ÉCOLE NORMALE SUPÉRIEURE DE LYON

Preferentially Master 2 Internship offer

Date of the offer: January-June 2026

Internship supervisor and Host laboratory:

Lab: Genome Mechanics

Team leader: Aurèle Piazza, CR CNRS

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Address of the internship: ENS de Lyon, LBMC, 46, allée d'Italie 69007 Lyon

Team Website : http://www.ens-lyon.fr/LBMC/equipes/mecanique-du-genome/

Languages spoken in the lab: French and English

Previous ENS student: Nicolas Mendiboure (4th year PhD in the lab)

A mechanical basis for homolog pairing in meiosis

(PhD position available!)

Keywords: Polymer modelling, Meiosis, Chromosome dynamics

Project description:

Meiosis is the specialized cell division at the basis of sexual reproduction. It involves the formation of hundreds of DNA double-strand breaks whose repair by homologous recombination drives recognition, pairing, and physical attachment via **crossover** (CO) of the parental homologs for their proper segregation at the first meiotic division. Three phenomena underlie this recombination-driven pairing process (see **Figure 1**):

Homolog bias: how does the repair occurs preferentially on the homologous chromosome rather than the nearby sister chromatid, such as in mitosis?

Obligatory CO: how at least one, and rarely more than one CO is formed per pair of homolog?

CO interference: how does the local CO designation decision can inhibit formation of subsequent COs at a distance of several dozens to hundreds of kilobases?

The mechanism(s) underlying these three phenomena, despite being central for meiosis success and thus sexual reproduction, remains unknown decades after their identification. We know it involves chromosome structure, organized as arrays of chromatin loops anchored on a semi-rigid protein axis, but how this cytological-scale organization mediates or provides input for the molecular-scale recombination process remains unknown. We make the hypothesis that active and uncoordinated chromosome movements generate tension at the level of pioneer inter-chromosomal recombination intermediates, and that this tension is the input committing to repair as a CO. Such commitment could explain the three aforementioned enigmatic phenomena of meiosis. The goal of the internship is to define the

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requirements and force regime governing this tension using a polymer model recapitulating the main features of meiotic prophase chromosomes in budding yeast.

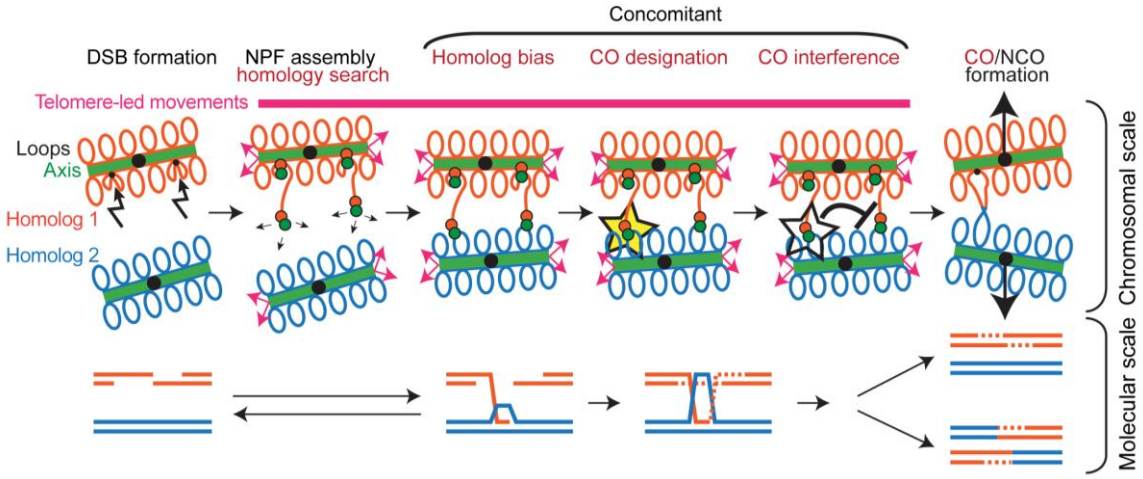

Figure 1: Overview of the molecular and chromosomal events of meiosis.

The goal of the student's internship will be to improve, interrogate, and play with a pre-existing polymer model of meiotic chromosomes developed in the laboratory by a PhD student who will oversee the candidate. A range of parameters are to be explored (chromosome length, rigidity, movement bursts and speed, etc) on first passage time and forces exerted between chromosomes. These results will in turn lead to predictions that will be tested experimentally by yeast geneticists in the laboratory thanks to an ambitious experimental system we recently developed in *S. cerevisiae*: a redesigned chromosomal region of 150-kb (SynIV) dedicated to the study of meiosis by Hi-C at high resolution (first version see Muller et al., MSB 2018). The student will have first-hand access to these data, to determine the influence of chromatin structure on chromosome pairing, homolog bias, CO designation and interference.

