Decoding

How well can we learn what the stimulus is by looking at the neural responses?

Two approaches:

- devise explicit algorithms for extracting a stimulus estimate
- directly quantify the relationship between stimulus and response using information theory

Predicting the firing rate

Starting with a rate response, r(t) and a stimulus, s(t),

the optimal linear estimator finds the best kernel K such that:

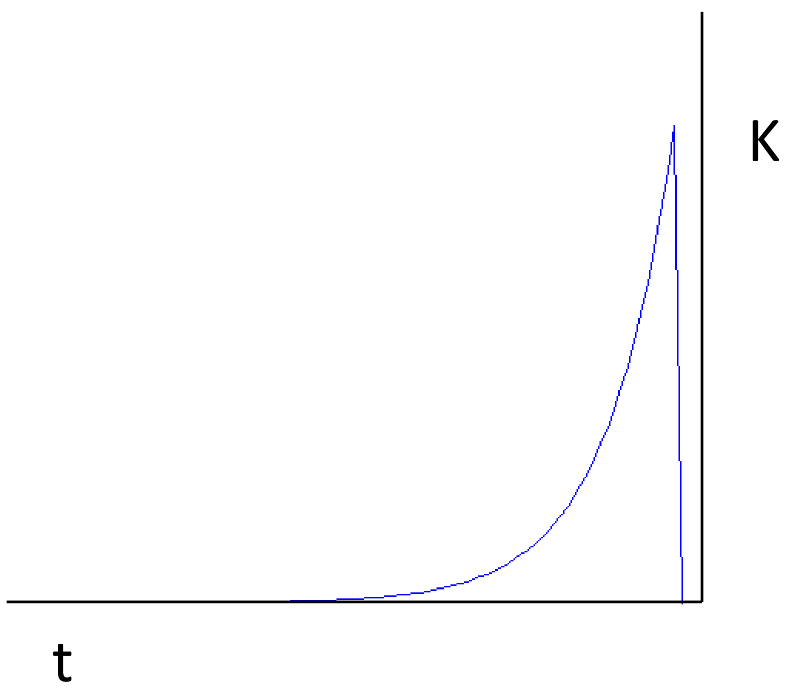
$$r_{\text{est}}(t) = \bar{r} + \int d\tau \, s(t-\tau)K(\tau)$$

is close to r(t), in the least squares sense.

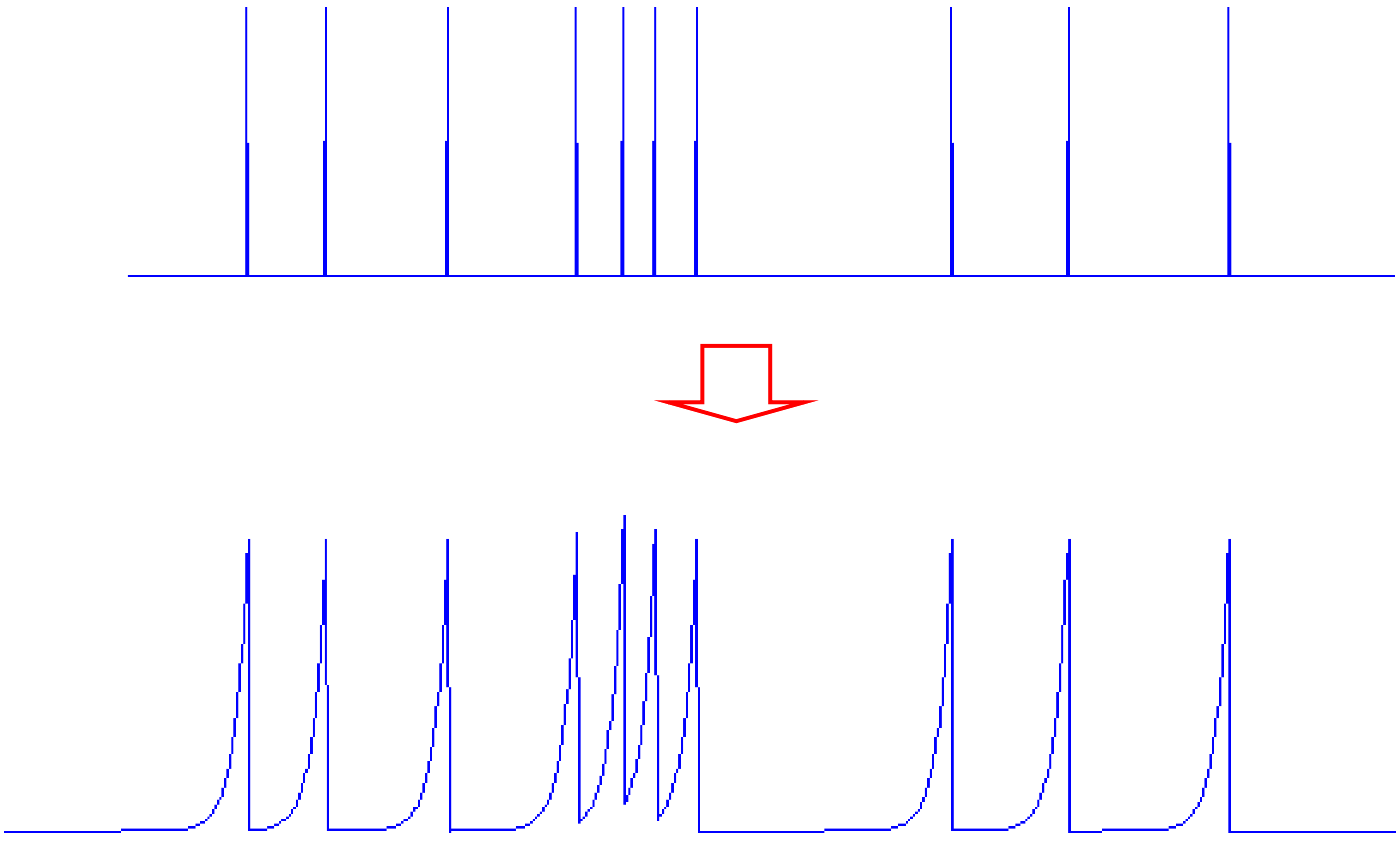
Solving for K(t),

$$K(t) = \frac{1}{2\pi}\int d\omega \, e^{-i\omega t}\frac{\tilde{C}_{rs}(-\omega)}{\tilde{C}_{ss}(\omega)}$$

