BUDGET DE LA NEUROTRANSMISSION GLUTAMATERGIQUE

- *Signalisation glutamatergique pré- et post-synaptique*

  Action post-synaptique : 140 000 molécules d' ATP/vésicule libérée (137 + 3)
  Recyclage (neurone - glie) : 11 000 molécules d' ATP
  Homéostasie calcique et libération pré-synaptique : 14 000 molécules d'ATP

---> 1.64 x 10^5 molécules d'ATP/vésicule libérée

- *2. Genèse et propagation du potentiel d'action*

  Rétablissement du gradient sodique dissipé par un PA (1.15 x 10^9 Na+)

----> 3.84 x 10^8 molécules d' ATP

(dont 82 % à l'axone, 14 aux dendrites et 4 au soma)

---> 1 PA peut évoquer la libération de glutamate au niveau de 8000 boutons synaptiques
mais probabilité de libération dépend de la fréquence
---> à 4 Hz ---> probabilité de 0.25
----> libération de 2000 vésicules depuis 8000 boutons

----> 3.28 x 10^8 molécules d'ATP

----> 7.1 x 10^8 molécules d'ATP/neurone/PA

Estimation du coût pour une fréquence à 4 Hz

4X

3.84×10^8 (PA)
+
3.28×10^8 (pré/post/recyclage)

$= 2.85 \times 10^9$ ATP/neurone/s

+ coût du maintien du potentiel de repos

3.42×10^8 (neurones)
1.02×10^8 (astrocytes)

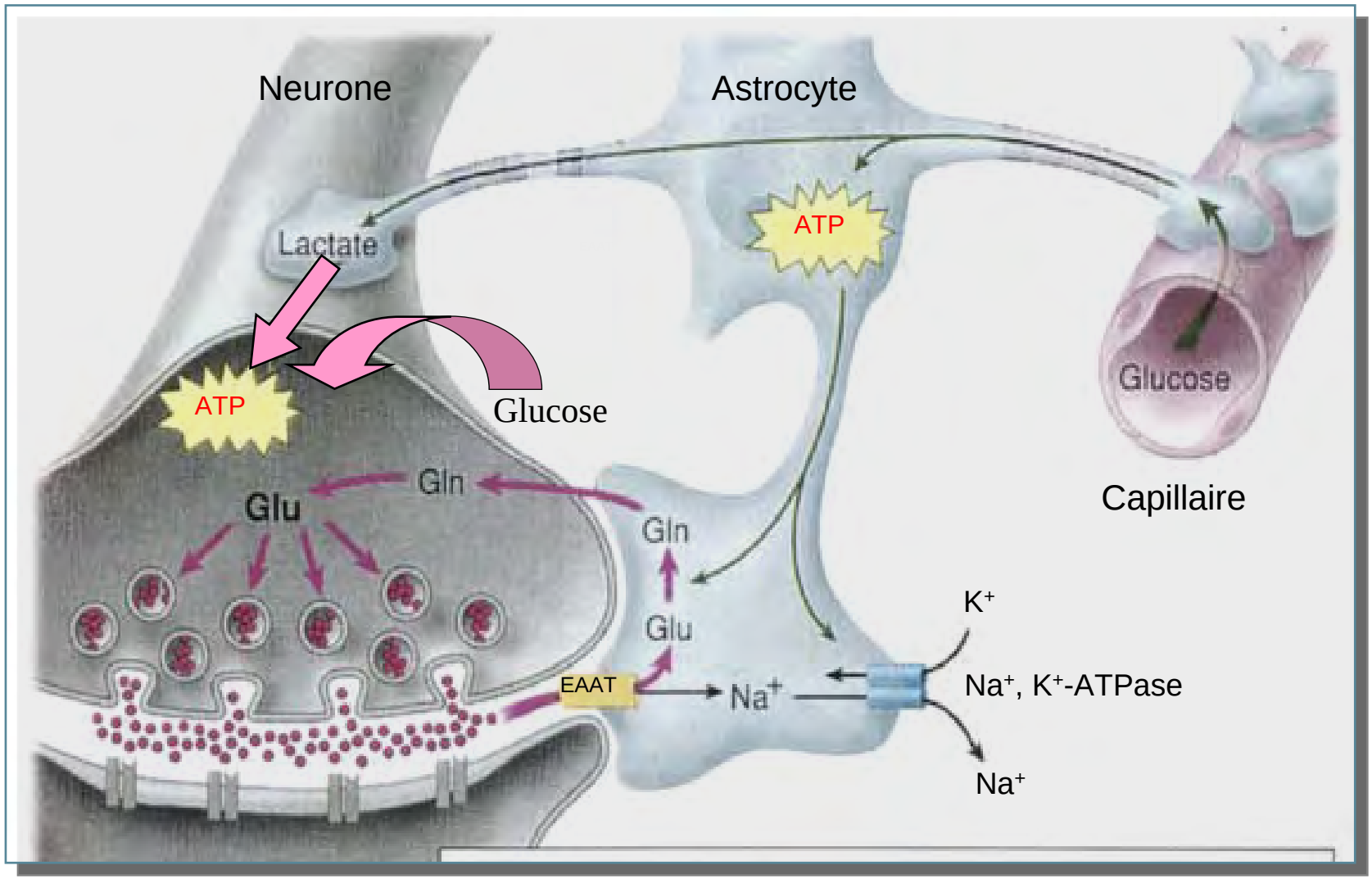
---> $3.29\ 10^9$ molécules d'ATP/ neurone/ s à 4 Hz

Si 9.2×10^7 neurones/cm^3 (donc ≈ par g) (Braitenberg et Schüz,1998)

Prédiction ---> 30 ATP ⌈mol/g/min consommés par MG
Mesure ---> 33 - 50 ⌈mol/g/min (Clarke et Sokoloff 1999)

-----> 1 PA/neurone/s ----> 6.5 ⌈mol ATP/g/min (car PA+pré/post/recyclage ≈ 85%)

L’unité neuroénergétique



Estimation chez le primate :

PPS

7×10^8 synapses/mm^3

40 000 neurones/mm^3 ---> 175 000 contacts synaptiques/neurone

1.2×10^9 molécules d'ATP pour PPS

Propagation PA

Axone: 100 mm / dendrite : 10 mm (≈2.5x> que rongeur)

9.2 x 108 molécules ATP pour PA

Présynaptique et recyclage

2.1×10^8 ATP

2.4×10^9 molécules d'ATPd'ATP/neurone/PA

(Rongeur :7.1×10^8 molécules d'ATP/neurone/PA)

Estimation chez le primate :

Densité neuronale > 3 x inférieure

Même densité synaptique

---> > 3 x plus de synapses/neurone

Coût/ neurone ≈ 3.3 x > c/o humain

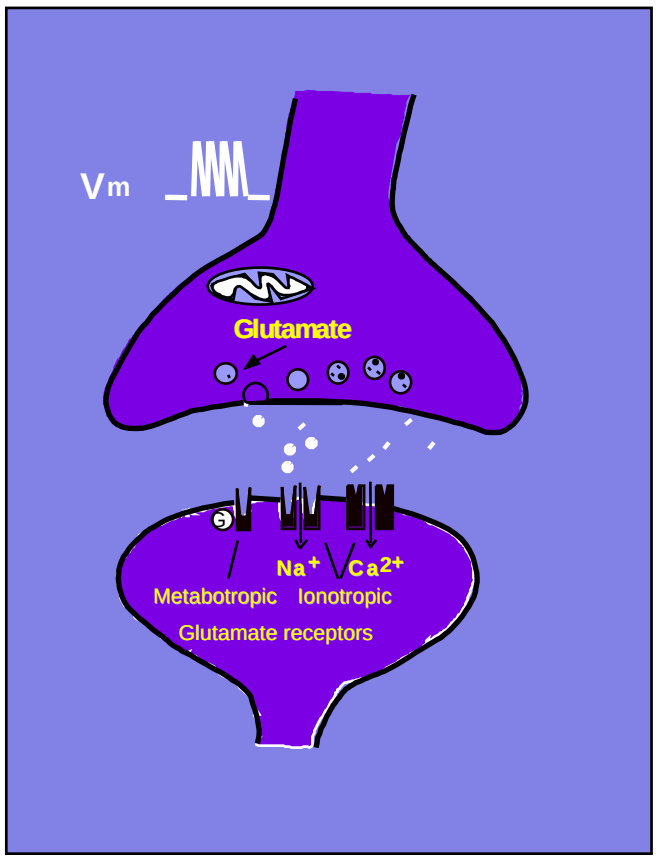
Consommation d'ATP :

Humain :14 ⌠mol/g/min
Rongeur : 30 ⌠mol/g/min

---> implications pour codage/fréquence

Comment l'activité neuronale est couplée au métabolisme et génère les signaux détectés par l'imagerie cérébrale

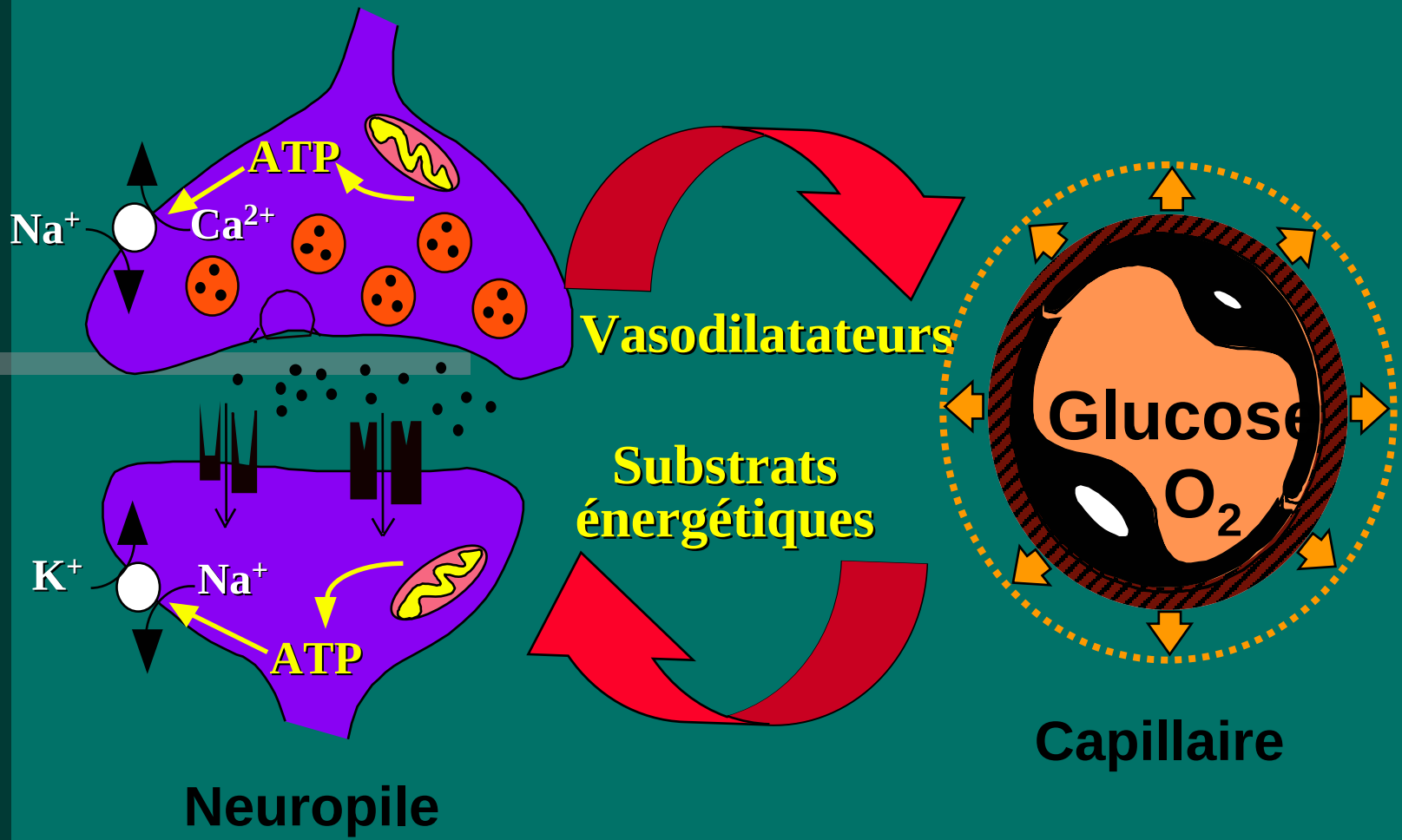
Activité neuronale ⟷ Réponses métaboliques et vasculaires → Imagerie fonctionelle

