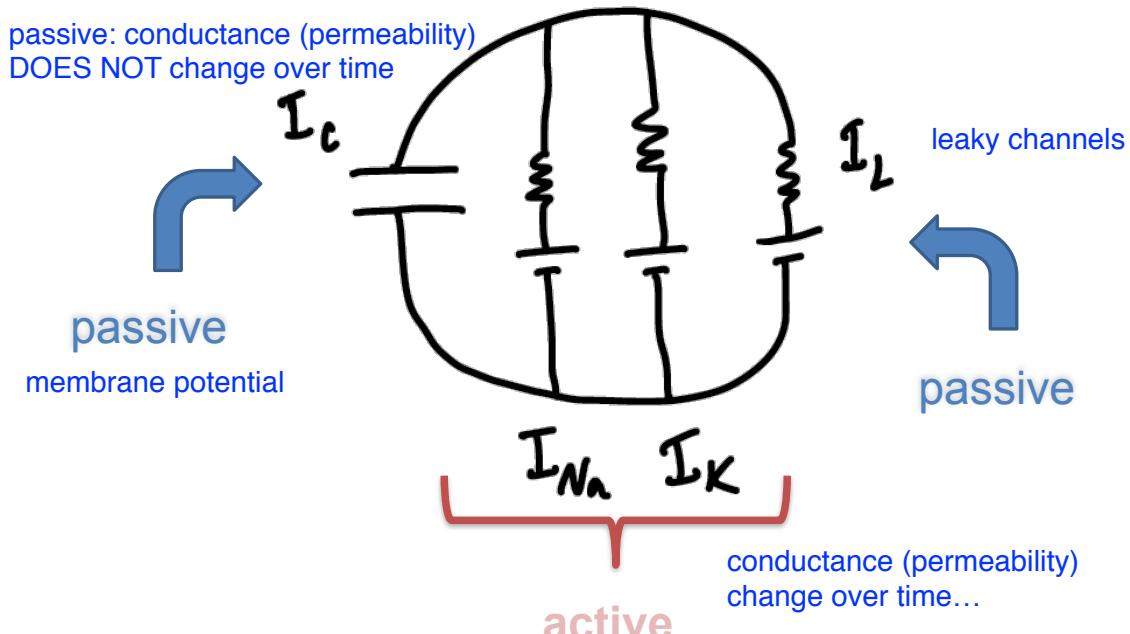


Thank you! Many slides by  
Drs. Gabrielle Gutierrez  
and  
Adrienne Fairhall

## Intrinsic neuron currents

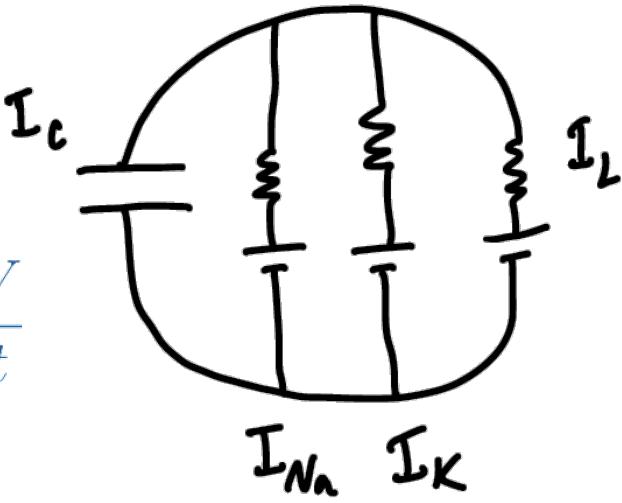
from the voltages, how do we get spikes?



