

An introduction to modern neurophysiology

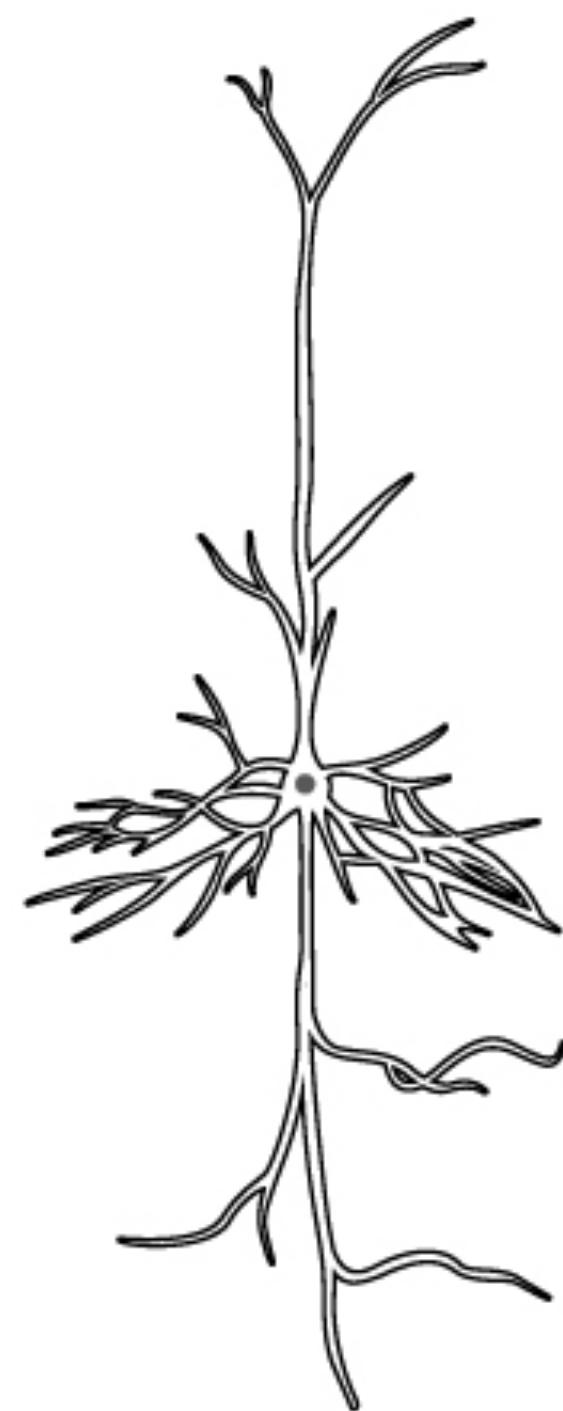
Computational modeling: the Leaky Integrate and Fire neuron



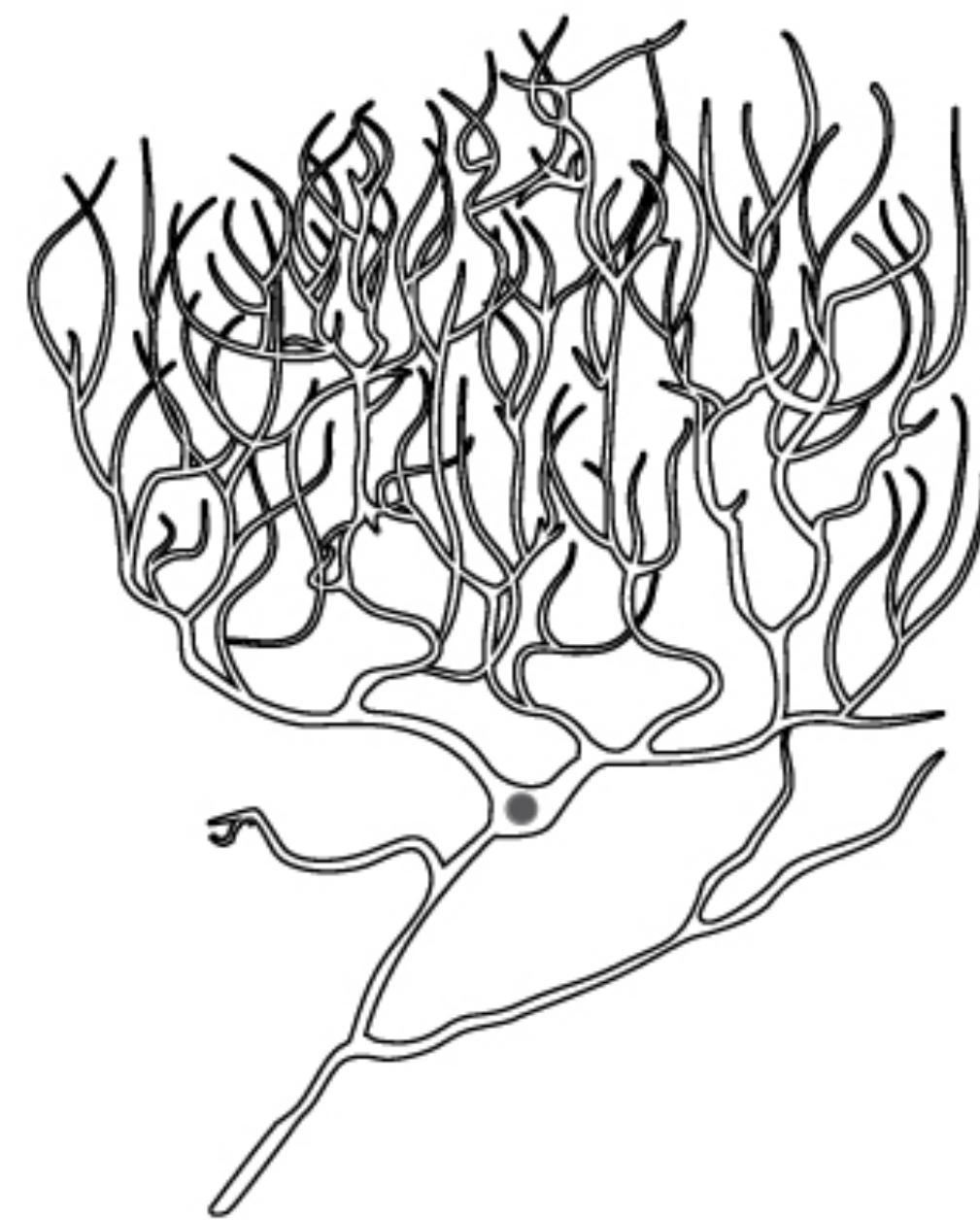
Modeling is simplifying complexity

How complex are we talking about?

