EpiGenSys

-

Systems Biological Determinatio

of the

Epigenomic Structure F

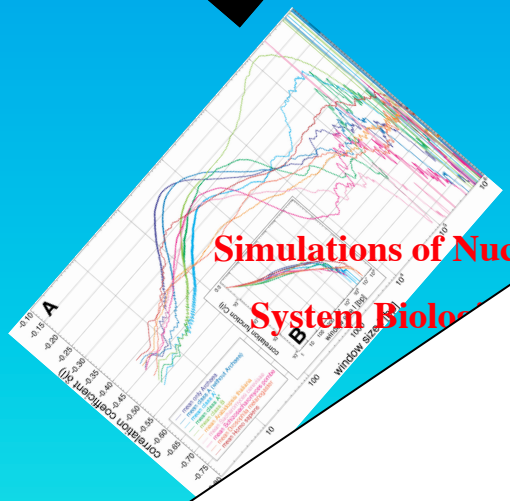
Nucleosomal

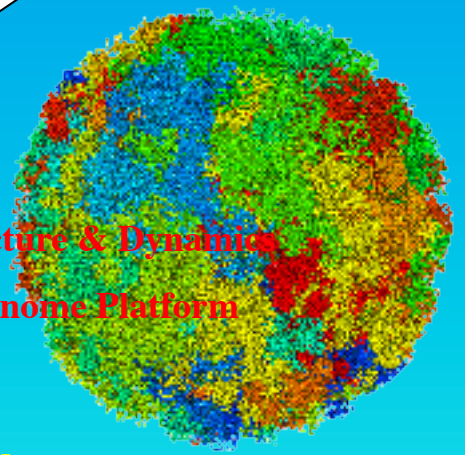
Intra/Inte re

Tra tionship

Simulations of Nucleo Chromosome Architecture & Dynamics

System Biolo ation via the GLOBE 3D Genome Platform





obias A. Knoch

Genomics & Erasmus Computing Grid

Pet Kippe, Gernot Längst, Gero Wedemann, & Frank G. Grosveld

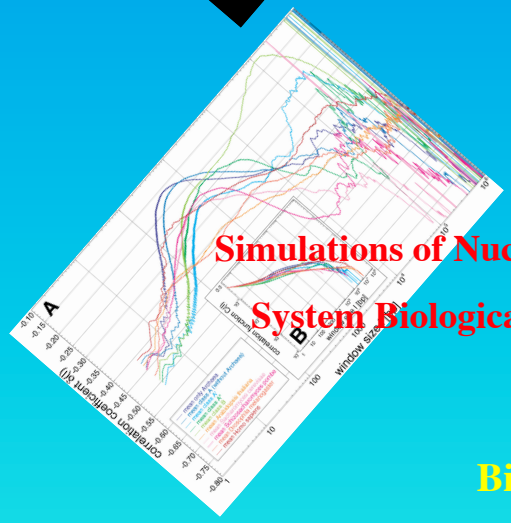
Sir W of Pathology, Genome Organization & Function, NWFIII/Biochemistry, System
Eng nformation Management, Cell Biology & Genetics - Clinical Genetics & Virology

Unive y of Oxford, BioQuant Centre / German Cancer Research Centre,
University of Regensburg, University of Applied Sciences Stralsund,
Erasmus Medical Centre

EpiGenSys

-

Systems Biological Determination of the Epigenomic Structure Function Relation



Nucleosomal Association Changes

Intra/Inter Chromosomal Architecture

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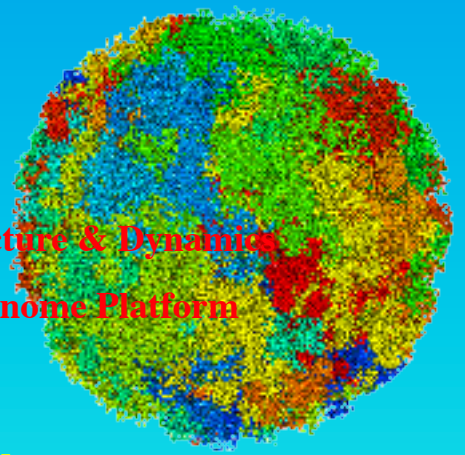
System Biological/Medical Result Integration via the GLOBE 3D Genome Platform



Tobias A. Knoch

Biophysical Genomics & Erasmus Computing Grid

Peter R. Cook, Karsten Rippe, Gernot Längst, Gero Wedemann, & Frank G. Grosveld

Sir William Dunn School of Pathology, Genome Organization & Function, NWFIII/Biochemistry, System Engeneering and Information Management, Cell Biology & Genetics - Clinical Genetics & Virology

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EpiGenSys

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Systems Biological Determinatio

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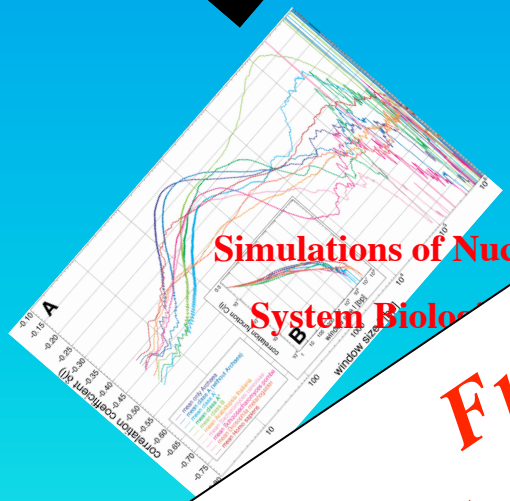

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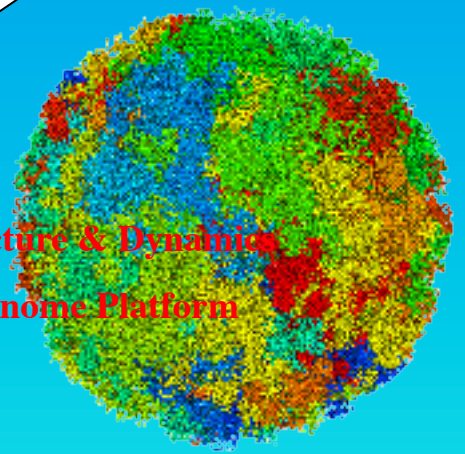

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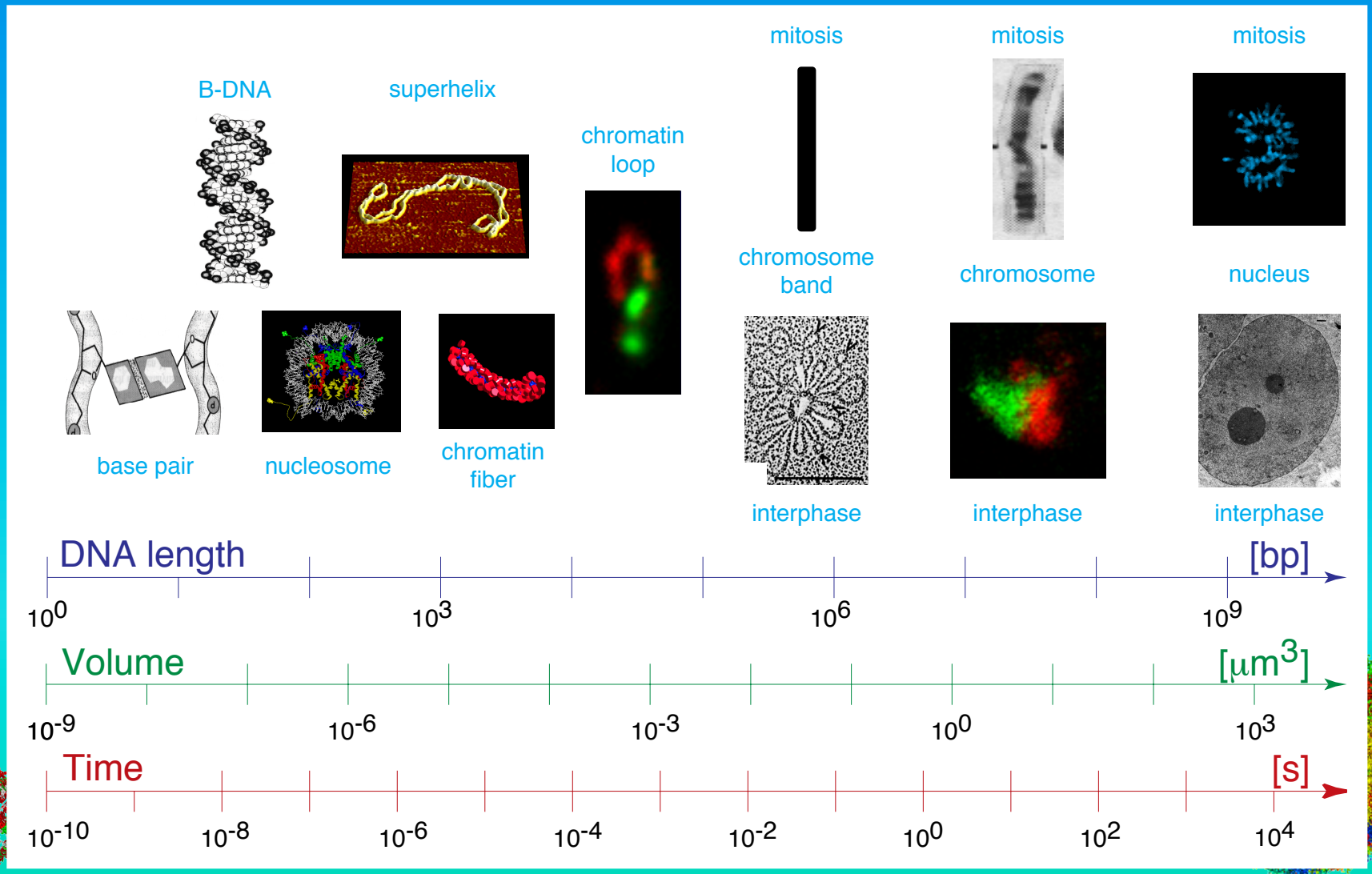
From Sequence to Morphology: Towards a Holistic Understanding of Genomes!

Dynamic and Hierarchical Genome Organization

The different organization levels of genomes bridge several orders of magnitude concerning space and time. How all of these organization levels connect to processes like gene regulation, replication, embryogeneses, or cancer development is still unclear?



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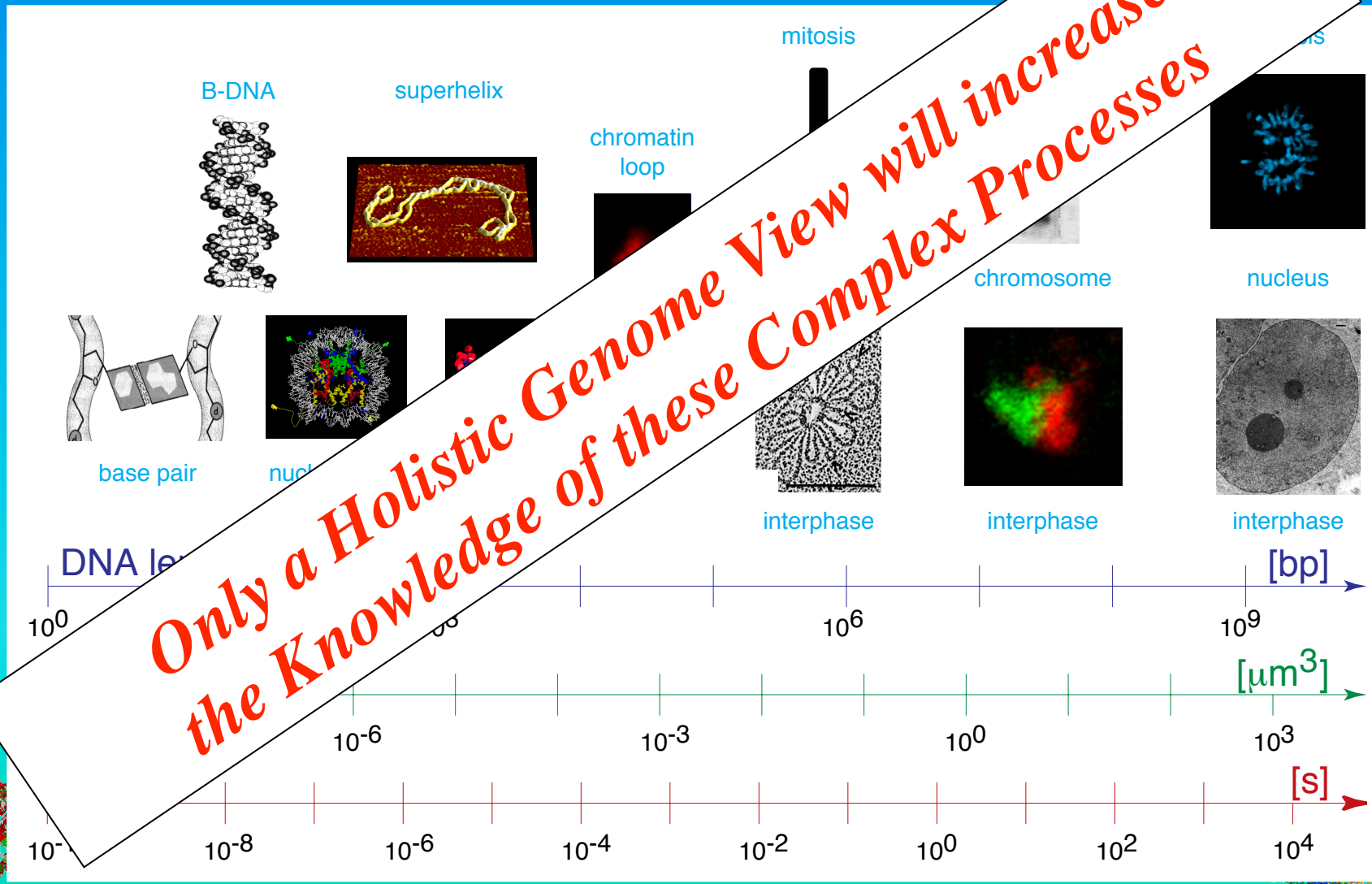
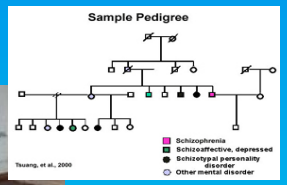


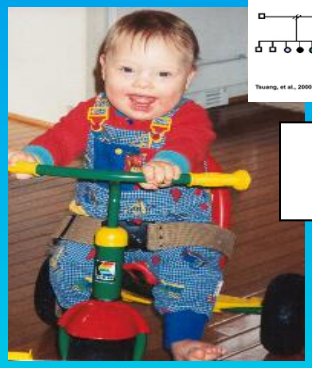
Only a Holistic Genome View will increase the Knowledge of these Complex Processes

Complexity of e.g. Cytogenetic Diagnostics & Treatment

The process of cytogenetic analysis requires proper patient and sample analysis as well asa comprehensive evaluation of the results.

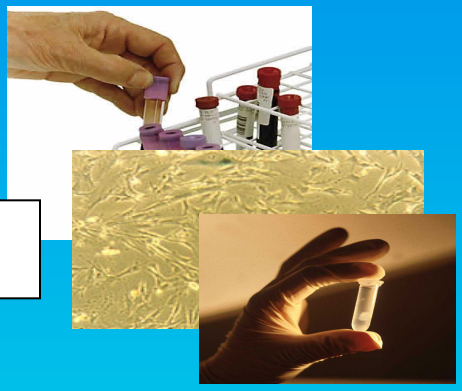
Patient

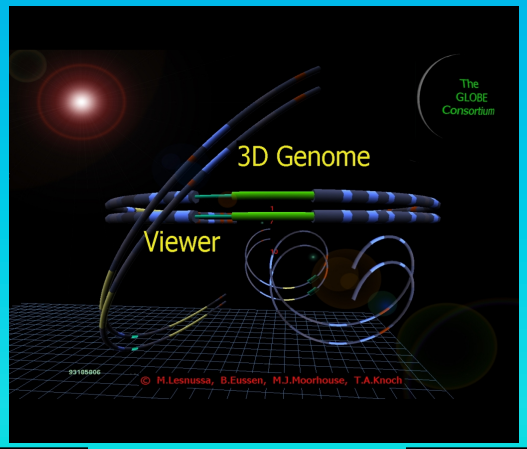


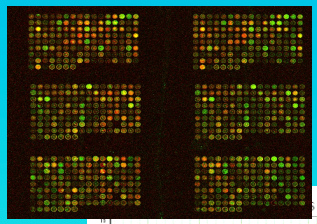


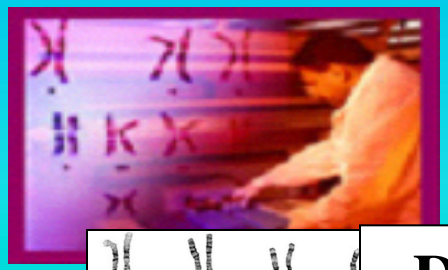
Treatment

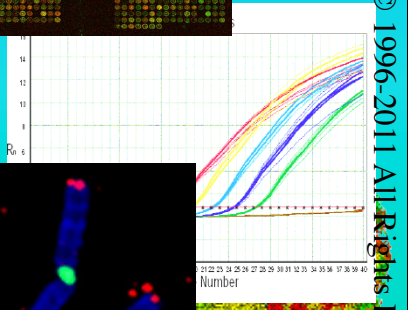
Sample





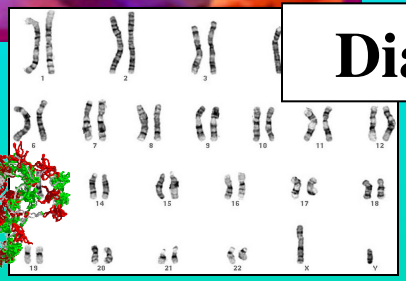


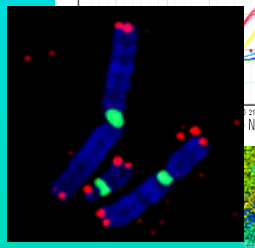




Diagnosis

Analysis





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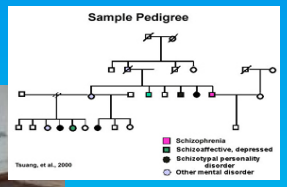

Patient

Treatment

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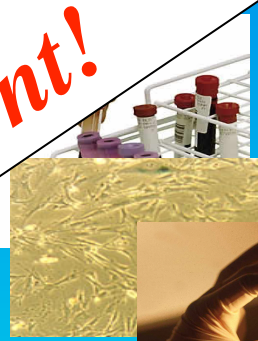

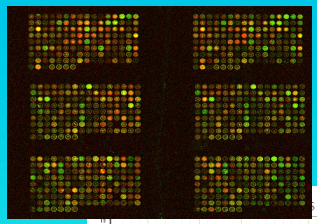

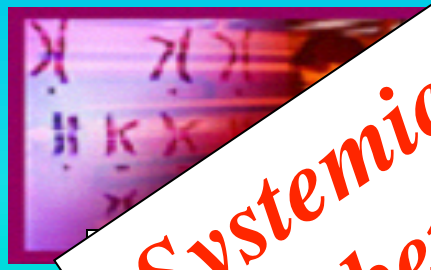

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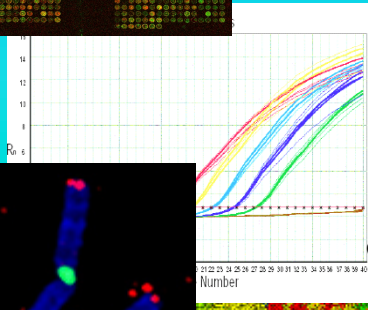
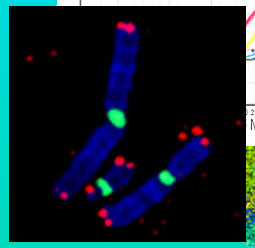
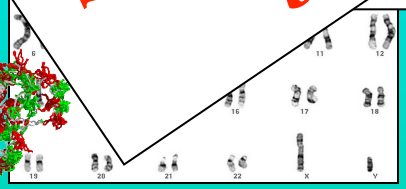
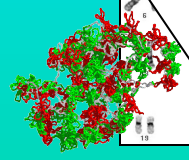




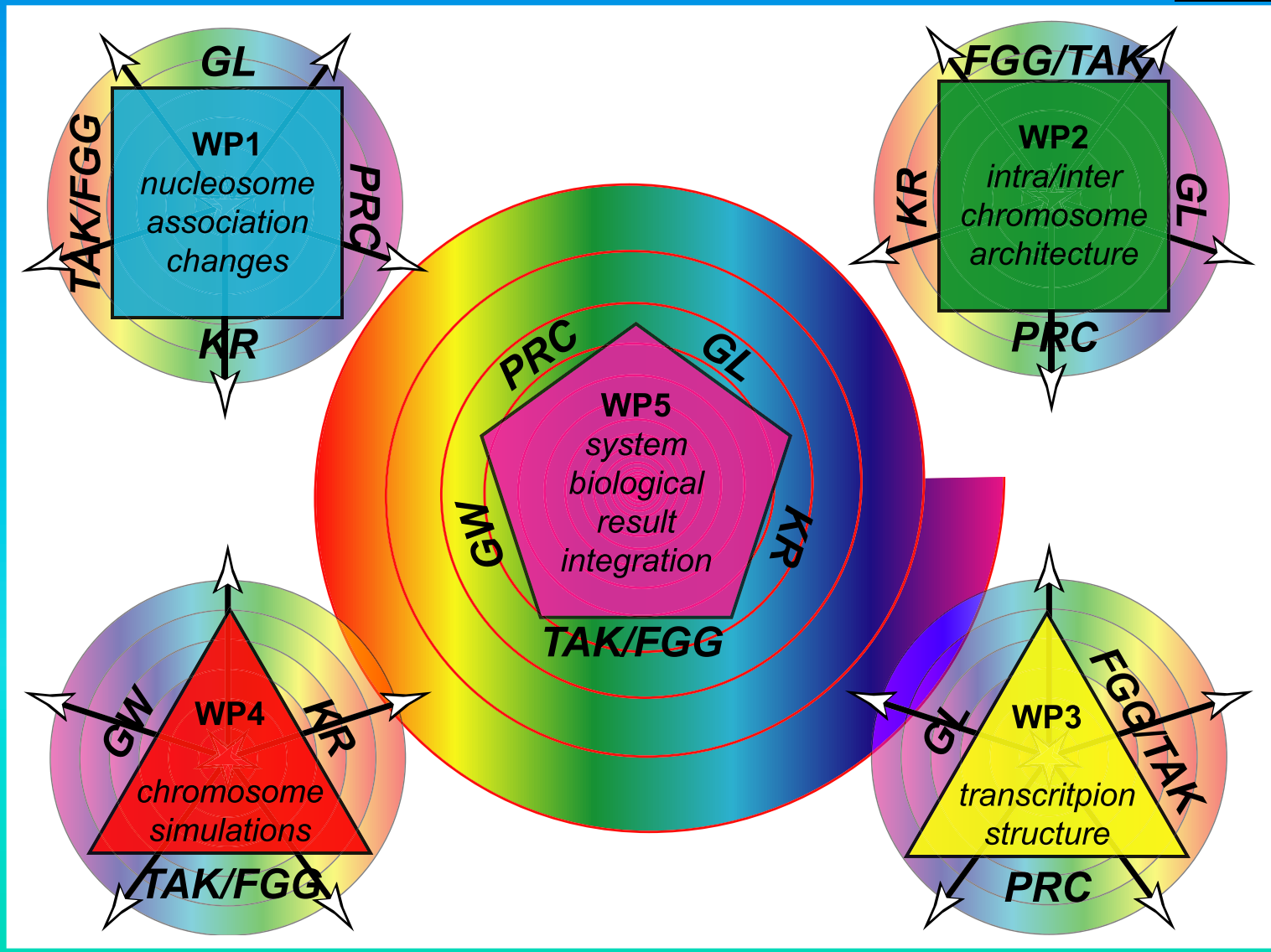




Systemic Genome Understanding Leads to better Diagnostics and Treatment!

