COMS30127: Computational Neuroscience

Lecture 19: Ion channels (j)

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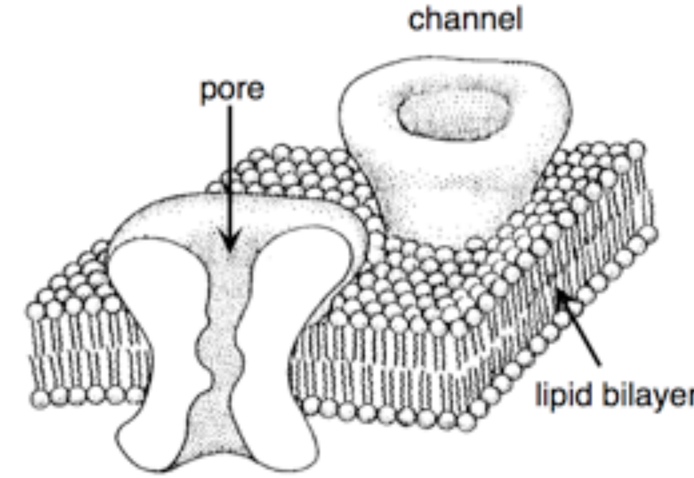
What we will cover today

- What are ion channels and what do they do?
- The different types of ion channels.
- How ion channels control the neuron’s nonlinear input-output function.
- Ion channels as an intrinsic source of noise in the brain.

What are ion channels?



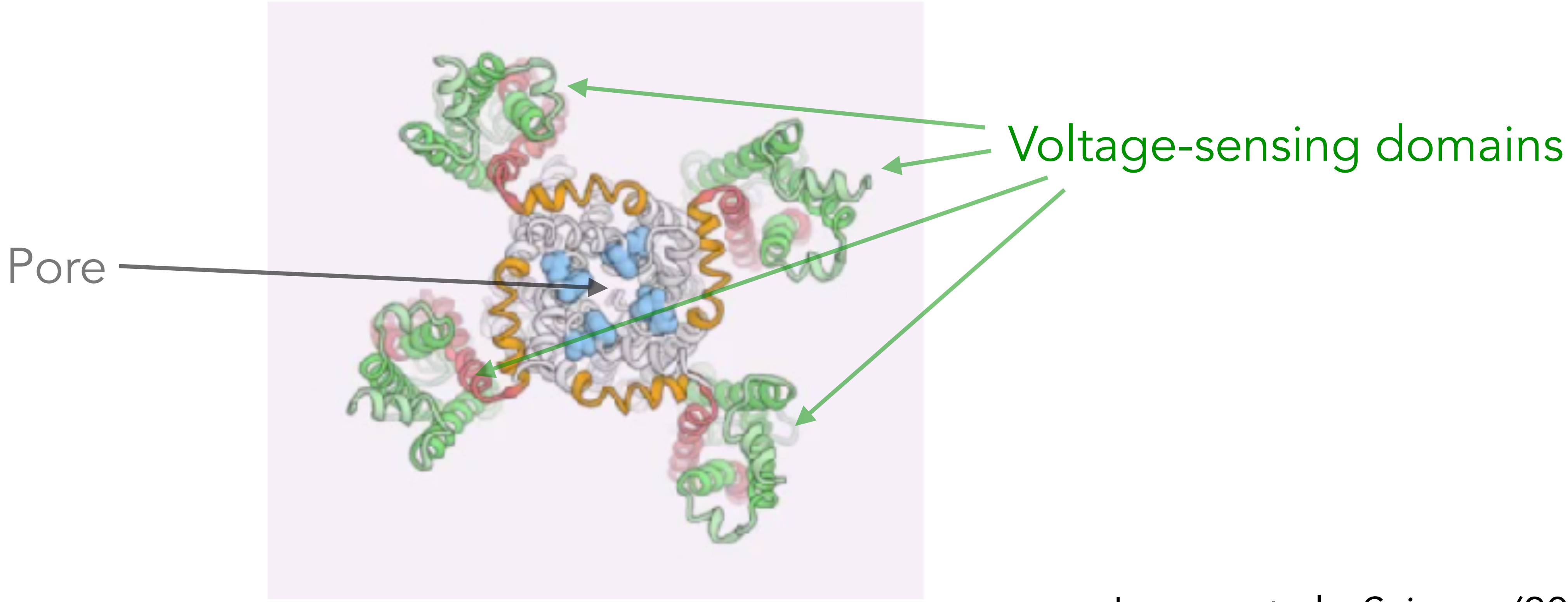
Hille (1992)

- Ion channels are ion-permeable pores in the lipid membrane of cells.
- A single neuron typically has hundreds of thousands to millions of ion channels embedded in its membrane.
- They open and close in response to stimuli (voltage, neurotransmitters, intracellular chemicals, pH, mechanical forces, temperature…), passing ions like Na^+, K^+, Ca^{2+}, Cl^-.
- Their currents mediate electrical signalling in the nervous system.
- The conductance of single ion channels vary between ~0.1 and 100 picoSiemens. For most channels it's around 10 pS.
- The flux through a single open channel can be millions of ions per second.

