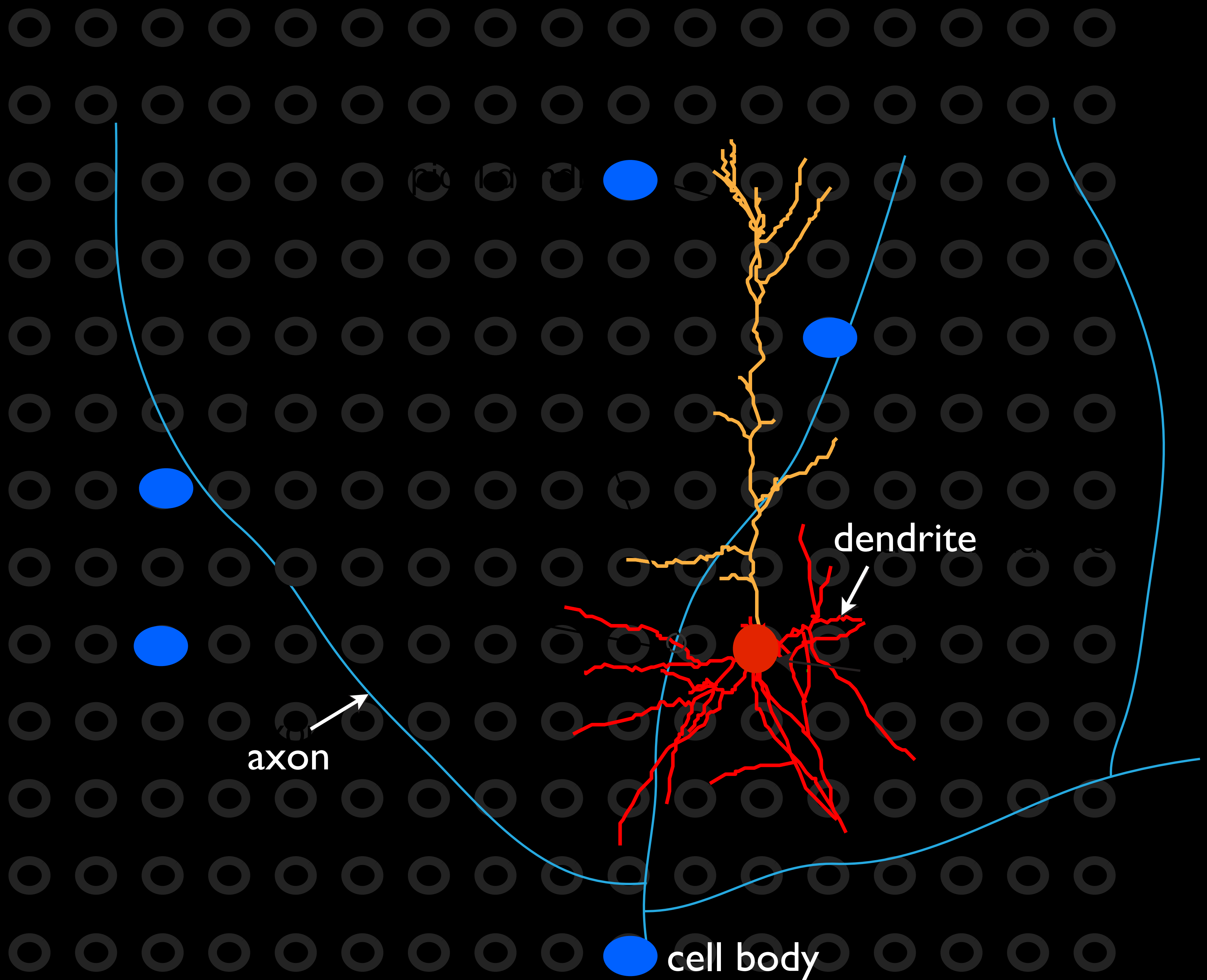
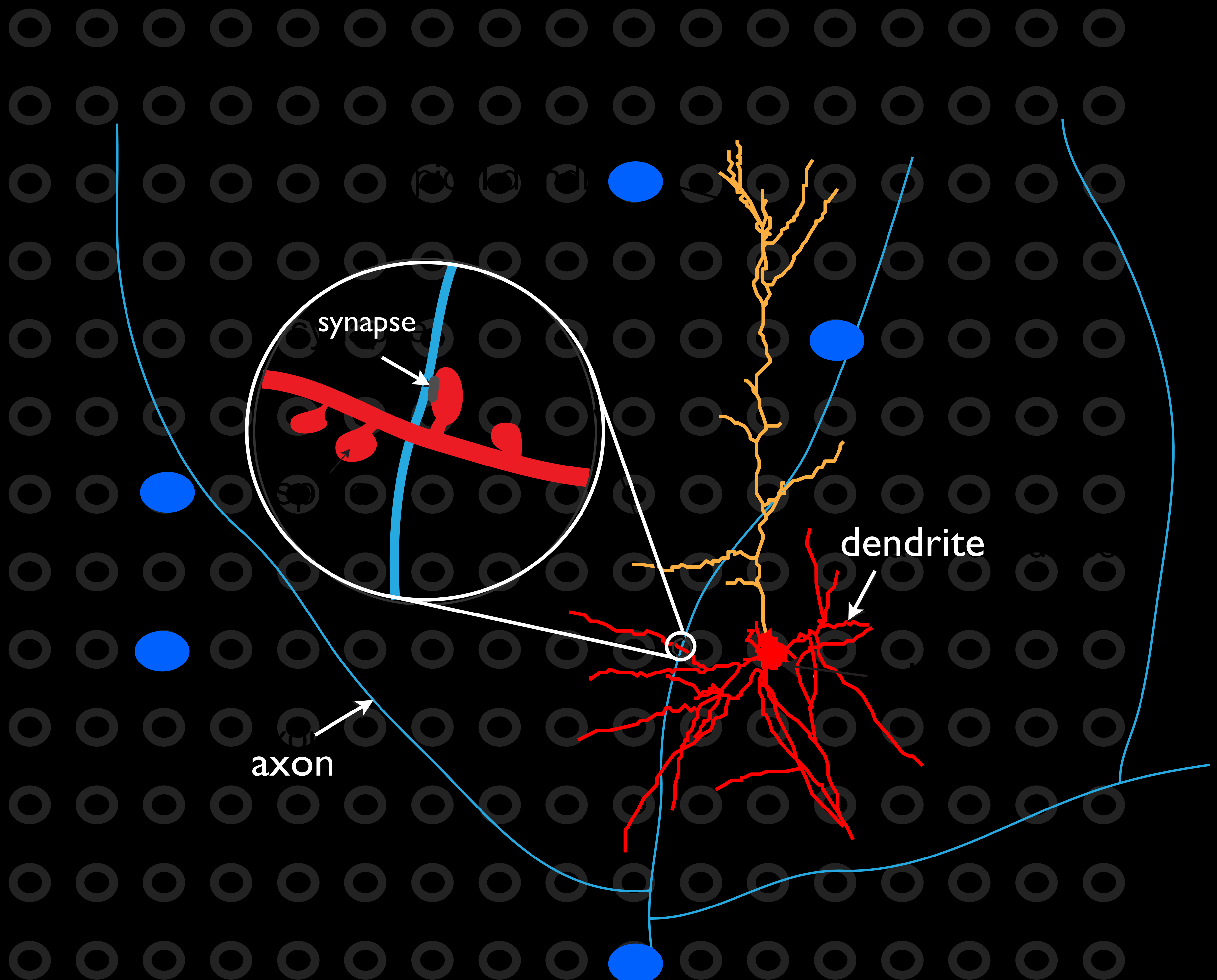
The Basic Organization of the Brain

The Neuron Doctrine


dendrite
axon
cell body



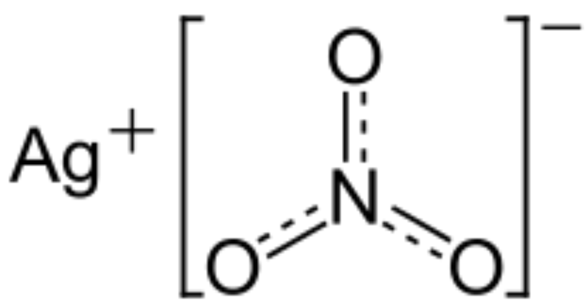
synapse
dendrite
axon

The Debate between Cajal and Golgi

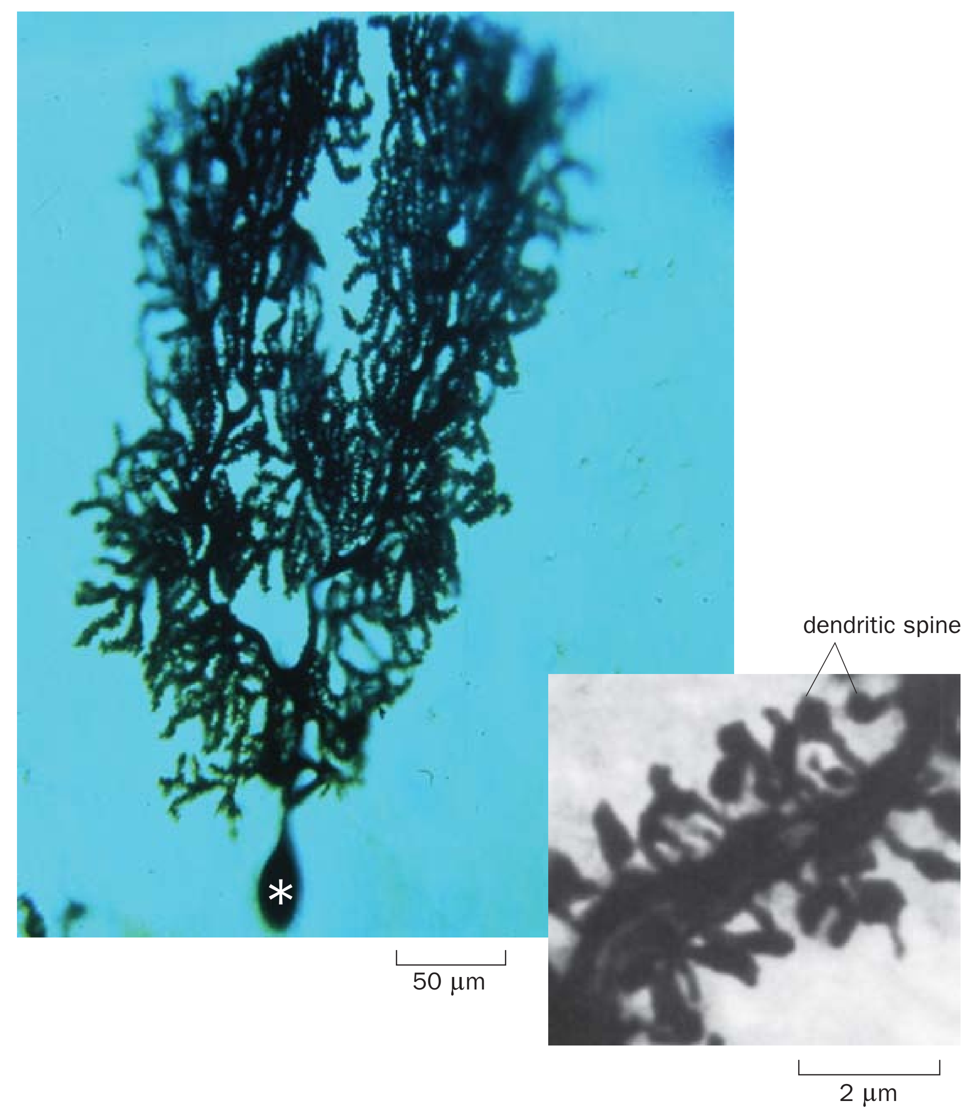
Ramon y Cajal

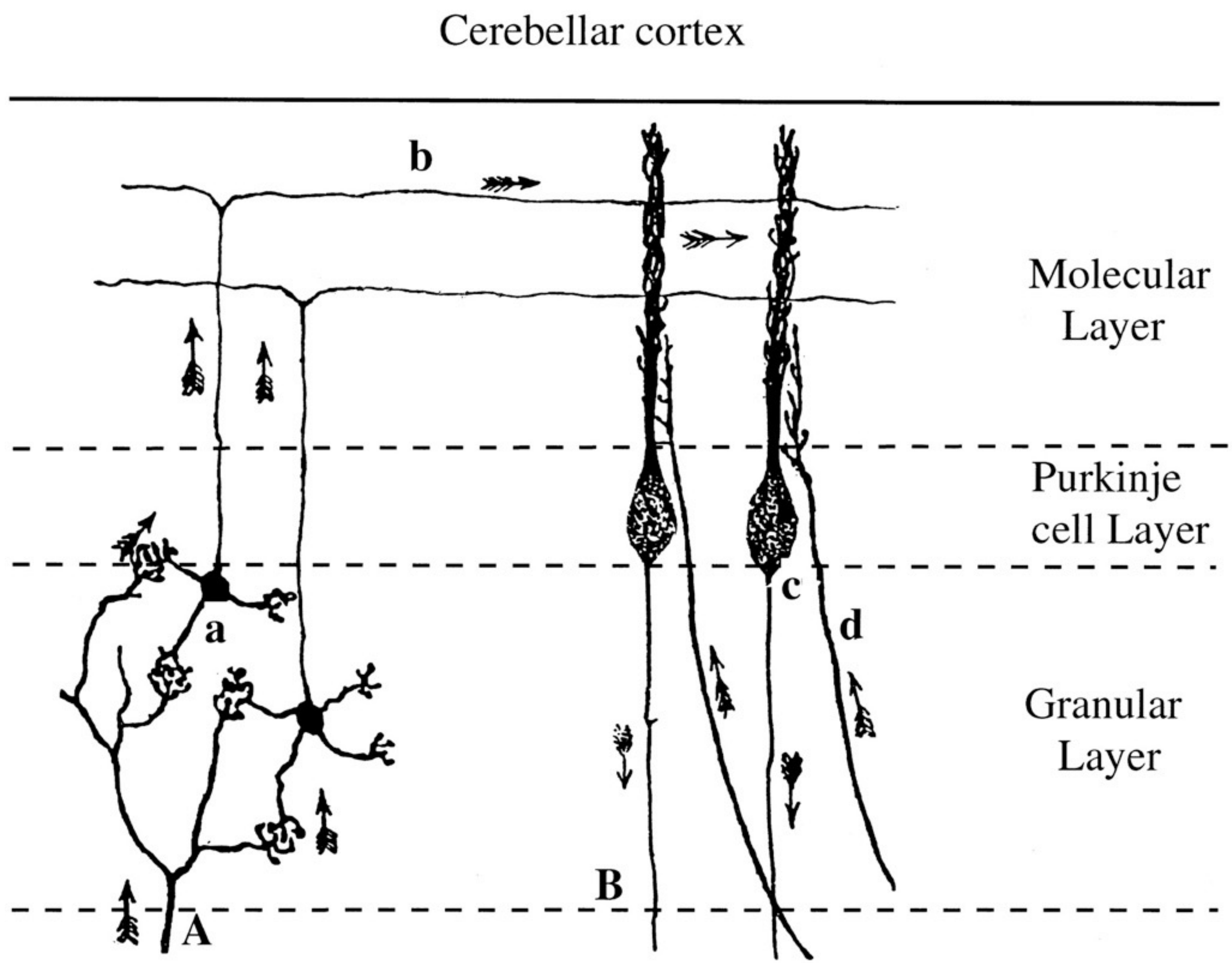
Camillo Golgi

Golgi Staining method



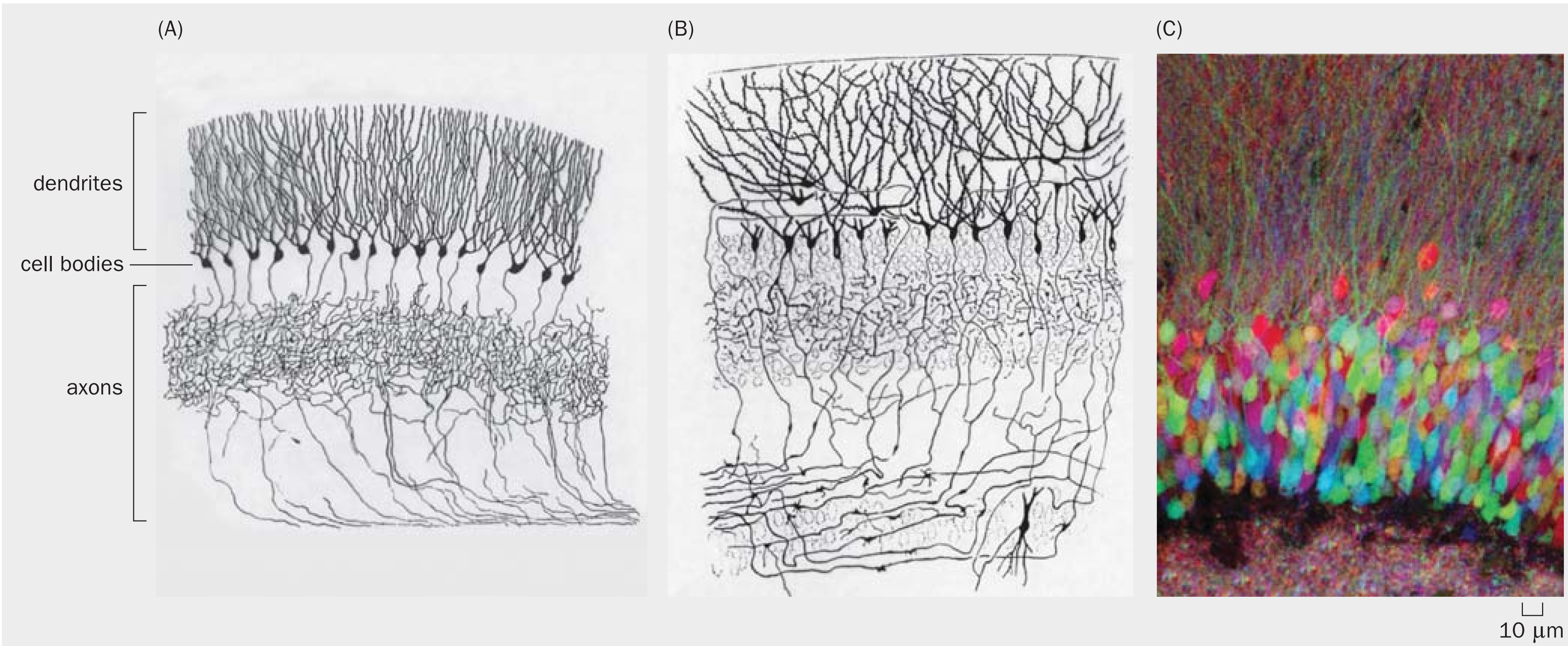
Silver nitrate





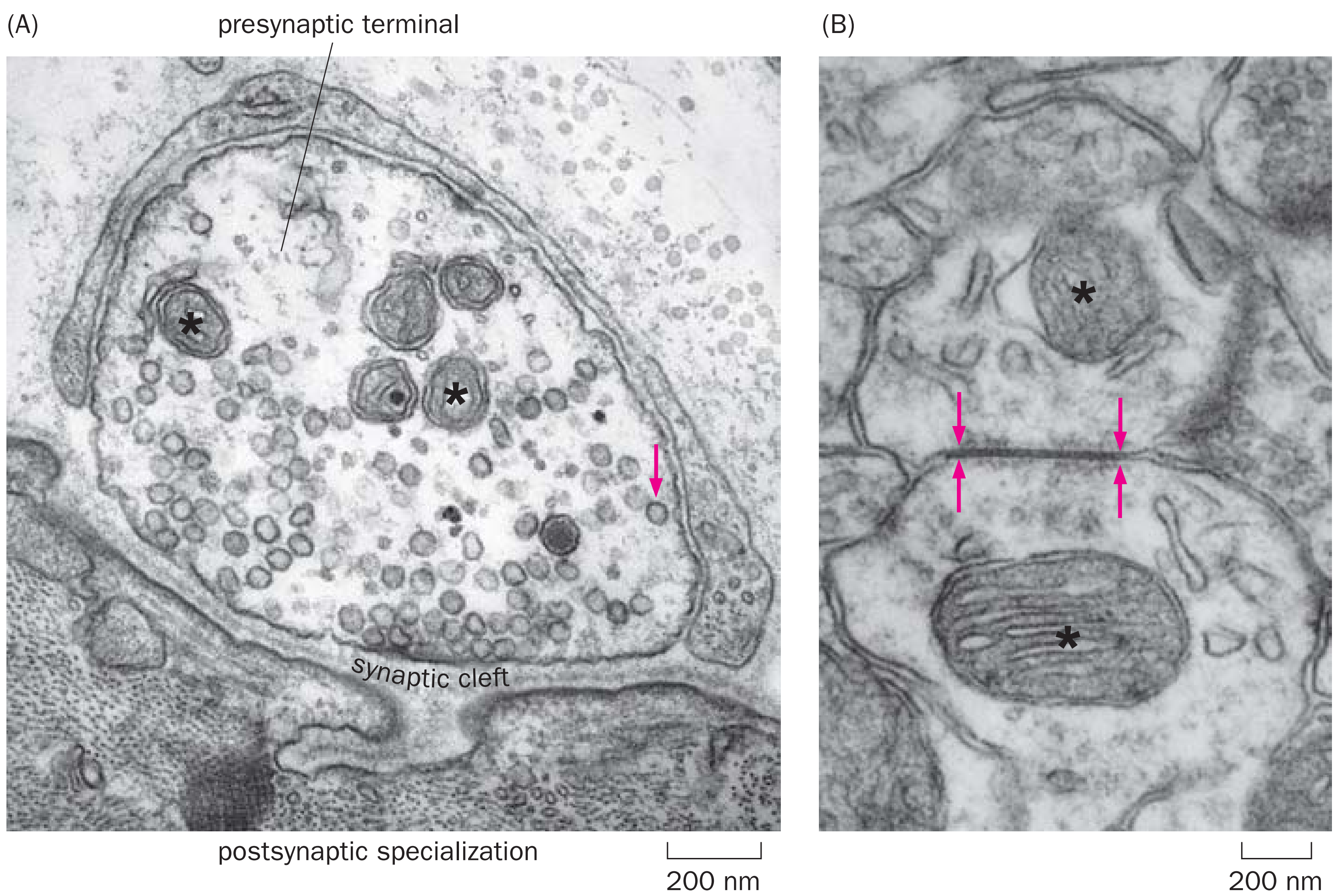
Cajal’s drawing of the cerebellar cortex

Reticular Theory vs Neuron Doctrine



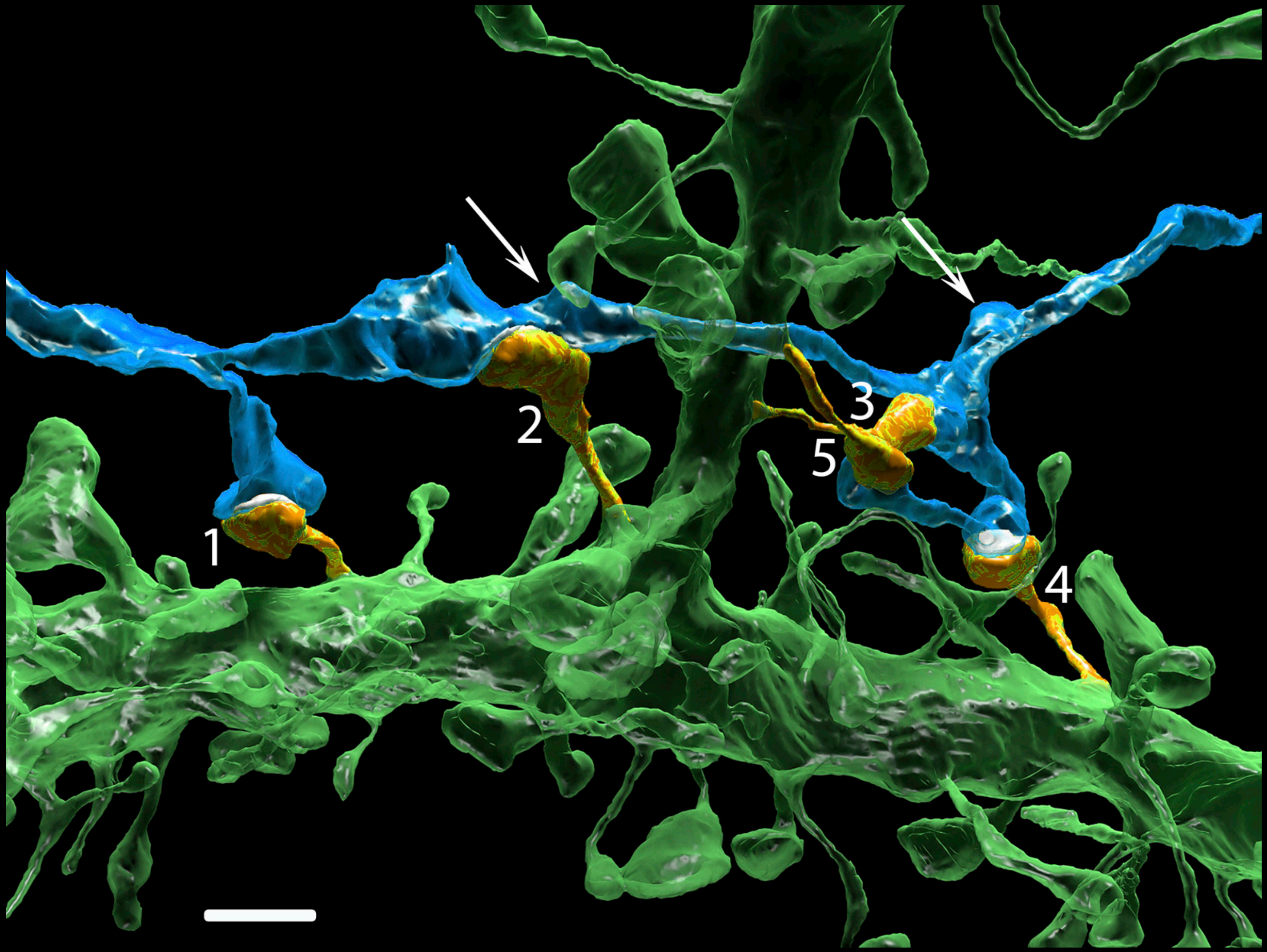
Synapse

How neurons communicate with each other?

