Introduction to neurons

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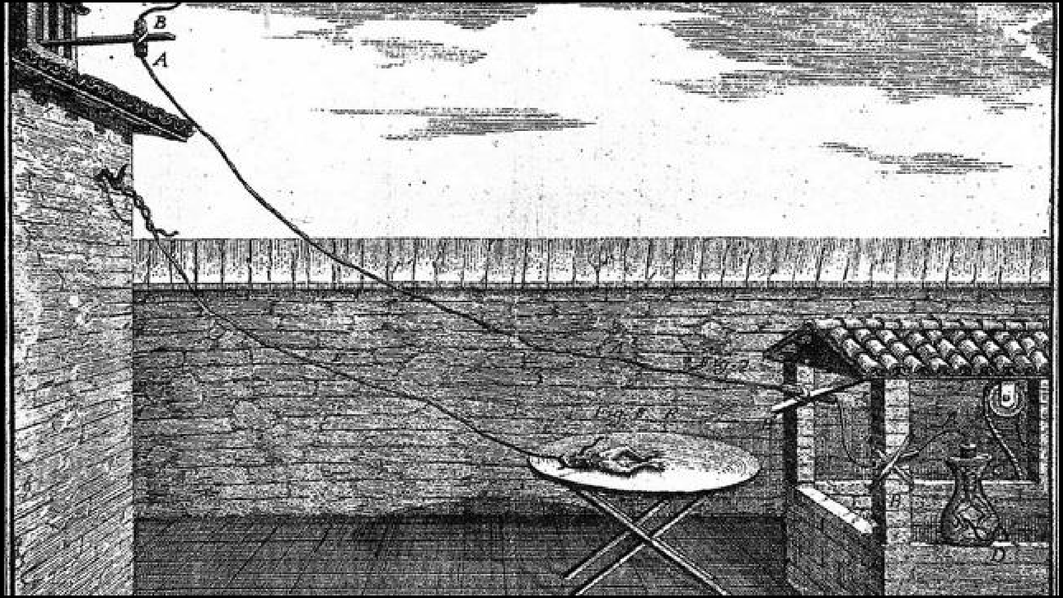
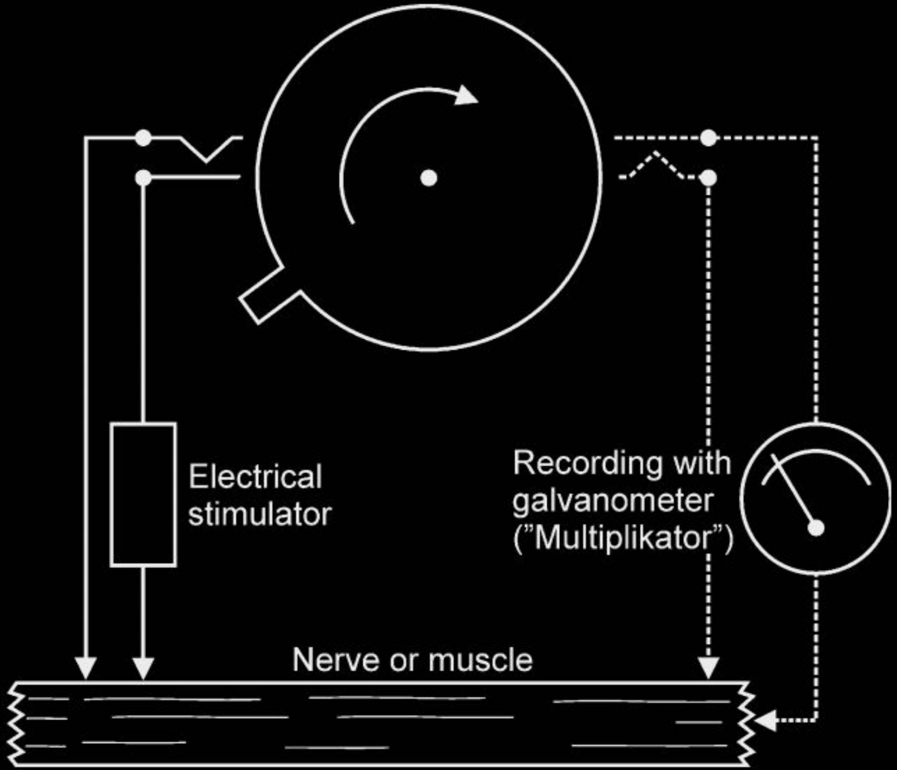
Neuroscience circa 1781

Galvani + Volta stimulating frogs legs



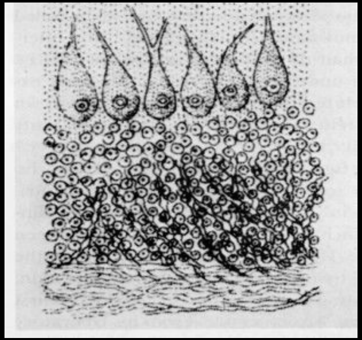
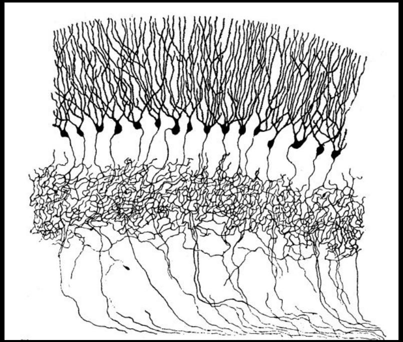
Discovery of the action potential



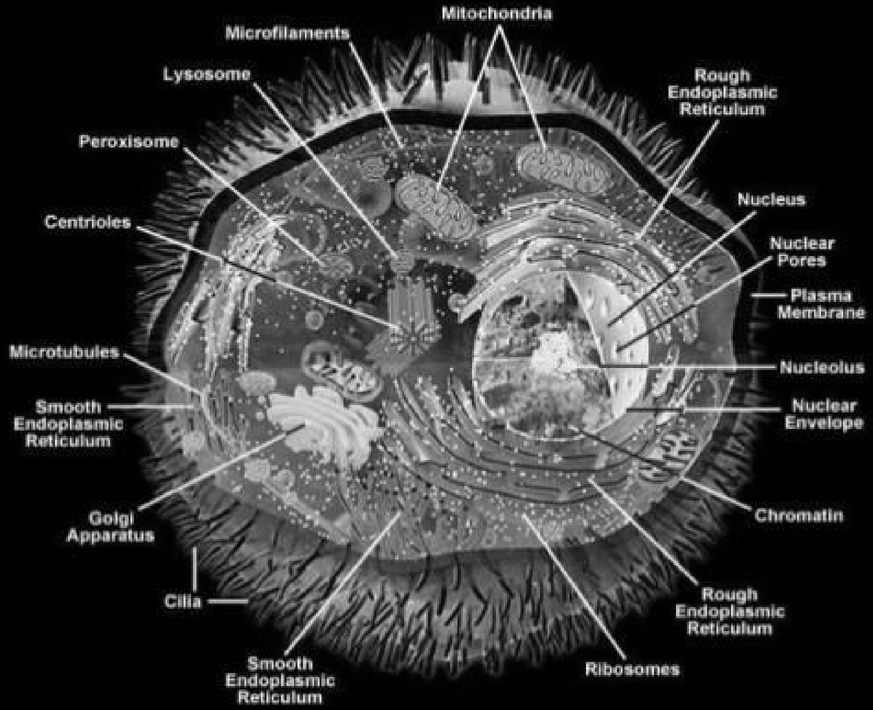
Operating du Bois-Reymond's Multiplikator

Discovery of neurons

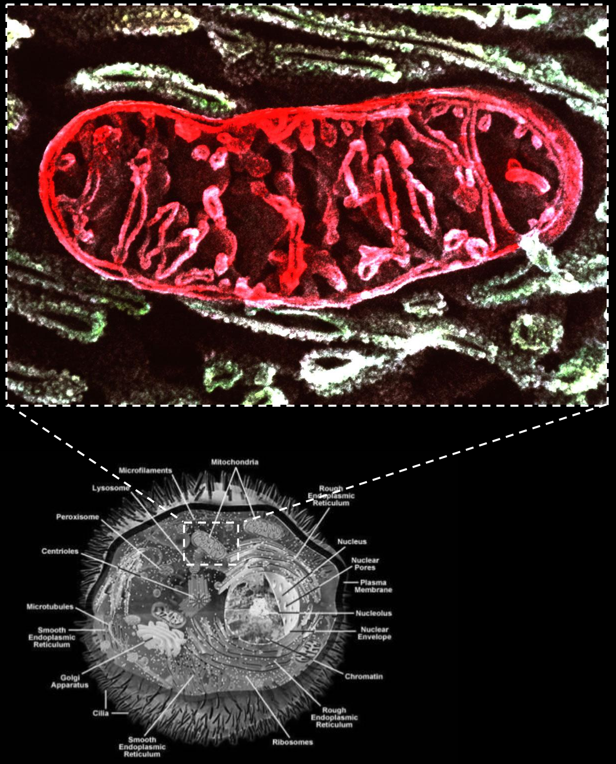
1906 Nobel Prize in Physiology

Neuron doctrine	Reticular theory
Cells 1 nucleus/cell	Syncytium Multiple nuclei
Evidence:	Evidence:
Golgi stain showed individual neurons	Neural tissue hard to observe
	