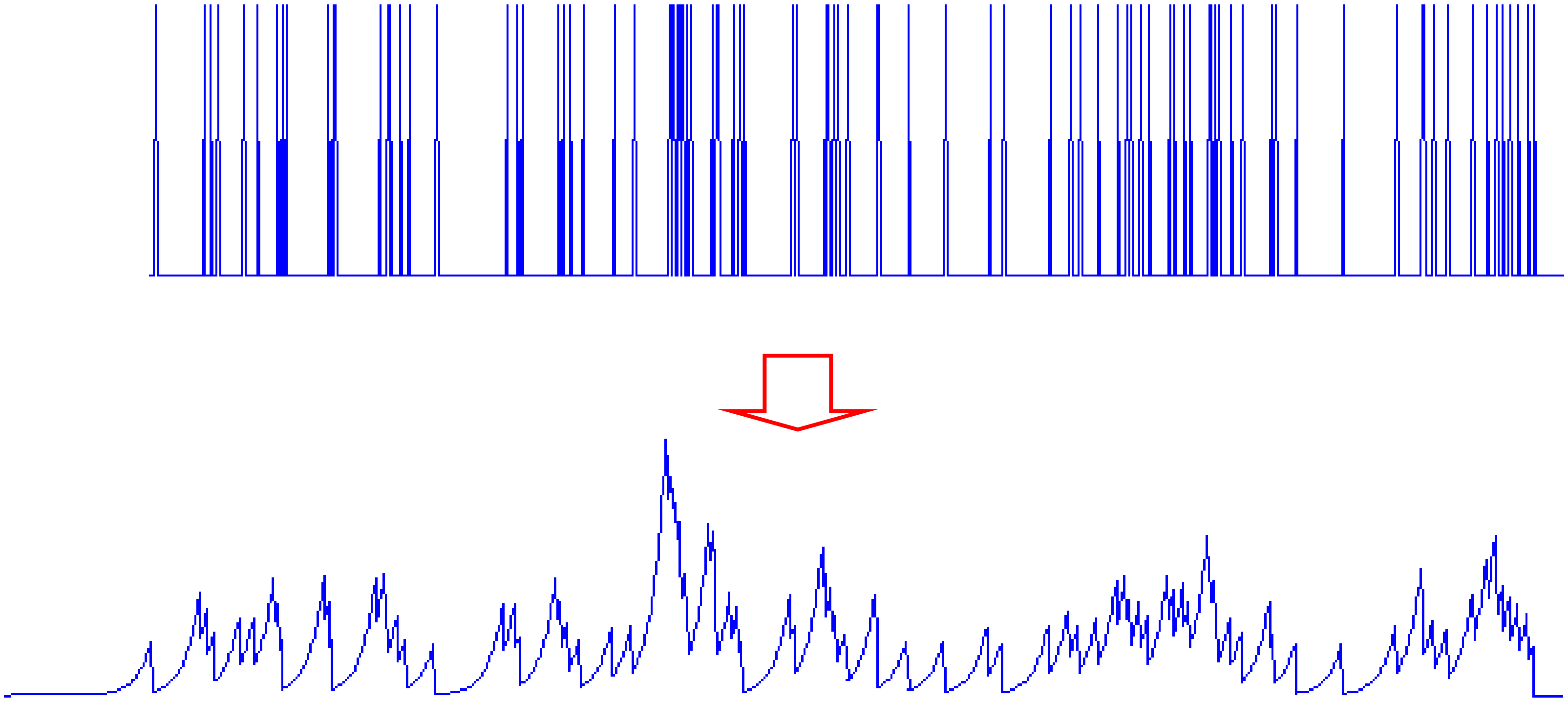
Stimulus reconstruction



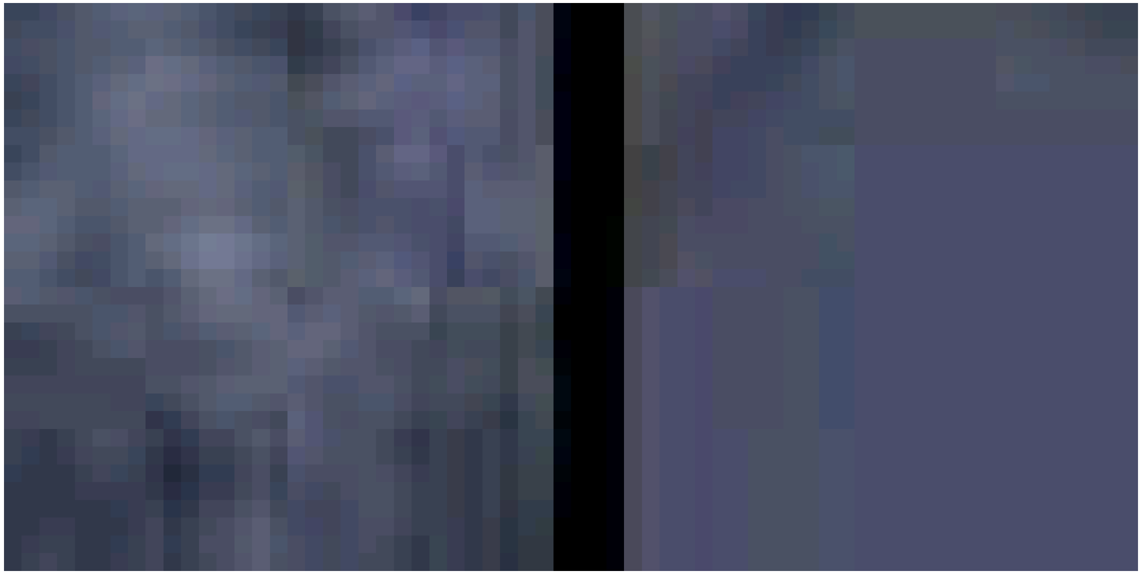
Stimulus reconstruction



Stimulus reconstruction



Reading minds: the LGN



Yang Dan, UC Berkeley

Computing in carbon

Basic elements of neuroelectronics

-- membranes
-- ion channels
-- wiring

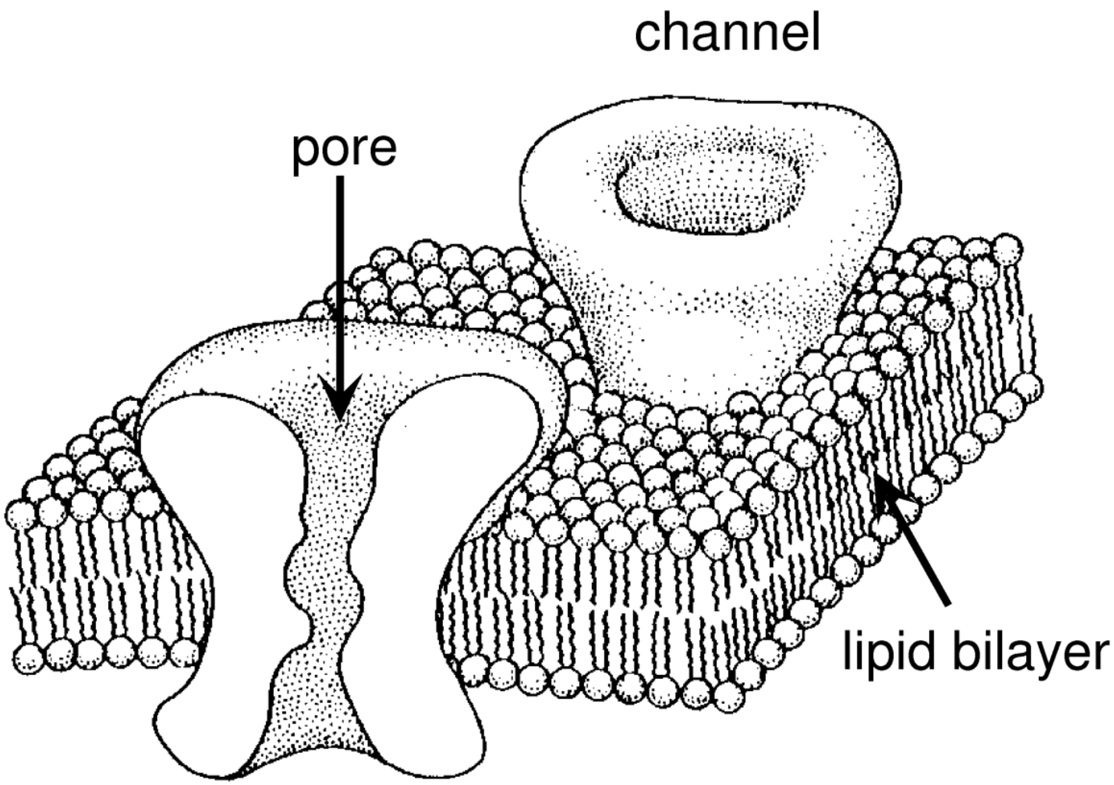
Elementary neuron models

-- conductance based
-- modelers' alternatives

Wiring neurons together

-- synapses
-- short term plasticity

Closeup of a patch on the surface of a neuron

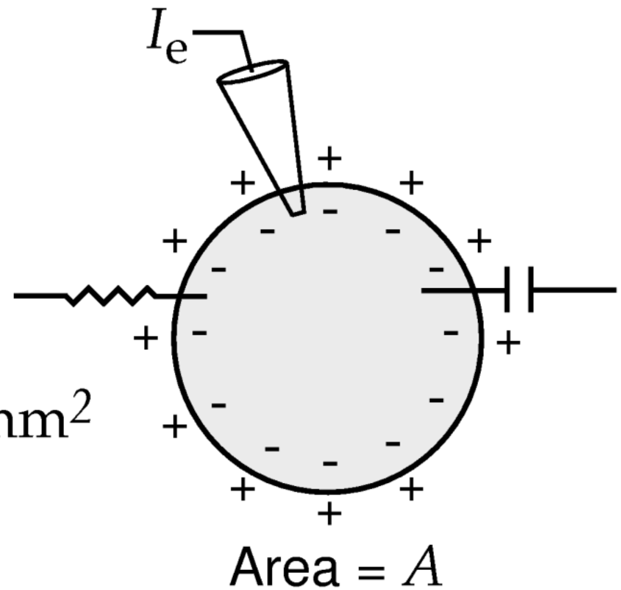


An electrophysiology experiment

$\Delta V = I_e R_m$

$R_m = r_m / A$

$r_m \approx 1\ \mathrm{M\Omega\ mm^2}$



$Q = C_m V$

$C_m = c_m A$

$c_m \approx 10\ \mathrm{nF/mm^2}$