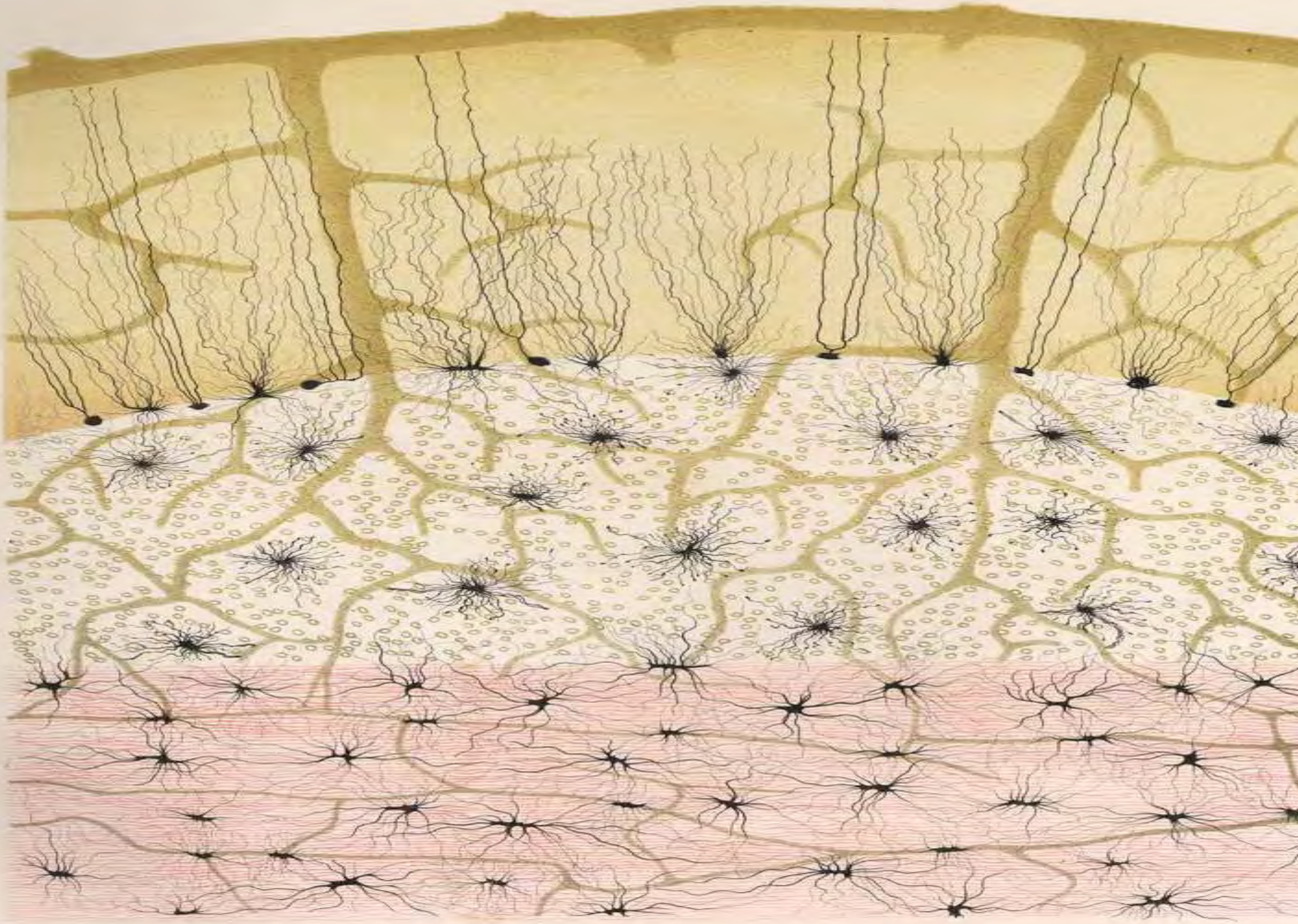


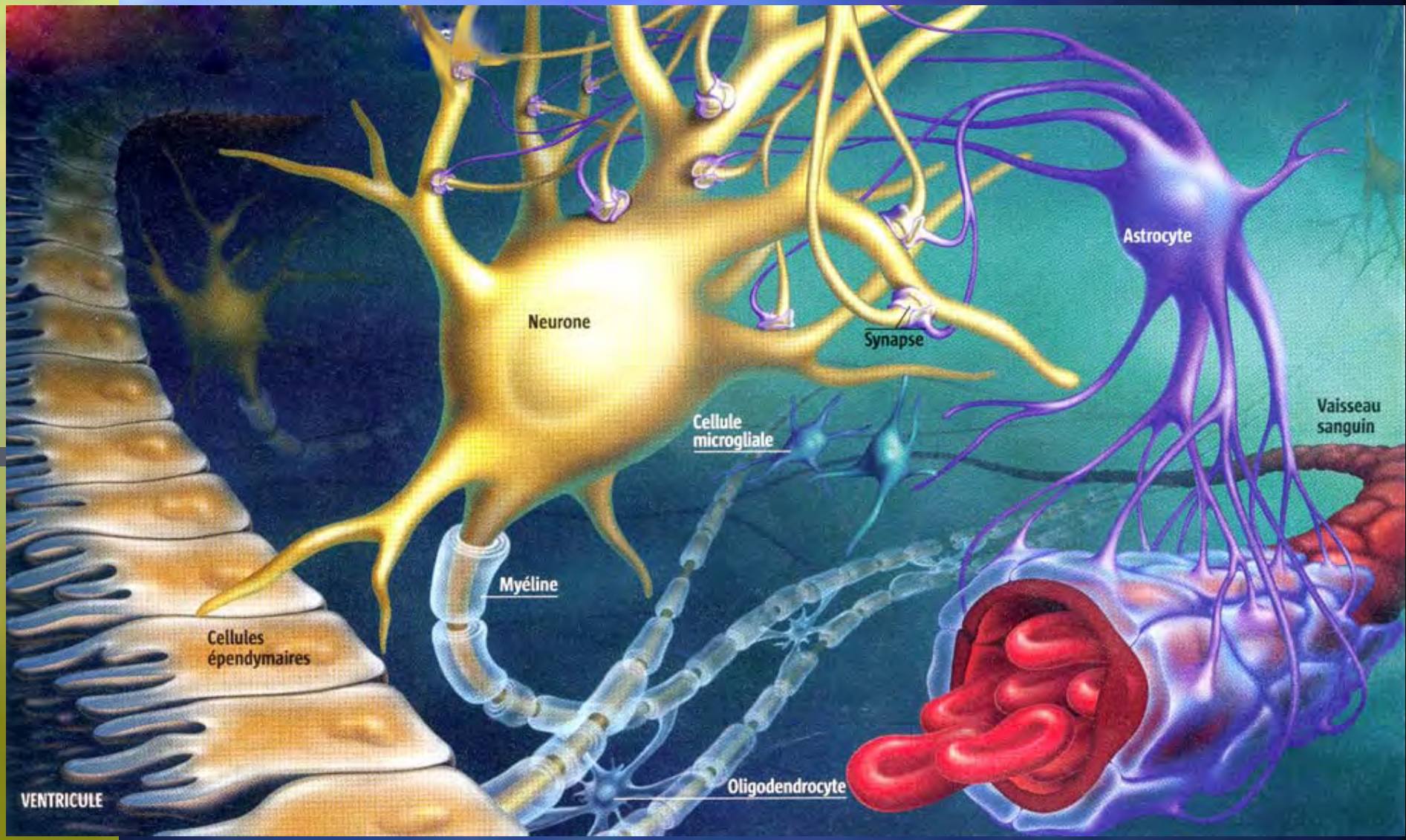
"Couplage"

?

Mécanisme classique proposé pour le couplage entre activité synaptique et consommation de glucose

