



Ústav  
experimentální  
medicíny AV ČR, v.v.i.  
EU Centre of Excellence



# ÚLOHA GLIOVÝCH BUNĚK V CNS, IONTOVÉ KANÁLY A RECEPTORY

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Ústav experimentální medicíny AVČR, v.v.i.



evropský  
sociální  
fond v ČR



EVROPSKÁ UNIE



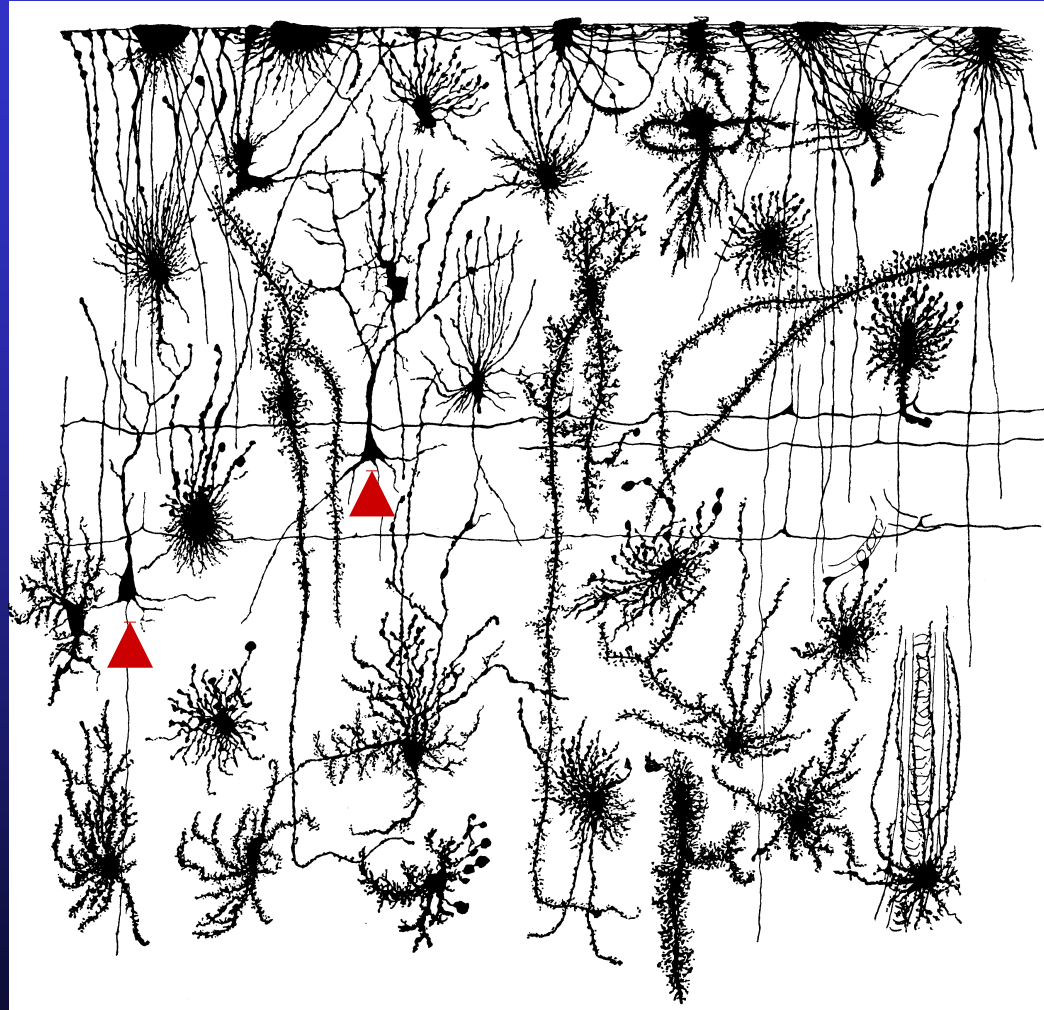
MINISTERSTVO ŠKOLSTVÍ,  
MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání  
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

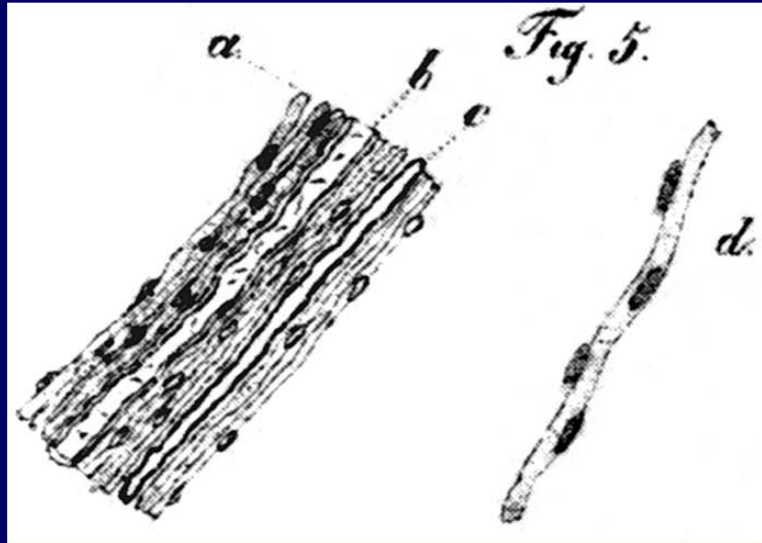
# Are they all neurons? How many glial?



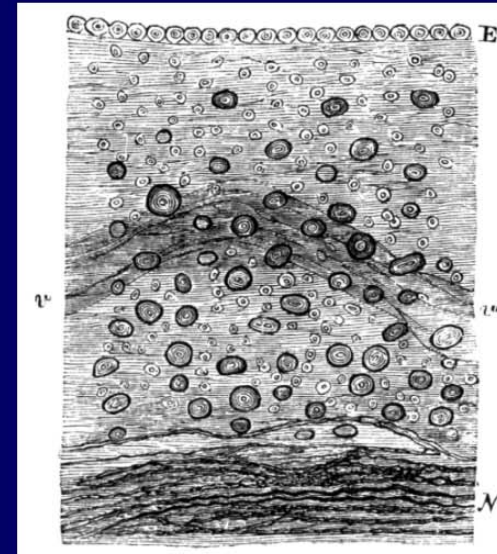
Gustaf Magnus Retzius (1842 - 1919) *Biologische Untersuchungen* (Stockholm: Samson and Wallin, 1890-1914). Vol. 6 (1894), plate ii, Fig. 5; Cortex of 45 cm long human embryo).

# History of glial cell research

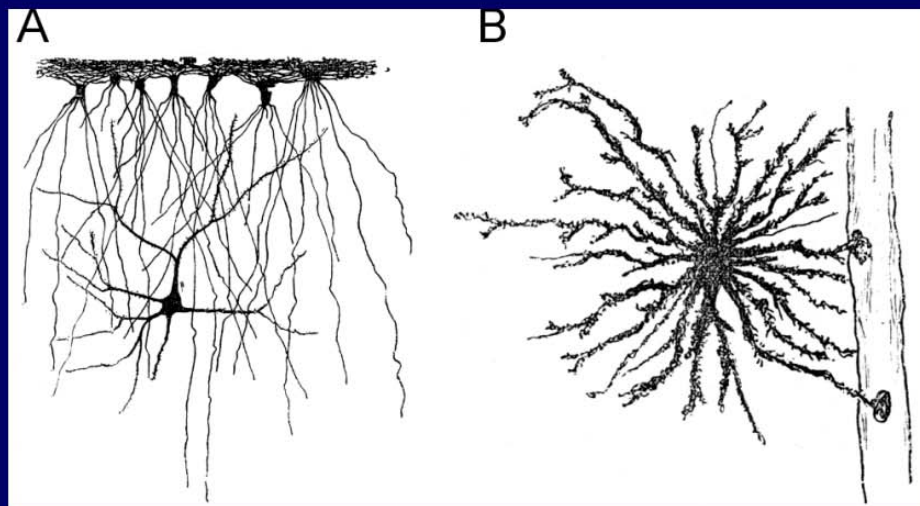
Rosenthal and Purkyně, 1839



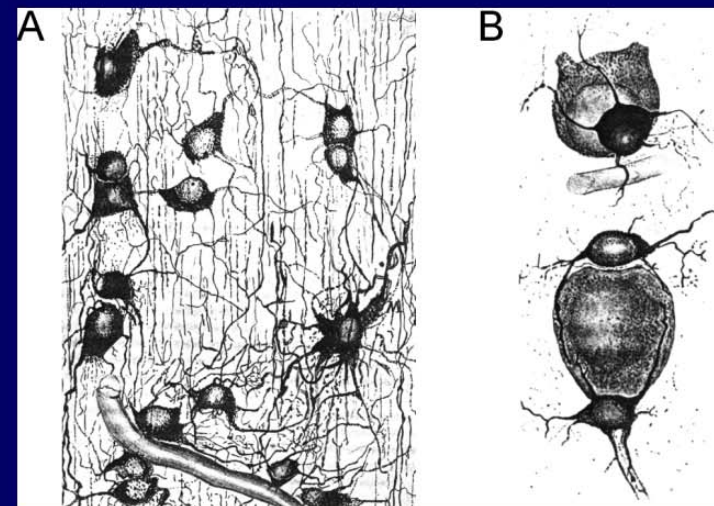
Virchow, 1858



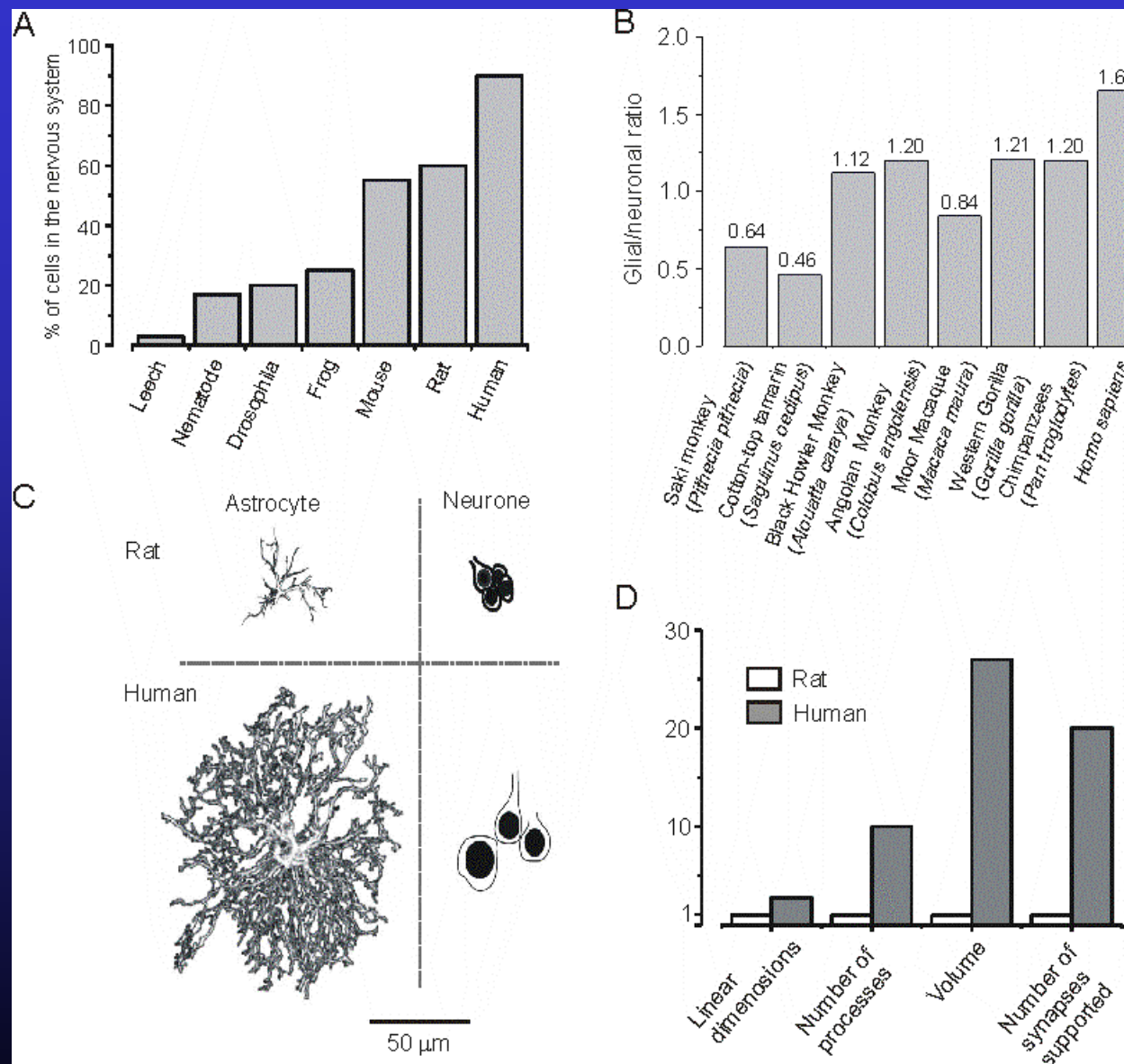
Andriezen, 1893



Penfield, 1924



# Phylogenetic advance of glia



Oberheim, Wang, Goldman, Nedergaard (2006): Trends Neurosci 29, 547-553.  
 Verkhratsky & Butt (2007): Glial Neurobiology, A Textbook; Wiley & Sons.

Gliové buňky jsou různorodé elementy, v nervové tkáni vedle sebe existují:

astrocyty

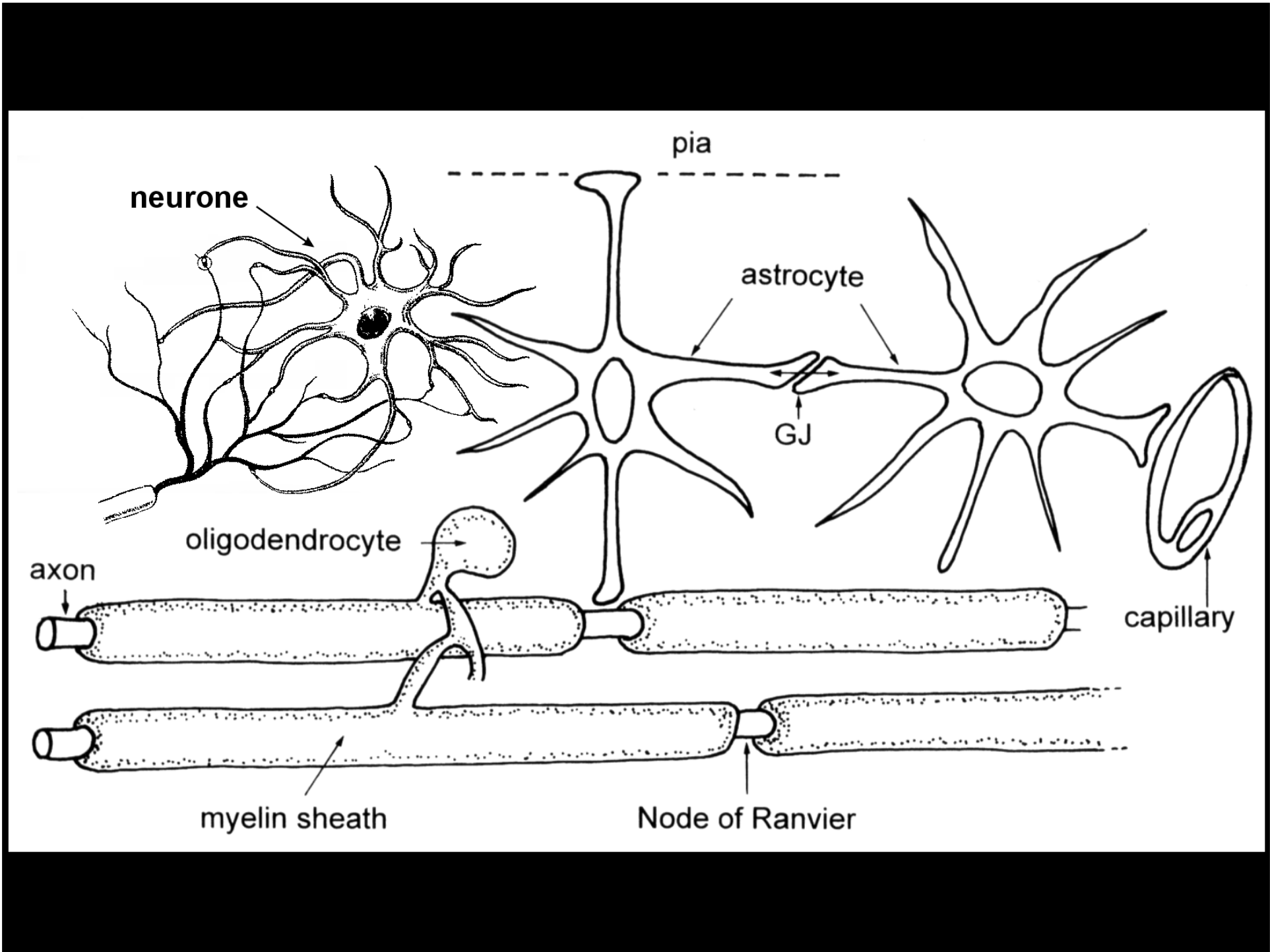
oligodendrocyty

Schwannovy buňky

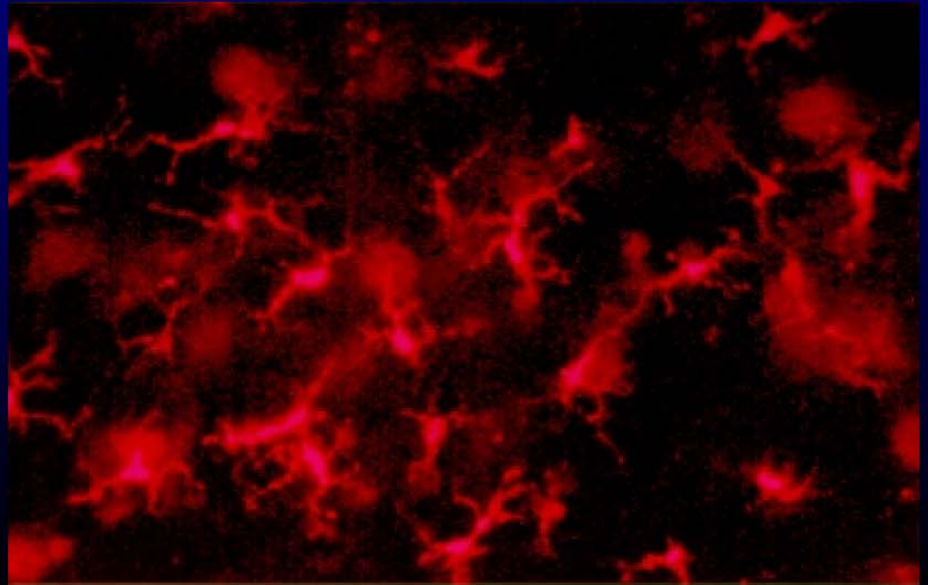
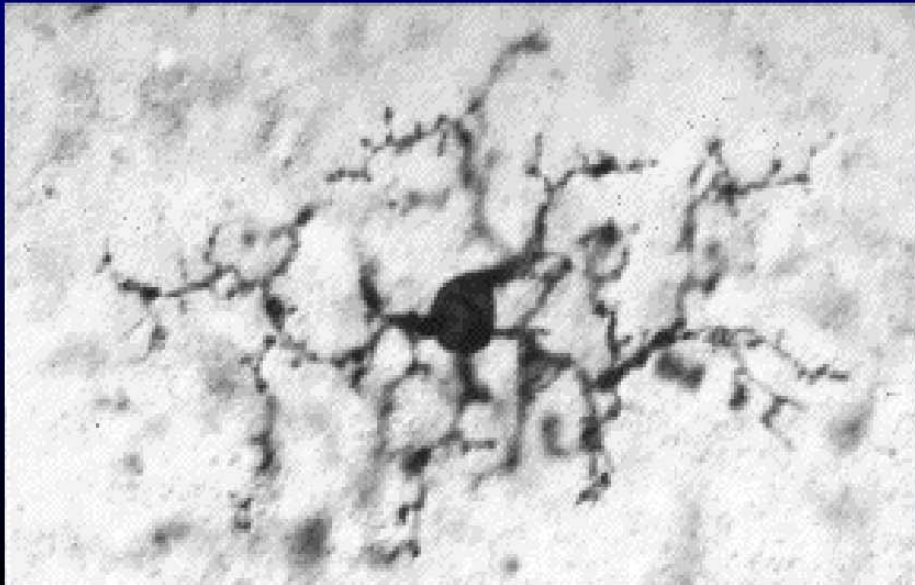
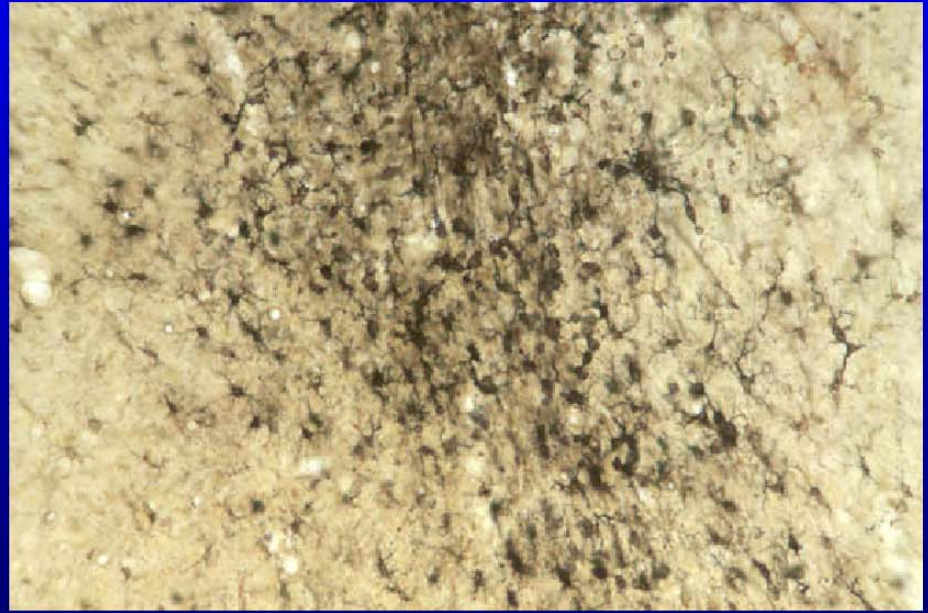
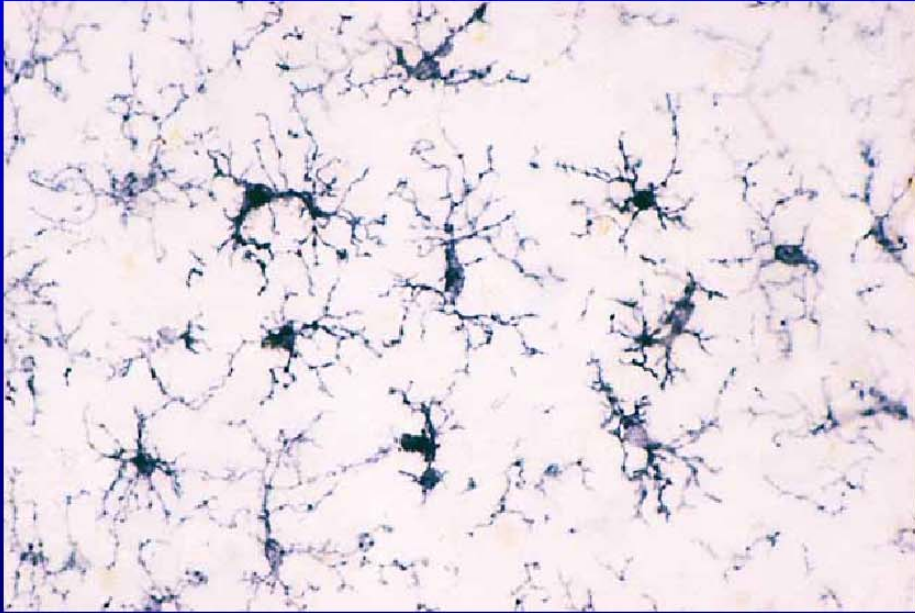
mikroglie

