COMS30017
Computational Neuroscience

Week 3 / Video 2 / Ion channels and dendritic integration

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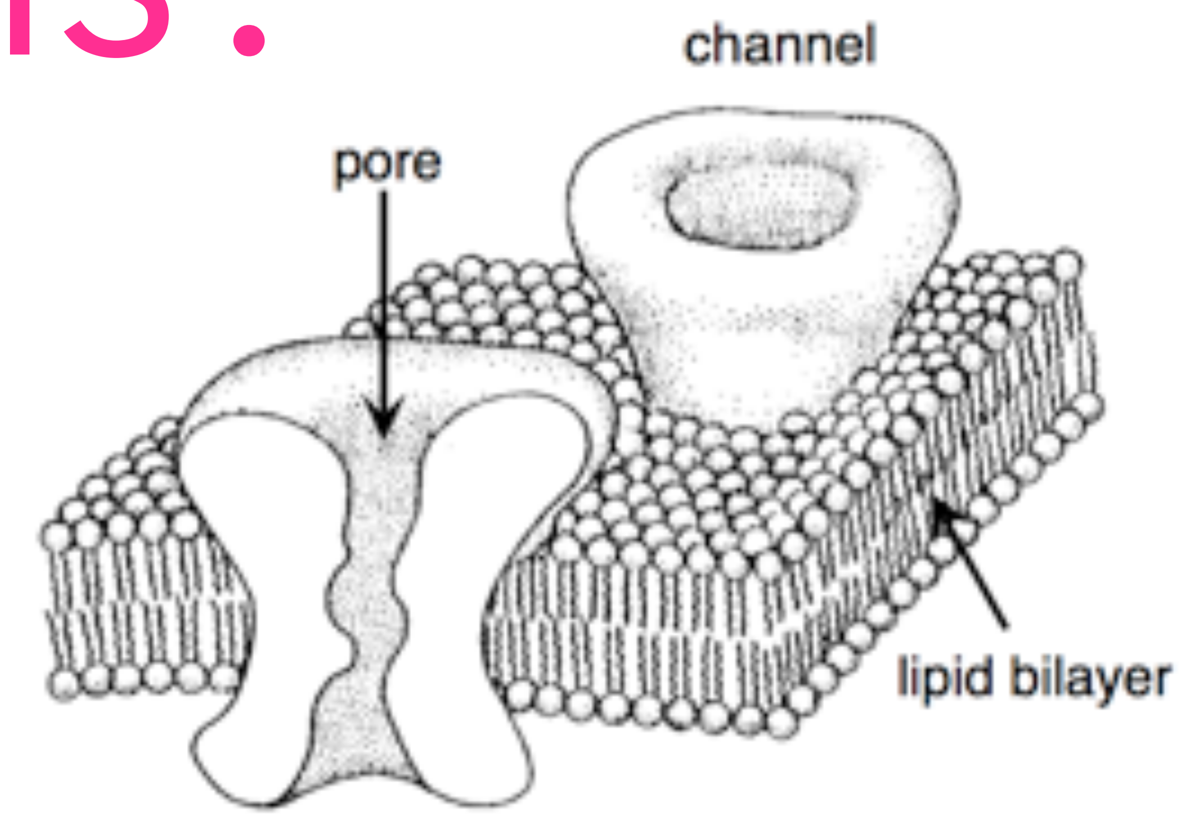
Intended learning outcomes

- Understand what ion channels are and what they do.
- Be able to write down a mathematical model of an ion channel current.
- Be able to explain how ion channels make the neuron's input-output function nonlinear.

