# To Spike or Not to Spike?

## Decisions from single neuron to simple networks

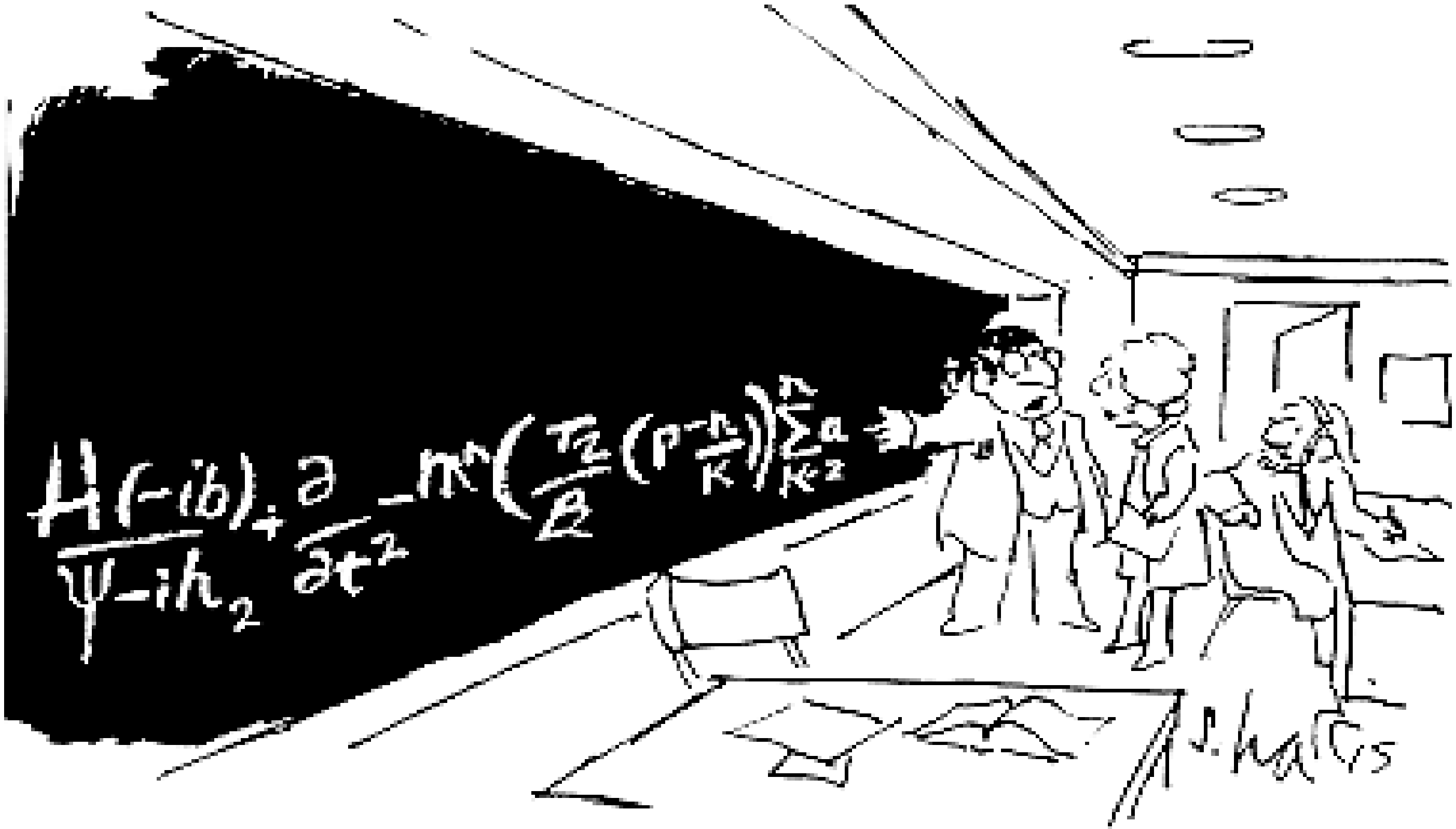
Boris Gutkin
GNT, DEC ENS

# Plan

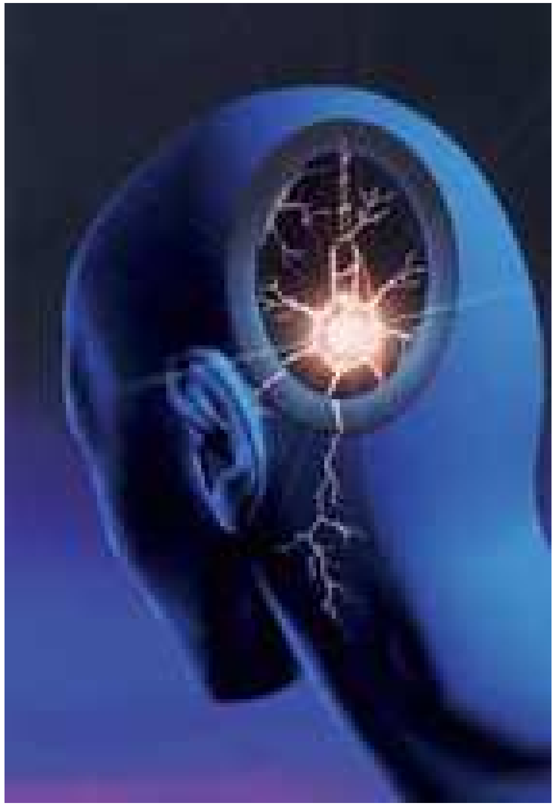
- How neurons integrate inputs
- Spike is a decision
- What is the threshold? What is the spike?
- Constructing a spike
- Constructing a network for decisions
  - 1 unit
  - 2 units: winner take all

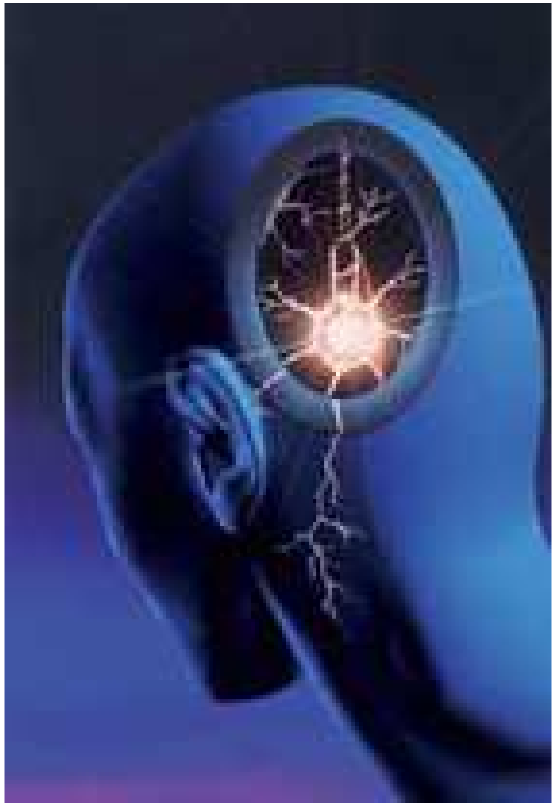
# Major Concepts

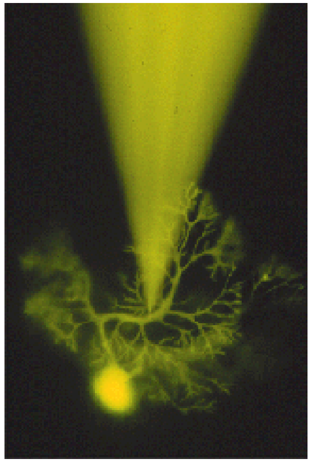
- All-or-none events
- Threshold crossing with no return
- Auto-catalysis: state-dependent positive feedback
- Reset: state-dependent delayed or slower negative feedback
- Memory/Forgeting: leak
- Winner-take-all dynamics

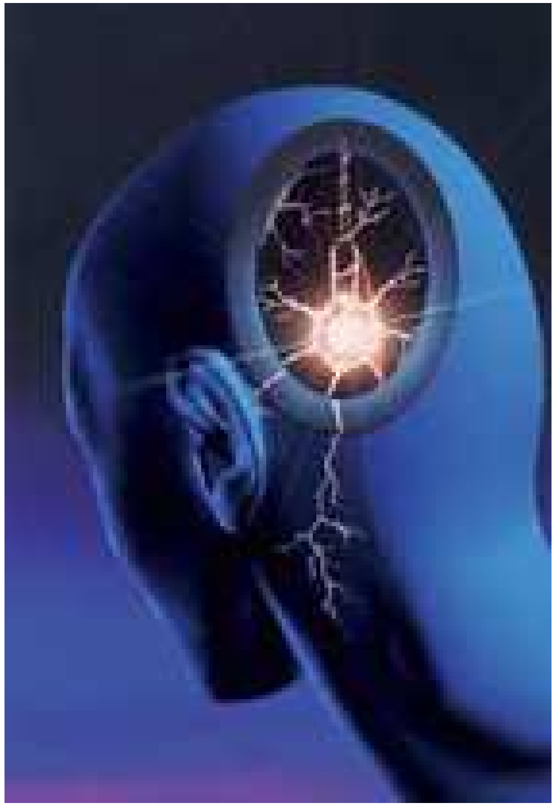


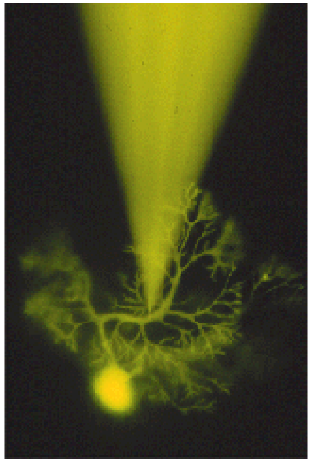
"But this *is* the simplified version for the general public."

