Biophysical modeling of the auto-assembly driving bacterial DNA segregation

PhD funding – start in October 2023

Laboratoire Charles Coulomb (L2C), Montpellier, France

Scientific topic. In bacteria, DNA segregation mainly relies on ParABS systems to faithfully partition DNA molecules during cell division. Our objective is to achieve a holistic, quantitative and molecular understanding of the mechanism driving the main bacterial DNA segregation system by using integrative and multidisciplinary approaches. We will perform **biophysical modeling** using the tools of theoretical physics. Our collaborators in the team of Jean-Yves BOUET (CBI, Toulouse) will perform experiments in genetics and genomics, cell biology and biochemistry to test our predictions. Built on an established collaboration, we aim to decipher the mechanisms that (i) drive the auto-assembly of the nucleoprotein complexes (ParB proteins) involved in the partition of the archetypical ParABS system of the plasmid F in *Escherichia coli.* This part involves a liquid-liquid phase separation of proteins on a polymer, and (ii) the subsequent splitting and positioning of complexes on either side of the division plane (through the action of ParA proteins). This part involves the coupled dynamics of different protein species. We will investigate both the interplay between the two dynamic auto-assemblies, ParA and ParB, that ensures DNA segregation, and the formation and inheritance of membrane-less organelles.

Objectives. This project is at the interface between polymer physics, colloid physics and active matter. We will first consider Lattice Gas-like (LG) models to characterize the phase transition leading to the formation of the ParB complexes. We will subsequently embed this LG onto a supercoiled polymer to decipher the role of the bridging and polymer compaction on this phase transition. We will finally add a second species of particles to this lattice gas to model the splitting of two replicated equilibrium droplets through the actions of the protein ParA. We will use both numerical and analytical approaches.

Candidate background. The applicant should have a background in theoretical physics. He/she will have skills in numerical simulations (e.g., Monte Carlo methods) and in developing analytical calculations. A strong interest in modeling biological processes will be needed.

Academic context. The host team *Complex System and Non Linear Physics* at Laboratory Charles Coulomb (Montpellier, France) is composed of 6 permanent researchers, several PhD students and postdotoral researchers working collaboratively on various topics in bacterial processes from the cellular scale with DNA organization and dynamics, genetic translation, flagellar motor motion, up to the scale of population dynamics. We have an established collaboration of over ten years with Jean-Yves BOUET from Toulouse, where experiments will be conducted.

The city & region. The city of Montpellier displays a vibrant atmosphere, with plenty of cultural and sporting activities. The city has a long history with a beautiful old city center and is surrounded by mountains to the North, the Mediterranean sea to the South, while Pyrénées and Alpes are nearby. The weather is mild and sunny most of the year.

Contact and Application. Please send a CV and motivation letter to Jean-Charles WALTER (jean-charles.walter@umontpellier.fr), researcher at Laboratory Charles Coulomb (Montpellier, France).