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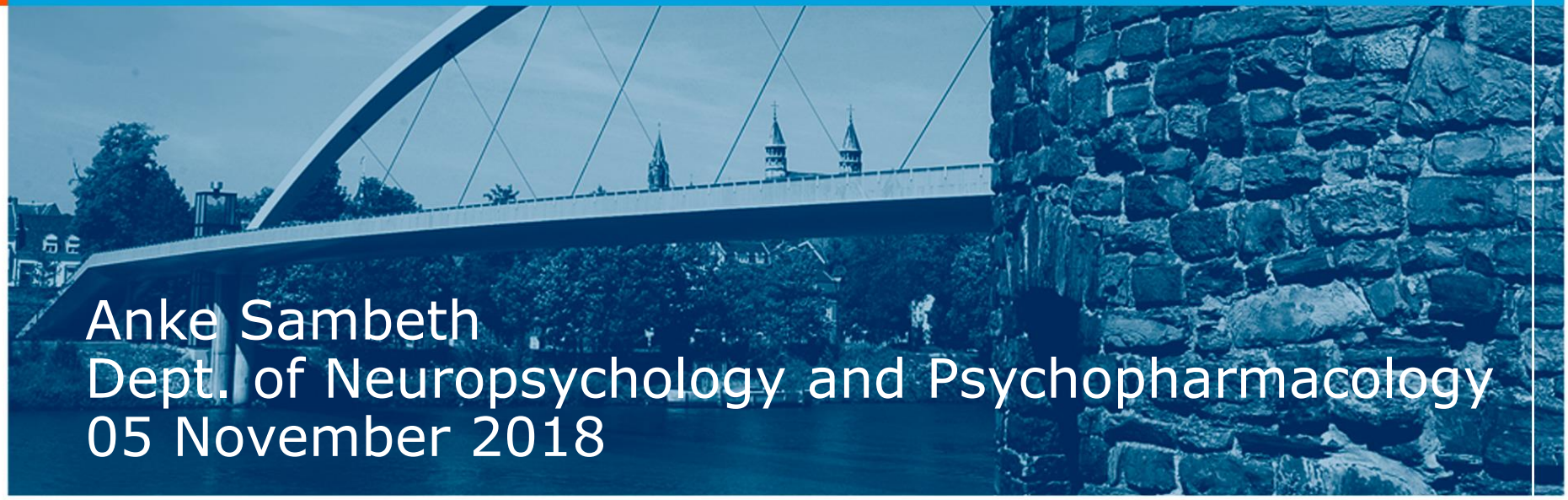
Electrophysiology and Neurotransmission



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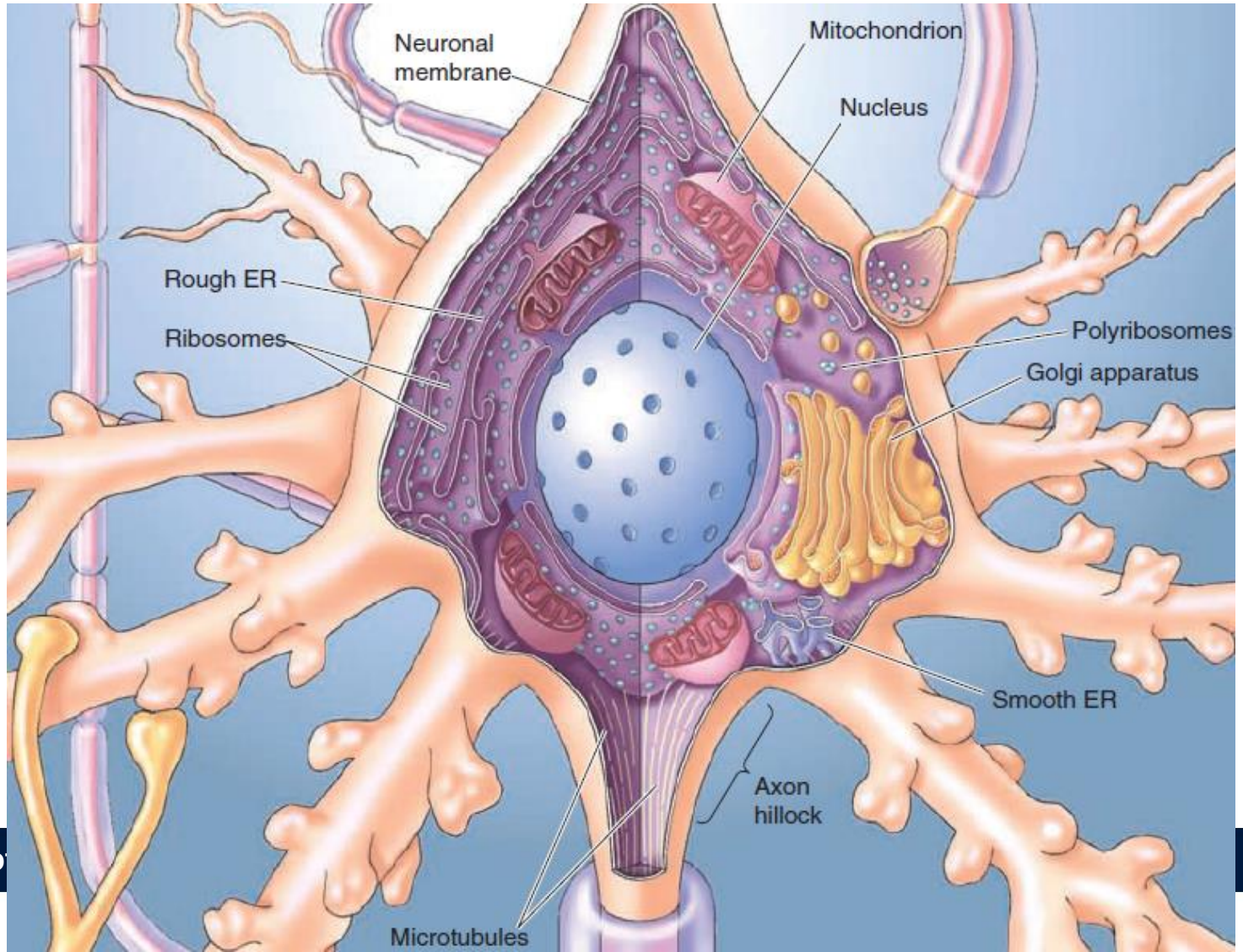
Dept. of Neuropsychology and Psychopharmacology
05 November 2018

Intro animation

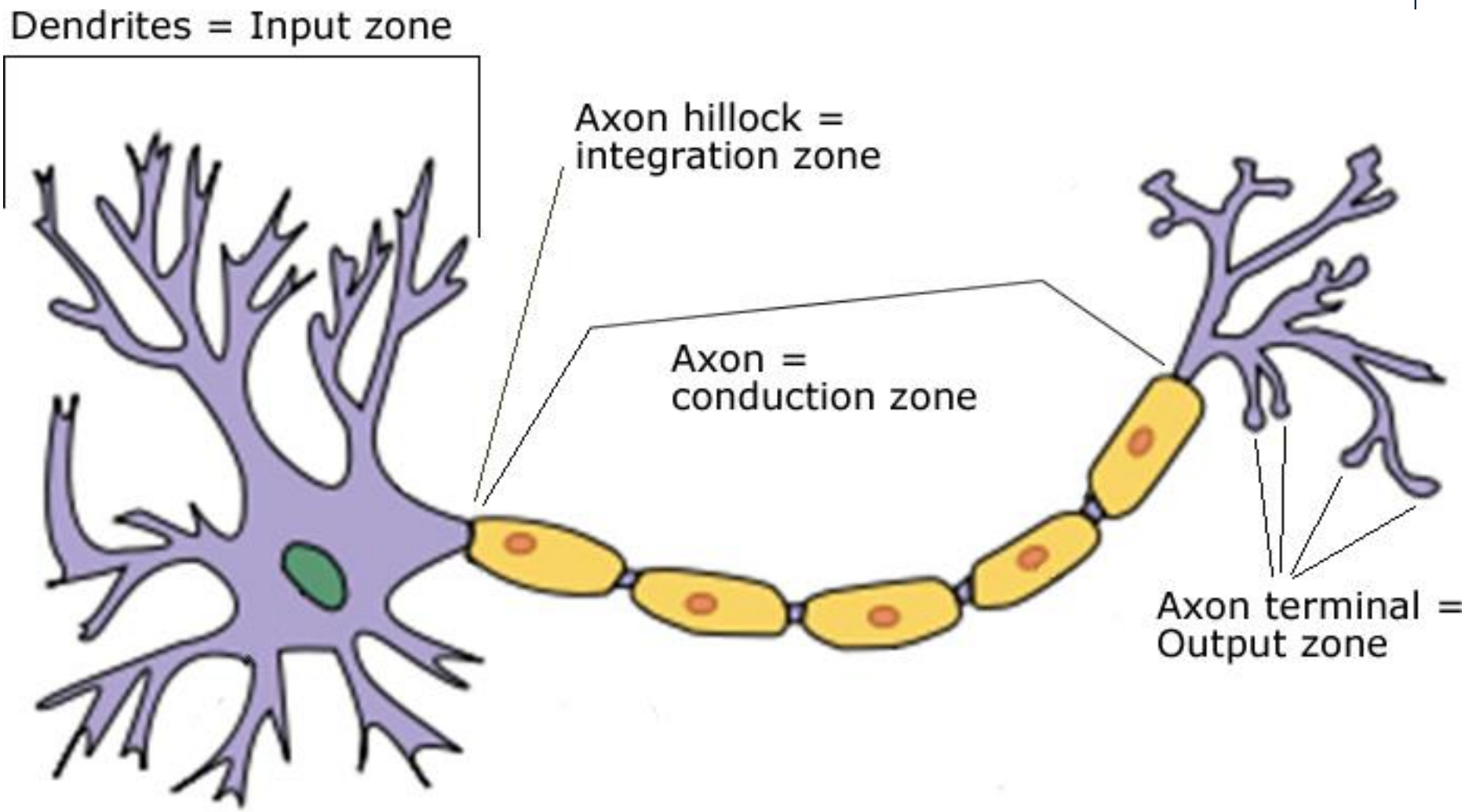
Outline of the lecture

- 1 – Action potentials
  - Resting potential
  - Disturbing the resting state potential
- 2 – Neurotransmission
  - Synapse
  - Steps in neurotransmission
  - Neurotransmitters
  - Role of 'drugs'

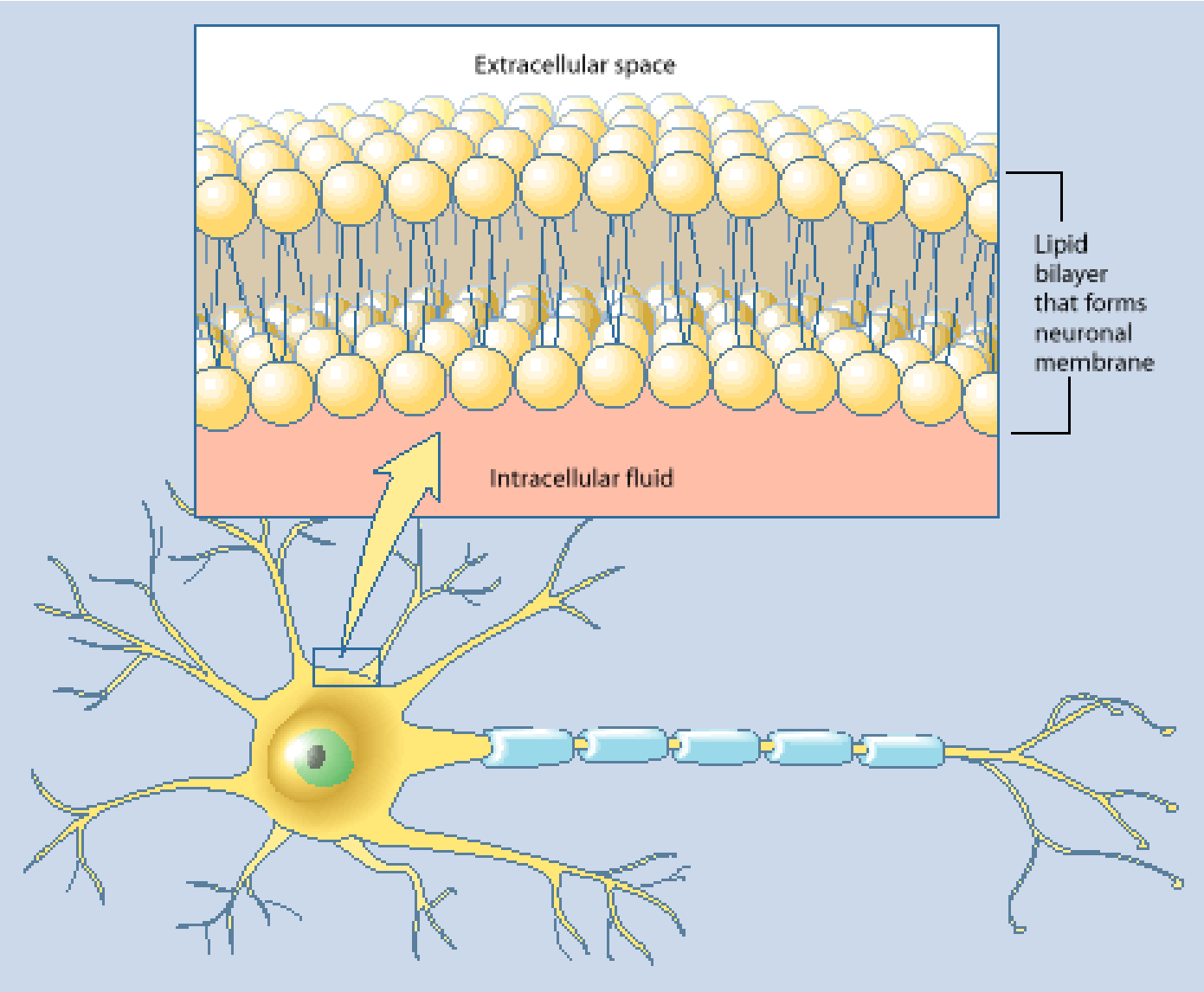
But first: Anatomy neuron



Anatomy neuron cntd.



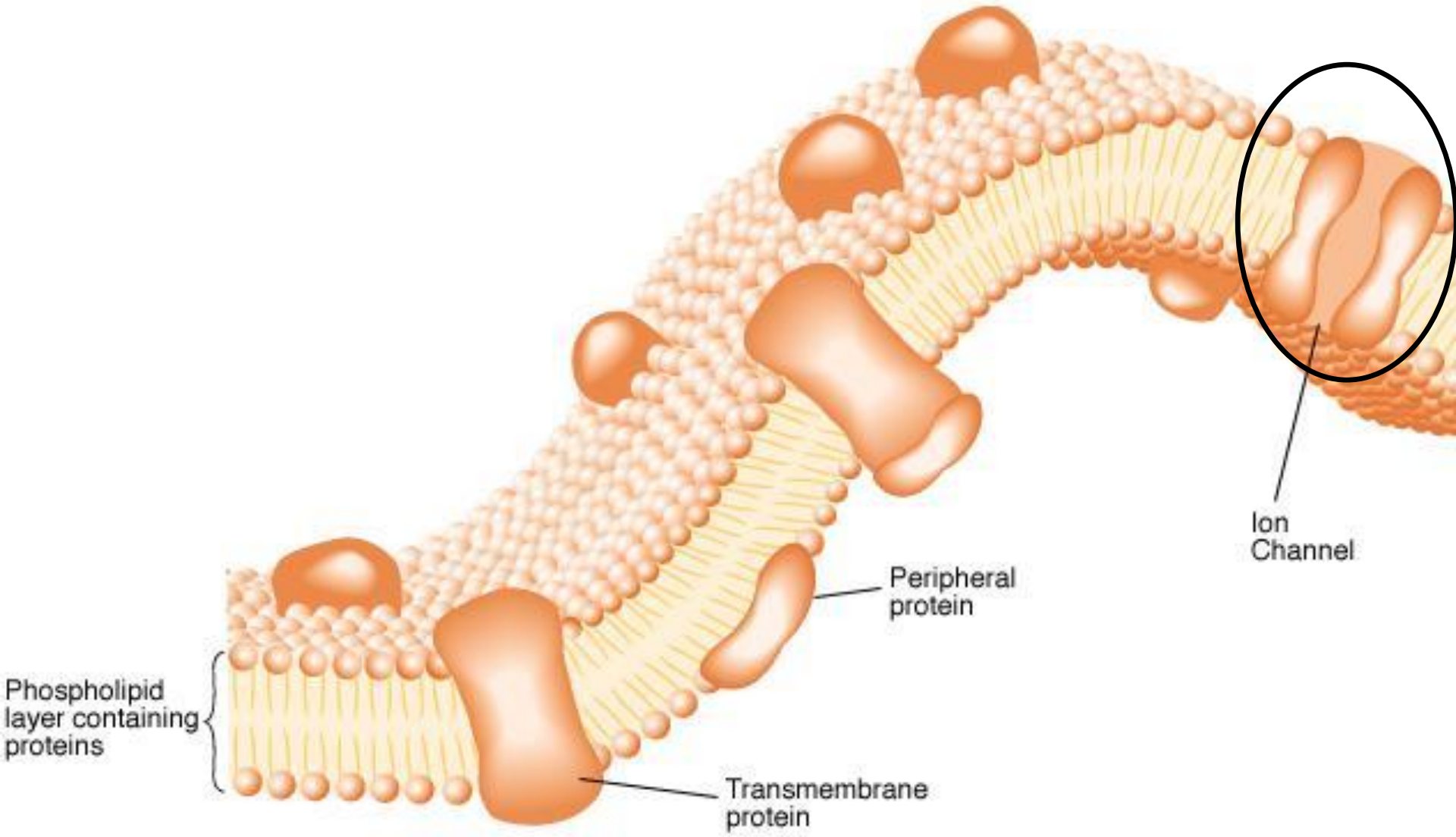
Lipid bi-layer membrane



Why lipid bi-layer? And is that all?

