School on Fundamentals of Complex Networks and Applications to Neuroscience
ICTP SAIFR
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An overview of single-cell and neural network models I

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CAPES

FAPESP
SÃO PAULO RESEARCH FOUNDATION

CNPq

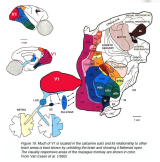
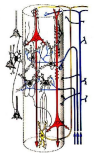
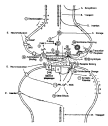
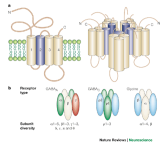
Ribeirão Preto, SP, pop. ~620,000 (2012), alt. 547 m (1,791 ft)

Campus of the University of São Paulo at Ribeirão Preto. Notice the campus lake and the Clinics Hospital.

Part 1

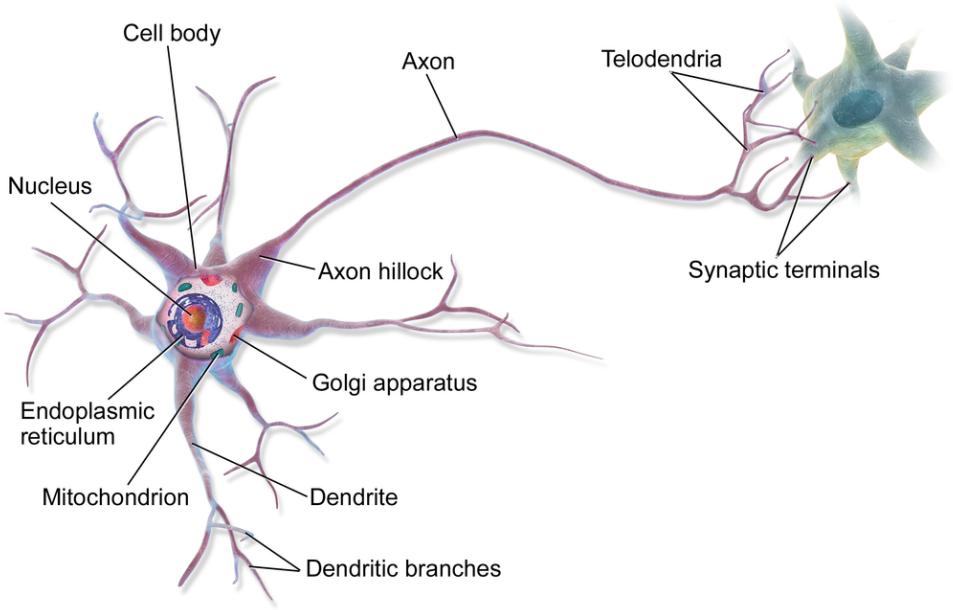
Basic Concepts

Spatial scales of the brain

$\sim$10cm	Whole brain	
$\sim$1cm	Brain structure/cortical areas	
100μm- 1mm	Local network/‘column’/‘module’	
10μm- 1mm	Neuron	
100nm- 1μm	Sub-cellular compartments	
$\sim$10nm	Channel, receptor, intracellular protein	

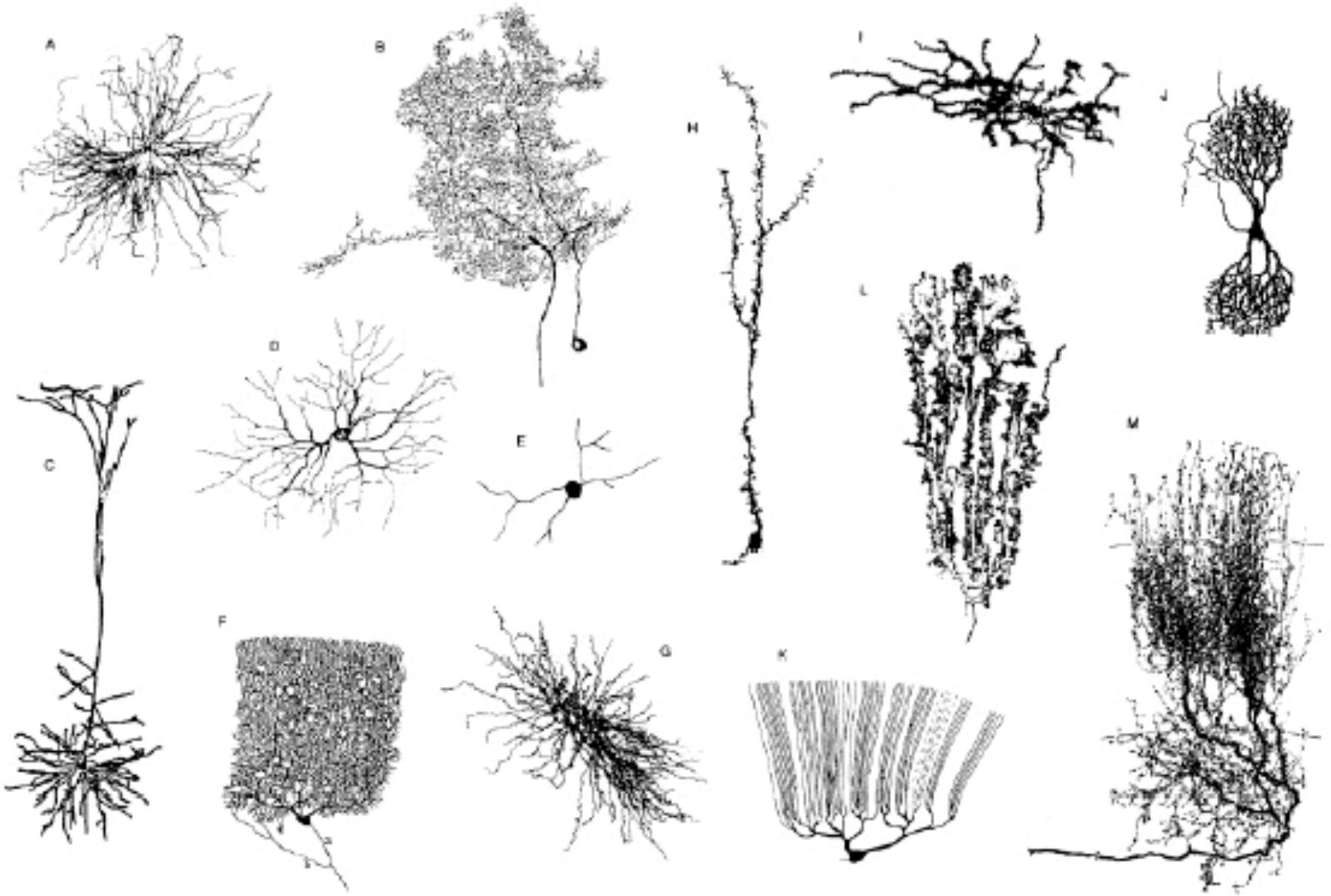
Neuron

- The brain is made of isolated cells – neurons and glia –, which are structurally, metabolically and functionally independent.
- **Neuron doctrine** (Ramon y Cajal, 1894): The neuron is the **basic functional unit of the nervous system**
- Neurons are specialized for intercellular communication



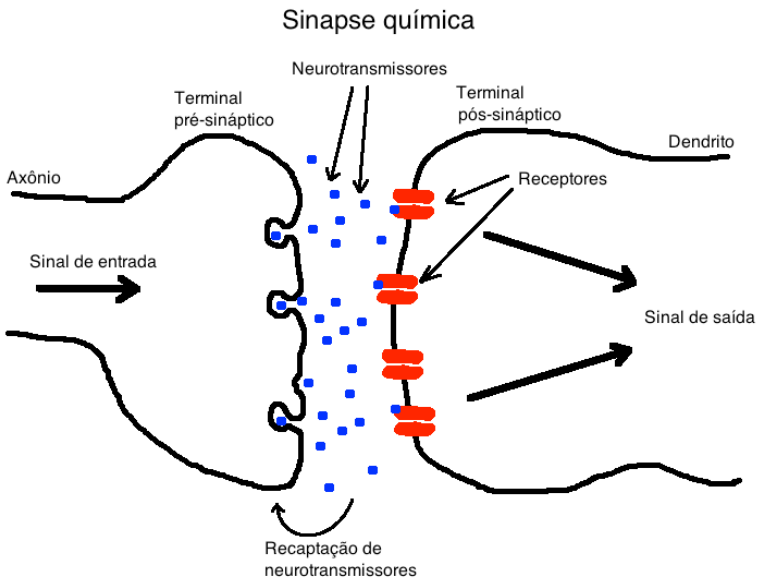
https://en.wikipedia.org/wiki/Neuron

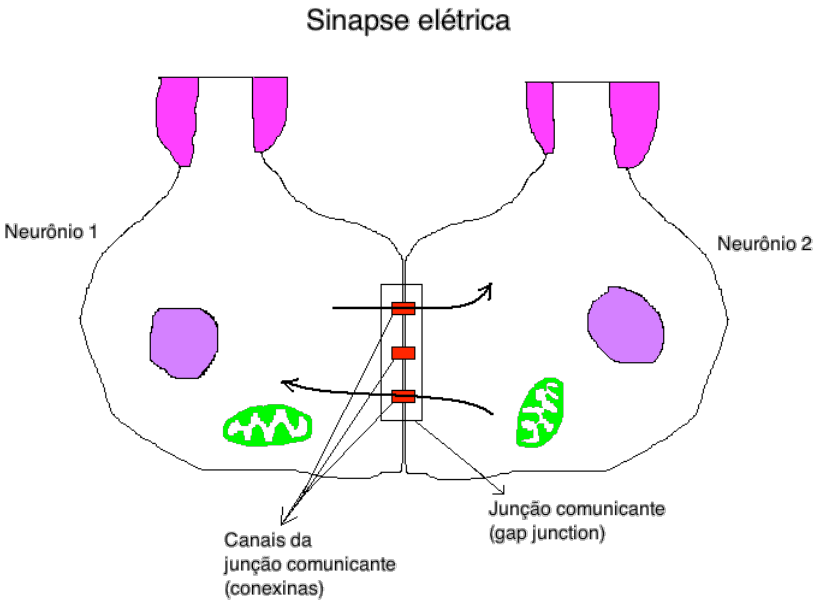
Neurons have many and diverse shapes



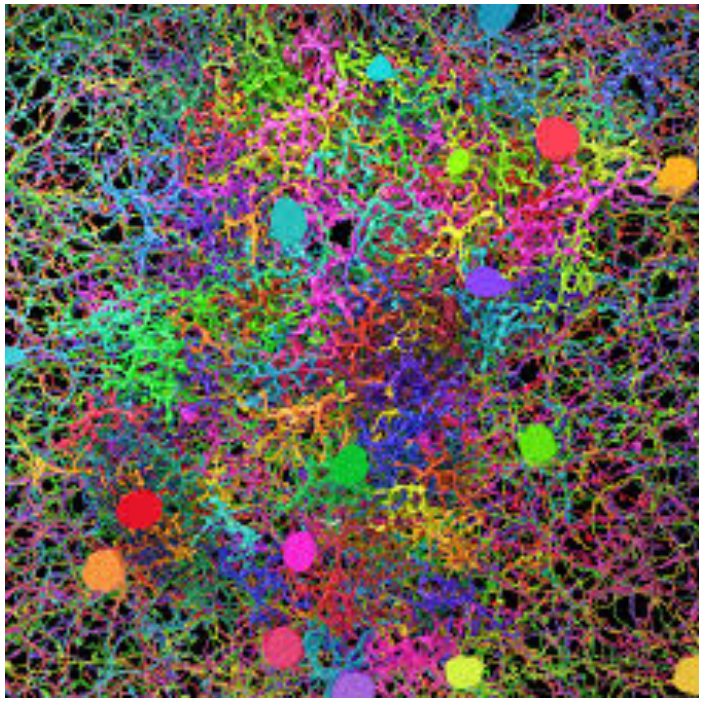
Synapse

- Specialized region in which a **pre-synaptic** cell makes contact with a **post-synaptic** cell
- Synapses may be chemical or electrical

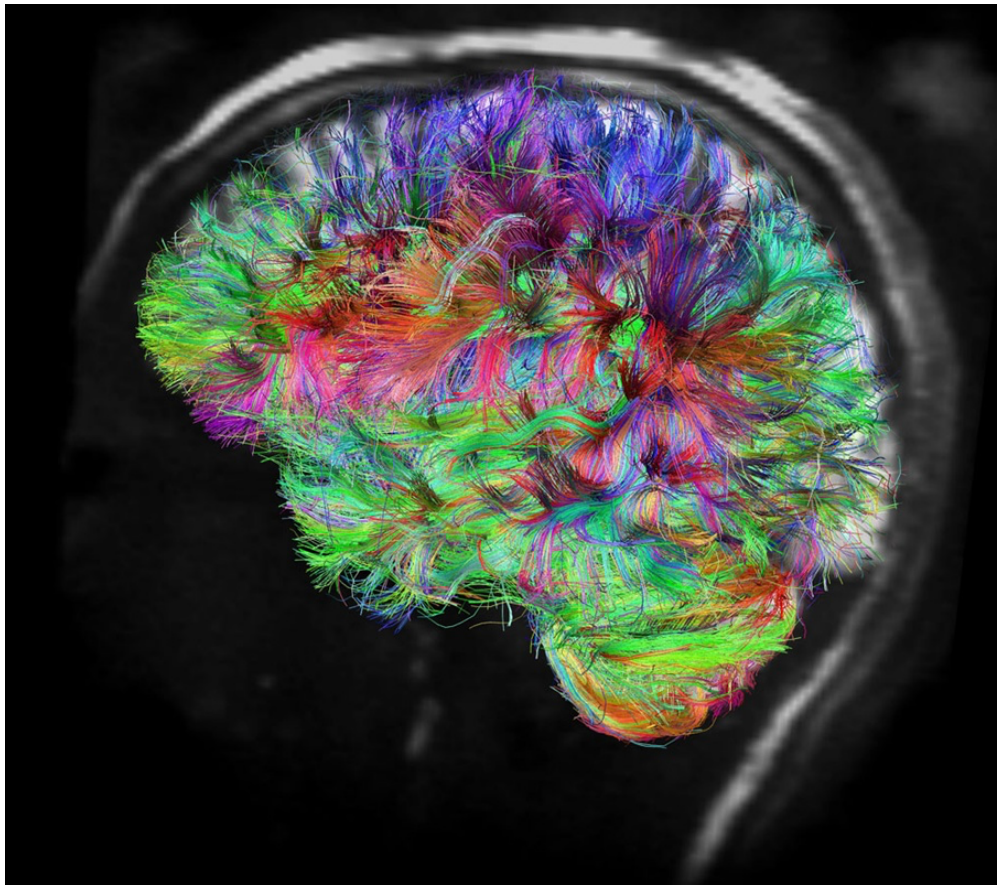




Neural circuits and networks



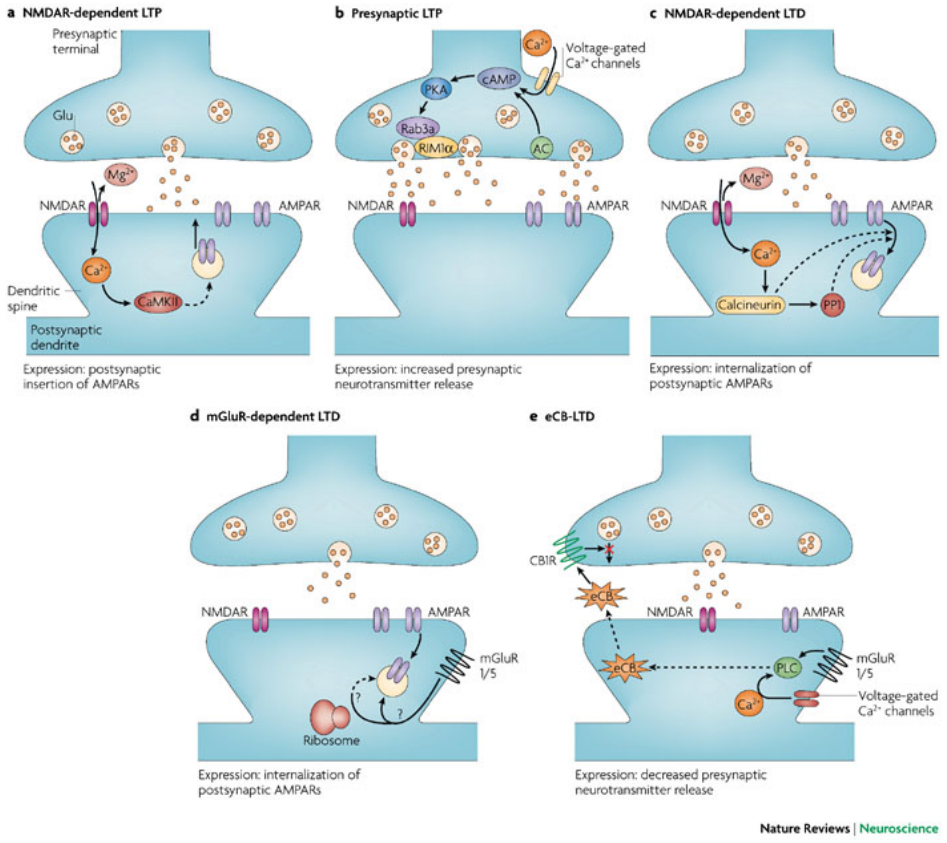
Alex Norton, EyeWire,
Seung Lab, MIT



V.J. Wedeen e L.L. Wald, Martinos Center for
Biomedical Imaging at Massachusetts General Hospital

Synaptic Plasticity

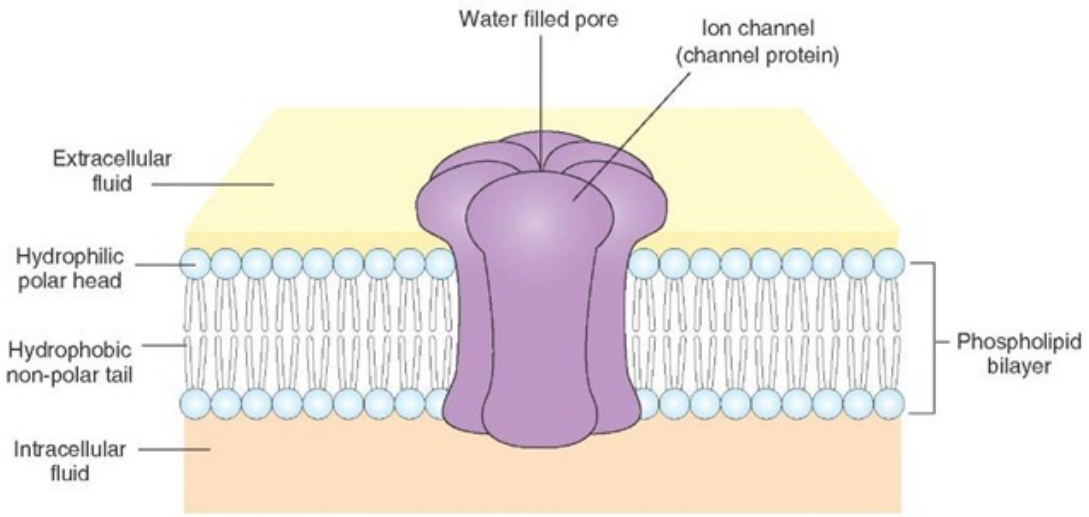
- Generic name given to any type of change (strengthening or weakening) in the efficacy of a synapse
- Synaptic plasticity can be of short or long duration
- Hypothetical mechanism underlying memory formation and learning



Kauer & Malenka (2007)

Neuronal Membrane

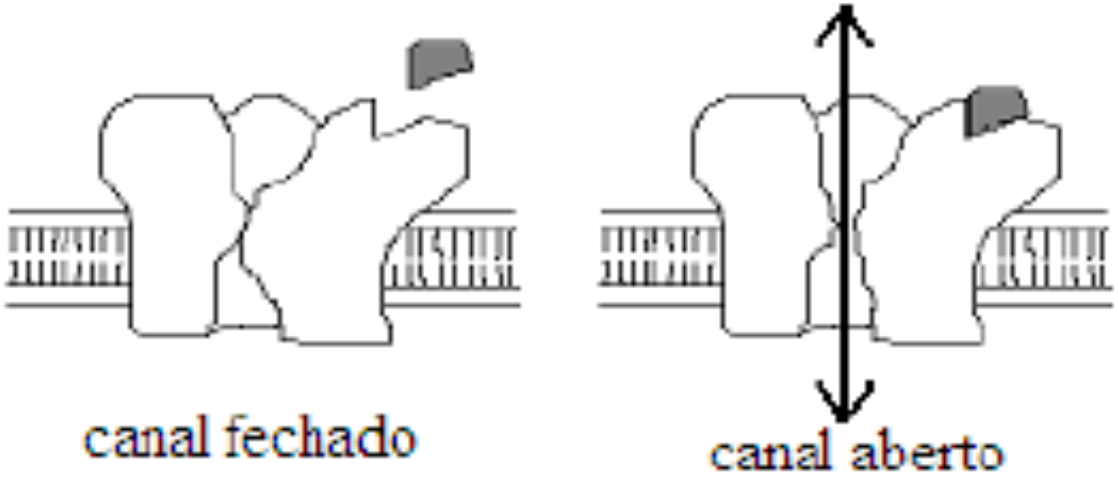
- Thin membrane (60-70 Å) that separates the cytoplasm from the extracellular space
- Made of a lipid bilayer in which proteins are immersed
- Some proteins cross the membrane forming ion channels



http://what-when-how.com/neuroscience/electrophysiology-of-neurons-the-neuron-part-1/

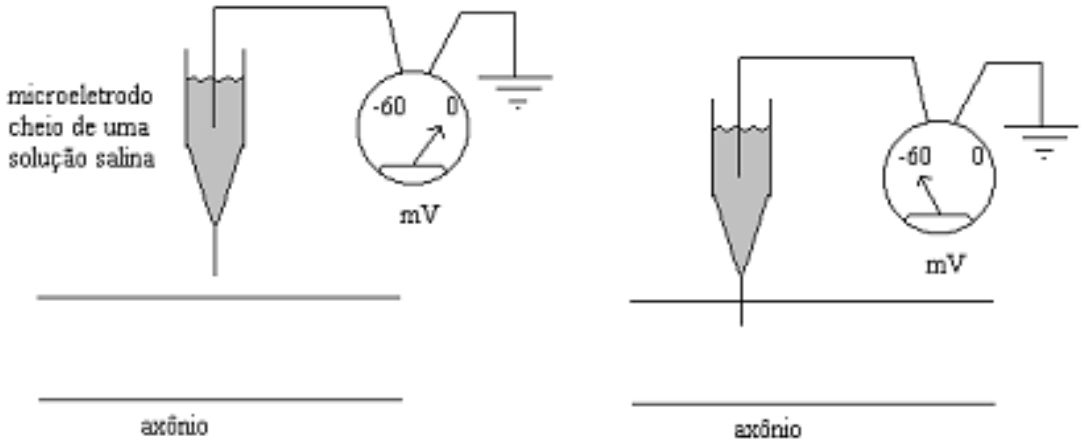
Ion channels

- Membrane proteins may undergo conformational changes under electrical and chemical control, thus regulating ionic flux
- The figure below illustrates a channel opening due to a protein-ligand binding



