Synapses et dynamique moléculaire

La synapse, une nanomachine stochastique

Molecules are starlings in the sky

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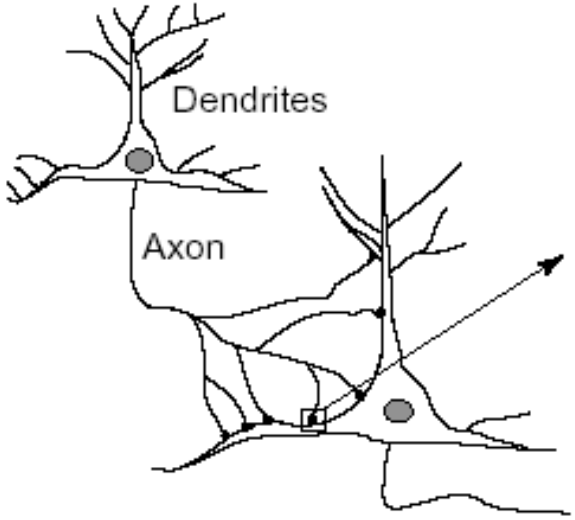
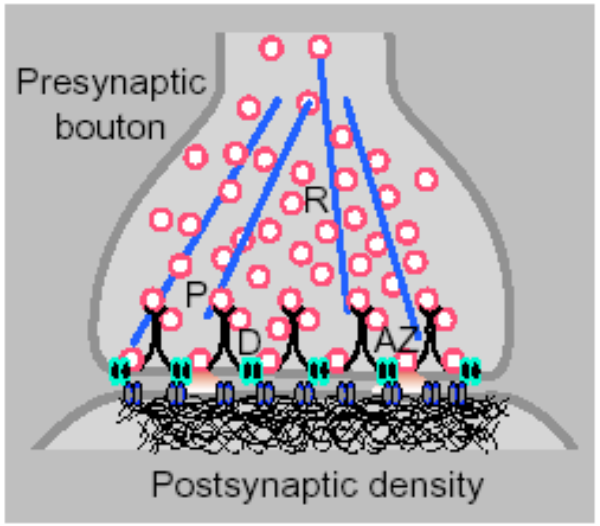
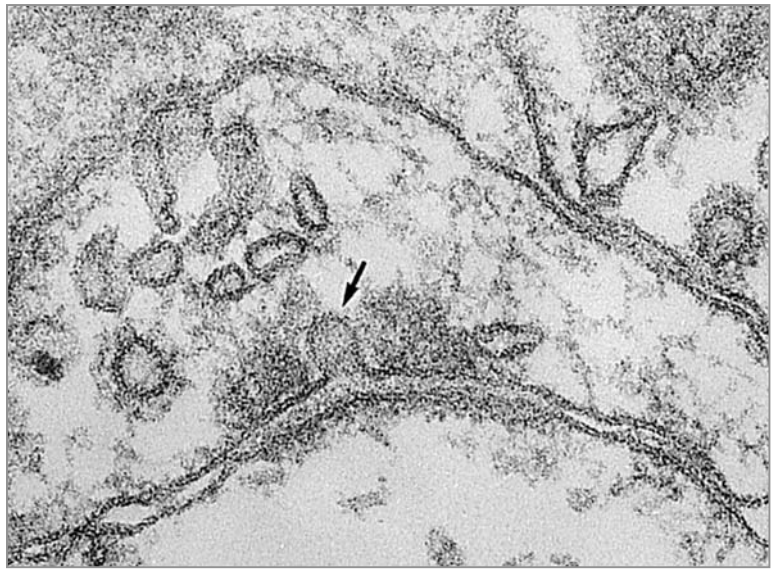
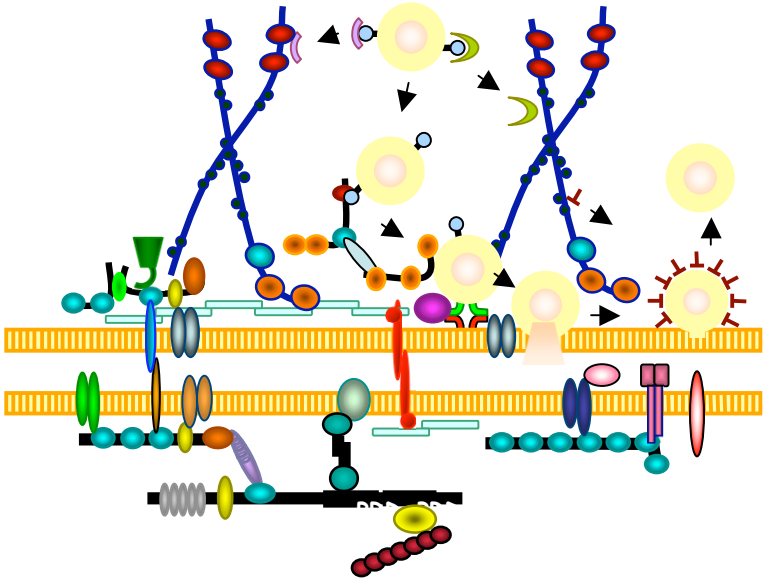
Communication between neurons take place at synapses

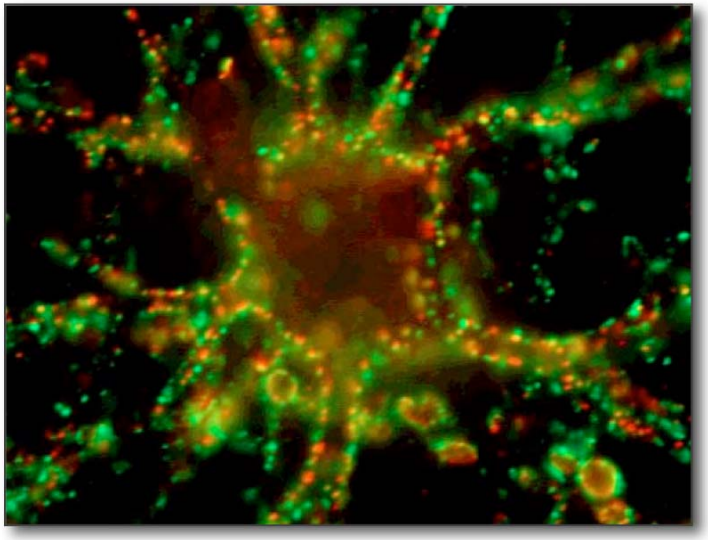




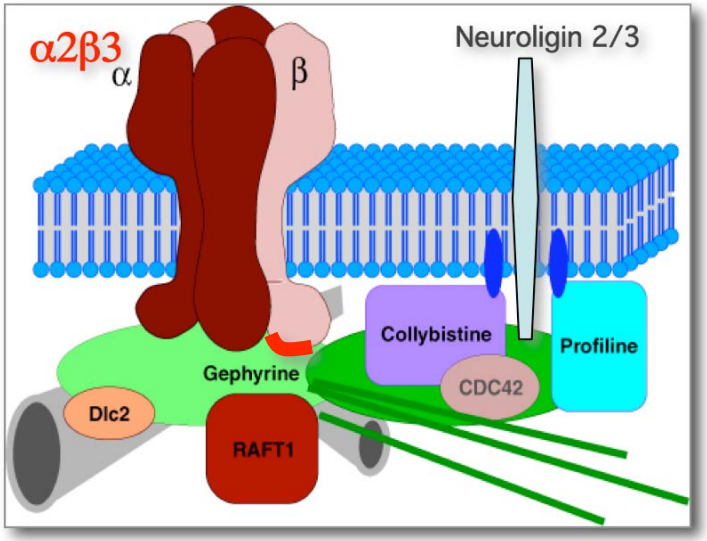




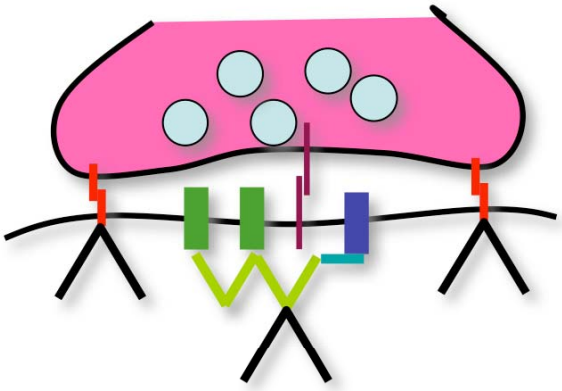
Most synaptic receptors form microdomains stabilized by scaffolds



