Medcelična signalizacija - 2

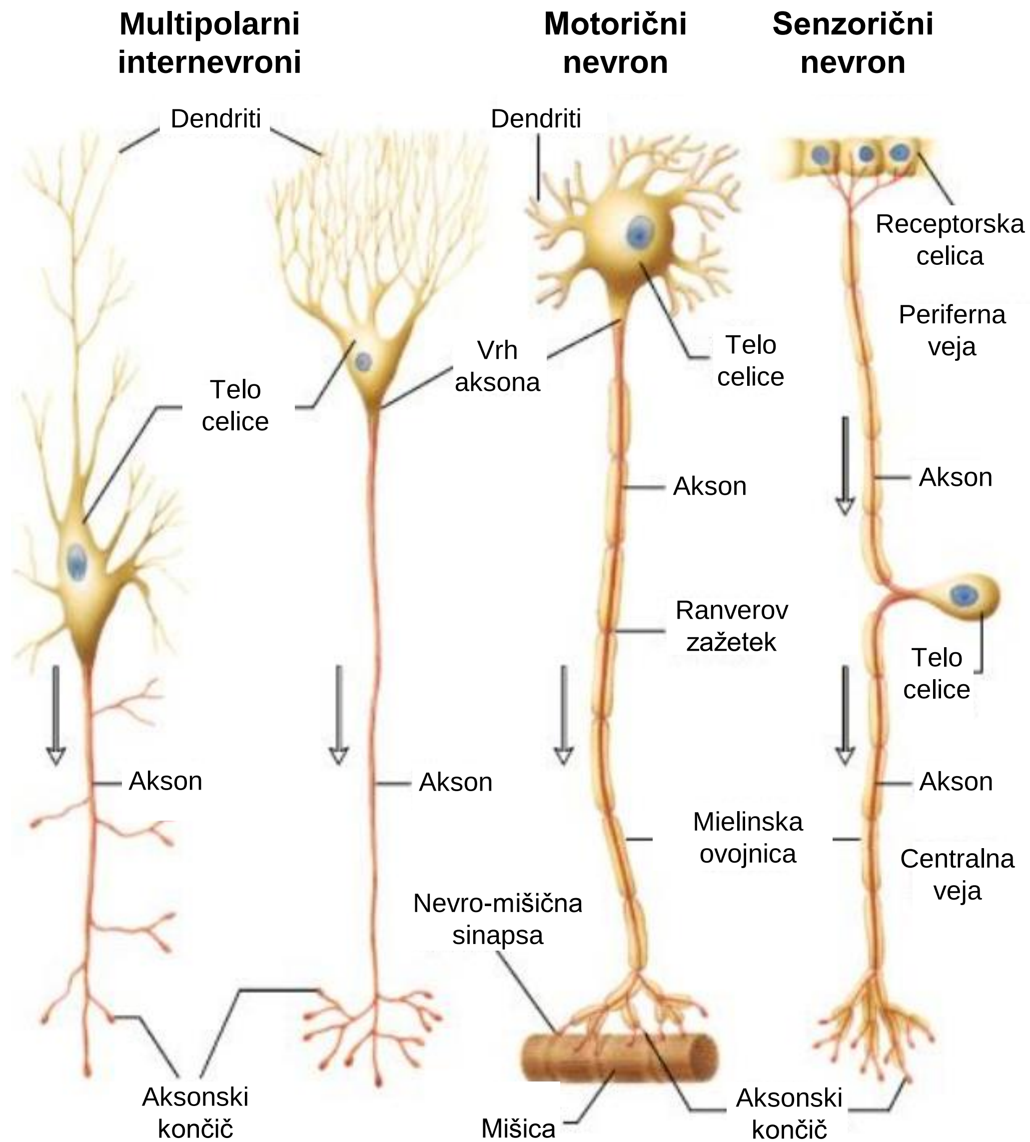
- Sprejem, prevajanje in prenos električnega signala.

- Ukrivljanje membran.

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

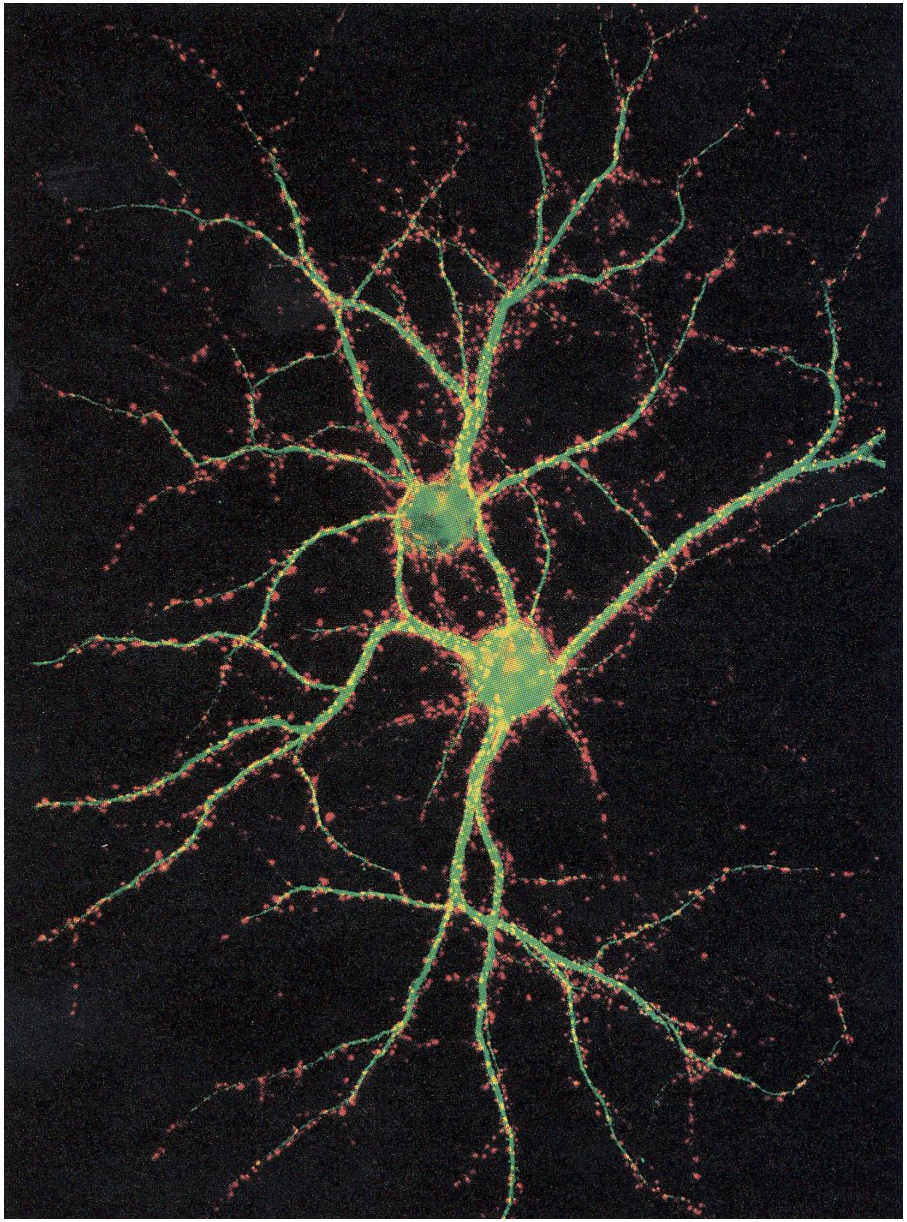
Sprejem, prevajanje, prenos električnega signala

Strukture tipičnih sesalskih nevronov



Nevroni se sporazumevajo s številnimi drugimi celicami

Hipokampalna internevrona



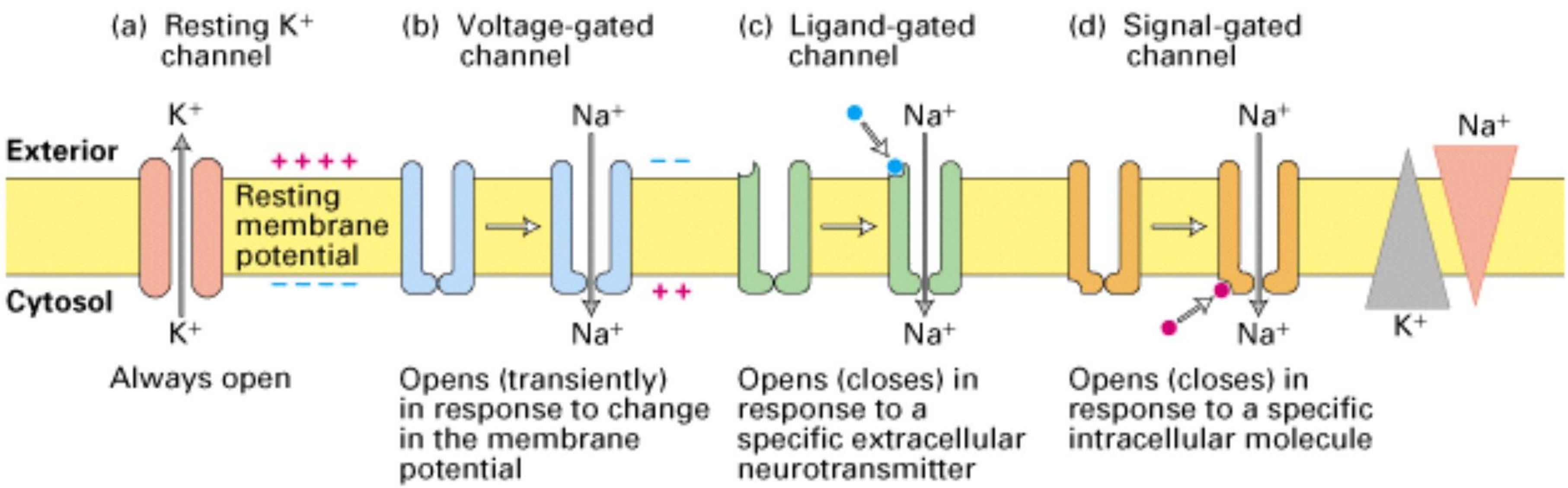
dendriti & telo celice - MAP2

aksonski končiči - sinaptotagmin

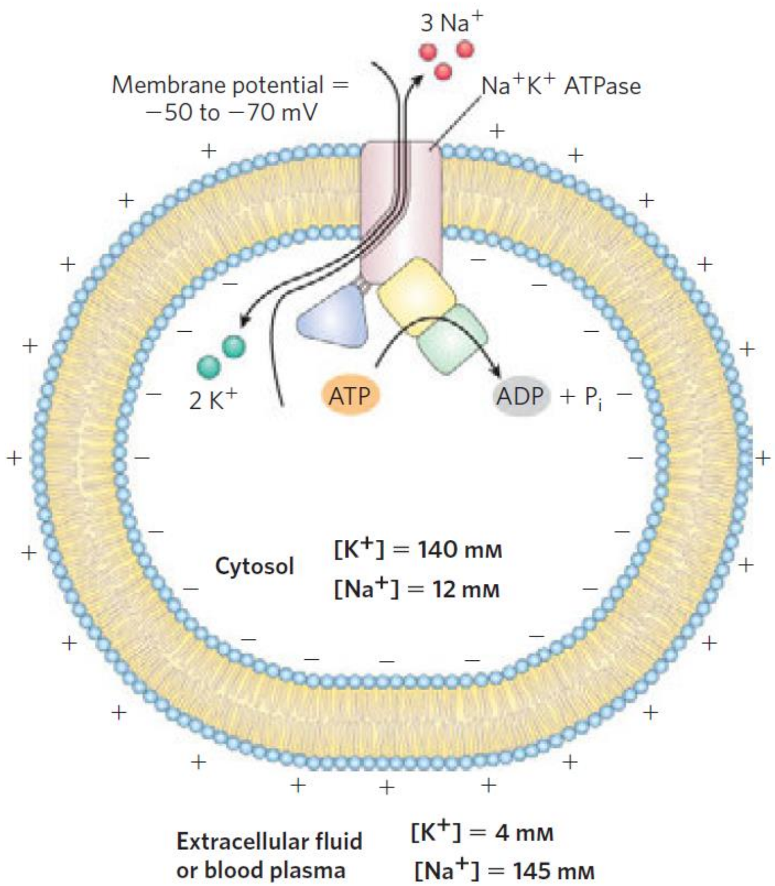
Kemična sinapsa

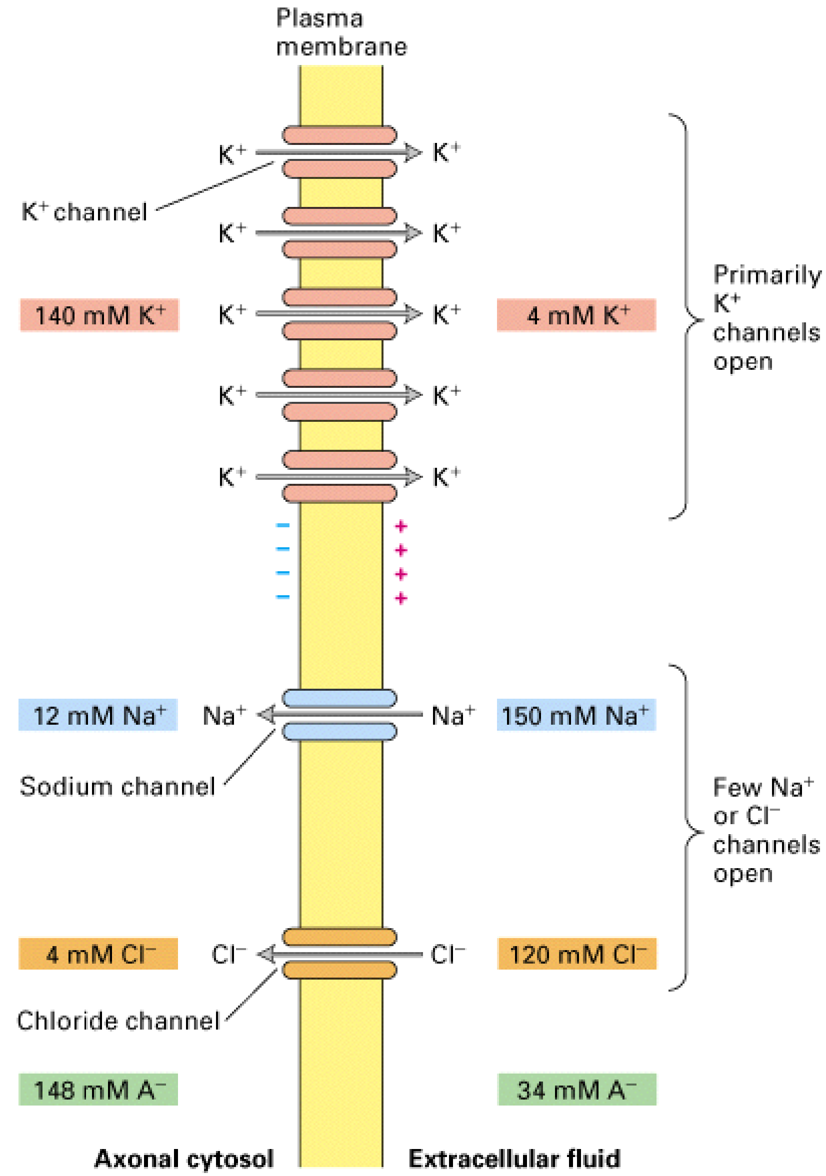
Sprejem, prevajanje in prenos električnega signala