- To take care that the intracellular and extracellular space remain separated
- To move molecules inside/outside
  - They communicate with outside world by transferring information
  - Every neuron has its own proteins
- Protein channels and pumps
  - Passive
  - Active

Proteins on membrane



Action potential introduction

- Resting potential
  - Diffusion
  - Equal distribution
  - Sodium / Potassium pump (Na^+/ K^+-pump)
- Disturbing resting potential / Action potential
  - Phases of action potential
  - Propagation
  - Excitatory / Inhibitory postsynaptic potentials

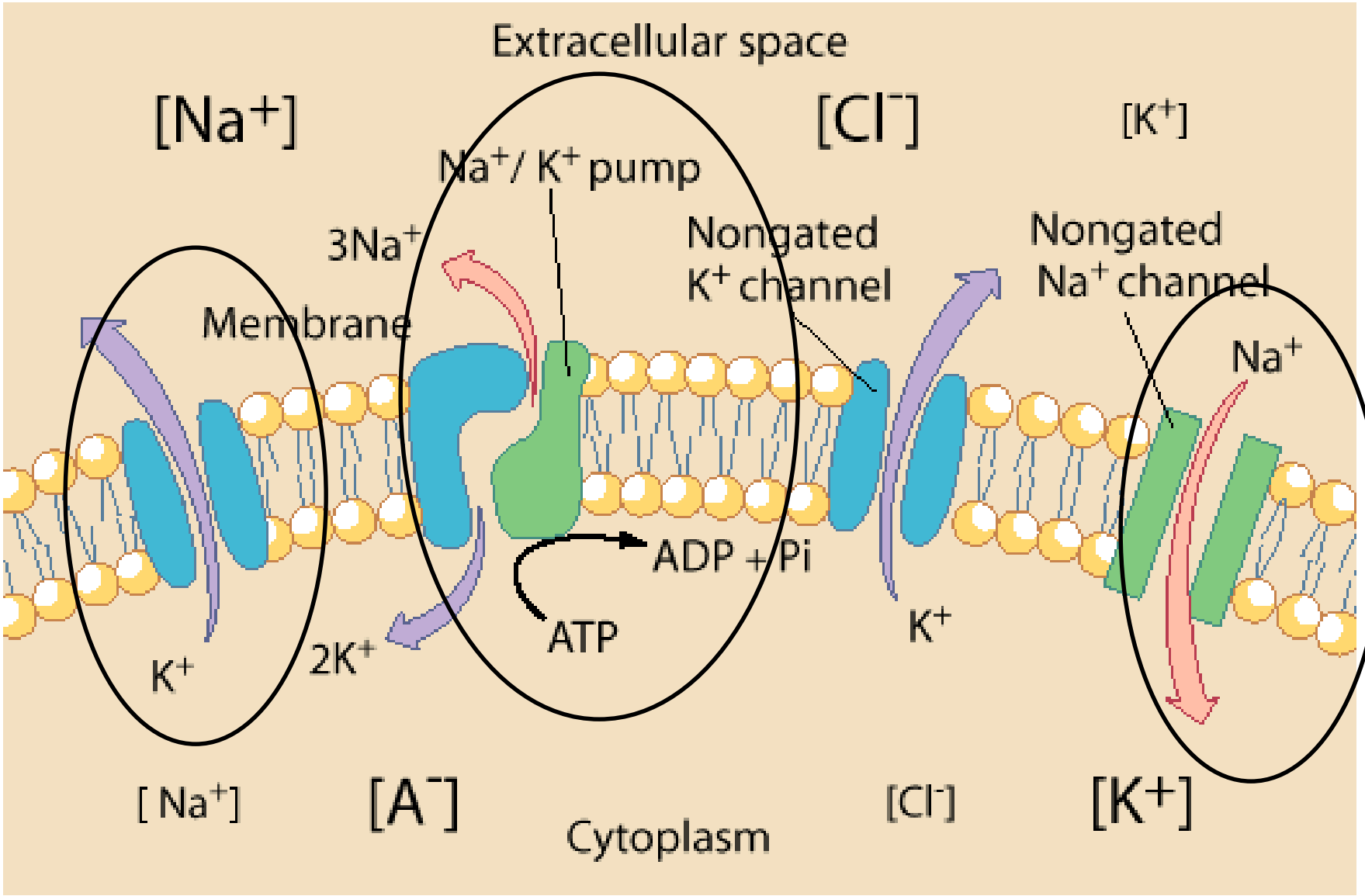
Resting potential

- Electrical gradient
  - ± -70 to -80 mV
- Motion / Diffusion
  - Na^+ (sodium) / K^+ (potassium) / Cl^- (chloride) / A^- (anions, various negatively charged ions)
  - Ion channels (gated, non-gated)
  - Selective permeability
  - Active / Passive motion

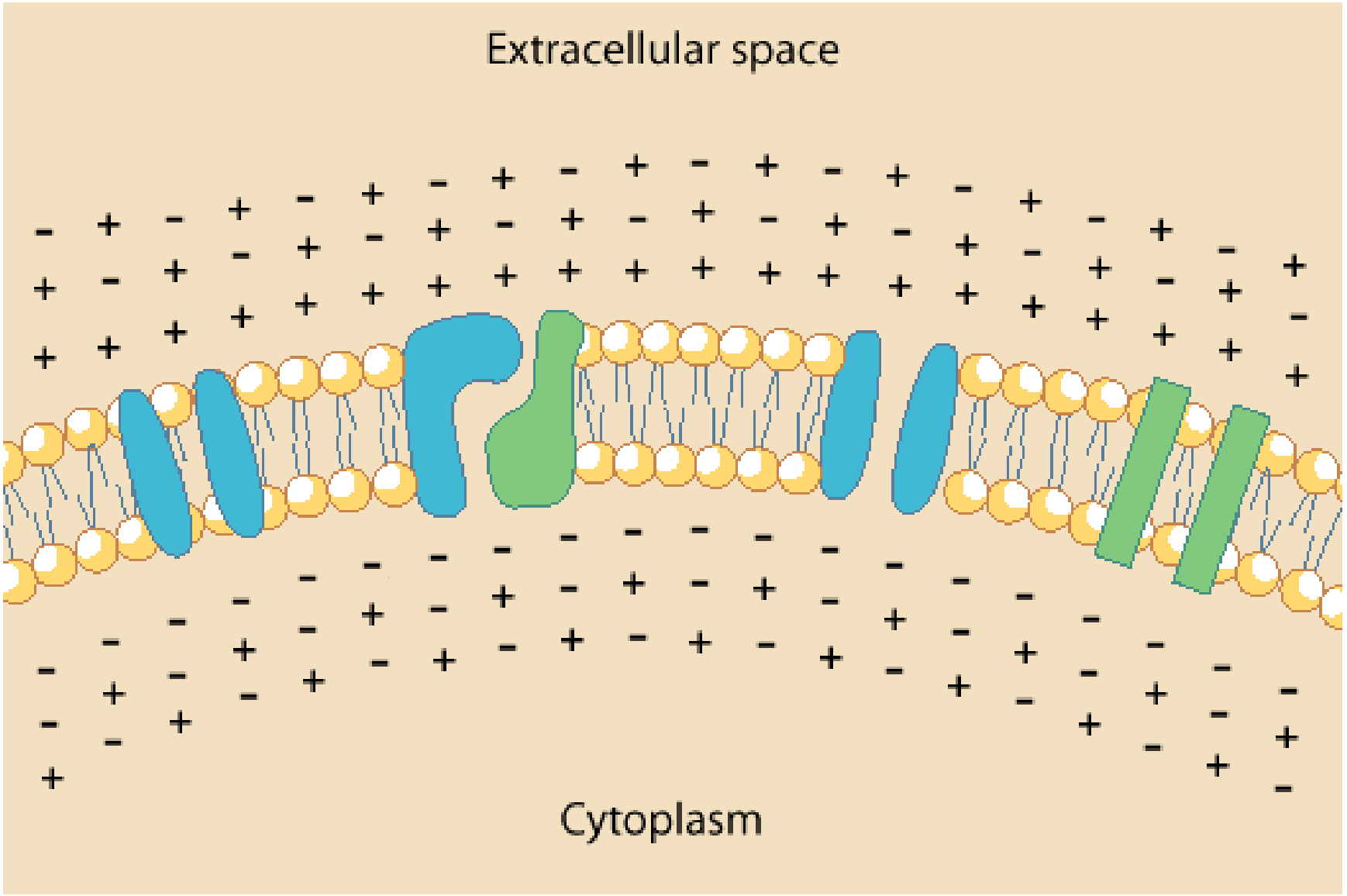
Resting potential continued

- Concentration gradient
  - Concentration inside vs. outside
  - Causes e.g., diffusion
- Electrical gradient
  - Opposites attract (+ likes – and – likes +)

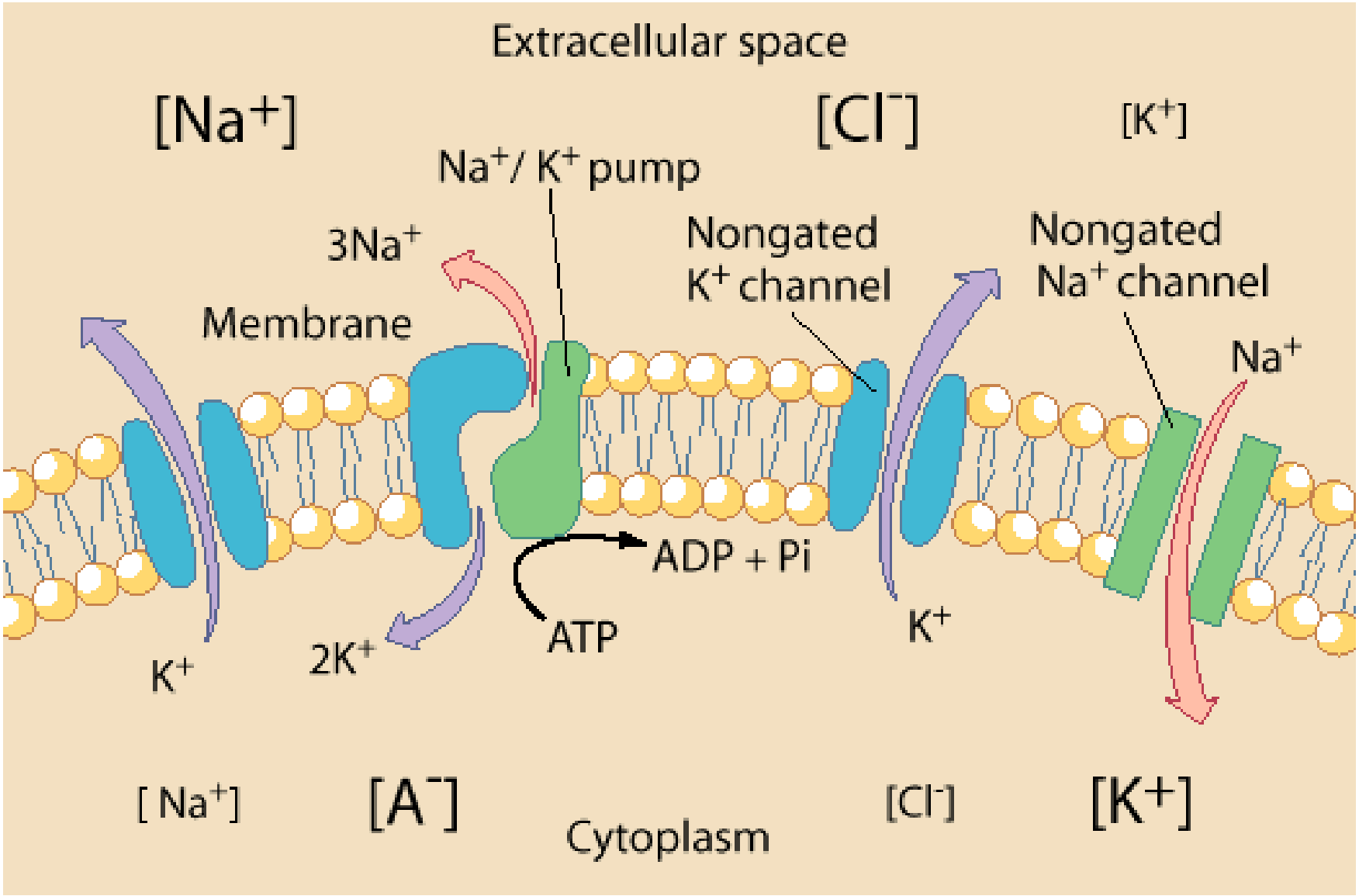
Concentration gradient



Electrical gradient



Concentration gradient again



Q1: How are potassium ions typically moved out of a neuron when the membrane is at rest?

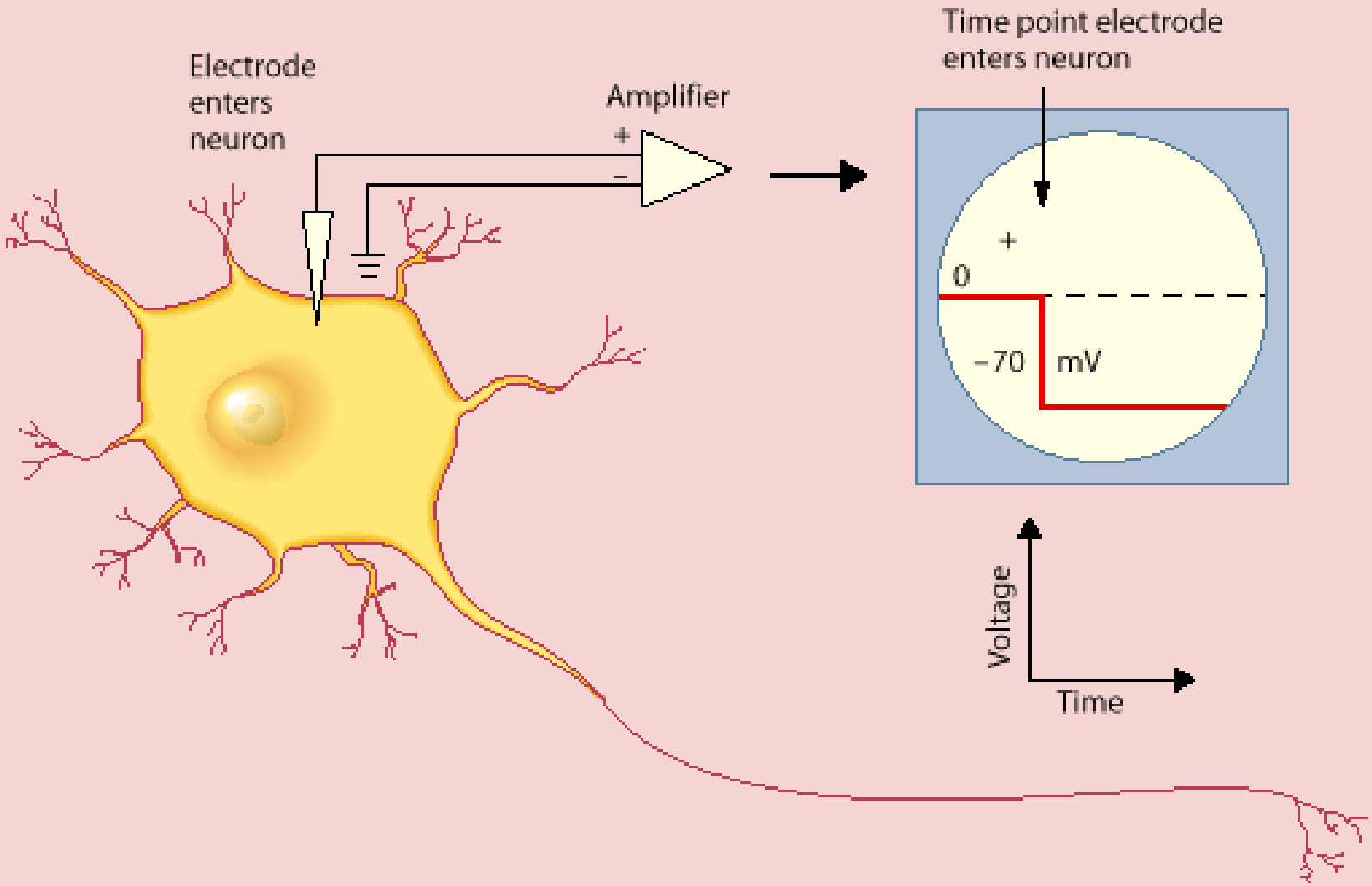
a) Electrical gradients move potassium out