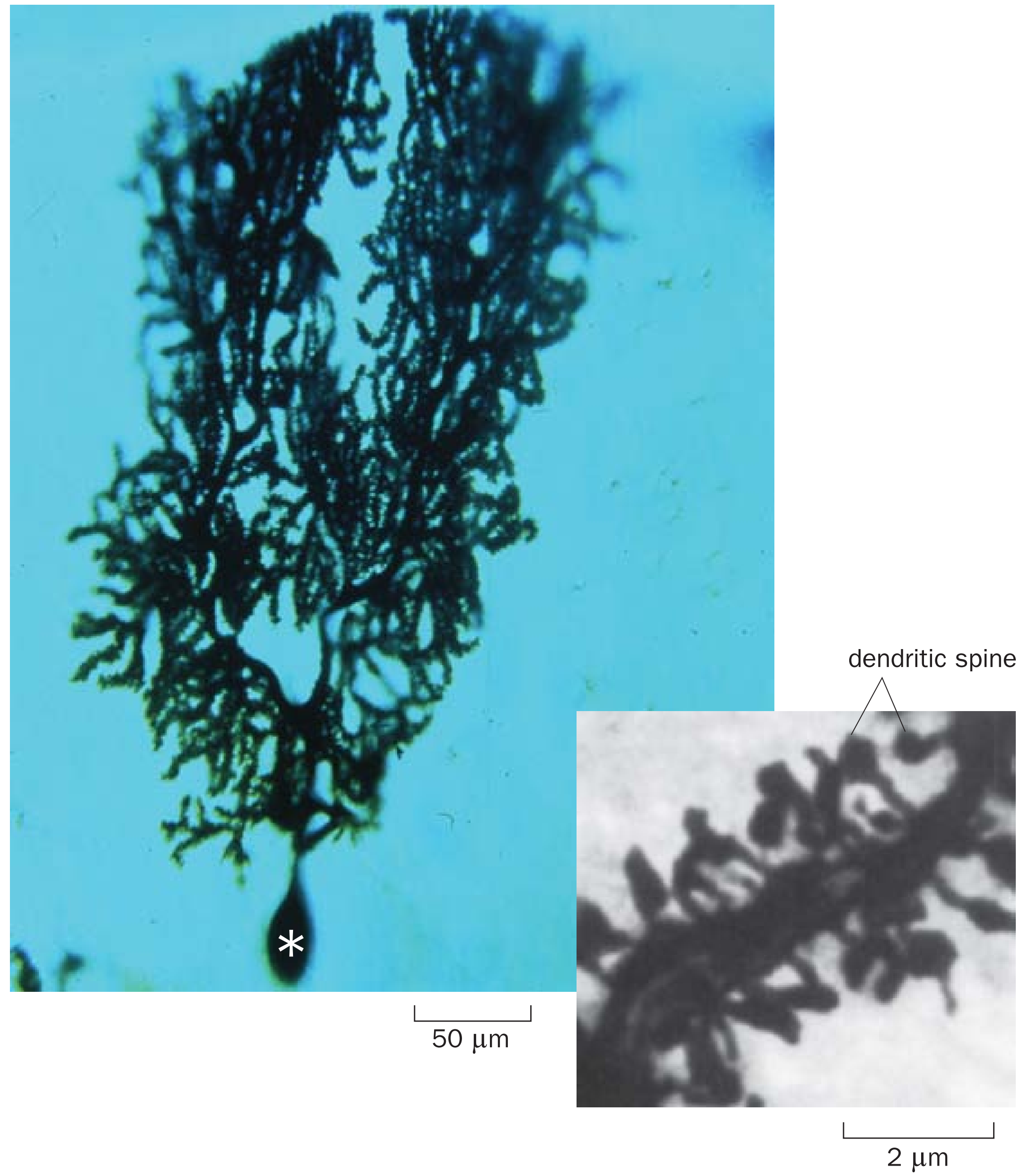


Chemical and electrical synapses

Synaptic Connectivity

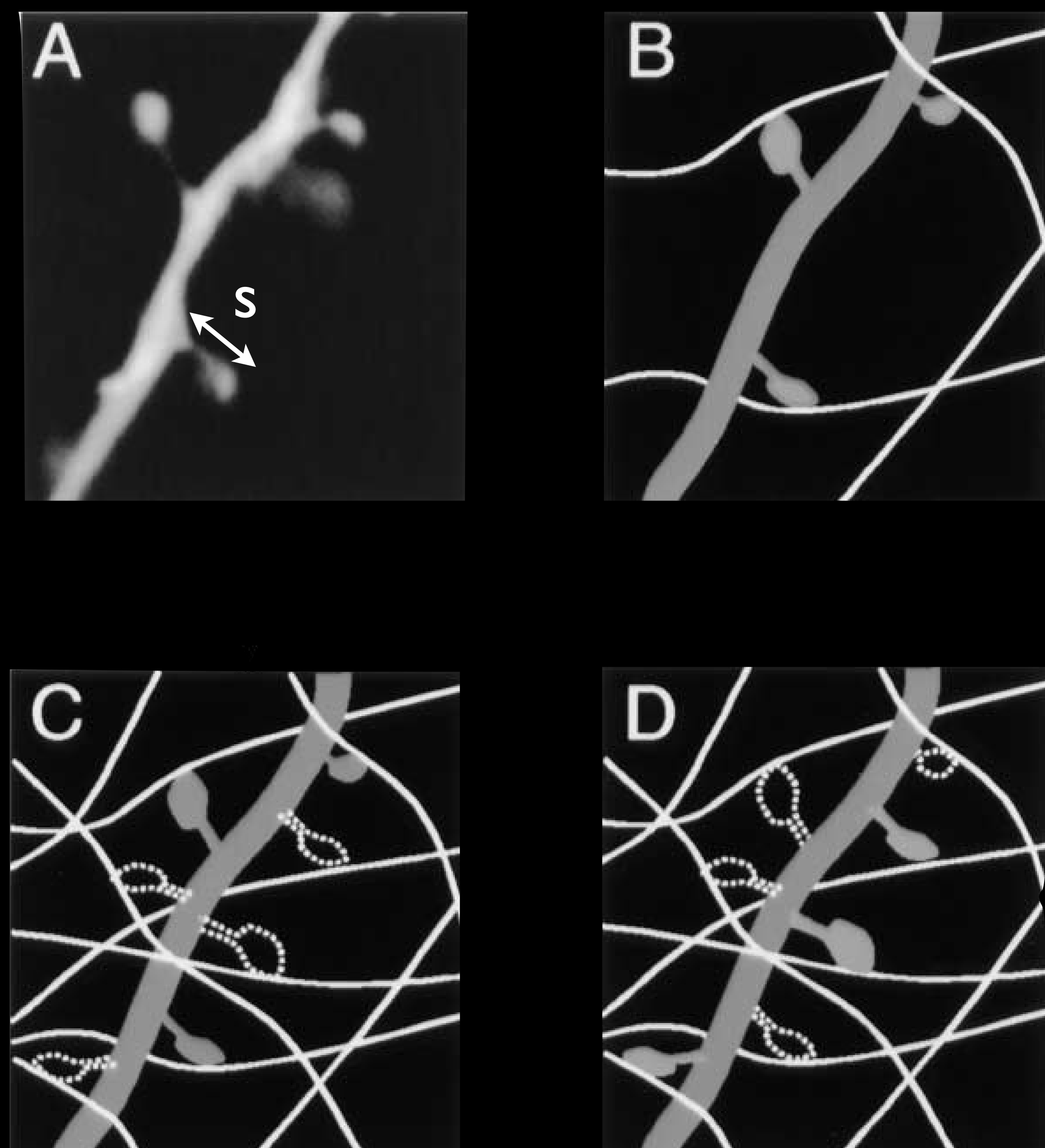


Kasthuri et. al, Cell 2015



Purkinjie cell in the cerebellum has the highest spine density in the brain

Structural Plasticity of Synaptic Connectivity



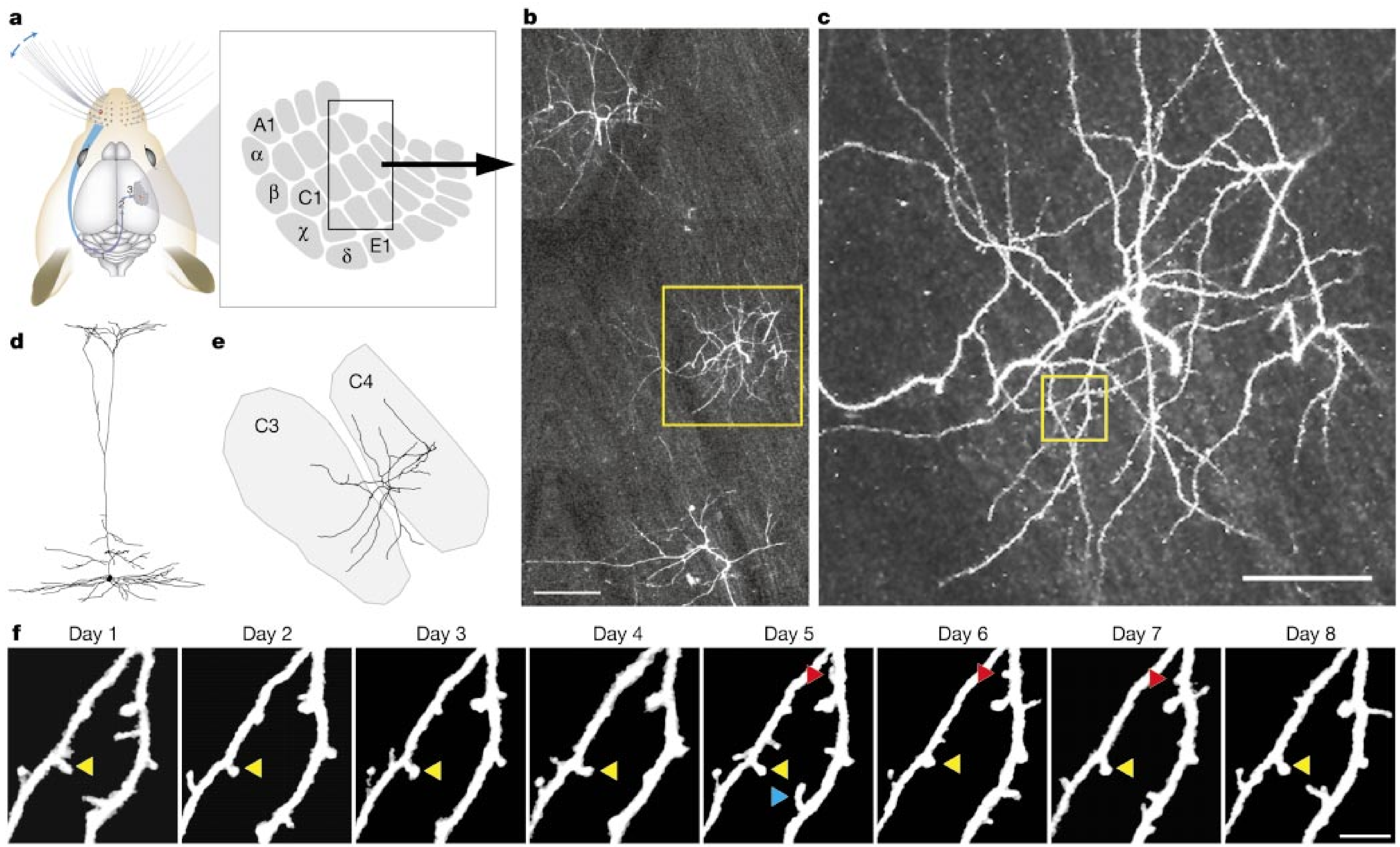
filling fraction = 3/7

$$f = \frac{2}{\pi s L_d b n}$$

s: spine length
L_d: total dendritic length per neuron
b: inter-bouton distance
n: neuronal density

Stepanyants et. al., *Neuron* 2001

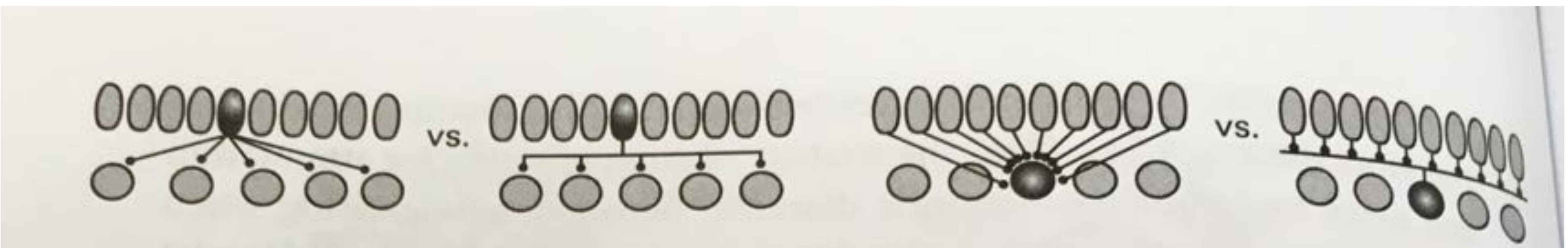
Structural Plasticity of Synaptic Connectivity



