Neuron is an electrical device that signals 0 or 1 (binary) in our brain, similar to the binary logic that chips use in computers. So, the binary logic as well as a carefully crafted electrical system to implement it was invented by nature long before humans invented computers!

SO FAR….

- Human brain has lots of electrical circuits…and some of that 'wiring' goes wrong in the spectrum of mental health challenges we face
- What are the biological components of a neuron?
- What is the power source of a neuron? – chemical potential set up via Nernst potential (uses 20-30% of the food you eat to set this up!)
- ………………………..

NEXT – let us demonstrate that neuron is an electrical device that was invented by nature long before humans invented similar electrical devices!

- We start with a basic neuron with only one type of channel, leak channel, and show how it is an actual electrical device (not analogy) [Adding channels such as Na+ and K+ will help make it generate 0 and 1 – in later modules]

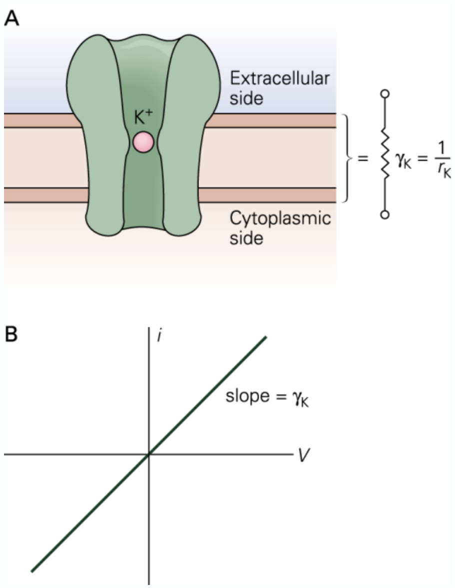
Review: Nernst and Rest Potentials

Watch this video for a quick review - https://www.youtube.com/watch?v=hk09AkV5_Kc

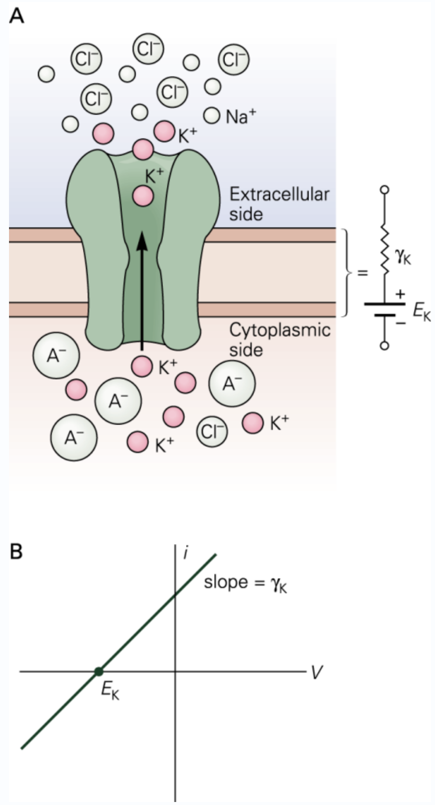
NERNST POTENTIAL – Consider a single ion in different concentrations across a cell membrane. Nernst potential is the membrane voltage across the phospho-lipid bilayer (cool video of general structure) when the flow of that ion due to the ***diffusion gradient*** = the flow in the other direction due to the ***electrostatic gradient***.

RESTING MEMBRANE POTENTIAL – Now consider multiple ions with their own concentration gradients. Resting membrane potential is the membrane voltage across the phospho-lipid bilayer when the NET flow of all ions due to their specific ***diffusion gradients*** = the NET flow in the other direction due to their specific ***electrostatic gradient***. That is, the equilibrium potential in this tug-of-war among the various ionic species

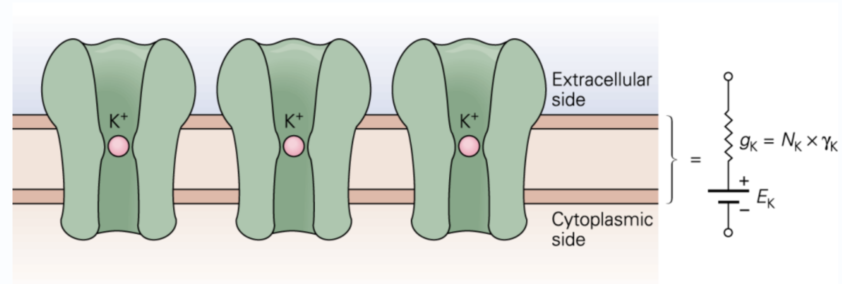
REVIEW: **Ion channels act as resistors allowing current flow across the membrane**



A single channel in the absence of a concentration gradient.



