Theory in neurobiology

Our goal is to make non-trivial, robust and experimentally testable predictions

- What? Creative theory-driven data analysis
- How? Mechanistic models of brain function
- Why? Constrained optimization of brain design and function

Basic principles of brain design and function

Wiring of the cortical column

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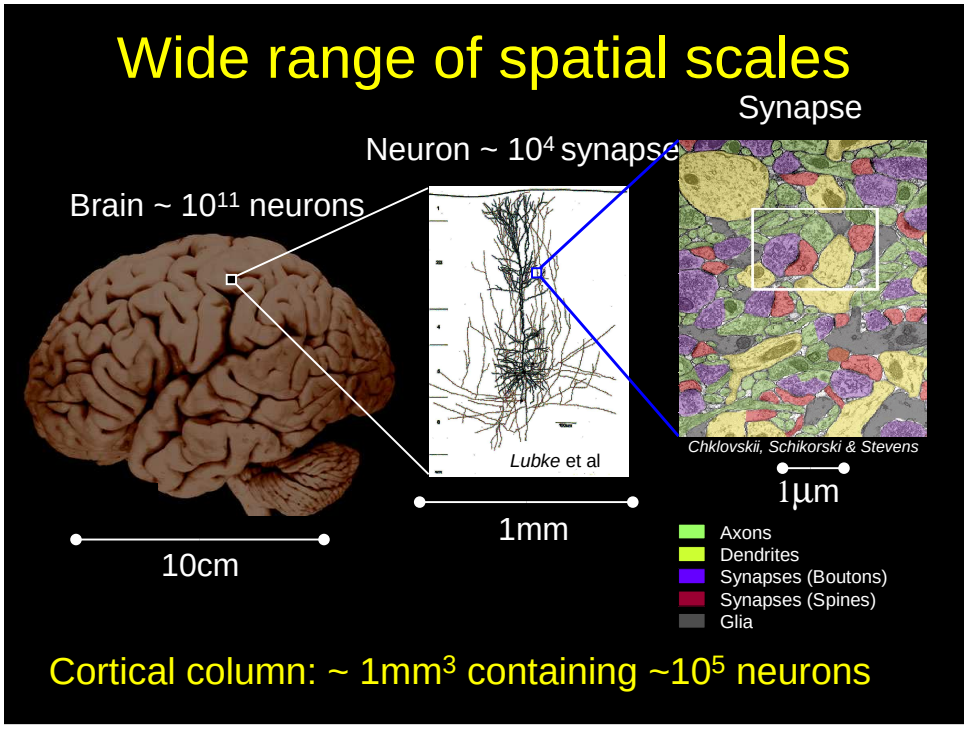
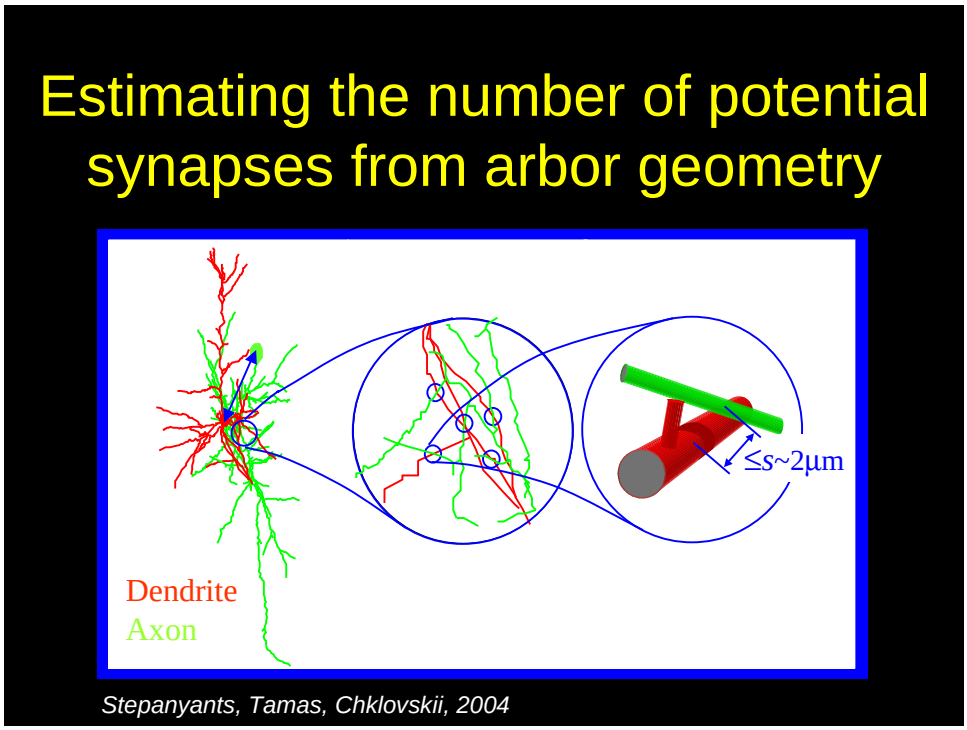
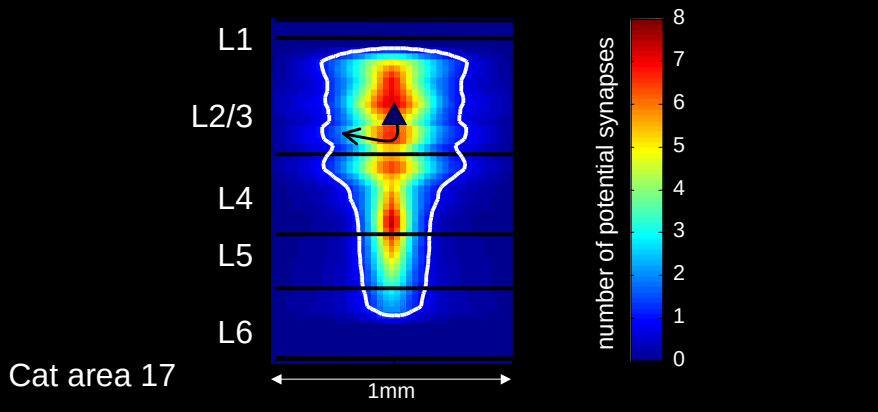

