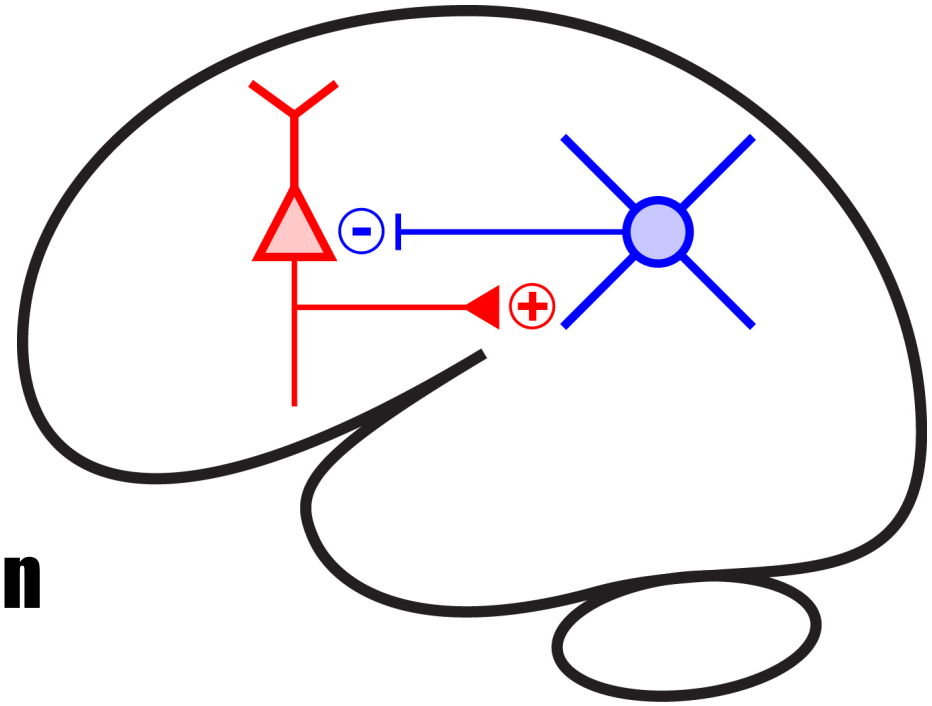
ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE



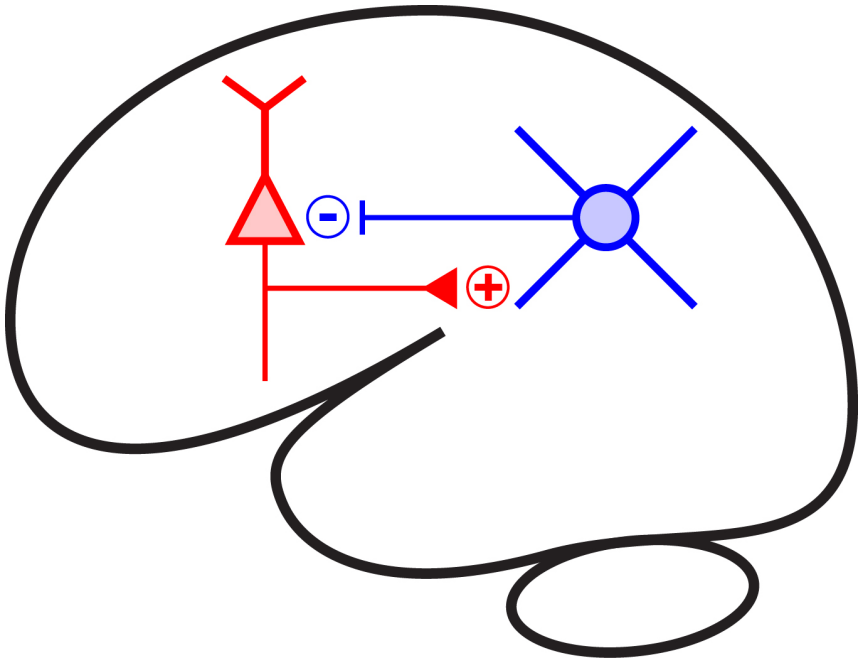
5.1 GABAergic inhibition

Cellular Mechanisms of Brain Function

Prof. Carl Petersen

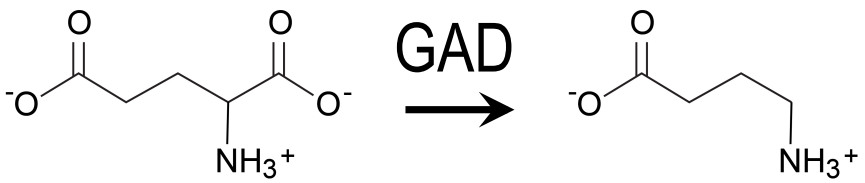
Inhibition

GABAergic inhibitory synaptic transmission



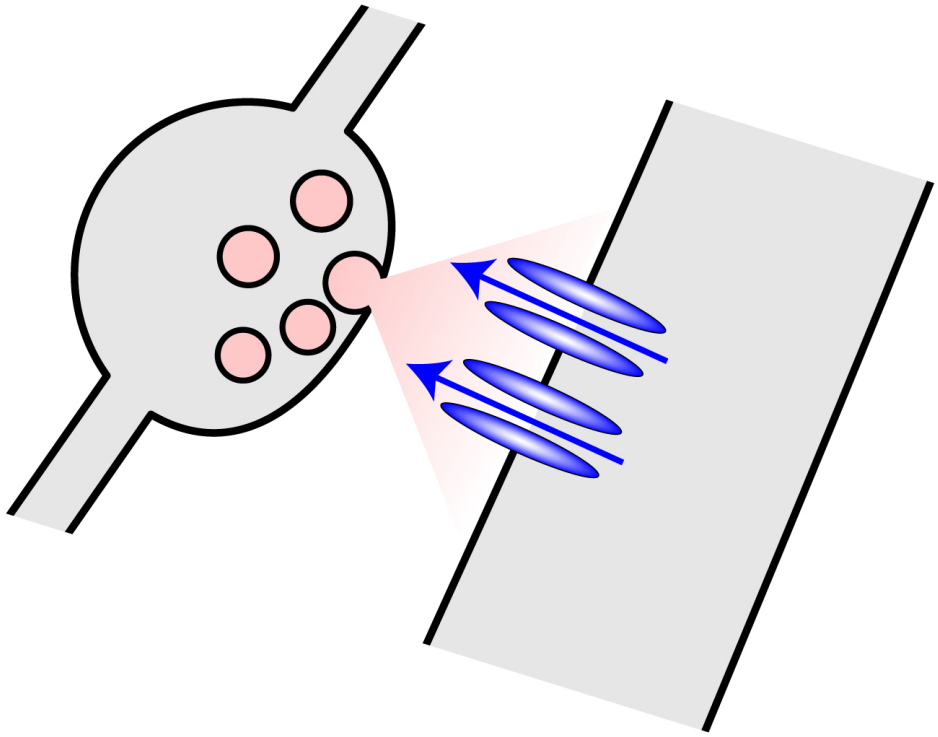
GABAergic synapses

Glutamate → GAD → GABA

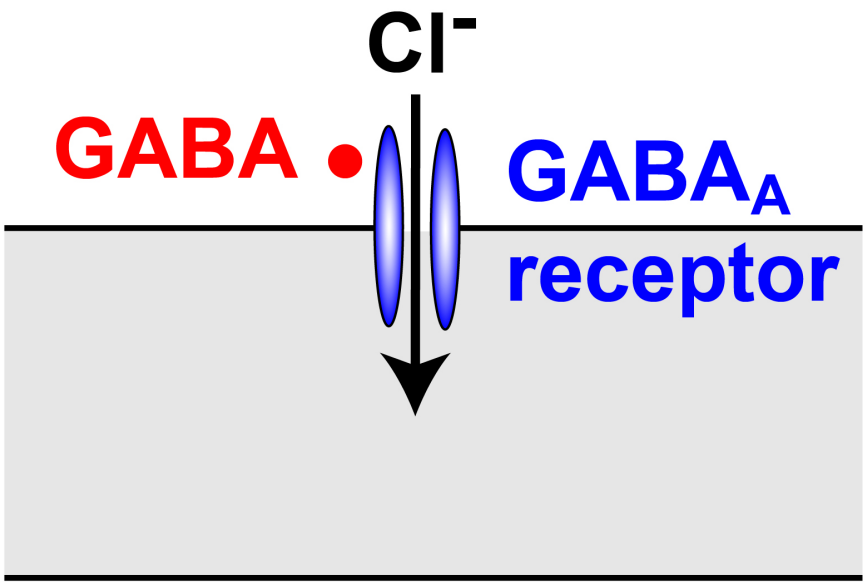


Vesicular GABA transporter
VGAT

Ionotropic GABA receptors
Outward postsynaptic current



$GABA_A$ receptors



Nernst equilibrium potential

$$E_{Cl} = \frac{RT}{zF} \ln \frac{[Cl^-]_i}{[Cl^-]_o}$$

$$E_{Cl} = 61.5 \log_{10} \frac{5}{120}$$

$$E_{Cl} = \sim -85 \text{ mV}$$

Cytosolic chloride concentration

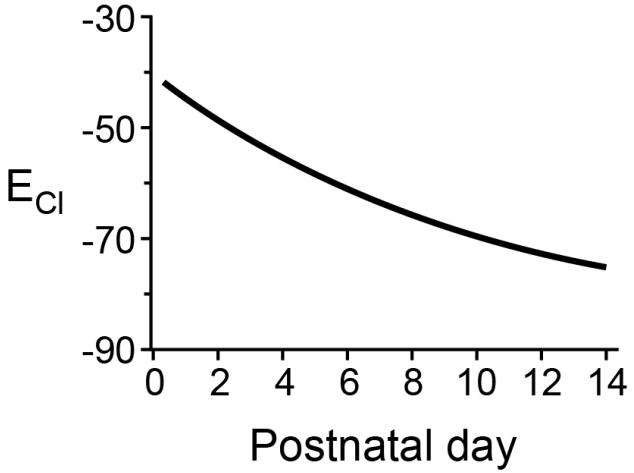
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