Current flow through a single channel subject to both chemical and electrical forces. Unitary conductance (γ).

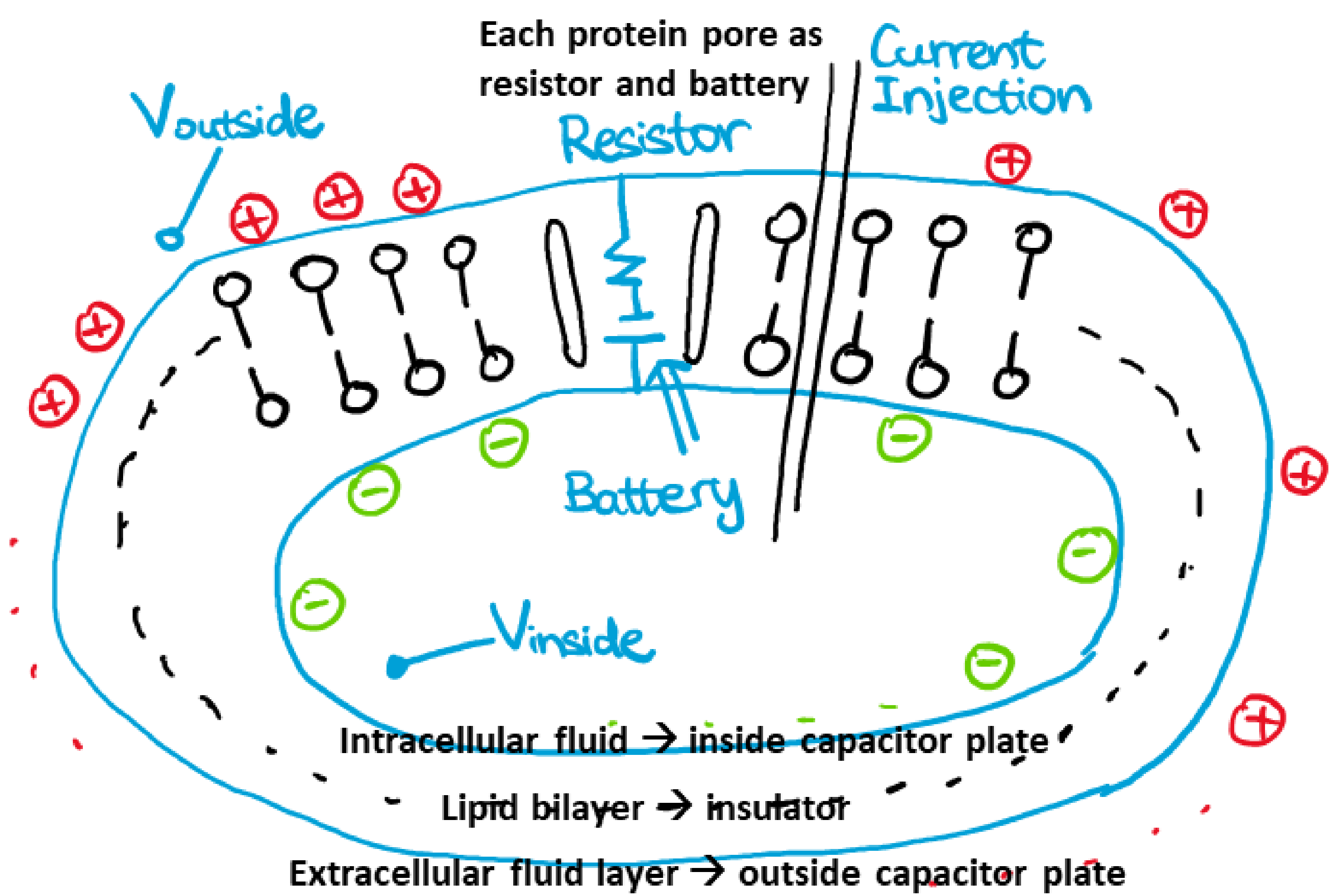


Total conductance represented by the unitary conductance of a single channel and the number of open channels.

