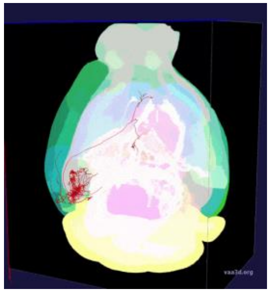
Neuron and action potential

Computational Neuroscience, Spring 2022

Xu Pan

The Misunderstood Brain

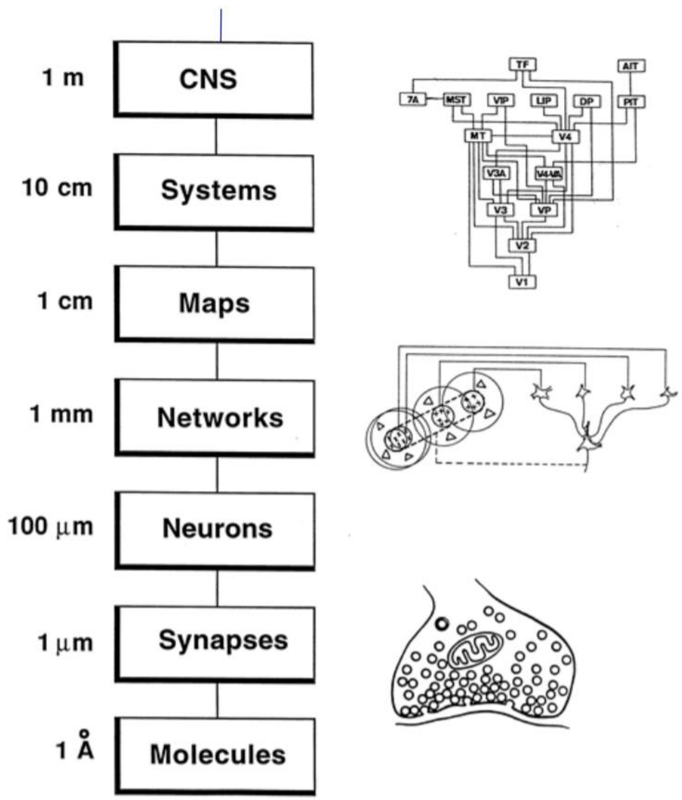


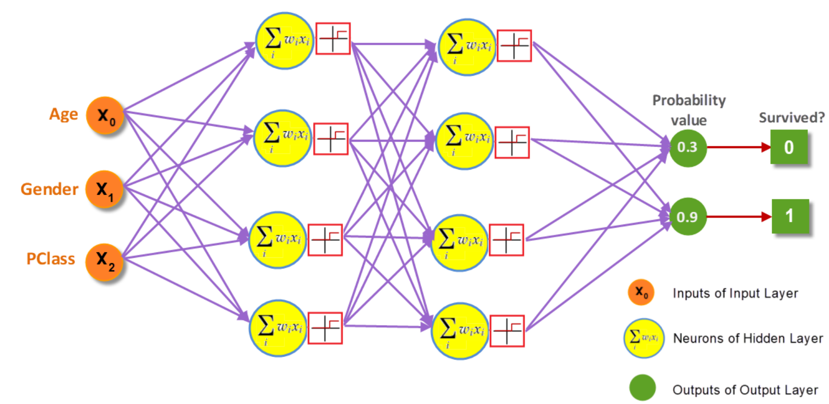
Allen Institute

- We know a lot about what makes neurons fire.
- We know a good deal about wiring patterns.
- We know only a little about how information is represented in the neural tissue.
- We know almost nothing about how information is processed.
- There is progress every month!

from David Touretzky

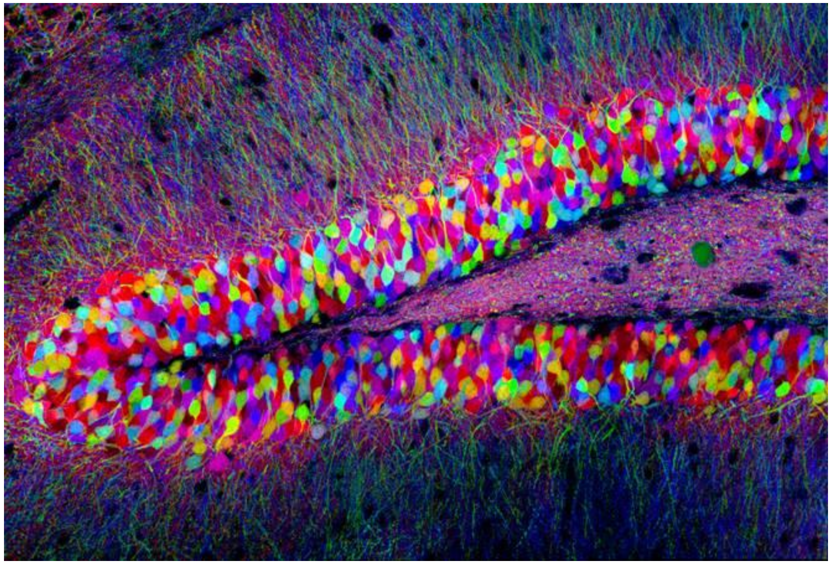
Brain v.s. Artificial Neural Networks (again...)





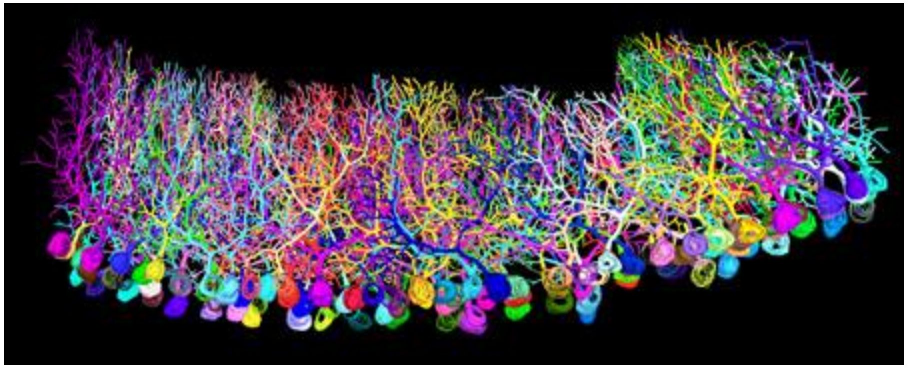
See some neurons

Hippocampus, CA3,
Memory formation.



By Tamily Weissman, Harvard University

Cerebellum, Purkinje cells,
Control motor movement.