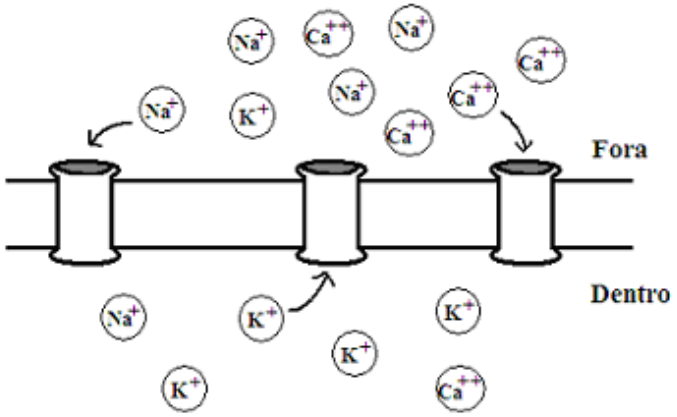
Membrane potential

- There is a difference of electrical potential between the two sides of the neuronal membrane
- Defining the zero of potential at the outside the inside is, in general, at a potential of –50 to –90 mV



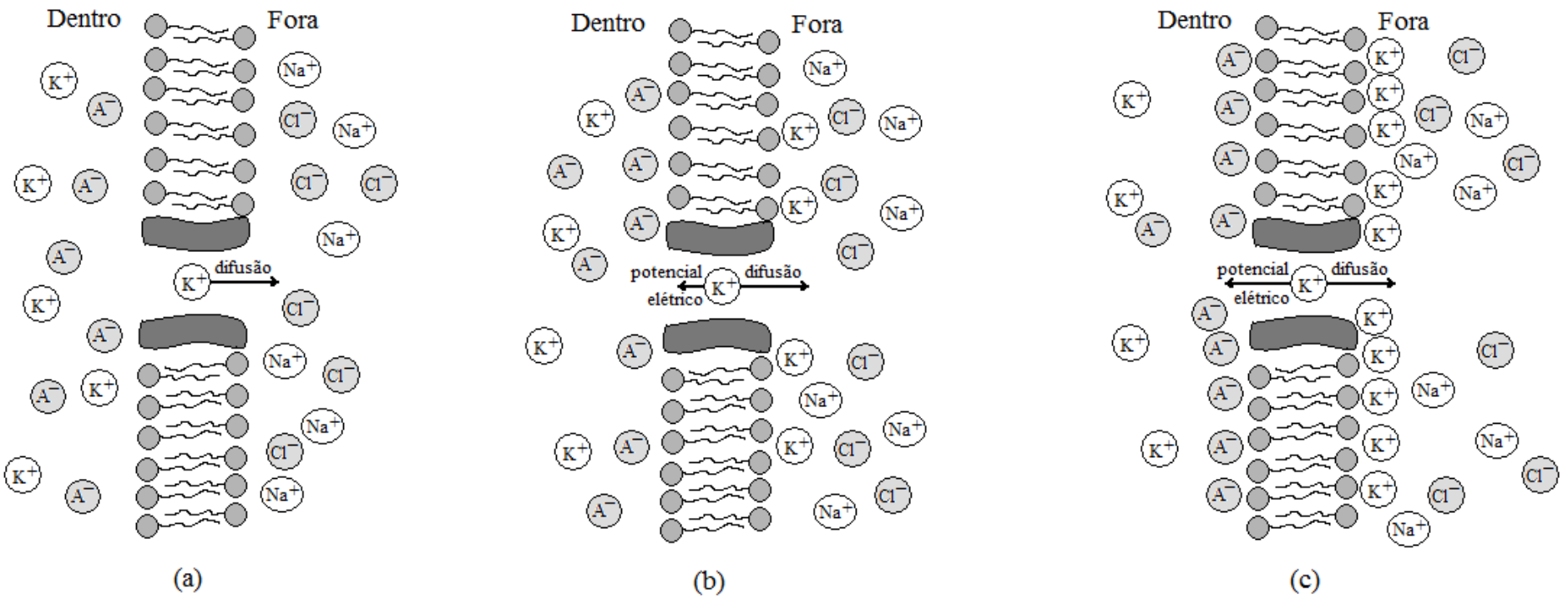
Ionic concentrations

- Ion concentrations are different on the two sides of the neuronal membrane



Ion	In (mM)	Out (mM)
Frog muscle (20°C)		
K^+	124	2,25
Na^+	10,4	109
Cl^-	1,5	77,5
Ca^{2+}	10^{-4}	2,1
Squid giant axon (20°C)		
K^+	400	20
Na^+	50	440
Cl^-	40-150	560
Ca^{2+}	10^{-4}	10
Typical mammalian cell (37°C)		
K^+	140	5
Na^+	5-15	145
Cl^-	4	110
Ca^{2+}	10^{-4}	2,5 - 5

Origin of the membrane potential



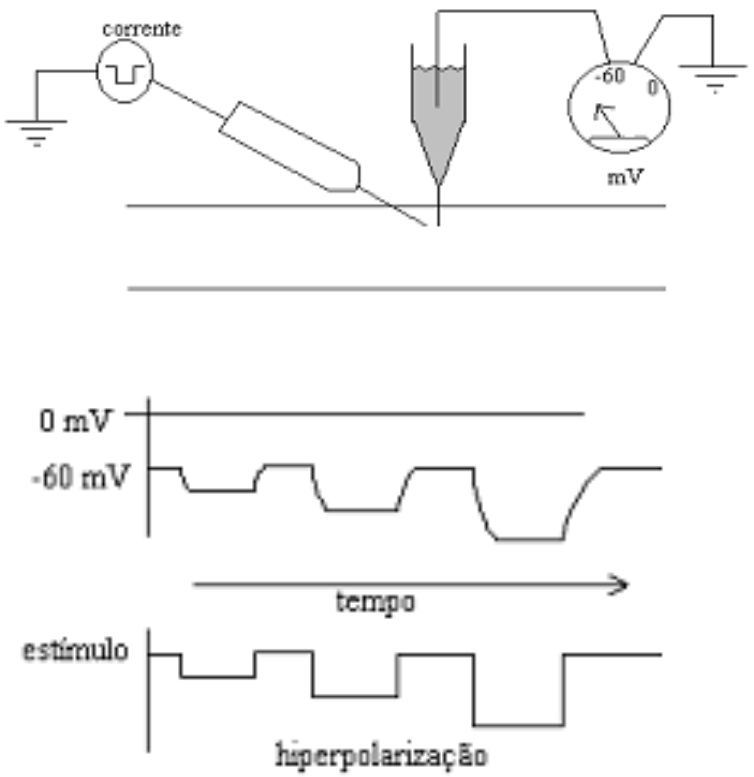
- Nernst potential

$$E = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$$

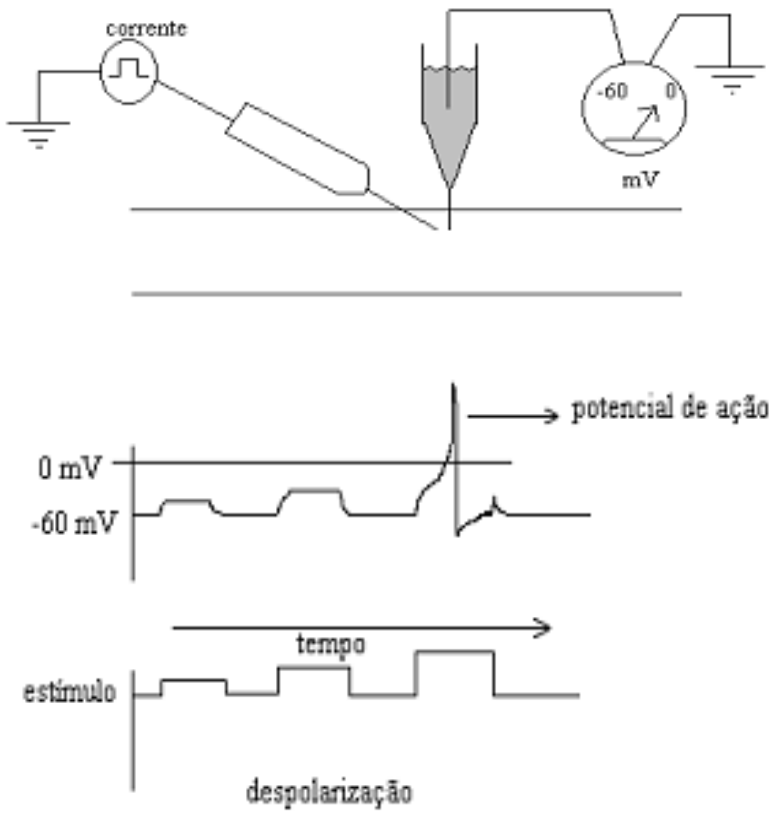
	Inside (mM)	Outside (mM)	Equilibrium protential (Nernst)
K^+	400	20	-75 mV
Na^+	50	440	+55 mV
Cl^-	40-150	560	-66 a -33 mV
Ca^{2+}	10^{-4}	10	+145 mV
A^- (organic ions)	385	—	—

Squid giant axon at 20°C

Depolarization and hyperpolarization



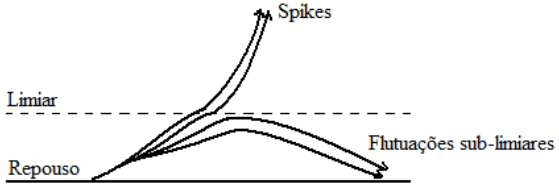
Graded variation

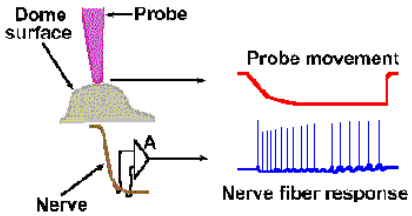


Action potential

Action potential

- Shape (width and amplitude) characteristic of each neuron
- Threshold phenomenon (all or none)
- Propagates unchanged while subthreshold voltage fluctuations are strongly attenuated
- Used by neurons to code and transfer information





Na figura da esquerda ilustra-se como a ponta de prova pressiona a superfície em forma de domo do mecanoreceptor e como as respostas do nervo são registradas. Na figura da direita, mostra-se um trem de disparos típico do nervo para uma pressão prolongada. O registro inteiro dura 40 ms.

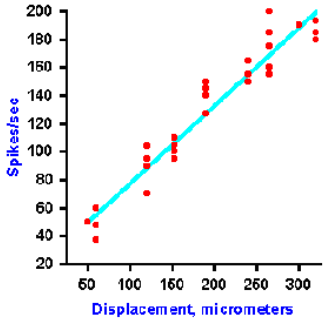
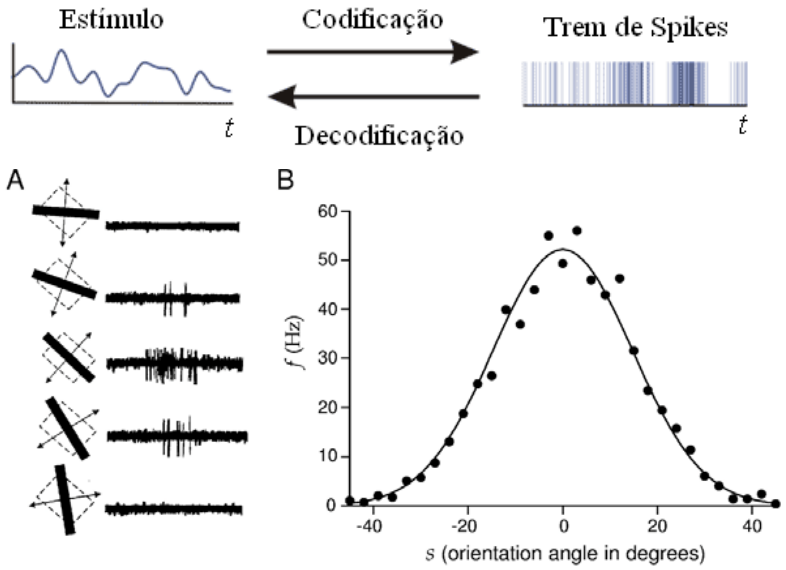
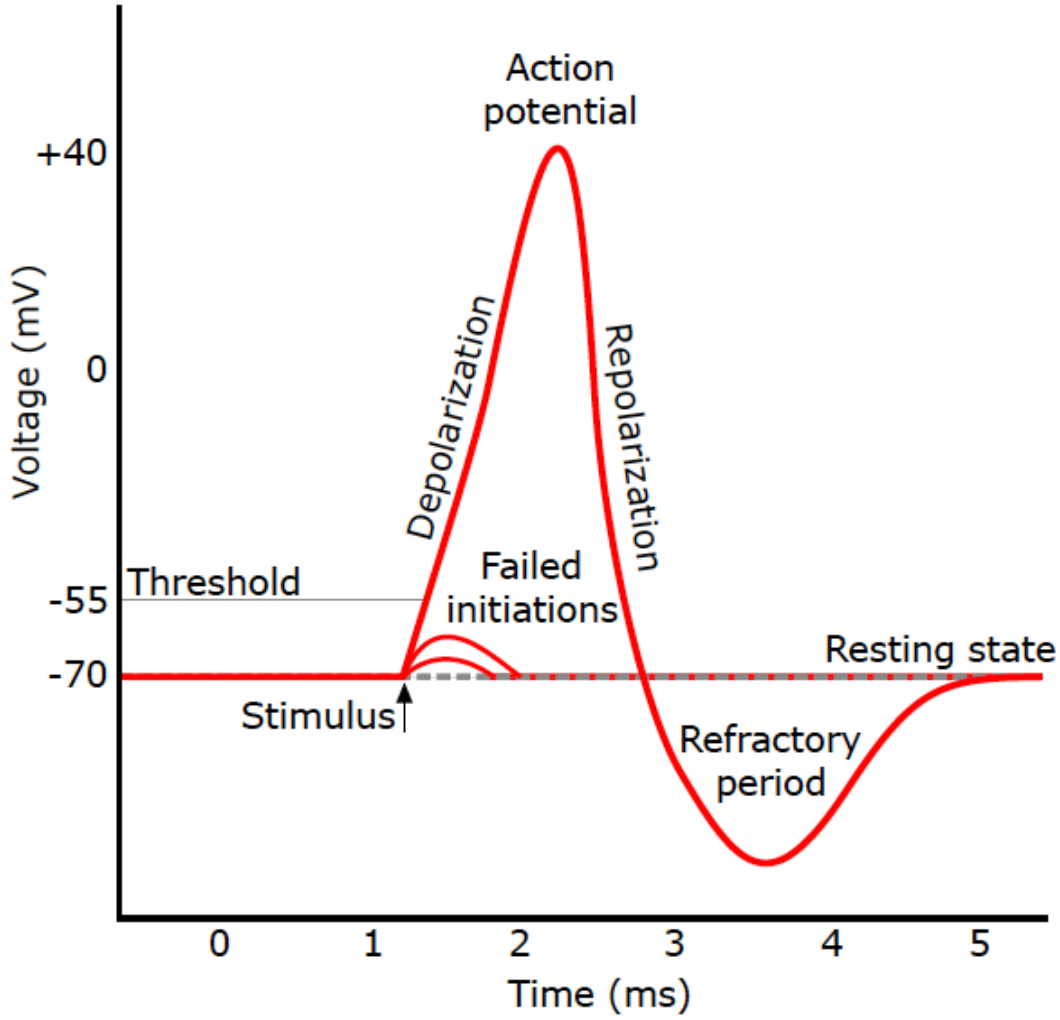


Gráfico da freqüência de disparos em função do deslocamento do receptor. Cada ponto corresponde a uma medida feita durante todo o tempo em que o deslocamento foi mantido constante (o platô na figura da esquerda). Dados adaptados de Tapper, D.N., Trans. NY Acad. Sci., 26:697-701, 1964.

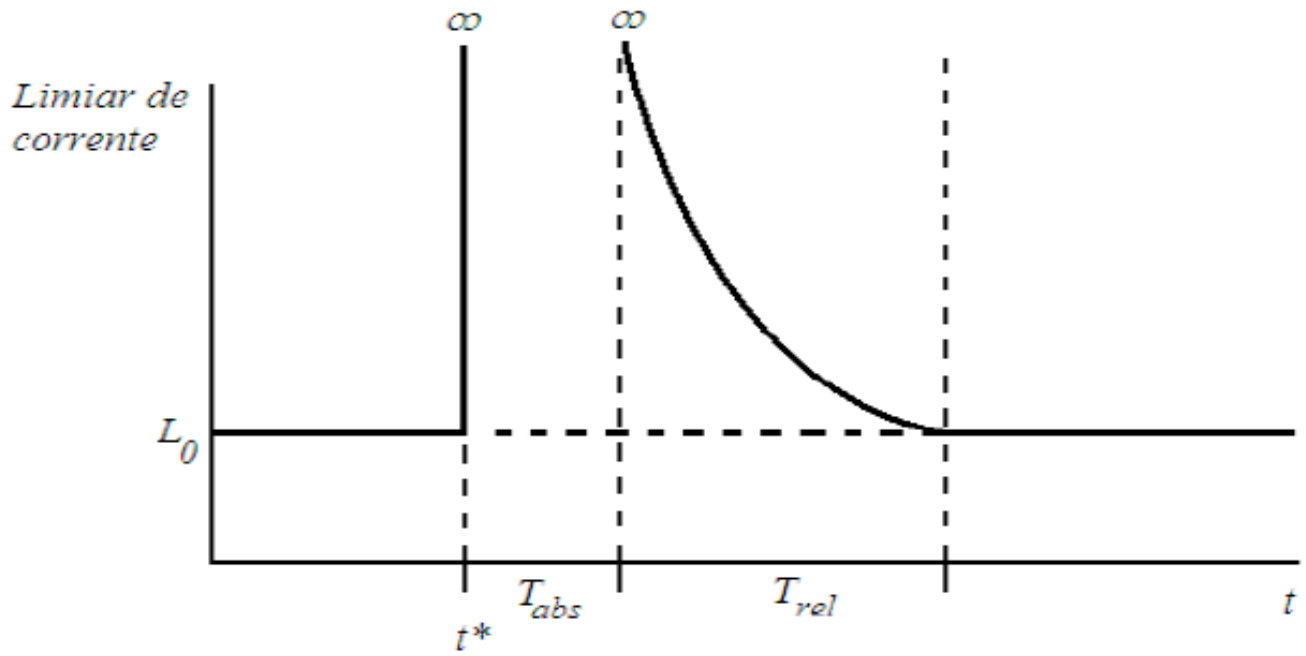




https://commons.wikimedia.org/wiki/File:Action_potential.svg#/media/File:Action_potential.svg

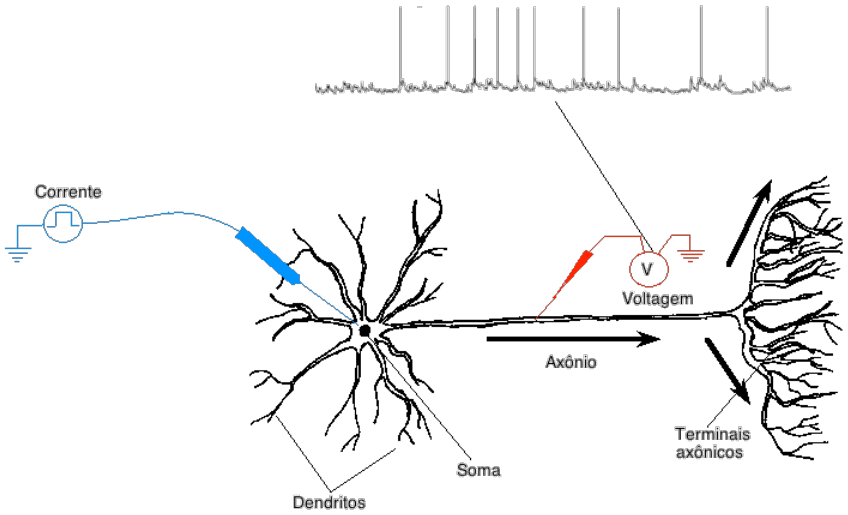
Refractory periods

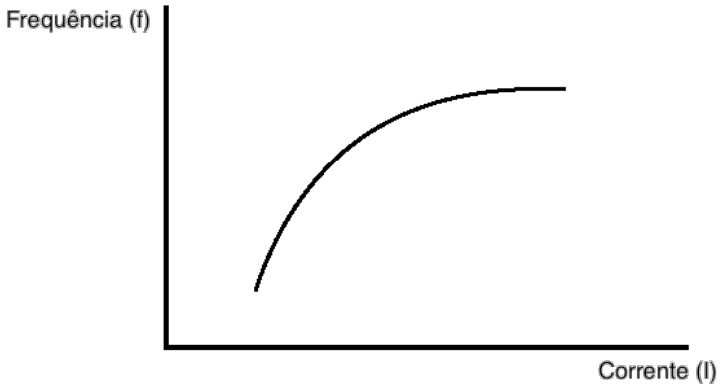
- **Absolute**: period during which a second stimulus (no matter how strong) will not lead to a second spike. It is as if the spike threshold were infinite
- **Relative**: period during which a second spike can be generated by a second stimulus stronger than the first. The strength of the second stimulus decays with time



F-I Curve

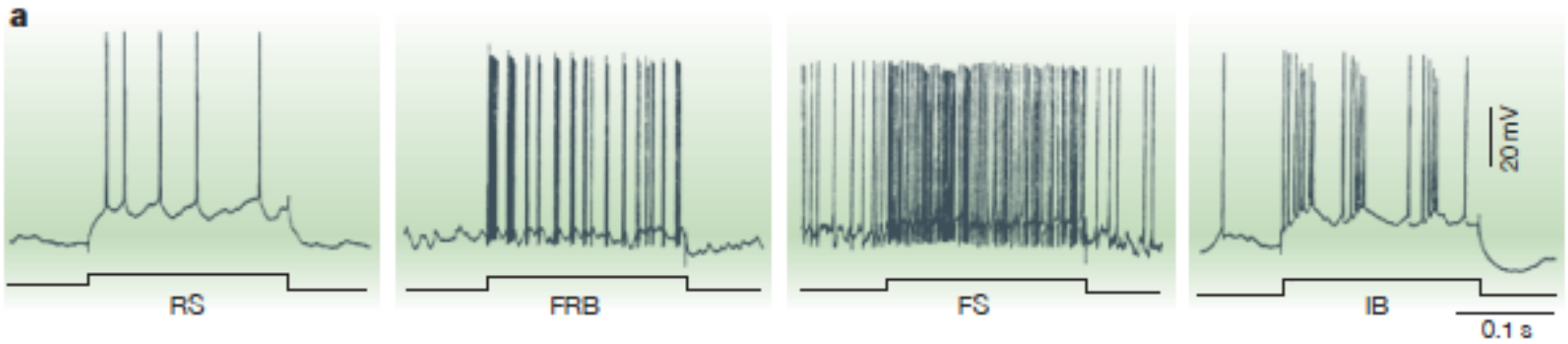
- Firing rate (F) of a neuron as a function of its input current (I)
- Each I value corresponds to a constant step current applied for a given time
- Describes the input-output transfer function of the neuron
- In general, F-I curves are nonlinear with saturation for high input values





