Medcelična signalizacija - 2

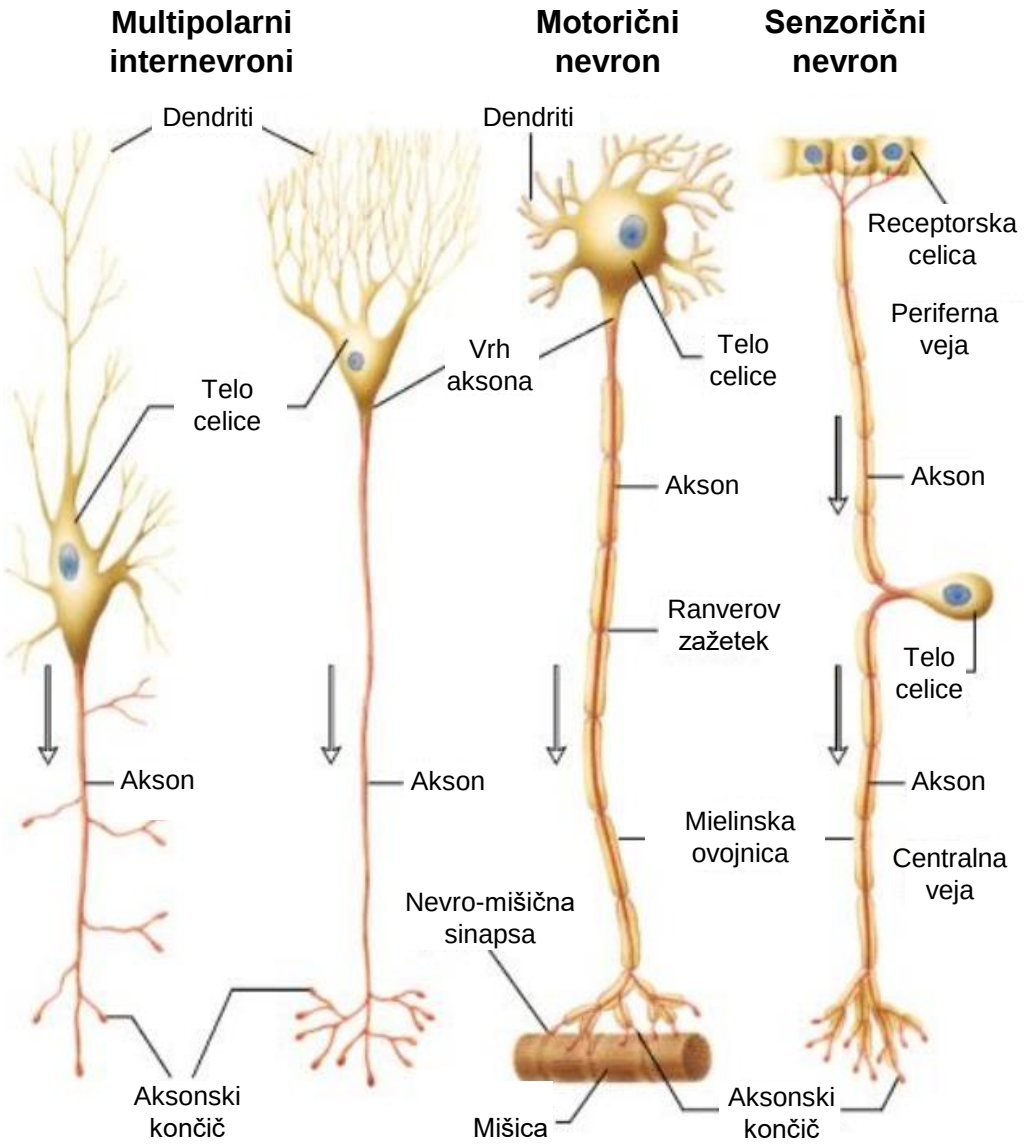
- Sprejem, prevajanje in prenos električnega signala.

- Ukrivljanje membran.

Lodish: Molecular cell biology, W.H. Freeman & Co., NY.
Alberts: Molecular Biology of the Cell, Garland Science, NY.

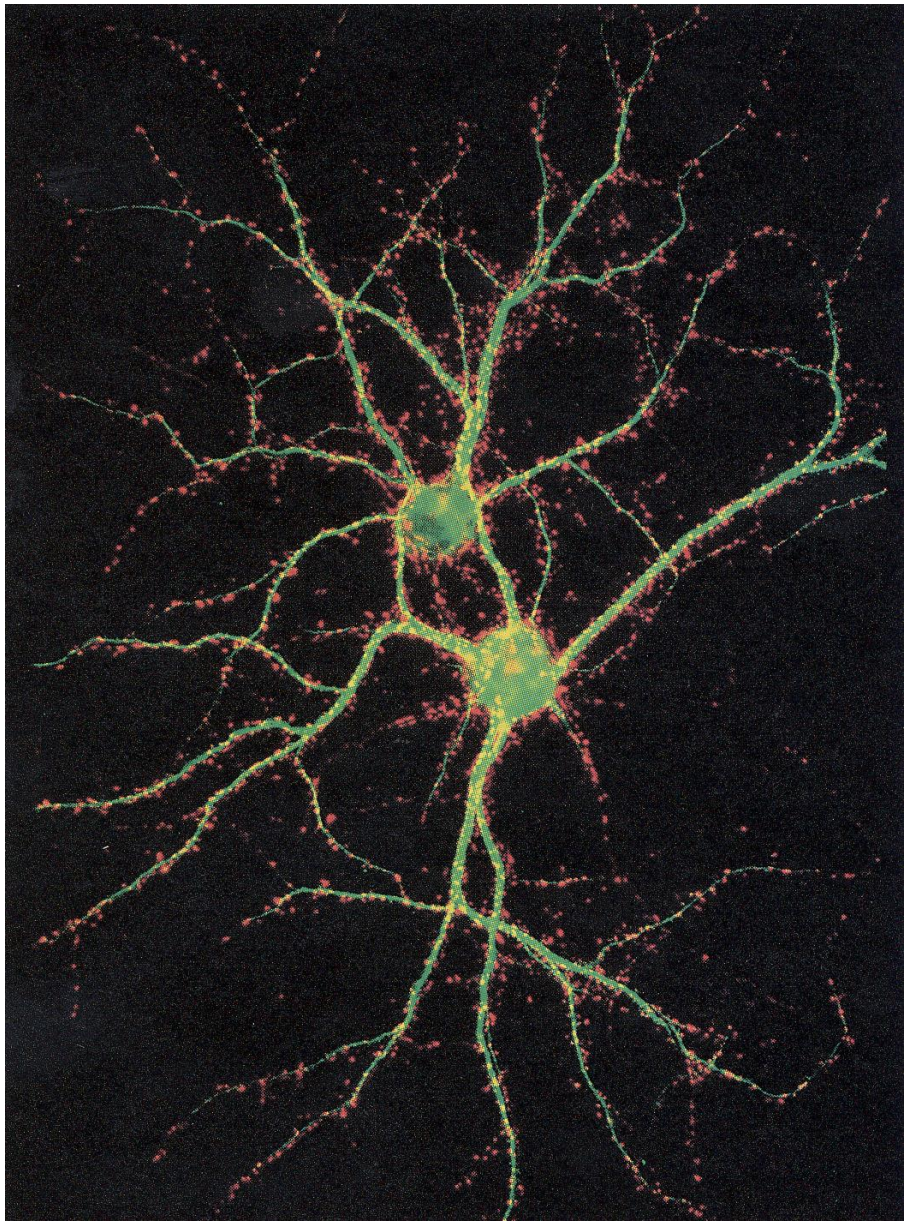
Sprejem, prevajanje, prenos električnega signala

Strukture tipičnih sesalskih nevronov



Nevroni se sporazumevajo s številnimi drugimi celicami

Hipokampalna internevrona



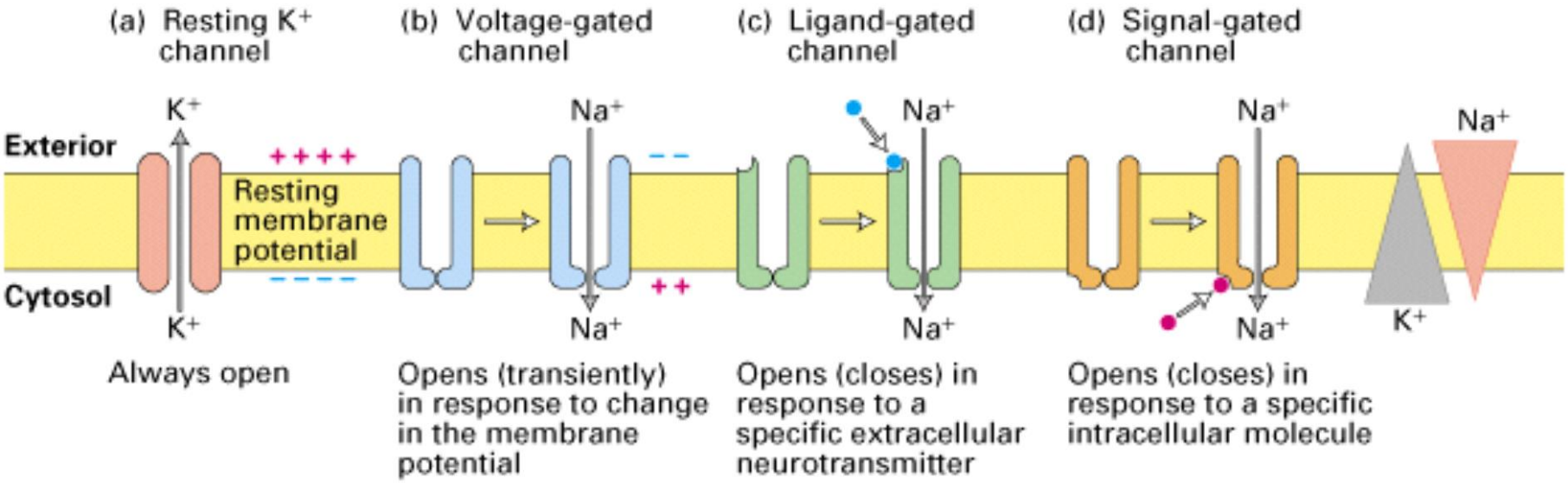
dendriti & telo celice - MAP2

aksonski končiči - sinaptotagmin

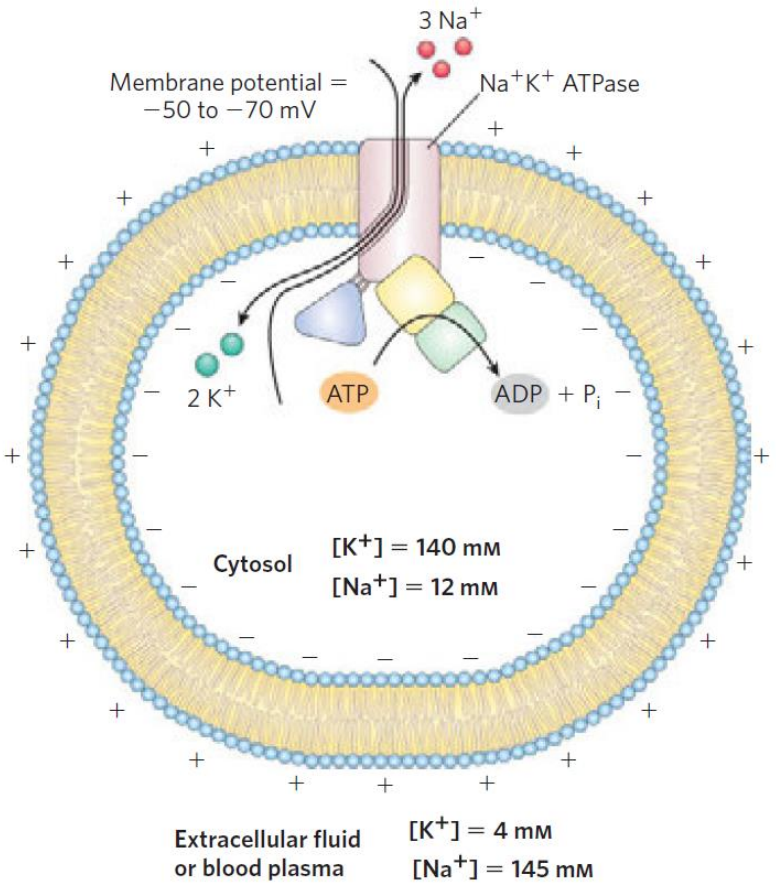
Kemična sinapsa

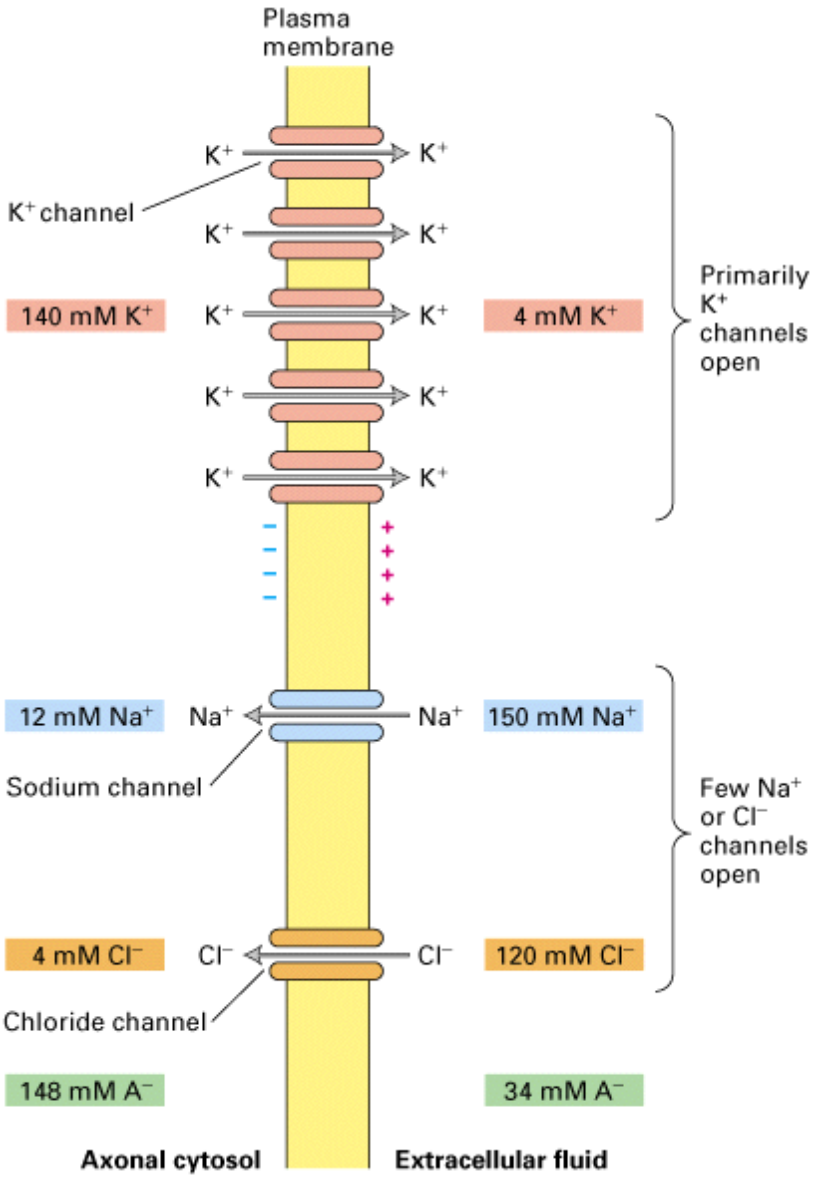
Sprejem, prevajanje in prenos električnega signala

