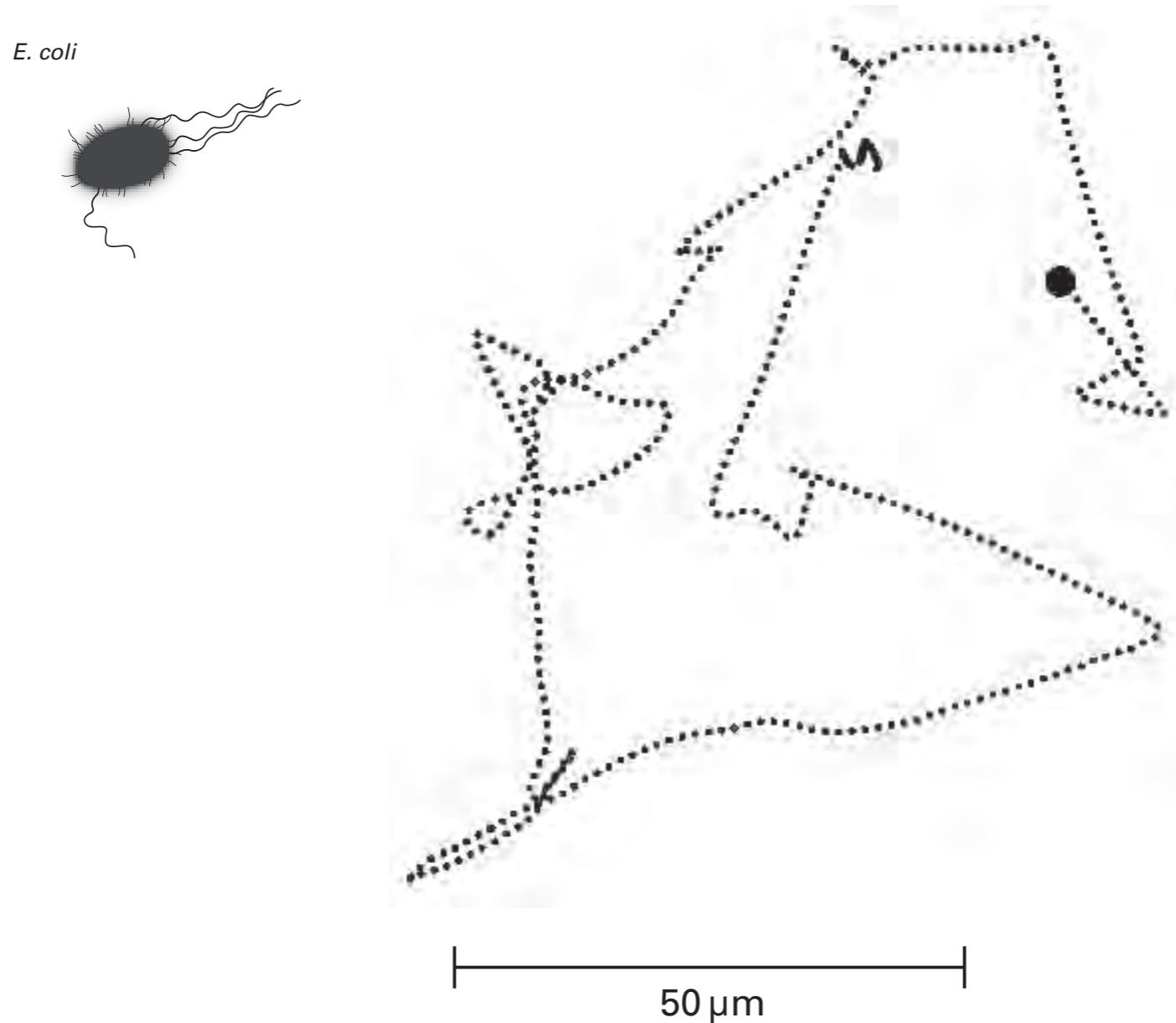


Connecting Neurons to Perform Computation

E. coli's biased random walk

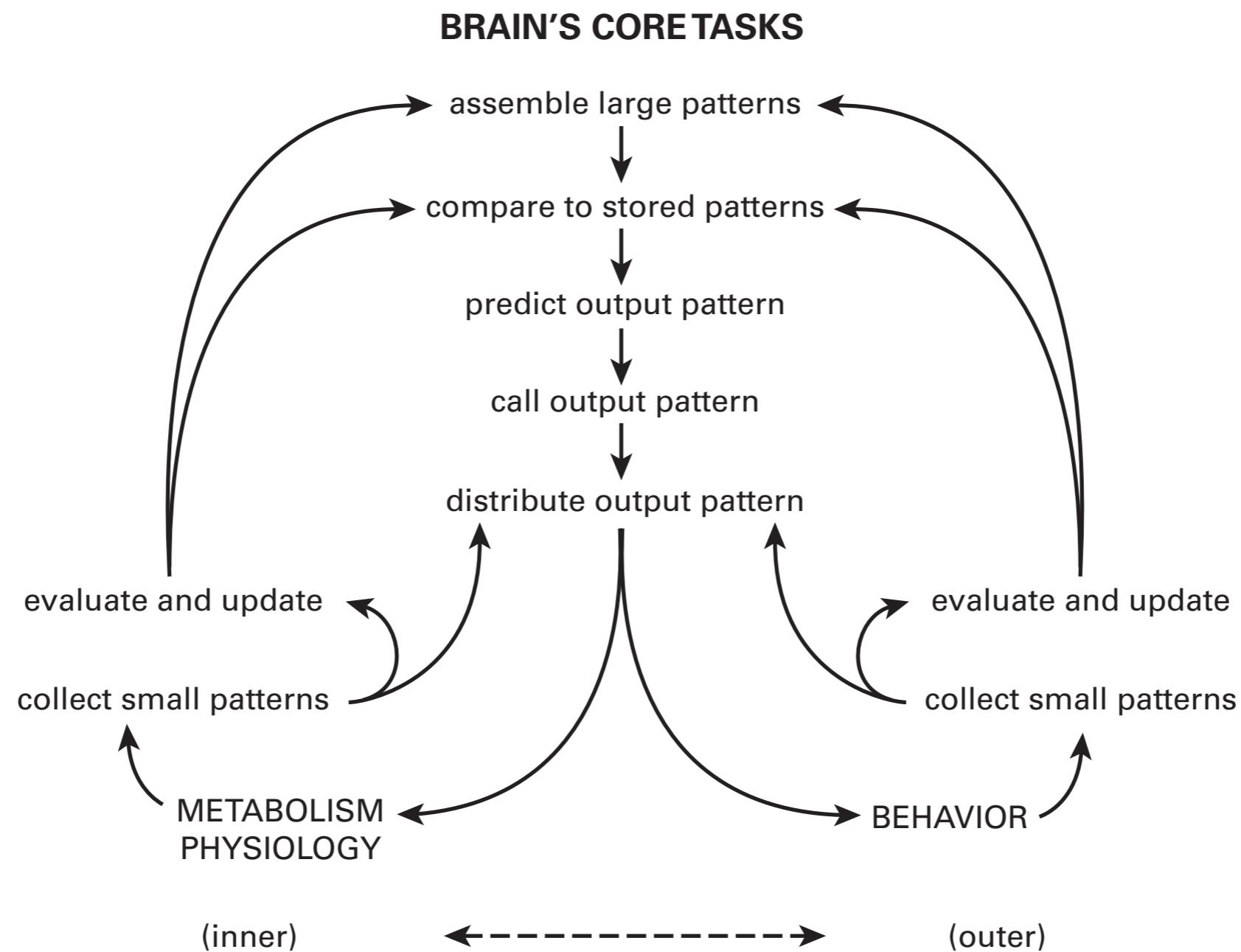


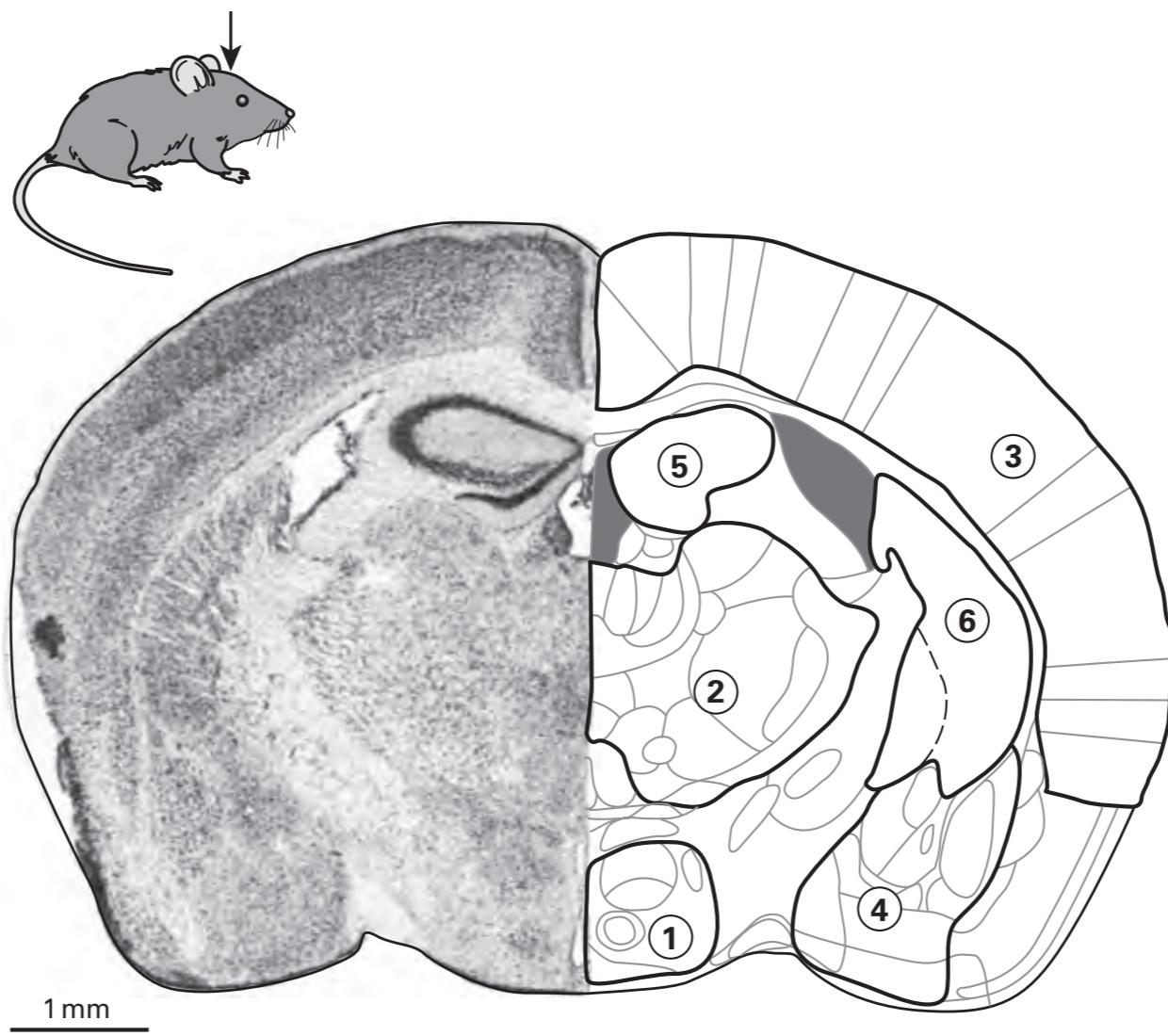
If life is getting better, enjoy more;
If life is getting worse, don't worry about it.

Why do we need a brain?

My brain is my second favorite organ.

Woody Allen

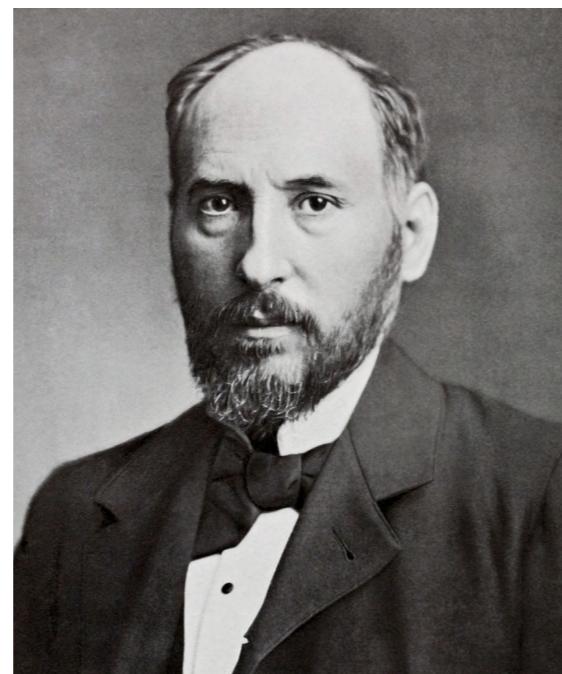




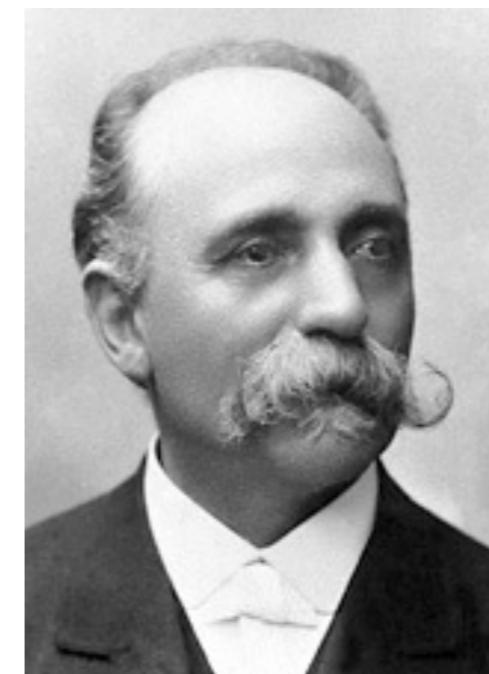
- ① Generate patterns for wireless signaling and appetitive behaviors.
- ② “Preprocessing” to shape signals for higher processing.
- ③ High-level processing: assemble larger patterns, choose behaviors.
- ④ “Tag” high-level patterns for emotional significance.
- ⑤ Store and recall.
- ⑥ Evaluate reward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

