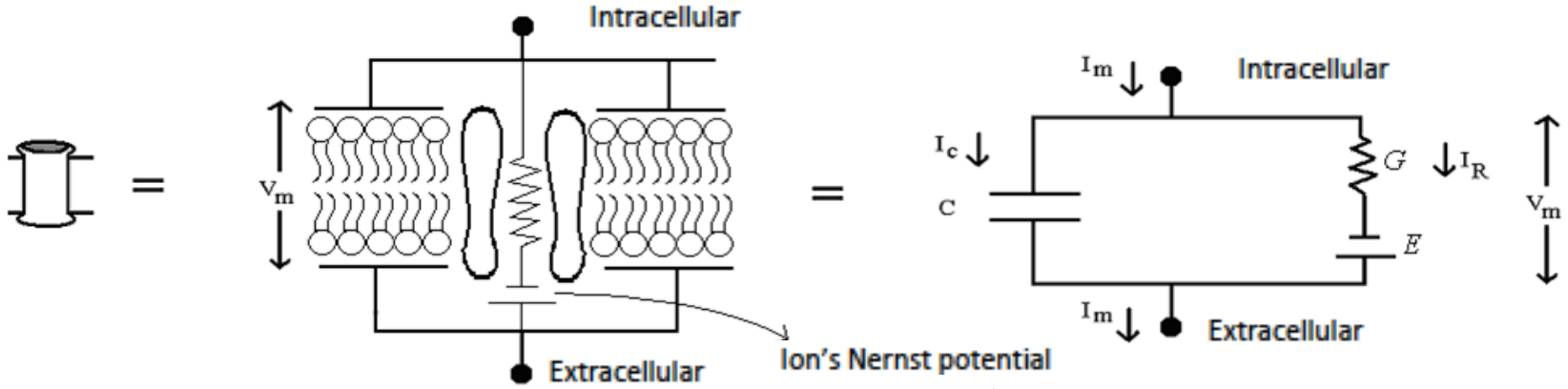
Part 2

Single neuron models

The membrane equation (passive)



$$E_{ion} = \frac{RT}{zF} \ln \frac{[Íon]_{out}}{[Íon]_{in}}.$$

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

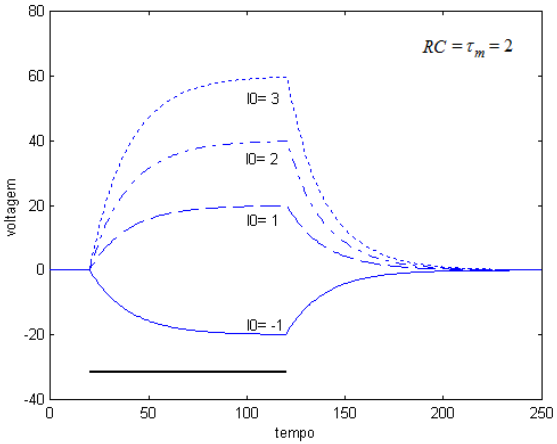
$$I_r = \frac{(V - E_N)}{r} = g(V - E_N) \quad \text{(1 open channel);}$$

$$I_R = Ng(V - E_N) = G(V - E_N) \quad (N \text{ open channels})$$

$$I_m = I_C + I_R = C \frac{dV_m}{dt} + G(V_m - E) = I_{inj}$$

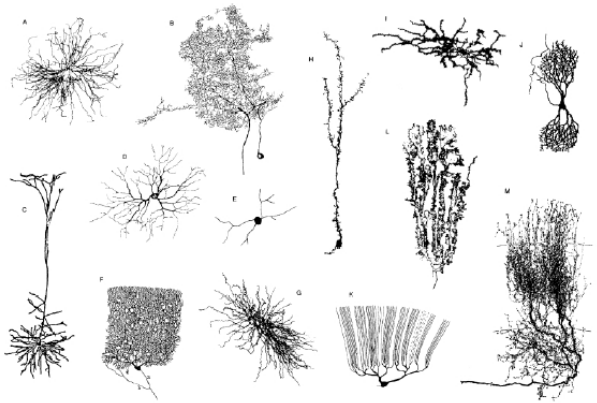
$$\tau_m \frac{dV_m(t)}{dt} = -V_m(t) + E + RI_{inj}(t)$$

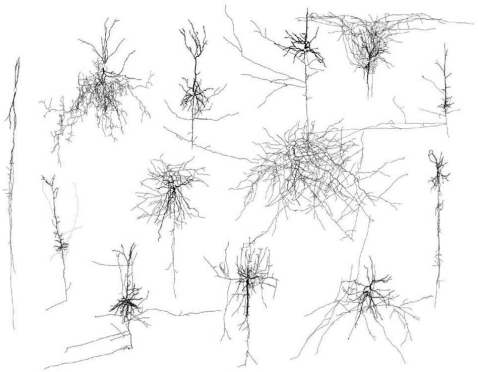
$$\tau_m = RC$$

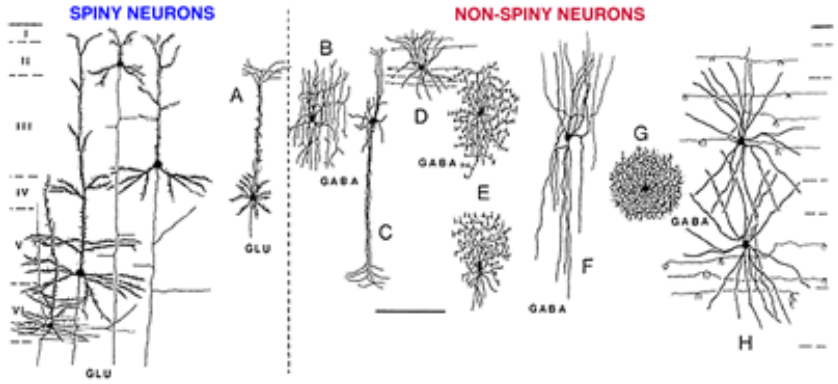


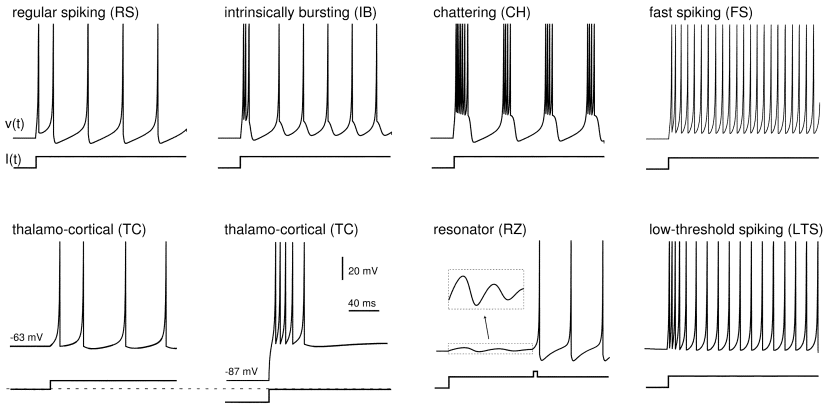
What to model in a neuron model?

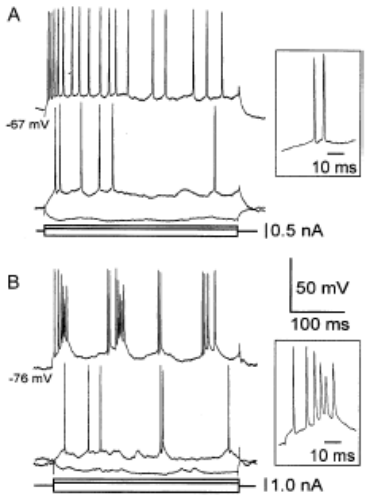
- Morphology (shape, axonal target, smooth or spiny);
- Electrophysiology (spike shape, pattern of spike train);
- Neurochemistry (neurotransmitter released at synapses);

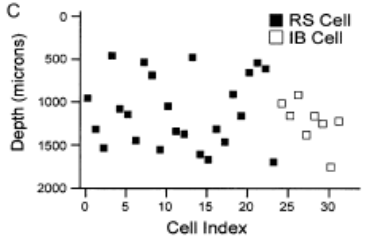












Neuron model

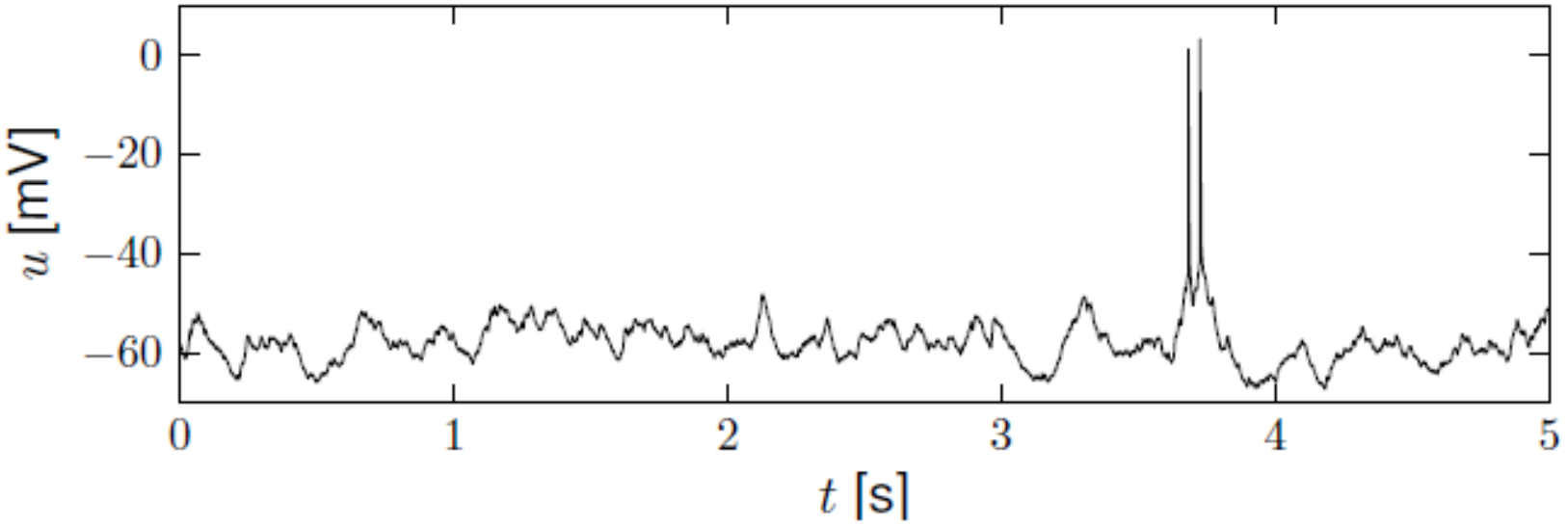
- Deterministic vs. Stochastic
- Firing rate vs. Spiking
- High-dimensional vs. Low dimensional
- More vs. Less biologically faithful

Why stochastic neuron models?

- *In vivo* and *in vitro* recordings of single neuron spike trains are characterized by a high degree of variability
- The following examples are taken from the book by Gerstner, Kistler, Naud and Paninski, *Neuronal Dynamics*, CUP, 2014

