Lecture 2

Equivalent Circuits

What is missing from our models?

- We can use Nernst and Goldman to predict a neuron’s membrane potential when the net flux (net current) is zero.

- What happens in the dynamic state, when the net current is not zero? For example, if we inject current into our isopotential neuron model?

We will apply basic principles of RC circuits to predict V_m across time.

First, let’s quickly review RC circuits.

Resistance

For a cylindrical block

$$R=\rho l/A$$

- ρ is resistivity (Ωcm)
- l is length of the cable (cm)
- A is cross sectional area (cm^2)

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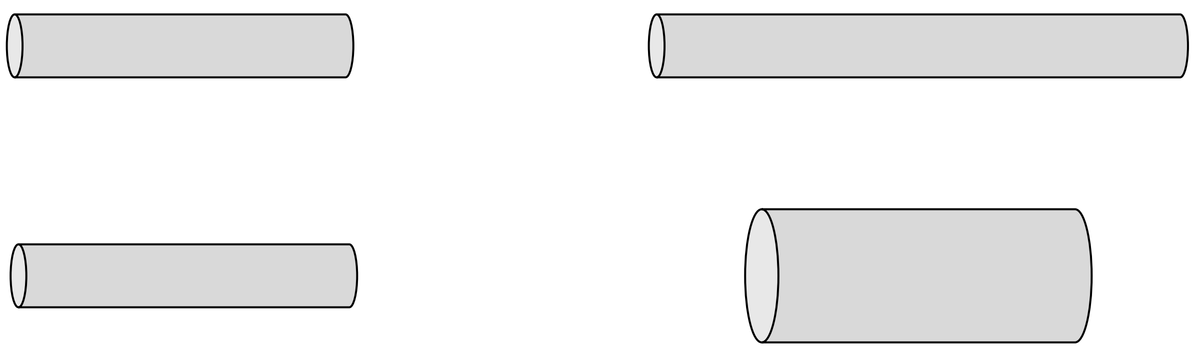

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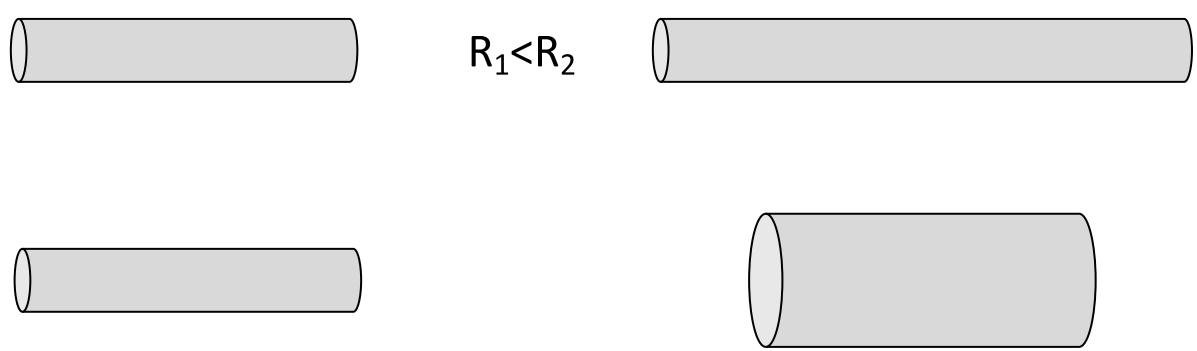

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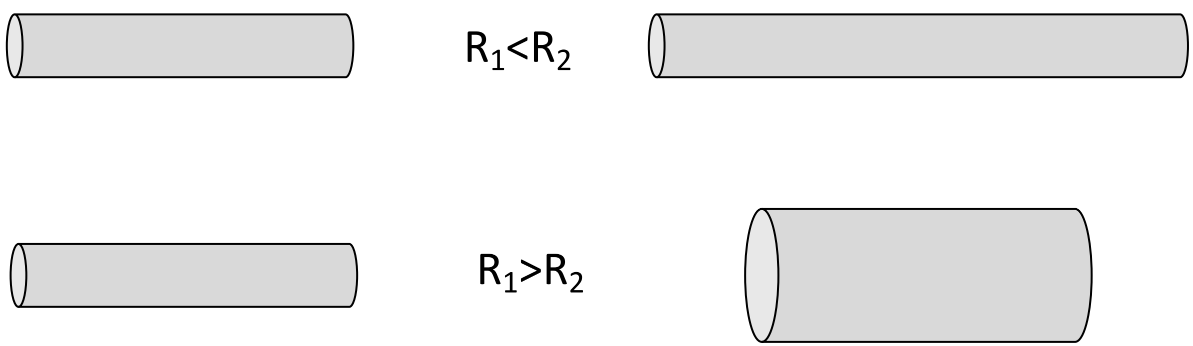


Resistance

For a cylindrical block

$$R=\rho l/A$$

- **ρ is resistivity (Ωcm)**
- l is length (cm)
- A is cross sectional area (cm^2)

The resistivity of mammalian saline is 60 Ωcm, while the resistivity of a pure phospholipid bilayer can reach 10^{15} Ωcm.

Ohm’s Law

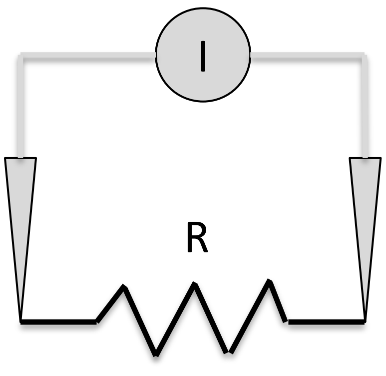
$$V=IR$$

or

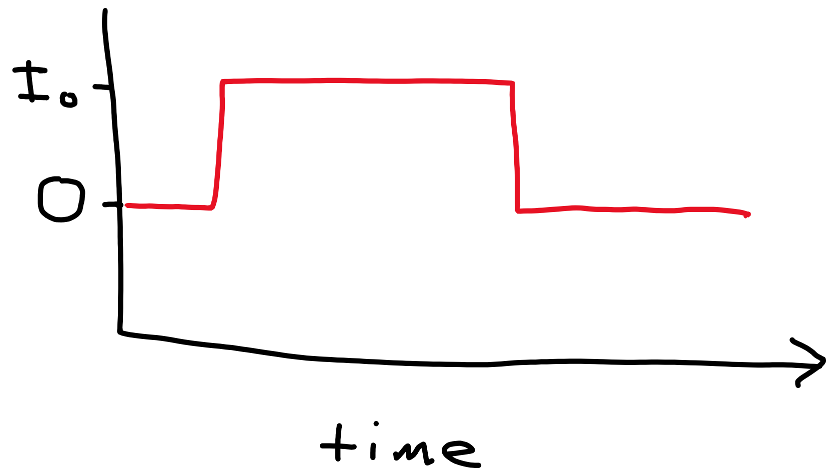
$$V=I/G$$

- R is resistance (in ohms, Ω)
- G is conductance (in siemens, S)
- V is potential difference (in volts, V)
- I is current (in amperes, A)
- Remember R=1/G

Injecting current across a resistor



V=?



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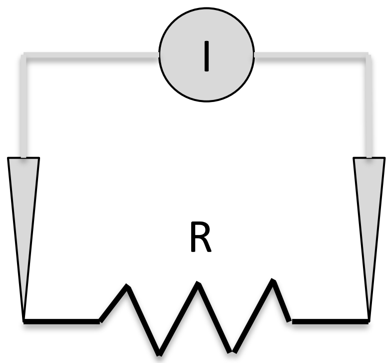

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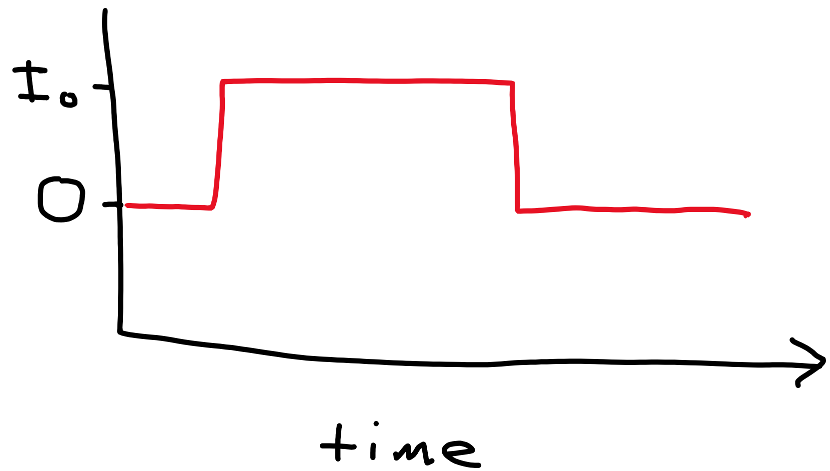

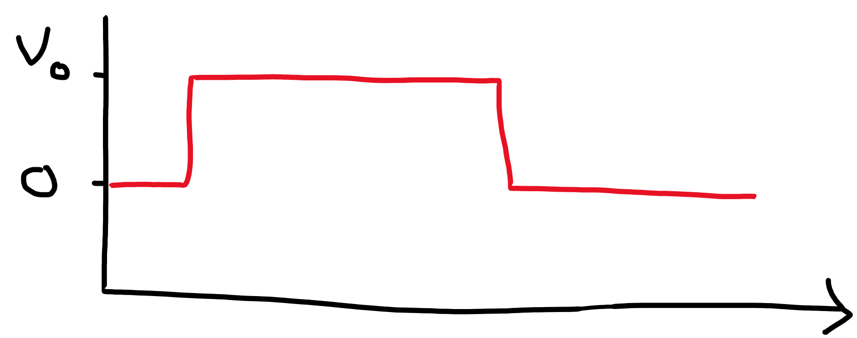

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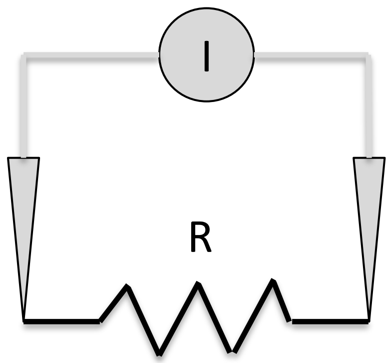

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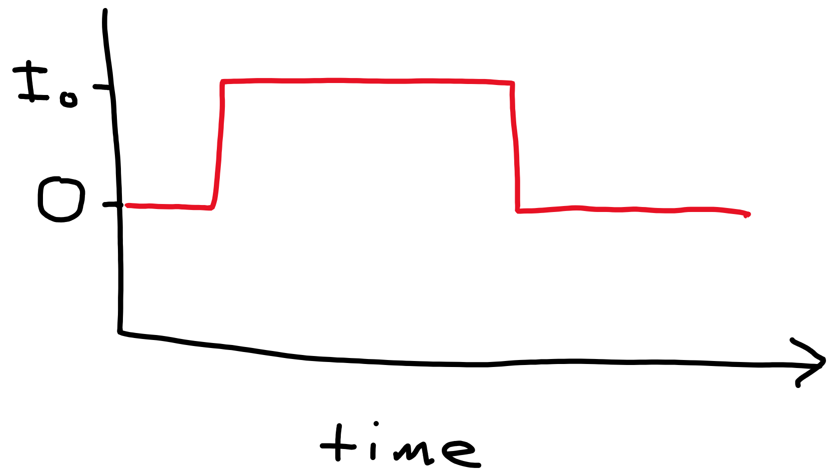
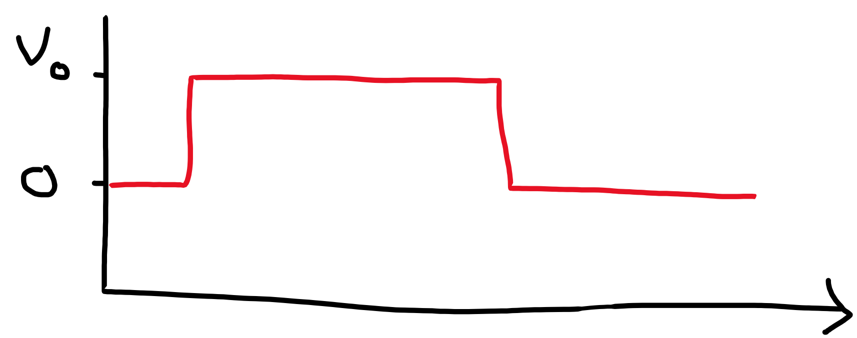
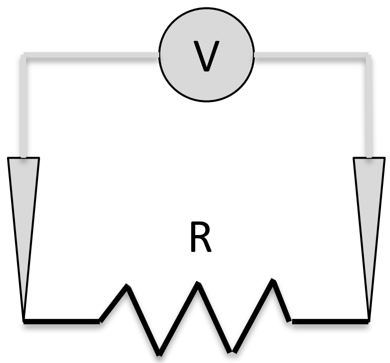


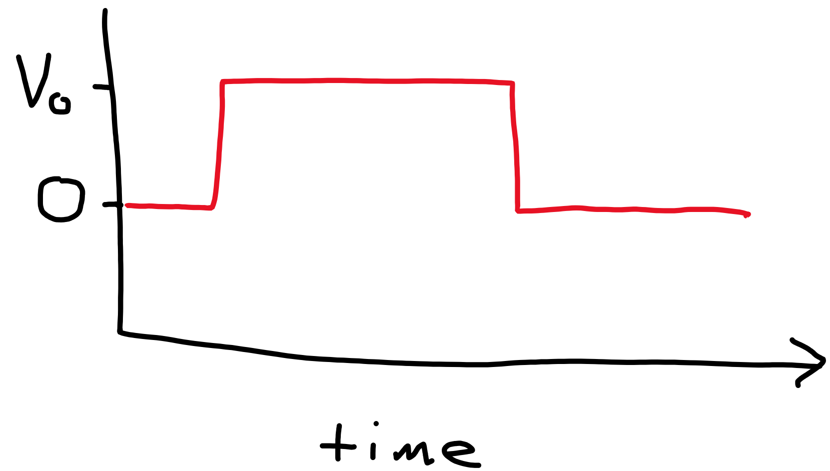
$V_0 = I_0 R$



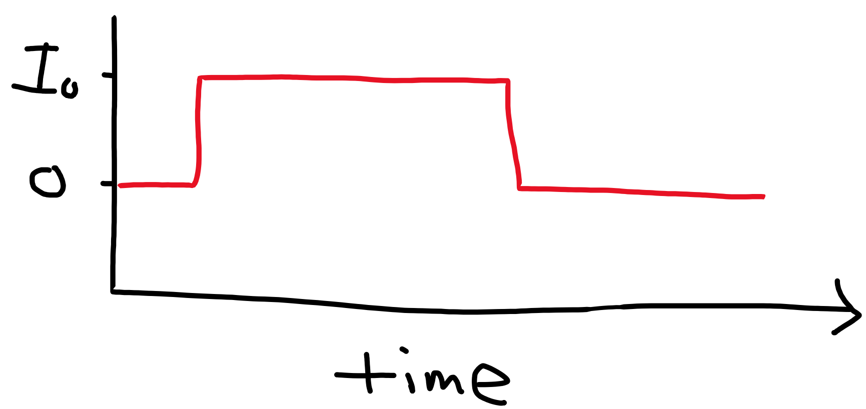
Clamping the voltage across a resistor



I=?