EpiGenSys

Systems Biological/Medical Determination of the Epigenomic Structure-Function Relation in:
i) the Beta-Globin locus, ii) the Immuno Globin loci, iii) the SAMD4 region, and iv) the Prader-Willi / Angelmann Syndrom region, in mouse and human active and inactive cell states and their global context.



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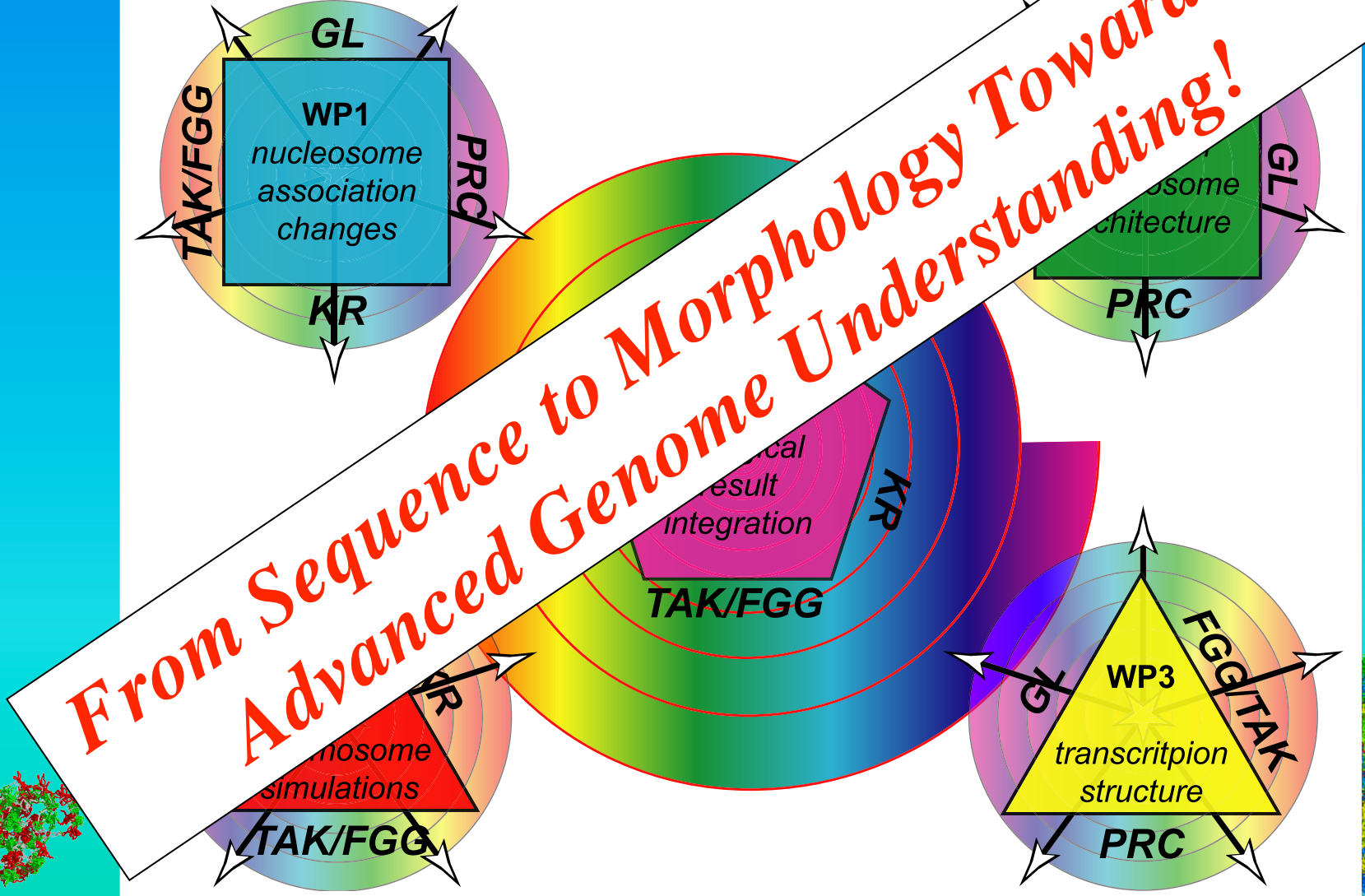


From Sequence to Morphology Towards an Advanced Genome Understanding!

Work Together and Communication in EpiGenSys

The work packages are implemented in such a way that they utilize the established expertise of individual partners (each with their own established network of contacts) while providing maximum benefit to the groups. Maximum output is guarantied by our virtual laboratory communication management.

WP1: **Nucleosomal association changes (Längst, Rippe, Wedemann, Knoch/Grosveld; T1-T5)**

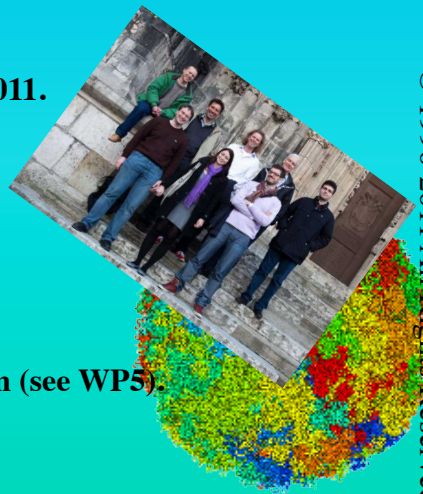
WP2 **Intra/inter chromosomal architecture (Grosveld/Knoch, Cook, Rippe, Längst; T1-T3)**

WP3 **Transcription structure relationship (Cook, Grosveld/Knoch, Längst; T1-T4)**

WP4 **Simulations of nucleosomal, chromatin fiber and chromosome architecture and their dynamics (Wedemann, Knoch/Grosveld, Rippe; T1-T3)**

WP5 **System biological result integration via the GLOBE 3D Genome Platform (Knoch/Grosveld, Cook, Rippe, Längst, Wedemann; T1-T5):**

1. **Two major meetings per year where all participants meet:**
   - **The first meeting took place in Den Haag from 7th to 8th July 2010.**
   - **The second meeting wass held in Regensburg from 6th to 8th April 2011.**
2. **A monthly online conference of lab heads according to theme.**
3. **Weekly conferences of the work force related to the specific tasks**
4. **Regular work meetings in participant labs with several exchanges.**
5. **Use of a web-based communication platforms with project database and forum (see WP5).**



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The EpiGenSys Virtual Laboratory is Working with ever Increasing Efficiency!

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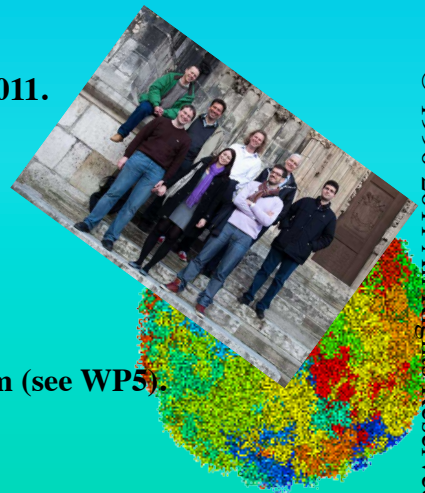
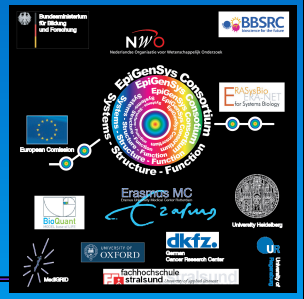


M&D Timeplan in EpiGenSys

The time plane according to the work packages is currently on track.



WP1

Milestones and deliverables:

WP1-1	months 6	Isolation of nucleosomal DNA by *in situ* MNase digestions; differential MNase digestion.
WP1-2	months 12	Sequencing analysis of nucleosomal positions and epigenetic modifications; annotation of DNA sequences obtained.
WP1-3	months 24	Effects of 'knocked-down/in' remodellers on nucleosomal position
WP1-4	months 27	Determination of nuclear localization of nucleosomal DNAs by FISH.
WP1-5	months 30	Bioinformatic analysis of nucleosomal sequences and epigenetic modifications.

WP2

Milestones and deliverables:

WP2-1	months 9	Availability of interaction maps obtained by deep sequencing.
WP2-2	months 18	Microscopic investigation of chromosome architecture.
WP2-3	months 24	Theoretical determination of 3D chromosome architecture.
WP2-4	months 36	Refined systems biological model of chromosome topology.

WP3

Milestones and deliverables:

WP3-1	months 6	Use of 3C established; 4C and expression arrays designed.
WP3-2	months 12	Use of 4C and expression arrays established, and first results.
WP3-3	months 18	Final 4C and expression results obtained.
WP3-4	months 24	Final results obtained for all egions; confirm selected 4C contacts using DNA FISH.
WP3-5	months 30	Confirm transcriptional activity of selected contacts by qRT PCR and RNA FISH.

WP4

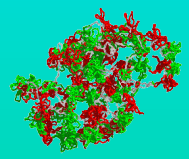
Milestones and deliverables:

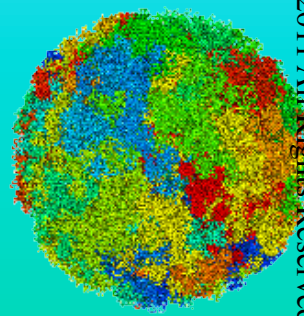
WP4-1	months 6	Implement a nucleosome chain model for variation of local nucleosome geometry, the nucleosomal interactions potential, the linker DNA length.
WP4-2	months 12	Simulations of fibers with ~500-1000 nucleosomes.
WP4-3	months 18	Implementation of the chromatin bead model for 20 Mb genomic regions.
WP4-4	months 30	Whole chromosome and nuclei simulation models.
WP4-5	months 36	Comparative analysis interaction maps by nucleosome and nuclei models.

WP5

Milestones and deliverables:

WP5-1	months 6	Central data base and the GLOBE 3D Genome Platform available to the consortium.
WP5-2	months 12	Integrating nucleosome positioning (experimental, sequence prediction, remodeller activity).
WP5-3	months 18	Predicting local fiber compaction from nucleosome positions and other signals (e. g. epigenetics).
WP5-4	months 24	Full integration of interaction maps, DNA FISH and RNA FISH data higher order simulation data.
WP5-5	months 36	Full system biological model of EpiGenSys.





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WP1-4	months 27	Determination of nuclear localization of nucleosomal DNAs by FISH.
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WP2

Milestones and deliverables:

WP2-1	months	sequencing.
WP2-2	mo	chitecture.
WP2-3		some architecture.
WP2-4		chromosome topology.

WP3

Milestones and deliverables:

WP3-1	months 6	Use of 3C established; 4C and expre
WP3-2	months 12	Use of 4C and expression arrays
WP3-3	months 18	Final 4C and expression resu
WP3-4	months 24	Final results obtained for DNA FISH.
WP3-5	months 30	Confirm transcripti FISH.

WP4

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WP4-3	months 18	Implementation of the chromatin bead model for 20 Mb genomic regions.
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WP4-5	months 36	Comparative analysis interaction maps by nucleosome and nuclei models.

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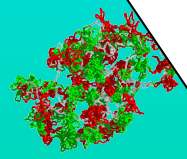
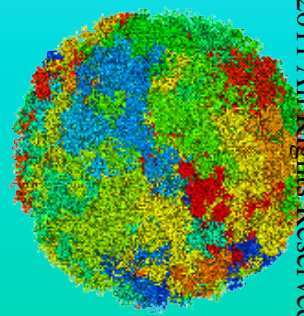
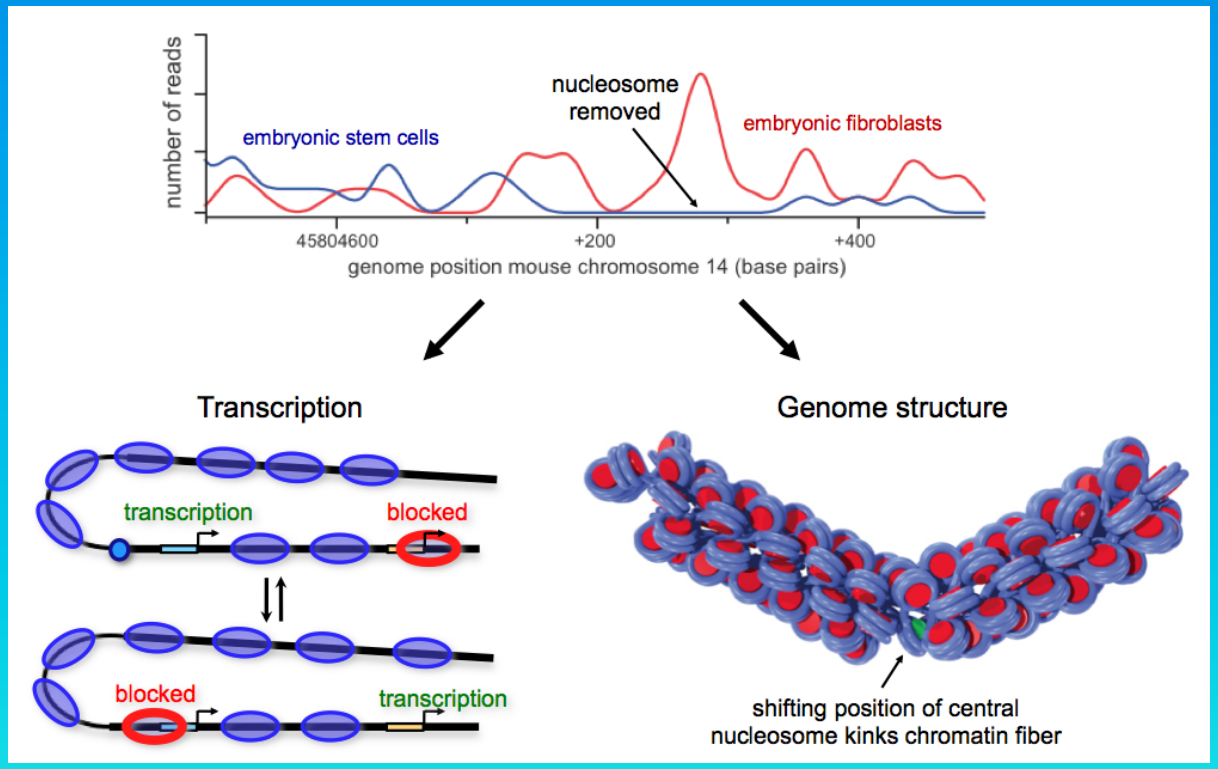
The EpiGenSys Project is on Track with the M&D Timeplan!

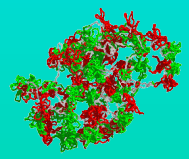


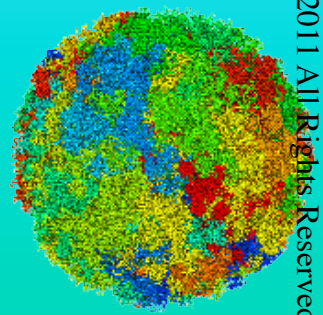


Nucleosomal Association Changes WP1

Nucleosomal association in relation to the DNA sequence, epigenetic modifications and the activity of ATP-driven chromatin remodelling complexes using high-throughput sequencing is evaluated. The results are directly put into simulations and related to DNA sequence predictions.







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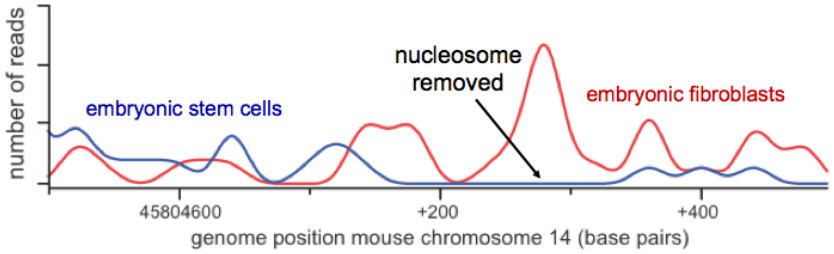

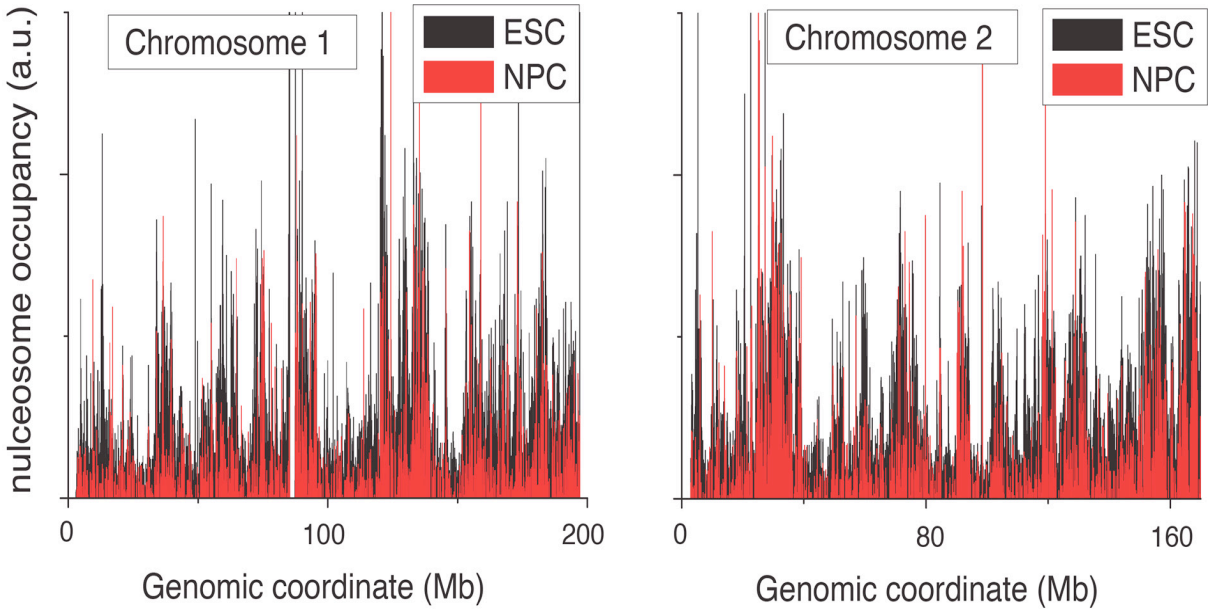

Nucleosomal Association Changes WP1

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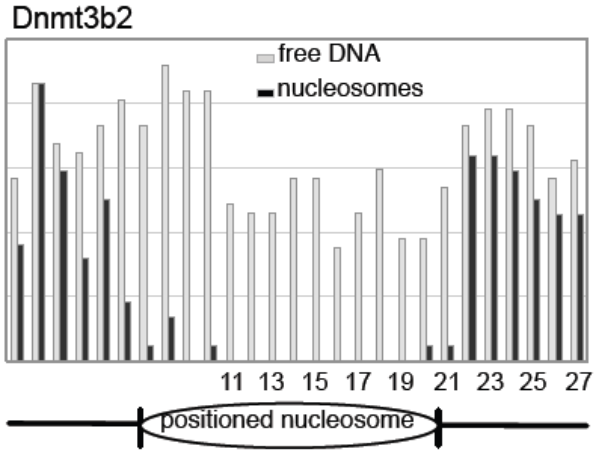
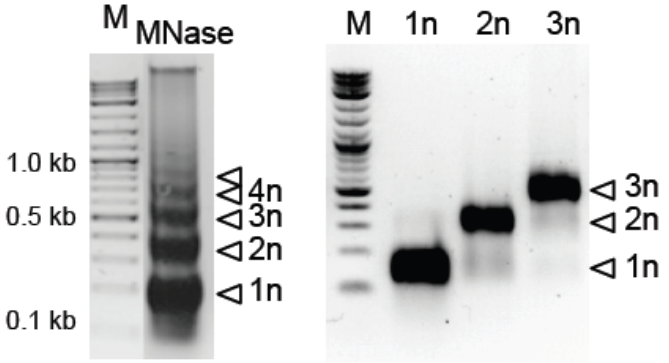
In vitro DNA methylation assay