Ionski kanalčki v PM nevrona:



Nastanek mirovnega potenciala na PM tipičnega vretenčarskega nevrona



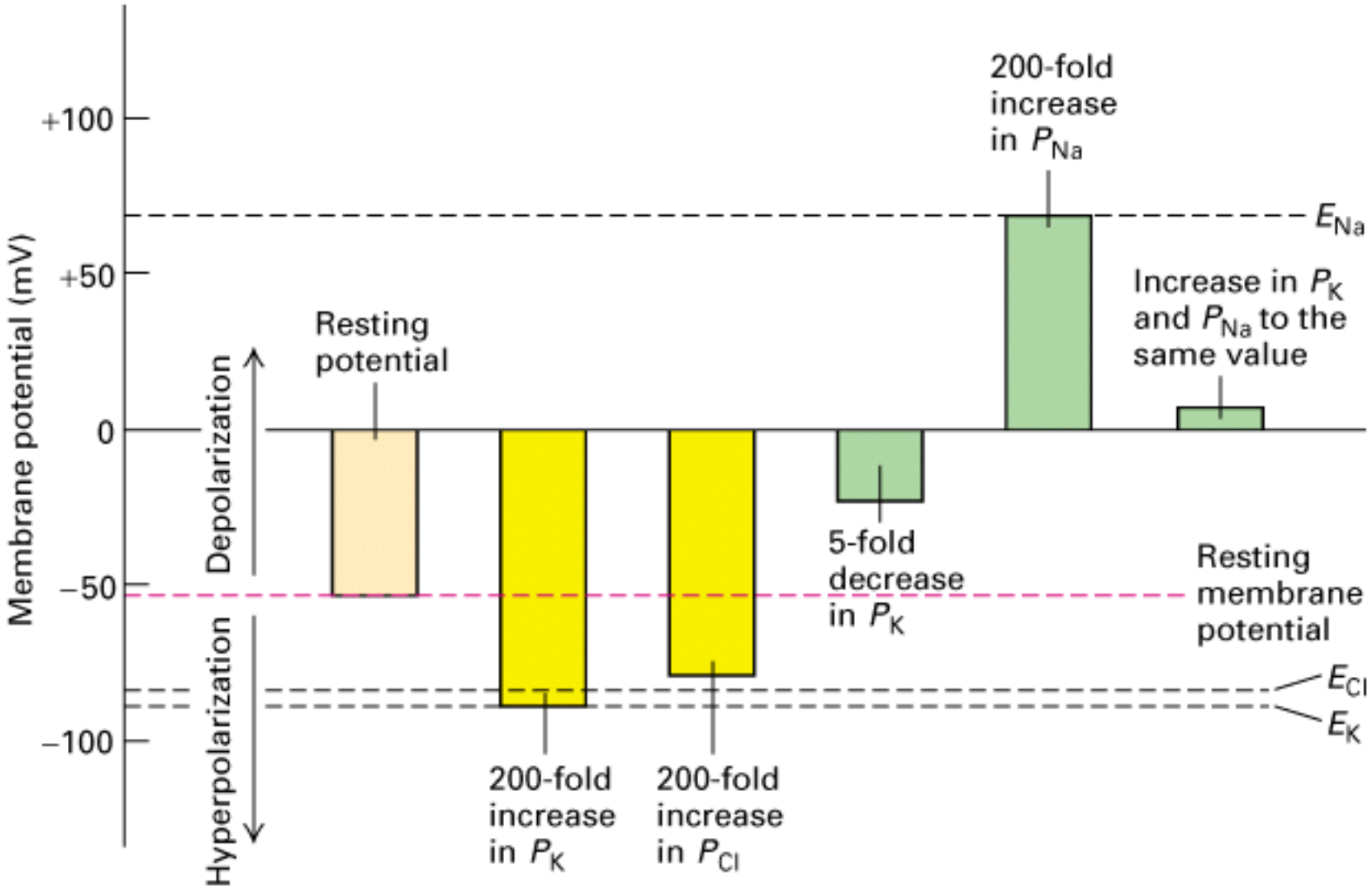


Električni potencial (E) PM celice

Nernstova enačba:

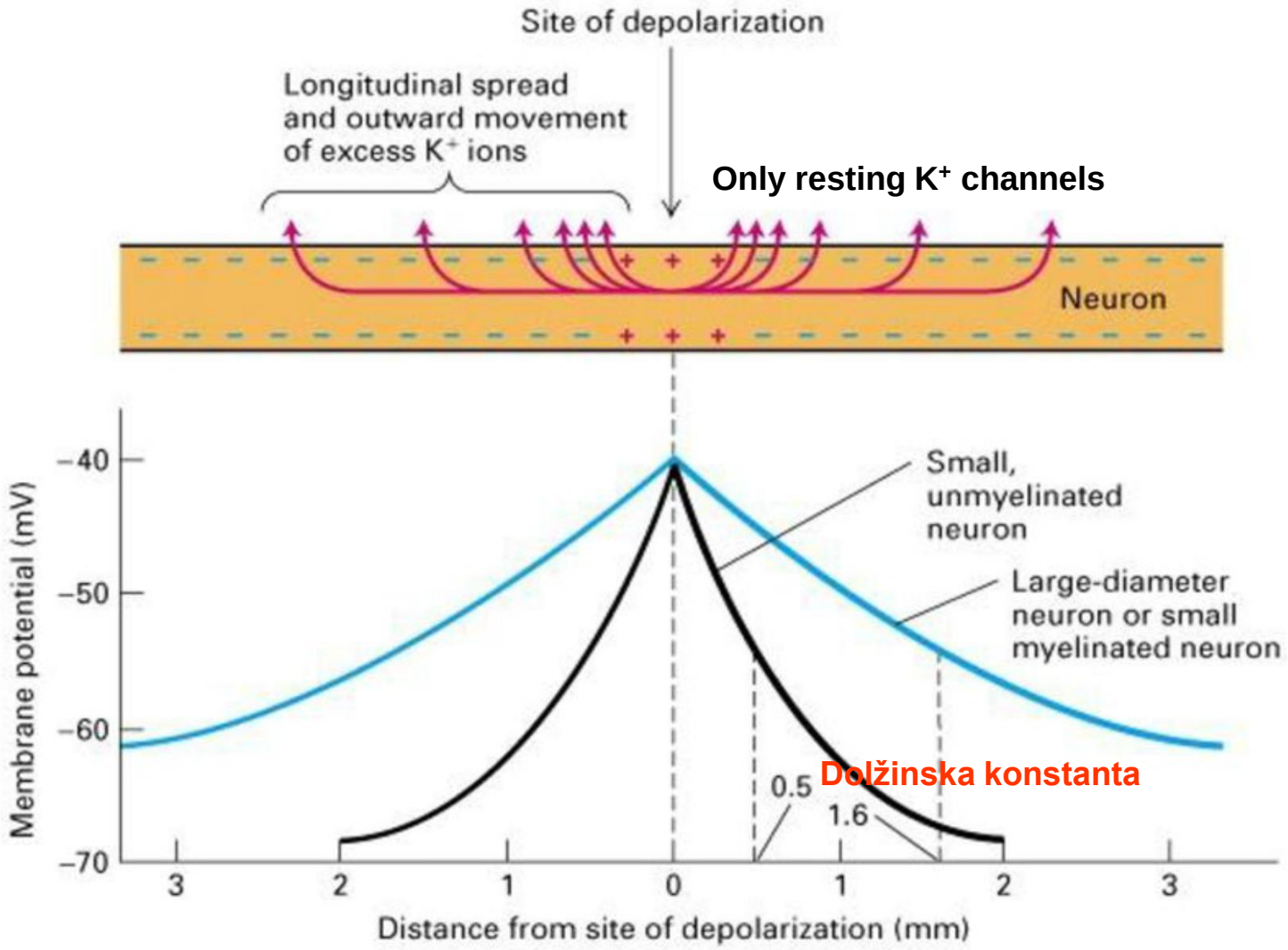
$$E = 59 \log_{10} \frac{[K_o] + [Na_o]\frac{P_{Na}}{P_K} + [Cl_i]\frac{P_{Cl}}{P_K}}{[K_i] + [Na_i]\frac{P_{Na}}{P_K} + [Cl_o]\frac{P_{Cl}}{P_K}}$$

