Three-Dimensional Organization of Chromosome Territories and the Human Cell Nucleus

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and
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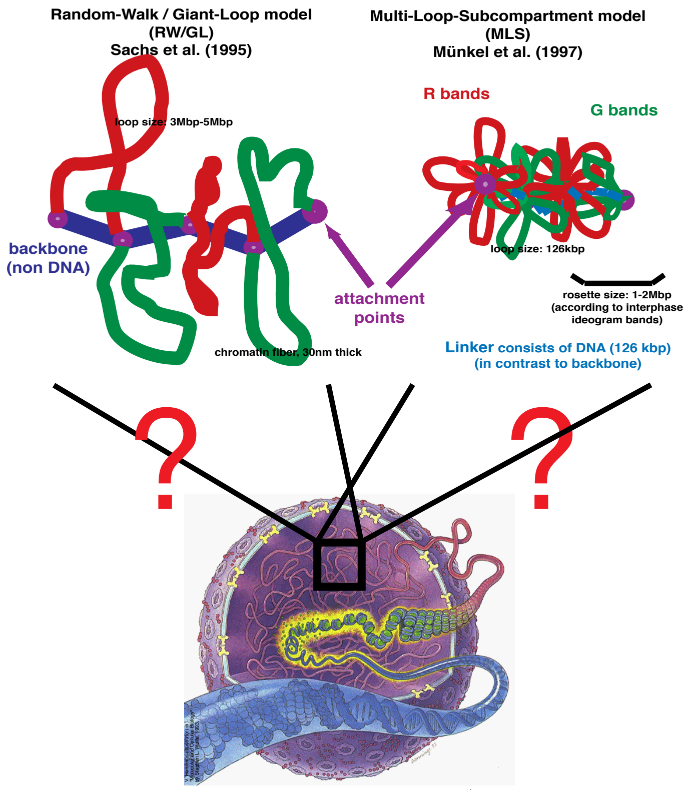
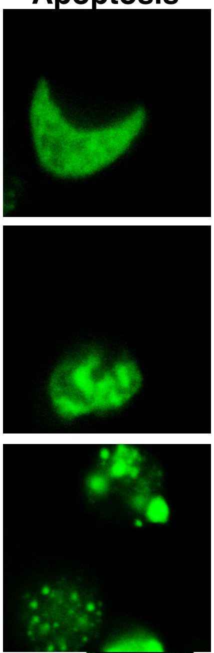
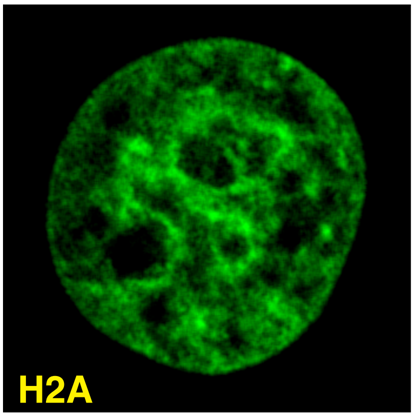
Biophysics of Macromolecules
DKFZ



