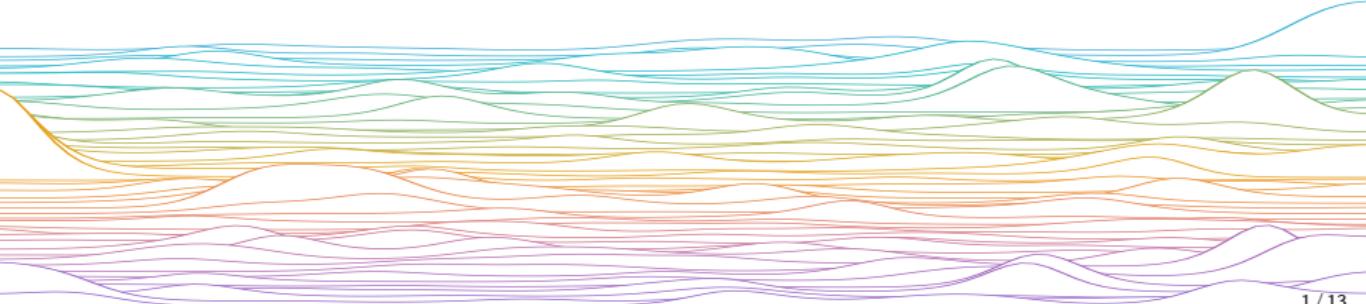


Ions

Computational Neuroscience
University of Bristol
Adapted from C O'Donnell's slides
M Rule

Learning outcomes:

- ▶ Understand what ion channels are and what they do
- ▶ Write down a mathematical model of an ion channel current
- ▶ Explain how ion channels make the neuron's input-output function nonlinear



Modelling Scales

... Quantum Chemistry, Molecular dynamics

Physiological,
Quantitative

Biological
Realism,
Data needed
to identify
parameters



Molecules	Gillespie, Master Equation
Concentrations	Mass-Action Kinetics
Conductance Models	Hodgkin–Huxley
Spiking Models	Leaky Integrate and Fire
Rate Neurons	Neural Mass/Field Models
Poisson Neurons	Generalized Linear Models
Binary Neurons	McCulloch–Pitts, Hopfield, Perceptron