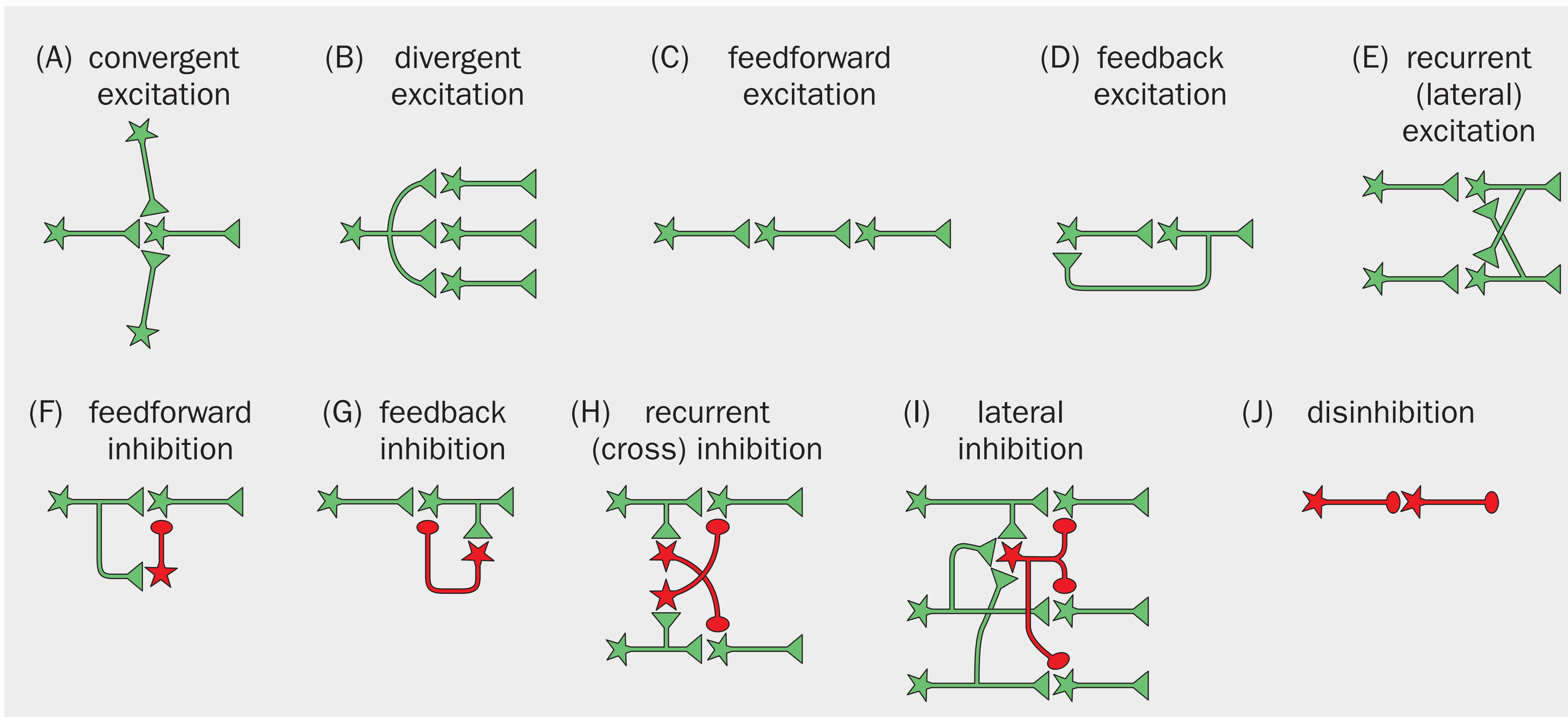
Trachtenberg et., al. *Nature* 2002

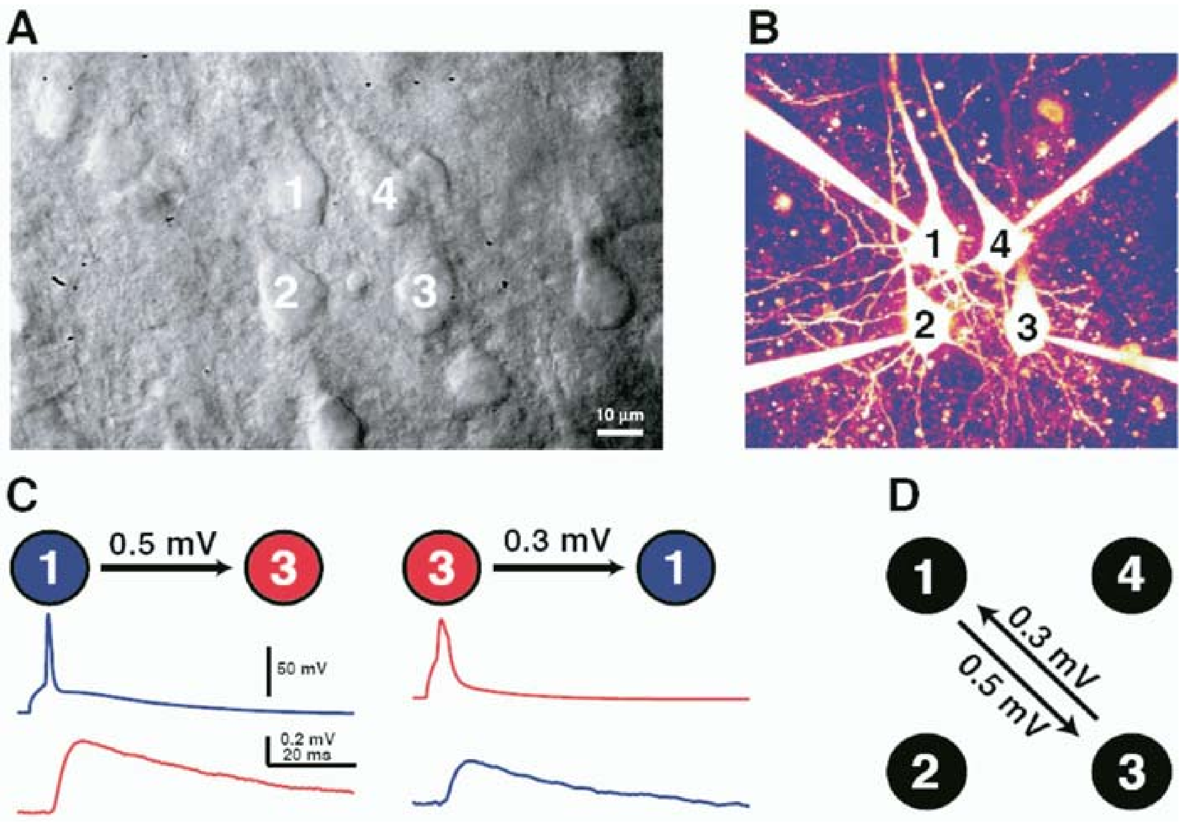
Circuit motif

Convergence and divergence

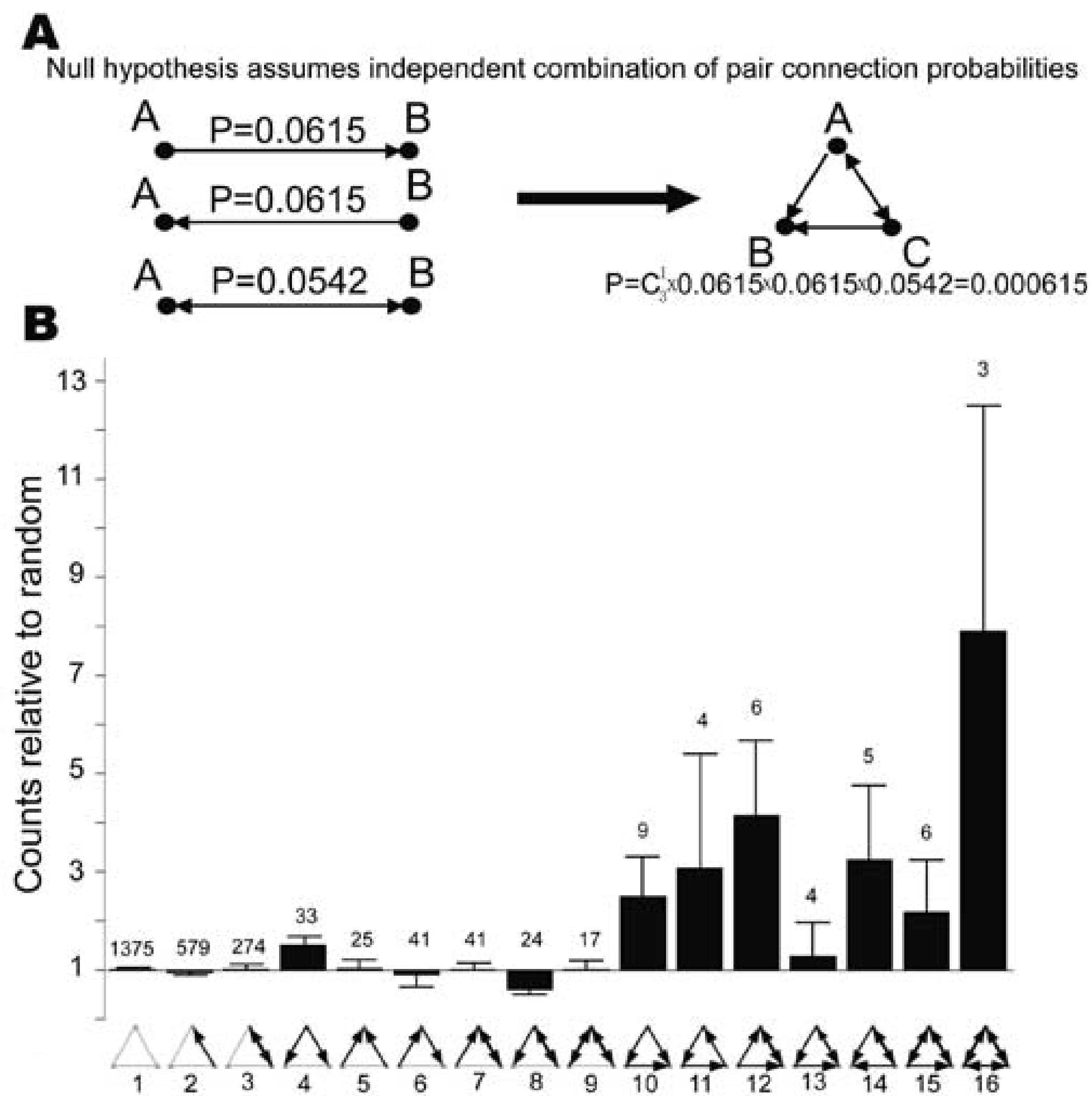


Circuit motifs




A
1
4
2
3
10 µm
B
1
4
2
3
C
1
0.5 mV
3
3
0.3 mV
1
50 mV
0.2 mV
20 ms
D
1
4
0.3 mV
0.5 mV
2
3

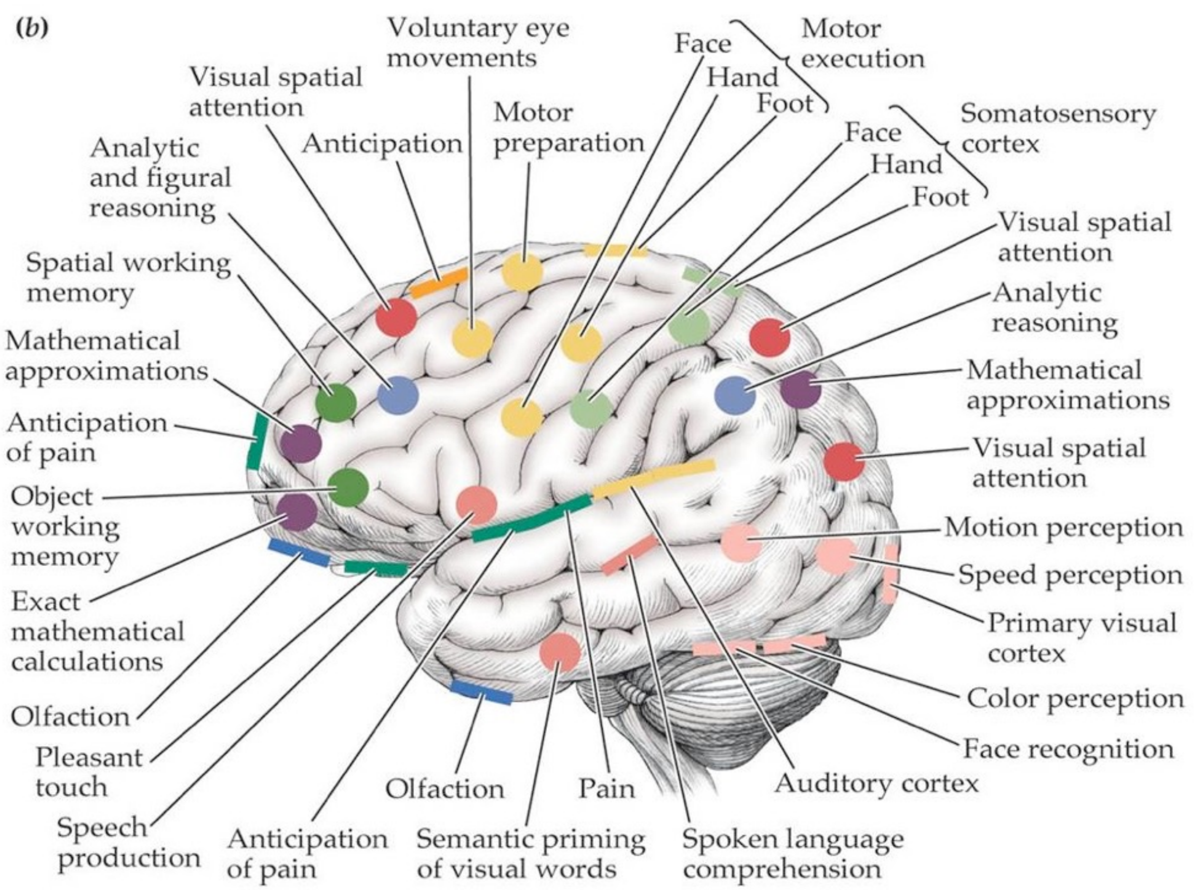
Some circuit motifs are over-represented



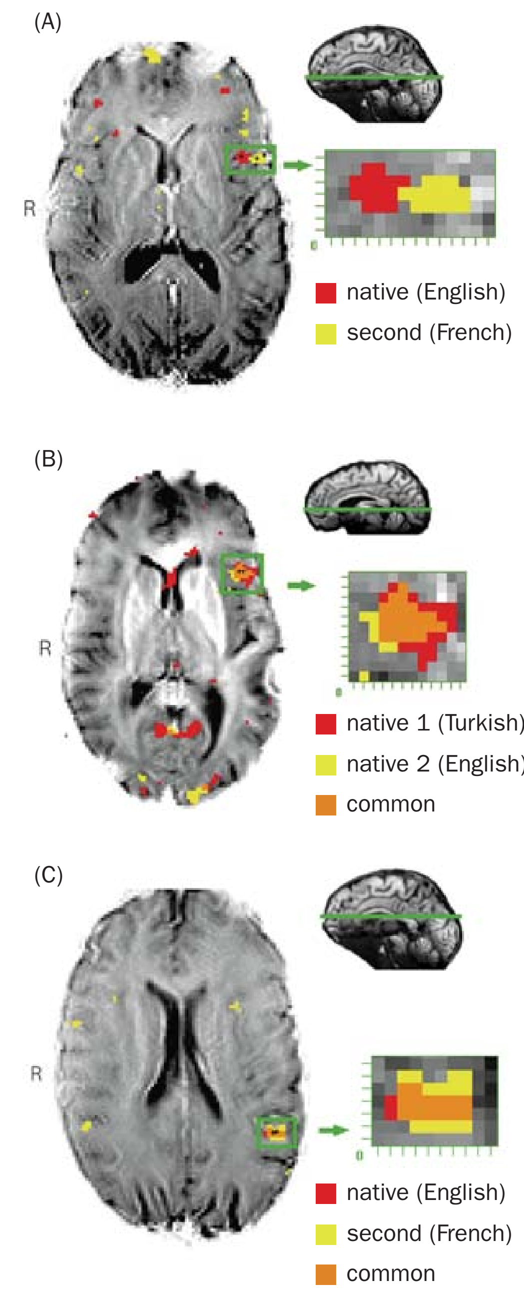
Song S, et.al, PloS Biology 2005

cortical map and column

Specific brain regions (columns) perform specialized brain functions

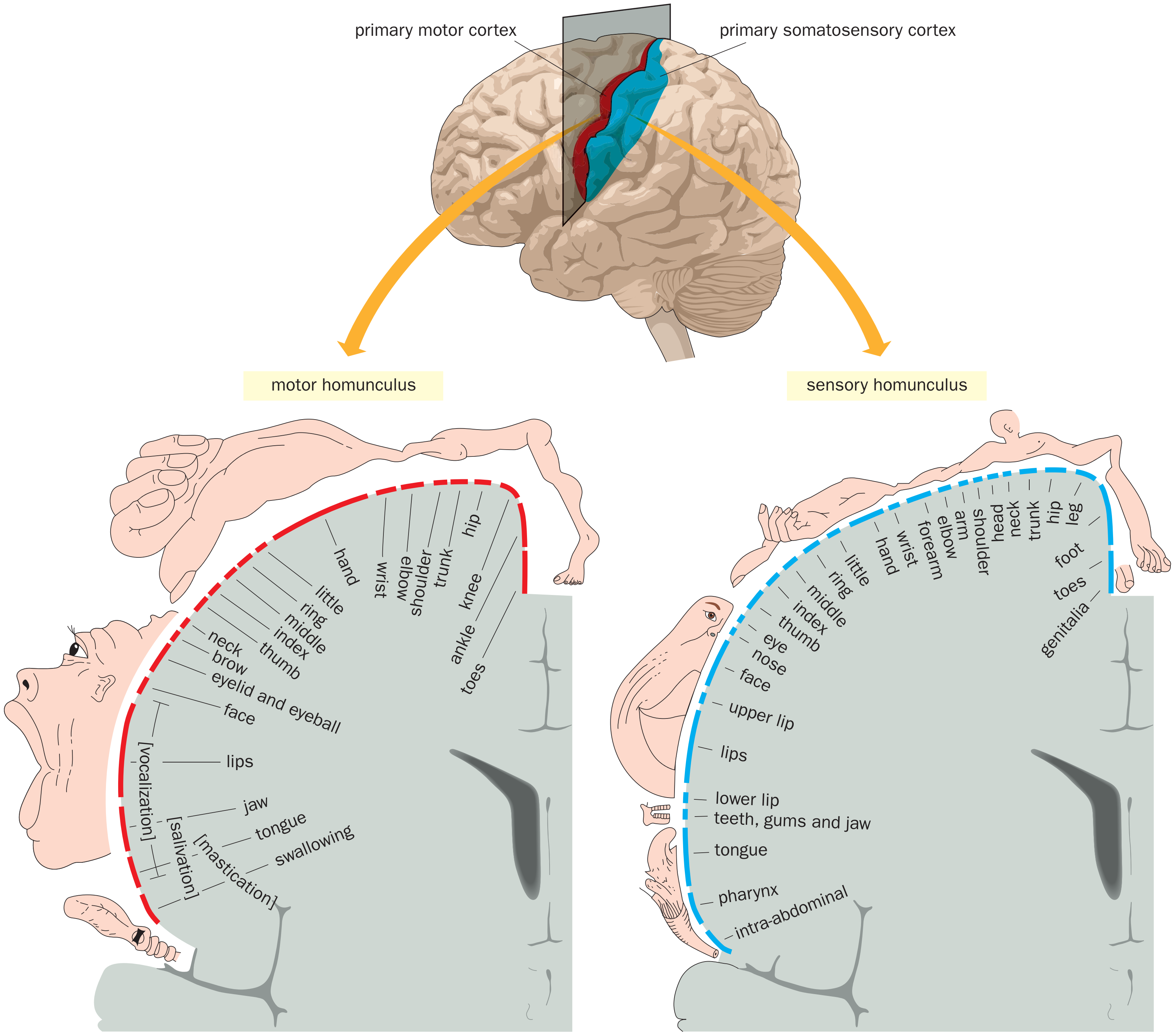


BIOLOGICAL PSYCHOLOGY, Fourth Edition, Figure 1.11 (Part 2) © 2004 Sinauer Associates, Inc.

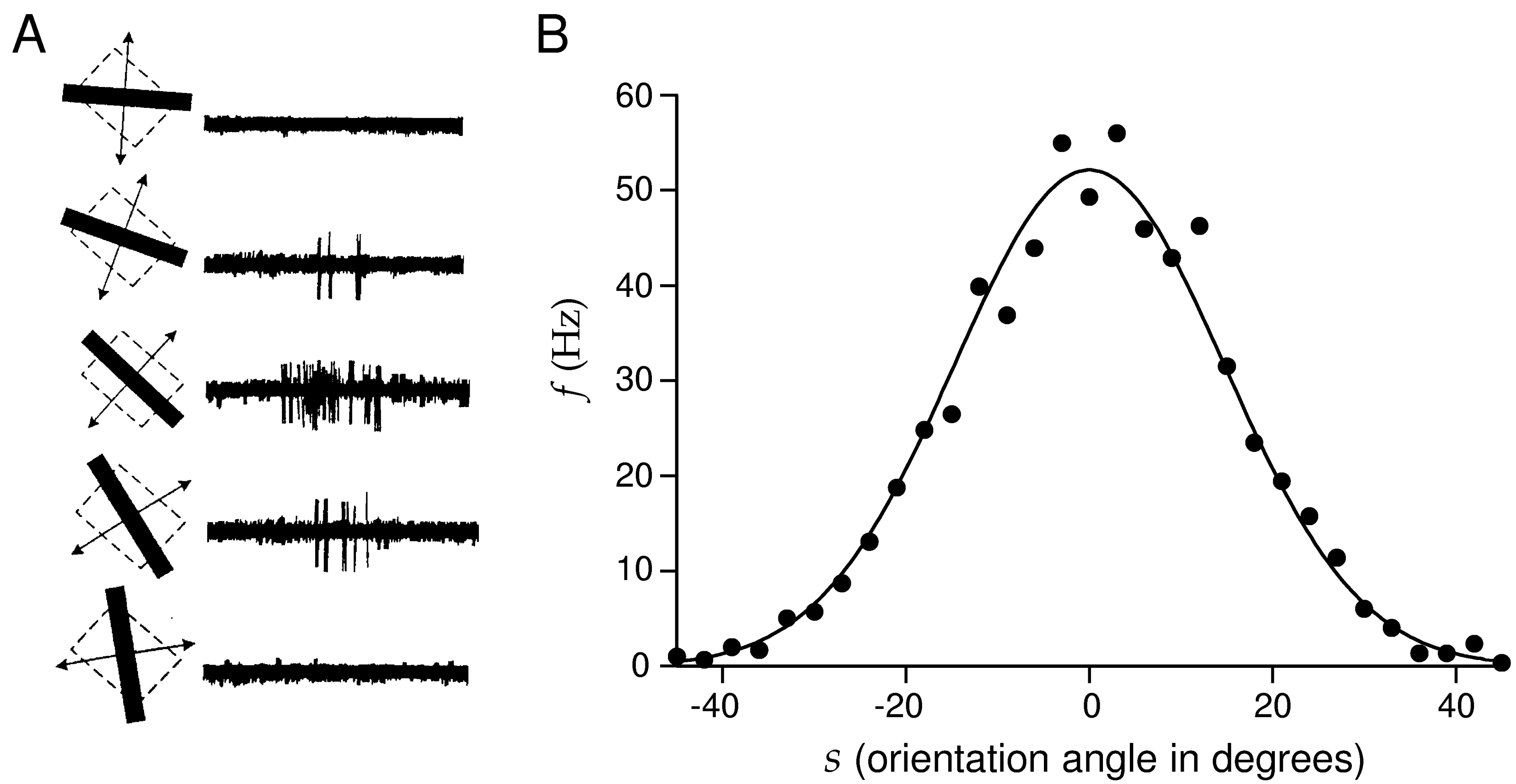


fMRI (functional magnetic resonance imaging)

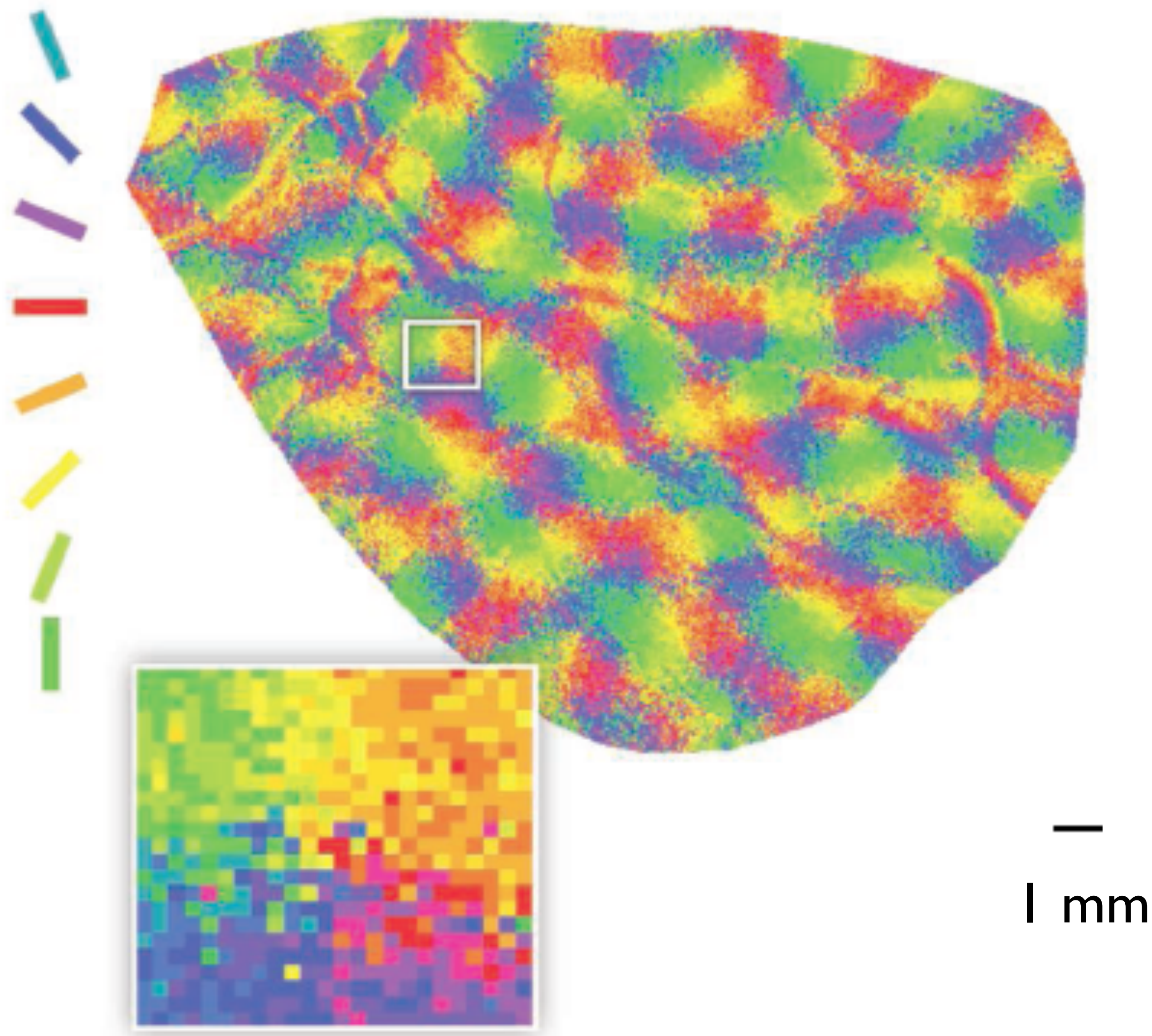
The cortex uses maps to organize information



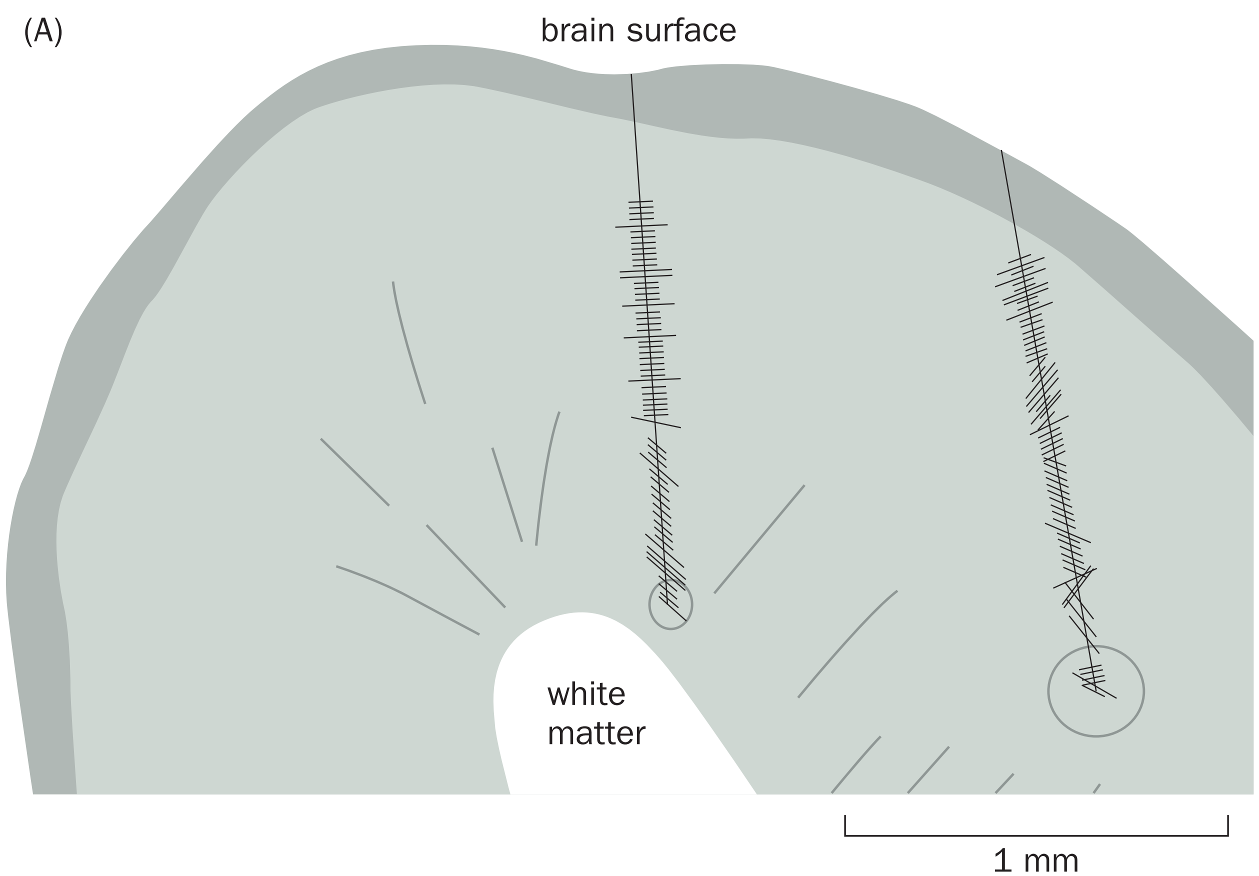
The cortex uses maps to organize information