Principles of Neural Design

The Debate between Cajal and Golgi

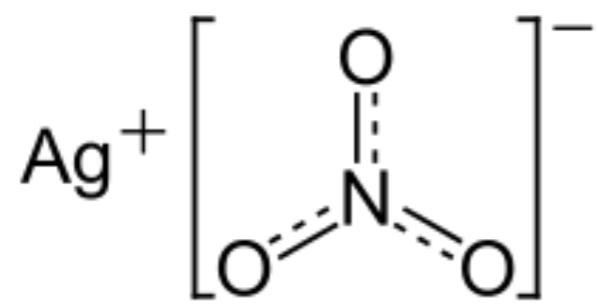


Ramon y Cajal

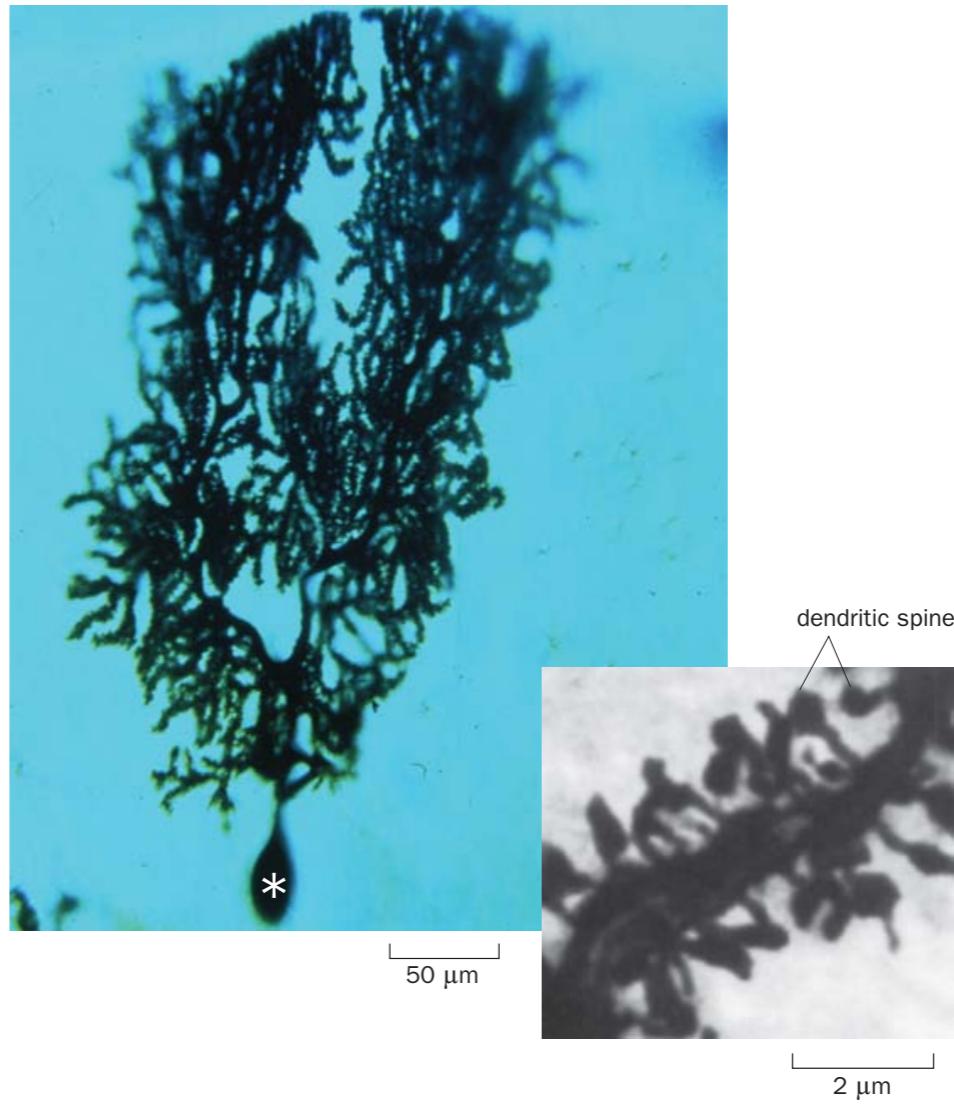


Camillo Golgi

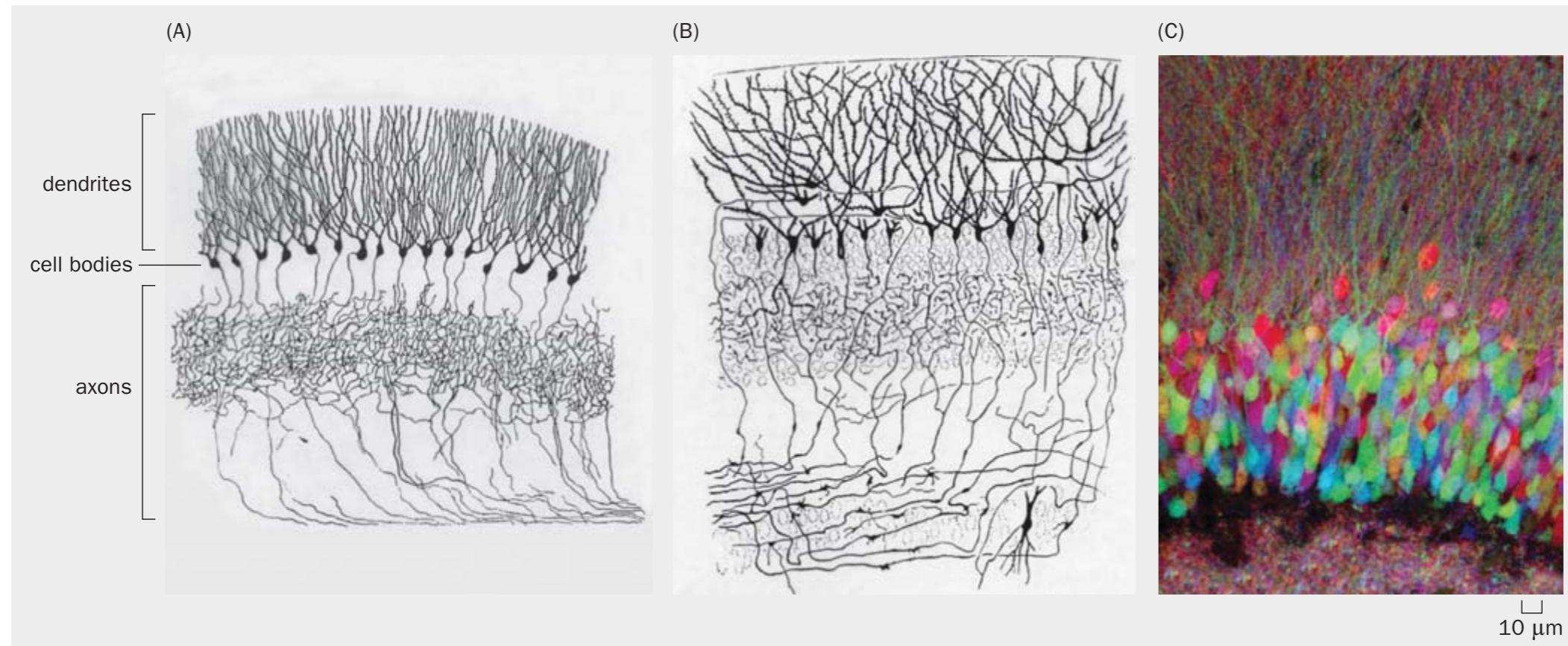
Golgi Staining method



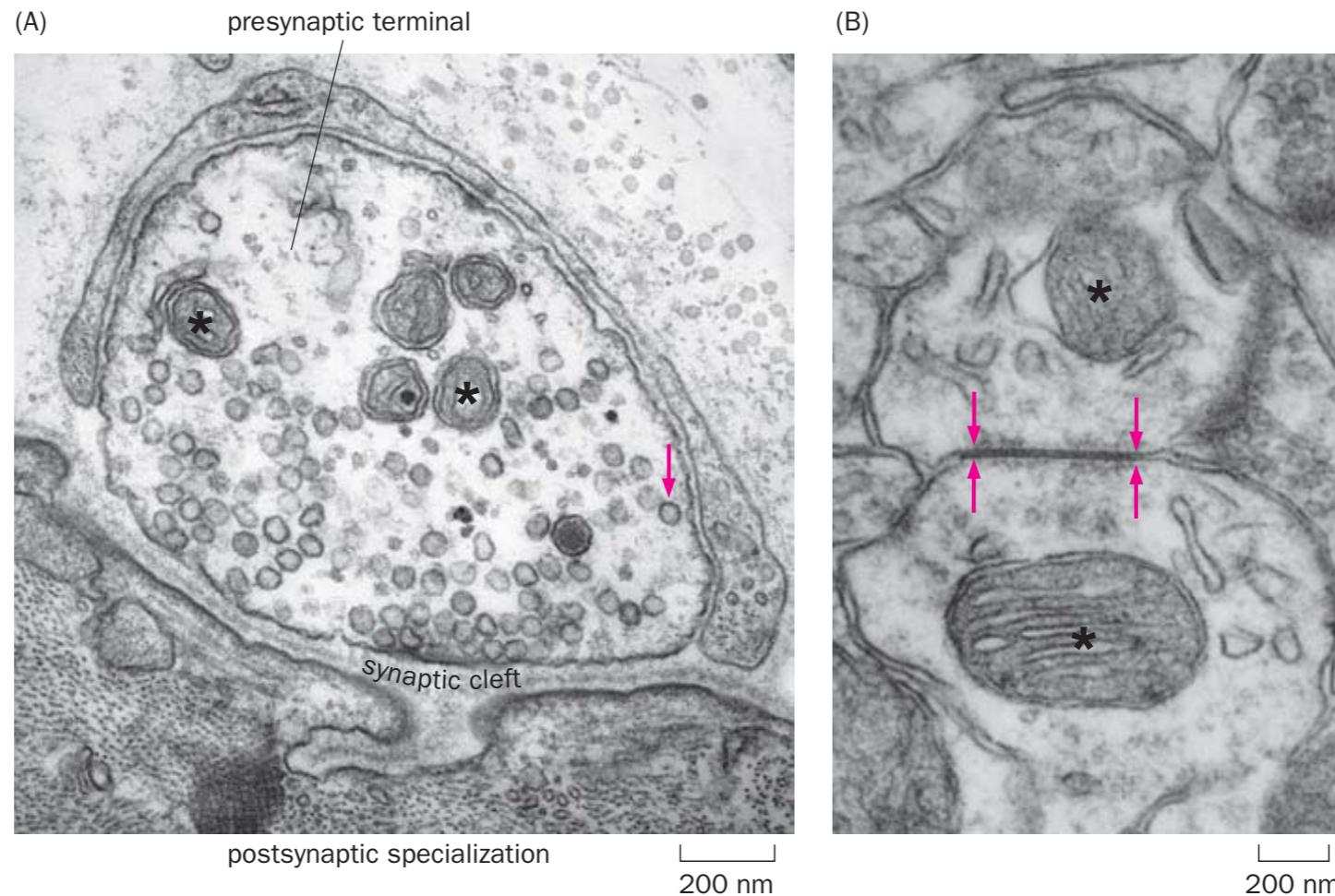
**Silver
nitrate**



Reticular Theory vs Neuron Doctrine

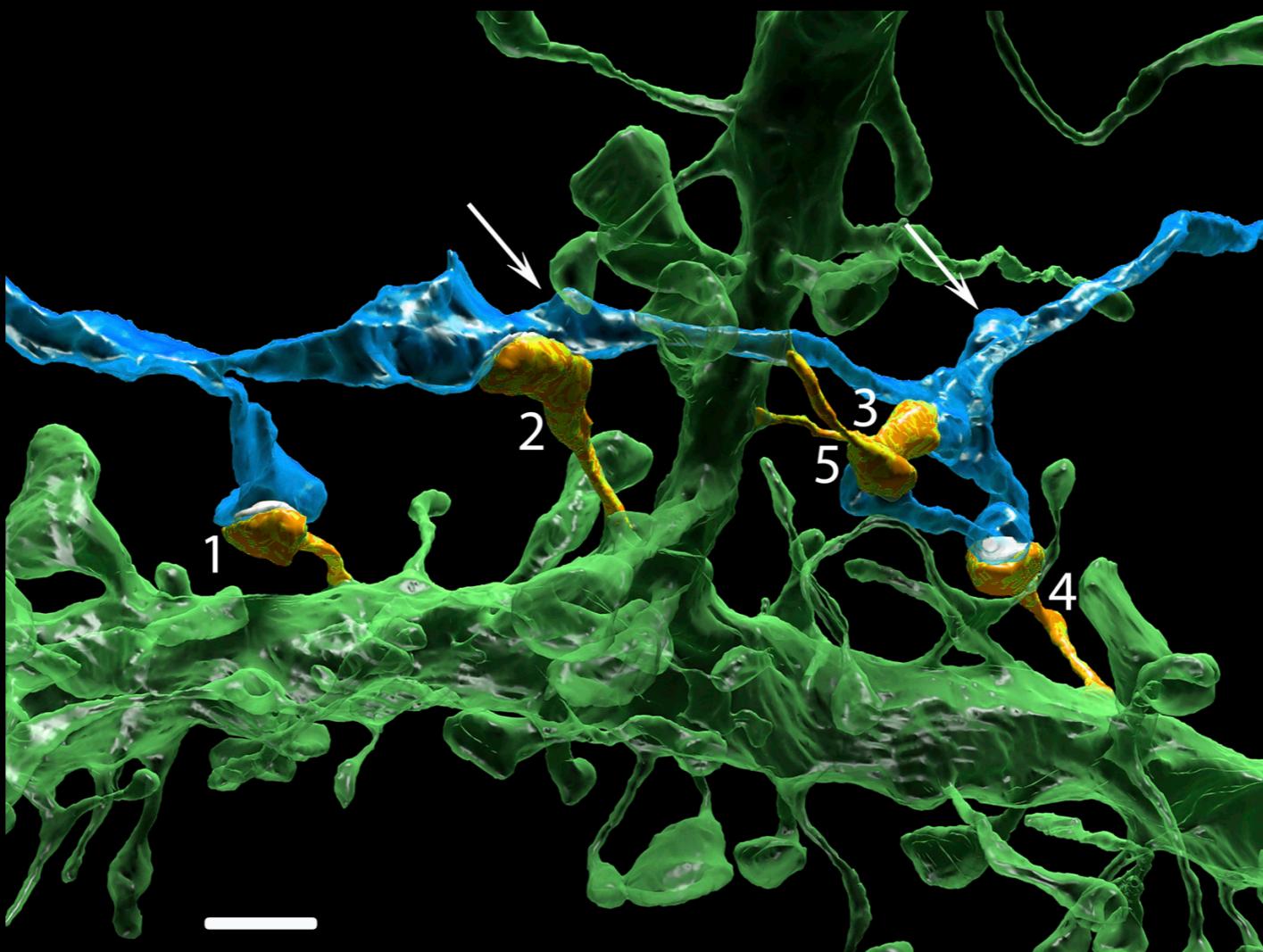


How neurons communicate with each other?



Chemical and electrical synapses

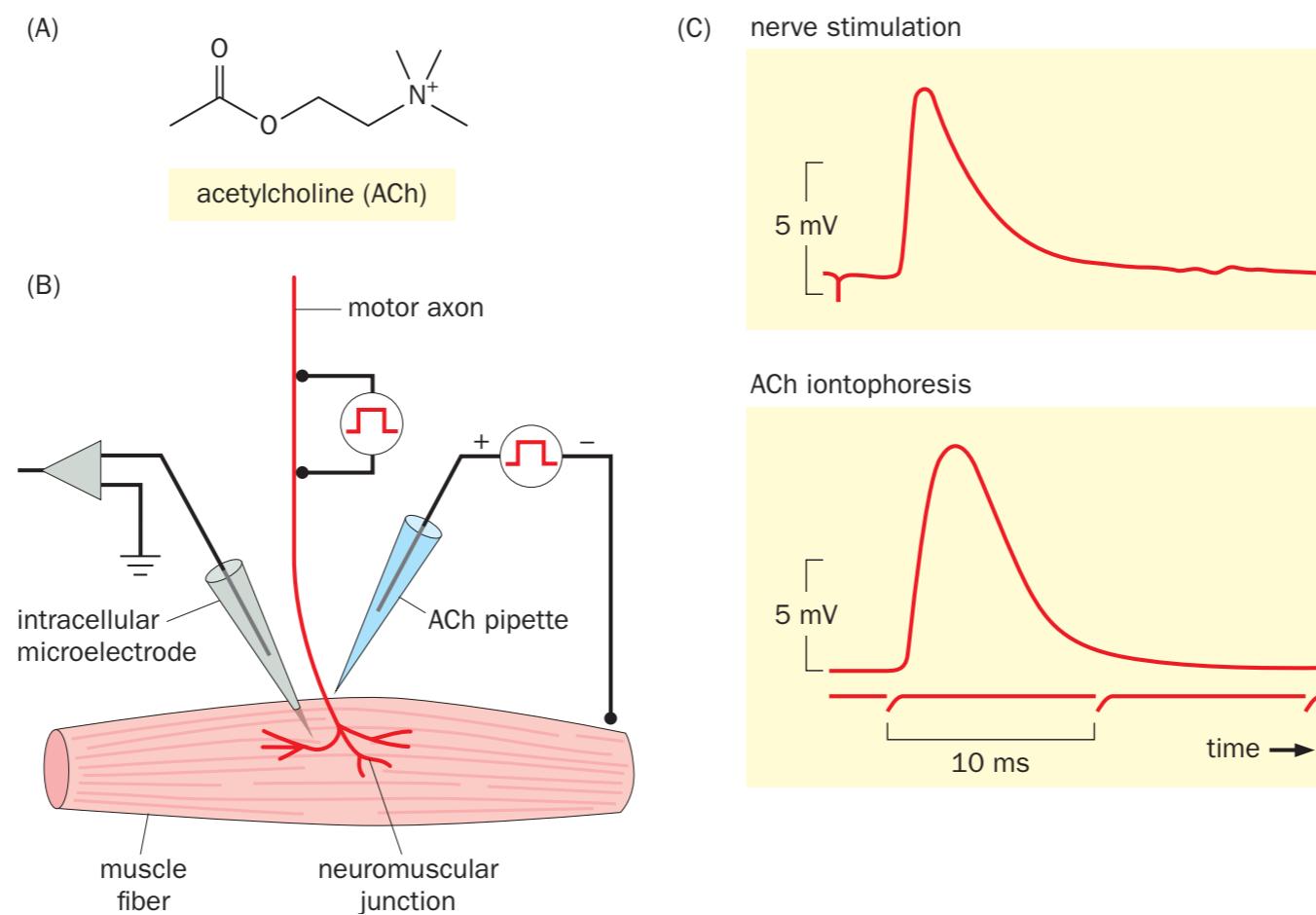
Synaptic Connectivity



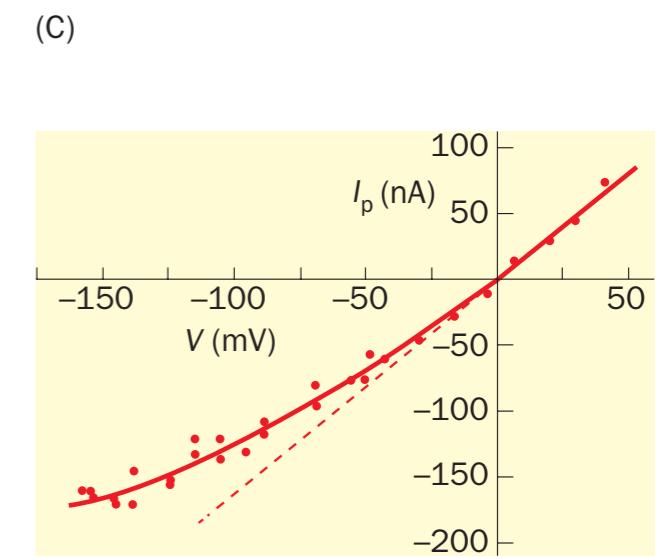
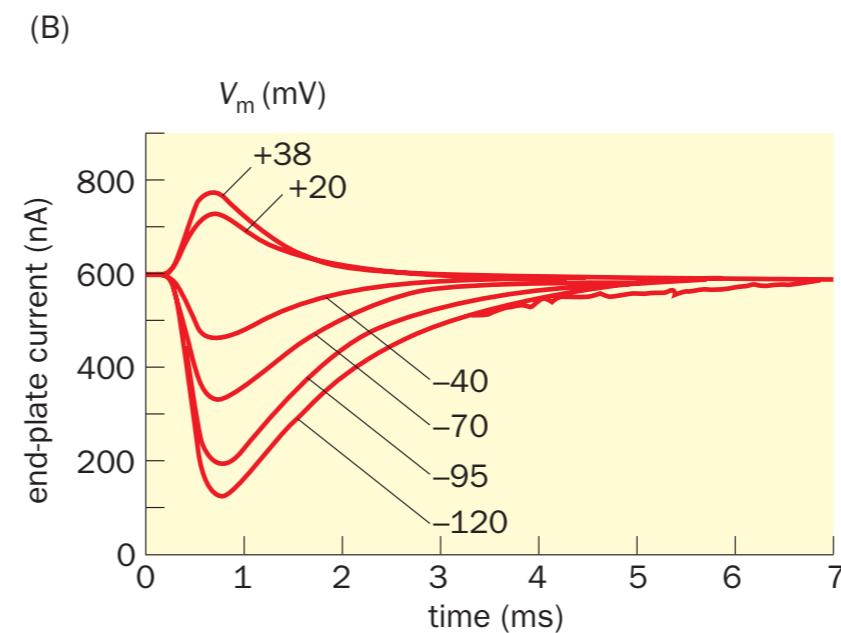
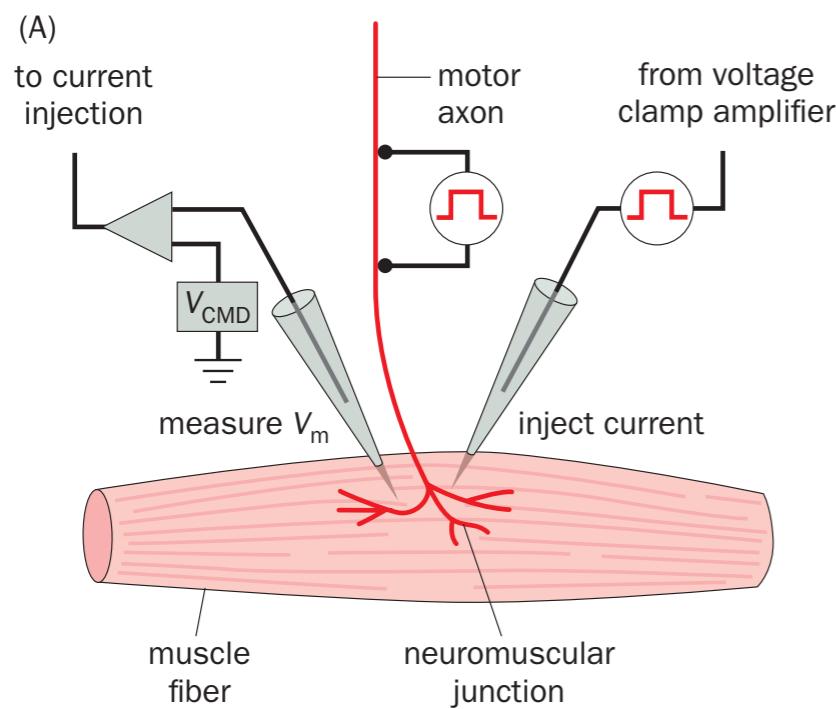
Kasthuri et. al, Cell 2015

Synaptic Transmission

Neurotransmitter release evokes membrane potential change in the postsynaptic neuron



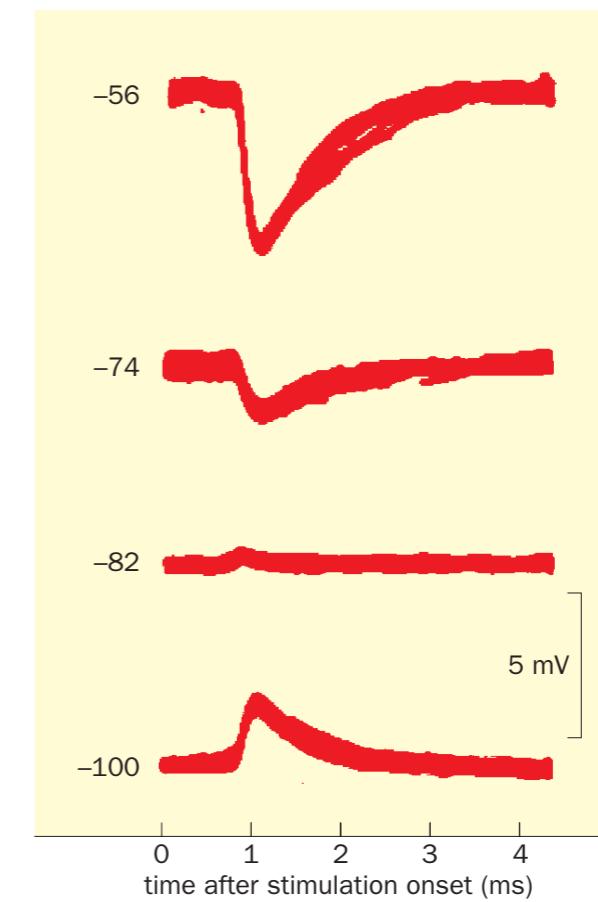
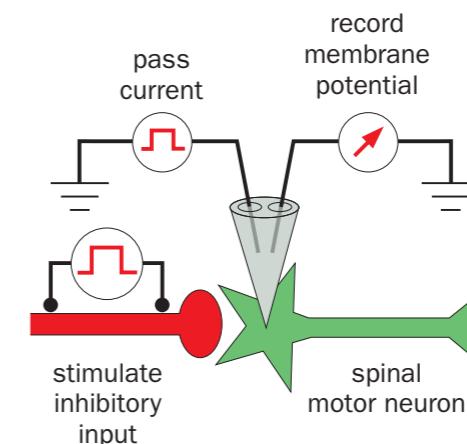
Reversal potential of a synapse