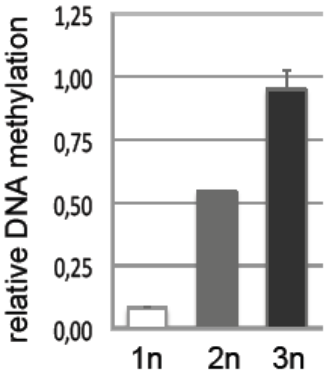
Isolation of cellular mono-, di- and trinucleosomes



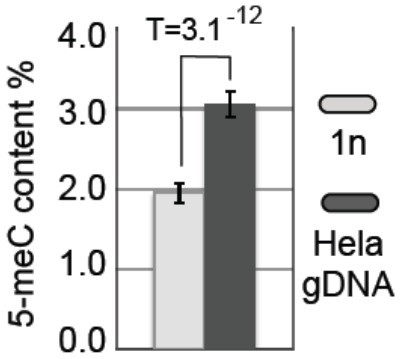
DNA methylation is enriched in the DNA linker region

enzymatic assay

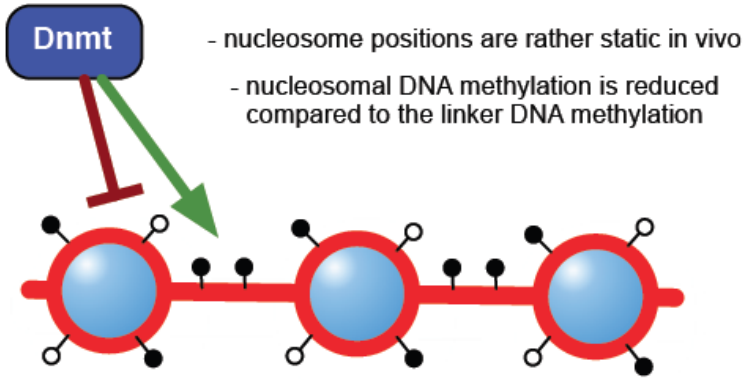
100 ng DNA



quantitative analysis of DNA methylation levels



Nucleosome positions determine the localization of methylated CpGs in vivo



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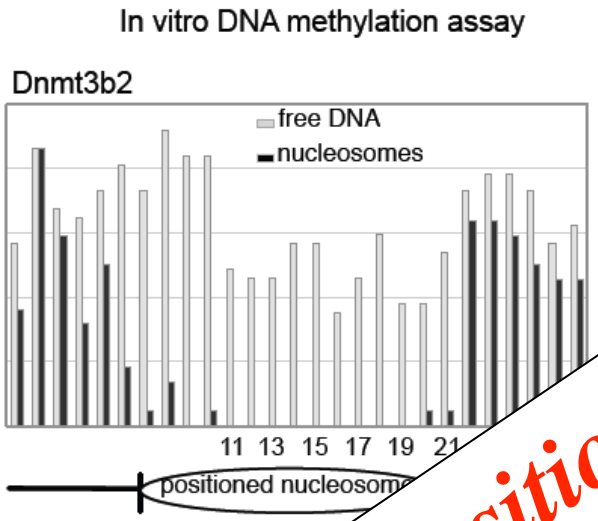

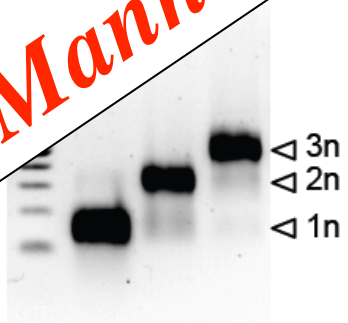

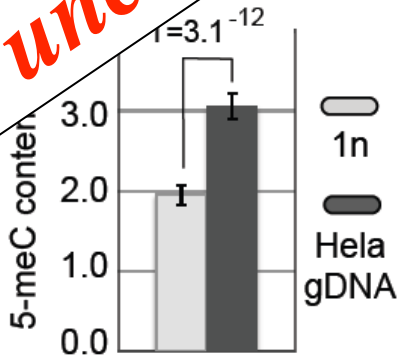

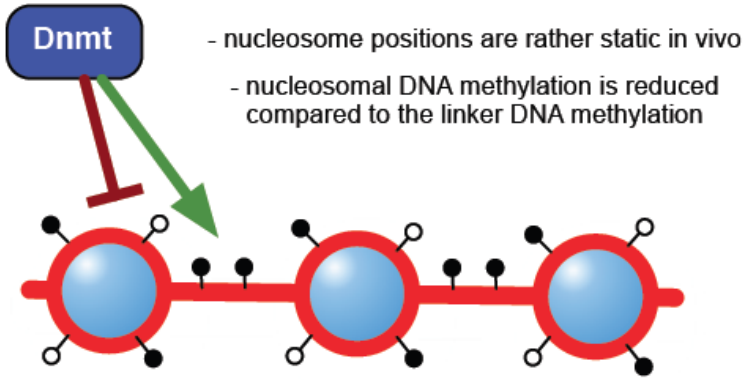

Nucleosomes Position According to Structure and Function in a Defined Manner!

Nucleosomal Positioning Prediction WP1

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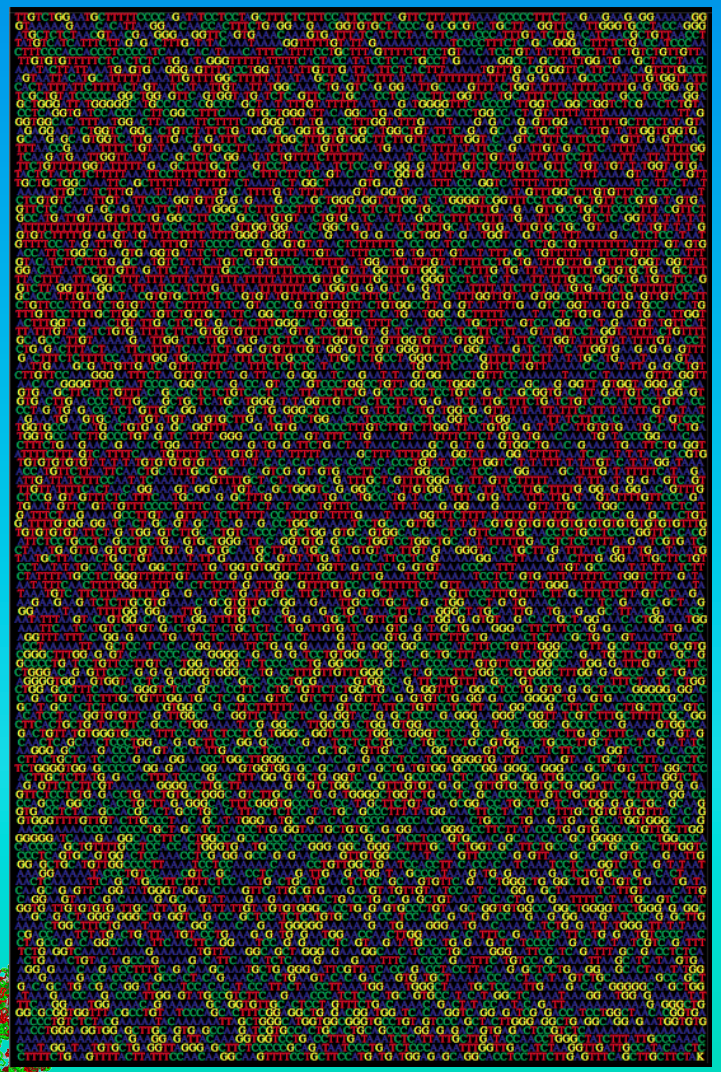

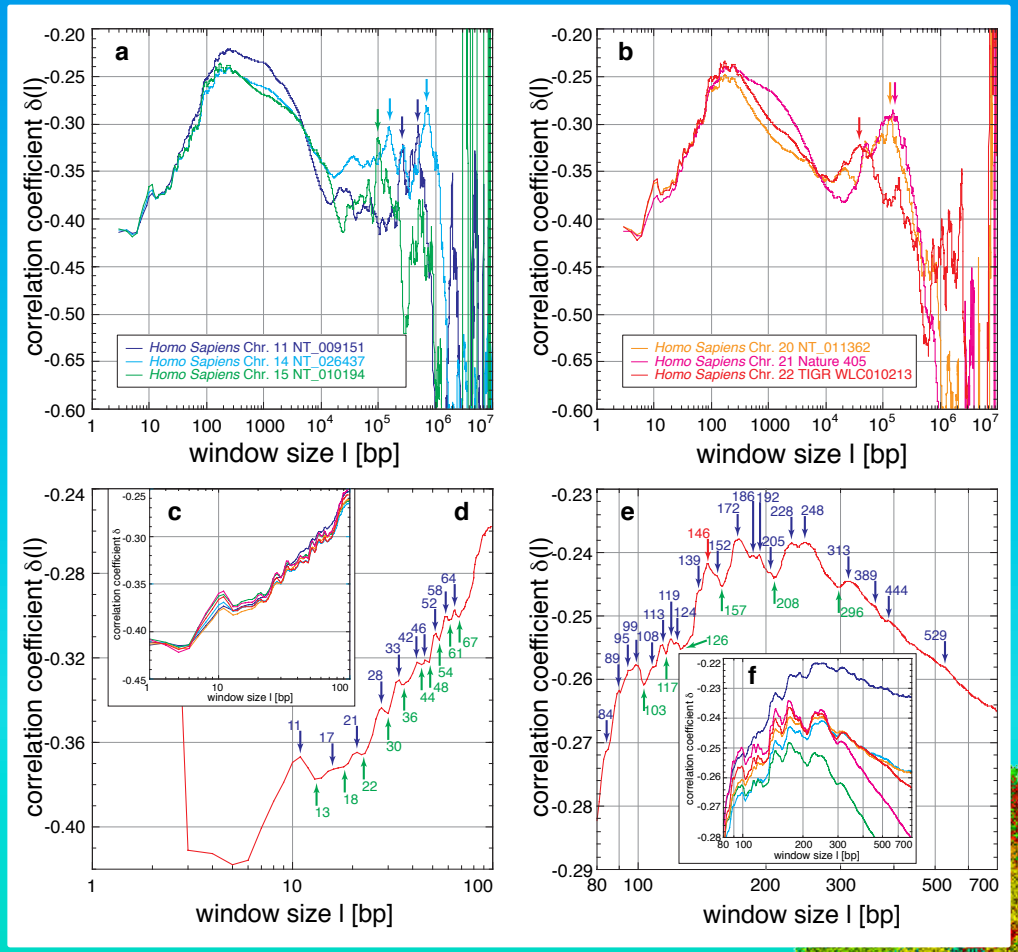

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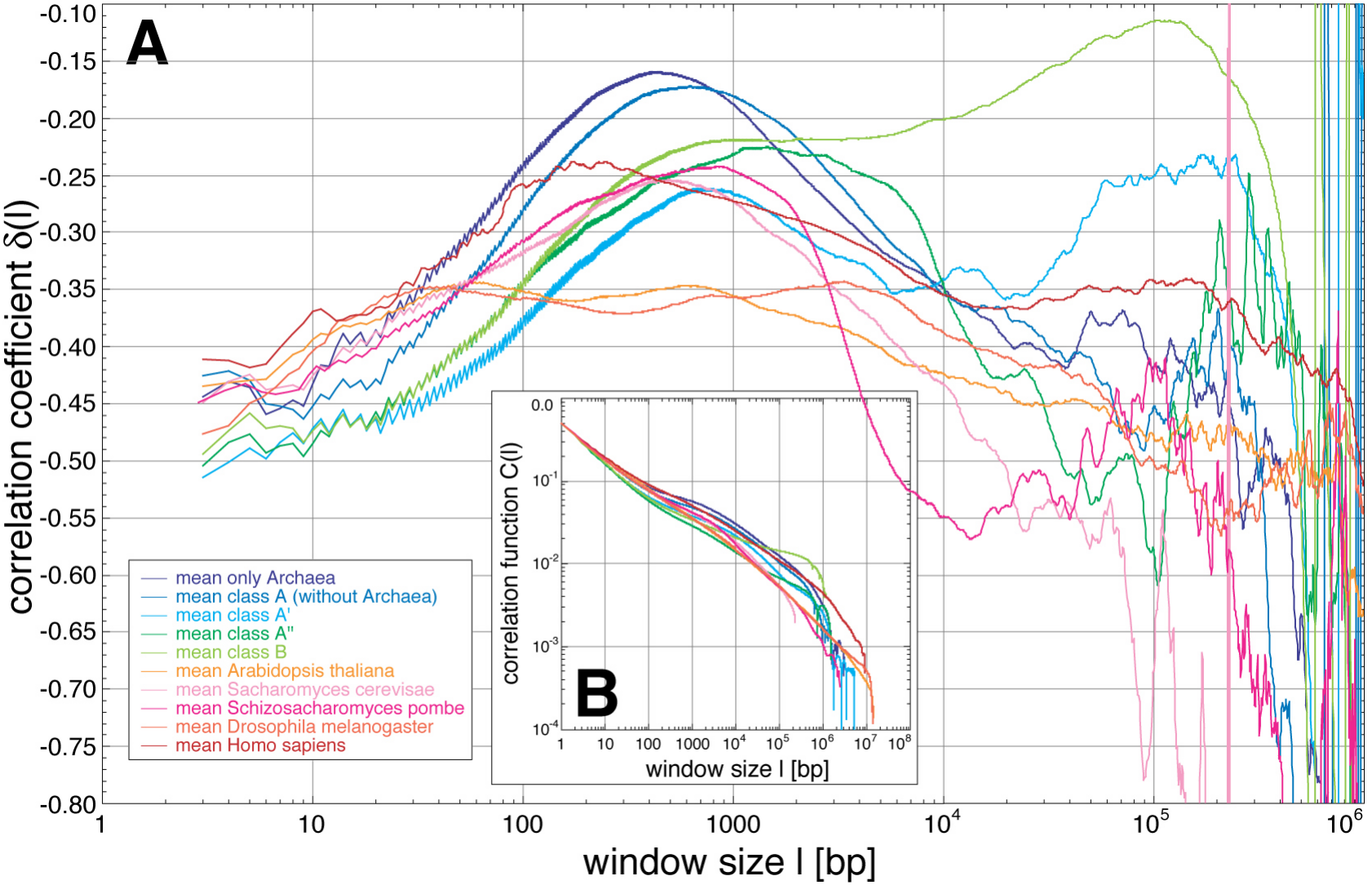

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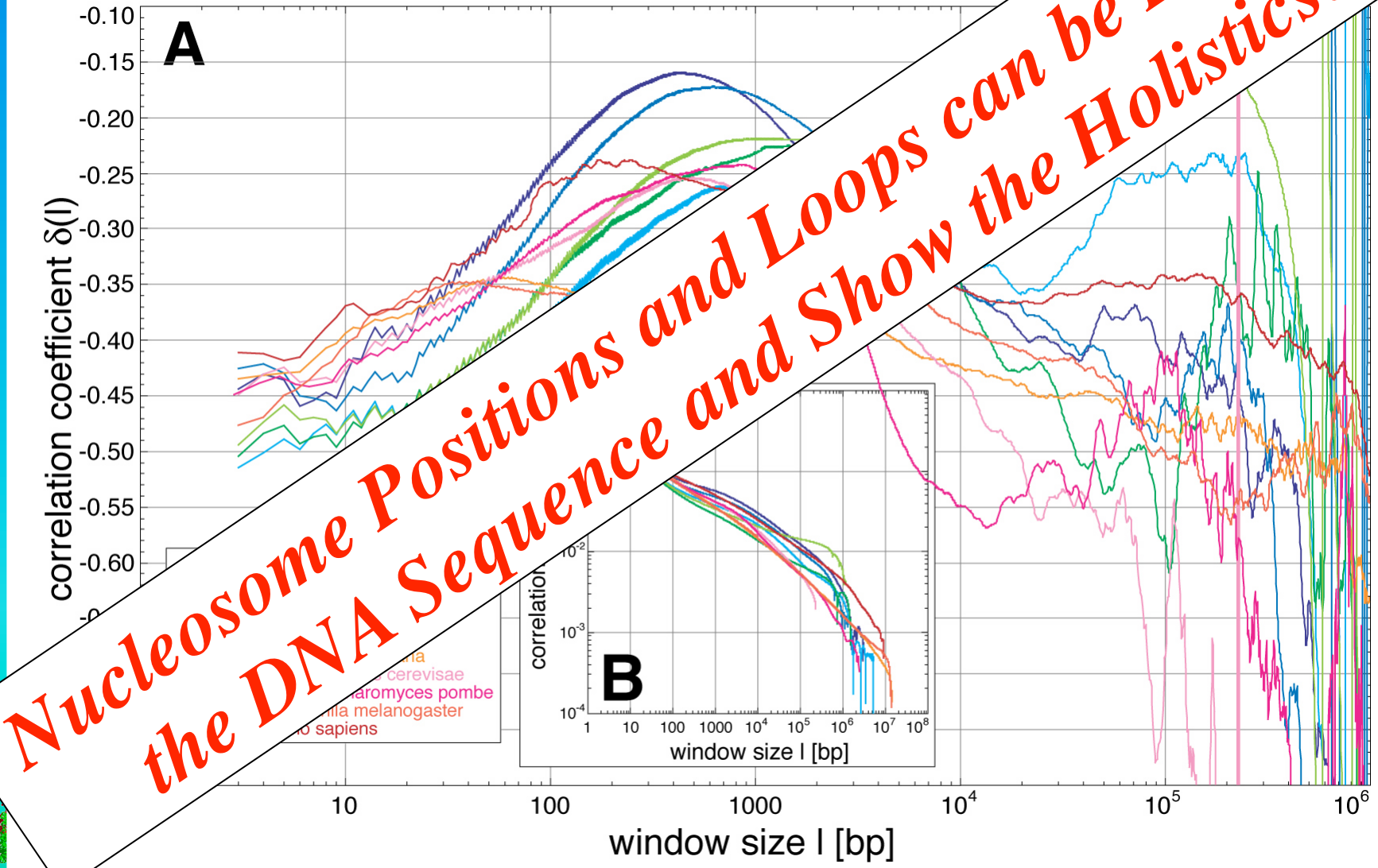
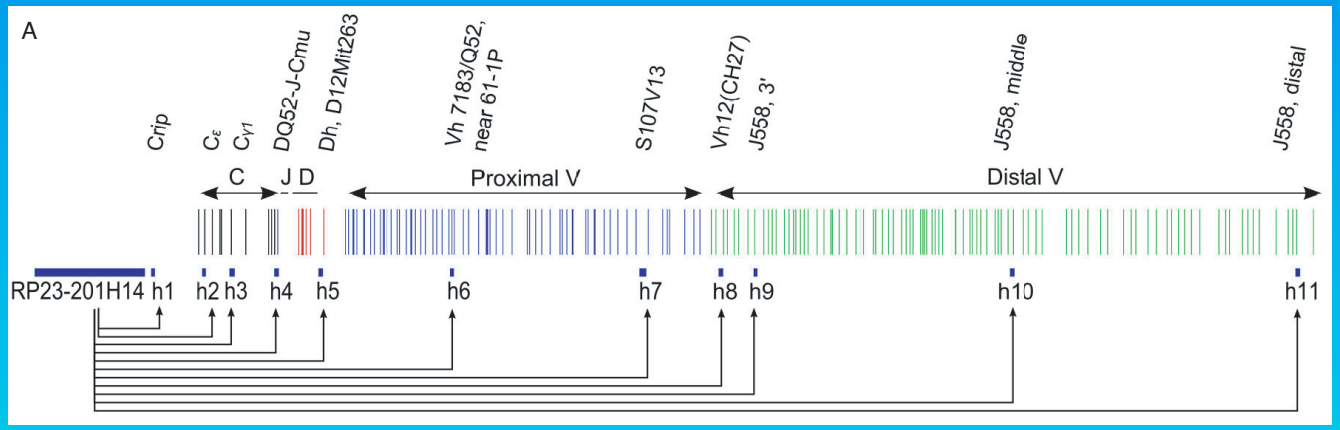
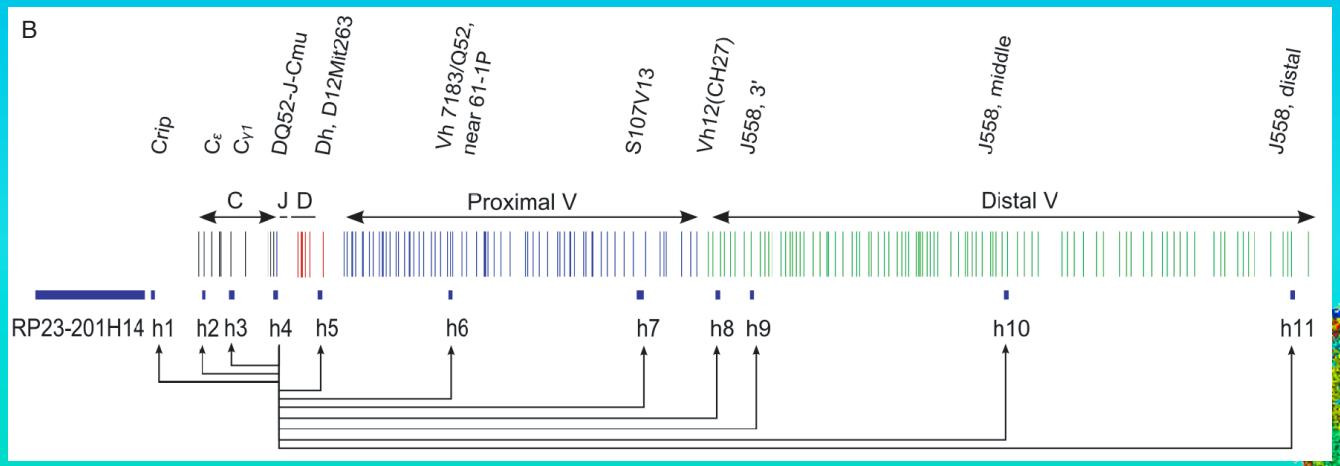


Nucleosome Positions and Loops can be Derived the DNA Sequence and Show the Holistics!

Intra/Inter Chromosomal Spatial Architecture WP2

Intra/inter chromosomal contacts are determined using a combination of chromosome conformation capture technology and highest-throughput deep sequencing. From the interaction maps 3D chromatin conformations and its higher-order structure is derived, i.e. its folding into loops and loop clusters.





