Recap

- **Computational level**: Identify the computational problem and task that the brain solves.

- **Algorithmic level**: Find the mathematical procedures that solve the problem.

- **Implementation level**: How the algorithms are realized by the nervous system.

top-down

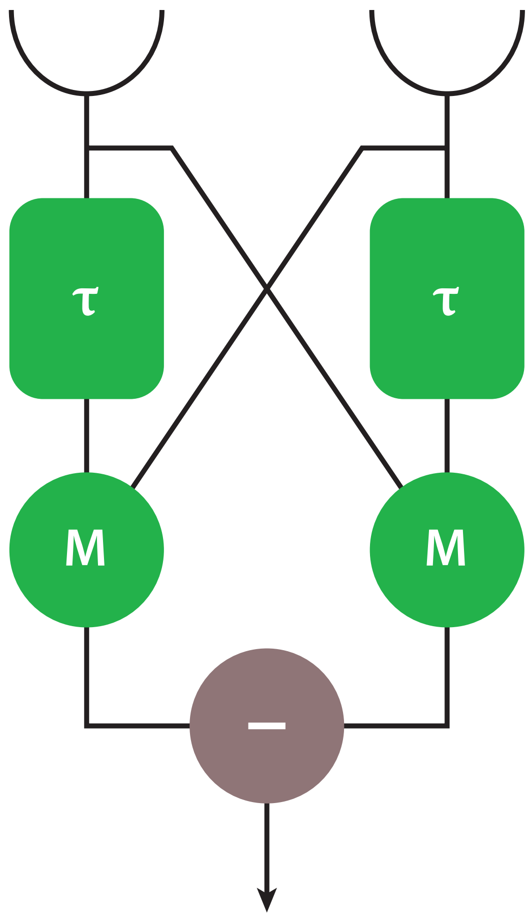
- **Systems level**: describe how population neural dynamics and behaviors emerge from ensembles of neurons.

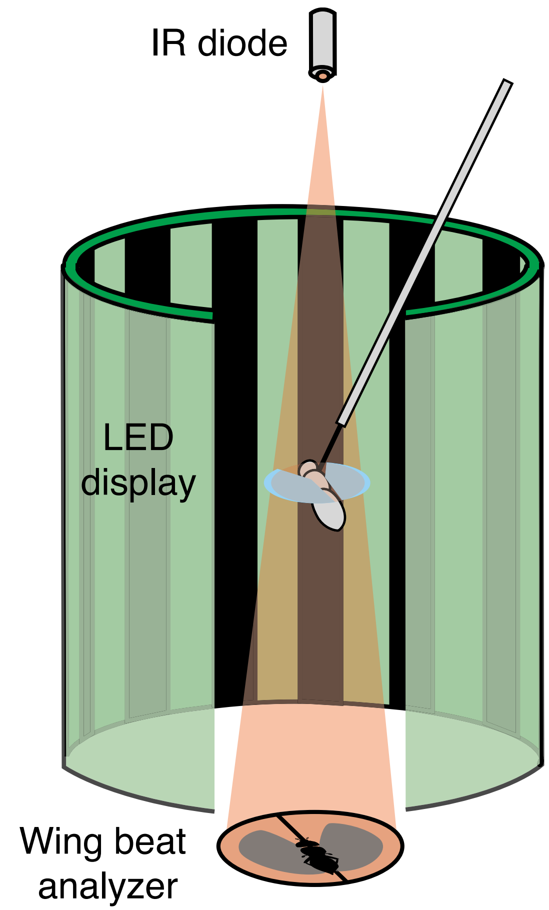
- **Cellular level**: develop biophysically accurate models to describe input-output relationships of different cell types.

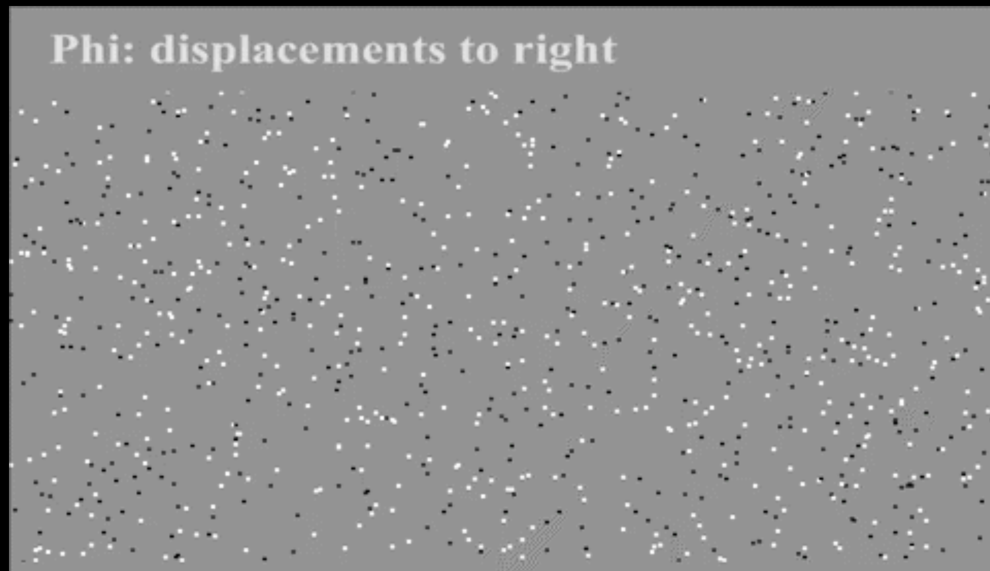
- **Structure level**: identify how neurons are statistically connected to each other in a circuit.

bottom-up

Hassenstein-Reichardt Detector Model







adapted from Damon Clark's slide

Little Fly,
Thy summer's play
My thoughtless hand
Has brush'd away.

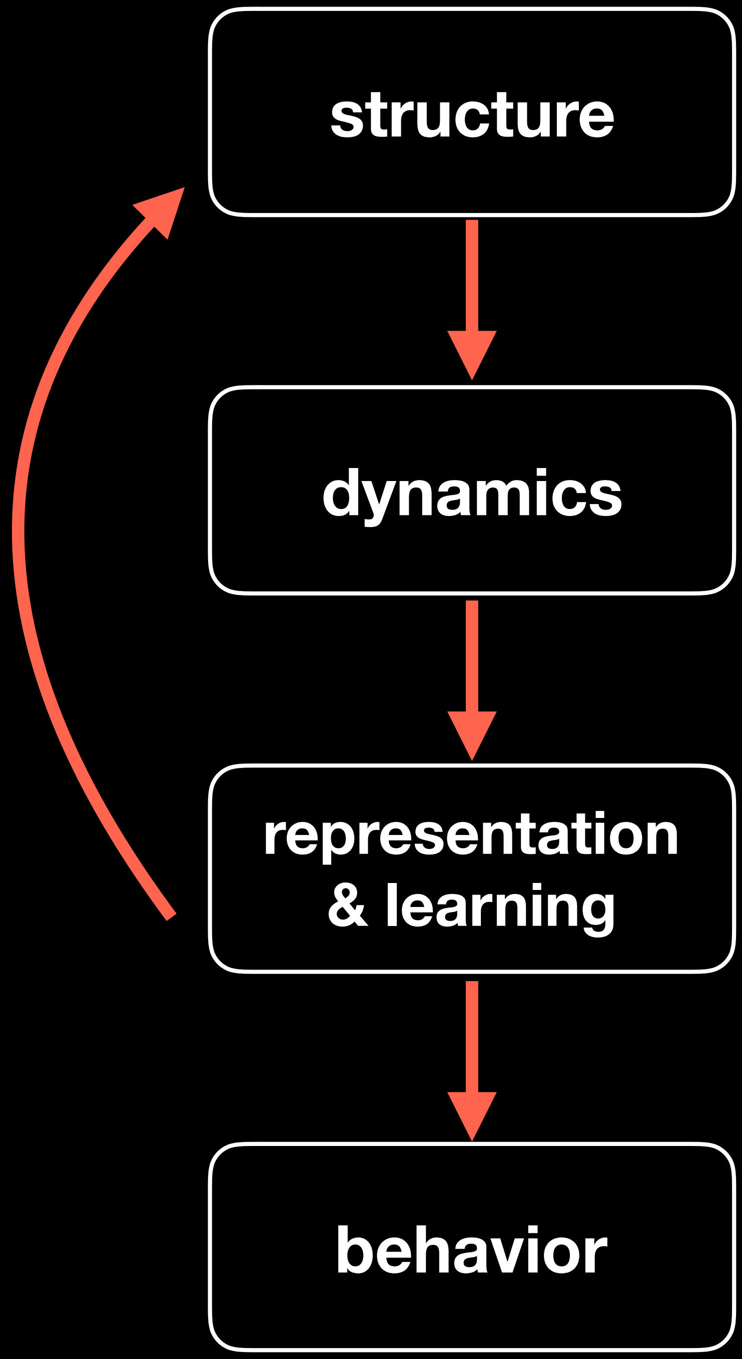
Am not I
A fly like thee?
Or art not thou
A man like me?