I ion = gion * (Vm – Eion)

or "the current is equal to the conductance times the driving force."

REVIEW: BIOLOGICAL COMPONENTS OF A NEURON

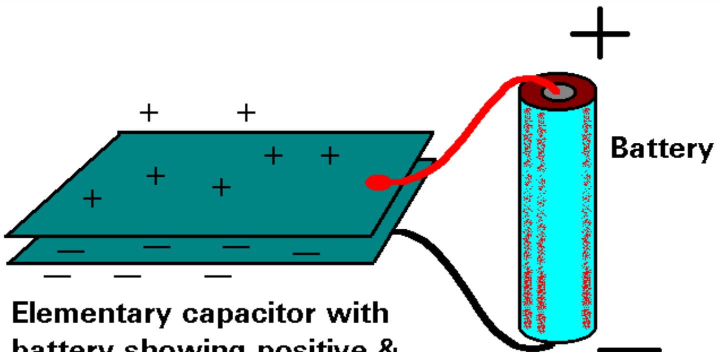


Now, how do we prove that a neuron is an electrical device? Let's begin with this simple sketch….and follow along with the video with the module

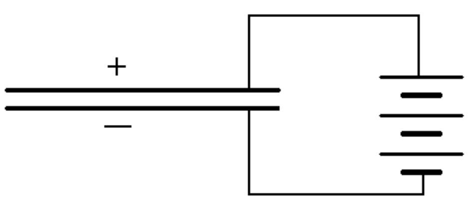
1. **Sketch a 9-volt battery connected to a capacitor on the left below**
2. **Then sketch a cell membrane showing the lipid bi-layer and charges**

Now focus on the cell membrane
- Cell membrane is a capacitor

Sketch a 9V DC battery connected to an LED. What charges really flow and how?

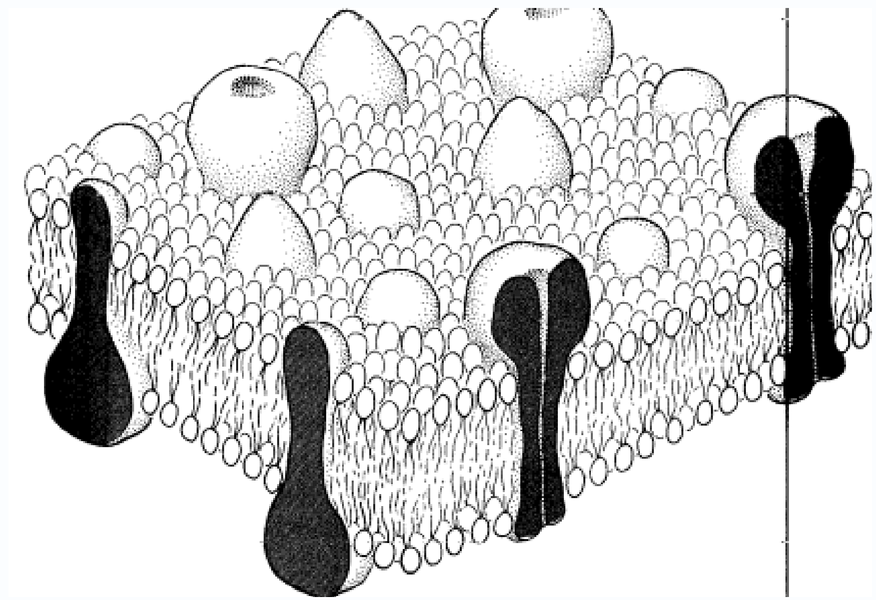


Elementary capacitor with battery showing positive & negative charges on its plates.



Schematic representation of capacitor and battery

Cell membrane



Cell membrane as a capacitor?

A capacitor consists of two conducting regions separated by an insulator. A capacitor works by accumulating a charge on one of the conducting surfaces. As this charge builds, it creates an electric field that pushes like charges on the other side of the insulator away. Capacitance may be defined two ways, 1) as an ability to store and separate charge, or 2) as the quantity of charge required to create a given potential difference between two conductors. A higher capacitance results in a lower potential difference.