Ionski kanali v PM nevrona:



Nastanek mirovnega potenciala na PM tipičnega vretenčarskega nevrona



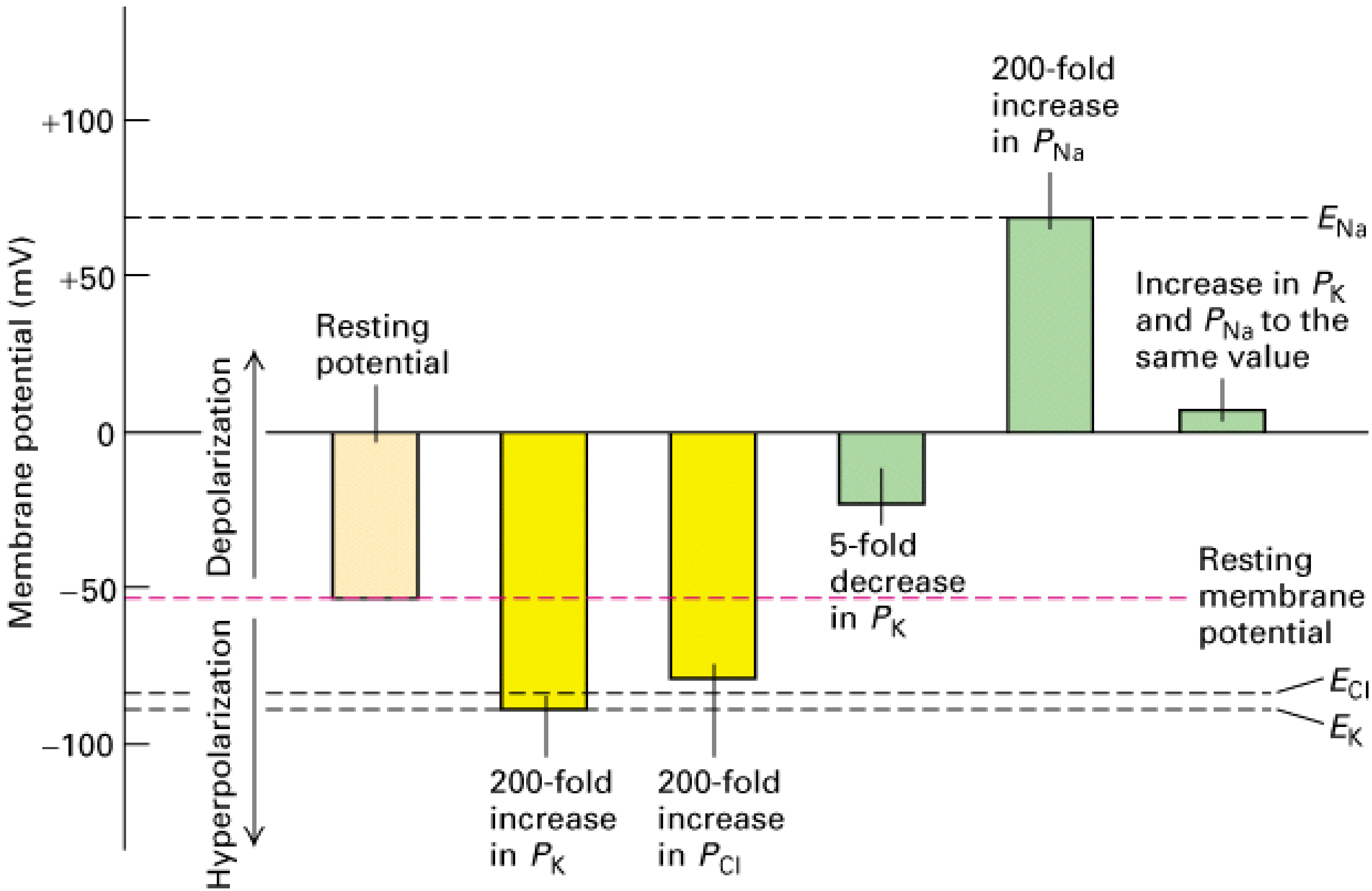


Ravnovesni električni potencial na PM celice

Nernstova enačba:

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

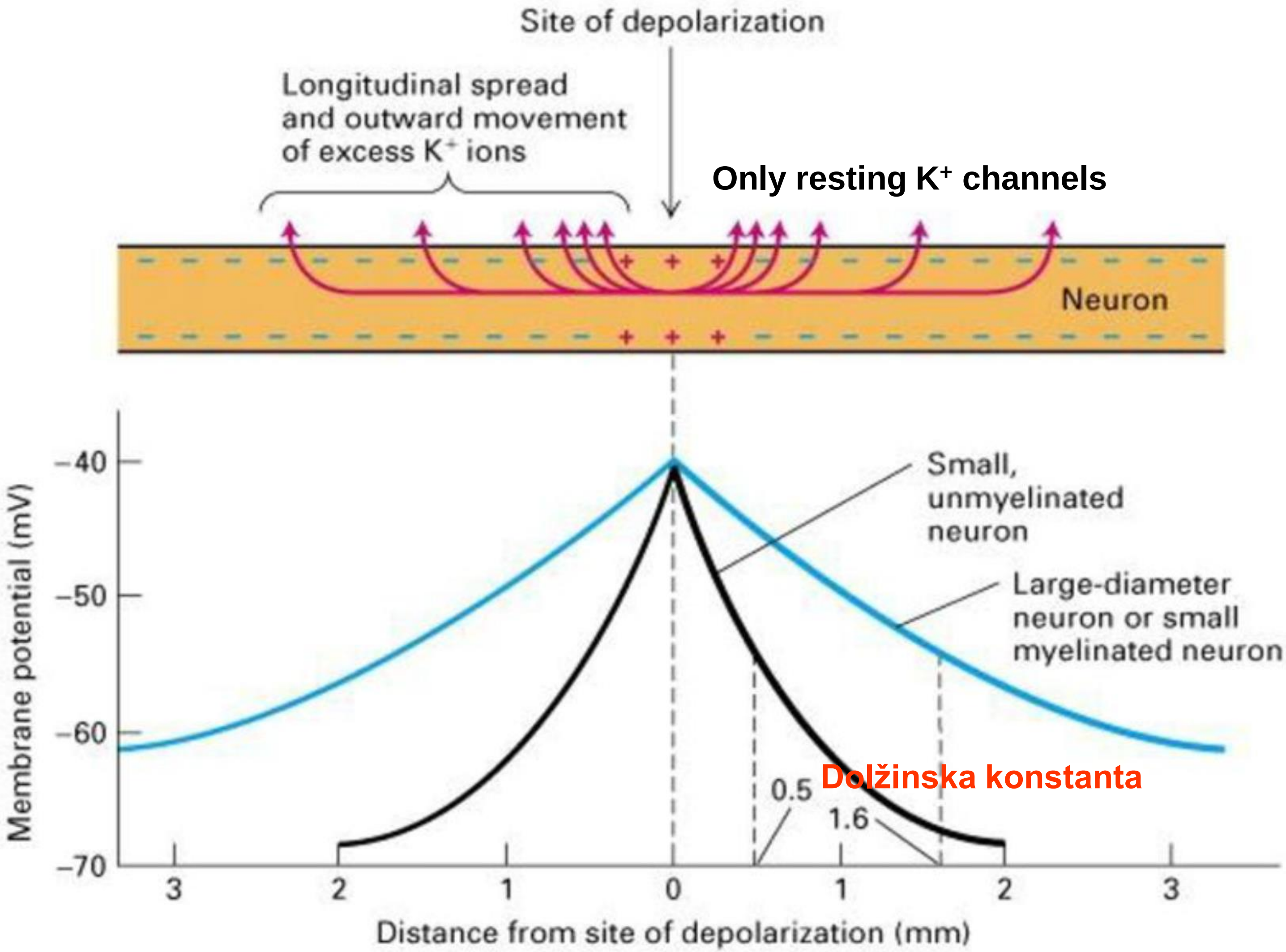
Odvisnost potenciala PM od prevodnosti za ione



Pasivno širjenje depolarizacije PM

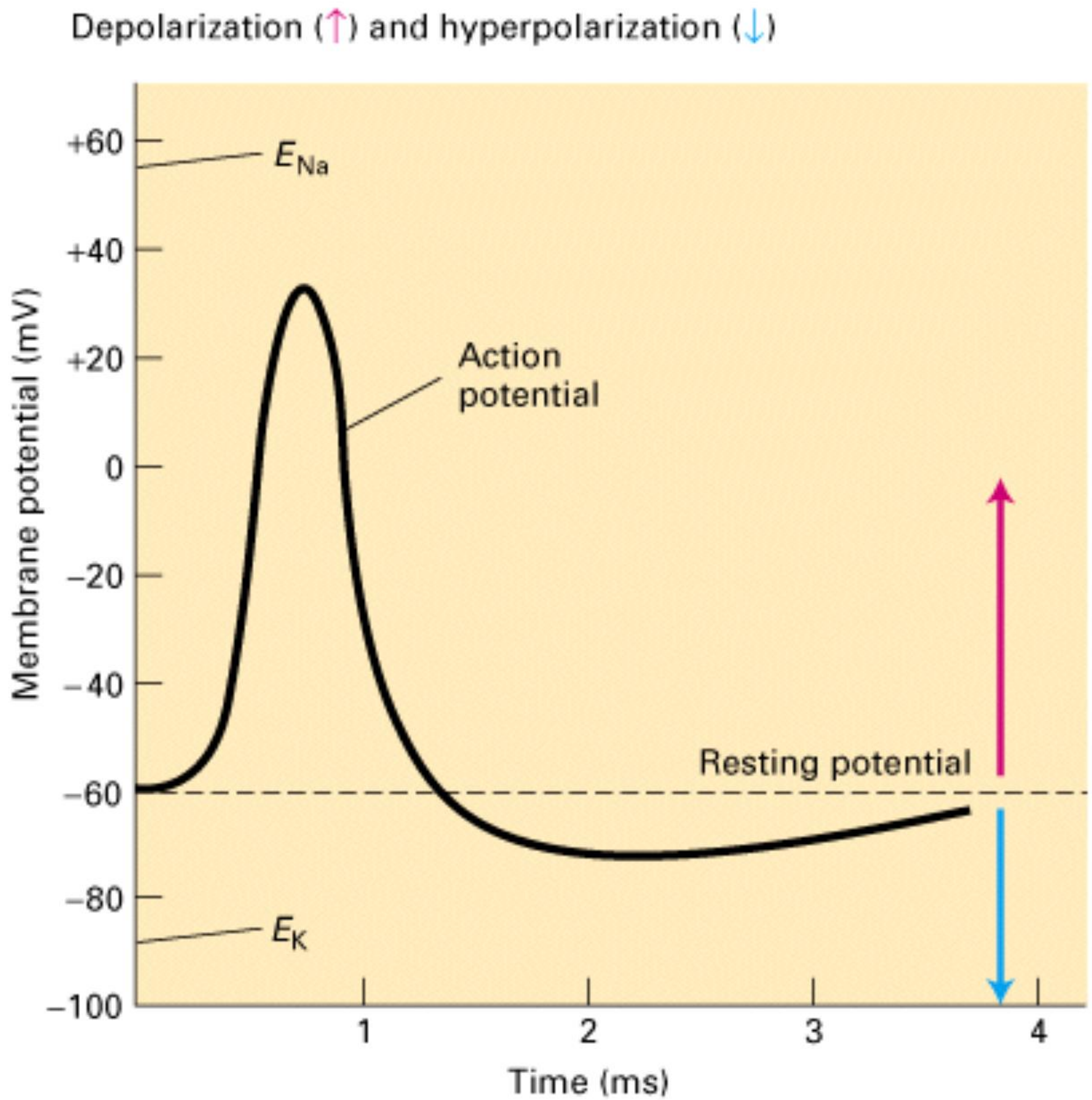
(brez napetostno-odvisnih ionskih kanalov)

