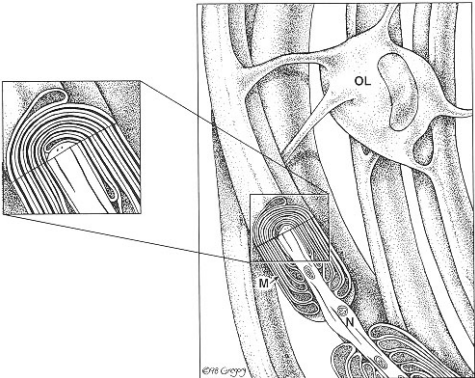
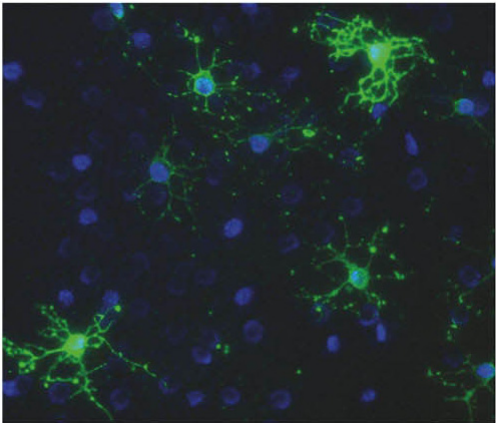
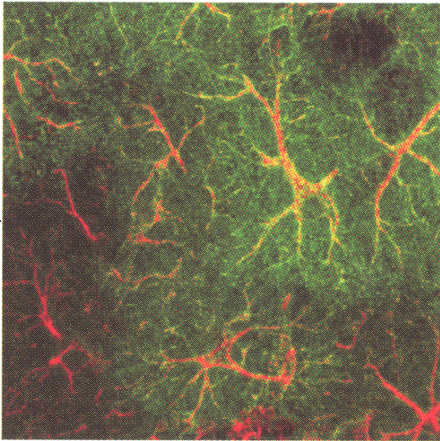
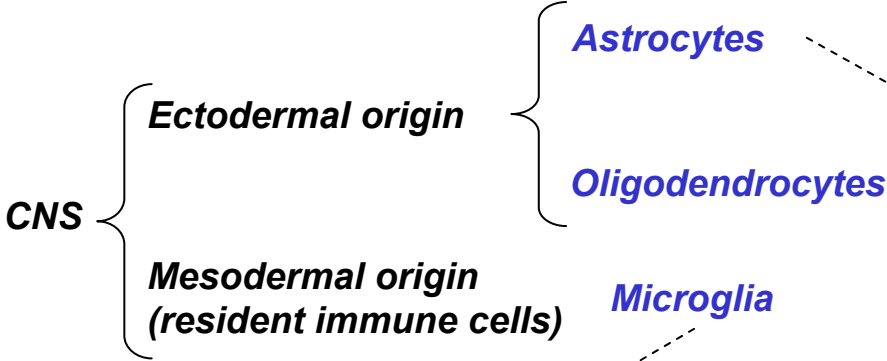
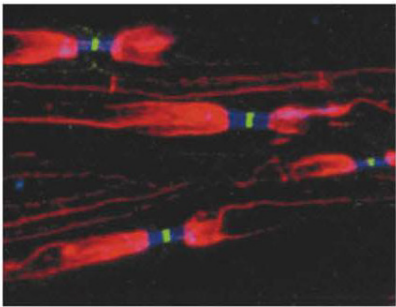


The glial cells in the nervous system

Diversity of glial cells

PNS : Schwann cells



Glial cells occupy 20% - 50% of the brain volume

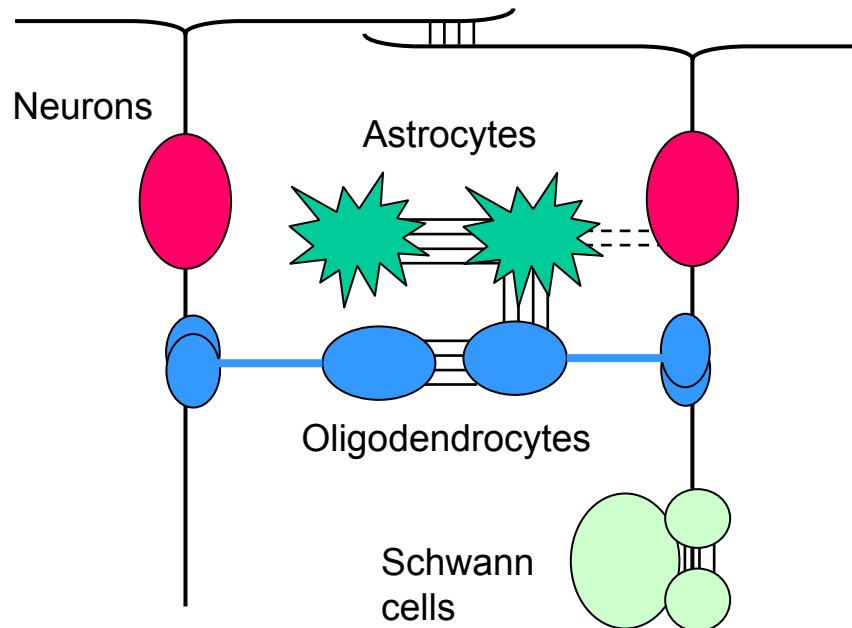
They outnumber the neurons by much!
10 glia : 1 neuron ratio in many brain areas!!