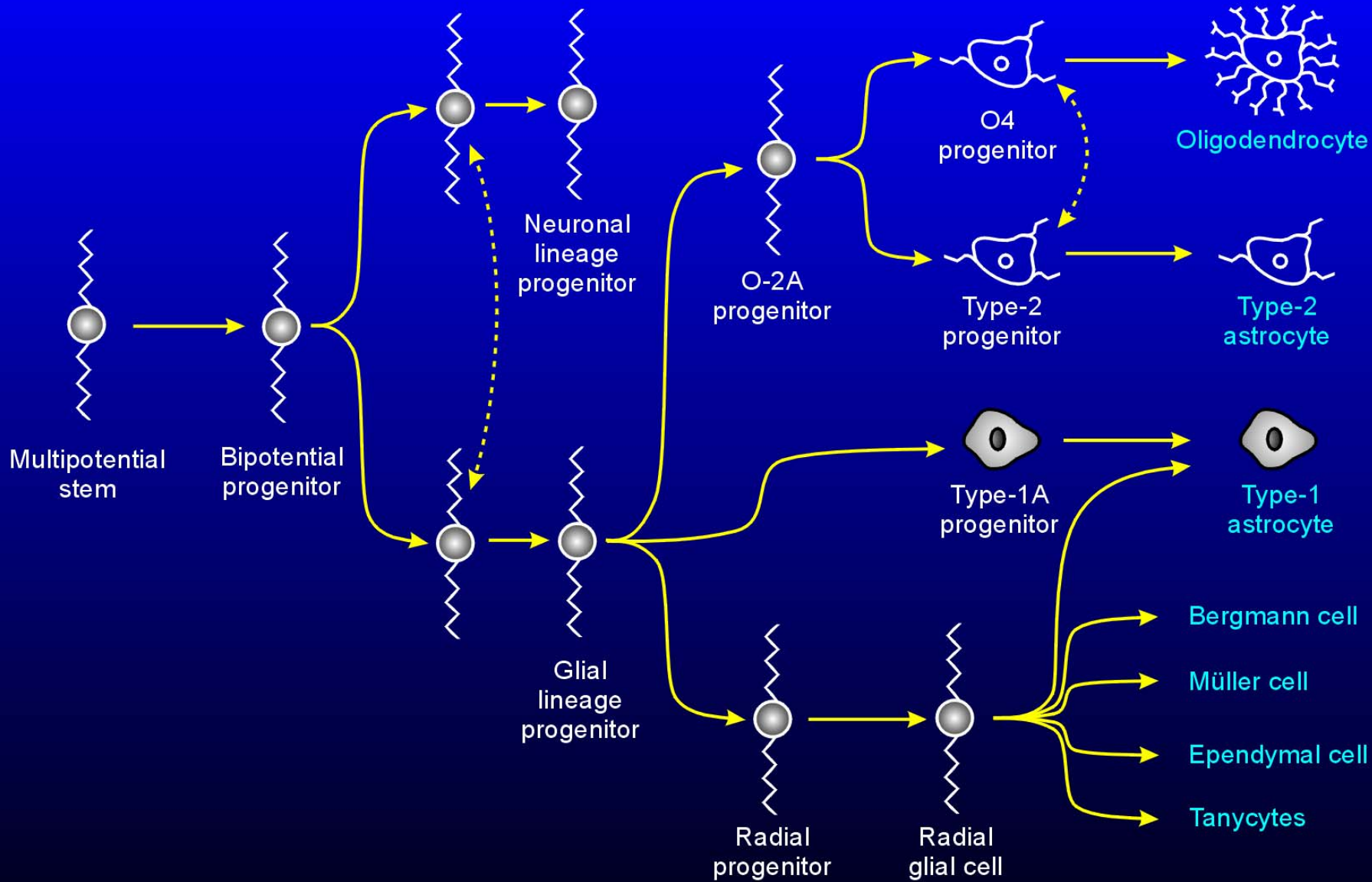
prekursorové buňky

proliferující a hypertrofující buňky

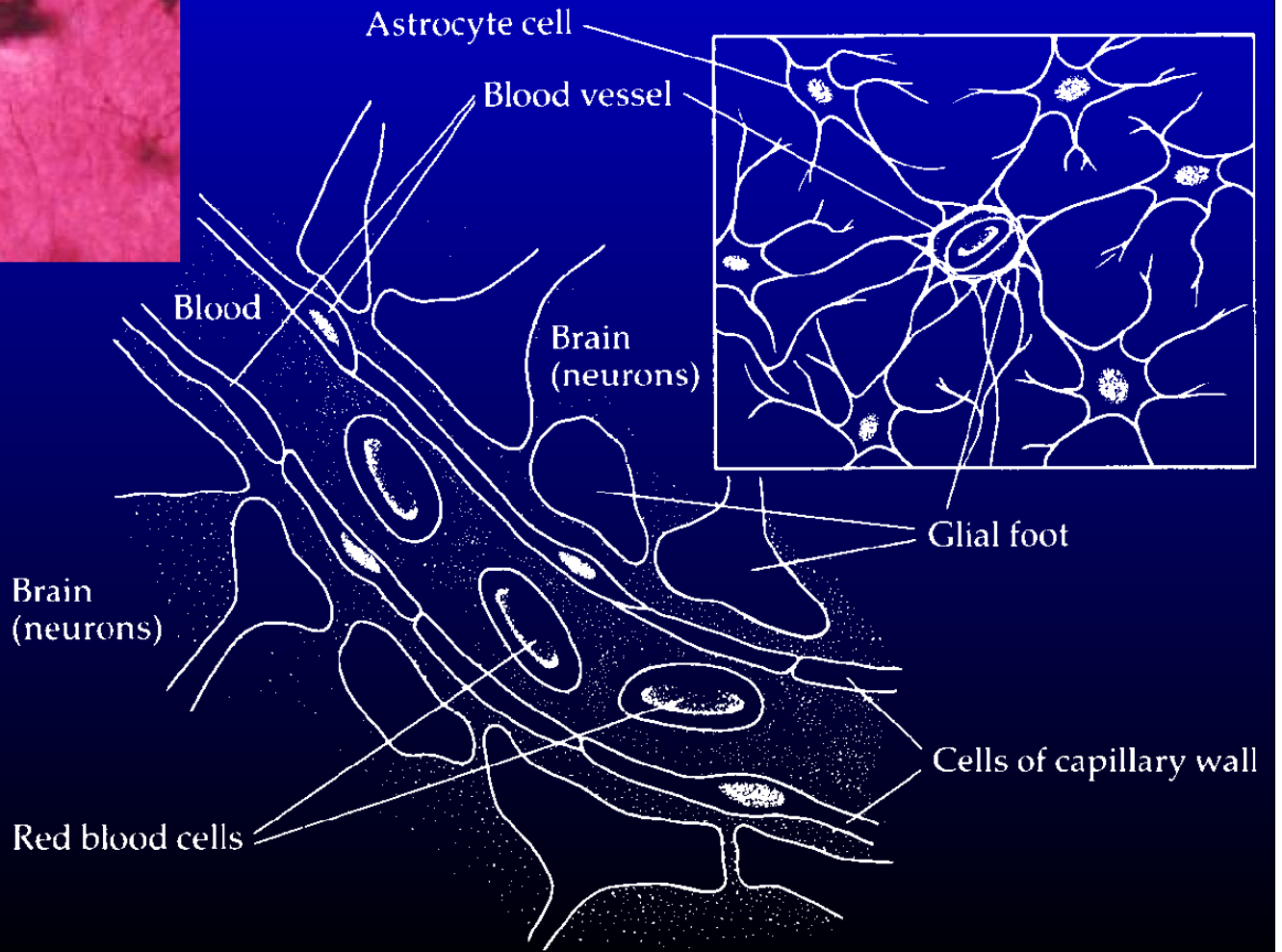
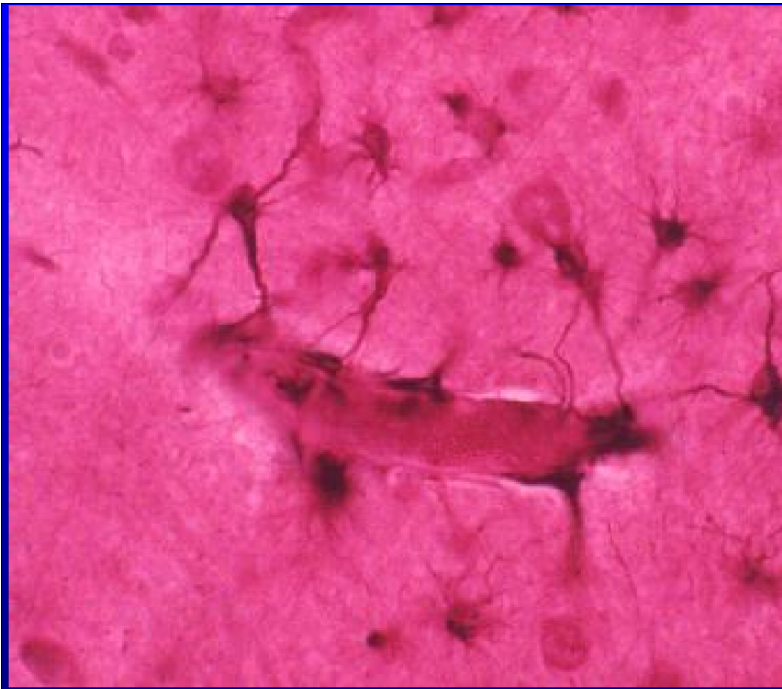


# Microglia





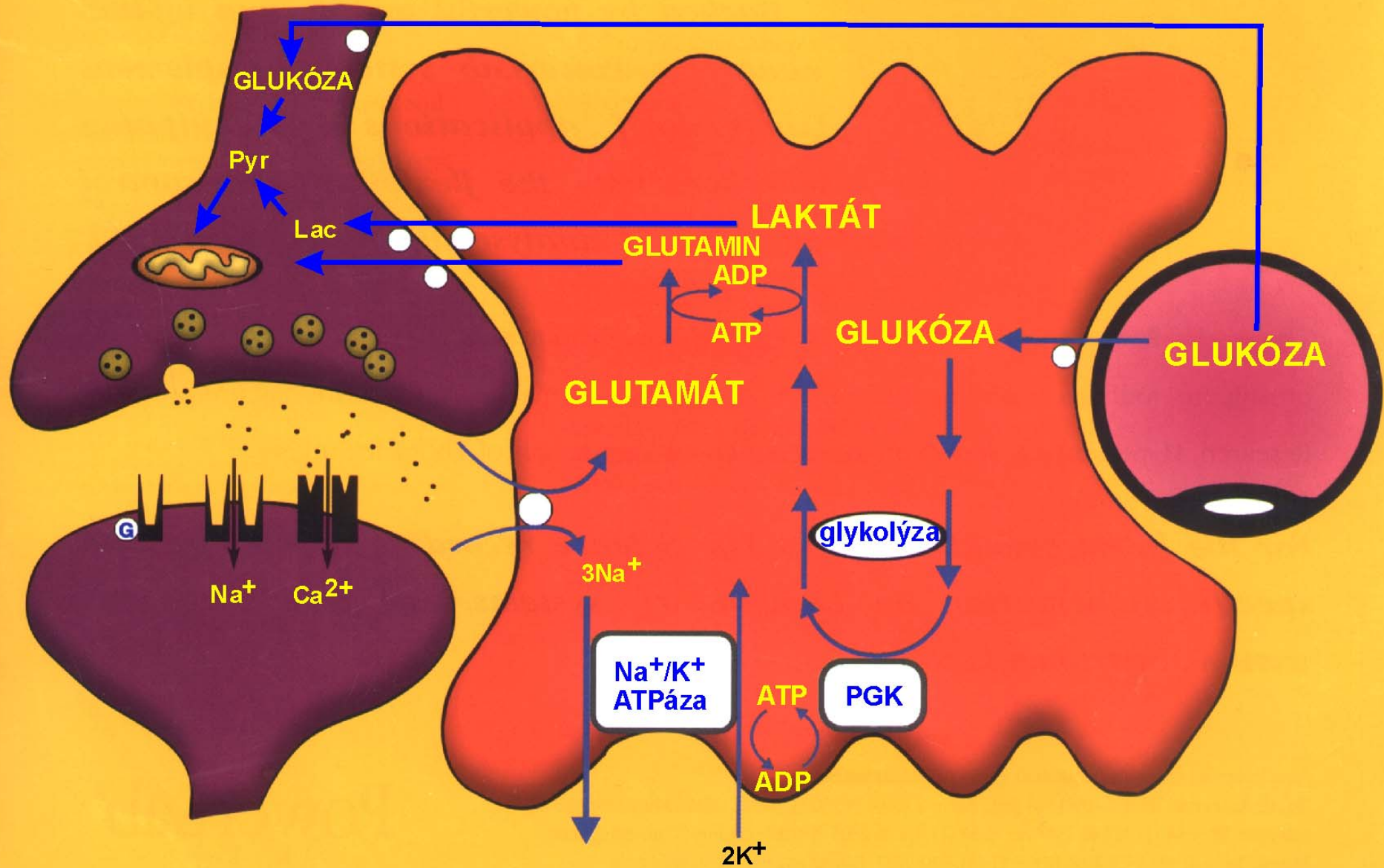
Adapted from: Cameron and Rakic, 1991

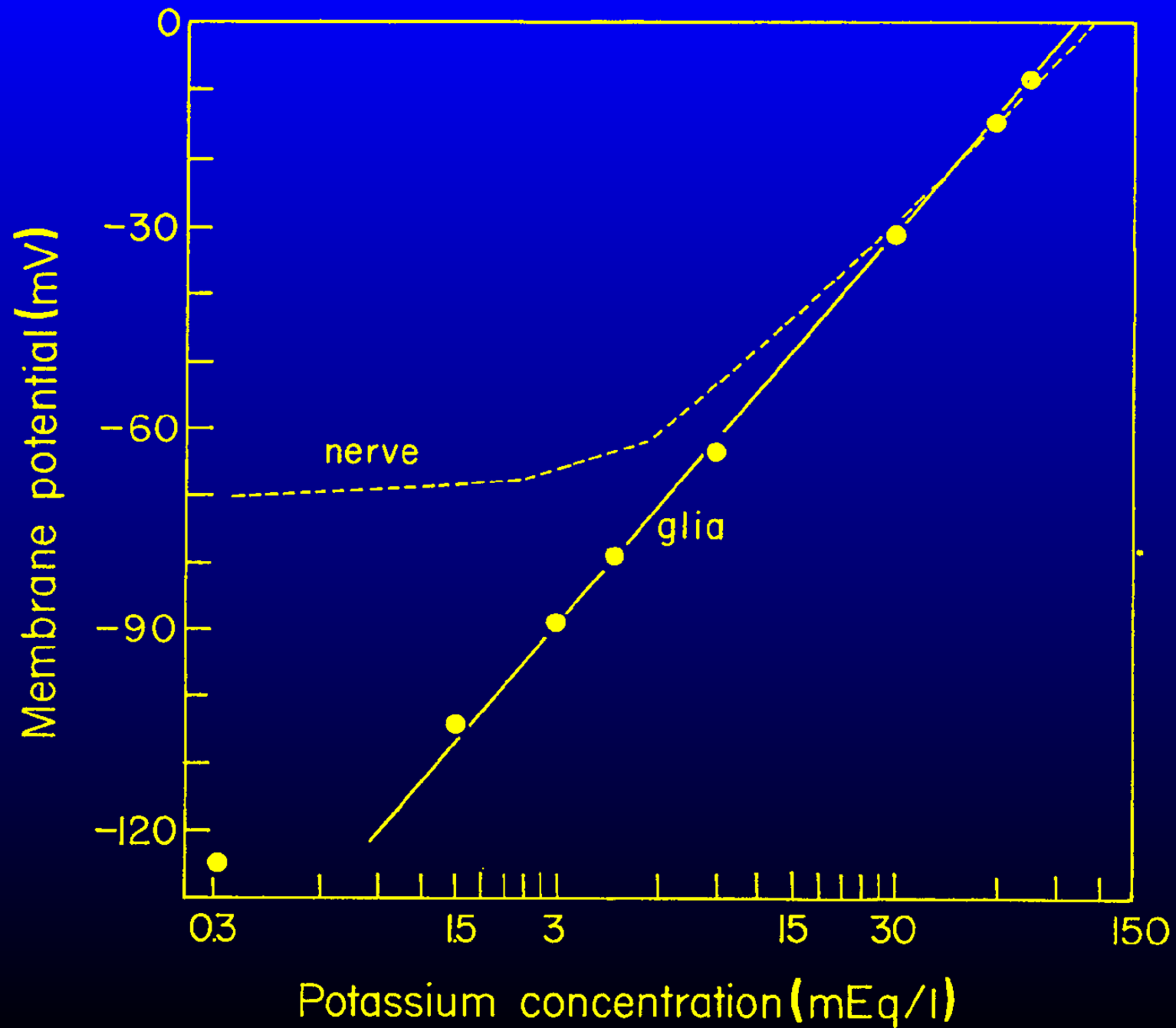


# Glutamátergنی synapse

# Astrocyt

# Kapilára





## Kanály a přenašeče určující elektrofyziologické vlastnosti gliových buněk

1. Pasívní iontové kanály (především pro  $K^+$ )
2. Napětově-závislé iontové kanály (např.  $Na^+$ ,  $K^+$  a  $Ca^{2+}$ )
3. Chemicky aktivované iontové kanály (např. GABA, glycín, glutamát)
4. ATP-závislé transportní mechanizmy (např. Na,K-ATPáza)  
kotransporty (např. Na-K-Cl, Na-HCO<sub>3</sub>, Na-Glu)  
antiporty (např. Na-H)

# IONTOVÉ KANÁLY

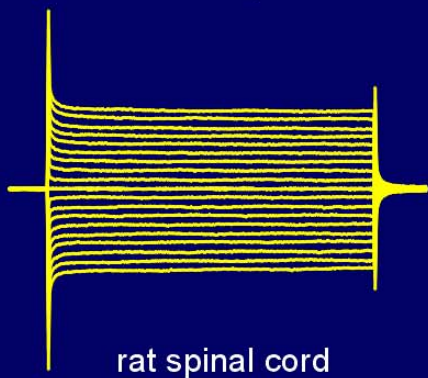
Stále otevřené  
(pasívní)

Řízené

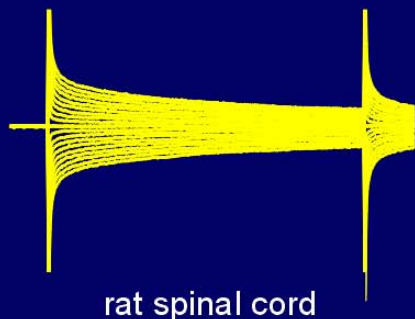
Napětově řízené  
( $K^+$ ,  $Na^+$ ,  $Cl^-$ ,  $Ca^{2+}$ )

Chemicky řízené  
(Glutamát, GABA, Glycín)

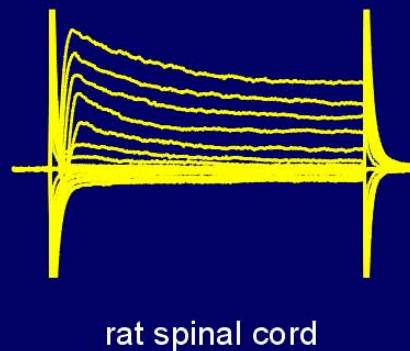
### Astrocytes



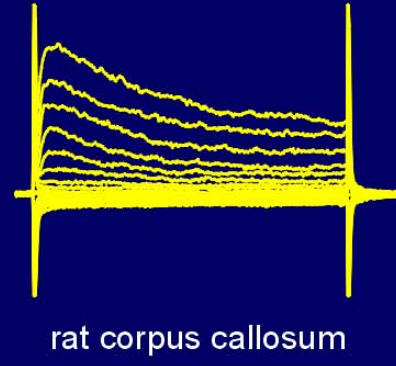
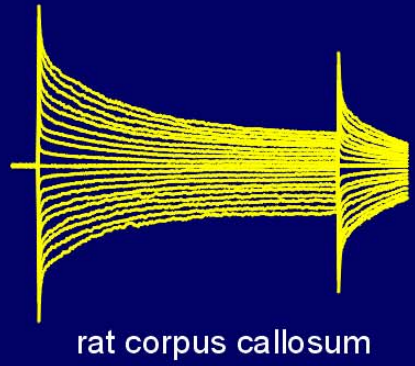
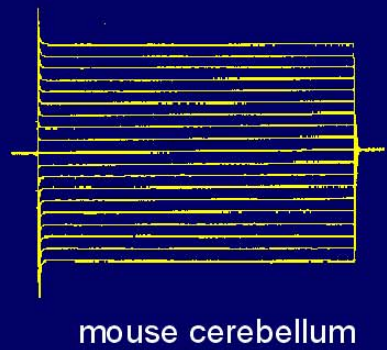
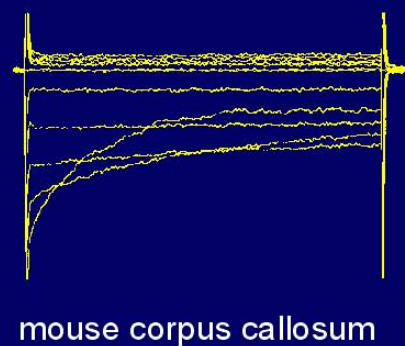
### Oligodendrocytes



