The Abdus Salam International Centre for Theoretical Physics

2415-7

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An engineer's view of brain anatomy: an economically wired highly interconnected neural network

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An engineer’s view of brain anatomy: an economically wired highly interconnected neural network

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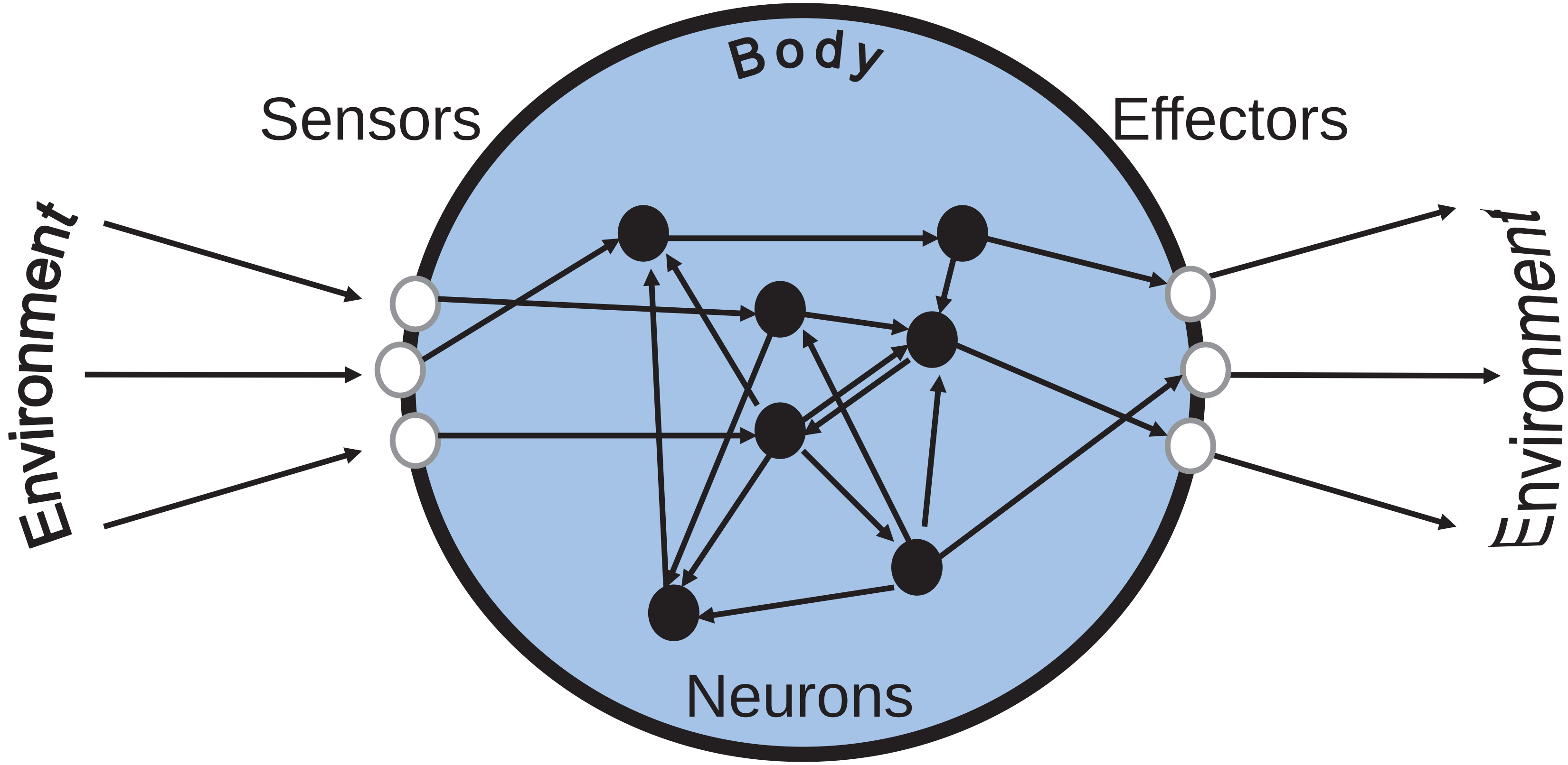
Why can't we model the brain?



Human brain: 10^{11} neurons,10^{15} connections ☹

Study simpler brains! ☺ Large parameter! ☺

Unknown level of abstraction ☹

Evolution is a blind engineer ☺

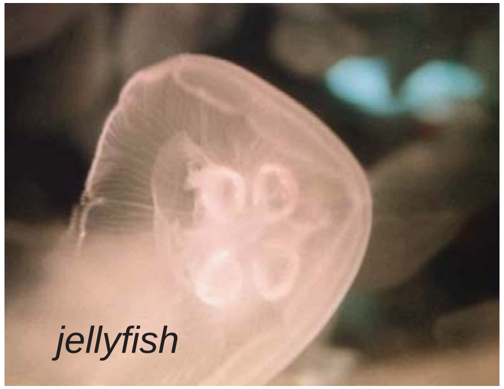
Normative theory of brain structure

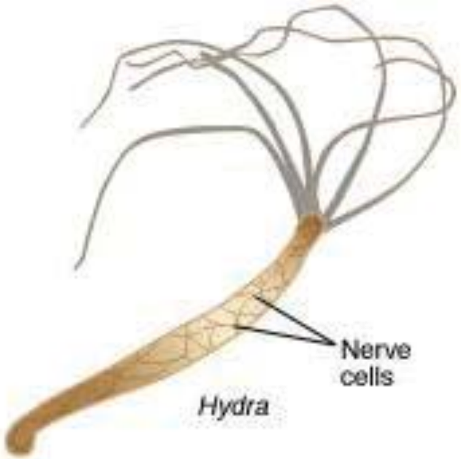
- Understand structure as a result of minimizing cost to the organism for given functionality

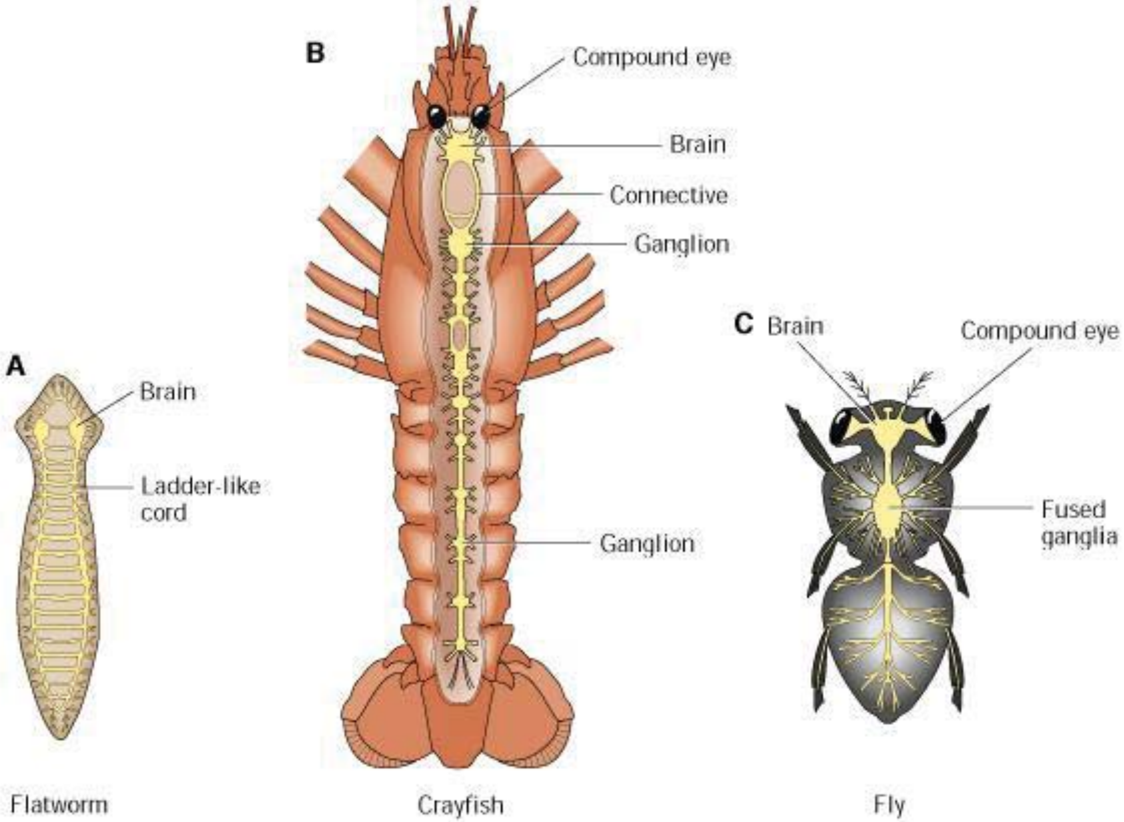
Example:

- Structure - placement of neurons
- Cost - wiring length (occupied volume, signal propagation delays and attenuation, metabolic energy)
- Functionality - wiring diagram, sensory inputs and motor outputs

Distributed vs. centralized nervous systems (Cajal 1899)





