of a movie by just looking at a few pixels on your screen," he says. Two-photon scanning microscopy captures more neuronal activity but reaches limits in terms of speed and the size of the brain volume that can be imaged. At depth, light-sheet microscopy has to battle scattering. The solution Vaziri devised is light sculpting based on temporal focusing (TeFo) in which the lateral and axial parameters of the microscope's laser beam are decoupled from one another. This approach let the scientists create spheres of excitation light that might be half the size of a neuron. At depths up to 500 μm these spheres were used to record neuronal activity rendered visual with calcium indicators.

The best way to excite these sculpted spheres is by giving each of them one pulse of light, says Vaziri. To do so, the team developed a laser with repetition high enough to allow fast acquisition rates by scanning and with a pulse that has enough energy to excite the calcium indicators in each voxel of brain tissue. The researchers scanned brain tissue quickly and over a large volume while sampling at single-neuron resolution. For example, in the cortex of awake, behaving mice, in a volume of 500 × 500 × 500 μm they captured activity three times a second from 4,000 neurons.

Vaziri hopes this technology can help labs explore cortical computation, the interaction between neurons in the cortex's layers and columns believed to be the canonical unit of computation in the brain. Using TeFo, labs could look at interacting neurons in multiple layers while an animal is solving a task, perhaps finding a hidden object. Next, he says, is to link such connectivity information to neuroanatomy. That's why he and his group recently duplicated the microscope.

The second microscope will be set up in David Cox's lab at Harvard University as part of a collaboration with neuroscientists there. Vaziri wants to disseminate his new technology. "We want people to use it, so we will try to be as helpful as possible," he says. Both a website and an annual workshop are in the works.

Vaziri obtained his PhD in physics from the University of Vienna, where he also did a postdoctoral fellowship. After a second postdoc at the National Institute of Standards and Technology in Washington and the University of Maryland, he joined Janelia Research Campus, where he learned firsthand about the tools sought in neuroscience. In 2011, he joined the IMP and the University of Vienna's center for molecular biology.

Even as a physics graduate student, Vaziri was fascinated by the brain, so he kept reading and attending talks on the subject. He knew he wanted to contribute to neuroscience. How to understand the brain, this tangible organ through which we perceive reality, is a fundamental question, he says. "We know that everything that is giving rise to all mysteries that we are after is ultimately confined in the piece of matter that is from you."

"I like also to draw."

Entering biology from physics takes some getting used to, says Vaziri. Physicists spend much time developing an experiment and putting it together. The actual experiment and data collection are often quick. It's the opposite in biology. Experimental design and building instruments take a fraction of the time needed to deal with biology because, he says, "it is valuable, it is to some extent unpredictable, and you need to just embrace the messiness of the biology."

Beyond work in the lab, Vaziri spends time with his family and takes his three-year-old son to museums, and the toddler also likes coming to the lab and watching. Vaziri enjoys mid-century modernism and, he says, "I like also to draw." His artistic tools of choice are charcoal and ink.

Vivien Marx

Prevedel, R. *et al.* Fast volumetric calcium imaging across multiple cortical layers using sculpted light. *Nat. Methods* **13**, 1021–1028 (2016).