Computing in carbon

Basic elements of neuroelectronics

-- membranes
-- ion channels
-- wiring

Elementary neuron models

-- conductance based
-- modelers' alternatives

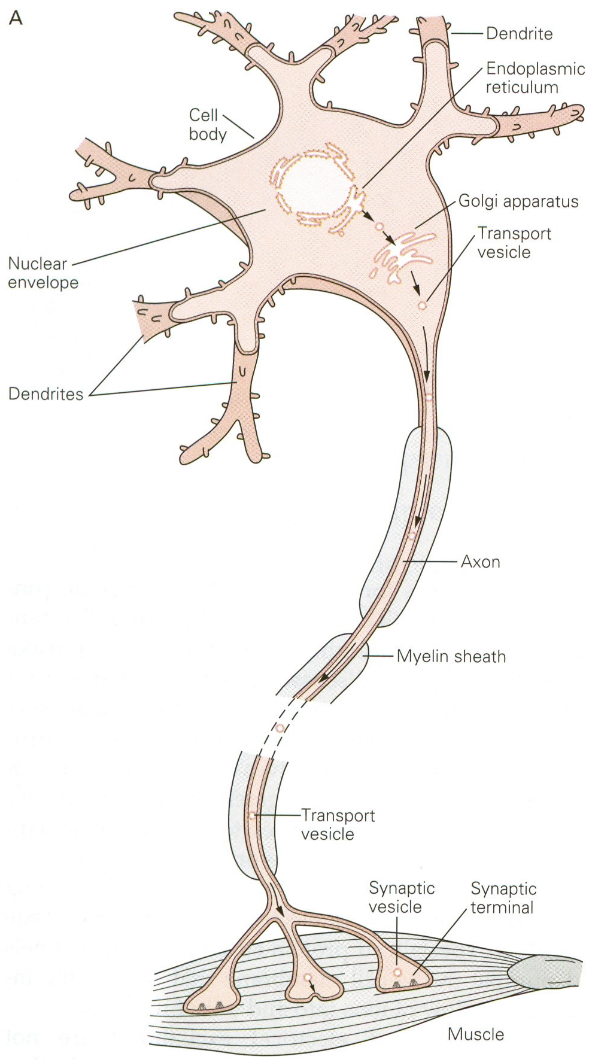
Wiring neurons together

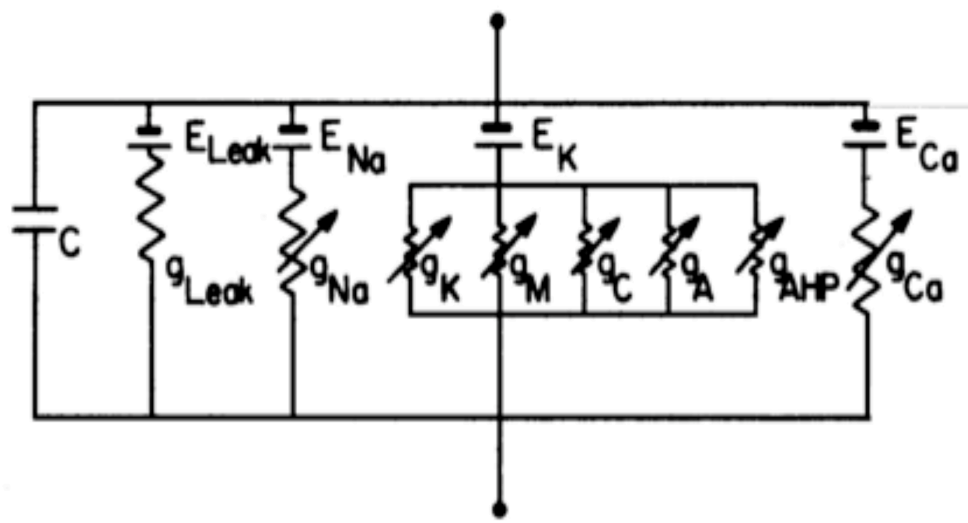
-- synapses
-- long term plasticity
-- short term plasticity

Wires

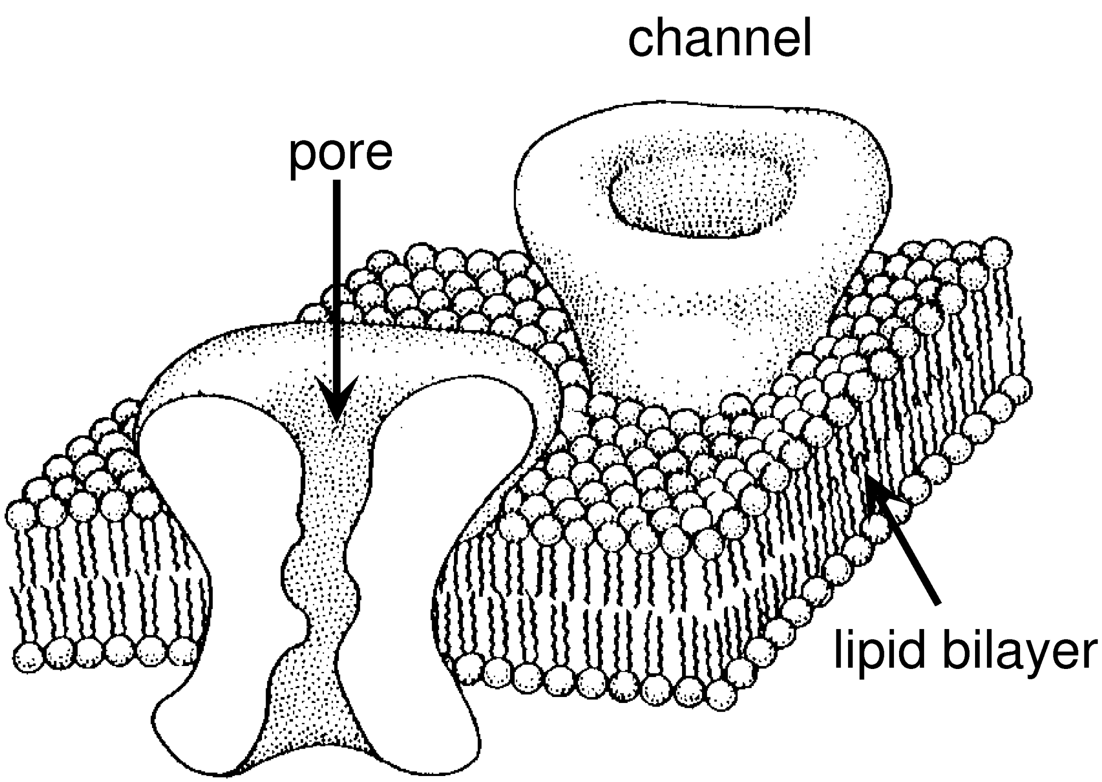
-- signal propagation
-- processing in dendrites