Excitatory and Inhibitory Synapses

Table 3–2: Commonly used neurotransmitters

Neurotransmitter	Major uses in the vertebrate nervous system ¹
Acetylcholine	motor neurons that excite muscle; ANS ² neurons; CNS excitatory and modulatory neurons
Glutamate	most CNS excitatory neurons; most sensory neurons
GABA	most CNS inhibitory neurons
Glycine	some CNS inhibitory neurons (mostly in the brainstem and spinal cord)
Serotonin (5-HT)	CNS modulatory neurons
Dopamine	CNS modulatory neurons
Norepinephrine	CNS modulatory neurons; ANS ² neurons
Histamine	CNS modulatory neurons
Neuropeptides	usually co-released from excitatory, inhibitory, or modulatory neurons; neurosecretory cells

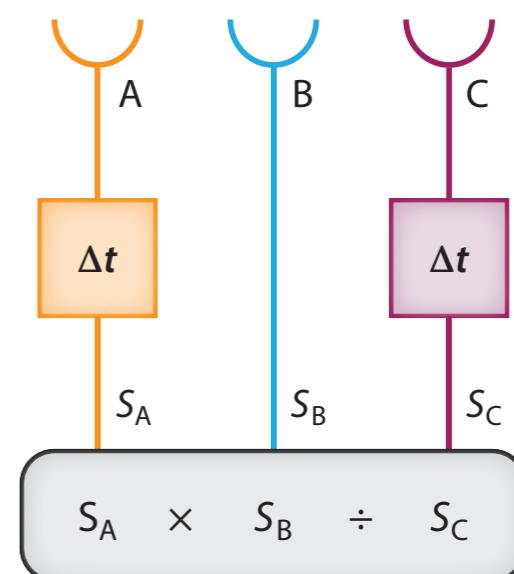
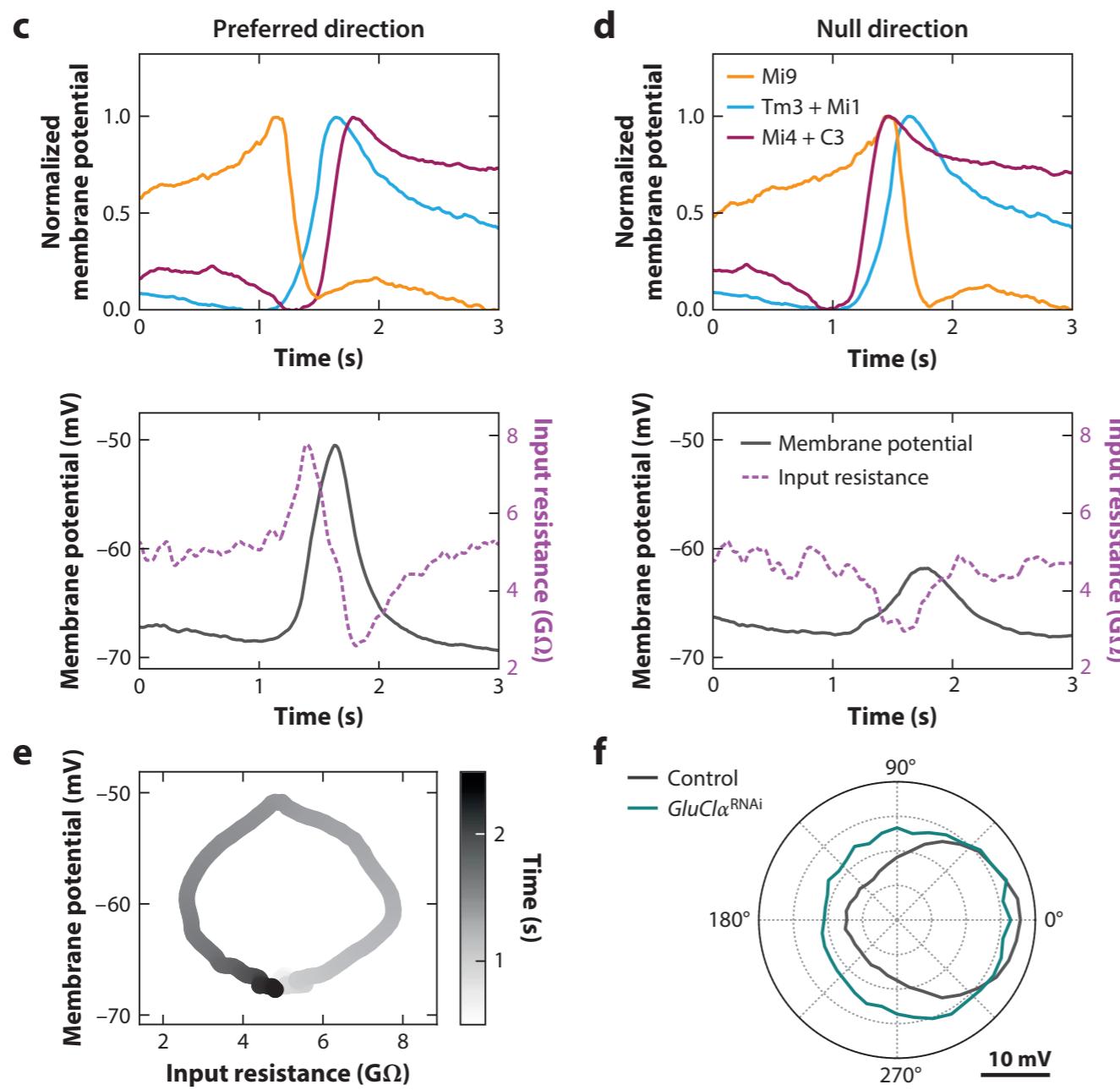
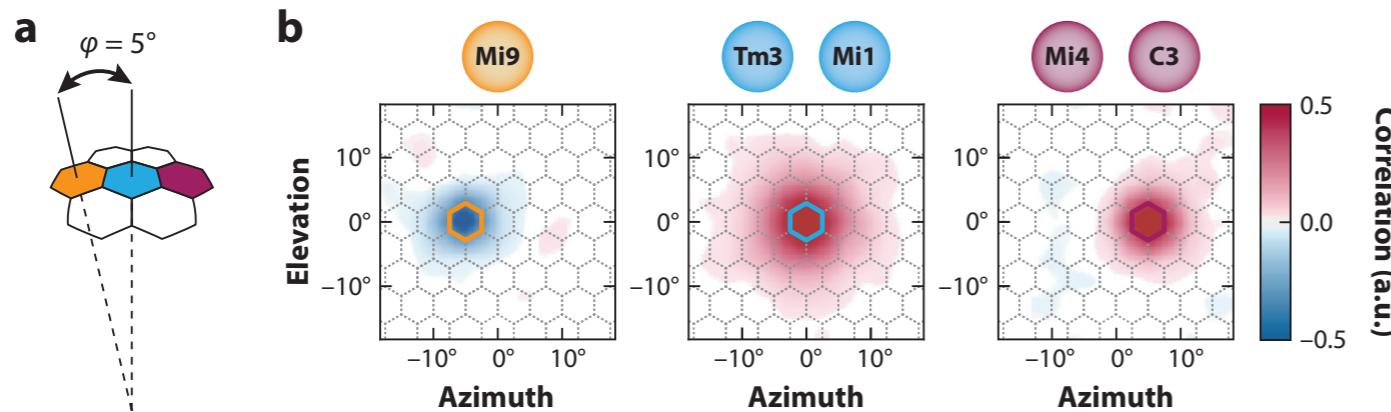


Shunting inhibition and divisive operation

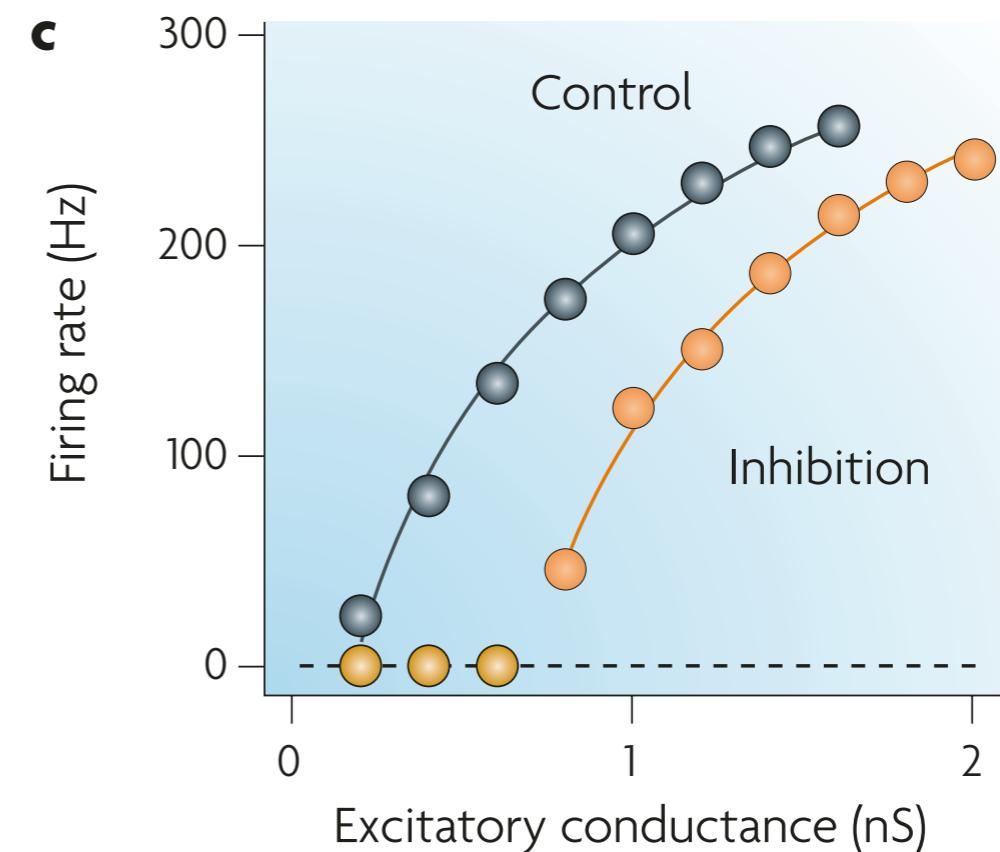
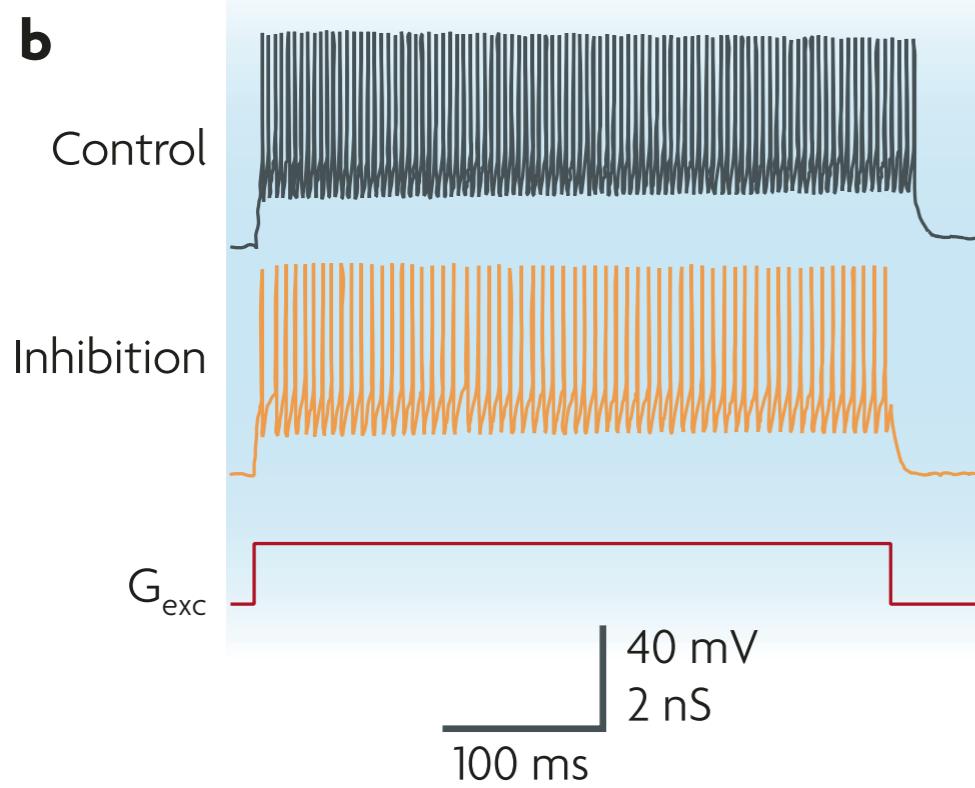
$$C_m \frac{dV}{dt} = -g_L(V - E_L) - g_{inh}(V - E_L) - g_{exc}(V - E_0)$$

$$V = \frac{(g_L + g_{inh})E_L + g_{exc}E_0}{g_L + g_{inh} + g_{exc}}$$

$$g_{inh} \gg g_L + g_{exc} \quad V \approx E_L + \frac{g_{exc}}{g_{inh}} E_0$$

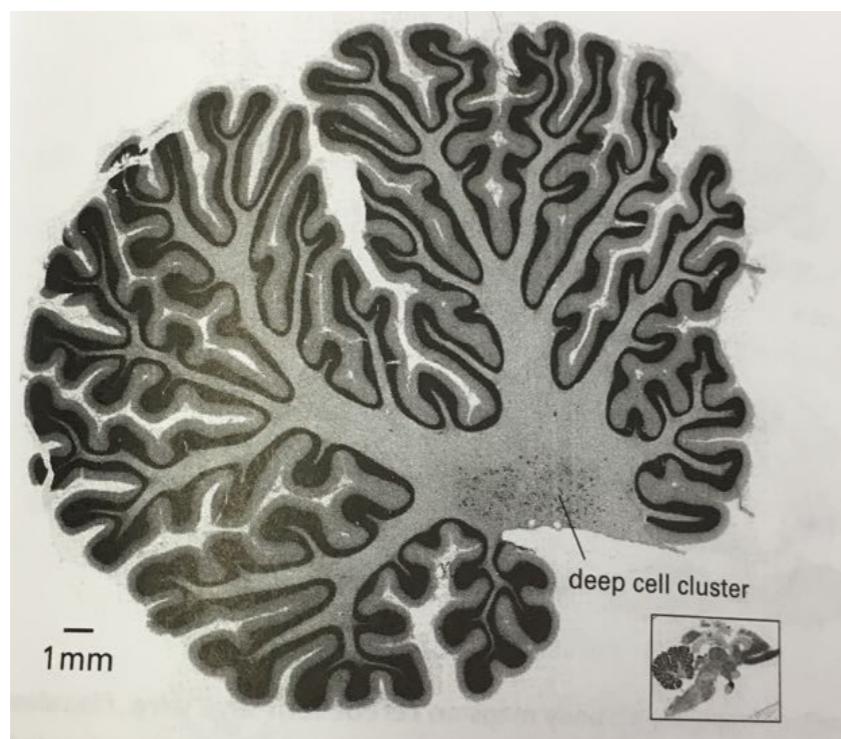


However, shunting inhibition becomes subtractive for firing rate

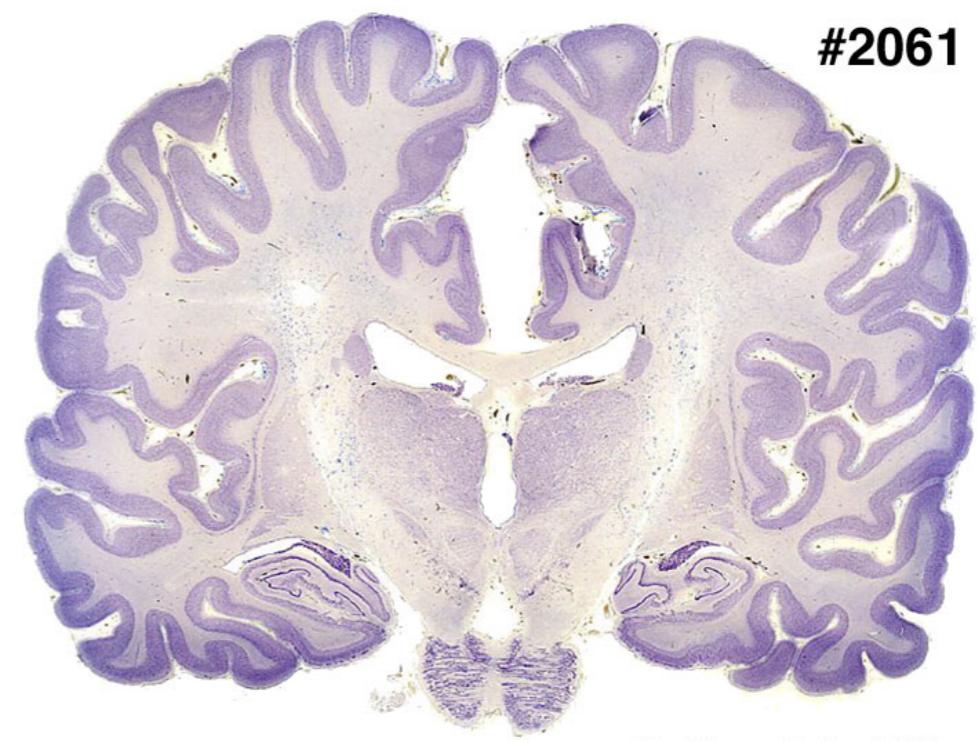


Why? (Your homework)

