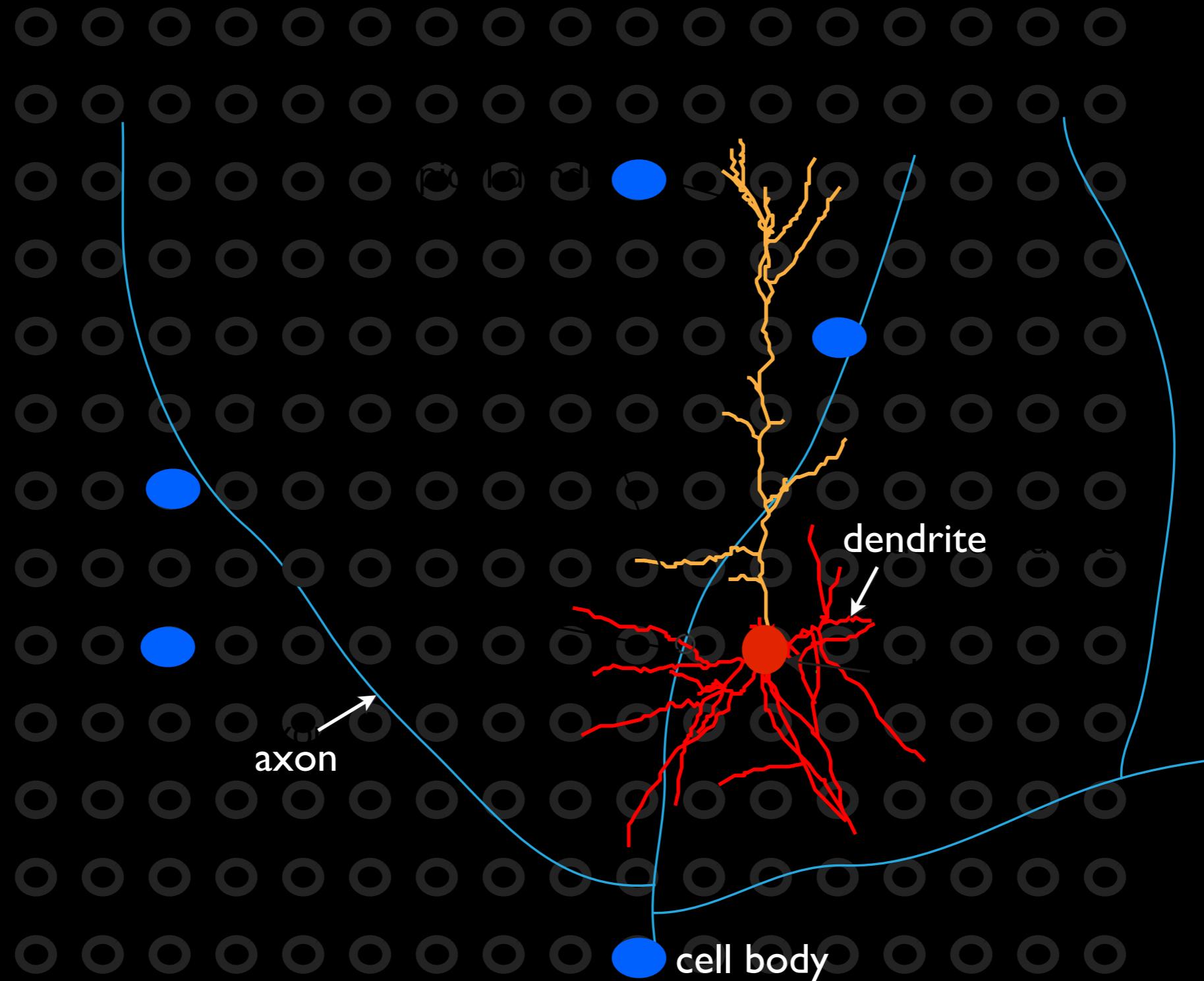
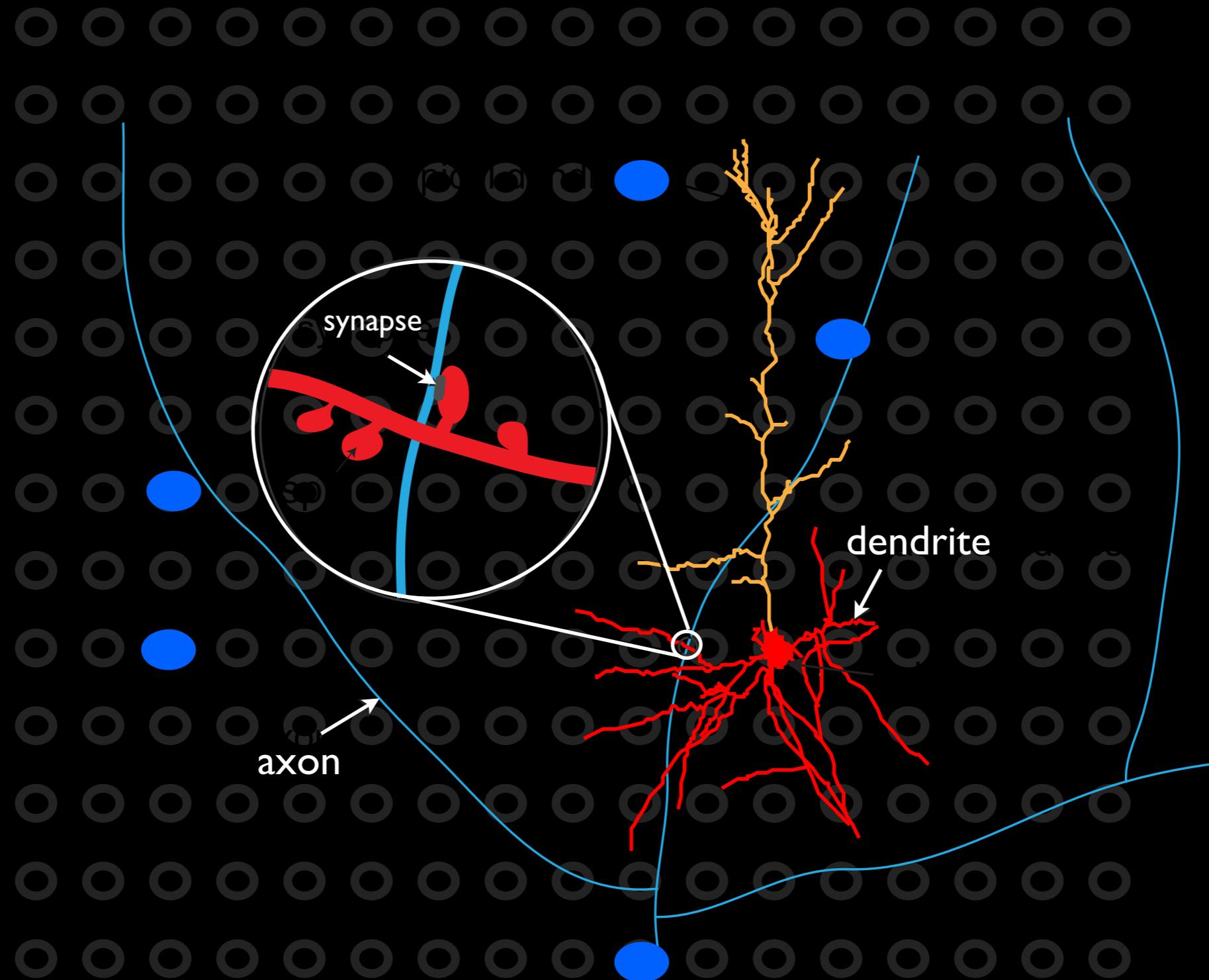