# Intrinsic neuron currents

Text

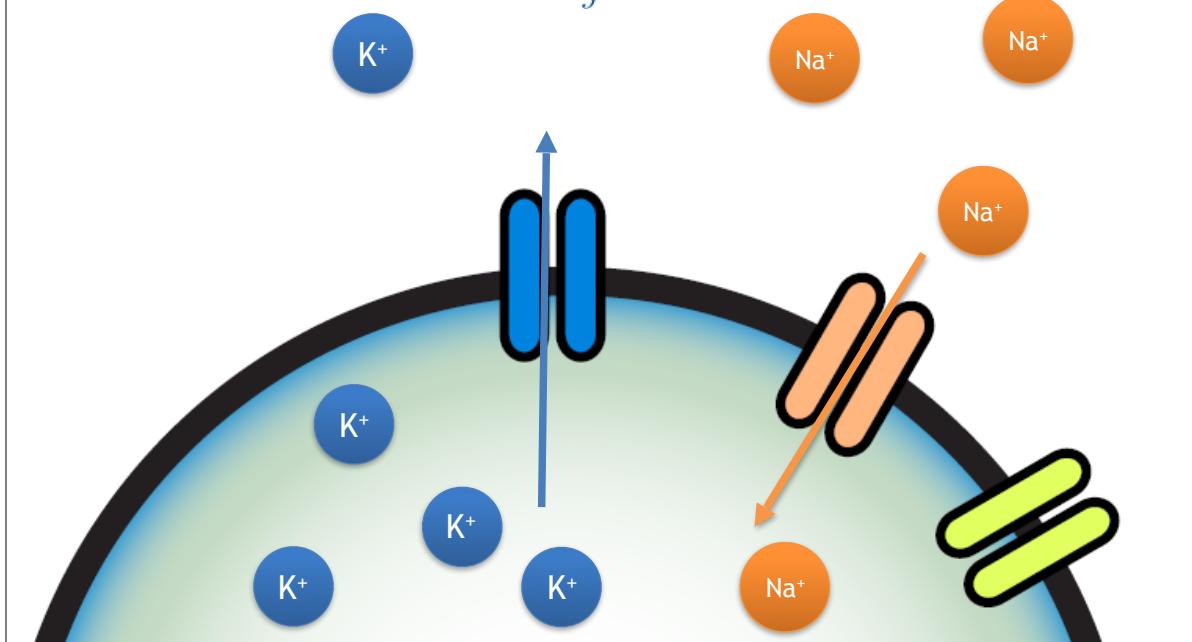
$$I_C = C \frac{dV}{dt}$$



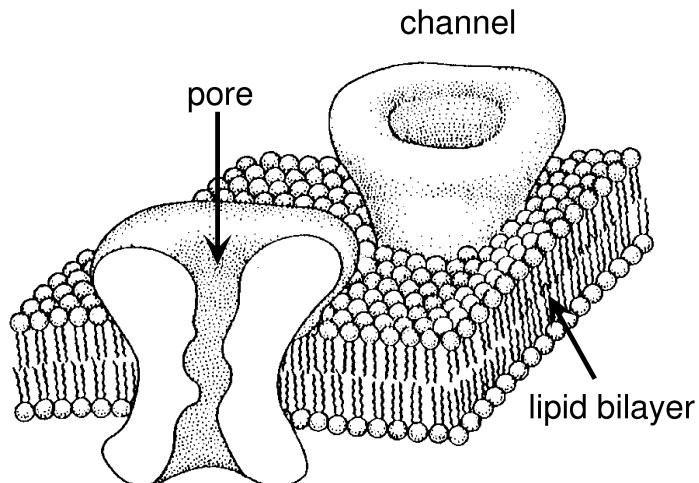
$$i_m = \sum_j g_j (V - E_j)$$

Driving force via  $E_j$ ; conductance  $g_j$

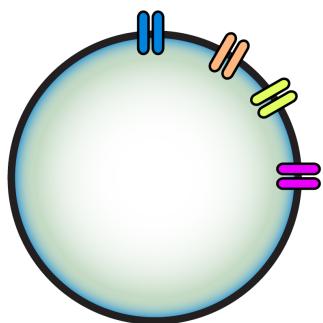
$$i_m = \sum_j g_j (V - E_j)$$



## Membrane patch



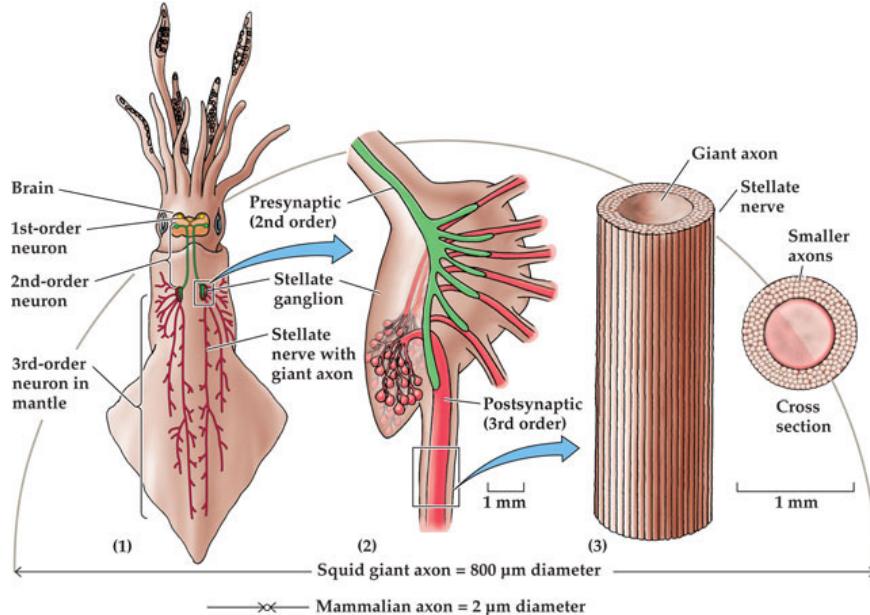
## The Hodgkin-Huxley model



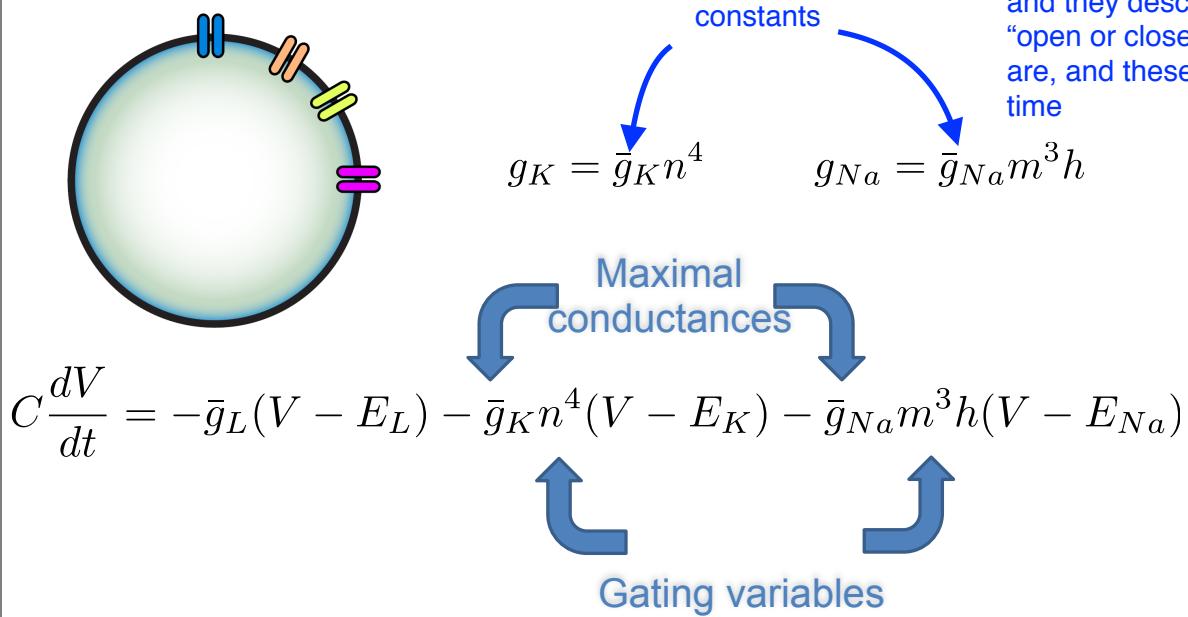
$$C_m \frac{dV}{dt} = -[I_L + I_K + I_{Na}]$$

# The Hodgkin-Huxley model

developed for a squid...



