The Integrate and Fire Neuron

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Outline

We'll develop different types of biophysical models of action potentials or "spikes".

- We'll begin with motivational data.

- We'll then consider some biophysics to construct:
  - The integrate and fire model **[today]**.
  - The Hodgkin-Huxley model **[next]**.

- Hands on: implement in Python.

Motivation

Goal: Create mathematical models that explain observations.

What is a model? spike train data

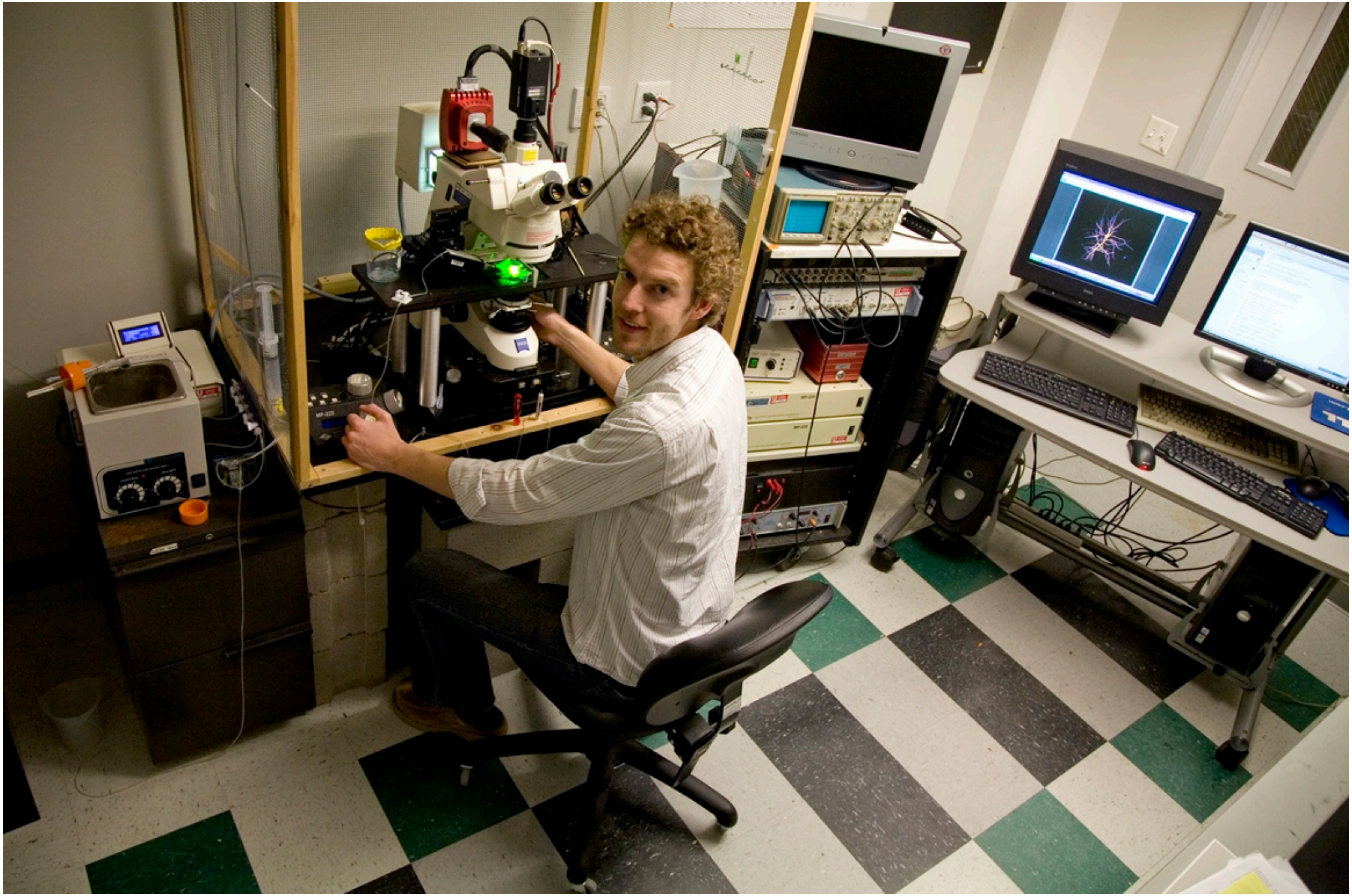
• Get the biophysics right:
  Integrate and fire model (I&F)
  Hodgkin-Huxley model (HH)

• Get the dynamics right:
  Izhikevich neuron
  FitzHugh-Nagumo model

Challenge: Rigorously link data and models ...

Consider an experiment:

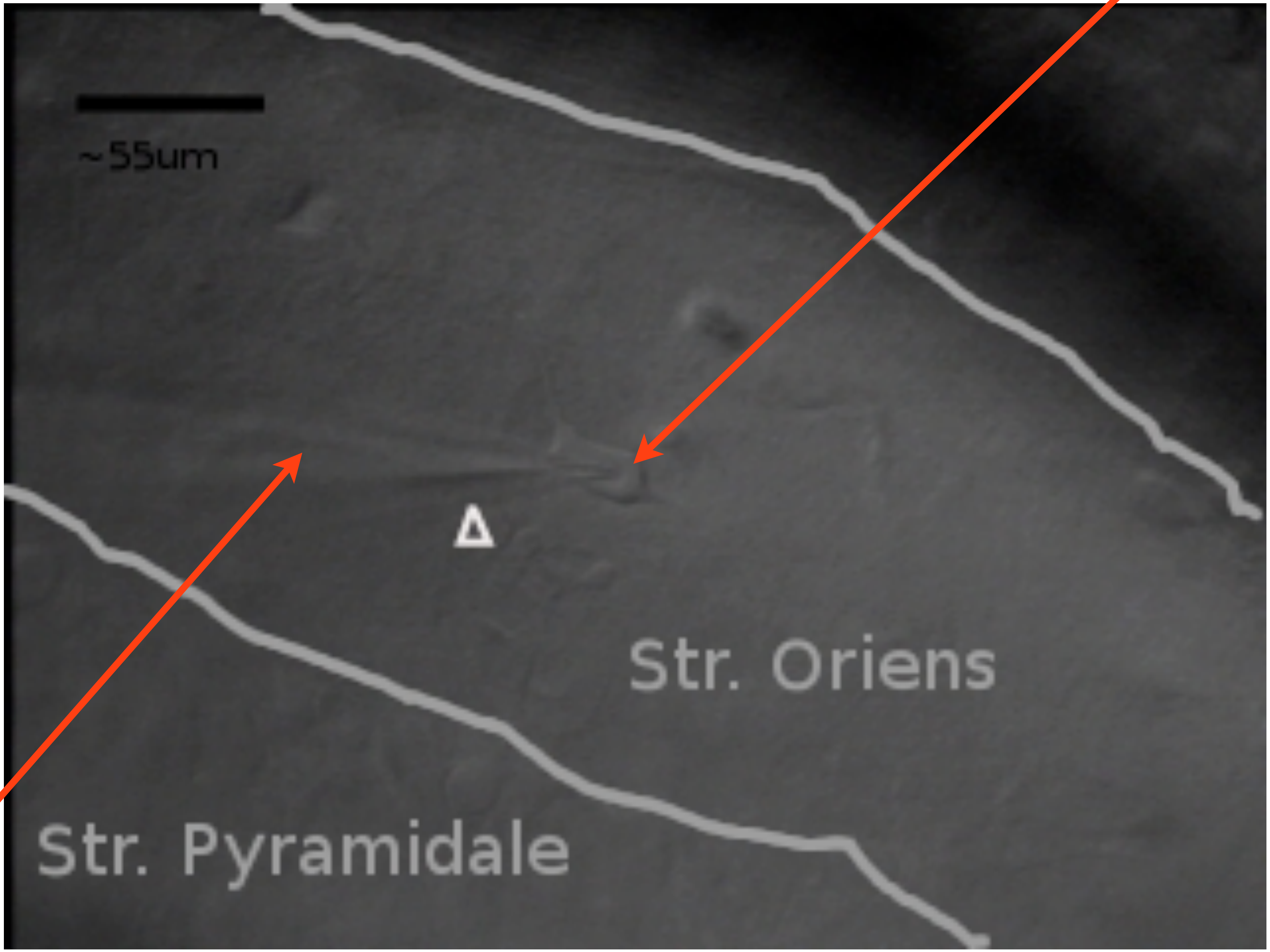
Our collaborator . . .



“Patch” the neuron

Ex. from hippocampus

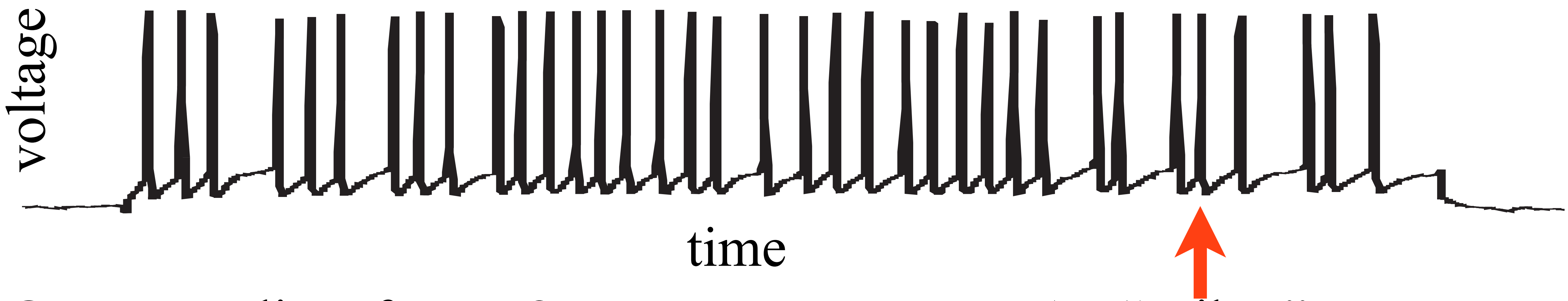
“patched” neuron



electrode

And records . . .

