Centre for Cognitive Science

Computational cognitive neuroscience: 2. Neuron

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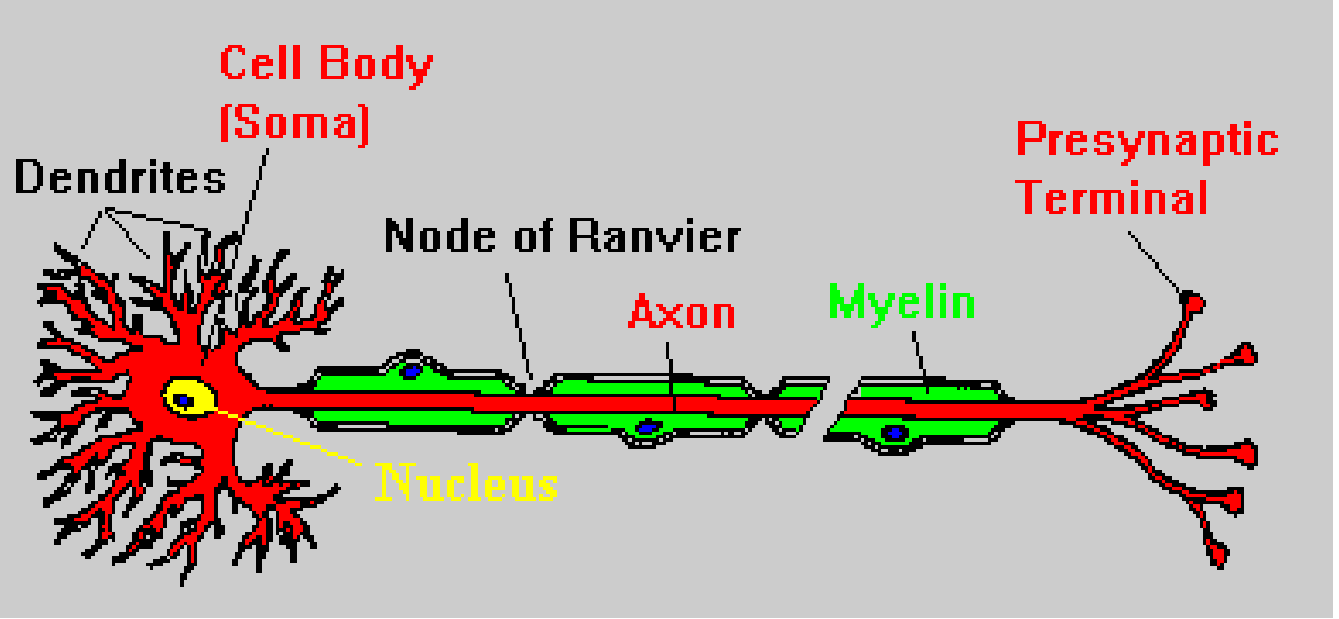
Neurons communicate via electric signals

- Neurons relay information from the outside world to the brain, and from the brain to the outside world (via muscles). Neurons do computations inside the brain that we call perception, thought, decisions, etc.

- These computations are based on **electrical pulses** called action potentials or spikes.

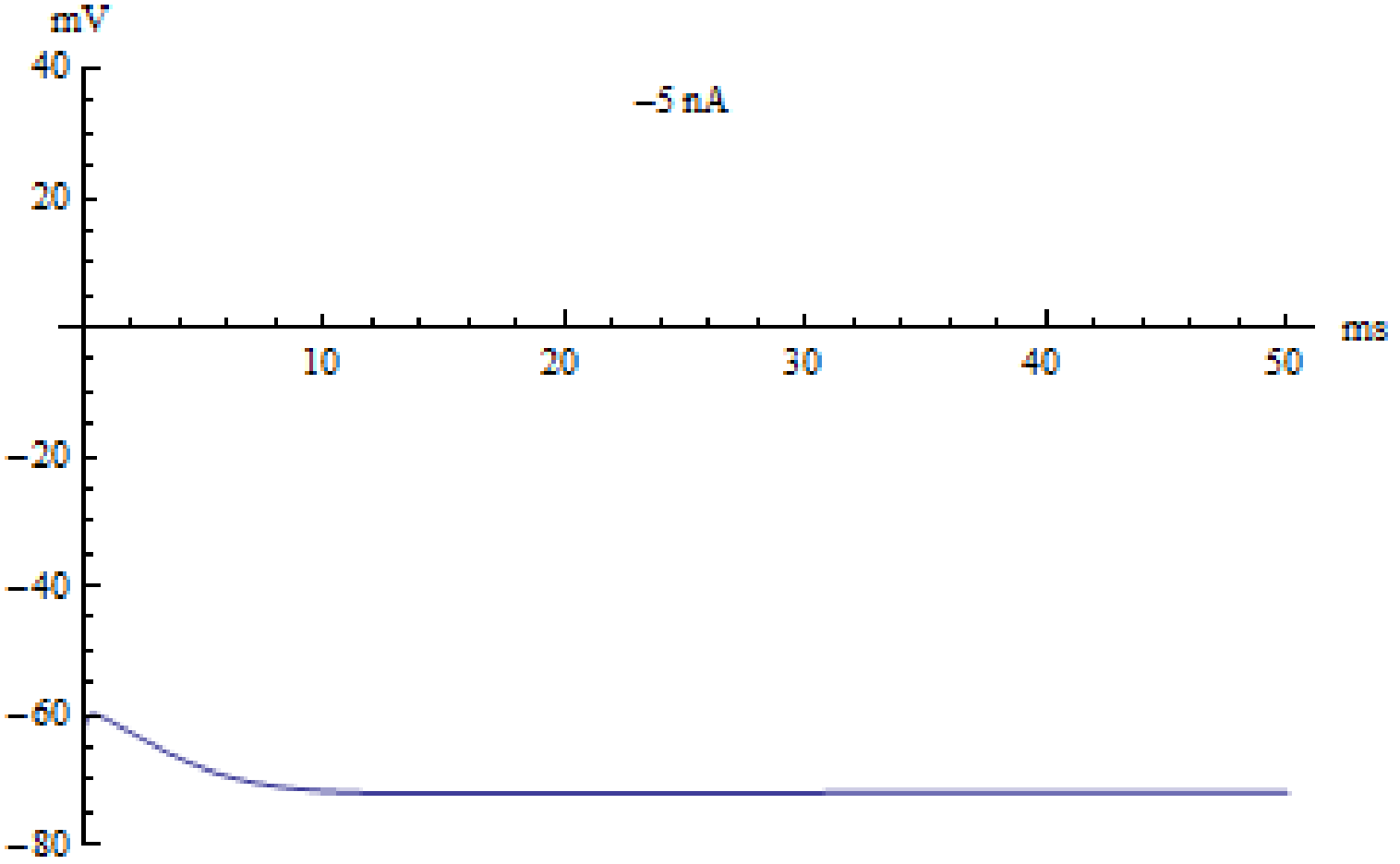
Spikes "jump" along axons like a Mexican wave



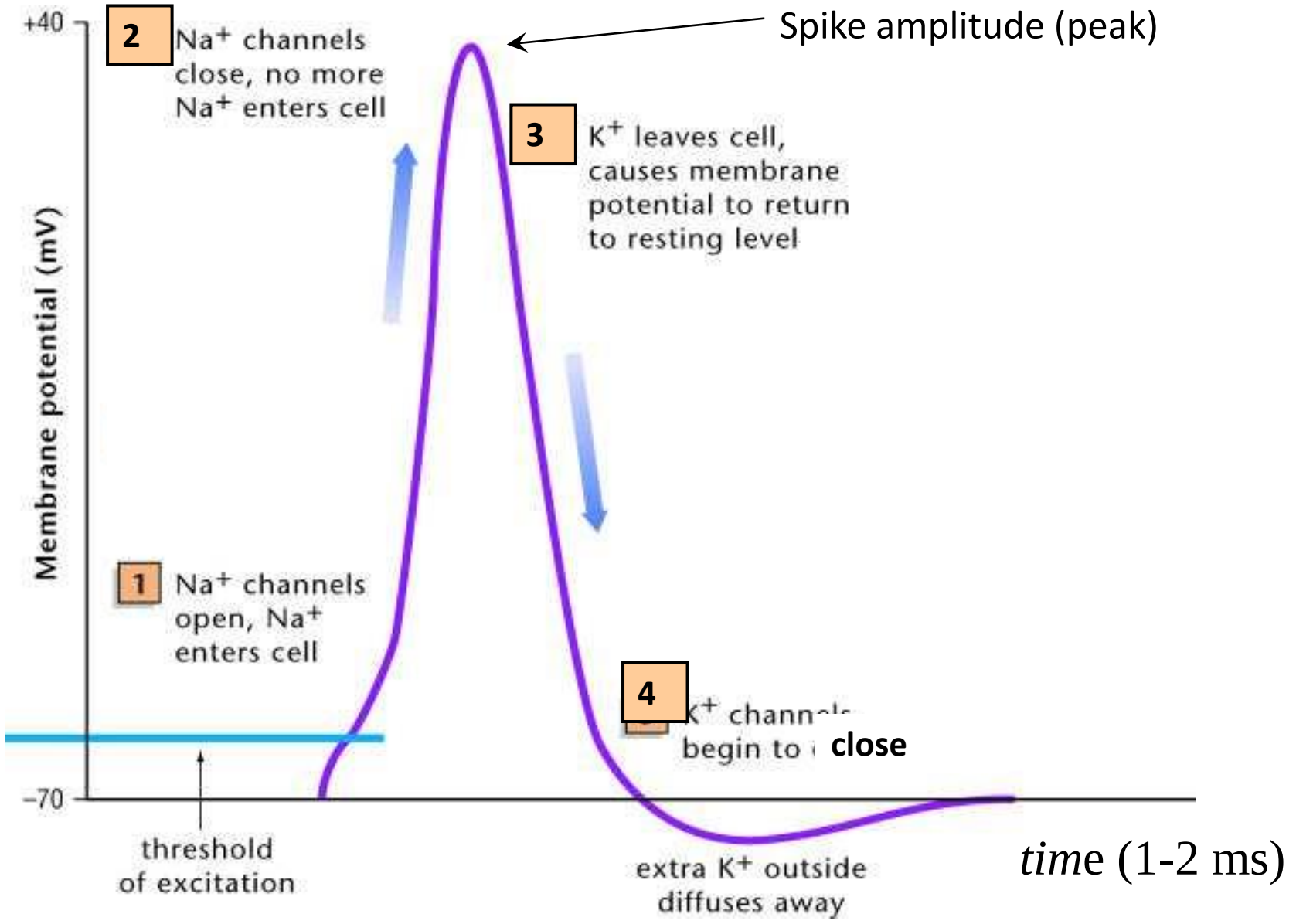
- Axons have a myelin sheath surrounding the axons, that makes up the "white matter" of the brain ("grey matter" are somas and dendrites).
- This speeds transmission, because the spike "jumps" between the gaps (nodes of Ranvier) and the myelin sheath provides electrical insulation.
- In each gap, the original amplitude of a spike is restored, so it's stays the same until it reaches presynaptic terminal of a synapse.

