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Researchers create most realistic computer models of brain cells

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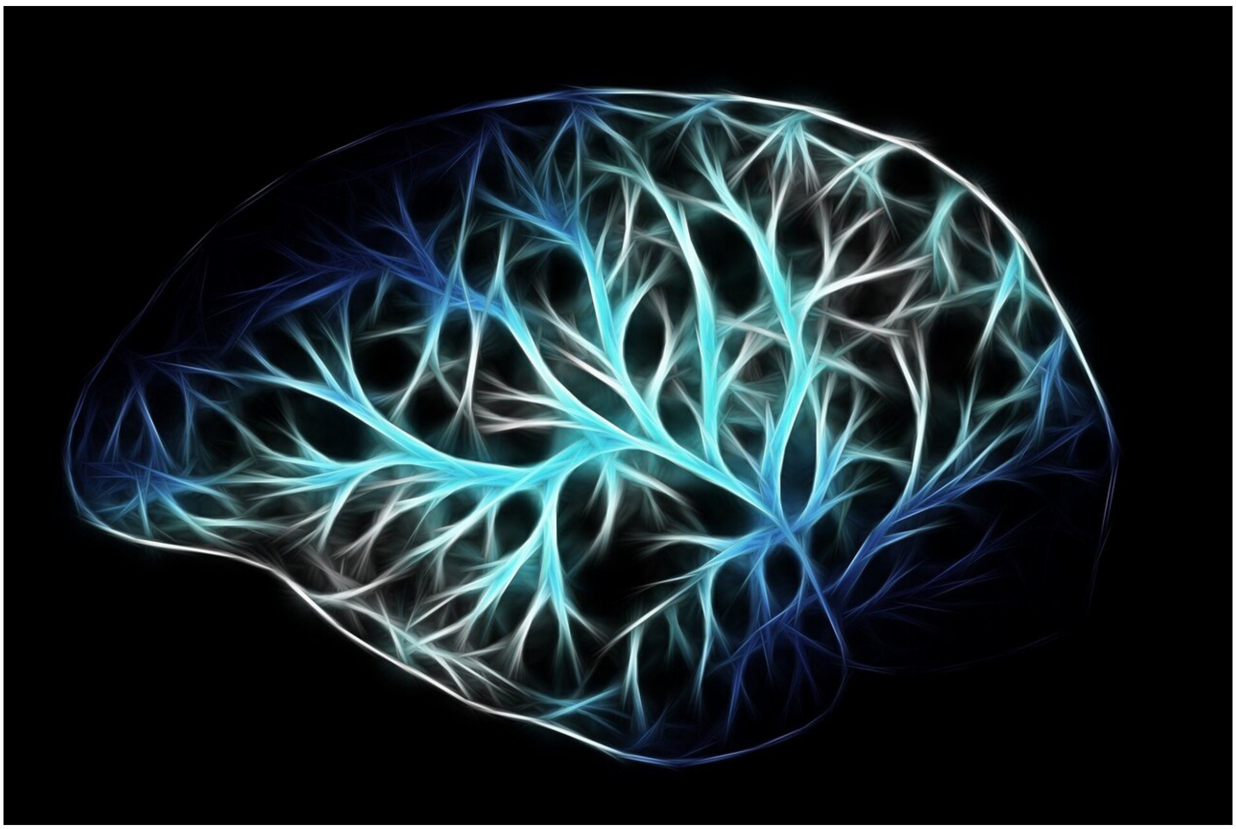

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Cedars-Sinai investigators have created the most bio-realistic and complex computer models of individual brain cells—in unparalleled quantity. Their research, published today in the peer-reviewed journal

Cell Reports, details how these models could one day answer questions about neurological disorders—and even human intellect—that aren't possible to explore through biological experiments.

"These models capture the shape, timing and speed of the electrical signals that neurons fire in order to communicate with each other, which is considered the basis of brain function," said Costas Anastassiou, Ph.D., a research scientist in the Department of Neurosurgery at Cedars-Sinai, and senior author of the study. "This lets us replicate brain activity at the single-cell level."

The models are the first to combine data sets from different types of laboratory experiments to present a complete picture of the electrical, genetic and biological activity of single neurons. The models can be used to test theories that would require dozens of experiments to examine in the lab, Anastassiou said.

"Imagine that you wanted to investigate how 50 different genes affect a cell's biological processes," Anastassiou said. "You would need to create a separate experiment to 'knock out' each gene and see what happens. With our computational models, we will be able to change the recipes of these gene markers for as many genes as we like and predict what will happen."

Another advantage of the models is that they allow researchers to completely control experimental conditions. This opens the possibility of establishing that one parameter, such as a protein expressed by a neuron, causes a change in the cell or a disease condition, such as epileptic seizures, Anastassiou said. In the lab, investigators can often show an *association,* but it is difficult to prove a *cause*.

"In laboratory experiments, the researcher doesn't control everything," Anastassiou said. "Biology controls a lot. But in a computational simulation, all the parameters are under the creator's control. In a model, I can change one parameter and see how it affects another, something that is very hard to do in a biological experiment."

To create their models, Anastassiou and his team from the Anastassiou Lab—members of the Departments of Neurology and Neurosurgery, the Board of Governors Regenerative Medicine Institute and the Center for Neural Science and Medicine at Cedars-Sinai, used two different sets of data on the mouse primary visual cortex, the area of the brain that processes information coming from the eyes.

The first data set presented complete genetic pictures of tens of thousands of single cells. The second linked the electrical responses and physical characteristics of 230 cells from the same brain region. The investigators used machine learning to integrate these two datasets and create bio-realistic models of 9,200 single neurons and their electrical activity.

"This work represents a significant advancement in high-performance computing," said Keith L. Black, MD, chair of the Department of Neurosurgery and the Ruth and Lawrence Harvey Chair in Neuroscience at Cedars-Sinai. "It also gives researchers the ability to search for relationships within and between cell types and to glean a deeper understanding of the function of cell types in the brain."

The study was conducted in collaboration with the Allen Institute for Brain Science in Seattle, which also provided data.

"This work led by Dr. Anastassiou fits in well with Cedars-Sinai's dedication to bringing together mathematics, statistics, and computer science with technology to address all the important questions in biomedical research and healthcare," said Jason Moore, Ph.D., chair of the Department of Computational Biomedicine. "Ultimately, this computational direction will help us understand the deepest mysteries of the human brain."

Anastassiou and his team are next working to create computational models of human cells to study brain function and disease in humans.

Provided by Cedars-Sinai Medical Center

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