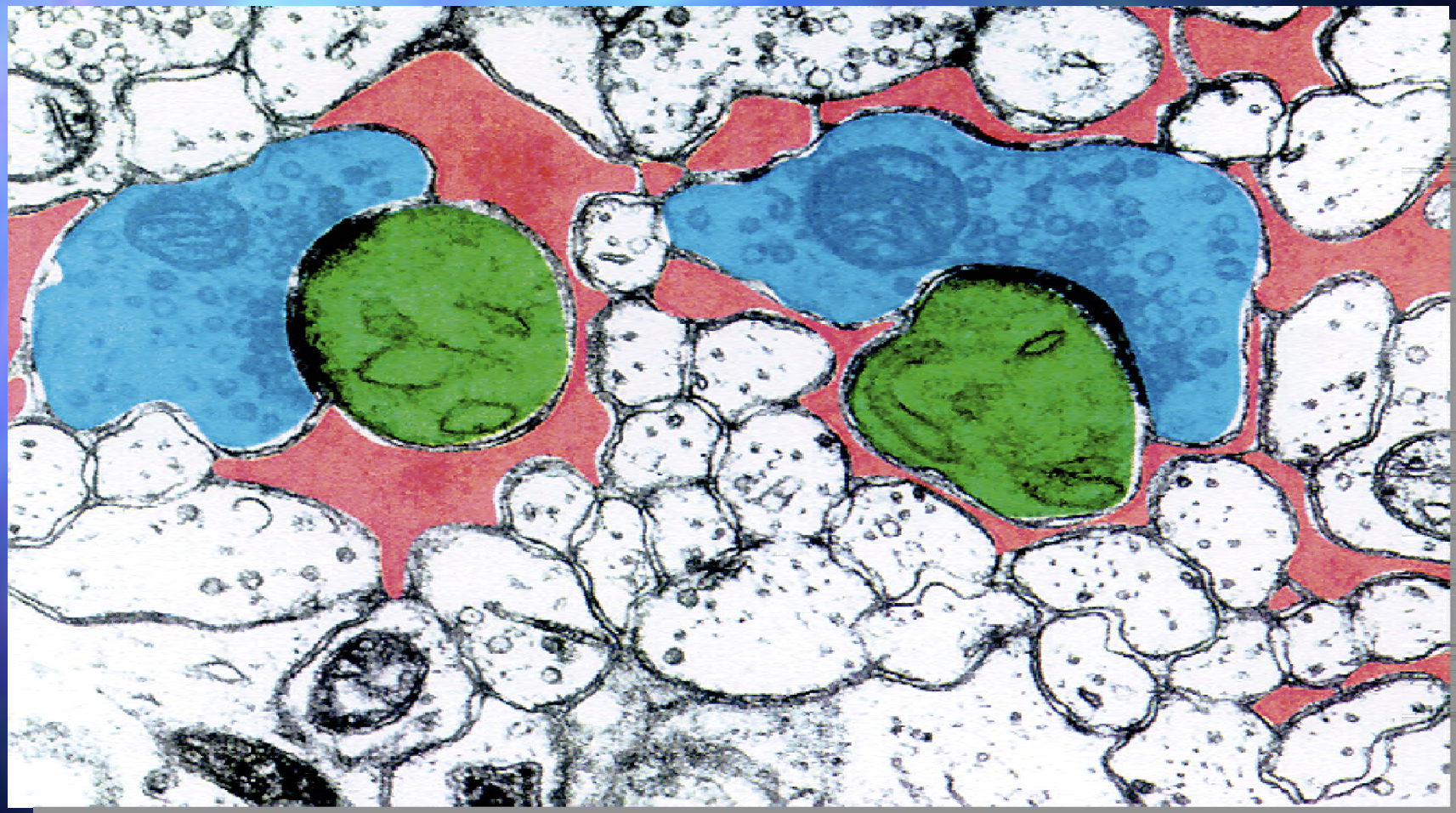






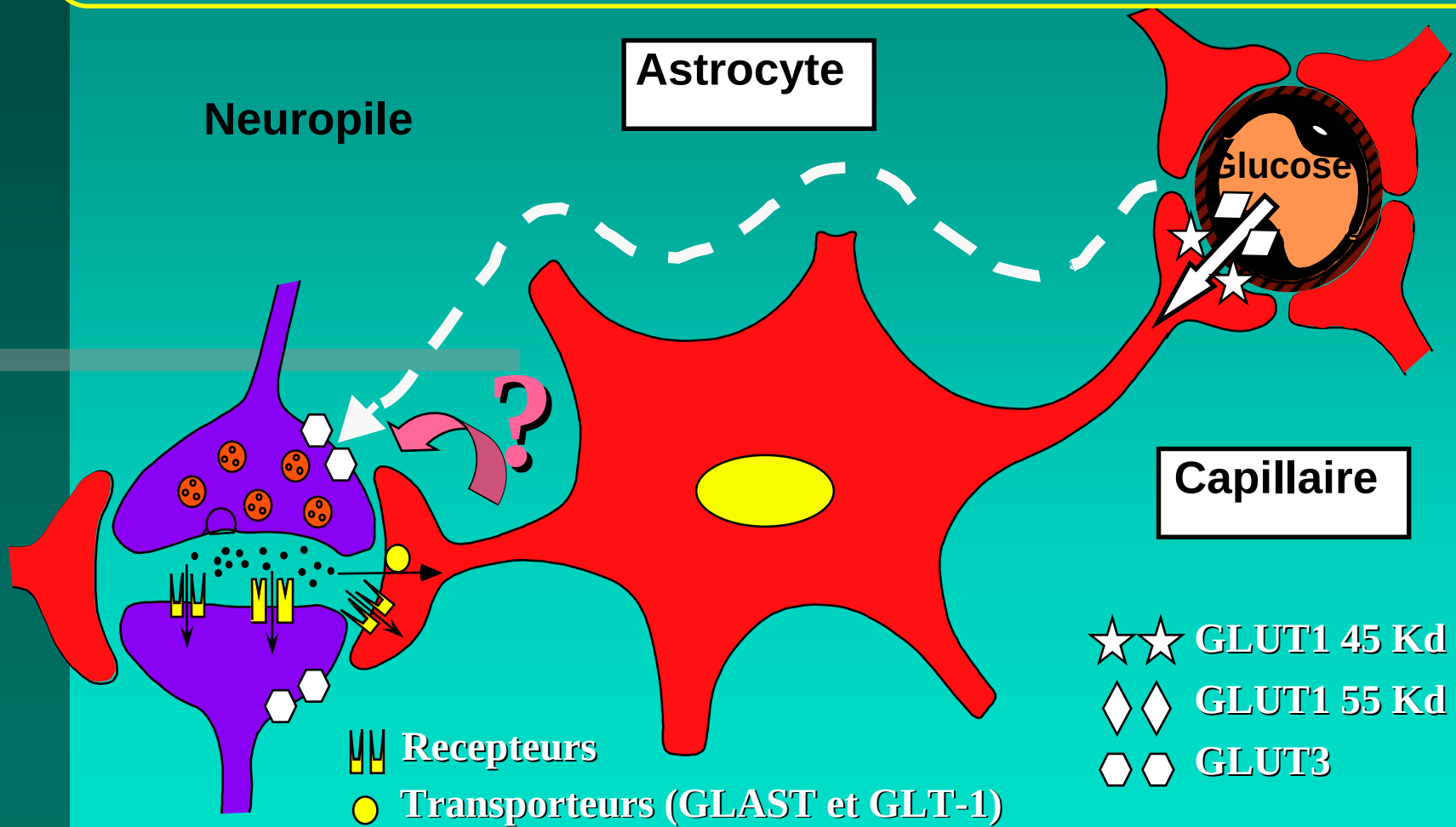
from F. Pfrieger and C. Steinmetz, La recherche, 2003 (361).

Astrocytes et synapses



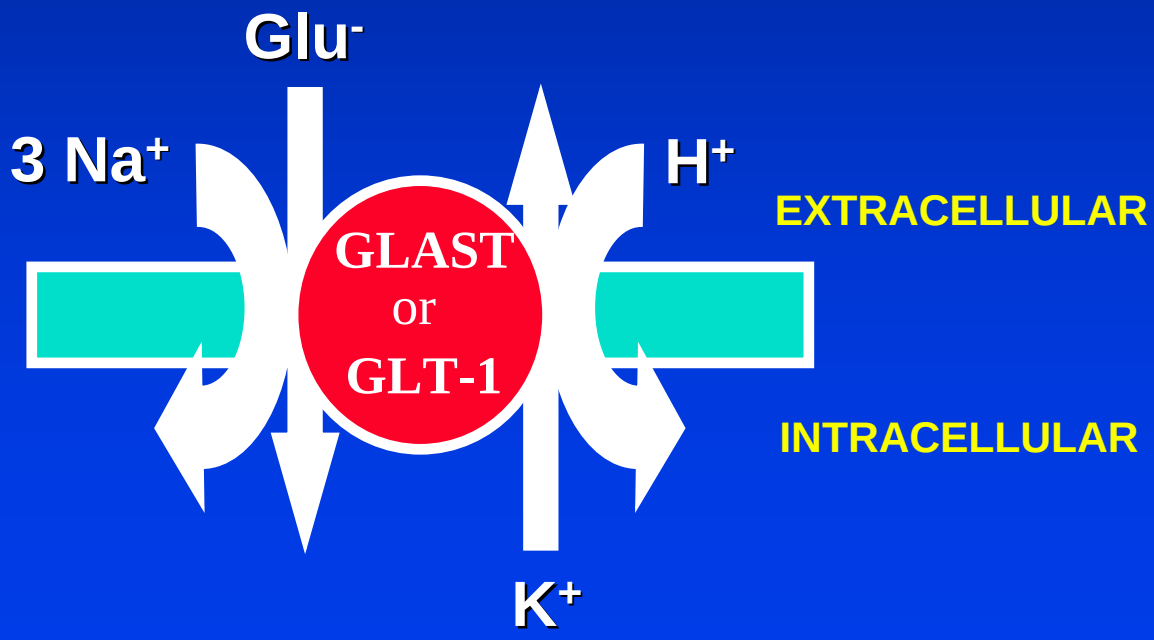
Tiré de: New views on synapse-glia interactions; F.W. Pfrieger and B.A. Barres; Current Opinion in Neurobiology 1996, 6:615-621

Role des astrocytes dans le couplage entre activité synaptique et consommation de glucose



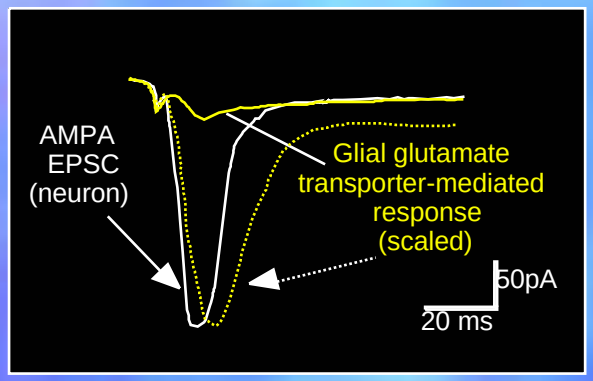
High-affinity Na^+-dependent glial glutamate transporters

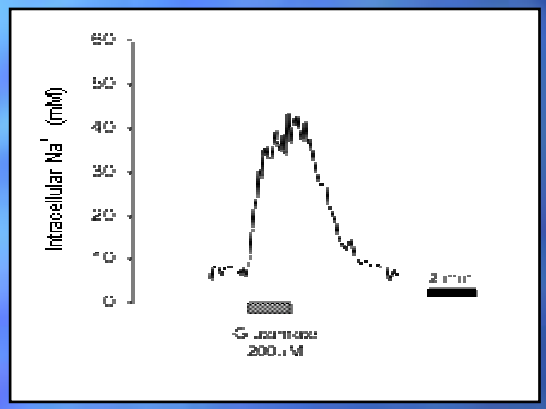
- GLAST and GLT-1
- Both expressed throughout the CNS
- On the same astrocytes but in variable proportions
- Together, responsible for the majority of glutamate uptake

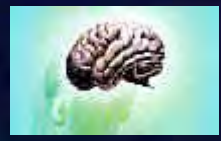


Synaptically released glutamate is avidly taken up by astrocytes where it generates a Na+ current