Doseg depolarizacije PM na pasiven način je kratek

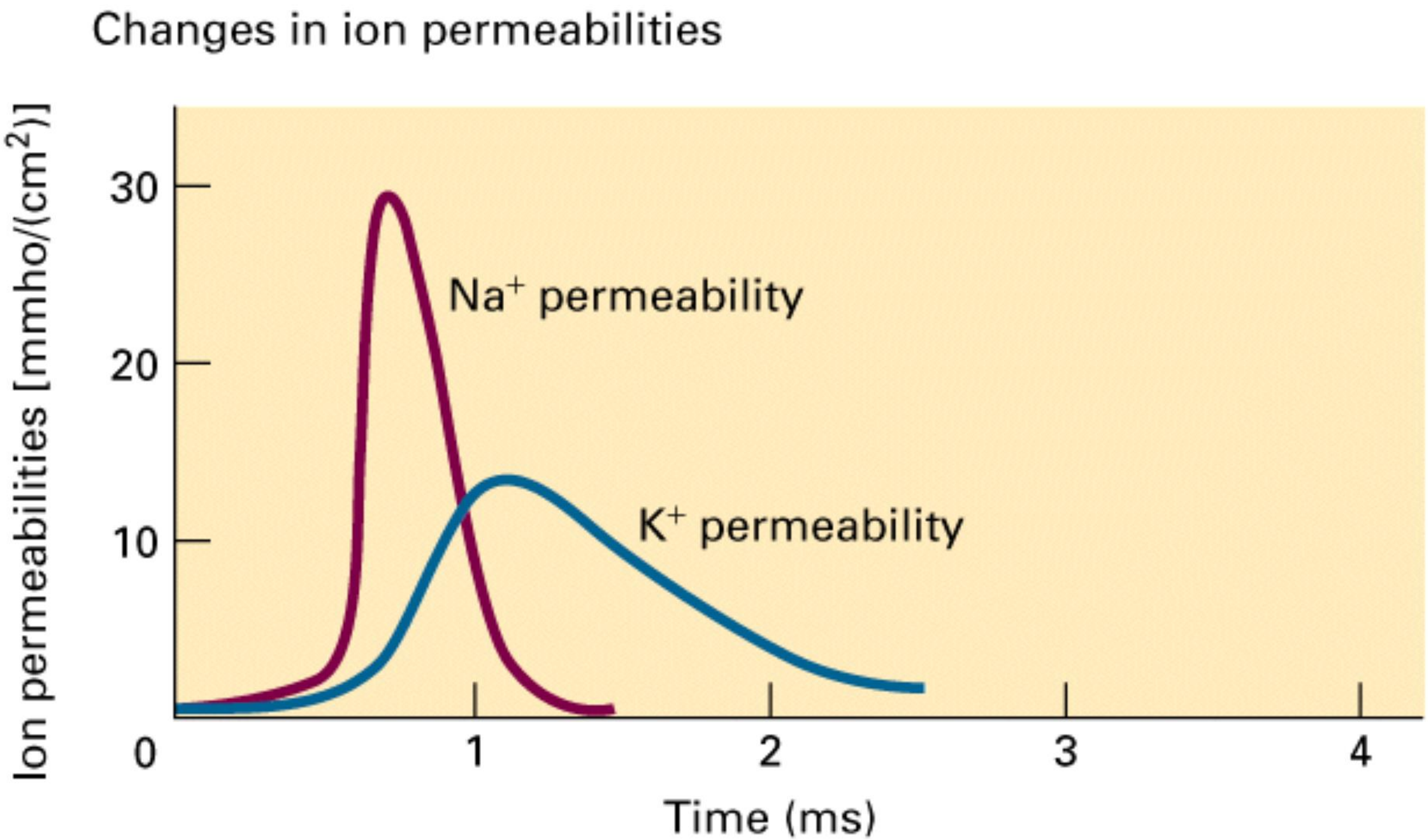


Napetostno-odvisni ionski kanali ustvarijo akcijski potencial

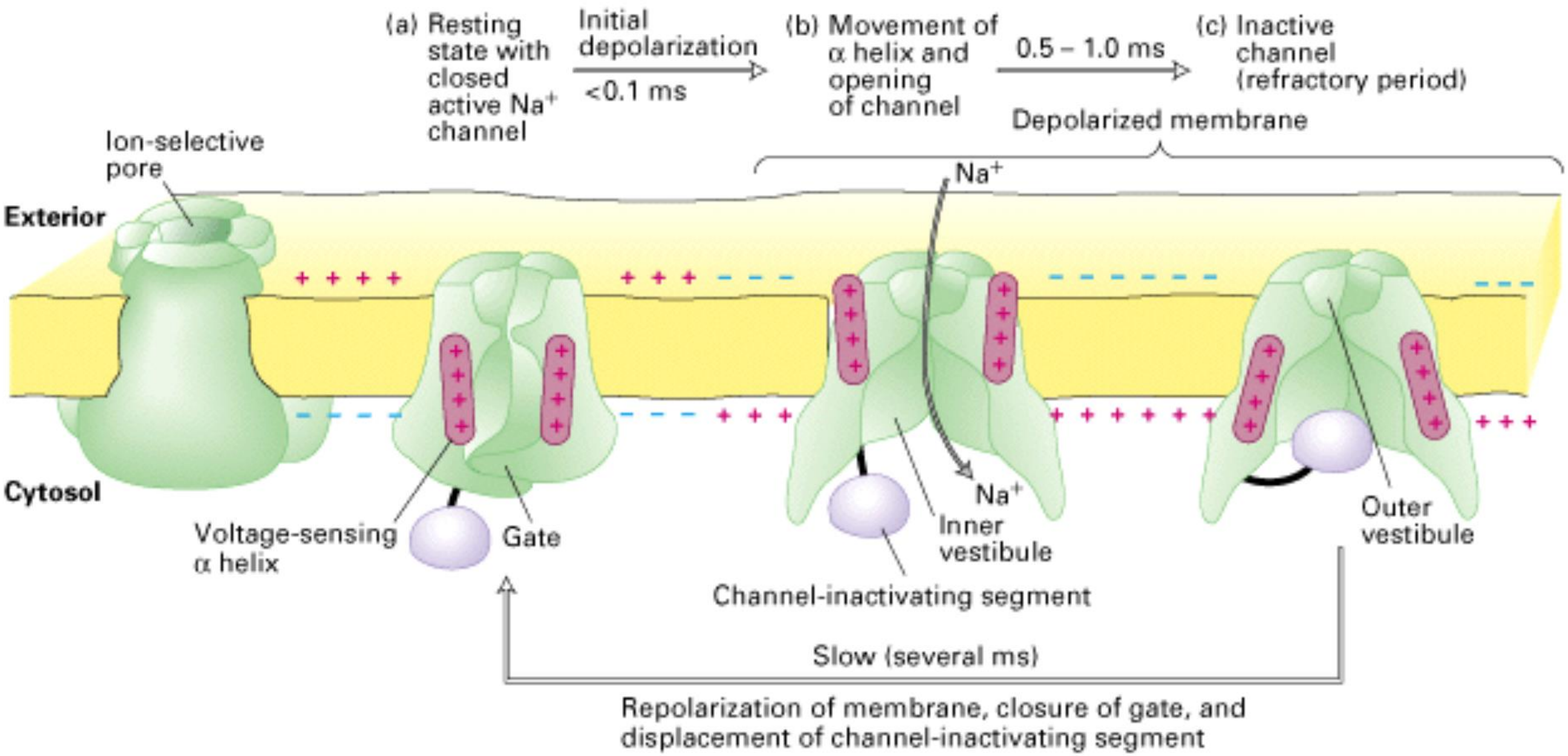
(depolarizacija, hiperpolarizacija in povratek membrane v mirovni potencial)



Ionska prevodnost PM med akcijskim potencialom



Struktura in funkcija napetostno-odvisnih Na^+ kanalov



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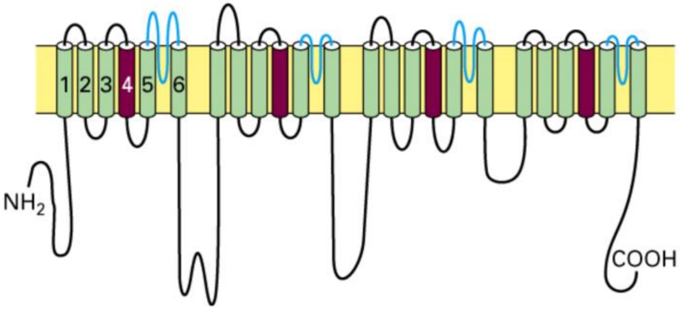
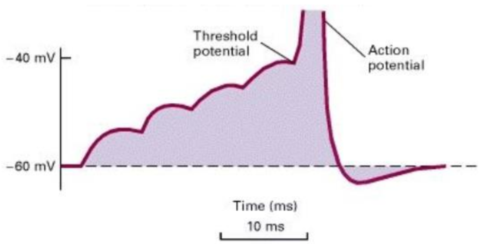
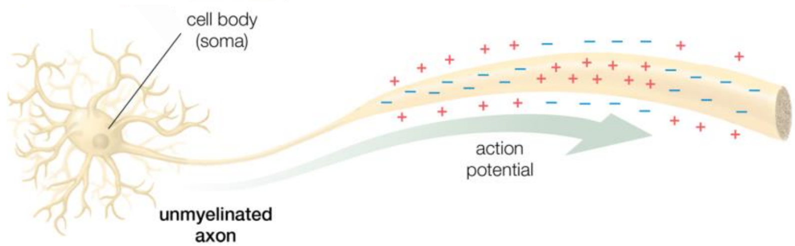
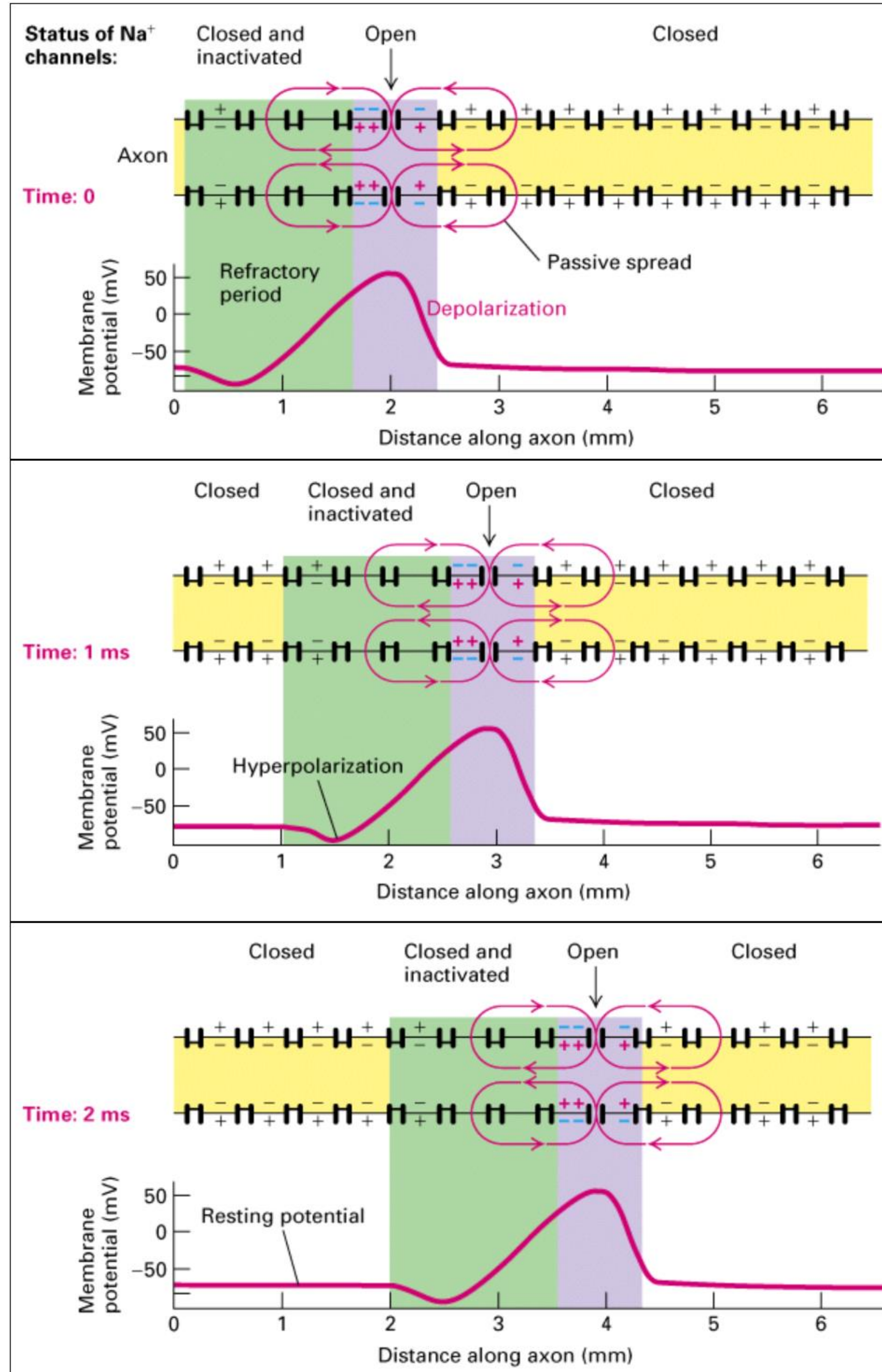


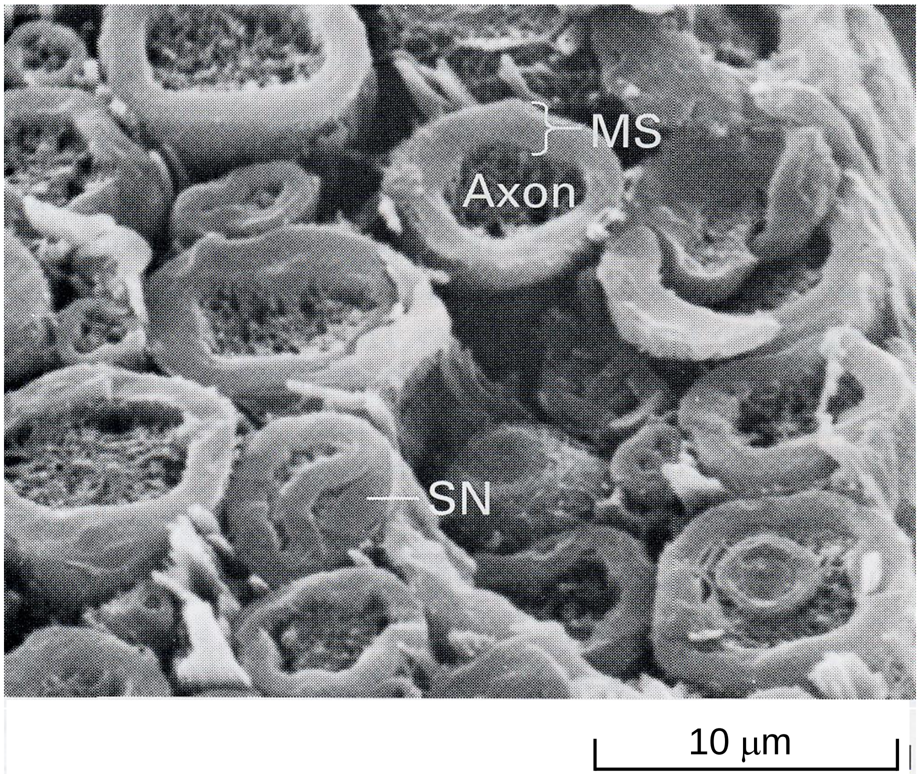
Širjenje akcijskega potenciala je enosmerno, proč od vira nastanka