The glial cells in the nervous system

Which of these functions are carried out by glial cells ?

- 1 To control the extracellular medium (e.g. K⁺ concentration)..... ☐
- 2 To recapture neurotransmitter from the synapses..... ☐
- 3 To form the blood-brain barrier..... ☐
- 4 To increase the conduction velocity of axons..... ☐
- 5 To produce transmitters active at the synapse..... ☐
- 6 To have receptors for neurotransmitters..... ☐
- 7 To have ionic channels..... ☐
- 8 To produce action potentials..... ☐
- 9 To form electrical synapses ☐
- 10 To react when the nervous system is injured..... ☐
- 11 To participate in the protection of neurons from toxic substances..... ☐
- 12 To control the flow of energy substrates from blood to neurons..... ☐

The nervous system has cellular compartments delimited by gap junctions



Two facts

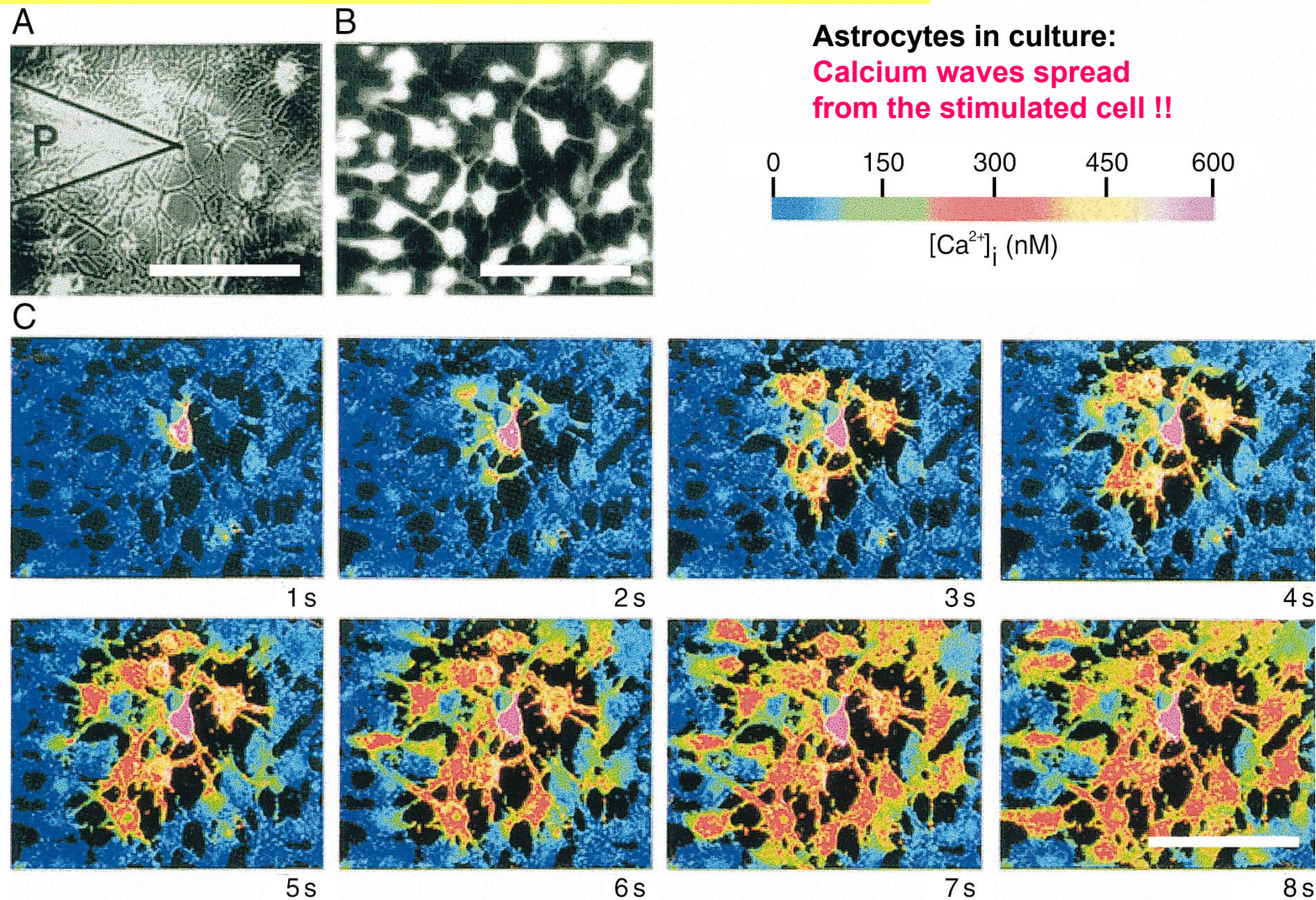
- Cells that are coupled to one another constitute a **functional syncytium**.
- The intracellular compartment of the nervous system is divided in **communication compartments**.

A prediction

- The activity of neuronal circuits **MUST** be affected by neighboring syncytia.