Spontaneous activity *in vivo*

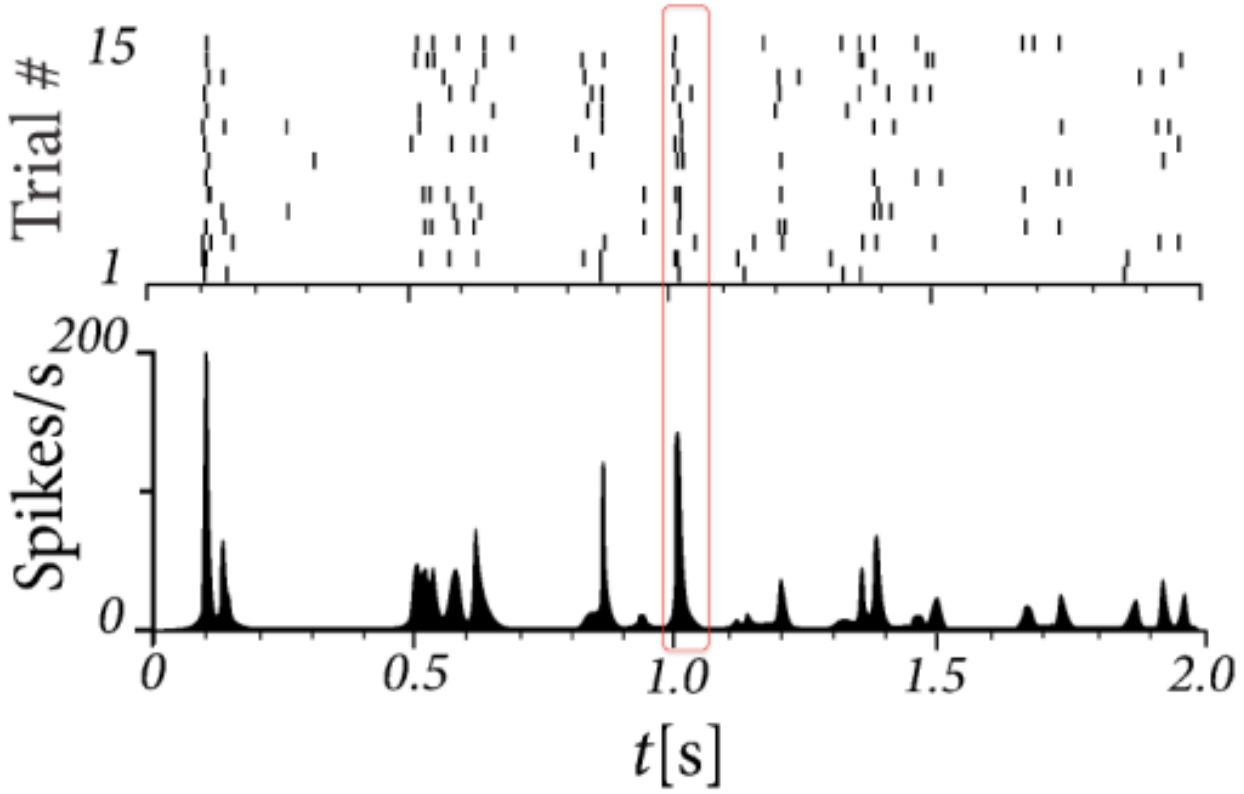
Awake mouse, cortex, freely whisking

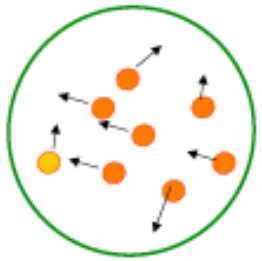


Crochet et al., 2011

Trial to trial variability *in vivo*

15 repetitions of the same random dot motion pattern

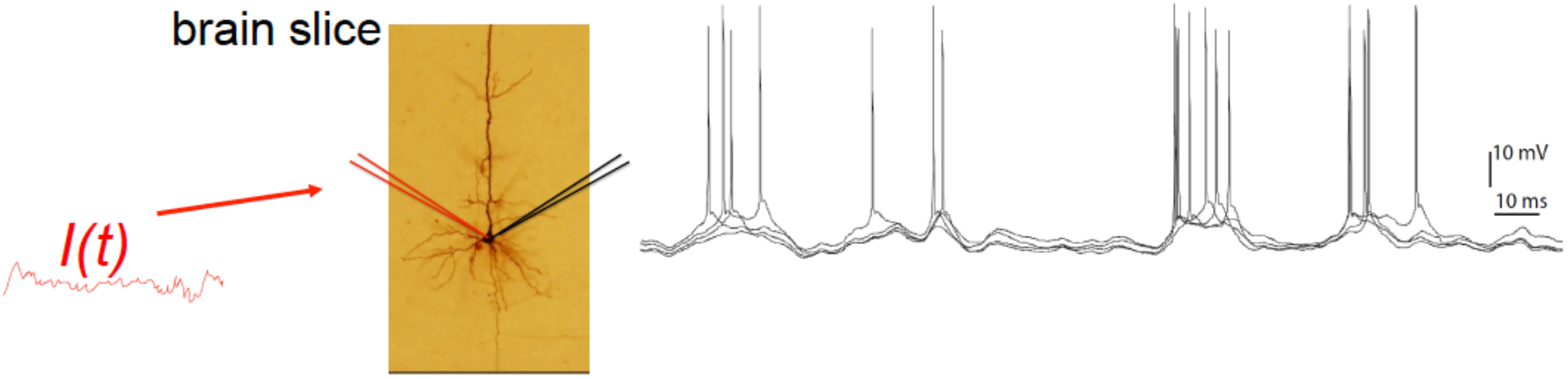




Adapted from Bair and Koch, 1996;
Data from Newsome, 1989

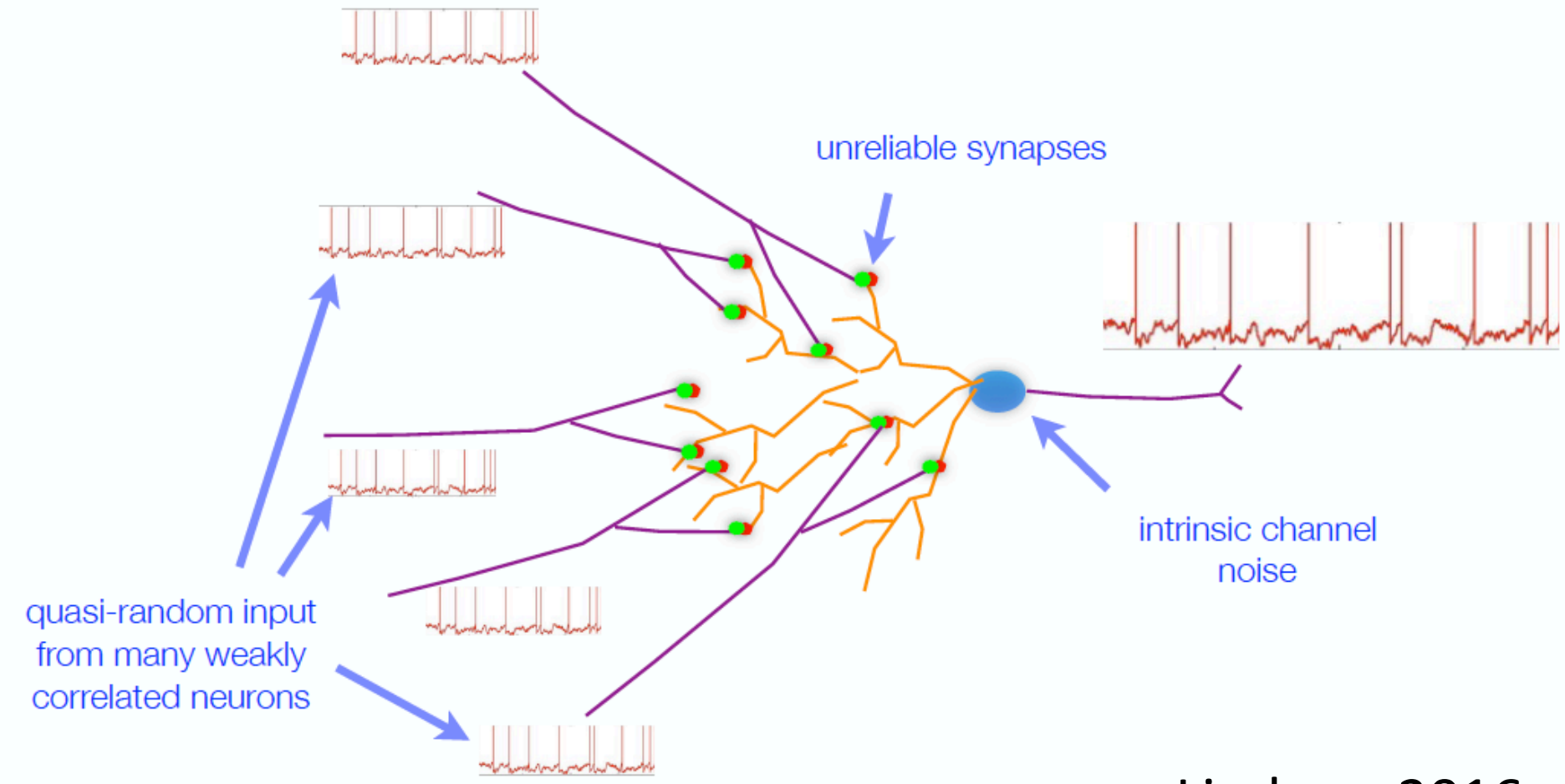
Trial to trial variability *in vitro*

4 repetitions of the same time-dependent stimulus



Modified from Naud and Gerstner, 2012

Sources of noise: extrinsic and intrinsic to neurons

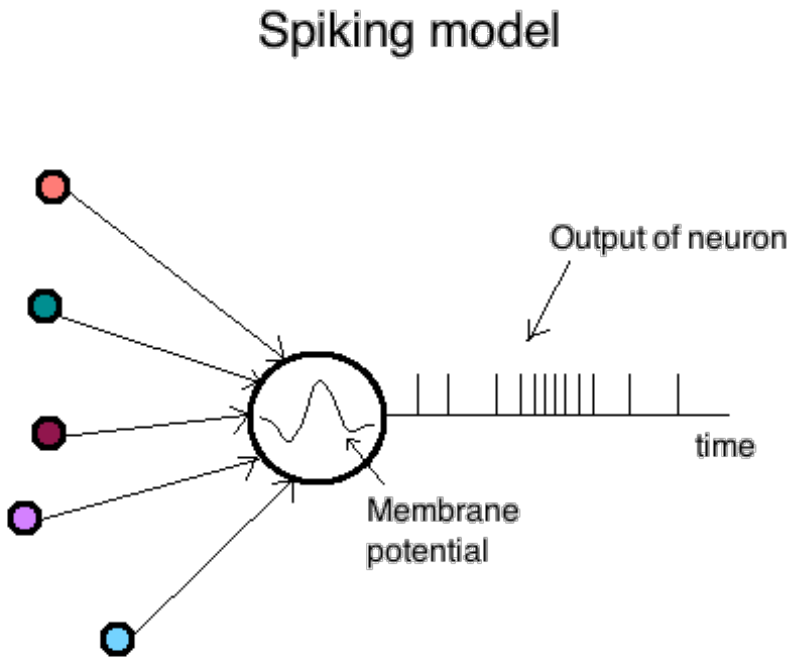


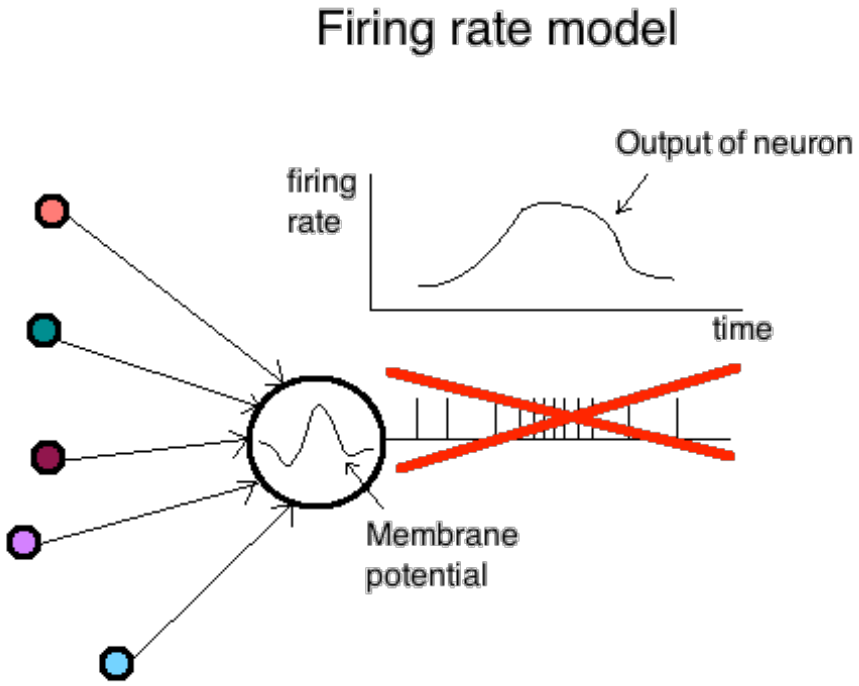
Lindner, 2016

Two types of noise model for a neuron

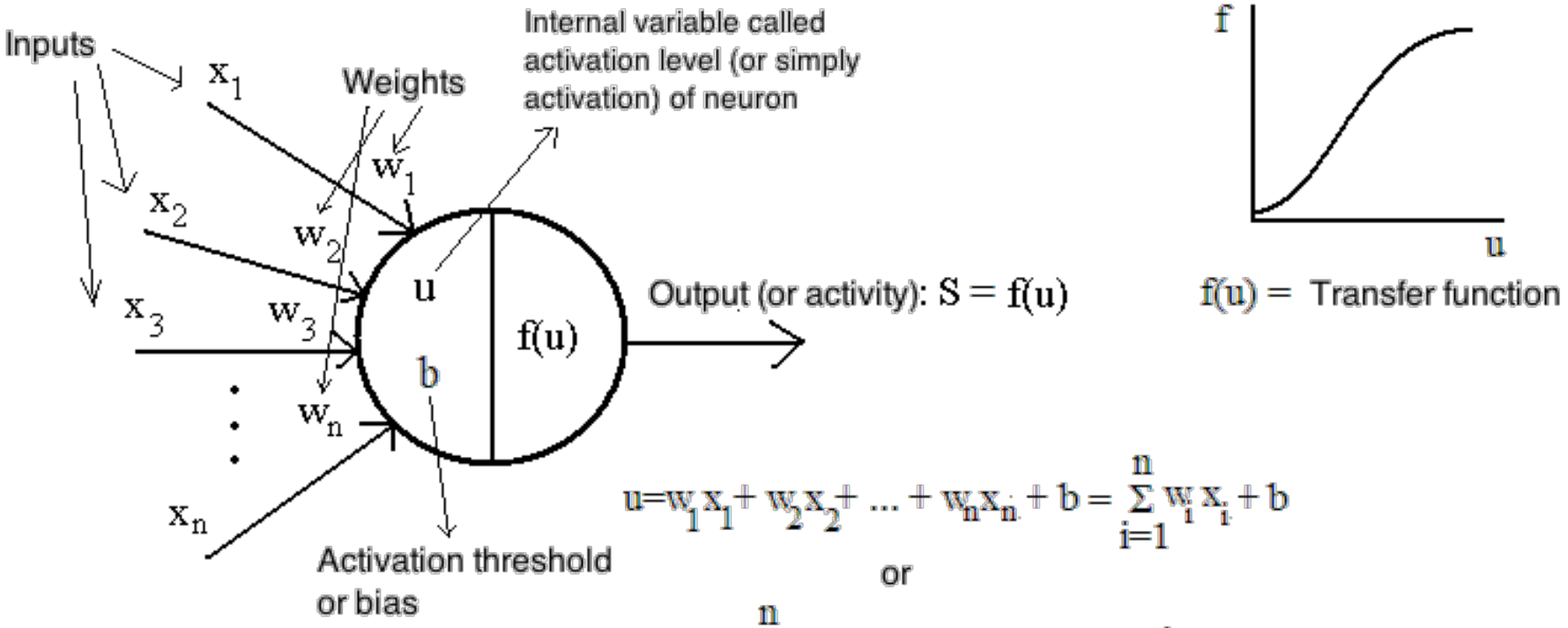
- Spike generation is directly modeled as a stochastic process
- Spike generation and synaptic transmission are modeled deterministically and noise enters the dynamics via additional stochastic terms

Spiking vs. firing rate





The firing rate neuron



$$u = w_1 x_1 + w_2 x_2 + \ldots + w_n x_n + b = \sum_{i=1}^{n} w_i x_i + b$$

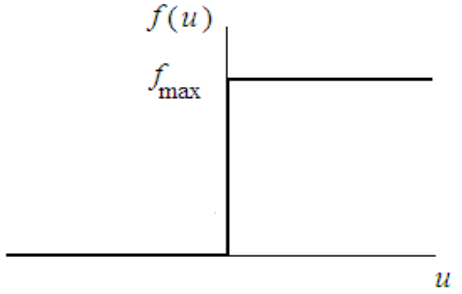
or

$$u = \sum_{i=0}^{n} w_i x_i \;,\; x_0 = 1 \quad \text{and} \quad w_0 = b$$

Transfer functions

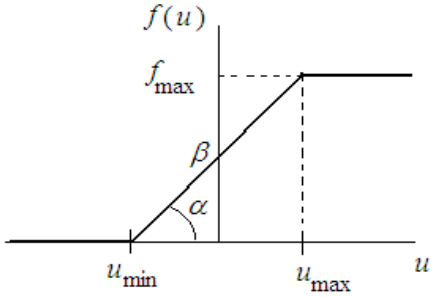
Step function:

$$S = f(u) = \begin{cases} f_{max} \text{ se } u \geq 0 \\ 0 \text{ se } u < 0 \end{cases}$$



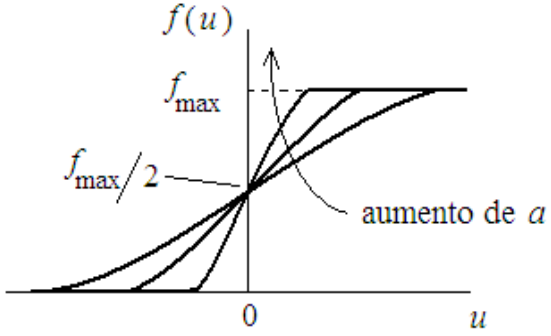
Piecewise linear:

$$S = f(u) = \begin{cases} f_{max} \text{ se } u \geq u_{max} \\ \alpha u + \beta \text{ se } u_{min} < u < u_{max} \\ 0 \text{ se } u \leq u_{min} \end{cases}$$



Sigmoid
(e.g. logistic):

$$S = f(u) = \frac{f_{max}}{1 + \exp(-au)}$$



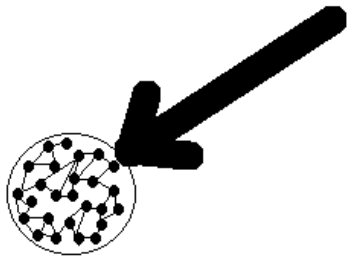
Comments

- Firing rate models are among the earliest forms of neuron modeling (late 1930s)
- They are the default neuron model used by Artificial Neural Networks (ANNs)
- In brain modeling, firing rate models are supposed to mimic not single cells but the "average" firing behavior of **cell populations**

Population rate model

- Suppose a population of neurons so close together that they can be considered as 'equivalent', i.e. they have similar properties and connectivity and receive the same input. Due to noise, which is assumed to be independent for each neuron, their response to the input can be different.
- The firing rate, or activity $A(t)$, of the population is given by

$$A(t) = \lim_{\Delta t \to 0} \lim_{N \to \infty} \frac{1}{\Delta t} \frac{n_{\text{spikes}}\left(t; t + \Delta t\right)}{N}$$



where n_{spikes} is the number of spikes of the population in the short time Δt

- Assume there are many groups of neurons. Each group *i* contains a large number of neurons and is described by its activity $A_i(t)$.
- The interaction between the different groups can be modeled by

$$A_j = f\left(\sum_i J_{ji} A_i\right)$$

where A_j is the population activity of group *j* which receives input from other groups *i*

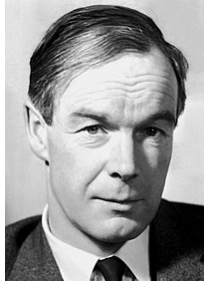
- In this equation, J_{ij} are no longer the weights of synapses between two neurons but an effective interaction strength between two groups of neurons.

Model dimension

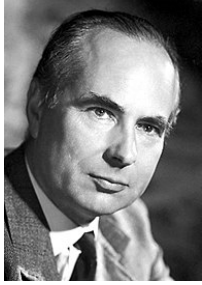
- The dimension of a model is the number of **variables** used by the model: 1, 2, 3, 4, etc
- In general, the higher the number of dimensions of a model, the more difficult to **understand** its behavior
- Each variable has an equation associated to it, so high dimensional models are more **computationally expensive**

Criteria for biological faithfulness

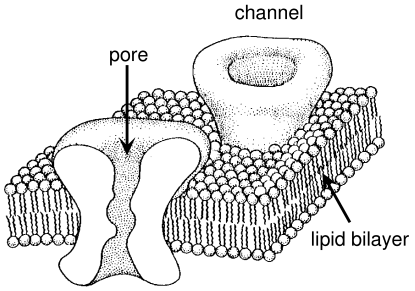
- Explicitness: model variables can be mapped to measured quantities;
- Number of details included: dendritic morphologies, ionic channel types, inhomogeneities in ion channel distributions, intracellular and biochemical mechanisms (calcium buffering, diffusion, second messengers pathways), extracellular potential
- How is a spike generated? By hand or naturally from the equations



Hodgkin-Huxley model

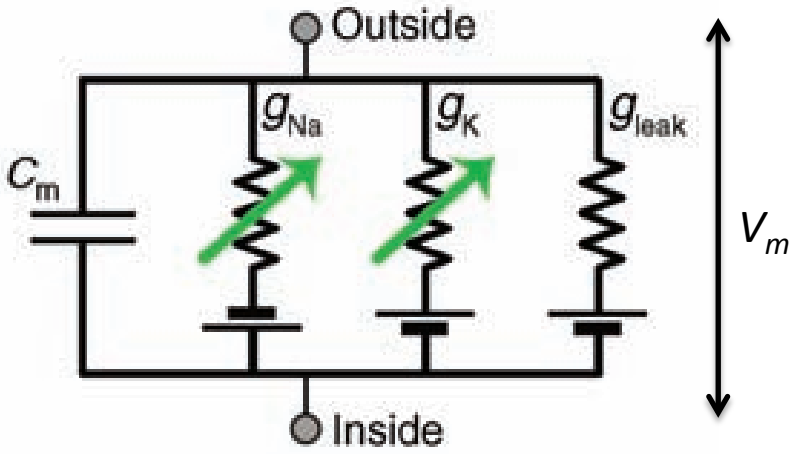


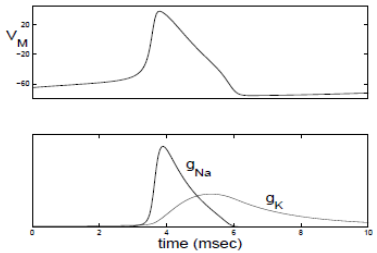
- 4D, single compartment, explicit (based on ionic conductances), spikes naturally generated

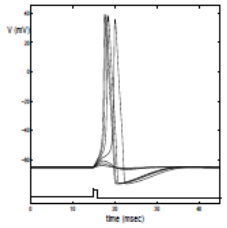


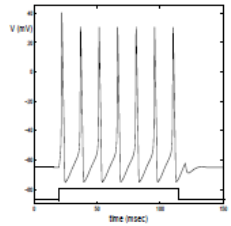
$$C\dot{V} = I - \overbrace{\bar{g}_{K+} n^4 (V - E_{K+})}^{I_{K+}} - \overbrace{\bar{g}_{Na+} m^3 h (V - E_{Na+})}^{I_{Na+}} - \overbrace{g_L (V - E_L)}^{I_L}$$

$$\dot{n} = (n_\infty(V) - n)/\tau_n(V)$$
$$\dot{m} = (m_\infty(V) - m)/\tau_m(V)$$
$$\dot{h} = (h_\infty(V) - h)/\tau_h(V)$$