# The Basic Organization of the Brain

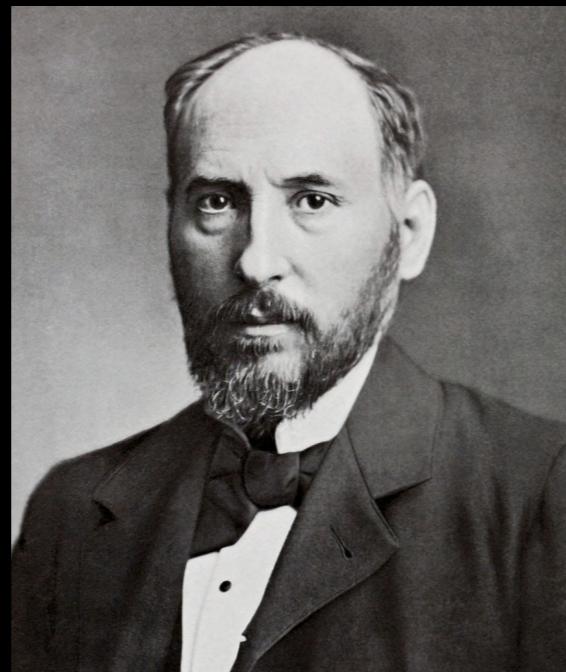
# The Neuron Doctrine



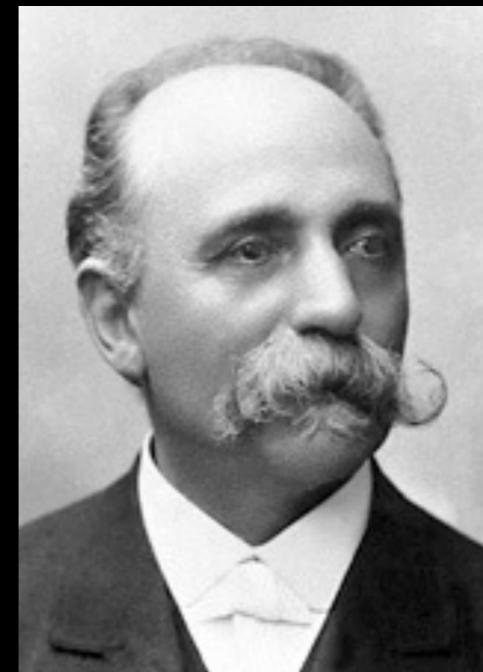




# The Debate between Cajal and Golgi

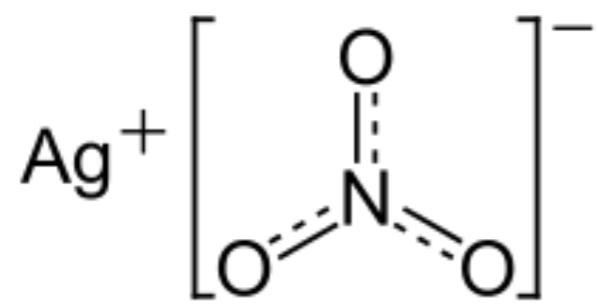


Ramon y Cajal

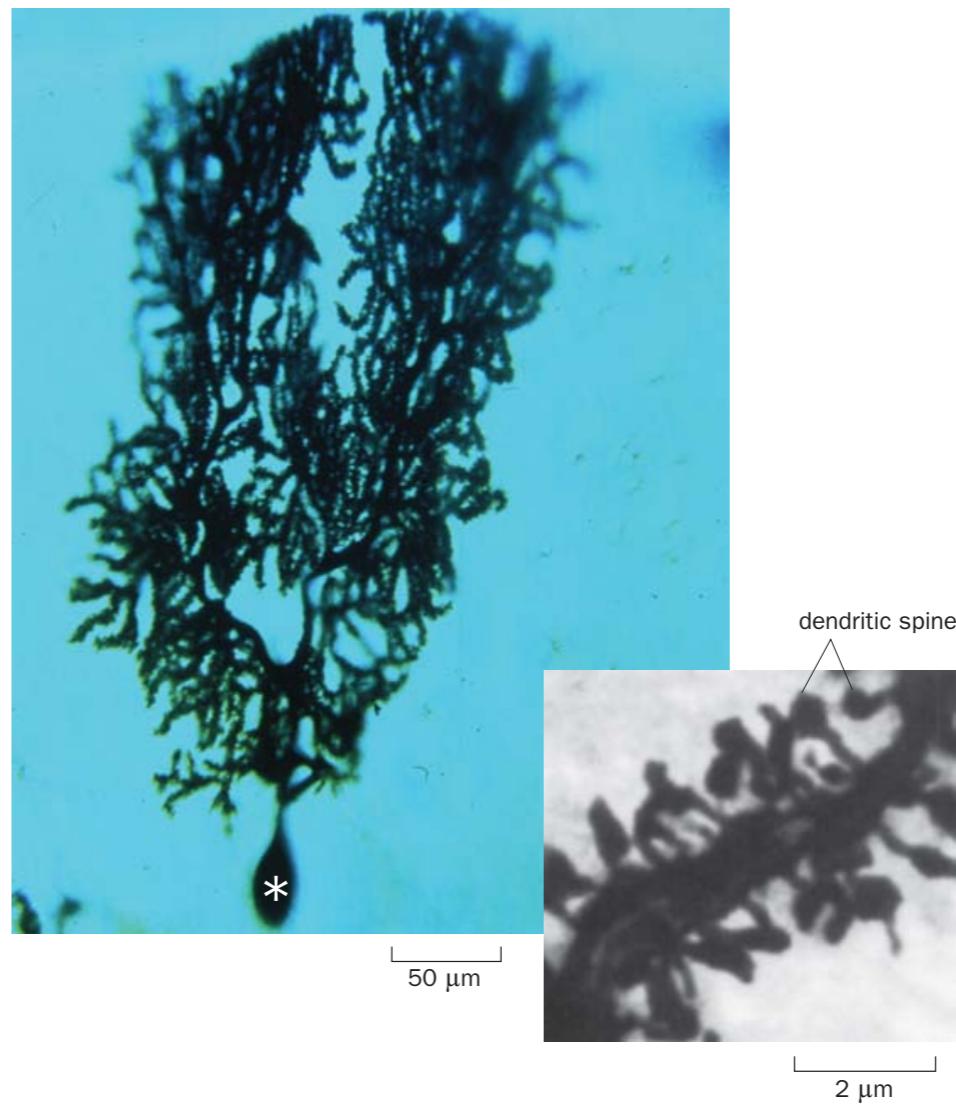


Camillo Golgi

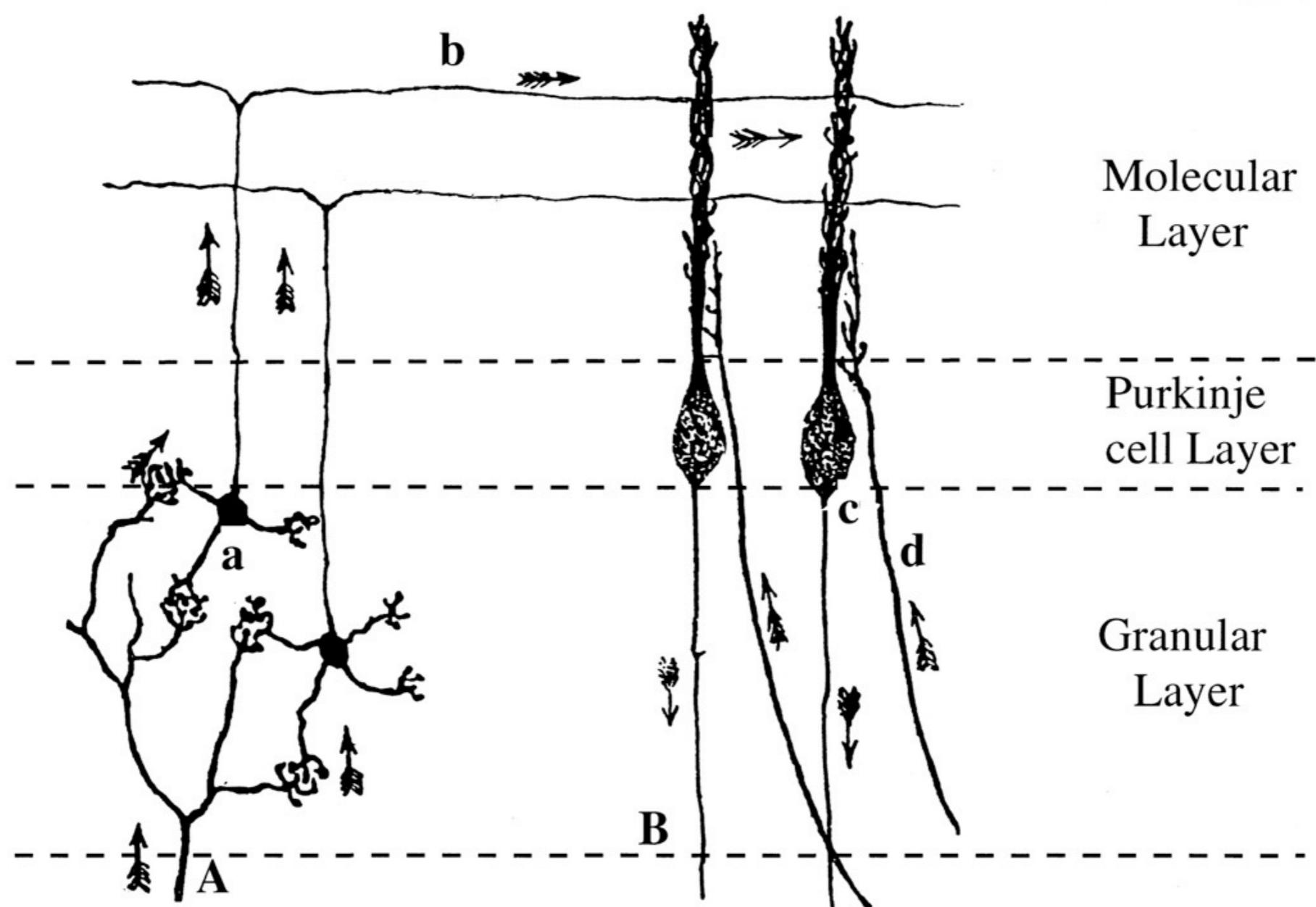
# Golgi Staining method



Silver nitrate

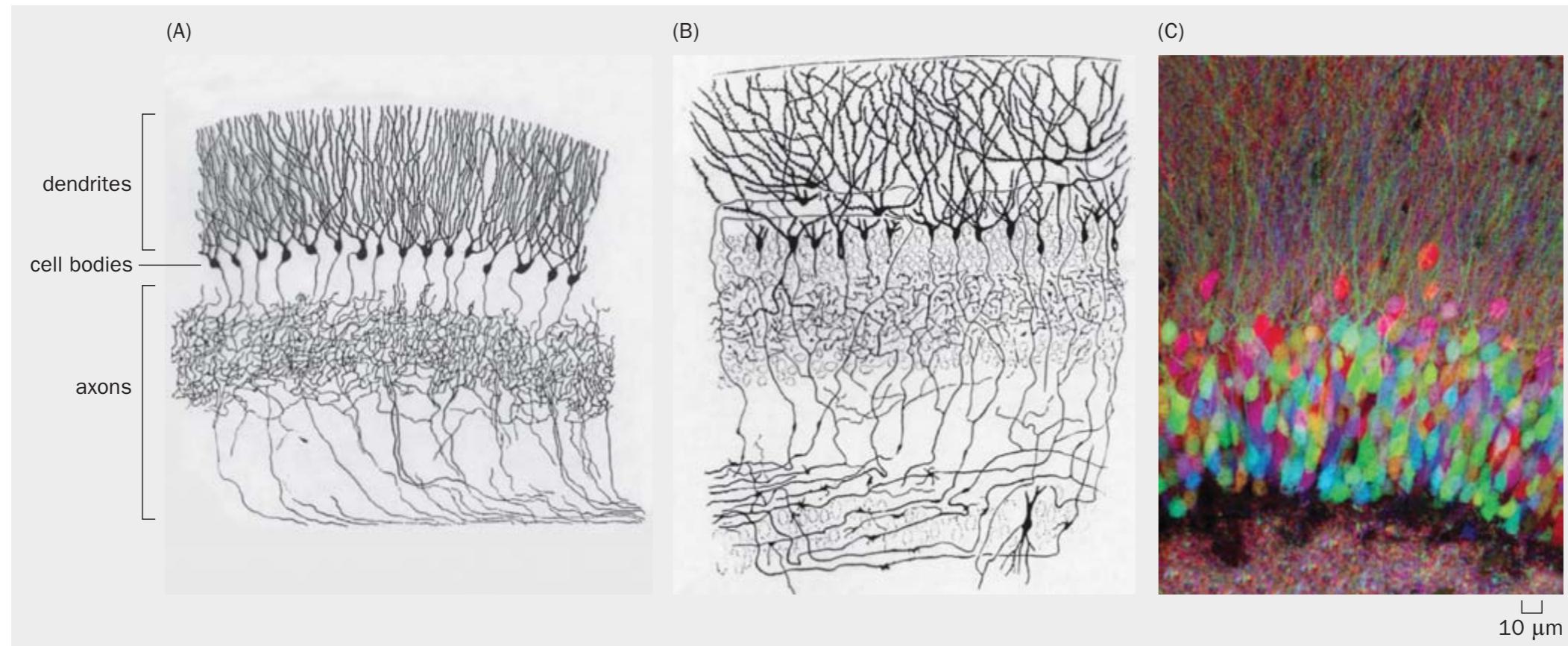


## Cerebellar cortex



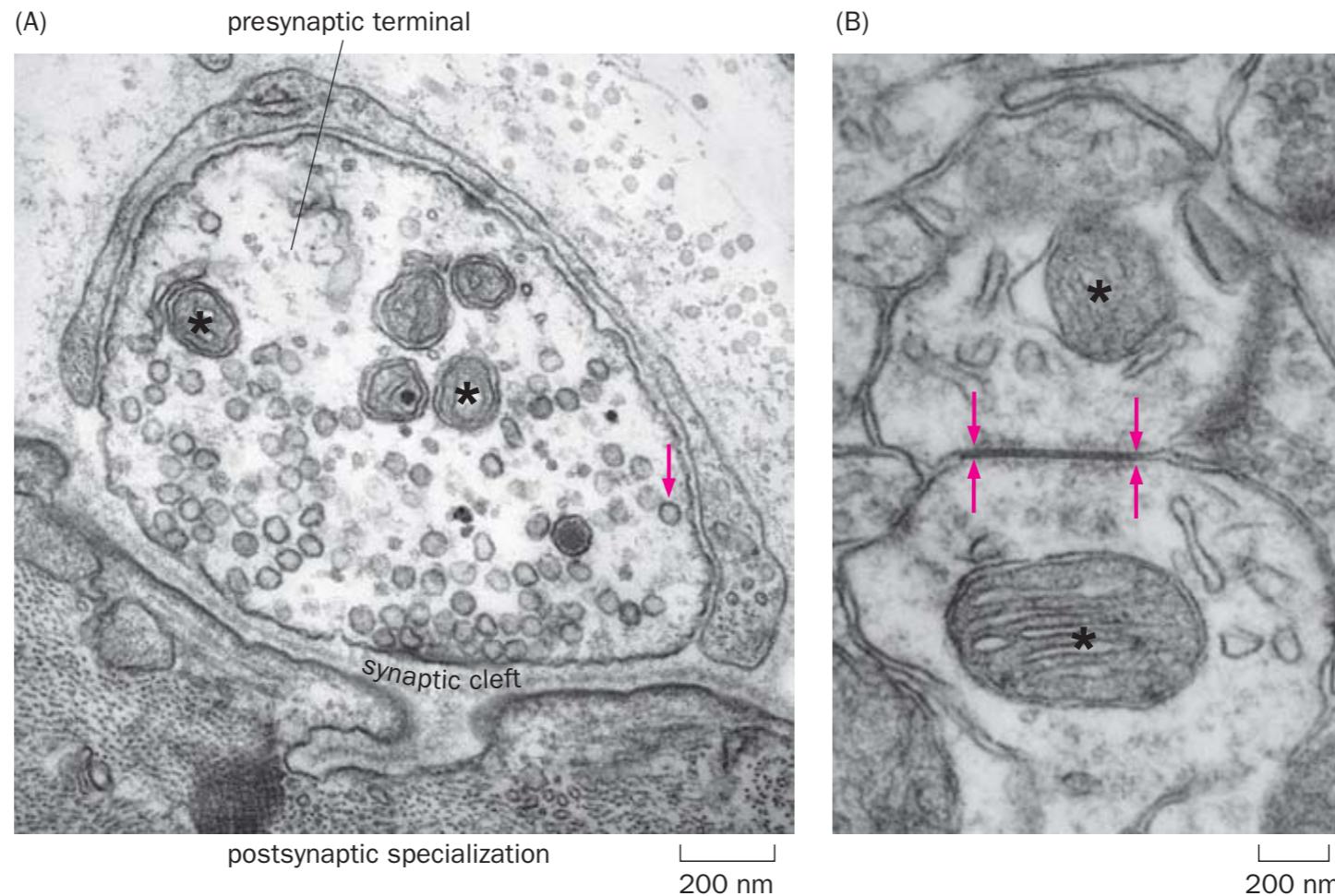
Cajal's drawing of the cerebellar cortex

# Reticular Theory vs Neuron Doctrine



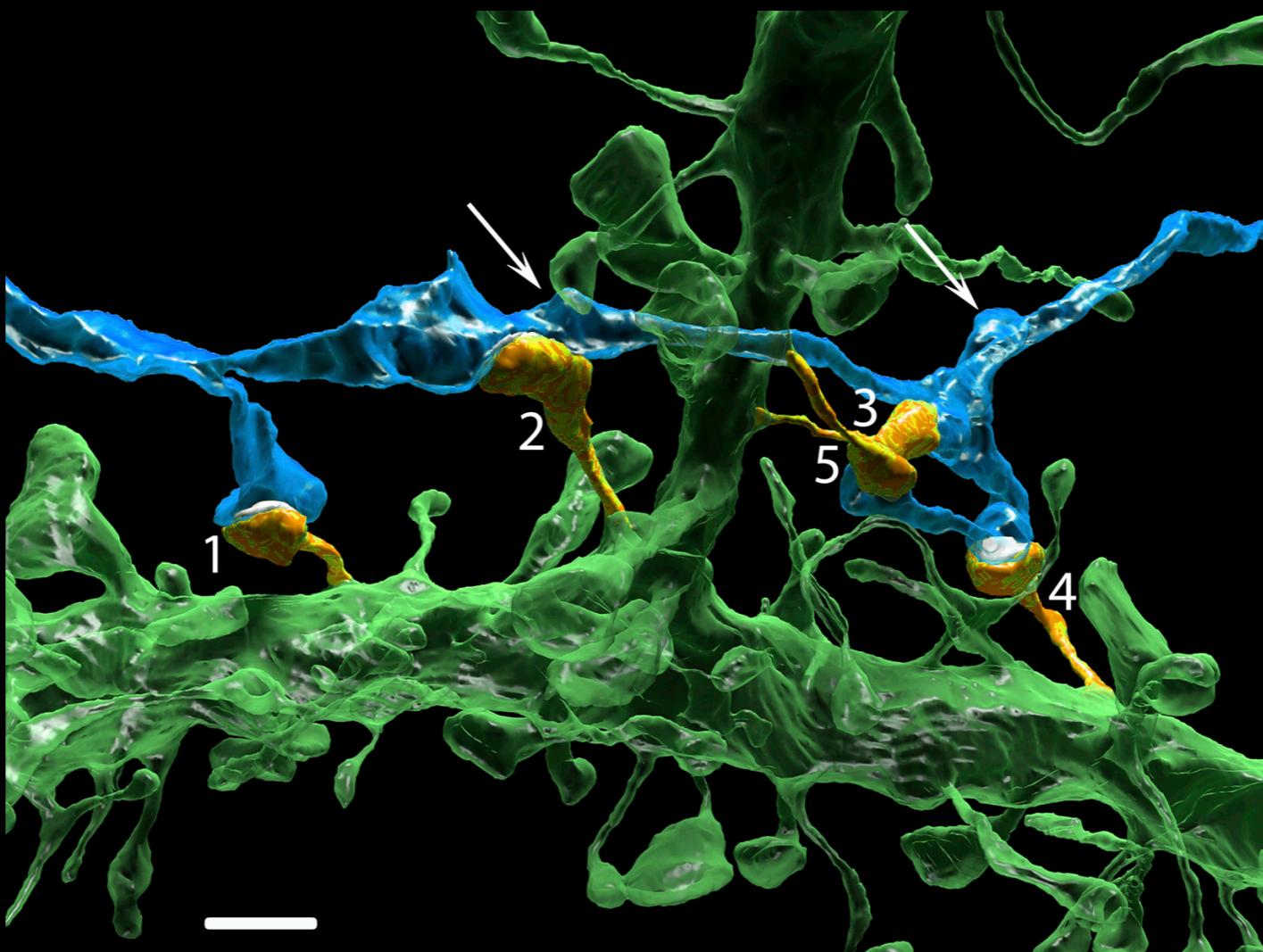
# Synapse

# How neurons communicate with each other?

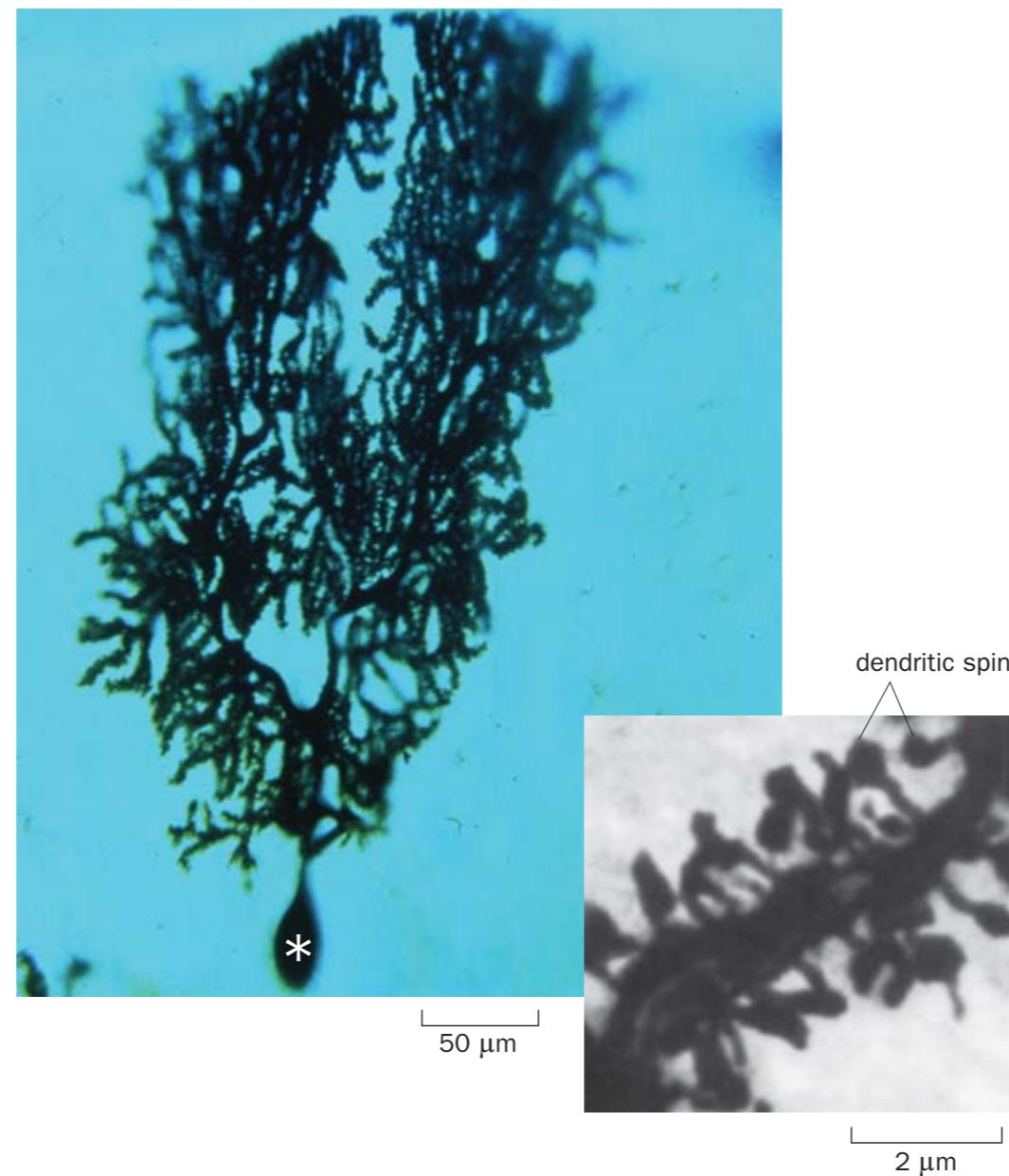


## Chemical and electrical synapses

# Synaptic Connectivity

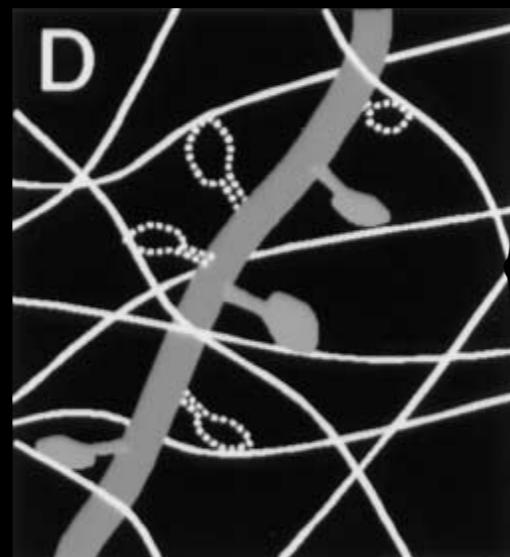
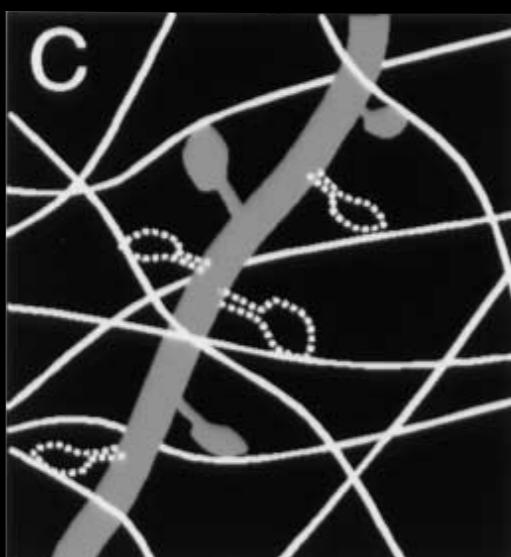
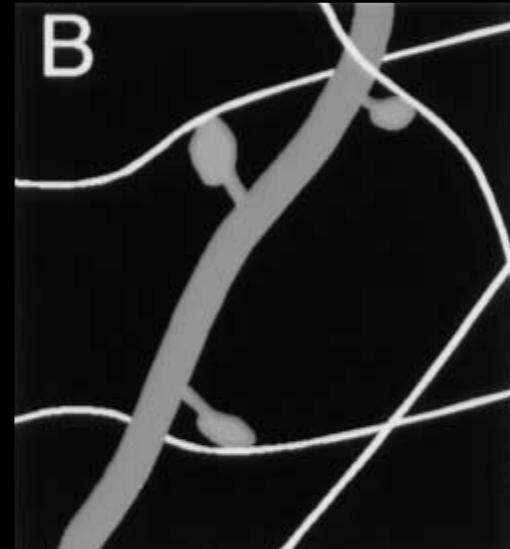
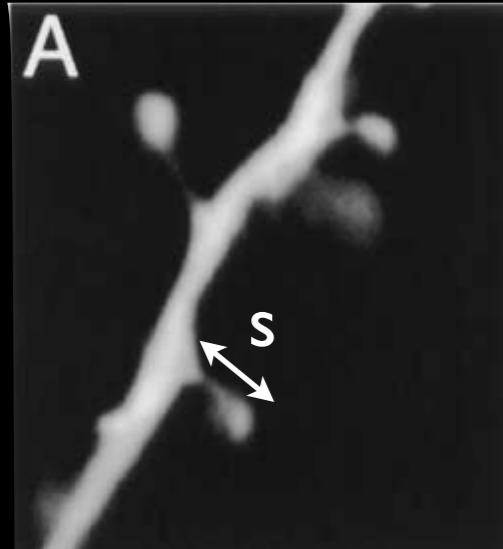