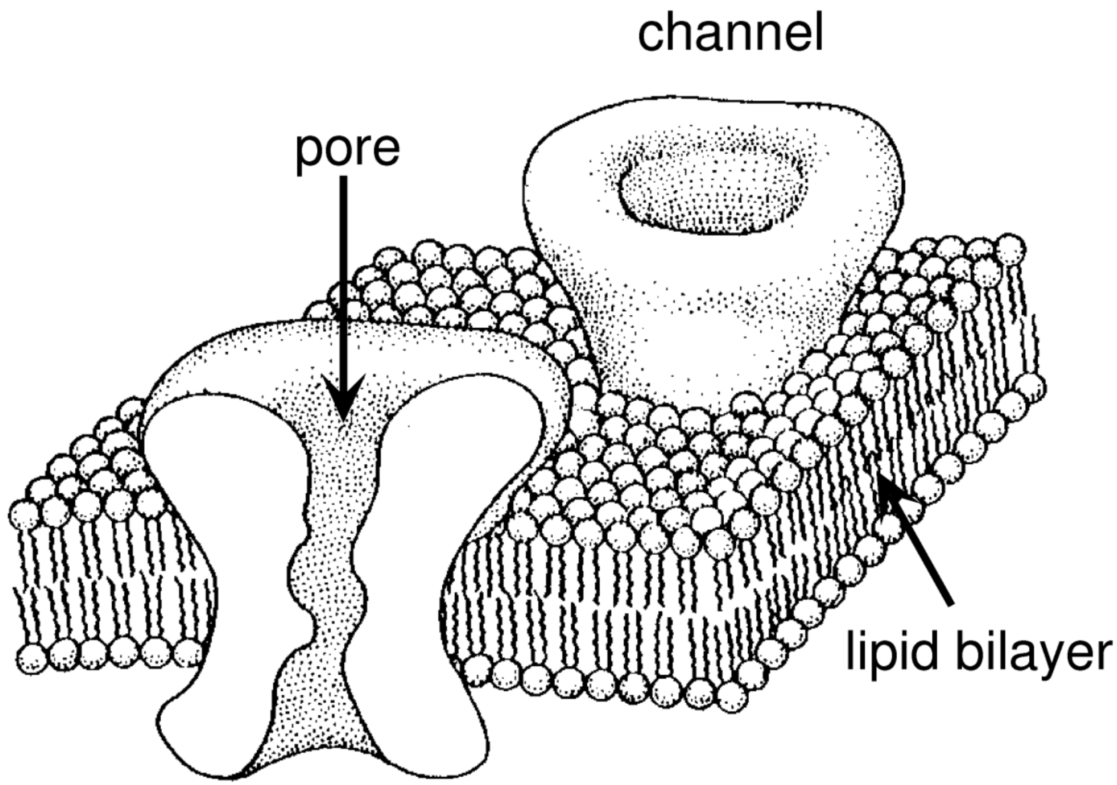
$= 1\ \mathrm{mF/cm^2}$

$$C_m \frac{dV}{dt} = \frac{dQ}{dt} = I_C$$

$$\tau_m = R_m C_m$$

Ion channels create opportunities for charge to flow
Potential difference is maintained by *ion pumps*

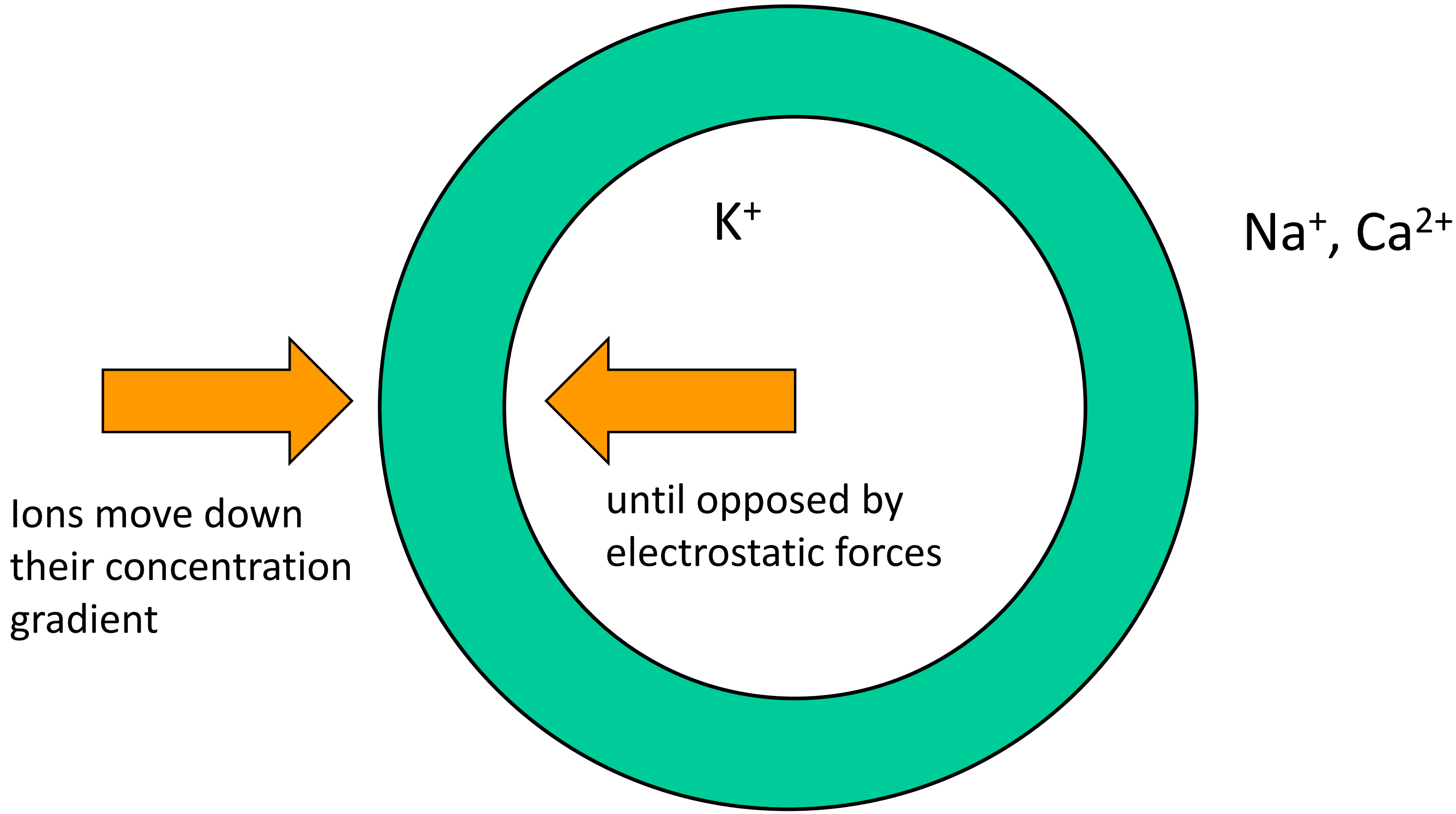
Movement of ions through the ion channels



Energetics: $qV \sim k_B T$

$V \sim 25mV$

The equilibrium potential



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

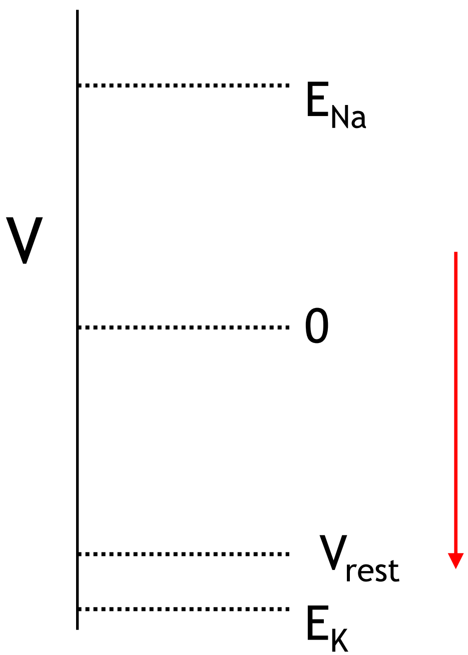
Different ion channels have associated *conductances*.

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

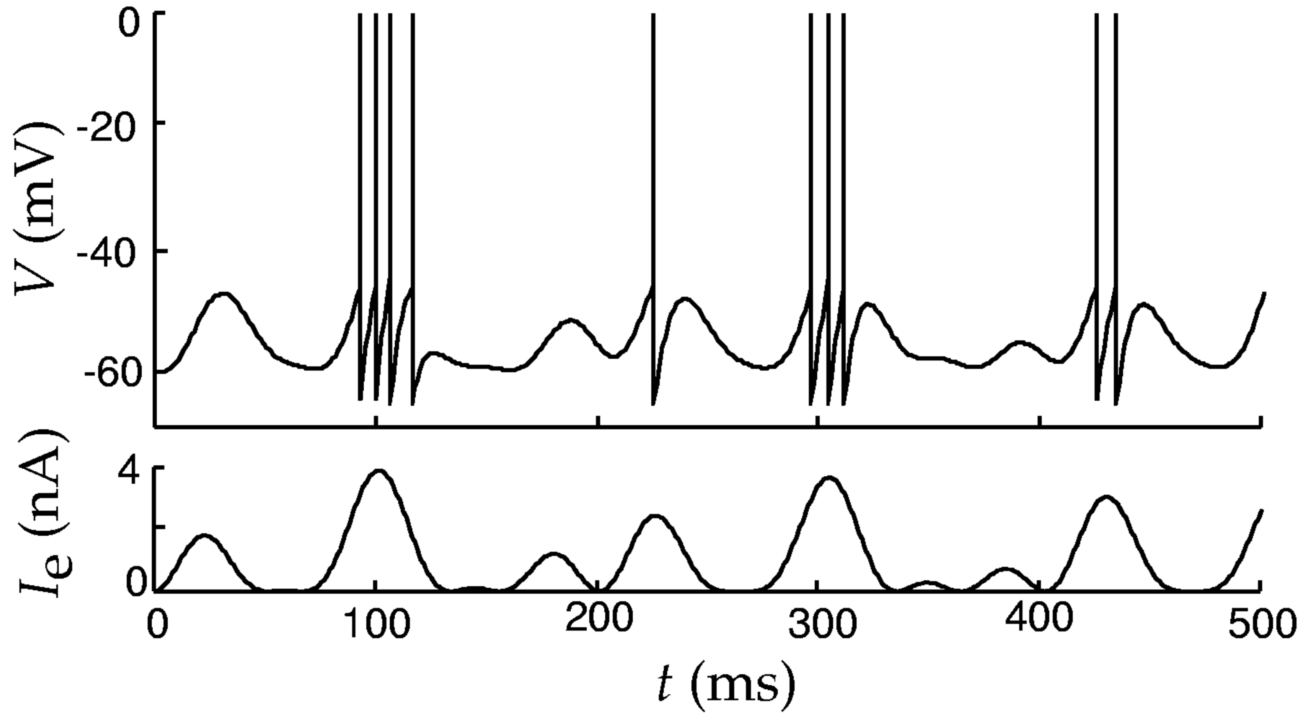
E_{Na}	~	50mV	depolarizing
E_{Ca}	~	150mV	depolarizing
E_K	~	-80mV	hyperpolarizing
E_{Cl}	~	-60mV	shunting