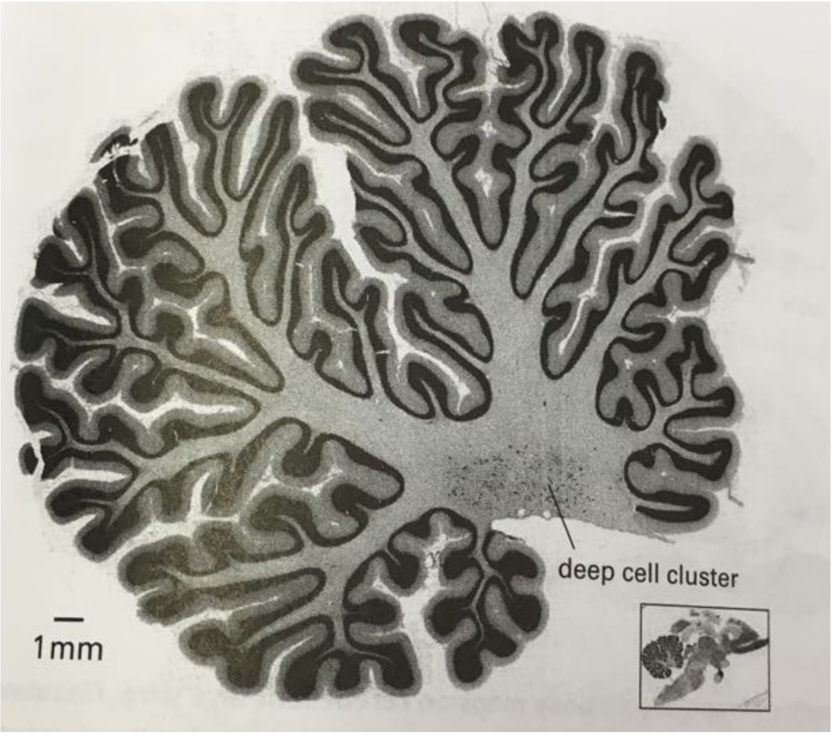
The cortex uses maps to organize information



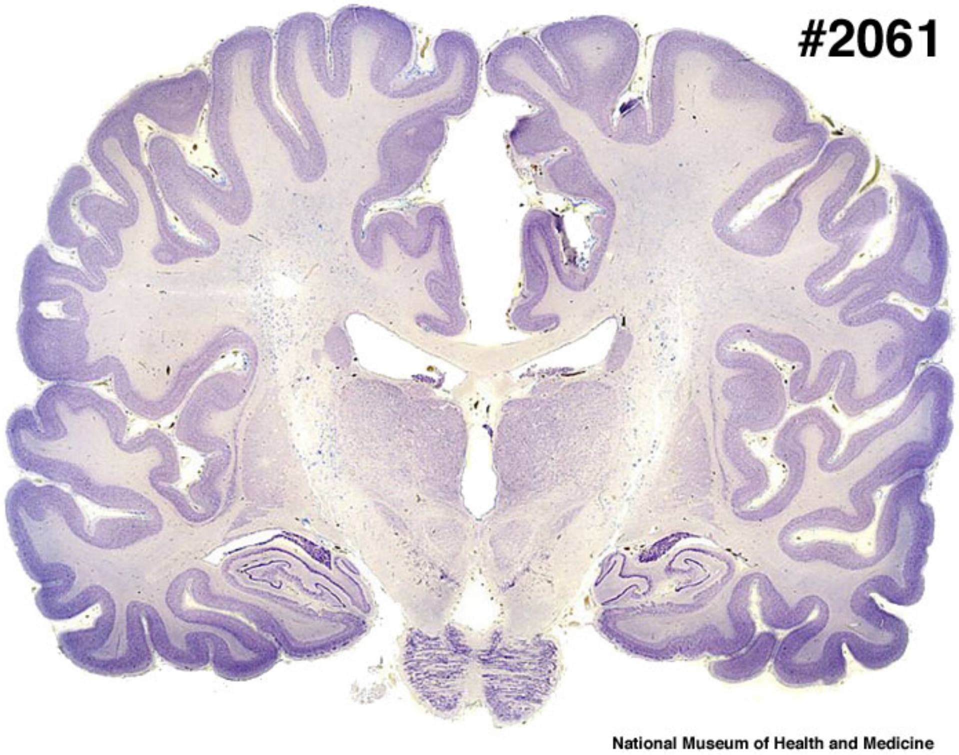
The Cortical Column



Hubel DH & Wiesel TN (1962) J Physiology 160: 106-154 cerebral cortex vs. cerebellar cortex



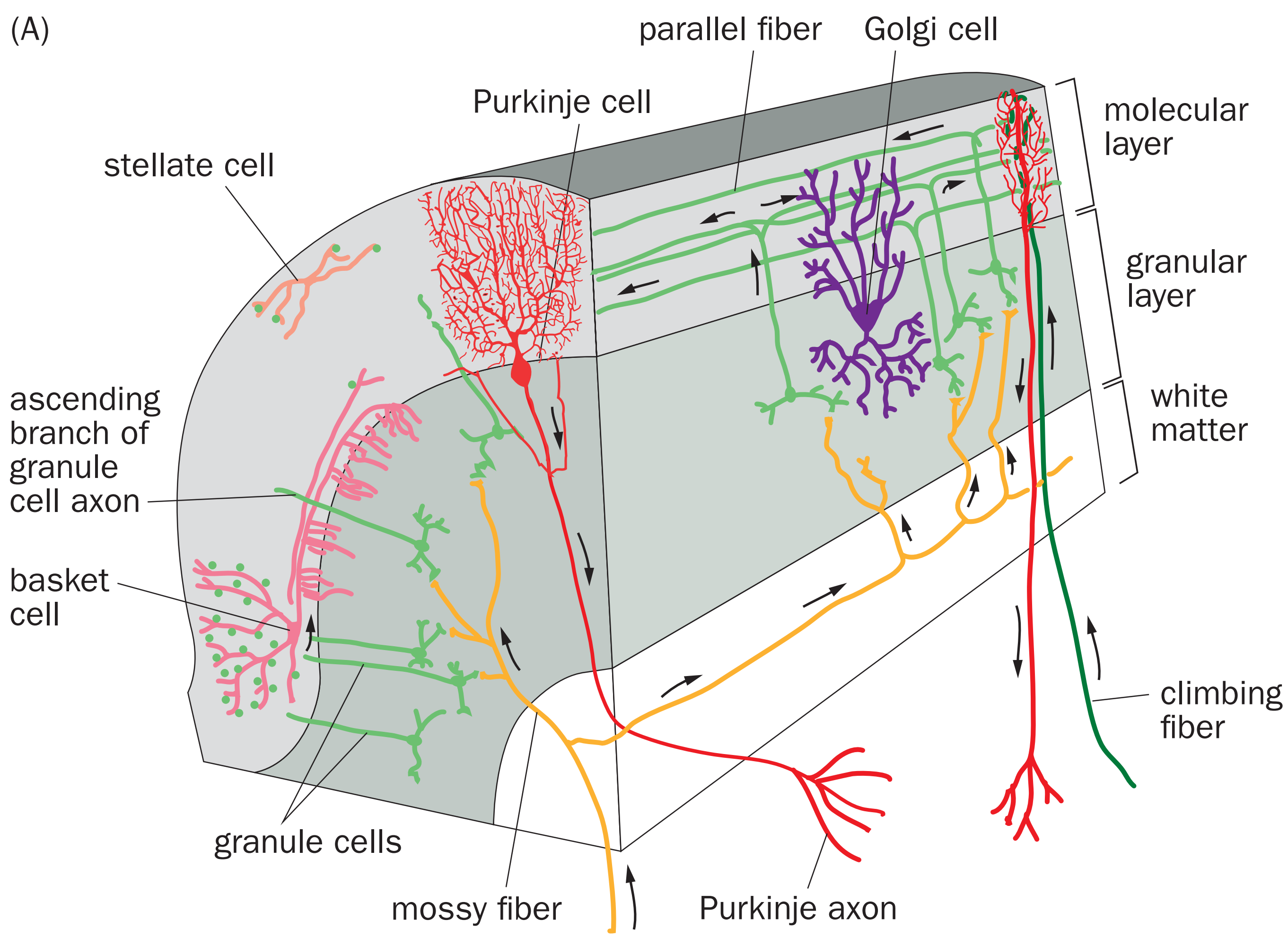
cerebellum



cerebral cortex

Connecting dense array to sparse array with extreme convergence and divergence

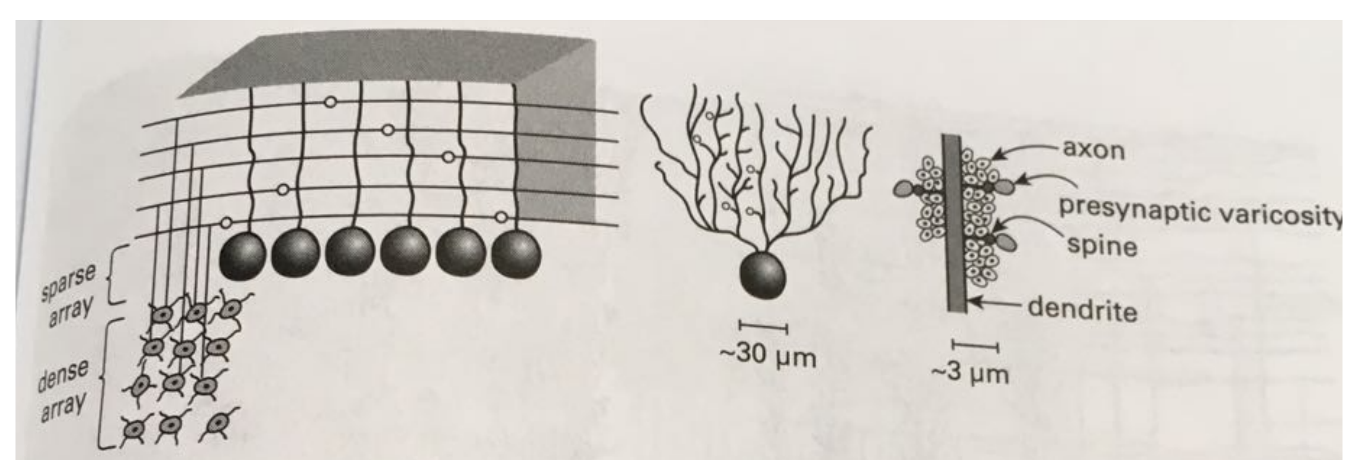
The organization cerebellar cortex



$$N_g D = N_p C$$

$$N_g \gg N_p$$

$$C \gg D$$



Connecting many dense arrays to many other dense arrays with moderate convergence and divergence

The organization of the cortical column

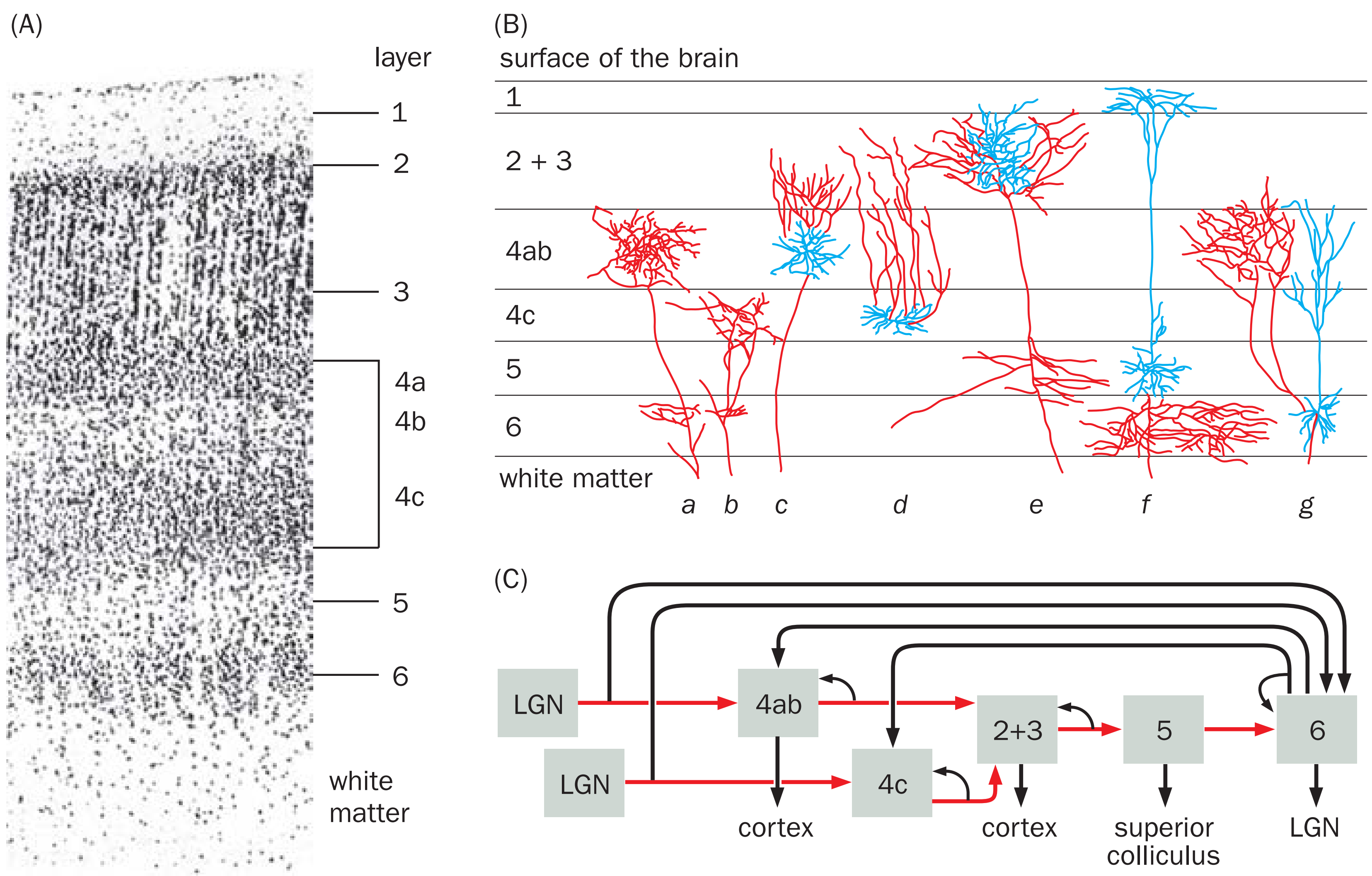
85% excitatory cells

15% inhibitory cells

10^5 neurons

10^9 synapses

5000 m wires



Why do we need axons and dendrites?

Single Cortical Neurons as Deep Artificial Neural Networks

[1]David Beniaguev, [1,2]Idan Segev and [1,2]Michael London

[1]The Edmond and Lily Safra Center for Brain Sciences and [2]Department of Neurobiology, The Hebrew University of Jerusalem, Jerusalem, Israel.

Communication: David Beniaguev - david.beniaguev@gmail.com

Can Single Neurons Solve MNIST? The Computational Power of Biological Dendritic Trees

Ilenna Simone Jones[1] and Konrad Kording[2]

[1]Department of Neuroscience, University of Pennsylvania
[2]Departments of Neuroscience and Bioengineering, University of Pennsylvania

September 4, 2020

Occam’s Razor

entities should not be multiplied without necessity.

奥卡姆剃刀定律

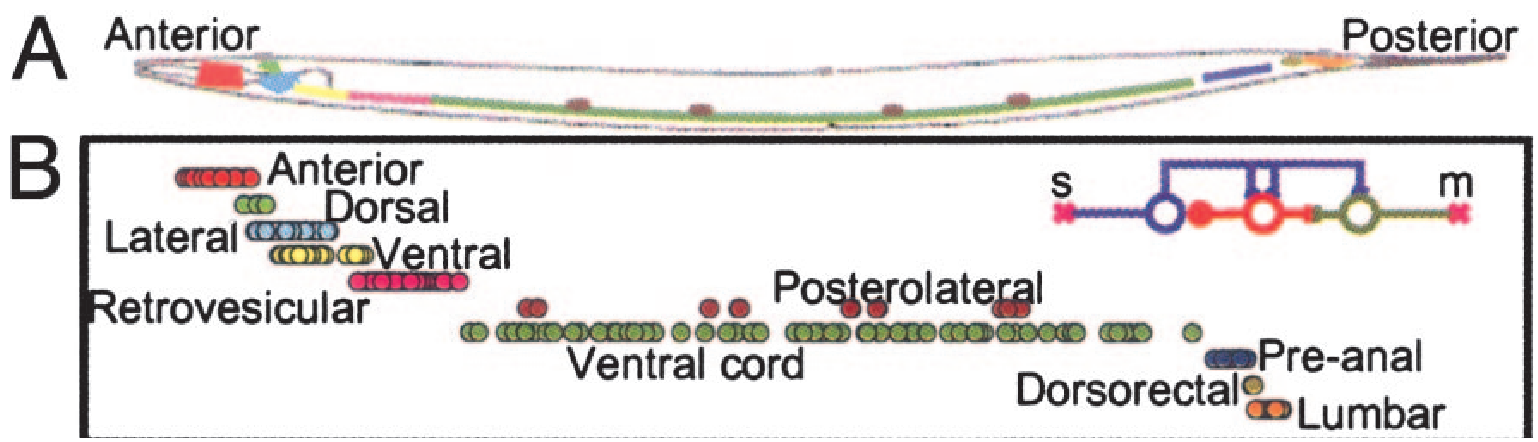
如无必要，勿增实体。简单有效原理。《箴言书注》：切勿浪费较多东西去做，用较少的东西，同样可以做好的事情。

Wiring Optimization of Neural Circuit

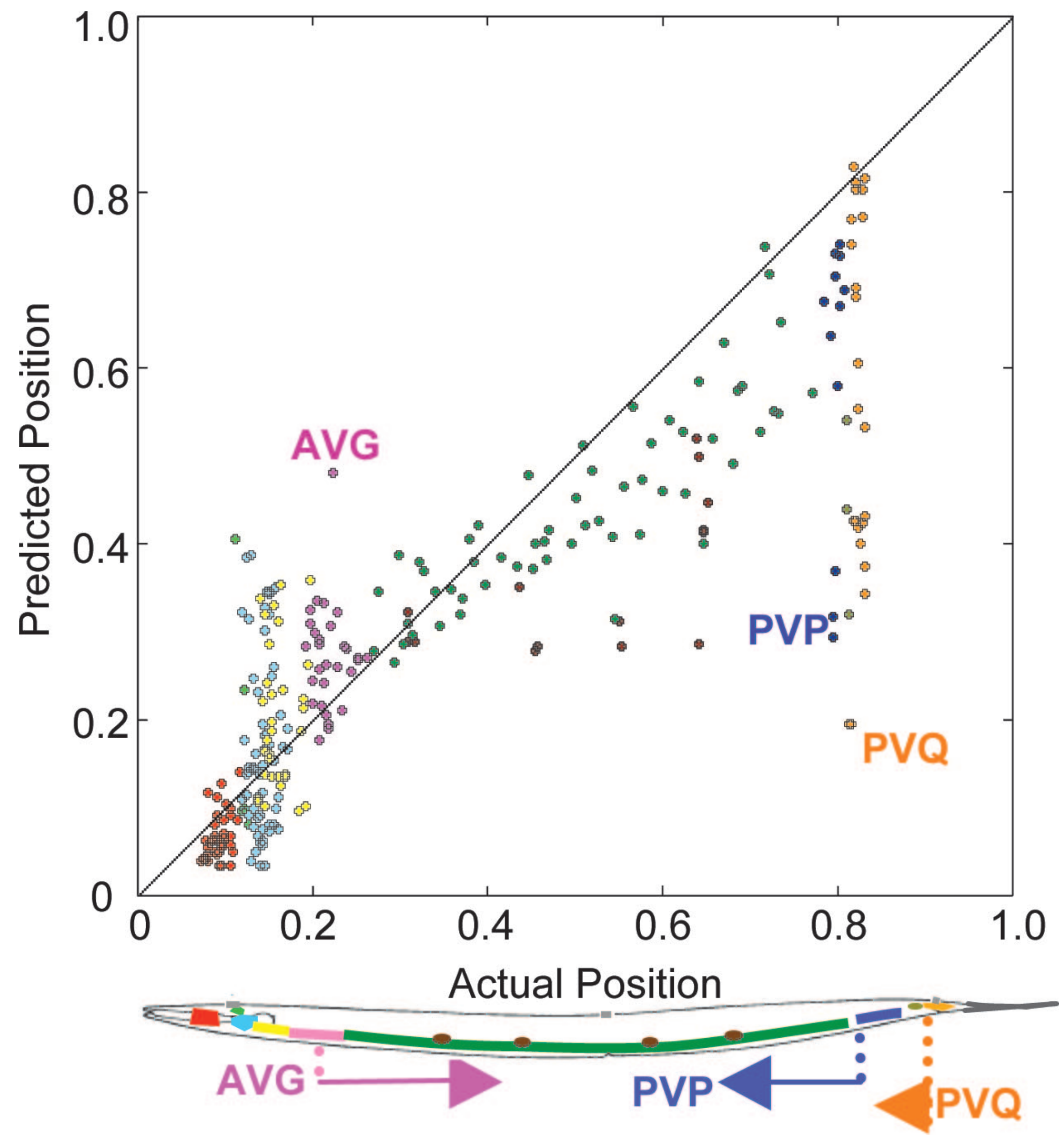
“After the many shapes assumed by neurons, we are now in a position to ask whether this diversity ... has been left to chance and is insignificant, or whether it is tightly regulated and provides an advantage to the organism. ... we realized that all of the various conformations of the neuron and its various components are simply morphological adaptations governed by laws of conservation for time, space, and material.”

