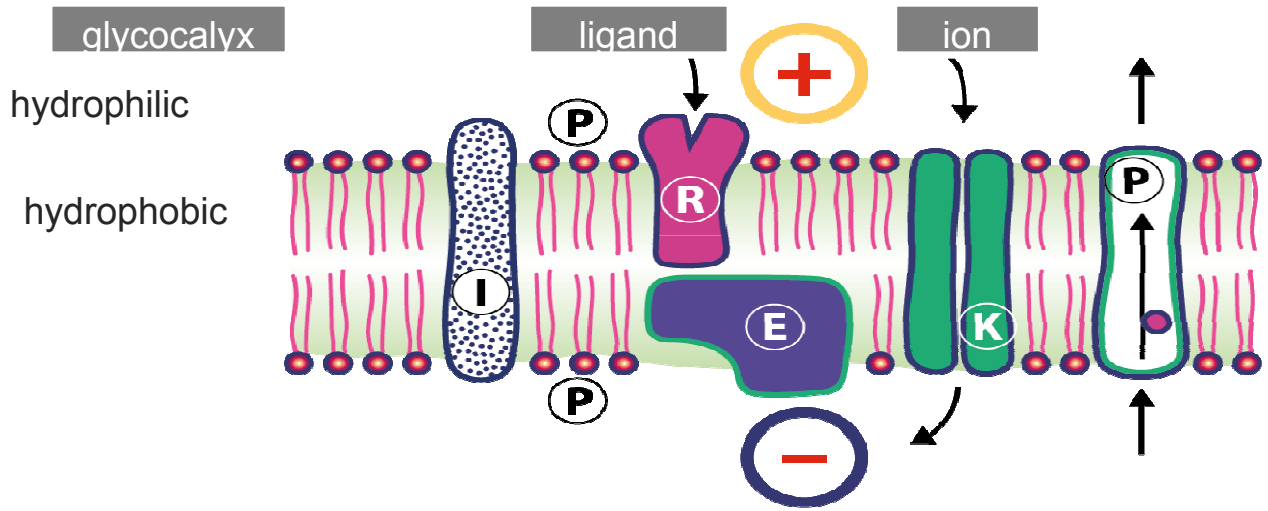
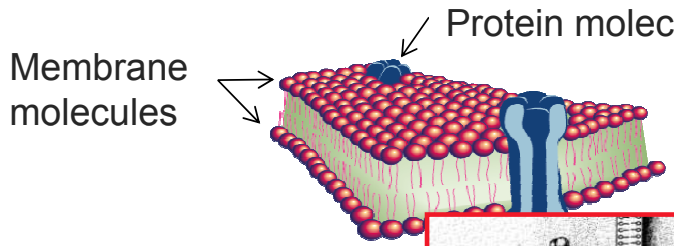
MUNI
MED

MEMBRANE OF EXCITABLE CELL. ELECTRICAL TRANSMISSION OF INFORMATION.

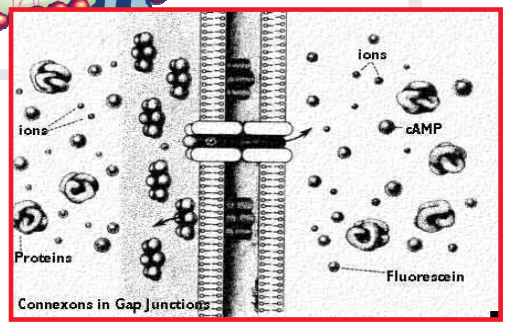
PLASMATIC MEMBRANE



I – integral protein
R – receptor
E – enzyme
K – channel (kanál)
P – pump (ATP-ase)



Nexus (gap junction) →



Marie Nováková, Department of Physiology, Faculty of Medicine, Masaryk University

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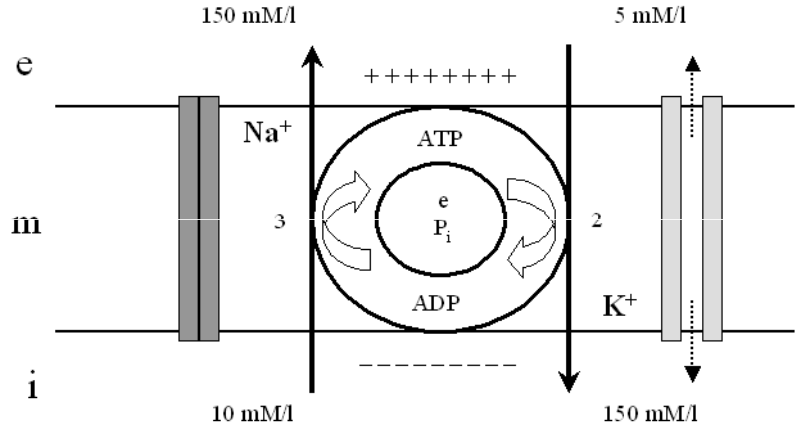
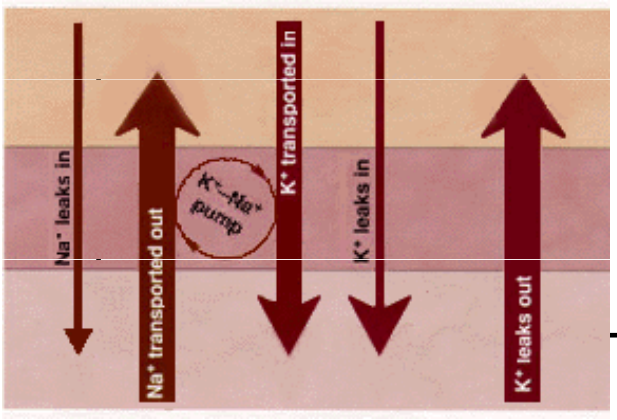
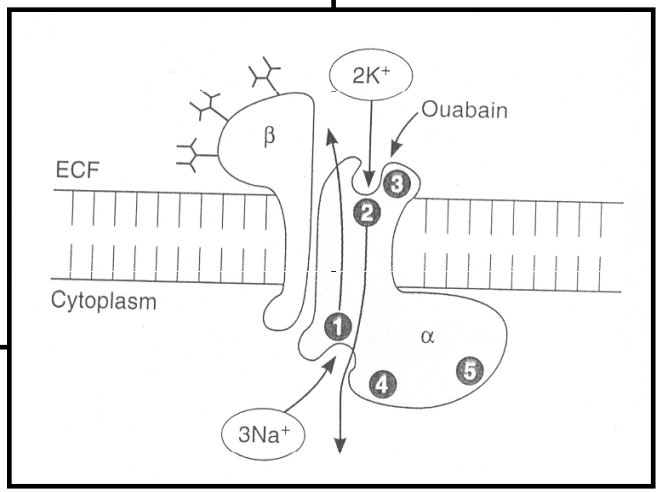
SODIUM-POTASSIUM EXCHANGER







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RESTING MEMBRANE POTENCIAL

It is the result of:

different cell membrane permeability for sodium (Na +)

and potassium (K+) ions

the presence of a sodium-potassium pump in cell membranes, which promotes this uneven distribution of intracellular and extracellular fluid ions

Phenomena occurring in the resting membrane potential

- ✓ Low membrane permeability for Na+
- ✓ High membrane permeability for K+
- ✓ Primarily active transport: Na+ out of the cell and K+ into the cell (given by the presence of Na+-K+ ATPase, in the ratio: 3 Na + out / 2 K + inwards)
- ✓ **Inside the cell remain anions of proteins and phosphates**

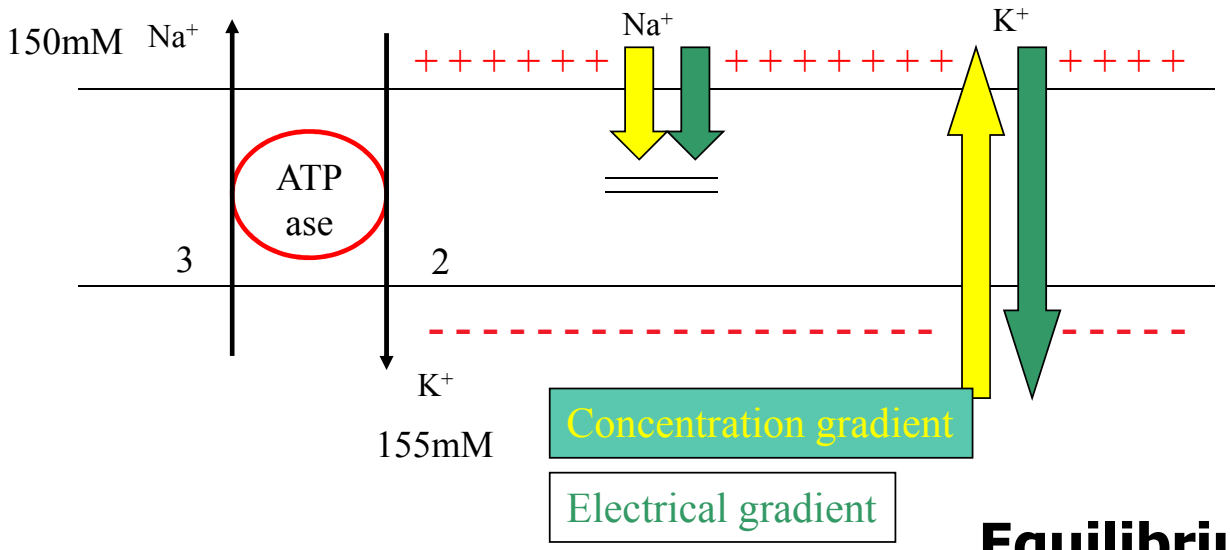
(thanks to this, we measure the electrical voltage between the outside and the inside of the cell)

We conclude that:

The cell membrane is

POLARIZED at rest

RESTING MEMBRANE VOLTAGE



Equilibrium potential

E_{Na} = +40 mV

E_K = -90 mV

E_{Cl} = -70 mV

E_{Ca} = +60 mV

E_r = -85 mV

Nernst equation:

$$Ex = \frac{R \cdot T}{F} \ln \frac{(Cx_{out})}{(Cx_{in})}$$

$$I_x = g_x \cdot (E - E_x)$$

I – current, E – voltage, g – specific voltage and time-dependent conductance

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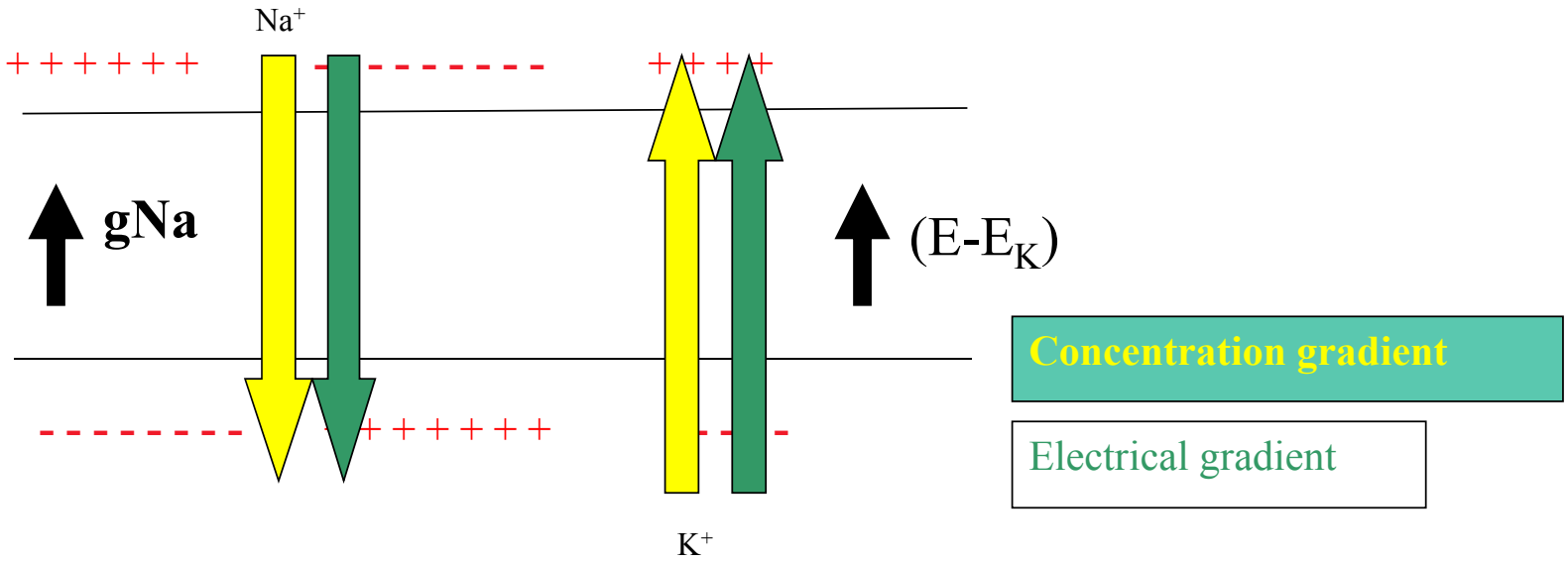
- For individual ions, we are able to calculate the so-called ions **EQUILIBRIUM potential** according to **NERNST EQUATION**

- In this context, potassium is most talked about, since its equilibrium potential is closest to the value of the resting membrane potential
- ($\mathbf{E_{k+}}$ = -70mV)
- $\mathbf{E_{k+}}$ – equilibrium potential of potassium means that the force driving the diffusion K+ outwards (chemical gradient) is just as great as the force of the potential acting in the opposite direction (electrical gradient)
- for sodium: $\mathbf{E_{Na}}$ = + 40mV

Physiological significance of resting membrane potential

- Cells use it to regulate their physiological functions, which include:
  - permeability of membranes of muscle and nerve cells for ions
  - intracellular calcium release for muscle contraction
  - release of nerve neurotransmiters (mediators) in the nervous system

ACTION POTENTIAL



Depolarisation
Transpolarisation

Repolarisation

(Hyperpolarisation)

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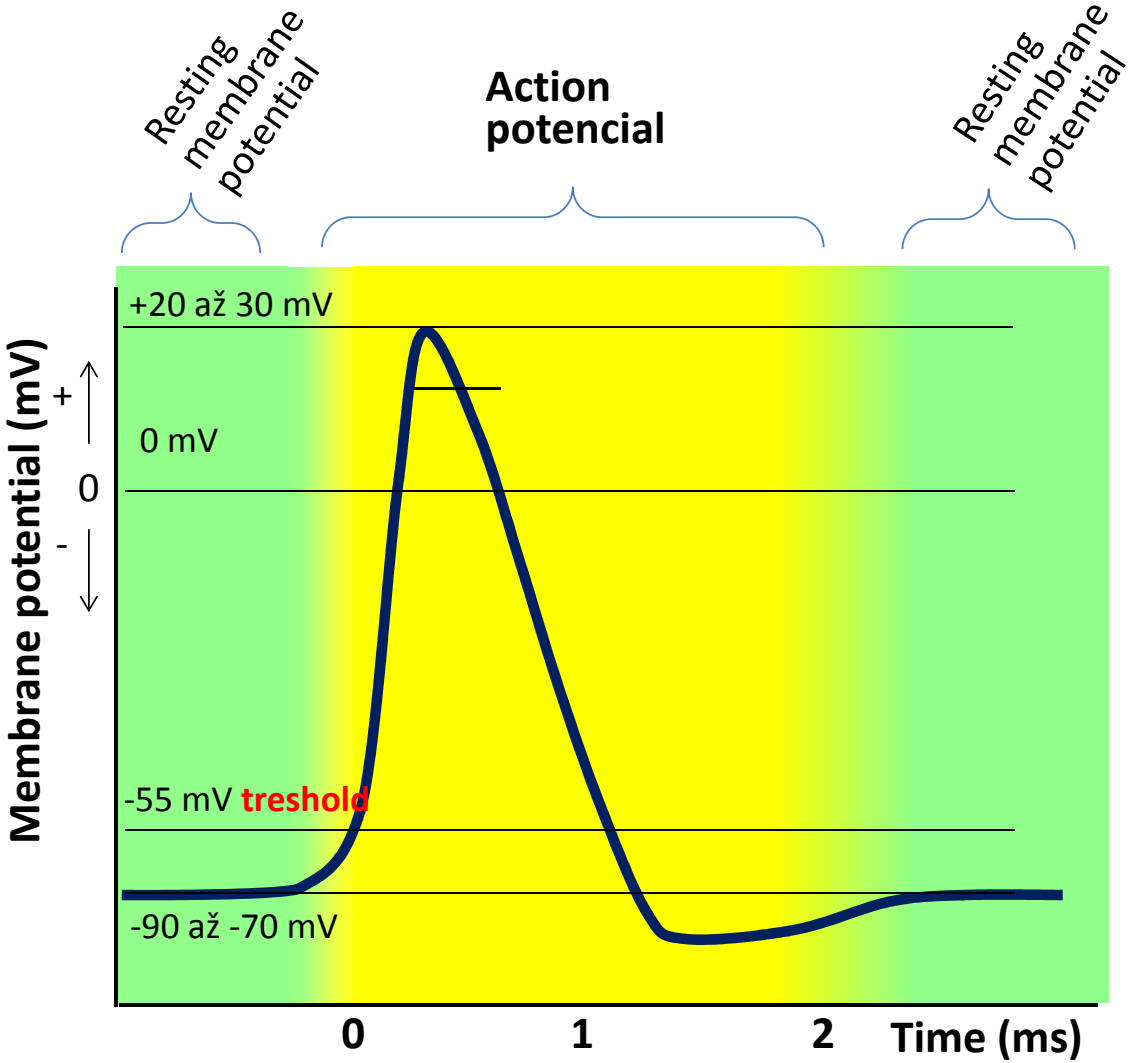
Resting membrane potential and action potential



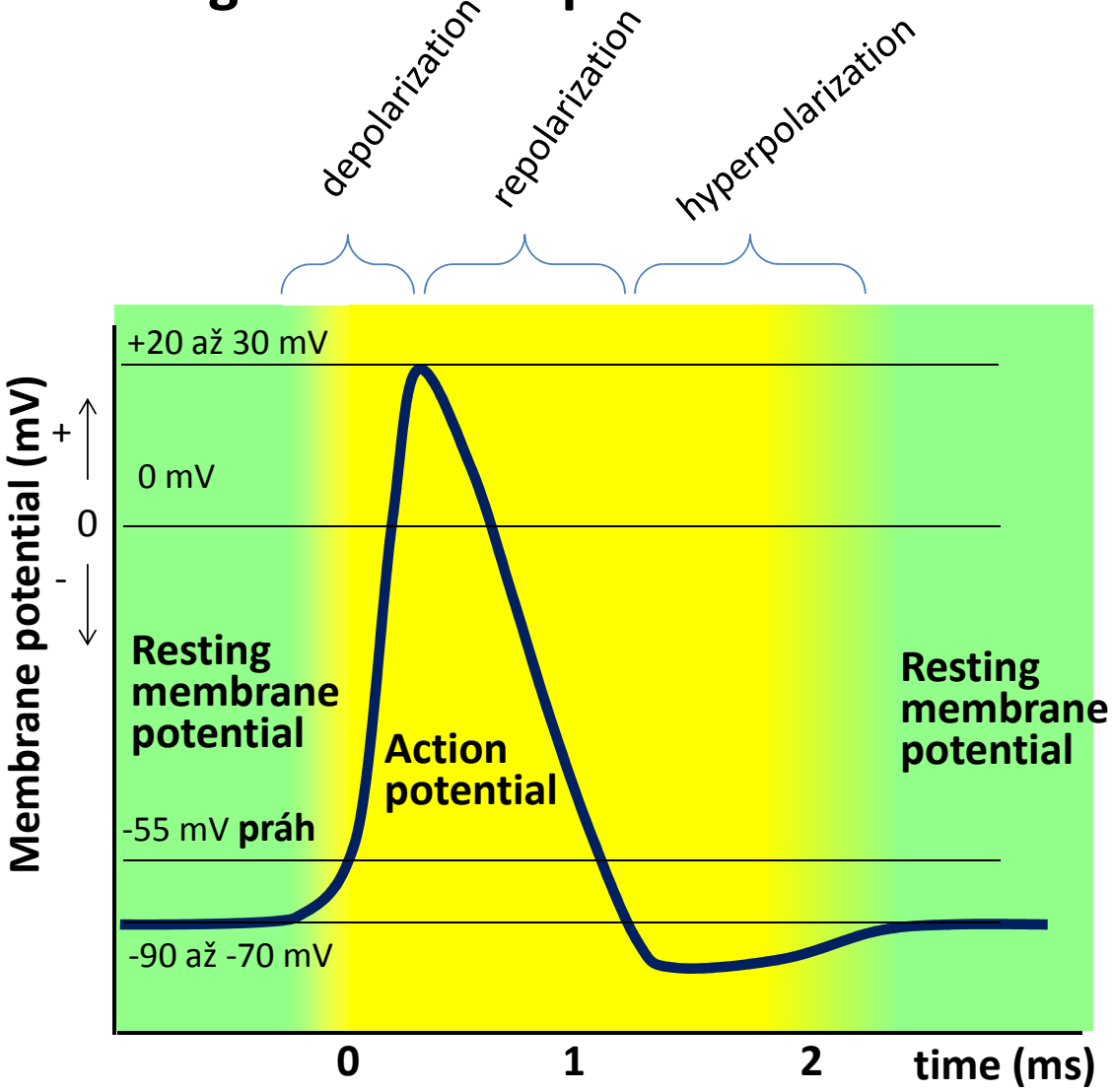
Resting membrane potencial:

- In the cell membrane at rest condition
- Inside the cell - negative charge, positive charge on the cell surface