cerebral cortex vs. cerebellar cortex



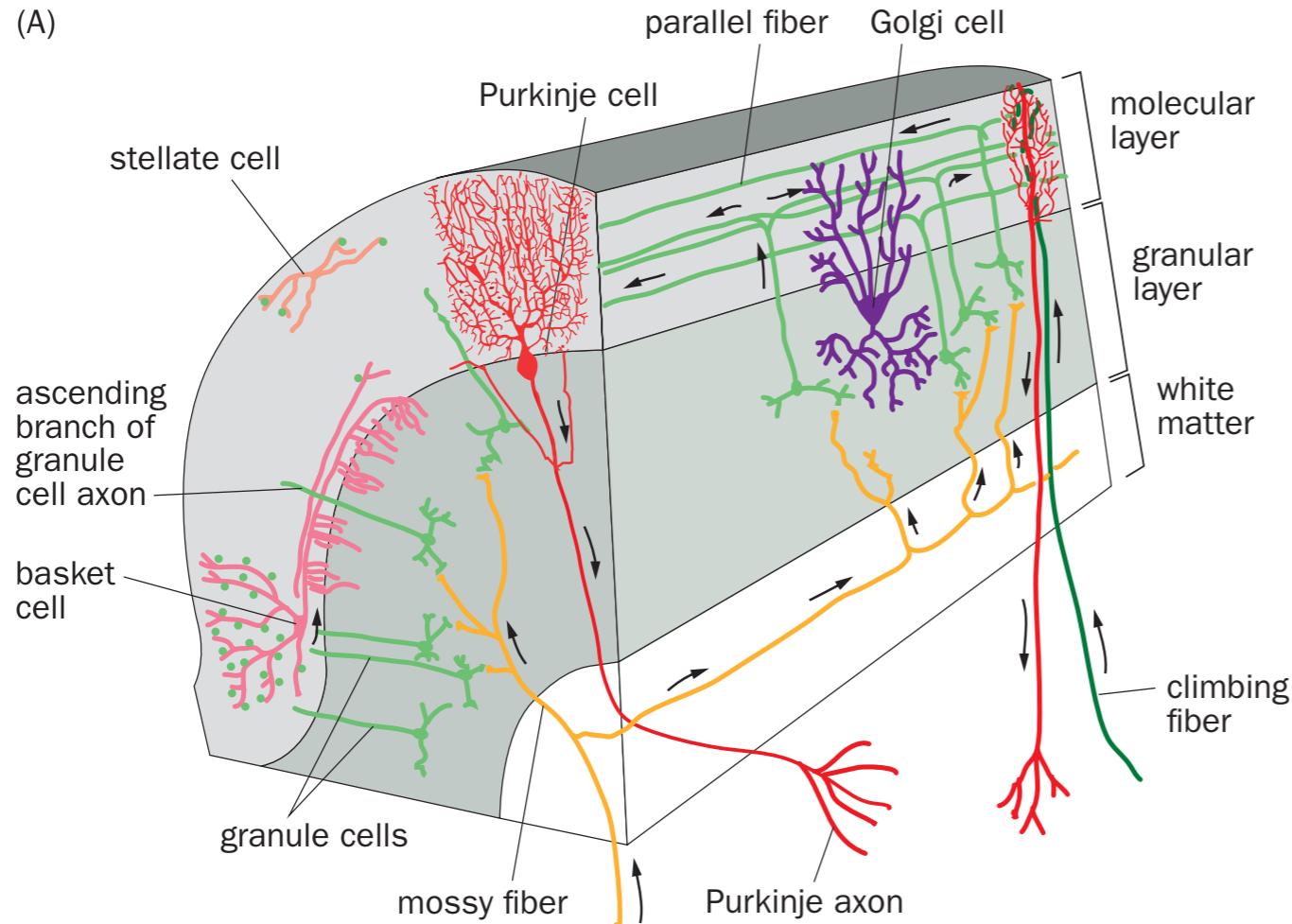
cerebellum



cerebral cortex

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

The organization of cerebellar cortex



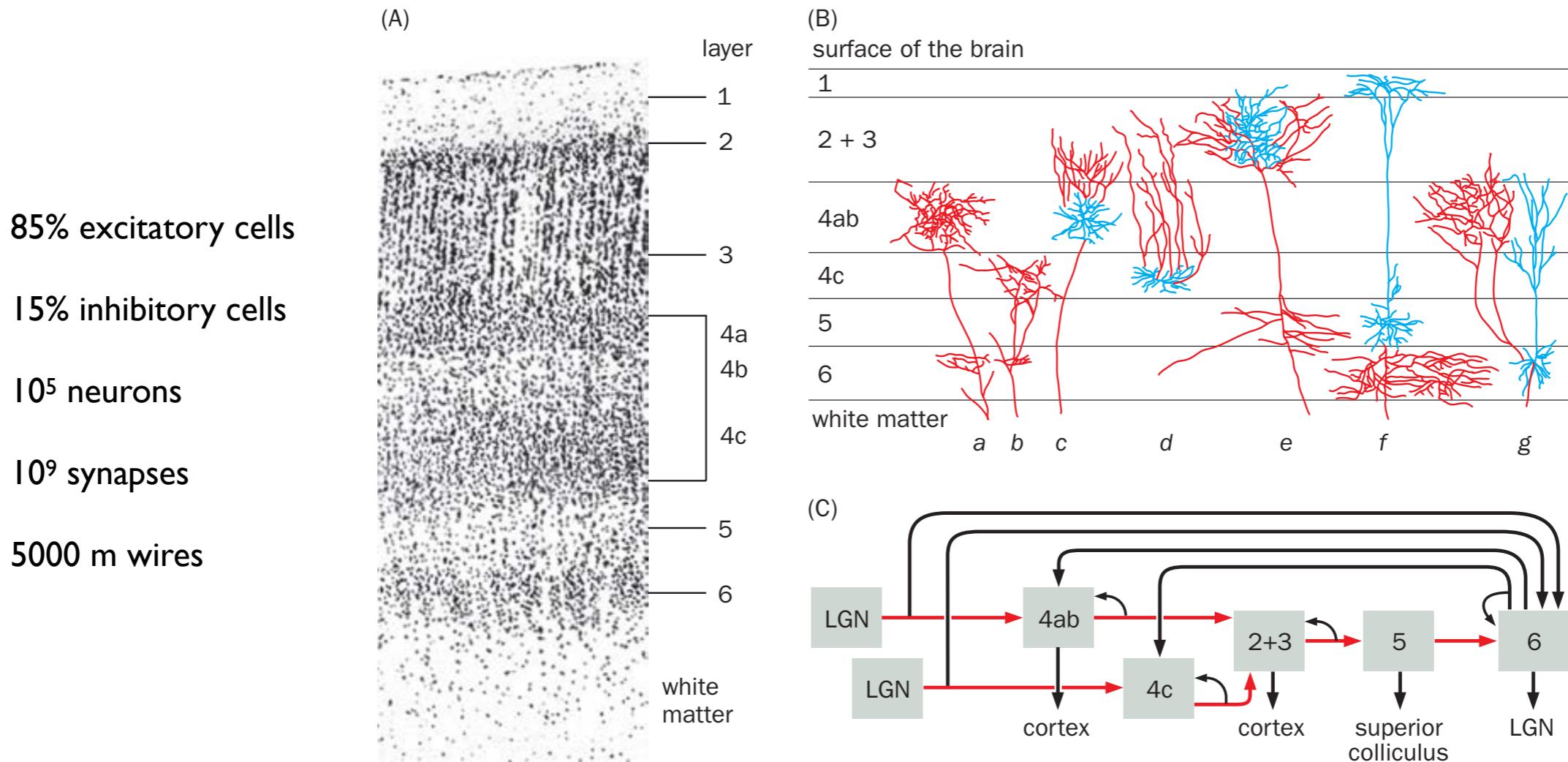
$$N_g D = N_p C$$

$$N_g \gg N_p$$

$$C \gg D$$

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

The organization of the cortical column





Why do we need axons and dendrites?

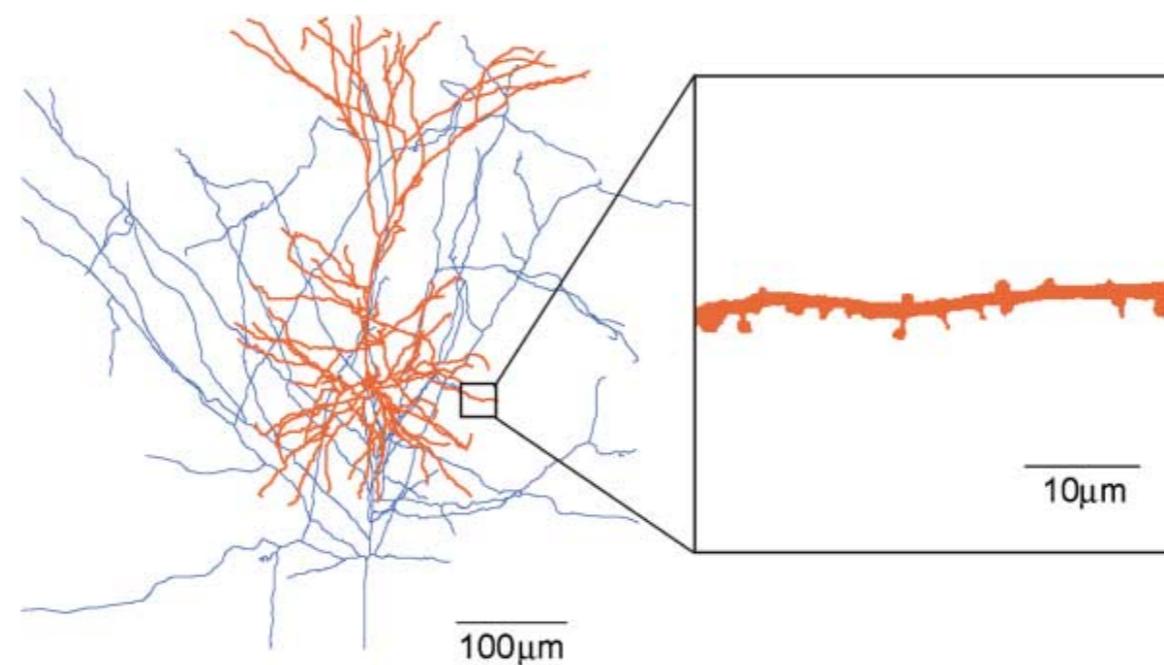


Wiring Optimization of Neural Circuit

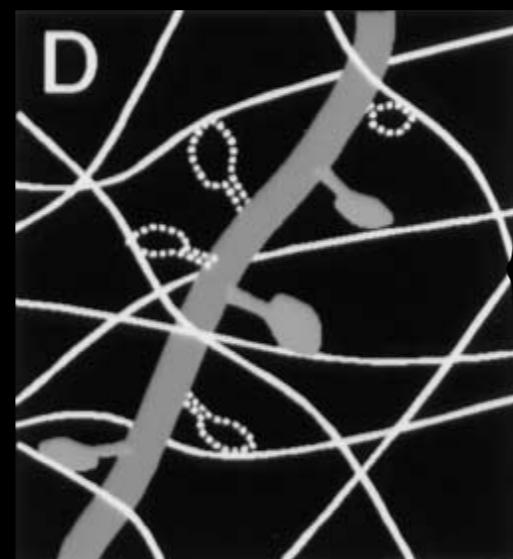
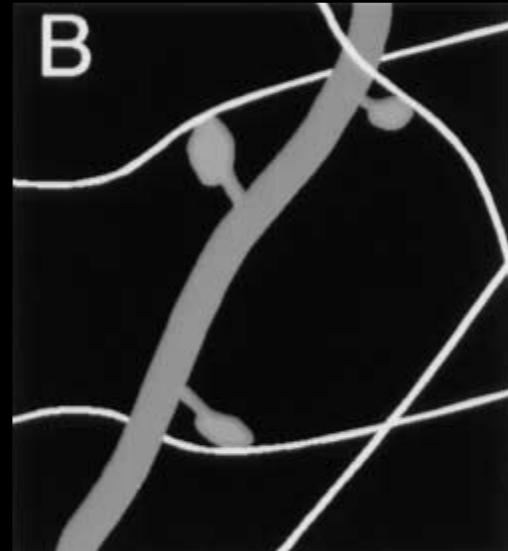
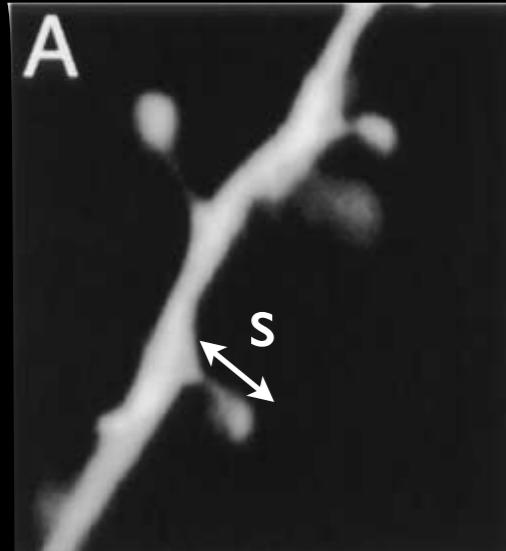
“After the many shapes assumed by neurons, we are now in a position to ask whether this diversity ... has been left to chance and is insignificant, or whether it is tightly regulated and provides an advantage to the organism. ... we realized that all of the various conformations of the neuron and its 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, dendrites and spines?