# The Hodgkin-Huxley model



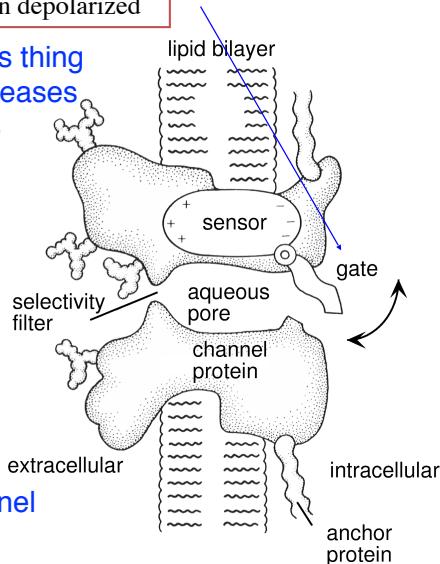
# The ion channel is a cool molecular machine

K channel: open probability increases when depolarized

chances this thing is open increases when cell is depolarized

$$P_K \sim n^4$$

probability of one channel being open



Persistent conductance

multiple subunits inside a channel  
 $n$  describes a subunit

$n$  is open probability  
 $1 - n$  is closed probability

Transitions between states occur at voltage dependent rates chance of subunit opening (changes over time with voltage)