Animation of an action potential (spike)

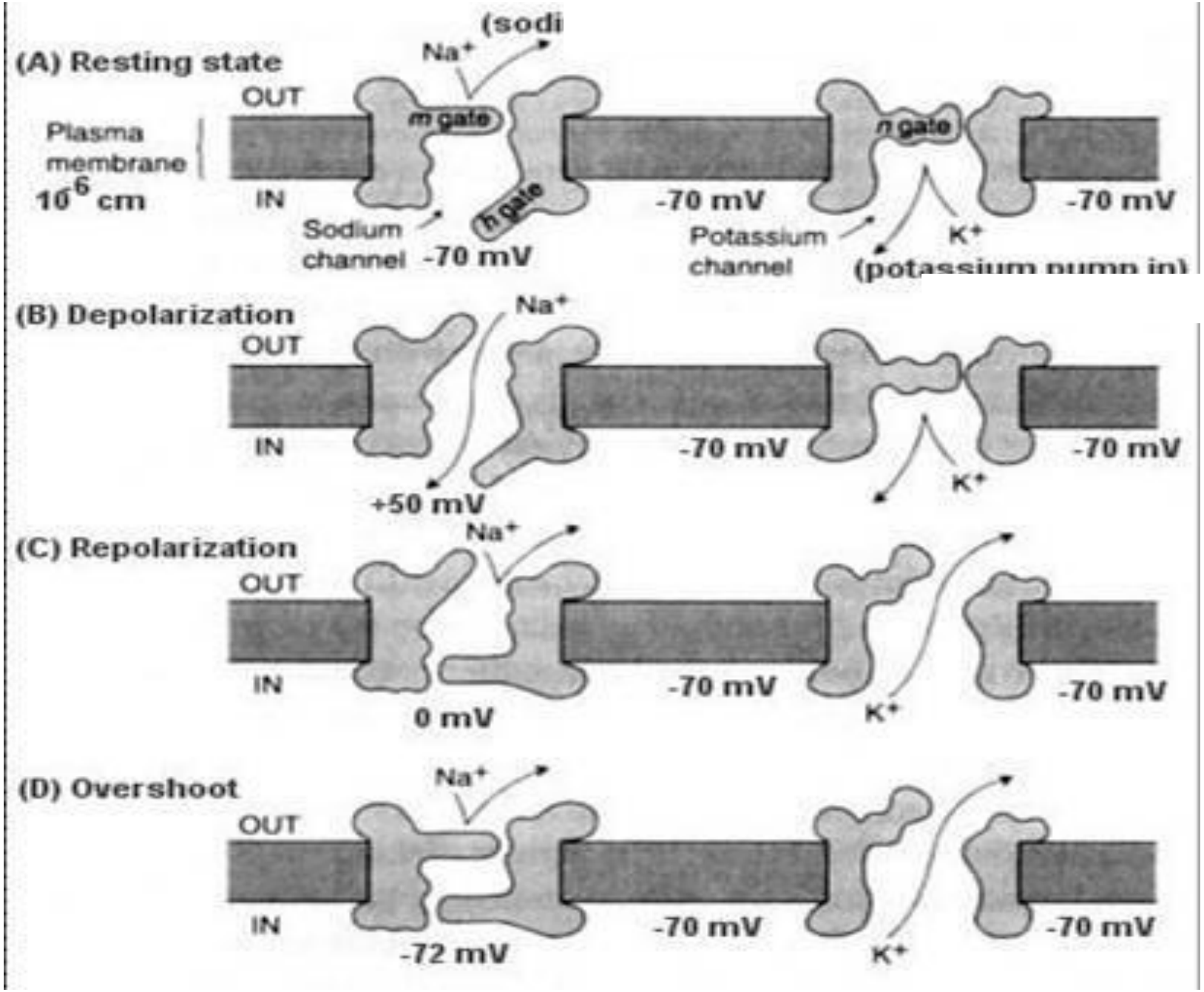
- The voltage V(t) (in mV) of the Hodgkin–Huxley model, graphed over 50 milliseconds. The injected current varies from −5 nA to 12 nA. The graph passes through three stages: an equilibrium stage, a single-spike stage, and a limit cycle stage (Wikipedia).



Change of membrane voltage during action potential



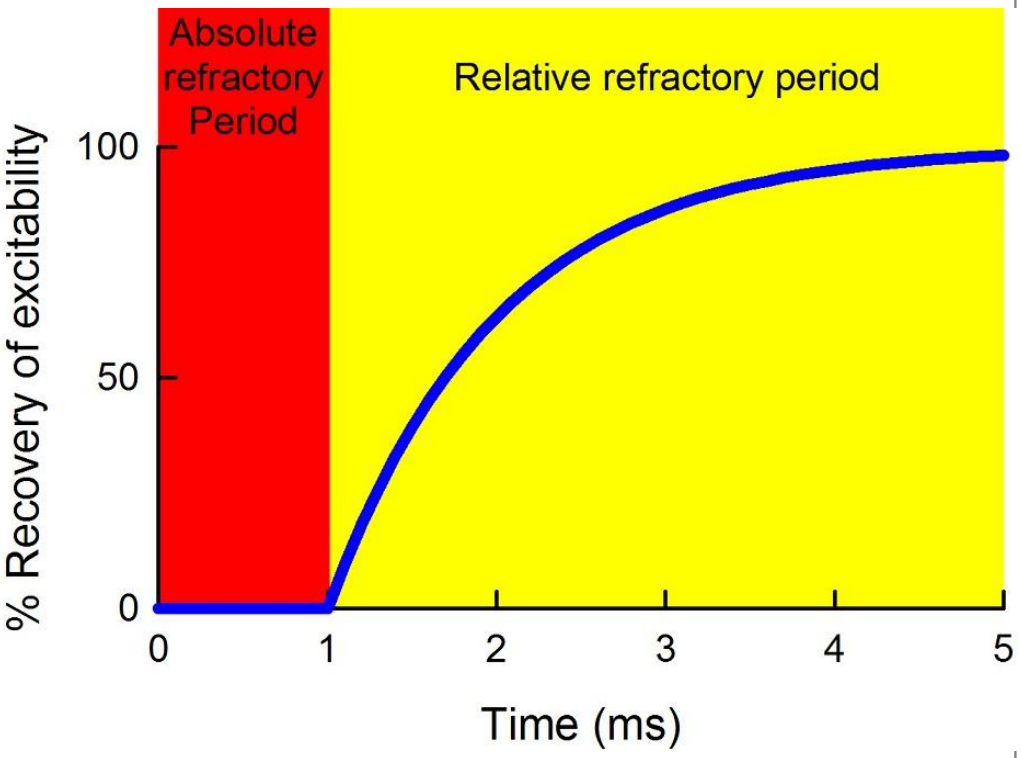
Ion channels in action potential (spike)



Refractory period

- The period from the initiation of the action potential to immediately after it is referred to as the absolute refractory period 1-2 ms. This is the time during which another stimulus given to the neuron (no matter how strong) will not lead to a second action potential.

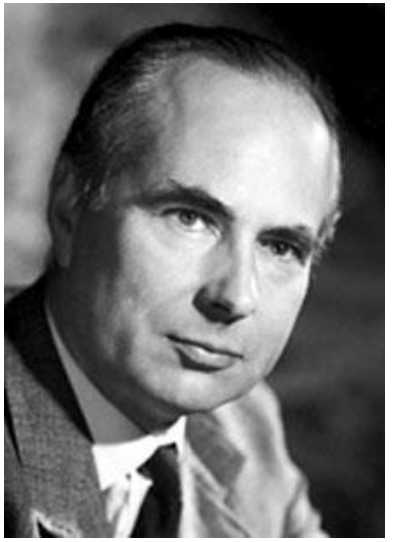
- The period immediately following the absolute refractory period is the relative refractory period 5-15 ms. The neuron can be excited if a stronger than normal stimulus is applied.



Hodgkin and Huxley

- In 1963, Brits Allan Hodgkin & Andrew Huxley received the Nobel prize in Physiology and Medicine for their work on axon potentials. (The 3rd laureate was Sir John Eccles for work on synapses.)

- H&H developed an action potential theory using one of the earliest applications of a technique of electrophysiology, known as the "voltage clamp“, which enabled to measure ionic currents flowing through the membrane.



- The equations describe mathematically how an action potential is generated when the total somatic potential rises above the firing threshold.

Hodgkin-Huxley model

- According to Ohm's law, $I = V/R = gV$, the membrane current I_m flowing through the ion channels during an action potential reads:

$$I_m = g_{Na} m^3 h (V - E_{Na}) + g_K n^4 (V - E_K) + g_L (V - E_L)$$

- Here: g is the electric conductance, Na = sodium, K = potassium, L is all other ions (the so-called leakage current). E denotes the equilibrium potential for that ion, V is the membrane voltage.

- Symbols m, n, h denote empirically derived parametric functions of the model that correspond to kinetics of individual subunits/gates of Na and K ion channels.

- This is historically the first computational model of biological neurons and applies to all axons (albeit with different values of parameters).