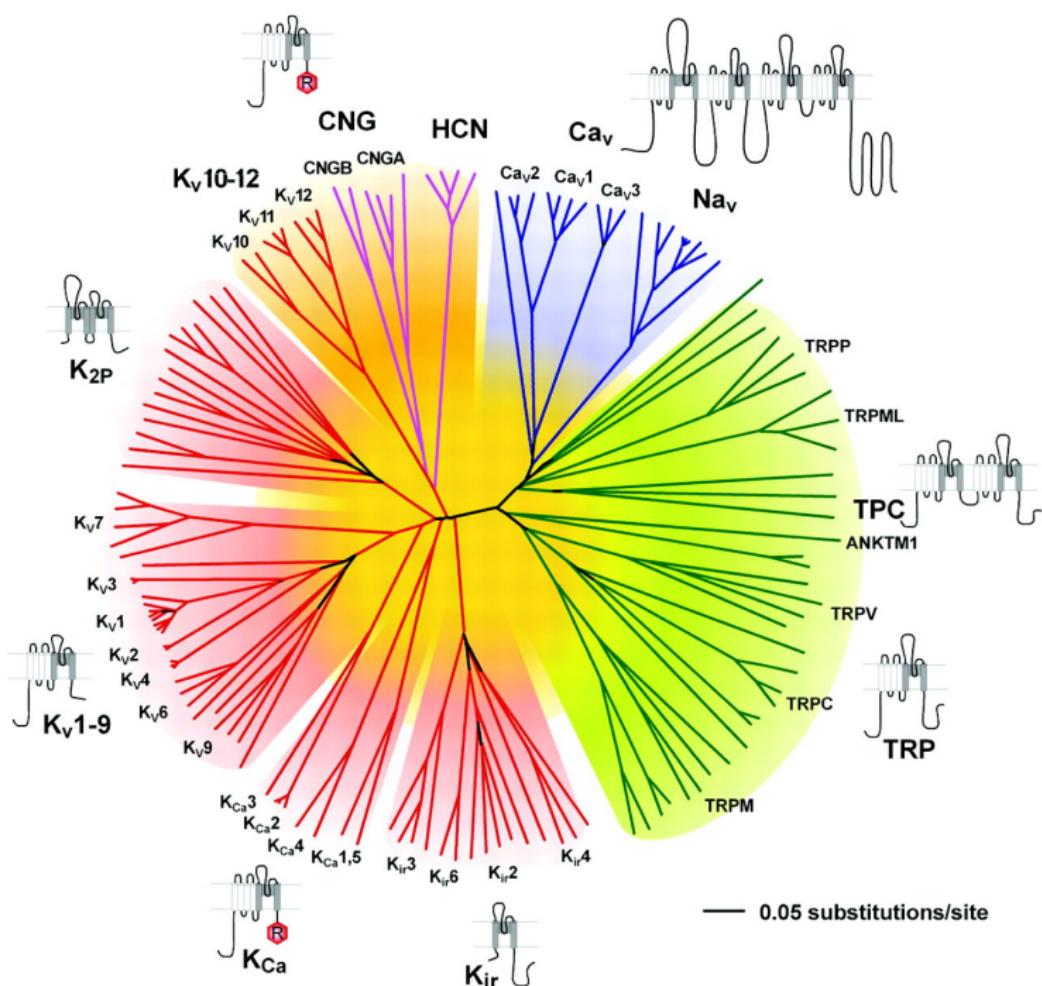
Computational
Efficiency,
Mathematical
Tractability

Phenomenological,
Qualitative

Cognitive Neuroscience, Psychology ...

What are ion channels?

- ▶ 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. Hille (1992)
- ▶ 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.



Ion channel types

Sodium (Na^+) channels mediate inward currents that depolarise the voltage.

- ▶ Fast gating, 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^+)

- ▶ Outward flux of + ions: lowers membrane volates
- ▶ 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+}) inward current of positive ions 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

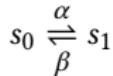
- ▶ Chloride (Cl^-) channels: involved in setting resting voltage.
- ▶ HCN channels: mixed Na^+/K^+ I_h current

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 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 .



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:

$$\dot{s}_1(t) = \alpha s_0(t) - \beta s_1(t)$$

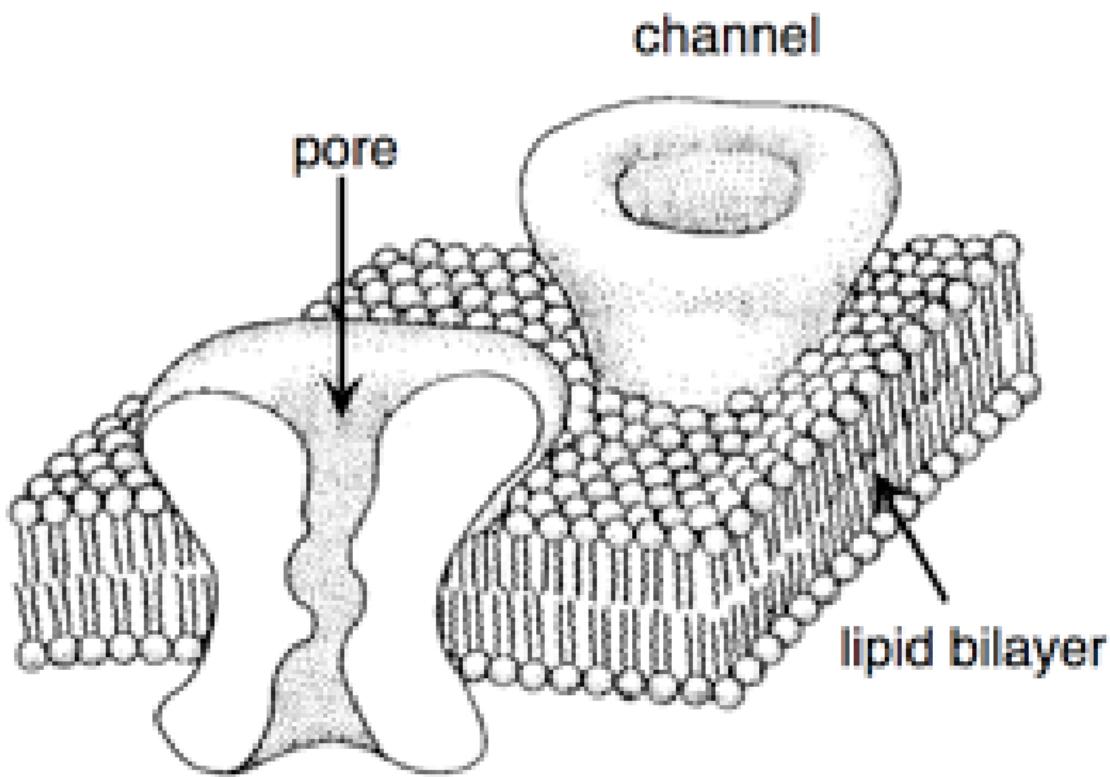
The steady state value s_∞ is found by setting $\dot{s}_1 = 0$, so

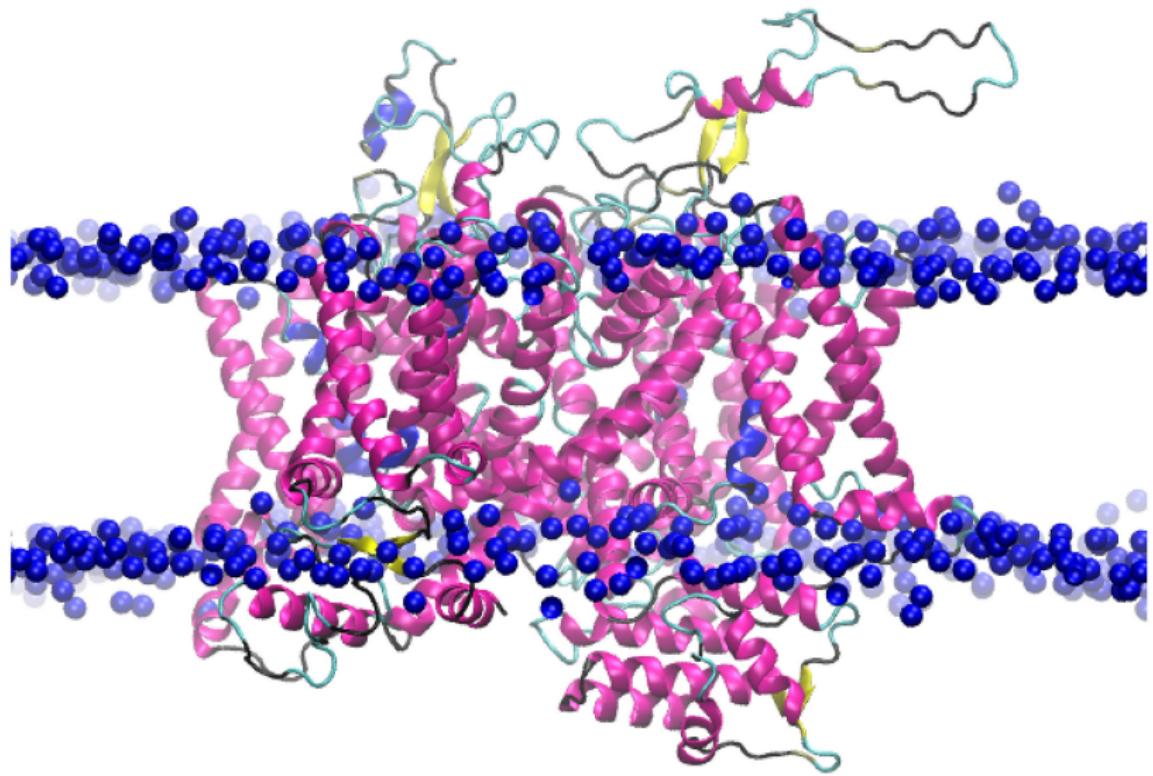
$$s_\infty = \frac{\alpha}{\alpha + \beta}$$