Electrophysiological classes

- Different types of neurons produce different spike train patterns in response to the same input current
- The different patterns are grouped in **electrophysiological classes** (four examples of cortical classes are shown below)



Steriade (2004)

Spike train measures

Spike train $S(t) = \sum_{i=1}^{n} \delta(t - t_i),$

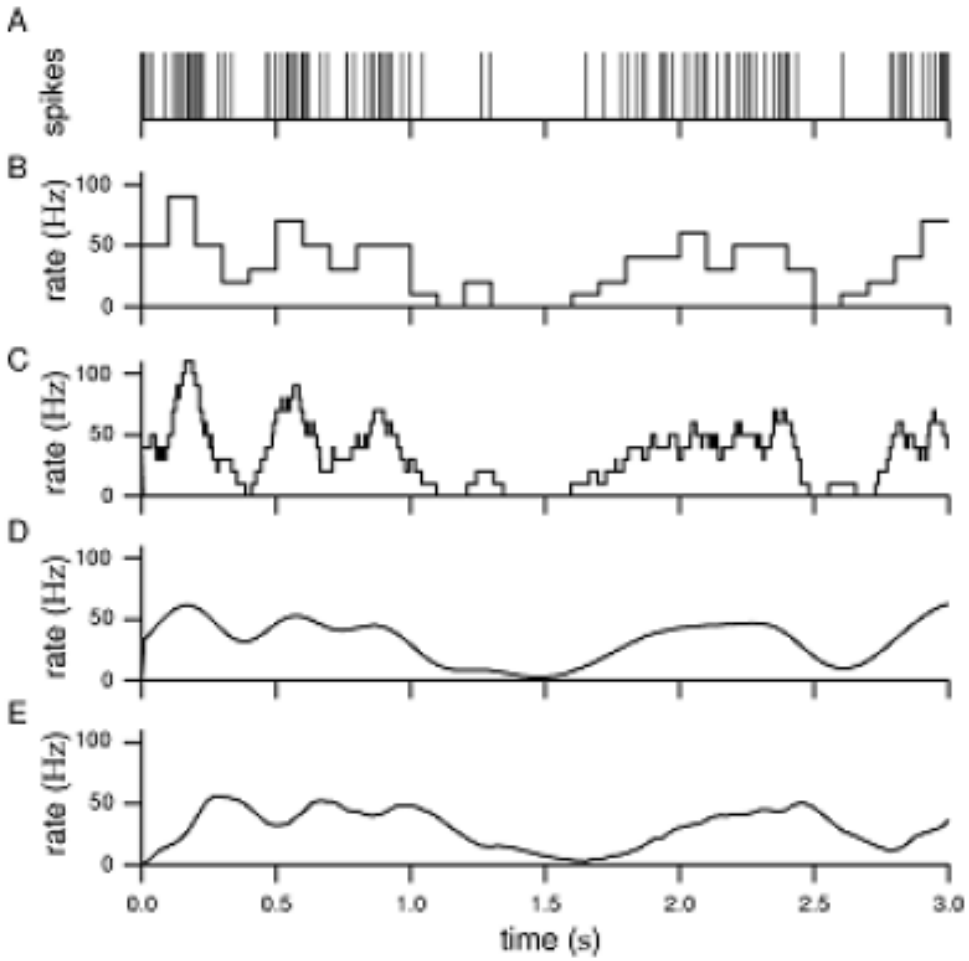
Spike count $r = \frac{n}{T} = \frac{1}{T}\int_0^T S(\tau)d\tau$

Time-dependent firing rate $r_1(t) = \frac{n(t; t+\Delta t)}{\Delta t}$

r(*t*) calculated with a sliding window $r_2(t) = \int_{-\infty}^{+\infty} w(\tau)S(t-\tau)d\tau$

C $w(t) = \begin{cases} 1/\Delta t & \text{se } -\Delta t/2 \le t \le \Delta t/2 \\ 0 & \text{caso contrário.} \end{cases}$

D $w(t) = \frac{1}{\sqrt{2\pi}\sigma_w} e^{-\frac{t^2}{2\sigma_w^2}}$



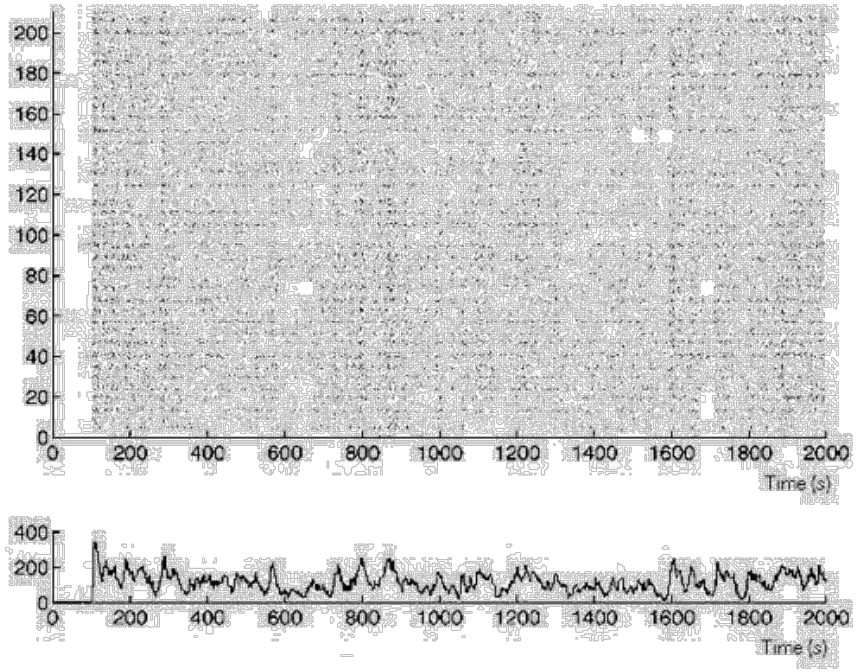
Dayan & Abbott (2001)

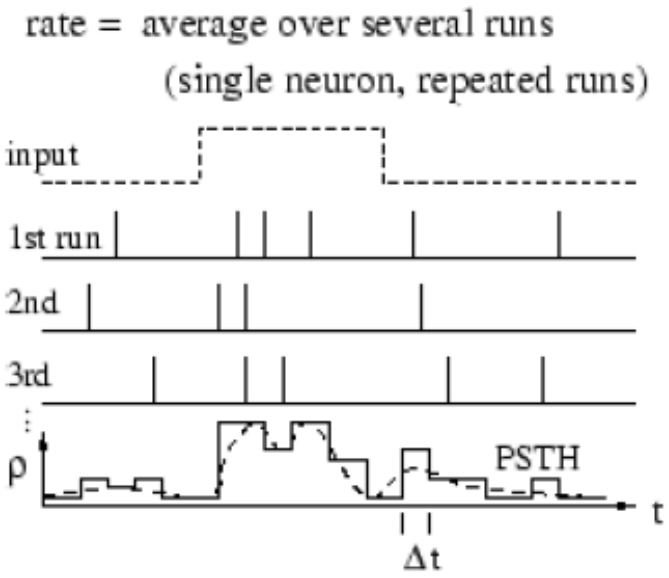
Raster plot and PSTH

Used to represent neuronal response because of neuronal variability

Each dot represents an action potential

Each line corresponds to a repetition of the same stimulus





spike density in **PSTH**

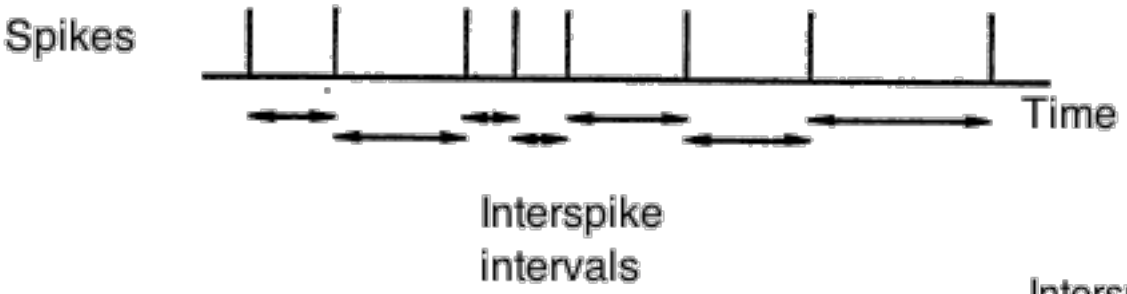
$$\rho = \frac{1}{\Delta t}\frac{1}{K} n_K(t; t+\Delta t)$$

PSTH: Peristimulus time histogram

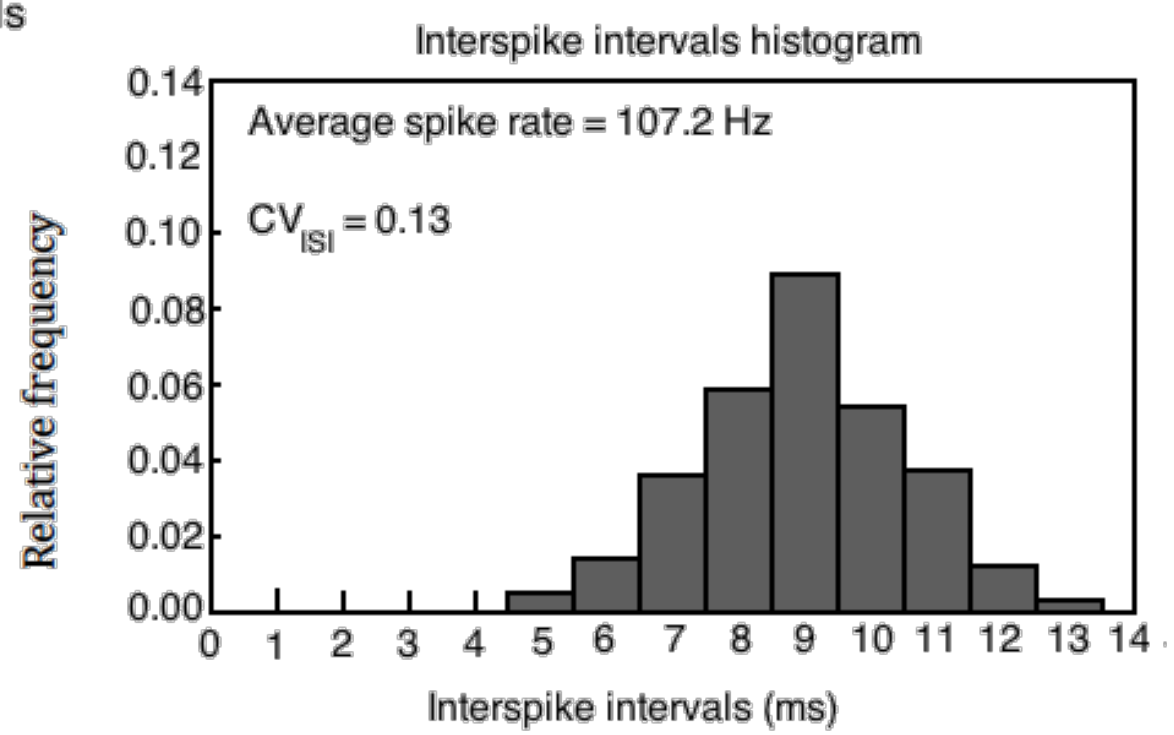
Gerstner & Kistler (2002)

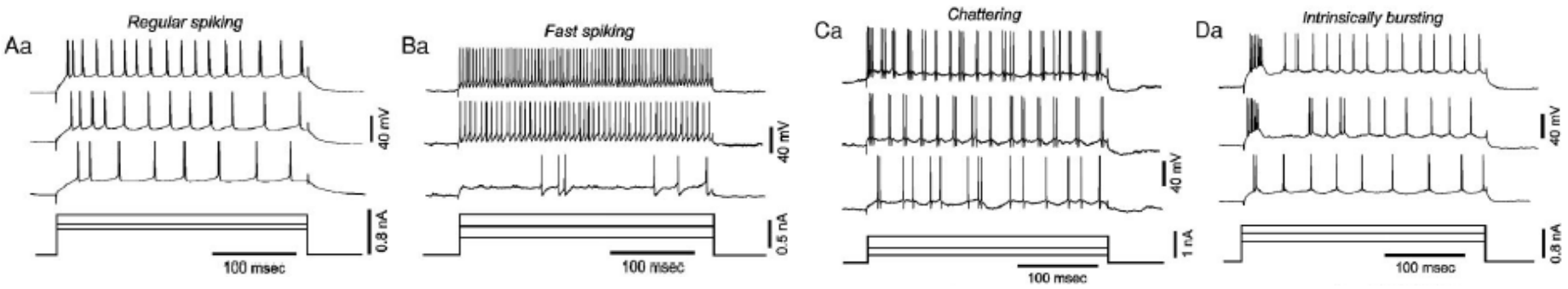
Interspike Intervals (ISIs)

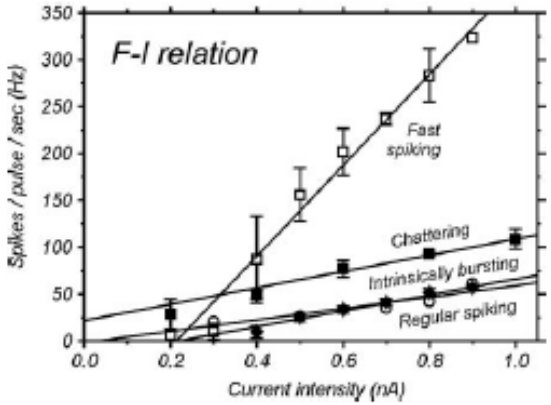
Another way to measure neuronal variability

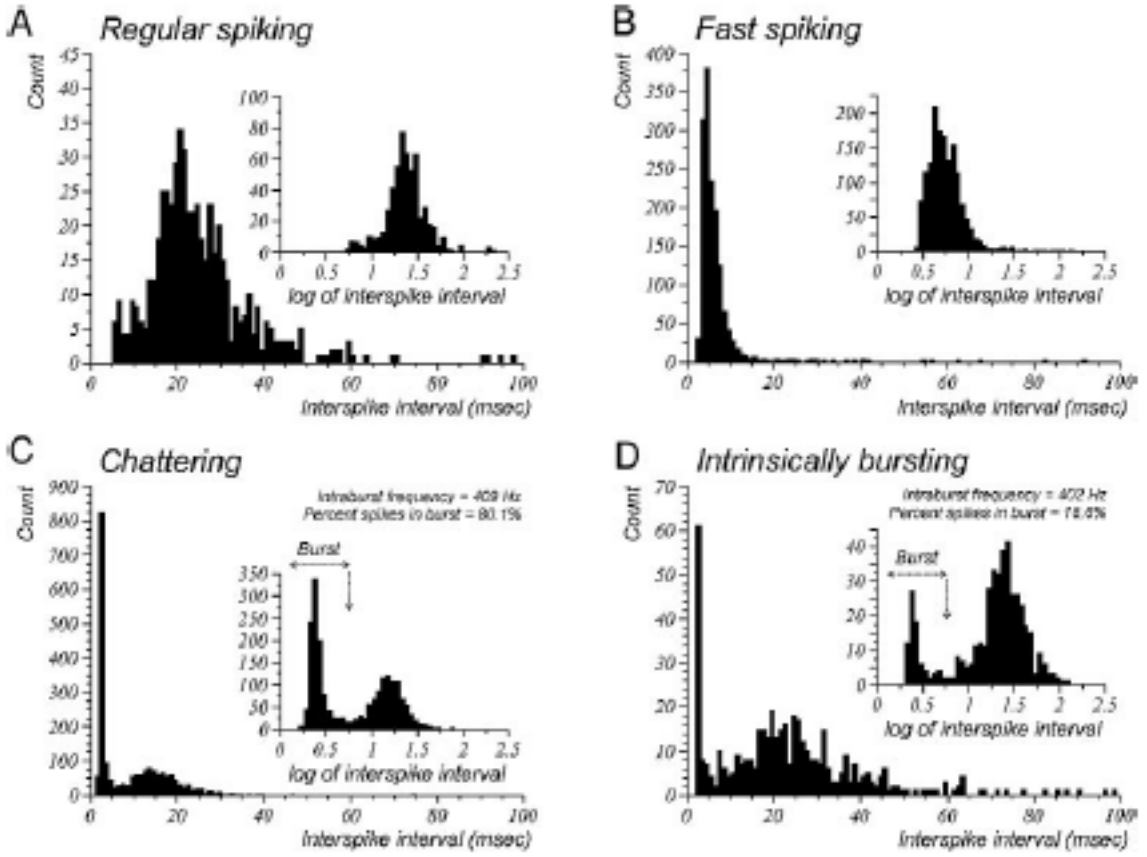


$$CV_{\mathrm{ISI}} = \frac{\sigma_{\mathrm{ISI}}}{\mu_{\mathrm{ISI}}}$$





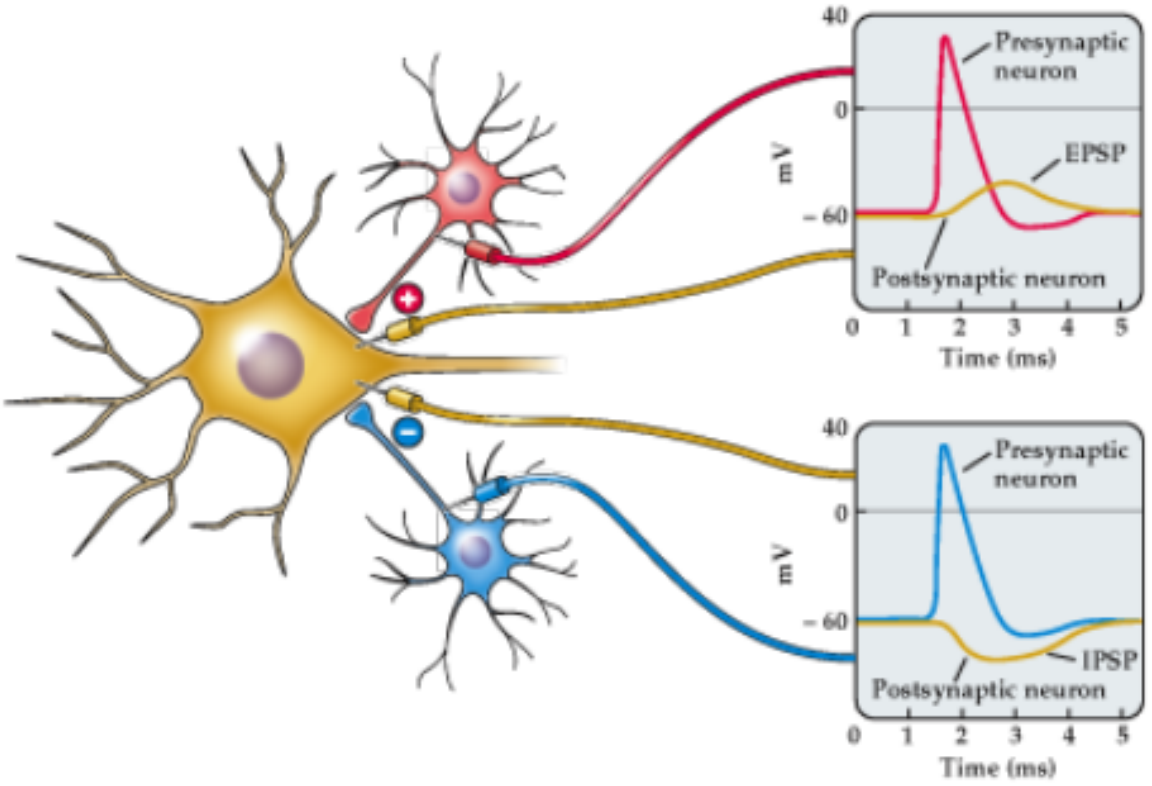




The graphs show two ways to quantify the responses of four types of cortical neurons: by the F-I curve and the histogram of ISIs

Nowak et al., J. Neurophysiol (2003)

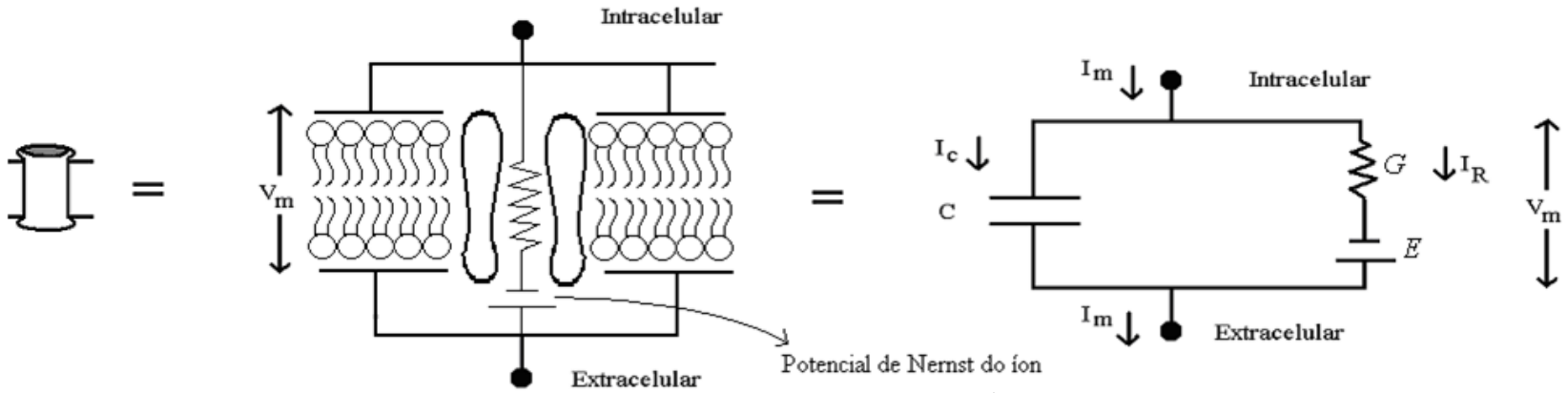
Postsynaptic potentials



EPSP: excitatory postsynaptic potential

IPSP: inhibitory postsynaptic potential

The membrane equation (passive)