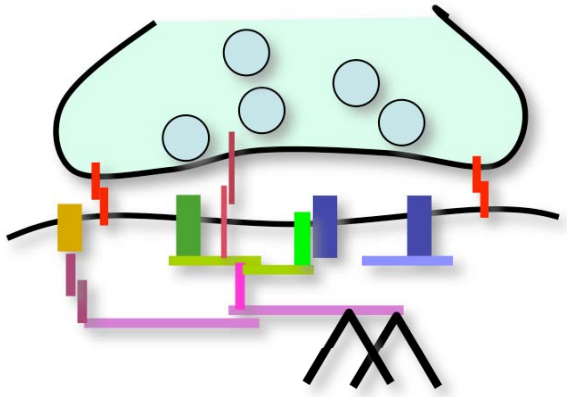
Spinal cord neuron



Betz et al. Since 1984

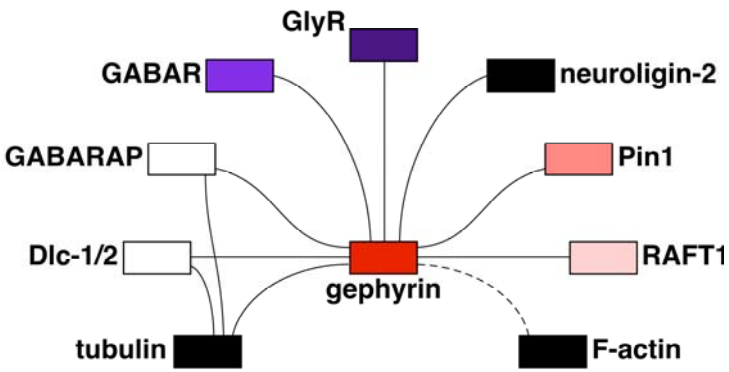


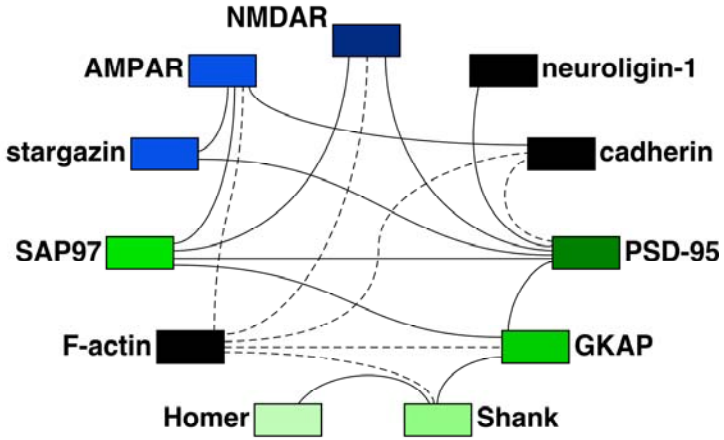
Inhibitory Synapse

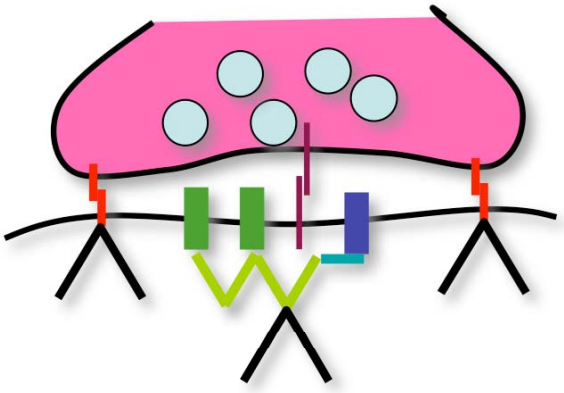


Excitatory Synapse

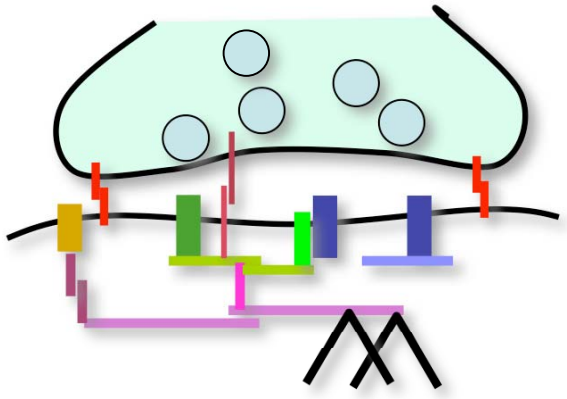
In fact, a network of molecular interactions, and some data on molecular localization