$I_0 = V_0/R$



Capacitance

Simple capacitor:

- Two parallel plate conductors of area A
- Conductors are separated by an insulator of thickness d and dialectric constant ε ($CV^{-1}m^{-1}$)
- Where ε_o is the natural constant

$$C = \frac{\varepsilon \varepsilon_o A}{d}$$

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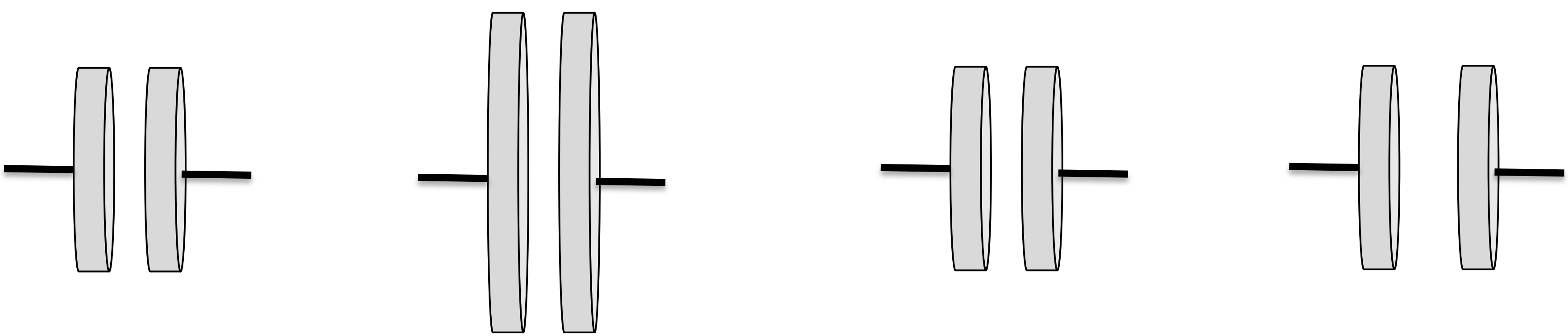

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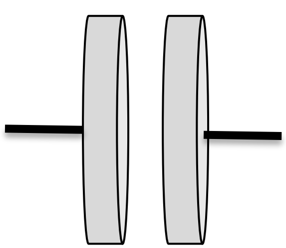
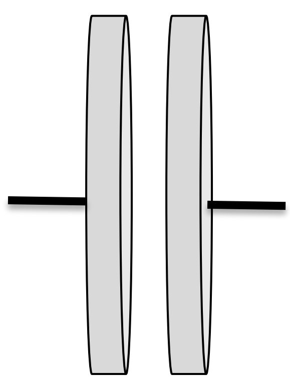
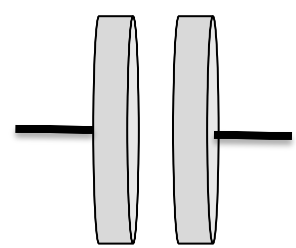
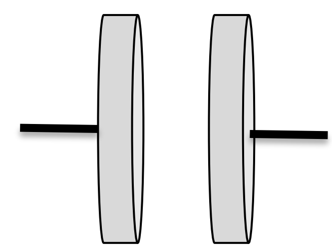


$C_1 < C_2$







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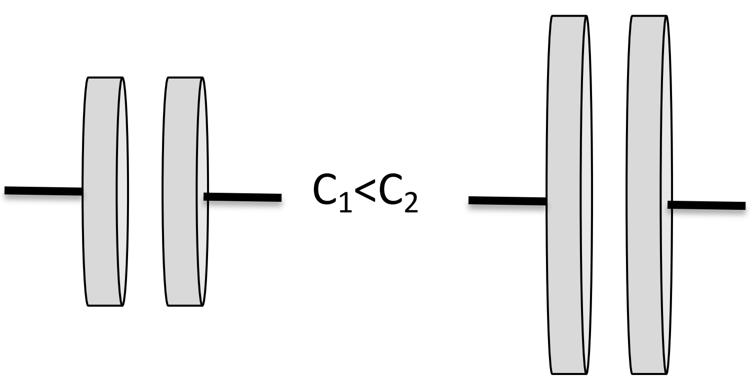
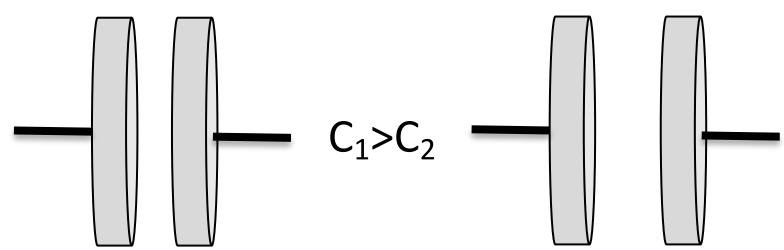




Capacitance

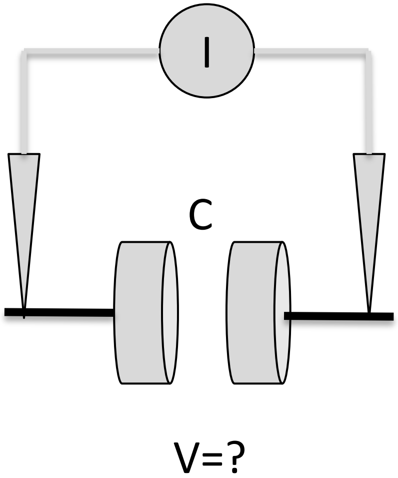
$$C = \frac{Q}{V}$$

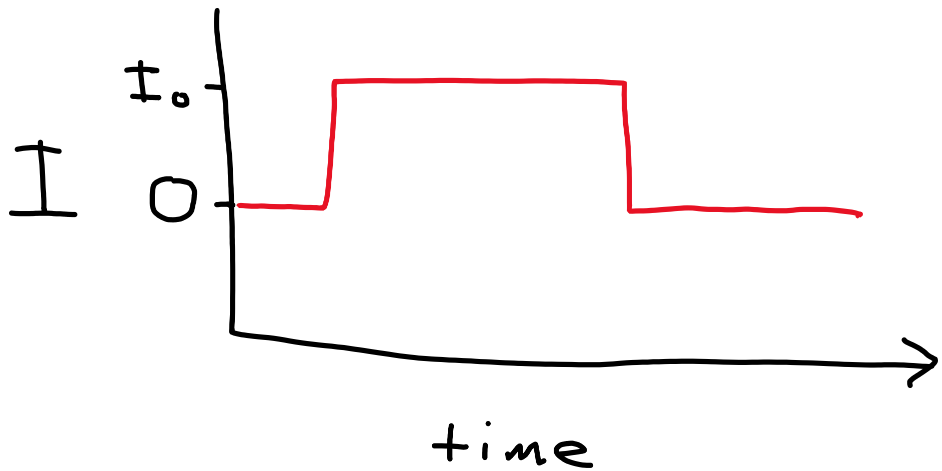
- C is capacitance (in farads, F)
- Q is charge (in coulombs, C)

$$\frac{dV}{dt} = \frac{I}{C}$$

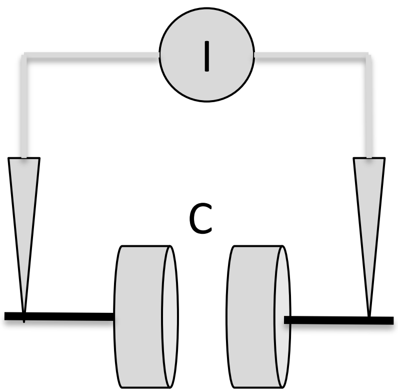
- Remember that $I = dQ/dt$

Injecting current across a capacitor

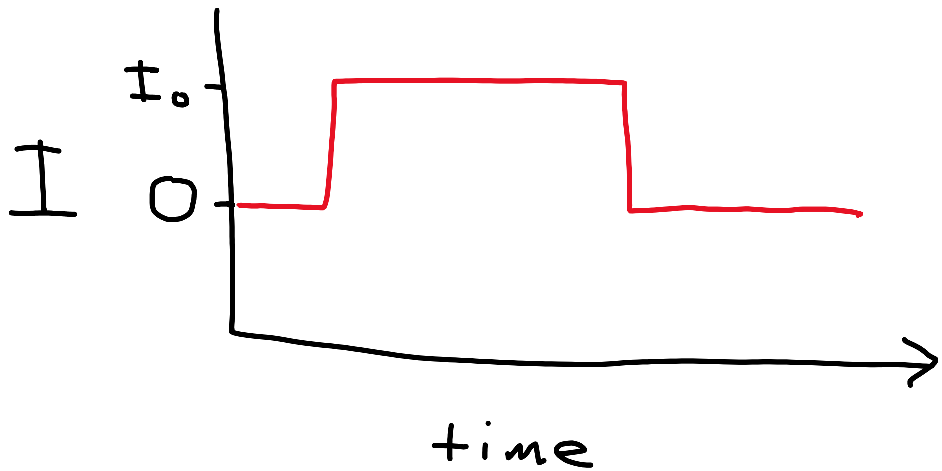




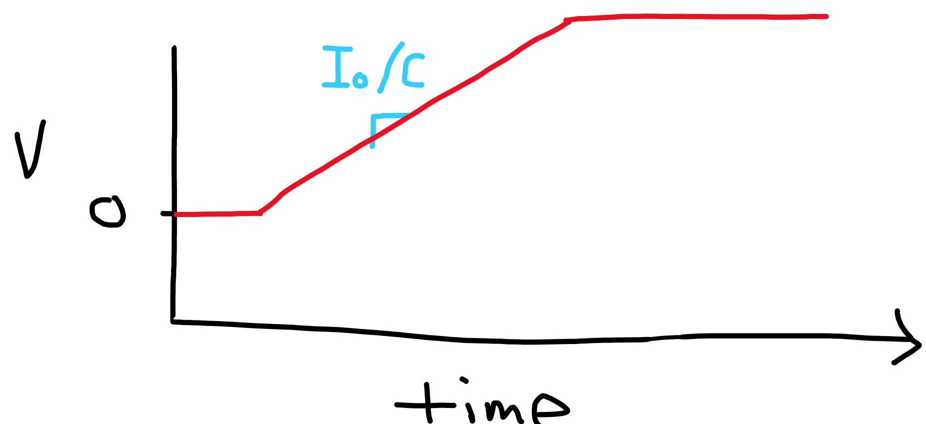
Injecting current across a capacitor



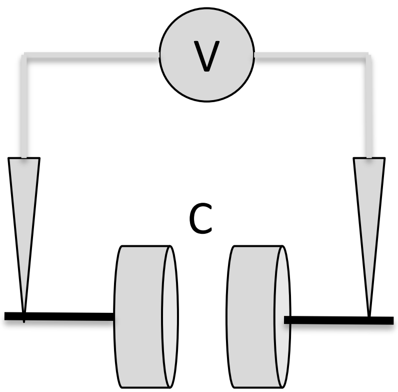
V=?

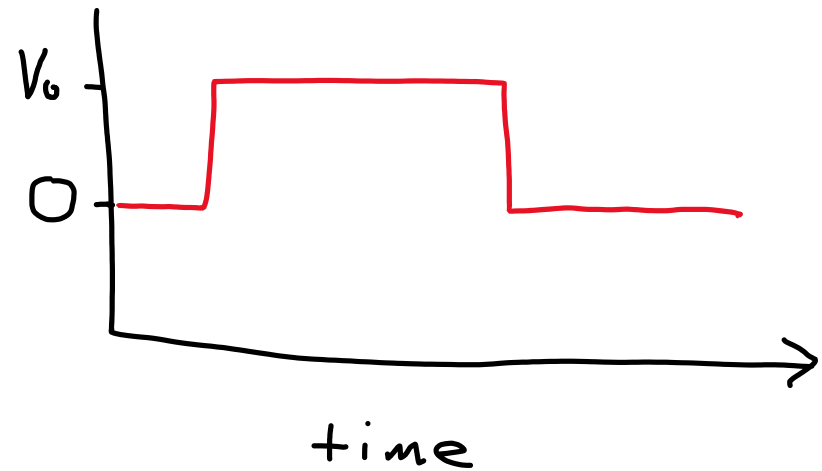


$dV/dt=I_0/C$



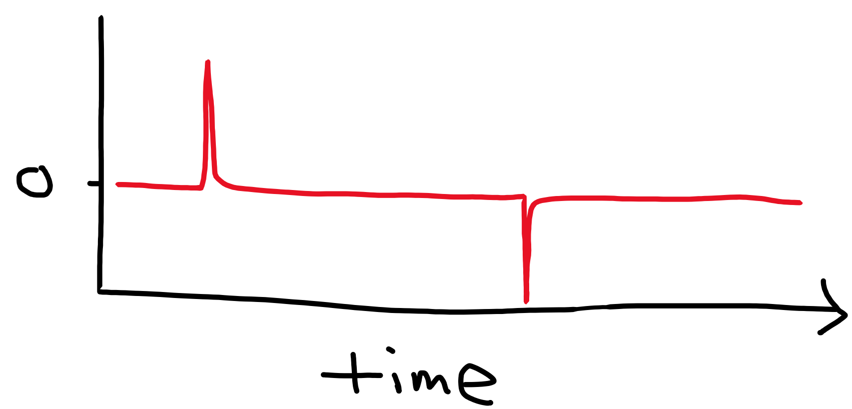
Clamping the voltage across a capacitor



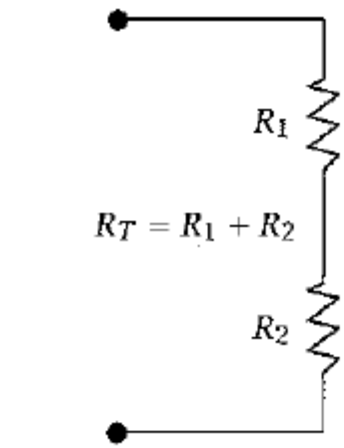


I=?

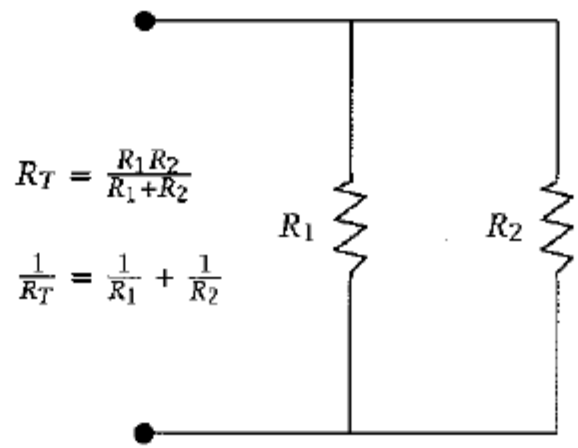
I= C(dV/dt)



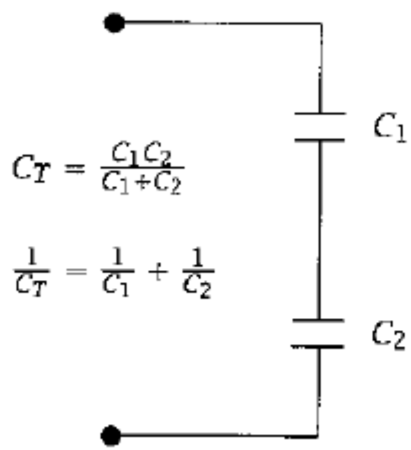
Lumped resistance and capacitance



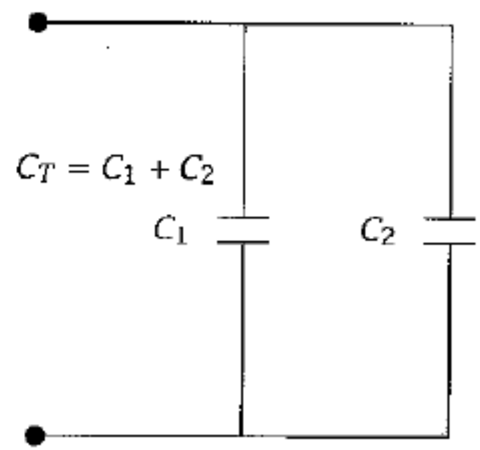
Resistances in Series



Resistances in Parallel

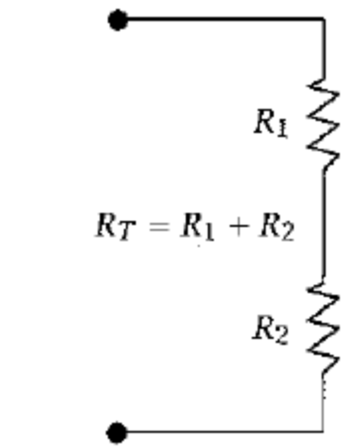


Capacitors in Series



Capacitors in Parallel

Lumped resistance and capacitance



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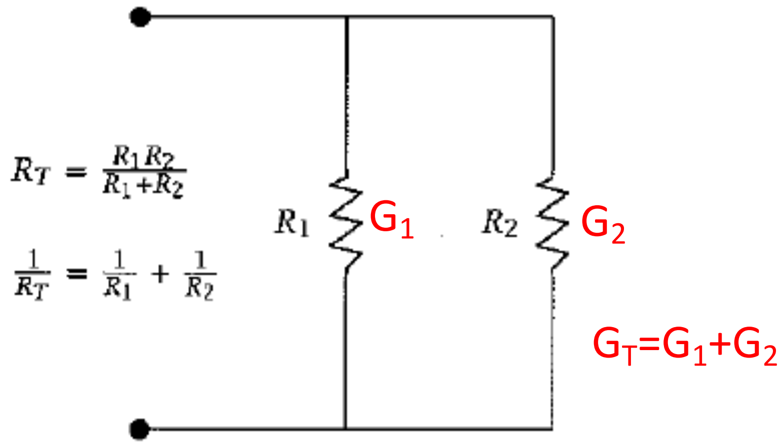

