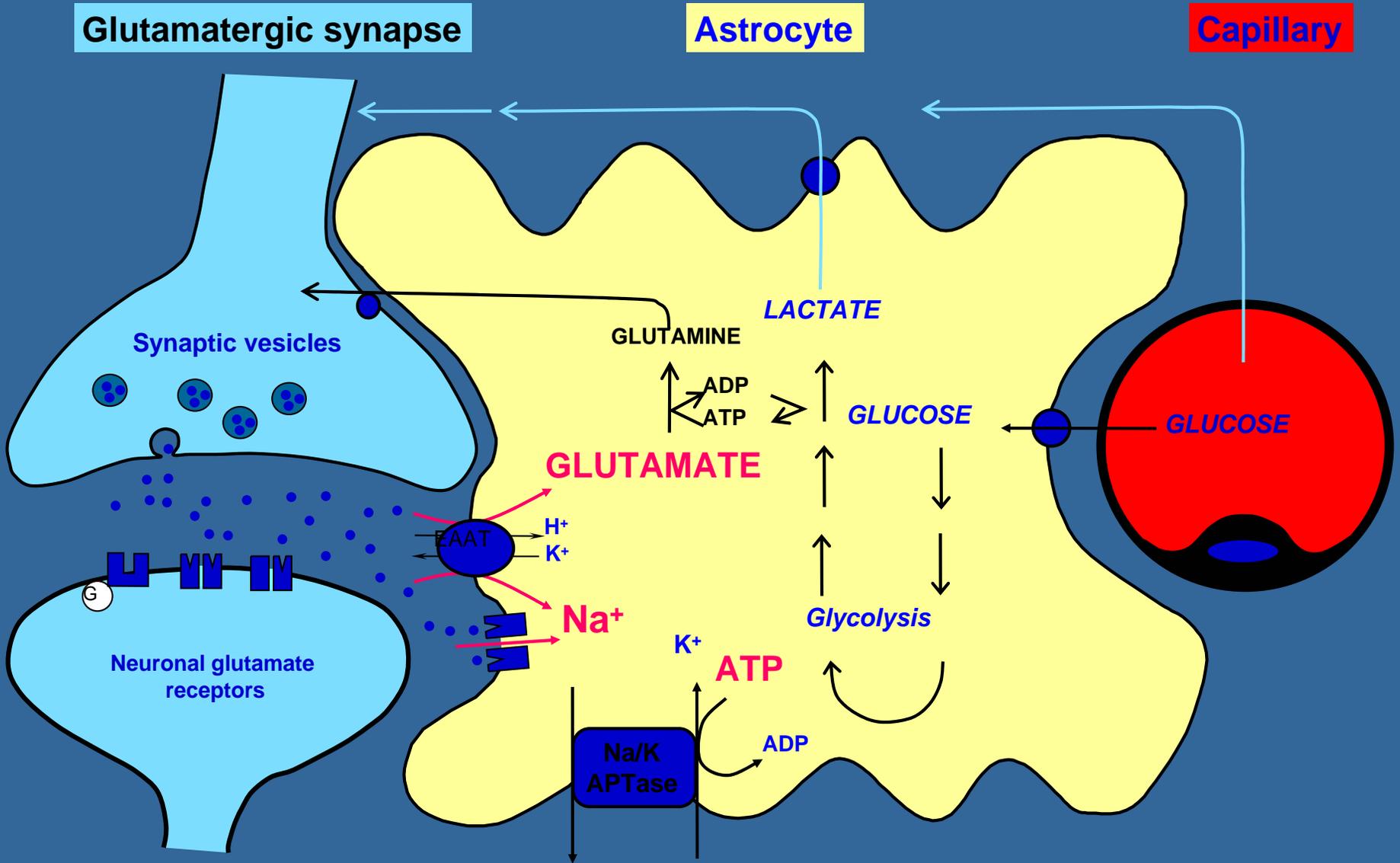


# Mechanism for Coupling Neuronal Activity to Glucose Utilization

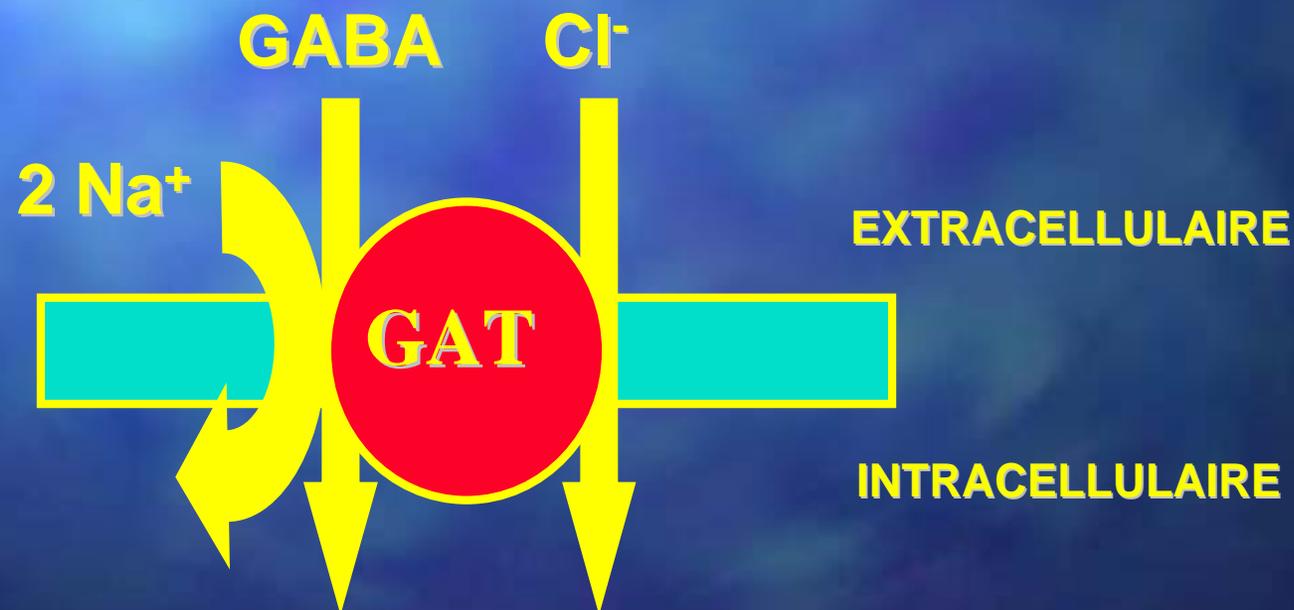




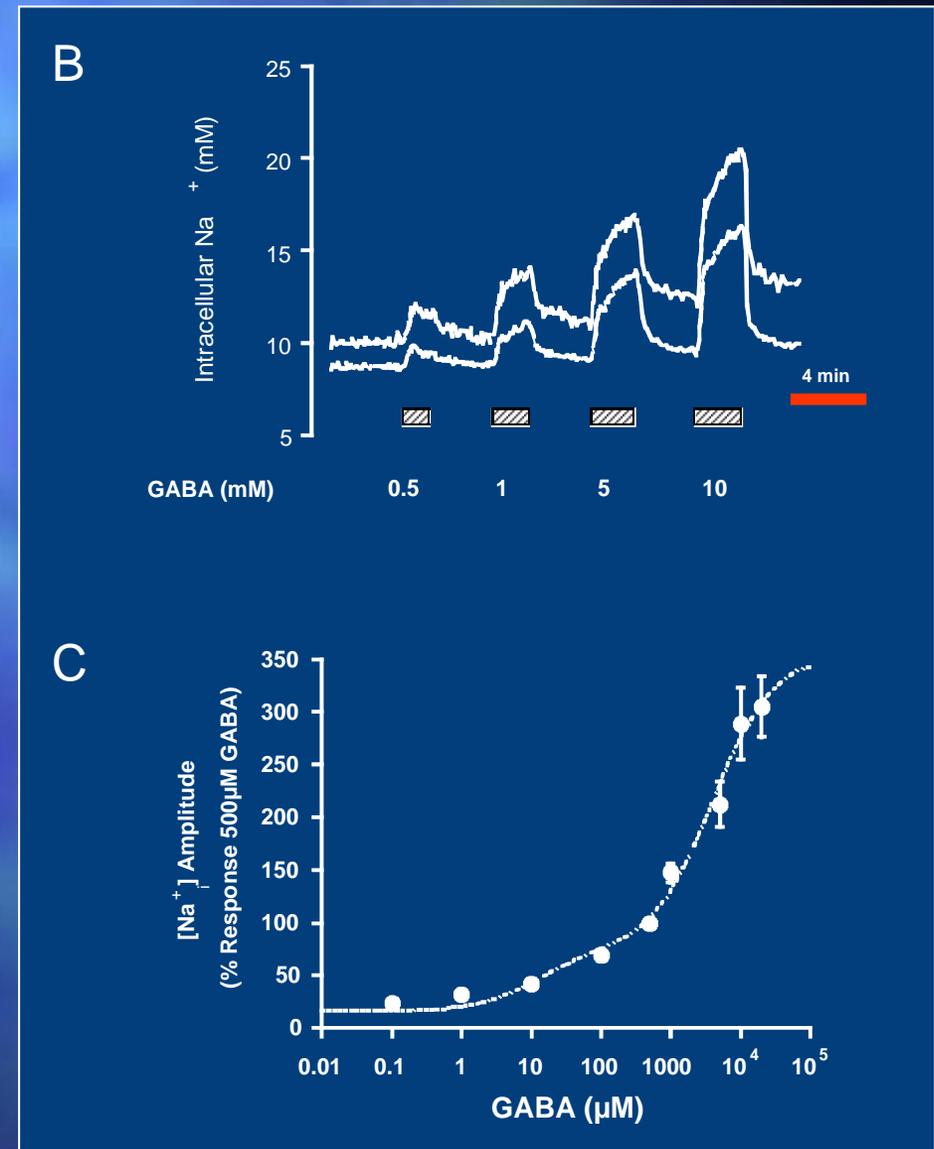
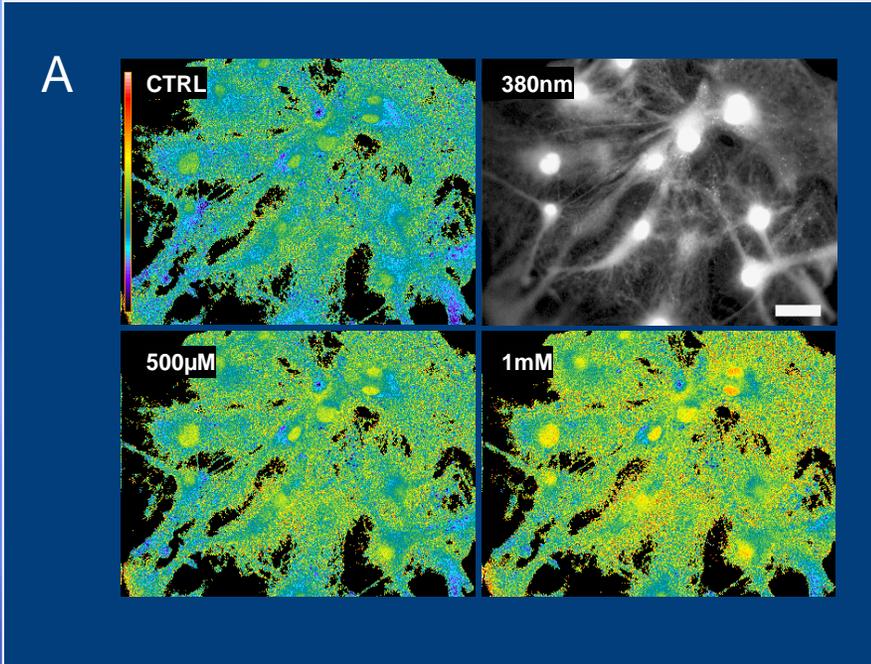
# Transporteurs au GABA

Haute affinité, dépendants du  $\text{Na}^+$ ,  $\text{Cl}^-$

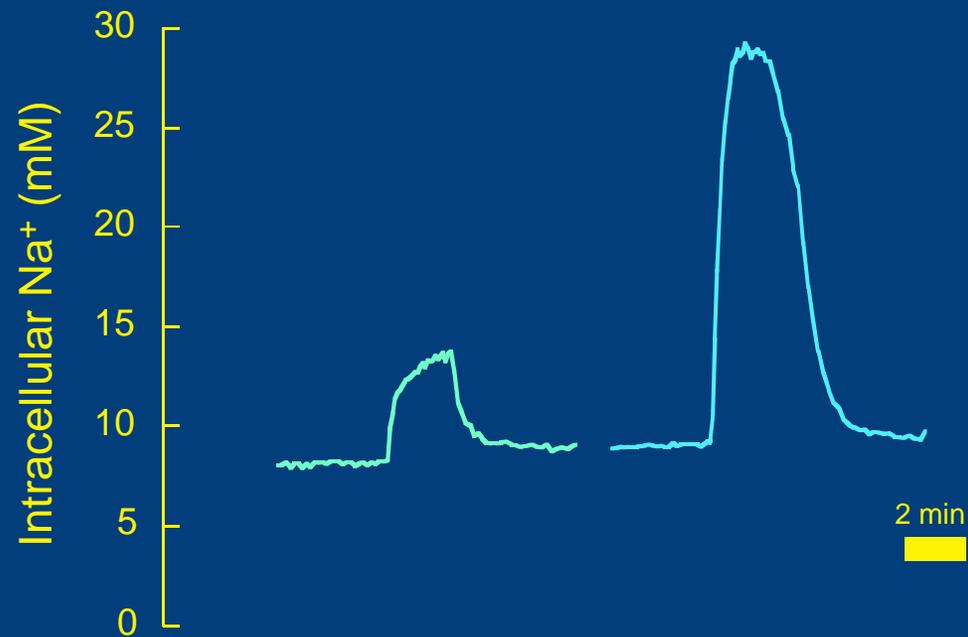
- ◆ **GAT1, GAT2, GAT-3, BGT-1**
- ◆ **Exprimés à travers le SNC**
- ◆ **Sur astrocytes et neurones**
- ◆ **Les transporteurs astrocytaires sont responsables de ~20% du recaptage de GABA**



# Sodium intracellulaire : réponse au GABA



# Sodium intracellulaire : réponse au GABA et glutamate

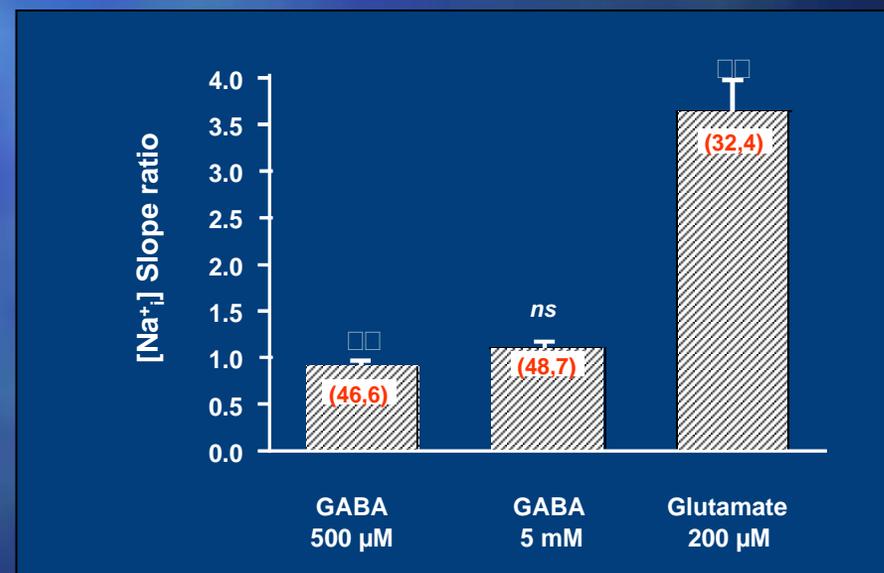
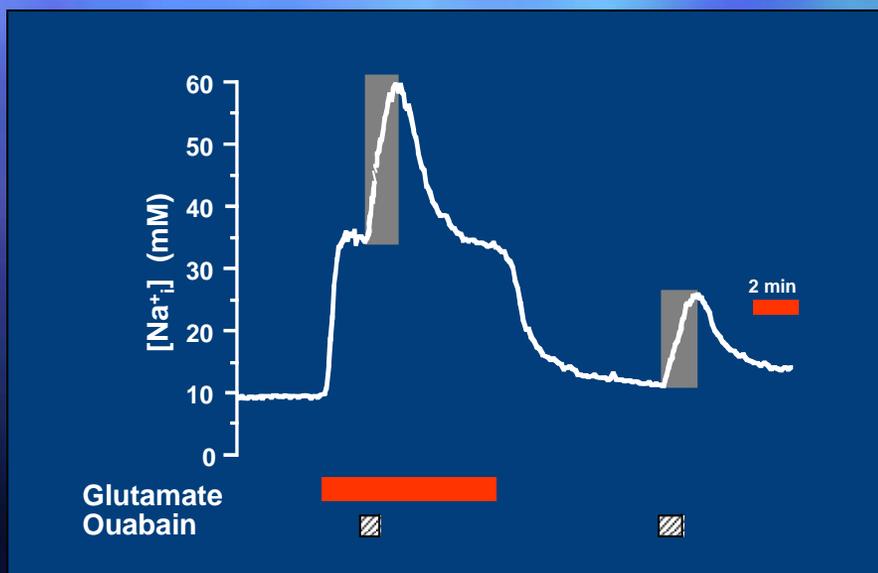
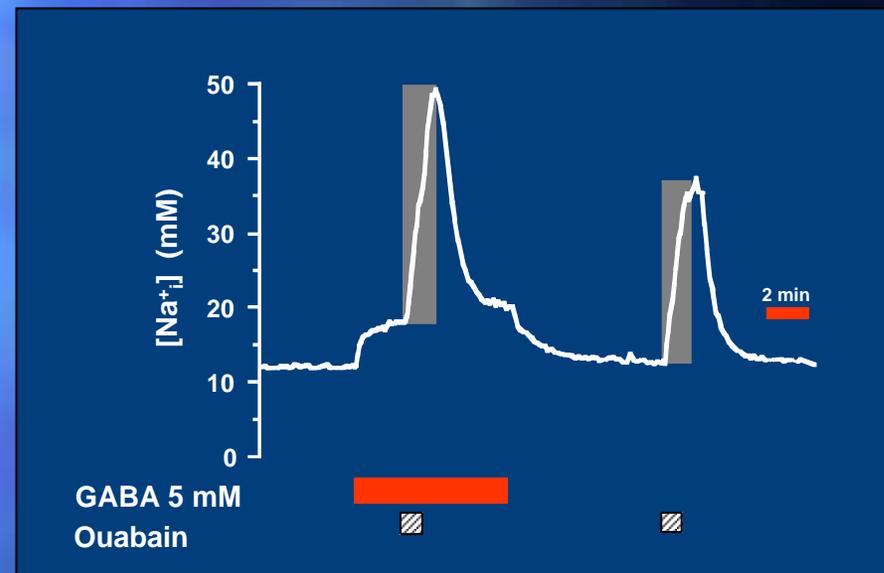
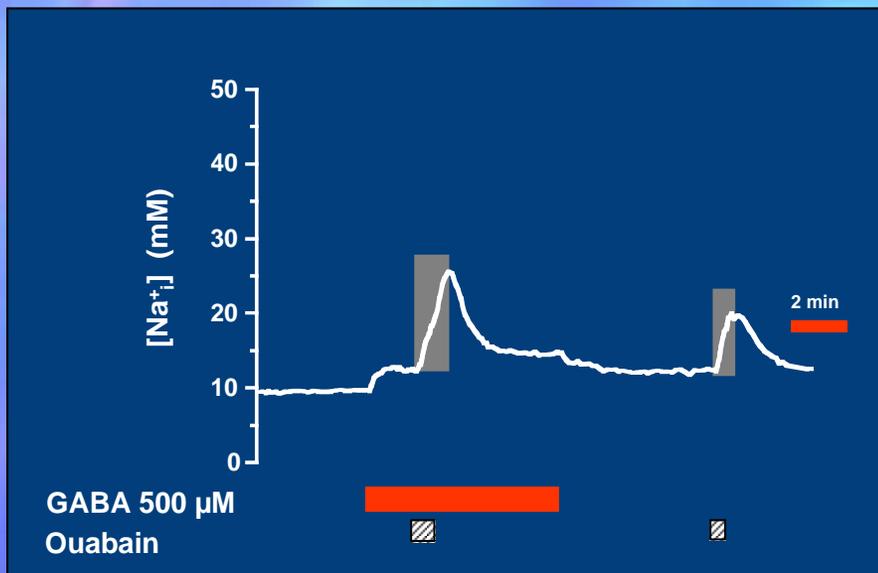


