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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Wiring of a Cortical Column

Wide range of spatial scales

Brain ~ \(10^{11}\) neurons

Cortical column: \(~1mm^3\) containing \(~10^5\) neurons

Estimating the number of potential synapses from arbor geometry

Dendrite
Axon

\[ <r \sim 2\mu m \]

*Stepanyants, Tamas, 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: $R=1\text{mm}$, $k=10^5$, $d=0.3\mu\text{m}$; $1\mu\text{m}$, $s=2.5\mu\text{m}$

<table>
<thead>
<tr>
<th>Design</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$R^3 \cdot k^3 d^3$</td>
</tr>
<tr>
<td>II</td>
<td>$R^3 \cdot k^{5/2} d^3$</td>
</tr>
<tr>
<td>III</td>
<td>$R^3 \cdot k^2 d^3$</td>
</tr>
<tr>
<td>IV</td>
<td>$R^3 \cdot k^2 d^4 / s$</td>
</tr>
</tbody>
</table>

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

\[
\begin{align*}
k &= 10^5 \\
d &= 0.3 \mu m \\
s &= 2.5 \mu m \\
\Rightarrow l &= 4 \text{mm} \\
\end{align*}
\]

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 \textit{in vivo}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image}
\caption{Genetically engineered mouse expresses GFP in a small subset of neurons.}
\end{figure}

\textit{Trachtenberg, ..., Svoboda, 2002}

\section*{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.