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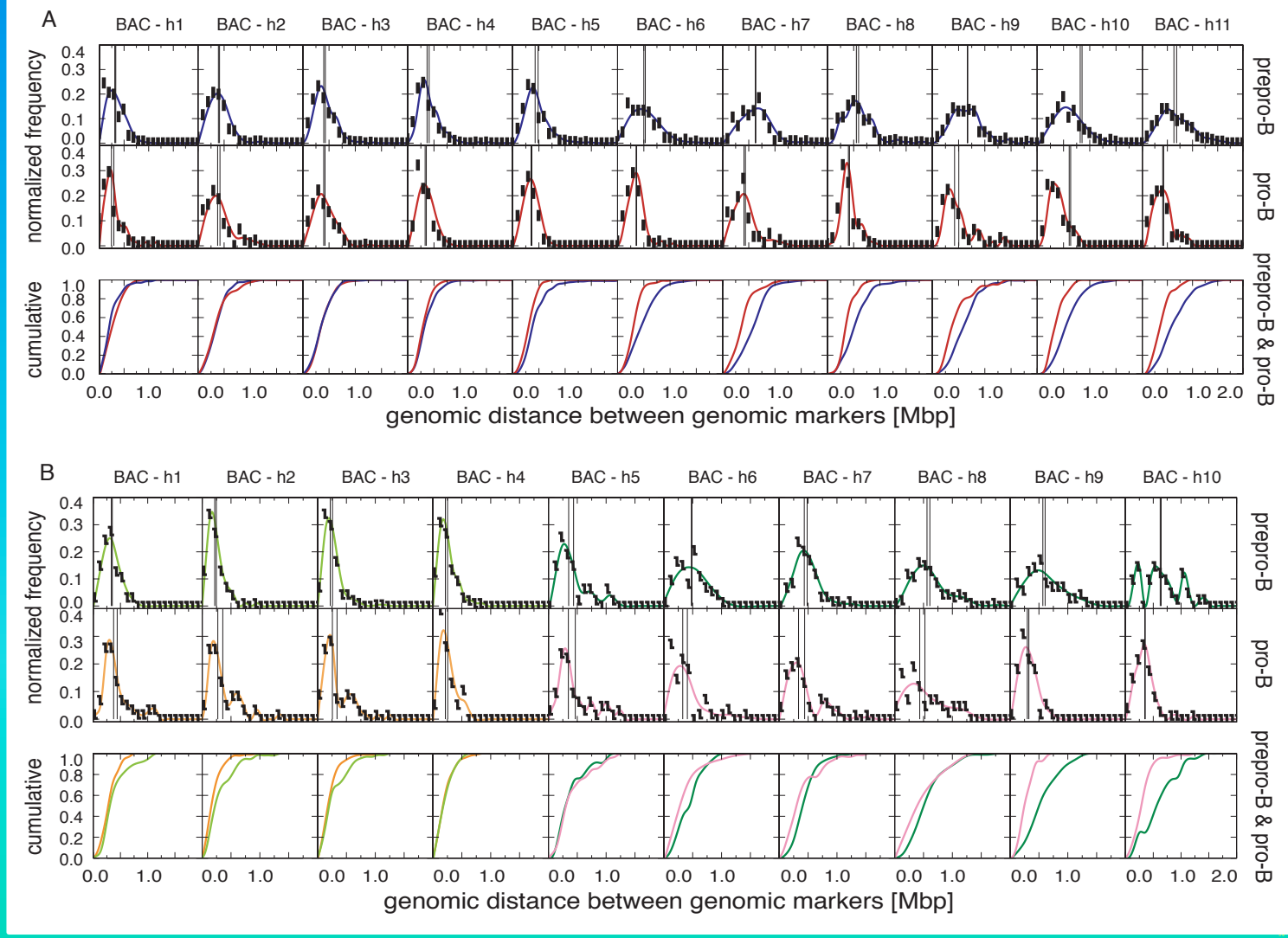

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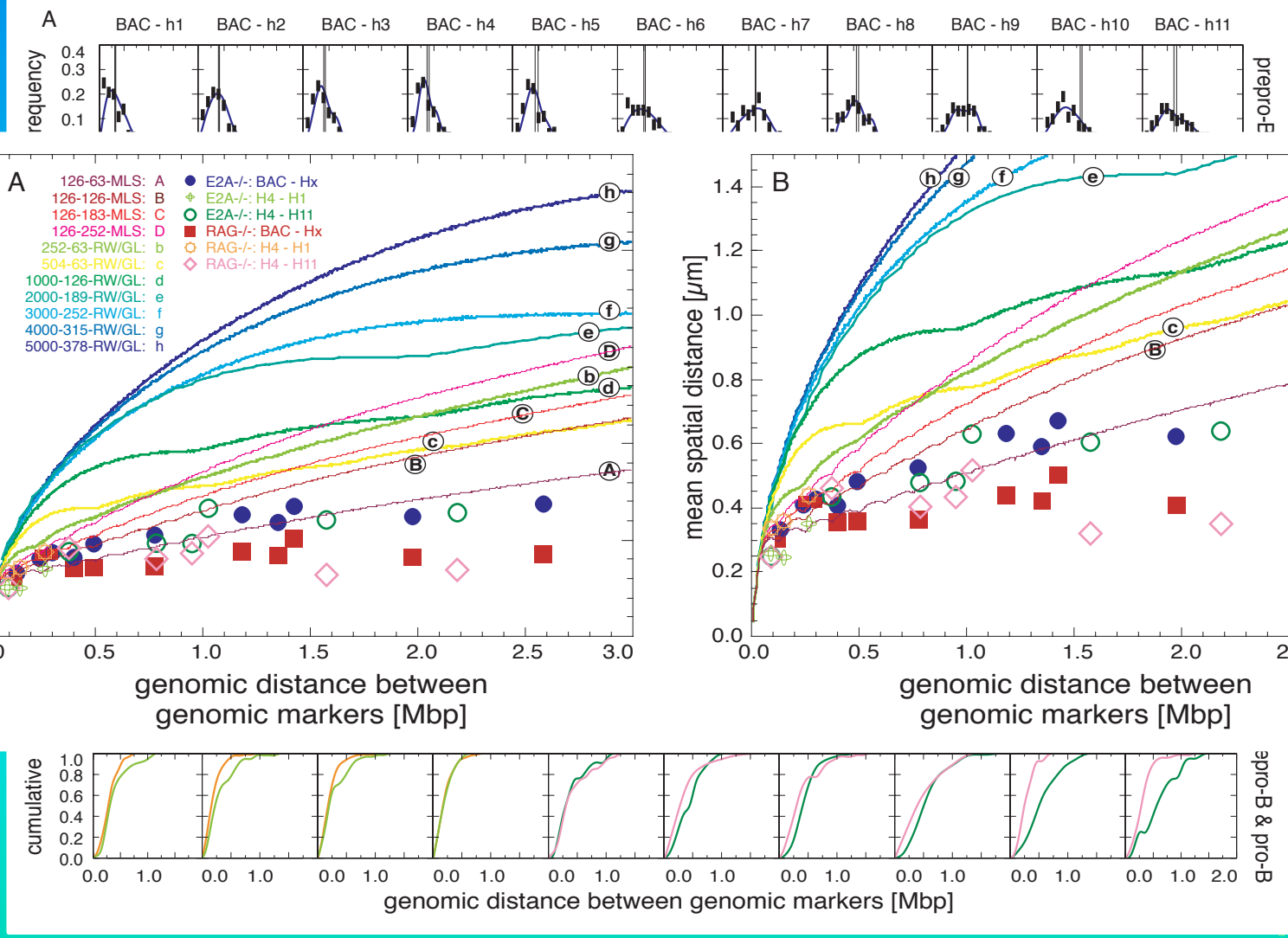

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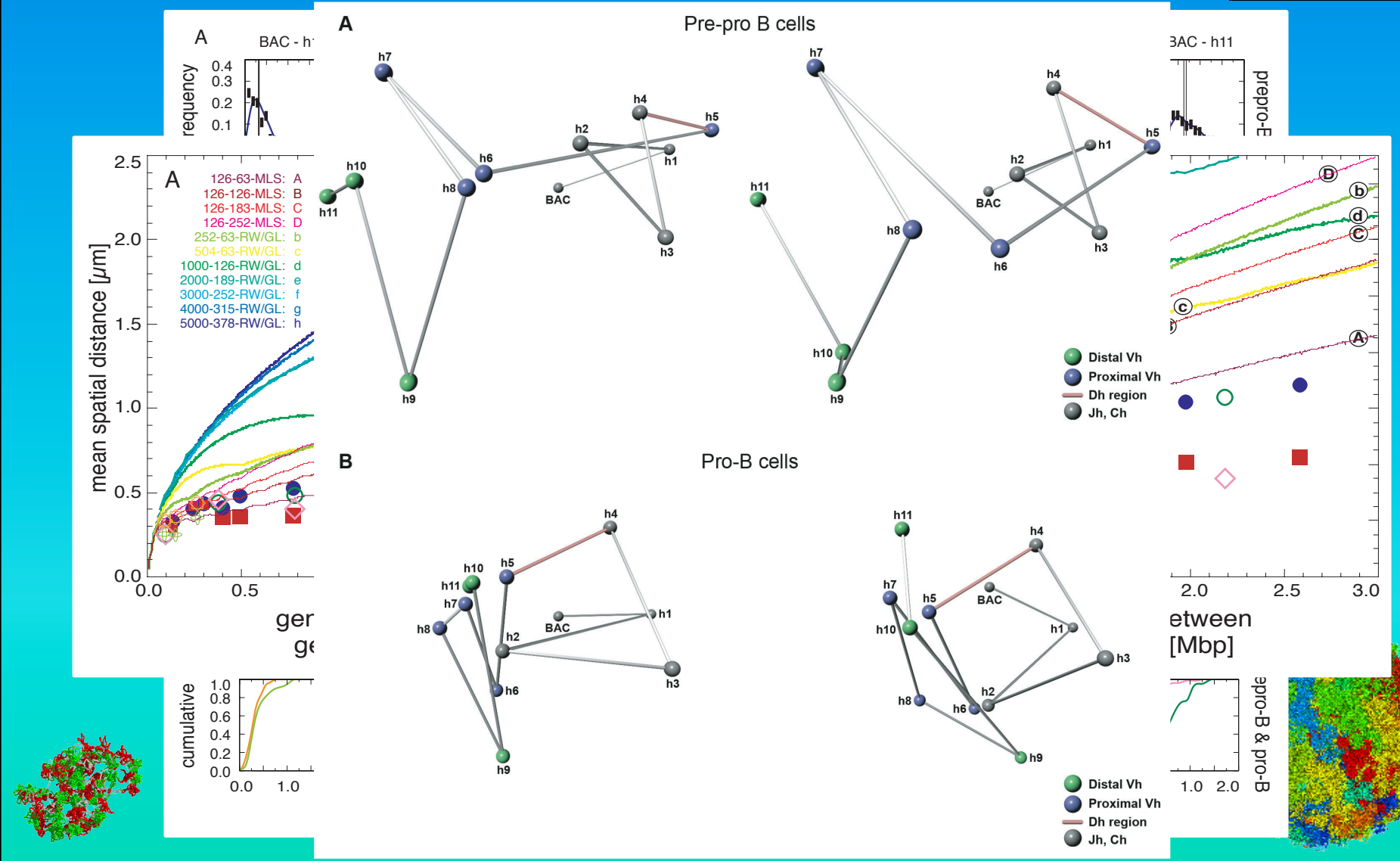

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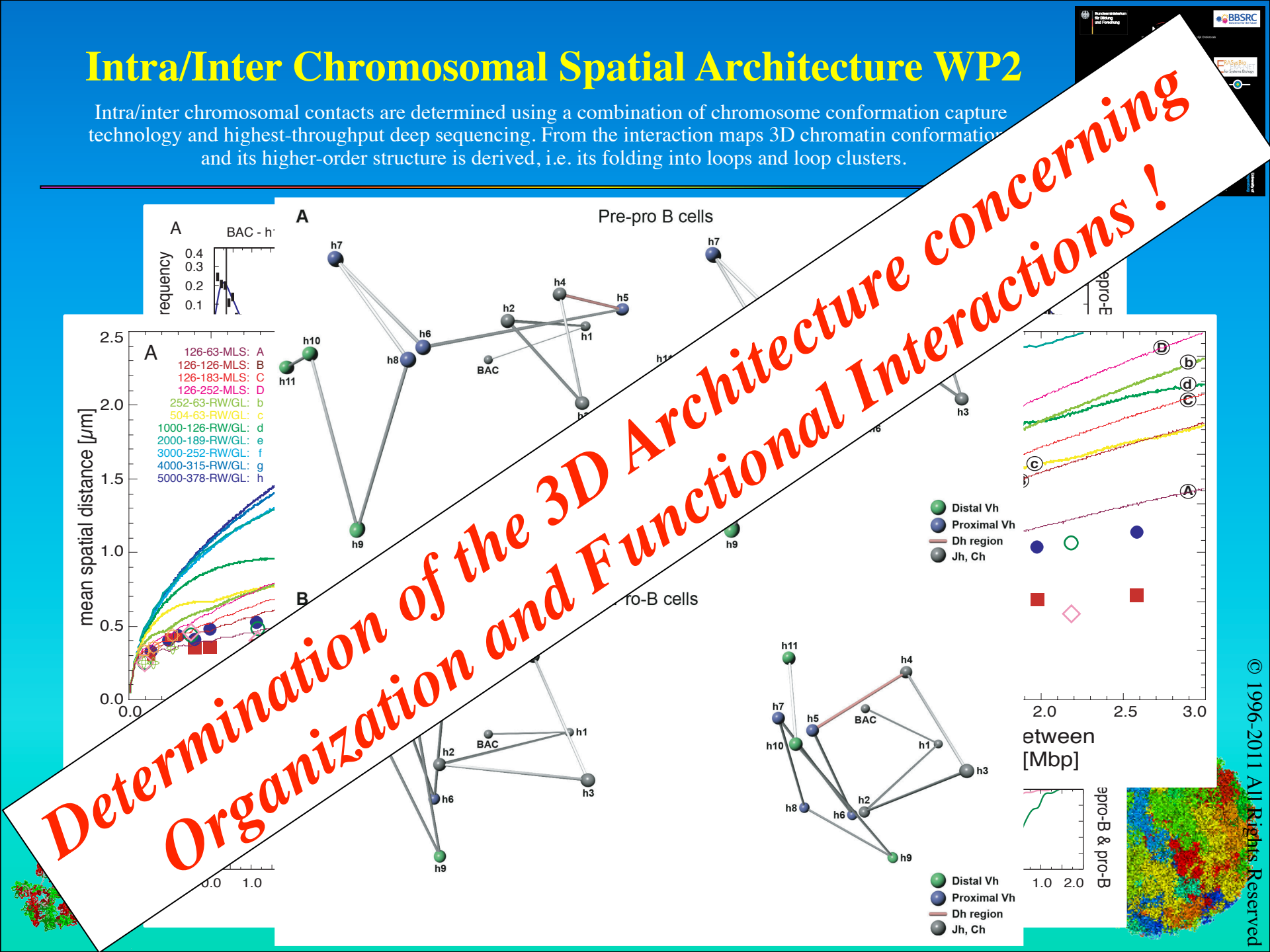

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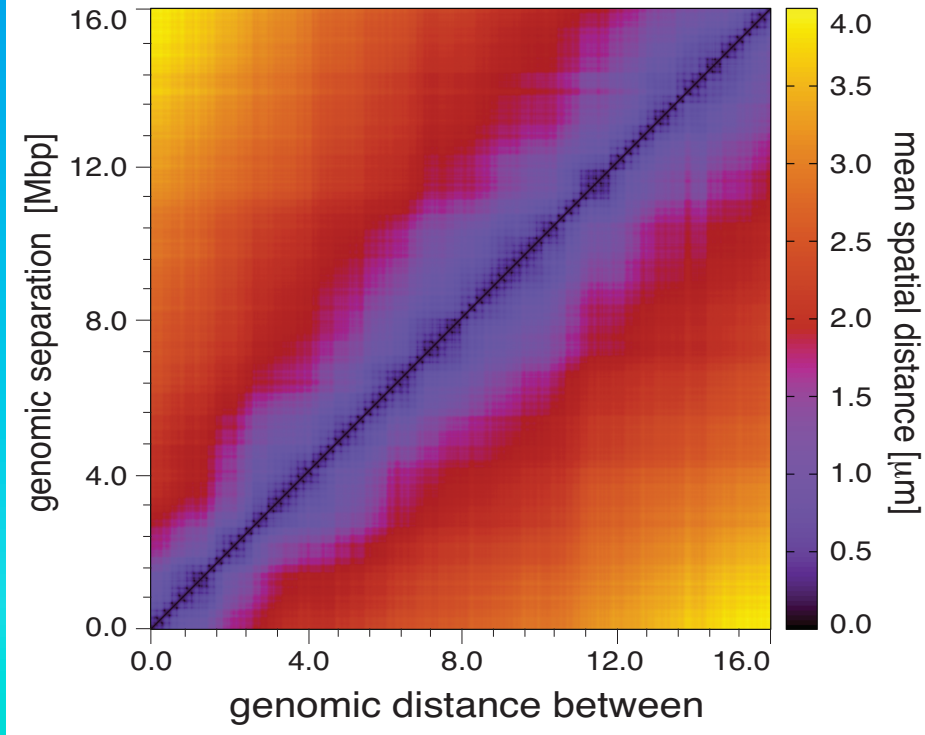
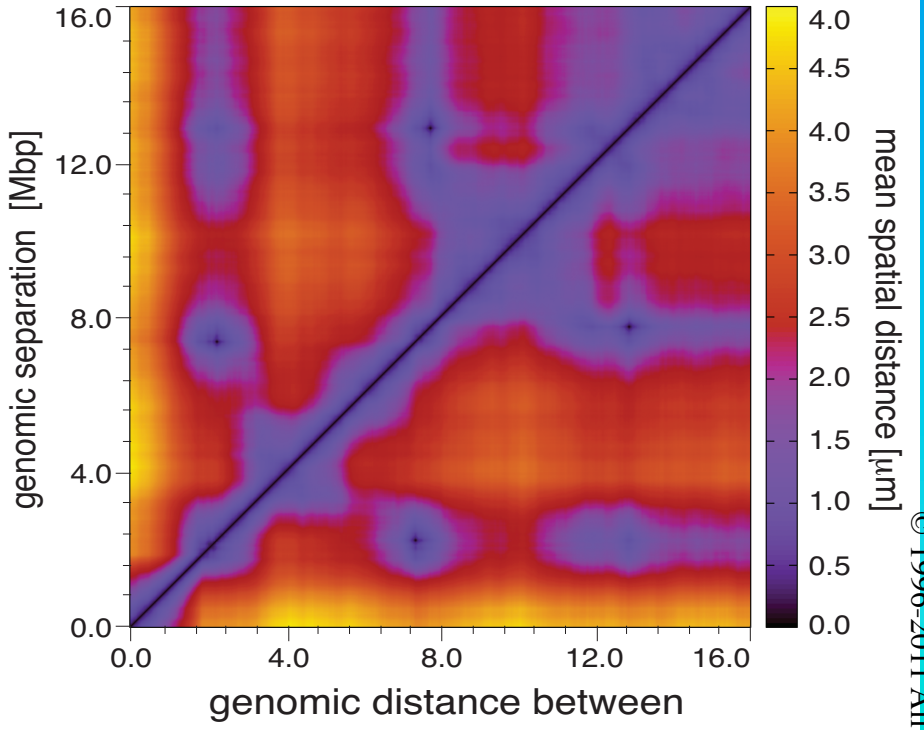
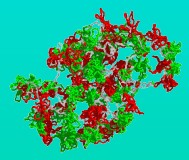
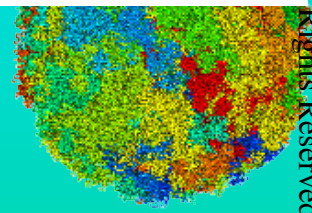
Small Chromatin Loops 126 kbp



Large Chromatin Loops 3 Mbp







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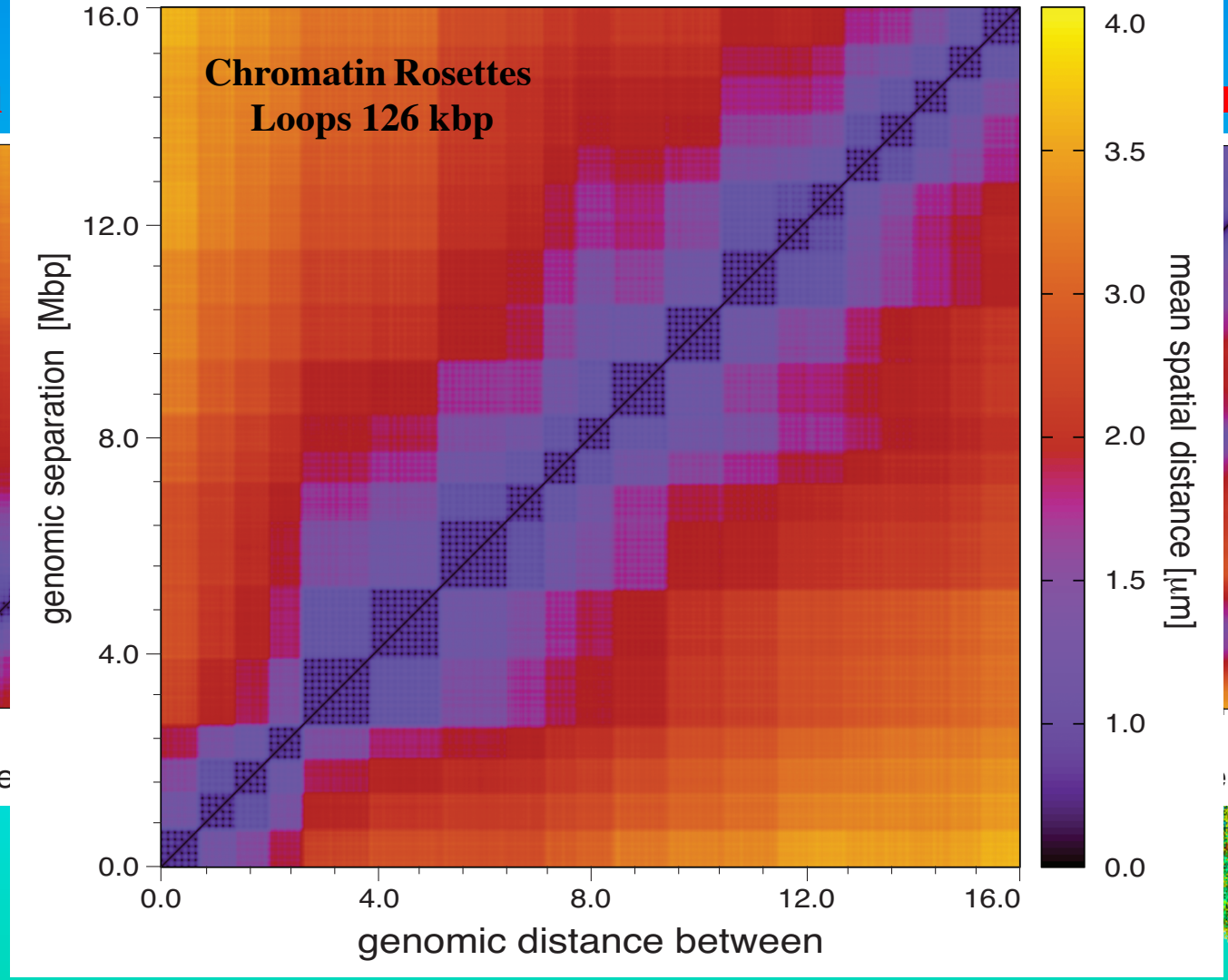