Equivalent circuit model of a neuron

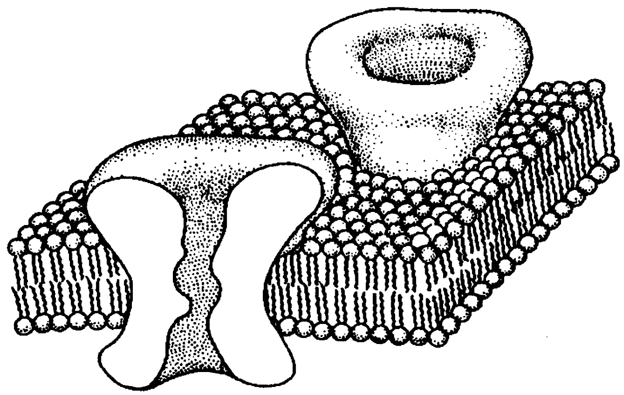


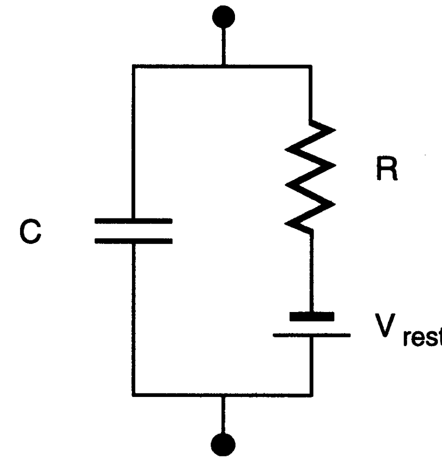


Closeup of a patch on the surface of a neuron



The passive membrane





Ohm's law: $V = I_R R$

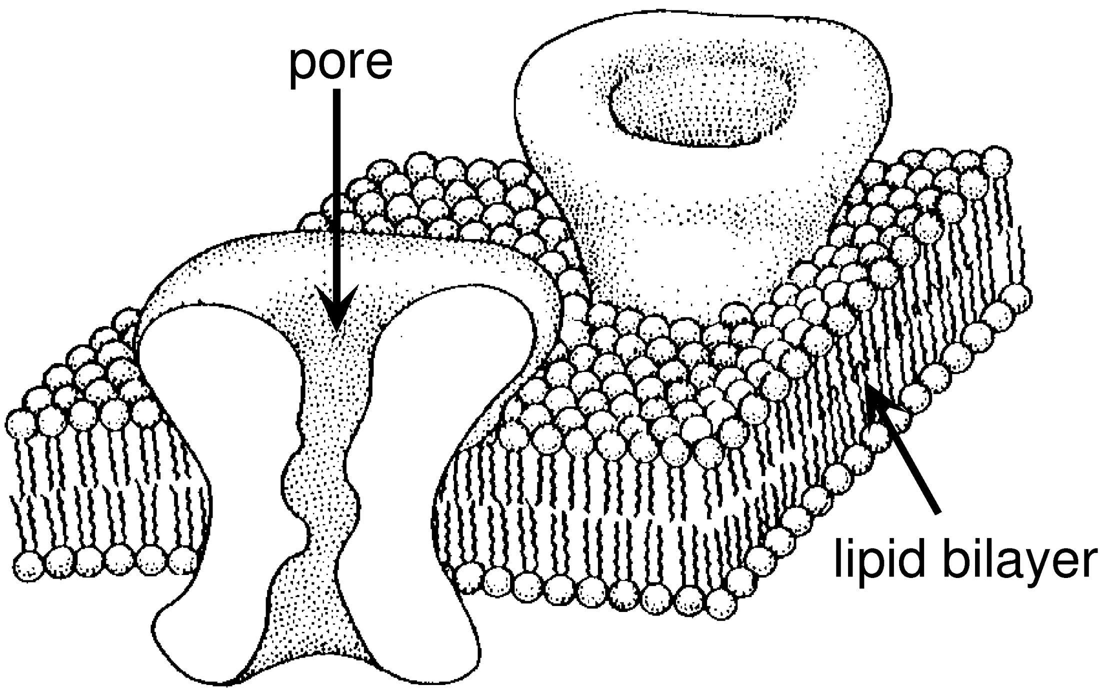
Capacitor: C = Q/V

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

Kirchhoff: $I_R + I_C + I_{\text{ext}} = 0$

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

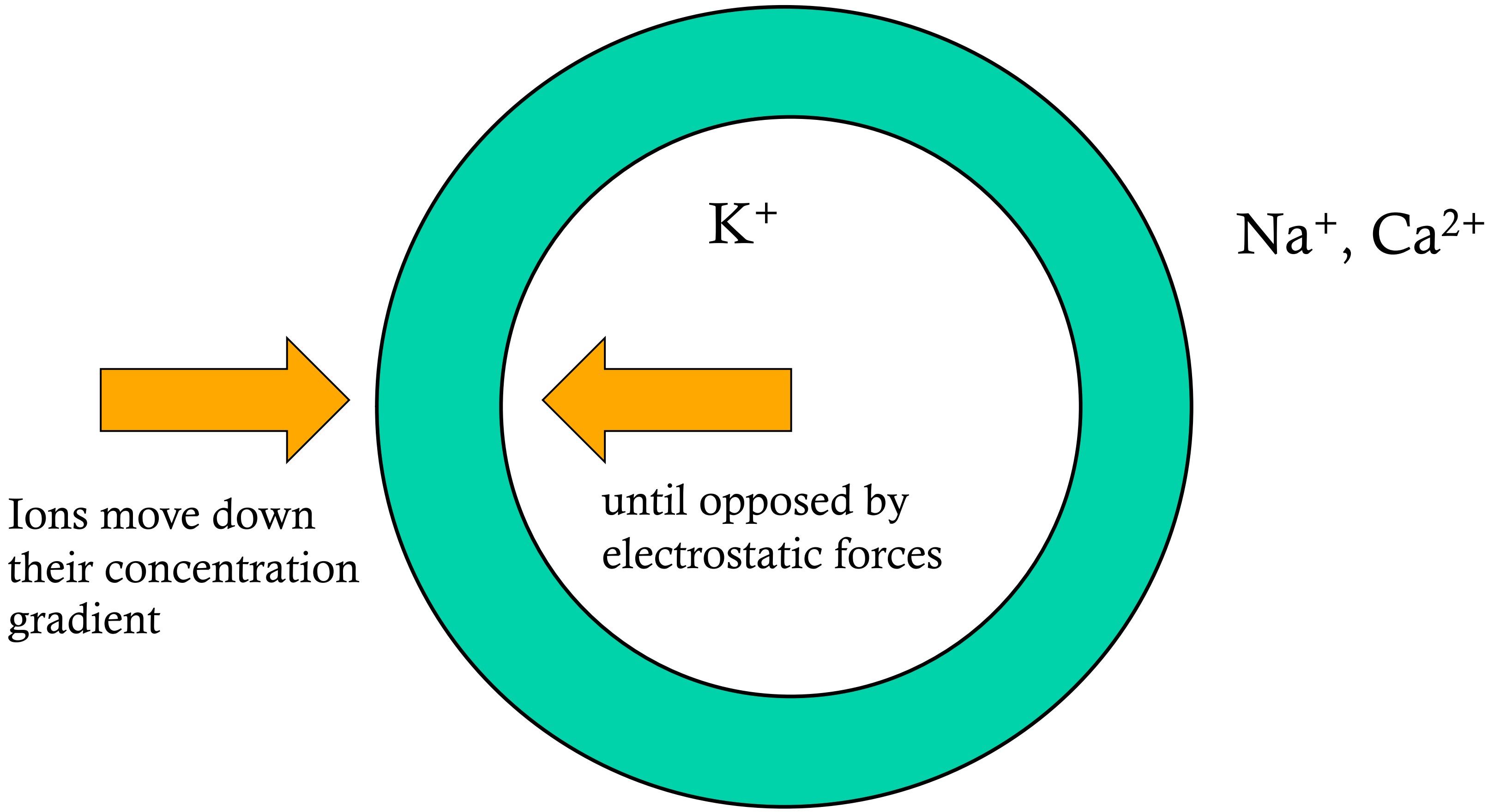
Movement of ions through ion channels



Energetics: $qV \sim k_B T$

$V \sim 25\text{mV}$

The equilibrium potential



Nernst: $$E = \frac{k_B T}{zq} \ln \frac{[\text{inside}]}{[\text{outside}]}$$

Each ion has an independent circuit path

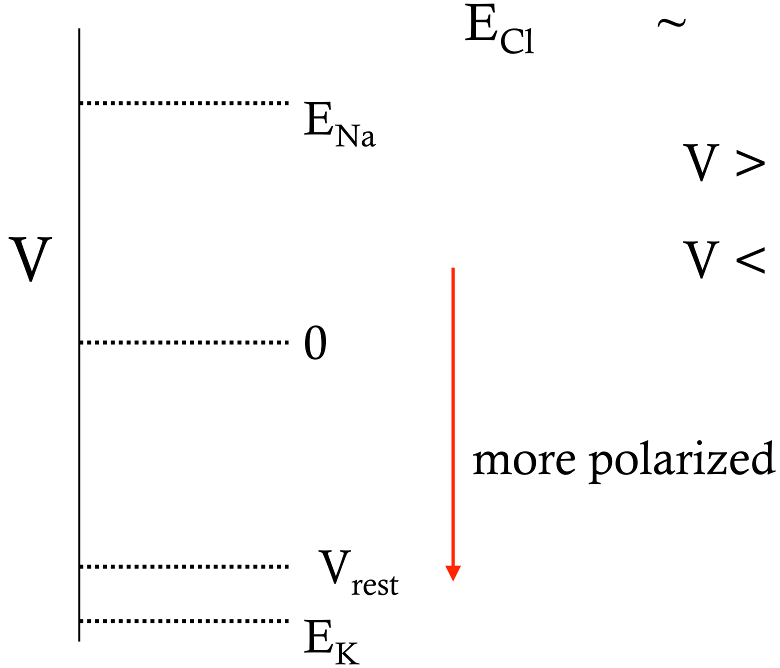
Different ion channels have associated *conductances*.

A given conductance tends to move the membrane potential toward the equilibrium potential for that ion

E_{Na}	~	50mV	depolarizing
E_{Ca}	~	150mV	depolarizing
E_{K}	~	-80mV	hyperpolarizing
E_{Cl}	~	-60mV	shunting

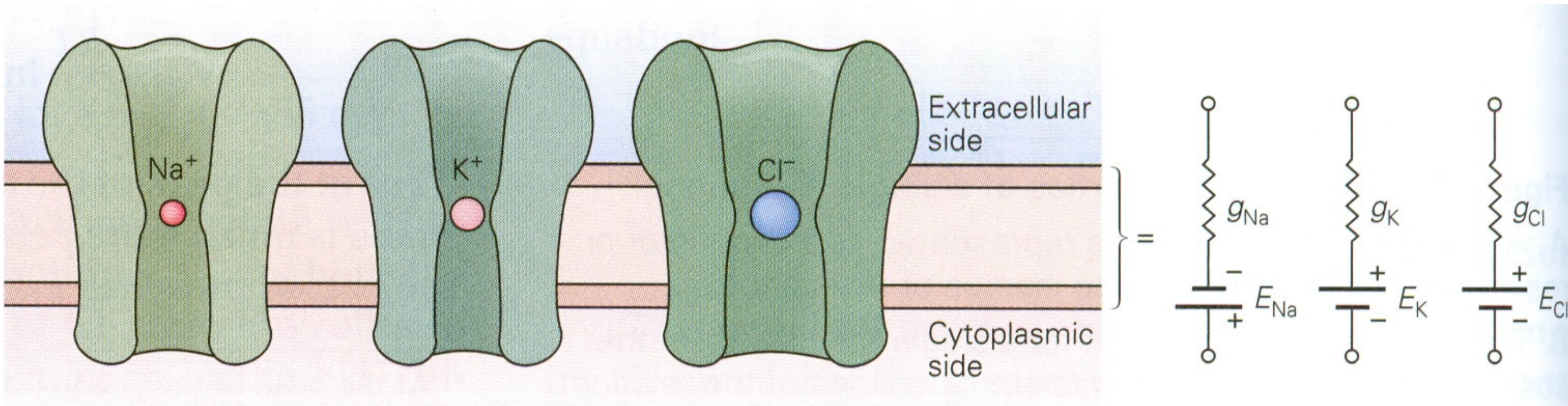
$V > E$ → positive current will flow outward

$V < E$ → positive current will flow inward

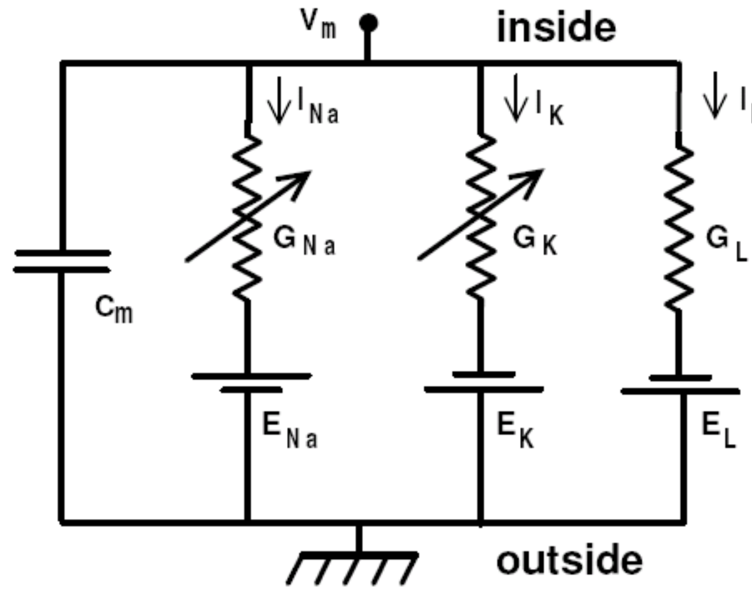


Parallel paths for ions to cross membrane

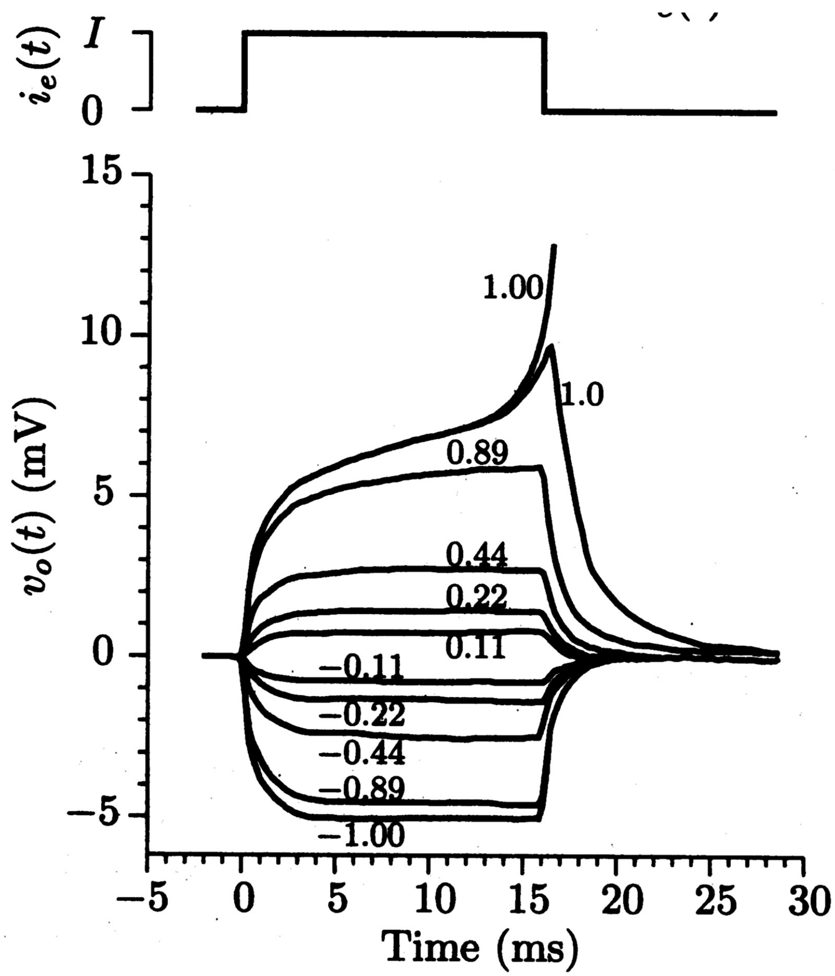
Several *I-V* curves in parallel:



New equivalent circuit:

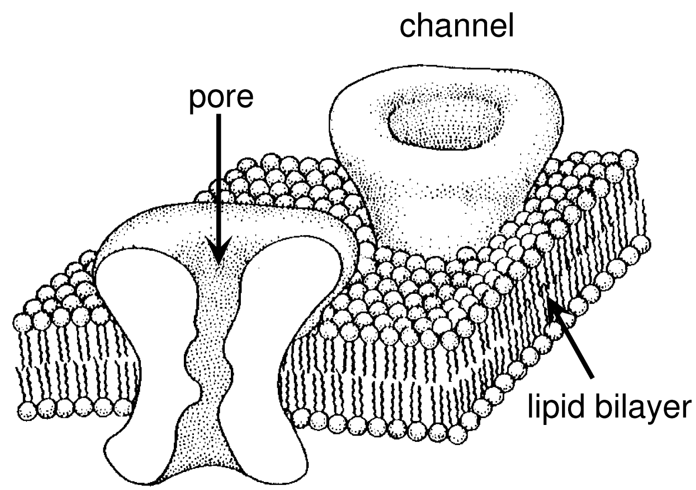


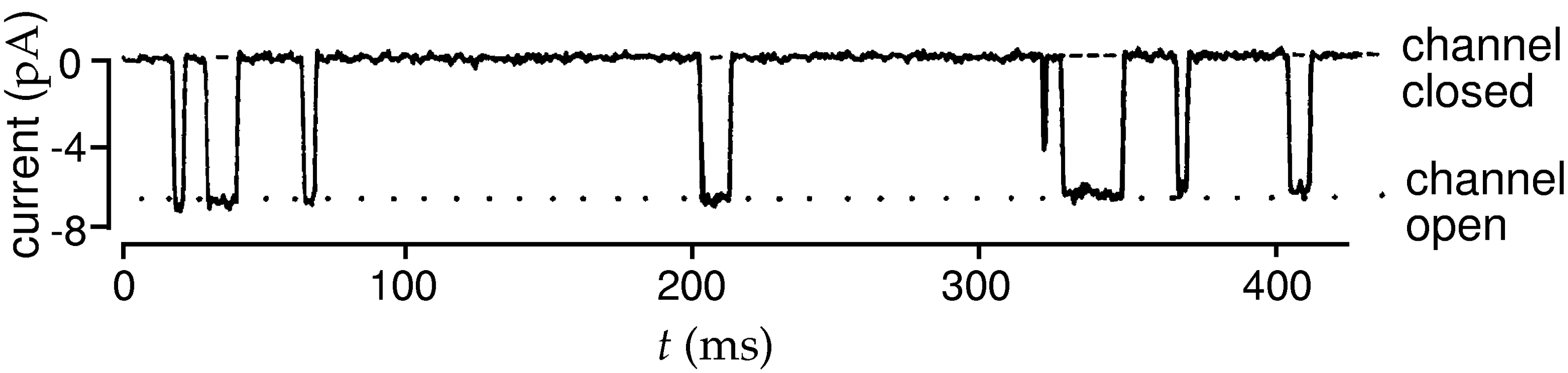
Neurons are excitable



Excitability arises from nonlinearity in ion channels

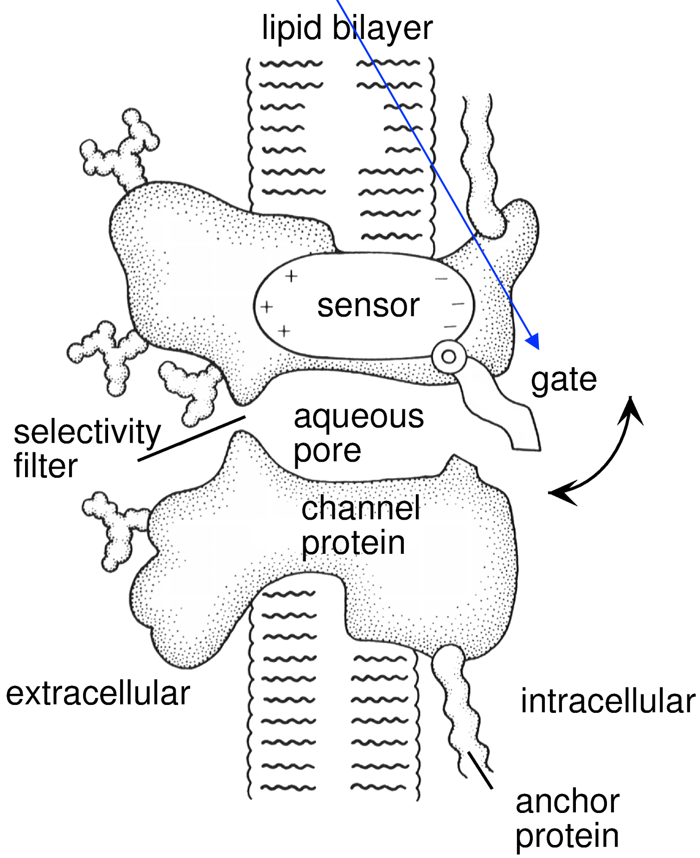
- Voltage dependent
- transmitter dependent (synaptic)
- Ca dependent