Structural Plasticity of Synaptic Connectivity



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

s: spine length

L_d : total dendritic length per neuron

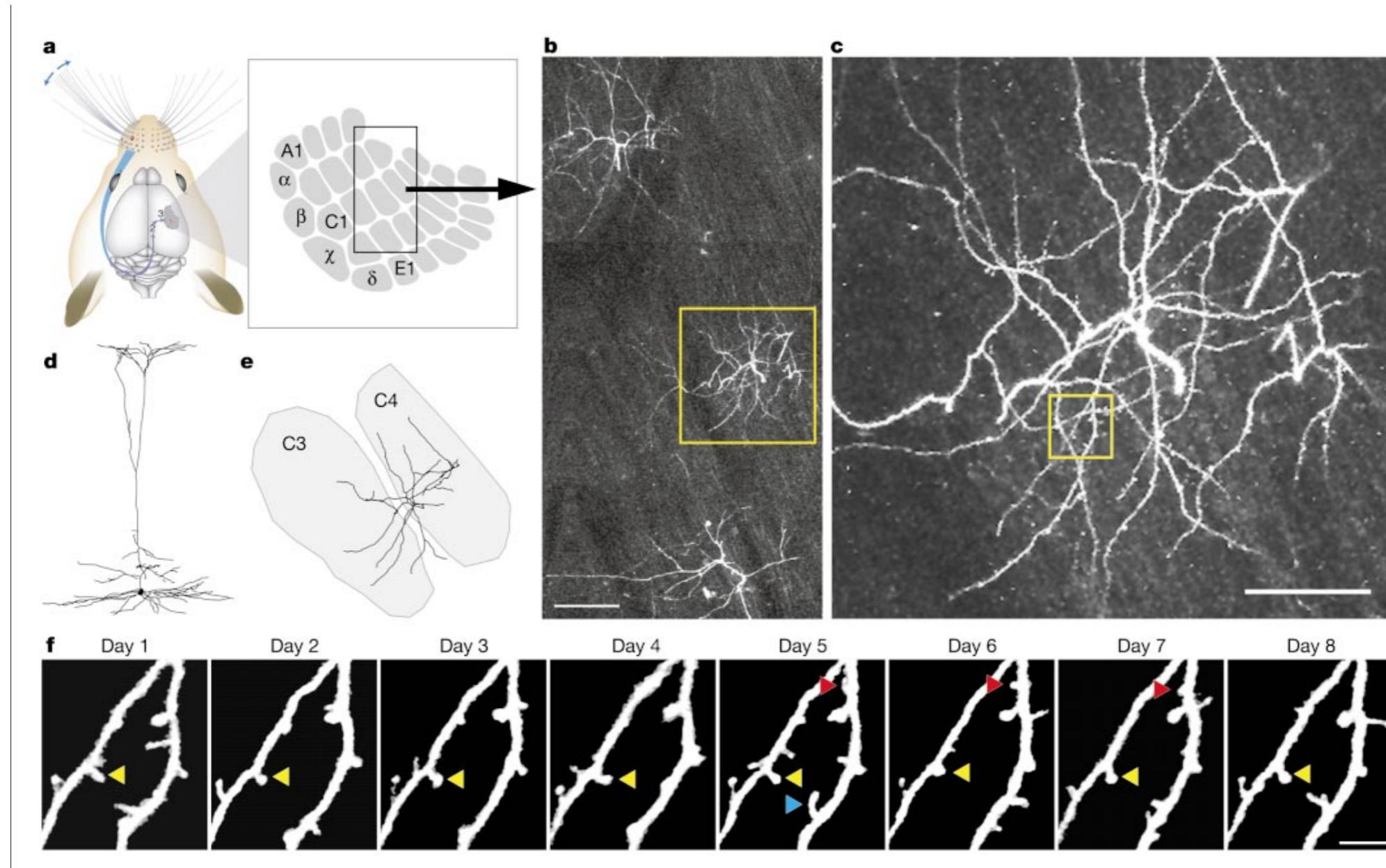
b: inter-bouton distance

n: neuronal density

filling fraction = 3/7

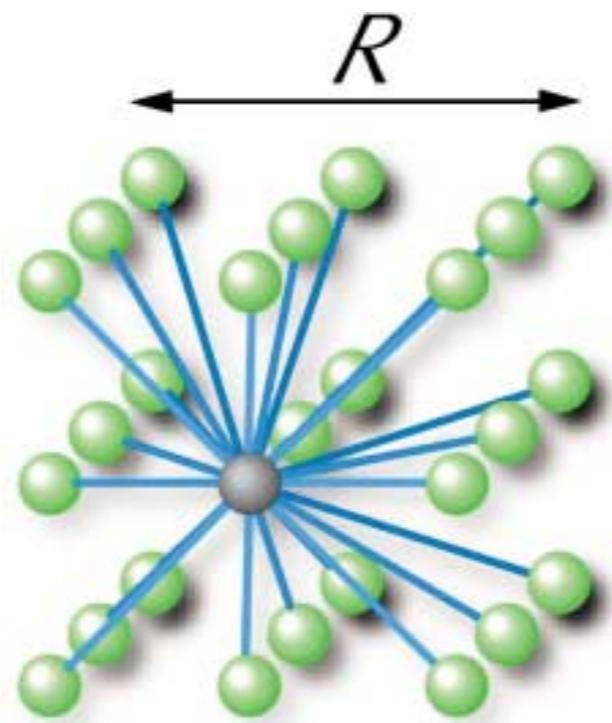
Stepanyants et. al., *Neuron* 2001

Structural Plasticity of Synaptic Connectivity



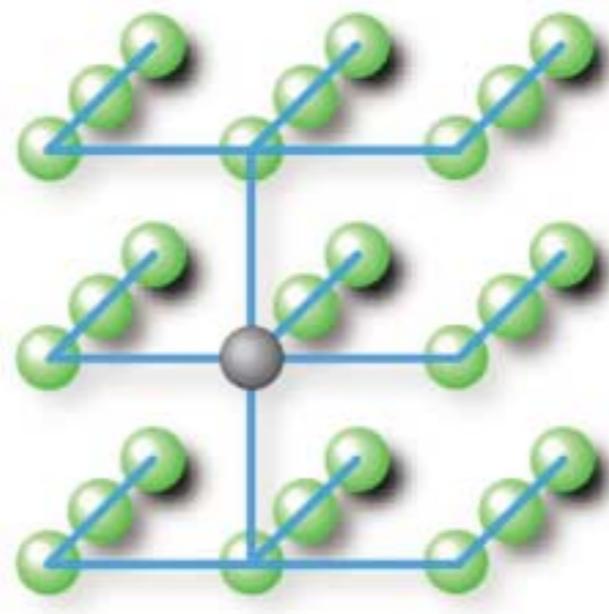
Trachtenberg et, al. *Nature* 2002

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



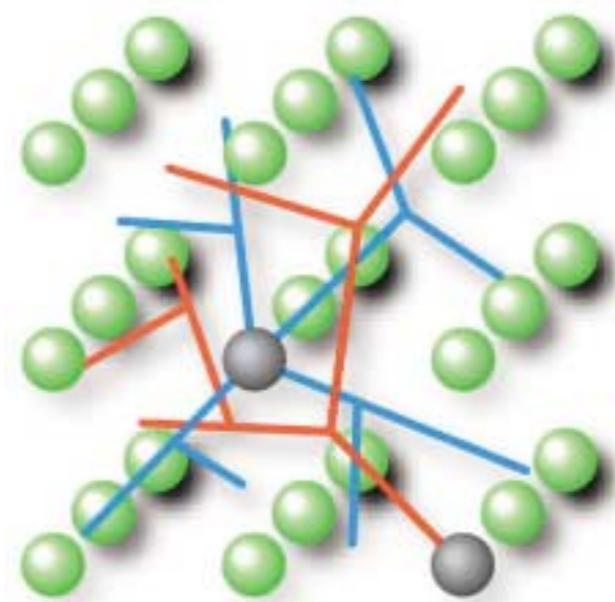
Design I

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



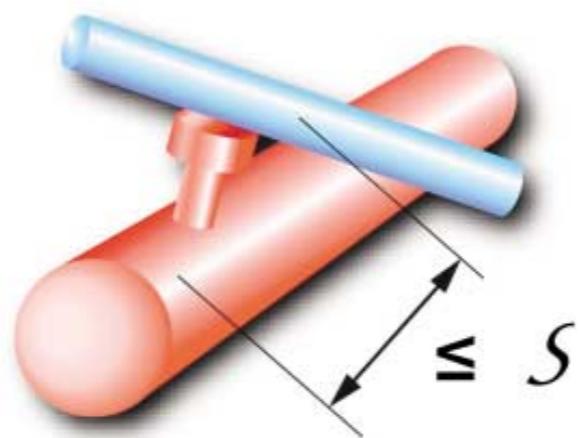
Design II

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



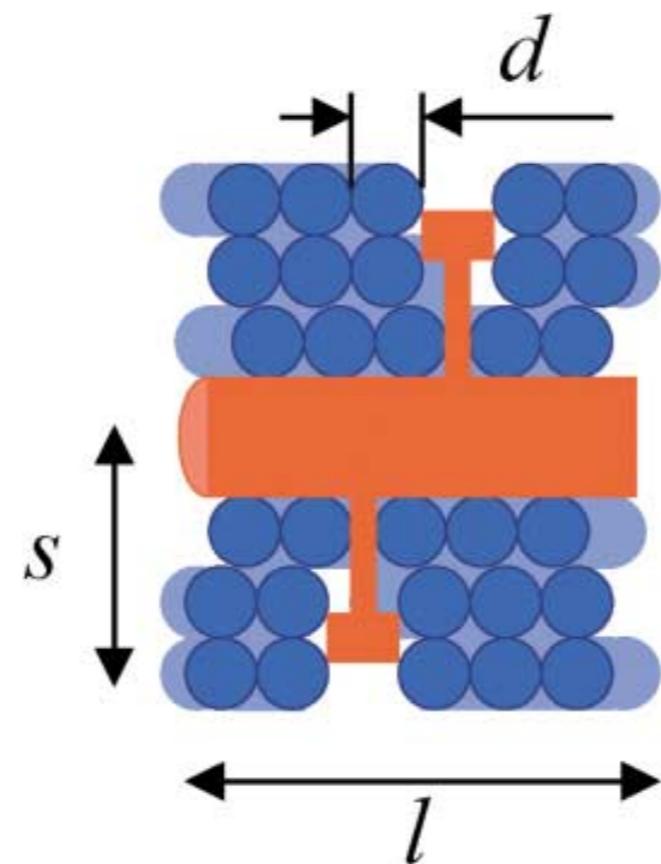
Design III

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



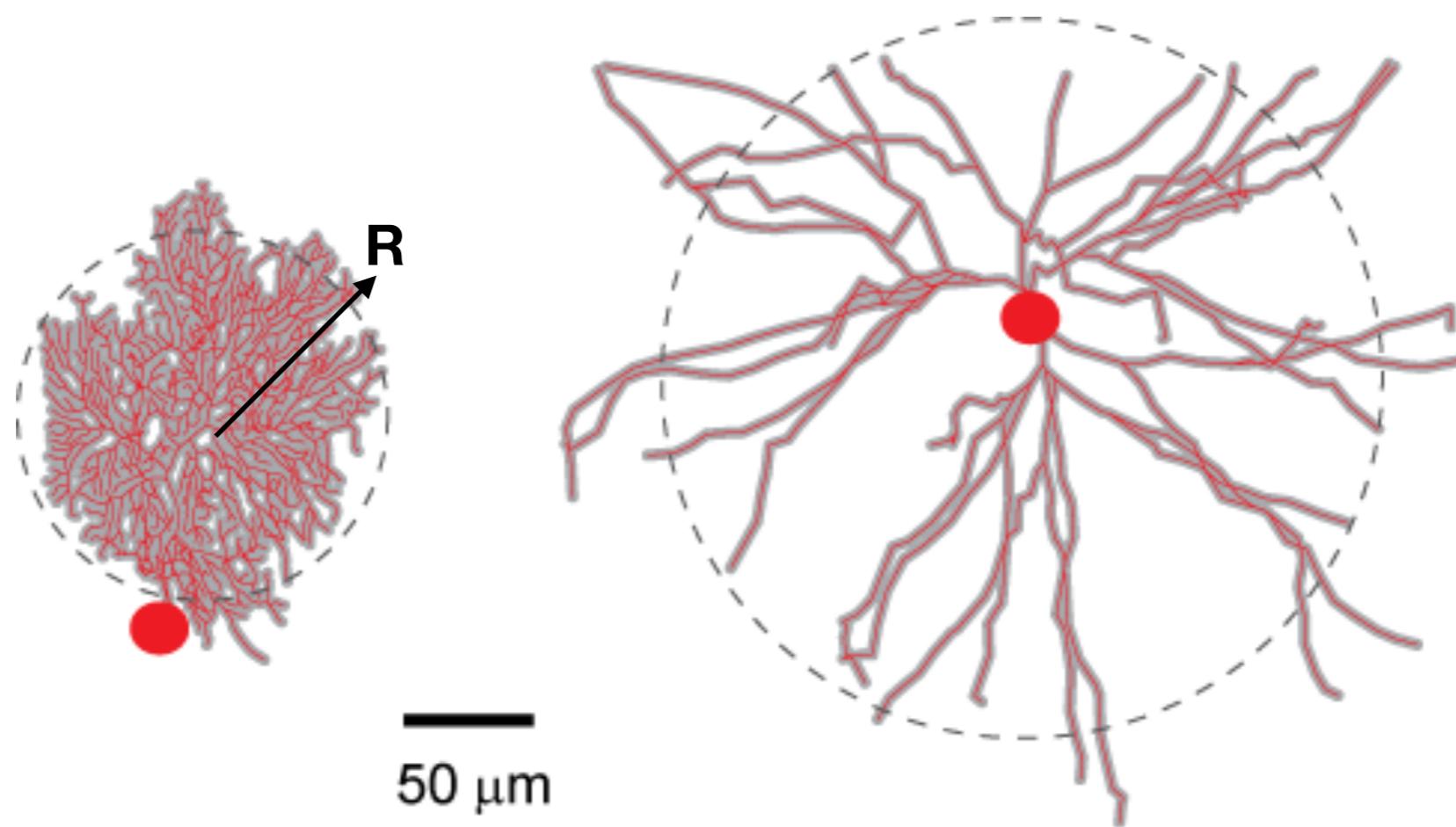
Design IV

Why do we need axons and dendrites?

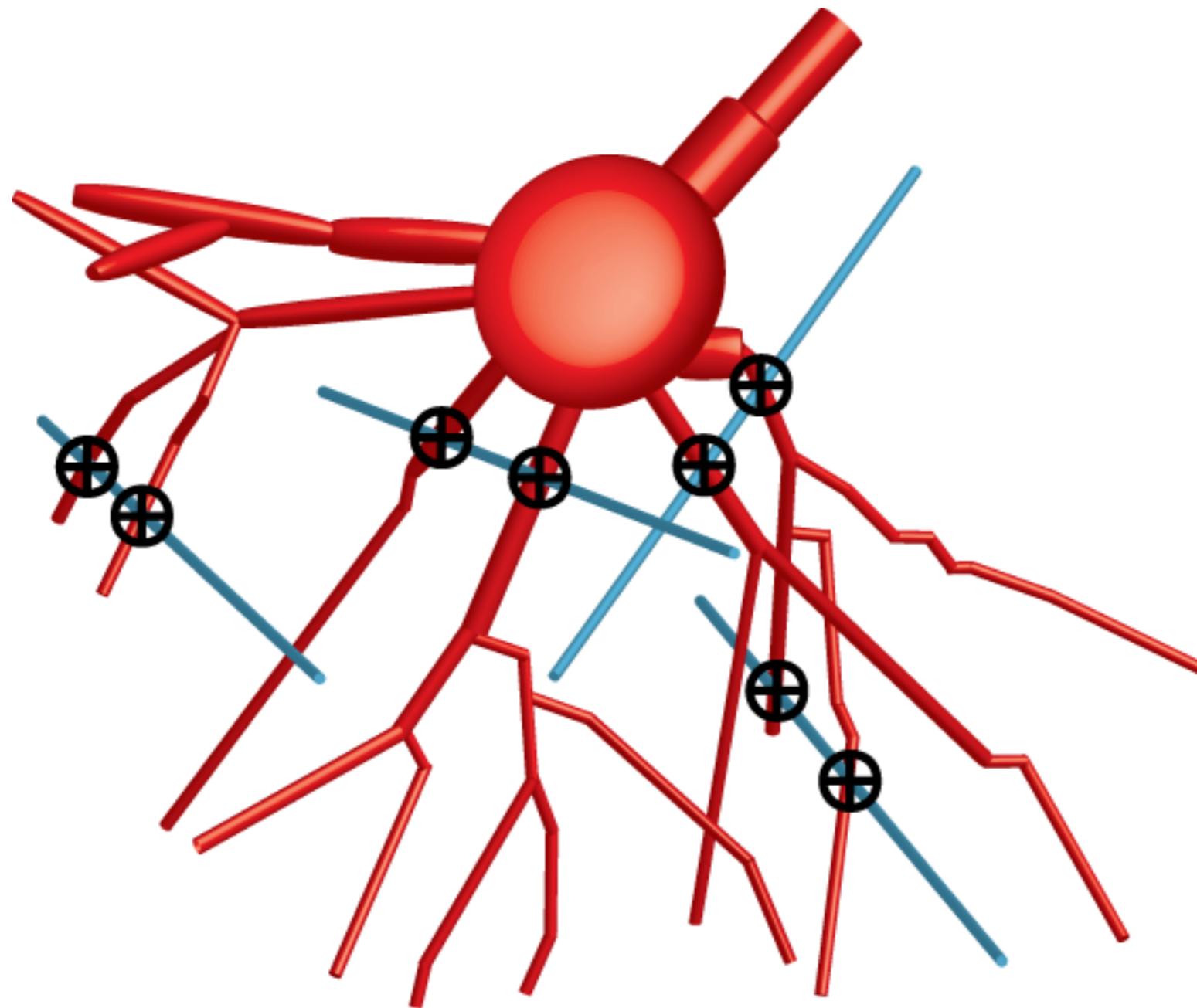


The Optimality of the design

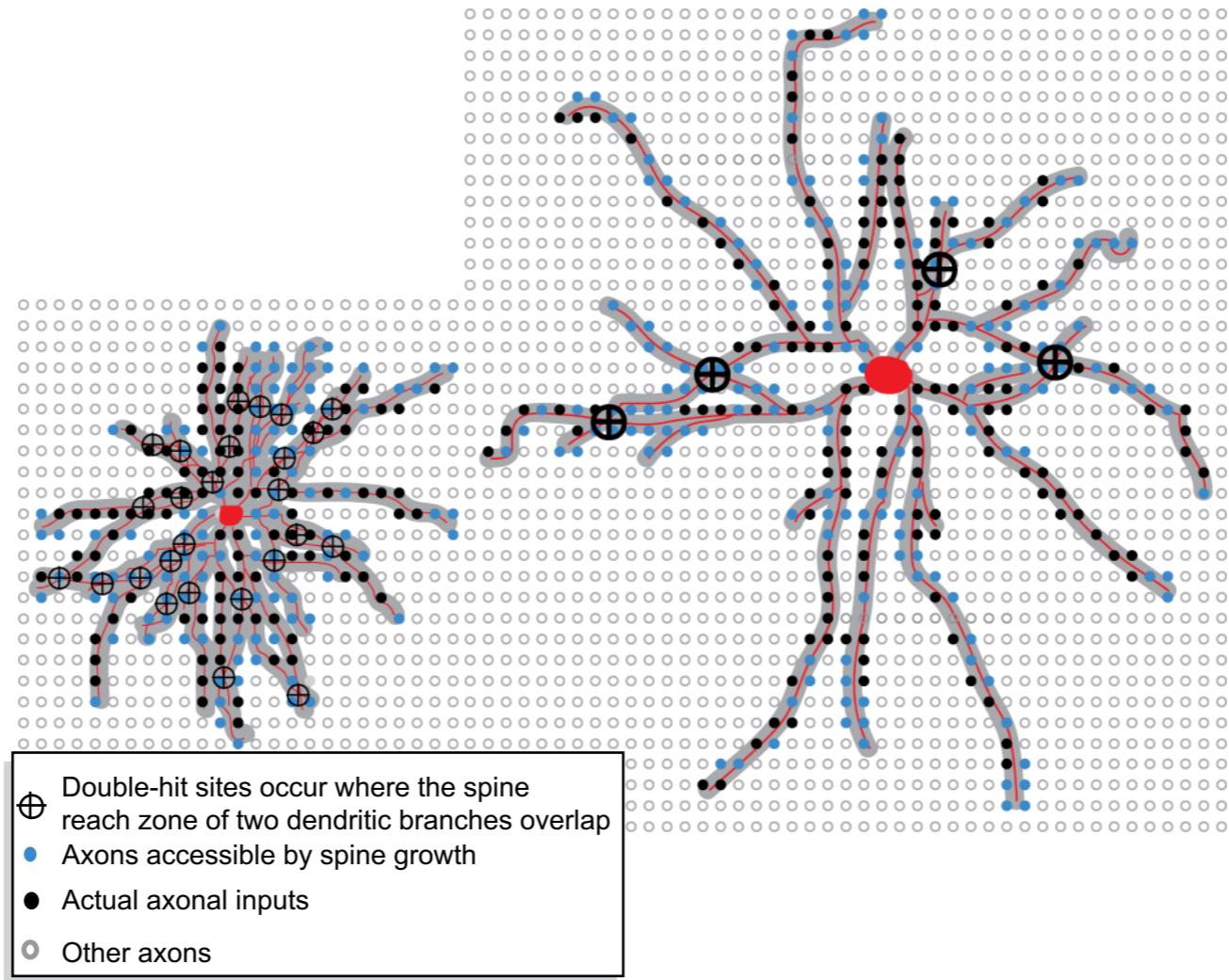
Why pyramidal dendrites appear much sparser than Purkinje dendrites?



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

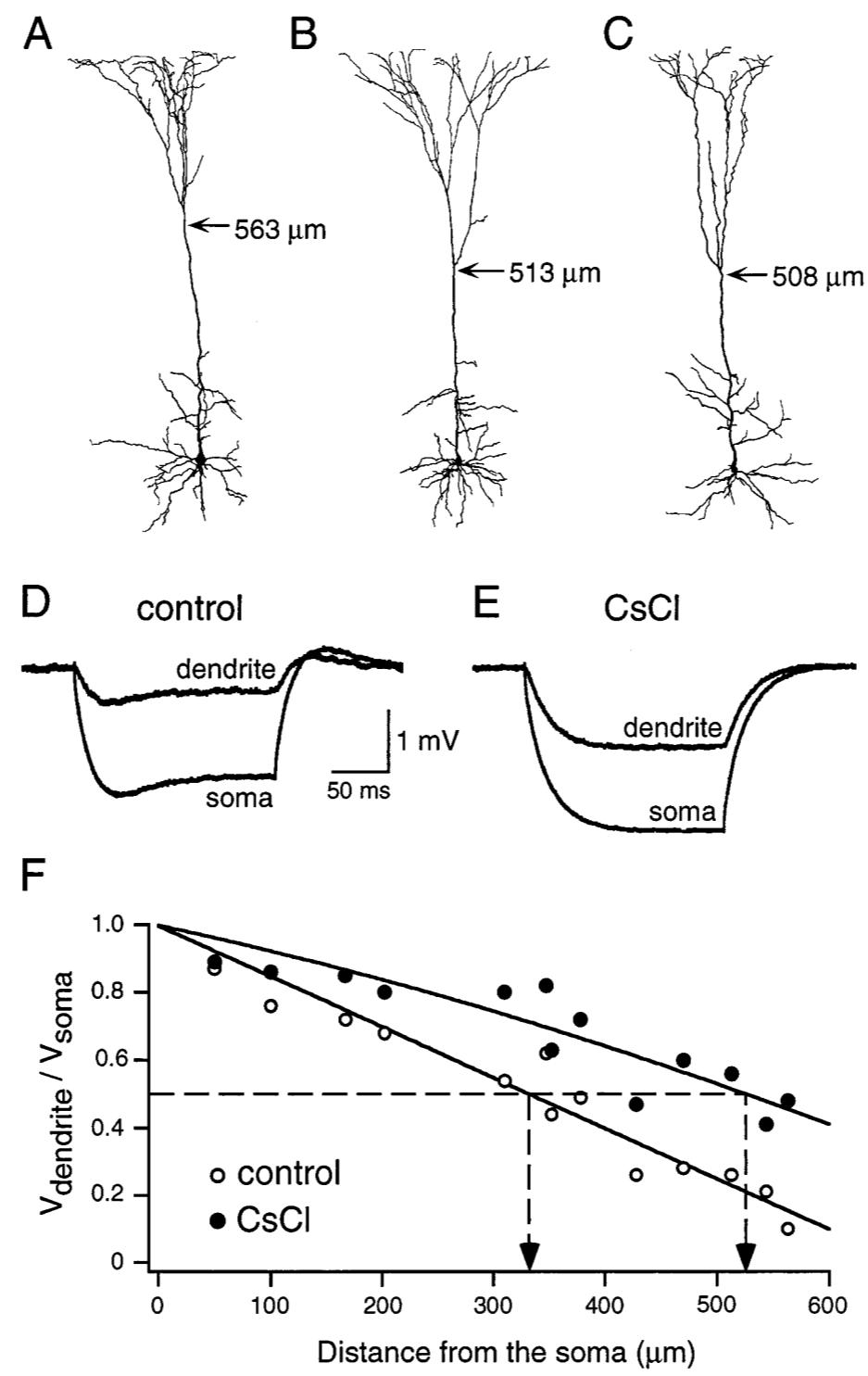


A sparse 3D dendritic arbor has fewer double-hits, and therefore, can access more axons, all other things being equal.



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.**





Wilfrid Rall

Wilfrid Rall and the cable equation

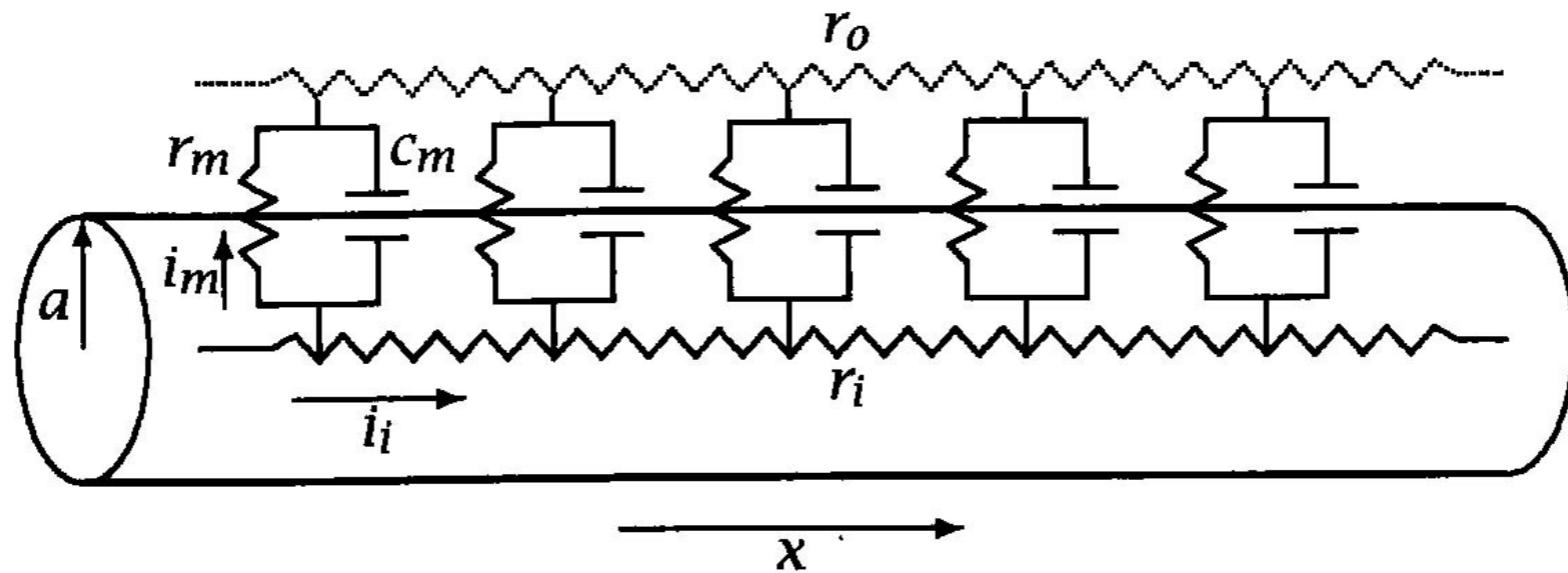
FUNDAMENTAL EQUATIONS

The derivation of the differential equation for distributions of passive electrotonic potential in uniform cylinders is well established in the theory developed for axons (5, 9, 20). In regions containing no sources or sinks of externally applied current, this differential equation can be expressed