- cell is impermeable to Na+
- inside the cell there is a higher concentration of K+, outside the cell there is a higher concentration of Na+
- the concentration of K+ inside is less than the concentration of Na+ outside

→ negative charge inside the cell

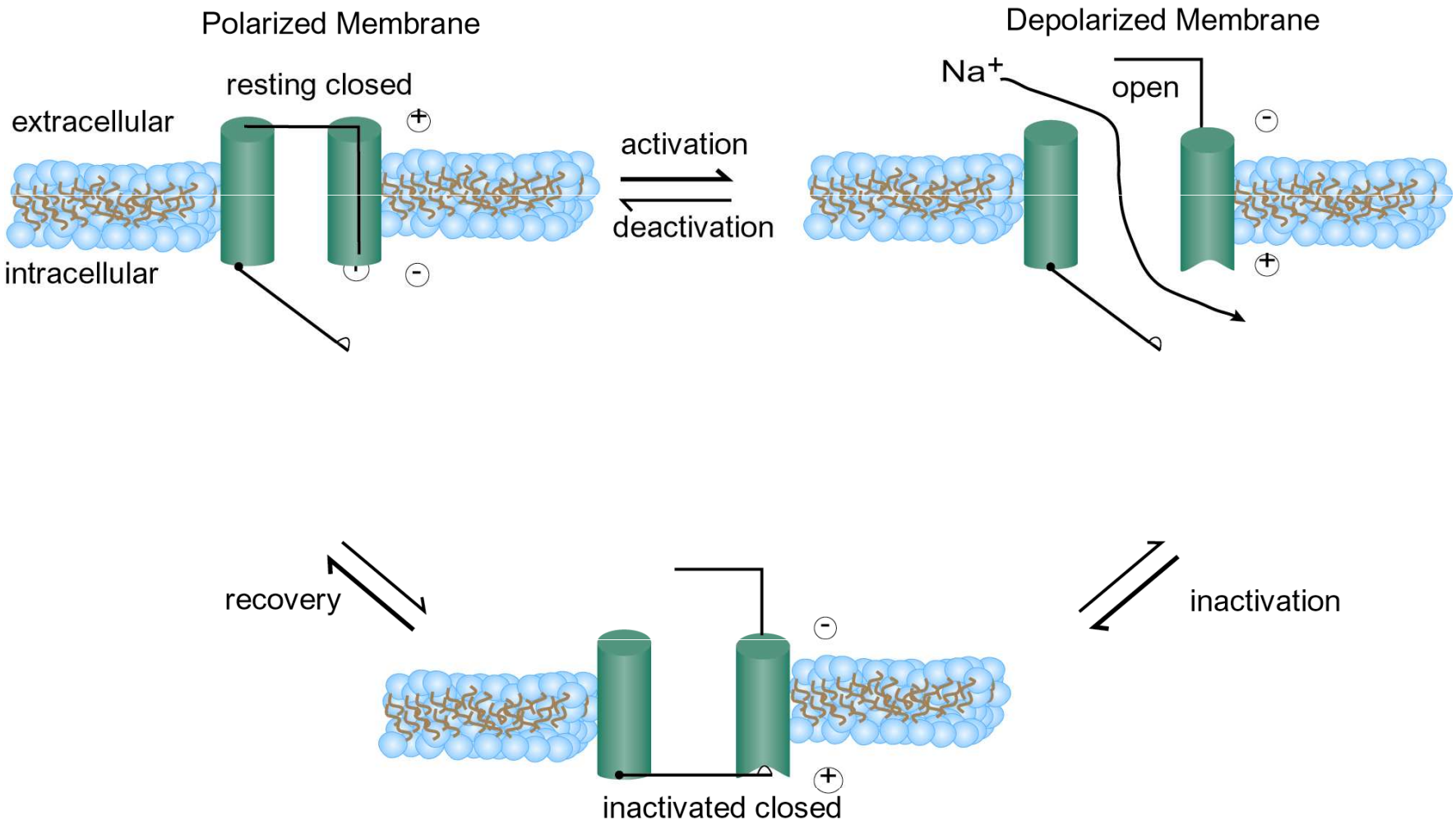
Resting membrane potential



Action potencial (AP)

- If the voltage threshold (-55 mV) is exceeded, an action potential is generated on the membrane

- **Depolarization phase**
  - Na+ channels open
  - Na+ enters the cell
  - Law „All or nothing“ – if the threshold is not exceeded, no AP, if the threshold is exceeded – the AP is created
- **Repolarization phase**
- Na+ channels are closed again (very fast inactivation)
- K+ channels are open- eflux of potassium
- Na+ is pumped out, K+ is pumped in
- Voltage gets back to rest values


Polarized Membrane
resting closed
extracellular
intracellular
activation
deactivation
Depolarized Membrane
Na+
open
recovery
inactivation
inactivated closed

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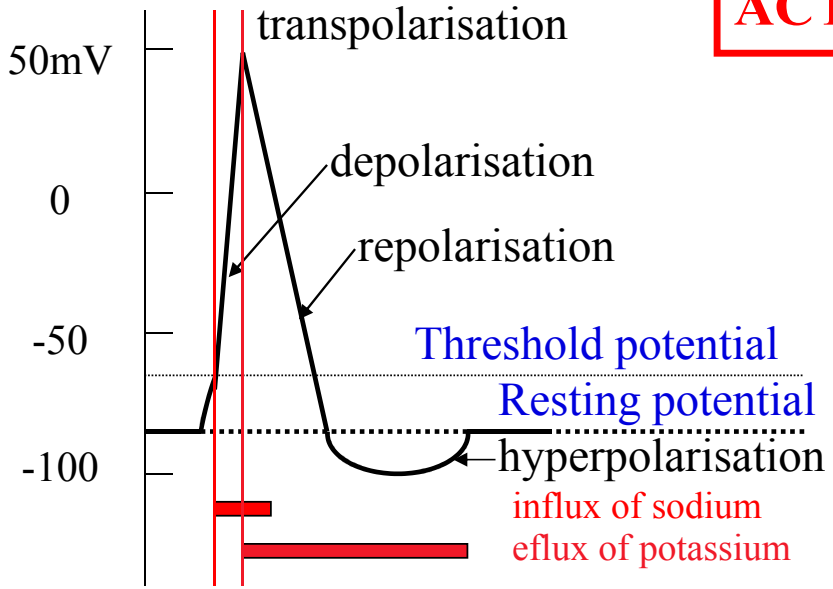
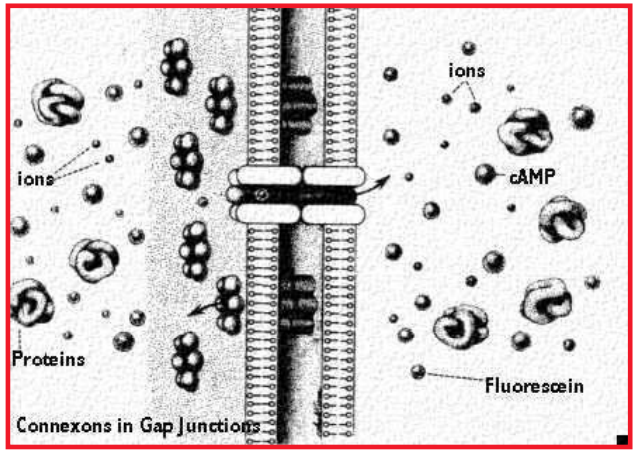
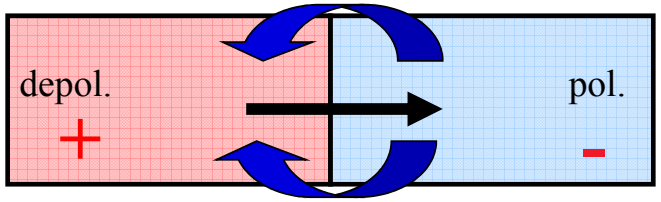
ACTION POTENTIAL



- Unit of excitation activity
- „All or nothing“ response
- Propagation without decrement („domino effect“)
- **Refracterity**



Local current



Propagation with decrement

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ACTION POTENTIAL (AP)

- **By irritating excitable cells (muscle or nerve), resting membrane potential can turn into ACTION potential**

- **AP is created according to the law: "all or nothing,,**

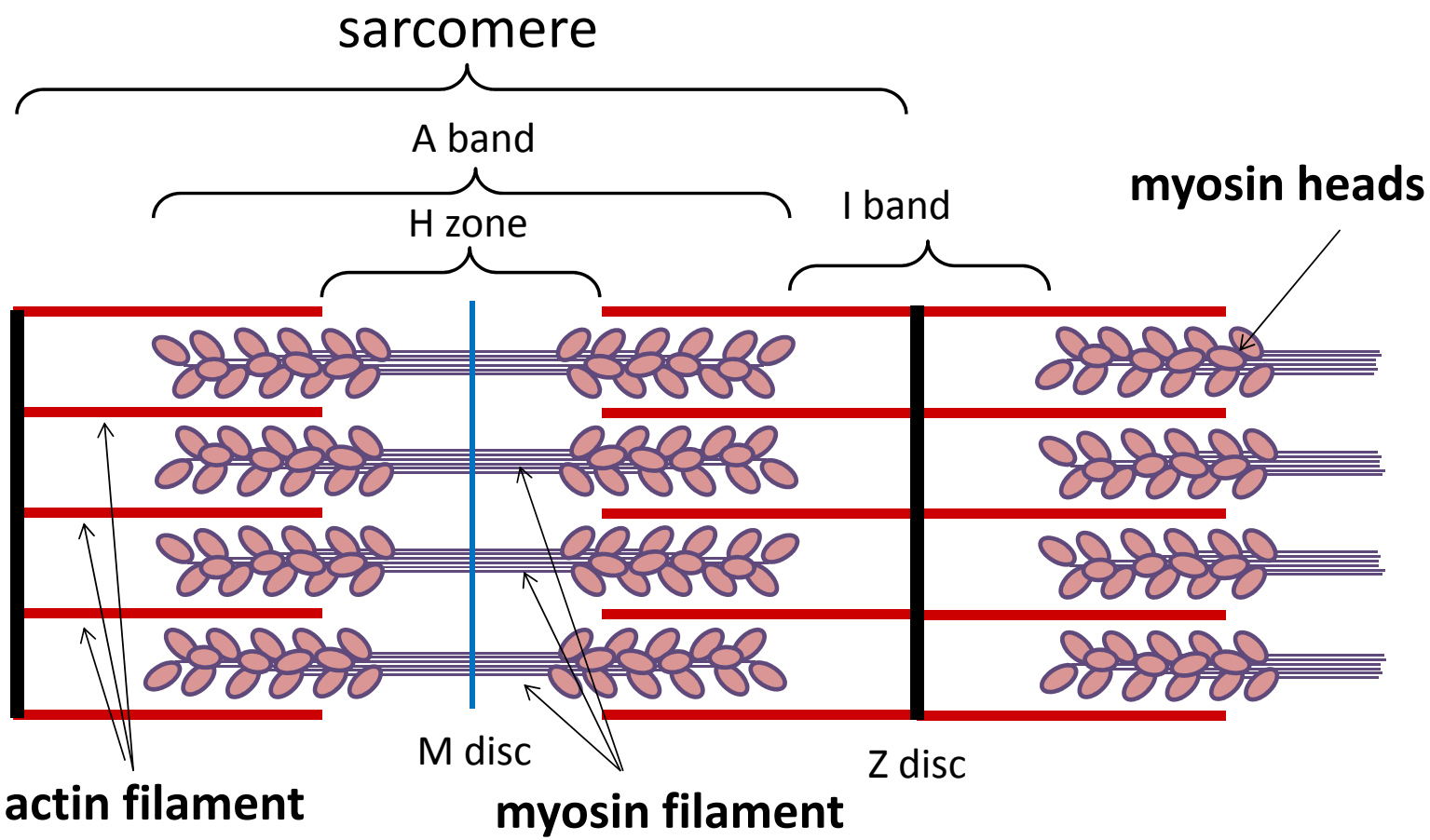
- a sufficiently strong stimulus (the so-called overtreshold stimulus) is needed for its creation

- its further spread takes place without losing its size

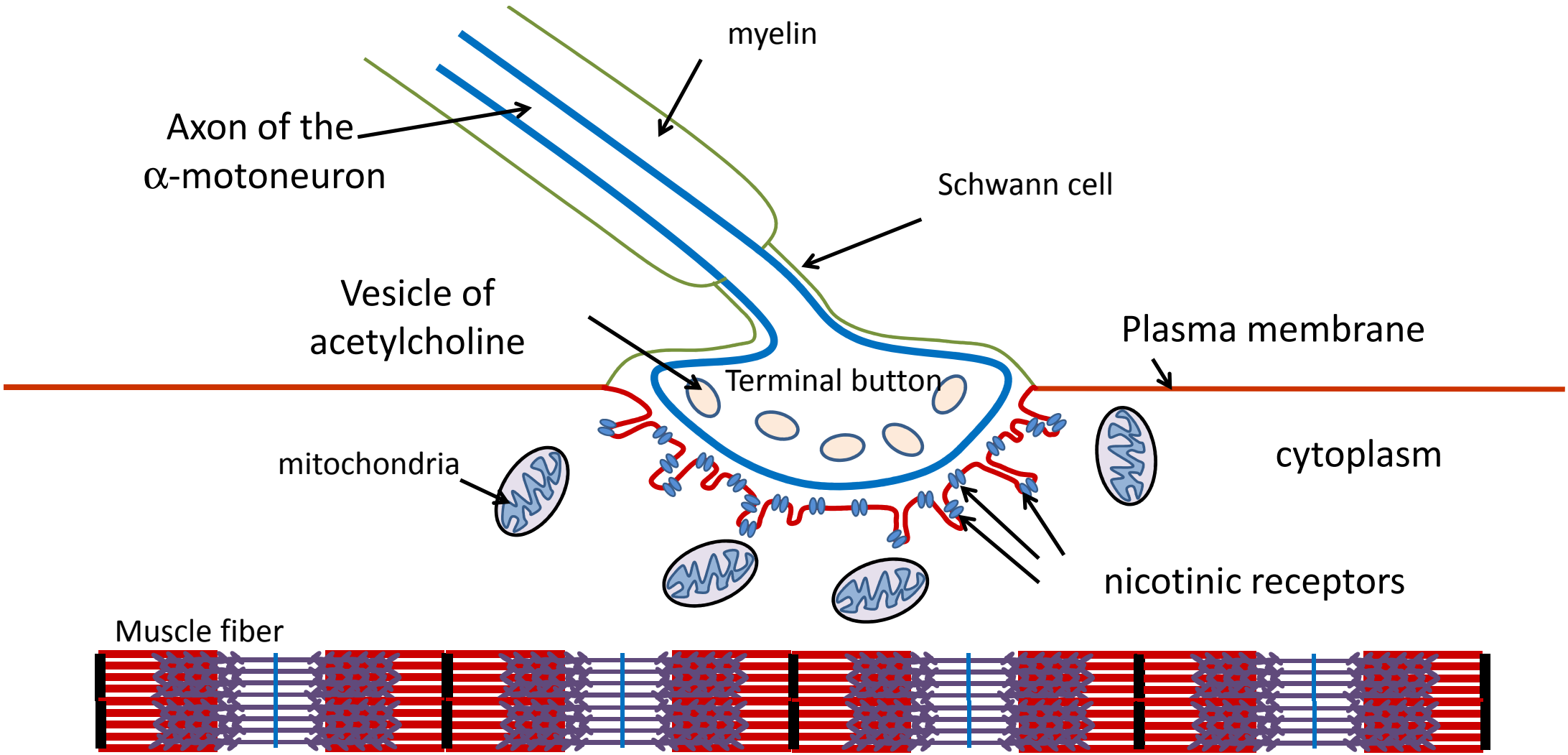
Physiological significance of action potential

- by changing the resting membrane potential into an action potential, the following occurs:
- encode and transmit information in living systems (nervous system)
- muscle contraction (musculature) is triggered

Morphology of the skeletal muscle fiber



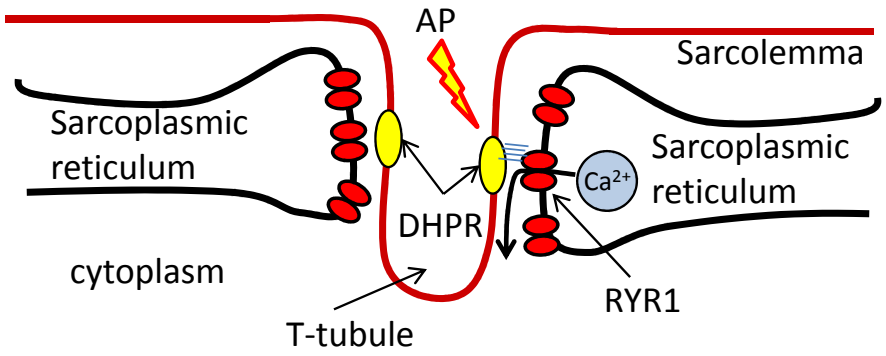
Motor end-plate



Excitation – contraction coupling

Excitation

- Action potential (AP) spreads on axon from alfa-motoneuron to neuro-moto end-plate
- Release of acetylcholine from vesicles to synaptic cleft
- Binding of acetylcholine with the nicotinic receptors placed on post-synaptic membrane
- Opening of Na^+ channels (connected with acetylcholine receptors) and intake of Na^+
- Local depolarization of the membrane
- Opening of voltage gaited channels for Na^+
- Formation of action potential

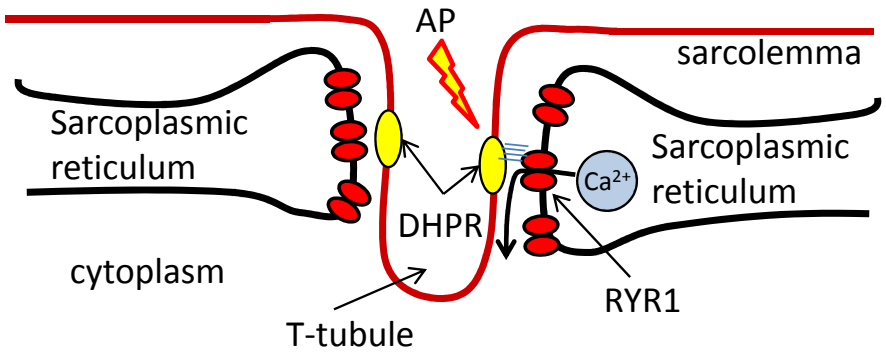


Excitation – contraction coupling

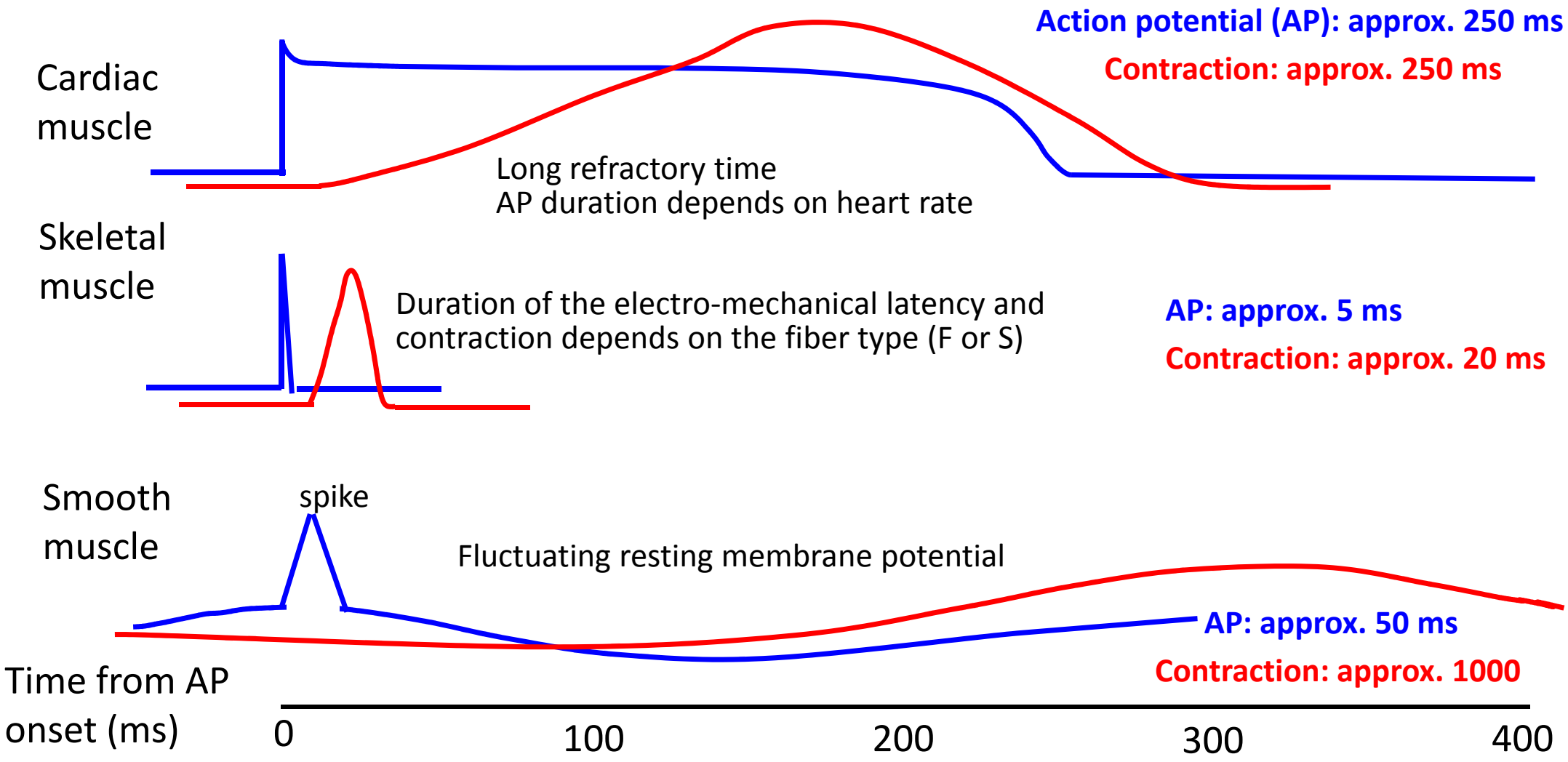
Contraction

- Spreading of action potential (AP) across fiber and into transversal tubule (T-tubule)
- Dihydropyridine receptors (DHPR) in the membrane changes its conformation
- Interaction of DHPR with ryanodine receptors (RYR1) in the membrane of sarcoplasmic reticules
- Opening of calcium channels in the sarcoplasmic reticulum and intake of Ca^{2+} into cytoplasm
- Binding of Ca^{2+} with troponin C
- Binding of myosin heads on actin
- If enough of Ca^{2+} and ATP in cytoplasm, myosin shifts along actin → contraction of muscle
- Contraction ends with decrease od Ca^{2+} concentration in the cytoplasm (Ca^{2+} is pumped by Ca-ATPase into the reticulum)