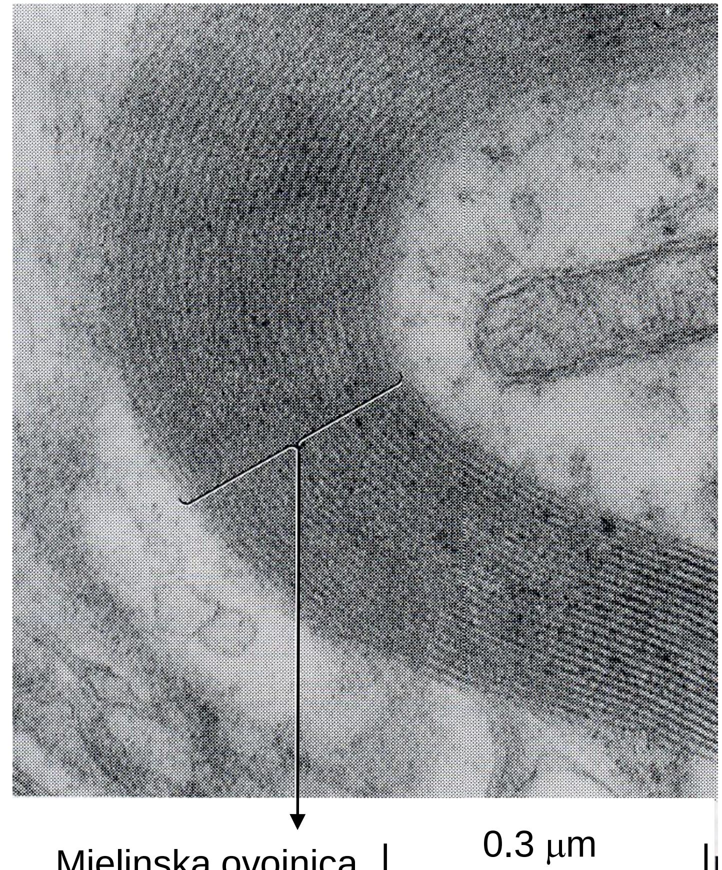






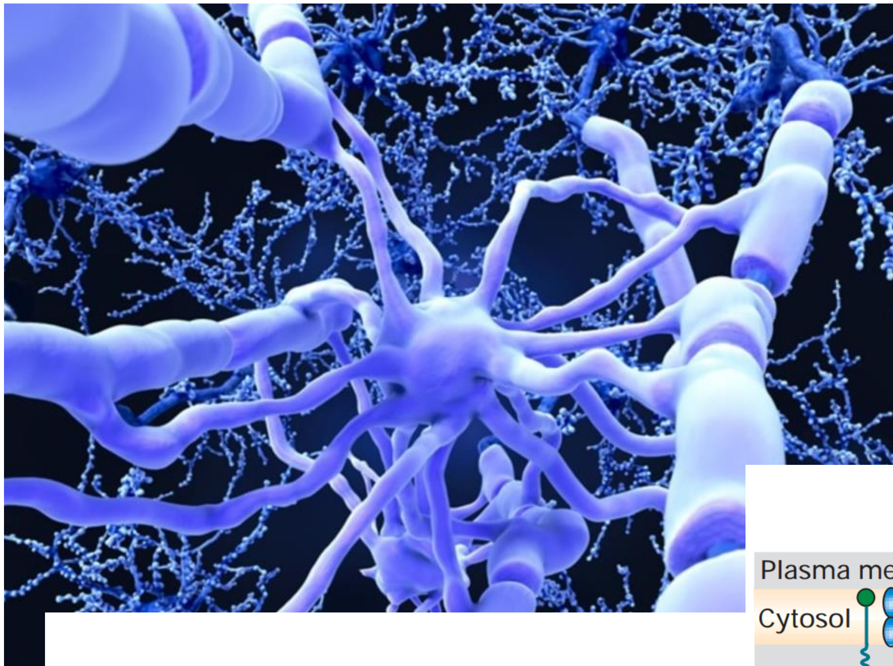
Mielinizacija aksonov

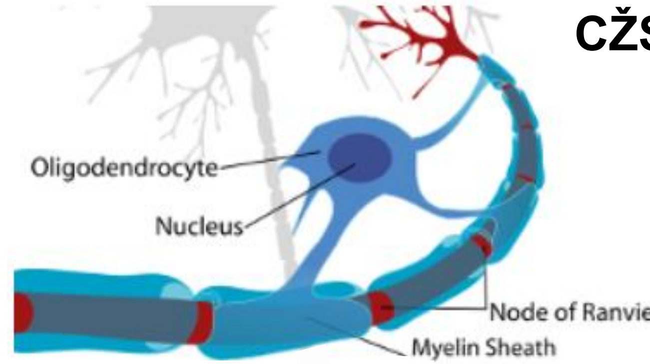




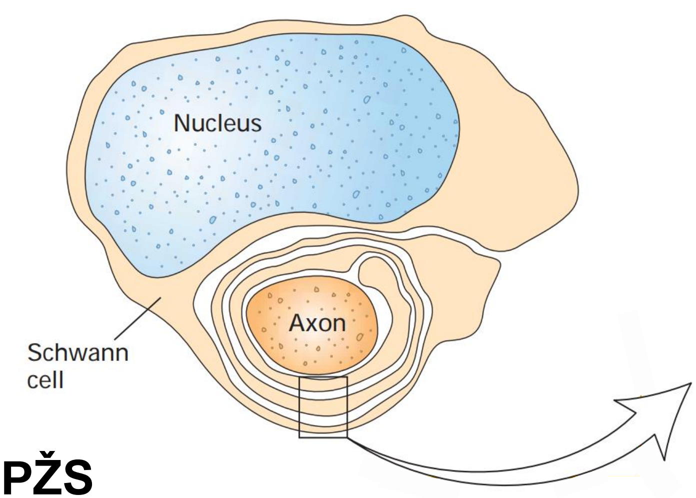
Mielinska ovojnica
50-100 membranskih plasti

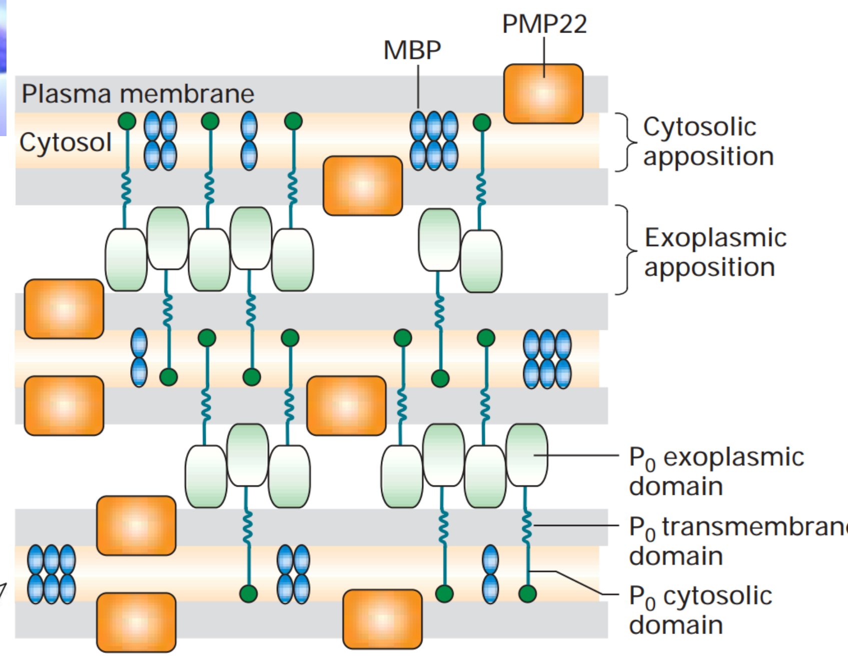
Struktura mielinske ovojnice



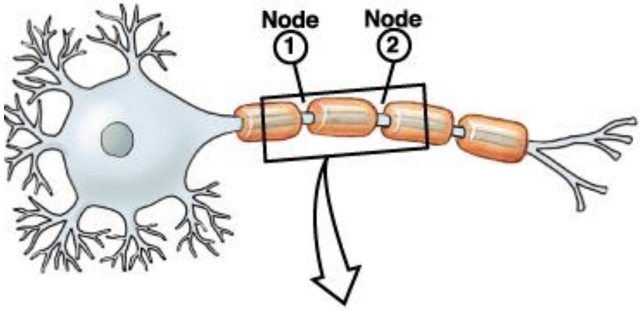


CŽS

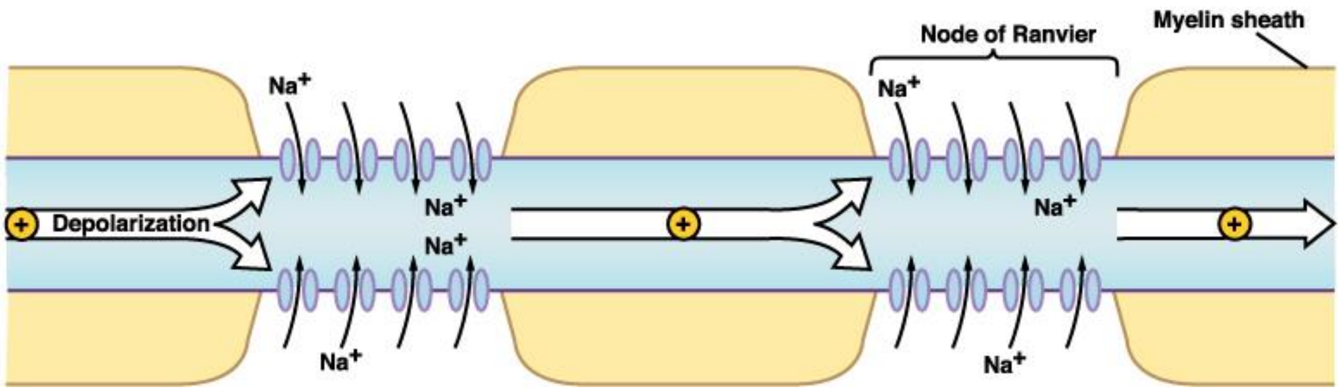




PŽS



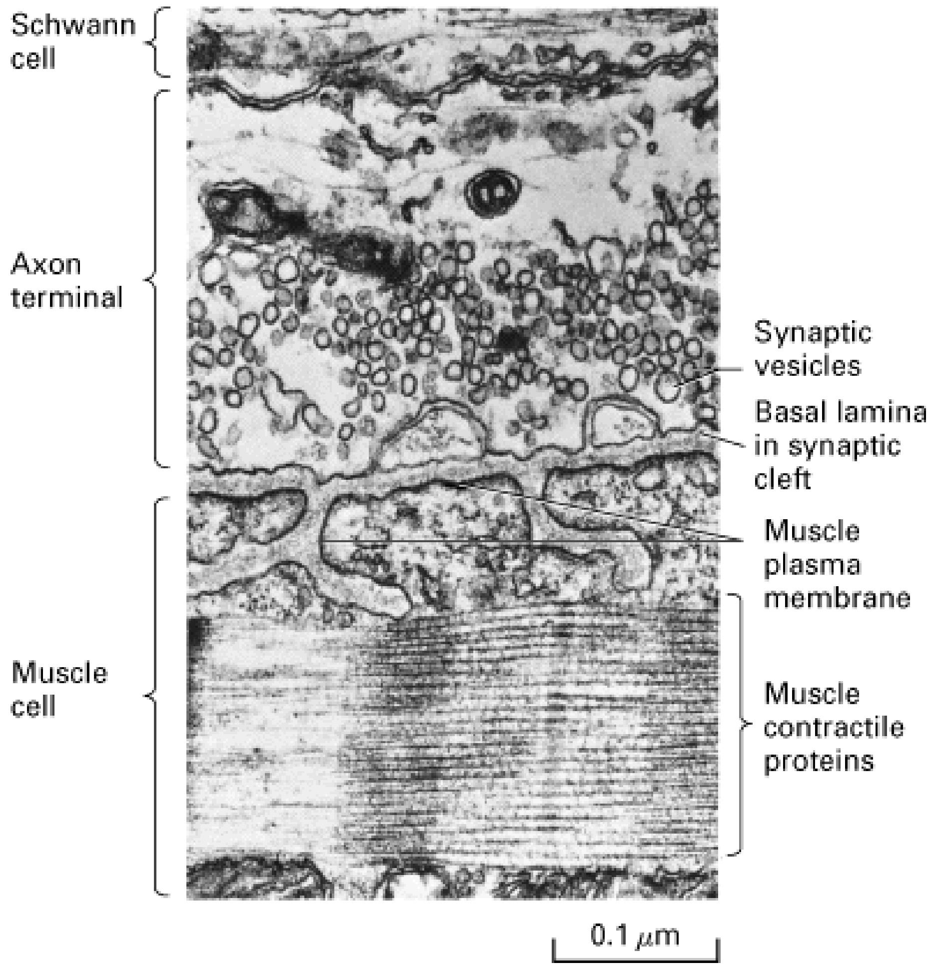
Mielinizacija poveča hitrost prevajanja Signala z ~1 m/s na 10-100 m/s.



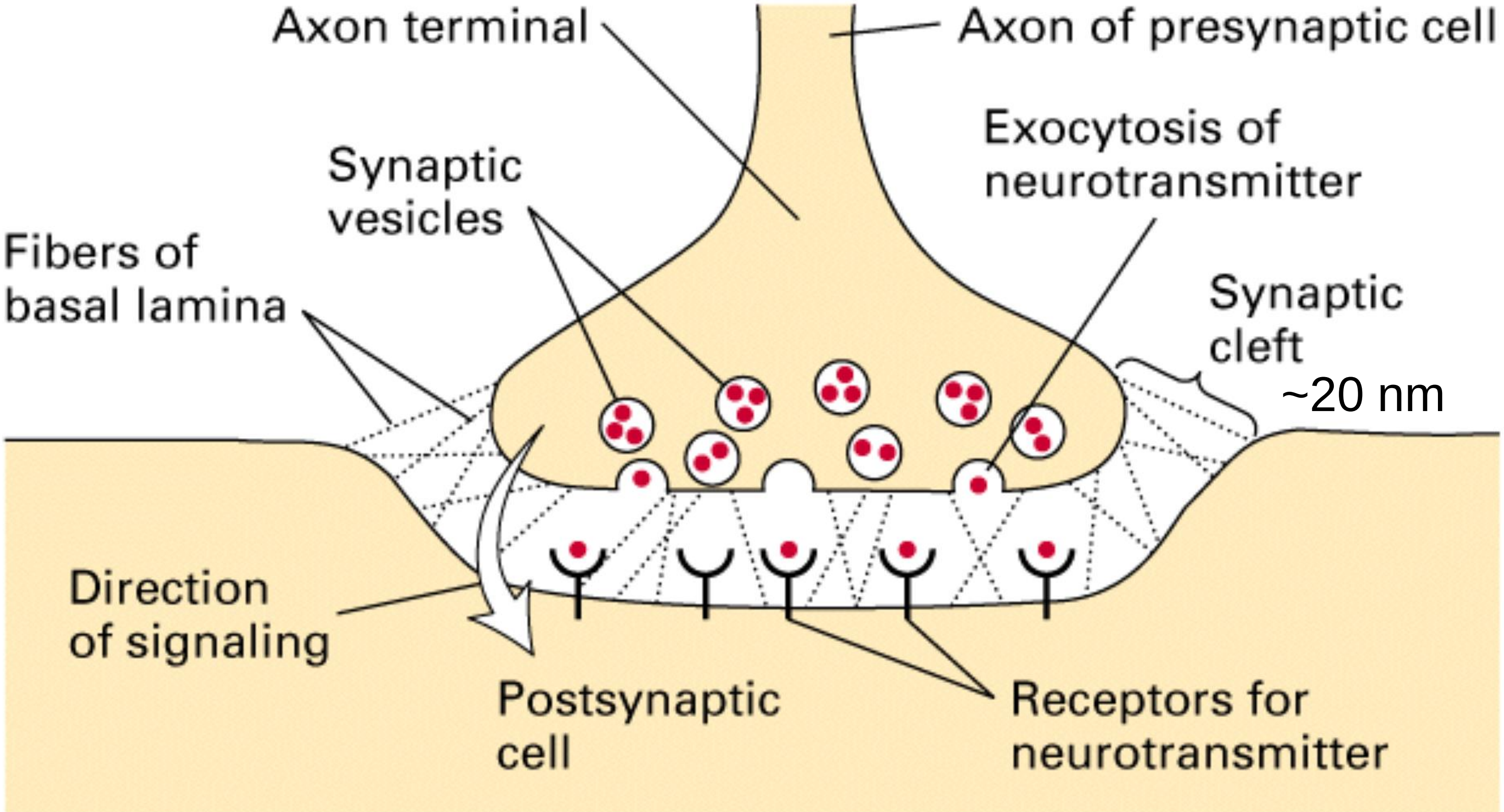
12 μm mieliniran vretenčarski akson
600 μm nemieliniran akson lignja
⇩
12 m/s
⇩
Radikalno zmanjšanje volumna nevrona & potrošnje ATP
⇩
Razvoj možganov pri vretenčarjih

Prenos signala v kemijski sinapsi

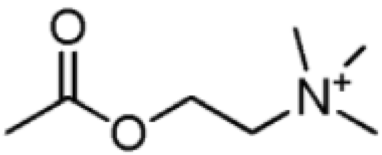
(žabji živčno-mišični stik)