The ion channel is a complex molecular machine

K channel: open probability increases when depolarized



$P_K \sim n^4$

Persistent conductance

n describes a subunit

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

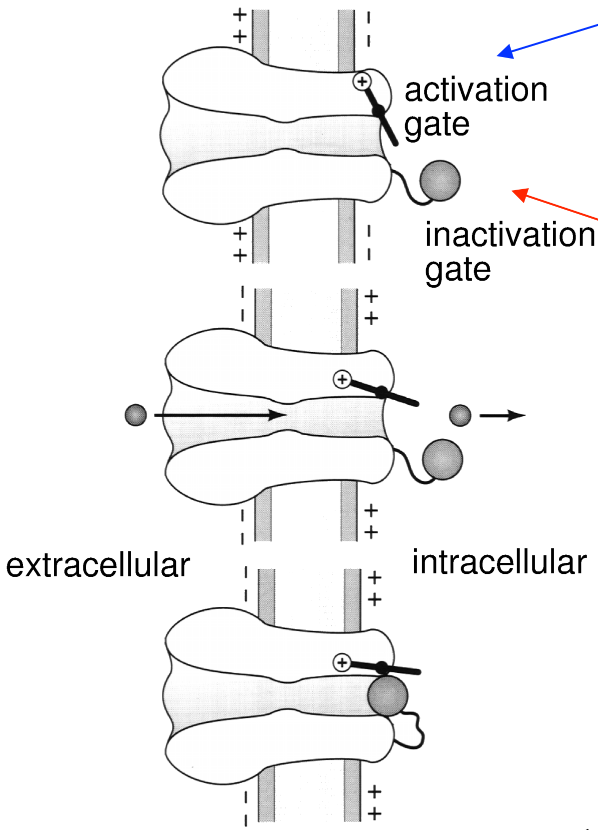
Transitions between states occur at voltage dependent rates

$\alpha_n(V)$ C → O

$\beta_n(V)$ O → C

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

Transient conductances



Gate acts as in previous case

Additional gate can block channel when open

$P_{Na} \sim m^3h$

m is activation variable
h is inactivation variable

m and *h* have opposite voltage dependences:
depolarization increases *m*, activation
hyperpolarization increases *h*, deinactivation

Activation and inactivation dynamics

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

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

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

We can rewrite:

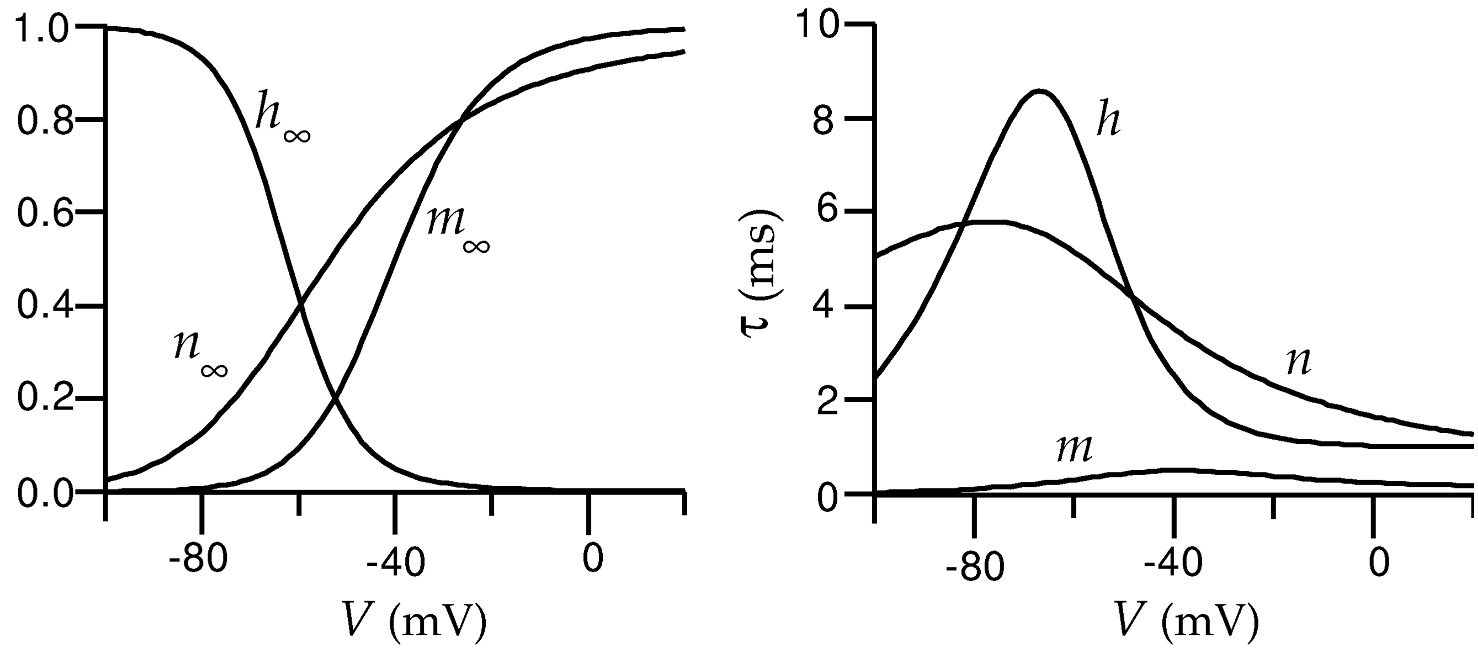
$$\tau_n(V)\frac{dn}{dt} = n_\infty(V) - n$$

where

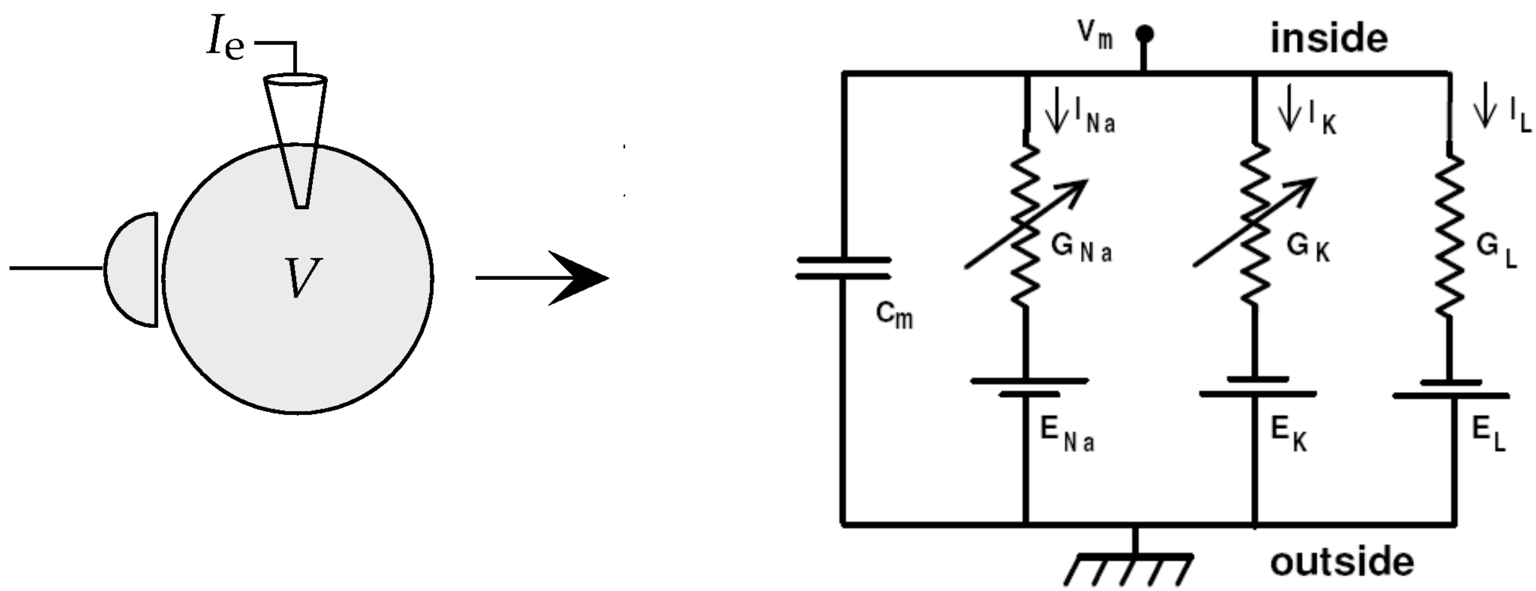
$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

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

Activation and inactivation dynamics



Putting it together



Ohm's law: $V = IR$ and Kirchhoff's law

$$-C_m \frac{dV}{dt} = \sum_i g_i (V - E_i) + I_e$$

Capacitative current

Ionic currents

Externally applied current

The Hodgkin-Huxley equation

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

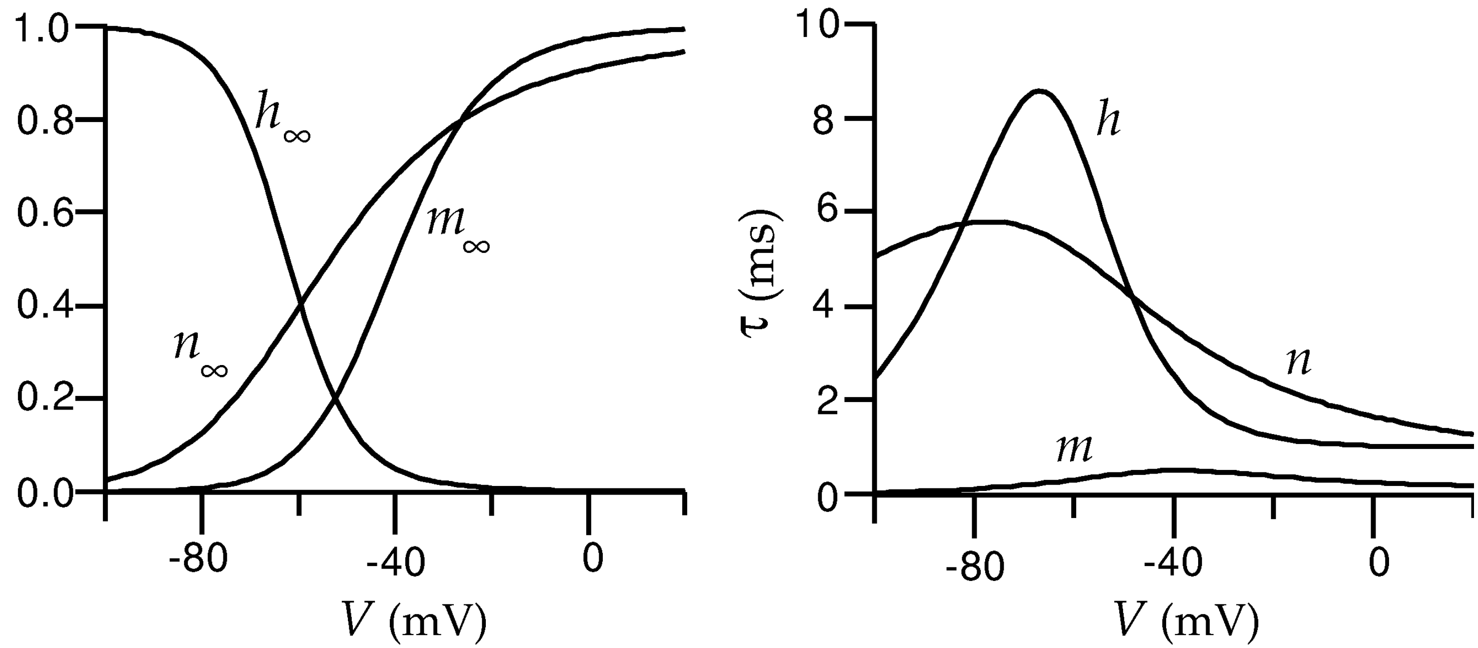
$$-C_m \frac{dV}{dt} = g_L (V - E_L) + \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) + \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})$$

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

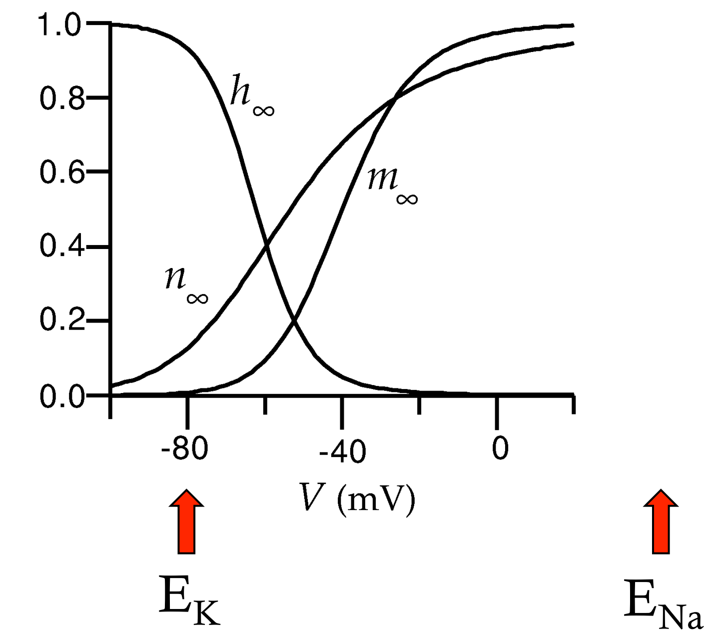
$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m$$

