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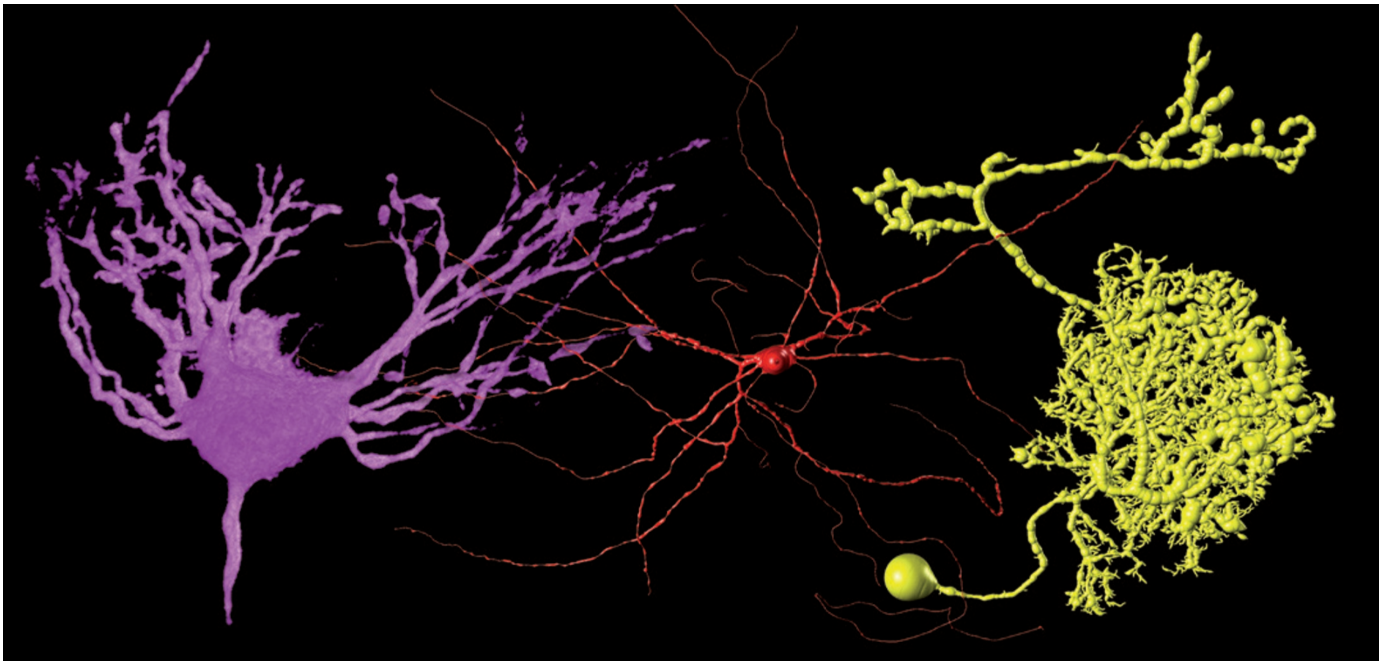
ALLEN INSTITUTE FOR BRAIN SCIENCE



Brain cells from a chick (purple), turtle (red) and fruit fly (yellow) illustrate the diversity of neuron shapes.

NEUROSCIENCE

Neuron encyclopaedia fires up to reveal brain secrets

But effort to catalogue brain's building blocks may stoke disagreements over classification.

BY HELEN SHEN

An ambitious plan is afoot to build the world's largest public catalogue of neuronal structures. The BigNeuron project, announced on 31 March by the Allen Institute for Brain Science in Seattle, Washington, is designed to help researchers to simulate and understand the human brain. The project might also push neuroscientists to wrestle with fundamental — sometimes even emotional — questions about how to classify neurons.

It is the era of the mega-scale brain initiative: Europe's Human Brain Project aims to model the human brain in a supercomputer, and the US BRAIN Initiative hopes to unravel how networks of neurons work together to produce thoughts and actions. Standing in the way of these projects is a surprising limitation. "We still don't know how many classes of neurons are in the brain," says neuroscientist Rafael Yuste at Columbia University in New York City.

BigNeuron aims to generate detailed descriptions of tens of thousands of individual neurons from various species, including fruit flies, zebrafish, mice and humans, and to suggest the best computer algorithms for extracting the finely branched shapes of these cells from microscopy data — a difficult and error-prone process.

Getting the details of the shapes right is crucial to accurately modelling the behaviour of neurons: their geometry helps to determine how they process and transmit information through electrical and chemical signals.

BigNeuron is not starting from scratch. Descriptions of neuron types date back to the Spanish neuroanatomist Santiago Ramón y Cajal, who in the late 1800s drew what he saw under the microscope. Stellate neurons are named after their starburst shape, and pyramidal neurons are recognizable by their pointed cell bodies.

But these definitions probably capture only a small slice of the diversity among the tens of millions of neurons in the mouse brain, ▶

or the tens of billions in the human one. "There are too many neurons in the brain, and we have only sampled a very, very small set," says the Allen Institute's Hanchuan Peng, who is leading the BigNeuron project.