—WILLIAM BLAKE,
"The Fly,"
from Songs of Experience

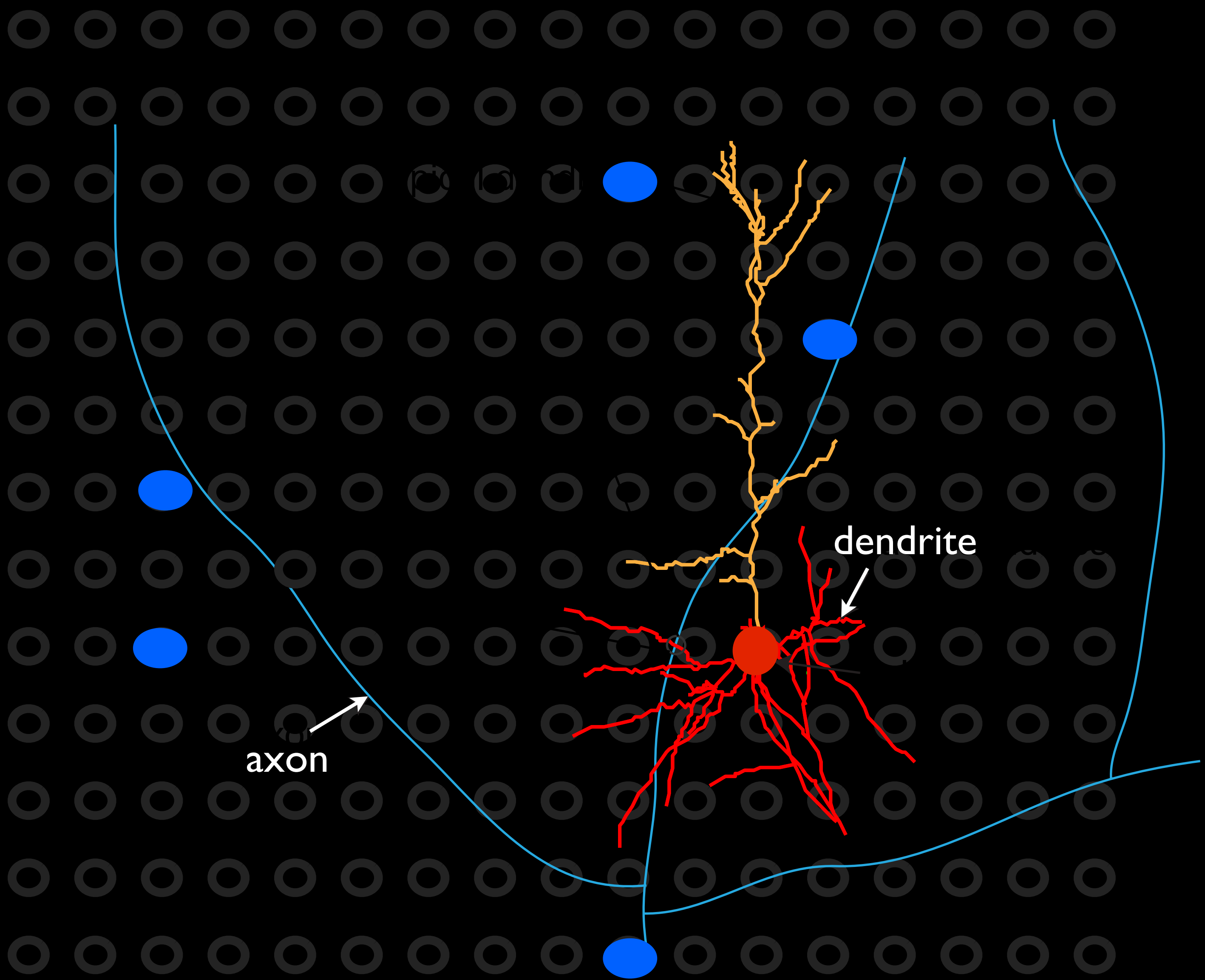
小小飞蝇
你夏日的游戏
已被我无心的手
拂之而去

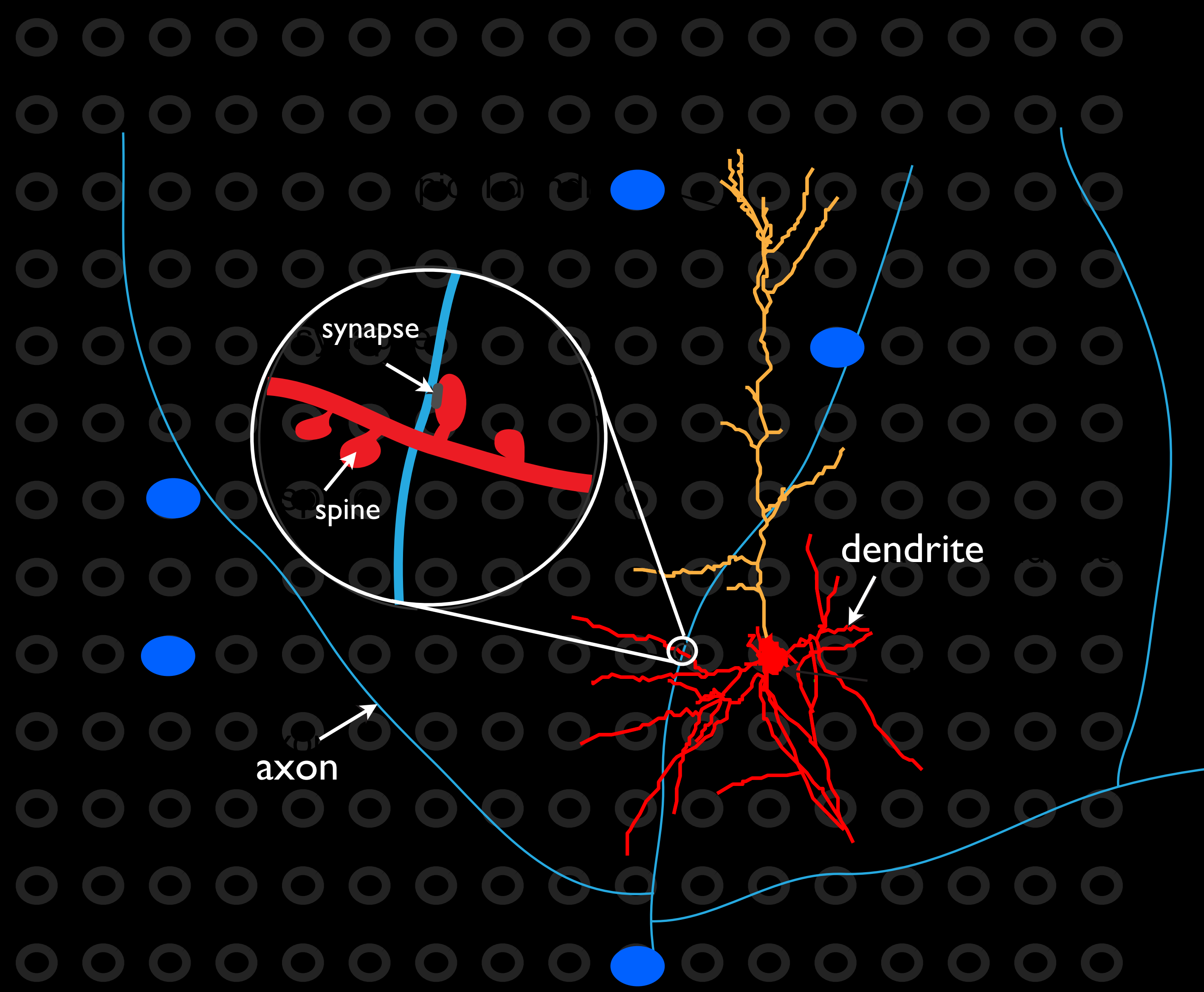
难道我不是
一只像你一样的蝇?
难道你不就是
一个像我一样的人?