From a single neuron record:



Q: Most salient feature? **A**: "spikes"

Build a model of spiking activity - increasing levels of realism

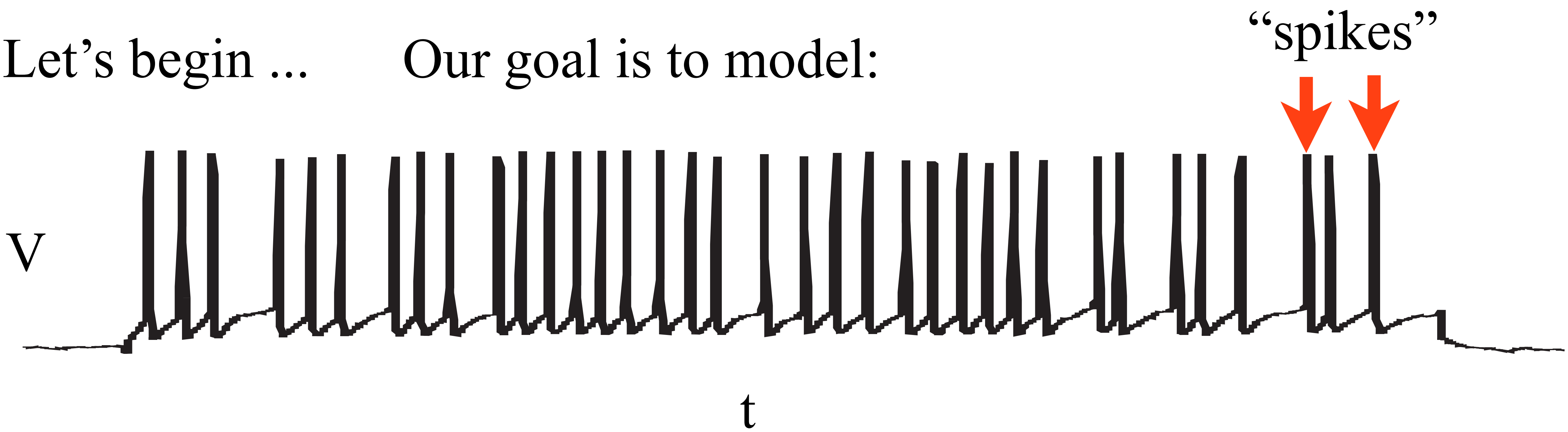
- Statistical
- Dynamical
- Biophysical

Q: "Analysis" of these spike train?

A: Propose candidate mechanisms that generate spikes.

Modeling the voltage: biophysics

Let's begin ... Our goal is to model:



Consider the general expression:

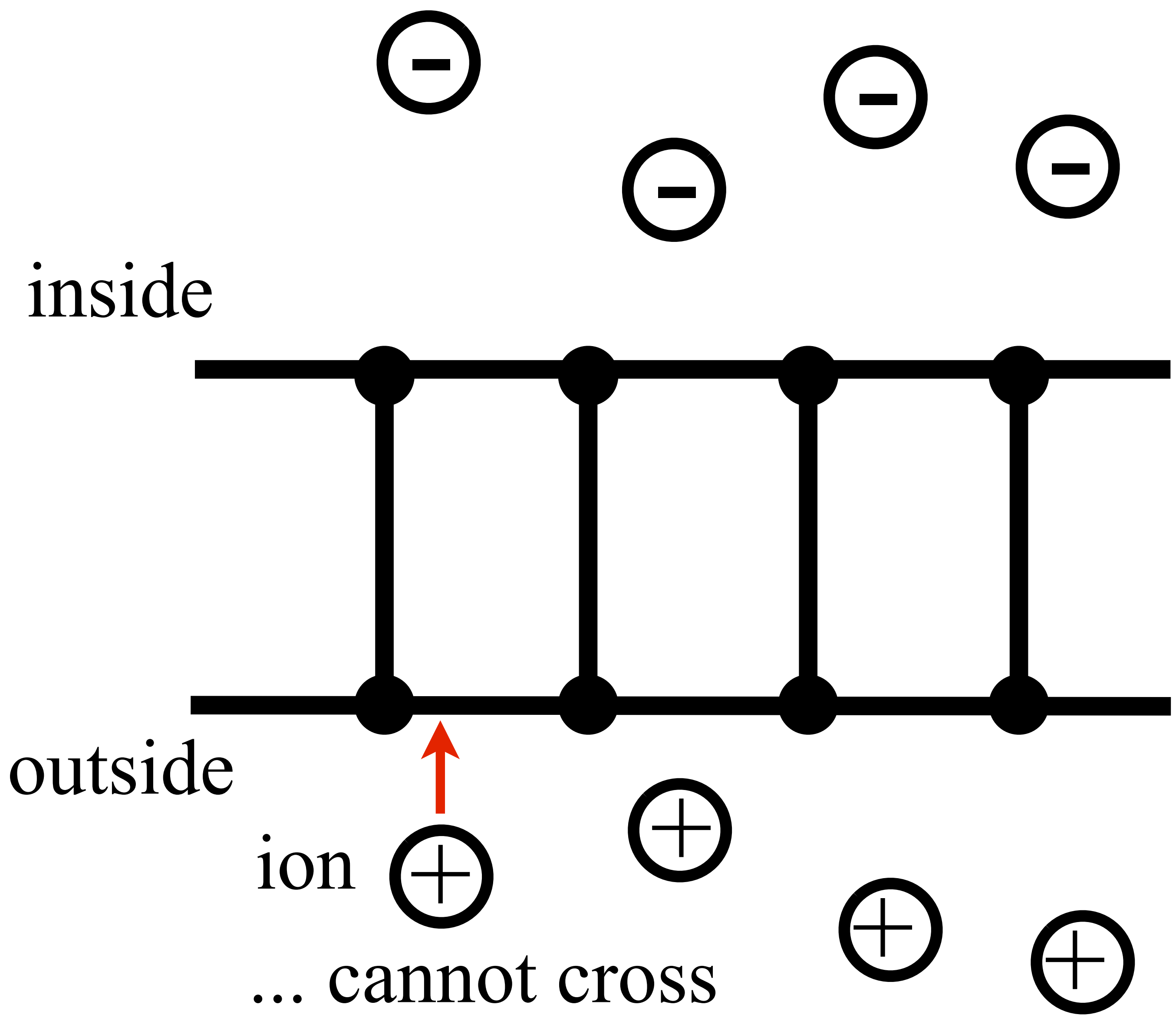
What else?

dV/dt = f (V, current inputs, time, ...)

We need to choose f ... biophysics.

Modeling the voltage: biophysics

Fact: The neuronal membrane is an impermeable lipid bilayer.



Negative charges inside the cell attracted to positive charges outside the cell

Positive charges want to reach this negative potential, but can't ...

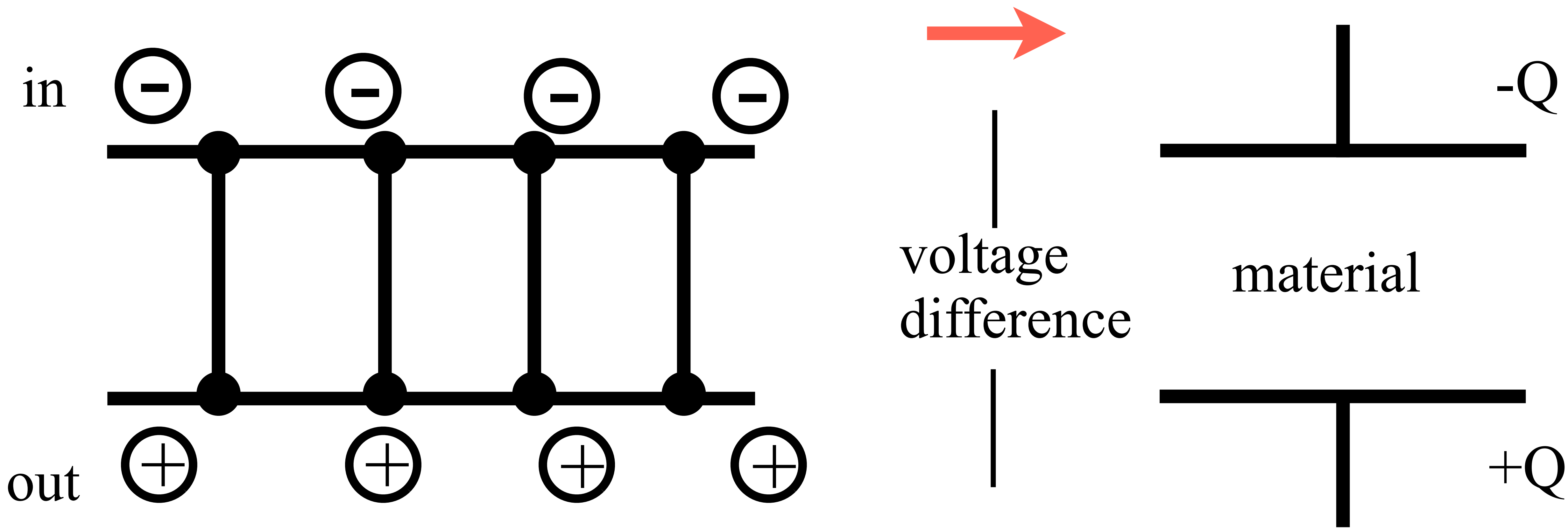
Fact: The inside has a negative voltage relative to the outside (-70 mV).