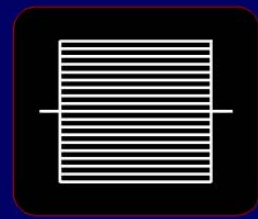
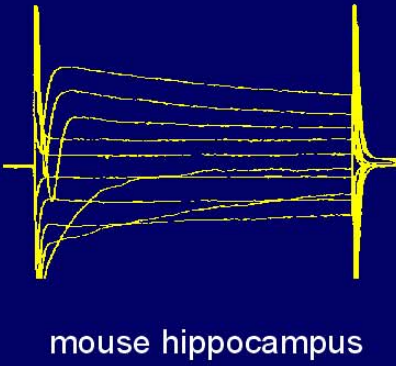
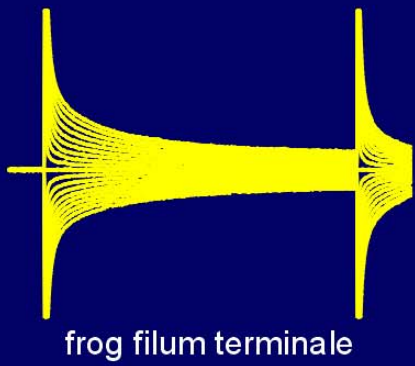
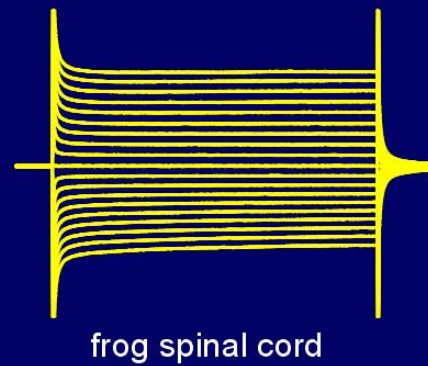
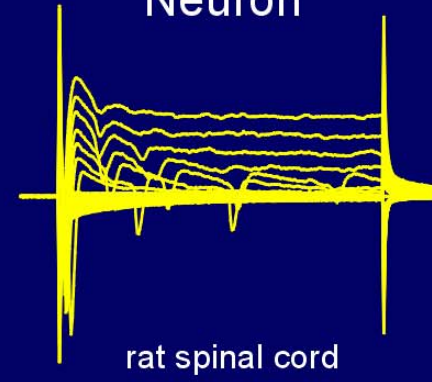
### Glial precursors

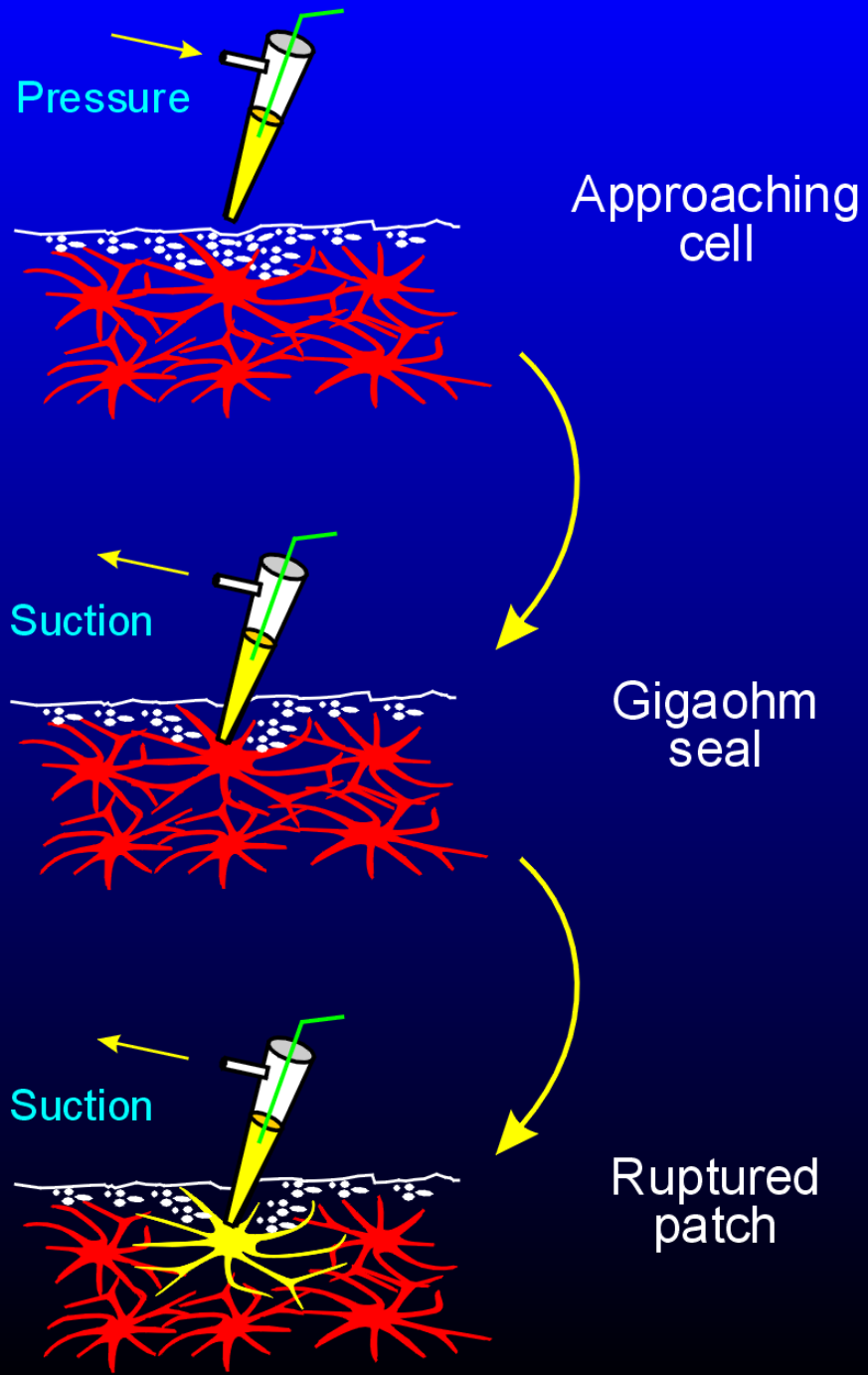


### Microglia

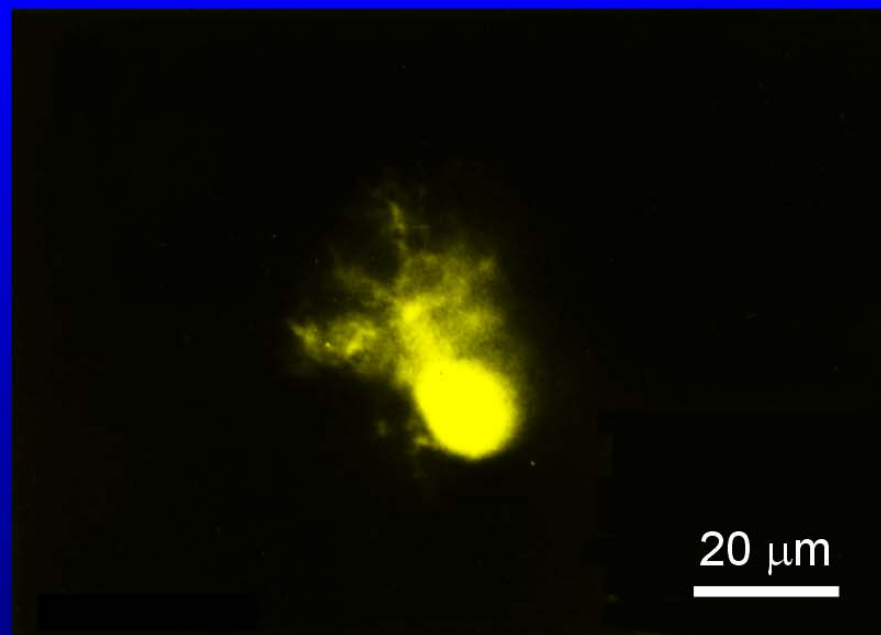
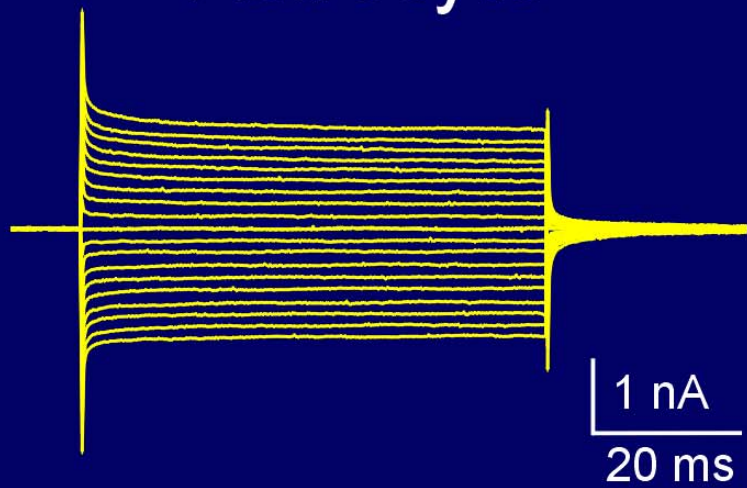


### Neuron





# Astrocyte

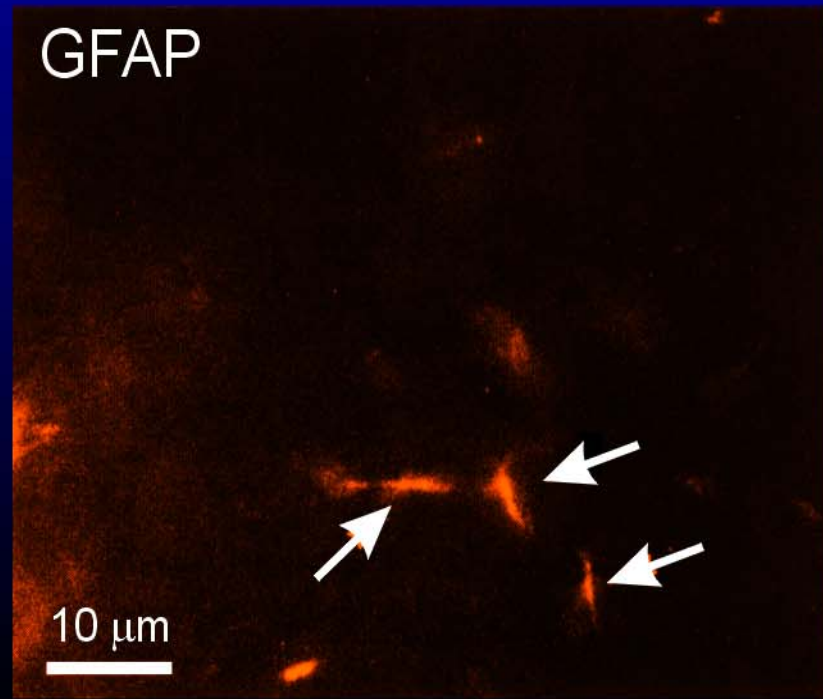
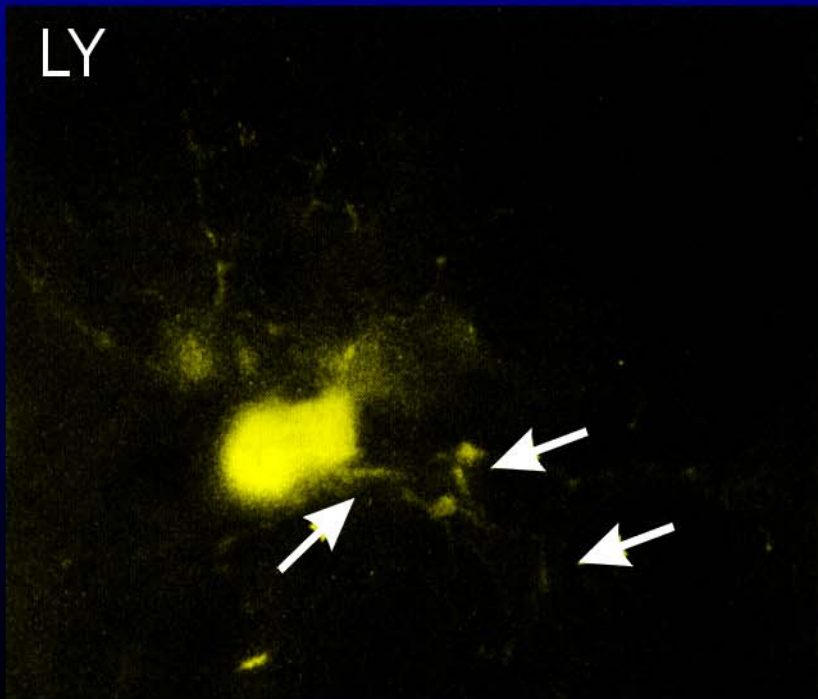
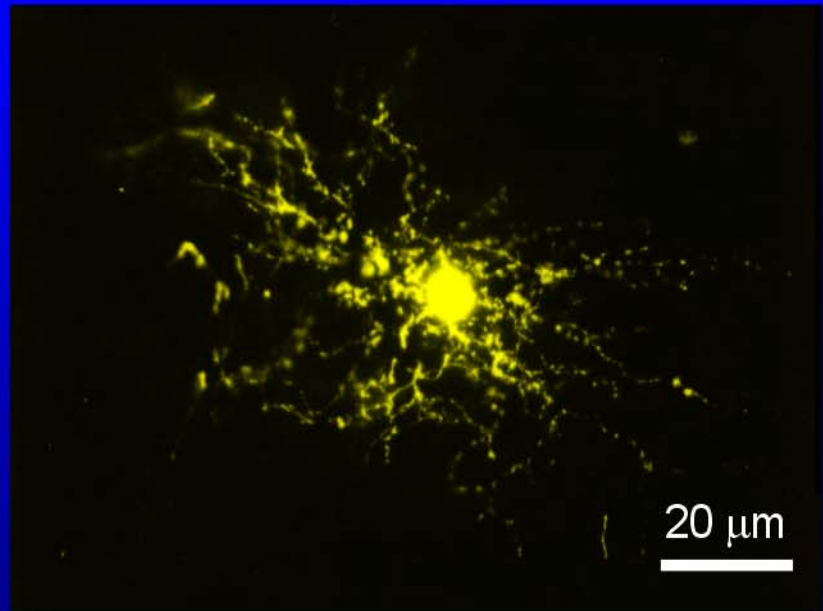
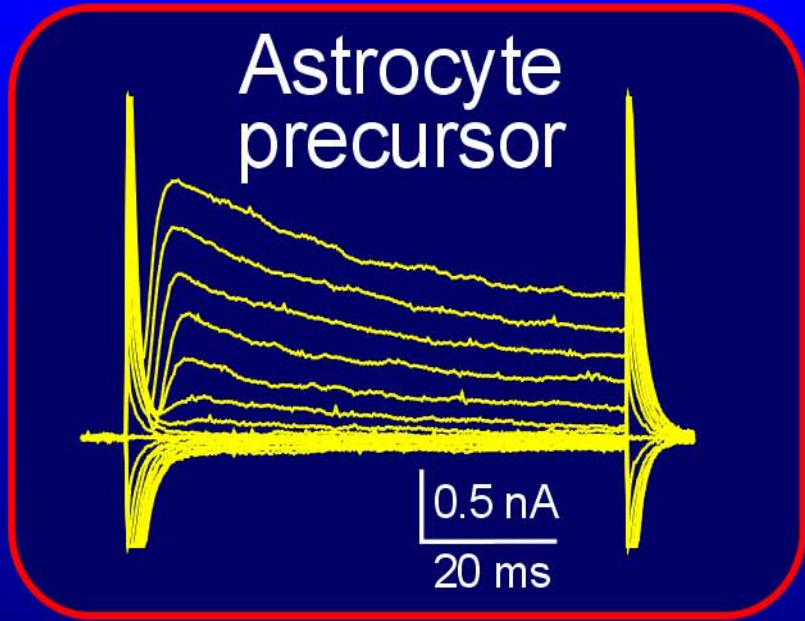


LY

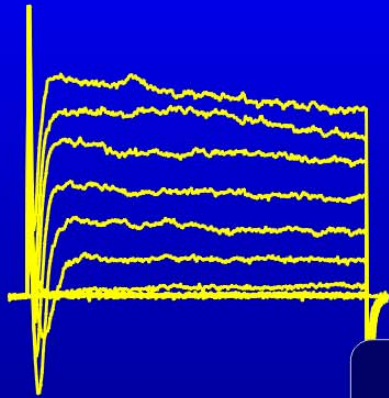


GFAP

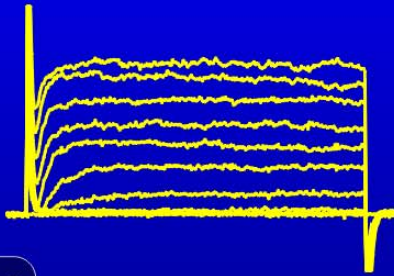




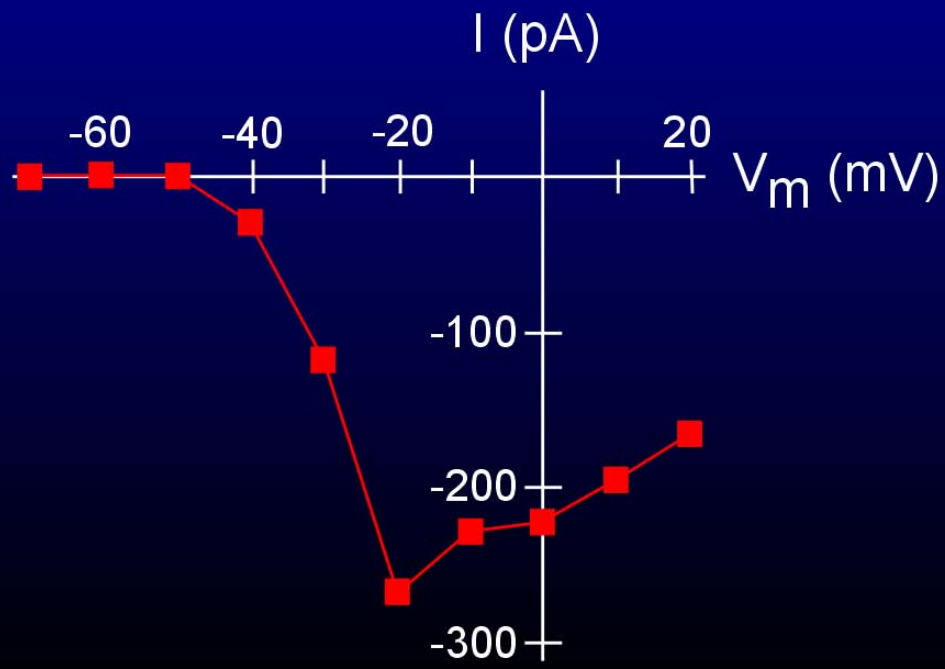
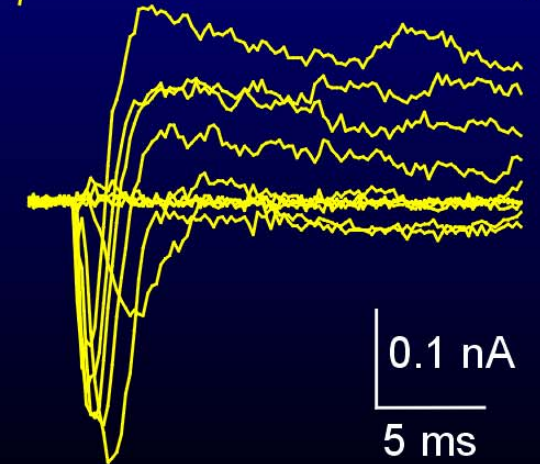
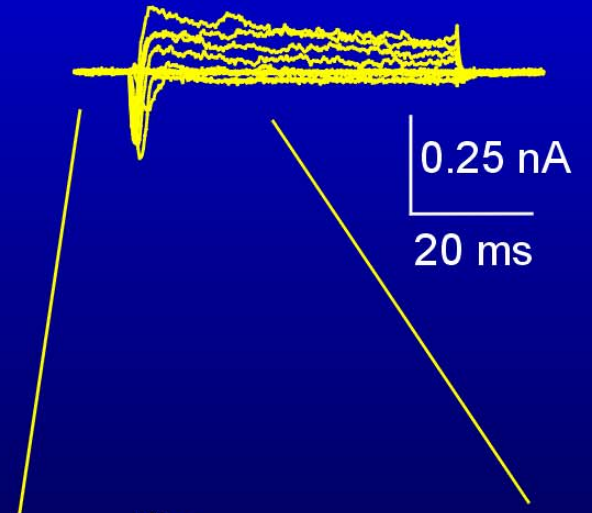
control



