By blowing up brain tissue to 20 times its size, scientists see unprecedented details

By Ryan Cross  |  Apr. 17, 2017, 11:00 AM

Microscopes reveal miniscule wonders by making things seem bigger. Just imagine what scientists could see if they could also make things bigger. A new strategy to blow brains up does just that. Researchers previously invented a method for injecting a polyacrylate mesh into brain tissue, the same water-absorbing and expanding molecule that makes dirty diapers swell up. Just add water, and the tissue enlarges to 4.5 times its original size. But it wasn’t good enough to see everything. The brain is full of diminutive protrusions called dendritic spines lining the signal receiving end of a neuron. Hundreds to thousands of these nubs help strengthen or weaken an individual dendrite’s connection to other neurons in the brain. The nanoscale size of these spines makes studying them with light microscopes impossible or blurry at best, however. Now, the same group has overcome this barrier in an improved method called iterative expansion microscopy, described today in *Nature Methods*. Here, the tissue is expanded once, the crosslinked mesh is cleaved, and then the tissue is expanded again, resulting in roughly 20-fold enlargement. Neurons are then visualized by light-emitting molecules linked to antibodies which latch onto specified proteins. The technique has yielded detailed images showing the formation of proteins along synapses in mice, as well as detailed renderings of dendritic spines (seen in the image above) in the mouse hippocampus—a center or learning and memory in the brain. The advance could enable neuroscientists to map the many individual connections between neurons across the brain and the unique arrangement of receptors that turn brain circuits on and off.

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