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

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

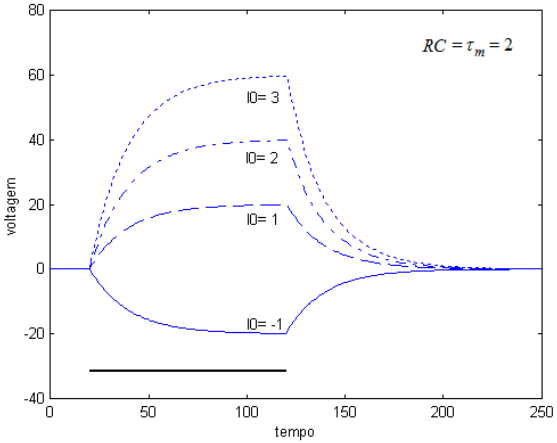
$$I_r = \frac{(V - E_N)}{r} = g(V - E_N) \quad \text{(1 open channel);}$$

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

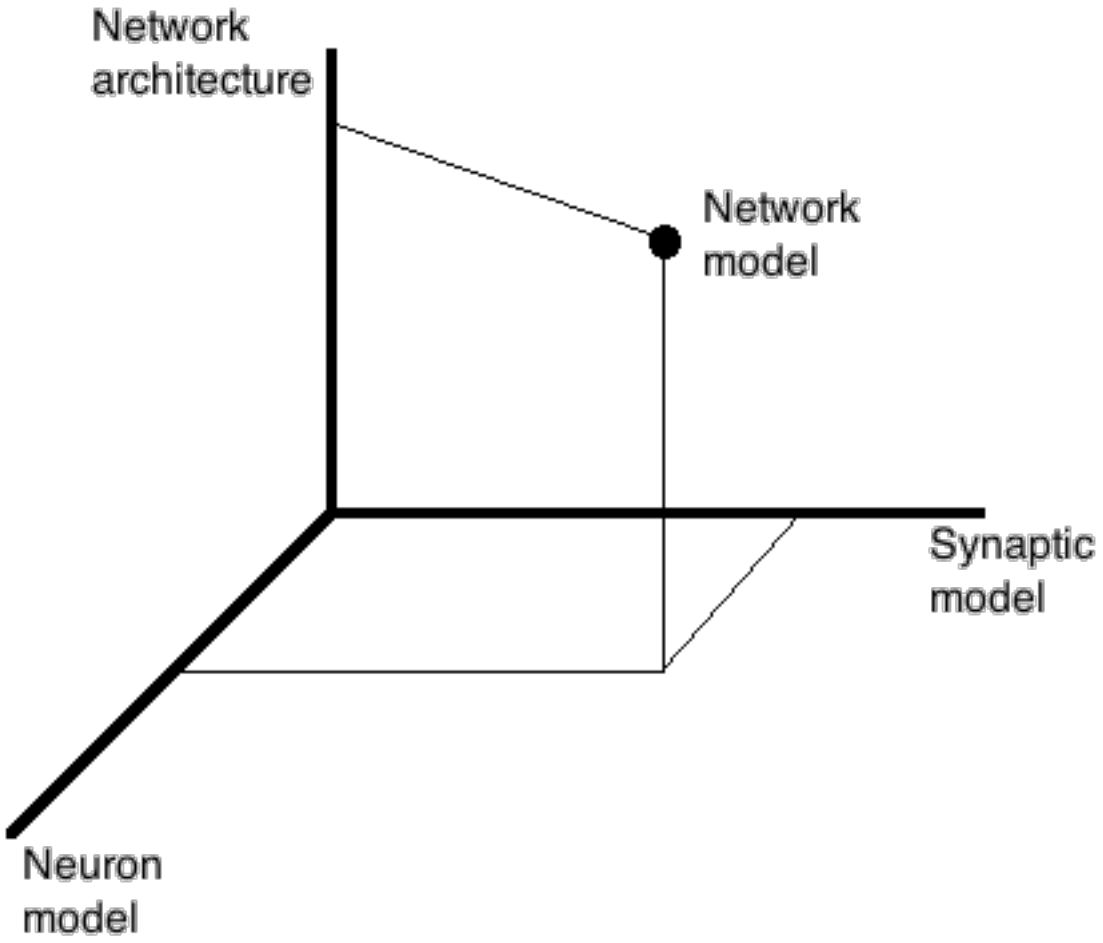
$$I_m = I_C + I_R = C\frac{dV_m}{dt} + G(V_m - E) = I_{inj}$$

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

$$\tau_m = RC$$



3D representation of a network model

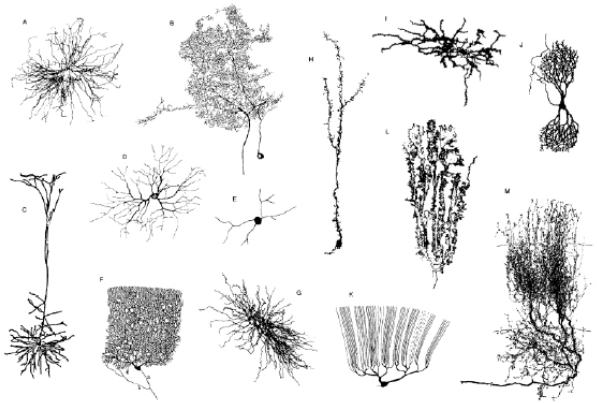


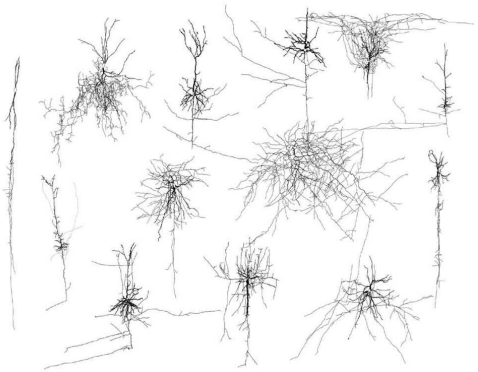
Part 2

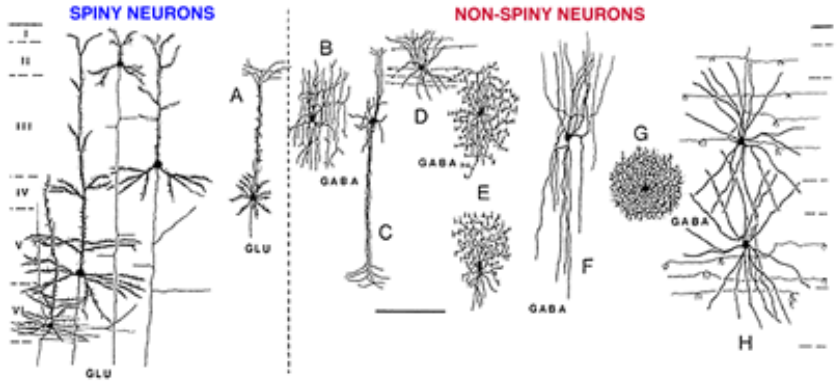
Single neuron models

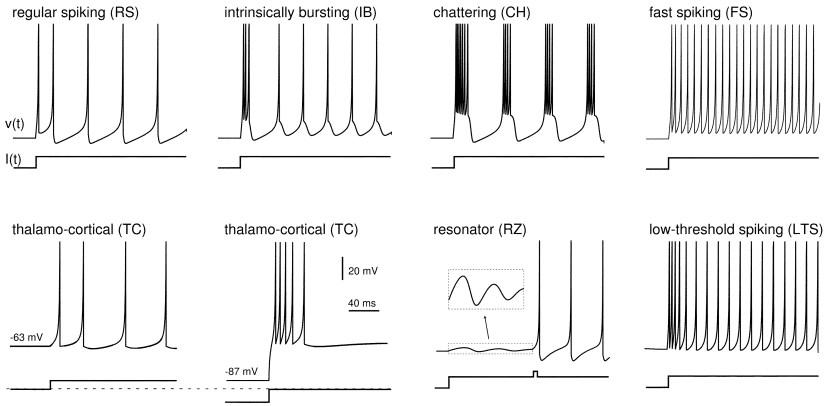
What to model in a neuron model?

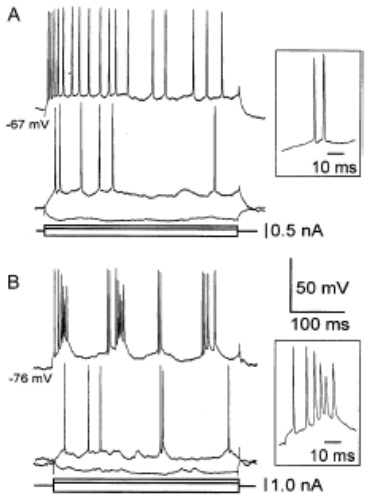
- Morphology (shape, axonal target, smooth or spiny);
- Electrophysiology (spike shape, pattern of spike train);
- Neurochemistry (neurotransmitter released at synapses);

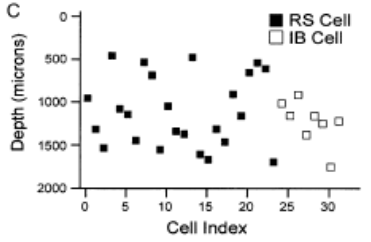








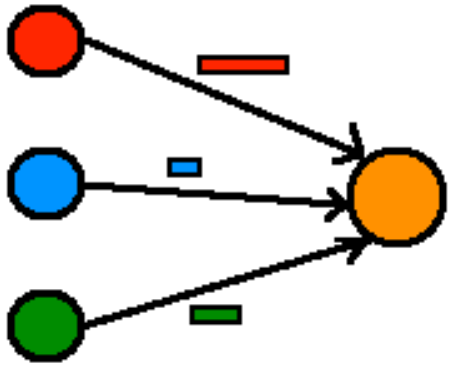


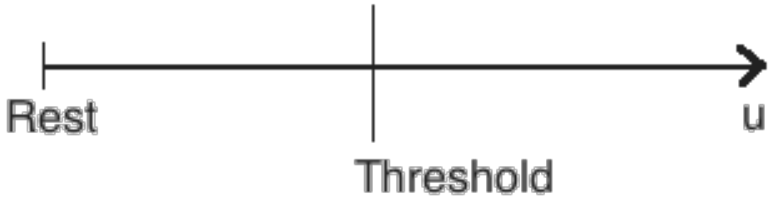


Neuron model

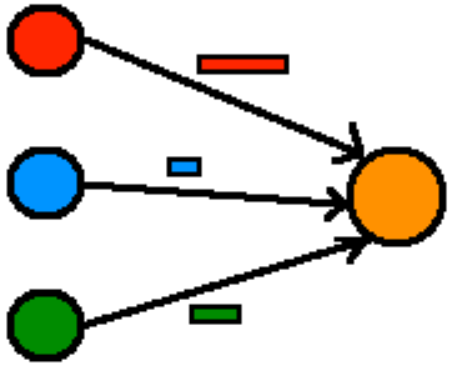
- Deterministic vs. Stochastic
- Firing rate vs. Spiking
- High-dimensional vs. Low dimensional
- More vs. Less Biologically Faithful

Deterministic

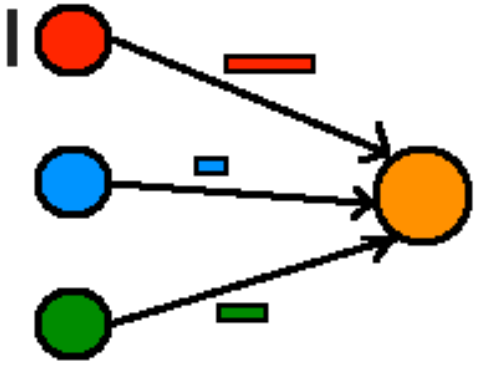




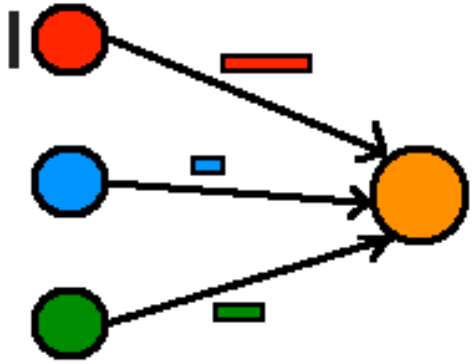
Stochastic

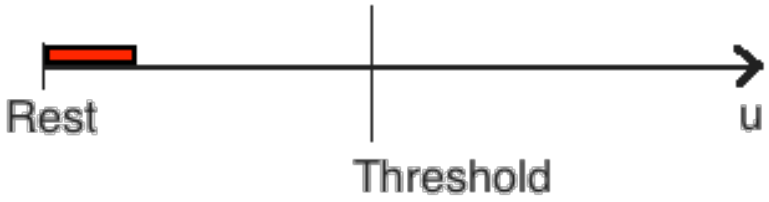


Deterministic

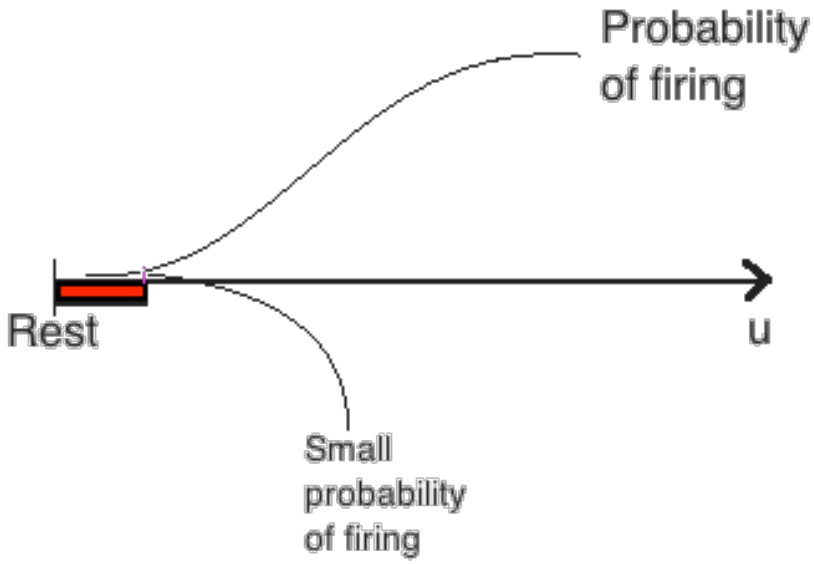


Stochastic

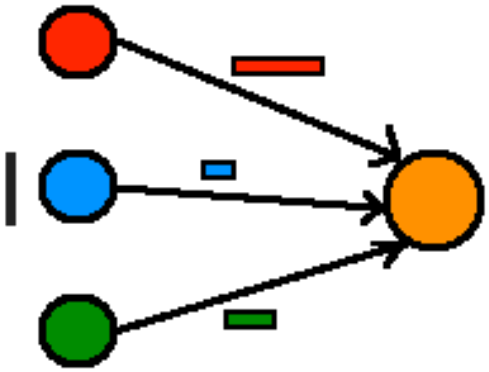




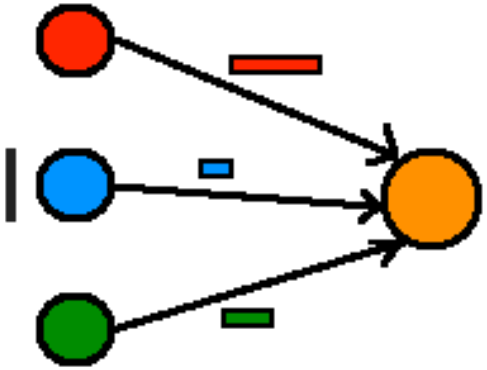
Do not fire

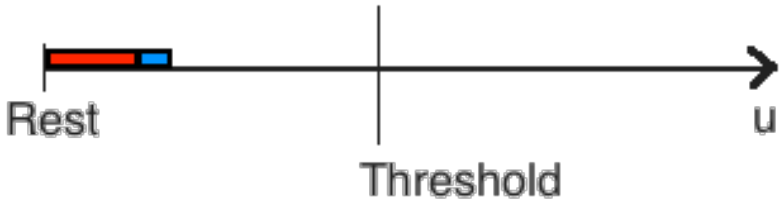


Deterministic

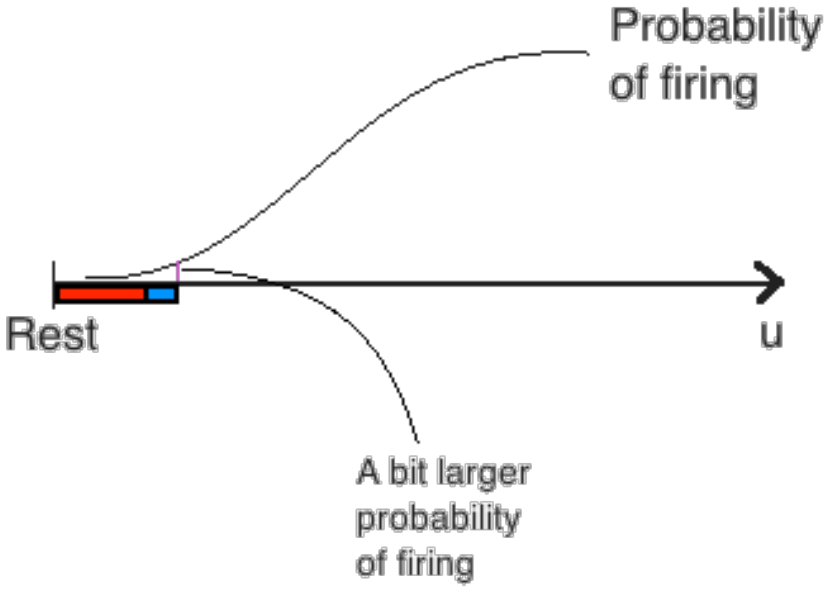


Stochastic

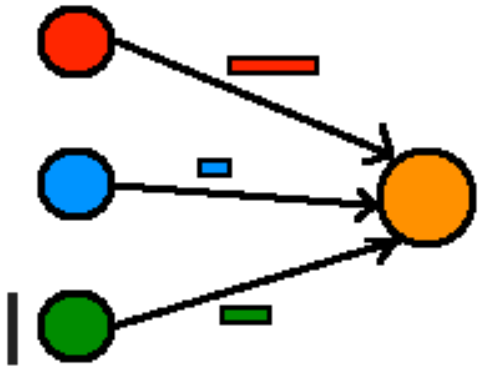




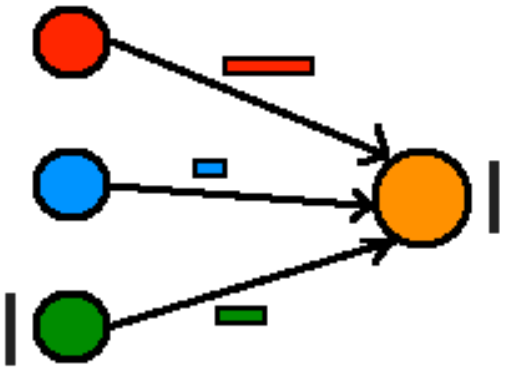
Do not fire

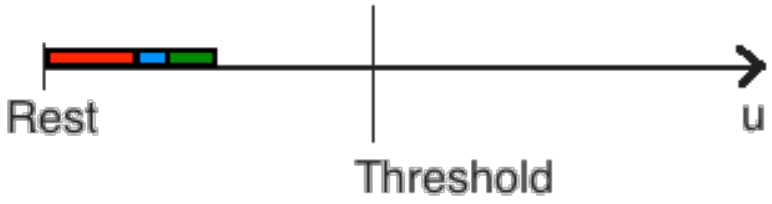


Deterministic

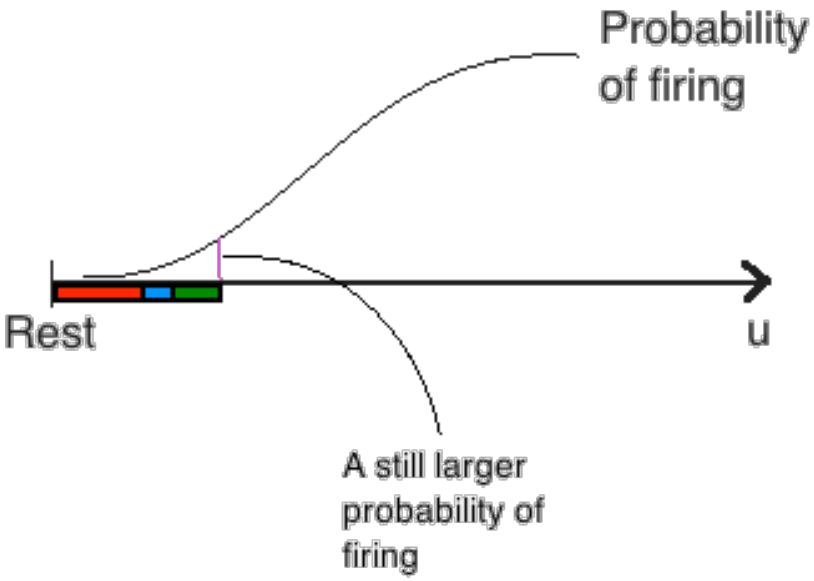


Stochastic



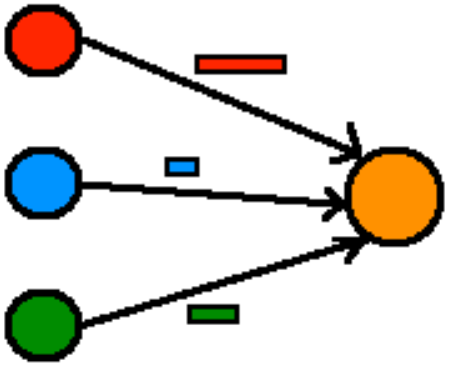


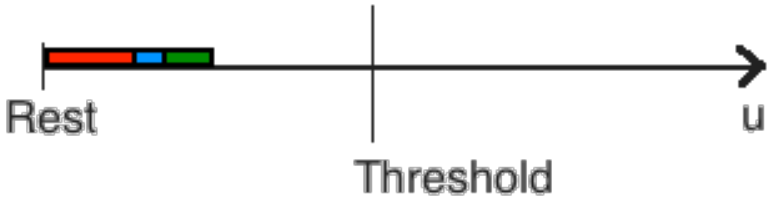
Do not fire



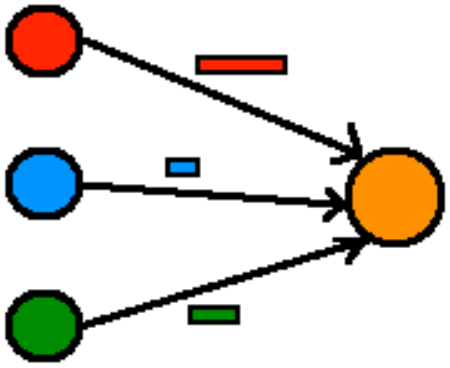
oops, neuron fired!