GABA 500 μM

Glutamate 200 μM

2 min

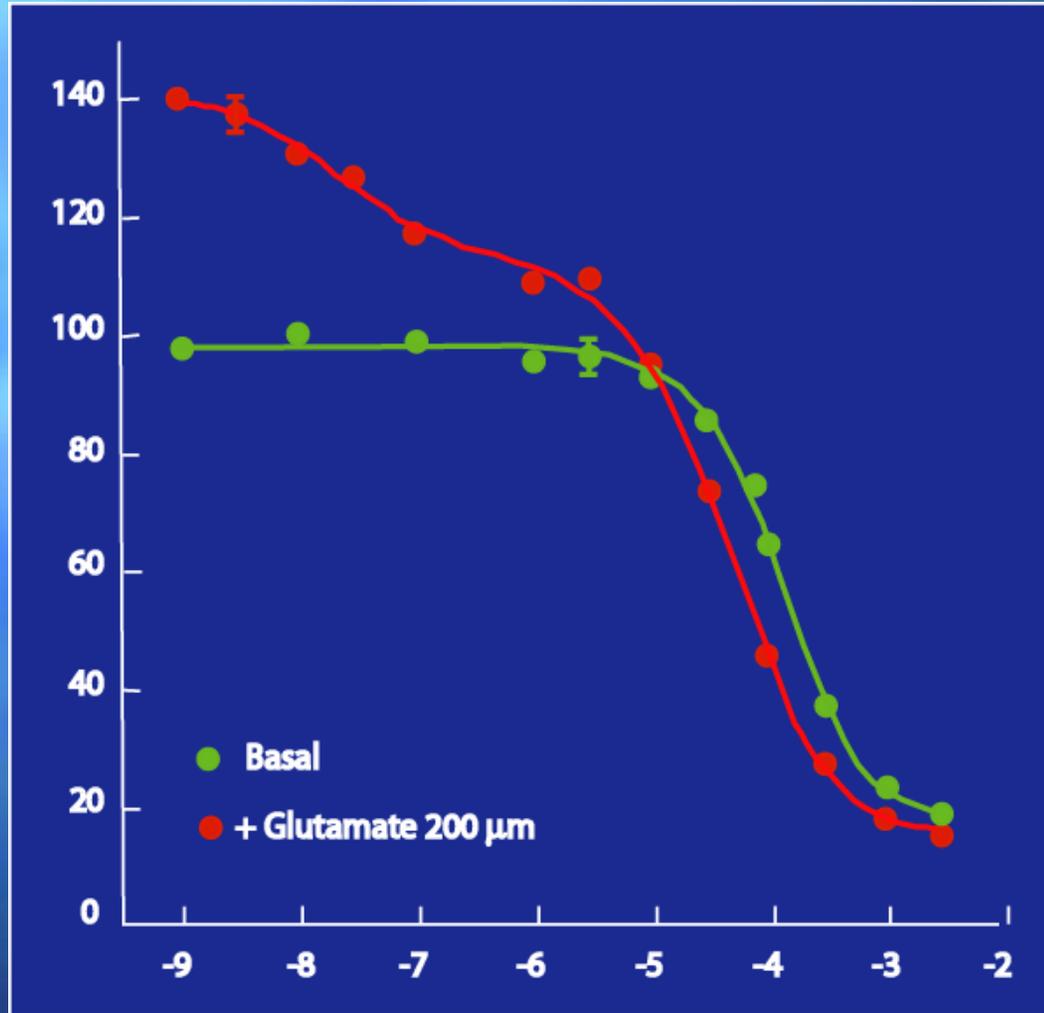
# Degré d'activation de la Na/K ATPase par le GABA et le glutamate



# Relations concentration - response de l'inhibition par la ouabaine de la capture de $^{86}\text{Rb}$ dans les astrocytes en présence ou en absence de glutamate



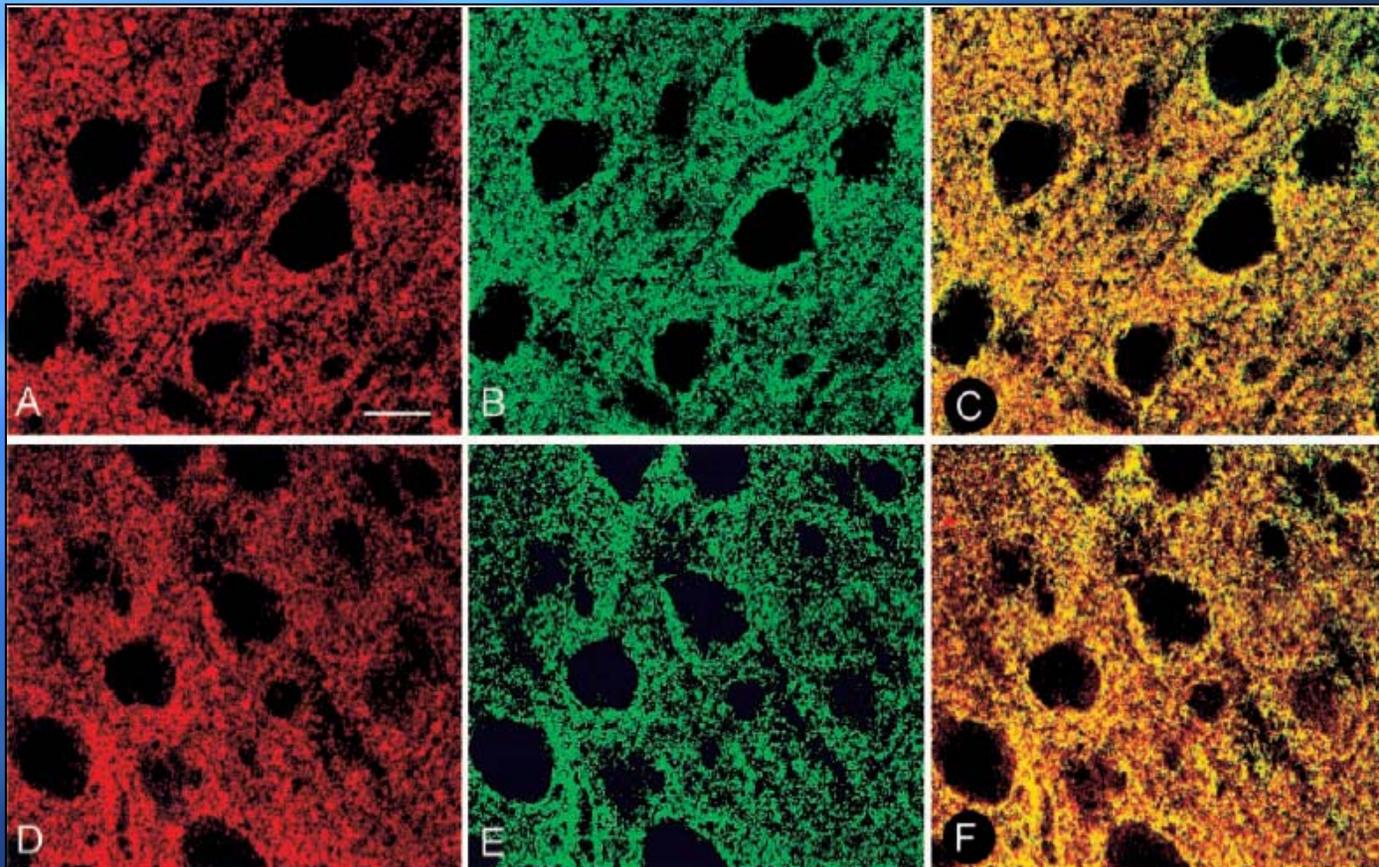
Activité NaK-ATPase (% Basal)



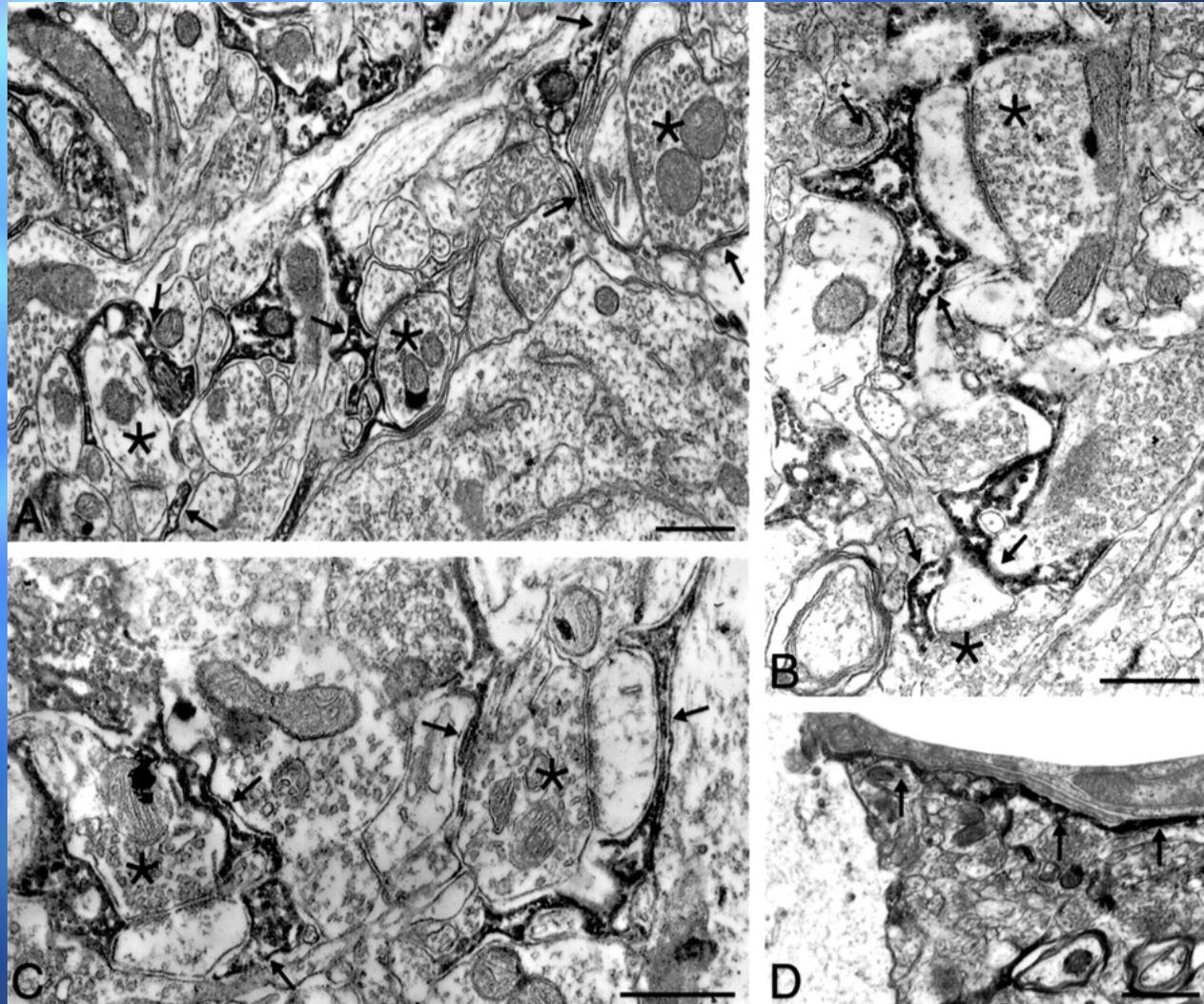
Ouabaine (M)



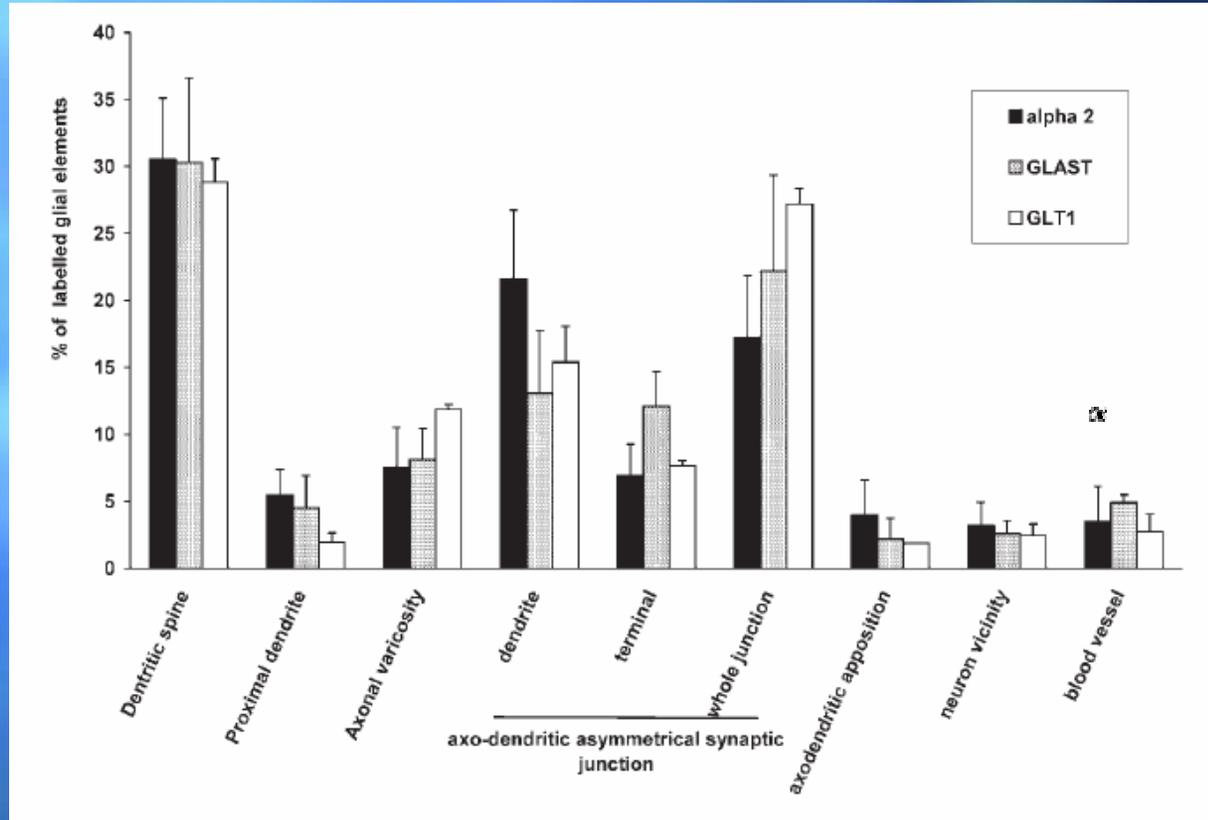
Marquage par double immunofluorescence  
de la sous-unité  $\alpha 2$  de la  $\text{Na}^+/\text{K}^+$ -ATPase (A et D),  
avec GLAST (C) ou GLT-1 (F) . (B GLAST, E GLT 1)



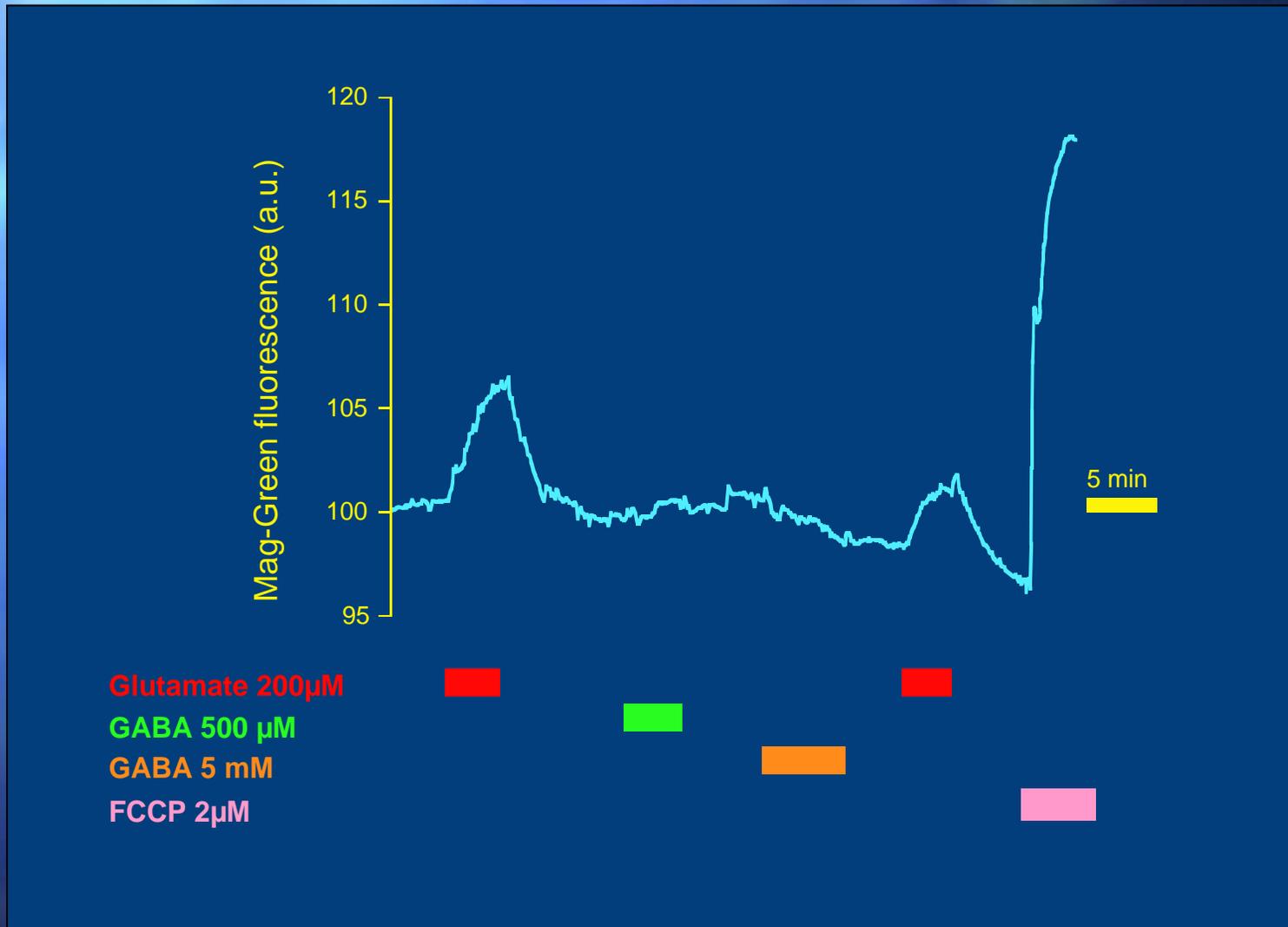
Immunocytochimie par microscopie électronique  
des 2 sous-unités de la  $\text{Na}^+/\text{K}^+$ -ATPase  
dans le cortex frontoparietal de rat (couches III à V)



# Histogramme de la distribution des éléments cellulaires engainés par les lamelles astrocytaires marquées immunohistochimiquement par $\alpha 2$ , GLAST or GLT-1 dans le cortex frontoparietal de rat

