Generation and propagation of axon potentials

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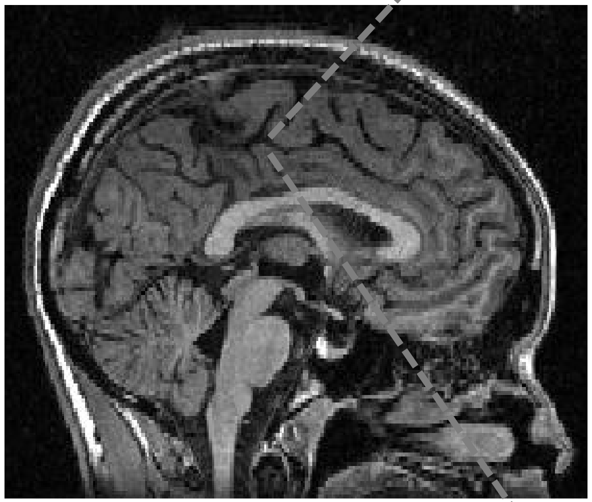
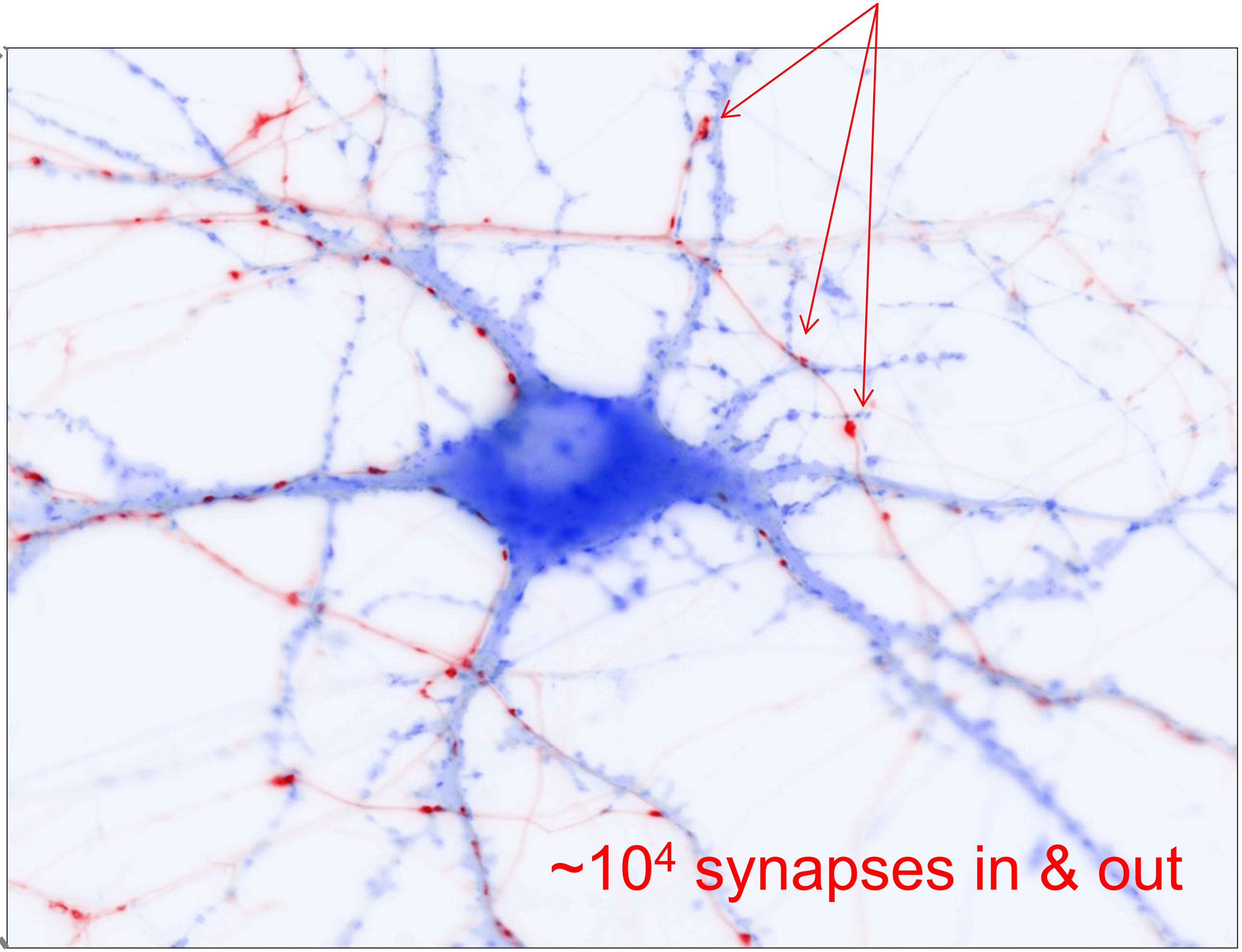
COSC422 – lecture 2

Brain is comprised of networks of neurons connected and communicating via synapses



~10^{12} neurons
(nerve cells)



Parts of neuron

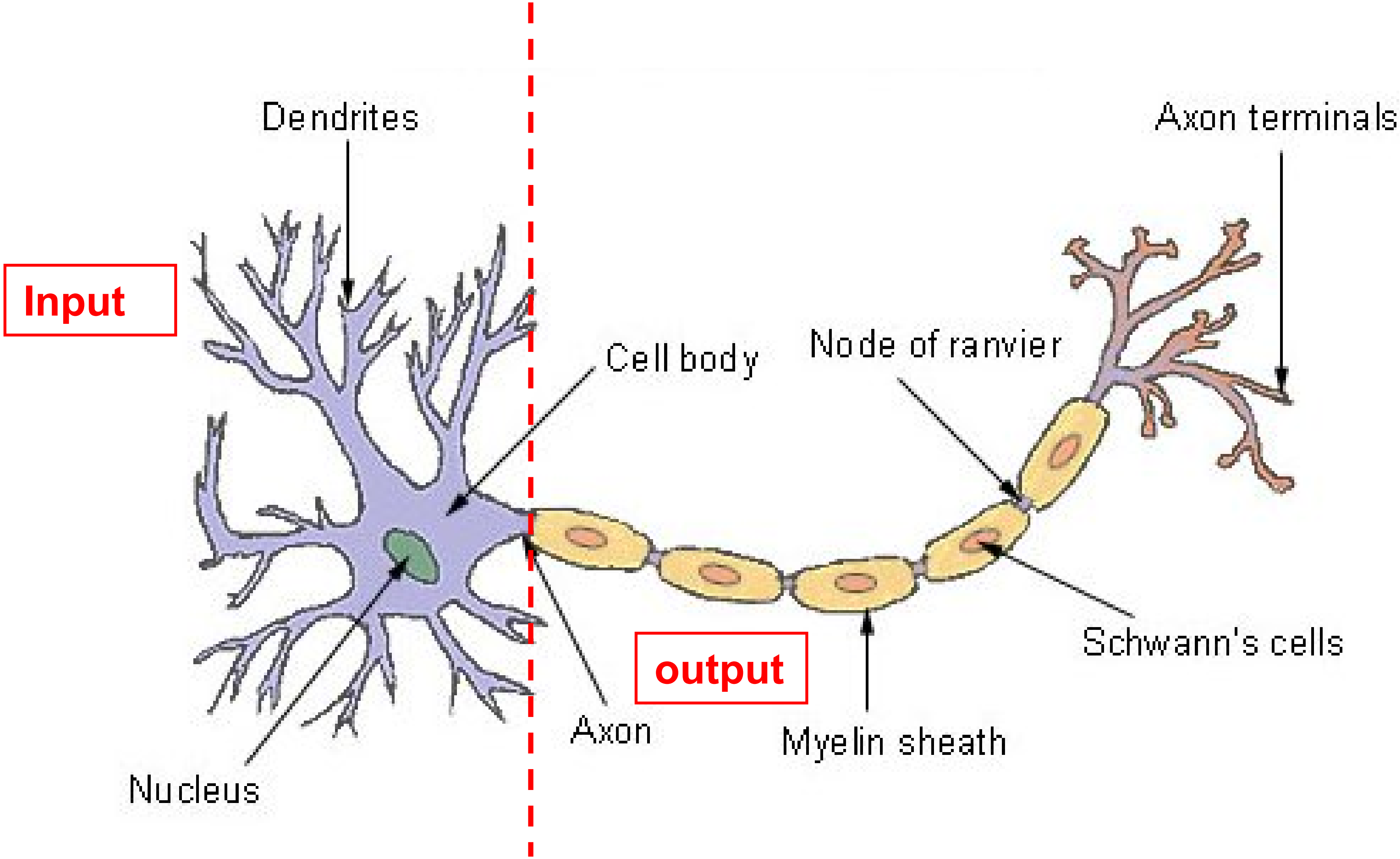
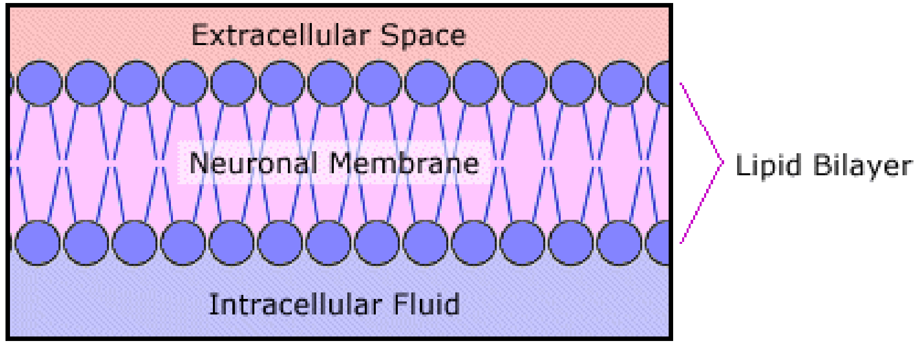