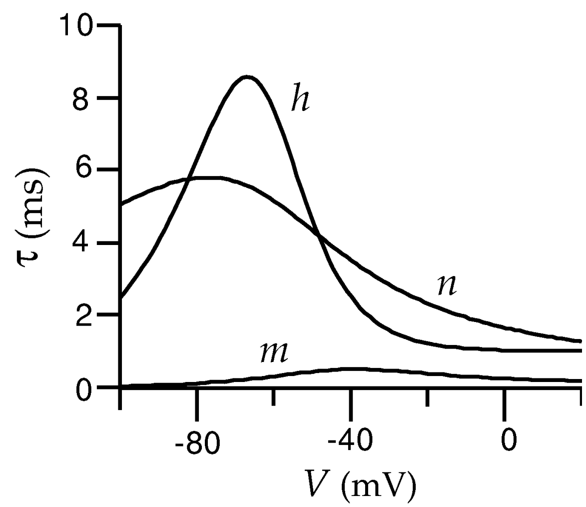
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

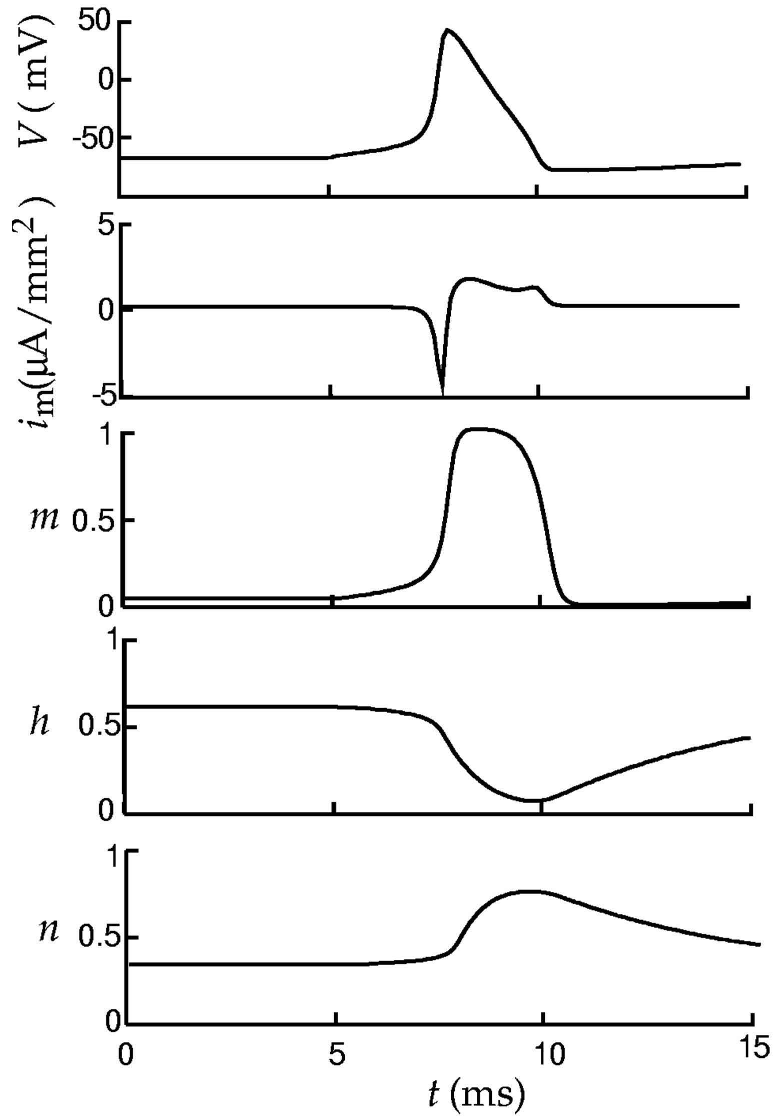
Activation and inactivation dynamics



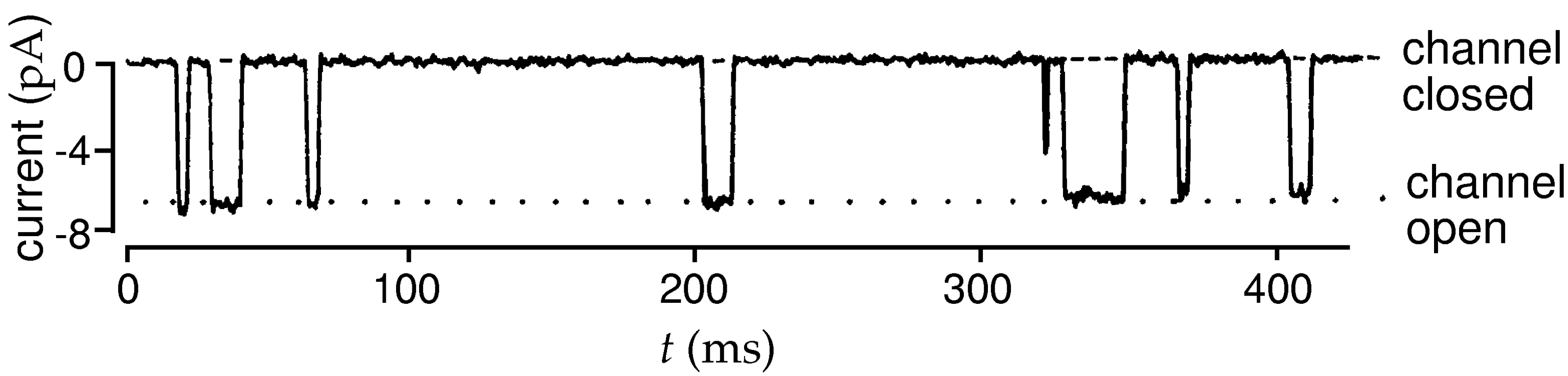
Dynamics of a spike



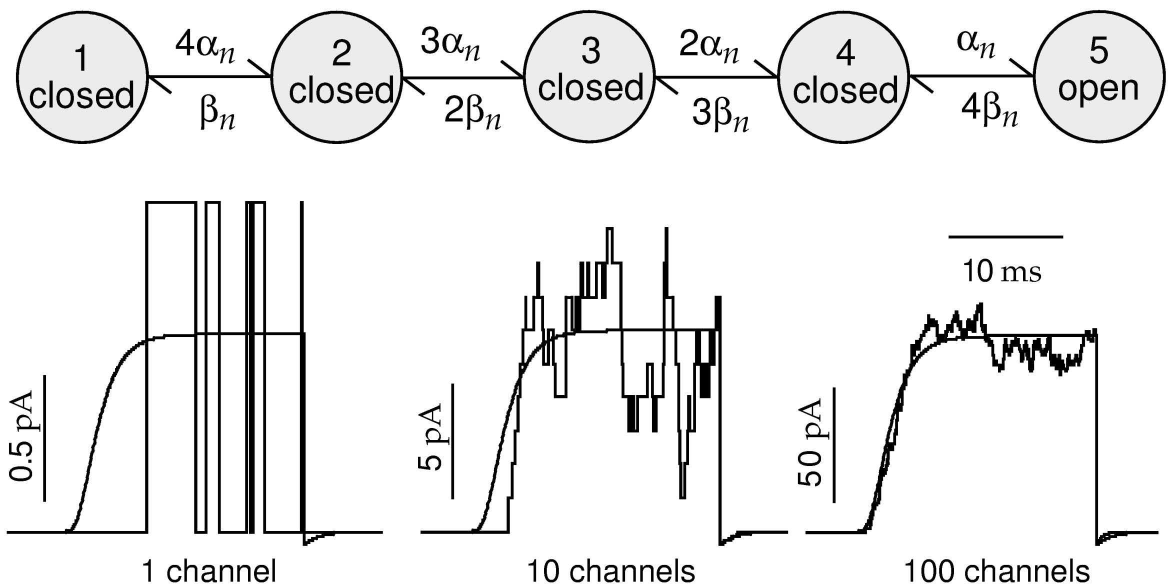




Ion channel stochasticity

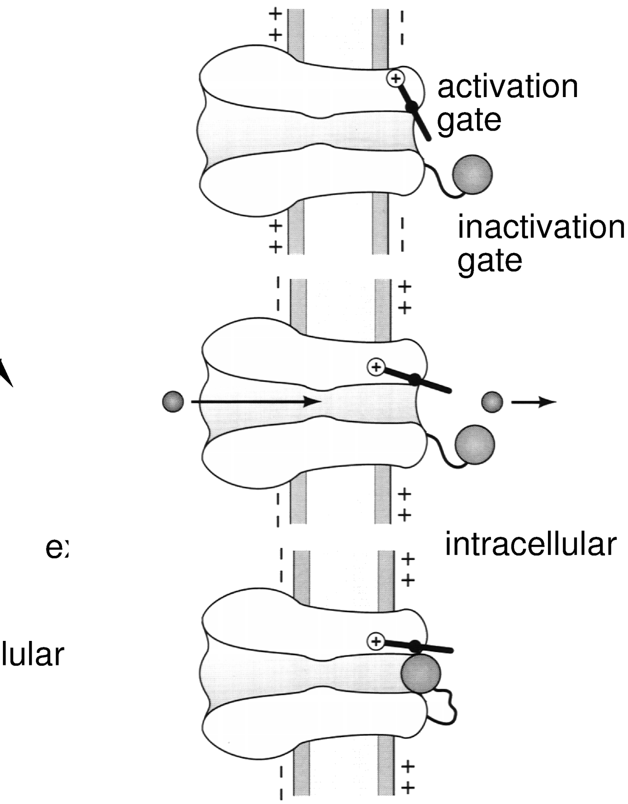


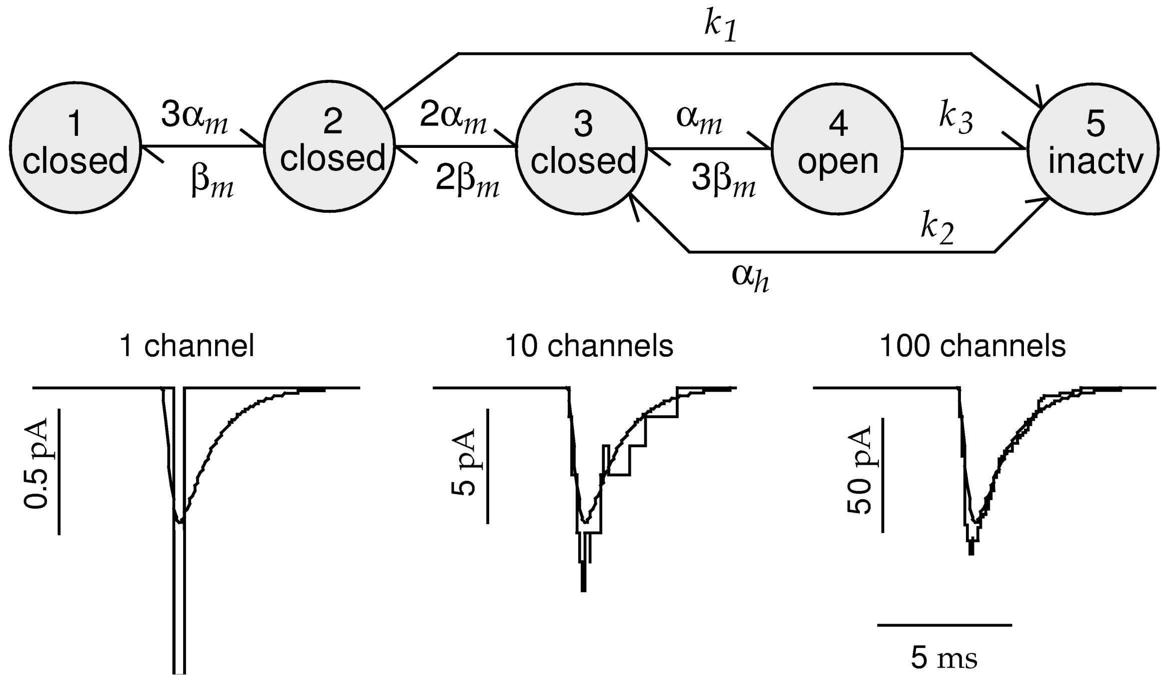
A microscopic stochastic model for ion channel function



approach to macroscopic description

Transient conductances





Different from the continuous model:

- interdependence between inactivation and activation
- transitions to inactivation state 5 can occur only from 2,3 and 4
- k_1, k_2, k_3 are *constant,* not voltage dependent

The integrate-and-fire model

Like a passive membrane:

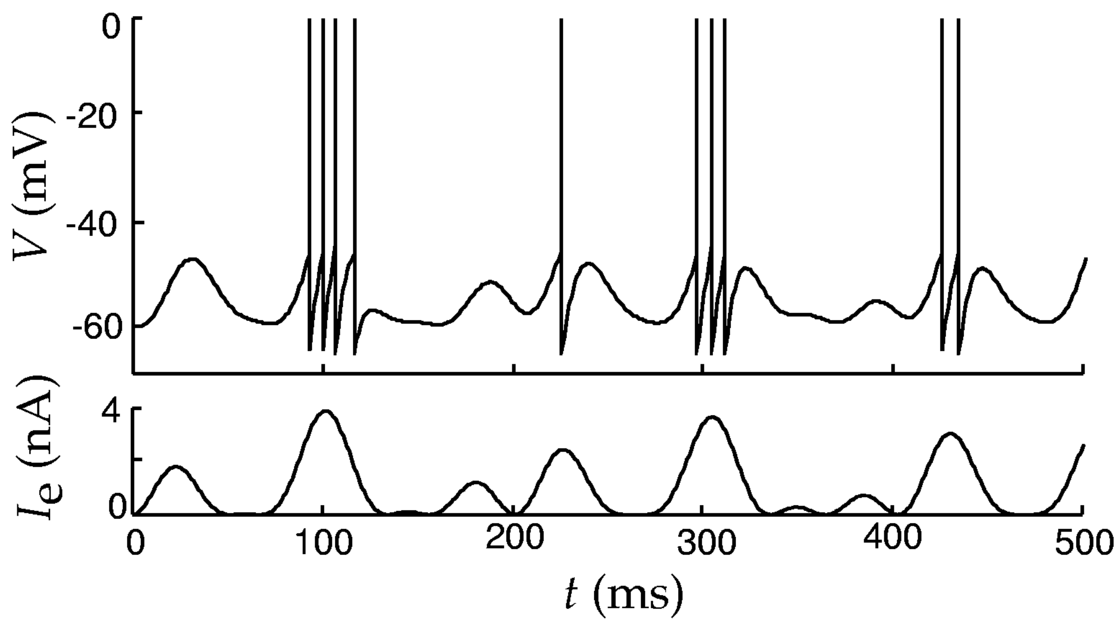
$$C_m \frac{dV}{dt} = -g_L(V - E_i) - I_e$$

but with the additional rule that

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

and $V \rightarrow V_{reset}$.