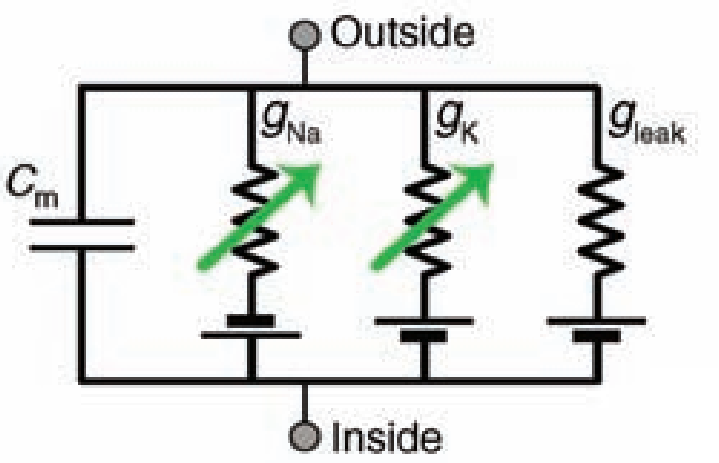




Hodgkin-Huxley (1949) demonstrated that:

- At rest, the conductance of the membrane of a squid axon to K^+ is 25 times higher than its conductance to Na^+: $G_K >> G_{Na}$;
- At the peak of an action potential, the membrane conductance to Na^+ is 20 times higher than its conductance to K^+: $G_K >> G_{na;}$
- During the after-hyperpolarization period, the membrane conductance to Na^+ is very low and its conductance to K^+ is larger than at rest: $G_{Na} \approx 0$ and $G_K > G_{K\_rest}$

HH explained the action potential



$$C\frac{dV}{dt} = -G_K\left(V - E_K\right) - G_N a\left(V - E_N a\right) - G_L\left(V - E_L\right) + I_{inj}$$

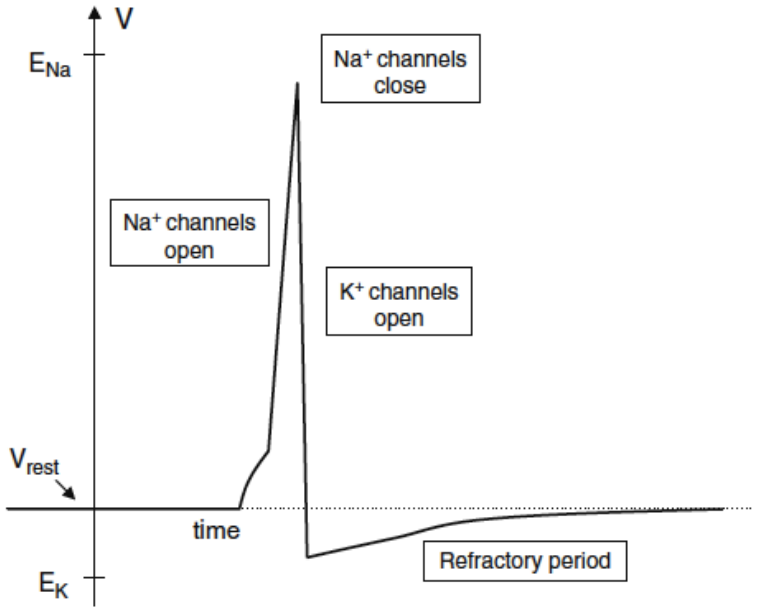
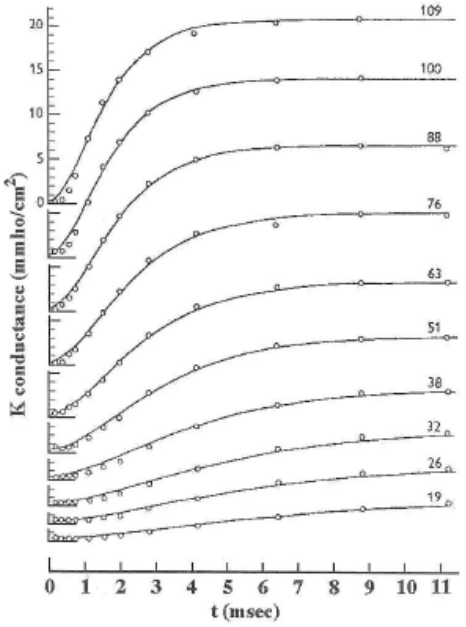


Fig. 1.7 The action potential. During the upstroke, Na^+ channels open and the membrane potential approaches the Na^+ Nernst potential. During the downstroke, Na^+ channels are closed, K^+ channels are open, and the membrane potential approaches the K^+ Nernst potential

Hodgkin-Huxley model

Mathematical fitting of experimental conductances (measured during voltage clamp conditions)

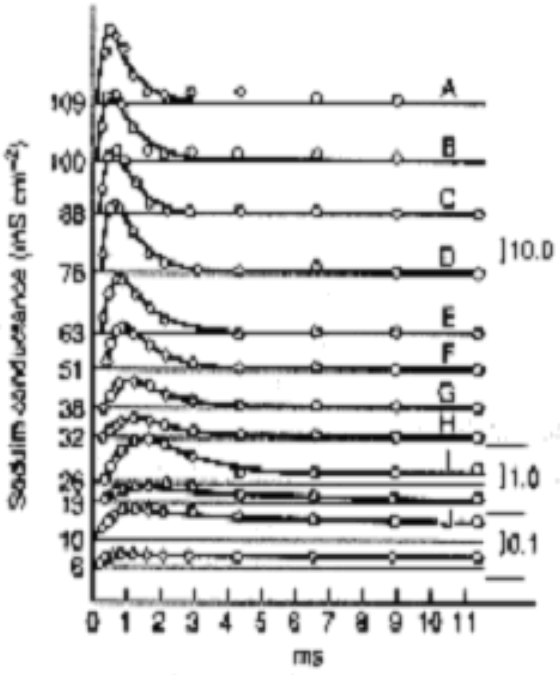


$$I_X = G_X p\,(V - E_X)$$

- G_X: maximal conductance;
- p: fraction of G_X attained at a given moment;
- E_X: Nernst potential if ion X.

$$p = m^r h^s$$

- m: activation variable (grows from 0 to 1 with increase of V);
- h: inactivation variable (decreases from 1 to 0 with increase of V)



K^+ conductance: persistent

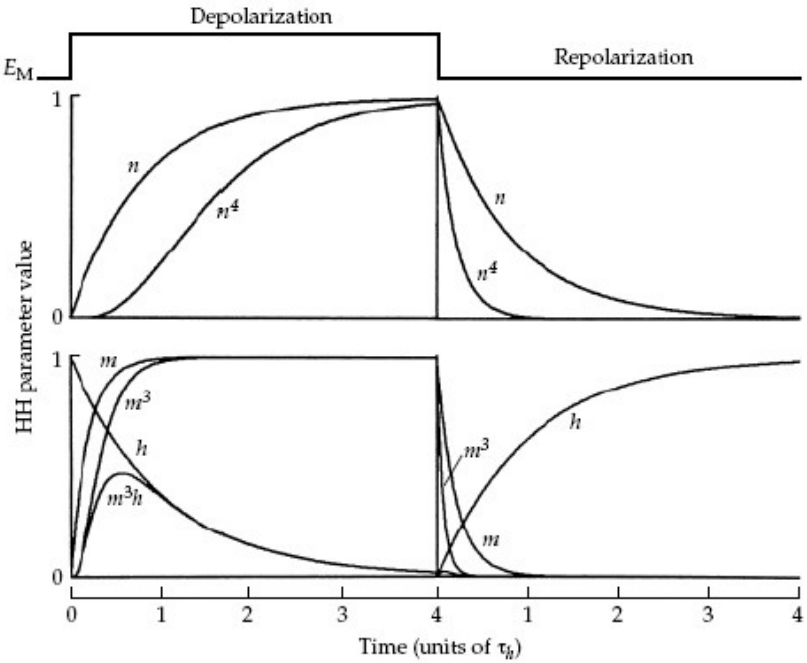
$r = 4$, $s = 0$

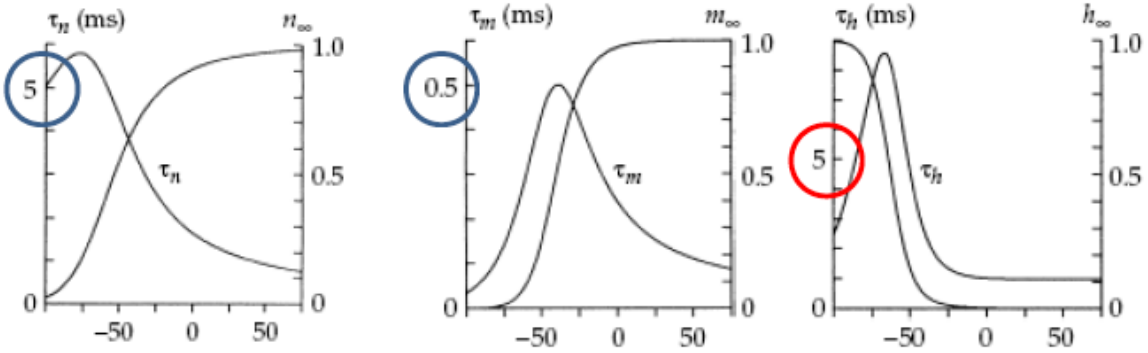
Do not inactivate

Na^+ conductance: transient

$r = 3$, $s = 1$

Inactivate

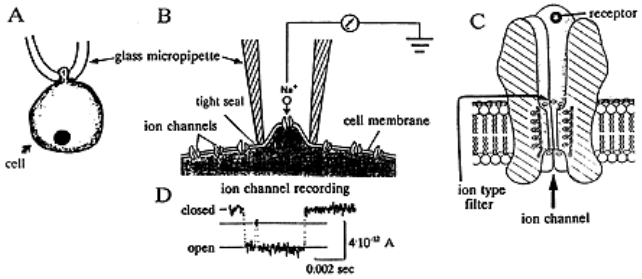

Depolarization
Repolarization
E_M
1
0
n
n^4
n
n^4
HH parameter value
m
m^3
h
m^3h
m^3
h
m
0 1 2 3 4 1 2 3 4
Time (units of τ_h)

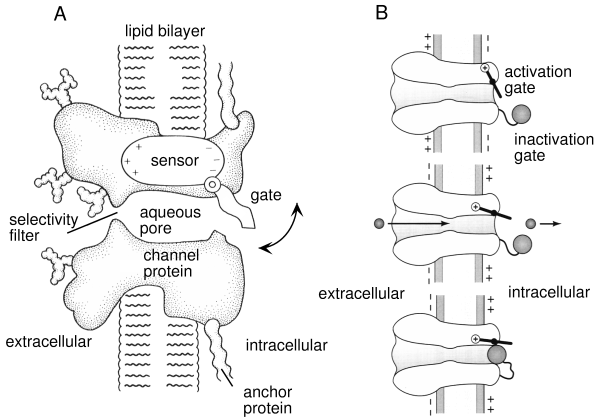

τ_n (ms)
n_∞
5
τ_n
1.0
0.5
0
−50 0 50
τ_m (ms)
m_∞
0.5
τ_m
τ_h (ms)
h_∞
5
τ_h

Voltage (mV)

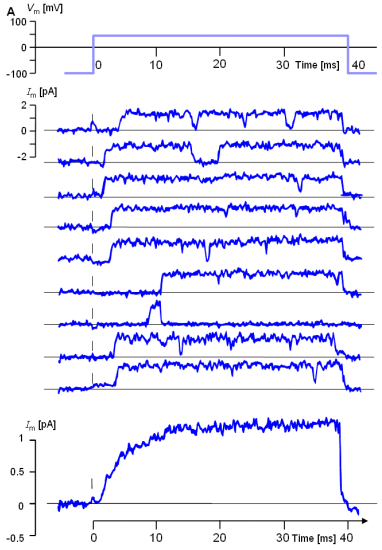
Hodgkin-Huxley formalism

Opening and closing of Individual channels is a stochastic process

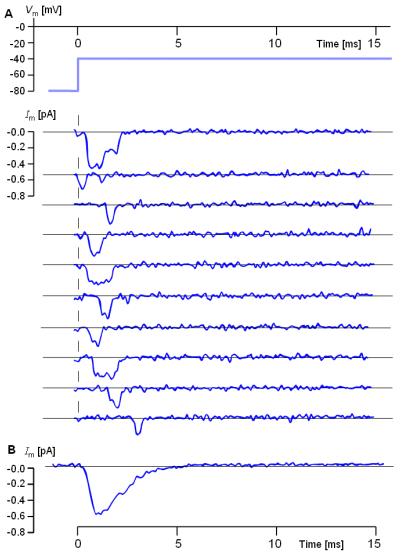




K^+ channel



Na^+ channel



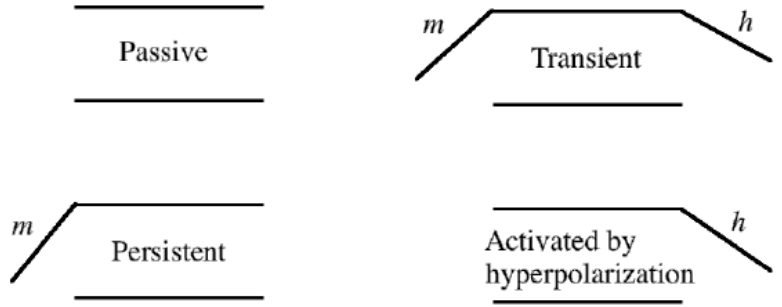
Ensemble average (deterministic)

$$I = \bar{g} \cdot p \cdot (V - E) \qquad p = \text{probability of open channel}$$

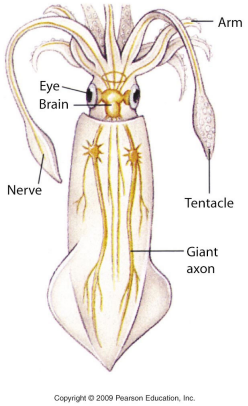
$$p = m^a h^b$$

m = fraction of open activation gates

h = fraction of open inactivation gates



Comment



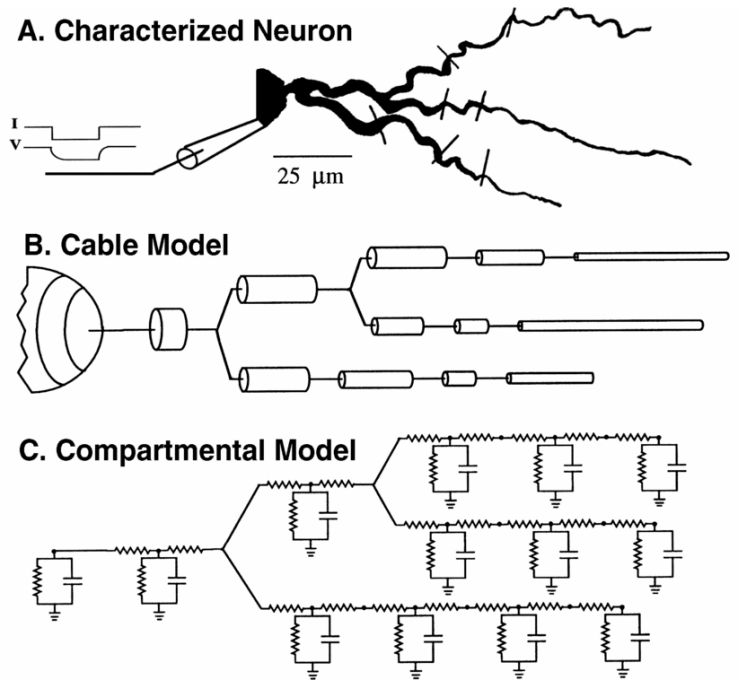
- Hodgkin and Huxley (1952) developed their model to describe action potential generation in the **squid giant axon**
- It is hugely different from mammalian cortical neurons
- But ionic currents in cortical neurons can be described in a similar way, hence “Hodgkin-Huxley-type models”

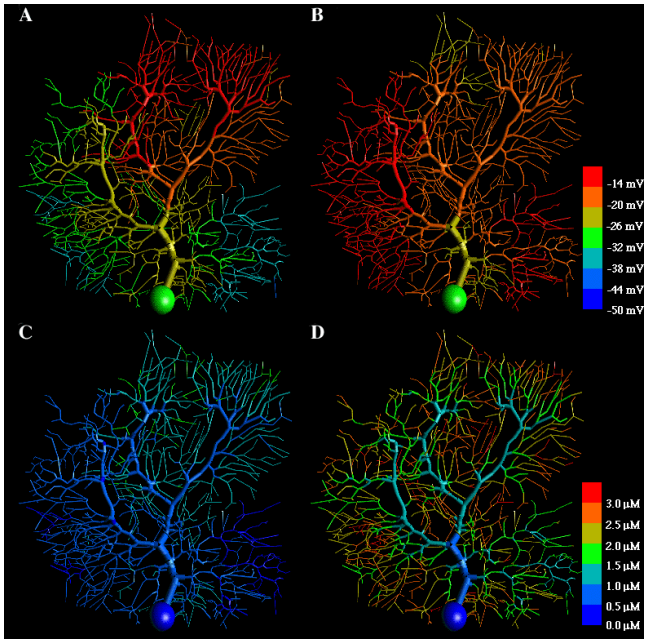
The zoo of ion channels

- **Fast Na** ($I_{Na)}$): transient; action potential generation
- **Slow Na** (I_{NaP}): slowly inactivating (persistent); keeps neurons depolarized (facilitating bursts)
- **Delayed rectifier K** (I_K): persistent; action potential termination
- **A current** (I_A): transient K current; creates spike delays
- **M current** (I_M): slow persistent K current; causes spike rate adaptation
- **Inward rectifier** (I_{kir}): activated by hyperpolarization; keeps resting potential near E_K
- **Ca dependent K channels** (I_C or I_{AHP}): persistent; depend on $[Ca^{2+}]$; responsible for afterhyperpolarizations (AHPs), spike frequency adaptation and bursting
- **Calcium channels** (I_{CaT} and I_{CaL}): transient and persistent; responsible for bursts and subthreshold voltage oscillations
- **h current** (I_h): slow; activated by hyperpolarization; mixture of Na and K ions; rhythmic firing and slow repolarization after hyperpolarizing

Detailed compartmental models

- D = $q(m+1)$; q = number of compartments; m = number of conductances
- Used mostly for **single-neuron** modeling (but the advent of fast computers is changing that)





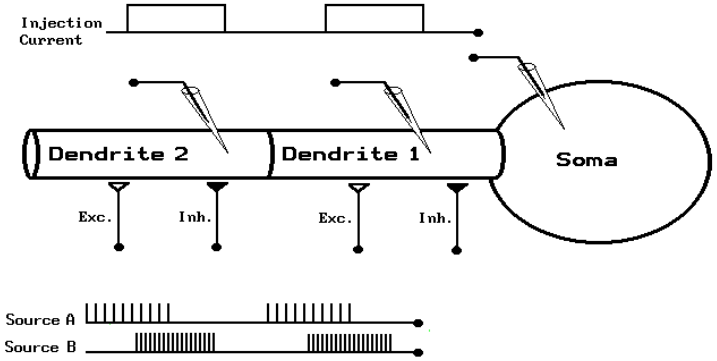
Model of a cerebellar Purkinje cell (De Schutter and Bower, 1994): 4550 compartments.

