How do we provide meaning to our environment? Cracking the neural code to the brain

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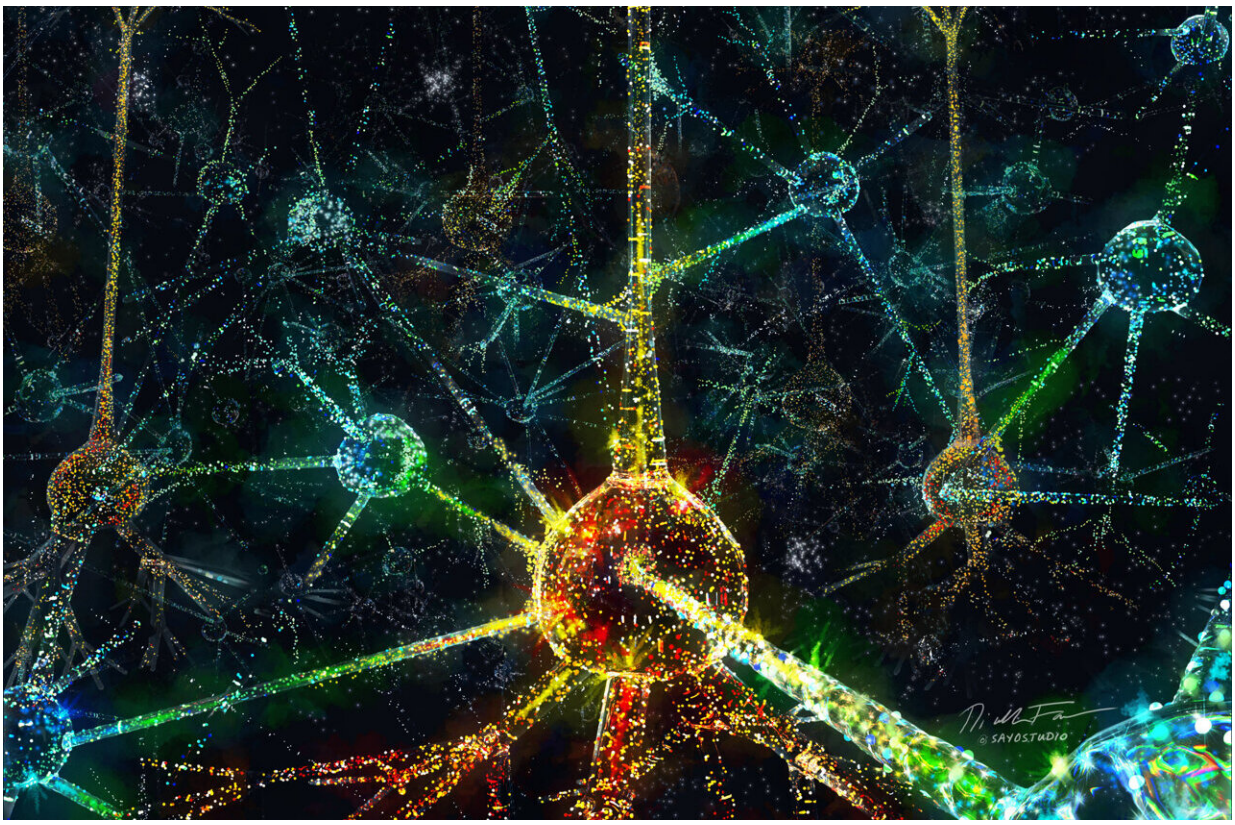

Jerry Chen, a Boston University College of Arts & Sciences assistant professor of biology, researches the neural code of the brain. He aims to better understand the relationship between the genetic and electrical influences that control cognitive functions like sensory processing, decision-making, and learning and memory. Credit: Nicolle Fuller, Sayo Studios

The brain is the most complex organ in our body—constantly absorbing and interpreting our surroundings, and guiding our movement, thoughts, behaviors and emotions. Although human beings share a fundamental understanding of our surrounding environment (i.e. ice is cold, fire is hot, knives are sharp) – each of us develops a unique interpretation of the information we process. For example, two people can have very different reactions after tasting the exact same meal, hearing the same sound, or leaving a shared social interaction.

Jerry Chen, a Boston University College of Arts & Sciences assistant professor of biology, researches the neural code of the brain. He aims to better understand the relationship between the genetic and electrical influences that control cognitive functions like sensory processing, decision-making, and learning and memory. "In order to crack the neural code," explains Chen, "you need to know at least two things. First, you need to be able to measure the activity of neurons in the brain as a subject is carrying out different cognitive tasks. And second, you have to know the identity of those neurons which we can learn about through the genes they express."

