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**Topology, structure and energy landscape of human chromosomes** BIN ZHANG, PETER WOLYNES, Rice University — The genomes' three-dimensional (3D) organization is crucial in regulating many biological processes, including gene regulation, DNA replication, and cell differentiation. We develop a statistically rigorous approach based on maximum entropy principle to determine a least-biased potential energy landscape that reproduces experimentally determined Hi-C contact frequency between genome pairs. The resulting energy landscape supports a knotless chromosome conformation, which has been highly anticipated since complex knotted conformations prohibit the access of gene information for transcription and hinder DNA replication. We further show that the topologically associating domain signal alone also enforces a chromosome structure free of knots. Our results highlight the importance of local interactions in determining the global topology of the chromosome structure. Finally, the derived landscapes for multiple chromosomes support the formation of territories that have long been observed in microscopy experiments. Together with Hi-C experiments, our approach provides a coherent picture of the 3D architecture of the genomes that is consistent with many the available experimental data.

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