Cell Biology: Organelles



Cell Biology: Mitochondria



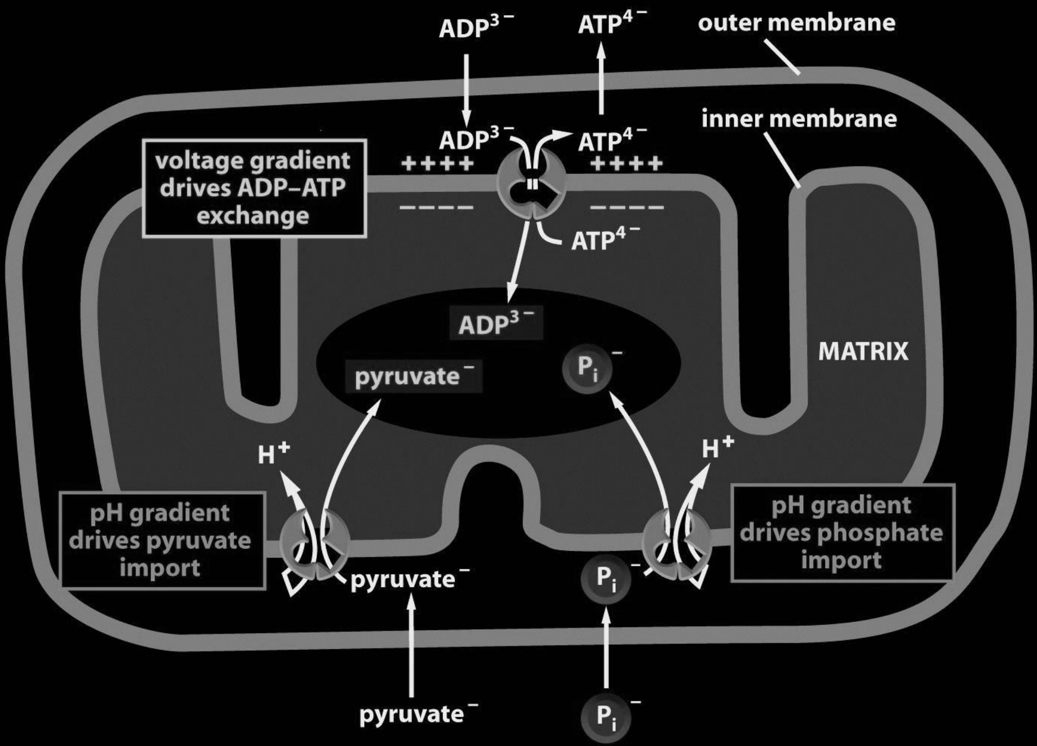
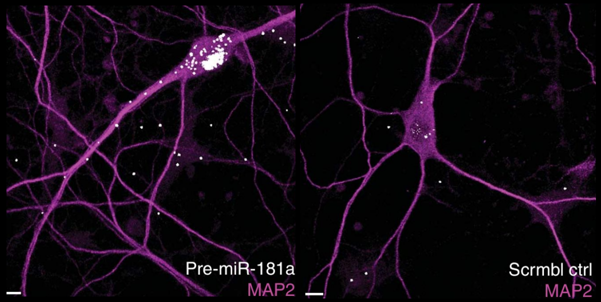
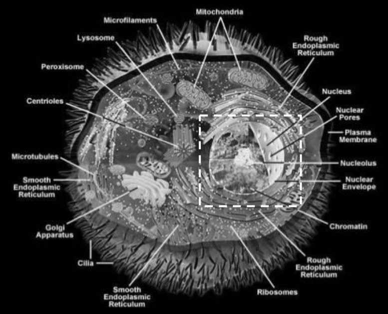


Figure 14-16 Molecular Biology of the Cell 5/e (© Garland Science 2008)

