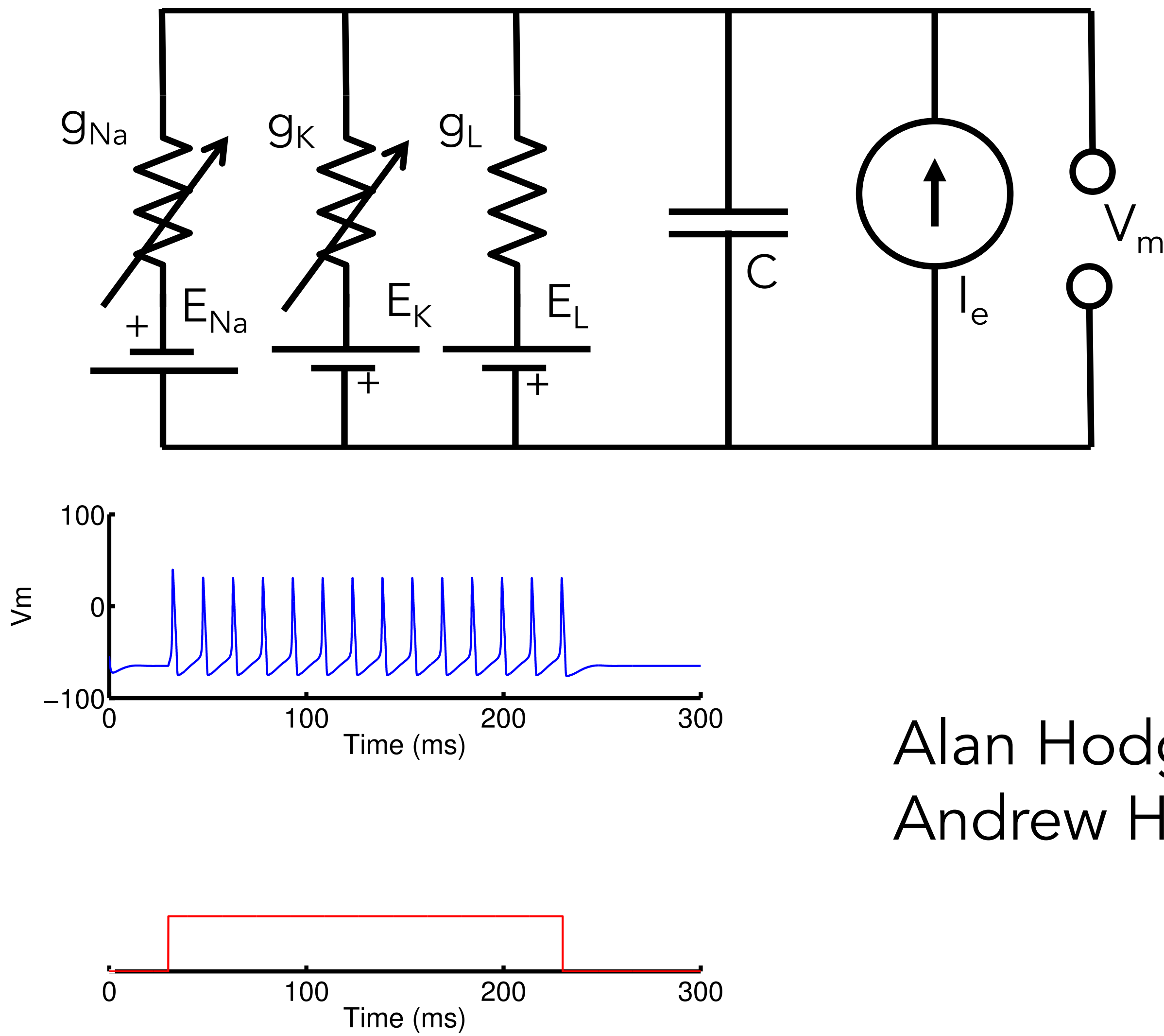
Introduction to Neural Computation

Michale Fee
MIT BCS 9.40 — 2018
Video Module on Nernst Potential
Part 1

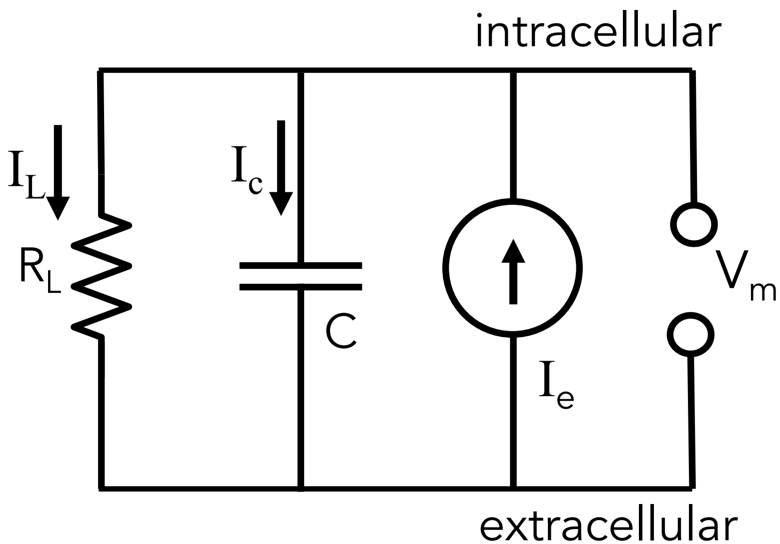
A mathematical model of a neuron

- Equivalent circuit model



Alan Hodgkin
Andrew Huxley, 1952

A neuron is a leaky capacitor



I_c = membrane capacitive current

I_L = membrane ionic current

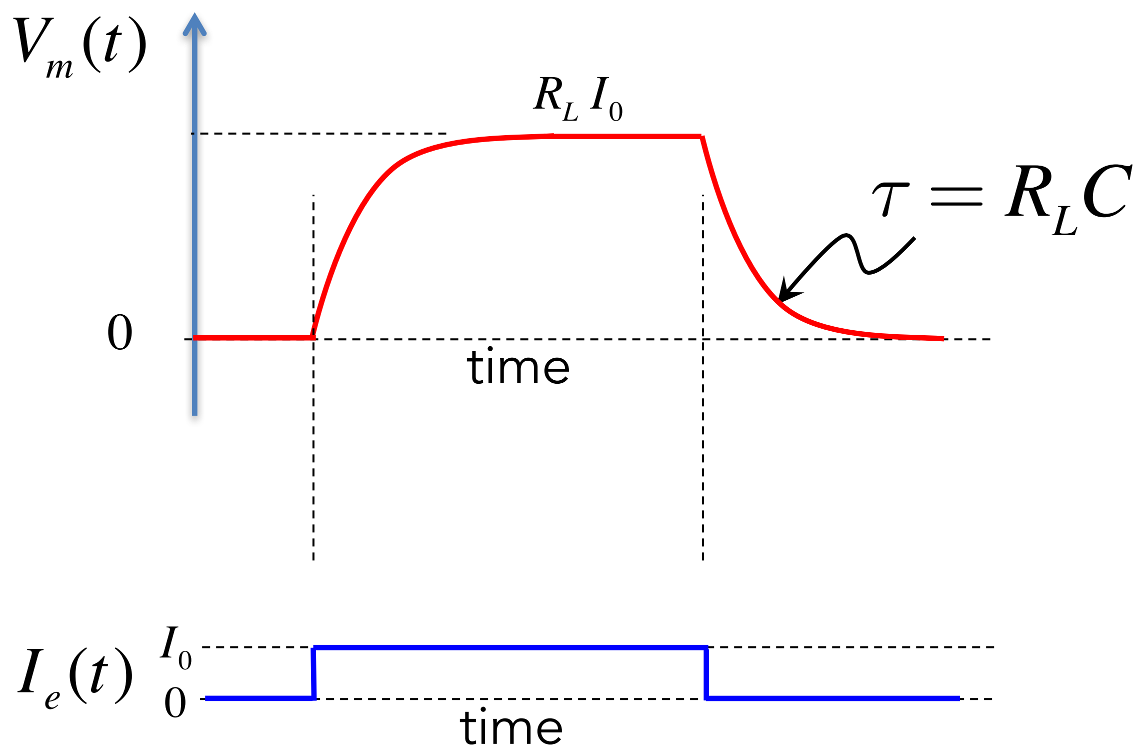
$$V_m + \tau \frac{dV_m}{dt} = V_\infty$$

where $\tau = R_L C$

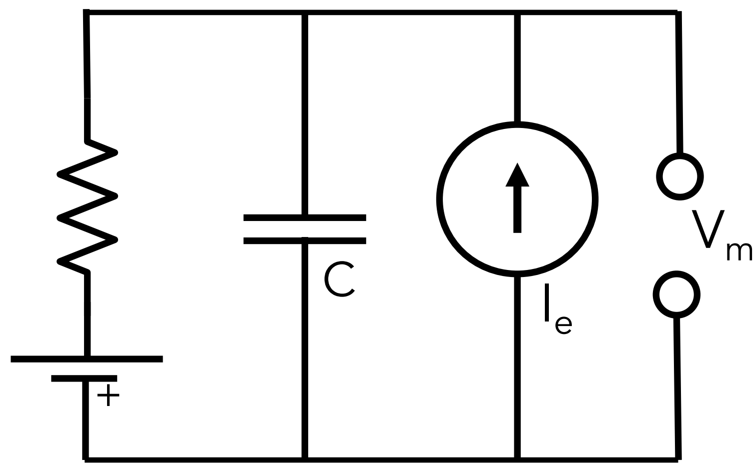
$$V_\infty(t) = R_L\, I_e(t)$$

Response to current injection

Let's see what happens when we inject current into our model neuron with a leak conductance.

