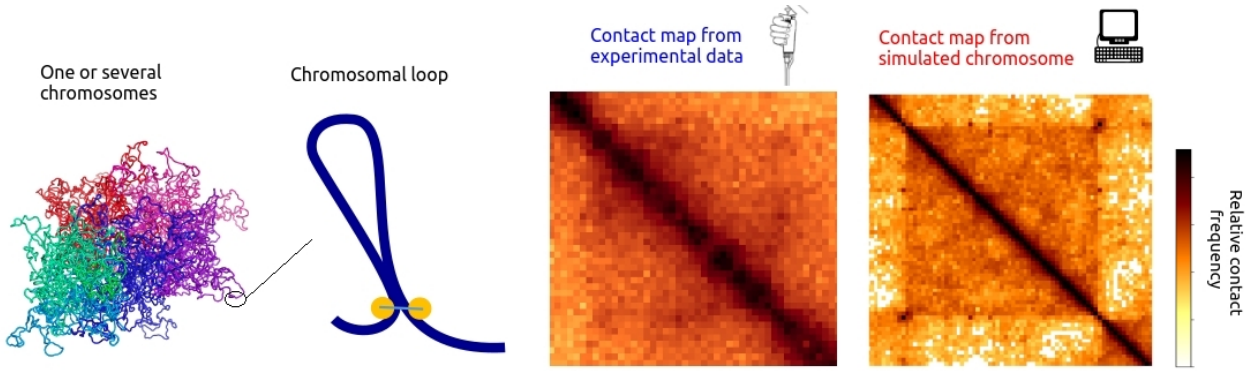
Internship and PhD PROPOSAL 2022

Project title: Long range chromosome loops in yeast

Laboratory: Spatial Regulation of Genomes (https://research.pasteur.fr/fr/team/spatial-regulation-of-genomes/) headed by Romain Koszul, Institut Pasteur, 28 rue Docteur Roux, 75015 Paris, France. *The internship can be extended by a thesis.*

PhD supervisor: Axel Cournac (ANR Jeune Chercheur, HDR to be submitted)

It is becoming increasingly clear that chromosome architecture is optimized for the proper execution of biological functions such as gene expression and replication, and that these in turn constrain the spatial organization of genomes on certain scales. Our community has recently identified several key proteins behind chromosome architecture and several associated mechanisms. The spatial organization of genomes can change during a cancer process (Taberlay et al. Genome Research 2016) or during a viral infection (Heinz et al., Cell 2018). A detailed knowledge of the mechanisms underlying chromosome architecture is thus important for a better understanding of certain pathologies.
The yeast *Saccharomyces cerevisiae* is a prime model organism. It is a eukaryotic cell that has the advantages of microorganisms (ease of cultivation, genetic manipulation) and several points in common with a human cell (rolling of DNA into nucleosomes, epigenetic etc). To observe the 3D structure of chromosomes, we use a technology called Hi-C (Lieberman-Aiden et al. Science 2009). This technique is based on the capture and sequencing at high throughput of DNA fragments that are close to each other (Dekker et al. 2002). This makes it possible to measure the contact frequencies between different loci within a chromosome or between two chromosomes and thus to infer the 3D organisation of genome. Our laboratory has recently identified stable chromosome loops of several tens of kilobases (kb) in yeast chromosomes during certain moments of the cell cycle (in mitosis: Garcia-Luis et al. NSMB 2019, in meiosis: Muller et al. MSB 2018).



We recently observed the presence of long range loops in different conditions that are independent of cohesin (unpublished data). The objective of this project is to **identify the biological and physical factors behind the formation and maintenance of this other type of loops.** These long-range loops could be linked to transcription activity and formed by collective processes like those of a phase transition.
> Techniques used: experimental classical molecular biology techniques (culture, PCR etc), computational (pipelines developed within the team in python language based on pattern detection or machine learning) and polymer simulations (molecular dynamics with GPU implementation). Depending on the abilities of the candidate, the student will have the choice to devote more time to the experimental or computer part of the project. For more information or apply, send an email to acournac@pasteur.fr.