Kasthuri et. al, Cell 2015



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

# Structural Plasticity of Synaptic Connectivity



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

s: spine length

$L_d$ : total dendritic length per neuron

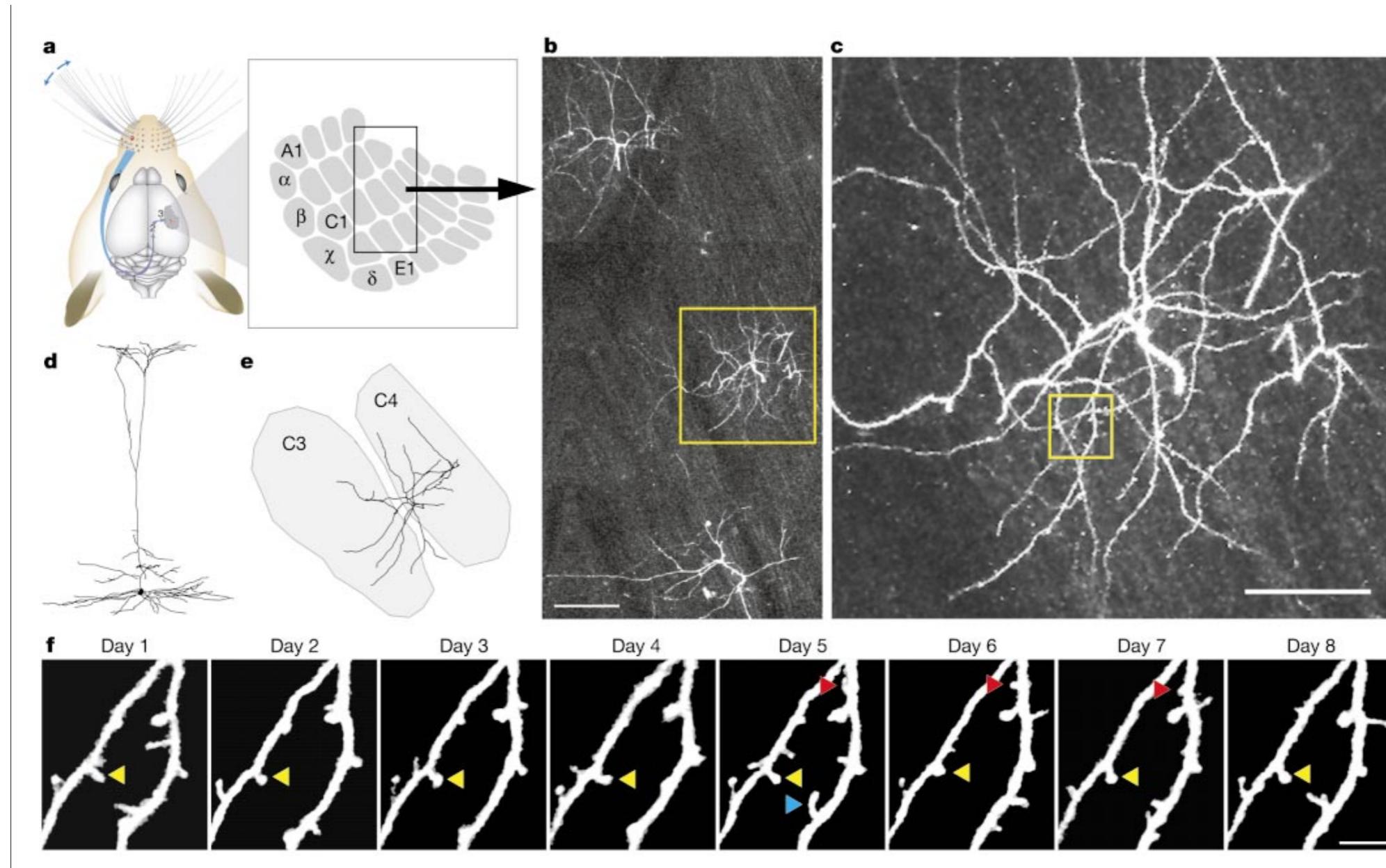
b: inter-bouton distance

n: neuronal density

filling fraction = 3/7

Stepanyants et. al., *Neuron* 2001

# Structural Plasticity of Synaptic Connectivity



Trachtenberg et, al. *Nature* 2002

# Why do we need a brain?

**My brain is my second favorite organ.**

**Woody Allen**

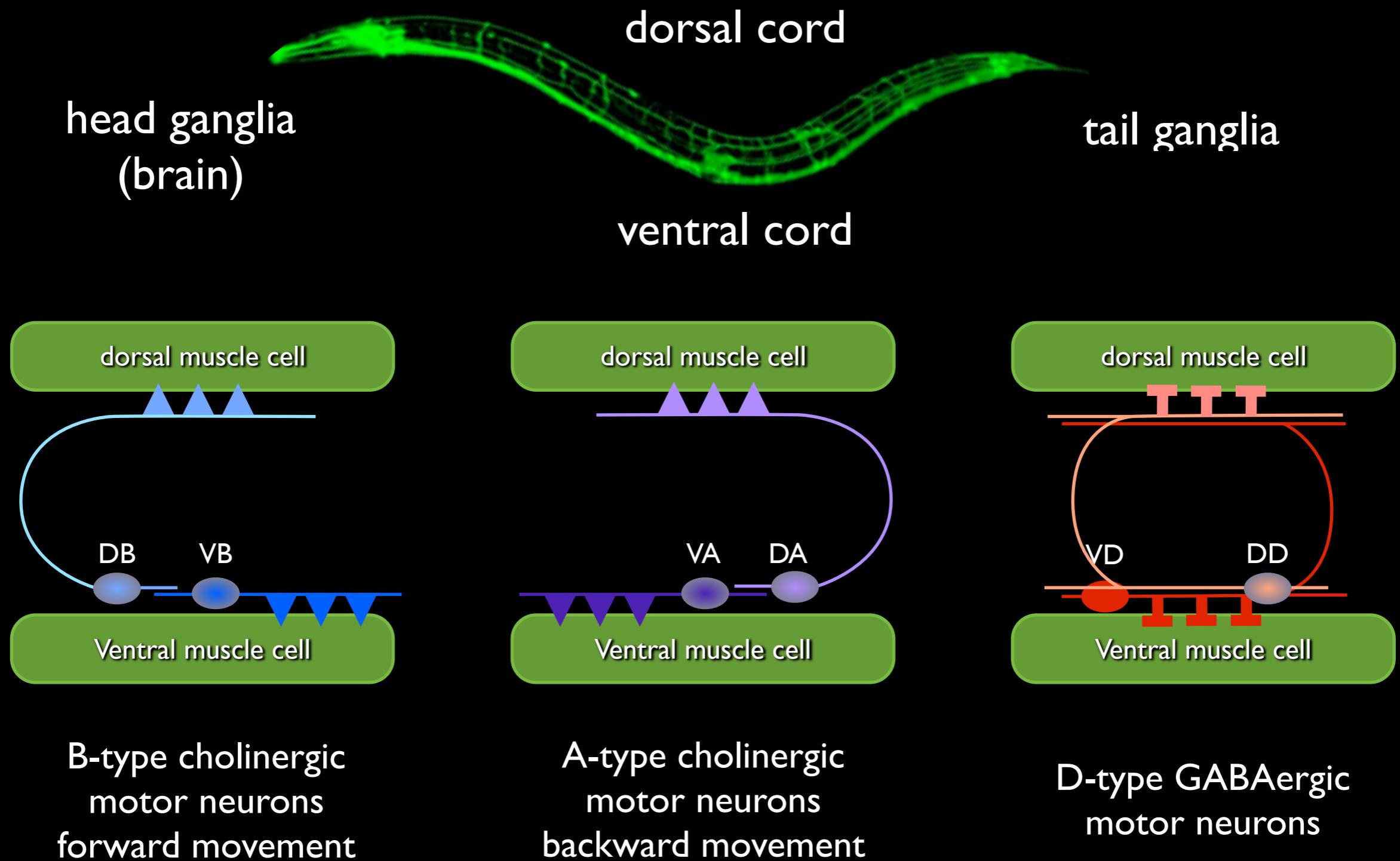
*Caenorhabditis elegans*

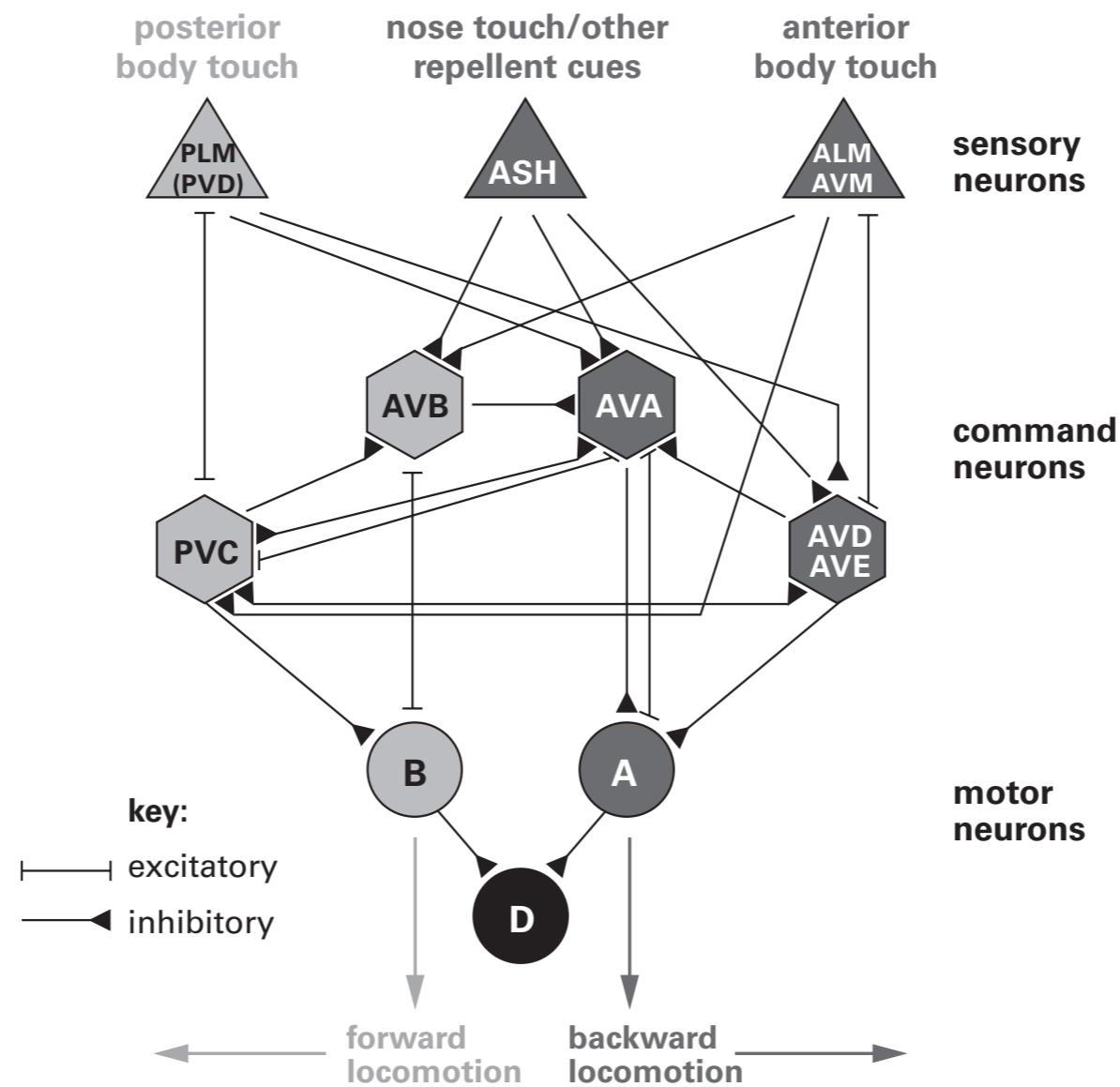


0.1 mm

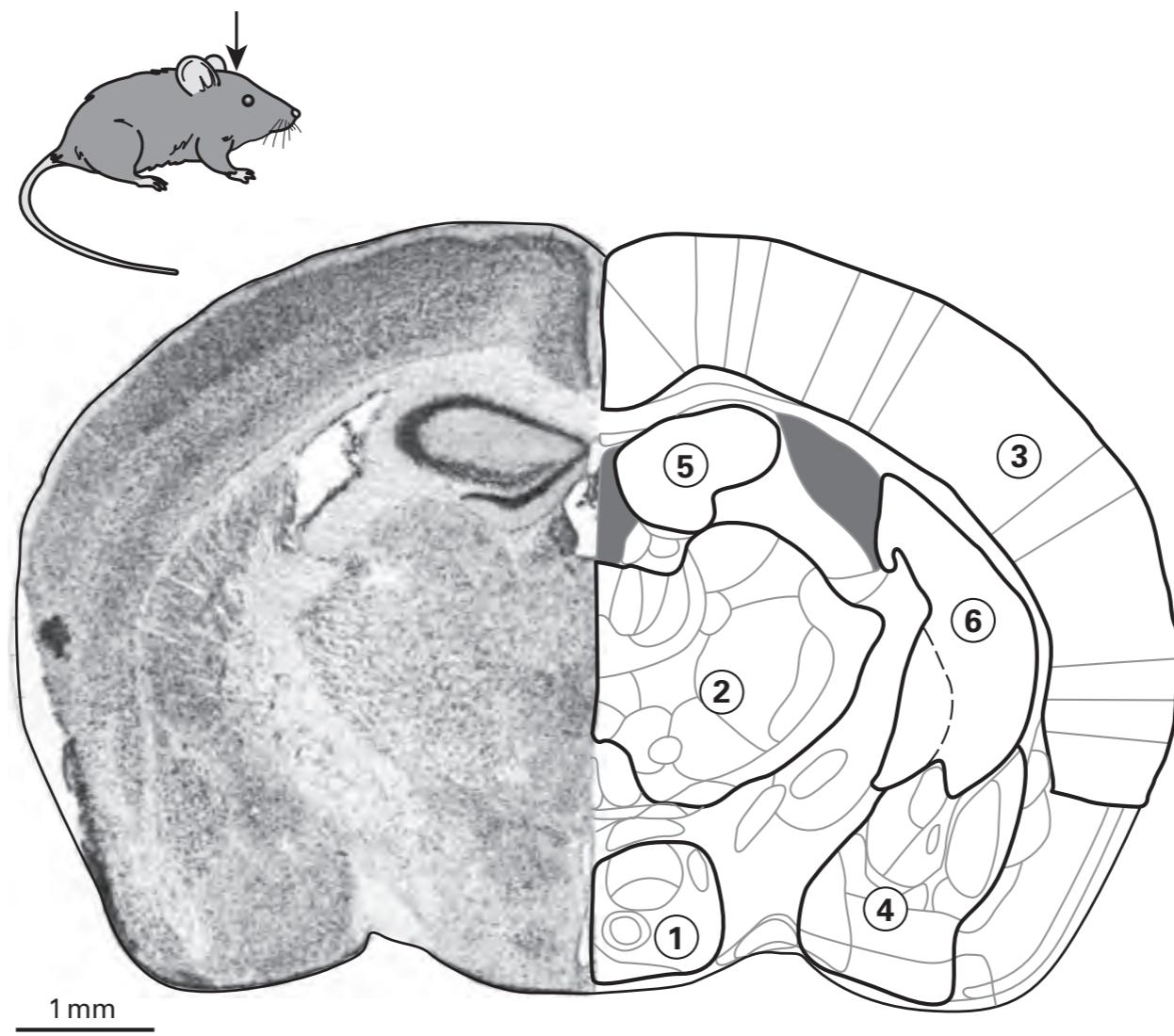
300 neurons

# Anatomy of *C. elegans* motor circuit

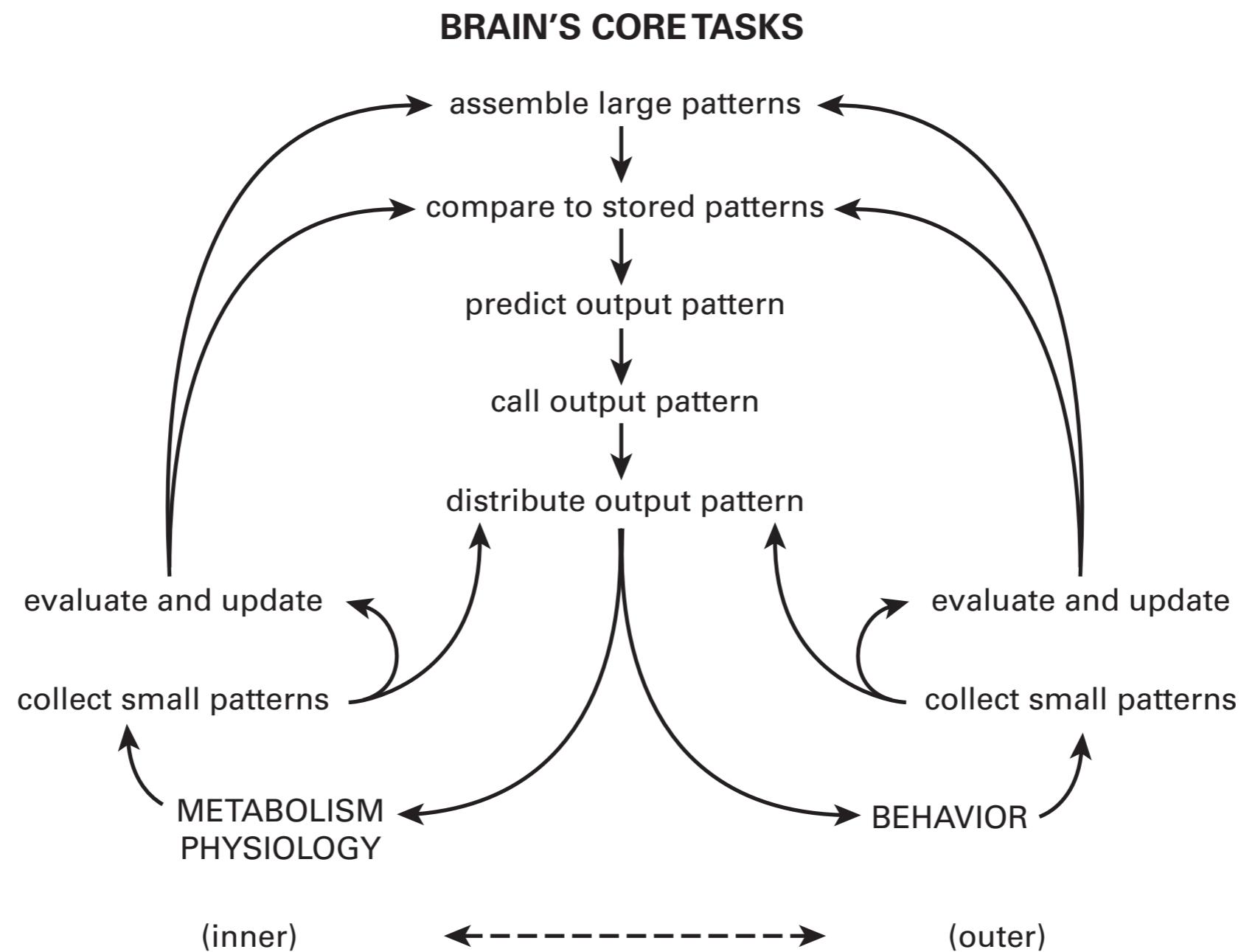




# Why a bigger brain?



- ① Generate patterns for wireless signaling and appetitive behaviors.
- ② “Preprocessing” to shape signals for higher processing.
- ③ High-level processing: assemble larger patterns, choose behaviors.
- ④ “Tag” high-level patterns for emotional significance.
- ⑤ Store and recall.
- ⑥ Evaluate reward predictions.



# Principles of neural design

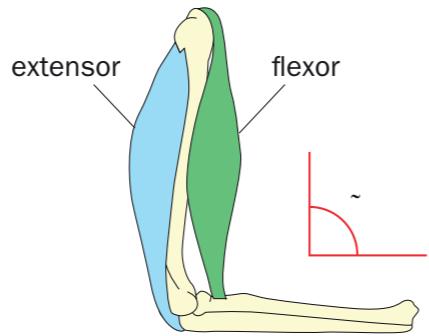
## 1. Minimize wire

*Compute locally if you can.*

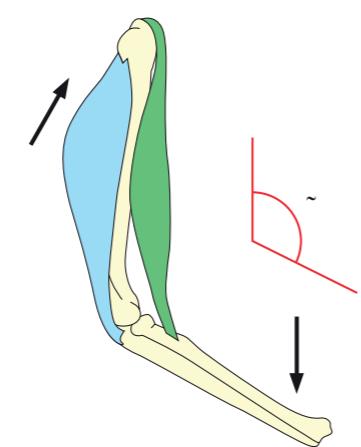
*Neurons that fire together should locate together.*

cortical map and column

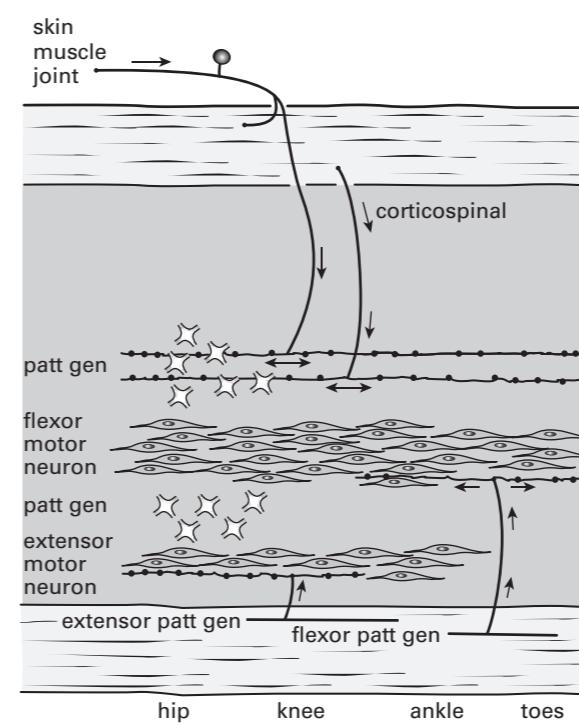
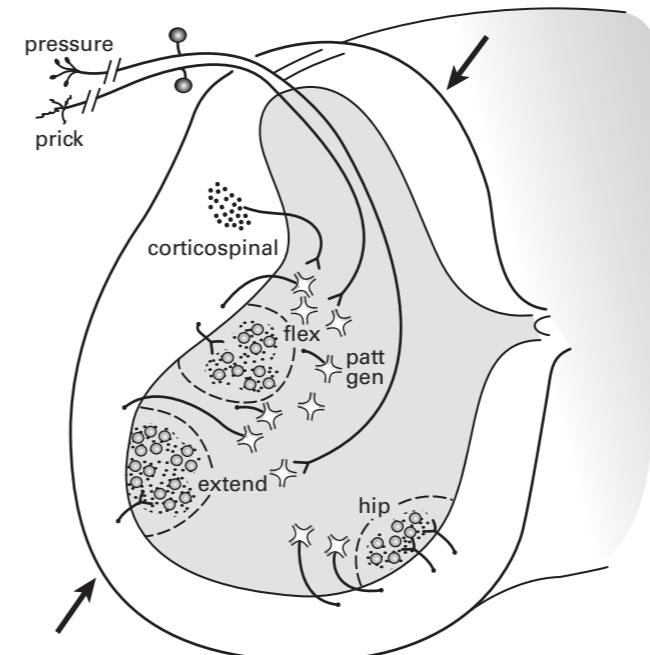
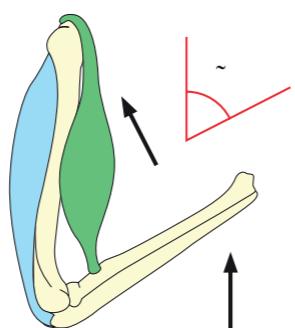
# Efficient wiring for integrated movements