E_L is the resting potential of the "cell".



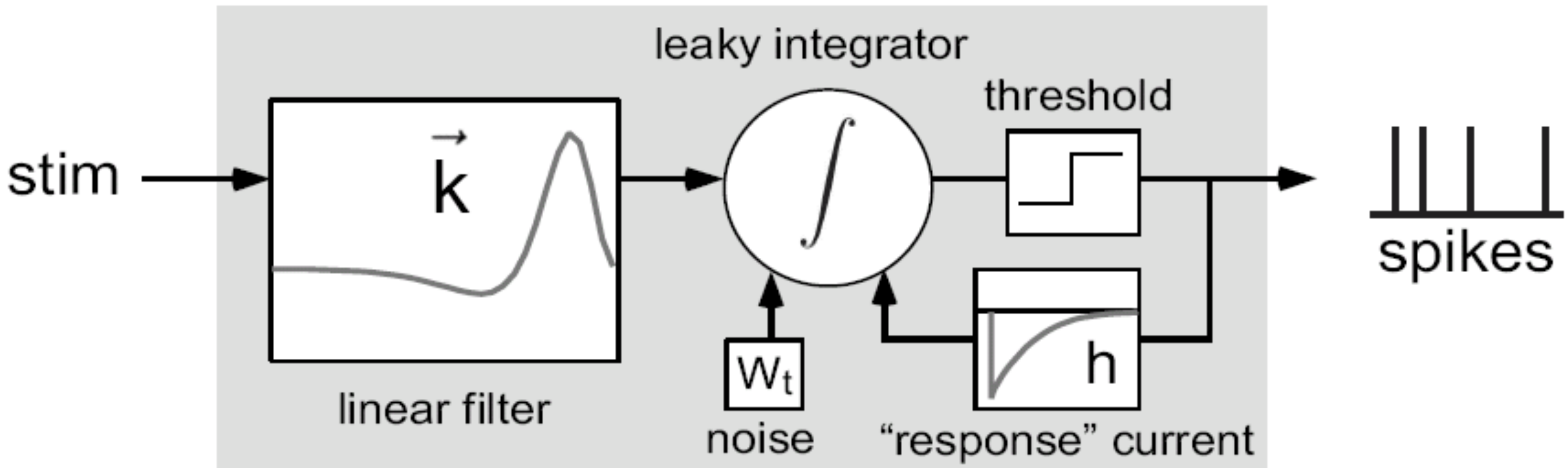
The spike response model

Kernel f for subthreshold response ← replaces leaky integrator
Kernel for spikes ← replaces "line"

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

Gerstner and Kistler

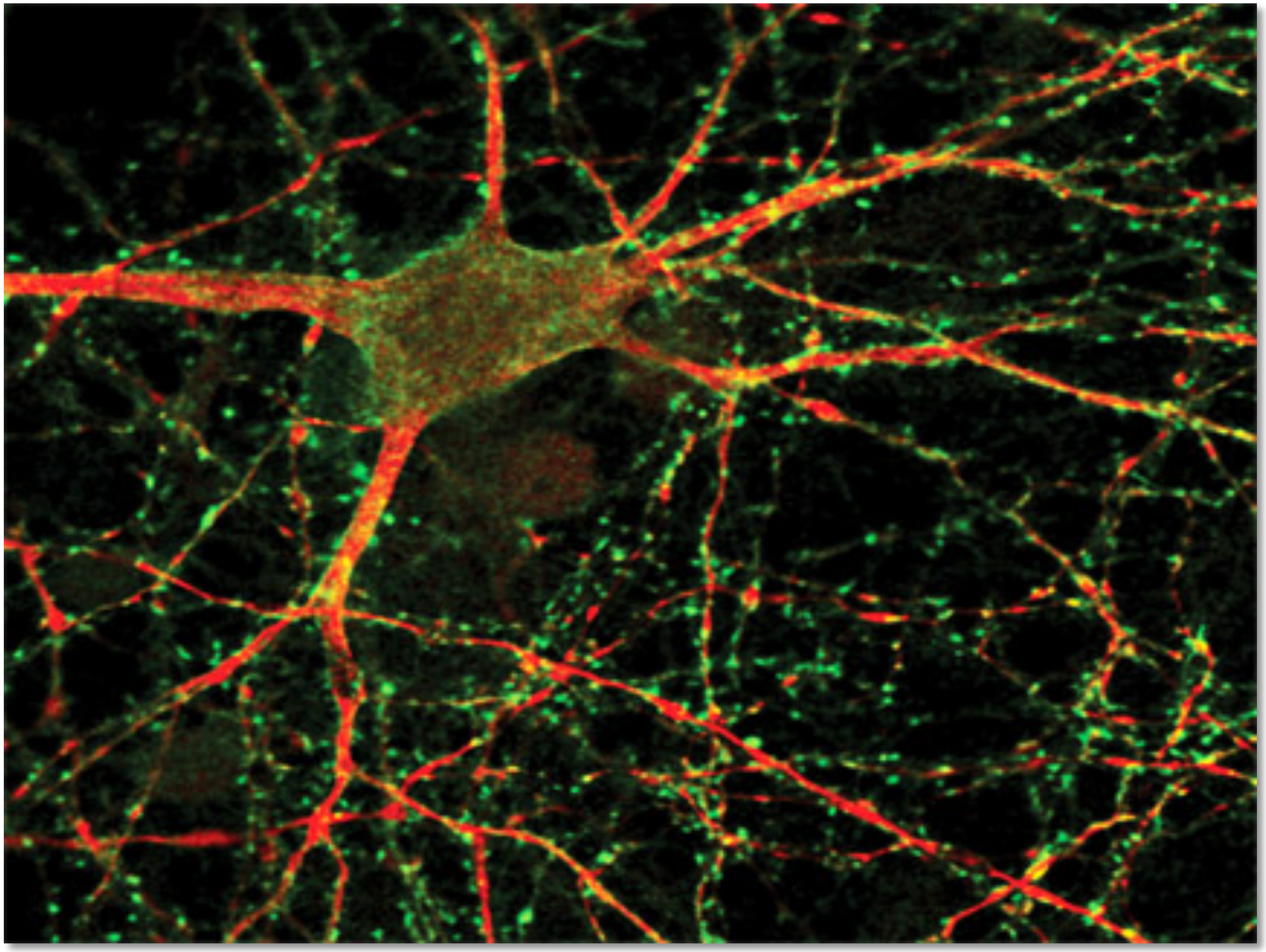
The generalized linear model



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

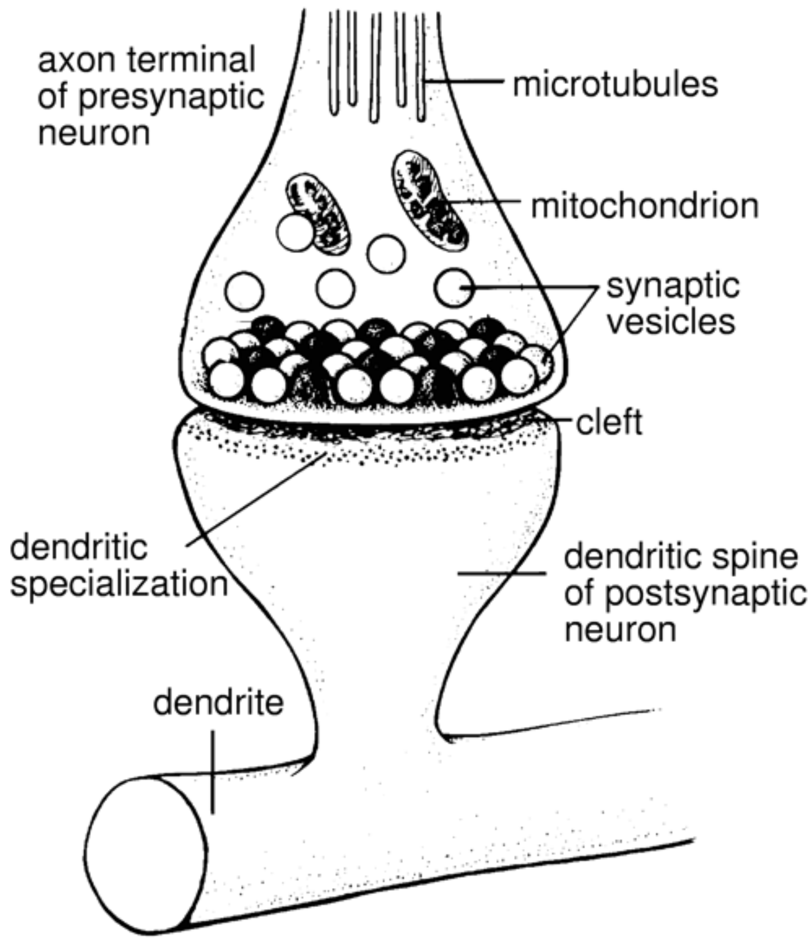
Truccolo and Brown, Paninski, Pillow, Simoncelli