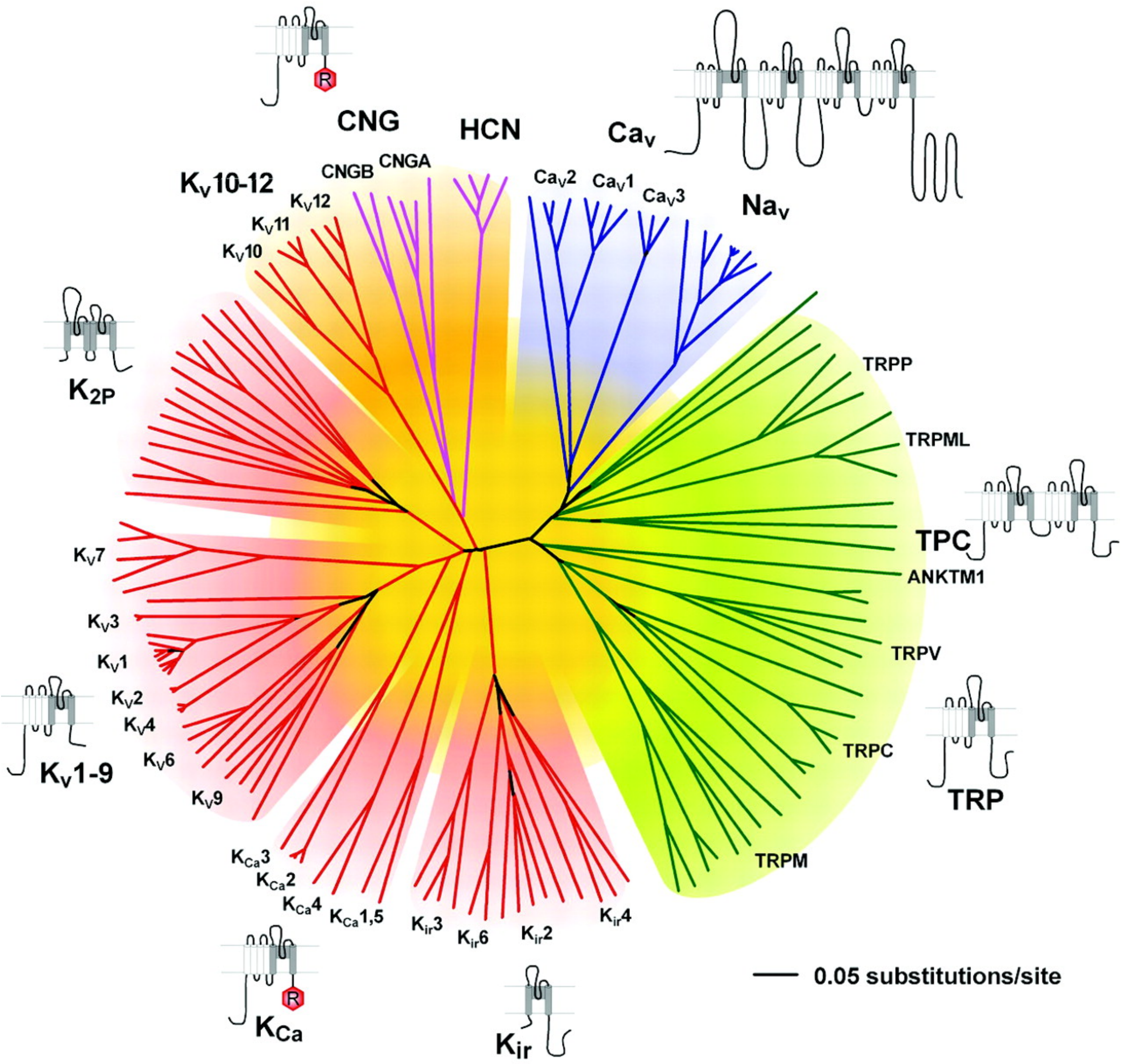
What are ion channels?



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.