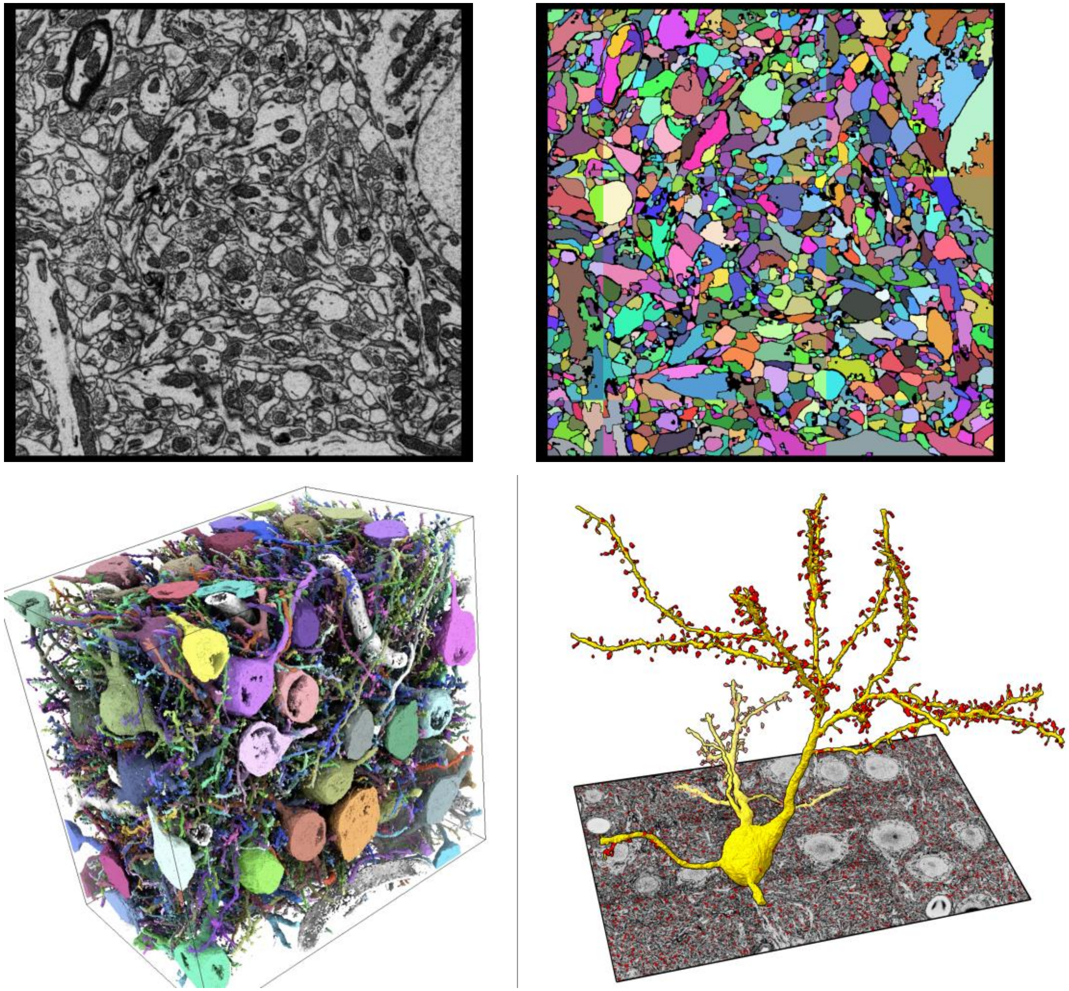


By Hermina Nedelescu

There are so many tools for imaging neurons! Above is Brainbow

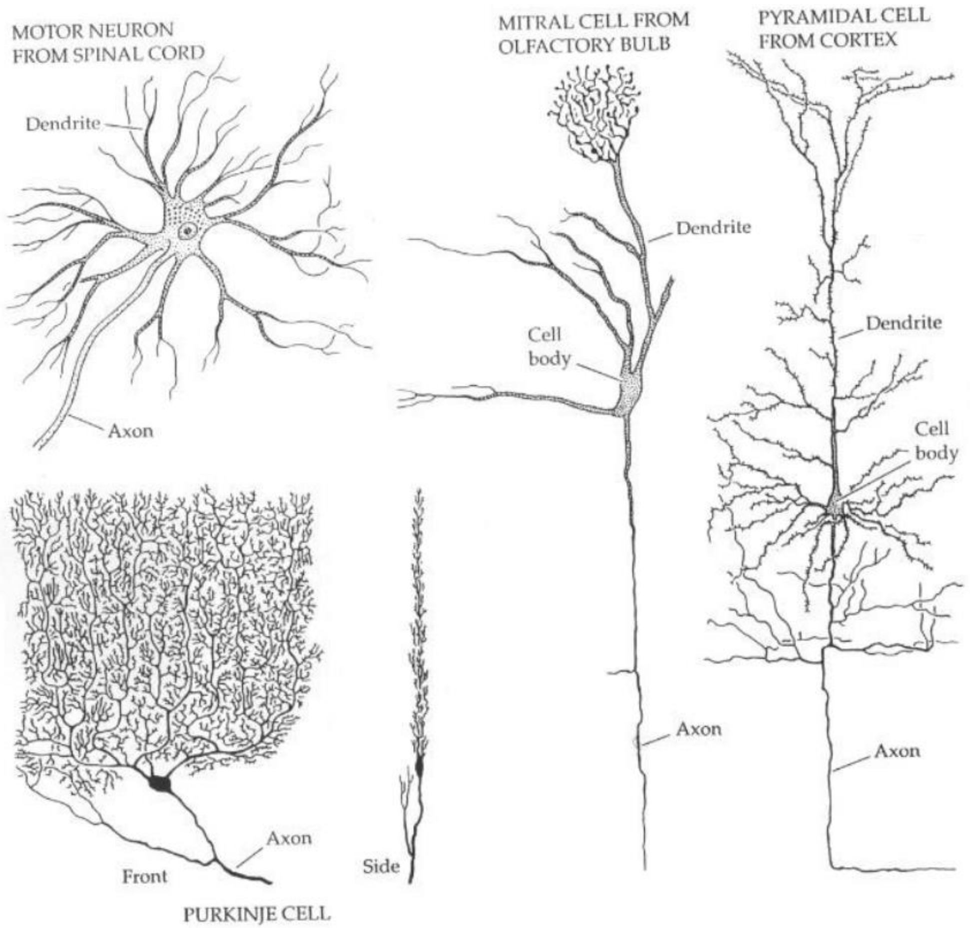
See some neurons

Electron microscopy
Layer 4 of
Somatosensory cortex



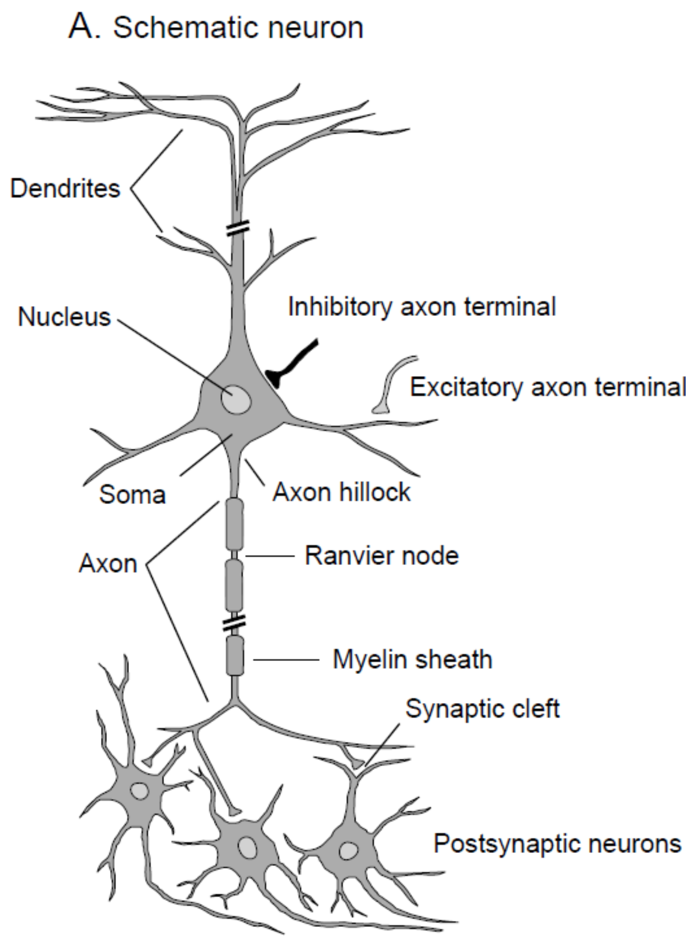
ALESSANDRO MOTTA, et. al. 2019

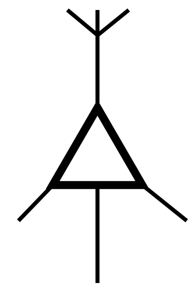
See some neurons