Ramon y Cajal

Neuronal layout in *C. elegans*

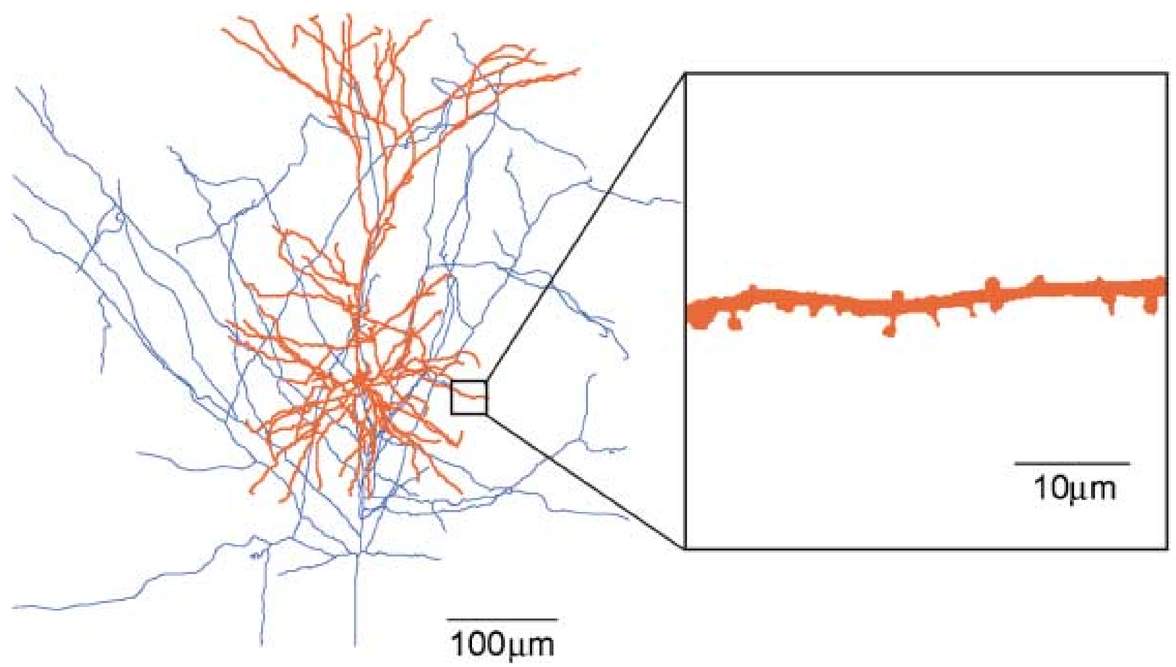


Neuronal layout in *C. elegans*

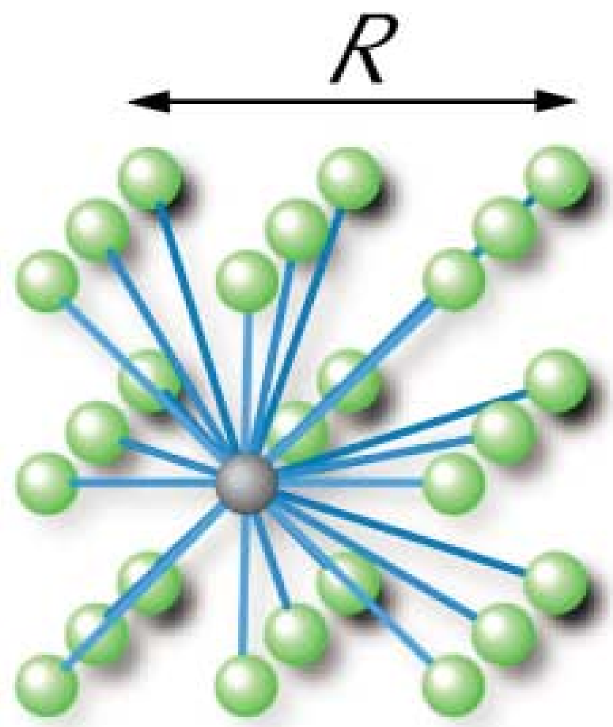


Beth Chen et. al., PNAS 2006

A toy problem: why do we need axons and dendrites?

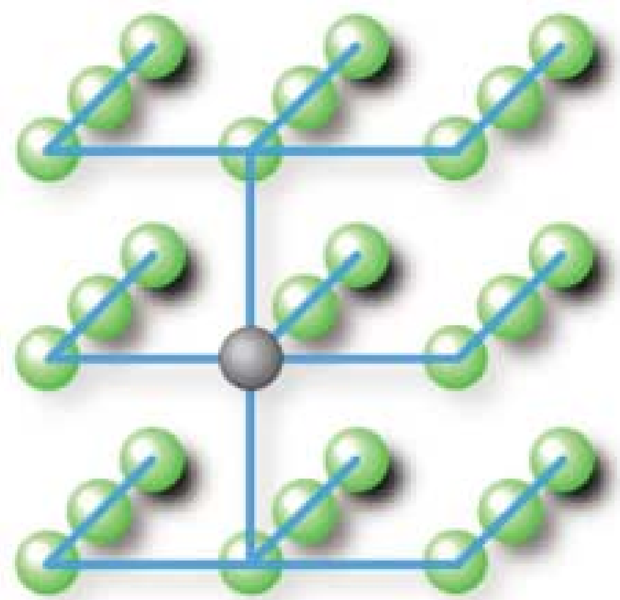


A toy problem: why do we need axons and dendrites?



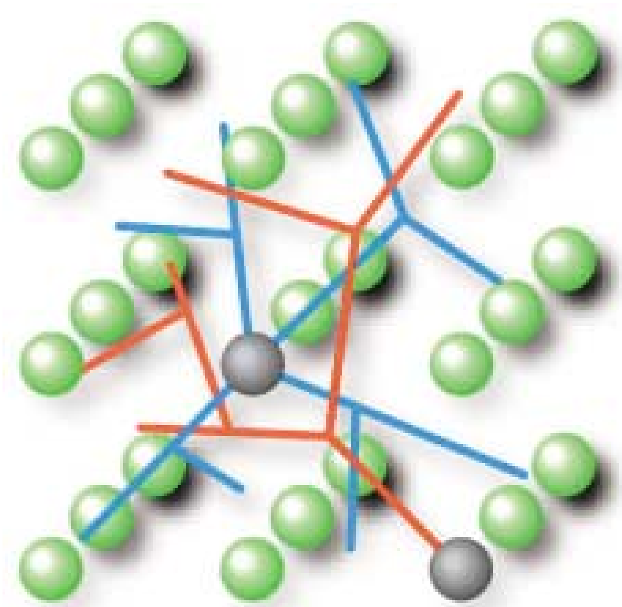
Design I

A toy problem: why do we need axons and dendrites?



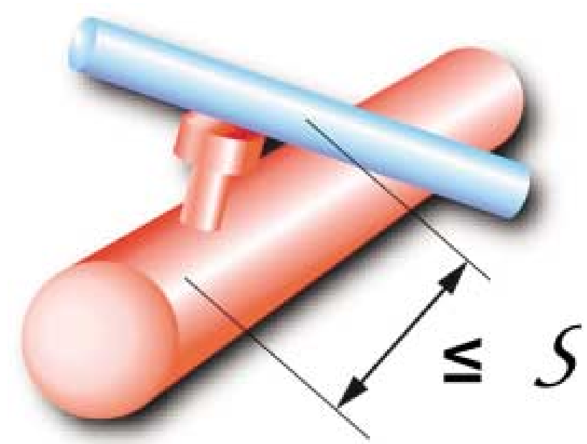
Design II

A toy problem: why do we need axons and dendrites?



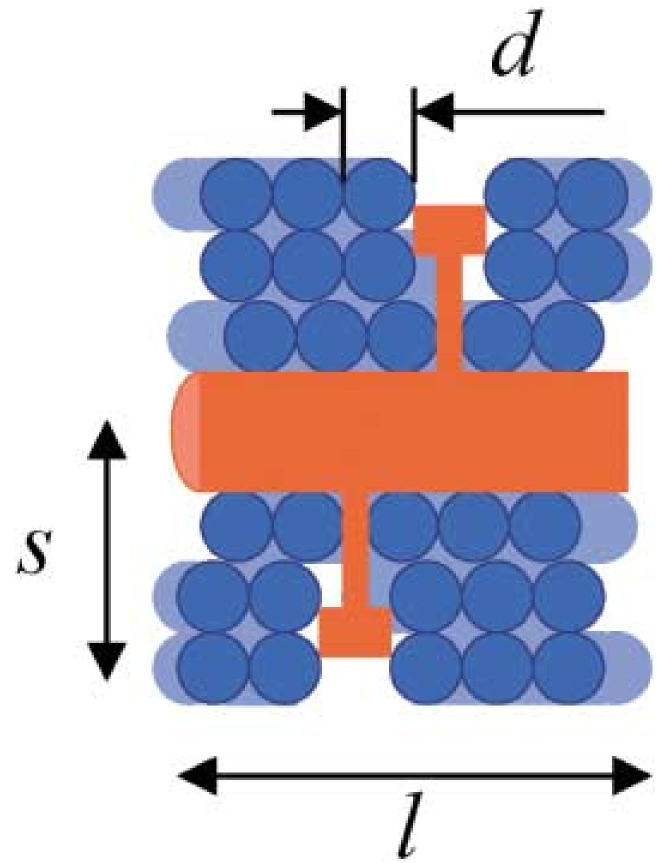
Design III

A toy problem: why do we need axons and dendrites?



Design IV

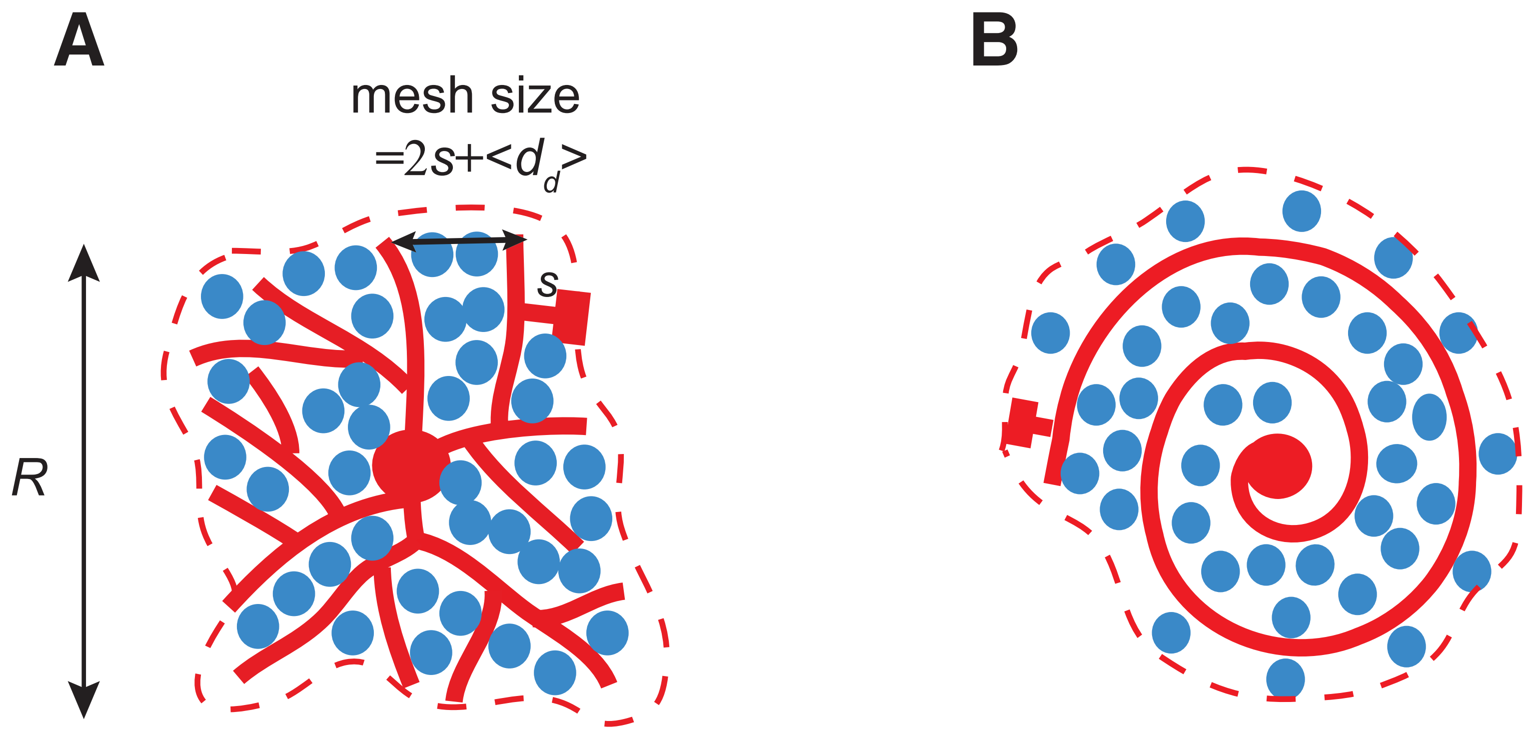
A toy problem: why do we need axons and dendrites?



The Optimality of the design

Chklovskii *Neuron* 2004

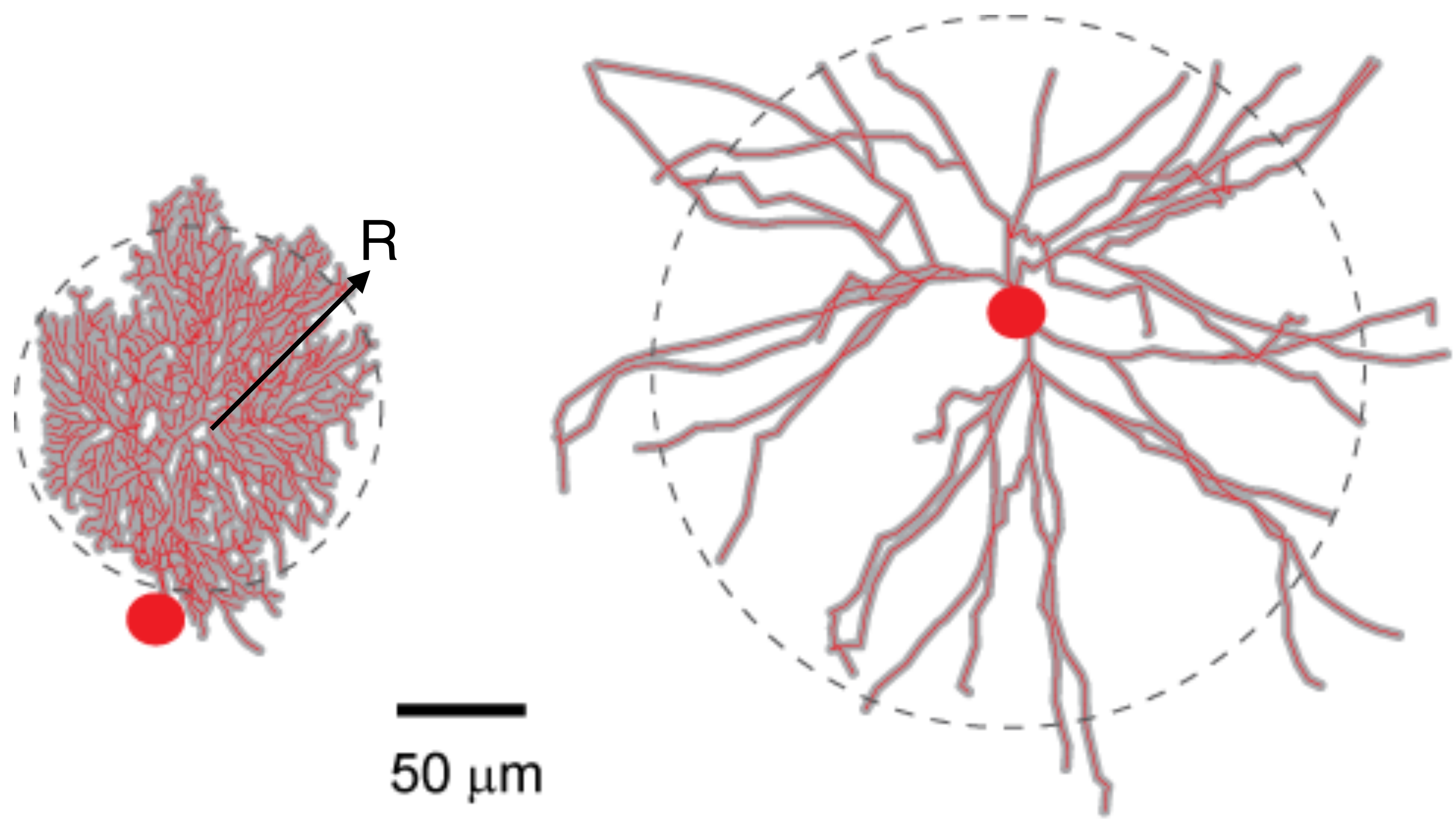
Why do we need branching dendrites and axons?



- Cost increases with the total length of a dendrite
- Cost increases with the path length from a synapse to the cell body

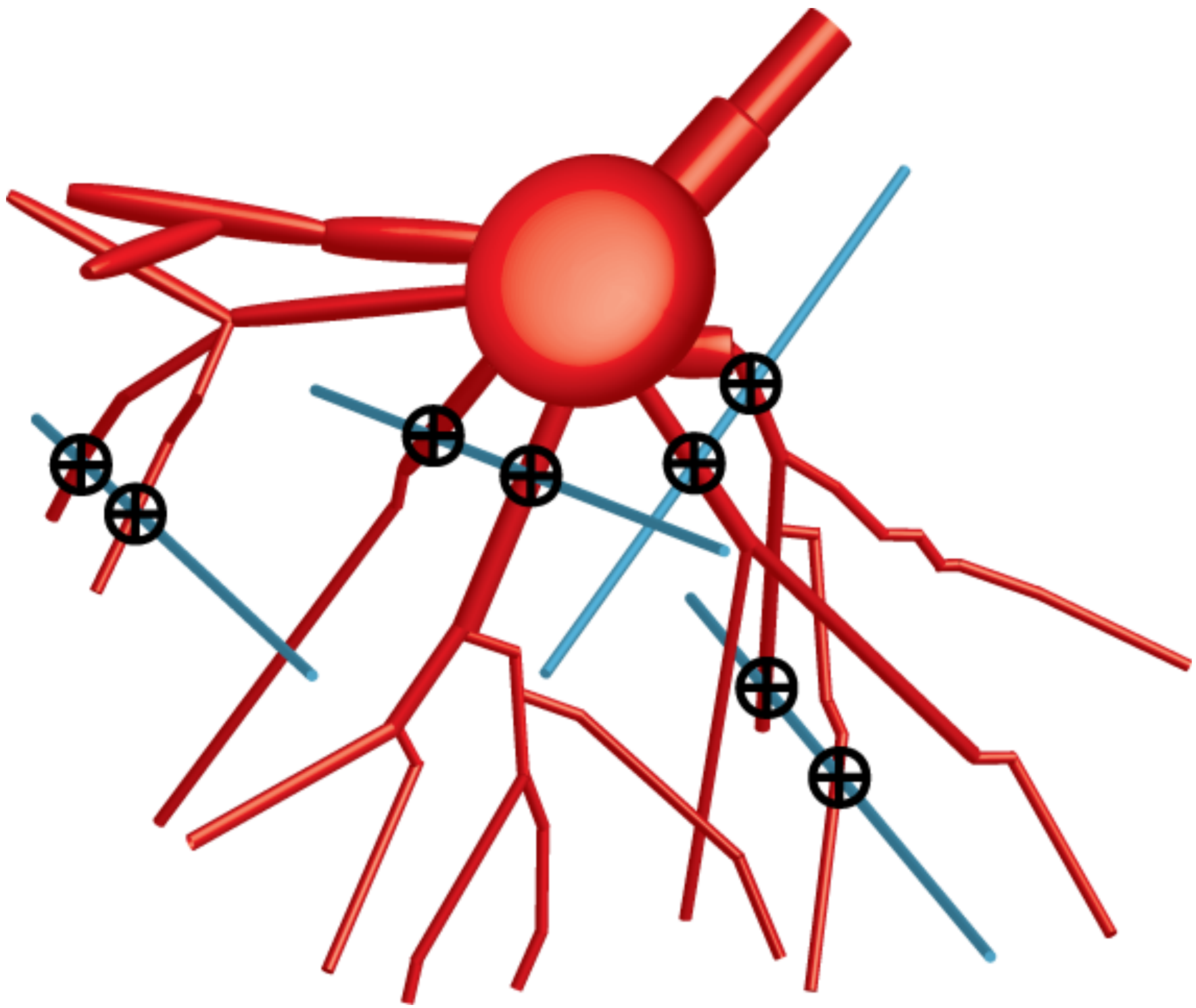
Wen, Chklovskii
Journal of Neurophysiology *2008*

Why pyramidal dendrites appear much sparser than Purkinje dendrites?

