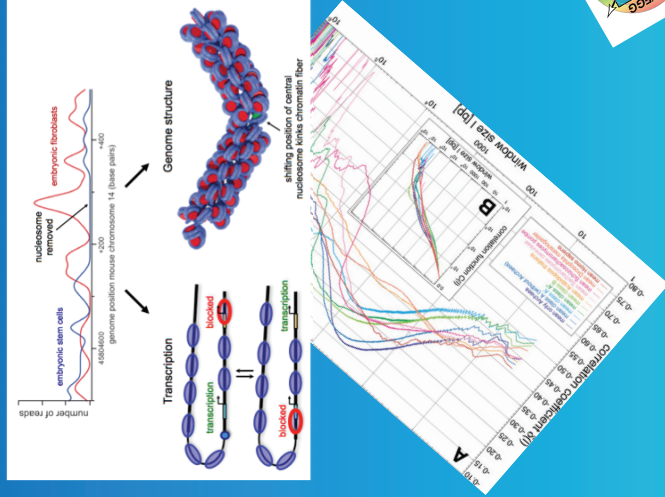
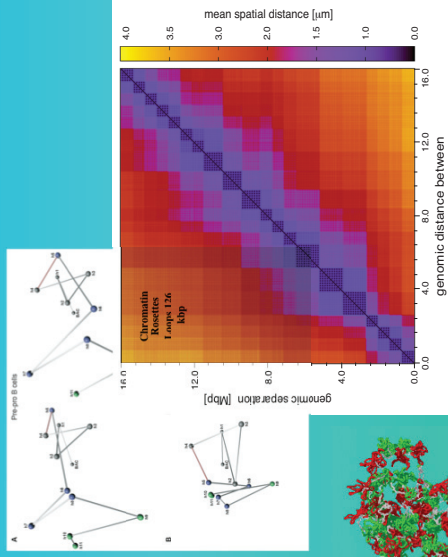


Nucleosomal Association Changes



Intra/Inter Chromosomal Architecture



EpiGenSys

Systems Biological Determination of the

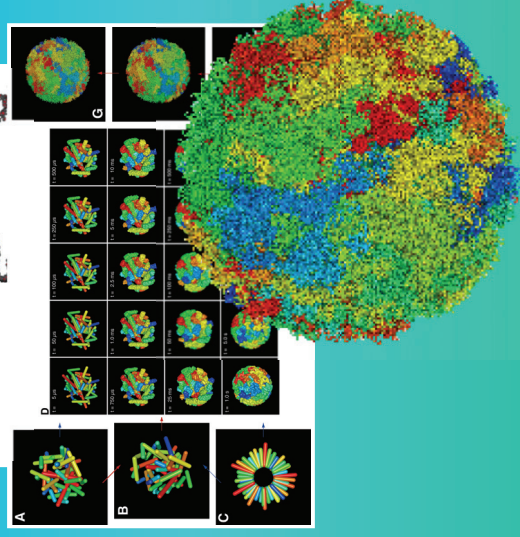
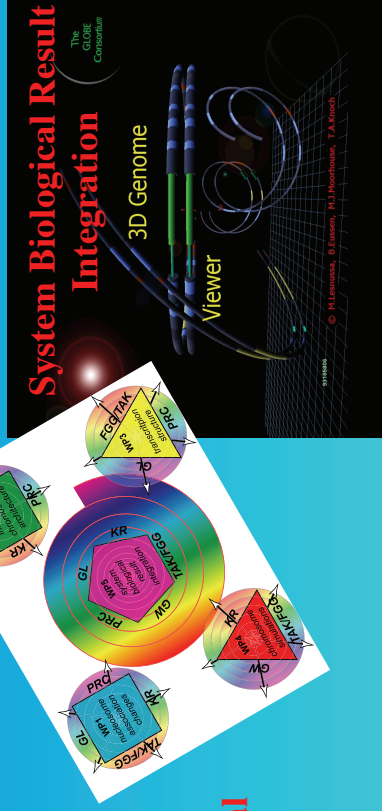
Epigenomic Structure Function Relation