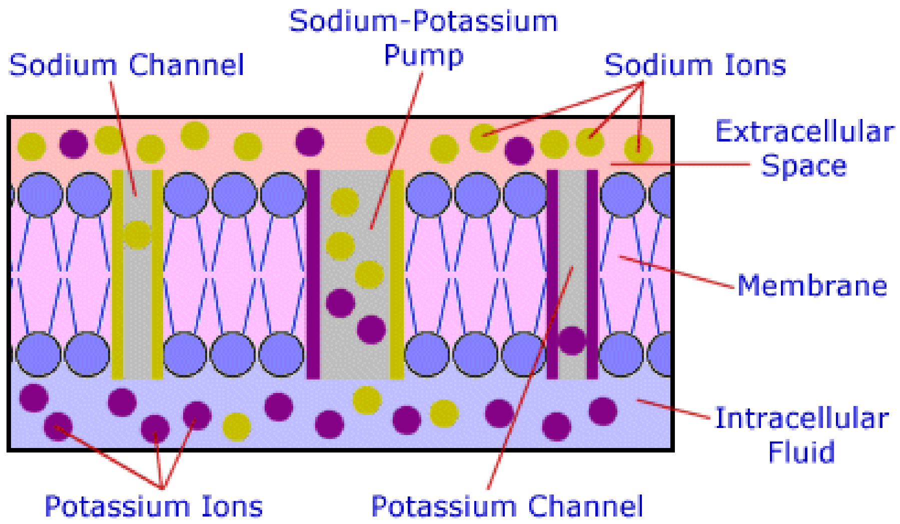
Image source: http://www.daviddarling.info/encyclopedia/N/neuron.html

Neuronal membrane

- Membrane is comprised of a double layer (bilayer) of lipids, i.e. molecules of fat.

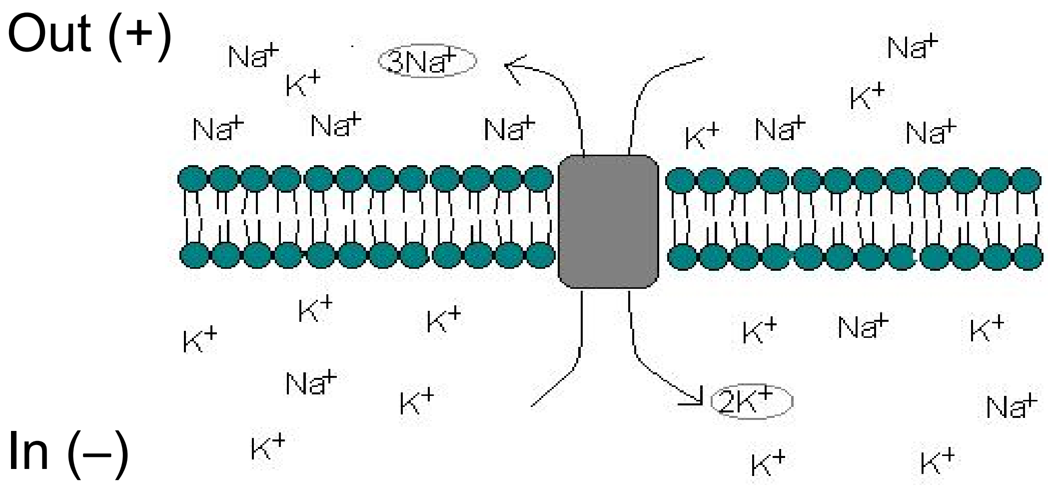


- The membrane also contains proteins that are:
  - Ion pumps that pump ions against their electric/ concentration gradients
  - Ion channels that pass ions along their concentration gradients
  - Receptors: proteins that bind some chemical and relay the signal to the inside of the cell.



Outside and inside neurons are charged **ions**

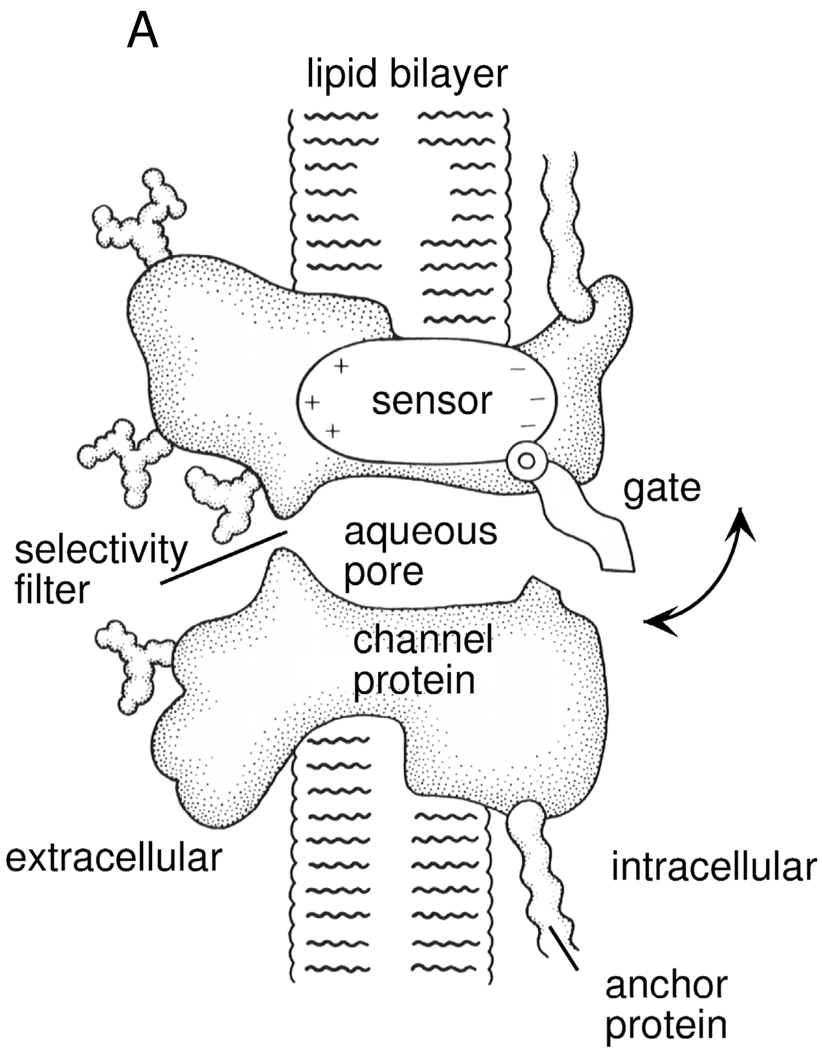
- In water, the salt NaCl molecule breaks down, and we get charged atoms, called ions: Natrium with a positive charge (Na^+) , and chlorine (Cl^-) with a negative charge. There are also potassium (K^+) ions.