Deterministic



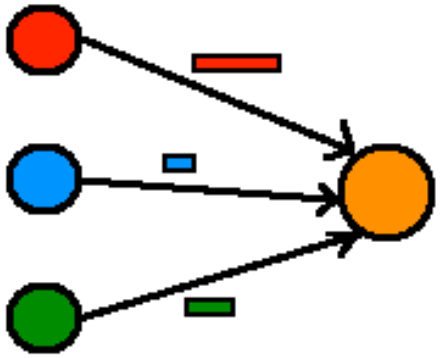


Stochastic

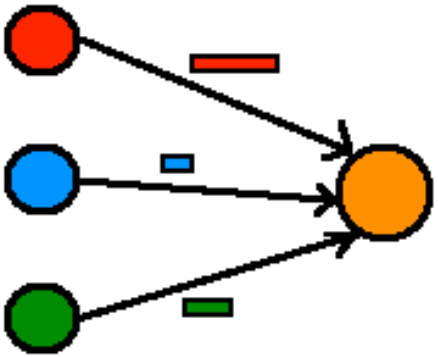


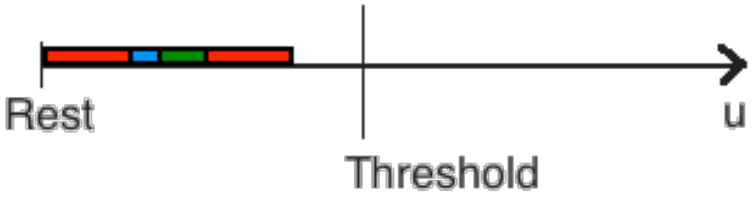
u is reset
after firing

Deterministic



Stochastic





Do not fire

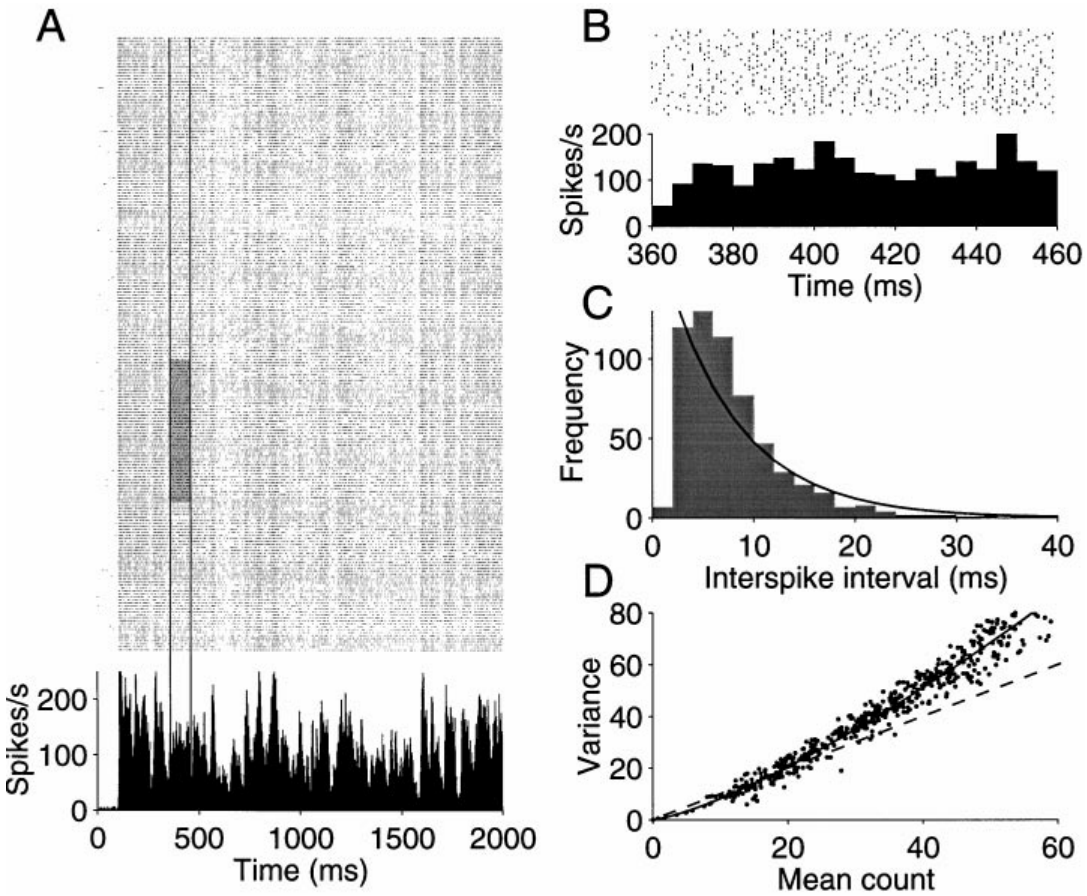
Small
probability
of firing

And so on...

Comments

- Stochastic neuron models may fire in the presence of **subthreshold** inputs
- Firing of stochastic neuron models is **not reproducible**, i.e. repetitions of the previous simulation with the same order of synaptic inputs produce firing patterns with different spike times

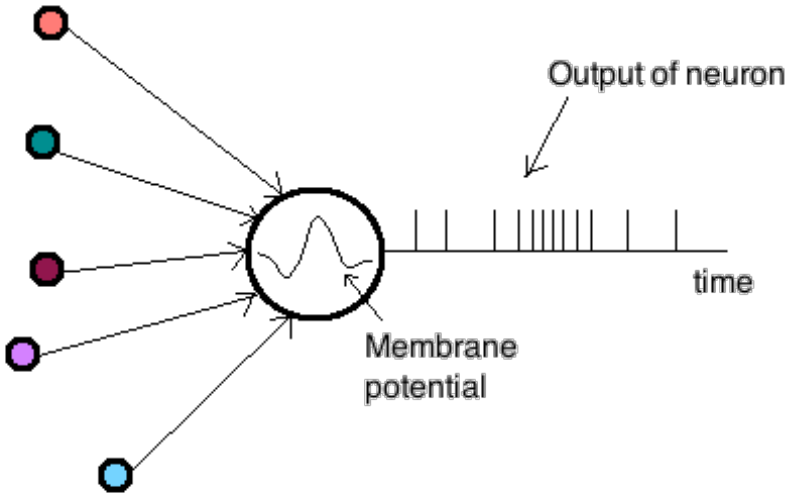
Neurons indeed show response variability



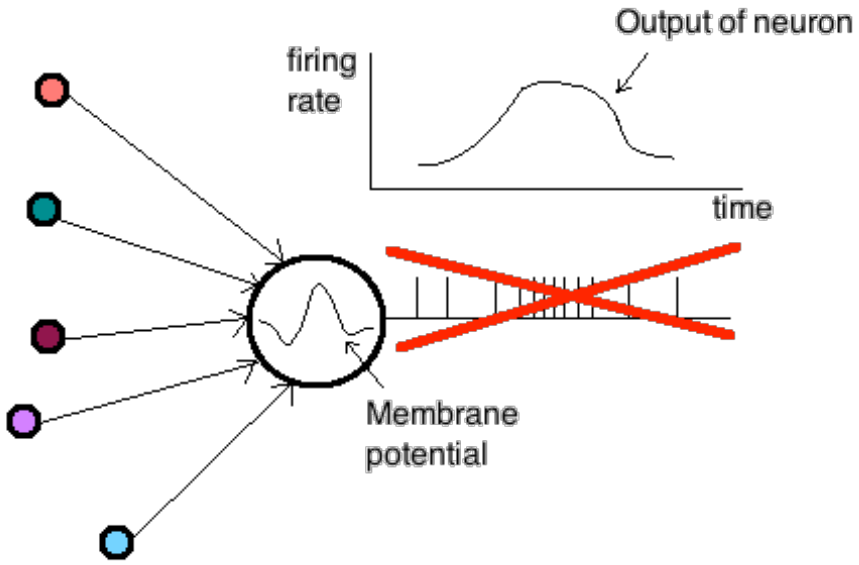
Shadlen & Newsome, 1998

Response variability of a neuron recorded from area MT of an alert monkey. **A**. Raster and PSTH depict responses for 210 presentations of an identical random dot motion stimulus. The motion stimulus was shown for 2 sec. The PSTH plots the spike rate, averaged in 2 msec bins, as a function of time from the onset of the visual stimulus. **Vertical lines** delineate a period in which spike rate was fairly constant. The **gray region** shows 50 trials from this epoch, which were used to construct **B** and **C**.
D. Variance of spike count vs. mean no. of spikes obtained from randomly chosen rectangular regions like the gray one in A. The dashed line is the expected relationship for a Poisson point process.

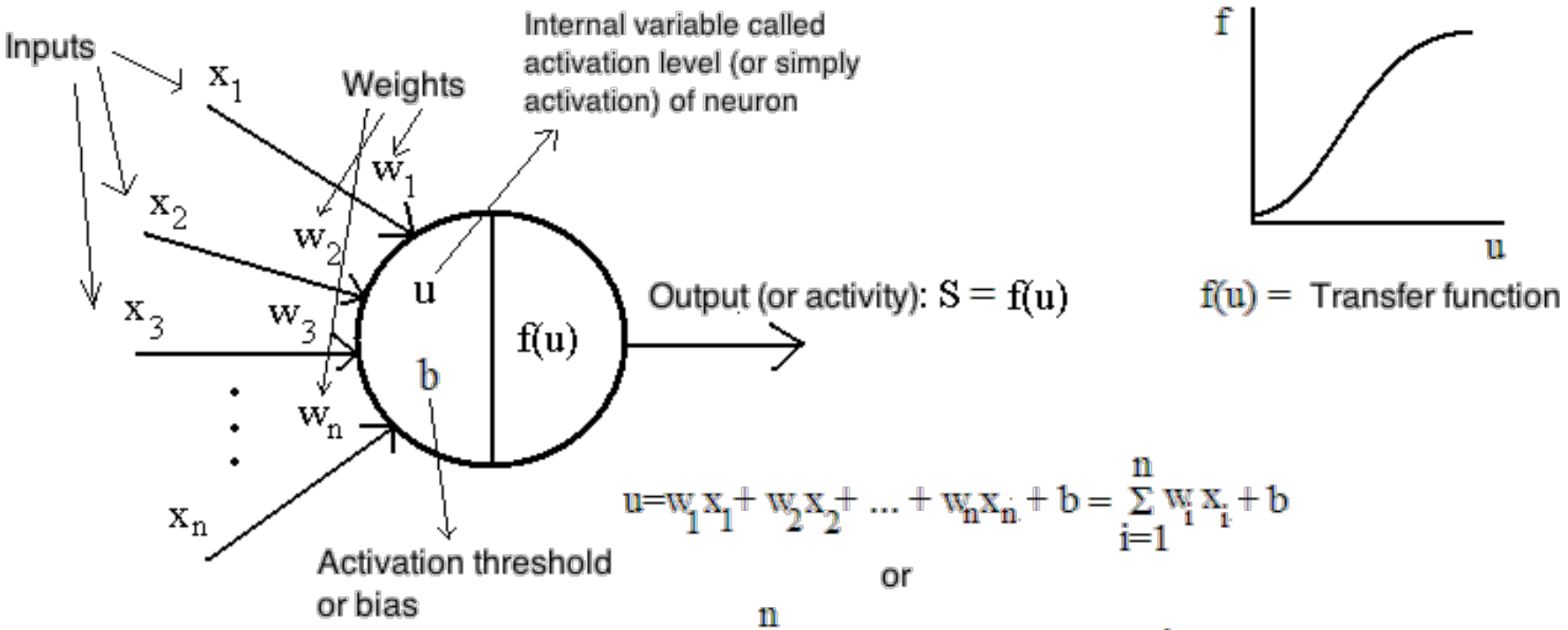
Spiking model



Firing rate model



The firing rate neuron



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

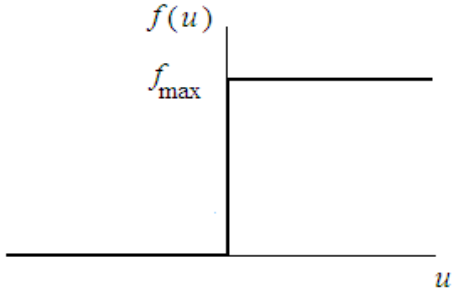
or

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

Transfer functions

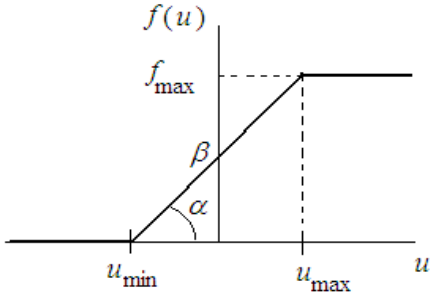
Step function:

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



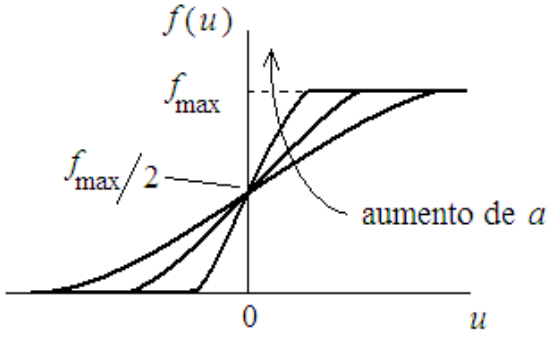
Piecewise linear:

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



Sigmoid
(e.g. logistic):

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



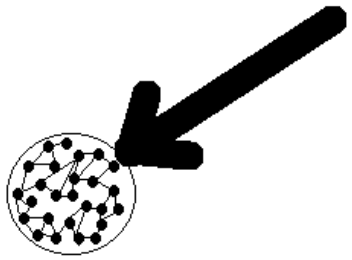
Comments

- 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

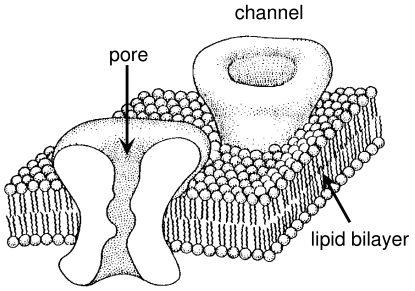
- The dimension of a model is the number of **variables** used by the model: 1, 2, 3, 4, etc
- In general, the higher the number of dimensions of a model, the more difficult to **understand** its behavior
- Each variable has an equation associated to it, so high dimensional models are more **computationally**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

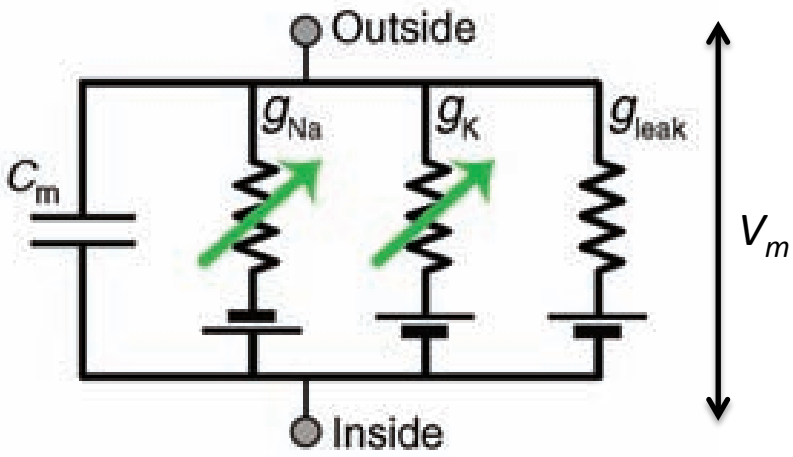
Hodgkin-Huxley model

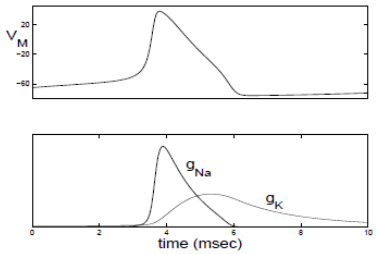
- 4D, single compartment, explicit (based on ionic conductances), spikes naturally generated

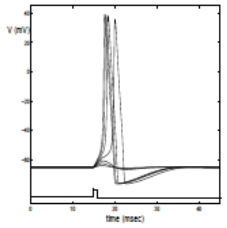


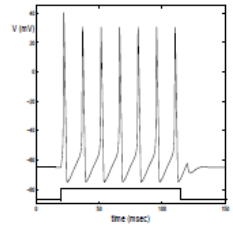
$$C\dot{V} = I - \overbrace{\bar{g}_{K+} n^4 (V - E_{K+})}^{I_{K+}} - \overbrace{\bar{g}_{Na+} m^3 h (V - E_{Na+})}^{I_{Na+}} - \overbrace{g_L (V - E_L)}^{I_L}$$

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







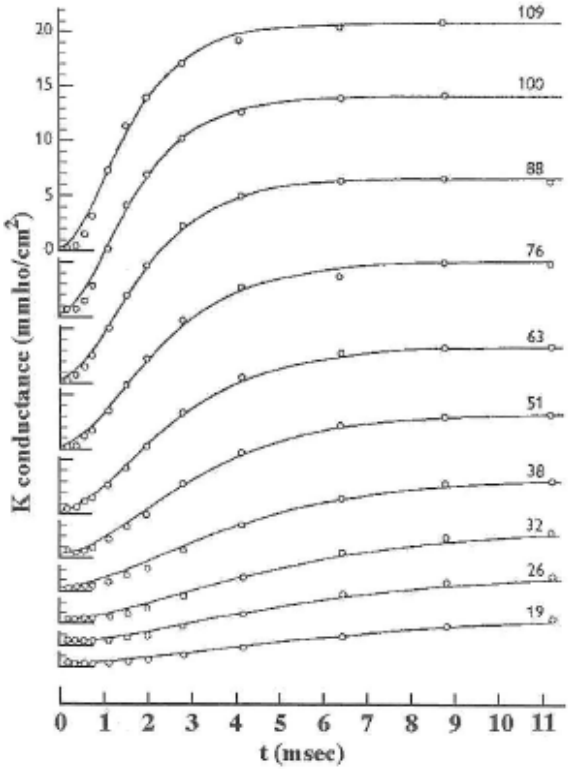


Hodgkin-Huxley model

Mathematical fitting of experimental conductances

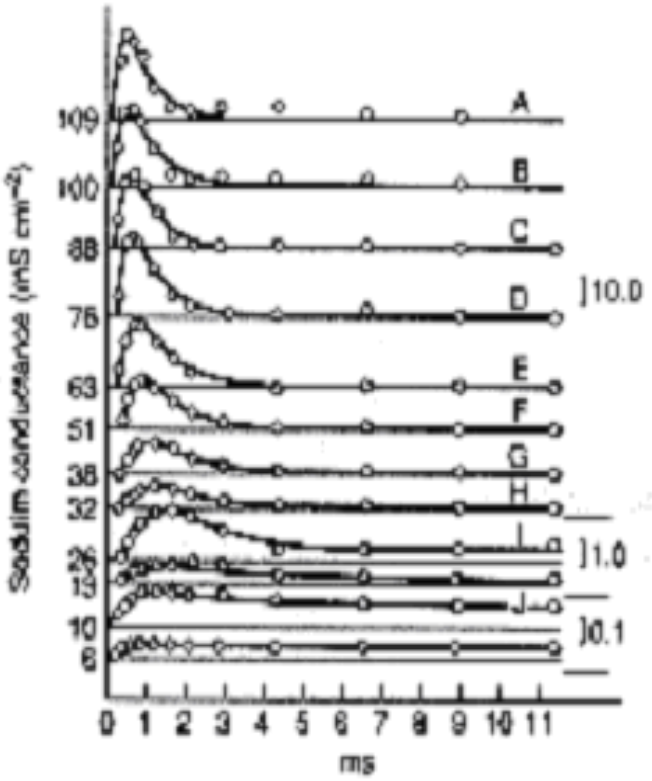
$$C\frac{dV_m(t)}{dt} + G(V,t)(V_m - E_{\text{rev}}) = I_{\text{inj}}(t) \qquad dV_m/dt = 0 \rightarrow$$

$$\rightarrow I_{\text{inj}}(t) = G(t)(V_m - E_{\text{rev}})$$

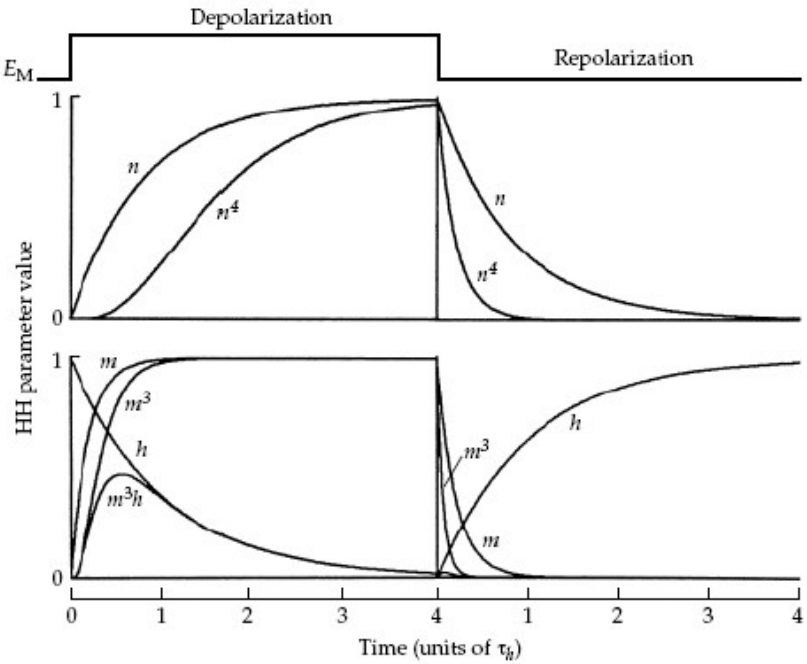


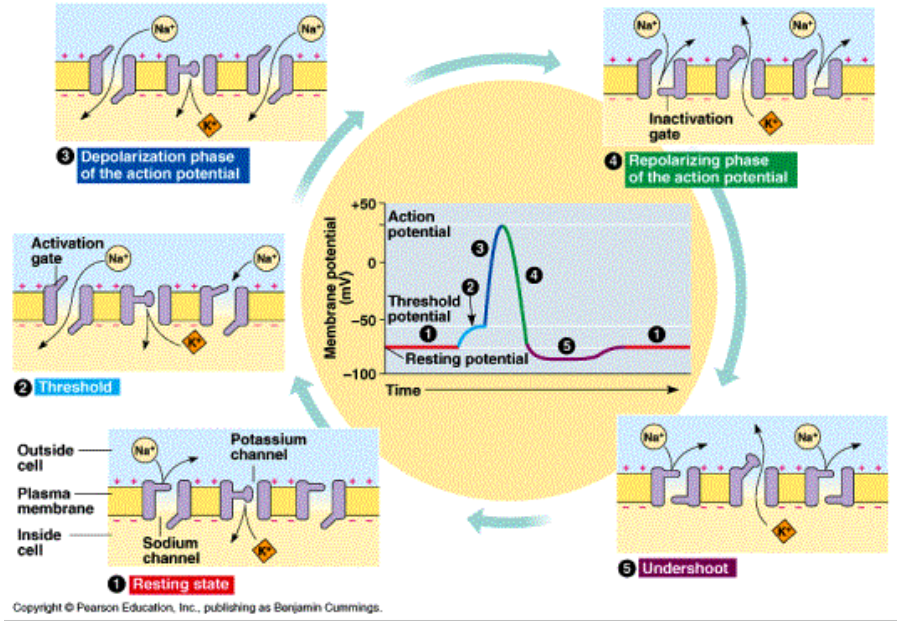
$$g_K(V,t) = \bar{g}_K n^4(V,t)$$

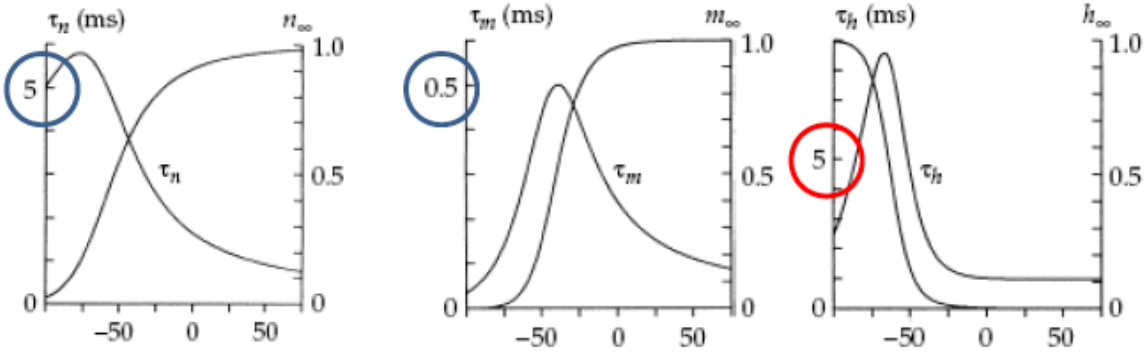
$$n(V,t) = n_\infty(V)\left(1 - e^{-t/\tau_n(V)}\right)$$