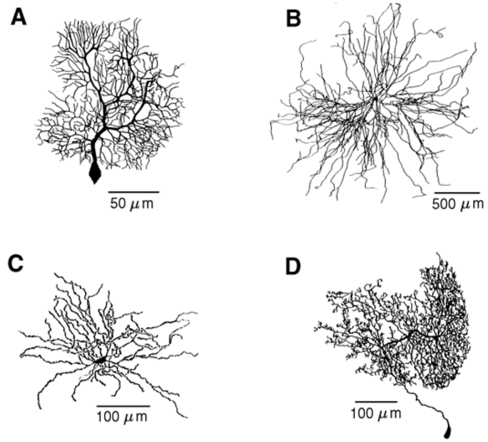


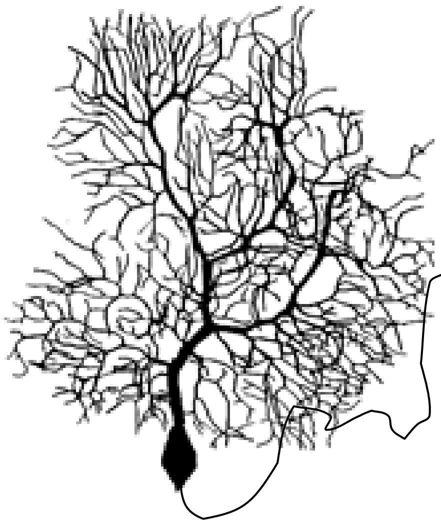
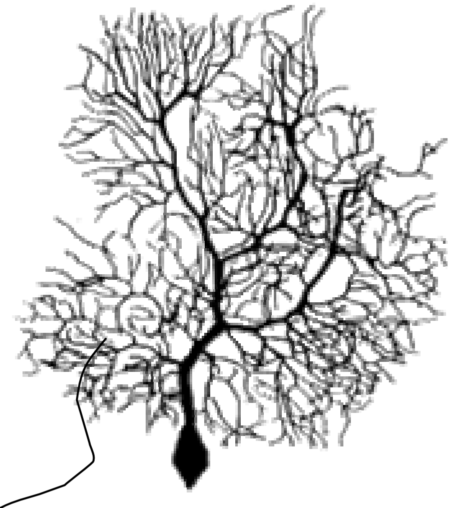