H-H model: parametric functions

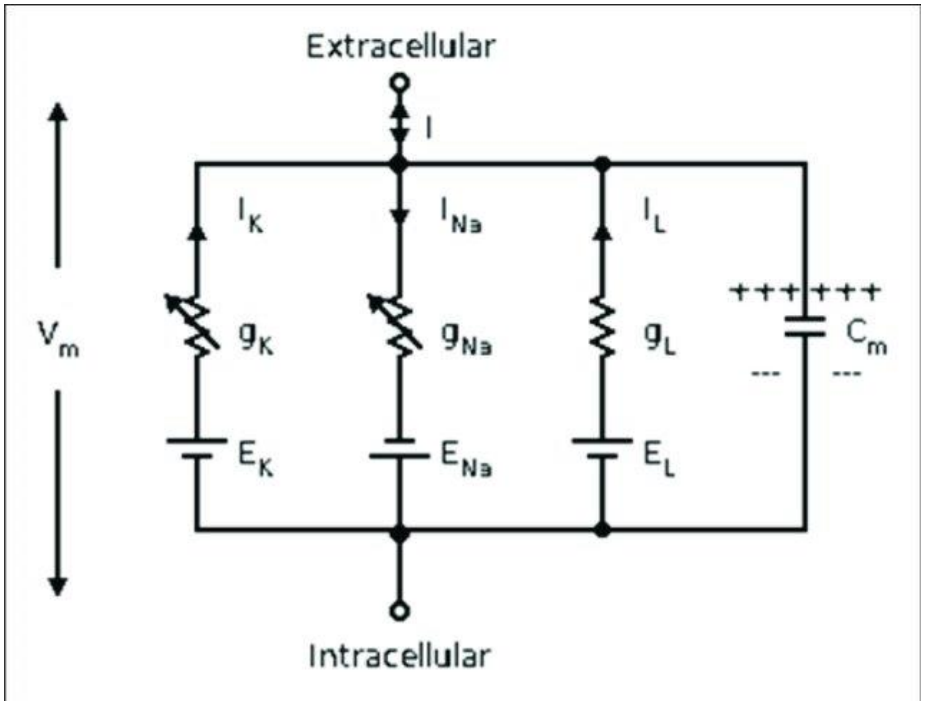
- The three variables m, n, and h are also called gating variables. They evolve according to the differential equations (V is voltage):

$$\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)\,m$$
$$\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)\,n$$
$$\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)\,h$$

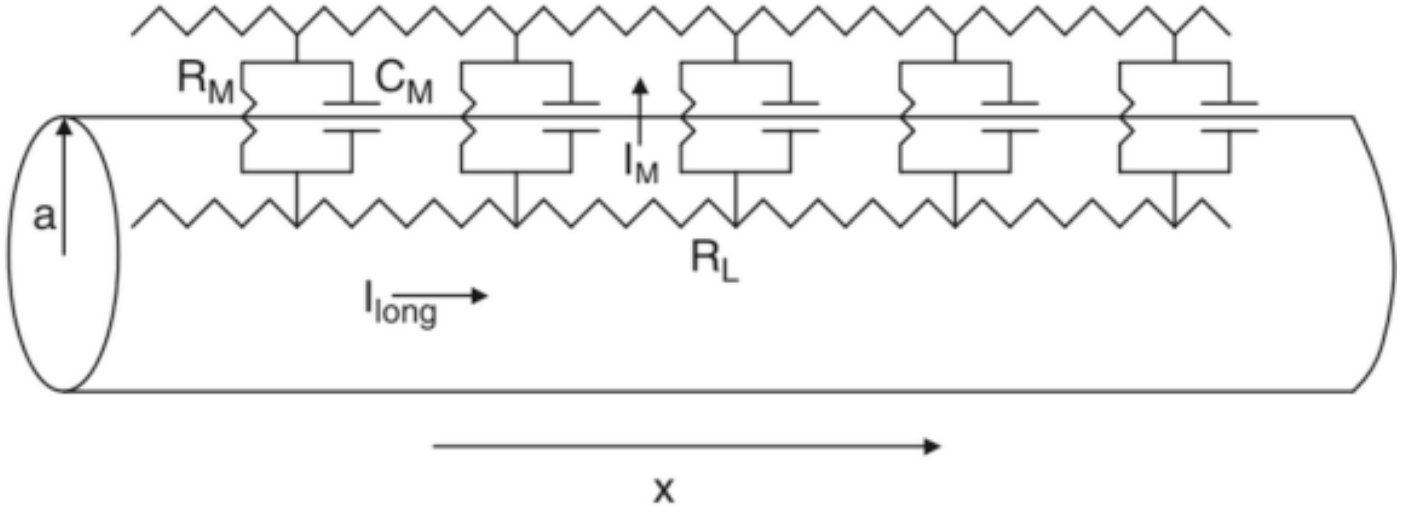
x	$\alpha_x(\mathrm{v}/\mathrm{mV})$	$\beta_x(\mathrm{v}/\mathrm{mV})$
n	$(0.1 - 0.01\,\mathrm{v}) / [\exp(1 - 0.1\,\mathrm{v}) - 1]$	$0.125\exp(-\mathrm{v}/80)$
m	$(2.5 - 0.1\,\mathrm{v}) / [\exp(2.5 - 0.1\,\mathrm{v}) - 1]$	$4\exp(-\mathrm{v}/18)$
h	$0.07\exp(-\mathrm{v}/20)$	$1 / [\exp(3 - 0.1\,\mathrm{v}) + 1]$

Equivalent electric circuit of axonal membrane

- Besides ionic conductances g, the membrane also has a capacitance C_m:



- Axon is also a long electric cable.



Hodgkin-Huxley model (continued)

- There is also a current related to the membrane capacitance C_{m} :

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

- Total membrane current is the sum: $I = I_{\mathrm{m}} + I_{\mathrm{C}}$

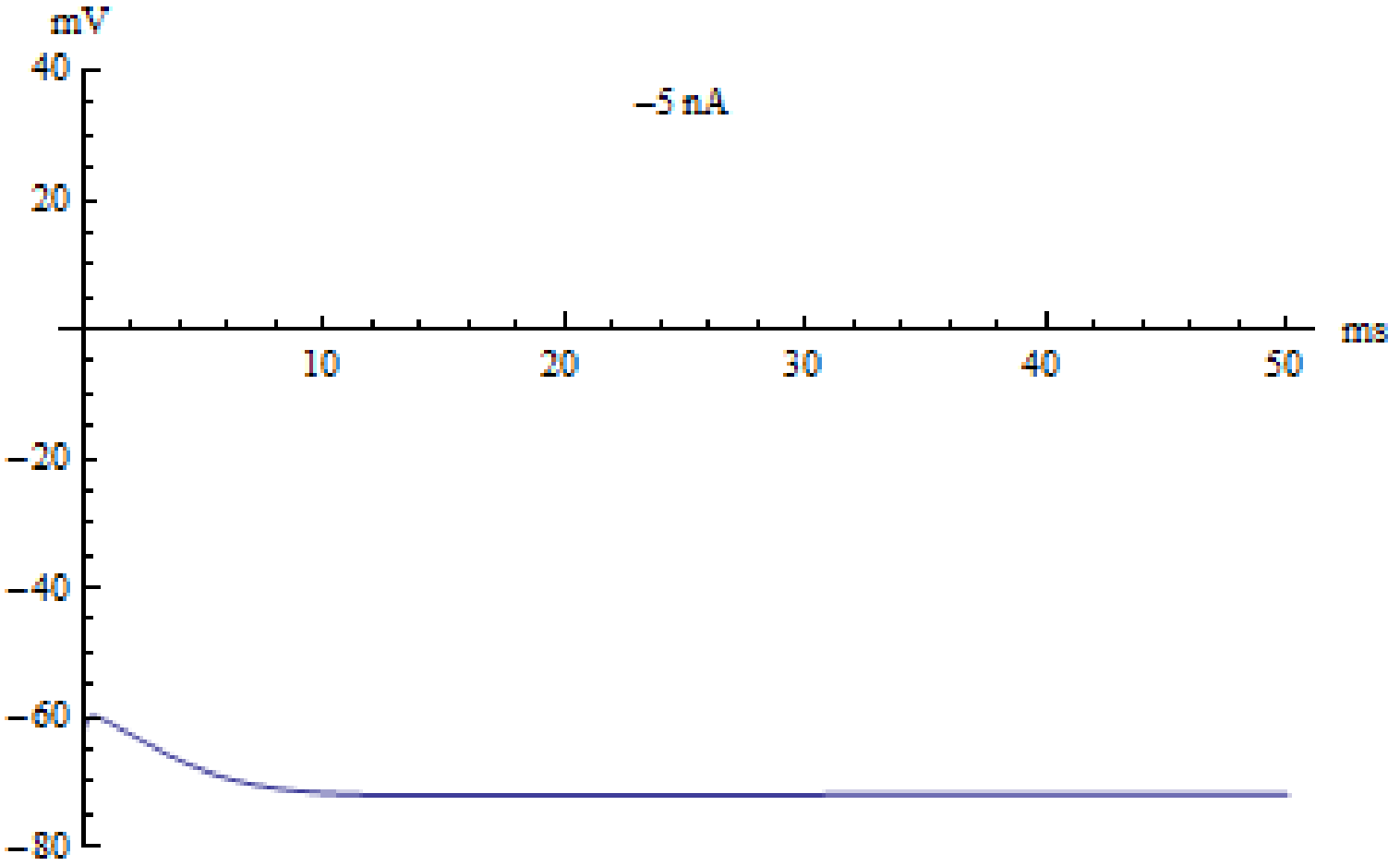
- From the so-called cable theory, we know that $I = \frac{a}{2R_{\mathrm{L}}} \frac{\partial^2 V}{\partial x^2}$

- where a is the radius of the axon, R_{L} is the specific resistance of the axoplasm, and x is the position along the axon. Substitution of this expression for I transforms the original set of equations into a partial differential equation, because the voltage V becomes a function of both x and t. Thus, the final equation for membrane voltage reads

