Post-doc at Bordeaux Neurocampus
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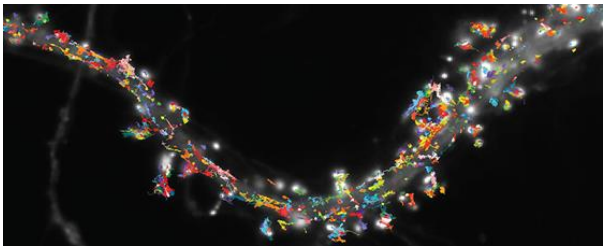

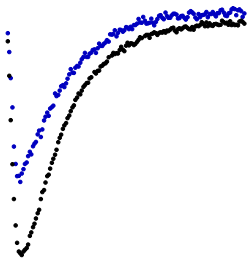

Project context:

Long term synaptic plasticity is thought to be essential for learning and memory. Long term potentiation (LTP) and depression (LTD) correspond to rapidly-induced and long-lasting increases and decreases in the efficacy of synaptic transmission, respectively. However, even if changes in synaptic strength have been the most studied parameter, it has been reported that the modification of synaptic plasticity is concomitant with structural plasticity. This plasticity includes the modification of the number of synapses to either reinforce or decrease the weight of a specific input regarding the sum of other inputs received by a neuron. The relationship between these two types of plasticity has not been explained.

In addition, our vision of synaptic transmission has been completely revisited. Indeed, development of super-resolution techniques, partly driven by our lab, highlighted the crucial role of both AMPARs nanoscale organization regarding release site. These findings have added a new unexpected level of complexity to our understanding of synaptic physiology that now requires to re-examine the mechanisms of synaptic plasticity, and more specifically synaptic depression through this new prism.

Moreover, it is now accepted that the induction of LTD at the post synapse triggers a multiphasic response. The initial phase results in the loss of AMPARs from synapses mainly due to endocytosis. At later time points, the long-lasting maintenance of a low synaptic strength has been attributed to new protein synthesis but remains poorly understood. Our preliminary results revealed a new complex molecular mechanism which can be the missing link between synaptic LTD, which affect synaptic response, and structural plasticity, responsible of the selection of only “useful” synapses.

Overall, the objective of this project is to use our technological advance in imaging coupled to electrophysiology to revisit LTD. In particular, we will redefine the respective modifications in AMPAR organization/ dynamic and synaptic transmission during the early and sustained phases of LTD. This will open the way to new approaches to control LTD, hence synaptic memory. In parallel, we will tightly describe structural plasticity induced by LTD. We will then determine the molecular link between these two plasticities.

Technical approaches:

Use our super-resolutions imaging techniques in both live and fixed tissues to characterize the organization and dynamics of AMPAR at the nanoscale;

Develop long term fluorescence imaging technique to follow structural plasticity both on cell culture and in brain slices.

Use electrophysiological technique on brain slices to measure synaptic modification throughout LTD

Realize d-STORM in slices to determine evolution of AMPAR content following LTD

Candidate profile:

Motivated neurobiologist with skills in super-resolution imaging techniques or electrophysiology and highly curious and enthusiast for science

References: (https://iins.u-bordeaux.fr/projectCHOQUET16)

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Compans et al. **Nat. Com**. 2021