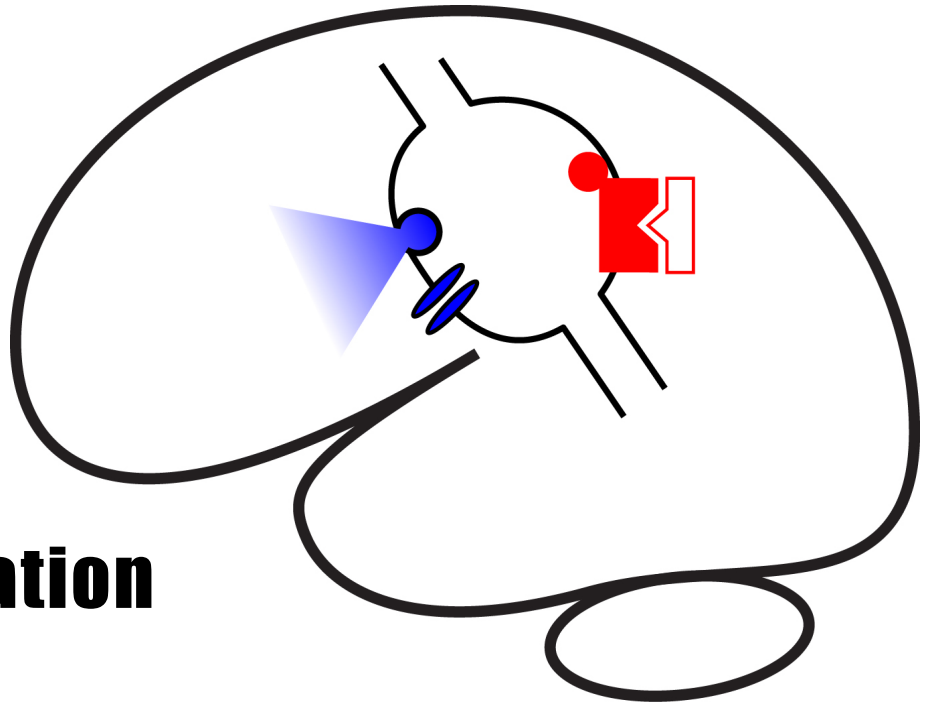
ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE



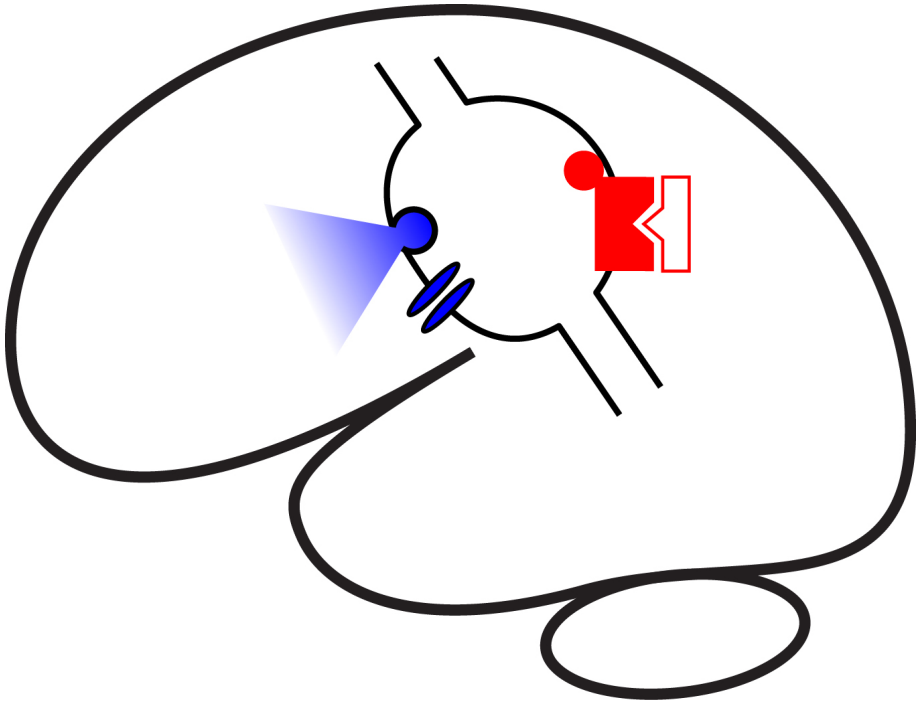
3.4 Presynaptic modulation

Cellular Mechanisms of Brain Function

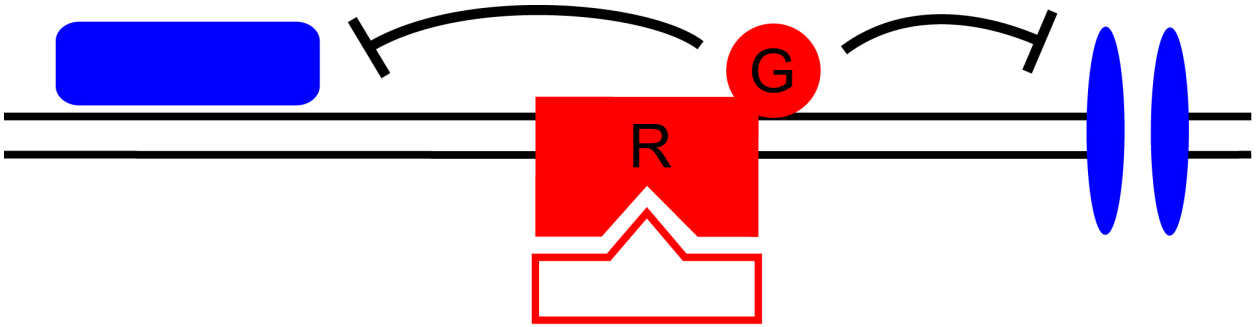
Prof. Carl Petersen

Presynaptic modulation by neurotransmitters

Presynaptic neuromodulation

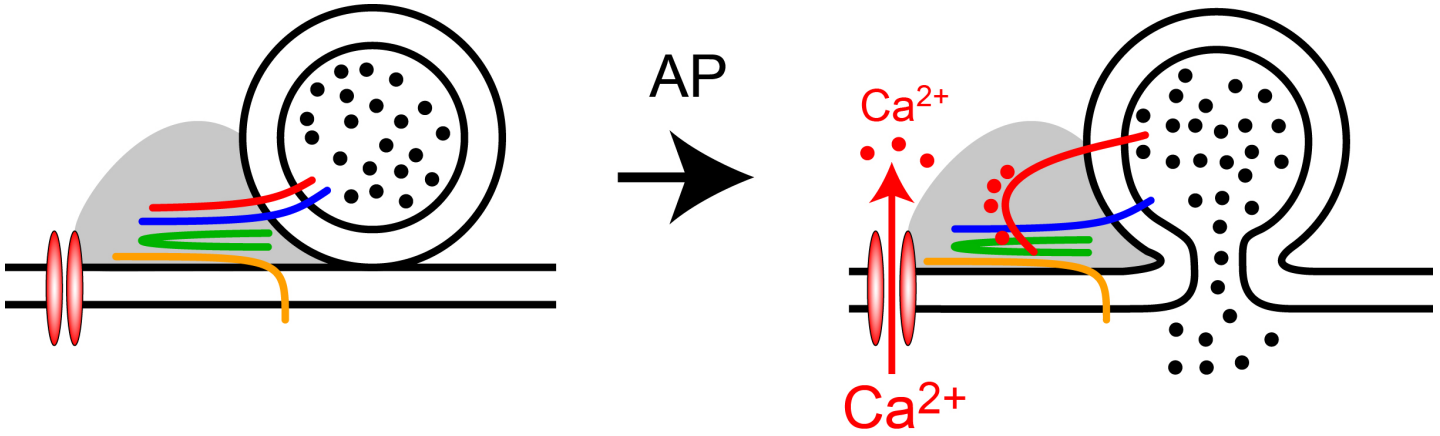


Presynaptic metabotropic receptors



Most metabotropic receptors are seven-transmembrane receptors (R), activating GTP-binding proteins (G), which signal via diverse pathways, including ion channels, second messenger systems and gene regulation.