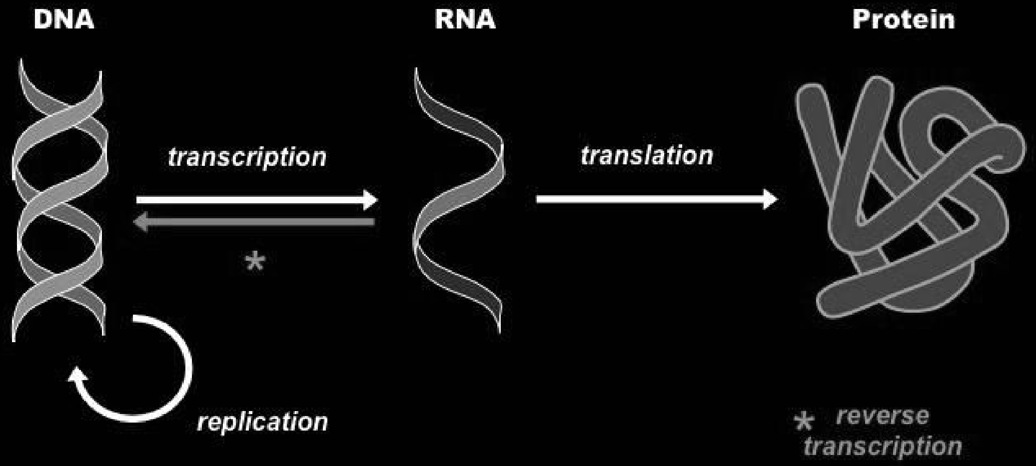
Molecular Biology: The Nucleus



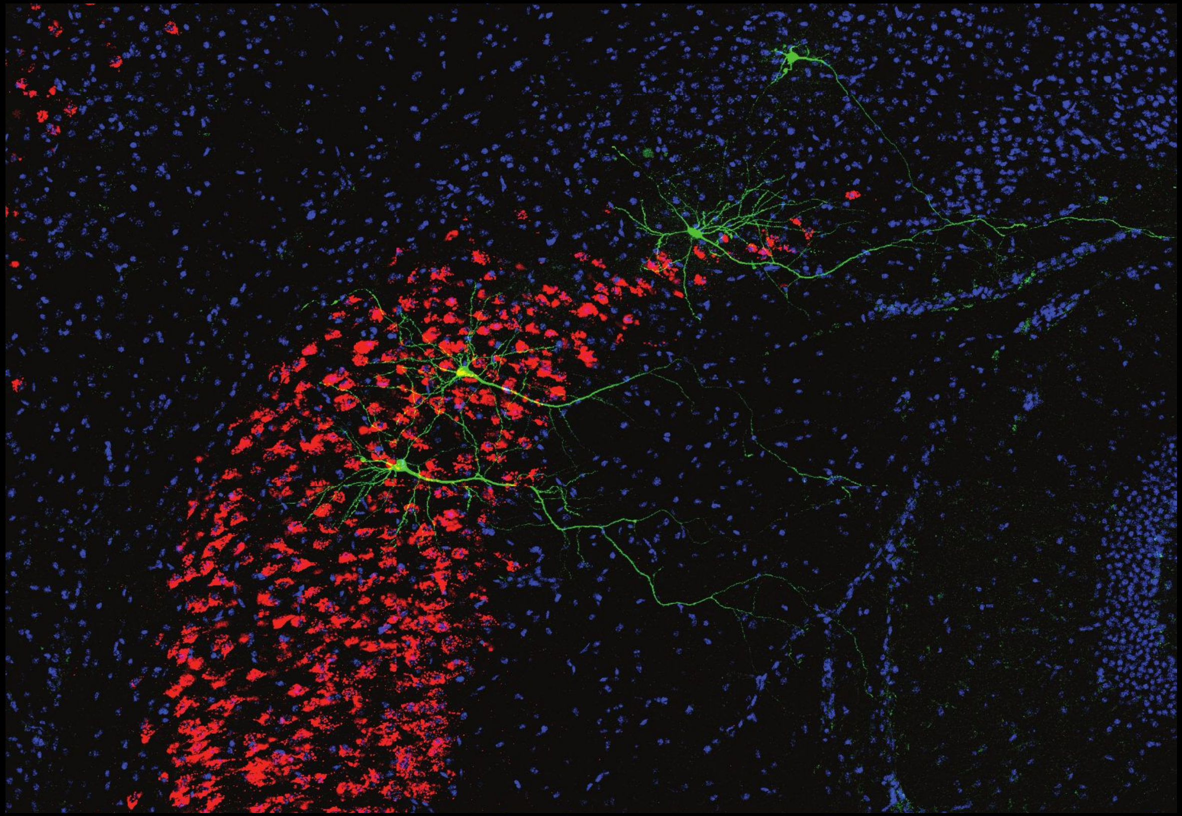


Central Dogma

Nucleus **Cytosol** **Ribosome**



Neuronal cell biology

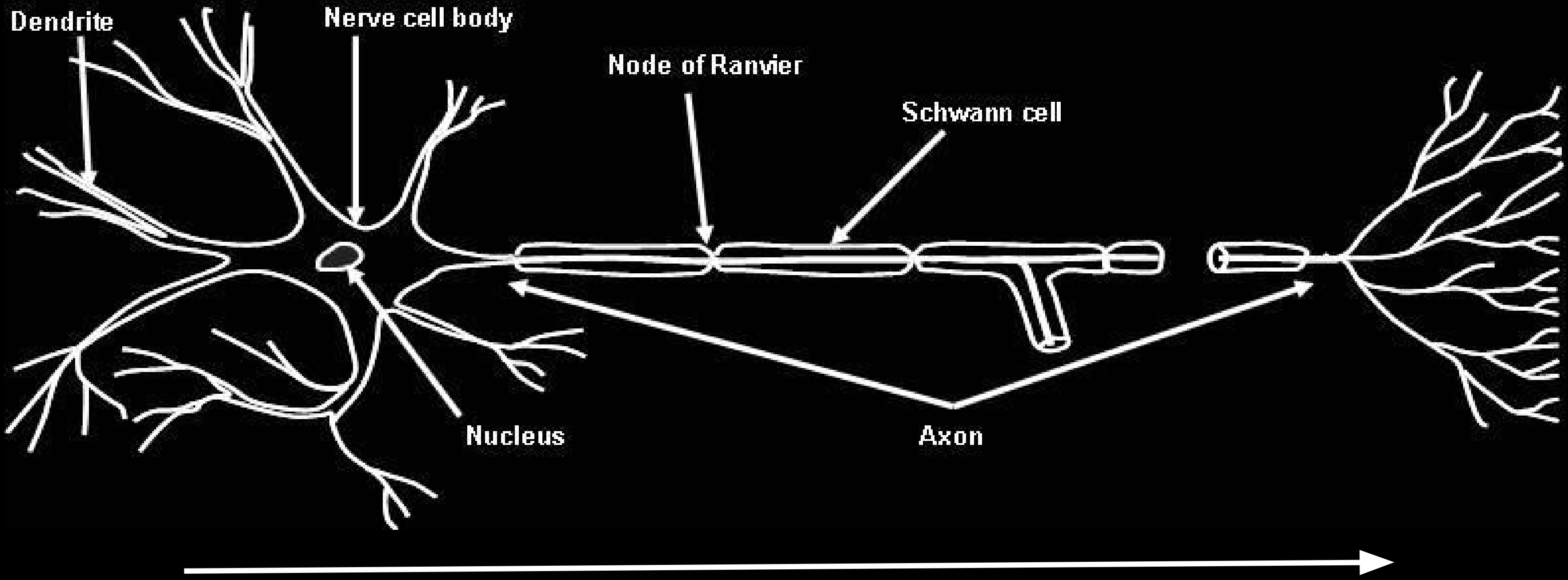


DAPI (nucleus)

Retrograde tracer (NAc)

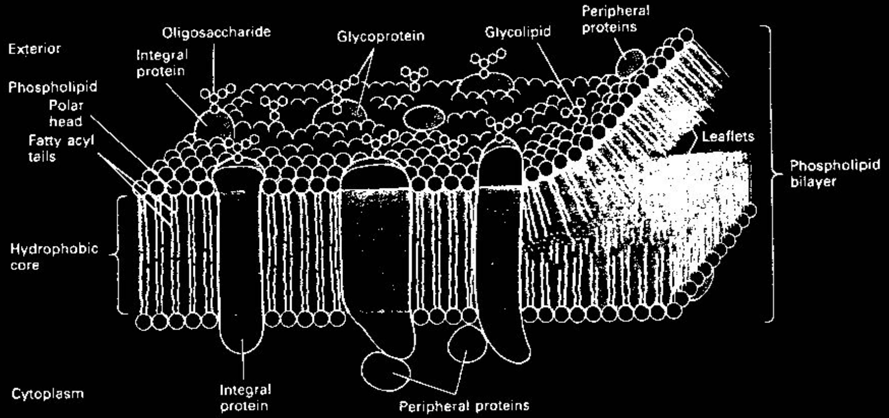
Biocytin

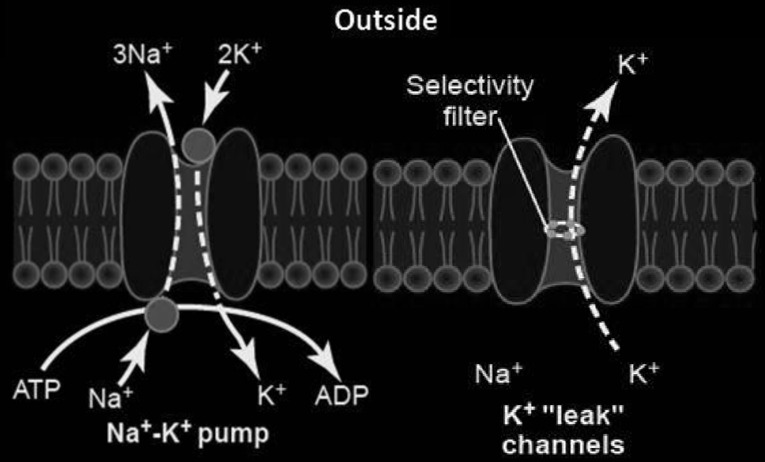
Neuronal cell biology



Direction of action potential

Generating a membrane potential





Nernst and Goldman Equations

Bernstein applied nernst equations to neurons

$$E_X = \frac{RT}{zF} \ln \frac{[X]out}{[X]in}$$

- Gas Constant: R
- Temp (°K): T
- Ion Concentration: $[X]out$
- Equilibrium Potential of X ion (eg. K+): E_X
- Valence of ion (-1, +1, +2): z
- Faraday constant: F
- Ion Concentration: $[X]in$

Equilibrium potentials:

K^+ = -90mV

Na^+ = +60mV

Cl^- = -70mV

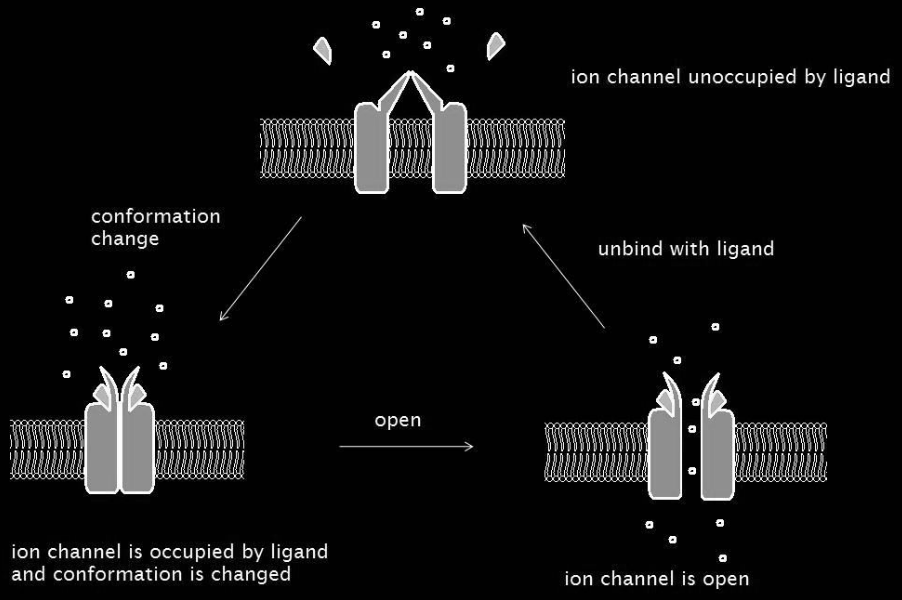
Nernst and Goldman Equations

Nernst equation generalized by Goldman

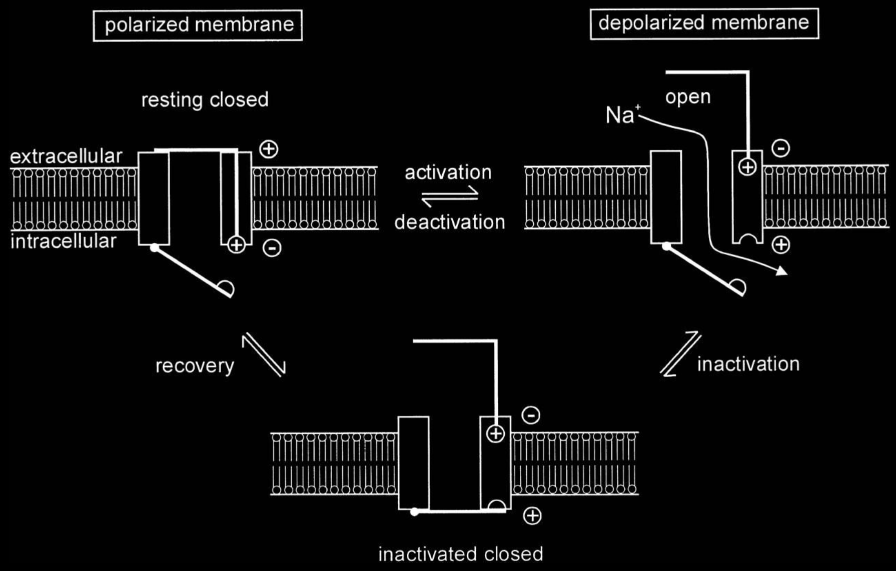
$$V_{\mathrm{m}} = \frac{RT}{F} \ln\left(\frac{p_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{o}} + p_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{o}} + p_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{i}}}{p_{\mathrm{K}}[\mathrm{K}^+]_{\mathrm{i}} + p_{\mathrm{Na}}[\mathrm{Na}^+]_{\mathrm{i}} + p_{\mathrm{Cl}}[\mathrm{Cl}^-]_{\mathrm{o}}} \right)$$