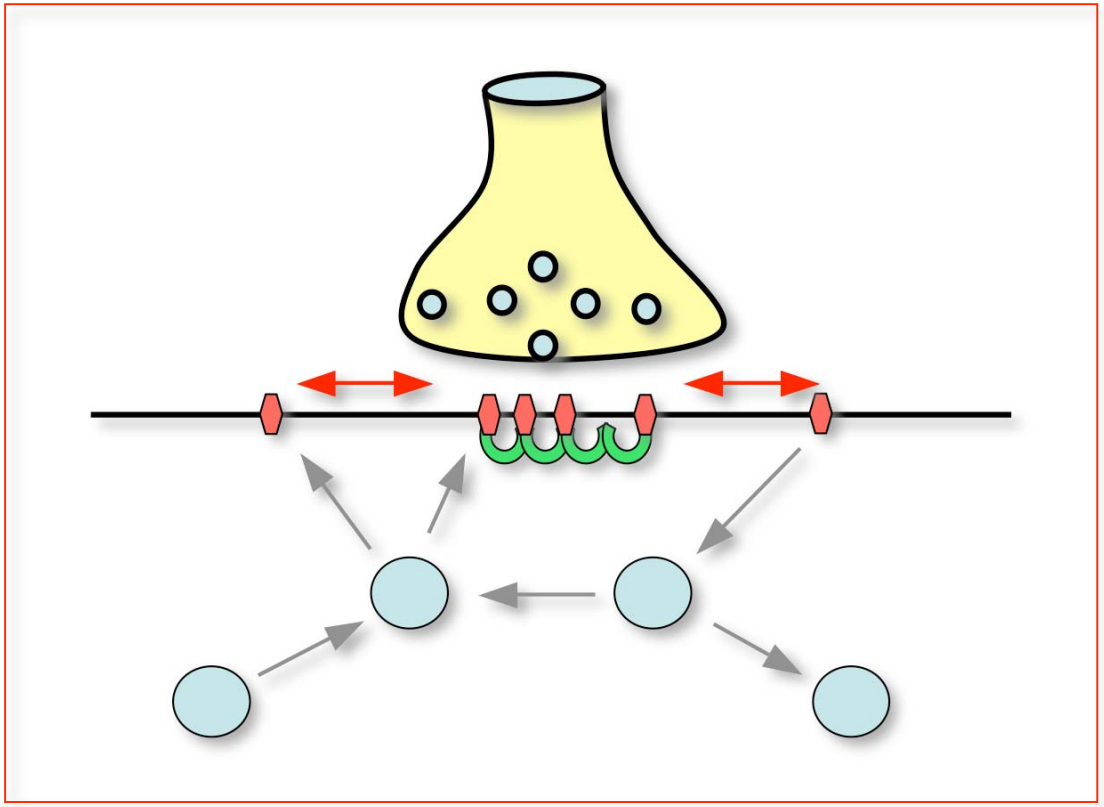


Inhibitory Synapse



Excitatory Synapse

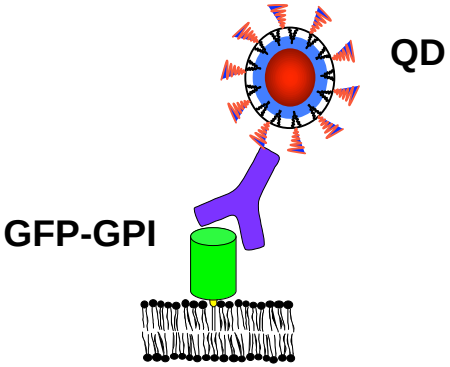
Constraints & cell biology

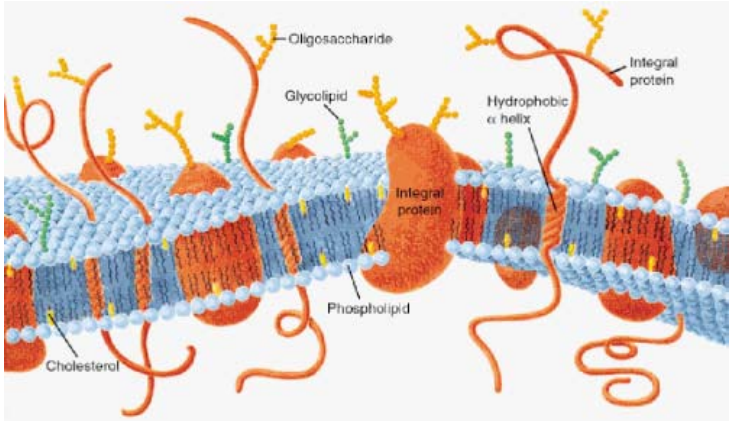


- Turnover of receptors (global and local)
- The number of receptors varies (development and plasticity)
- Most receptors are inserted and removed at non-synaptic loci

Singer-Nicholson the fluid mosaic model (1972)

Diffusion result from a collective behavior of proteins and lipids





Renner J Neurosci 2009

Singer-Nicholson the fluid mosaic model (1972)

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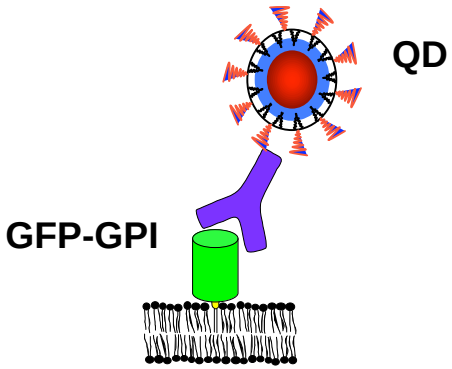
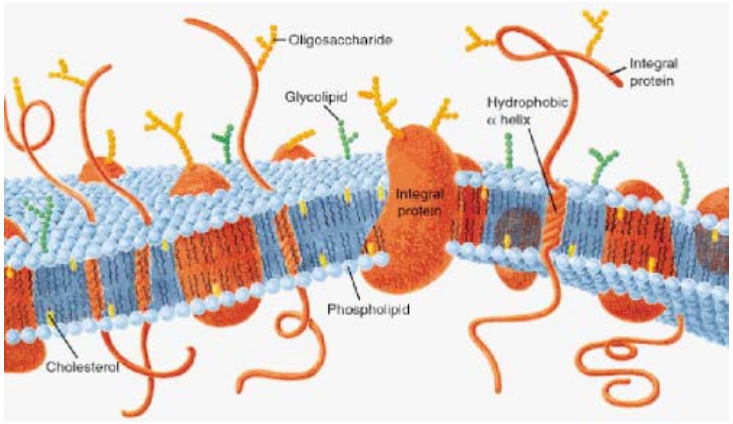
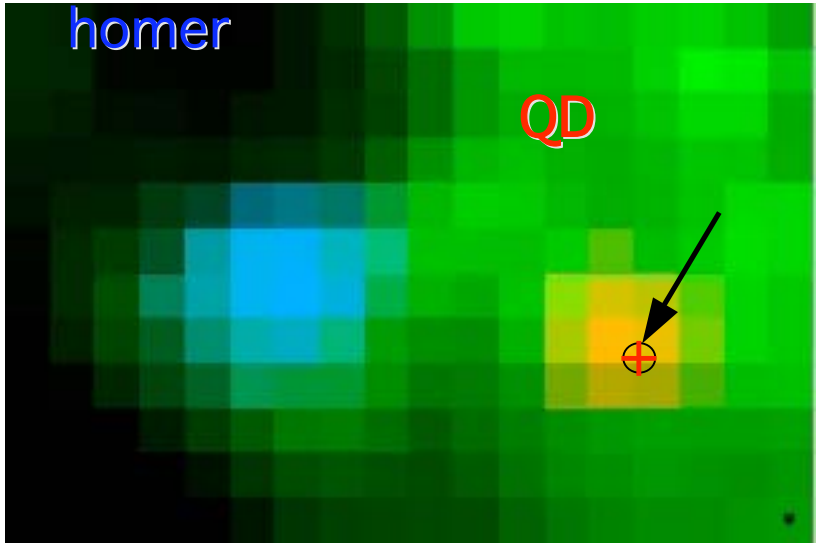
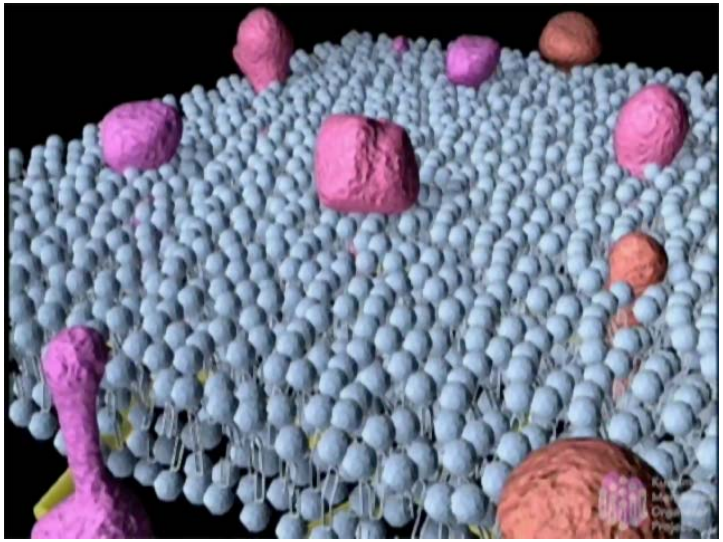






Cultured hippocampal neurons (24 DIV)