Vpliv sprememb v prevodnosti ionov na potencial PM



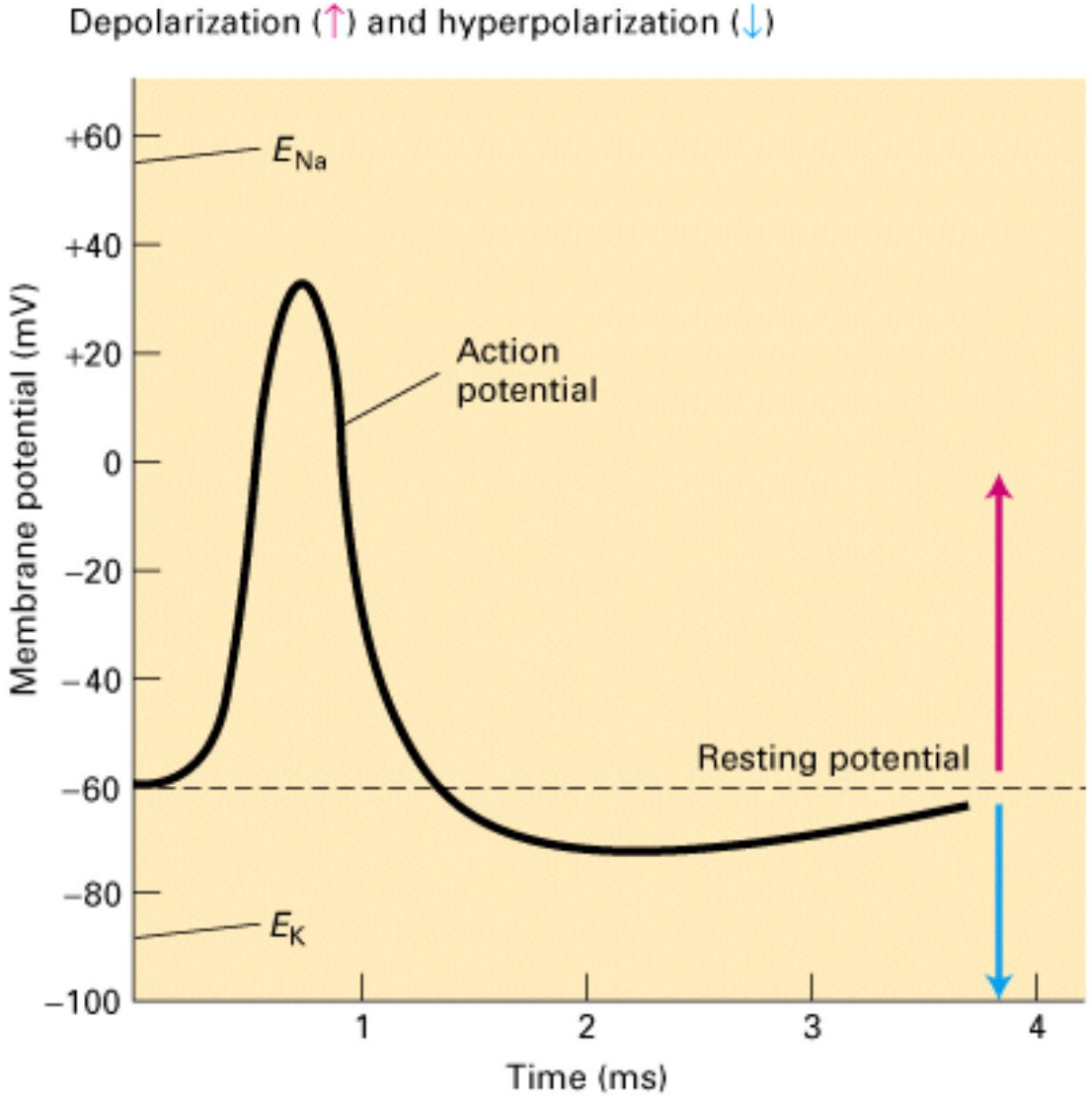
Pasivno širjenje depolarizacije PM

Doseg depolarizacije PM na pasiven način je kratek

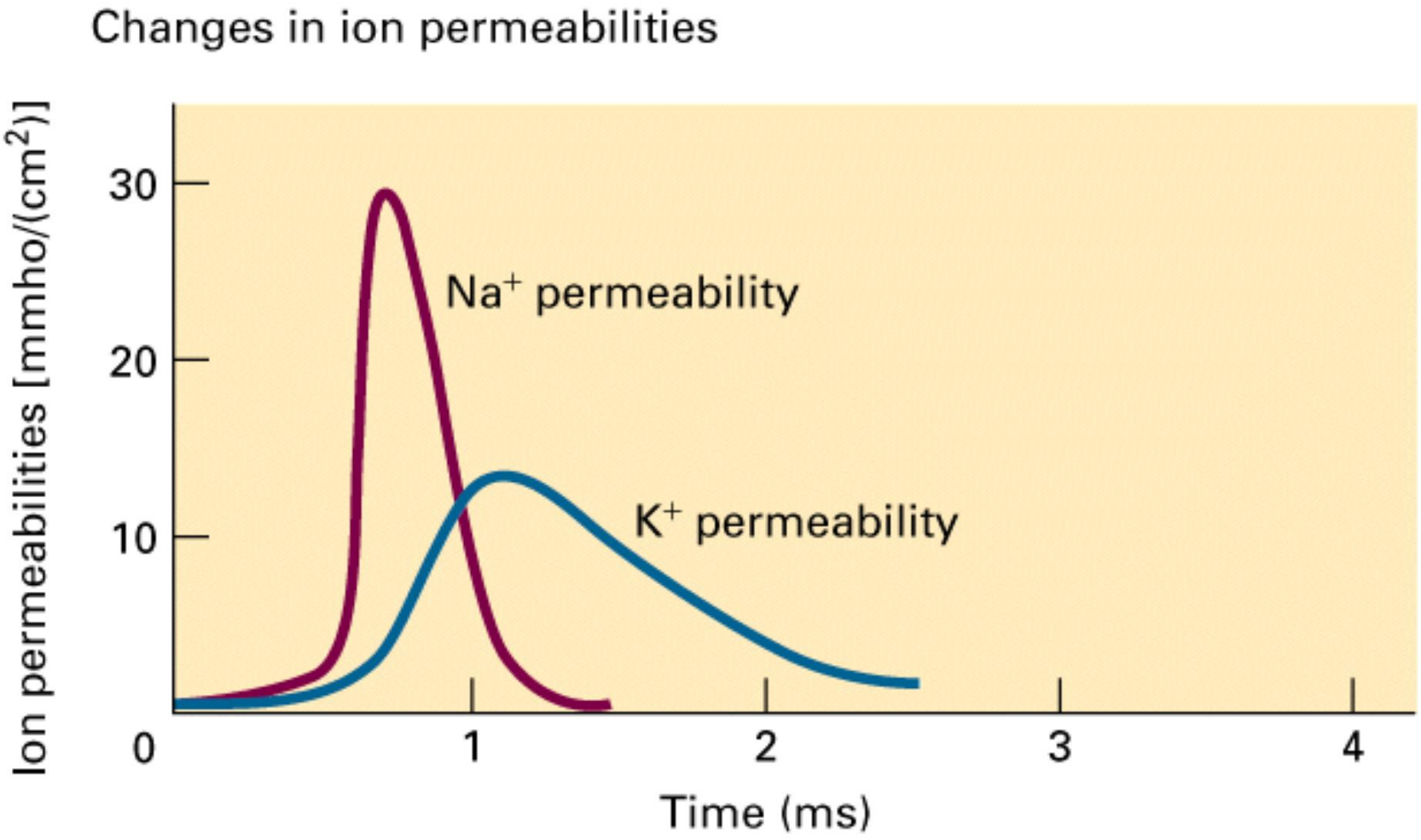


Napetostno-odvisni ionski kanalčki ustvarijo akcijski potencial

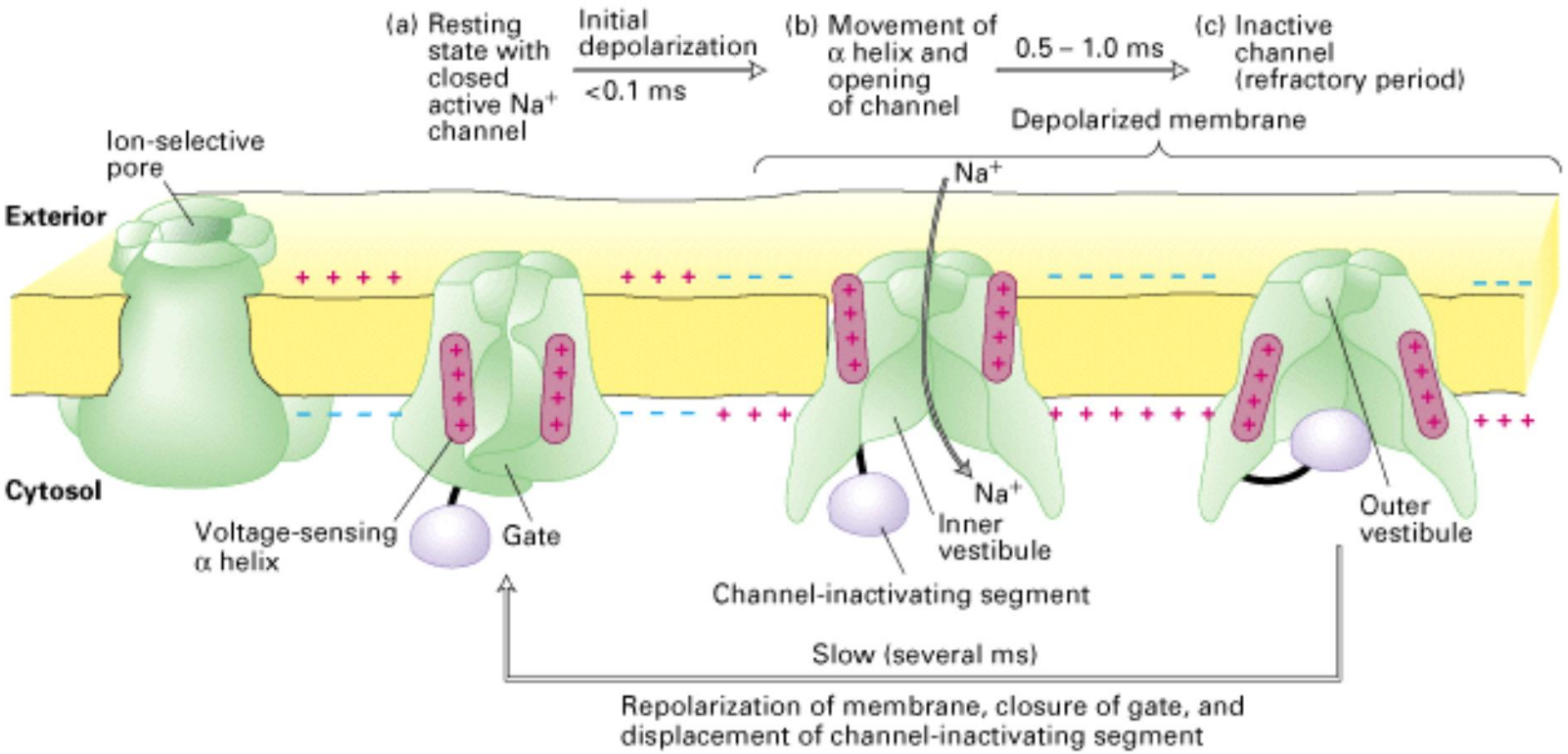
(depolarizacija, hiperpolarizacija in povratek membrane v mirovni potencial)

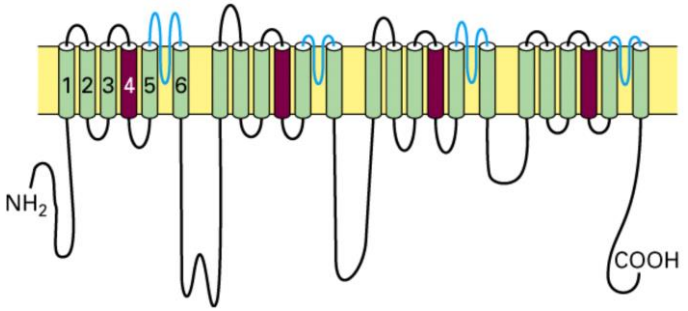


Ionska prevodnost PM med akcijskim potencialom



Struktura in funkcija napetostno-odvisnih Na^+ kanalčkov

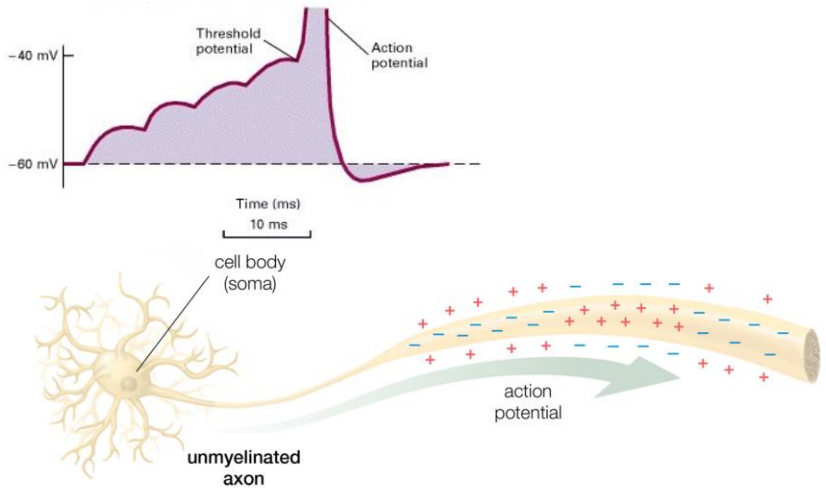


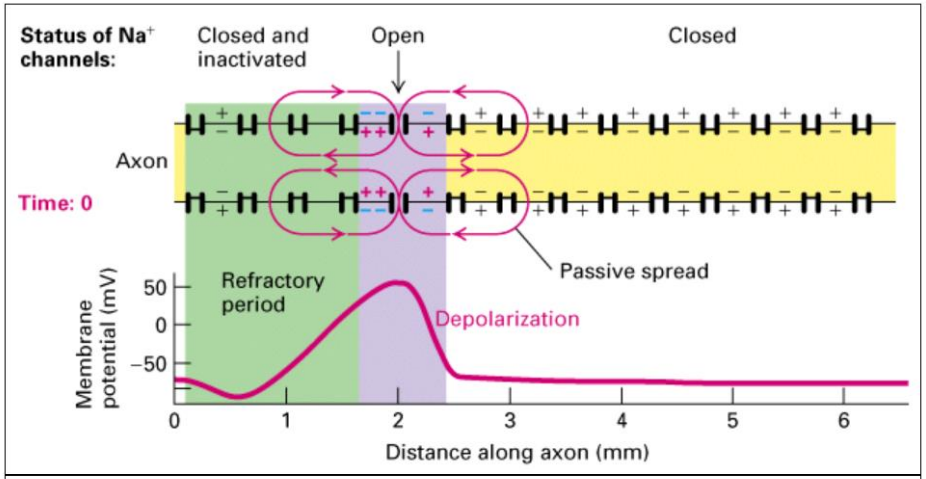


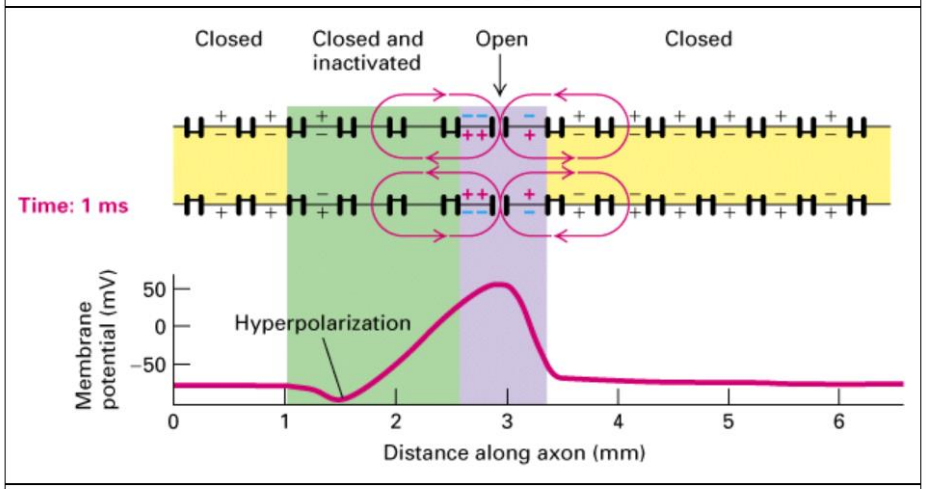
Seminar 23.12.2020

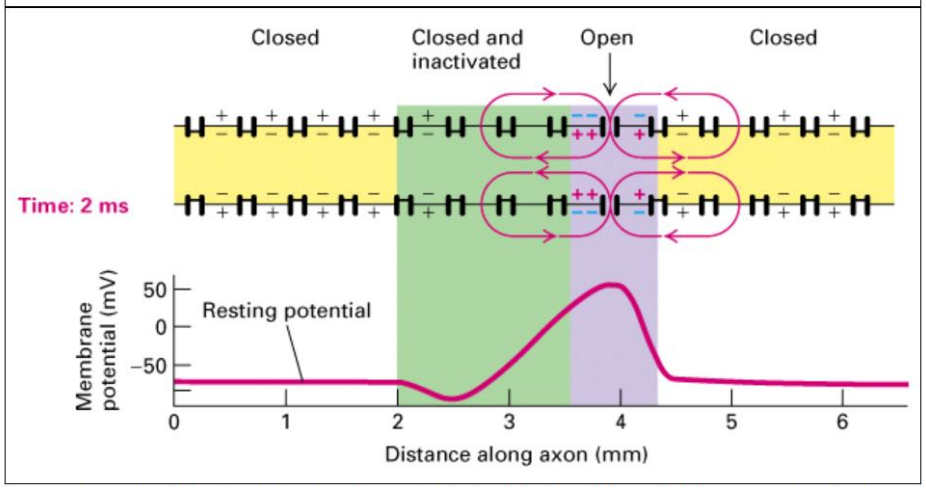
Liza Ulčakar, Luka Gnidovec,
Nika Mikulič Vernik

