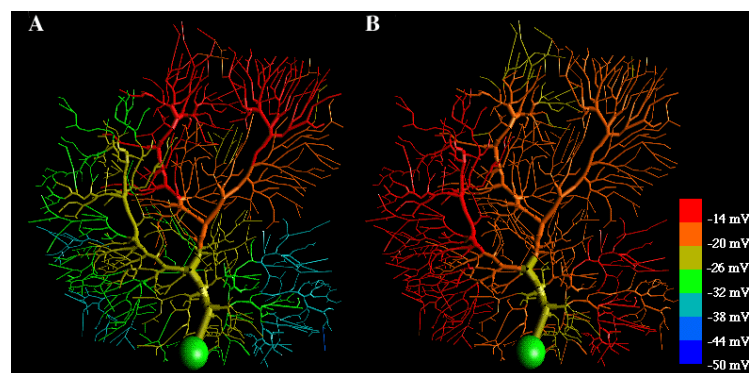
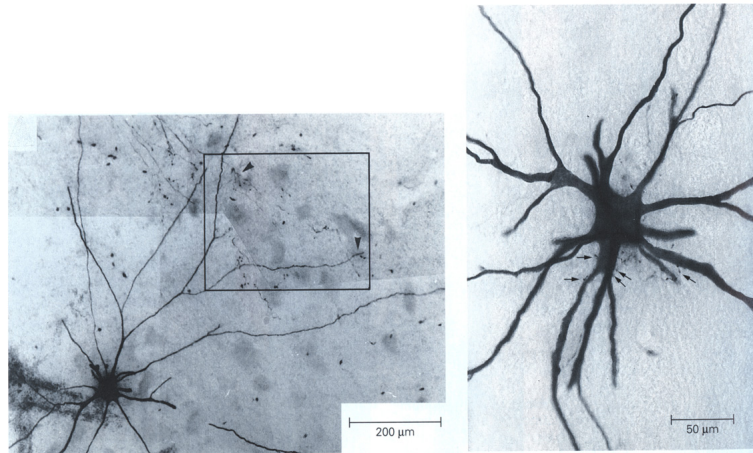


Neurons are not a single isopotential compartment! The figures below show two snapshots of the membrane potential in a model of the dendritic tree of a Purkinje cell from the cerebellum during a dendritic action potential. Note the substantial differences in potential across the dendrites and also how potential spreads through the tree with time.



(from De Schutter and Smolen, <http://www.bbf.uia.ac.be>)

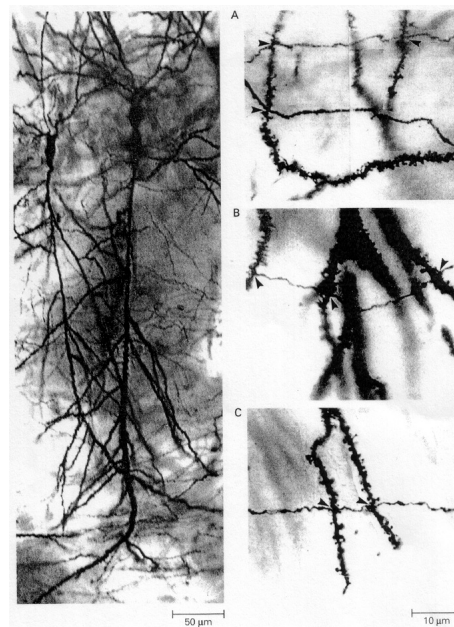
Dendritic trees are sometimes smooth like this spinal cord motorneuron . . .



Kandel et al.

. . . but other neurons have spiny dendrites, like these hippocampal pyramidal cells.

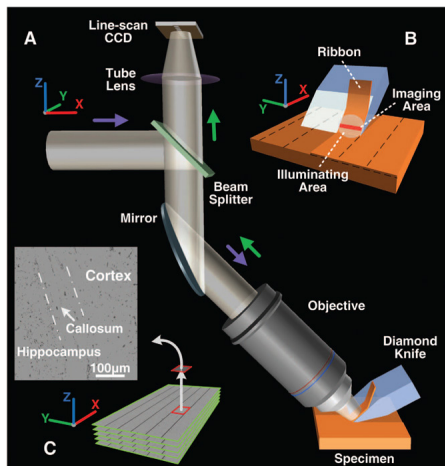
The figures at right show details of the spiny dendrites, with axons that make synapses on them.