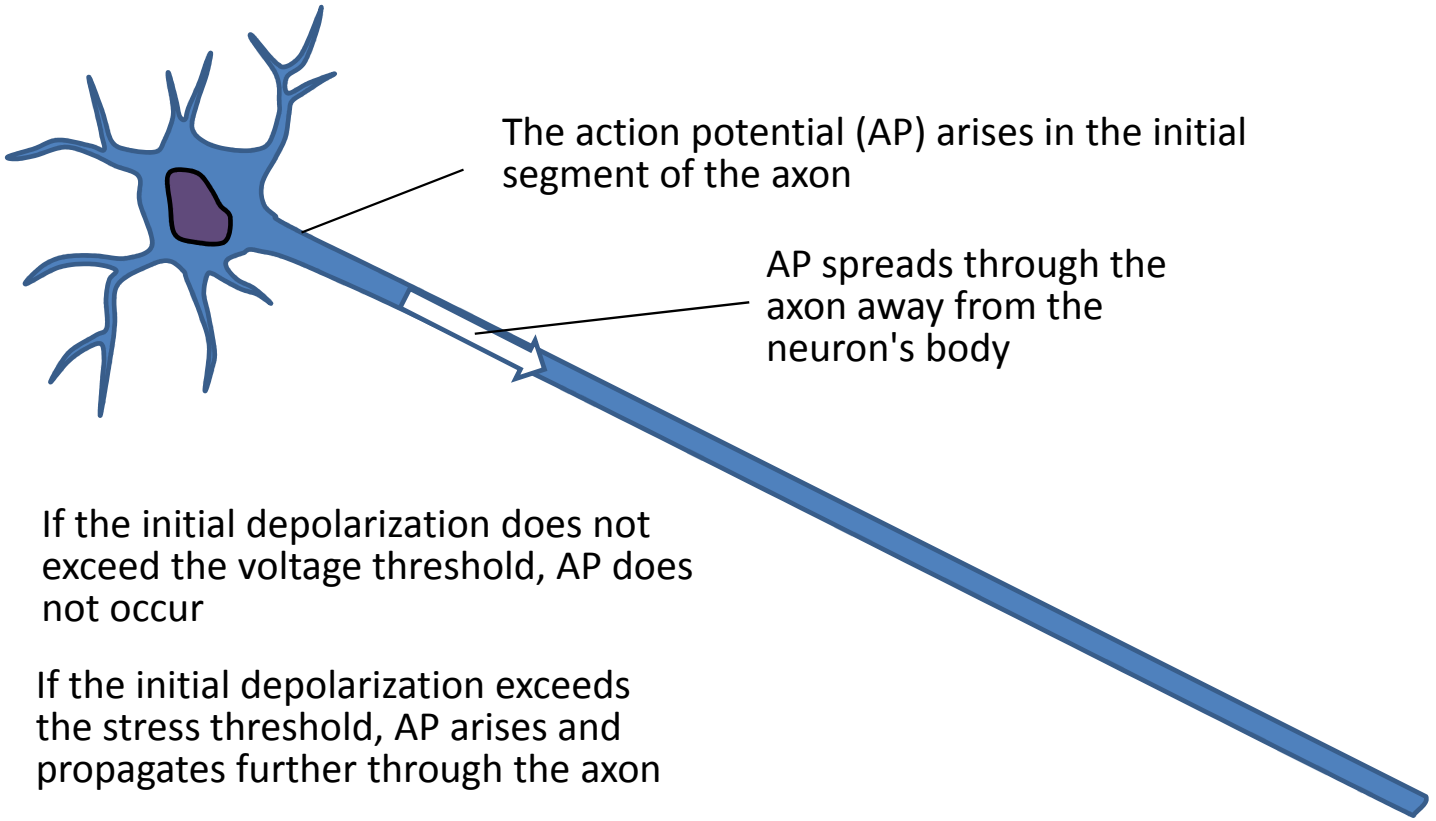
Rigor mortis – caused by ATP deficit → formation of strong link between actin and myosin



Skeletal, cardiac and smooth muscle – action potential and contraction



Propagation of action potential (unmyelinated fiber)

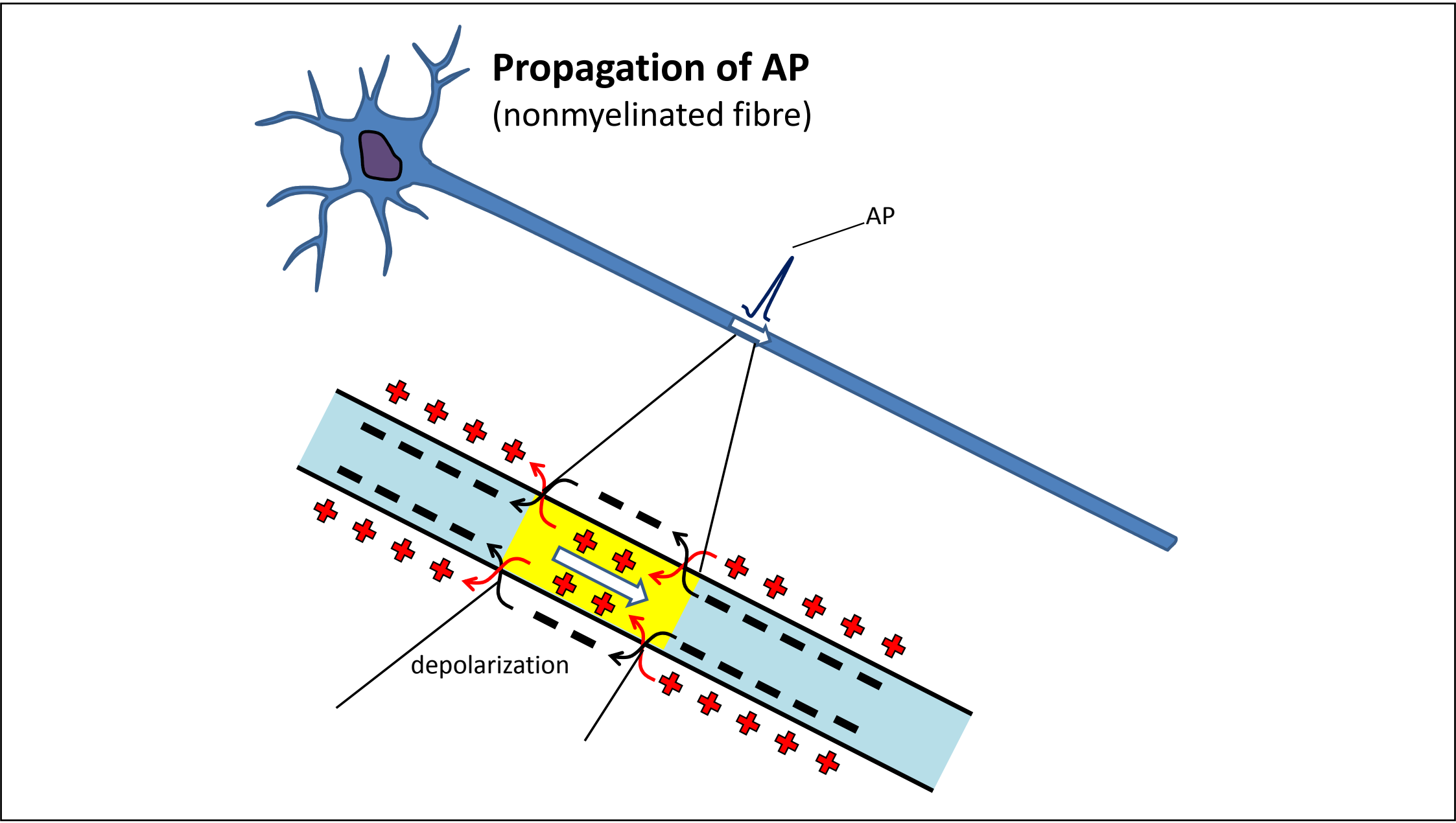


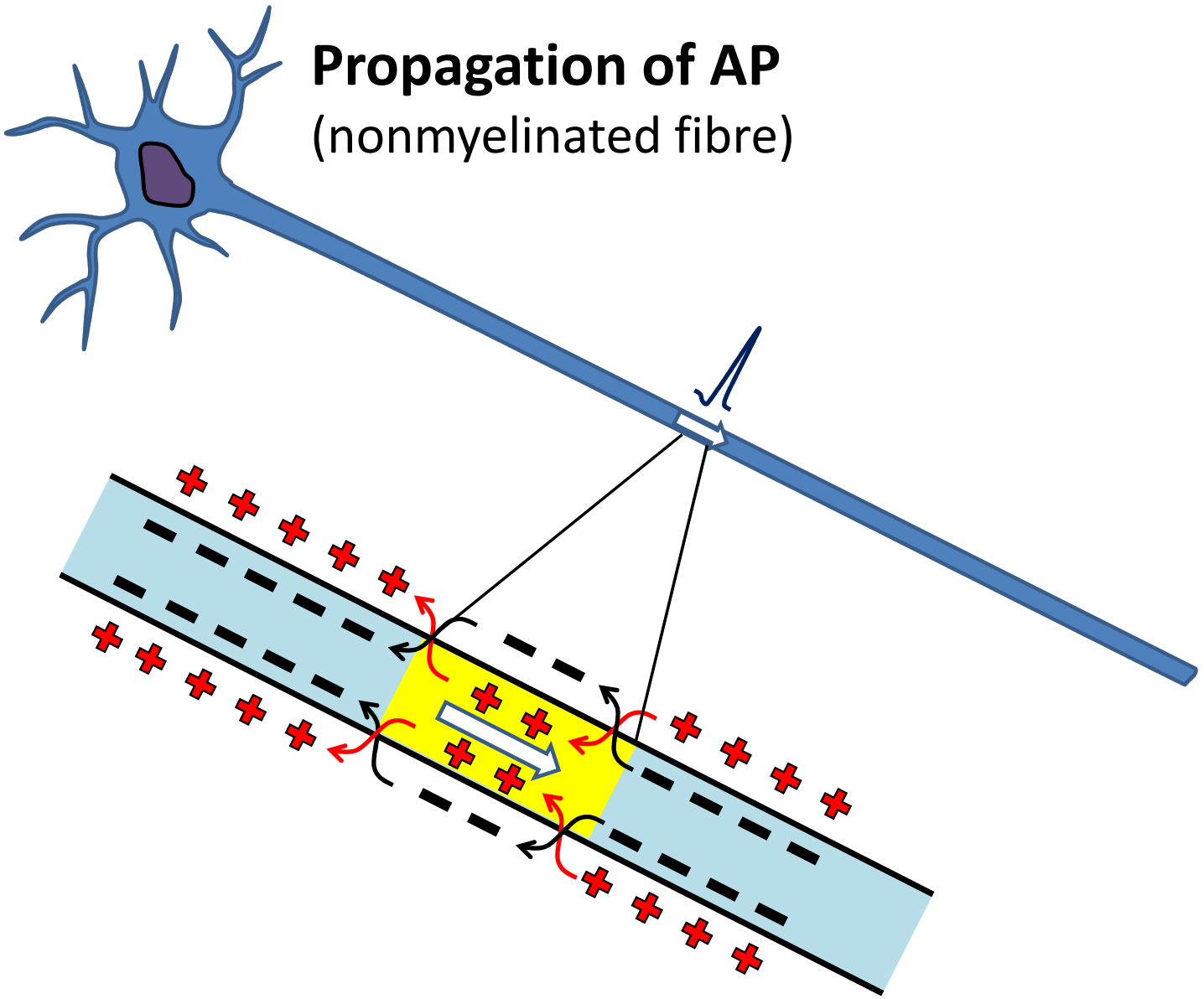
The action potential (AP) arises in the initial segment of the axon

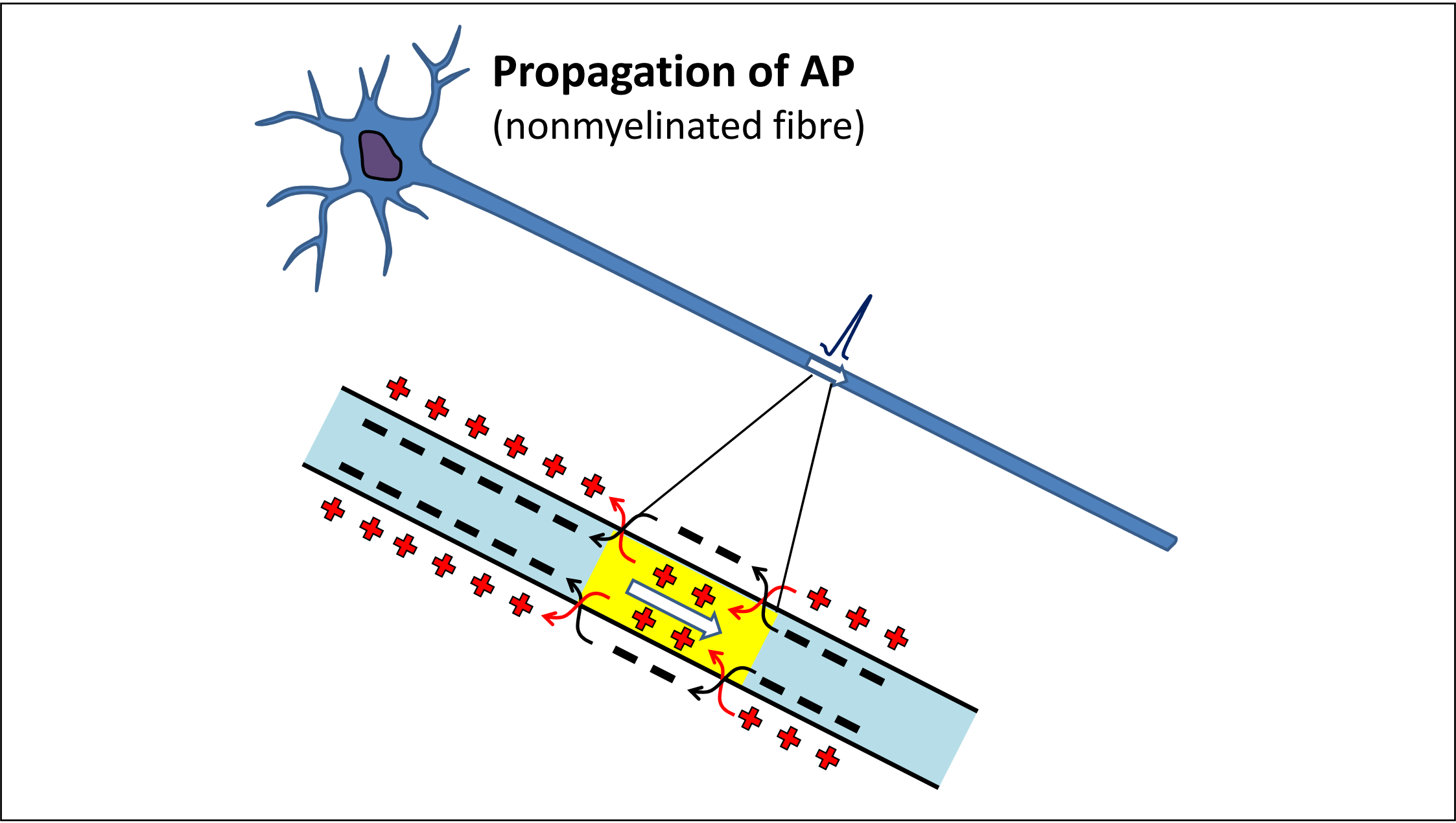
AP spreads through the axon away from the neuron's body

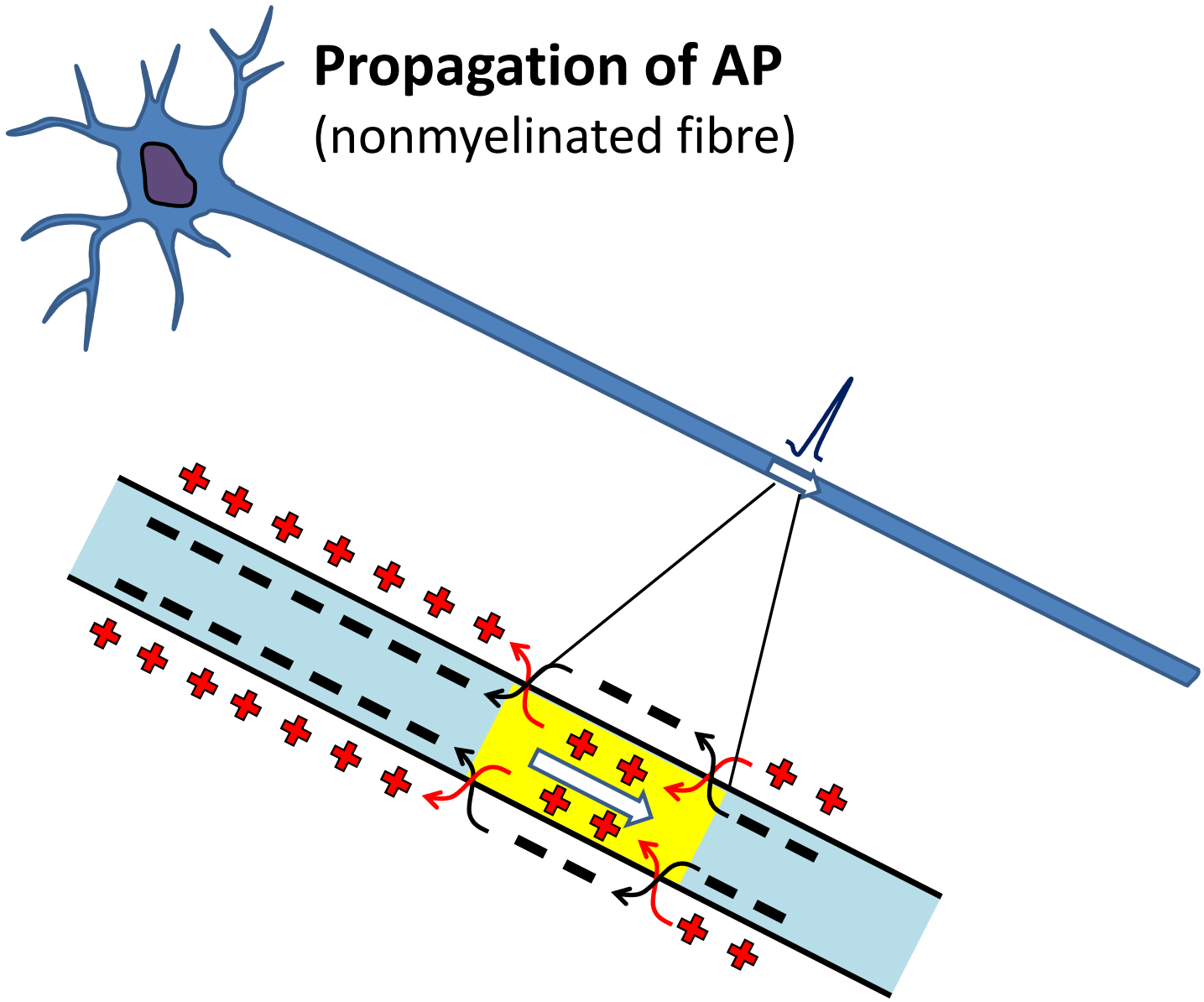
If the initial depolarization does not exceed the voltage threshold, AP does not occur