Excess negative charge inside the cell ...

Modeling the voltage: biophysics

The cell membrane acts like a simple circuit element ...

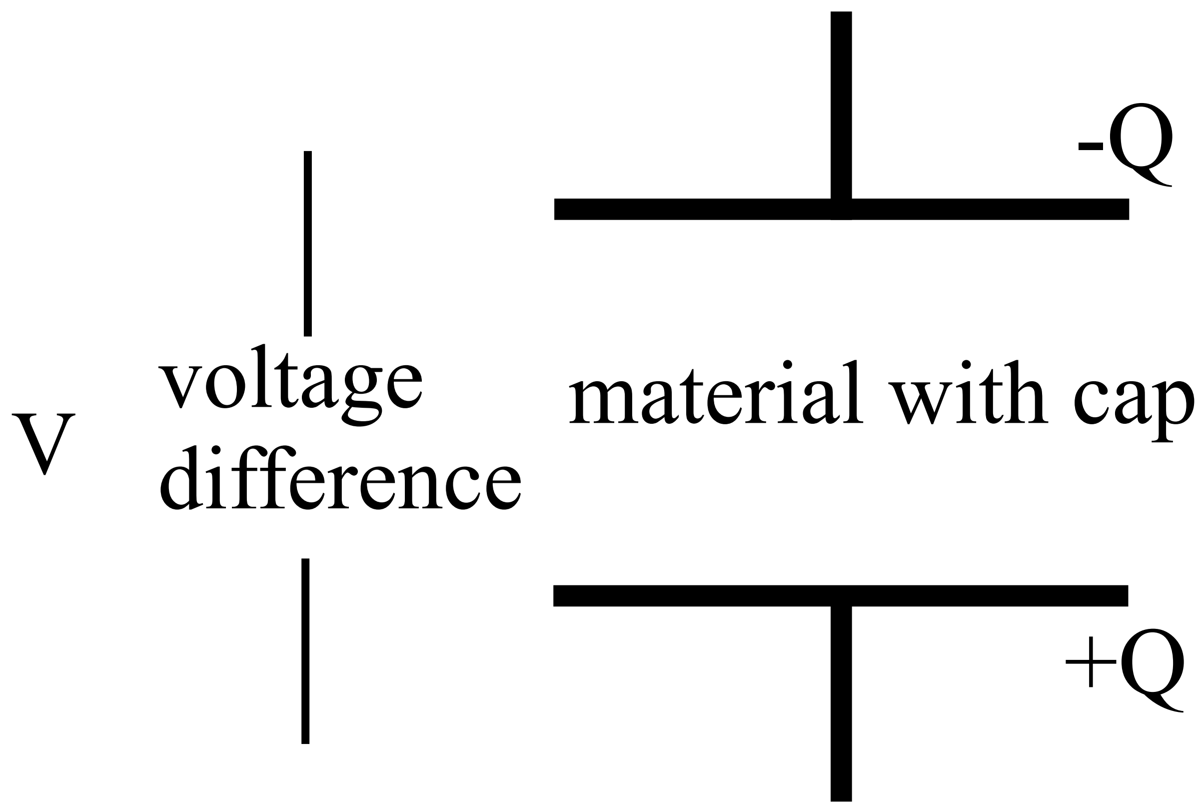
<u>Equivalent circuit</u>: replace the neuronal membrane with a **<u>capacitor</u>**



Q: Circuit element? **A: capacitor**

Modeling the voltage: biophysics

Q: Why is this useful? For a capacitor, relate three quantities:

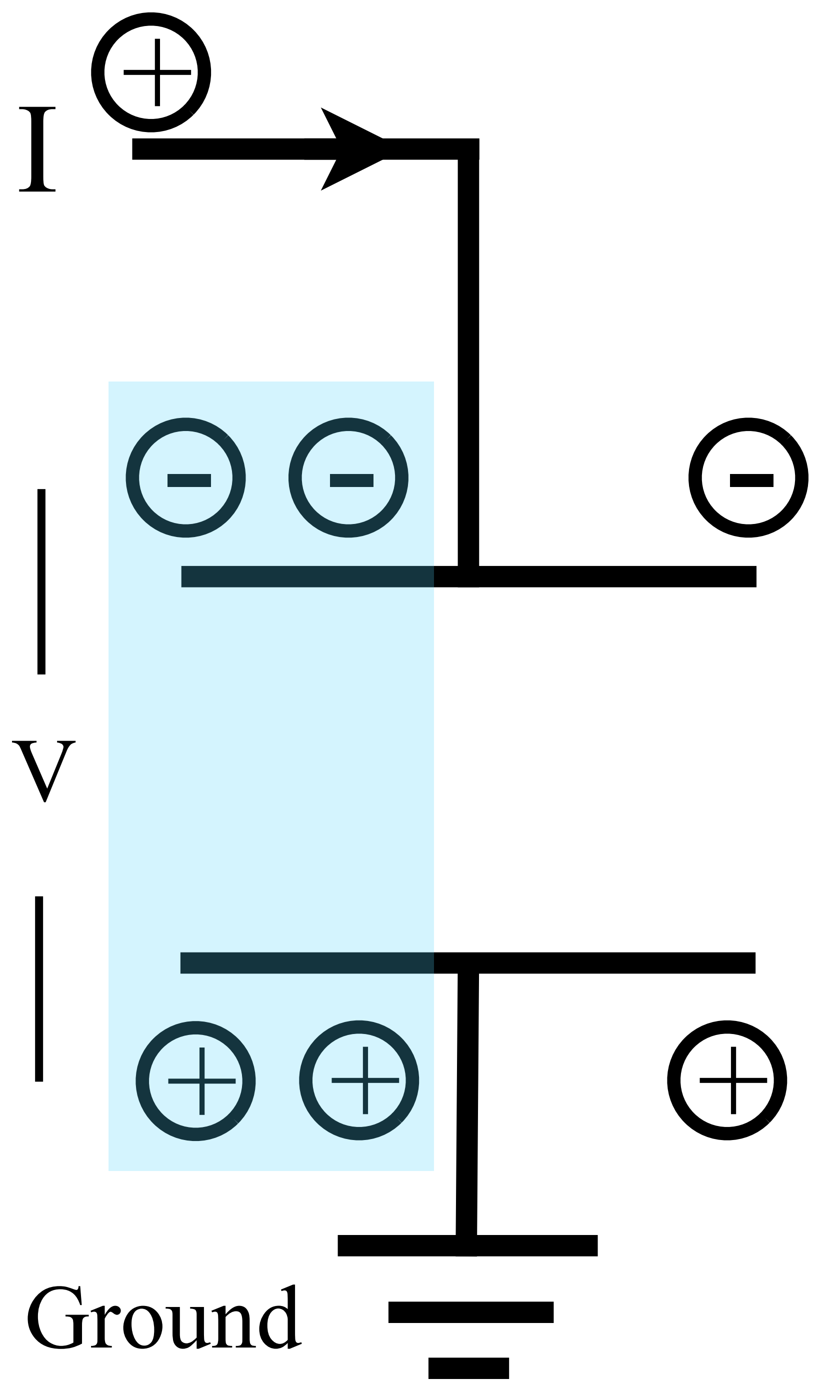


Relate these variables: $\boxed{Q = C\,V}$

We'll use this to build our mathematical model ...

Modeling the voltage: biophysics

Let's inject current to one side of the capacitor:



Maintain equal & opposite net charge across plates ...

The charge Q changes:

$$dQ/dt = I$$

... which changes the voltage

$$Q = CV$$

$$I = C\,dV/dt$$

Modeling the voltage: biophysics

Rearrange for a simple model ...

General model: $dV/dt = f\,(V, \text{current inputs}, \text{time}, \ldots)$

Equivalent circuit with capacitor: $I = C\, dV/dt$

$$\boxed{dV/dt = I/C}$$

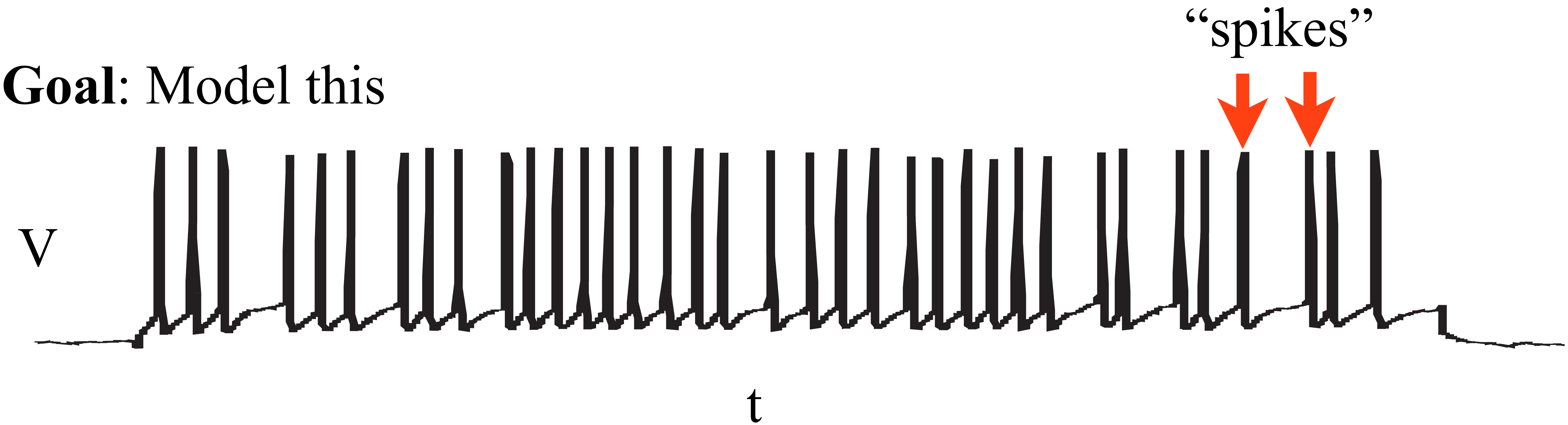
Our first model ... motivated by biophysics.

