V. Biological Neural Networks

A. Overview

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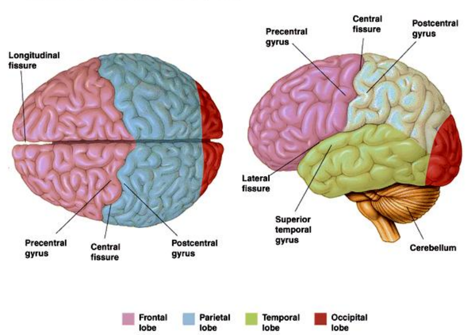
A Very Brief Tour of Real Neurons

(and Real Brains)

► The Lobes of the Cerebral Hemispheres



3/25/15 (fig. from internet) 3

Left Hemisphere

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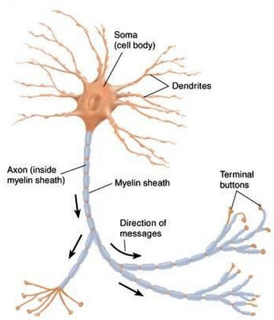
Typical Neuron



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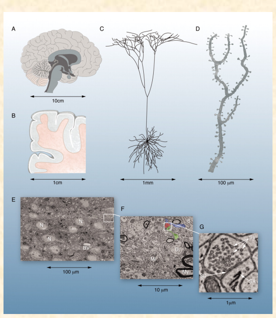
The brain is organized over sizes that span 6 orders of magnitude



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

Science AAAS

Published by AAAS

Overview of Brain to Neurons

<http://www.youtube.com/watch?v=DF04XPBj5uc>

(play flash video)

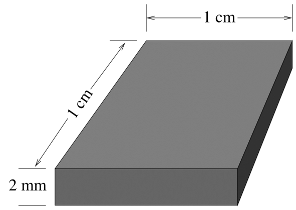
Animation of Neuron

- 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

(fig. from Carter 1998)

Neural Density in Cortex



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

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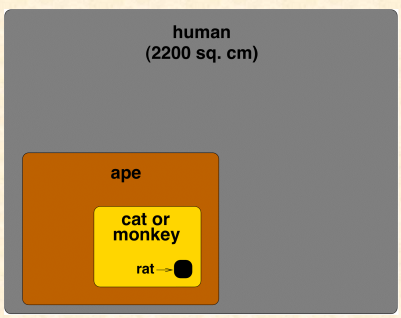
Cortical Areas



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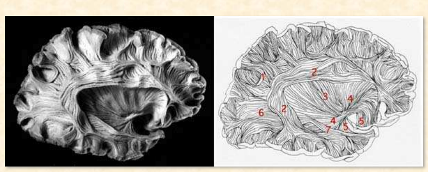
Intercortical Connections



- (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

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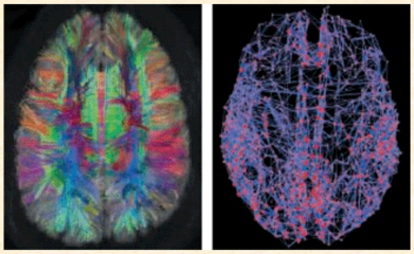
Intercortical Connections
(diffusion spectrum imaging)

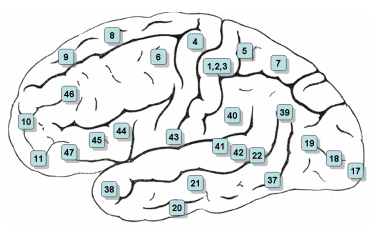


G. Miller Science 330, 164 (2010) (2010)

Published by AAAS

3/25/15 13

Brodmann's Areas



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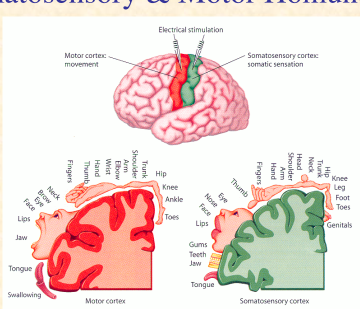
Somatosensory & Motor Homunculi