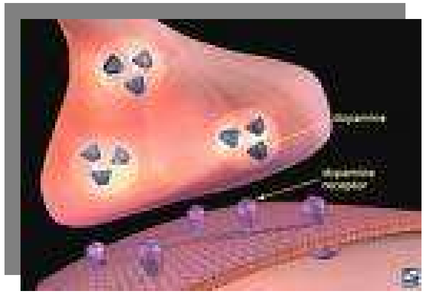


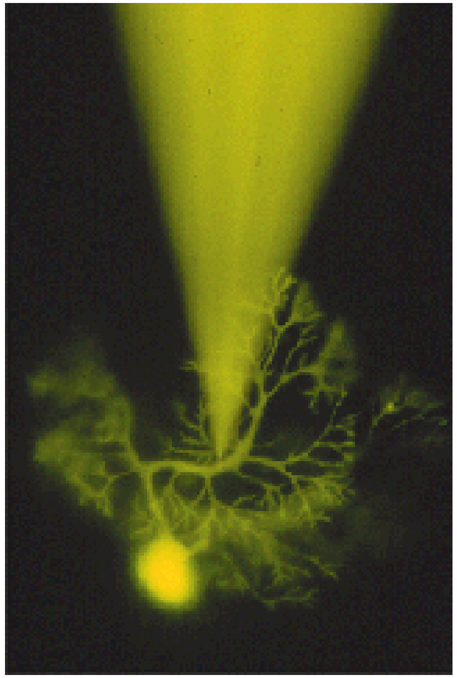


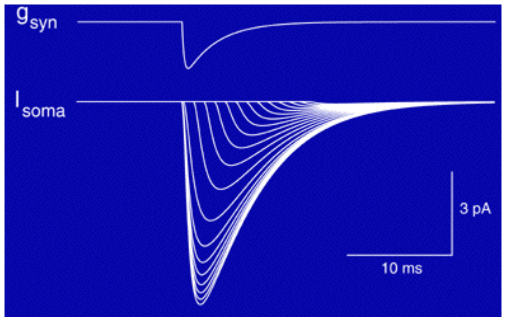



A
50 μm
B
500 μm
C
100 μm
D
100 μm

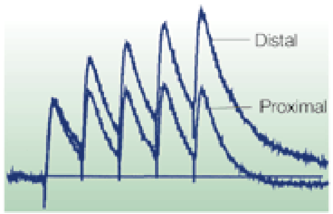





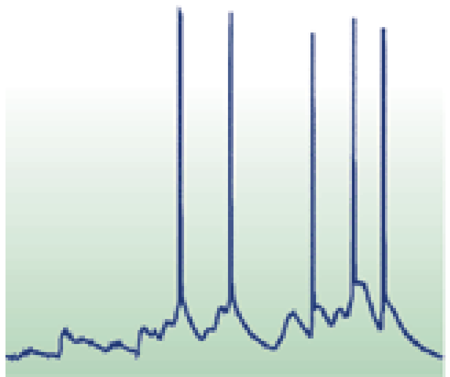




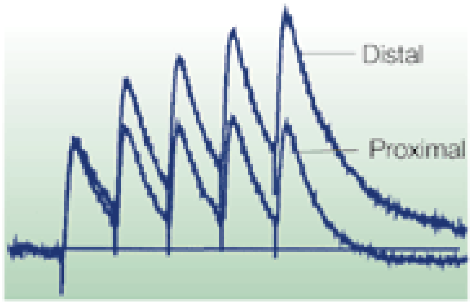
$g_{syn}$
$I_{soma}$
3 pA
10 ms

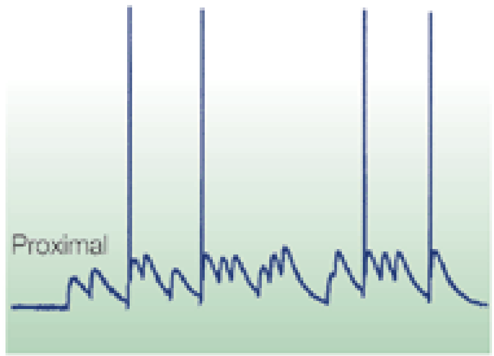



Distal
Proximal

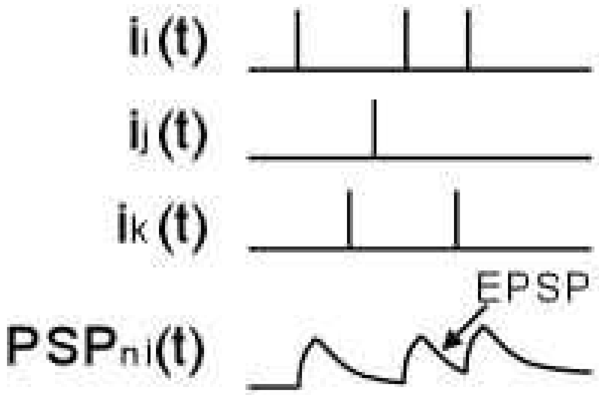



# Basic Operation: Integration



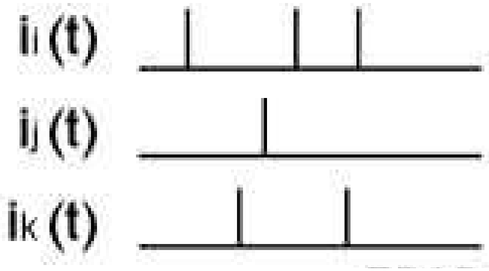

Neuron adds up its inputs




$$\sum input - currents(t_i)$$

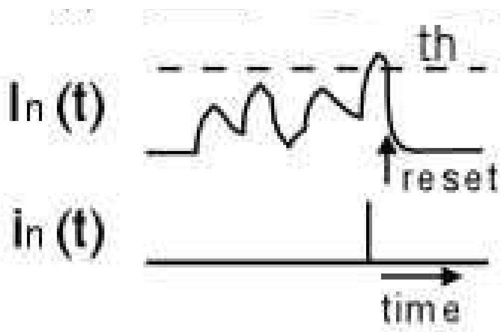
$$\frac{dV}{dt} = I = \sum EPSC(t_i)$$

# Perfect Integrator.



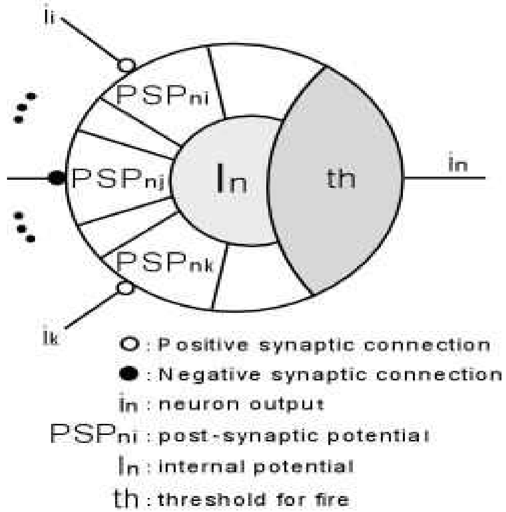

$$\sum input - currents(t_i)$$

$$\frac{dV}{dt} = I = \sum EPSC(t_i)$$




+ Threshold to create a spike

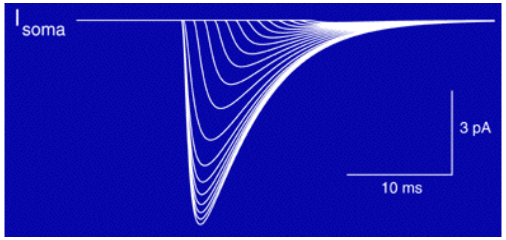
+ Reset Voltage



# Perfect Integrator

$$\frac{dV}{dt} = I(t) = \sum EPSC(t - t_i)$$

$$\int_{V(0)}^{V} \frac{dV}{dt} = \int_0^t I(t)dt = \int_0^t \sum EPSP(t_i)dt$$

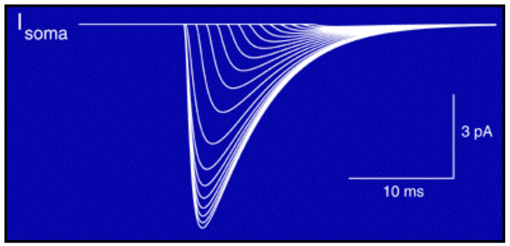



$$EPSC(t) = 0 \text{ for } t<t_i$$

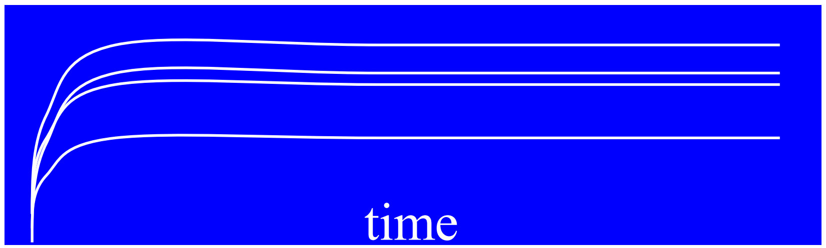
$$= e^{-t-t_i}$$

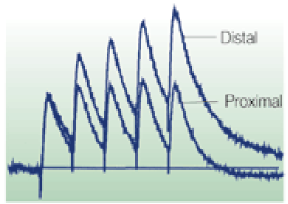
$$\int_{V(0)}^{V} \frac{dV}{dt} = 0 + \int_{t_i}^{t} e^{-(t-t_i)}dt = 1 + e^{(t-t_i)}$$

As time gets big, V(t) -> 1+V(0)

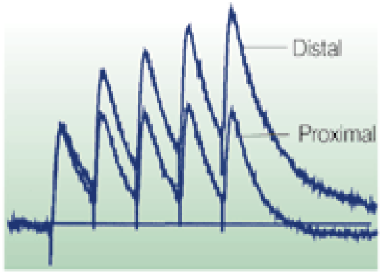



V



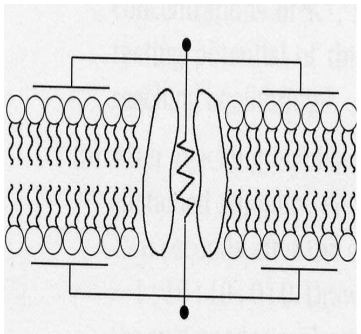
# Leak: forgetting

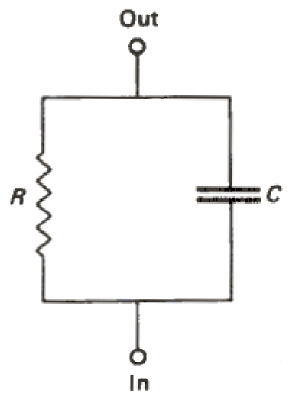


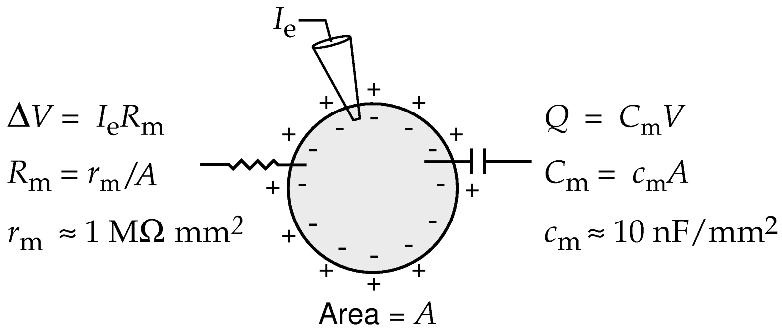

$$\tau \frac{dV}{dt} = -V + I(t) = -V + \sum EPSC(t - t_i)$$


$$\tau \frac{dV}{dt} = -(V - E_m) + I(t) = -(V - E_m) + \sum EPSC(t - t_i)$$

Get here from Ohm's Law

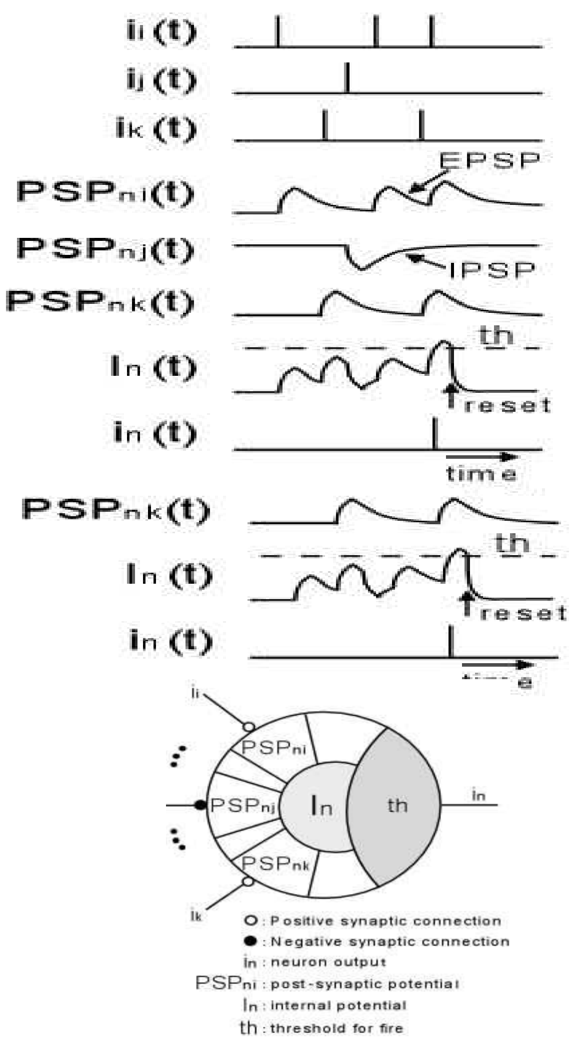


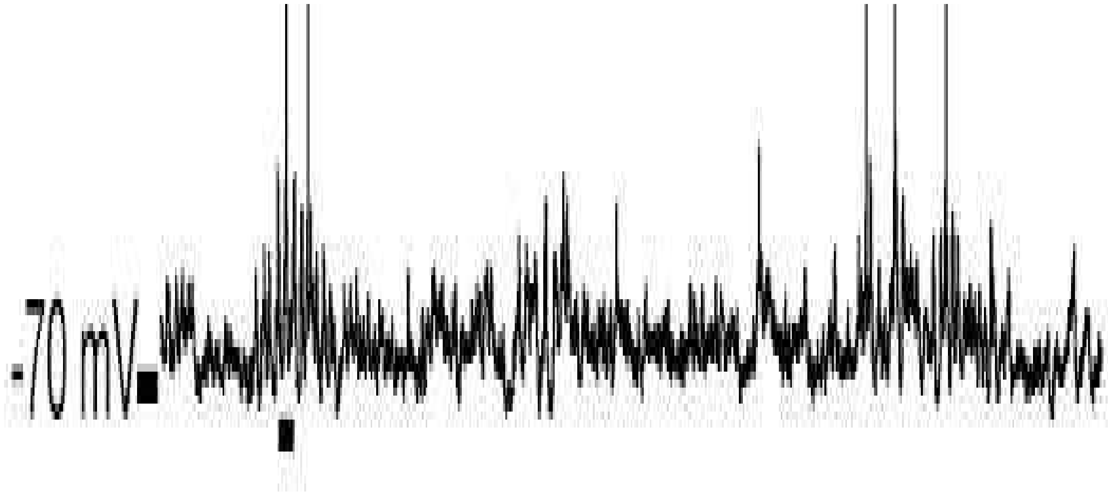



Lapicque (1907)