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

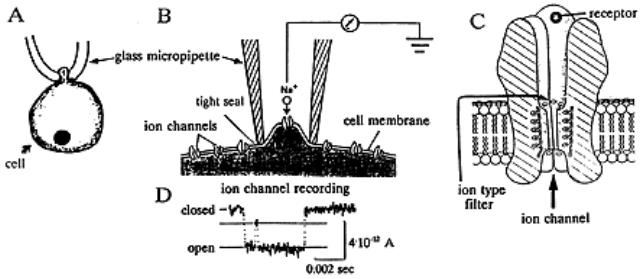

Depolarization
Repolarization
E_M
1
0
n
n^4
n
n^4
HH parameter value
m
m^3
h
m^3h
m^3
h
m
0 1 2 3 4 1 2 3 4
Time (units of τ_h)

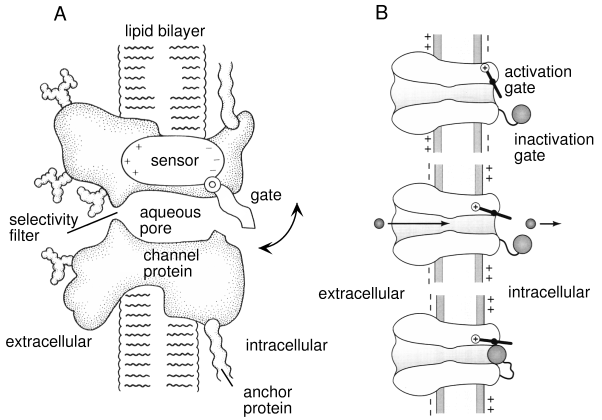

Na+
K+
3 Depolarization phase of the action potential
Inactivation gate
4 Repolarizing phase of the action potential
Activation gate
2 Threshold
Action potential
Threshold potential
Resting potential
Membrane potential (mV)
+50
0
−50
−100
Time
Outside cell
Plasma membrane
Inside cell
Potassium channel
Sodium channel
1 Resting state
5 Undershoot
Copyright © Pearson Education, Inc., publishing as Benjamin Cummings.


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)

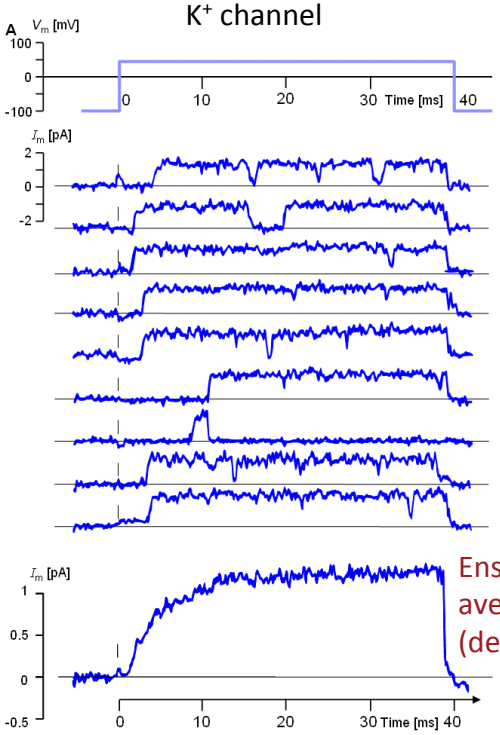
Hodgkin-Huxley formalism

Opening and closing of Individual channels is a stochastic process



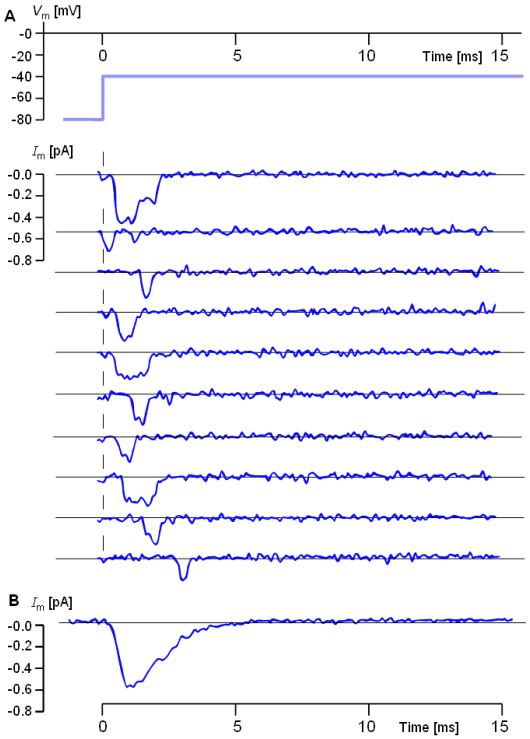


K⁺ channel



Ensemble average (deterministic)

Na⁺ channel

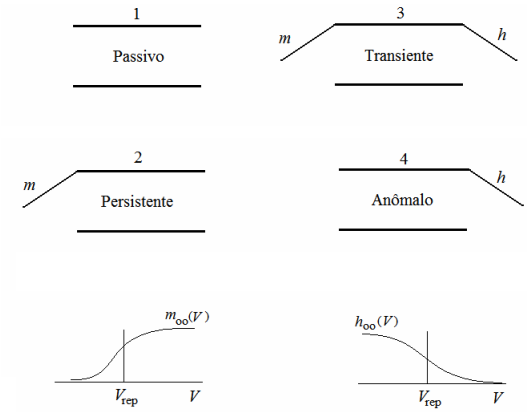


$$I = \bar{g} \cdot p \cdot (V - E)$$

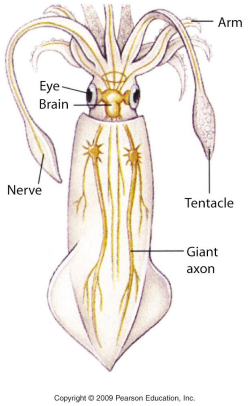
$\bar{g}$ = maximal conductance

p = probability of open channel

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



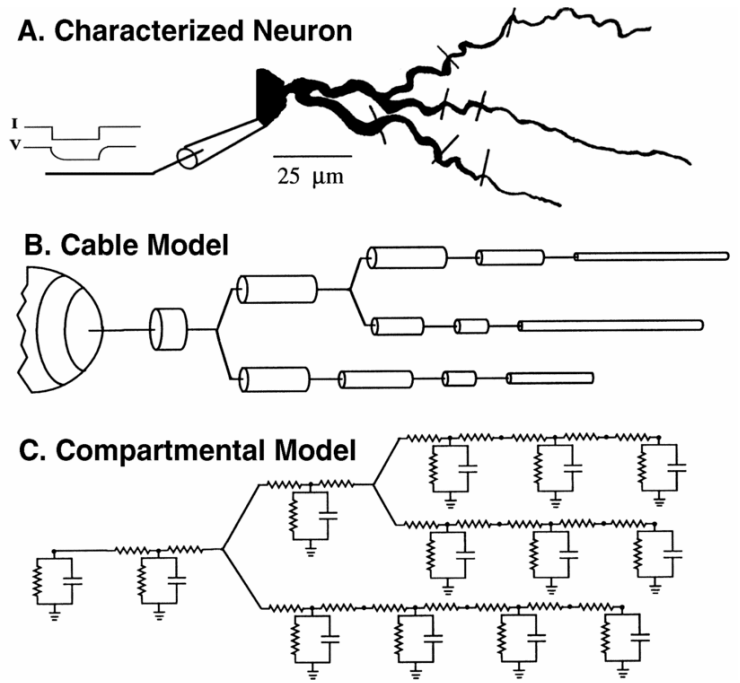
Comment

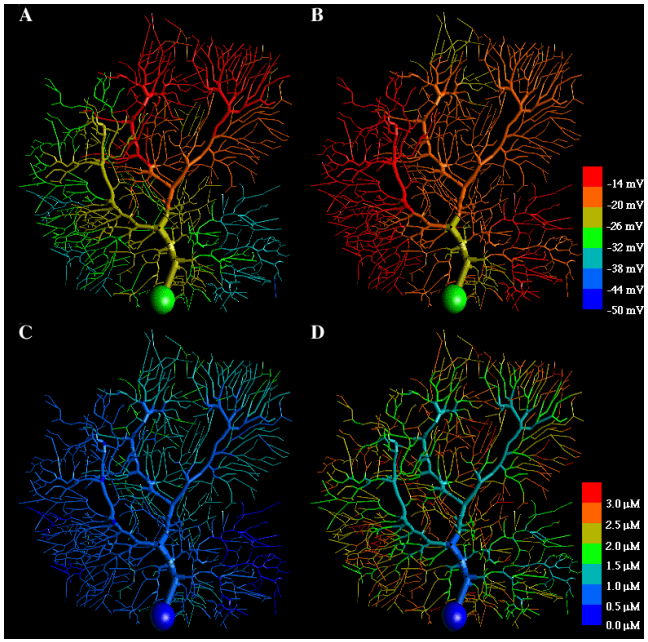


- Hodgkin and Huxley (1952) developed their model to describe action potential generation in the **squid giant axon**
- It is hugely different from mammalian cortical neurons
- But ionic currents in cortical neurons can be described in a similar way, hence “Hodgkin-Huxley-type models”

Detailed compartmental models

- D = $q(m+1)$; q = number of compartments; m = number of conductances
- Used mostly for **single-neuron** modeling





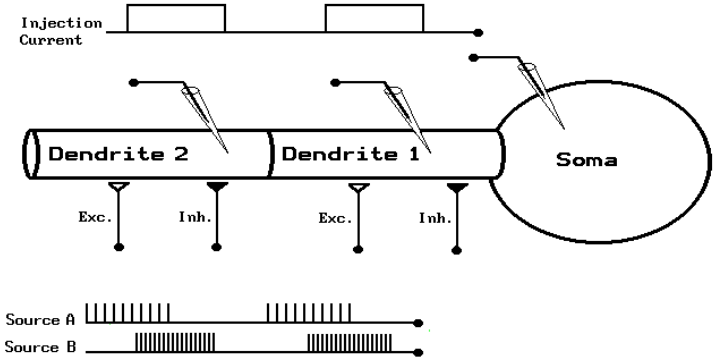
Model of a cerebellar Purkinje cell (De Schutter and Bower, 1994): 4550 compartments.

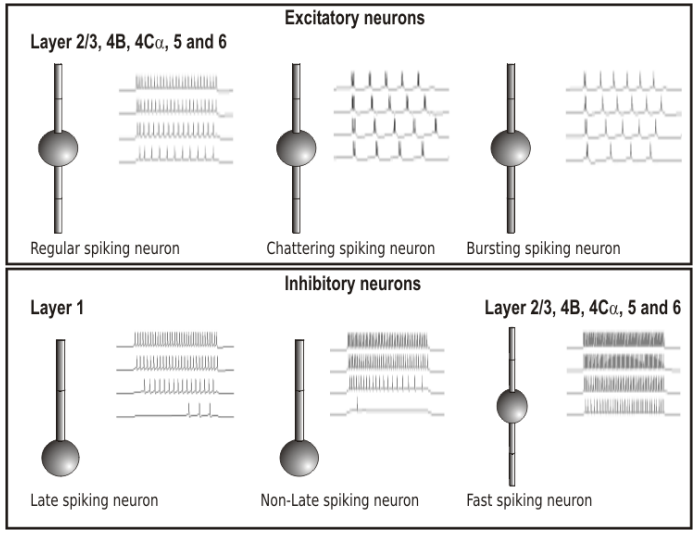
Comment

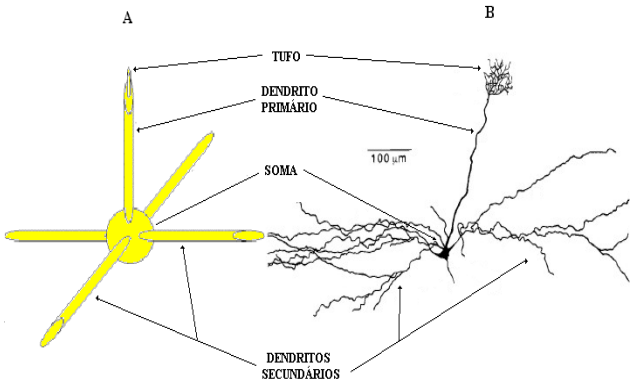
- The addition of more and more compartments to a neuron model seems to be a good strategy to get closer to the "real thing"
- However, increased complexity not necessarily always lead to better models:
  - Each new compartment requires the modeler to decide which conductances to put in it and with what 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?)

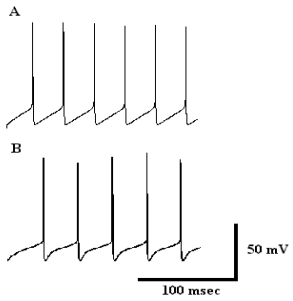
Reduced compartmental models

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





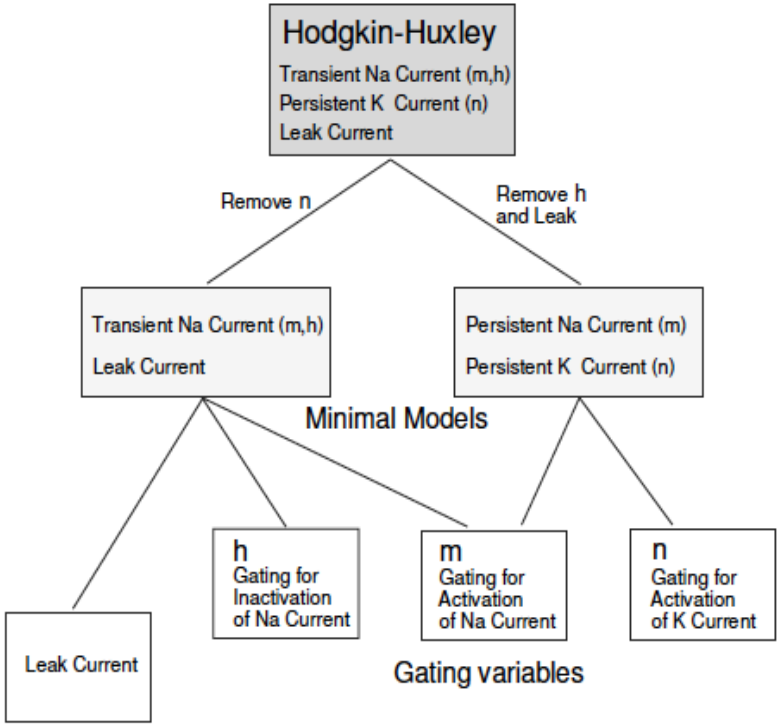




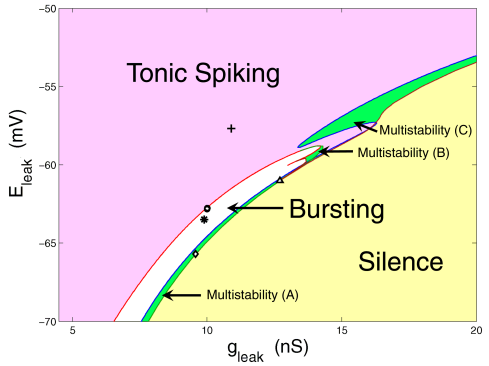
Model

Real

Reduced HH models



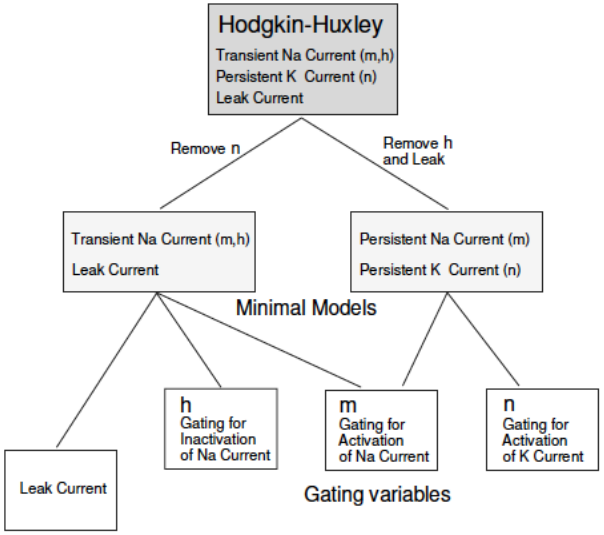
Izhikevich (2007)

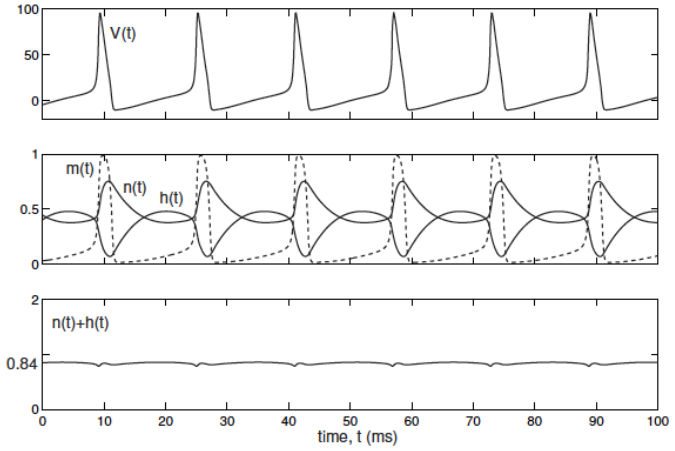


Cymbalyuk

- 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

Reduced HH models

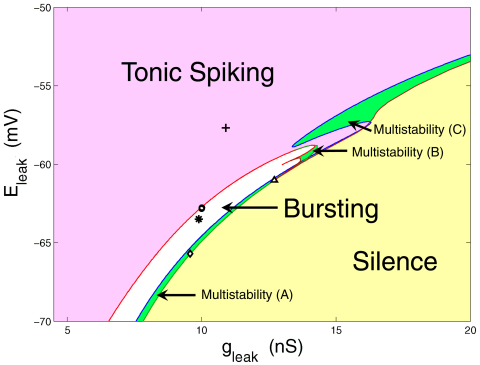


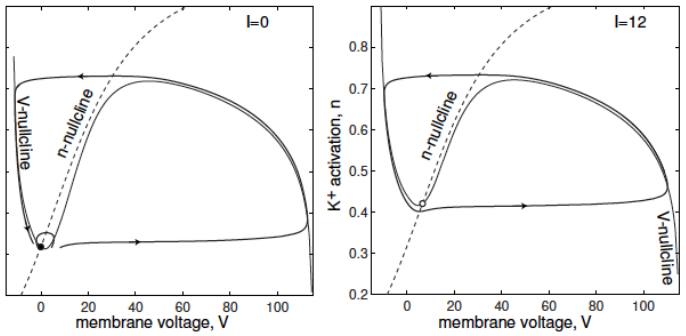


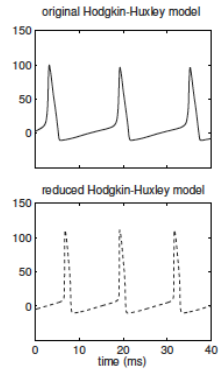
V, m: fast variables
N, h: slow variables

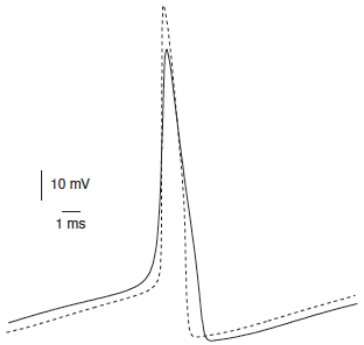
$m(t) \rightarrow m_\infty$
$n(t) = 0.84 - h(t)$

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







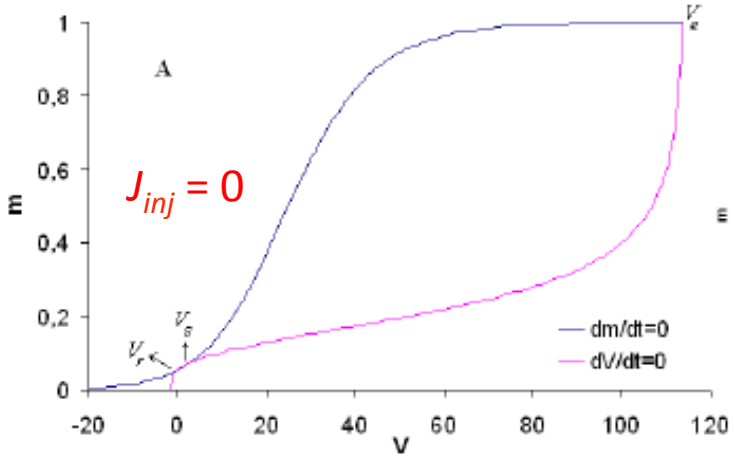


Reduced models can be analyzed in the phase plane using dynamical systems tools: equilibrium points, limit cycles, bifurcations

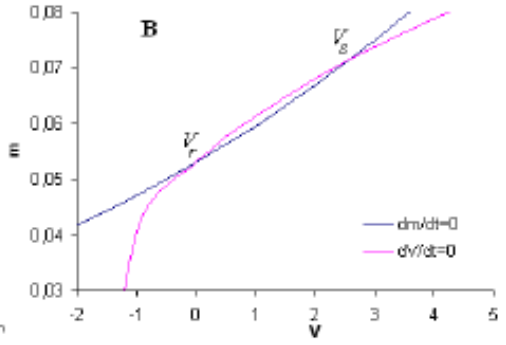
Fast variables (V, m)