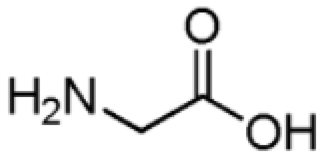


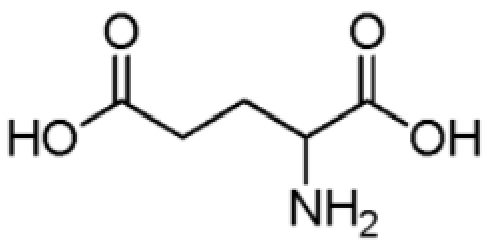
Kemijska sinapsa - shematsko

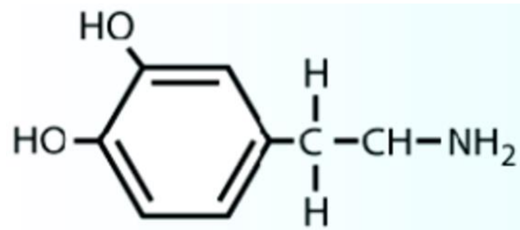


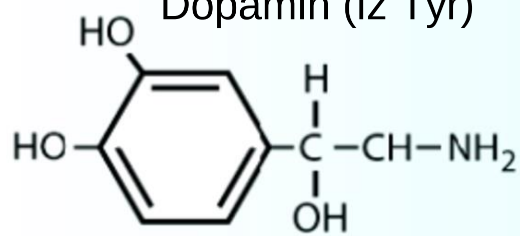
Klasični nevrotransmiterji

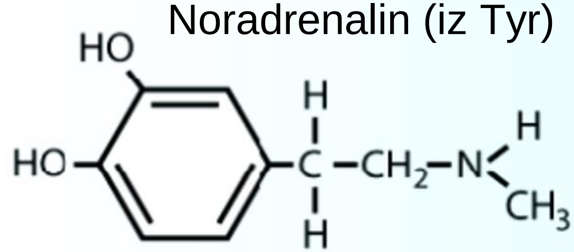

Acetilholin

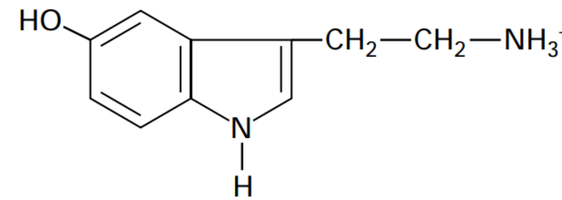

Glicin

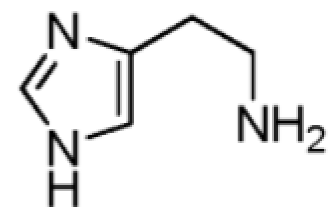

Glutamat

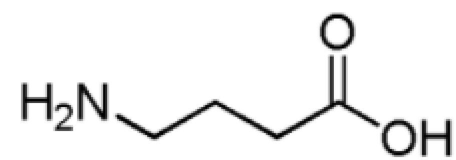

Dopamin (iz Tyr)


Noradrenalin (iz Tyr)


Adrenalin (iz Tyr)

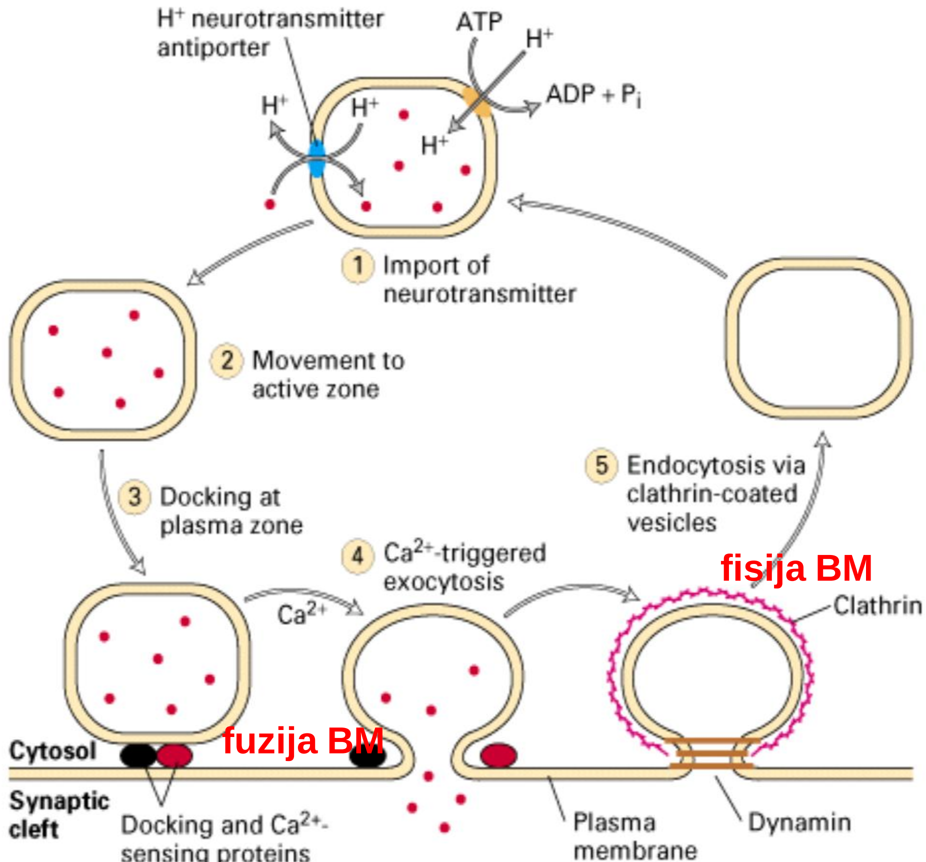

Serotonin (iz Trp)

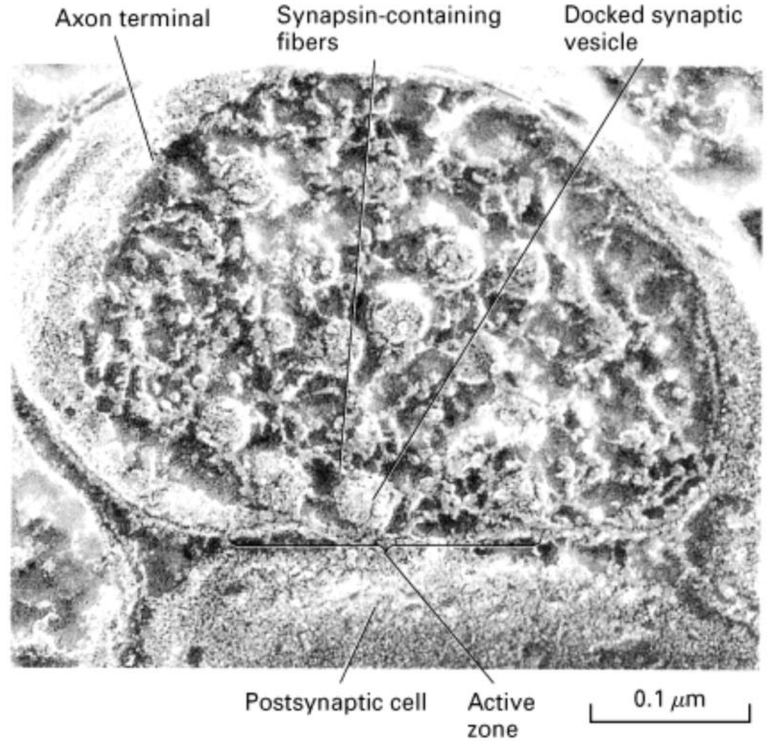

Histamin (iz His)

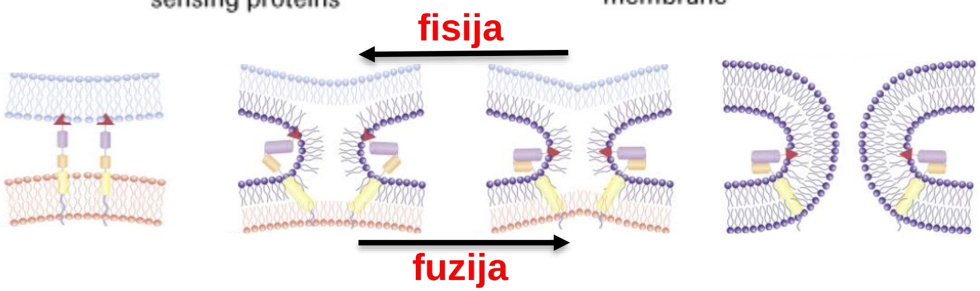

γ-Aminomaslena kislina (GABA; iz Glu)

Cikel sinaptičnega mešička

Biološke membrane se združujejo/zlivajo in razdružujejo/cepijo

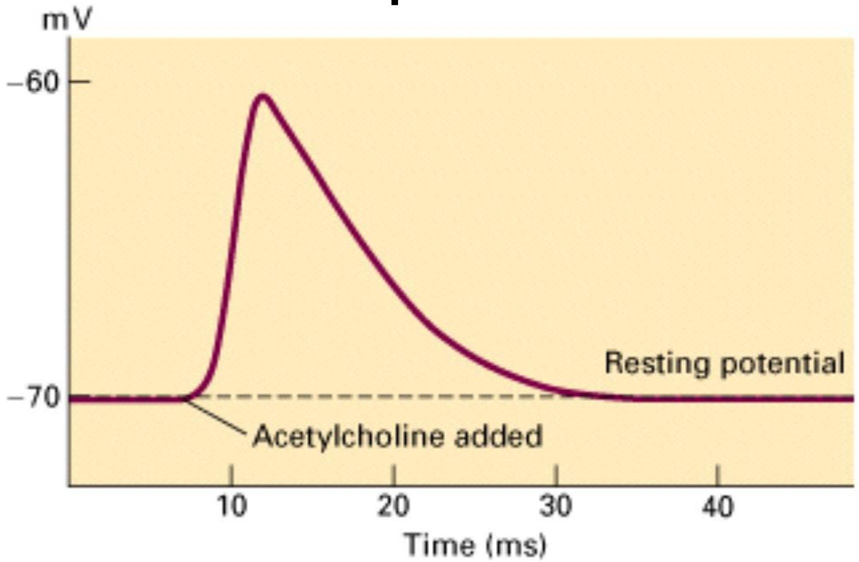






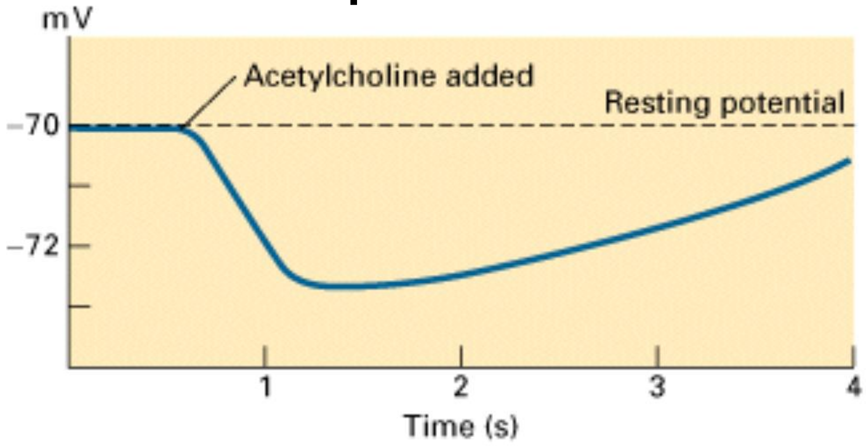
Ekscitatorni in inhibitorni odziv postsinaptične celice

Ekscitatorna sinapsa



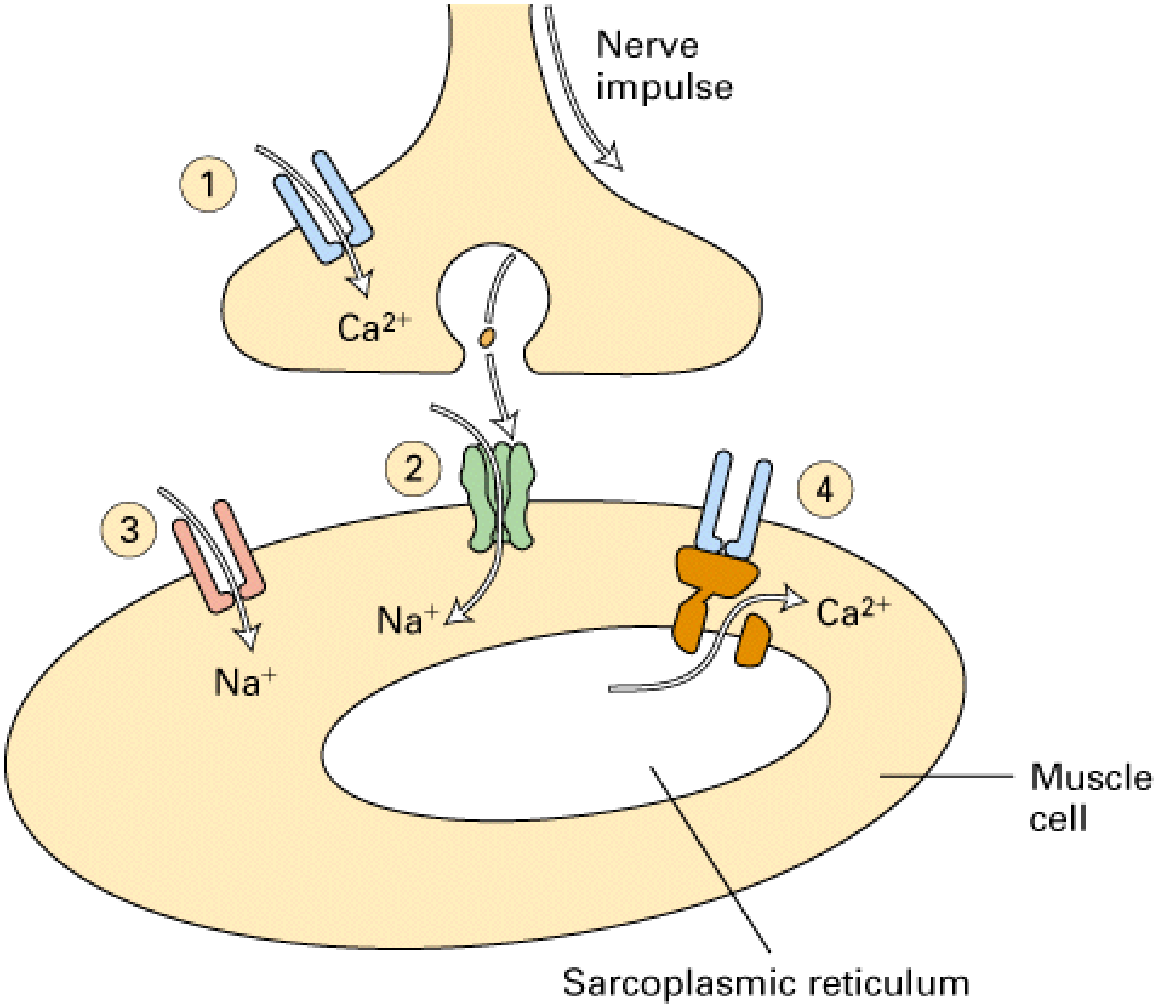
Žabja skeletna mišica
- nikotinski AChR
(**ekscitatorni receptor**)