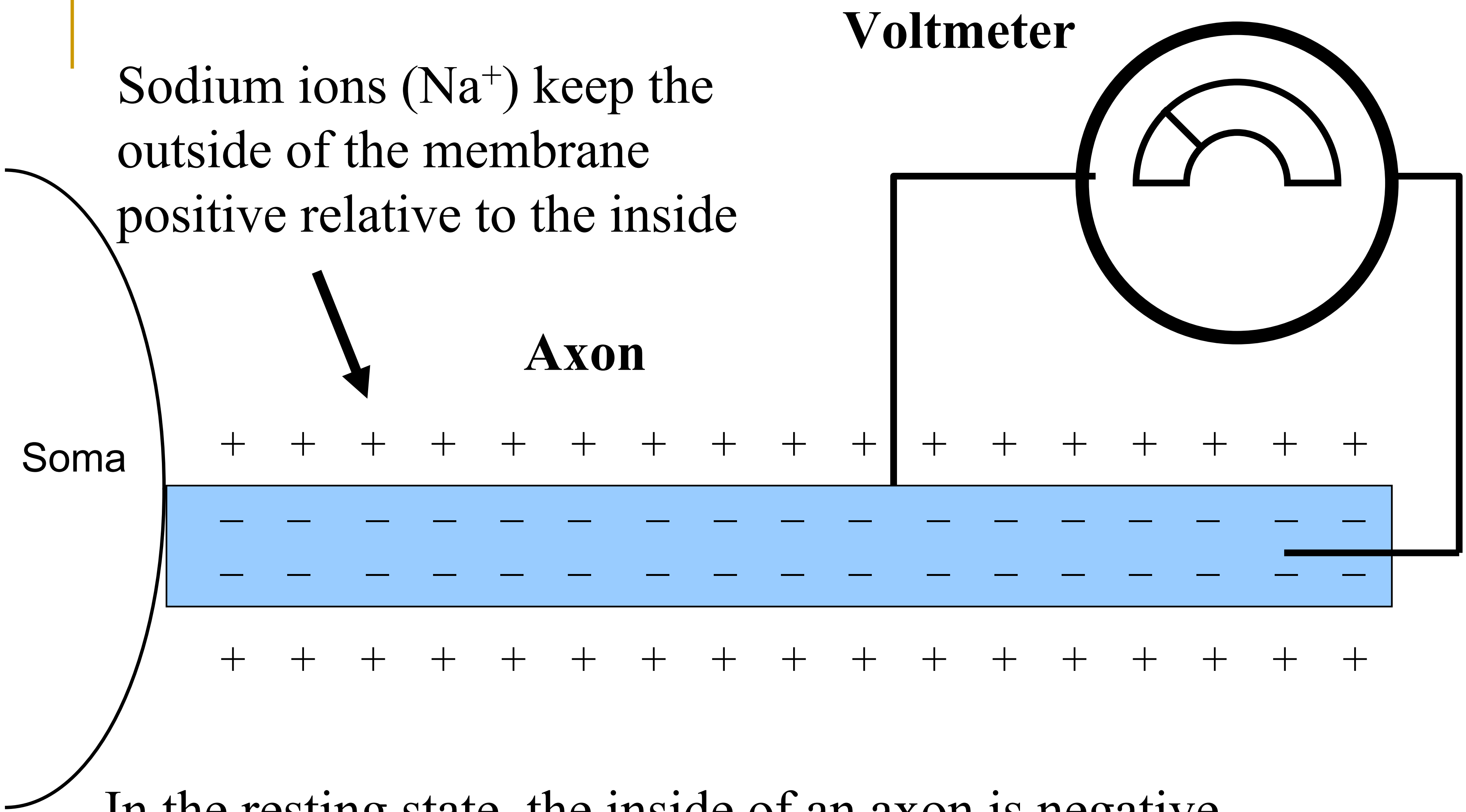
$$V = V_{in} - V_{out} \approx -70 \text{ mV}$$

- Molecular pumps in the membrane keep the Na^+ ions outside the membrane of the neuron and K^+ inside, thus creating a voltage difference between the inside and the outside of neuron membrane.

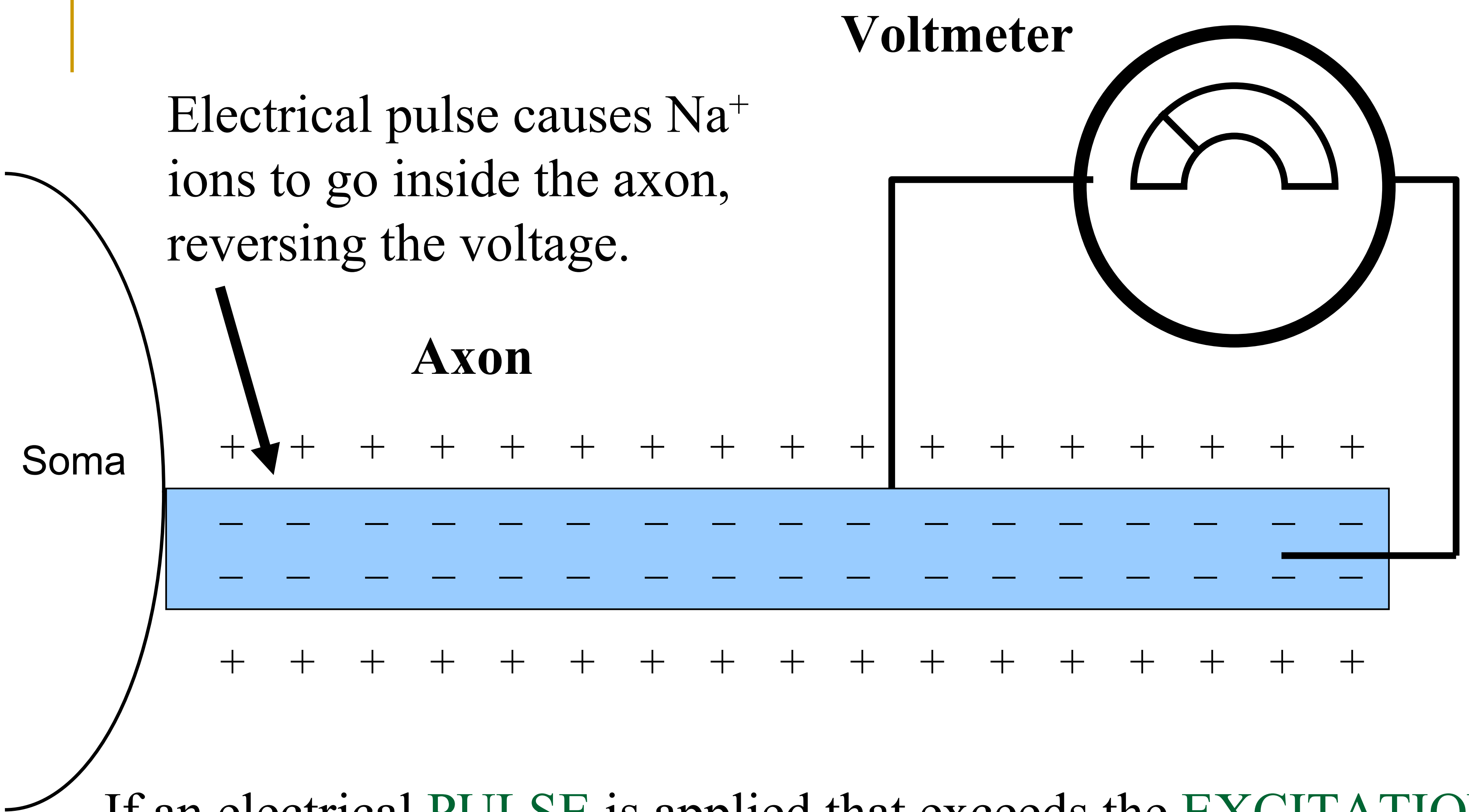
Electrical pulses depends on ion channels