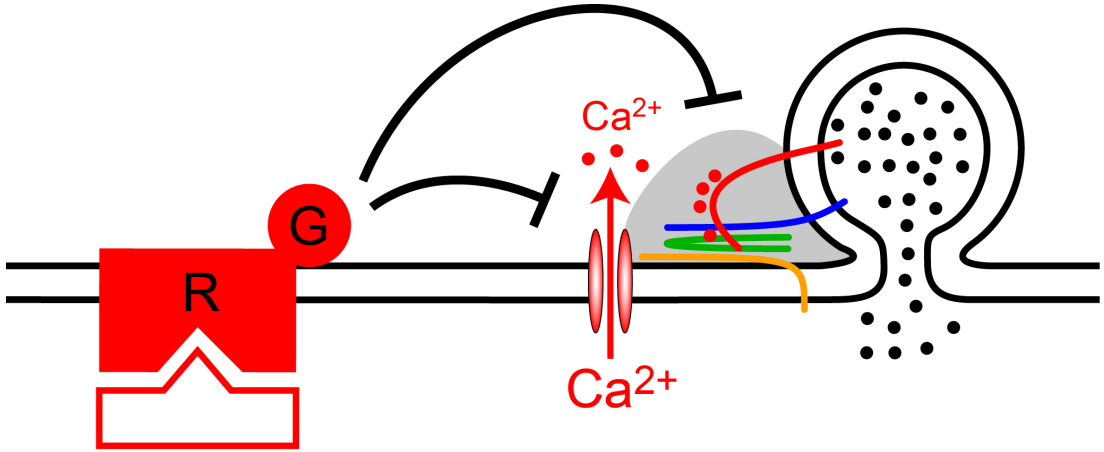
Presynaptic modulation of synaptic transmission



Many targets for modulating synaptic transmission:

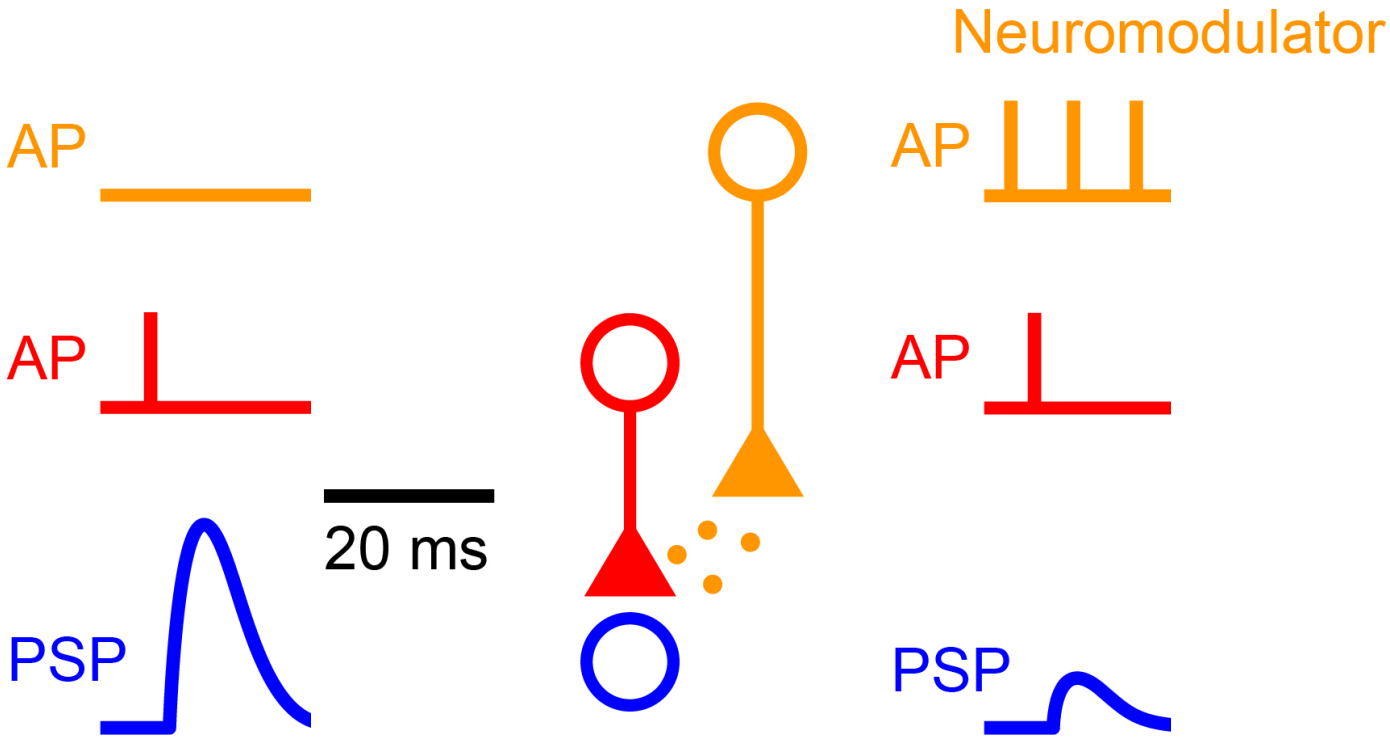
AP, Ca^{2+}, Synaptotagmin, Synaptobrevin, SNAP-25, Syntaxin, Rab3/27, NSF, MUNC13/18, RIM/RIM-BP, Complexin, Vesicular transporters ...

