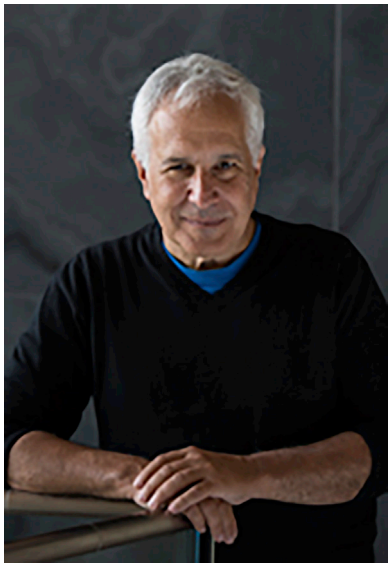
CellPress

Jeff Lichtman

Jeff Lichtman is interested in understanding the development of synapses and how they change as a result of experience. His work has championed the field of "connectomics." In an interview with *Neuron*, he discusses his approach to science and the challenges faced in the age of big data.

Jeff Lichtman is the Jeremy R. Knowles Professor of Molecular and Cellular Biology and the Ramón y Cajal Professor of the Faculty of Arts and Sciences at Harvard. His research interest is neural developmental and particularly the way in which early experience alters nervous system organization in long-lasting ways. He has participated in the development of methods that help describe neural connectivity at the level of individual synapses (connectomics) and how these networks change over time using fluorescence tools such as Brainbow and automated serial electron microscopical methods. Much of his work has centered on the mammalian peripheral nervous system, which undergoes profound activity-dependent circuit reorganizations in early life, causing axons to prune most of their branches while strengthening a small subset (synapse elimination). Professor Lichtman graduated from Bowdoin College with a degree in Biology and from Washington University School of Medicine in 1980 with a PhD in Neurobiology (mentored by Dale Purves) and an MD. After postdoctoral work with Eric Frank at Harvard Medical School, he joined the faculty of Washington University and remained there for 20 years before moving to the department of Molecular and Cellular Biology at Harvard in 2004. He is a member of the Center for Brain Science and the faculty director of the Harvard Center for Biological Imaging. He is a member of the National Academy of Sciences.



Jeff Lichtman
Harvard University

What do you think are the big questions to be answered next in your field?

We do not yet understand the way our experiences are encoded in the nervous system. To me this is the still unknown "central dogma" of neuroscience: a means for information transfer between individuals over generations based not on passing on genetic information, but rather on the transfer of learned information from one generation to the next.

Which aspect of science, your field or in general, would you wish the general public knew more about?

Because we all have brains and we all know they are important, it is disappointing how little the general public actually knows about the nervous system and neurobiology.

To tackle your favorite research question, is there a tool that either needs to be developed or is currently available that could be implemented in a novel way?

My personal hope is that comparative connectomics will eventually be possible. In this way, connectivity motifs that are different because of different learning experiences, diseases of cognition, different developmental stages, etc. might be ferreted out. This is a tremendously difficult graph analysis problem that will require not only routine methods to generate huge and complicated wiring diagrams but mathematics to analyze them.

Who were your key early influences?

Victor Hamburger, Rita Levi-Montalcini, Bernard Katz, Dale Purves, David Hubel, and Torsten Wiesel.

What's your favorite experiment?

Stanley Cohen's "accidental " pathway to discovery of epidermal growth factor by seeing that salivary extract caused premature opening of the eyes of young rodents.

What motivated you to become a scientist?

I grew up with a Leica microscope in my bedroom room as a child that my father had previously used in medical school. I spent a lot of time just looking at things and got hooked.

What is your view on big data-gathering collaborations as opposed to hypothesis-driven research by small groups?

I believe we scientists are beginning the painful transition from an age of big ideas to an age of big data. I see these two perspectives (ideas and data) as if they sit on opposite sides of a see saw. The more data, the harder it is to formulate a big idea (at least an idea that can be expressed in words). In my view, the biggest causality of big data is big ideas. So when people say to me that, sure we don't understand something yet, but eventually we will, I think quite the opposite, that more information only makes understanding

harder. If you want big ideas, look back in time.

What do you think are the biggest problems/challenge science as a whole is facing today?

What replaces the traditional idea of ''understanding'' when a biologist confronts a massive amount of detailed data. This is for me the crisis of modern biology, that things are not getting easier but harder to understand even though our description of the biological universe is getting ever more accurate. I think learning to handle and leverage big data is an exciting future for all of biology (genomics is farther along than any field in biology) but in my view handling big data is fundamentally different than the more straightforward hypothesis testing that drove so much neuroscience in the past half century.

How do you view the level of crosstalk between disciplines, (for example, physics, mathematics, engineering, humanities, and social sciences)?

I see computer science and mathematics playing an ever larger role in biology.

What advice do you find yourself giving to your students and postdocs?

I tell them to ask themselves when they pose a research question if they don't do it (let's say they get hit by a truck), will the experiment likely be done by someone else. If the answer is yes, it is the wrong question to ask.

How do you find inspiration?

By looking at the biological sample. The great embryologist Victor Hamburger said, ''Our real teacher has been and still is the embryo, who is, incidentally, the only teacher who is always right.''

What do you do when you're not in the lab?

Garden and play piano.

What career paths did you consider other than a scientist?

Pianist, composer, writer—but I wasn't good enough at any of them.

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