$$\alpha_n(V) \quad C \rightarrow O$$

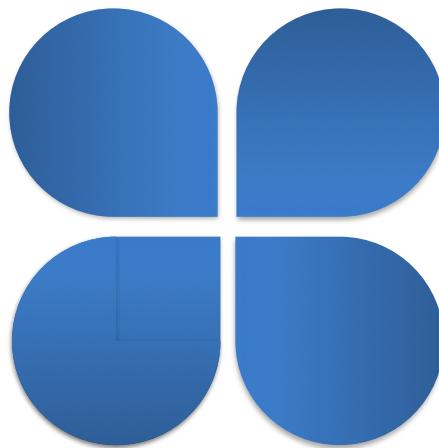
$$\beta_n(V) \quad O \rightarrow C$$

chance of subunit closing over time

$$\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n$$

rate of change of subunits openings

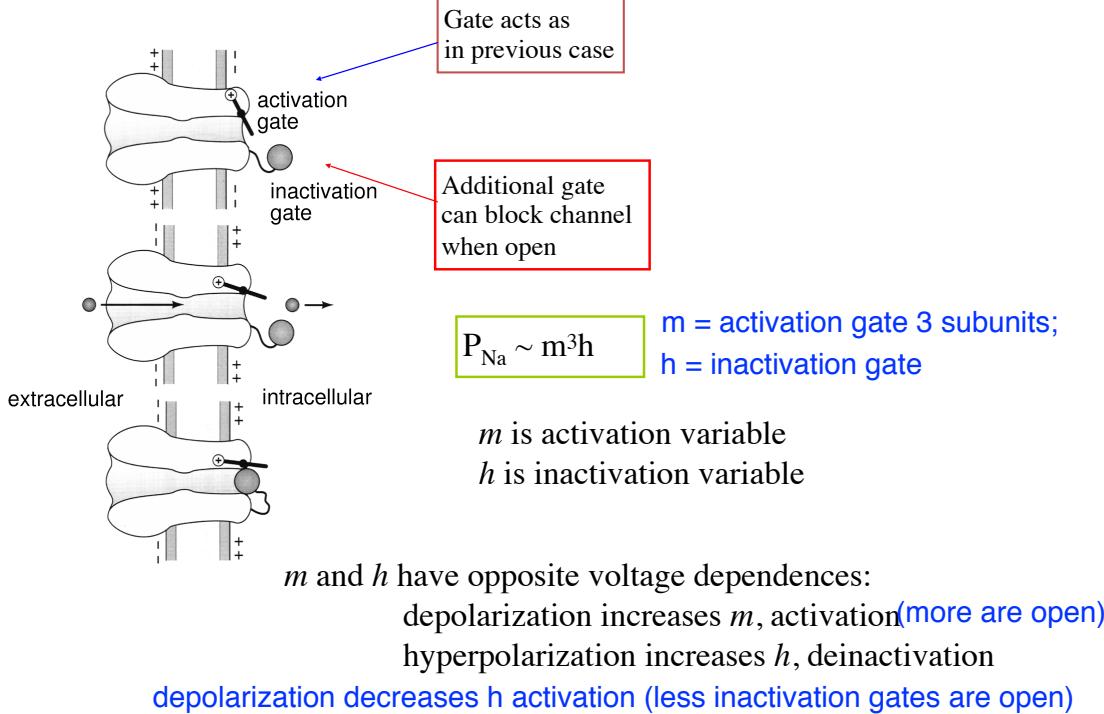
There are 4 “independent” subunits in the K channel



$$proba(1 \text{ subunit open}) = n$$

$$proba(\text{ all 4 subunits, and hence channel open}) = n^4$$

## Transient conductances



## Dynamics of activation and inactivation

$$\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n$$

$$\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V)m$$

$$\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V)h$$

what your  $n$  is approaching at a particular voltage  $V$

We can rewrite:

how fast  $n$  approaches its equilibrium. Large  $T$  = slow approach. Small  $T$  = fast

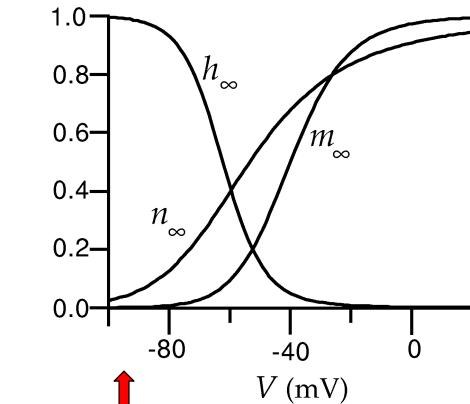
where

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}$$

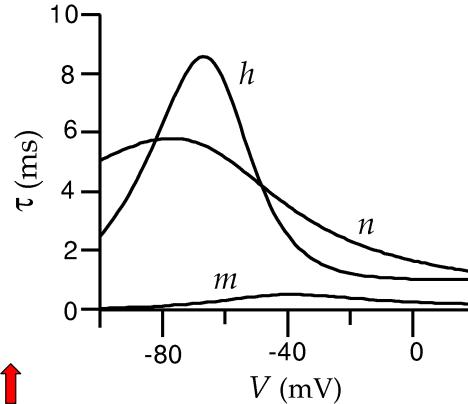
## Anatomy of a spike

where you are going as a function of t



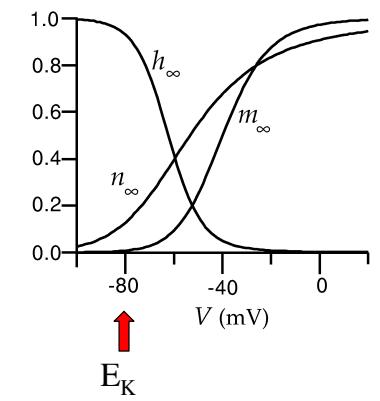
$E_K$   
one has high permeability  
at low potential, the other at high  
 $g_{Na} \sim m^3 h$

how fast you approach your equilibrium  
Low T = fast approach

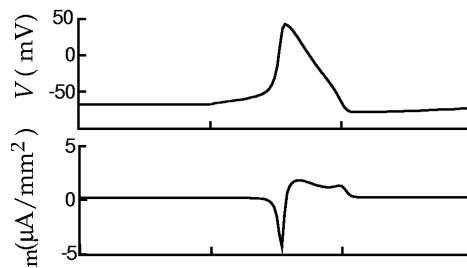
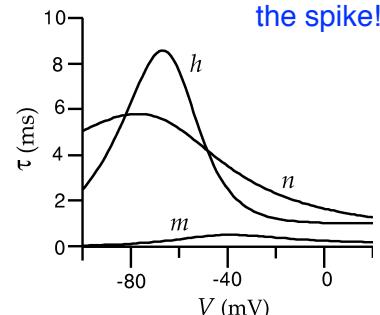