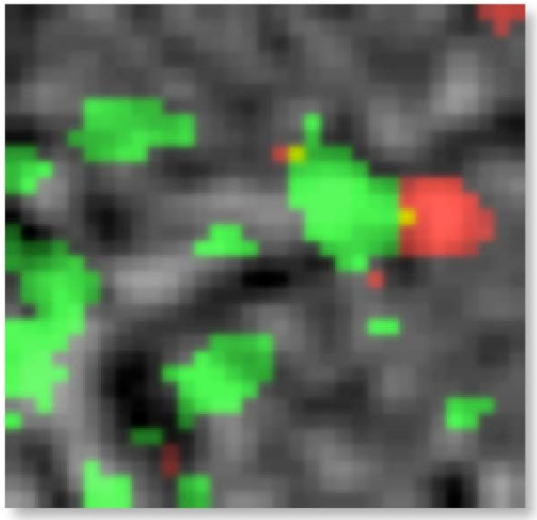


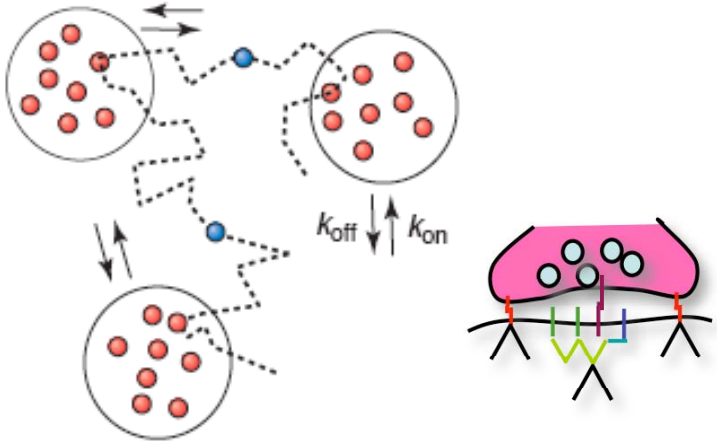
From Kusumi

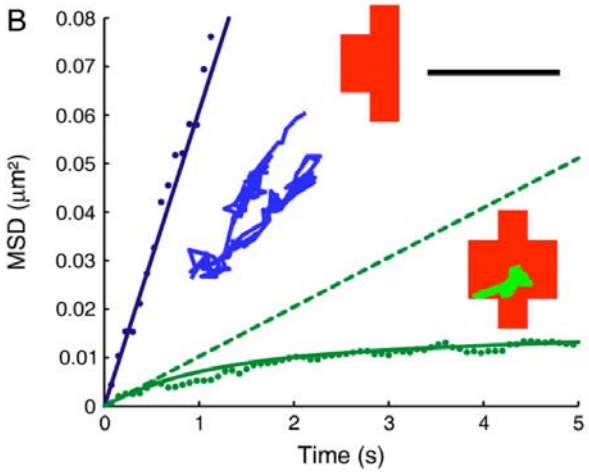
Renner J Neurosci 2009

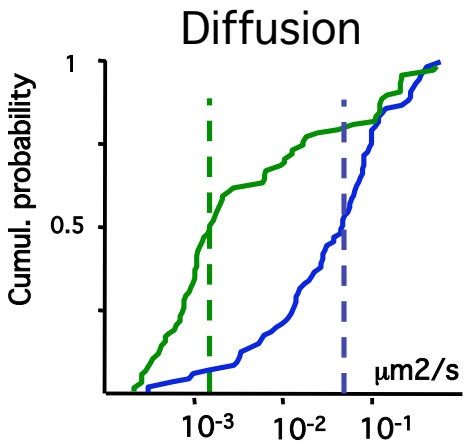
Membrane exploration & dynamics of GlyR-Qdots