Nichols et al., From Neuron to Brain

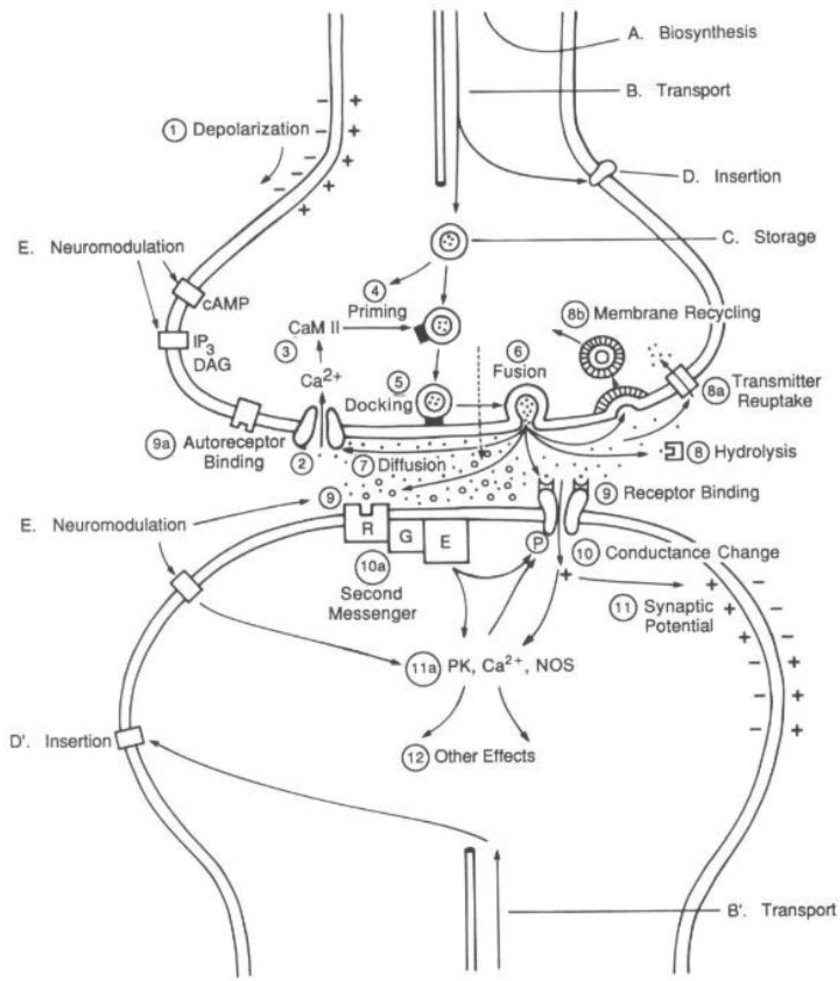
Neuron





Thomas Trappenberg, 2010

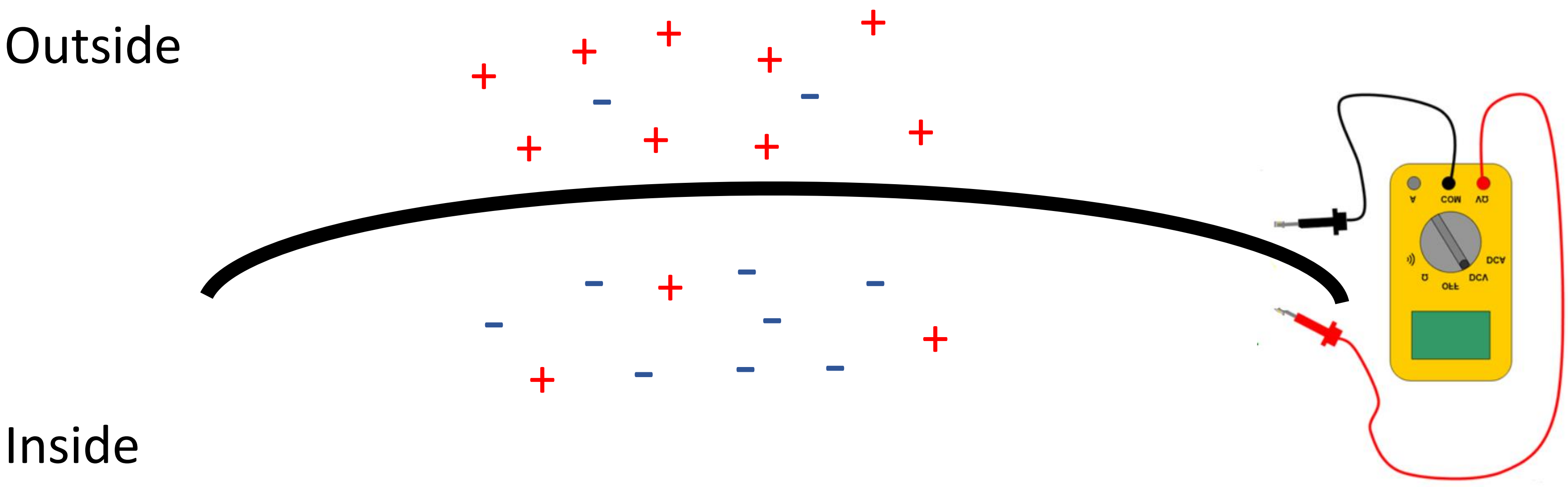
Synapse



Gordon Shepherd, The Synaptic Organization of the Brain

Membrane potential

- The more positive ions, the higher potentials.
- Higher potential means more difficult for positive ions to move there.

