

Perspectives & Opinions

The Theory Connection

Neuroscientist Jeremy Freeman believes scientific theory is all about making connections: between people, between labs, between biological systems. And he considers Janelia Research Campus, where he's a group leader, to be an ideal environment for fostering those relationships.

WE ALL LEARNED the scientific process. Formulate a hypothesis, collect exactly the right data to test the hypothesis, and then evaluate it. But it's never that straightforward. More often, we collect not-really-the-right data and end up swimming in observations, many of them unexpected.

Some are curious, some are trivial, some are groundbreaking. How do we sort through them? How do we plan the next experiment? How do we put it all together?

To me, theory is a collection of strategies, tools, and concepts for making sense of experimental data. It's the halfway point between data and ideas. By design, I rarely enter a collaboration or experiment with a preconceived notion of what I hope or expect to find. I let my thinking be driven by the data, and allow myself to be surprised. But data analysis quickly suggests hypotheses

and more targeted experiments. I do my best to sit in the middle of that loop.

This approach becomes all the more pressing as we study increasingly complex systems. The magnitude of data being collected and the experimental capabilities, at Janelia and elsewhere, are outpacing our ability to analyze the data, let alone develop principles for what they mean and what experiments to do next. We have unprecedented access to the inner workings of the nervous system and can do experiments that a few years ago would have seemed impossible. To keep up, we need to modernize our analysis, making it more efficient, more collaborative. And do it fast enough to adjust our experiments in real time.

One great example is my lab's collaboration with Nick Sofroniew, in Karel Svoboda's lab. Nick has designed an incredible virtual reality system that simulates a tactile environment through which a real mouse can navigate, running on a ball while walls move back and forth stimulating its whiskers. We can monitor neural responses over increasingly large portions of the animal's brain while

it performs this behavior.

The complexity is daunting – not only of the data themselves, but the sheer number of possible behavioral paradigms and experimental manipulations. One way to start paring down that list is to analyze the data online.

This lets us make experimental decisions or manipulate neurons

based on the measured data, all while the mouse is still on the ball. Some of what we're developing is specific to this system, but much of it is general – both the techniques and the ideas – and we're actively collaborating with others to develop similar approaches in other systems.

Establishing a computational collaboration starts with making a personal connection. We need to open and maintain conversations, between theorists and experimental groups, and among different groups who might find it

useful to be exposed to each other's ideas. I don't think it's a surprise that most of the great discoveries in science have two or more names attached to them, and that will only continue as we tackle larger and more complex problems – together.

Janelia is a phenomenal place to do computation and theory because there are almost no barriers to building these relationships. Everyone is so open to looking at the experimental data with others. Janelians want to collaborate.

The physical space in which we work matters a lot, especially when it comes to proximity. Janelia is relatively small, so it's easy to run into people. On a big, sprawling campus it would be harder to get collaborations off the ground. At Janelia, if I just sit all day by the coffee bar, I'll have a chance to talk with all of my collaborators – and probably end up with new ones.

Theorists' activities at Janelia are diverse, but one thing we have in common is that we work across different systems. Theorists at Janelia have a unique opportunity to sit at the intersection between labs, revealing principles that span animals and modalities, and sharing ideas and techniques. Part of my own work is building platforms for analysis of neural data that make it easier to collaborate and coordinate. As that effort grows beyond our campus and into the broader neuroscience community, Janelia itself has been a model for what openness and collaboration can, and should, look like.

I often hear that neuroscience needs more theorists. Maybe it's not that we need more; it's just that we need to dissolve the barriers to making connections. All scientists should work closer to the intersections. We'd all be thinking a little more theoretically, a little more computationally. And that's where the big ideas will come from.

–Interview by Nicole Kresge

Jeremy Freeman

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Jeremy Freeman is a group leader at the Janelia Research Campus.

Jeremy Freeman
applies computational
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