Širjenje akcijskega potenciala je enosmerno, proč od vira nastanka

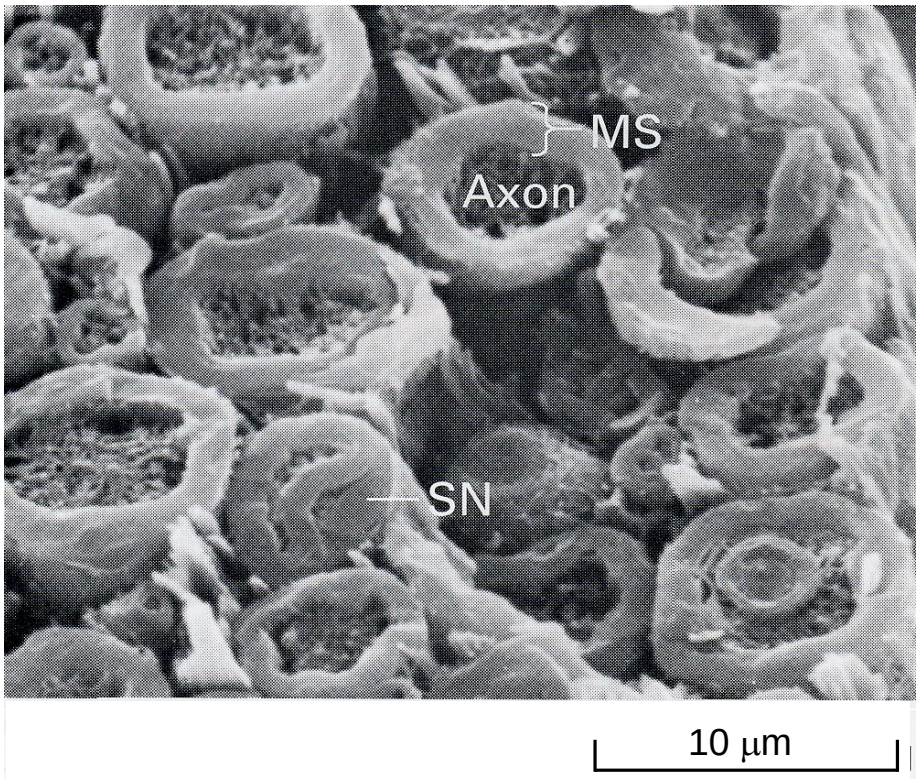


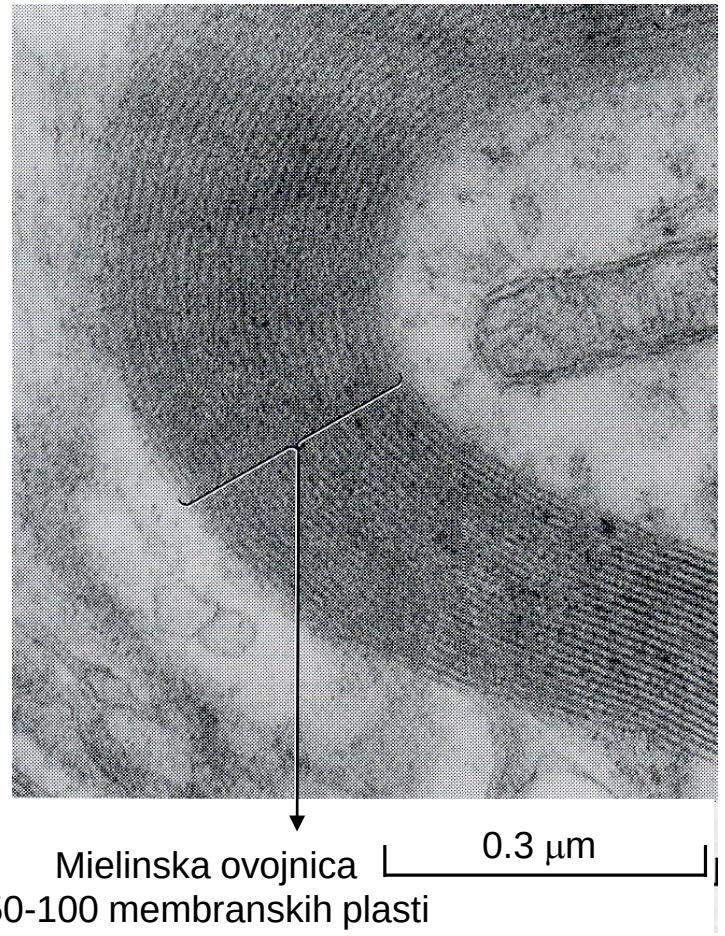






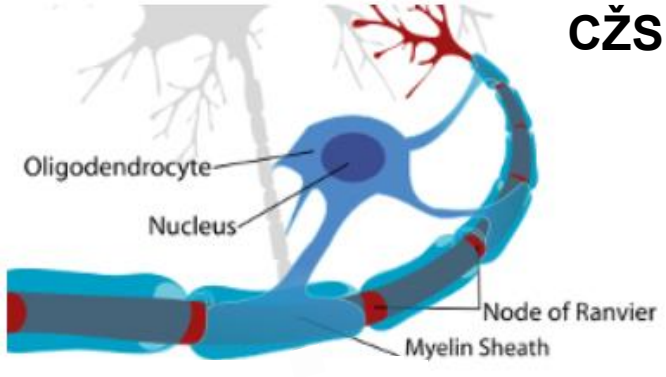
Mielinizacija aksonov

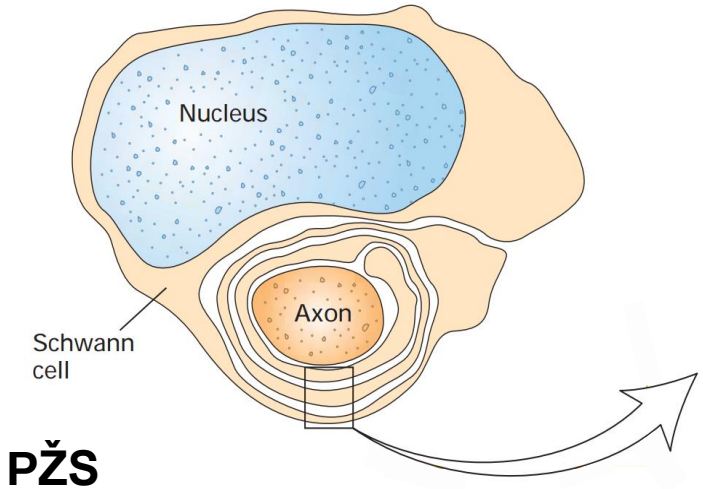




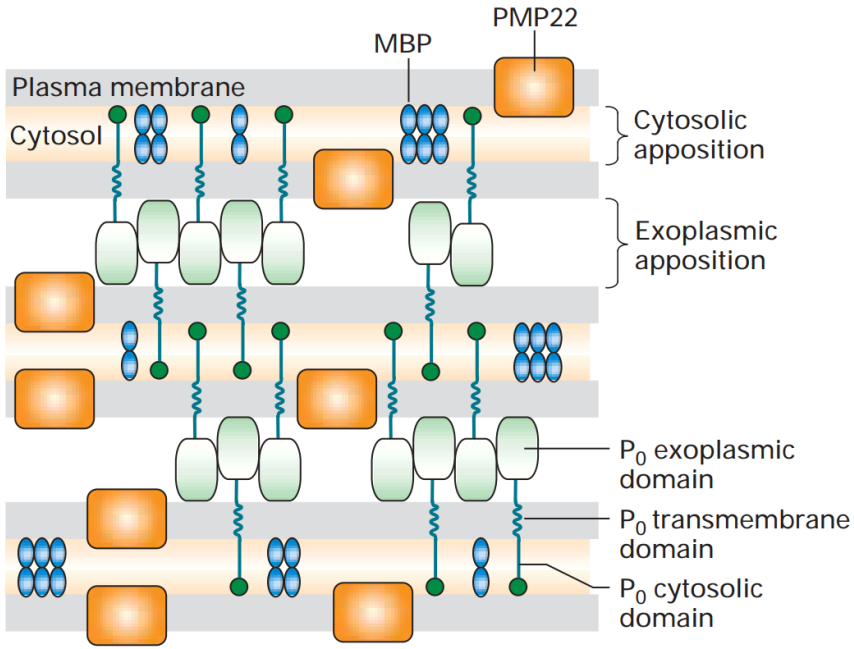
Struktura mielinske ovojnice

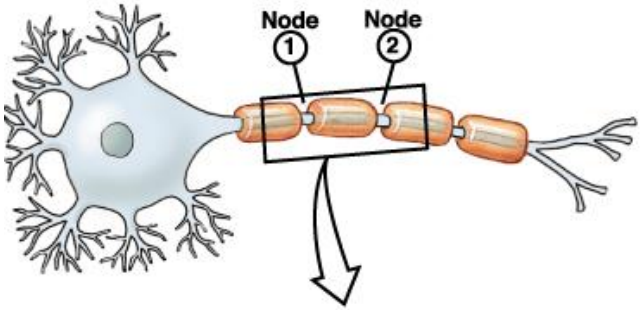
CŽS



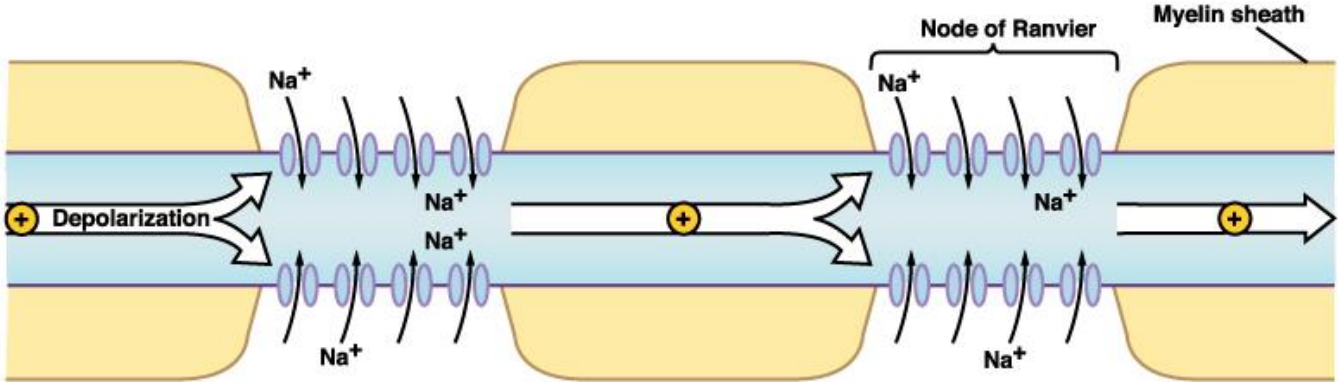


PŽS





Mielinizacija poveča hitrost prevajanja Signala z ~1 m/s na 10-100 m/s.



12 μm mieliniran vretenčarski akson
600 μm nemieliniran akson lignja

⇩

12 m/s

⇩

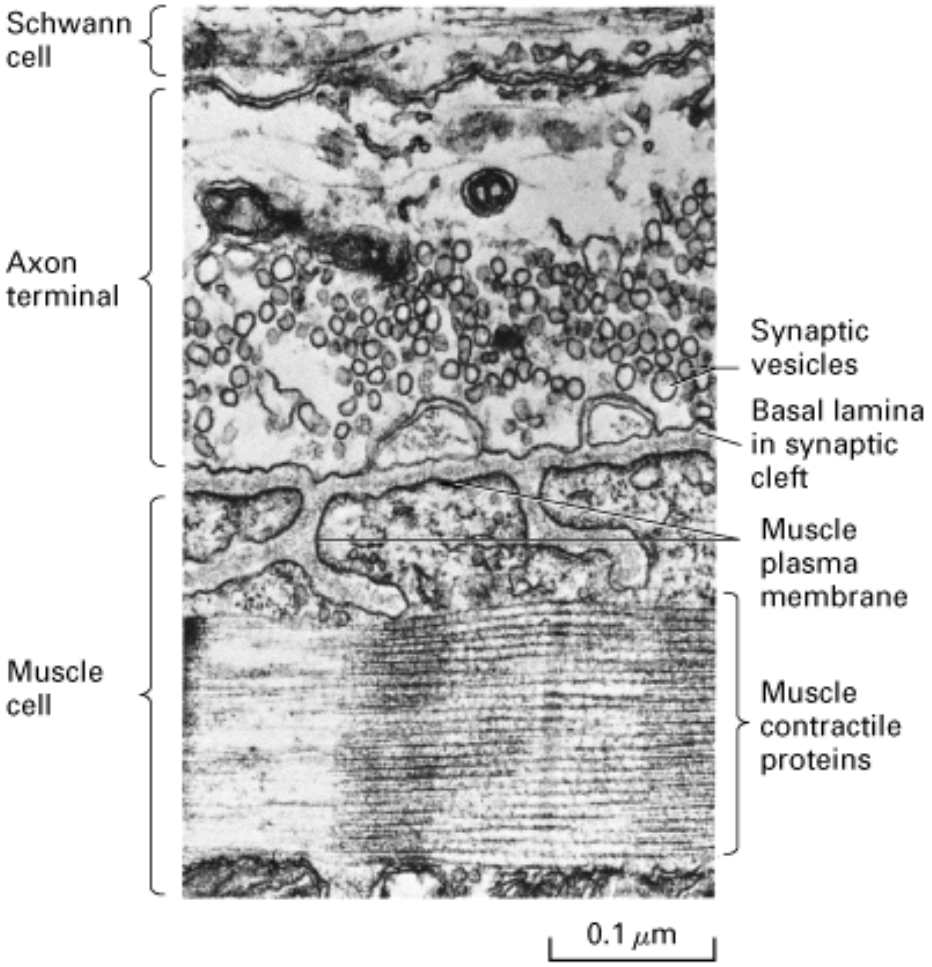
Radikalno zmanjšanje volumna nevrona & potrošnje ATP

⇩

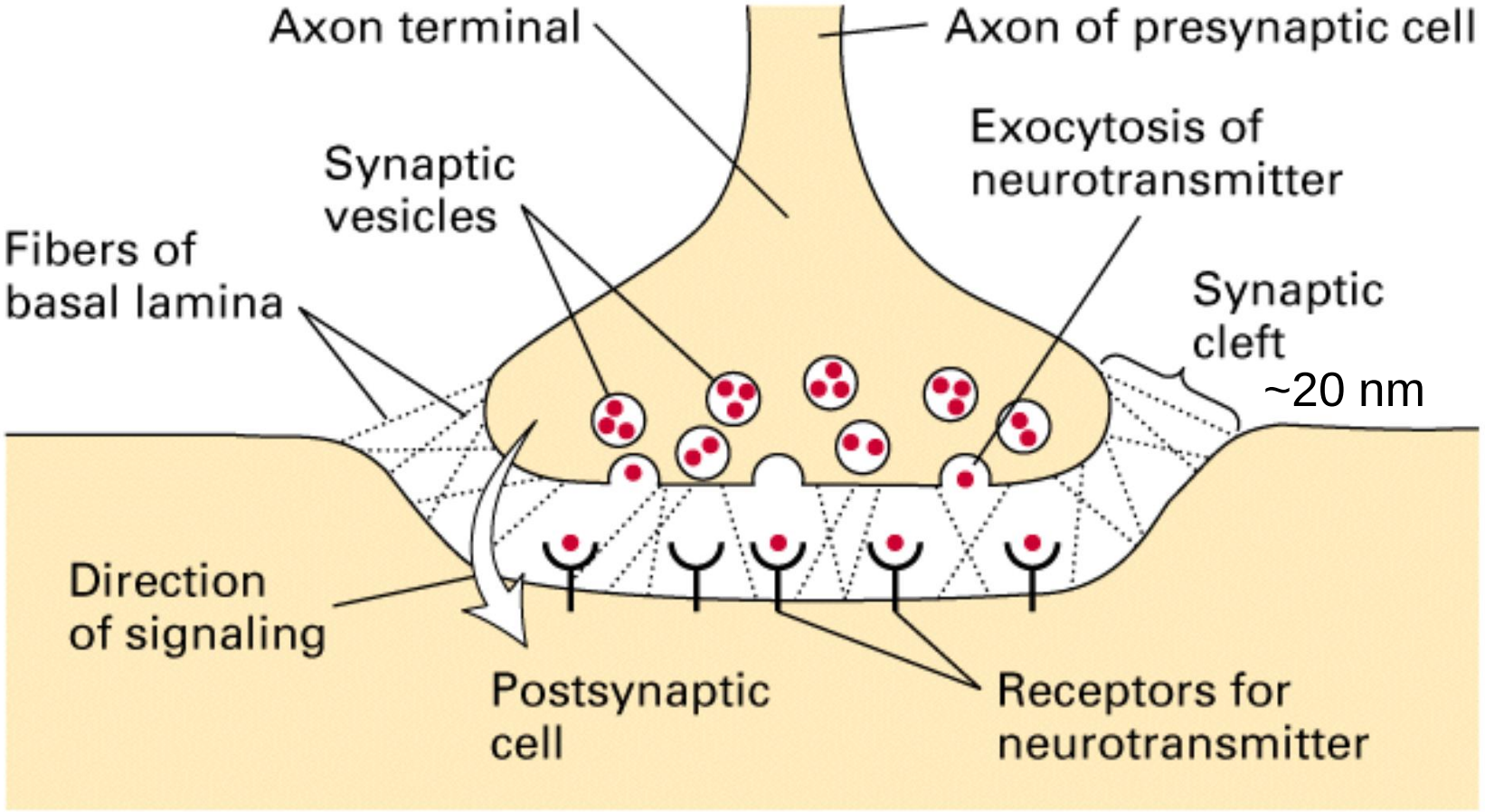
Razvoj možganov pri vretenčarjih

Prenos signala v kemijski sinapsi

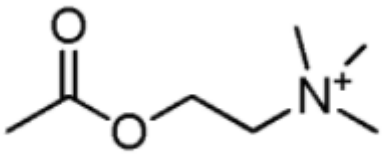
(žabji živčno-mišični stik)



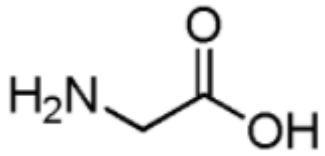
Kemijska sinapsa - shematsko



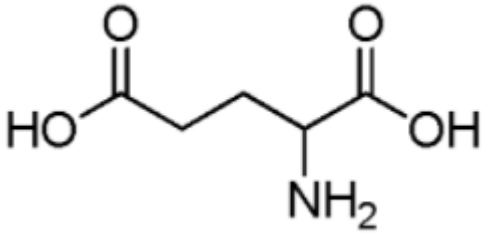
Klasični nevrotransmiterji



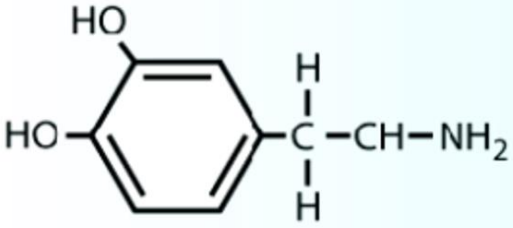
Acetilholin



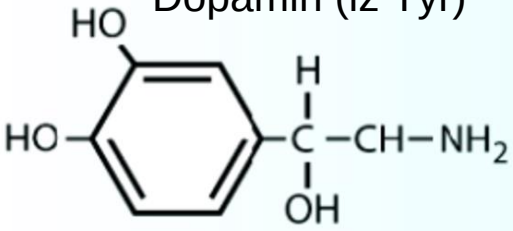
Glicin



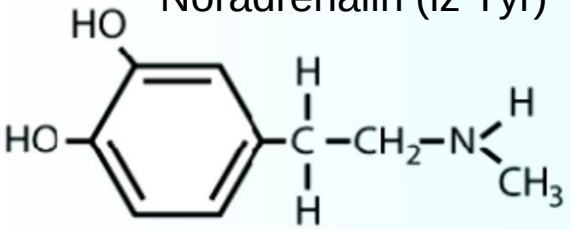
Glutamat



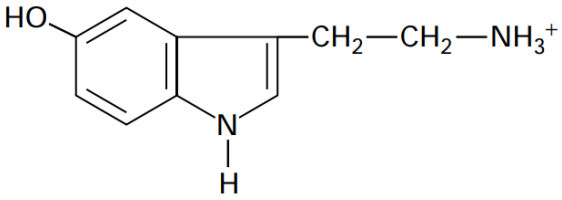
Dopamin (iz Tyr)