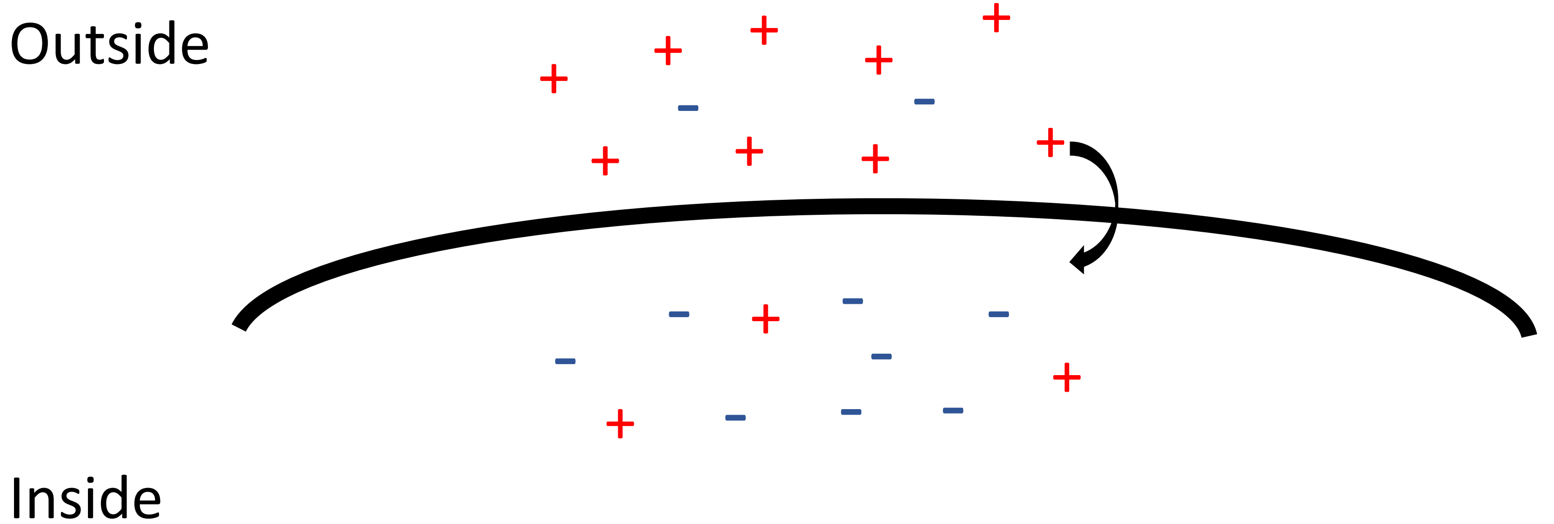


Membrane potential $V_m = V_{in} - V_{out}$

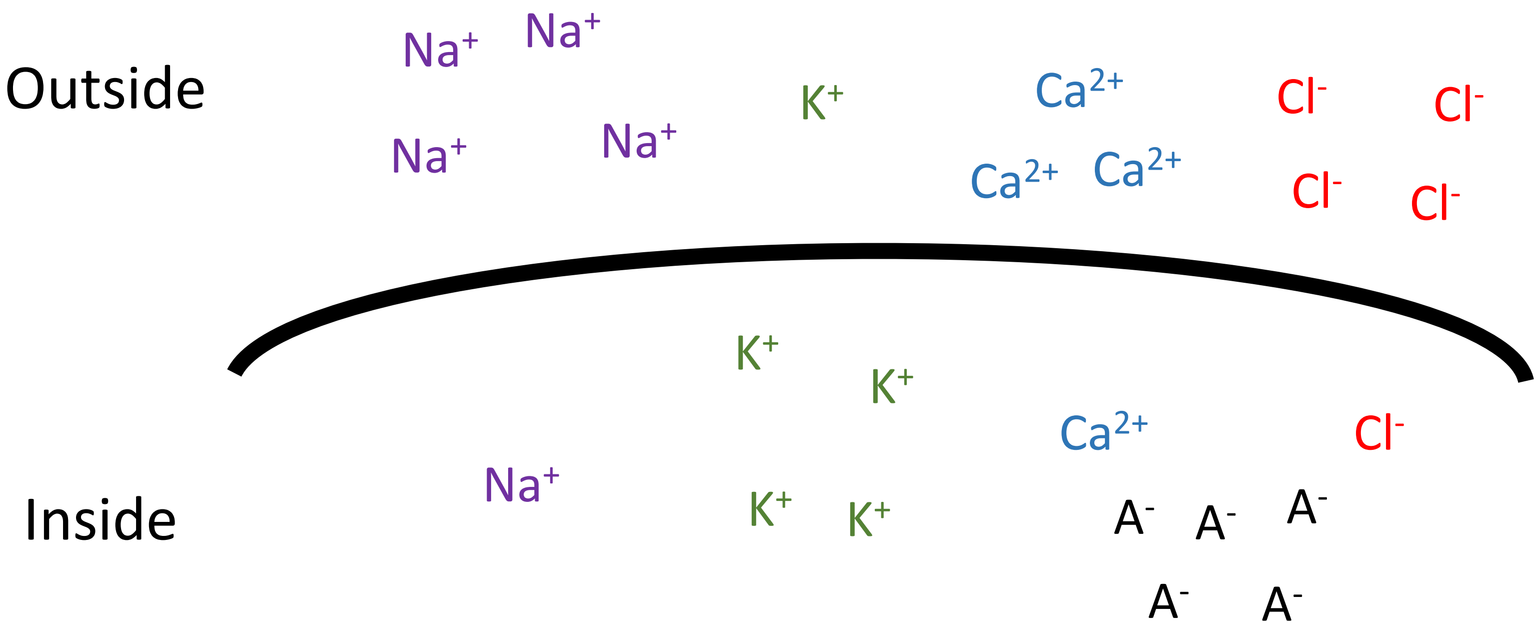
For a typical neuron, this number is -70 mV

Depolarize / Hyperpolarize

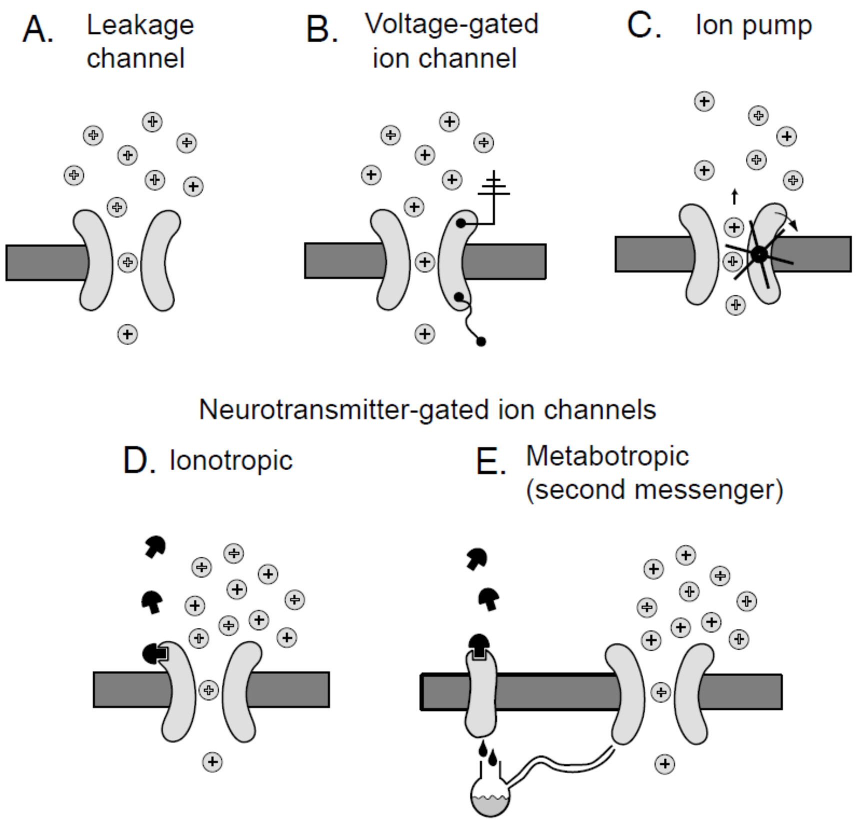
- Influx of positive ions (outflux of negative ions) increases V_m. Depolarize
- Influx of negative ions (outflux of positive ions) increases V_m. Hyperpolarize



When we talk about current, I, its direction (sign) is inward.


Outside
Na+ Na+
Na+ Na+
K+
Ca2+ Ca2+ Ca2+
Cl- Cl- Cl- Cl-
Inside
K+ K+ K+ K+
Na+
Ca2+
Cl-
A- A- A- A- A-

Ion channels

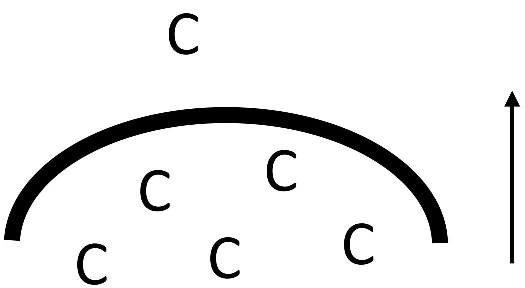


Thomas Trappenberg, 2010

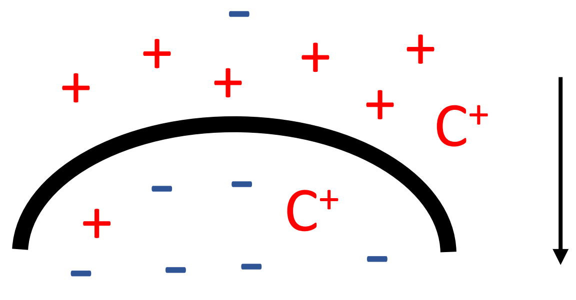
Nernst equation

- Relationship between $V_m, [C]_{in}, [C]_{out}$.
- There are two passive "forces" that can drive ions across the membrane, i.e. change inside / outside concentrations.

Diffusion "Force"

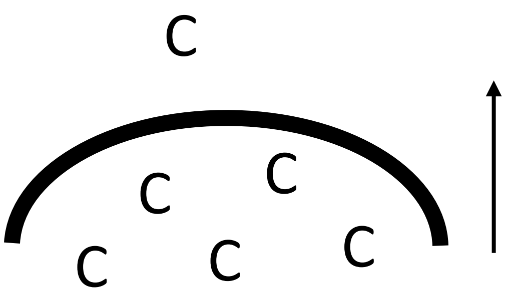


Electric Force

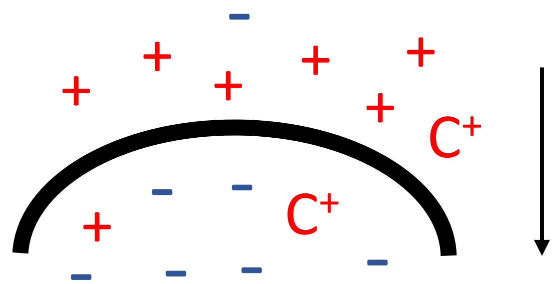


Nernst equation

Diffusion "Force"



Electric Force



Fick's law

$$J_{diff} = -D\,\frac{\partial [C]}{\partial x}$$

Ohm's law

$$J_{drift} = -\mu z [C]\,\frac{\partial V}{\partial x}$$

$$J_{diff} = J_{drift} \quad \Rightarrow \quad \boxed{V_{eq} = -\frac{RT}{zF}\,ln\,\frac{[C]_{in}}{[C]_{out}}}$$

Nernst equation

$$E_c = V_{eq} = -\frac{RT}{zF} ln \frac{[C]_{in}}{[C]_{out}}$$

This is called *Nernst potential, equilibrium potential,* or *reversal potential.*

These 3 numbers are "constant".
Tiny changes in them lead to drastic changes in Vm.

