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Transcription-dependent genome folding

It is well known that the enhancer-promoter interactions are essential for gene expression, but the role of RNA Polymerase II (Pol II)-mediated activity on genome folding is remain controversial. Here by investigating Micro-C data for mESCs and Drosophila embryo, we show a significant correlation between gene compaction and Pol II occupancy inside the gene, independent of cohesin-dependent loop extrusion activity. To rationalize these observations, we develop a biophysical model for the transcription-dependent folding of the genome by coupling a mathematical description of gene transcription (binding, initiation, elongation, termination of Pol II) and a polymer model of chromosome organization integrating effective Pol II-Pol II attractive interactions. Systematic analysis of the model allows to mechanistically investigate the role of gene length, gene activity or transcriptional bursting on the spatio-temporal dynamics of gene, in agreement with experimental observations. Our work provides solid proofs that transcriptional activity shapes the 4D genome via (micro)phase separation mediated by Pol II.

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