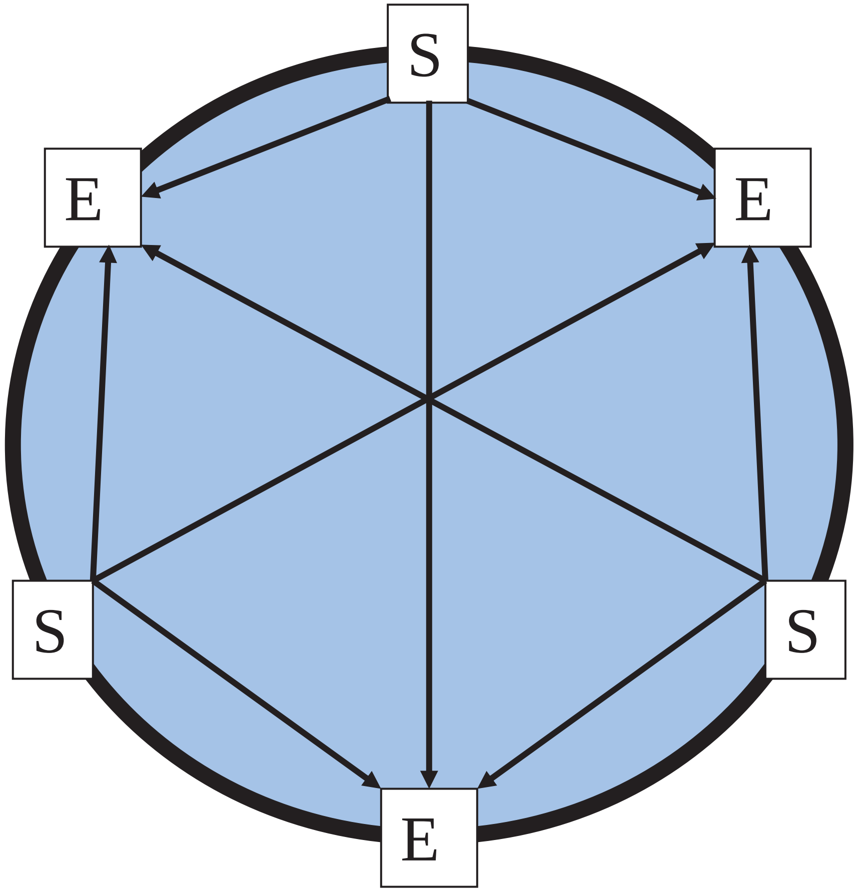


10^3 neurons

10^5 neurons

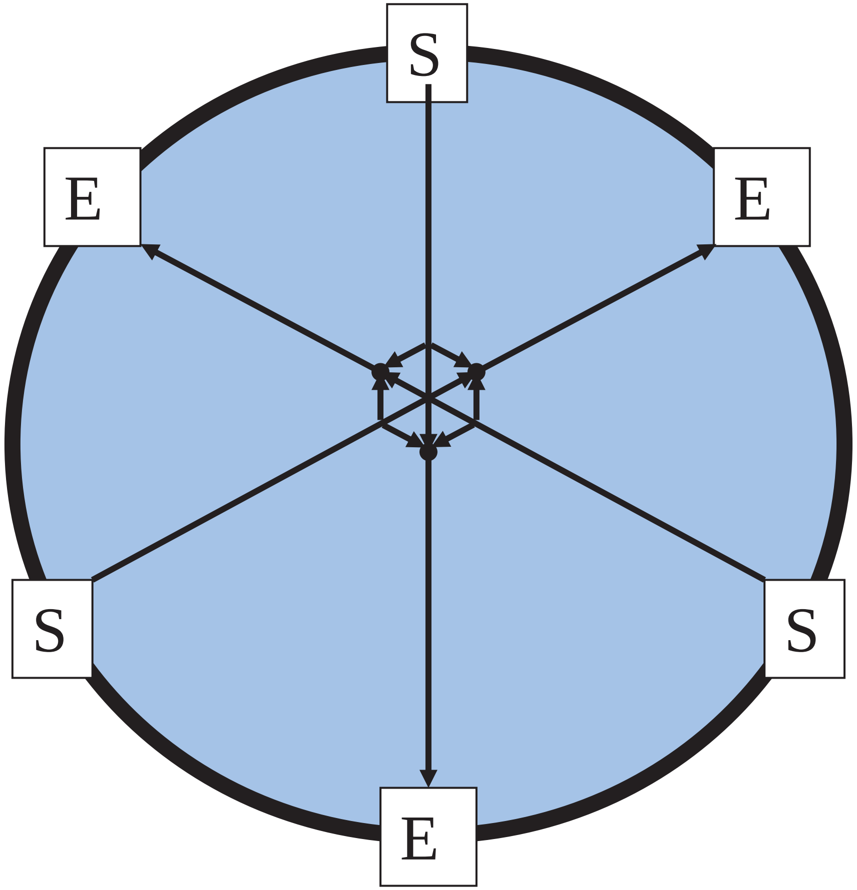
Which design is less costly?

Distributed nervous system



$N_{Wires} = N_S N_E$

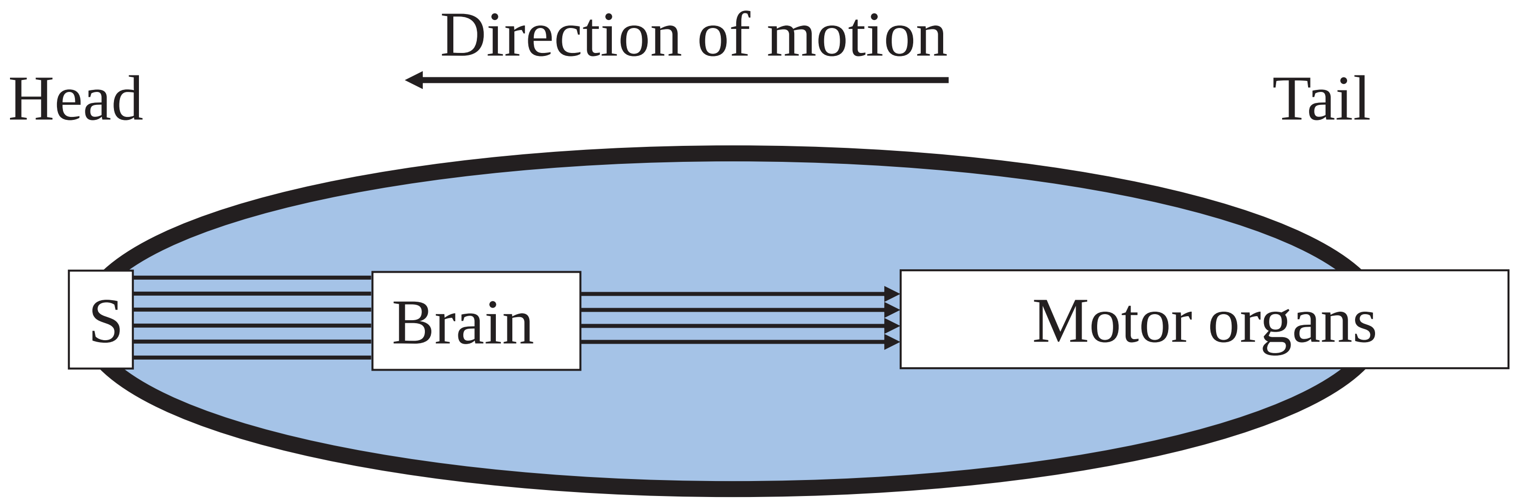
Centralized nervous system



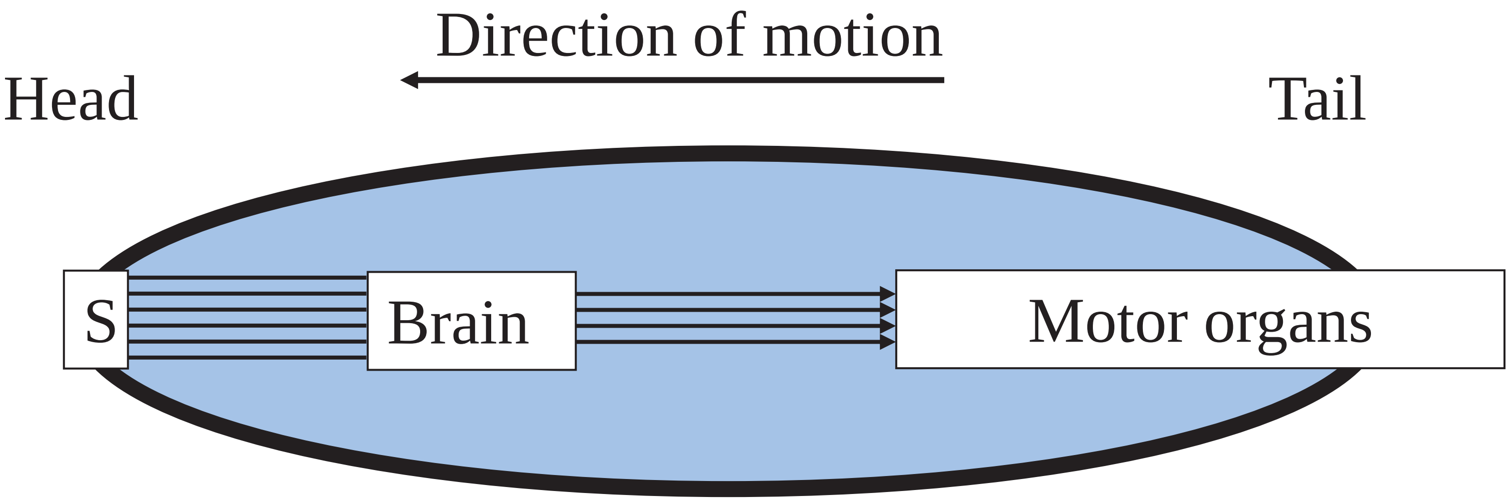
$N_{Wires} = N_S + N_E$

$N_S = N_E = 10^6$: 10^{12} $2\text{x}10^6$

What determines brain placement?



What determines brain placement?

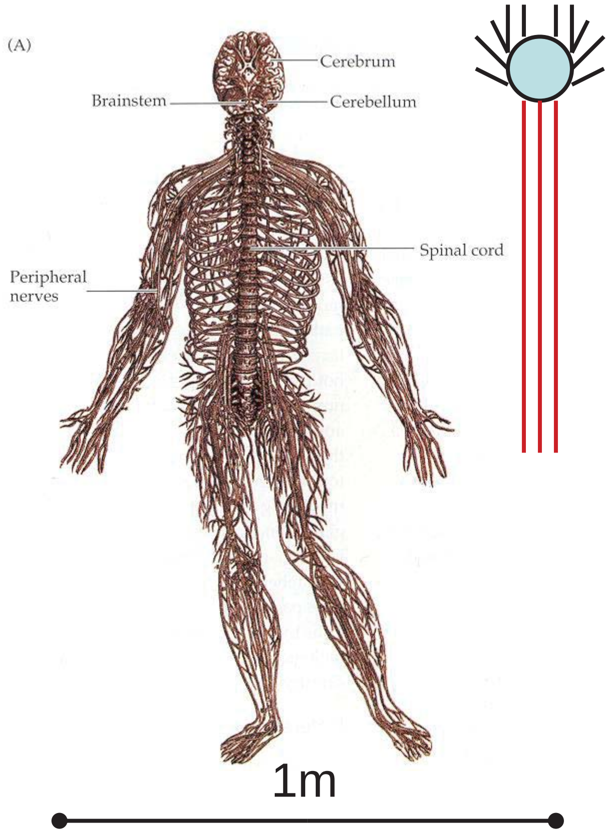


Brain location is biased towards the dominant source of connections

Numbers of connections to the human brain

Anterior: Cranial nerves

Olfactory	10,000K
Optic	2,000K
Oculomotor	60K
Trochlear	6K
Trigeminal	300K
Abducens	14K
Facial	20K
Cochlear	60K
Vestibular	40K
Glossopharyngeal	7K
Vagus	70K
Accessory	7K
Hypoglossal	15K