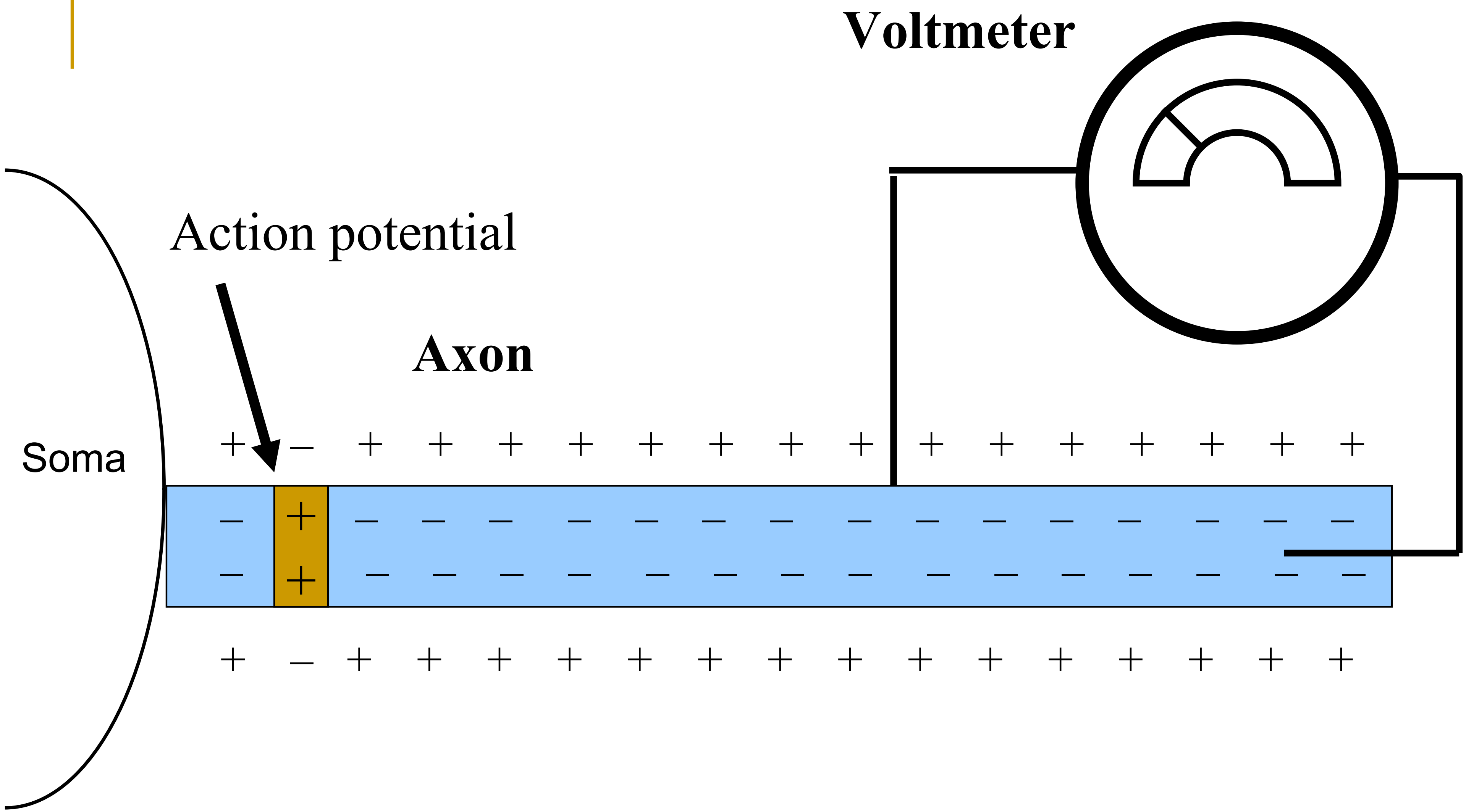
- In addition to Na/K pumps, there are various types of ion channels in the membrane of neurons.
- These ion channels are specifically permeable for different ions thus we speak about Na channels, K channels, Cl channels.
- Cl channels are always open. Na and K channels open and close when the membrane voltage V changes.



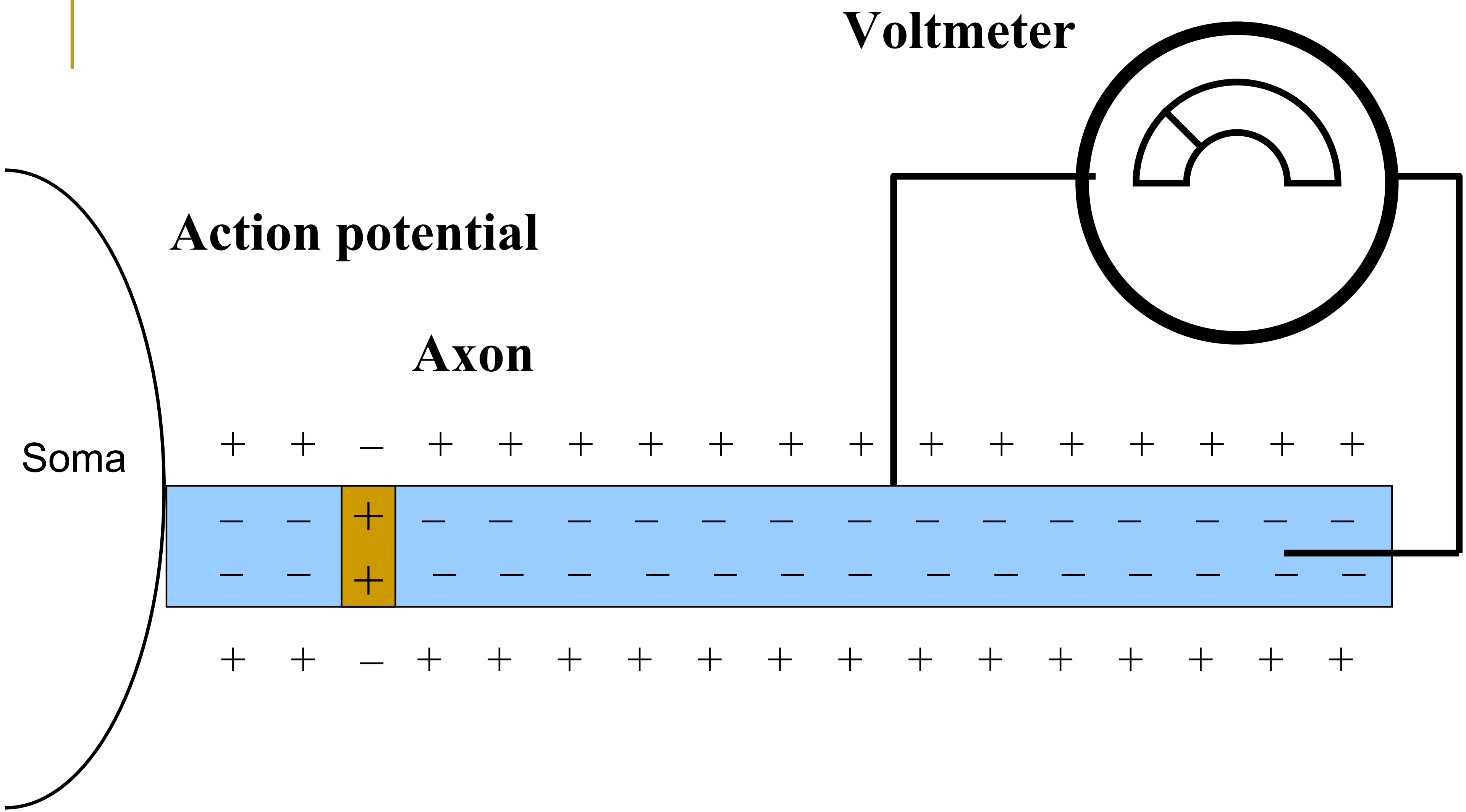
In the resting state, the inside of an axon is negative with respect to the outside, by about –70 millivolts (mV). This is called the RESTING POTENTIAL V_0



