Physical modeling of chromosome dynamics

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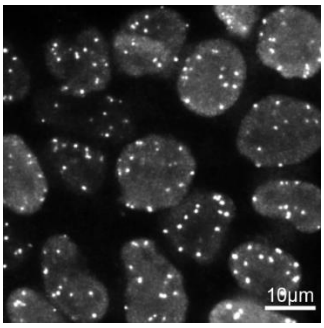
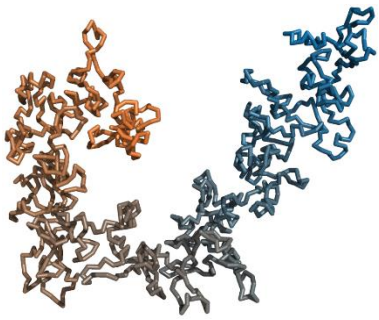
Transcriptional regulation and cis-regulatory elements, such as distal enhancers, are essential for cell life. In mammals, many lines of evidence suggest that cohesin, a protein complex that extrudes loops of DNA, mediates proximal interactions on a scale up to 1 Mb[1]. Cohesin can extrude loops until it stops at a “barrier” protein (CTCF) bound to DNA in the specific orientation[2]. However, it is unclear how loop extrusion affects chromosome dynamics globally and reciprocal dynamics at the scale of a topologically associating domain. On the one hand, being an active process, loop extrusion could increase the dynamics of chromosome fiber; on the other hand, it could decrease it by introducing constraints.

To address these questions, we perform live-cell imaging in mouse embryonic stem cells (mESCs) and build a physical model based on Langevin molecular dynamics[3]. A polymer model allows us to isolate and explain the effects of cohesin and CTCF on chromosome dynamics. By utilizing experimental or physically relevant parameters, we estimate the cohesin-mediated CTCF loop lifetime.

Our results of chromosomal contact dynamics provide a novel quantitative framework to link chromosome structure to function and show that cohesin and CTCF stabilize otherwise highly dynamic chromosome structures to facilitate selected subsets of chromosomal interactions.





References.

[1] de Wit, Elzo, and Elphège P. Nora. "New insights into genome folding by loop extrusion from inducible degron technologies." *Nature Reviews Genetics* 24.2 (2023): 73-85.

[2] Fudenberg, Geoffrey, et al. "Formation of chromosomal domains by loop extrusion." *Cell reports* 15.9 (2016): 2038-2049.

[3] Mach, Pia, Kos, Pavel, et al. "Cohesin and CTCF control the dynamics of chromosome folding." *Nature Genetics* (2022): 1-12.