New and Notable

Chromosome Condensation: Amorphous or Structured

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Since eukaryotic chromosome condensation and segregation was first observed in the light microscope more than a century ago, the process has attracted the imagination of nearly all students with the opportunity to observe the dynamics of this process. As the understanding of the structural components of the metaphase chromosome has become clarified, molecular reductionism has been increasingly challenged by this process. A chromatid of a human chromosome contains a single DNA molecule with a length of several centimeters and a diameter of 20 angstroms. In the course of the cell cycle, this DNA molecule is confined to a volume with a largest linear dimension of approximately 5 microns, and upon replication, the two daughter molecules are resolved or segregated with the complete elimination of entanglements. It is not surprising that the mechanisms of condensation and decondensation, and the mechanisms of packing the DNA molecule into structural fibers would attract the attention of polymer theorists. The article by Sikorav and Jannink (1993) entitled "Kinetics of chromosome condensation in the presence of topoisomerases: a phantom chain model" discusses the condensation of chromosome as though it is caused by the change of solvent from good solvent to poor solvent. On the basis of existing theories that deal with polymer aggregation accompanied by solvent exclusion in polymer melts, the observed kinetics of chromosome condensation are far too rapid to fit the theoretical condensation rates predicted by this model.

The "phantom chain model" allows polymer chains to pass through each other, thus enhancing the predicted rates of the condensation process to values consistent with chromosome condensation rates. The topo II activity known to be associated with chromosomes is considered to be the rationalization of this "pass through" or "phantom" model. The application of classical polymer hydrodynamic theories has been historically important for our understanding of the properties of biological macromolecules, and for this reason alone, such analyses should be encouraged and accepted for publication. Only in this way will they be subjected to scientific scrutiny. There are, however, serious issues, ignored in this manuscript, that are an important part of the DNA and chromatin literature.

First, the concentration of nucleoprotein in metaphase chromosomes is difficult to estimate, but I believe it is less than that of a pure melt that would exclude all solvent. In fact, my estimate is that even at metaphase, the nucleoprotein occupies, at best, 6% of the volume of the chromosome, the rest being occupied by solvent.

Second, a theory based on reptation is very sensitive to the existence of polymer ends and to the mechanical properties of the polymer fibers. The interphase and metaphase chromosome fibers contain essentially no ends, making reptation in the absence of further assumptions of looping and pairing of fibers a very speculative model to deal with.

Third, there is a rather unusual oversimplification and classification of topological constraints in this paper into two categories: "plectonemic supercoiling of the DNA duplex" or an "ordinary polymeric constraint." Such an analysis ignores the possibility of higher order helicity, for example, plectonemic forms of the 11-nm- or 30-nm fibers, which I consider to be far more likely mechanisms for chromosome condensation than simple "precipitation."

Finally, the cleavage and rejoining by topo II in a DNA melt environment is a very hazardous mechanism to advocate for chromosome condensation, for at such high concentration, what provides the free energy to create a systematic direction for such an activity? Extensive entanglement and knotting of the DNA would be likely, and undoing such a process might very well be the undoing of life itself.

Although the article by Sikorav and Jannink is intellectually of interest and of high quality, I am of the opinion that a more systematic mechanism must be at the heart of chromosome condensation.

REFERENCES

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The Complexities of Cardiac Cables: Virtual Electrode Effects

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When the heart is stimulated by a cathodal (negative) current pulse applied by a point electrode, the resulting depolarization of a small region of tissue at the electrode triggers a propagating, depolarization wavefront that expands outward from the electrode. This wavefront can be detected by optical measurements of the transmembrane potential, microelectrode measurements of the intracellular potential, extracellular measurements of the voltage gradients associated with the extracellular current, or magnetic measurements of the combined intracellular and

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