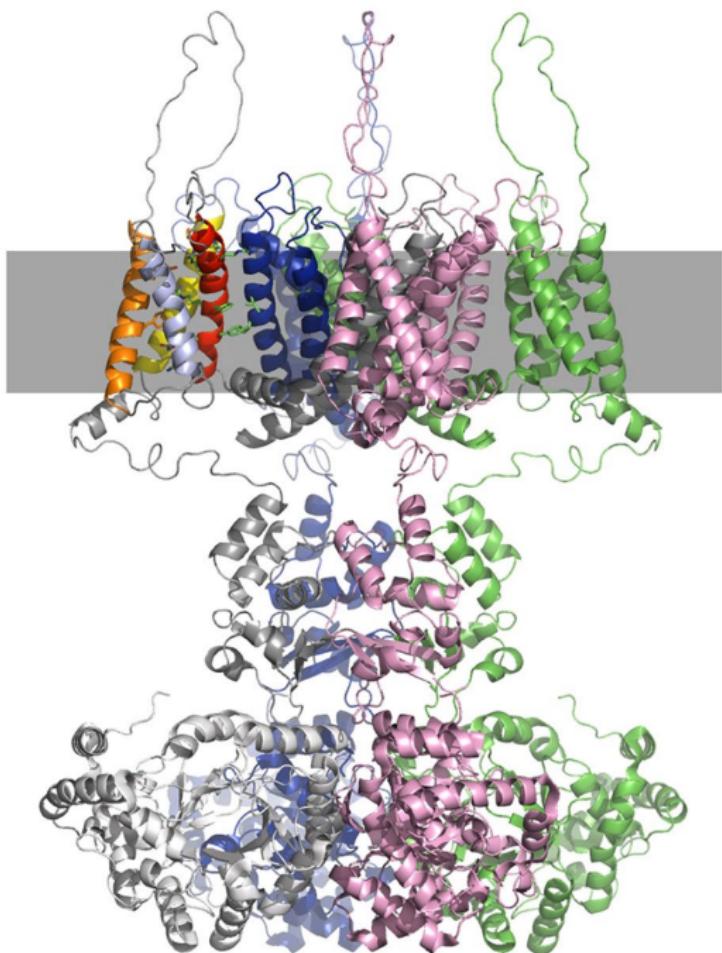
Then we can rewrite the right hand side of the dynamics equations as

$$\dot{s}(t) = \frac{s_\infty - s_1(t)}{\tau}$$

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







Modelling ion channels

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

$$I(t) = \bar{g} \cdot s(t) \cdot [E_{\text{rev}} - v(t)]$$

I am using the electrical engineering and physics current convention here. In electrophysiology the RHS will actually be the negative current. This is a historical artefact related to Hodgkin and Huxley's experimental setup and how they chose current direction conventions in nodal analysis. Hodgkin and Huxley used a voltage-clamp experimental setup where an amplifier in negative feedback supplied current to cancel the synaptic current, holding the cell at a fixed voltage. They measured the output of the amplifier, hence the change in sign convention.

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 transitions rate (α , β) functions of voltage.

We will go through a famous example of 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](#)

[Channelpedia](#)

[ICGenealogy](#)

end