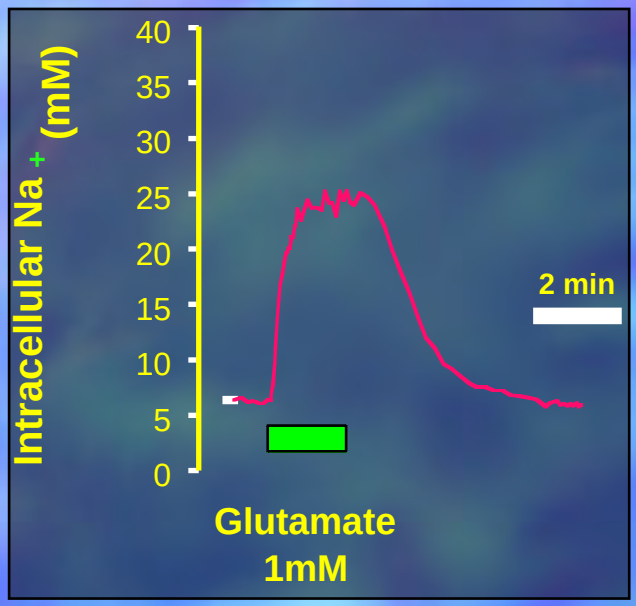
adapted from Bergles & Jahr
Neuron 19:1297-1308 (1997)

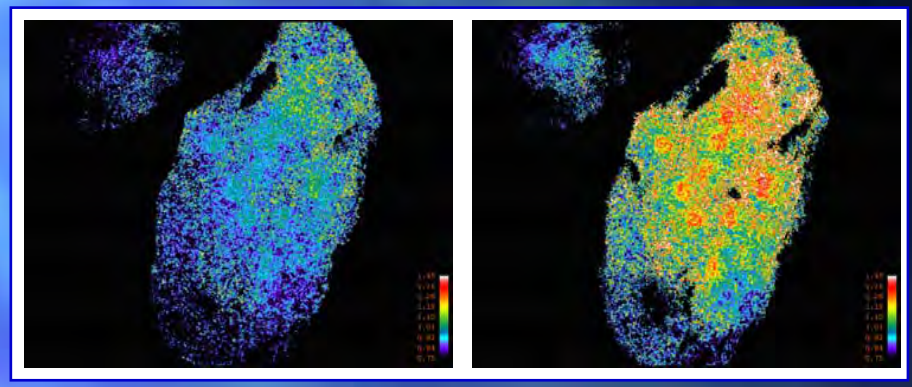


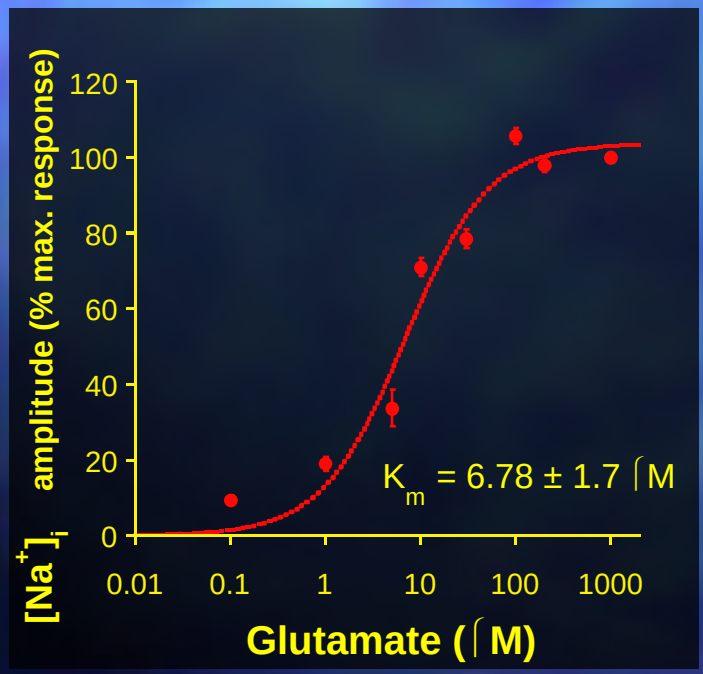


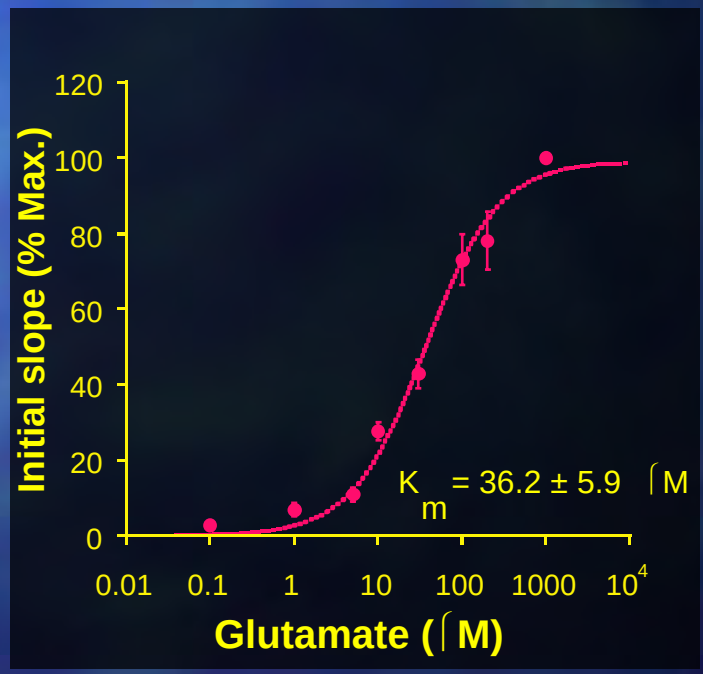


Glutamate and Na imaging



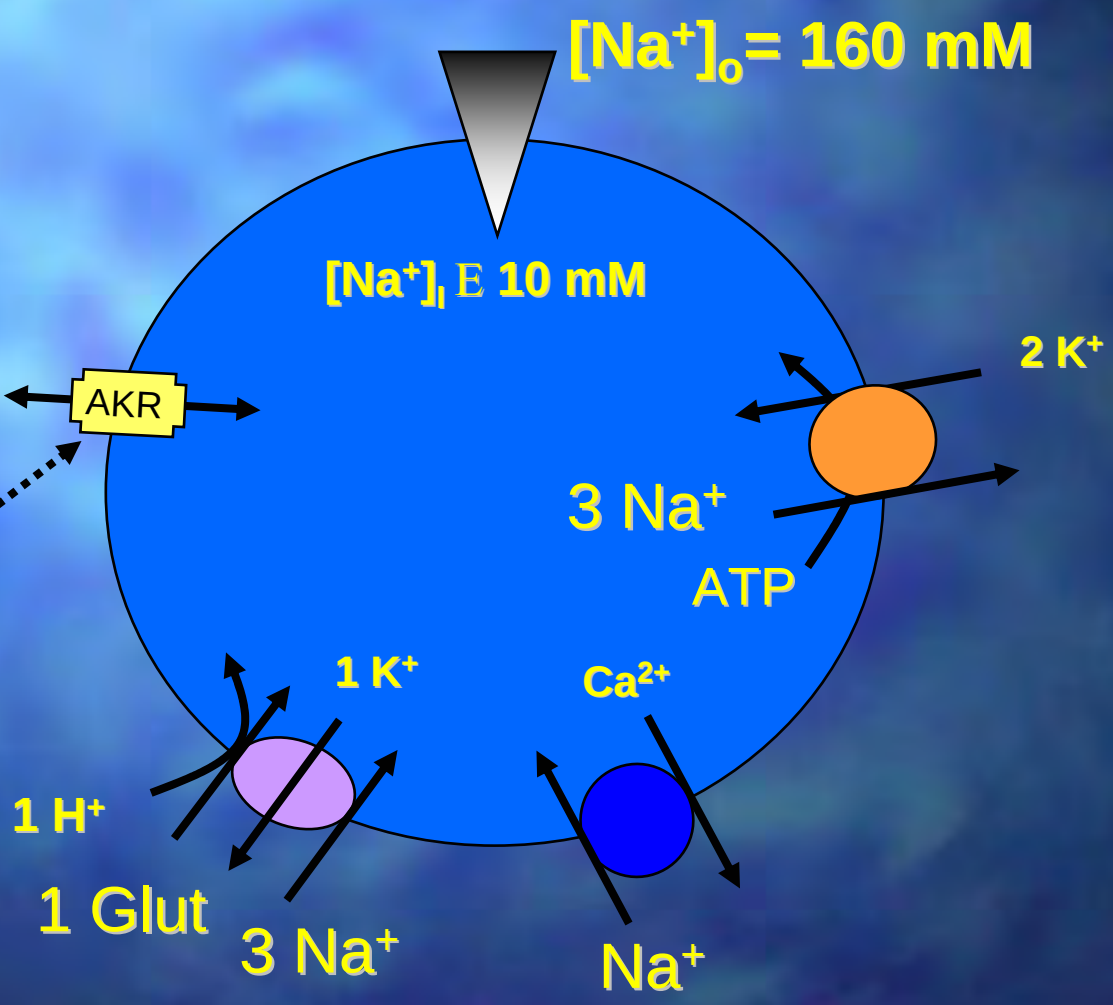


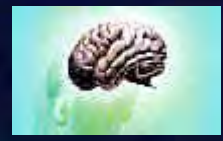




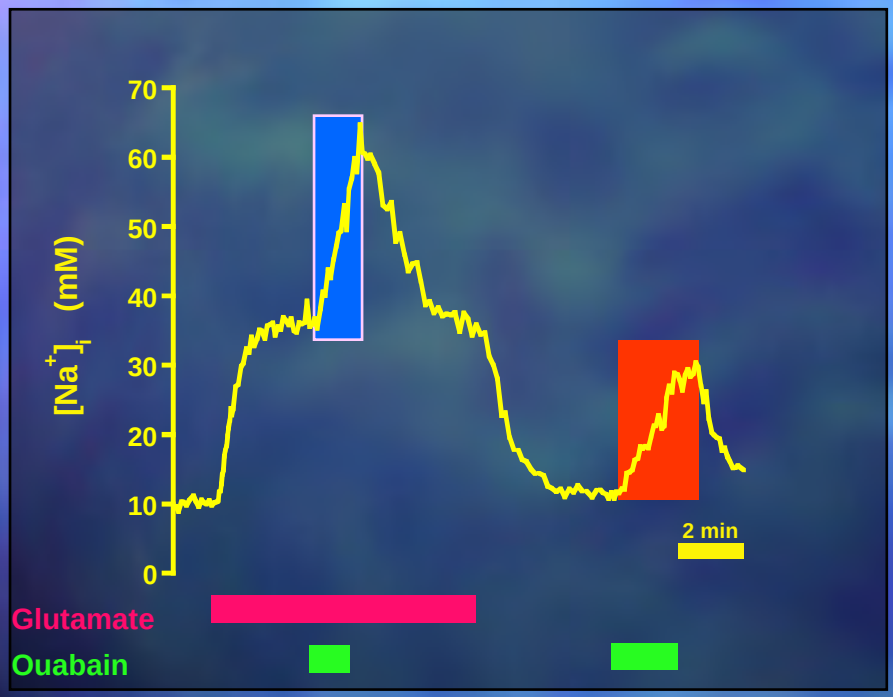
Homeostasie du sodium dans les astrocytes