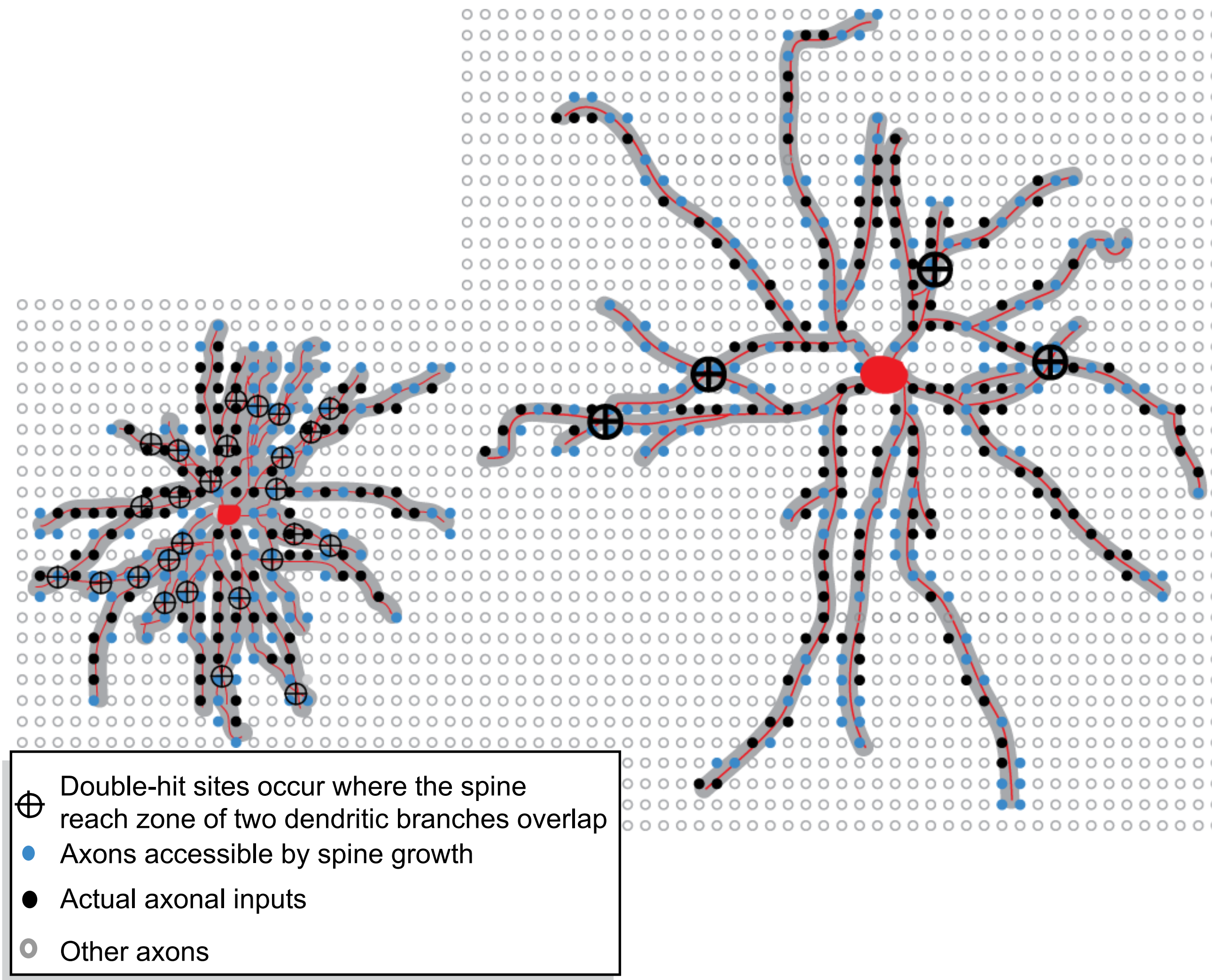


Wen et. al., PNAS 2009

Double-hits reduce the number of axons accessible to a 3D dendritic arbor



A sparse 3D dendritic arbor has fewer double-hits, and therefore, can access more axons, all other things being equal.

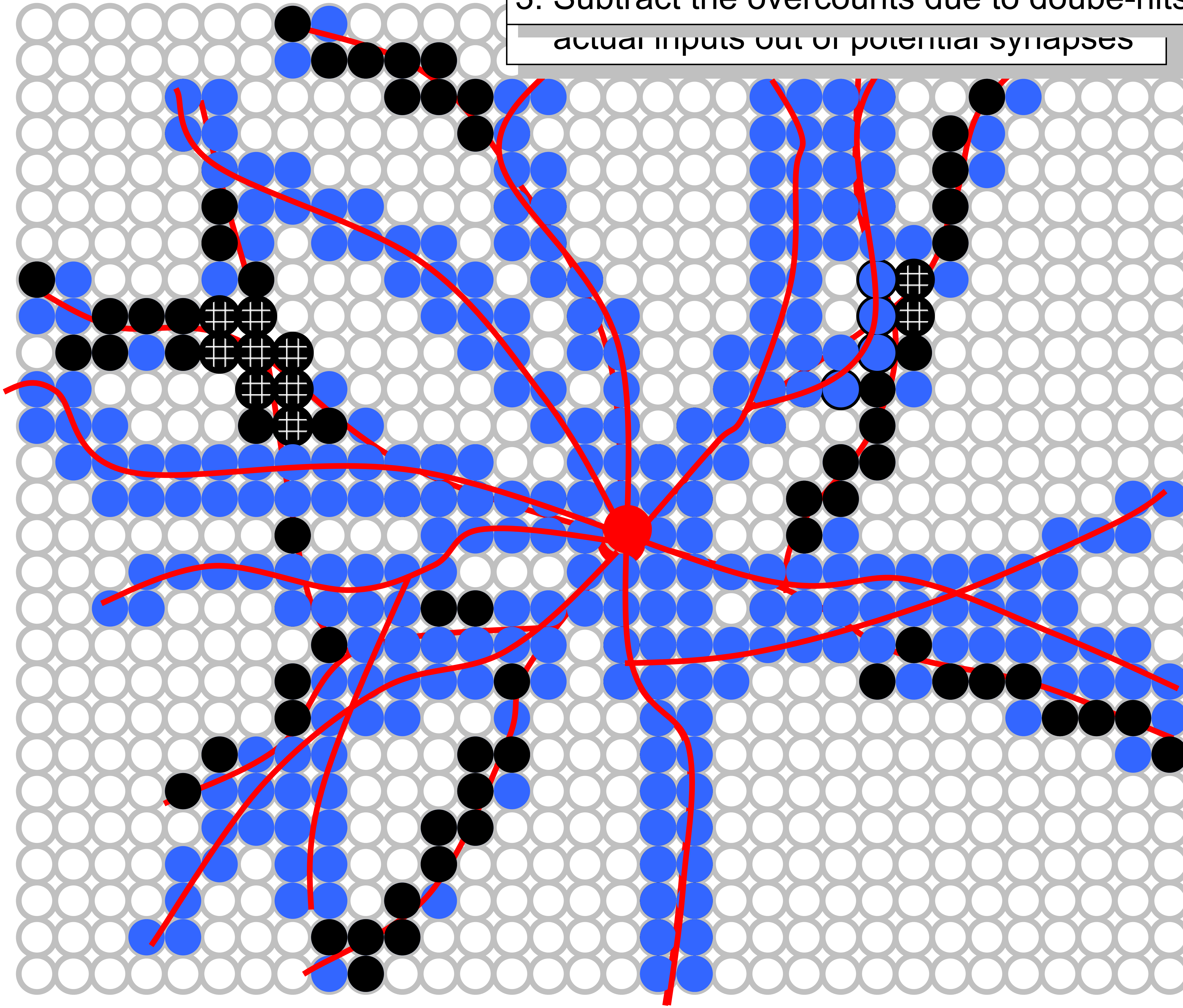


Why access a large number of axons?

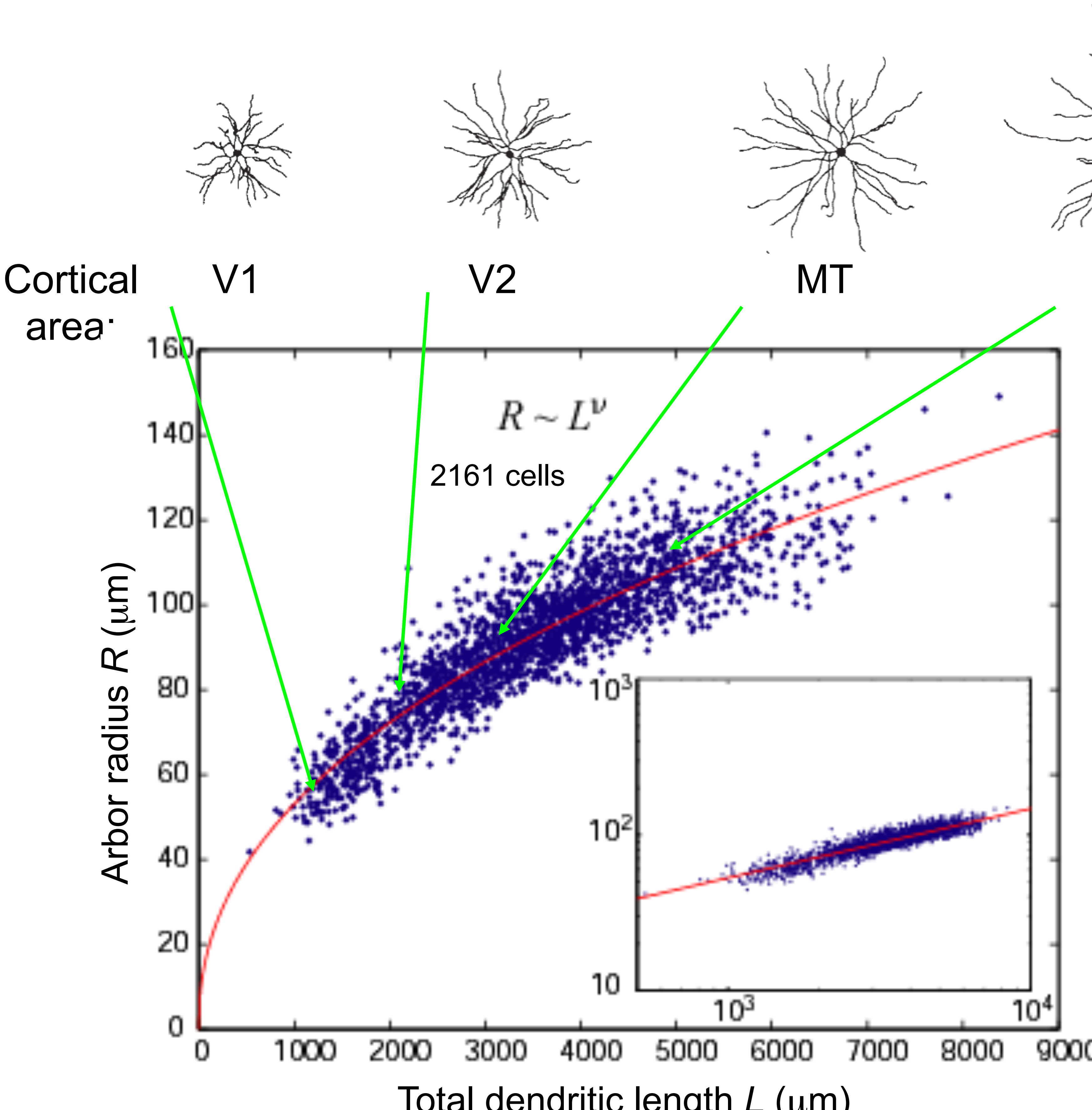
- The functionality of a dendritic arbor benefits from having a large connectivity repertoire, which is defined as the the number of combinations of axons synapsing on a dendritic arbor .

- **The shape of a dendritic arbor maximizes the connectivity repertoire while minimizing the dendritic cost.**

3. Subtract the overcounts due to doube-hits



Scaling of basal pyramidal dendrites

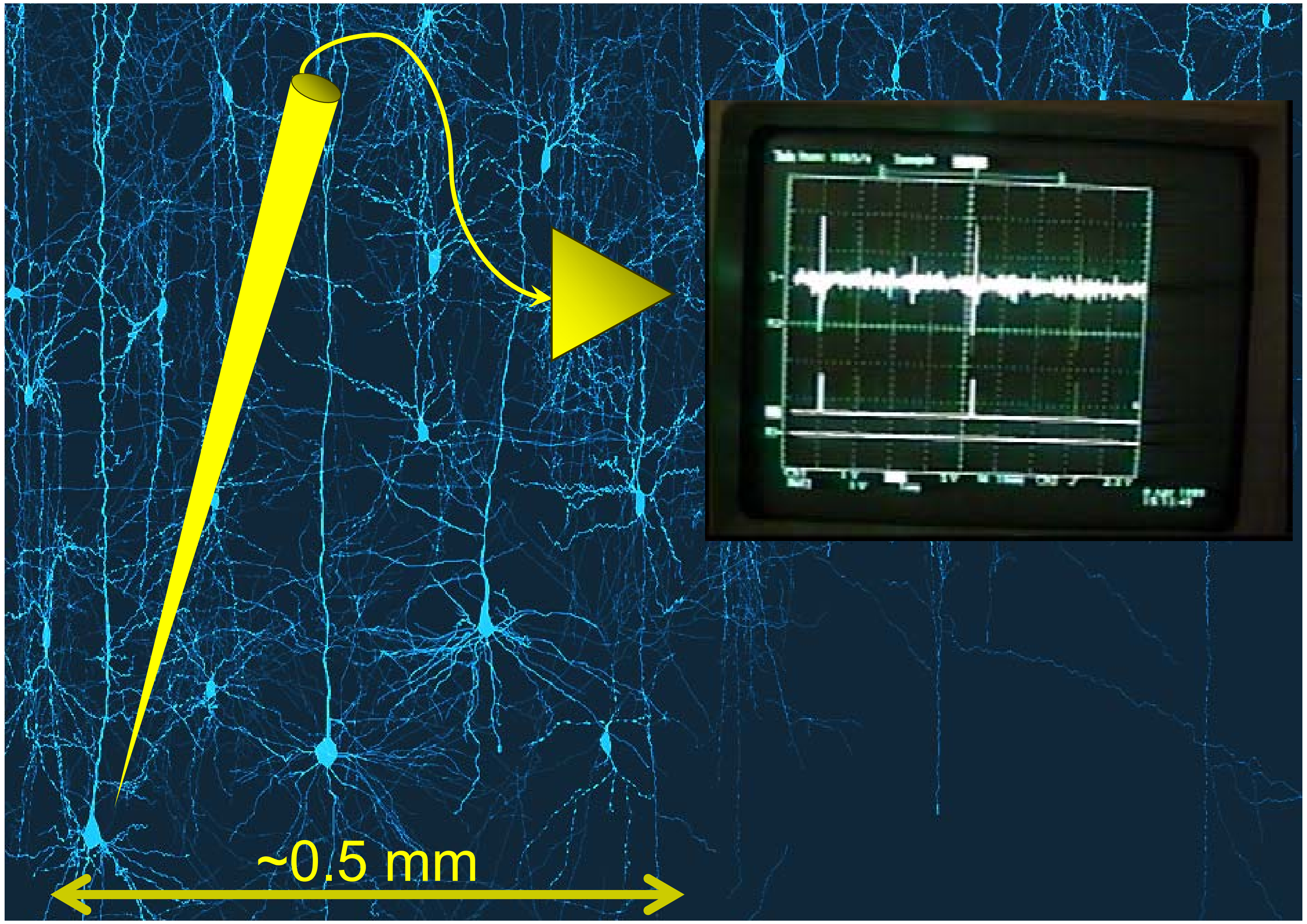


$\nu = 0.44 \pm 0.01,$

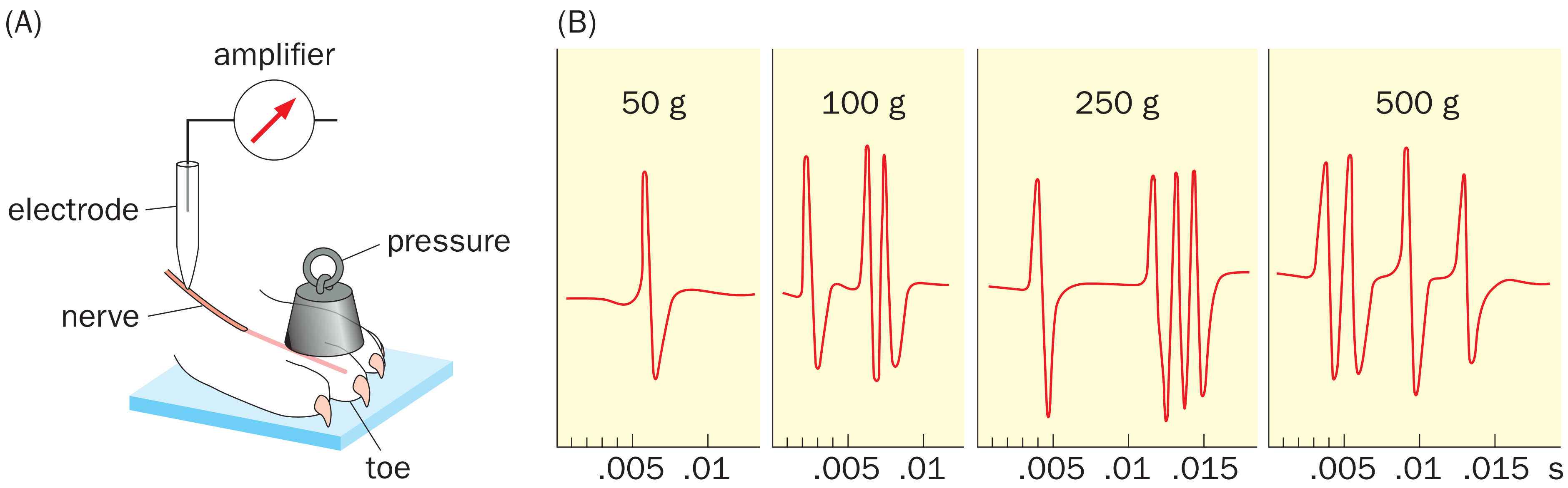
$\nu_{theory} = 0.43$

Wen et. al., PNAS 2009

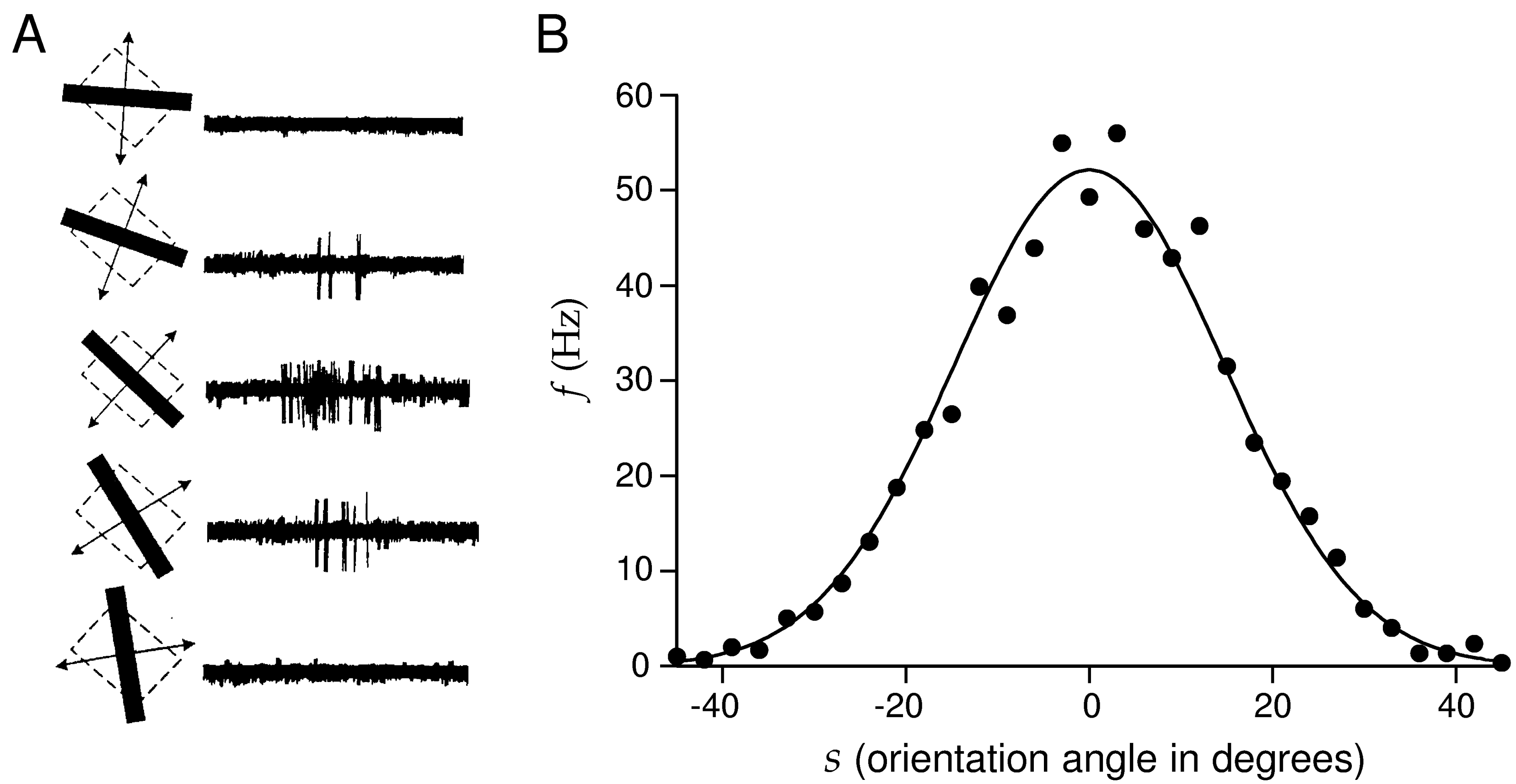
Action potential as the basic unit to transmit information between neurons



What is the neural code?

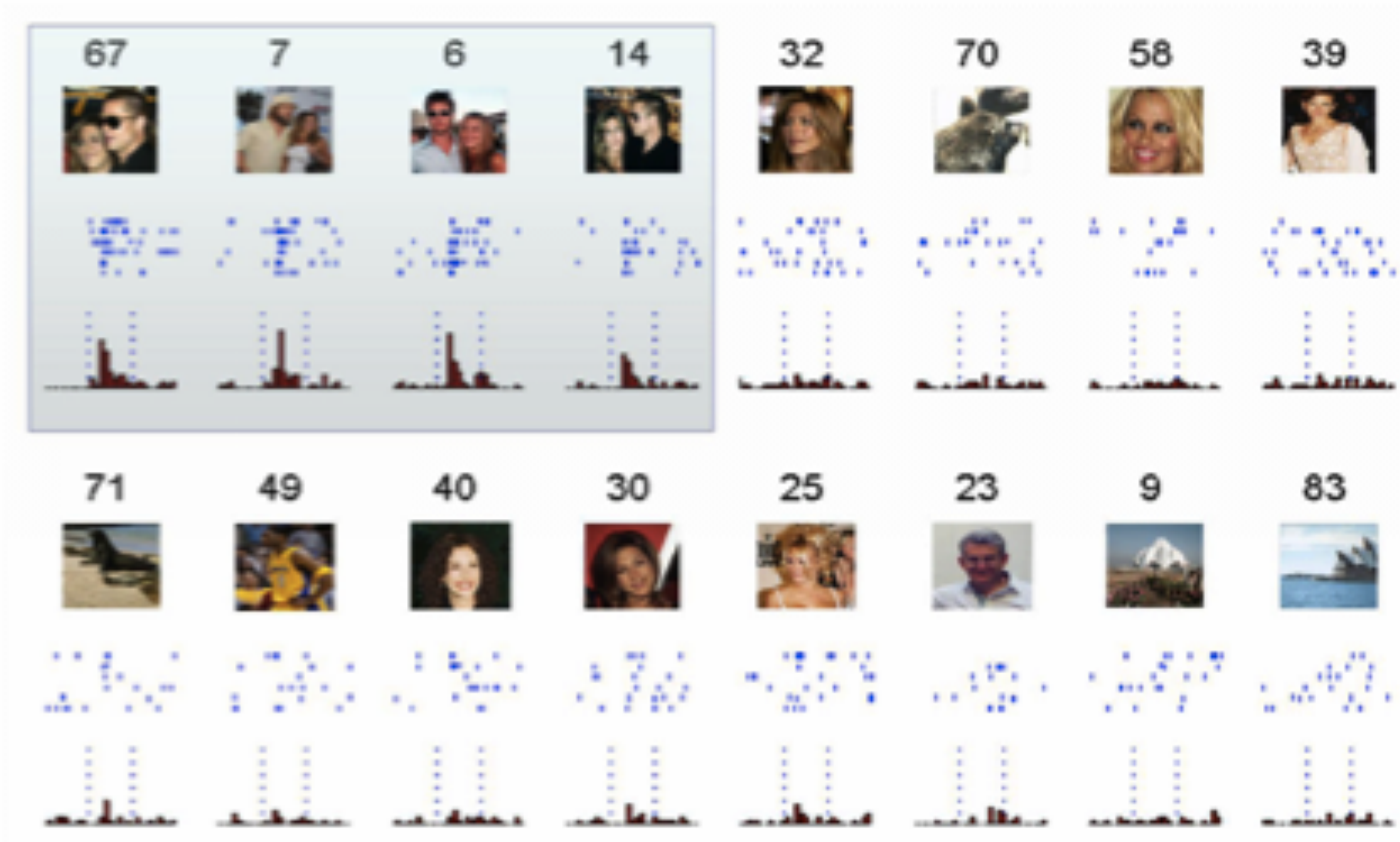


What is the neural code?