$E_{Na}$   
 $g_K \sim n^4$

## Anatomy of a spike

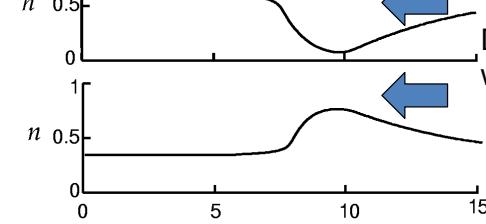


$E_K$   
this delay allows for  
the spike!



as voltage gets a higher,  
 $m$  approaches a higher  
value (closer to its max)  
Runaway +ve feedback

Low T so  $m$   
rises quickly  
As  $V$  rises,  $h$  drops low, dropping  $Na^+$  permeability...  
But  $h$  is slower to change as it has a large T (leads to delay)

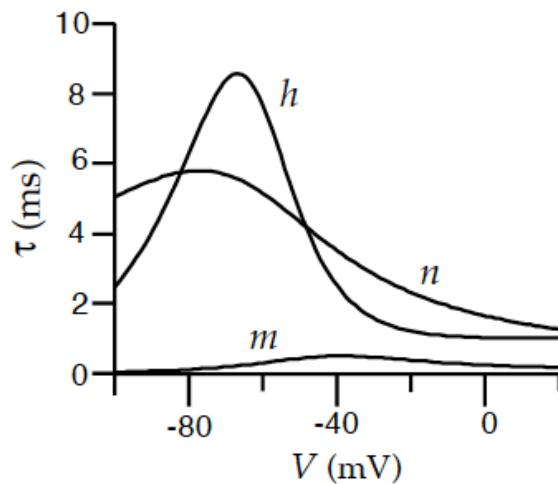
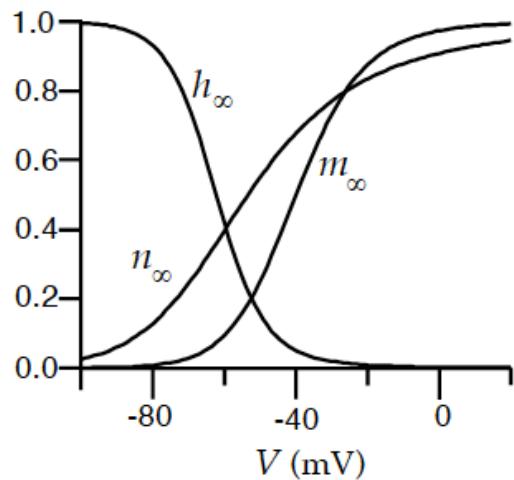


Double  
whammy

$n$  has a large T so it is slow to change... But at larger  
voltages, it approaches a high value increasing  $K^+$   
permeability

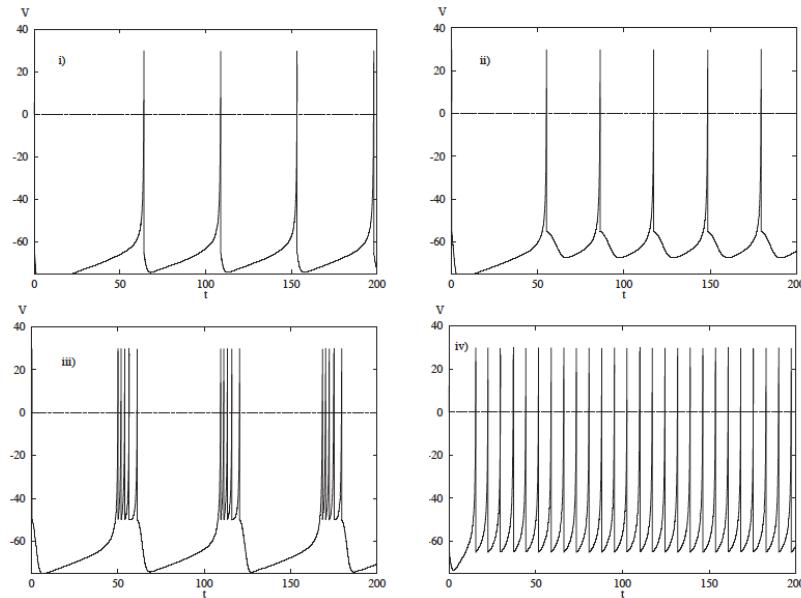
# Gating Variables

$$\tau_n(V) \frac{dn}{dt} = n_\infty(V) - n$$



HH code

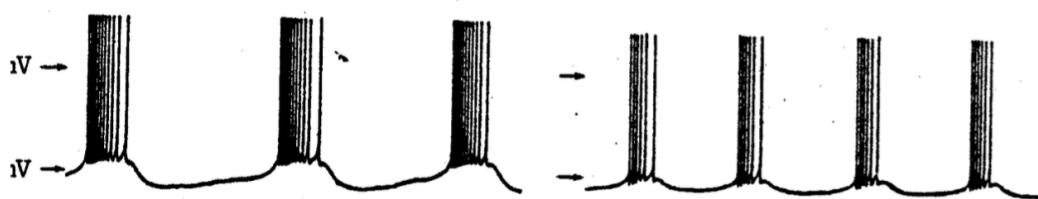
# Ion channel types, what are they good for?