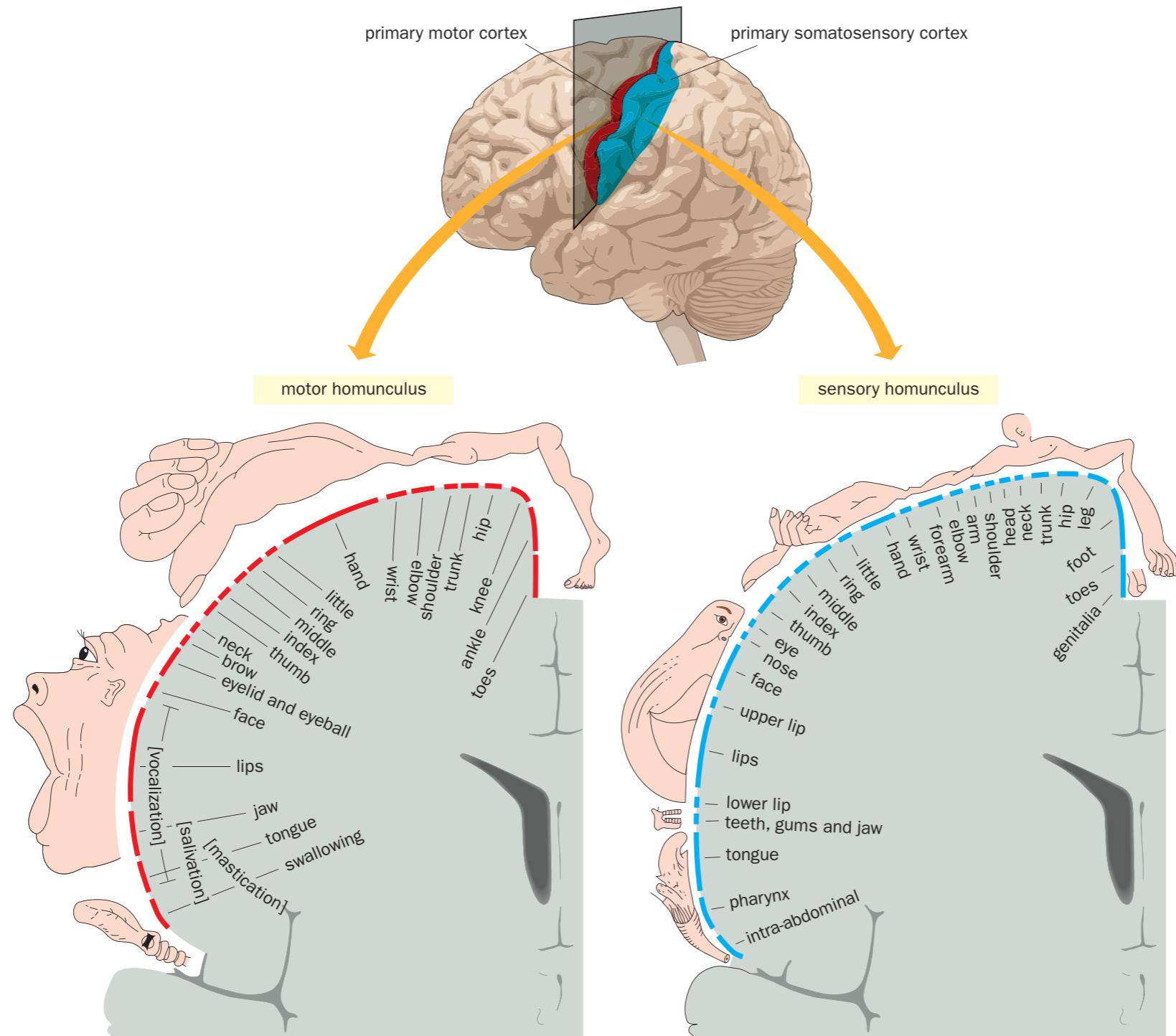
extensor contraction



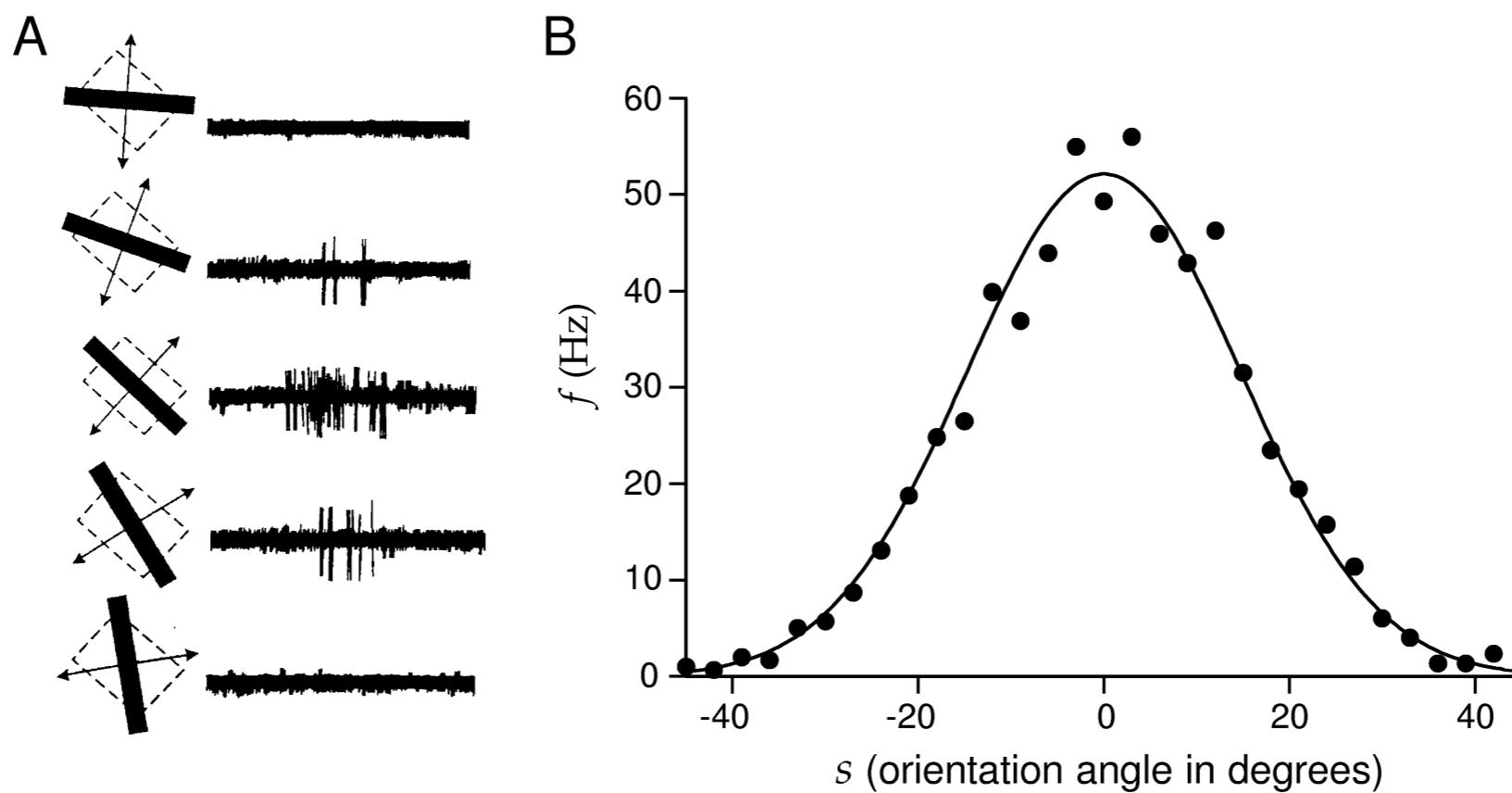
flexor contraction



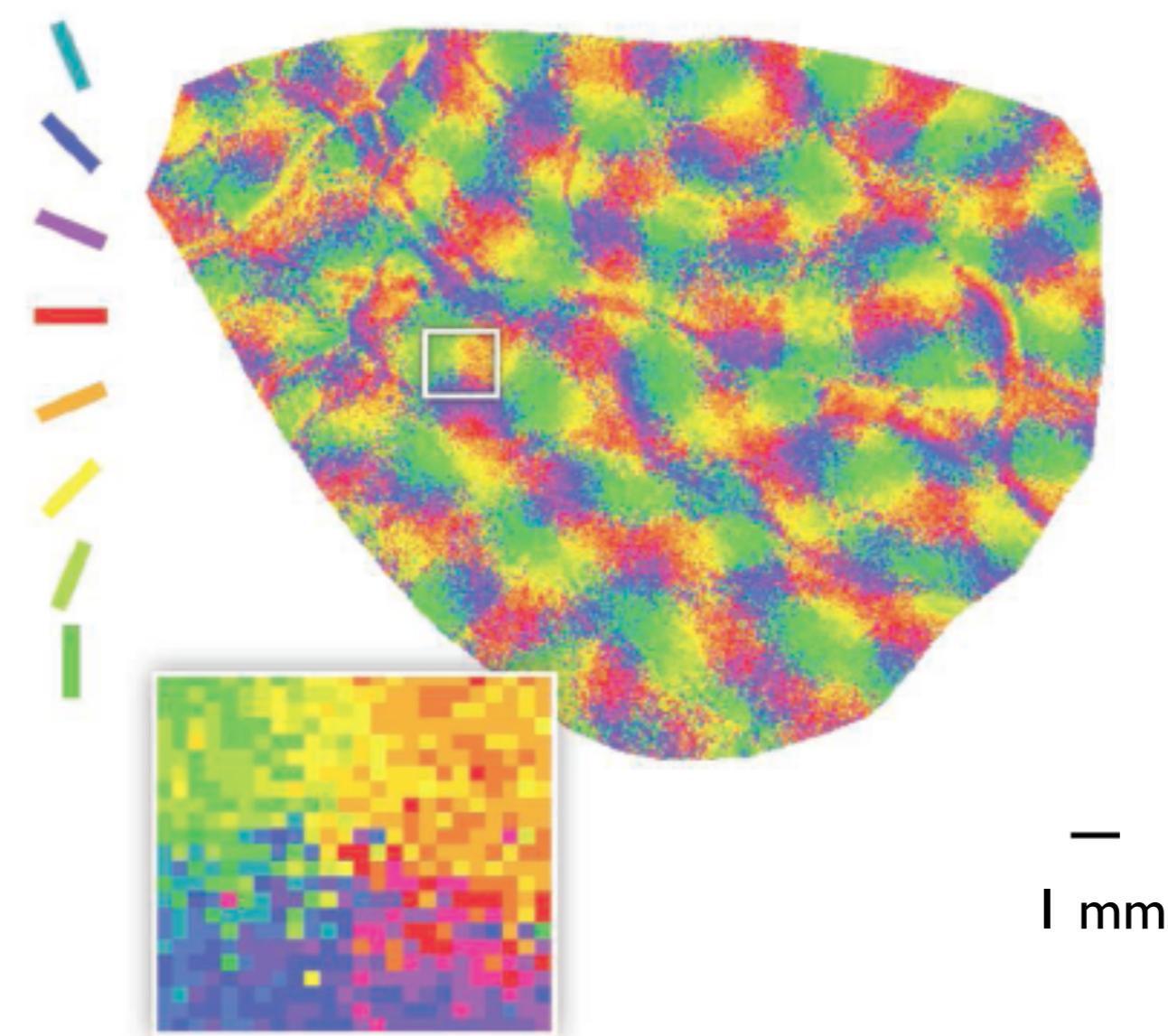
# The cortex uses maps to organize information



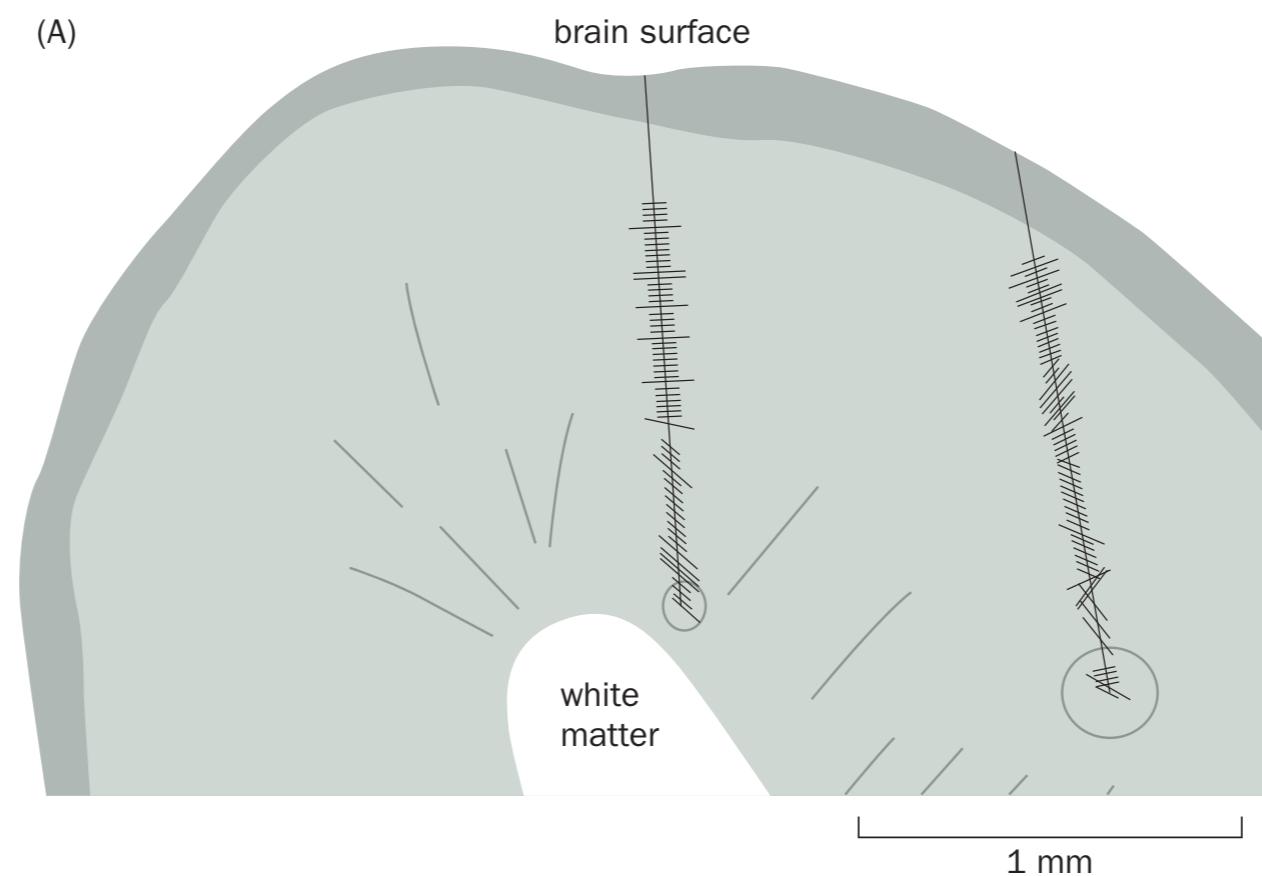
# The cortex uses maps to organize information



# The cortex uses maps to organize information

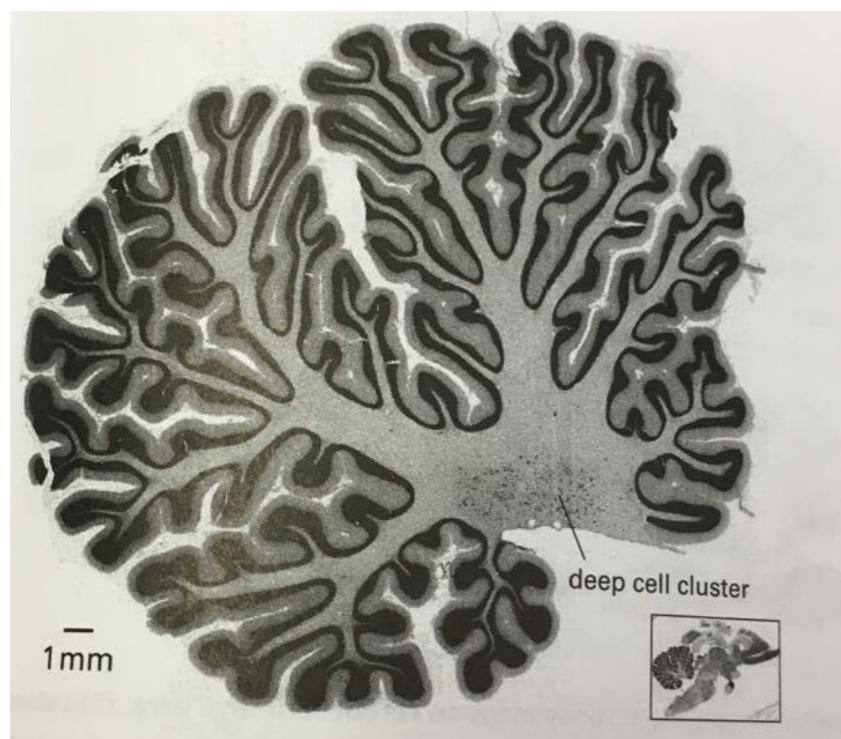


# The Cortical Column

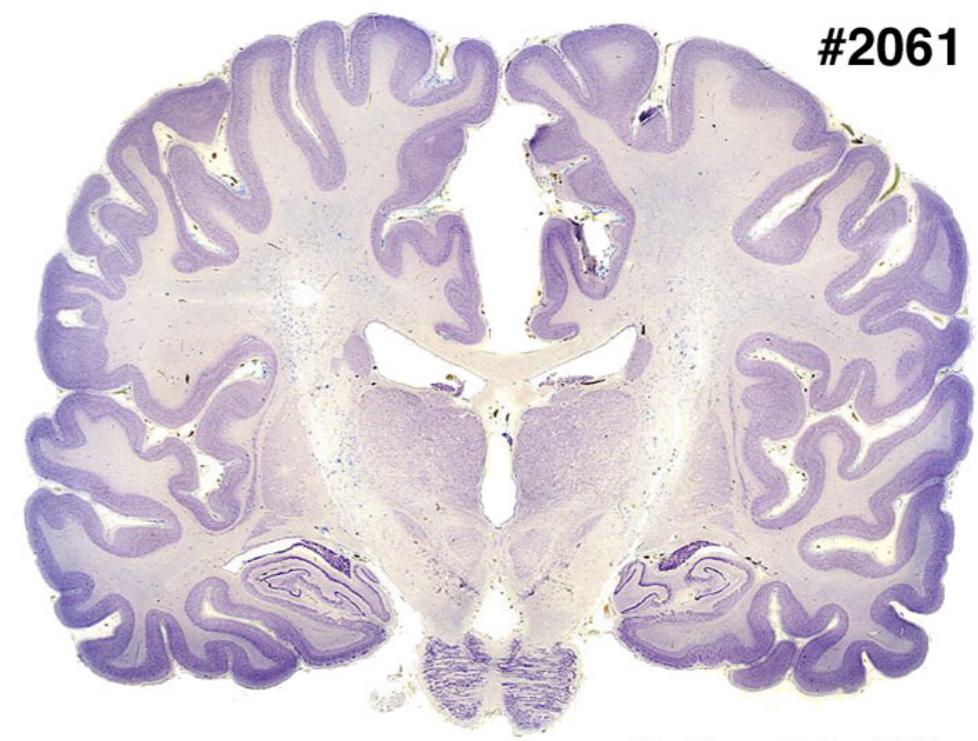


Hubel DH & Wiesel TN (1962) J Physiology 160: 106-154

cerebral cortex vs. cerebellar cortex



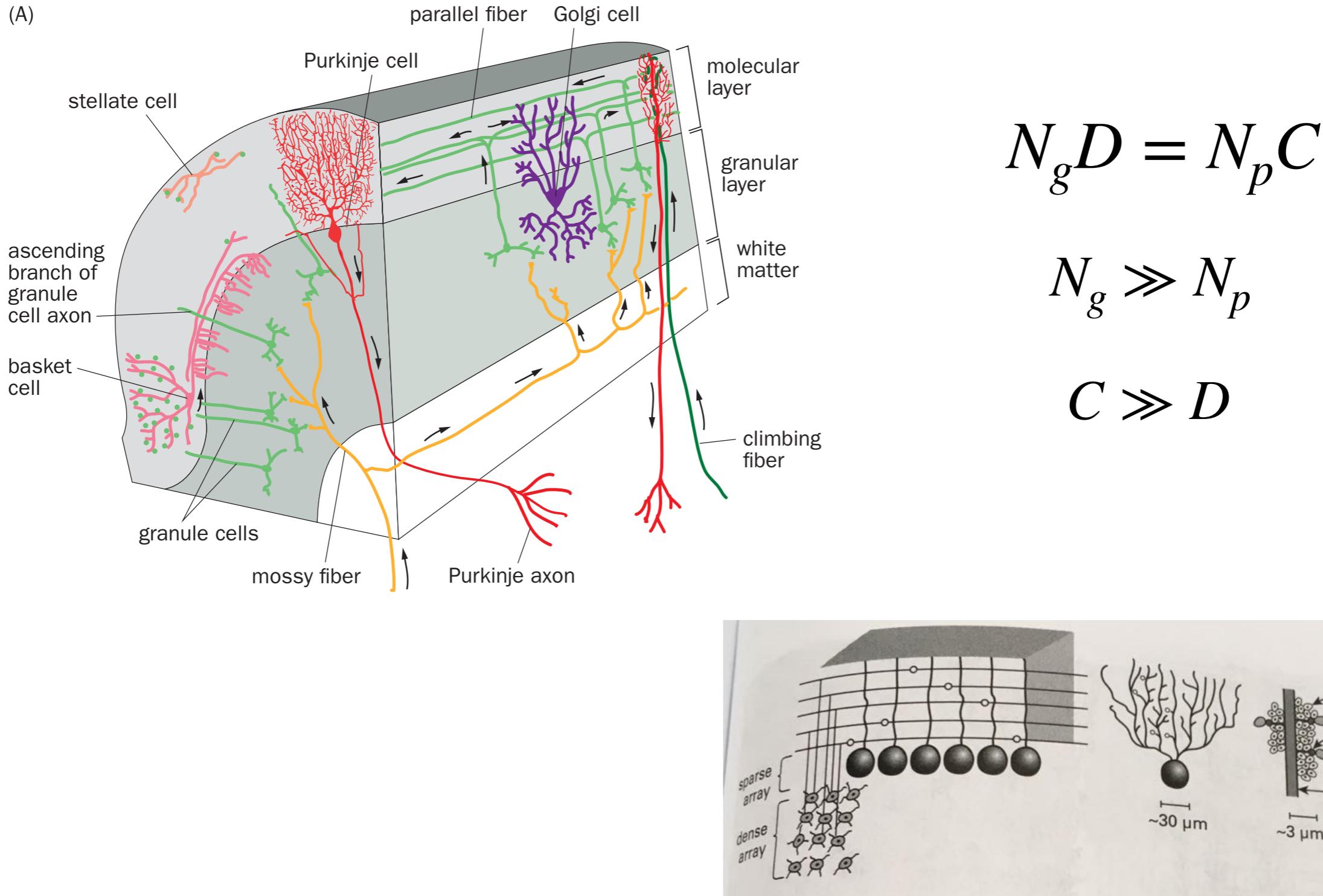
cerebellum



cerebral cortex

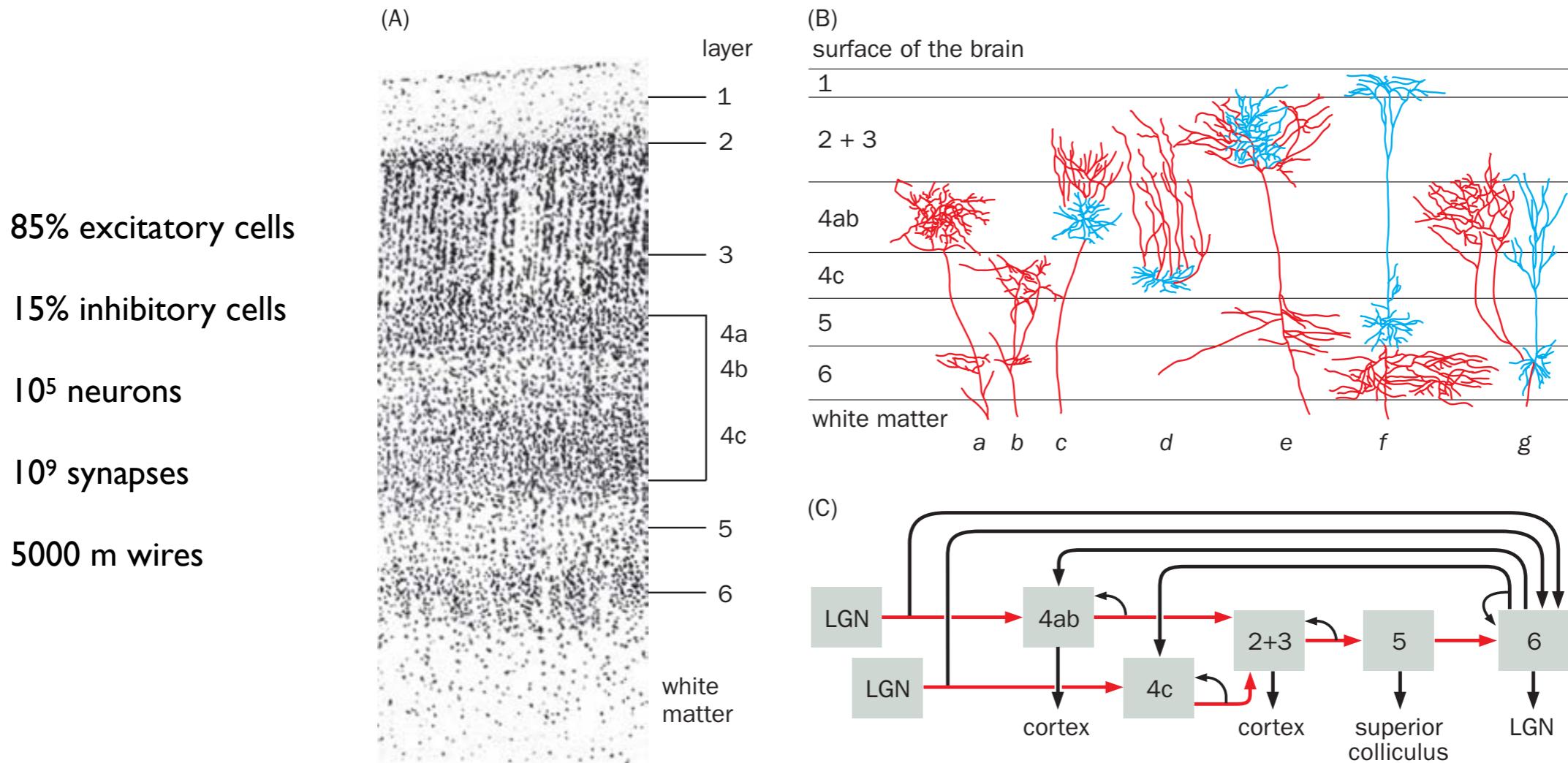
**Connecting dense array to sparse array with  
extreme convergence and divergence**