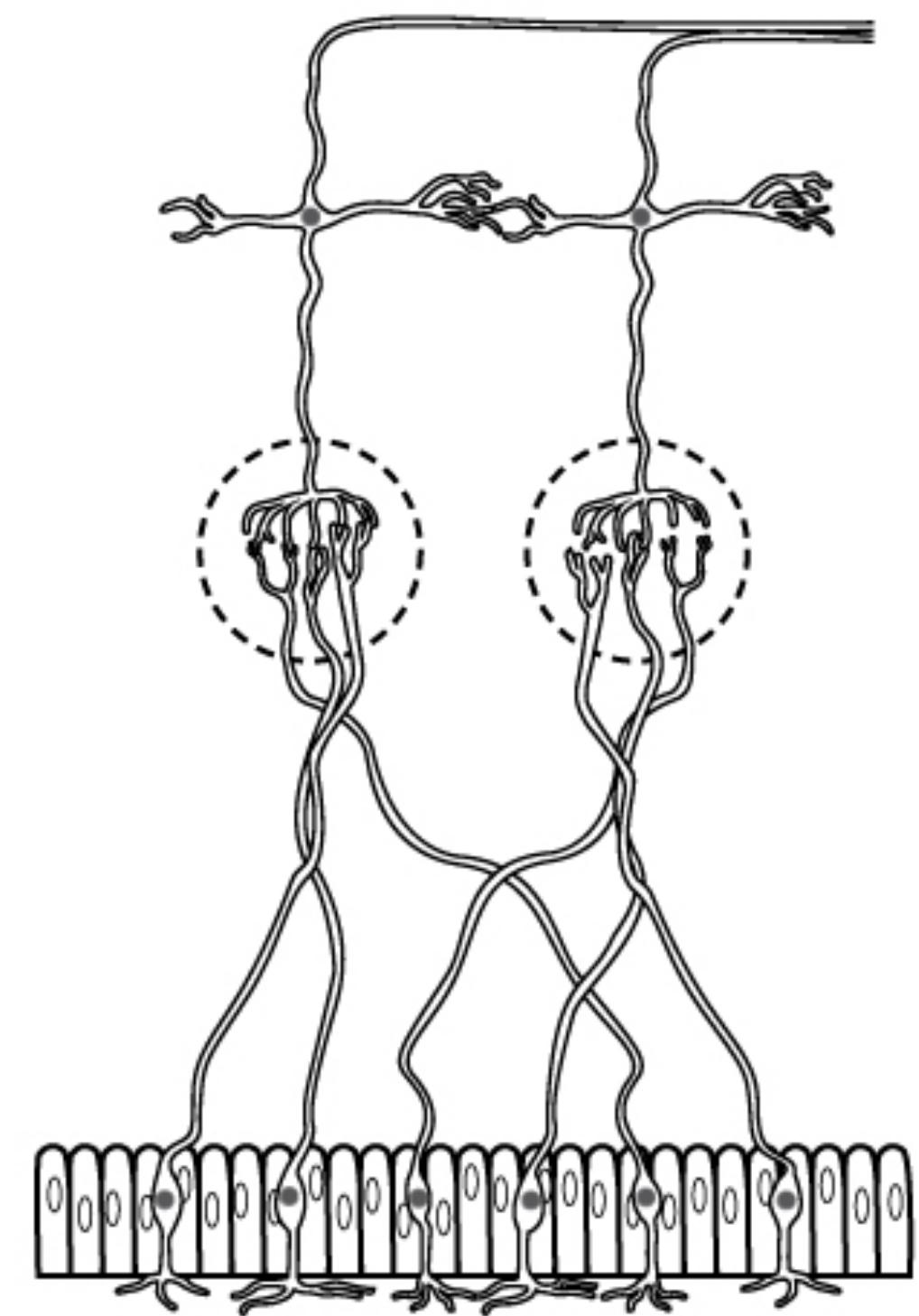
86 billion neurons
Different morphology
Different function (excitatory vs inhibitory)



(a) Pyramidal cell of the cerebral cortex



(b) Purkinje cell of the cerebellar cortex



(c) Olfactory cells in the olfactory epithelium and olfactory bulbs

Credits to OpenStax Anatomy and Physiology.
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Anatomy of a neuron

Neurons, like all cells, are extremely complex systems:

- Machinery to keep them alive
- Machinery to allow for electrical signaling

Multiple parts:

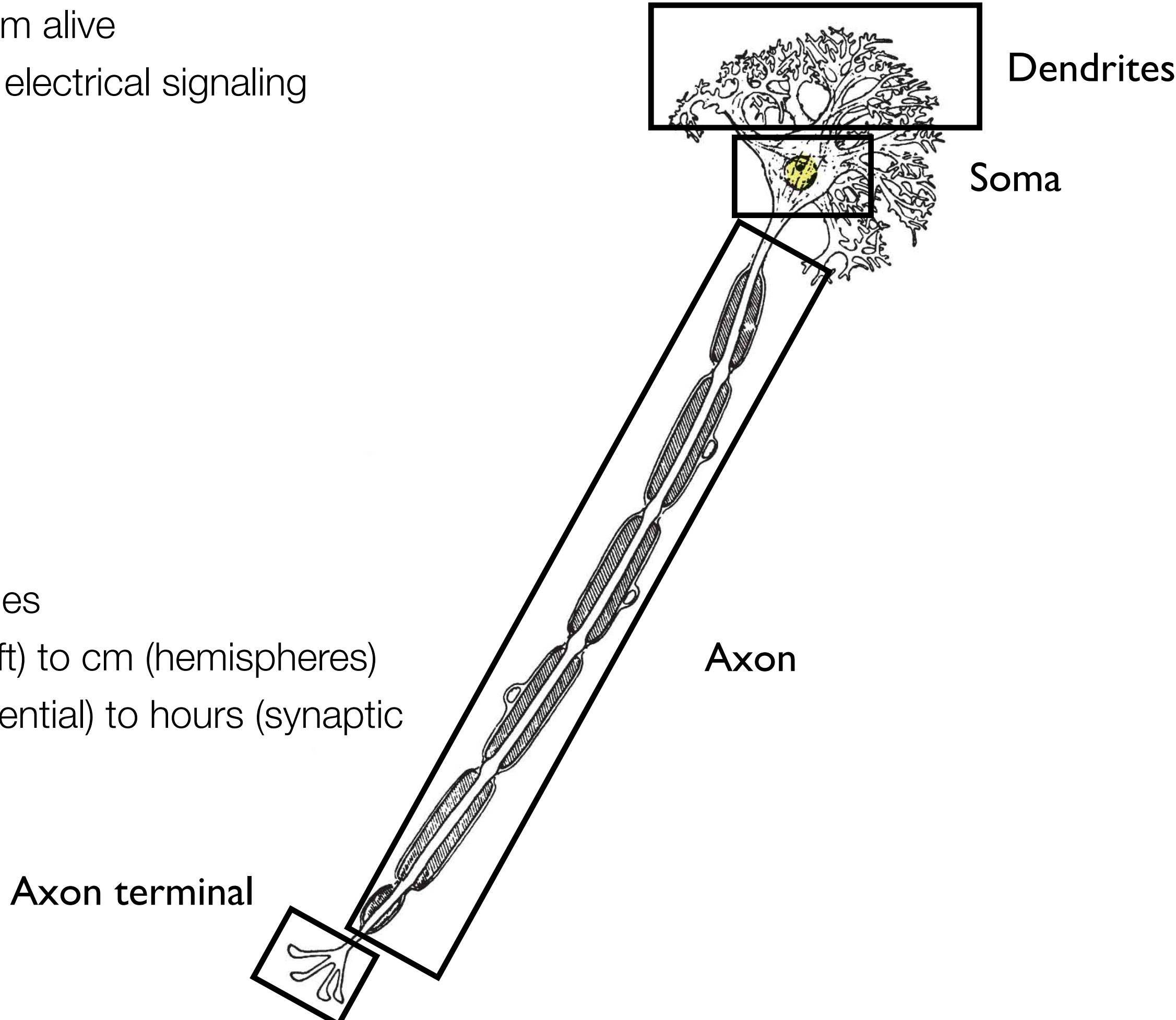
- Dendrites
- Soma
- Axon
- Axon terminal