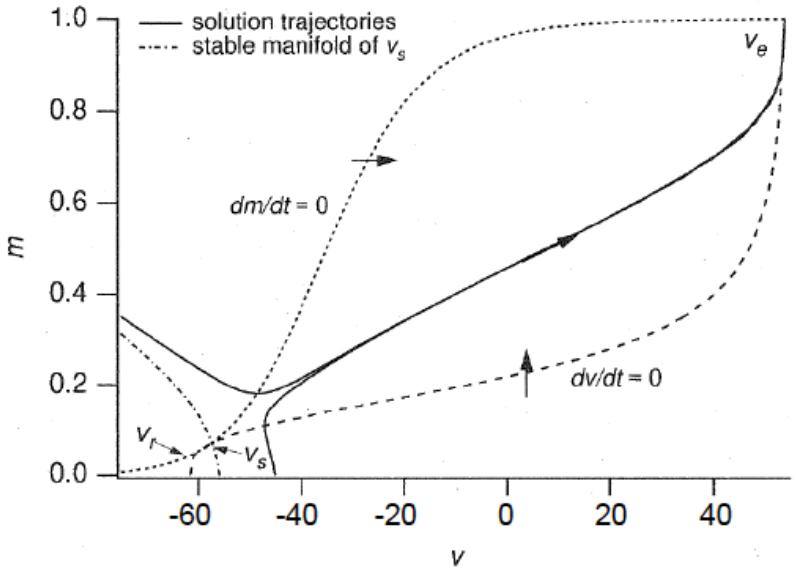
$$C_m \frac{dV}{dt} = -\bar{g}_K n_0^4 (V - E_K) - \bar{g}_{Na} m^3 h_0 (V - E_{Na}) - \bar{g}_V (V - E_V) + J_{inj}$$

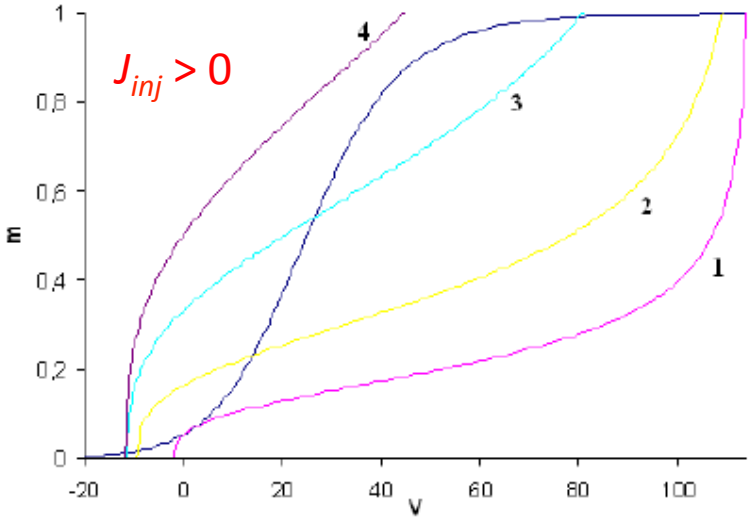
$$\tau_m \frac{dm}{dt} = m_\infty - m$$



nullclines







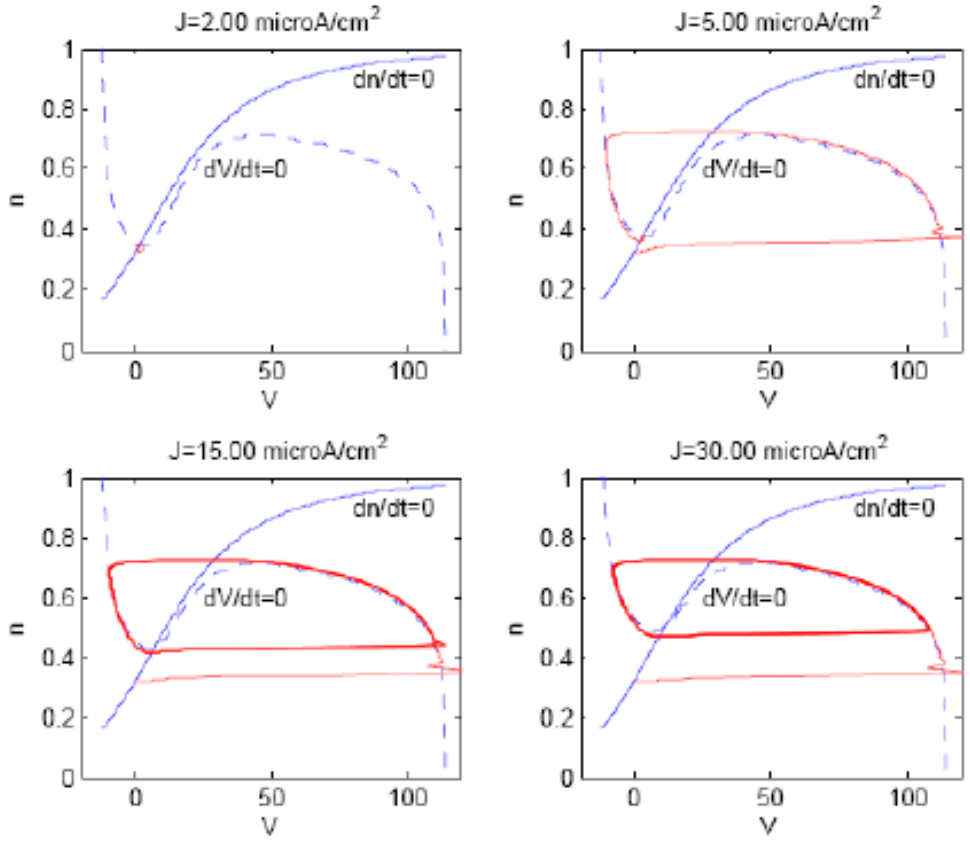
V and *n* (fast and slow variables)

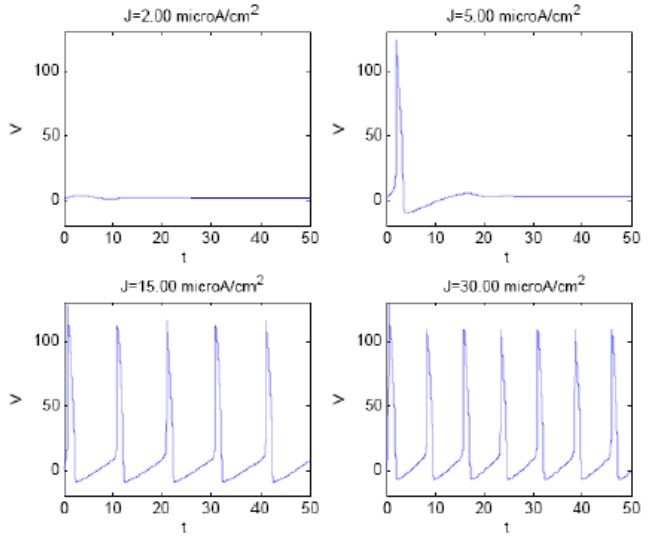
$$C_m \frac{dV}{dt} = -\bar{g}_K n^4 (V - E_K) - \bar{g}_{Na} m_\infty^3 (V)(0{,}8 - n)(V - E_{Na}) - \bar{g}_V (V - E_V) + J_{inj}$$

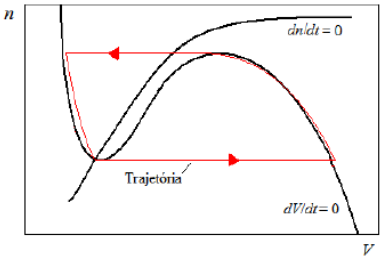
$$\tau_n \frac{dn}{dt} = n_\infty - n$$

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

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







Fitzhugh-Nagumo Model

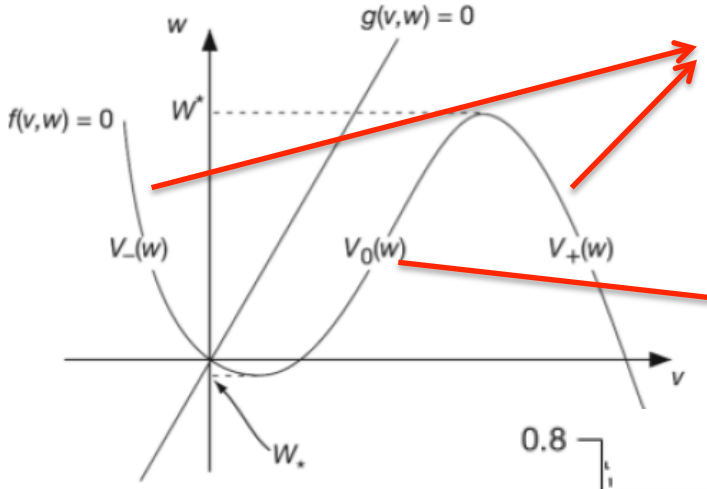
2-D system that has the same qualitative characteristics of the fast-slow phase plane

Cubic

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

v = voltage;

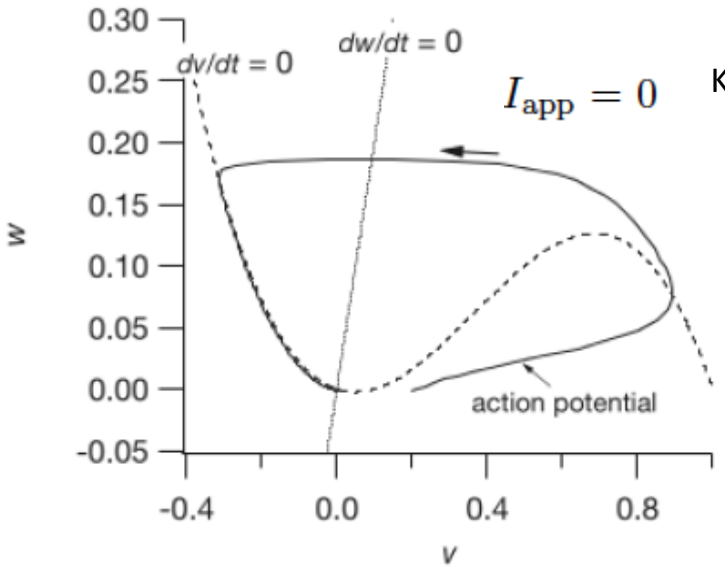
w = recovery variable



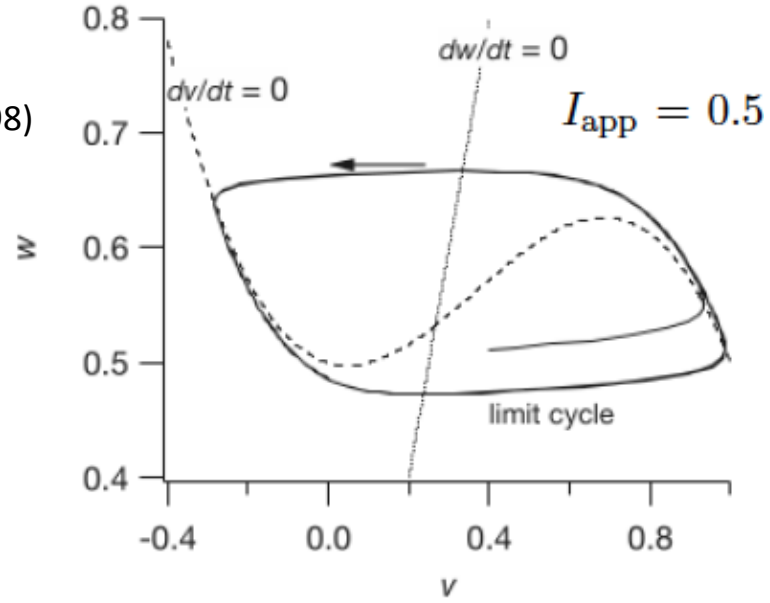
Stable branches

Unstable branch

Keener & Sneyd (1998)

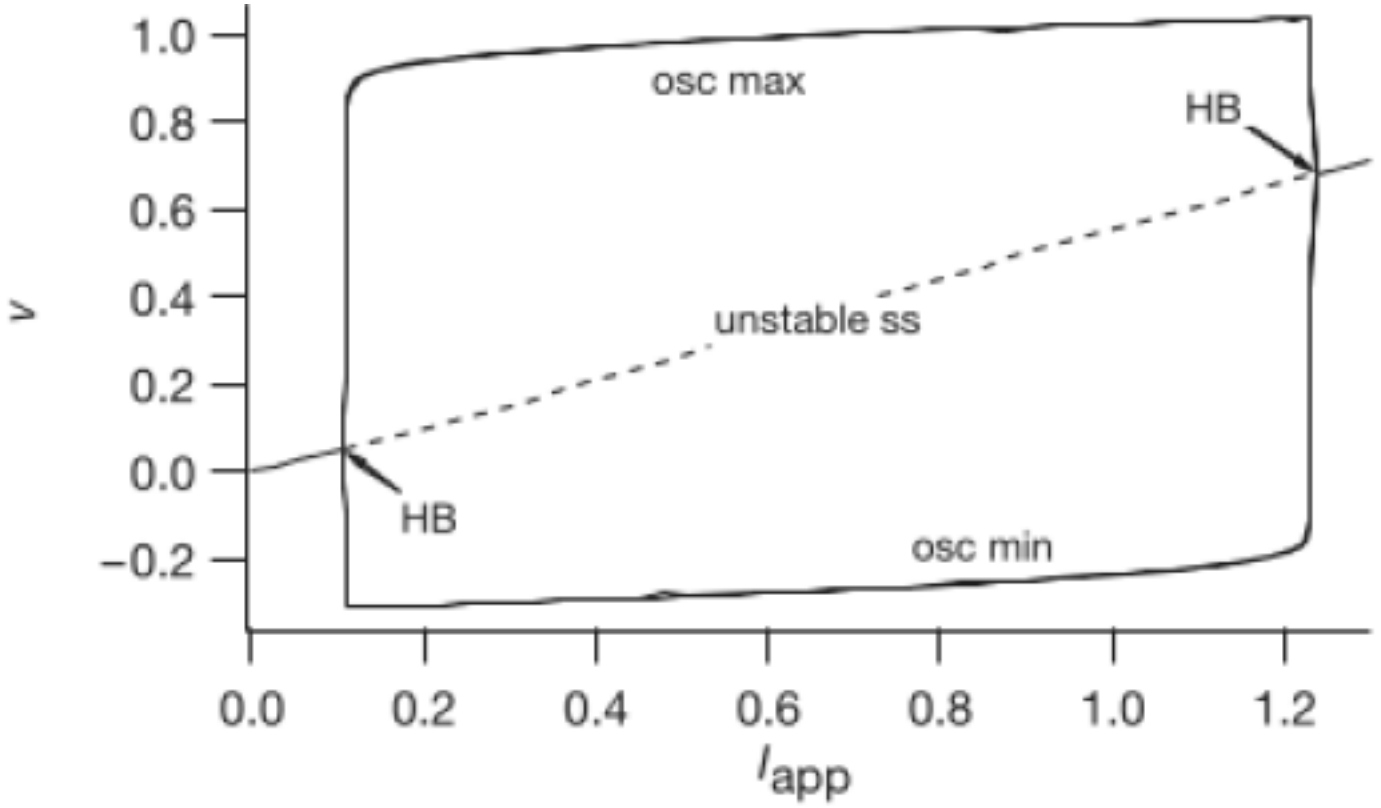


System has a stable resting state and is excitable



The resting state is unstable and there is a periodic orbit

Fitzhugh-Nagumo model (Bifurcation diagram)



Keener & Sneyd (1998)

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

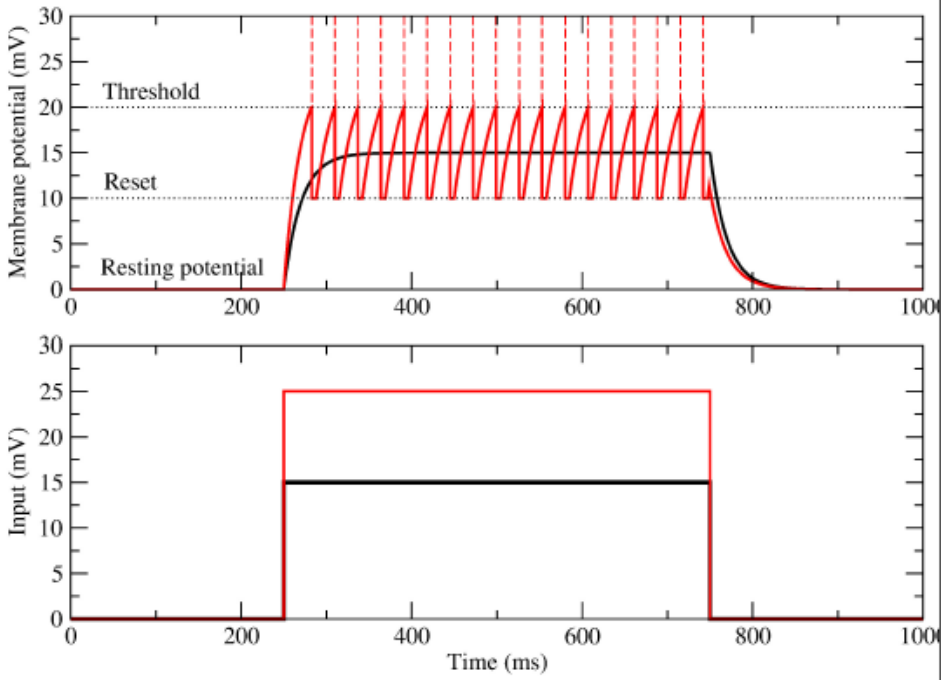
$$I_{\mathrm{th}} = \frac{V_{\mathrm{th}} - V_{\mathrm{rest}}}{R}$$

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

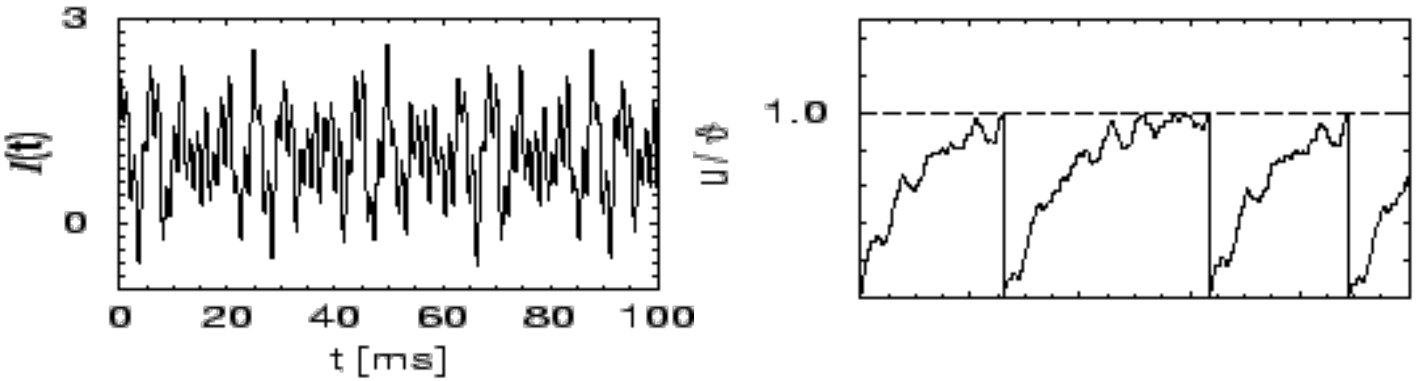
$$\tau \frac{dV}{dt} = -\left(V - V_{\mathrm{rest}}\right) + R \cdot I$$

- 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 $I(t)$



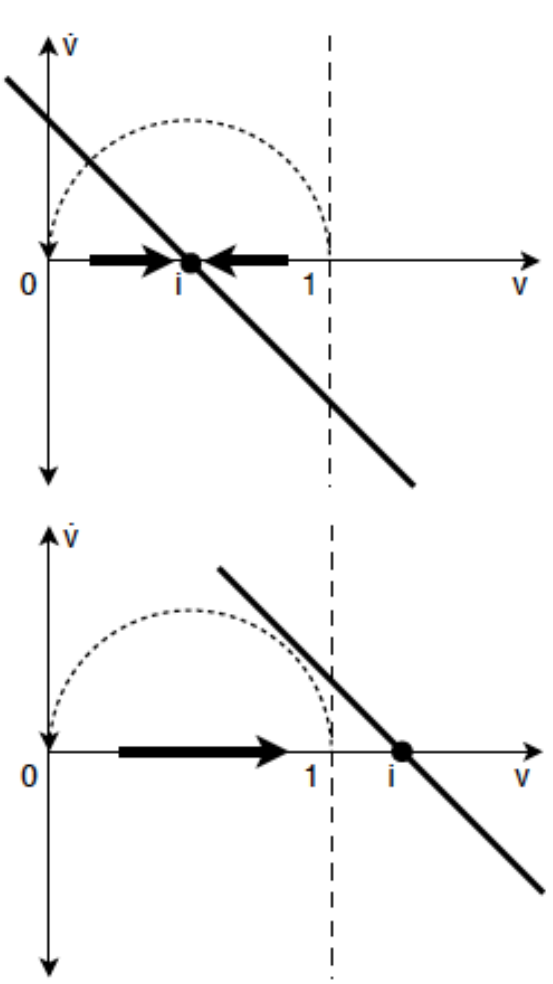
Dynamics of the LIF model

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

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

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

  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

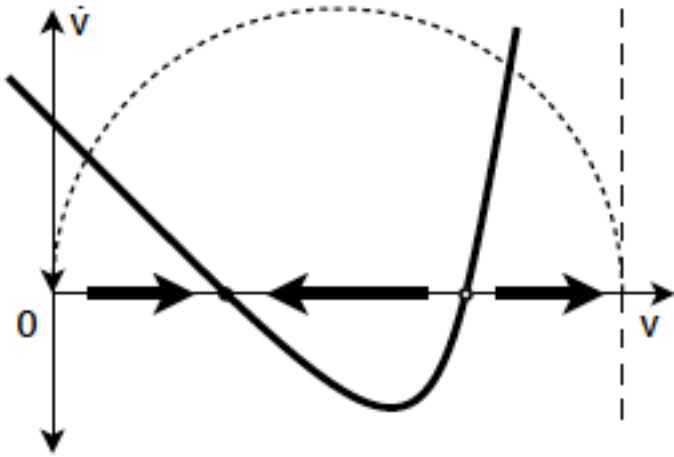
- Extensions of the LIF model given by

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

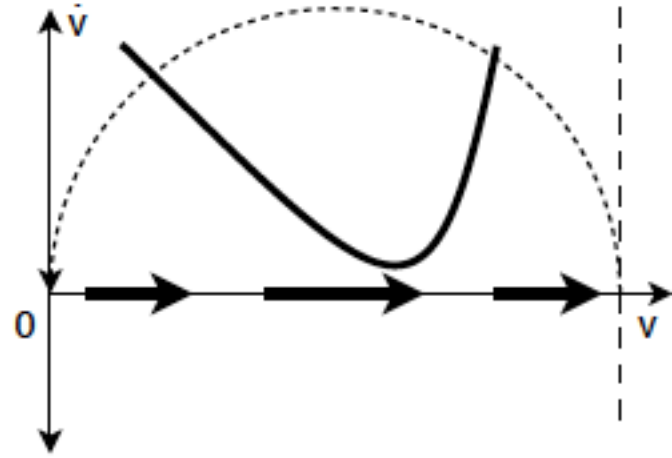
with

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

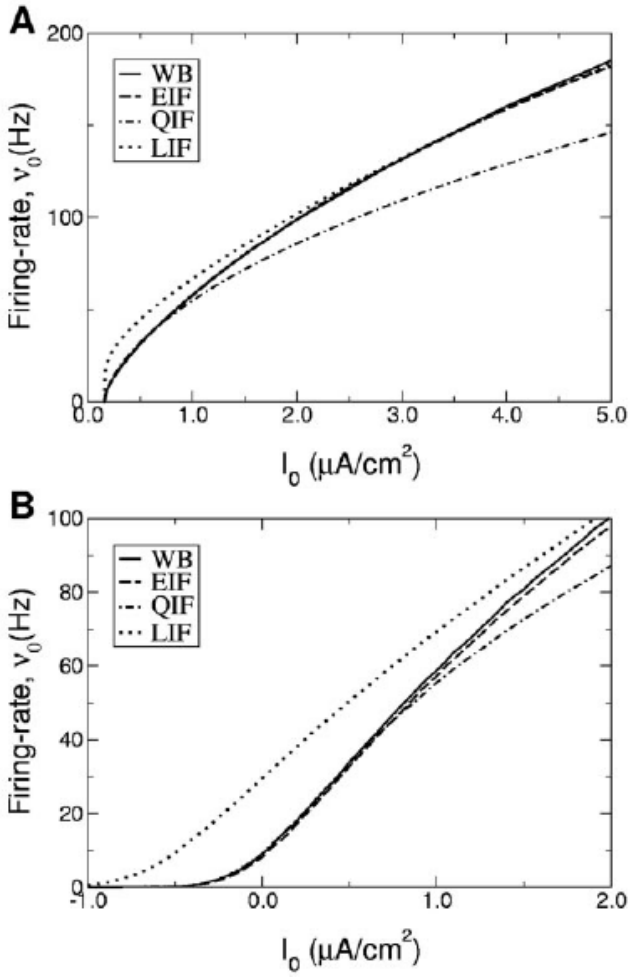
$$\phi(v) = -v + ae^{v-b} \quad \text{(exponential IF model, EIF)}$$