Astrocytes in the nervous system

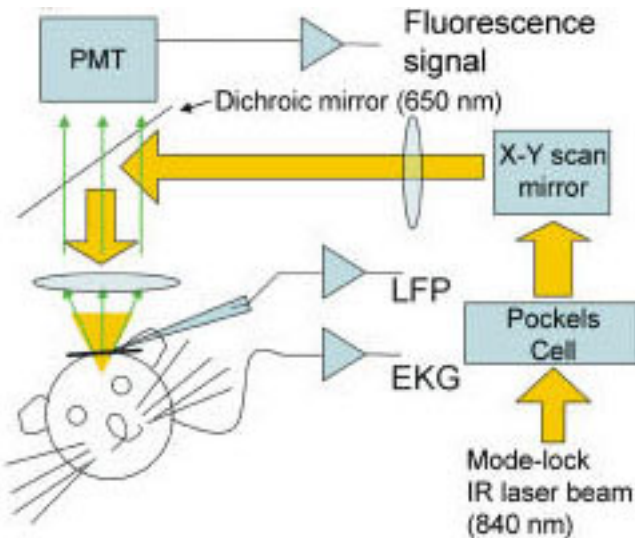
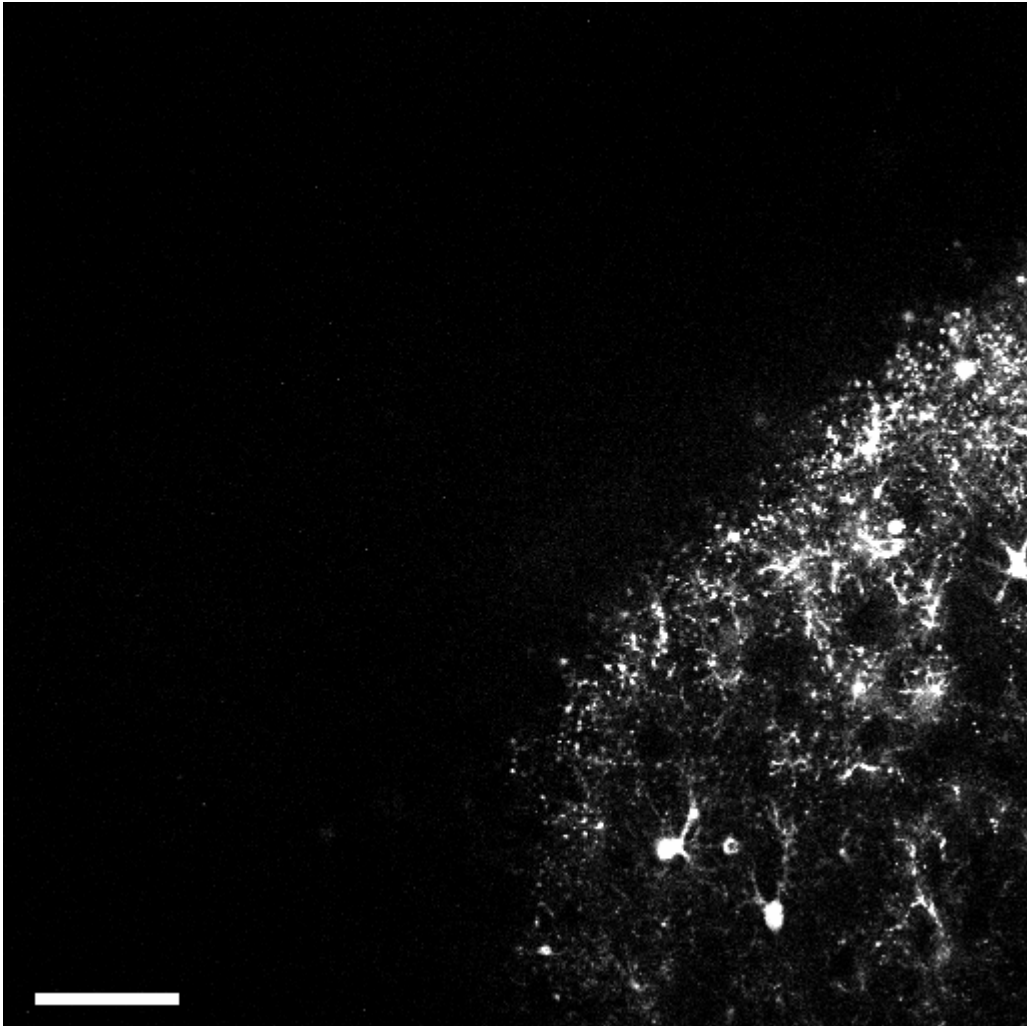
Astrocytes form a functional syncytium communicated through gap junction (electric synapses)



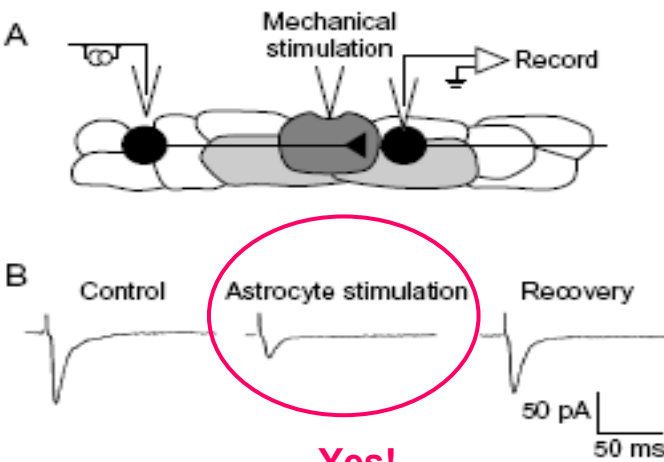
Astrocytes in the nervous system

The functional syncytium seen in vivo, in the somatosensory cortex of a rat

Astrocytes alive!!
Spontaneous Ca^{2+} waves



Do these Astrocyte Calcium Waves affect the Activity of Neuronal networks?