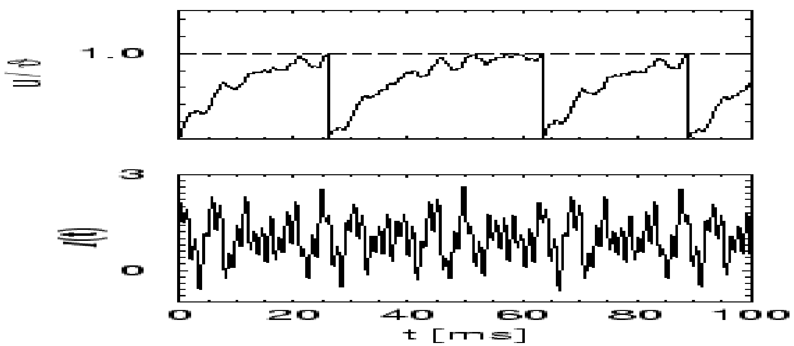
# Leaky Integrate and Fire Model



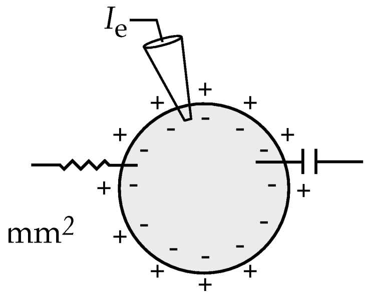

$$\tau \frac{dV}{dt} = -(V - E_m) + I(t) = -(V - E_m) + \sum EPSC(t - t_i)$$

+ threshold and reset



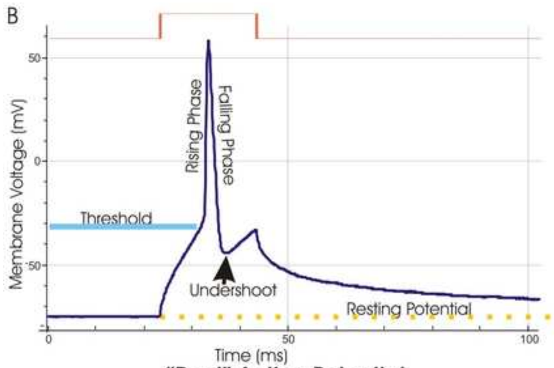
# What is the threshold?
# How is the spike made?

Biophysics

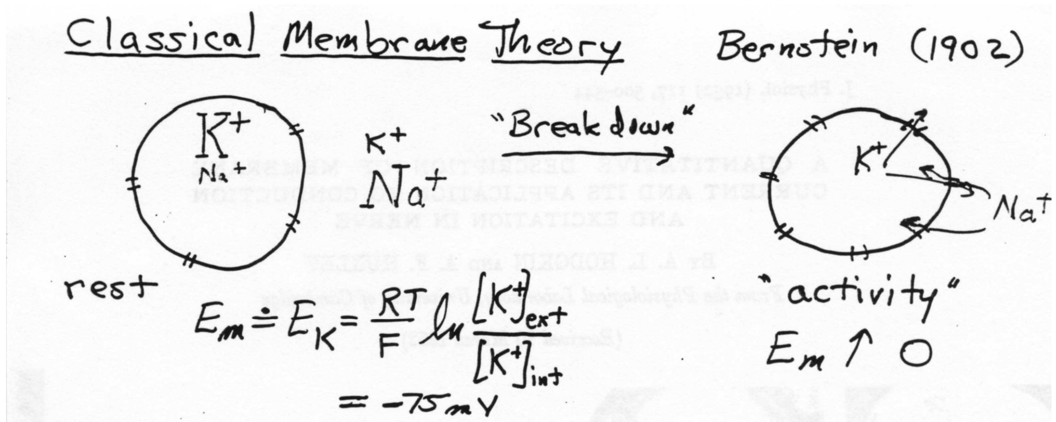



Break Down Model

Capacitance/resistance breaks down

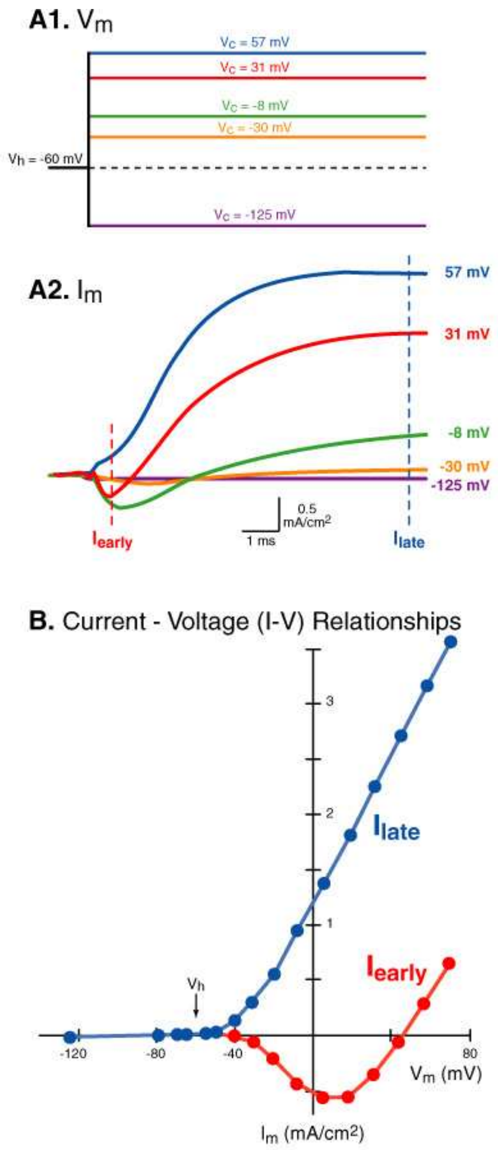



"Real" Action Potential




$$RC\frac{dV}{dt} = -V + I(t)$$

# Current Across Membrane




Pass a constant input current

Track the voltage

Record Current-Voltage Function
I-V Curves

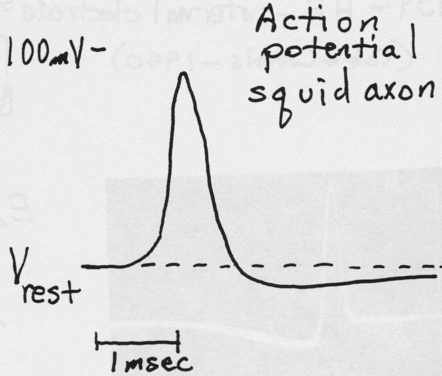
J. Physiol. (1952) 117, 500–544

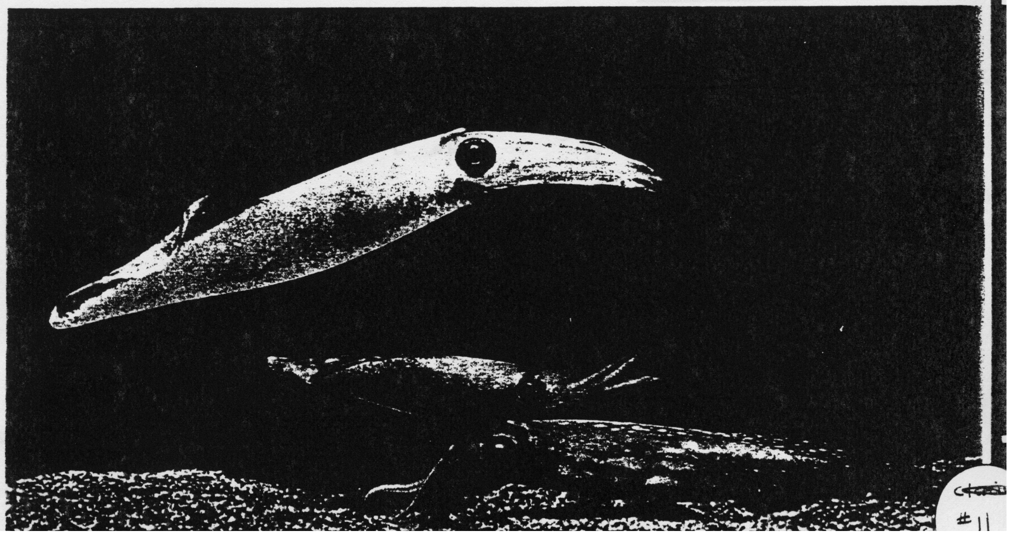
# A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

By A. L. HODGKIN and A. F. HUXLEY
*From the Physiological Laboratory, University of Cambridge*

(*Received* 10 *March* 1952)

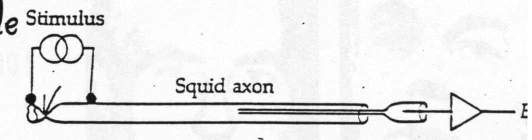
Alan Lloyd Hodgkin     Andrew Fielding Huxley

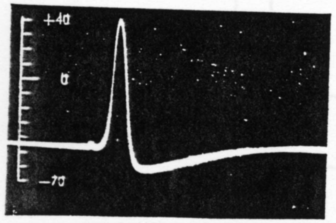


Nobel Prize, 1959

1939 – HH – internal electrode
(Cole + Curtis – 1940)




$E_m$ reverses —
Bernstein disproved.

