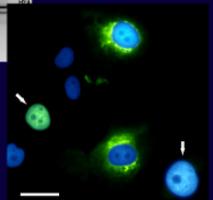
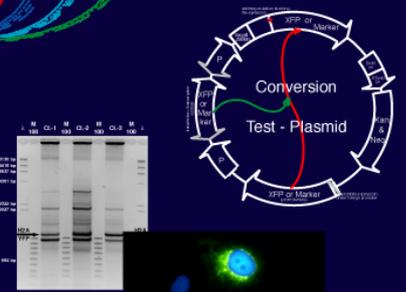
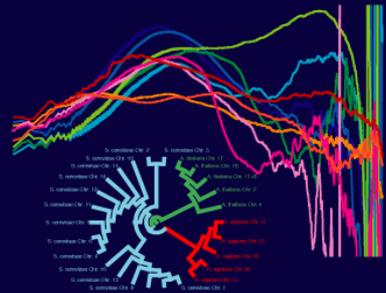
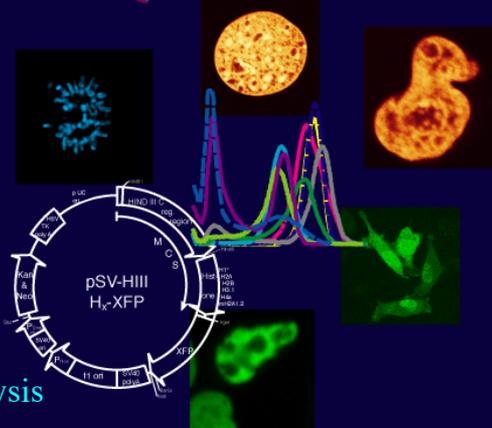
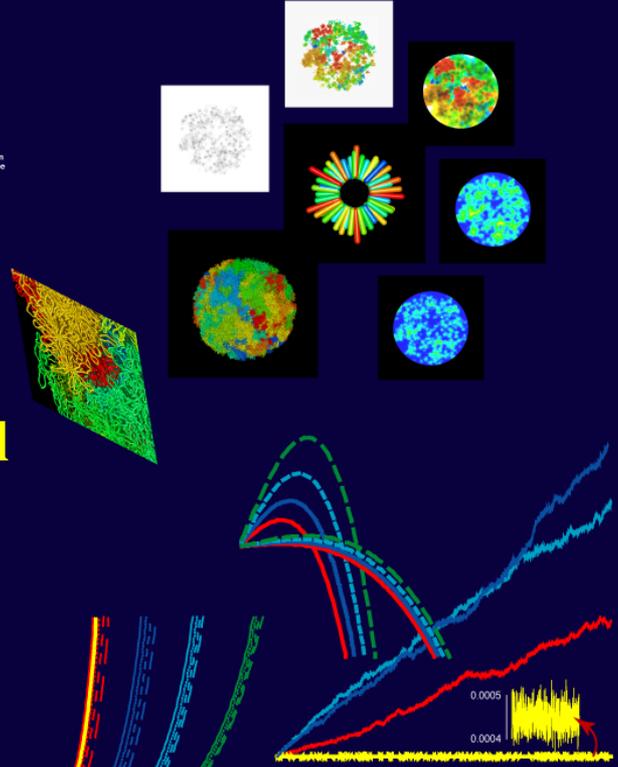
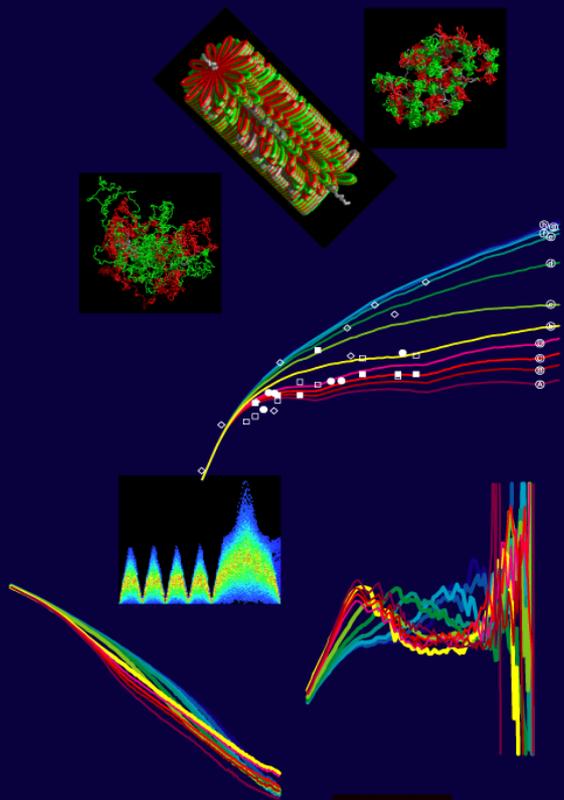


# Approaching the Three-Dimensional Organization of the Human Genome

Tobias A. Knoch

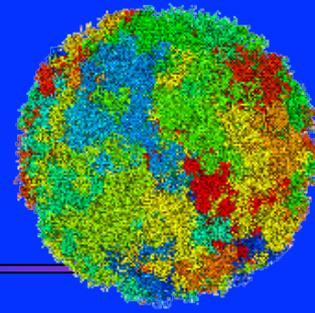


Construct Conversions in Simultaneous Co-Transfections

In Vivo Analysis of the Chromatin Distribution

Long-Range Correlations in Completely Sequenced Genomes

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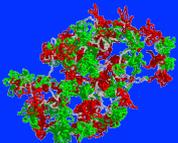
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**Approaching the Three-Dimensional Organization and Dynamics  
of the  
Human Genome**

**Knoch, T. A.**

*Klaus Görtler Prize Lecture, 15th Heidelberg Cytometry Symposium, German Cancer  
Research Centre (DKFZ), Heidelberg, Germany, 17th - 19th October, 2002.*

***Abstract***

*To approach the still largely unknown sequential and three-dimensional organization of the human cell nucleus, the structural-, scaling- and dynamic properties of interphase chromosomes and cell nuclei were simulated on the 30nm chromatin fiber level with Monte Carlo, Brownian Dynamics and parallel computing methods. Differences between used models explain various experimental conditions, favouring a Multi-Loop-Subcompartment model with 63-126kbp loops aggregated to possibly rosettes connected by 63-126kbp linkers, and predict correctly the transport of molecules by moderately obstructed diffusion excluding the Inter-Chromosomal Domain hypothesis. Correlation analyses of completely sequenced Archaea, Bacteria and Eukarya chromosomes revealed fine-structured positive long-range correlations due to codon, nucleosomal or block organization of the genomes, allowing classification and tree construction. By construction and expression of fusion proteins from the histones H1, H2A, H2B, H3, H4 and mH2A1.2 with the auto-fluorescent proteins CFP, GFP, YFP, DsRed-1 and DsRed-2, the chromatin morphology could be investigated in vivo during interphase, mitosis or apoptosis and revealed different interphase morphologies for cell lines, quantifiable by scaling analyses. Finally, construct conversions in simultaneous co-transfections due to recombination/ repair/replication were discovered in  $\leq 25\%$  of cells and led to a variety of new applications.*

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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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