

## **Semi-analytical modeling of chromatin loop-extrusion**

At the scale of  $10^5$ - $10^6$  base pairs, human chromosomes are structured in topologically associated domains (TADs). These are regions of the chromosome within which contacts are more frequent than with adjacent regions, as measured by 'chromosome conformation capture' experiments such as Hi-C. TADs have been shown to result from the action of cohesin, a molecular motor. Cohesin binds to chromatin, reel it in, and extrude it as a loop. This process is called "loop extrusion" (Fudenberg et al. 2016). In this realm, theoretical modelling is able to answer the following questions: How much energy should the cell spend to maintain these structures? with how many concurrent motors? how fast? and how frequently? The current approach to simulate loop extrusion uses explicit molecular dynamics simulations. This approach, while very flexible, limits our possibility (i) to explore the parameter space in an efficient manner and (ii) to dissect the observed effects under the lenses of a coherent analytical theory. I will present our original approach to simulate loop extrusion, that exploits an analytical solution of the probability distribution over a conformational space for the polymer model, and the action of extruders simulated in 1D. I will show how this approach allows highlighting the hallmarks of the out-of-equilibrium processes on chromatin conformation observed in experiments. Finally, this approach permits the definition of the Gibbs entropy of chromosome conformation. I will show how the application of this concept to simplified toy-models increases our analytical understanding of the loop extrusion process.

Fudenberg G, Imakaev M, Lu C, Goloborodko A, Abdennur N, Mirny LA. 2016. Formation of Chromosomal Domains by Loop Extrusion. *Cell Reports* 15: 2038–2049.

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