# The organization cerebellar cortex



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

# The organization of the cortical column



**Why do we need axons and dendrites?**



# **Single Cortical Neurons as Deep Artificial Neural Networks**

<sup>1</sup>David Beniaguev, <sup>1,2</sup>Idan Segev and <sup>1,2</sup>Michael London

<sup>1</sup>The Edmond and Lily Safra Center for Brain Sciences and <sup>2</sup>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<sup>1</sup> and Konrad Kording<sup>2</sup>

<sup>1</sup>Department of Neuroscience, University of Pennsylvania

<sup>2</sup>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

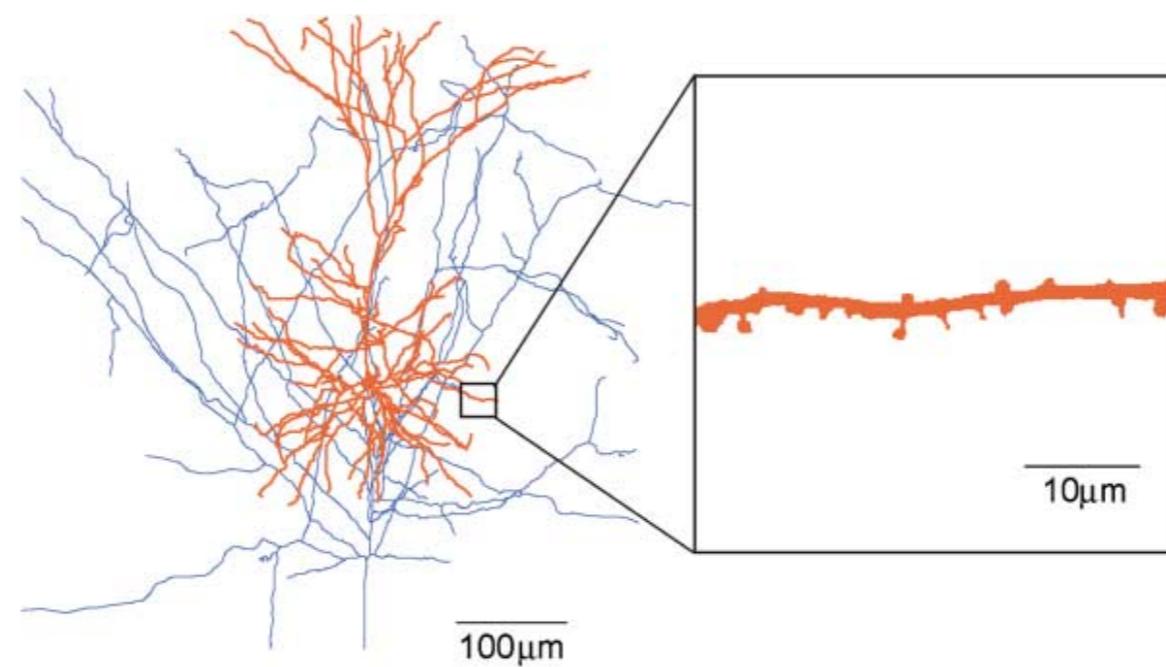
如无必要，勿增实体。简单有效原理。《箴言书注》：切勿浪费较多东西去做，用较少的东西，同样可以做好的事情。

# Wiring Optimization of Neural Circuit

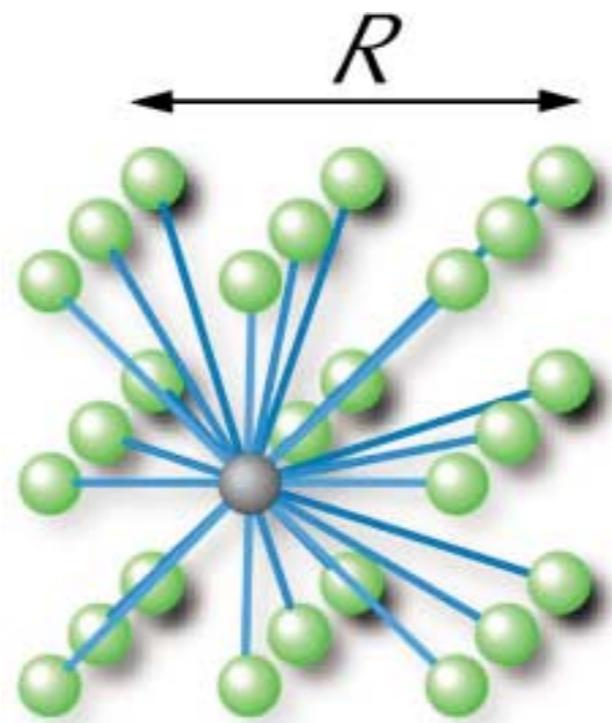
“After the many shapes assumed by neurons, we are now in a position to ask whether this diversity ... has been left to chance and is insignificant, or whether it is tightly regulated and provides an advantage to the organism. ... we realized that all of the various conformations of the neuron and its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

Ramon y Cajal

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

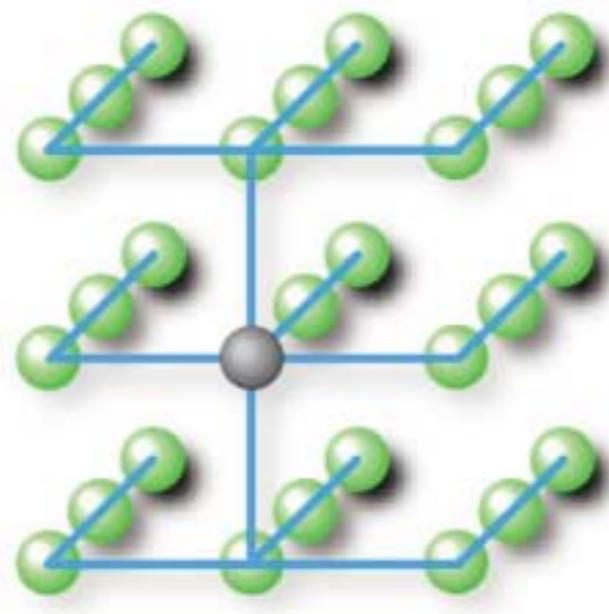


A toy problem: why do we need axons and dendrites?



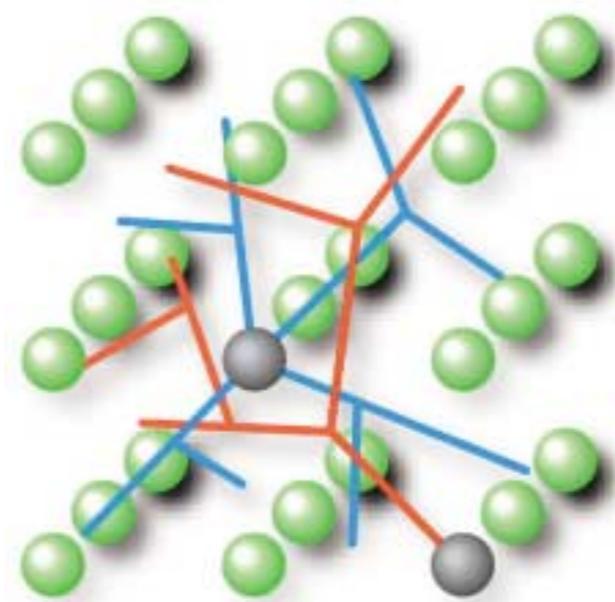
Design I

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



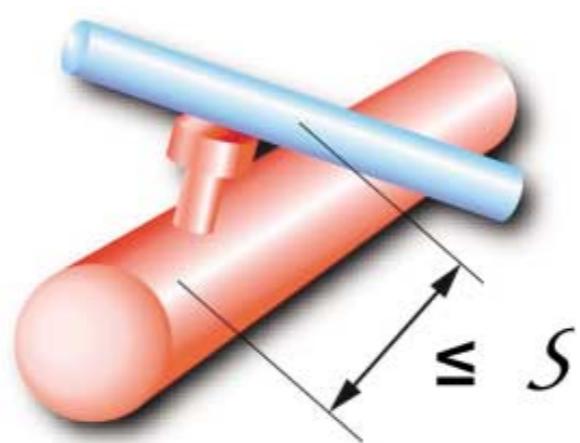
Design II

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



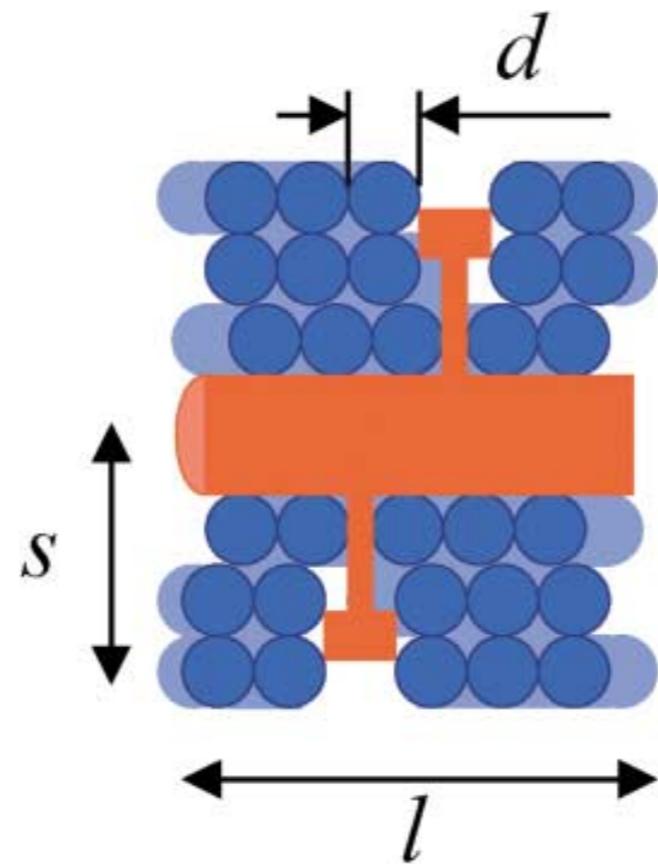
Design III

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



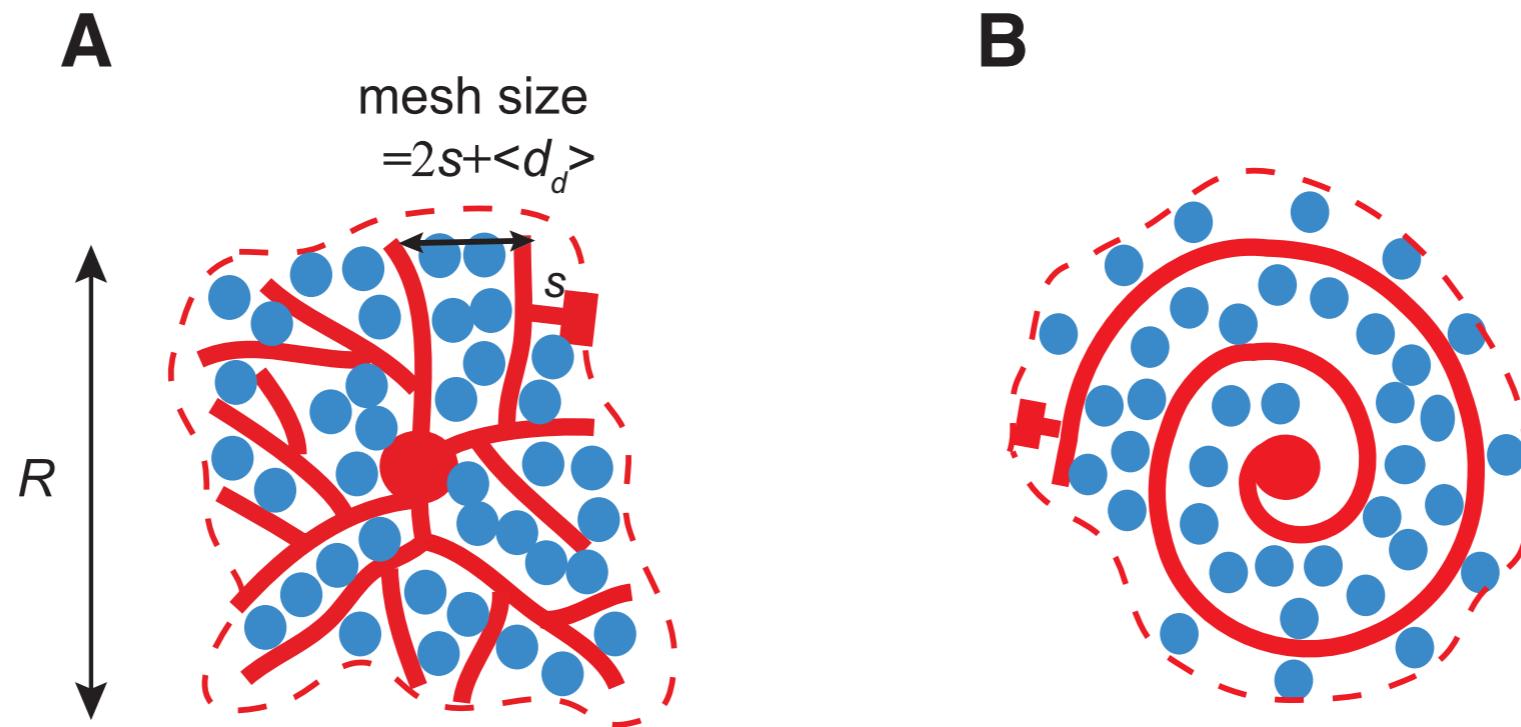
Design IV

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



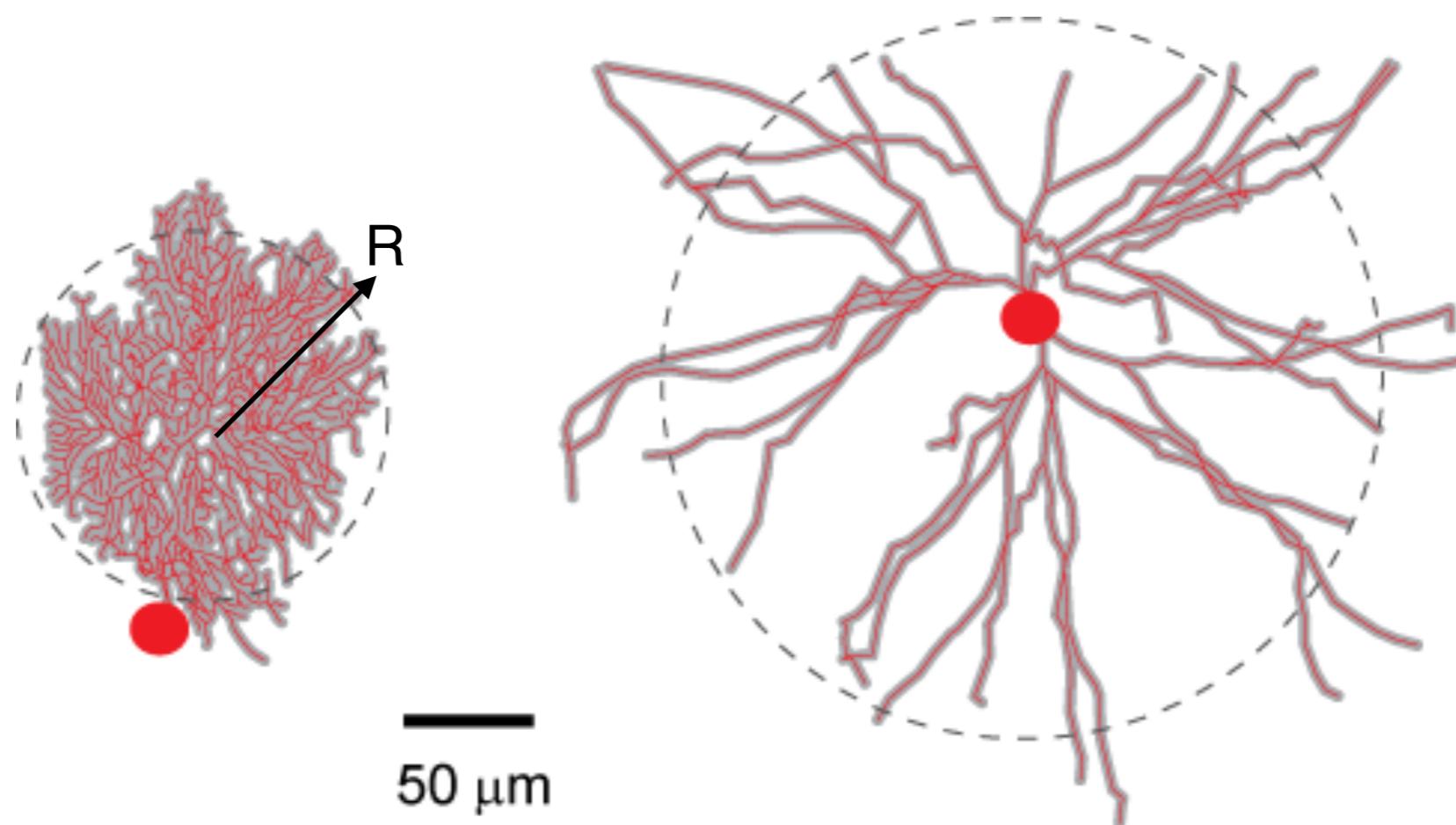
The Optimality of the design

# Why do we need branching dendrites and axons?



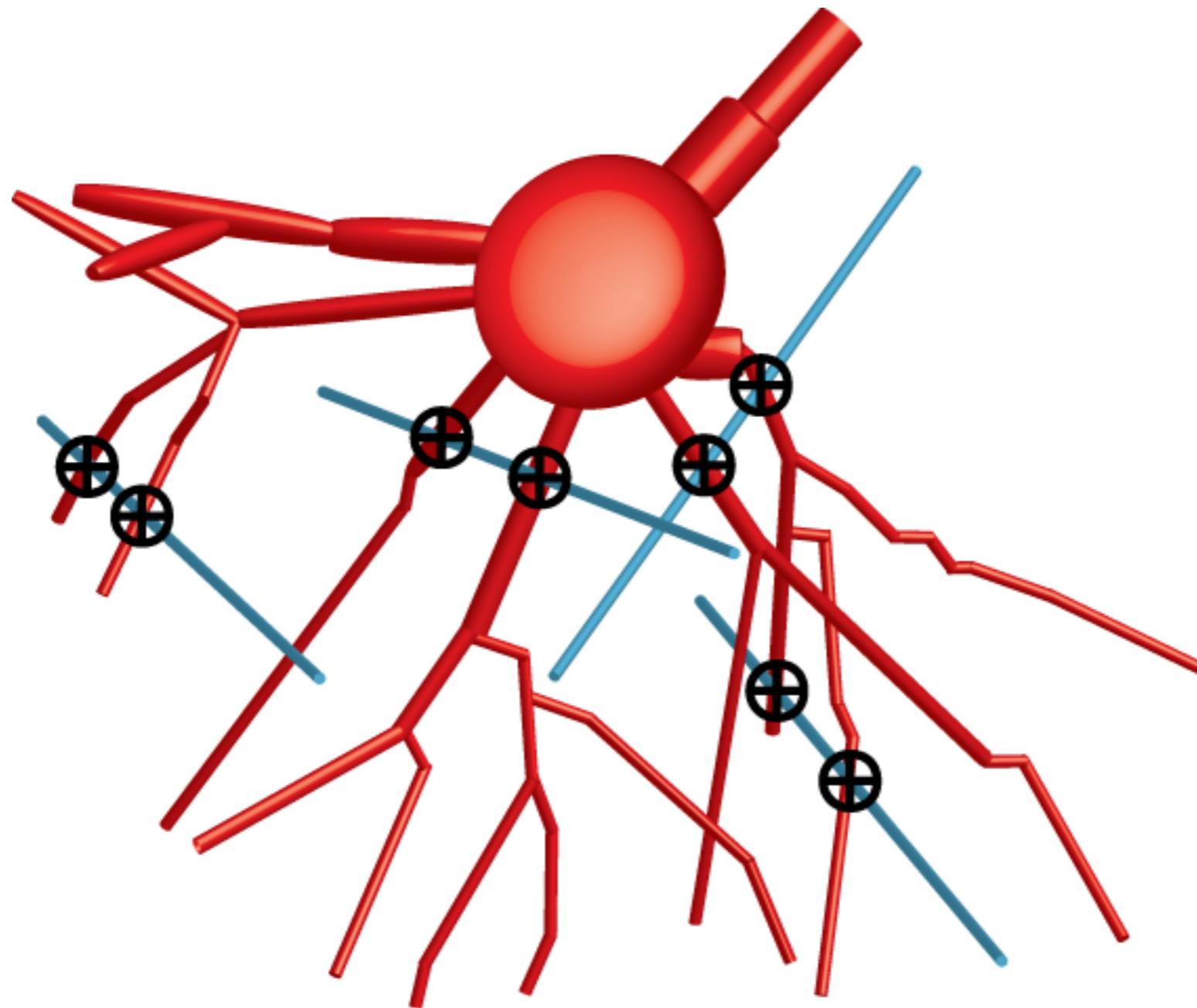
- Cost increases with the total length of a dendrite
- Cost increases with the path length from a synapse to the cell body