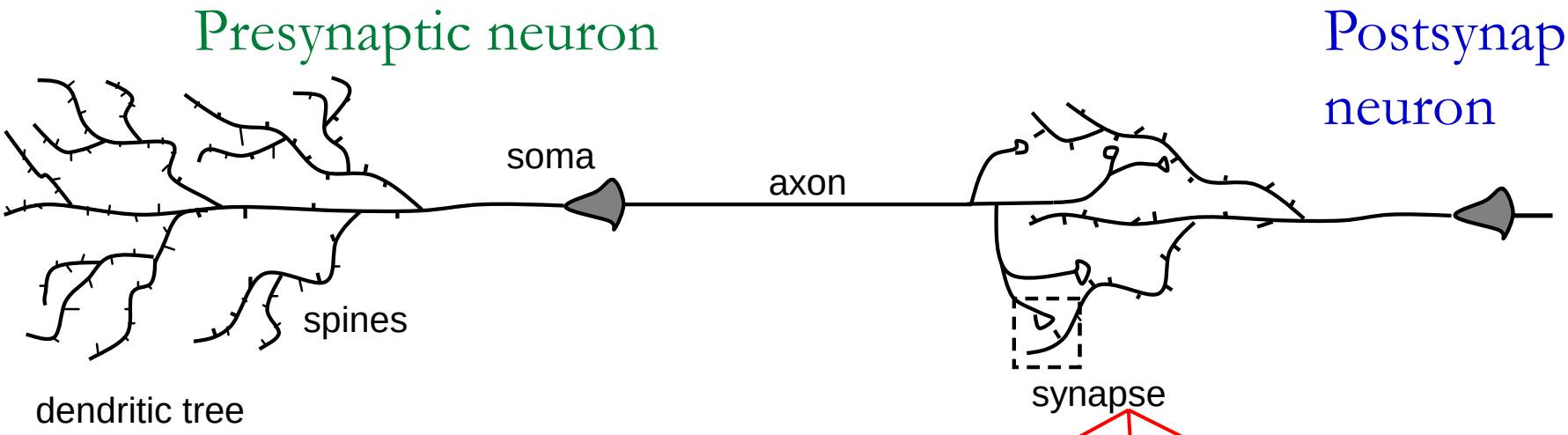
$$(a/2R)\frac{\partial^2 V}{\partial x^2} = C_m \frac{\partial V}{\partial t} + g_{Na}\, m^3 h(V - E_{Na}) + g_K n^4 (V - E_K) + g_L (V - E_L)$$

Animation of an action potential (spike)

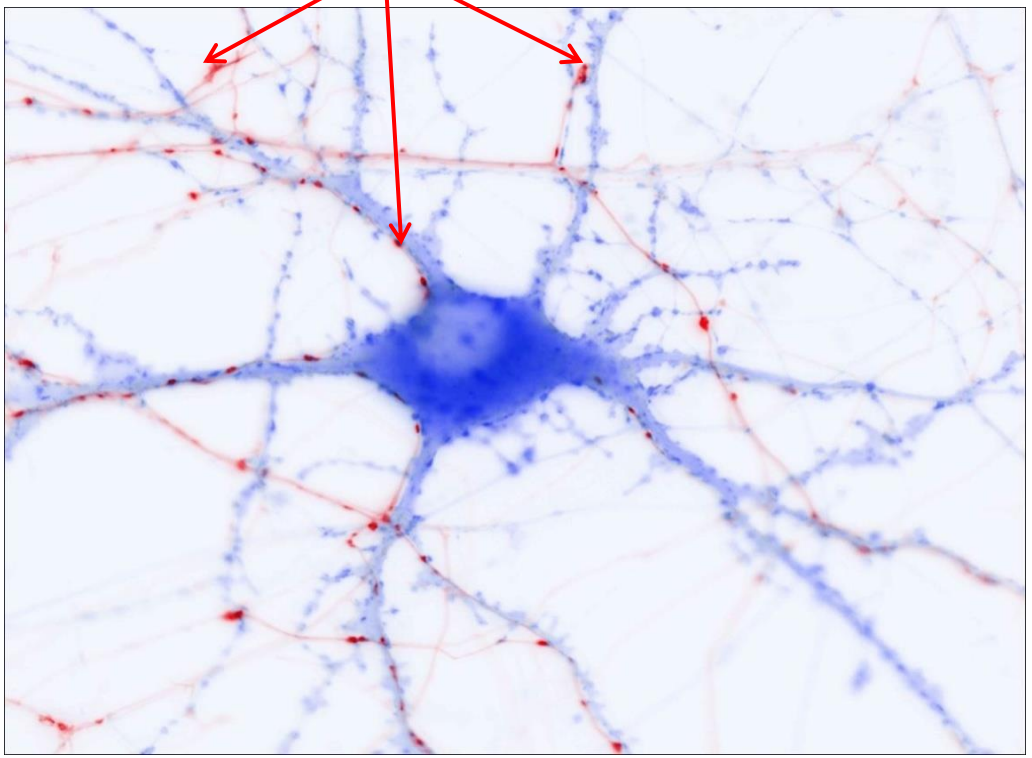
- The voltage V(t) (in mV) of the Hodgkin–Huxley model, graphed over 50 milliseconds. The injected current varies from −5 nA to 12 nA. The graph passes through three stages: an equilibrium stage, a single-spike stage, and a limit cycle stage (Wikipedia).



Presynaptic and postsynaptic neurons

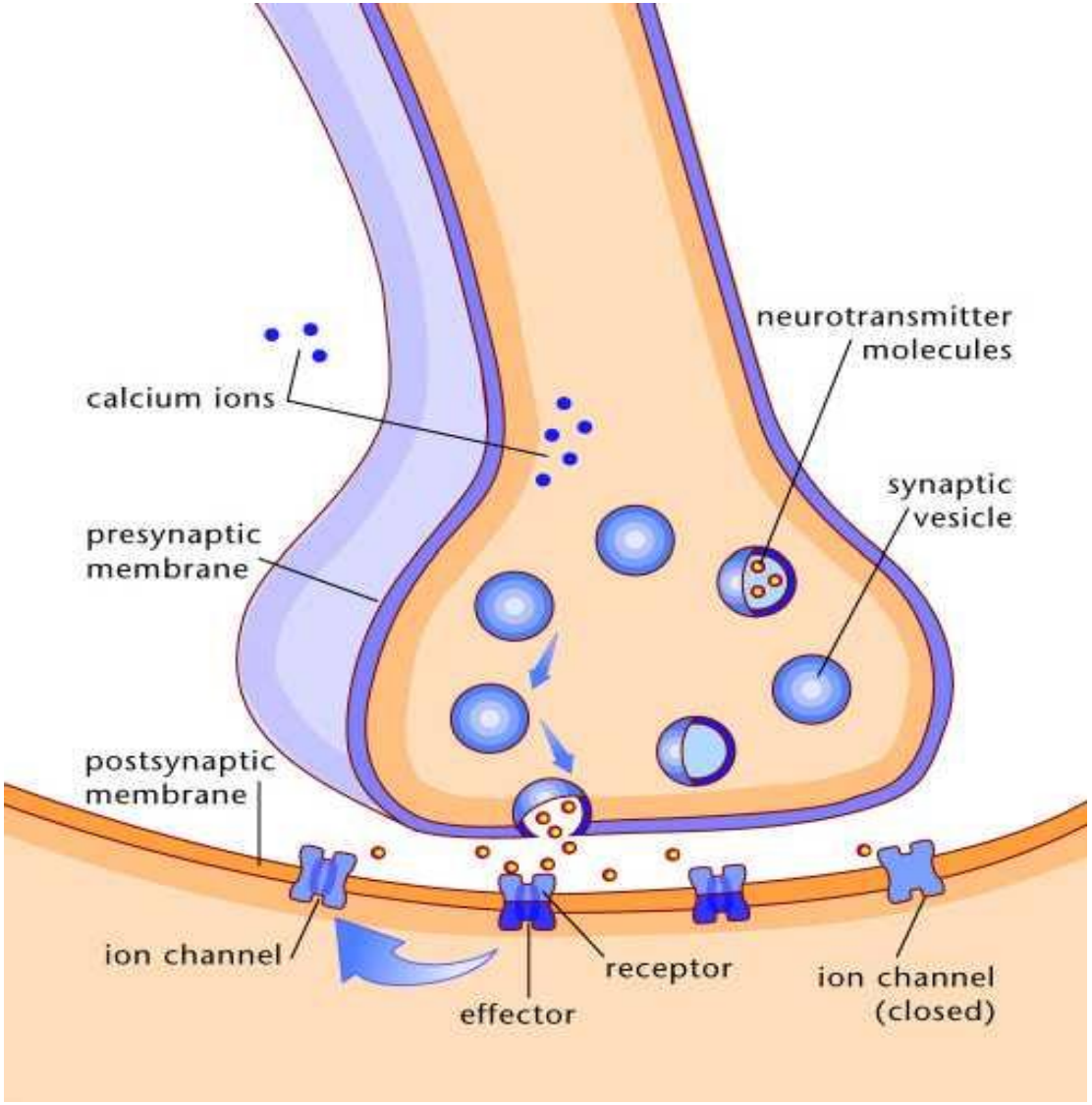


Axons of presynaptic neurons make synapses (little blobs) on the soma and dendrites of the postsynaptic neuron(s).



Synapse: from Greek "sunapsis", point of contact

- Synapse consists of 3 parts:
  - Presynaptic terminal – contains vesicles filled with neurotransmitter.
  - Synaptic cleft – filled with tiny filaments that attach terminal to the postsynaptic neuron (they are not shown).
  - Postsynaptic membrane contains – receptors associated with various effectors, passive and voltage-gated ion channels.

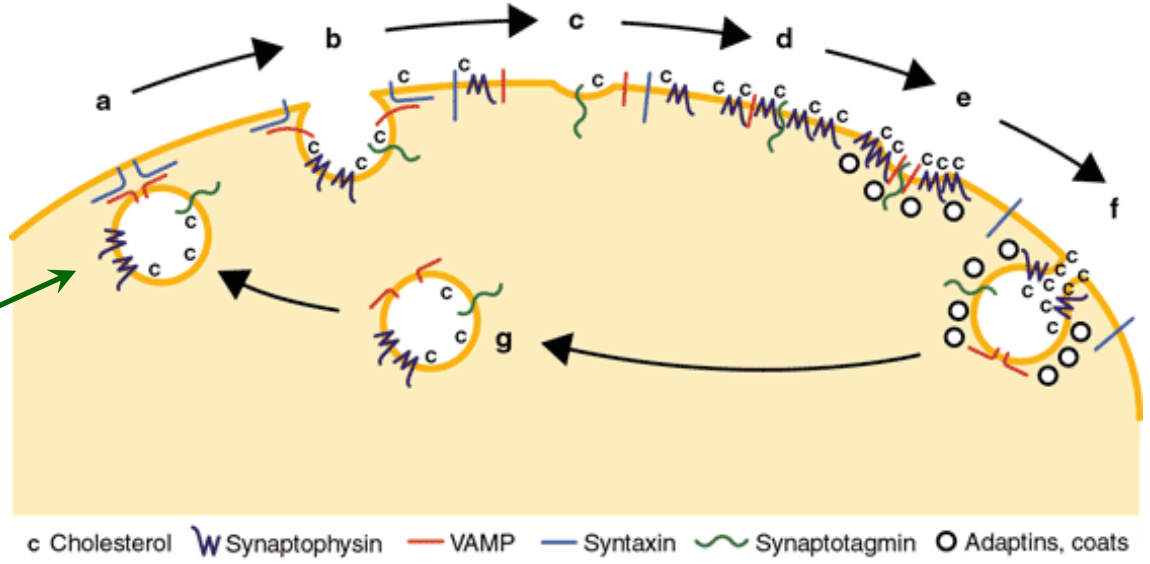


Role of calcium in release of presynaptic vesicles

- When a presynaptic spike (action potential, AP) arrives at the presynaptic terminal, voltage-gated ion channels for calcium in the terminal's membrane open and let ions of Ca^{2+} enter to the terminal.