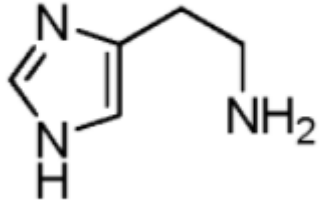
Noradrenalin (iz Tyr)



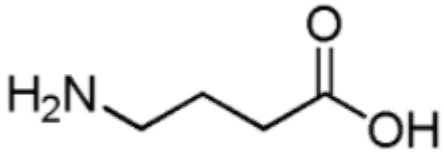
Adrenalin (iz Tyr)



Serotonin (iz Trp)



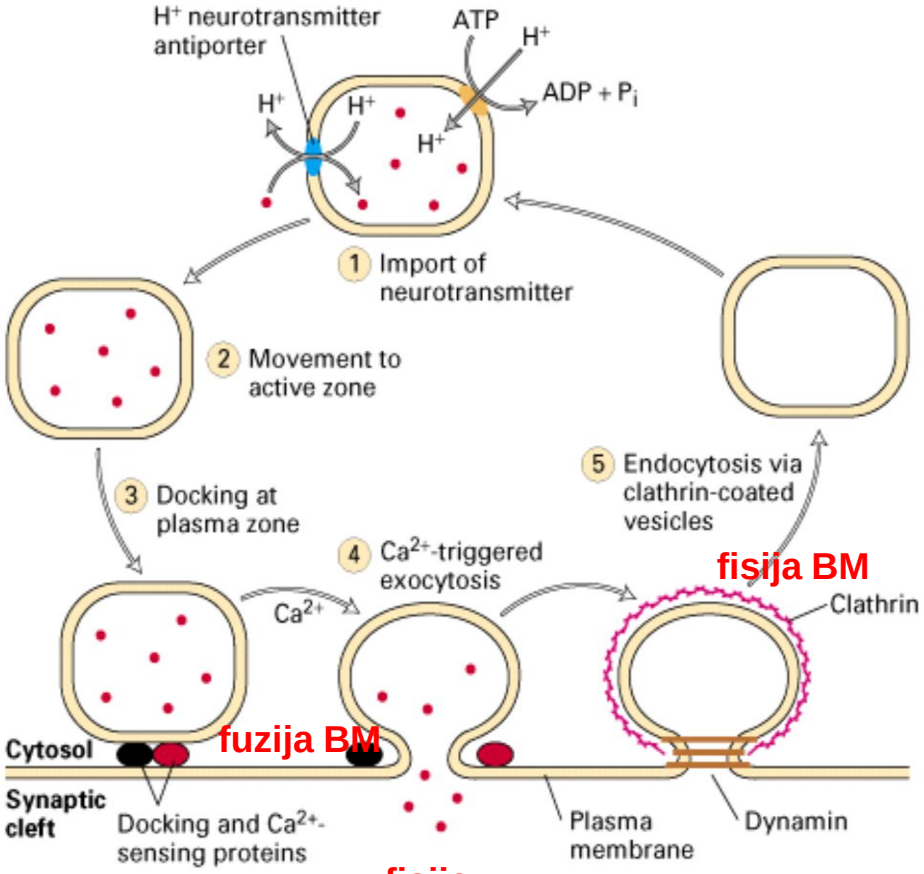
Histamin (iz His)

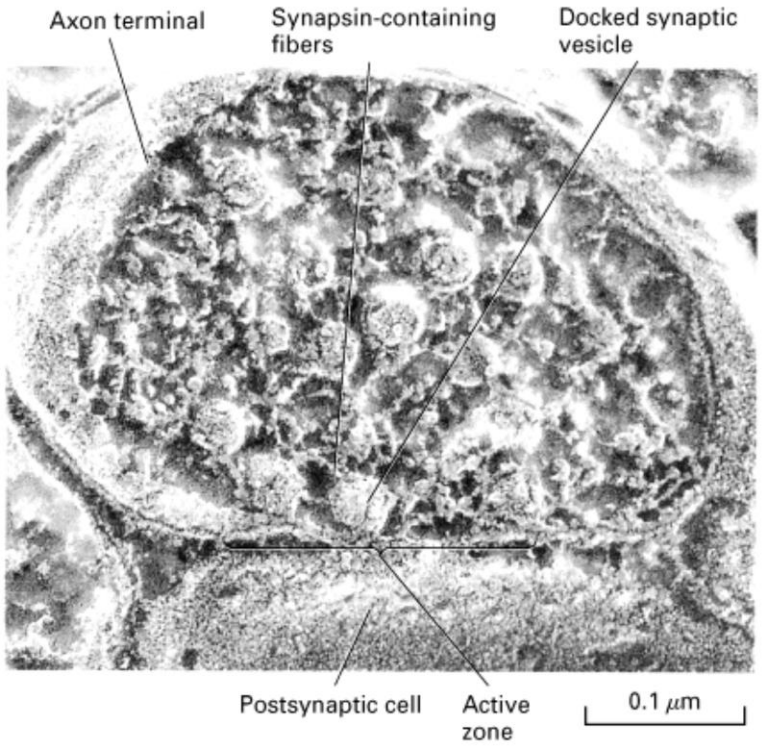


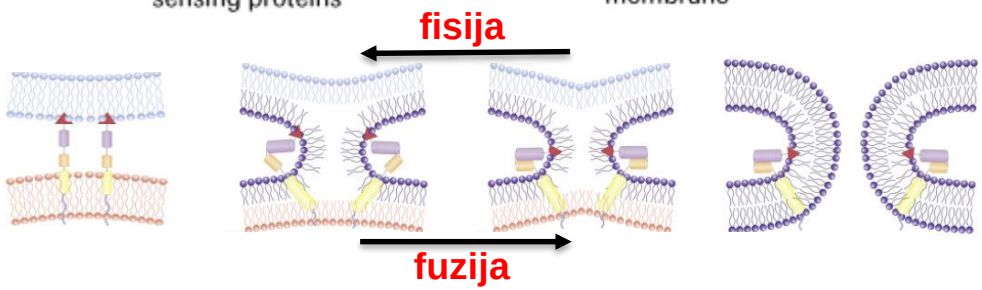
γ-Aminomaslena kislina (GABA; iz Glu)

Cikel sinaptičnega mešička

Biološke membrane se združujejo/zlivajo in razdružujejo/cepijo

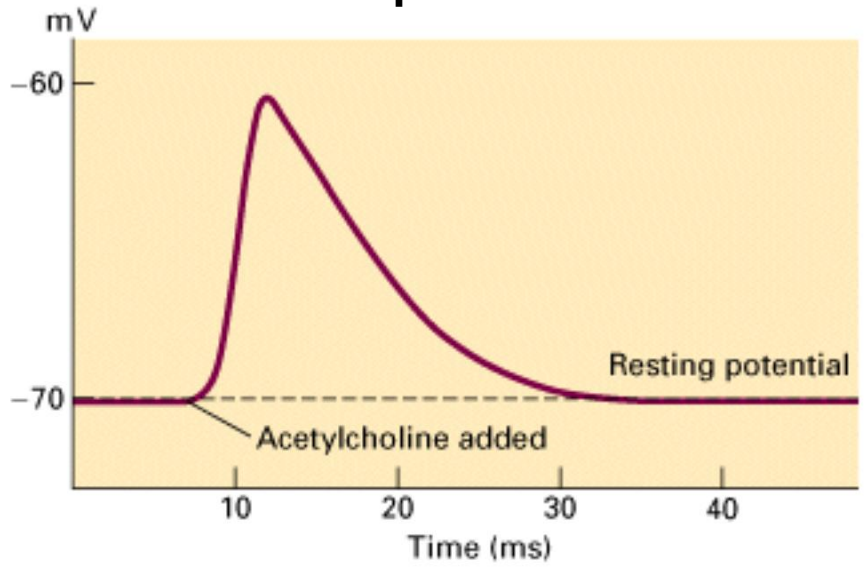






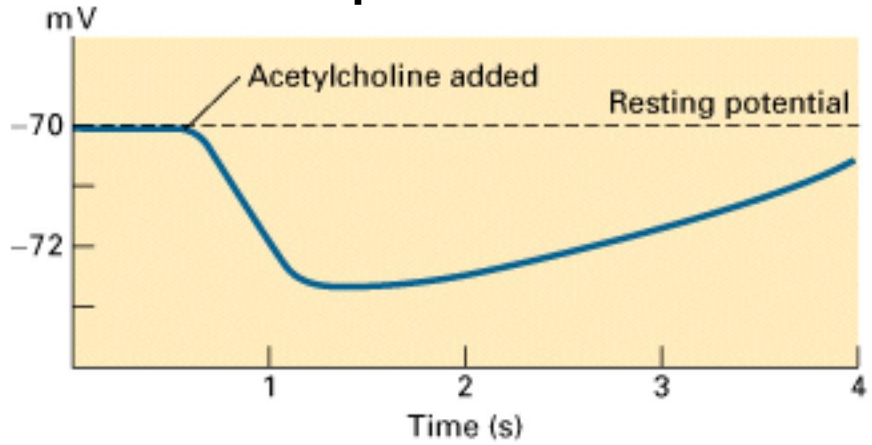
Ekscitatorni in inhibitorni odziv postsinaptične celice

Ekscitatorna sinapsa



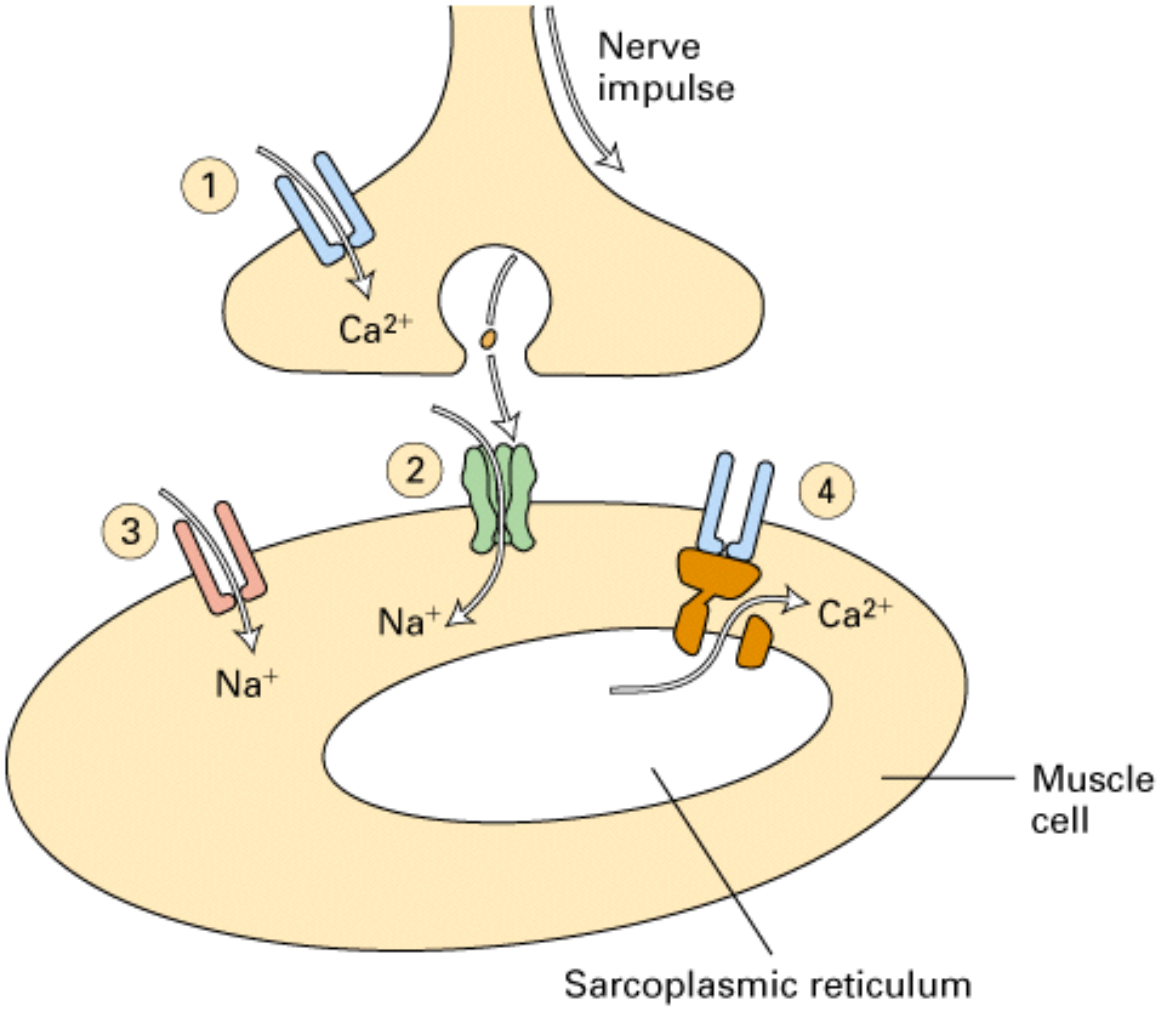
Žabja skeletna mišica
- nikotinski AChR
(**ekscitatorni receptor**)