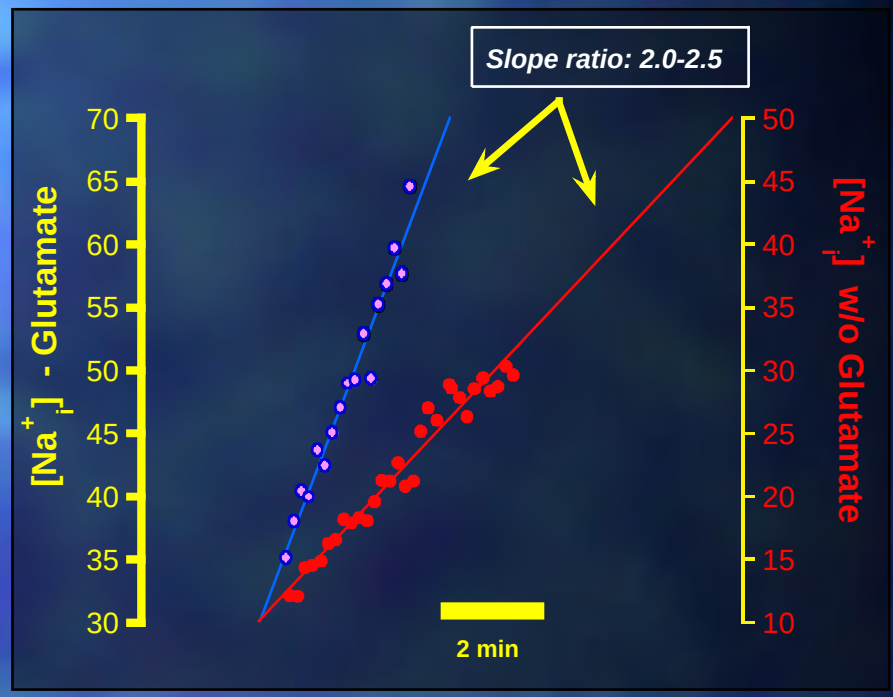
(modèle simplifié)





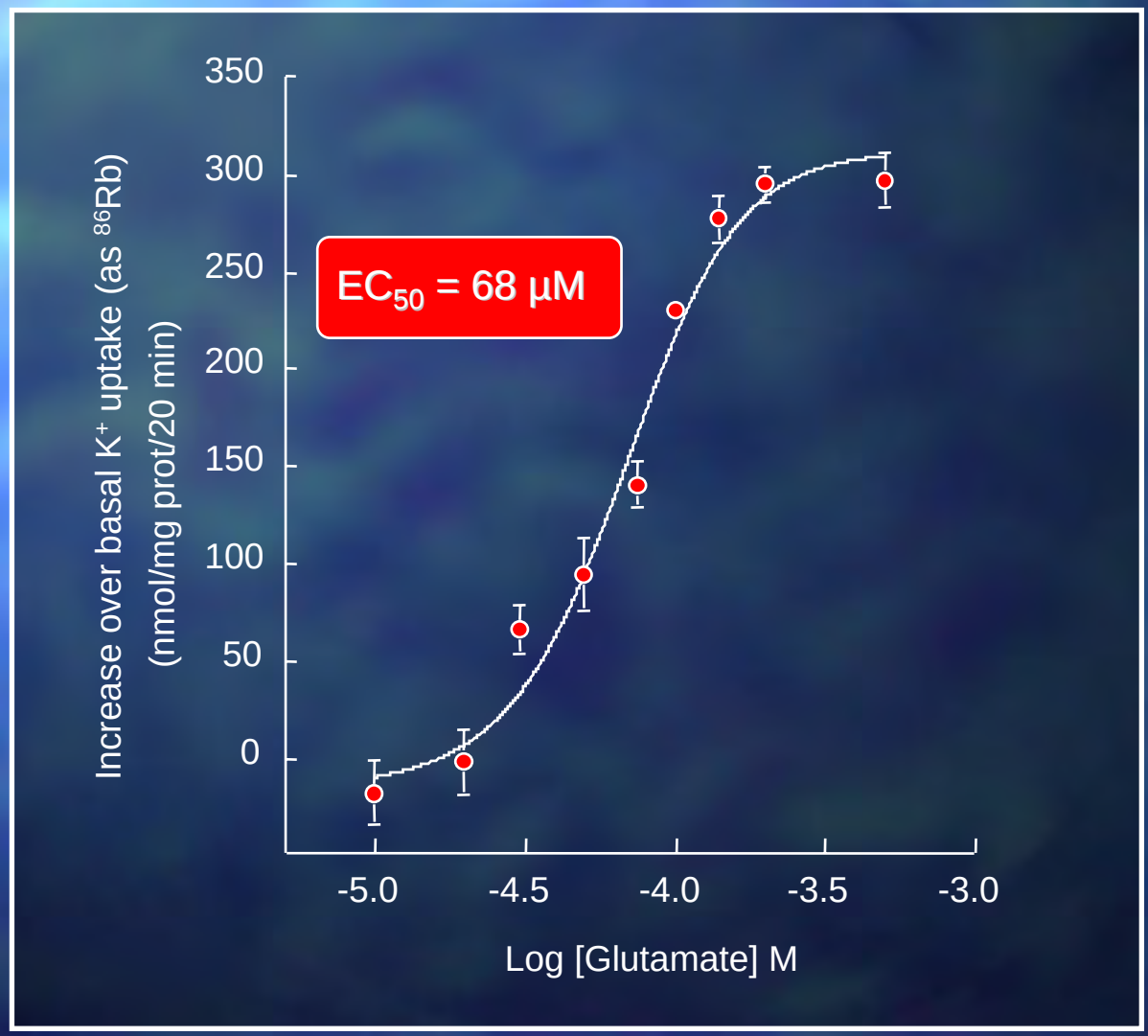
Glutamate effect on Na^+/K^+ ATPase activity



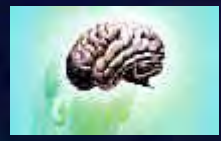


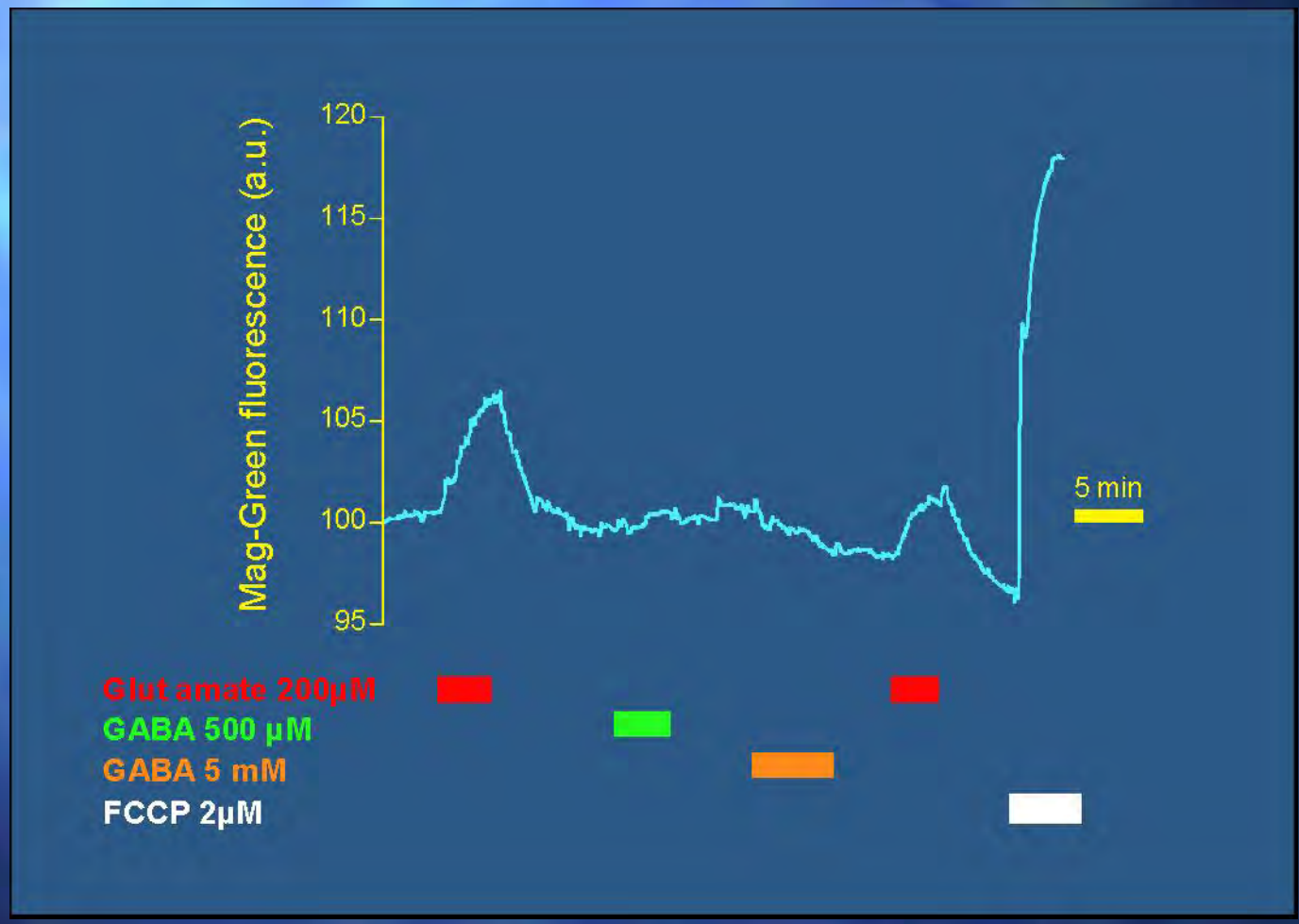
L'application de glutamate double la consommation d'ATP associée à l'activité de la Na/K.ATPase

Glutamate Stimulates the Activity of the Na+/K+ ATPase in a Concentration-Dependent Manner