Inhibitorna sinapsa



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

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



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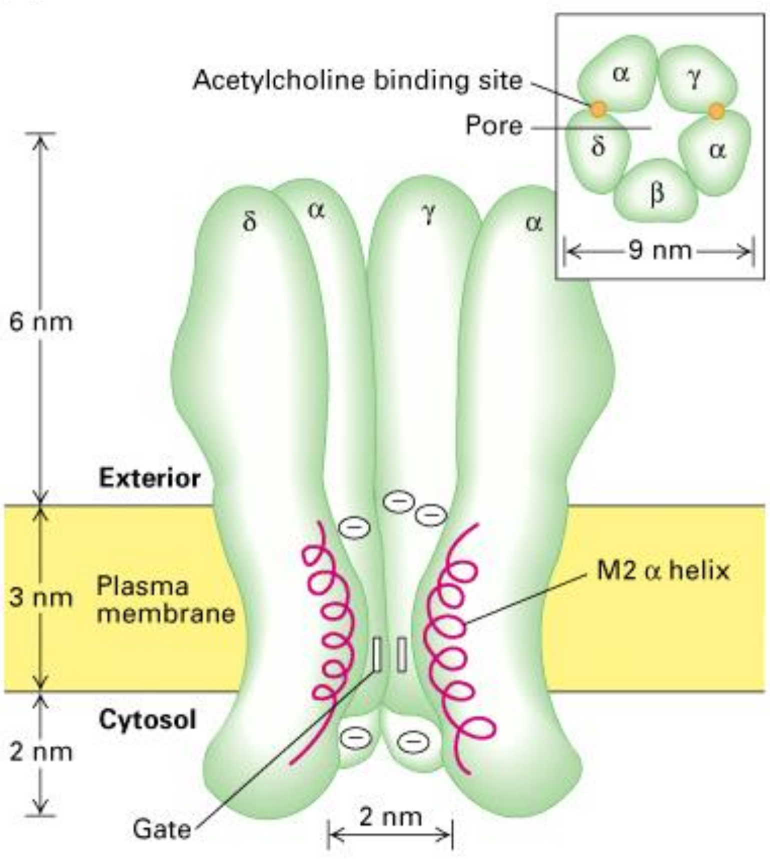
Nikotinski ACh receptor



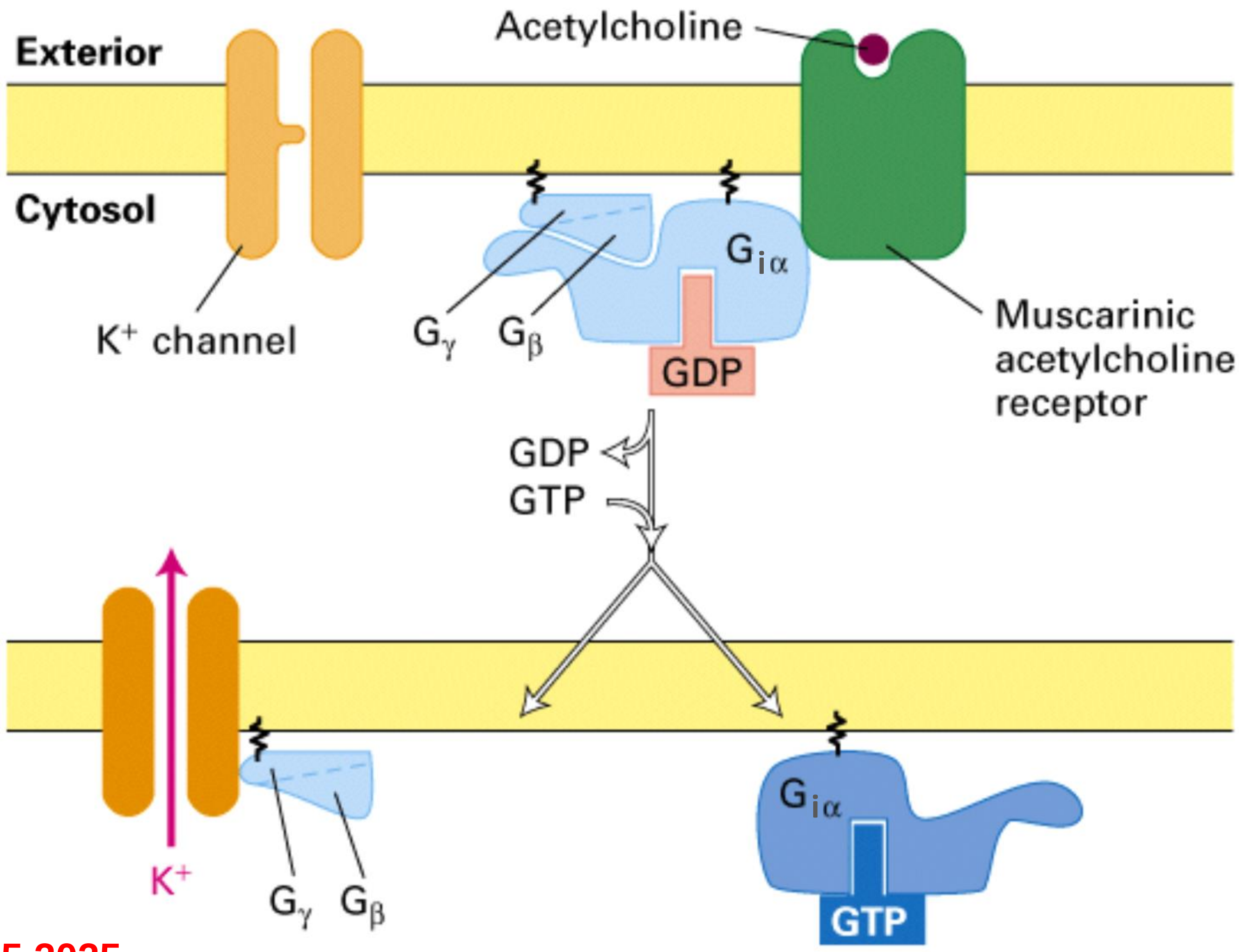
Hitre sinapse

Nevrotransmiterski receptorji, z ligandi-regulirani ionski kanali		
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 kanali so navedeni v oklepaju.

[2] N-metil-*D*-aspartat

Muskarinski ACh receptor v PM srčne mišice (M2)



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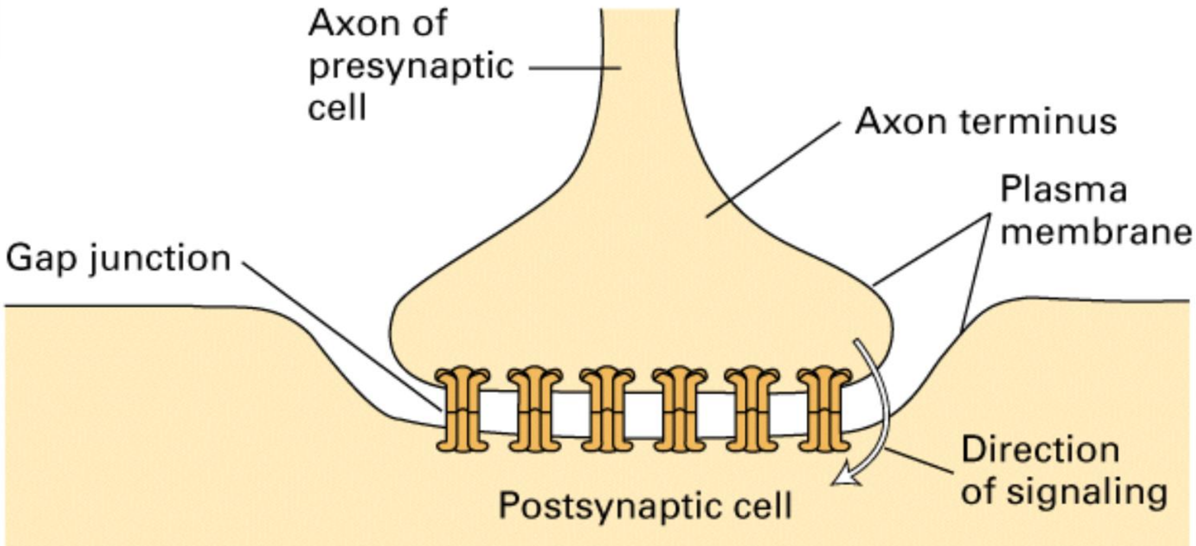
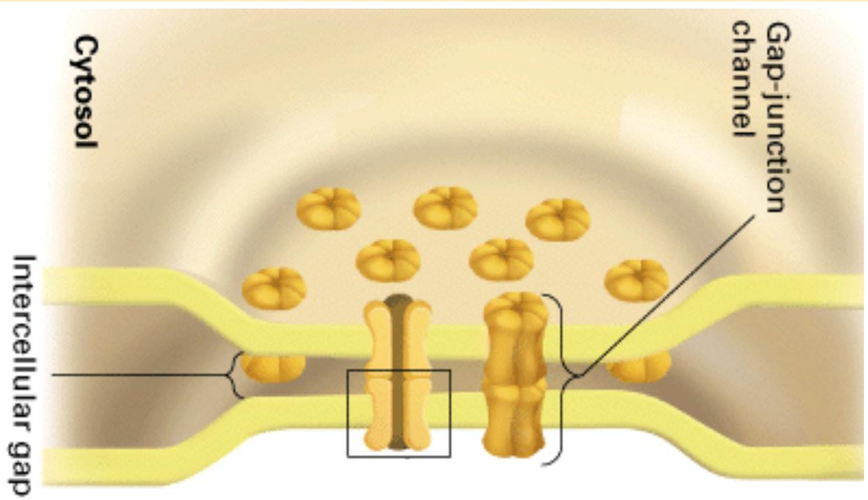
Počasne sinapse

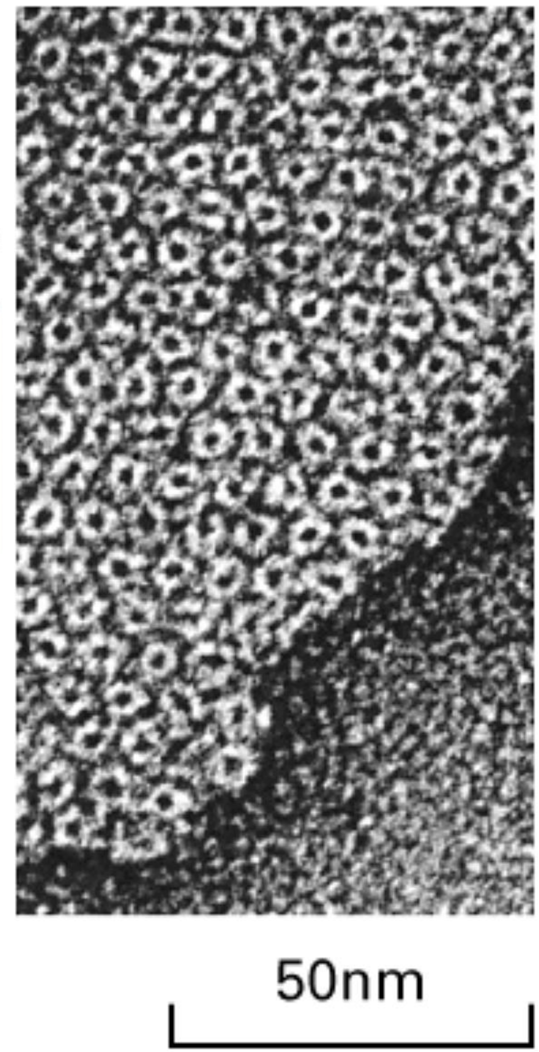
Primeri GPCR za nevrotransmiterje in nevropeptide	
GPCR za klasične nevrotransmiterje	
Acetilholin* (muskarinski receptor)	γ-Aminomaslena kislina* (GABA, B-razred)
Adenozin	Glutamat*
ATP	Histamin
Dopamin	Serotonin* ($5HT_1$, $5HT_2$, $5HT_5$ receptorji)
Adrenalin, noradrenalin	
GPCR za nevropeptide	
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 kanale.
Njihovi GPCR so navedeni v oklepaju.

