Quantitative super-resolution microscopy of proteins at the inhibitory synapse

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Synapses are crucial structures in neurons whose size is below the diffraction limit of conventional optical microscopies. In the last few years, super-resolution optical microscopies, in particular Single-Molecule Localization (SML) techniques, have provided very helpful means to achieve a detailed characterization of density and spatial organization of synaptic proteins [1]. Moreover, many computational methods employing clustering analysis algorithms [2] have been developed to extract quantitative information from SML data sets.

Recently, it has been reported that during synaptic plasticity, chemically induced by long-term potentiation of inhibitory synapse (iLTP), GABAA receptors are immobilized and confined at the post-synaptic site in cultured hippocampal neurons, enhancing GABAergic synaptic currents. iLTP expression relies on the recruitment and accumulation of the scaffold protein gephyrin at synaptic areas [3], promoting the clustering of synaptic GABAA receptors. In our work, we use Stochastic Optical Reconstruction Microscopy (STORM) imaging combined with clustering analysis and DNA origami calibration [4] to investigate the inhibitory synapse at a nanoscale level and to quantify synaptic proteins in cultured post-natal mouse hippocampal neurons under plasticity conditions.

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