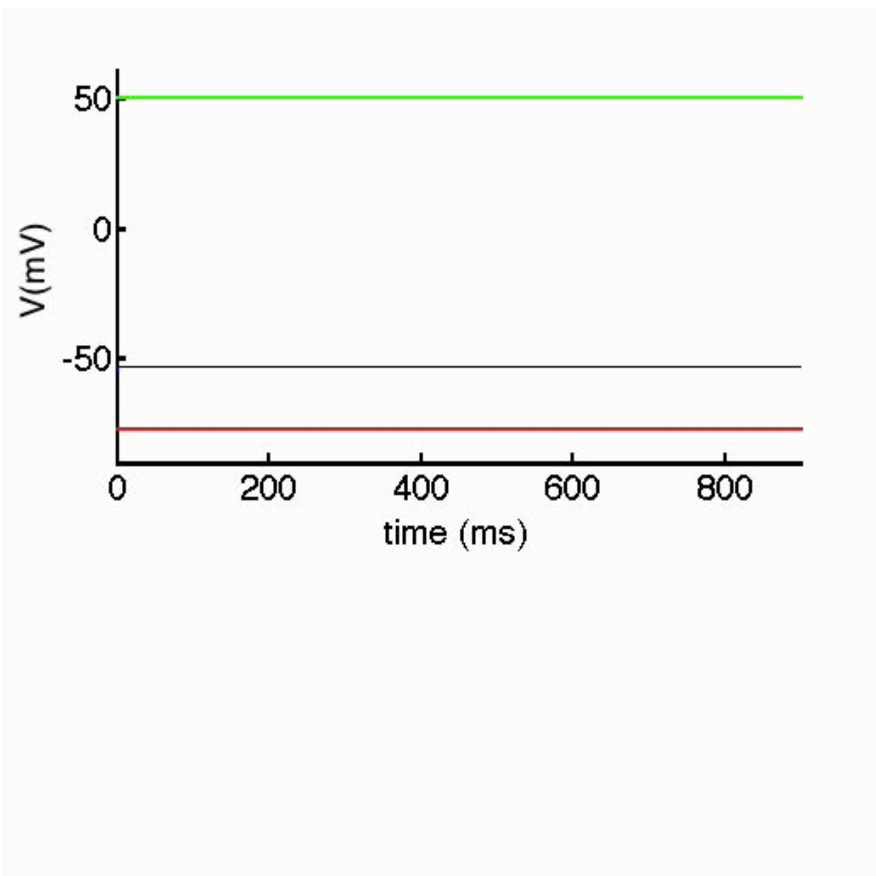


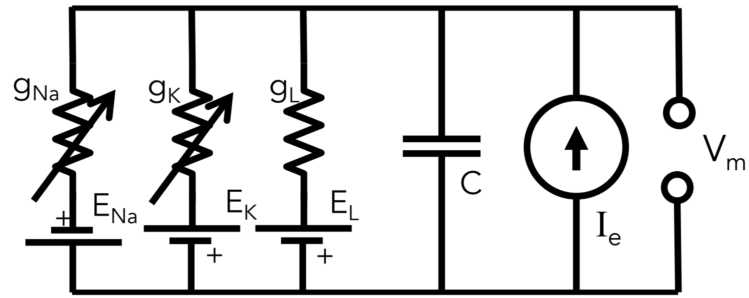
A neuron is a leaky capacitor



Outline of HH model

Voltage and time-dependent ion channels are the ‘knobs’ that control membrane potential.



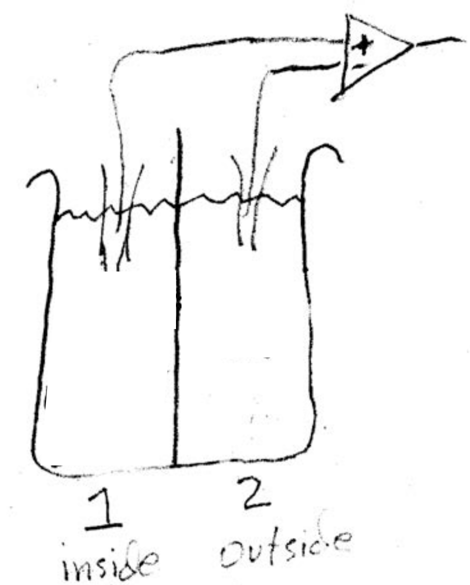


- Some ion channels push the membrane potential positive.
- Other ion channels push the membrane potential negative.
- Together these channels give the neural machinery flexible control of voltage!

Where do the batteries of a neuron come from?

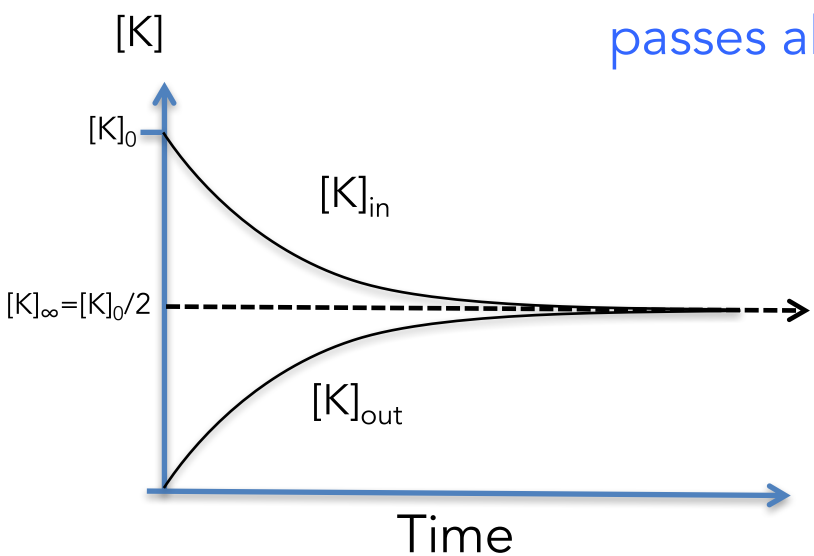
1) Ion concentration gradients

2) Ion-selective permeability of ion channels

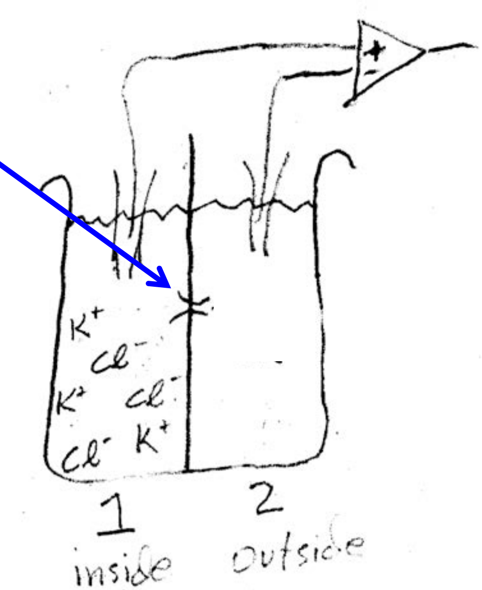


Neurons have batteries

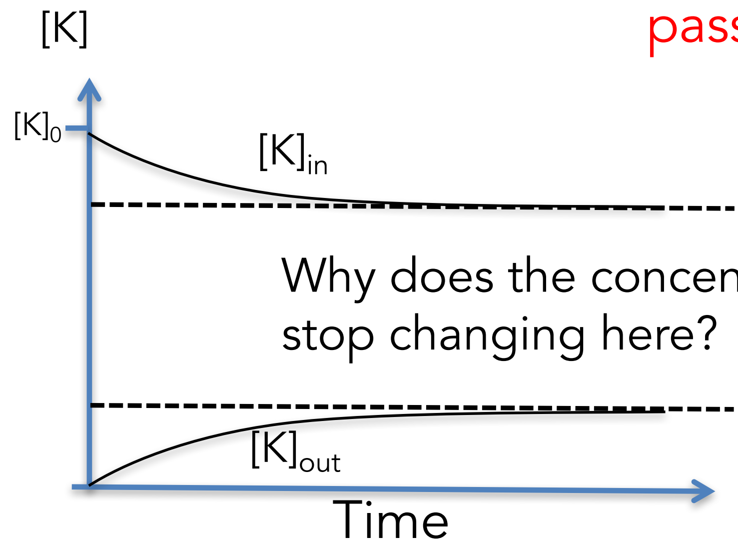
‘Non-selective’ pore
passes all ions



(a long time)

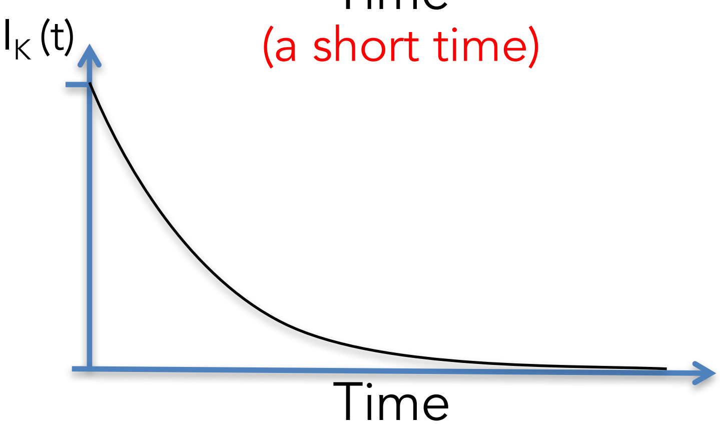


Neurons have batteries

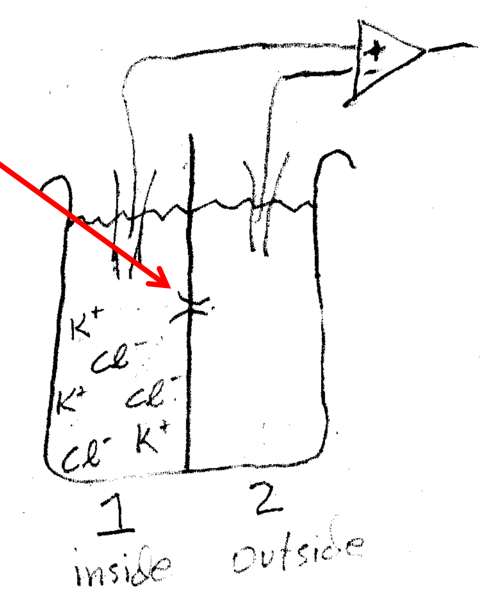


Why does the concentration stop changing here?

(a short time)

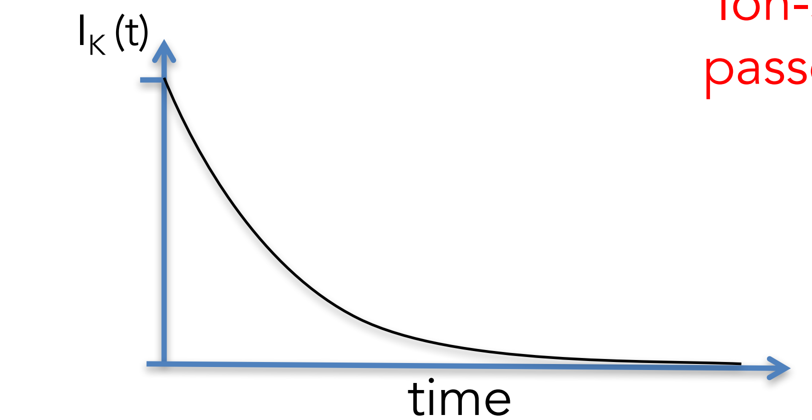


'Ion-selective' pore passes only K^+ ions

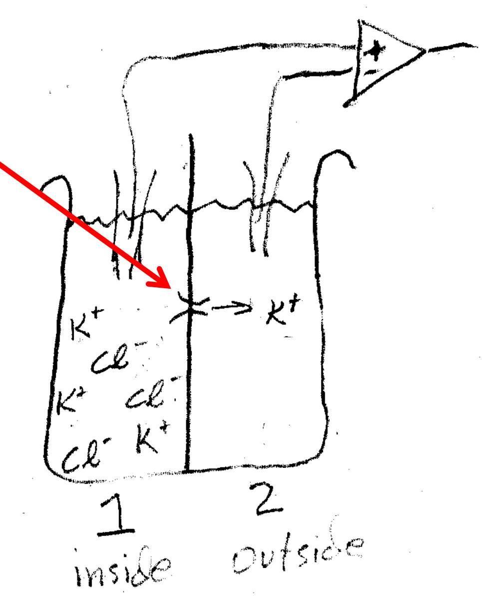


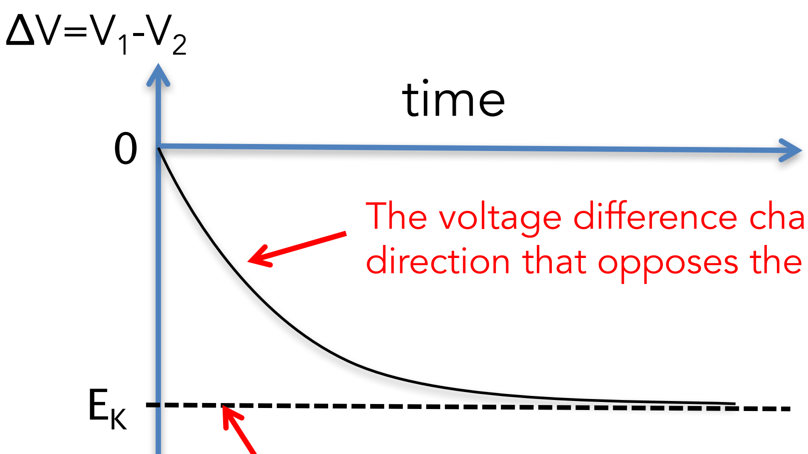
Why do the ions stop flowing from side 1 to side 2?