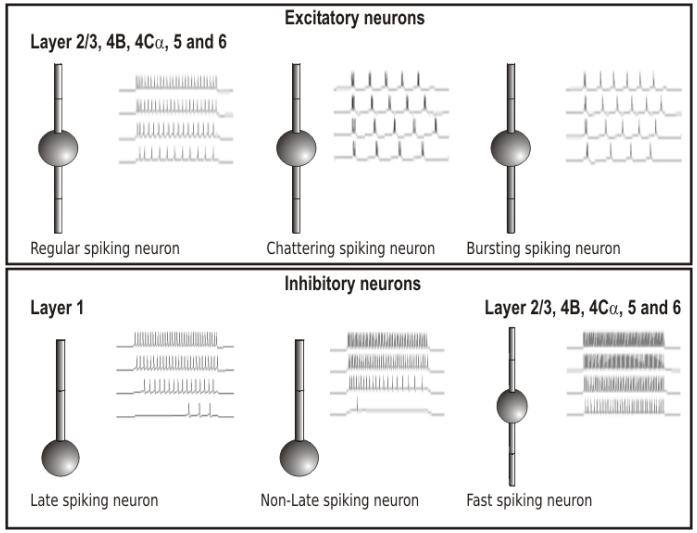
Comment

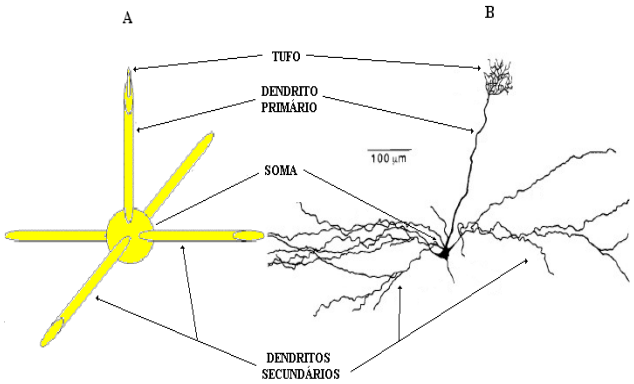
- The addition of more and more compartments to a neuron model seems to be a good strategy to get closer to the "real thing".
- However, increased complexity not necessarily always lead to better models:
  - Each new compartment requires the modeler to decide which conductances to put in it and with what parameters, and there are few cases in which these are known (so the modeler has to "guess").
  - As the number of parameters increase so does the number of parameter combinations that produce similar behavior (how unique is a model?).

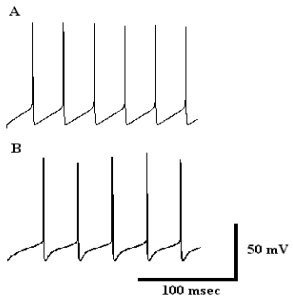
Reduced compartmental models

- Few compartments (e.g. ball-and-stick model)
- Used in “realistic” network models





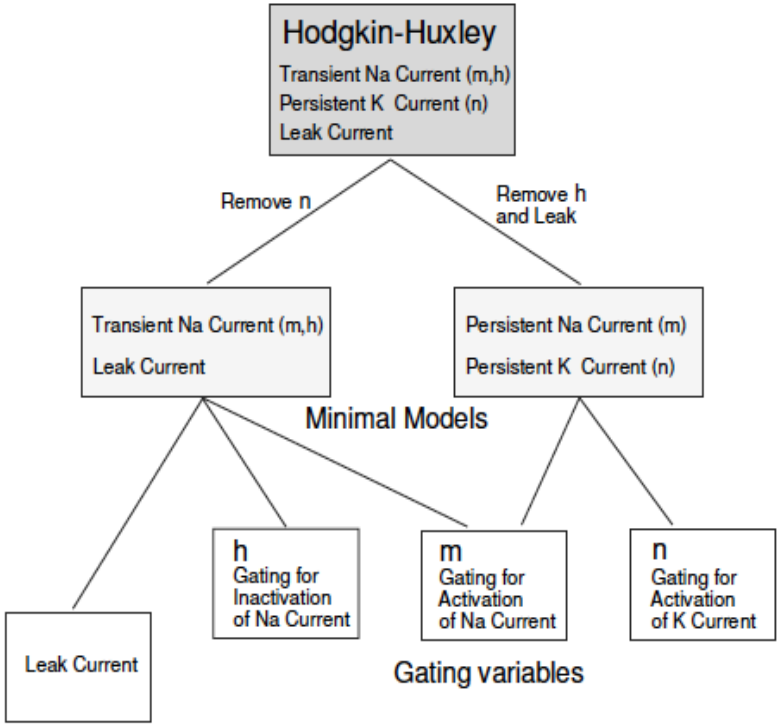




Model

Real

Reduced HH models



Izhikevich (2007)

- Single compartment models with only 2 or 3 variables (one being *V*)
- Can replicate a number of properties of the HH model, including the genesis of an **action potential**
- Can be analyzed in the phase plane using **dynamical systems** tools: equilibrium points, limit cycles, bifurcations

Example of reduced HH model:
V and *n* (fast and slow variables)

$$C_m \frac{dV}{dt} = -\bar{g}_K n^4 (V - E_K) - \bar{g}_{Na} m_\infty^3(V)(0{,}8 - n)(V - E_{Na}) - \bar{g}_V (V - E_V) + J_{inj}$$

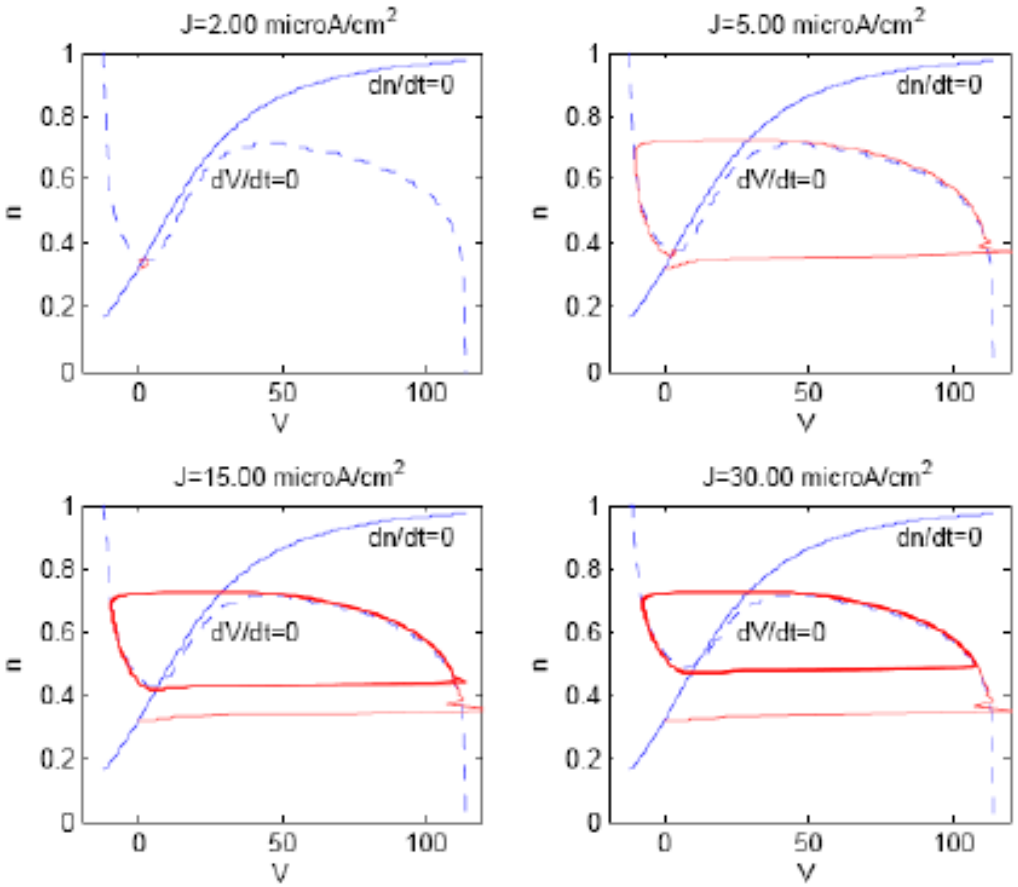
$$\tau_n \frac{dn}{dt} = n_\infty - n.$$

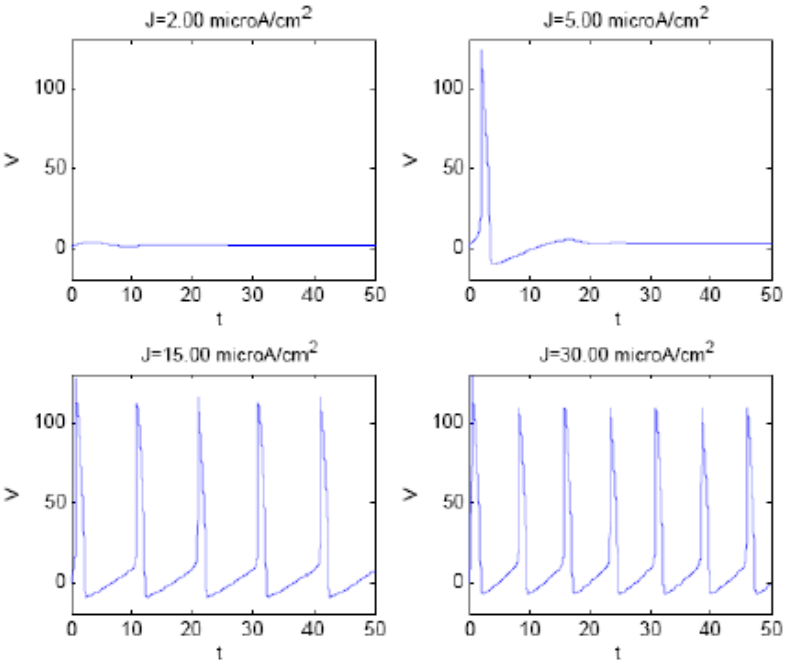
Nullclines: dV/dt = 0; dn/dt = 0

V, m: fast variables
n, h: slow variables

$m(t) \rightarrow m_\infty$
$n(t) = 0.84 - h(t)$

Model with 2 variables:
V(t) and n(t)





Fitzhugh-Nagumo Model

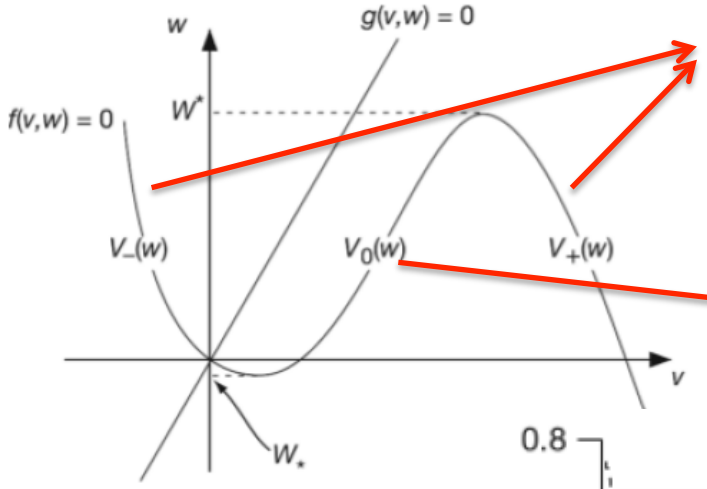
2-D system that has the same qualitative characteristics of the fast-slow phase plane

Cubic

$$\frac{dv}{dt} = f(v) - w + I_{\text{app}}$$
$$\frac{dw}{dt} = \epsilon(v - \gamma w).$$

v = voltage;

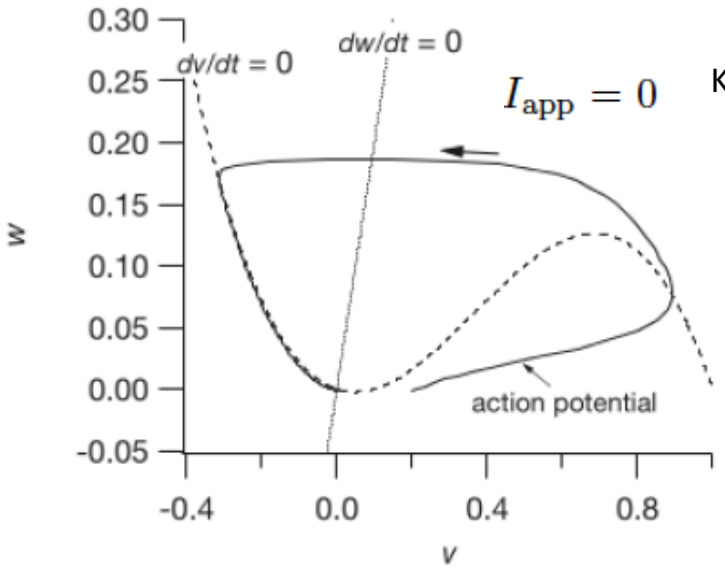
w = recovery variable



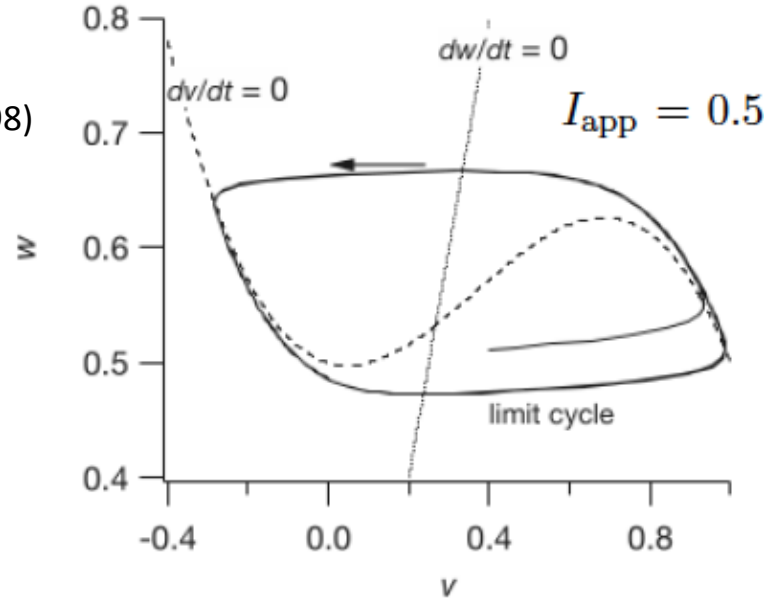
Stable branches

Unstable branch

Keener & Sneyd (1998)



System has a stable resting state and is excitable



The resting state is unstable and there is a periodic orbit

Simple spiking neuron models

- 1D or 2D, non-HH type models (not explicit)
- Emphasis on neuronal response (spike trains)
- Spikes generated by hand
- Examples:
  - Leaky integrate-and-fire (LIF) model (Lapicque 1907)
  - Non-linear LIF models (quadratic, exponential)
  - Izhikevich model
  - Adaptive exponential integrate-and-fire (AdEx) model

The LIF model

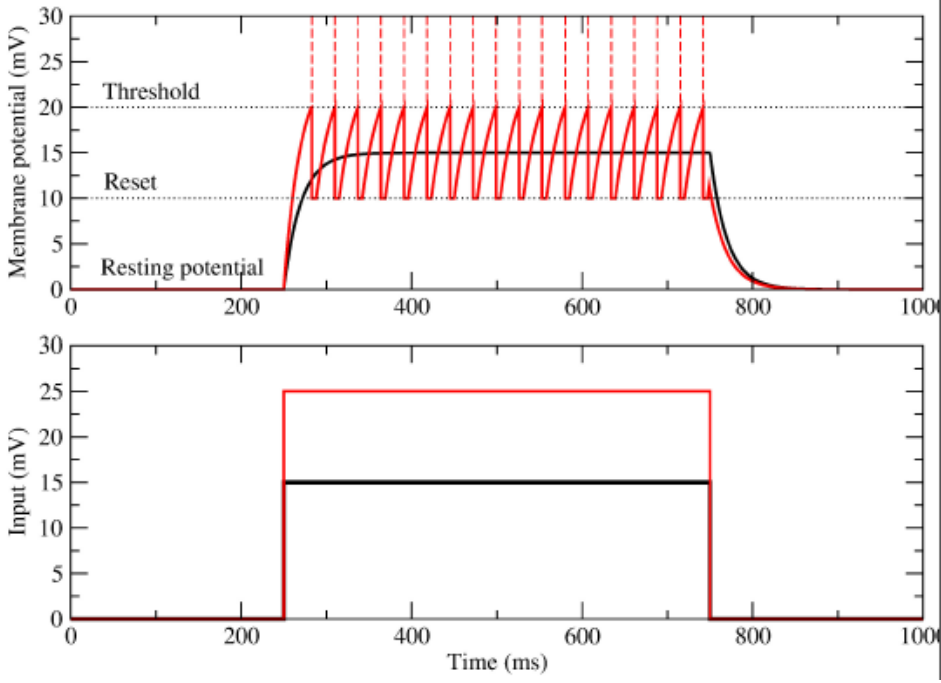
$$I_{\mathrm{th}} = \frac{V_{\mathrm{th}} - V_{\mathrm{rest}}}{R}$$