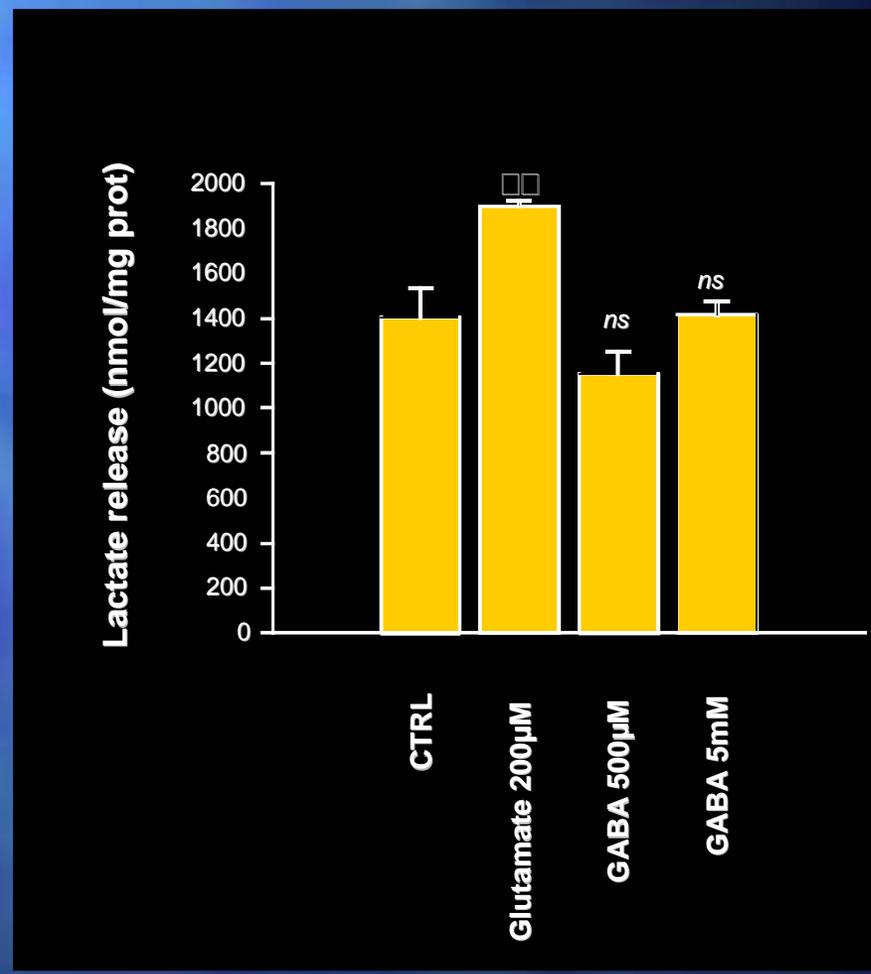
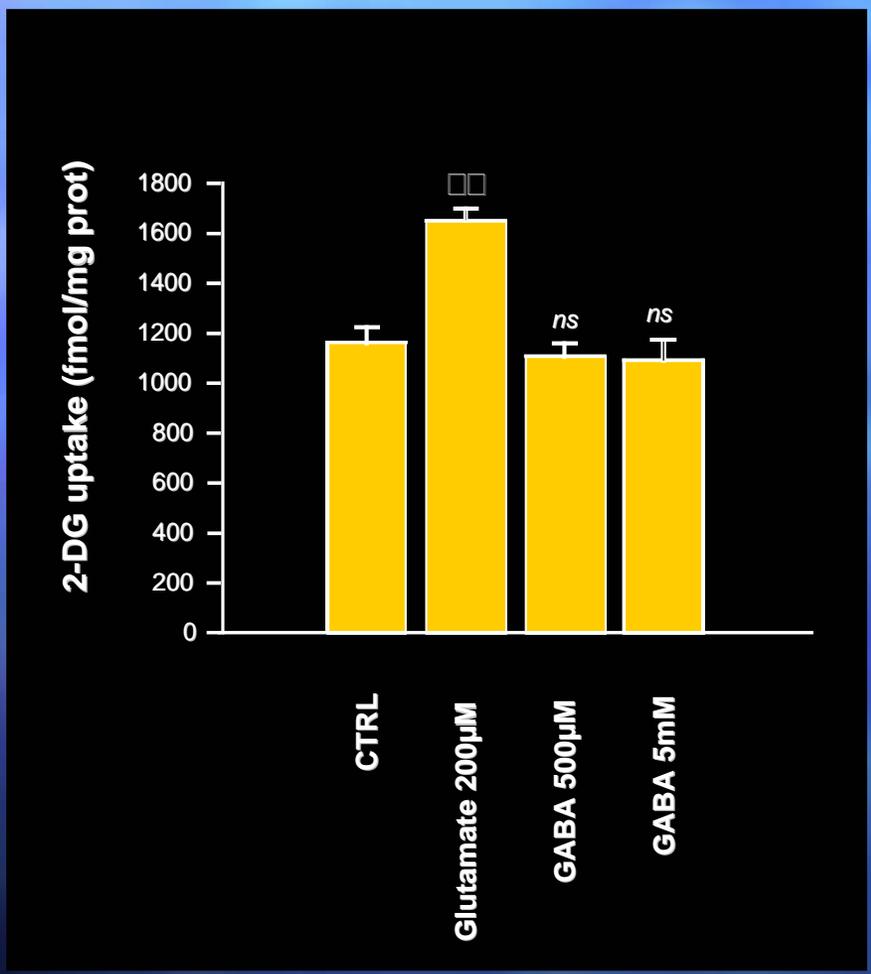