V > E → positive current will flow outward

V < E → positive current will flow inward

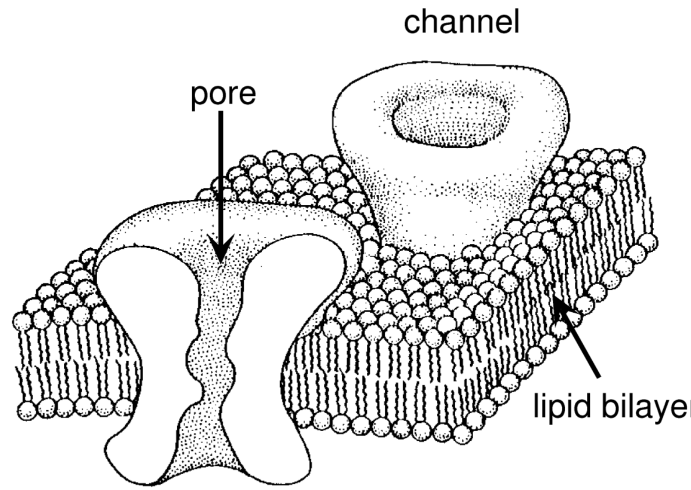


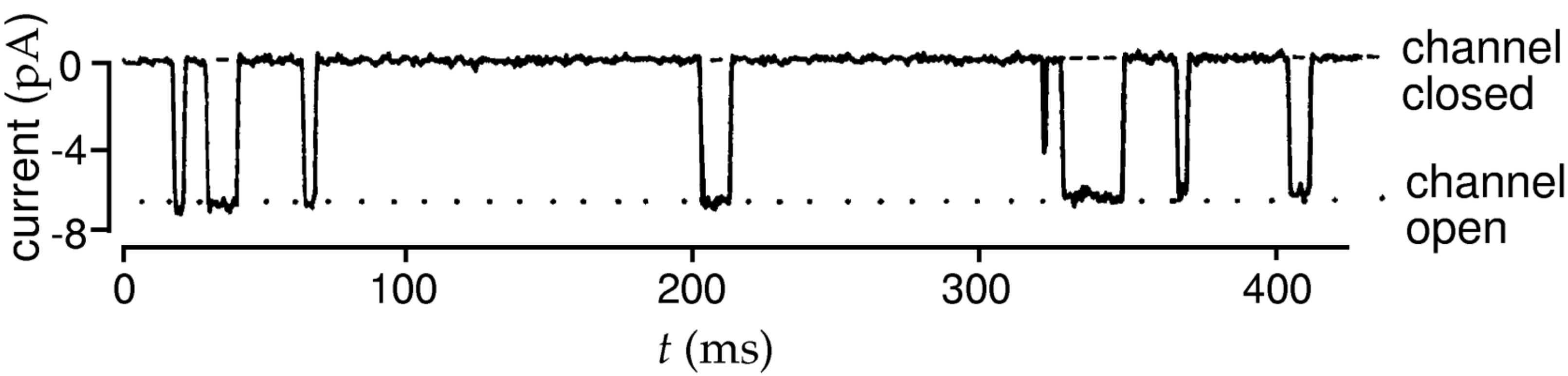
The neuron is an excitable system



Excitability is due to the properties of ion channels

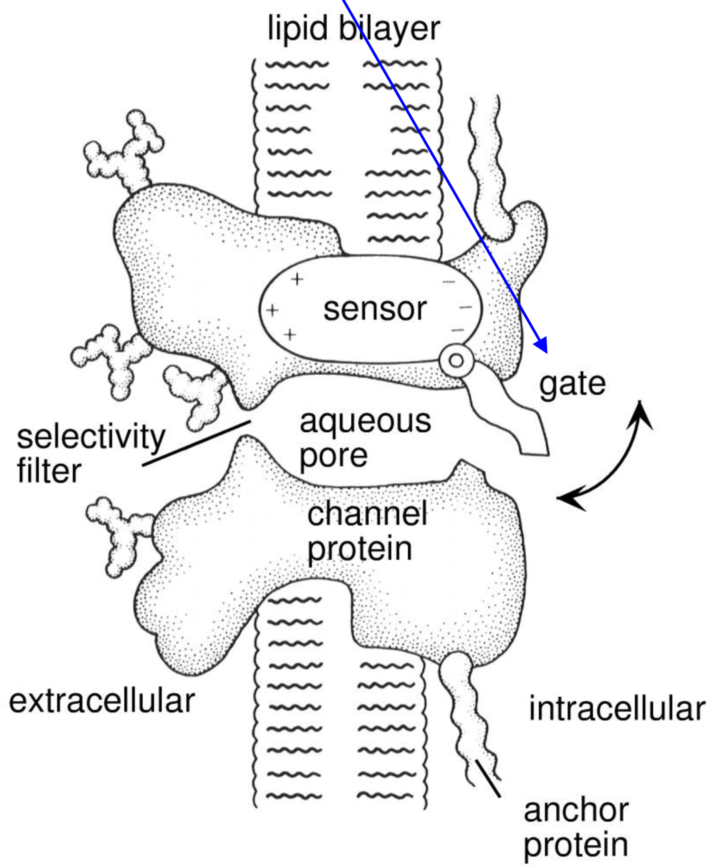
- Voltage dependent
- transmitter dependent (synaptic)
- Ca dependent





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

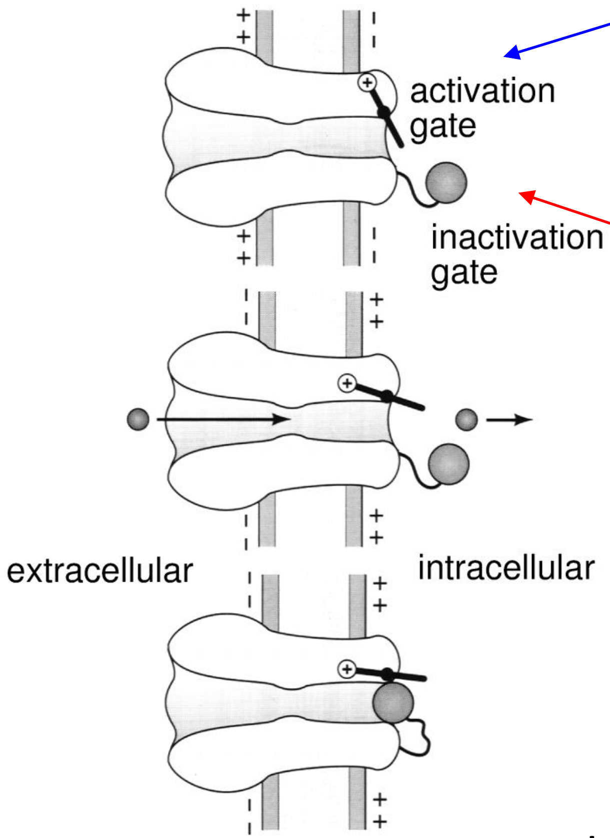
Transitions between states occur at voltage dependent rates