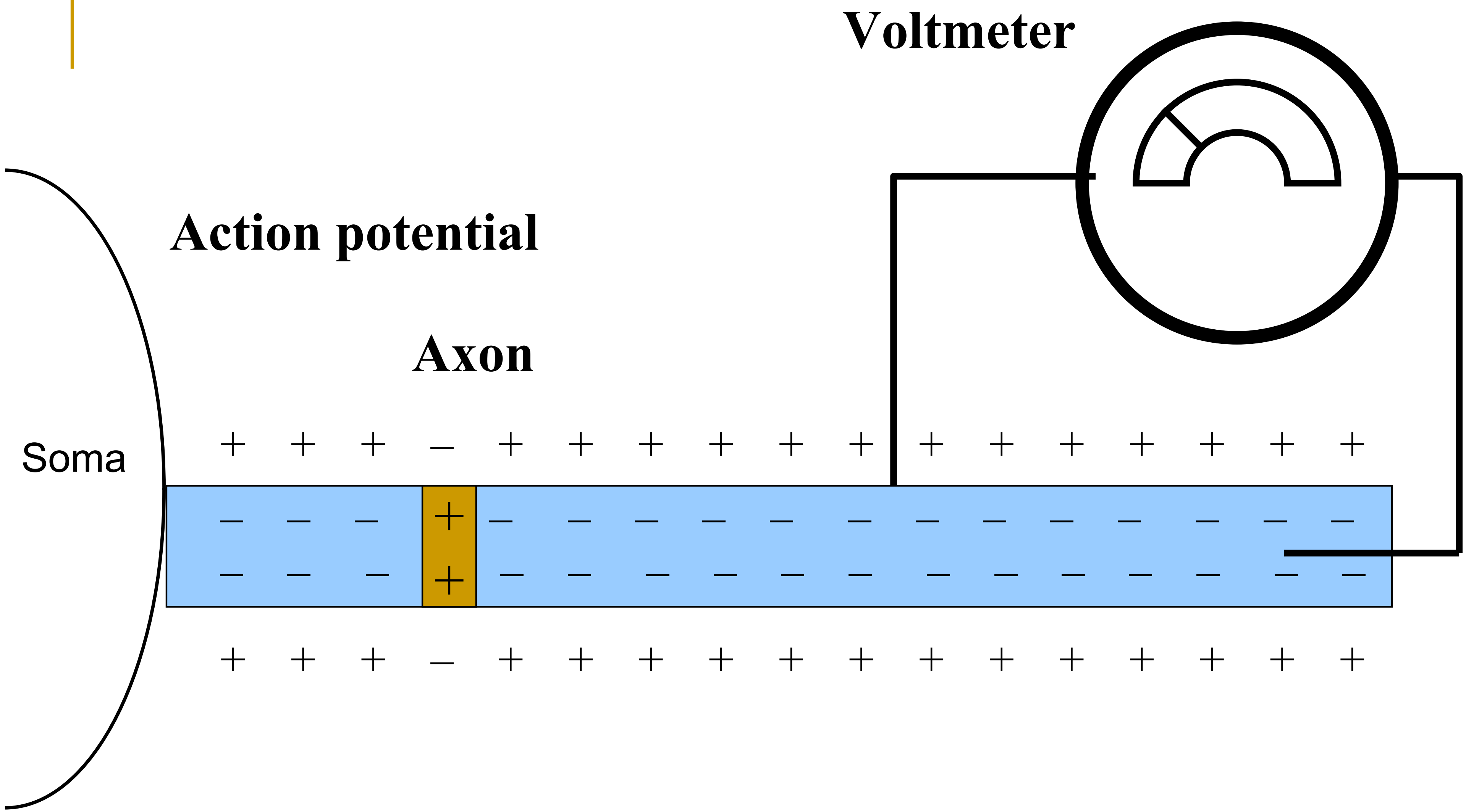
If an electrical PULSE is applied that exceeds the EXCITATION THRESHOLD (about –55 mV), then an ACTION POTENTIAL also called SPIKE is generated.



Action potential is generated in the axon hillock and causes the inside to swing positive relative to the outside in a small patch of membrane.



This action potential progresses along the axon, like a Mexican wave



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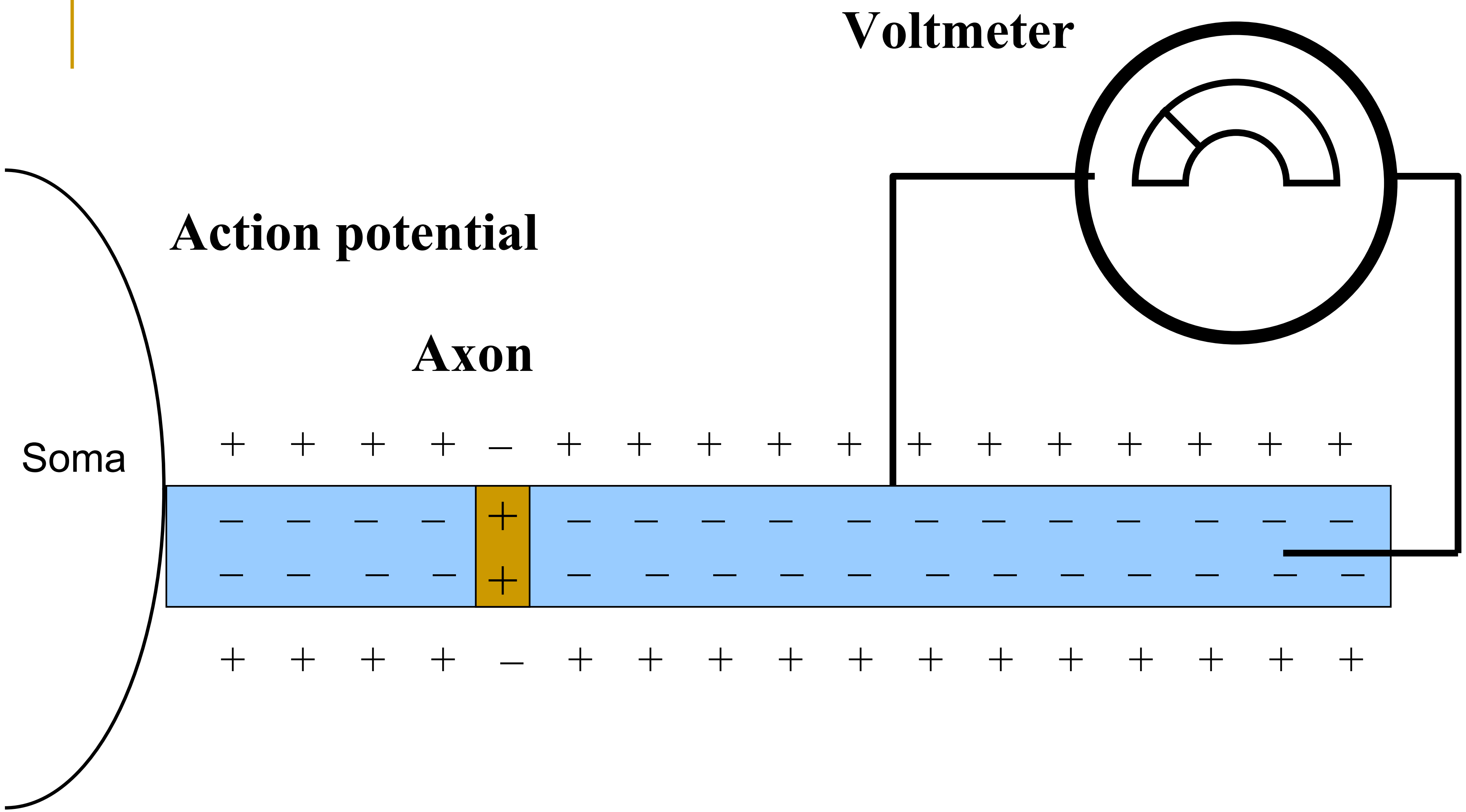