Inhibitorna sinapsa

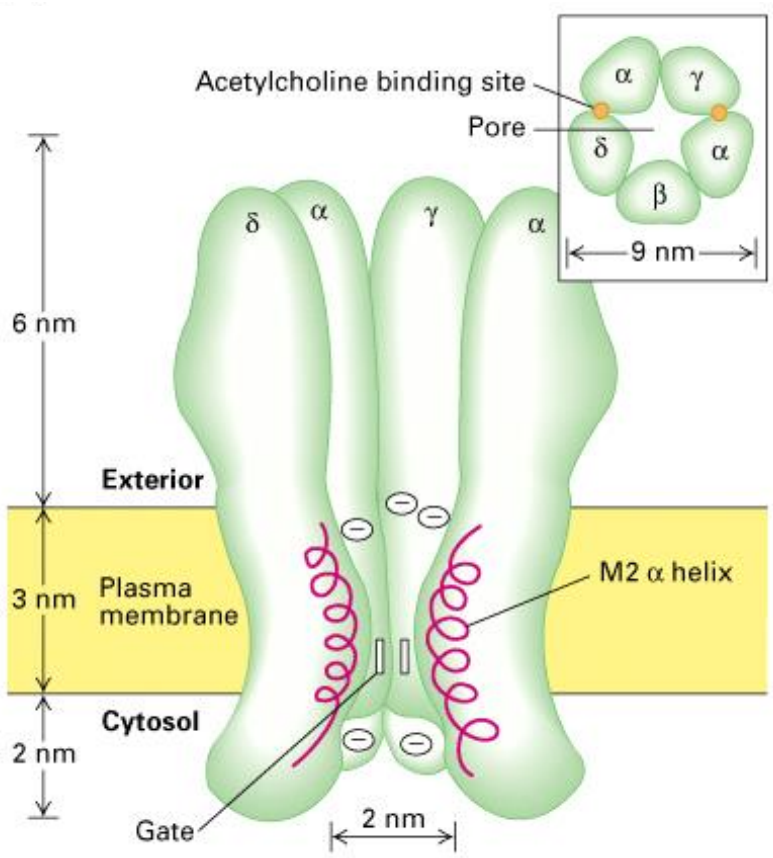


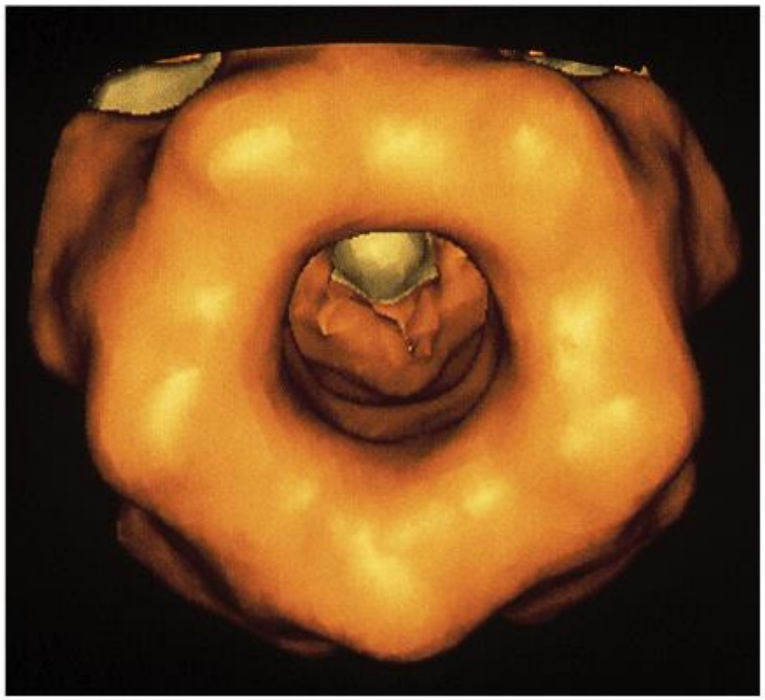
Žabja srčna mišica
- muskarinski AChR
(**inhibitorni receptor**)

Aktivacija z ligandi-uravnavanega ionskega kanalčka v živčno-mišičnem stiku



Nikotinski ACh receptor



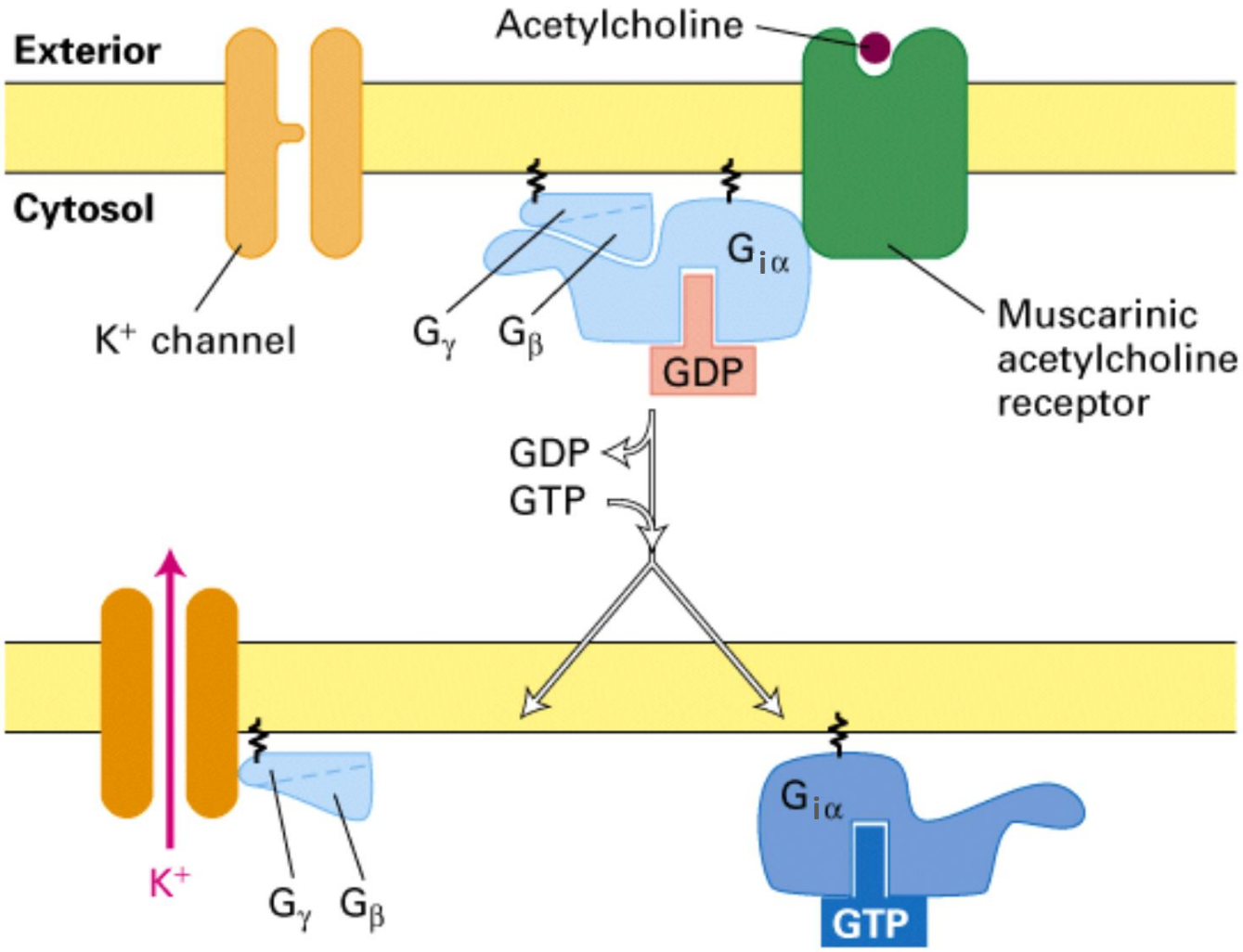


Hitre sinapse

Nevrotransmiterski receptorji, z ligandi-regulirani ionski kanalčki		
Funkcijski tip	**Ligand[1]**	**Prevaja**
Ekscitatorni receptorji	Acetilholin (nikotinski receptor)	Na^+/K^+
	Glutamat (NMDA[2] receptor)	Na^+/K^+ in Ca^{2+}
	Glutamat (ne-NMDA[2] receptor)	Na^+/K^+
	Serotonin ($5HT_3$ receptor)	Na^+/K^+
Inhibitorni receptorji	γ-Aminomaslena kislina (GABA, A-razred)	Cl^-
	Glicin	Cl^-

[1] Večina teh ligandov se veže tudi na receptorje, ki so sklopljeni z G-proteini (GPCR). Njihovi receptorji–ionski kanalčki so navedeni v oklepaju.
[2] N-metil-*D*-aspartat

Muskarinski ACh receptor v PM srčne mišice (M2)

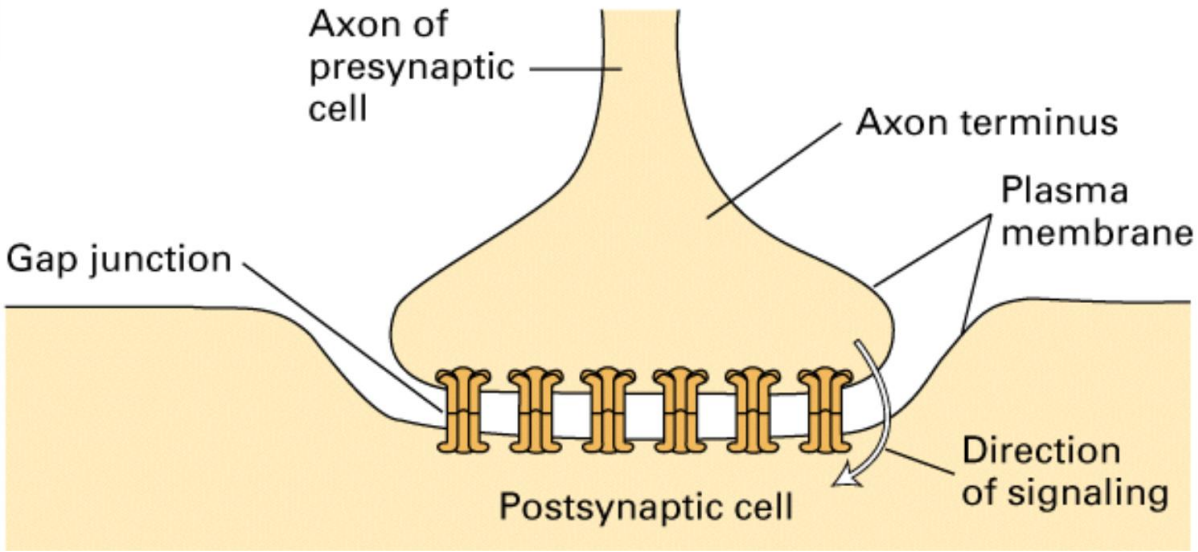


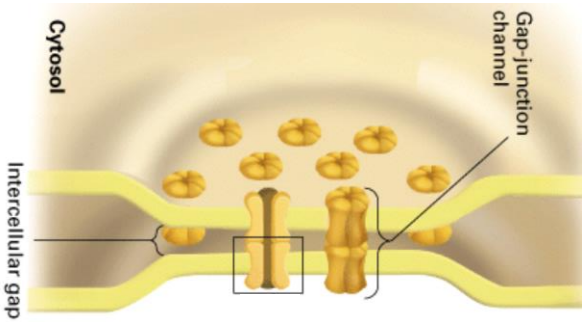
Počasne sinapse

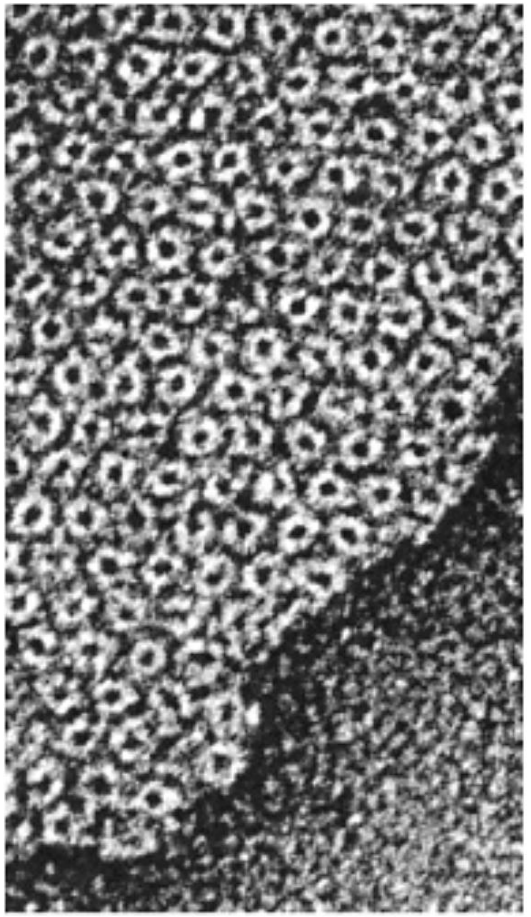
Primeri GPCR za nevrotransmiterje in nevropeptide	
GPCR za klasične nevrotransmiterje	
Acetilholin* (muskarinski receptor)	γ-Aminomaslena kislina* (GABA, B-razred)
Adenozin	Glutamat*
ATP	Histamin
Dopamin	Serotonin* ($5HT_1$, $5HT_2$, $5HT_5$ receptorji)
Adrenalin, noradrenalin	
GPCR za nevropeptide	
Adrenokortikotropni hormon (ACTH)	Opioidi (npr. β-endorfin)
Bradikinin	Oksitocin
Kolcistokinin (CCK)	Tahikinini (npr. substanca P)
Endotelin	Tirotropin-sproščujoči hormon (TRH)
Gastrin	Vazoaktivni črevesni peptid (VIP)
Luteinizirajoči hormon-sproščujoči hormon (LHRH)	Vazopresin

*Ti nevrotransmiterji se veže tudi na receptorje, z ligandi-regulirane ionske kanalčke.
Njihovi GPCR so navedeni v oklepaju.