Q: Does this model reproduce the data? Python

Modeling the voltage: biophysics

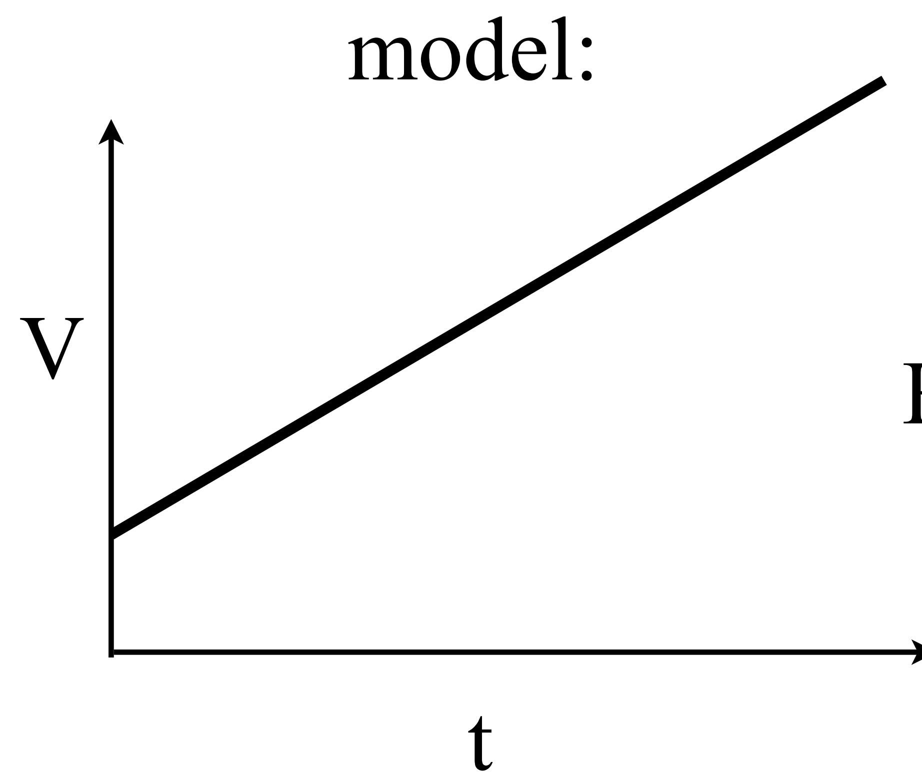
Q: Does this model produce "spiking"?

Goal: Model this



Consider I > 0, C > 0,

Then: $V[t] = V[0] + I/C\ t$



Hmm ...

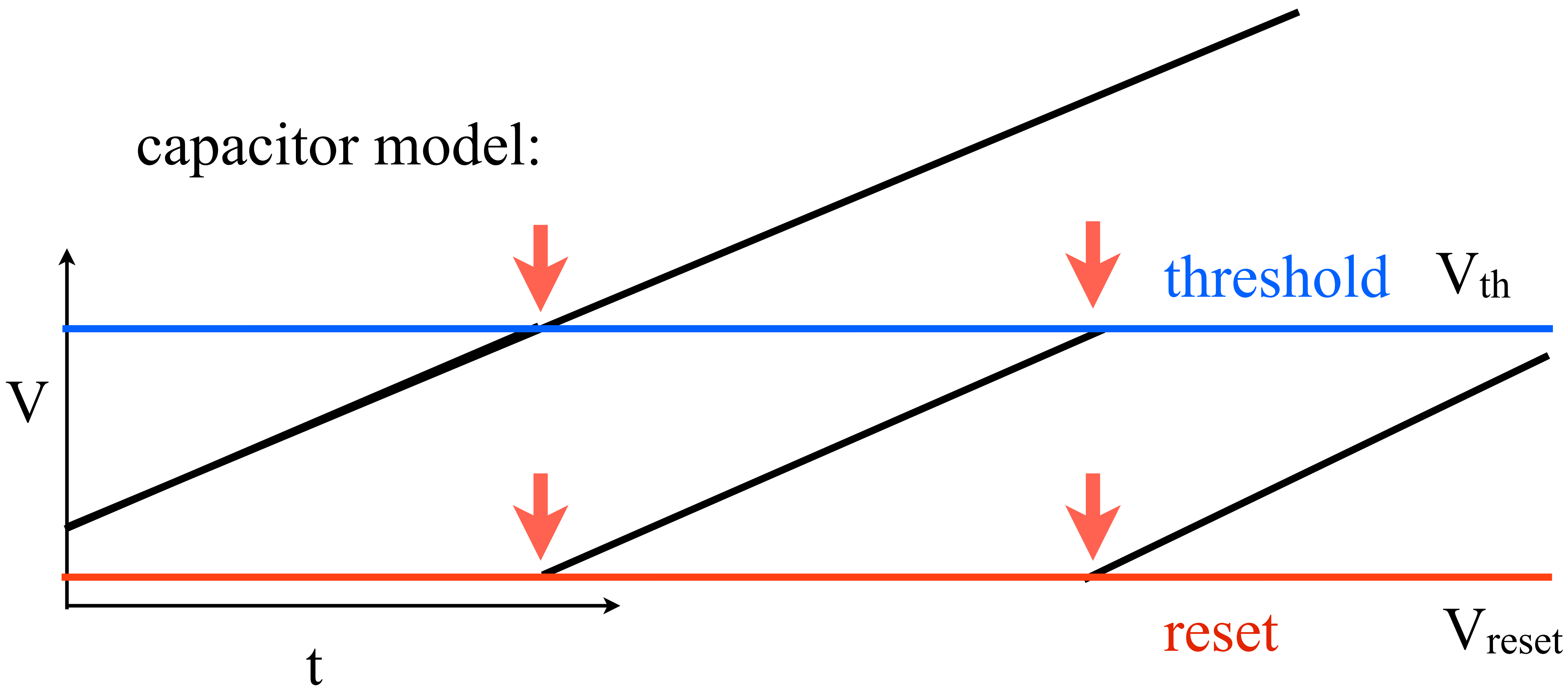
Model 1: Integrate and fire

To make our model spike ... a hack.

add **threshold & reset**

<u>Idea</u>: when the voltage becomes large enough (threshold), then reset it to a lower value.

capacitor model:



Model 1: Integrate and fire

The complete I&F model:

$$\boxed{\begin{array}{l} dV/dt = I/C \\[2em] \text{if } V > V_{th}\text{ , then } V = V_{reset} \end{array}}$$

(motivated by capacitor)

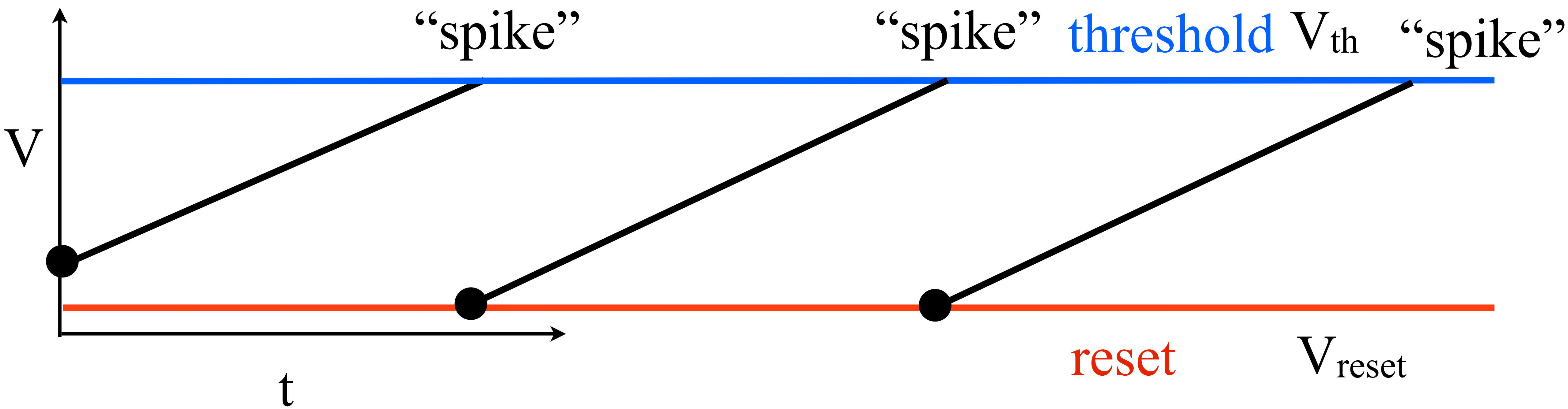
(threshold & reset)

V	voltage across membrane
I	injected current
C	capacitance
V_{th}	voltage threshold
V_{reset}	voltage reset

Python

Model 1: Integrate and fire

Each time threshold reached, we say the model "spikes" ...