b) The sodium-potassium pump moves them out

c) Concentration gradients move potassium out

Animation 1: Resting potential

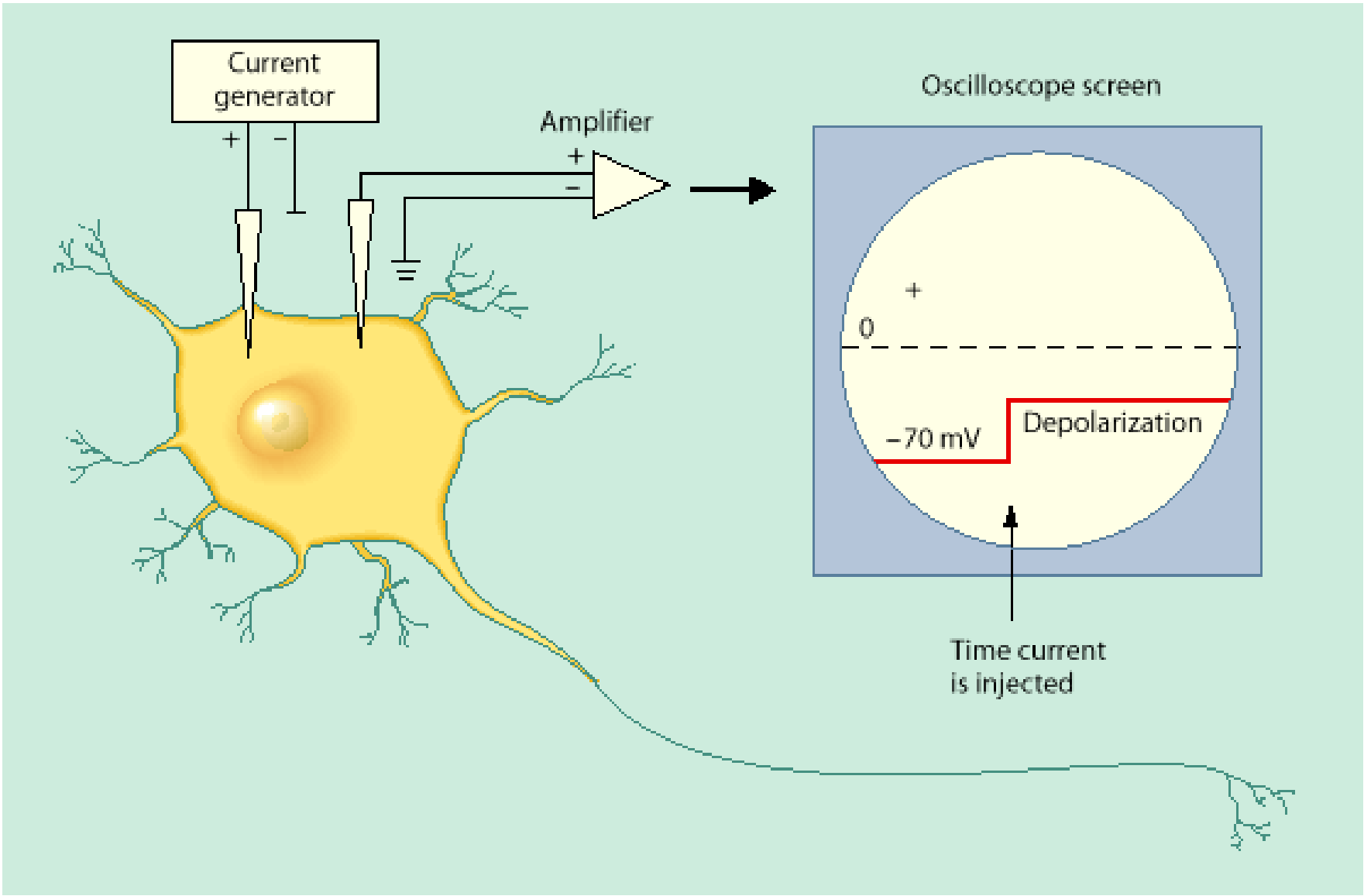
Resting potential measured



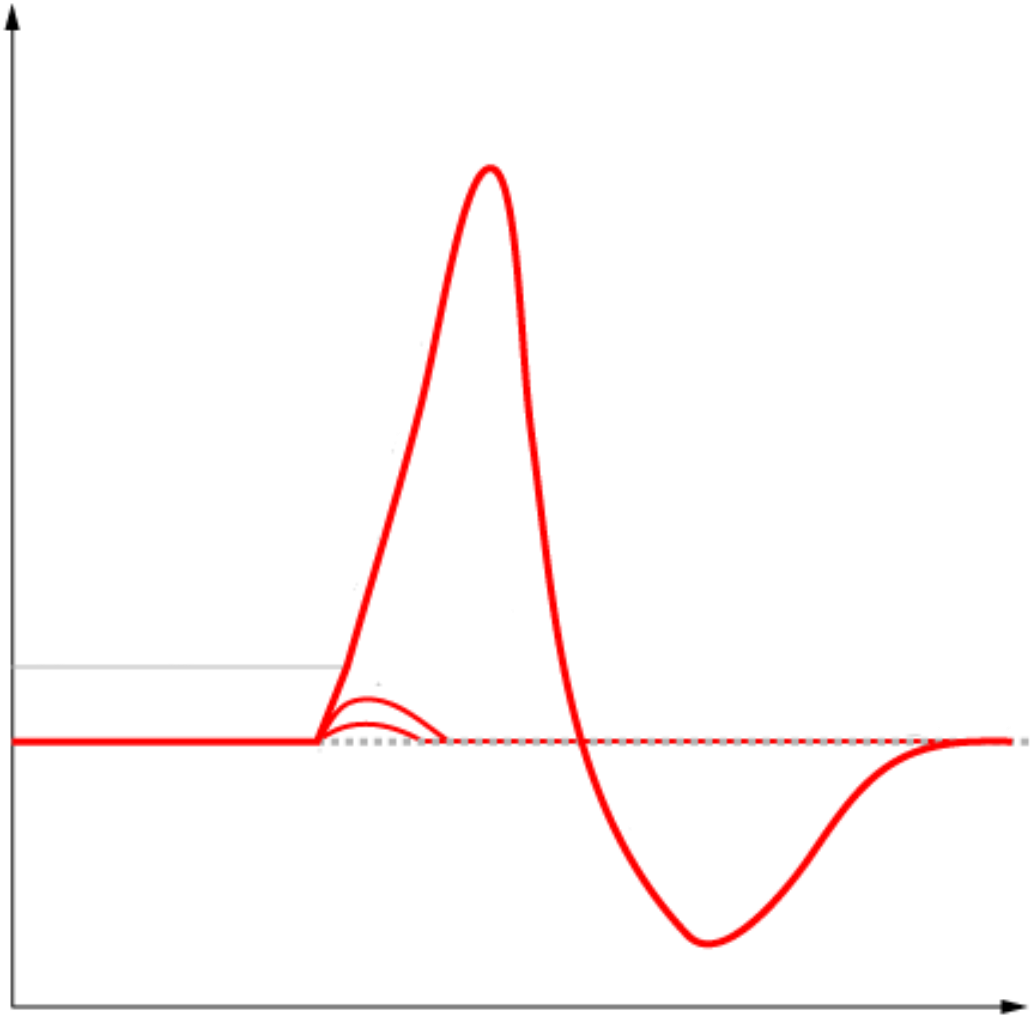
Action potential generation

- Stimulus
- Negative or positive charge?
- Hyperpolarization / Depolarization

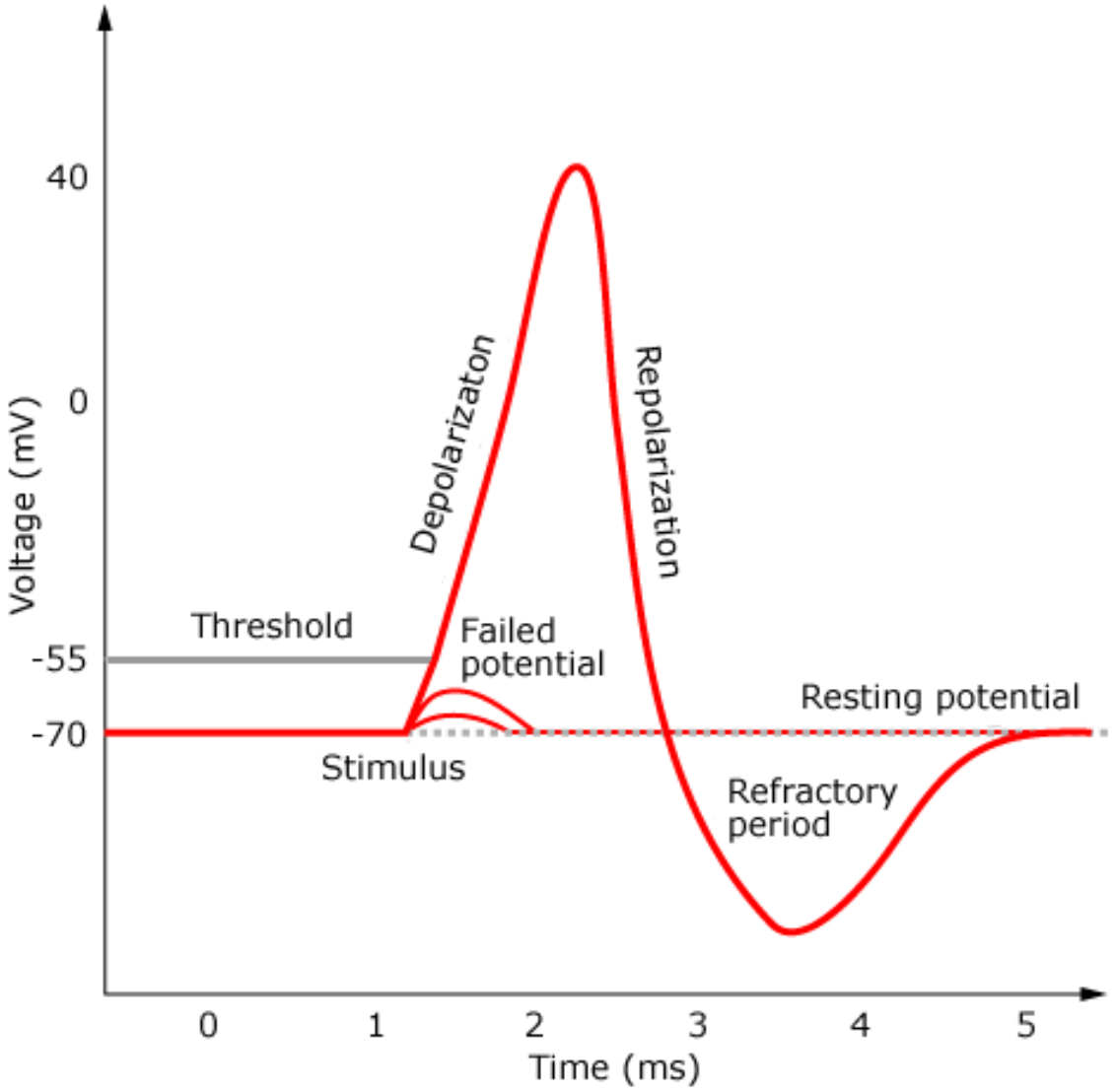
Action potential measured



Action potential (AP)



Action potential (AP)

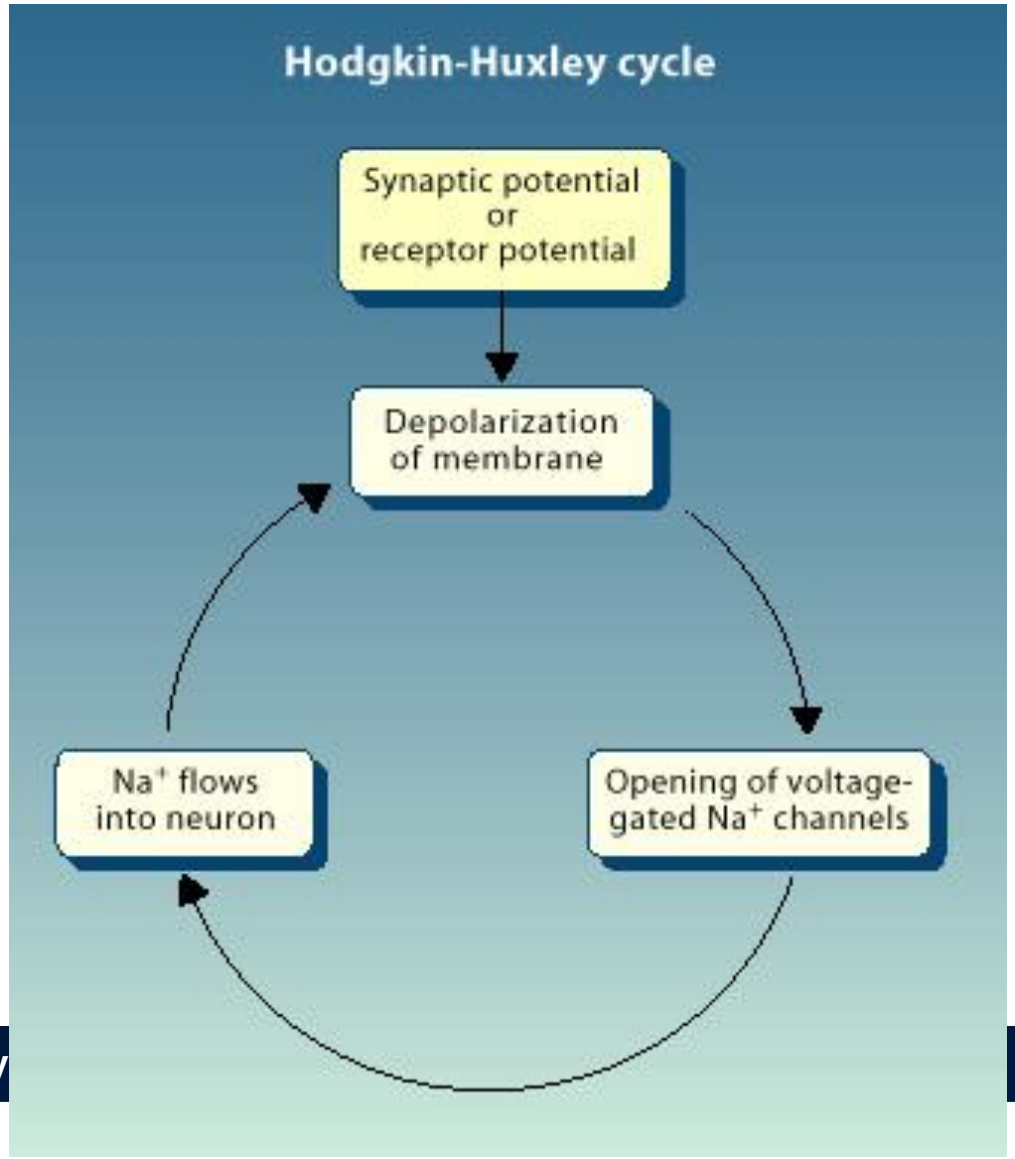


Q2: The action potential is a transient change in the resting membrane potential from -70 mV to +30 mV, then back to -70 mV. This change is caused by the opening of first …, then … voltage-gated channels.

a) K^+, then Na^+

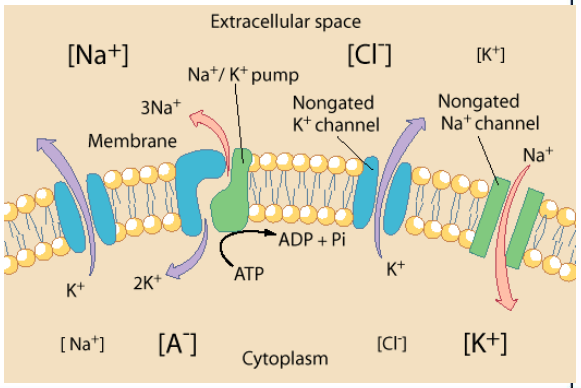
b) Na^+, then K^+

Na^+ flow to evoke AP

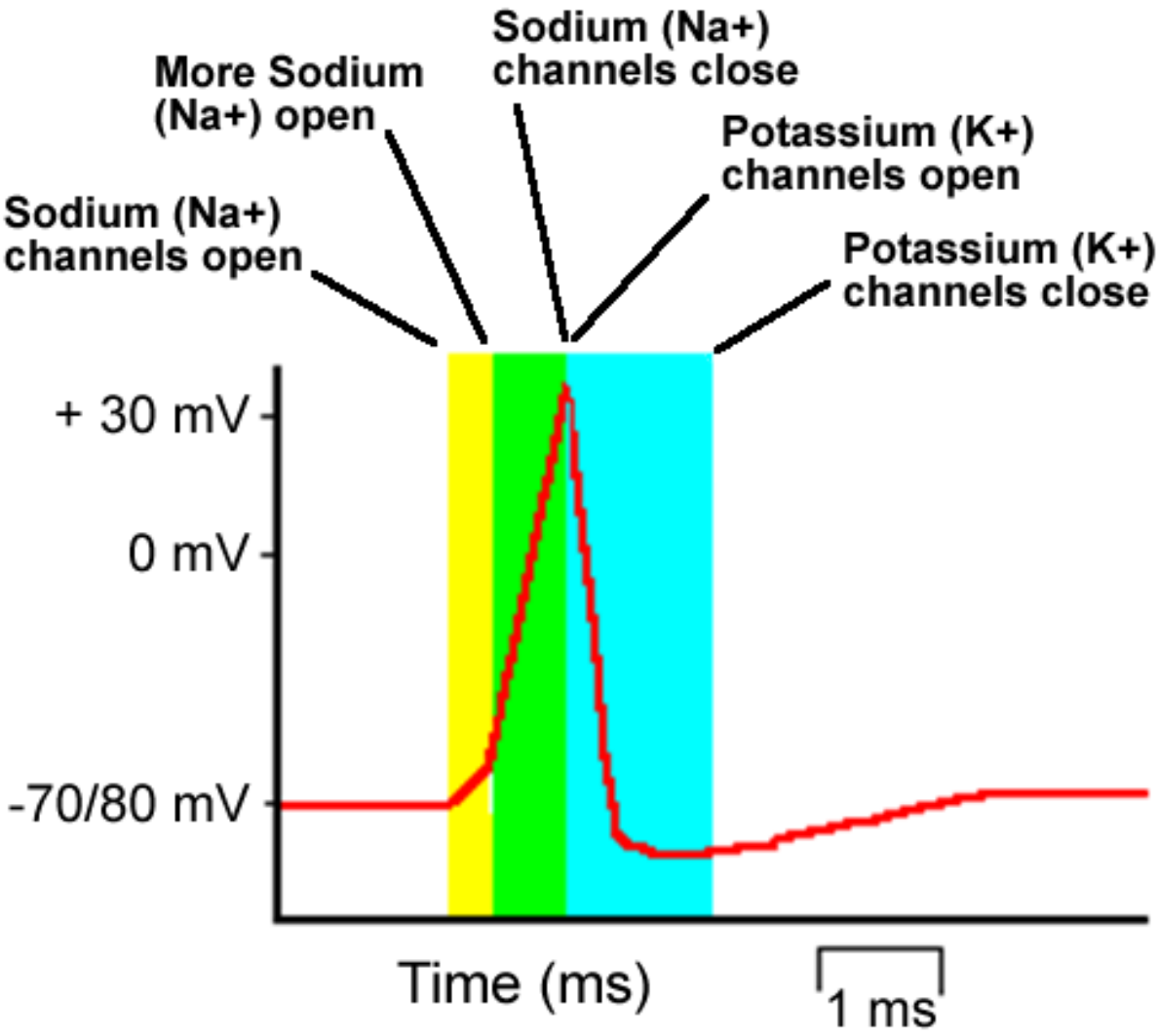


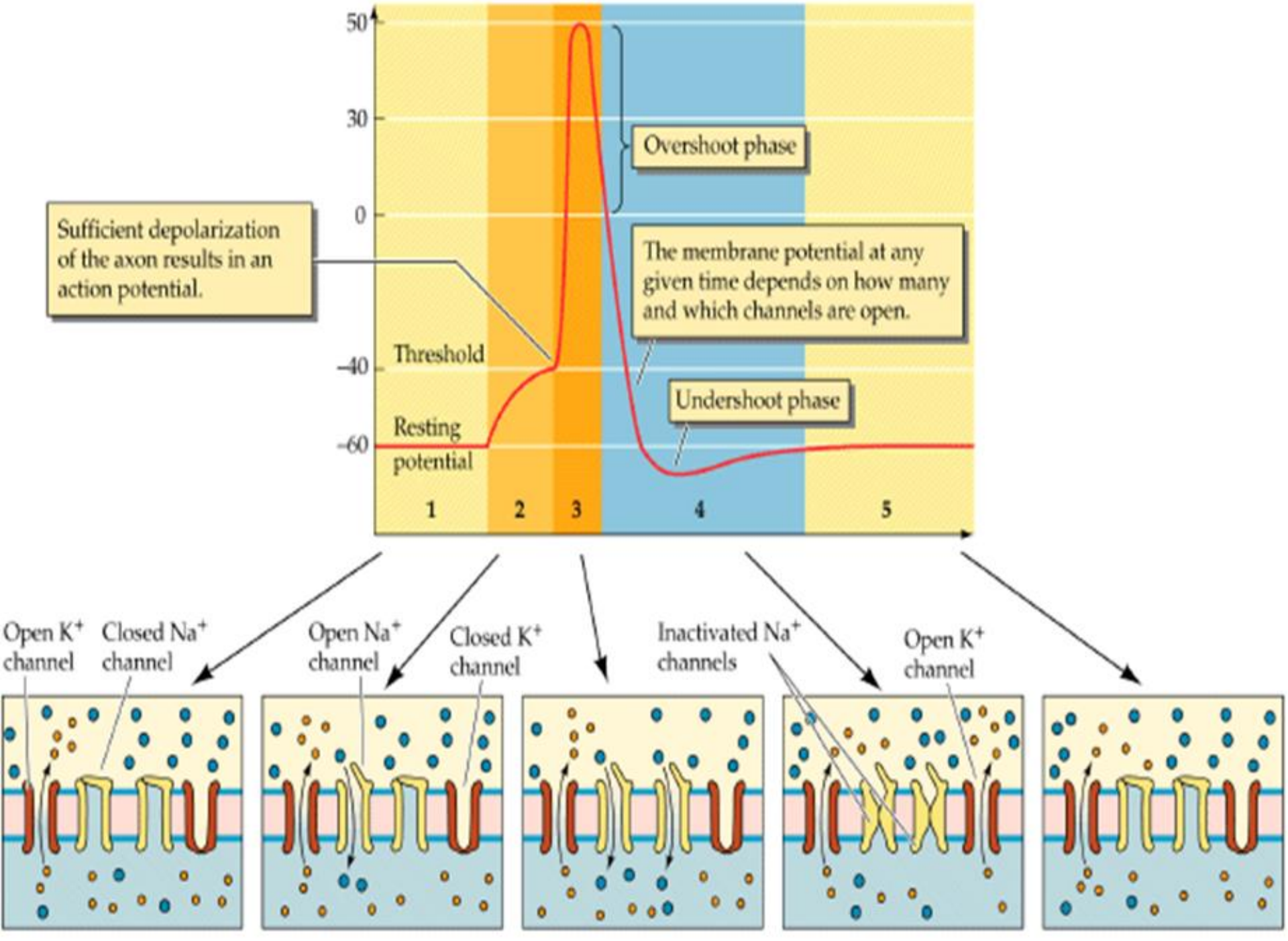
Na^+ and K^+ flow during AP

- Thus, Na^+ channels open and Na^+ flows into neuron
- After slight delay K^+ channels open and K^+ flows out of neuron
- Repolarization / Undershoot
- Refractory period
  - Absolute
  - Relative