$C = Q/V$, where C is the capacitance, Q is the total charge and V is the voltage across the plates. So, we get $I = dQ/dt$ = current flowing into the capacitor = C*dV/dt.

In the neuron the membrane is the insulator between the two conducting surfaces (represented by the aqueous intra and extracellular fluids). A neuron's capacitance is proportional to it's membrane surface area, so large neurons have larger capacitances. Capacitance also decreases with the distance between the two conducting surfaces. Capacitance plays an important role in the axon, and is involved in action potential generation and propagation. Myelin plays a very important role in this too. Myelination not only increases the membrane resistance of the axon (there is very little ion exchange across the membrane in myelinated regions of the axon), but increases the distance between the conducting surfaces, and so decreases membrane capacitance. These factors lead to more rapid conduction of action potentials down the axon and is responsible for the phenomenon known as saltatory conduction.

Sketch a cell membrane with only leak channels ('passive membrane') on the left below. Then add a pipette representing current injection. Assume the membrane potential starts at V_rest (value?). With CONSTANT +ve current injection for 100 ms, plot on the right the following: Vm vs. time at top, and current injection below it. Assume t is from -10 to 200 ms, and Ek = -65 mV for leak channel. How is time constant defined, and what is it for the Vm vs. time plots? **(<u>parallel exercise</u> – how is this problem similar to filling a bucket with a 1-inch diameter hole at the bottom with water from a constant faucet?)**

Explain at the ionic level, what really happens from t=-10 to 200 ms. Assume Ek = -65 mV for leak channel.

To follow up on your explanation, assume that 10 +ve ions flow through the pipette per ms, fill in the table below:

Time (ms)	Influx via pipette	Net efflux from cell	Stick on inside wall	Vm

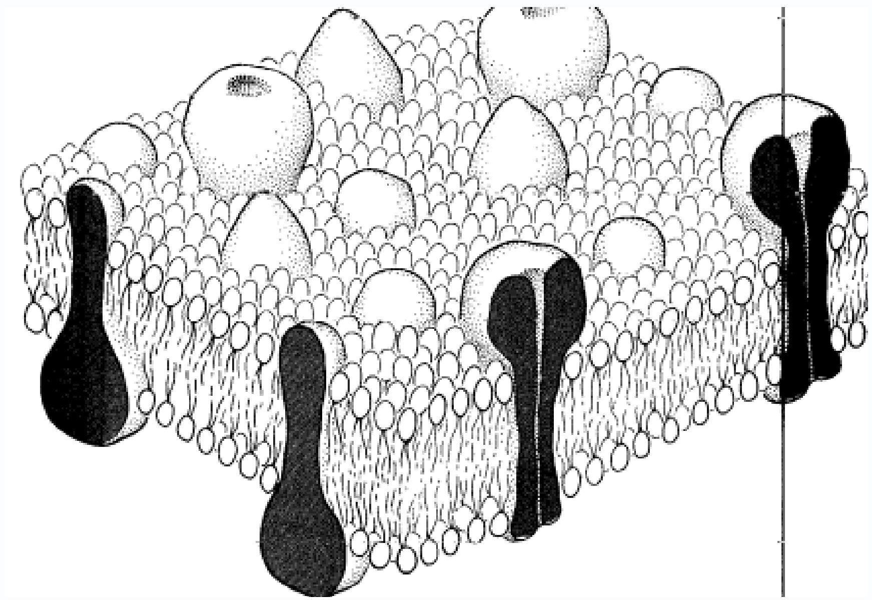
Following up on the previous slide, sketch the elements (first) of the electrical circuit, and then put them all together, following the logic on the previous slides. (<u>parallel exercise – do the same with the bucket example</u>)

time	influx	eflux	stick on the wall	Voltage
0-1	10	0	10	-65
1-2	10	2	8	-63
2-3	10	4	6	-61
3-4	10	6	4	-59
4-5	10	8	2	-57
5-6	10	10	0	-55
6-7	10	10	0	-55
7-8	10	10	0	-55