- Subthreshold dynamics ($V < V_{\mathrm{th}}$):

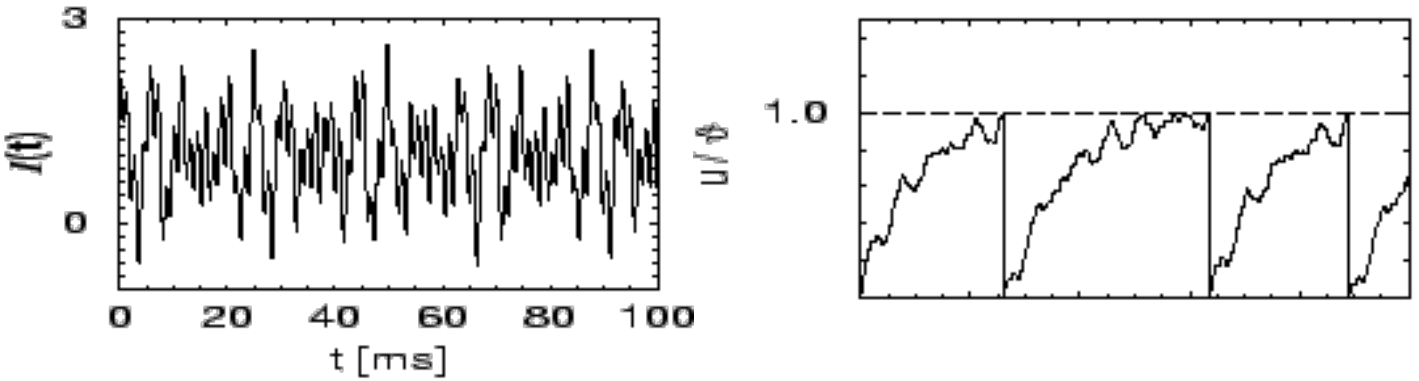
$$\tau \frac{dV}{dt} = -\left(V - V_{\mathrm{rest}}\right) + R \cdot I$$

- Spike emitted (by hand) at $t = t_{sp}$ when $V = V_{\mathrm{th}}$
- Then voltage reset to $V = V_{\mathrm{reset}}$
- (Optional) refractory period:

$$V(t) = V_{\mathrm{reset}} \text{ for } t_{sp} < t < t_{sp} + \tau_{\mathrm{ref}}$$



Response to noisy input $I(t)$



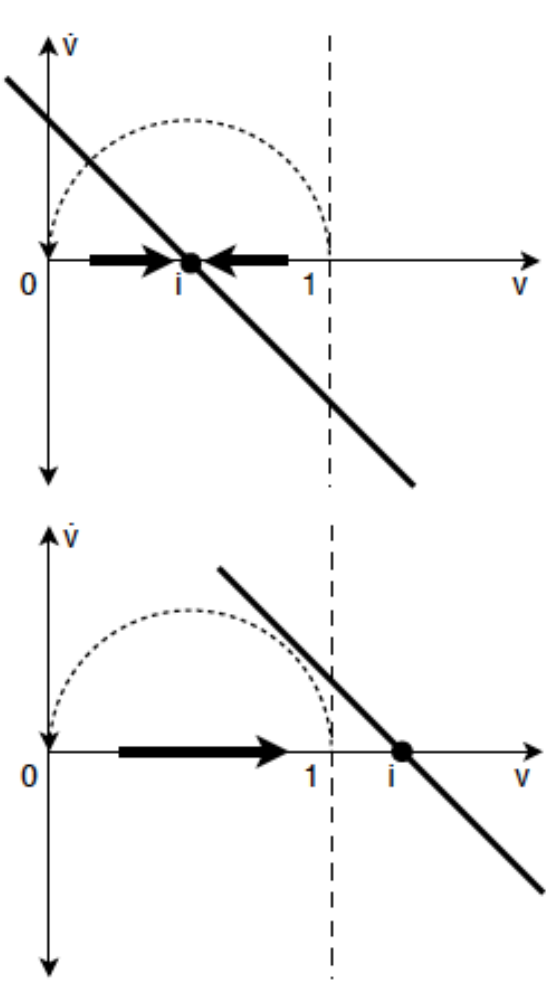
Dynamics of the LIF model

- Rescaling $\tau \frac{dV}{dt} = -(V - V_{\text{rest}}) + R \cdot I$:

$$v \equiv \frac{V - V_{\text{rest}}}{V_{\text{th}} - V_{\text{rest}}}; \quad i \equiv \frac{RI}{V_{\text{th}} - V_{\text{rest}}}; \quad t' \equiv t / \tau \Rightarrow$$

$$\Rightarrow \frac{dv}{dt'} = -v(t') + i$$

  with threshold at $v = 1$
- Stable fixed point at $v = i$
- For $i < 1$ the membrane potential goes to the fixed point and stays there (no spikes)
- For $i > 1$ the membrane potential gets to the threshold and a spike occurs
- After the spike the membrane potential is reset to 0 and the process starts again
- The neuron keeps firing regularly while the above threshold stimulus is on



Non-linear I&F models

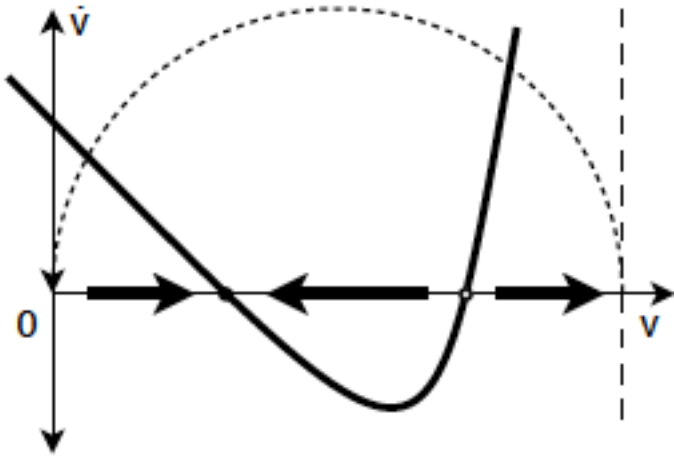
- Extensions of the LIF model given by

$$\tau \frac{dv}{dt} = \phi(v) + i$$

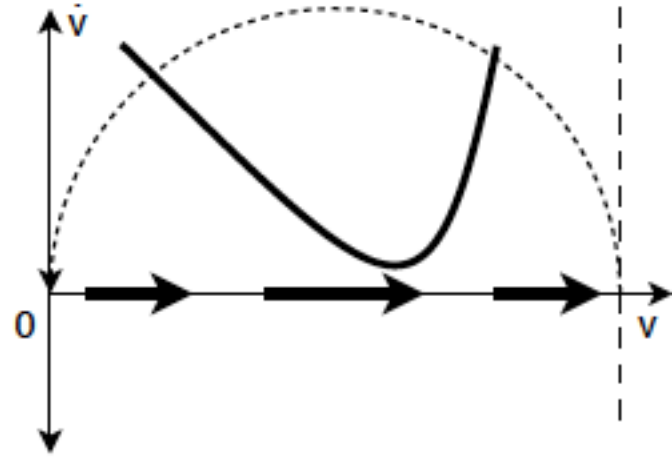
with

$$\phi(v) = a(v-b)^2 \quad \text{(quadratic IF model, QIF)}$$

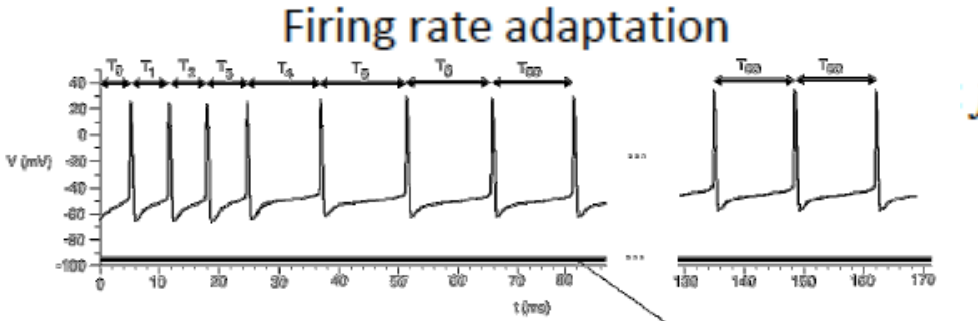
$$\phi(v) = -v + ae^{v-b} \quad \text{(exponential IF model, EIF)}$$



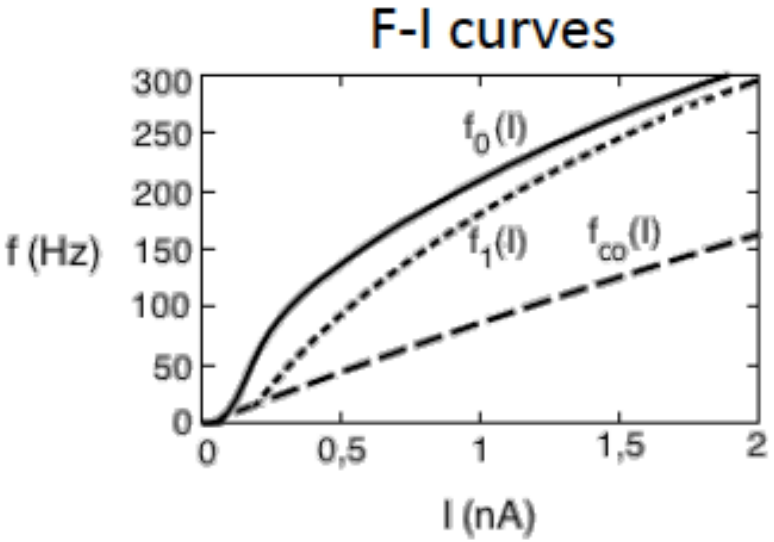
- The black dot in the top graph is a stable fixed point and the white dot is an unstable fixed point
- The voltage value of the white dot is the critical voltage for spike initiation by a short current pulse
- The bottom graph shows the case for a constant super-threshold current: the result is repetitive firing
- Notice that a strong inhibitory current can push the curve below the d*v*/d*t* = 0 line and disrupt the repetitive firing

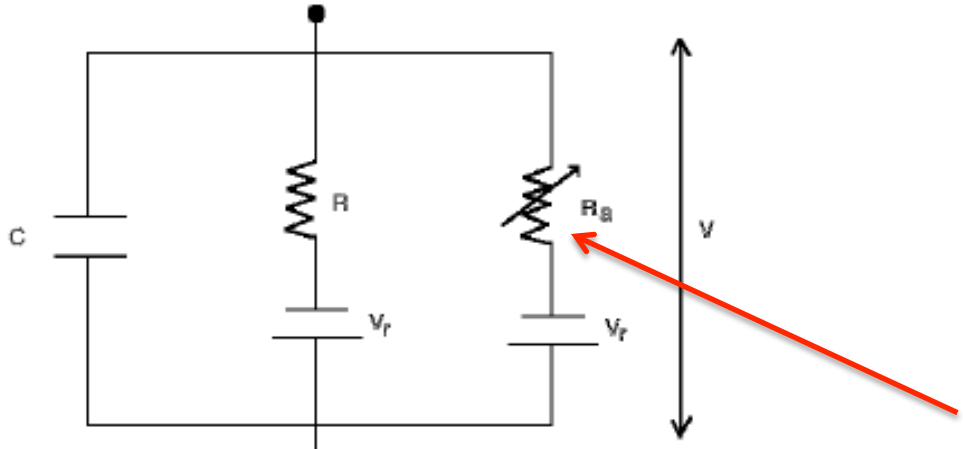


LIF with adaptive variable



$$f_0 = 1/T_0, f_1 = 1/T_1, f_2 = 1/T_2, \ldots, f_\infty = 1/T_\infty$$





$$C\frac{dV}{dt} + \frac{(V - V_r)}{R} + g_a(V - V_r) = I$$

$$\tau \frac{dV}{dt} = -(V - V_r)(1 + Rg_a) + RI$$

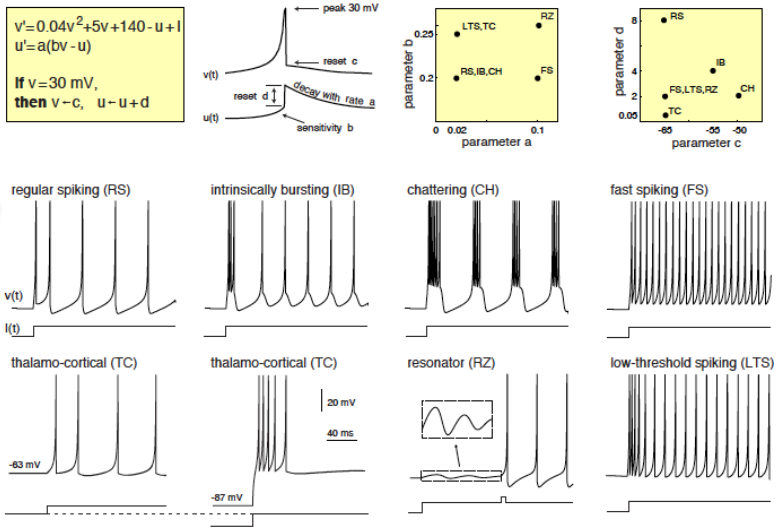
$$\tau_a \frac{dg_a}{dt} = -g_a$$

Adaptation conductance (recovery variable): incremented after each spike to provide negative feedback on *V* and drive it towards V_r thus making it more difficult for *V* to reach threshold.

Izhikevich and AdEx models

www.izhikevich.com

- Nonlinear I&F models with a second variable (recovery variable)
- Can replicate many neuronal **spiking patterns**
- Proposed by Izhikevich in 2003 and Brette and Gerstner in 2005

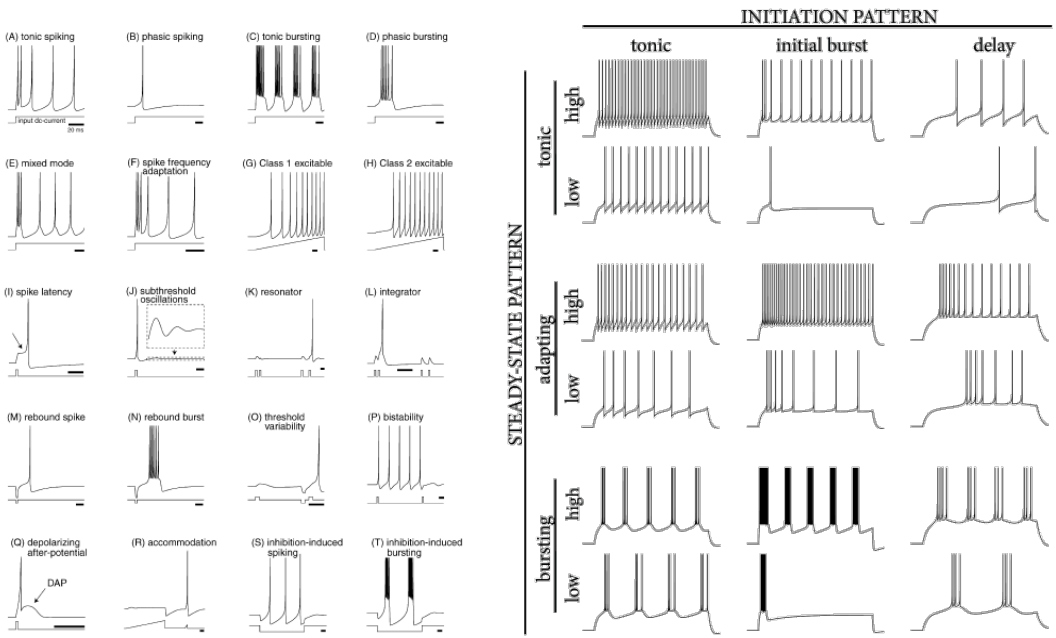


$$C\frac{dV}{dt} = -g_L(V - E_L) + g_L\Delta_T \exp(\frac{V - V_T}{\Delta_T}) - w + I$$

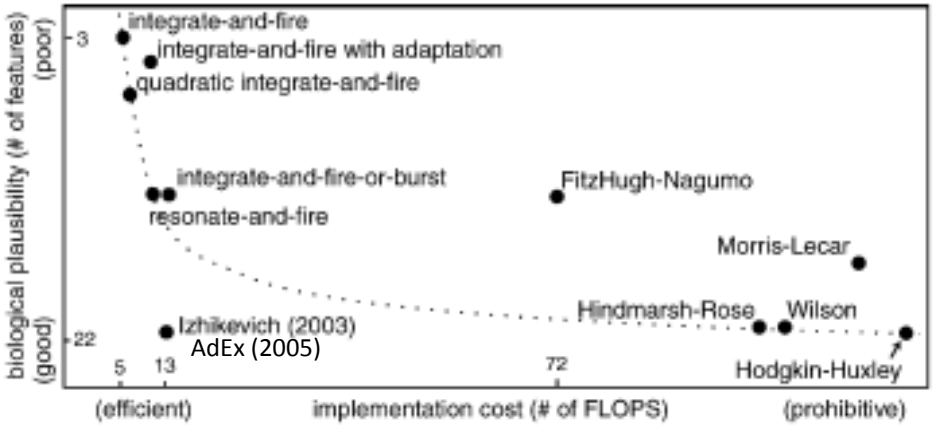
$$\tau_w \frac{dw}{dt} = a(V - E_L) - w$$

