Researchers uncover key mechanisms in chromosome structure development

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Researchers at Rice University are making strides in understanding how chromosome structures change throughout the cell's life cycle. Their study on motorized processes that actively influence the organization of chromosomes appears in the *Proceedings of the National Academy of Science.*

"This research provides a deeper understanding of how motorized processes shape chromosome structures and influence cellular functions," said Peter Wolynes, study co-author and the D.R. Bullard-Welch Foundation Professor of Science. Wolynes is also a professor of chemistry, biosciences, physics and astronomy and the co-director of the Center for Theoretical Biological Physics (CTBP).

The research introduces two types of motorized chain models: swimming motors and grappling motors. These motors play distinct roles in manipulating chromosome structure.

Swimming motors, similar to RNA polymerases—enzymes that copy DNA sequences into RNA—help expand and contract the chromatin fiber as the genes are decoded. Grappling motors bring distant segments of chromatin fibers together, creating long-range correlations that are needed to keep the chromosome knot-free.

Motor proteins, which consume chemical energy, are pivotal in shaping the architecture of chromosomes. The researchers explored how these proteins impact ideal polymer chains.

They found that swimming motors can lead to either contraction or expansion depending on the forces exerted. In contrast, grappling motors produce consistent long-range effects, aligning with the patterns seen in Hi-C experiments, which identify chromatin interactions in the cell nucleus during interphase, a stage in the cell cycle when a cell is not dividing and chromosomes are decondensed and spread throughout the nucleus. The motors that do this are particularly weak and would easily stall when forming loops, so the researchers looked for a way to speed them up.

"This study is notable for its use of theoretical modeling of chromosome chain organization by motor proteins," said Zhiyu Cao, study co-author and a graduate student at CTBP.

Using a statistical mechanics approach, the researchers created a self-consistent description that predicts the spatial distribution of loop extrusion probabilities. This model resolved how the motors' responses to the forces exerted by the randomly tumbling DNA can be overcome, so they can still carry out the packing needed to fit the long chain of chromosomes into the microscopic cell nucleus.

The three-dimensional organization of the chromosomes affects vital biological processes such as DNA replication and the differentiation of cells as embryos develop.

More information: Zhiyu Cao et al, Motorized chain models of the ideal chromosome, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2407077121

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