2020 *Fall Course Program*


structure
dynamics
representation & learning
behavior

The Neuron Doctrine


dendrite
axon

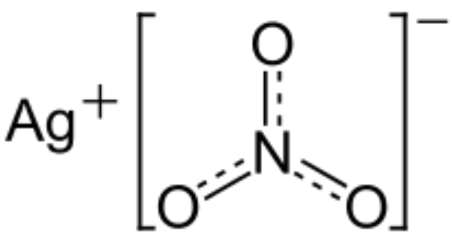

synapse
spine
dendrite
axon

The Debate between Cajal and Golgi

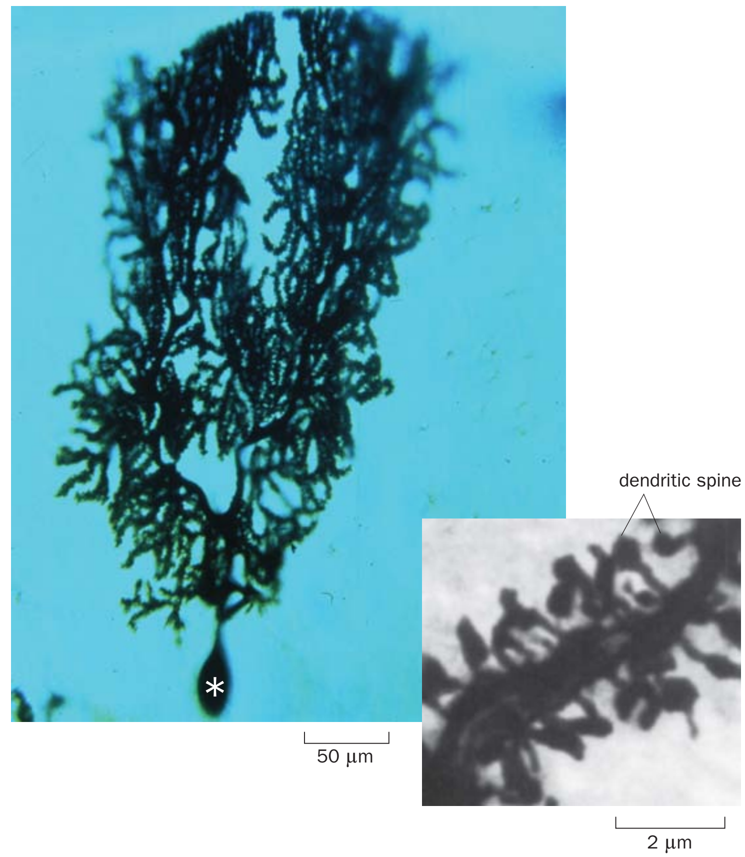
Ramon y Cajal

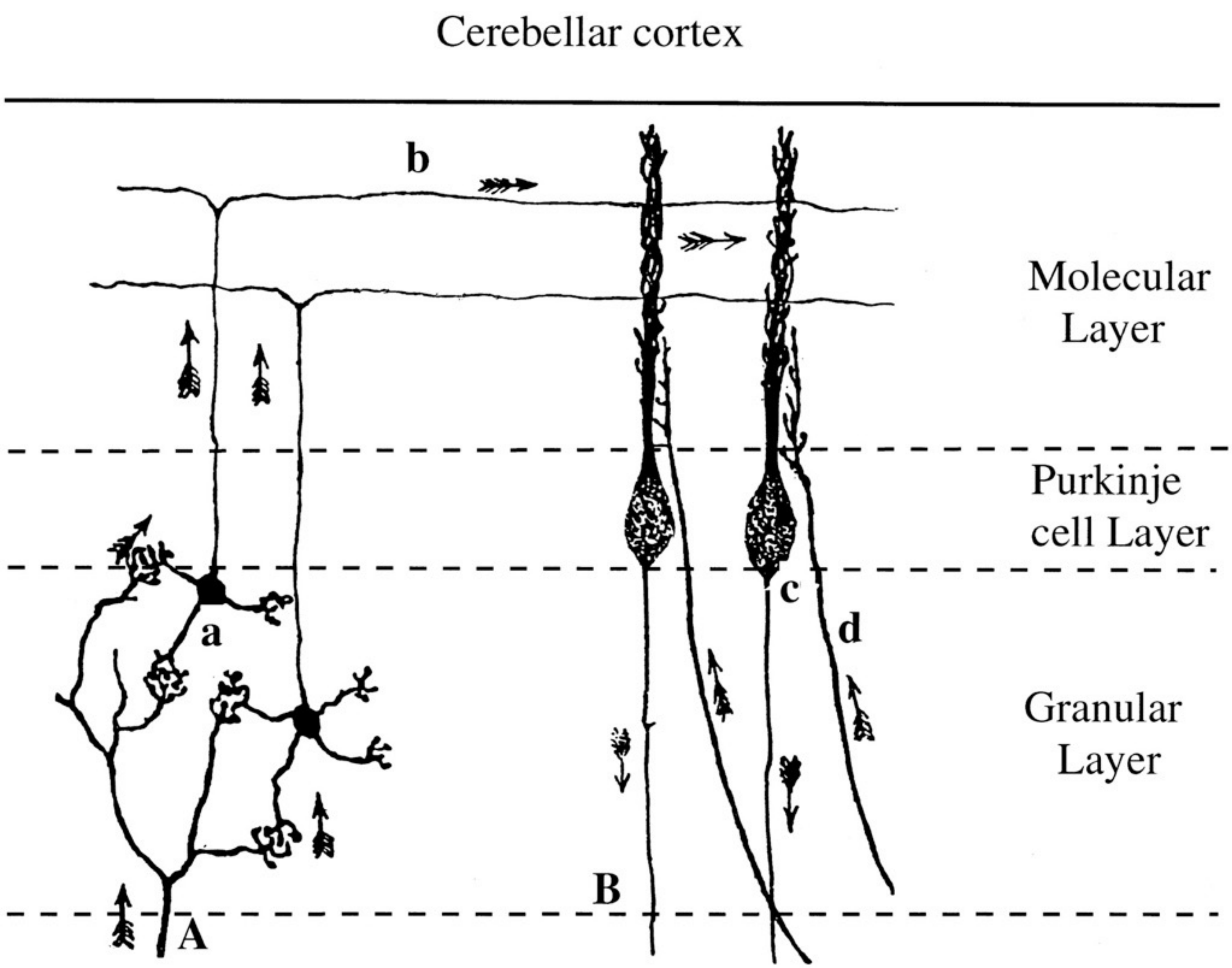
Camillo Golgi

Golgi Staining method



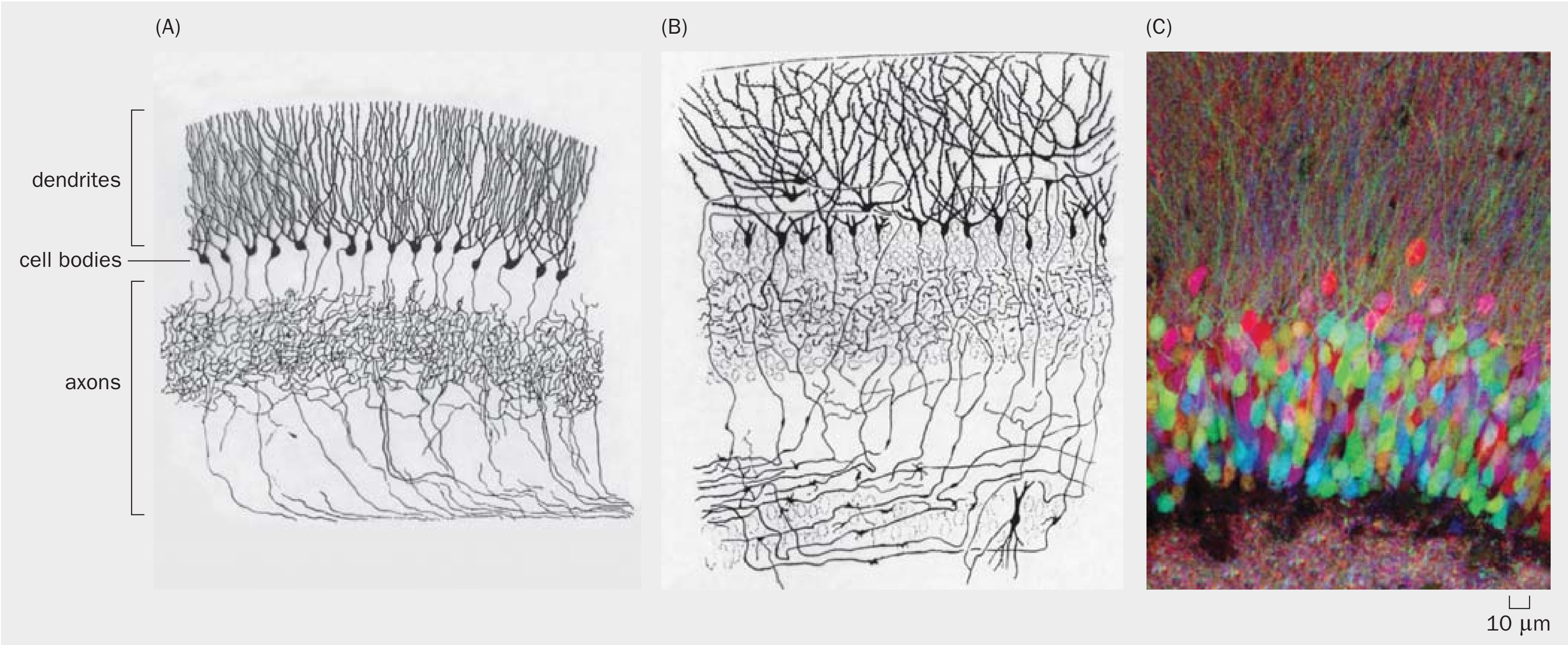
Silver nitrate





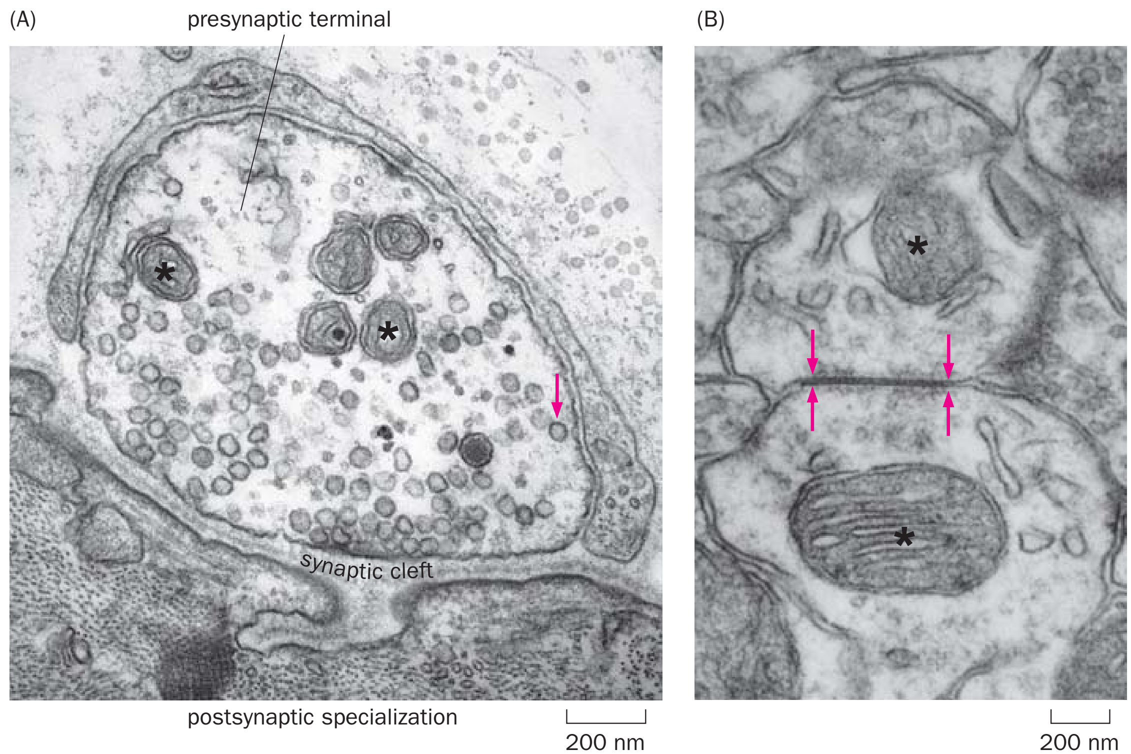
Cajal’s drawing of the cerebellar cortex

