From single molecule imaging to synapse understanding

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A complex molecular assembly accounts for receptor accumulation at synapses and “synaptic plasticity” derives partly from modifications of postsynaptic receptor number resulting from receptor trafficking. New concepts now emerge from imaging of receptor movements at the single molecule level. Inhibitory glycine or GABA receptors, and the excitatory AMPA and NMDA glutamate receptors are mobile in synapses, switch between extrasynaptic and synaptic localizations by lateral diffusion and can be exchanged between synapses through lateral diffusion in the plane of the extrasynaptic plasma membrane. This dynamic behavior can be tuned by the cytoskeleton or by the synaptic activity. Variations in receptor numbers at postsynaptic sites is therefore likely to depend, not only on regulated exo-endocytotic processes but also on regulation of diffusion by modification of the structure of the membrane and/or by transient interactions with scaffolding proteins. This diffusive behavior, provides a new framework for the understanding of synaptic strength regulations. Because receptors diffuse in the plasma membrane, in the same way that particles do in a two-dimensional field, they could be transiently trapped at specific loci corresponding to postsynaptic densities. We will present new data on the regulation of the diffusive properties of inhibitory receptors by excitatory activity. This open new routes towards understanding not only the dynamic equilibrium accounting for receptor number at synapses, but also the mechanisms underlying the excitation–inhibition balance during modifications induced by so-called plasticity within neuronal networks.