What are ion channels?

- Voltage-gated ion channels typically have a pore domain made up of four identical, or similar, channel subunits arranged in a ring. The ion pore is made along the axis where they meet.
- The channel also has secondary voltage-sensing domains, that deform in response to changes in the transmembrane voltage.
  These drag the pore-domain components to switch the channel open or closed.

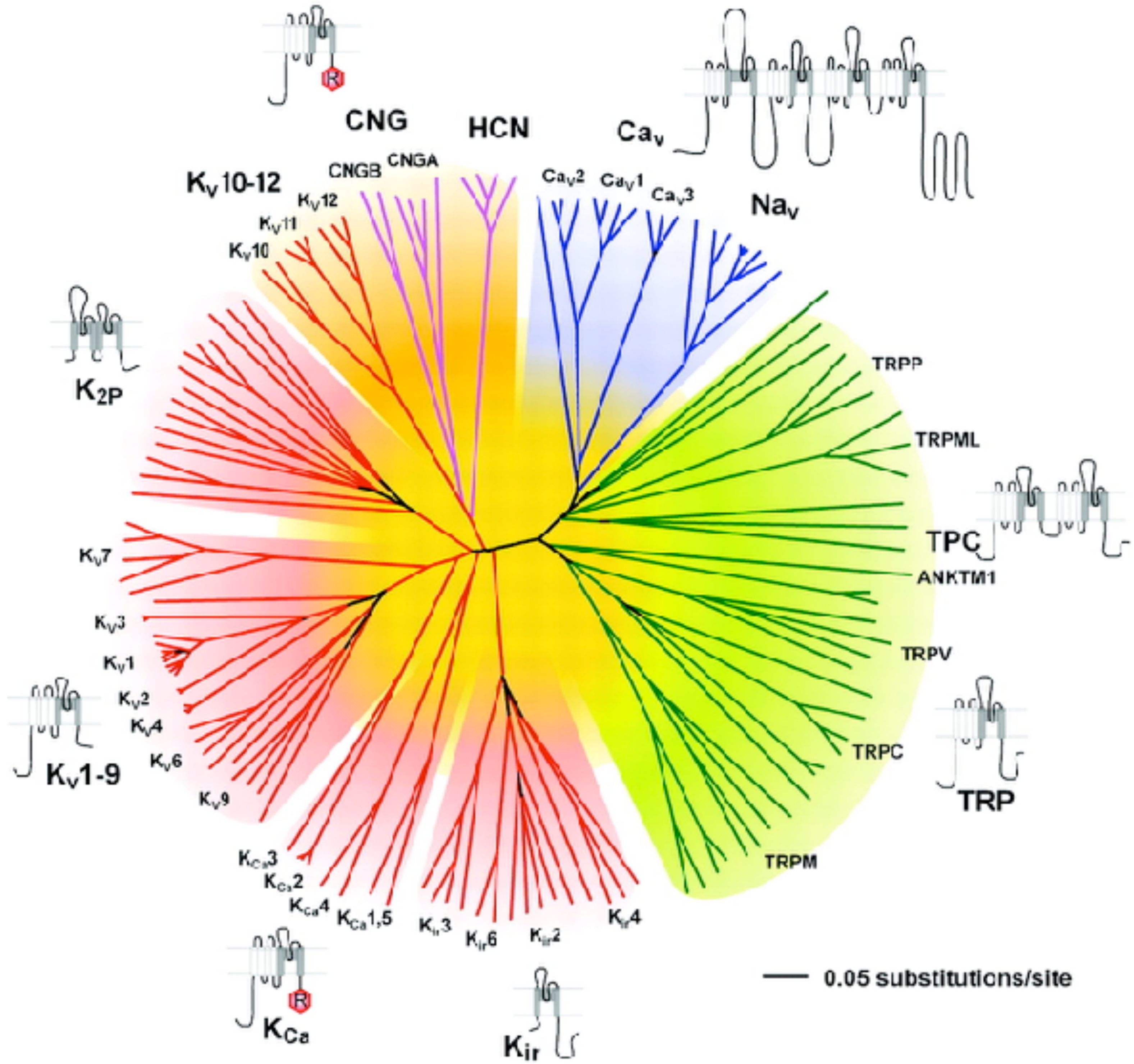
Bottom-up view of a potassium channel (from inside the cell)



Jensen et al., *Science* (2012)

Ion channel types

The ion channel zoo



Yu et al., *Pharm Rev* (2005)