# Détermination indirecte des niveaux d' ATP par imagerie au free Mg<sup>2+</sup>: comparaison entre GABA et glutamate

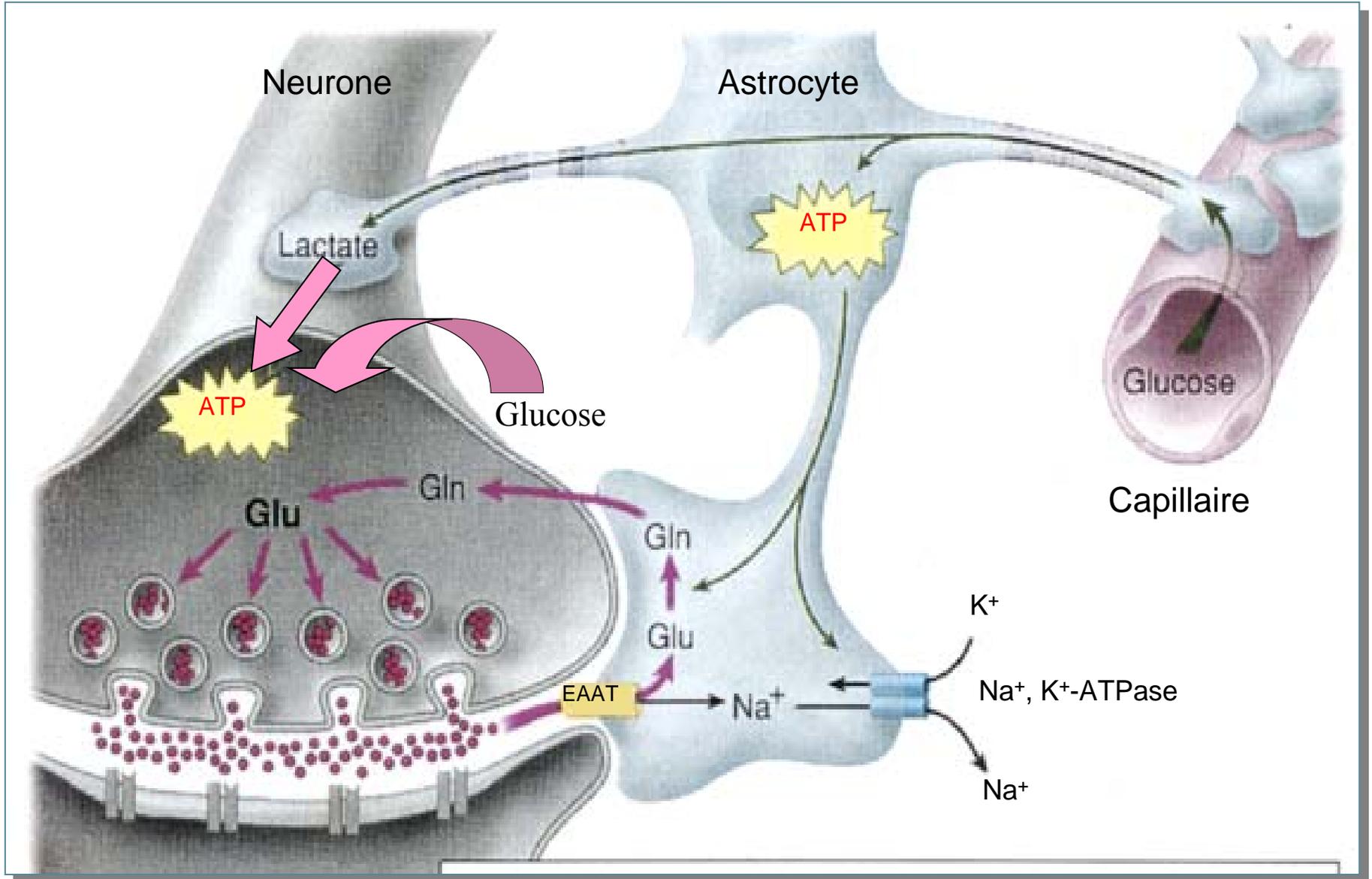


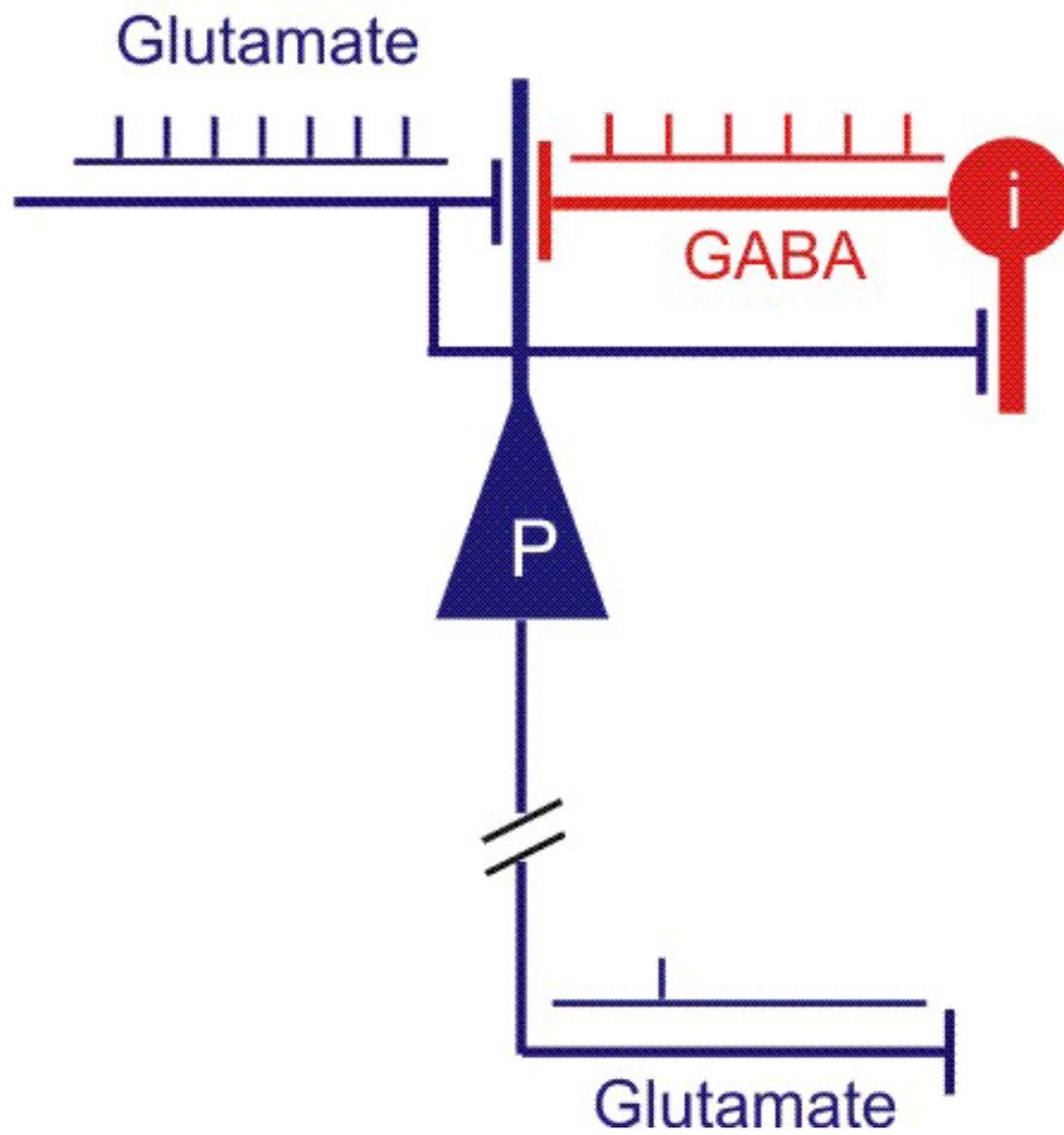


# Réponses métaboliques au GABA et au glutamate

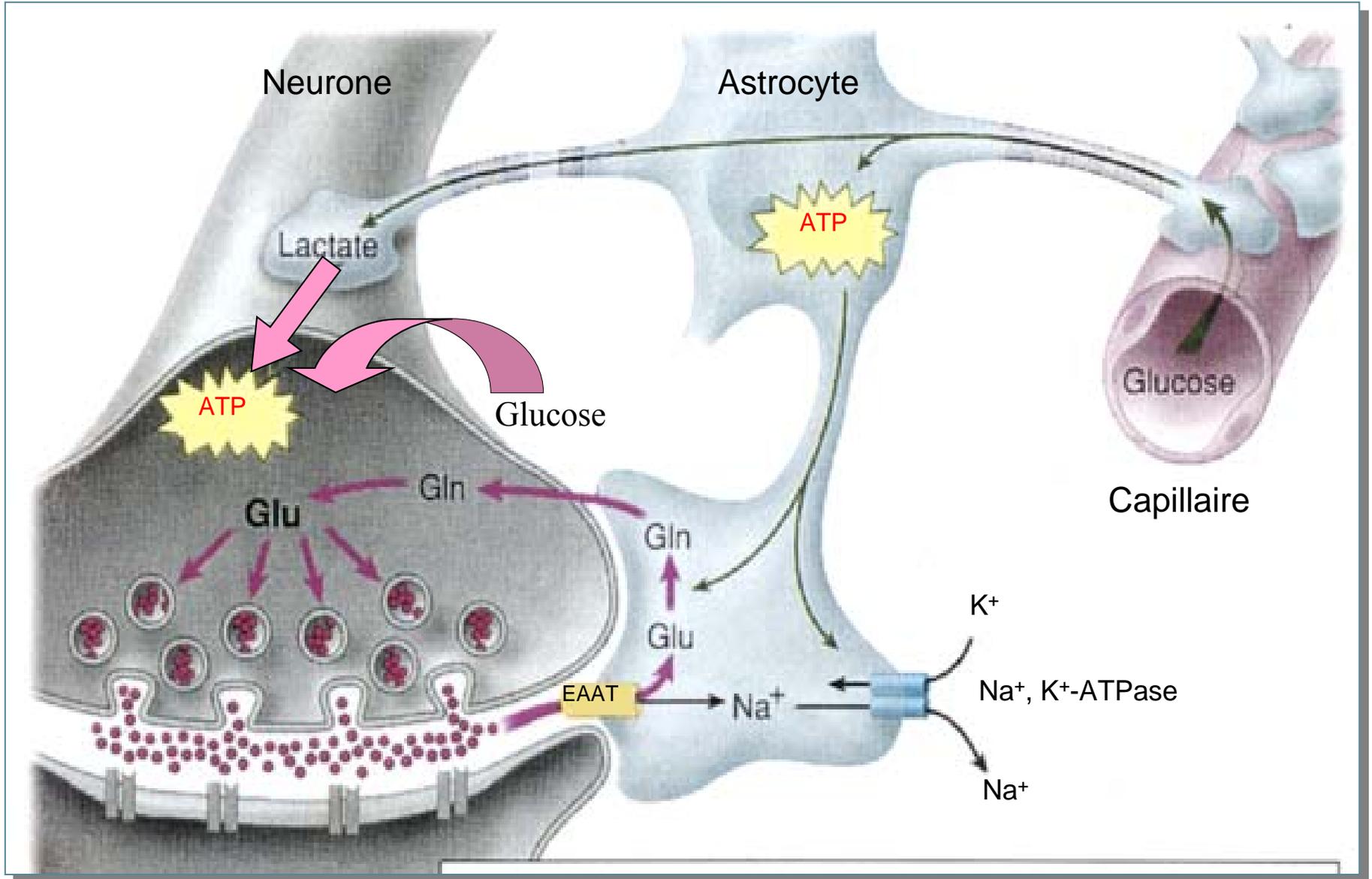


# L'unité neuroénergétique

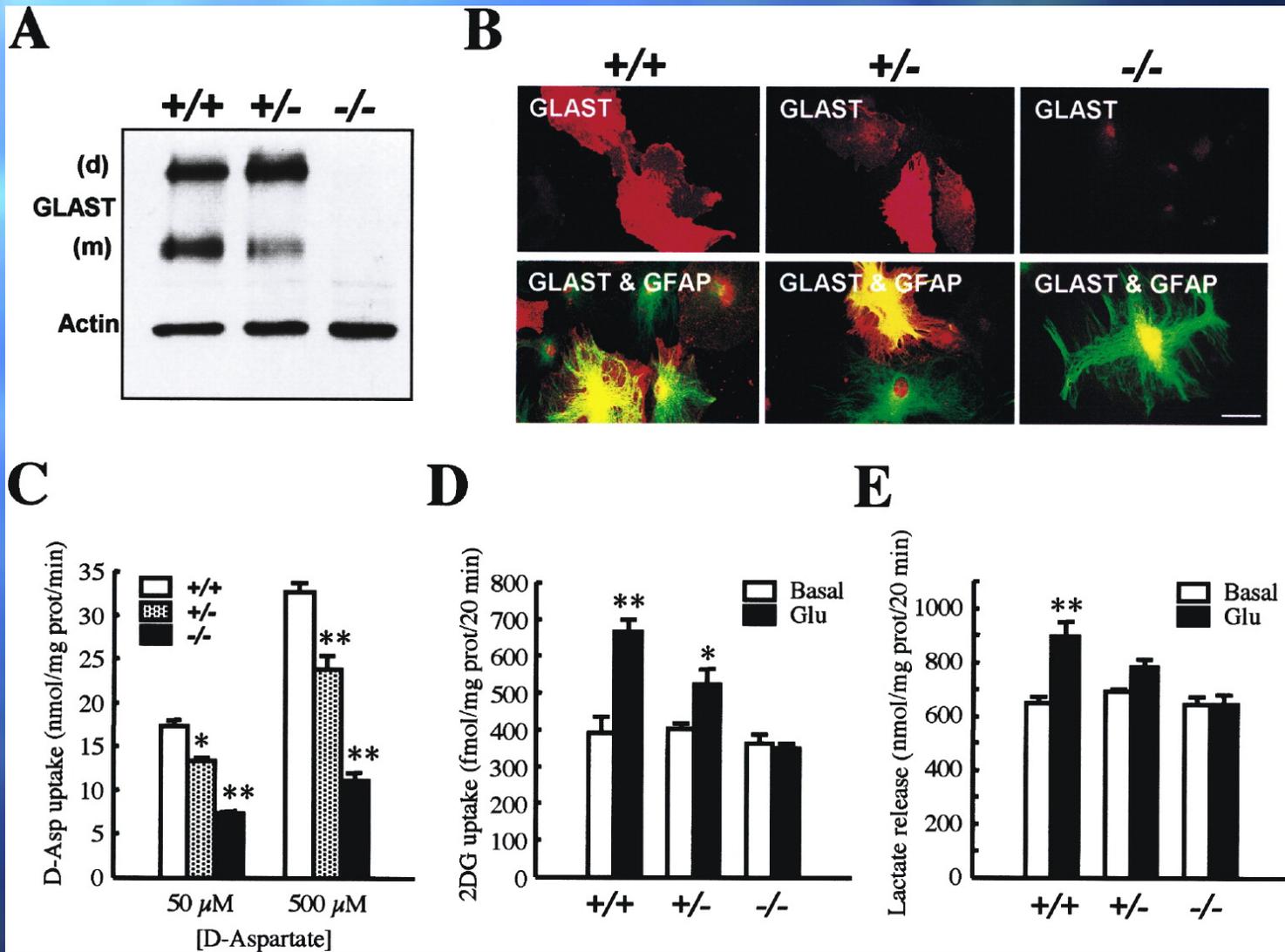




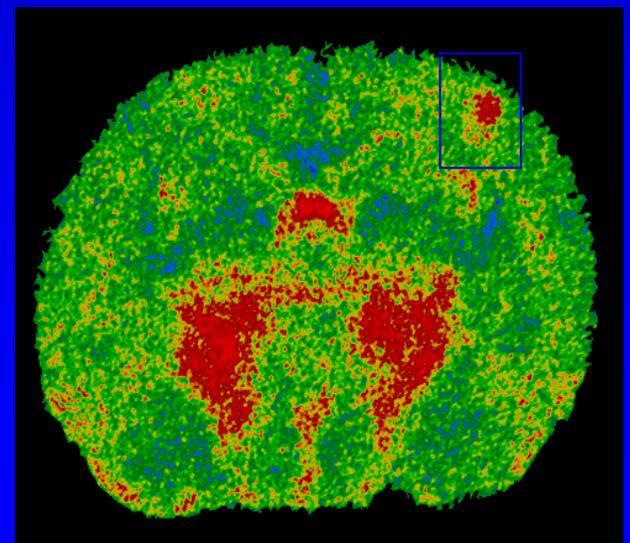
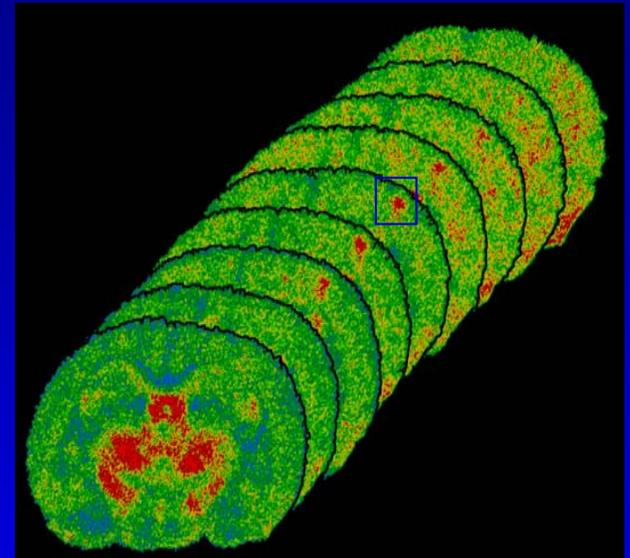
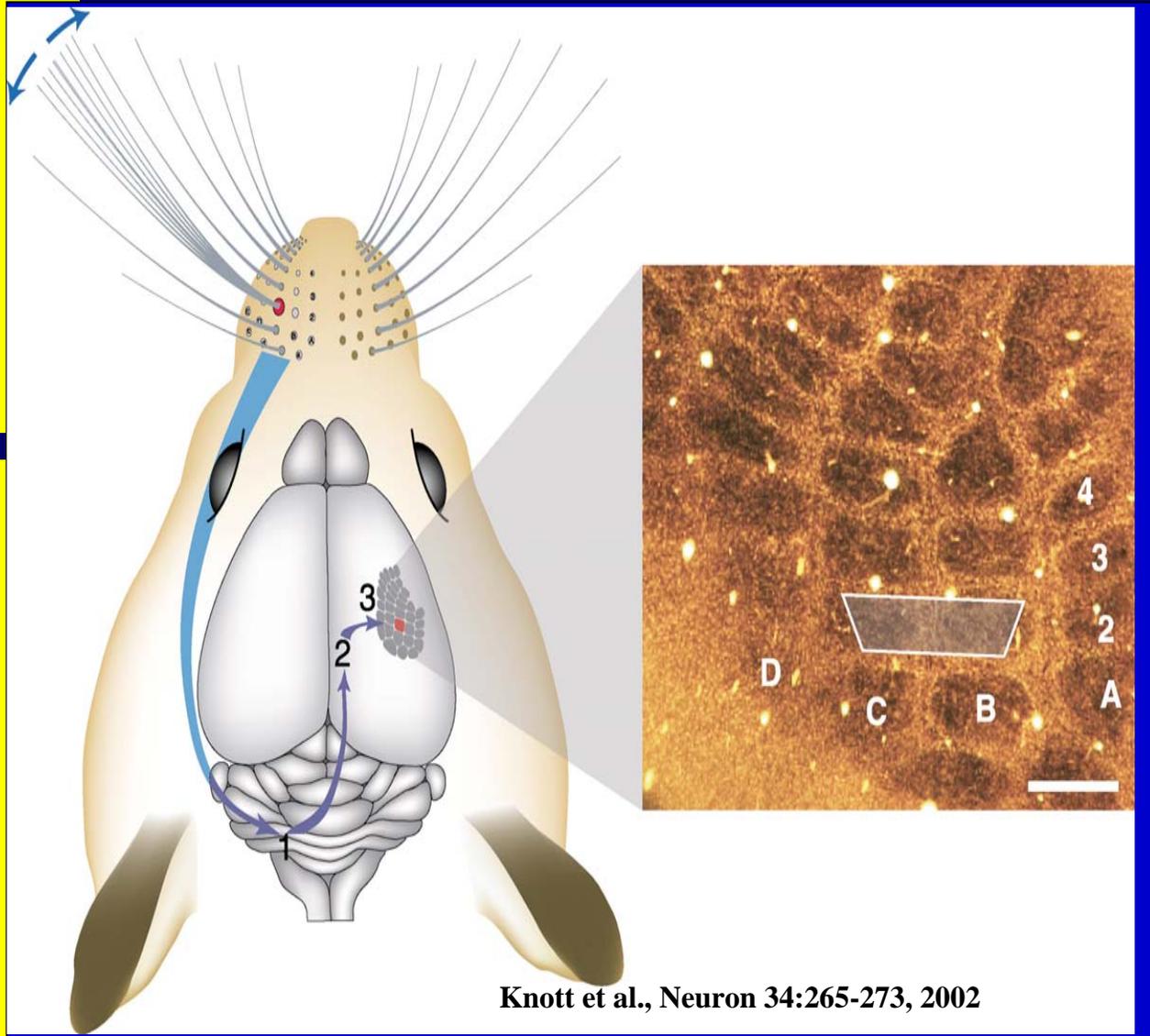
# L'unité neuroénergétique



# Cultures primaires d'astrocytes préparées à partir de souris KO GLAST



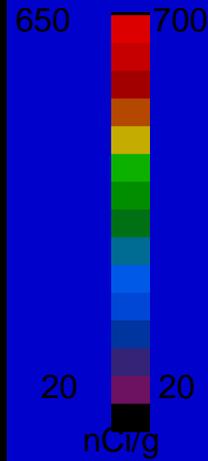
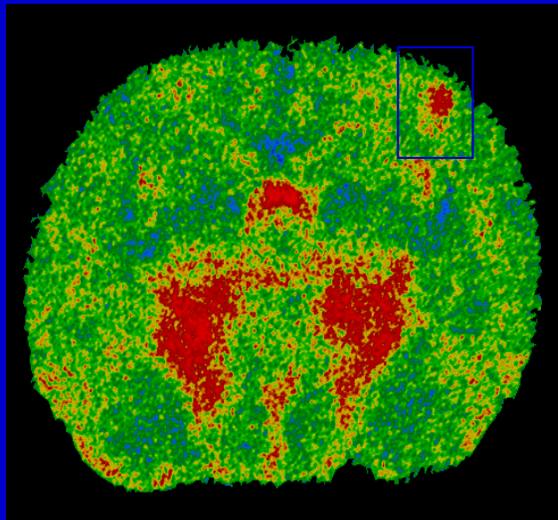
# Visualisation par by Autoradiographie au Deoxyglucose de l'Activité la voie Vibrisses-Barils (Whisker-to-Barrel)



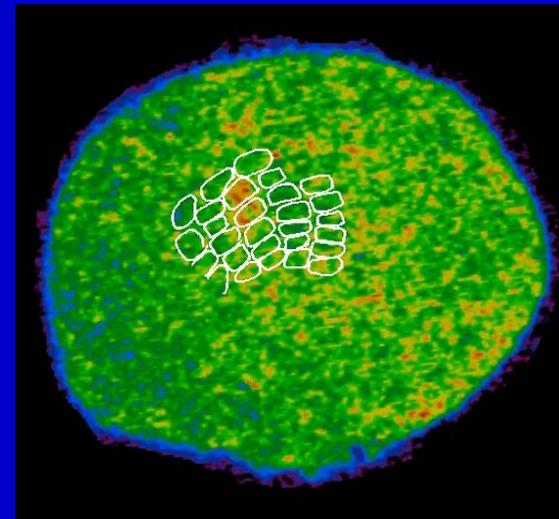
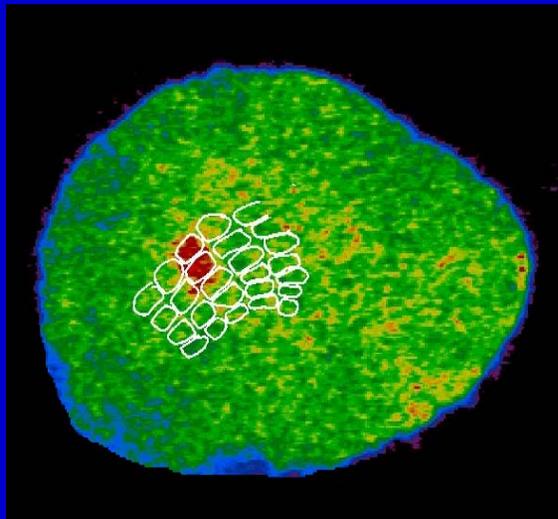
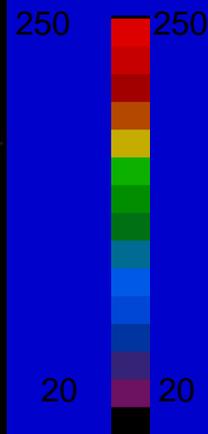
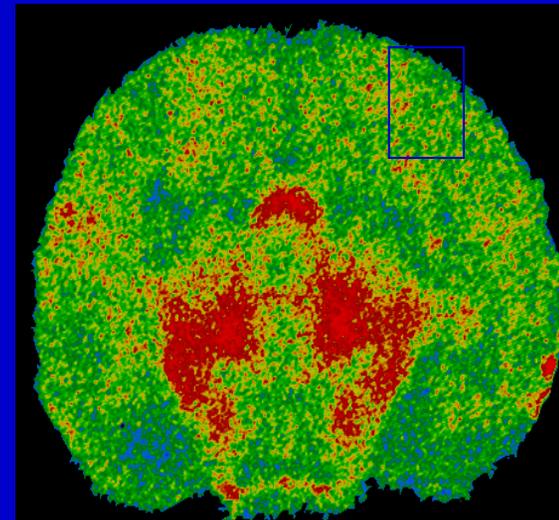
# Réduction de la réponse métabolique suite à une stimulation des vibrisses chez les souris GLAST KO

Voutsinos-Porche et al 2003

P10 GLAST +/+

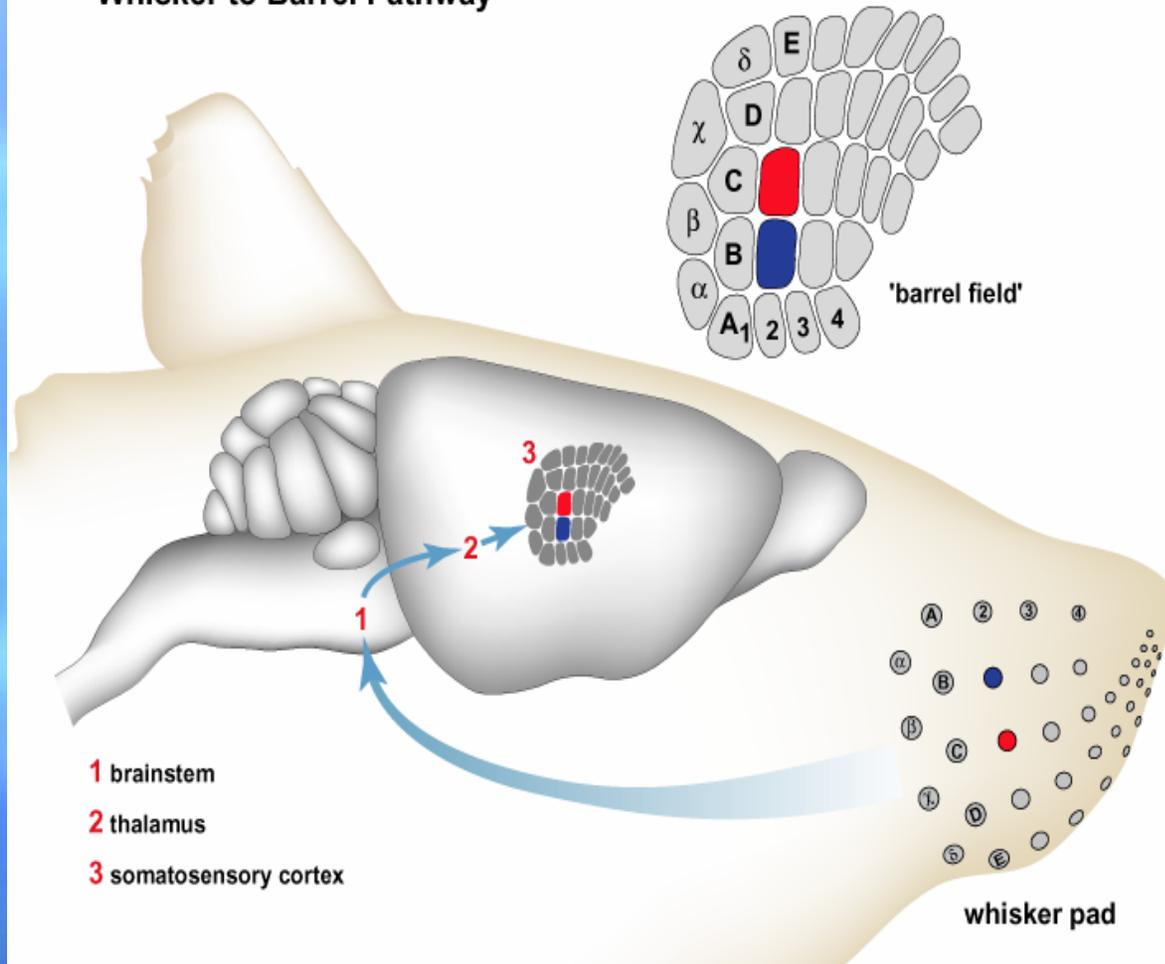


P10 GLAST -/-



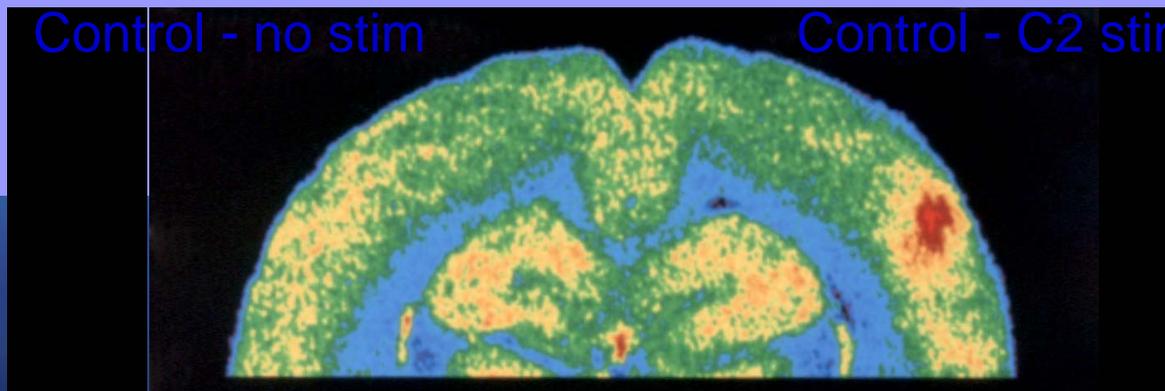


# 'Whisker to Barrel Pathway'



Control - no stim

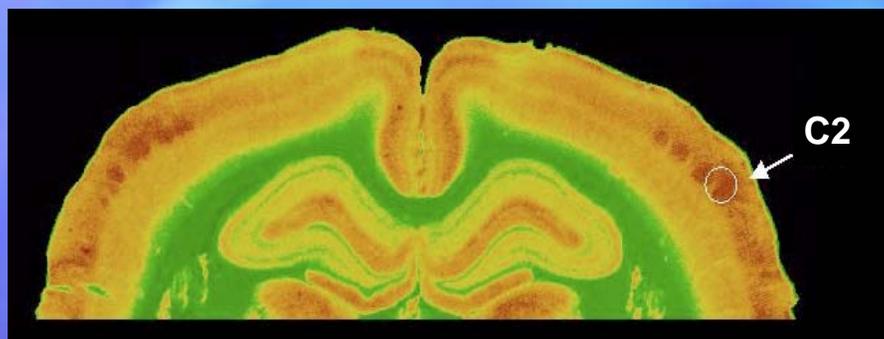
Control - C2 stim



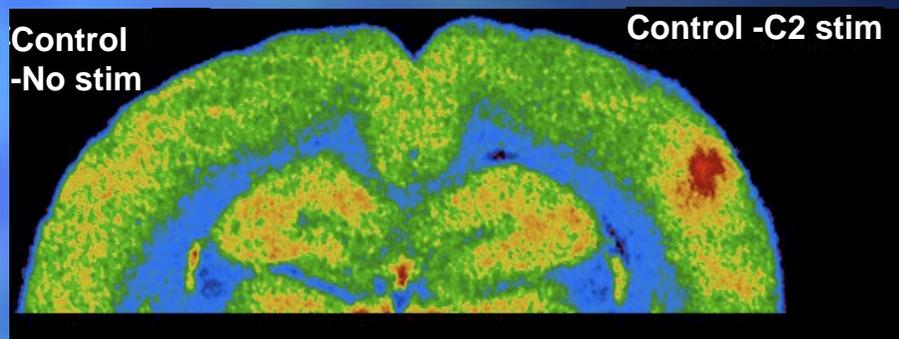
# GLAST Antisense Reduces Whisker-Stimulated Glucose Utilization in the Rat Somatosensory Cortex