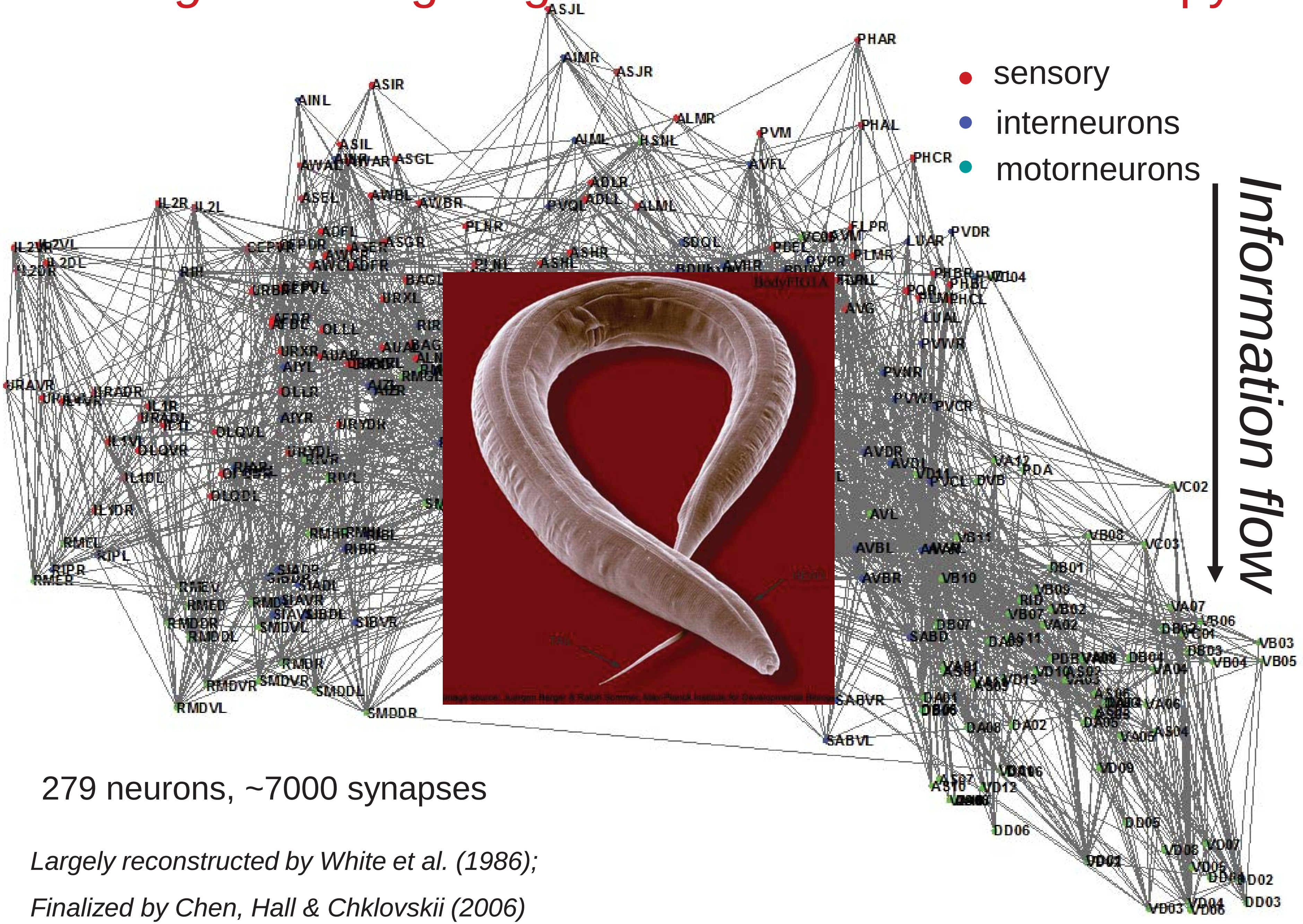
Posterior: Spinal cord

Dorsal	2,000K
Ventral	400K

Anterior/posterior ratio > 1 is consistent with forward brain placement

Cherniak, 1994

C. elegans wiring diagram from electron microscopy



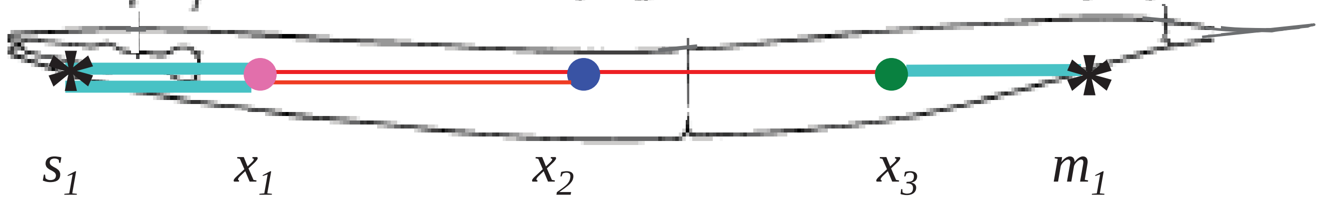
279 neurons, ~7000 synapses

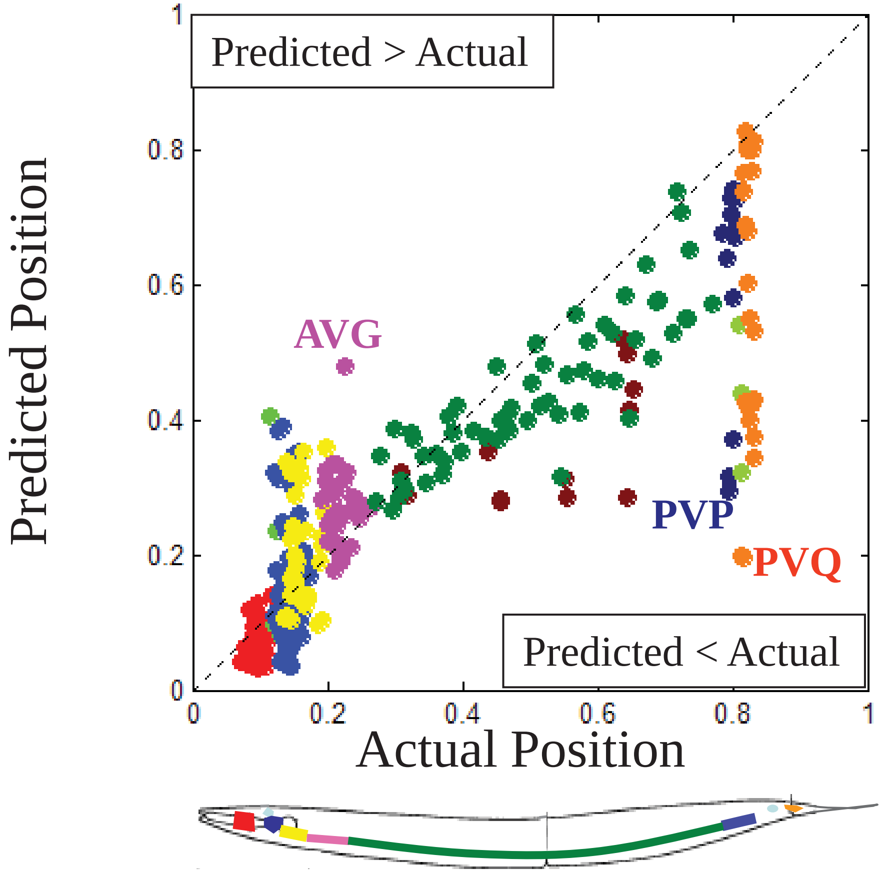
Largely reconstructed by White et al. (1986);

Finalized by Chen, Hall & Chklovskii (2006)

Neuronal layout optimization in *C. elegans*

$$Cost = \frac{1}{2\alpha}\sum_i\sum_j A_{ij}|x_i - x_j|^{\zeta} + \sum_i\sum_k S_{ik}|x_i - s_k|^{\zeta} + \frac{1}{\alpha}\sum_i\sum_l M_{il}|x_i - m_l|^{\zeta},$$





- Avg deviation: 9.7%

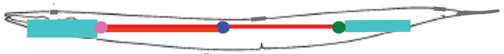
- Biggest outliers are pioneer neurons
- Motorneurons are seemingly sub-optimal:

  Predict proprio-sensory function

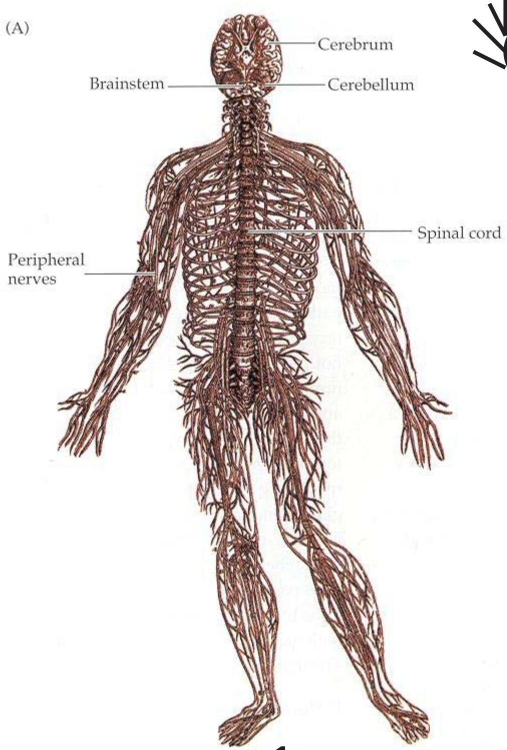
Chen, Hall & Chklovskii 2006

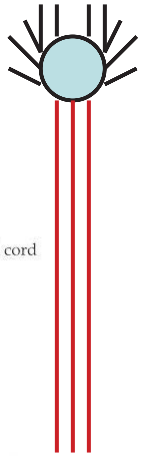
For given connectivity, wiring optimization largely predicts neuronal layout in invertebrates and long-range connections in vertebrates