DOI: 10.1016/j.physd.2011.05.012

1. Calcium processing can cause single neurons to autonomously produce rich dynamical behavior (much discovered at UW):

Tritonia “bursting pacemaker” cells, Smith thesis ‘77  
Mechanism: Ca-gated K current ( $I_{K,Ca}$ ):



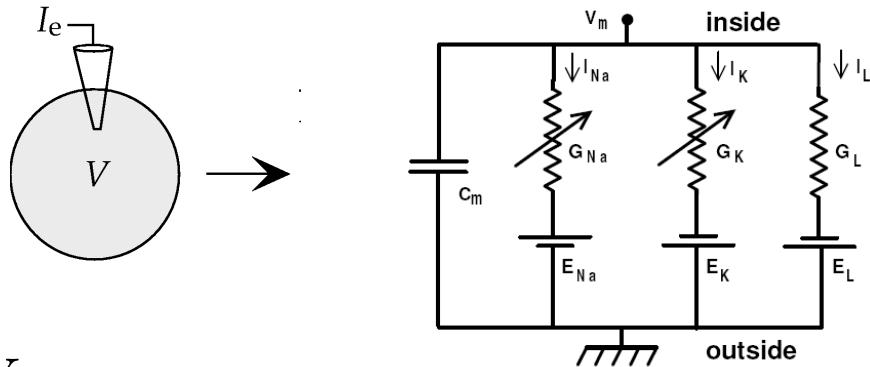
## GOAL : MODEL THIS BURSTING PROCESS

When neuron spikes, Ca flows into cell

This opens Ca-gated K channels

... which increases K conductance, switching off a burst

## Modeling Ca dynamics:



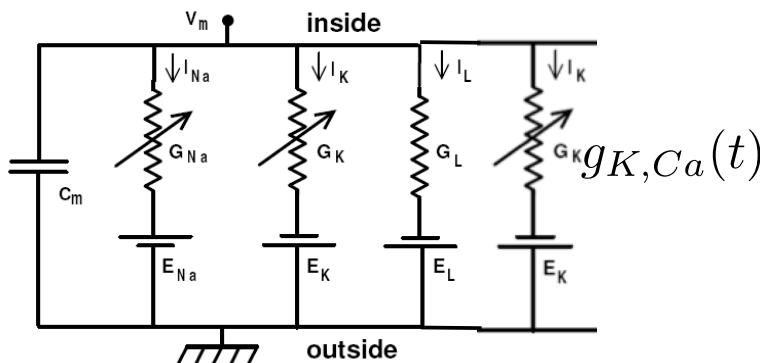
$$C \frac{dV}{dt} = \sum_j g_j(t)(E_j - V) + I_e(t)$$

Voltage-gated conductances  
("standard" HH:)

Calcium-dependent conductances  
(Smith, Connor/Stevens, ...)

$$\frac{dg_j}{dt} = F_j(g_j, V) \quad \frac{dg_j}{dt} = F_j(g_j, Ca)$$

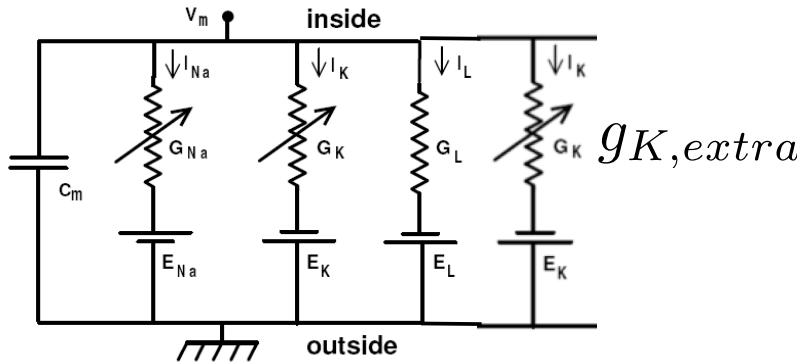
Model  $I_{K,Ca}$  as added current in HH equation.



$$C \frac{dV}{dt} = \dots + g_{K,Ca}(t)(E_K - V)$$

$\dots$  = standard HH terms

Warmup lab exercise: add constant K conductance



$$C \frac{dV}{dt} = \dots + g_{K,extra}(E_K - V)$$

... = standard HH terms

Warmup Lab exercise.

Start with HH.m code from website.