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = V + \tau \frac{\partial V}{\partial t}, \quad [1]$$

where $V = V_m - E$ is the electrotonic potential, x represents distance along the axis of the cylinder, $\tau = R_m C_m$ is the membrane time constant, and $\lambda = [(d/4)(R_m/R_i)]^{1/2}$ is the characteristic length constant.³

The basic assumption of cable theory: dendrites are cylinders!



r_i = axial resistance (Ω/cm)

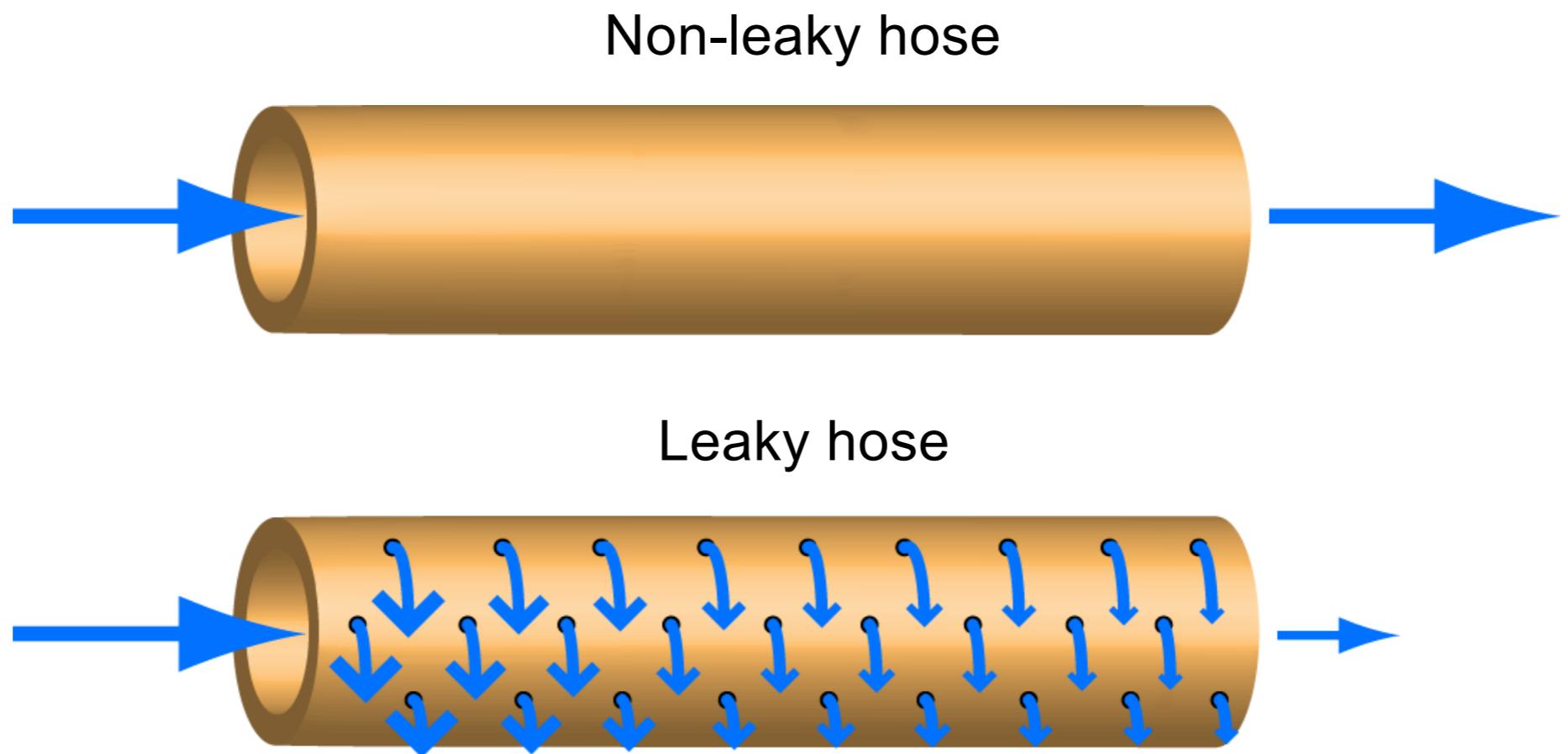
r_m = membrane resistance ($\Omega\cdot\text{cm}$)

C_m = membrane capacitance (F/cm)

Simplifying assumptions:

1. Extracellular resistance $r_o=0$
2. Membrane properties are uniform throughout, for all parts of the cylinder and are independent of membrane potential – no voltage gated channels.
3. Current flow is along a single dimension, x . So, there's no radial current

Cable equation: a garden hose analogy

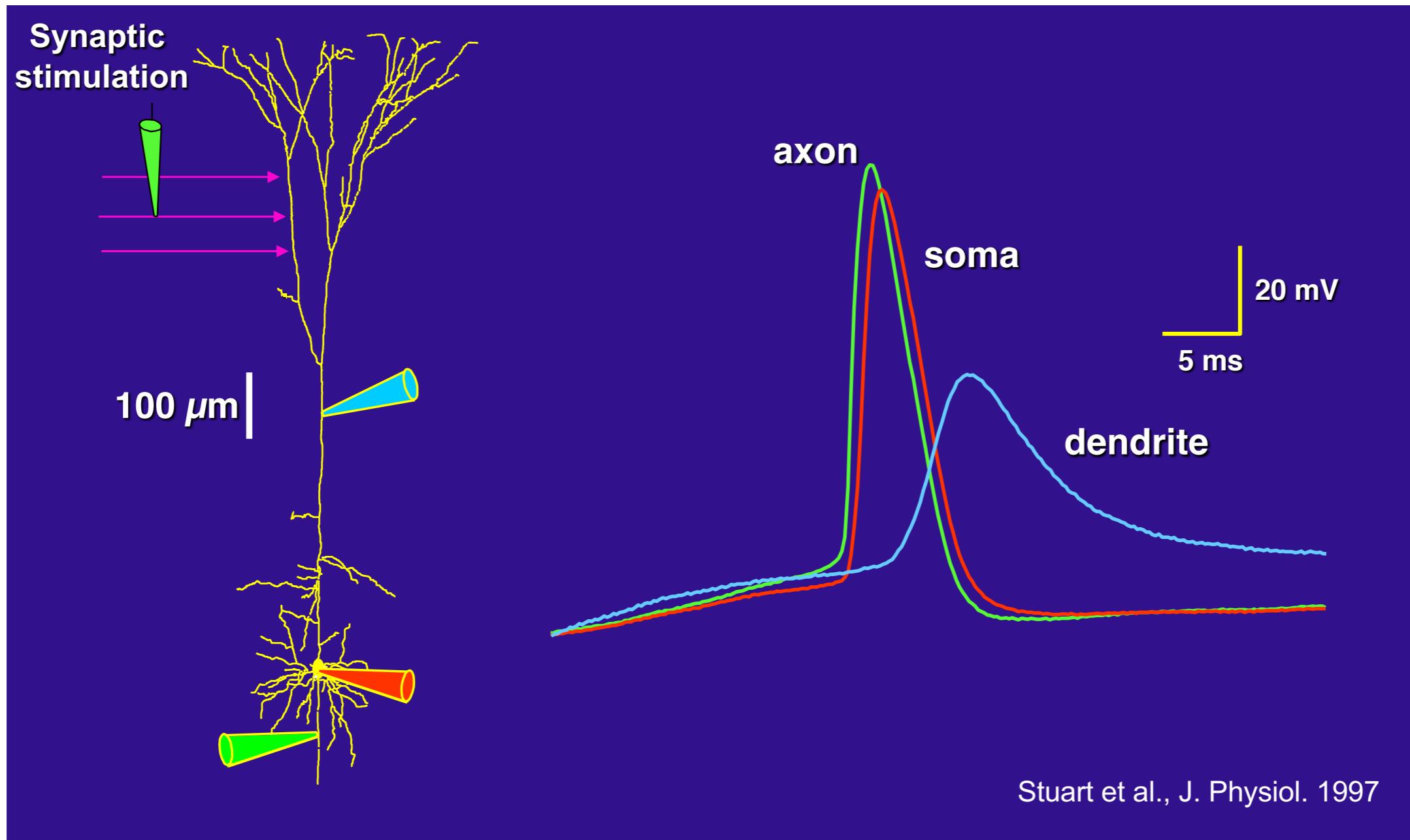


Propagation through neuronal dendrites is similar to
water flow through a leaky hose!