Multiple physical processes:

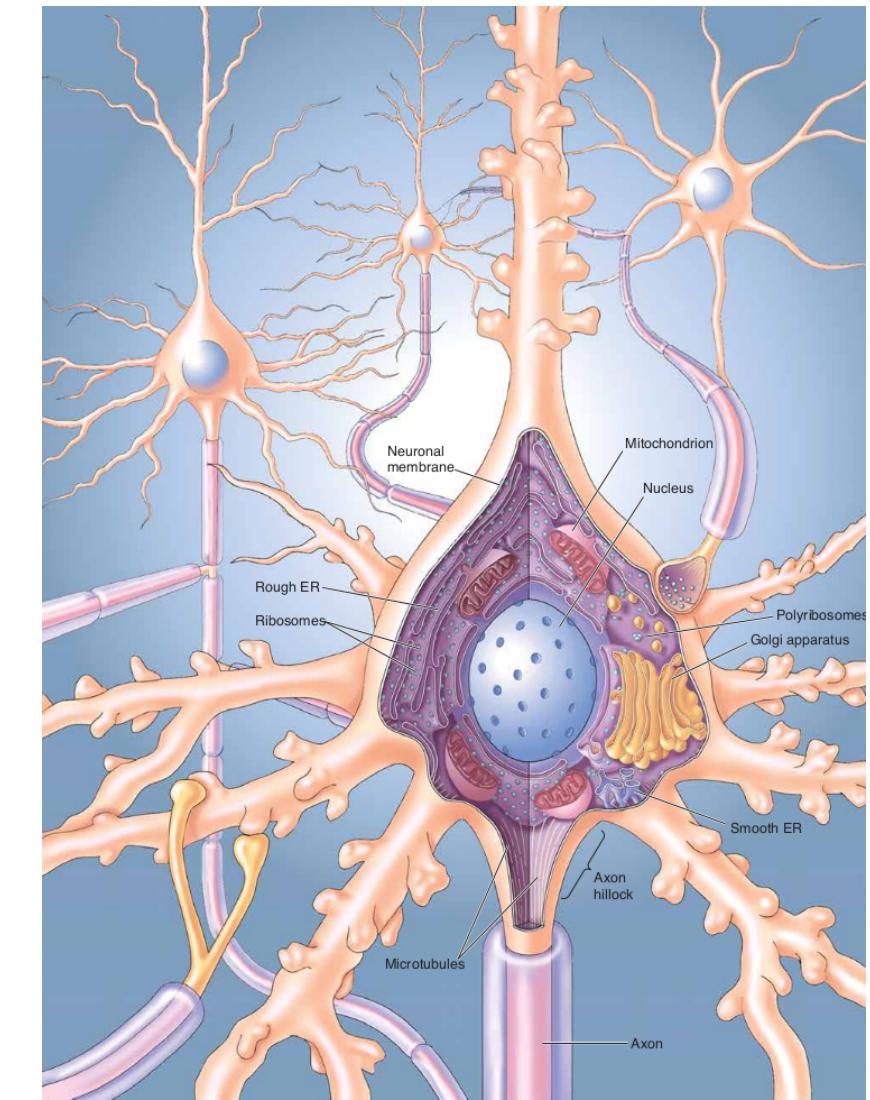
- Biochemical
- Electrical

Multiple spatial and time scales

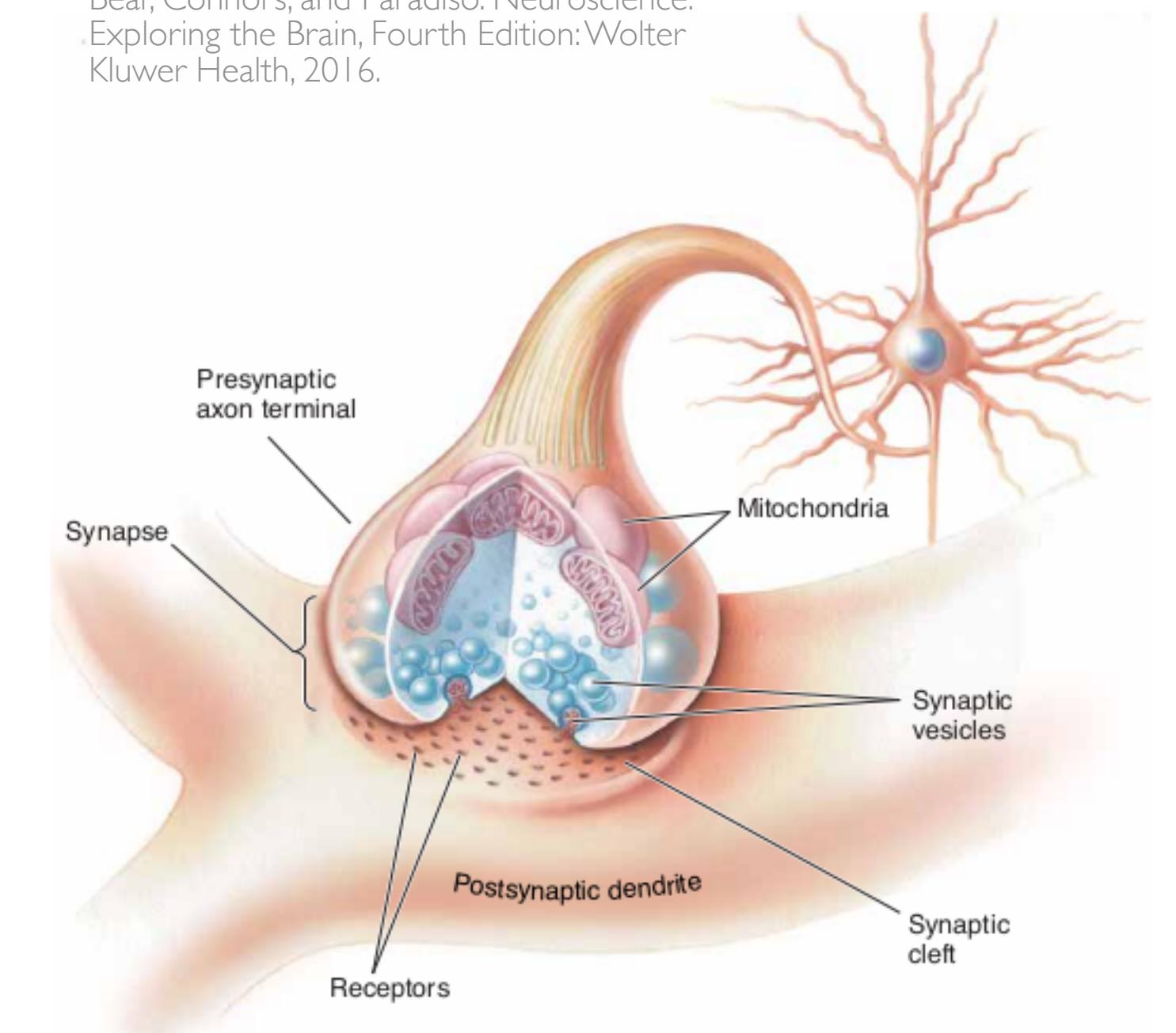
- From nm (synaptic cleft) to cm (hemispheres)
- From < ms (action potential) to hours (synaptic plasticity)