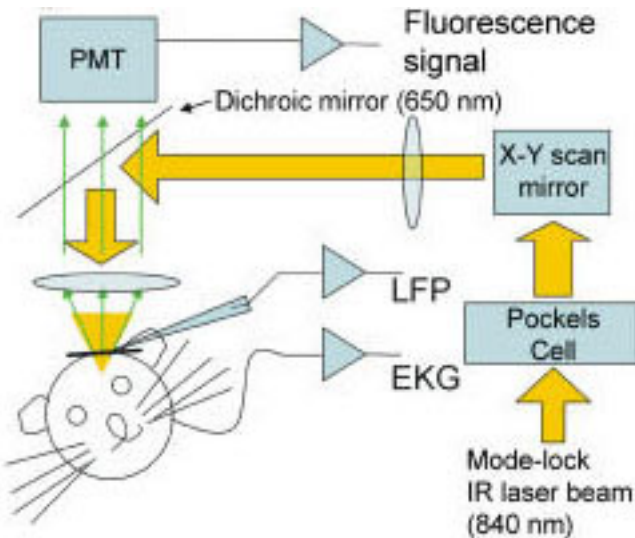
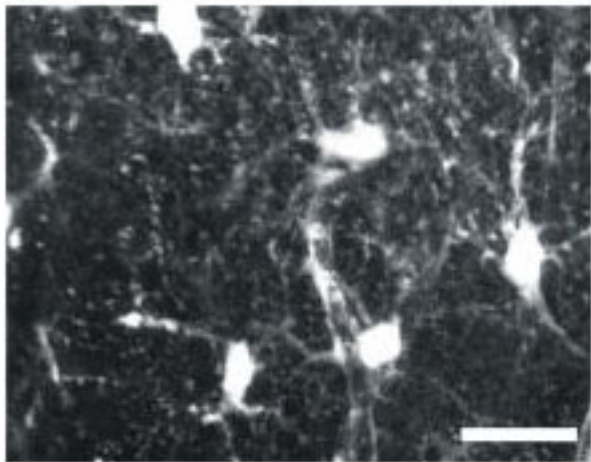
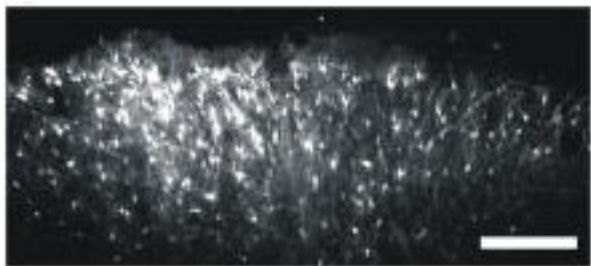
Yes!

Astrocytes in the nervous system

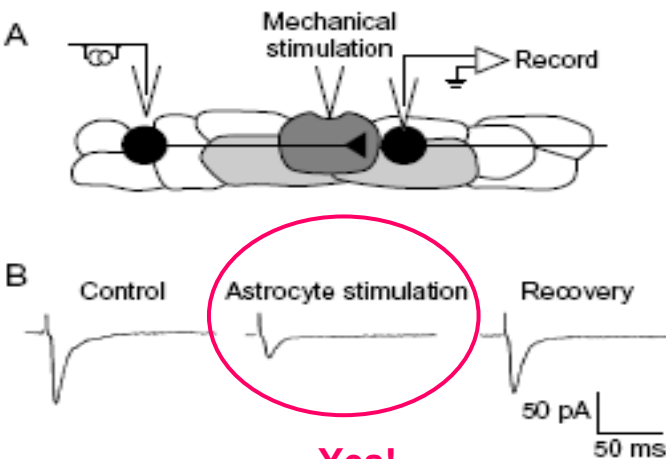
The functional syncytium seen in vivo, in the somatosensory cortex of a rat

Astrocytes alive!!
Spontaneous Ca^{2+} waves

Static views:



Do these Astrocyte Calcium Waves affect the Activity of Neuronal networks?