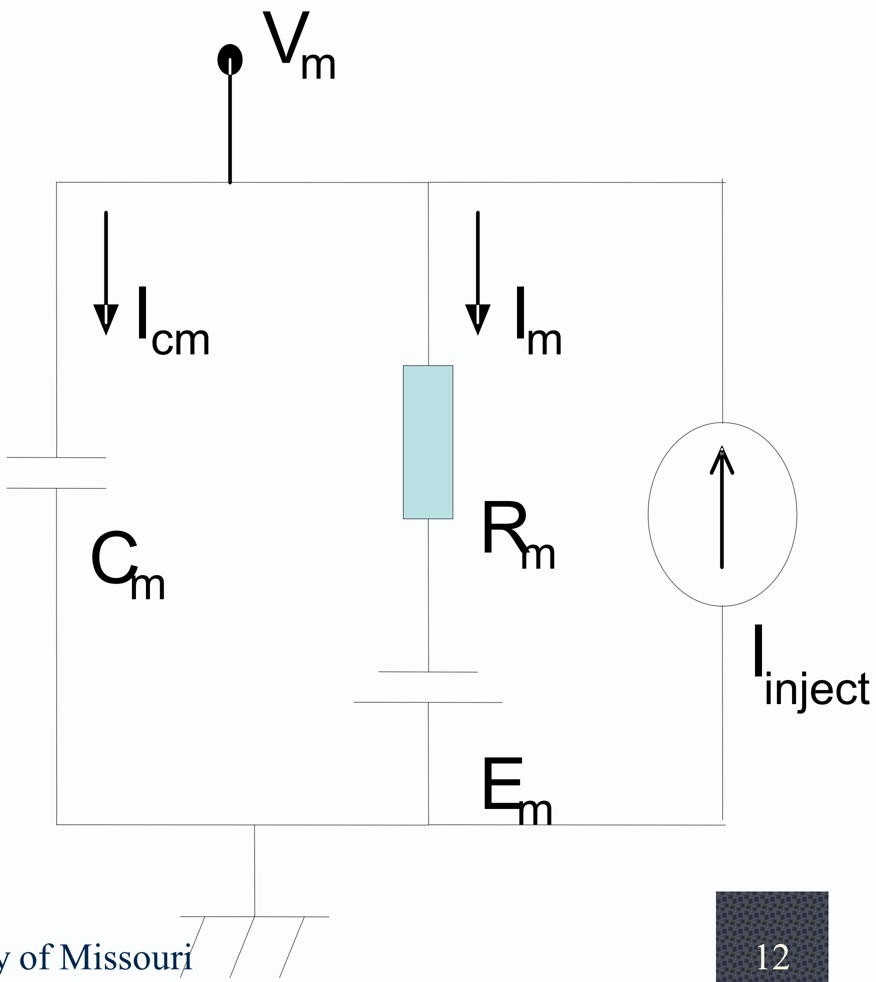
When inject a current into the cell, Ohm's law will decide how many ions/ms flow outside the cell (eflux). At the beginning, there will be 0 ions/ms. As the voltage increase, eflux will increase until it's 10 ions/ms. Conservation of charge law will decide how many ions/ms stick on the wall (stick on the wall = influx - eflux). At the beginning it's 10 ions/ms, it will decrease as eflux increase and reach to 0 ions/ms. And we can use capacitor equation to calculate how voltage change.