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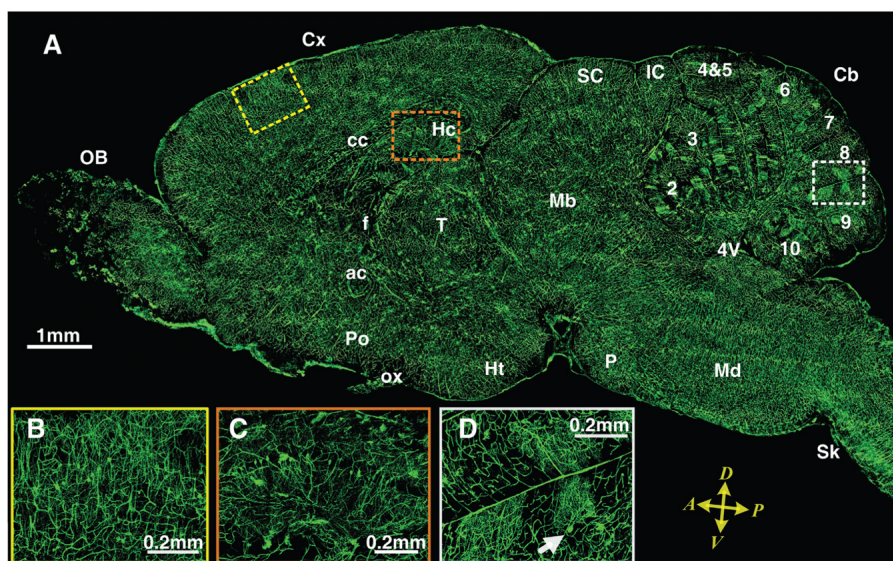
To improve the understanding of brain structure, several groups are using automatic imaging of fixed tissue blocks. This works best if the neurons of interest are stained, but the ultimate goal is to reconstruct whole tissue. This shows a light microscopic method, but this work is also being done with EM.

**Fig. 1.** (A) Schematic representation of the MOST system. The specimen is mounted in a chamber, the motion of which is controlled by a series of mechanical translation stages that can move in three directions (the chamber and stages are not shown). Slicing is performed by moving the specimen along the *x* axis to generate ribbons, and each ribbon is simultaneously imaged. The illuminating beam passes through the beam splitter, mirror, and objective and irradiates the ribbon. After it passes through the mirror, beam splitter, and tube lens, the imaging beam collected by the objective is then recorded by a line-scan CCD. (B) Schematic representation of slicing. The slicing produces ribbons that glide forward along the knife face. The illuminating and imaging areas are indicated by a circle and a red line, respectively. To expand the detection range, we performed slicing with a lateral and an axial scan (LS). (C) An image stack acquired using MOST. The stack is composed of many subimages. The subimages aligned along the *x* axis were produced from a ribbon. These image sequences reconstitute the entire cross section of the specimen along the *y* axis. A subimage of the cortex, hippocampus, and corpus callosum is also indicated.



Li, Gong, Zhang, et al. Science 330:1404 (2010)

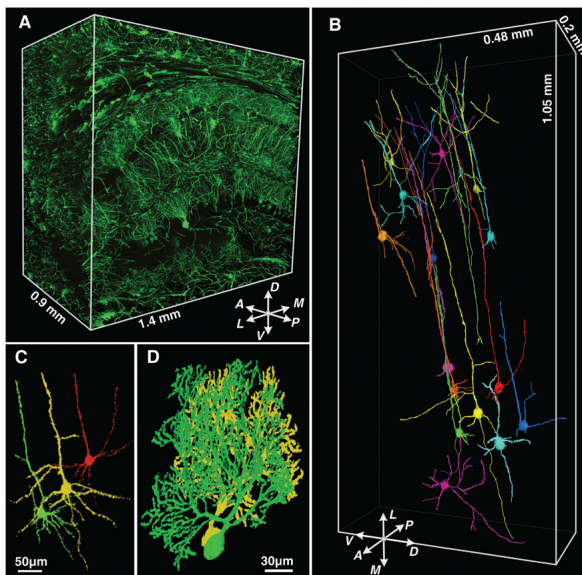
Wow!



Li, Gong, Zhang, et al. Science 330:1404 (2010)

Some examples of reconstructions of segments of brain using Golgi staining.

Golgi stains only a fraction of the neurons present in a tissue, so that individual neurons can be seen clearly and some relationships among neurons can be seen. However the structure of the tissue is greatly simplified.