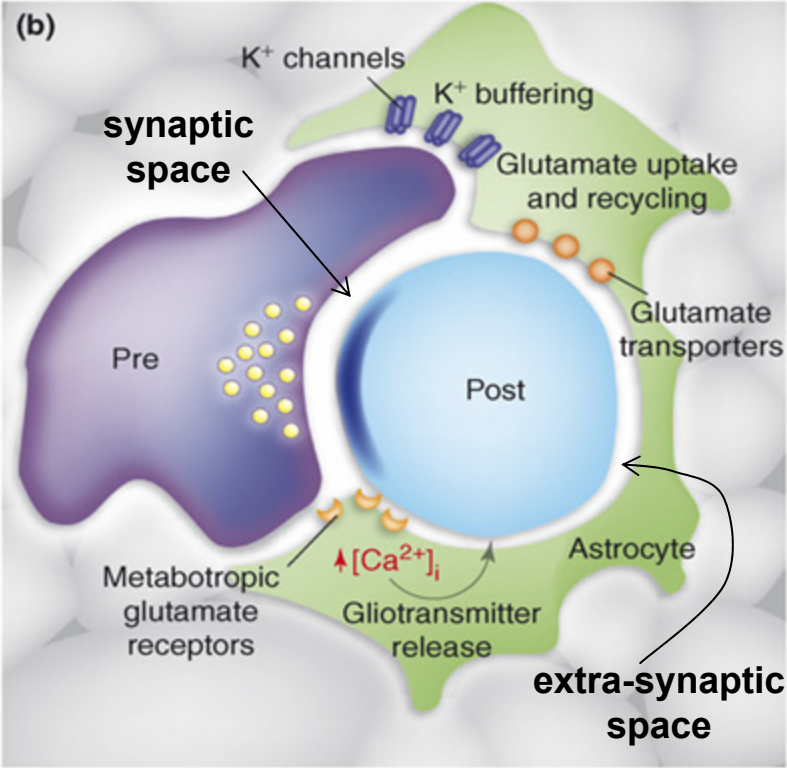
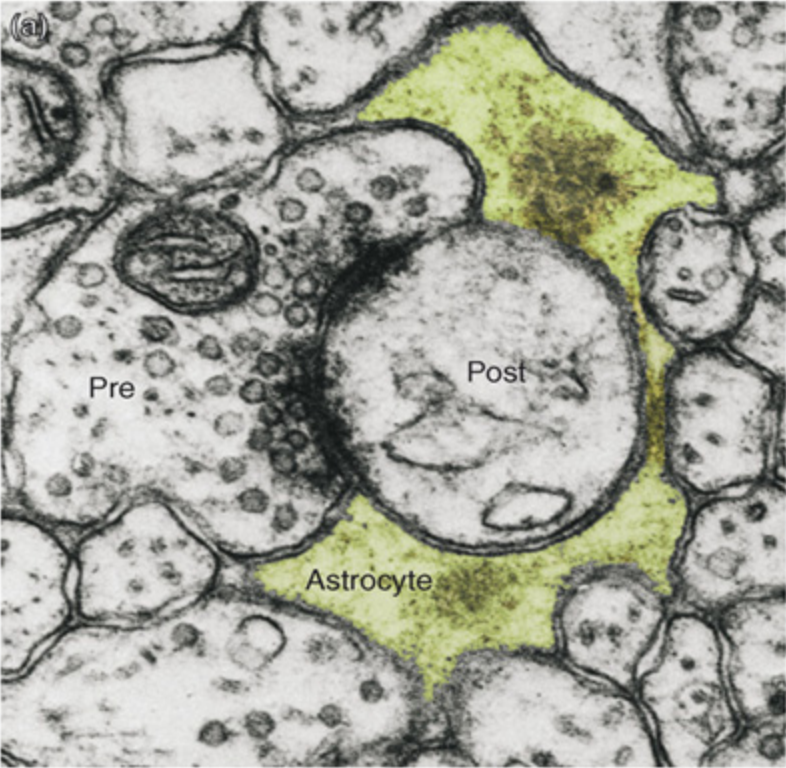


Yes!

Astrocytes in the nervous system:

Astrocytes sense and integrate synaptic activity

How? → **THE TRIPARTITE SYNAPSE**



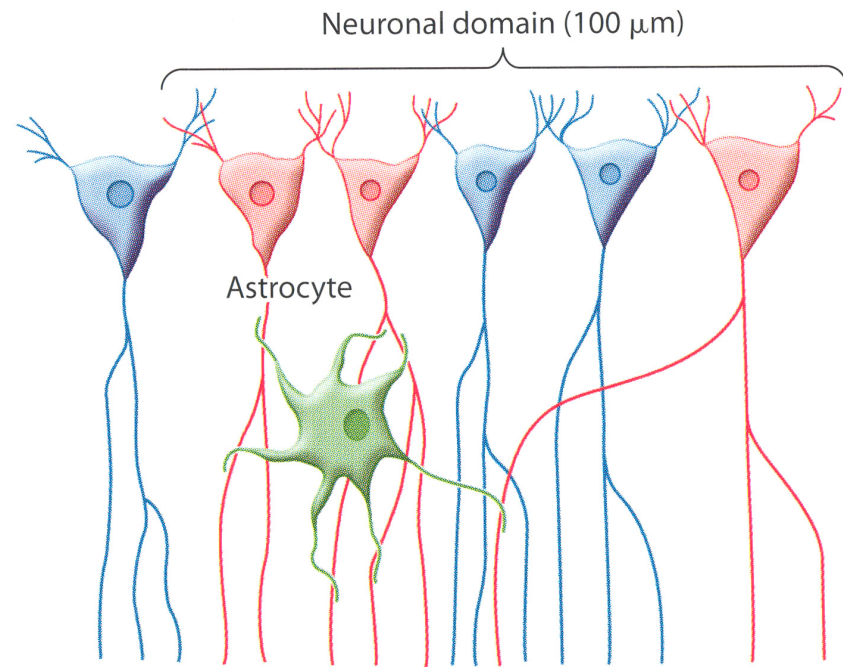
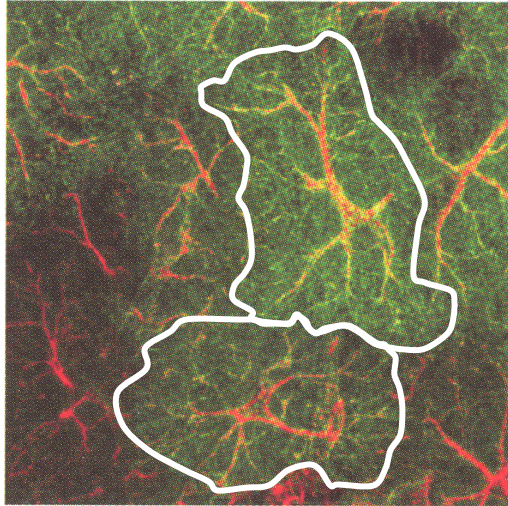
TRENDS in Molecular Medicine