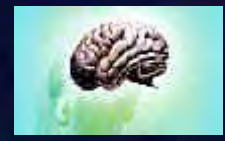


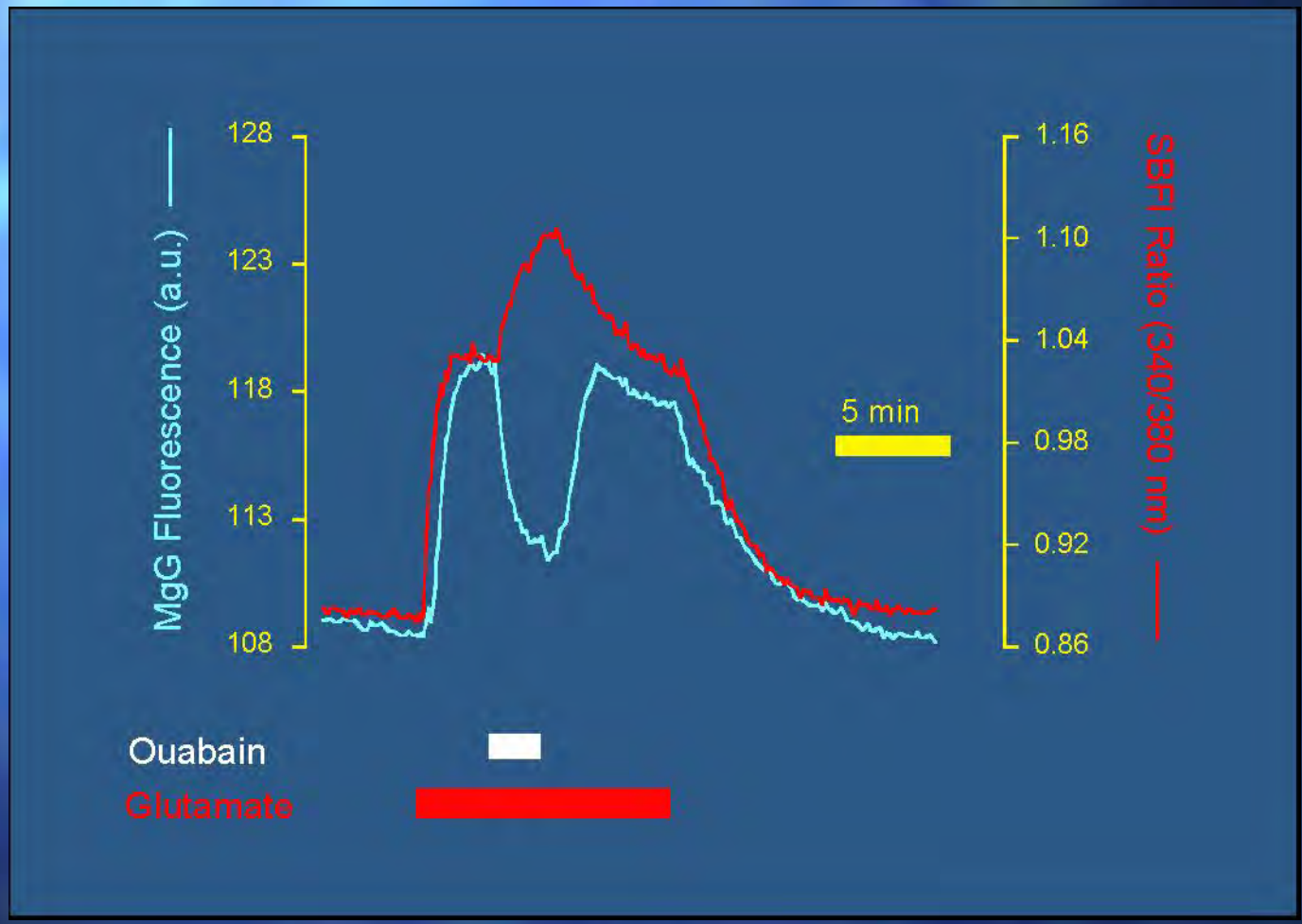
Indirect ATP levels measurement by free Mg^{2+} imaging





Simultaneous Intracellular Na^+ and Free Mg^{2+}





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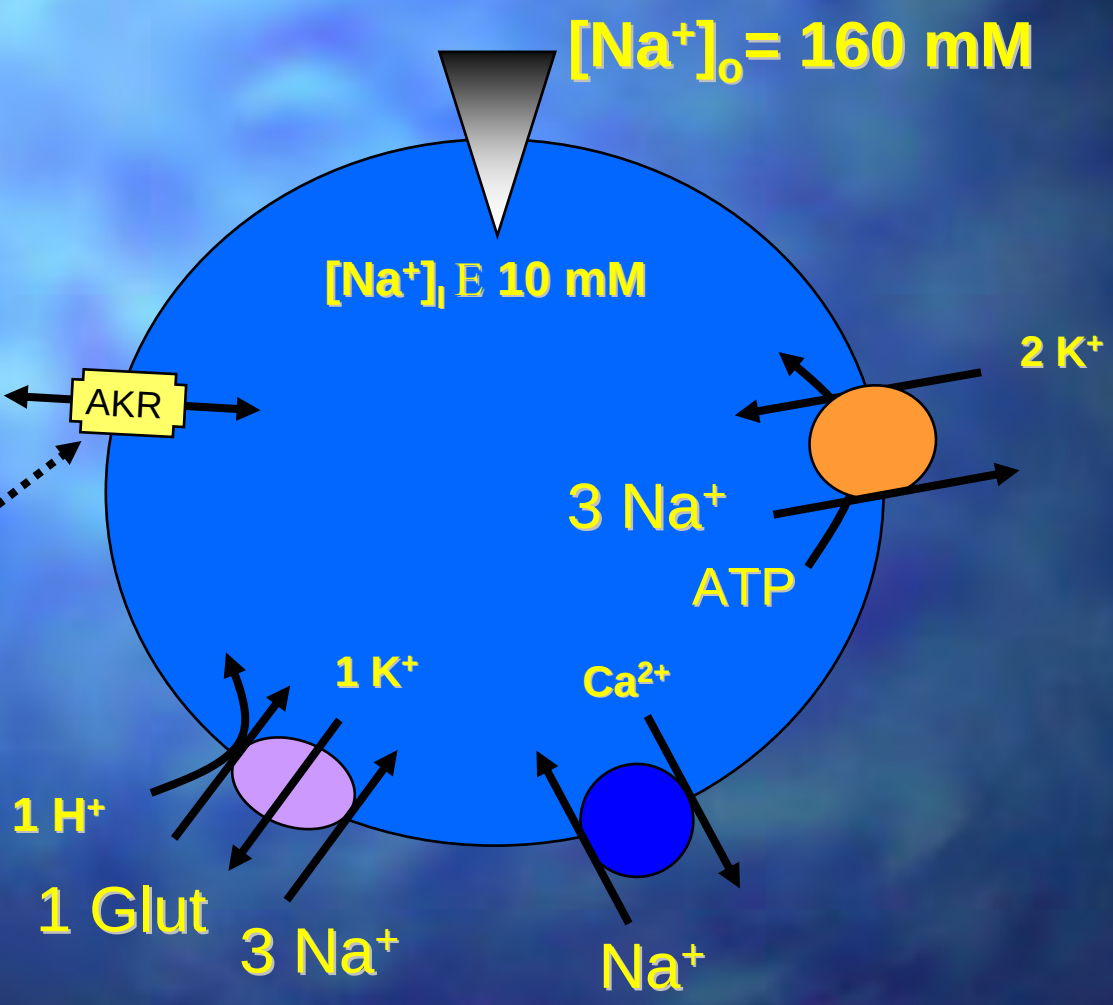
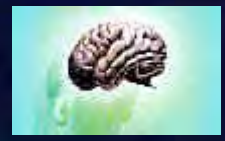
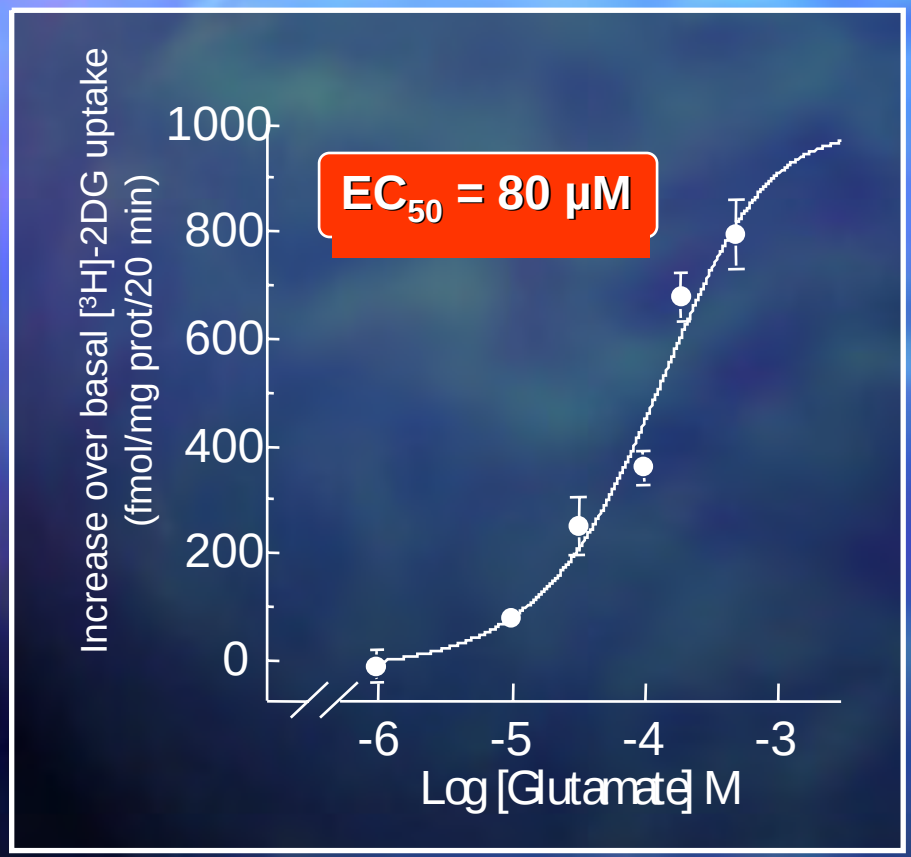


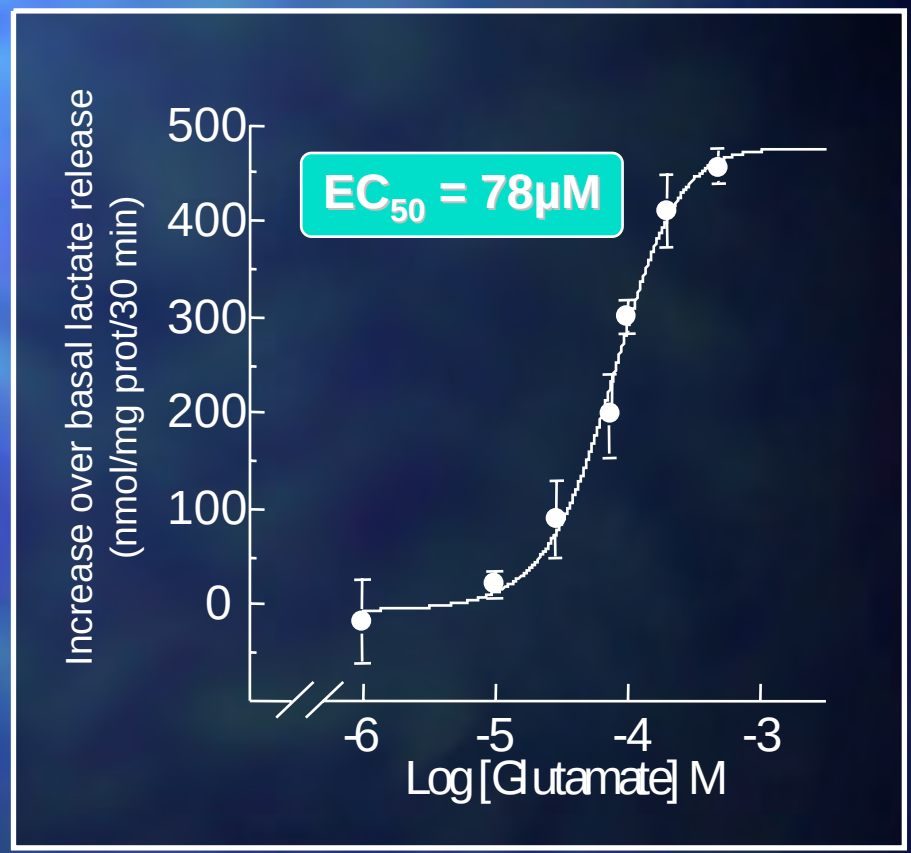
Glutamate Stimulates Aerobic Glycolysis in Astrocytes