$\alpha_n(V)$ 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

First order rate equations

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

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

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

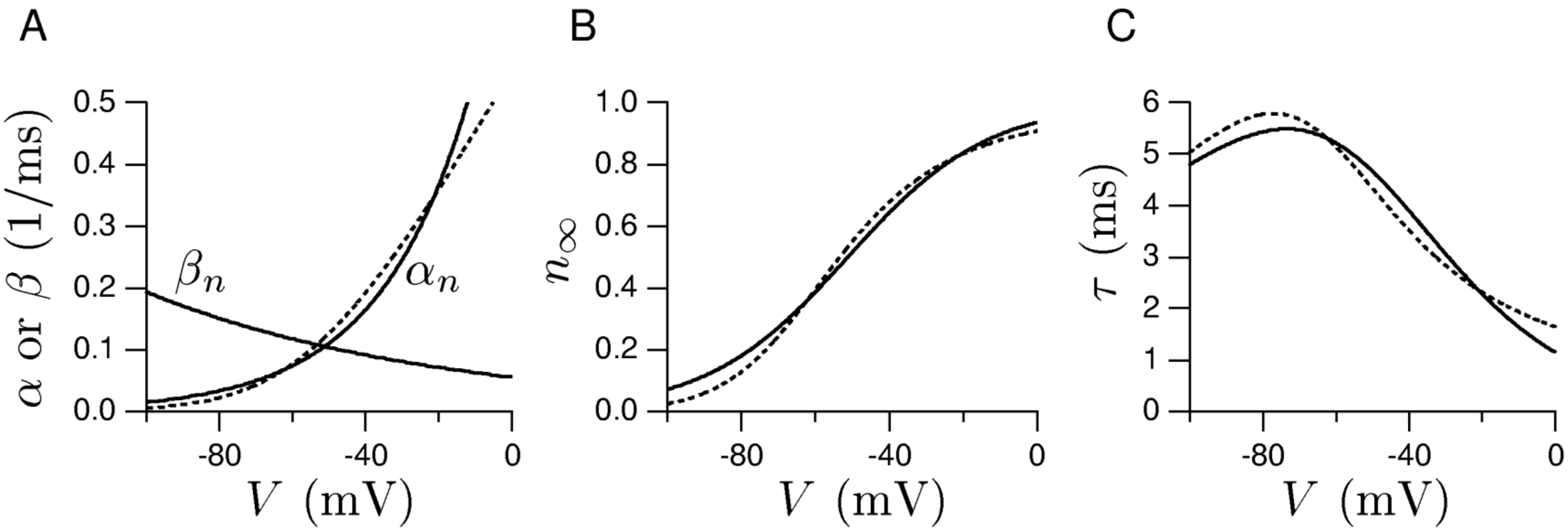
We can rewrite:

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

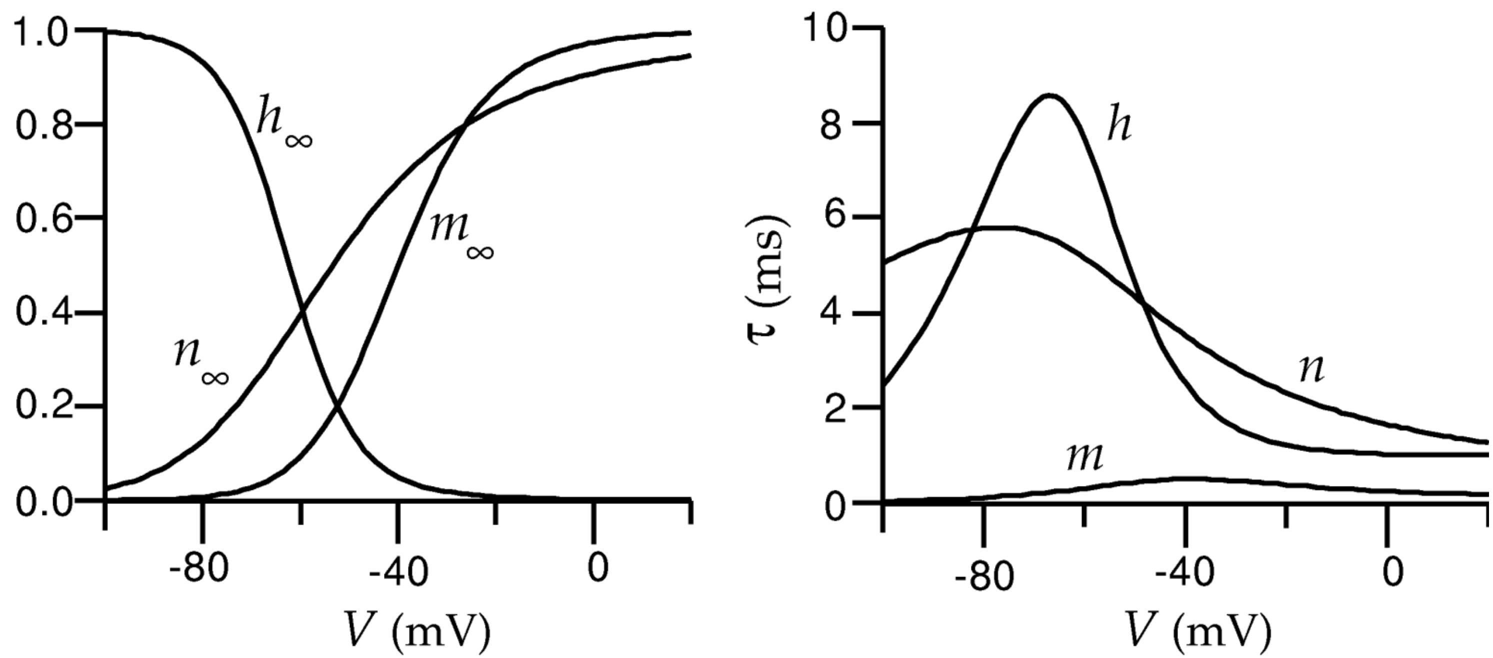
where

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

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

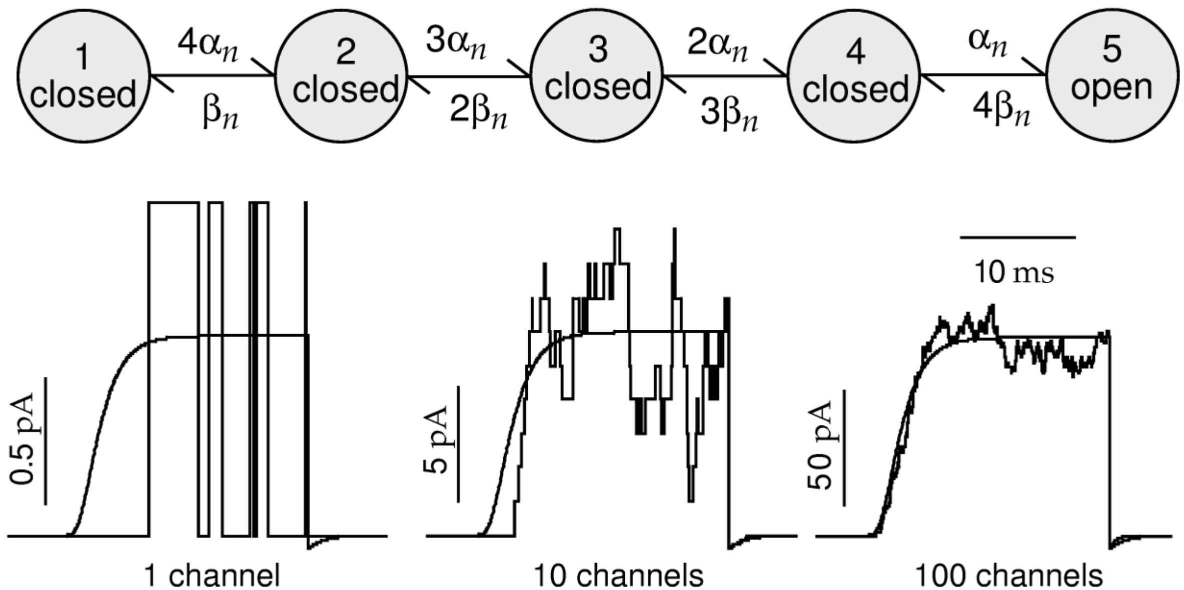


A
B
C
α or β (1/ms)
β_n
α_n
n_∞
τ (ms)
V (mV)
V (mV)
V (mV)