Gliotransmitters: {
Glutamate
ATP
D-serine
... and more

Receptors for Gliotransmitters {
in the post-synaptic neuron
in the pre-synaptic neuron

Astrocytes in the nervous system:

The Neuronal domain of Astrocytes



An astrocyte can directly control synapses located within a 100 μm radius

It can control more than 100 000 synapses!!

They Control:

- Clearance of Neurotransmitters (neurotransmitter transporters)
- Clearance of K^+ ions (K^+ channels and Na^+-K^+ ATPase)

They Produce:

- Intracellular Ca^{2+} increase in response to Neurotransmitters (neurotransmitter receptors)
- Secretion of Gliotransmitters in response to the Ca^{2+} increase

Functions of Gliotransmission in the nervous system

The Gliotransmitter produced by an astrocyte can regulate...

- Other astrocytes (controlling the Ca^{2+} waves)
- The neurons within its domain $\xrightarrow{\text{controlling}}$

{
Excitability
Neurotransmission
Synchronization

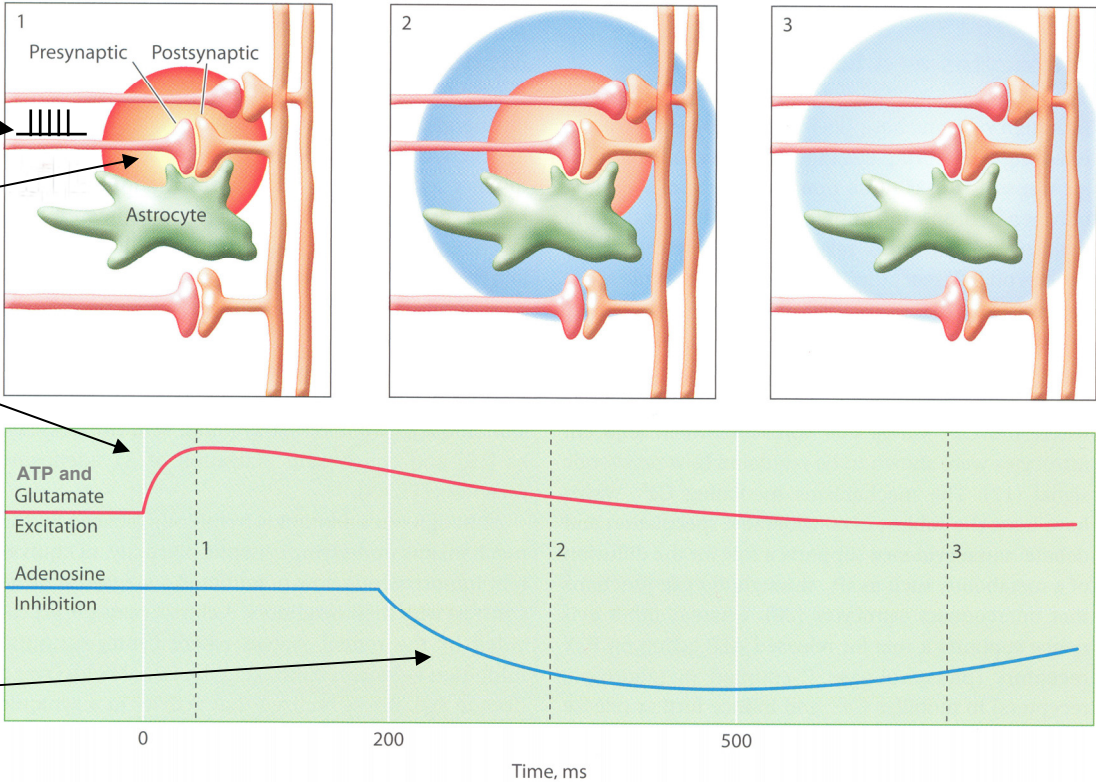
An example of control of synapses: Time and Space / Activation and Inhibition

1. A neuron fires action potentials
The activated astrocyte releases Glutamate and ATP (red)
Both gliotransmitters increase the activity of that synapse and of the ones very close to it.