Building circuits



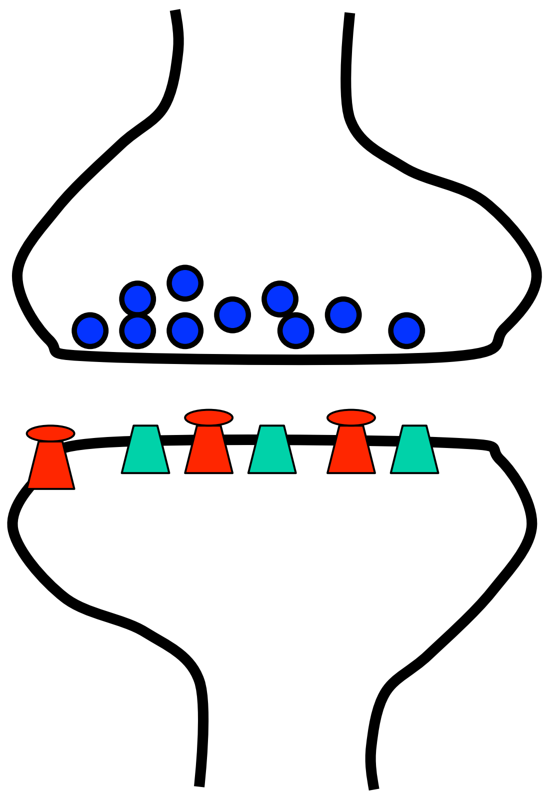
Eickholt lab, Kings College London

Synapses

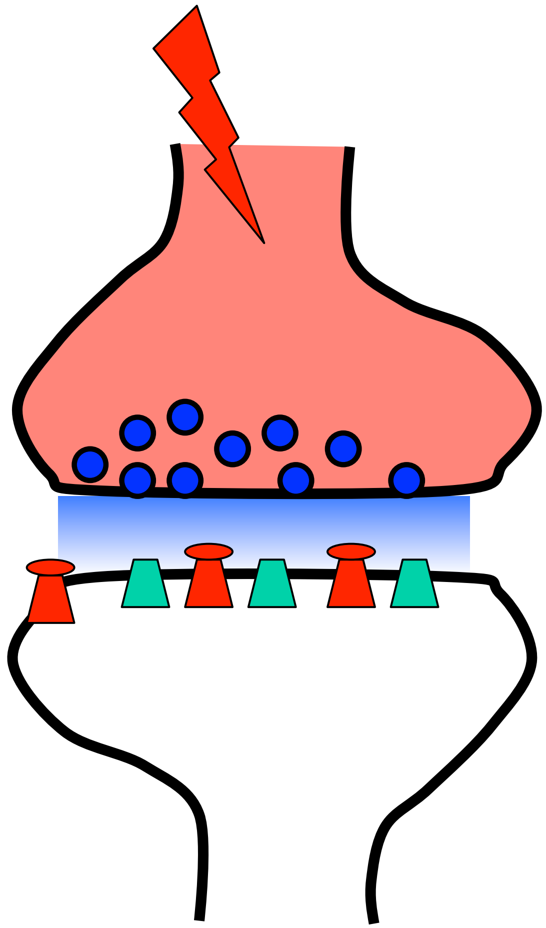


Signal is carried chemically across the synaptic cleft

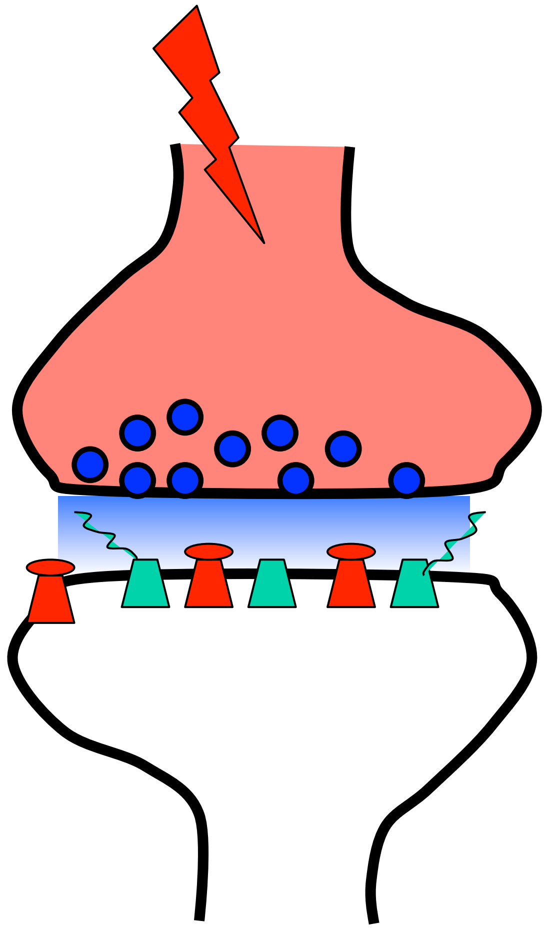
Synaptic signalling



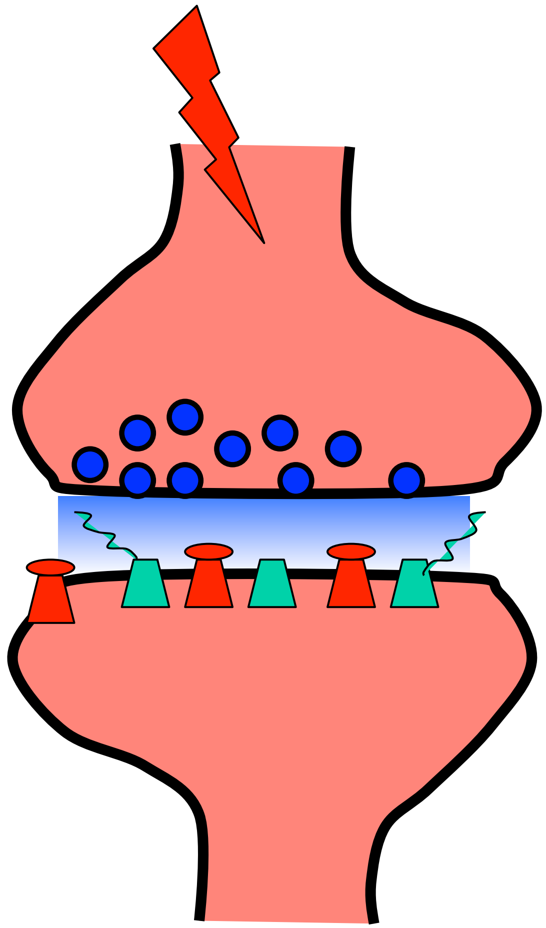
Synaptic signalling



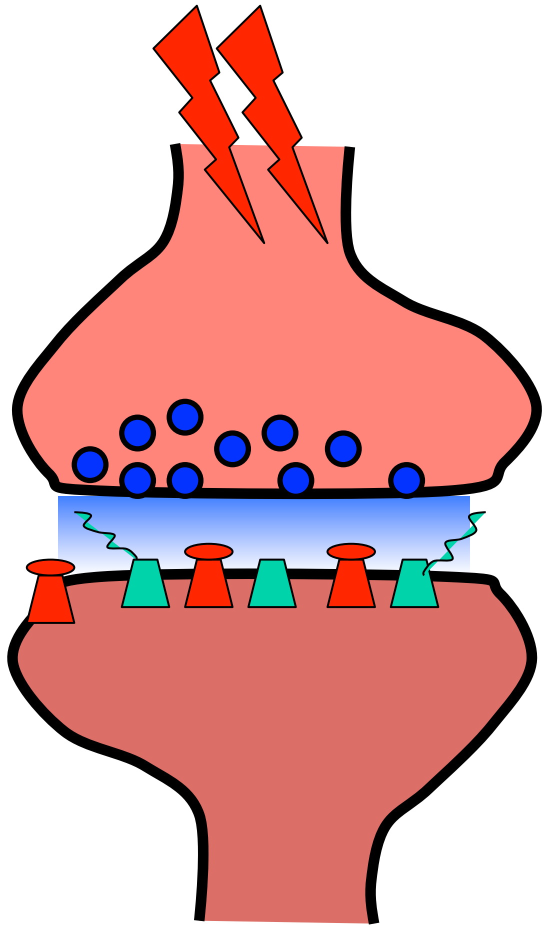
Synaptic signalling



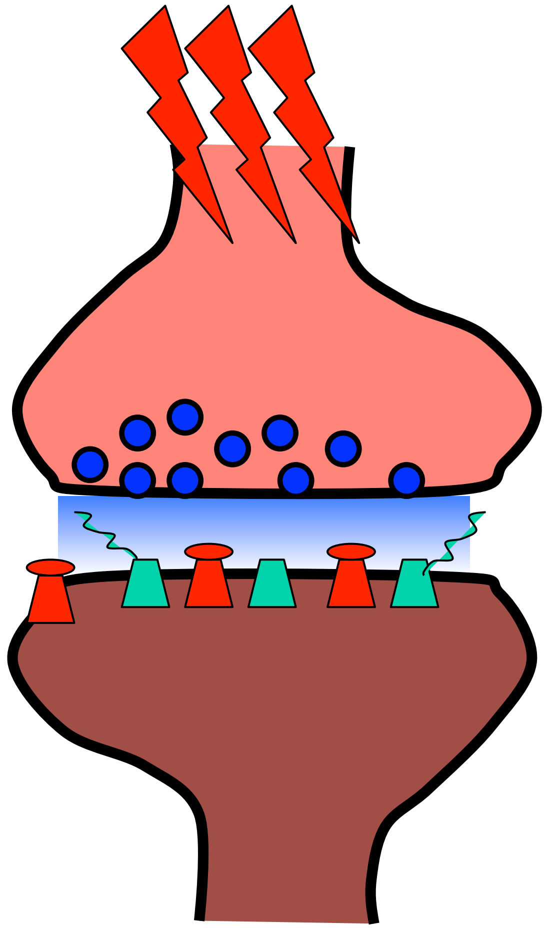
Synaptic signalling



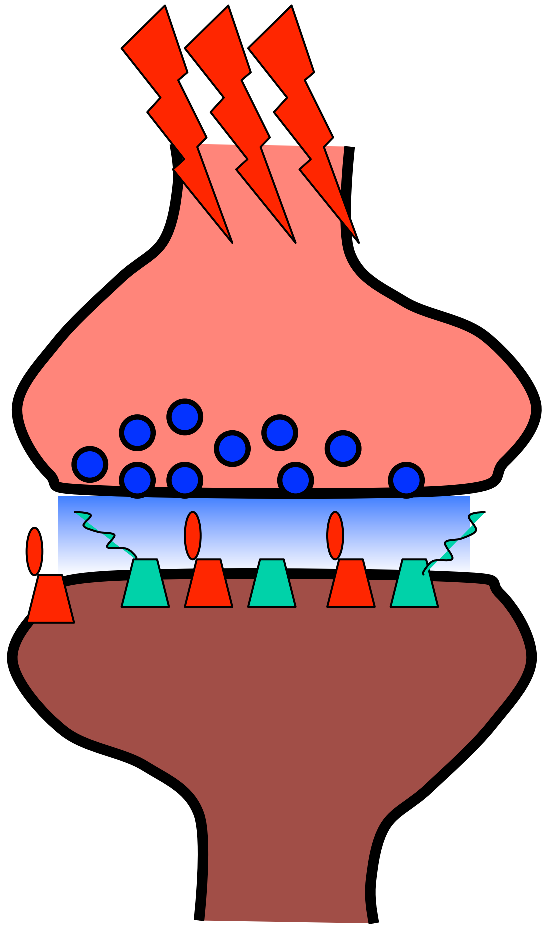
Synaptic signalling



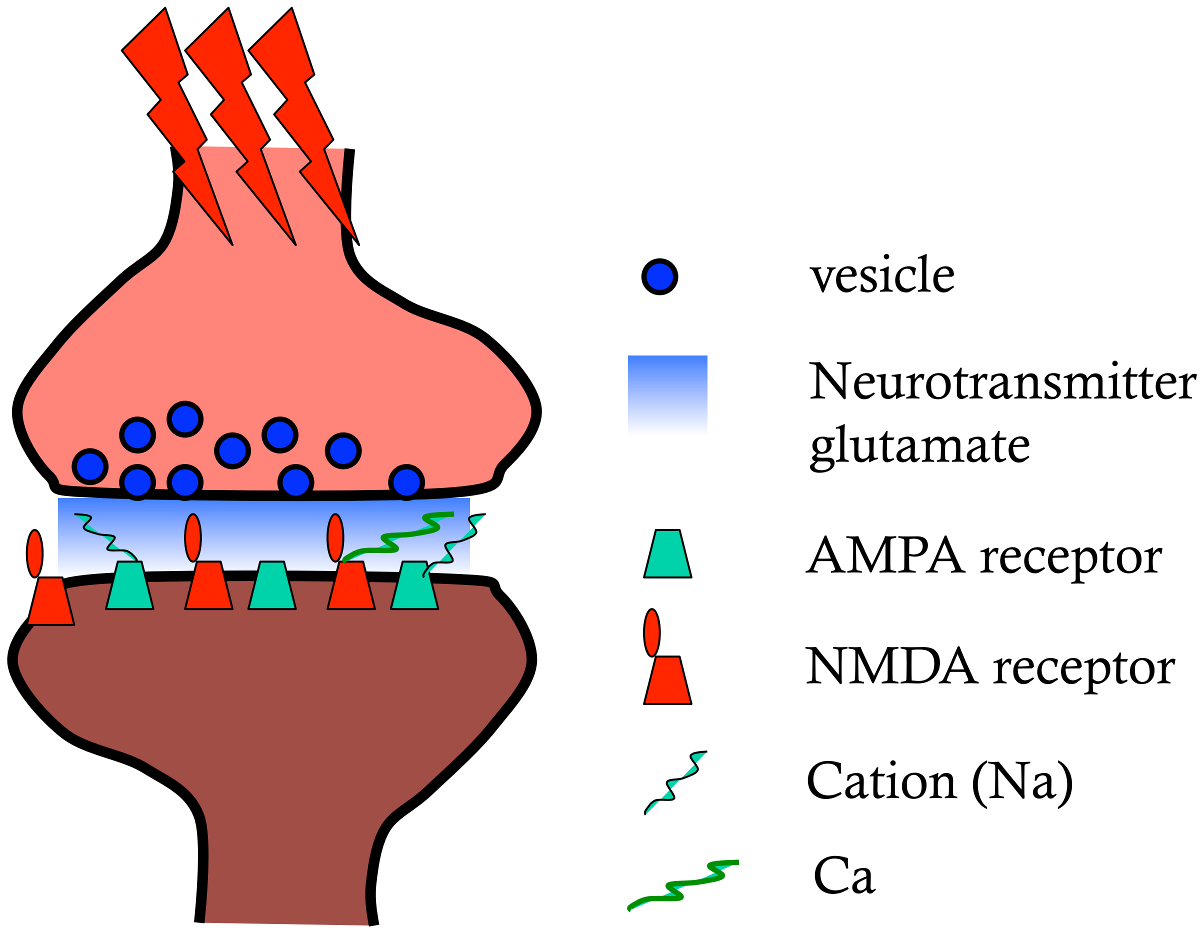
Synaptic signalling