Cherniak, Mitchison, Van Essen, Klyachko & Stevens, de Polavieja

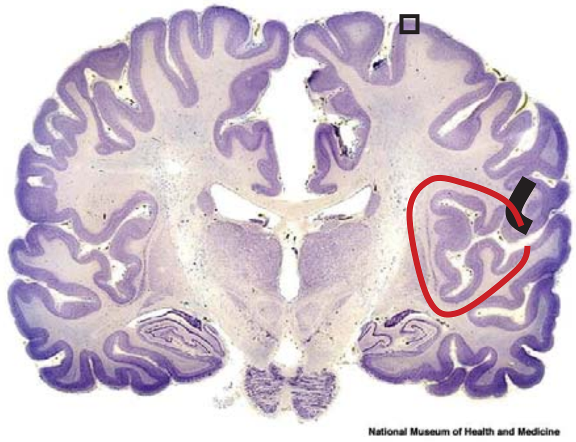


1mm



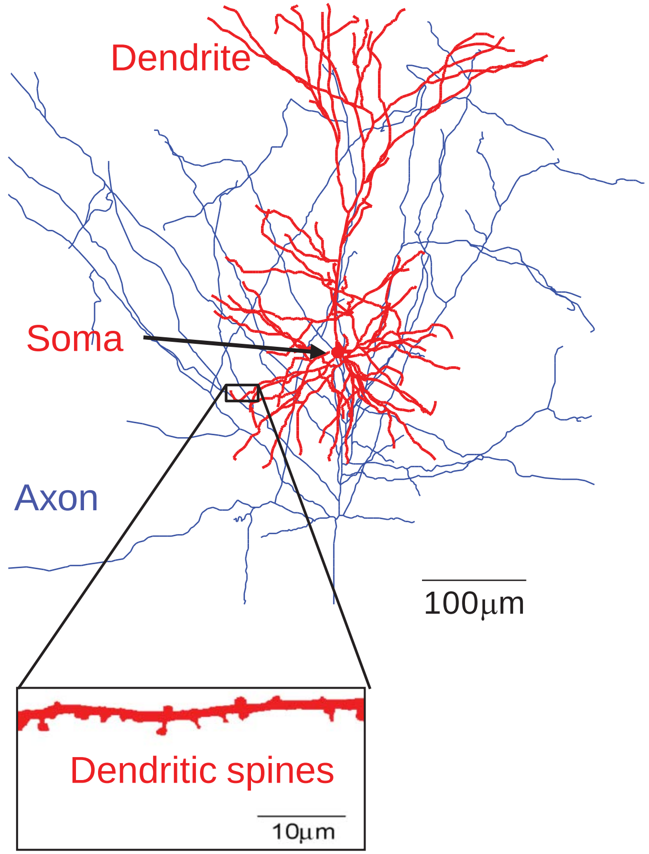


1m



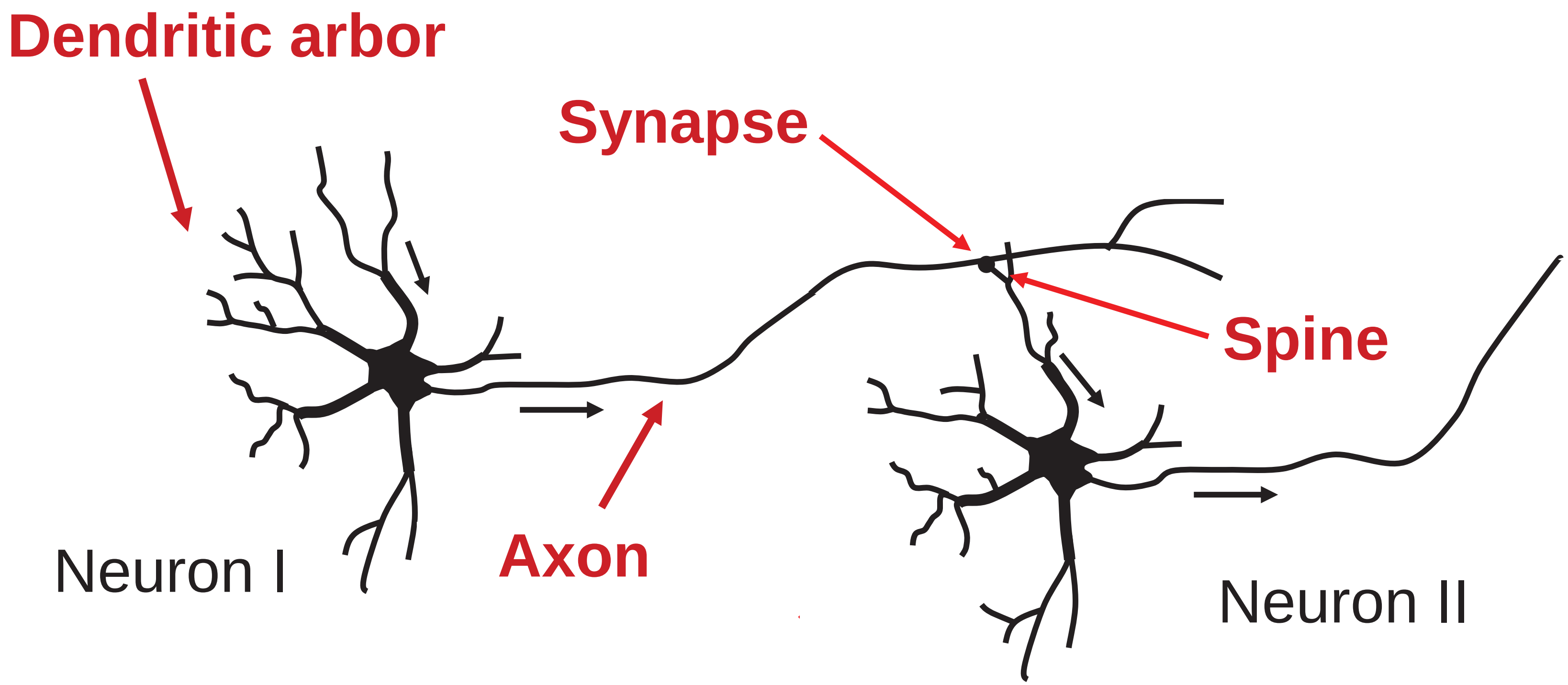
10cm

Pyramidal neuron



Courtesy: G. Shepherd

Computational function of a neuron

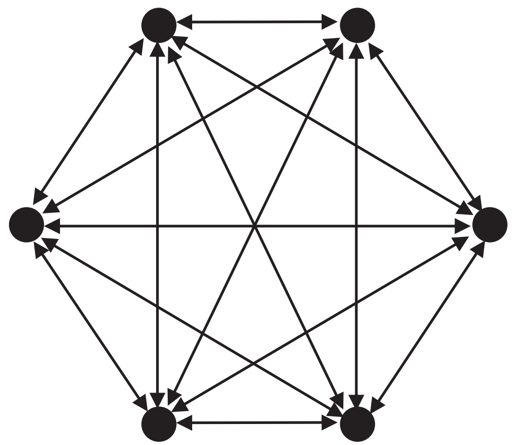


Is this an appropriate level of abstraction?

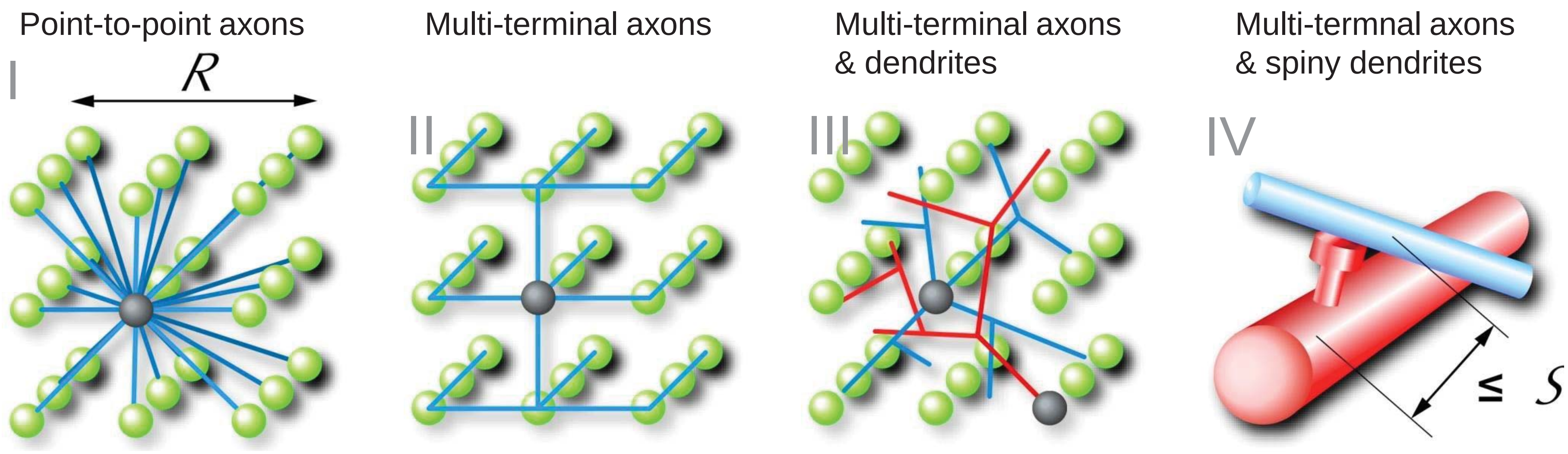
Wiring problem

What is the smallest volume of the all-to-all connected network of N neurons with wires of diameter d ?

Example, $N = 6$:



Wiring designs for an all-to-all network

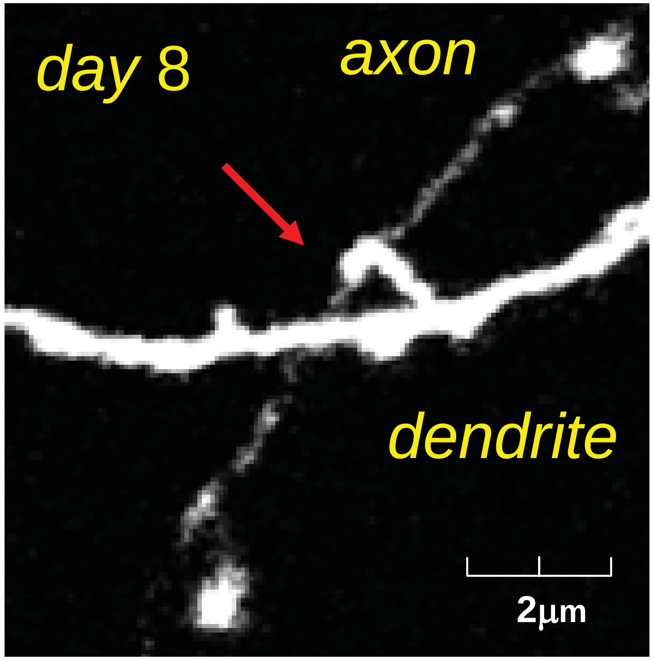


$R^3 \sim N^3 d^3$ $R^3 \sim N^{5/2} d^3$ $R^3 \sim N^2 d^3$ $R^3 \sim N^2 d^4/s$

Cortical column: N=10^5, d=0.2μm ; 0.5μm, s=1.5μm, R=1mm

8,000mm^3 30mm^3 2mm^3 0.6mm^3

Synaptic connectivity in mammalian cortex can change with time: possible memory mechanism



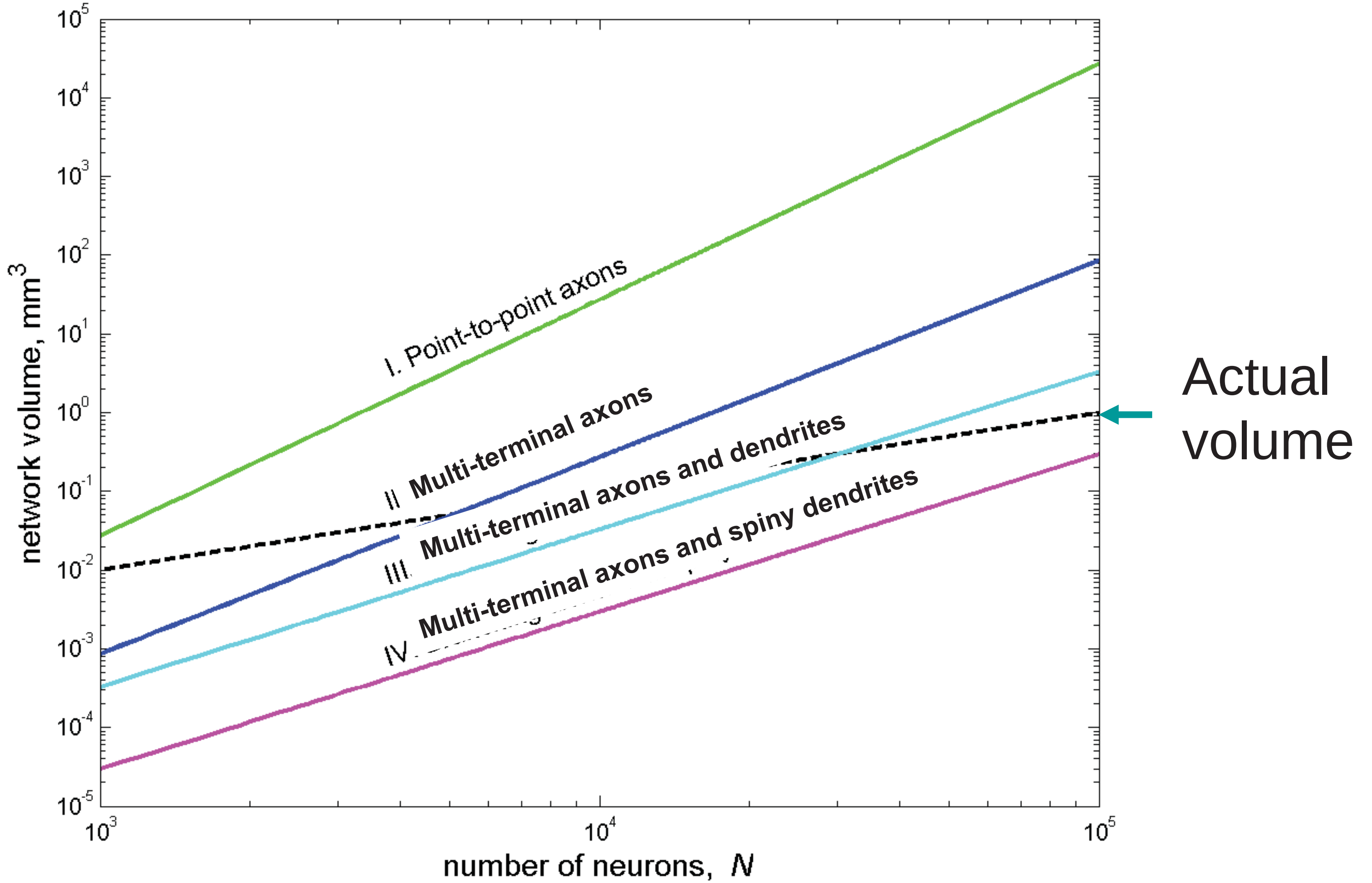
Trachtenberg, Chen, Knott, Feng, Sanes, Welker, Svoboda, 2002

Potential synapse - a proximity between a dendrite and an axon that can be bridged by a spine

Stepanyants, Hof & Chklovskii (2002)