The neuron's input-output function

a.k.a. synaptic integration

Non-linear synaptic integration

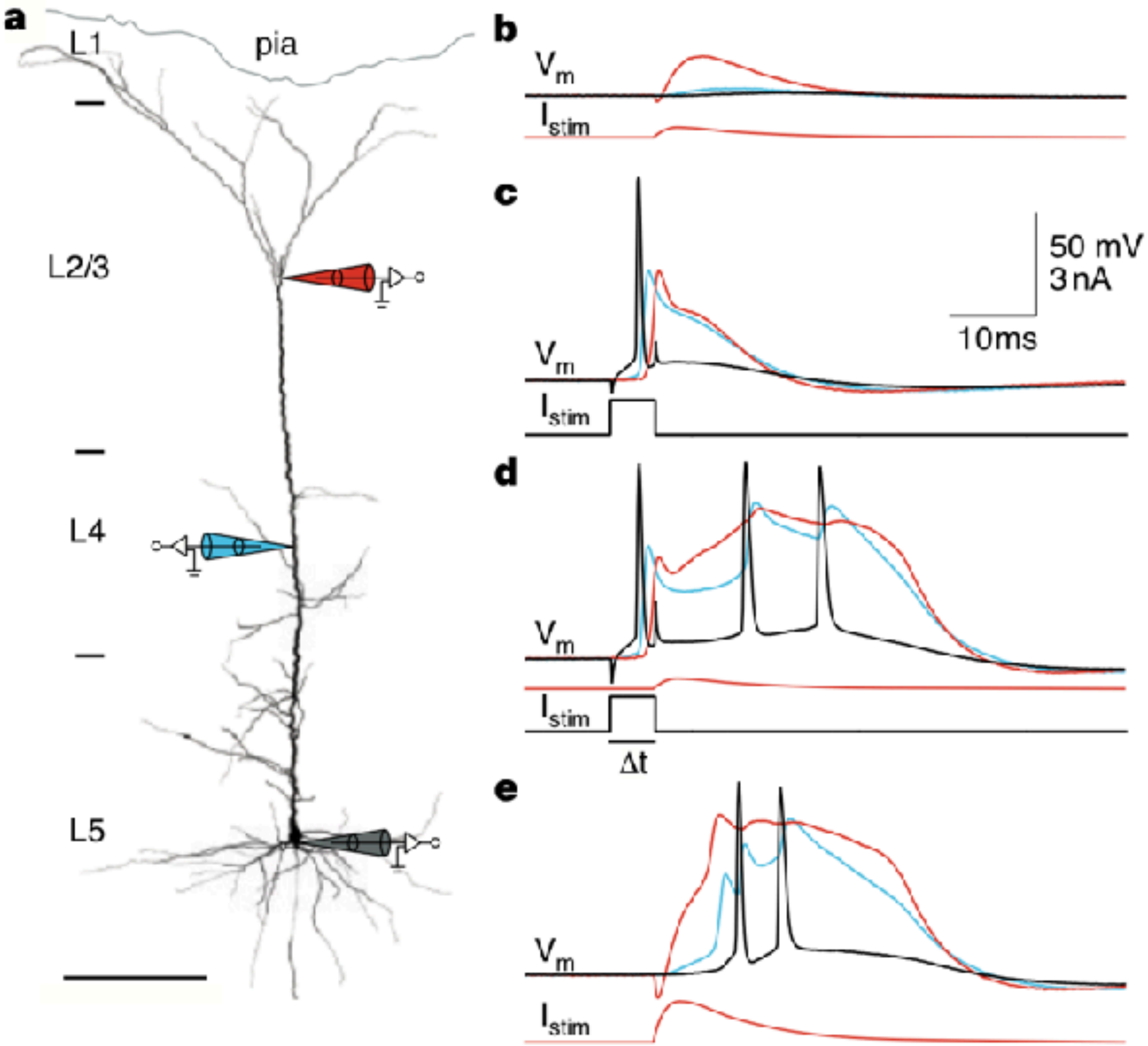
- Neurons receive multiple temporal patterns of spike trains as input, and produce a single spike train as output.
- “Point” neuron models typically assume that the soma performs a weighted linear sum of the synaptic currents.
- However, real neurons differ from this idealisation in two key aspects:
  1. Neurons have dendrites, which implies a spatial layout of synaptic inputs.
  2. Dendrites have voltage-dependent (active) ion channels which makes synaptic integration non-linear.

Synaptic location matters

- An otherwise identical synapse will give a smaller response if it is located at a distal dendritic site.

- However, the local voltage change tends to be higher for distal synapses.

