ID de Contribution: **35** Type: **Non spécifié**

Probing genome organization with intra-nuclear mechanical micro-manipulation

Over the past decades, our understanding of the physical organization of the genome has improved tremendously. Developments in imaging and chromatin conformation capture have uncovered how eukaryotic chromosomes are structured at different scales (territories, compartments, TADs, loops) and how each level of organization relates to genome functions. A lot of effort is currently put on observing this organization in 4D and building physical models and concepts from observations. However, perturbation approaches to validate these concepts are often rather indirect. The lack of tools to directly exert and measure forces on nuclear and genomic structures in vivo fundamentally limits our understanding of their physical nature.

To address this gap, we are developing a novel tool to actively manipulate individual genomic loci using magnetic forces in the nucleus of living cells. It consists in targeting iron-containing nanoparticles to a genomic locus of interest and applying a controlled magnetic field. Through this approach, we are able for the first time to physically move an individual genomic locus through the nuclear space. The ability to mechanically manipulate genomic structures and observe their response in real time as they unfold offers a unique opportunity to probe their material properties at various spatial, temporal and force scales.

We will present the very first data obtained through this approach, already revealing non-trivial physical properties of chromatin, such as strongly heterogenous viscoelastic properties –reflective of different nuclear structures –and partial reversibility –as one would expect for reactive living matter. This technique opens obvious roads to probe how the physical properties of the genome at various scales relate to key genome functions, including transcription, DNA damage/repair, replication, chromosome segregation and genome integrity.

Auteurs principaux: KEIZER, Veer (Institut Curie); KOLAR-ZNIKA, Lorena (Institut Curie); BAROUX, Remi (Institut Curie); AIZEL, Koceila (Institut Curie); HOFFMANN, Sebastian (Institut Curie); FACHINETTI, Daniele (Institut Curie); DAHAN, Maxime (Institut Curie); COULON, Antoine (Institut Curie)

Orateur: COULON, Antoine (Institut Curie)