13 Hz
75 ms
integration





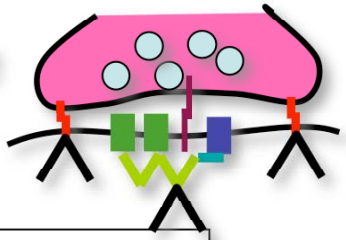


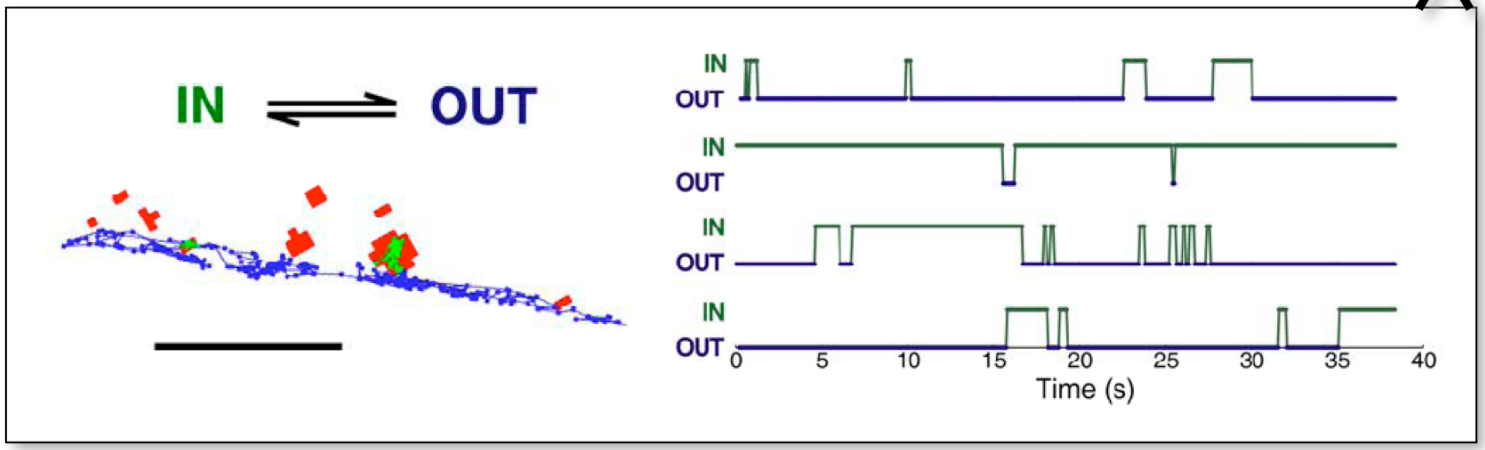


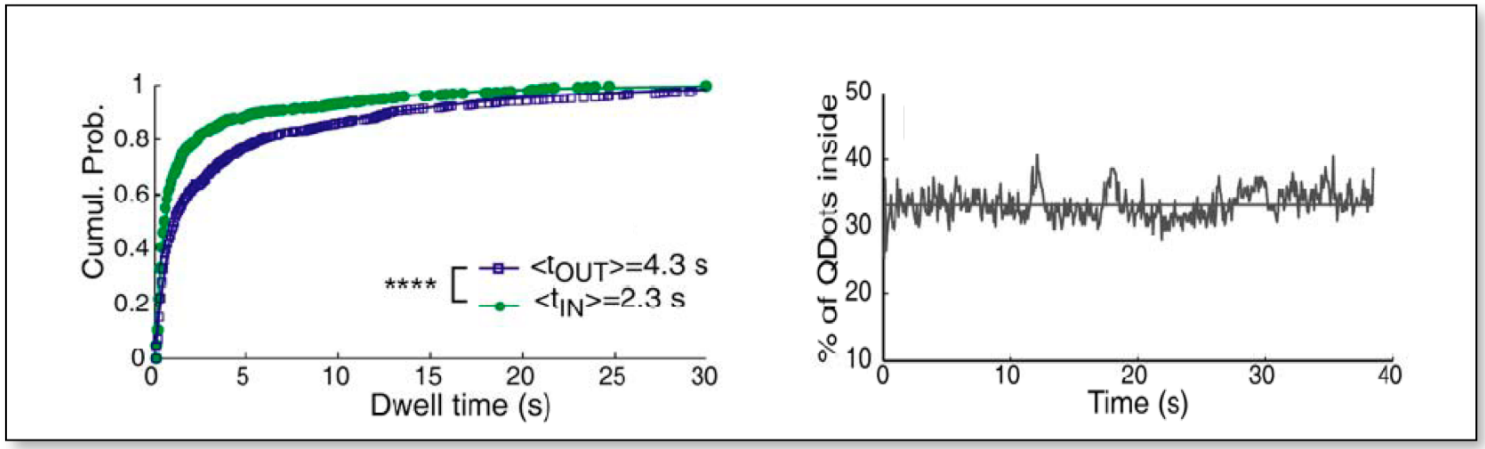
Cultured spinal cord neuron

Dahan, Lévi et al. *Science 03*

The “in-out” equilibrium at steady state

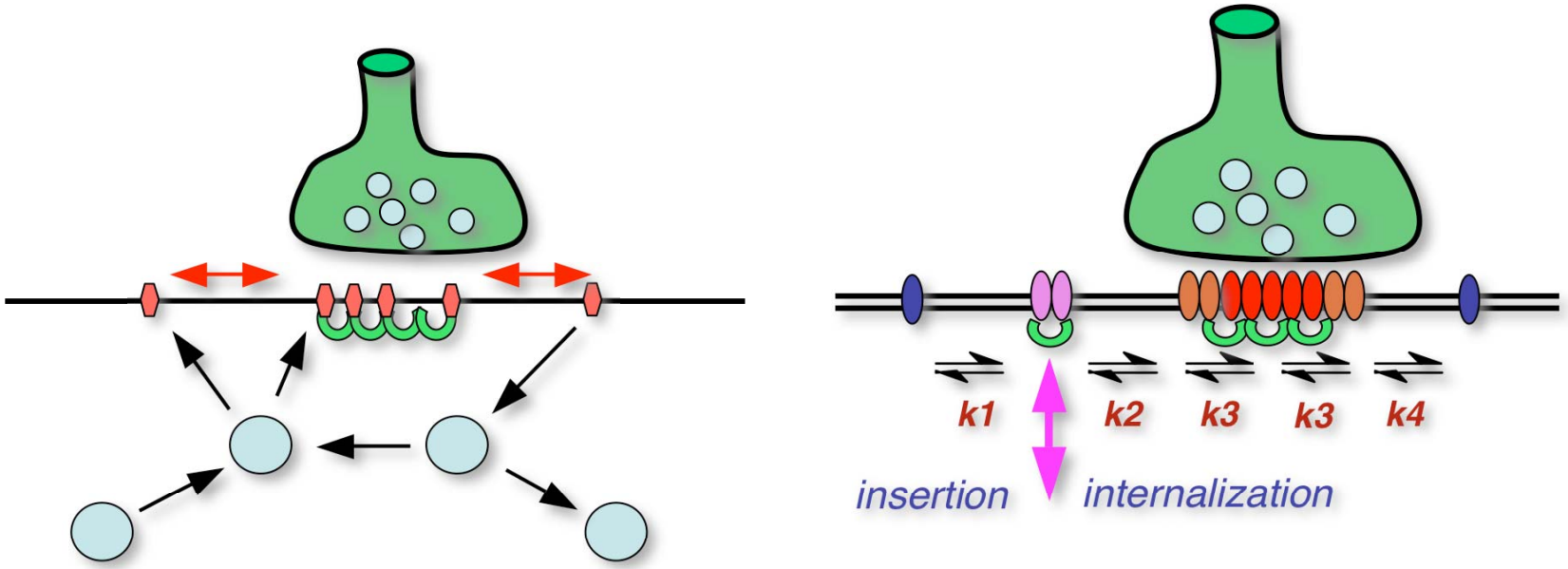


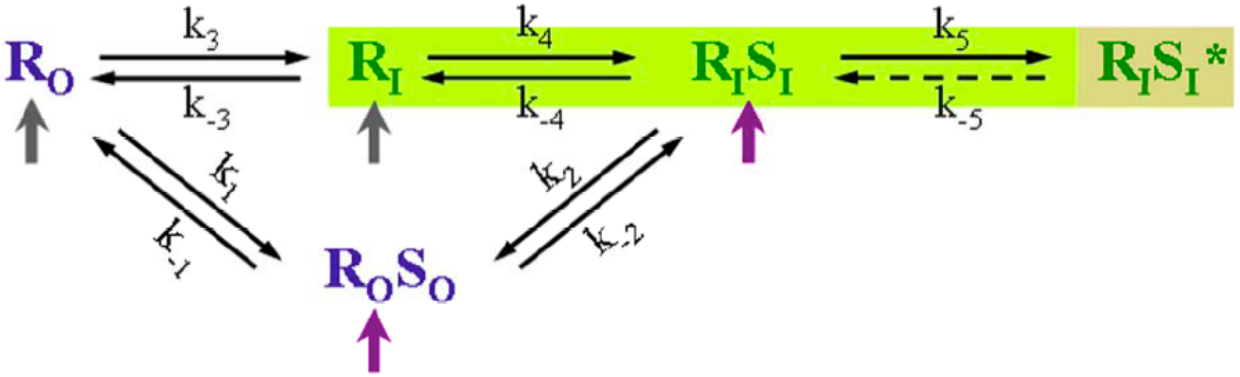




Ehrensperger & al. *Biophys. J* 2007

Stable synapse and kinetics at equilibrium

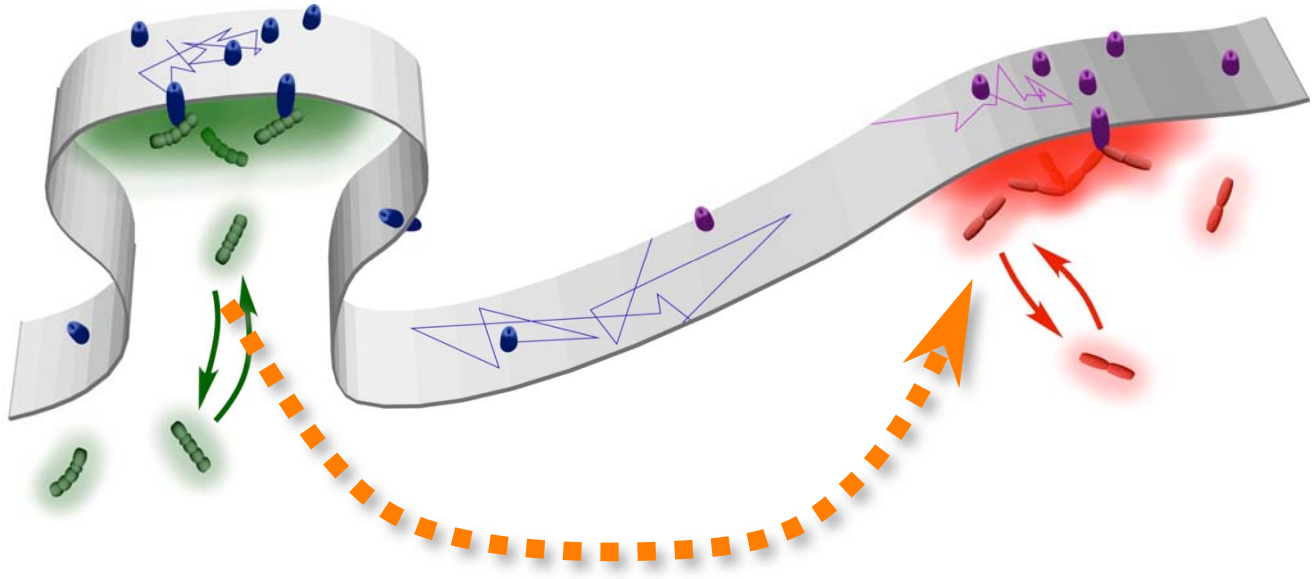




Triller and Choquet *Neuron* 2008
Ehrensperger *Biophys. J* 2007

The synapse paradox:
plasticity despite stability, stability despite plasticity

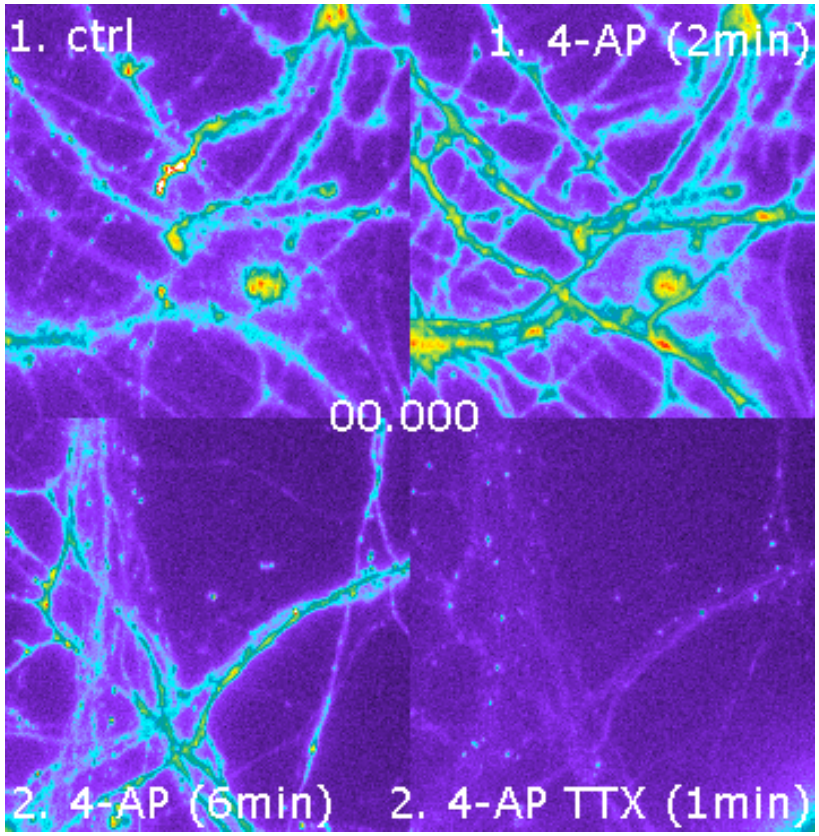
Compatibility between itinerant receptors and stable postsynaptic structure

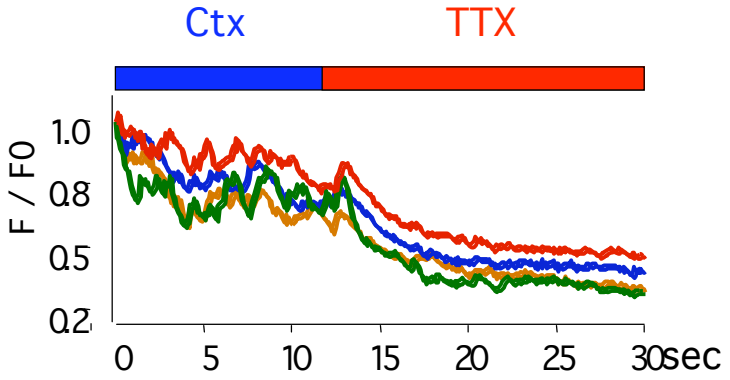


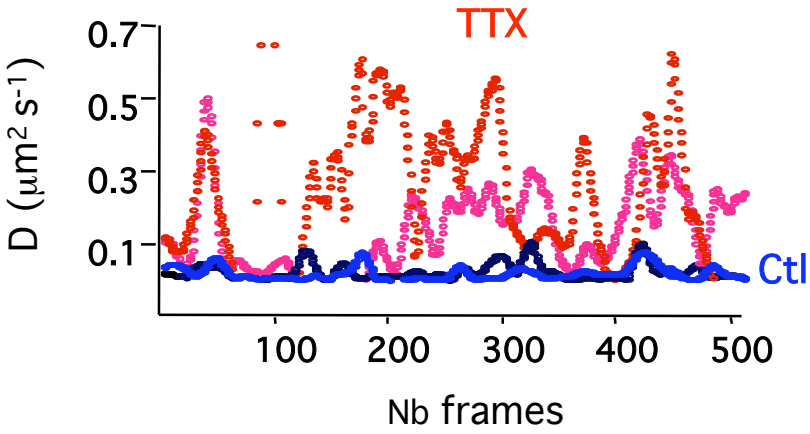
Stabilization ⟷ Dynamic Equilibrium

Regulated confinement

Synaptic activity modify intracellular calcium & control GlyR lateral diffusion





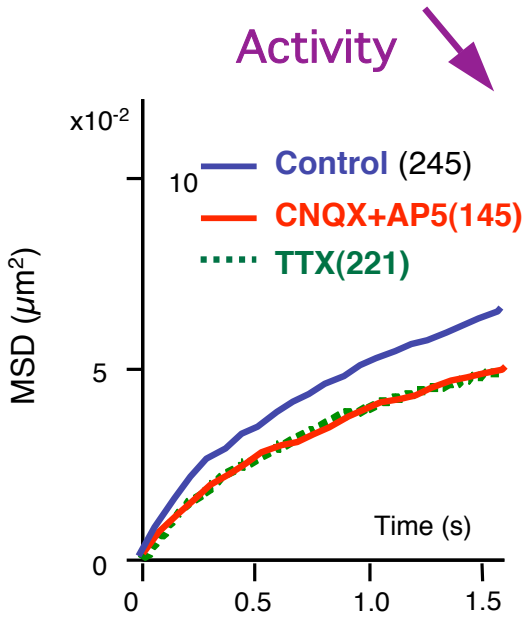


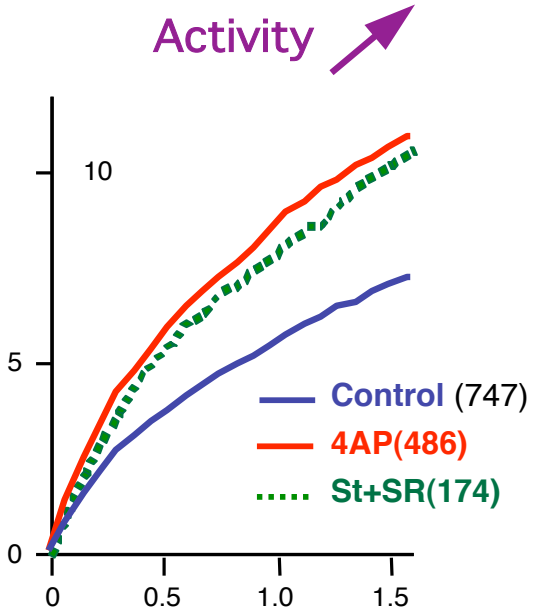
4-AP 50mM and TTX 1mM
9div spinal cord neurons loaded with Fluo4