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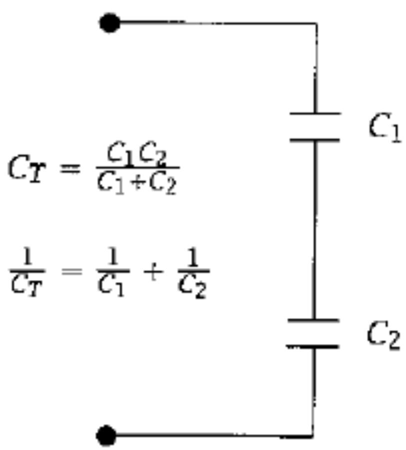

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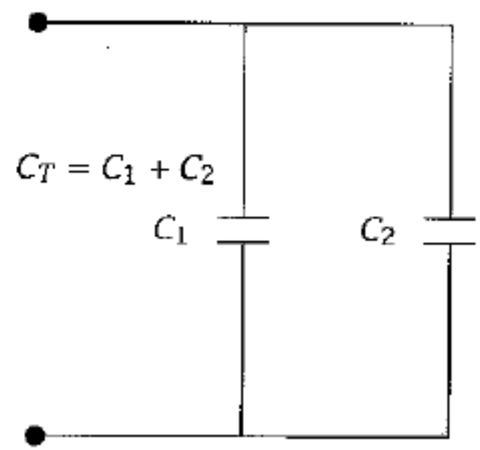
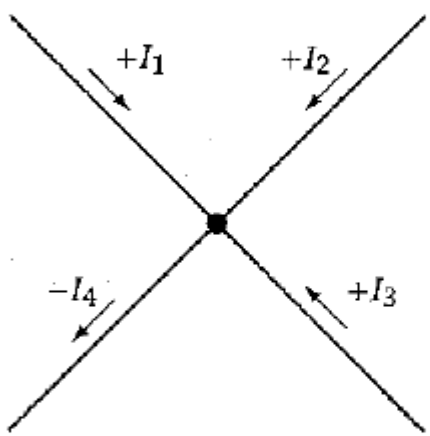


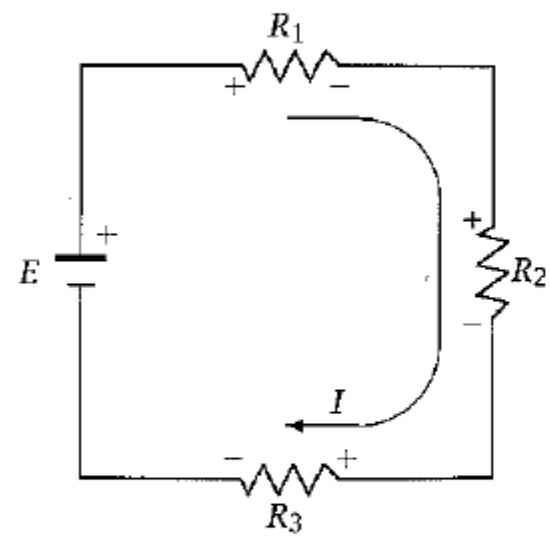
Capacitors in Parallel

Kirchhoff’s Laws

1. Current: Conservation of Charge
2. Voltage: Conservation of Current



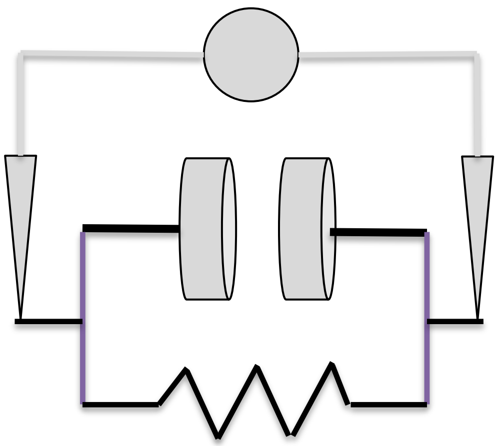
$$I_1 + I_2 + I_3 - I_4 = 0$$



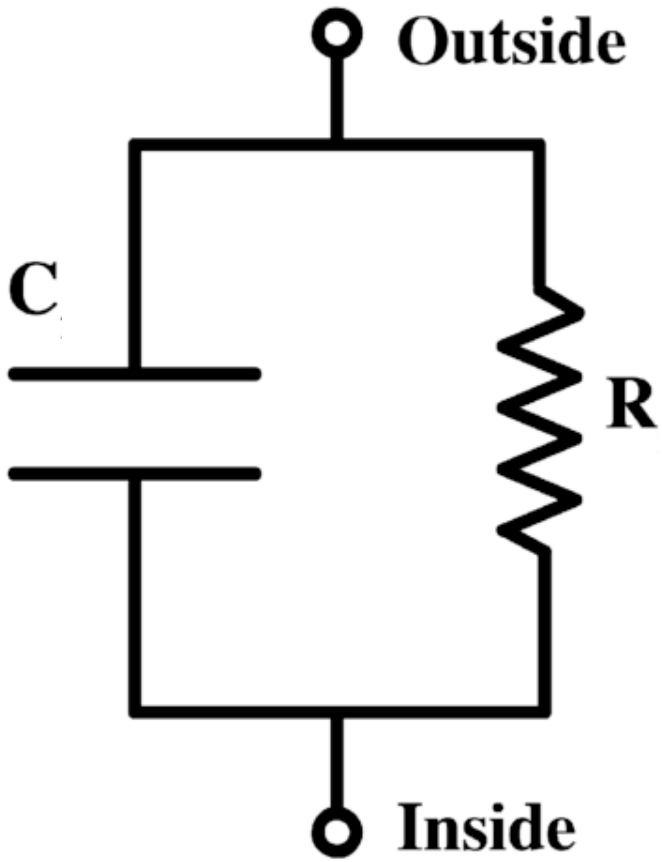
$$E - IR_1 - IR_2 - IR_3 = 0$$

Figure from Foundations of Cellular Neurophysiology Appendix A

Resistors and Capacitors



R and C in parallel (RC circuit)



$$I = C\frac{dV}{dt} + \frac{V}{R}$$

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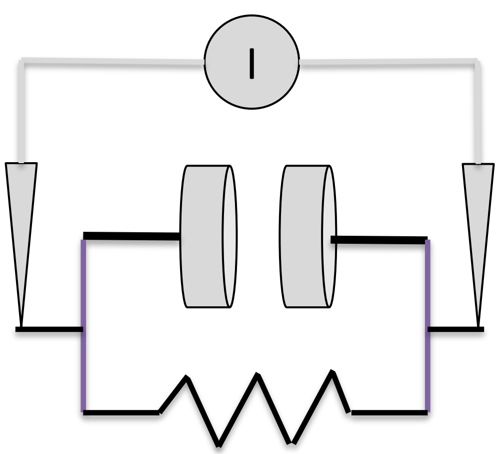
One simple solution: Discharging an RC circuit

$$I = C\frac{dV}{dt} + \frac{V}{R}$$

V=V_o at t=0 and I=0



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$$I = C\frac{dV}{dt} + \frac{V}{R}$$

$V=V_o$ at $t=0$ and $I=0$

$$0 = C\frac{dV}{dt} + \frac{V}{R}$$

$$-\frac{V}{R} = C\frac{dV}{dt}$$

$$-\frac{1}{RC}\int dt = \int \frac{1}{V}\, dV$$

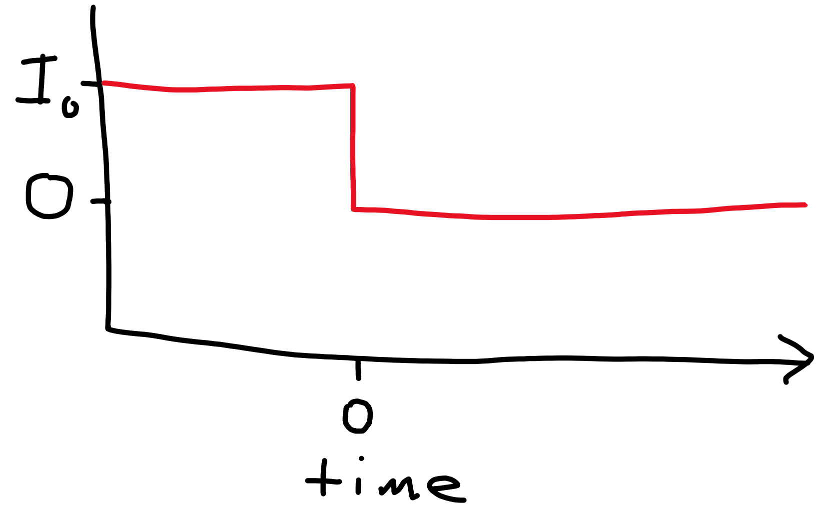
$$-\frac{1}{RC}t + C = \ln V$$

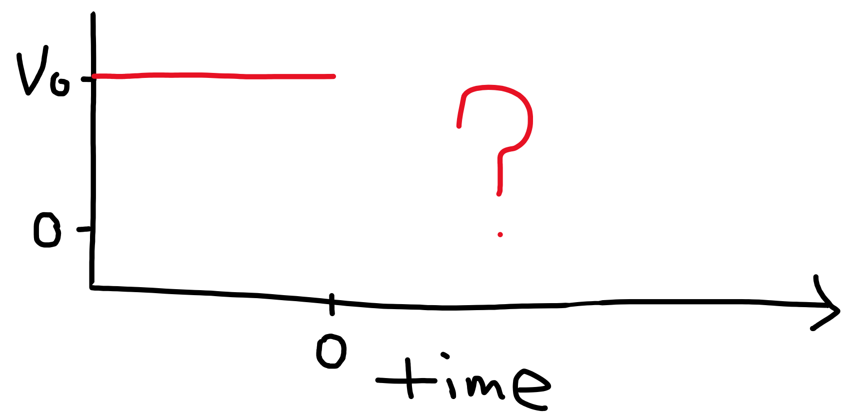
$$e^{-\frac{t}{RC}+C} = V$$

$$V = V_0 e^{-\frac{t}{RC}}$$

One simple solution: Discharging an RC circuit

$$V = V_0 e^{-\frac{t}{RC}}$$

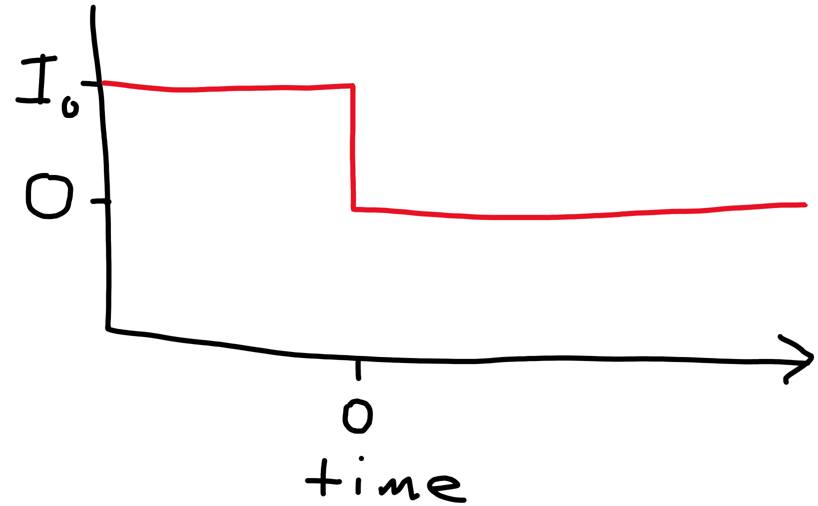


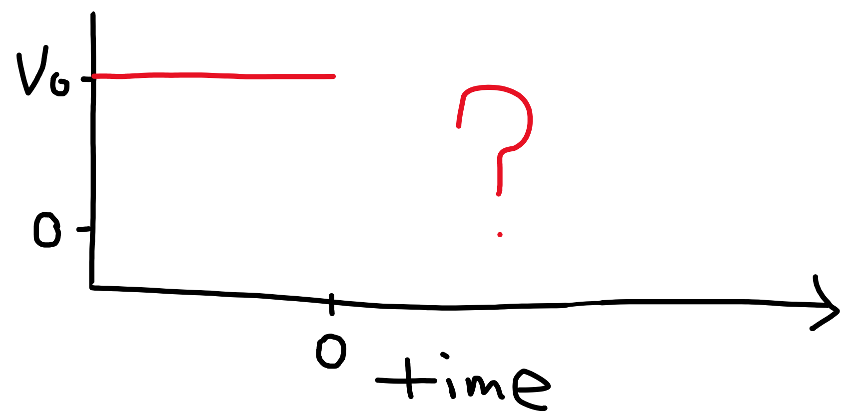


One simple solution: Discharging an RC circuit

$V = V_0 e^{-\frac{t}{RC}}$

- *When t=0, V*=V_0
- *When* t=RC=τ_m
  V= $V_0 e^{-1}$=0.368V_0





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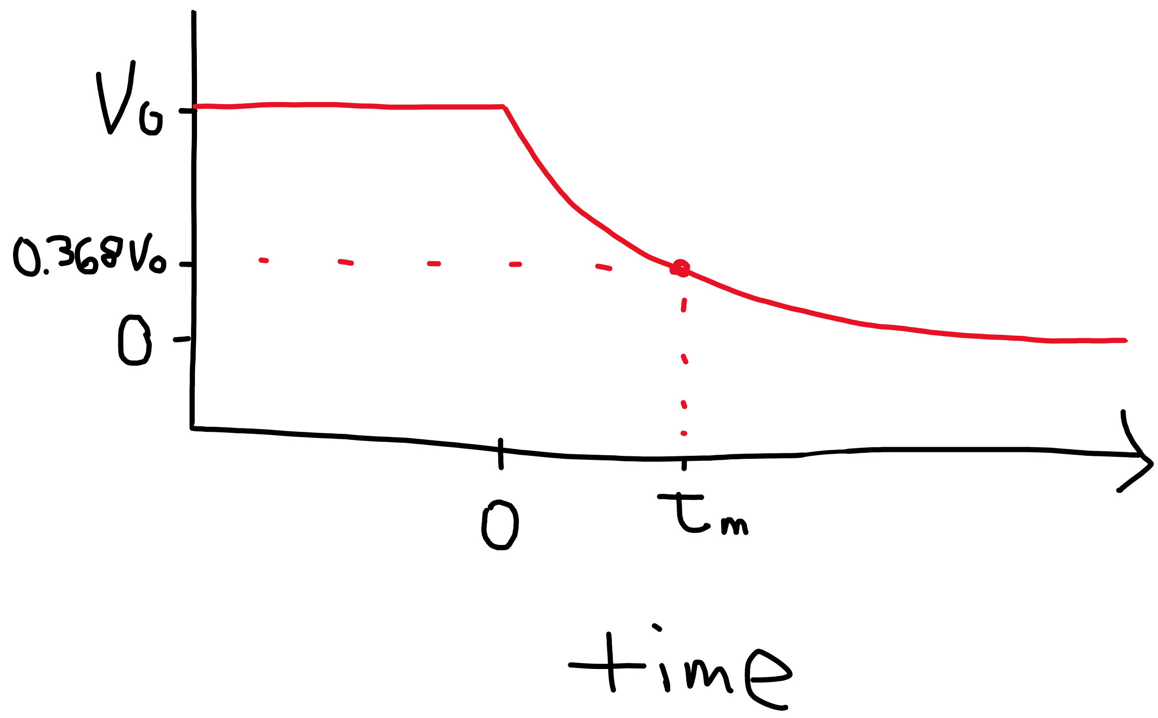