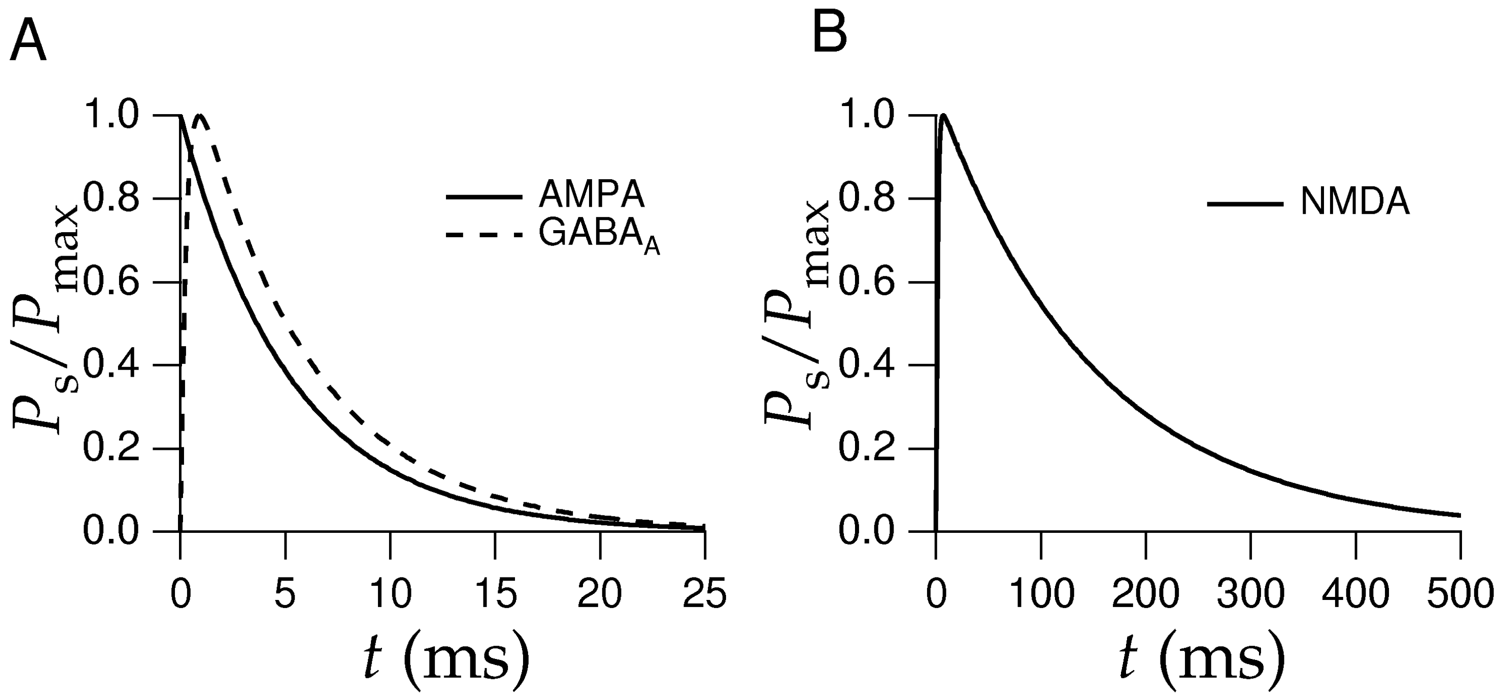
Synaptic signalling



Synaptic signalling

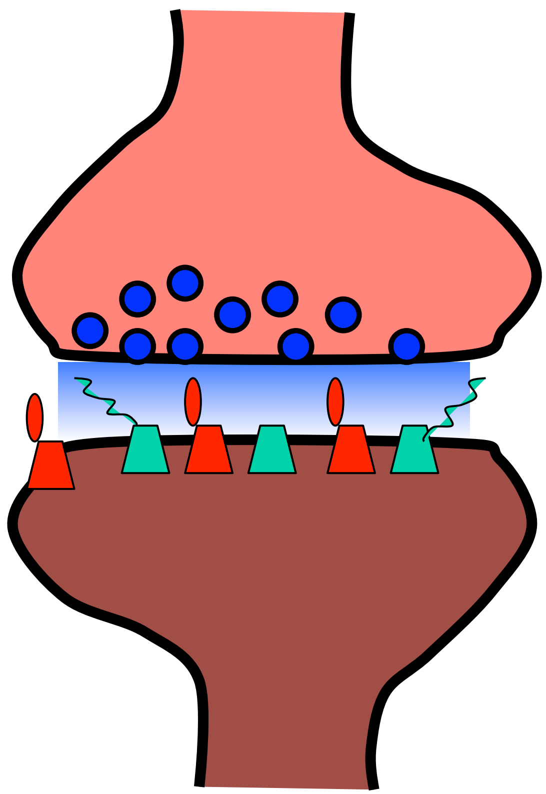


Post-synaptic conductances



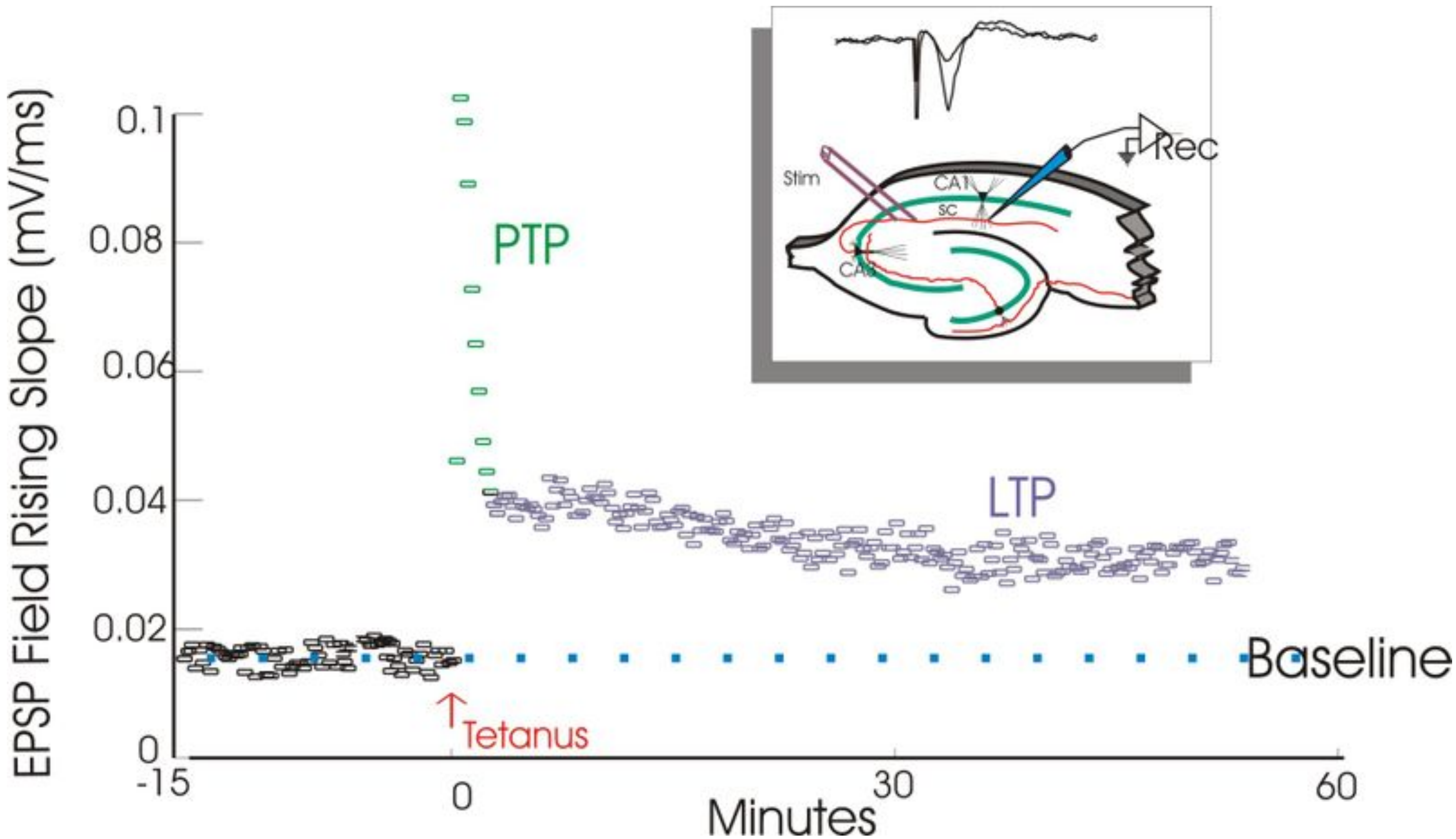
Requires pre- and post-synaptic depolarization

Connection strength



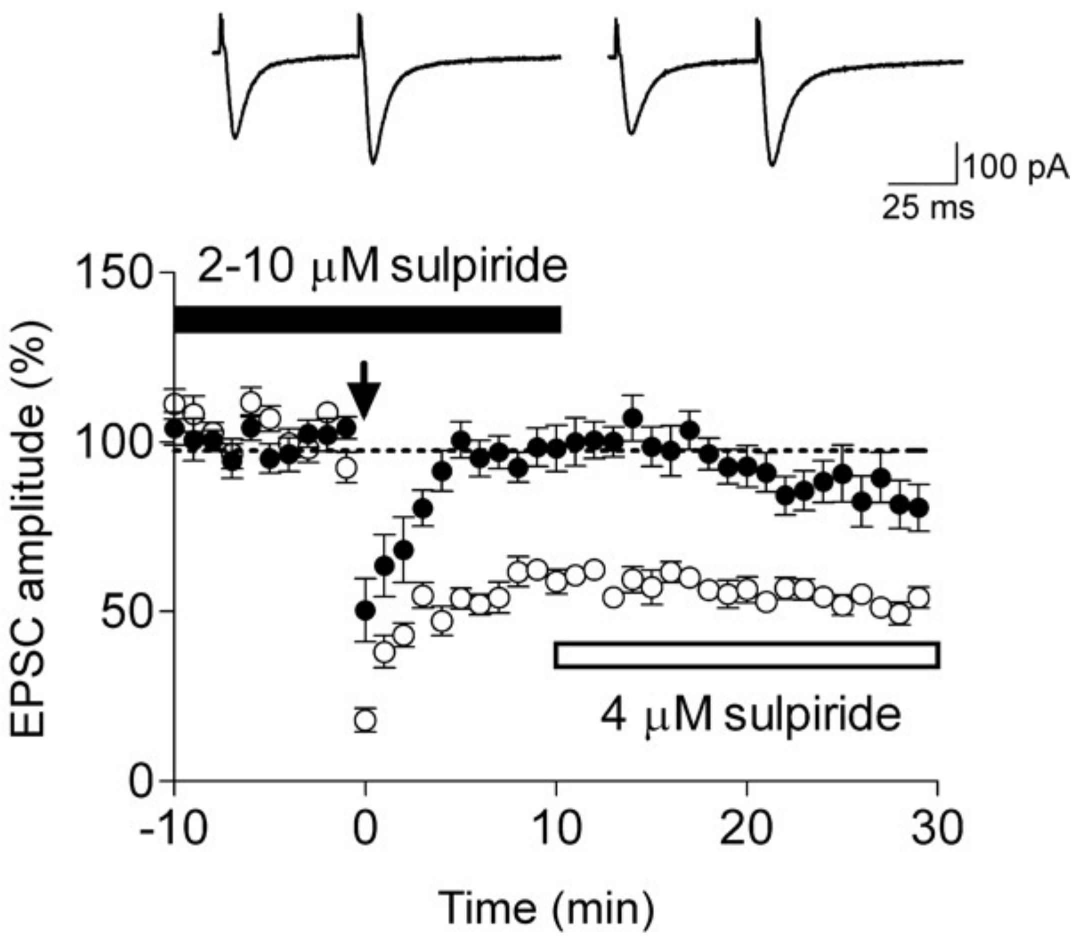
w = npq

Long-term potentiation



Wiki commons

Long-term depression



Ronesi and Lovinger, J Physiol 2005

Empirical model

$$\frac{dW_i(t)}{dt} = \frac{1}{\tau([Ca^{2+}]_i)}\left(\Omega([Ca^{2+}]_i) - W_i\right)$$

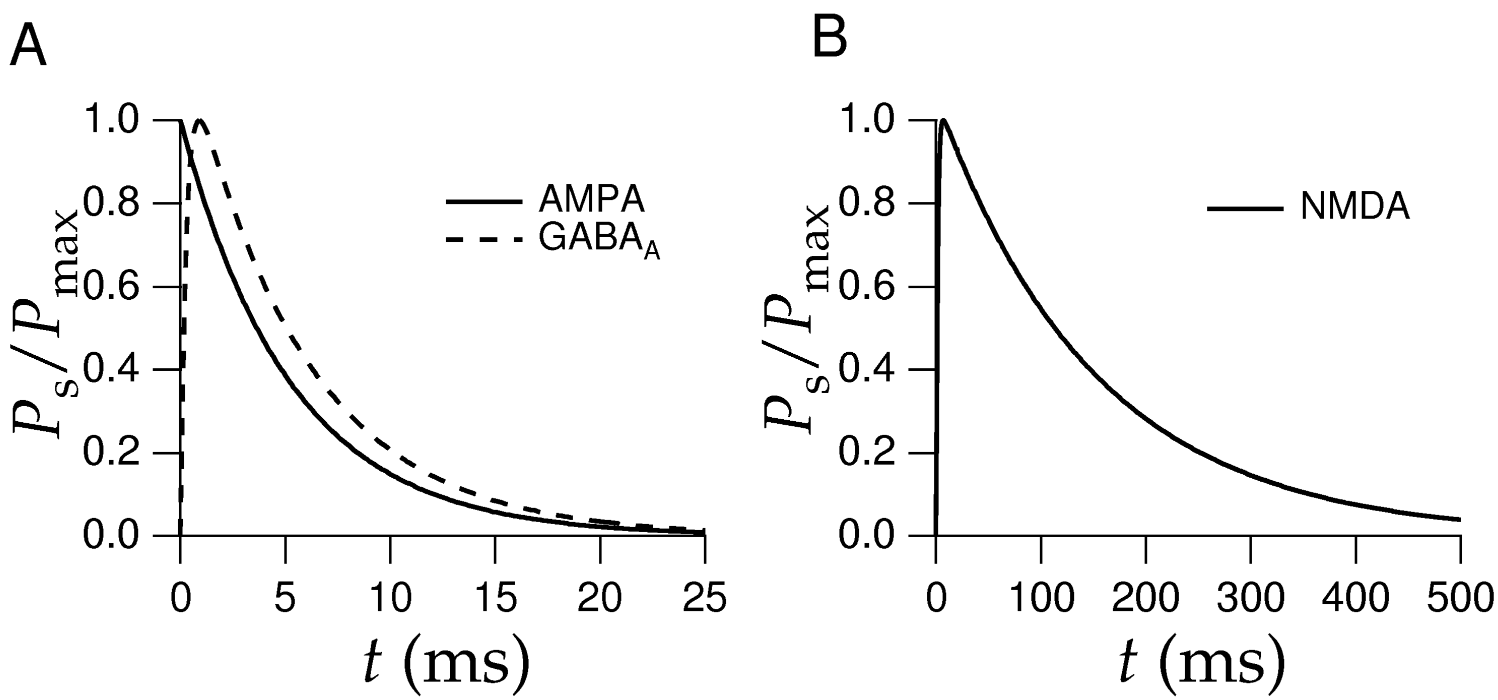
Shouval, .., Cooper, Biological Cybernetics 2002

