SORBONNE UNIVERSITÉ

Interfaces pour le vivant

Title of the research project: **Image analysis methods development for *in vitro* and *in situ* cryo-electron tomographyn studies of conformational variability of biomolecular complexes: Case of nucleosome structural and dynamics studies**

Thesis supervisor: **JONIC Slavica**

Email address of the thesis supervisor: slavica.jonic@upmc.fr

Doctoral School : ED130

Subject description:

Recent progress in instrumental and software developments for cryo-electron microscopy (cryo-EM) has allowed near-atomic structural resolution of various biomolecular complexes from single particle analysis (SPA) and electron tomography (ET) images. While SPA allows collecting structural data of isolated complexes, ET allows structural data collection in the cellular environment. One of the main current cryo-EM challenges is the data interpretation in terms of continuous conformational changes of complexes (an uncountable number of intermediate conformational states) contrary to the traditional description of the conformational variability in terms of discrete conformational changes (a countable number of conformational states). Different conformations can coexist and their individual characterization is crucial to understand the functional mechanisms of complexes and develop new drugs. While a few methods have already been developed to interpret SPA data in terms of continuous conformational variability, no method is currently available to describe this type of variability from cryo-ET data. One part of this PhD thesis will be focused on image analysis methods development to allow analyzing continuous conformational changes of complexes from cryo-ET data and will be supervised by Dr. Jonic (image processing group). The other part of the PhD thesis will be focused on application of the new methods to cryo-ET studies of the nucleosome structure and dynamics (conformational variability) and will be supervised by Dr. Leforestier (biology group). The new methods will be used to analyze extensively the conformational variability of the nucleosome that was detected by the Leforestier group in their recently collected unprecedented cryo-ET data of nucleosomes *in vitro* (in solution) and *in situ* (in the cellular environment).