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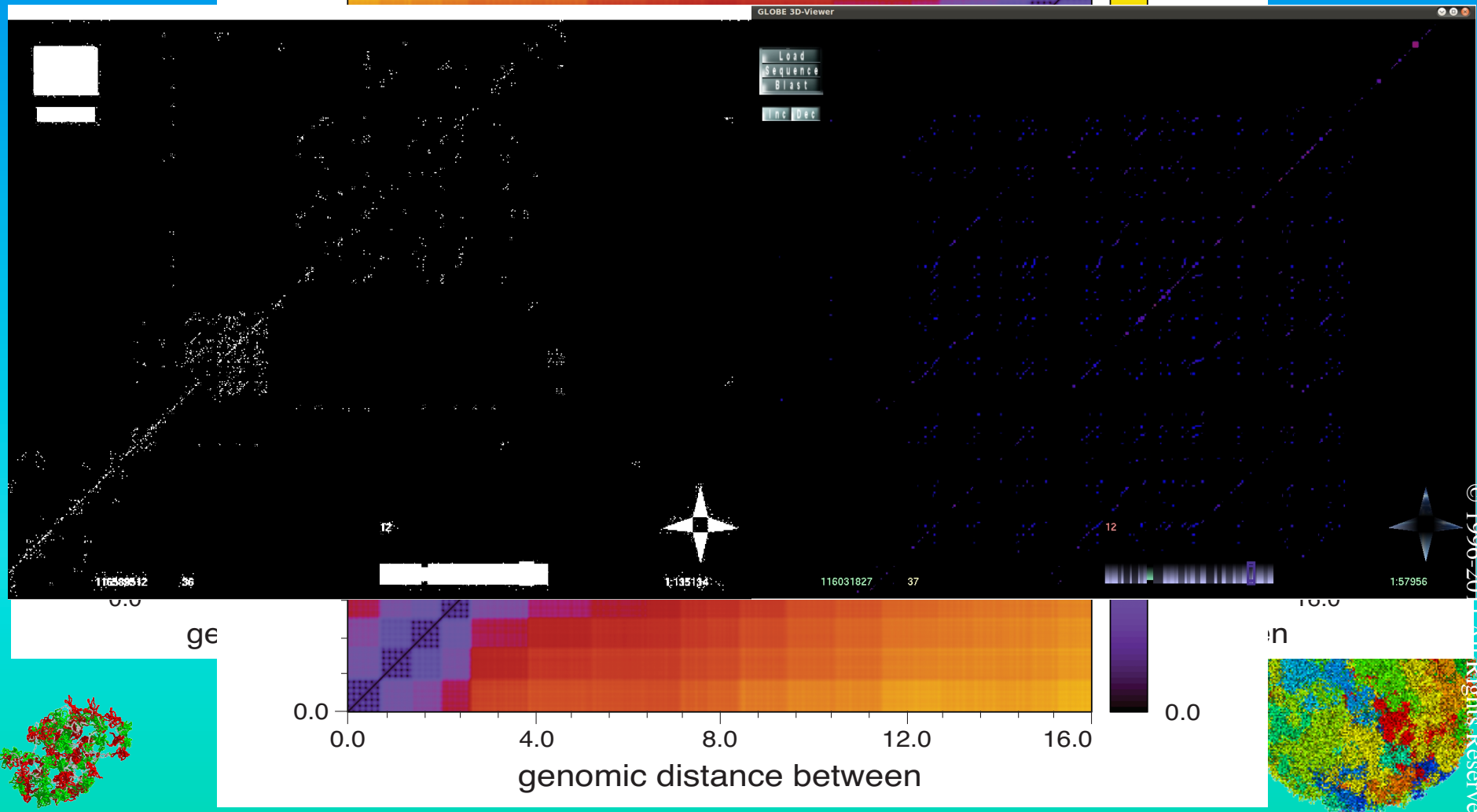

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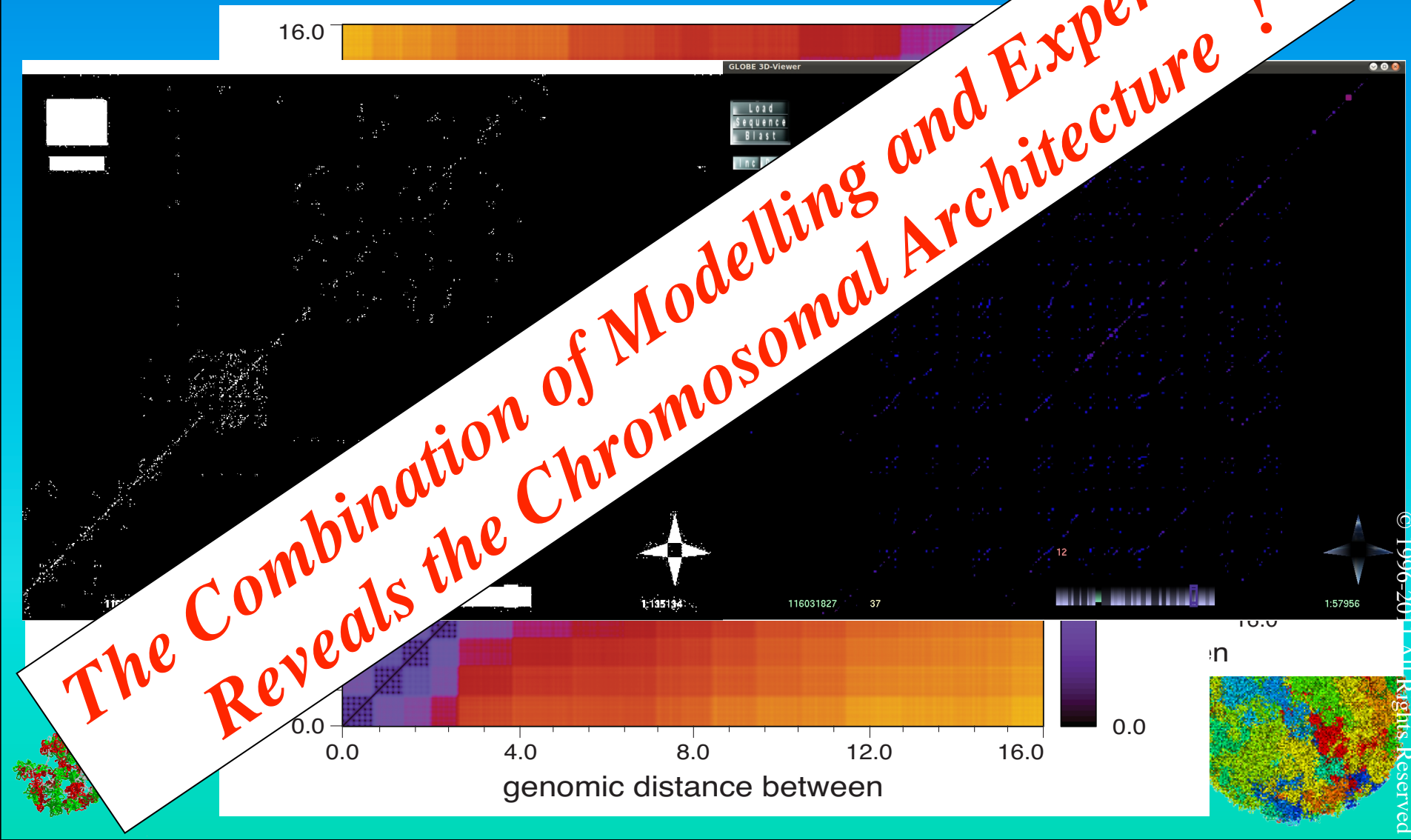
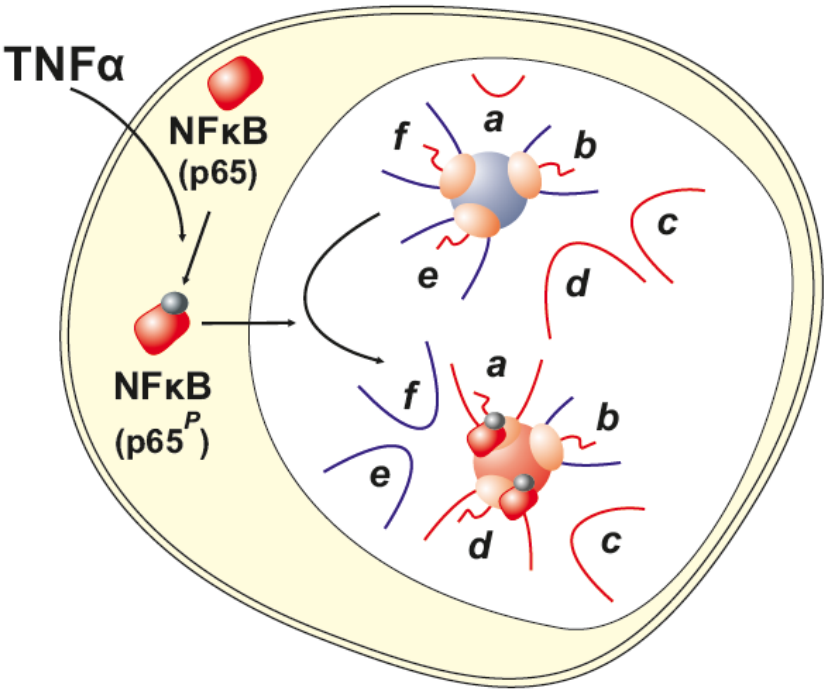


The Combination of Modelling and Experiment Reveals the Chromosomal Architecture !

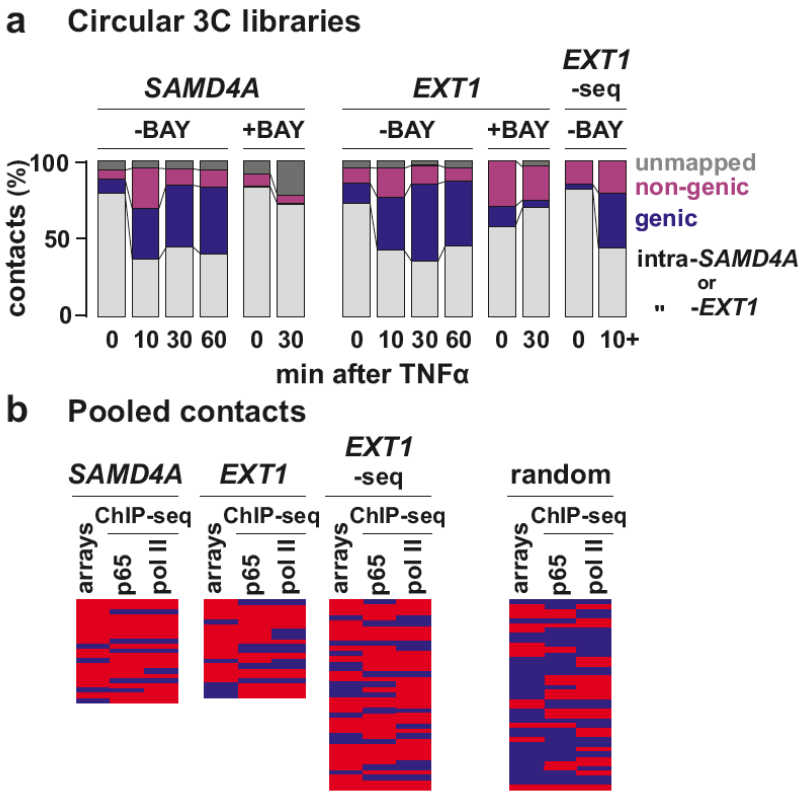
Transcription Structure-Function Relationship WP3

Transcription rates are determined by qRT-PCR, RNA and DNA FISH using intronic probes and high-resolution laser scanning and single molecule imaging. Transcription-dependent changes of active and inactive loci compared result in the transcription structure-function relationship.

Hypothesis Transcriptionfactories



TNFα induces SAMD4A/EXT1 to Associate with other Responsive Genes



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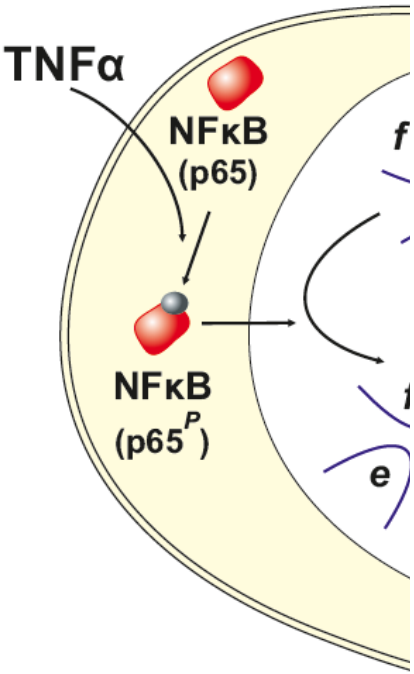
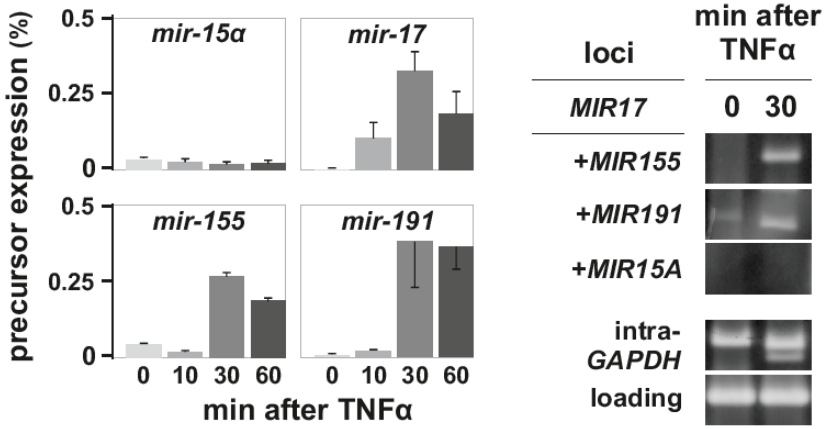
TNFα-Responsive Genes hosting miRNAs Co-Associate

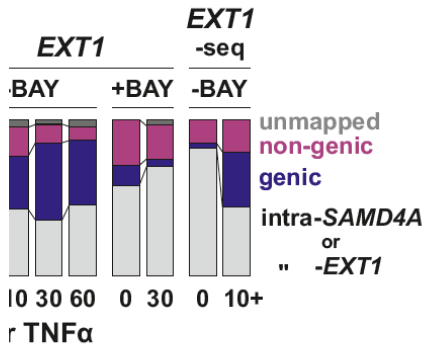
Hypothesis Tra

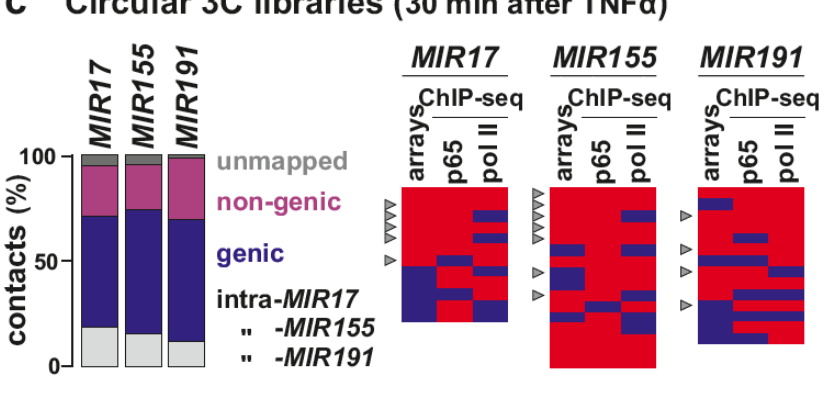
SAMD4A/EXT1

her Responsive Genes









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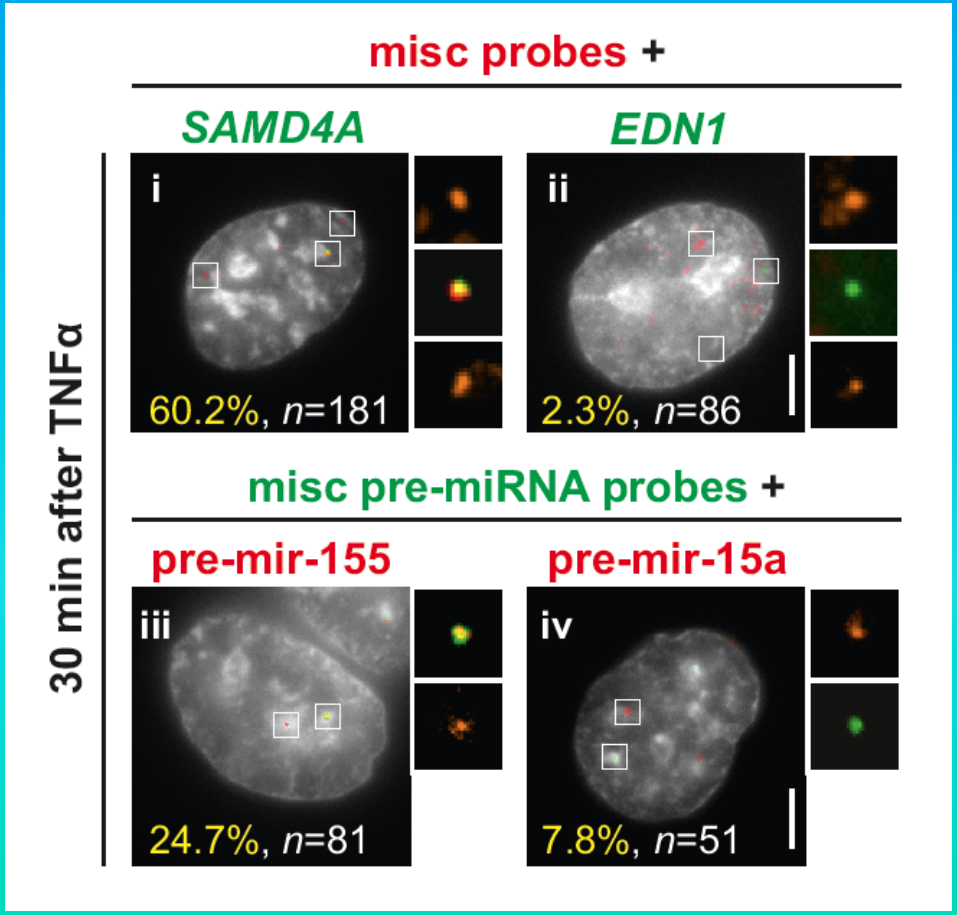
Nascent Transcripts Colocalize with Responsive Genes



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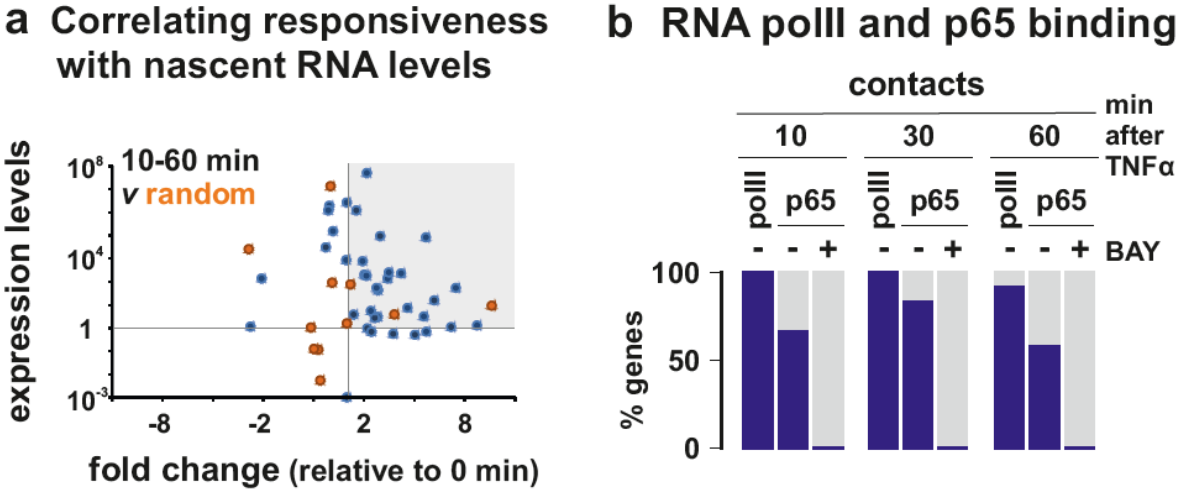
Range of Responsiveness & RNA Polymerase II and NFκB