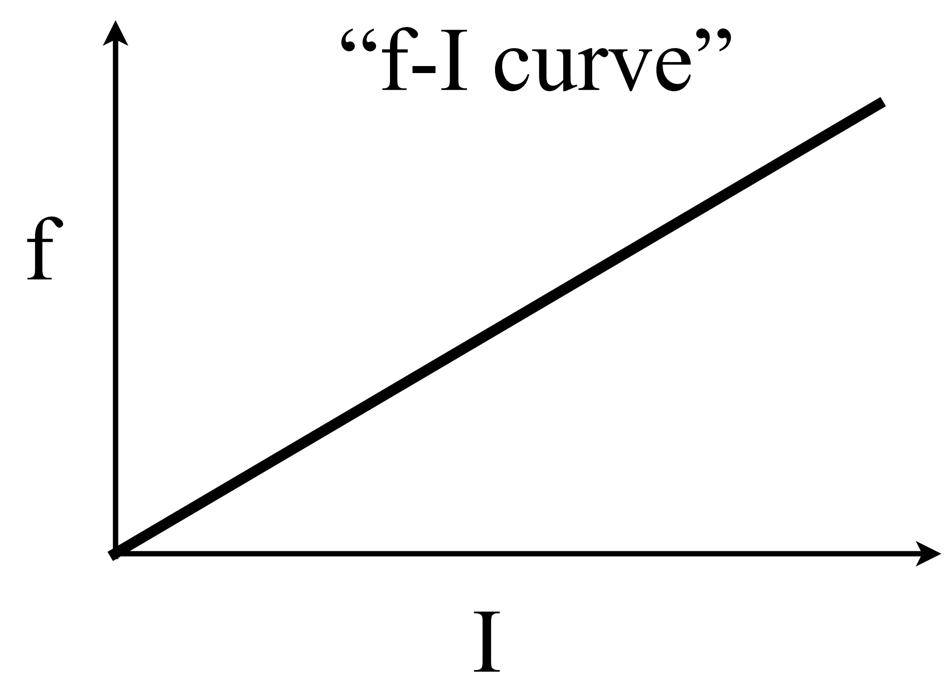


Q: What is the rate of spiking?

A: It's constant ...

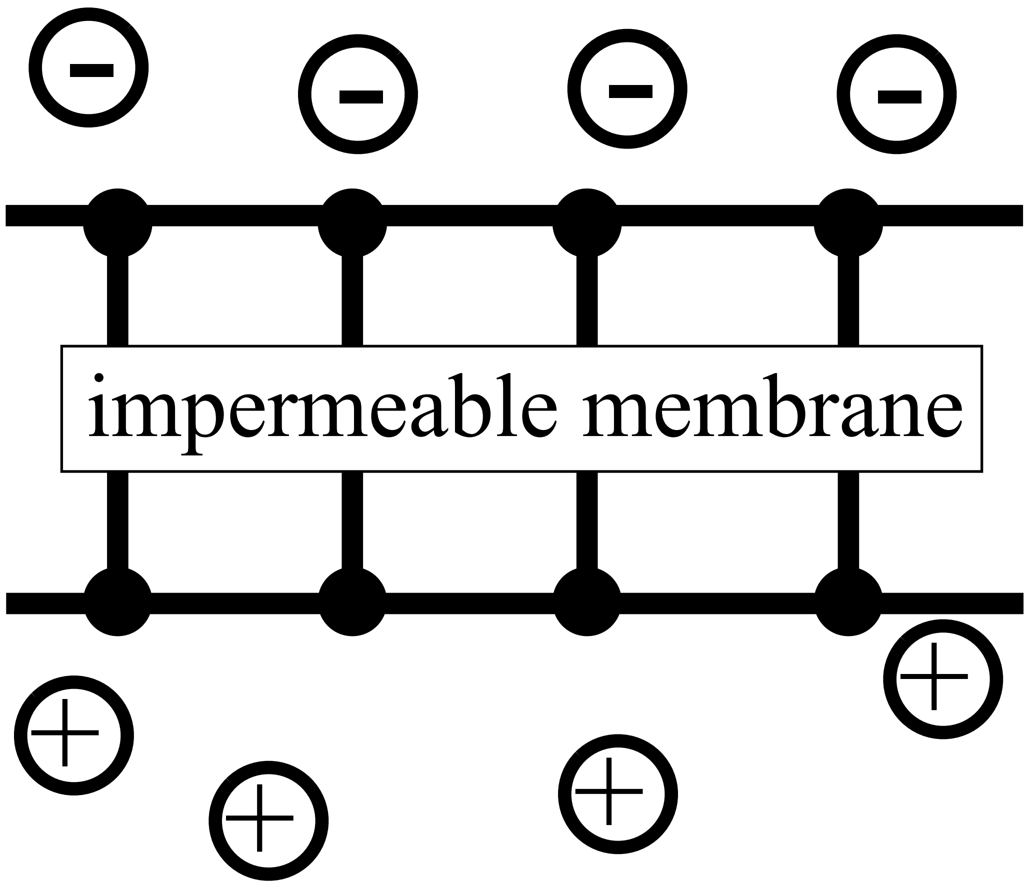
firing rate = $I \,/\, ((V_{th} - V_{reset})\, C)$

plot it versus I ...

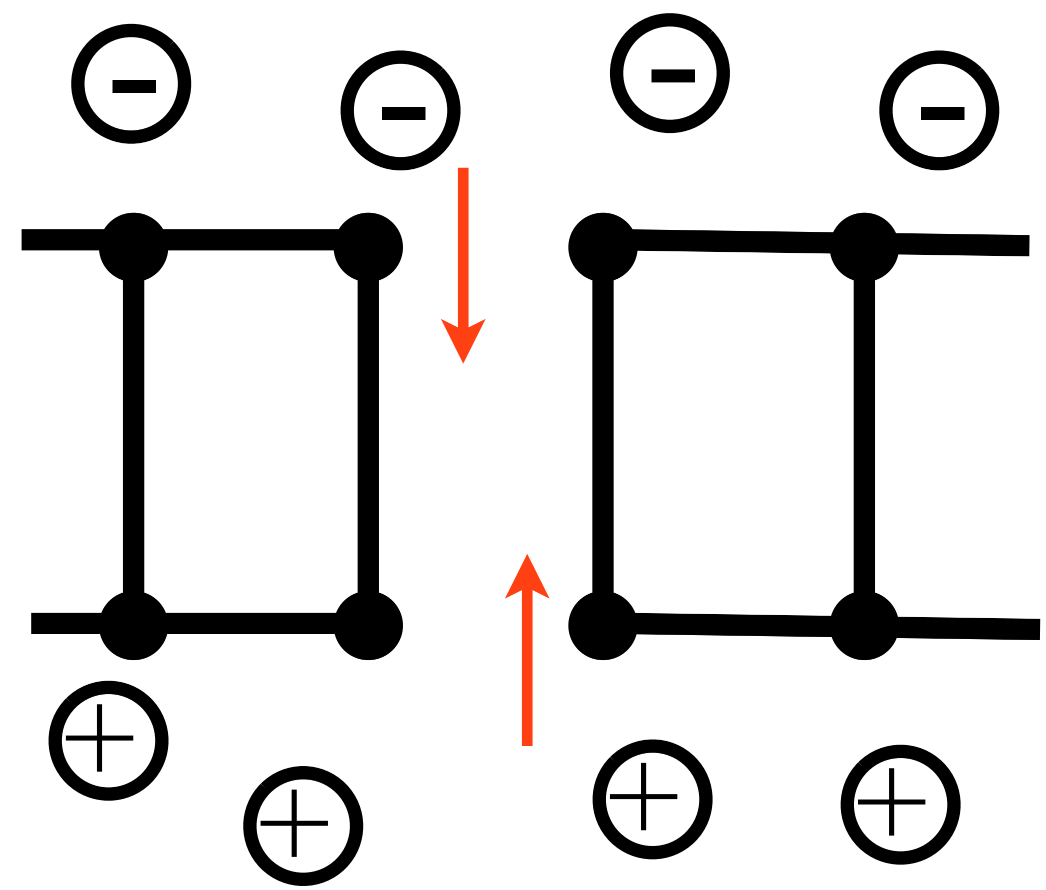


Modeling the voltage: more biophysics

Our initial cell model was boring ... ions **cannot** pass through.