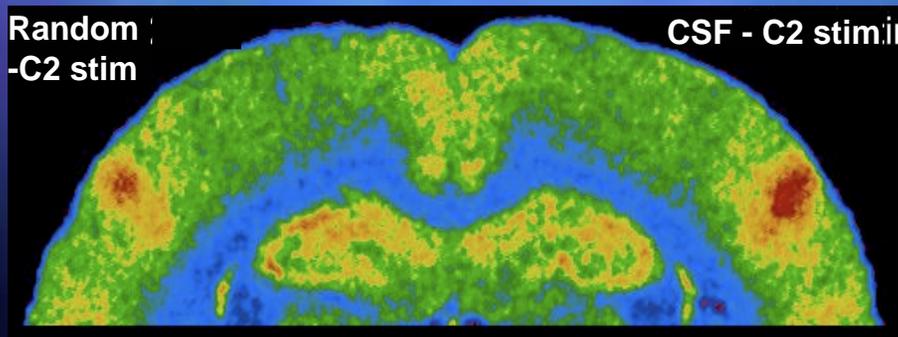
## Cytochrome Oxidase



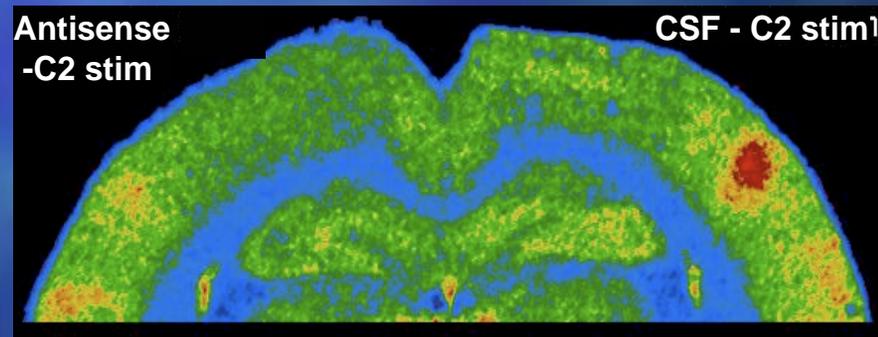
## Utilisation de Glucose



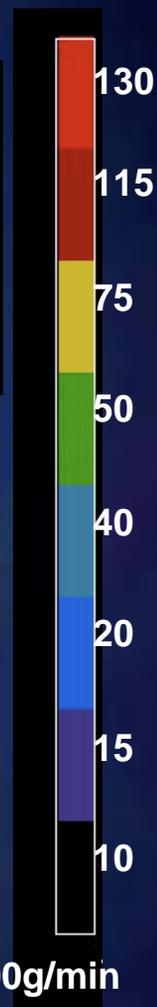
### Groupe I



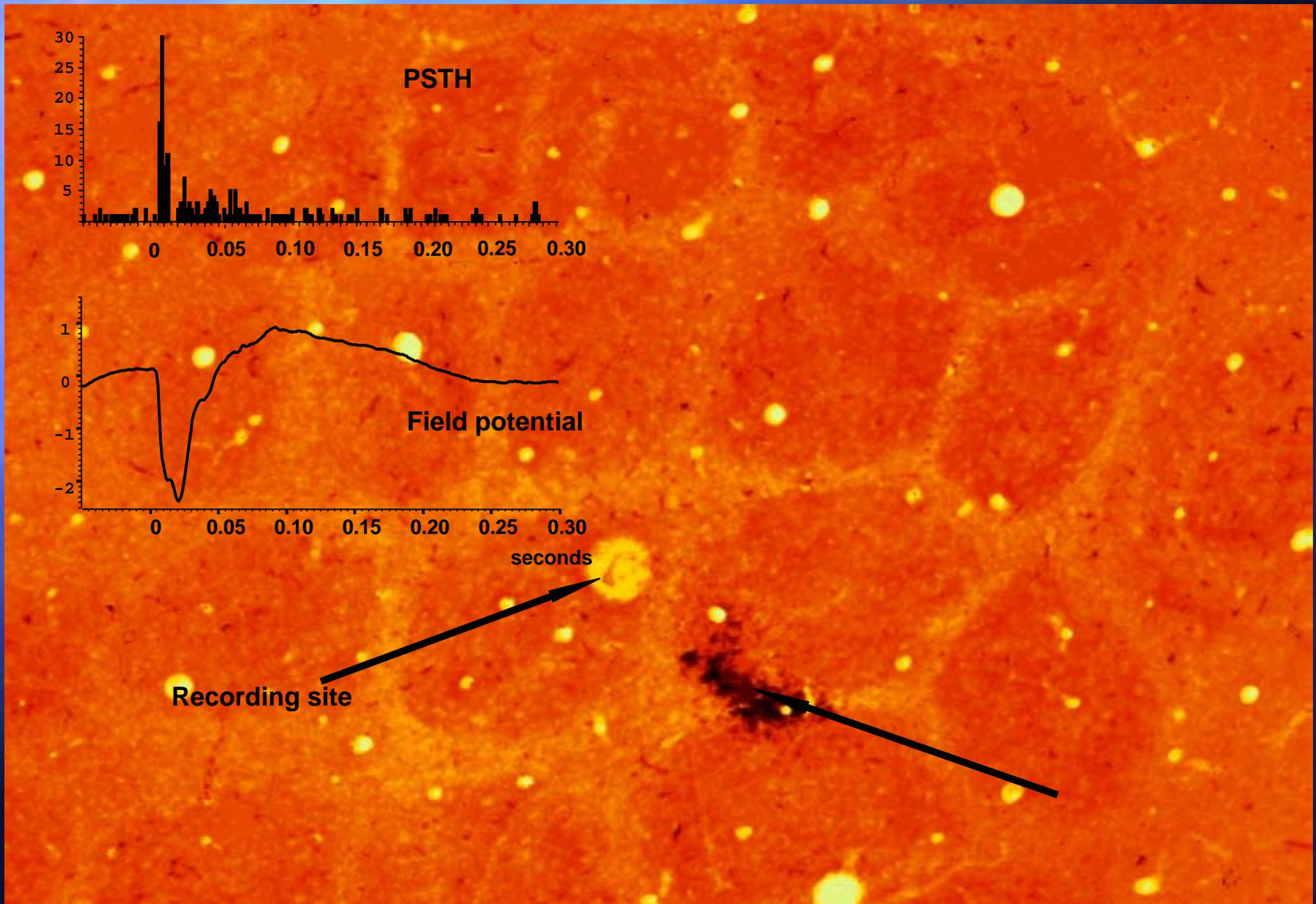
### Groupe II



### Groupe III



# Barrel recording



PSTH

Field potential

Recording site

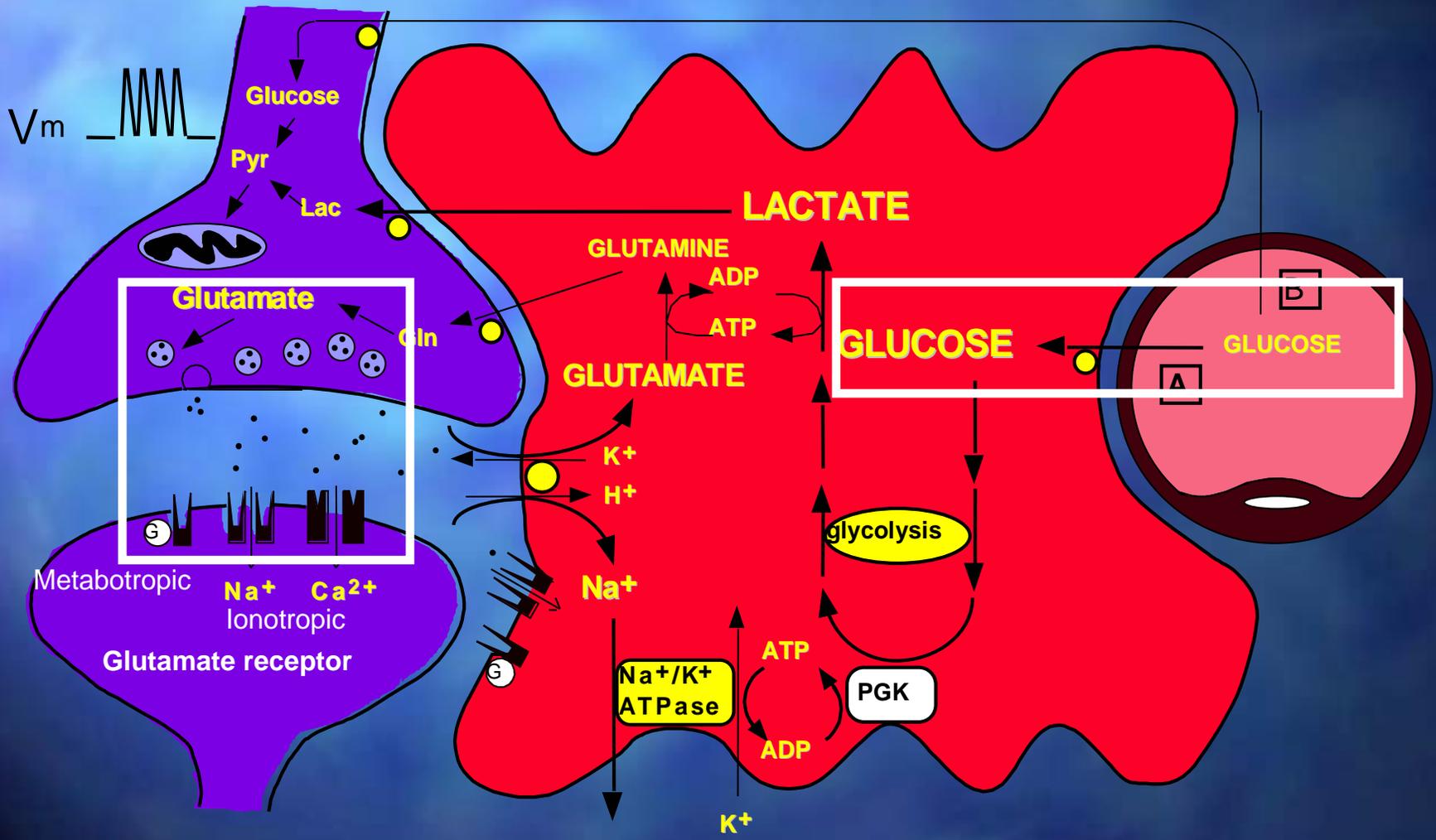
seconds



Synapse glutamatergique

Astrocyte

Capillaire

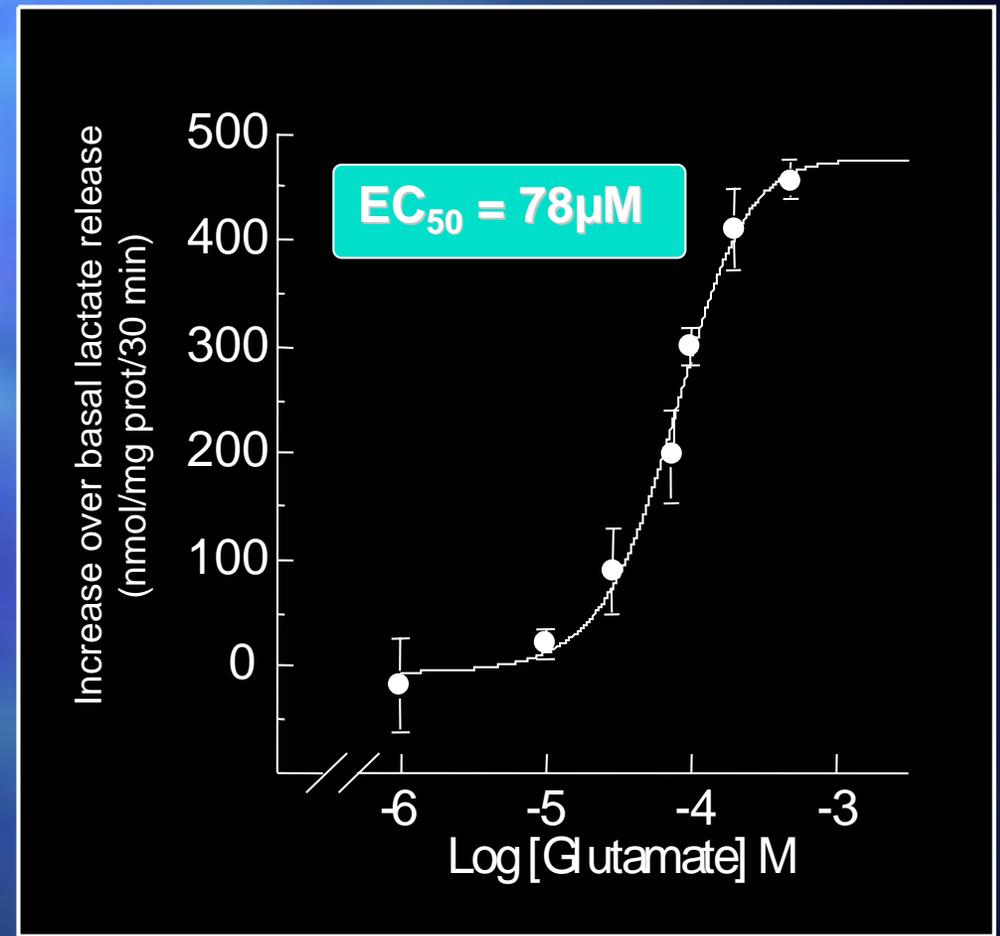
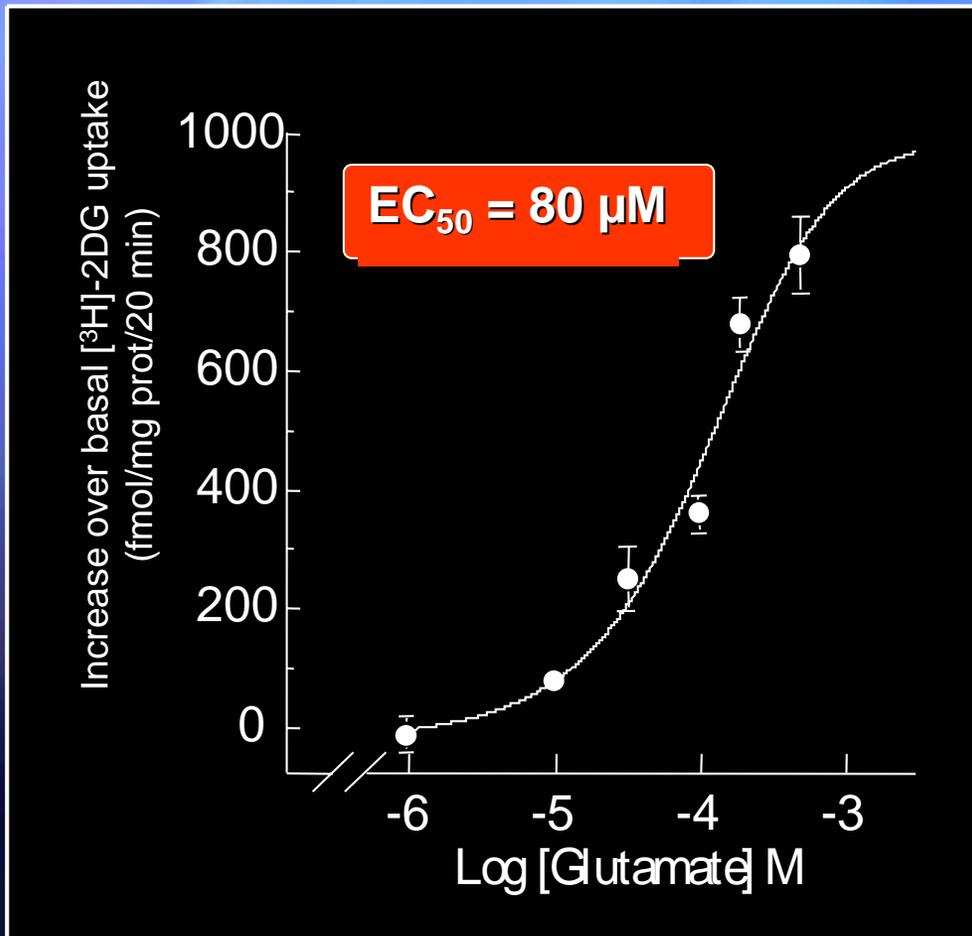