Biophysical model of a cell with a passive channel

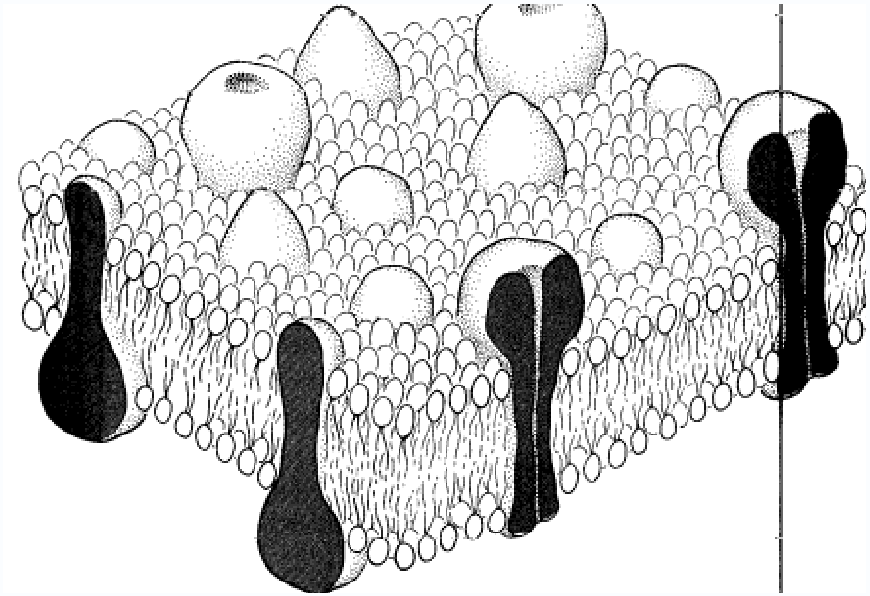
Cell membrane



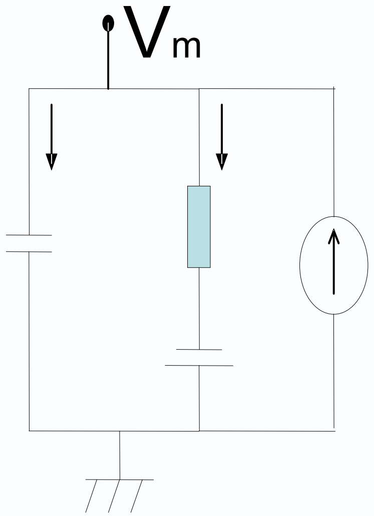
Corresponding 'model'



Repeat yourself: Explain what happens with current injection - assume 20 +ve ions/ms are injected into the cell, and Vm,init = Ek



- Assume there is only one ion species, 'leak' ions; Vm,init = Vm(time=0) = Vm(0)
- As a first step, label all components and variables in the figure below
- Why is Vm(0) = E_rev = Ek = E_leak ?
- Now answer the question above in the space below using a table as before:



How do we model this 'dynamic' system - a passive membrane with current injection?

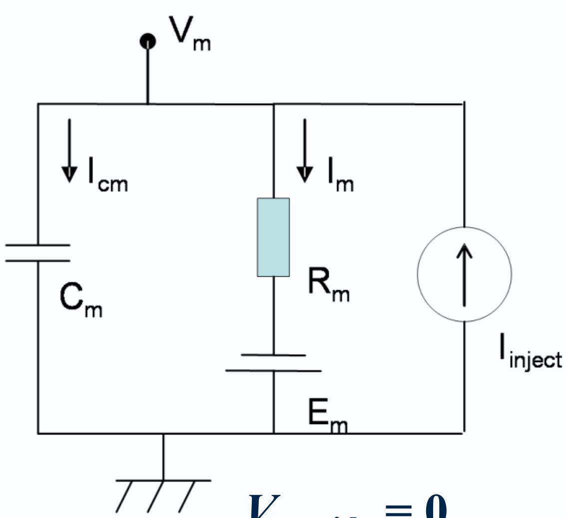
CONVENTION:

(i) Voltages are measured with respect to the outside of the cell, i.e., $V_{outside}=0$.

(ii) Current OUT of the cell is considered positive by convention (biologists and neuroscientists)

(iii) By convention, I_{inject} is positive if it goes into the cell

$V_{inside} = V_m$



$V_{outside} = 0$

Basic Laws used in modeling this capacitor with passive channels:

1. __Ohm's Law__ – to calculate the current flowing in the presence of a voltage difference between the outside and inside of the cell

2. __Capacitor charging law__ – accumulation of charge on the capacitor (cell membrane) plates leads to an increase in voltage across the capacitor (cell membrane)

3. __Nernst potential__ - the diffusion and electrostatic forces are always present. This Nernst potential is used as a 'battery' source

4. __Conservation of charge__ – What equation does this law give?

Can you now derive the equation for the circuit above?

The ‘Modeling’ process – membrane equation

STEP 1: What are the laws at work here?

STEP 2: Write in words, how the various laws interact to help attain equilibrium

STEP 3: How do we go from step 2 to equations?

How do we model this ‘dynamic’ system - a passive membrane with current injection?