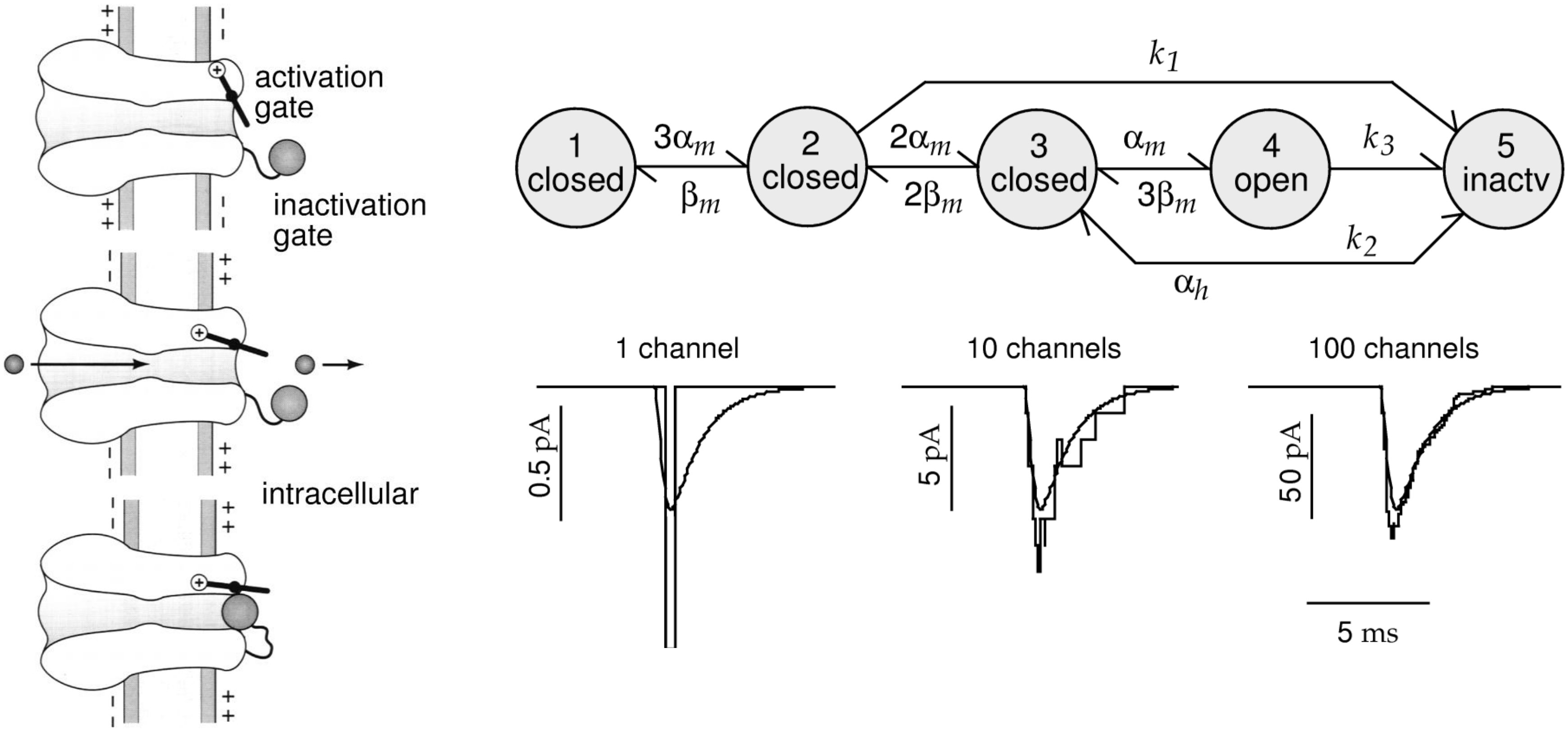
1.0
0.8
0.6
0.4
0.2
0.0
h_∞
m_∞
n_∞
-80
-40
0
V (mV)
10
8
6
4
2
0
τ (ms)
h
n
m
-80
-40
0
V (mV)

A microscopic stochastic model for ion channel function



approach to macroscopic description

Transient conductances



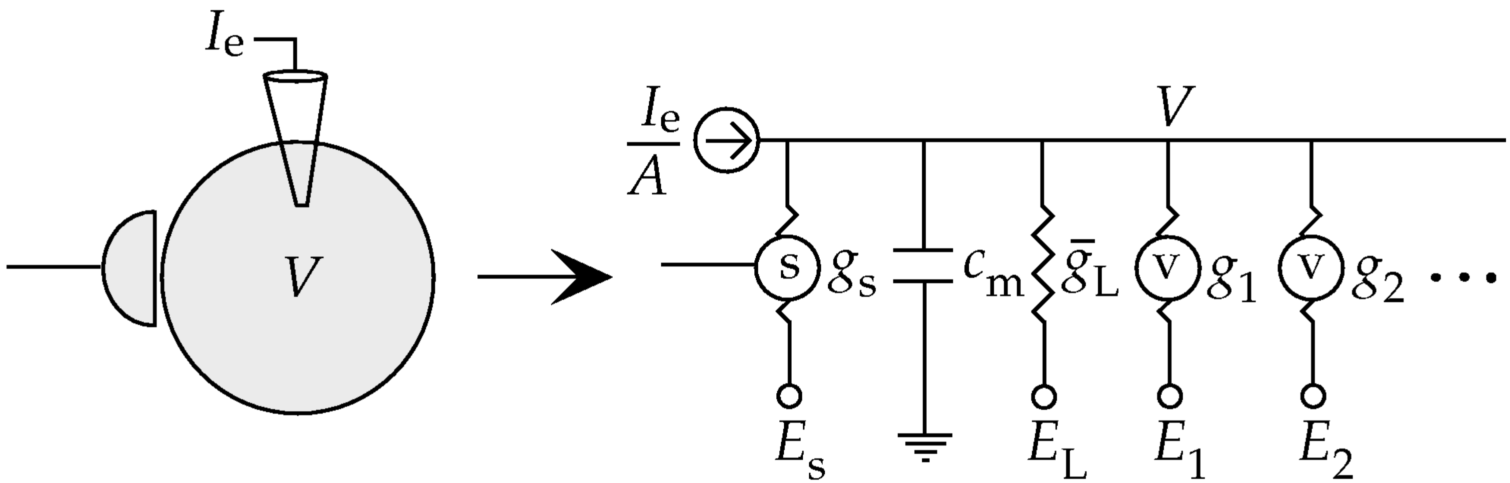
Different from the continuous model:

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

Putting it back 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

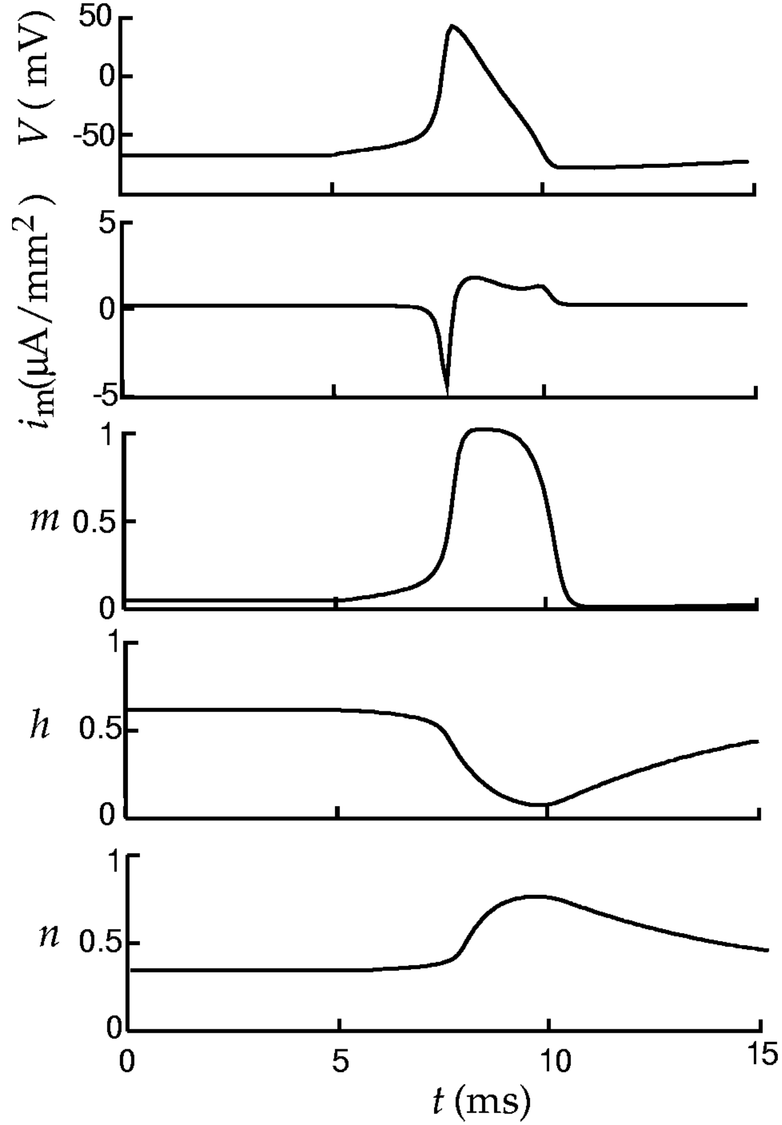
Externally applied current

The Hodgkin-Huxley equation

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

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

Anatomy of a spike



The integrate-and-fire model

Like a passive membrane:

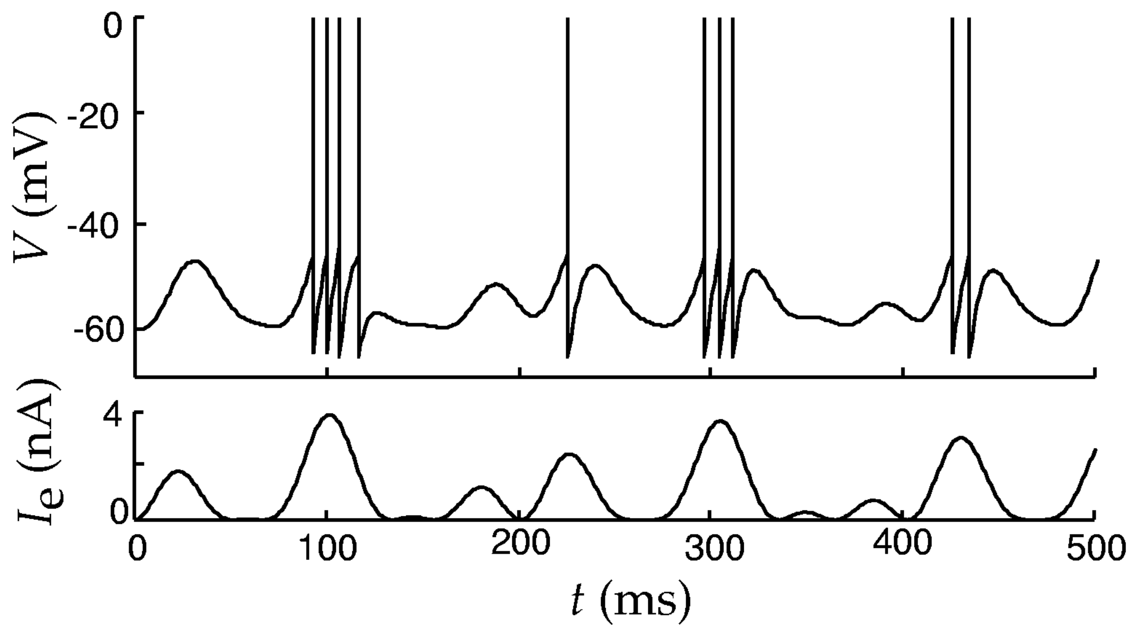
$$C_m \frac{dV}{dt} = -g_L(V - E_i) - I_e$$

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

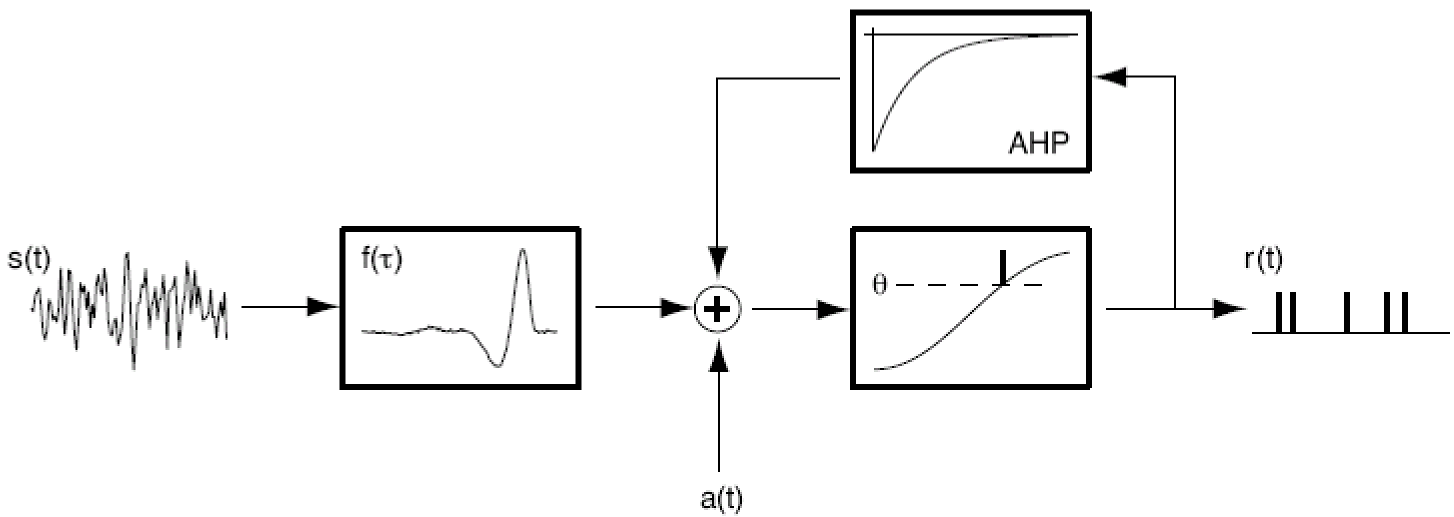
Gerstner and Kistler

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

An advanced spike response model

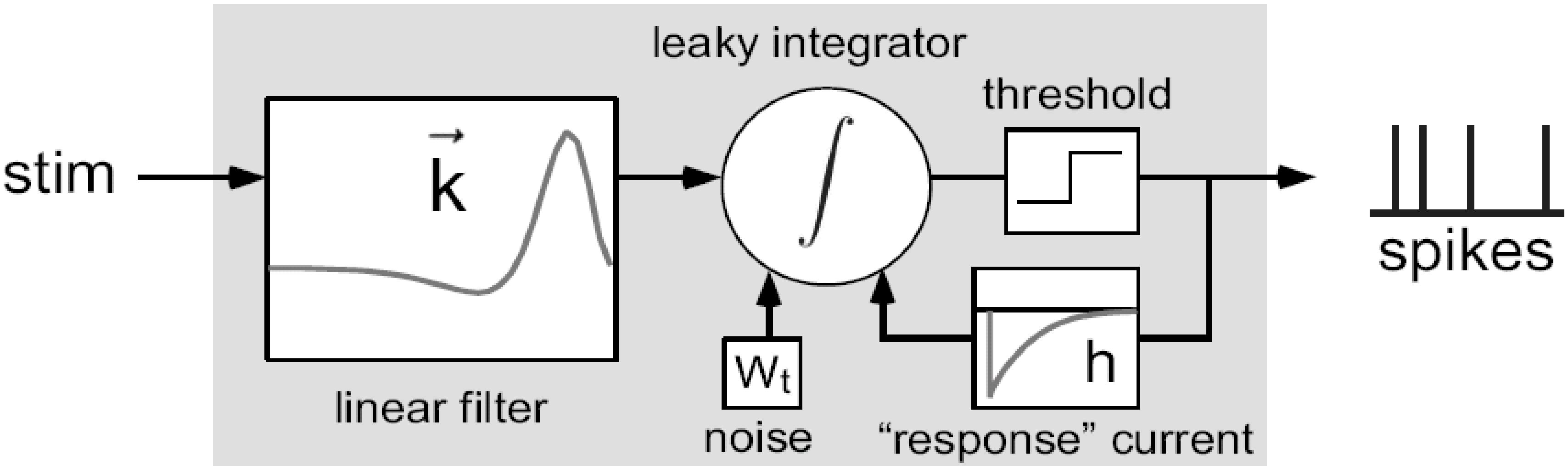
Keat, Reinagel and Meister



- AHP assumed to be exponential recovery, A $\exp(-t/\tau)$
- need to fit all parameters