2. Glutamate is cleared soon from the extracellular space, so it does not go far.

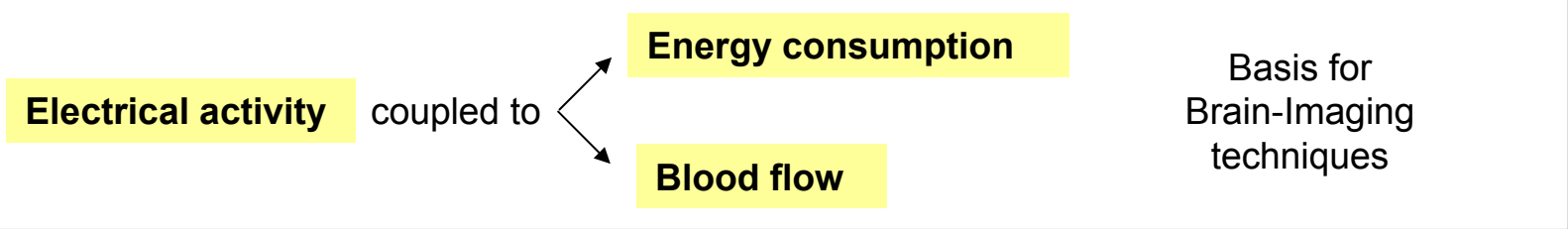
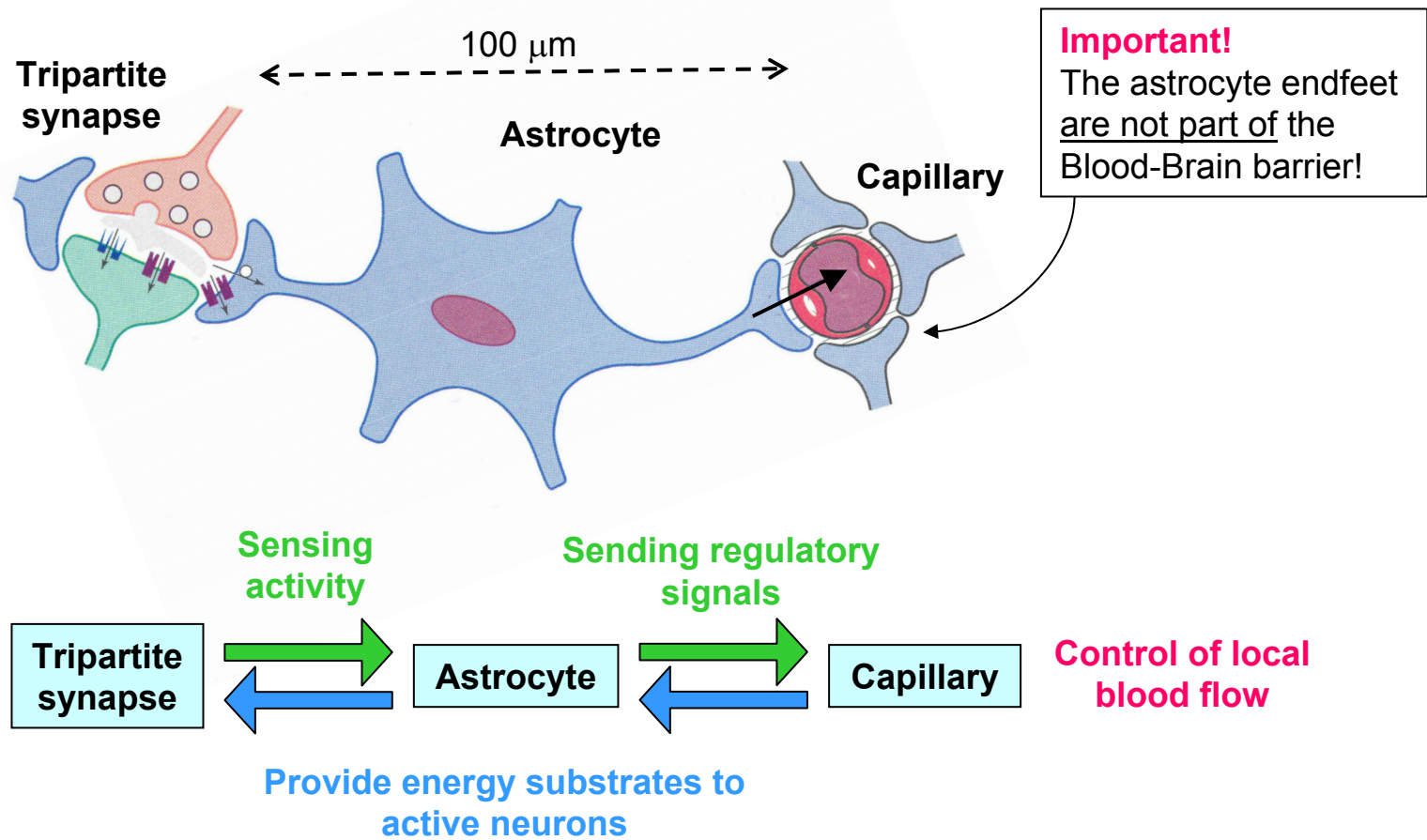
ATP is degraded to Adenosine and diffuses further away (blue)