Ion conductance

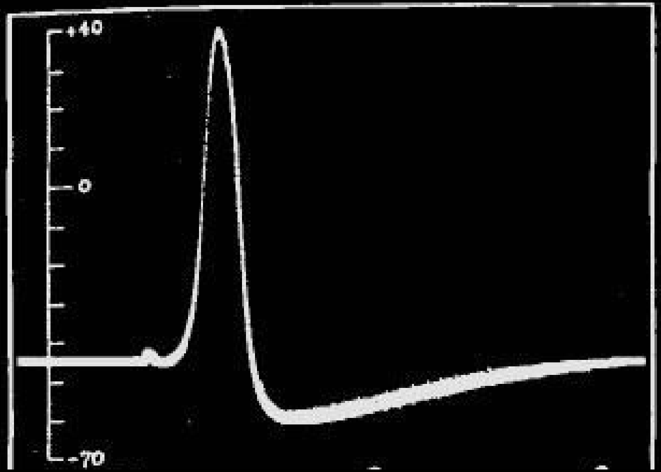
Ligand gated ion channel



Voltage gated ion channel



Action potential: Hodgkin-Huxley



$$I = C_m \frac{\mathrm{d}V_m}{\mathrm{d}t} + \bar{g}_{\mathrm{K}} n^4 (V_m - V_K) + \bar{g}_{\mathrm{Na}} m^3 h (V_m - V_{Na}) + \bar{g}_l (V_m - V_l),$$

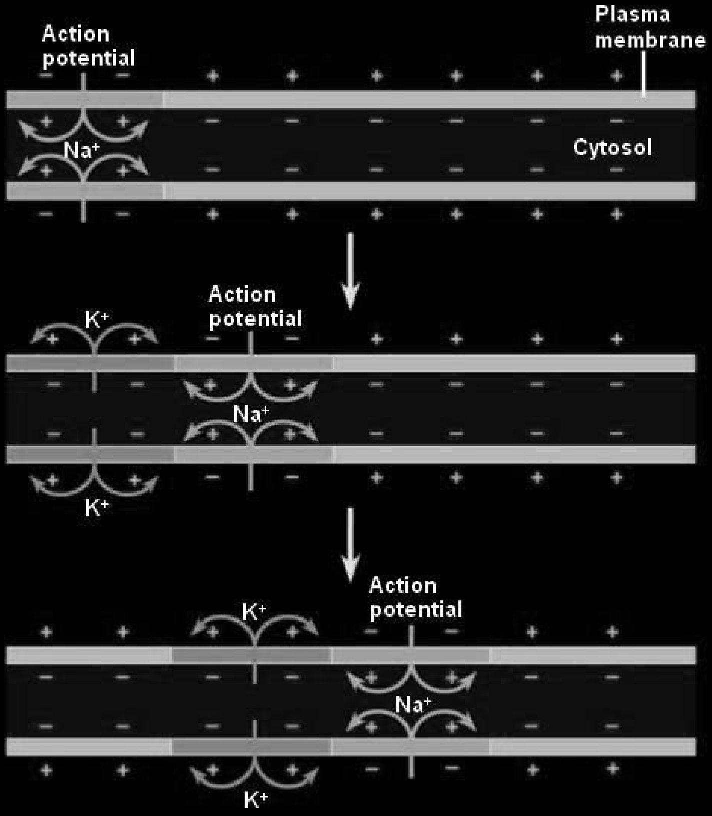
$$\frac{dn}{dt} = \alpha_n(V_m)(1-n) - \beta_n(V_m)n$$

$$\frac{dm}{dt} = \alpha_m(V_m)(1-m) - \beta_m(V_m)m$$

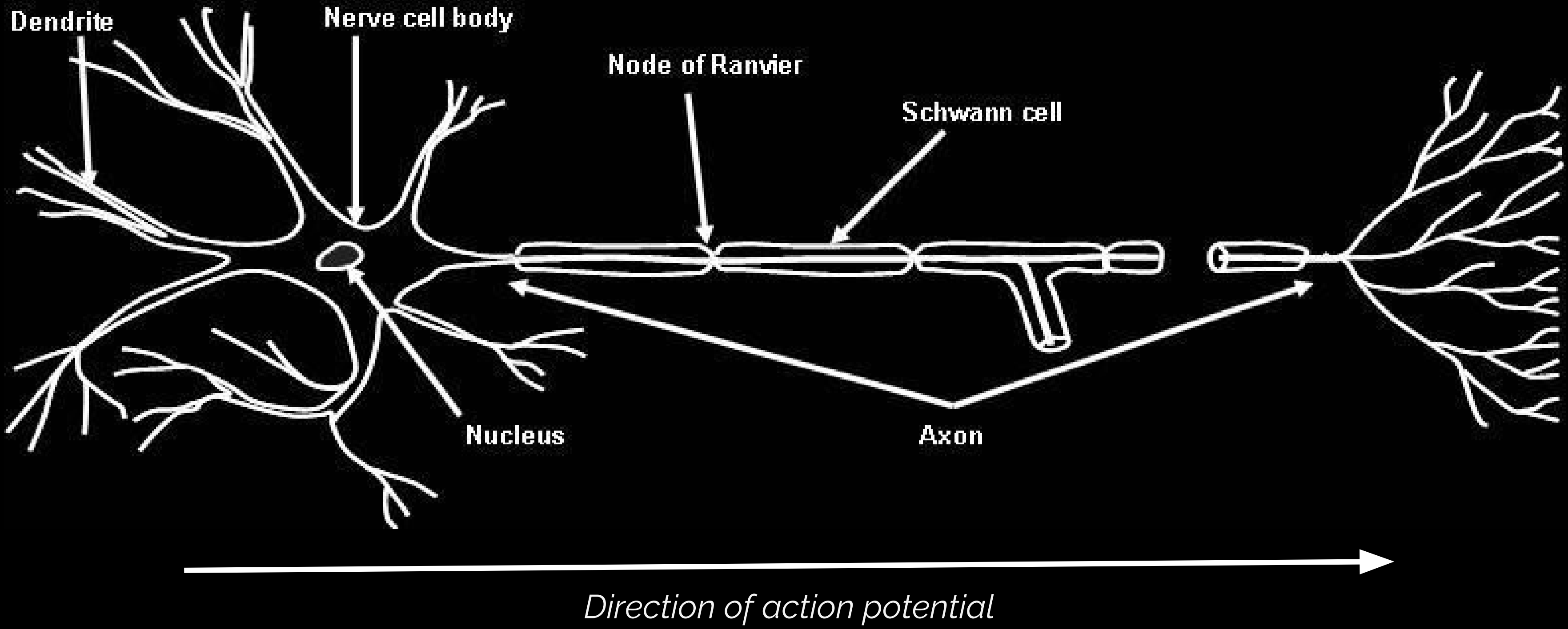
$$\frac{dh}{dt} = \alpha_h(V_m)(1-h) - \beta_h(V_m)h$$