Električna sinapsa

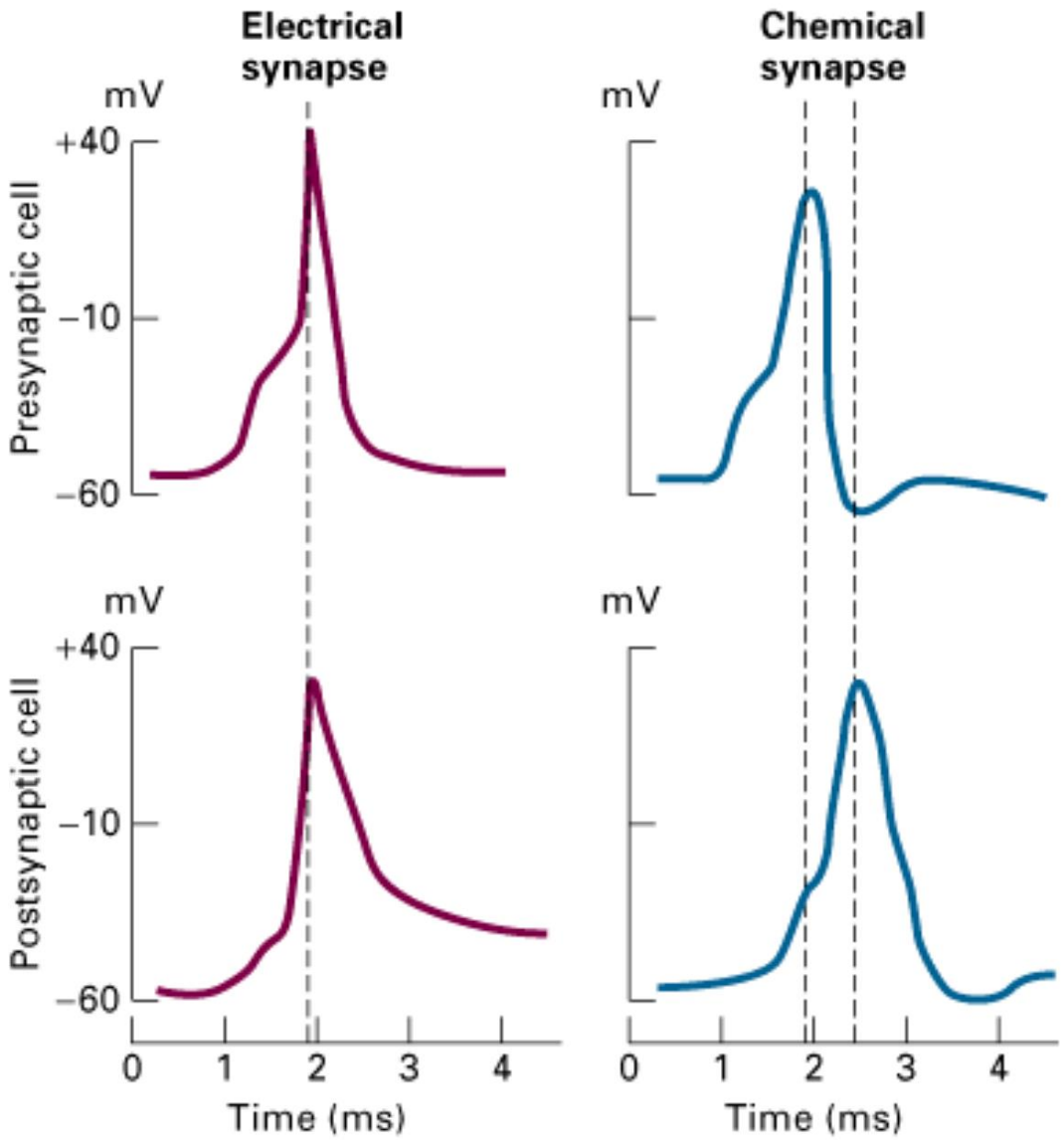






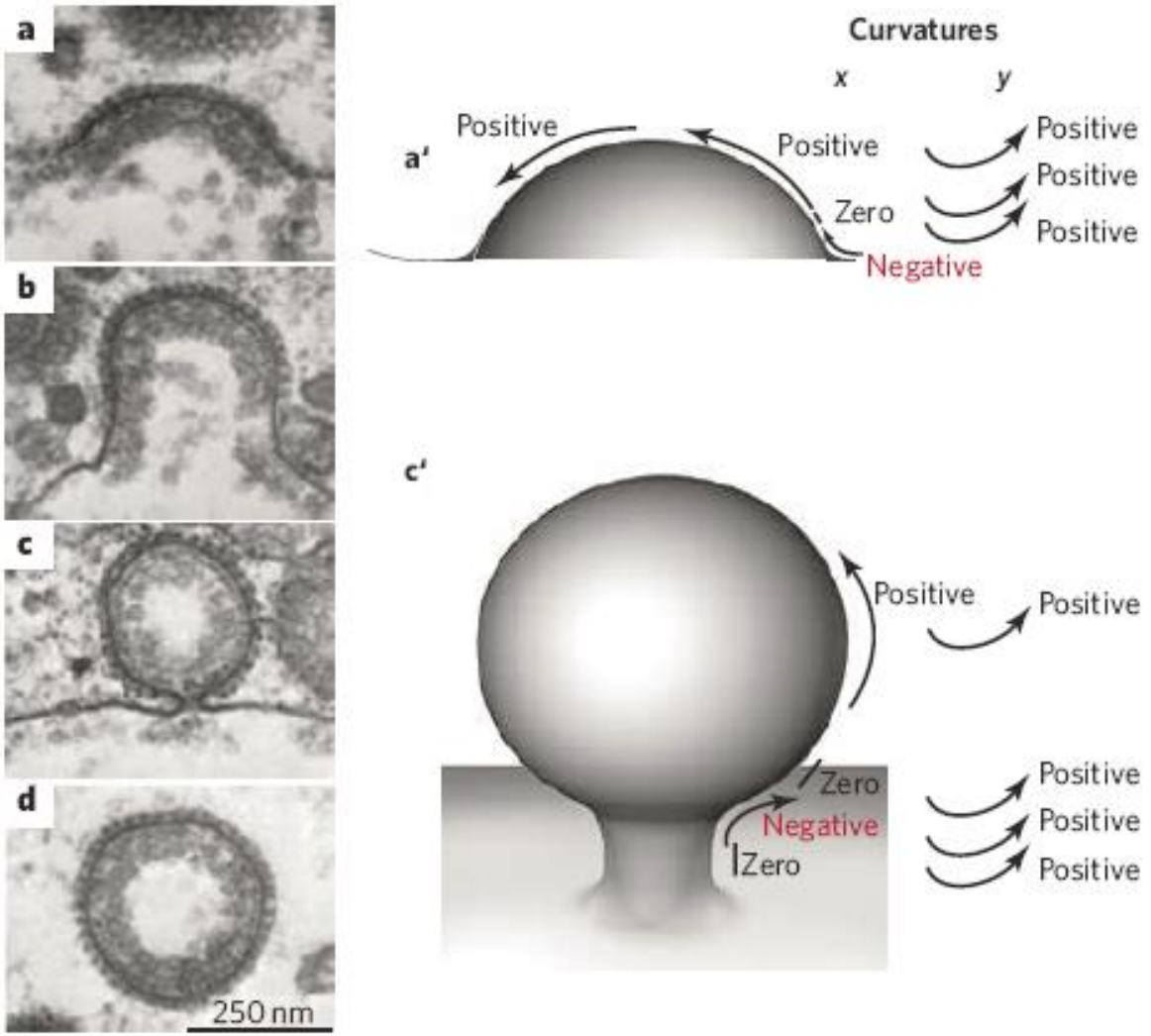
Seminar 6.1.2021

Andrej Race, Andrej Ivanovski, Mateja Žvipelj, Neža Pavko

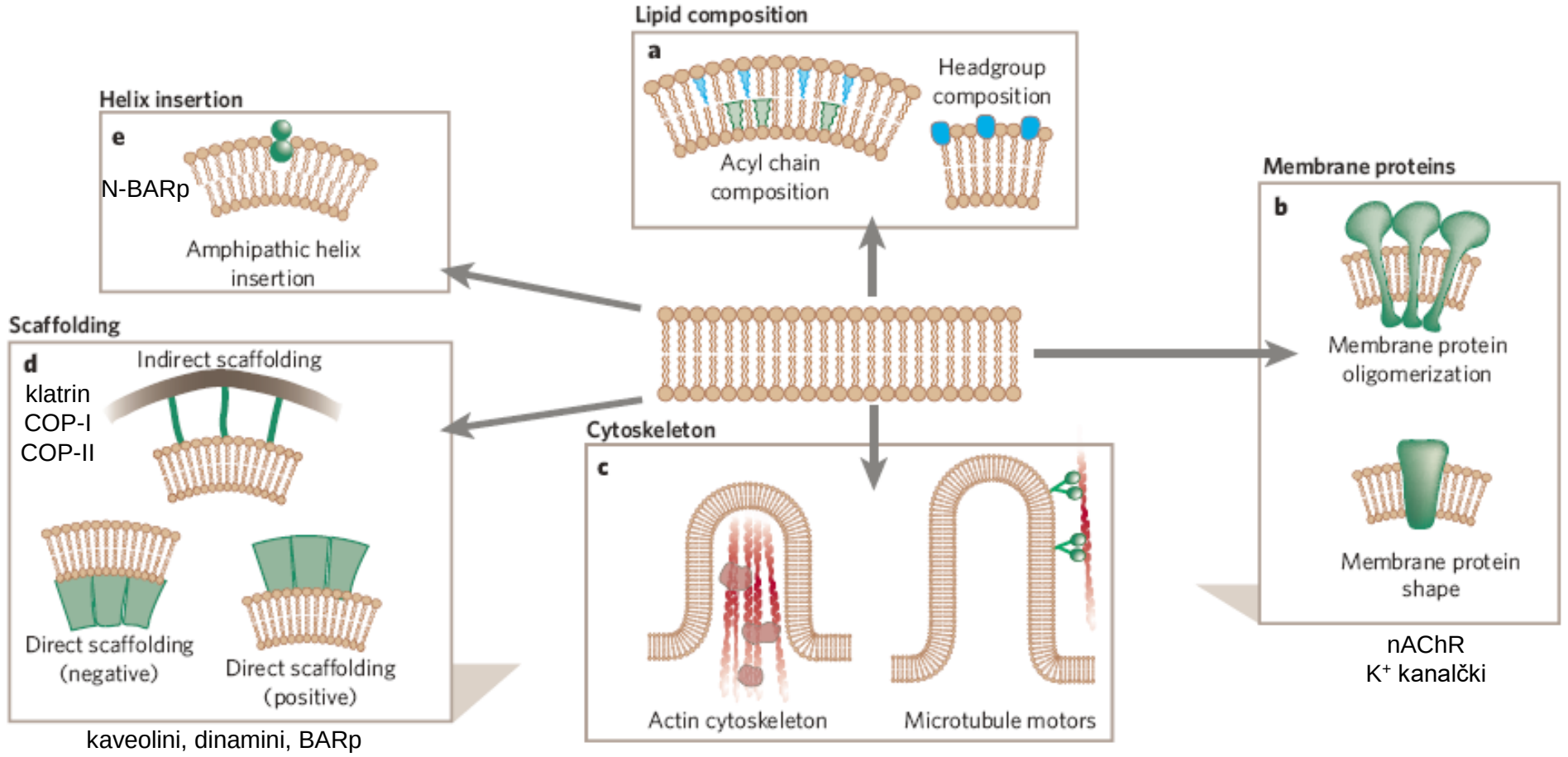

Electrical synapse
Chemical synapse
mV
+40
−10
−60
Presynaptic cell
Postsynaptic cell
0
1
2
3
4
Time (ms)

Ukrivljanje membran

Vnos snovi v celico s klatrin-posredovano endocitozo



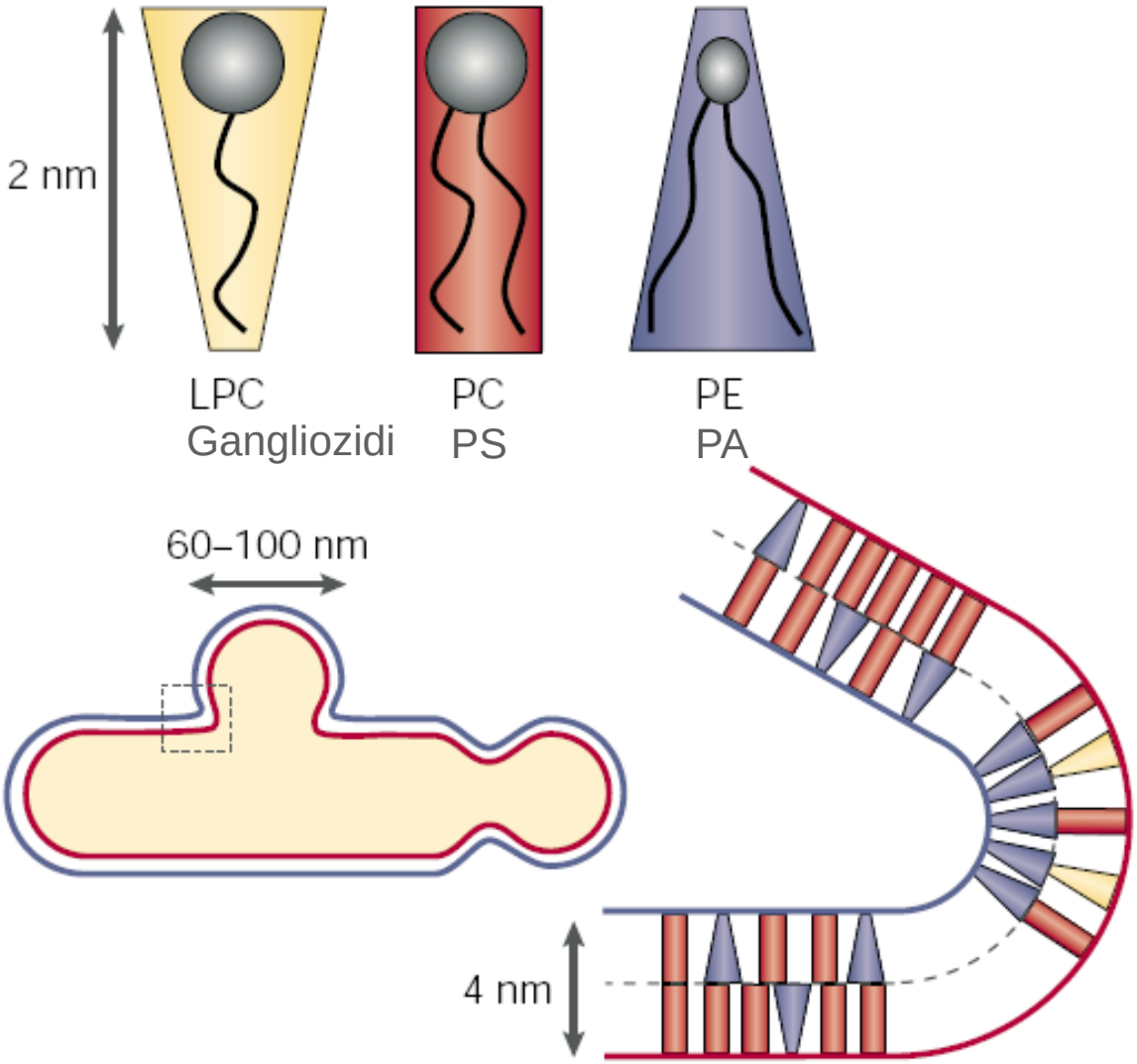
Mehanizmi ukrivljanja lipidnega dvosloja



kaveolini, dinamini, BARp

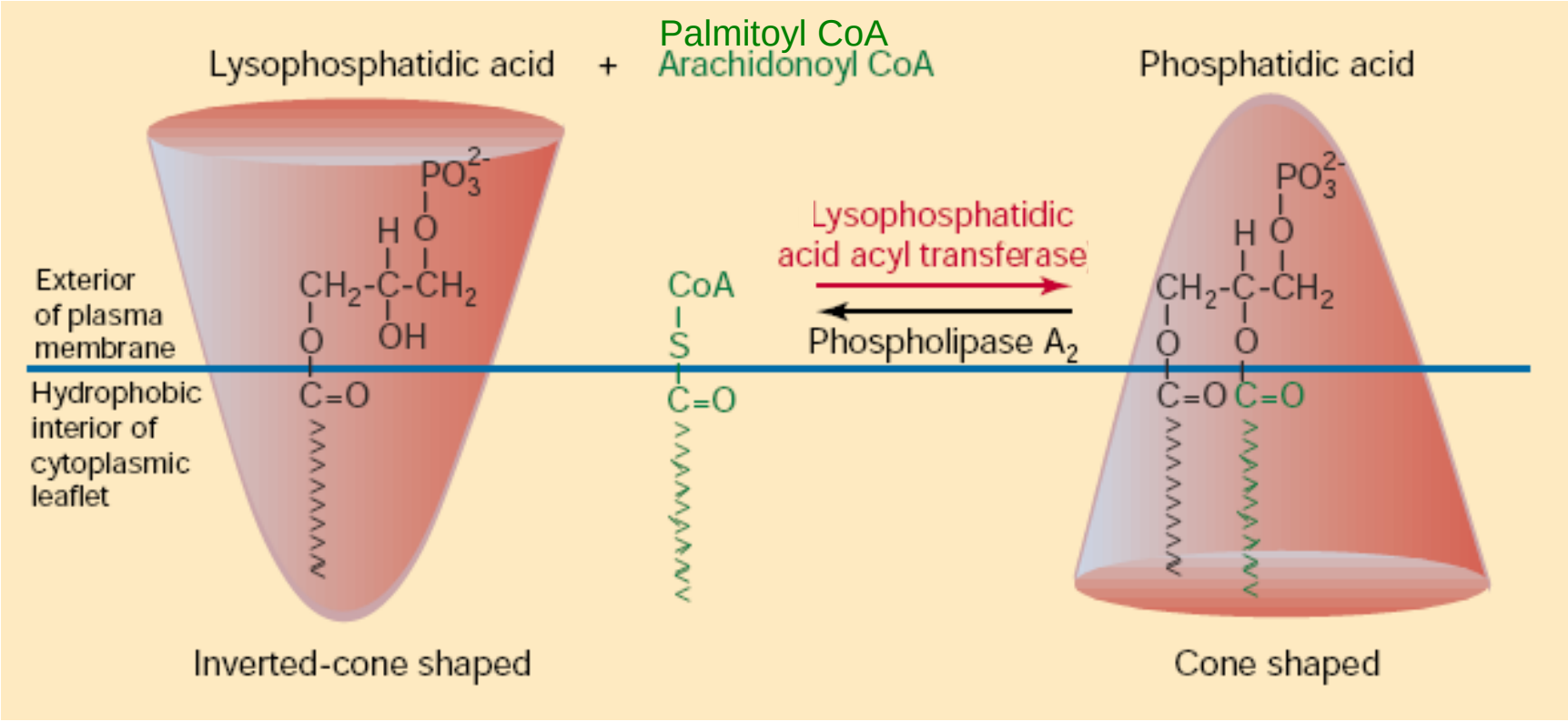
nAChR
K^+ kanalčki

Fosfolipidi so različnih oblik - njihova oblika in razporeditev vplivata na ukrivljenost membrane