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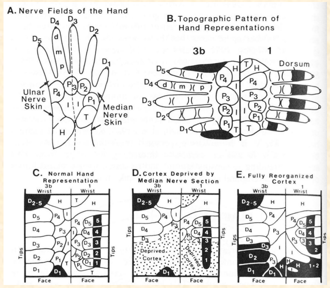
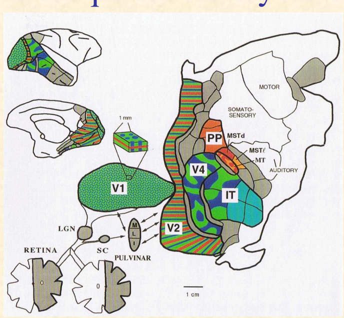
Reorganization of Cortex



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

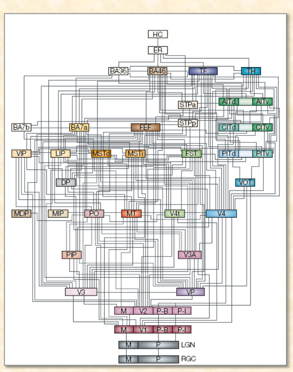
3/25/15 (fig. < McClelland & al, *Par. Distr. Proc.* II) 16

Macaque Visual System



3/25/15 (fig. from Clark, *Being There*, 1997) 17

Hierarchy of Macaque Visual Areas



3/25/15 (fig. from Van Essen & al. 1992) 18

B. Neurons

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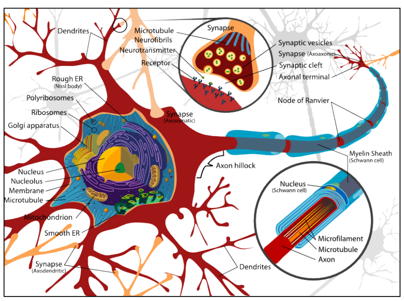
Typical Neuron



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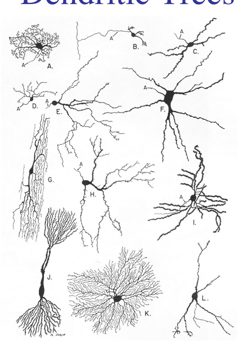
Dendritic Trees of Some Neurons



- A. inferior olivary nucleus
- B. granule cell of cerebellar cortex
- C. small cell of reticular formation
- D. small gelatinosa 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)

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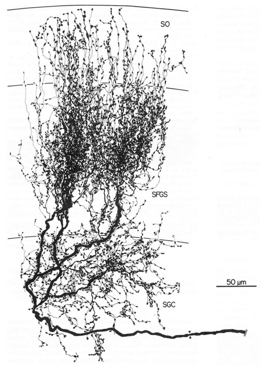
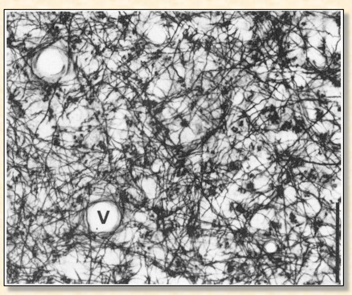
Axonal Terminations
(Tectum of Turtle)



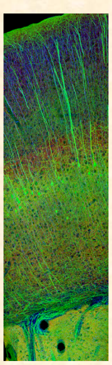
3/25/15 (fig. from Sereno & Ulinski 1987) 22

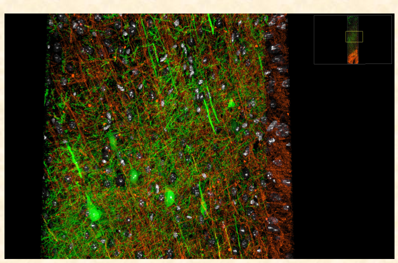
Axonal Net



3/25/15 (fig. from Arbib 1995) 23

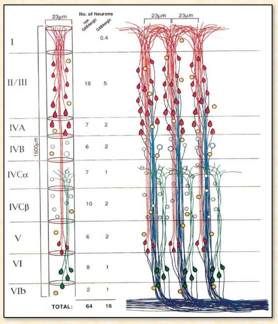
Neural Connections





3/25/15 (array tomography by O’Shea at SmithLab, Stanford) 24

Minicolumn



- Up to ~100 neurons
  - 75–80% pyramidal
  - 20–25% interneurons
- 20–50μ diameter
- Length: 0.8 (mouse) to 3mm (human)
- ~ $6{\times}10^5$ synapses
- 75–90% synapses outside minicolumn
- Interacts with $1.2{\times}10^5$ other minicolumns
- Mutually excitable
- Also called *microcolumn*