The ion channel zoo



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

Ion channel types

- Sodium (Na^+) channels mediate inward currents that depolarise the voltage.
  - Fast gating and activated by depolarisation (positive feedback).
  - Responsible for upswing of the action potential, and boosting subthreshold inputs in dendrites.
  - Targets for some anaesthetics (e.g. lidocaine, pufferfish venom)
- Potassium (K^+) channels mediate outward currents that hyperpolarise the voltage.
  - Can be fast or slow gating, activated by depolarisation (negative feedback).
  - Voltage-independent K^+ channels mediate the 'leak' current.
  - Very genetically diverse (around 50 types in mammals).
- Calcium (Ca^{2+}) channels, like sodium, mediate inward currents that depolarise the voltage.
  - Fast gating, but not as strongly expressed as sodium so have weaker effect on the voltage.
  - Responsible for some forms of dendritic spikes.
  - Generate intracellular calcium signals that the cell uses to monitor its electrical activity.
- Other channels include
  - Chloride (Cl^-) channels: involved in setting resting voltage.
  - HCN channels: mixed sodium/potassium permeability, active at resting voltage, inactivated by depolarisation (negative feedback), heavily expressed in dendrites).

Modelling ion channels

Modelling ion channels

- In most neuroscience applications we don't care about all the molecular details of the ion channel, we just want a simple model that captures their dynamics.
- Usually this involves state-based modelling.
- We assume that each channel can be in one of a small number of of discrete states. The channel can transition between states, with transition rates that depend on the cell's voltage.

Modelling ion channels

Consider a 2-state ion channel model with transitions between the closed s_0 and open s_1 states, with transition rates α and β:

$$s_o \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} s_1$$

If we imagine a large population of such channels, we could think of s_1 as representing the proportion of the population in the open state.
Then we can write down a differential equation to describe its dynamics:

$$\frac{ds_1(t)}{dt} = \alpha s_o(t) - \beta s_1(t)$$

The steady state value s_∞ is found by setting $\frac{ds_1}{dt} = 0$, so $s_\infty = \frac{\alpha}{\alpha + \beta}$

Then we can rewrite the right hand side of the dynamics equations as

$$\frac{ds_1(t)}{dt} = \frac{s_\infty - s_1(t)}{\tau}$$

Where we have introduced the time constant $\tau = 1/(\alpha + \beta)$

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Modelling ion channels

The electrical current flowing through a large population of such channels is

$$I(t) = s_1(t)\bar{g}(V(t) - E_{rev})$$

Total current

Fraction of channels open
(time-varying)

Maximum conductance

Voltage
(time-varying)

Reversal potential

Modelling ion channels

- This was a very simple 2-state channel example. Most real channels are too complicated to describe so compactly, so their models often have many more states.
- The voltage dependence is built into these channel models by making the the transitions rate (α and β) functions of voltage.
- We will go through a famous example of the this in the next video: the Hodgkin-Huxley squid axon model.
- You can find lots of example computational models of ion channel types in several good online repositories:
  - ModelDB: https://senselab.med.yale.edu/modeldb/
  - Channelpedia: https://channelpedia.epfl.ch
  - ICGenealogy: https://icg.neurotheory.ox.ac.uk

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.