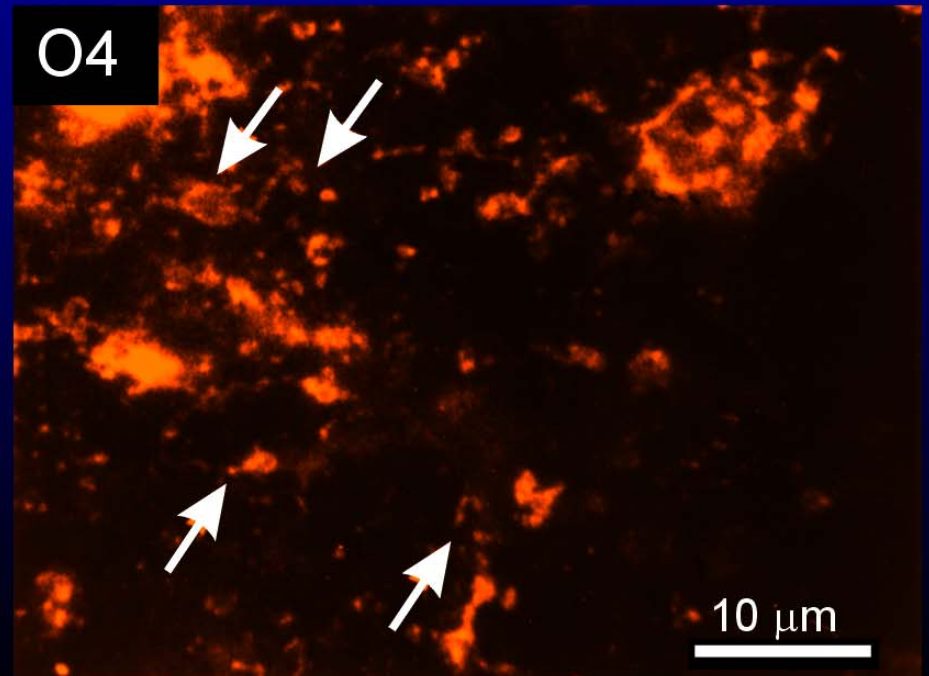
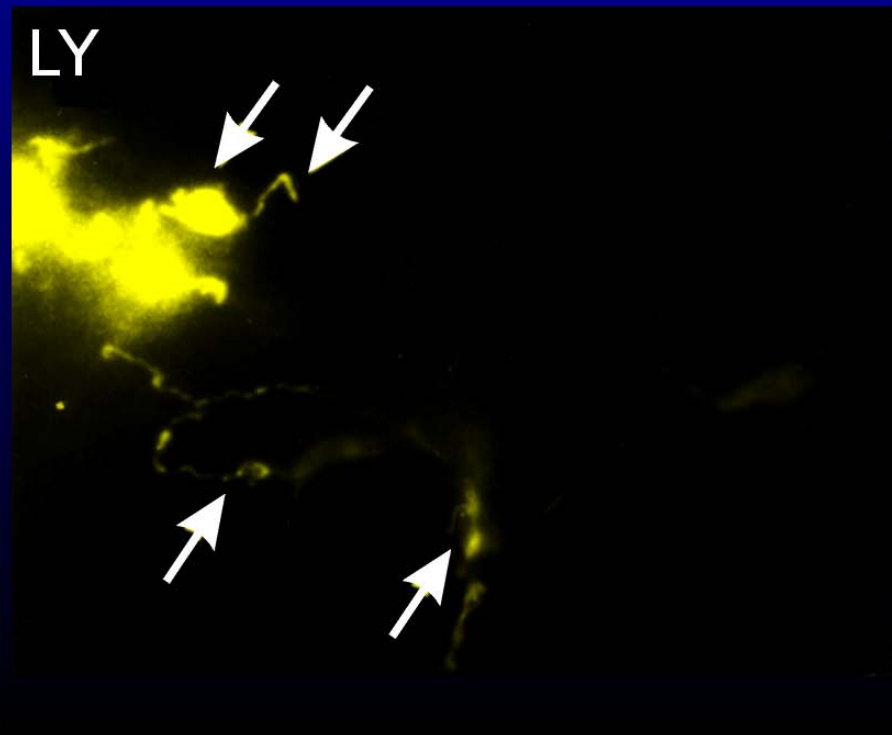
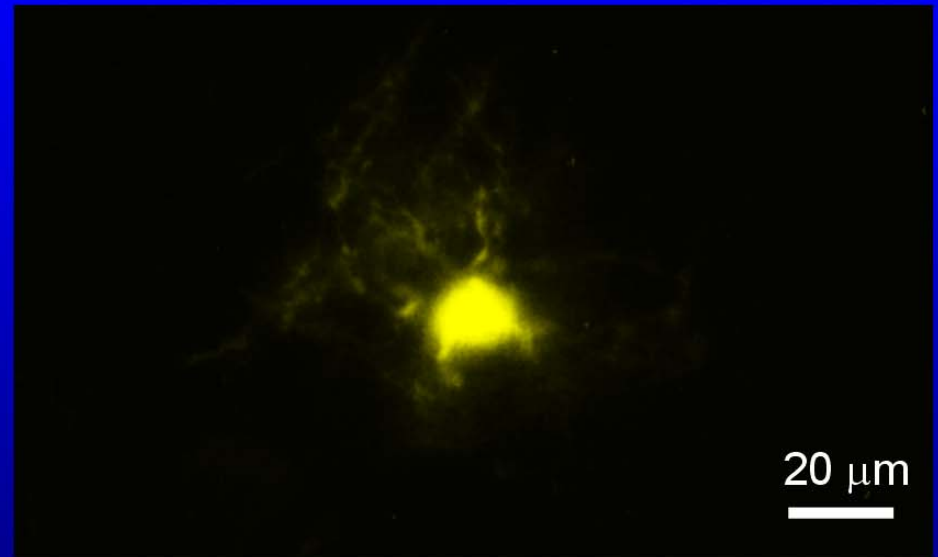
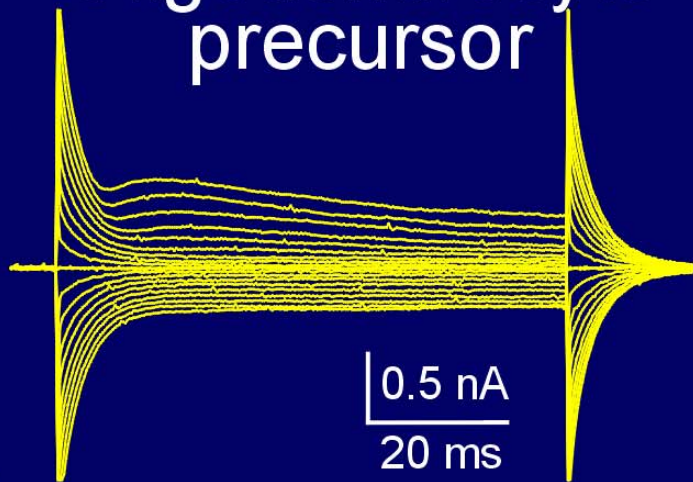
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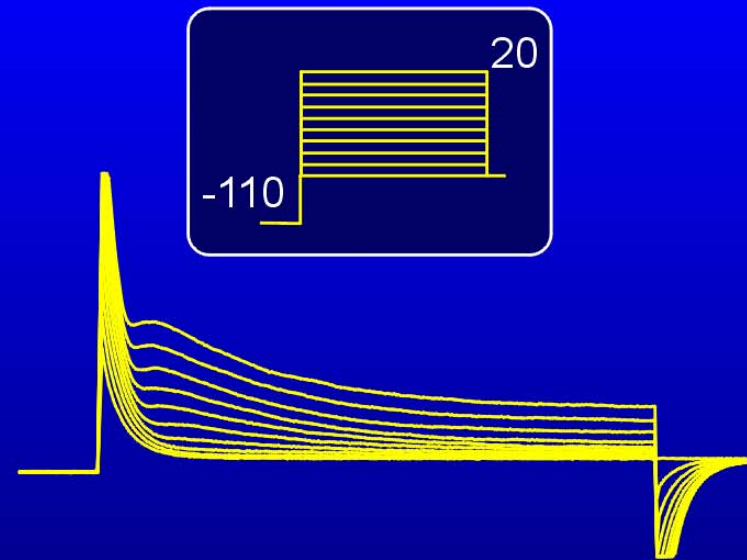
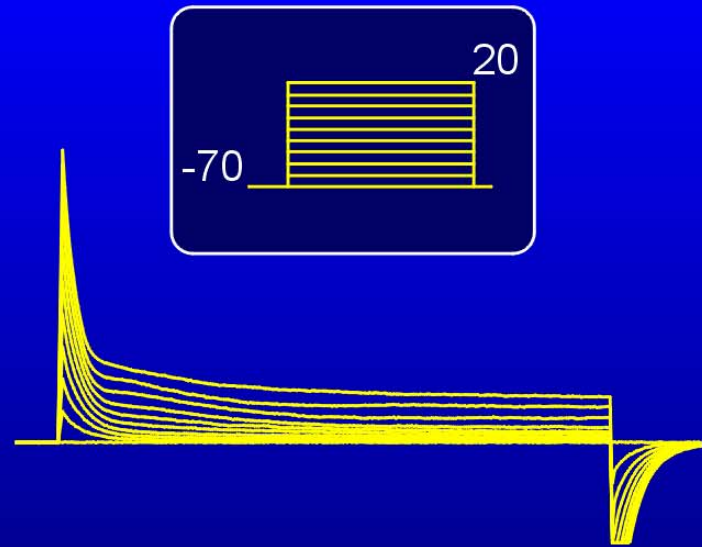


Na<sup>+</sup>-sensitive current



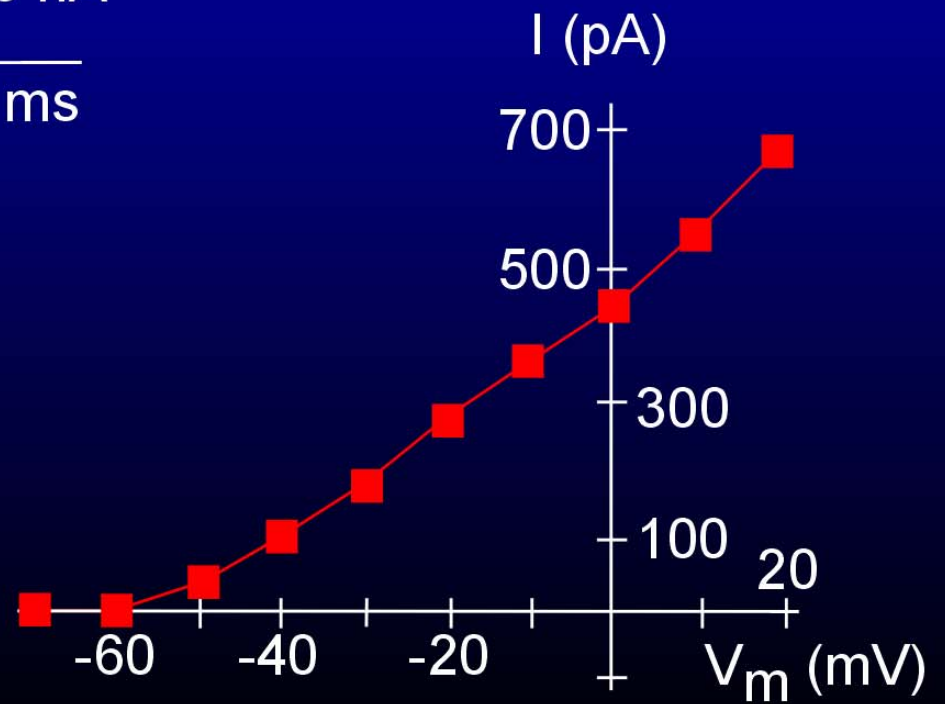
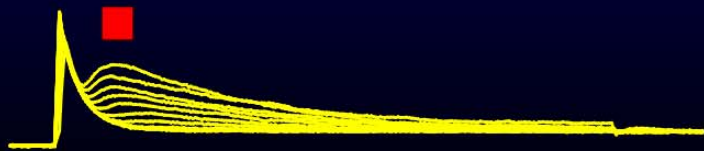
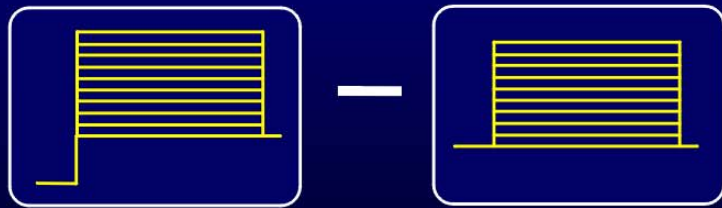
# Oligodendrocyte precursor





1.5 nA  
15 ms

A-current

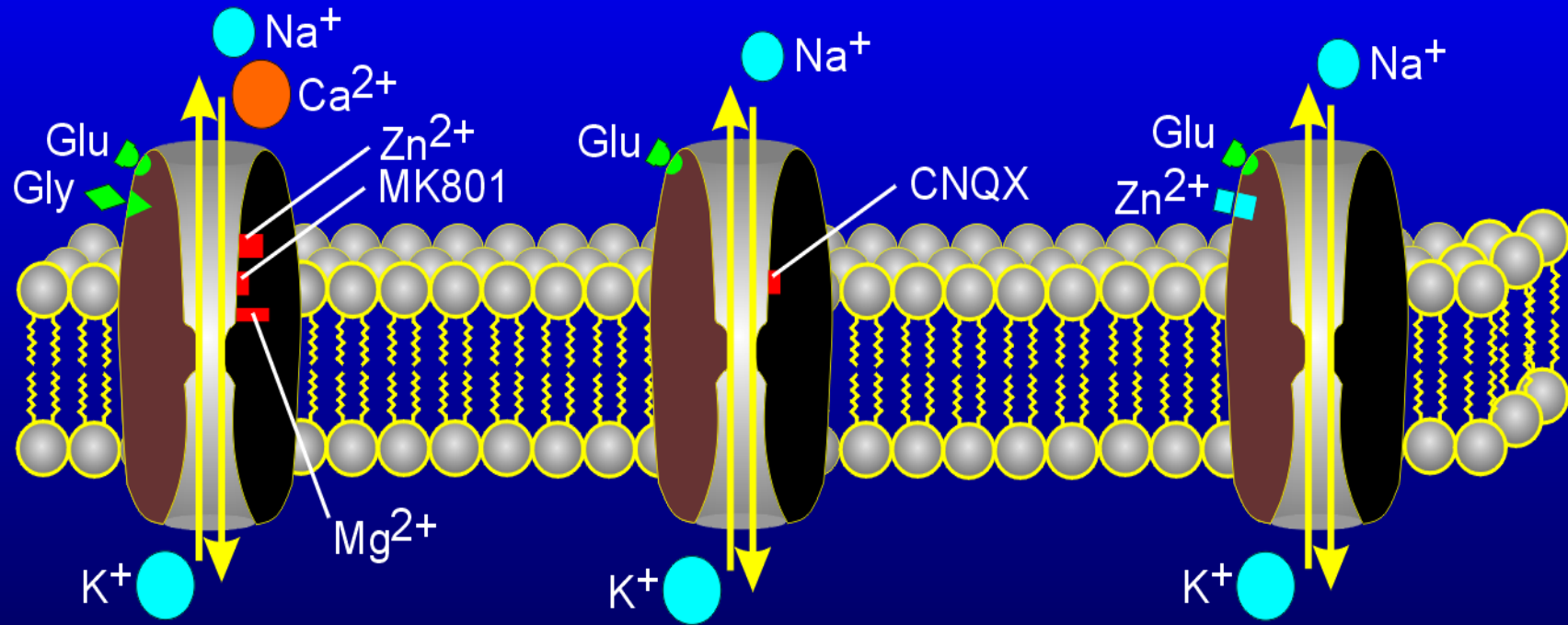


Iontový kanál	Astrocyty	Oligodendrocyty	Neurony
Na <sub>V</sub>	Ano	Ne	Ano
Ca <sub>T</sub>	Ano	Ne	Ano
Ca <sub>L</sub>	Ano	Ne	Ano
Ca <sub>N</sub>	Ne	Ne	Ano
K <sub>D</sub>	Ano	Ano	Ano
K <sub>A</sub>	Ano	Ano	Ano
K <sub>Ca</sub>	Ano	Ne	Ano
K <sub>IR</sub>	Ano	Ano	Ano
Cl <sub>V</sub>	Ano	Ano	Ano

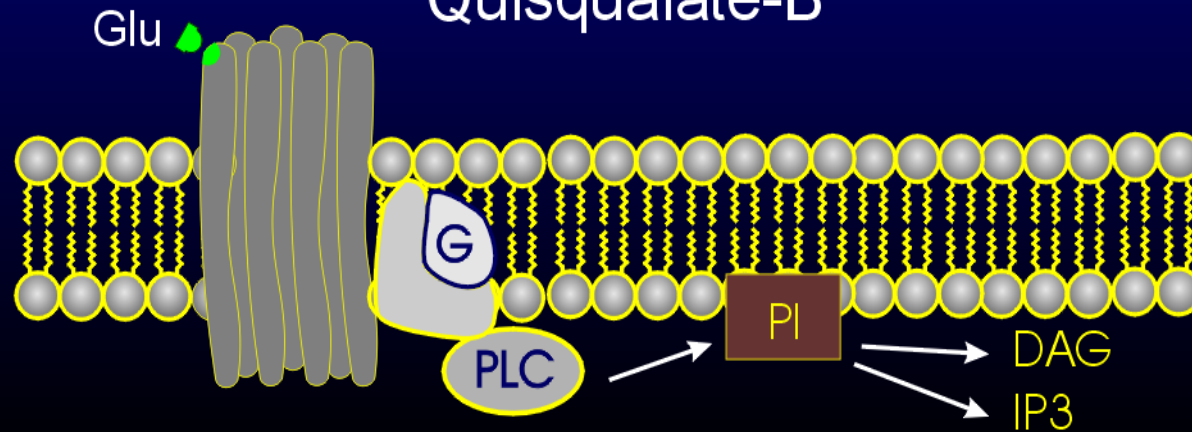
NMDA

Kainate (AMPA)

Quisqualate-A (AMPA)



Quisqualate-B

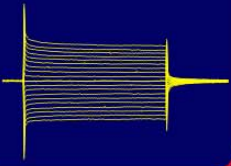


L-Glutamate

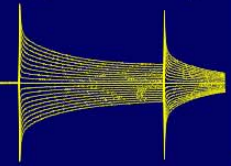
Kainate

NMDA

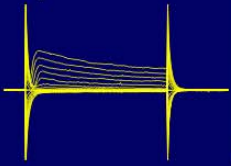
Astrocyte



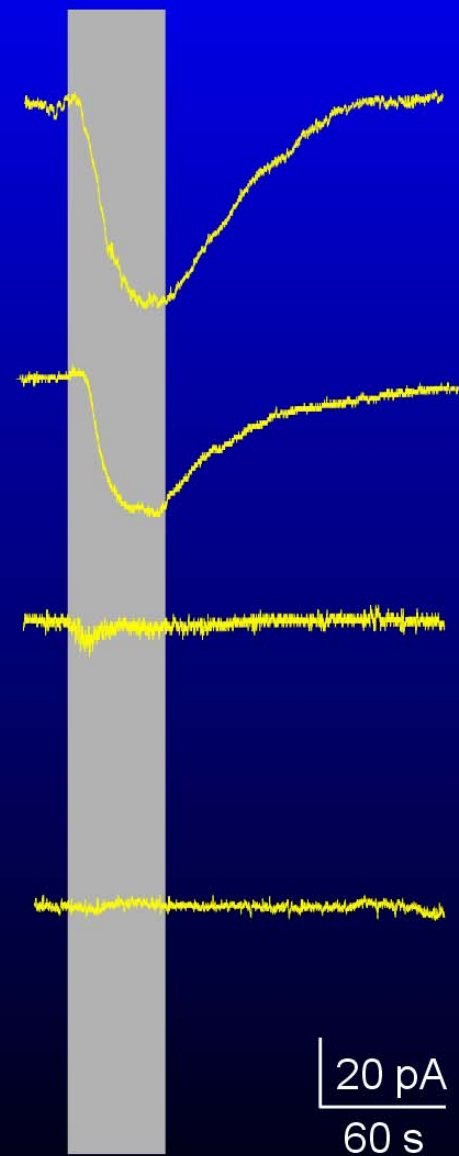
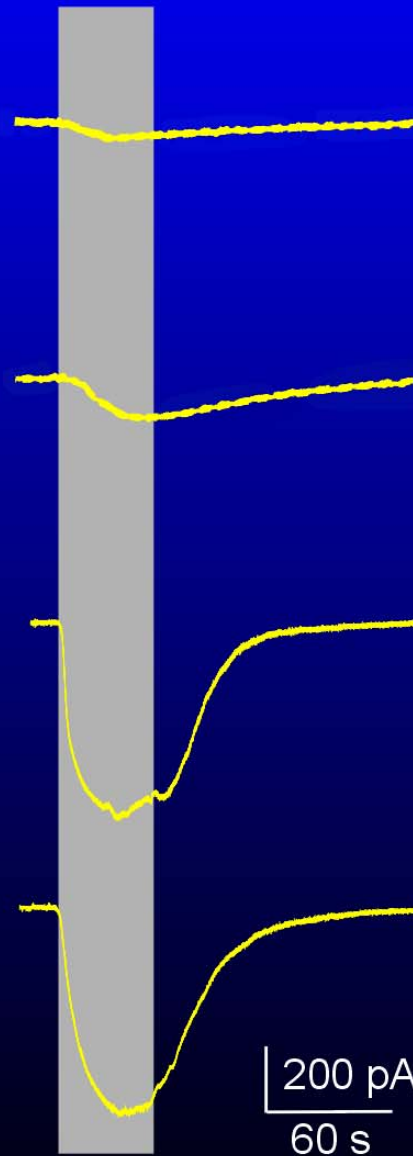
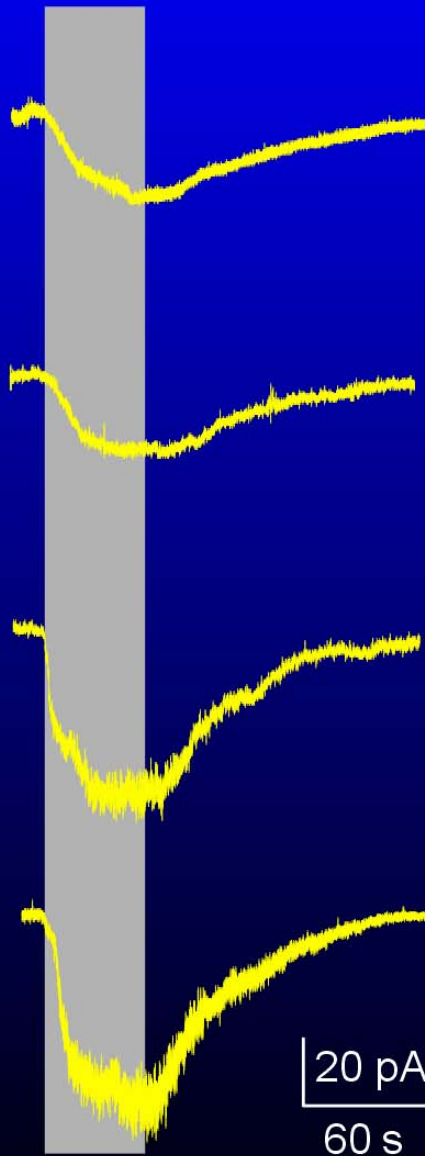
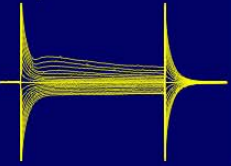
Oligodendrocyte