Wide range of spatial scales
Synapse
Neuron ~ 10^4 synapse
Brain ~ 10^11 neurons
Lubke et al
Chklovskii, Schikorski & Stevens
1µm
1mm
10cm
Axons
Dendrites
Synapses (Boutons)
Synapses (Spines)
Glia
Cortical column: ~ 1mm^3 containing ~10^5 neurons


Estimating the number of potential synapses from arbor geometry
≤s~2µm
Dendrite
Axon
Stepanyants, Tamas, Chklovskii, 2004

Number of potential synapses made by a pyramidal neuron in the visual cortex



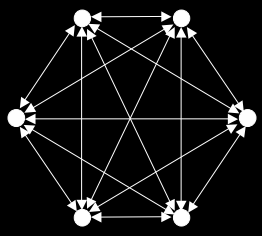
Stepanyants, Hirsch, Martinez, Kisvarday, Ferecsko and Chklovskii (2004)

A cortical neuron is capable of synapsing onto most neurons in its column

Wiring problem

Fully connected (all-to-all) network of k neurons

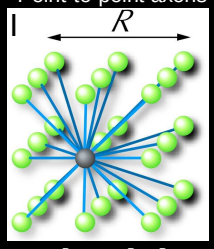
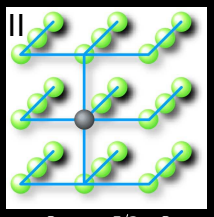
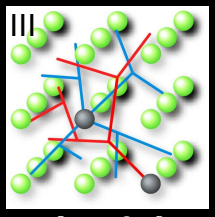
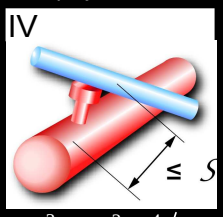
Example, $k = 6$:



To implement such network using wires of diameter d in the smallest possible volume

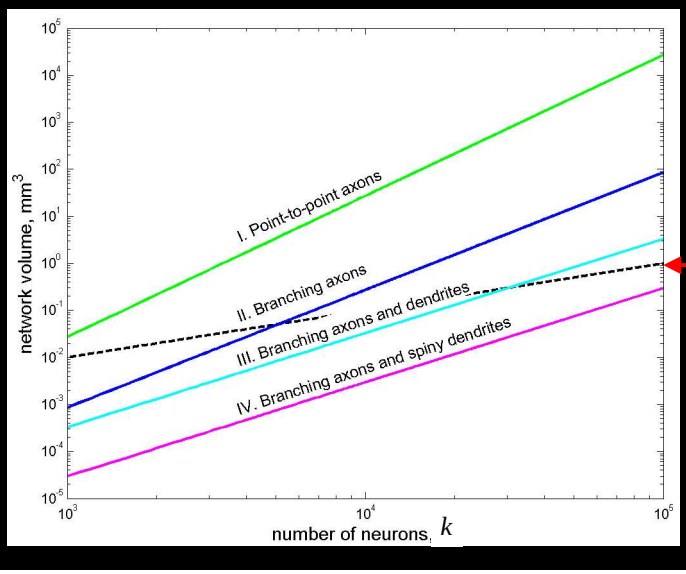
Network volume for different wiring designs

Cortical column: R=1mm, k=10^5,d=0.3μm;1μm, s=2.5μm

Point-to-point axons	Branching axons	Branching axons & dendrites	Branching axons & spiny dendrites
I	II	III	IV
			