Ion	Inside (mM)	Outside (mM)	Equilibrium Potential $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
Mammalian cell			$T = 37°C$
K^+	140	5	$62 \log \frac{5}{140} = -89.4mV$
Na^+	5-15	145	$62 \log \frac{145}{5-15} = +90-(+61)mV$
Cl^-	4	110	$-62 \log \frac{110}{4} = -89mV$
Ca^{2+}	10^{-4}	2.5-5	$31 \log \frac{2.5-5}{10^{-4}} = +136-(+145)mV$

More about Nernst potential

- If the membrane is only permeable to one type of ion, for example, K^+.
- Its Nernst potential is eventually where V_m get to.
- The influx / outflux of K^+ depends on the sign of (V_m-E_k)

Vm > -89.4 mV, outflux.
Vm < -89.4 mV, influx.

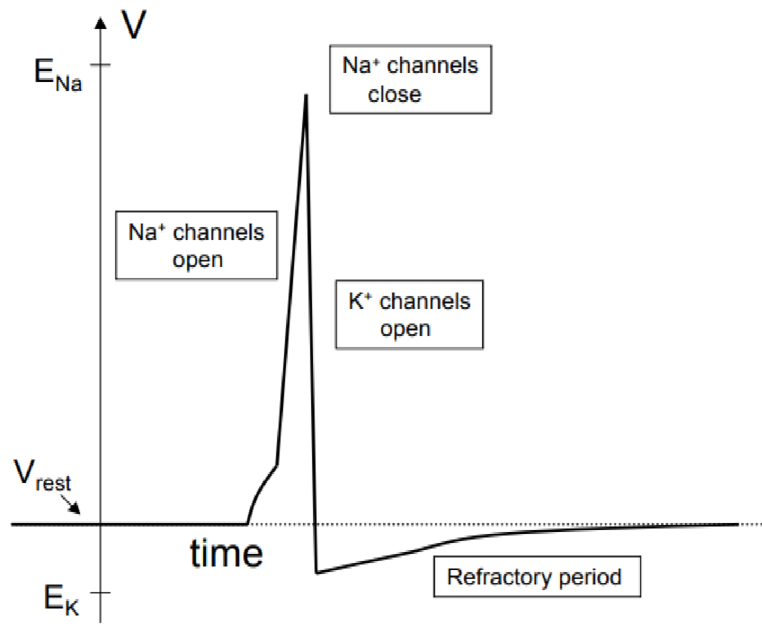
Ion	**Inside (mM)**	**Outside (mM)**	**Equilibrium Potential** $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
K^+	140	5	$62 \log \frac{5}{140} = -89.4mV$

Goldman-Hodgkin-Katz Equation

$$\mathrm{V}_m = \frac{RT}{F} ln \frac{P_K[\mathrm{K}^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{out}}{P_K[\mathrm{K}^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{in}}$$

- Similar to Nernst equation, but assume multiple permeable ions.
- Each ion try to bring V_m to its own Nernst potential. The “strength” is their permeability, P.
- P is **not** constant and can change according to the state of the neuron. (We will model its dynamics.)

Goldman-Hodgkin-Katz Equation



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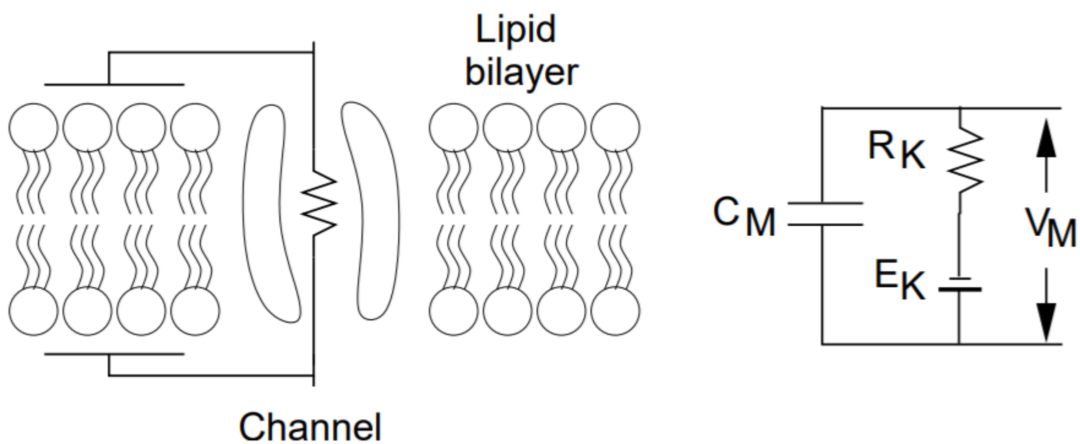
Equivalent circuit model

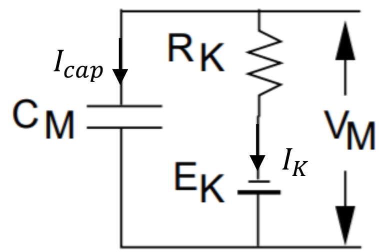


- 1) Resistor represents ion channel permeability
- 2) Battery represents Nernst potential.
- 3) Capacitor represents the ability of the neuron to store charge.

Equivalent circuit model

- Capacitor can store charge

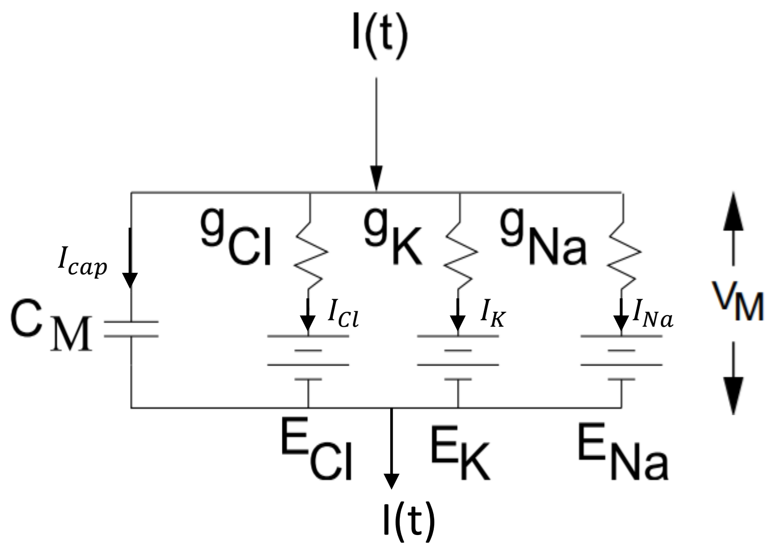
$$q = C_m V_m \qquad I_{cap} = C_m \frac{dV_m}{dt}$$



$$I_K = g_K(V_m - E_k)$$

Kirchhoff's Laws $\quad I_{cap} + I_K = 0 \quad \boxed{C_m \frac{dV_m}{dt} + g_K(V_m - E_k) = 0}$

Equivalent circuit model



$$I(t) = I_{cap} + I_K + I_{Cl} + I_{Na}$$

$$\boxed{C_m \frac{dV_m}{dt} = -g_K(V_m - E_k) - g_{Cl}(V_m - E_{Cl}) - g_{Na}(V_m - E_{Na}) + I(t)}$$

Equivalent circuit model

- Now we can derive how V_m respond to an input I.

$$C_m \frac{dV_m}{dt} = -g_K(V_m - E_k) - g_{Cl}(V_m - E_{Cl}) - g_{Na}(V_m - E_{Na}) + I(t)$$