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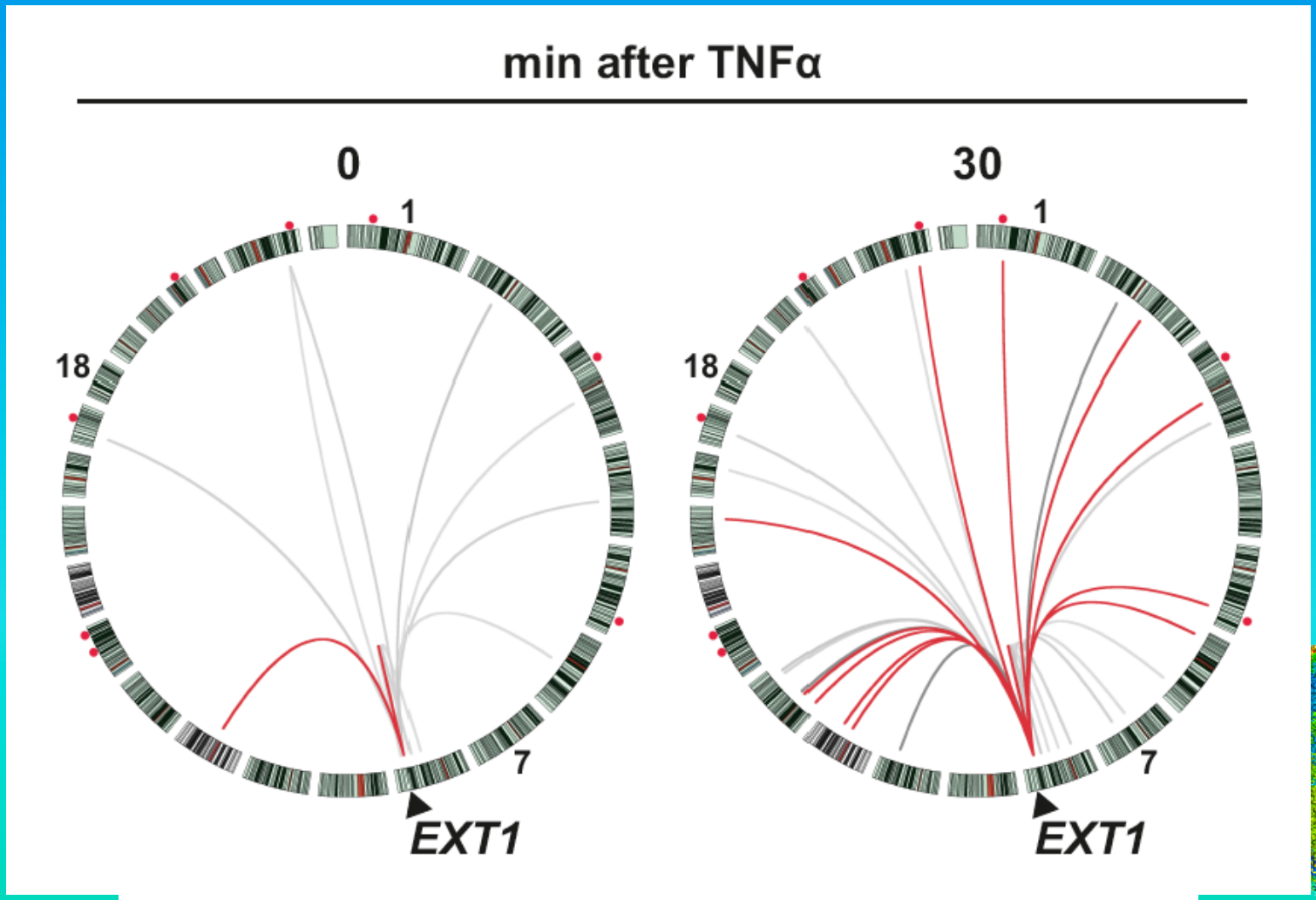
Contacts Evolve over Time



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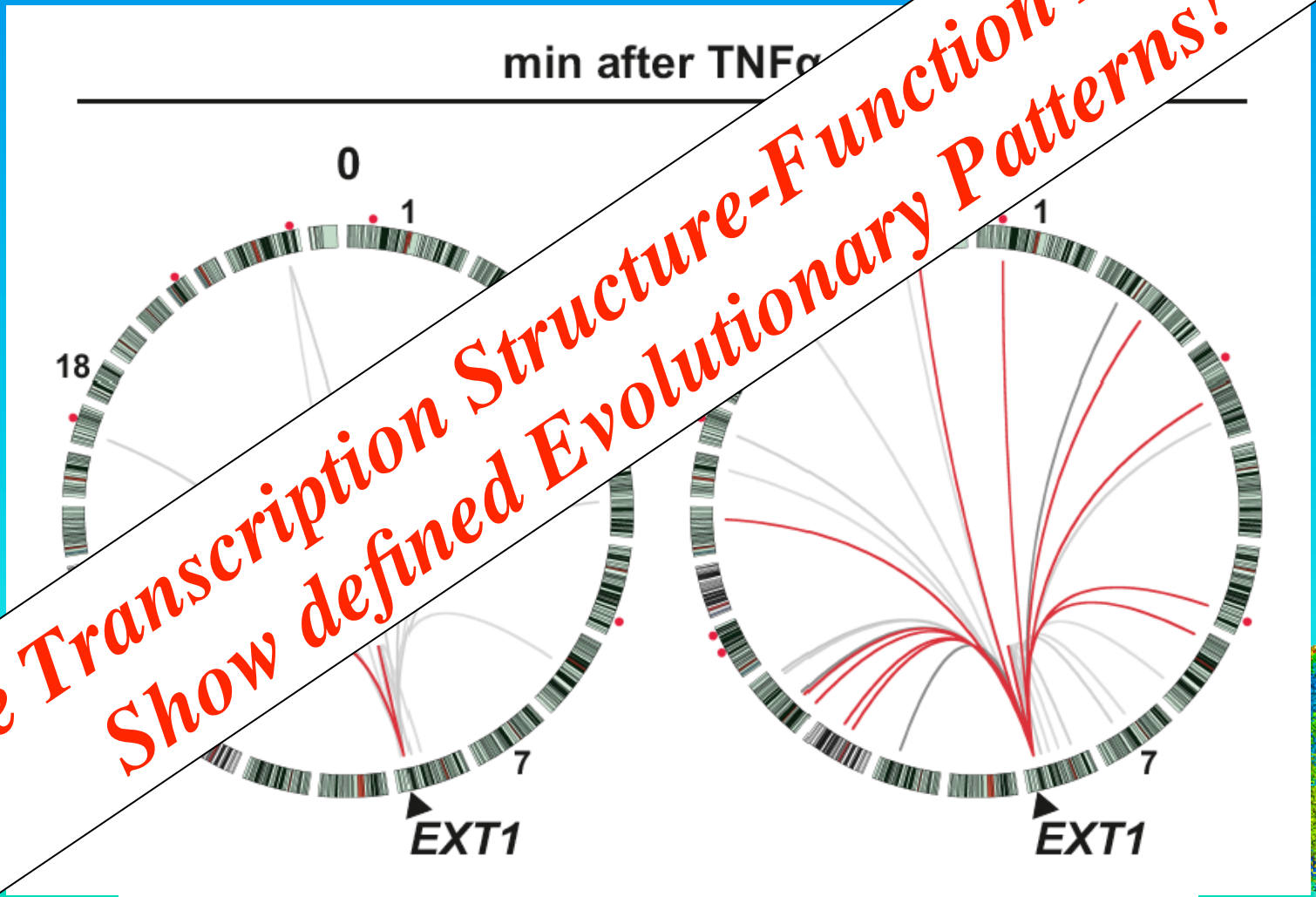
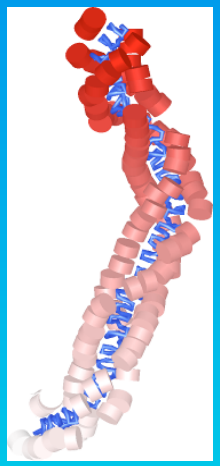


The Transcription Structure-Function Relation Show defined Evolutionary Patterns!

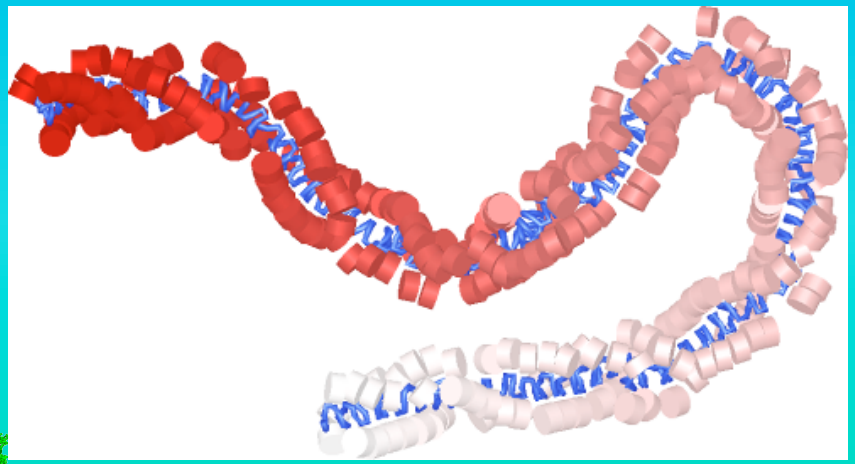
Simulation of Nucleosomes & Chromatin WP4

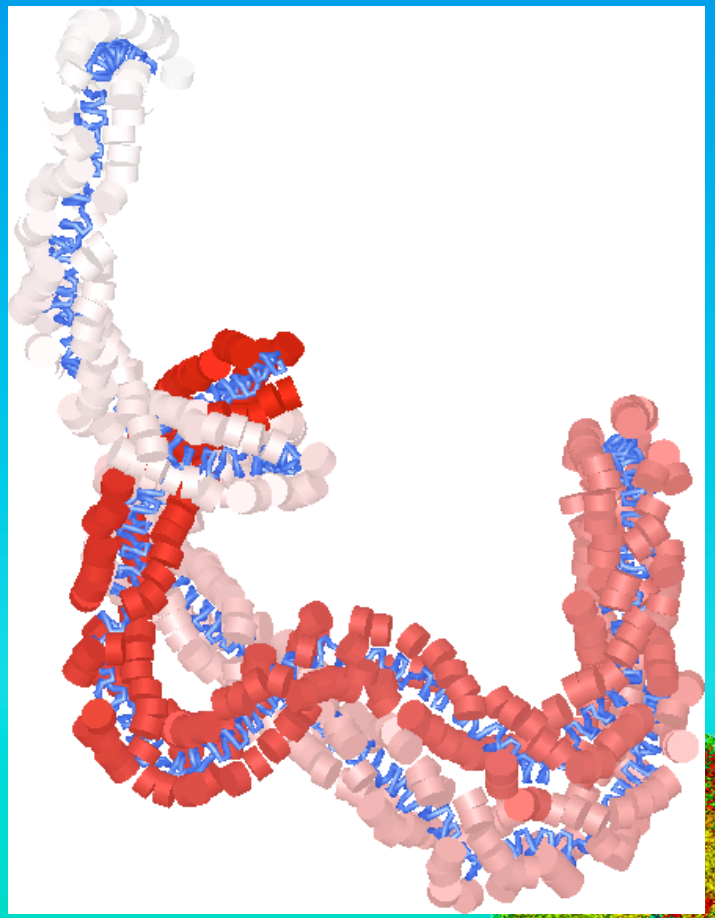
By parallel super-computer simulations using novel algorithms allow to simulate nucleosome and chromatin fibers up to 1000 nucleosomes, with variations of the nucleosomal position and linker length inbetween. The unprecedented scale and variation leads to new before unseen chromatin states.



100 nucleosomes

250 nucleosomes





500 nucleosomes

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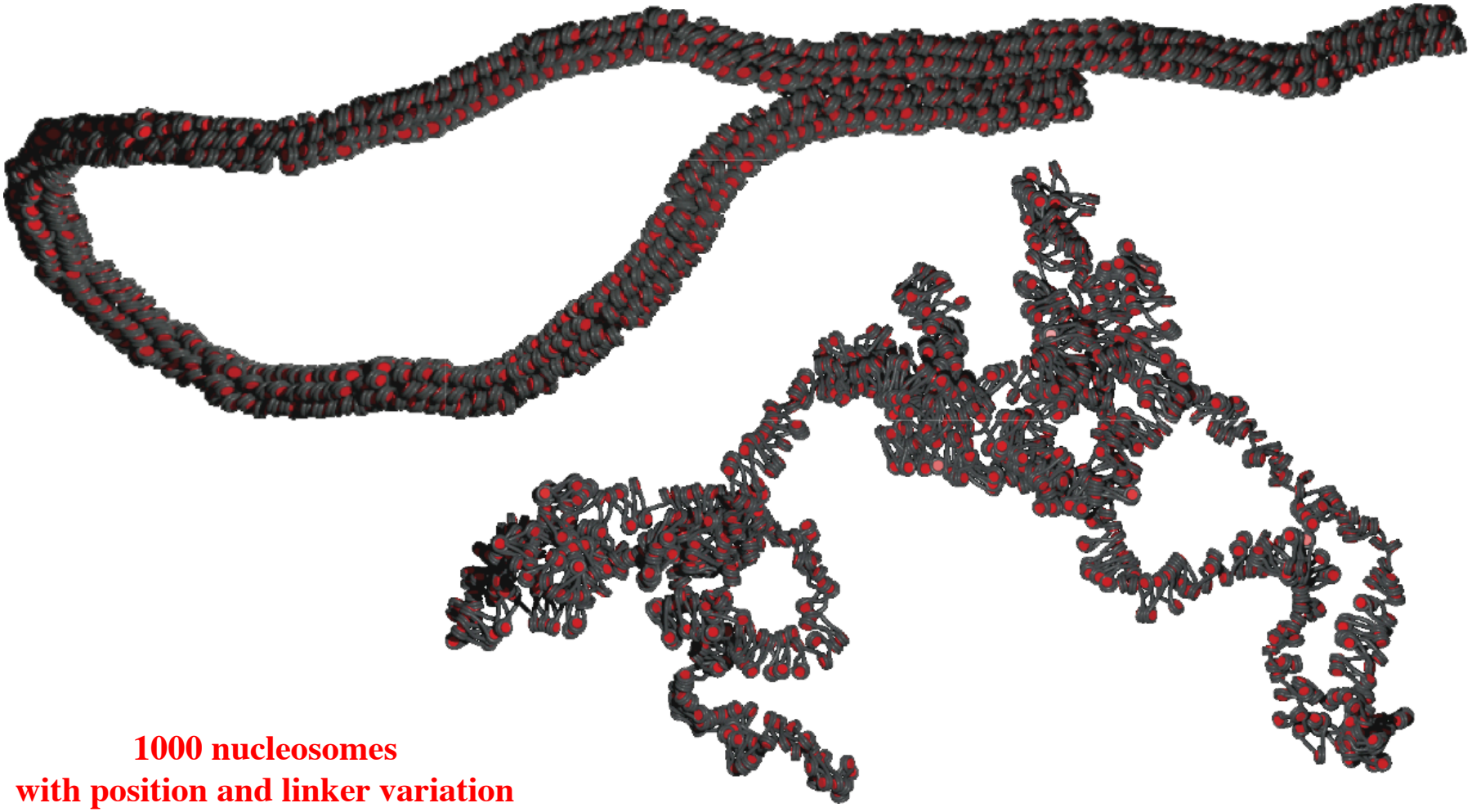

1000 nucleosomes
with position and linker variation

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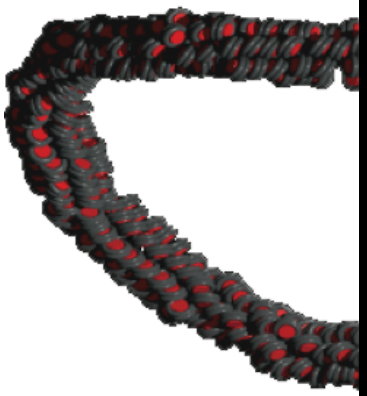