Neurons have batteries



'Ion-selective' pore
passes only K^+ ions



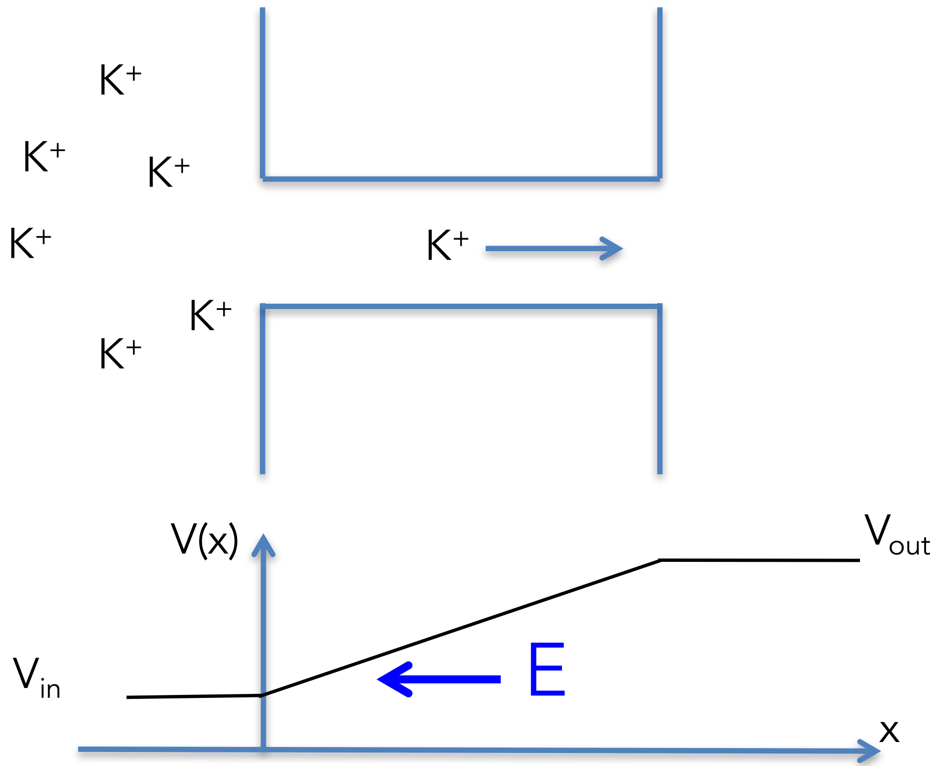


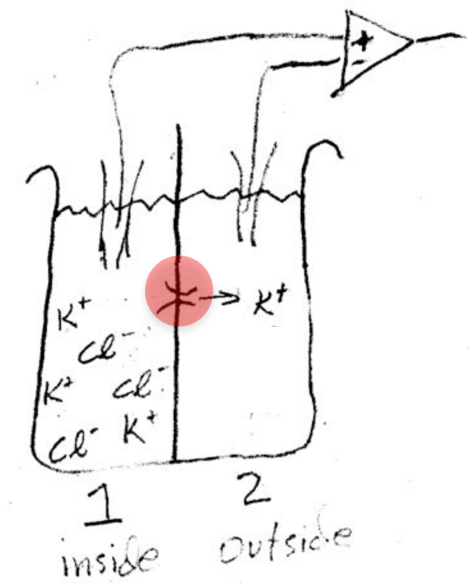
The voltage difference changes in a direction that opposes the flow of ions.

It reaches an 'equilibrium potential' at a value that gives zero net flow of ionic current.

This voltage difference is a battery for our model neuron!!

Neurons have batteries





There will be some electric field strength such that the 'drift' will exactly balance the diffusion produced by the concentration gradient…

Nernst Potential

Neurons have batteries

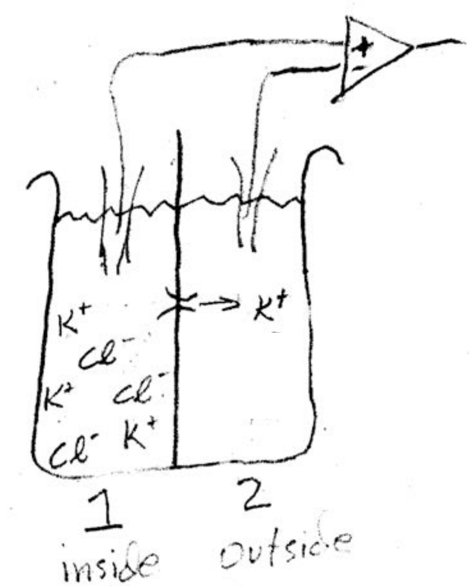
- Where do the 'batteries' of a neuron come from?

    1) Ion concentration gradients

    2) Ion-selective pores (channels)

- How big is the battery (how many volts?)

    This is determined by a balance between diffusion down a concentration gradient balanced by 'drift' in the opposing electric field.



Electrodiffusion and the Nernst Potential

One can use Ohm's law and Fick's first law to derive the Nernst potential

— At this voltage, the drift current in the electric field exactly balances current due to diffusion

$$I_{Tot} = I_{Drift} + I_{Diffusion} = 0$$

Ohm's Law

$$I_{Drift} = \frac{Aq^2\varphi(x)D}{kT}\frac{\Delta V}{L}$$

Fick's First Law

$$I_{Diffusion} = -AqD\frac{\partial \varphi}{\partial x}$$

$$\Delta V = \frac{kT}{q}\ln\left(\frac{\varphi_{out}}{\varphi_{in}}\right)$$ at equilibrium

Derive Nernst potential using the Boltzmann equation

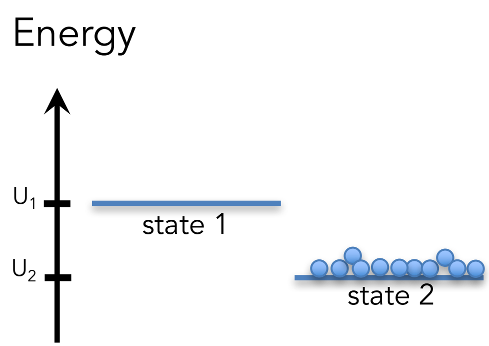
The Boltzmann equation describes the ratio of probabilities of a particle being in any two states, at thermal equilibrium:

$$\frac{P_{state1}}{P_{state2}} = e^{-\left(\frac{U_1 - U_2}{kT}\right)}$$

$k =$ Boltzmann constant (J/K)

$T =$ temperature (K) = 273 + T_C

$kT =$ thermal energy (J)



$kT = 0$

$$\frac{P_{state1}}{P_{state2}} = 0$$

Derive Nernst potential using the Boltzmann equation

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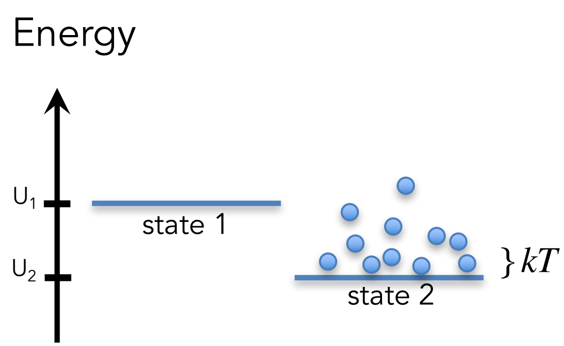

$$kT > 0$$

$$\frac{P_{state1}}{P_{state2}} > 0$$

Derive Nernst potential using the Boltzmann equation

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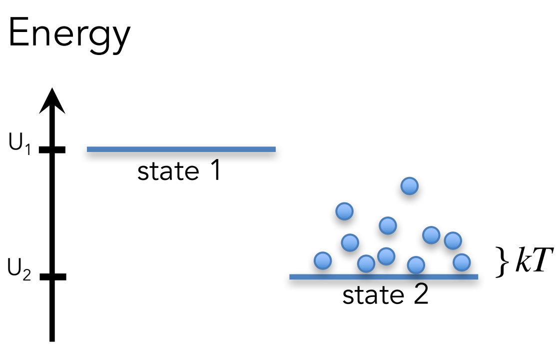
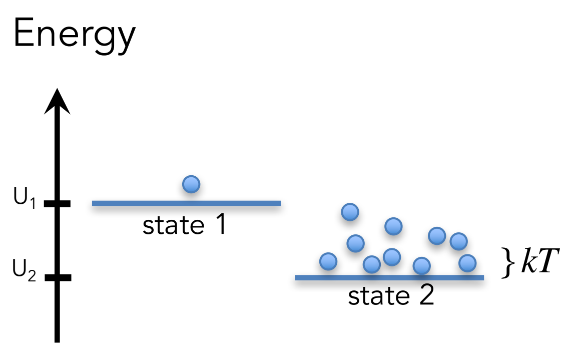


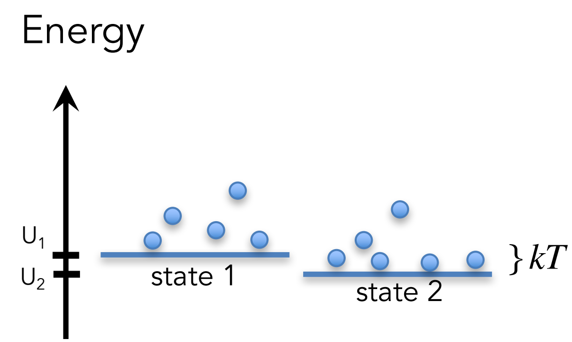
$$\Delta U >> kT$$

$$\frac{P_{state1}}{P_{state2}} \approx 0$$



$$\Delta U = 2kT$$

$$\frac{P_{state1}}{P_{state2}} = e^{-2}$$



$$\Delta U < kT$$

$$\frac{P_{state1}}{P_{state2}} \approx 1.0$$

Nernst Potential

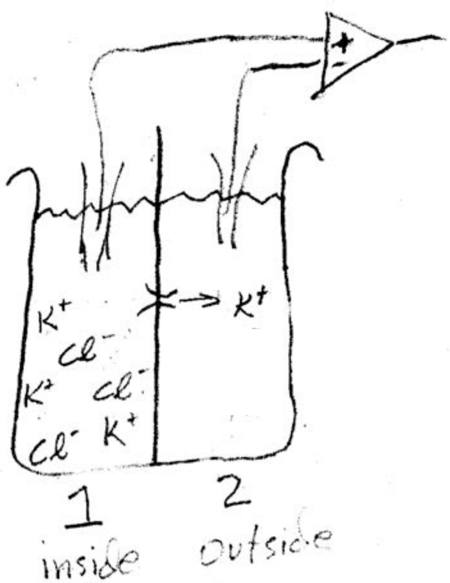
We can compute the equilibrium potential using the Boltzmann equation:

$$\frac{P_{in}}{P_{out}} = e^{-\frac{U_{in}-U_{out}}{kT}} = e^{-\frac{q(V_{in}-V_{out})}{kT}}$$