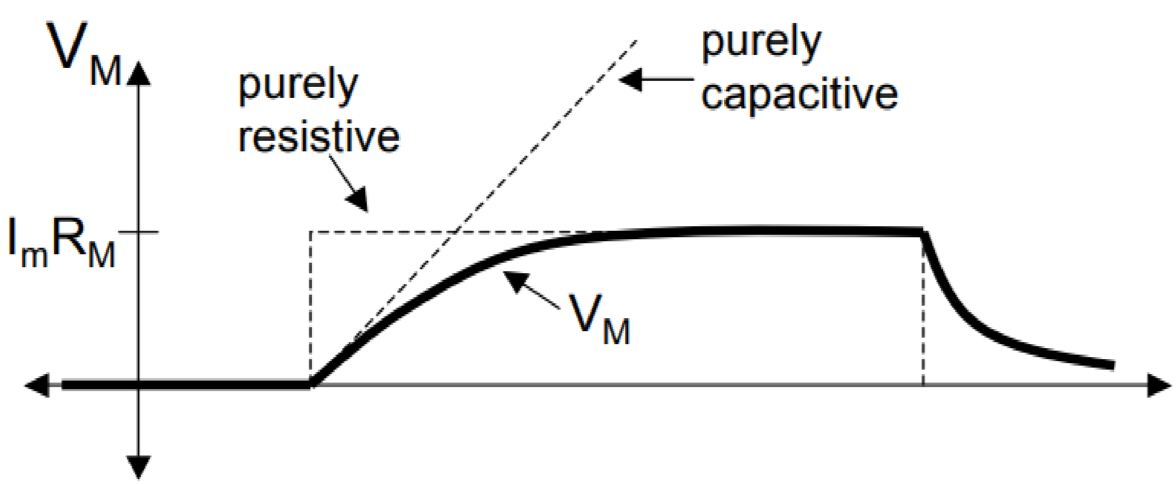
$$C_m \frac{dV_m}{dt} = -g_m(V_m - E_m) + I(t)$$

$$I(t) = \begin{cases} I_0 & if\ 0 < t < T \\ 0 & otherwise \end{cases}$$

$$V_m = \begin{cases} \frac{I_0}{g_m}\left(1 - e^{-\frac{t}{\tau_m}}\right) & if\ 0 < t < T \\ V_m(T)e^{-t/\tau_m} & otherwise \end{cases} \qquad \tau_m \equiv C_m/g_m$$

Equivalent circuit model

$$V_m = \begin{cases} \dfrac{I_0}{g_m}\left(1 - e^{-\frac{t}{\tau_m}}\right) & if\ 0 < t < T \\ V_m(T)e^{-t/\tau_m} & otherwise \end{cases} \qquad \tau_m \equiv C_m/g_m$$



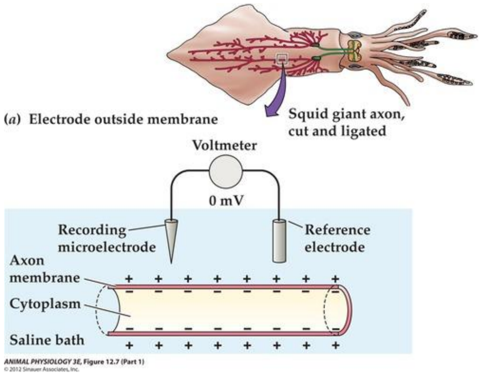
Hodgkin-Huxley model

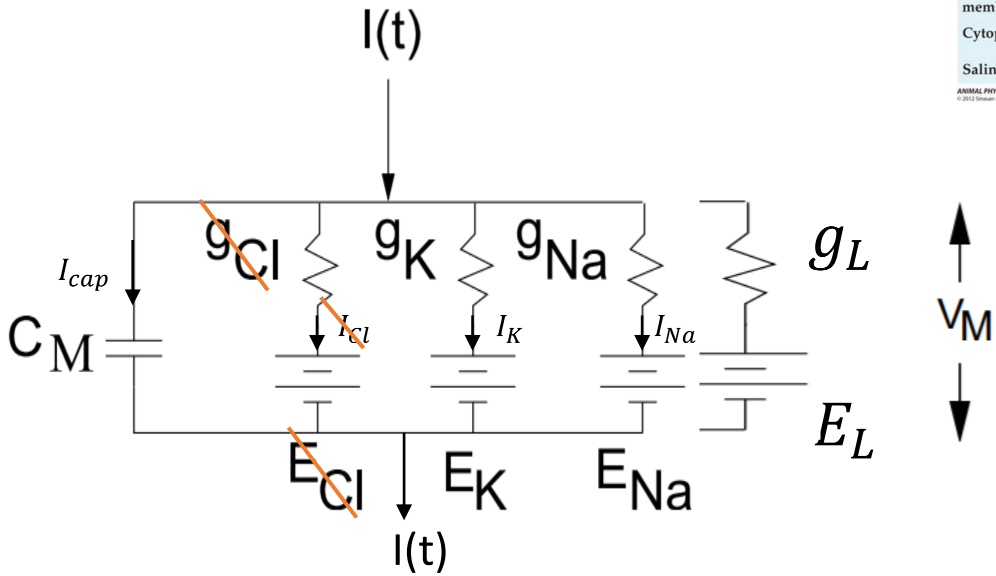
Now we have good knowledge about a passive neuron whose g_K and g_{Na} are constant.

But this neuron cannot not generate spikes. It only follows the input, I(t), with a delay.

Let's look at how g_K and g_{Na} responde to the change of V_m.

Hodgkin-Huxley model



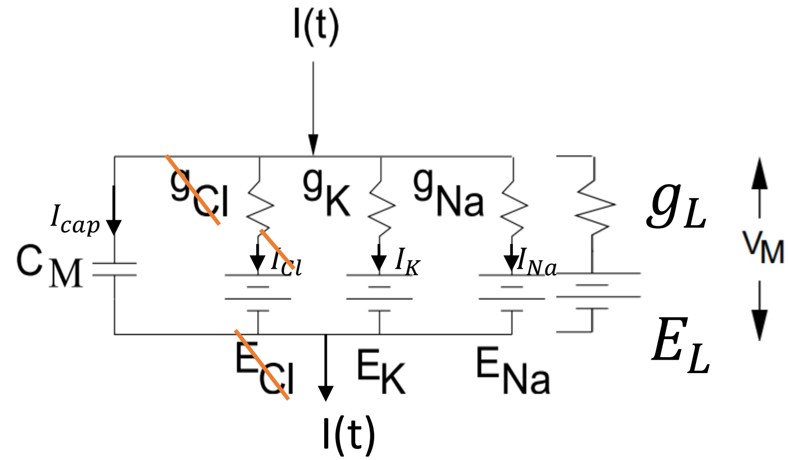


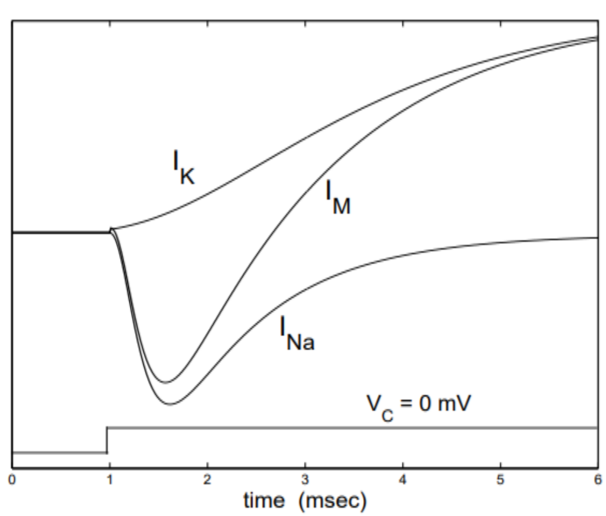
$$g_L = \frac{I_M}{(V_m - E_L)}$$

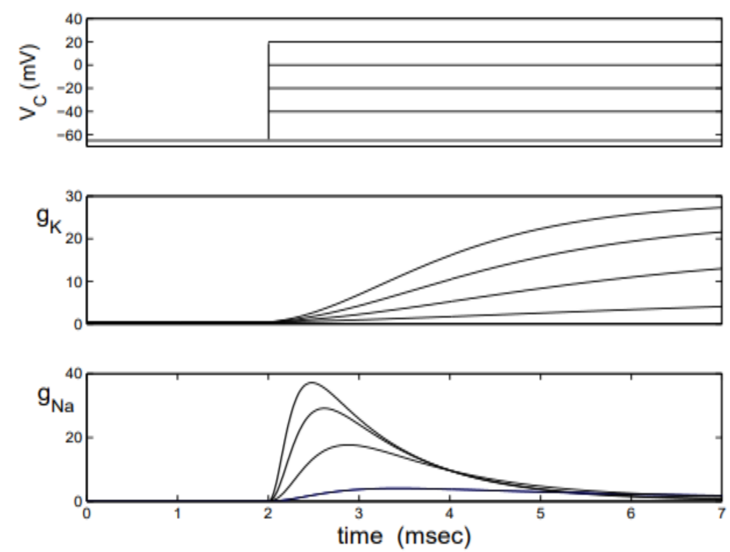
Measure this by hyperpolarize the neuron (Na and K voltage-gated channels are closed)