If $V = V_{peak}$ (e.g. 0 mV or +20 mV),

$$V \rightarrow V_r \qquad w \rightarrow w + b$$



https://neuronaldynamics.epfl.ch/online/Ch6.S1.html



Models	biophysically meaningful	tonic spiking	phasic spiking	tonic bursting	phasic bursting	mixed mode	spike frequency adaptation	class 1 excitable	class 2 excitable	spike latency	subthreshold oscillations	resonator	integrator	rebound spike	rebound burst	threshold variability	bistability	DAP	accommodation	inhibition-induced spiking	inhibition-induced bursting	chaos	# of FLOPS
integrate-and-fire	-	+	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	5
integrate-and-fire with adapt.	-	+	-	-	-	-	+	+	-	-	-	-	+	-	-	-	-	+	-	-	-	-	10
integrate-and-fire-or-burst	-	+	+		+	-	+	+	-	-	-	-	+	+	+	-	+	+	-	-	-		13
resonate-and-fire	-	+	+	-	-	-	-	+	+	-	+	+	+	+	-	-	+	+	+	-	-	+	10
quadratic integrate-and-fire	-	+	-	-	-	-	-	+	-	+	-	-	+	-	-	+	+	-	-	-	-	-	7
Izhikevich (2003)	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	13
FitzHugh-Nagumo	-	+	+	-		-	-	+	-	+	+	+	-	+	-	+	+	-	+	+	-	-	72
Hindmarsh-Rose	-	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	120
Morris-Lecar	+	+	+	-		-	-	+	+	+	+	+	+	+		+	+	-	+	+	-	-	600
Wilson	-	+	+	+			+	+	+	+	+	+	+	+	+	+		+	+				180
Hodgkin-Huxley	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	1200

Neuron models: detailed vs. simplified

- Conductance-based (HH) and compartmental models are useful to study single neurons:
  - Propagation of membrane potentials along the dendritic tree
  - Pharmacological manipulations
  - Functional properties of single neurons
- But to model neural networks it is necessary to know/ estimate parameters for **all neurons**, a phenomenal task
- IF model and its variants are too simple to be used as biophysical neuron models
- But are useful for the construction of large-scale network models and study:
  - Spiking activity patterns in networks
  - Functional properties of networks or network parts

Part 3

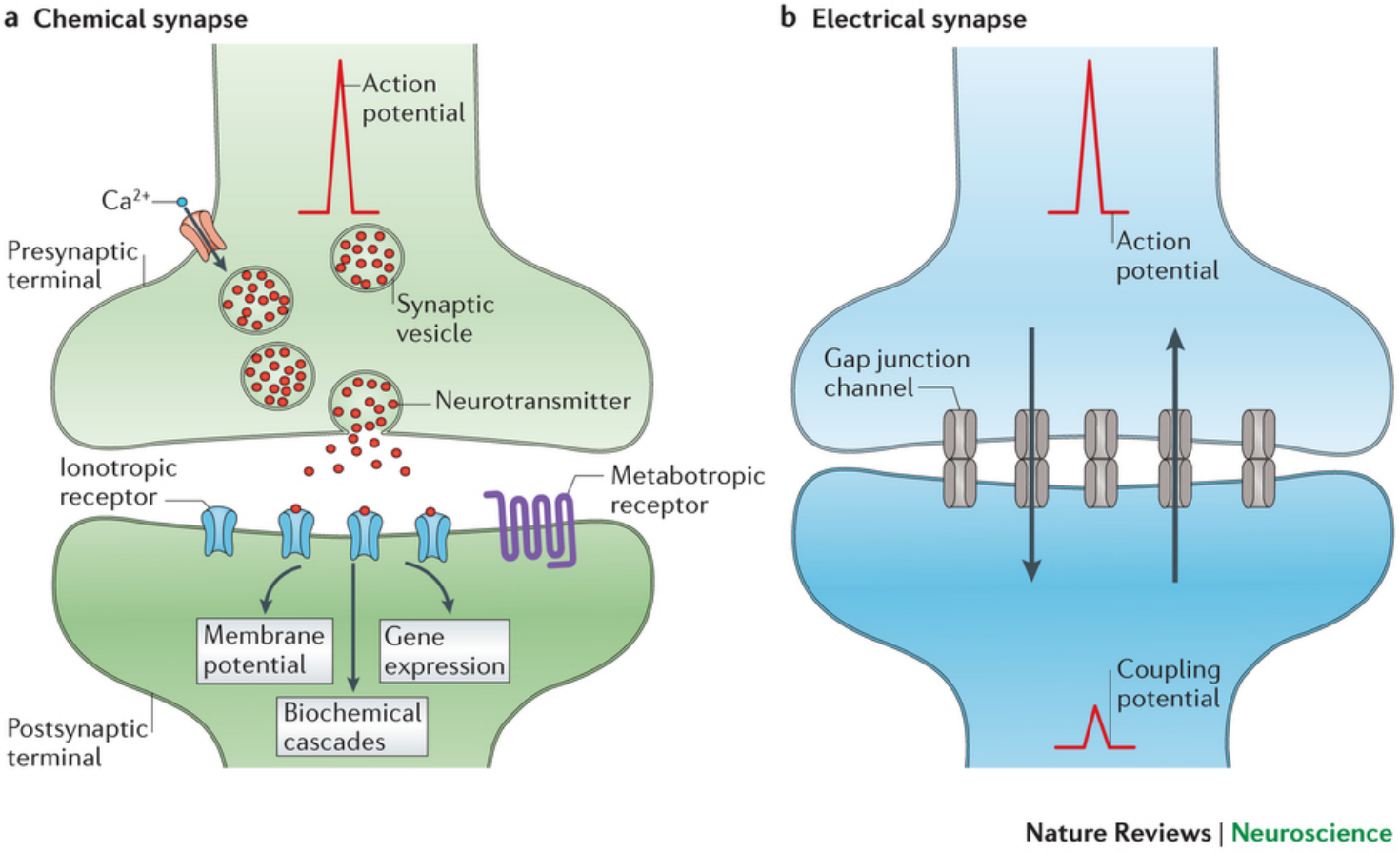
Synaptic models

Purpose of synaptic modeling

- To capture the following facts:

1. Some neurons have stronger and more lasting influences over a given neuron than others
2. Some of these influences are excitatory (increase the likelihood of spike emission) while some are inhibitory (decrease this likelihood)
3. The strength of the influence of a neuron over another one changes over time as a function of the activities of both neurons (synaptic plasticity)

Types of synapses



Pereda, 2014

Types of synapses

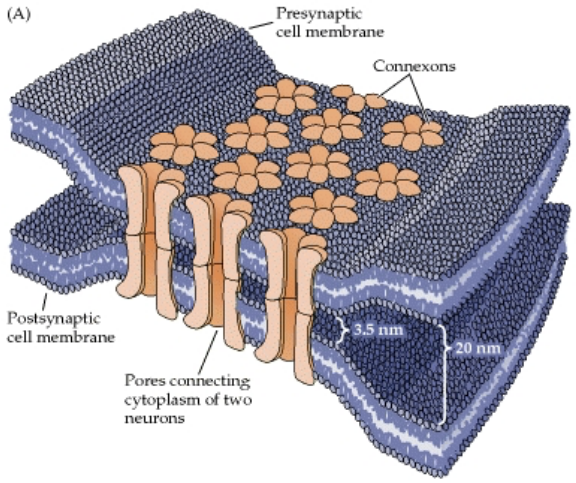
Electrical

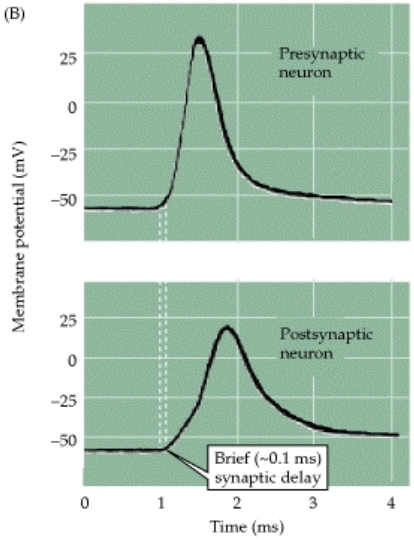
- 2 neurons linked together by gap junctions
- Rapid communication
- Bidirectional communication
- Excitation/inhibition at the same synapse
- Occur between neurons and glia

Chemical

- Signal transduction
- Excitatory or inhibitory
- Slower communication
- Unidirectional communication
- More plastic

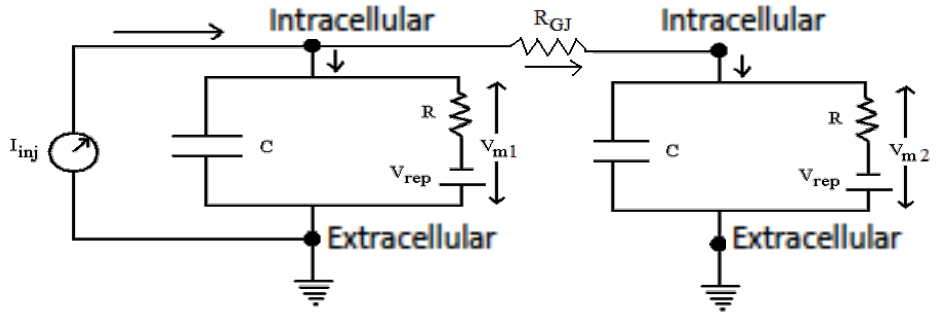
Electrical synapse





An action potential in the presynaptic neuron causes the postsynaptic neuron to be depolarized within a fraction of millisecond

Neuroscience. 2nd edition.
Purves D, Augustine GJ, Fitzpatrick D, et al., editors.
Sunderland (MA): Sinauer Associates, 2001

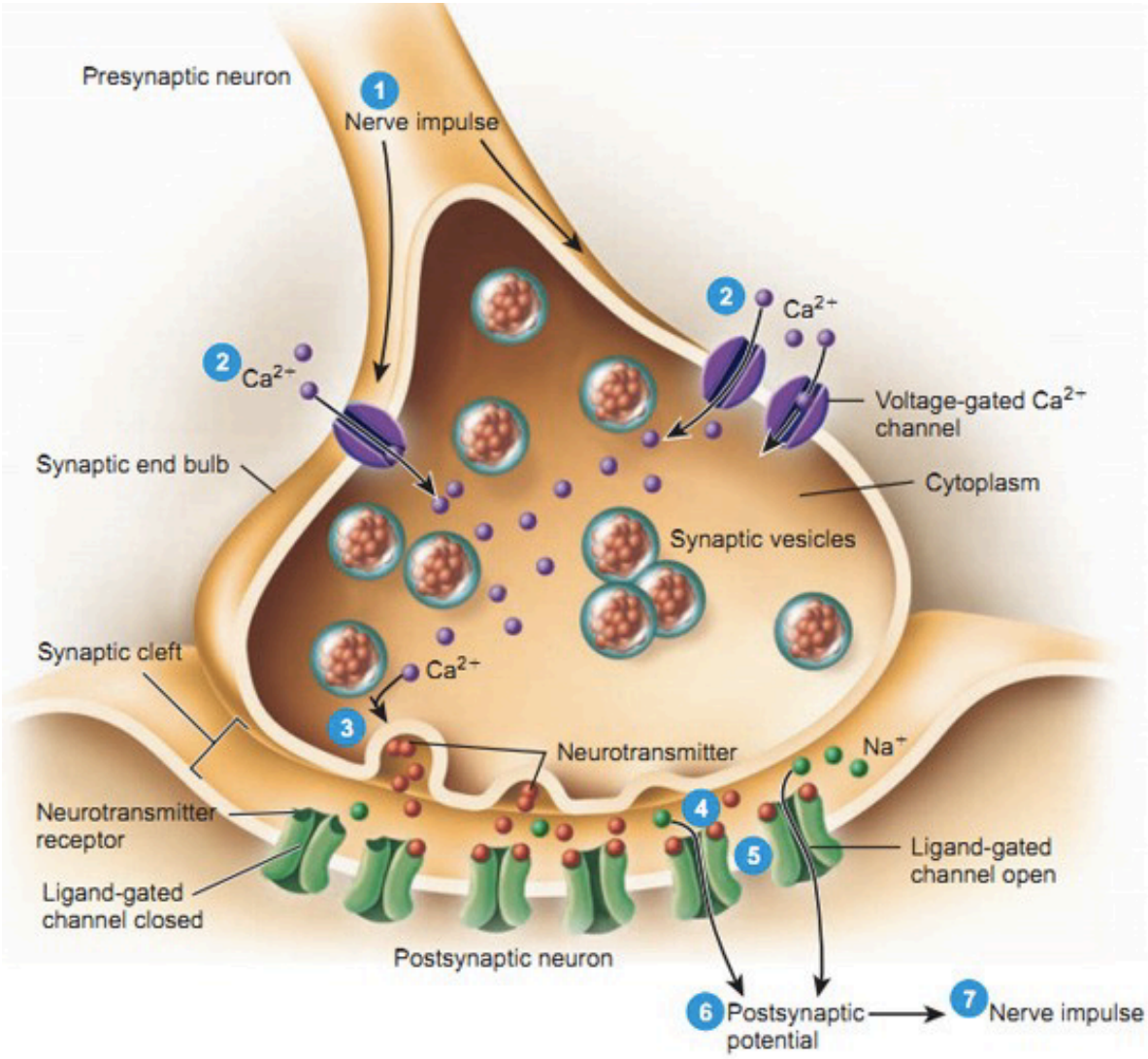


$$V_2 = kV_1$$

$$I_{GJ} = G_{GJ}\left(V_1 - V_2\right)$$

Gap junction coupling can be modeled by a single resistance connecting the 2 cells (see equivalent circuit to the left). The corresponding equations are given below the figure. The cell-cell coupling coefficient is *k* and the transjunctional current is I_{GJ}

Chemical synapse (generic steps)

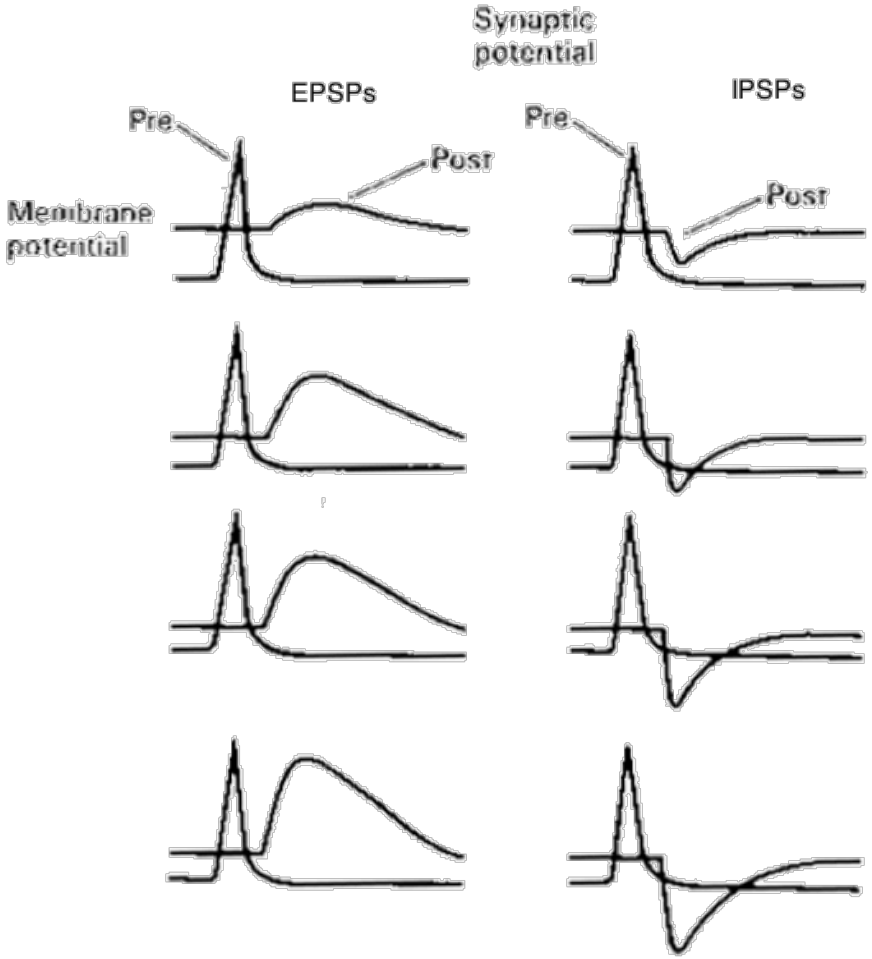


Chemical Synapses

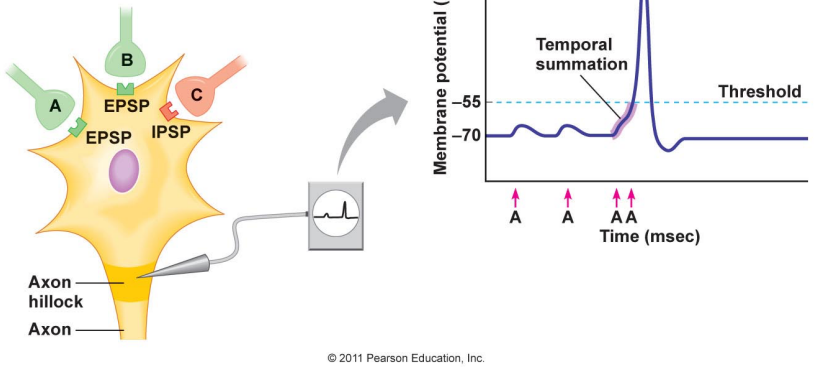
- Excitatory or inhibitory
- Ionotropic (fast) and metabotropic (slow)
- Many neurotransmitters, but the most common in the cortex are:
  - Glutamate (usually excitatory)
  - γ-aminobutyric acid (GABA) (usually inhibitory)
- Dynamics depends on receptor type:
  - Glutamate receptors: AMPA/Kainate and NMDA
  - GABA receptors: $GABA_A$ and $GABA_B$
- Short-term and long-term synaptic plasticity