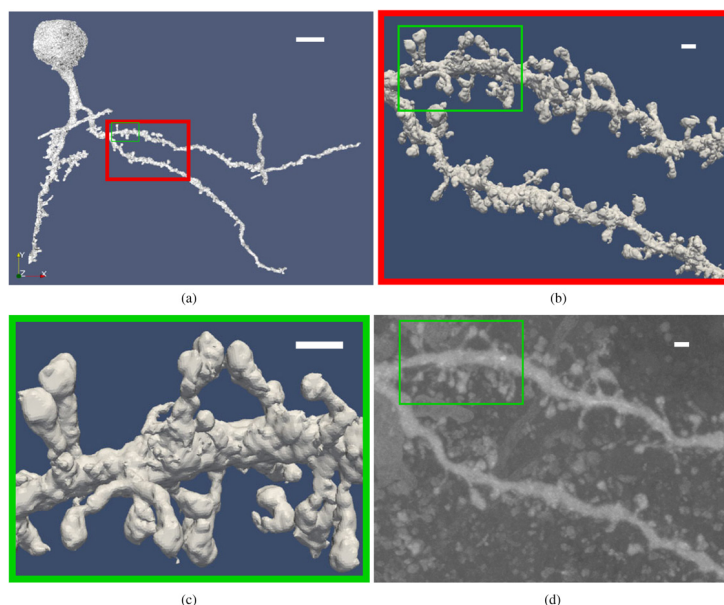


**Fig. 4.** (A) A large volumetric reconstruction of a partial hippocampus of the mouse brain. The cube volume is 1.4 mm by 1.5 mm by 0.9 mm. The multi-layered structure of the hippocampus and a large number of transverse fibers of the corpus callosum are clearly visible. Dorsal-ventral, anterior-posterior, and left-medial axes are indicated. (B) We traced the neurites of 17 neurons in the ectorial cortex, indicated by a dashed box in Fig. 2H. (C) Three-dimensional reconstruction of three neighboring pyramidal cells in layer 5 of the ectorial cortex as in (B). These three cells are distinguished by different colors; other cells, neurites, and blood vessels that densely cover the three cells are not shown. (D) Three-dimensional reconstruction of a pair of neighboring Purkinje cells in the ninth lobule of the cerebellum. The Purkinje cell in green can also be seen in Fig. 3D, indicated by an arrow.

Li, Gong, Zhang, et al. Science 330:1404 (2010)

Reconstruction of a cell that has been filled with biocytin from serial EM sections. Note the details of the spines.

(Done using a similar automated method, with automated reconstruction of neurons).

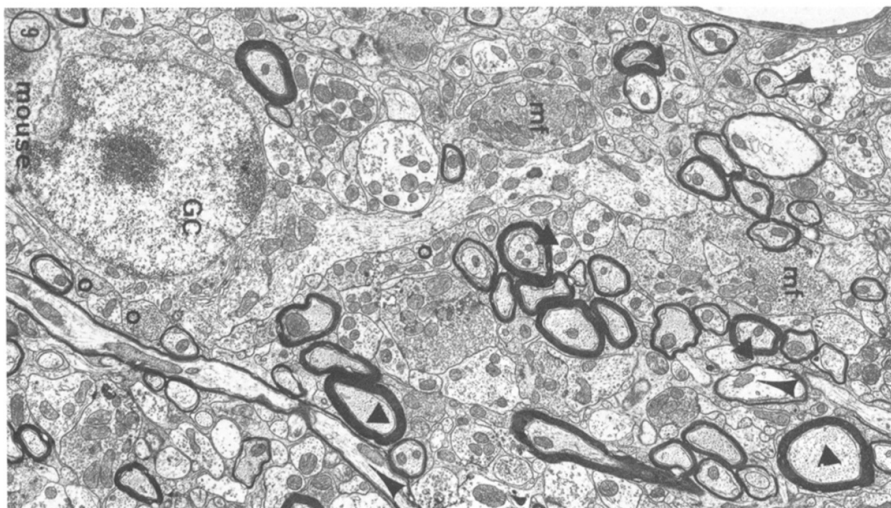


**Fig. 9** Surface reconstruction of a spiny L4 cell from Dataset II: (a) soma with dendrites. (b) details of the dendritic branch complex and spines in direct comparison with (d) a projection of the experimental data. (c) zoom of a spiny dendrite section. The area shown corresponds to the region that is marked green in (b). White length bars are 10  $\mu$ m in (a), 1  $\mu$ m otherwise