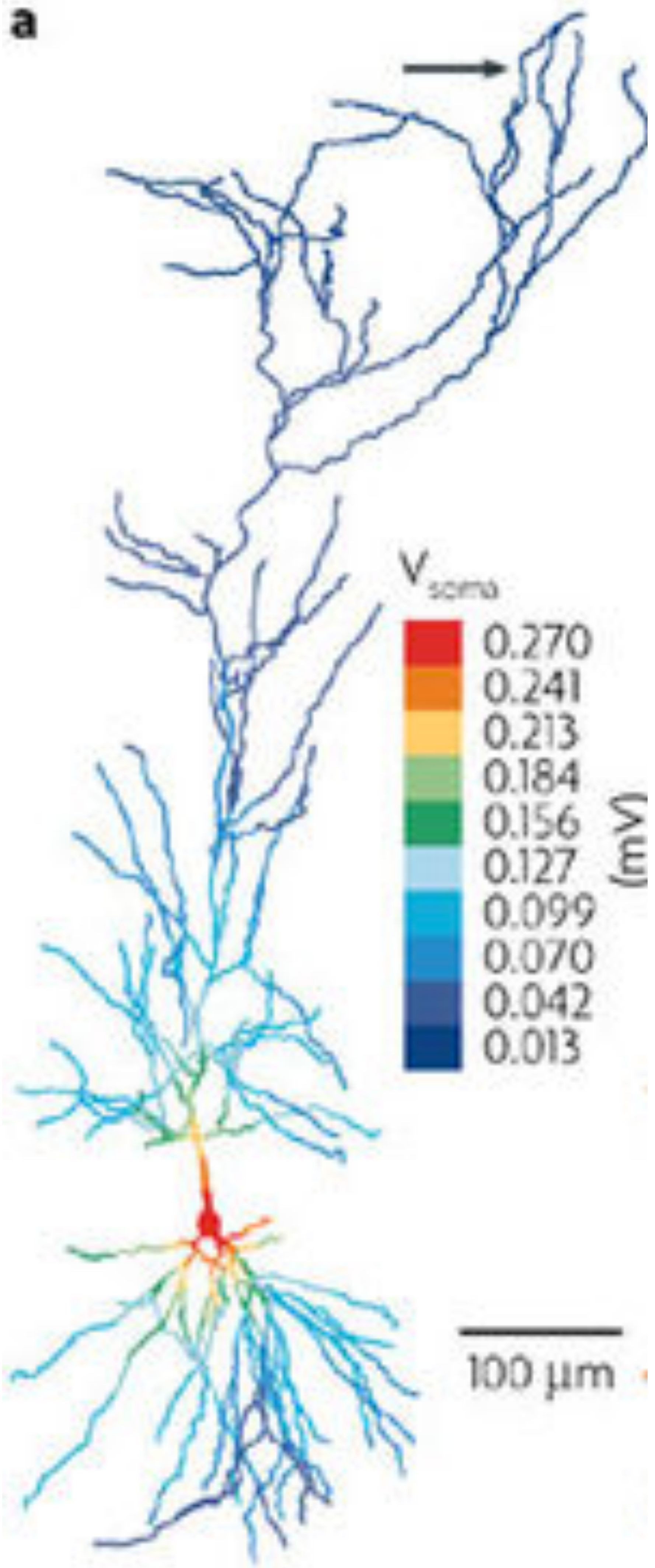
- "Point" neuron models (like the integrate-and-fire) assume that the soma performs a weighted linear sum of the synaptic currents.

