Internship/PhD in System Biophysics of membranes

Spatiotemporal regulation of the cell activity by multi-scaled dynamics

Contact : Stéphanie Bonneau (stephanie.bonneau@sorbonne-universite.fr)

Project and objectives

Metabolic activity is a hallmark of living systems, by which they maintain their out-of-equilibrium state. This activity takes place in a highly dynamic, crowded and structured environment. Today, the multi-scale spatiotemporal organization emerges as organizing and coordinating cellular behaviour. A major challenge now is to link the nano-scaled and molecular levels with the classical micron-scale cell description, in terms of dynamics, mechanics and remodelling. In particular, insight are lacking for the 50-500 nm scale (corresponding to the so-called meso-scale biology), due to specific experimental limitations. In this con-text, the major issue of our project is to understand how the spatiotemporal dynamics of this meso-scale organization influence the biological activity. For this purpose, we will focus on a key membrane, of which state and activities relate with key points of the cellular physiological and thermodynamical state: the plasma membrane, which is directly coupled to the activity of the cytoskeleton. One of its major function is the control of the cellular exchanges, including by endo- and exocytosis via specific receptors. In this context, our objectives are to: 1) follow the meso- and nano-scaled dynamics within living cells of controlled state, 2) for each level, characterise the motions, 3) establish correlations between these organizations and the biological activity 4) produce a theoretical model to support the interpretation of these correlations and couplings.

Internship/PhD programm

For plasma membrane, the meso-organization (Figure) is related to in-plane patterning called lipid rafts (R). Rafts represent the so-called lateral compartmentalization of lipids and protein-receptors at the cell surface. Internalization of ligands and receptors by these domains occurs via a specific process defined as raft-dependent endocytosis (E).

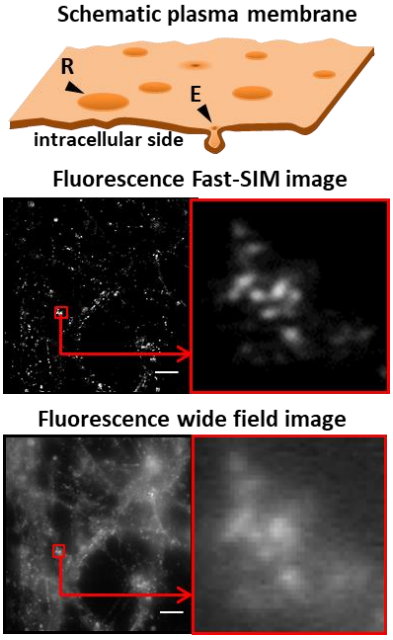

Fig. *Schematic of lipid rafts and comparison between WF and Fast-SIM in primary HD neurons. Bar 10µm.*

The successful candidate will be in charge of the experimental part of the project, in particular super-resolution imaging. She/he will work in the Laboratoire Jean Perrin (UMR 8237 CNRS and Sorbonne University) in the Biomembrane group, under the supervision of Prof. S. Bonneau. The team has a homemade Fast-SIM set-up, of which innovative approach increases the acquisition rate and enable fast, large field and non-aggressive (low light) imaging of the samples. Experiments on living cells already demonstrate a lateral resolution of ~100 nm at raw data acquisition rate of 15 frames per second for a wide field of 85µmx85µm. In collaboration with the Neuroscience Lab of IBPS (Prof S. Betuing), experiments will be performed on primary cells cultures of cortical neurons, from wild type mice and from models of Huntington Disease (HD). Our strategy is to track the cholesterol-rich lipid rafts (Cholera-toxin B Alexa-488) and the receptors (GluN2B-Cherry subunit). Quantitative data will be derived from image analysis (rafts number and size distribution, mean square displacement, fission/fusion events, dif-fusion mode…) to analyse topology and dynamics. Those data are characteristic of the out-of-equilibrium state of the cell. They will be correlated with data obtained from biochemical analysis and functional imaging, which give access to the biological activity.