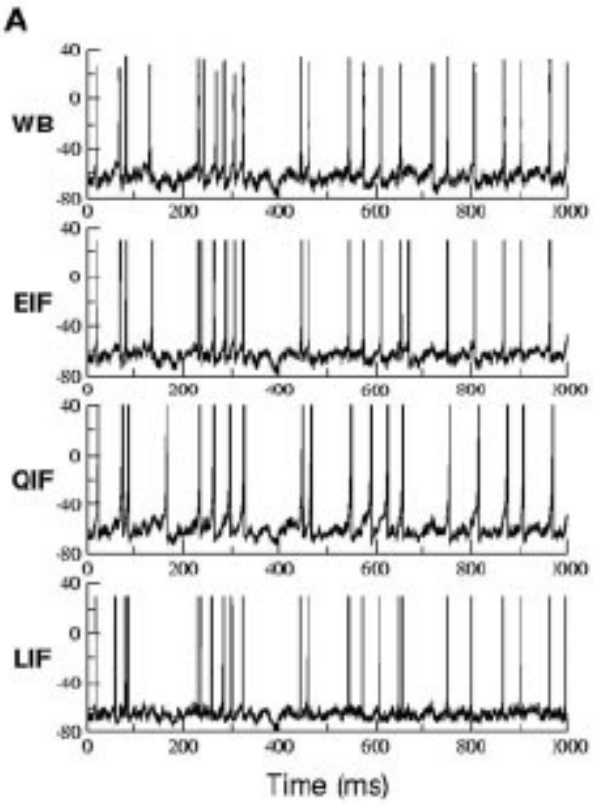
- The black dot in the top graph is a stable fixed point and the white dot is an unstable fixed point
- The voltage value of the white dot is the critical voltage for spike initiation by a short current pulse
- The bottom graph shows the case for a constant super-threshold current: the result is repetitive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

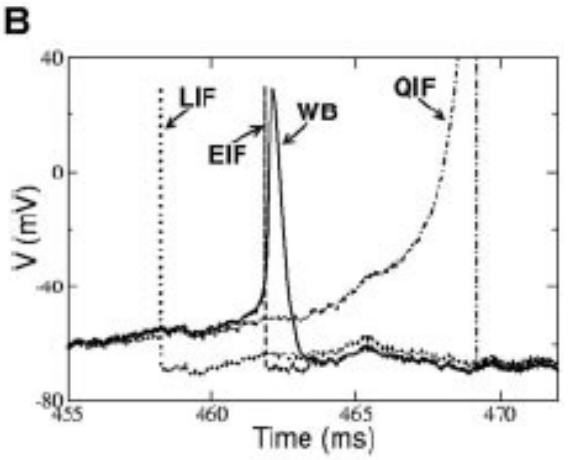


Firing behavior of IF models



F-I curves of IF models for a constant input current (**A**) and a noisy input current (**B**)

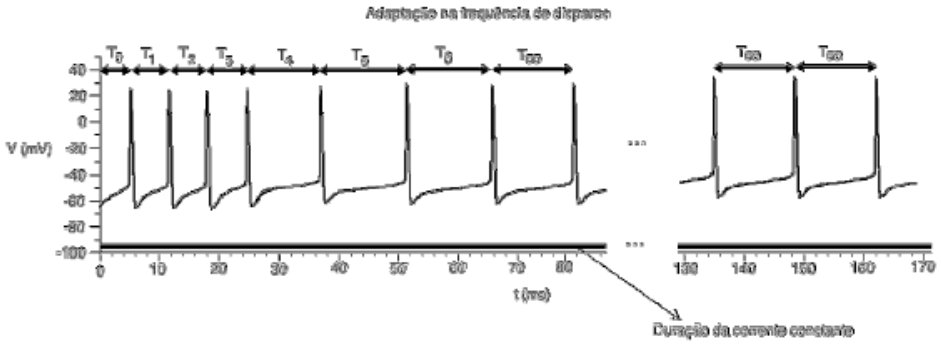




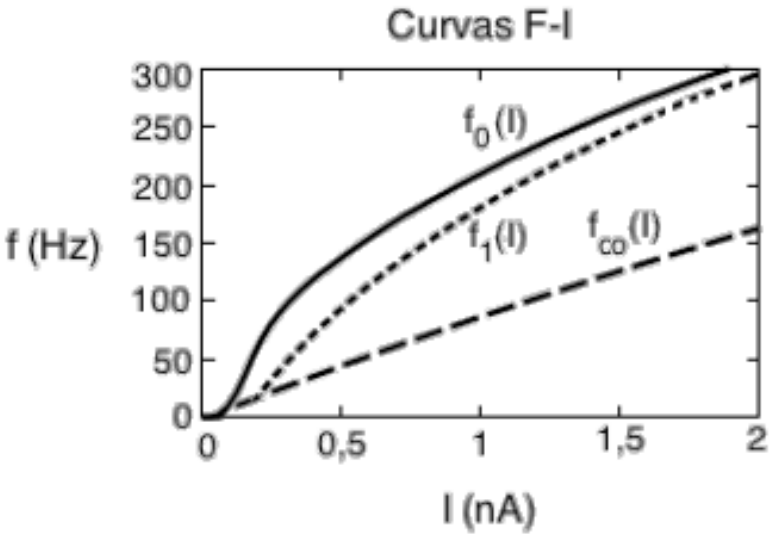
Voltage traces of IF models for the same noisy input current. **B** shows a higher resolution for a short time interval in which a spike has been generated in all models

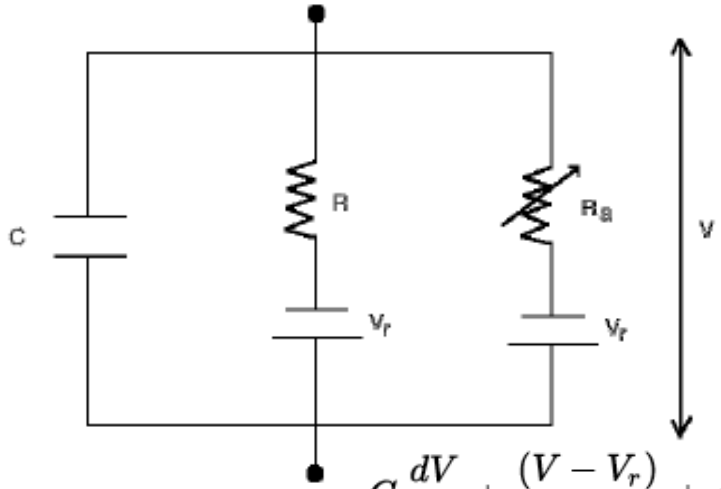
Fourcaud-Trocmé et al. (2003)

LIF with adaptive variable



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





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

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

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

g_a is incremented after each spike so that the stronger I_a current forces the voltage to V_r, thus making it more difficult for the voltage to reach threshold

Izhikevich model

Quadratic integrate-and-fire with recovery variable (*v* and *u*).

v nullcline: quadratic

u nullcline: linear

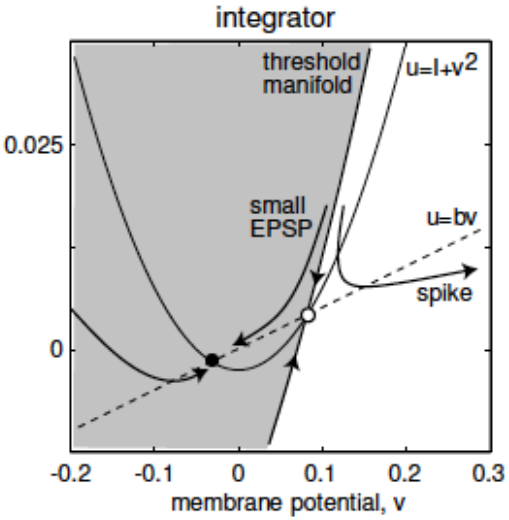
$$v' = 0.04v^2 + 5v + 140 - u + I$$

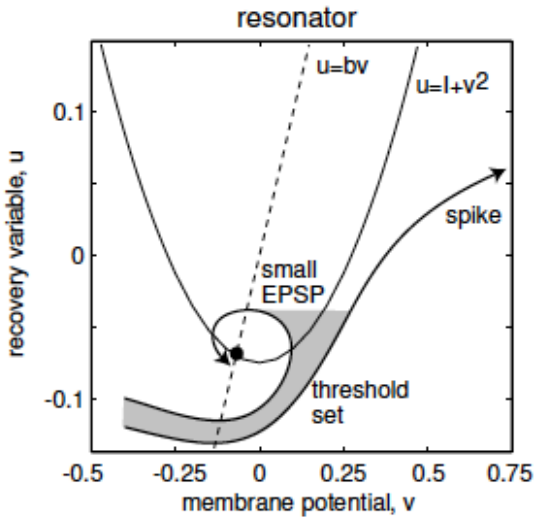
$$u' = a(bv - u)$$

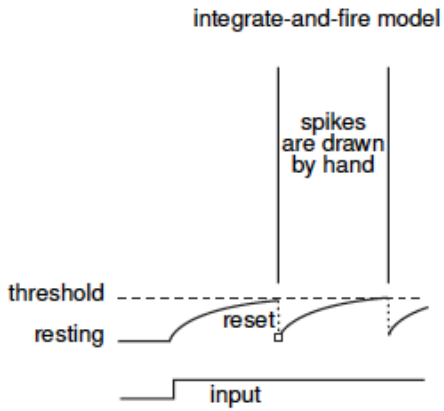
$$\text{if } v \geq 30\,\text{mV}, \text{ then } \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases}$$

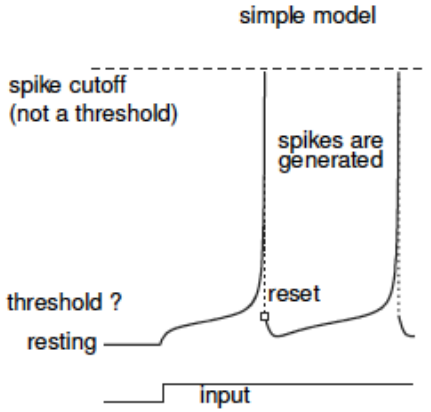
v can escape to infinity (modeling spike initiation) but the voltage is reset when it reaches the peak value (defined by hand).

In the Izhikevich model the voltage reset occurs not at the threshold but at the peak of the spike









Izhikevich, 2007

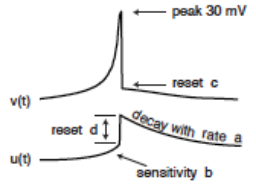
Izhikevich model

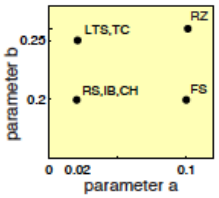
By adjusting the four parameters (*a*, *b*, *c*, *d*) of the model to experimental data, Izhikevich was able to mimic the firing behavior of a large number of cell types

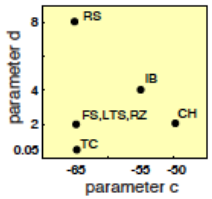
$v' = 0.04v^2 + 5v + 140 - u + I$

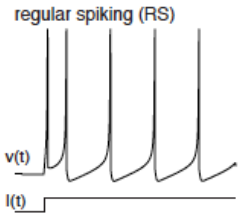
$u' = a(bv - u)$

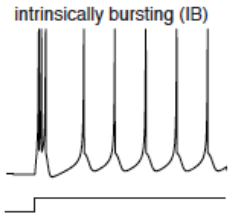
If $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$

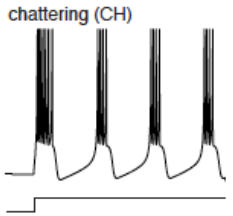


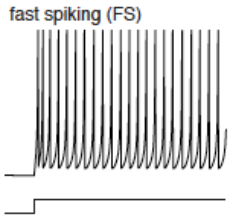


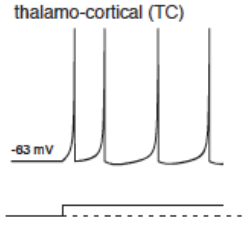


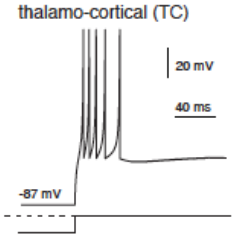


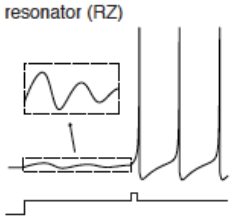


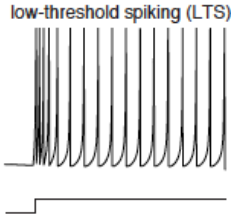


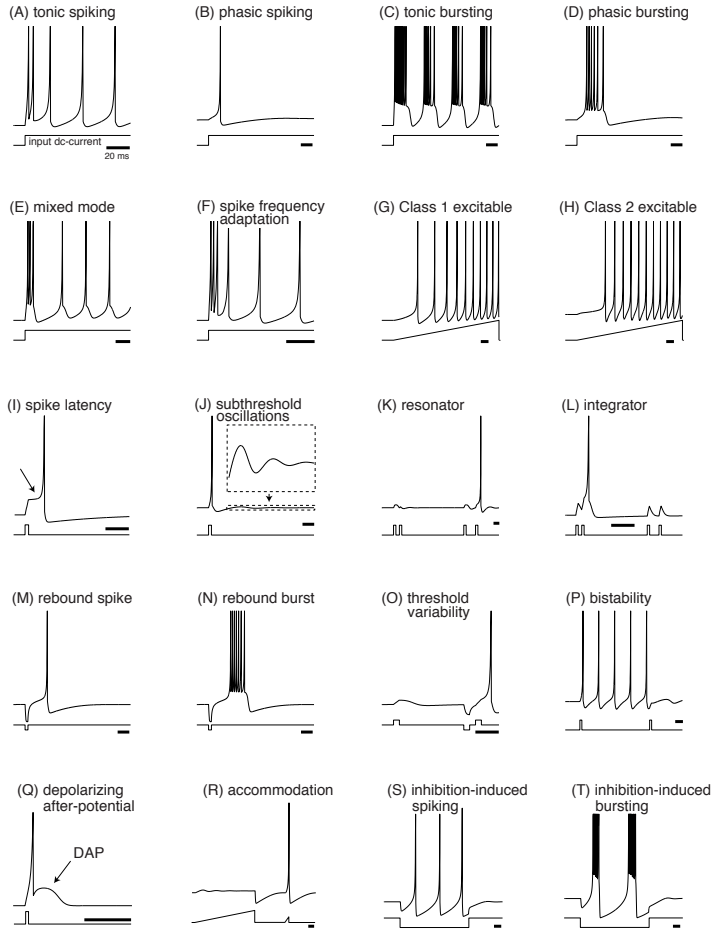












www.izhikevich.com

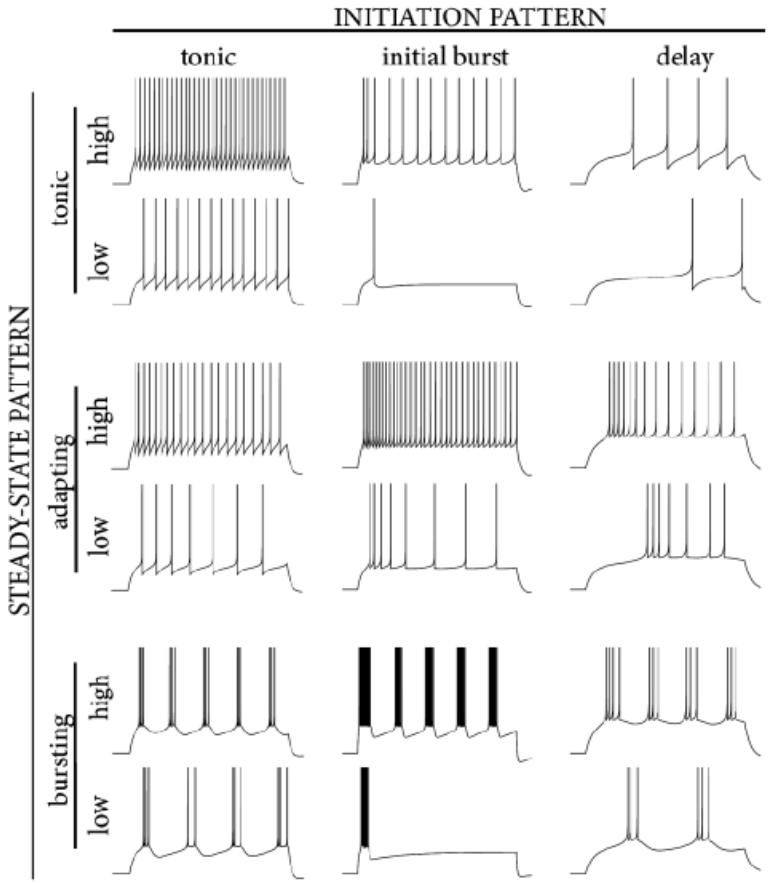
Adaptive EIF model (AdEx)

Exponential integrate-and-fire with recovery variable (*v* and *u*)

$$\tau_V \frac{dV}{dt} = -(V - V_r) + \Delta_L \exp\left(\frac{V - V_L}{\Delta_L}\right) - Ru + RI$$

$$\tau_u \frac{du}{dt} = a(V - V_r) - u$$

$$\text{se } V \geq V_{\text{pico}}, \quad \text{então} \quad \begin{cases} V \leftarrow V_{\text{reset}} \\ u \leftarrow u + b. \end{cases}$$



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

AdEx vs Izhikevich

The main differences of the Izhikevich model and the AdEx model are:

quadratic voltage dependence in the voltage equation of the Izhikevich model versus exponential dependence in the AdEx model;

upswing of the action potential is too slow in the Izhikevich model (Izhikevich 2007) compared to real neurons and more realistic in the AdEx model because of the exponential voltage dependence (Badel et al. 2008);

the Izhikevich model shows unrealistic nonlinearities in the subthreshold regime, whereas the AdEx model is linear in agreement with experiments (Badel et al. 2008);

attenuation of high frequency inputs as $1/f^2$ for a model with quadratic voltage dependence like in the Izhikevich model vs. $1/f$ for models with exponential voltage dependence (Fourcaud et al, 2003);

the choice of the voltage cut-off value for spikes is critical in the Izhikevich model but less so in the AdEx model (In the absence of a cut-off the adaptation variable *w* diverges in the Izhikevich model during the upswing of the action potential but does not diverge in the AdEx model.);

extraction of the voltage dependence from experiments suggests a combination of linear and exponential terms as in the AdEx model (Badel et al. 2008), rather than a quadratic dependence as in the Izhikevich model;

while qualitative fits to firing patterns are possible with both models, the AdEx model allows better quantitative fits to voltage traces (Naud et al. 2008).

http://www.scholarpedia.org/article/Adaptive_exponential_integrate-and-fire_model

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REVIEW

What Is the Most Realistic Single-Compartment Model of Spike Initiation?

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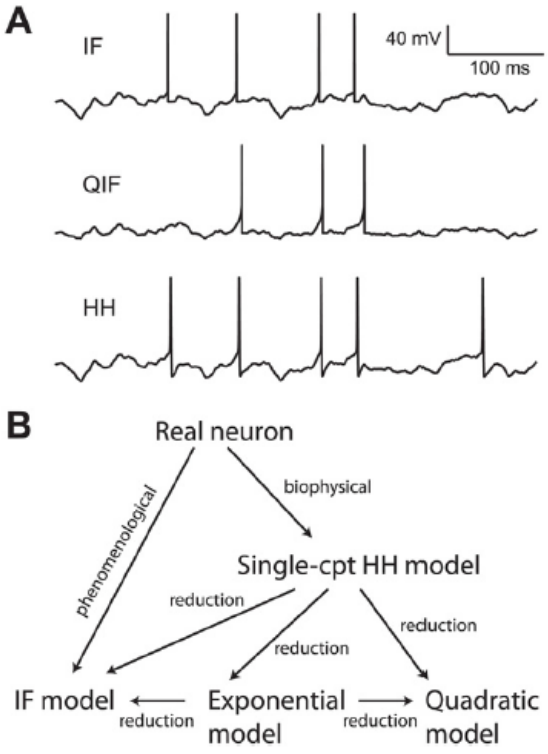

Kink at onset