Consider the passive membrane (leak current only) with the following parameters:
C =1.4884e-10 Farads; Asoma = 6.3428e-4 cm^2; gleak =2.0e-5 Seimens/cm^2; Eleak = -0.07 V. Take *Vm*(t=0) = *Vm*(0) = -0.06V.
(Note: Rm is the same as Rleak, and 1/Rm = 1/Rleak = Gleak; Also, Em = Eleak)

What is the mathematical model for this membrane? What really happens?
A passive membrane is a capacitor with only the leak channels permitting ionic flows (with its own E_{leak}). The ‘law’ that governs this system is as follows (Kirchoff current law):

“Charge accumulating on the capacitor per second = charge flowing into it thro’ the leak channel per second + charge injected into it per sec by an external source”

Recall that flow of charges per second is “current”, and it is measured in Amperes. For the passive membrane the equation above in words becomes,

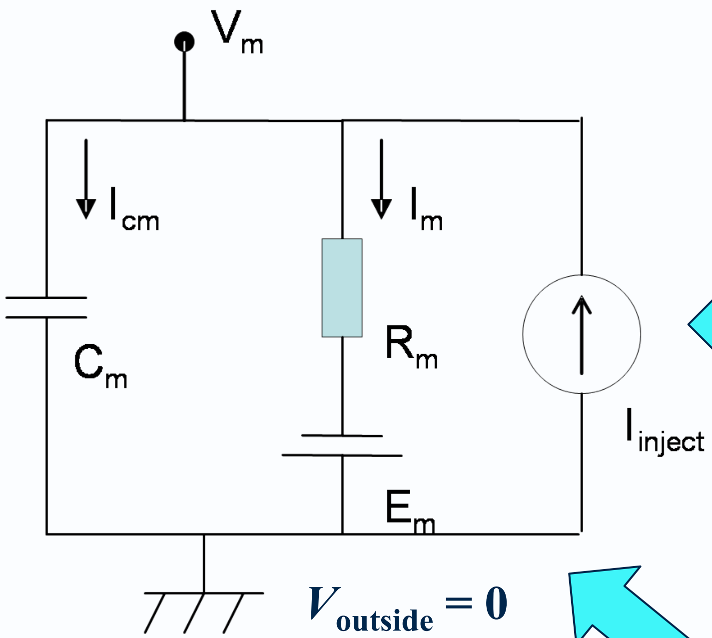
$$I_{cm} = - I_m + I_{inject} \quad \textit{(using notation on earlier slide)}$$

$$C*dV_m/dt = - G_{leak}*(V_m-E_{leak}) + I_{inject}$$

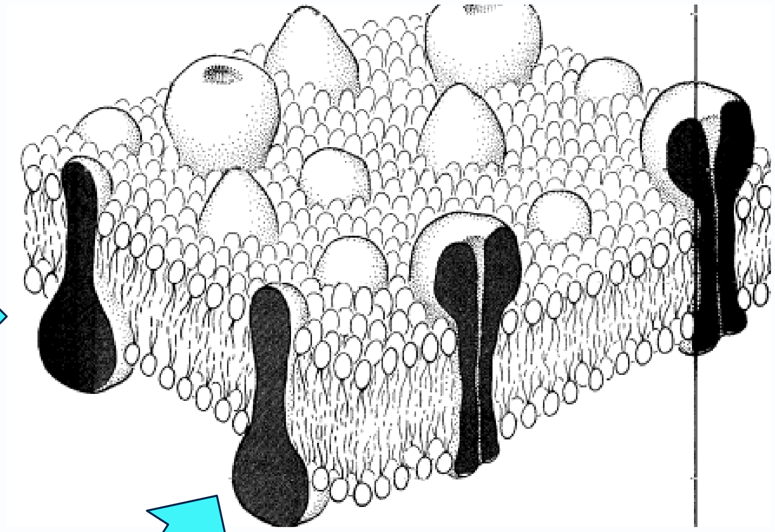
$$= - A*gleak*(V_m-E_{leak}) + I_{inject}$$

NEURON IS AN ELECTRICAL DEVICE!

$V_{\mathrm{inside}} = V_{\mathrm{m}}$



$V_{\mathrm{outside}} = 0$



$$C*dV_m/dt = -\,G_{leak}*(V_m - E_{leak}) + I_{inject}$$

$$= -\,A*gleak*(V_m - E_{leak}) + I_{inject}$$

What is the expression for time constant?