V. Biological Neural Networks

A. Overview

A Very Brief Tour of
Real Neurons

(and Real Brains)

The Lobes of the Cerebral Hemispheres
The brain is organized over sizes that span 6 orders of magnitude

J W Lichtman, W Denk Science 2011;334:618-623

Published by AAAS
Overview of Brain to Neurons

Animation of Neuron

• An animated film about nicotine addiction
• A good visualization of a single neuron
• ©2006, Hurd Studios
• Winner of NSF/AAAS Visualization Challenge
• View flash video

Grey Matter vs. White Matter
Part 4B: Real Neurons

Neural Density in Cortex

- 148,000 neurons / sq. mm
- Hence, about 15 million / sq. cm

Cortical Areas

Intercortical Connections

- (1) Short arcuate bundles, (2) Superior longitudinal fasciculus, (3) External capsule, (4) Inferior occipitofrontal fasciculus, (5) Uncinate fasciculus, (6) Sagittal stratum, (7) Inferior longitudinal fasciculus
Intercortical Connections (diffusion spectrum imaging)

Brodman’s Areas

Somatosensory & Motor Homunculi
Reorganization of Cortex

- Median nerve sectioned to show fluidity of cortical organization
- (C) before
- (D) immediately after
- (E) several months later

Macaque Visual System

Hierarchy of Macaque Visual Areas

Fig. from Clark & al., "Being There," 1997

Fig. from Van Essen & al., 1992
B. Neurons

Typical Neuron

Dendritic Trees of Some Neurons

A. inferior olivary nucleus
B. granule cell of cerebellar cortex
C. small cell of reticular formation
D. small gelatinous cell of spinal trigeminal nucleus
E. ovoid cell, nucleus of tractus solitarius
F. large cell of reticular formation
G. spindle-shaped cell, substantia gelatinosa of spinal chord
H. large cell of spinal trigeminal nucleus
I. putamen of lenticular nucleus
J. double pyramidal cell, Ammon’s horn of hippocampal cortex
K. thalamic nucleus
L. globus pallidus of lenticular nucleus

Fig. from Trues & Carpenter, 1964
Axonal Terminations
(Tectum of Turtle)

Axonal Net

Neural Connections
(array tomography by O’Shea at SmithLab, Stanford)
Minicolumn
- Up to ~100 neurons
  - 75–80% pyramidal
  - 20–25% interneurons
- 20–50 µ diameter
- Length: 0.8 (mouse) to 3 mm (human)
- ~6x10^5 synapses
- 75–90% synapses outside minicolumn
- Interacts with 1.2x10^6 other minicolumns
- Mutually excitable
- Also called microcolumn

Layers and Minicolumns

Macrocolumns
- ~70 inhibitory-coupled minicolumns in humans
- 70% of minicol. connections are within macrocol.
- Basket neurons provide shunting inhibition between minicolumns
- Winner-takes-all networks
- Represent microfeatures
Part 4B: Real Neurons

Intracortical Connections

- Dendrites extend 2–4 minicol. diameters
- Axons extend 5× (or even 30–40×) minicol. diameter
- Periodic spacing of axon terminal clusters causes entrainment
- ∼2×10^7 connections to macrocolumn

Neural Networks in Visual System of Frog
Chemical Synapse

1. Action potential arrives at synapse
2. Ca ions enter cell
3. Vesicles move to membrane, release neurotransmitter
4. Transmitter crosses cleft, causes postsynaptic voltage change

Typical Receptor

video by Hybrid Medical Animation
Fig. 3 Activity-dependent modulation of pre-, posts-, and trans-synaptic components.

V M Ho et al. Science 2011;334:623-628
Published by AAAS

Fig. 4 Local regulation of the synaptic proteome.

V M Ho et al. Science 2011;334:623-628
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Fig. 3: A 3D model of synaptic architecture.