Set  $I=16.35$ ; %baseline current well into periodic spiking regime

Adjust initial conditions (typical values with this I)

$v\_init=-65$ ; %the initial conditions

$m\_init=.052$ ;

$h\_init=.596$ ;

$n\_init=.317$ ;

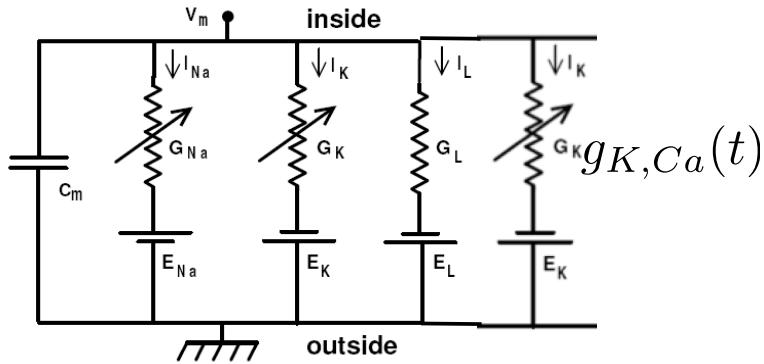
Add constant conductance  $g_{K,extra}$ . Thus, you should be simulating

$$C \frac{dV}{dt} = \dots + g_{K,extra}(E_K - V)$$

How large does  $g_{K,extra}$  need to be to terminate periodic spiking?

Solution code: HH\_increase\_constant\_gK\_terminate\_spiking.m

Model  $I_{K,Ca}$  as added current in HH equation.



$$C \frac{dV}{dt} = \dots + g_{K,Ca}(t)(E_K - V)$$

$\dots$  = standard HH terms

Blackboard: discussion of how we do this!

Step through HW problem pdf

Quick lab exercise:

Download HH\_burst\_via\_gK\_Ca\_conductance.m from our website

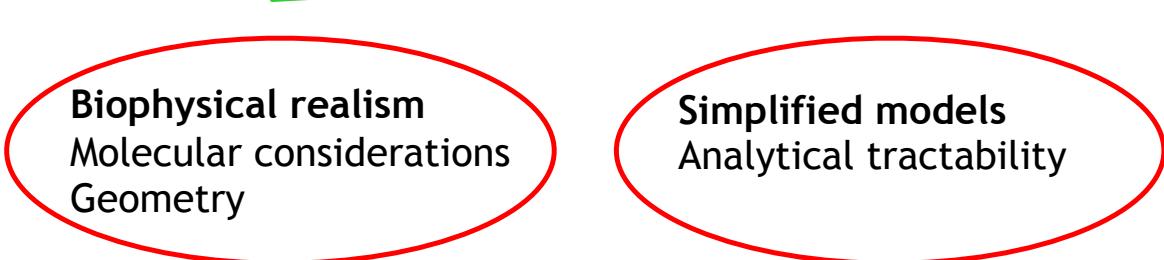
Explain to your neighbor, line by line, how the  $g_{K,Ca}$  conductance is implemented

See if you can find parameters that implement a burst.

gK\_Ca\_bar=0; to start  
gK\_Ca\_bar=10; gives burst

## Where to from here?

Hodgkin-Huxley



## The integrate-and-fire neuron

Like a passive membrane:

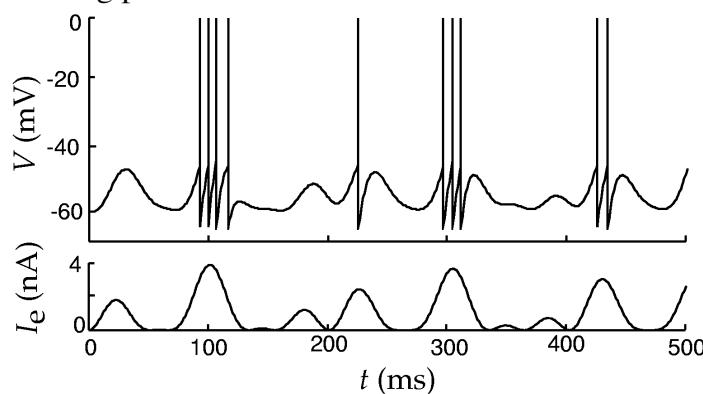
$$C_m \frac{dV}{dt} = -g_L(V - E_i) - I_e$$

but with the additional rule that

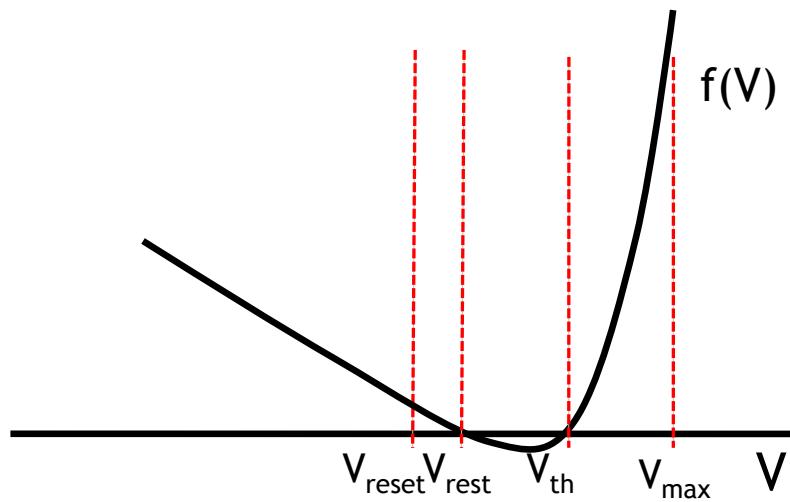
when  $V \rightarrow V_T$ , a spike is fired

and  $V \rightarrow V_{\text{reset}}$ .