Schematic Na^+ and K^+ flow



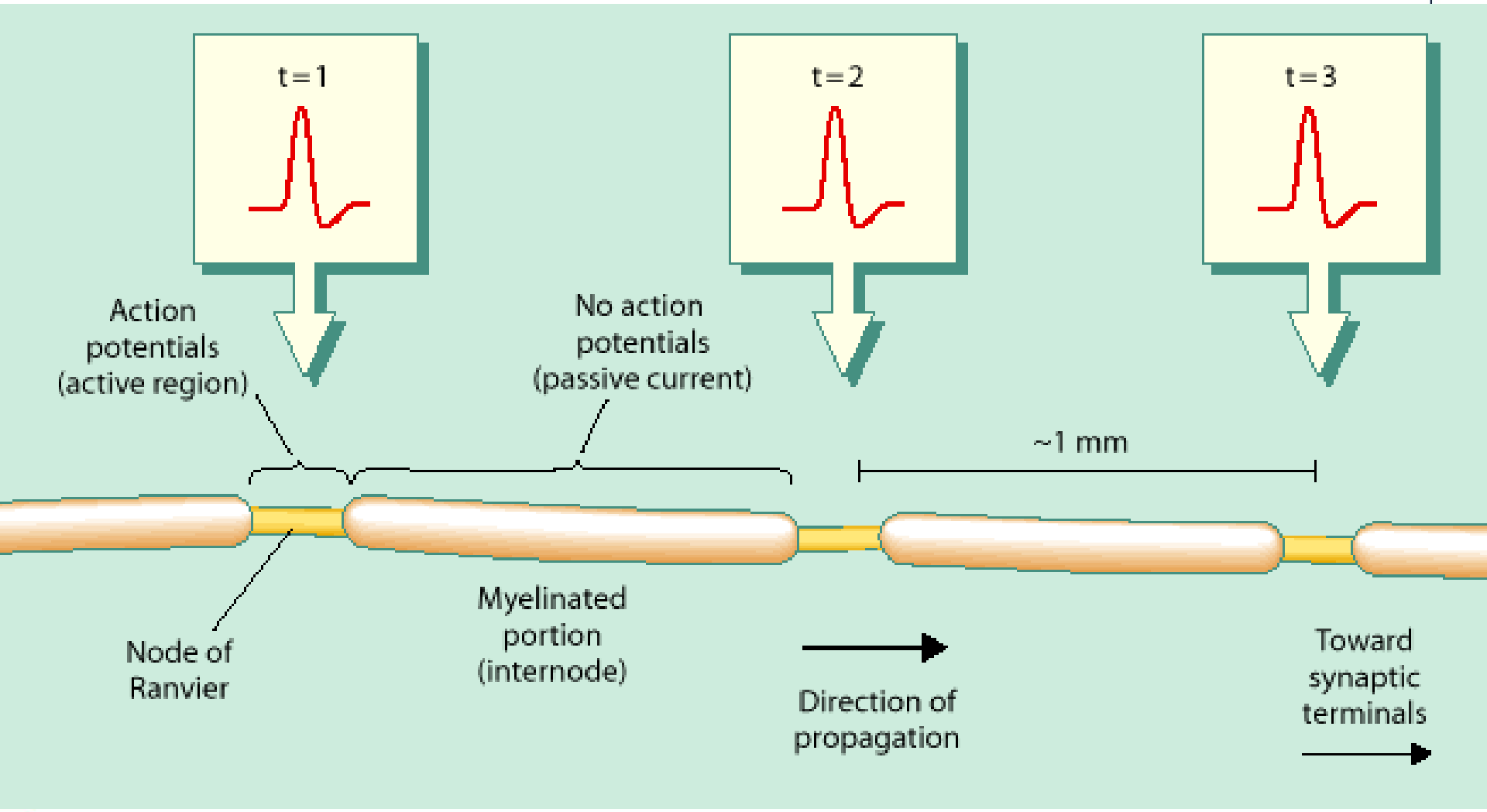

50
30
0
−40
−60
Overshoot phase
Sufficient depolarization of the axon results in an action potential.
The membrane potential at any given time depends on how many and which channels are open.
Threshold
Undershoot phase
Resting potential
1
2
3
4
5
Open K+ channel
Closed Na+ channel
Open Na+ channel
Closed K+ channel
Inactivated Na+ channels
Open K+ channel

Animation 2: Action potential

Q3: As the axon hillock depolarizes, voltage-gated Na^+ channels open and Na^+ moves … the cell causing further …

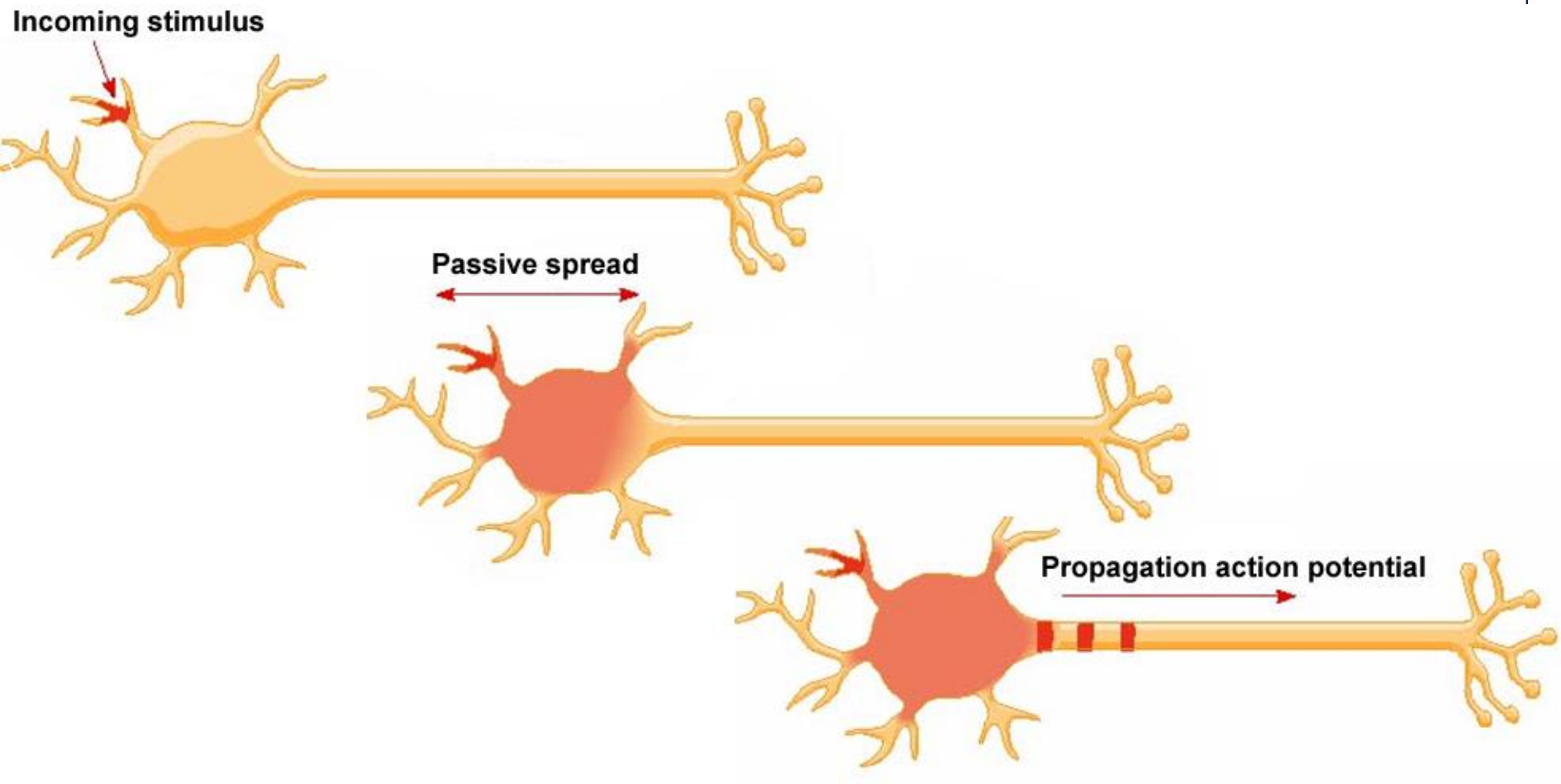
a) Out of; repolarization
b) Into; repolarization
c) Out of; depolarization
d) Into; depolarization

Propagation action potential



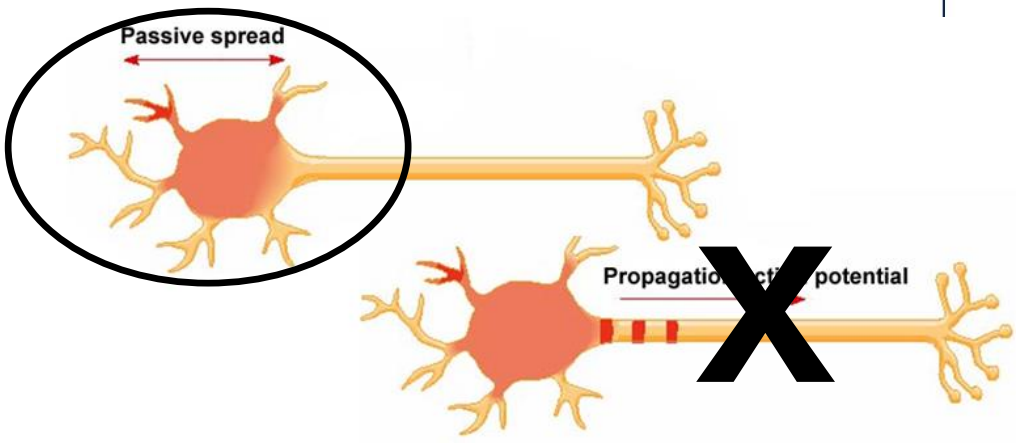
Animation 3: Propagation

Propagation continued

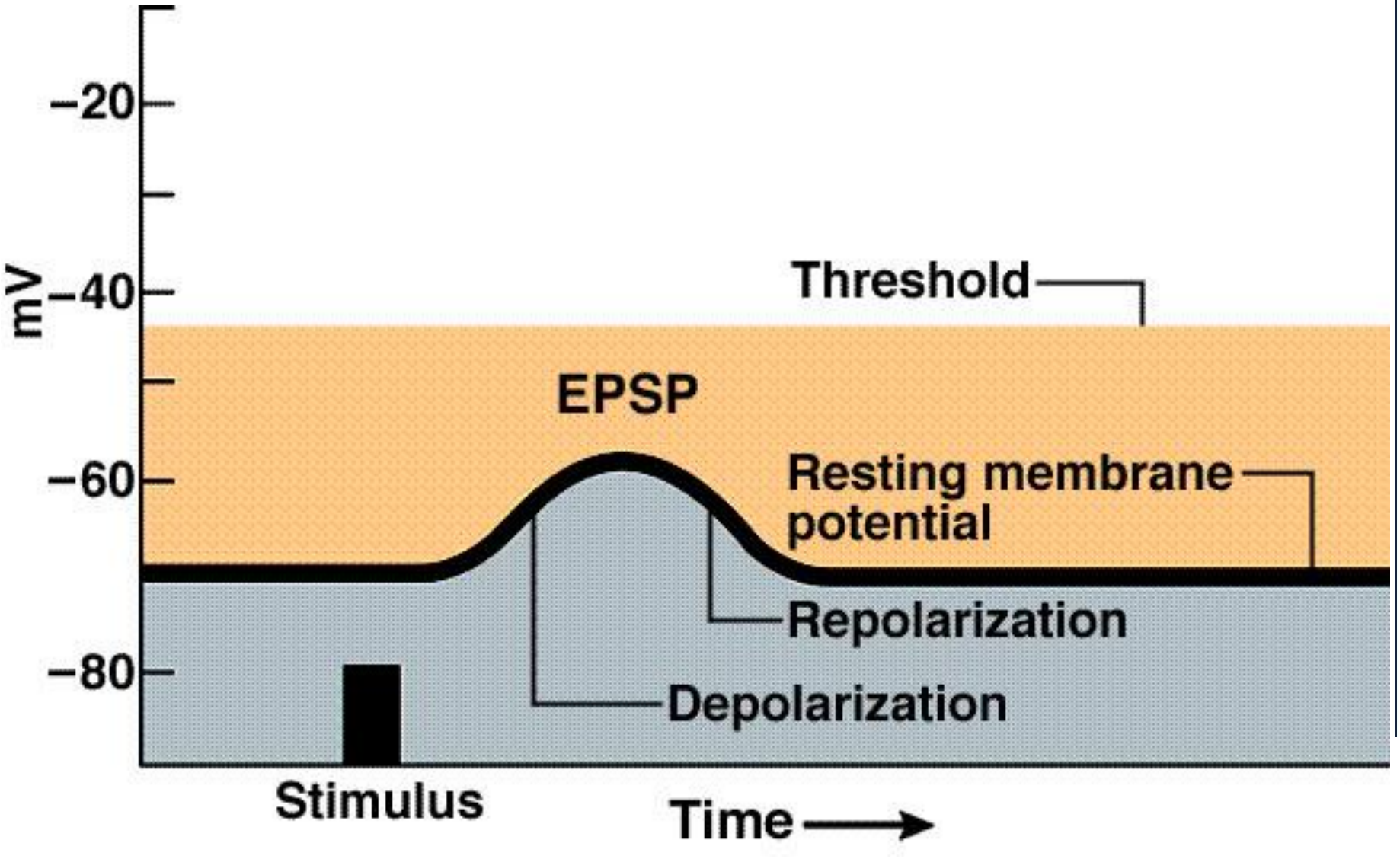


EPSP or IPSP? Graded potentials!

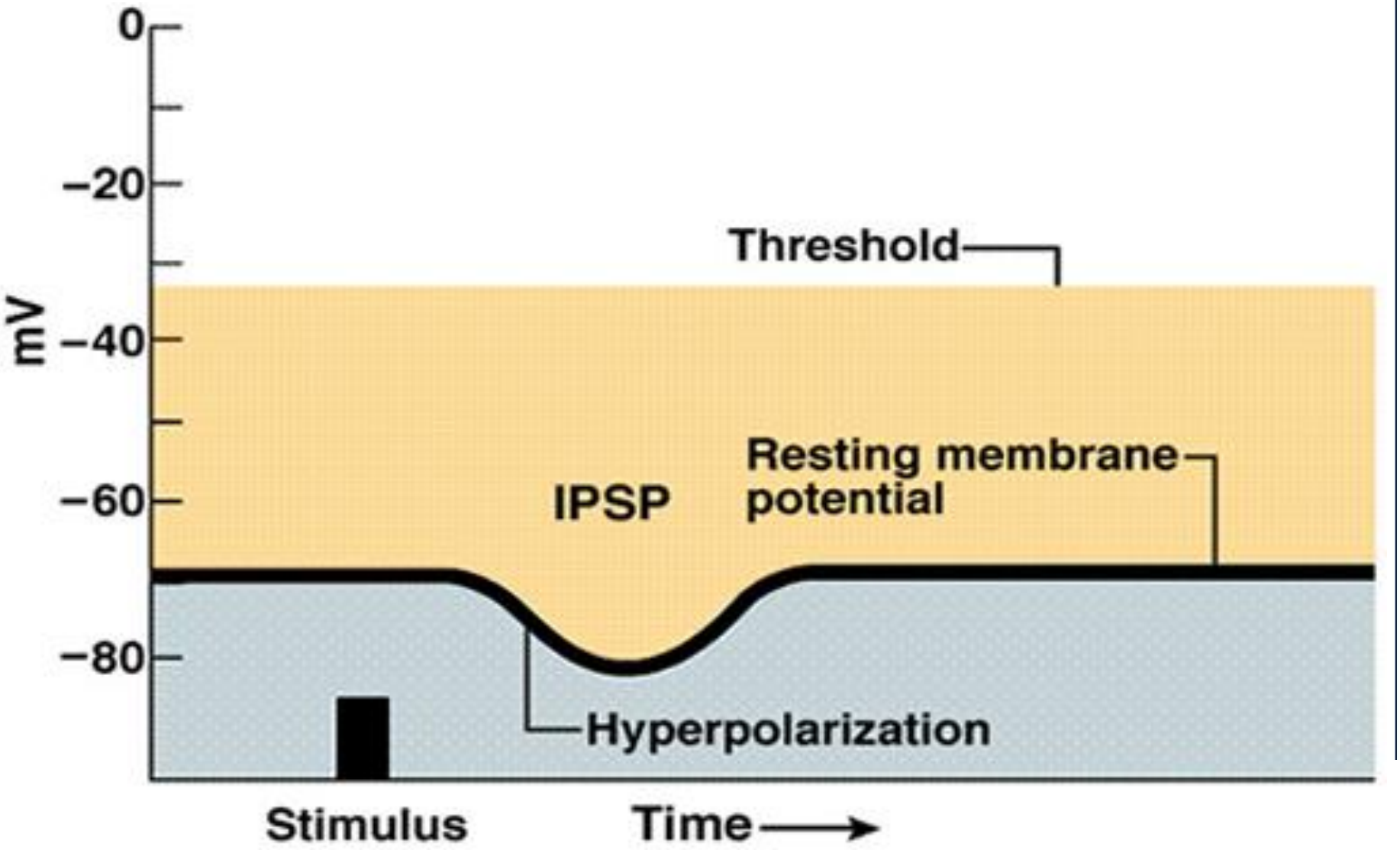
- Partial de- or hyperpolarization
- Graded
- Fast
- Decremental
- Temporal / Spatial summation