# Why pyramidal dendrites appear much sparser than Purkinje dendrites?

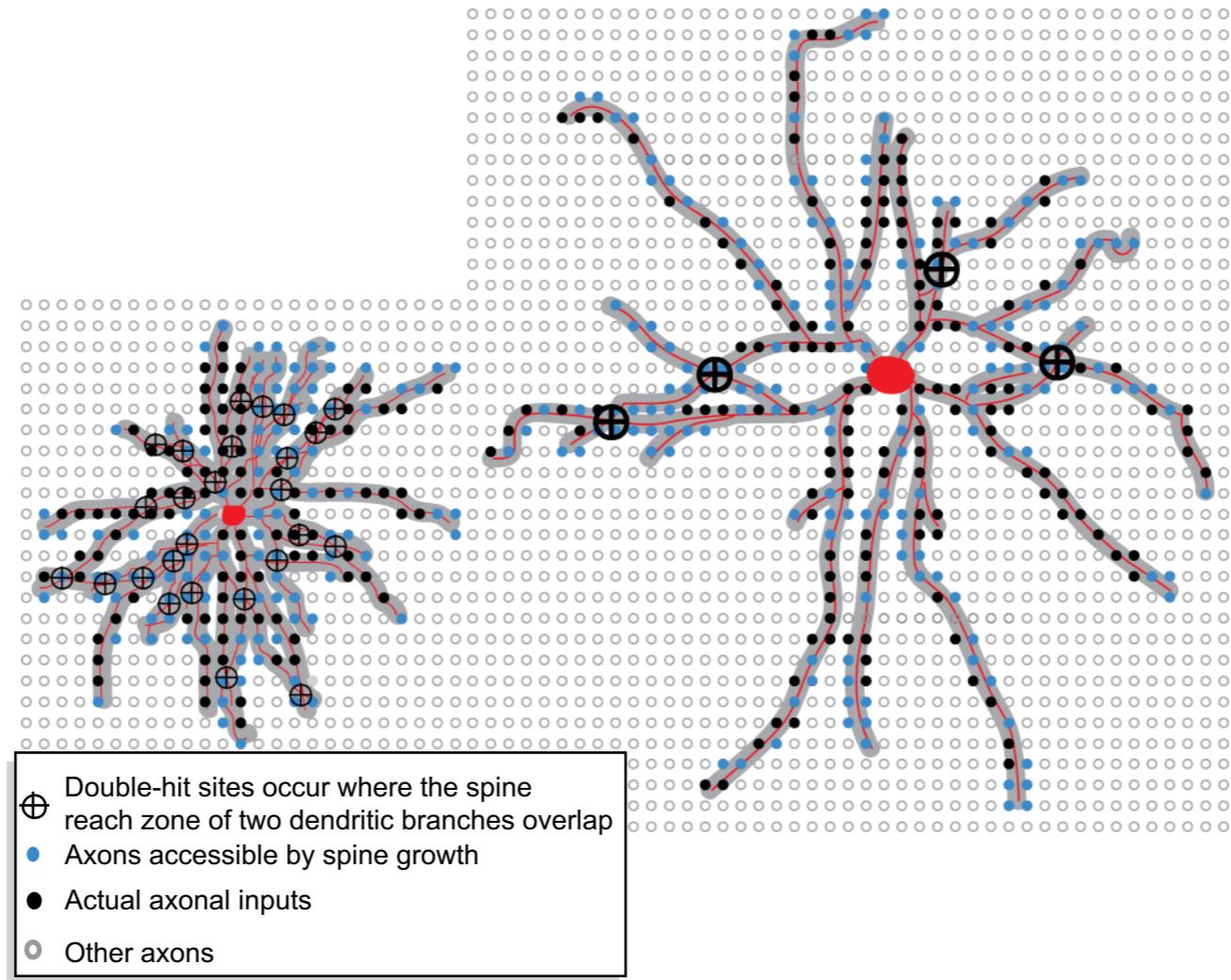


Wen et. al., PNAS 2009

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.*

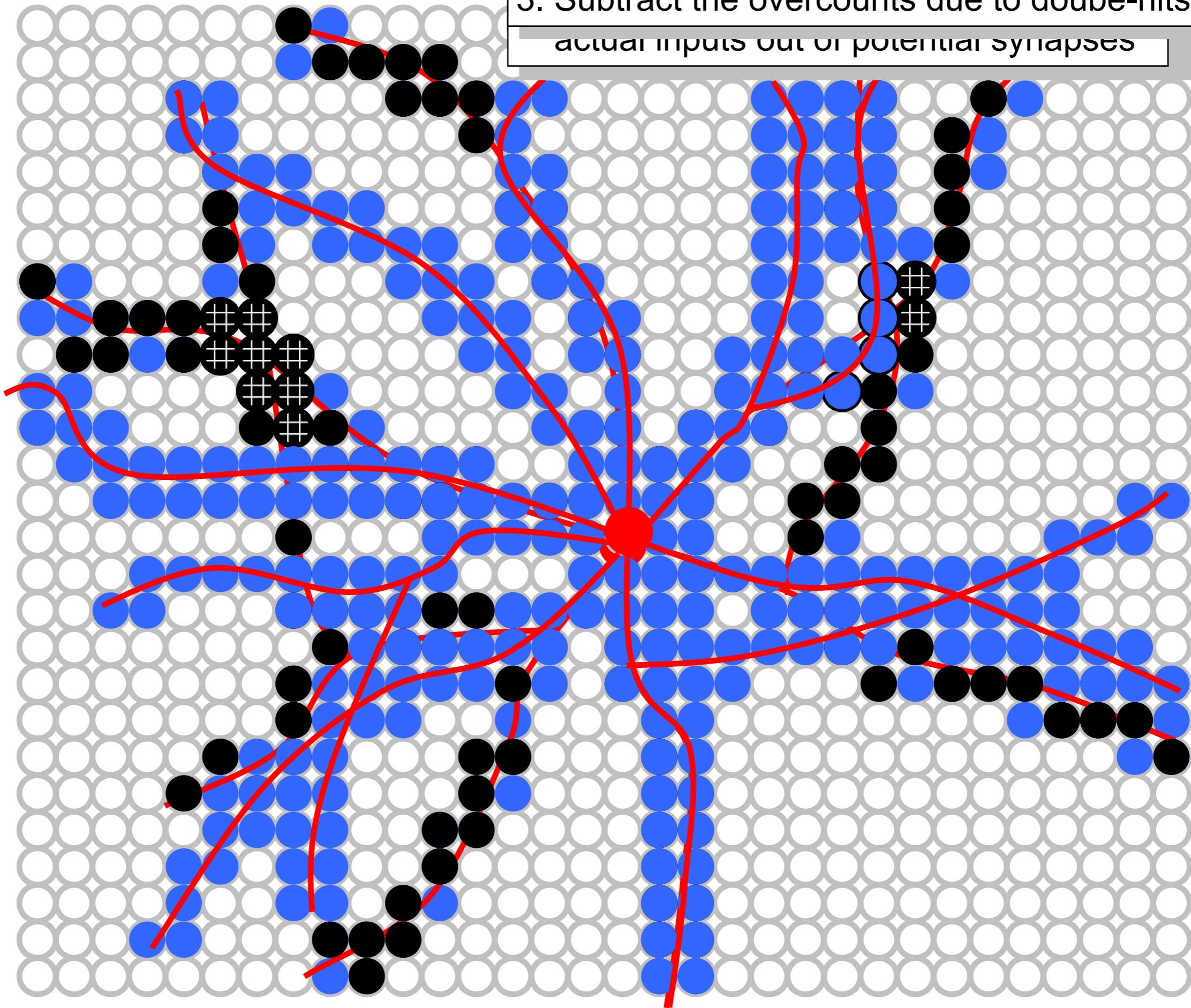


# Why access a large number of axons?

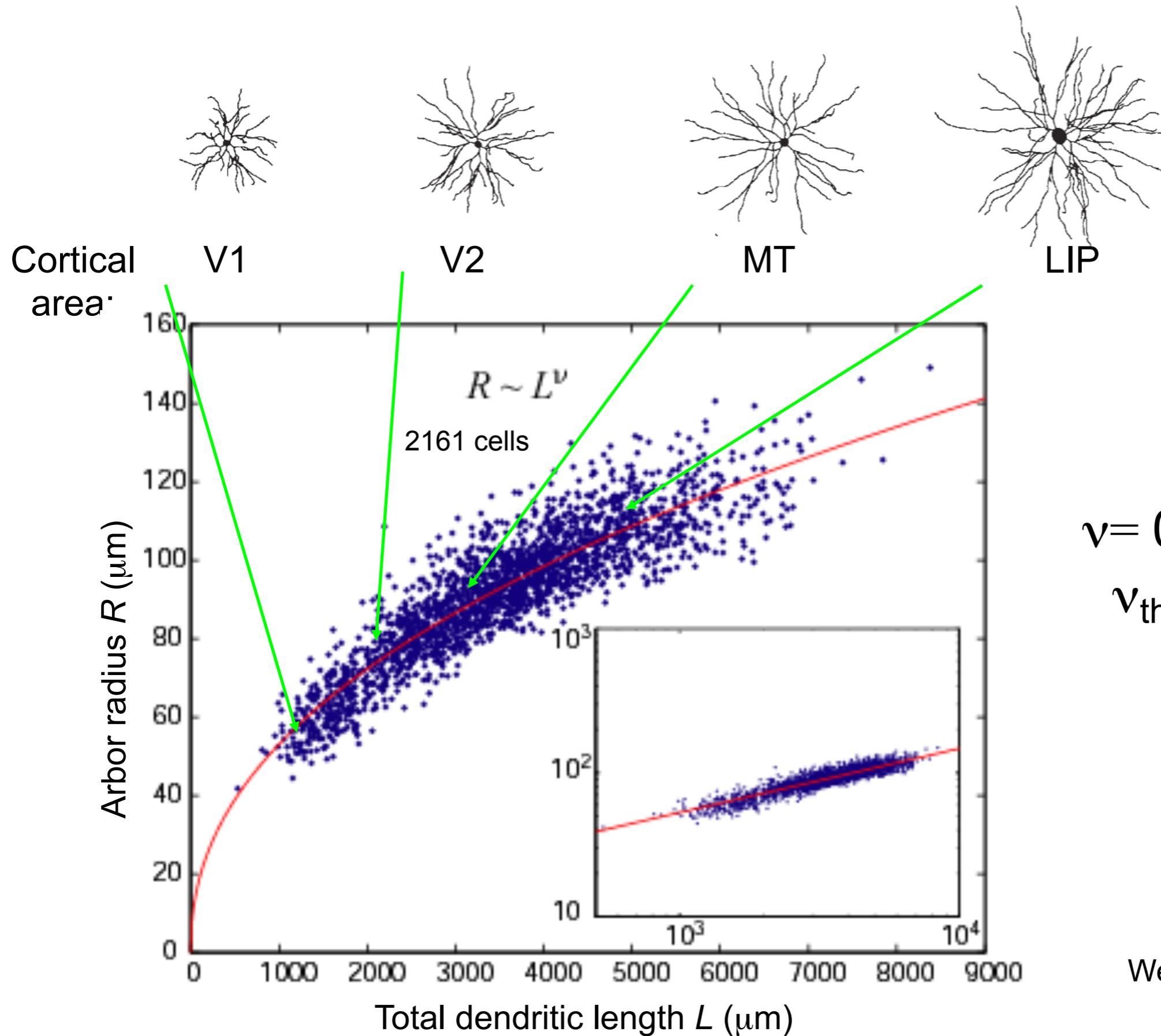
- The functionality of a dendritic arbor benefits from having a large connectivity repertoire, which is defined as the the number of combinations of axons synapsing on a dendritic arbor .
- **The shape of a dendritic arbor maximizes the connectivity repertoire while minimizing the dendritic cost.**