3. Adenosine has inhibitory effects on more distant synapses



Astrocytes and Brain Metabolism

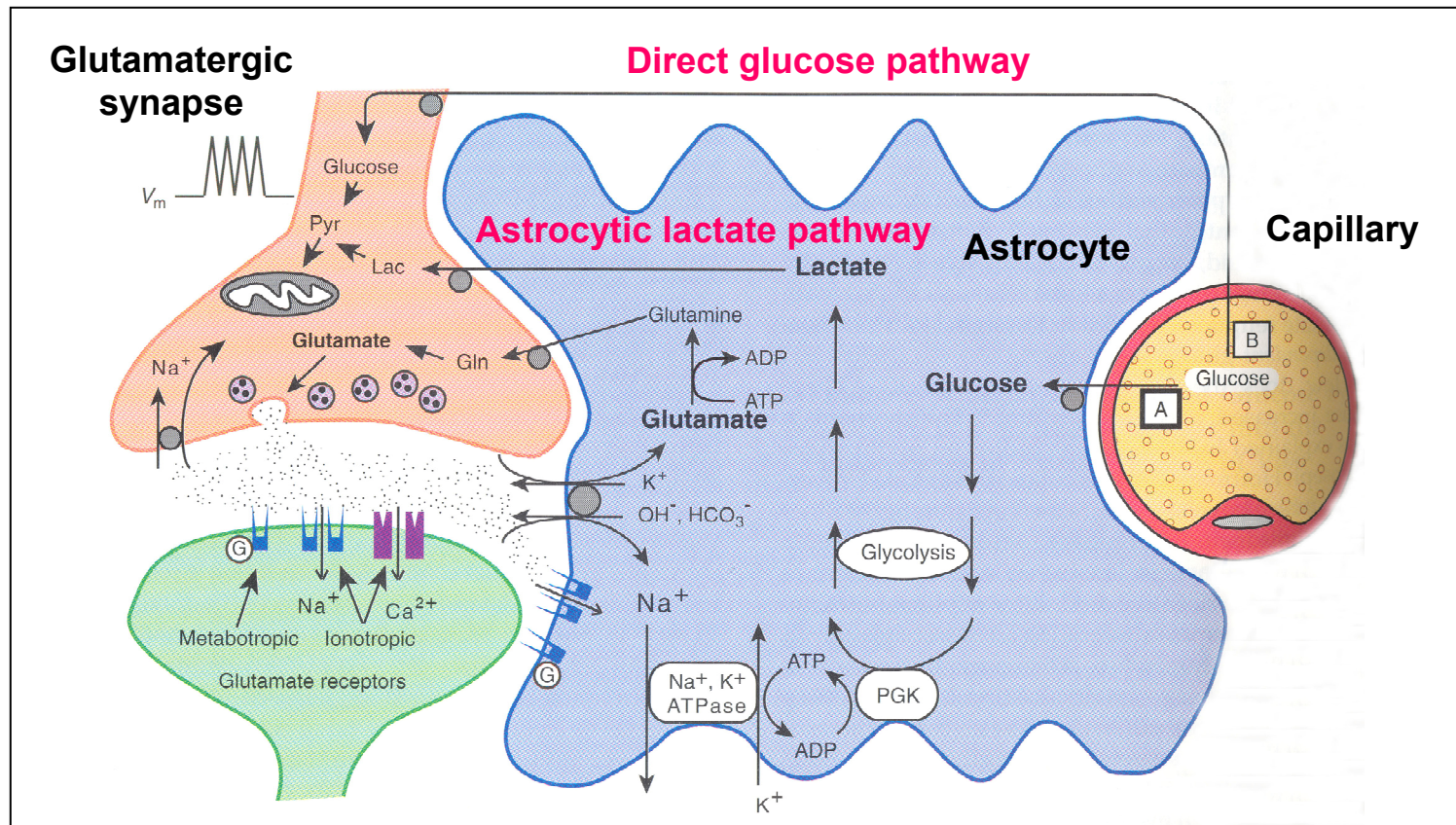
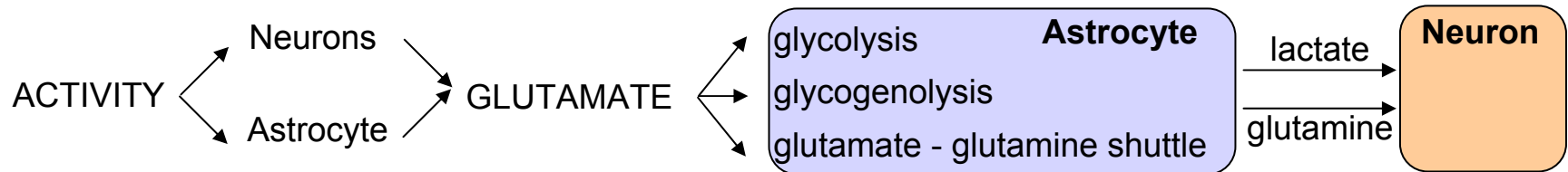
Astrocytes are a bridge between synapses and the blood flow



Astrocytes and Brain Metabolism

Astrocytes shuttle lactate and glutamine to neurons in an activity-dependent way

Glucose → obligatory energy substrate for the brain
→ Neurons and Glia consume glucose



“Glyopathologies”: The most recent hypotheses on pathologies related to glial malfunction

What happens when astrocytes do not work well?

- Ca^{2+} wave uncontrolled → too many astrocytes activated → too many neurons activated synchronously → EPILEPSY
- Astrocyte activity decreased → neurons are not well coordinated → SCHIZOPHRENIA
- A decrease in the number of astrocytes → DEPRESSION
- Less neurotransmitter uptake by astrocytes → neurotoxicity → NEURODEGENERATION
- INJURY → Reactive astrogliosis (activation and proliferation of astrocytes)
- ALZHEIMER'S → Reactive astrocytes surround the amyloid plaques

What happens when oligodendrocytes do not work well?

- Demyelination of CNS neurons → Demyelinating diseases (e.g. MULTIPLE SCLEROSIS)

What happens when Schwann cells do not work well?

- Altered myelination of PNS neurons → PERIPHERAL NEUROPATHIES

We should **know more** about GLIAL CELLS and we **SHOULD TAKE CARE** of them!