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Out of equilibrium dynamics of a cross-linking polymer: chromatin as a case study

The structural investigation of large macro-molecular assemblies is an essential step towards understanding the molecular mechanisms at work in cells. Due to the very unstable and labile nature of these assemblies most assays rely on a fixation step, typically achieved using formaldehyde cross-linking, to freeze and capture contacts made by proteins and nucleic acids. Propelled by rapid technological advances such as ChIP-seq and Hi-C chromatin structure is today field of intense activity. Here we use Hi-C which maps contacts between genomic regions both within and between chromosomes in order to quantify the chromatin distortion induced by irreversible cross-link. The analysis of the polymeric structure emerging from the contact maps shows the presence of two different organizations at short and long distances. The large distance behavior reflects the in-vivo structure of the chromosomes and can be interpreted in terms of classical equilibrium polymer model. On the other hand, the short distance behavior depends on the concentration of the cross-linking agent and on exposure time and cannot be interpreted by an equilibrium dynamics. By modeling the cross-linking effect as a polymer irreversible collapse we were able to quantitatively describe this short distance polymeric structure.

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