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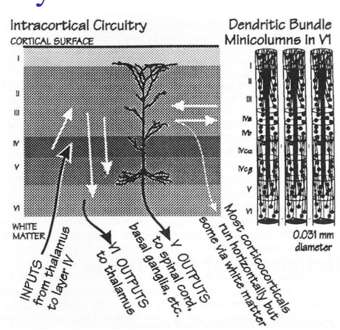
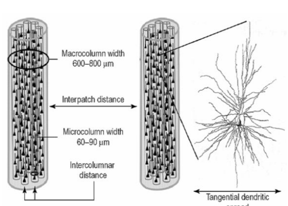
Layers and Minicolumns



3/25/15 (fig. from Arbib 1995, p. 270) 26

Macrocolumns



- ~70 inhibitorally-coupled minicolumns in humans
- 70% of minicol. connections are within macrocol.
- Basket neurons provide shunting inhibition between minicolumns
- Winner-takes-all networks
- Represent microfeatures

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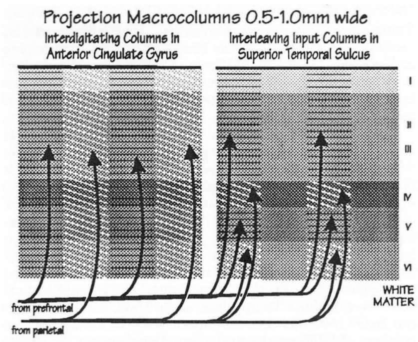
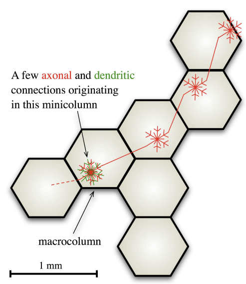


3/25/15 (fig. from Arbib 1995, p. 270) 28

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



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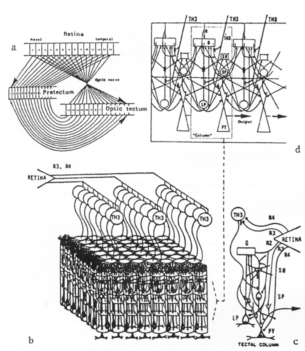
Neural Networks in Visual System of Frog



3/25/15 (fig. from Arbib 1995, p. 1039) 30

Synapses

video by Hybrid Medical Animation

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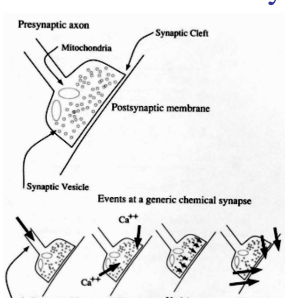
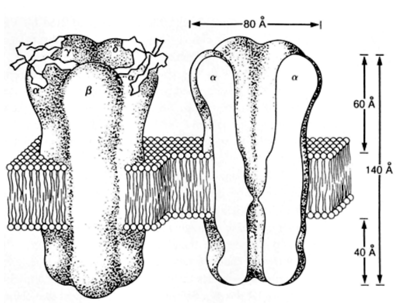
Chemical Synapse