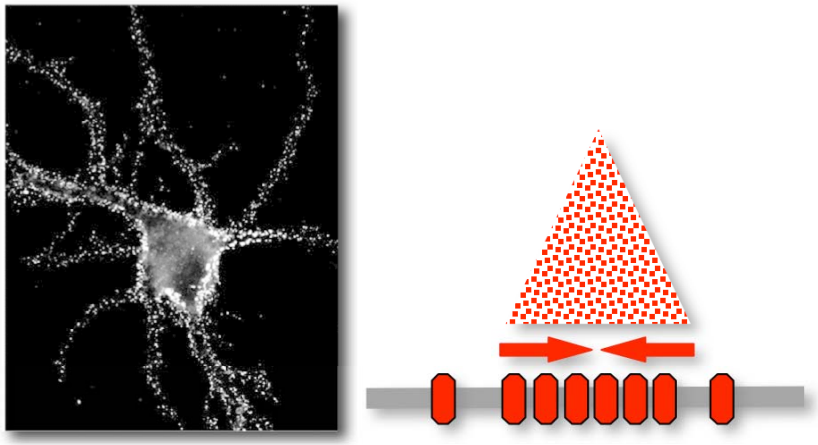
Cultured spinal cord neurons

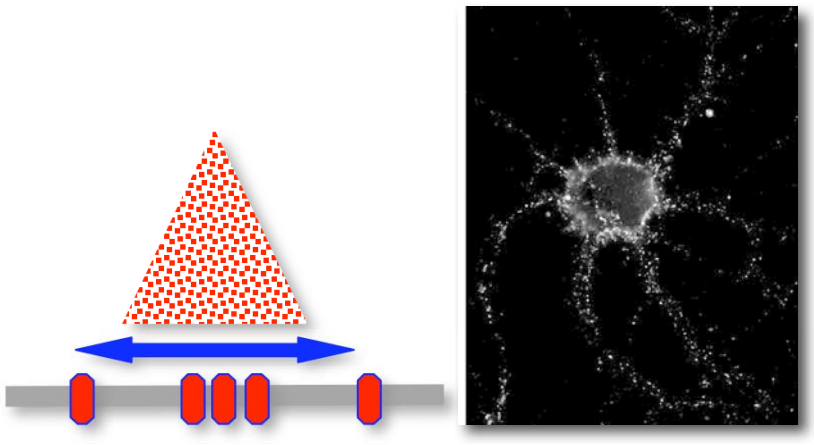
Sabine Lévi et al. *Neuron* 2008

Activity regulates $GABA_A\gamma2R$ confinement at synapses







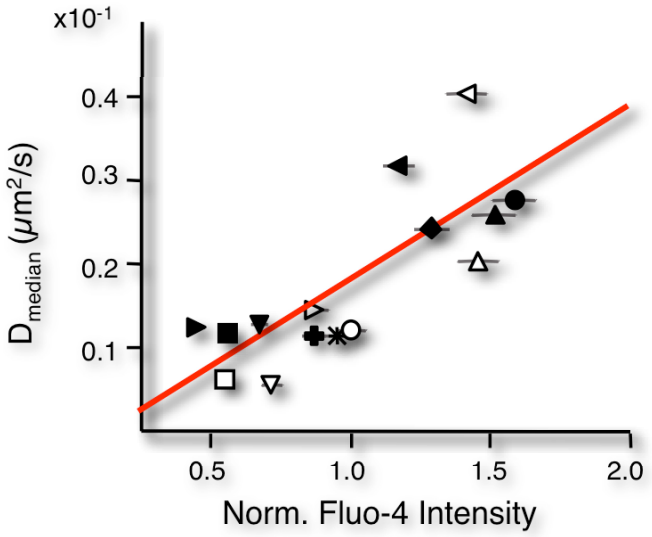


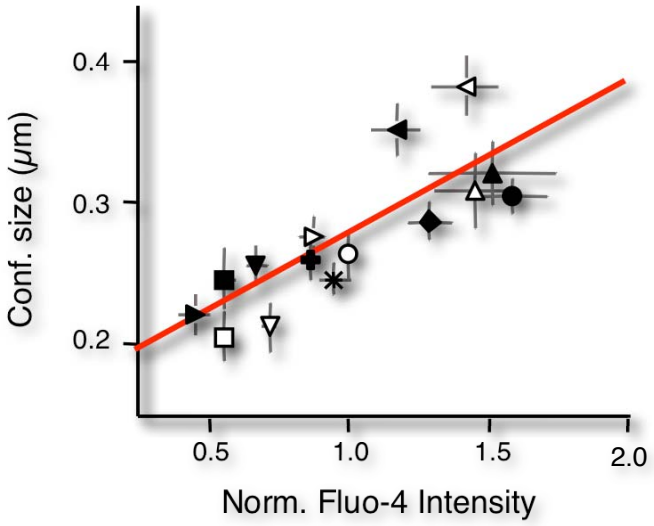
Hippocampal neurons 21 days IV

Bannai et al *Neuron 2009*

Correlation between Ca^{2+} and GABAγ2R Mobility

Winthin synapses



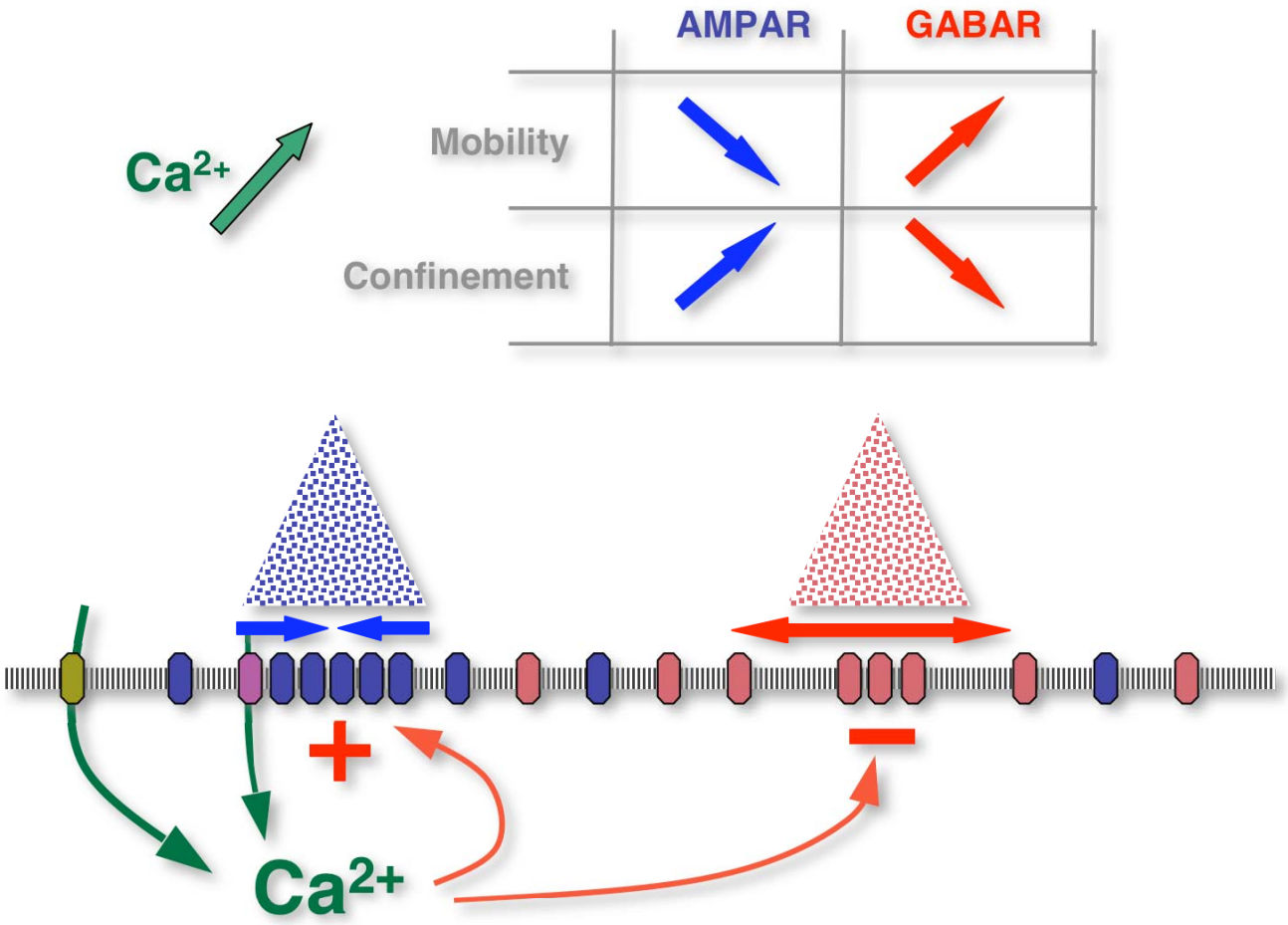


○ Control ▽ TTX □ CNQX+APV ✚ 4AP+CNQX ◆ 4AP+APV ▼ 4AP+TTX

● 4AP △ St+Gz ▲ 4AP+St+Gz ▶ 4AP+EGTA ◀ 4AP+ 2APB+ Ry ⋉ 4AP+ nife ■ 4AP+CNQX+APV

Bannai et al *Neuron 2009*

Reactive Ca^{2+} tuning of excitation/inhibition