- Calcium triggers a chain of processes that lead to the fusion of vesicles with the membrane and release of their content into the synaptic cleft.

Influx of calcium triggers fusion (exocytosis)



Vesicles are "recycled" while re-uptaking the neurotransmitter from the cleft (note: molecules of neurotransmitter are not shown here)

Source: T.F.J. Martin, Nature Cell Biology, doi:10.1038/71392

Neurotransmitter binds to postsynaptic receptors

- Postsynaptic receptors are associated with ion channels, in fact they form one big molecule.
- When neurotransmitter (ligand) binds to the receptor part, that opens the ion channel.
- Receptors are specific for given neurotransmitter and ion channels are specific for concrete ions.
- Ions that are allowed to move through the channel then flow in or out (according to electro-chemical gradient).

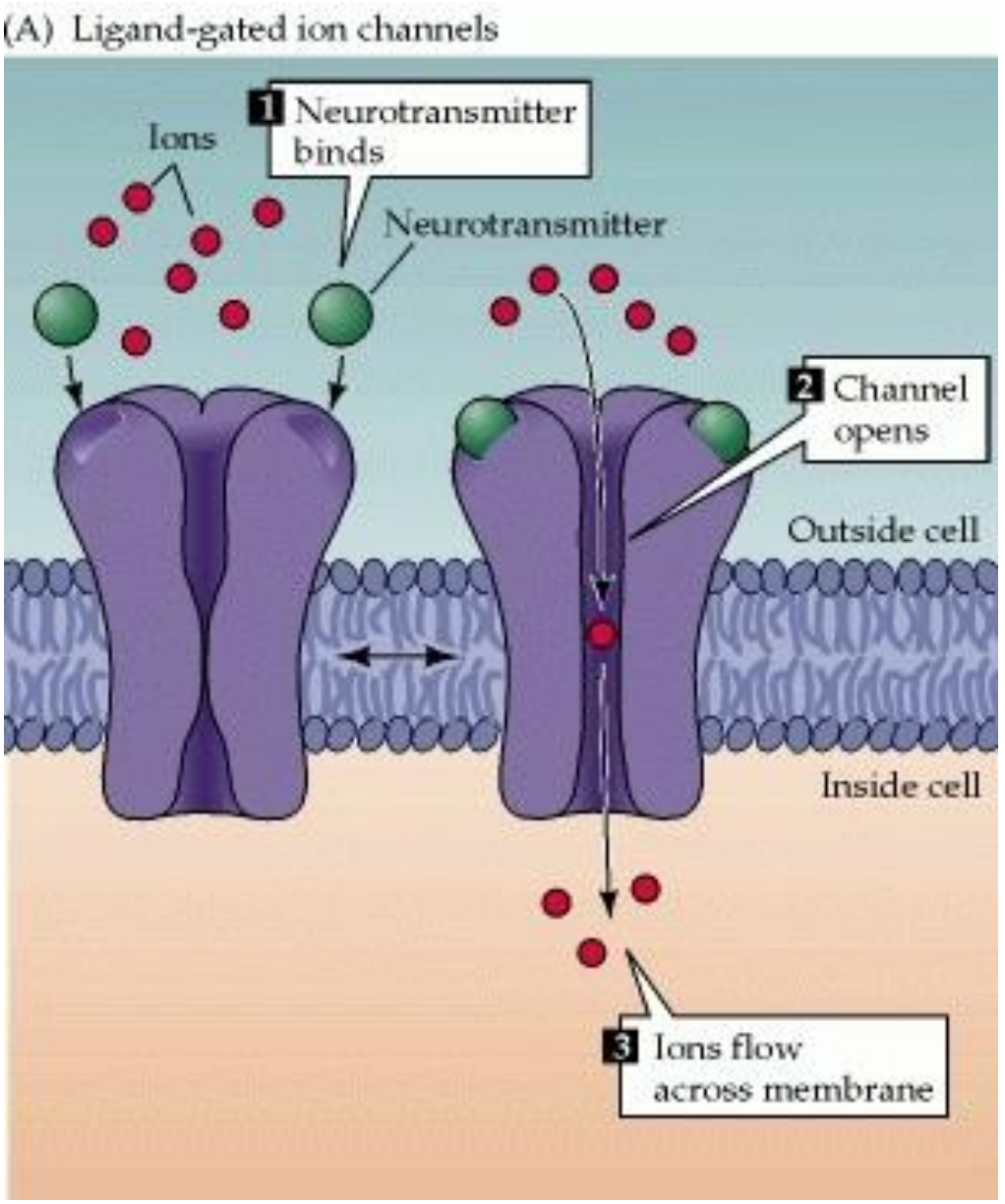


Image source: http://www.ncbi.nlm.nih.gov/books/NBK10855/

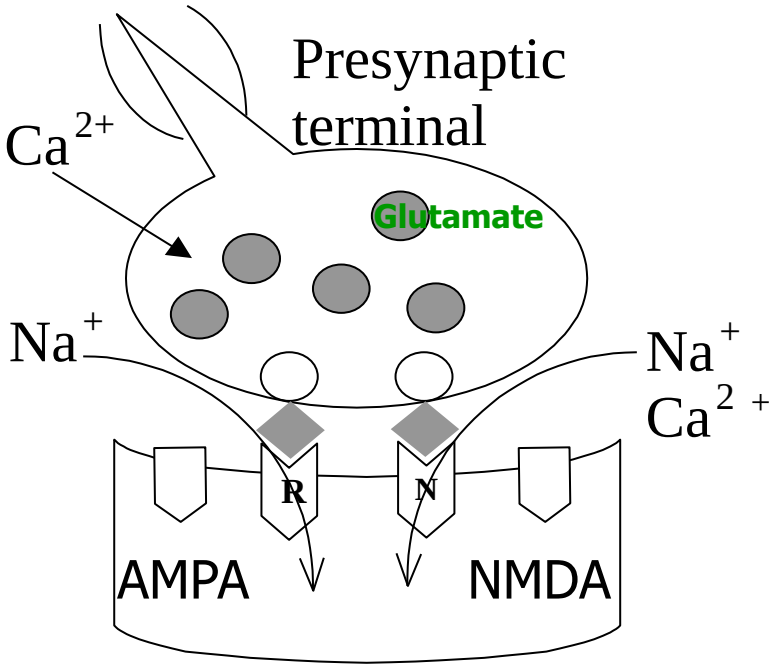
Receptor/ion channels: excitation versus inhibition

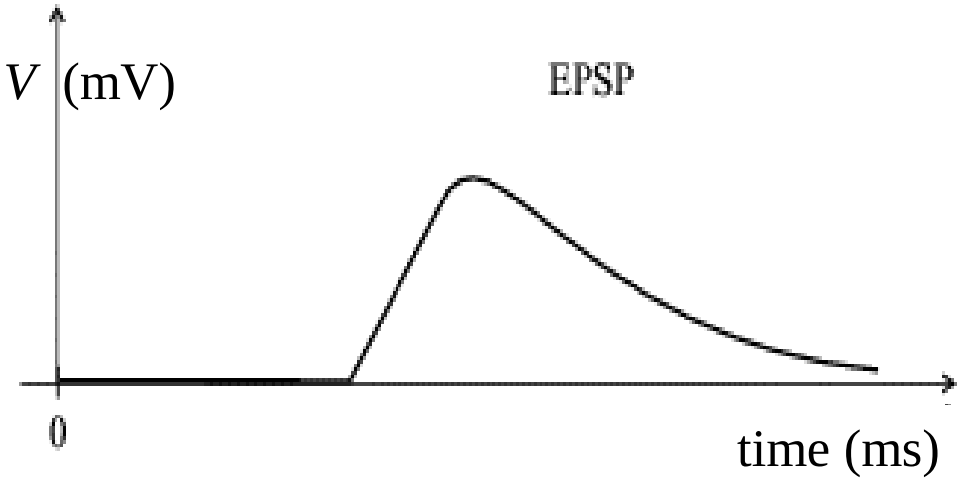
- When nothing is happening, postsynaptic membrane is polarized at $V_0 \cong -70$ mV (the resting potential).

- If the neurotransmitter interacts with receptor/ion channels that cause **depolarization** of the postsynaptic membrane towards positive values – then we speak about **excitation.**
  - Major excitatory neurotransmitter in the brain is glutamate (Glu).

- If the neurotransmitter interacts with receptor/ion channels that cause **hyper-polarization** of the postsynaptic membrane towards more negative values – then we speak about **inhibition**.
  - The major inhibitory neurotransmitter in the brain is γ-aminobutyric acid (GABA).