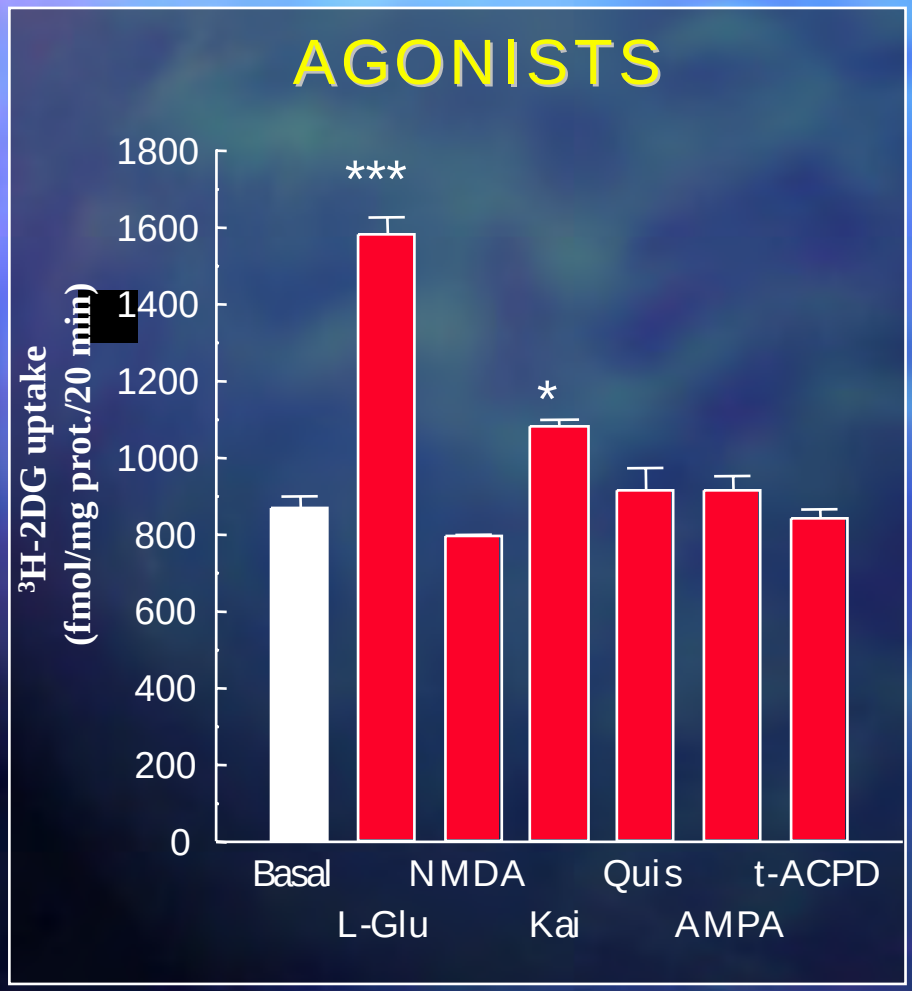
Glucose utilization

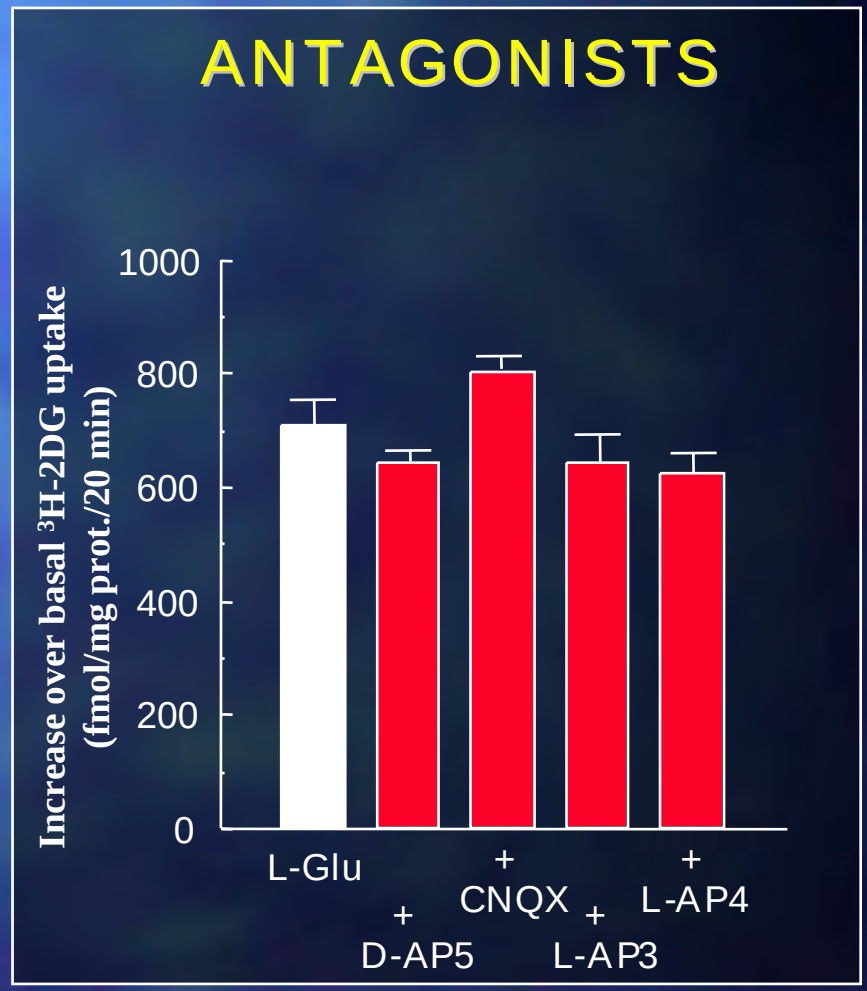


Lactate production

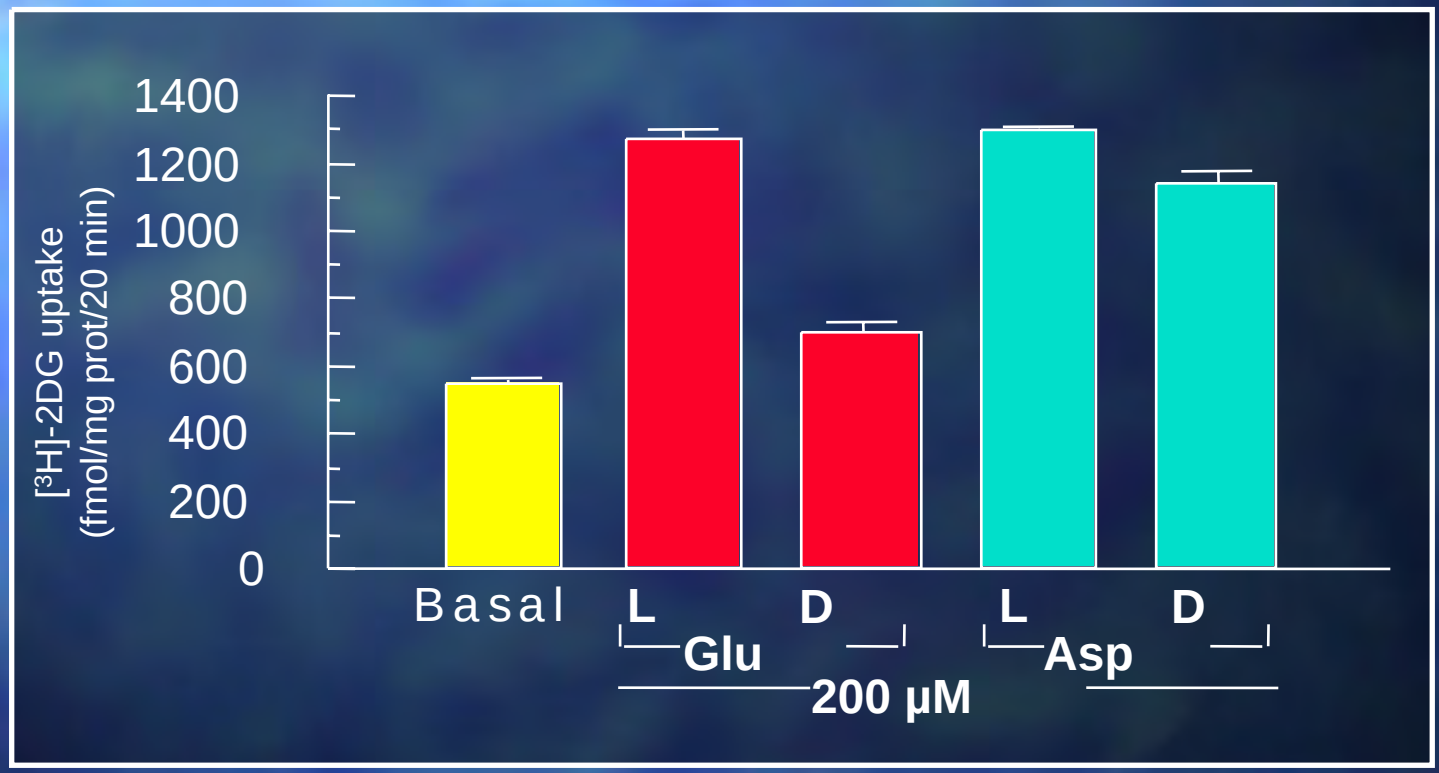


Glutamate-Stimulated Glucose Utilization Is not Mimicked nor Prevented by Glutamate Receptor Agonists or Antagonists