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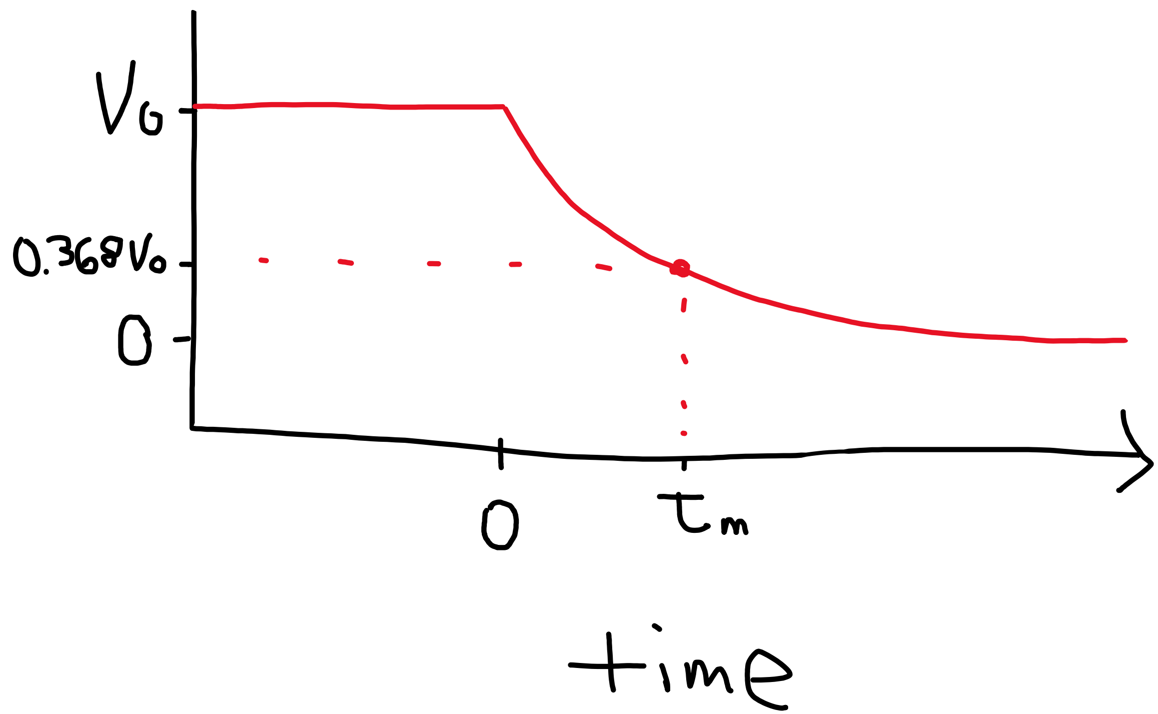
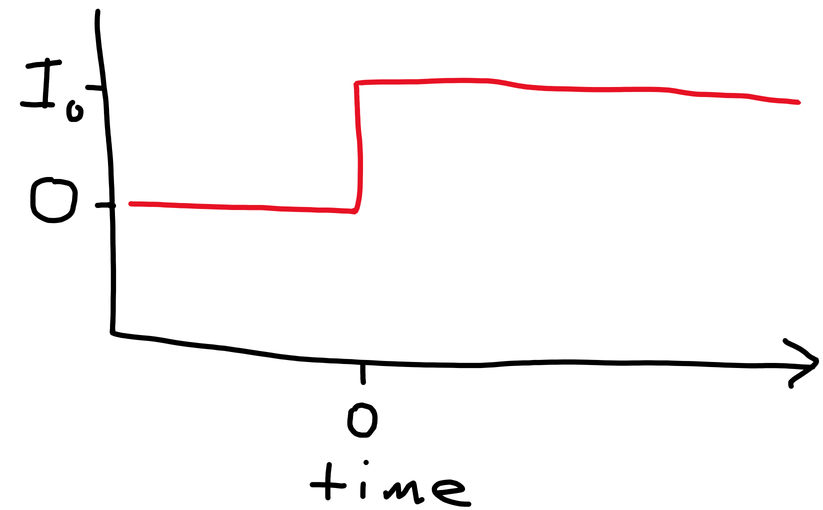
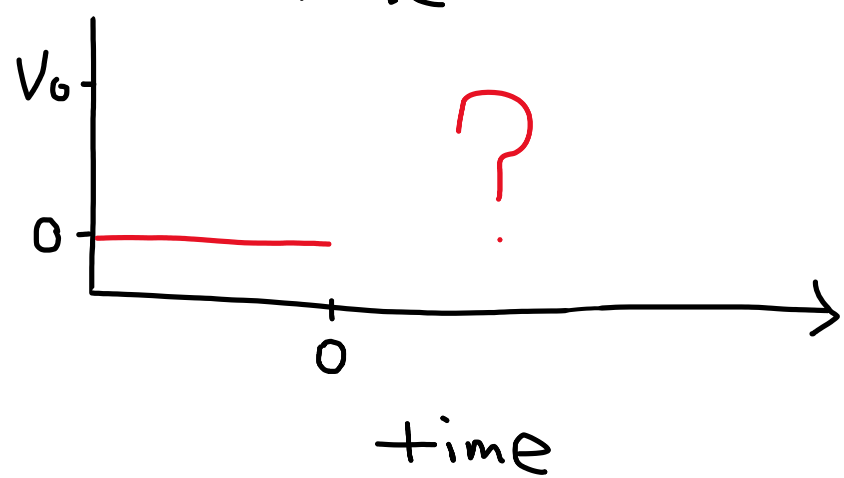


The time constant $\boldsymbol{\tau}_m$ = RC
Voltage follows an exponential decay.
Every $\boldsymbol{\tau}_m$ seconds the voltage becomes 1/*e* (0.368) of its previous value.

One simple solution: Charging an RC circuit

$$V = V_0\left(1 - e^{-\frac{t}{RC}}\right)$$





One simple solution: Charging an RC circuit

$$V = V_0\left(1 - e^{-\frac{t}{RC}}\right)$$

- *When t=0, V=0*
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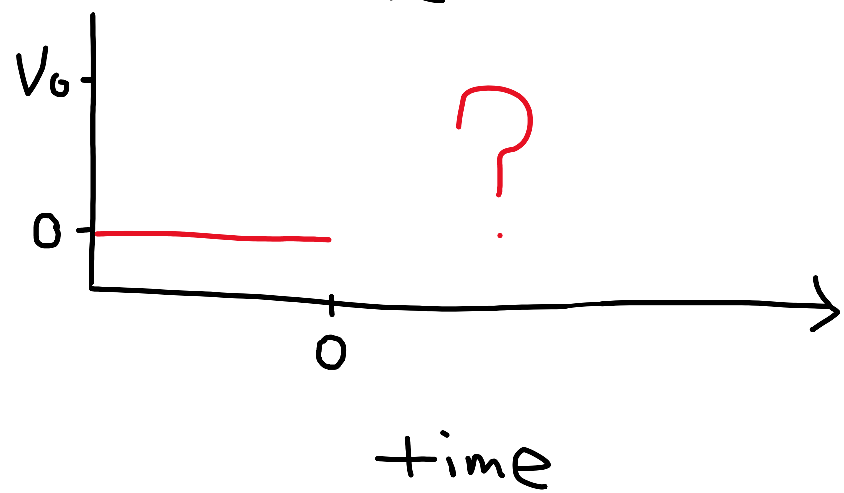
  V= $V_0(1\text{-}e^{-1})$=0.632V_0



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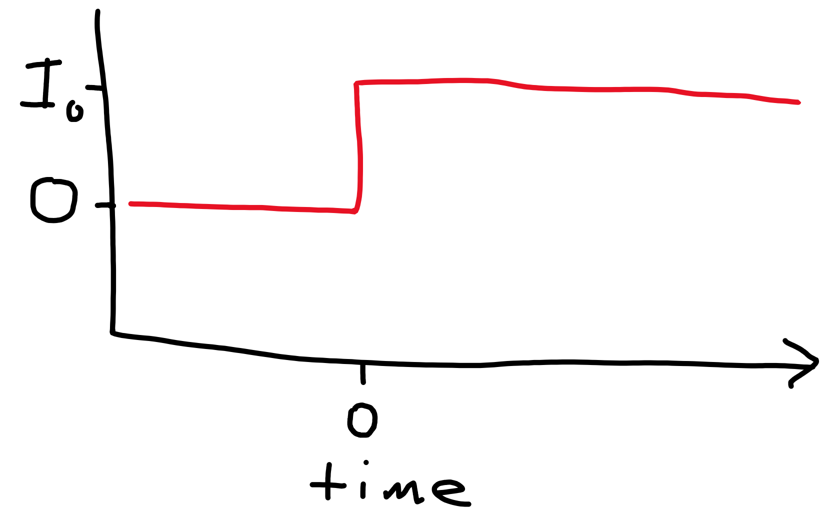
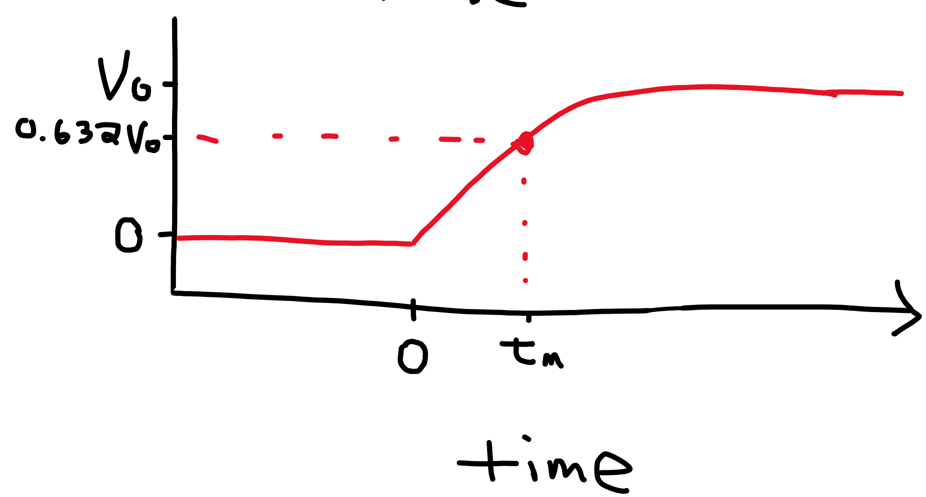
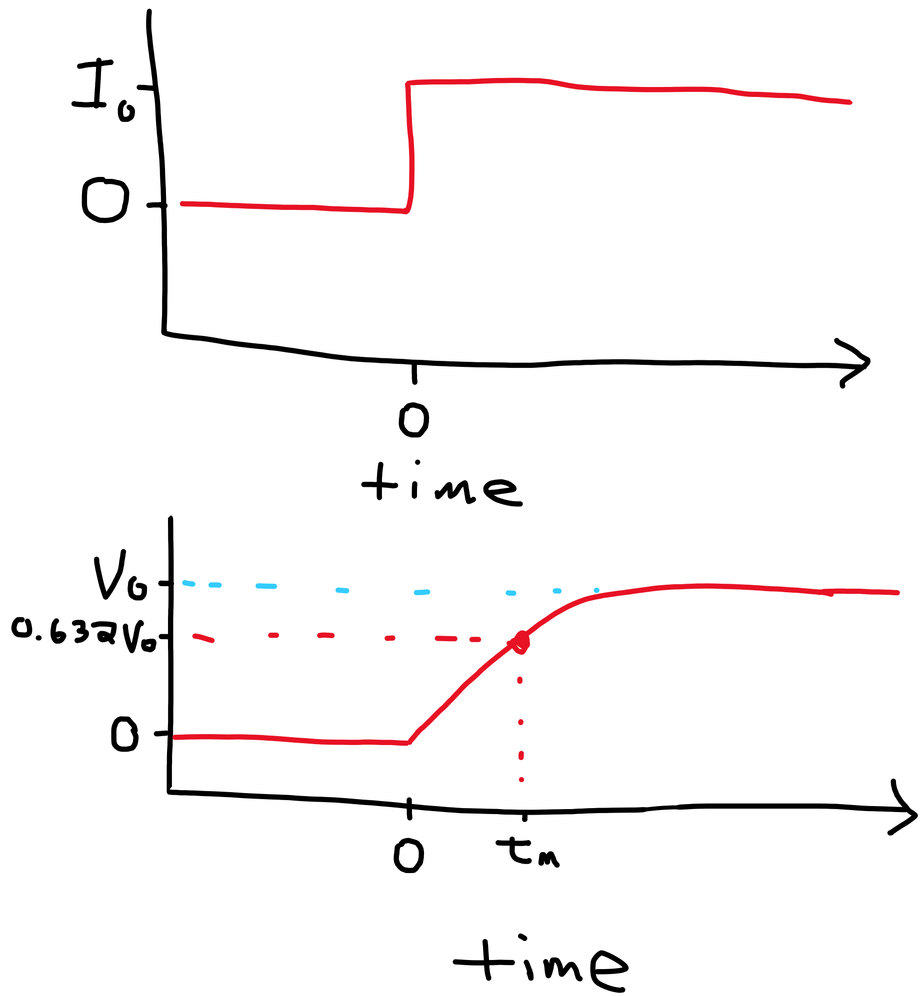




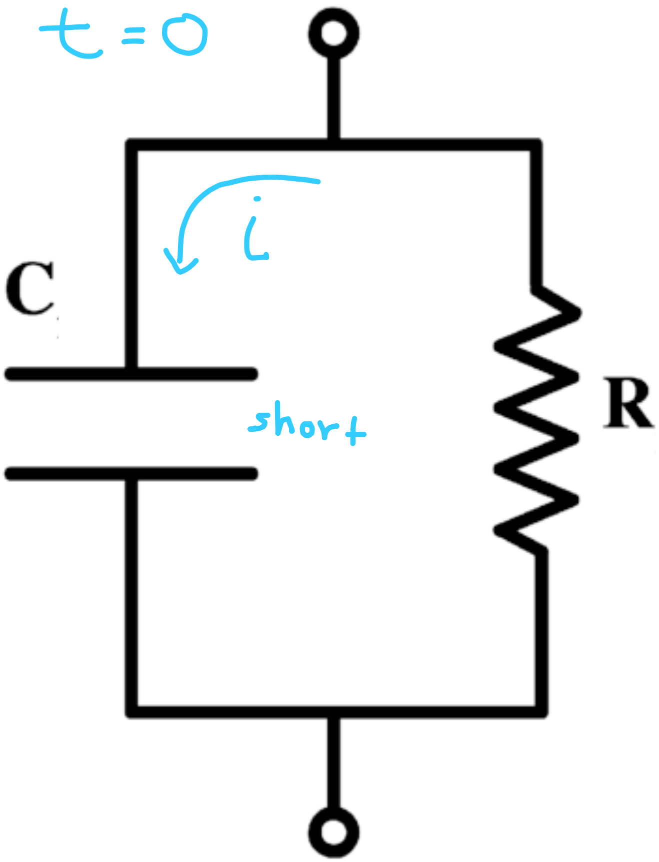
One simple solution: Charging an RC circuit

$$V = V_0\left(1 - e^{-\frac{t}{RC}}\right)$$

- When $t=0$, $V=0$
- When $t=RC=\tau_m$
  $V= V_0(1-e^{-1})=0.632V_0$
- When t>>0 (steady state)
  $V=V_0=I_0R$



R and C in parallel (RC circuit)