Hodgkin-Huxley model

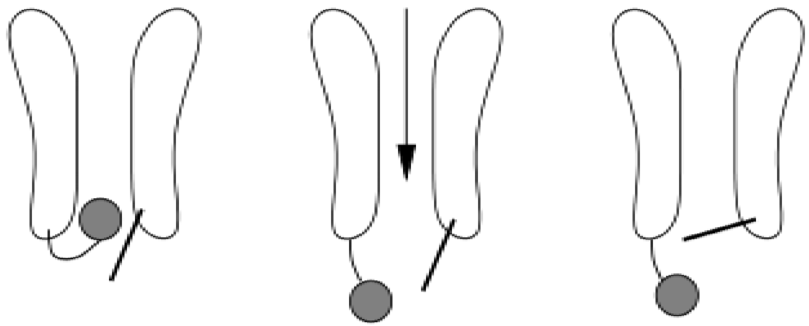
$$g_K(t) = \frac{I_K(t)}{(V_m - E_k)}$$



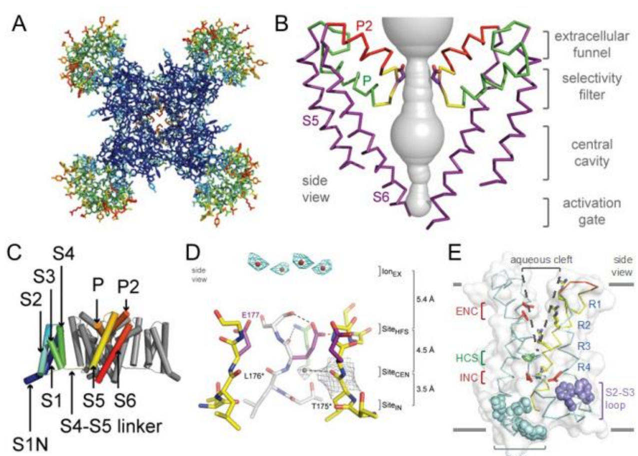




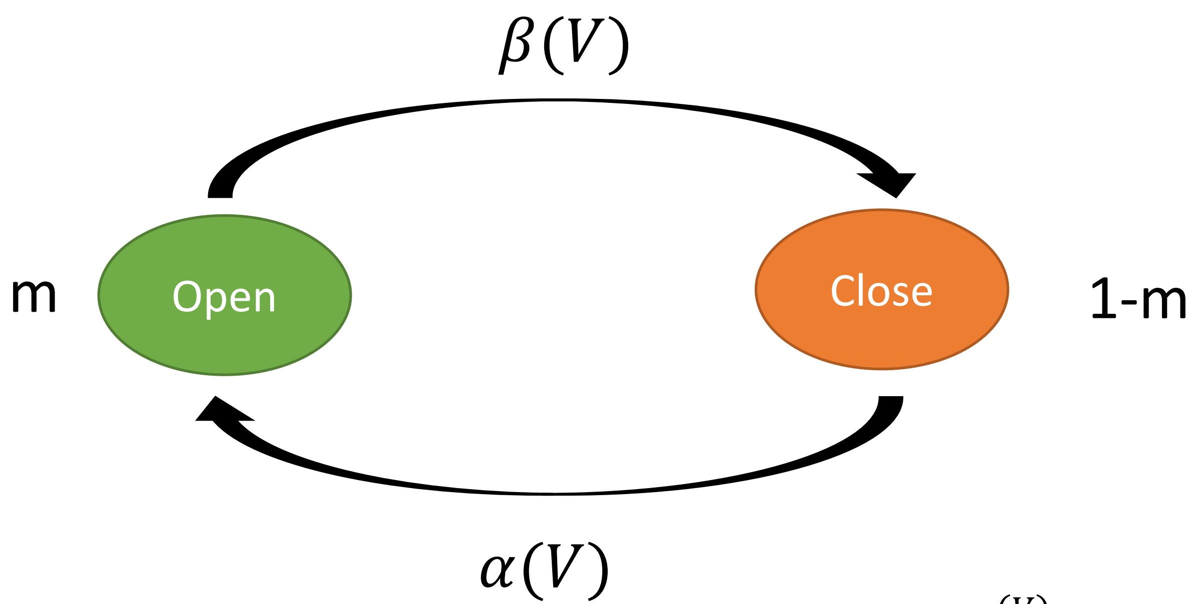
Hodgkin-Huxley model



Voltage-gated sodium channel



Voltage-gated channels



$$m_\infty(V) = \frac{\alpha(V)}{\alpha(V) + \beta(V)} \qquad \tau(V) = \frac{1}{\alpha(V) + \beta(V)}$$

$$\frac{dm}{dt} = \alpha(V)(1 - m) - \beta(V)m = (m_\infty(V) - m)/\tau(V)$$

$$m(t) = m_\infty(V) + (m(0) - m_\infty(V))e^{-t/\tau(V)}$$

Hodgkin-Huxley model

$$g_K = \bar{g}_K n^4 \quad \text{and} \quad g_{Na} = \bar{g}_{Na}\mathrm{m}^3\mathrm{h}$$

$$\frac{d\mathrm{n}}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n = (n_\infty(V) - n)/\tau_n\,(V)$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m = (m_\infty(V) - m)/\tau_m(V)$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h = (h_\infty(V) - h)/\tau_h(V)$$

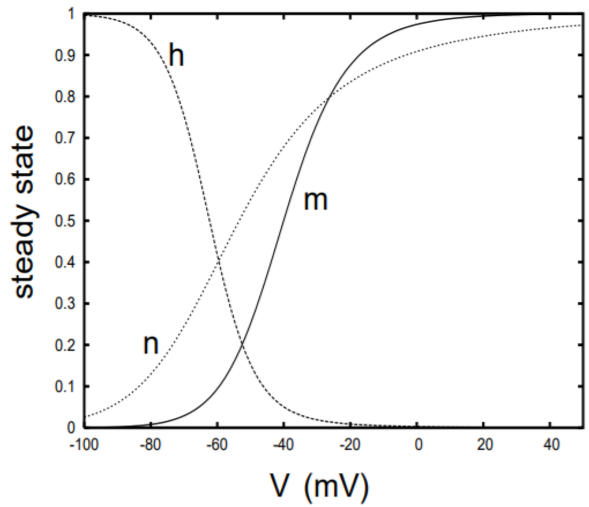
$$C_m\frac{dV_m}{dt} = -g_K(V_m - E_k) - g_{Na}(V_m - E_{Na}) - g_L(V_m - E_L) + I(t)$$

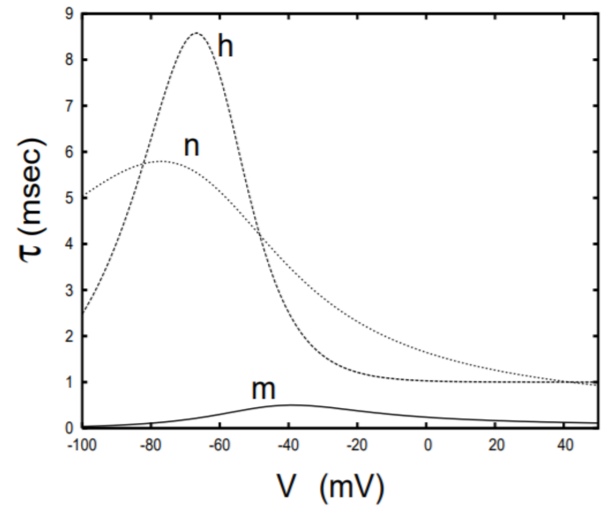
Hodgkin-Huxley model

$\bar{g}_K = 120\ mS/c\mathrm{m}^3$, $\bar{g}_{Na} = 36\ mS/c\mathrm{m}^3$, $\bar{g}_L = 0.3\ mS/c\mathrm{m}^3$,
$\mathrm{E}_{Na} = 50\ mV$, $\mathrm{E}_K = -77\ mV$, $\mathrm{E}_L = -54\ mV$,