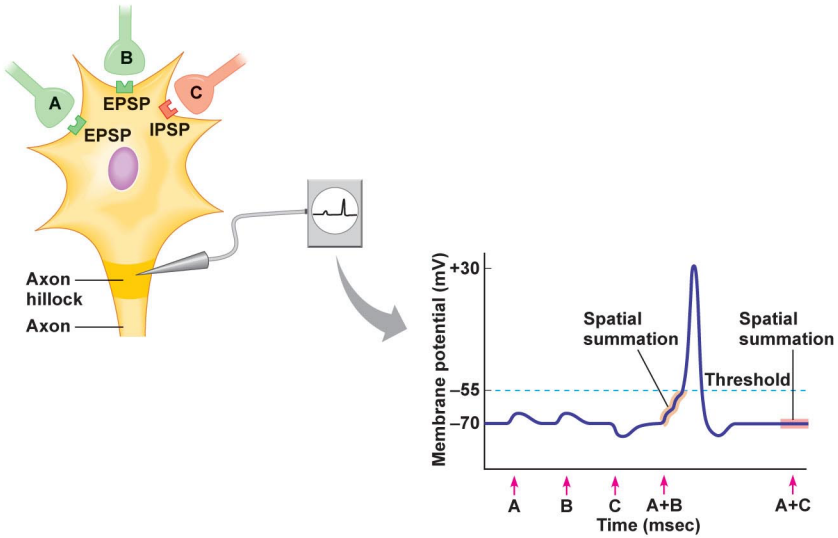
Postsynaptic potentials

- Excitatory postsynaptic potential (**EPSP**): Transient depolarization of the postsynaptic membrane by presynaptic release of neurotransmitter
- Inhibitory postsynaptic potential (**IPSP**): Transient hyperpolarization of the postsynaptic membrane by presynaptic release of neurotransmitter



Postsynaptic potentials summation

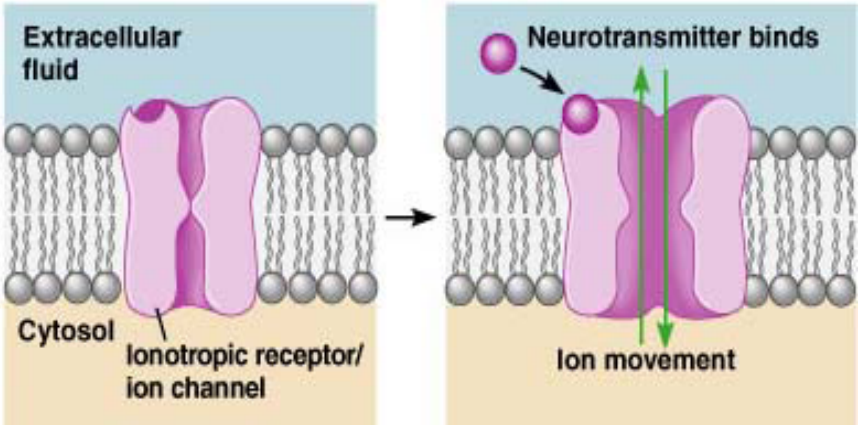




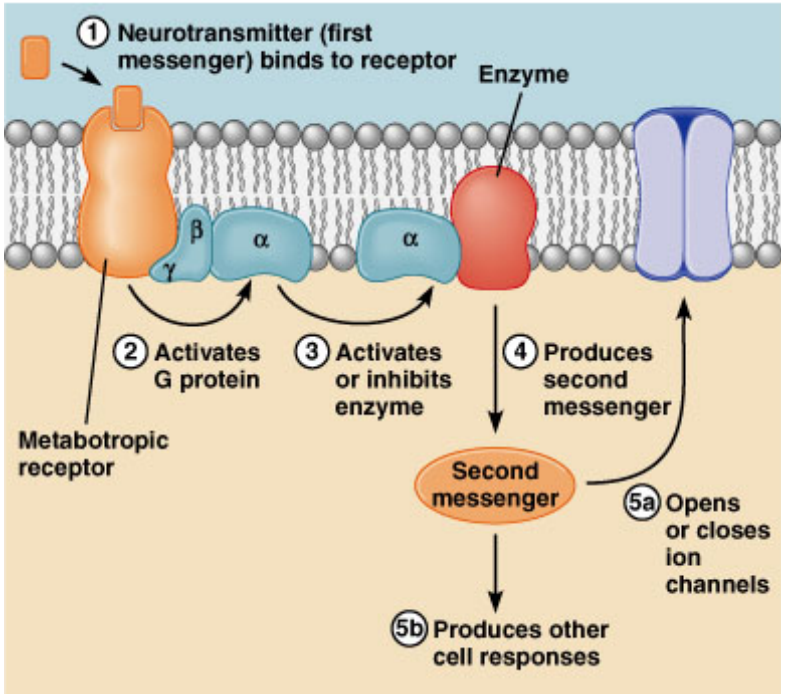
Temporal summation:
(spikes from the **same** cell arriving at successive times)

Spatial summation:
(spikes from **different** cells arriving at the same time)

Ionotropic and Metabotropic Synapes



Ionotropic: fast



Metabotropic: slow

Synaptic receptors

Glutamate

- Ionotropic
  - AMPA/Kainate: early EPSP
  - NMDA: activated when cell is already depolarized (late EPSP)

GABA

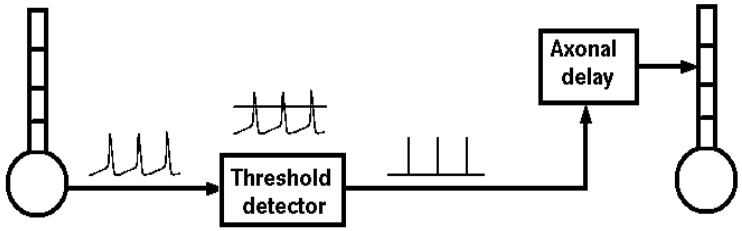
- Ionotropic
  - $GABA_A$
- Metabotropic
  - $GABA_B$

Synaptic models

- There are many models, the most common in network models assumes a **synaptic current**

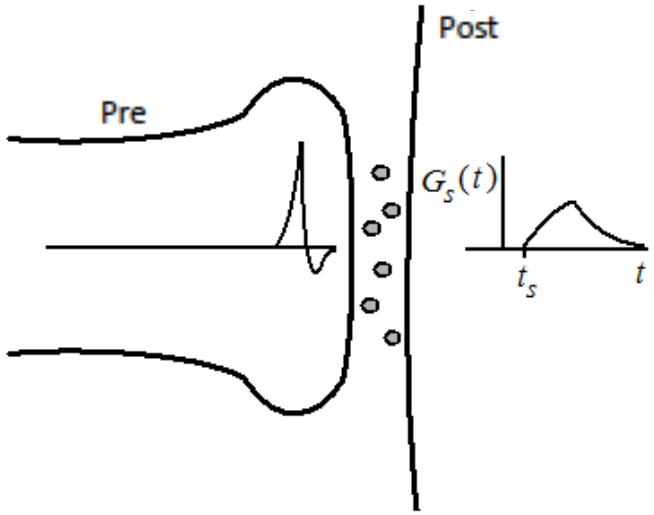
$$I_{\text{syn}} = g(t)\left(V_{\text{post}} - V_{\text{rev}}\right)$$

- V_{rev} = −75 mv (inhibitory synapses) and V_{rev} = 0 (excitatory synapses)
- $g(t)$ = synaptic conductance of **postsynaptic** cell
- Synaptic delays can also be introduced

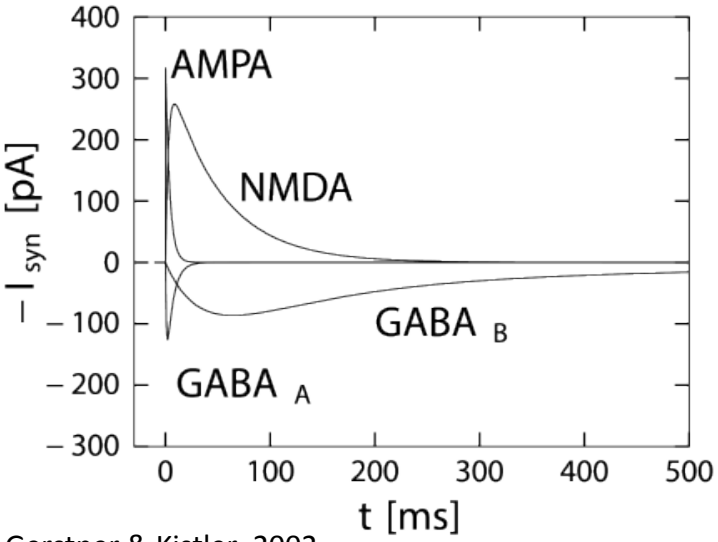


Synaptic conductance

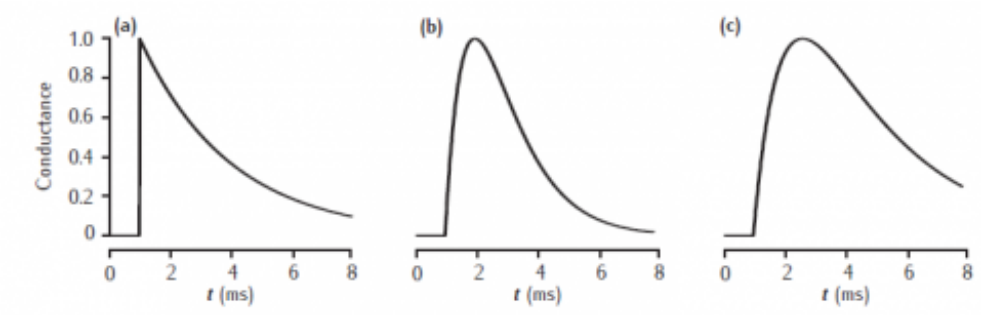
- The time course of $g(t)$ can be modeled by kinetic equations but in general **fixed** time course functions are used



Fixed functions used to model $g(t)$



Gerstner & Kistler, 2002



(a) $$g(t) = \bar{g} \exp\left(-\frac{t - t_j}{\tau}\right)$$

(b) $$g(t) = \bar{g} \frac{t - t_j}{\tau} \exp\left(-\frac{t - t_j}{\tau}\right)$$

(alpha function)

(c) $$g(t) = \bar{g} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left(\exp\left(-\frac{t - t_j}{\tau_1}\right) - \exp\left(-\frac{t - t_j}{\tau_2}\right)\right)$$

Synaptic inputs in the LIF model
(also valid for other IF models)

- Current-based model: Each presynaptic spike generates a postsynaptic **current** pulse in neuron *i*

$$\tau \frac{dV_i}{dt} = -V_i + RI_i^{syn}(t)$$

$$I_i^{syn}(t) = \sum_j w_{ij} \sum_f \alpha\left(t - t_j^{(f)}\right)$$

Fixed function

- $t_j^{(f)}$ are the spike times of presynaptic neuron *j*
- w_{ij} is the synaptic efficacy (weight) of the synapse from neuron *j* to neuron *i*

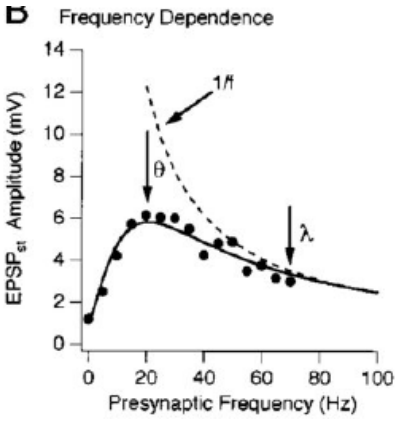
Synaptic inputs in the LIF model
(also valid for other IF models)

- Conductance-based model: Each presynaptic spike generates a **change in the conductance** of the postsynaptic membrane with time course $g(t - t_j^{(f)})$

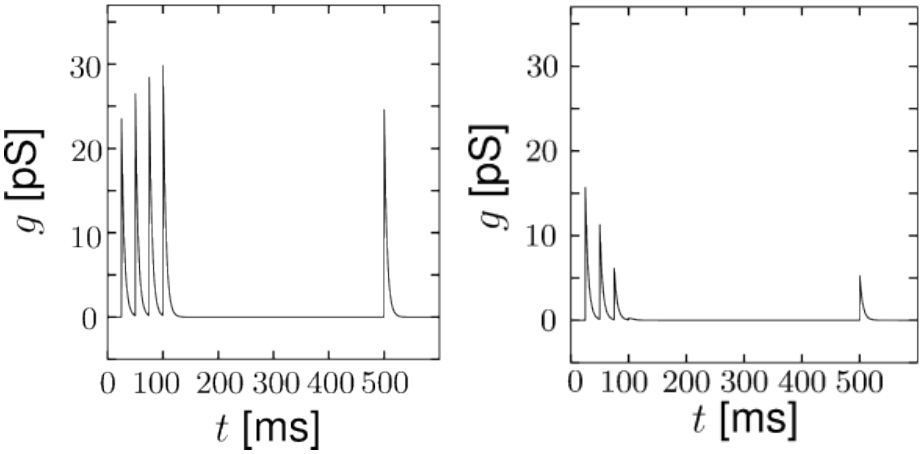
$$\tau \frac{dV_i}{dt} = -V_i + RI_i^{syn}(t)$$

$$I_i^{syn}(t) = -\sum_j w_{ij} \sum_f g\left(t - t_j^{(f)}\right)(V_i(t) - V_{rev})$$

Short-term plasticity



Above. Facilitation of excitatory cortical synapse in a slice of rat somatosensory cortex. Right. Frequency dependency of facilitation and depression. Markran et al., 1998.



Simulation of facilitation (left) and depression (right): sequence of 4 presynaptic spikes followed by a 5th spike 400 ms after (Gerstner & Kistler, 2002)

- Synaptic conductance given by

$$g(t) = \bar{g} p_s p_{rel}$$

- p_s = probability that a postsynaptic channel opens given that a transmitter was released by presynaptic neuron → modeled by an α function
- p_{rel} = probability that a transmitter is released by presynaptic neuron following the arrival of an action potential
- p_{rel} is affected by synaptic **facilitation** and **depression**

$$\tau_p \frac{dp_{rel}}{dt} = p_0 - p_{rel} + f_F (1 - p_{rel}) \sum_j \delta(t - t_j)$$

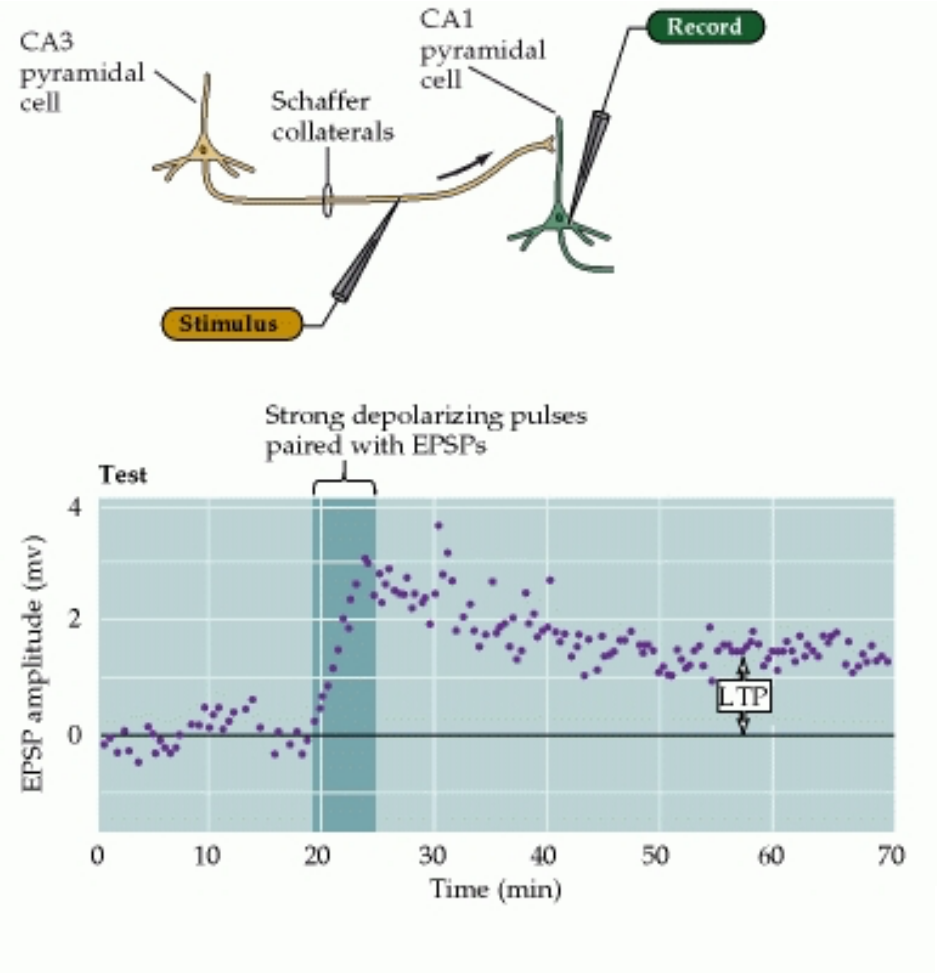
$$\tau_p \frac{dp_{rel}}{dt} = p_0 - p_{rel} - f_D p_{rel} \sum_j \delta(t - t_j)$$