WW II – '39-'47

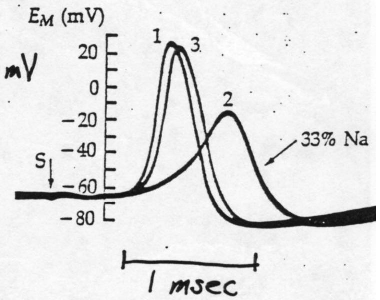
<u>Sodium</u> <u>Hypothesis.</u>
Selective change

Hodgkin + Katz (1949)
$g_{Na} > g_K$ during a.p.

rest: $g_K >> g_{Na} \Rightarrow E_m \doteq E_K$

a.p.: $g_{Na} >> g_K \Rightarrow E_m \uparrow E_{Na} = +60\,mV$

∴ $[Na^+]_{ext}$ affects a.p.



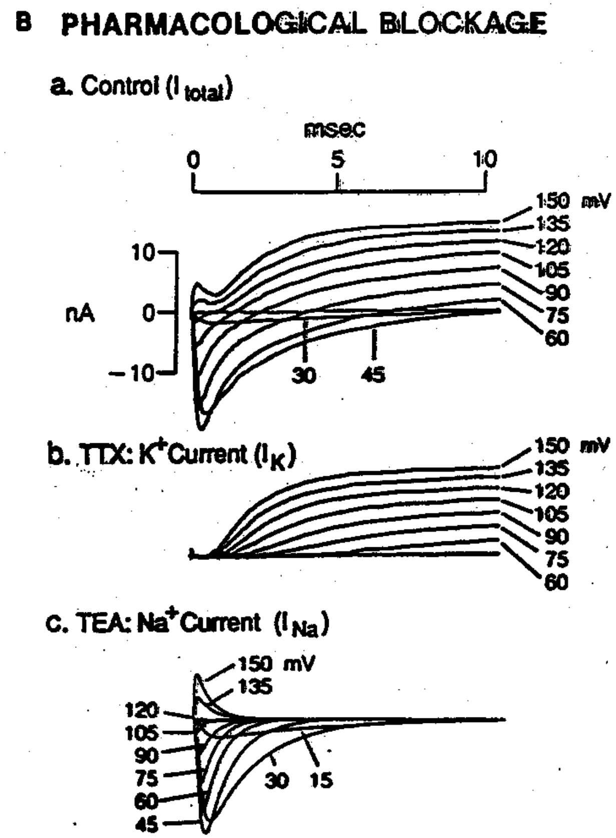




**Figure 7.** *B*, Separation of ionic currents by use of nerve poisons. *a*, Response in normal seawater; different amplitudes of voltage steps are indicated on the right (in mV). *b*, Response due to $I_K$ when $I_{Na}$ is blocked by tetrodotoxin (TTX). *c*, Response due to $I_{Na}$ when $I_K$ is blocked by tetraethylammonium (TEA). (From Hille, 1977).

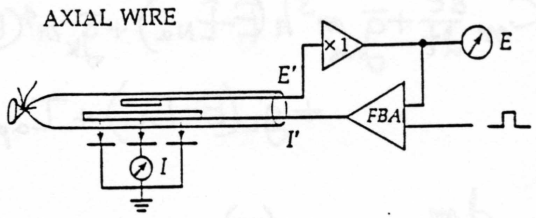
ing into the cell) followed by an outward movement of positive current (see Figure 9; solid line).

At this point, we need to define a bit of terminology that will be useful. In simple terms, ionic current through excitable membranes is controlled by two factors: (1) an ion-selective pore through which only certain ions can flow, and (2) a gate or gates that open(s) and close(s) the pore to allow ionic flux. The turning on of a current is known as the *activation* of the current and the opposite of activation is known as *deactivation*. These processes occur when an *activation gate* opens or closes. If a current turns on and then off despite a constant change in membrane potential, it is said to *inactivate*. The reverse of inactivation is *deinactivation*. Inactivation and

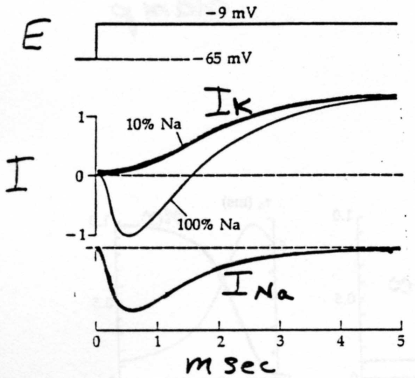
## Quantitate $I_K$, $I_{Na}$

Space clamp $\Rightarrow \frac{\partial E}{\partial x} = 0$ Cole, Marmont, HH ~ '48, '49

Voltage clamp $\Rightarrow \frac{\partial E}{\partial t} = 0$




1952 — HH — 5 papers




Separate by ion substitution

$$g_K = \frac{I_K}{E - E_K} \quad , \; \ldots$$

### Dependence on E

fit

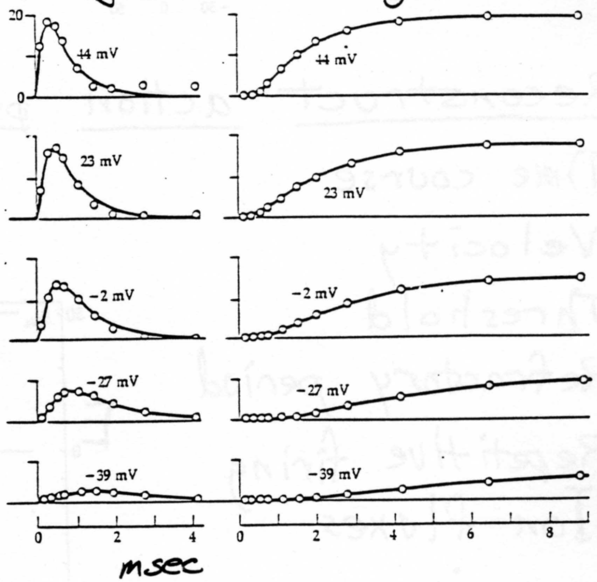
$$g_K(t) = \bar{g}_K \, n^4(t)$$

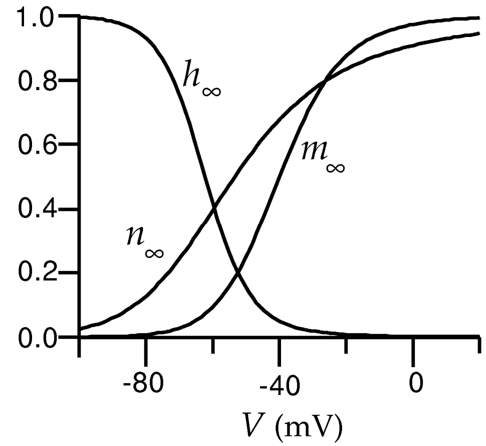
$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n$$

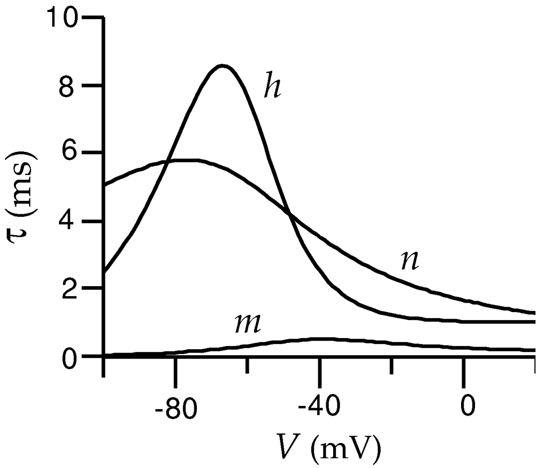
open $K^+$ channel requires 4 "particles" in active state

$$P \underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}} P^*$$

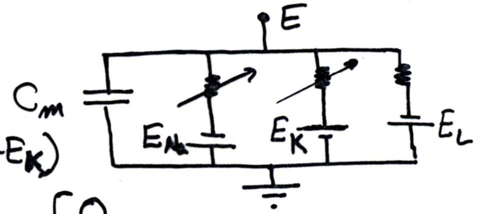
$$g_{Na}(t) = \bar{g}_{Na} \, m^3(t) \, h(t)$$



# HH Eqns




$$C_m \frac{dE}{dt} + \bar{g}_{Na} m^3 h (E - E_{Na}) + \bar{g}_K n^4 (E - E_K)$$
$$+ g_L (E - E_L) + I_{app} = \begin{cases} 0 \\ \frac{d}{4R} \frac{\partial^2 E}{\partial x^2} \end{cases}$$
– cable w/o space clamp