- 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

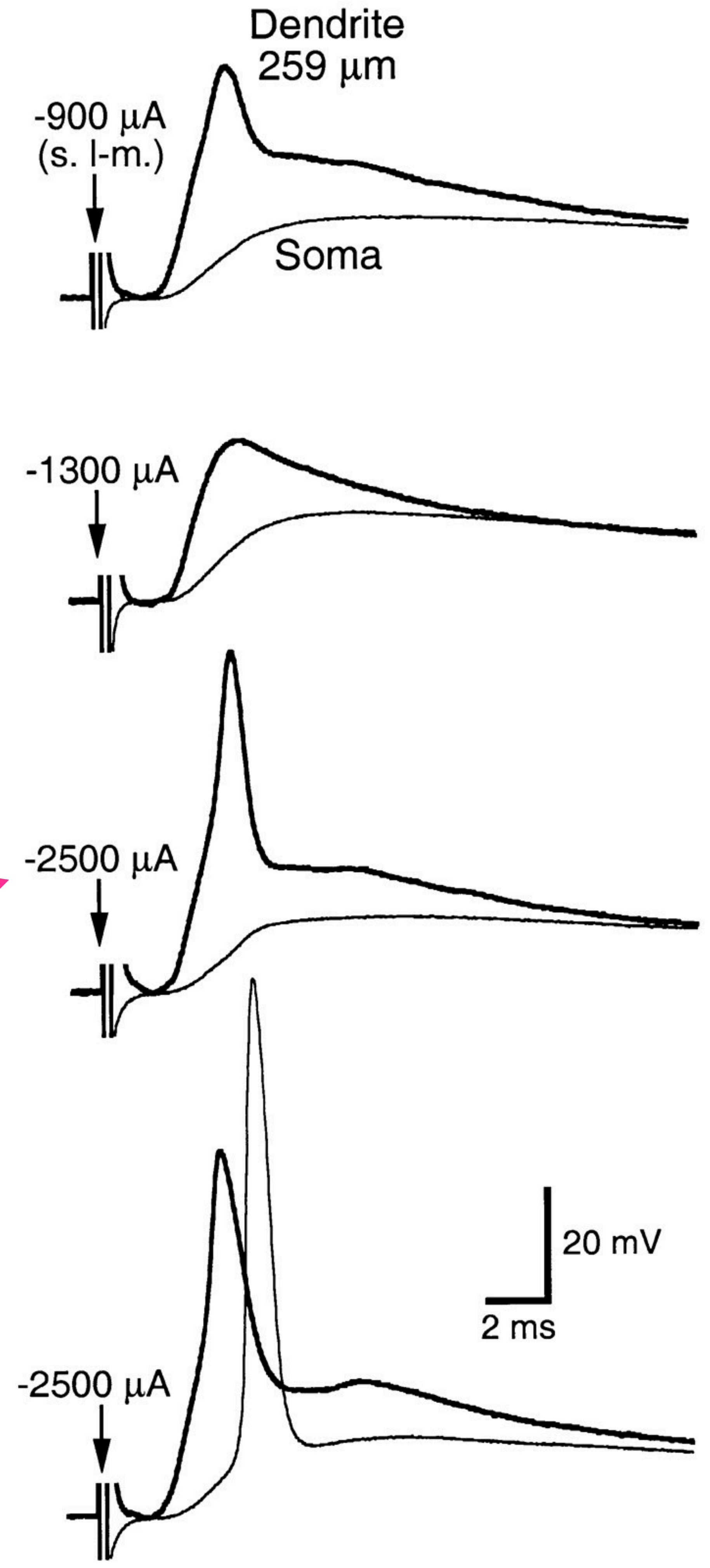
- The figure on the right is a trace of the dendritic tree of a CA1 pyramidal cell from a rat.
- The colour indicates the amplitude of the voltage response (EPSP) at the soma, when the synapse is placed at the corresponding location on the dendritic tree.
- Without any "boosting", a synapse would give a smaller somatic response if it was located at a distal dendritic site.
- However it turns out that voltage-dependent ion channels in dendrites can boost synaptic inputs to amplify their effect at the soma.



Spruston, *Nat Rev Neurosci* (2008)