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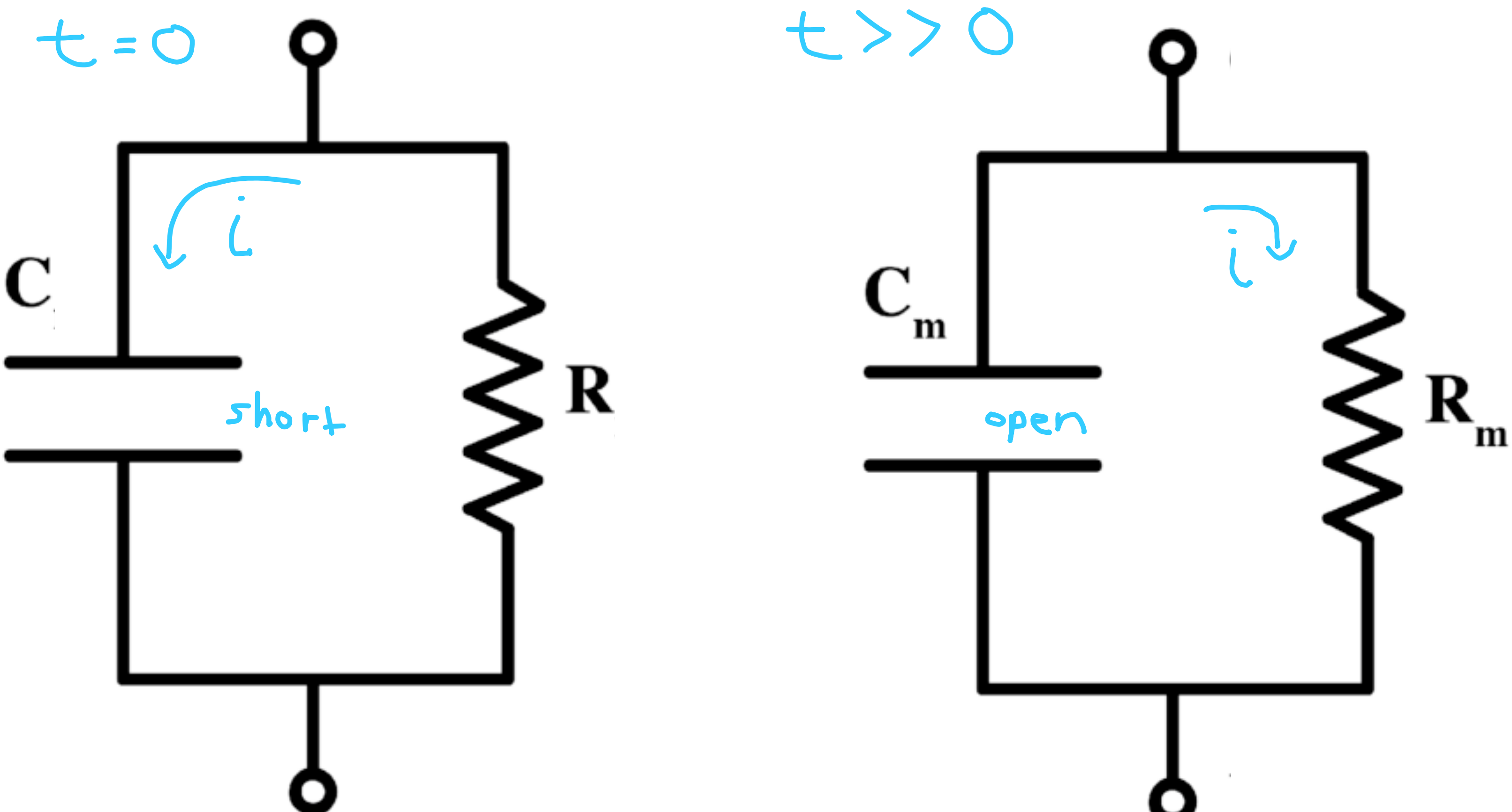

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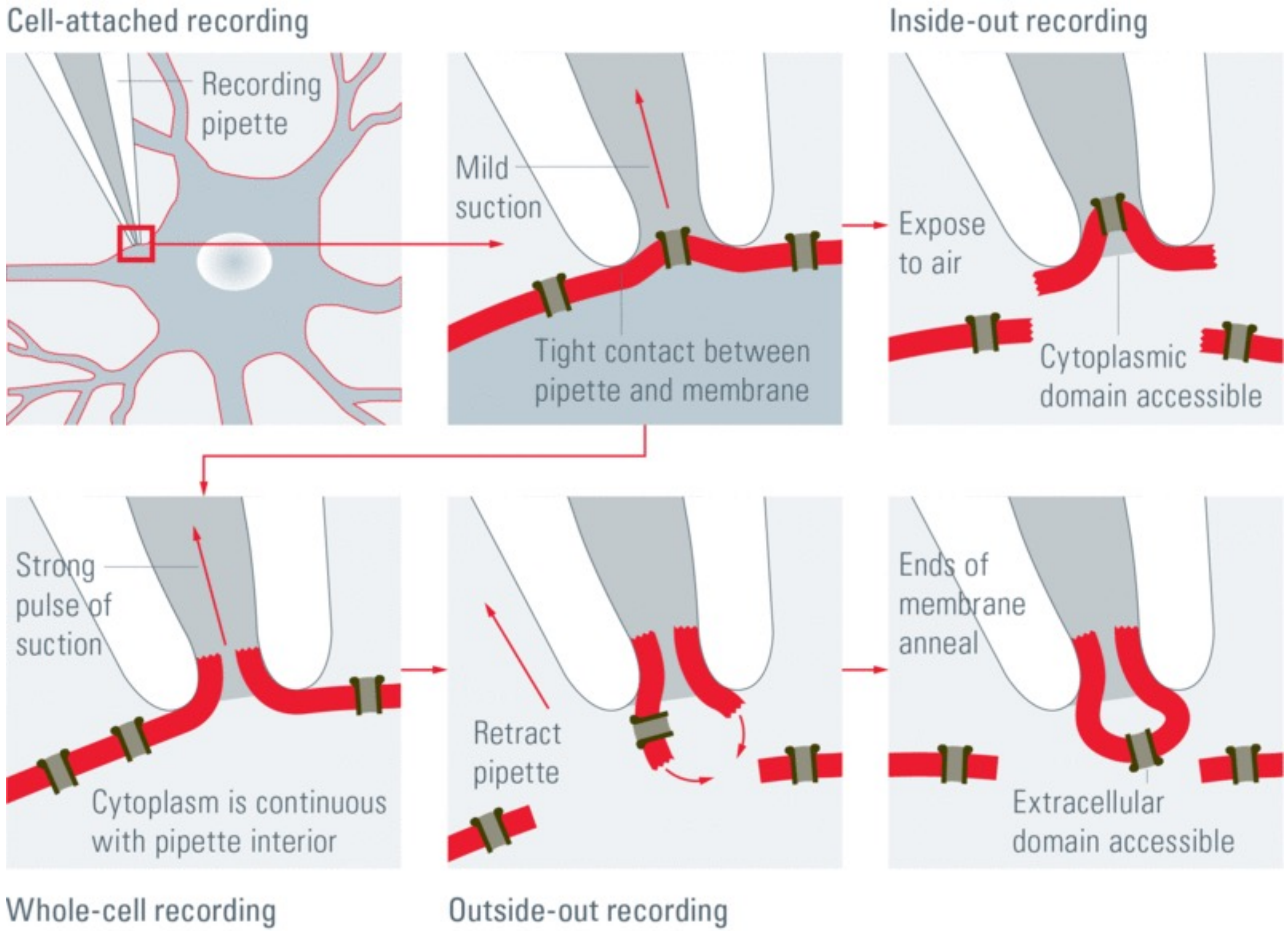
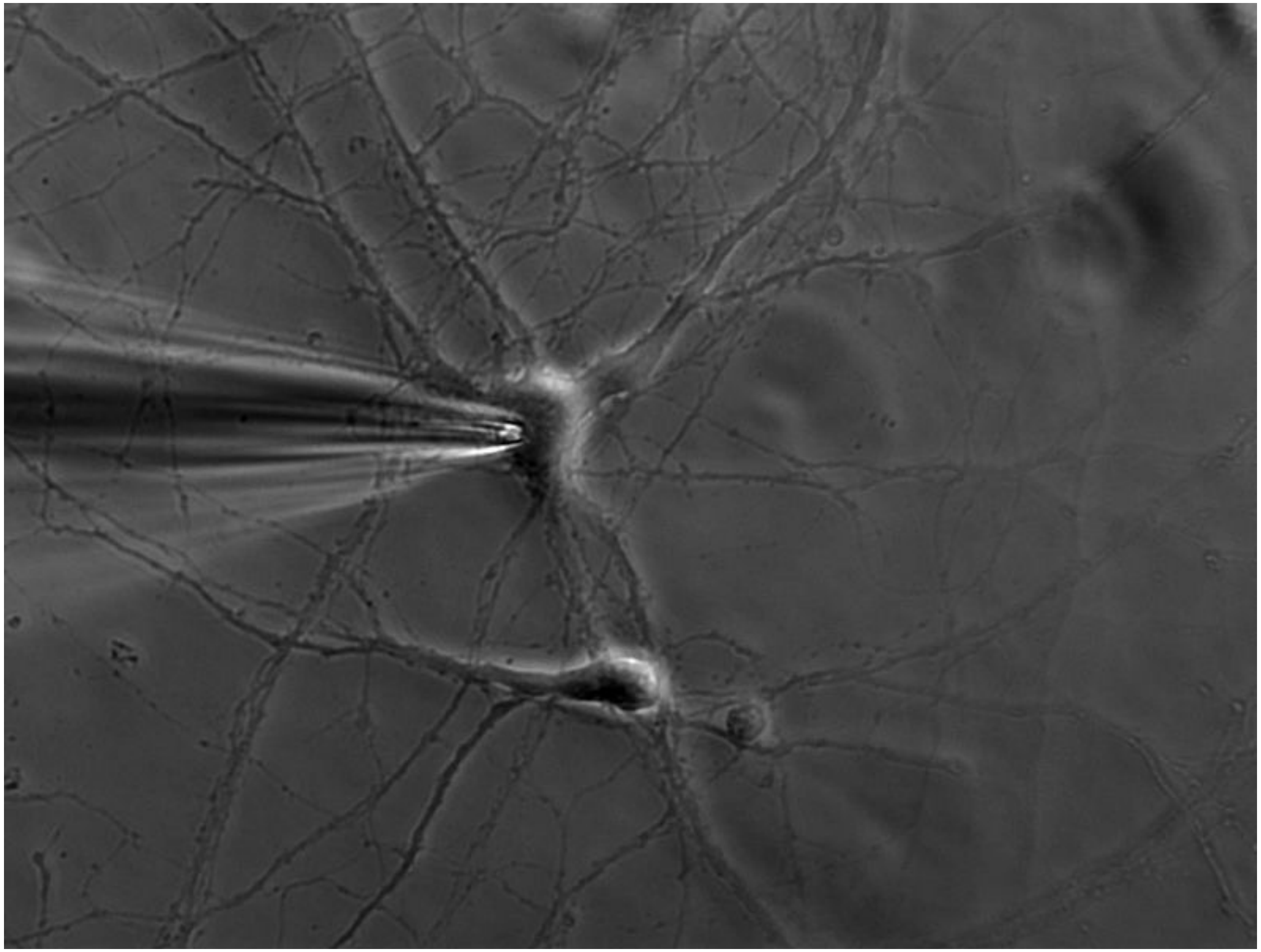
Acquiring neural data

Whole-cell, patch-clamp electrophysiology

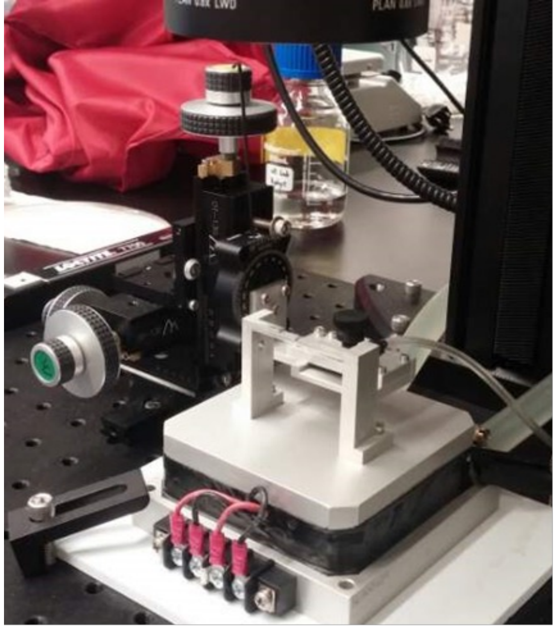


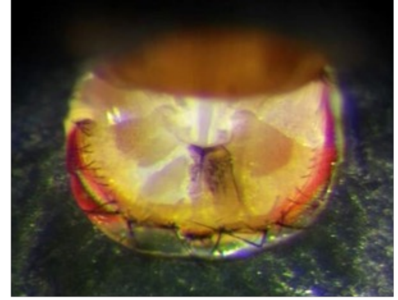
https://www.leica-microsystems.com/science-lab/the-patch-clamp-technique/

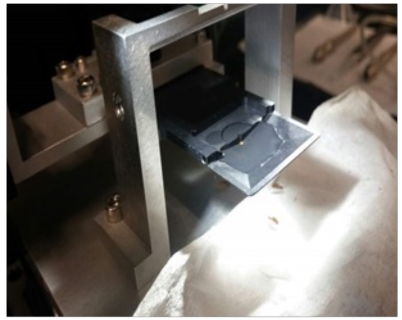
Patching neurons in vitro

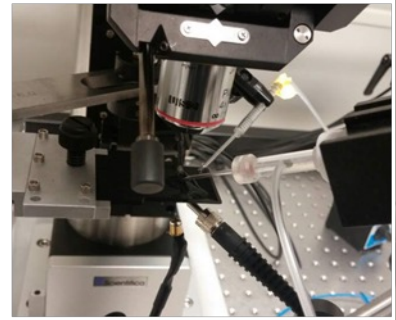


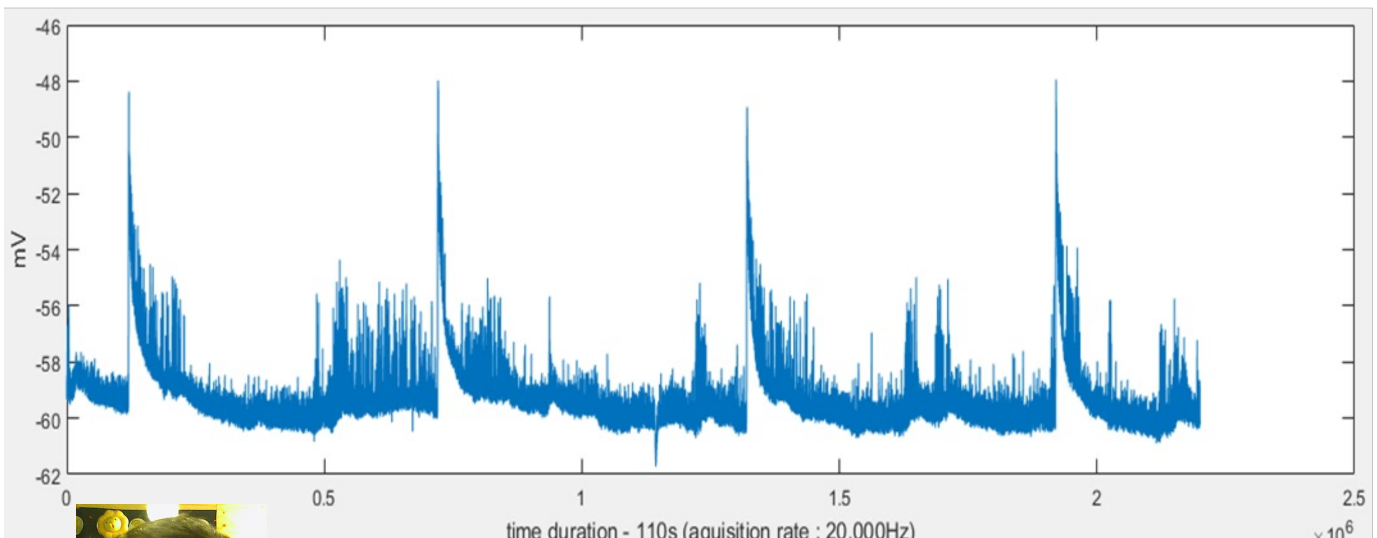
https://www.leica-microsystems.com/science-lab/the-patch-clamp-technique/