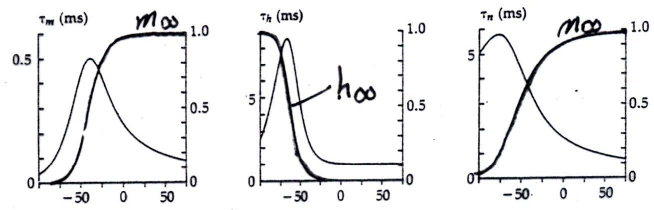
$E = V_m$, membrane potential

$$\frac{dm}{dt} = \phi \frac{m_\infty(E) - m}{\tau_m(E)}$$

$$\frac{dh}{dt} = \phi \cdots$$

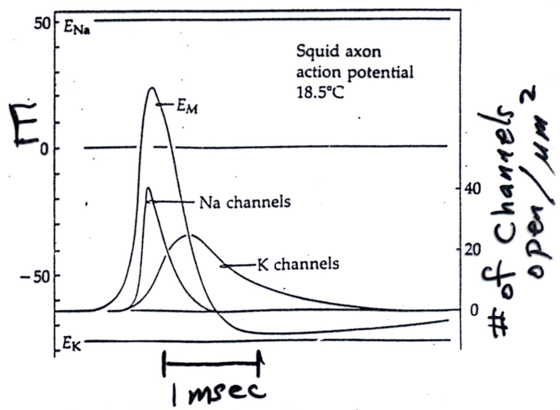
$$\frac{dn}{dt} = \phi \cdots$$

$\phi \sim$ Temperature

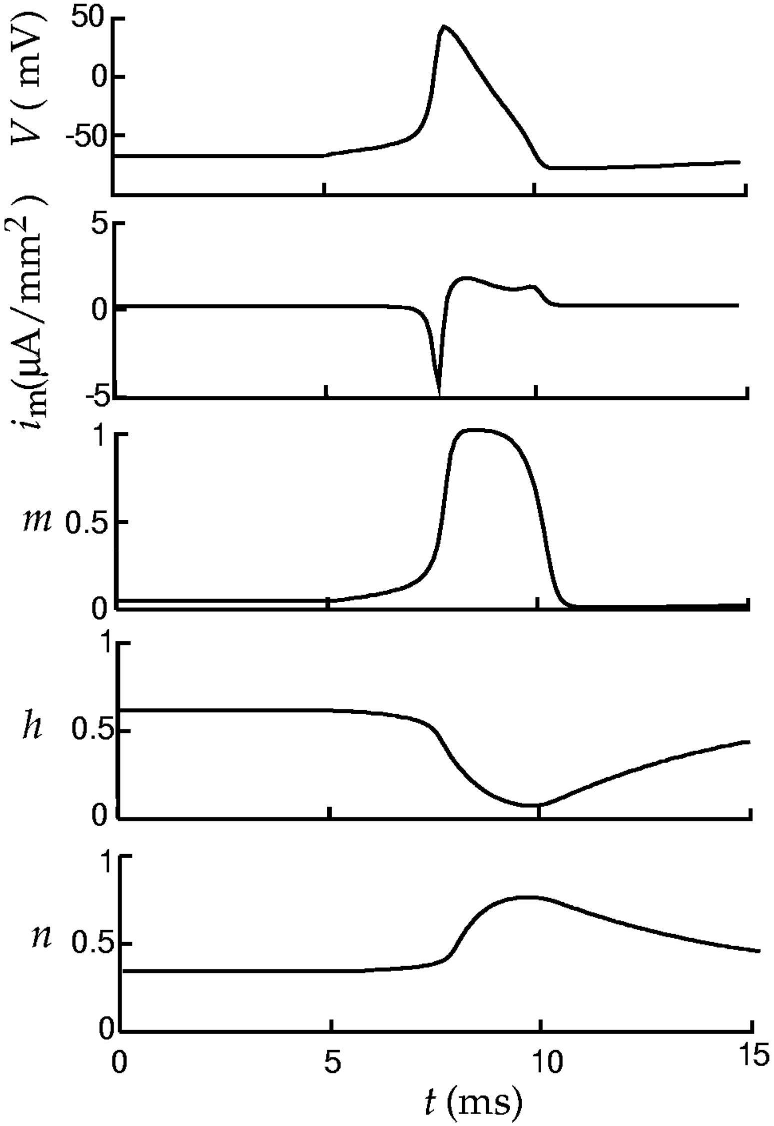



## Reconstruct action potential

Time course
Velocity
Threshold
Refractory period
Repetitive firing
Ion fluxes
⋮



# The Action Potential: players




Voltage event

Current -- $V'(t)$

Na Activation

fast

Na inactivation

K activation

slow

Simulation (by DeFelice et al, 1993) of patch of HH membrane w/ channels treated stochastically.

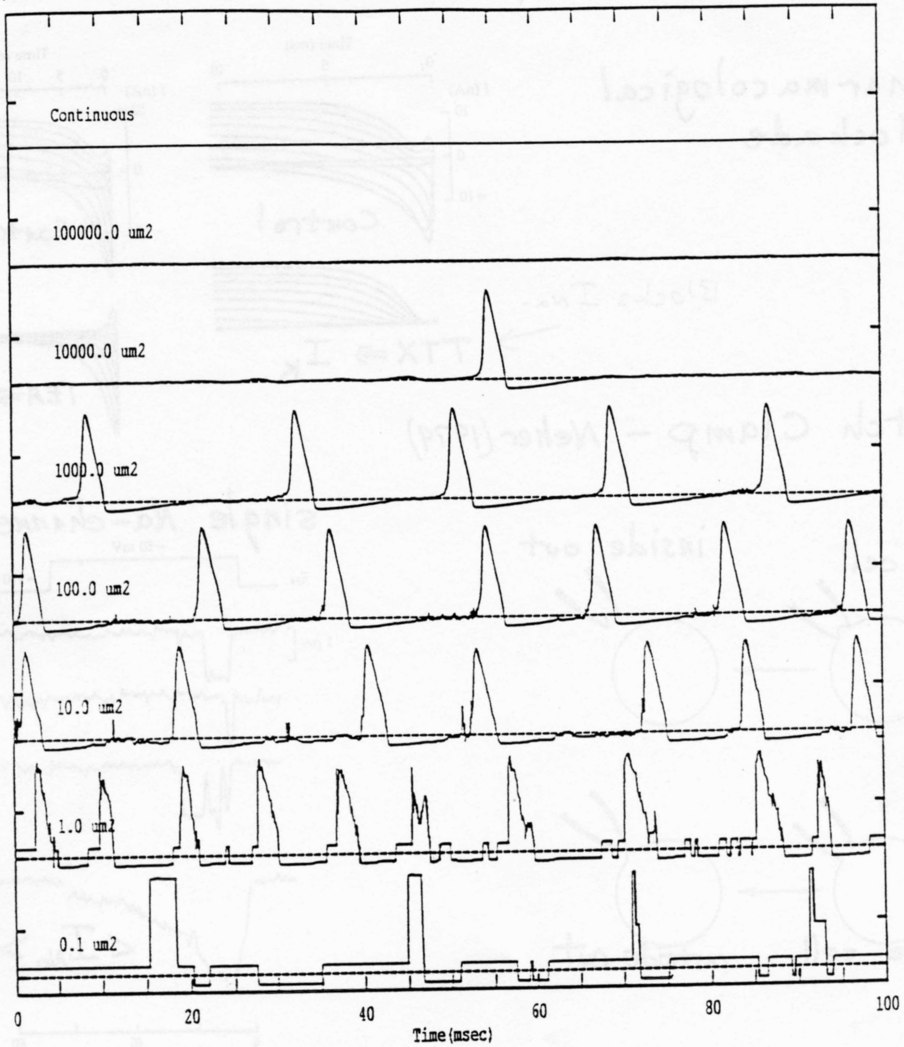


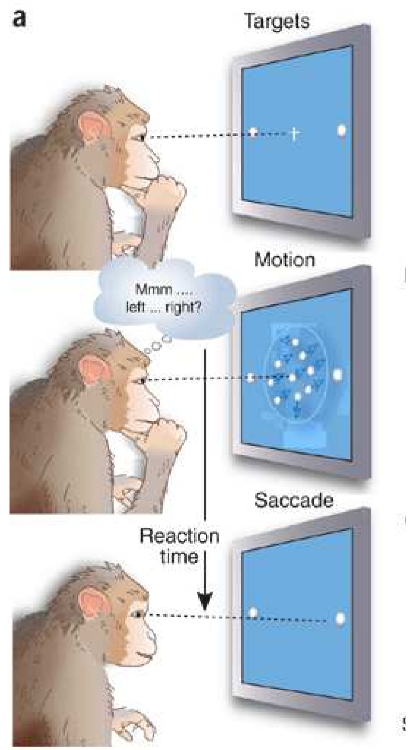

**Figure 3: Membrane Response without Injection Current**
The membrane model is simulated with standard biophysical parameters for squid axonal membrane ($C_m, E_{Na}, E_K, E_L, g_L$) and with no current injection ($I_{\text{inject}} = 0 \frac{pA}{\mu m^2}$). The continuous Hodgkin-Huxley equations and the discrete channel populations are used alternatively to represent the membrane conductances $g_{Na}$ and $g_K$. As the membrane surface area is increased, the response from the channel model converges to the response from the standard Hodgkin-Huxley model. Both models predict that no activity occurs when no current is injected. However, as the membrane surface area is decreased, the active behavior predicted by the channel model diverges dramatically from the lack of activity predicted by the Hodgkin-Huxley model.

# In order to produce the spike

- Integrate inputs
- State dependent positive feedback: autocatalysis
- Cross-threshold:
    - **Point of no return** for Na
- All-or-none action (potential)
    - **Fast Positive feedback**
    - **Slower NEGATIVE FEEDBACK**
- **Forgetting: leak**

# So a spike is like a decision

- Neuron integrates inputs
- Decides if they are above threshold
- Take a all-or-none action
- Resets to start again




•Observer collects evidence

•Decides if his/her certainty threshold is reached

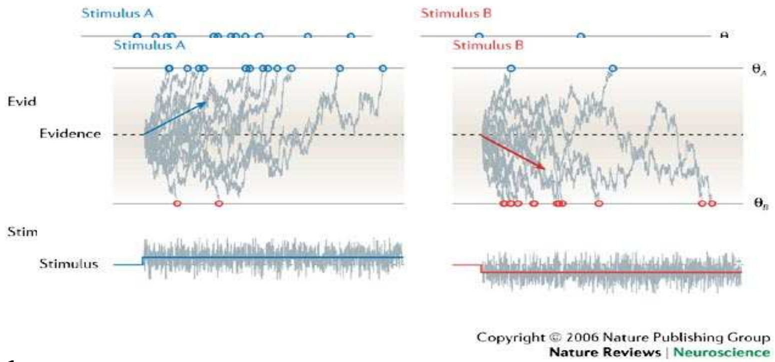
•Takes the action
•Starts over again

When the inputs (evidence) come randomly in time
Voltage does a random walk to threshold
Classical models of decision making: diffusion models

Leak: forgetting the evidence!