$U = qV$ = electrical potential (J)

q = charge of ion

$q = 1.6\text{x}10^{-19}$C for monovalent ion



Nernst Potential

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$U = qV =$ electrical potential (J)

$q =$ charge of ion

$q =$ $1.6\text{x}10^{-19}$C for monovalent ion

$$V_{in} - V_{out} = -\frac{kT}{q}\ln\left(\frac{P_{in}}{P_{out}}\right)$$

$$\frac{kT}{q} = 25mV \text{ for monovalent ion}$$

$$\Delta V = V_{in} - V_{out} = 25mV \ln\left(\frac{P_{out}}{P_{in}}\right)$$

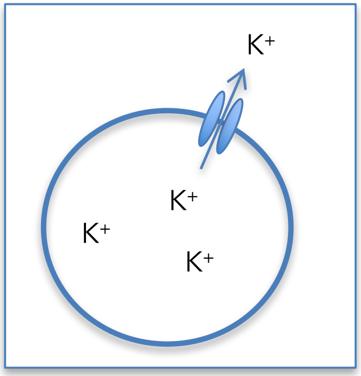
$$\Delta V = 25mV \ln\left(\frac{[K]_{out}}{[K]_{in}}\right) = E_K$$

Don't get confused by this notation. E_K is the equilibrium potential (voltage) for the K ion. 'E' here does not refer to an electric field.

The Nernst potential for potassium

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75

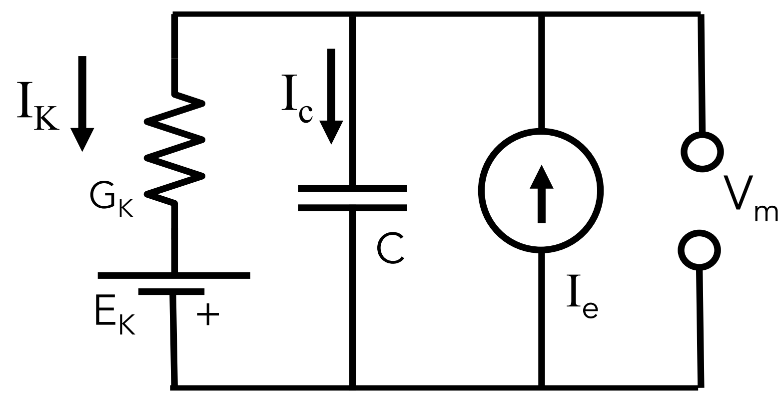


$$E_k = \frac{kT}{q}\ln\left(\frac{20}{400}\right)$$

$\frac{kT}{q}$ = 25mV at 300K (room temp) for monovalent ion

$$E_K = 25mV(-3.00) = -75mV$$

How to implement an ion specific conductance as a battery in our model neuron



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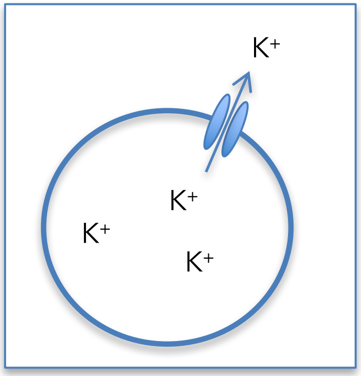
Video Module on Nernst Potential
Part 2

The Nernst potential for potassium

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75



$$\Delta V = \frac{kT}{q}\ln\left(\frac{[K]_{out}}{[K]_{in}}\right)$$

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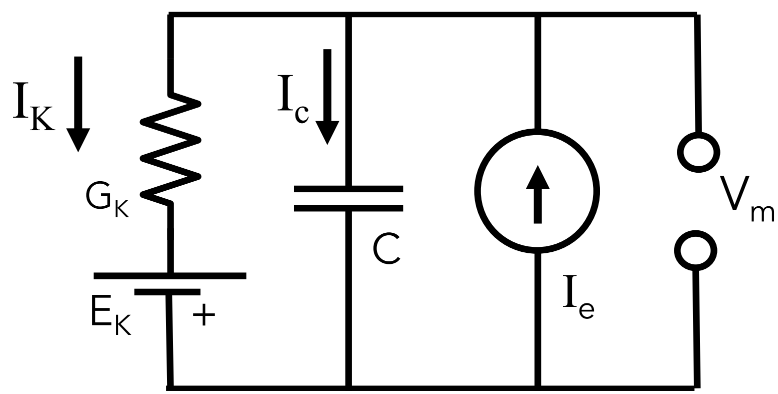
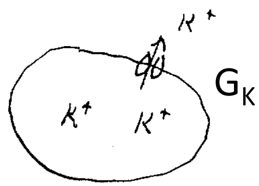
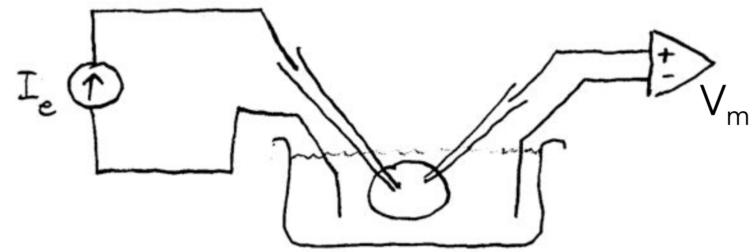


Potassium I-V relation

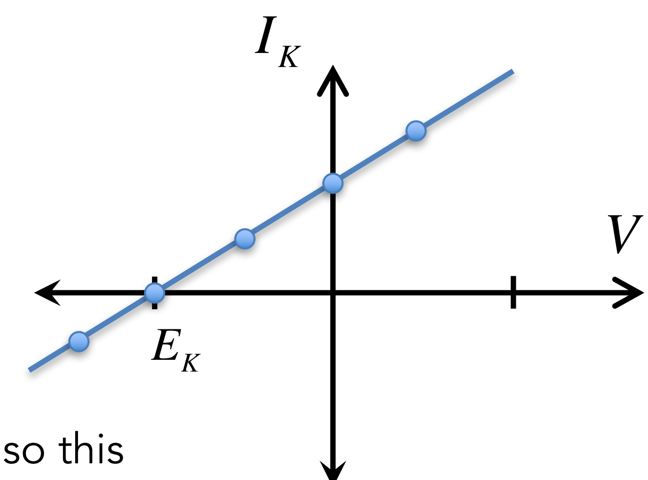
One of the best ways to study the function of an ion channel is to plot the current-voltage relation (I-V curve). This can be measured as the current required to hold the neuron at a given voltage.





For a potassium conductance

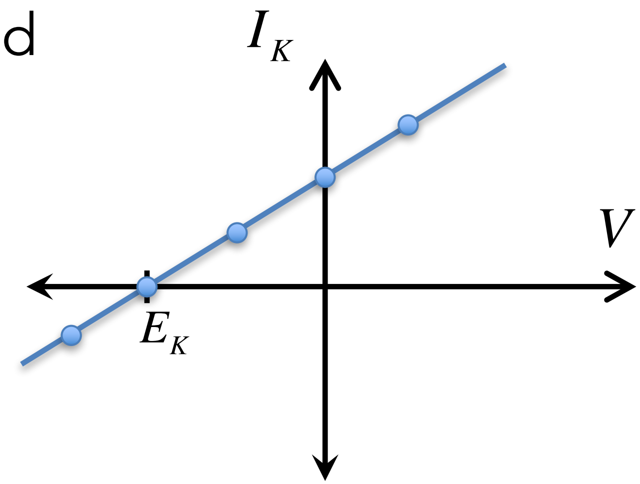
- If you hold the voltage above the equilibrium potential, K current will flow out through the membrane (positive current)
- If you hold the cell below E_K, then the current will flow into the cell.



Note that the current <u>reverses</u> at the equilibrium potential, so this is often referred to as the 'reversal potential'

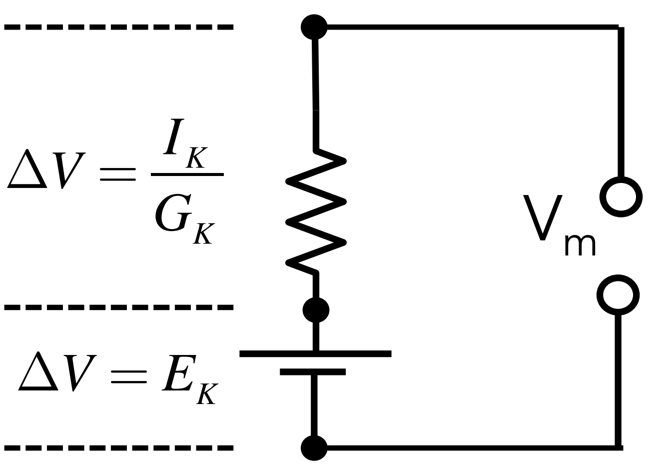
I-V relation

This relation turns out to be monotonic and roughly linear for ion channels in the open state. So we can write:



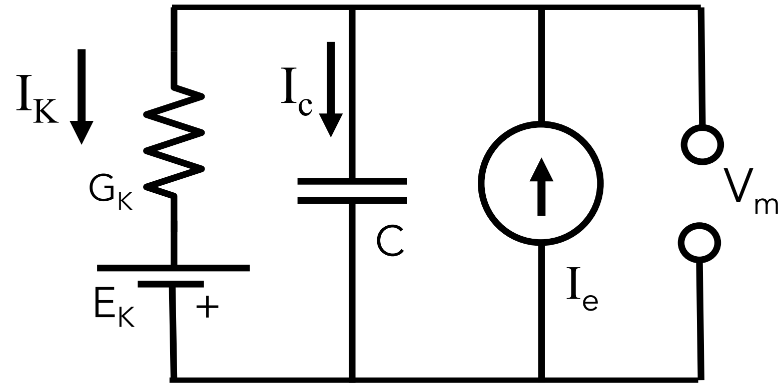
$$I_K = G_K(V - E_K)\ , \qquad G_K = R_K^{-1}$$

We can model this as a battery in series with a resistor! Why?



$$V_m = E_K + \frac{I_K}{G_K} \Rightarrow I_K = G_K\underbrace{(V - E_K)}_{\text{driving potential}}$$

Our equation is now:



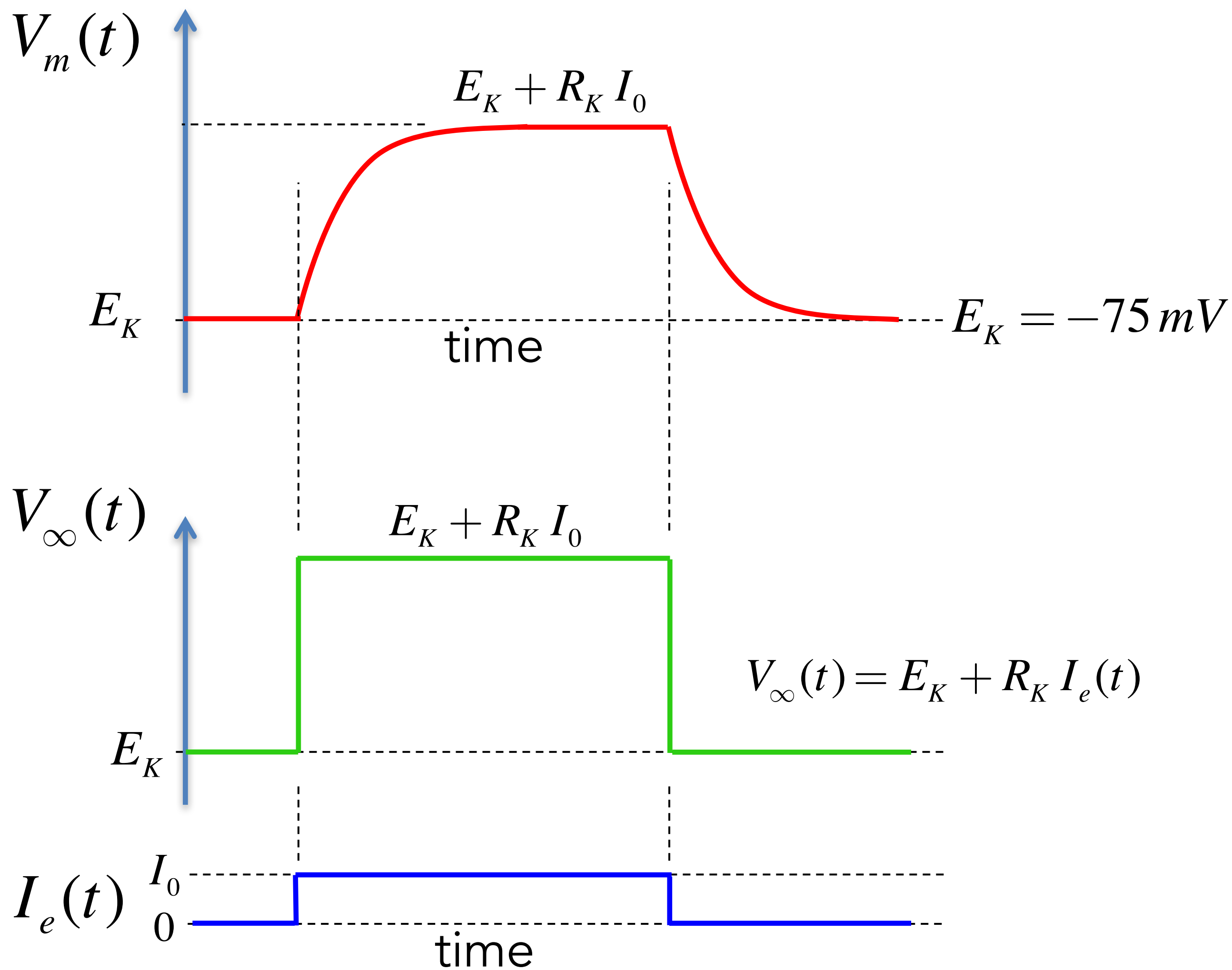
$$I_K + C\frac{dV}{dt} = I_e$$

$$G_K(V - E_K) + C\frac{dV}{dt} = I_e \quad , \qquad R_K = G_k^{-1} \;\; , \;\; \tau = R_K C$$

$$V + \tau\frac{dV}{dt} = \underbrace{E_K + R_K I_e}_{V_\infty}$$

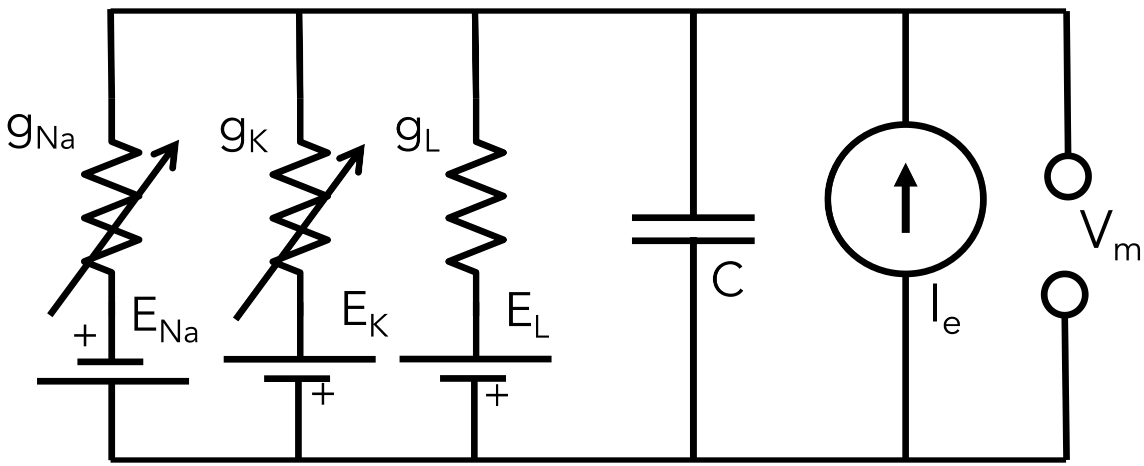
$$V + \tau\frac{dV}{dt} = V_\infty , \qquad V_\infty = E_K + R_K I_e$$

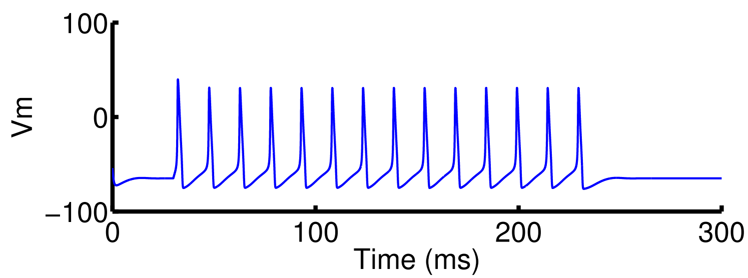
Response to current injection

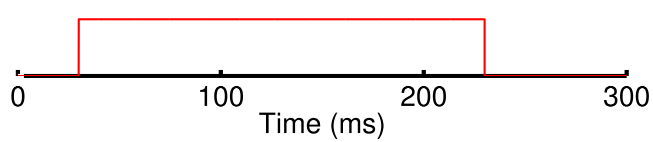


A mathematical model of a neuron

- Equivalent circuit model







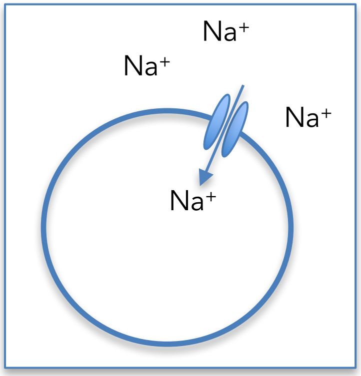
Alan Hodgkin
Andrew Huxley, 1952

The Nernst Potential is different for different ions

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75
Na^+	50	440	

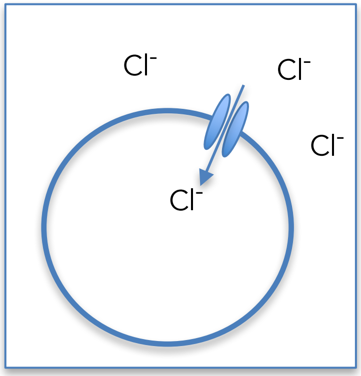
$$E_{Na} = 25mV \ln\left(\frac{440}{50}\right) = 25mV(2.17) = 54.3mV$$



The Nernst Potential is different for different ions

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75
Na^+	50	440	+54
Cl^-	52	560	



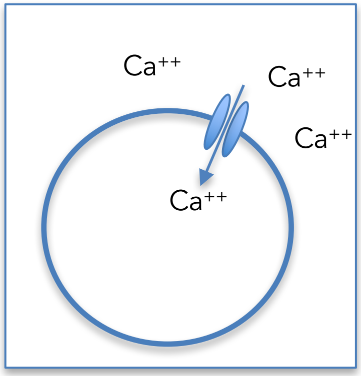
$$E_{Cl} = -25mV \ln\left(\frac{560}{52}\right) = -25mV(2.38) = -59.4\,mV$$

The negative here comes from the negative charge of the Cl^- ion (q=-e)

The Nernst Potential is different for different ions

Intracellular and extracellular concentrations of ionic species, and the Nernst potential

Ion	Cytoplasm (mM)	Extracellular (mM)	Nernst (mV)
K^+	400	20	-75
Na^+	50	440	+55
Cl^-	52	560	-59
Ca^{++}	10^{-4}	2	+124

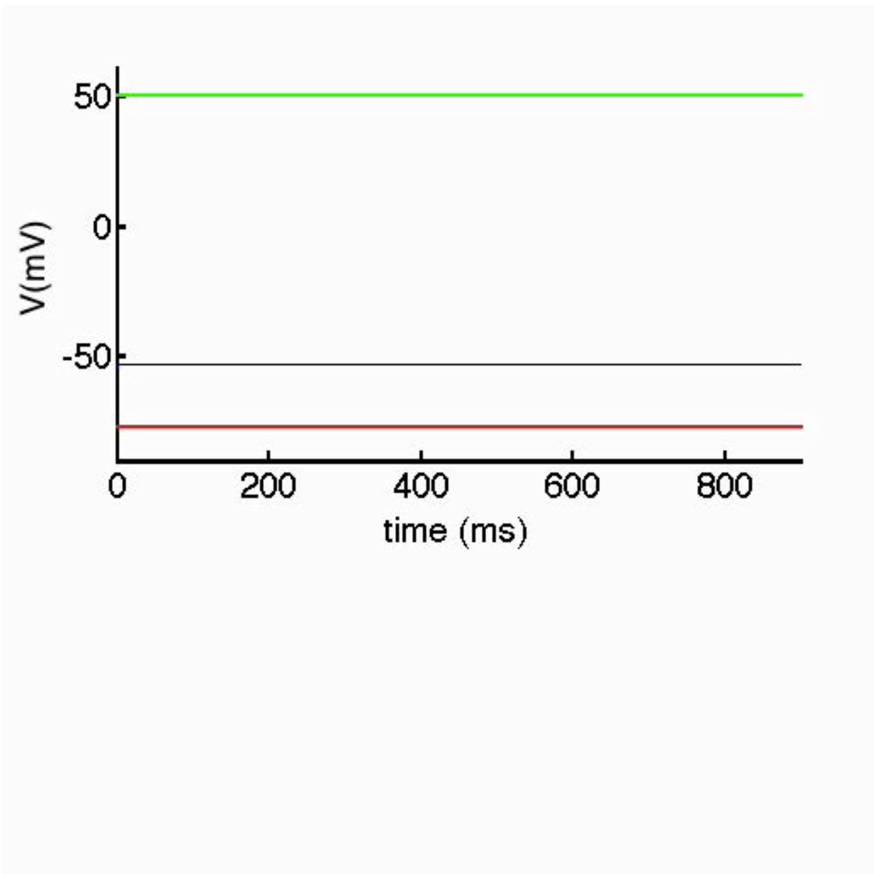


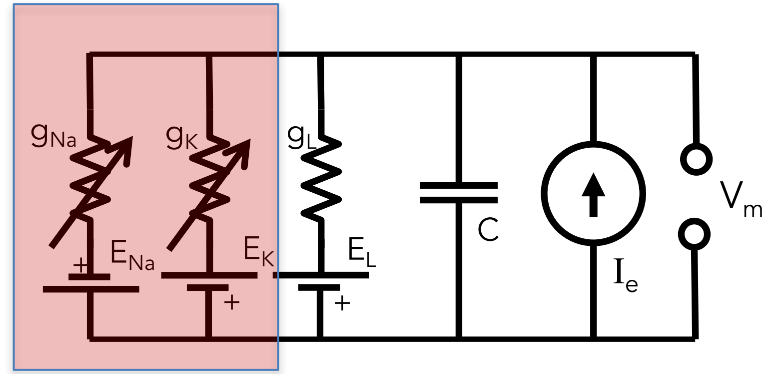
$$E_{Ca} = 12.5mV \ln\left(\frac{2}{.0001}\right) = 124mV$$

Why is this 12.5mV?