In his latest research breakthrough, published in *Science*, Chen and his collaborators uncovered how a mouse brain understands sensory information—specifically focusing on the perception of touch. His team's new discovery has relevance for a range of neurological disorders such as stroke, to neuropsychiatric diseases such as Autism Spectrum Disorder, where an individual's sense of perception can be altered. Additionally, the new findings have exciting implications for targeted treatments and interventions for psychological and neurological disorders.

Jerry Chen weighs in on the study's goals, methodology, findings and impact in the Q&A below.

What did you aim to study with your research? What made you want to examine this issue?

Our lab is interested in studying the neural basis for perception and cognition. The brain is the most complex organ in the body. That complexity is partially defined by the fact that billions of the neurons in the brain are not all the same. There are hundreds of thousands of different types of neurons—serving different functions and carrying out different computations. To really understand how the brain operates, we need to deconstruct the brain down to its individual components and then start asking how these components interact during behavior.

Can you please explain the first-of-its-kind "neuron catalog" technology that contributed to this study—and its impact?

Our collaborators from the Allen Institute for Brain Science had a goal of creating a "neuron catalog" by generating a census of all of the types of cells in the brain. This is part of a collective effort by several teams across multiple institutions.

The catalog only describes the molecular composition of the neurons but it doesn't necessarily say anything about the function of the neurons or the computations they perform. The technology that my research team developed leverages this new information from the catalog, and adds the next layer of information, which is the activity patterns of the cells. It allows us to hone in and study the function of the cells in the catalog in a comprehensive manner. This is why we call it **C**omprehensive **R**eadout of **A**ctivity and **C**ell type Mar**K**ers, or CRACK (ie. a pun on "cracking neural circuits"). Our CRACK technology will pave the way for a "catalog 2.0," allowing researchers to collect both molecular and functional information about all of the cells in the brain.

How did you apply this technology within your study?

We applied the CRACK platform to study a specific part of the cortex involved with our perception of touch. We looked at how the different neurons from the catalog process information and talk to other neurons when an animal touches objects in their environment. We also looked at how the neurons adapt when the environment changes.

What did the findings reveal?

When you're perceiving the world around you, your brain does a combination of processing the stimuli that makes up the scene—but it also tries to fill information based on what you've learned in the past to help you interpret what you're sensing. For example, let's say you're rummaging through a bag feeling around for your car keys. Your brain has learned what keys feel like and so it's filling in information as you are feeling objects of different textures or shapes to guide your search. However, there are times when you feel something, like a sharp edge, that really jumps out and tells you that you're on the right track and that you've maybe found your keys. Our findings essentially uncover that there is a dedicated circuit composed of specific cells in the catalog that we call "hub cells." These cells help to alert the brain that you've come across a salient feature that needs to be investigated further.

What was the most surprising finding?

A surprising finding is that the "hub cells," that we identified to be important for "feature detection," also respond in interesting ways when your environment changes. There are a certain set of genes that are known to be important for learning and adaptability, that can go up or down depending on changing environments. We found that those genes are always "on" in hub cells, which goes against some current principles.

When environments change, these cells respond by trying to compensate for these changes. We think this could be a way for the circuit to "remember" or "not forget" how to process information in the old environment.

What is the significance of these findings?

Our findings have relevance for a range of neurological disorders such as stroke, to neuropsychiatric diseases such as Autism Spectrum Disorder, where an individual's sense of perception can be altered. Rather than viewing the brain as a homogenous piece of tissue, understanding which specific cell types are the most relevant will allow us to develop treatments that can be highly targeted. This marks exciting progress toward directly treating the underlying cause of specific symptoms—while also potentially avoiding unwanted side effects from other therapeutics and interventions.

What do you hope to study next?

There are a lot of directions that we're going in based on our new technology and findings. The idea of dedicated circuits for neuronal plasticity composed of specific cell types in the catalog—or the surprise finding in our study—is especially intriguing. This is one area that we're following up on; we're specifically looking at potentially similar types of circuits in other parts of the brain and how they function both during learning and memory, and across time.

More information: Cameron Condylis et al, Dense functional and molecular readout of a circuit hub in sensory cortex, *Science* (2022). DOI: 10.1126/science.abl5981.
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