A major bottleneck in cataloguing more neurons has been extracting the three-dimensional structure from a stack of hundreds or thousands of two-dimensional microscope images. Neurons often turn sharply, loop back on themselves and cross over each other. So tracking all the branches can be tricky, both for humans and for machines. A simple neuron might take a few days to reconstruct by hand; a more complex cell could take months.

Computers tend not to trace neurons as well as people can, but some programs can tackle a tough case in just a few hours. Their success depends on the input data and on experimental conditions.

To make it possible to characterize thousands of neurons, the first phase of BigNeuron is to figure out which algorithms are best for specific jobs. Over the next few months, code developers will be invited to submit their best reconstruction algorithms and neuroscientists their imaging data. Next, supercomputers will run the algorithms on the contributed data. The various reconstructions will be compared against each other and, where available, against human reconstructions, which are still considered the 'gold standard'. All the data and algorithms will be made open-access.

The Human Brain Project, the Wellcome Trust in London and the Janelia Farm Research Campus in Ashburn, Virginia, are among those who have pledged to sponsor meetings and workshops for BigNeuron. Oak Ridge National Laboratory in Tennessee and Lawrence Berkeley National Laboratory in California will join the Human Brain Project in contributing supercomputing resources. The Allen Institute has no formal estimates yet of the project's cost.

By 2016, project organizers hope to have a massive, annotated database of neuron morphologies. But Yuste thinks that BigNeuron will magnify another major challenge: researchers will have to agree on where to draw the boundaries between cell types.

Researchers generally agree on some neuron types, such as the chandelier cell. Other classes are not so clear, including the classic pyramidal cells, which make up about 80% of neurons in the cerebral cortex. Some researchers have proposed that the category actually encompasses many different types, whereas others see a single class of somewhat heterogeneous cells.

Egos are at stake, too, because several cell types are named after the researchers who described them. "People are very emotional about this," Yuste says.

The problem, says Yuste, is that neuronal taxonomy has historically been based largely on qualitative descriptions and subjective assessment of microscope images. As imaging technologies and automated analysis algorithms improve, they will provide more-detailed data and quantitative measures to classify cells.

"I guarantee there are going to be new neurons that no one has ever described before, and neuron types that people have previously described that are going to get blown away," says Yuste. ■

CLIMATE CHANGE

Global-warming limit of 2 °C hangs in the balance

Panel creates scientific baseline for debate about climate reparations.

BY JEFF TOLLEFSON

In preparation for international climate talks in Paris this December, a scientific panel has completed a technical evaluation of the meeting's official goal — to keep the global average temperature within 2 °C of pre-industrial levels. Scheduled for release as soon as 3 April, the panel's report will assess prospects for meeting this goal as well as impacts on environment and society that are likely to occur well before that threshold is breached, feeding into a potentially explosive debate about whether the target should be set even lower.

"We have provided a substantive basis for the political discussion," says Andreas Fischlin, an ecological modeller at the Swiss Federal Institute of Technology in Zurich and co-facilitator of the process.

The 2 °C goal encountered intense opposition when it was formally adopted in Cancún, Mexico, in 2010. Led by low-lying island nations and many of the poorest countries — which are likely to be hit hardest by rising seas and extreme weather — a solid majority of nations in the United Nations Framework Convention on Climate Change called for a formal review into whether the goal should be lowered to 1.5 °C. The bulk of support for the 2 °C goal comes from wealthier industrialized nations, which can more easily adapt to the changing climate.

For many poor countries, the debate is about social justice, says Petra Tschakert, a geographer at Pennsylvania State University in University Park who participated in the process. Scientifically, Tschakert says, a goal of 1.5 °C is clearly more protective of vulnerable populations. But developing countries recognize that meeting the 2 °C goal, let alone 1.5 °C, will be exceedingly difficult on the basis of current emissions trends. What they seek, she says, is a benchmark that they can use in Paris to fight for 'loss and damages' — monetary compensation paid by the biggest greenhouse-gas emitters to the poorer countries most harmed by warming.

"The science tells us that 1.5 °C might be considerably better."

"The real question is whether or not the high-income countries, the big polluting countries, are willing to pay loss and damages to countries that bear the brunt of the impacts," she says. "Vulnerable countries have no other leverage within this political process."

The history of the 2 °C goal extends back four decades. At the time, researchers argued that it would be wise to keep Earth's average temperature below the upper bound of the 10 °C range that has prevailed naturally over the past few hundred thousand years. It has become increasingly clear, however, that temperatures are destined to soar well beyond anything that humans have ever witnessed. Even if countries keep to the emissions pledges they have made up to now, climate models predict that the world is on track for about 3 °C of warming this century.

At the same time, a growing body of research suggests that ecological and economic impacts are already occurring with the 0.8 °C of warming that has already occurred. These impacts will increase in severity as temperatures rise. Damage to coral reefs and Arctic ecosystems, as well as more extreme weather, can all be expected well