

Modelling and Engineering Genome Architecture

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Laboratory

Epigenomics Project CNRS UPS3201
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Subjects / Tools-Methodologies

- 1 : Integrative Biology/systems and synthetic biology
- 2 : Chromosome structure and evolution/molecular genetics and microbiology
- 3 : Functional organization of cell nucleus/nucleoid/bioinformatics

Summary of lab's interests

GIP Genopole® hosts an Institute of Complex Studies dedicated to modelling and simulation of complex biological processes in the post-genomic era, called the Epigenomics Project, and headed by F. Képès. The Epigenomics Project is a CNRS Unit and is the object of contracts between GIP Genopole® and University of Evry. This lab includes computer scientists, physicists and biologists / bioinformaticists. It has a long-standing tradition of multidisciplinary projects.

Summary of project

The present project aims at rationally producing a marked conversion of transcriptional regulations by moving one gene along the chromosome through directed mutagenesis. This cannot be achieved without an understanding of the interrelation between chromosomal architecture and transcriptional regulation. Such an understanding is now within reach in the form of the solenoidal model of chromosomes that was proposed in 2003 by François Képès on the basis of genomic and transcriptomic data, and developed in subsequent years with his colleagues. This model suggests a strong connection between the chromosomal architecture and the global scheme of transcriptional regulation in microorganisms. The present project aims at exploring in-depth this connection, thus paving the way to a rational engineering of whole microbial genomes. At stakes are an integrated spatio-temporal understanding of the functional organization of the cell nucleus/nucleoid, and an assessment of the impact of transcriptional dynamics in shaping genome architecture. A combination of synthetic biology, genetic engineering, systems biology and bioinformatics approaches is proposed to tackle the following new issues: - The function that relates gene expression level to global gene position along the chromosome; - The importance of transcription in the evolutionary forces that shape a chromosome; - The transcription-related mechanisms that fix evolutionarily genes at particular locations along a chromosome; - The compromise between gene position and promoter quality in determining the level of gene expression; - The physiological effects of the observed gene positional regularities; - The extent of our understanding and of our engineering capability for large-scale transcriptional regulation; - Evolutionary insights into chromosomal architecture; - Bio-inspired tools for evolutionary multi-objective optimization algorithms; - Dynamically reachable highly ordered structures of the DNA polymer. Finally, it must be noted that the understanding thus generated will provide an essential handle for any future attempt at engineering microbial genomes at a global scale for practical purposes.