Astrocyte precursor



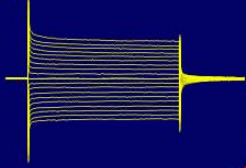
Oligodendrocyte precursor



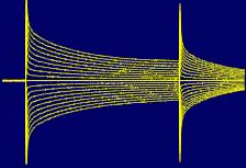
GABA

Glycine

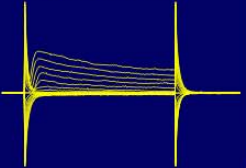
Astrocyte



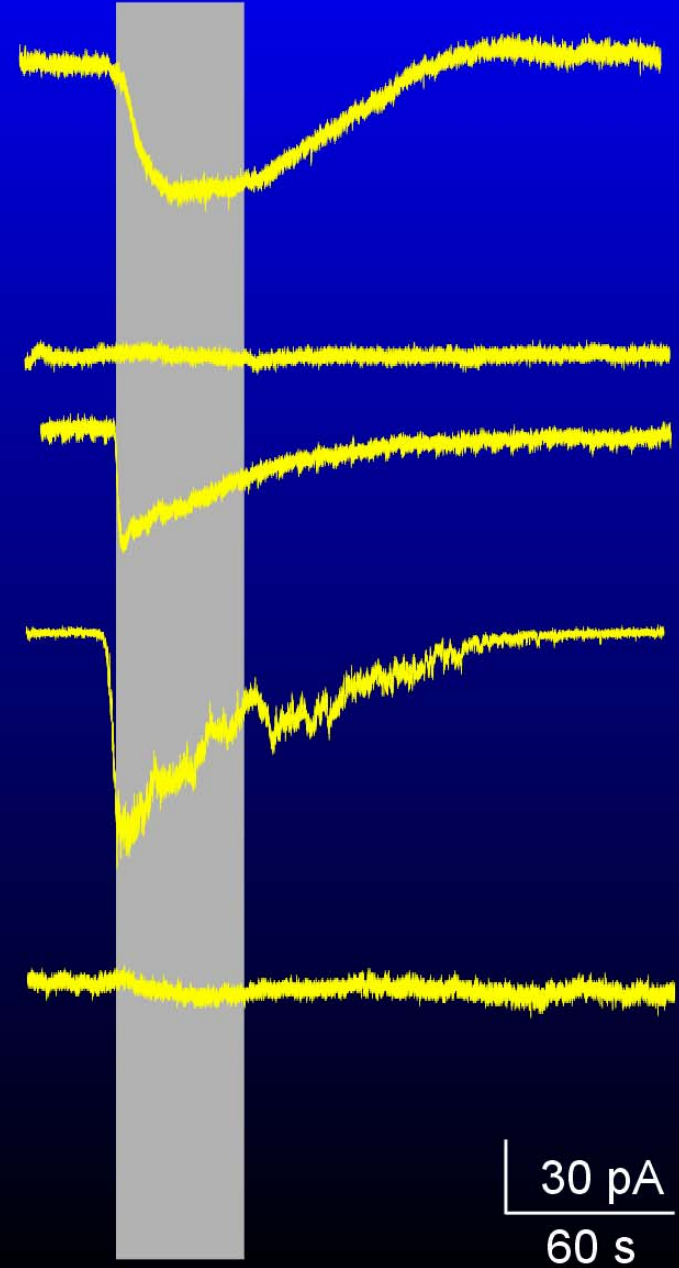
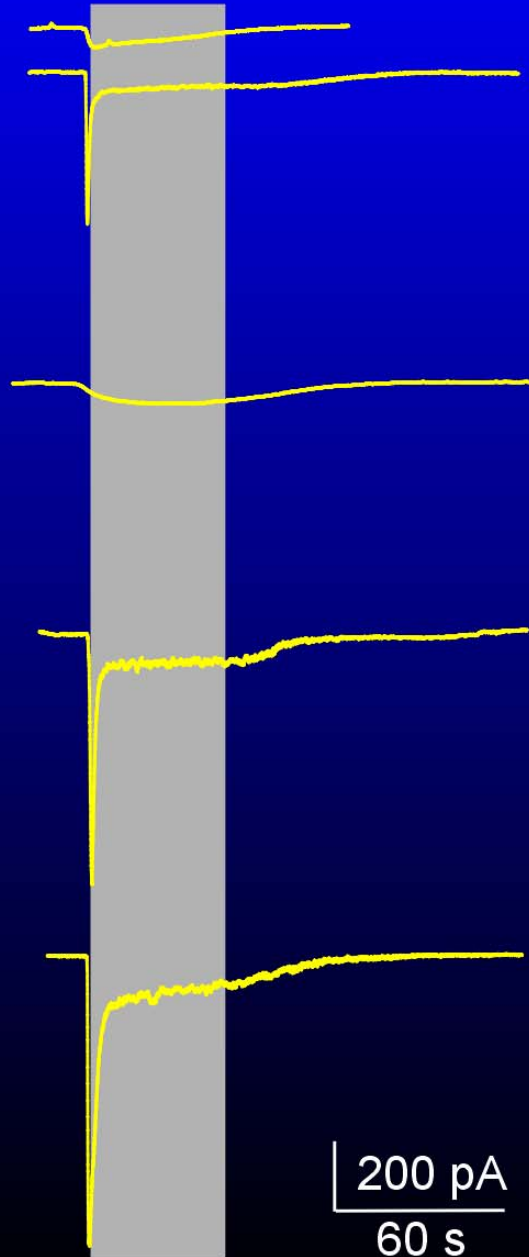
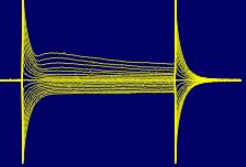
Oligodendrocyte



Astrocyte precursor

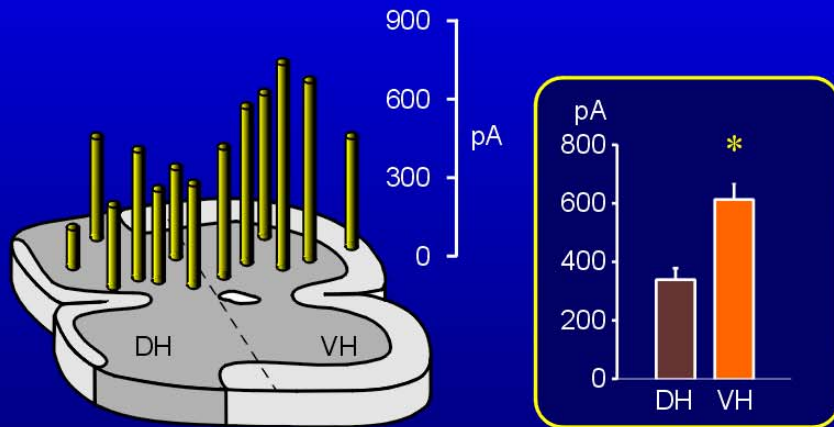


Oligodendrocyte precursor

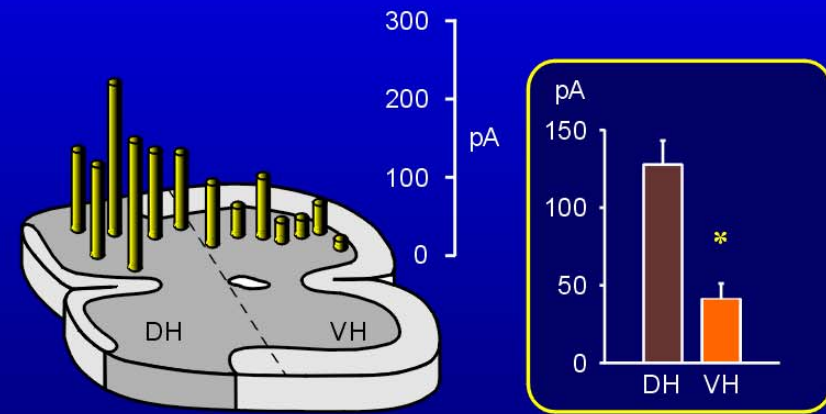


# Kainate-evoked currents

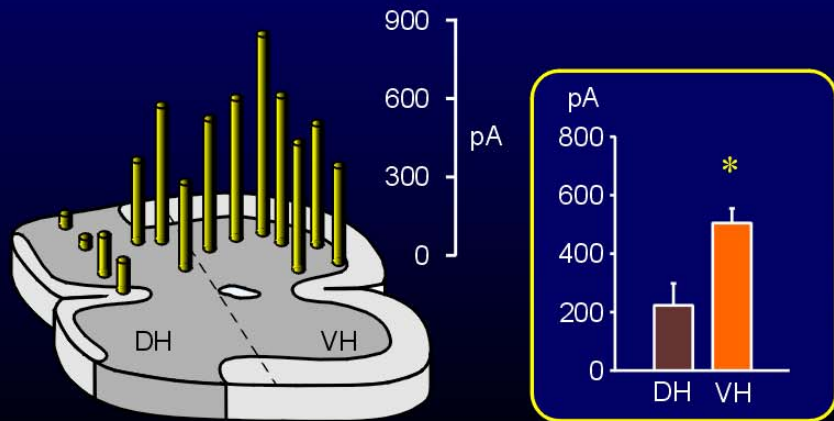
## Astrocyte precursors



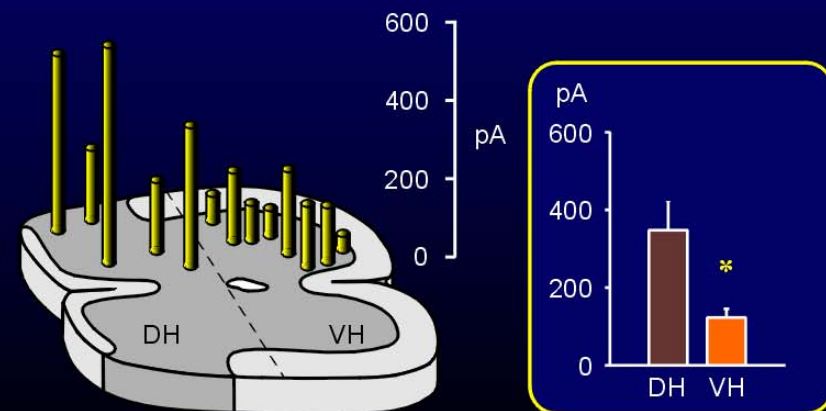
## Astrocytes

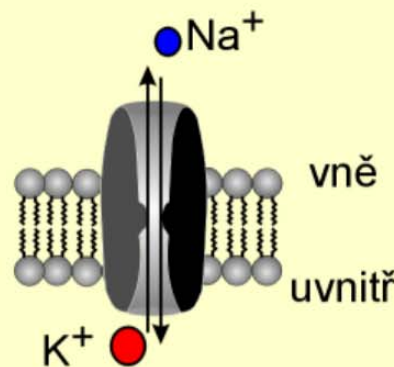
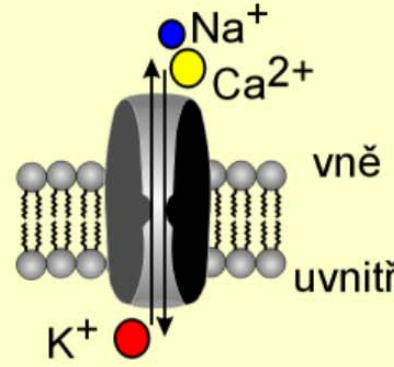
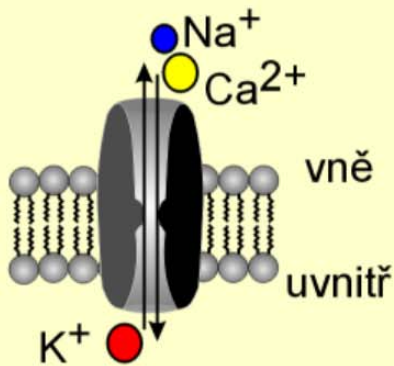
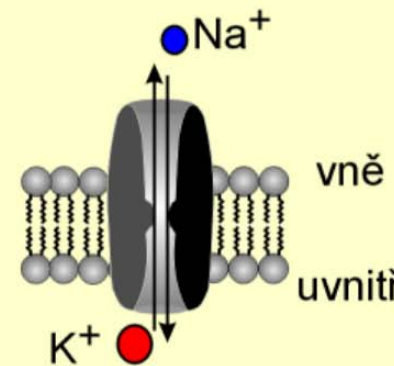
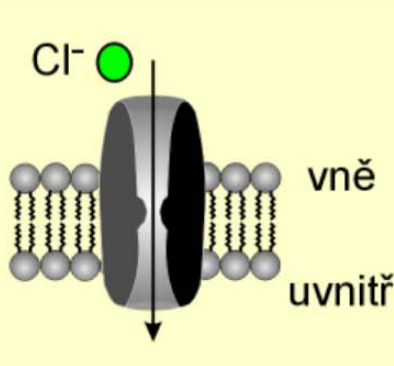
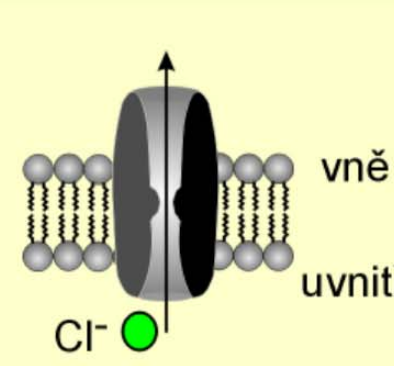


## Oligodendrocyte precursors



## Oligodendrocytes

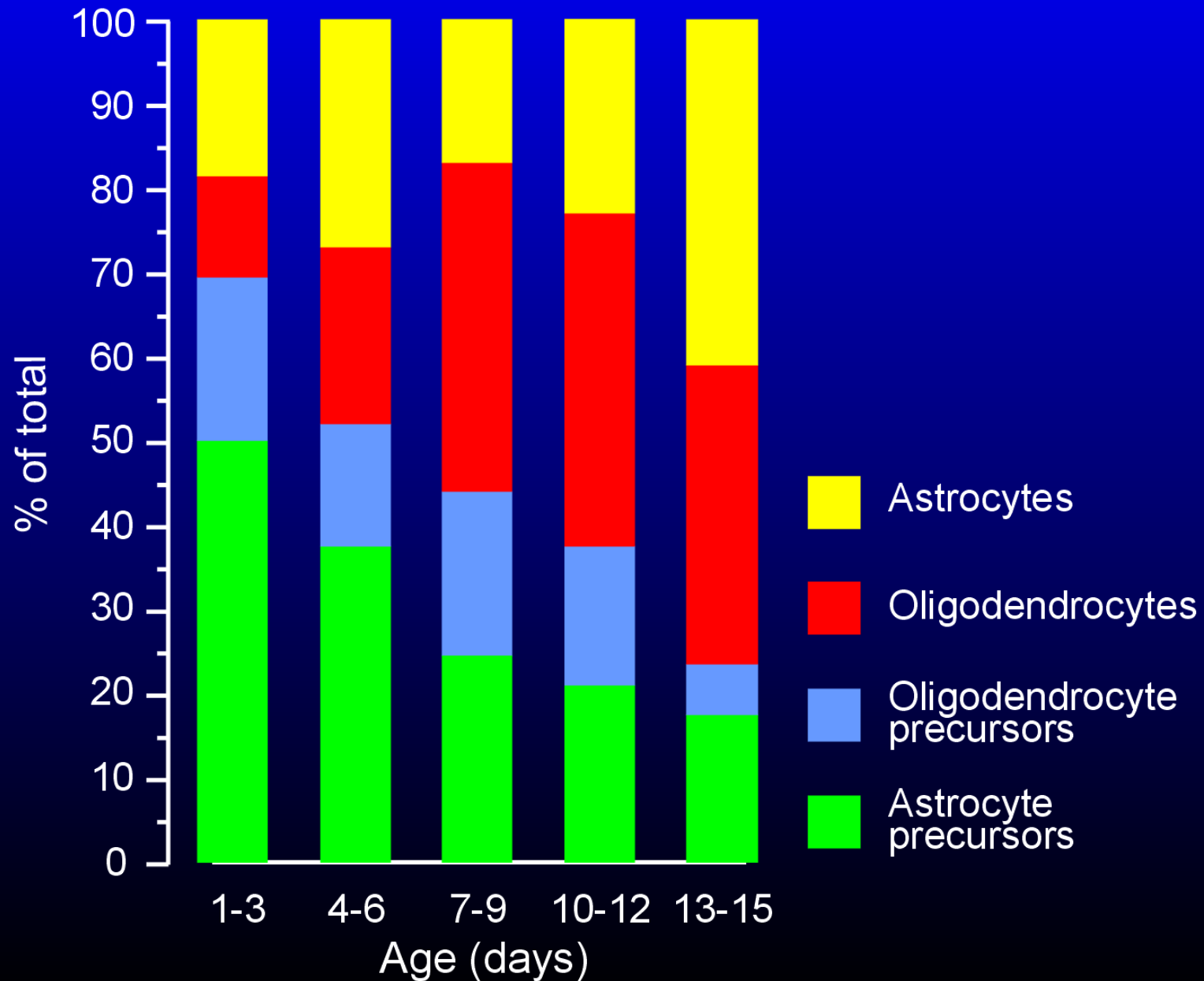


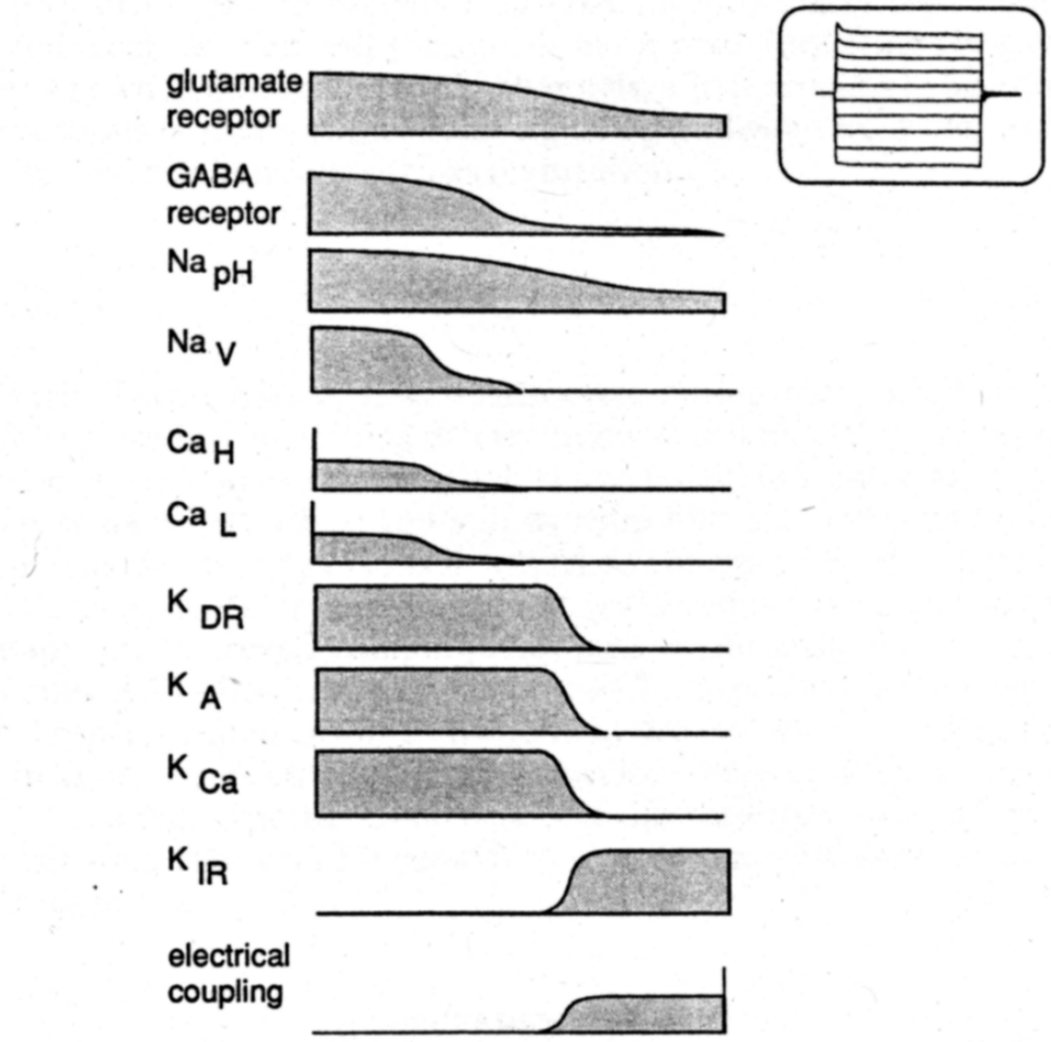
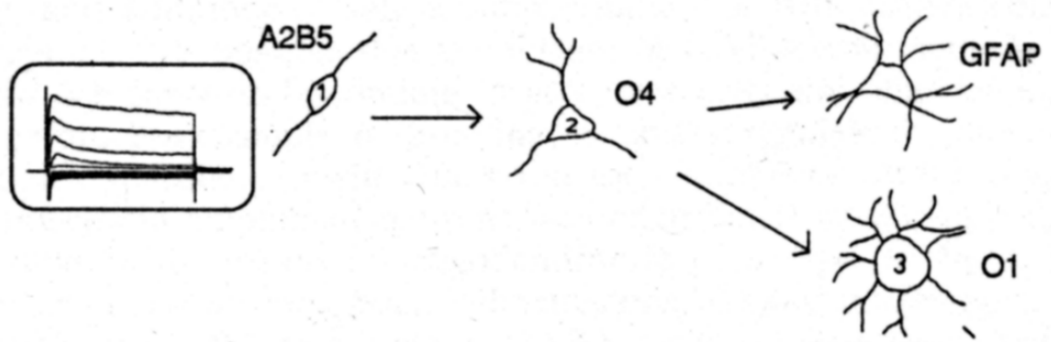
receptor	neurony	gliové buňky
AMPA / kainátový		 <p>hipokampus mozeček mícha oční sítnice</p>
NMDA		 <p>hipokampus mozeček mícha oční sítnice kůra mozková</p>
GABA <sub>A</sub>		 <p>hipokampus mozeček mícha oční sítnice</p>
glycin		<p>mícha</p>