"Myelinated motor neuron" by National Institutes of Health (NIH) is licensed under CC BY-NC 2.0.
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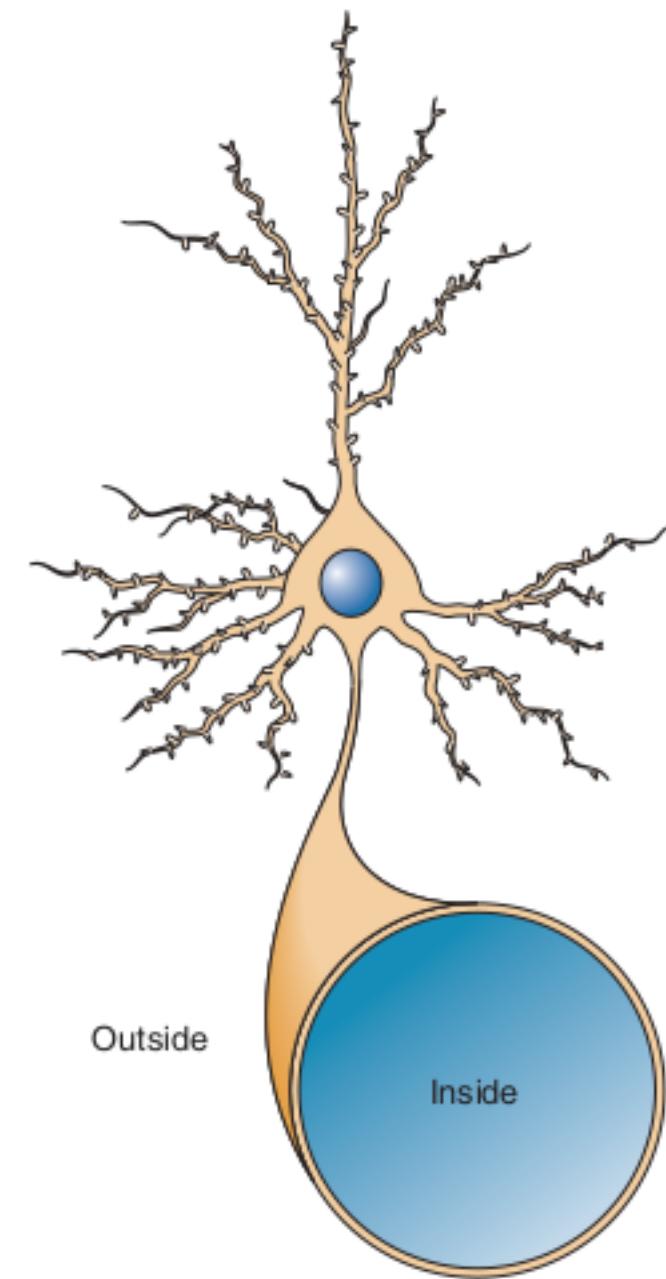


Bear, Connors, and Paradiso. Neuroscience: Exploring the Brain, Fourth Edition: Wolter Kluwer Health, 2016.



Bear, Connors, and Paradiso. Neuroscience: Exploring the Brain, Fourth Edition: Wolter Kluwer Health, 2016.