Peter R. Cook, Karsten Rippe, Gernot Längst,

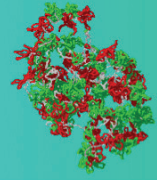
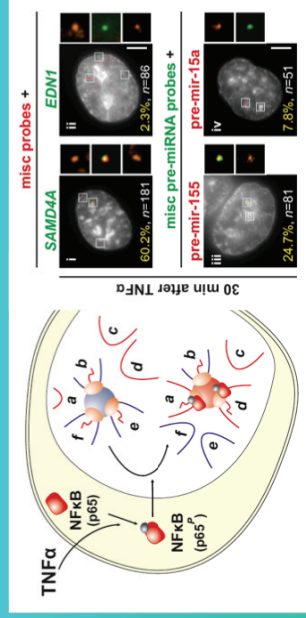
Gero Wedemann, Frank G. Grosveld,

Tobias A. Knoch

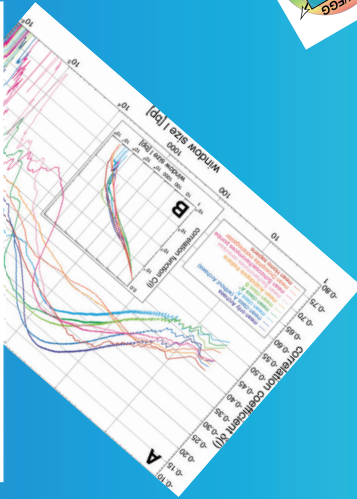
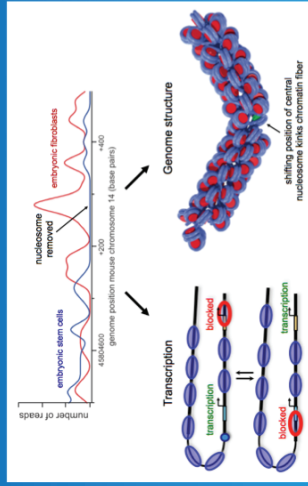
Simulation Nucleosome & Chromatin Fibre Architecture/Dynamics



Transcription <-> Structure



Nucleosomal Association Changes



Intra/Inter Chromosomal Architecture

EpiGenSys

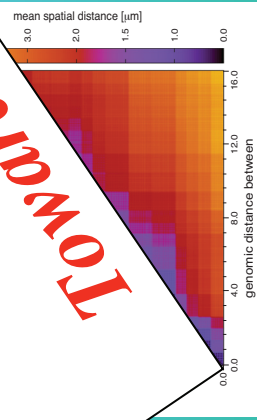
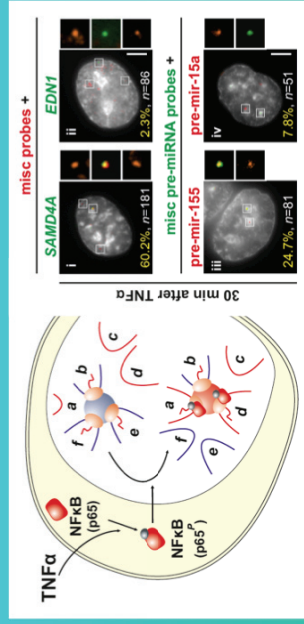
Systems Biological Determination of the Epigenomic Structure Function Relationship