Reticular Theory vs Neuron Doctrine



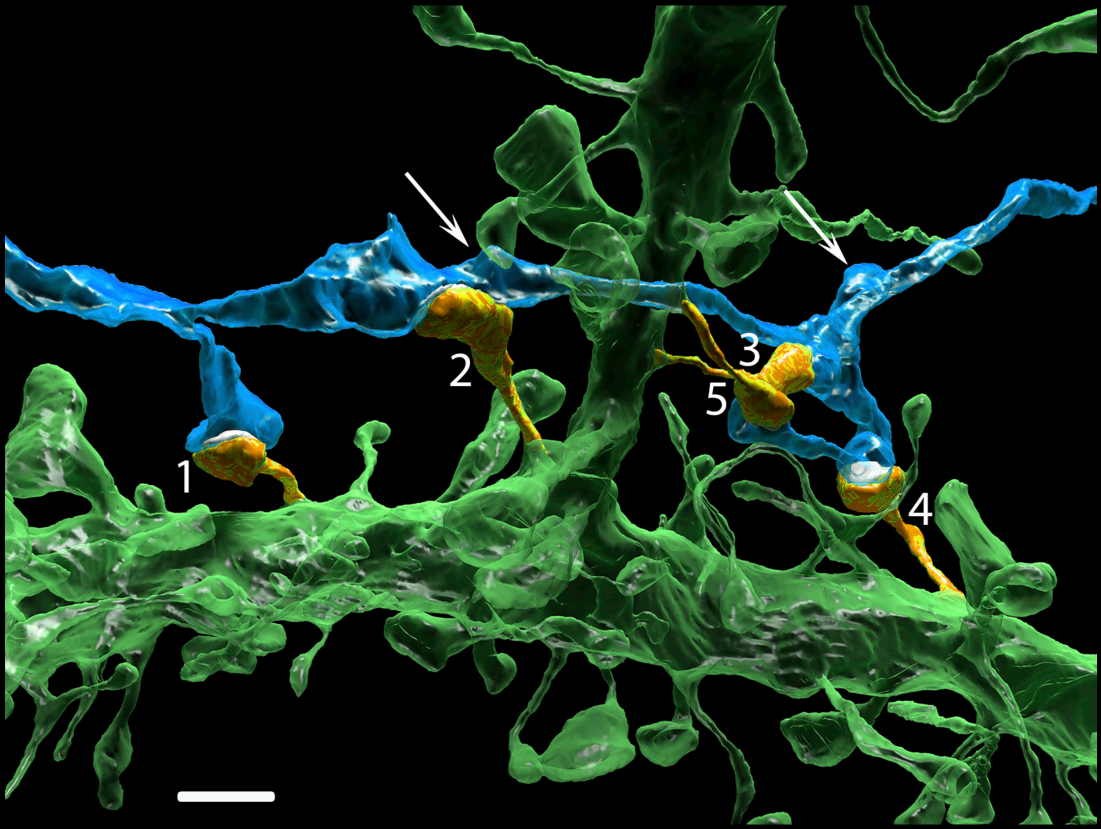
Synapse

How neurons communicate with each other?



Chemical and electrical synapses

Synaptic Connectivity

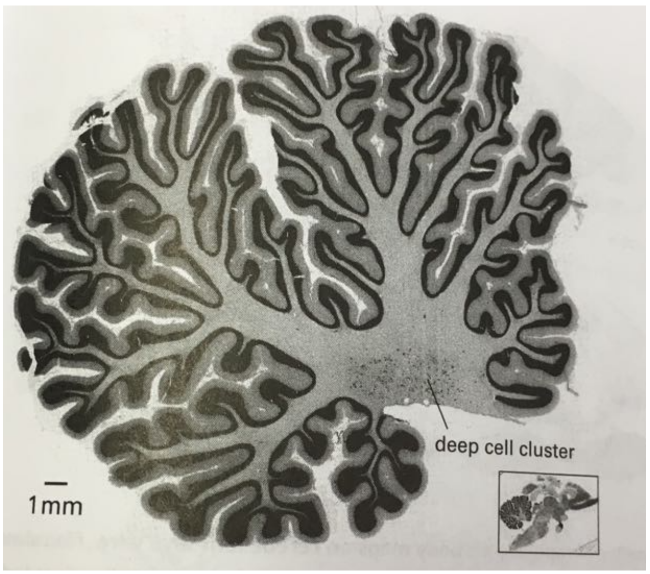


Kasthuri et. al, Cell 2015

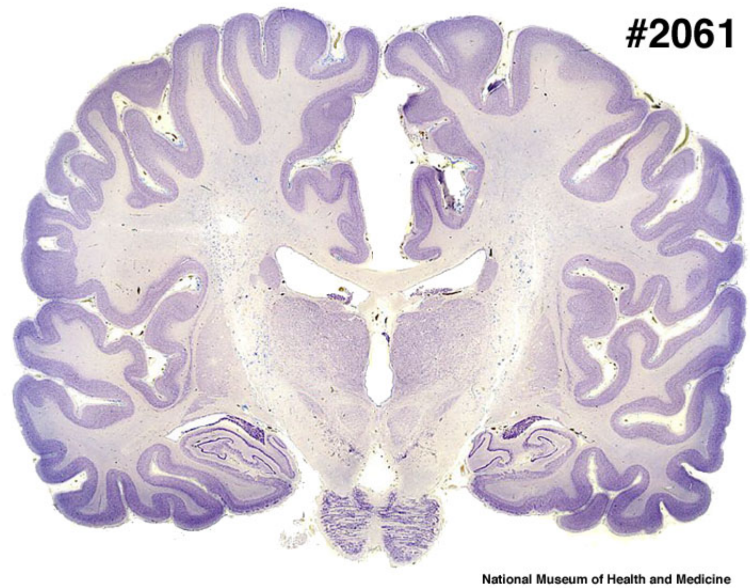
divergence: number of outputs per neuron

