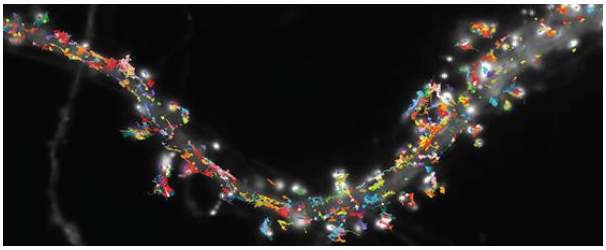
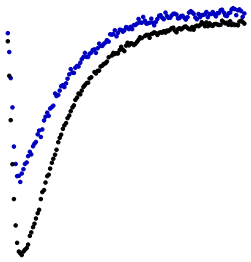
PhD at Bordeaux Neurocampus
(Contact: eric.hosy@u-bordeaux.fr)





Project context:

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by impairments of social interaction and communication accompanied by a pattern of repetitive and restrictive behavior. Since several autism risk genes affect the function of specialized structures that allow the communication between neurons, studies in the last few years have suggested that pathogenesis of ASD may be attributed to deficits in synaptic function. Mutations in the SHANK3 gene, coding for a scaffolding protein located at excitatory synapses, account for 1-2% of all ASD cases and although autistic phenotype has been described across individuals with SHANK3 deficiency, heterogeneity in the severity of the phenotype has been reported. Here we hypothesize that heterogeneity in the phenotype is the consequence of the interplay between genetic and environmental factors (double-hits). Using human pluripotent stem cells differentiated into neurons or microglia, and exploiting genetic/environmental double hits mouse models we will identify the mechanisms underlying inflammation/gene interaction. The ultimate goal of InflASD is to also identify new strategies to treat ASD caused through the spectrum of the inflammatory response.
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 glutamate receptor 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 some neurodevelopmental pathologies as ASD.
Overall, the objective of this project is to use our technological advance in imaging coupled to electrophysiology to revisit ASD at the synaptic level.

Technical approaches:
Use our super-resolutions imaging techniques in both live and fixed tissues to characterize the organization and dynamics of glutamate receptors 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

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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