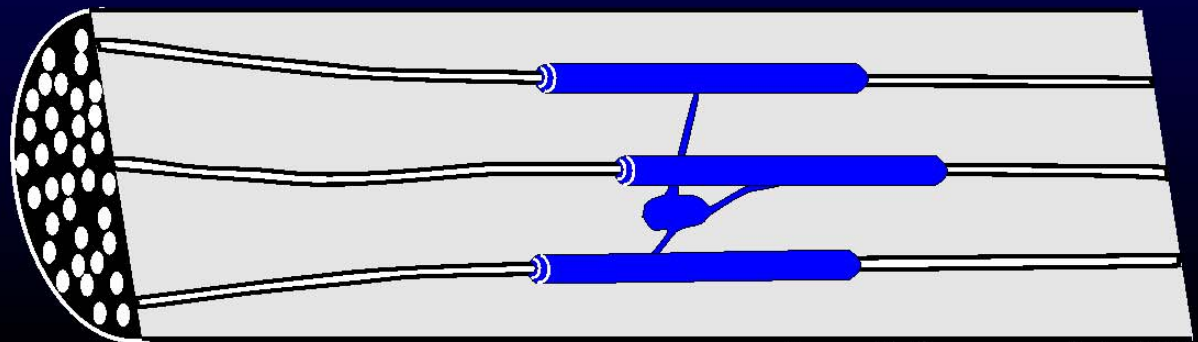
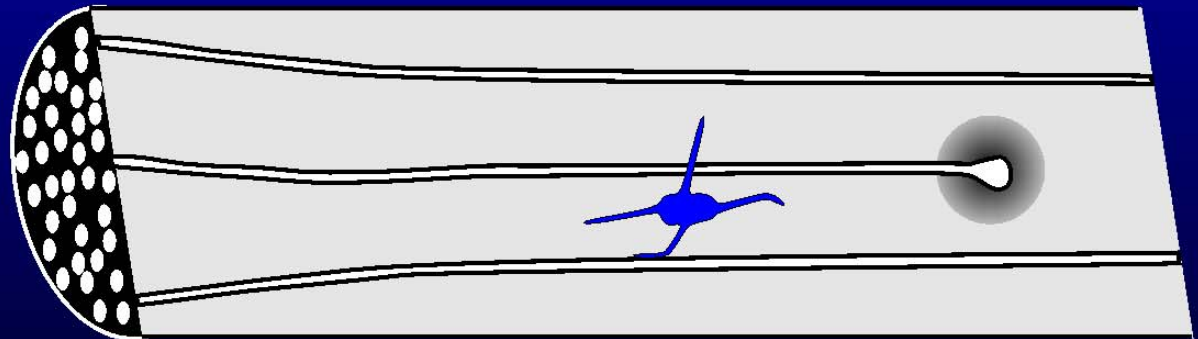
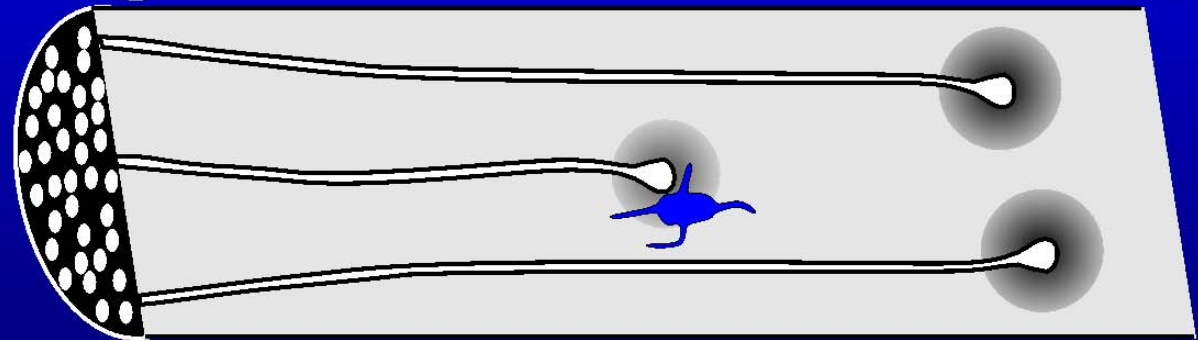
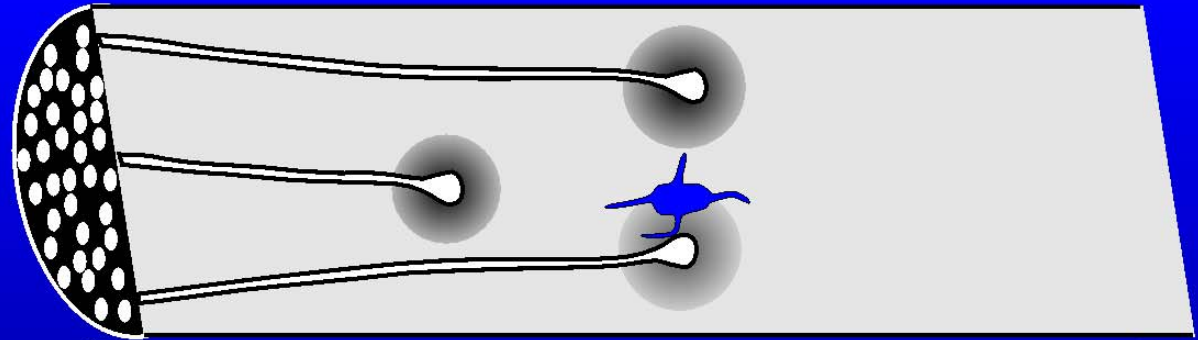
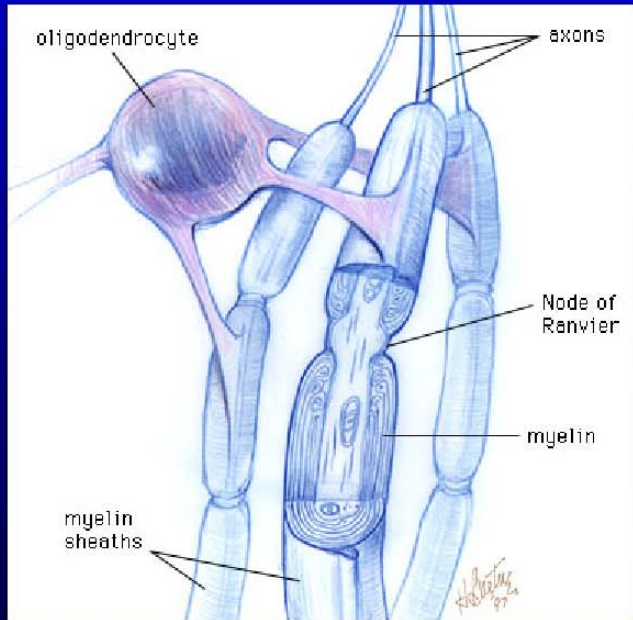
## Metabotropní receptory astrocytů *in vivo*

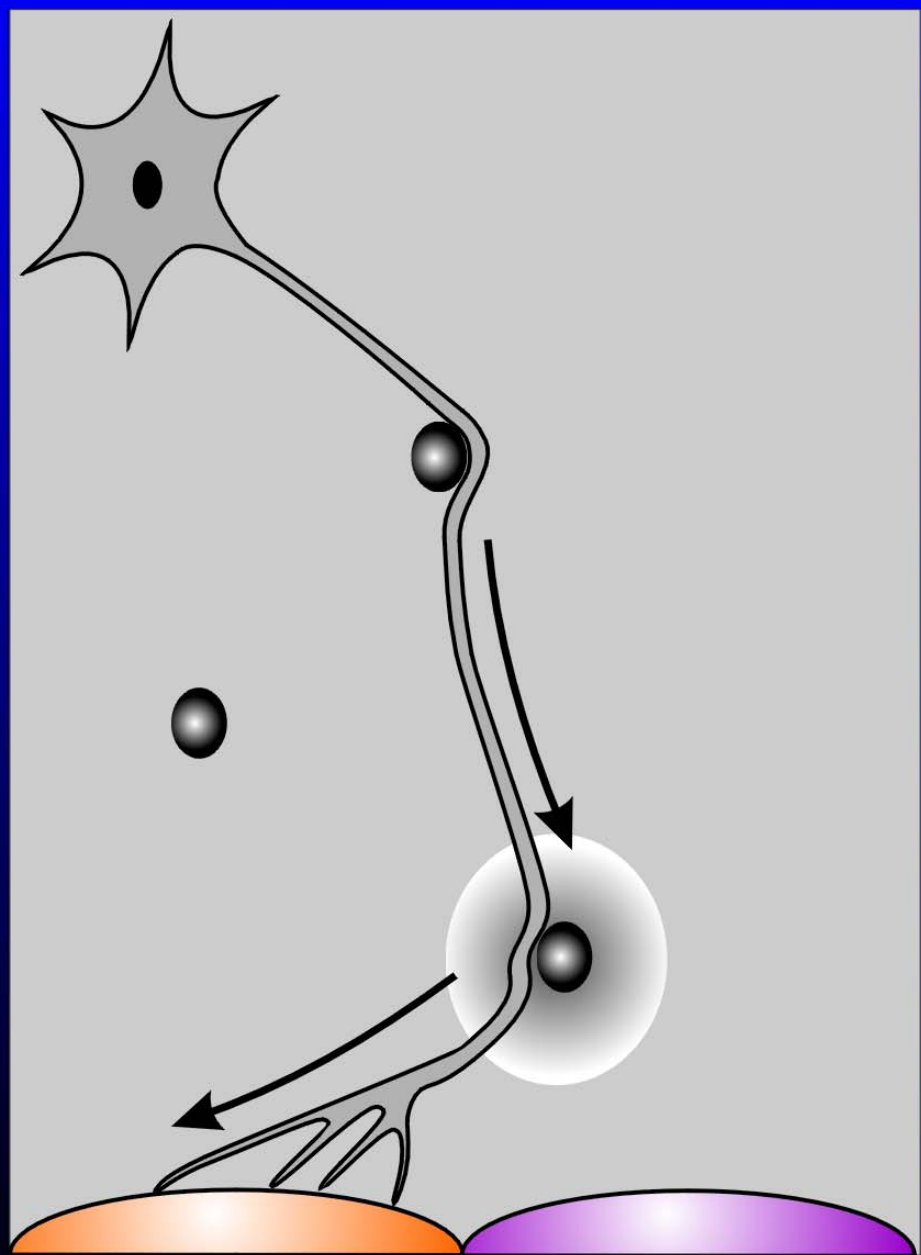
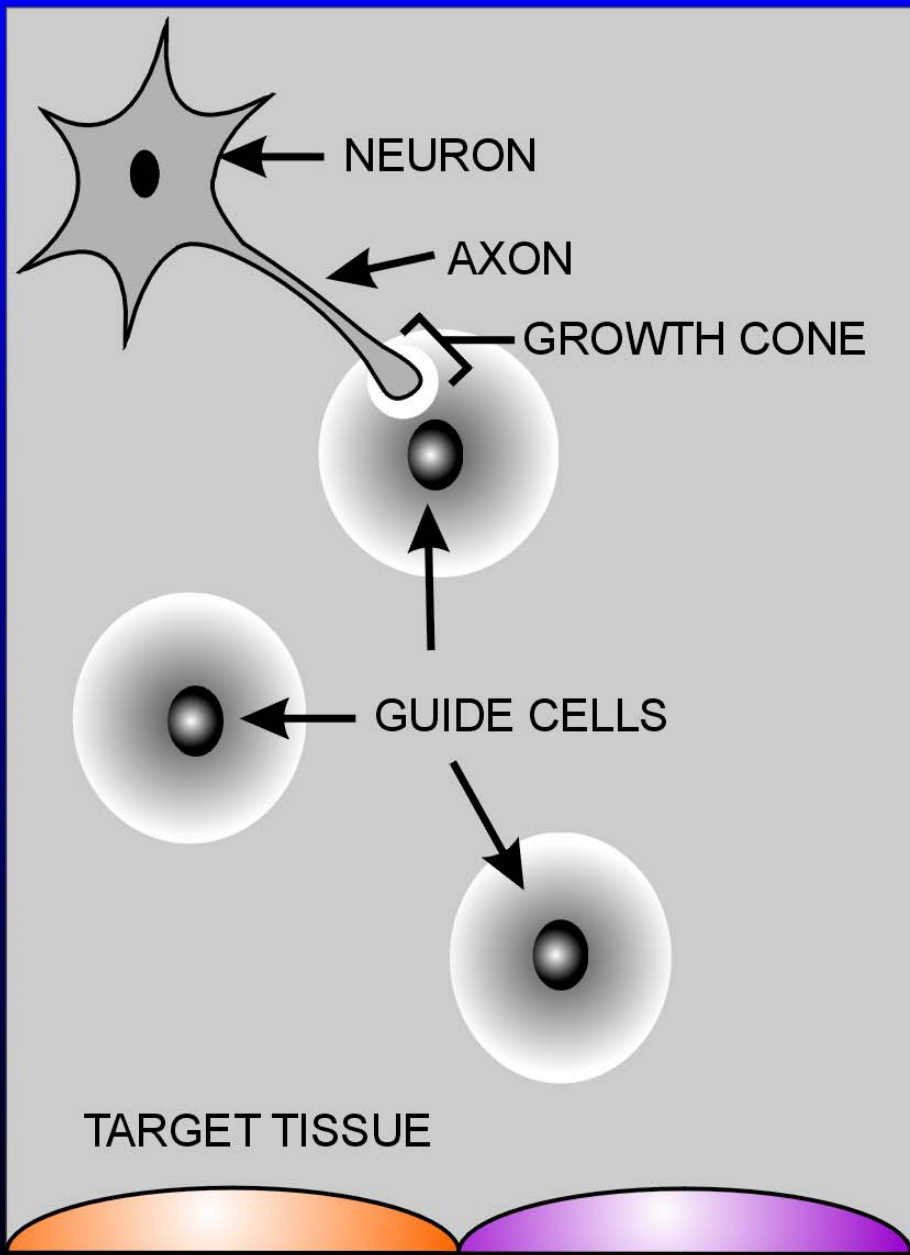
Receptor	Oblast CNS	Efekt
mGlu	hipokampus, kůra mozková	fosfolipáza C
β2 adrenergní	mozeček, kůra mozková	adenylát cykláza
α1 adrenergní	mozeček, kůra mozková, striatum	fosfolipáza C
adenozín	hipokampus	fosfolipáza C
ATP	hipokampus, mozeček	zvýšení $[Ca^{2+}]_i$
serotonin	hipokampus, corpus callosum, kůra mozková	?
mACH	hipokampus, corpus callosum, kůra mozková	?
histamín	mozeček	zvýšení $[Ca^{2+}]_i$
somatostatin	hipokampus, amygdala, hypotalamus	?
substance P	při reaktivní astroglióze v optickém nervu	?
κ opioidní	Pituicyty	?
natriuretický faktor	hipokampus, amygdala	zvýšení cGMP

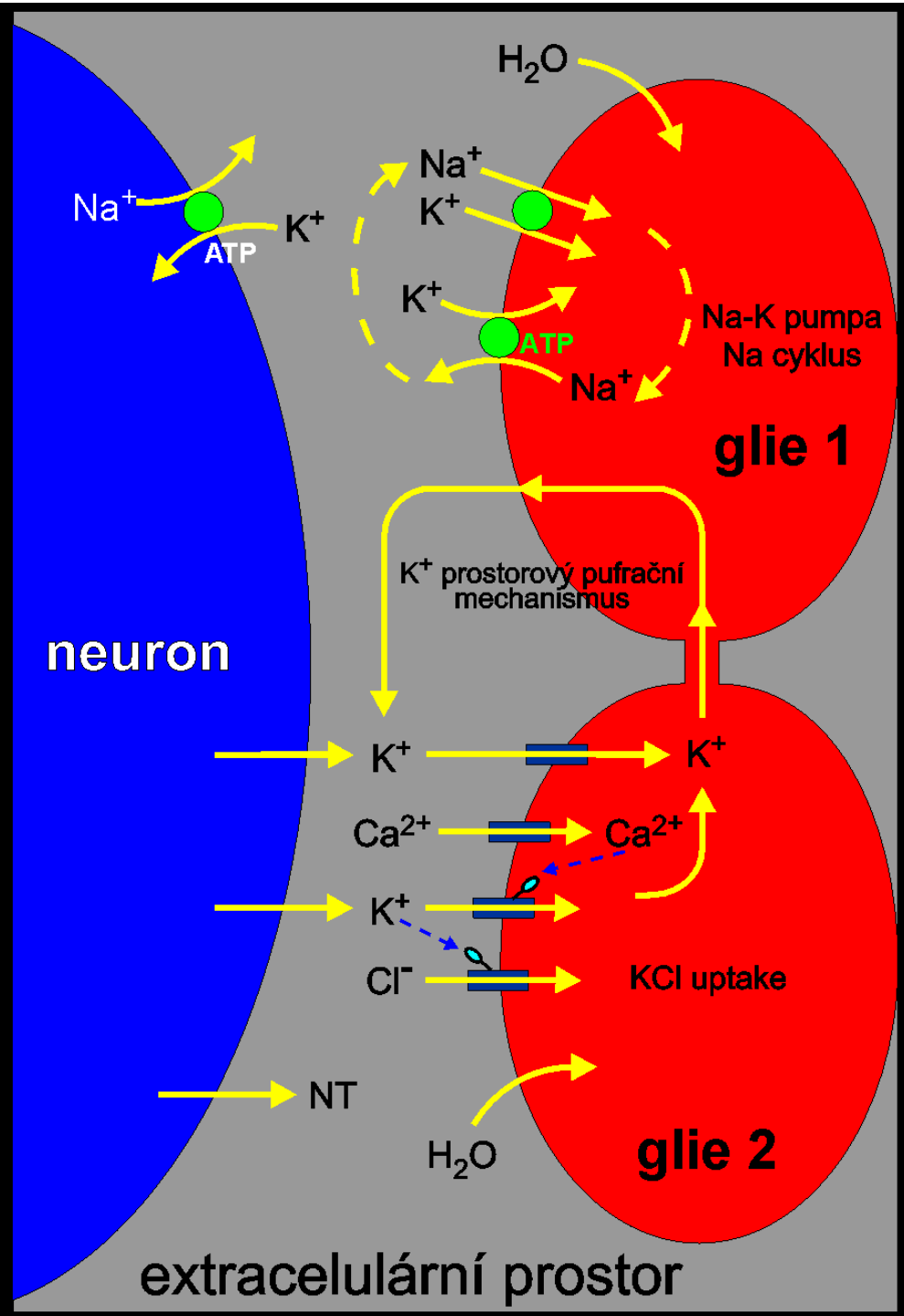
# Rat spinal cord gray matter









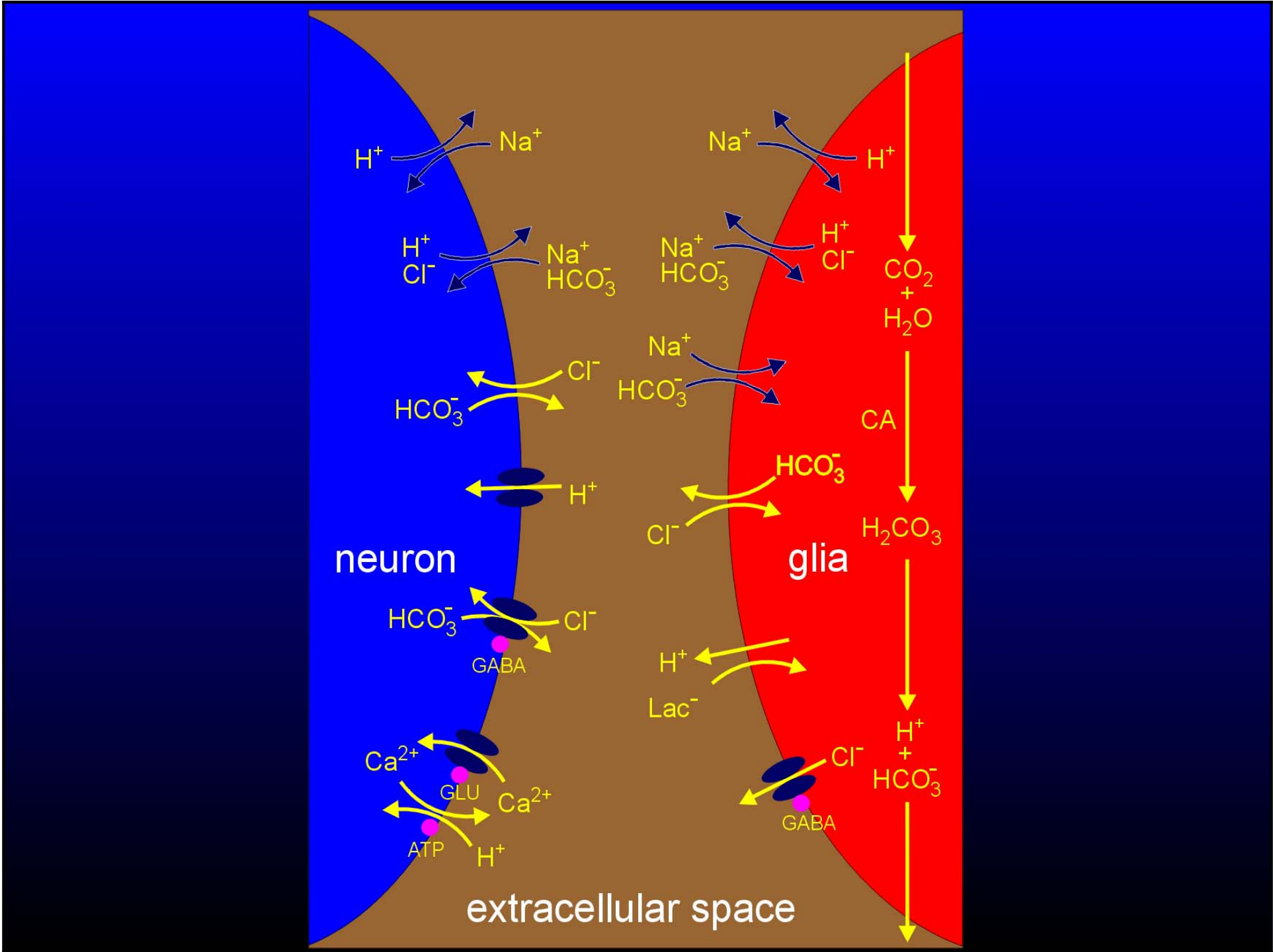


neuron

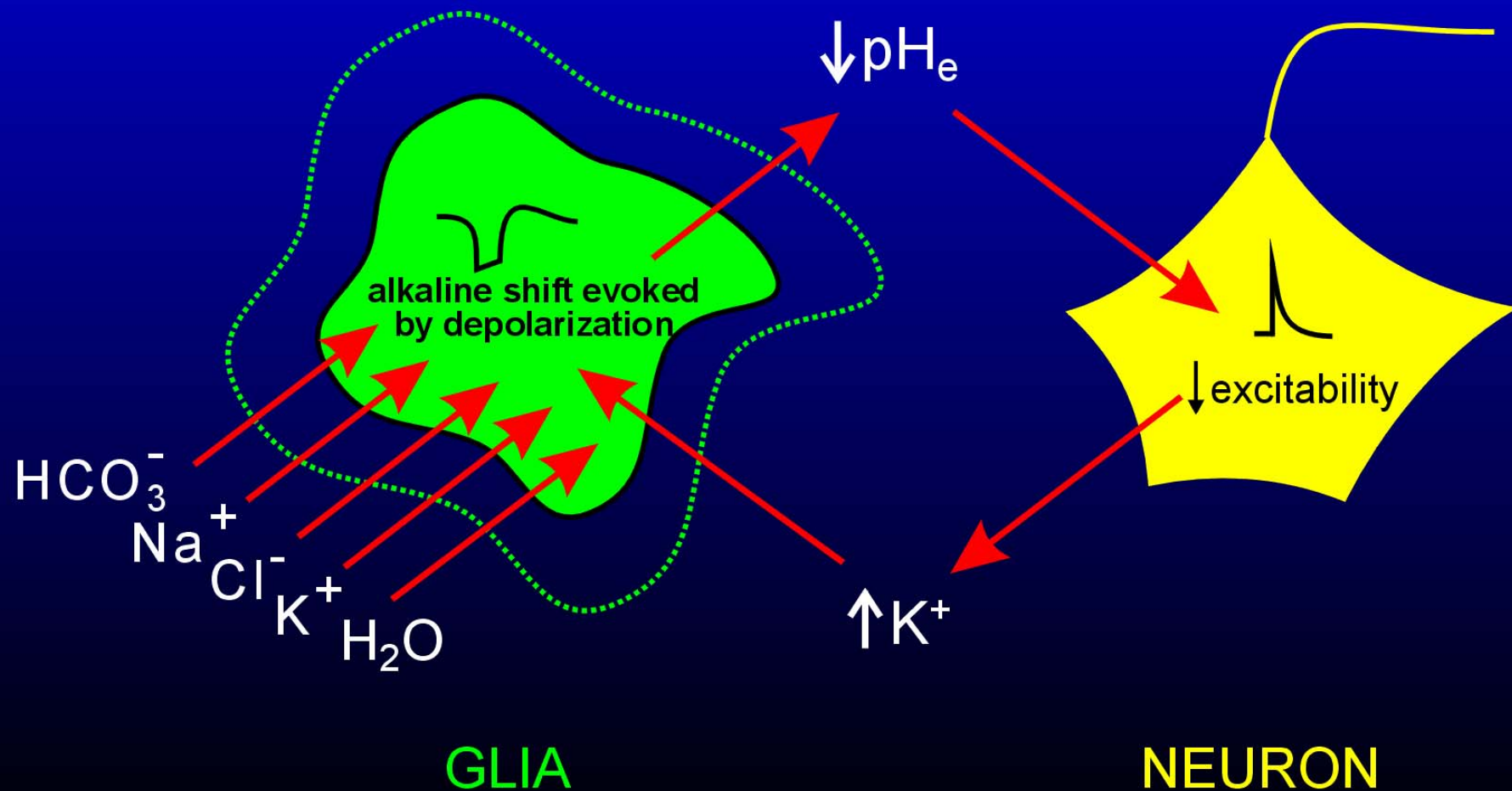
glie 1

glie 2

extracelulární prostor

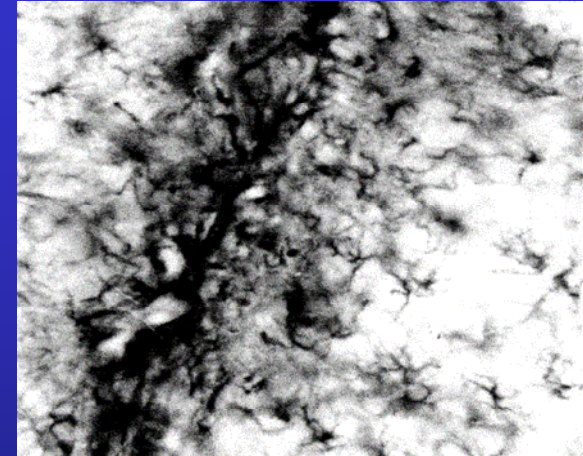
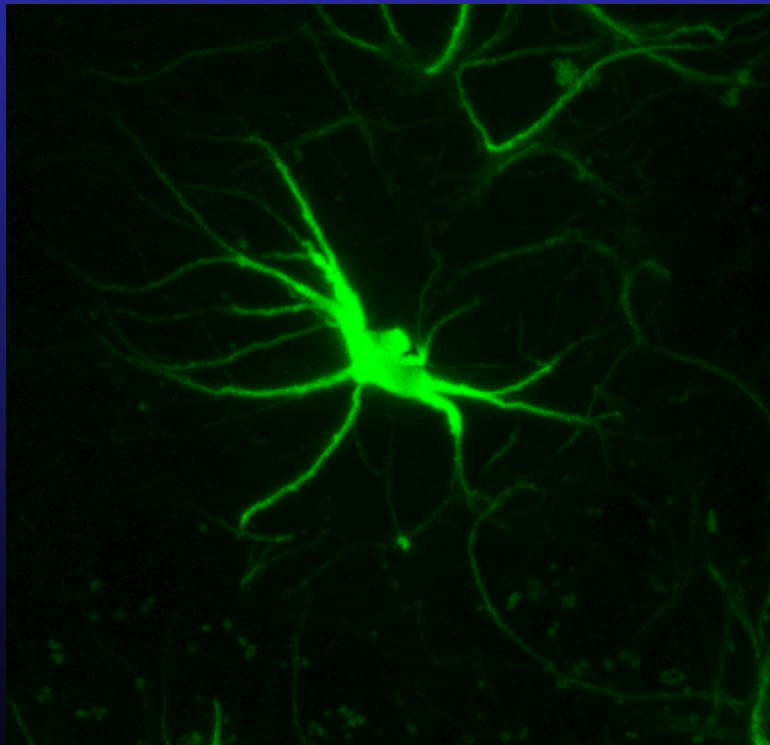