convergence: number of inputs per neuron

The synaptic organization of cerebral cortex vs. cerebellar cortex

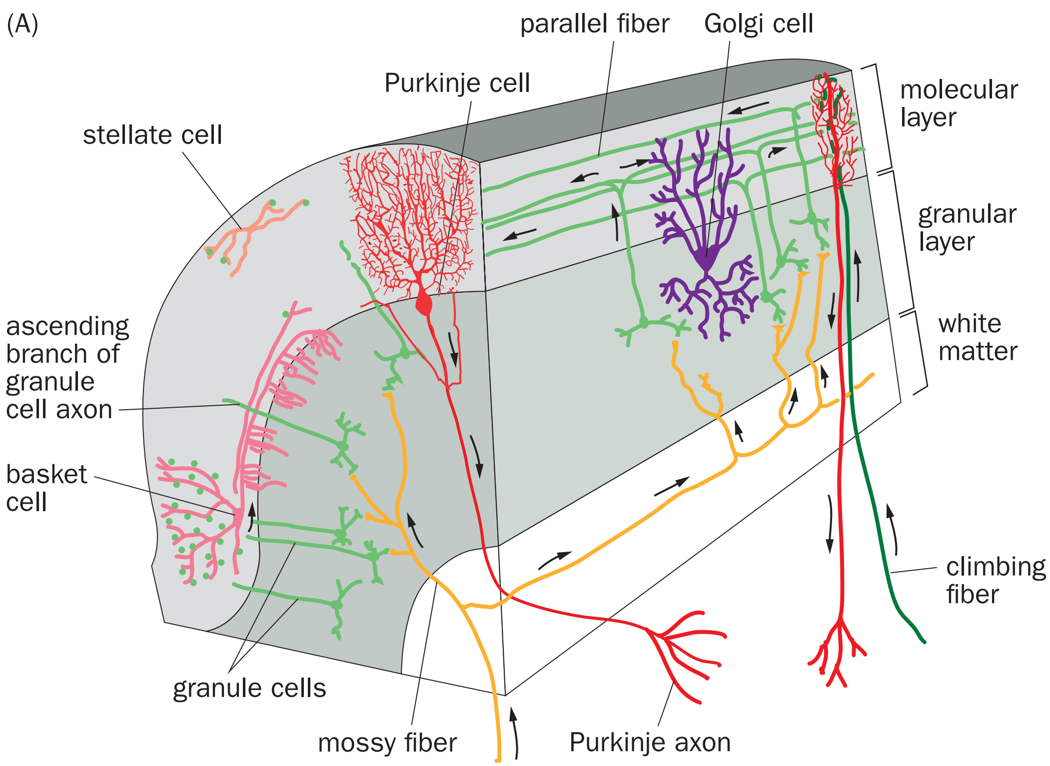


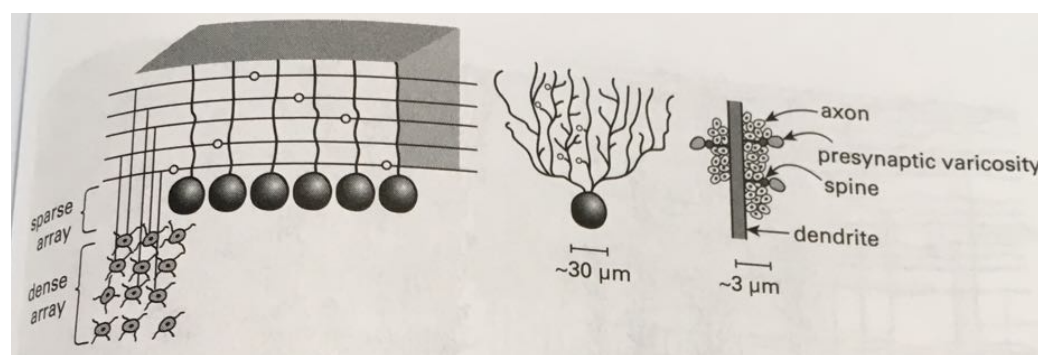
cerebellum

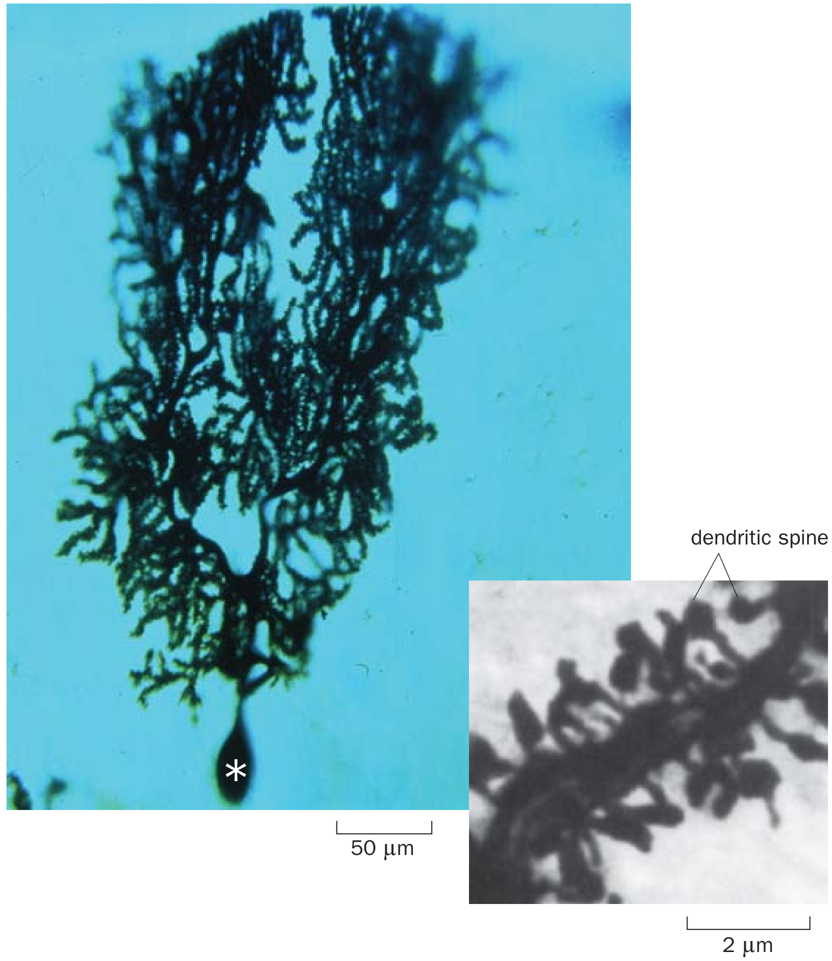


cerebral cortex

The organization cerebellar cortex







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

Cerebellar cortex: connecting dense array to sparse array with extreme convergence and divergence

The organization of the cortical column

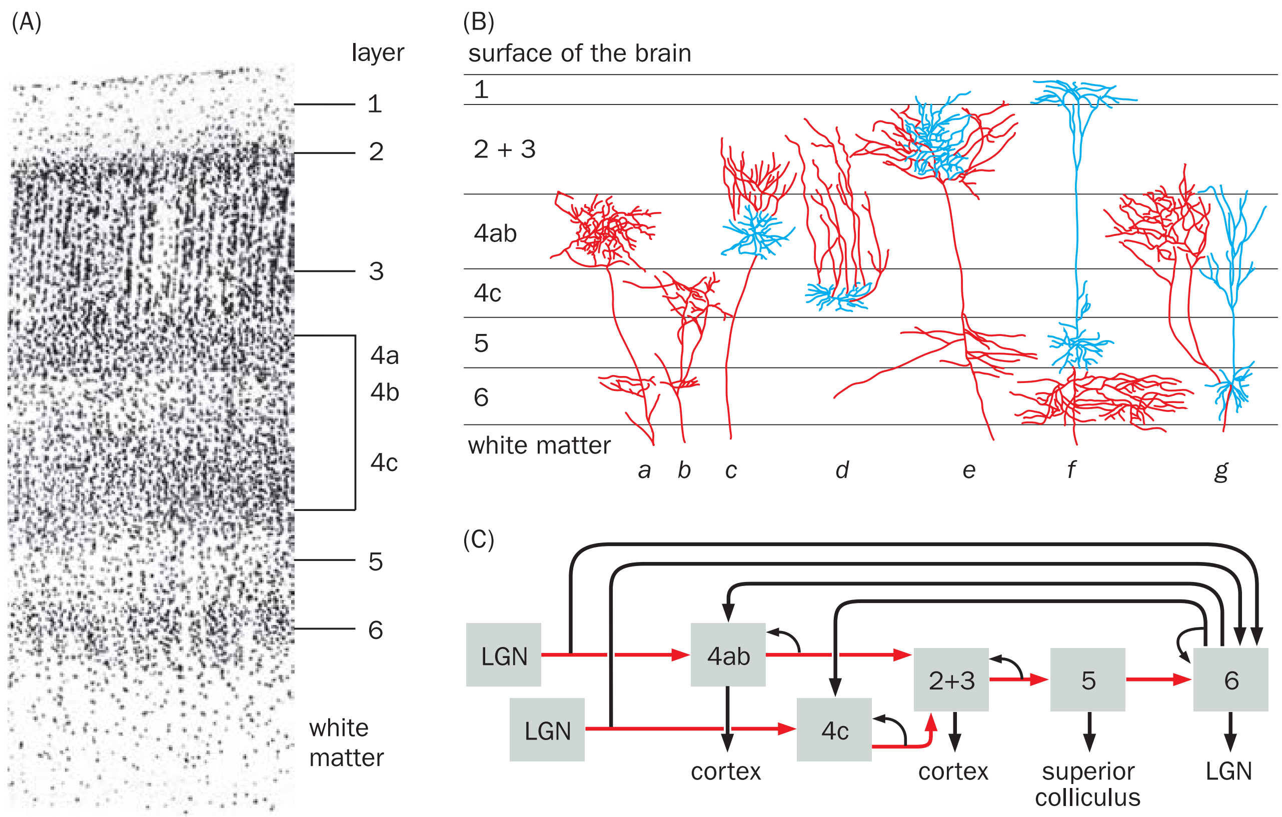
85% excitatory cells

15% inhibitory cells

10^5 neurons

10^9 synapses

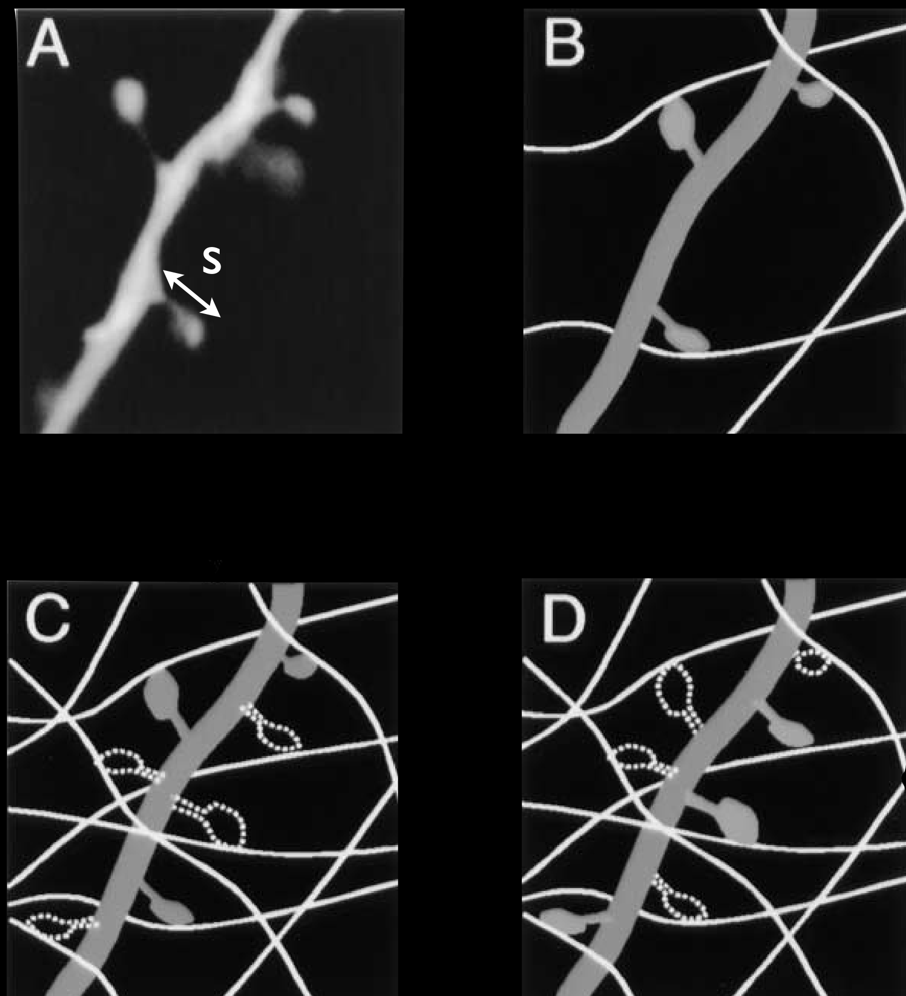
5000 m wires



Cerebellar cortex: connecting dense array to sparse array with extreme convergence and divergence

Cerebral cortex: connecting many dense arrays to many other dense arrays with moderate convergence and divergence