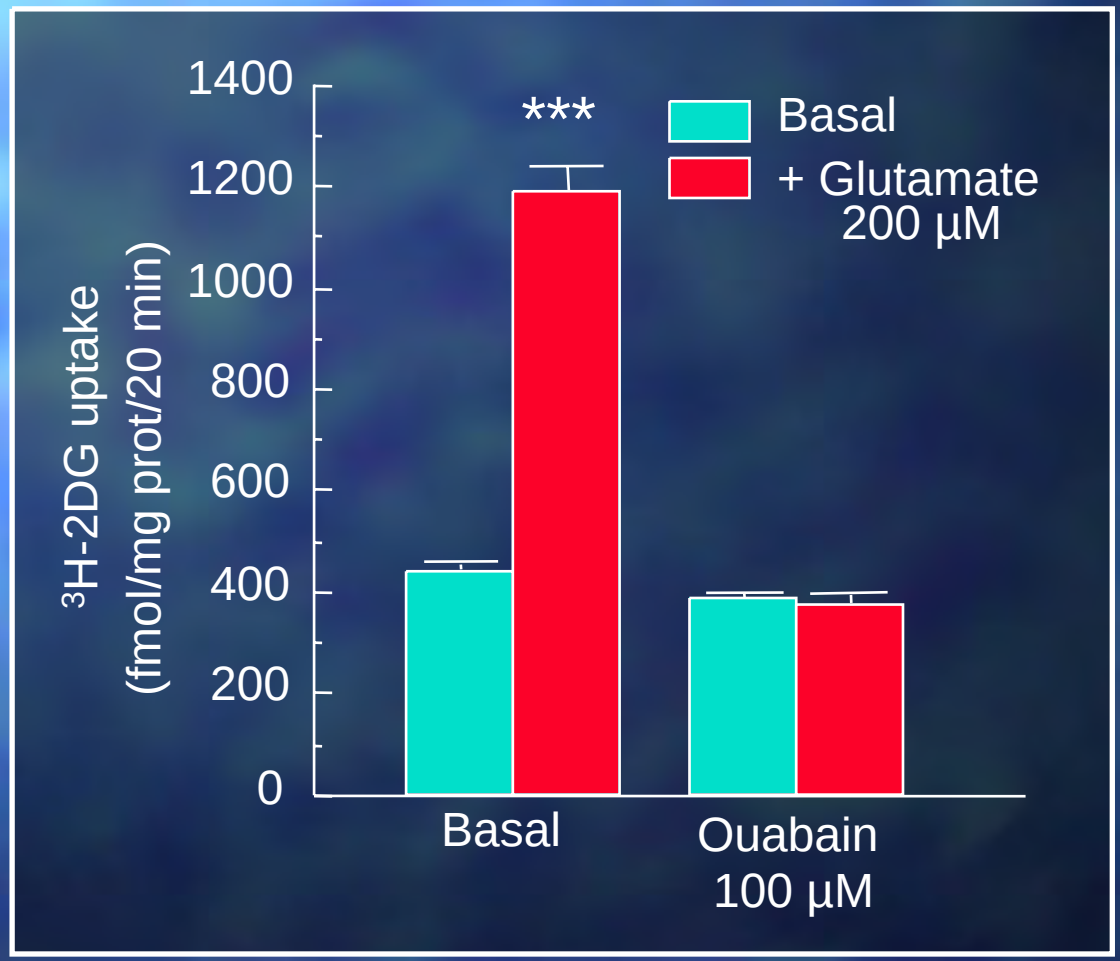




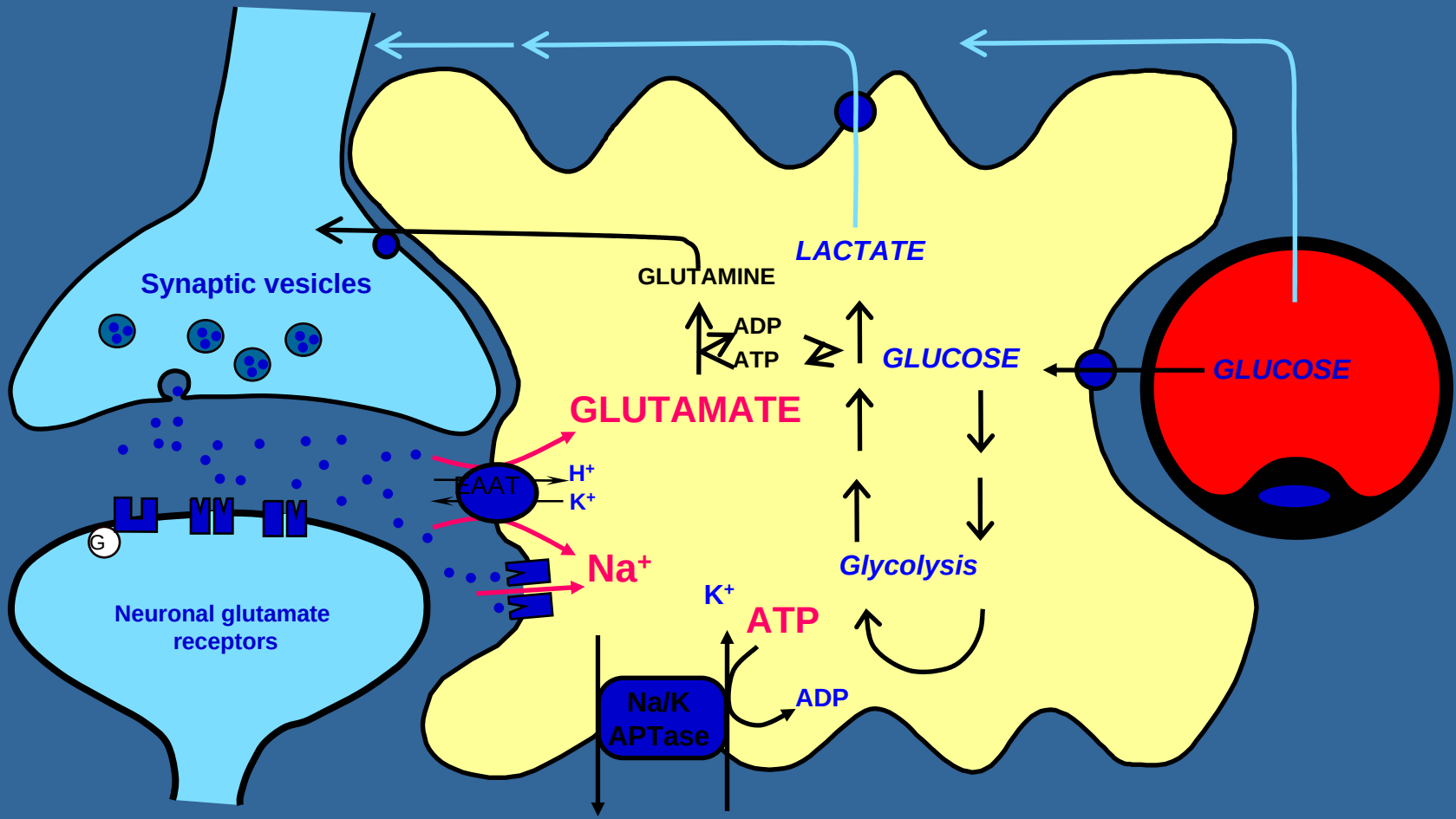
The Effect of Glutamate but not Aspartate on Glucose Utilization in Astrocytes is Stereospecific



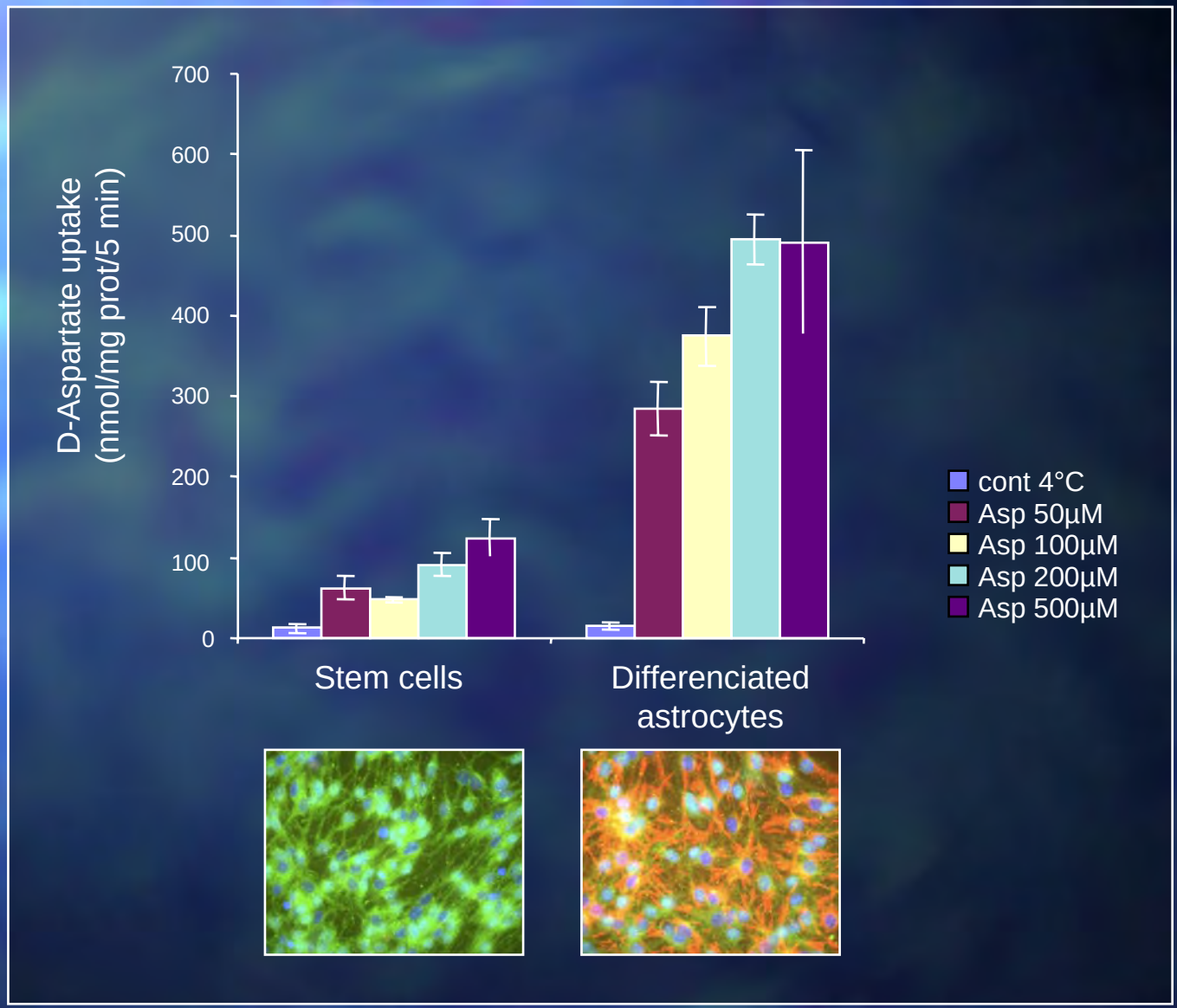
Na+/K+ ATPase inhibitor ouabain prevents the stimulation of glucose utilization by glutamate



Mechanism for Coupling Neuronal Activity to Glucose Utilization



D-aspartate uptake



Glucose utilisation – lactate release