update the model to include **channels** or "pores" in the membrane

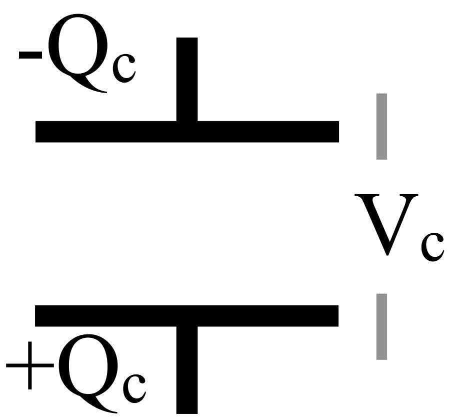


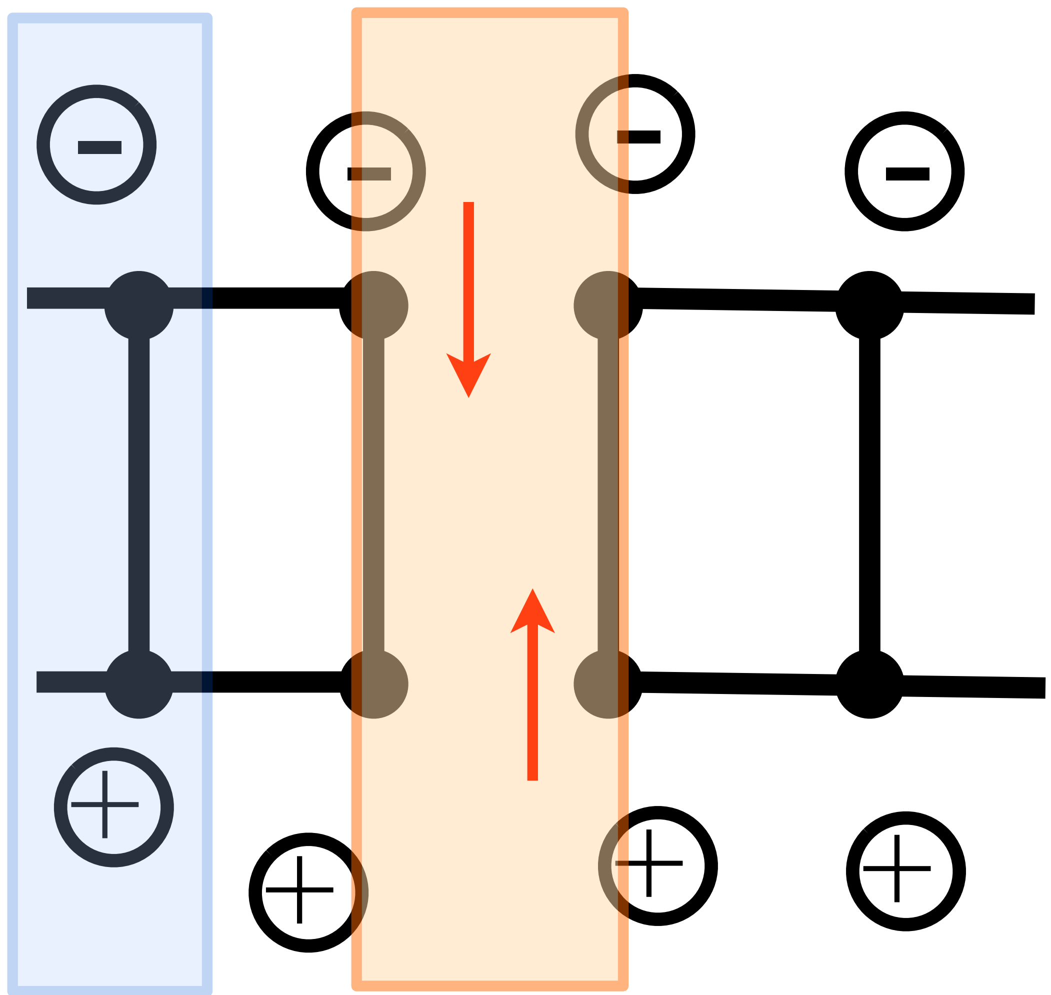
To start, consider an <u>always-open</u> channel ...

Modeling the voltage: more biophysics

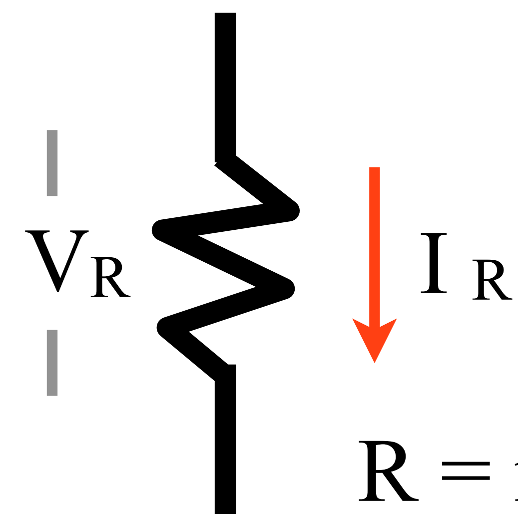
Q: How do we build a model? **A:** Consider an <u>equivalent circuit</u>.

acts like capacitor





Q: Acts like ...
A: a resistor



R = resistance

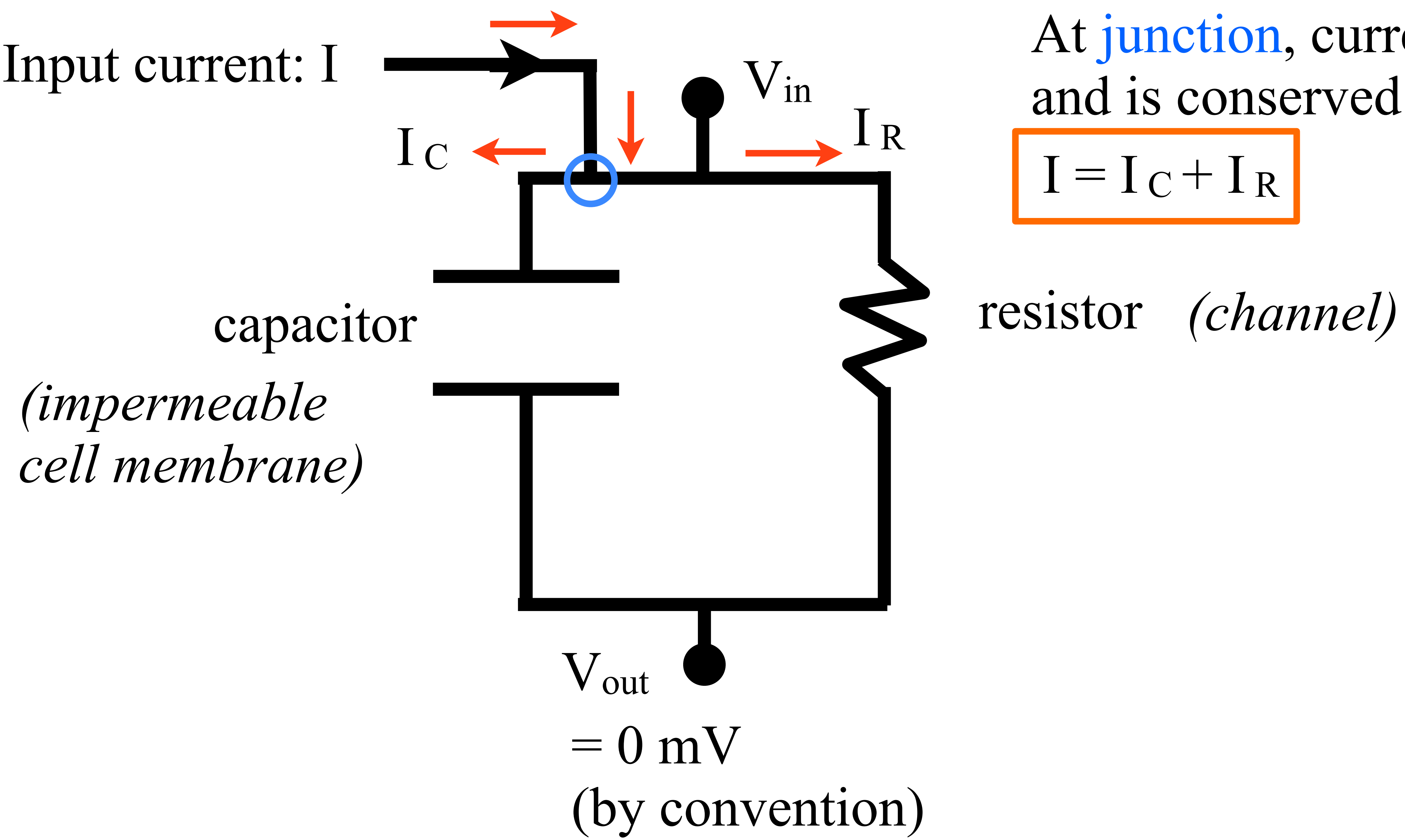
$Q_C = CV_C$

$V_R = R\,I_R$

Combine elements to form a simple circuit ...