A. L. Hodgkin, A. F. Huxley, and B. Katz, 1952. J Physiol

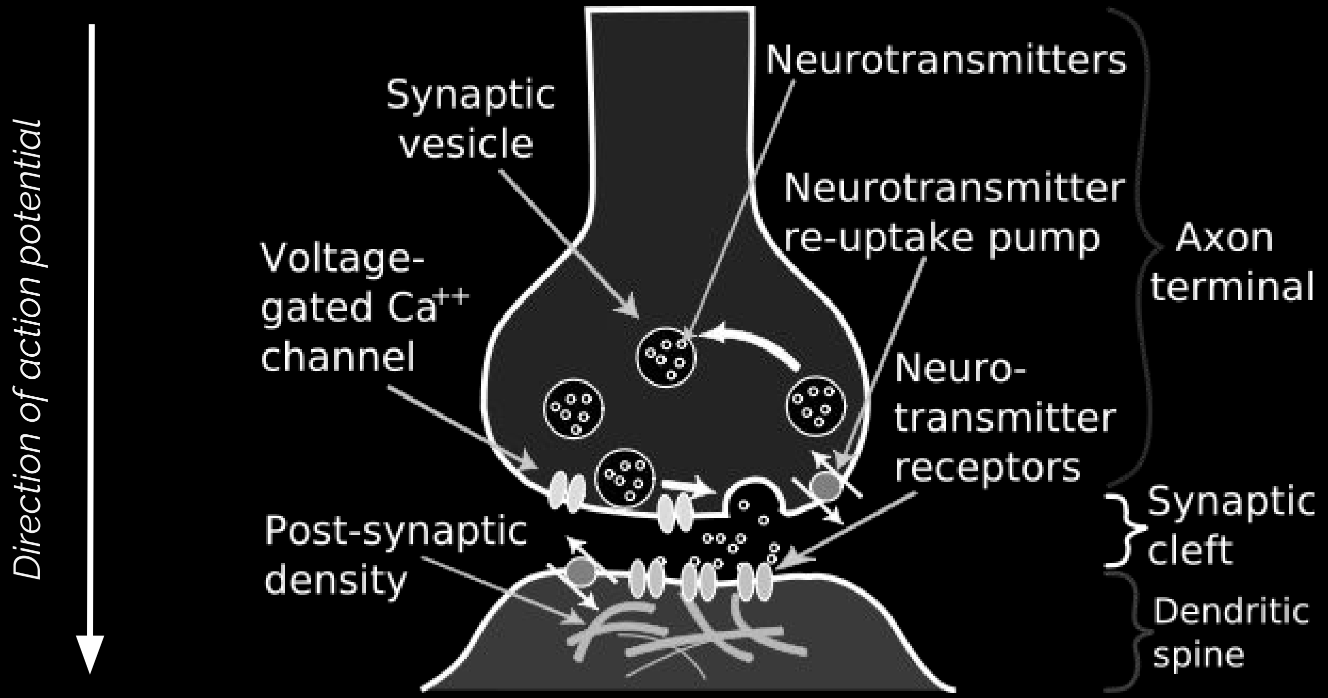
Action potential: propagation



Neuronal cell biology -- synapses



Synapses

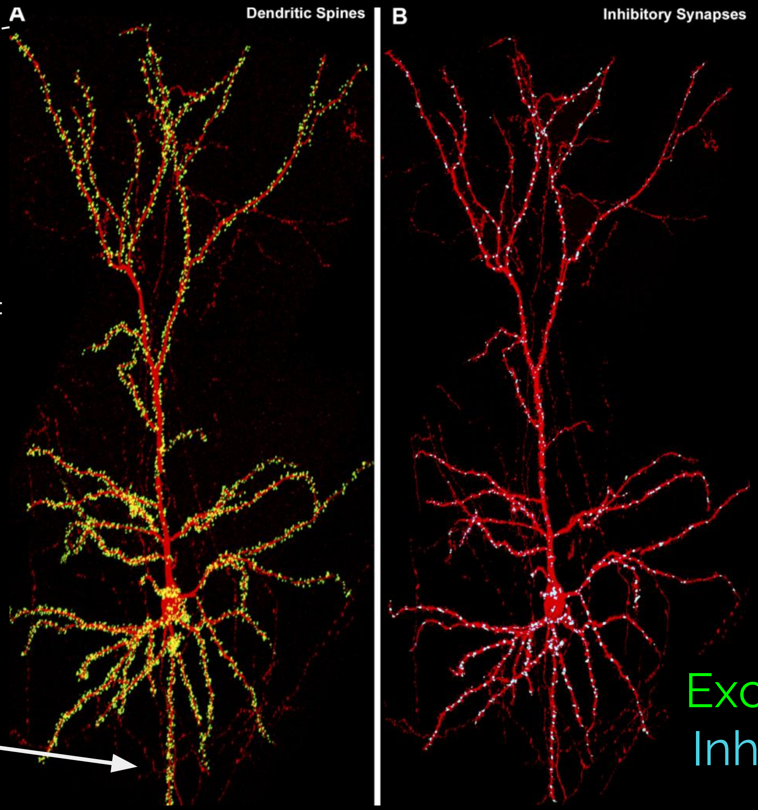

Direction of action potential
Synaptic vesicle
Neurotransmitters
Neurotransmitter re-uptake pump
Voltage-gated Ca++ channel
Neuro-transmitter receptors
Axon terminal
Synaptic cleft
Post-synaptic density
Dendritic spine

Anatomy of a neuron

Apical Dendrites

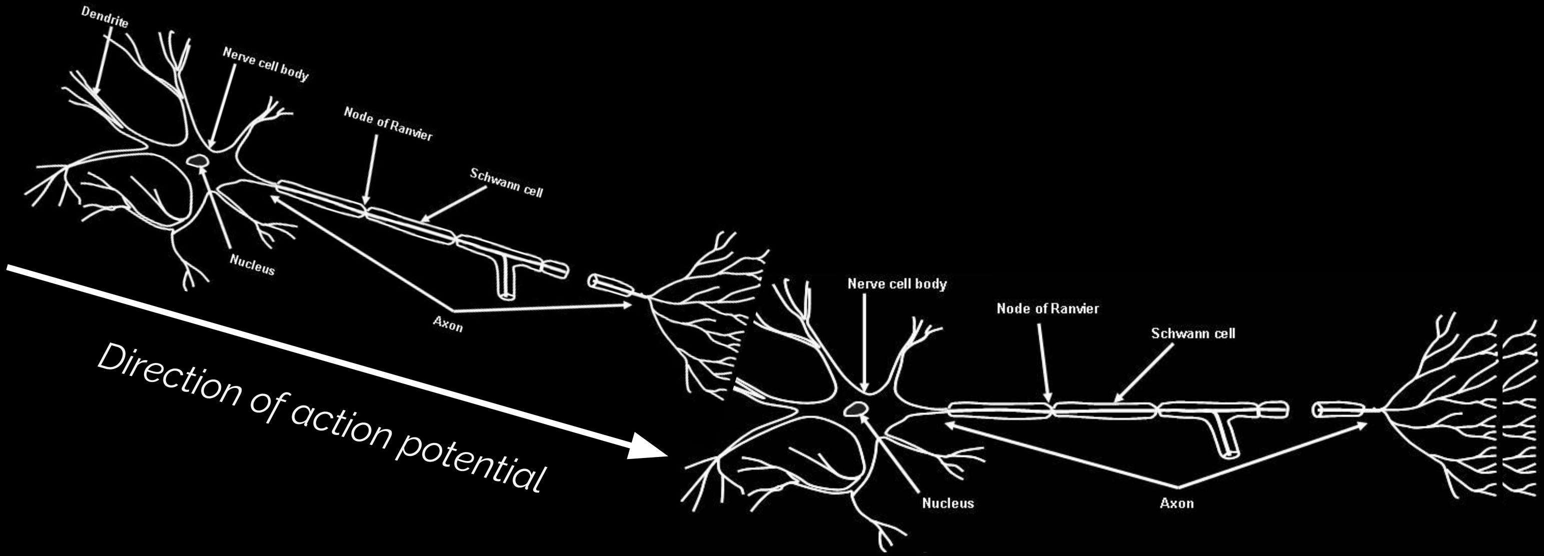
Proximal Dendrites

Axon



Neuron
Excitatory synapse
Inhibitory synapse

Neuronal cell biology -- dendritic integration



Passive dendritic integration: timing

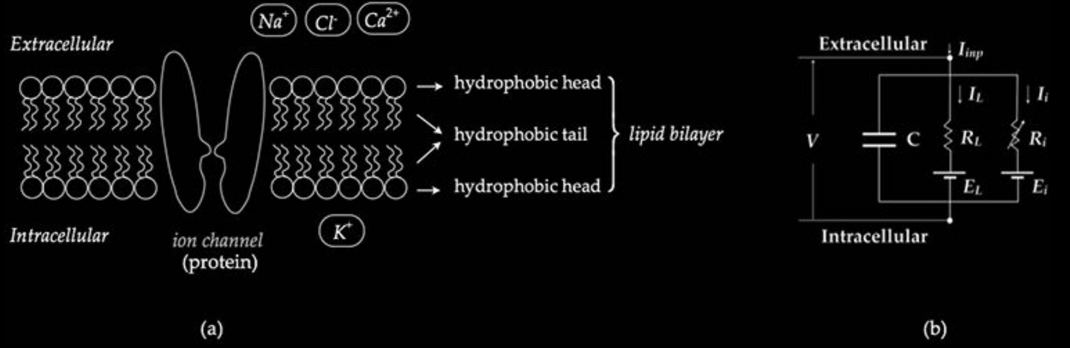
Resistor-capacitor circuit (RC)