Outline of HH model

Voltage and time-dependent ion channels are the 'knobs' that control membrane potential.





- Na^+channels push the membrane potential toward +50mV.
- K^+ channels push the membrane potential toward -80mV.
- Together these channels give the neural machinery flexible control of voltage!
- - for example to generate an action potential

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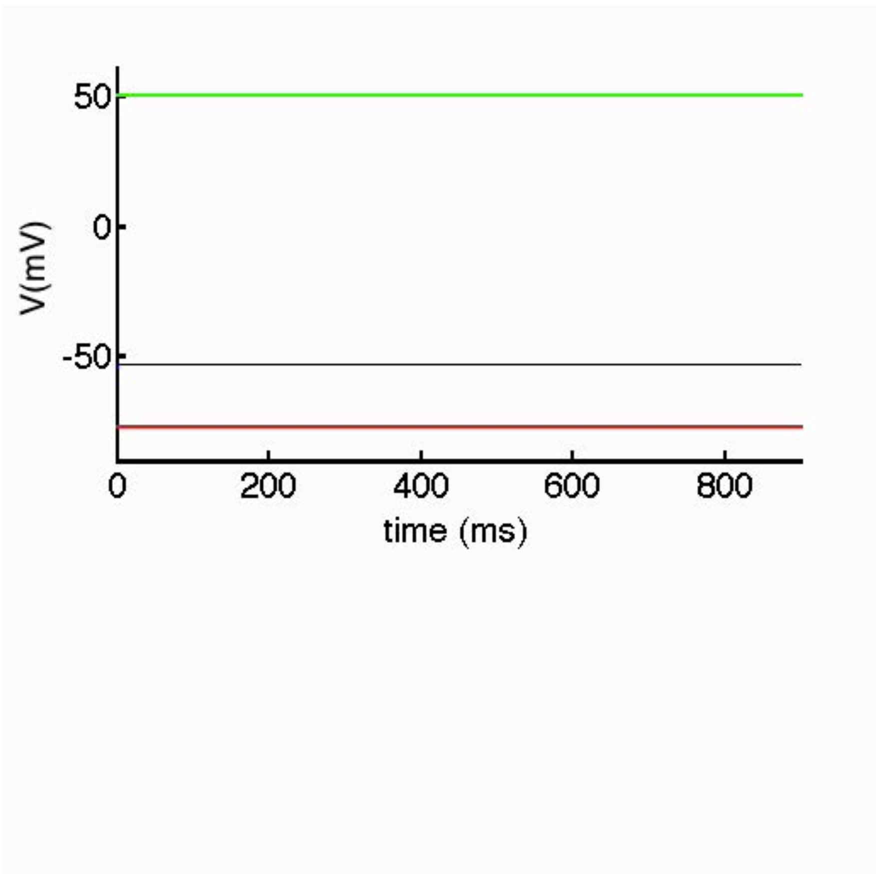
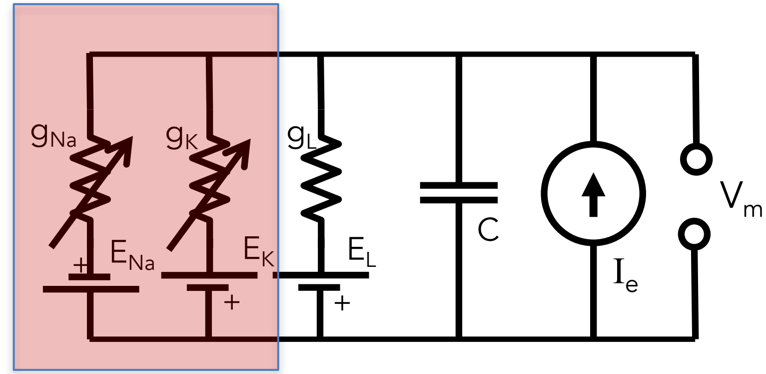
Video Module on Integrate and Fire Neuron

Outline of HH model

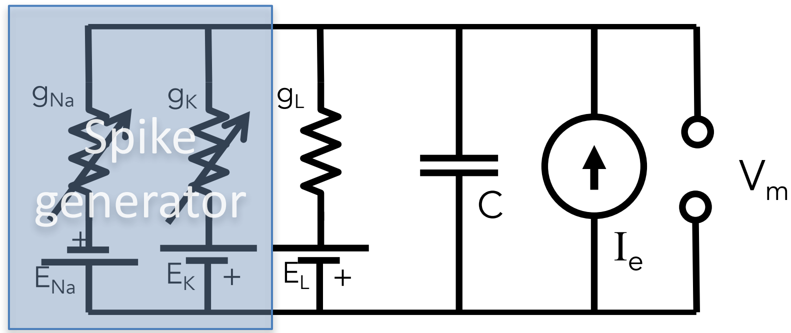
Voltage and time-dependent ion channels are the 'knobs' that control membrane potential.



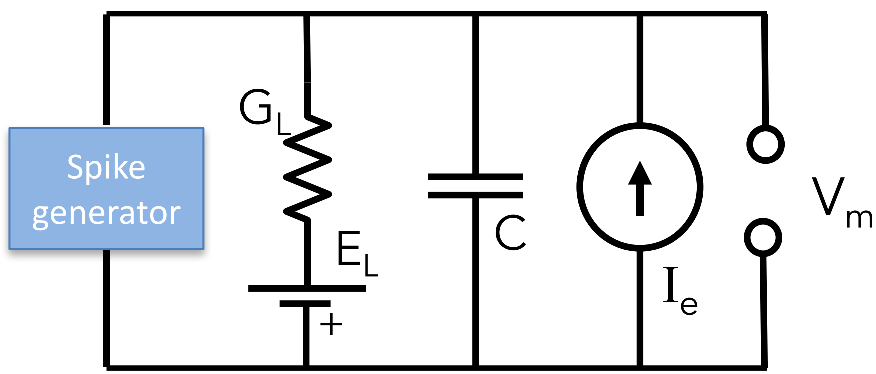


- Na^+ conductance pushes the membrane potential toward +55mV.
- K^+ conductance pushes the membrane potential toward -75mV.
- Together these conductances (and batteries) give the neuron flexible control of voltage!
- - for example to generate an action potential

Integrate and Fire model of a neuron



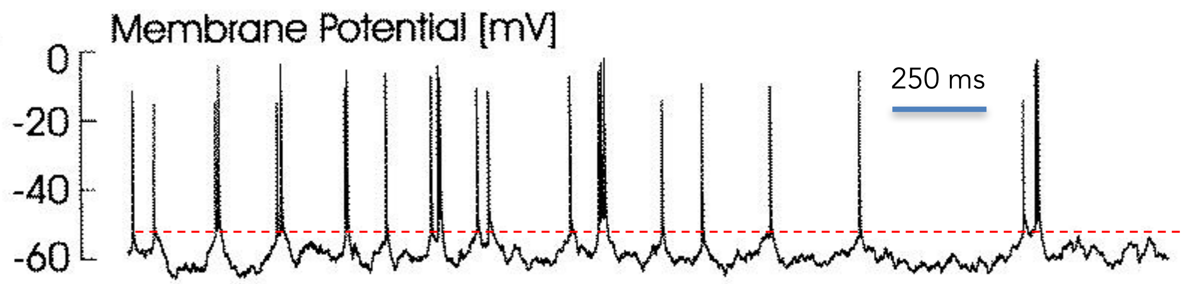
We are going to replace the fancy spike generating mechanism in a real neuron with a simplified 'spike generator'.



Louis Lapique, 1907

Knight, 1972

A simplified model of a neuron



spikes as $\delta -$ functions

- While APs (spikes) are important, they are not what neurons spend most of their time doing. Spikes are very fast (~1ms in duration).

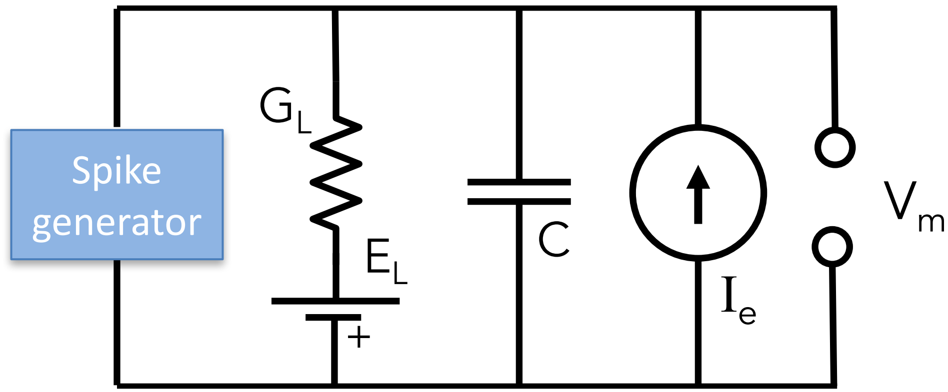
- This is much shorter than the typical interval between spikes (~100ms). Most of the time, a neuron is 'integrating' its inputs. (Separation of timescales)

- All spikes are the same. (No information carried in the details of action potential waveforms.)

- Spikes tend to occur when the voltage in a neuron reaches a particular membrane potential, called the spike threshold.

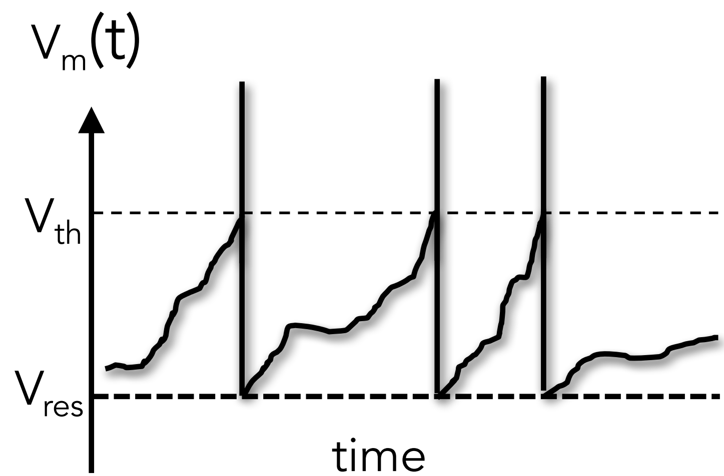
Integrate and Fire model of a neuron

The spike generator is very simple. When the voltage reaches the threshold V_{th}, it resets the neuron to a hyper-polarized voltage V_{res}.