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

3/25/15 (fig. from Anderson, *Intr. Neur. Nets*) 32

Typical Receptor



3/25/15 (fig. from Anderson, *Intr. Neur. Nets*) 33

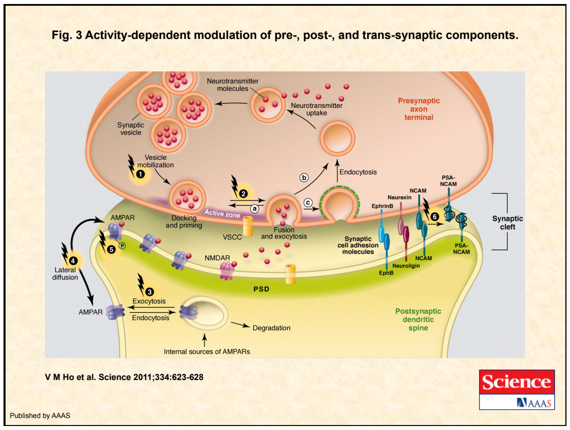


Fig. 3 Activity-dependent modulation of pre-, post-, and trans-synaptic components.
Neurotransmitter molecules
Neurotransmitter uptake
Presynaptic axon terminal
Synaptic vesicle
Vesicle mobilization
Endocytosis
Docking and priming
Active zone
Fusion and exocytosis
VSCC
AMPAR
NMDAR
Lateral diffusion
Synaptic cell adhesion molecules
EphrinB
Neurexin
NCAM
PSA-NCAM
Neuroligin
EphB
Synaptic cleft
PSD
Exocytosis
Endocytosis
Degradation
Internal sources of AMPARs
Postsynaptic dendritic spine
V M Ho et al. Science 2011;334:623-628
Science
AAAS
Published by AAAS

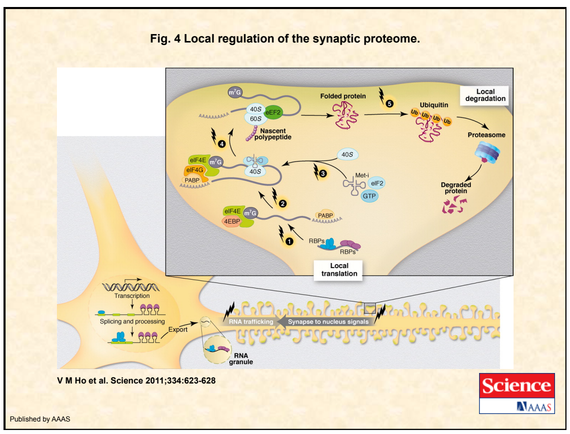


Fig. 4 Local regulation of the synaptic proteome.
Folded protein
Ubiquitin
Local degradation
Nascent polypeptide
Proteasome
Degraded protein
Local translation
Transcription
Splicing and processing
Export
RNA trafficking
Synapse to nucleus signals
RNA granule
V M Ho et al. Science 2011;334:623-628
Science
AAAS
Published by AAAS

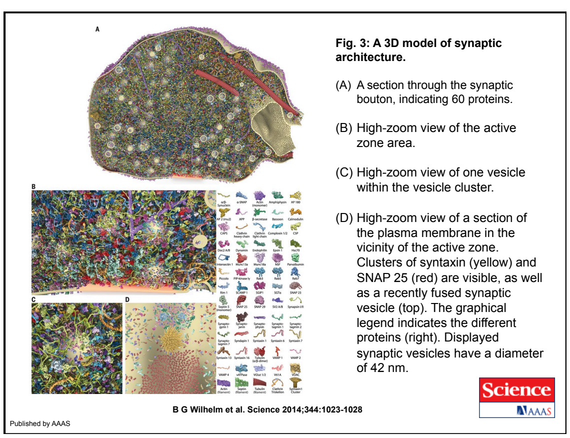
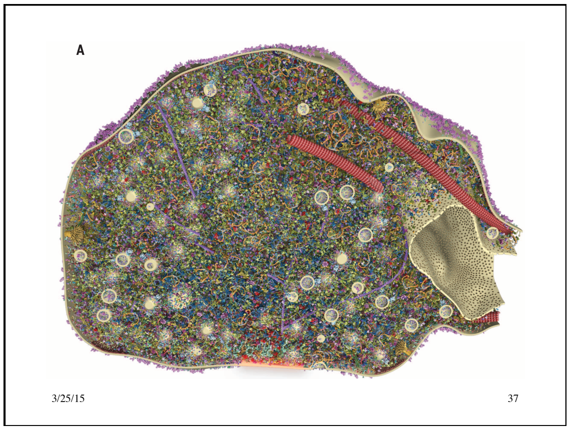
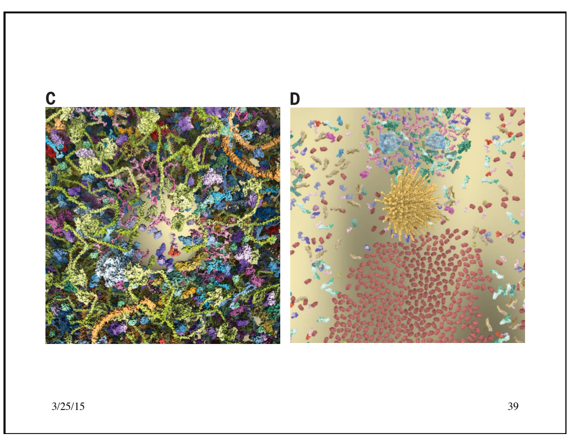