Characterize neuronal functionality by the number of potential synapses

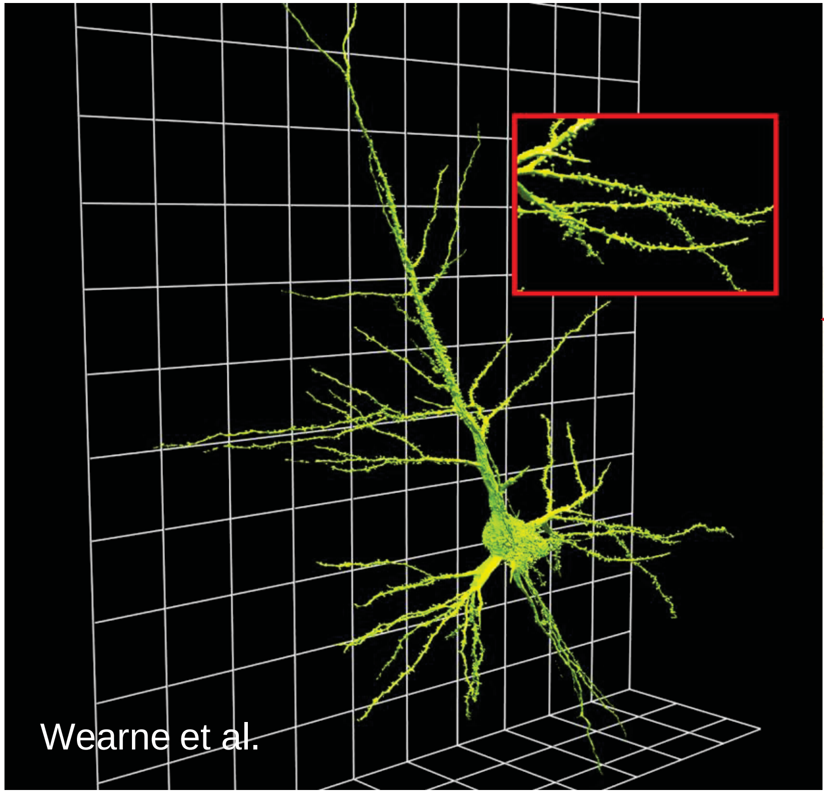
Network volume for different designs

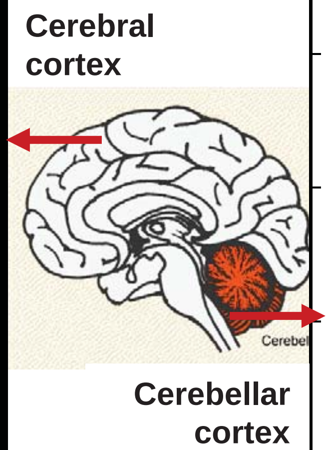


Chklovskii, 2004

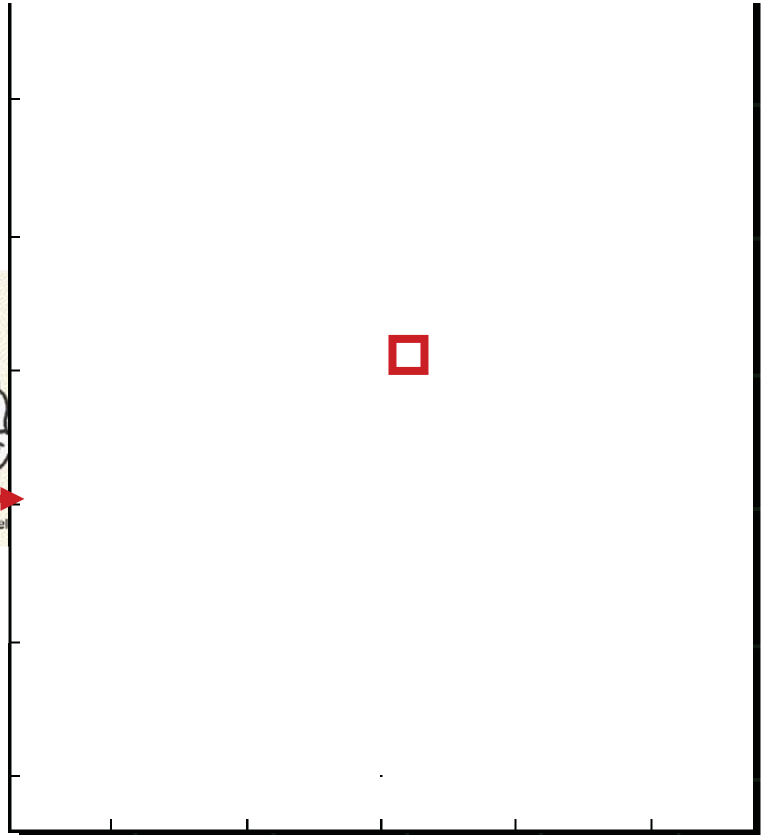
Do shapes of mammalian neurons reflect interesting computations in dendrites or just wiring cost minimization for given connectivity?

Pyramidal cell



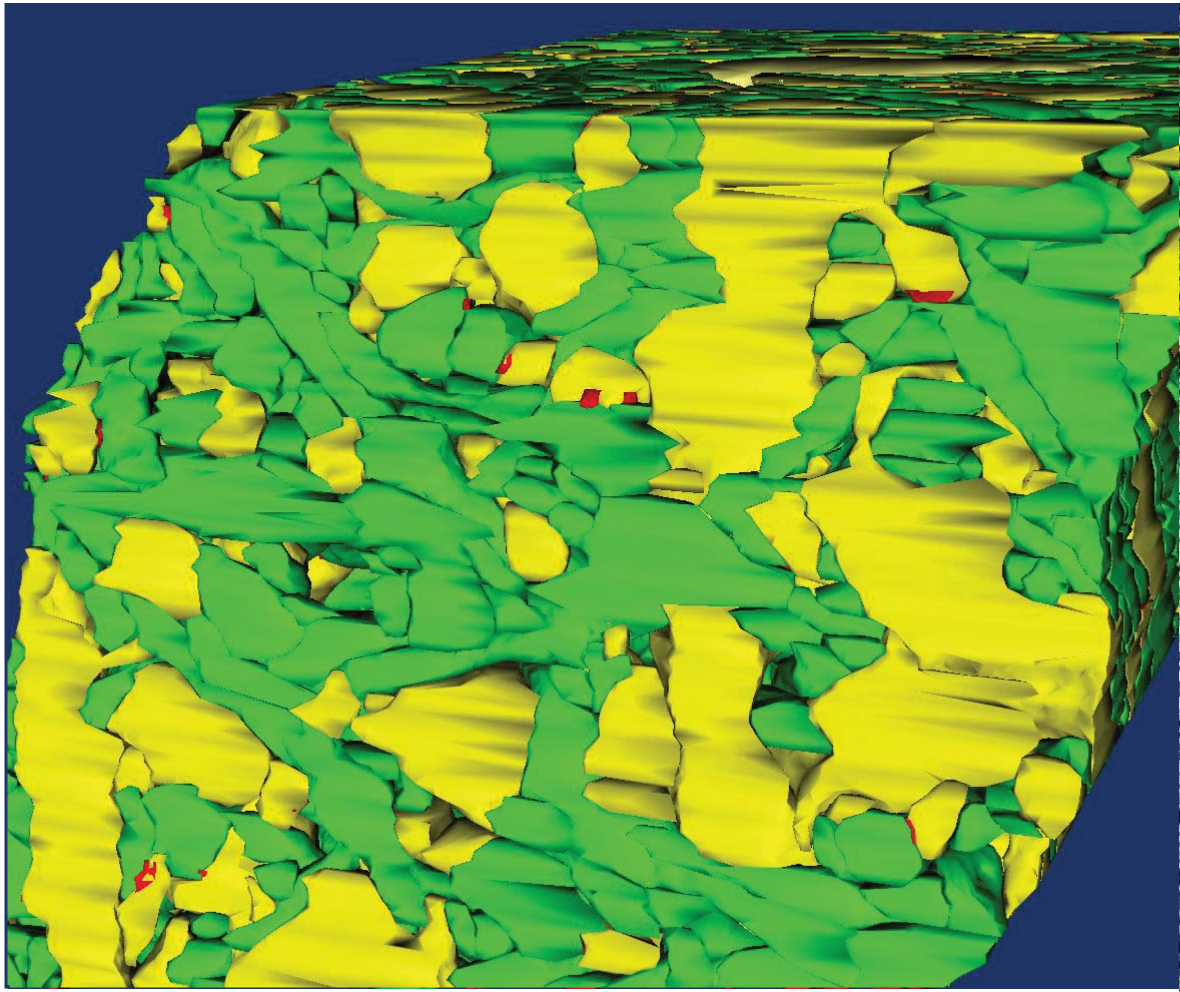


Purkinje cell



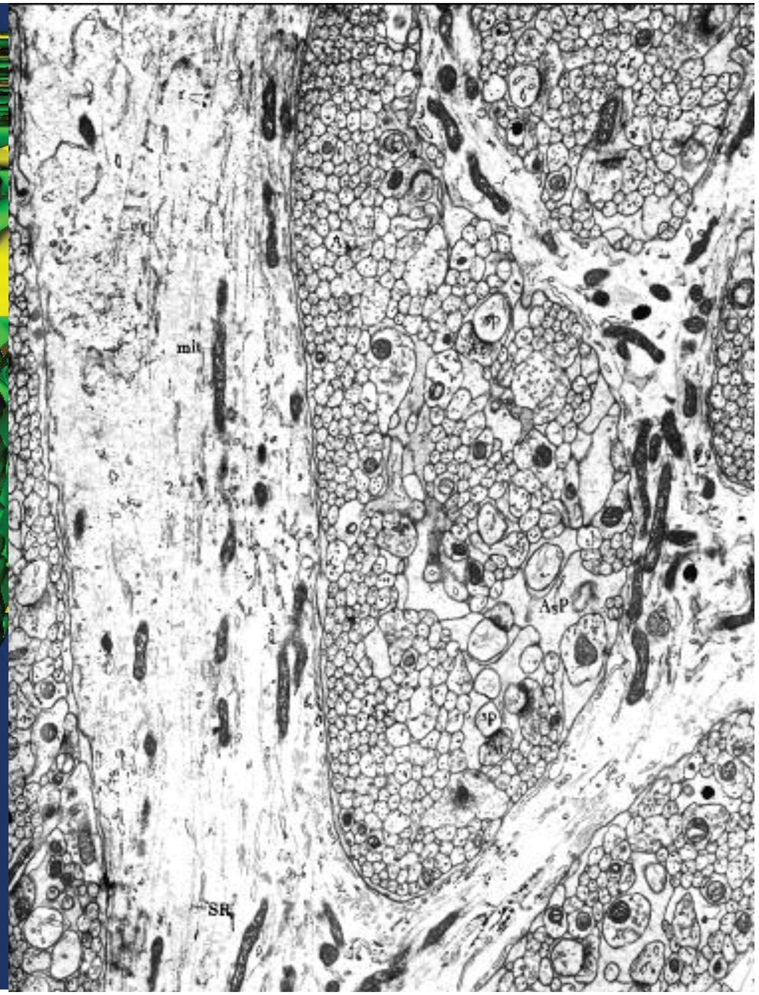
Mammalian neurons: 10^4-10^5 synapses - Large parameter! ☺

Packing of axons and dendrites is space-filling



Hippocampus: axons in all directions

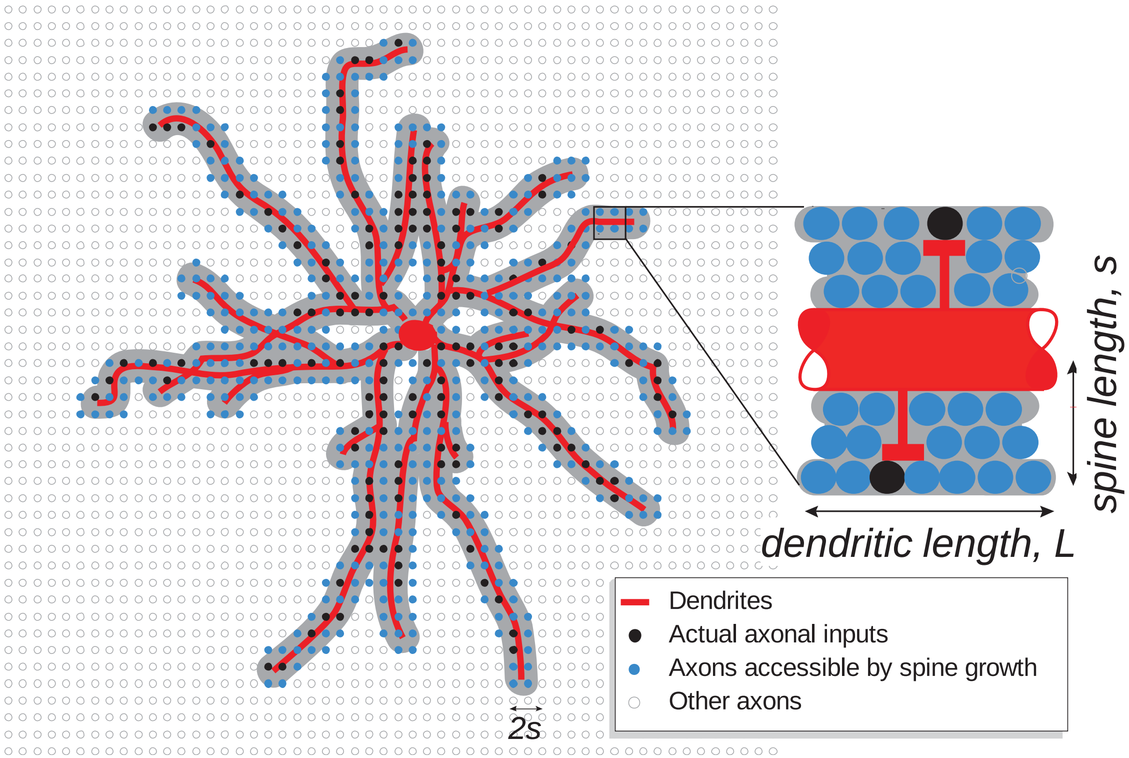
Mishchenko,Spacek,Mendenhall,Harris,Chklovskii