Anatomy of an action potential

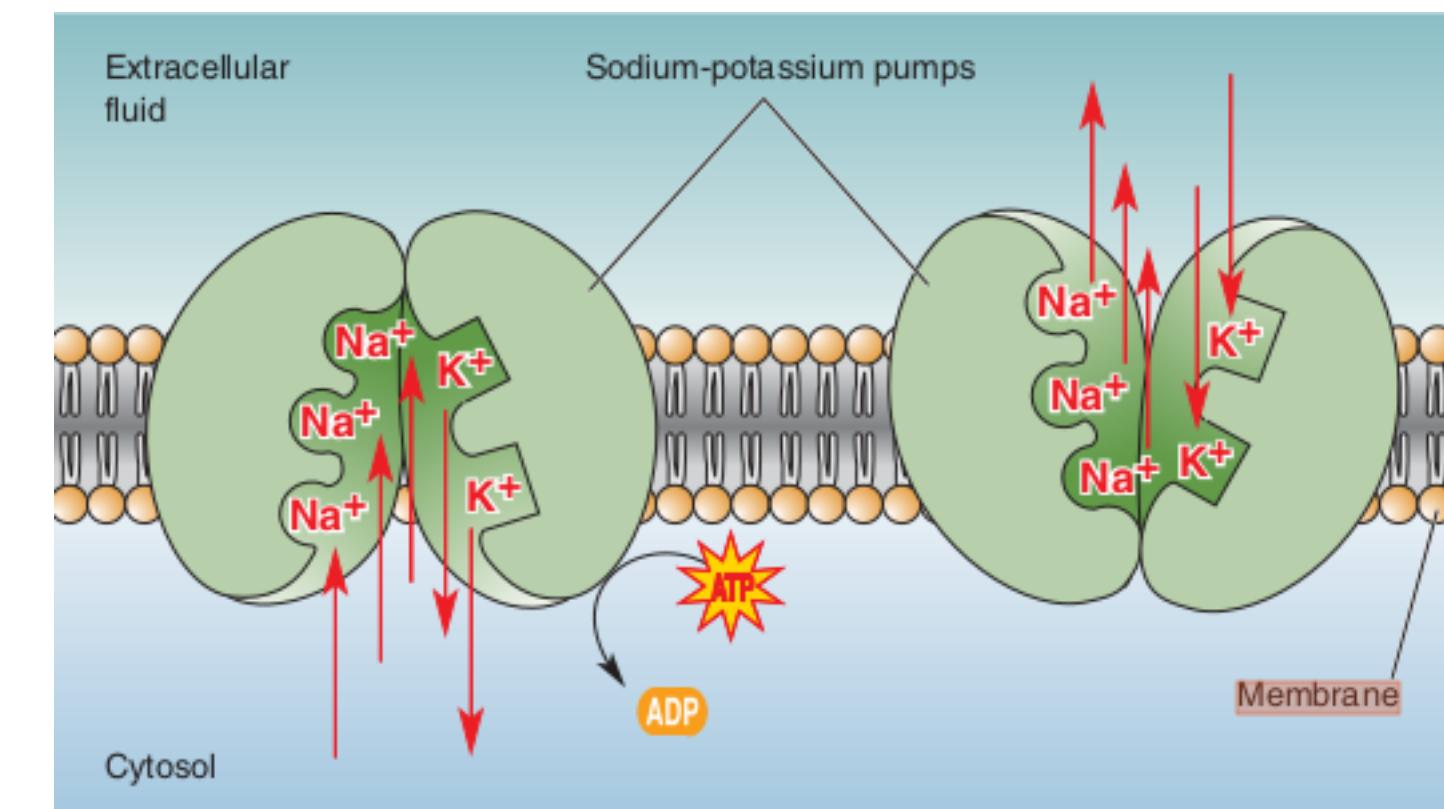


Ion	Concentration outside (in mM)	Concentration inside (in mM)	Ratio Out : In	E_{ion} (at 37°C)
K ⁺	5	100	1 : 20	-80 mV
Na ⁺	150	15	10 : 1	62 mV
Ca ²⁺	2	0.0002	10,000 : 1	123 mV
Cl ⁻	150	13	11.5 : 1	-65 mV

Bear, Connors, and Paradiso. Neuroscience: Exploring the Brain, Fourth Edition: Wolter Kluwer Health, 2016.

Ion pumps maintain membrane charge

- Sodium out
- Potassium in



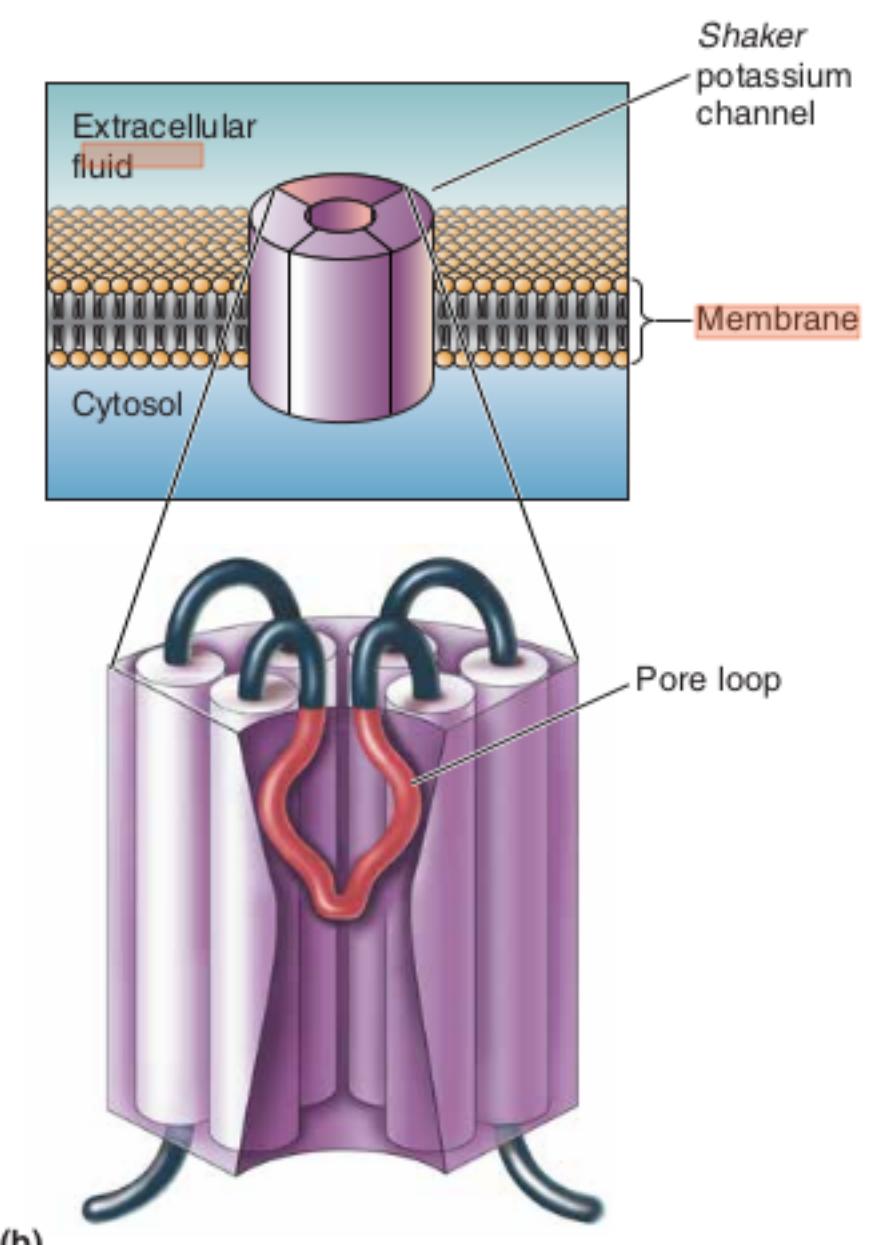
Bear, Connors, and Paradiso. Neuroscience: Exploring the Brain, Fourth Edition: Wolter Kluwer Health, 2016.