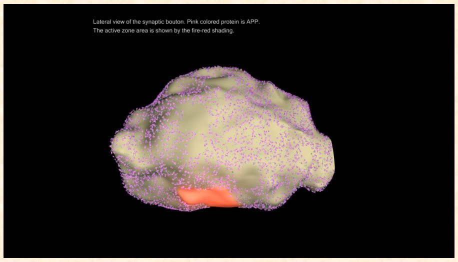
Fig. 3: A 3D model of synaptic architecture.
(A) A section through the synaptic bouton, indicating 60 proteins.
(B) High-zoom view of the active zone area.
(C) High-zoom view of one vesicle within the vesicle cluster.
(D) High-zoom view of a section of the plasma membrane in the vicinity of the active zone. Clusters of 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.
B G Wilhelm et al. Science 2014;344:1023-1028
Science
AAAS
Published by AAAS


A
3/25/15
37


B
3/25/15
38


C
D
3/25/15
39

Video of 3D Model



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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

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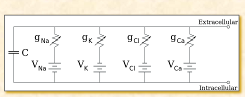
Membrane Potential (Variables)

- g_e = excitatory conductance
- E_e = excitatory potential (~ 0 mV)
- g_i = inhibitory conductance
- E_i = inhibitory potential (–70 mV)
- g_l = leakage conductance
- E_l = leakage potential
- V_m = membrane potential
- θ = threshold



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Membrane Potential

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

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

Change in membrane potential: $\dot{V}_m = CI_{\text{net}}$ (C is rate constant)

$$\dot{V}_m = C\left[g_e\left(E_e - V_m\right) + g_i\left(E_i - V_m\right) + g_l\left(E_l - V_m\right)\right]$$

Equilibrium $V_m = \dfrac{g_e E_e + g_i E_i + g_l E_l}{g_e + g_i + g_l}$

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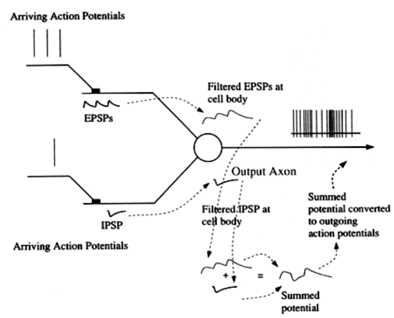
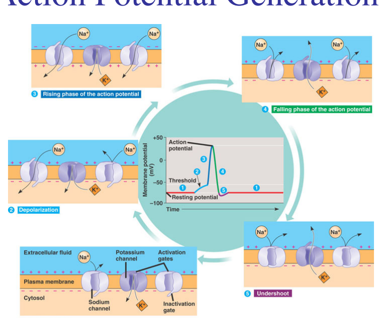
Slow Potential Neuron