$E_L$  is the resting potential of the “cell”.



## Exponential integrate-and-fire neuron



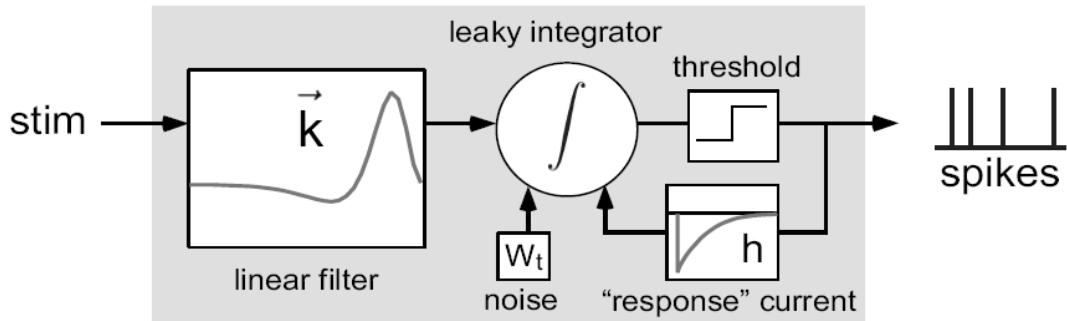
$$f(V) = -V + \exp([V-V_{\text{th}}]/\Delta)$$

## The spike response model

Kernel  $f$  for subthreshold response  $\leftarrow$  replaces leaky integrator  
Kernel for spikes  $\leftarrow$  replaces “line”

- determine  $f$  from the linearized HH equations
- fit a threshold
- paste in the spike shape and AHP

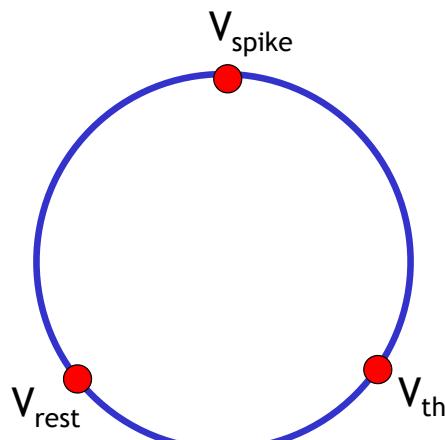
## The generalized linear model



- general definitions for  $k$  and  $h$
- robust maximum likelihood fitting procedure

Truccolo and Brown, Paninski, Pillow, Simoncelli

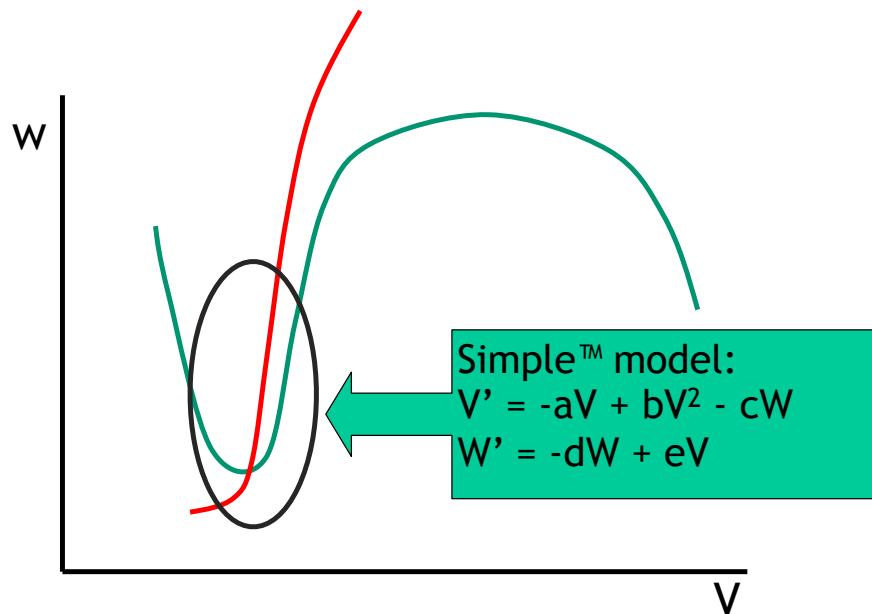
## The theta neuron



$$\frac{d\theta}{dt} = 1 - \cos \theta + (1 + \cos \theta) I(t)$$

Ermentrout and Kopell

## Two-dimensional models



## Where to from here?

Hodgkin-Huxley



Biophysical realism  
Molecular considerations  
Geometry

Simplified models  
Analytical tractability