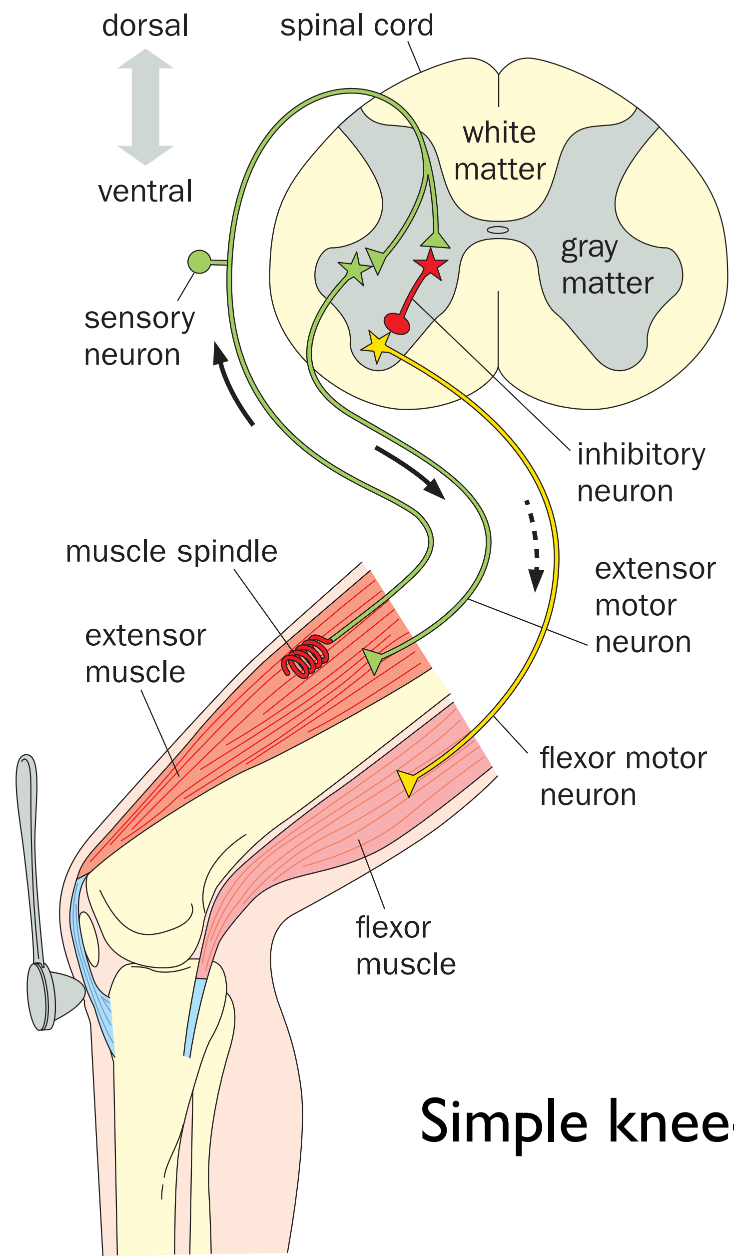
Gaussian tuning curve of a neuron in the primary visual cortex (V1)

What is the neural code?



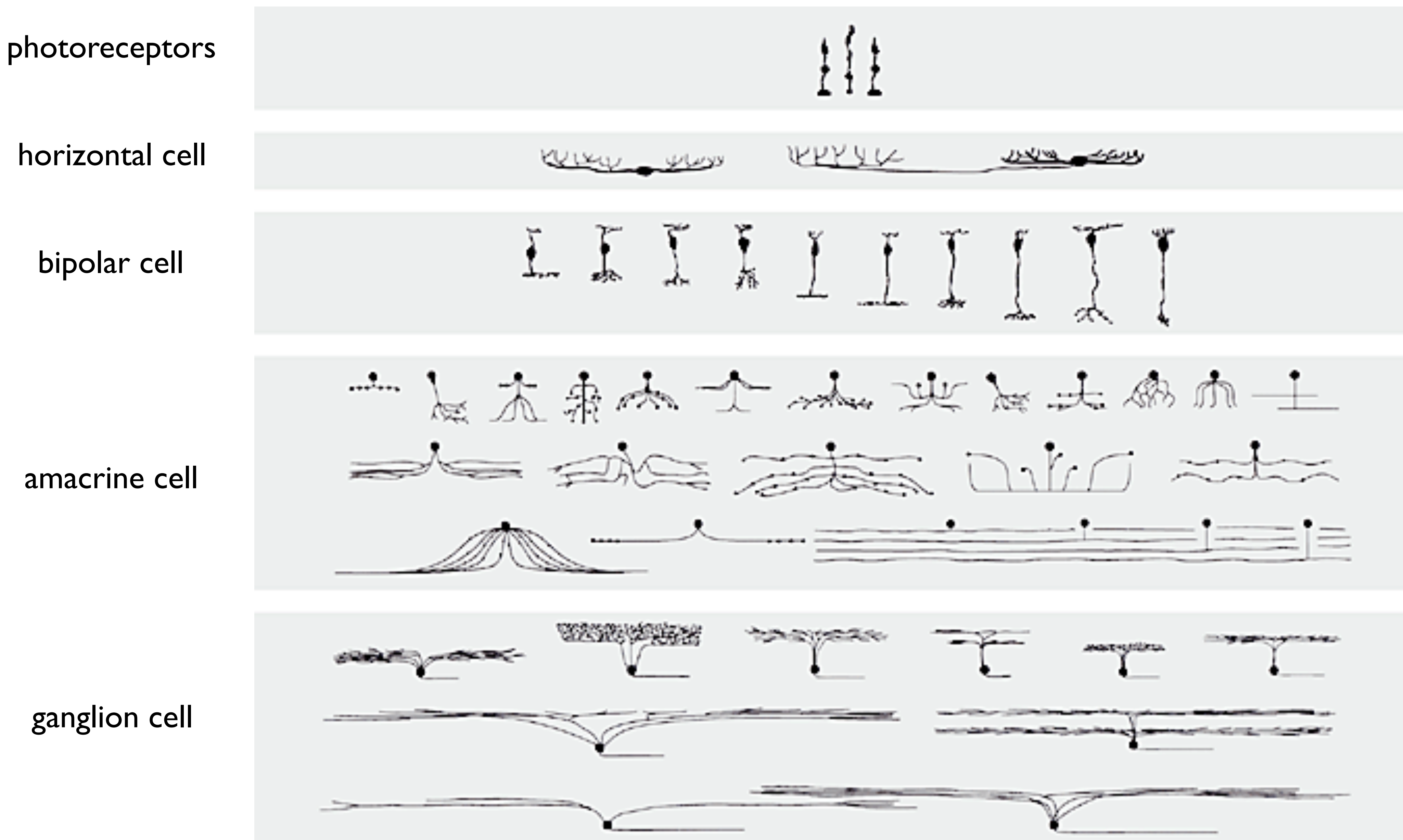
High brain areas represent increasingly complex features

Neurons perform their functions in the context of neural circuit

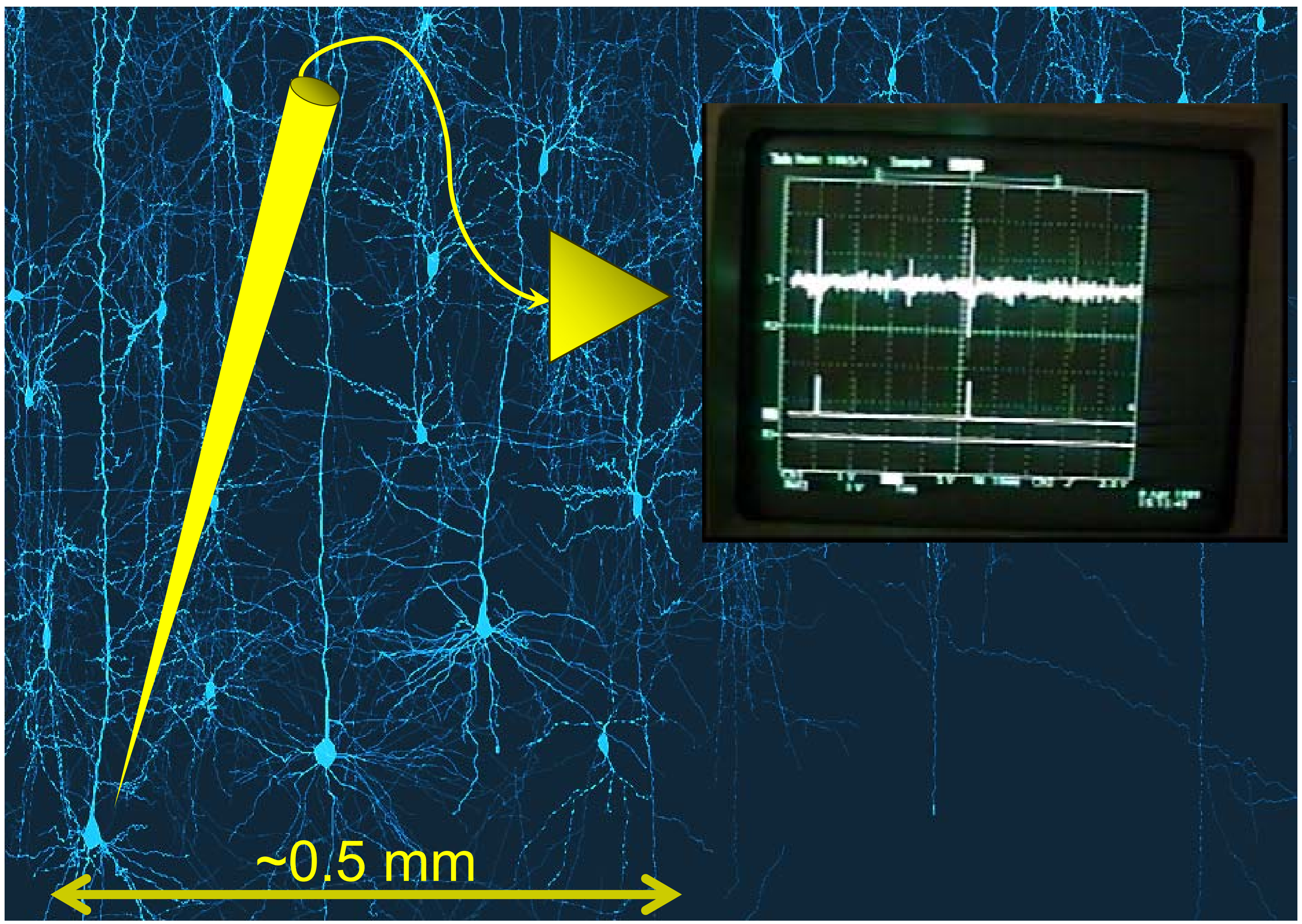


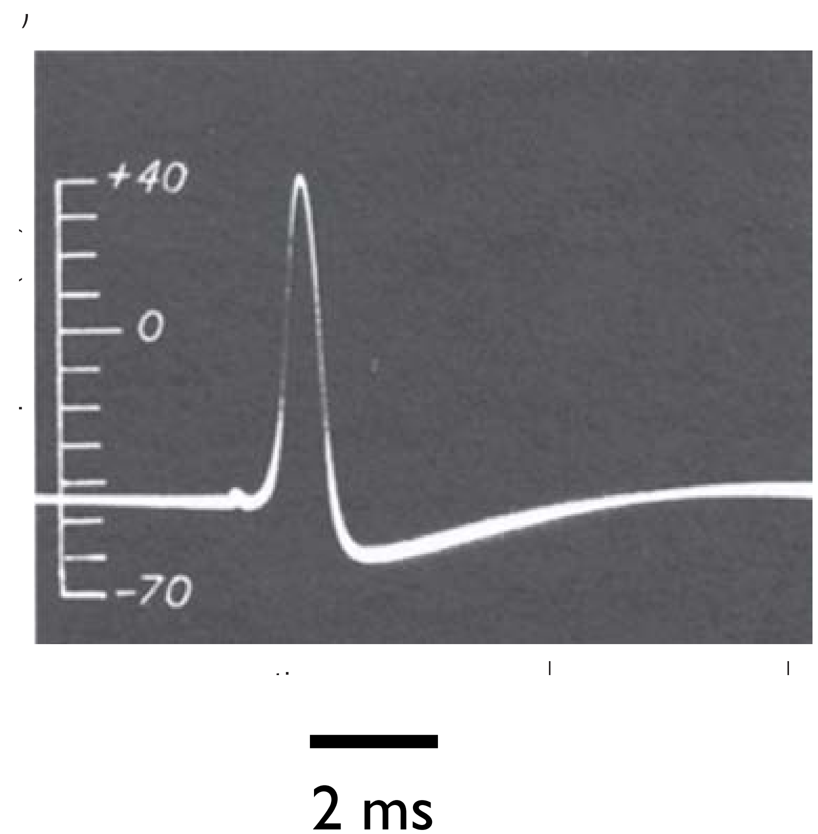
Simple knee-jerk reflex circuit

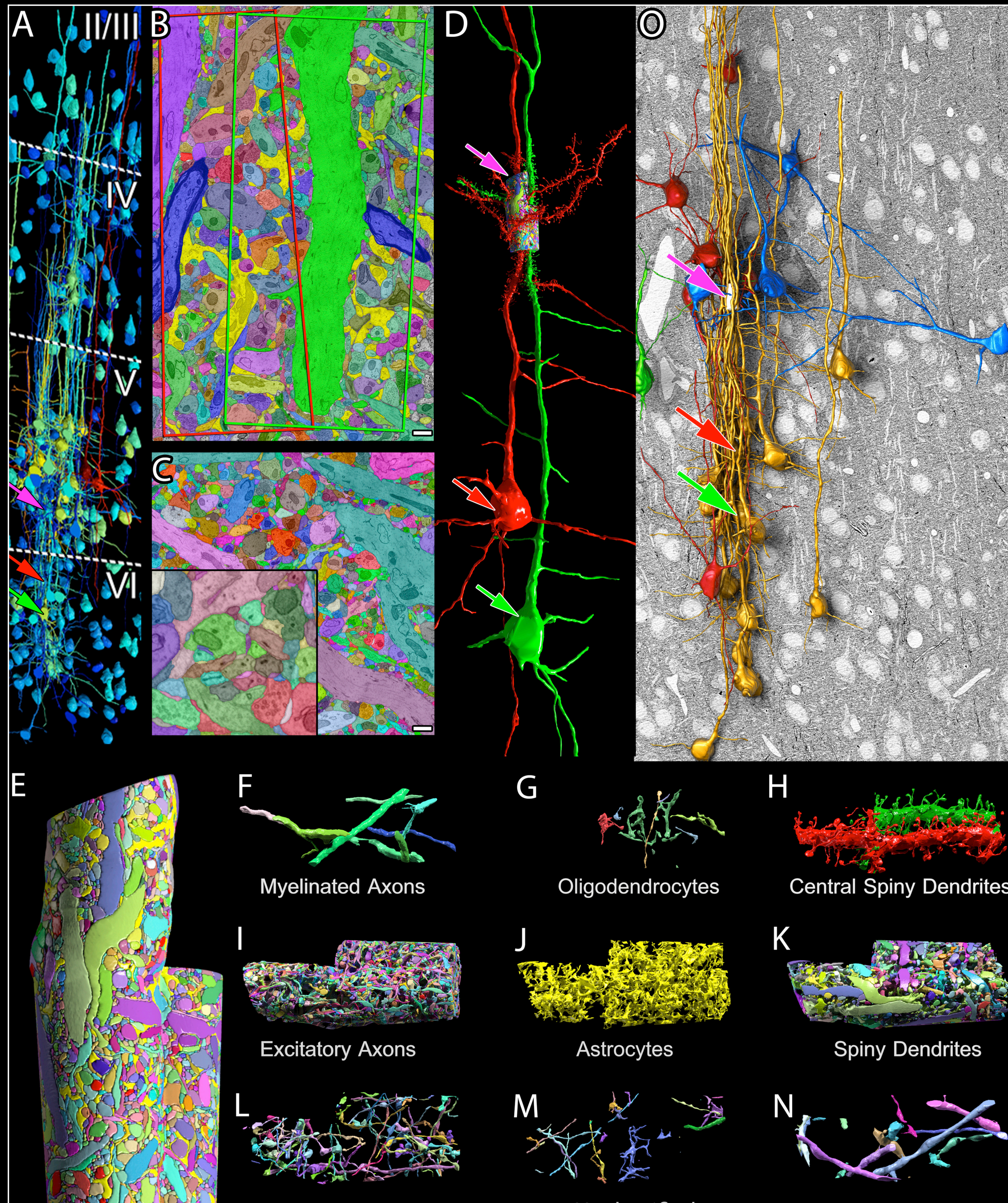
Diverse cell types in the brain



How neurons communicate with each other?







Kasthuri et. al,
Cell 2015

The organization of the cortical column

Table 1. List of reconstructed neurons

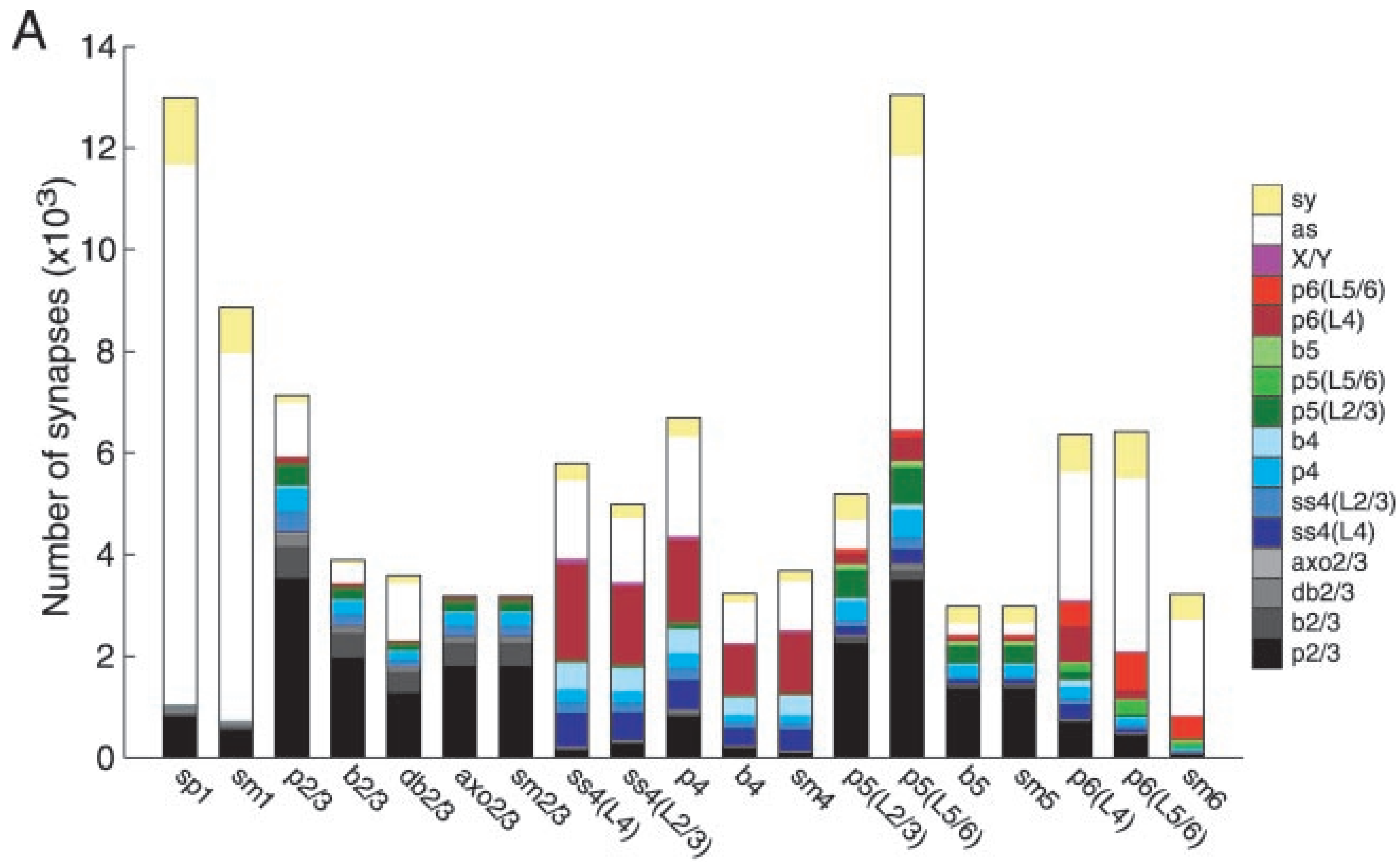
Cell type	Abbreviation	Axon	Dendrite
Pyramidal cell in layer 2/3	p2/3	6	6
Basket cell in layer 2/3	b2/3	6	4
Double bouquet cell in layer 2/3	db2/3	1	1
Spiny stellate cell with axon in layer 4	ss4(L4)	2	2
Spiny stellate cell with axon in layer 2/3	ss4(L2/3)	3	3
Pyramidal cell in layer 4	p4	3	3
Basket cell in layer 4	b4	5	3
Pyramidal cell in layer 5 with axon in layer 2 and 3	p5(L2/3)	1	1
Pyramidal cell in layer 5 with axon in layer 5 and 6	p5(L5/6)	1	1
Basket cell in layer 5	b5	1	
Pyramidal cell in layer 6 with axon in layer 4	p6(L4)	6	6
Pyramidal cell in layer 6 with axon in layer 5 and 6	p6(L5/6)	1	1
Thalamic afferent of type X or Y	X/Y	3	

Each row shows a description of the cell type (first column), its abbreviation used in this study (second column), and the number of neurons of which the axon and dendrites were reconstructed (third and fourth columns).

