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How the genome folds[1]

EREZ LIEBERMAN AIDEN, Harvard Society of Fellows

I describe Hi-C, a novel technology for probing the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing. Working with collaborators at the Broad Institute and UMass Medical School, we used Hi-C to construct spatial proximity maps of the human genome at a resolution of 1Mb. These maps confirm the presence of chromosome territories and the spatial proximity of small, gene-rich chromosomes. We identified an additional level of genome organization that is characterized by the spatial segregation of open and closed chromatin to form two genome-wide compartments. At the megabase scale, the chromatin conformation is consistent with a fractal globule, a knot-free conformation that enables maximally dense packing while preserving the ability to easily fold and unfold any genomic locus. The fractal globule is distinct from the more commonly used globular equilibrium model. Our results demonstrate the power of Hi-C to map the dynamic conformations of whole genomes.

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