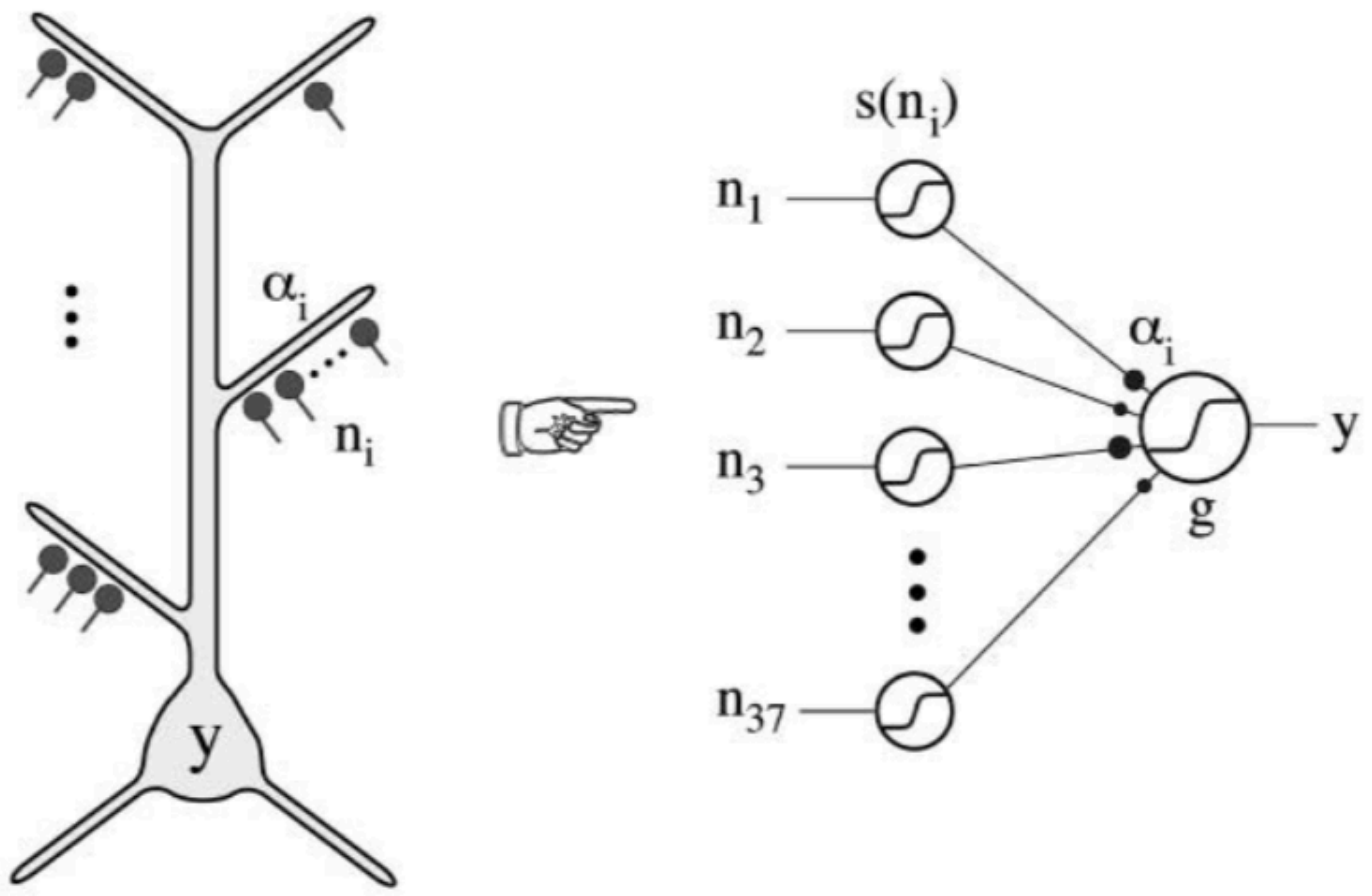
Dendritic spikes

- Some neurons have enough voltage-gated ion channels in their dendrites to enable purely dendritically-generated action potentials.
- These dendritic spikes tend to be weaker and less all-or-none that axonal action potentials (note variable dendritic amplitudes in each plot on right).
- A single dendritic spike is not always sufficient to trigger an axonal spike.



Golding and Spruston, *Neuron* (1998)

The single neuron as two-layer neural network



- The existence of dendritic spikes means we can almost think of a single pyramidal neuron as a multi-layer neural network. Each dendritic does a nonlinear operation on its inputs before passing the signal to the soma.
- Voltage-gated ion channels expand the brain's computational power.

Poirazi and Mel, *Neuron* (2003)

Summary

- Ion channels are protein complexes that let electrical current flow in and out of the neuron.
- They mediate neurons' electrical dynamics.
- Kinetic models of neurons are commonly described using ODEs.
- Ion channels' voltage dependence makes the neuron's input-output function highly non-linear.
- Single neurons can in principle approximate a 2-layer artificial neural network.