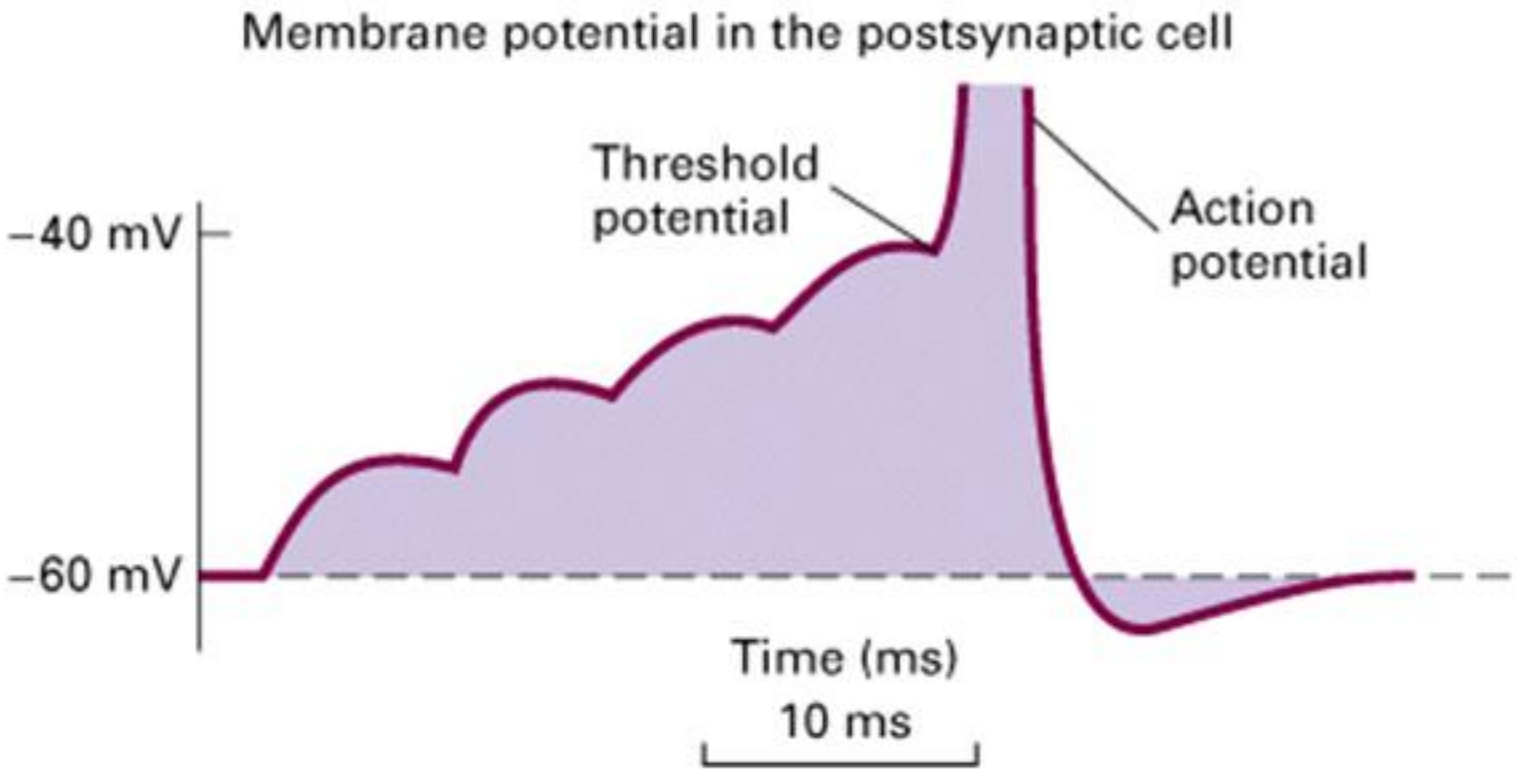
Excitatory PostSynaptic Potential



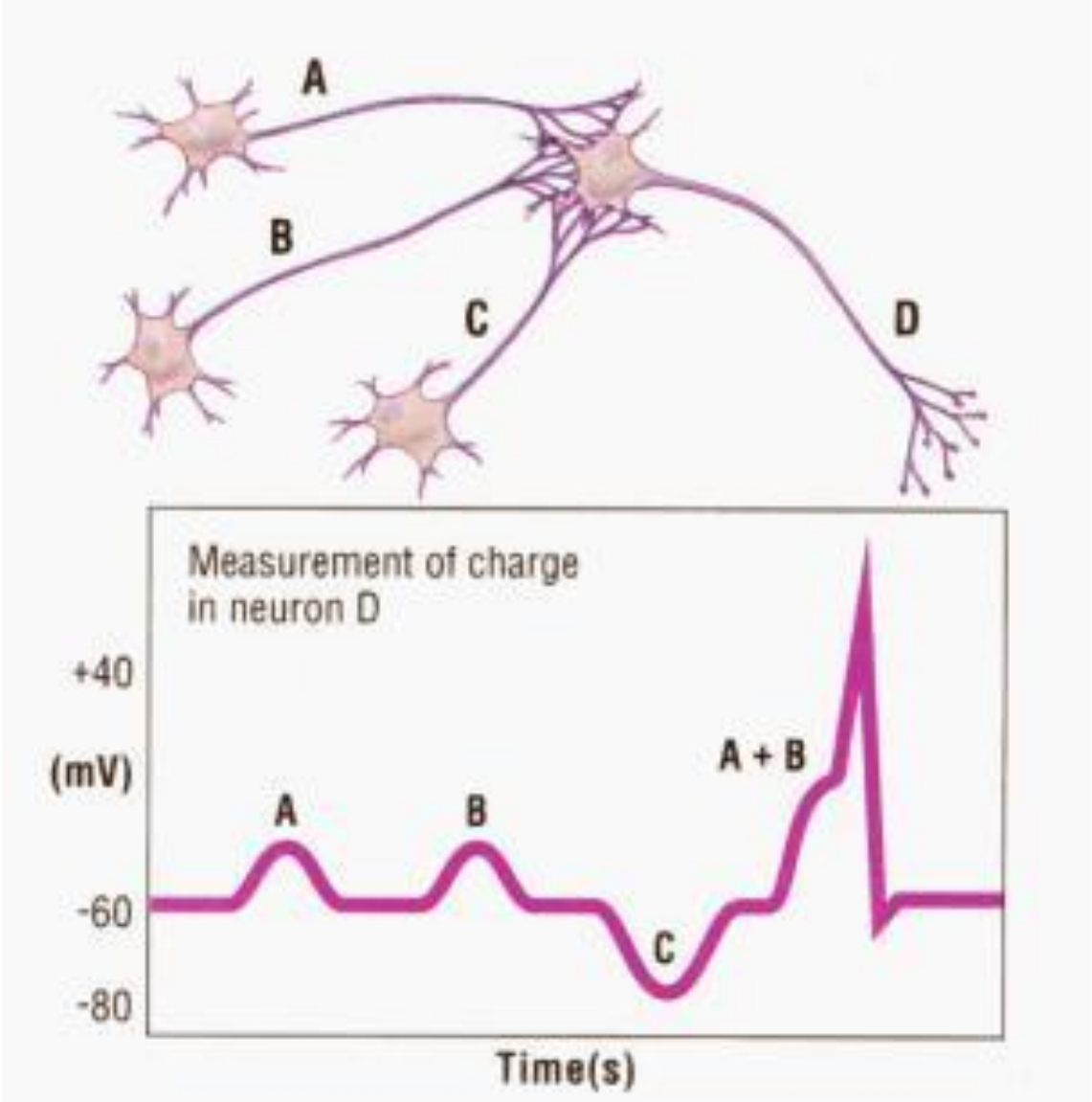
Inhibitory PostSynaptic Potential



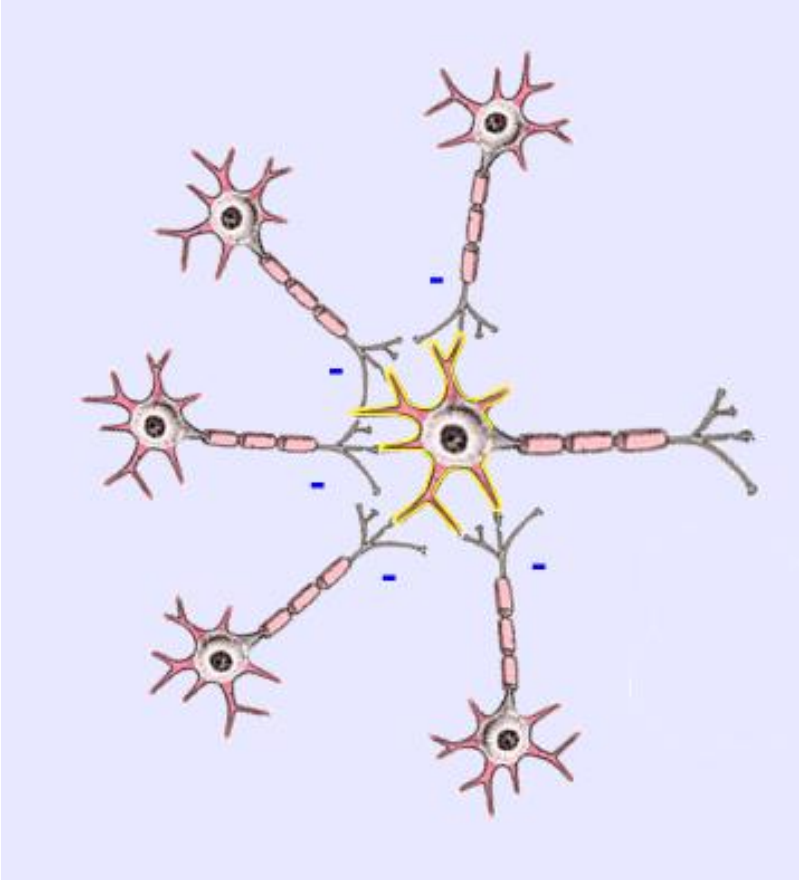
Temporal summation



Spatial summation



Summation continued



http://learntech.uwe.ac.uk/synapsesNeuro/Default.aspx?pageid=1916

Q4: Which of the following is false?

a) Refractory periods are not associated with graded potentials, but are associated with action potentials

b) Graded potentials are always hyperpolarizing, but action potentials are always depolarizing

c) Graded potentials are always decremental, whereas action potentials are always non-decremental

d) Graded potentials are proportional to the magnitude of the stimulus, whereas action potentials are 'all-or-none'

Summary action potentials

- Resting potential
- Action potential
- Na^+ / K^+ / Cl^- / A^- molecules
- Propagation
- Temporal and spatial summation

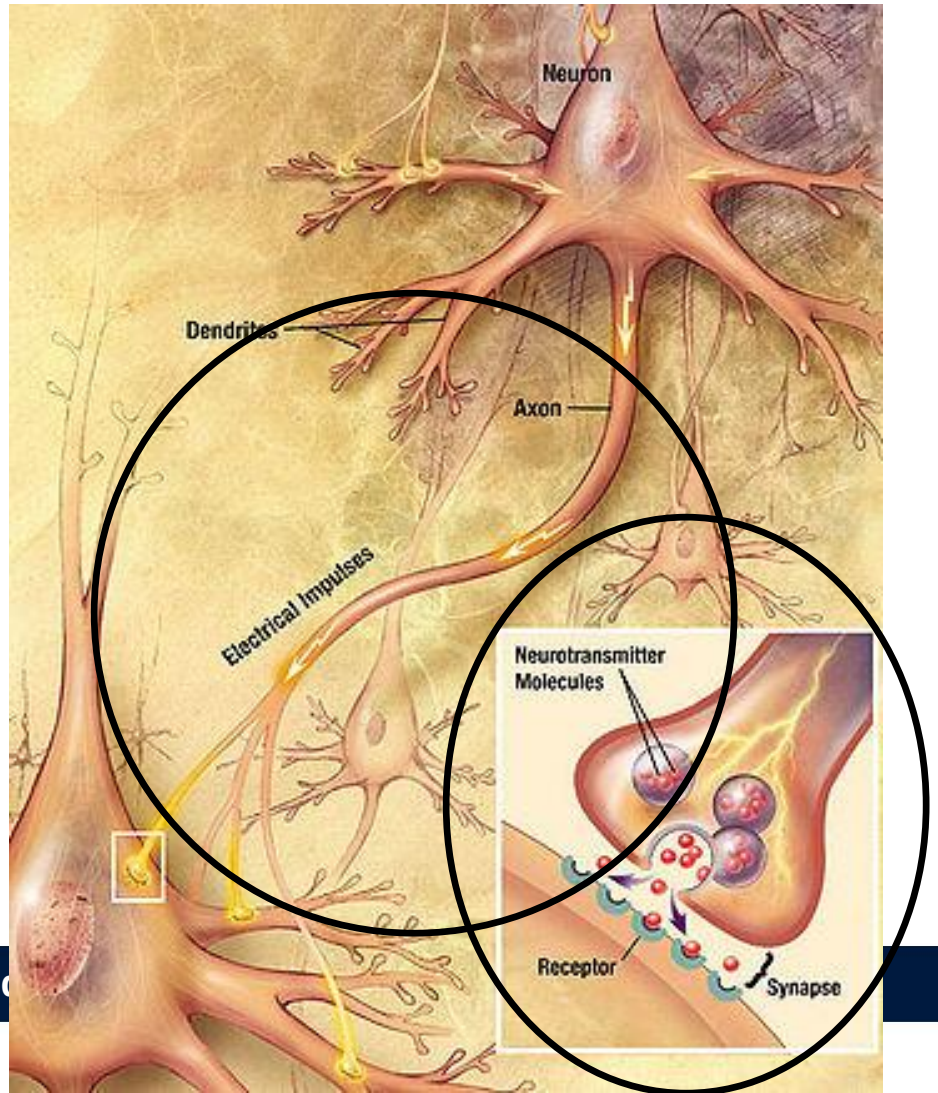
After break animation

Neurotransmission

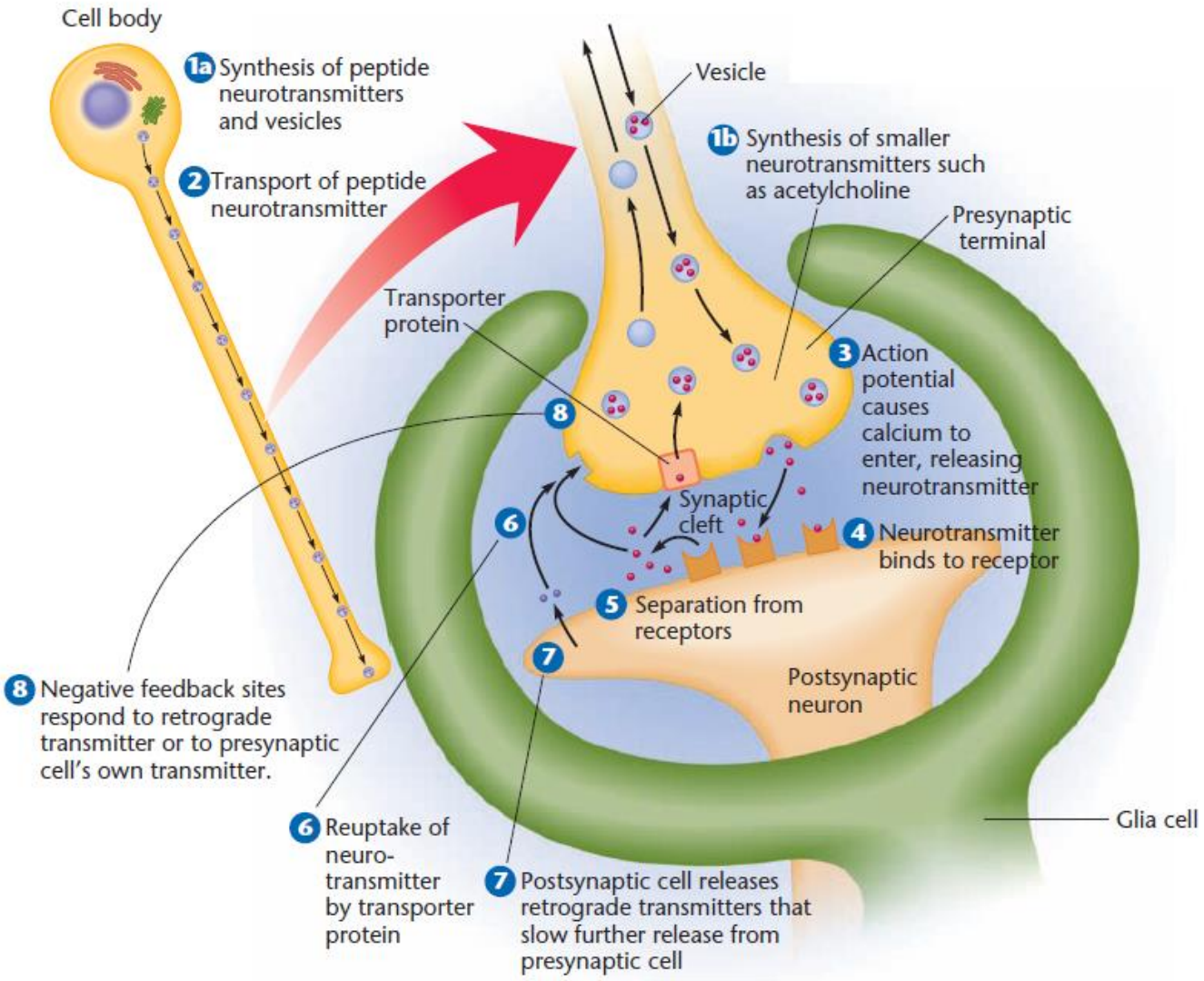
- Steps in neurotransmission
- Synapse
- Neurotransmitters
- Drugs and their effects on neurotransmission

