Quantitative super-resolution imaging of the nanoscale organization of the inhibitory synapse

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Super-resolution and in particular techniques provide the capability to quantitatively investigate sub-cellular structures and protein distribution at the molecular scale [1]. In particular, the advent of single molecule localization microscopy techniques played a significant role in modern neuroscience progress, allowing new insights into the protein organization and dynamics at the synaptic level [2]. In this work we exploit PALM (Photo-Activatable Localization Microscopy) and STORM (stochastic optical reconstruction microscopy) in order to study the functional organization and distribution of gephyrin, a scaffold protein of the inhibitory synapses that mediates the anchoring of GABAA receptor [3, 4]. A quantitative approach based on clustering analysis coming from graph theory [5] allow us to quantitatively monitor the rearrangement of the gephyrin clusters in response to a chemically induced form of long-term potentiation of inhibitory synapses (chem-iLTP) [3]. This approach suggested that, during the expression of chem-iLTP, gephyrin is redistributed from extra-synaptic to synaptic compartments. We also show that the increase of synaptic gephyrin is strictly linked to an increase of heterogeneity in the inner organization of the scaffold protein at the synapse that rearranges in nanodomains.

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