$R^3 \sim k^3 d^3$	$R^3 \sim k^{5/2} d^3$	$R^3 \sim k^2 d^3$	$R^3 \sim k^2 d^4/s$
30,000mm^3	100mm^3	2mm^3	0.6mm^3

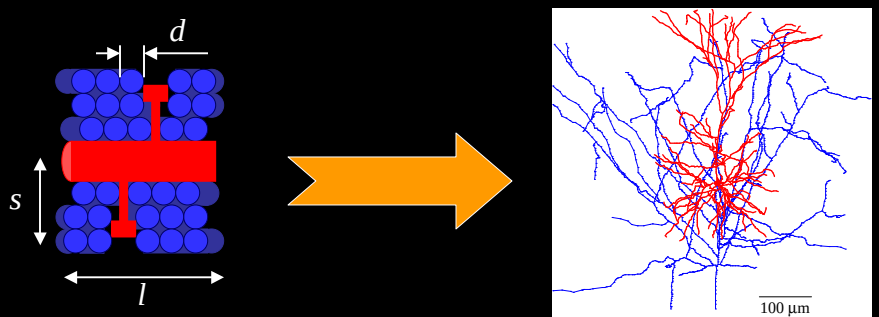
Chklovskii, 2004

Network volume for different designs



Actual volume

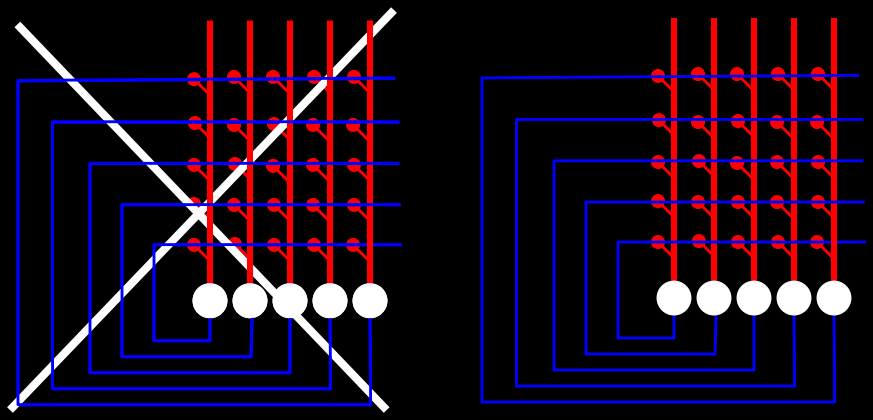
Axons and dendrites are just long enough to make potential synapses with every neuron in a column



Minimal length of a dendrite with k potential synapses: $l \sim kd^2/s$, same as design IV

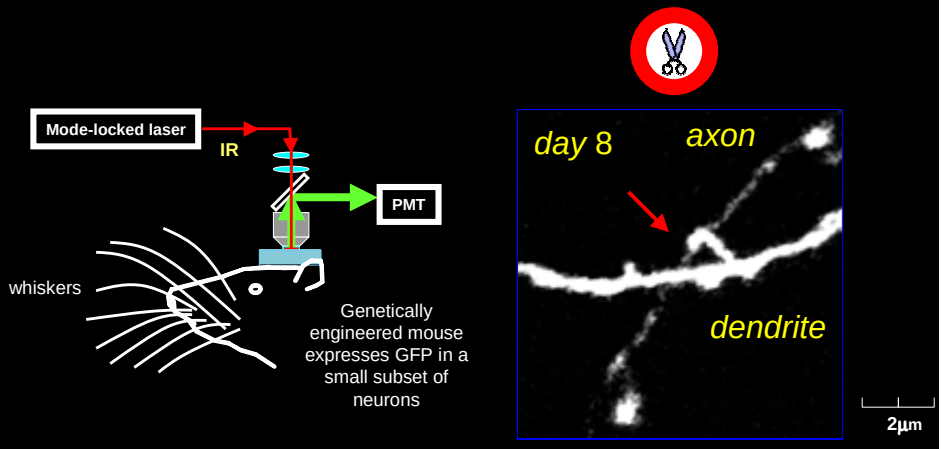
$k=10^5$ $d=0.3\mu m$ $s=2.5\mu m$ $\Rightarrow l=4mm$ *(Braitenberg)*

What fraction of potential synapses are actual synapses?



Circuit re-wiring through formation & elimination of spines is a potential memory mechanism with high information storage capacity (*Stepanyants, Hof, Chklovskii, 2002*)

Two-photon imaging provides evidence of synapse re-arrangement *in vivo*



Trachtenberg, …, Svoboda, 2002

Summary

- Dimensions of axons and dendrites are optimized for high potential connectivity in a small volume
- Circuit re-wiring through formation and elimination of spines is a potential memory mechanism with high information storage capacity