# Building the Yeast linkage disequilibrium map

Location: **Institut Curie**, Paris. '**Nuclear Dynamics**' and '**Physical Chemistry**' units.

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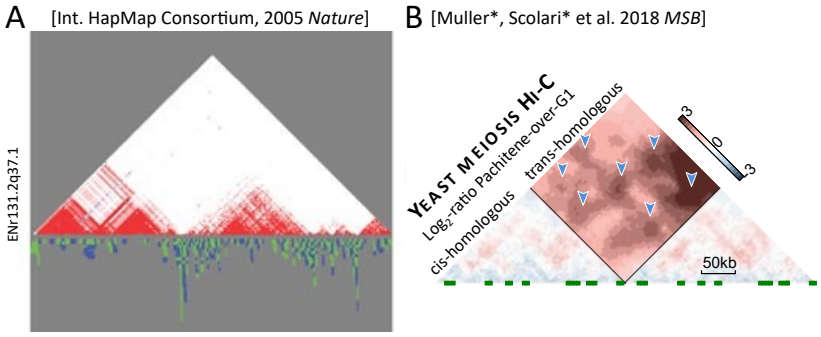
A key function of the polymeric nature of DNA is to link genes to each other and orderly pass them through generations. To ensure genetic diversity, during meiosis, genes are recombined from different chromosomes. We are interested in integrating 3D genome conformational data with evolutionary data, with the objective of modeling the propagation of genetic diversity in absence of selection, which is key to the propagation of hereditary traits and diseases (Penman et al., 2009).




(A) Linkage disequilibrium map on a region of human chromosome measured by the International HapMap Consortium (Altshuler et al., 2005), this is obtained by sequencing thousands of samples from a variety of human populations, blocks similar to TADs that represent genes/alleles whom presence is highly correlated in the population, are visible on the bottom, and recombination rates can be estimated by this block structure (lower bars). (B) Unpublished re-analysis of the Hi-C contact map on a synthetic region of chromatin specifically designed to measure trans-homologous interactions during Meiosis in Yeast, obtained in KoszulLab, in this representation it is possible to see regions of trans-homologous contacts between the bases of the Rec8 cohesin, that hints to an tightly regulated chromosomal folding in Yeast during meiosis.

## *Background*

Homologous recombination, a physiological process highly conserved from bacteria to metazoans and used for DNA repair damage, with the emergence of sexual reproduction in eukaryotes and conjugation in bacteria, has been hijacked as the elected way of combining genes from different lineages through generations. The logical consequence of this is that homologous recombination, when performing this function, should be tightly regulated to prevent hereditary diseases emerging from incompatibilities between different genes, or disruptive insertions in the case of conjugation. On the human genome, linkage disequilibrium maps, obtained by looking at the co-variance of genetic variants on samples of the human populations, show a peculiar blocky structure that points to the fact that meiosis recombination is not uniform along the genome (Altshuler et al., 2005; Figure A). Understanding how much of this can be explained by natural selection is an open question. In the case of Yeast, Hi-C studies seem to suggest that the chromatin conformation during meiosis is tightly constrained (Muller*, Scolari* et al., 2018; Figure B) and our working hypothesis is that these constraints play the fundamental role in regulating homologous recombination and the linkage disequilibrium of the genomes.

## *In practice*

At the moment, integrating data from chromatin conformation (Hi-C and FISH experiments) with evolutionary data as linkage disequilibrium map in Yeast is impeded by the fact that we currently lack a linkage disequilibrium maps for the *S. cerevisae* specie. This project will take the task of reanalyzing published data on the diversity of Yeast isolates (1011 different isolates sequenced; Peter et al., 2018) in order to obtain a linkage disequilibrium map in Yeast. This is a network/matrix of single nucleotide polymorphisms correlations, currently non-existent. And, a priory, it may look very different from the human map, or even not representable in the same format, considering that Yeast might possess different kind of variabilities and resilience to genomic instabilities. As such, the project might require the conception and development of new algorithms and theories.

## *Profile*

A naïve attempt to apply the same tools used on the Human genome with default parameters in Yeast will not give a positive outcome to the project. To calculate the Linkage Disequilibrium in Yeast, we are searching for a student with a skillset in programming and data analsys and an vibrant enthusiasm to go deep in a complex datasets. The project will require the reimplementation of known algorithms or their readaptation to be used on the Yeast 1,011-genomes raw dataset.

## *Context*

Our team studies the physical organization of the genome –in space and in time– in the nucleus and its relationship with transcriptional regulation or other functional genomic processes. We take a quantitative and interdisciplinary approach at the physics-biology interface, combining advanced microscopy, mechanical micro-manipulation and physical modeling.

Our team is part of the '**Physical Chemistry**' unit (UMR168), with physicists working on diverse biological topics and the '**Nuclear Dynamics**' unit (UMR3664), with biologists studying different aspects of the cell nucleus.

Institut Curie is a major player in cancer research. It consists of a Research Center for basic research and Hospital group for translational and clinical research. It has more than 1000 employees and is strongly international. It is an inclusive, equal opportunity employer and is dedicated to the highest standards of research integrity.

## *Application*

Contact us at vittore.scolari@curie.fr with your CV and a letter explaining your interest in joining our lab.

## *References*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