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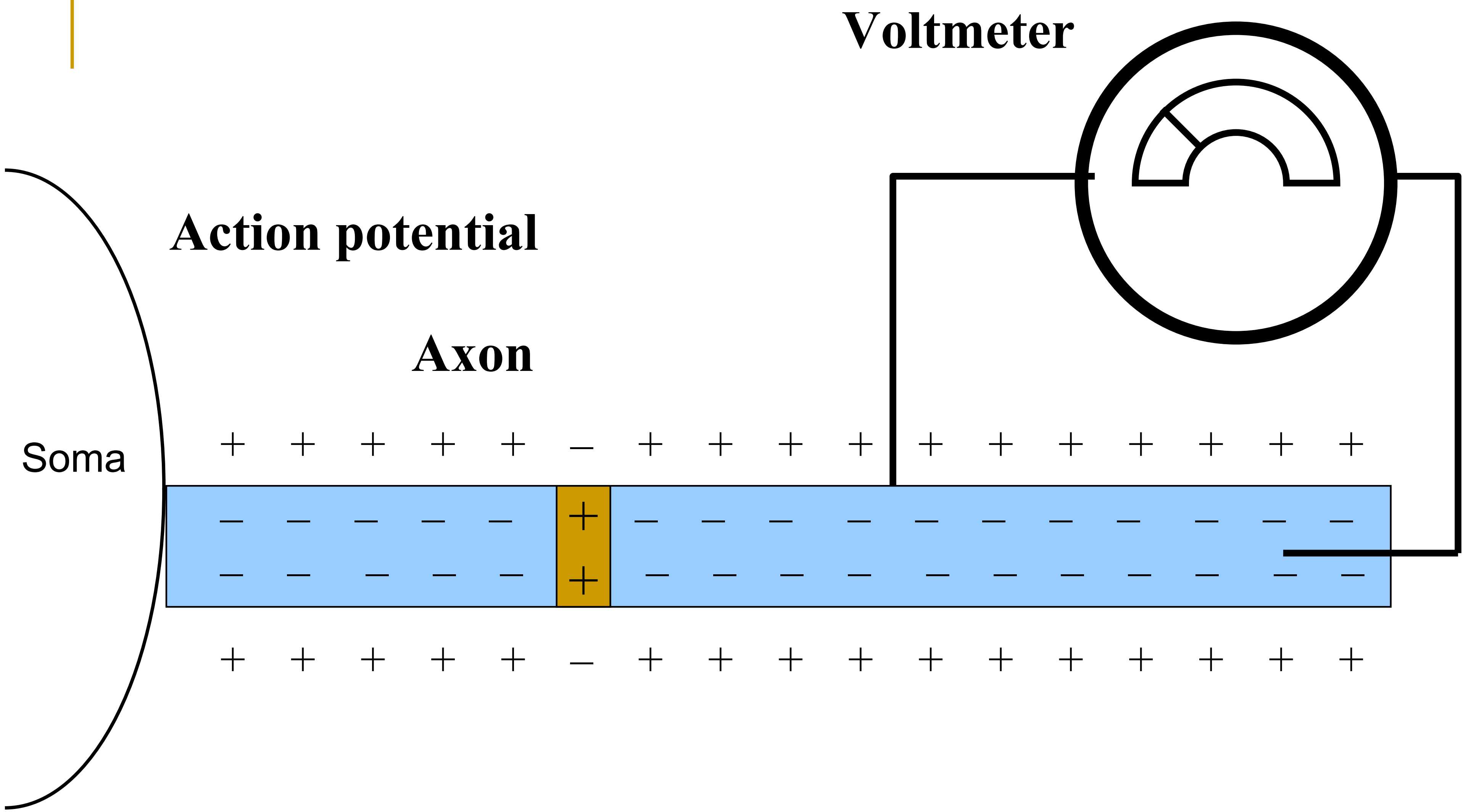
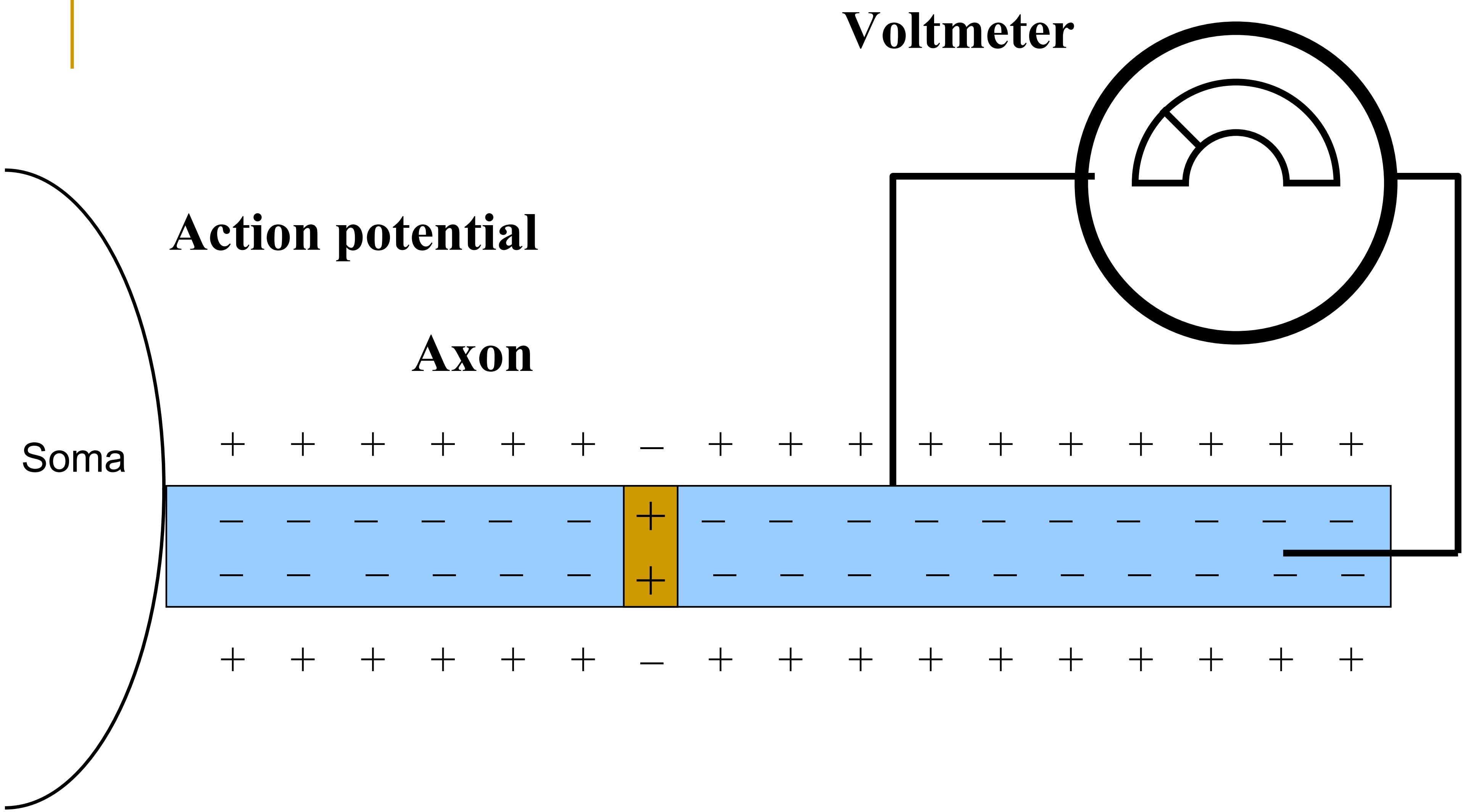


This action potential progresses along the axon, like a Mexican wave.

Action potential



This action potential progresses along the axon, like a Mexican wave.