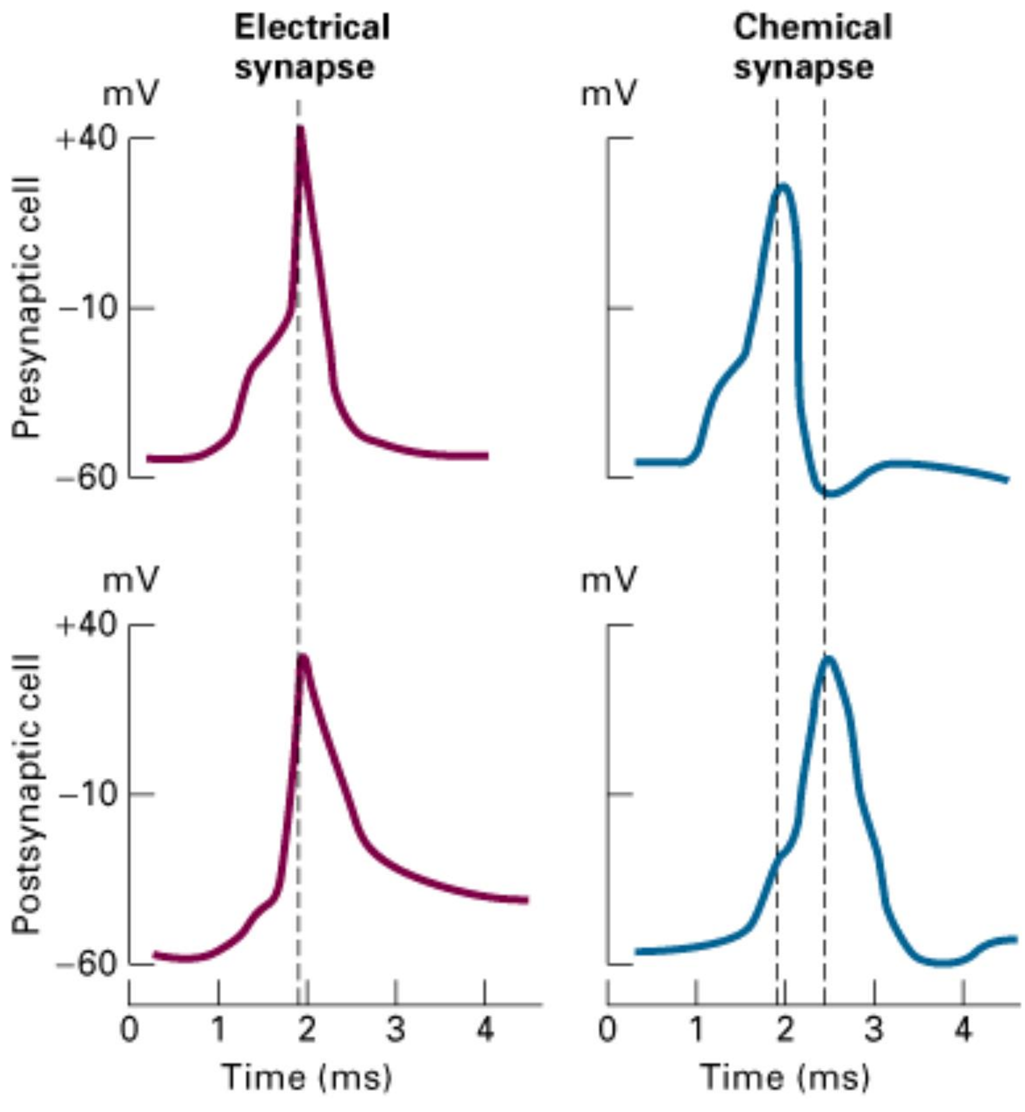
Električna sinapsa





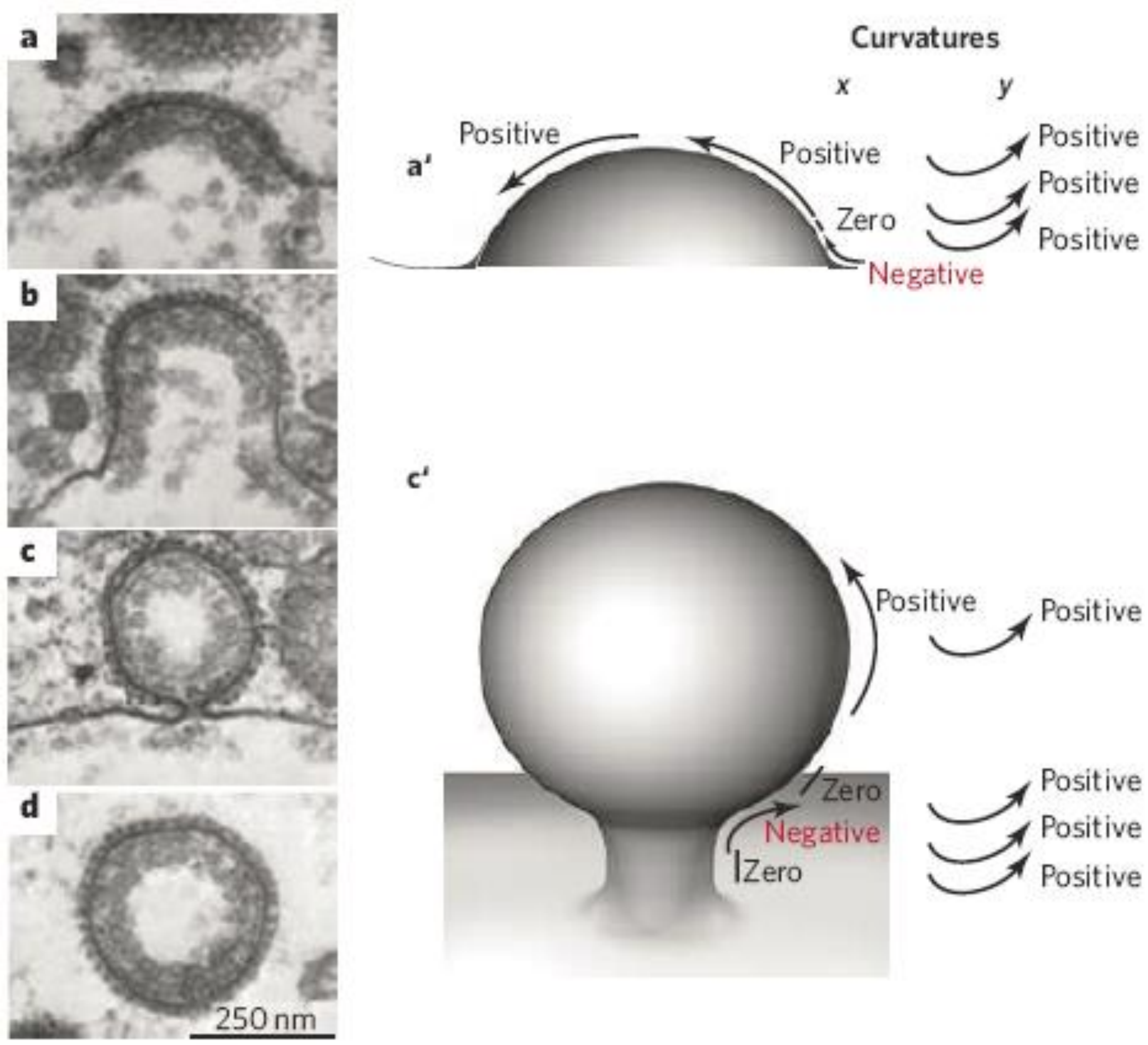


Prednosti električne sinapse pred kemijsko: zanesljivost, hitrost in usklajenost

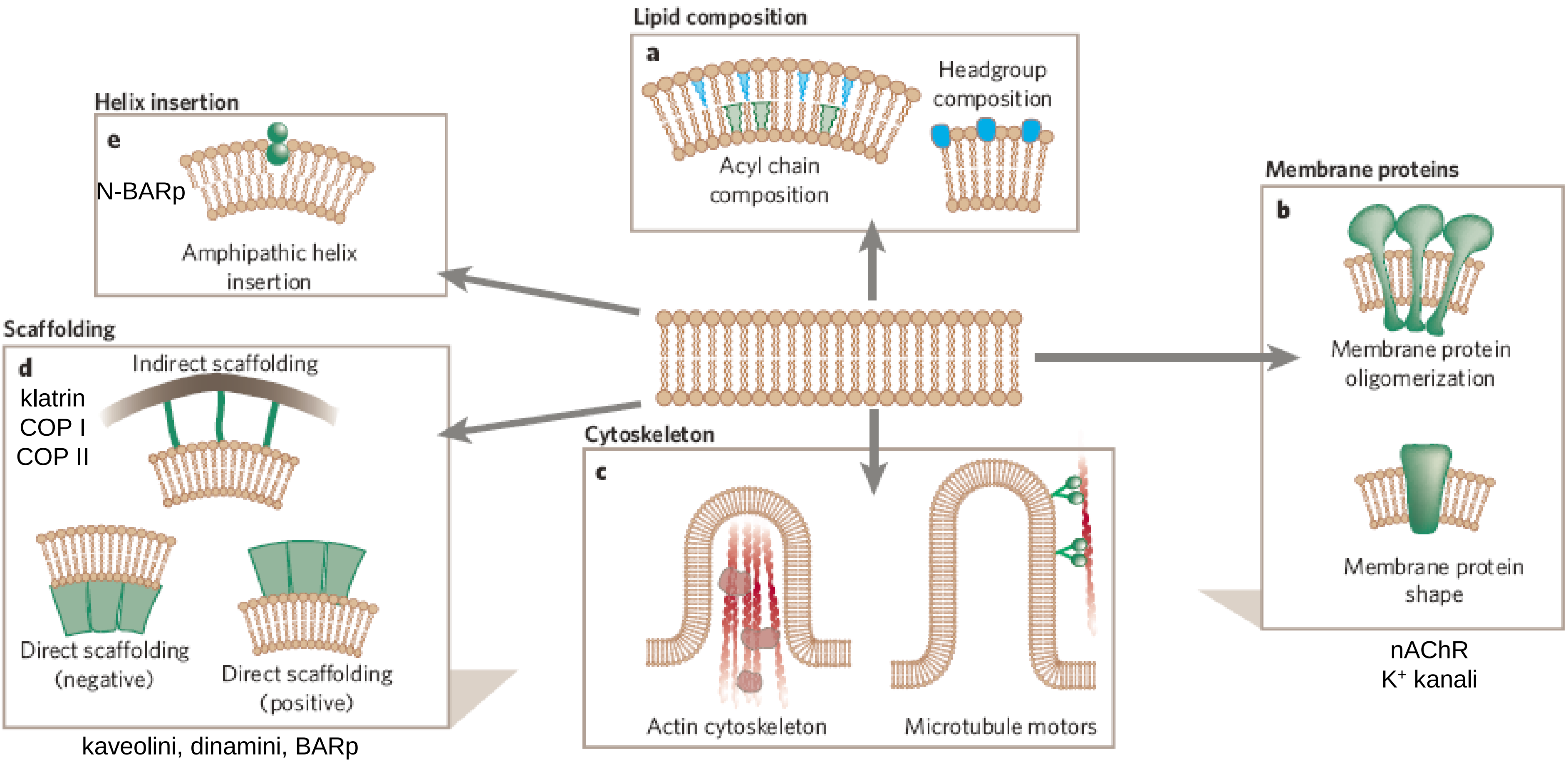


Ukrivljanje bioloških membran

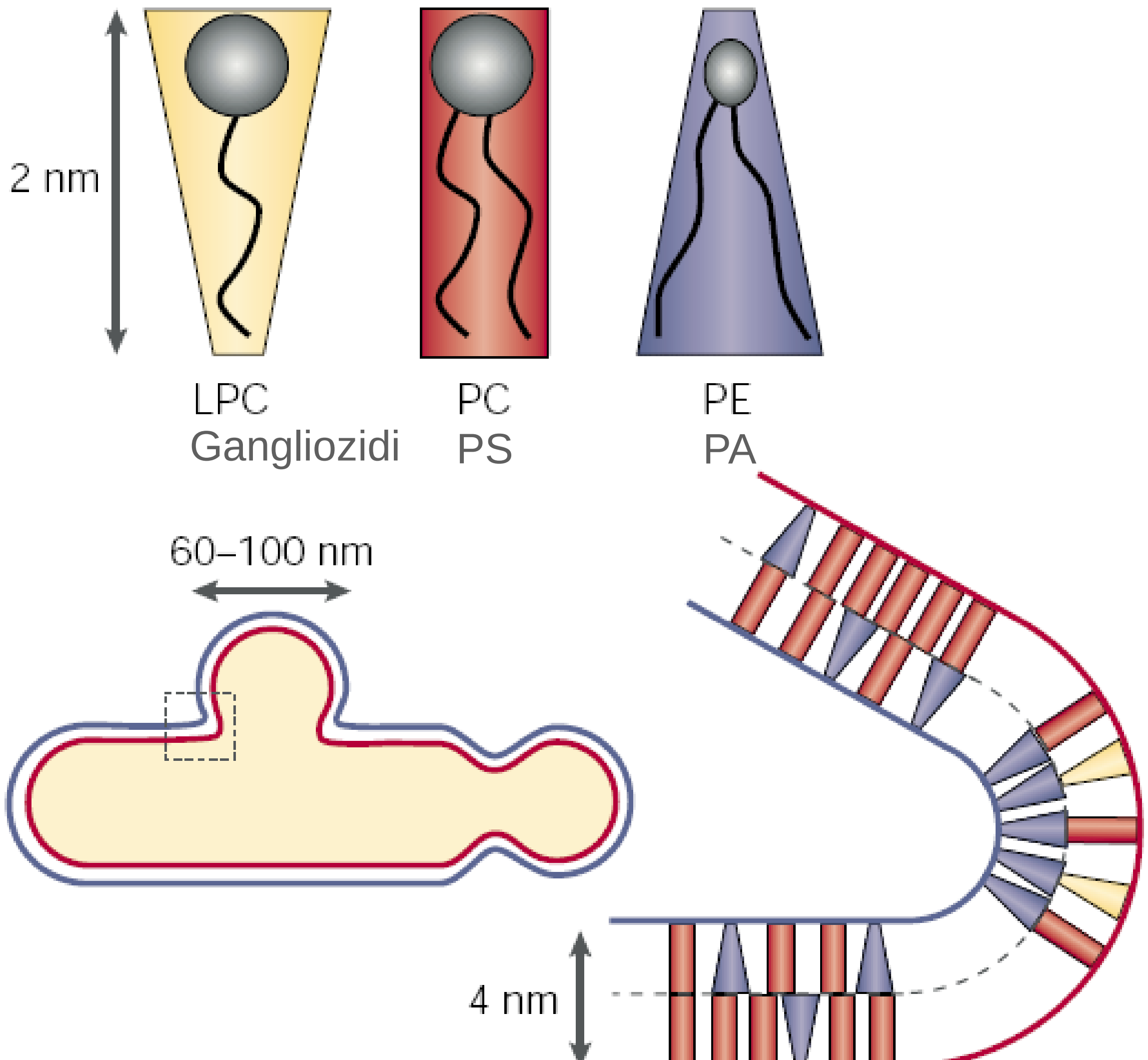
Vnos snovi v celico s klatrin-posredovano endocitozo



Mehanizmi ukrivljanja lipidnega dvosloja

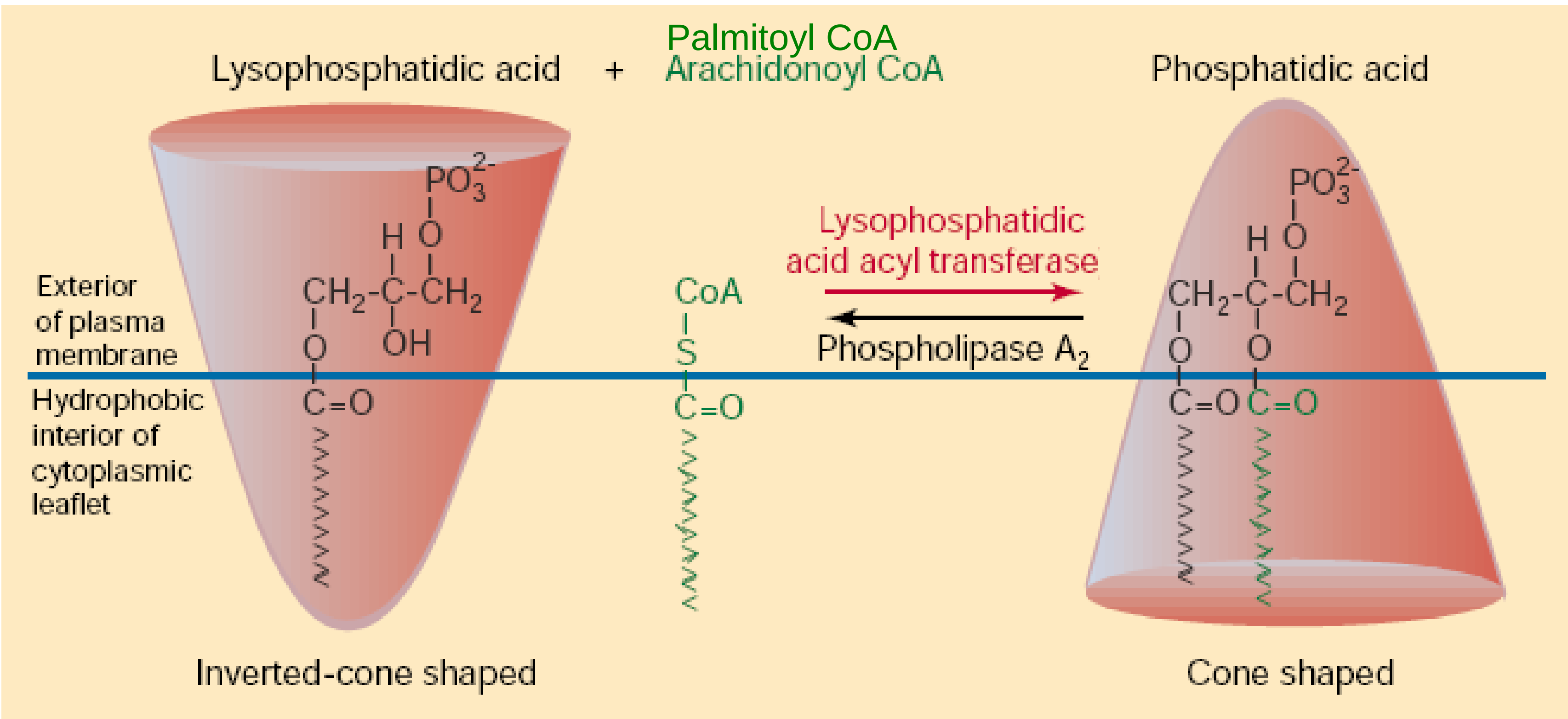


Fosfolipidi so različnih oblik - njihova oblika in razporeditev vplivata na ukrivljenost membrane