Cerebellum: axons orthogonal to dendrites

Sanford Palay

What determines the total length of dendrites?
The airport terminal theory



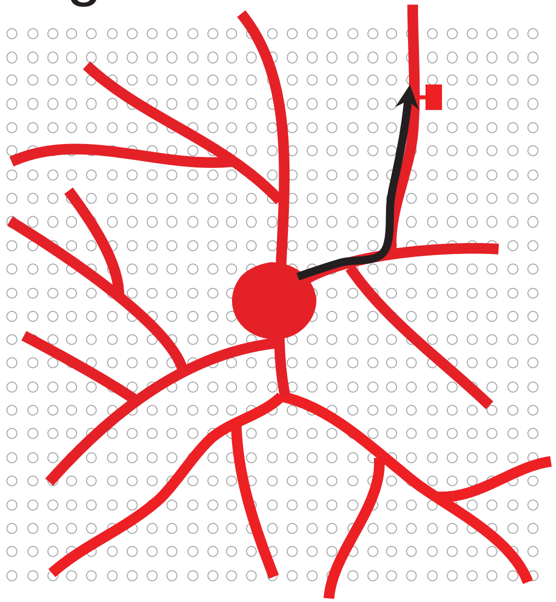
New York JFK airport

Total dendritic length, *L*, is determined by the number of potential synapses, *N*: $L \sim Nd^2/s$

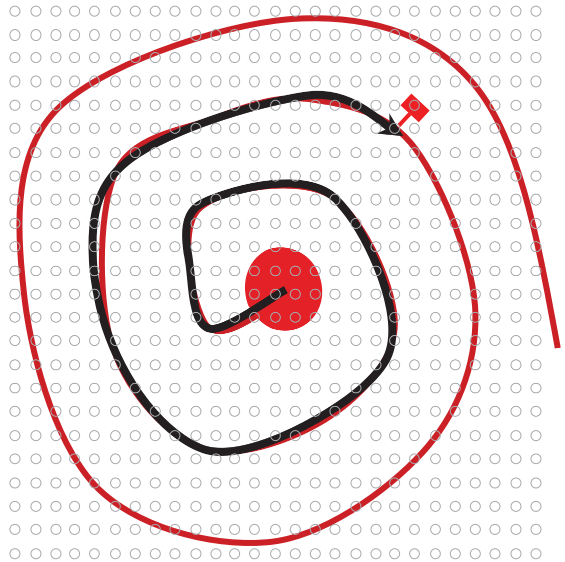
Pyramidal cells: $N = 10^5$ $d = 0.2\mu m$ $s = 1.5\mu m$ $\Longrightarrow$ $L = 2.6mm$

Why do dendrites branch?

Two dendrite designs with the same total length and number of potential synapses



Branching arbor



Non-branching arbor

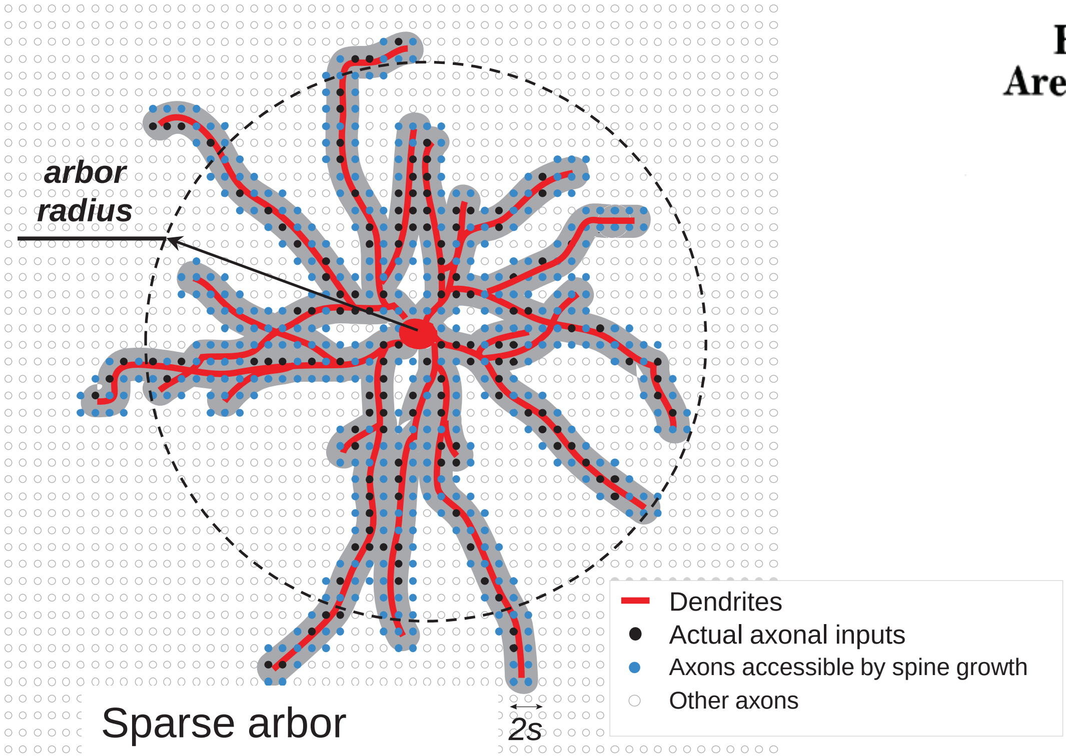
Chicago O’Hare airport

Branching dendrites have shorter path from synapses to cell body

Cuntz, Borst & Segev (2007), Wen & Chklovskii (2008)

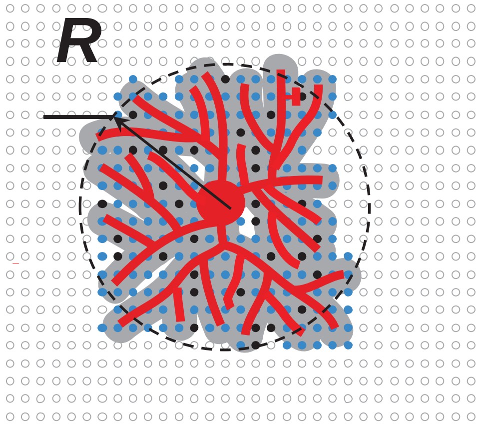
Compact arbor minimizes path length for a given total dendritic length

THE JOURNAL OF COMPARATIVE NEUROLOGY 361:479–490 (1995)



Retinal Neurons and Vessels Are Not Fractal But Space-Filling

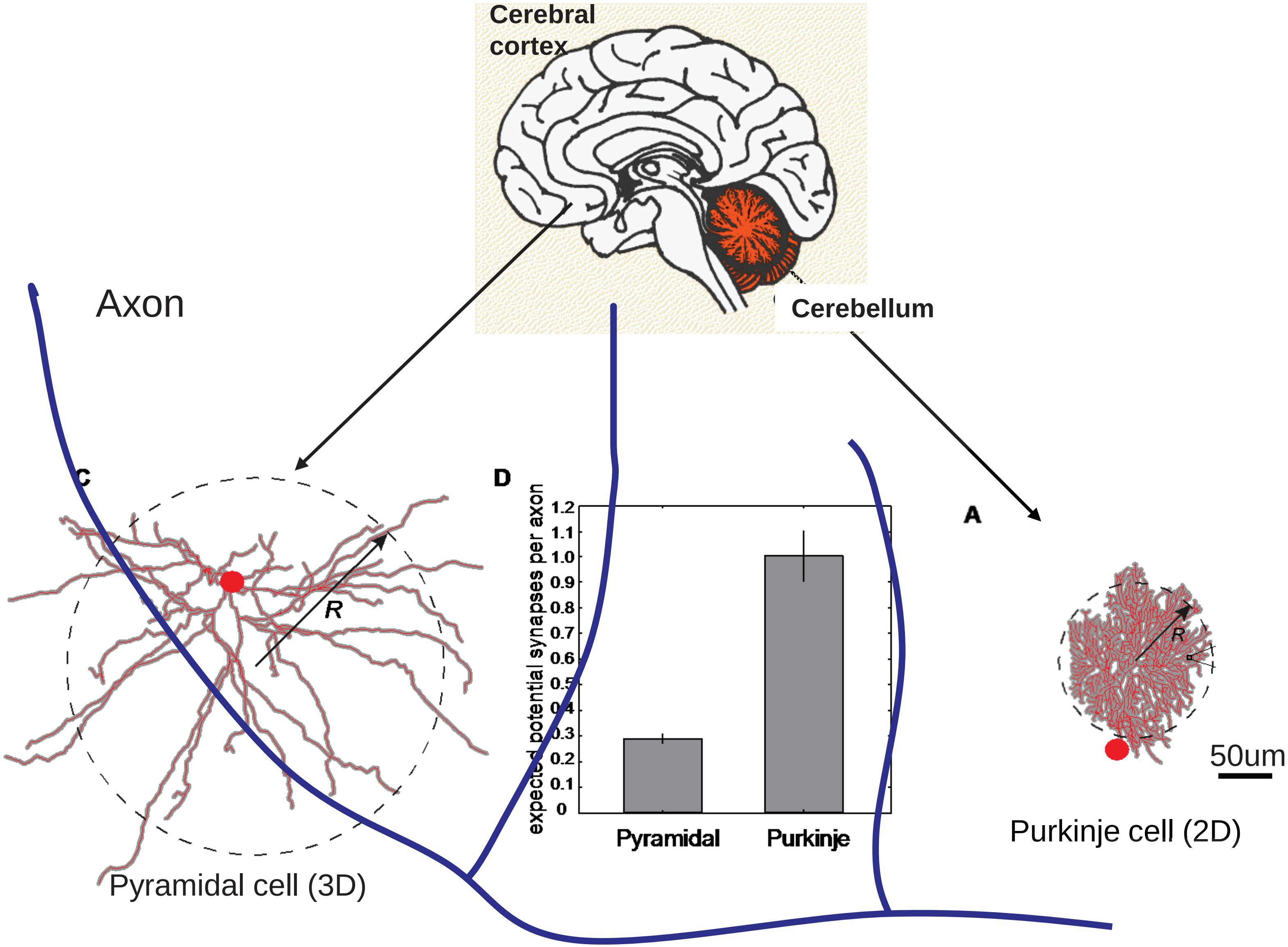
JOSEPH PANICO AND PETER STERLING
Department of Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6058