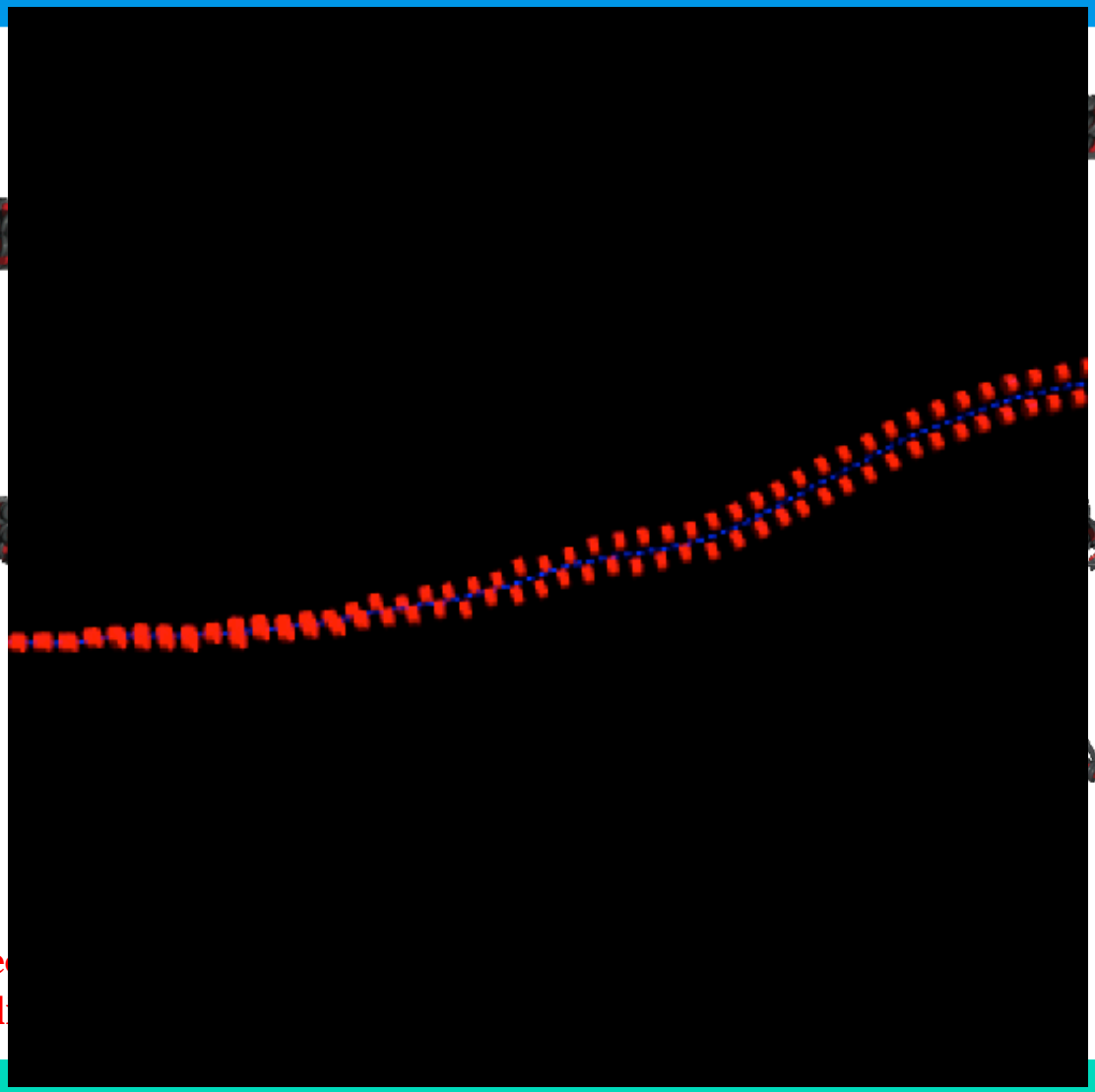

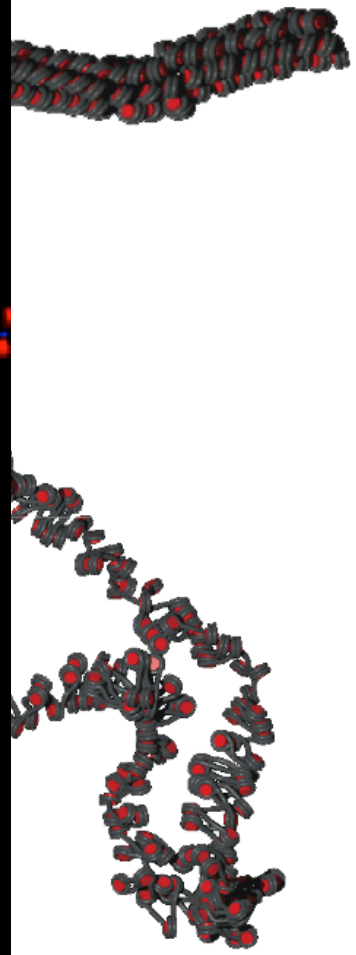

1000 nucle
with position and l

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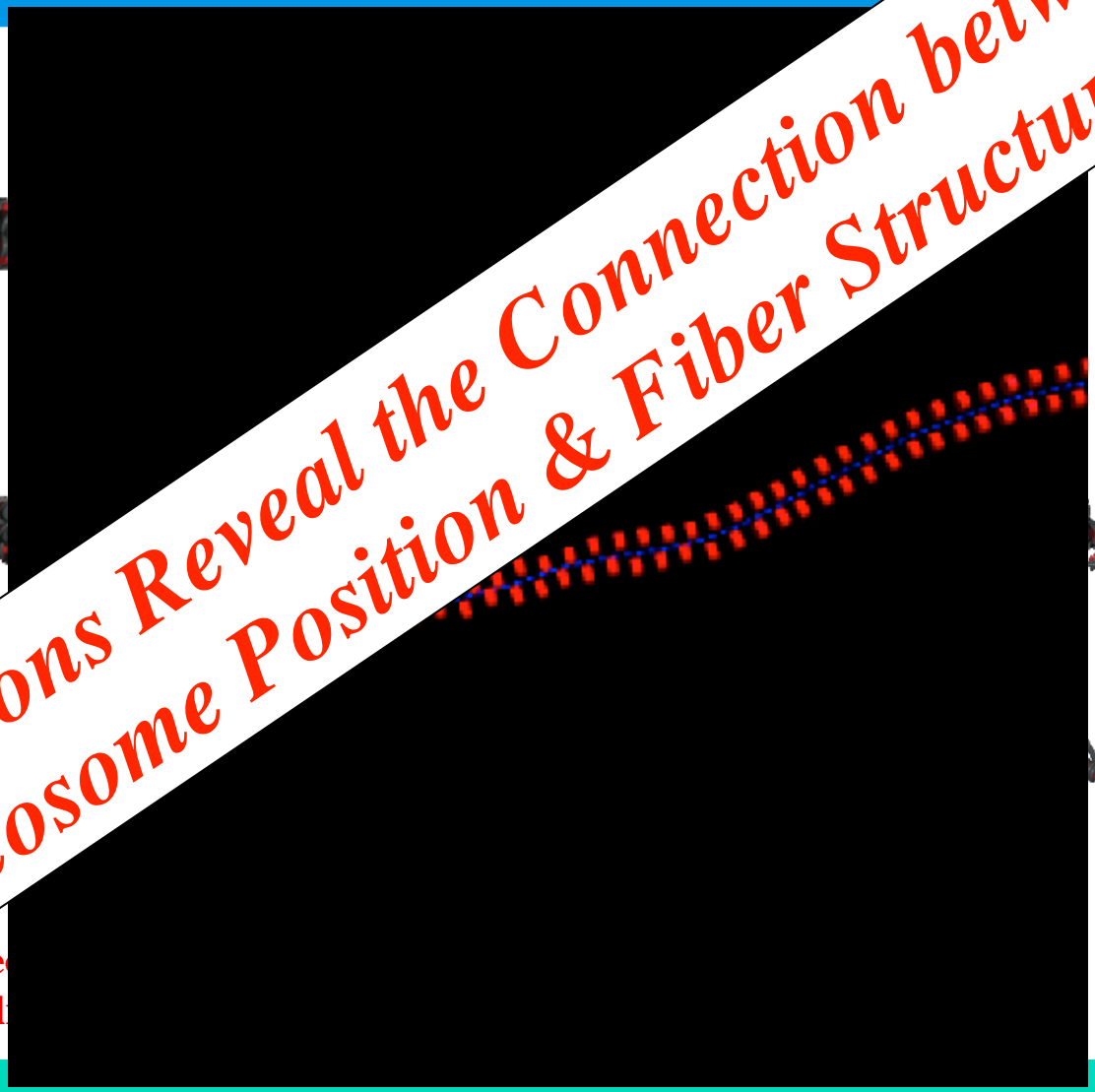
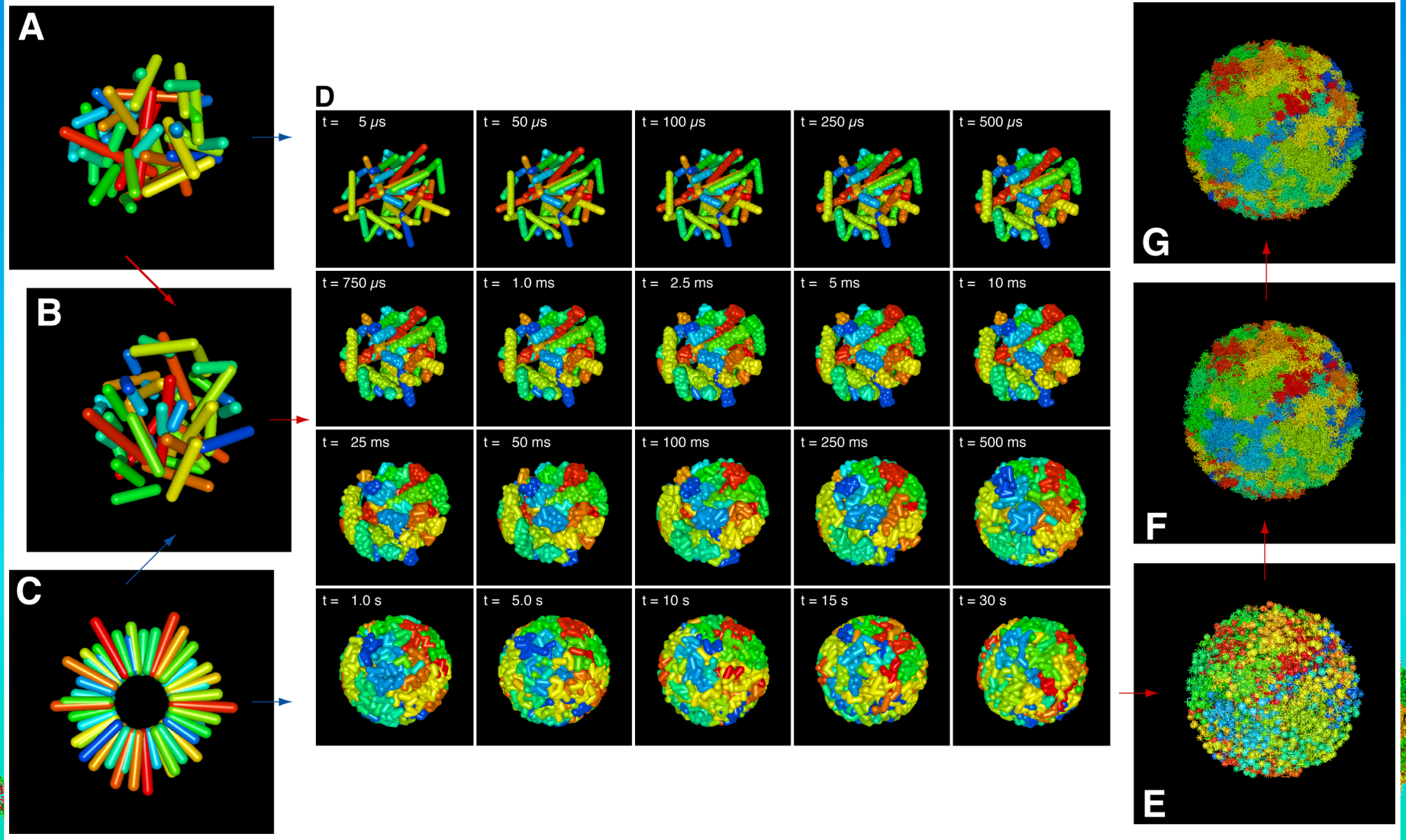


Simulations Reveal the Connection between Nucleosome Position & Fiber Structure !

with ion and l

Simulation of Nucleosomes, Chromatin, & Nuclei WP4

By parallel super-computer simulations using novel Monte Carlo and Brownian Dynamics approaches simulate chromosomes and whole nuclei with unprecedented resolution, resulting in novel predictions for the detailed folding of the chromatin fiber with corresponding impact on the experimental evaluation.



Simulation of Nucleosomes, Chromatin, & Nuclei WP4

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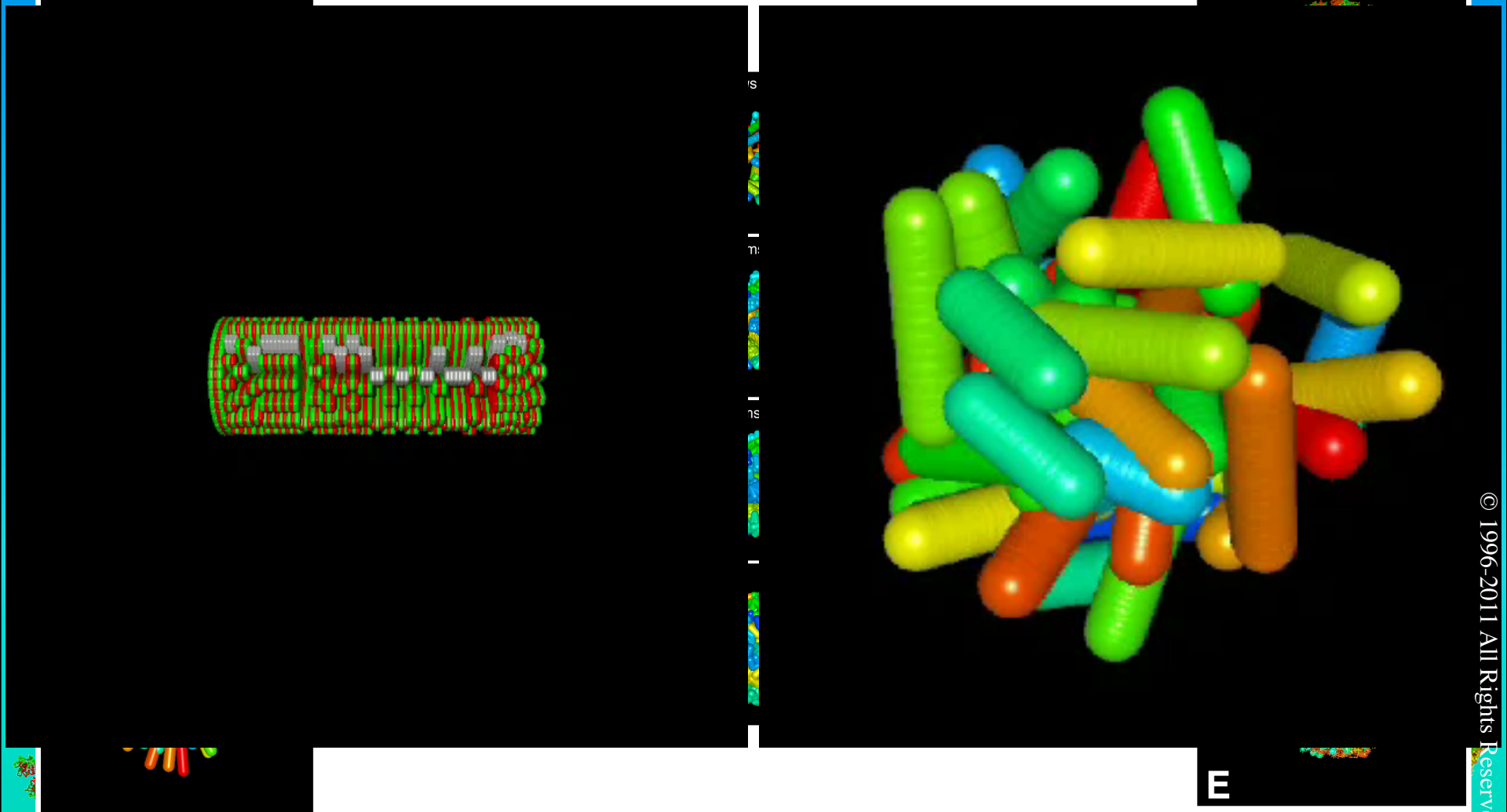

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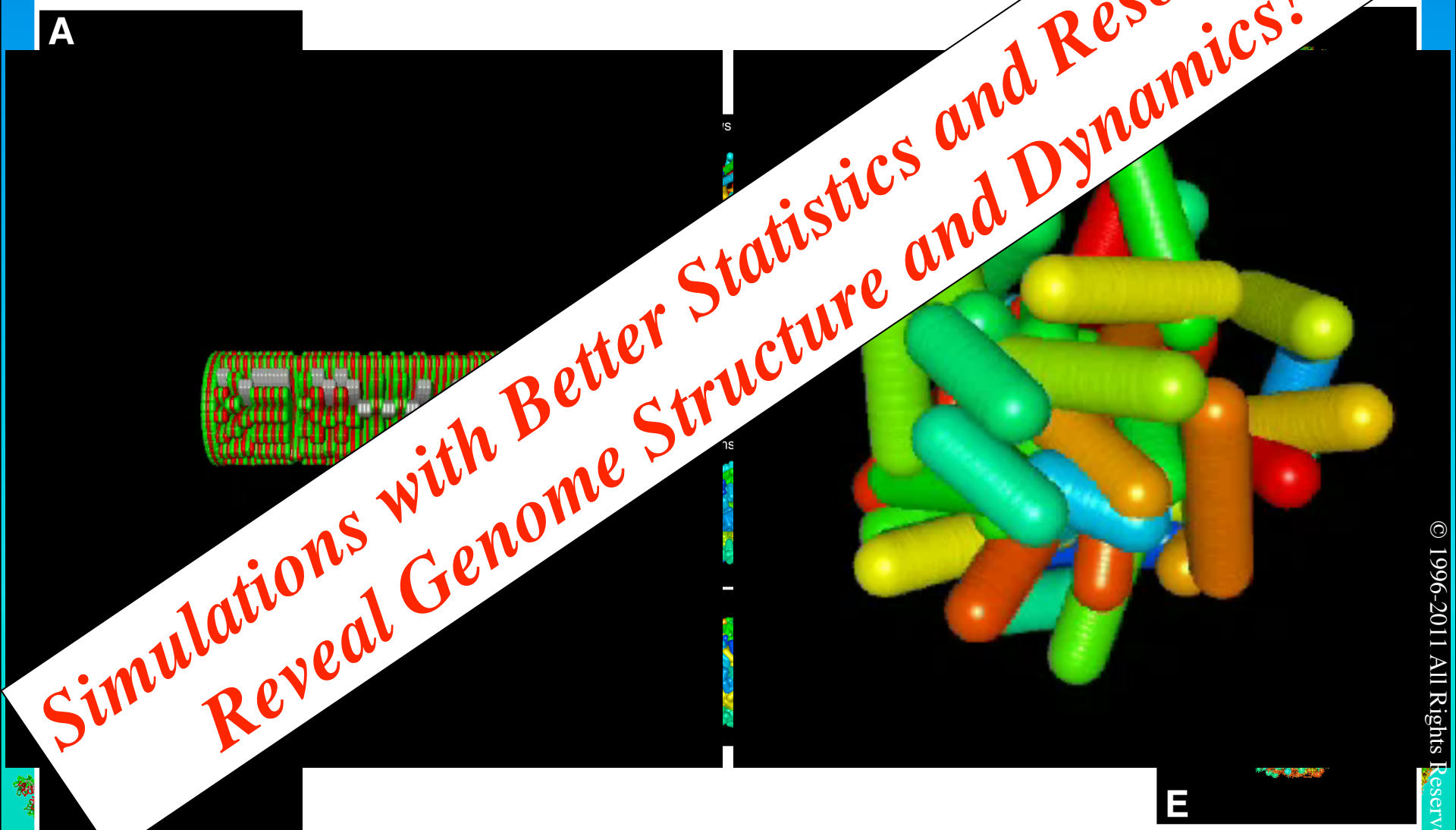
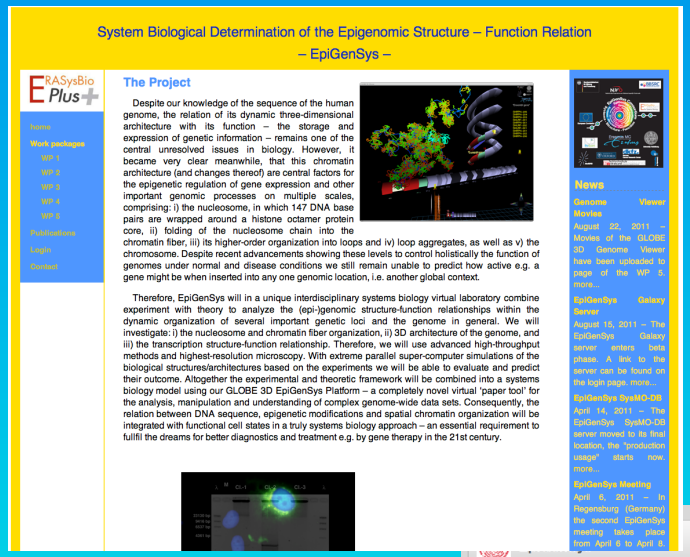


Simulations with Better Statistics and Resolutions Reveal Genome Structure and Dynamics!

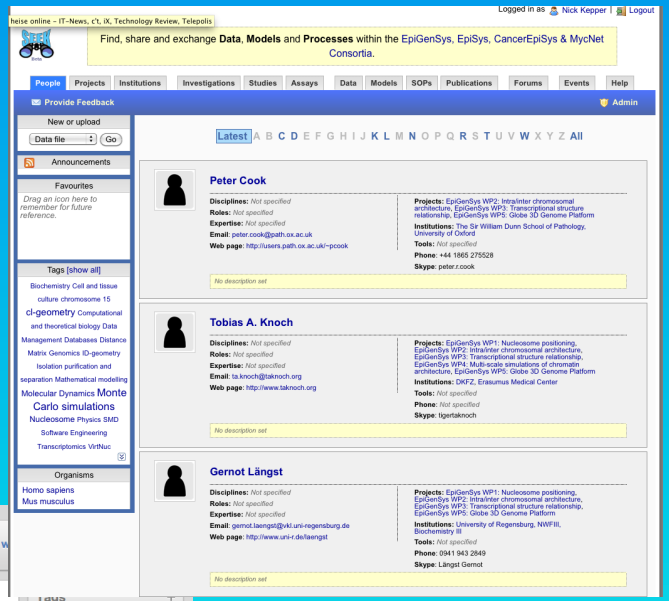
Systems Biological Result Communcation via Internal and External Communication Windows WP5

Three classic internal and external communication windows were opened: i) the EpiGenSys website communicates with the public, ii) the EpiGenSys Wiki functions is used for exchange, and iii) the EpiGenSys SysMO DB archives in a virtual labnote the data. All allow access to the systems and are the basis for the GLOBE 3D Genome Platform.

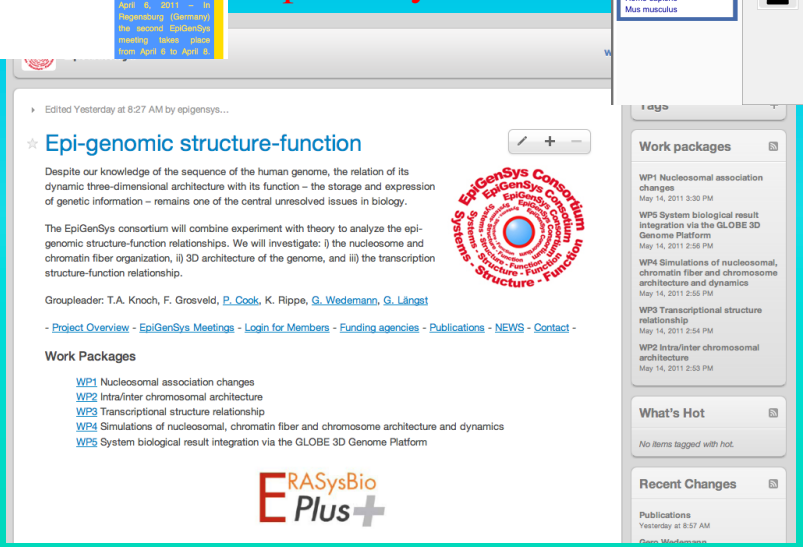
EpiGenSys Public Website



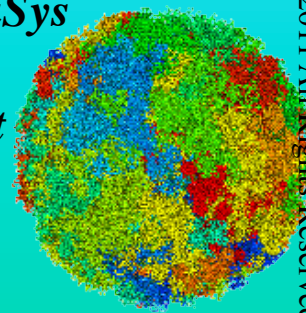
EpiGenSys SysMO DB

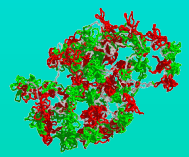


EpiGenSys Wiki



Joined with:
EpiGenSys
CancerEpiSys
EpiSys
MycNet





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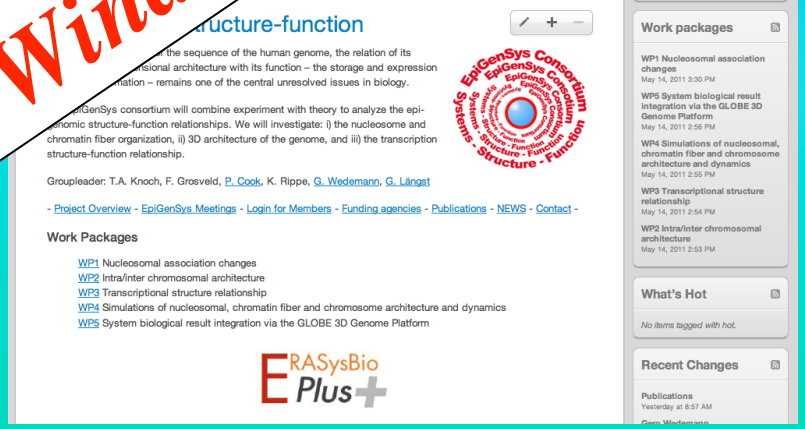
EpiGenSys Public Website

EpiGenSys has Three Internal and External "Classic Windows" for Communication!