Restoration of the resting potential

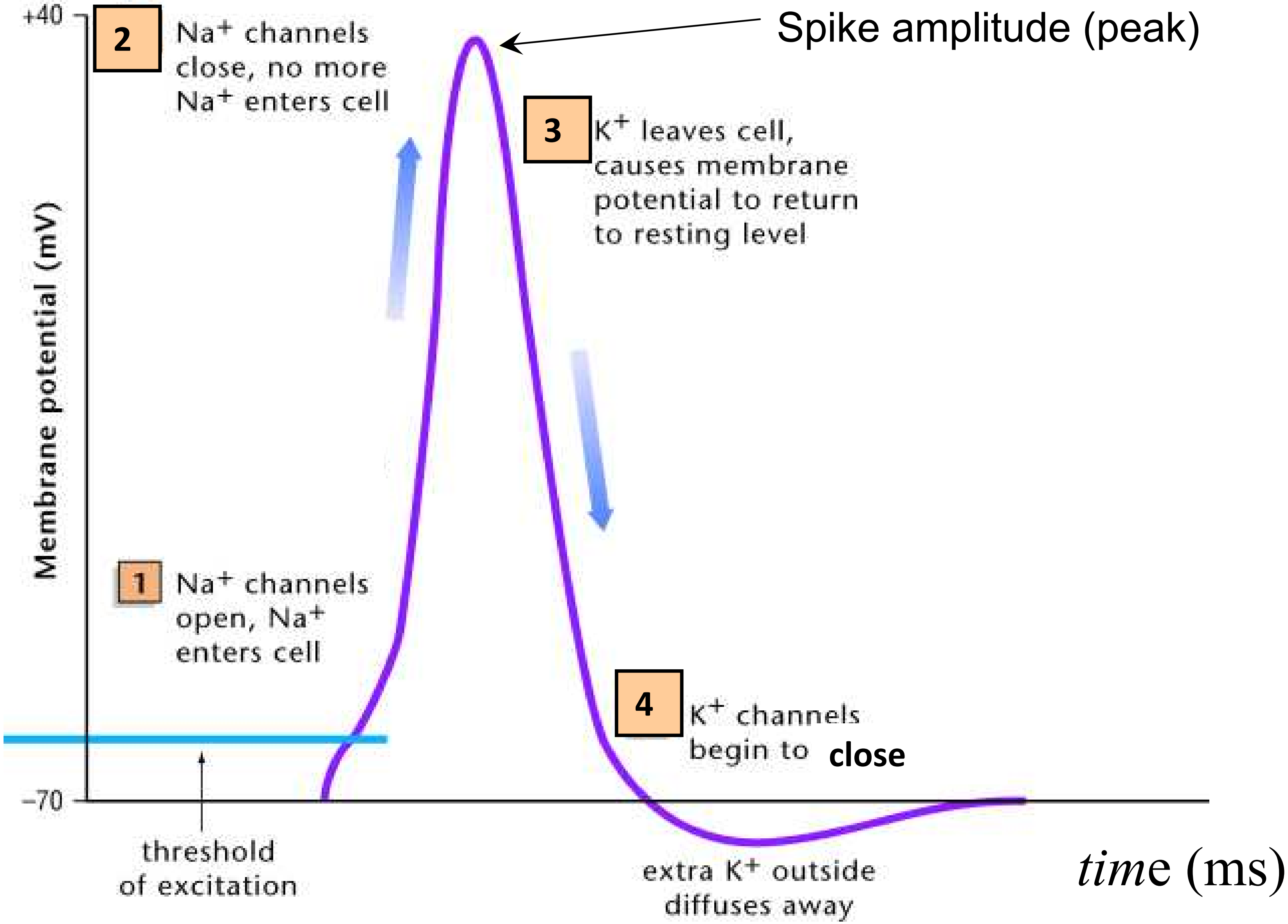
- After the surge of Na^+ inside the neuron, the resting potential is restored first by closing the Na^+ channels and then by opening the K^+ channels and letting out K^+ ions.

- Then Na+ ions are pumped out and K+ in via pumps until the equilibrium is established again.

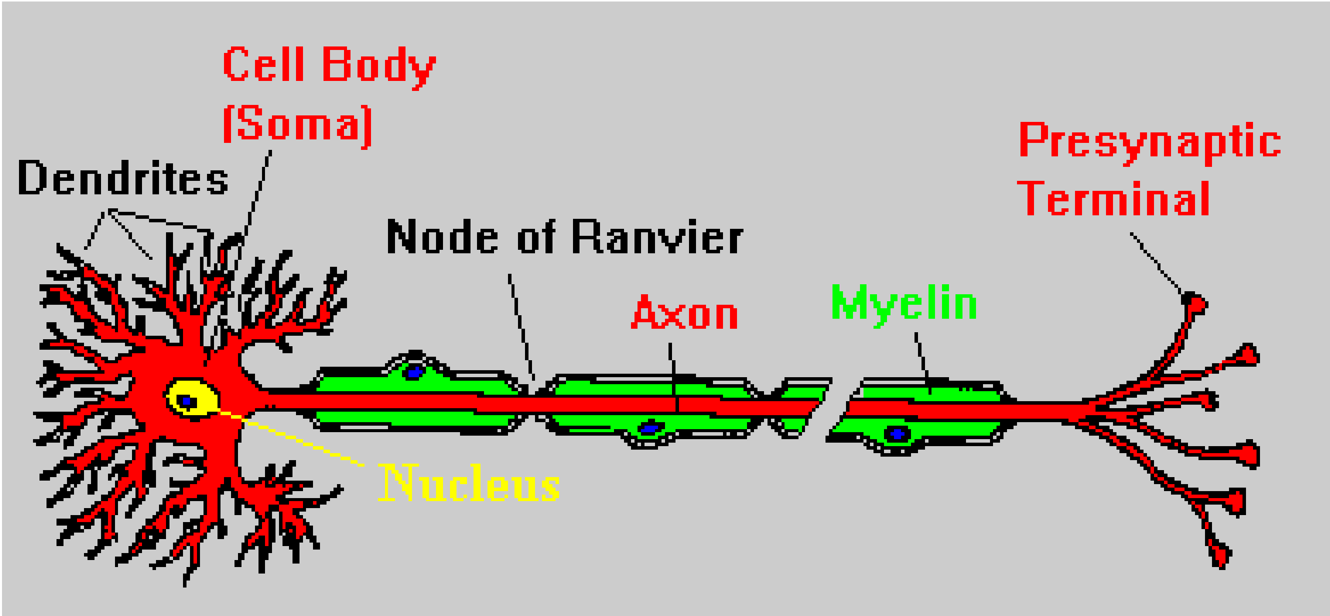
- All this takes time, creating a **refractory period** when the cell can't fire again, i.e. can't generate a new axon potential.

- Absolute refractory period lasts 1-2 ms, but it's followed by 5 ms of relative refractory period when the firing threshold is elevated.

Change of voltage during action potential

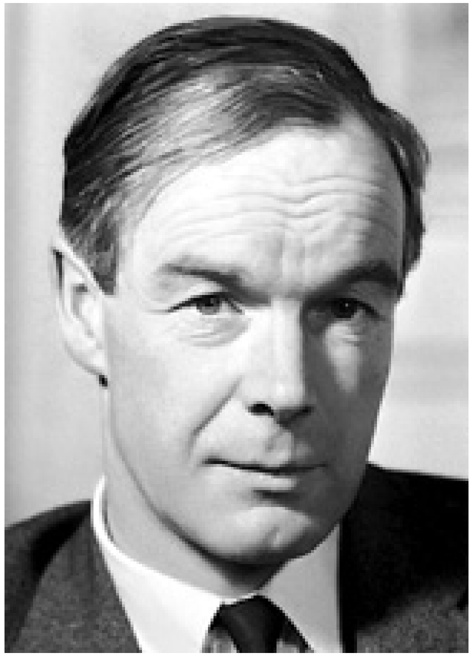


Spikes "jump" along axons

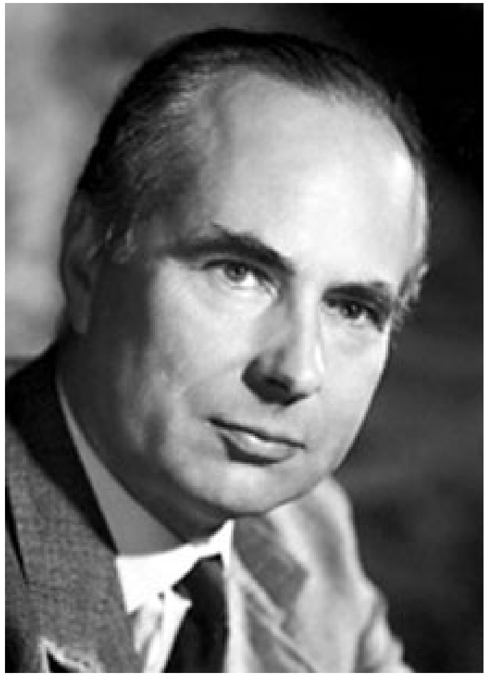


- Axons have a myelin sheath surrounding the axons, that makes up the "white matter" of the brain (grey matter are somas and dendrites).
- This speeds transmission, because the spike jumps between the gaps (nodes of Ranvier) and the sheath provides electrical insulation.
- In each gap, the original amplitude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

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 representing one of the earliest applications of a technique of electrophysiology, known as the "voltage clamp".
- Another critical element was the use of the giant axon of Atlantic squid, which enabled them to record ionic currents using the techniques of the time.



Hodgkin-Huxley model

- Besides measuring membrane currents and voltages in the axon they also developed the first mathematical model of axon potential generation.

- This is historically the first model of biological neurons explaining the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon (1952).

- The Hodgkin–Huxley model applies to all axons and is still used today:

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

Hodgkin-Huxley model contd.

- It describes mathematically how an action potential is generated when the total somatic potential rises above the firing threshold:

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

- Here: i_m is the total electric current flowing through the axonal membrane, 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.

- Symbols m, n, h denote empirically derived parametric functions of the model.