Ion channels selectively let ions in

- Voltage gated
- Ligand gated
- Mechanically gated



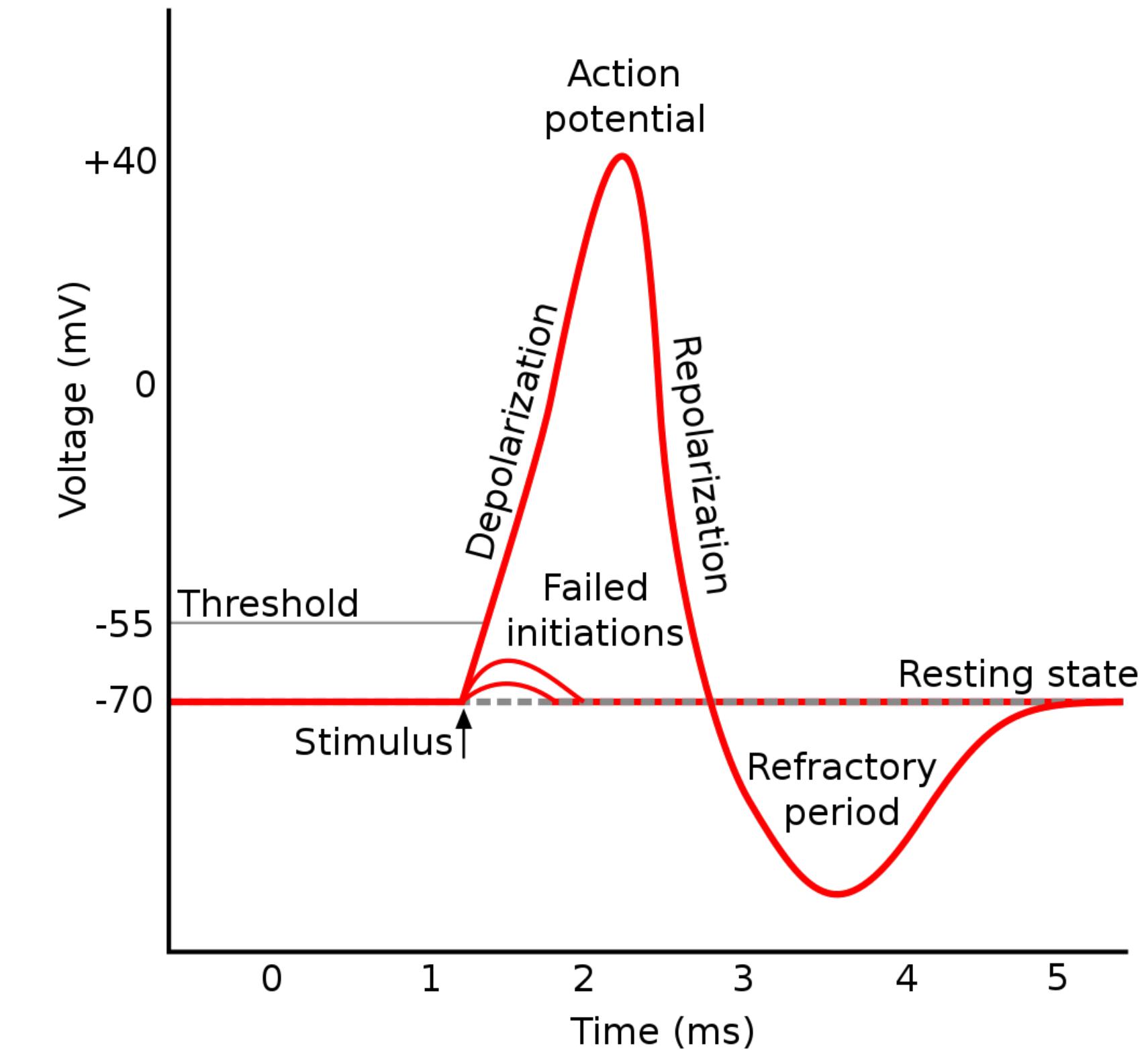
(a)



(b)

Anatomy of an action potential

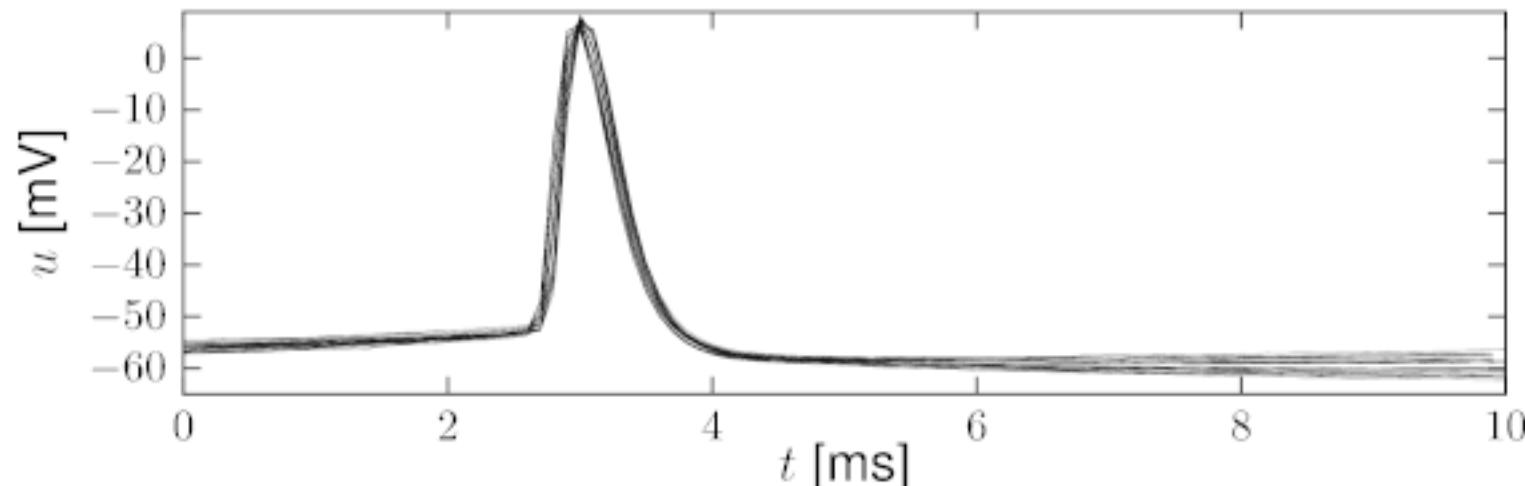
1. Stimulus arrives at synaptic cleft
2. Neurotransmitter released
3. If neurotransmitters bind to receptors in post-synaptic neuron they cause opening of ion channels in dendrites
4. If sodium enters the cell, we have a EPSP (Excitatory Post Synaptic Potential)
5. If stimulation is strong enough that the membrane potential reaches a threshold value, voltage gated sodium channels open
6. Positively charged sodium enters the cell: depolarization
7. Sodium channels inactivate (refractory period)
8. Voltage gated potassium channel open
9. Positively charged potassium out: repolarization + hyperpolarization
10. Sodium channels close
11. During all this sodium-potassium pumps are still working and will bring back the membrane to its resting state



Different neuronal types have different detailed mechanisms for generating action potentials!

[Bean, B. The action potential in mammalian central neurons. *Nat Rev Neurosci* 8, 451–465 (2007). <https://doi.org/10.1038/nrn2148>]

Do we need to model all this?