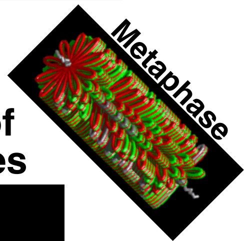
Apoptosis

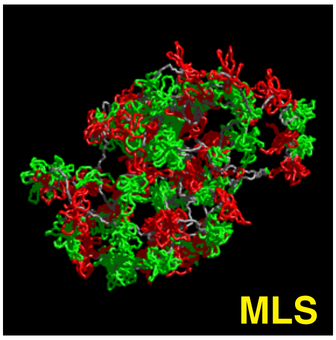


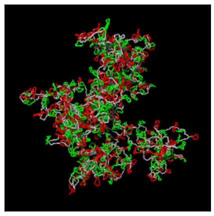
Chromatin Labeling in vivo

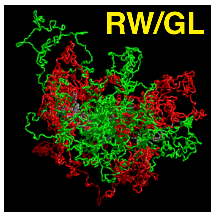


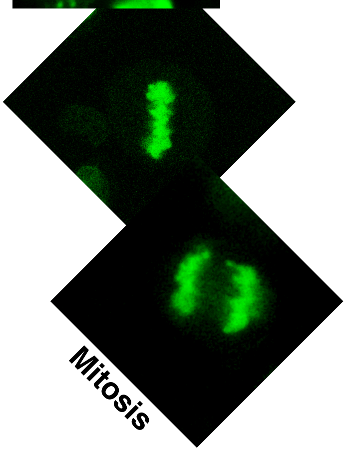
Simulation of Chromosomes

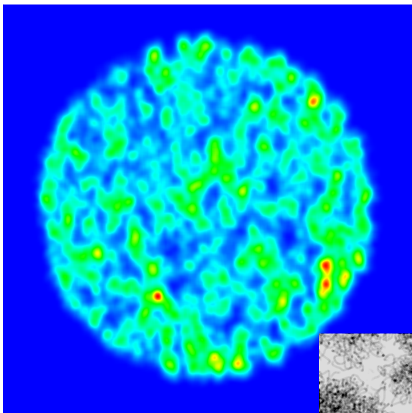




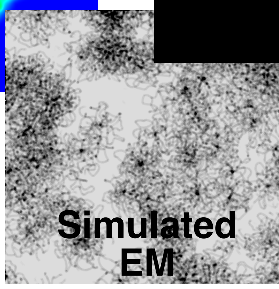






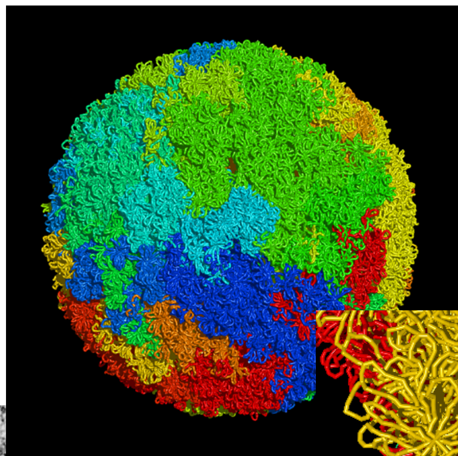


Simulated Confocal Image



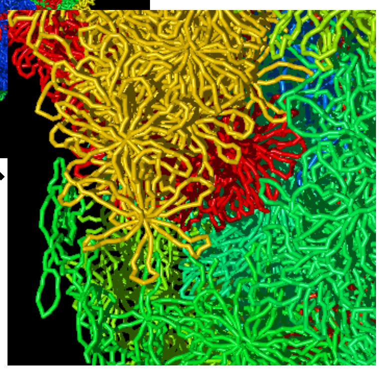
Simulated EM

Simulation of Nuclei



Diffusion

Dynamics of Structure



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an the
Human Cell Nucleus

Knoch, T. A.

Three-dimensional organization of chromosome territories and the human cell nucleus.
SBD, Heidelberg, Germany, Dezember, 1999.

Abstract

To study the three-dimensional organization of chromosome territories and the human interphase cell nucleus we developed models, which could be compared to experiments. Despite the successful linear sequencing of the human genome its 3D-organization is widely unknown. Using Monte Carlo and Brownian dynamics simulations we managed to model the chromatin fiber as a wormlike-chain polymer. A typical chromosome consists of 20.000 and a nucleus with all 46 chromosomes of 1.200.000 polymer chain segments. The parallel simulations are performed on a SP2512 and a Cray T3E. With fluorescent in situ hybridization and confocal microscopy we determined genomic marker distributions and chromosome arm overlap.

Best agreement between simulations and experiments is reached for a Multi-Loop-Subcompartment model (126 kbp loops connected to rosettes connected by a 126 kbp chromatin linker). A fractal analysis of simulations leads to multi-fractal behaveour in good agreement with porous network research. The formation of chromosome territories was shown as predicted and low overlap of chromosomes and their arms was also reached in contrast to other models.

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Keywords:

Genome, genomics, genome organization, genome architecture, structural sequencing, architectural sequencing, systems genomics, coevolution, holistic genetics, genome mechanics, genome function, genetics, gene regulation, replication, transcription, repair, homologous recombination, simultaneous co-transfection, cell division, mitosis, metaphase, interphase, cell nucleus, nuclear structure, nuclear organization, chromatin density distribution, nuclear morphology, chromosome territories, subchromosomal domains, chromatin loop aggregates, chromatin rosettes, chromatin loops, chromatin fibre, chromatin density, persistence length, spatial distance measurement, histones, H1.0, H2A, H2B, H3, H4, mH2A1.2, DNA sequence, complete sequenced genomes, molecular transport, obstructed diffusion, anomalous diffusion, percolation, long-range correlations, fractal analysis, scaling analysis, exact yard-stick dimension, box-counting dimension, lacunarity dimension, local nuclear dimension, nuclear diffuseness, parallel super computing, grid computing, volunteer computing, Brownian Dynamics, Monte Carlo, fluorescence in situ hybridization, confocal laser scanning microscopy, fluorescence correlation spectroscopy, super resolution microscopy, spatial precision distance microscopy, autofluorescent proteins, CFP, GFP, YFP, DsRed, fusionprotein, in vivo labelling.

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