Excitatory synapses

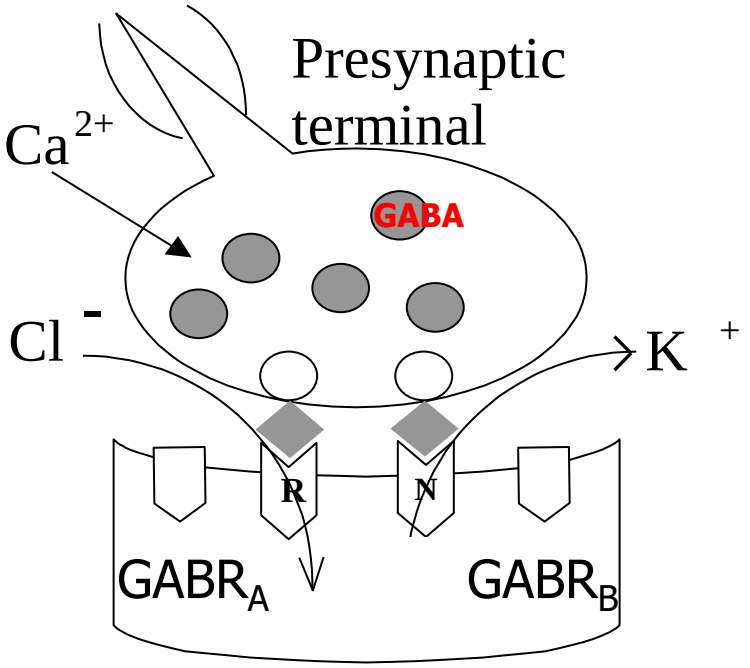


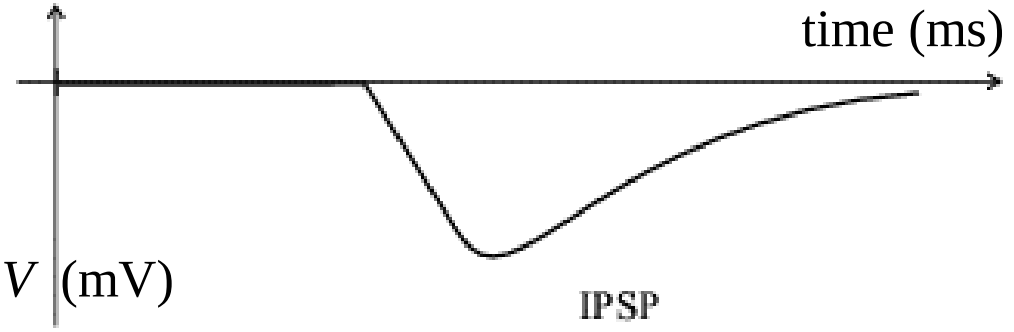


- Neutrotransmitter: glutamate.
- Postsynaptic receptors associated with ion channels are called AMPAR and NMDAR, (there are also metabotropic receptors there that are not associated with ion channel).
- When we measure the electric potential *V* at the postsynaptic membrane, we see a positive deviation from the resting potential, which is called **excitatory postsynaptic potential (EPSP).**

Inhibitory synapses

- Neutrotransmitter: GABA
- Postsynapstic receptors GABRA and GABRB, ion channels for K^+ and Cl^-
- When we measure the electric potential *V* at the postsynaptic site, we see a negative deviation from the resting potential, which is called **inhibitory postsynaptic potential (IPSP).**





Postsynaptic potential (PSP)

- PSP (either EPSP or IPSP) is the result of electric current *I* that flows through the receptor-gated ion channels and obeys the equation:

$$I_{syn}(t) = g_{syn}(t)\left(V(t) - E_{syn}\right)$$

- Where the effect of neurotransmitter binding to and opening the postsynaptic receptors/ion channels is a conductance change, g_{syn} of the postsynaptic membrane.

- V is the momentary value of the membrane potential (voltage).

- E_{syn} is the reversal potential of those ion channels (Na, K, Cl, Ca) that mediate that particular synaptic current (excitatory or inhibitory) in the postsynaptic membrane.

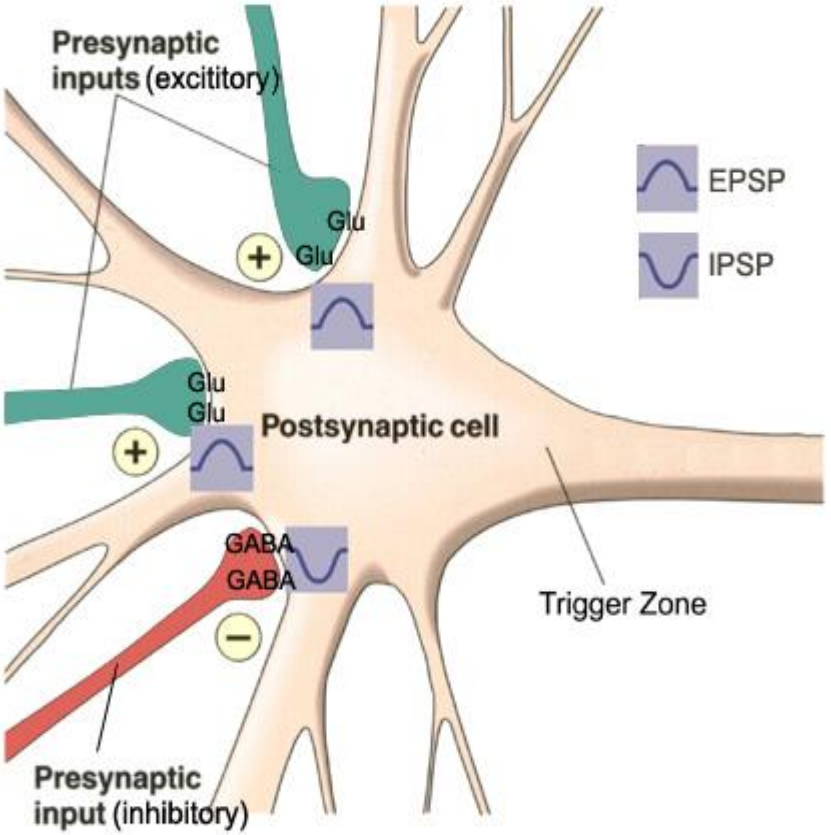
Summation of EPSPs and IPSPs in space

- Let's have only n =3 synapses on the soma. The total PSP is the sum of all synaptic PSPs, i.e.:

$$PSP_{syn}^{soma}(t) = \sum_{i=1}^{n} PSP_{syn,i}$$

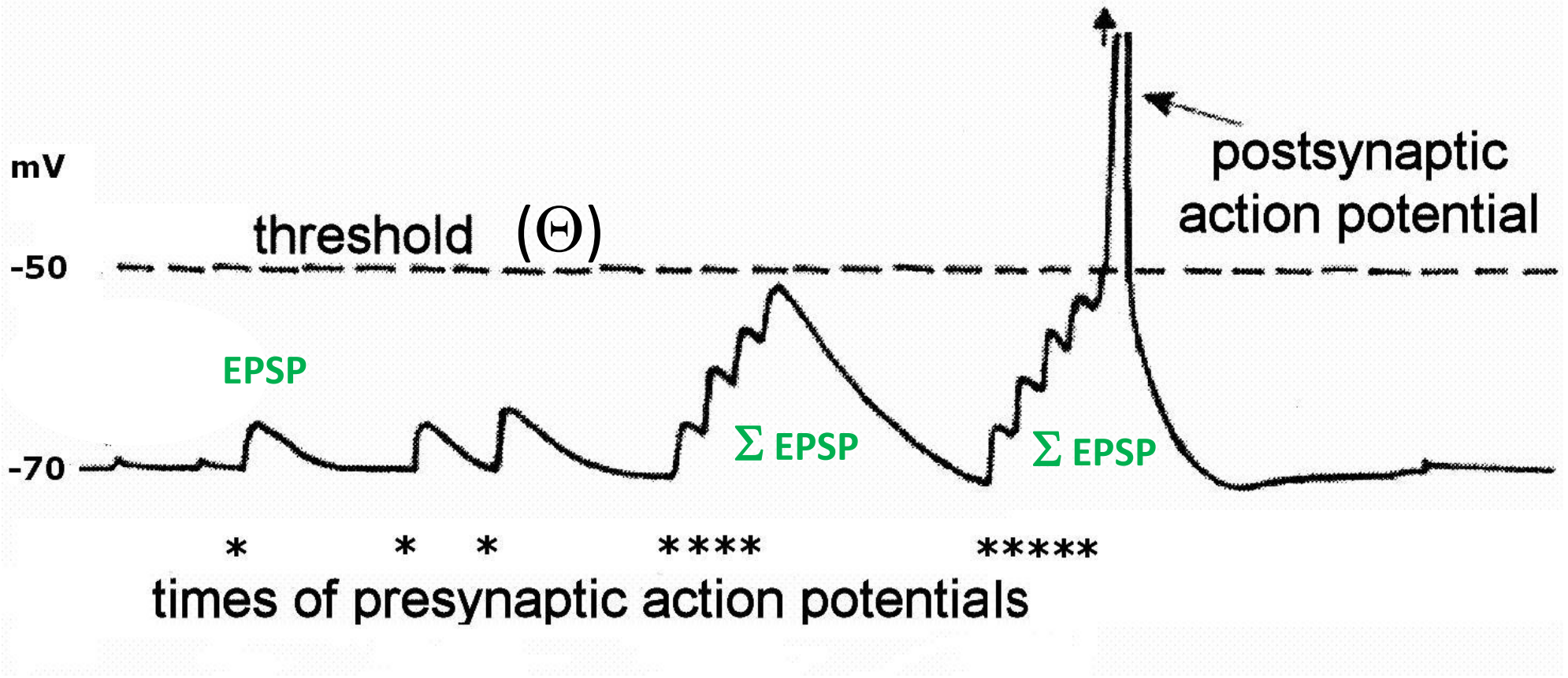
- All the EPSPs and IPSPs add up instantly (soma is equipotential).

- If $PSP_{total} = EPSP_{total} - IPSP_{total} > \Theta$, (firing threshold) then an action potential is generated in the trigger zone between soma and axon (axonal hillock).

