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Researchers combine the power of artificial intelligence and the wiring diagram of a brain to predict brain cell activity

Information in the brain is transmitted via electrical signals between specialized cells called neurons. The activity within a large network of such neurons controls sensations, behavior, and cognition. Scientists have long sought ways to simulate the neural networks in the brain with computers in order to understand how it works. Now, researchers have combined new measurements of the wiring diagrams of the fruit fly with artificial intelligence methods to build a neural network that can do what few thought possible: To predict the activity of individual neurons without making a single measurement in a living brain.

The research, published in the scientific journal *Nature* today, was carried out by University of Tübingen scientists, Prof. Dr. Jakob Macke and PhD candidate Janne Lappalainen, in collaboration with Dr. Srinivas Turaga and colleagues from HHMI's Janelia Research Campus.

For decades, neuroscientists have spent countless hours in the lab painstakingly measuring the activity of neurons in living animals to tease out how the brain enables behavior. These experiments have yielded groundbreaking insights into how the brain works, but they have only scratched the surface, leaving much of the brain unexplored.

Now, researchers are using artificial intelligence and the connectome – a map of neurons and their connections created from brain tissue – to predict the role of neurons in the living brain. Using only information about the connectivity of a neural circuit gleaned from the fruit fly visual system connectome and a guess of what the circuit is supposed to do, researchers created an AI simulation of the fruit fly visual system that can predict the activity of every neuron in the circuit. “We now have a computational method for turning measurements of the connectome into predictions of neural activity and brain function, without first starting with difficult-to-acquire measurements of neural activity for every neuron,” says Janelia Group Leader Srini Turaga, a senior author on the new research.

The team of scientists from HHMI’s Janelia Research Campus and the University of Tübingen used the connectome to build a detailed deep mechanistic network simulation of the fly visual system, where each neuron and synapse in the model corresponds to a real neuron and synapse in the brain. Although they didn’t know the dynamics of every neuron and synapse, data from the connectome allowed the team to use deep learning methods to infer these unknown parameters. They combined this information with knowledge about the circuit’s goal: motion detection. “At that point, everything fell into place, and we could finally figure out if this connectome-constrained model gives us a good model of the brain,” says Janne Lappalainen, a PhD candidate at Tübingen University who led the research.

Scientists use the connectome to build a detailed deep mechanistic network simulation of the fly visual system that can predict neural activity in living brains.
The new model predicts the neural activity produced by 64 neuron types in the fruit fly visual system in response to visual input and accurately reproduces more than two dozen experimental studies performed over the past two decades. By enabling researchers to predict the activity of individual neurons using only the connectome, the new work has the potential to transform how neuroscientists generate and test hypotheses about how the brain works. In principle, scientists can now use the model to simulate any experiment and generate detailed predictions that can be tested in the lab.

The new research provides more than 450 pages of predictions gleaned from the new model, including identification of cells not known to be involved in motion detection previously, that can now be examined in living flies. The group’s work provides a strategy for turning the wealth of connectomic data now being generated by Janelia and other research institutions into advanced understanding of the living brain, according to the researchers. “There is a big gap between the static snapshot of the connectome and the dynamics of real-life computation in the living brain, and the question was, can we bridge that gap in a model? This paper, for the specific example of the fruit fly, shows a strategy for bridging that gap,” says Jakob Macke, a senior author on the paper and a professor at the University of Tübingen. This approach makes it possible to create artificial neuronal networks that are similar to the brain of fruit flies, and which can be used for a variety of future investigations: For example, they could be used to investigate how biological neural networks are able to be so much more energy efficient than artificial neural networks.

Janne Lappalainen is a PhD student at Tübingen University and the International Max Planck Research School `Intelligent Systems', and a visiting scientist at HHMI's Janelia Research Campus. Professor Jakob Macke leads the `Machine Learning in Science' Group, which is part of the Tübingen Cluster of Excellence „Machine Learning: New Perspectives for Science", the Tübingen AI Center and the "Bernstein Center for Computational Neuroscience Tübingen". The project has been funded, in part, by the ERC Consolidator grant DeepCoMechTome.

Publication:

Janne K. Lappalainen, Fabian D. Tschopp, Sridhama Prakhya, Mason McGill, Aljoscha Nern, Kazunori Shinomiya, Shinya Takemura, Eyal Gruntman, Jakob H. Macke, Srinivas C. Turaga: "Connectome-constrained networks predict neural activity across the fly visual system", *Nature*, 2024

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