# In order to make decision for two choices?

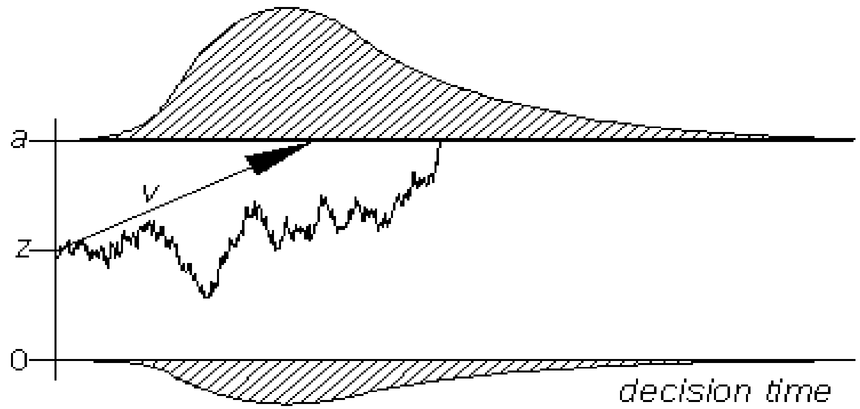
- Imagine neuron
  - Choice 1 + inputs
  - Choice 2 - inputs



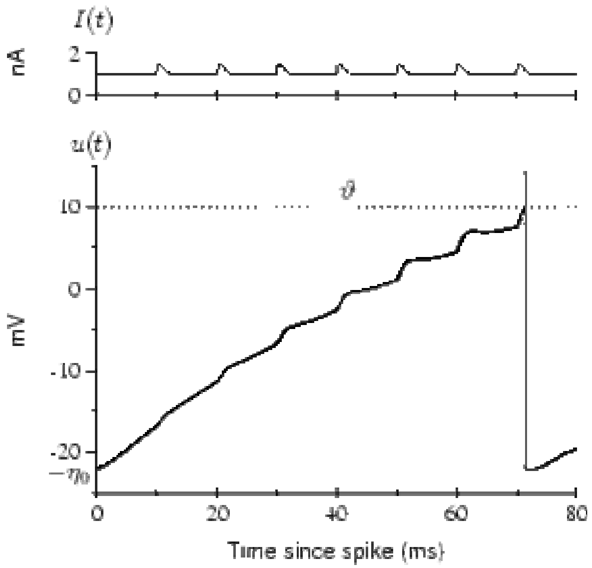

- Integrate to two thresholds
- Two neurons
  - Neuron 1 - choice 1
  - Neuron 2 - choice 2

# Decision Time

- How long does it take to reach the decision criterion




- Spike Time
  - How long does it take to reach the threshold
- Force/rate of evidence
- Rate of forgetting
  - Time constant



# Interactions Between Choices

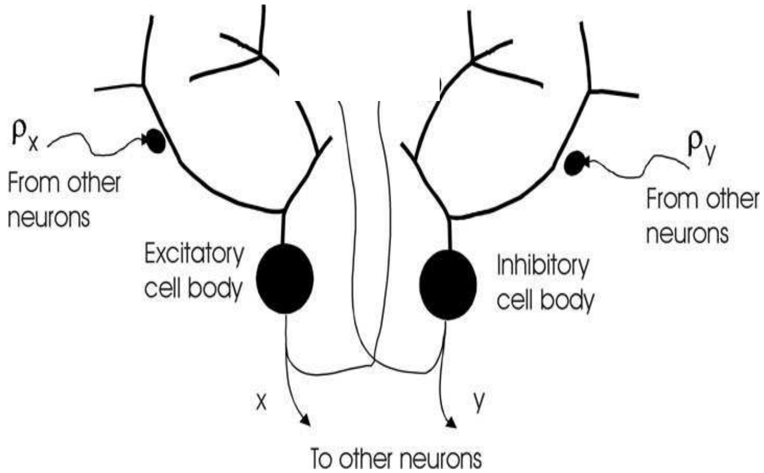
- No interactions -- both choices are possible at same time
  - Cogmaster AND Sleep
- **Alternative choice**
  - Cogmaster OR Sleep
- Exclusive spiking: winner-take-all
- Inhibition between neurons

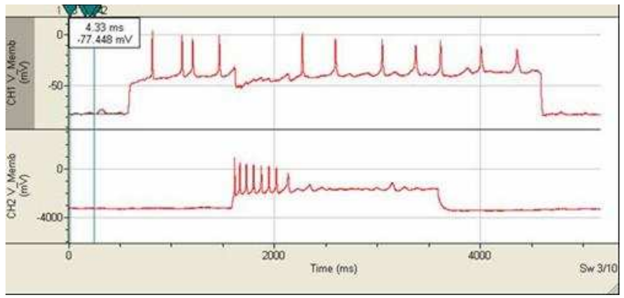
$$\frac{dV_1}{dt} = -\frac{V_1}{\tau} + I_A(t) - s_{12}$$