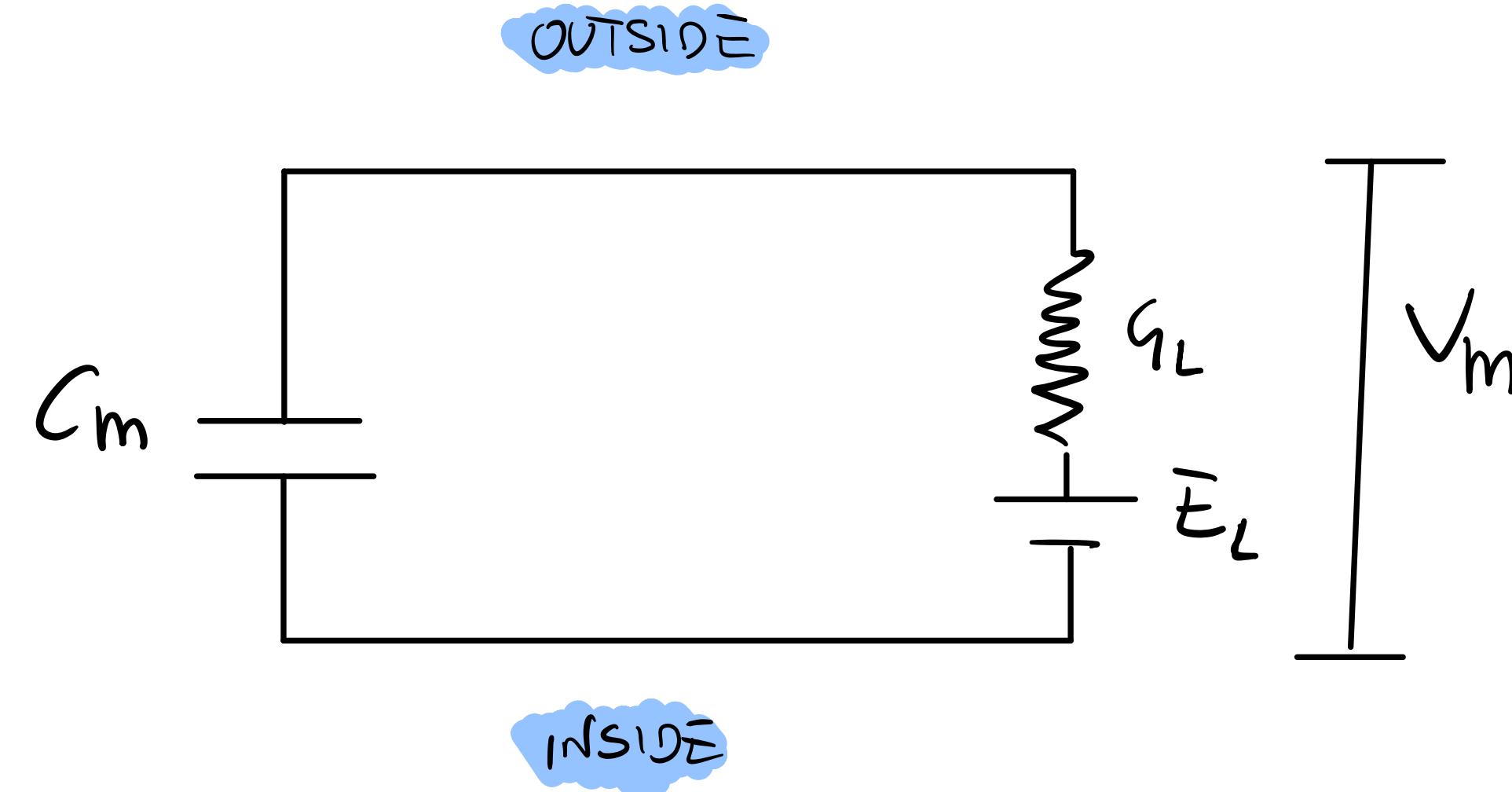


Gerstner, Wulfram, et al. Neuronal dynamics: From single neurons to networks and models of cognition. Cambridge University Press, 2014.

Action potentials form the basis of neural signaling and are largely stereotypical (see e.g. [de Polavieja, Gonzalo G., et al. Journal of Neuroscience (2005)] for another view on the typical assumption that APs are stereotyped)

We could be happy with a model that just produces spikes, without dealing with all the intricacies of the biochemistry behind...

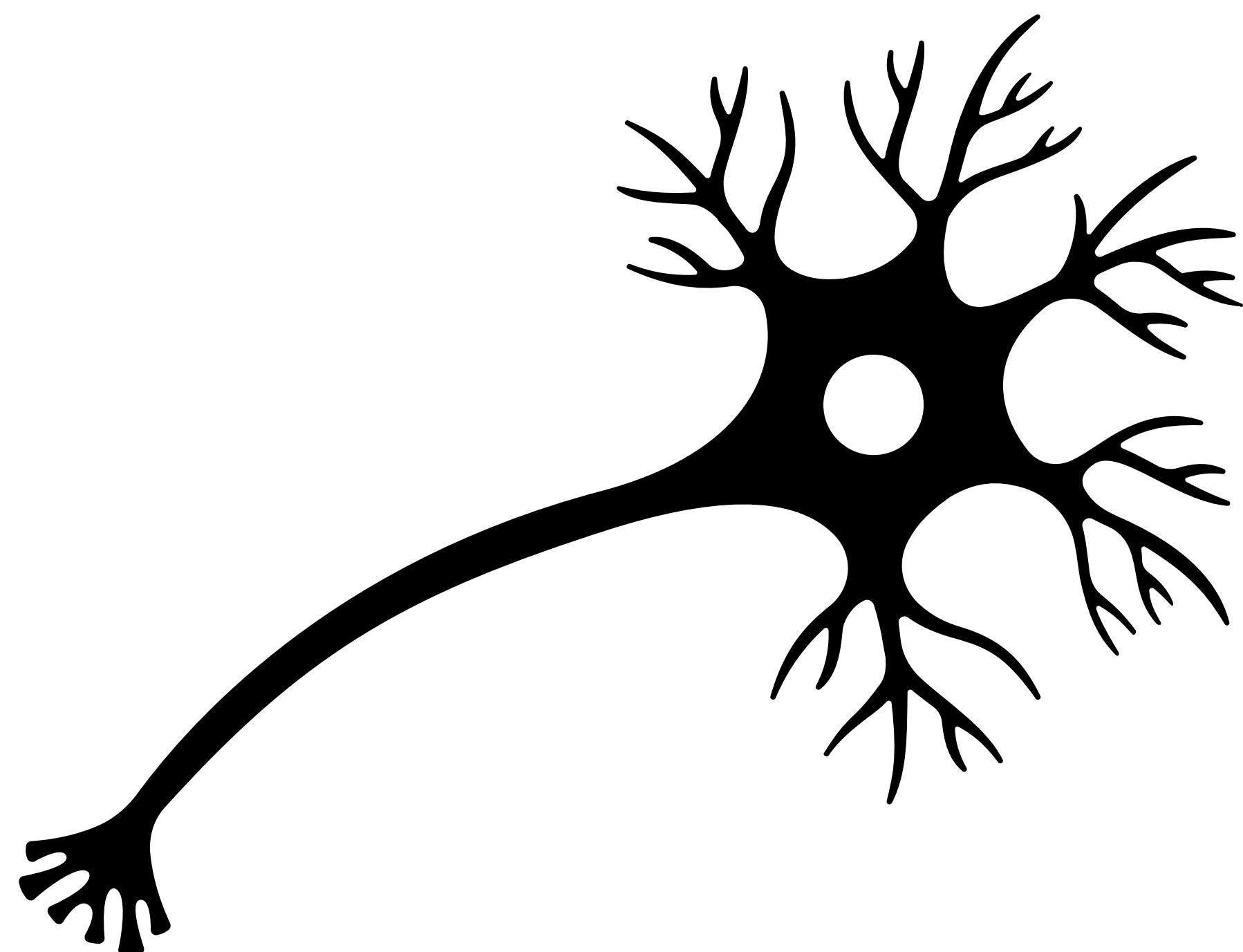
We will only work with transport of electrical charges, without including any biochemistry