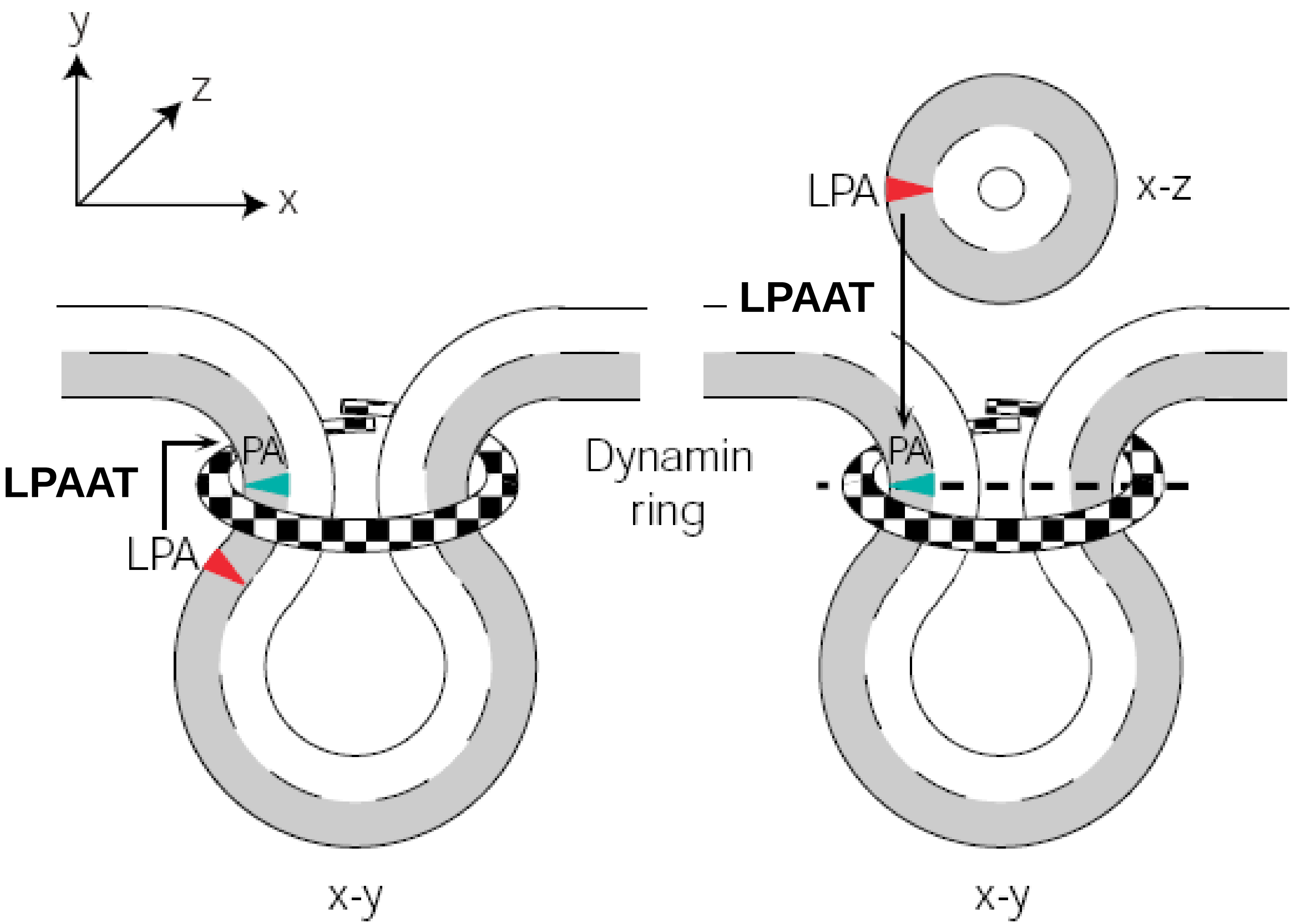
Spreminjanje geometrije lipidov

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

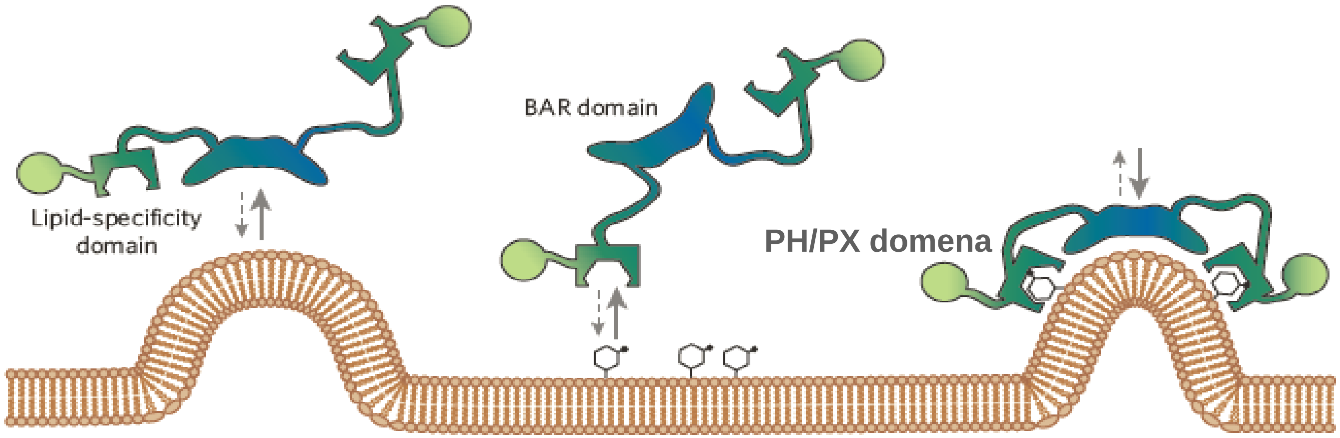


- Encimi, ki vplivajo na velikost lipidne 'glave'

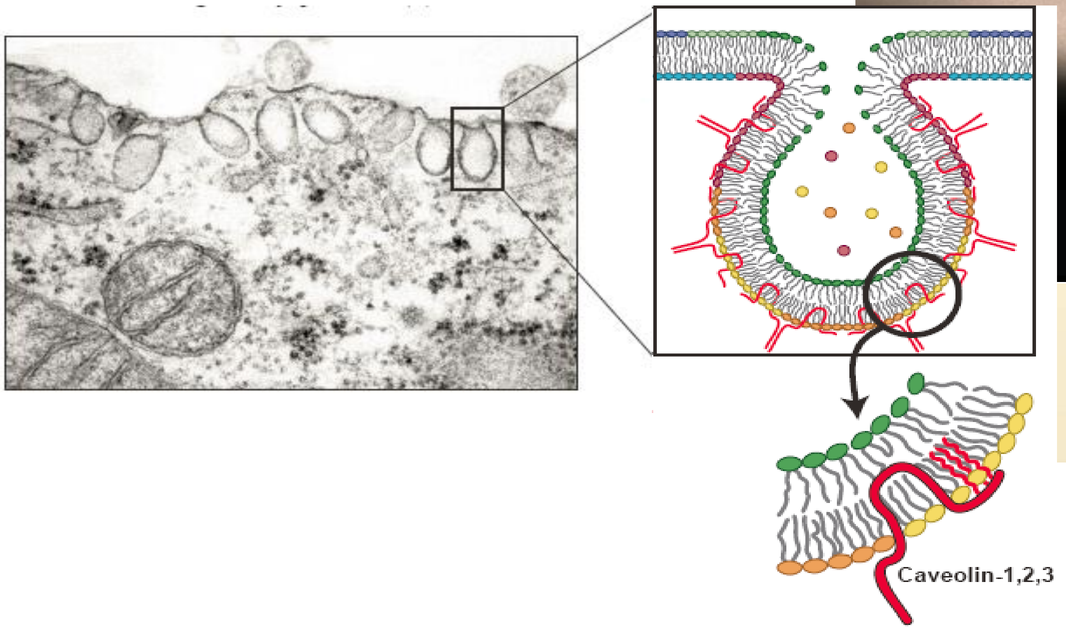
Vloga LPAAT-posredovane pretvorbe LPA v PA v eni od stopenj tvorbe sinaptičnega vezikla (odcepitev)

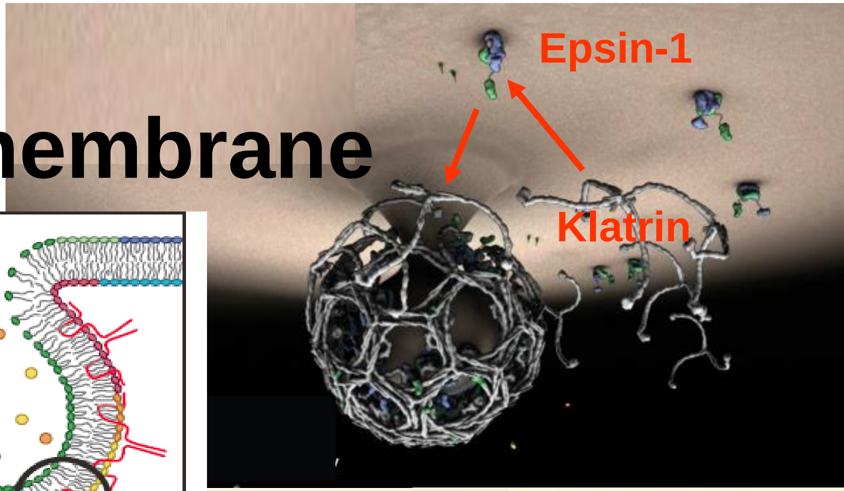


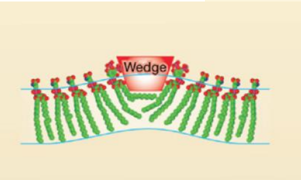
Posredno ukrivljanje membrane

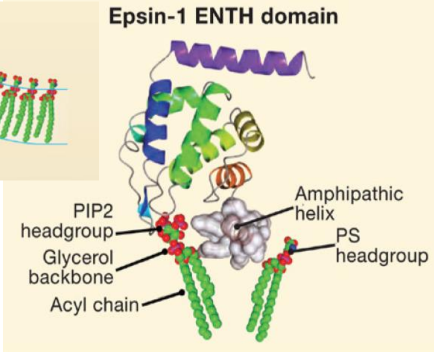


Neposredno ukrivljanje membrane

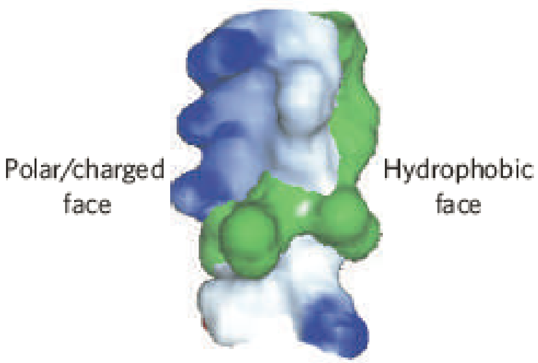


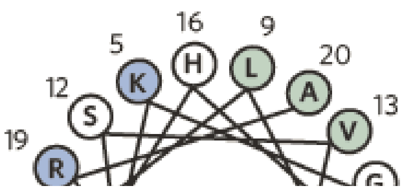


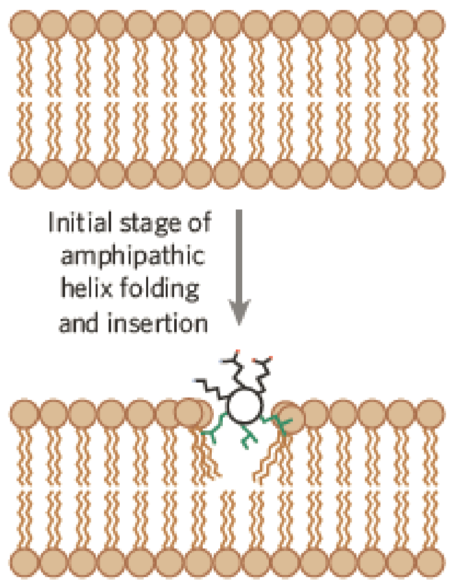


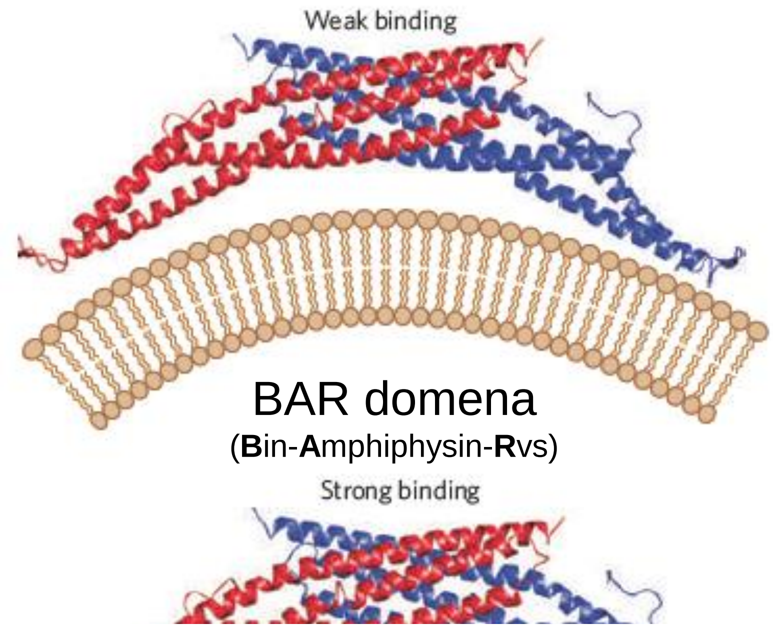


Amfipatična vijačnica in ukrivljanje membrane

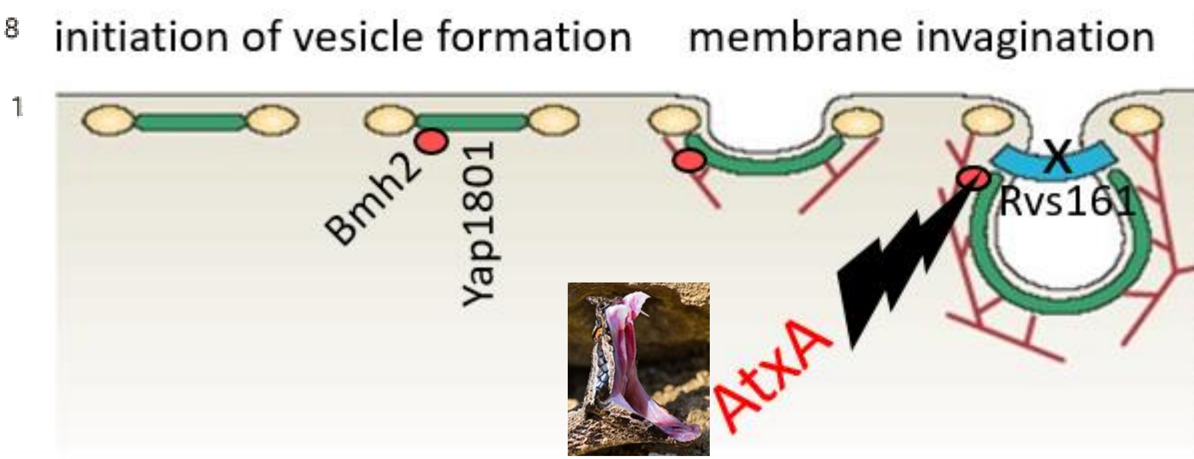








BAR domena
(**B**in-**A**mphiphysin-**R**vs)



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.