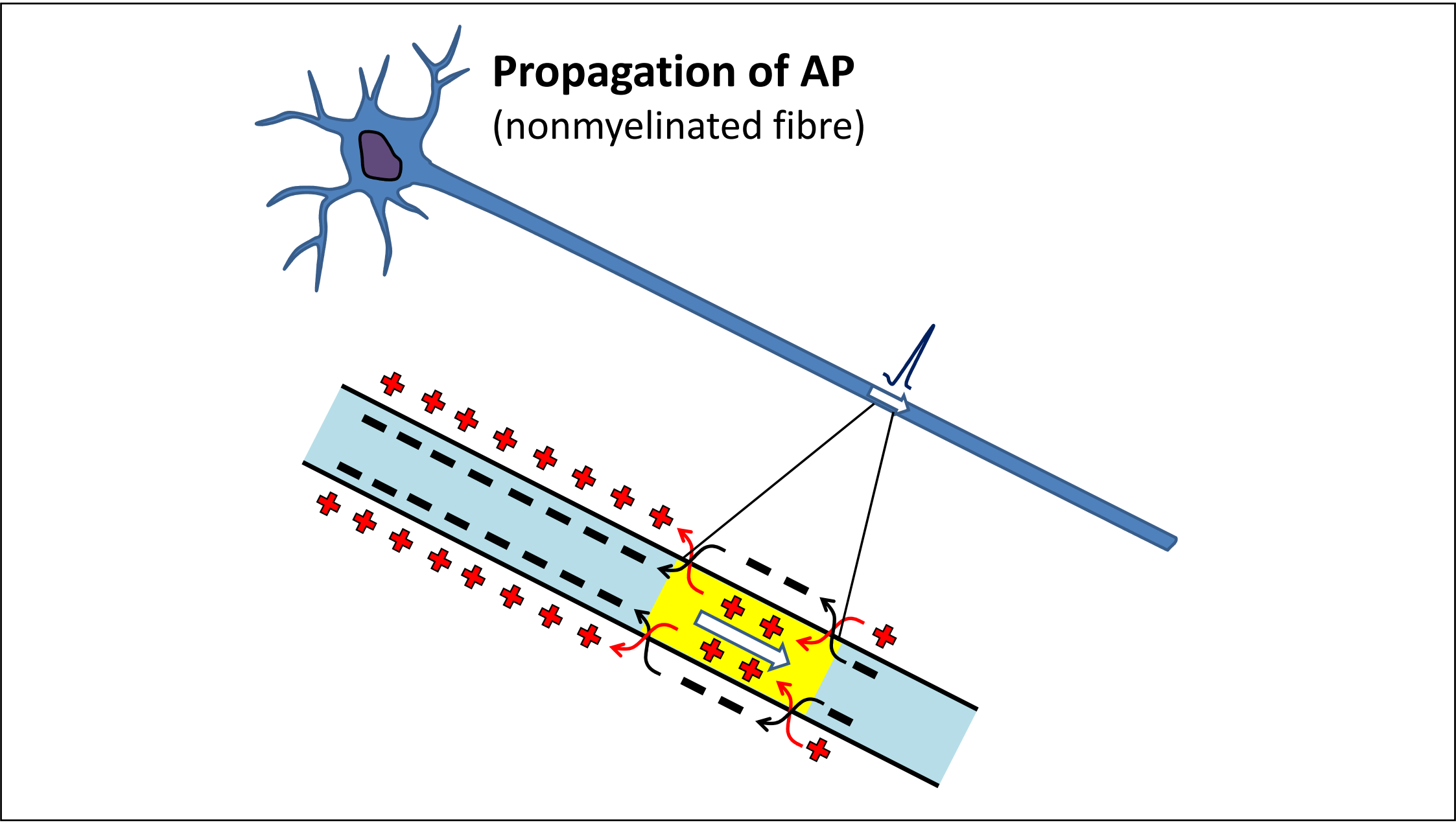
If the initial depolarization exceeds the stress threshold, AP arises and propagates further through the axon


Propagation of AP
(nonmyelinated fibre)
AP
depolarization


Propagation of AP
(nonmyelinated fibre)

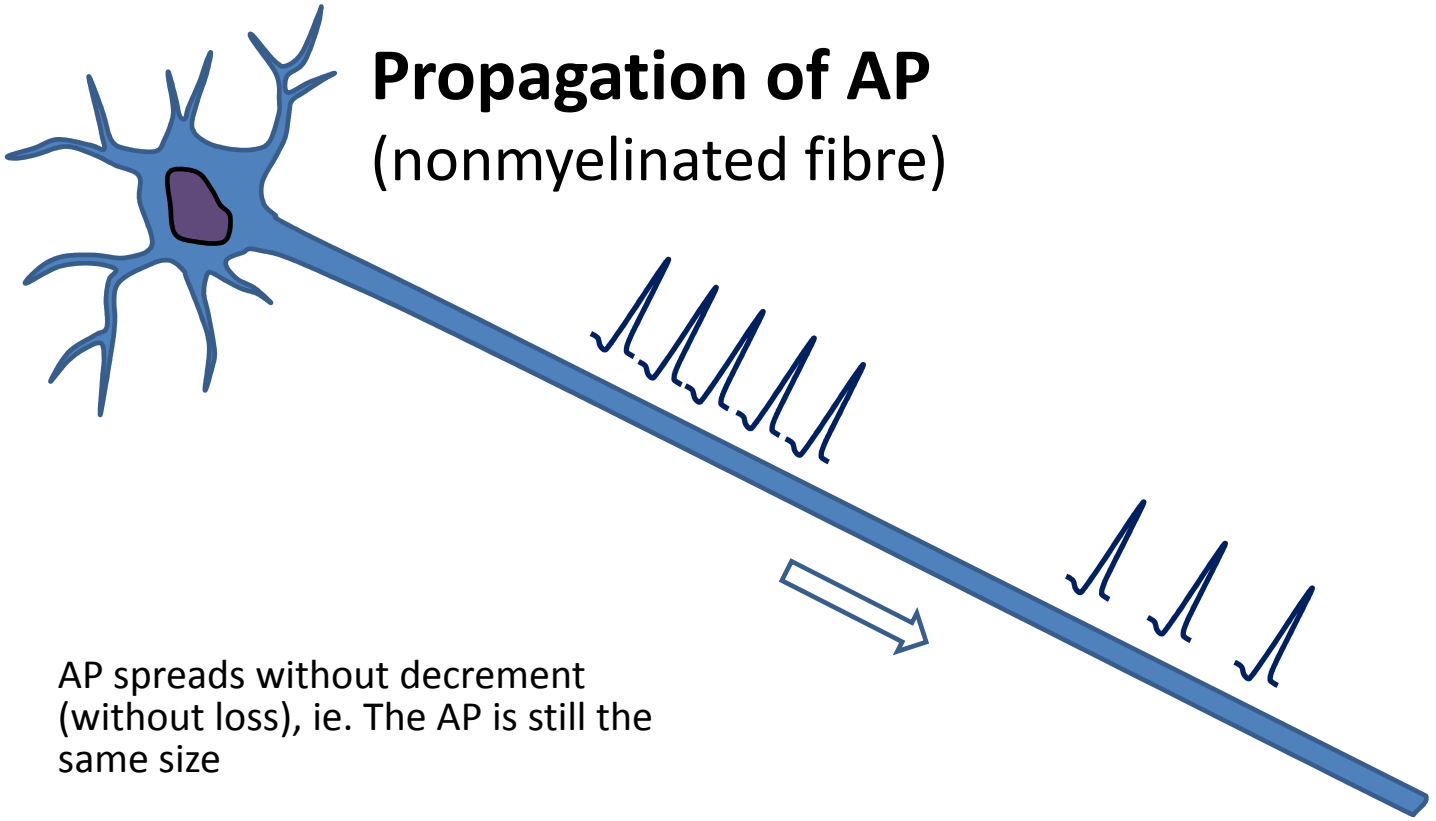

Propagation of AP
(nonmyelinated fibre)


Propagation of AP
(nonmyelinated fibre)


Propagation of AP
(nonmyelinated fibre)

Propagation of AP

(nonmyelinated fibre)



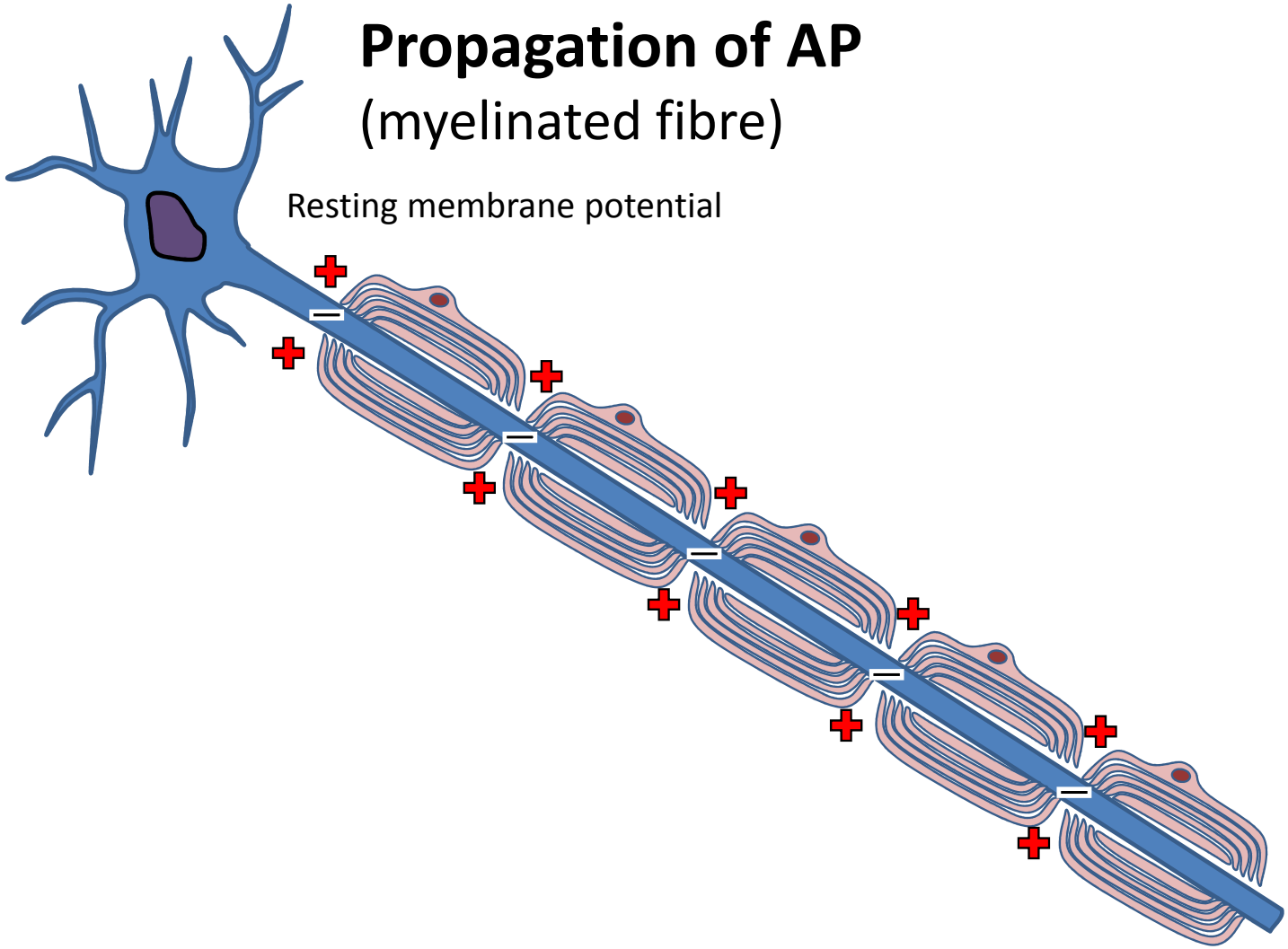
AP spreads without decrement (without loss), ie. The AP is still the same size

Because the AP is still the same size, the transmitted information is encoded in the AP frequency

Propagation of AP

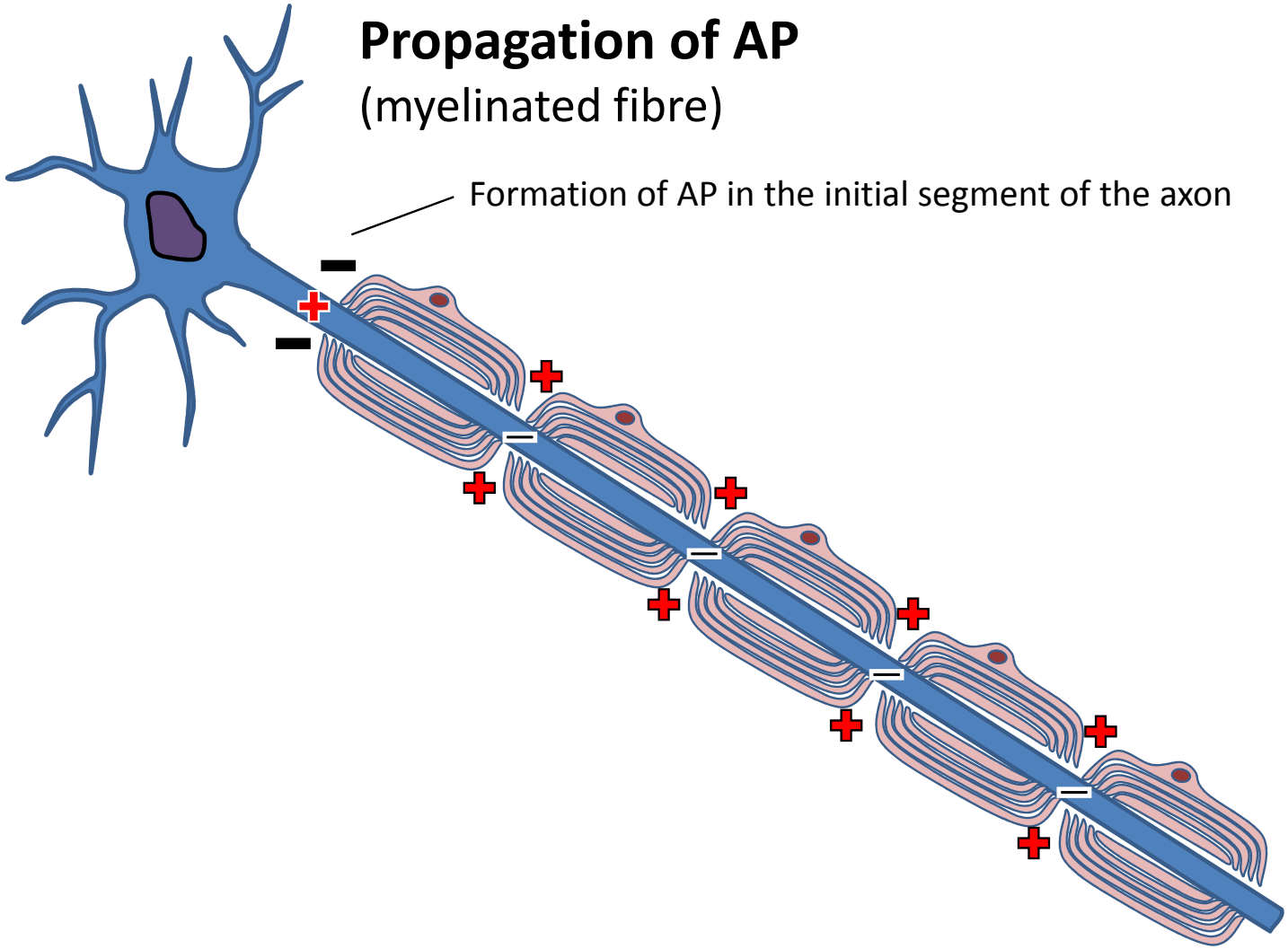
(myelinated fibre)

Resting membrane potential



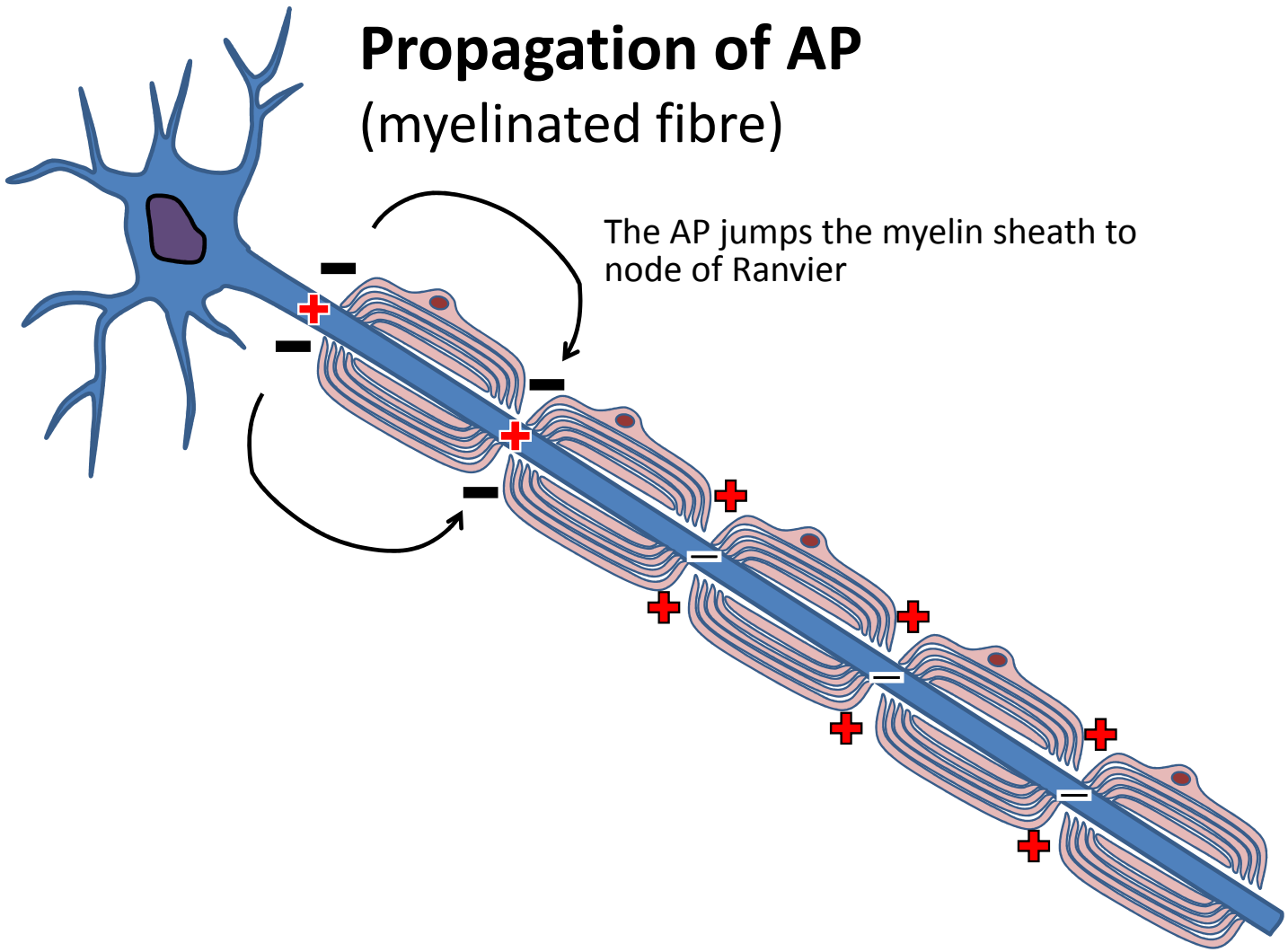
Propagation of AP

(myelinated fibre)



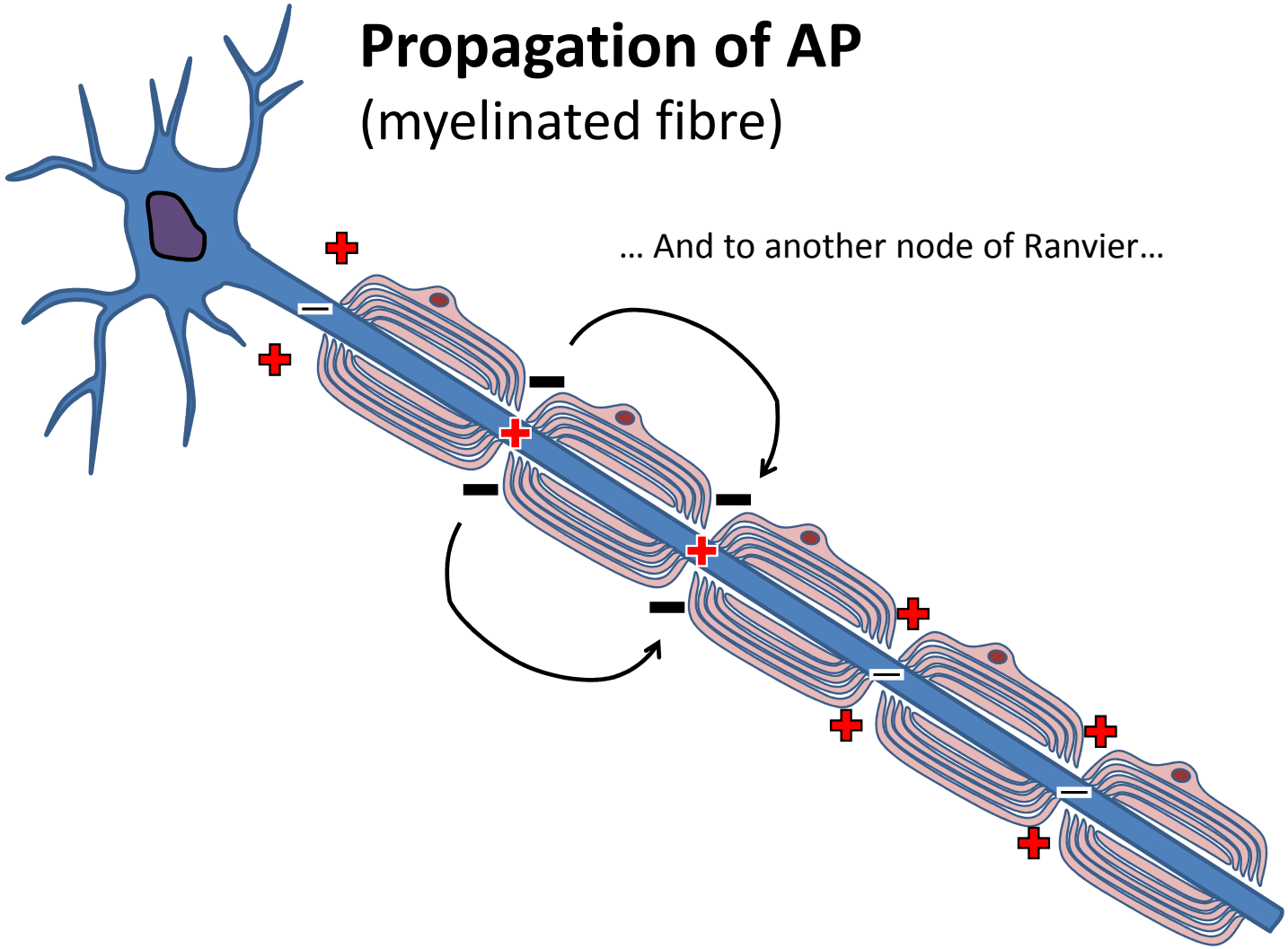
Propagation of AP

(myelinated fibre)