Structural Plasticity of Synaptic Connectivity



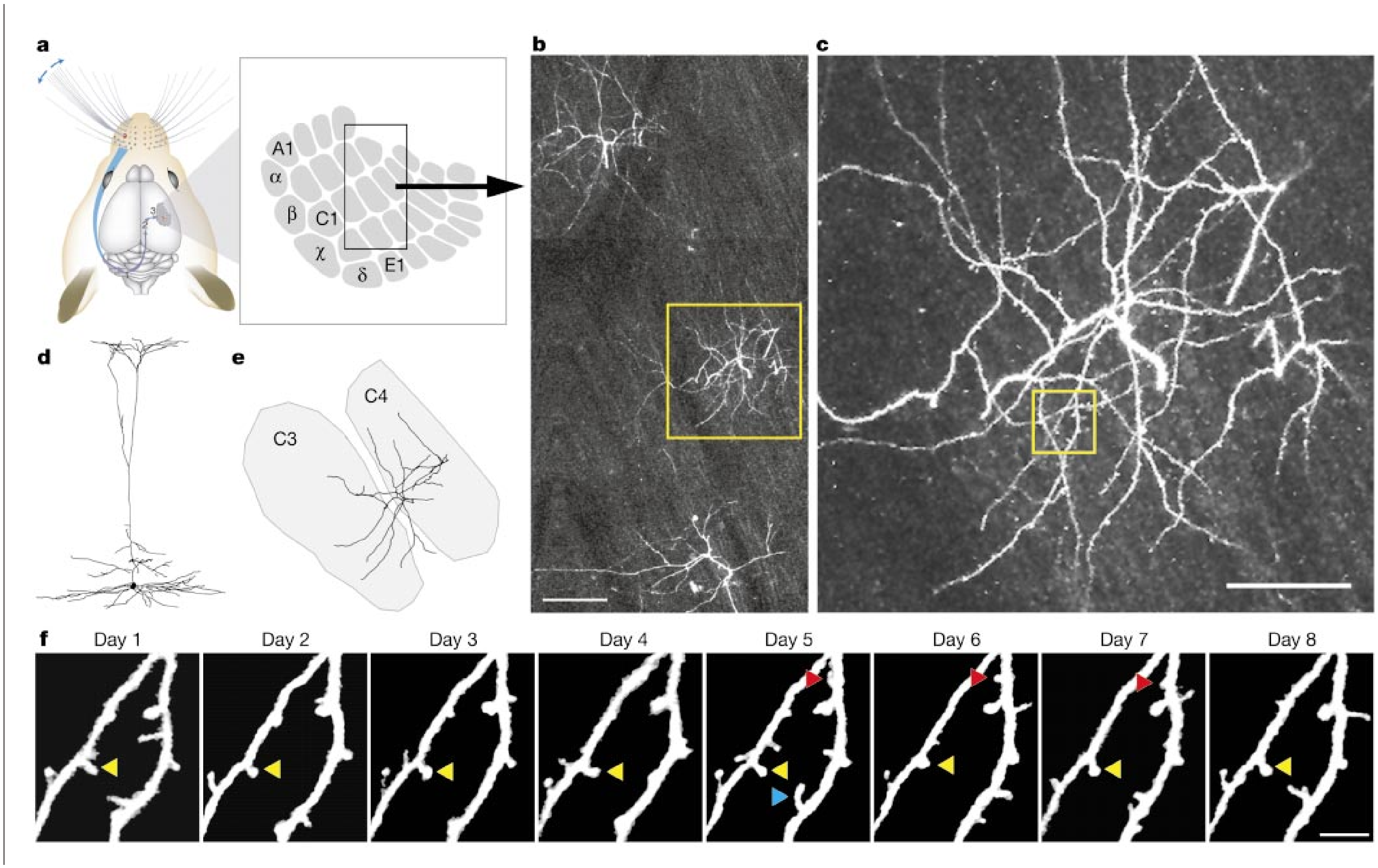
filling fraction = 3/7

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

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

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

Occam’s Razor

entities should not be multiplied without necessity.

奥卡姆剃刀定律

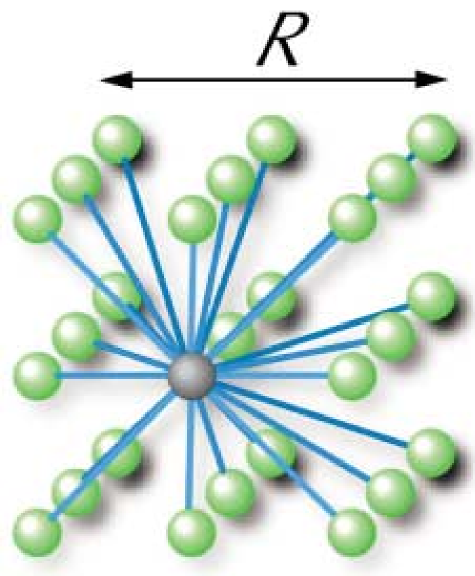
如无必要，勿增实体。简单有效原理。《箴言书注》：切勿浪费较多东西去做，用较少的东西，同样可以做好的事情。

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

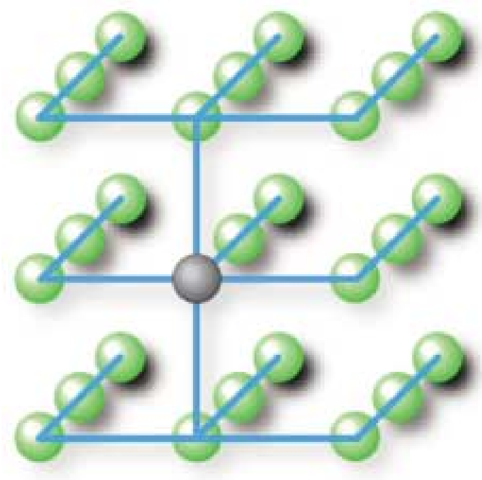
Why do we need axons and dendrites?



N: number of neurons
d: process diameter
R: network linear size

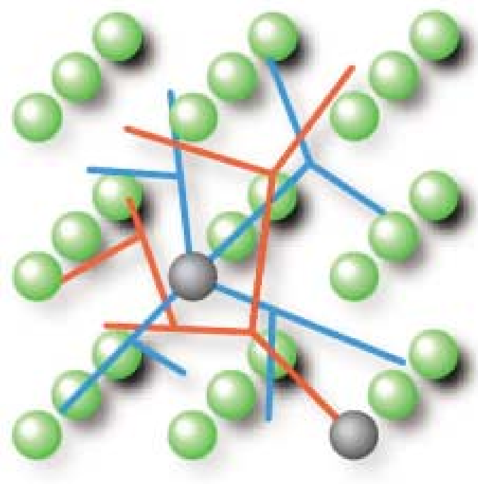
Design I

Why do we need axons and dendrites?



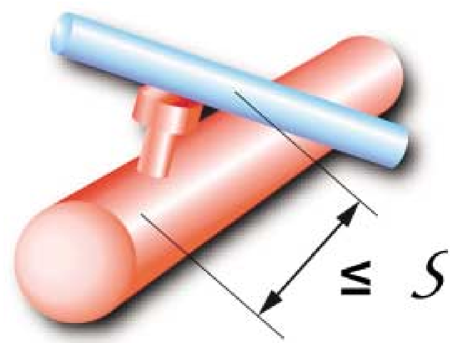
Design II

Why do we need axons and dendrites?



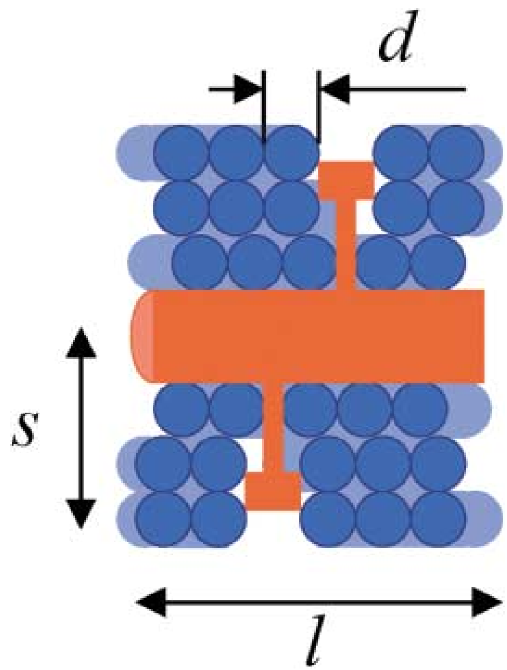
Design III

Why do we need axons and dendrites?