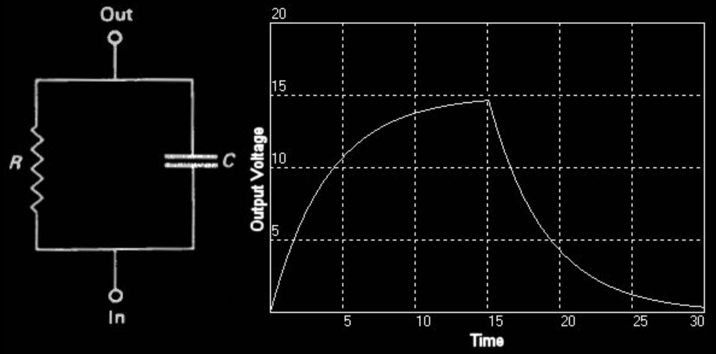
The time to reach 1/e of the original value:

$$\tau = RC$$

Change in voltage:

$$\Delta V_m(t) = I_m R(1 - e^{-t/\tau})$$





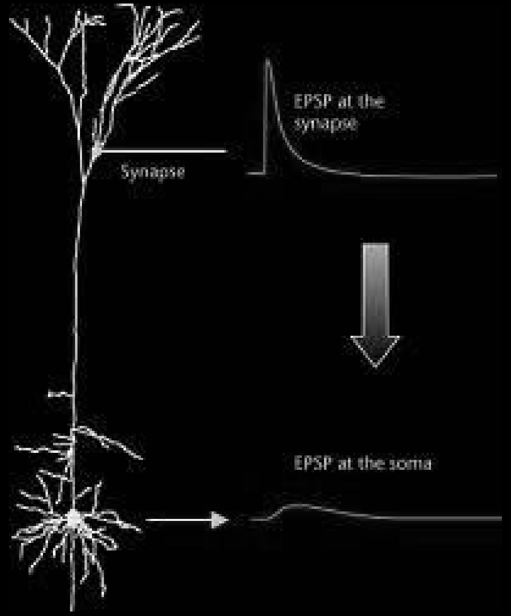
Passive dendritic integration

Length constant:

$$\lambda = \sqrt{\frac{rm}{ra}}$$

Length constant and relation to attenuation of VM =

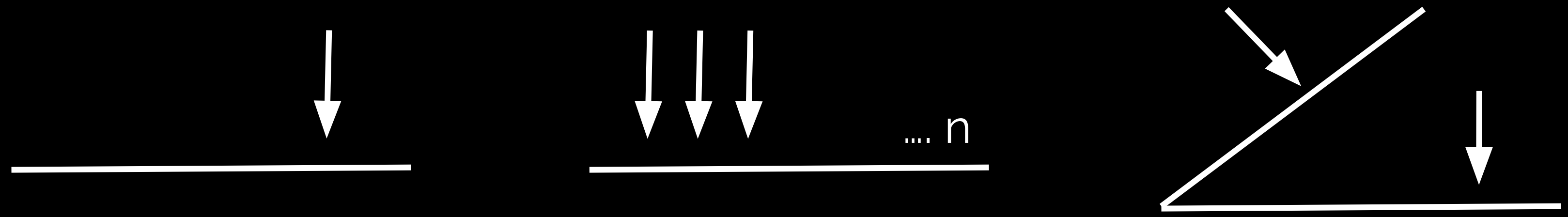
$$\Delta V_m(x) = \Delta V_0 e^{-x/\lambda}$$

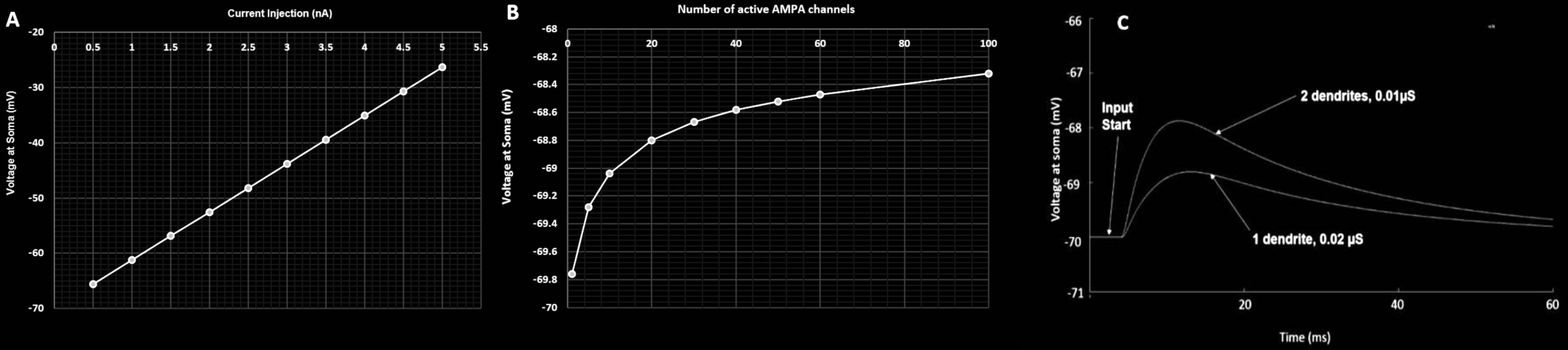


r_{in} = impedance to the transmembrane flow of charge.

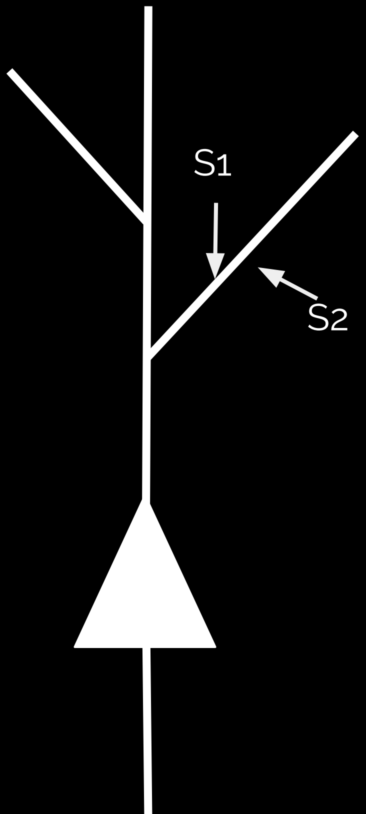
r_a = impedance to the flow of charge through the cytoplasm.

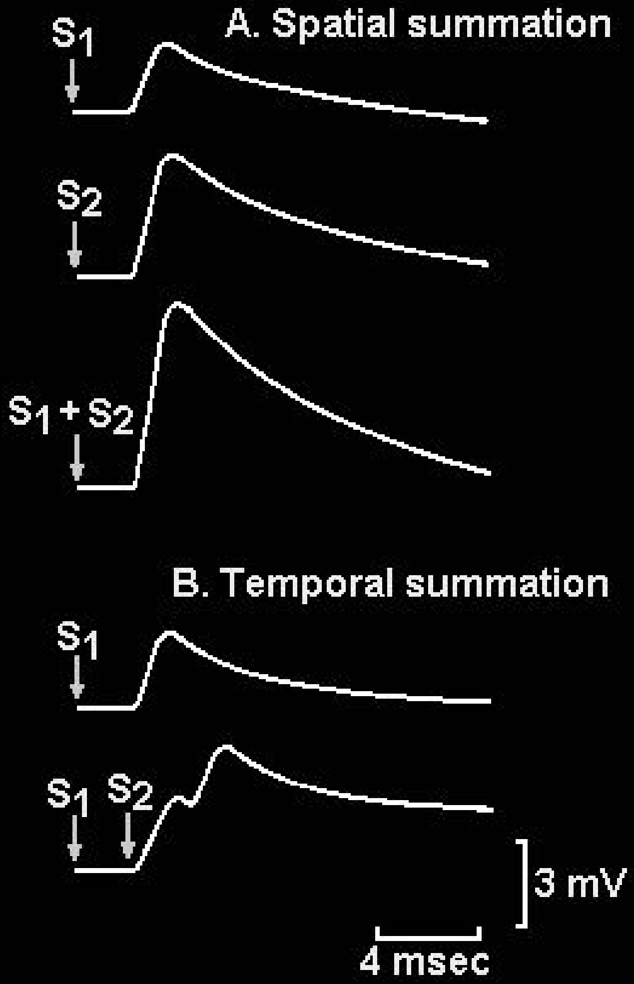
Passive dendritic integration: sublinear integration