(A) A section through the synaptic bouton, indicating 60 proteins.
(B) High-zoom view of the active zone area.
(C) High-zoom view of one vesicle within the vesicle cluster.
(D) High-zoom view of a section of the plasma membrane in the vicinity of the active zone. Clusters of synaptobrevin (yellow) and SNAP 25 (red) are visible, as well as a recently fused synaptic vesicle (top). The graphical legend indicates the different proteins (right). Displayed synaptic vesicles have a diameter of 42 nm.

B G Wilhelm et al. Science 2014;344:1023-1028
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Fig. 3. A 3D model of synaptic architecture. (A) Action through the synapse, indicating 60 proteins. The proteins are shown in the colors indicated in tables S1 and S2 and in positions determined according to the imaging data (Fig. 2 and fig. S6) and to the literature (see fig. S6 for details). (B) High-zoom view of the active zone area. (C) High-zoom view of synaptic vesicles with vesicle clusters. (D) High-zoom view of the plasma membrane in the vicinity of the active zone. Clusters of syntaxin (yellow) and SNAP 25 (red) are visible, as well as a recently fused synaptic vesicle (top). The graphical legend indicates the different proteins (right). Displayed synaptic vesicles have a diameter of 42 nm.
Video of 3D Model

Input Signals

- **Excitatory**
  - about 85% of inputs
  - AMPA channels, opened by glutamate

- **Inhibitory**
  - about 15% of inputs
  - GABA channels, opened by GABA
  - produced by inhibitory interneurons

- **Leakage**
  - potassium channels

- **Synaptic efficacy:** net effect of:
  - presynaptic neuron to produce neurotransmitter
  - postsynaptic channels to bind it

Membrane Potential (Variables)

- $g_e = \text{excitatory conductance}$
- $E_e = \text{excitatory potential (}-0\text{ mV})$
- $g_i = \text{inhibitory conductance}$
- $E_i = \text{inhibitory potential (}-70\text{ mV})$
- $g_l = \text{leakage conductance}$
- $E_l = \text{leakage potential}$
- $V_m = \text{membrane potential}$
- $\theta = \text{threshold}$
Membrane Potential

Currents: $I_x = g_x(E_x - V_m)$, $x = e, i, l$

Net current: $I_{net} = I_e + I_i + I_l$

Change in membrane potential: $V_m = C \frac{dV_m}{dt}$ (C is rate constant)

$V_m = C g_x(E_x - V_m) + g_i(E_i - V_m) + g_l(E_l - V_m)$

Equilibrium $V_m = \frac{g_x E_x + g_i E_i + g_l E_l}{g_x + g_i + g_l}$

Slow Potential Neuron

Action Potential Generation
Part 4B: Real Neurons

Frequency Coding

Variations in Spiking Behavior

Dendritic computation in pyramidal cells.
Rate Code Approximation

- Rate-coded (simulated) neurons:
  - short-time avg spike frequency
  - avg behavior of microcolumn (~100 neurons) with similar inputs and output behavior
- Rate not predicted well by $V_m$
- Predicted better by $g_e$ relative to a threshold value $g_e^\theta$

\[
\theta = \frac{g_e^\theta E_s + g_i E_i + g_e E_i}{g_e^\theta + g_i + g_e}
\]

Rate Code Approximation

- $g_e^\theta$ is the conductance when $V_m = \theta$
- Rate is a nonlinear function of relative conductance
- What is $f$?

\[
y = f(g_e - g_e^\theta)
\]

Activation Function

- Desired properties:
  - threshold (~0 below threshold)
  - saturation
  - smooth
- Smooth by convolution with Gaussian to account for noise
- Activity update:
  \[
y_{out} = y_t + C(y - y_t)
\]

\[
y = \frac{x}{x+1} \text{ where } x = \eta[g_e - g_e^\theta]
\]

\[
y = \frac{1}{1 + \frac{1}{\eta[g_e - g_e^\theta]}}
\]