Co-incidence detection via active dendrites



Weak distal stim alone

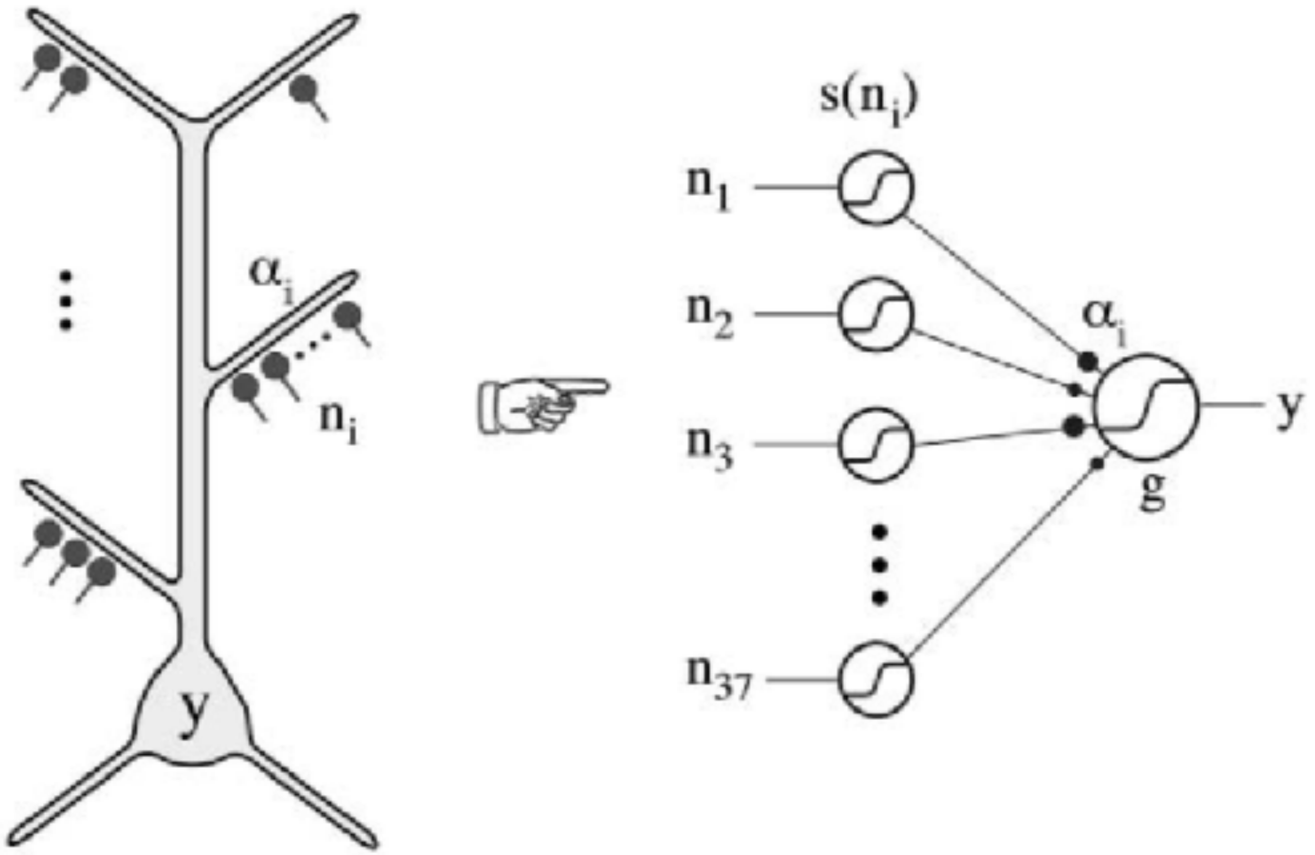
Somatic stim alone

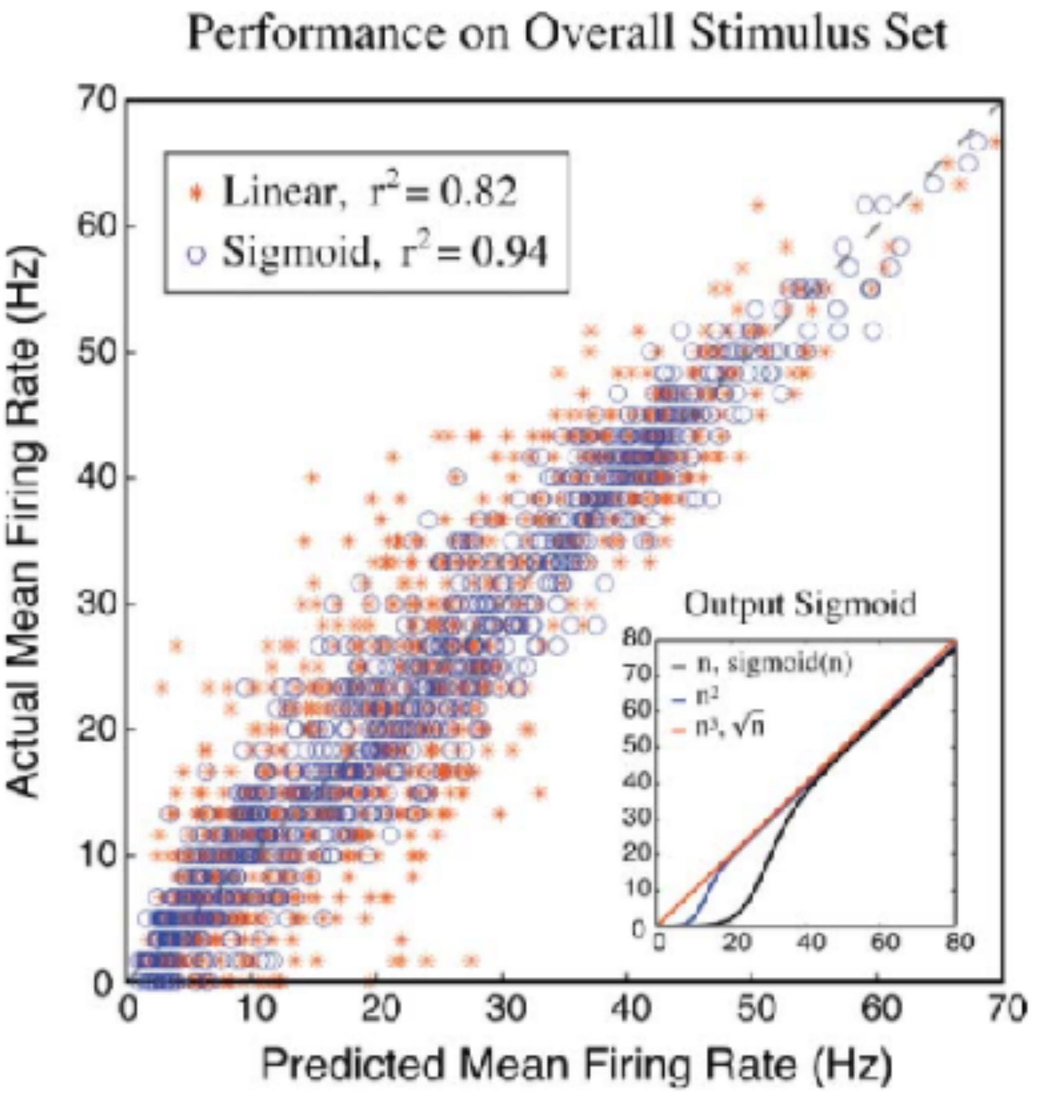
Weak distal + somatic stim