Lang et al. J. Comput. Neurosci. (2011) DOI 10.1007/s10827-011-0316-1

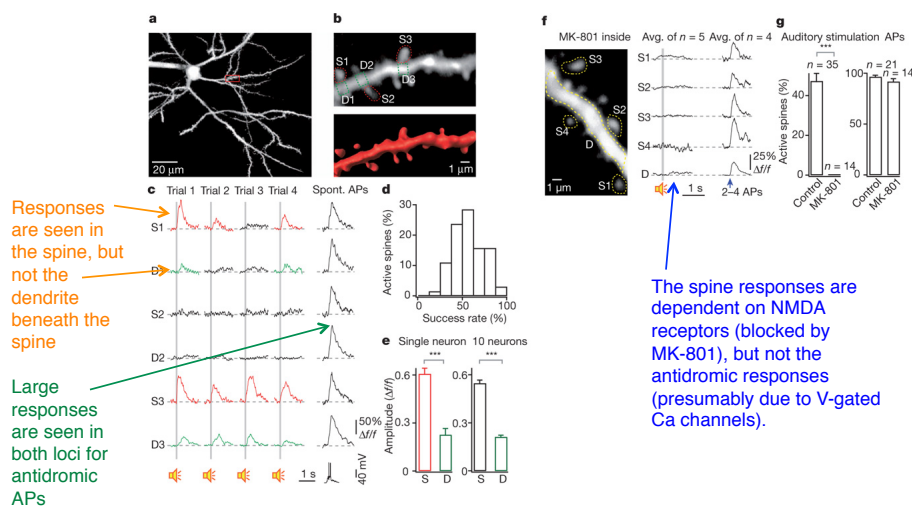


What the brain really looks like up close. An electron micrograph showing a neuron (GC) with part of its primary dendrite and the associated neuropil. The complexity of the structure along with the unreliable demarcation of components makes automated reconstruction difficult.



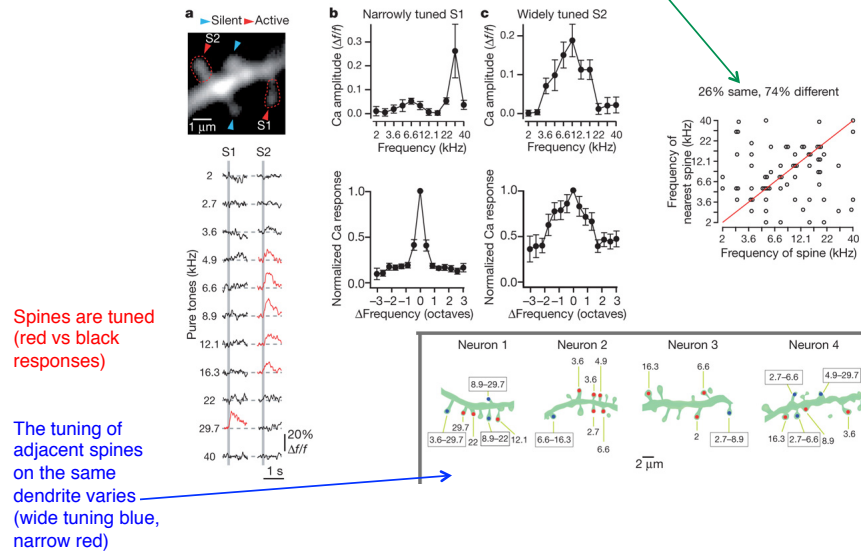
Mugnaini et al. 1980

How are inputs distributed on dendritic trees? The answer is beginning to emerge from studies of calcium imaging of dendritic spines in cortical neurons. Below are calcium signals from spines in auditory cortex neurons, showing responses to sound.



Chen, Leischner, Rochefort, Nelken, Konnerth. Nature (2011) doi:10.1038/nature10193

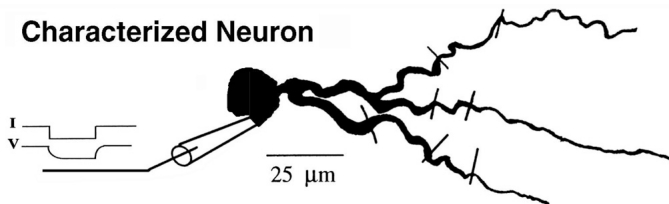
Auditory neurons are generally tuned to different frequencies. Surprisingly, inputs to adjacent spines on a cortical neuron can have **widely different frequency tuning**.



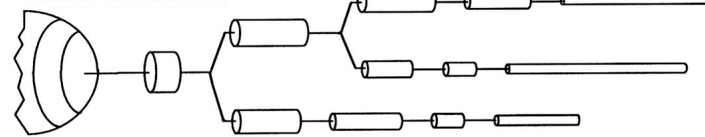
Chen, Leischner, Rochefort, Nelken, Konnerth. Nature (2011) doi:10.1038/nature10193

The direct approach to modeling dendritic trees is to reduce them to compartments and model each compartment using standard patch-of-membrane techniques.

### Characterized Neuron



### Cable Model



### Compartmental Model