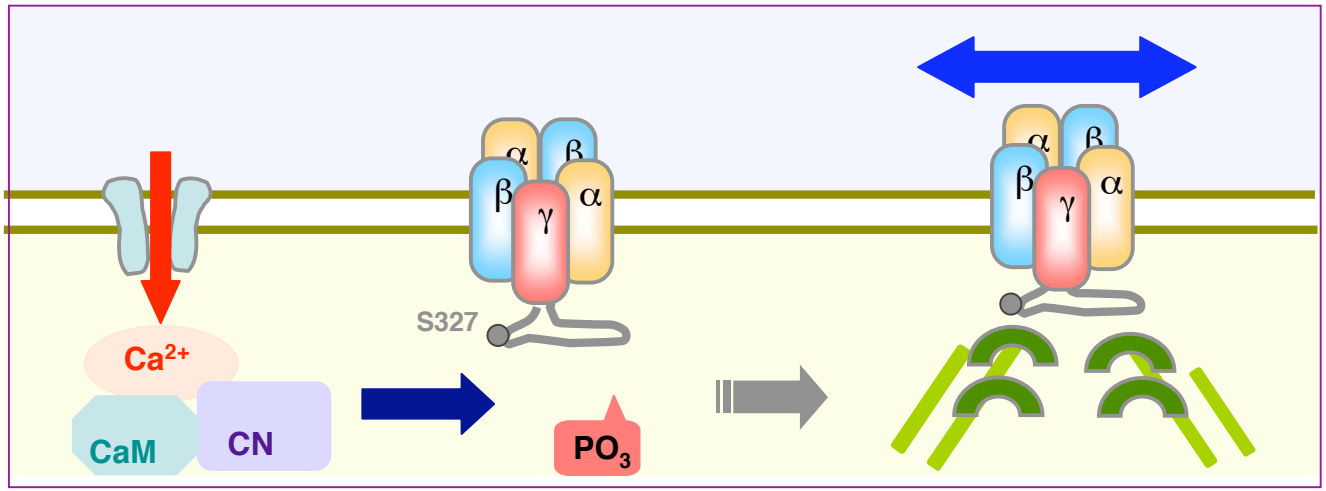
Borgdorf & Choquet 2002,Tardin et al. 2003

Bannai et al *Neuron 2009*

Diffusion parameters & “synaptic reactivity”

GABA receptor: anti-homeostatic reactivity

hippocampal neurons

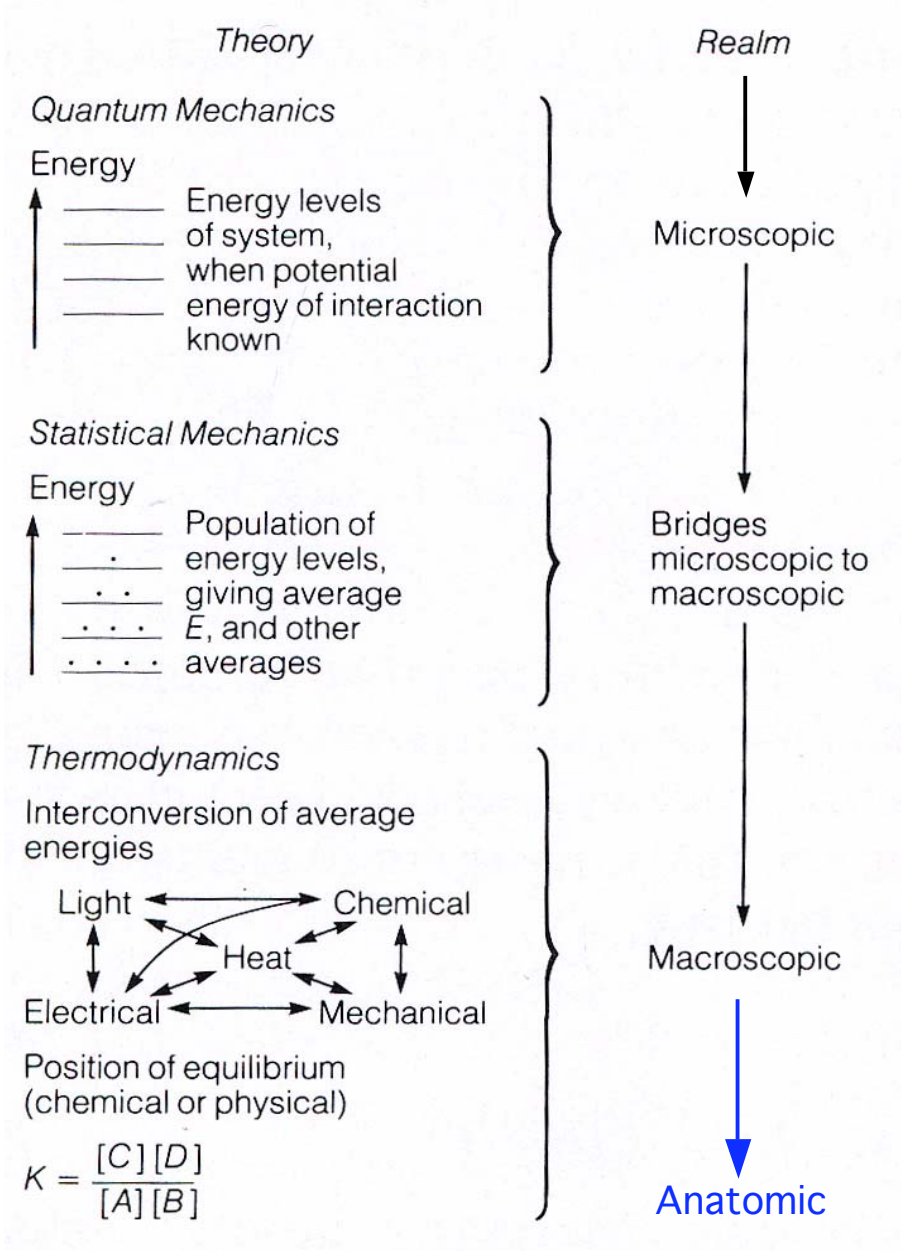


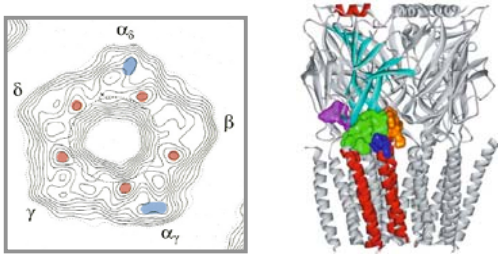
“Synaptic Reactivity” results form the diffusion in the PM

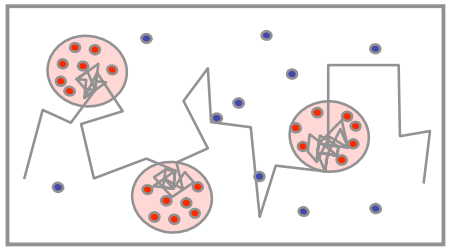
Lateral diffusion is regulated by biological process

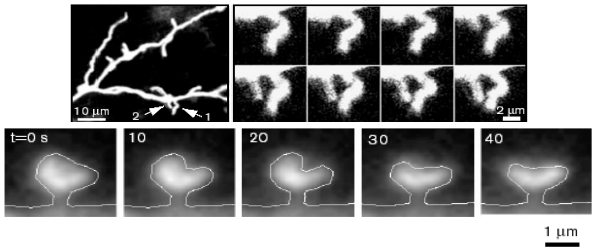
--> Rapid and reversible regulation of synaptic inhibiton

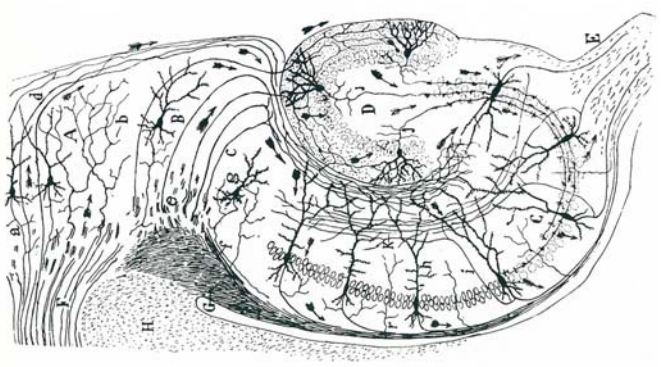
The scale jump











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