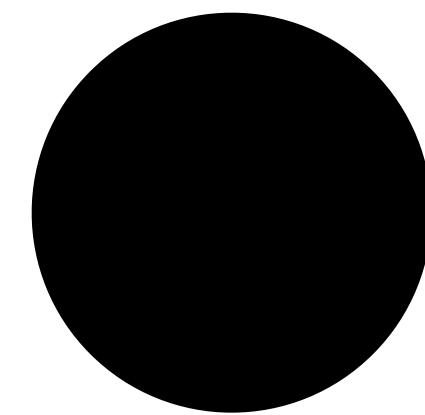
$$C_m \frac{dV_m}{dt} = g_L(E_L - V_m) + I_{app}$$

if $V_m > V_{th}$ then $V_m \mapsto V_{reset}$

What we're left with?



=



Point neuron models

Maybe we over simplified things?

A simple model should always be preferred if it's adequate for our needs: it favors interpretability!

In any case the best way is to test it out, in our case we will do this in the tutorial, where we'll build on top of this simple LIF model to more complex ones.

Behind this simplification there are lots of (important?) assumptions!

You are discarding:

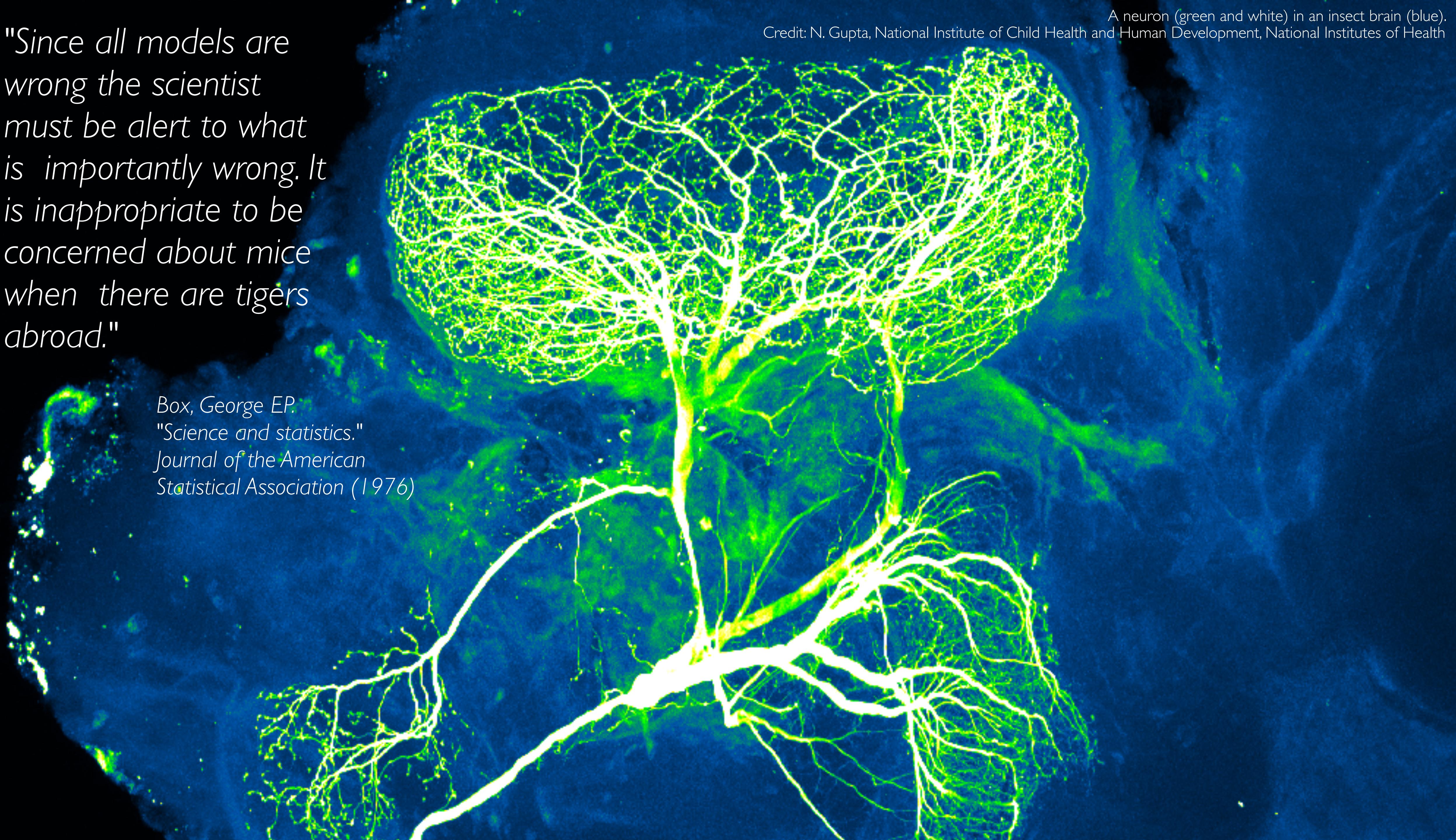
- the details of chemical transmission
- the influence of specific ions on the membrane potential
- the details of the kinetics of specific ions in and out of the cell
- the effect of specific neurotransmitters
- differences between what happens in dendrites vs soma vs axon
- the effect of the distribution of specific ion channels on the cell membrane
- a lot of biochemical details that happen within the cell
- sub-threshold activity and suppose that an action potential is the basis of the communication between neurons
-

Important to know everything you left out of your model as it may be the reason why you cannot fit your model to the data!

"Since all models are wrong the scientist must be alert to what is importantly wrong. It is inappropriate to be concerned about mice when there are tigers abroad."

Box, George EP.
"Science and statistics."
Journal of the American Statistical Association (1976)

A neuron (green and white) in an insect brain (blue).
Credit: N. Gupta, National Institute of Child Health and Human Development, National Institutes of Health



A note on time integration of differential equation

$$\frac{dV_m}{dt} = \lim_{\Delta t \rightarrow 0} \frac{V_m(t + \Delta t) - V_m(t)}{\Delta t} \approx \frac{V_m(t + \Delta t) - V_m(t)}{\Delta t}$$

$$C_m \frac{V_m(t + \Delta t) - V_m(t)}{\Delta t} = \varsigma_L (E_L - V_m) + I_{app}$$

$$V_m(t + \Delta t) = V_m(t) + \frac{\Delta t}{C_m} \left[\varsigma_L (E_L - V_m(t)) + I_{app} \right]$$

First order forward Euler method