Modeling the voltage: more biophysics

Consider an equivalent circuit: capacitor & resistor



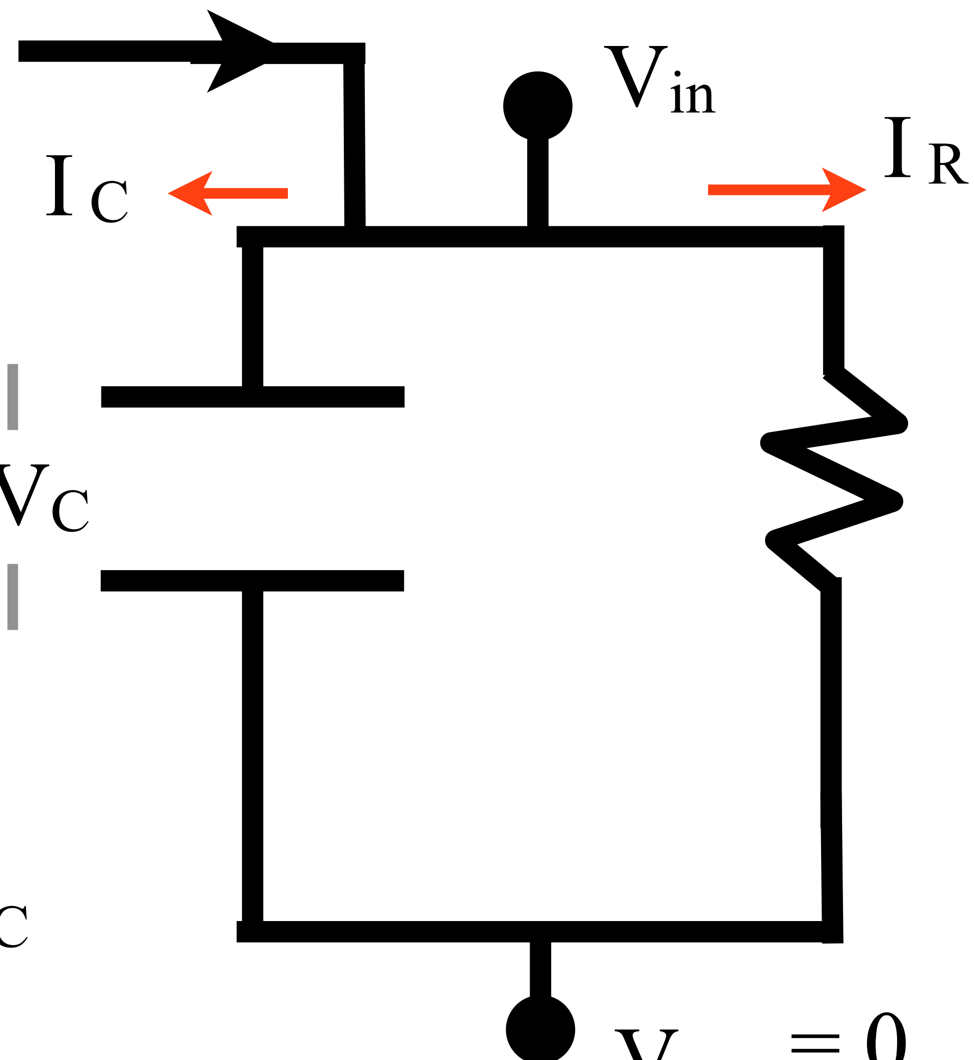
At junction, current splits and is conserved

$$\boxed{I = I_C + I_R}$$

Let's analyze the behavior of this model ...

Modeling the voltage: more biophysics

Consider the case: $I = 0$, "equilibrium". The equivalent circuit ...



$V_{in} - V_{out} = V_C$

0

so $Q_C = C\, V_C$

$Q_C = C\, V_{in}$

$Q_C = C\, V_{out} = 0$

no fixed charge on capacitor

"at equilibrium"

$= 0$

$V_R = V_{in} - V_{out} = I_R\, R$

so $V_{in} = V_{out} = 0$

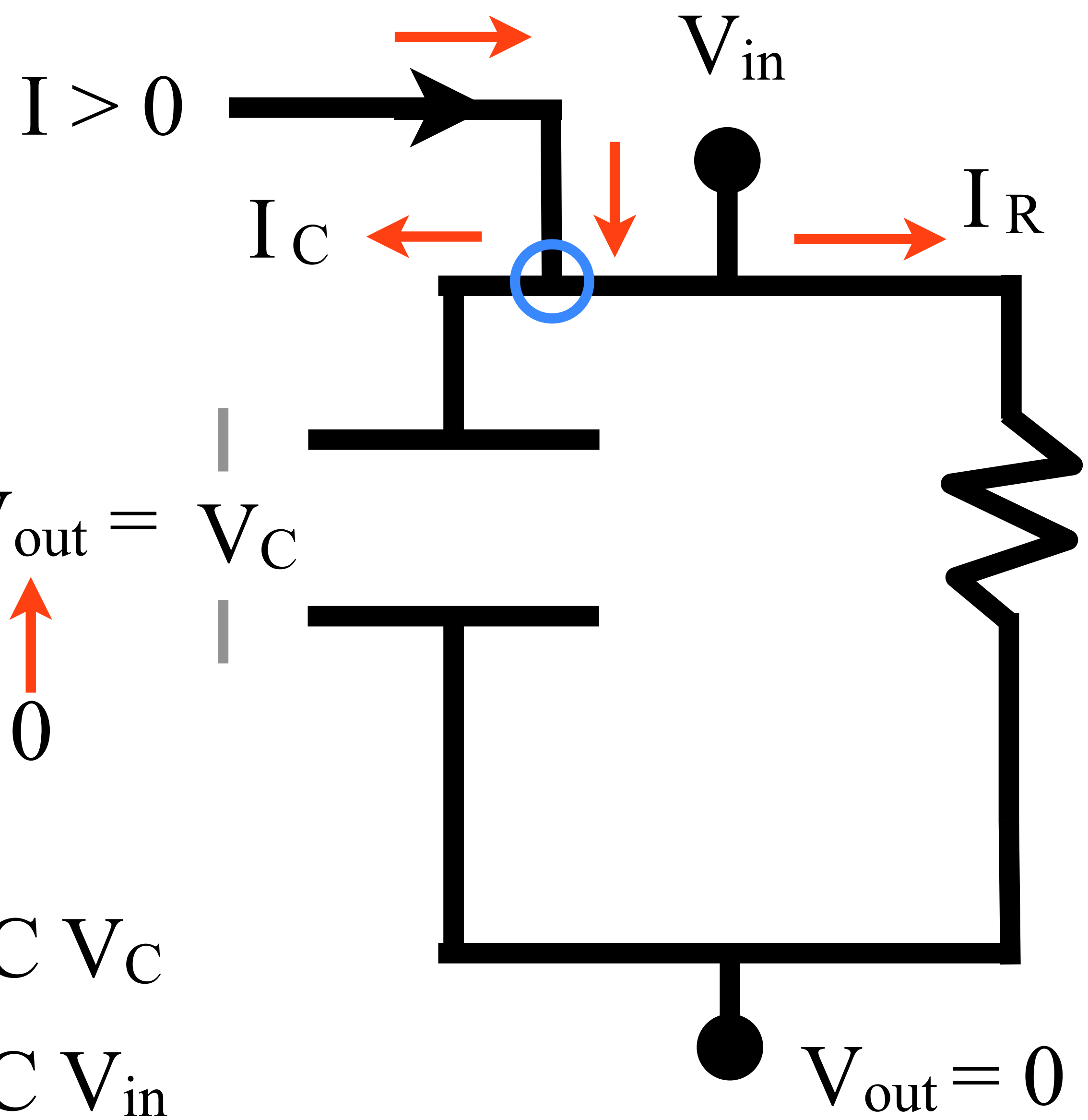
cell voltage "at rest"

at equilibrium ...

Modeling the voltage: more biophysics

Now, inject current: $I > 0$

The equivalent circuit ...



At junction, current splits and is conserved

$$\boxed{I = I_C + I_R}$$

$$V_{in} - \underbrace{V_{out}}_{0} = V_C$$

$$V_R = V_{in} - \underbrace{V_{out}}_{0} = \boxed{I_R}\, R$$

so $Q_C = C\, V_C$

$Q_C = C\, V_{in}$

$\boxed{I_C} = C\, dV_{in}/dt$

substitute in:

$$I = C\, dV_{in}/dt + V_{in}/R$$

$$\boxed{dV_{in}/dt = -\,(V_{in} - V_*)\,/\,\tau}$$

where $V_* = R\, I$ “target voltage”

$\tau = R\, C$ “time constant”

Modeling the voltage: more biophysics

Behavior of the RC-circuit:

$$dV_{in}/dt = -(V_{in} - V_*)/\tau$$

$$V_{in} \rightarrow V_*$$

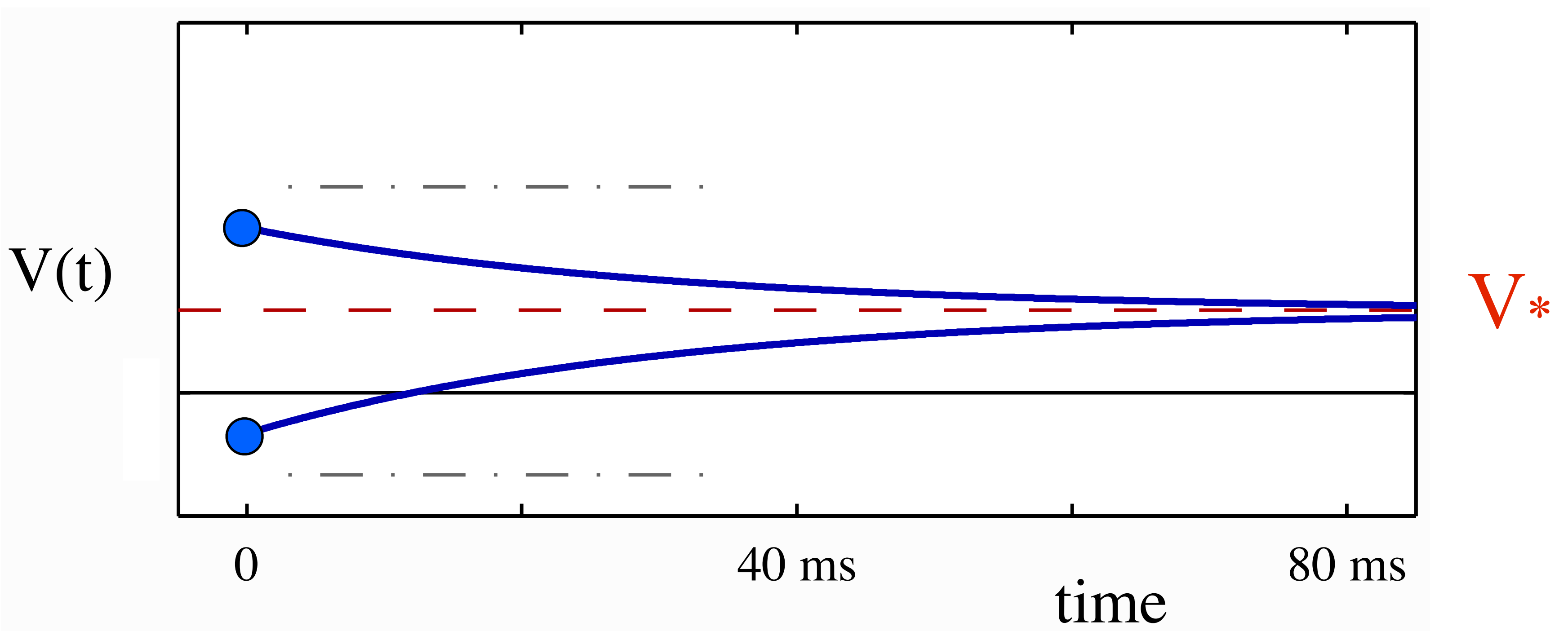
Consider I = constant

$V_* = R\,I =$ constant

$\tau = R\,C =$ constant

In words: Voltage across the membrane approaches the <u>target voltage</u>.

