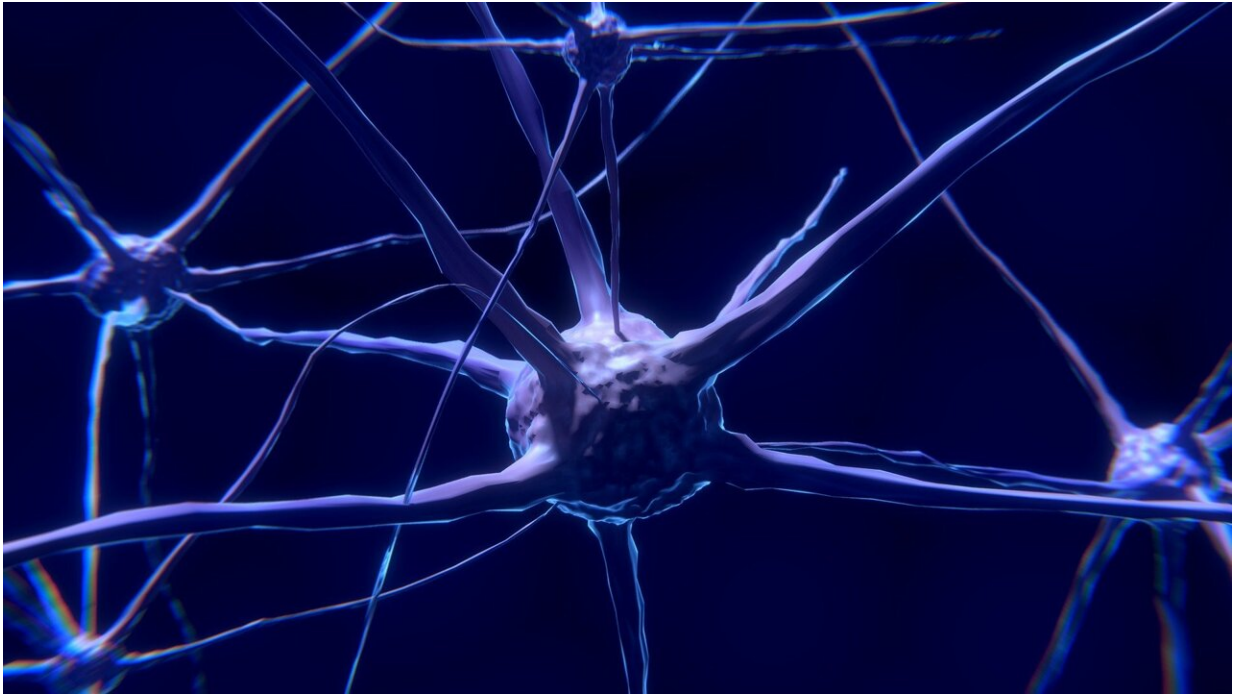


Building artificial neurons with mathematics

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EPFL's Blue Brain Project has found a way to use only mathematics to automatically draw neurons in 3D, meaning we are getting closer to being able to build digital twins of brains.

Santiago Ramón y Cajal, a Spanish physician from the turn of the 19th century, is considered by most to be the father of modern neuroscience. He stared down a microscope day and night for years, fascinated by

chemically stained neurons he found in slices of human [brain](#) tissue. By hand, he painstakingly drew virtually every new type of neuron he came across using nothing more than pen and paper. As the Charles Darwin for the brain, he mapped every detail of the forest of neurons that make up the brain, calling them the "butterflies of the brain."

Today, 200 years later, Blue Brain has found a way to dispense with the human eye, pen and paper, and use only mathematics to automatically draw neurons in 3D as digital twins. Math can now be used to capture all the "butterflies of the brain," which allows us to use computers to build any and all the billions of neurons that make up the brain. And that means we are getting closer to being able to build digital twins of brains.

These billions of neurons form trillions of synapses—where neurons communicate with each other. Such complexity needs comprehensive neuron models and accurately reconstructed detailed brain networks in order to replicate the healthy and disease states of the brain. Efforts to build such models and networks have historically been hampered by the lack of experimental data available. But now, scientists at the EPFL Blue Brain Project using algebraic topology, a field of Math, have created an algorithm that requires only a few examples to generate large numbers of unique cells. Using this algorithm—the Topological Neuronal Synthesis (TNS), they can efficiently synthesize millions of unique neuronal morphologies.

The TNS algorithm is of huge importance for the rapidly growing field of computational neuroscience, which increasingly relies on biologically-realistic models from the single cell level to large-scale neuronal networks. Accurate neuronal morphologies, in particular, lie at the heart of these efforts as they are essential for defining [cell types](#), discerning their functional roles, investigating structural alterations associated with diseased brain states and, identifying what conditions make brain networks sufficiently robust to support the complex cortical processes

that are fundamental for a healthy brain. Therefore, it is essential to accurately reconstruct detailed brain networks in order to replicate the healthy and disease states of the brain.

In a paper published in *Cell Reports*, a team led by Lida Kanari has applied the Topological Morphology Descriptor (TMD) introduced in Kanari et al. 2018, which reliably categorizes dendritic morphologies, to digitally synthesize dendritic morphologies from all layers and morphological types of the rodent cortex. The advantages of this topology-driven approach are multiple, as the new TNS algorithm, is generalizable to new types of cells, needs little input data and does not require fine tuning because it captures feature correlations.

Enabling the rapid digital reconstruction of entire brain regions from relatively few reference cells

The TNS algorithm driven by the topological architecture of dendrites generates realistic morphologies for a large number of distinct cortical neuronal cell types with realistic morphological and [electrical properties](#). This has enabled the rapid digital reconstruction of entire brain regions from relatively few reference cells, thereby allowing the investigation of links between neuronal morphologies and brain function across different spatio-temporal scales and addressing the challenge of insufficient biological reconstructions. A multi-stage validation documented in the paper ensures that the synthesized cells reproduce the shapes of reconstructed neurons with respect to three modalities: 1. Their morphological characteristics, 2. The electrical activity of single cells and, 3. The connectivity of the network they form.

Lida Kanari explains that "the findings are already enabling Blue Brain to build biologically detailed reconstructions and simulations of the mouse brain, by computationally reconstructing brain regions for

simulations which replicate the anatomical properties of neuronal morphologies and include region specific anatomy. We address one of the fundamental problems for neuroscience—the scarcity of experimental neuronal reconstructions since the topological synthesis requires only a few examples to generate large numbers of unique cells. Using the TNS algorithm, we can efficiently synthesize millions of unique neuronal morphologies (10 million cells in a few hours)," she concludes.

Facilitating medical applications

"Comprehensive neuron models are essential for defining cell types, discerning their functional roles and investigating structural alterations associated with diseased brain states," affirms Blue Brain Founder and Director, Prof. Henry Markram. "The researchers synthesized cortical networks based on structural alterations of dendrites associated with medical conditions and revealed principles linking branching properties to the structure of large-scale networks."

"As the TNS algorithm is implemented in an [open source software](#), this will allow the modeling of brain diseases in terms of single cells and networks, as it provides a tool to directly investigate the link between local morphological properties and the connectivity of the neuronal network they form. This approach is of particular interest for [medical applications](#) as it enables the investigation of diseases in terms of the emergence of global network pathology from local structural changes in neuron morphologies," he concludes.

More information: Lida Kanari et al, Computational synthesis of cortical dendritic morphologies, *Cell Reports* (2022). [DOI: 10.1016/j.celrep.2022.110586](#)

Topological Neuron Synthesis Algorithm: portal.bluebrain.epfl.ch/resou

[...al-neuron-synthesis/](#)

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