INTERNSHIP PROPOSAL

Laboratory name: Laboratoire Jean Perrin
CNRS identification code: UMR 8237
Internship director'surname: Claude LOVERDO
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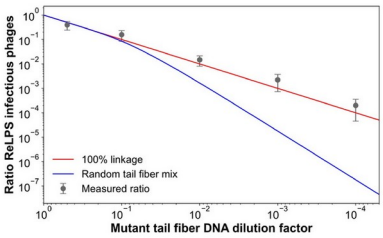
Internship location: Sorbonne Université (Paris 5e)

Thesis possibility after internship: YES
Funding: YES If YES, which type of funding: ANR

Modelling of genotype to phenotype coupling in phage replication

Bacteriophages play critical roles in nature, from molecular to ecological scales. Our understanding of phages' life cycles is incomplete, due to limitations of quantitative in vivo studies. Building biological systems in vitro has proven as an effective method to address biological questions in minimal settings more amenable to quantitative measurements. In the ANR project "Phabeta: Unravelling and harnessing phages' biophysical and evolutionary traits in a cell-free system" we plan to develop an in vitro framework to understanding phage cycles: how can a phage cycle be built from first principles? What is the inherent capacity of genotype to phenotype coupling of phages, independent of cellular compartmentalization? What are the biophysical characteristics of phage-membrane interactions underlying infection and lysis? We will address these using quantitative methods and theory. We plan to exploit the ability to synthesize phages in a cell-free system to develop an acellular phage cycle by quantitatively addressing phage self-assembly and potential inherent genotype/phenotype linkage. We will then characterize the minimal components necessary for phage infection of synthetic cells to capture the role of the biophysical and biochemical variables involved in such a process using liposome-based synthetic cells. Lastly, combining these components, we wish to achieve a synthetic cell-based phage cycle to understand the inherent evolutionary, biophysical constraints and their trade-offs.

This project is a collaboration between experimentalists (teams led by Ariel Lindner, David Tareste, and Vincent Noireaux) and theoreticians (This internship+PhD).



The master 2 internship will be centered on the capacity of genotype to phenotype coupling of phages, independent of cellular compartmentalization: when phages are produced with a mix of 2 closely related types of phage DNA, it has been observed experimentally that there is more association of DNA with related proteins than the null model [1]. A simple explanation is that, as proteins of a given type are produced close to the genome of this type, then the proportion of the matching protein is higher than the overall proportion of this protein type in the solution. A first model considering a local and a global protein concentration has already been developed. In the internship, the student will develop a more realistic model taking into account the out-of-equilibrium kinetics of protein production, assembly, and diffusion, using a combination of numerical simulation and analytical calculations, to test whether this more detailed model gives similar results, and link with physical parameters that may be tuned in new experiments, which would enable to compare with model predictions.

[1] Levrier et al. Nature Communications (15) 2223 (2024) https://www.nature.com/articles/s41467-024-46585-1

Condensed Matter Physics: NO Soft Matter and Biological Physics: YES
Quantum Physics: NO Theoretical Physics: YES