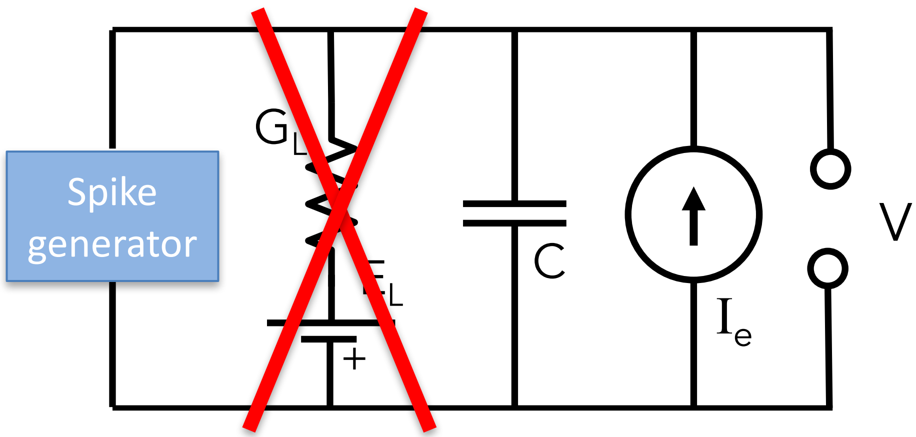
Louis Lapique, 1907

Removed due to copyright restrictions: Figure 2D1: Subthreshold membrane potential oscillations in RA neuron. Mooney, R. "Synaptic basis for developmental plasticity in a birdsong nucleus." Journal of Neuroscience 1 July 1992, 12 (7) 2464-2477.



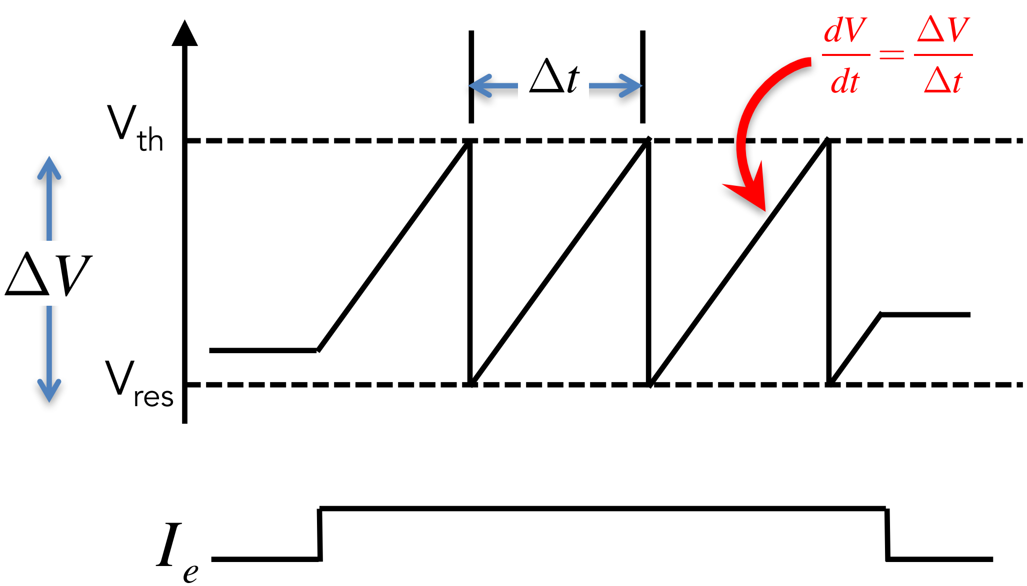
Integrate and Fire model of a neuron

- Let's calculate the firing rate of our neuron



We'll first consider the case where there is no leak.

$$f.r. = \frac{1}{\Delta t} \qquad \Delta V = V_{th} - V_{res}$$

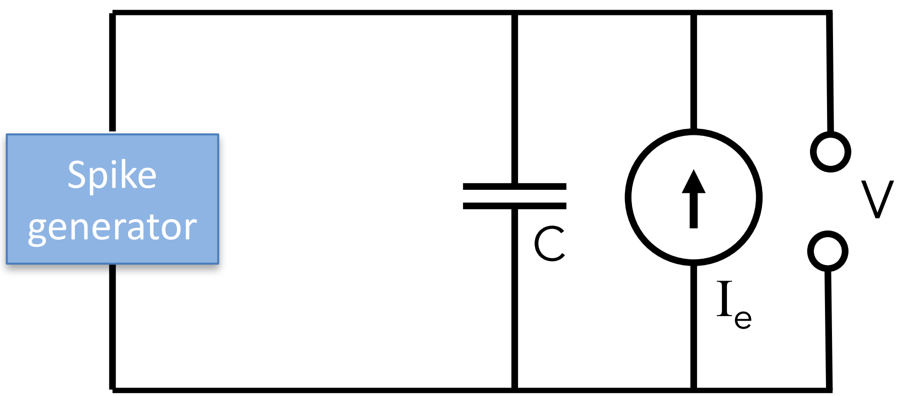


$$C\frac{dV}{dt} = I_e \qquad C\frac{\Delta V}{\Delta t} = I_e$$

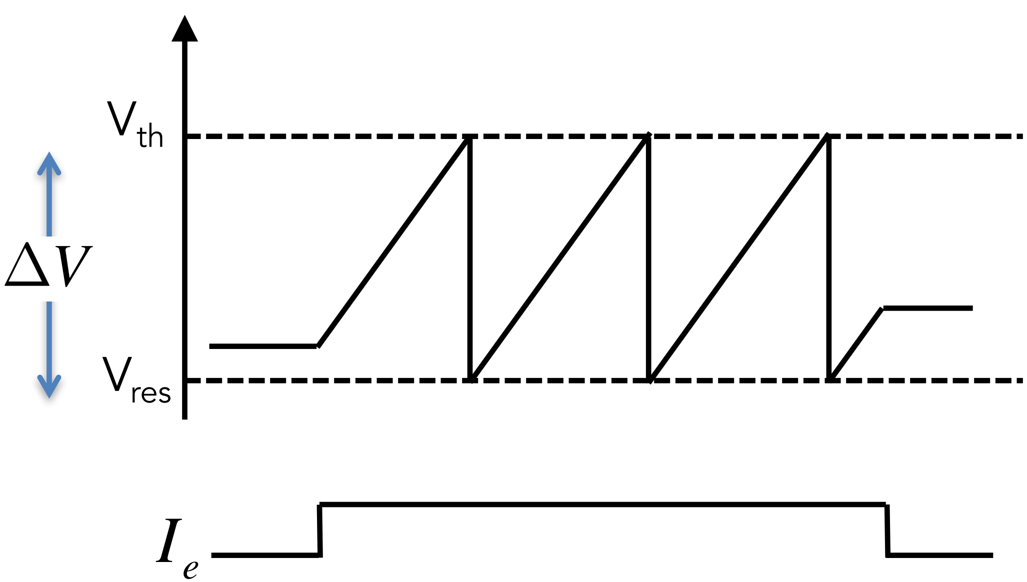
$$f = \frac{1}{\Delta t} = \left(\frac{1}{C\Delta V}\right) I_e$$

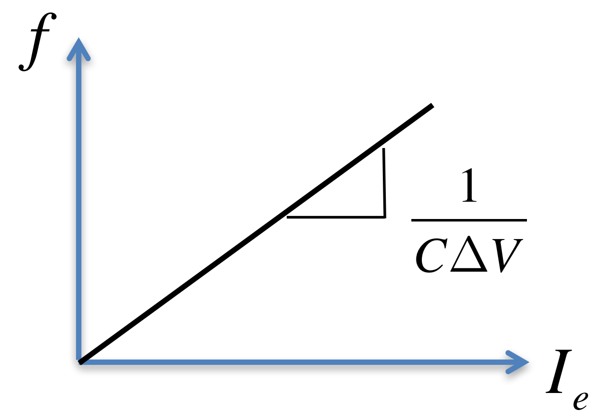
Integrate and Fire model of a neuron

- Let's calculate the firing rate of our neuron



We'll first consider the case where there is no leak.

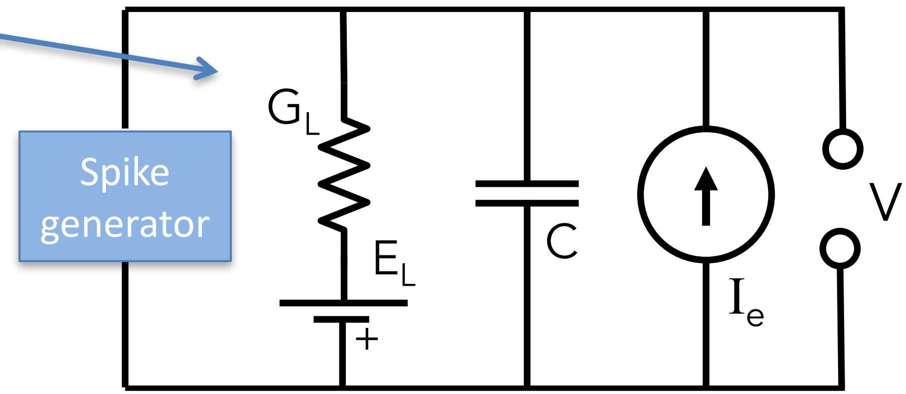




$$f = \left(\frac{1}{C\Delta V}\right) I_e$$

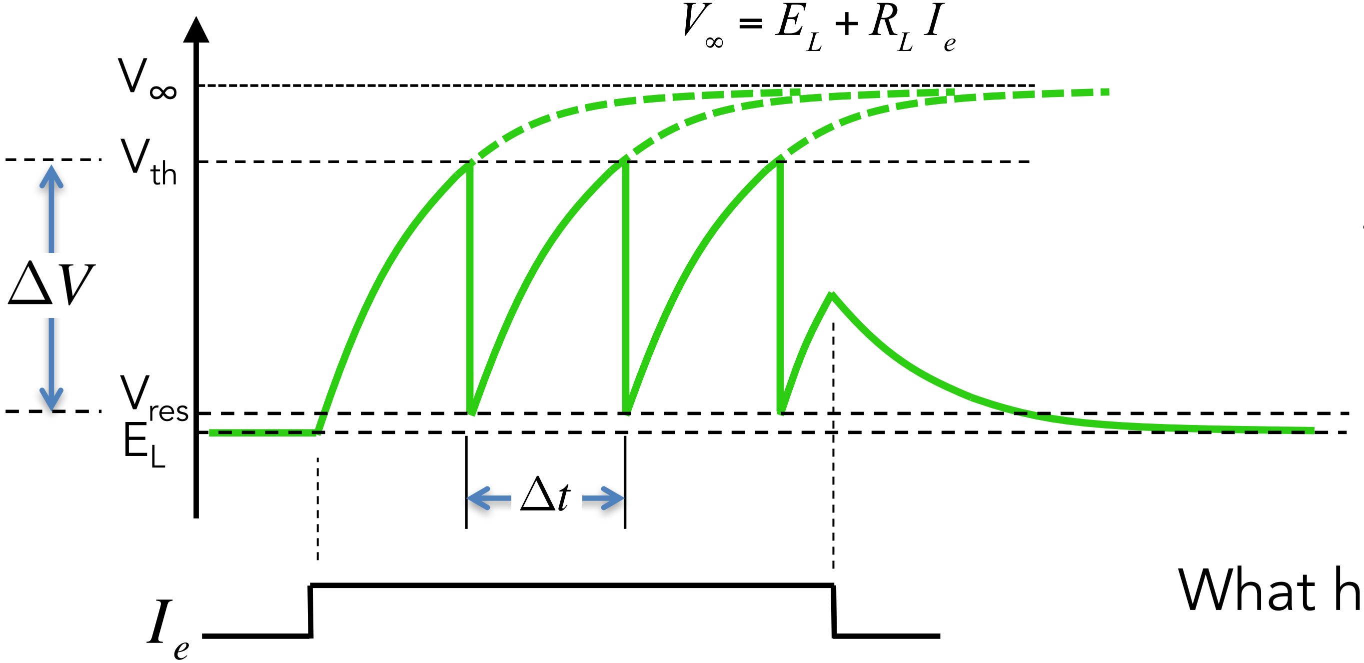
Integrate and Fire model of a neuron

Now we'll put our leak conductance back in.