$$R \sim (Ls)^{1/2}$$

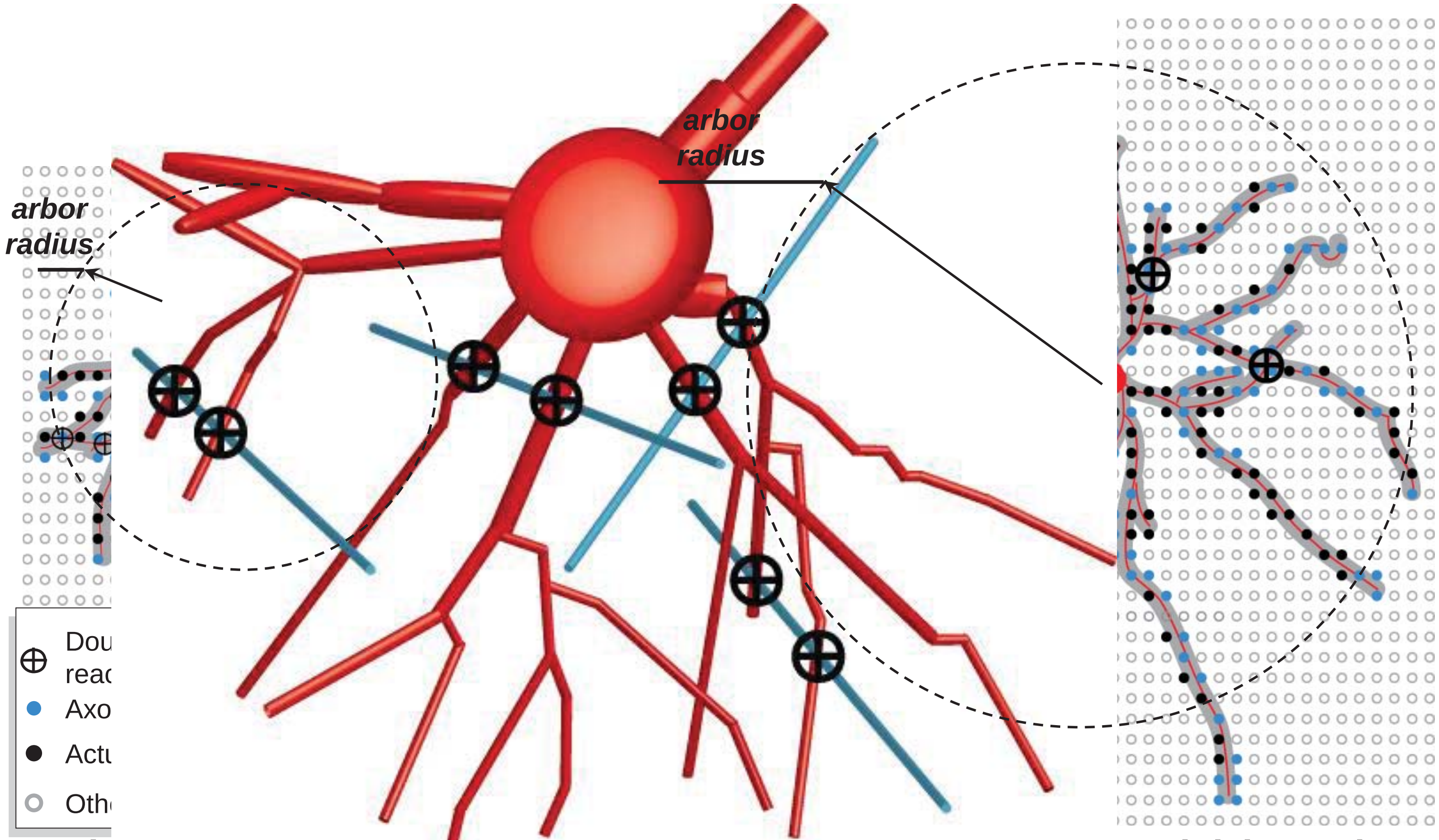
Compact arbor

For a given number of potential synapses, flat compact arbor minimizes wiring cost



Why are pyramidal cells sparse?

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



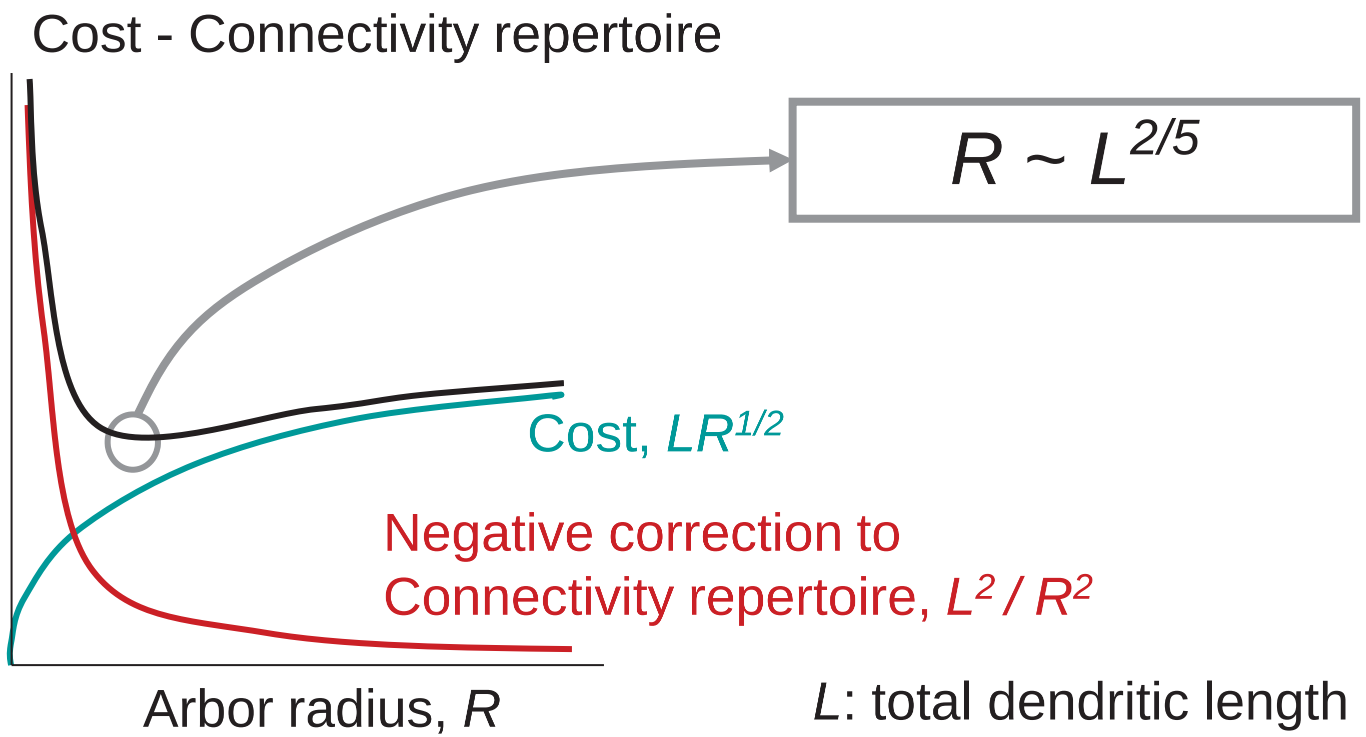
For a given total dendritic length, sparse 3D dendritic arbor has fewer double-hits, and, therefore, can access more axons

Statistical preference for sparse arbors, or self-repulsion

Samsonovich & Ascoli (2003)

Airport terminal with double-hits

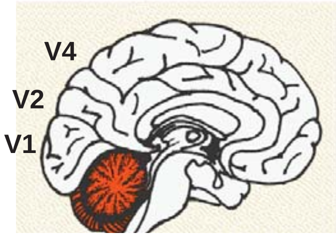
Arbor radius maximizes connectivity repertoire while minimizing cost
= min{Cost - Connectivity repertoire}