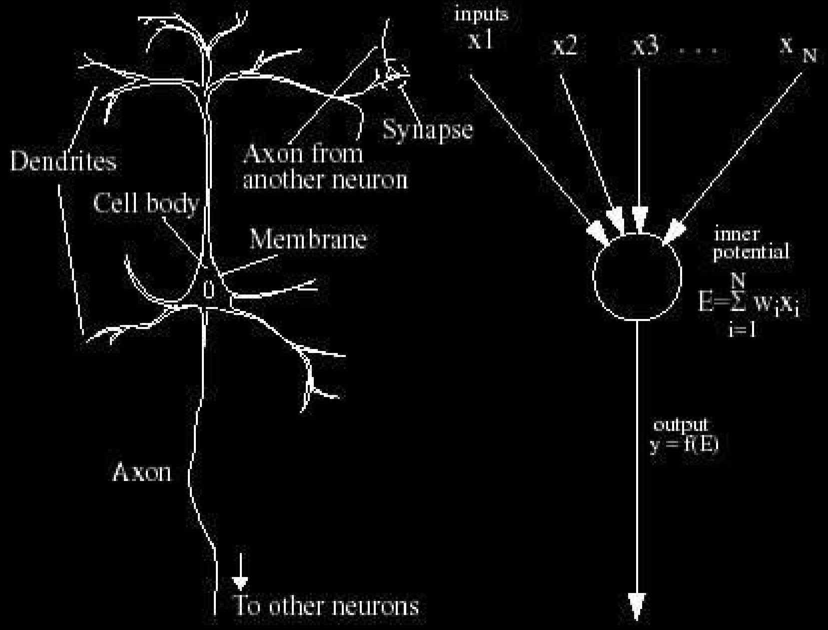


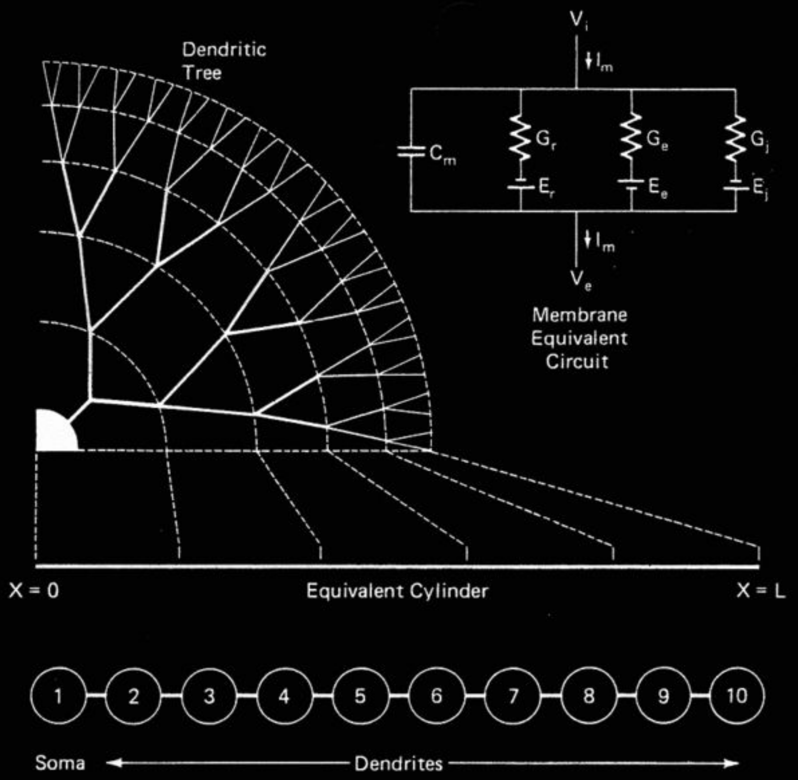
Summation


S1
S2

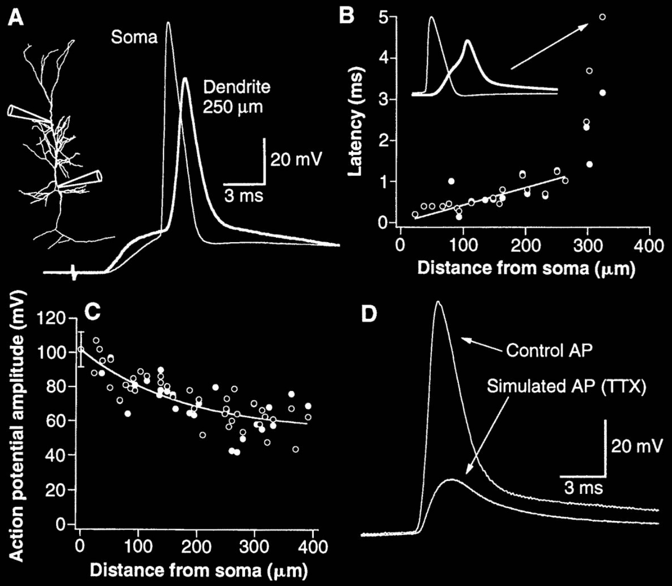

A. Spatial summation
S1
S2
S1 + S2
B. Temporal summation
S1
S1 S2
3 mV
4 msec

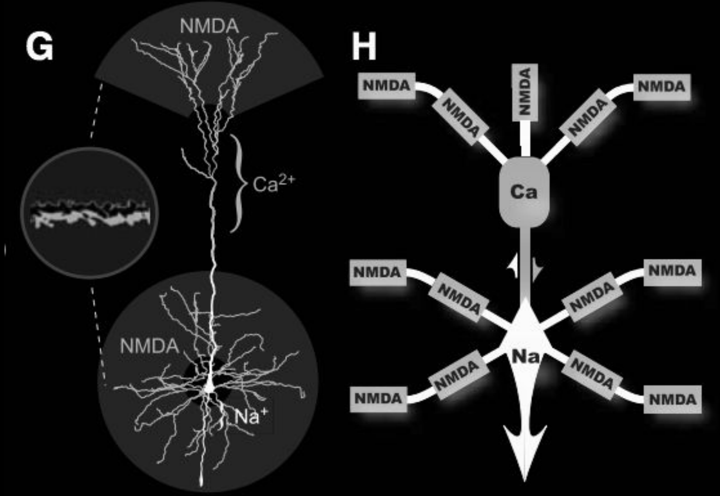
Models of neurons





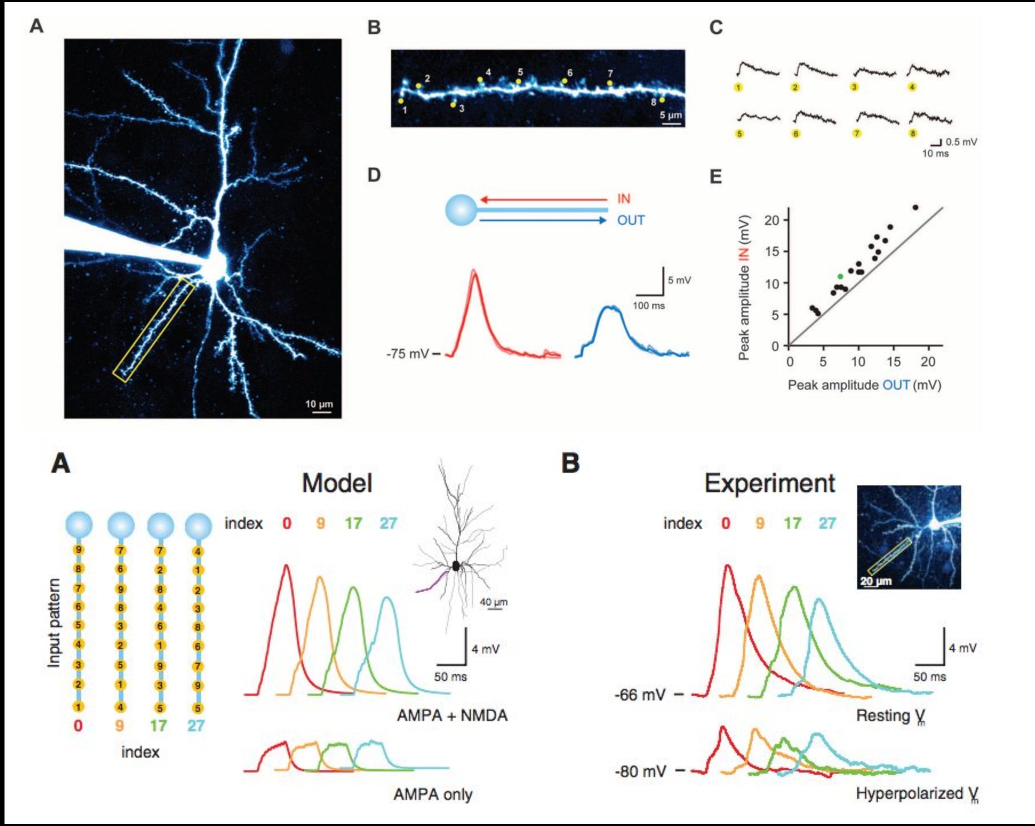
Voltage-dependent dendritic integration (i.e. supralinear)