H-H model: dynamics of variables

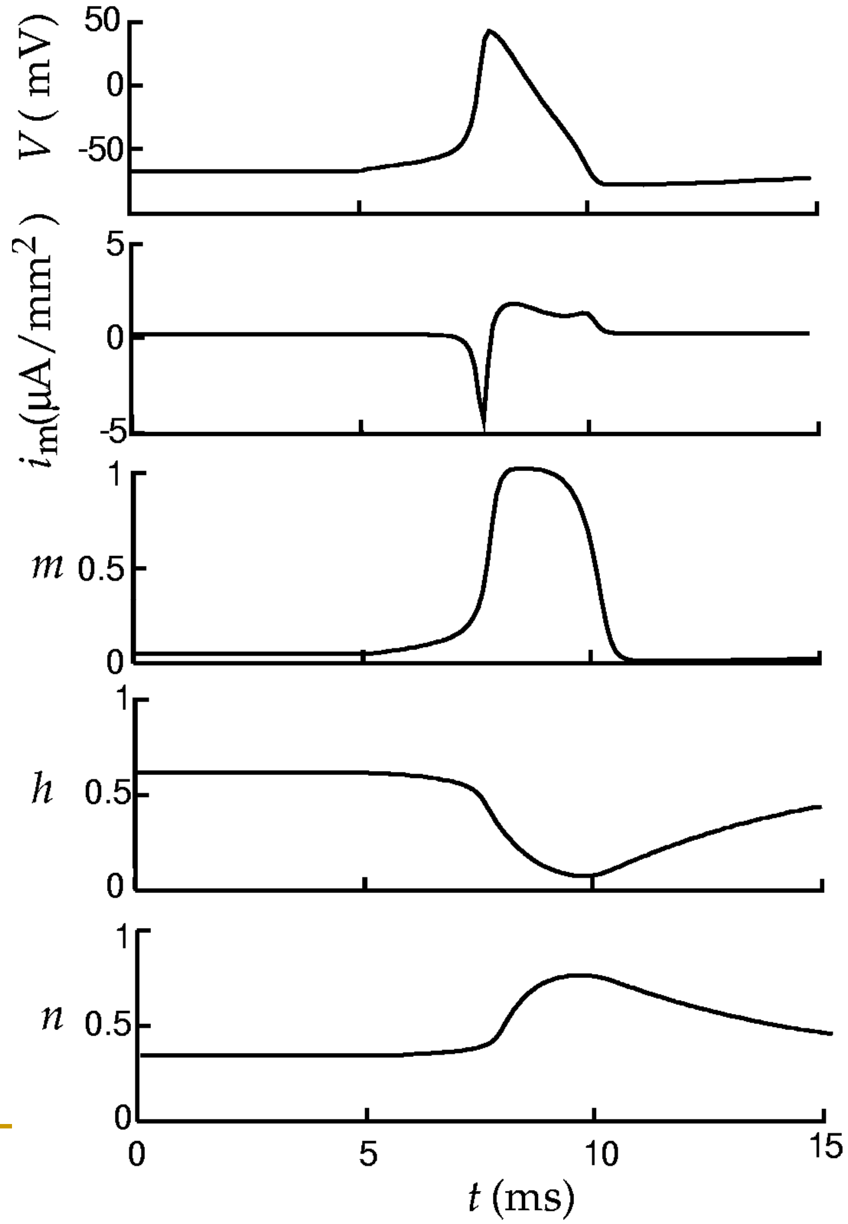
- The three variables *m, n*, and *h* are called gating variables. They evolve according to the differential equations (*V* is voltage):

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

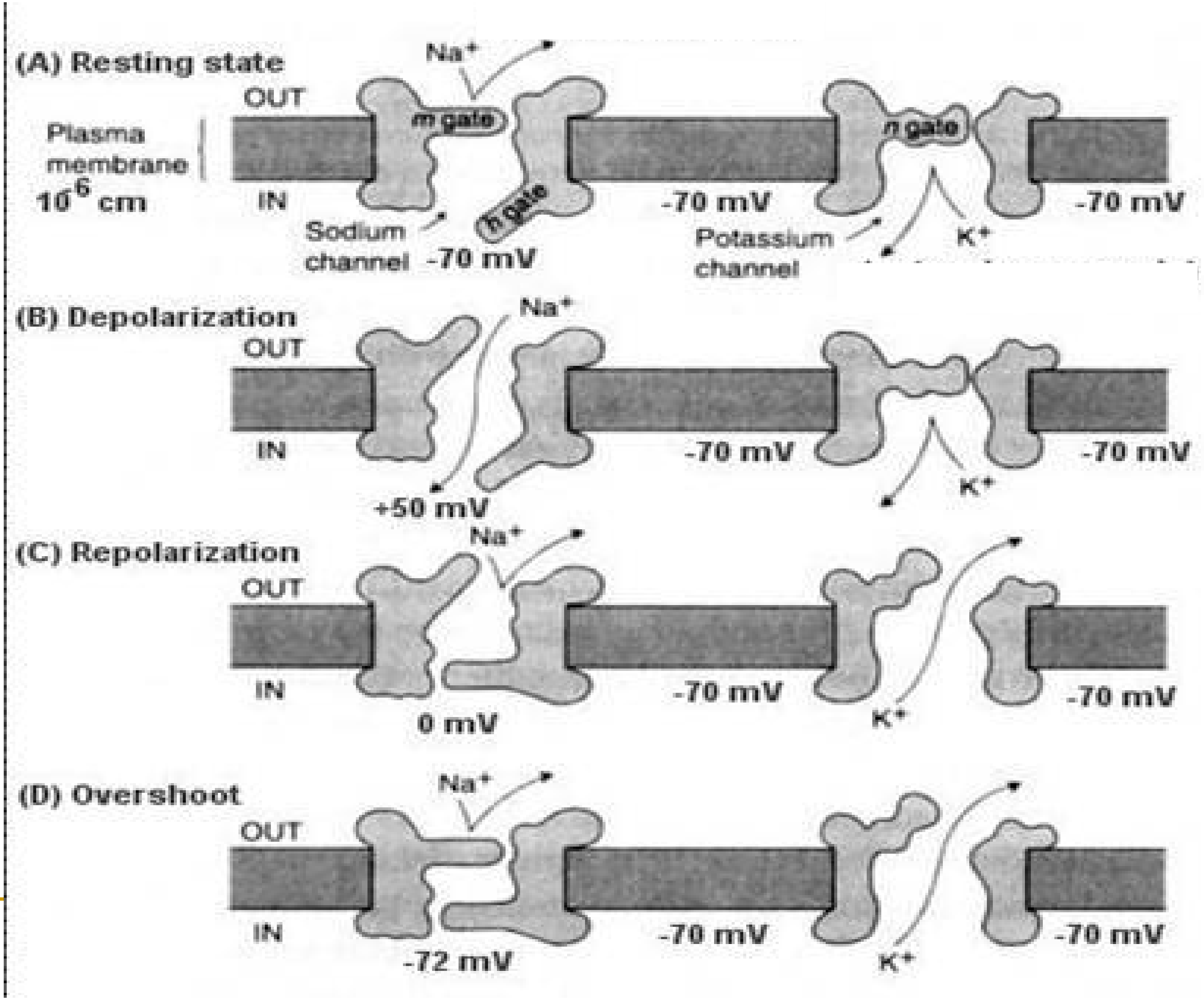
x	$\alpha_x(V/\mathrm{mV})$	$\beta_x(V/\mathrm{mV})$
n	$(0.1 - 0.01V)/[\exp(1 - 0.1V) - 1]$	$0.125\exp(-V/80)$
m	$(2.5 - 0.1V)/[\exp(2.5 - 0.1V) - 1]$	$4\exp(-V/18)$
h	$0.07\exp(-V/20)$	$1/[\exp(3 - 0.1V) + 1]$

H-H model: dynamics of variables

- Resulting time course of the membrane voltage V during spike:
- Underlying time course of the membrane current i_m :
- Time course of the variable m:
- Time course of the variable h:
- Time course of the variable n:



Ion channels in action potential (spike)



Conclusion

- The 4 phases of spike generation correspond to particular states (open, close) of Na and K ion channels in the membrane of an axon.

- *m, n, h* , the empirically derived parametric functions of the H-H model, were later discovered to correspond to kinetics of individual subunits/gates of Na and K ion channels.

- Software NEURON numerically solves HH equation. We will build soma next time because the spike is generated where the soma becomes an axon (axon hillock).