# Le glutamate stimule la glycolyse aérobie dans les astrocytes



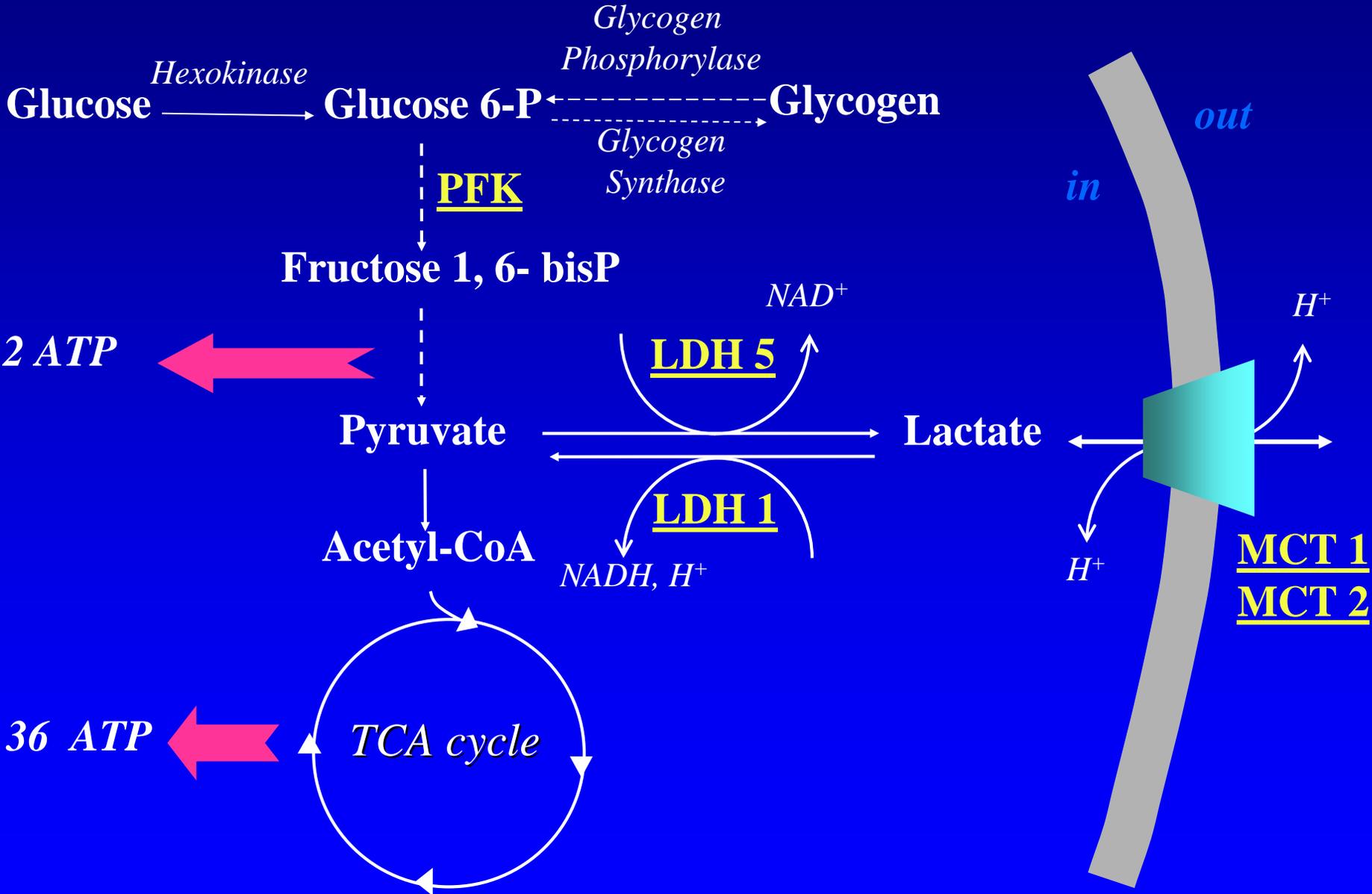
## Utilisation de glucose

## Production de lactate





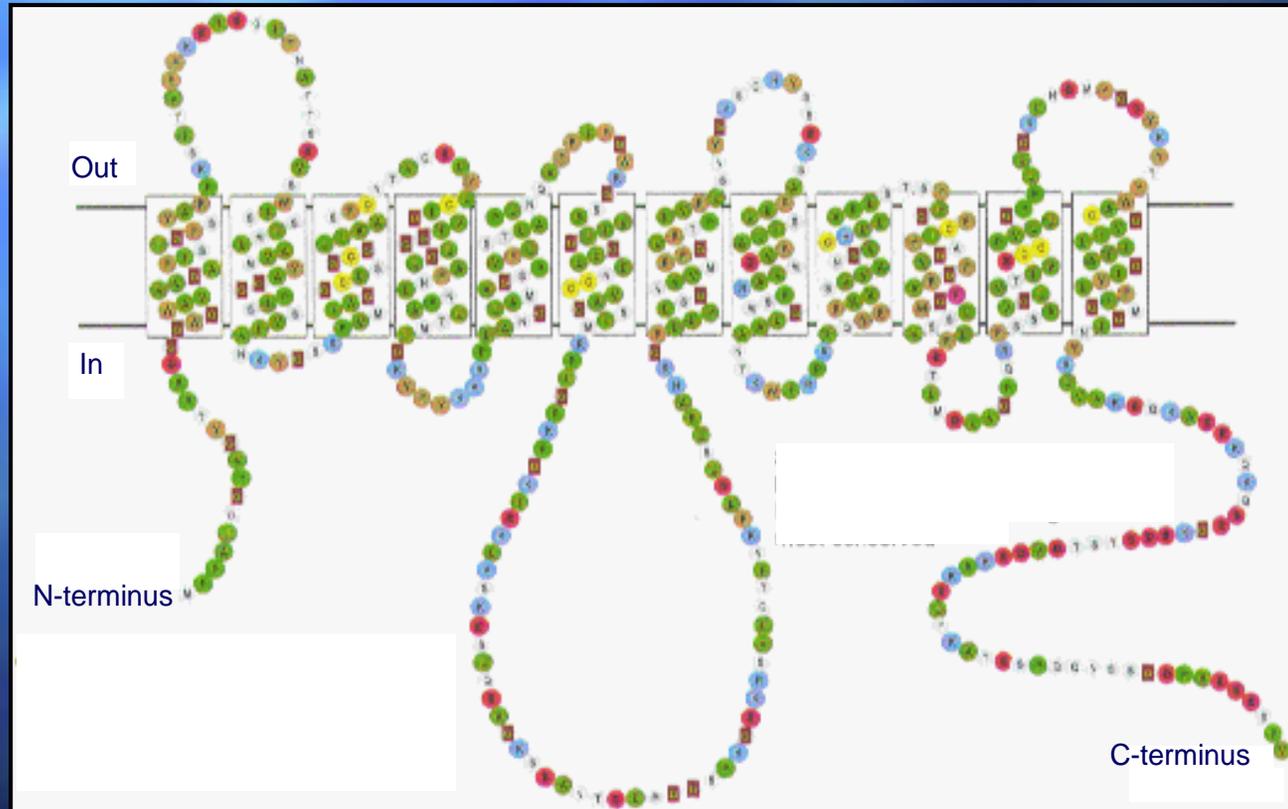
# Métabolisme du lactate



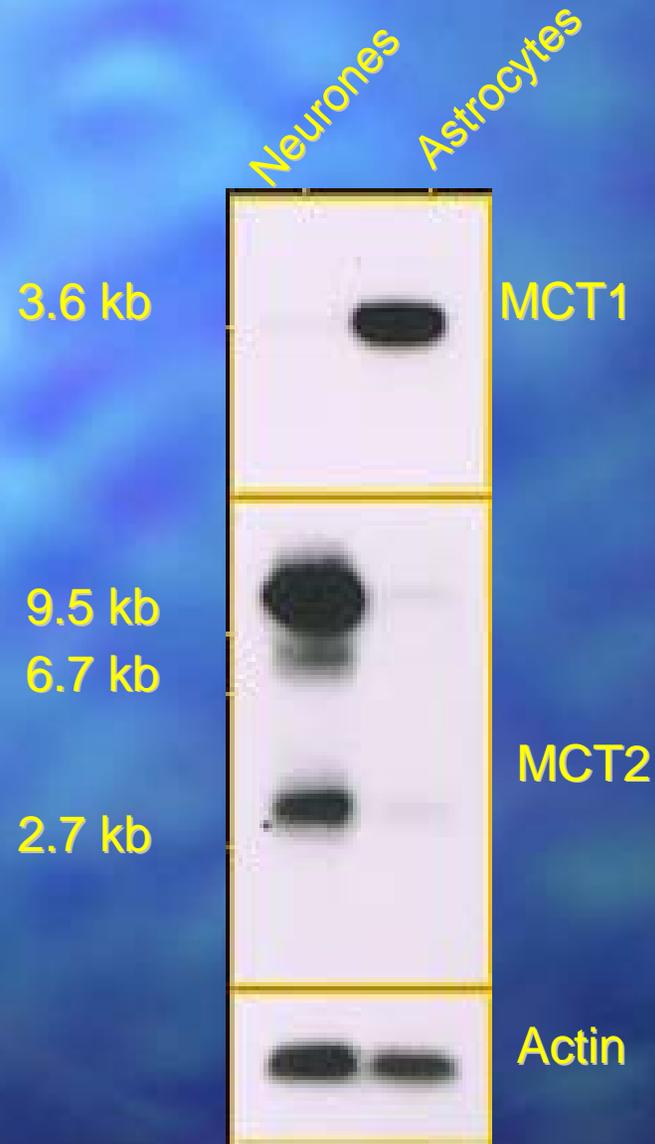
# Transporteurs aux monocarboxylates



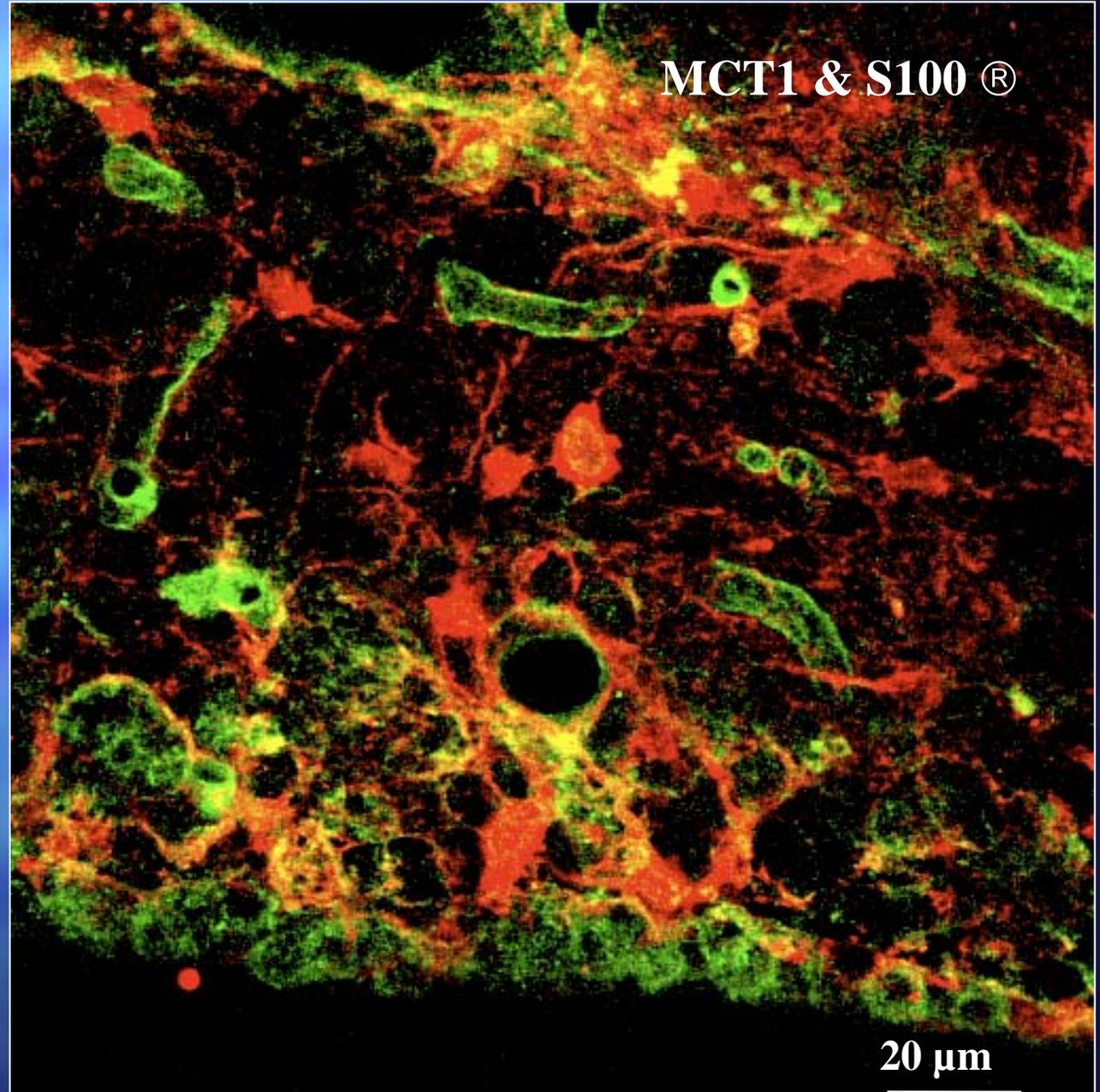
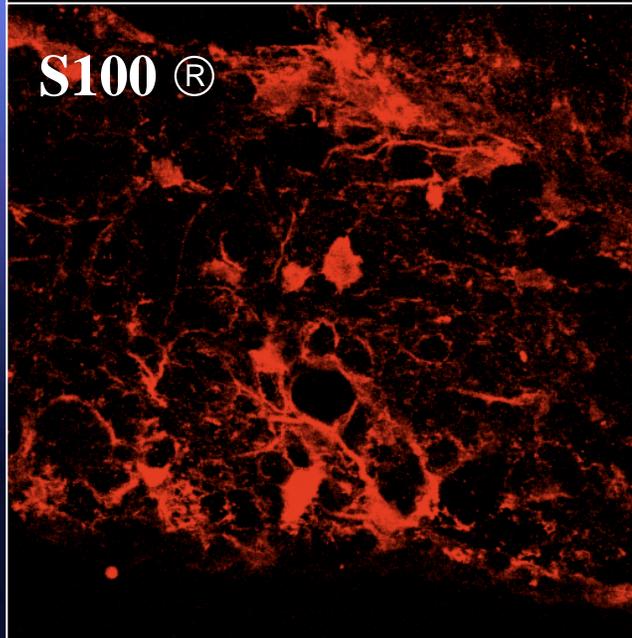
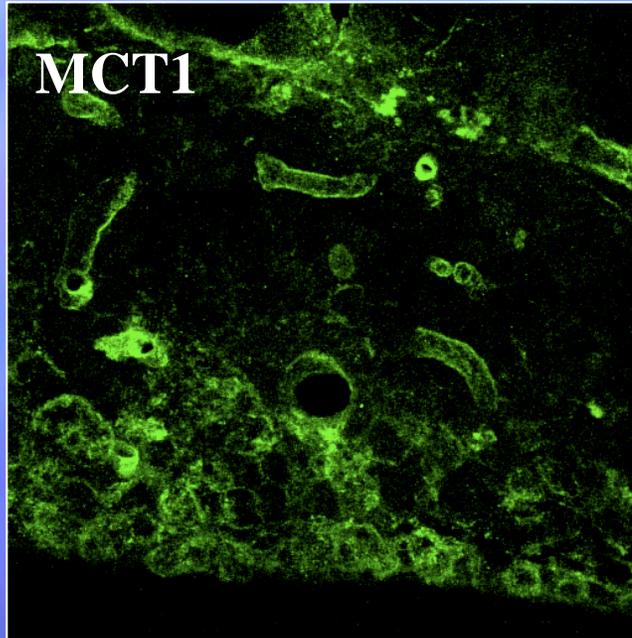
- **MCT1-9 ont été identifiés par homologie de séquence**
- **Spécifiques pour le L-lactate, le pyruvate et les corps cétoniques**
- **Co-transport avec H<sup>+</sup>**
- **K<sub>m</sub> : 0.1-1 mM      K<sub>m</sub> MCT1 > MCT2**



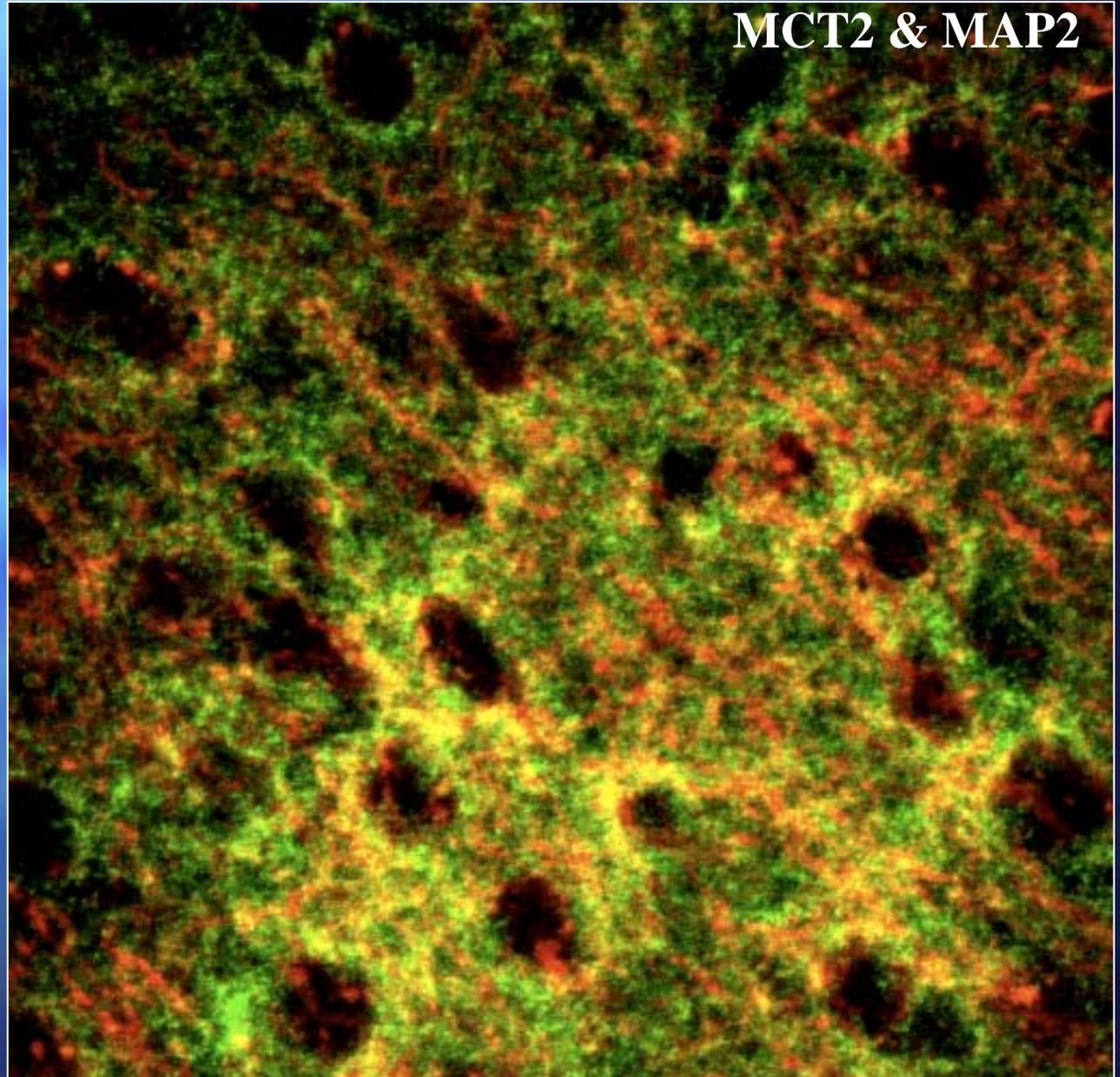
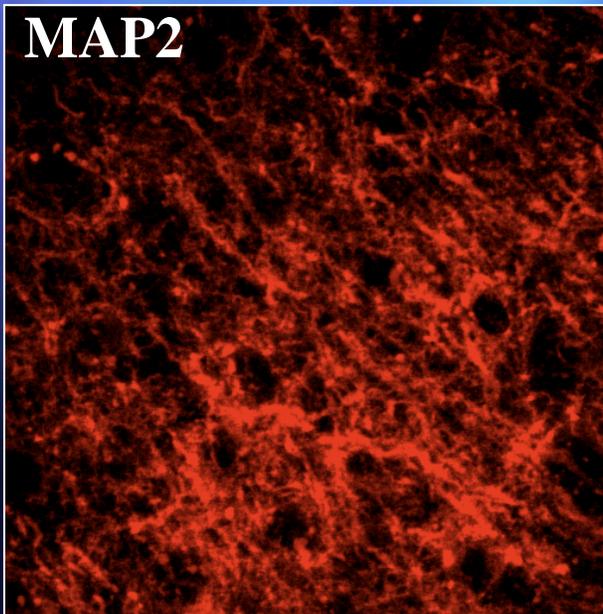
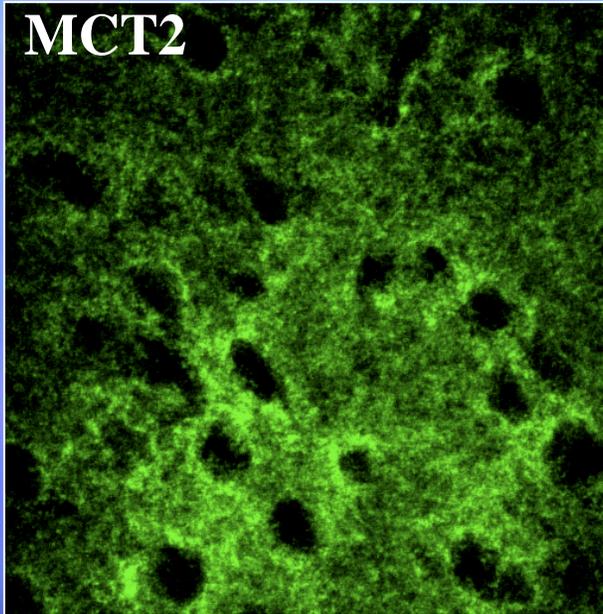
# Expression de MCT1 et MCT2 mRNAs dans des cultures primaires de neurones et astrocytes corticaux



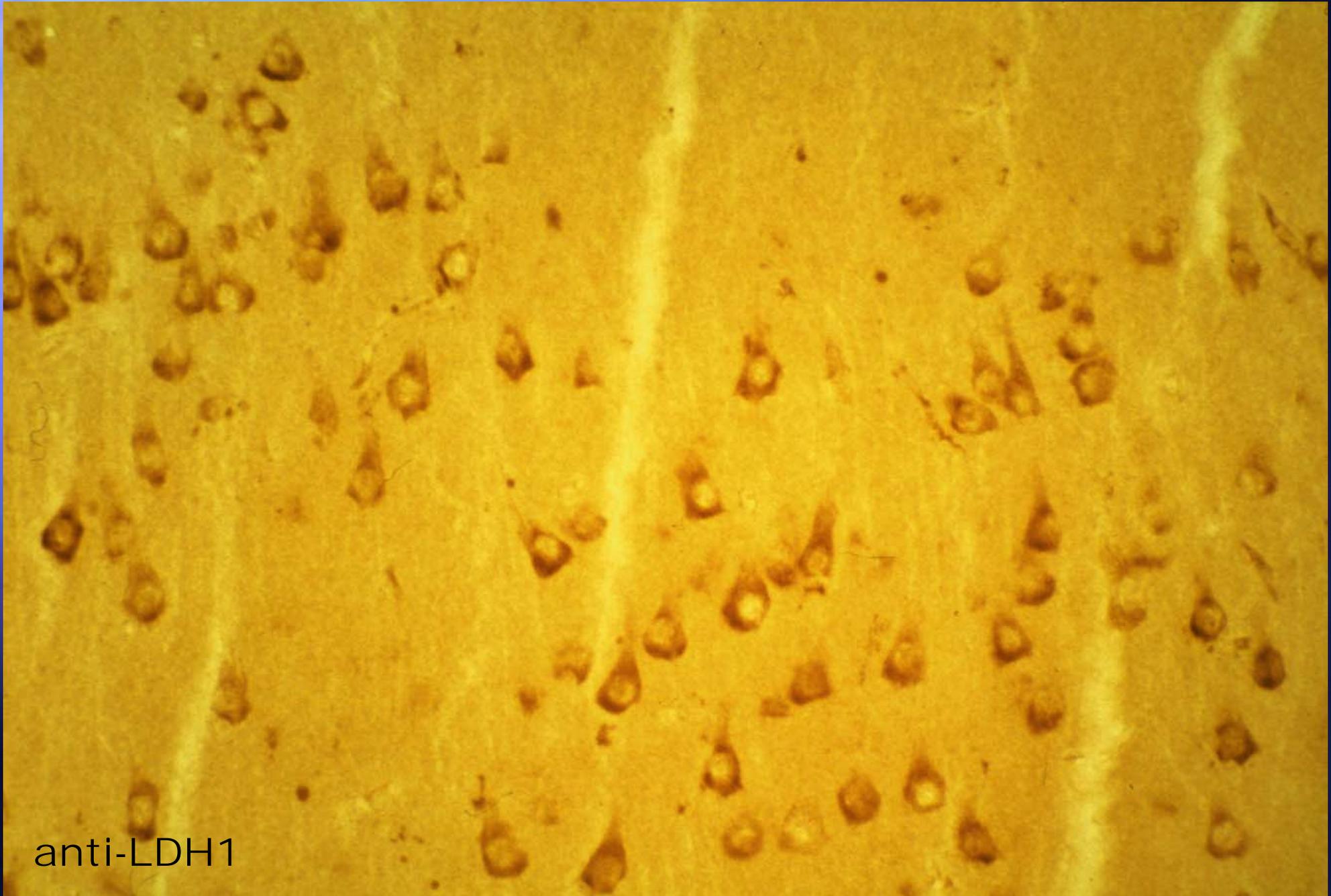
# Colocalisation de MCT1 et S100<sub>B</sub> dans le cerveau de souris