Presynaptic inhibition

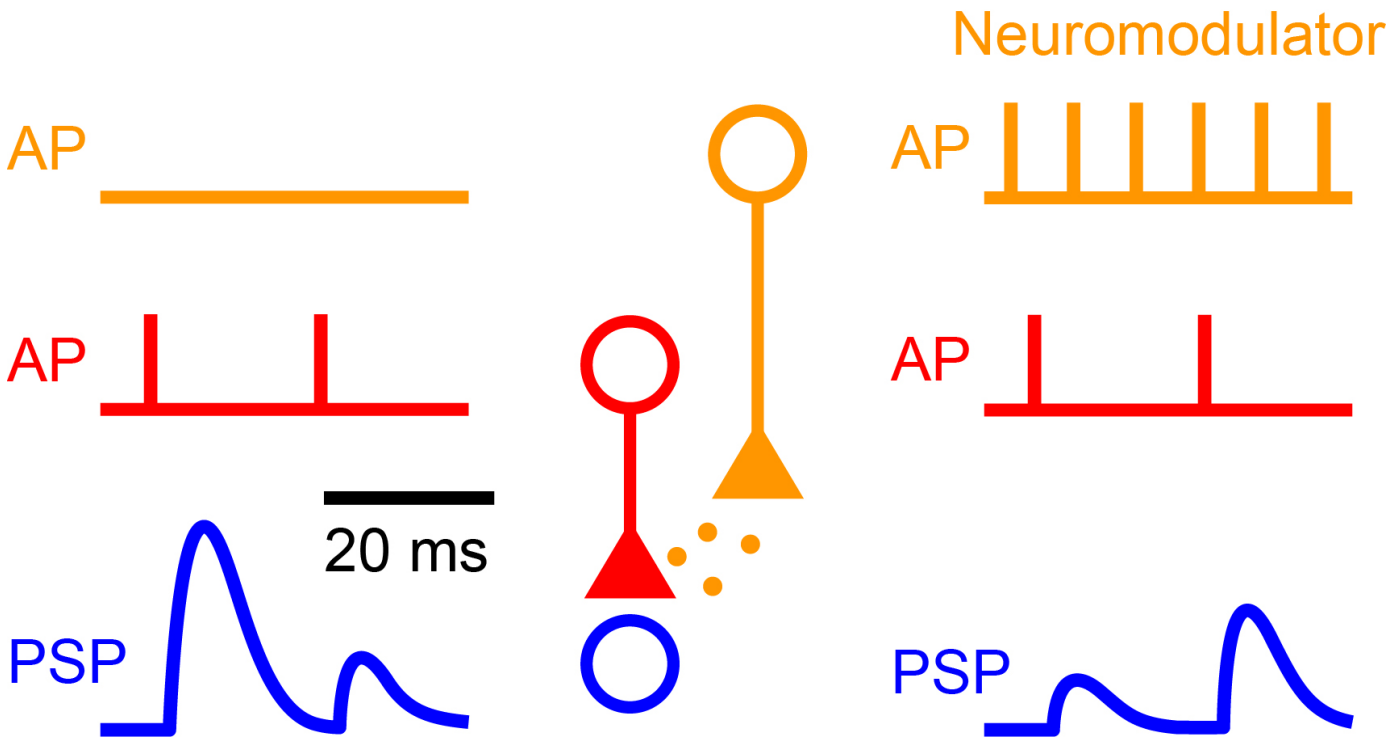


Neuromodulators can presynaptically inhibit neurotransmitter release, through seven-transmembrane receptors (R) activating GTP-binding proteins (G), which act to reduce calcium influx and inhibit release machinery.