Design IV

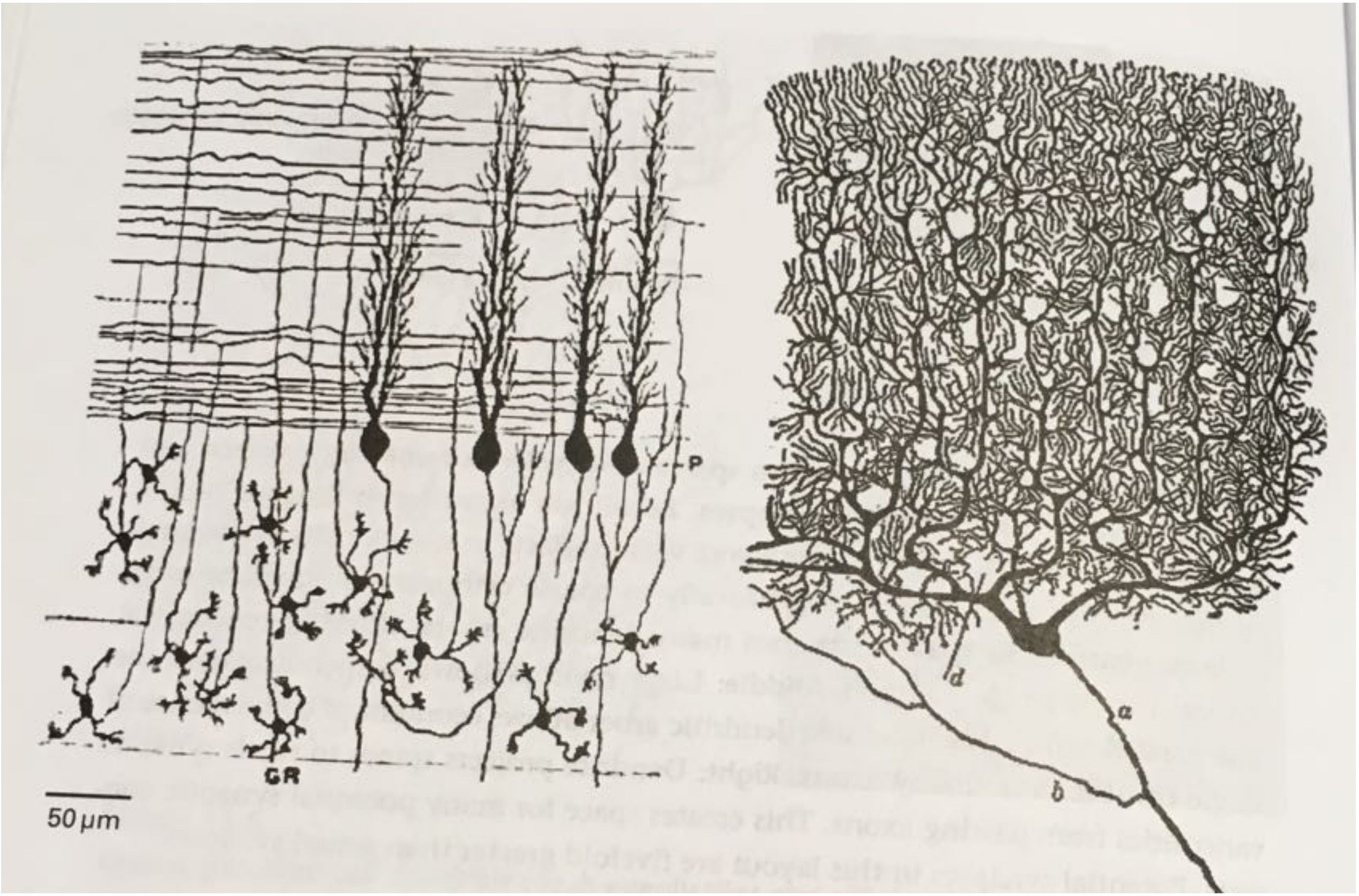
Why do we need axons and dendrites?



The Optimality of the design

Chklovskii *Neuron* 2004

The cerebellar cortex



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

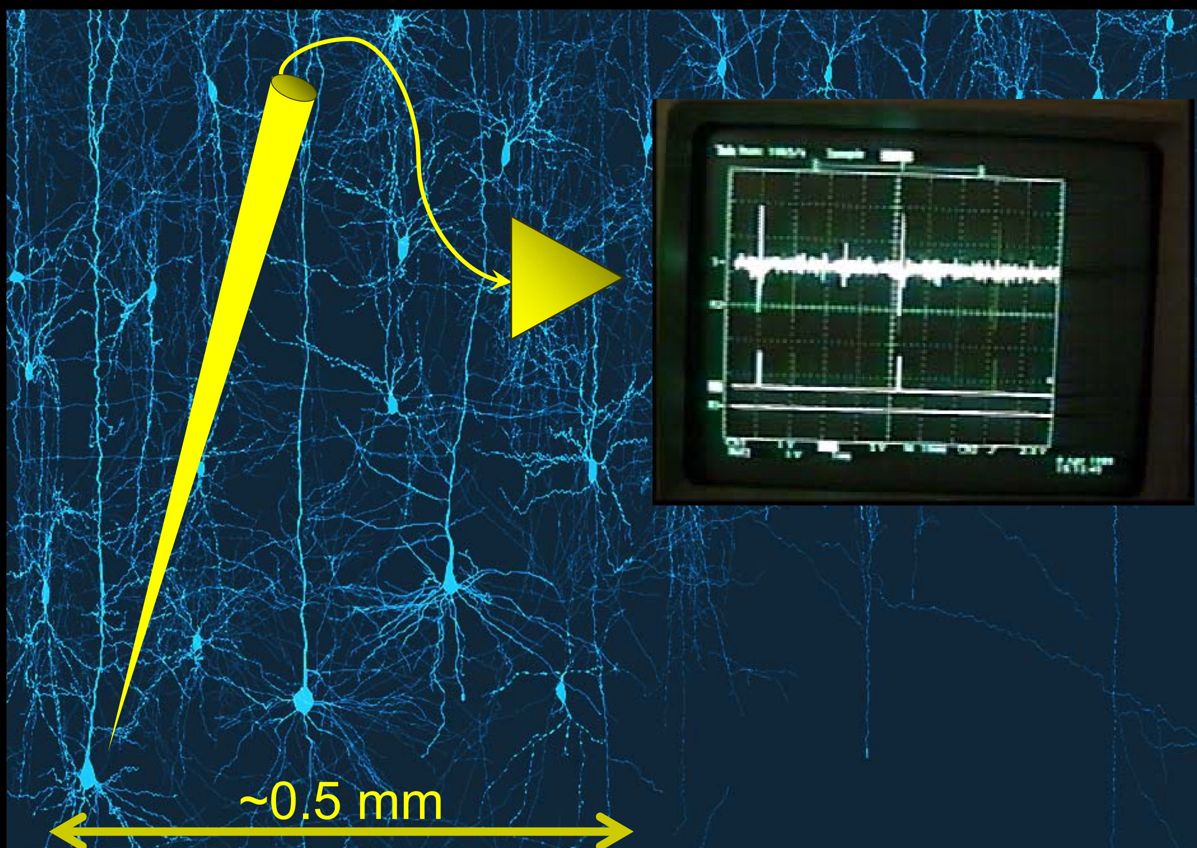
Can Single Neurons Solve MNIST? The Computational Power of Biological Dendritic Trees

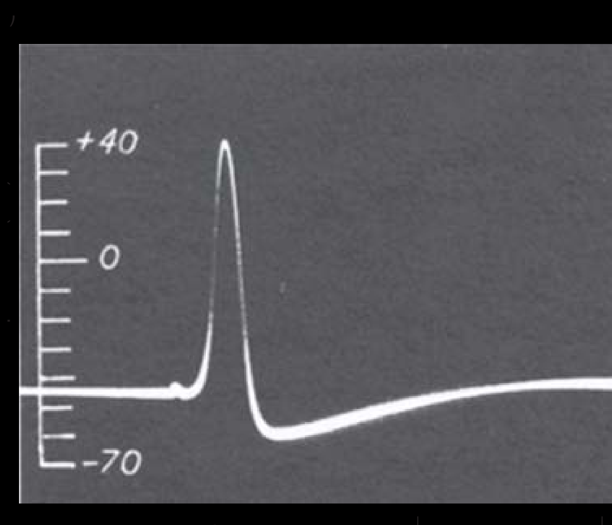
Ilenna Simone Jones[1] and Konrad Kording[2]

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

September 4, 2020

Action potential



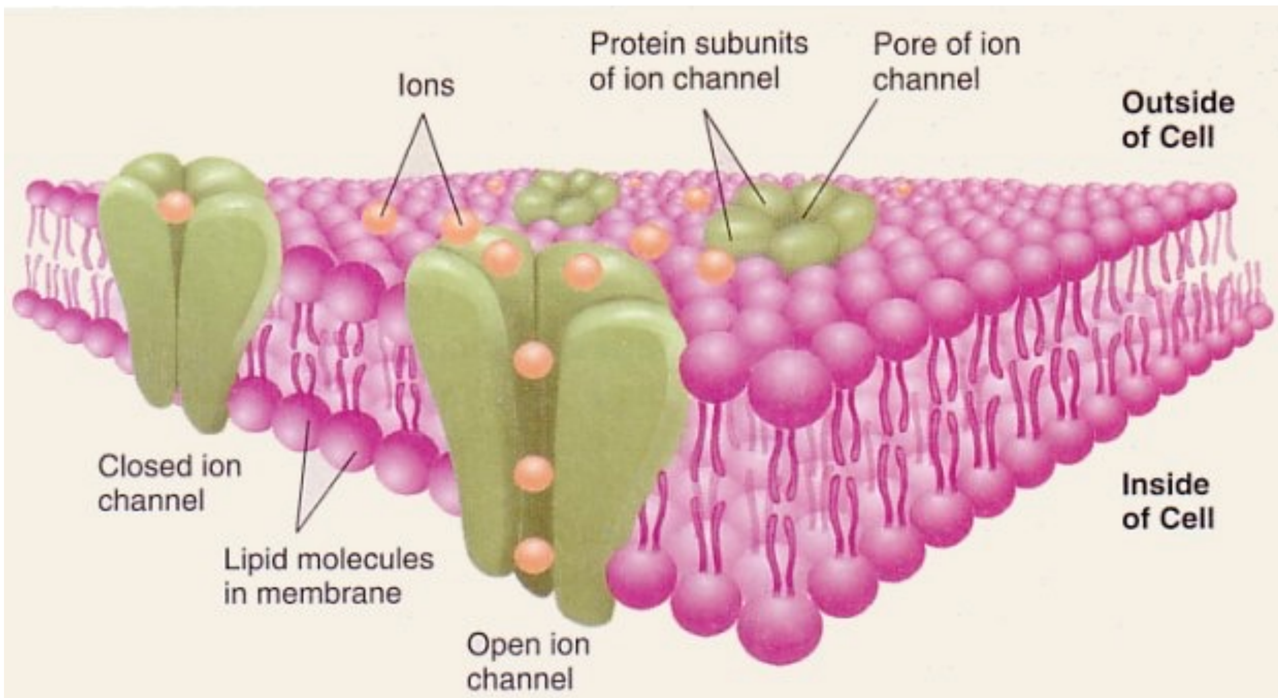


2 ms

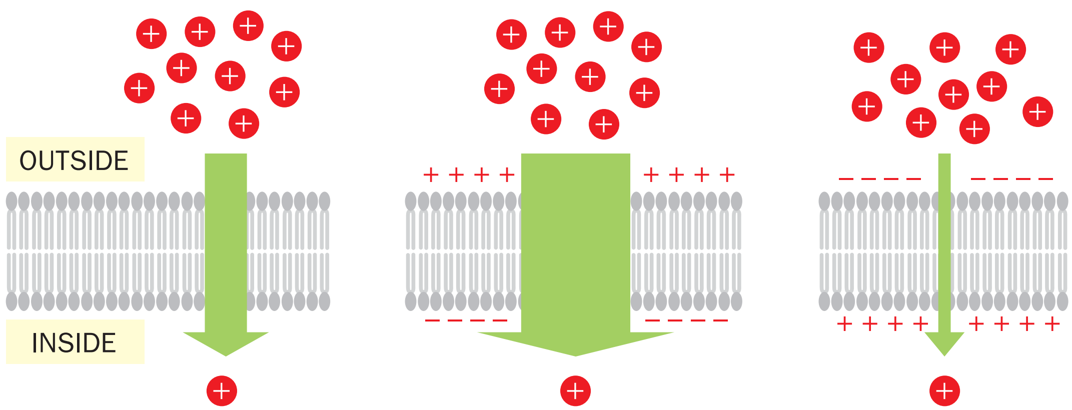
How does a neuron generate an action potential?