# Colocalisation de MCT2 et MAP2 dans le cerveau de souris

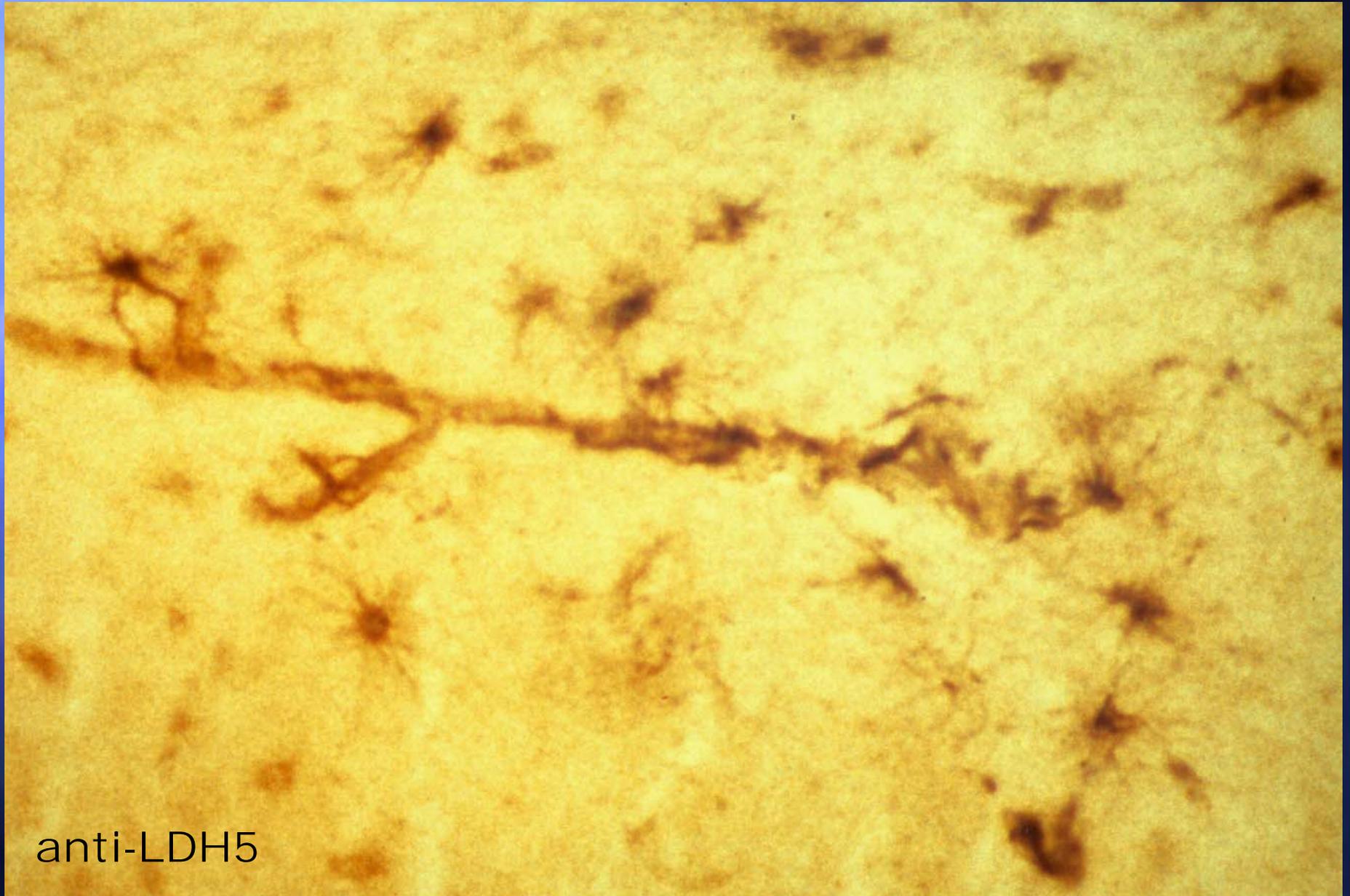


# LDH 1 : Neurones



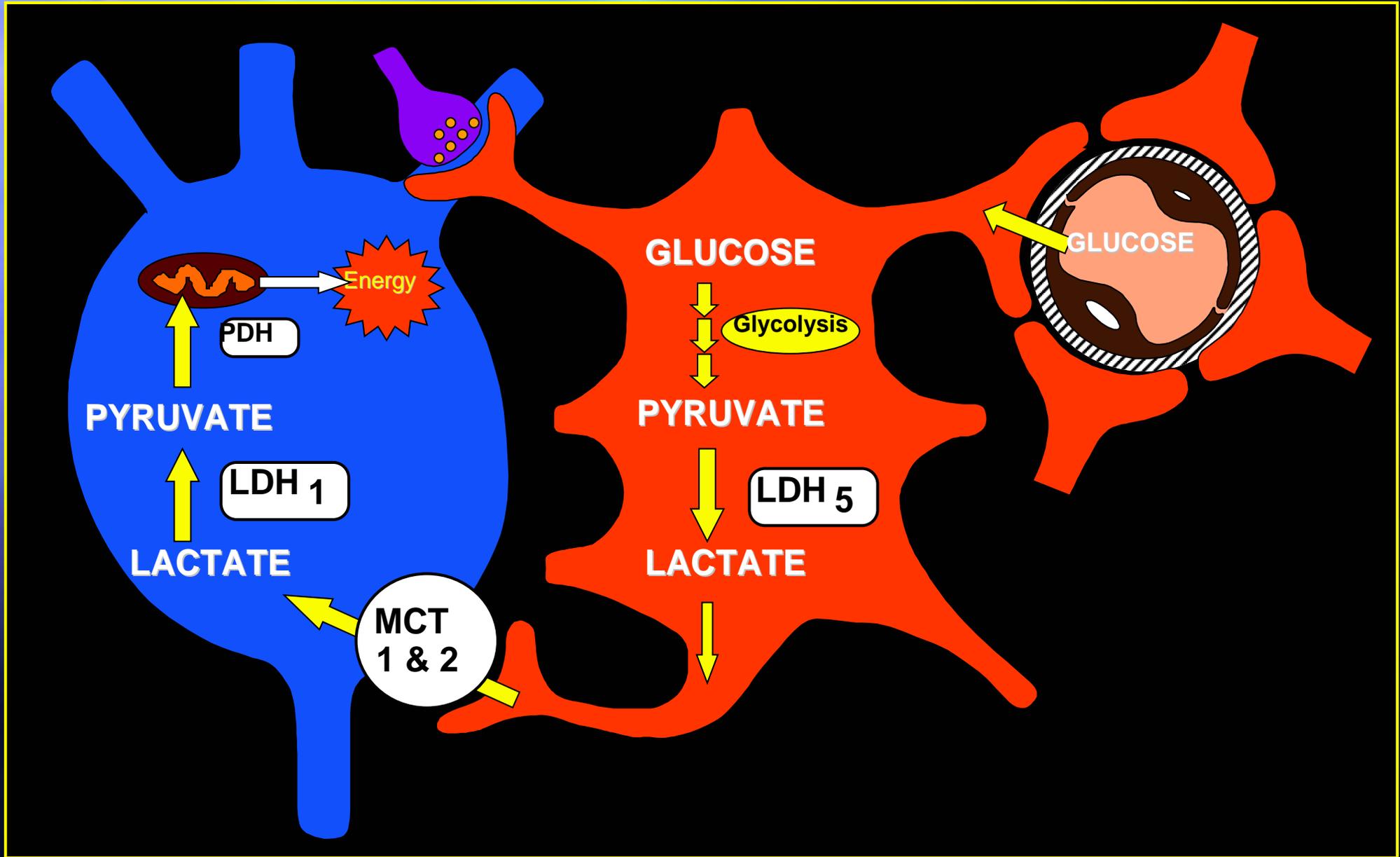
anti-LDH1

# LDH 5 Astrocytes



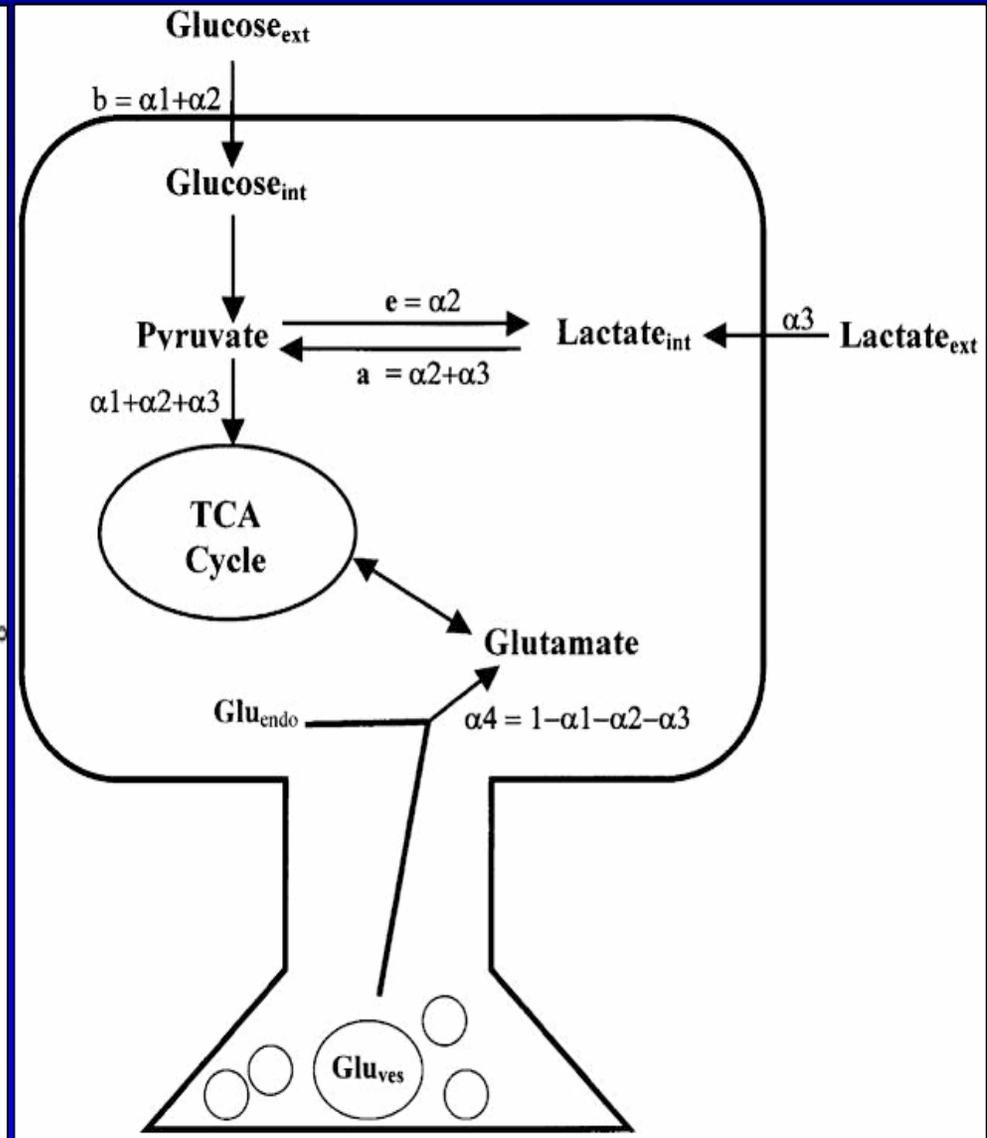
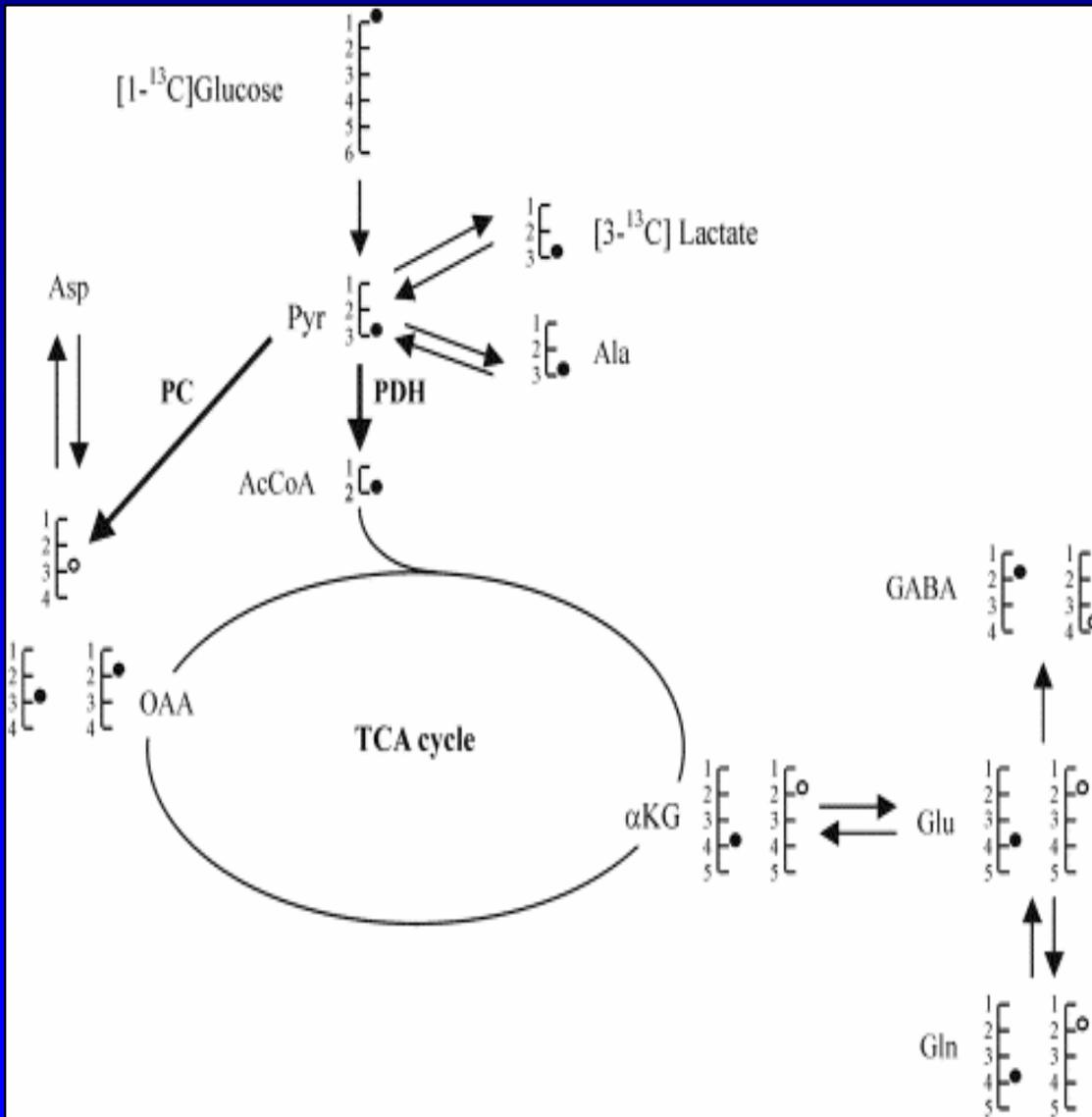
anti-LDH5

# ASTROCYTE-NEURON LACTATE SHUTTLE NAVETTE LACTATE ASTROCYTE - NEURONE





# Participation de substrats au métabolisme oxydatif peut être déterminé par RMN $^{13}\text{C}$





## Contribution relative du glucose et du lactate au métabolisme oxydatif neuronal

<b>[Lactate] (mM)</b>	<b>Glucose exogène (⟨1 + ⟨2)</b>	<b>Lactate exogène (⟨3)</b>
<b>1.1</b>	<b>53.28%</b>	<b>46.72%</b>
<b>5.5</b>	<b>10.05%</b>	<b>89.95%</b>
<b>11</b>	<b>7.09%</b>	<b>92.91%</b>

***Concentration de glucose : 5.5 mM***



Constantes de temps différentes pour  
l'activité synaptique et la réponse  
métabolique

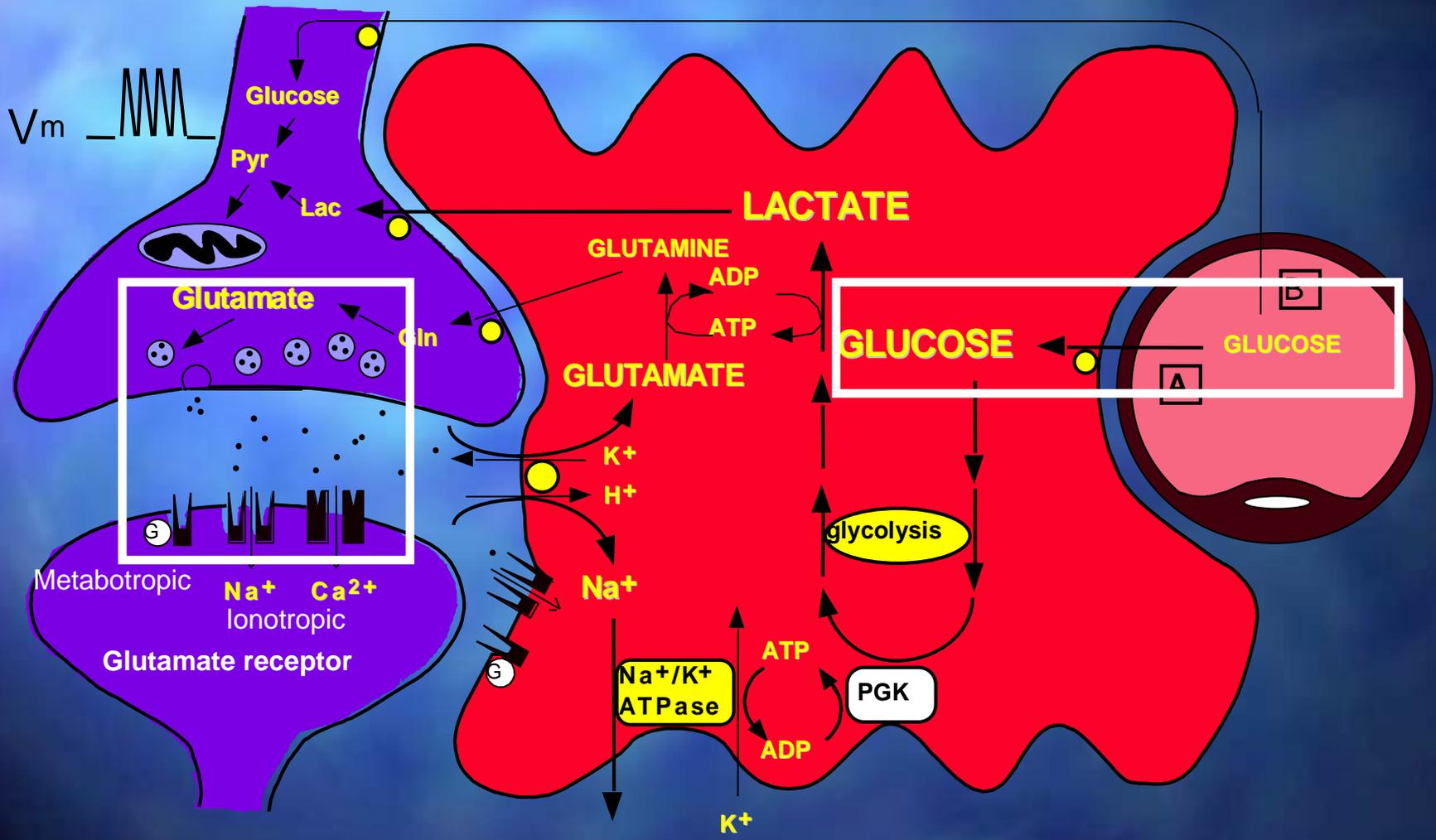
Rôle de l'espace extracellulaire comme  
tampon *spatial* et temporel