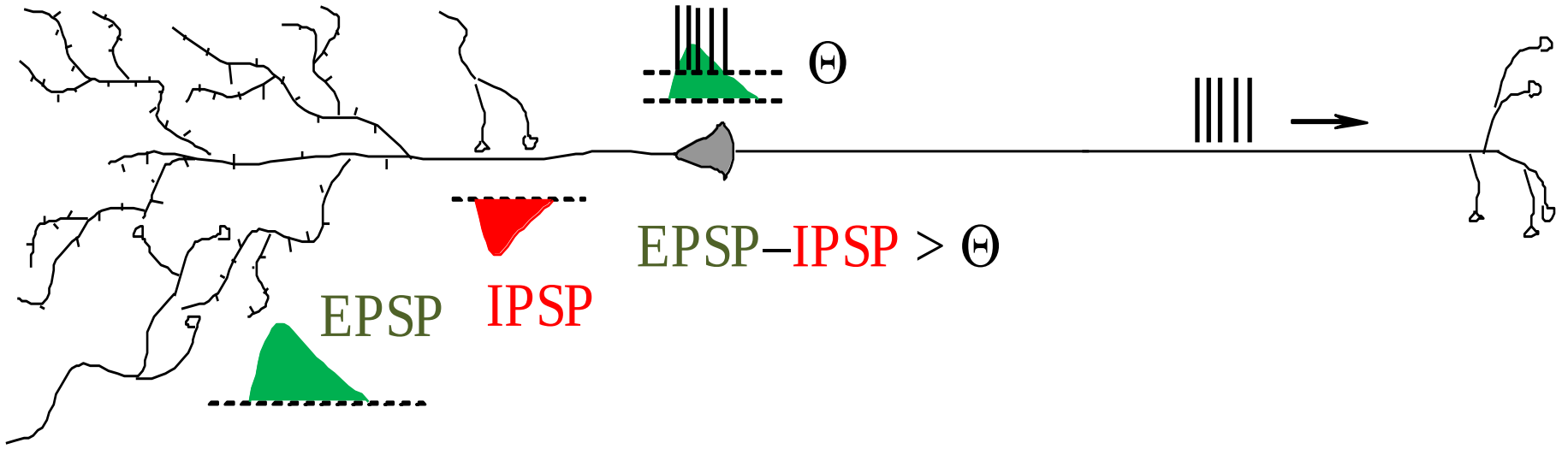


Summation of individual PSPs at soma

- Each presynaptic electric pulse (spike) causes a single EPSP "bump" at the postsynaptic site that propagates to soma.
- On arrival of many EPSPs in close succession, these EPSPs sum up on the top of each other and if the cumulative sum crosses the firing threshold Θ, the neuron generates an output spike (action potential).



Neuron: an analogue-digital converter



- Since the inhibitory synapses can be activated as well, the total *V* at soma = ΣEPSP-ΣIPSP. If it is > Θ, neuron generates an output spike train during the time when the total PSP at soma > Θ. We call it a **spike train**.

- The number and frequency/rate of spikes within the output spike train are proportional to the duration and magnitude of *V* at the soma.

- Spike train then propagates towards synapses, where it causes release of a neurotransmitter.

Synaptic weight

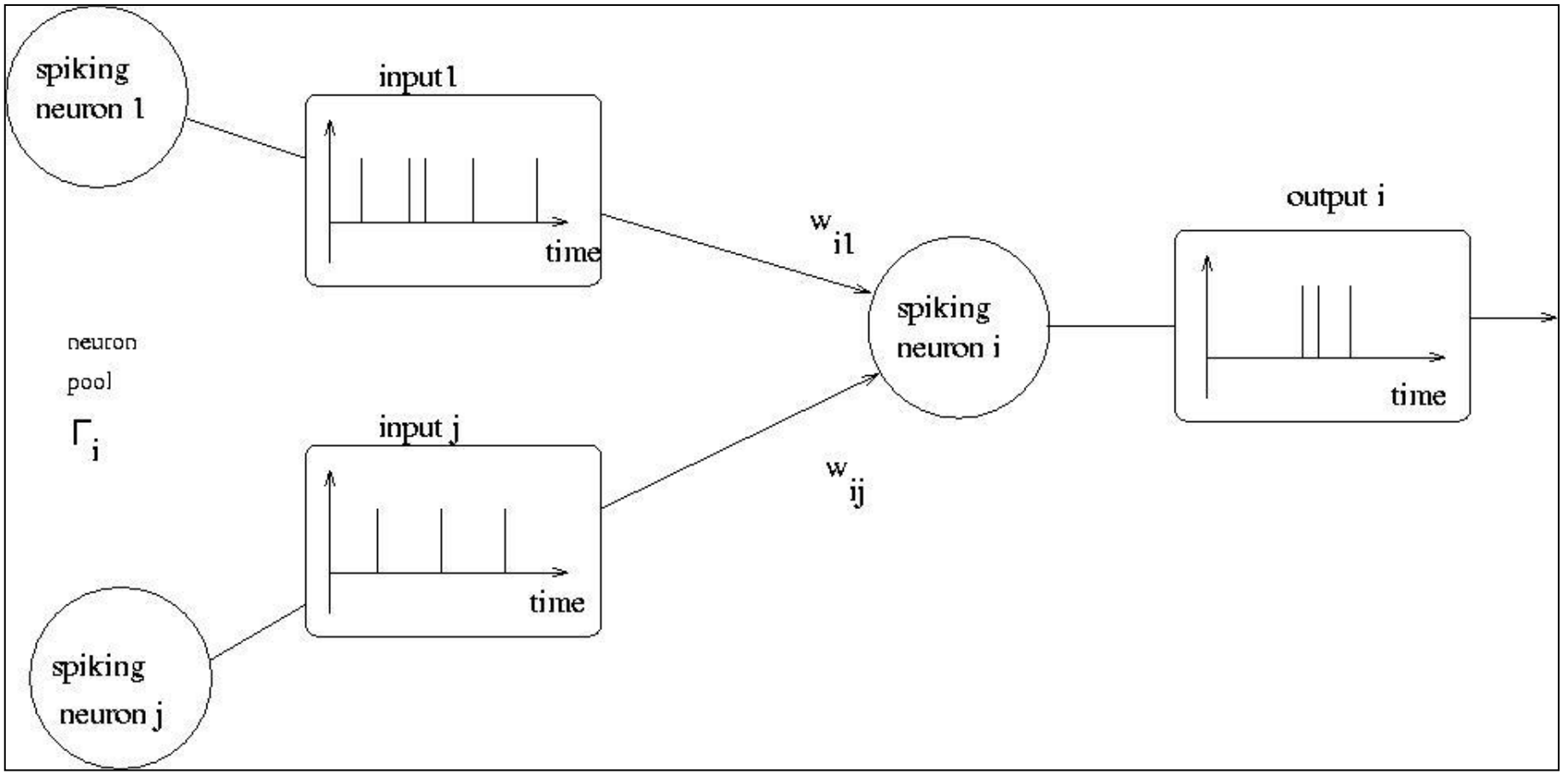
- Each synapse has a measurable strength or weight (essentially a function of PSP overall conductance.) Synaptic weight reflects synapse's impact upon firing the neuron.

- Synapses direct information traffic in the network, influencing which neurons will be activated.

- Increase or decrease in the strength of a synapses can change the directions of the flow of information in neural circuits.

Towards a simplified model of a neuron

- We want a simplified computational model of a neuron, in which the number of variables and parameters will be reduced as much as possible, yet it will precisely simulate the input / output dynamics of a biological neuron.



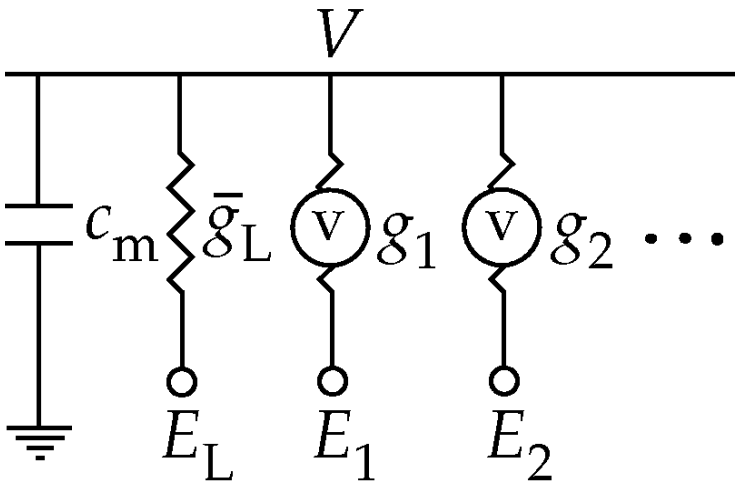
Integrate and fire (I&F) models

- The dependent variable is the membrane voltage V, the independent variable is time t.
- Action potentials (spikes) occur when the membrane potential V reaches a firing threshold Θ (parameter of the model).
- Leaky I&F: after firing, the membrane potential is reset to the value of the resting potential V_0 (parameter of the model).
- I&F can be modelled at various levels of rigour depending on more or less simple assumptions used.

Integrate & fire model

Electric scheme equivalent to an integrate and fire I&F model

$$i_k(t) = g_k(t)(V(t) - E_k)$$



- C_m is the capacitance, g_k is the conductance for ion of type k = 1, 2, ..., L means leakage and E is the equilibrium potential for a given type of an ion.
- In this circuit **the electric current flowing through the capacitance equals the sum of** the leakage current and **ionic currents** $I = \Sigma\, i_k$ (by convention capacitance current is 'plus' while other current is 'minus'):

$$c_m \frac{dV}{dt} = -g_L(V - E_L) - I$$

Integrate & fire model

- The simplest model of a spiking neuron is described by this equation:

$$c_m \frac{dV}{dt} = -g_L(V - E_L) - I$$

if $V \geq \Theta$ a postsynaptic spike is fired

- Where: $I = \Sigma\, i_k$ is the sum of all excitatory and inhibitory ionic currents mediated by ions of type k
- The symbol L denotes the so-called leak current that is always present.
- Dependent variables: V, ionic conductances g_k, and I.
- Parameters: c_m, g_L, Θ, and all the equilibrium potentials E.