$$\frac{dV_2}{dt} = -\frac{V_2}{\tau} + I_B(t) - s_{21}$$

$$\frac{ds_{ij}}{dt} = \frac{\delta(t - t_j)}{\tau_s}$$

+threshold
+ reset



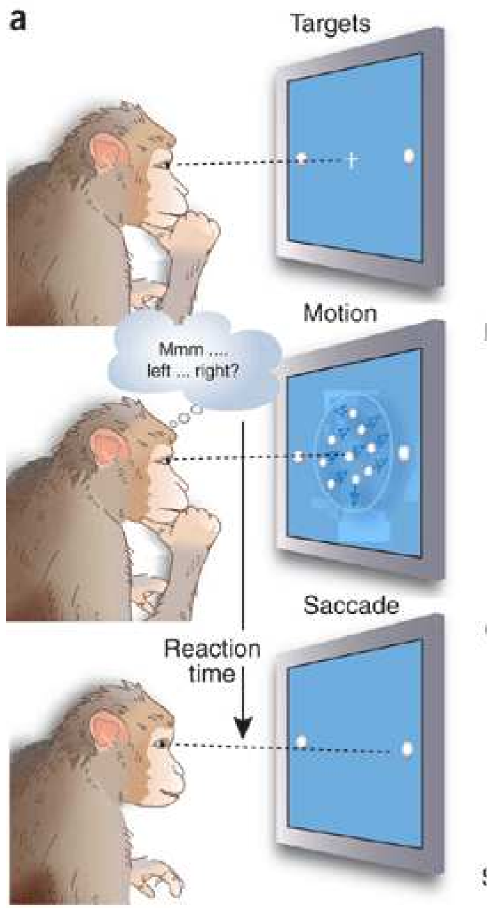



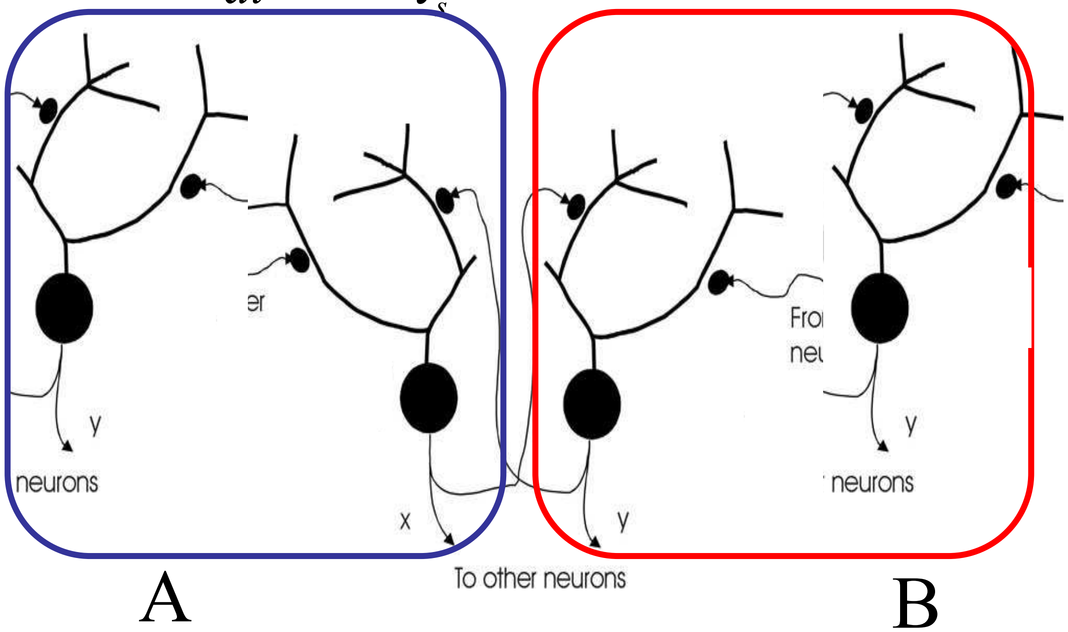
# - Forgetting at rate of leak

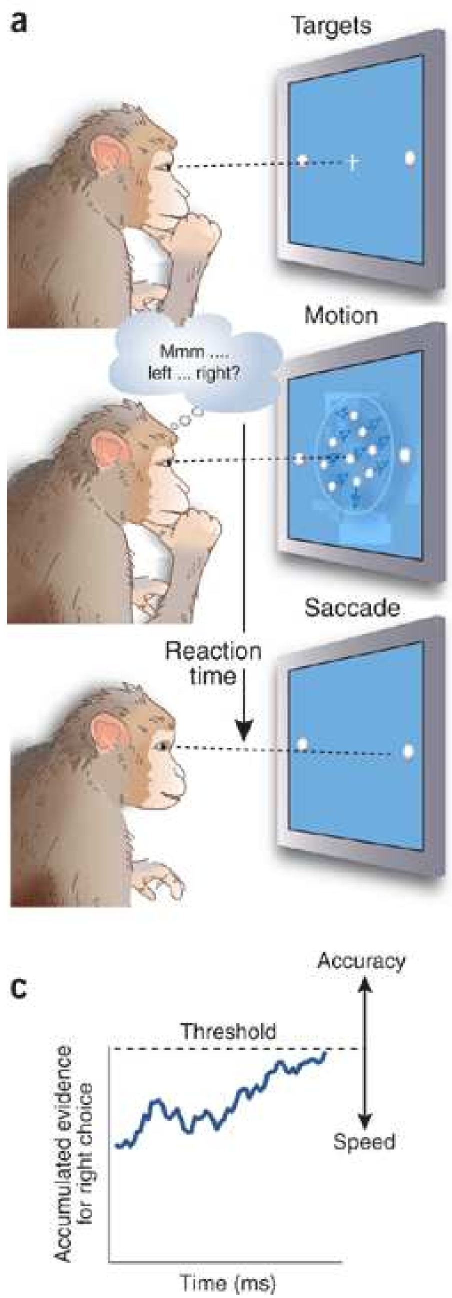
$$\frac{dV_1}{dt} = -\frac{V_1}{\tau} + I_A(t) - s_{12}$$

$$\frac{dV_2}{dt} = -\frac{V_2}{\tau} + I_B(t) - s_{21}$$

$$\frac{ds_{ij}}{dt} = \frac{\delta(t - t_j)}{\tau_s}$$






# Mutual excitation of like neurons gives memory

$$\frac{dV_1}{dt} = -\frac{V_1}{\tau} + I_A(t) + \sum s_{ijA} - \sum s_{ijB}$$

M

$$\frac{dV_{iA}}{dt} = -\frac{V_{iA}}{\tau} + I_A(t) + \sum s_{ijA} - \sum s_{ijB}$$

$$\frac{dV_{1B}}{dt} = -\frac{V_{1B}}{\tau} + I_B(t) + \sum s_{ijB} - \sum s_{ijA}$$

M

$$\frac{dV_{iB}}{dt} = -\frac{V_{iB}}{\tau} + I_B(t) + s_{ijB} - s_{ijA}$$

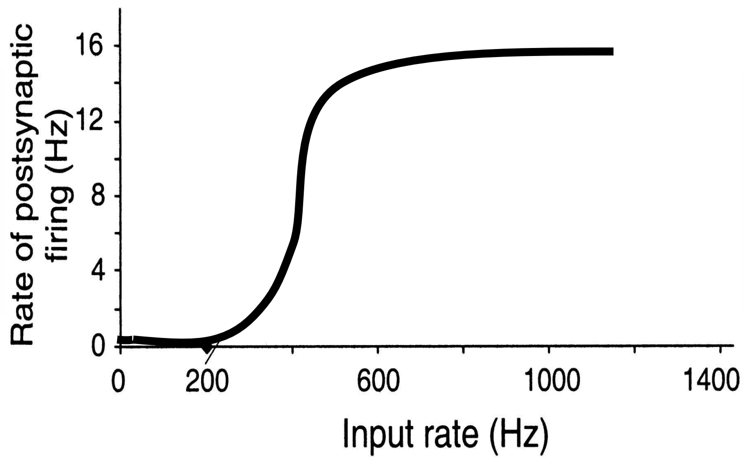
$$\frac{ds_{ij}}{dt} = g\frac{\delta(t - t_j)}{\tau_s}$$

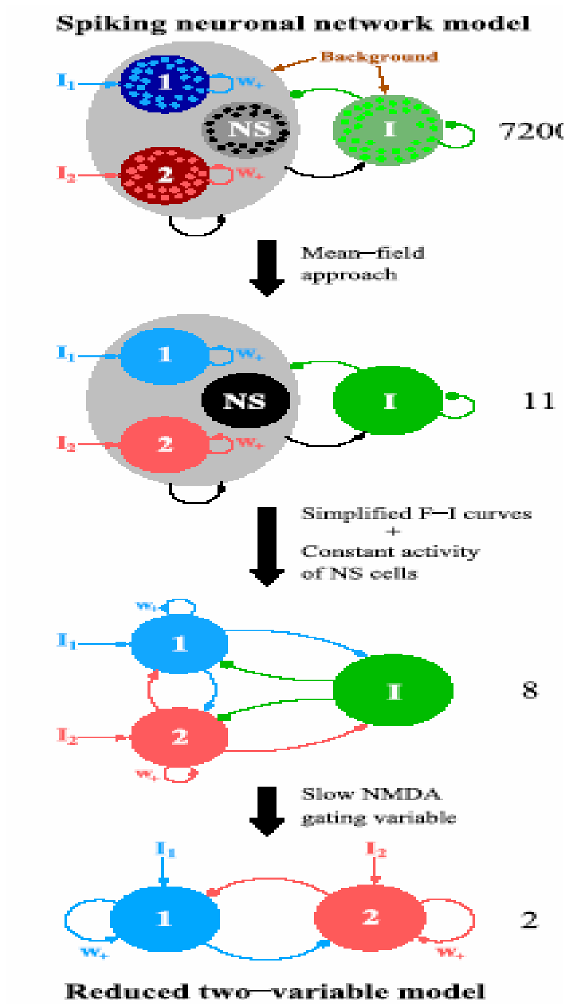
# From single neuron to networks

- Winner-take all in networks of firing rate units.

$$\frac{dU_1}{dt} = -\frac{U_1}{\tau} + S[I_A(t) + s_{11}U_1 - s_{12}U_2]$$

$$\frac{dU_2}{dt} = -\frac{U_2}{\tau} + S[I_B(t) + s_{22}U_2 - s_{21}U_1]$$

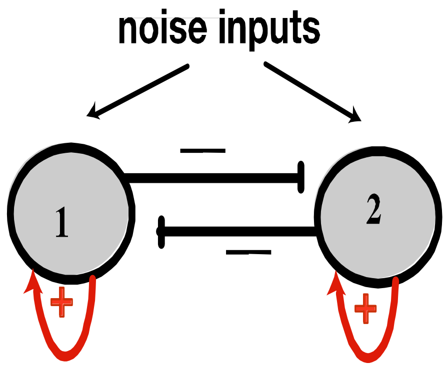


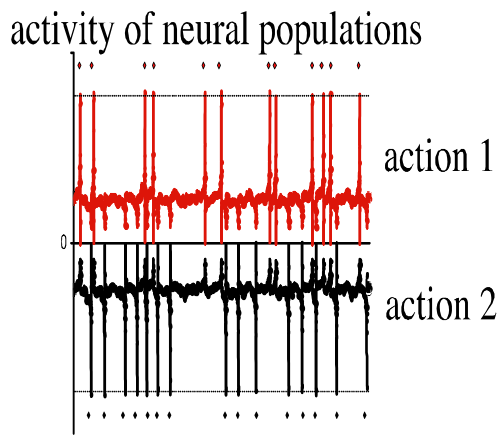



# Making the Decision

- Triple well: weak interactions
- Stronger interactions, no data:
  - Double well
- Data comes in: push off the well

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.



# Decision time

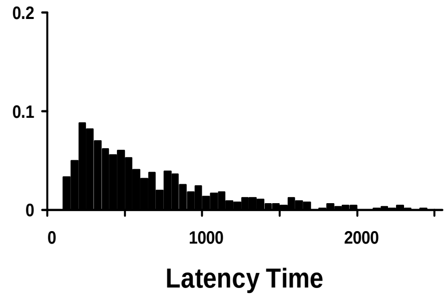
1

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.

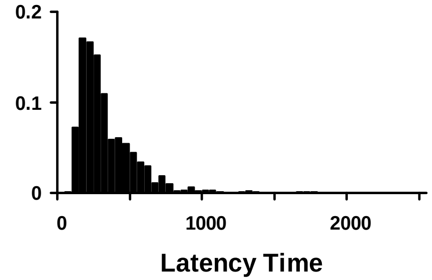
2

Decision time distribution




Recurrent interactions stronger

Shorter mean
Lower spread



# Major Concepts

- Integration
- Threshold -- point of no return
- Positive self-feedback: memory
- Leak: forgetting
- Negative Slower Feedback: competition/reset

# Decision Task