<u>Example</u> (RC-circuit):



Q: Does the RC-circuit “spike”?

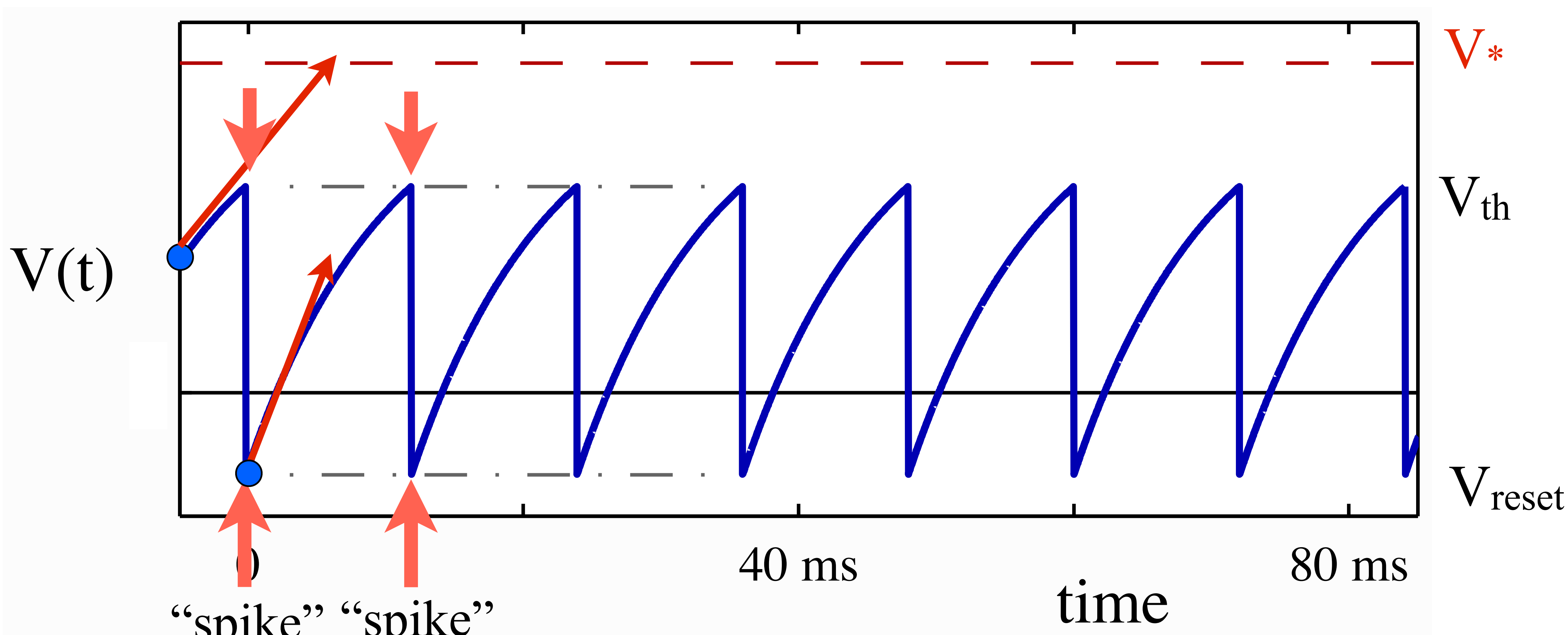
Model 2: Leaky integrate and fire

To make our model spike ... a hack.

add **threhsold & reset**

<u>Idea</u>: when the voltage becomes large enough (threshold), then reset it to a lower value.

<u>Example</u> (I&F):



Model 2: Leaky integrate and fire

The complete leaky I&F model:

$$\boxed{\begin{array}{l} dV_{in}/dt = -(V_{in} - V_*) / \tau \\ \text{if } V > V_{th} \text{, then } V = V_{reset} \end{array}}$$

(motivated by RC-circuit)

(threshold & reset)

where $V_* = R\,I$ "target voltage"

$\tau = R\,C$ "time constant"

An extension of the I&F model - the cell membrane has a hole.

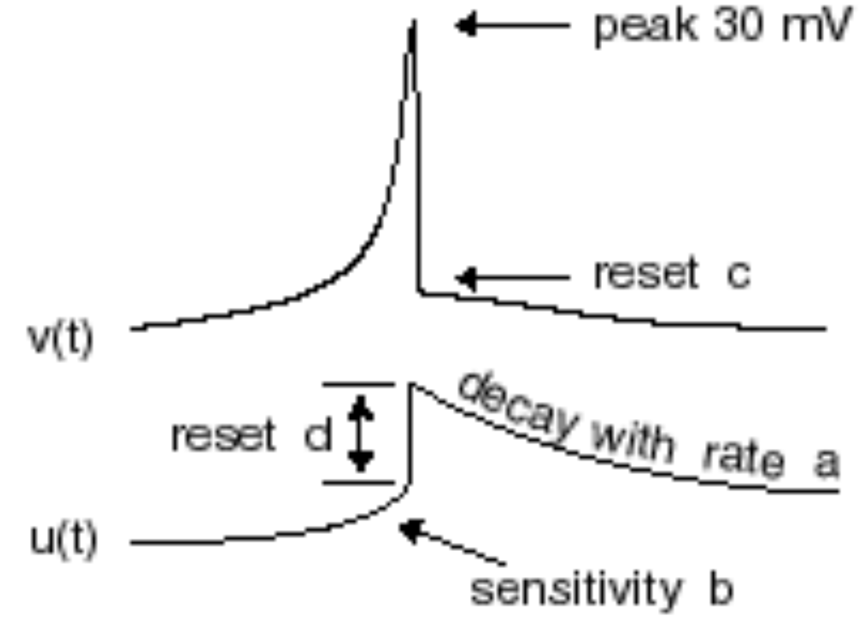
Extensions of I&F models

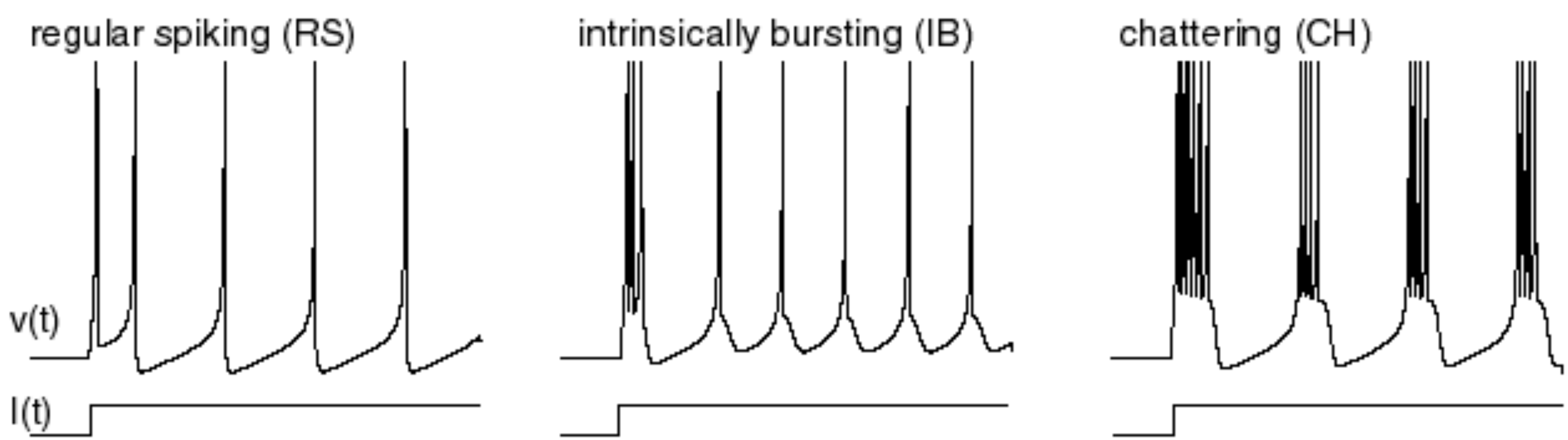
Quadratic I&F: $dV/dt = I + V^2$, if $V > V_{th}$, then $V = V_{reset}$

Izhikevich neuron:

$$v' = 0.04v^2 + 5v + 140 - u + I$$
$$u' = a(bv - u)$$

if $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$





http://www.izhikevich.org/publications/spikes.htm

Challenge

Simulate the LIF model in Python

https://mark-kramer.github.io/BU-MA665-MA666/IF.html