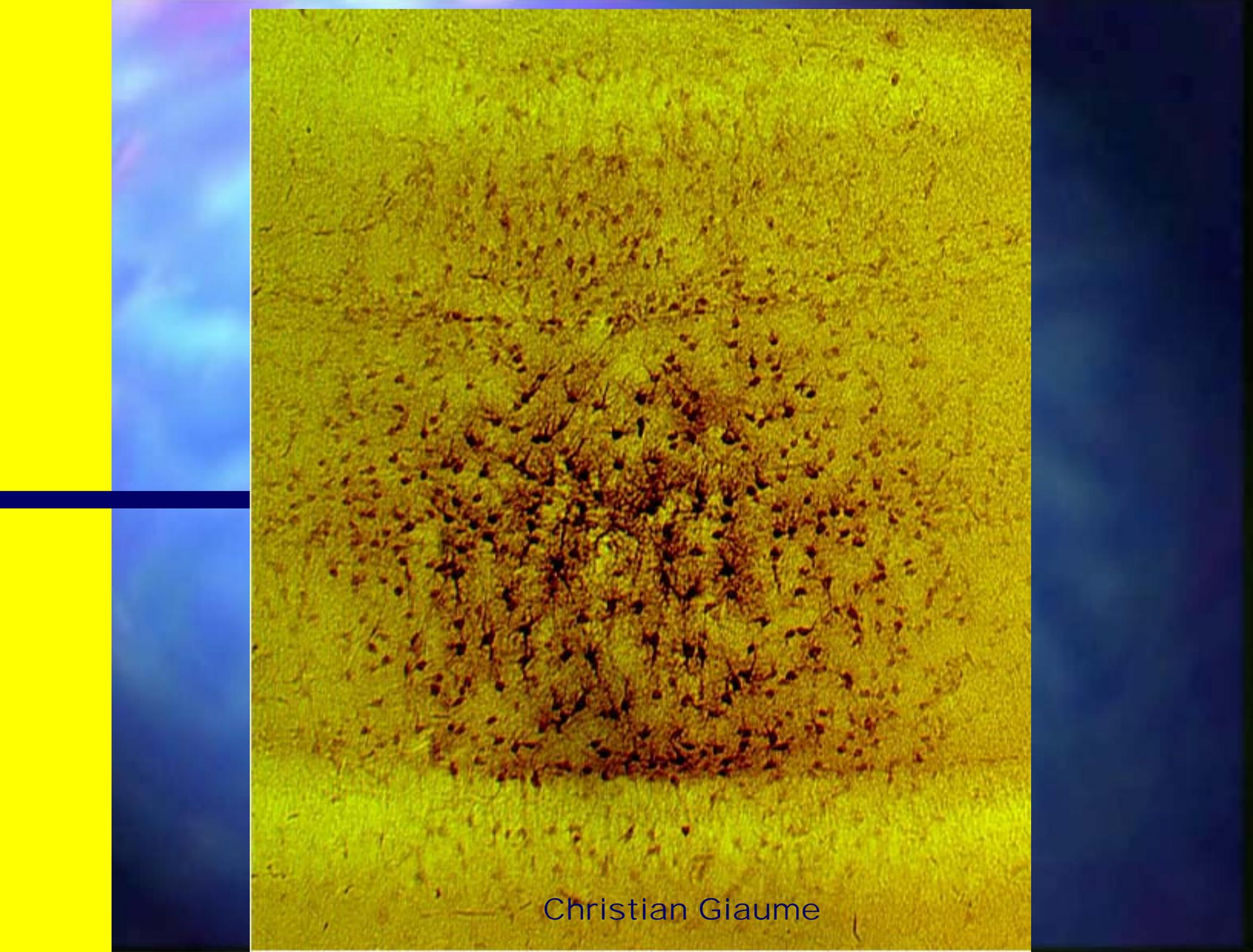


Synapse glutamatergique

Astrocyte

Capillaire





Christian Giaume

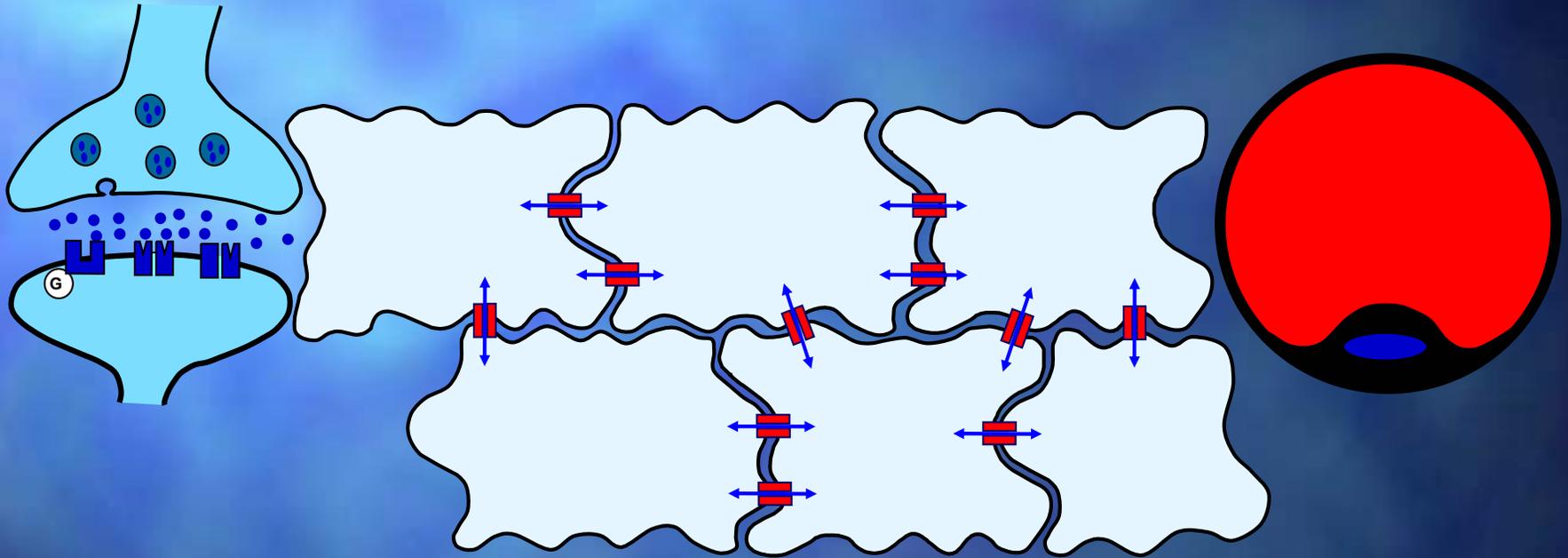


# Mechanism for Coupling Neuronal Activity to Glucose Utilization

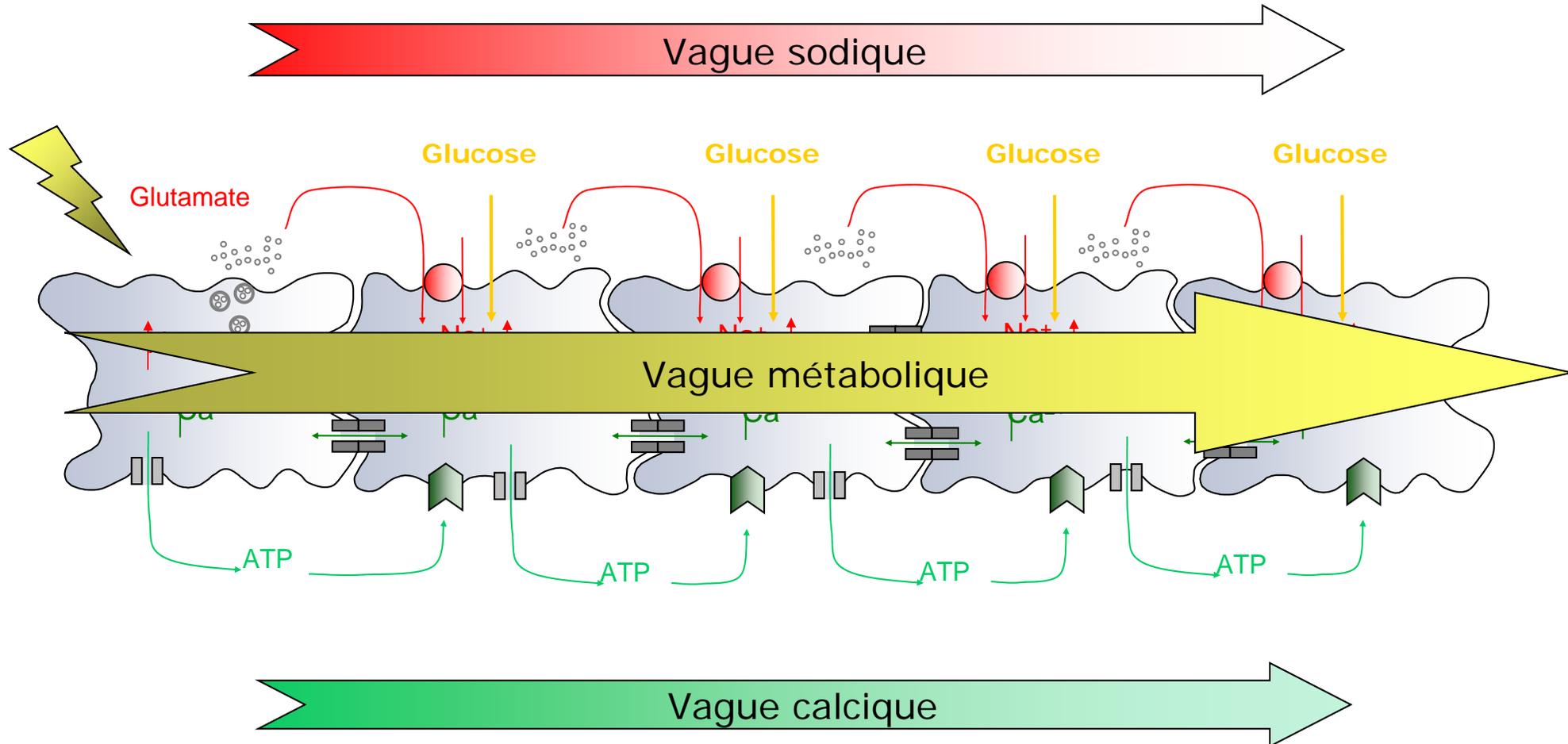
Synapse Glutamatergique

Réseau astrocytaire

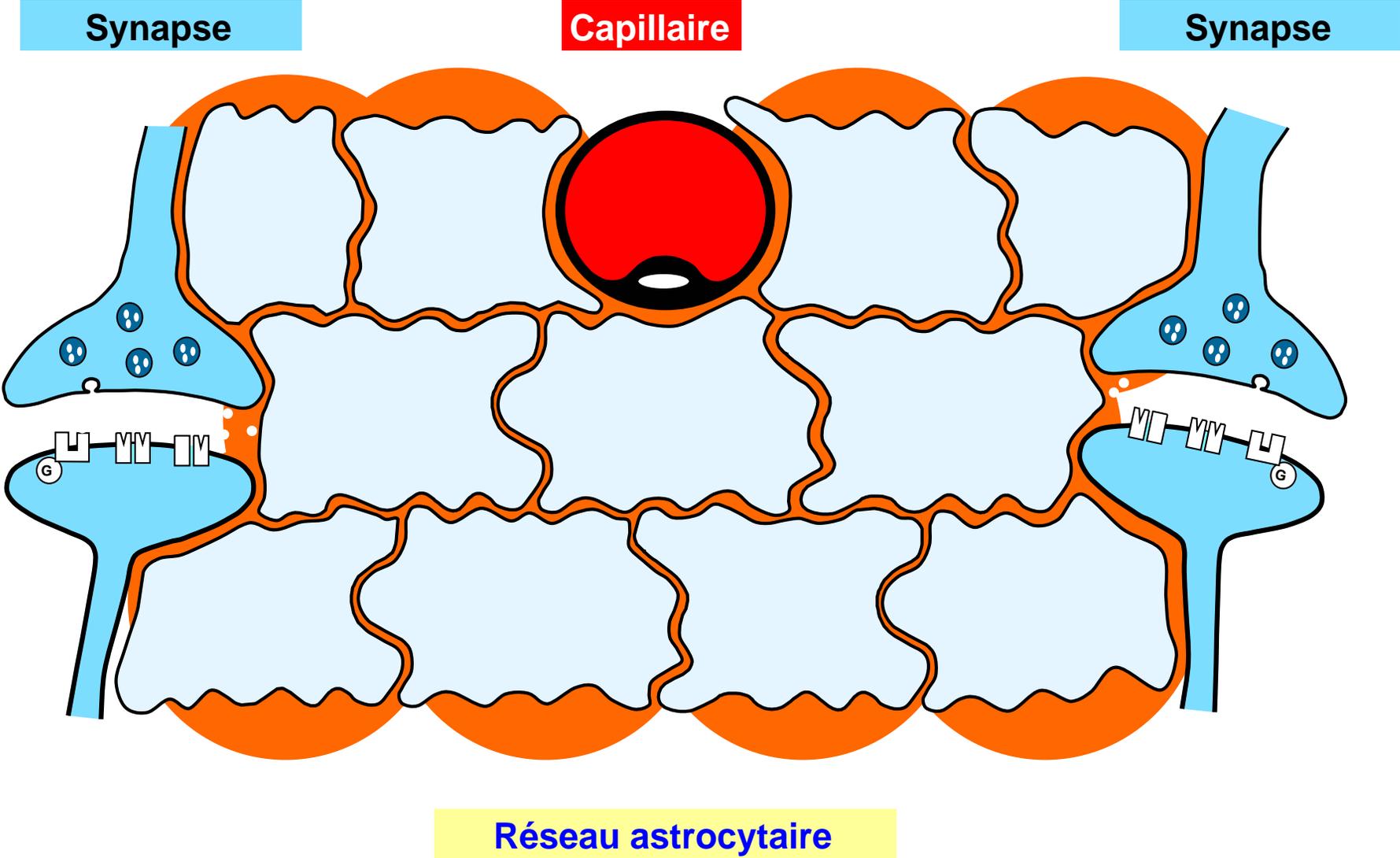
Capillaire

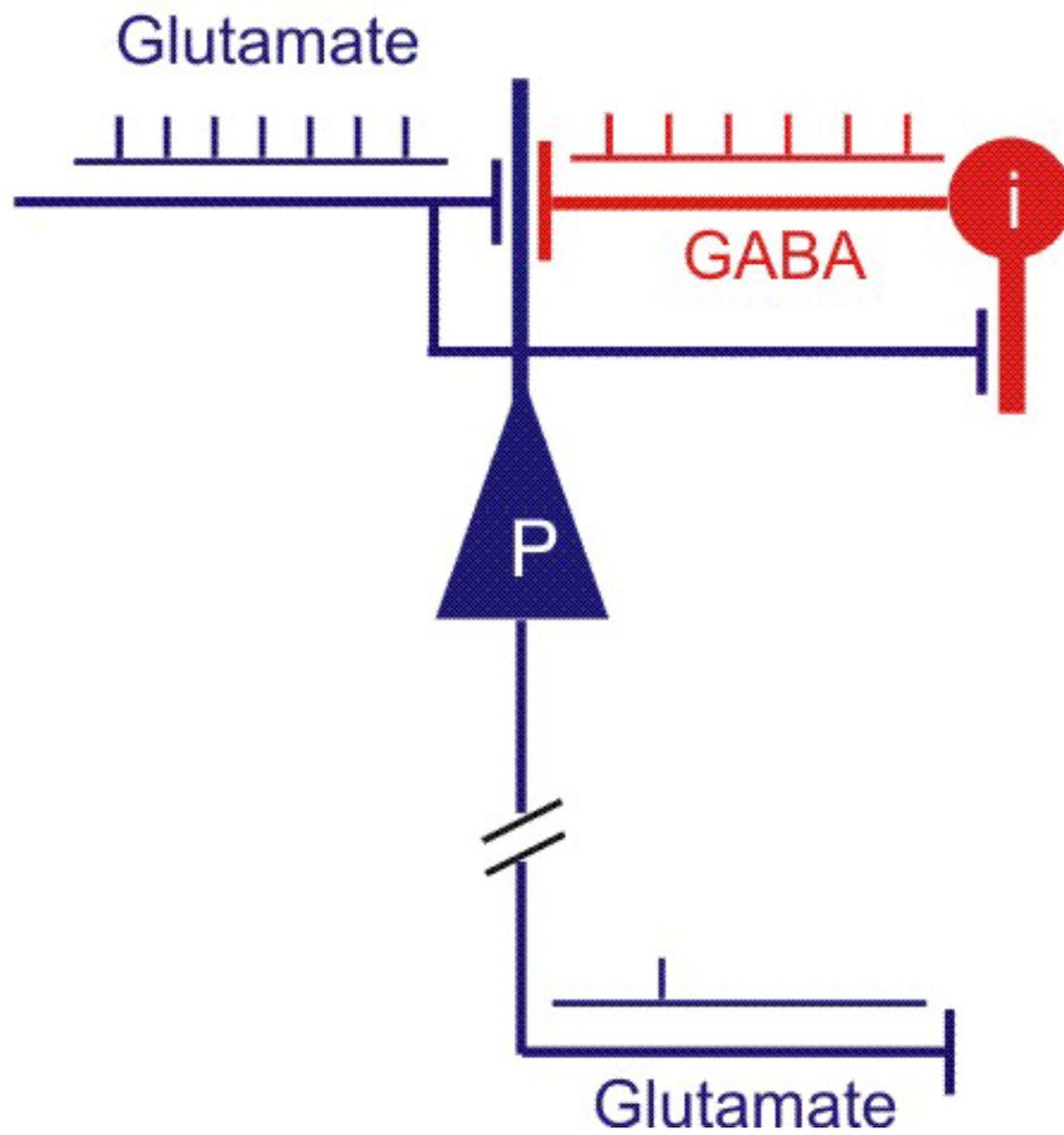


# Vagues intercellulaires calciques, sodiques et métaboliques



# Mécanisme d'amplification du couplage neurométabolique







Constantes de temps différentes pour  
l'activité synaptique et la réponse  
métabolique

Rôle de l'espace extracellulaire comme  
tampon spatial et temporel