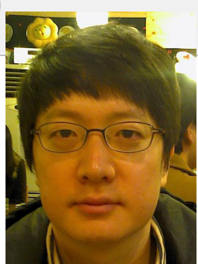










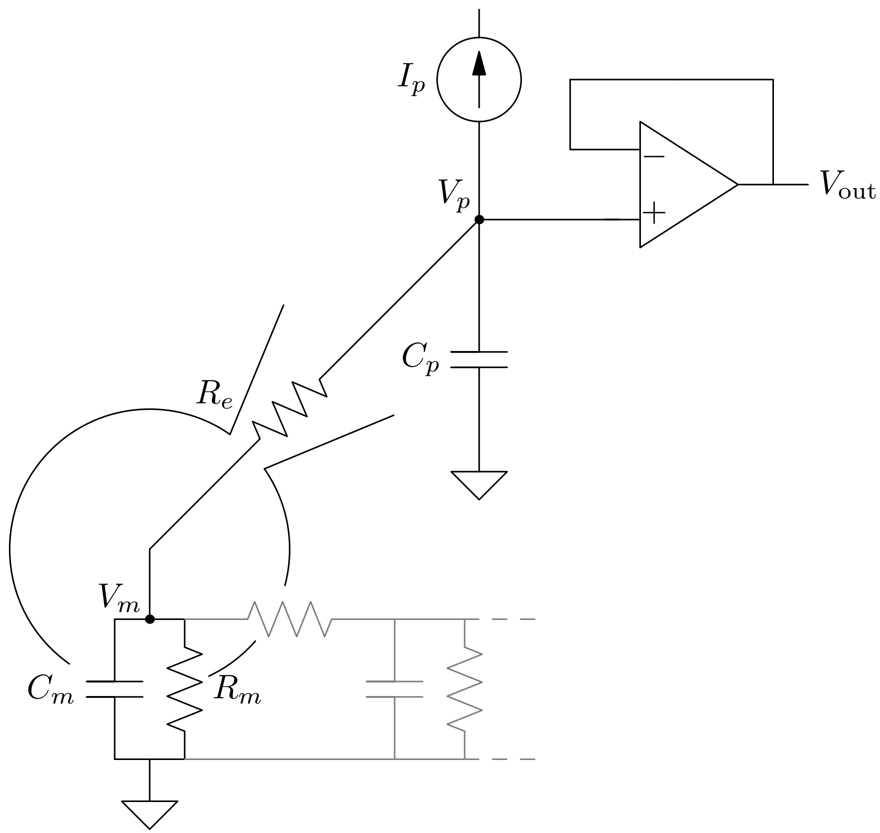


Patching neurons in vivo

HyoJong Jang

DREXEL UNIVERSITY College of Medicine

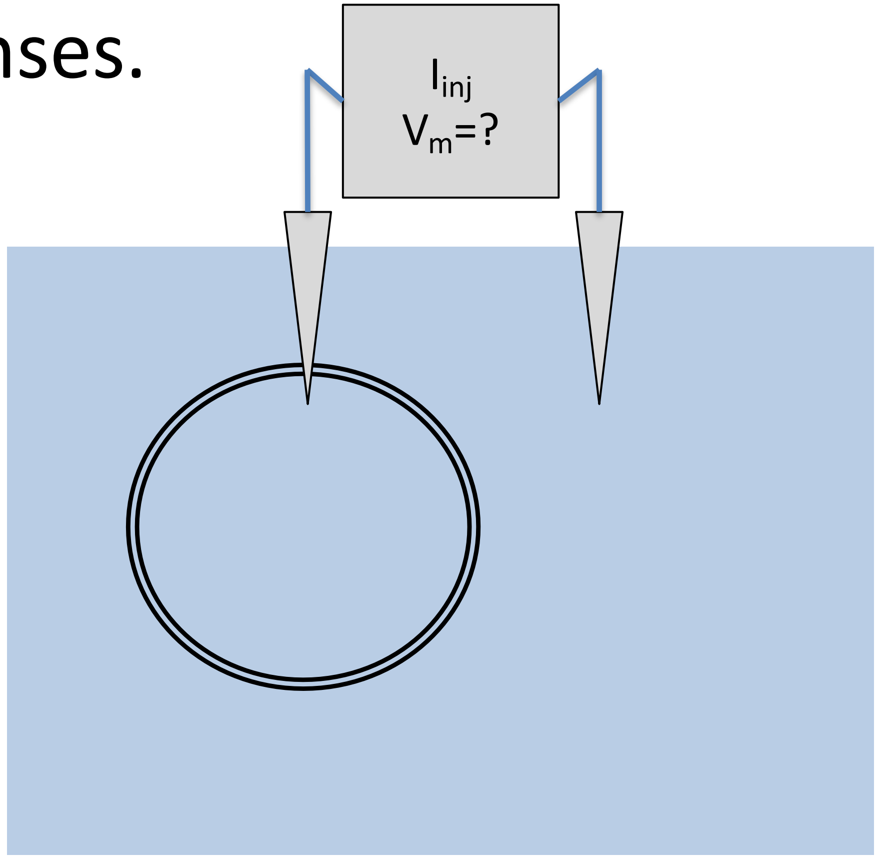
Current clamp uses a "voltage follower" op-amp configuration



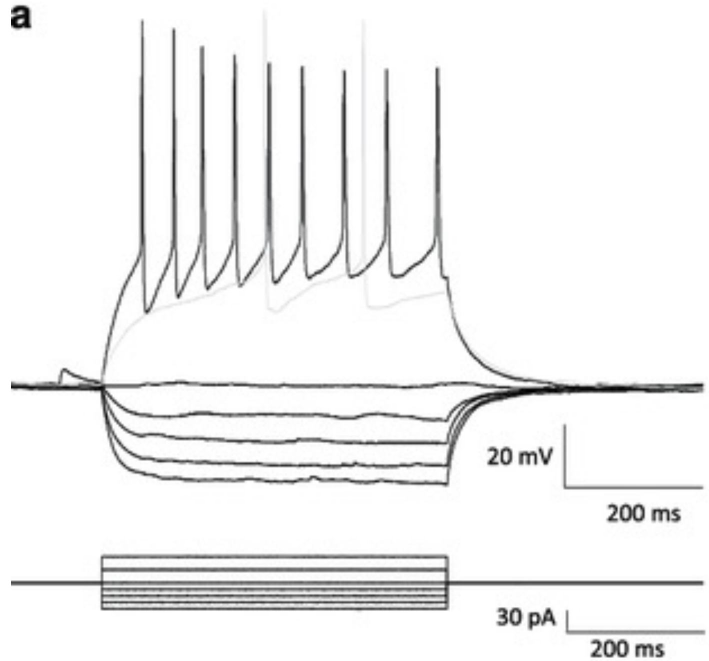
Barbour B, Electronics for electrophysiologists, 2014

Acquiring neural data

- Current clamp – not really "clamping" but actually just injecting current and measuring voltage responses.



Real current injection experiments



-60 mV

V_{rest}=-60mV

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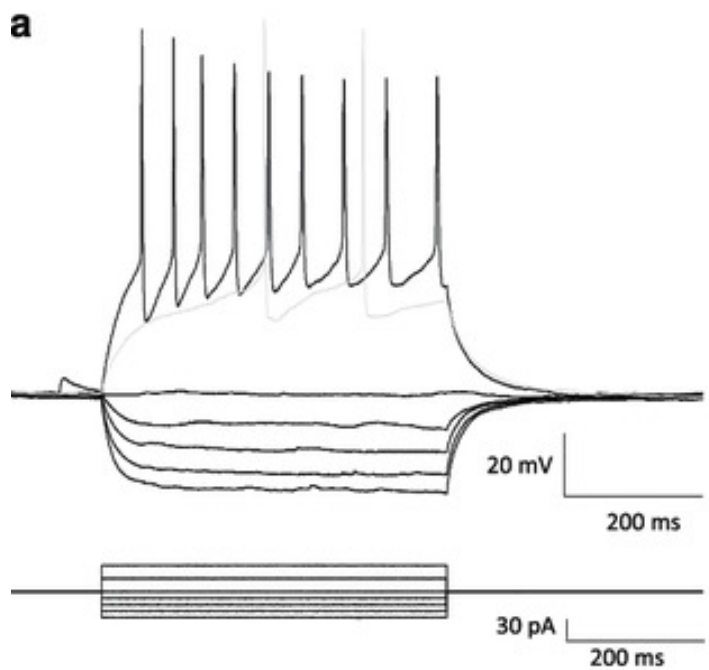
Real current injection experiments

Positive currents
depolarize the membrane



-60 mV

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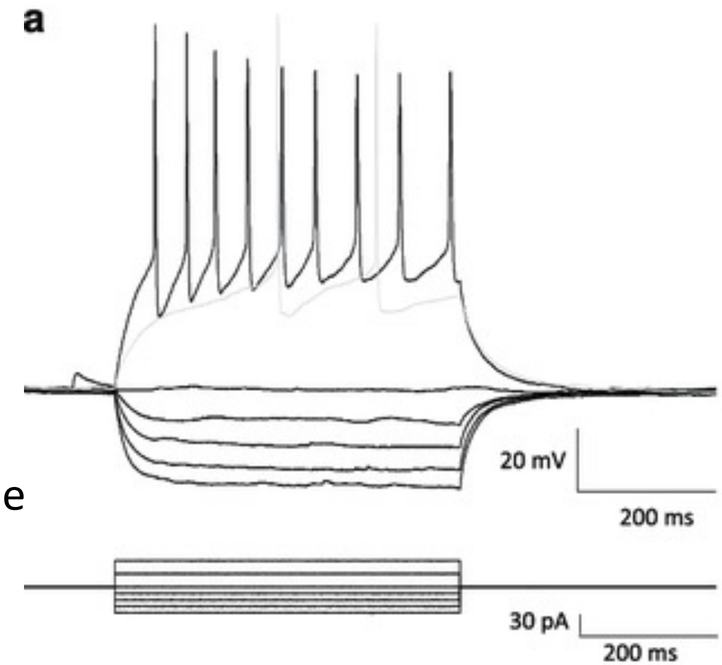
Real current injection experiments



-60 mV

Negative currents **hyperpolarize** the membrane

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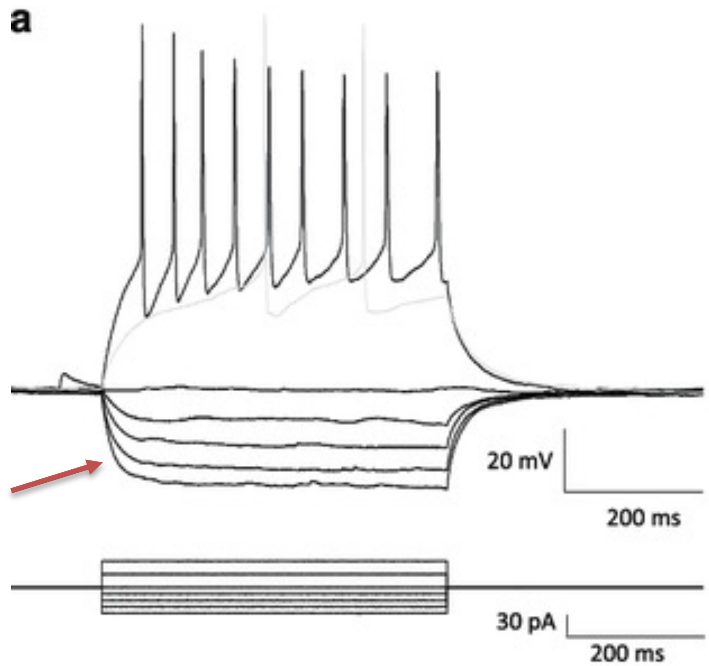
Real current injection experiments



-60 mV

We can model this part
with simple RC circuits

Gunhanlar et al. Molecular Psychiatry 2018

Membrane properties

Neurons have membrane properties that impact electrical signaling:

1. Ions flow across the membrane…

   Membrane resistance, R_m

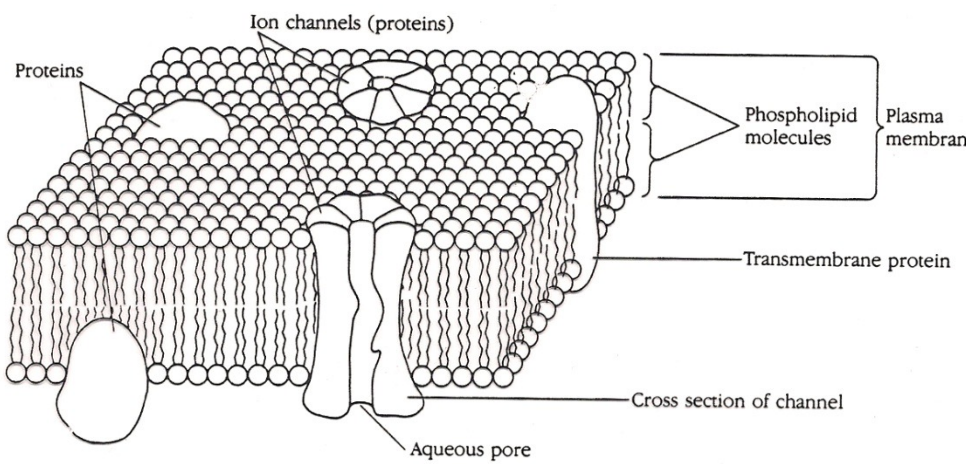
2. Flow of ions induces charge separation…

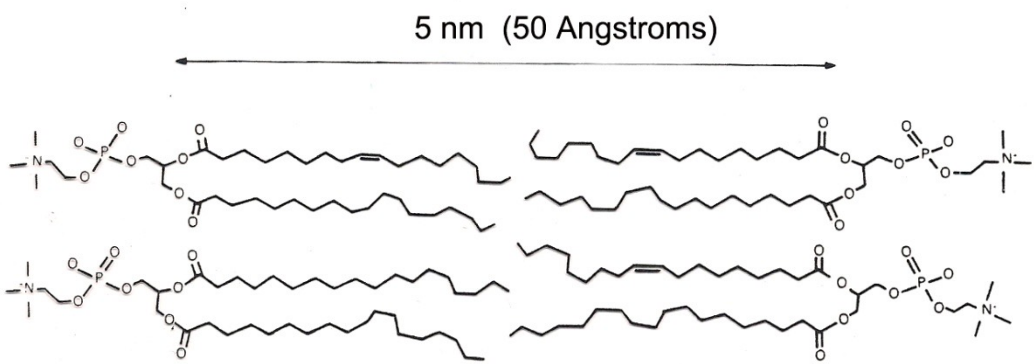
   Membrane capacitance, C_m

3. Ions flow down the length of a process…

   Axial membrane resistance, R_a

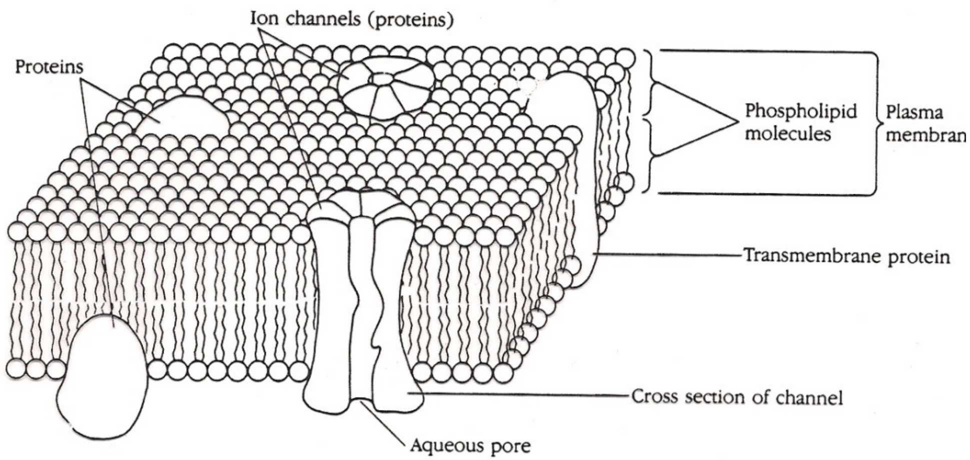
The membrane is a capacitor…





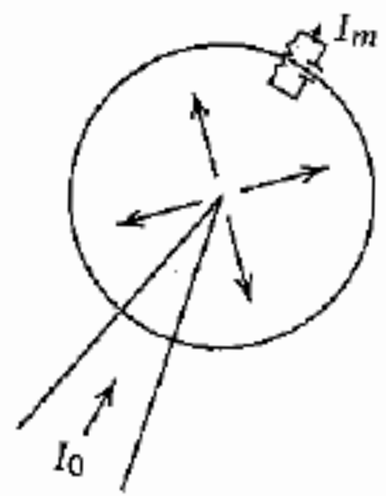
- The cell membrane is an insulator surrounded by a conductor (saline).