Animation 4: Neurotransmission

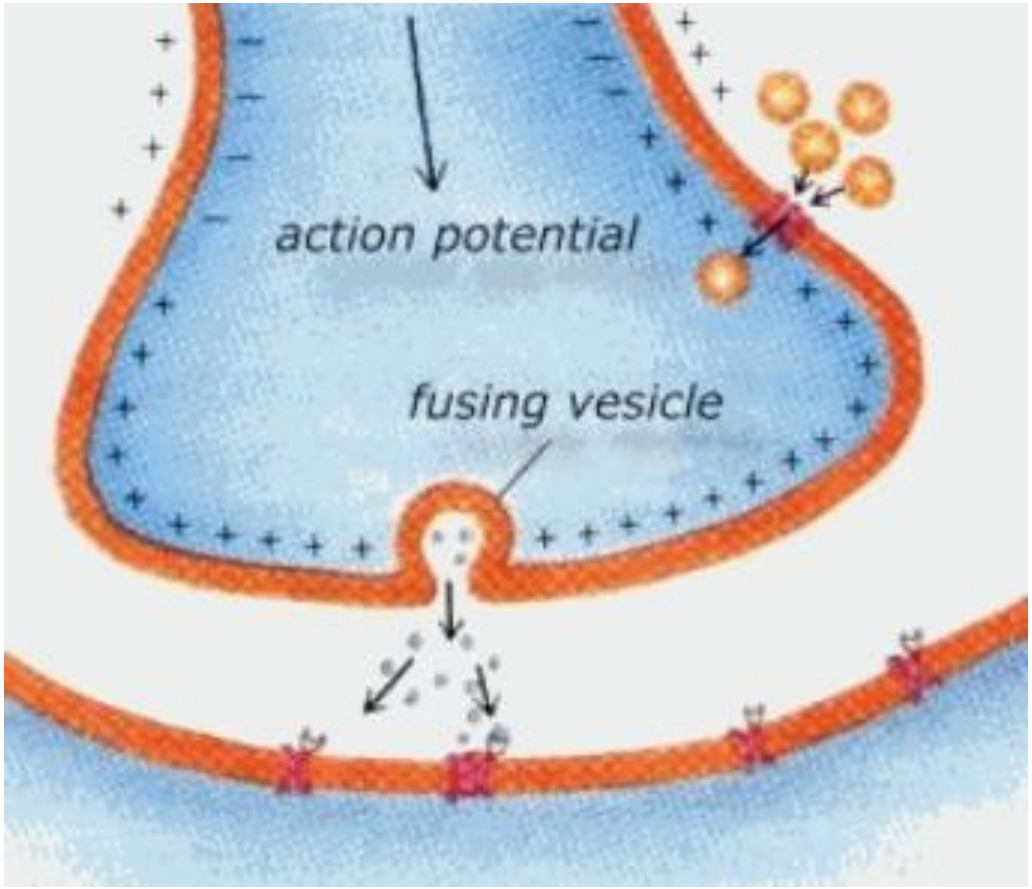
Chemically addressed nervous system



Steps in neurotransmission

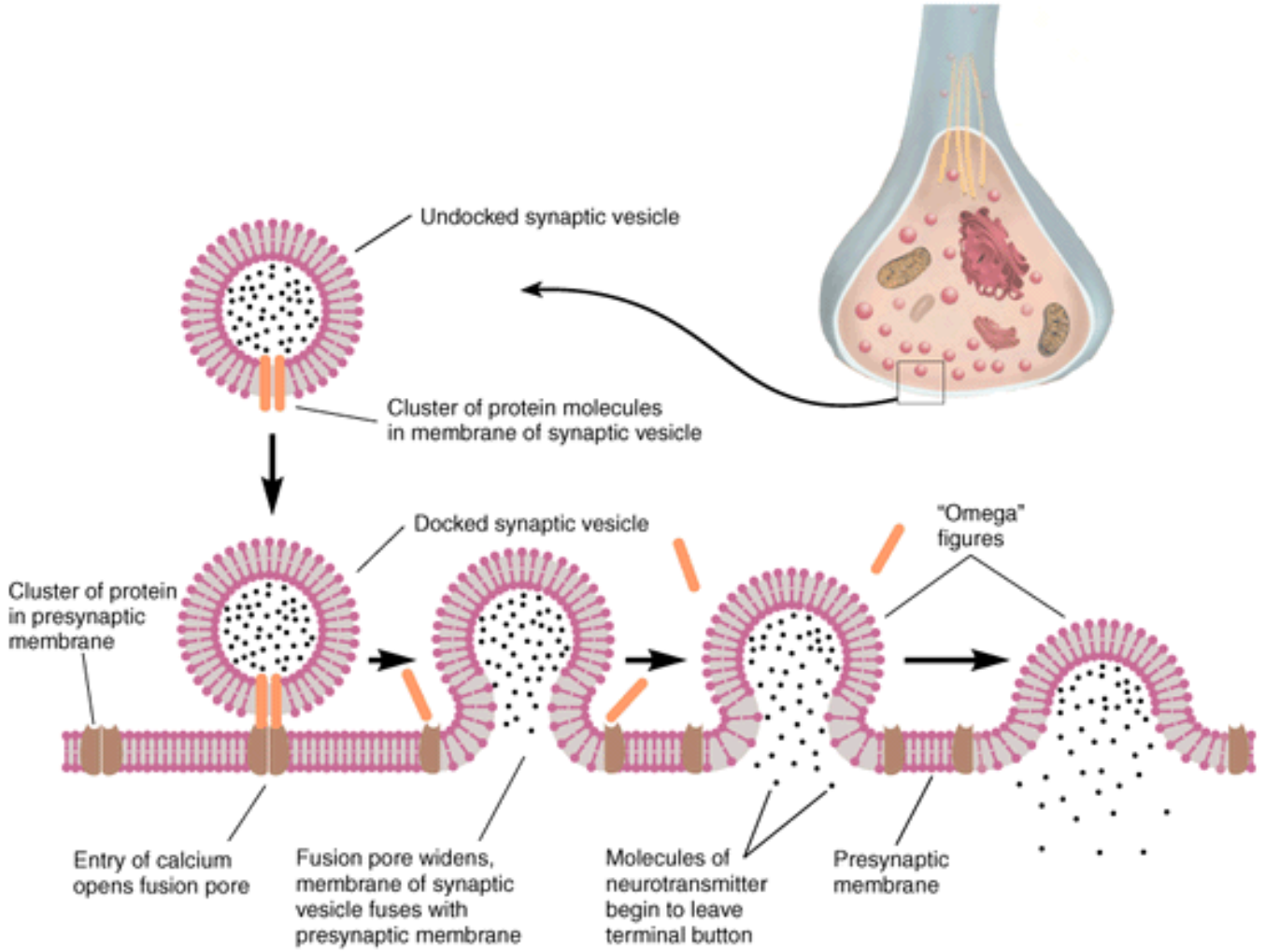


Action potential causes nt. release

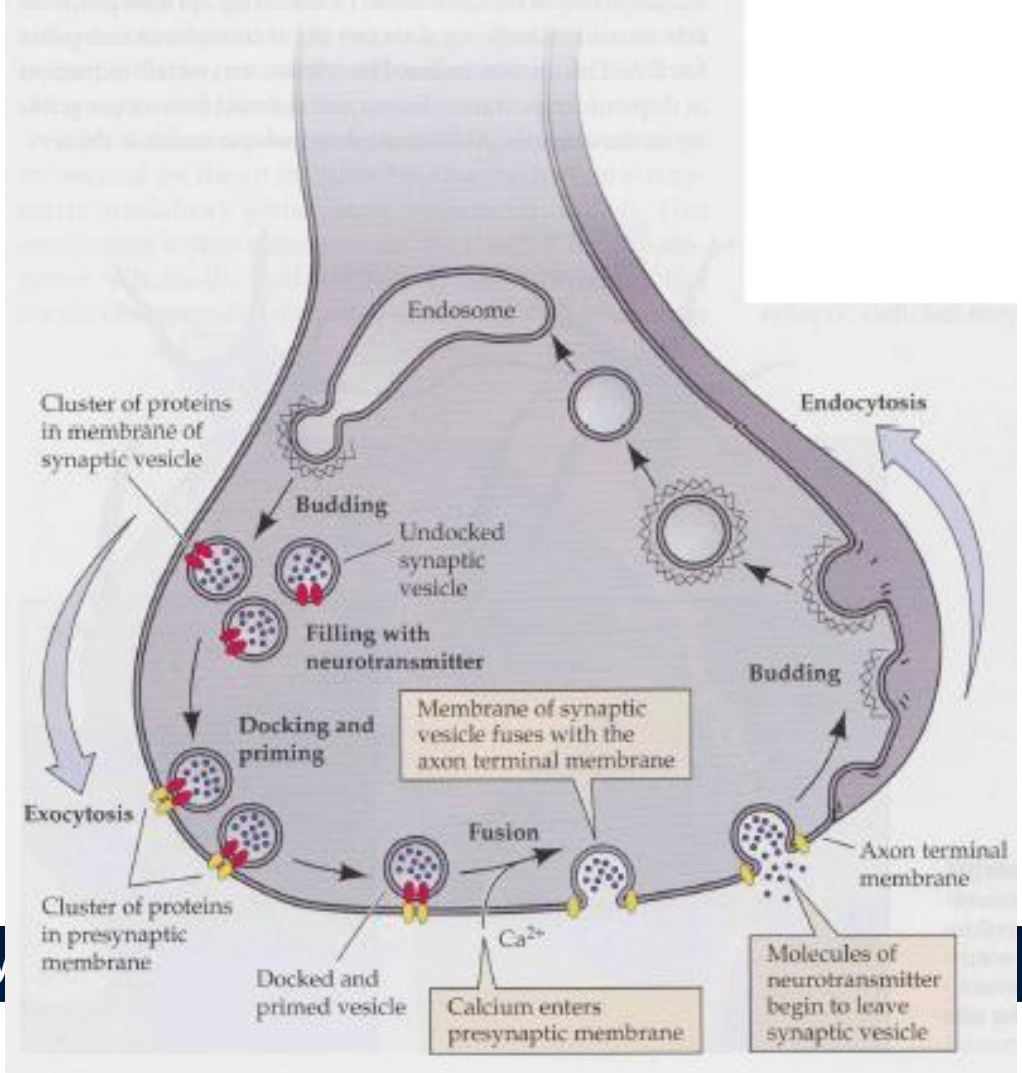


Release: vesicle function

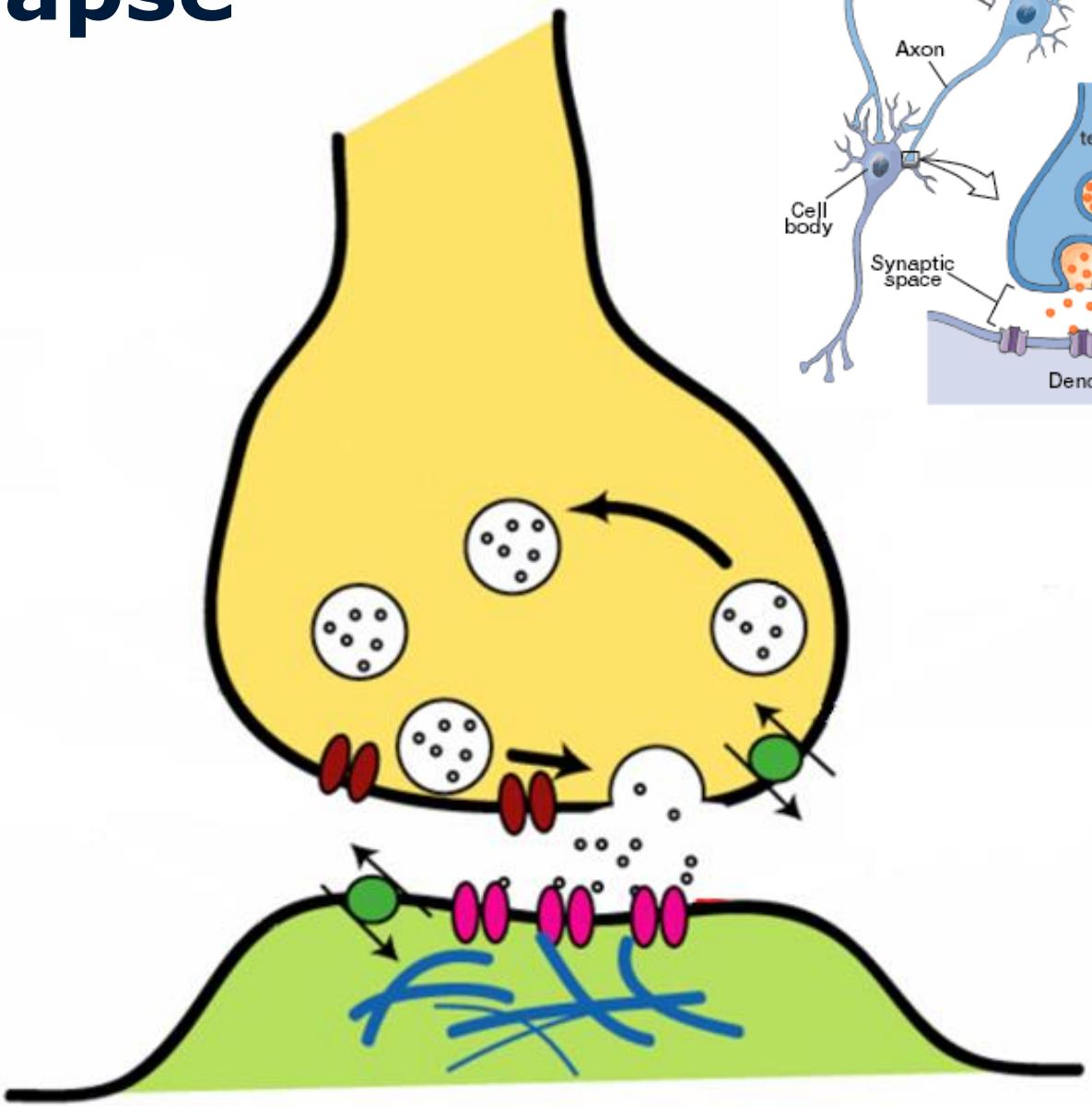
- Release of Neurotransmitter

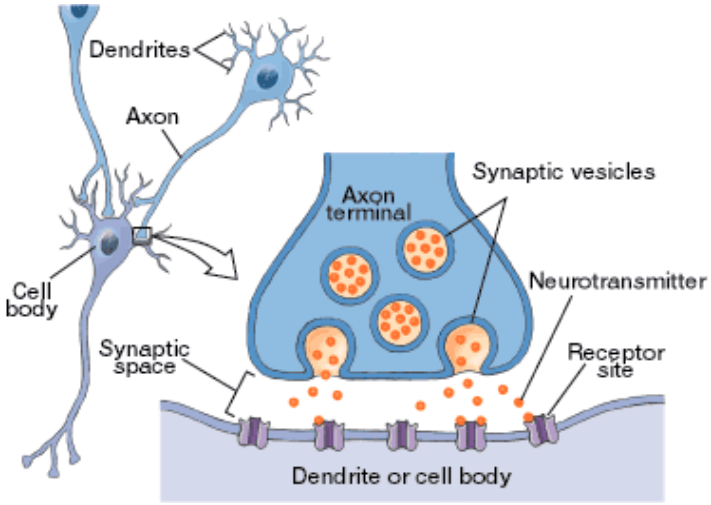


Life cycle of a vesicle

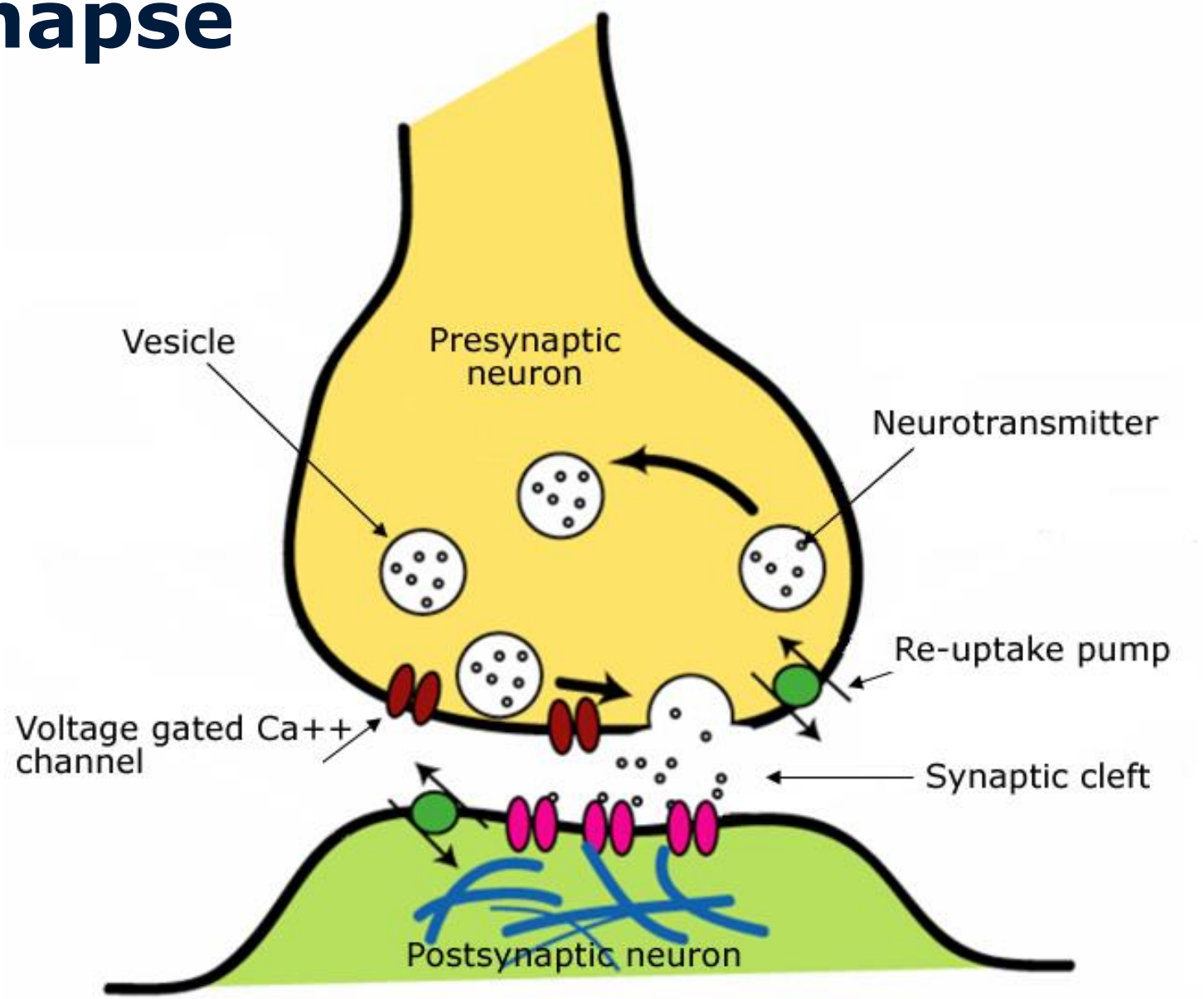


Synapse




Dendrites
Axon
Synaptic vesicles
Axon terminal
Cell body
Neurotransmitter
Synaptic space
Receptor site
Dendrite or cell body

Synapse


Vesicle
Presynaptic neuron
Neurotransmitter
Re-uptake pump
Voltage gated Ca++ channel
Synaptic cleft
Postsynaptic neuron

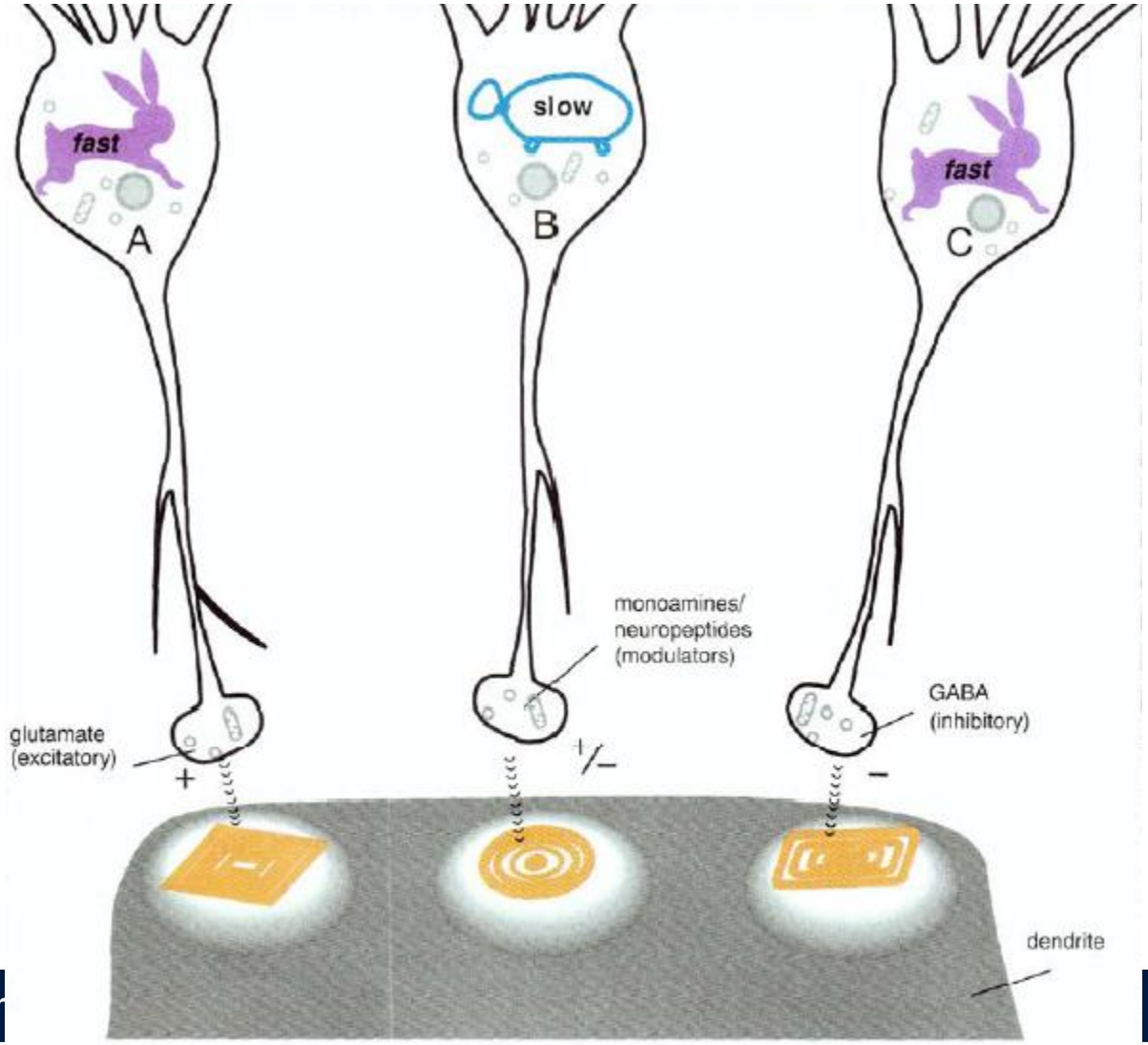
Animation 5: Neurotransmission

Types of neurotransmitters

- Acetylcholine (nicotinic, m_1 – m_5)
- Indolamines
  - Serotonin ($5\text{-}HT_1$ – $5\text{-}HT_7$)
- Catecholamines
  - Dopamine (D1 – D5)
  - Noradrenaline (α – β)
- Amino Acids
  - Glutamate NMDA, AMPA
  - GABA $GABA_A$, $GABA_B$