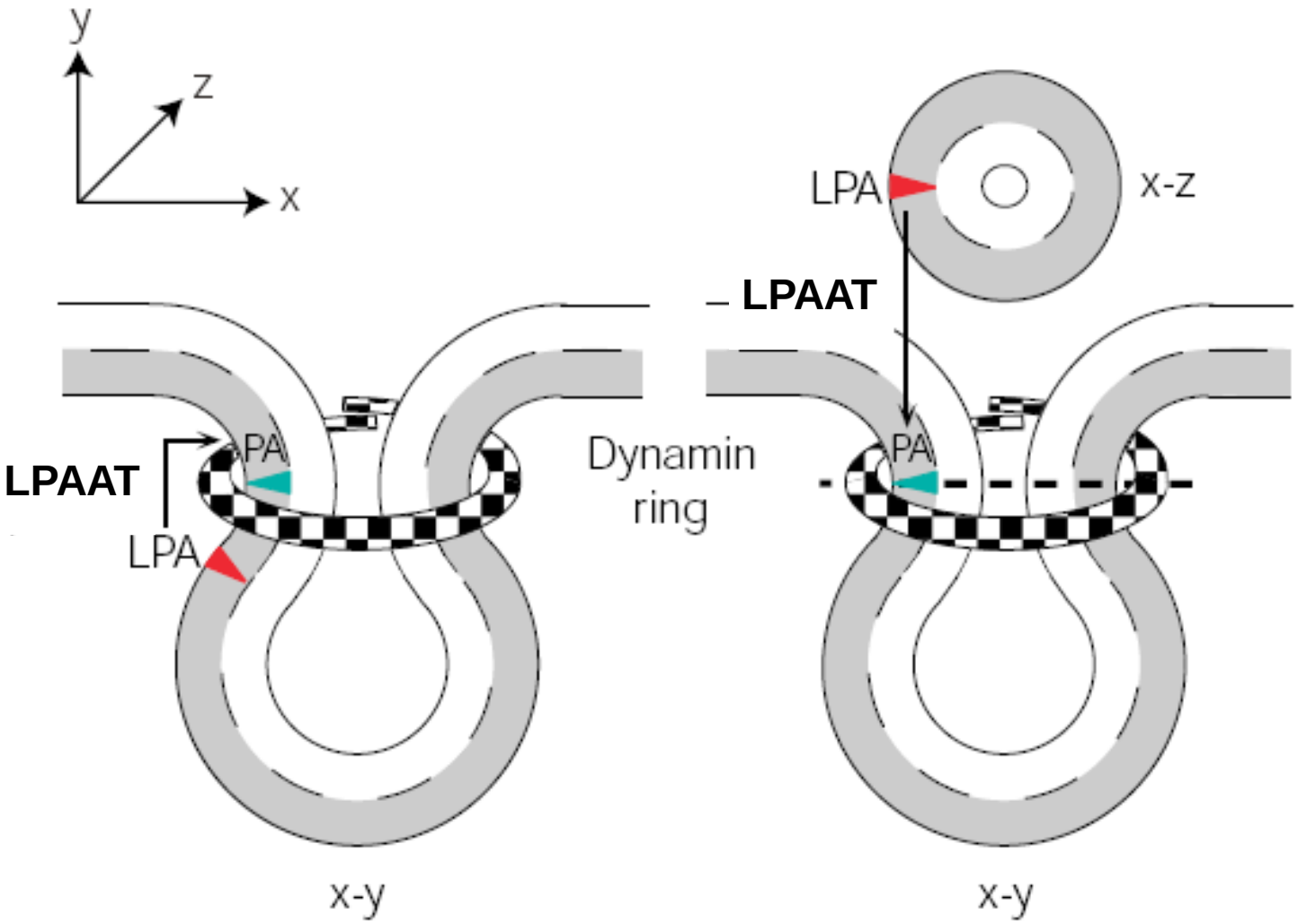
Spreminjanje geometrije lipidov

- Encimi, ki vplivajo na vsebnost in tip acilnih skupin v lipidih

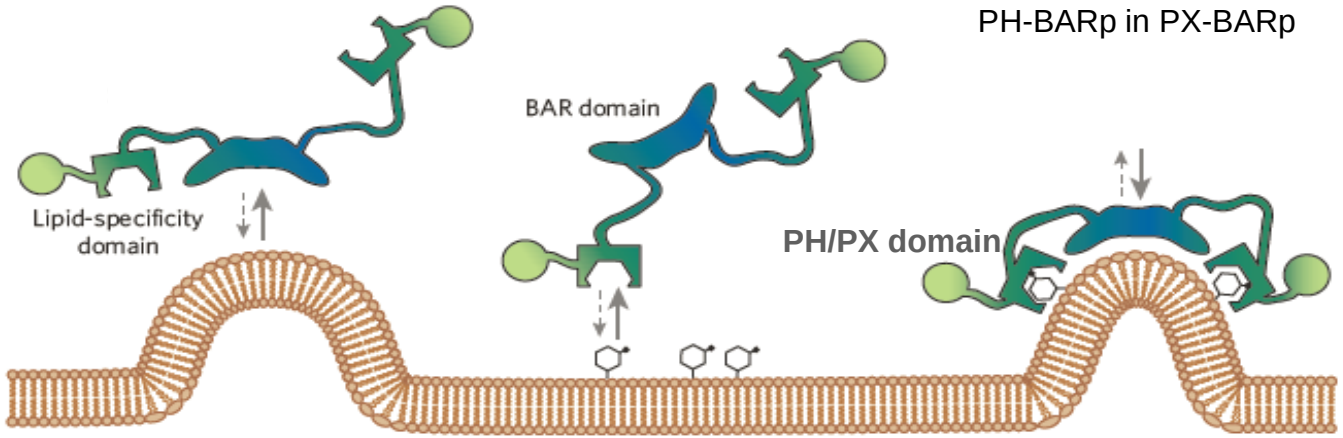


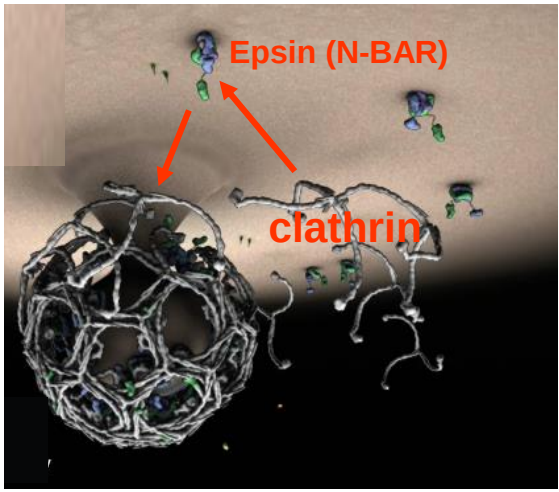
- Encimi, ki vplivajo na velikost lipidne „glave“

Vloga LPAAT-posredovane pretvorbe LPA v PA v eni od stopenj tvorbe sinaptičnega vezikla (odcepitev)

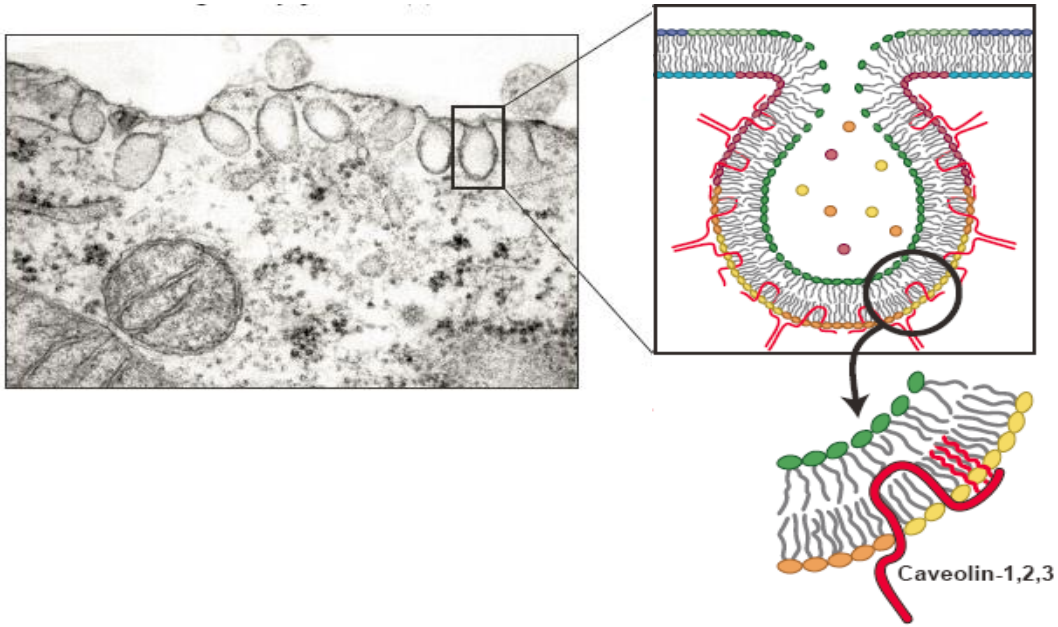


Posredno ukrivljanje membrane

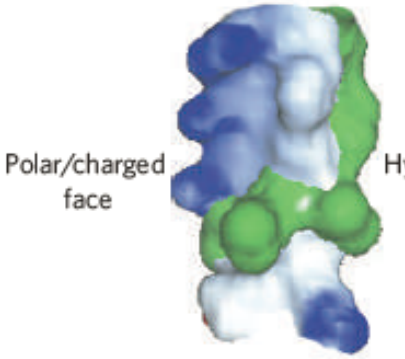


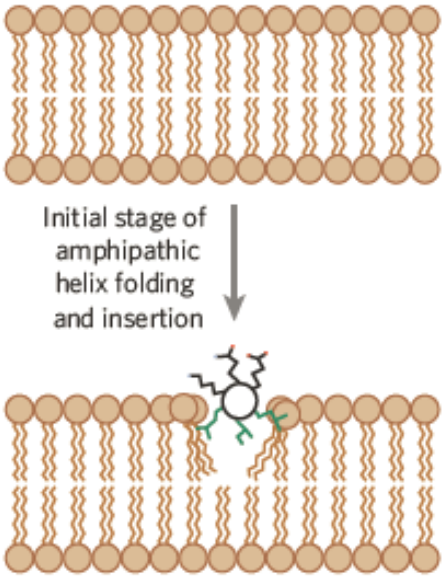


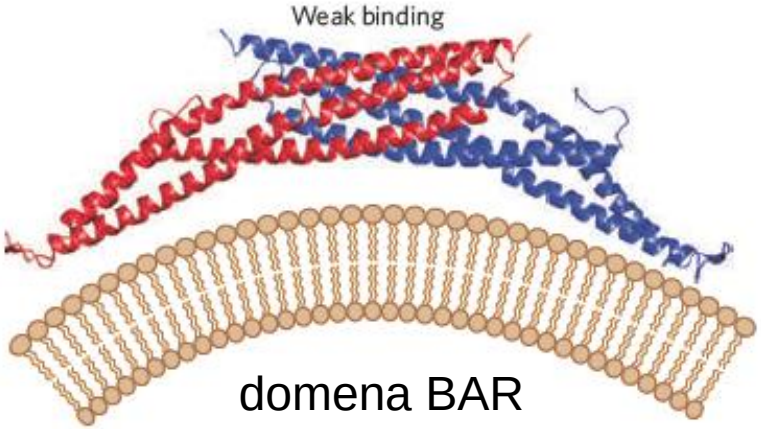
Neposredno ukrivljanje membrane



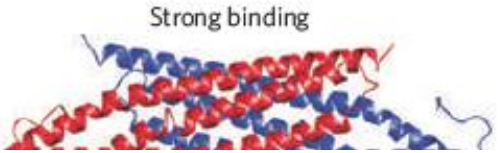
Amfipatična vijačnica in ukrivljanje membrane

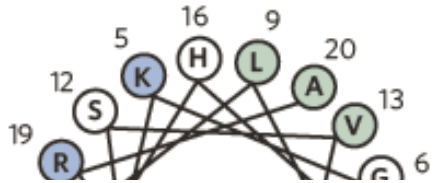


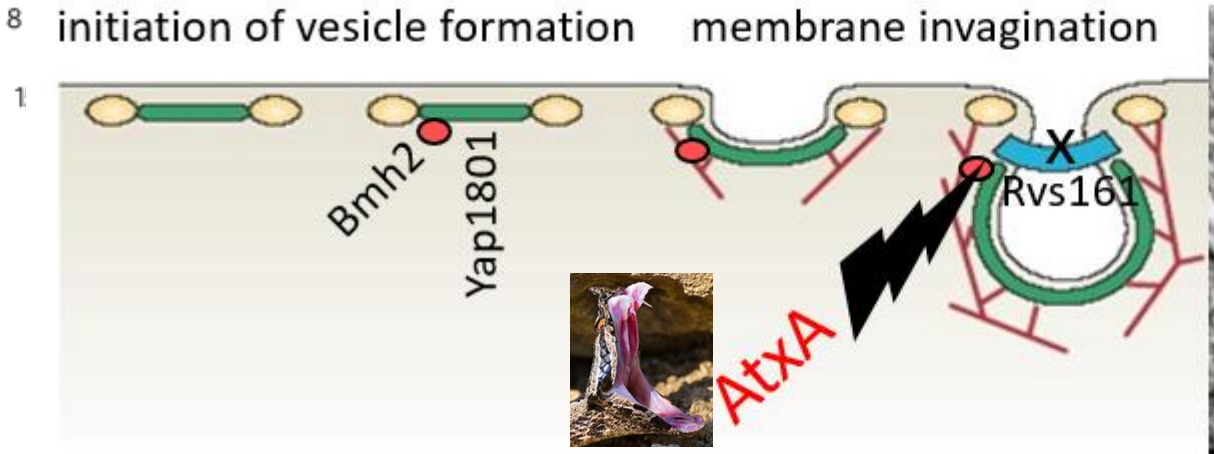




domena BAR
(**B**in-**A**mphiphysin-**R**vs)







Mattiazzi et al. (2012) PLoS One 7, e40931

Dodatno branje

McMahon, H.T. et al. (2010): Membrane curvature in synaptic vesicle fusion and beyond. Cell 140, 601-605.

Robinson, C.V. et al. (2019): Tools for understanding nanoscale lipid regulation of ion channels. Trends Biochem. Sci. 44, 795-806.