Strong distal stim alone

Larkum, Zhu and Sakmann, *Nature* (1999)

The single neuron as two-layer neural network

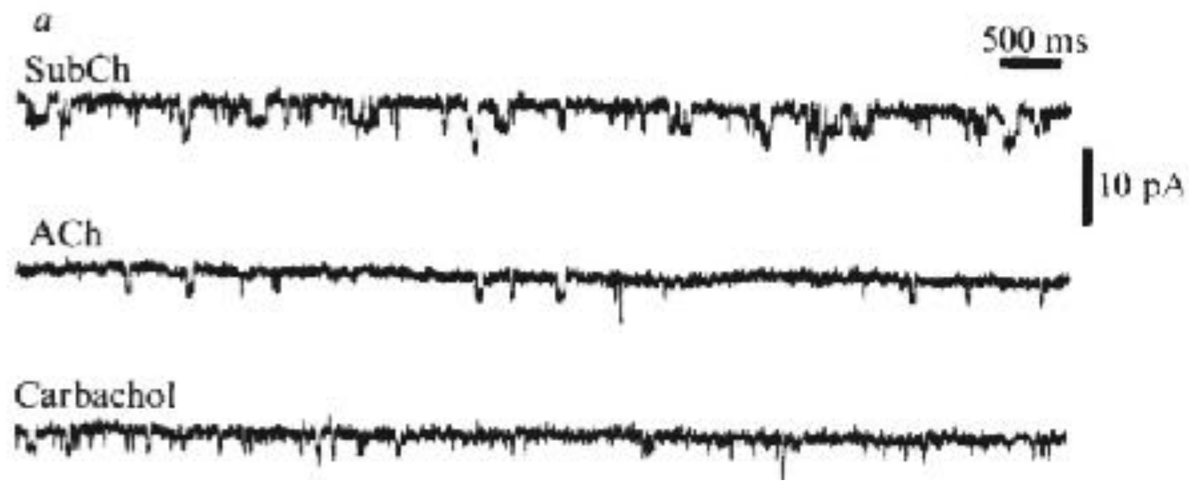




Poirazi and Mel, *Neuron* (2003)