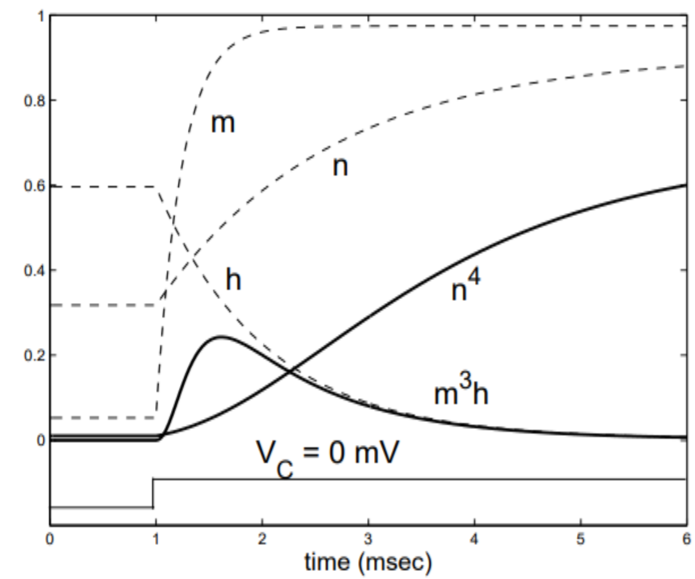
$$\begin{aligned}
\alpha_n(V) &= 0.01(V+55)/(1-\exp(-(V+55)/10)) \\
\beta_n(V) &= 0.125\exp(-(V+65)/80) \\
\alpha_m(V) &= 0.1(V+40)/(1-\exp(-(V+40)/10)) \\
\beta_m(V) &= 4\exp(-(V+65)/18) \\
\alpha_h(V) &= 0.07\exp(-(V+65)/20) \\
\beta_h(V) &= 1/(1+\exp(-(V+35)/10)).
\end{aligned}$$

Hodgkin-Huxley model





$$g_K = \bar{g}_K n^4$$
$$g_{Na} = \bar{g}_{Na} \mathrm{m}^3 \mathrm{h}$$



Hodgkin-Huxley model

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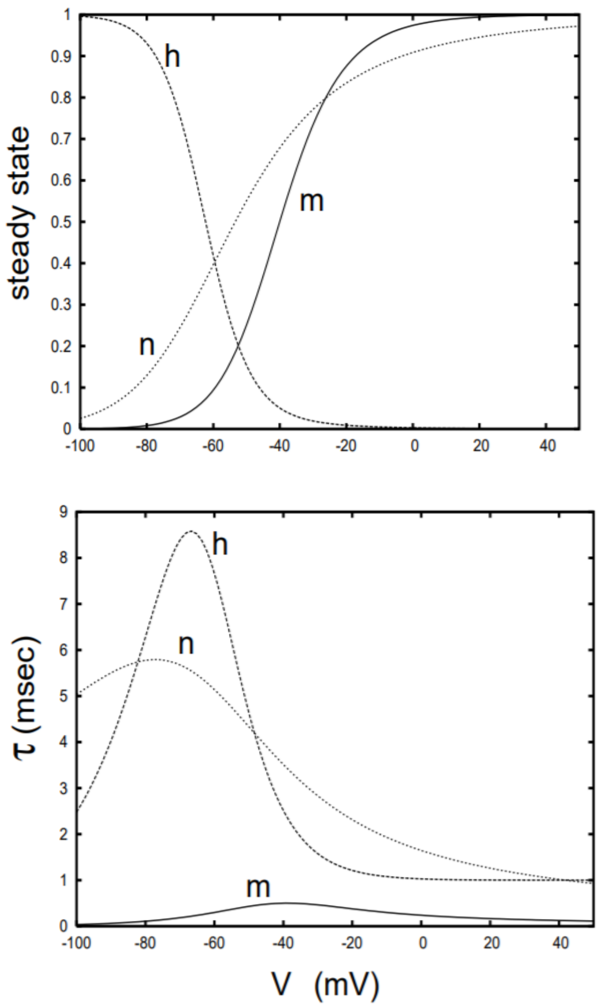
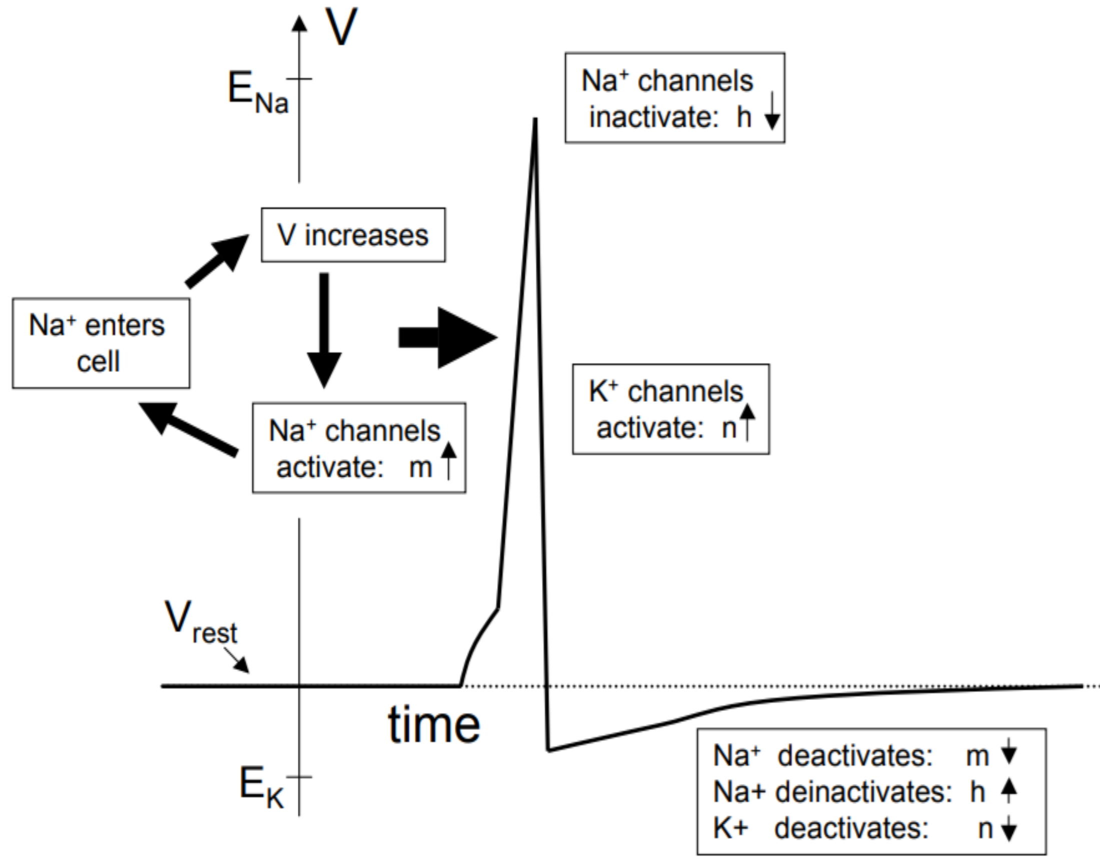
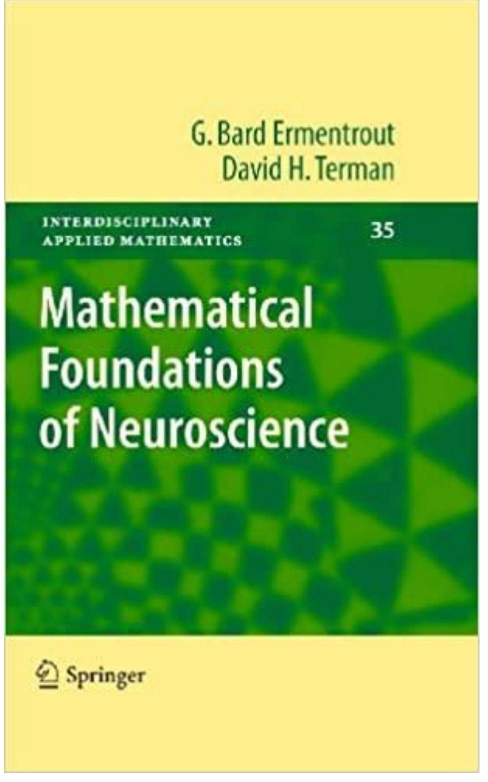




Further reading



Chapter 1