$GABA_A$ reversal potential ~ -80 mV. Resting membrane potential ~ -70 mV. The membrane potential helps keep a low cytosolic chloride concentration.

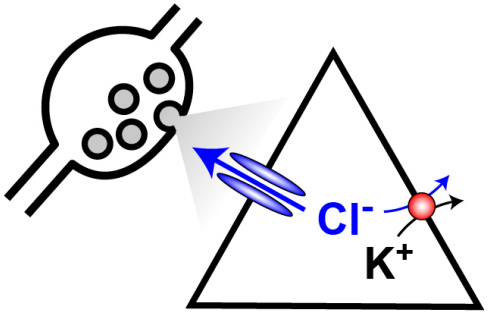
Chloride transporters (notably KCC2) also contribute importantly.

Chloride concentration during early development

Chloride reversal potential

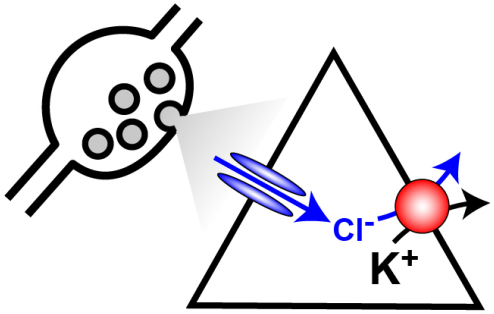


Early development



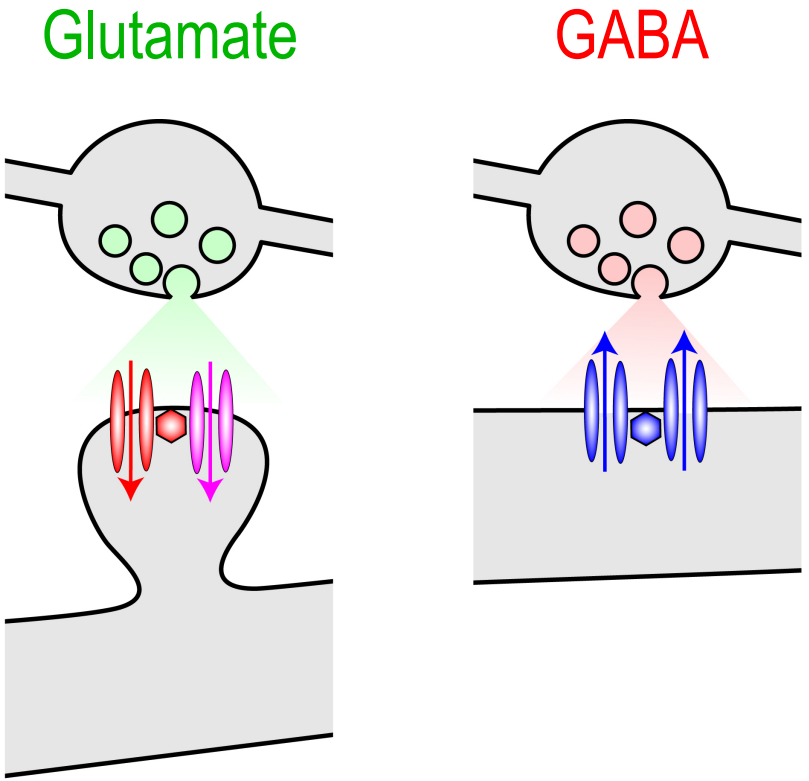
Low KCC2 expression
High cytosolic chloride

Adult brain



High KCC2 expression
Low cytosolic chloride

Glutamatergic vs GABAergic synapses



VGluT

AMPA/NMDA
PSD95

Spine

VGAT

$GABA_A$
Gephyrin

Shaft or soma

$GABA_B$

$GABA_B$ receptors activate K^+ channels and inhibit Ca^{2+} channels.

Glycine

Glycine is the major inhibitory neurotransmitter in the brainstem and the spinal cord.

GABAergic inhibition

- GABA is the main inhibitory neurotransmitter in the brain.
- $GABA_A$ receptors are ligand-gated chloride channels, thus having hyperpolarised reversal potentials in the adult brain.
- $GABA_B$ receptors activate postsynaptic K^+ channels and pre-/post-synaptically inhibit Ca^{2+} channels.