# Mechanism of non-specific feedback suppressing neuronal activity

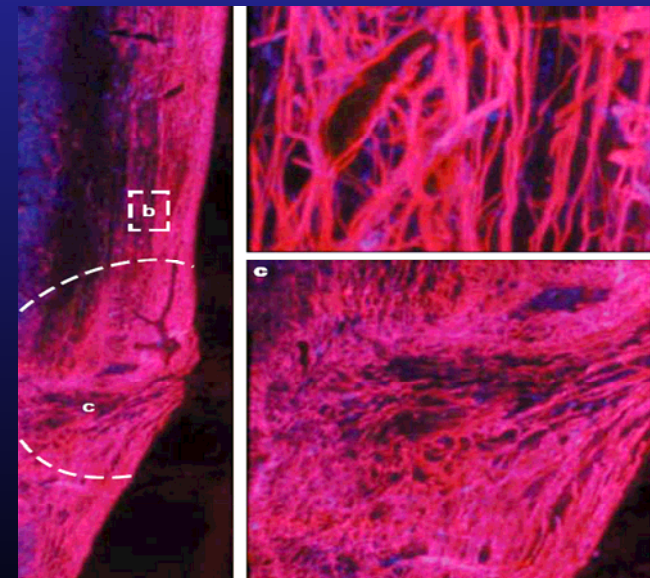


# Astrocyte pathophysiological response

- Astrogliosis
- Glia scar

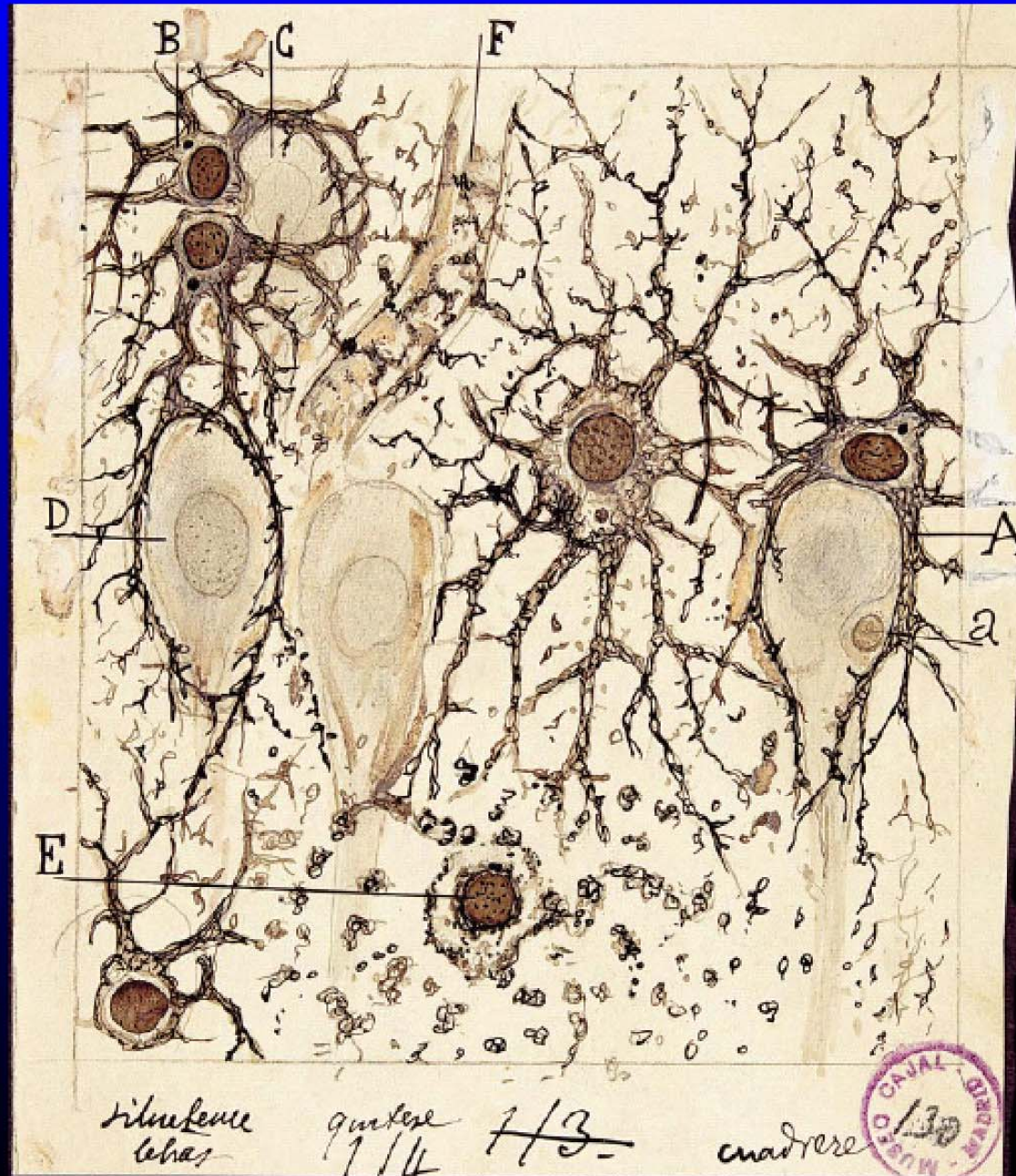


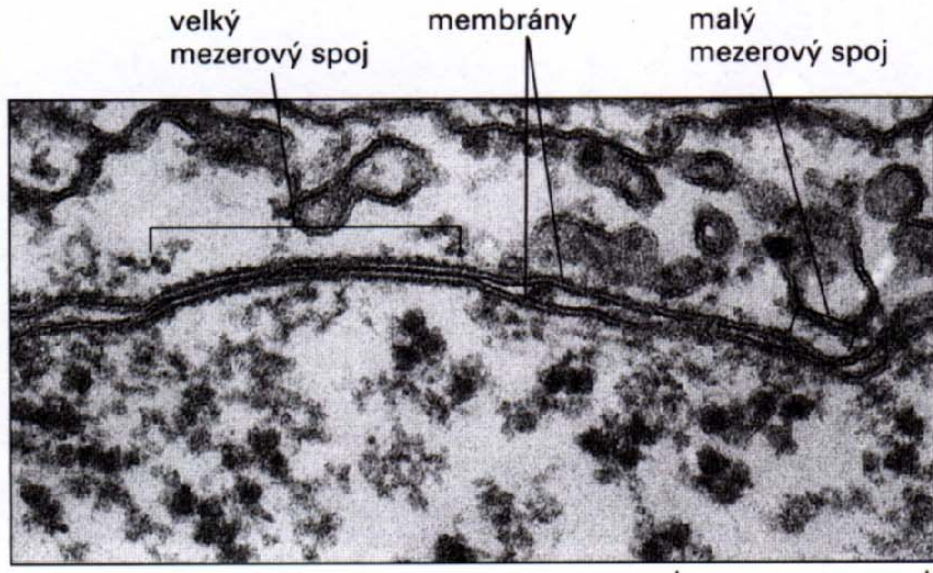
Monzón-Mayor et al. *Brain Res.* 865:245-258, 2000



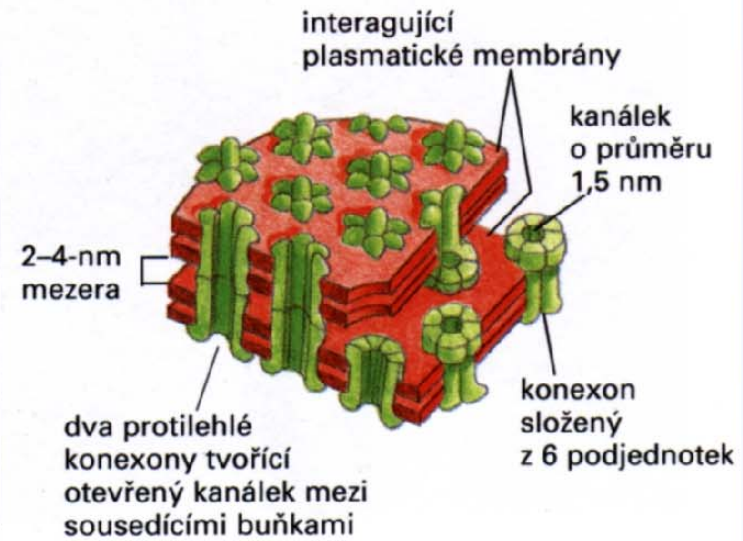
Silve and Miller. *Nature Rev Neurosci* 5: 146-156

# Neuroglia of the pyramidal layer and stratum radiatum of the Ammon horn

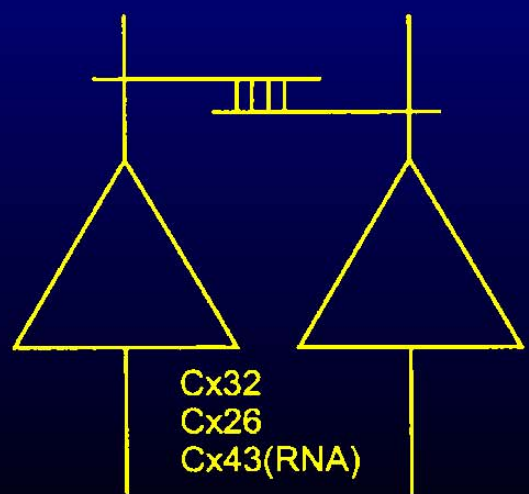




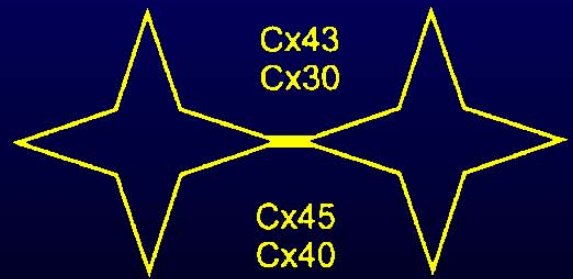
(A)



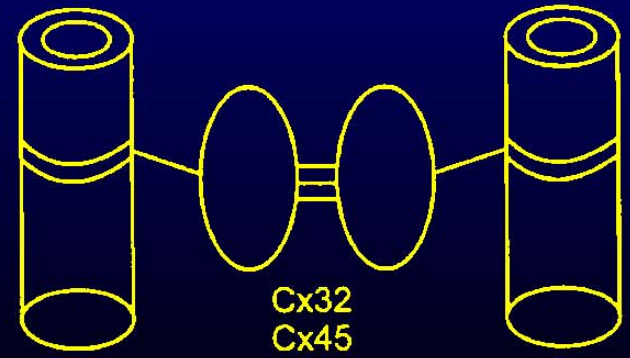
(B)



Neurons

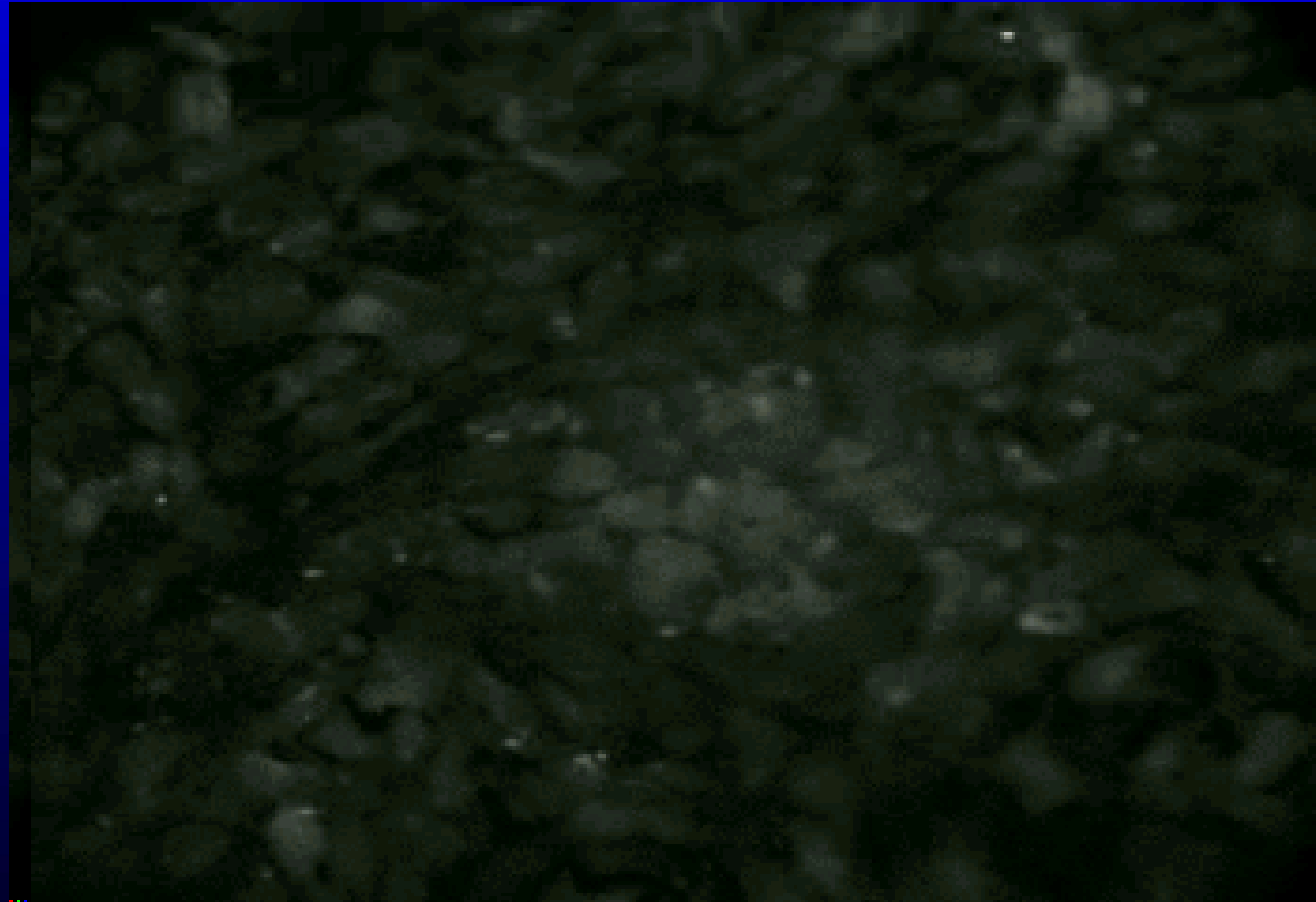


Astrocytes



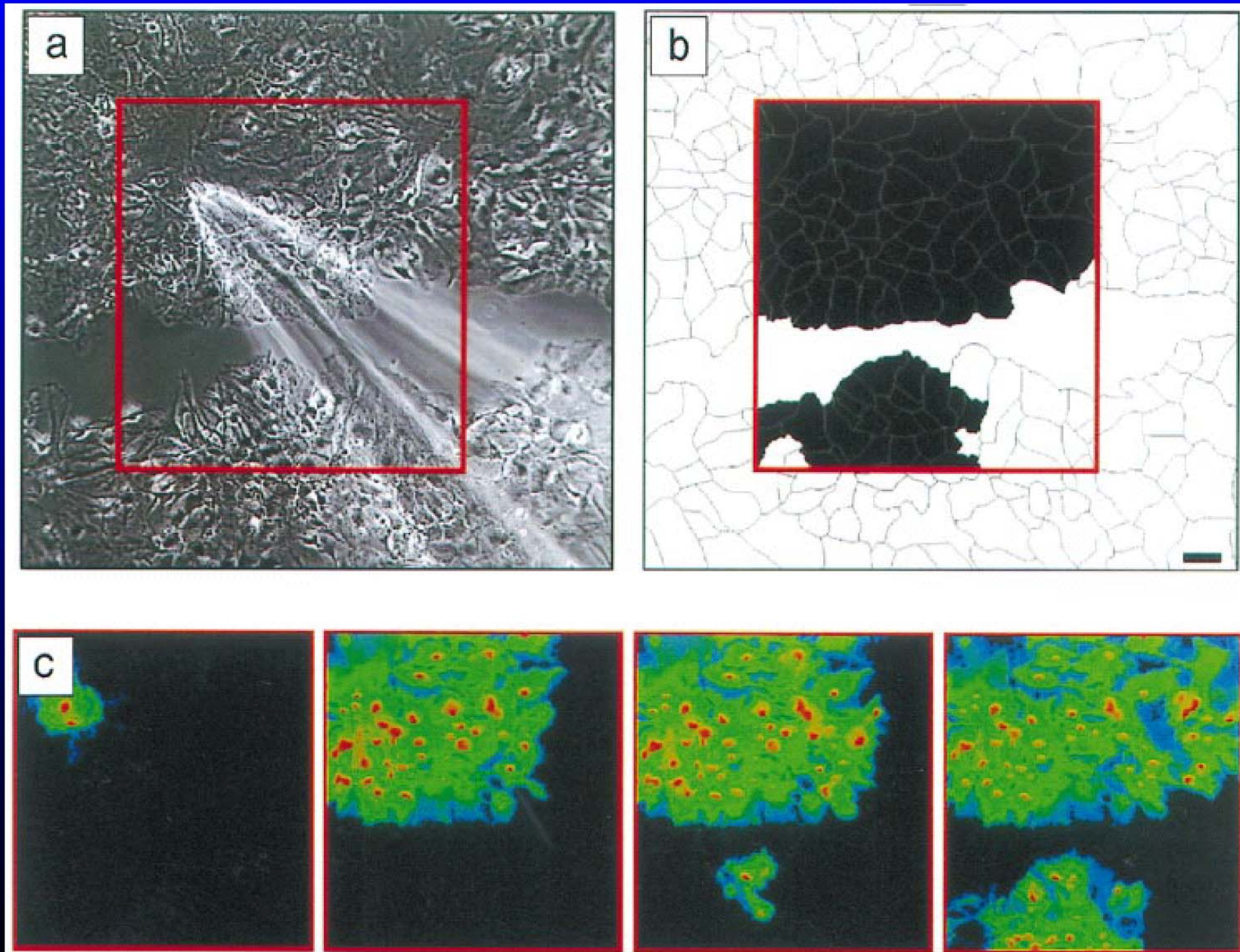
Oligodendrocytes

Stimulation of glial cells evokes a radially propagating wave of elevated calcium

