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To knot or not to knot

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The enzyme topoisomerase II catalyzes the passage of one DNA duplex across another, modulating chromosome supercoiling, condensation, and catenation during essential eukaryotic cell processes. In principle, microscopically these DNA topology relaxing enzymes may create or relax entanglements. In order for macroscopic scale relaxation to occur, this symmetry must somehow be broken. An interplay between network connectivity and topology-relaxing activity must govern the propagation of stresses across long length scales.

In addition to canonical membrane-bound organelles, eukaryotic cells contain membraneless compartments, or biomolecular condensates, that concentrate specific collections of proteins and nucleic acids. Many of these compartments form through liquid-liquid phase separation (LLPS), and the principles, mechanisms and regulation of their assembly and cellular functions are emerging. Eukaryotic topoisomerase II has been shown to form condensates with DNA by LLPS.

We exploit this LLPS as a platform for studying the strand passage activity in a tunable condensation environment. Our work contributes biophysical understanding of these condensates and specific novel insights into the strand passage activity of the topology relaxing enzyme through a combination of in vitro creation of this physiologically relevant state, quantitative fluorescence imaging, and active and passive microrheology.

Keyword-1

Keyword-2

Keyword-3

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