Think of this G_L like a small potassium conductance that is constantly on. It has no voltage dependence and no time dependence. E_L = -75mV.

$$V_\infty = E_L + R_L I_e$$



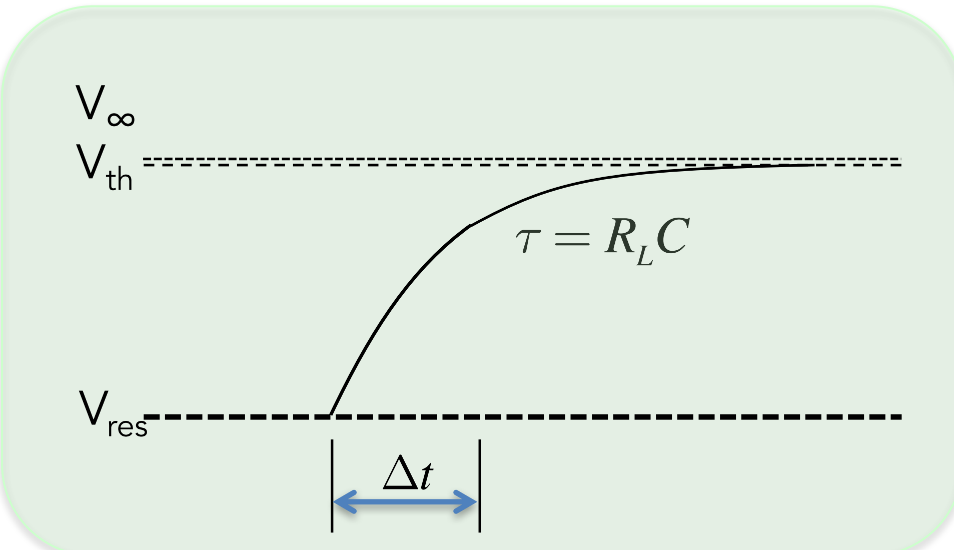
$$f.r. = \frac{1}{\Delta t}$$

What happens when

$$V_\infty < V_{th} \ ?$$

Integrate and fire with leak

What happens just at threshold?



Lets calculate the injected current required to reach threshold (rheobase).

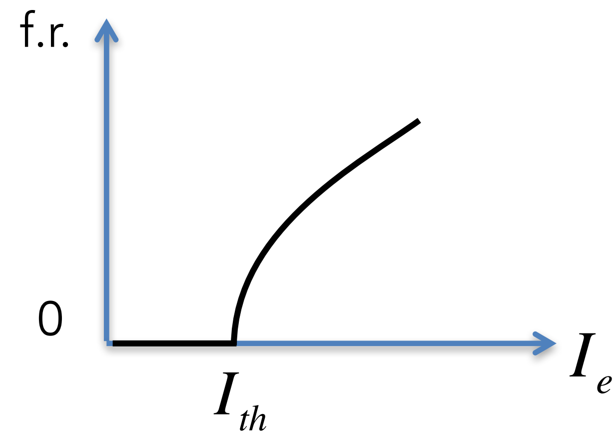
$$V_\infty = V_{th}$$

$$E_L + R_L I_e = V_{th}$$

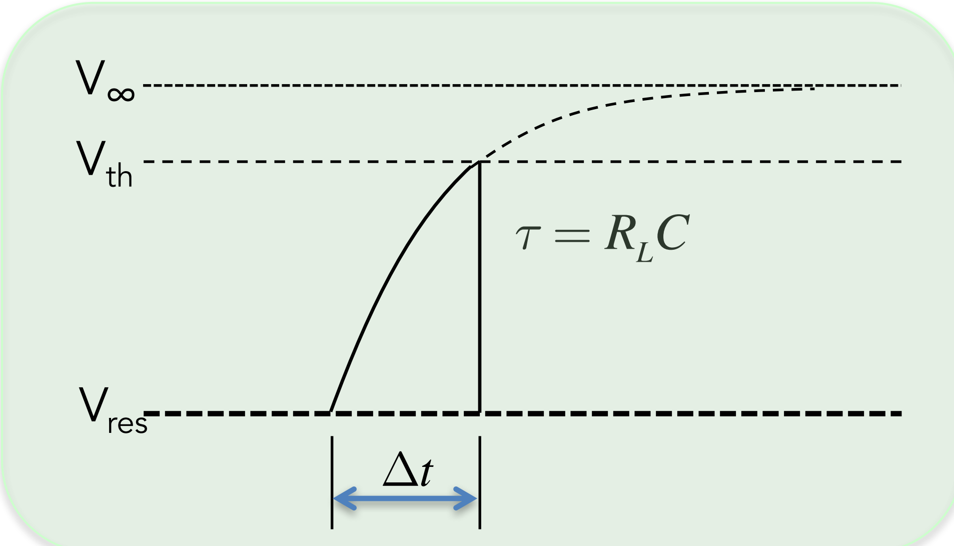
$$I_{th} = I_e = G_L (V_{th} - E_L)$$

The time to reach threshold (Δt) is:

- very long
- very sensitive to injected current



Integrate and fire with leak



$$e^{-\Delta t/\tau} = \frac{V_\infty - V_{th}}{V_\infty - V_{res}}$$

$$\Delta t = -\tau \ln\left(\frac{V_\infty - V_{th}}{V_\infty - V_{res}}\right)$$

$$V(t) - V_\infty = (V_0 - V_\infty)e^{-t/\tau}$$

$$V_{th} - V_\infty = (V_{res} - V_\infty)e^{-\Delta t/\tau}$$

$$f = \Delta t^{-1} = \left[\tau \ln\left(\frac{V_\infty - V_{res}}{V_\infty - V_{th}}\right)\right]^{-1}$$

Integrate and fire

At high input currents, the solution has a simple approximation

$$f = \left[\tau \ln\left(\frac{V_\infty - V_{res}}{V_\infty - V_{th}}\right)\right]^{-1}$$

$$V_\infty \gg V_{th}, V_{res}$$

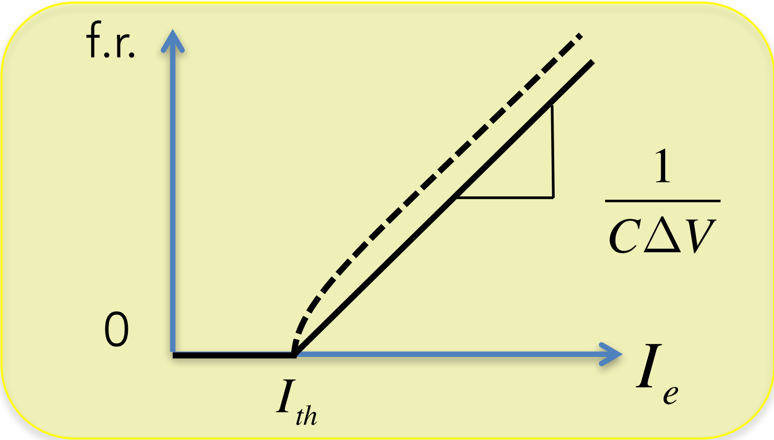
$$\ln(1+\alpha) \sim \alpha$$

$$\boxed{f = \frac{1}{C\Delta V}\left(I_e - I_{th}\right)}$$

$$I_{th} = G_L\left(V_{th} - E_L\right)$$

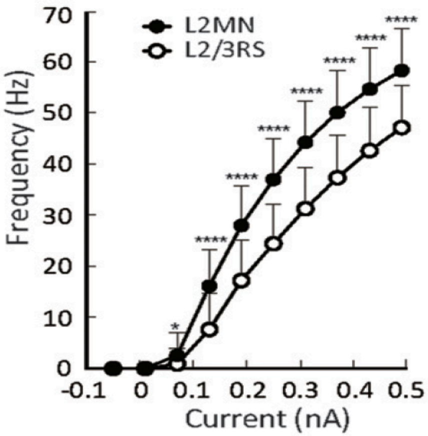
Integrate and fire

This equation is linear in injected current I_e , just like the case of no leak!



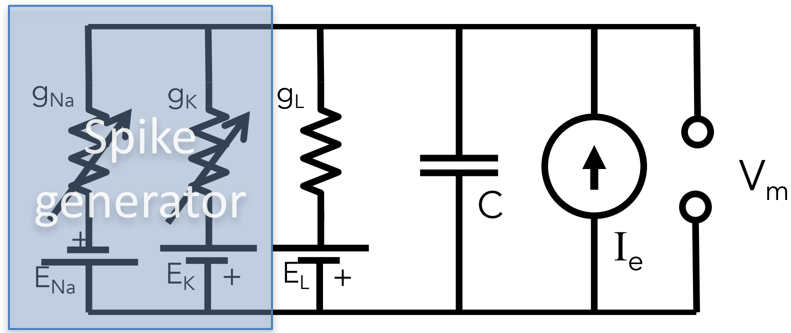
$$f = \frac{1}{C\Delta V}(I_e - I_{th})$$

The F-I curve of many neurons look approximately like this!

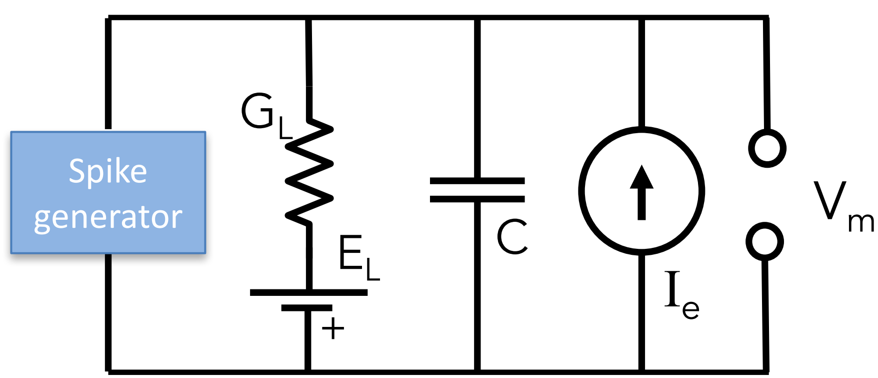


Luo et al 2017

Integrate and Fire model of a neuron



We have replaced the fancy spike generating mechanism in a real neuron with a simplified 'spike generator'.



Louis Lapique, 1907

Knight, 1972