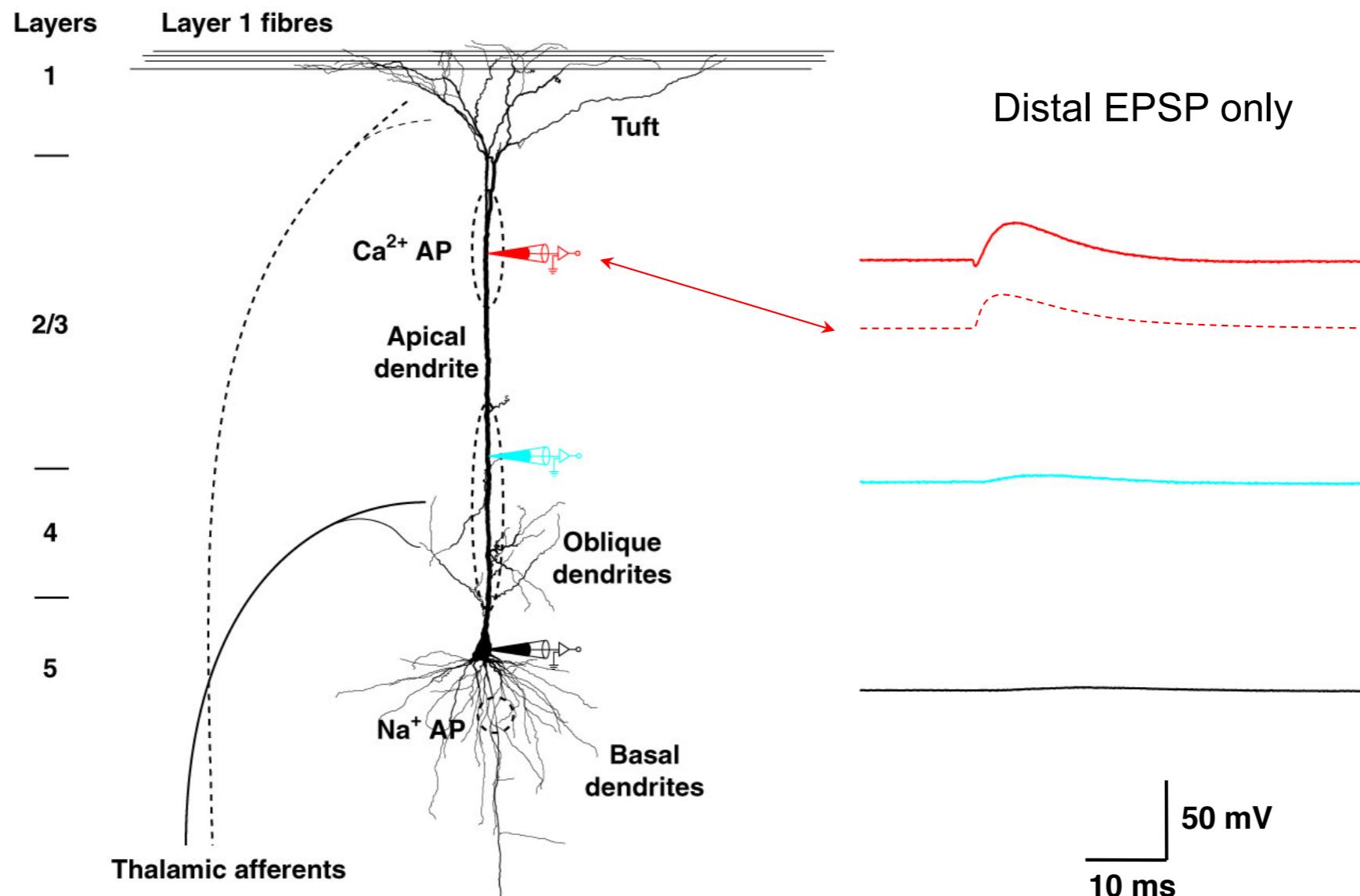
A derivation

The roles of dendrites beyond connectivity

Action potential generation and back propagation in dendrites

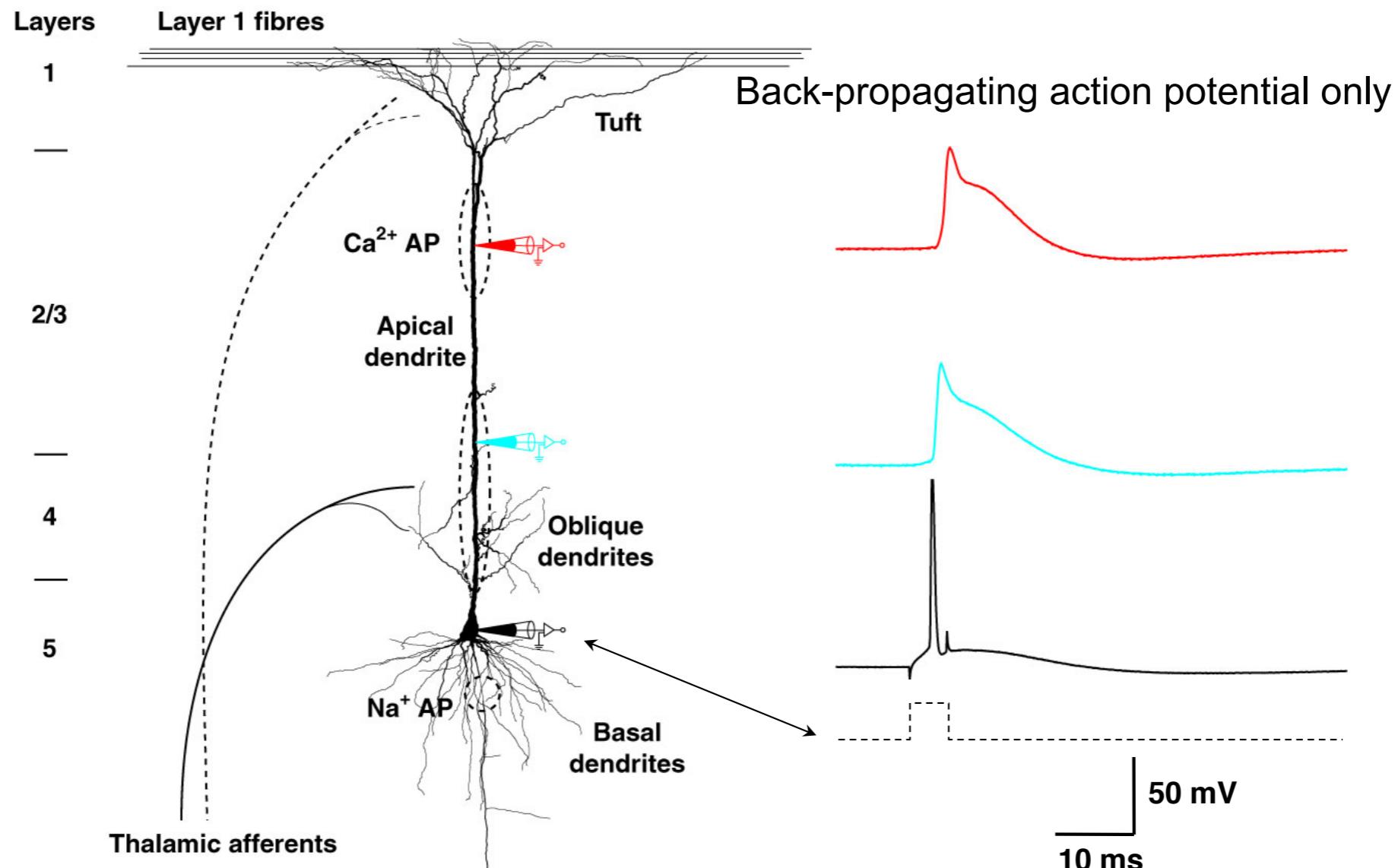


Interaction between back-propagation of action potentials and Ca^{2+} spike



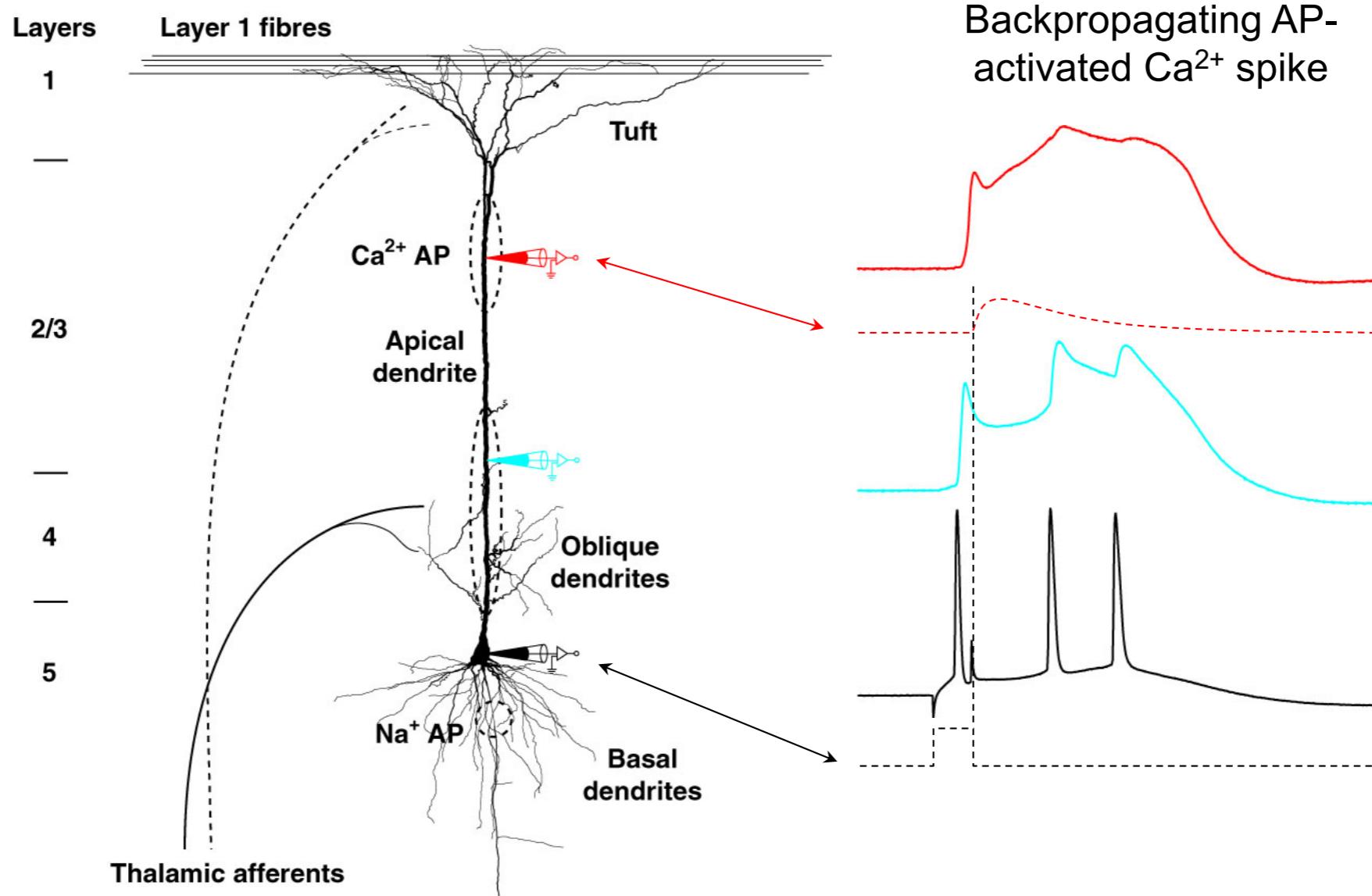
Larkum, Zhu & Sakmann - Nature, 1999

Interaction between back-propagation of action potentials and Ca^{2+} spike



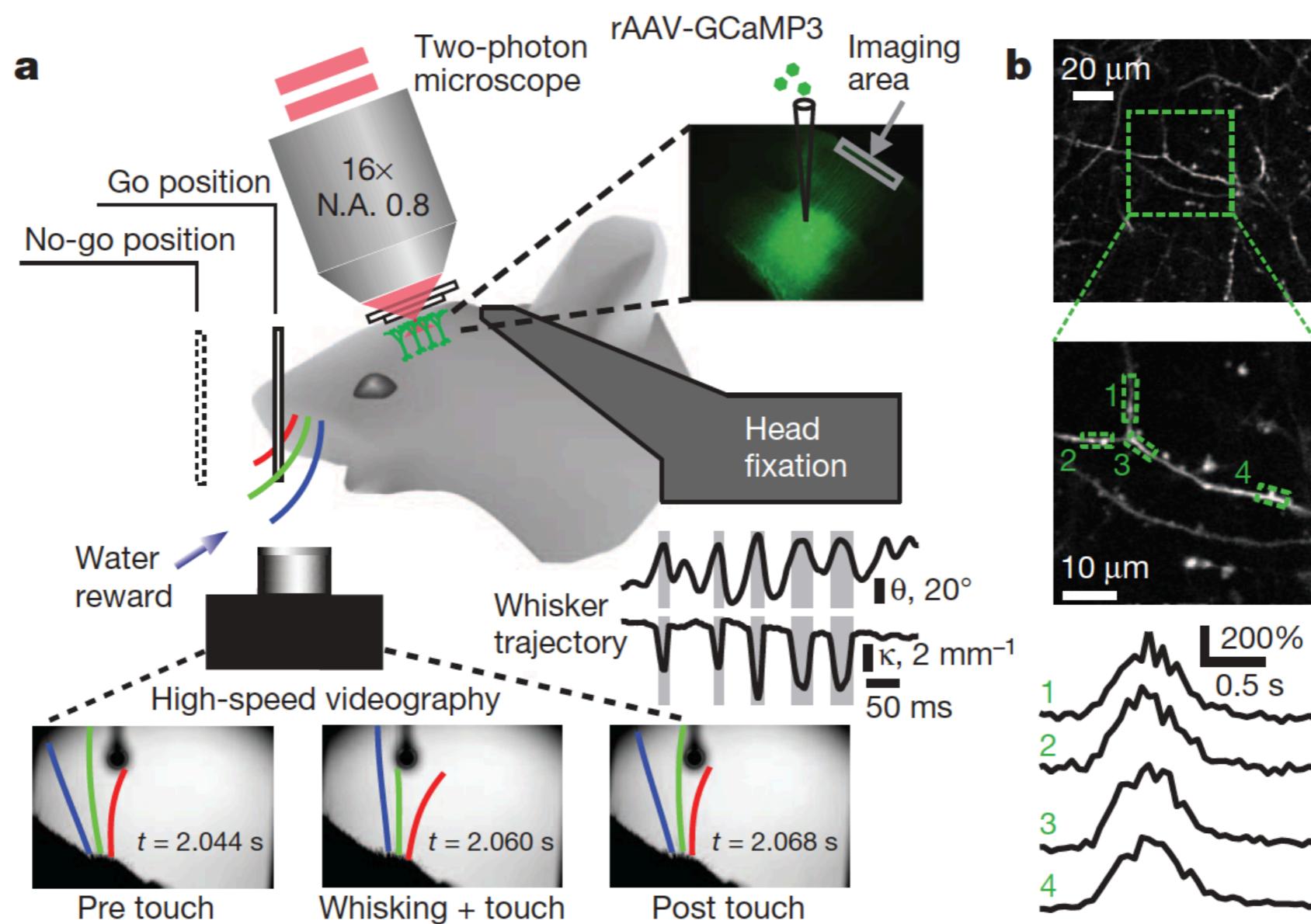
Larkum, Zhu & Sakmann - Nature, 1999

Interaction between back-propagation of action potentials and Ca^{2+} spike



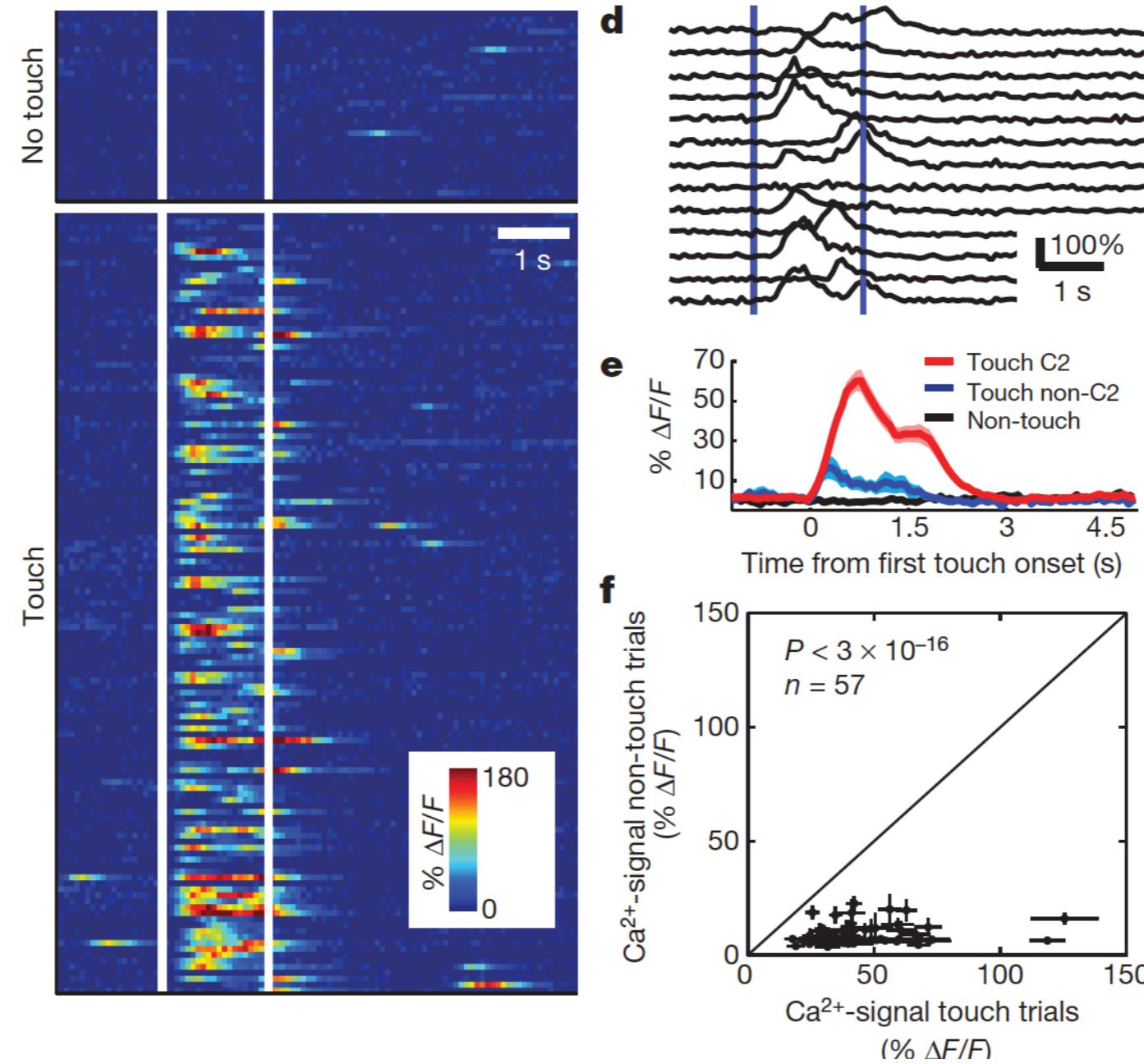
Larkum, Zhu & Sakmann - Nature, 1999

Specific dendritic Ca^{2+} signal during active sensing

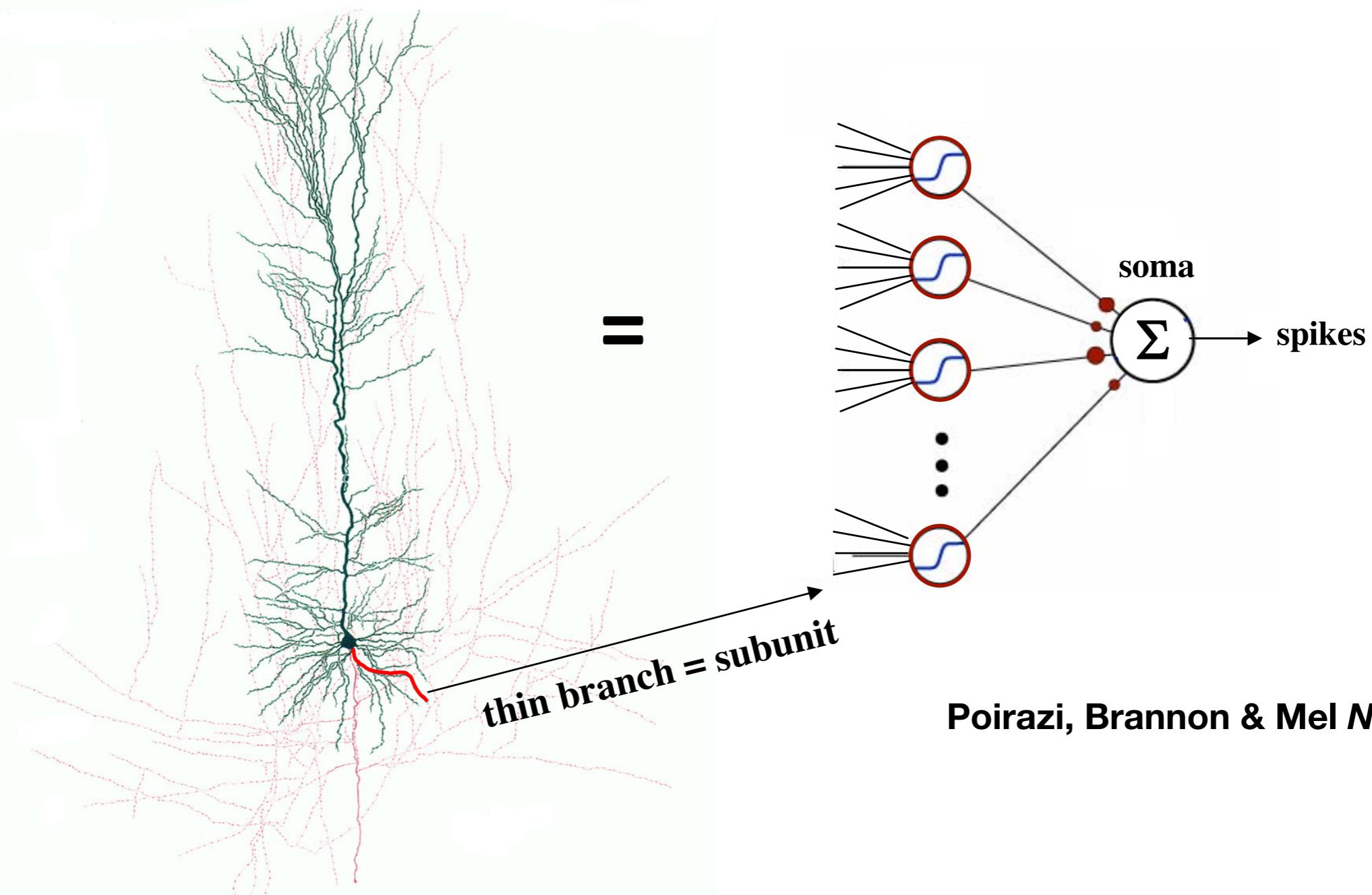


Xu et al *Nature* 2012

Specific dendritic Ca^{2+} signal during active sensing



Dendritic compartment and nonlinear integration



Single Cortical Neurons as Deep Artificial Neural Networks

¹David Beniaguev, ^{1,2}Idan Segev and ^{1,2}Michael London

¹The Edmond and Lily Safra Center for Brain Sciences and ²Department 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

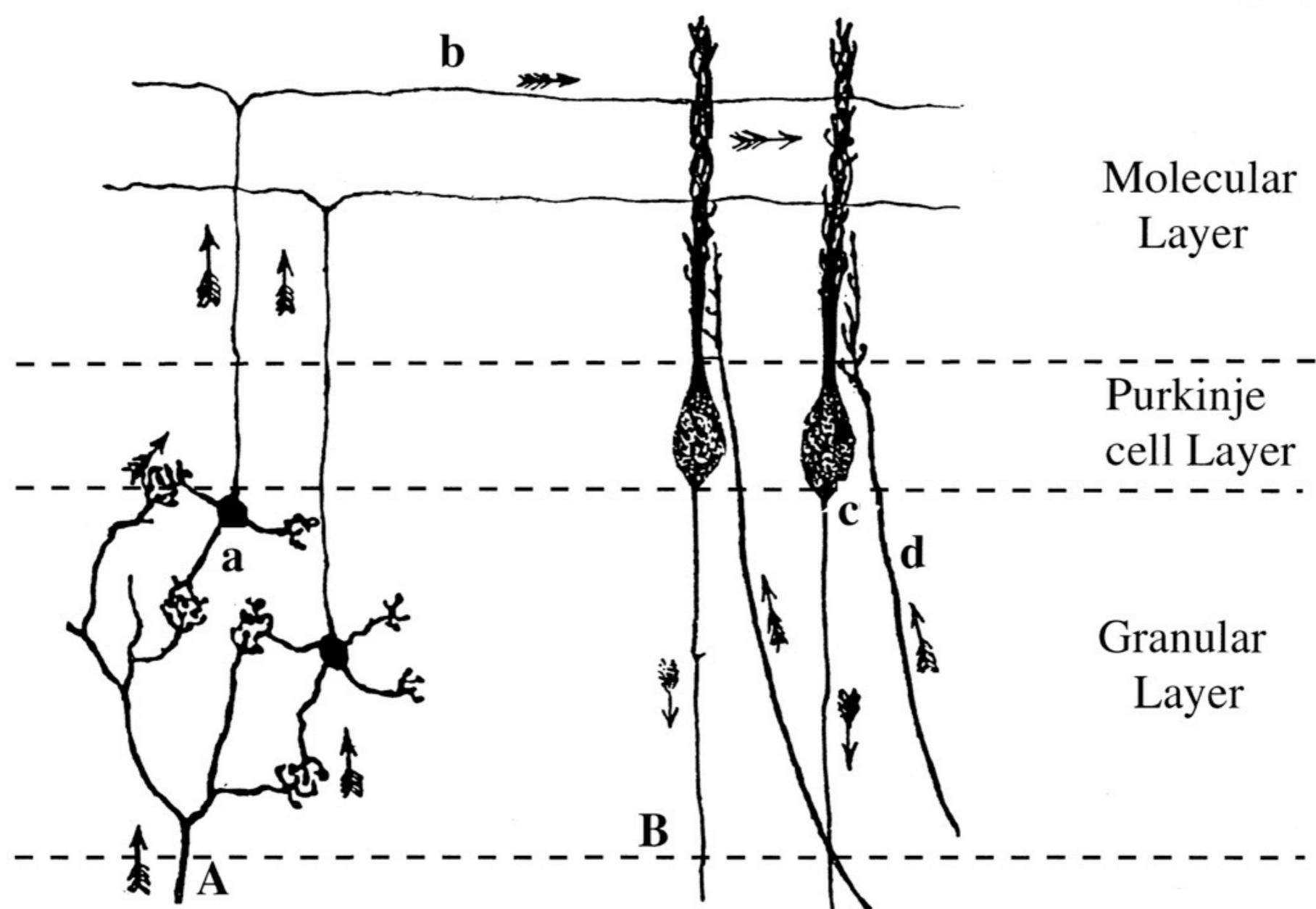
Ilenna Simone Jones¹ and Konrad Kording²

¹Department of Neuroscience, University of Pennsylvania

²Departments of Neuroscience and Bioengineering, University of Pennsylvania

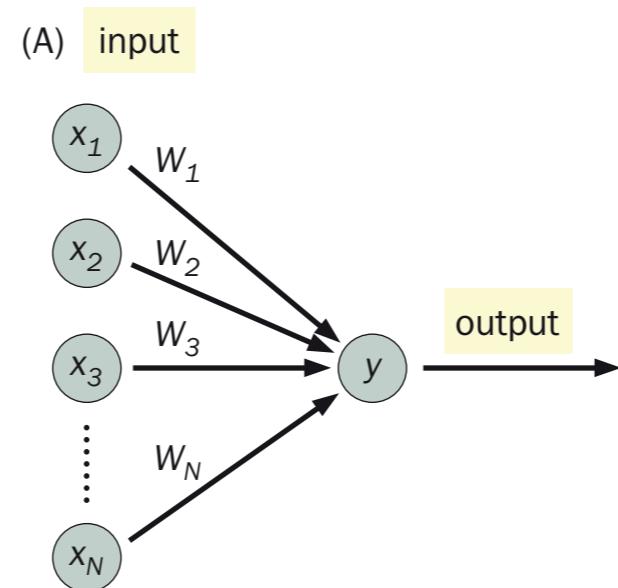
September 4, 2020

Cerebellar cortex



Cajal's drawing of the cerebellar cortex

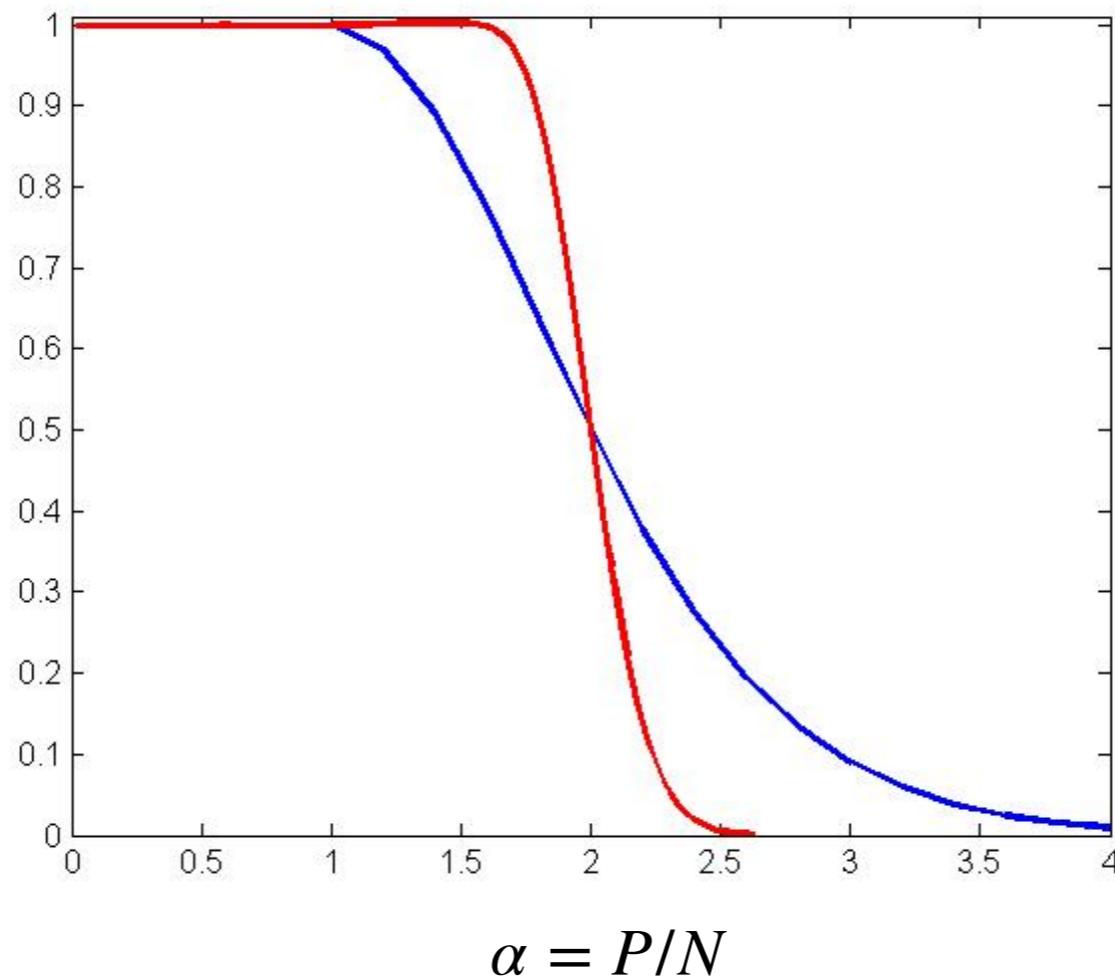
McCulloch-Pitts neuron and the Perceptron model



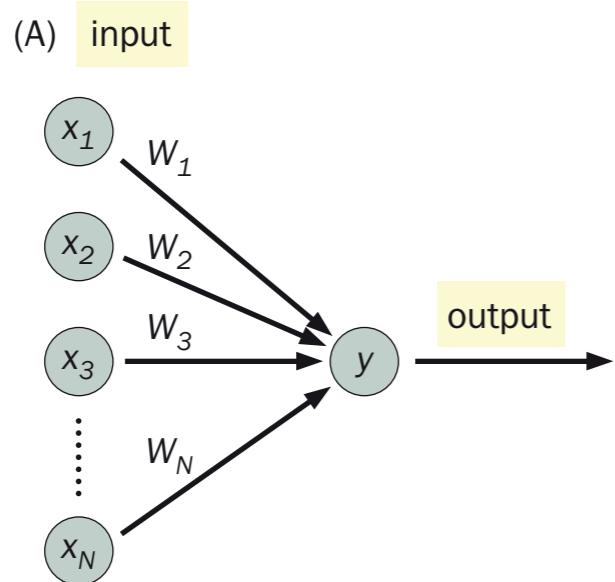
$$y = \text{sign} \left(\sum_{i=1}^N W_i x_i - \theta \right)$$

Critical Capacity

$$\frac{C(P, N)}{2^P}$$



The Perceptron learning algorithm



$$y = \text{sign} \left(\sum_{i=1}^N w_i x_i - \theta \right)$$

$$\mathbf{W} \leftarrow \mathbf{W} + \eta(y_0^n - y)\mathbf{X^n}$$

J. Physiol. (1969), **202**, pp. 437–470

With 1 plate and 2 text-figures

Printed in Great Britain

A THEORY OF CEREBELLAR CORTEX

By DAVID MARR*

From Trinity College, Cambridge

(Received 2 December 1968)

SUMMARY

1. A detailed theory of cerebellar cortex is proposed whose consequence is that the cerebellum learns to perform motor skills. Two forms of input-output relation are described, both consistent with the cortical theory. One is suitable for learning movements (actions), and the other for learning to maintain posture and balance (maintenance reflexes).