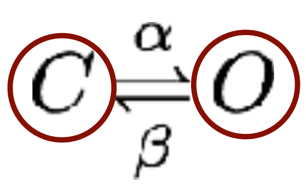
Stochasticity of ion channels

Ion channels are discrete and stochastic

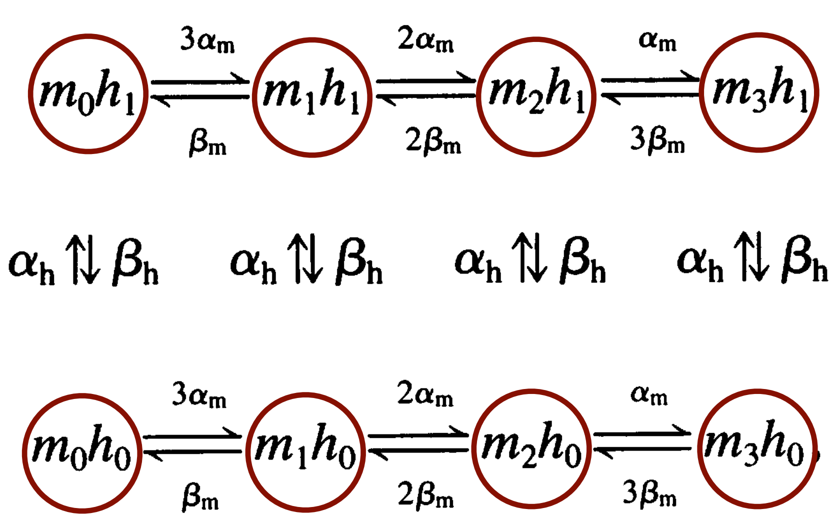


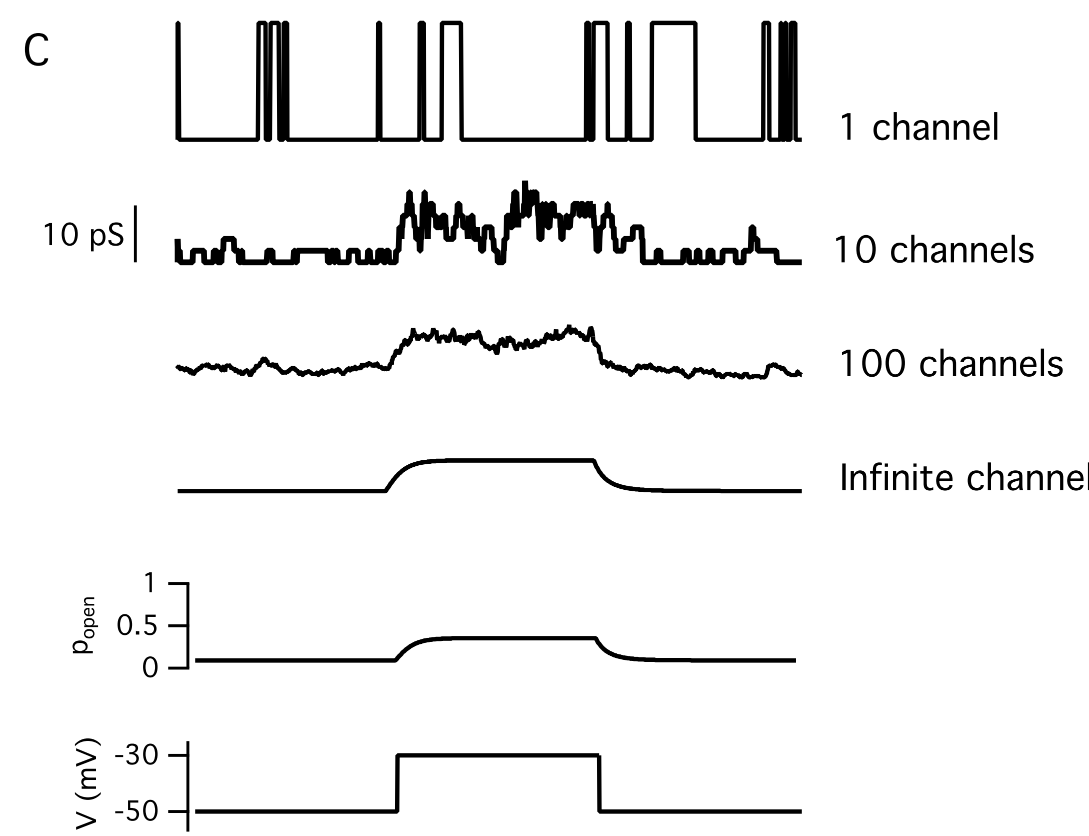
Neher & Sakmann, Nature (1976)

2-state:



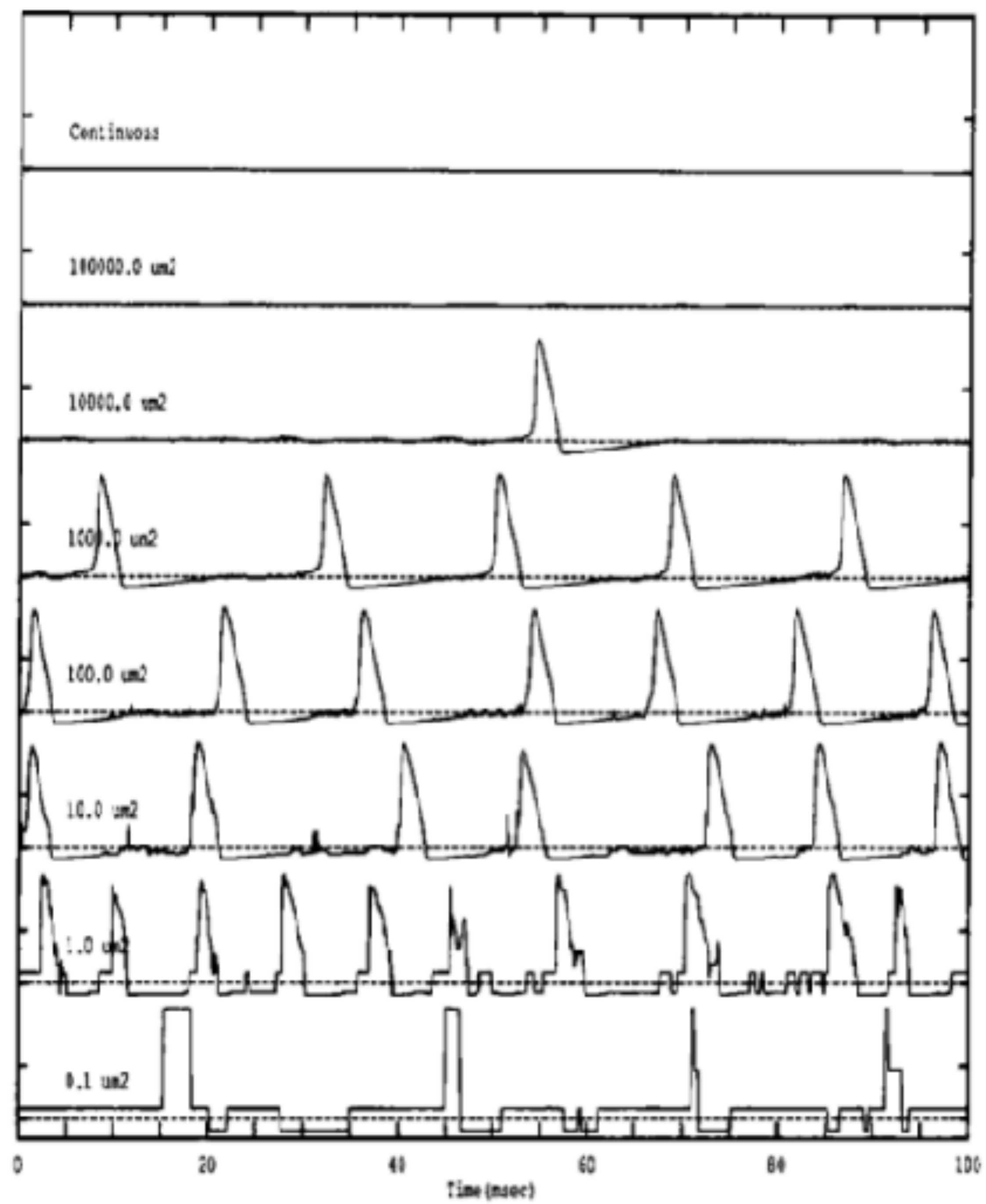
8-state:





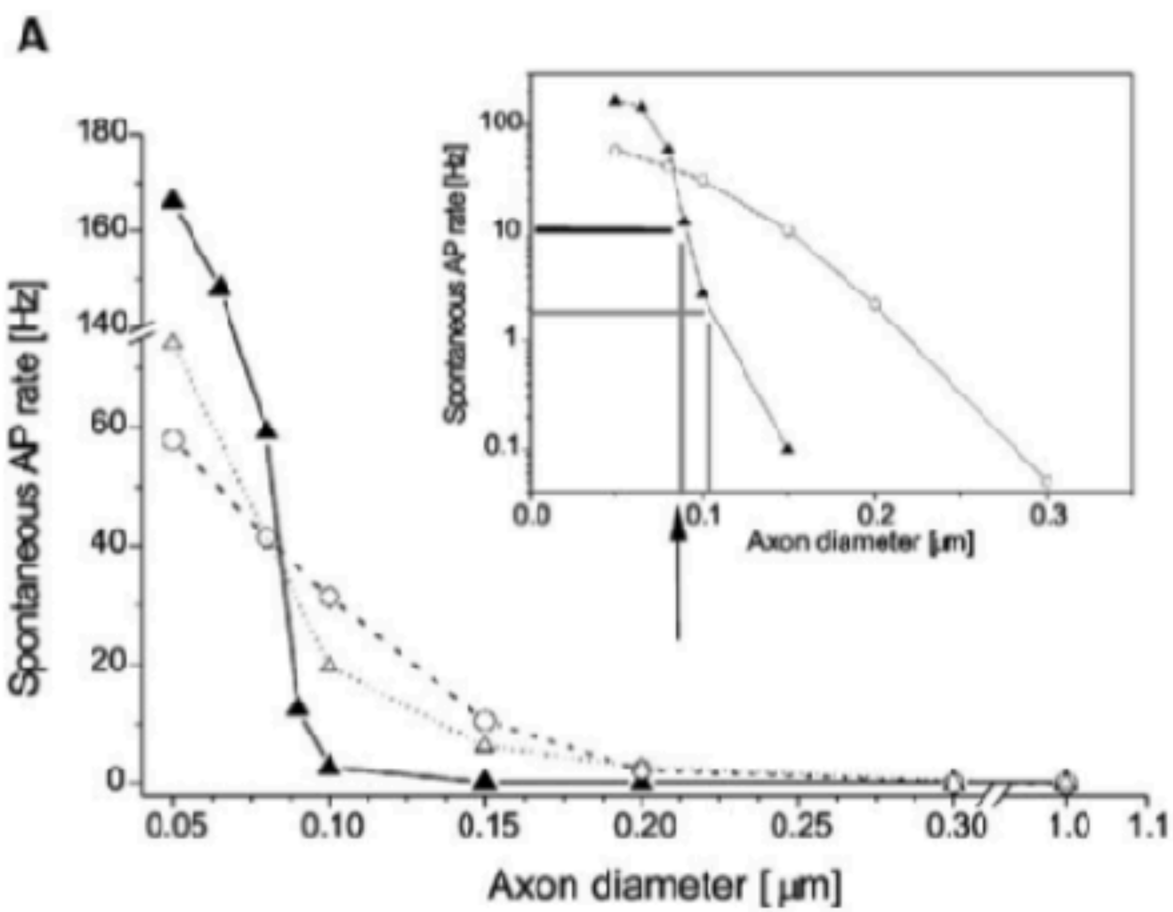
O'Donnell & Nolan (2014)