Binzegger T, et.al, *Journal of Neuroscience 2004*

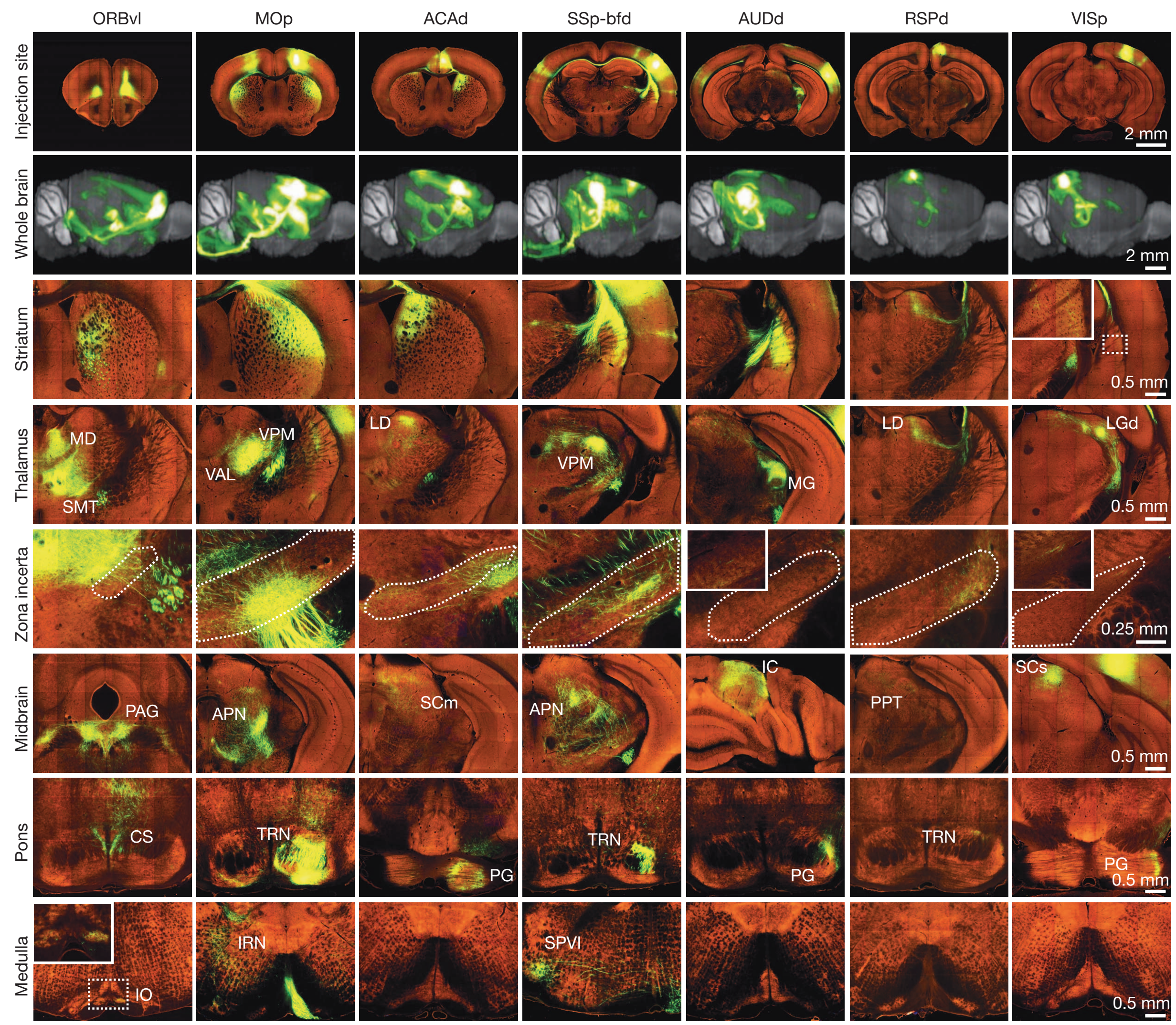
The organization of the cortical column

Binzegger T, et.al, *Journal of Neuroscience 2004*



Where is the dark matter?

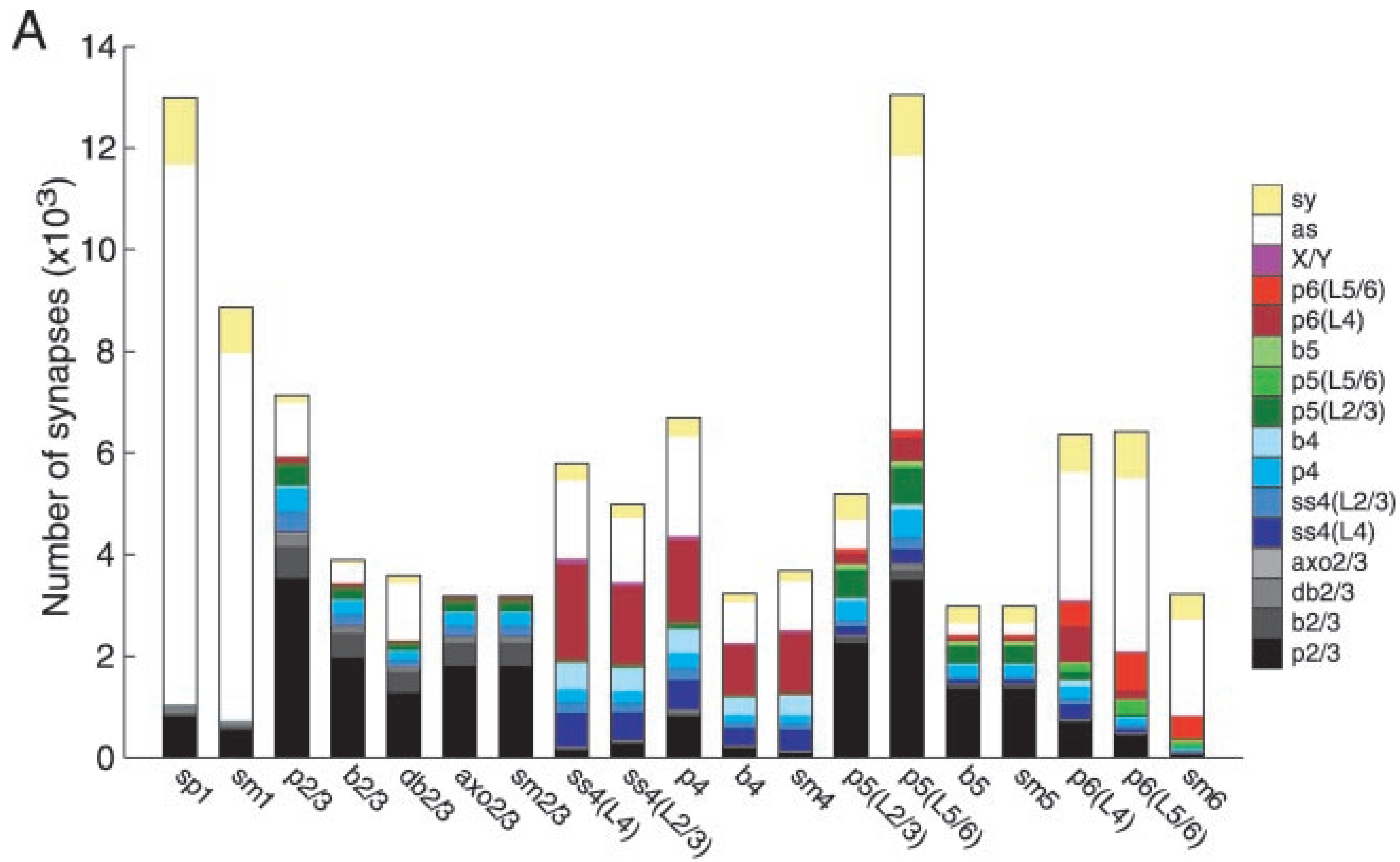
A mesoscale mouse connectome



Oh SW et. al, Nature 2014

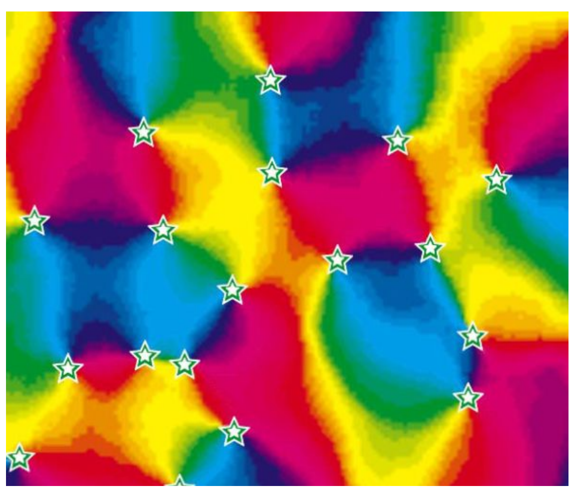
The organization of the cortical column

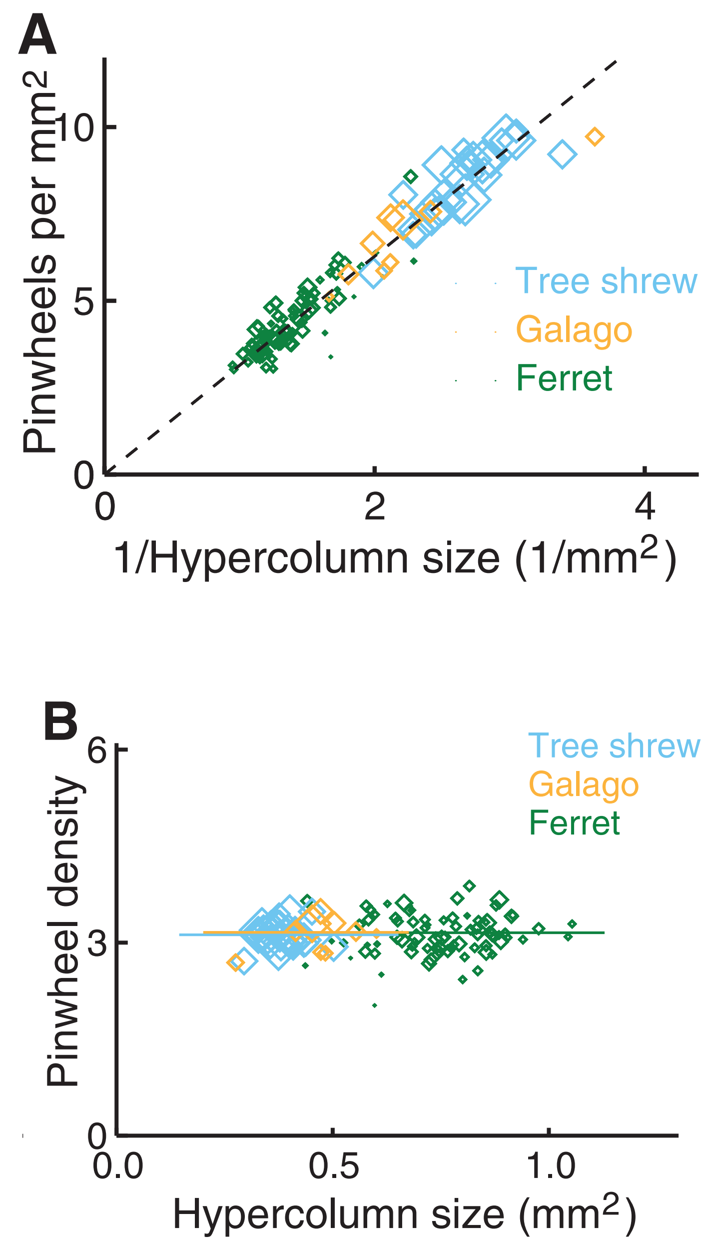
Binzegger T, et.al, *Journal of Neuroscience 2004*



~ 80% of the synapses are inter-areal long-range connections

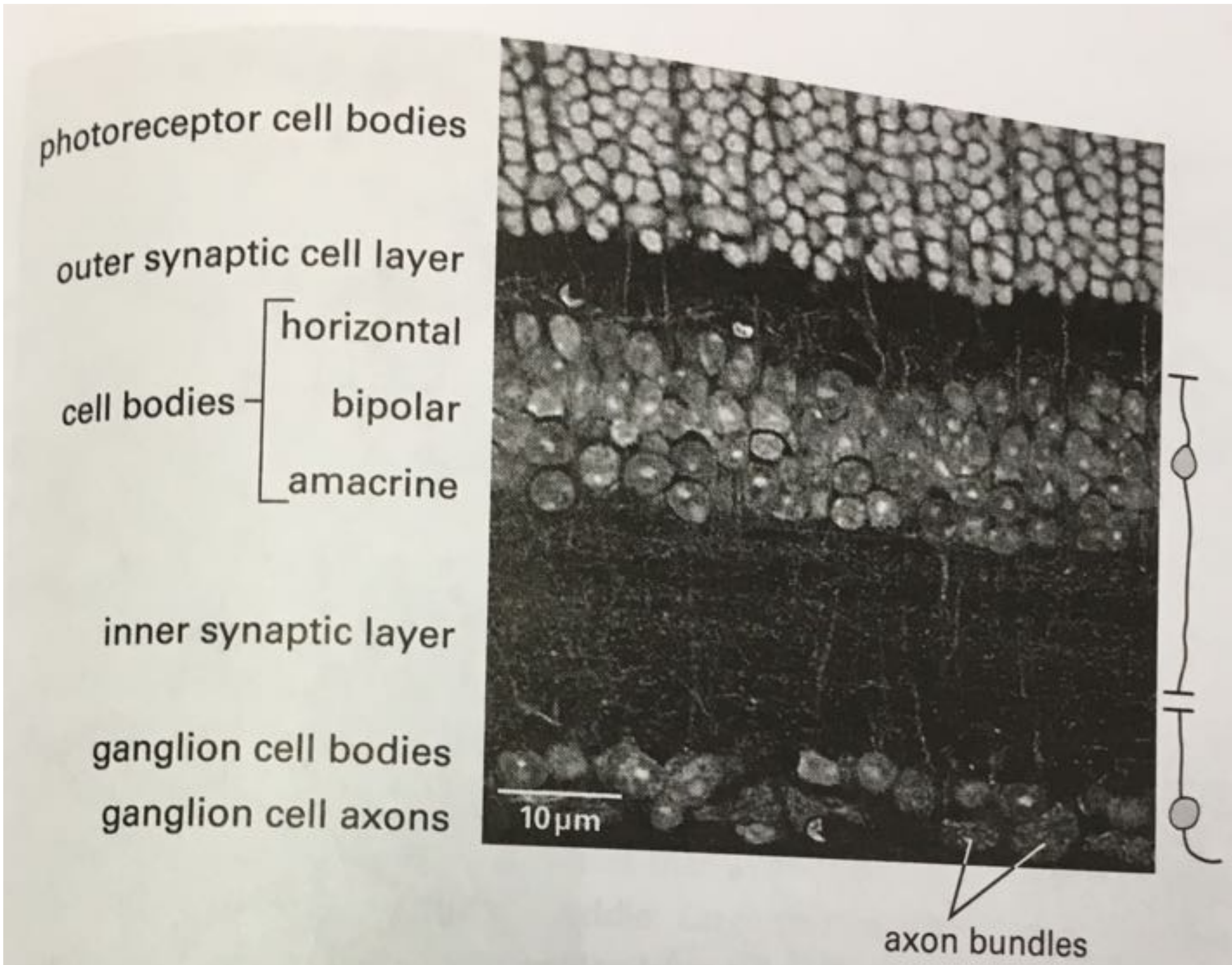
Pinwheel density approaches $\pi = 3.14$



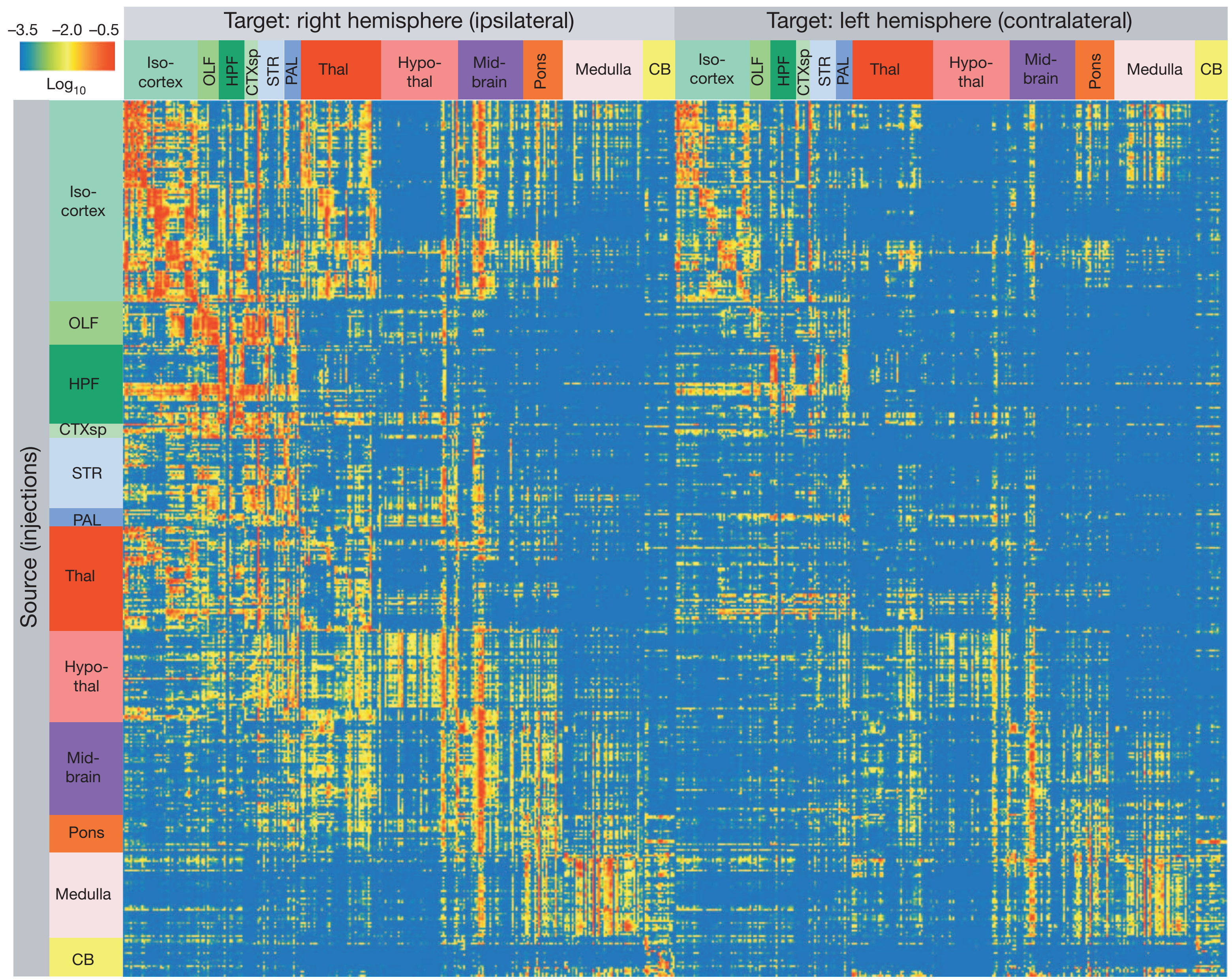


Kaschube M, et. al, Science 2010

Segregation of cell bodies and axon bundles

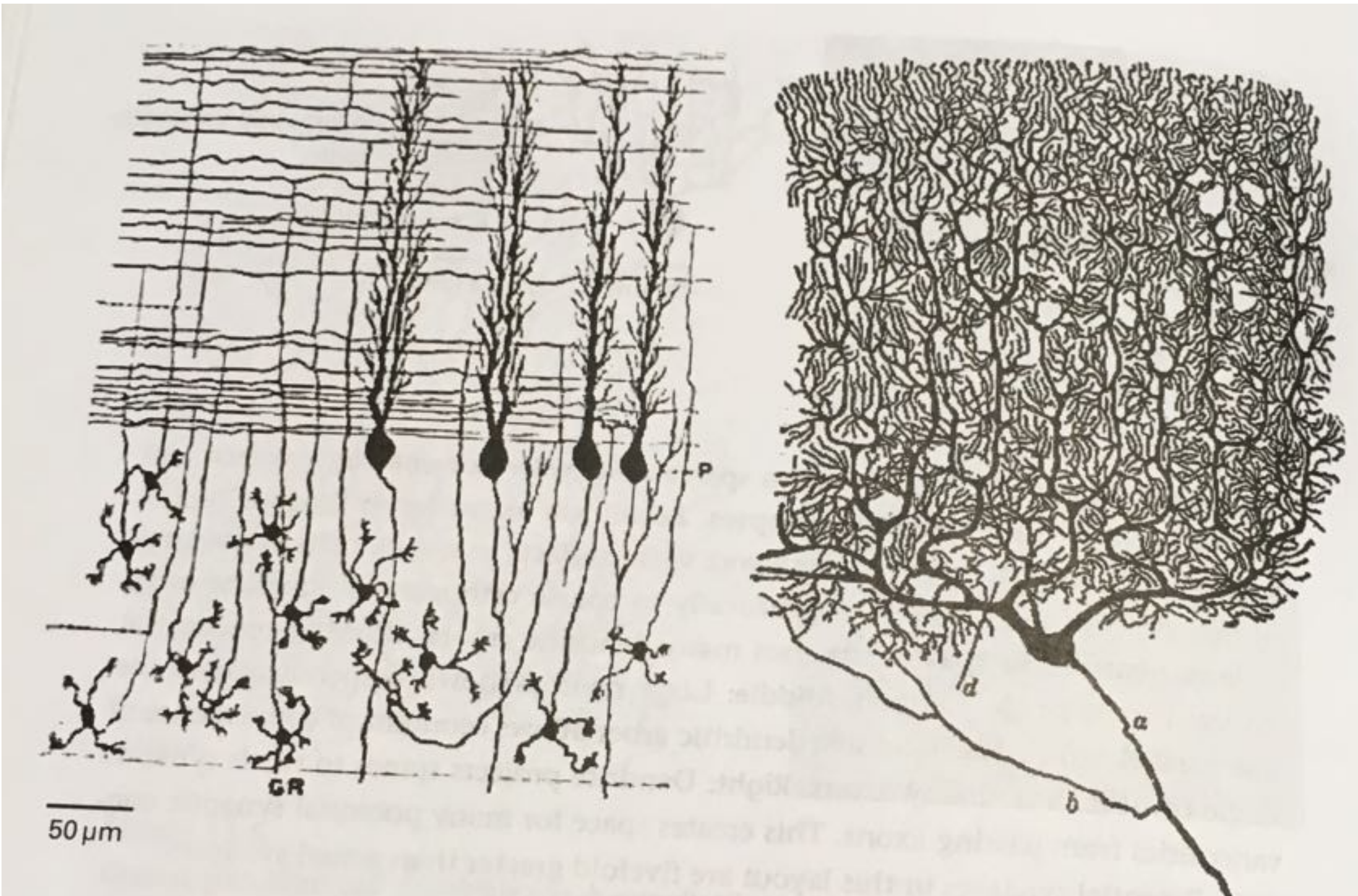


A mesoscale mouse connectome



Oh SW et. al, Nature 2014

The cerebellar cortex



Differences between a computer and a brain

- *Brain is analogue; computer is digital*
- *Brain uses content-addressable memory*
- *Brain is a massively parallel machine; computer is modular and serial*
- *Processing speed is not fixed in the brain; there is no central clock*
- *Short-term "working" memory is not like RAM*

Differences between a computer and a brain

- *Synapses are far more complex than electrical logical gate*
- *Unlike computers, processing and memory are performed by the same components in the brain*
- *The brain is a self-organizing system*
- *Brain has bodies*