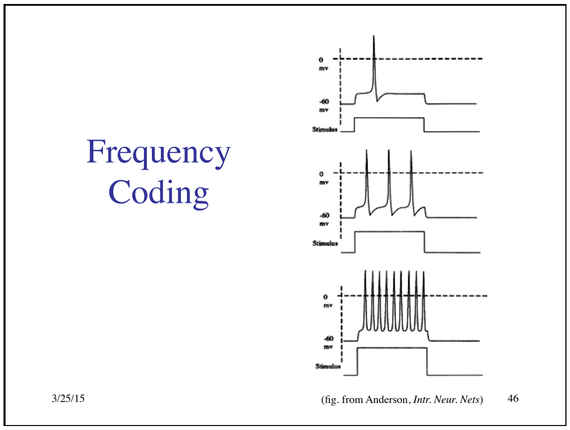


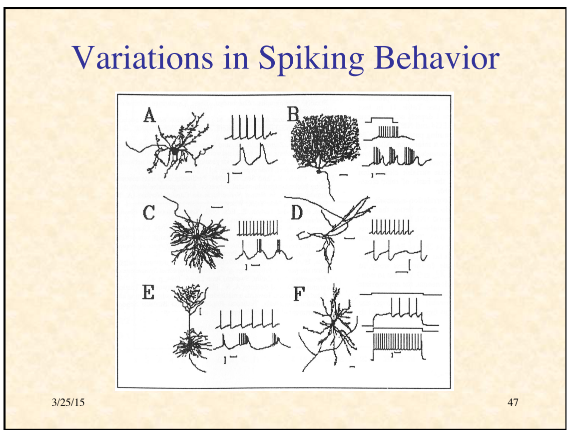
3/25/15 (fig. < Anderson, *Intr. Neur. Nets*) 44

Action Potential Generation



3/25/15 45


Frequency Coding
0 mv
-60 mv
Stimulus
3/25/15
(fig. from Anderson, *Intr. Neur. Nets*)
46


Variations in Spiking Behavior
A
B
C
D
E
F
3/25/15
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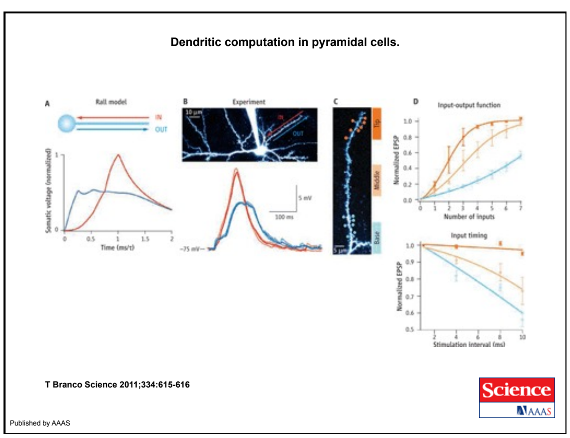
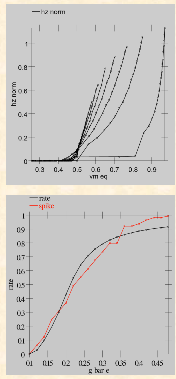

Dendritic computation in pyramidal cells.
A
Rall model
B
Experiment
C
D
Input-output function
Number of inputs
Input timing
Stimulation interval (ms)
T Branco Science 2011;334:615-616
Published by AAAS
Science

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^θ



(fig. < O'Reilly, *Comp. Cog. Neurosci.*)

Rate Code Approximation

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

$$\theta = \frac{g_e^\theta E_e + g_i E_i + g_l E_l}{g_e^\theta + g_i + g_l}$$

$$g_e^\theta = \frac{g_i(E_i - \theta) + g_l(E_l - \theta)}{\theta - E_e}$$

$$y = f(g_e - g_e^\theta)$$

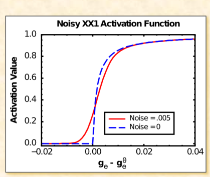
Activation Function

- Desired properties:
  - threshold (~0 below threshold)
  - saturation
  - smooth
- Smooth by convolution with Gaussian to account for noise
- Activity update:

$$y_{t+1} = y_t + C(y - y_t)$$

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

$$y = \frac{1}{1 + \dfrac{1}{\eta\left[g_e - g_e^\theta\right]^+}}$$



(fig. < O'Reilly, *Comp. Cog. Neurosci.*)