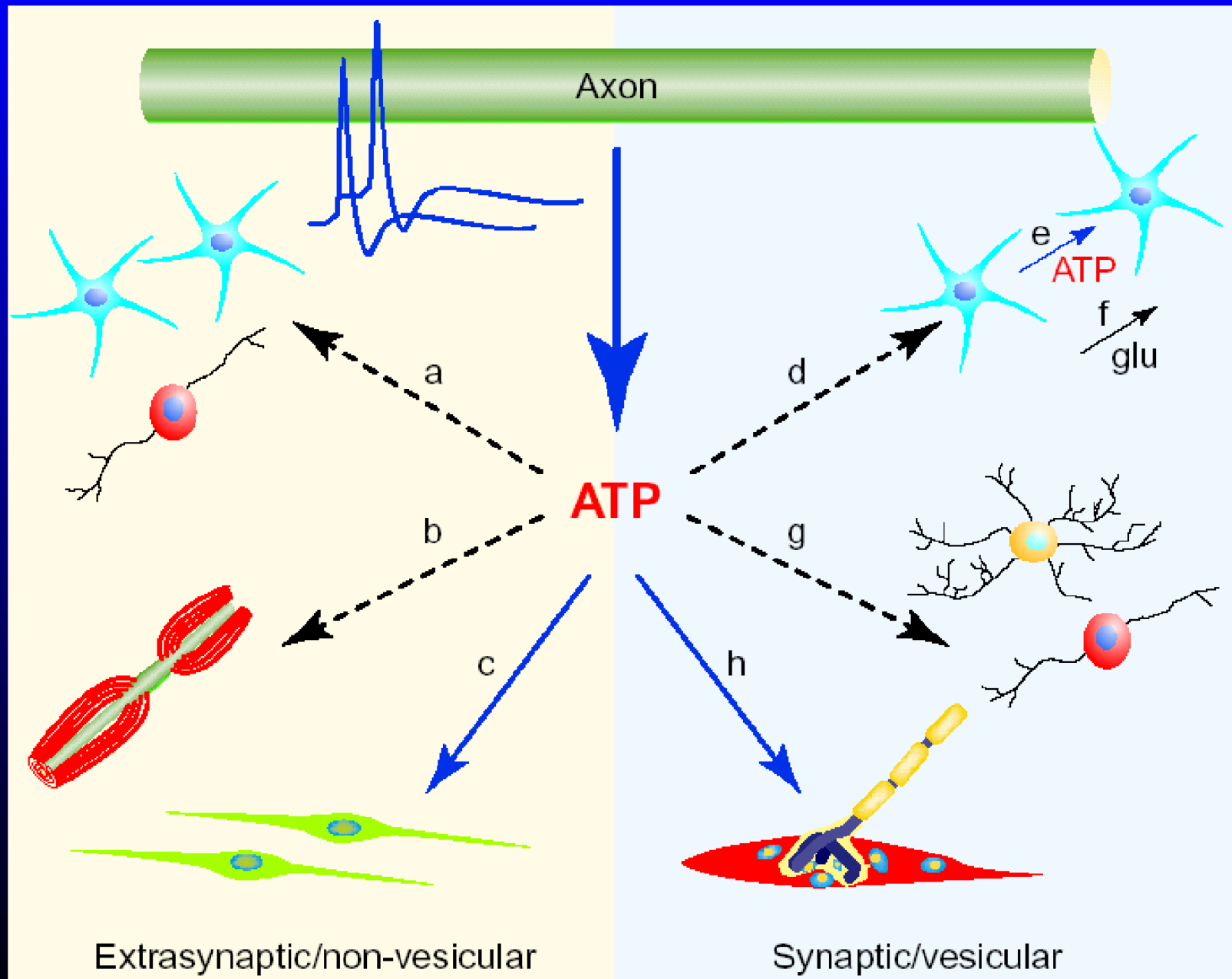


*P. Haydon, Nature Rev Neurosci 2, 2001*

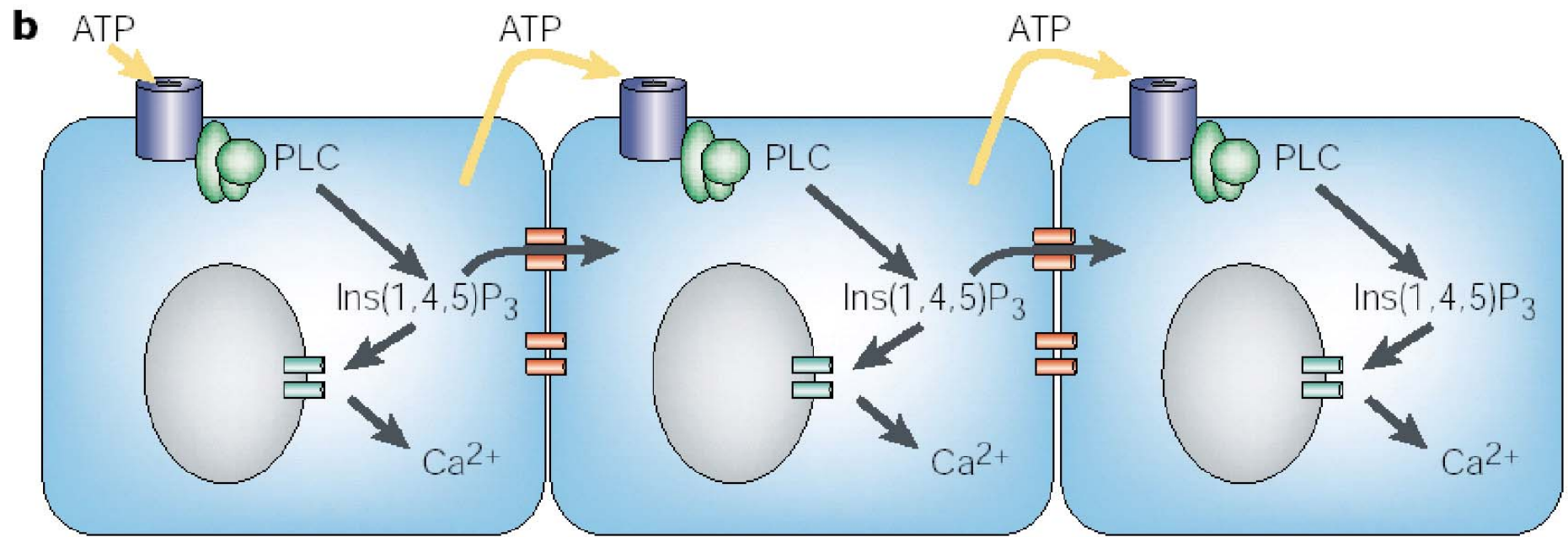
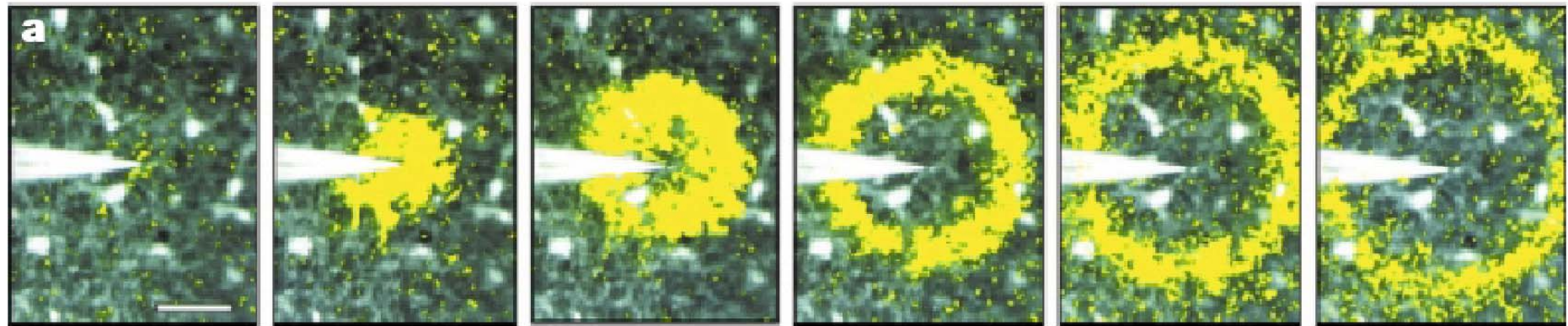
## Extracellular component in astrocytic calcium wave propagation



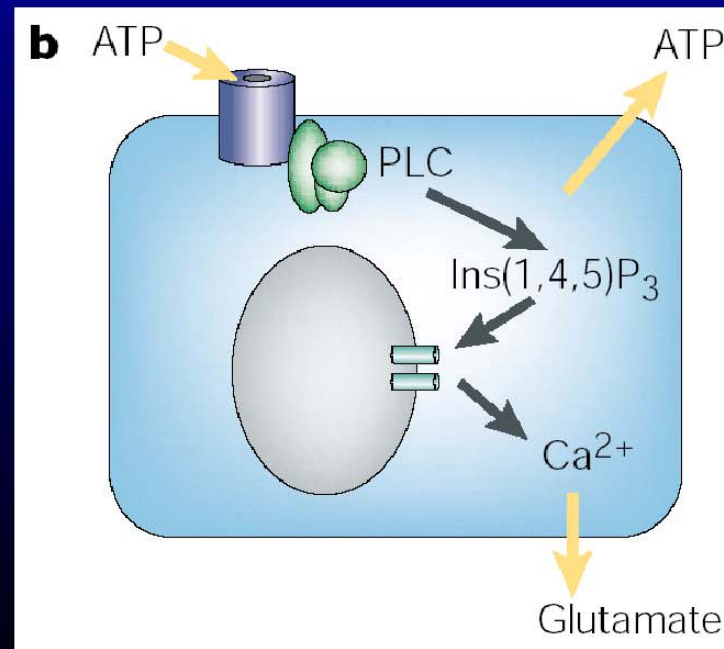
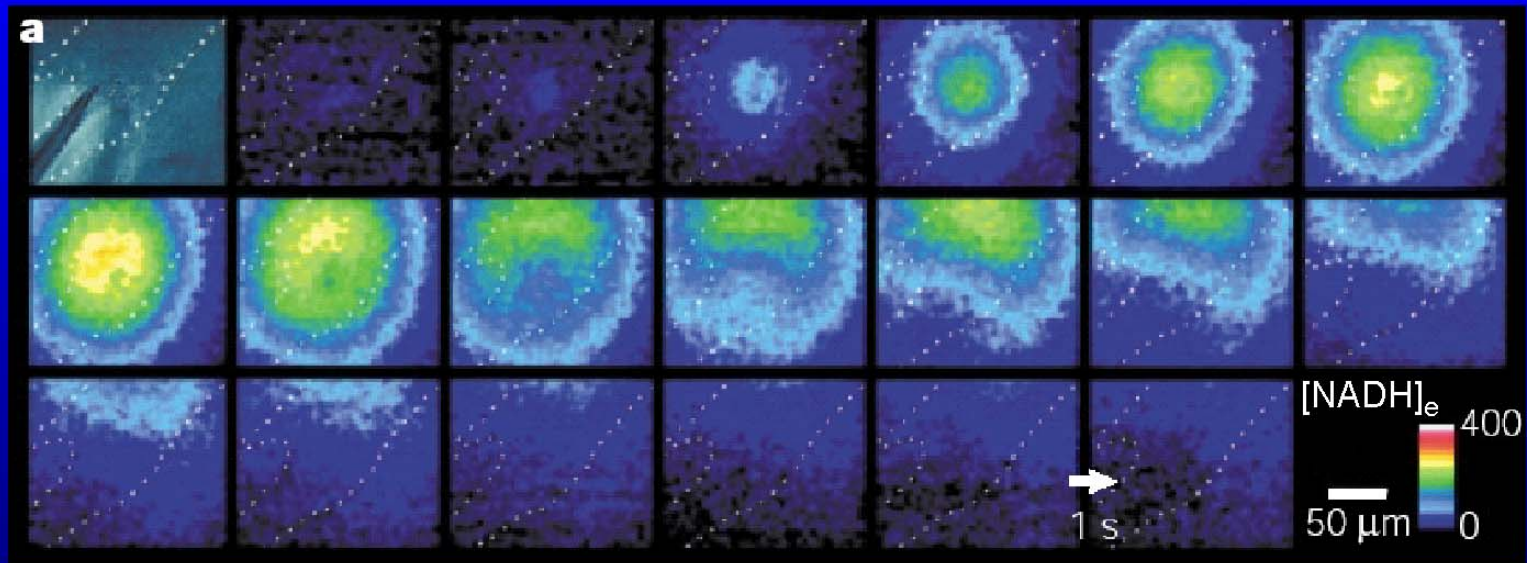
# ATP-mediated communication from the axon to glial cells



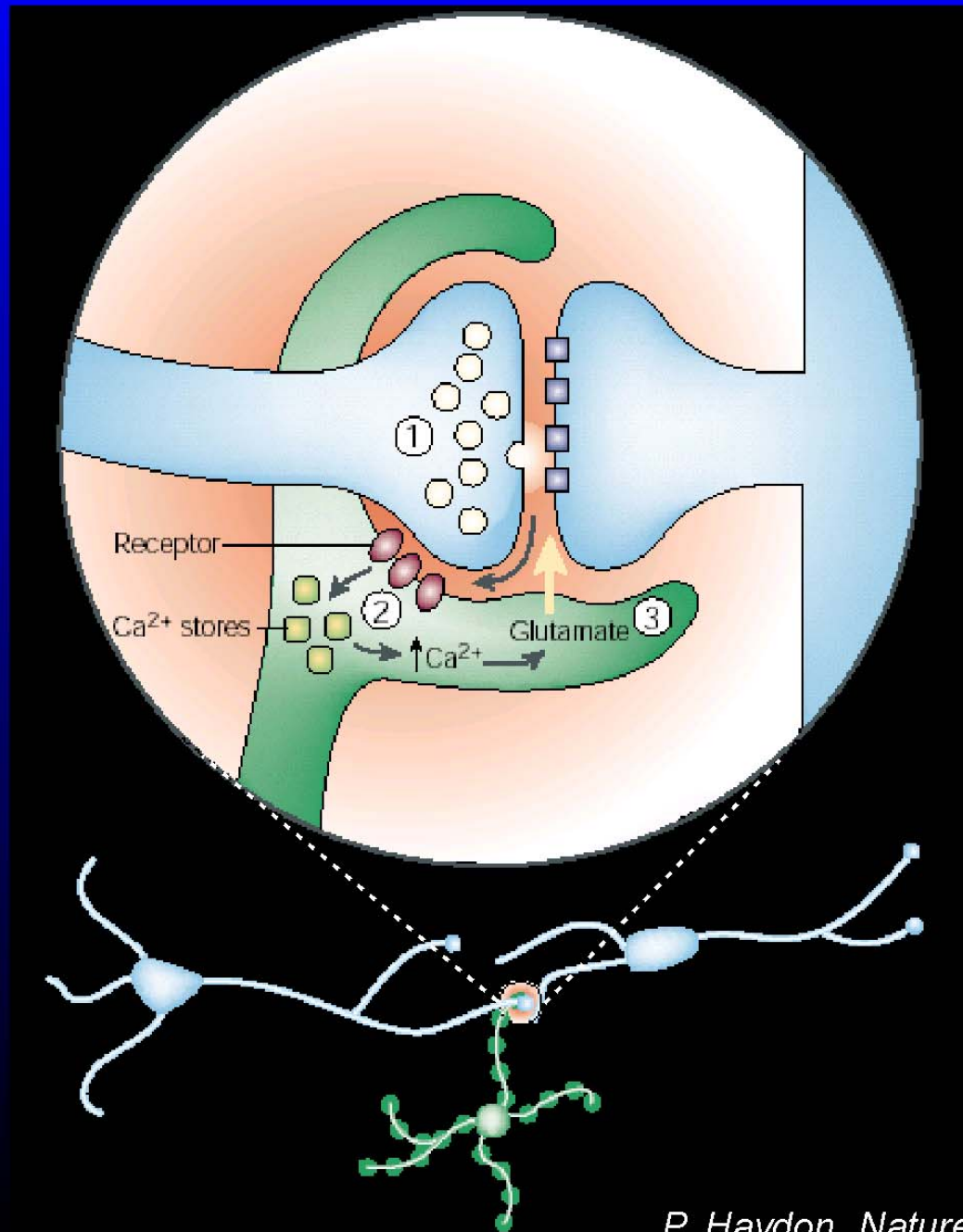
# Stimulation of glial cells evokes a radially propagating wave of elevated calcium



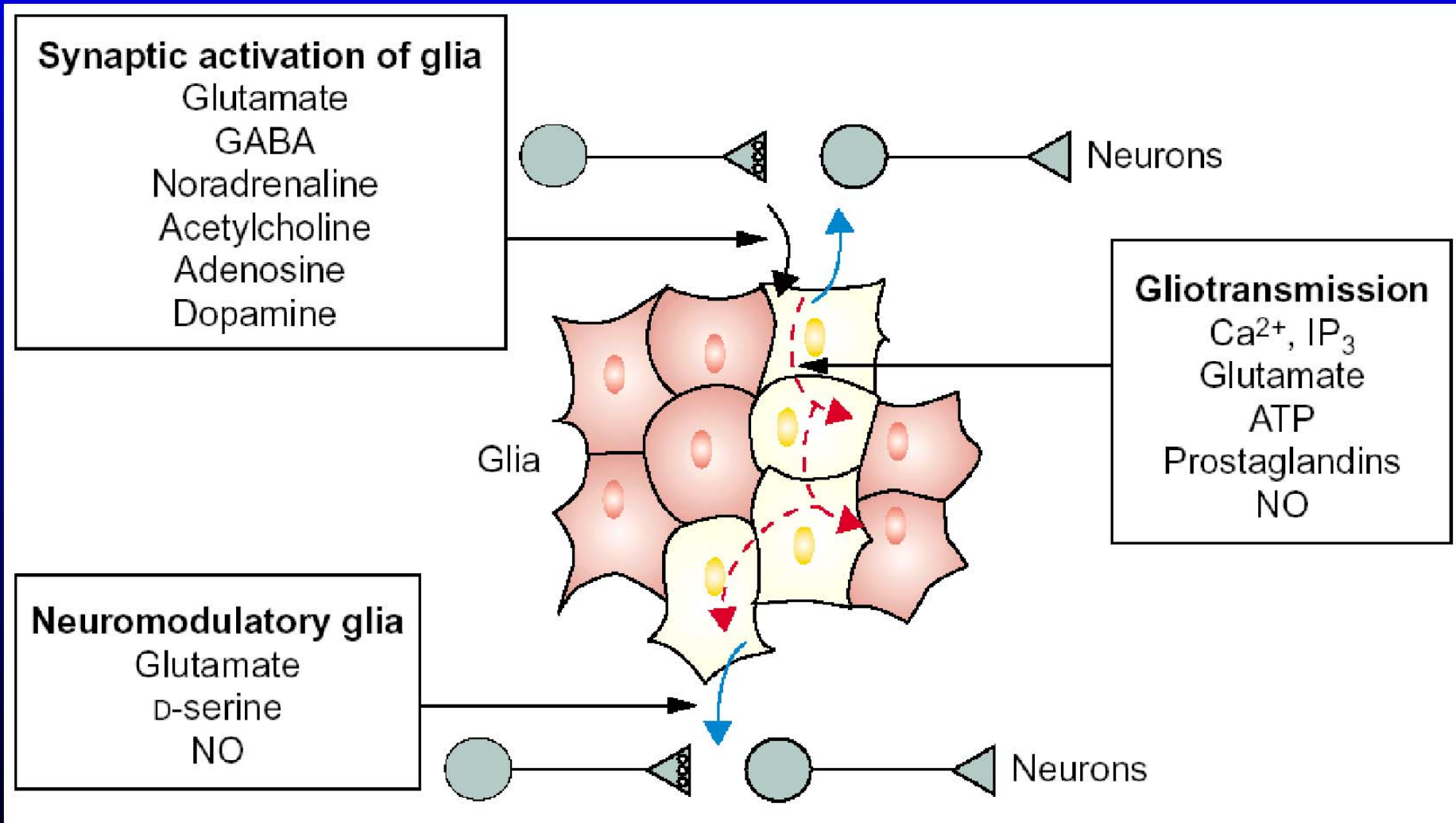
# Astrocytic calcium waves cause the calcium-dependent release of glutamate

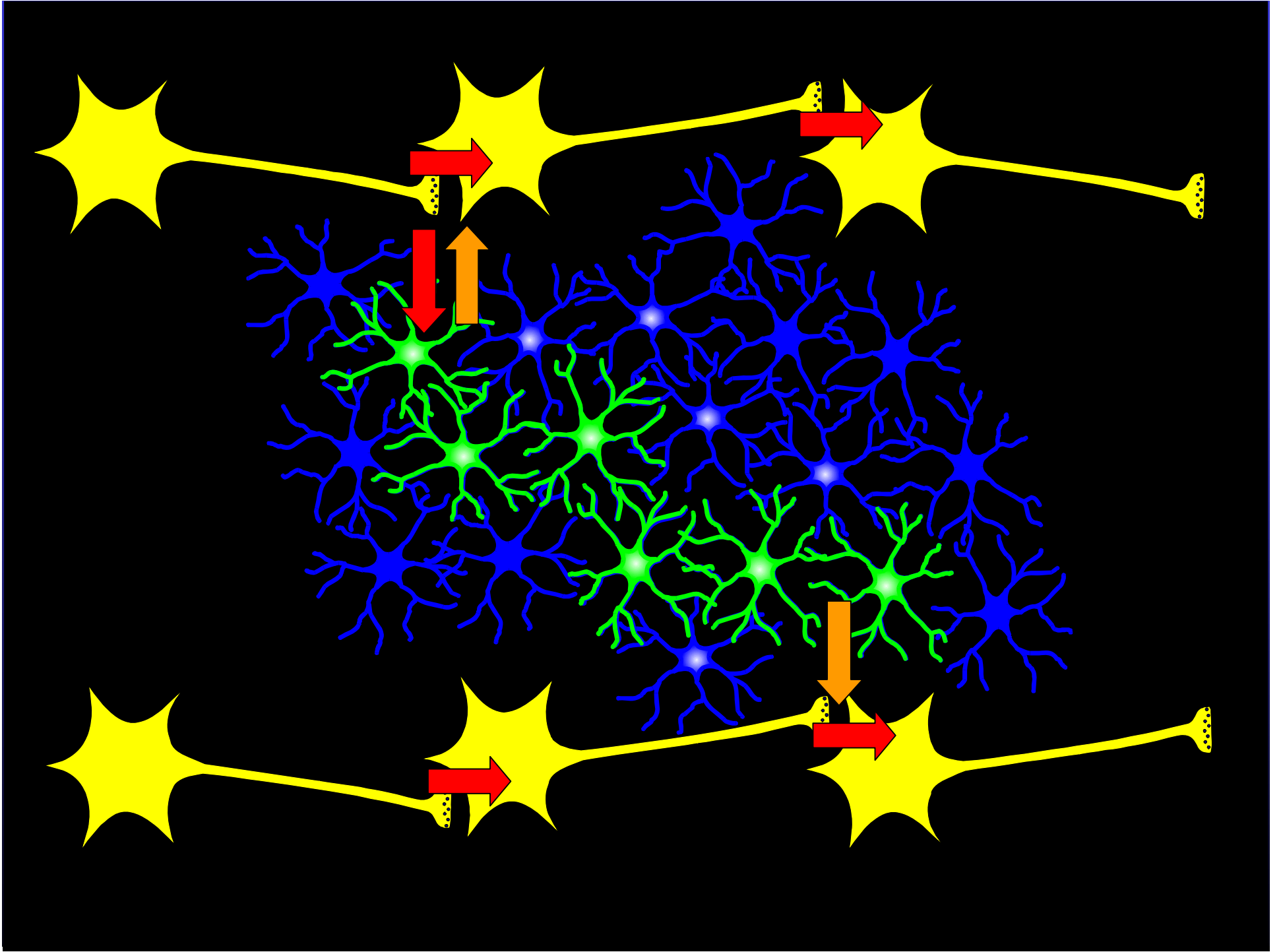


Intercellular signalling between neurons and astrocytes have a local modulatory action



# Bi-directional signaling between astrocytes and neurons





## Současná představa o funkci gliových buněk:

1. Strukturální opora neuronů, gliální sítě, hematoencefalická bariéra, izolace axonů - myelin.
2. Mají napětově-závislé iontové kanály ( $K_{IR}$ ,  $K_D$ ,  $K_A$ ,  $Na_G$ ,  $Na_N$ ,  $Ca_T$ ,  $Ca_L$ ,  $Cl^-$ ).
3. Mají chemicky-aktivované iontové kanály (glutamát, GABA, glycin).
4. Neurony ovlivňují tvorbu kanálů v gliových buňkách.
5. Syntetizují a uvolňují mediátory (ACh, glutamát, GABA).
6. Zajišťují homeostázu energetického metabolismu (energetická zásobárna, glykogen, glykogenolýza).
7. Zajišťují iontovou homeostázu ( $K^+$ , pH,  $Ca^{2+}$ ).
8. Zajišťují objemovou homeostázu (dynamické změny objemu).
9. Hypertrofují, prolifерují, tvoří gliální jizvy, reparace, remyelinizace.
10. Interakce neuron-glie, signalizace, plastické změny.