Peter R. Cook, Karsten Rippe, Gero Wedemann, Frank

Tobias

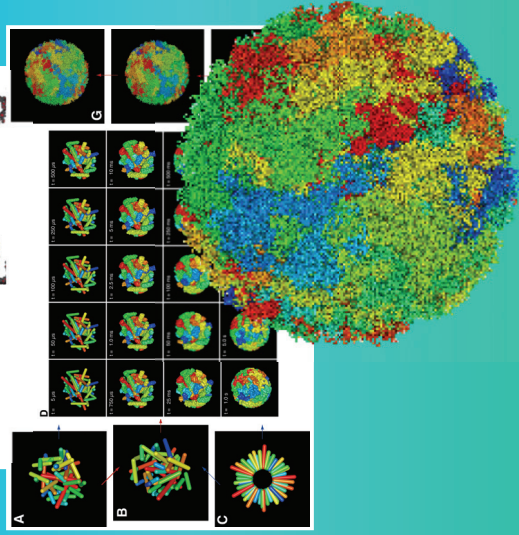
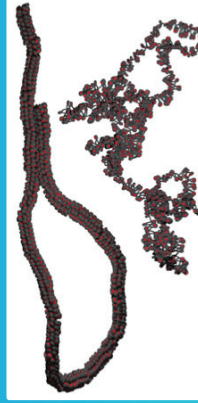


Transcription <-> Structure



From Sequence to Morphology: Understanding of Genomes!

Simulation Nucleosome & Chromatin Fibre Architecture/Dynamics



BBSRC
EMASysBio
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Consortium
University of Regensburg
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Fachhochschule
JKU Linz
JKU Linz
JKU Linz

On the Detailed
3D Multi-Loop Aggregate/Rosette Chromatin Architecture
and
Functional Dynamic Organization
of the
Human and Mouse Genome

Knoch, T. A.

EpiGenSys EU Funding Meeting, June, 2012.

Abstract

Although the sequence of the human genome is known, the relation of its three-dimensional dynamic architecture with its function – the storage and expression of genetic information – remains one of the central unresolved issues of our time. Here we show how simulations of the structural-, scaling- and dynamic properties of interphase chromosomes and cell nuclei with Monte Carlo and Brownian Dynamics methods (WP4) can be combined with experimental structure preserving 3D FISH combined with high-resolution fluorescence microscopy that allows determination of the centre of mass of target fluorophors at a resolution of ~30 nm – beyond the classical resolution limit (WP2), *in vivo* chromatin labelling (WP2) as well as our newly developed combination of chromosome conformation capture technology and high-throughput deep sequencing (WP2). Best agreement is reached both for the Prader-Willi/Angelmann region and the Immunoglobulin heavy-chain (Igh) locus for a Multi-Loop-Subcompartment (MLS) model of chromosome organization predicting 60-150 kbp loop aggregates separated by a similar linker. Beyond, DNA sequence correlation analysis of completely sequenced genomes reveals fine structured multi-scaling long-range correlations. The fine structure in the human case is attributable to nucleosome positioning (WP1) and transcription (WP3). In summary, genomes show a complex sequential and three-dimensional organization related closely to each other in a system biological/medical co-evolutionarily developed entity.

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Keywords:

Genome, genomics, genome organization, genome architecture, structural sequencing, architectural sequencing, systems genomics, coevolution, holistic genetics, genome mechanics, genome statistical mechanics, genomic uncertainty principle, multilism genotype-phenotype, 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 quasi 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, polymer model, analytic mathematical model, Brownian Dynamics, Monte Carlo, fluorescence *in situ* hybridization (FISH), targeted chromatin capture (T2C) confocal laser scanning microscopy, fluorescence correlation spectroscopy, spatial precision distance microscopy, super-resolution microscopy, two dimensional fluorescence correlations spectroscopy (2D-FCS) auto-fluorescent proteins, CFP, GFP, YFP, DsRed, fusion protein, *in vivo* labelling, information browser, visual data base access, holistic viewing system, integrative data management, extreme visualization, three-dimensional virtual environment, virtual paper tool, human ecology, e-human grid ecology, society, social systems, e-social challenge, inverse tragedy of the commons, grid phenomenon, micro-sociality, macro-sociality, autopoietic tragedy of social sub-systems, micro subsystems, macro subsystems, micro operationality, macro operationality, grid psychology micro riskmanagement, macro riskmanagement.

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