Presynaptic inhibition



Presynaptic inhibition affects dynamics

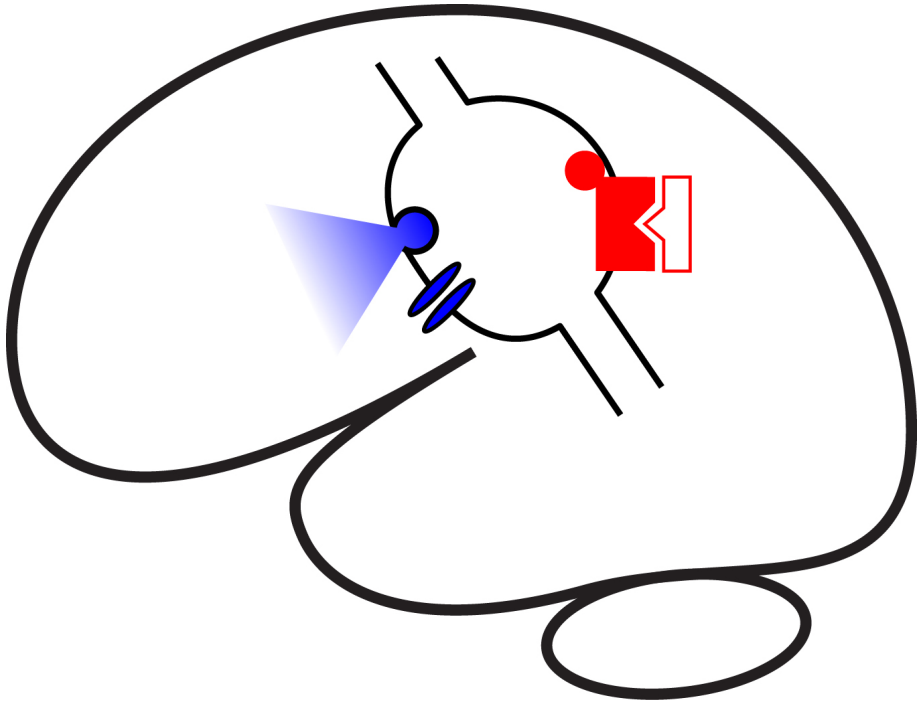


Neuromodulatory transmitters

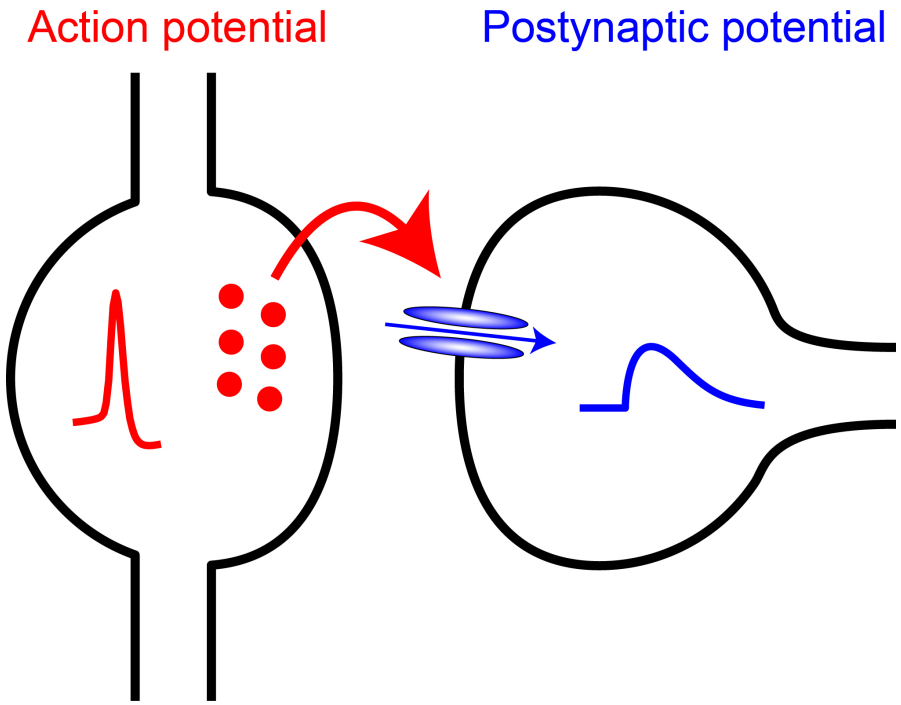
Glutamate
GABA
Acetylcholine (ACh)
Dopamine (DA)
Serotonin (5-HT)
Adenosine
Adrenaline
Noradrenaline
Histamine

Glycine
Orexin
Anandamide
2-arachidonoylglycerol (2-AG)
Enkephalin
Endorphin
Substance P
Oxytocin
…

Presynaptic modulation by neurotransmitters



Postsynaptic neuromodulation



Clinical relevance of neuromodulation

Examples

Depression: Fluoxetine / Sertraline – selective serotonin reuptake blockers

Antipsychotic: Risperidone – blocker of specific DA, 5HT, adrenergic receptors

Neuromodulation

- Neuromodulators signal over long spatial and temporal scales.
- Neuromodulators act upon metabotropic receptors affecting diverse signalling pathways.
- Presynaptic inhibition, reducing release probability, is prominent, mediated by inhibition of Ca^{2+} channels and release machinery.