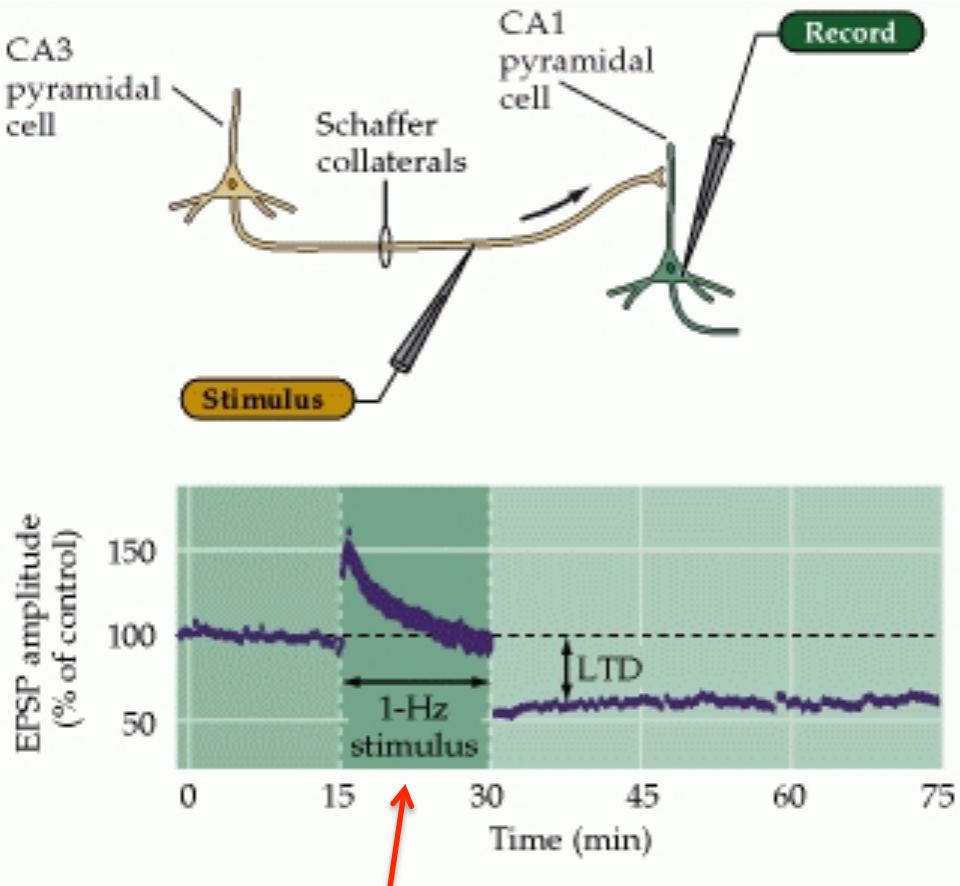
Activity-dependent synaptic plasticity

- Widely believed as the basic phenomenon underlying learning and memory
- Hebb (1949): if input from neuron A often contributes to the firing of neuron B, then the synapse from A to B should be strengthened
- More recently, Hebb's suggestion has been generalized to include decreases in strength arising from repeated failure of neuron A to be involved in the activation of neuron B

LTP and LTD

long-term potentiation and long-term depression



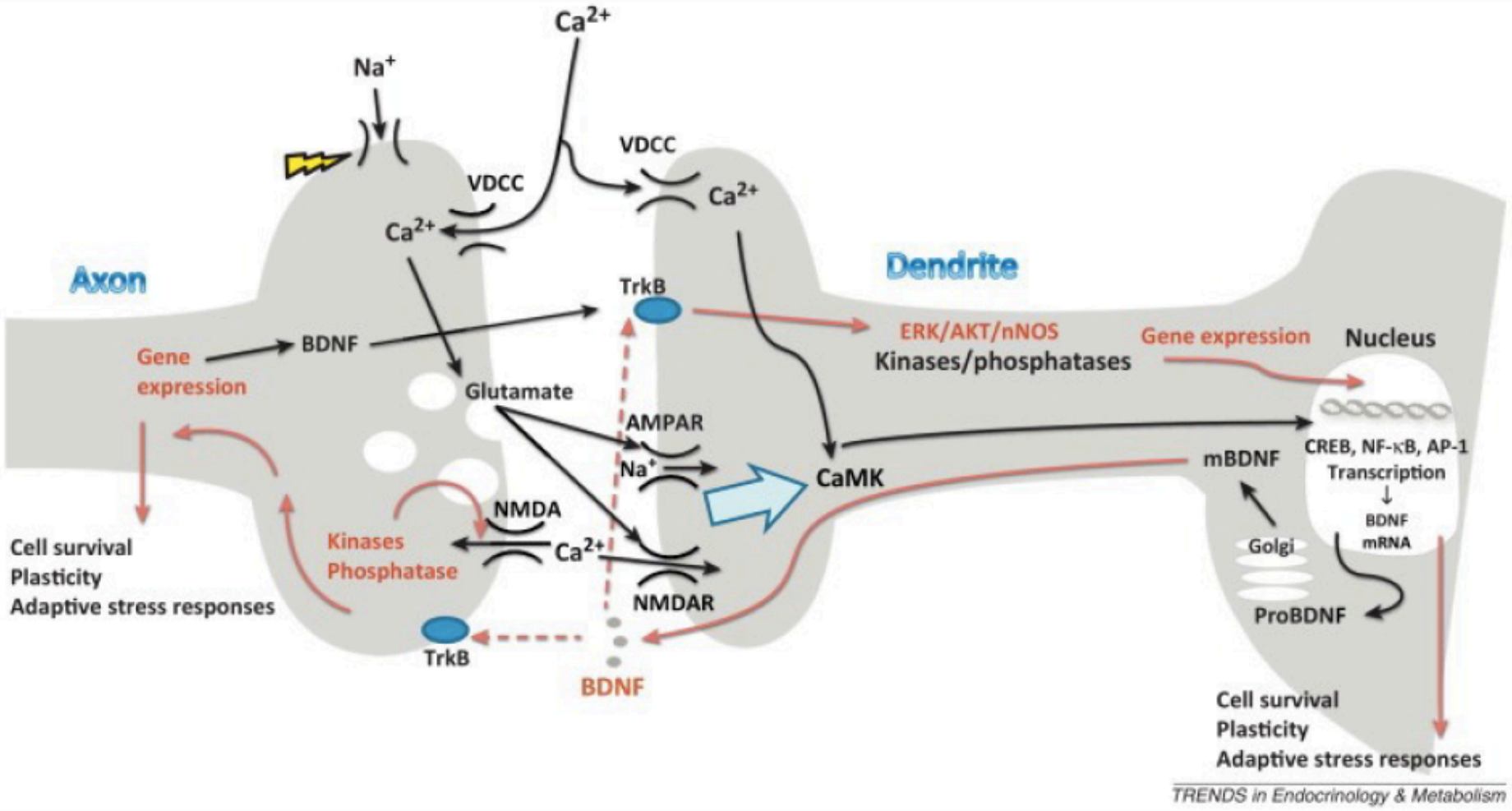


Low-frequency stimulation

Purves et al. (2001)

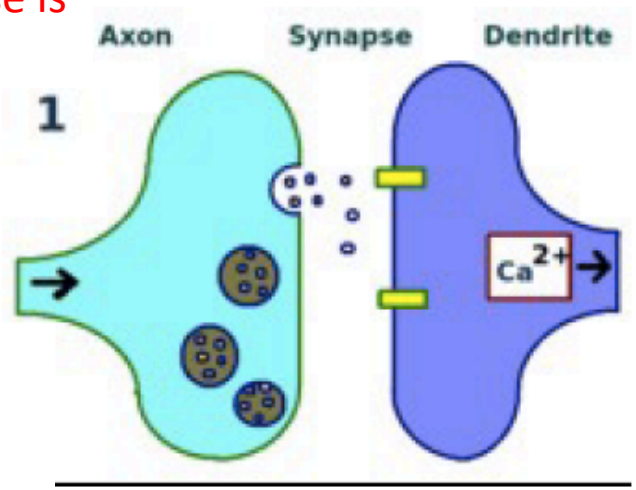
LTP and LTD

Very complicated mechanisms not completely understood

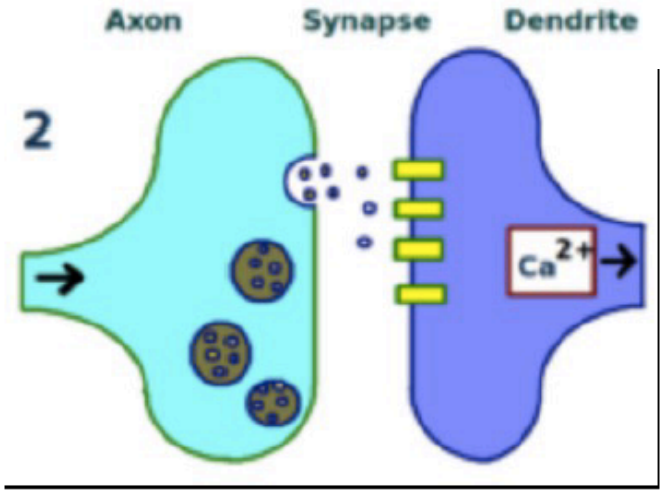


The generic mechanism of synaptic plasticity should be like this

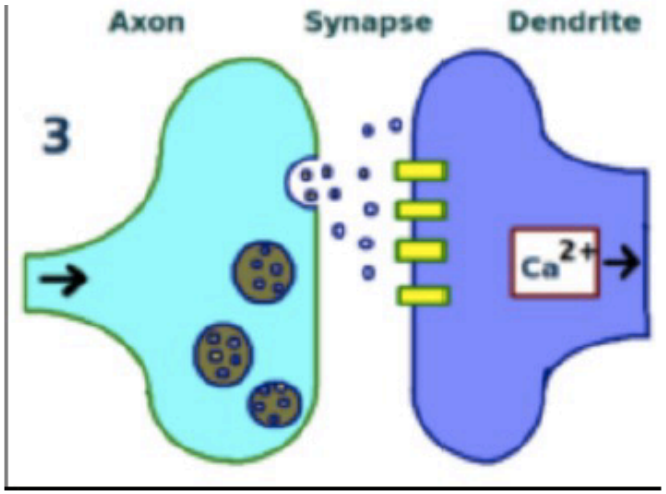
The synapse is stimulated

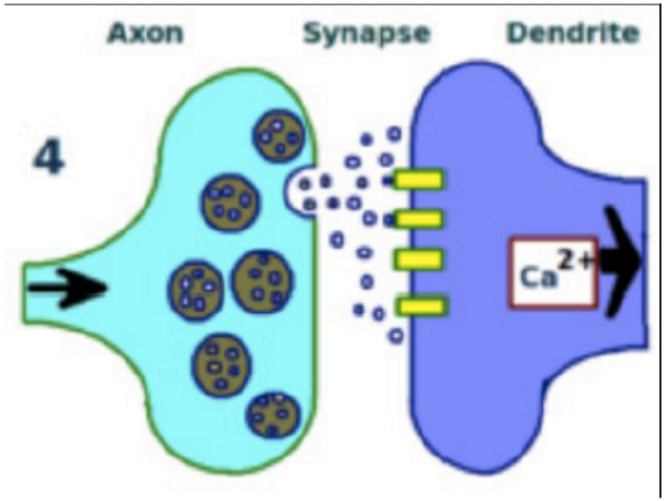


More receptors



More neuro-transmitters





Now there is a stronger link

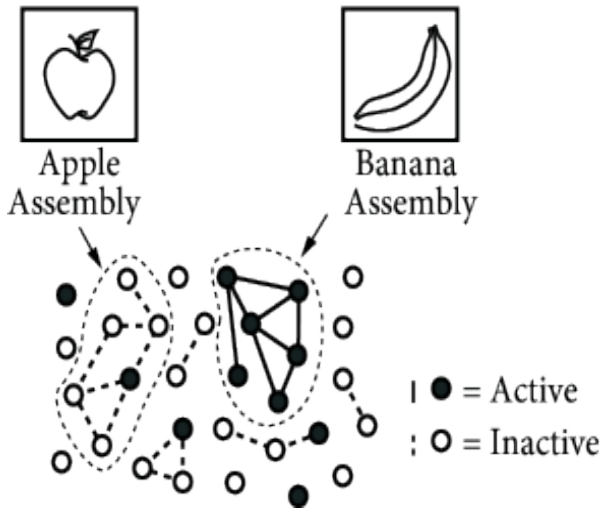
Synaptic plasticity and memory

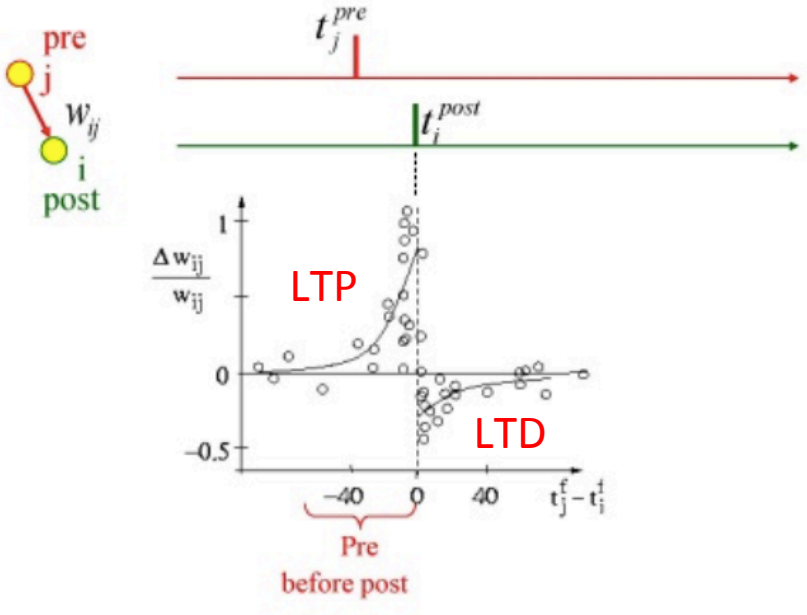
- Morris (1986) showed that LTP was necessary for the formation of memories *in vivo*.

- Animals where the NMDA receptors were blocked were unable to learn the position of the platforms where they could stand without swimming.
- In vitro analysis showed that LTP was indeed blocked.
- Tonegawa (1996) showed that genetically altered mice with impaired NMDA receptors showed poor spatial navigation capabilities.

Hebbian plasticity

- Mechanism of **synaptic weight change** proposed by Hebb in 1949 to implement formation of cell assemblies and learning
- The weight of the synapse between two neurons grows whenever their firing activity is correlated: **neurons that fire together wire together**
- *Spike-timing dependent plasticity* (STDP): experimental protocol of synaptic plasticity induction discovered by Markram in 1995. **Causal** version of Hebb's rule: the spike of pre-synaptic neuron must **precede** the spike of post-synaptic neuron for their weight to increase, otherwise the weight decreases



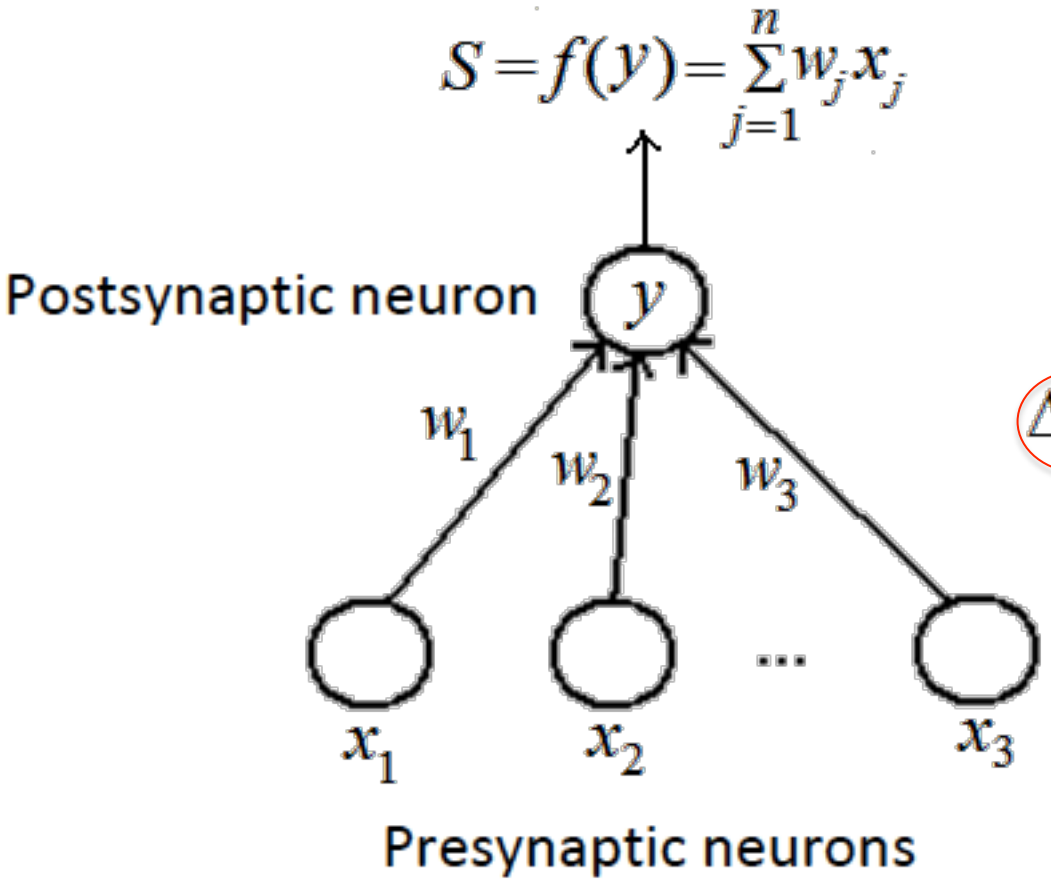


Models of long-term plasticity

$$I_{\text{syn}} = \bar{g} \cdot s(t) \cdot \left(V_{\text{post}} - V_{\text{rev}} \right)$$

- Changes in $\bar{g}$ (maximal synaptic conductance) to model incorporation or removal of channels
- Implemented by hand or through a **learning rule** (e.g. Hebb's rule)
- The time-scale of changes in $\bar{g}$ is **much slower** than the one of membrane potential dynamics

Hebbian rule for rate-based neurons



$\Delta w_i = \beta S x_i$

Change in *i*th synaptic weight (Hebb's rule)

β = learning rate;
S = activity of postsynaptic neuron;
x_i = activity of *i*th presynaptic neuron

BCM model

- Bienenstock, Cooper and Munro (1981) introduced a unified framework to treat potentiation and depression.
- The BCM model incorporates a sliding threshold that separates potentiation from depression.
- It can be proved that under some conditions it can be derived from STDP.

- x: presynaptic activity;
- y: postsynaptic activity;
- w = synaptic weight
- $dw/dt = \phi(y)x - \varepsilon w$