### 3. Subtract the overcounts due to double-hits

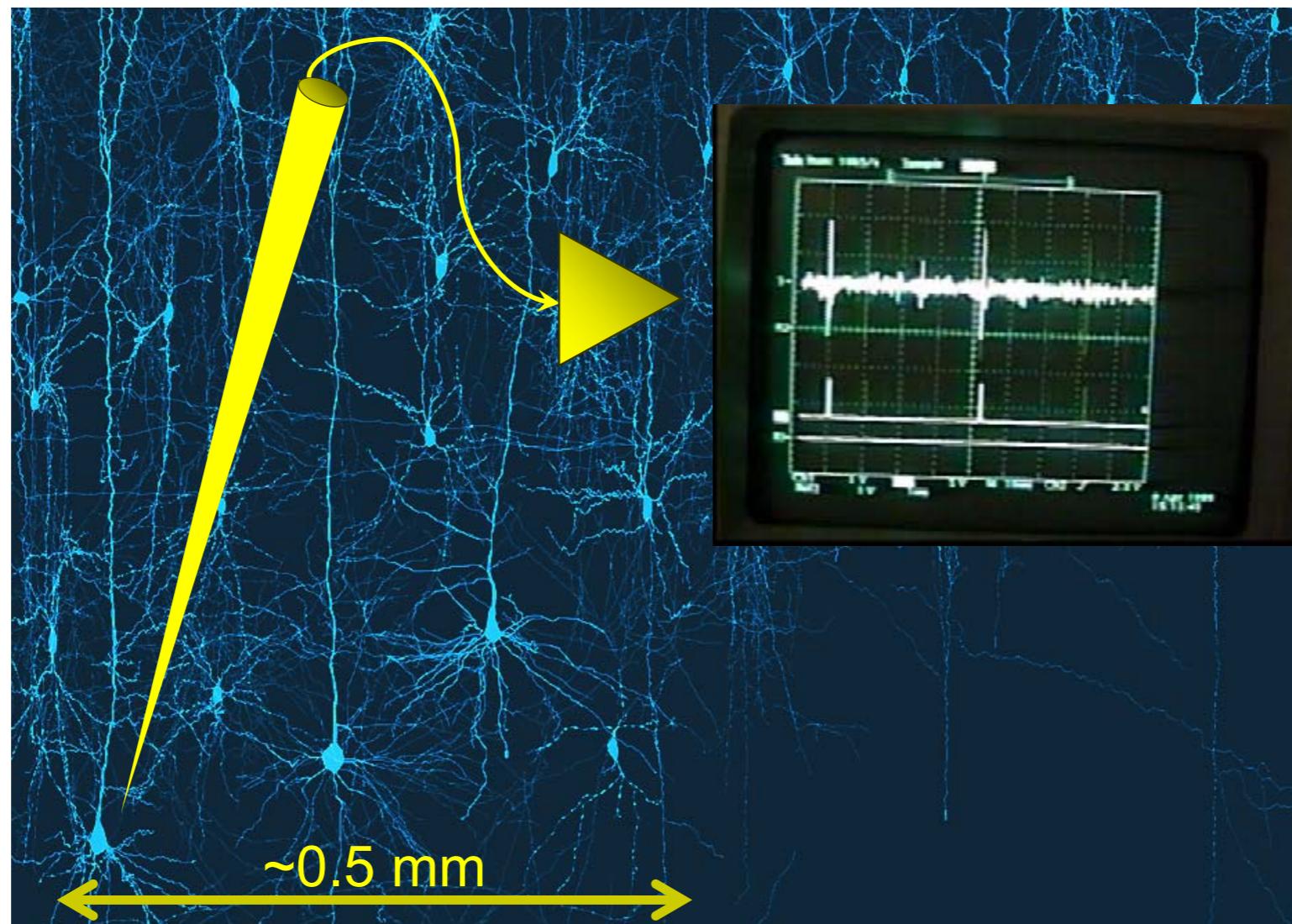
actual inputs out of potential synapses



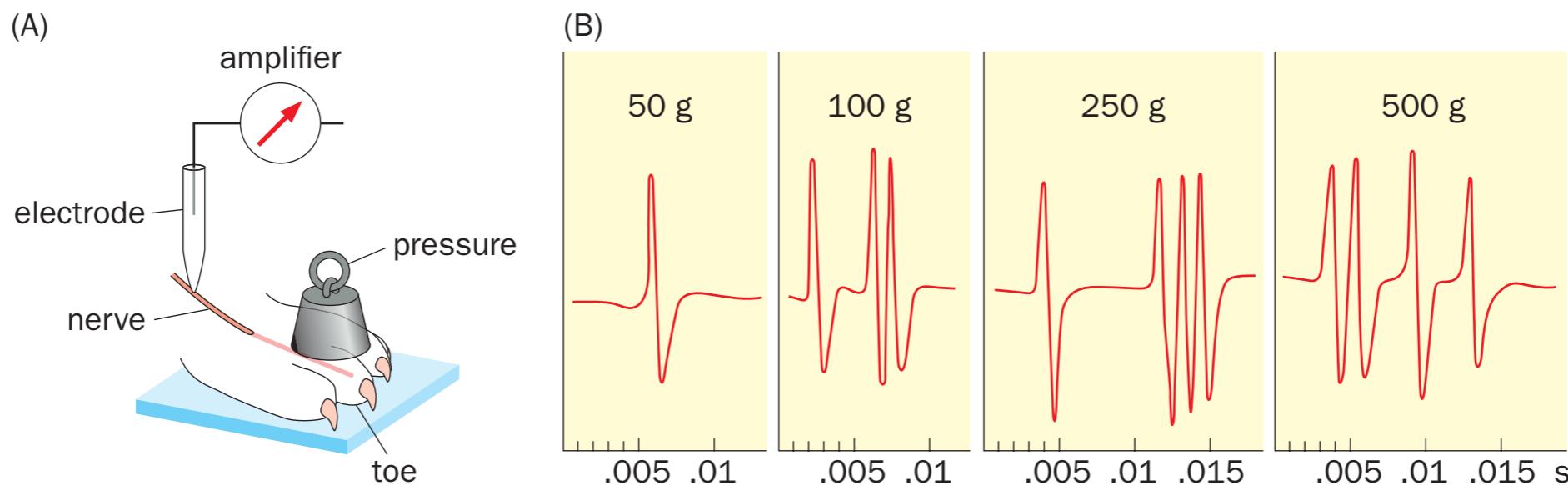
# Scaling of basal pyramidal dendrites



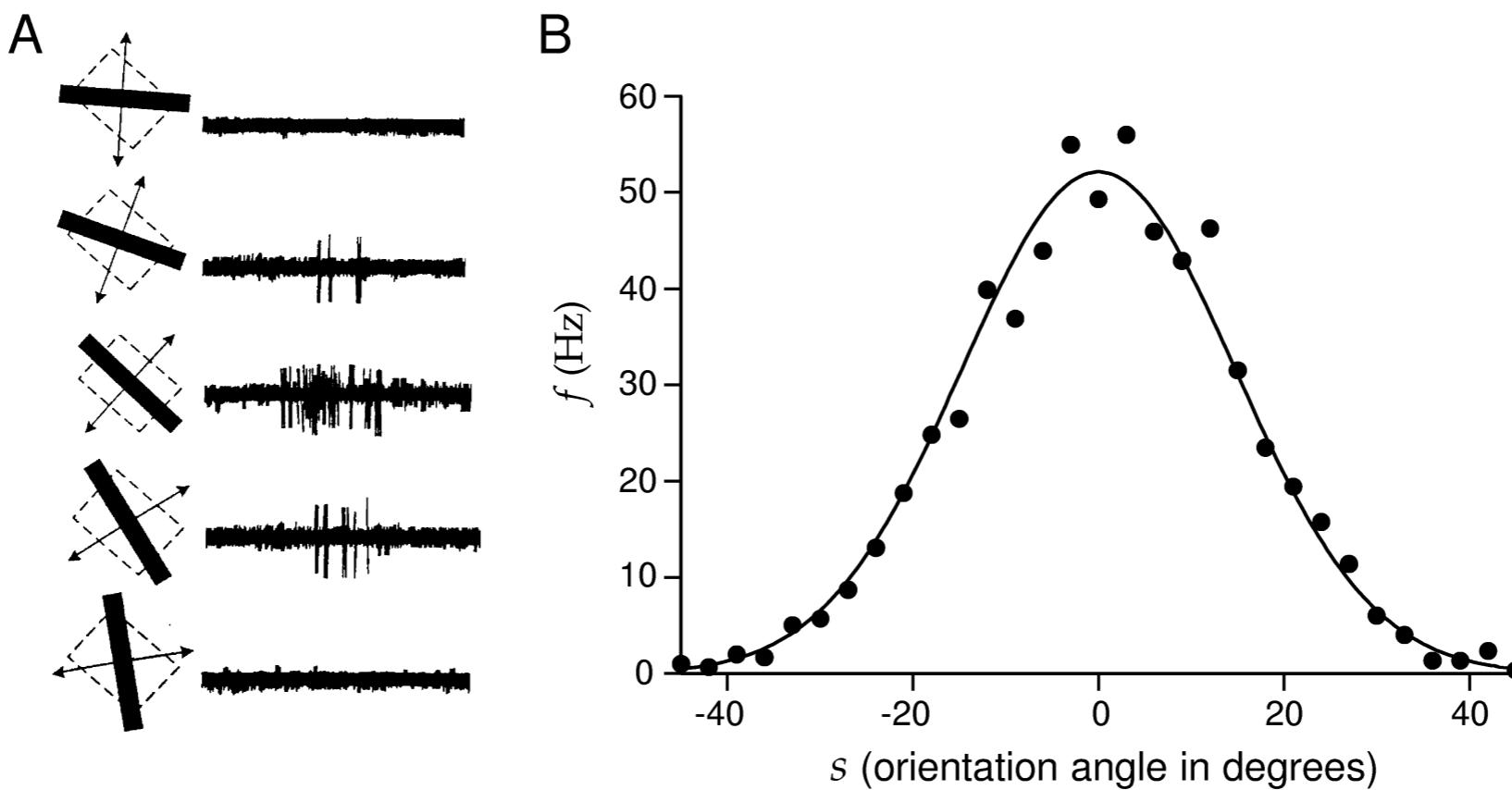
# Action potential as the basic unit to transmit information between neurons



# What is the neural code?

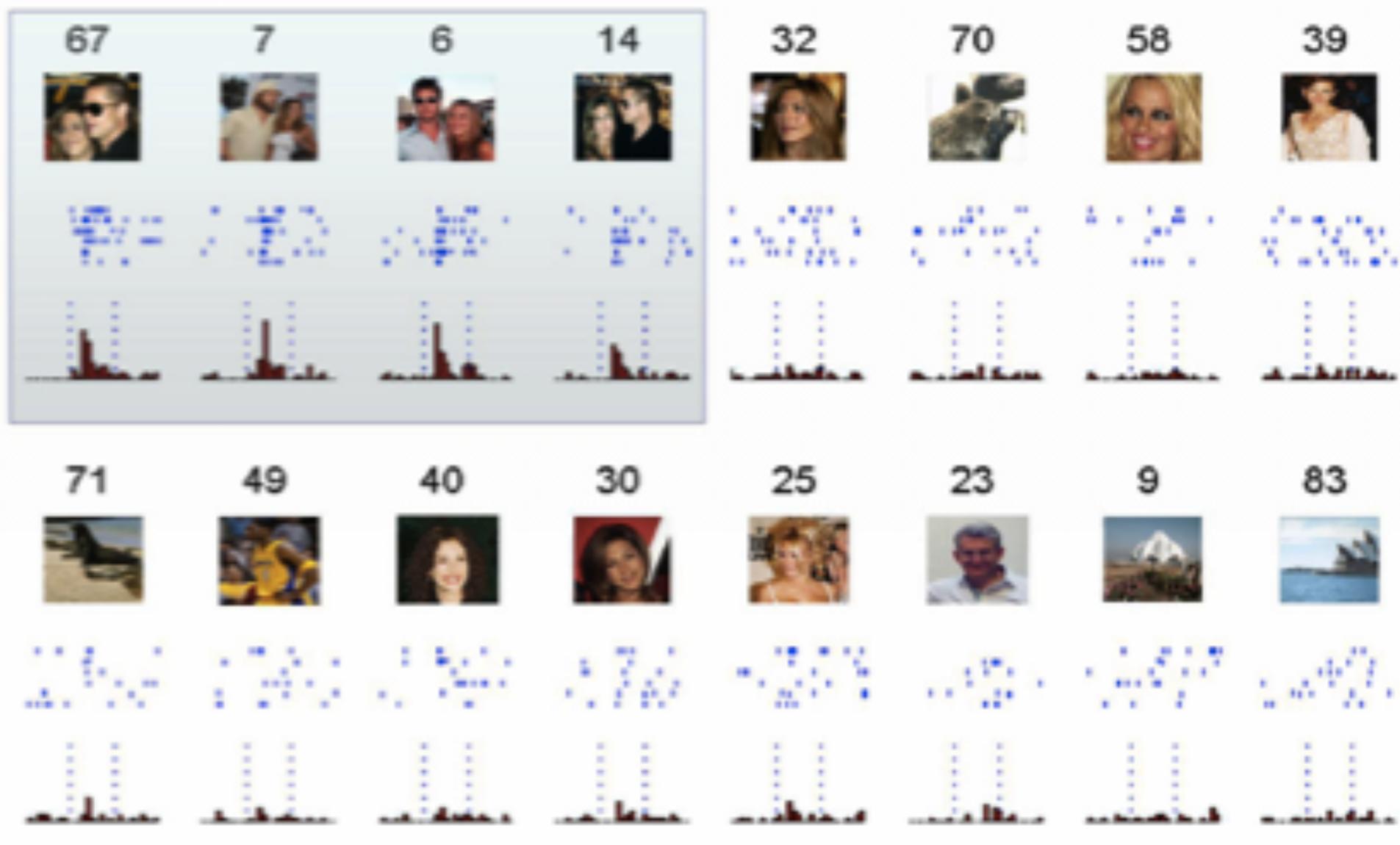


# What is the neural code?



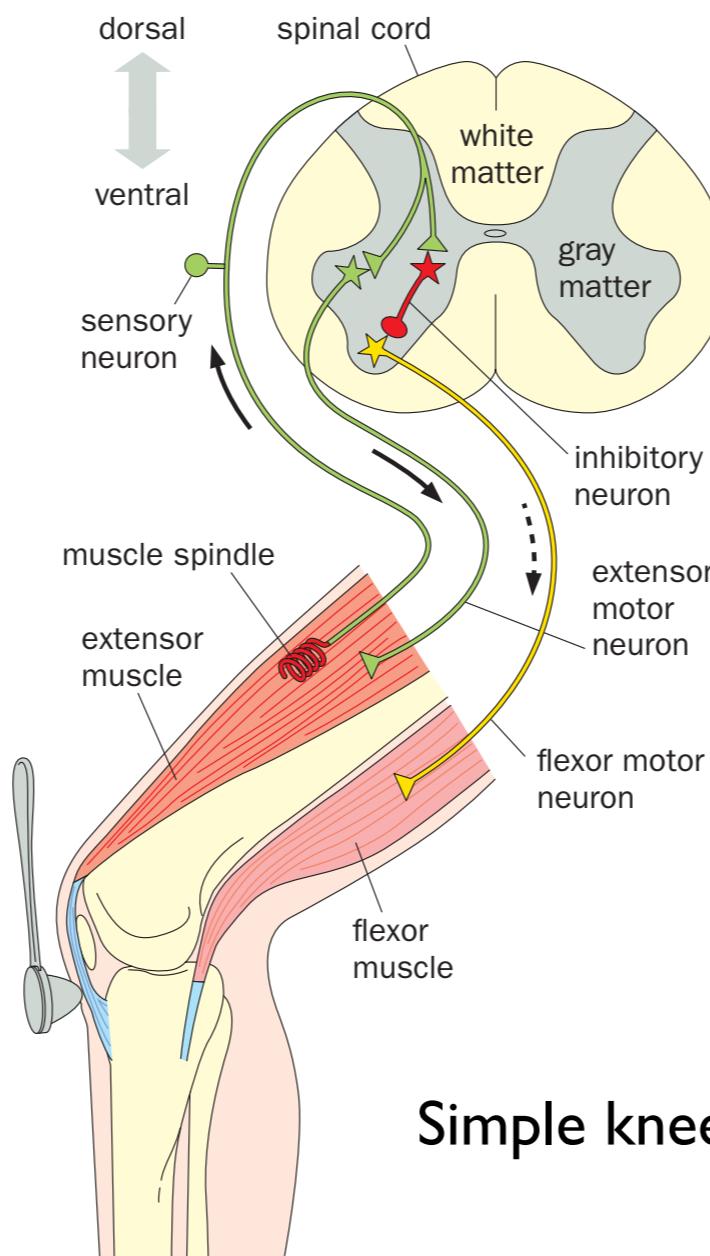
Gaussian tuning curve of a neuron in the primary visual cortex (V1)

# What is the neural code?



High brain areas represent increasingly complex features

# Neurons perform their functions in the context of neural circuit

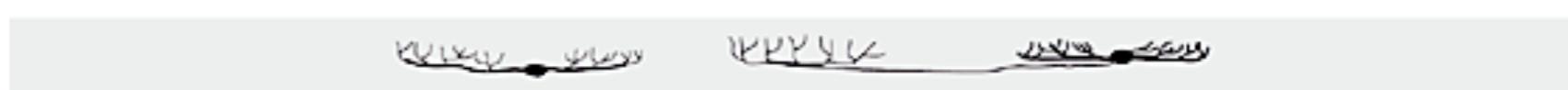


# Diverse cell types in the brain

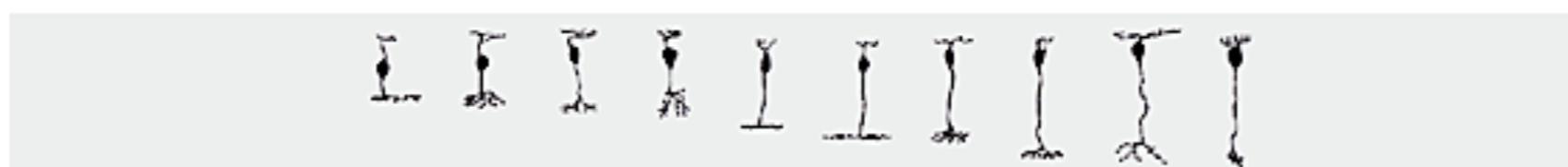
photoreceptors



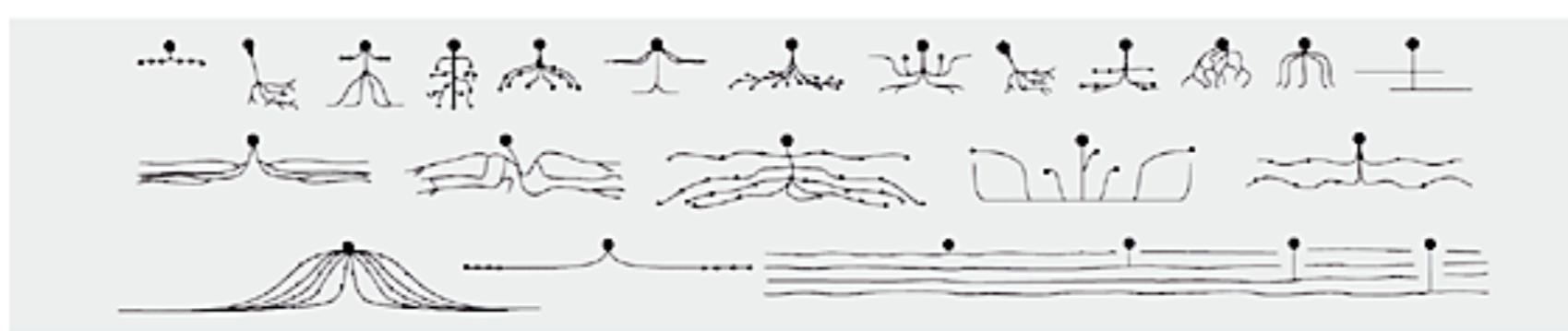
horizontal cell



bipolar cell



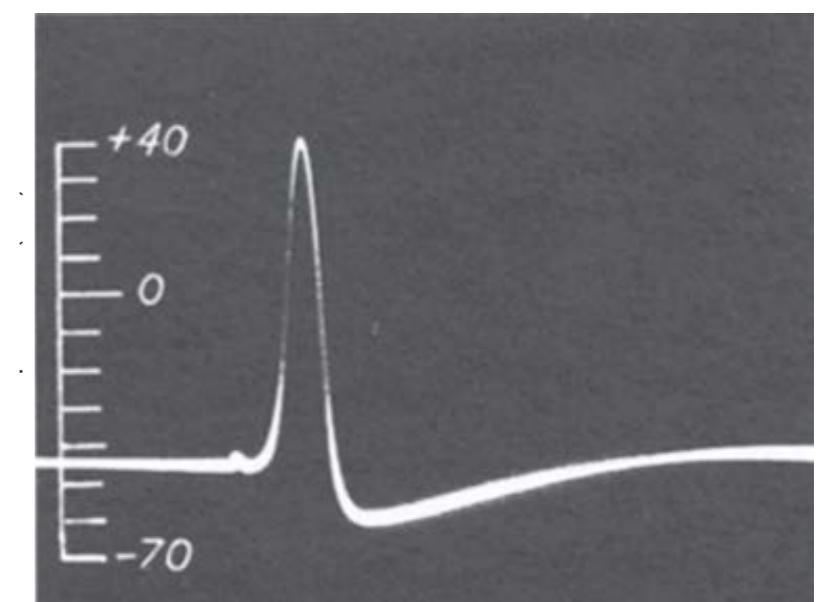
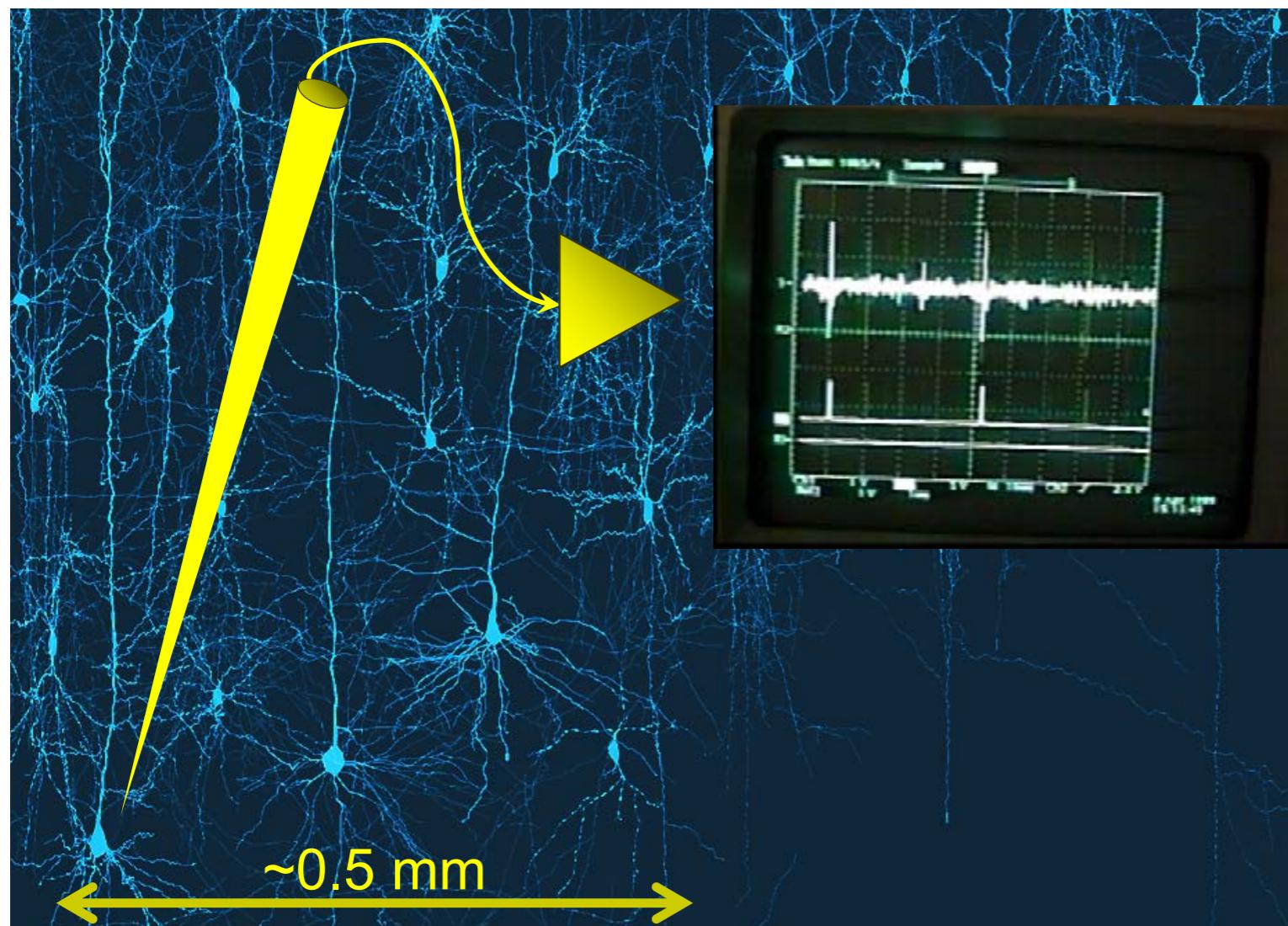
amacrine cell