Hebbian plasticity

$$\Delta w_{ij} = \eta x_i x_j$$

Hebb, 1949

Post-synaptic conductances

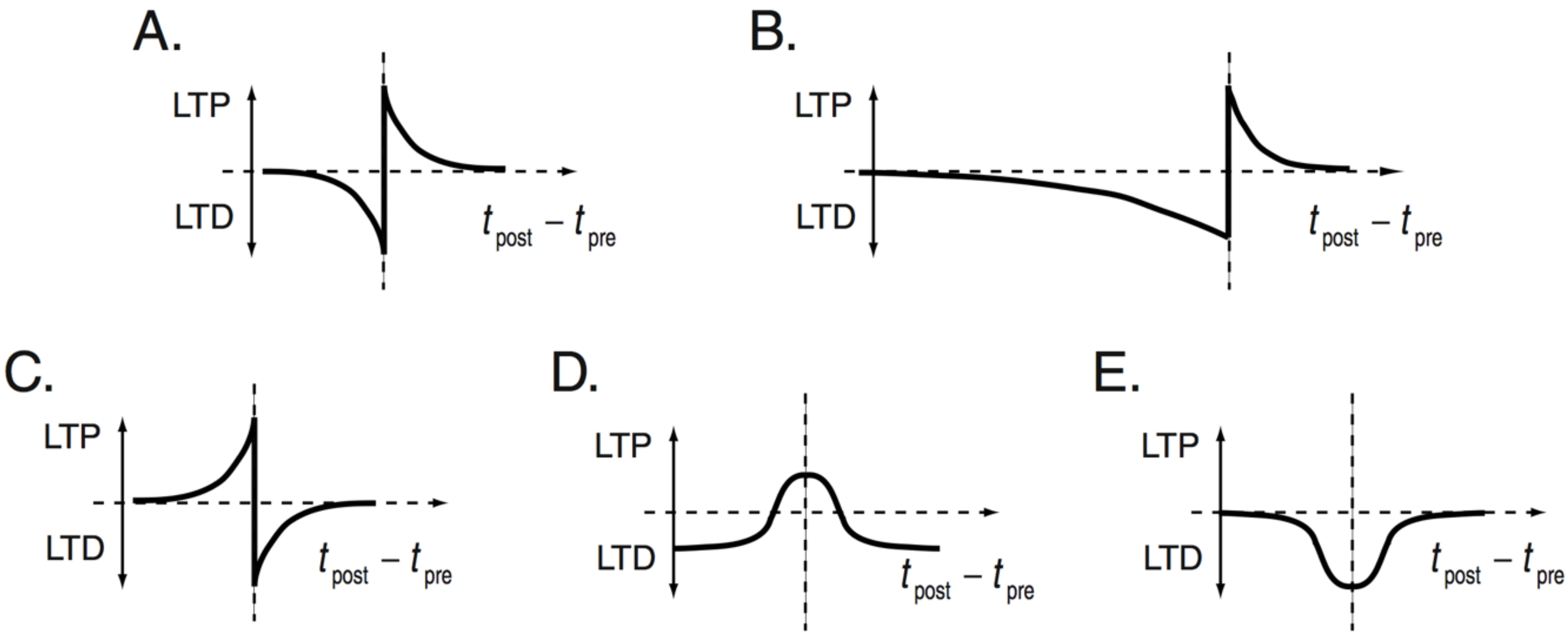


$$\Delta w_{ij} = \eta x_i x_j$$

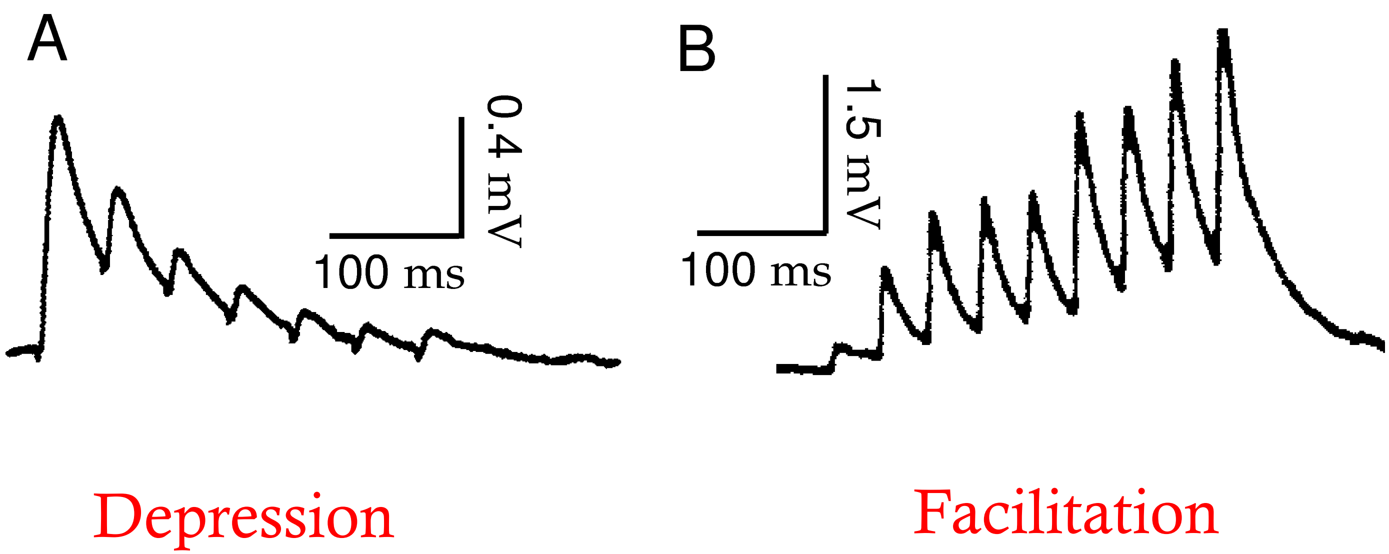
Requires pre- and post-synaptic depolarization

Coincidence detection, Hebbian

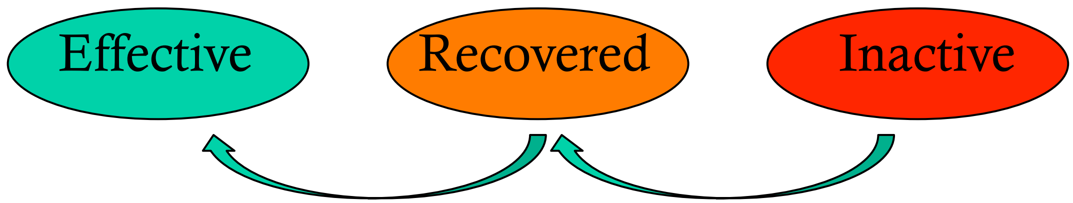
Spike-timing dependent plasticity



Short-term synaptic plasticity



Modeling short-term synaptic plasticity



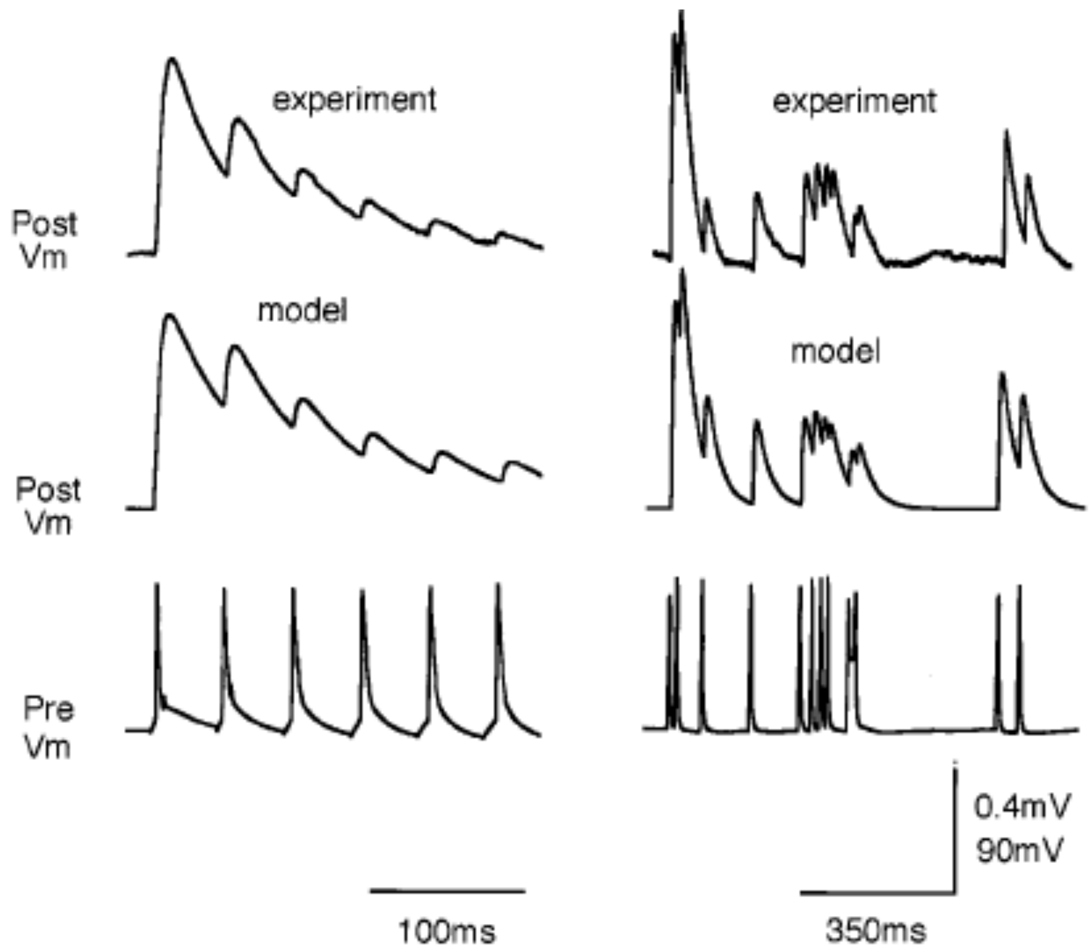
$$\frac{dR}{dt} = \frac{I}{\tau_{rec}}$$

$$\frac{dE}{dt} = -\frac{E}{\tau_{inact}} + U_{SE} \cdot R \cdot \delta(t - t_{AP})$$

$$I = 1 - R - E,$$

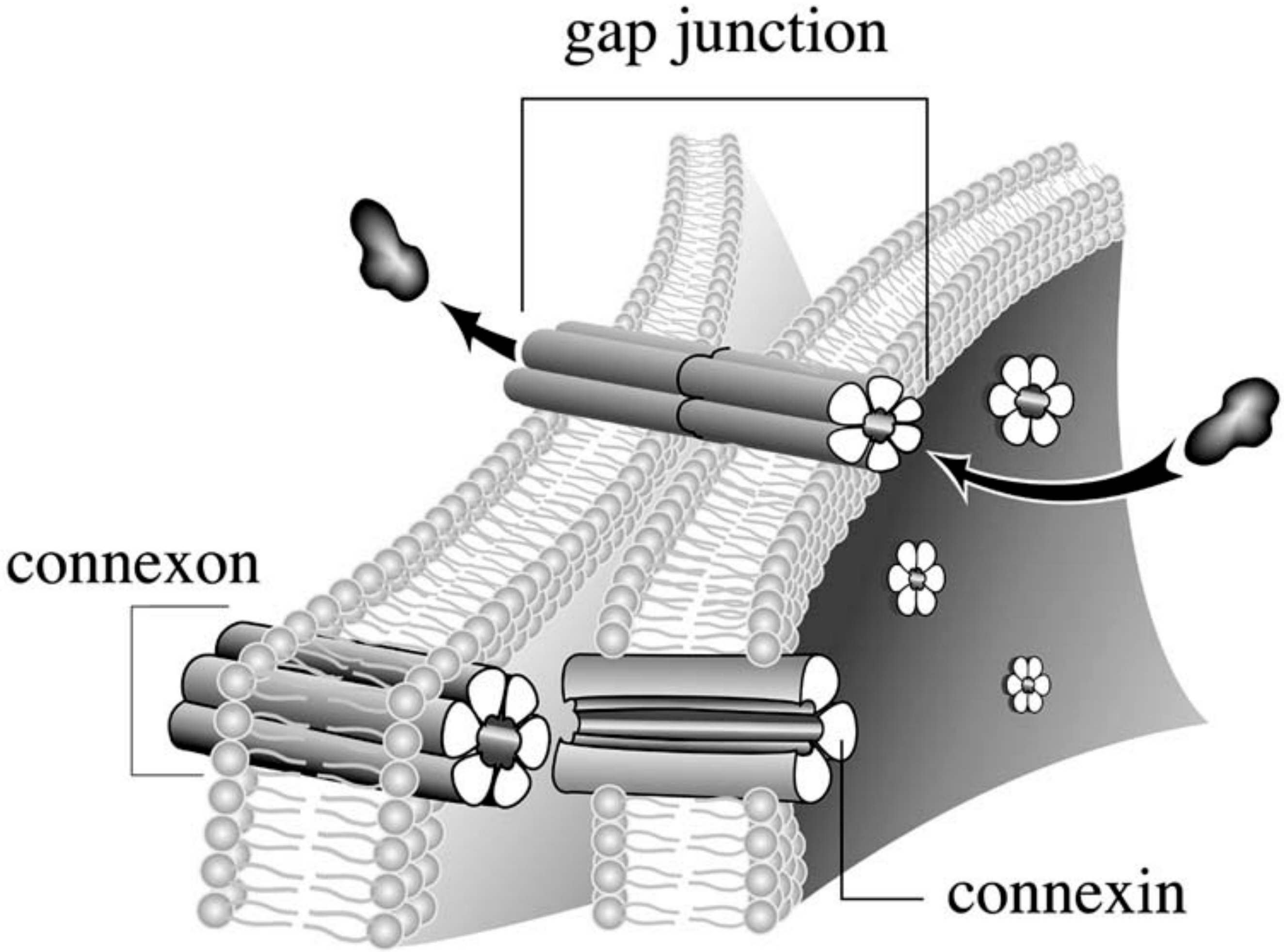
Tsodyks and Markram, 1997

Modeling short-term synaptic plasticity



Tsodyks and Markram, 1997

Gap junctions



Echevaria and Nathanson