Animation 6: How neurons use neurotransmitters

Speed of neurotransmission

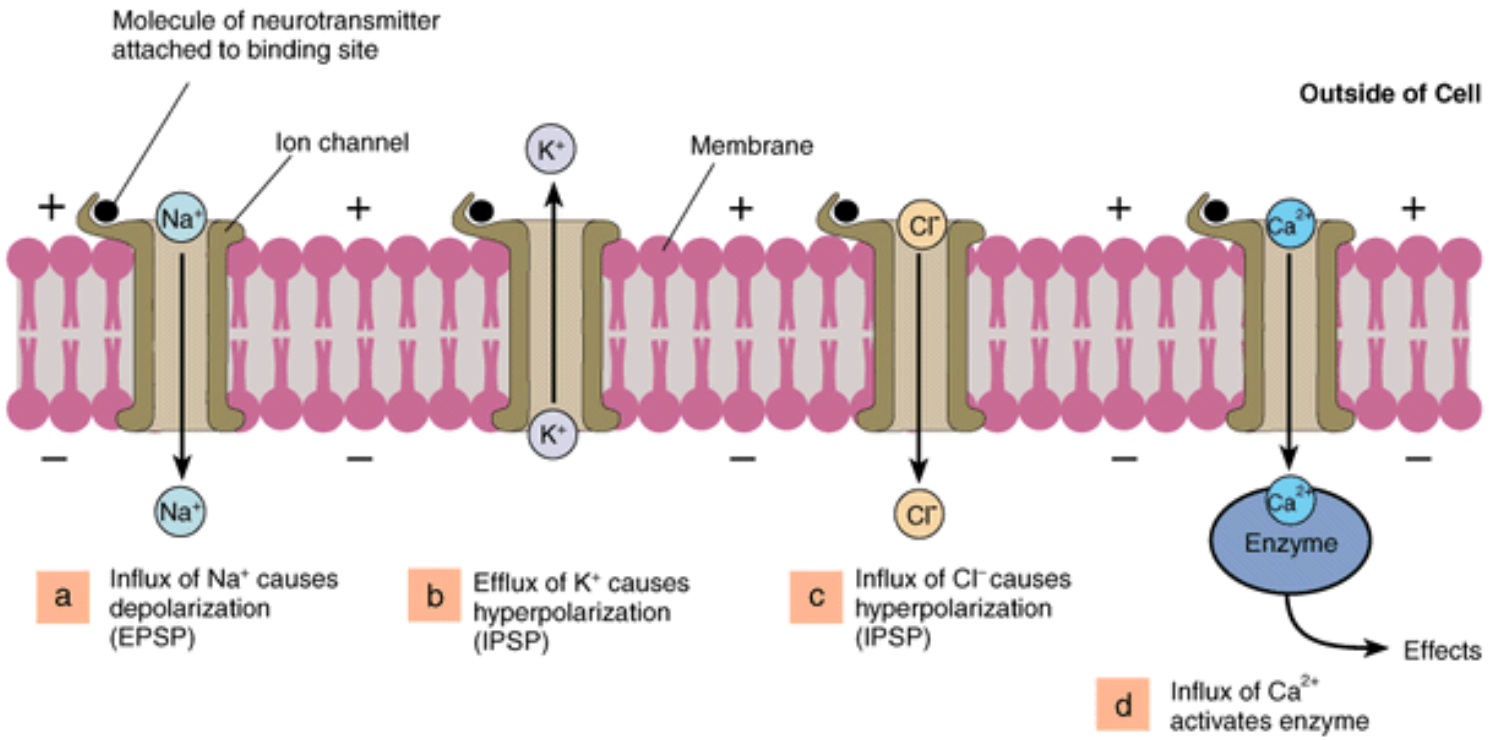


Two types of receptors

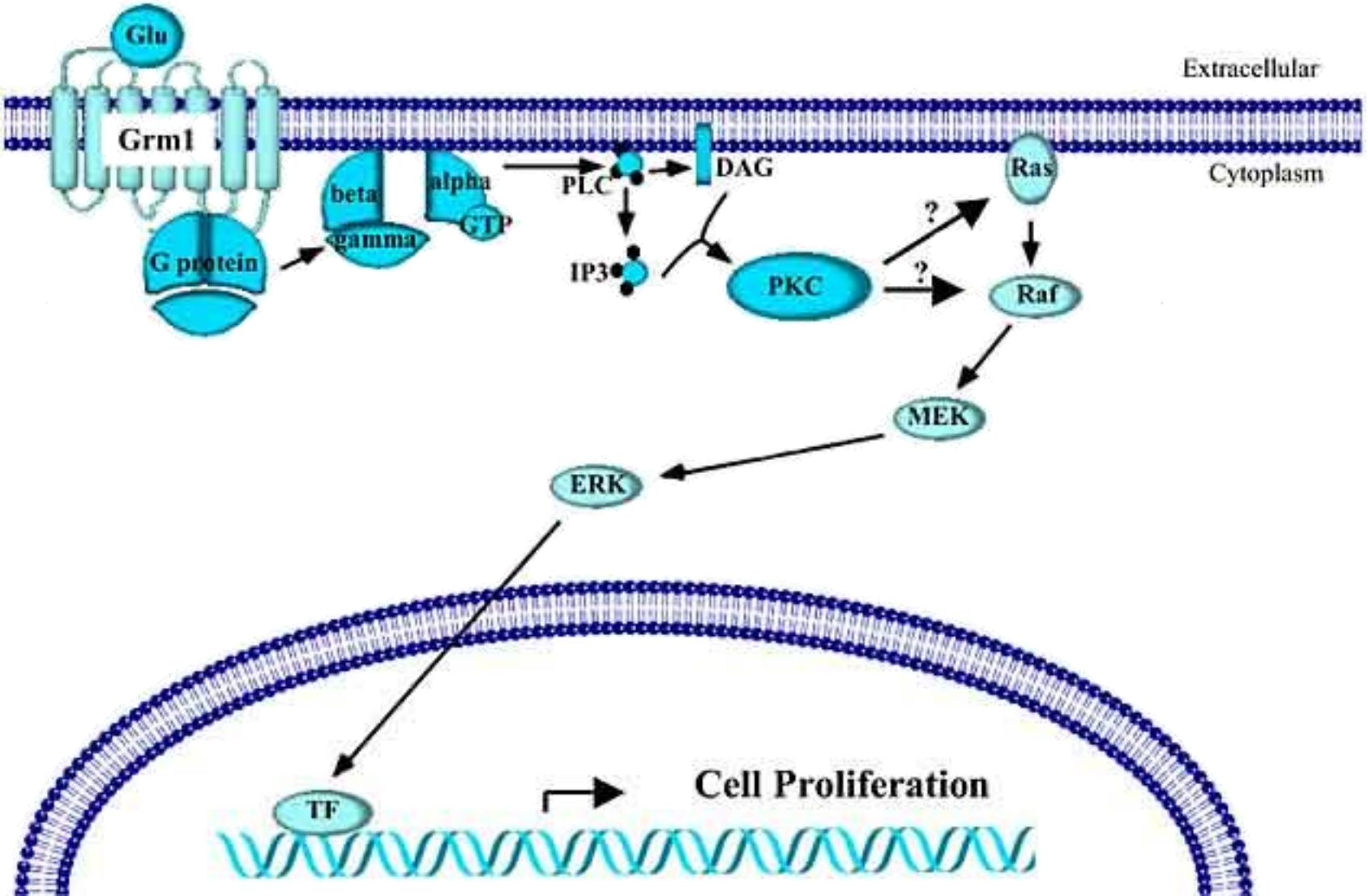
- Ionotropic: transmitter gated ion-channels
  - Direct gating
  - Fast, chemical synaptic transmission
  - Short-lasting effects
    - *EPSP (excitatory postsynaptic potential): e.g. AMPA-gated ion channels cause influx of Na^+ resulting in depolarization*
    - *IPSP (inhibitory postsynaptic potential): e.g. $GABA_A$-gated ion channels cause influx of Cl^- resulting in hyperpolarization*
- Metabotropic: G-protein coupled receptors
  - Indirect gating
  - Slow transmission
  - Long-lasting effects

Ionotropic receptors

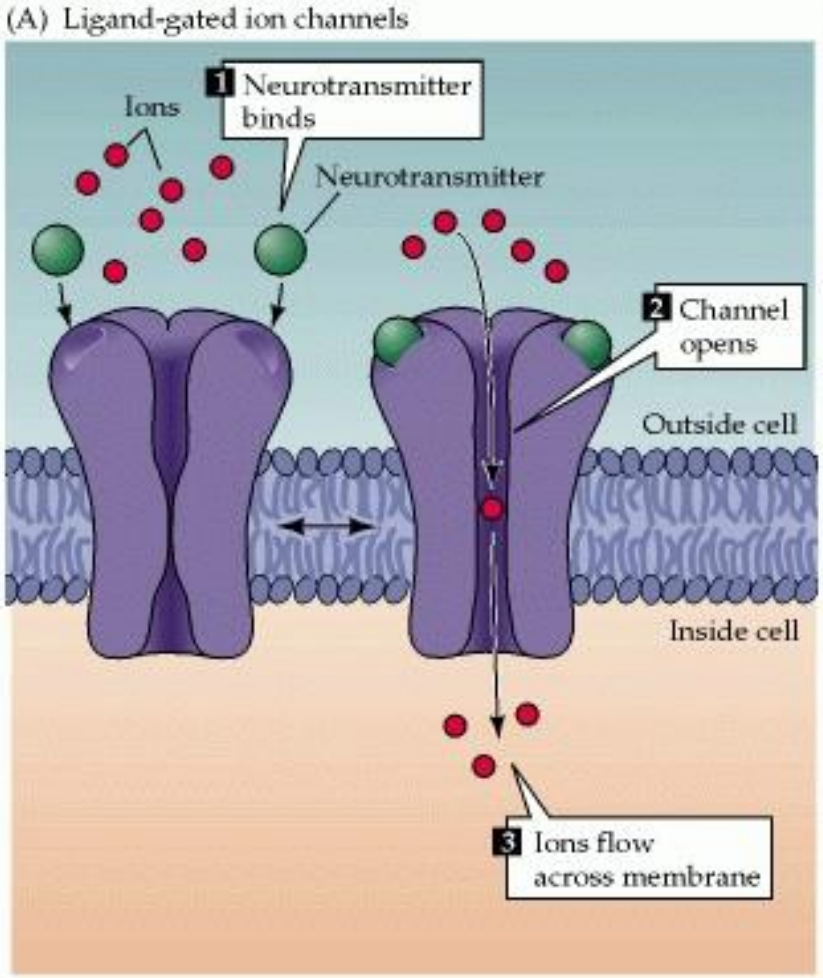
- Ionic Movements During Postsynaptic Potentials

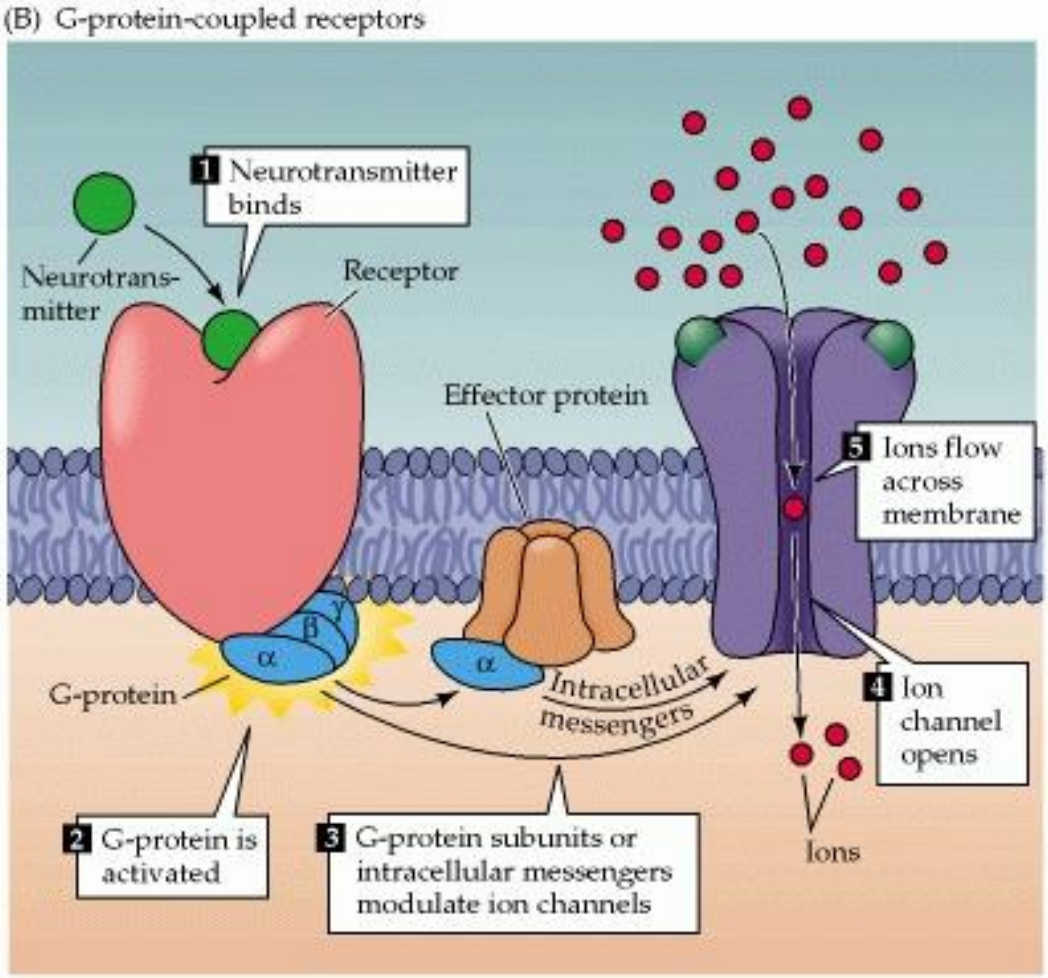


Metabotropic receptors



Ionotropic vs. metabotropic



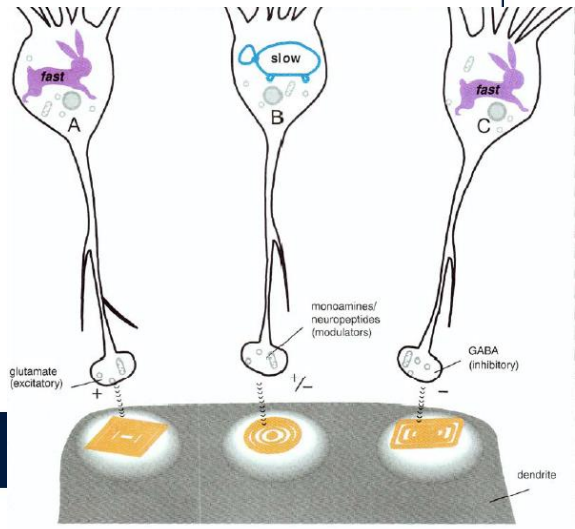


Glutamate and GABA
Our main nt. in the brain!

- Glutamate produces EPSPs
  - Thus excitatory
  - Mainly interacts with ionotropic NMDA or AMPA receptors
- GABA produces IPSPs
  - Thus inhibitory
  - Partly ionotropic (GABAa), partly metabotropic (GABAb)

Neuromodulators

- Alter the action of systems of neurons that transmit information using either glutamate or GABA
- The other neurotransmitters
  - ACh
  - 5-HT
  - DA
  - NE
- Mainly metabotropic processes



Q5: Which ONE of the following neurotransmitters would you expect to find in the synapse during fast inhibitory synaptic transmission?

a) GABA
b) Acetylcholine
c) Noradrenaline
d) Glutamate

Animation 7: Memorize the neurotransmitters!

Q6: If a neurotransmitter binds to a receptor on the target cell and produces depolarizations, the neurotransmitter...

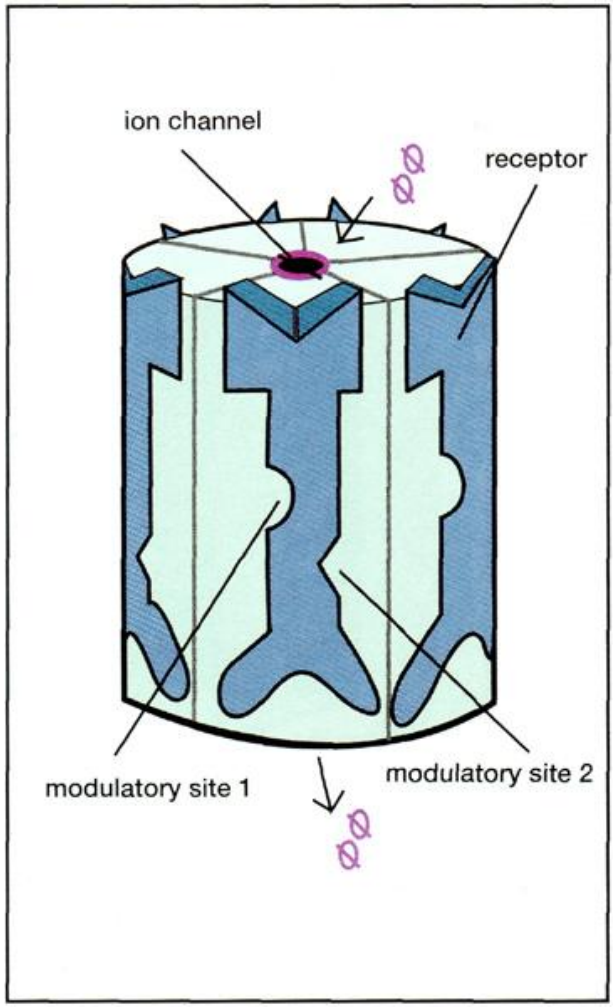
a) Was probably stimulating the flow of K^+ ions out of the cell
b) Produced an excitatory postsynaptic potential
c) Produced an inhibitory postsynaptic potential
d) Was probably stimulating the flow of Cl^- ions into the cell

'Drugs' and their interaction with receptor

- Drug mimics actions of neurotransmitter at same site
- It binds to nearby site and facilitates neurotransmitter binding

