

Image-based reconstruction of nuclear organization

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Subjects / Tools-Methodologies:

- 1 : nuclear organization / computational data analysis
- 2 : chromosomes / physical models
- 3 : epigenetics / super-resolution microscopy

website: <http://www.pasteur.fr/ip/easysite/go/03b-000011-022/objectives>

Summary of lab's interests

Our group develops computational imaging and modeling techniques to gain a quantitative understanding of cell biological processes. We combine approaches from applied mathematics, physics and cell biology, either within the group or through collaborations. We develop computational methods to extract massive and high accuracy information from imaging data, which we use to constrain and test physics based models. We also implement microscopy techniques that break traditional limits of spatial resolution by coupling instrumentation with computational analysis methods. Our current work focuses on the spatial organization and dynamics of genes and chromosomes inside the nuclear volume.

Summary of project

The spatial organization of genes and chromosomes inside eukaryotic cell nuclei is not random and plays an important role in gene expression, and in the replication and repair of the genome. Despite this fundamental functional importance, the dynamic architecture of the genome remains largely uncharted. Our project aims to build a physical model of chromosomes in yeast, allowing to predict the probabilistic position of genes relative to nuclear landmarks and to each other. The proposed approach is to combine first-principle chromosome models with high throughput and high resolution experimental data obtained thanks to novel data analysis techniques. As first steps, we have recently developed a computational method to generate probabilistic maps of gene positioning with ~100 nm resolution by analyzing images containing thousands of cells (Berger et al. Nat. Meth. 2008). We have also developed a first rigid body simulation of interphase yeast chromosomes. Initial results are encouraging and suggest that gene positioning may be predictable with a relatively simple model. The PhD student is expected to play a central role in this project and will join a team currently consisting of 2 postdocs and 1 research engineer, and several collaborators. Depending on interests and coordination within the group, the proposed PhD research may include both experimental and analytical components: development of statistical methods to reconstruct chromosome conformation from different partial data sets; development of algorithms to increase resolution and throughput of imaging data; dynamic 3D imaging of living cells, with a commercial and an experimental high-resolution microscope; construction of fluorescently tagged cell lines; chromosome conformation capture experiments; physics based simulations. We seek a highly motivated student with a solid background in physics or mathematics. We expect a strong interest and willingness to participate in a highly collaborative and interdisciplinary project.