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Biophysical models of the genome structural organization

The eukaryotic genome in interphase is organized in distinct layers. Chromosomes occupy different positions in the nucleus (chromosome territories) with limited overlaps and segregate into active (A) and inactive (B) compartments spanning several mega-bases (Mb) of DNA. At the sub-Mb level, chromatin is organized into self-interacting regions (topologically associating domains or TADs) and loops. The combination of experiments and computation showed that these layers are regulated by biophysical mechanisms: limited crossing between distinct chromosome regions favors a territorial organization, (micro-)phase-separation leads to compartmentalization, and the loop-extrusion mechanism can form TADs and loops. These layers, which are referred to as the 3D Genome, do not behave like a static structure but a highly dynamic scaffold that contributes to regulating gene expression by bringing into spatial proximity genes with their activating (or silencing) regions. However, understanding the fundamental mechanisms driving the crosstalk between 3D Genome and gene expression is still lacking. In my talk, I will present examples where chromatin simulations helped to link the rearrangements of the 3D Genome during differentiation [1] or hyperacetylation treatment [2] to perturbations of the biophysical properties of chromatin in mouse cells.

References

[1] Jerkovíc et al. A Scaffolding Element Rewires Local 3D Chromatin Architecture During Differentiation. **doi**: https://doi.org/10.1101/2024.05.23.595561

[2] Paldi et al. Transient histone deacetylase inhibition induces cellular memory of gene expression and three-dimensional genome folding. **doi**: https://doi.org/10.1101/2024.11.21.624660

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