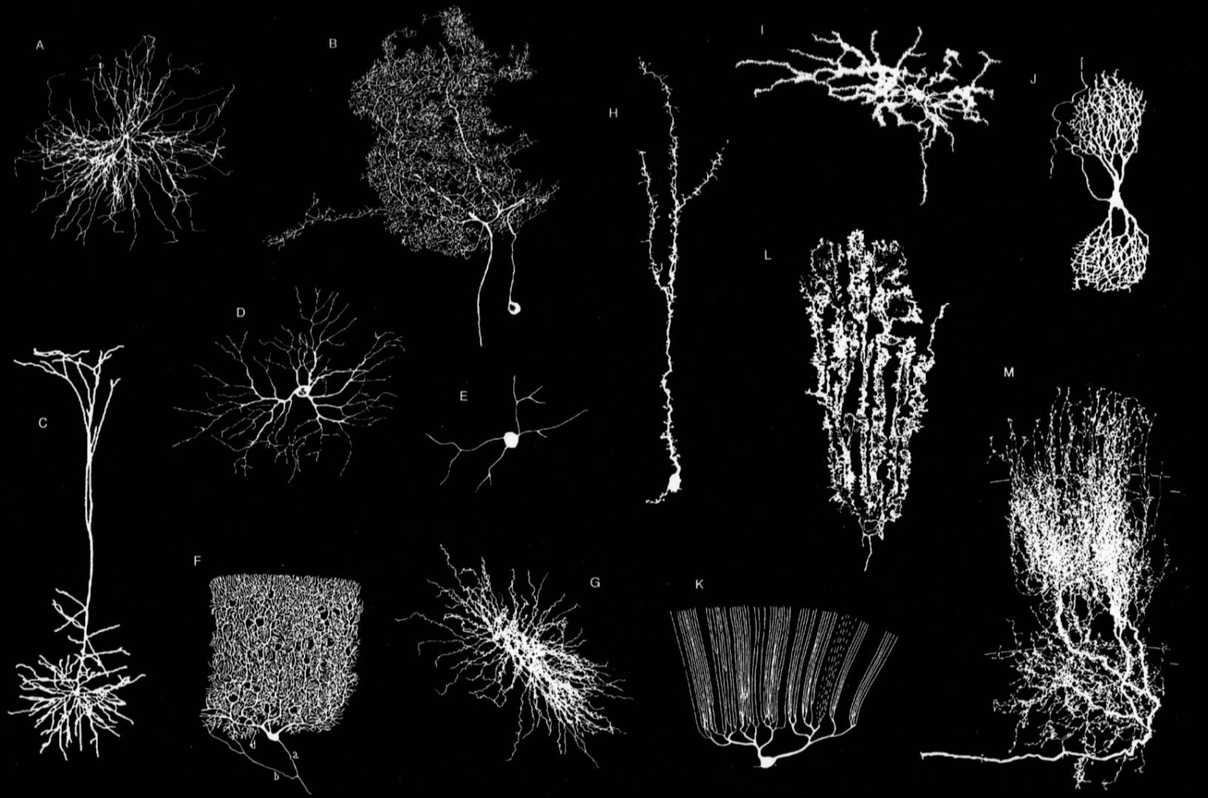
Spruston et al., 1995. Science;
Larkum et al., 2009. Science

Dendritic integration: discriminating temporal sequences



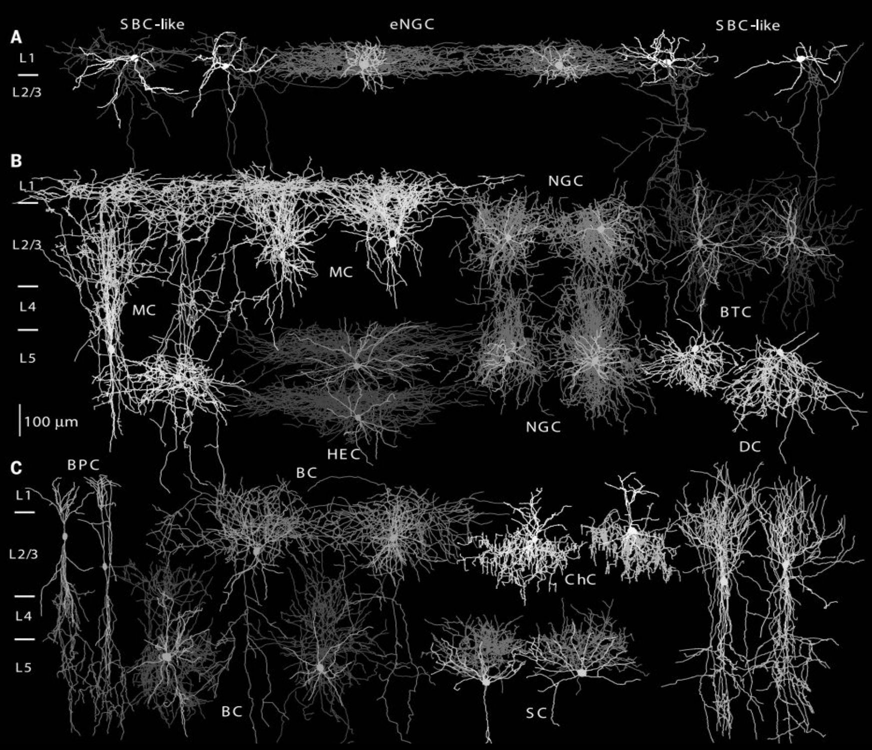
Branco et al., 2010. Science

Neuronal diversity: anatomy



‘Beautiful Brain: The Drawings of Santiago Ramon y Cajal)

Neuronal diversity: electrophysiology and connectivity



Jiang et al., 2015. Science

Neuronal diversity: gene expression

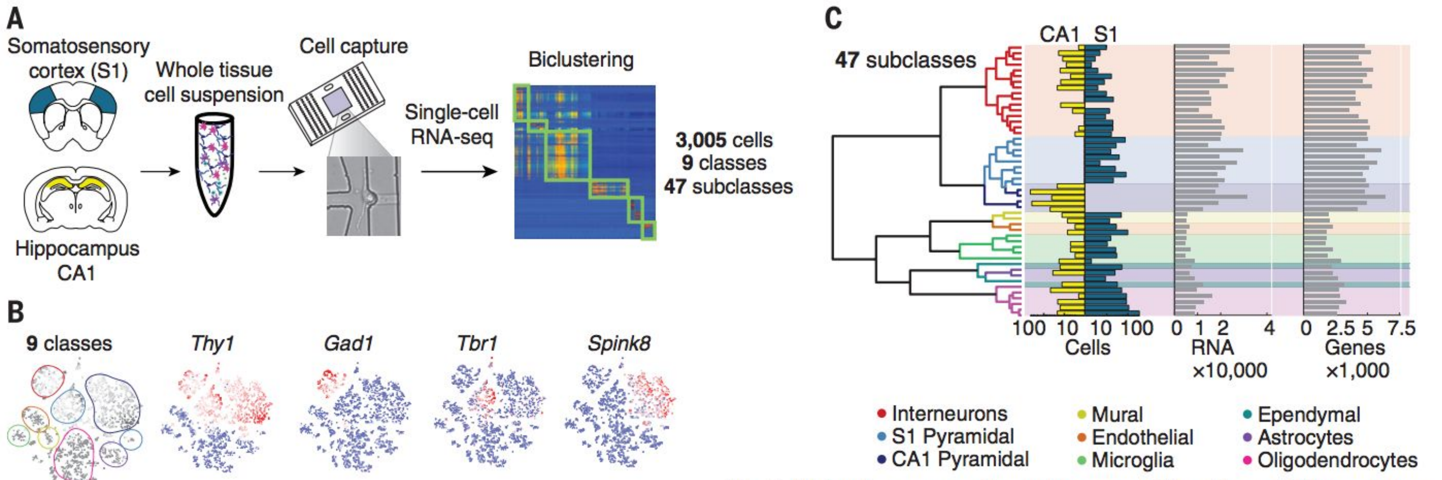


Fig. 1. Molecular census of somatosensory S1 cortex and hippocampus CA1 by unbiased sampling and single-cell RNA-seq. (**A**) Workflow for obtaining and analyzing single-cell RNA-seq from juvenile mouse cortical cells, from dissection to single-cell RNA-seq and biclustering. (**B**) Visualization of nine major classes of cells using t-distributed stochastic neighbor embedding (tSNE). Each dot is a single cell, and cells are laid out to show similarities. Colored contours correspond to the nine clusters in (A) and fig. S3. Expression of known markers is shown using the same layout (blue, no expression; white, 1% quantile; red, 99% quantile). (**C**) Hierarchical clustering analysis on 47 subclasses. Bar plots show number of captured cells in CA1 and S1, number of detected polyA+ RNA molecules per cell, and total number of genes detected per cell.

Ziesel et al., 2015. Science

Takeaways

- Neurons look cool -- you should care about them
- Membrane potential generated via impermeable membrane + proteins
- Action potential via synaptic input, dendritic integration, and voltage dependent conductance
- Integration of inputs can be linear, supralinear or sublinear
- Neurons are diverse