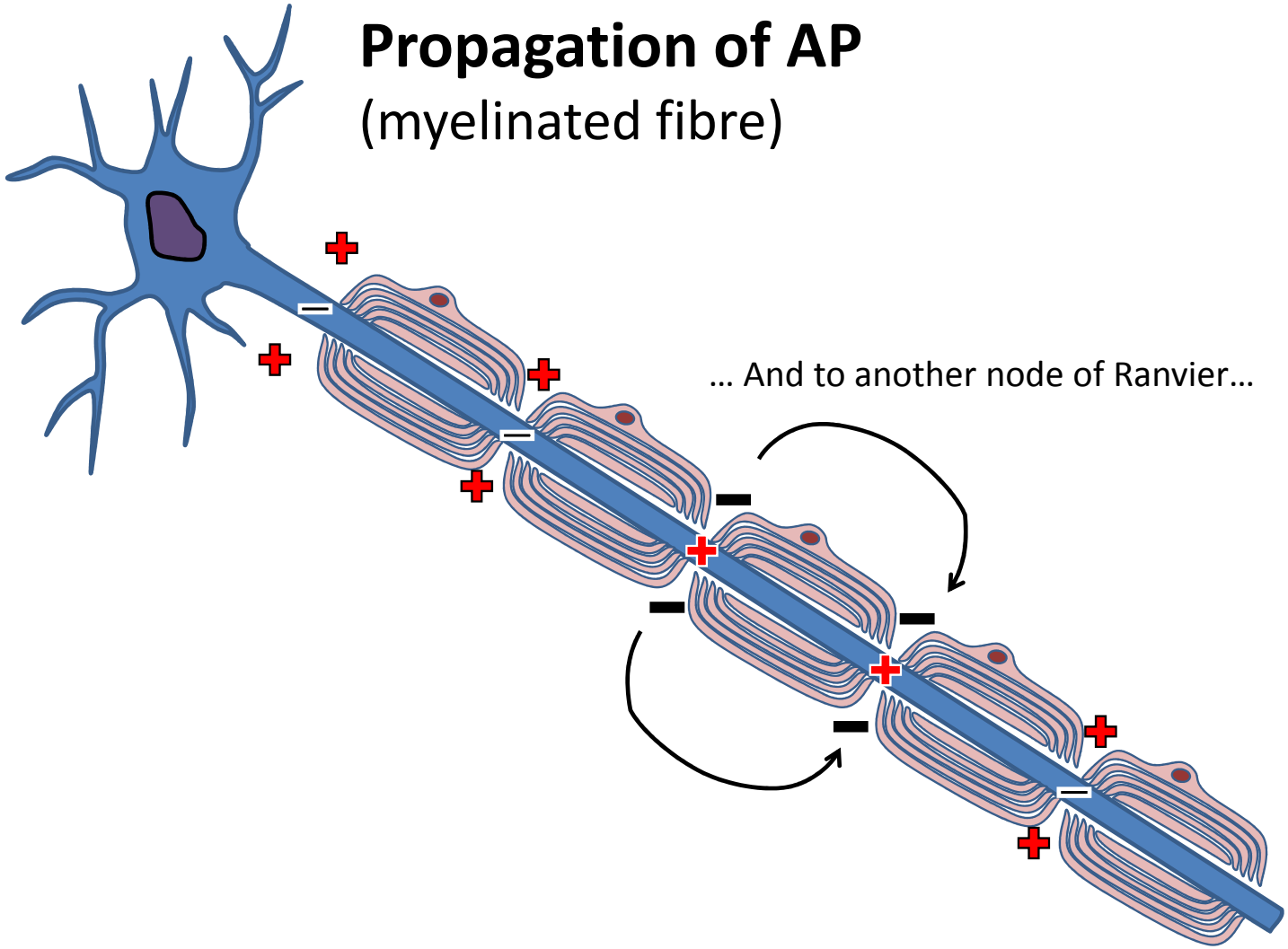
Propagation of AP

(myelinated fibre)



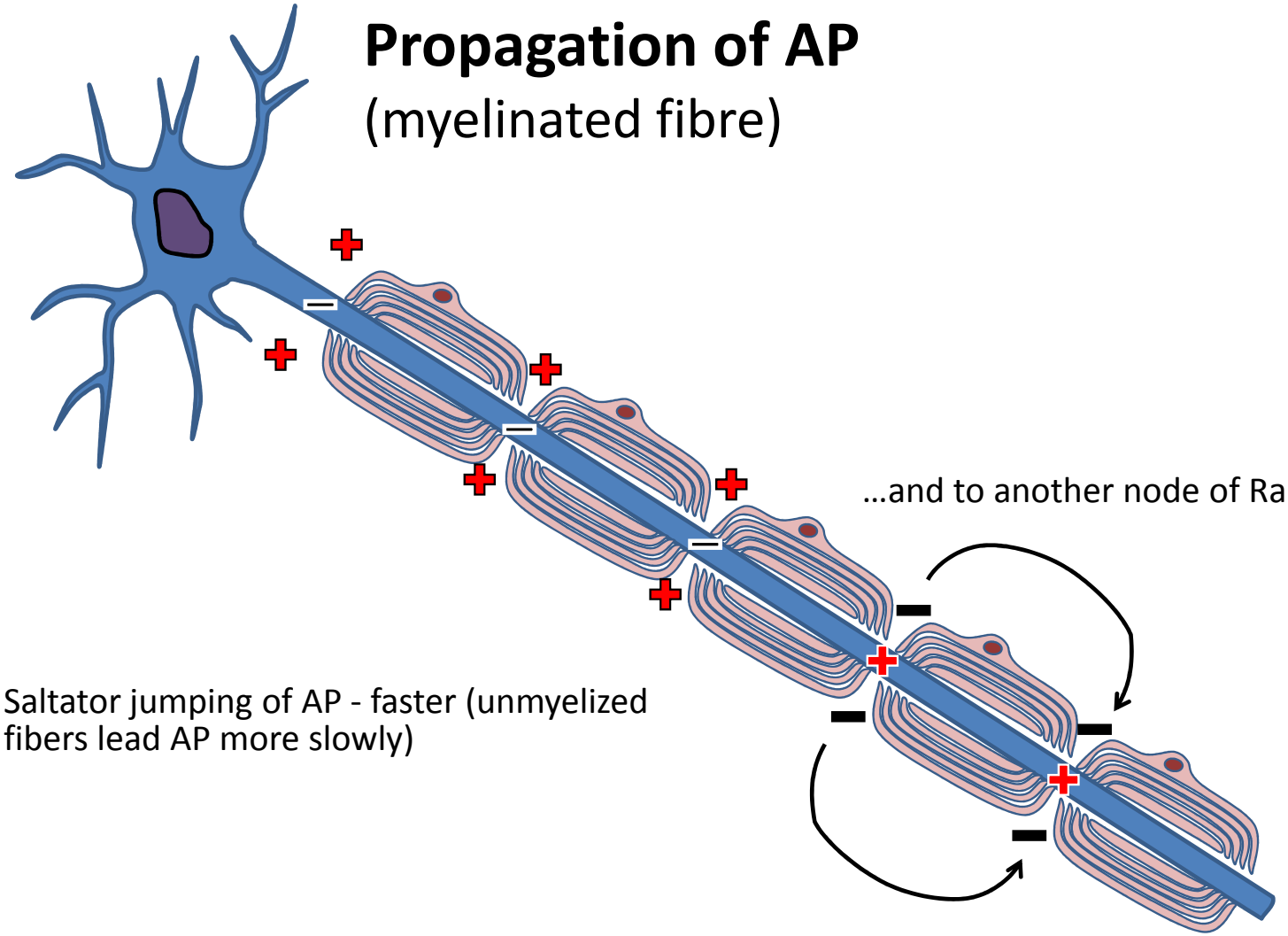
Propagation of AP

(myelinated fibre)



Propagation of AP

(myelinated fibre)



…and to another node of Ranvier…

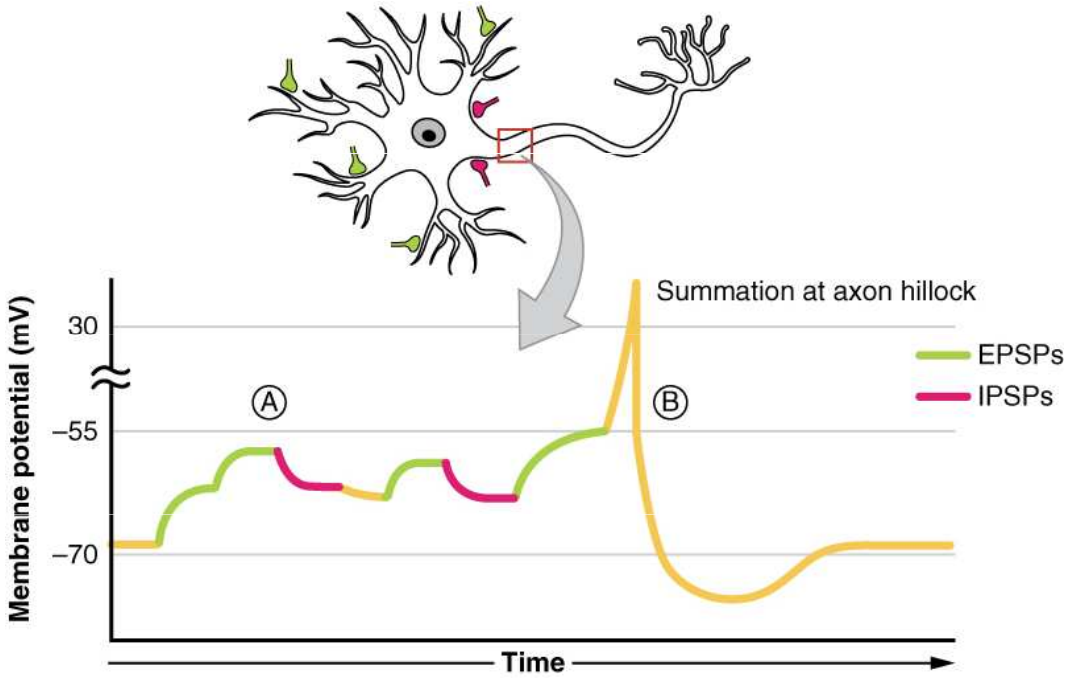
Saltator jumping of AP - faster (unmyelized fibers lead AP more slowly)

LOCAL RESPONSE of MEMBRANE POTENTIAL

- evolutionarily older type of membrane reaction to irritation
- we find it in lower animals, but also in the human nervous system

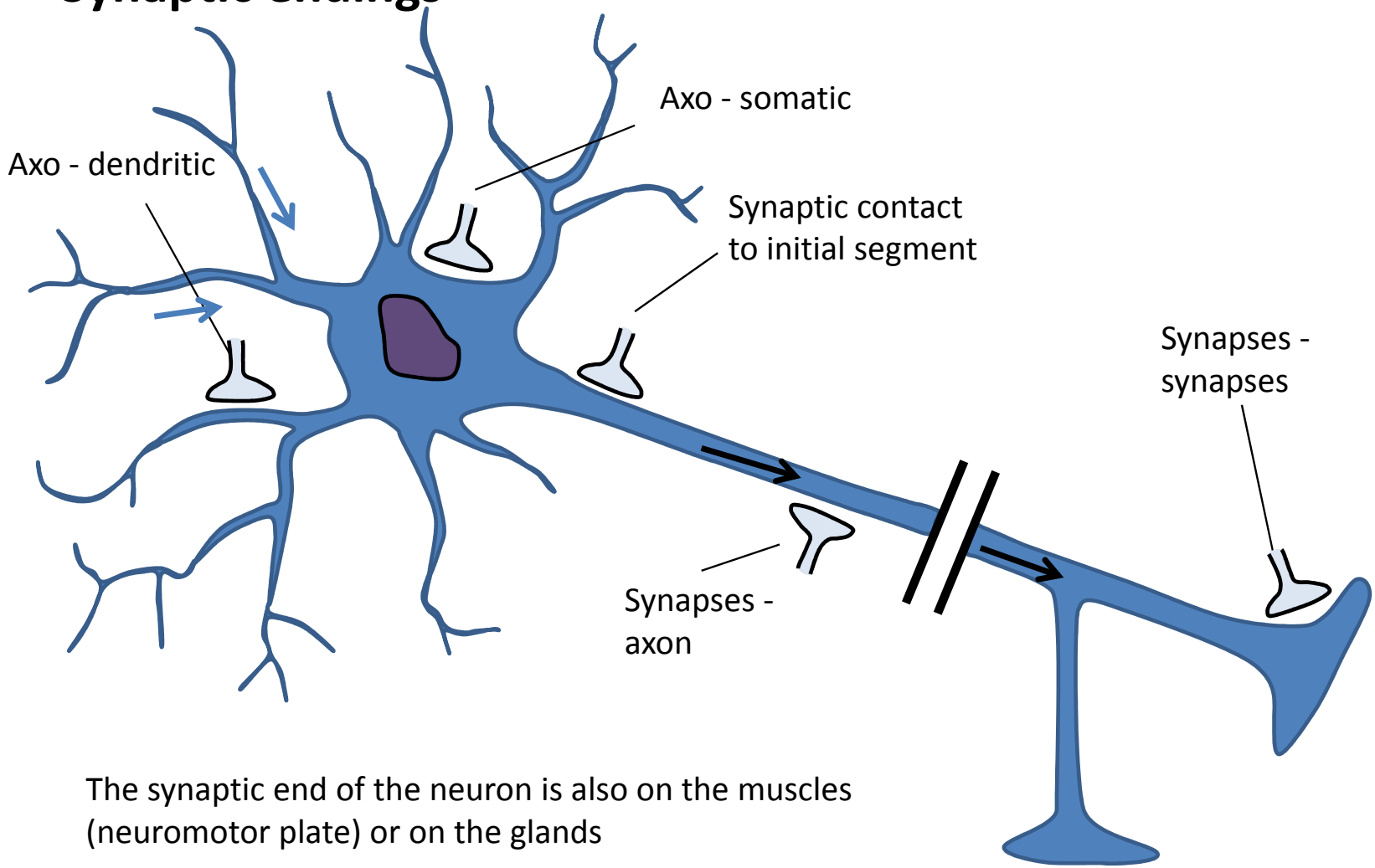
  it has its function
- its properties (unlike AP):
  - depends on the intensity of the stimulus
  - spreads with decrement
  - refractery period is absent

e.g.: we find it as a reaction to irritation of sensory cells –“ receptor potential“, mainly on the synapses of our NS (postsynaptic potencial – excitatory-inhibitory), endplate potential in neuromuscular junction



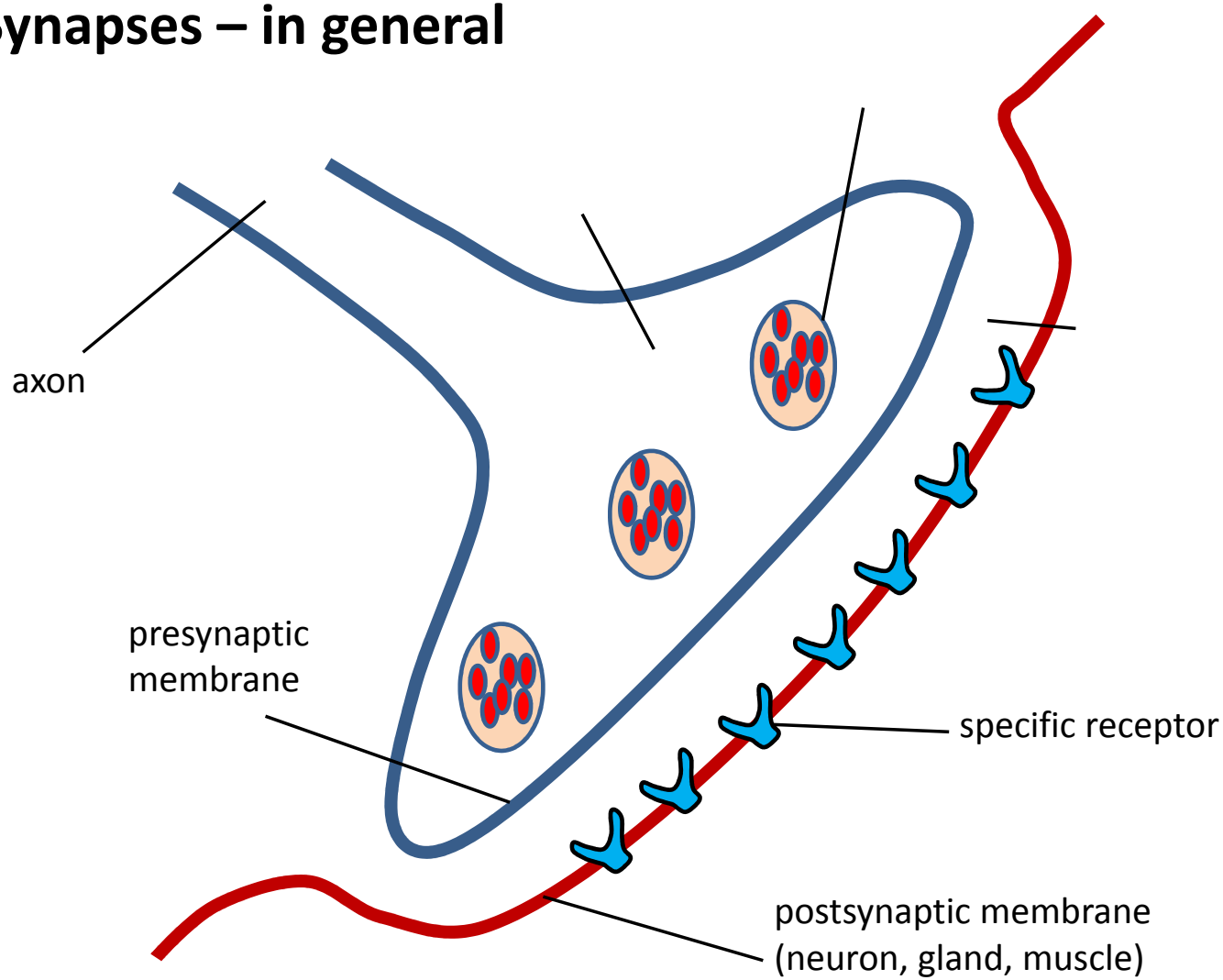
https://oerpub.github.io/epubjs-demo-book/resources/1224_Post_Synaptic_Potential_Summation.jpg

Synaptic endings

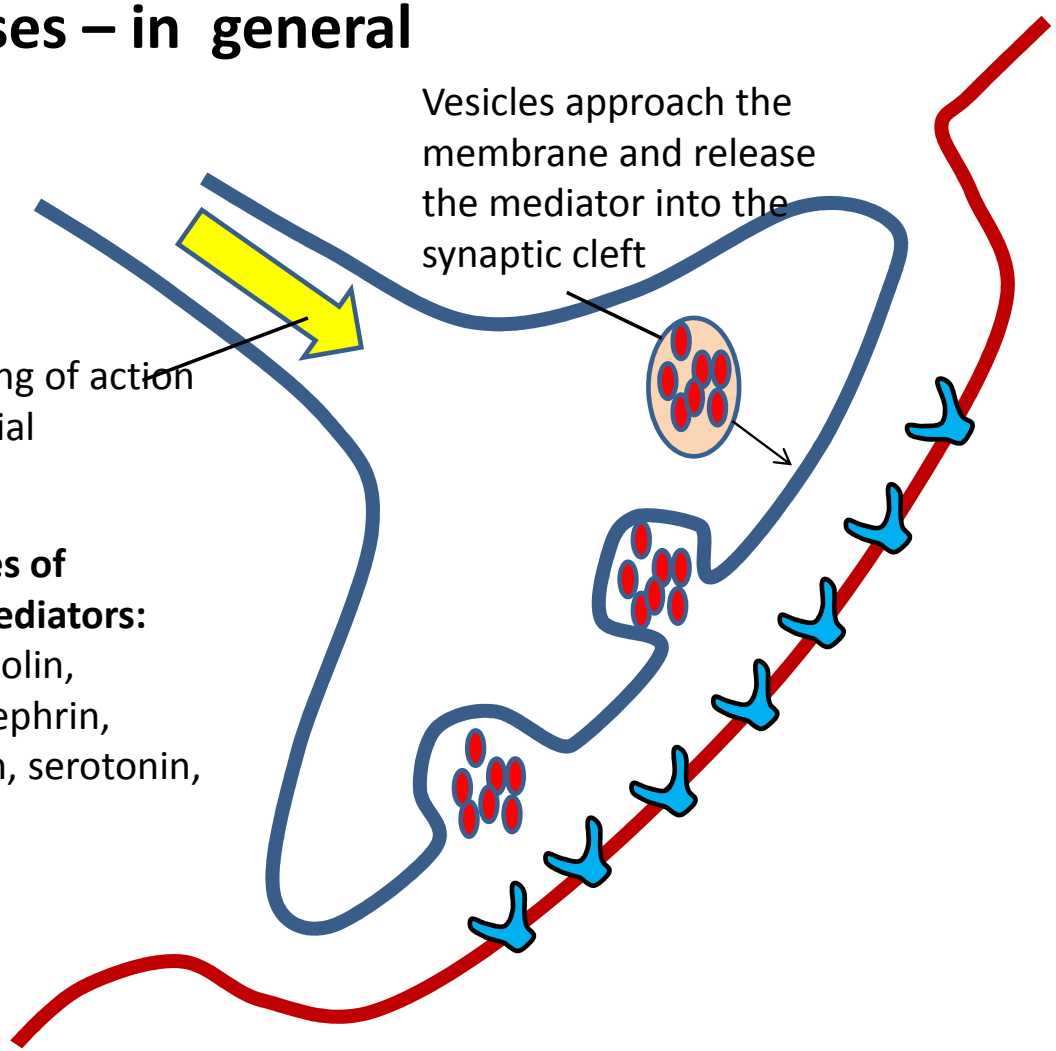


The synaptic end of the neuron is also on the muscles (neuromotor plate) or on the glands