Adaptive exponential integrate-and-fire model **AdEx**

- AdEx was introduced by Gerstner and Brette:

$$c_m \frac{dV}{dt} = f(V) - w + I$$

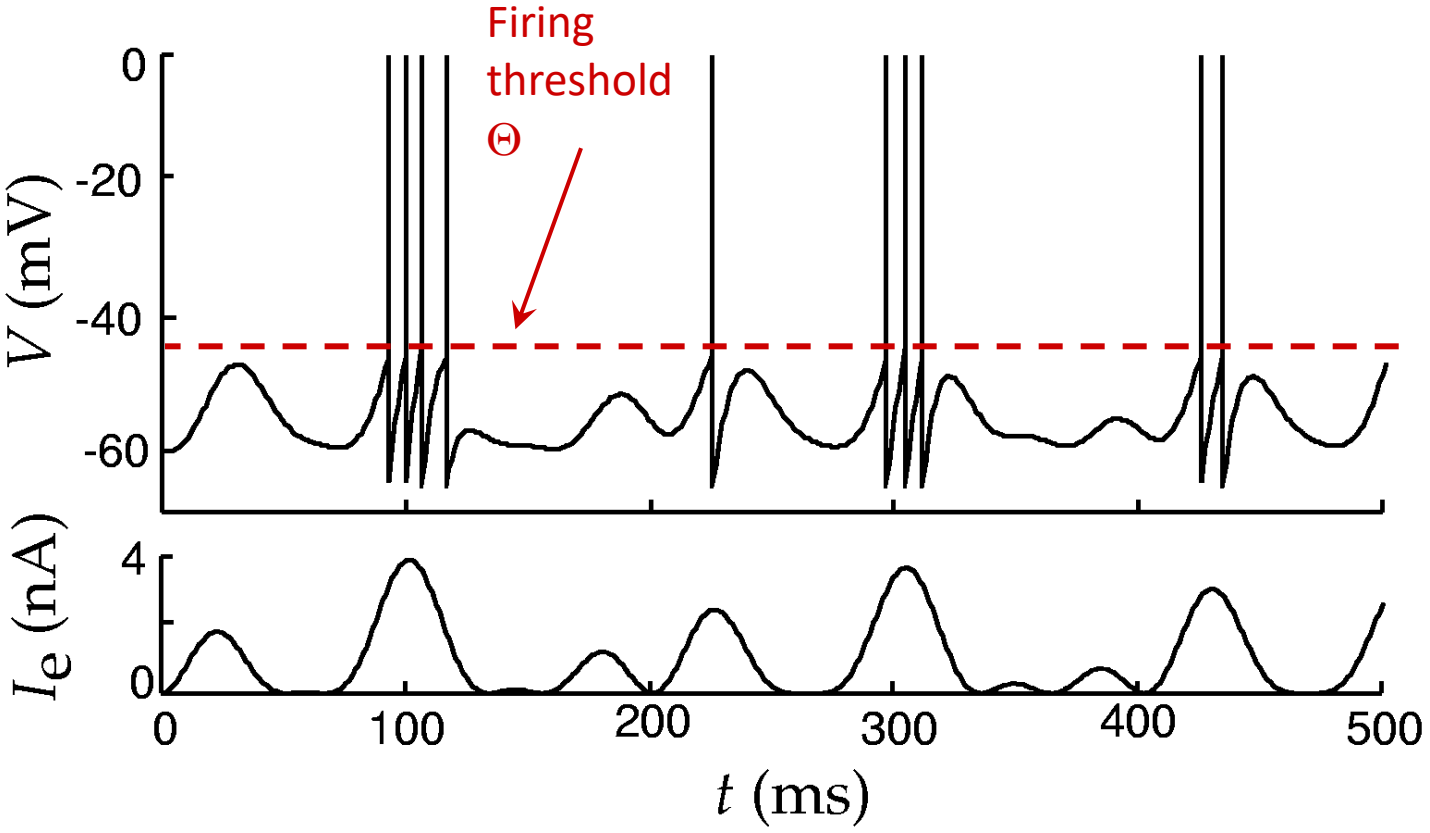
$$f(V) = -g_L(V - E_L) + g_L \Delta_T \exp\left(\frac{V - \Theta}{\Delta_T}\right)$$

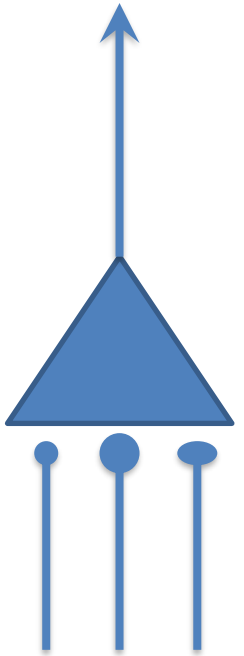
$$\tau_w \frac{dw}{dt} = a(V - E_L) - w$$

- if $V \geq \Theta$, then three events happen
  - Postsynaptic neuron fires a spike
  - V is reset to a reset potential, for instance V_0 and
  - leakage current variable w is reset to $w + b$

- Dependent variables: ***V***, ***I***, and variable ***w***.
- Parameters: c_m, g_L, Θ, Δ_T, a, b, and all the equilibrium potentials E.

Behaviour of AdEx model in response to excitatory inputs I_e





- Excitatory synaptic inputs are waveforms of electric current I_e evoked by synapses of different strengths (weights).
- The stronger synapse, the higher the waveform. Stronger synapses manage to cross the firing threshold and fire the neuron model.

Izhikevich's model of spiking neuron

- reproduces firing behavior of many types of cortical neurons. It combines the biologically plausibility of Hodgkin-Huxley-type dynamics and the computational efficiency of integrate-and-fire neurons. (http://www.izhikevich.org/publications/spikes.htm)

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I$$

$$\frac{du}{dt} = a(bv - u)$$

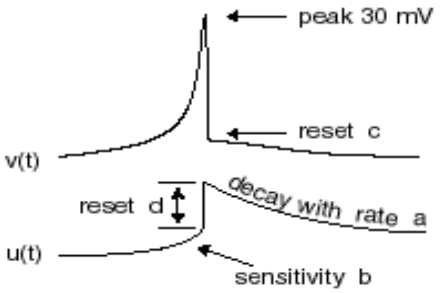
$$\text{if} \quad v \geq peak, \quad \text{then} \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases}$$

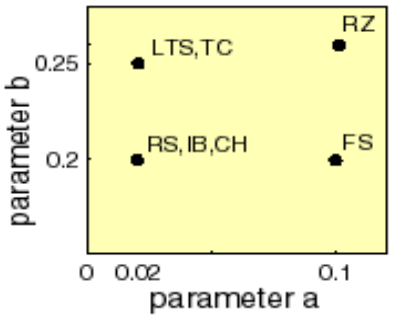
- Dependent variables: ***I***, ***v*** and ***u***
- Parameter *peak* is the value of the spike peak.
- Parameters: a, b, c, d – these determine a particular spiking pattern.

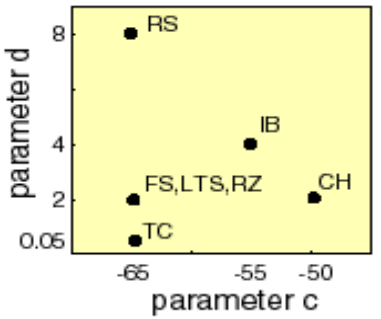
The project: Simple spiking model of Izhikevich

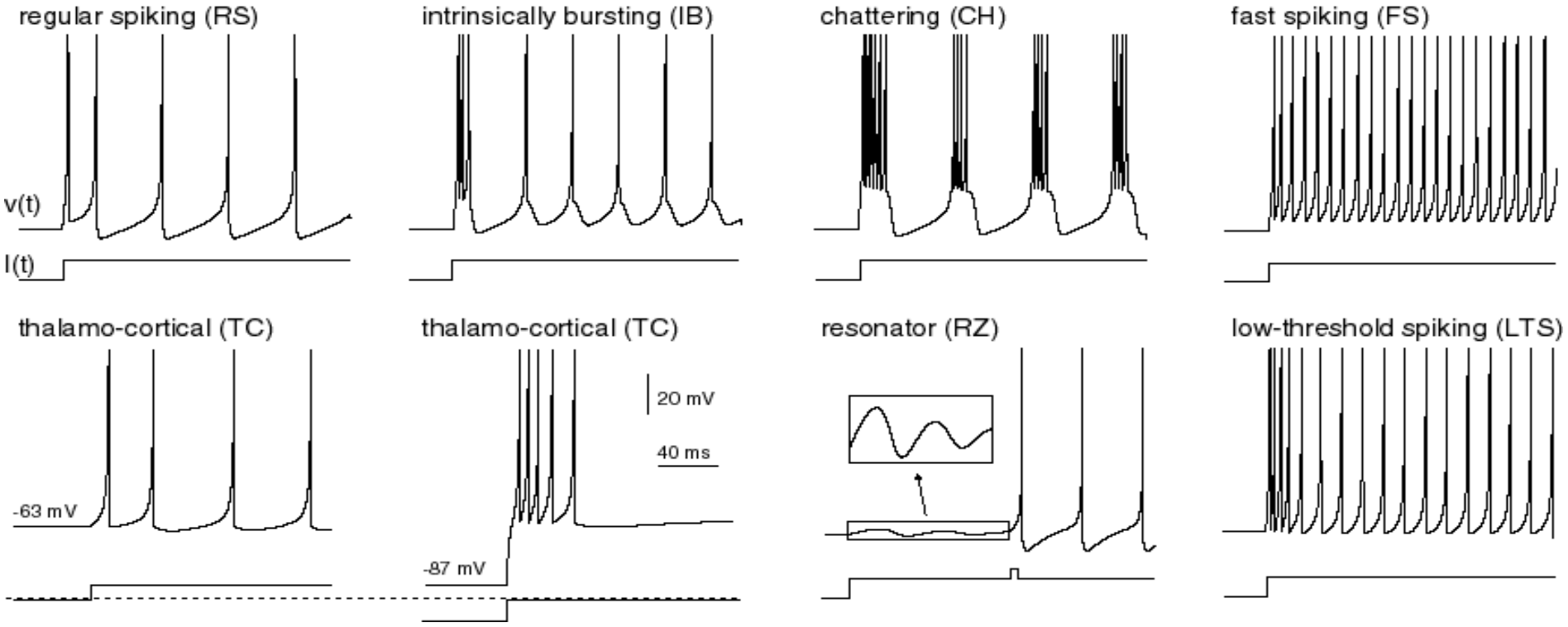
$v' = 0.04v^2 + 5v + 140 - u + I$
$u' = a(bv - u)$

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









Summary for I&F

- There are many modifications of the basic I&F model
  - Adaptive exponential I&F model AdEx of Brette and Gerstner;
  - Simple spiking model of Izhikevich;
  - And many more models tailored to specific types of neurons.

Figure 1.8: Neurons are dynamical systems.