… and a resistor



- Membrane resistance is set by channels embedded in the membrane. (Without channels, the resistance would be extremely high, and there would be no way for current to flow across the membrane)

Consider the cell membrane as an RC circuit



$$I_m = \underbrace{C_m \frac{dV_m}{dt}}_{\text{Current from the membrane capacitance}} + \underbrace{\frac{V_m}{R_m}}_{\text{Current from the membrane resistance}}$$

- Current injected will distribute uniformly across the surface
- Current across a unit of area is the **sum** of the current through the capacitor and the resistor

Finite step of current for a time interval 0<T<t, across the membrane:

$$I(t) = C_m \frac{dV_m}{dt} + \frac{V_m}{R_m}$$

$$I(t) = \begin{cases} 0 & t < 0 \\ I_{inj} & 0 < t < T \\ 0 & t > T \end{cases}$$

$$V_m = \begin{cases} 0 & t < 0 \\ I_m R_m \left(1 - e^{-\frac{t}{\tau_m}} \right) & 0 < t < T \\ I_m R_m e^{-\frac{t}{\tau_m}} & t > T \end{cases}$$

Figure from: C. Koch, Biophysics of computation: information processing in single neurons, 2004

Finite step of current for a time interval 0<T<t, across a unit of area of membrane:

$$I(t) = C_m \frac{dV_m}{dt} + \frac{V_m}{R_m}$$

$$I(t) = \begin{cases} 0 & t < 0 \\ I_{inj} & 0 < t < T \\ 0 & t > T \end{cases}$$

$$V_m = \begin{cases} 0 & t < 0 \\ I_m R_m \left(1 - e^{-\frac{t}{\tau_m}}\right) & 0 < t < T \\ I_m R_m e^{-\frac{t}{\tau_m}} & t > T \end{cases}$$

Here, I_m=I_{inj} and V_{ss}=$I_{inj}R_m$

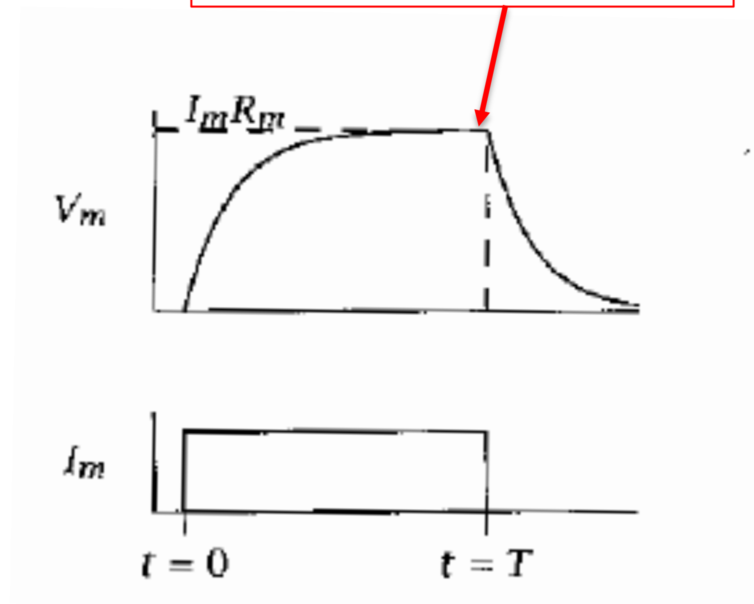


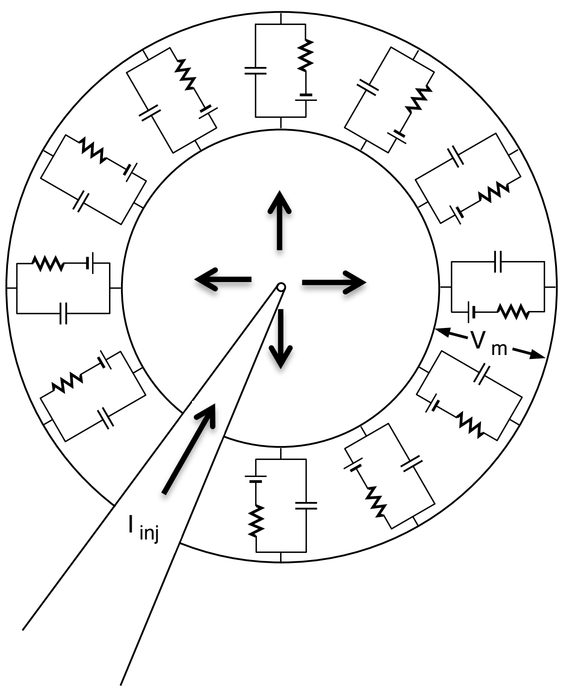
Figure from: C. Koch, Biophysics of computation: information processing in single neurons, 2004

Adding the resting membrane potential

- Our RC model takes into consideration the membrane resistance and capacitance, but how do we incorporate the resting membrane potential?

Adding a voltage source to the RC model

- Model the entire neuron using the RC circuit model
- Use a voltage source to account for V_{rest}



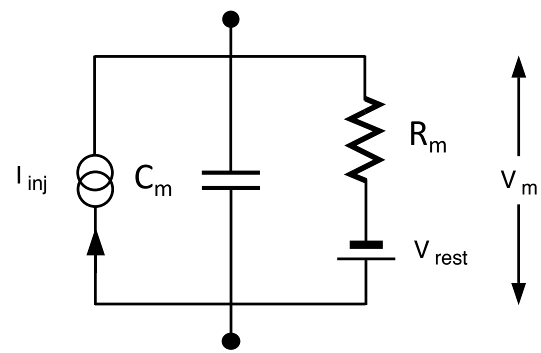
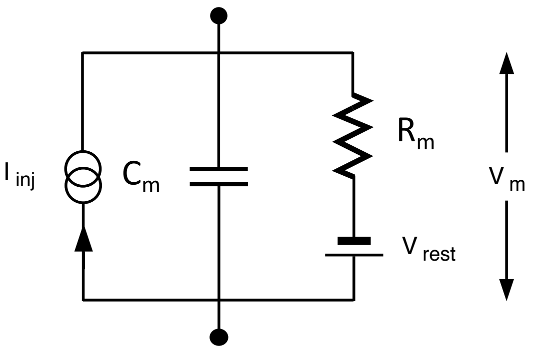


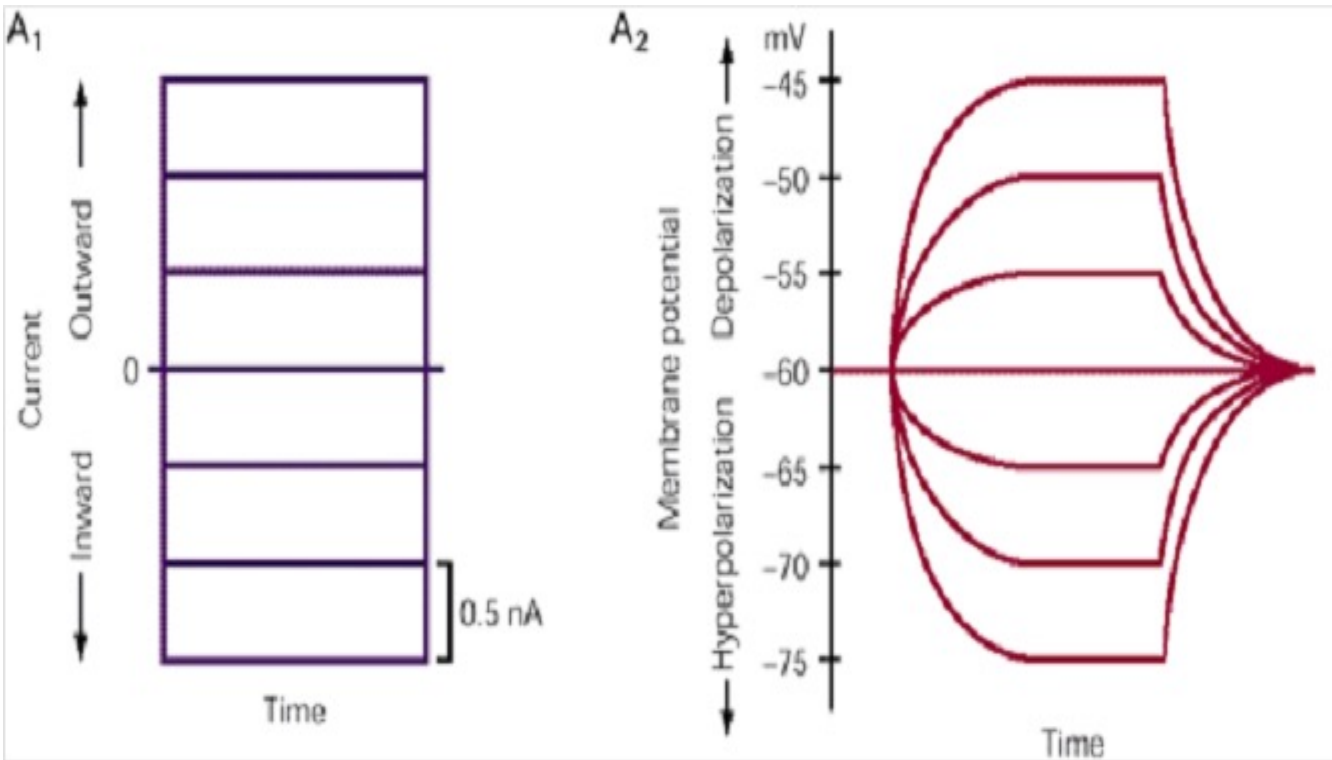
Figure from: C. Koch, Biophysics of computation: information processing in single neurons, 2004

Current equation for isopotential cell



$$I_{inj} = Cm\frac{dV_m}{dt} + \frac{(Vm - Vrest)}{R_m}$$

Current injection across the isopotential cell



Calculating the membrane resistance

- How can you use a current injection step to experimentally measure the membrane resistance for an isopotential cell?

Isopotential cell: membrane resistance

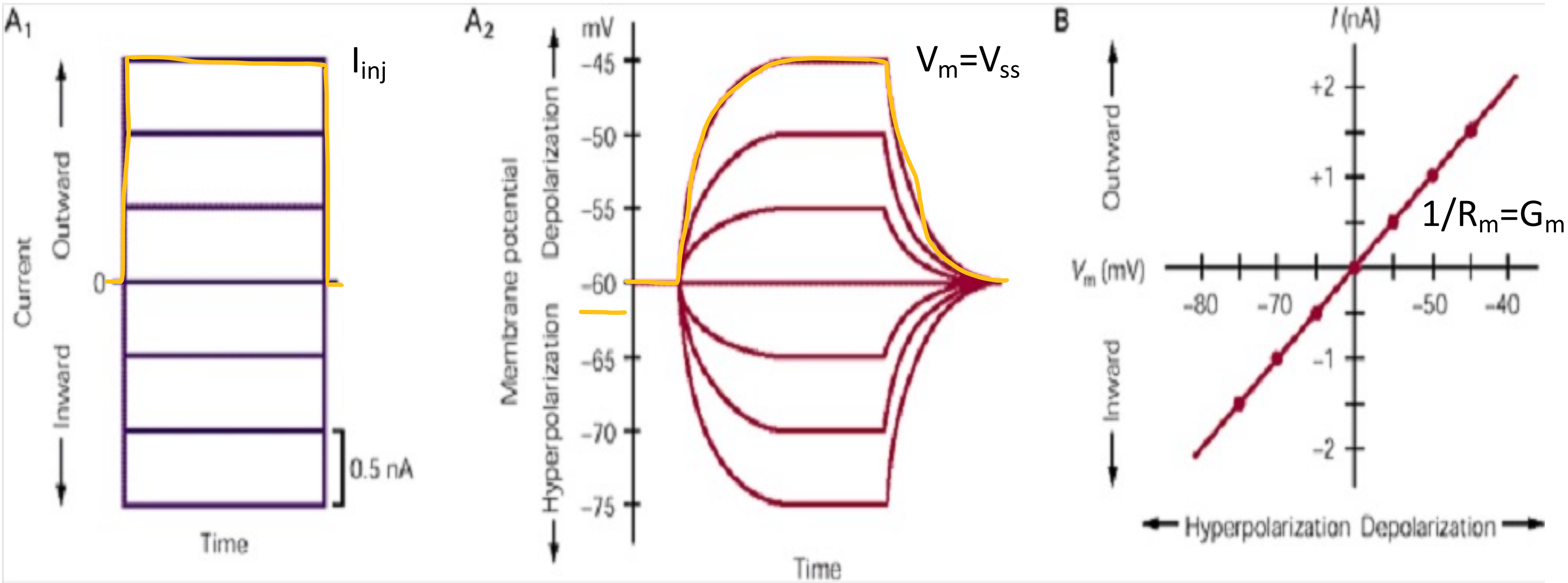
- Once V_m reaches steady state, the governing equation for the entire cell is:

$$V_m - V_{rest} = I_{inj} R_m$$

- where R_m represents the membrane resistance of the entire cell

Isopotential cell: membrane resistance

$R_m = (V_m - V_{rest}) / I_{inj}$



Calculating the membrane capacitance

- How do you experimentally measure the membrane capacitance for an isopotential cell?

$V = V_0\left(1 - e^{-\frac{t}{RC}}\right)$

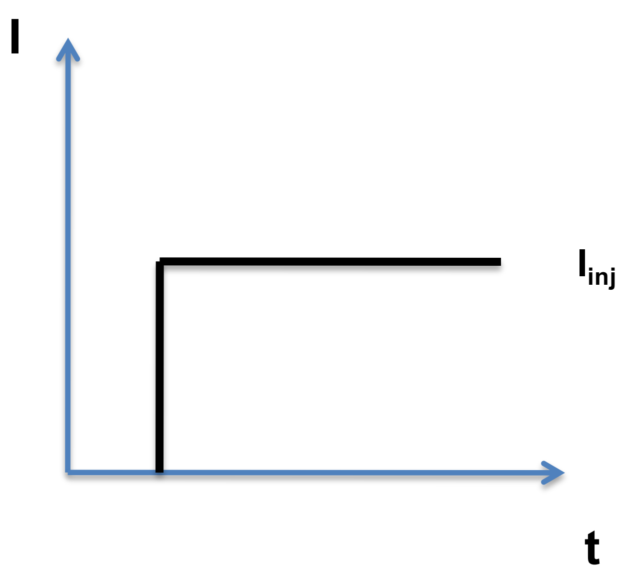
e=2.718
1/e =0.368
1-1/e=0.632

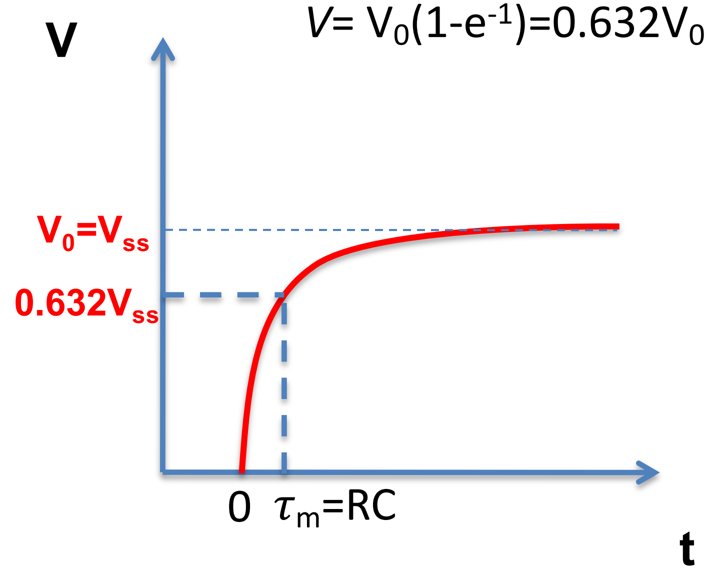
Isopotential cell : membrane capacitance

- How do you experimentally measure the membrane capacitance for an isopotential cell?

$$V = V_0\left(1 - e^{-\frac{t}{RC}}\right)$$

- $V_0 = V_{ss} = I_{inj} * R$
- *When* $t = RC = \tau_m$
  $V = V_0(1 - e^{-1}) = 0.632V_0$





e=2.718
1/e =0.368
1-1/e=0.632

How do C_m and R_m establish the input (current injection) and output (V_m) relationship for the isopotential neuron?