Synapses – in general

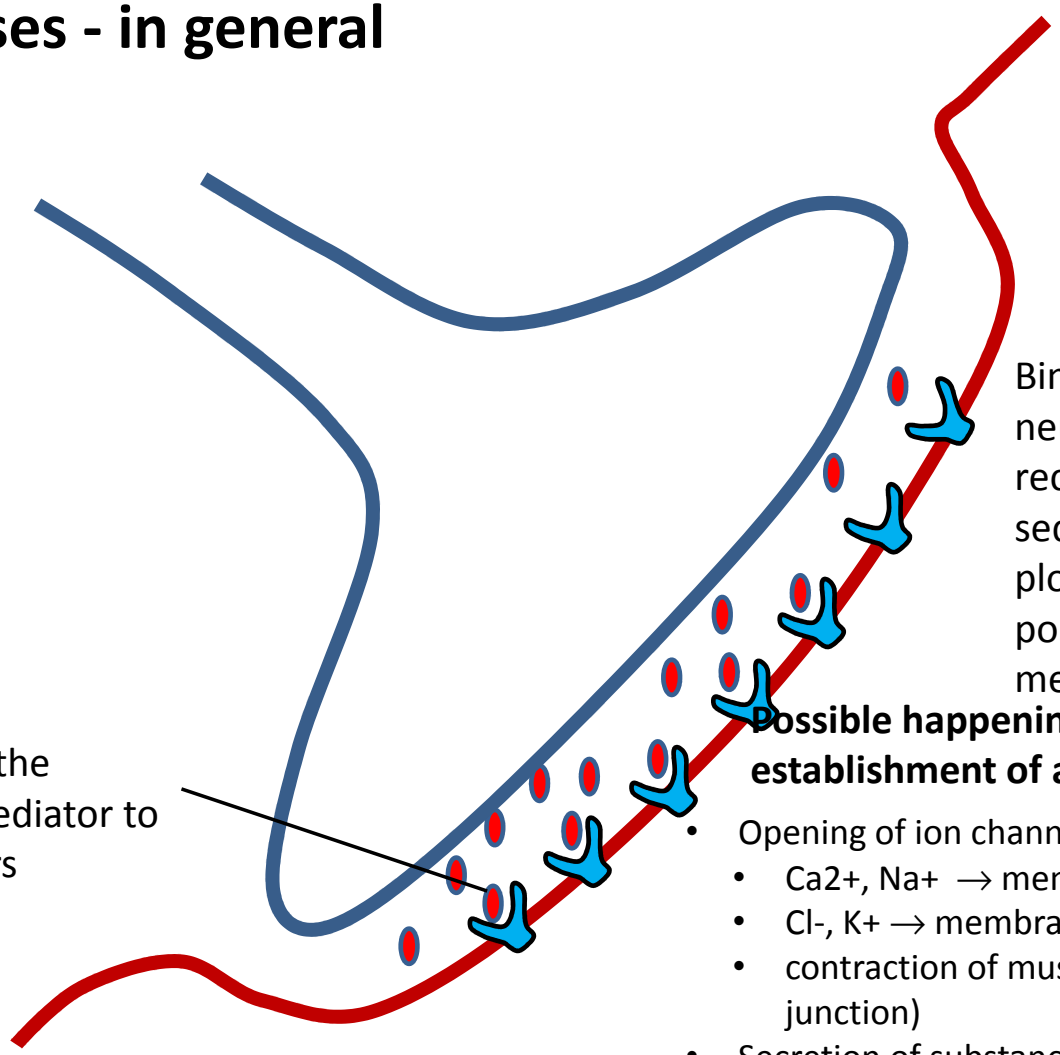


Synapses – in general



Examples of neuromediators:
Acetylcholin, norepinephrin, dopamin, serotonin, GABA,…

Synapses - in general



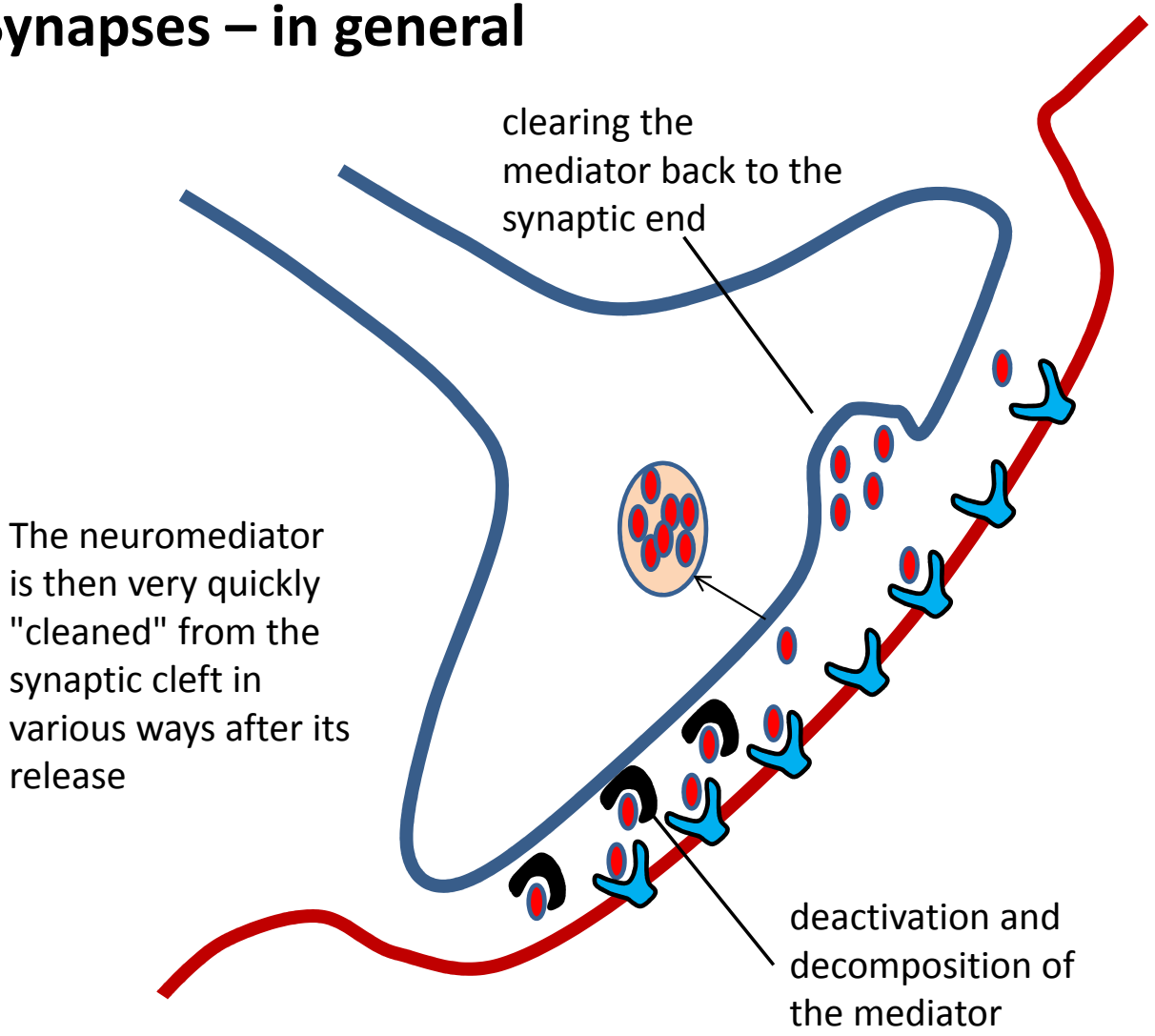
Binding the neuromediator to receptors

Binding the neuromediator to receptors triggers sequence of other plots on the postynaptic membrane

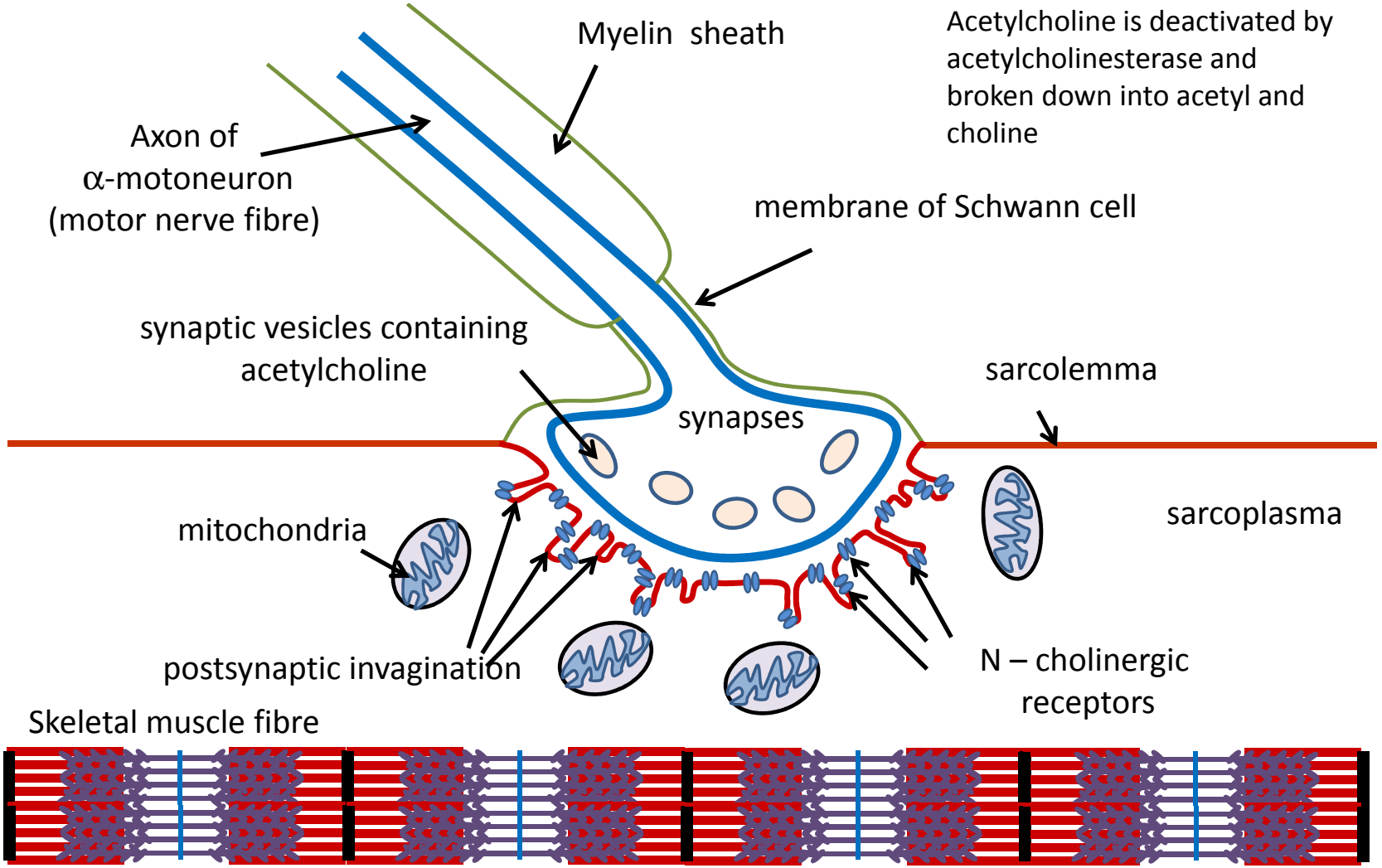
Possible happenings caused by the establishment of a synaptic mediator:

- Opening of ion channels for:
  - Ca2+, Na+ $\rightarrow$ membrane depolarization
  - Cl-, K+ $\rightarrow$ membrane hyperpolarization
  - contraction of muscle (neuromuscular junction)
- Secretion of substances (in glands)
- Changes of metabolism, etc.……

Synapses – in general



Neuromuscular junction

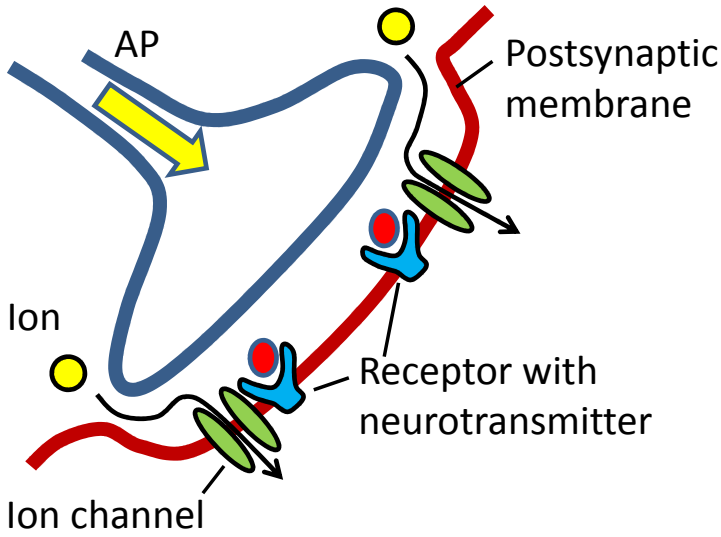


Postsynaptic potencial (PSP)

Neurotransmitters bound to certain types of receptors of the postsynaptic membrane cause ion channels to open and ions to move from/to the cell
→ change of potentials on the postsynaptic membrane
→ creates **postynaptic potential**

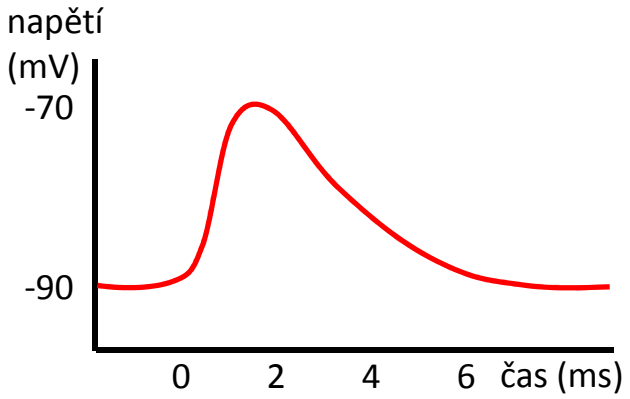
Postsynaptic potencial

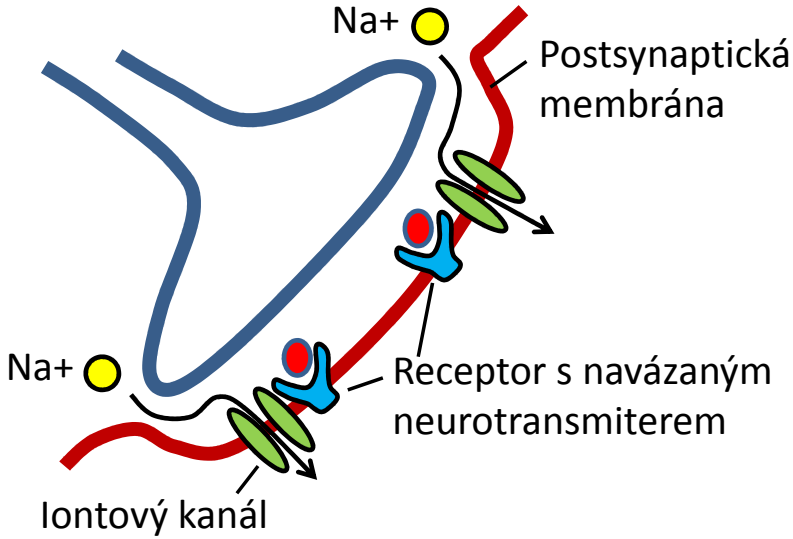
- is weak (many times weaker than AP)
- spreads from synapse with decrement (loss) – shrinks as it distances itself from the synapse (gradually disappears)



Excitatory postsynaptic potencial (EPSP)

Postsynaptic potencial inducing cell depolarization (but much weaker than AP)
Cation input to a cell (e.g. Ca2+ or Na+)

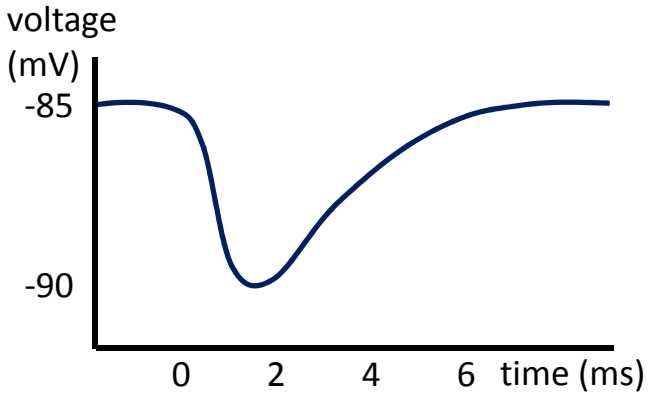


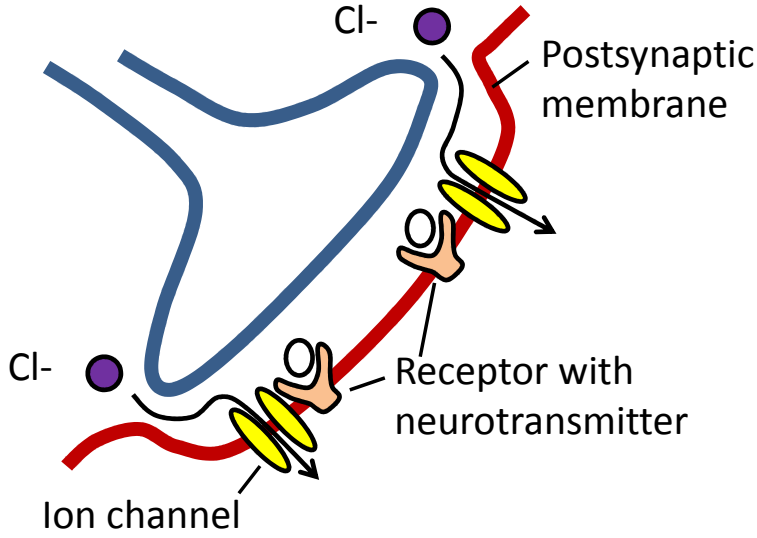


One type of neurotransmitter binds to one type of receptor and opens one type of ion channels
E.g. nicotine receptor-bound acetylcholine causes the Na+ channel to open and the Na+ to enter the cell

Inhibitory postsynaptic potencial (IPSP)

Postsynaptic potencial inducing cell hyperpolarization
Anion input to a cell (e.g. Cl-) or cation output from a cell (K+)