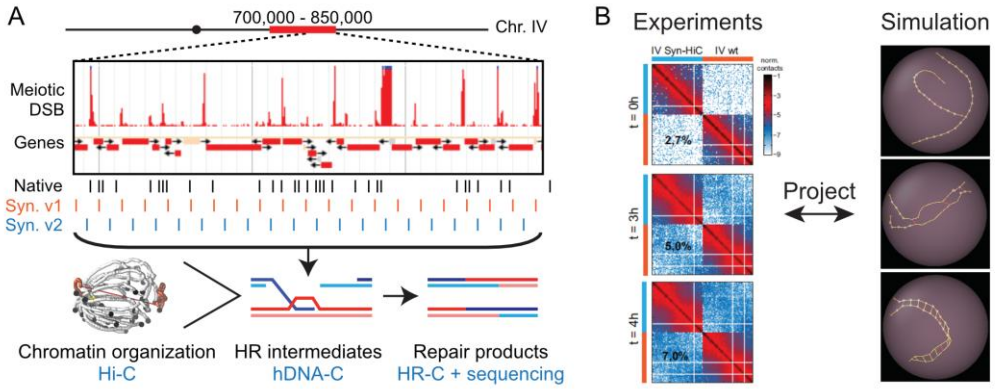

Figure 2: Experimental system to study the chromosomal and molecular events of meiosis. (A) *Redesigned region on chr. IV containing 22 meiotic hotspots.* ***(B)*** *Detection of individual homolog's structure and pairing in meiosis, obtained with the first version of the system (ref. 4). (**C**) Polymer model of meiotic chromosomes developed by a biophysicist in the lab. The project will allow comparing data and simulation to extract physical parameters dictating homologs' pairing.*

Supervision: The student will be supervised by a PhD student, the PI, and Daniel Jost (physicist in the research unit).

Techniques the candidate will learn: HiC data analysis, polymer modelling under HooMD Blue.

Research fields the candidate will gain expertise in: 3D genome organization, chromosome dynamics meiosis, polymer modeling.

Lab publications related to the subject:

1. Djeghmoum Y, **Piazza A**✉, *Donor transcription suppresses D-loops in cis and promotes genome stability*, **The EMBO Journal** 2025 doi: 10.1038/s44318-025-00541-x
2. Piveteau V, Salari H, Dumont A, Savocco J, Dupont C, Jost D, **Piazza A**✉, *Condensin loop extrusion properties, roadblocks, and role in homology search in S. cerevisiae*, **BioRxiv**, 2024 doi: https://doi.org/10.1101/2024.09.12.612585 (revision at **The EMBO Journal**)
3. Dumont A, Mendiboure N, Savocco J, Anani L, Moreau P, Thierry A, Modolo L, Jost D, **Piazza A**✉, *Mechanism of homology search expansion during recombinational DNA break repair in Saccharomyces cerevisiae*, **Molecular Cell**, 2024 Aug;632(8027):1165-1173.doi: 10.1038/s41586-024-07770-w.
4. Reitz D, Djeghmoum Y, Watson AR, Rajput P, Argueso JL, Heyer WD✉, **Piazza A**✉, Delineation of two multi-invasion-induced rearrangement pathways that differently affect genome stability, **Genes and Development**, 2023 Aug 4. doi: 10.1101/gad.350618.123. *co-last authors
5. **Piazza A***✉, Bordelet H*, Dumont A, Thierry A, Savocco J, Girard F, Koszul K✉, Cohesin regulates homology search during recombinational DNA repair, **Nature Cell Biology**, 2021 Nov;23(11):1176-1186 *co-first and °co-last authors
6. **Piazza A**, Shah SS, Wright WD, Gore SK, Koszul R, Heyer WD, *Dynamic processing of displacement loops during recombinational DNA repair*, **Molecular Cell**, 2019 Mar 21;73(6):1255-1266.e4
7. Muller, H, Scolari, VF, Agier, N, **Piazza, A**, Thierry, A, Mercy, G, Descorps-Declere, S, Lazar-Stefanita, L, Espéli, O, Llorente, B, and others (2018). *Characterizing meiotic chromosomes' structure and pairing using a designer sequence optimized for Hi-C,* **Molecular systems biology**, 14(7).