Specific membrane resistance and capacitance

You can also estimate the membrane resistance and capacitance if you know the cell’s

1. Geometry
2. Specific membrane resistance
3. Specific membrane capacitance

Specific membrane resistance

R_M is the specific membrane resistance$(\Omega \cdot \text{cm}^2)$.

- This value differs significantly between neural cell types.
- How would you calculate the total resistance for the entire cell membrane (R_m)?

Membrane resistance for an isopotential cell

$$R_m = \frac{R_M}{4\pi a^2}$$

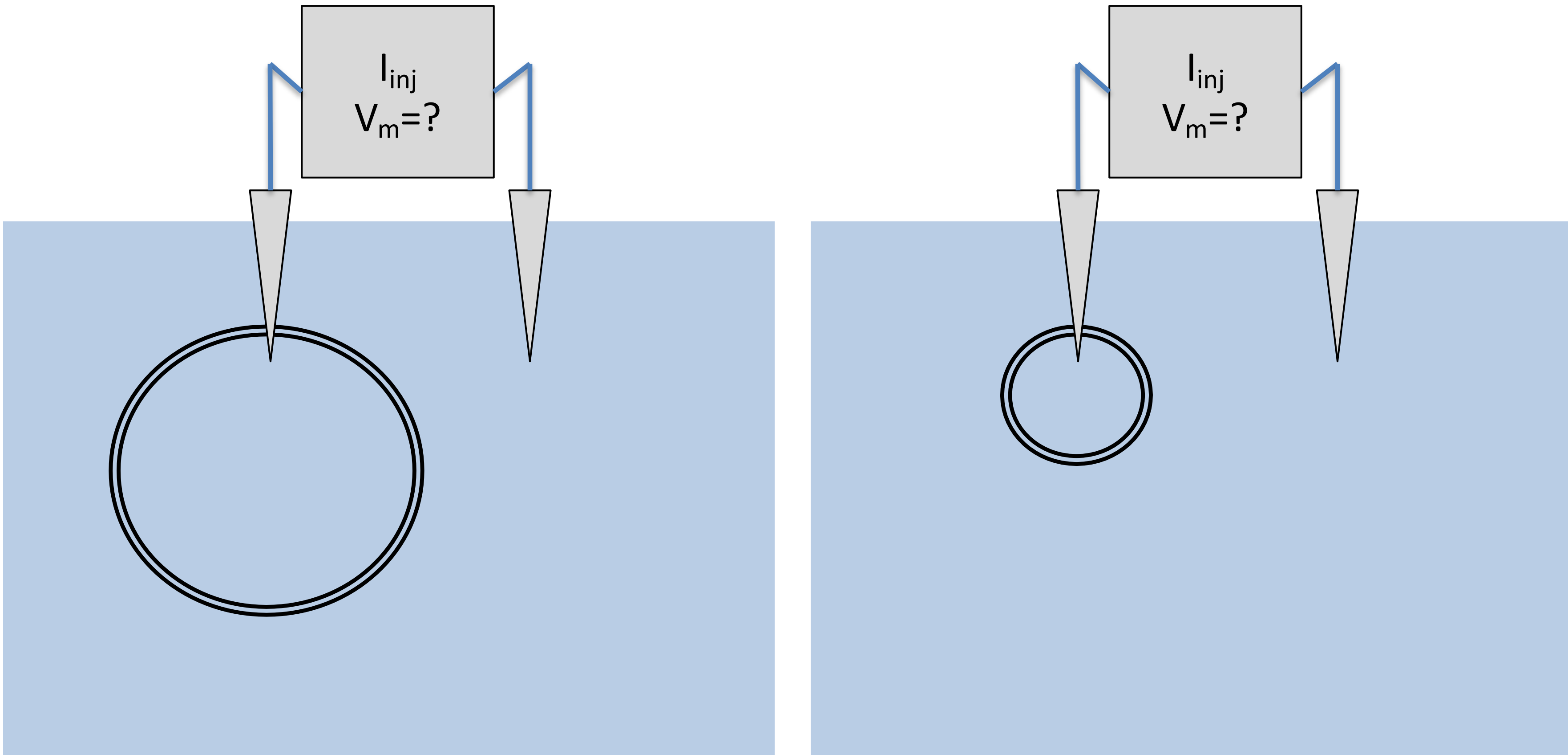
- a is the spherical cell's radius
- R_m is proportional to R_M
  - R_m is not the same for every neuron → different membrane surface areas or different R_M
- How does the size of the cell affect its R_m?

Membrane resistance for an isopotential cell

$$R_m = \frac{R_M}{4\pi a^2}$$

- a is the spherical cell's radius
- R_m is inversely proportional to the surface area
  - the smaller the radius, the higher the R_m

Which one has a higher V_m with I_{inj}?



Specific membrane capacitance

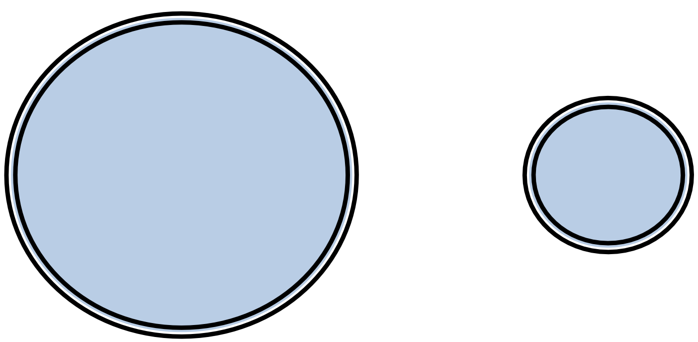
C_M is the specific membrane capacitance ($\mu F/cm^2$).

- This value remains highly consistent across neural cell types (approximately $1\mu F/cm^2$).
- How would you calculate the capacitance for the entire cell membrane?

Specific membrane capacitance

C_M is the specific membrane capacitance ($\mu F/cm^2$).

- This value remains highly consistent across neural cell types (approximately $1\mu F/cm^2$).
- Which cell has the larger capacitance?



Limitations for our isopotential cell model, Part 1

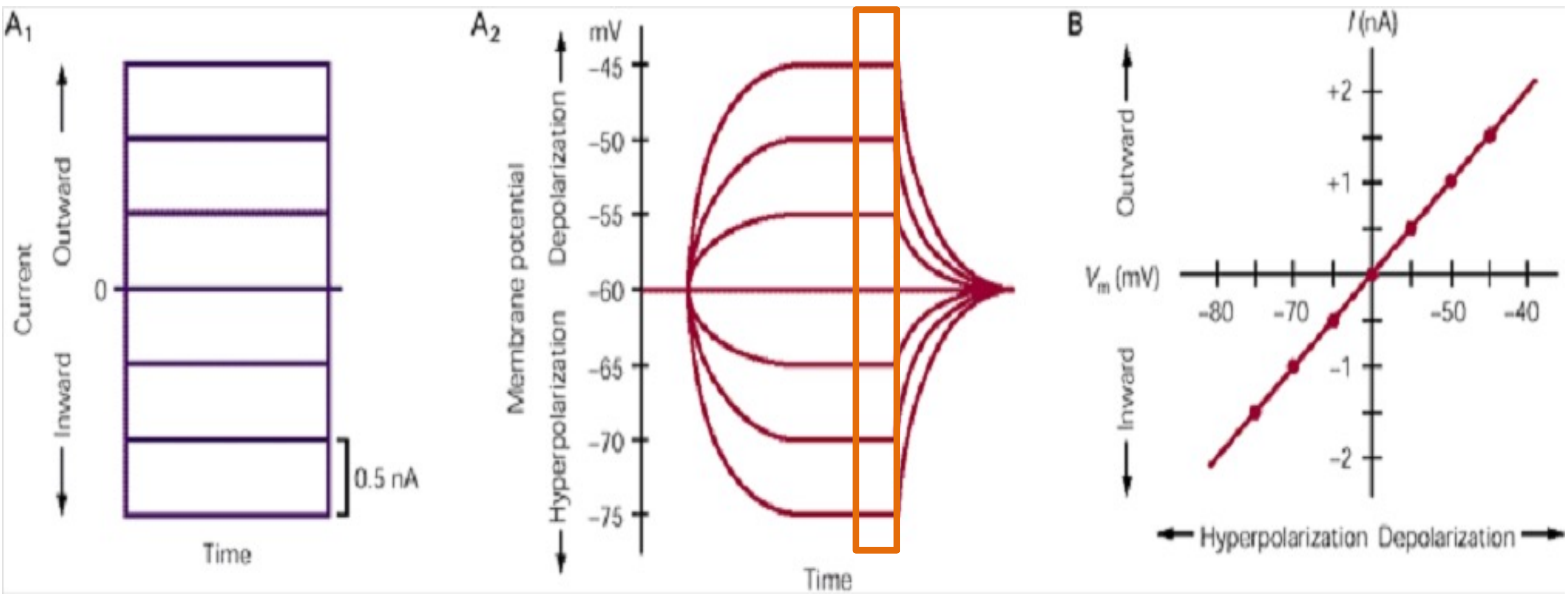
- Subthreshold signals traverse the whole cell, not just the soma
  - Dendrites
  - Axons
- The signals decrease in amplitude as a function of distance travelled
- We ignore axial resistance R_a in our models (because our neuron is a sphere) but will return to it in the next lecture

Limitations for our isopotential cell model, Part 2

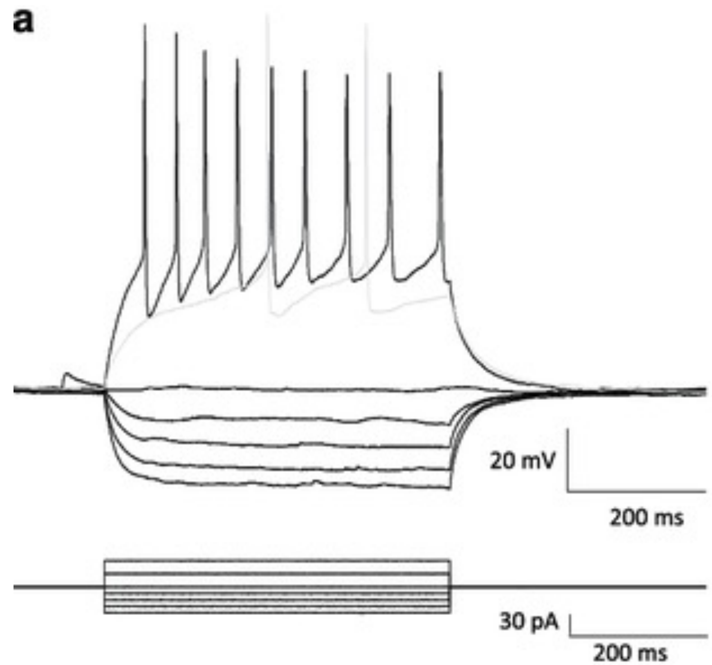
- With our simple RC circuit model of an isopotential cell, we can estimate ***passive*** membrane properties from current clamp experiments.

- However, our model does not accommodate ***active*** membrane properties (ex. Spikes!!). This will be covered in future lectures.

Current injection across an isopotential cell



Real current injection experiments



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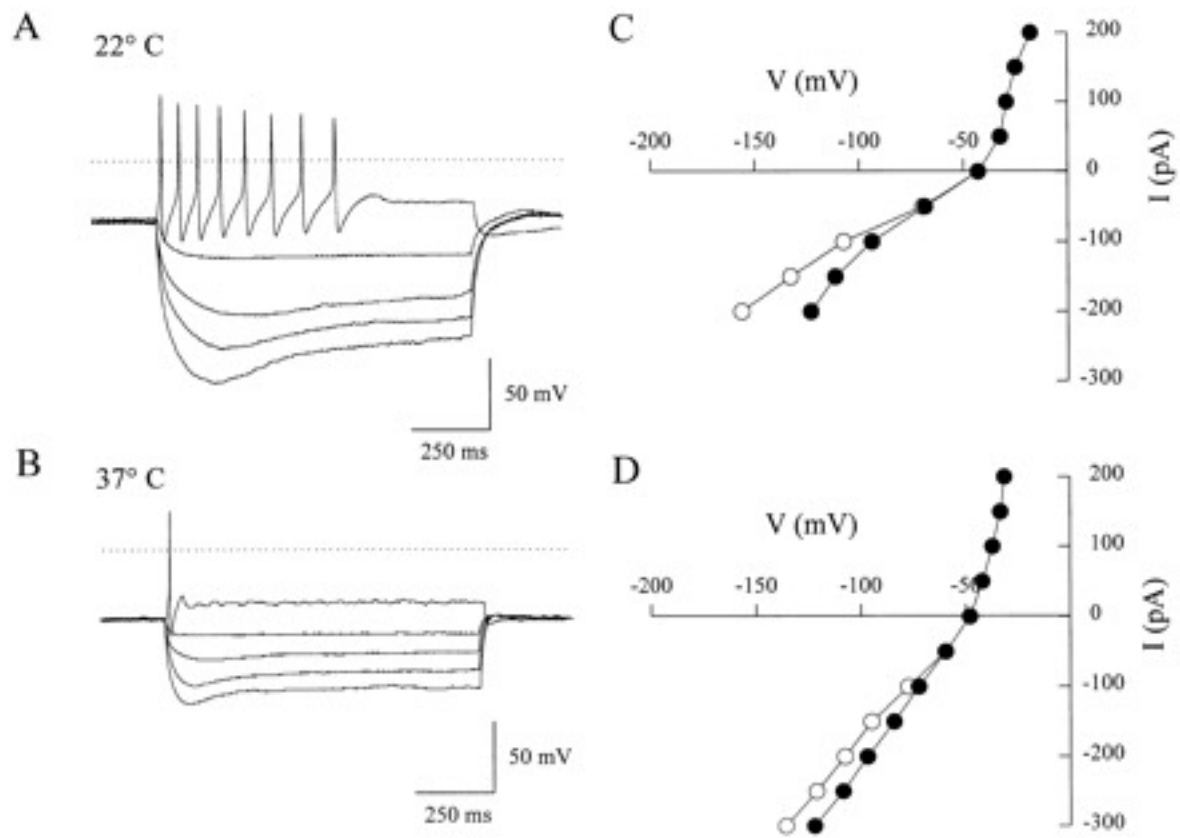
Real current injection experiments



J. Cuevas et al. Journal of Neurophysiology. 1997

Additional Readings

Paul Miller

Ch 2.2

An Introductory Course in
COMPUTATIONAL NEUROSCIENCE

Electronics for electrophysiologists

Boris Barbour*†

September 17, 2014

Chapter 1
The Hodgkin–Huxley Equations

G.B. Ermentrout and D.H. Terman, *Mathematical Foundations of Neuroscience*,
Interdisciplinary Applied Mathematics 35, DOI 10.1007/978-0-387-87708-2_1,
© Springer Science+Business Media, LLC 2010

Reading Ahead

Neuron

Obituary

Wilfrid Rall (1922–2018)

Chapter 1
The Hodgkin–Huxley Equations

G.B. Ermentrout and D.H. Terman, *Mathematical Foundations of Neuroscience*,
Interdisciplinary Applied Mathematics 35, DOI 10.1007/978-0-387-87708-2_1,

Next time

- Introduction to cable theory (Video on Bb Learn will be available Tuesday)

Lab 1 is due Monday at 11:59 PM