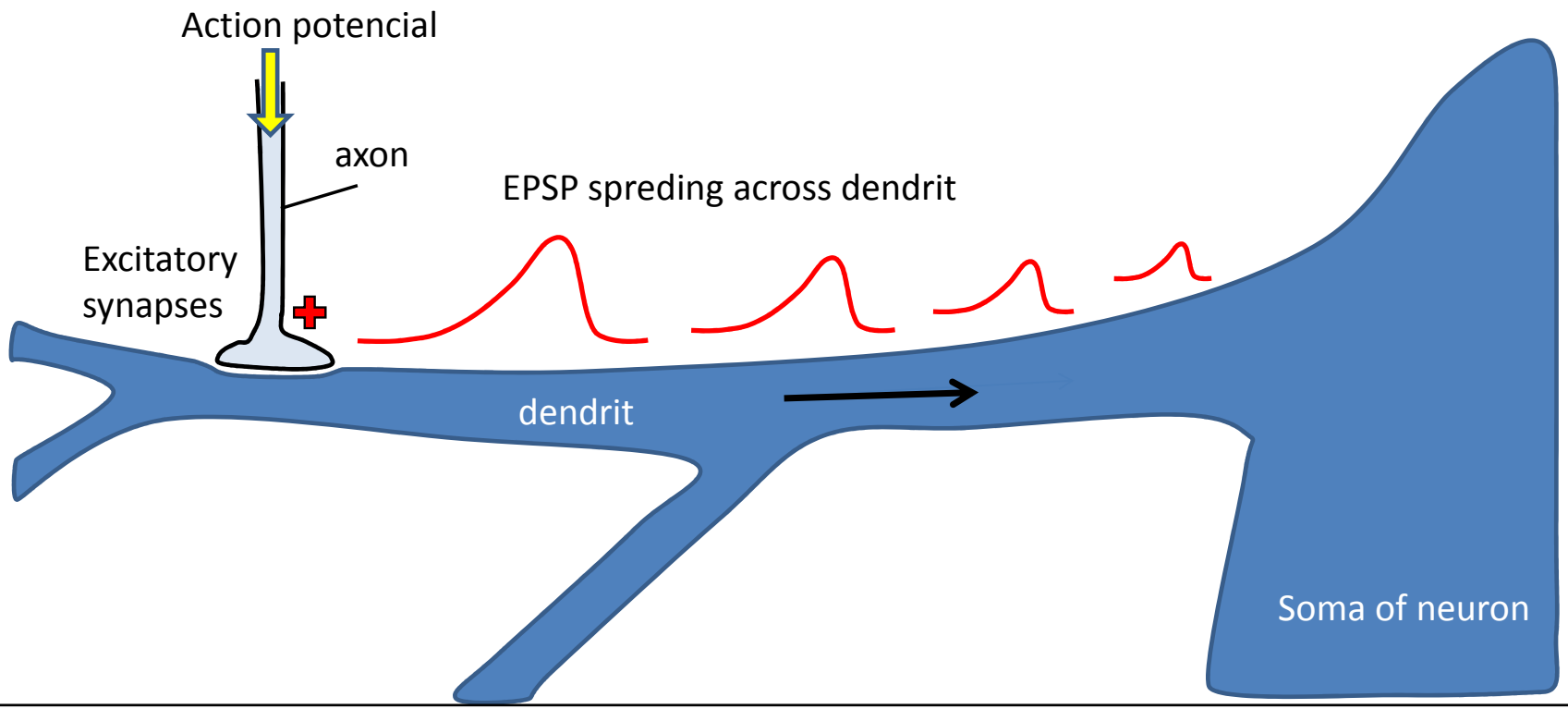


One type of neurotransmitter binds to one type of receptor and opens one type of ion channels
E.g. GABA bound to GABA A causes the CL- channel to open and the CL- to enter the cell

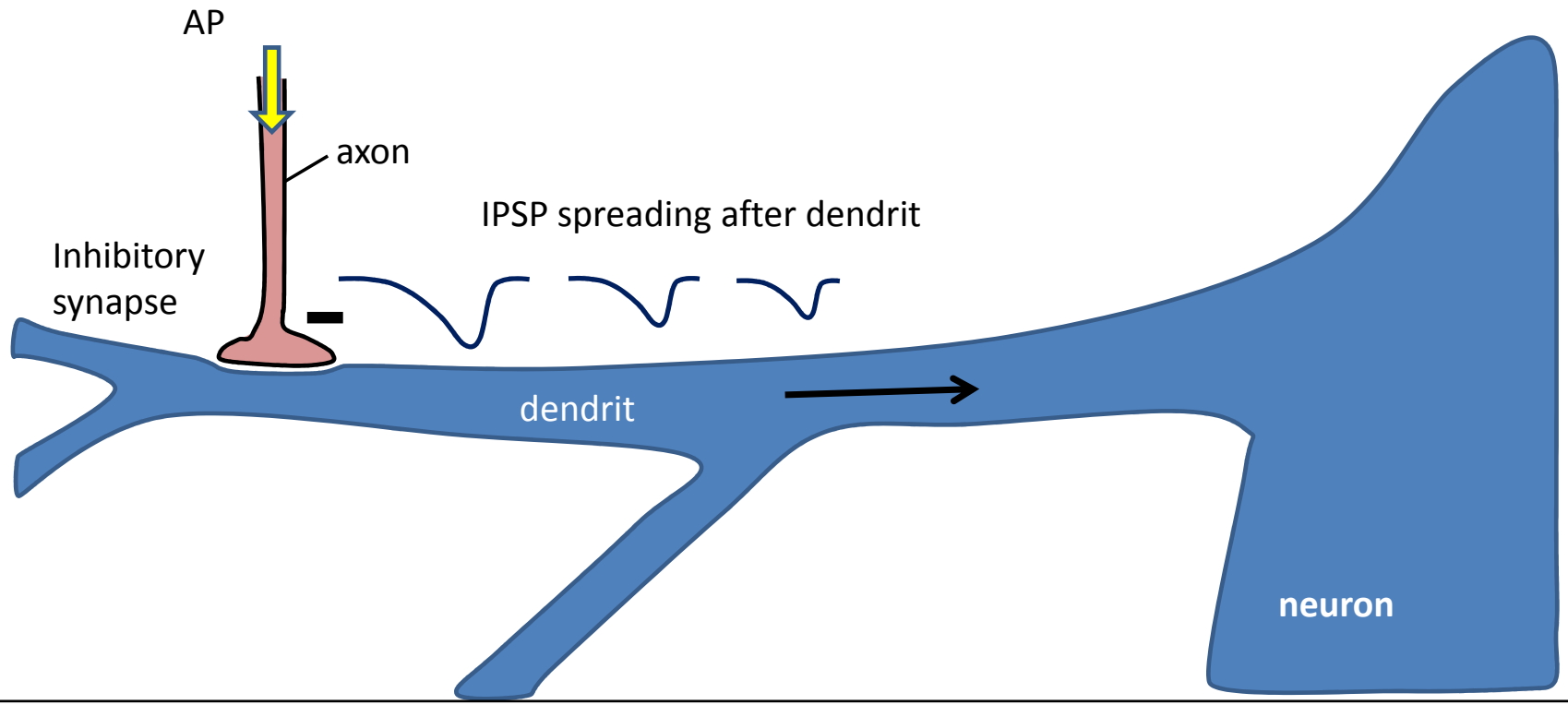
Spread EPSP

PSP

- Is weakly than AP
- Spread with decrement (with loss), gradually disappears



Spread IPSP

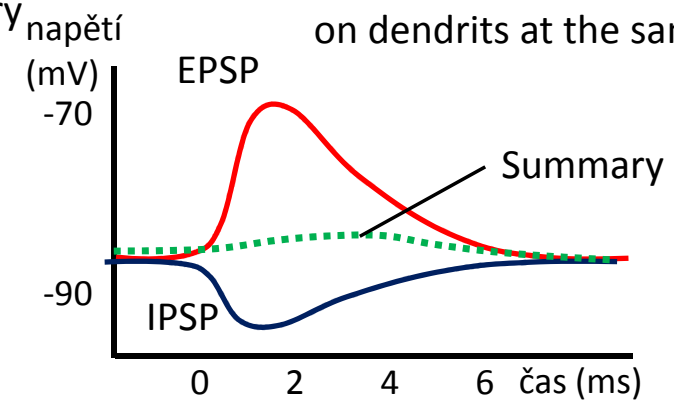

AP
axon
IPSP spreading after dendrit
Inhibitory
synapse
dendrit
neuron

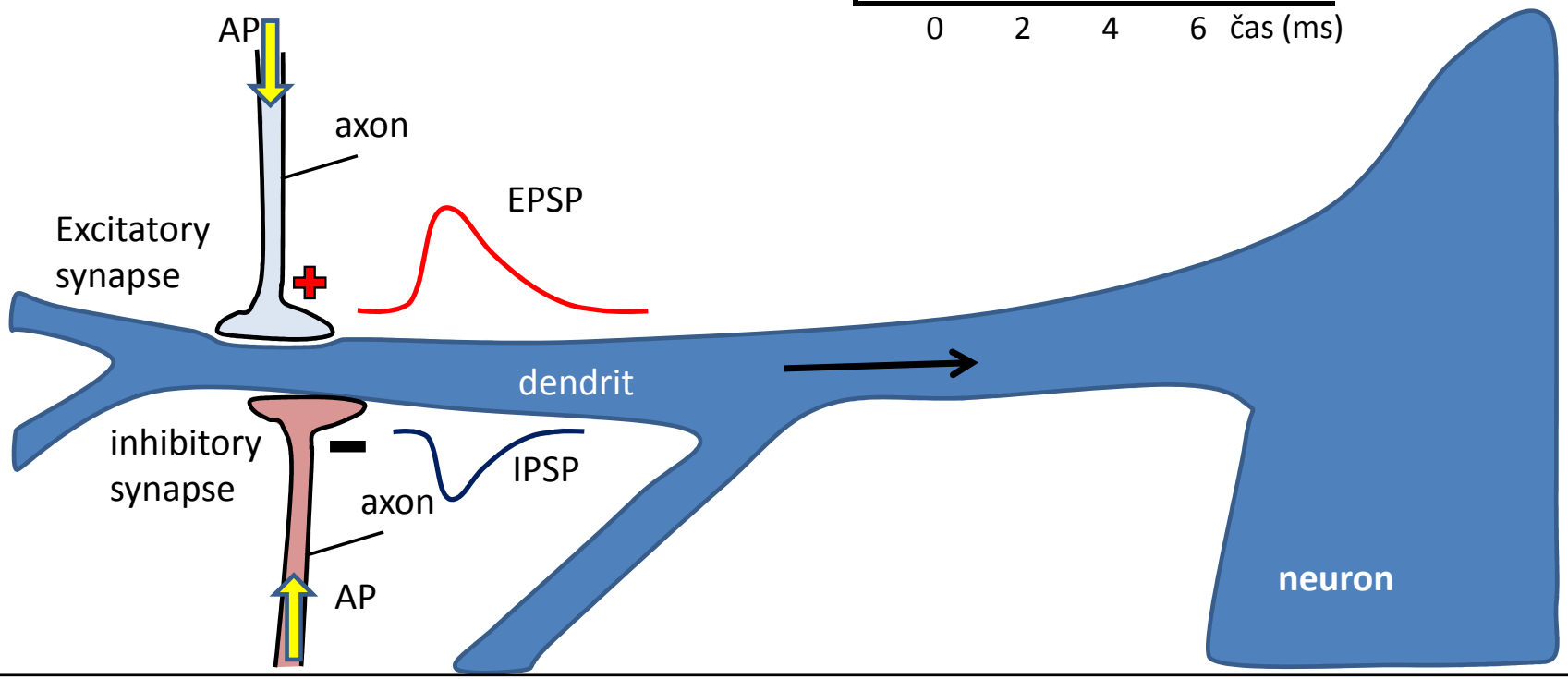
Summation of postsynaptic potencials

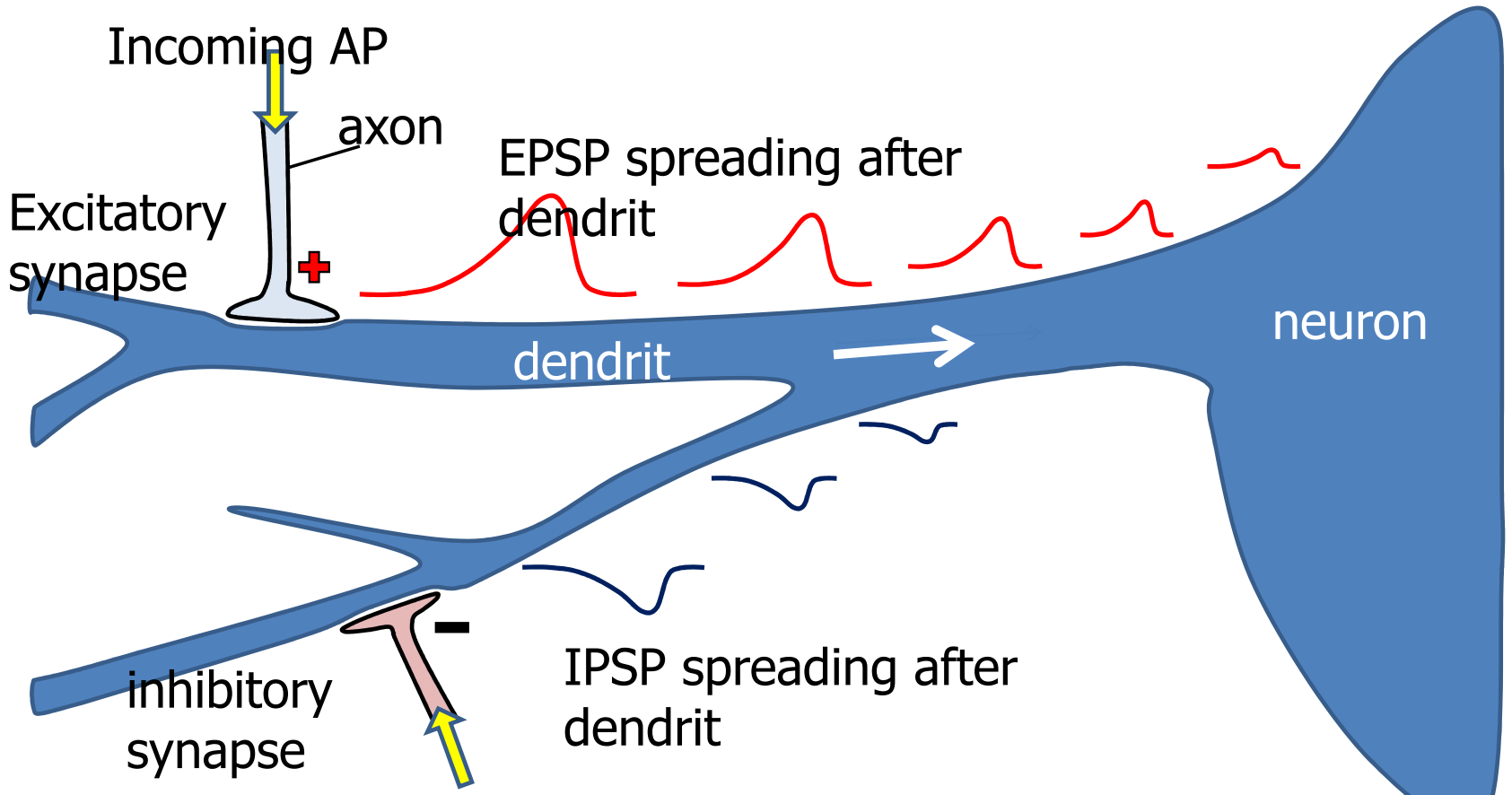
There may be both excitatory and inhibitory synapses on the neuron's body - EPSP and IPSP - add up

- Predominance of IPSP – hyperpolarization of membrane
- Predominance EPSP – depolarization of membrane

EPSP and IPSP that originated on dendrits at the same time

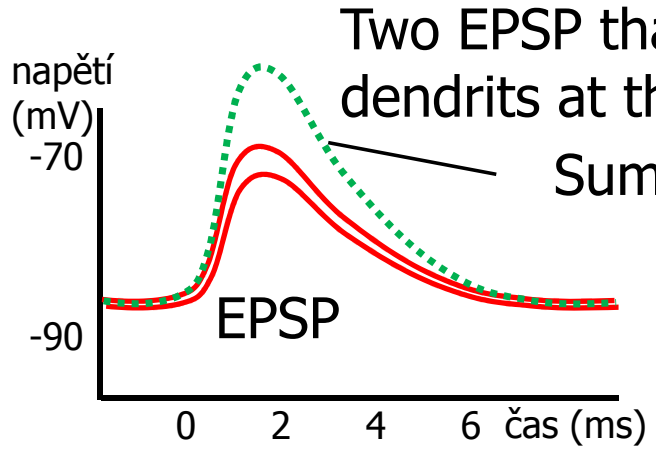





Incoming AP
axon
EPSP spreading after dendrit
Excitatory synapse
dendrit
neuron
inhibitory synapse
IPSP spreading after dendrit

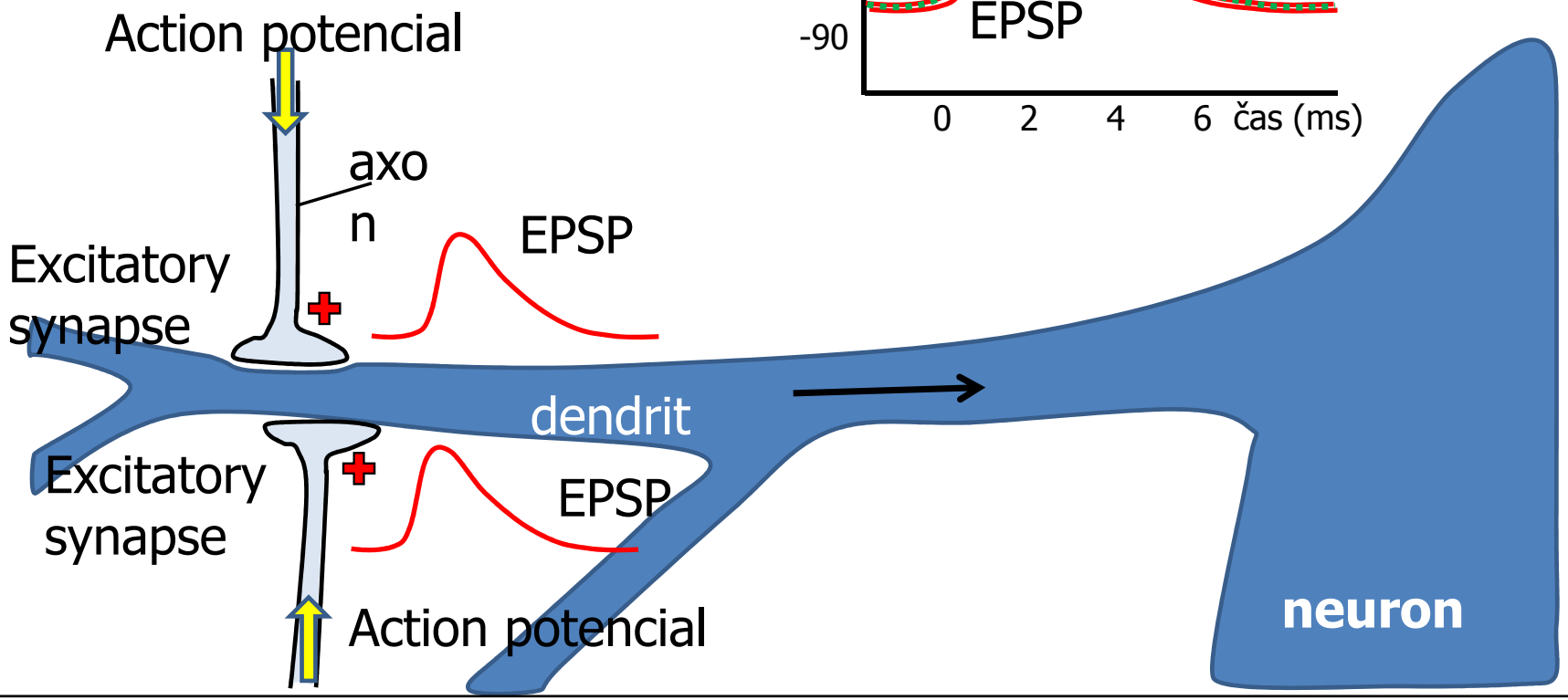
Summation of postsynaptic potencials

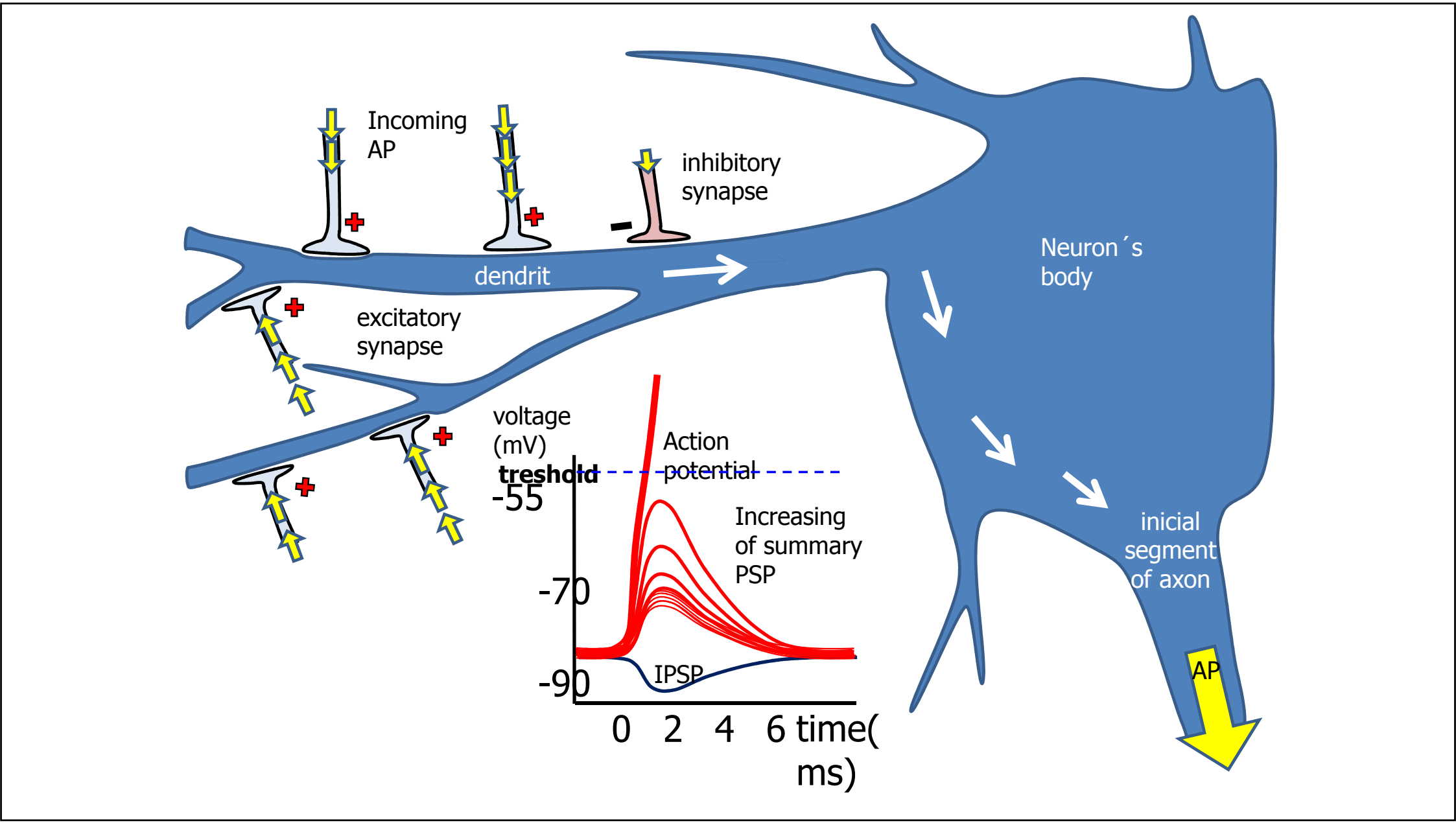
There may be both excitatory and inhibitory synapses on the neuron's body - EPSP and IPSP - add up