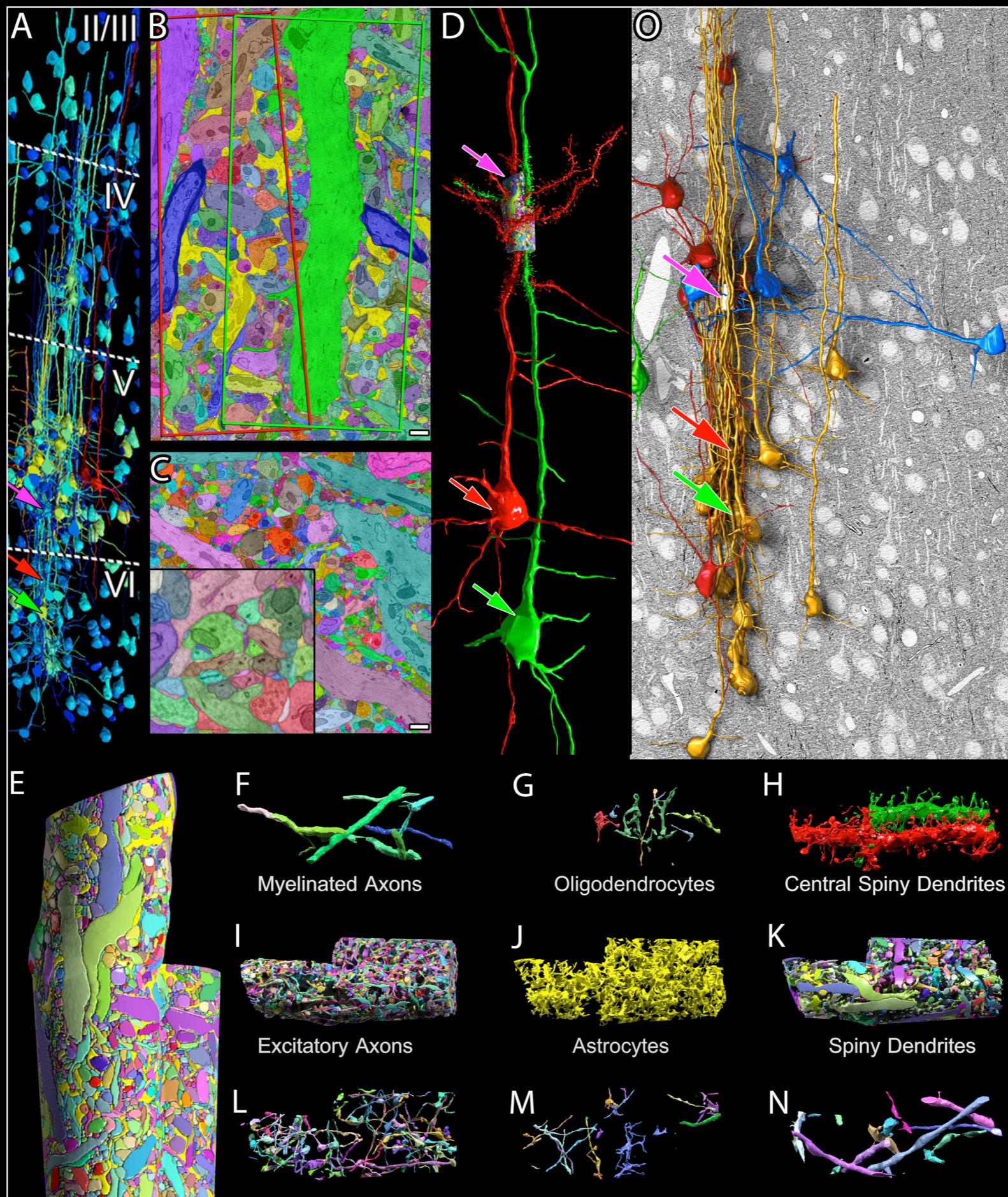


ganglion cell



# 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    |          |

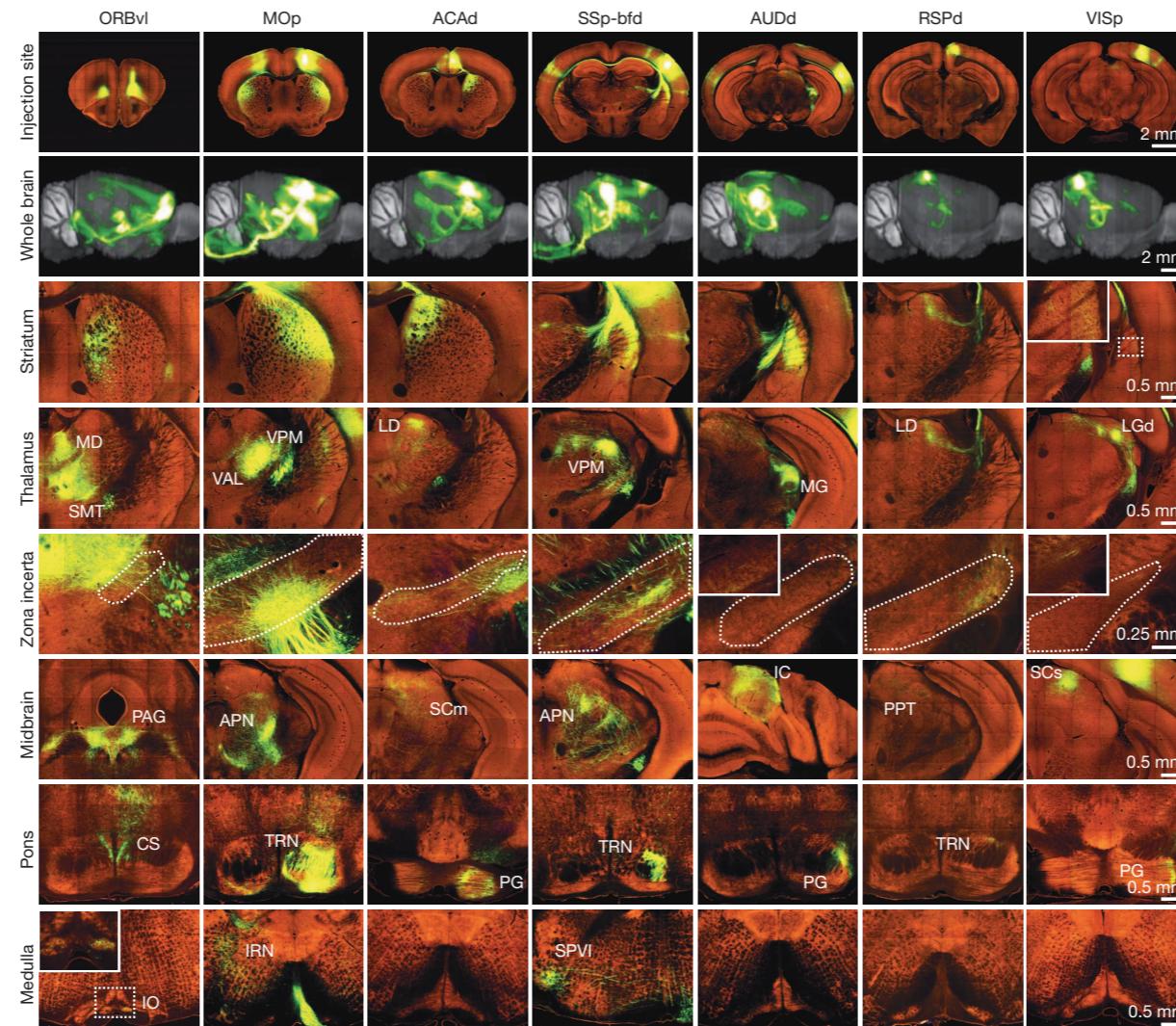
Each row shows a description of the cell type (first column), its abbreviation used in this study (second column), and the number of neurons of which the axon and dendrites were reconstructed (third and fourth columns).

# The organization of the cortical column

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

Where is the dark matter?

# A mesoscale mouse connectome



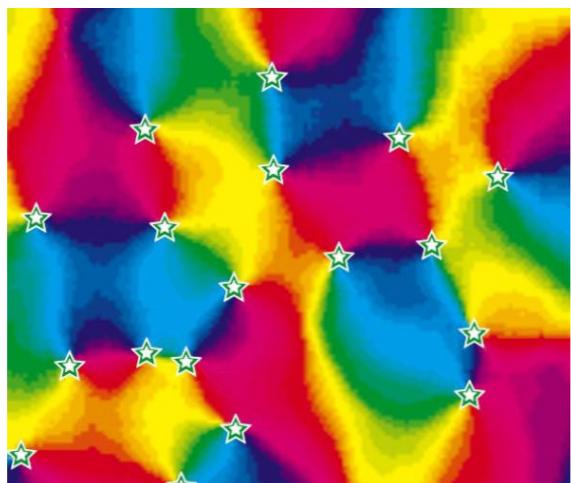
Oh SW et. al, Nature 2014

# The organization of the cortical column

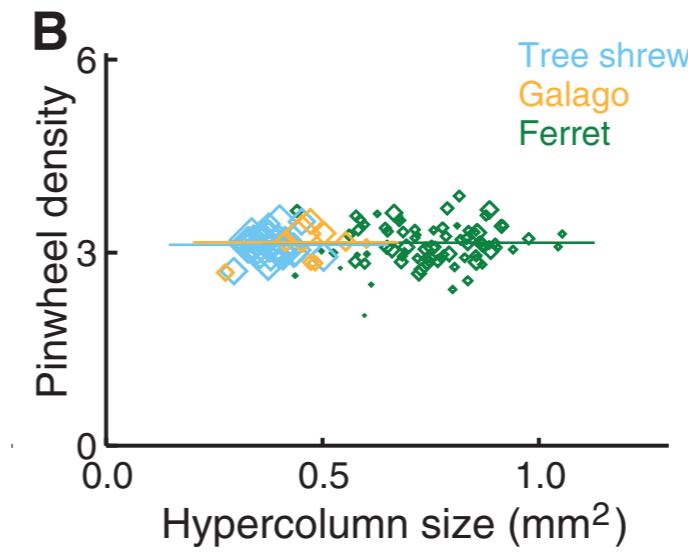
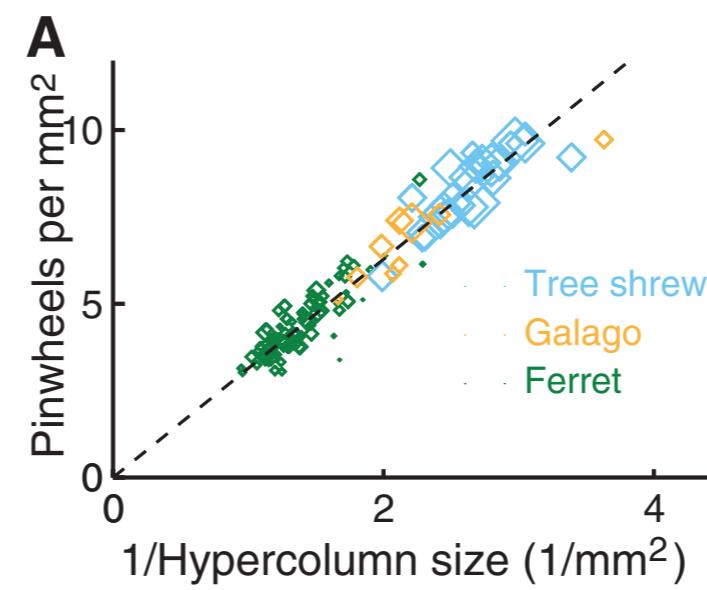
Binzegger T, et.al, *Journal of Neuroscience* 2004

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

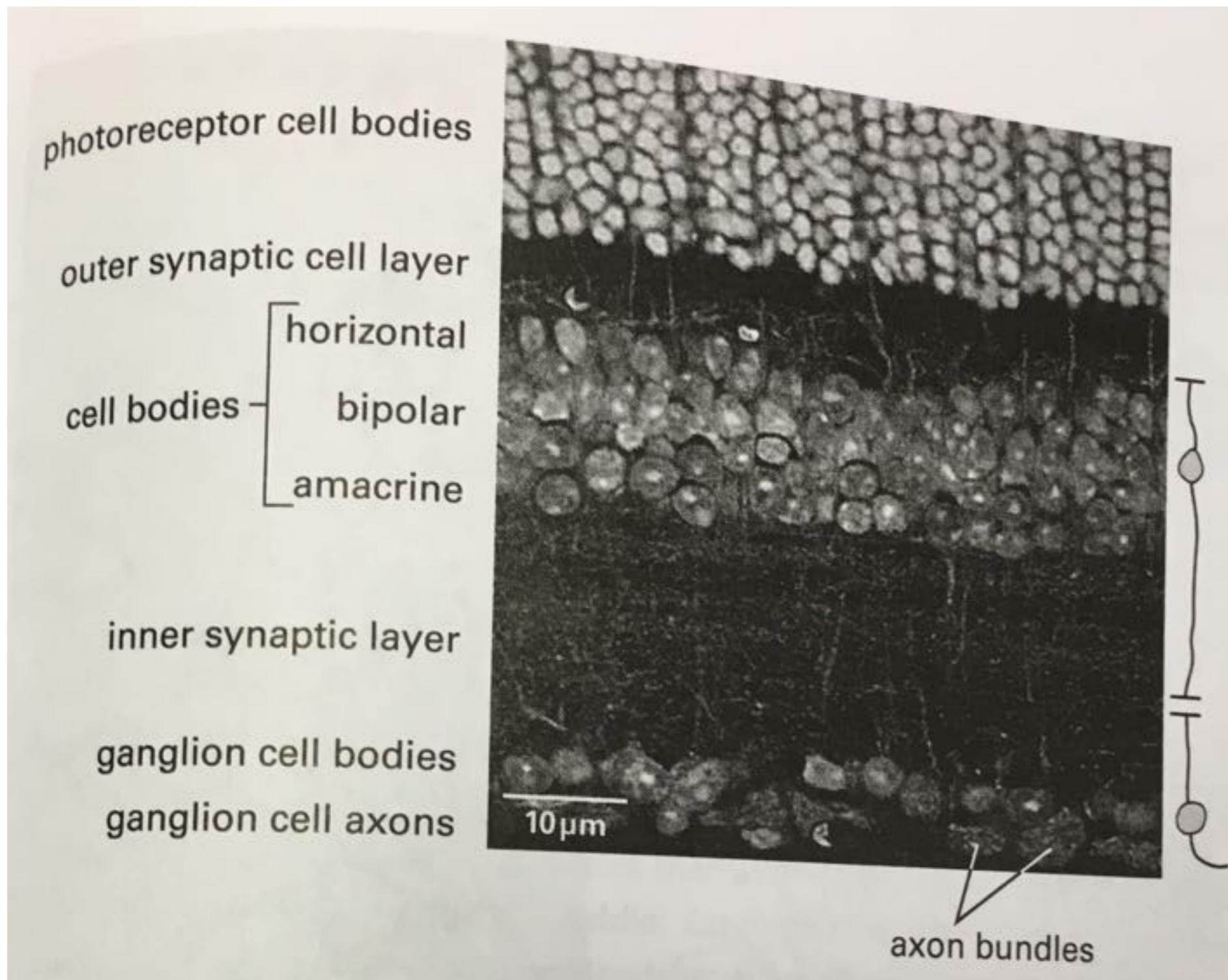
# Pinwheel density approaches $\pi = 3.14$



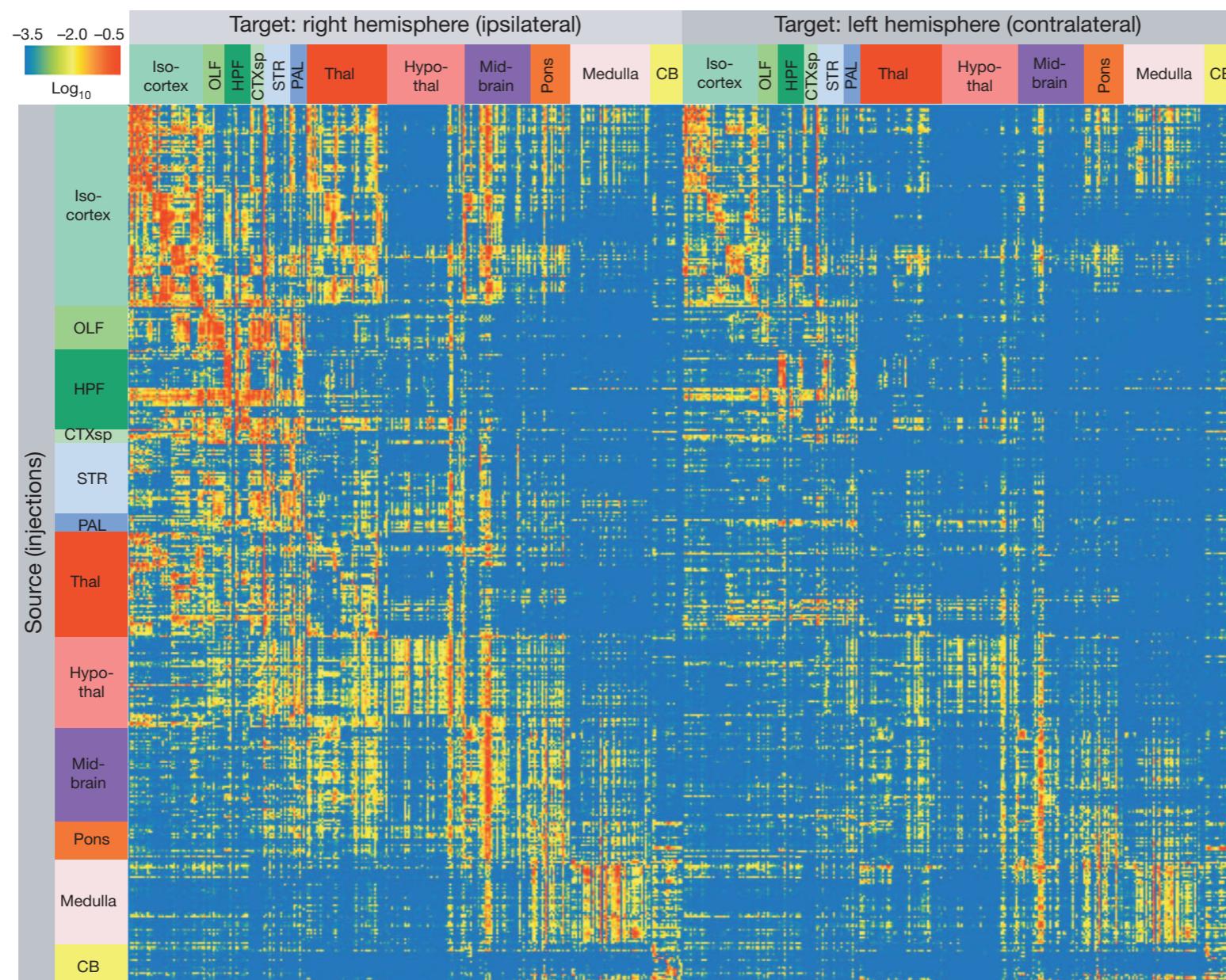
Kaschube M, et. al, Science 2010



# Segregation of cell bodies and axon bundles

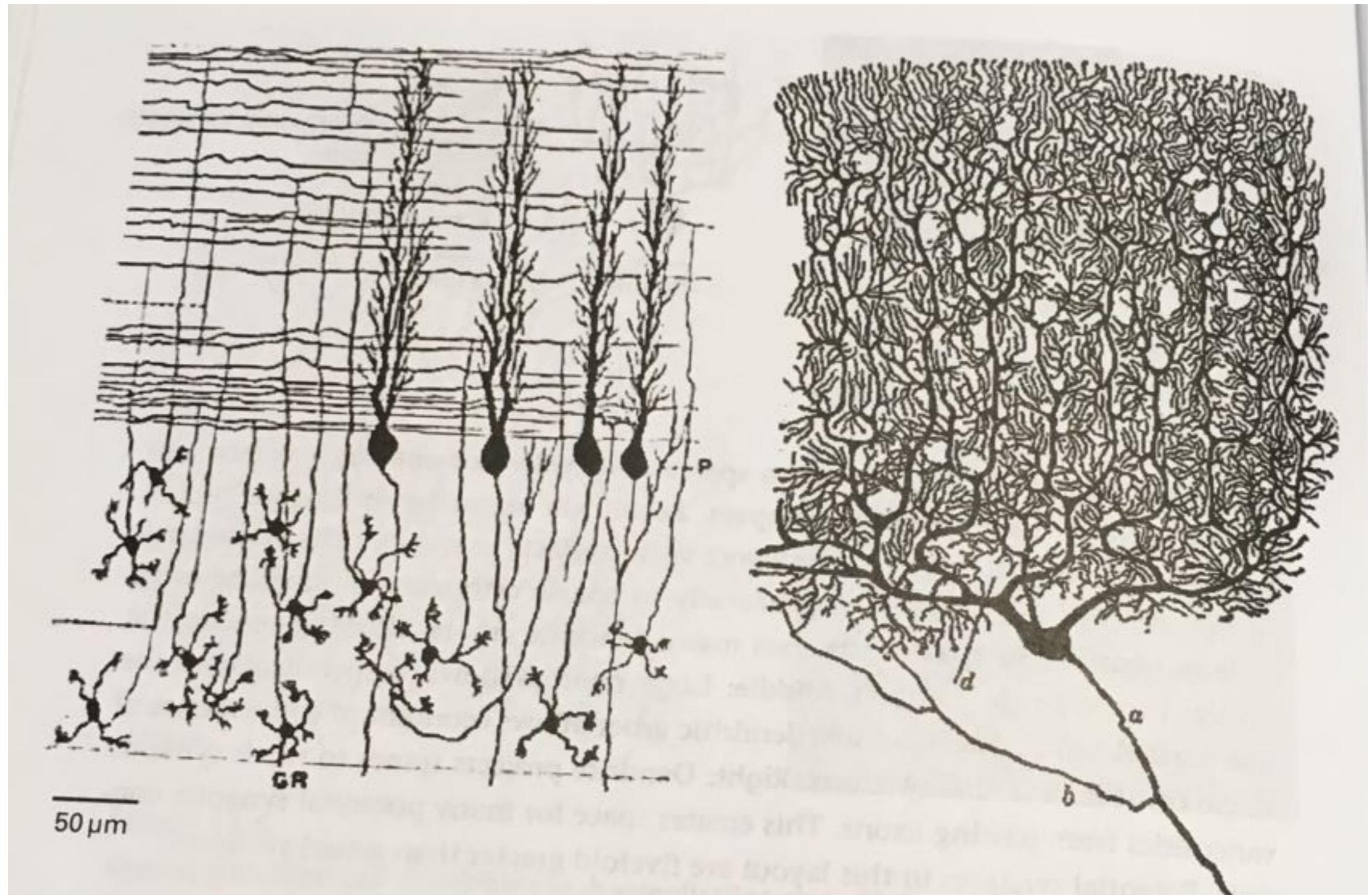


# A mesoscale mouse connectome



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*