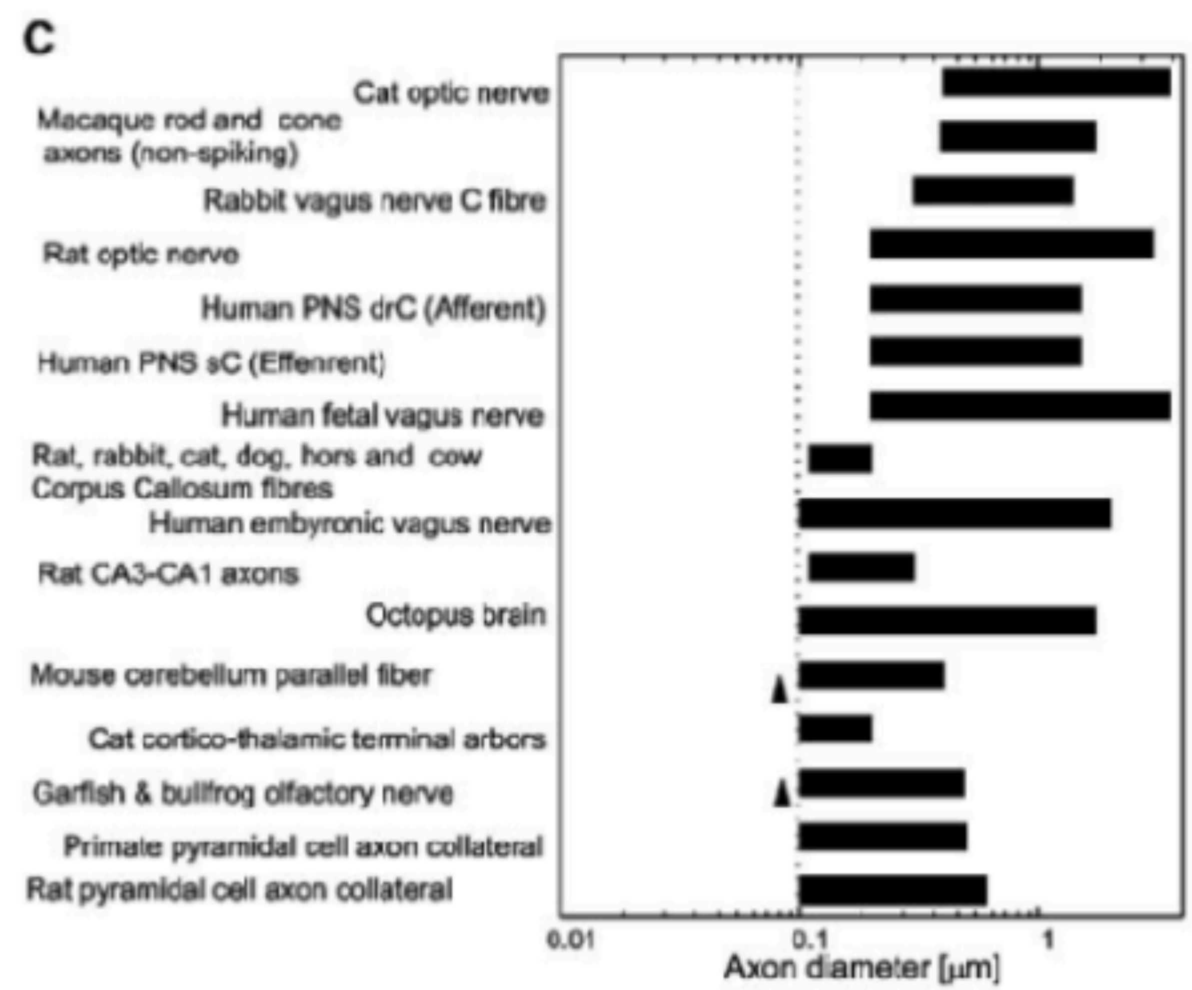
Spontaneous spikes from ion channel noise



Strassberg & DeFelice, *Neural Comput* (1993)

A lower limit on axon diameter due to ion channel noise





Faisal et al., *Curr Biol* (2005)

Further reading

- Scholarpedia article by Hille: http://www.scholarpedia.org/article/Ion_channels
- Spruston, Nelson. 2008. "Pyramidal Neurons: Dendritic Structure and Synaptic Integration." *Nature Reviews Neuroscience* 9 (3): 206–21