Two EPSP that originated on dendrits at the same time

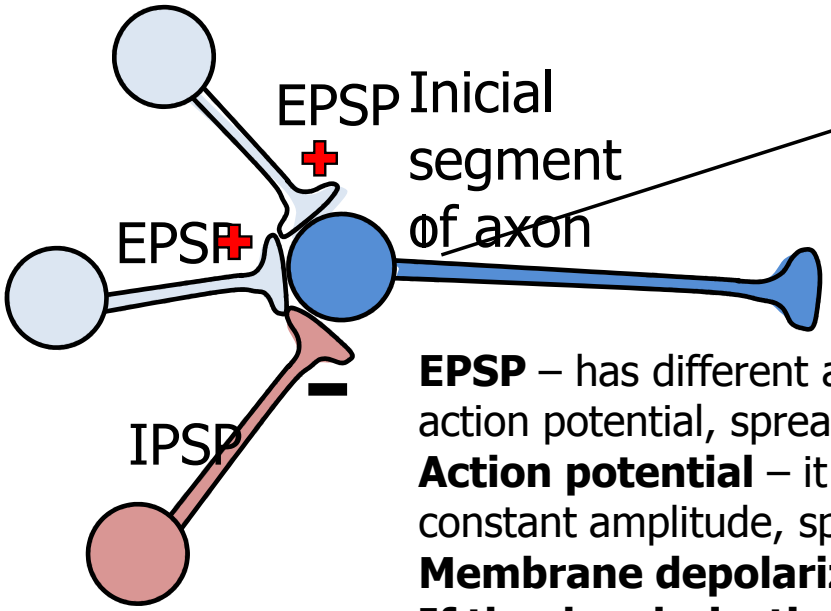
Summary

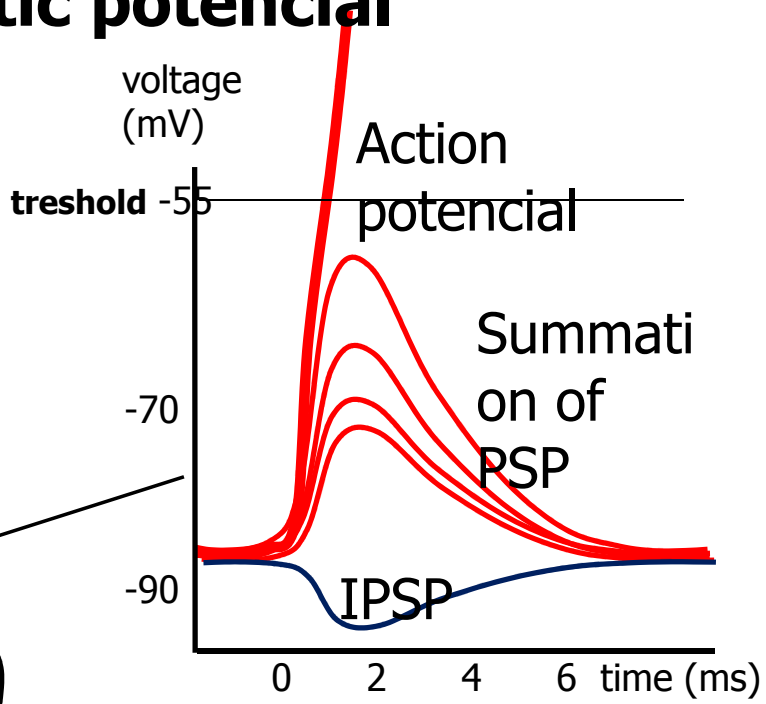



Incoming
AP
inhibitory
synapse
dendrit
excitatory
synapse
Neuron´s
body
voltage
(mV)
treshold
-55
-70
-90
Action
potential
Increasing
of summary
PSP
IPSP
0 2 4 6 time(
ms)
inicial
segment
of axon
AP

Summation of postsynaptic potencial

All EPSP and IPSP that came to the neuron at the same time add up.
If the sum of all PSP exceeds the threshold (around -55mV), the action potential is created.

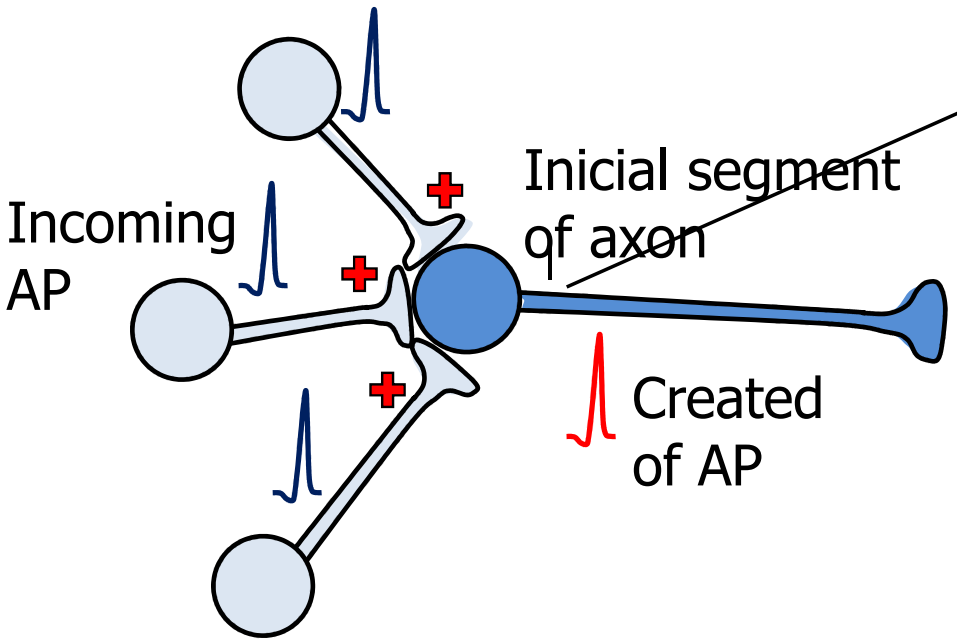


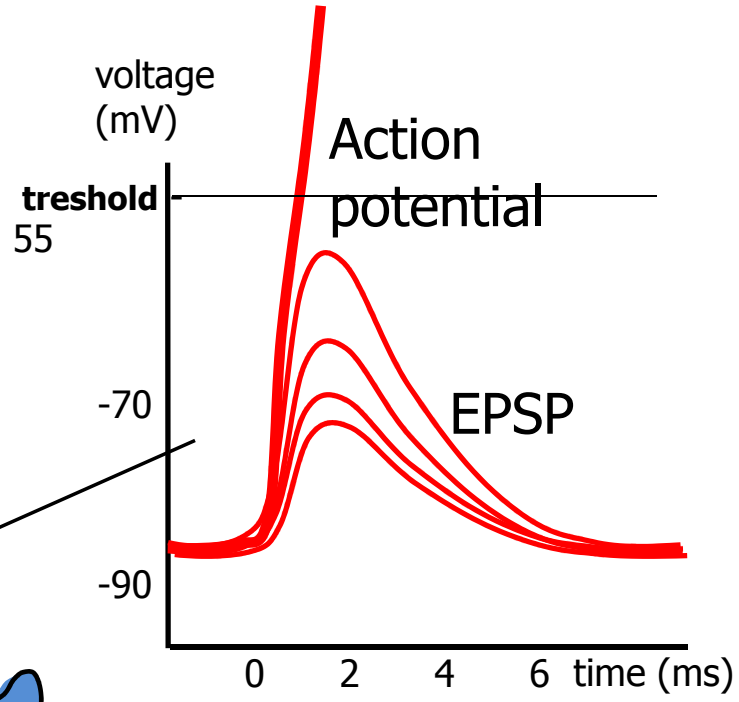


EPSP – has different amplitudes, but is smaller than the amplitude of action potential, spreads with decrement
Action potential – it arises only after crossing the threshold, has a constant amplitude, spreads without decrement
Membrane depolarization may not lead to AP
If the depolarization does not exceed the threshold, the AP does not create

Space summation

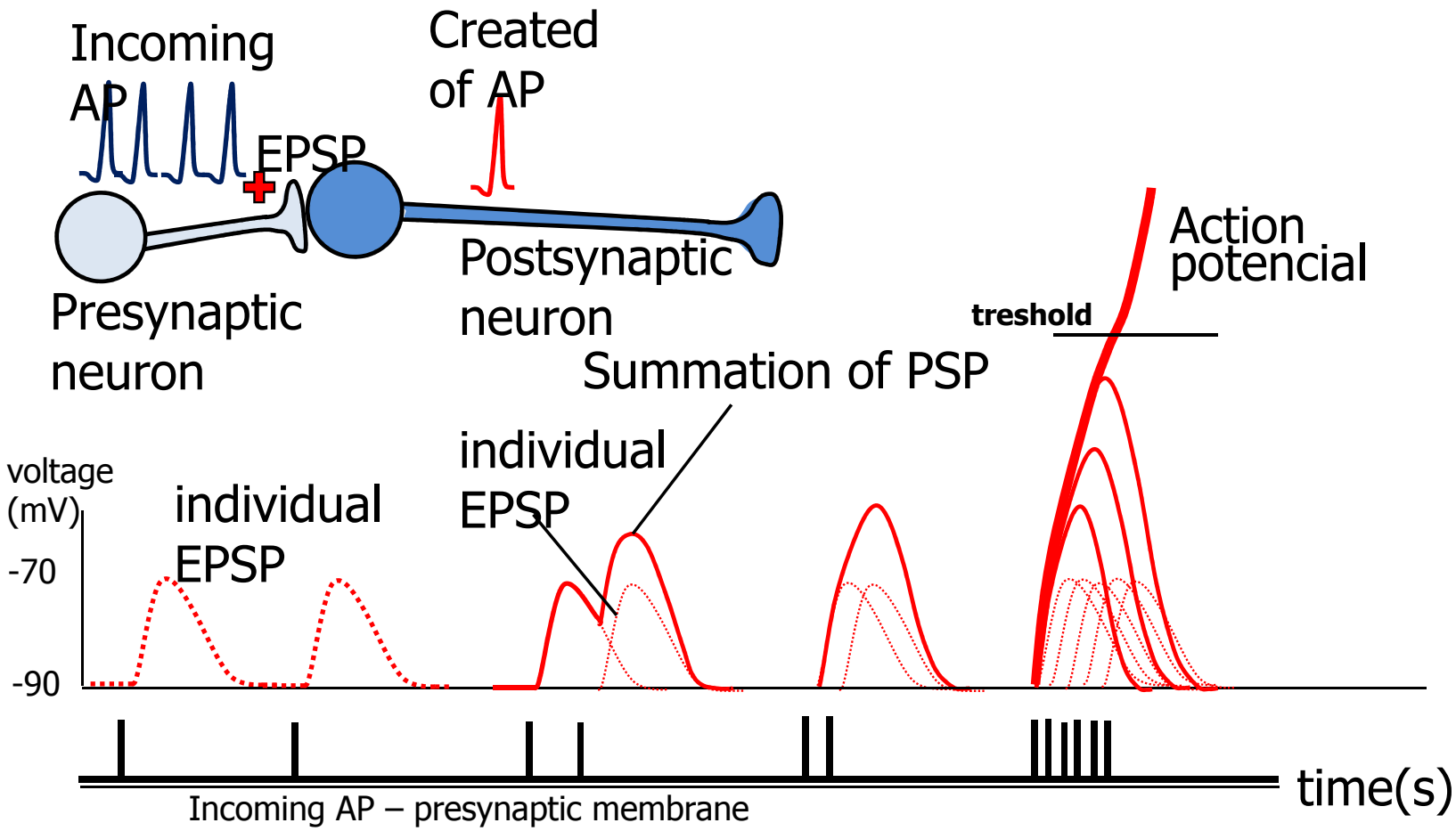
The more excitatory synapses on the neuron, which the AP came up with at the same time, the more EPSP was created and the easier it was to reach the threshold for the formation of AP on the postsynaptic neuron





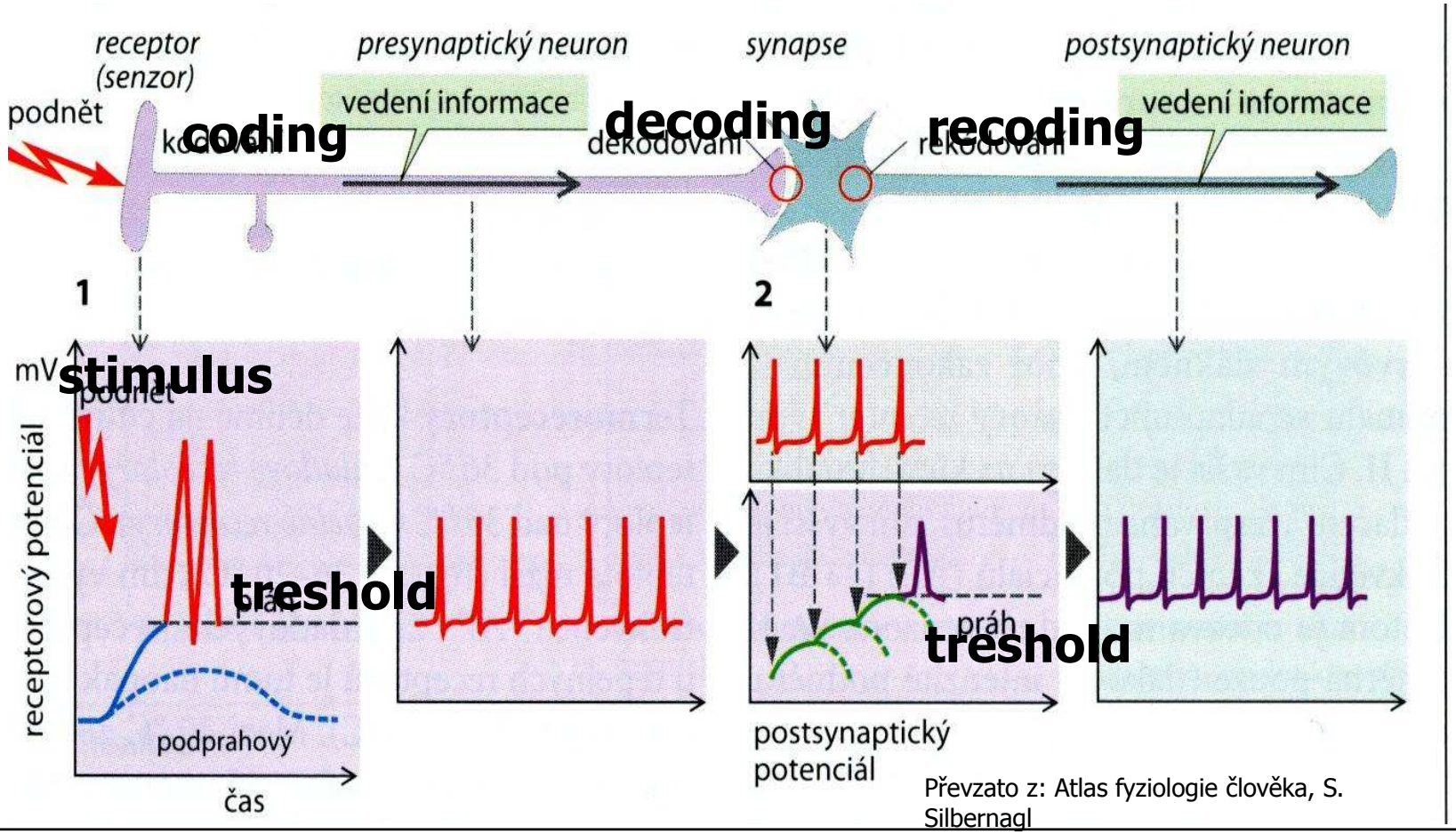
Time summation

The higher the frequency of AP coming to synapses, the greater the summation of PSP and the sooner the AP threshold on the postsynaptic neuron is reached



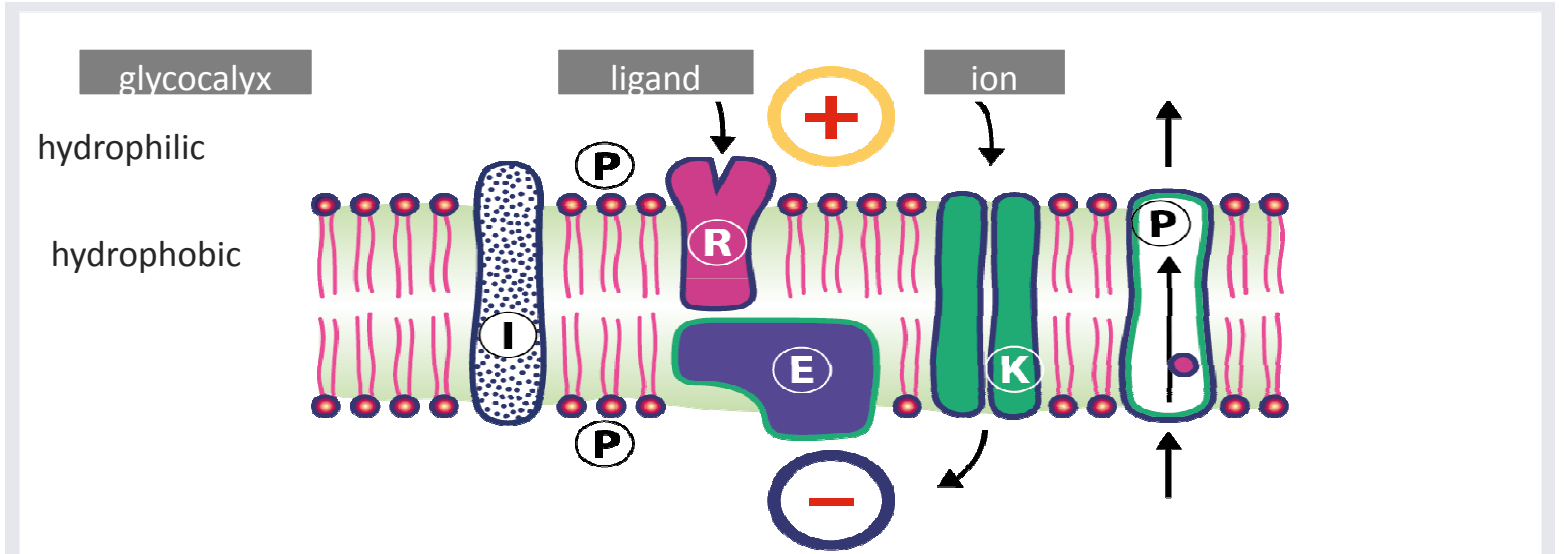
Coding information

- Coding – intensita of stimulus recorded by the receptor is recoded to AP frequency
- Decoding – on synapses - frequency of AP is transformed into PSP
- Recoding - if the sum of all PSP exceeds the threshold, creates AP

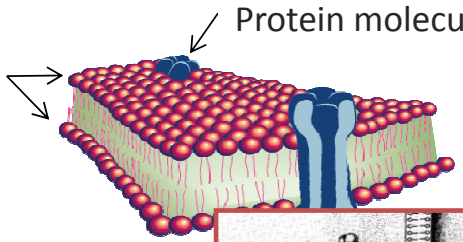


Převzato z: Atlas fyziologie člověka, S. Silbernagl

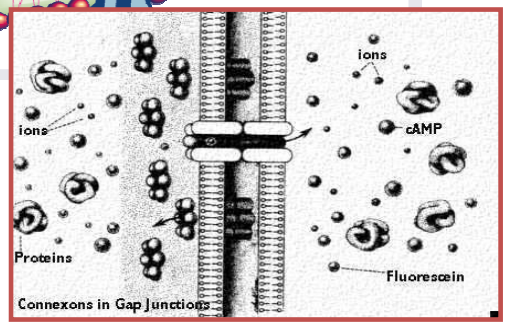
ELECTRIC SYNAPSES



I – integral protein
R – receptor
E – enzyme
K – channel
P – pump (ATP-ase)



Nexus (gap junction) →



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MUNI MED

- **RESTING MEMBRANE POTENTIAL IS A CONDITION OF EXCITABILITY**
- **IT DEPENDS ON HIGH RESTING MEMBRANE CONDUCTIVITY FOR POTASSIUM**

ACTION POTENTIAL IS A PROPAGATED ELECTRICAL SIGNAL GENERATED BY FAST SODIUM CURRENT INTO THE CELL

- **ACTION POTENTIAL REPRESENTS UNIT OF INFORMATION**
- **CODING OF INFORMATION IN THIS SYSTEM IS PERFORMED BY CHANGED FREQUENCY OF ACTION POTENTIALS**