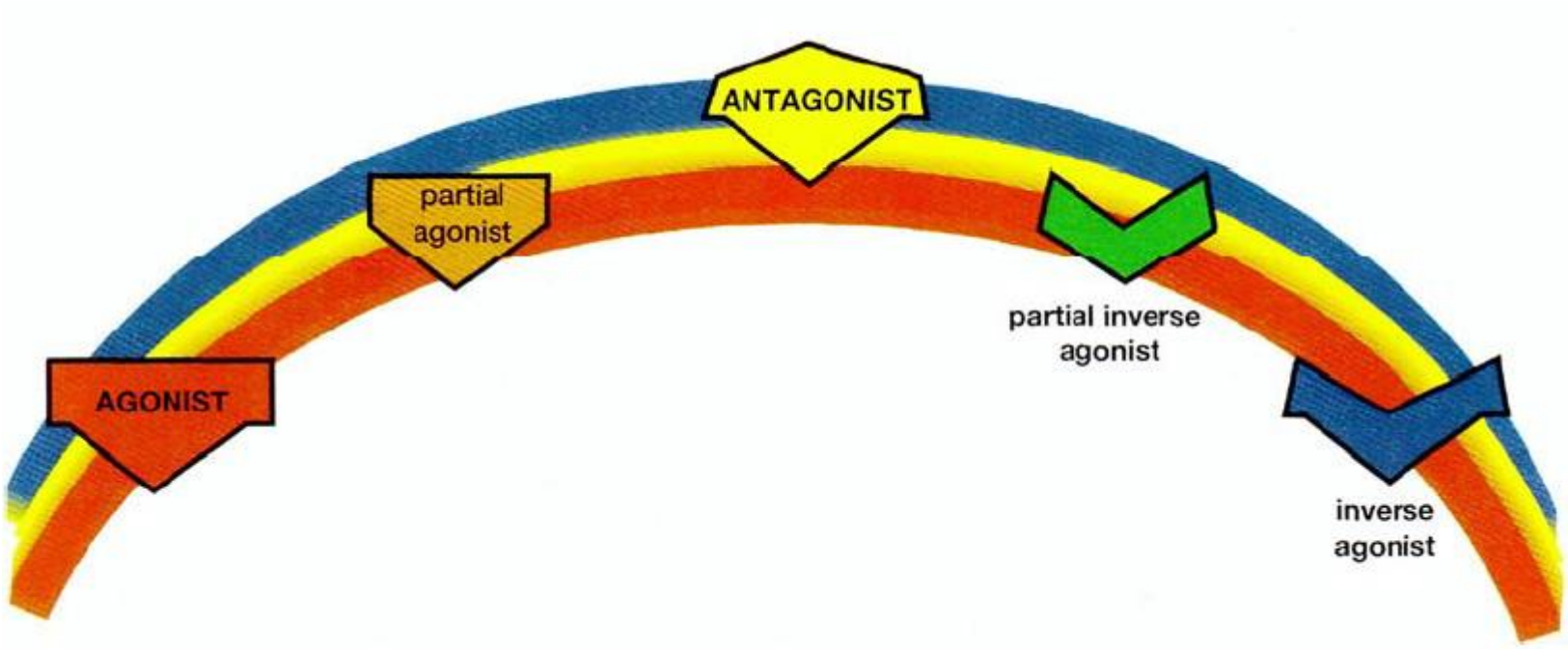
Drug-receptor interaction continued

SUPERFAMILY 1

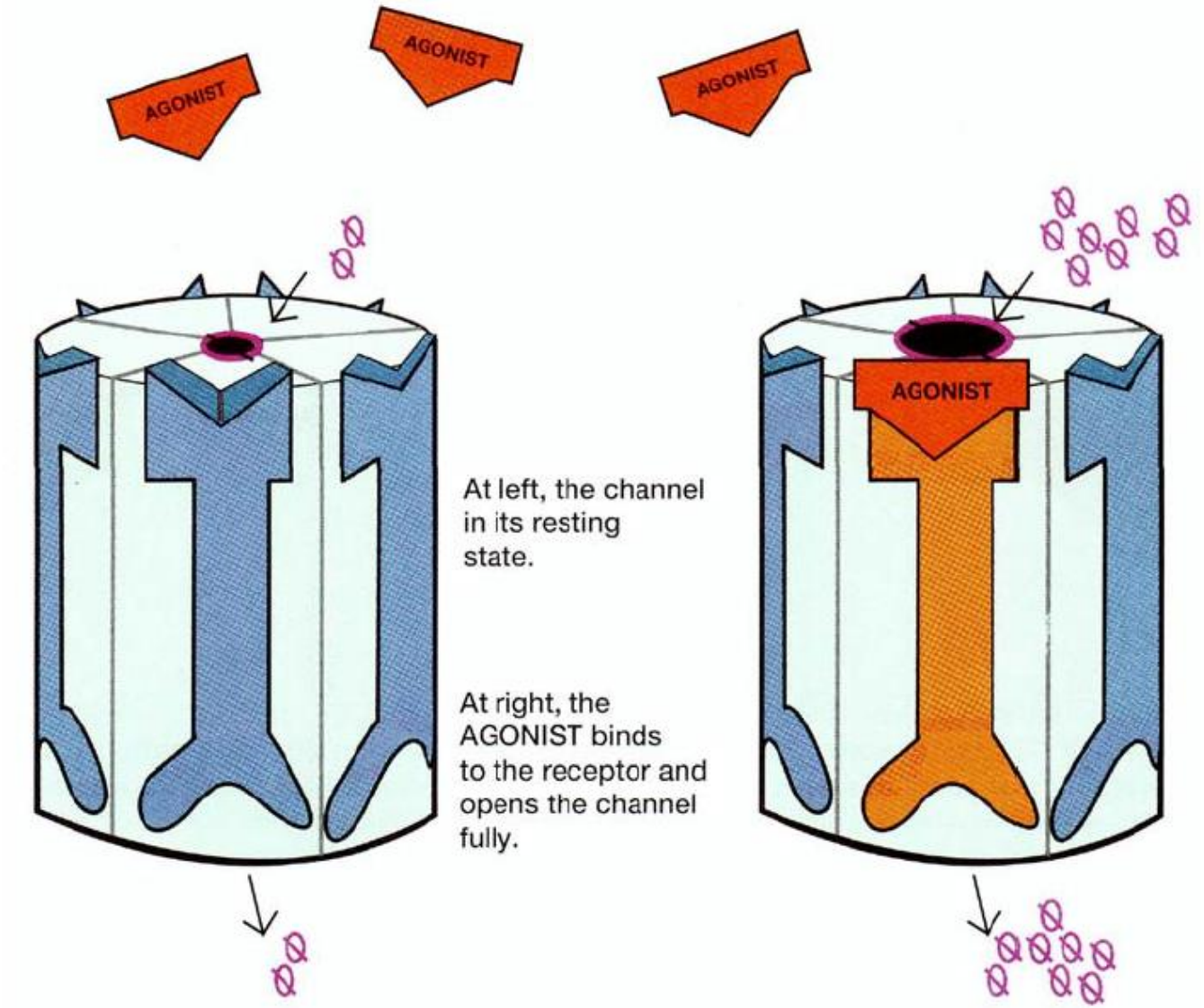


SUPERFAMILY 2; Channel in resting state

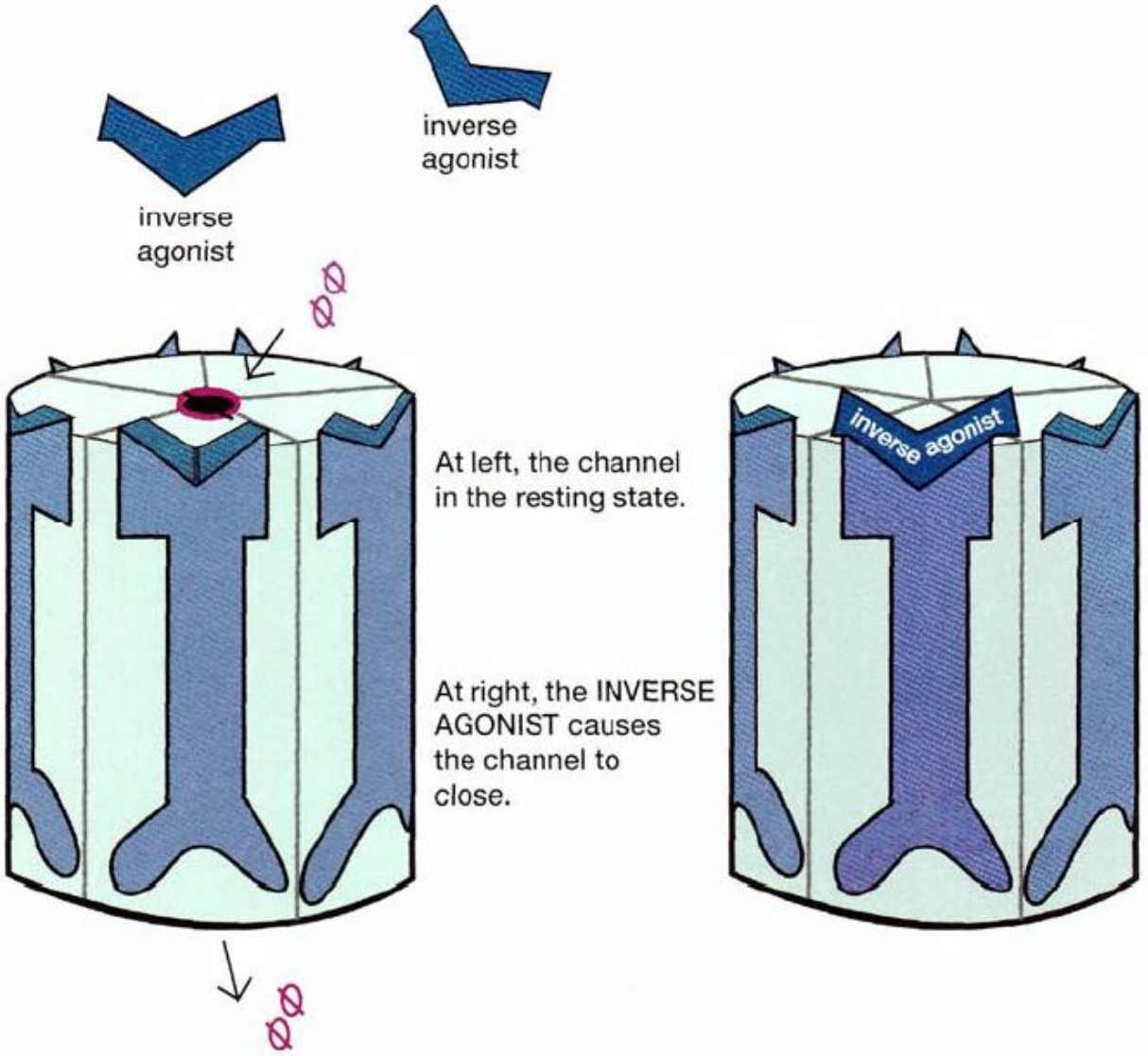
Drugs agonist spectrum



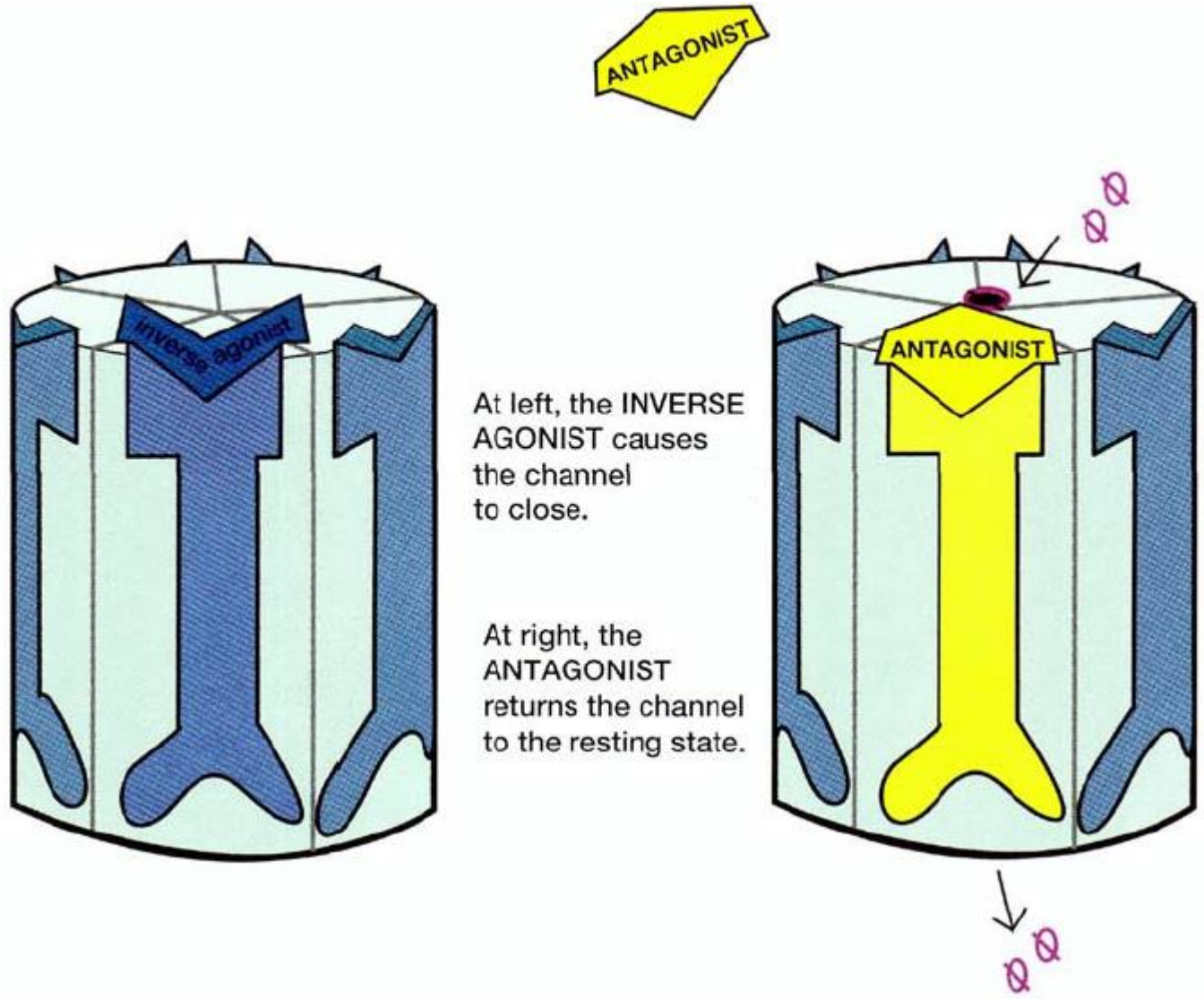
Agonist


AGONIST
AGONIST
AGONIST
AGONIST
At left, the channel in its resting state.
At right, the AGONIST binds to the receptor and opens the channel fully.

Inverse agonist



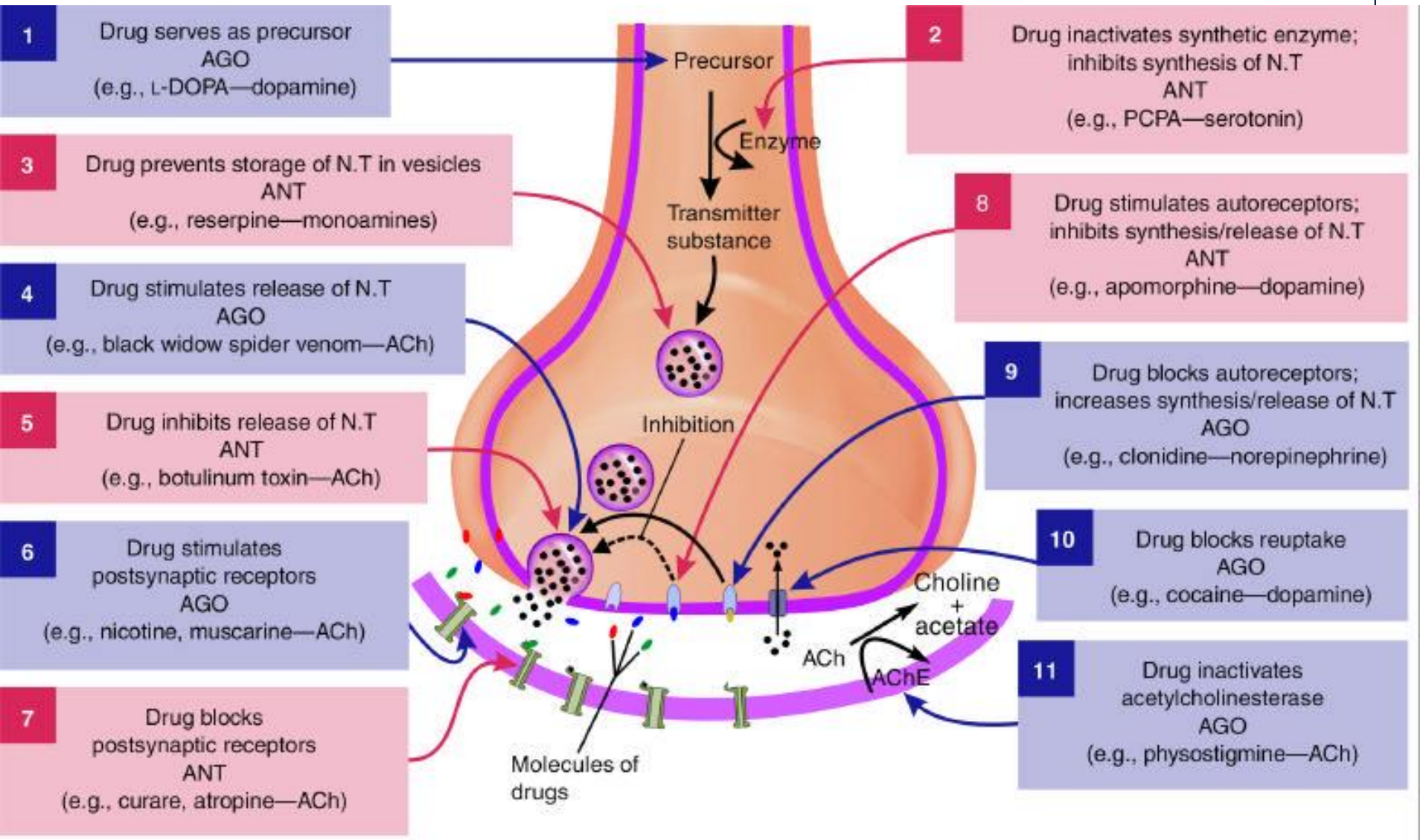
Antagonist


ANTAGONIST
inverse agonist
ANTAGONIST
At left, the INVERSE AGONIST causes the channel to close.
At right, the ANTAGONIST returns the channel to the resting state.

Q7: Which of the following actions is NOT used to inhibit the stimulatory effects of monoamines released from presynaptic vesicles?

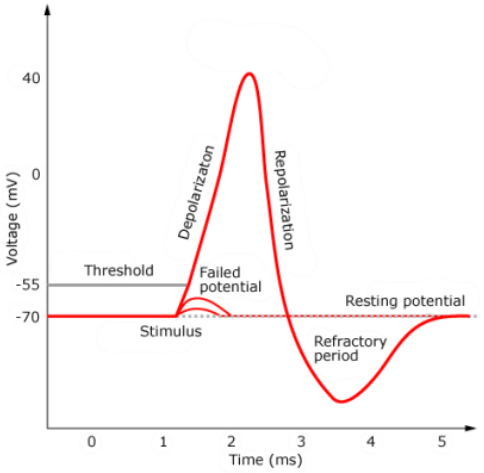
a) Re-uptake into the presynaptic neuron ending
b) Enzyme degradation(breakdown) by monoamine oxidase enzymes
c) Blockade of the receptor and inhibition by specific receptor antagonists

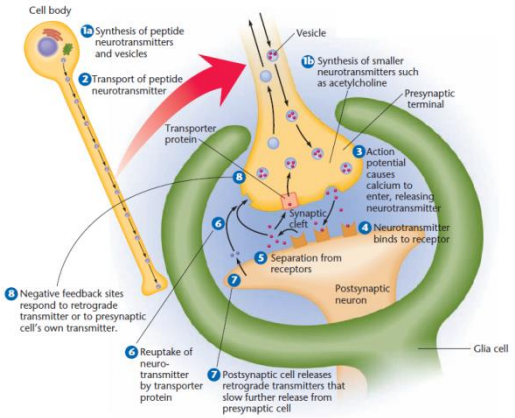
Drugs affect various stages nt.



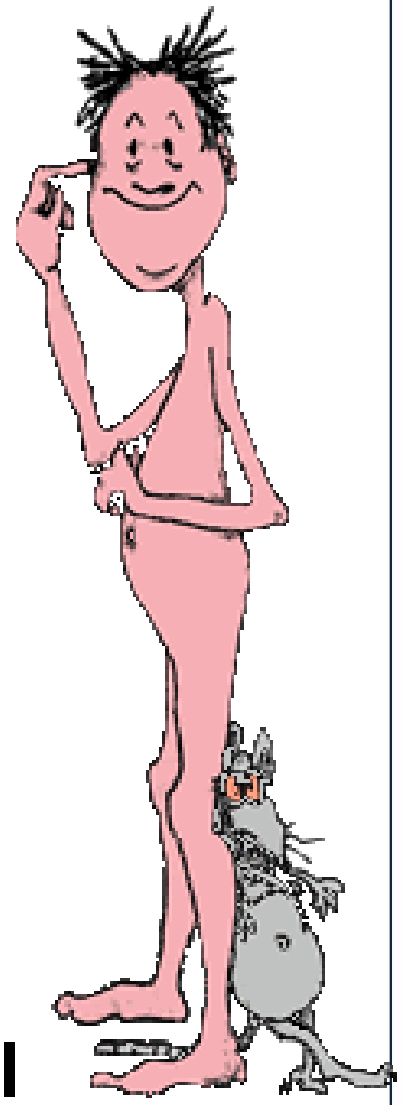
General summary

- Action potentials
  - Resting potentials and action potentials
  - Propagation and summation
- Neurotransmission
  - Steps in neurotransmission
  - Synapses and receptors
  - Drugs affect neurotransmission





Questions?



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