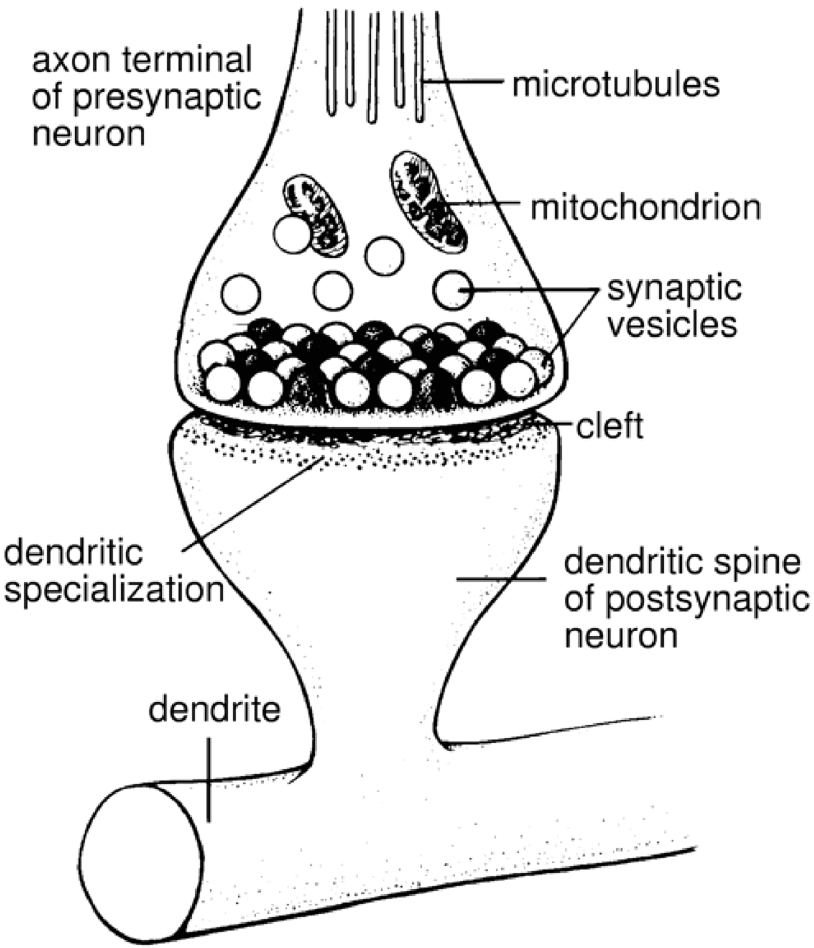
The generalized linear model

Paninski, Pillow, Simoncelli



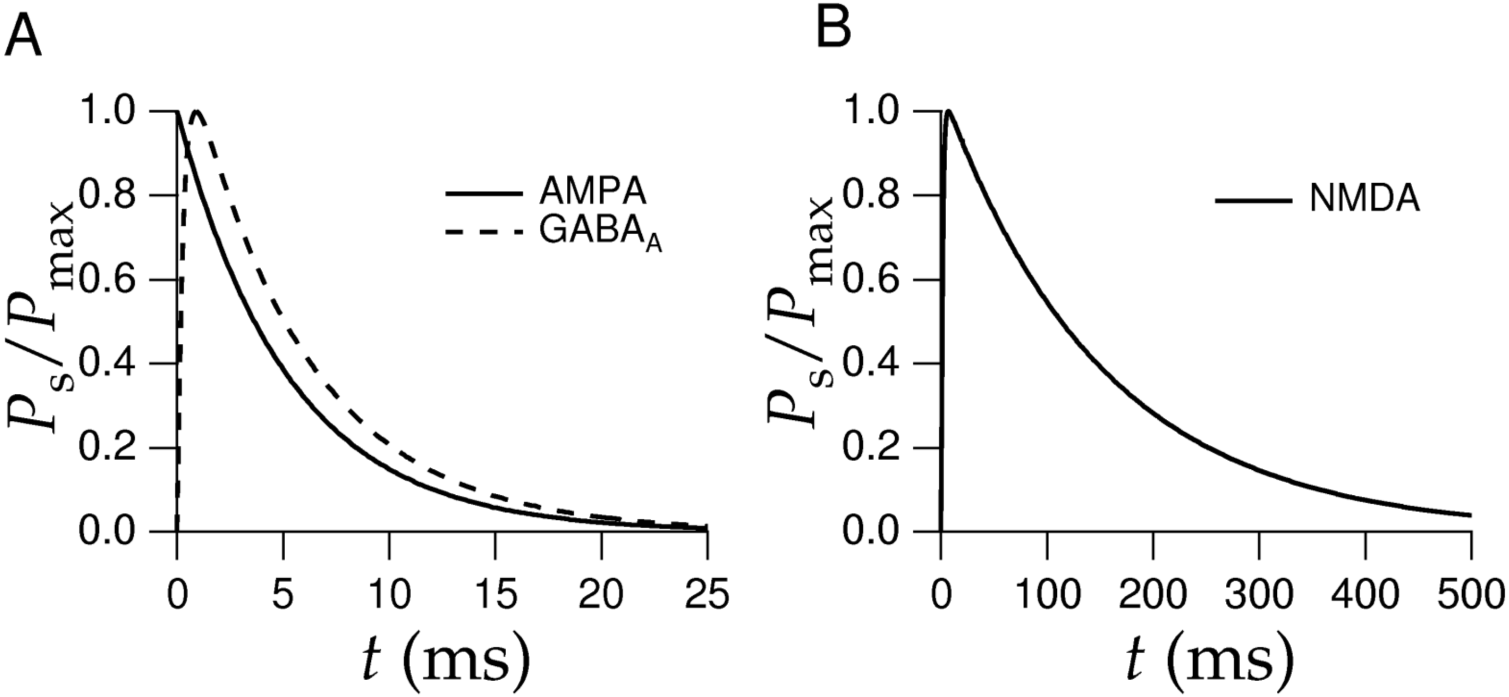
- general definitions for k and h
- robust maximum likelihood fitting procedure

Synapses



Signal is carried chemically across the synaptic cleft

Post-synaptic conductances



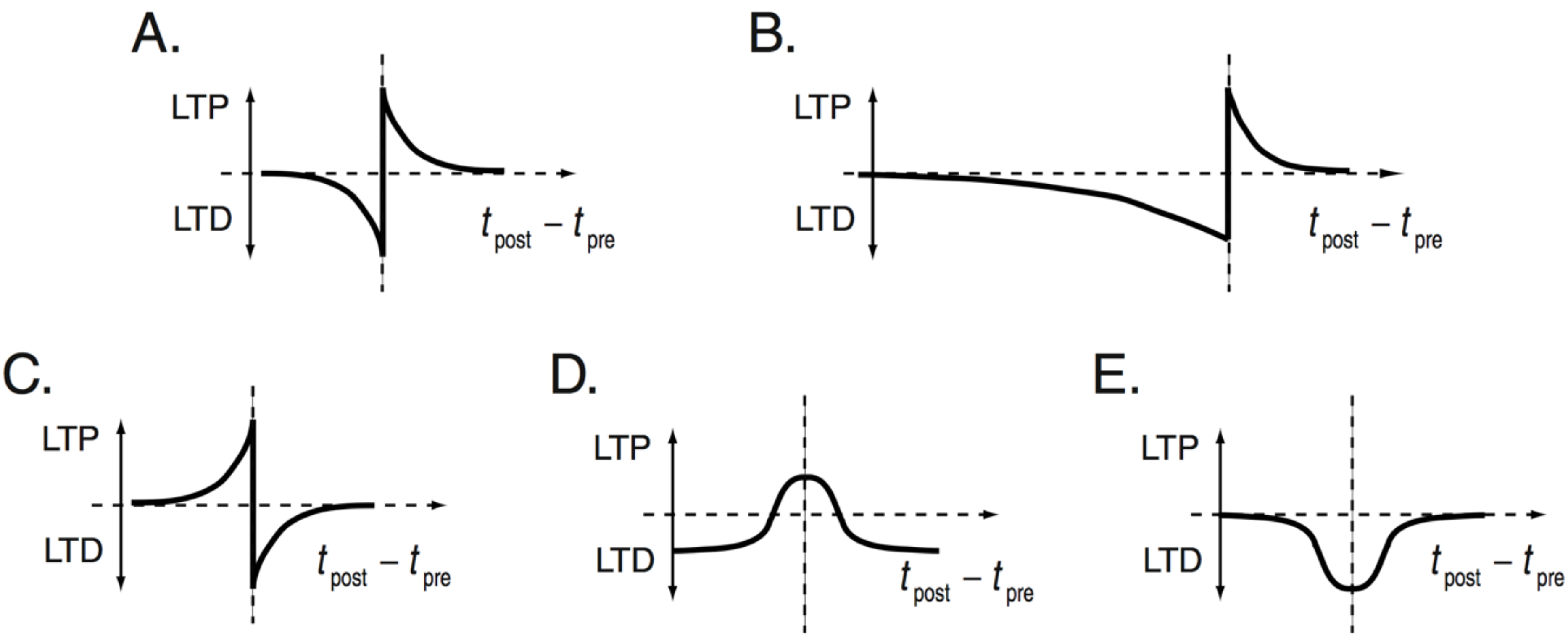
Requires pre- and post-synaptic depolarization

Coincidence detection, Hebbian

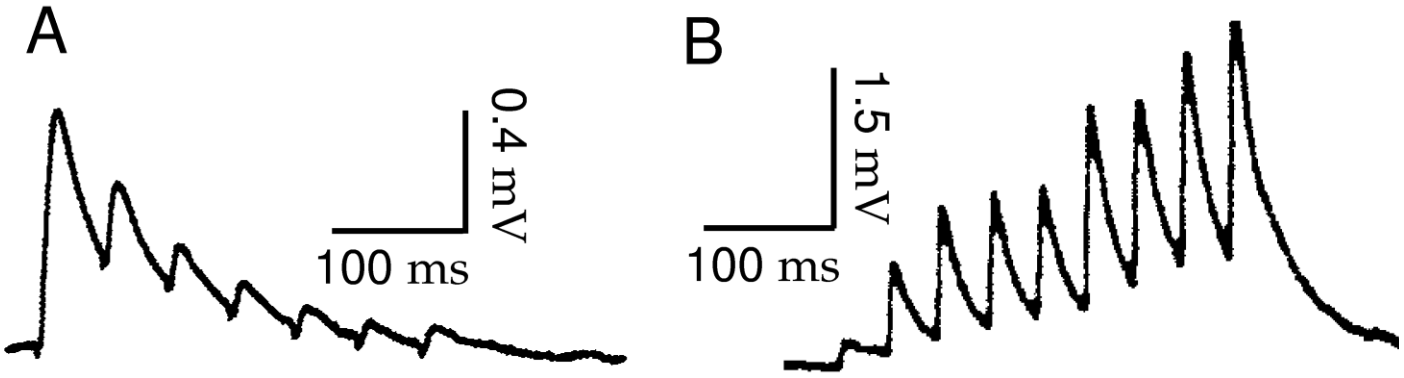
Synaptic plasticity

1. LTP, LTD

2. Spike-timing dependent plasticity



Short-term synaptic plasticity



Depression

Facilitation