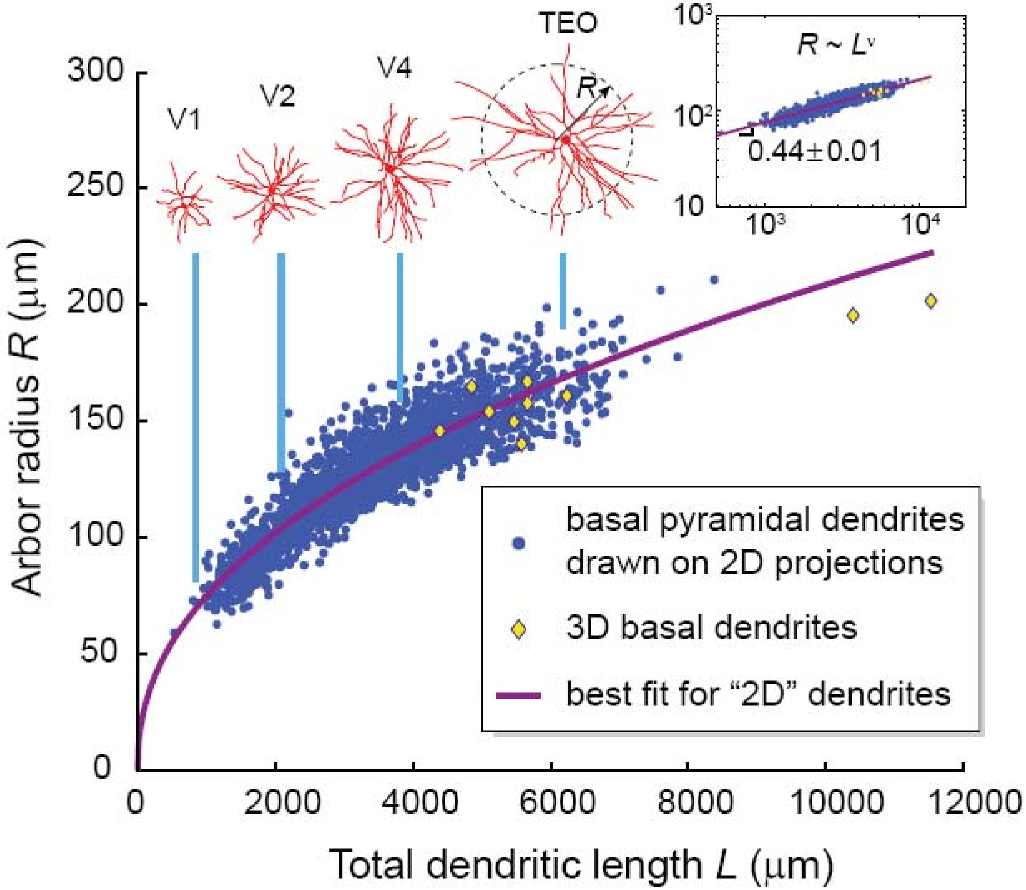


Free energy = Energy - Entropy

Scaling of basal dendrites of pyramidal cells

Cortical areas

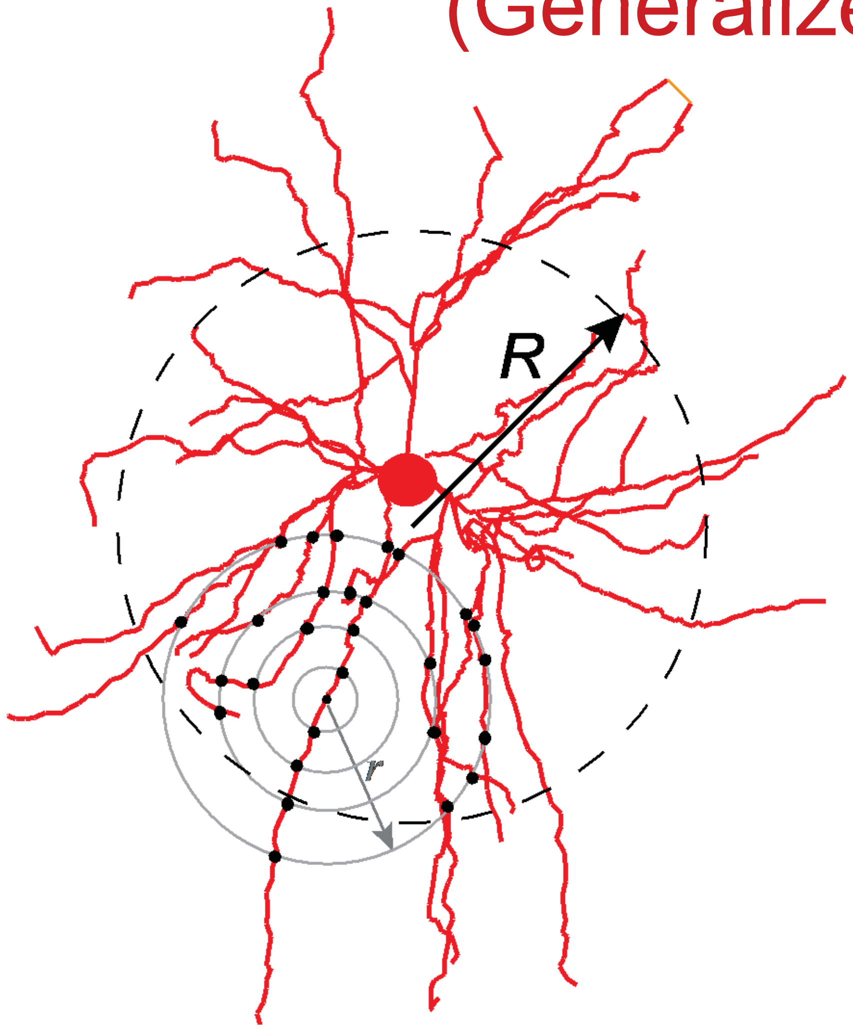


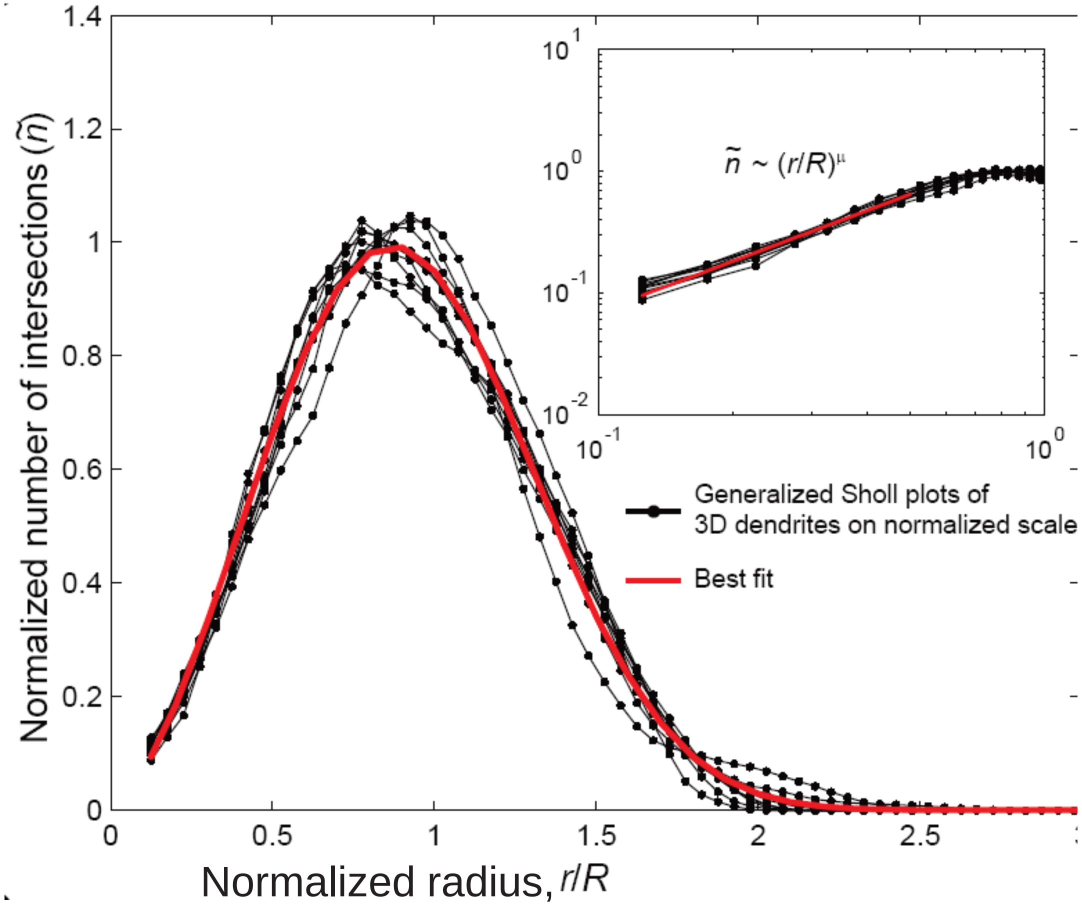


$R \sim L^{\nu}$ $\nu = 0.44 \pm 0.01$

$\nu_{theory} = 0.4$

Two-point correlation function (Generalized Sholl analysis)



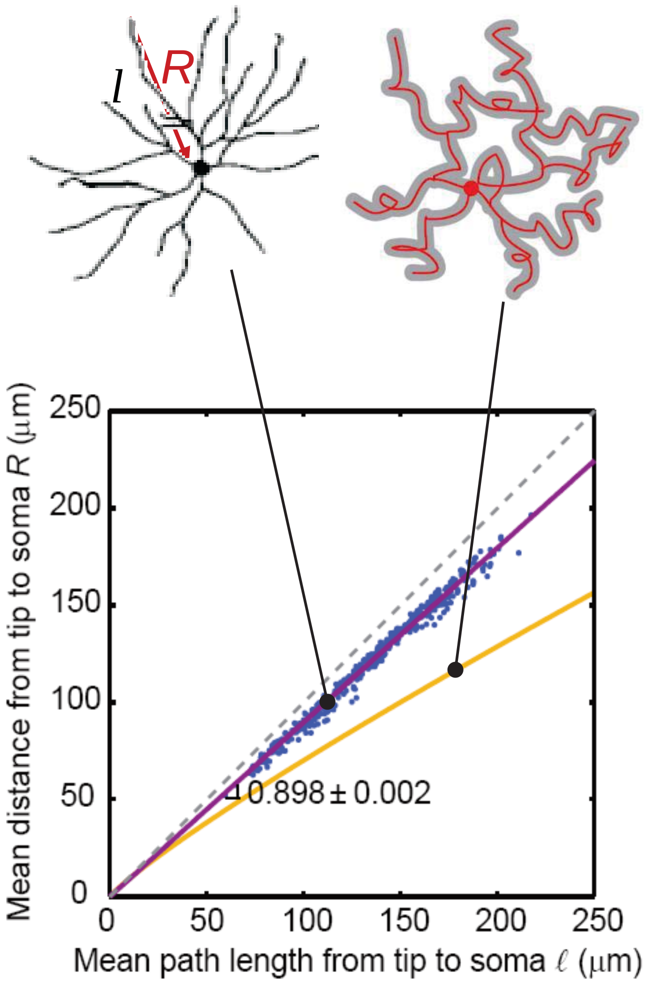


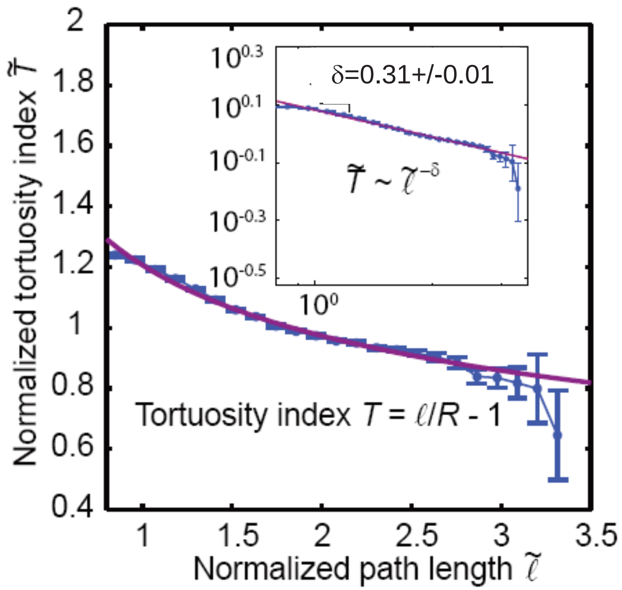
$$\tilde{n} = g(r/R)^{1/\nu - 1} \exp[-h(r/R)^{\gamma}]$$

Dendrites are “stretched” by the path length cost

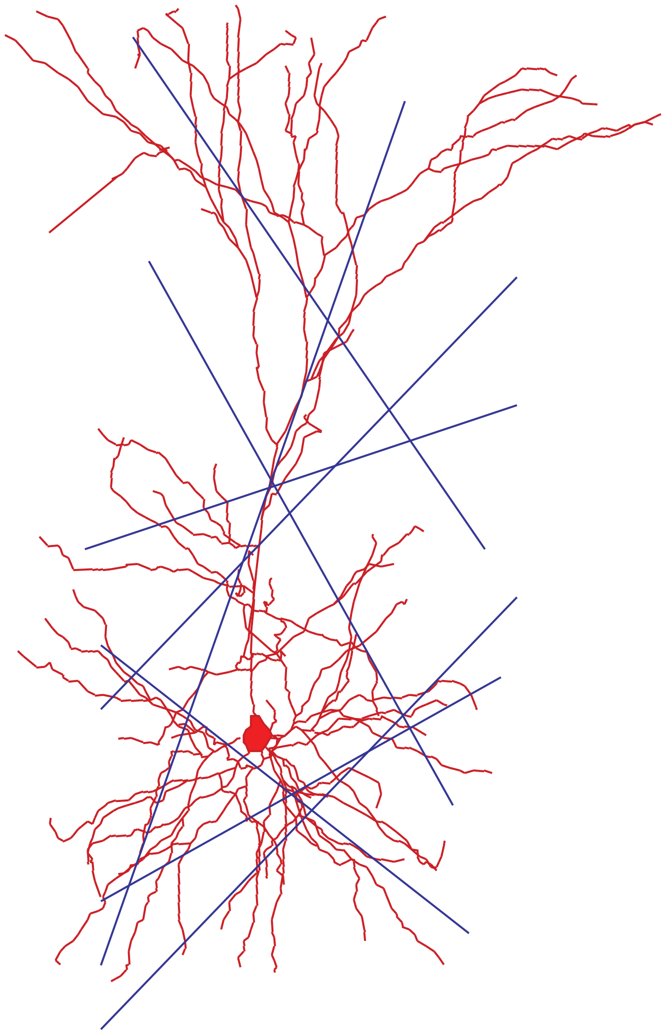
$$\mathcal{J} \sim \frac{L^2}{R^2} - \frac{L}{a}\log(1-R/\ell) + \beta L \ell^{\delta}$$

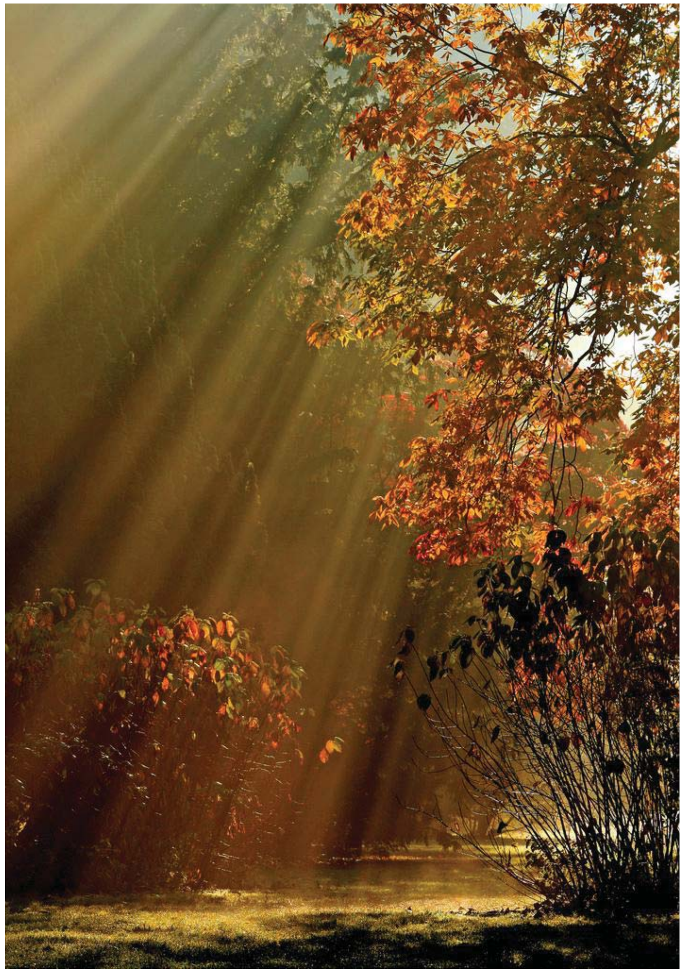
$$\frac{\ell}{R} - 1 = \frac{1}{\delta\beta\ell^{\delta}a}$$





Why do neurons and trees look alike?





Minimize: Wiring cost

Maximize: Connectivity repertoire

Summary

- Minimizing wiring cost for given connectivity explains neuronal layout in invertebrates and long-range connections in vertebrates

- Minimizing wiring cost while maximizing connectivity repertoire can account for the shape of mammalian neurons

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