437

A Theory of Cerebellar Function

JAMES S. ALBUS

Cybernetics and Subsystem Development Section

Data Techniques Branch

Goddard Space Flight Center

Greenbelt, Maryland

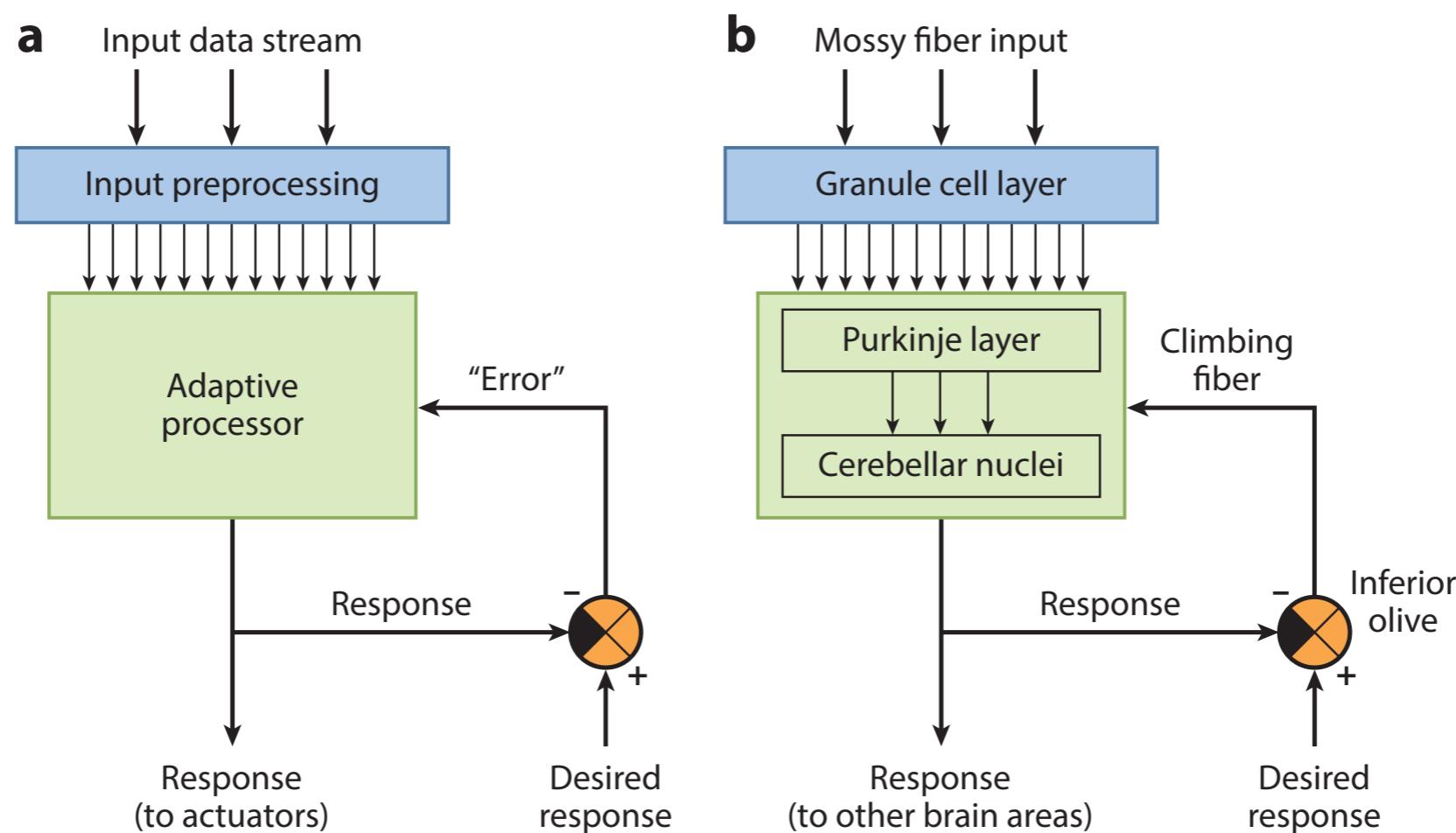
Communicated by Donald H. Perkel

ABSTRACT

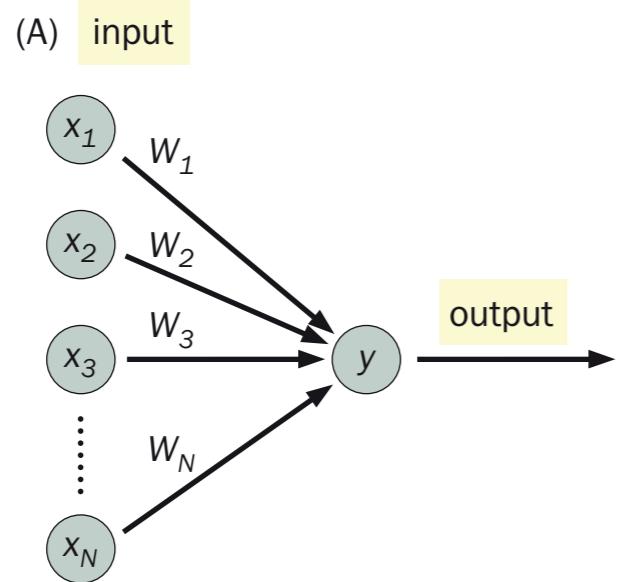
A comprehensive theory of cerebellar function is presented, which ties together the known anatomy and physiology of the cerebellum into a pattern-recognition data processing system. The cerebellum is postulated to be functionally and structurally equivalent to a modification of the classical Perceptron pattern-classification device. It is suggested that the mossy fiber → granule cell → Golgi cell input network performs an expansion recoding that enhances the pattern-discrimination capacity and learning speed of the cerebellar Purkinje response cells.

Parallel fiber synapses of the dendritic spines of Purkinje cells, basket cells, and stellate cells are all postulated to be specifically variable in response to climbing fiber activity. It is argued that this variability is the mechanism of pattern storage. It is demonstrated that, in order for the learning process to be stable, pattern storage must be accomplished principally by weakening synaptic weights rather than by strengthening them.

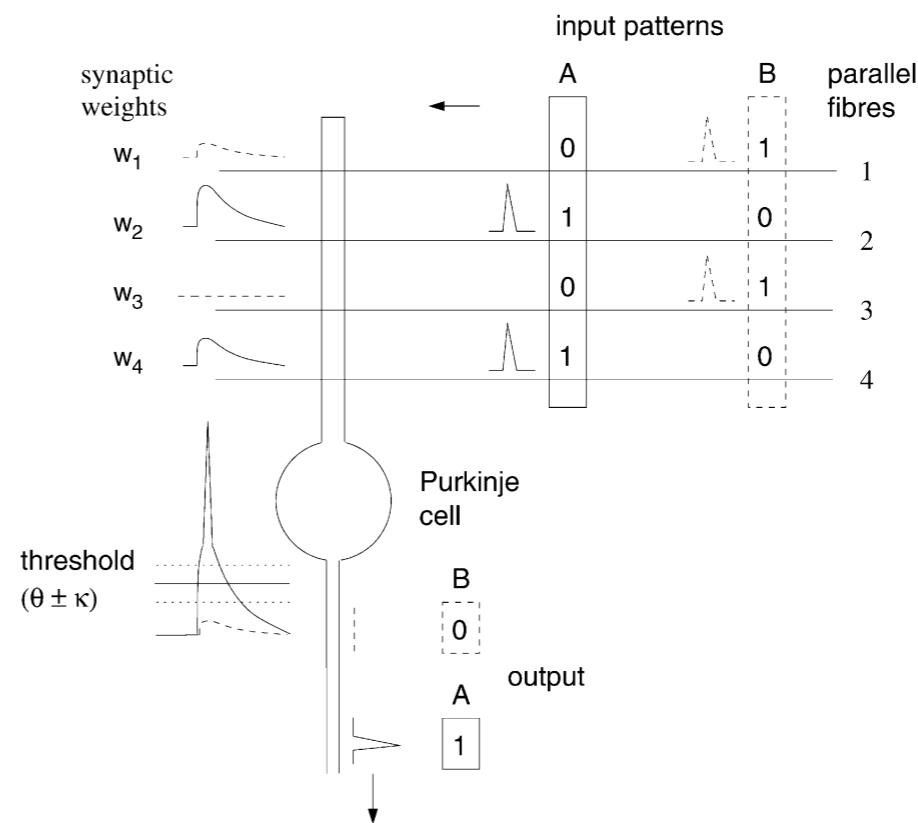
Cerebellum, a supervised learning machine?



Cerebellar Cortex and more realistic Perceptron model

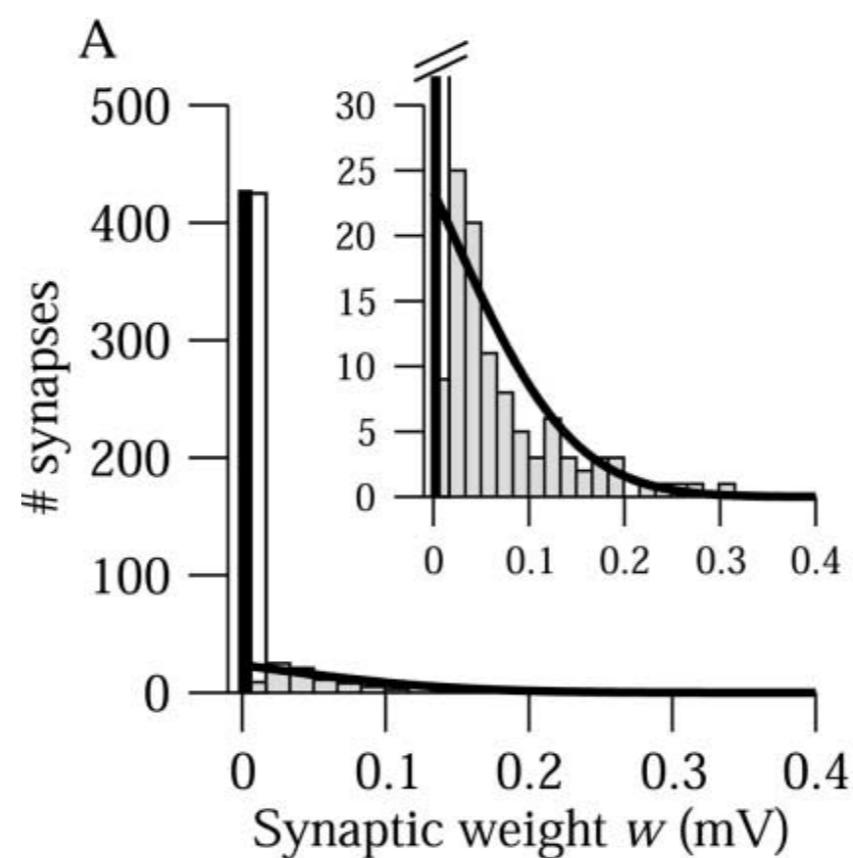


$$y = \text{sign} \left(\sum_{i=1}^N W_i x_i - \theta \right)$$



- Weights are all positive
- Fixed and marginal stability of the threshold

Optimal Information Capacity and the Distribution of Synaptic Weights

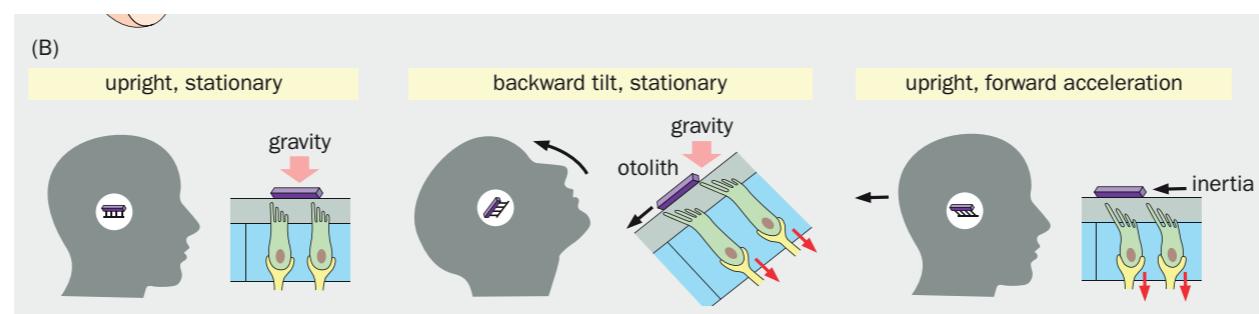


Training vs Generalization

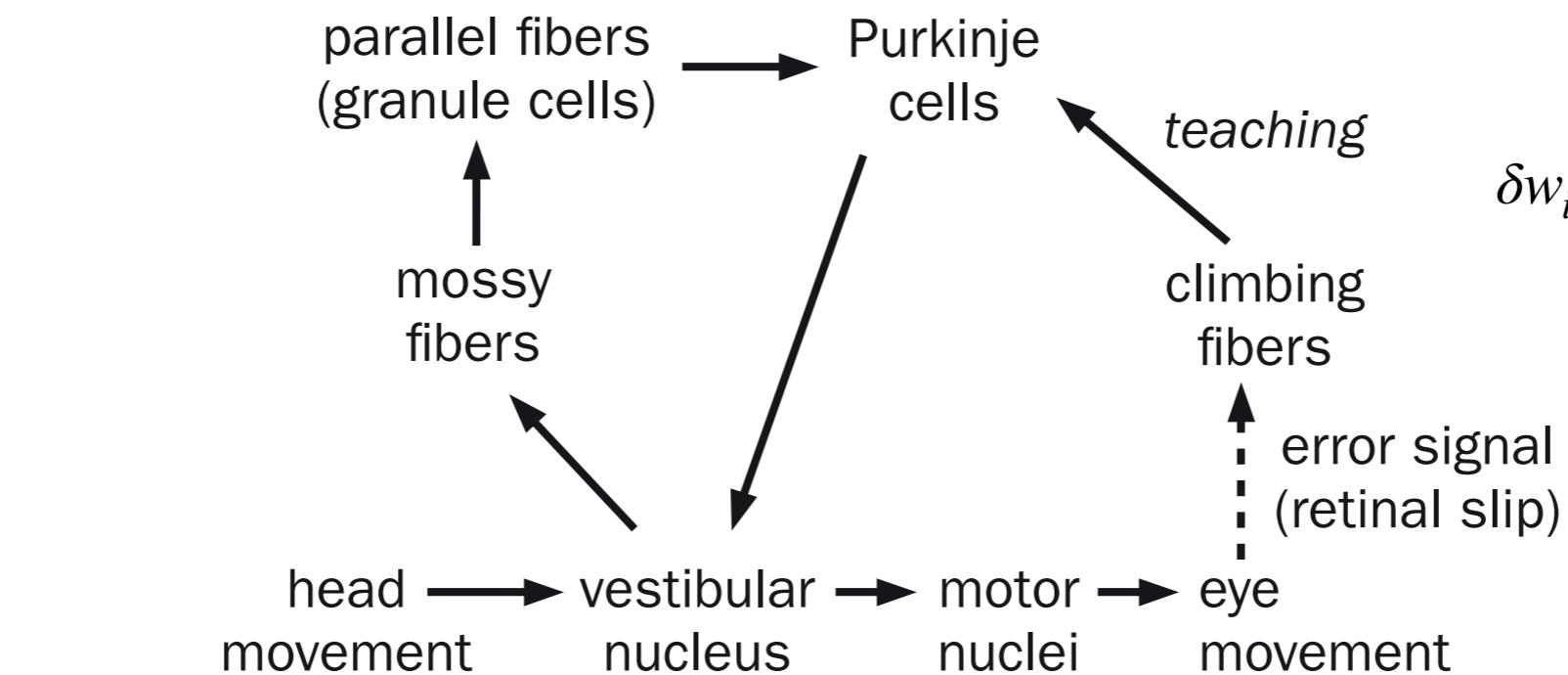
- The notion of generalization. Do we have sufficient data?
- The optimal separation planes
- The limitation of linear separability

Classification or Regression?

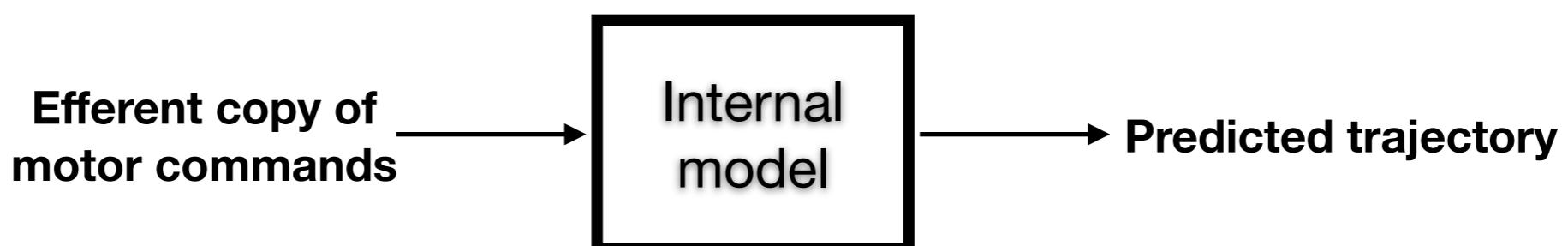
Cerebellar function in Vestibulo-ocular reflex



(A)



$$\delta w_i = -\epsilon(CF - \bar{CF})x_i$$



Masao Ito