Single Neuron Dynamics

— point neuron model


Ions
Protein subunits of ion channel
Pore of ion channel
Outside of Cell
Closed ion channel
Lipid molecules in membrane
Open ion channel
Inside of Cell

What determines the resting potential of a neuron?



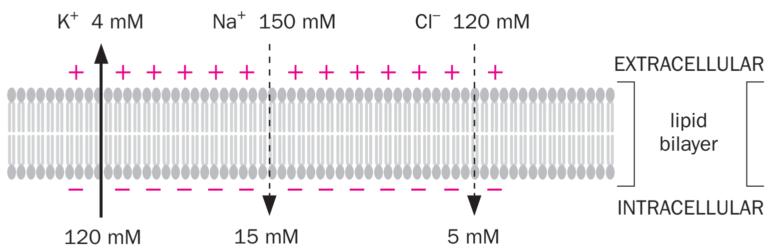
chemical gradient alone; no membrane potential

chemical gradient and electrical gradient driving ion movement in the same direction

chemical gradient and electrical gradient driving ion movement in opposing directions

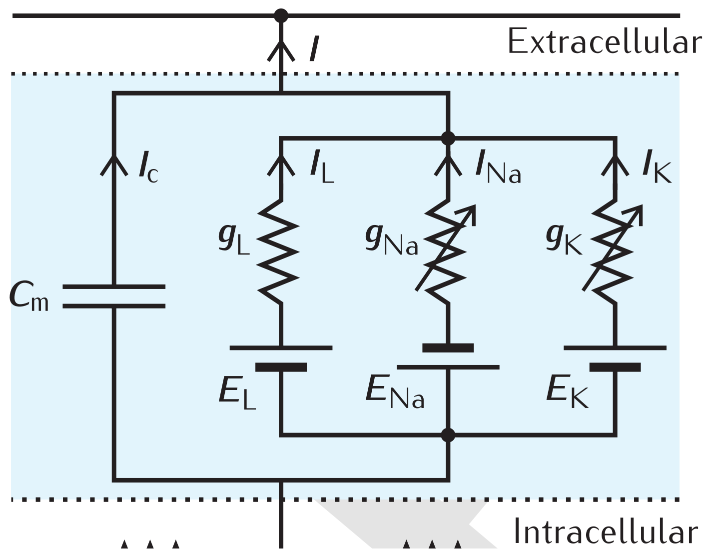
Ion pump

(A)



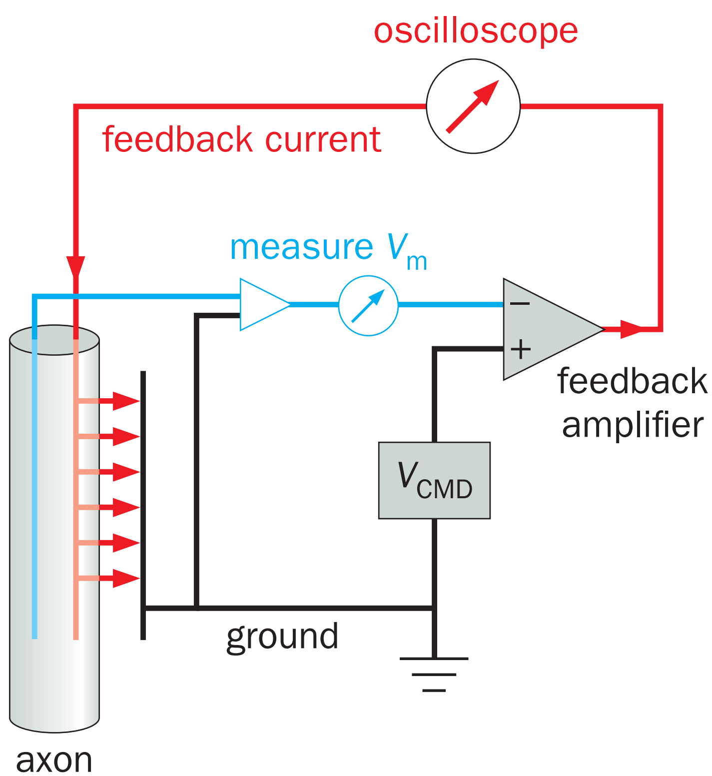
K+ 4 mM
Na+ 150 mM
Cl− 120 mM
EXTRACELLULAR
lipid bilayer
INTRACELLULAR
120 mM
15 mM
5 mM

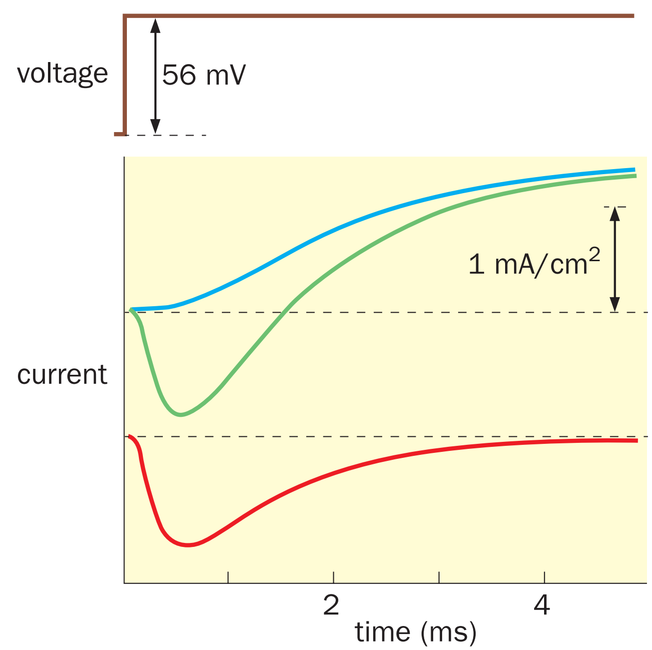
The Equivalent Electronic Circuit of a Neuron



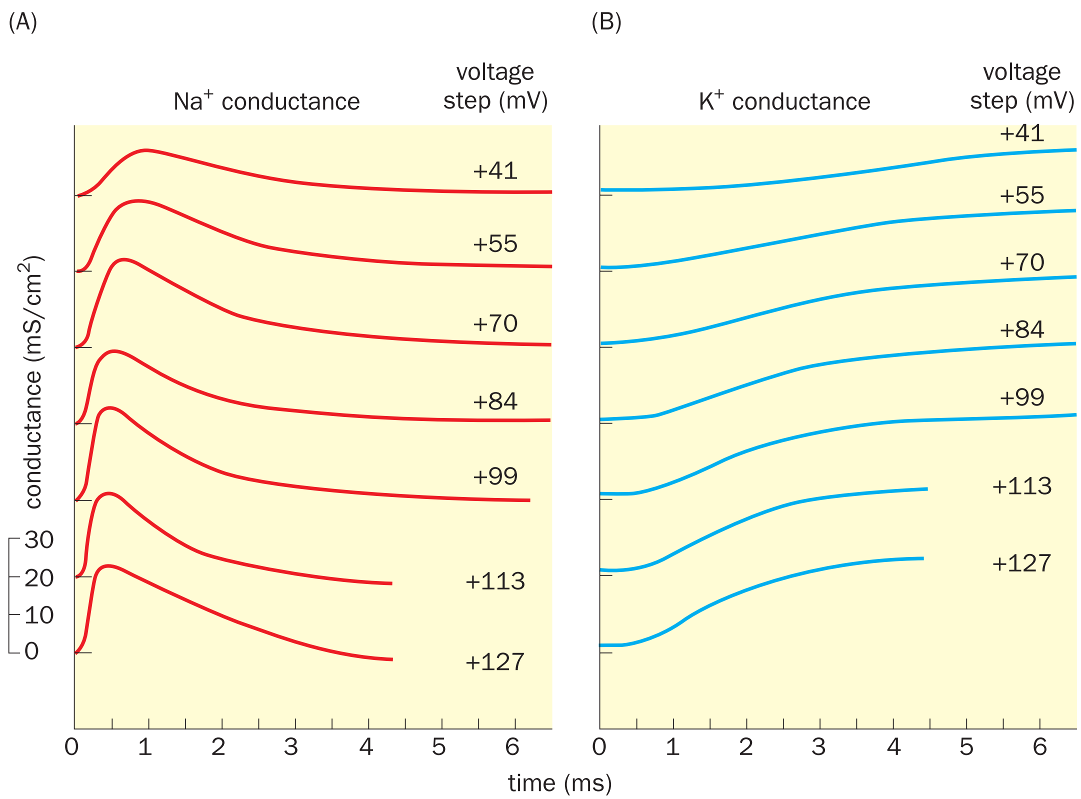
$$C_m \frac{dV}{dt} = -\sum_i g_i(V)(V - E_i) - \bar{g}_L(V - E_L) + I_e$$

Voltage Clamp Recording





Voltage-gated Conductance



Qualitative explanation of action potential generation