EpiGenSys Wiki



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EpiGenSys International Large-Scale High-Throughput Data Analysis Centers and Grid Gateway WP5

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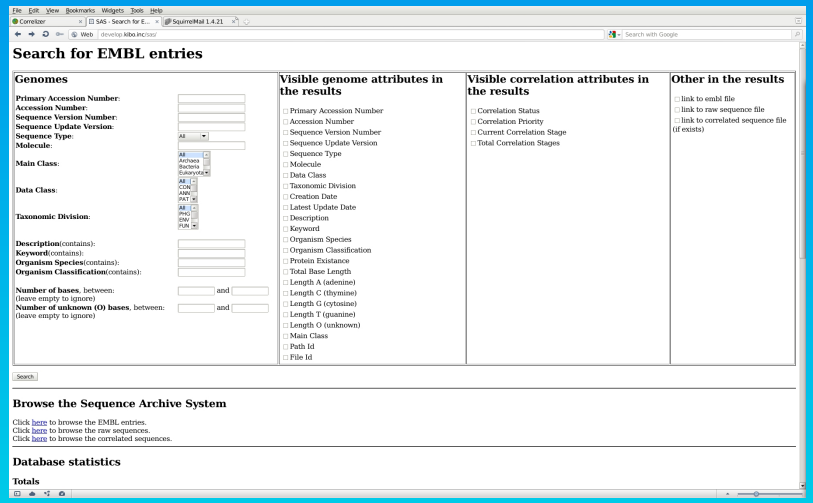
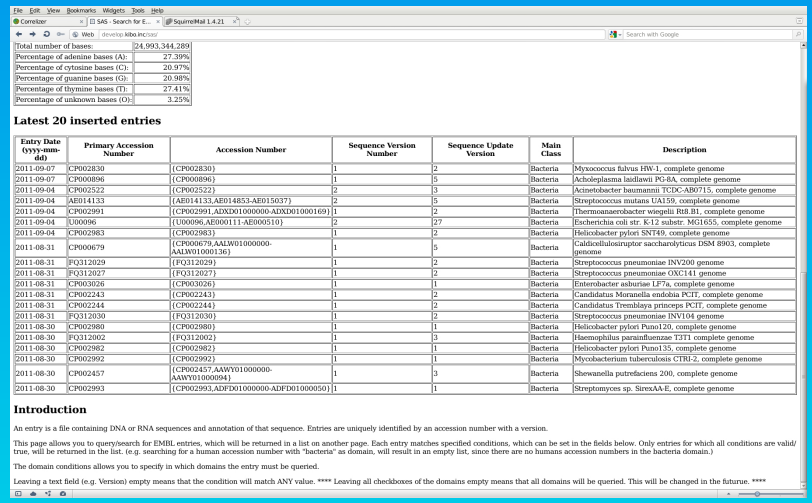
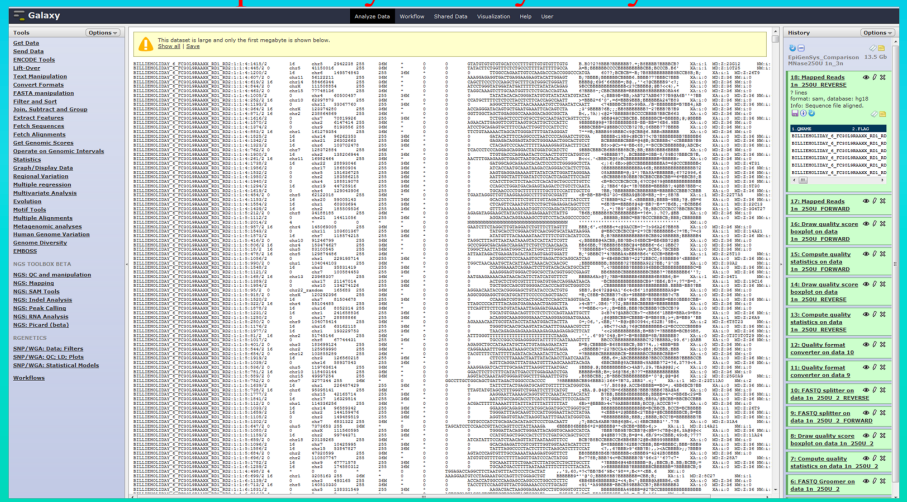
EpiGenSys Sequence Archiving Systems of Completely Sequenced Genomes





EpiGenSys Galaxy Analysis



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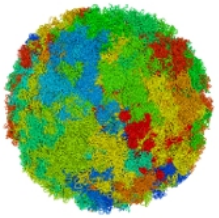

Project

- Correlizer
- Background
- Publications
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- Joining
- Acknowledgements

Participants

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- Server Status
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Comunity

- Teams
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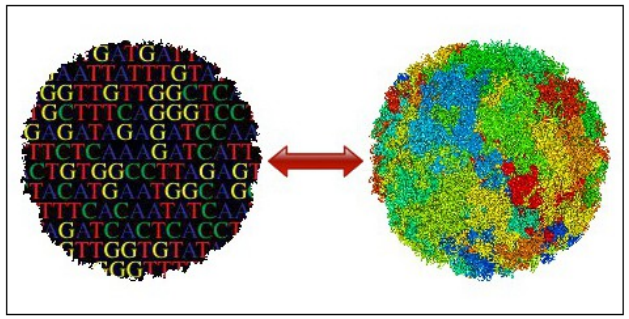
Revealing the Mysteries of Genome Organization

Genomes are fantastic keepers of genetic information and are the outcome of evolutionary replication, mutation and selection. Genomes organize functions from the cellular level, via the organismic level, up to the complex basis of mind. In human cells the genetic information controlling most processes from the cellular level, over embryogenesis to cognitive ability, manifests in a diploid set of 23 DNA molecules (chromosomes), combined they consist of ~3x10^9 base pairs (bp) stored in ~2.80 GB of data. This whole genome, whose added molecular length totals ~2m, is kept in comparably small cell nuclei with typical diameters of ~10 µm or volumes of 500 µm^3. The sequential organization of genomes, i.e. the relations between distant base pairs and regions within sequences, and its connection to the three-dimensional architectural organization of genomes is still a largely unresolved problem.



Correlizer has been set up to unravel these mysteries, and we found long-range power-law correlations on almost the entire observable scale of 132 completely sequenced chromosomes of 0.5 x 10^6 to 3.0 x 10^7 bp. Varying from Archaea, Bacteria, Arabidopsis thaliana, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster, and Homo sapiens. The local correlation coefficients show a species-specific multi-scaling behavior: close to random correlations on the scale of a few base pairs, a first maximum from 40 to 3,400 bp (for Arabidopsis thaliana and Drosophila melanogaster divided in two submaxima), and often a region of one or more second maxima from 10^5 to 3 x 10^5 bp. Within this multi-scaling behavior, an additional fine-structure is present and attributable to codon usage in all except the human sequences, where it is related to nucleosomal binding.

Computer-generated random sequences assuming a block organization of genomes, the codon usage, and nucleosomal binding explain these results. Mutation by sequence reshuffling destroyed all correlations. Thus, the stability of correlations seems to be evolutionarily tightly controlled and connected to the spatial genome organization, especially

User of the Day

Jeff17

I work in information technology. My primary interest is in the mathematical projects, but I have recently picked up an interest in some of the biology projects as well.

Jeff17
Correlizer

Credits:	56,038
BSrac:	862
Rank:	42
Rank%:	91.102

BOINC STATS boincstats.com user stats

News

... more

News is available as an RSS feed RSS

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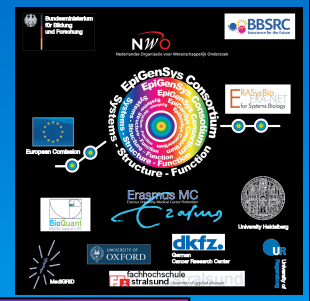

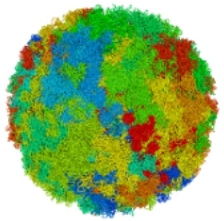

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Project status

Server software version: 23903M / 7 Sep 2011 | 12:34:36 UTC

Server status

Program	Host	Status
data-driven web pages	svahesrv2	Running
upload/download server	svahesrv2	Running
scheduler	svahesrv2	Running
feeder	svahesrv2	Running
transitioner	svahesrv2	Running
file_deleter	svahesrv2	Running
db_purge	svahesrv2	Running
ego_validator	svahesrv2	Running
ego_assimilator	svahesrv2	Running
ego_beta_validator	svahesrv2	Running
ego_beta_assimilator	svahesrv2	Running

Running: Program is operating normally

Not Running: Program failed or the project is down

Disabled: Program is disabled

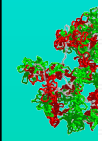
Computing status

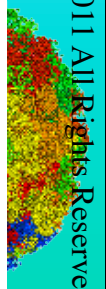
Work	#
Tasks ready to send	28,078
Tasks in progress	50,451
Workunits waiting for validation	1
Workunits waiting for assimilation	1
Workunits waiting for file deletion	3
Tasks waiting for file deletion	2
Transitioner backlog (hours)	0

Users	#
with recent credit	435
with credit	472
registered in past 24 hours	4
Computers	**#**
with recent credit	1,158
with credit	1,262
registered in past 24 hours	16
current GigaFLOPs	1,422

Tasks by application

application	unsent	in progress	avg runtime of last 100 results in h (min-max)	users in last 24h
BioMedical Genome Correlations	26,860	45,034	0.48 (0.29 - 1.07)	165
Correlizer Beta Applications	834	5,779	0.46 (0.15 - 1.07)	30





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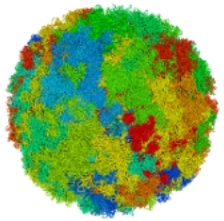

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db_purge		
ego_validator		
ego_assi		
eg		

ng
g normally
d or the project is
ram is disabled

Computing

	451
	1
mation	1
file deletion	3
file deletion	2
backlog (hours)	0

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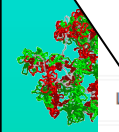
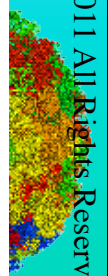
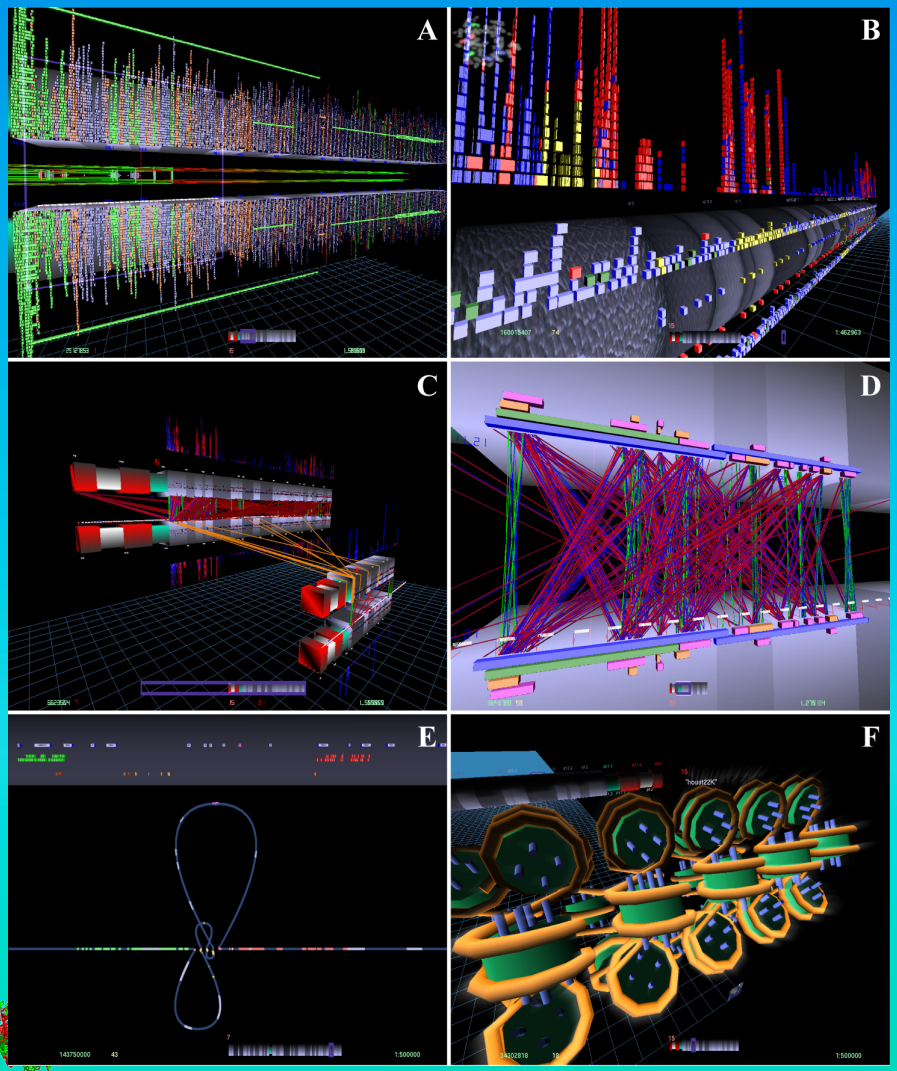
EpiGenSys created New Data Analysis Centers and a Volunteer Grid with High Public Impact!

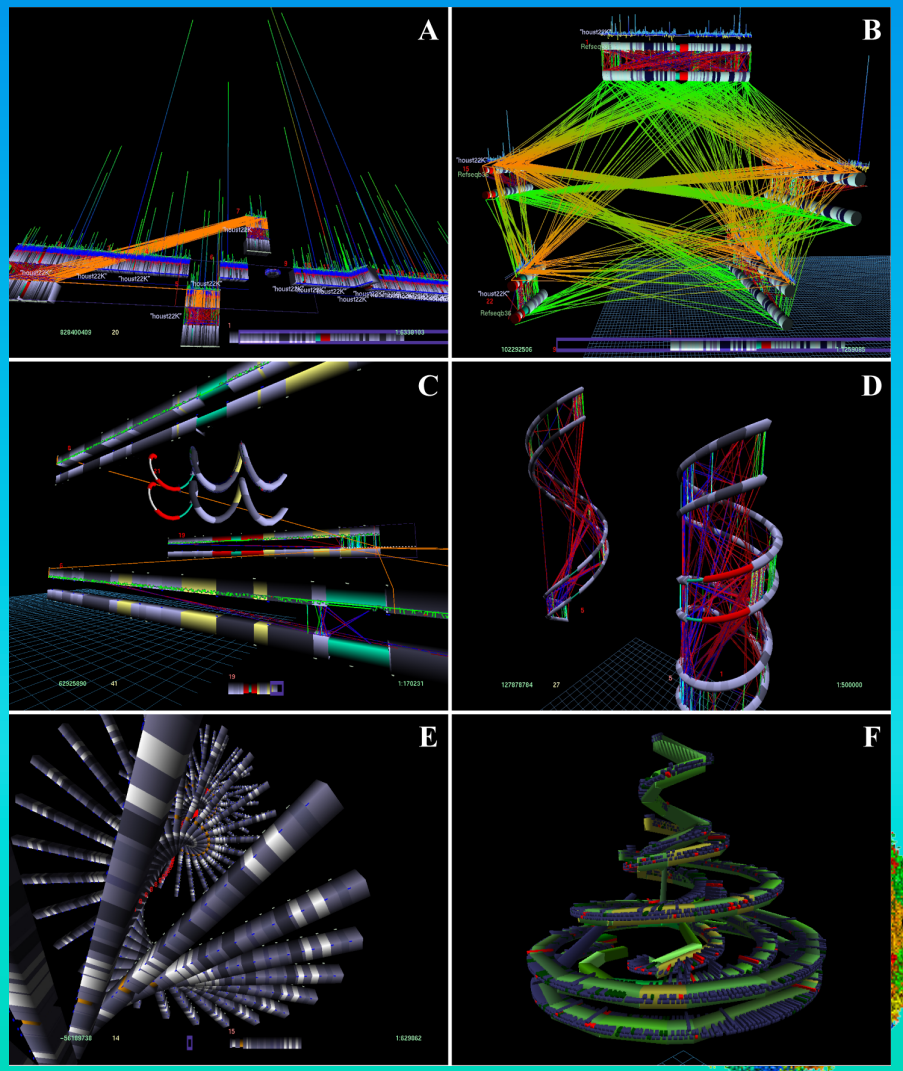




EpiGenSys Systems Biological Result Integration via the GLOBE 3D Genome Platform WP5

All results will be integrated using our GLOBE 3D Genome Platform, established for analysis, manipulation and understanding of multi-dimensional complex genome wide data. Thus in reiterative cycles between experiments and simulations a systems biological/medical genome model will be achieved.





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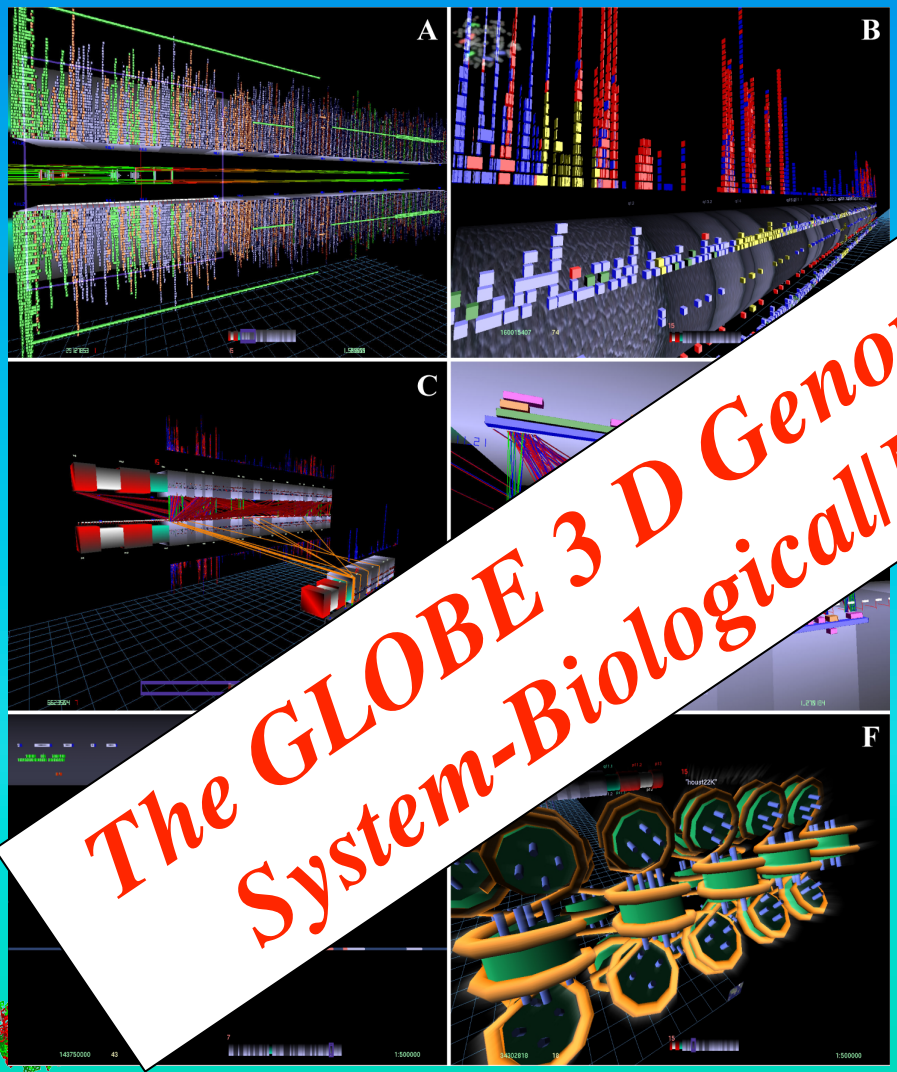

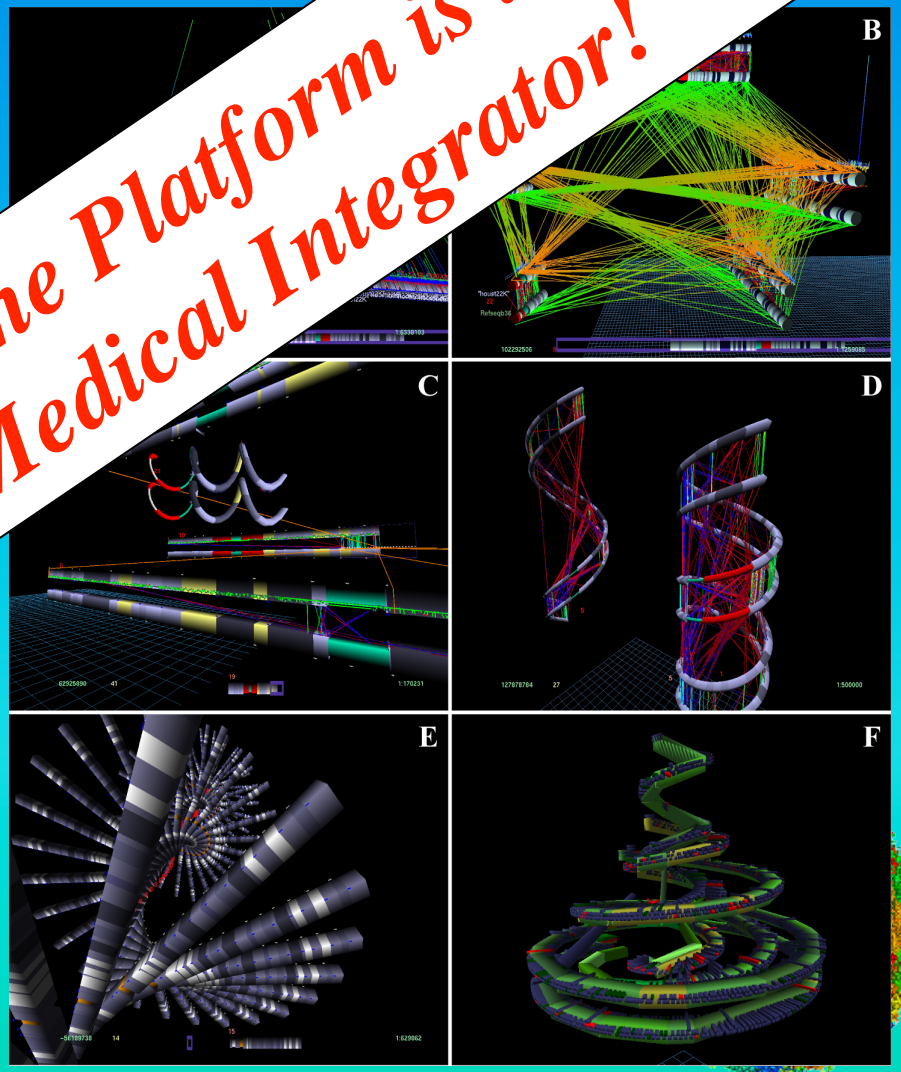

The GLOBE 3 D Genome Platform is the System-Biological/Medical Integrator!

Publications of EpiGenSys

The EpiGenSys consortium approach will be exploited and disseminated in interdisciplinary research publications. Until know 12 research articles and reviews are published or in press. Currently, several are under way and will be published soon.

Research Articles:

1. Melnik, S., Deng, B., Papantonis, A., Babbo, S., Carr, I.M. & Cook, P.R. The proteomes of transcription factories containing polymerases I, II, or III. *Nat. Methods*, in press.
2. Ettig, R., Kepper, N., Stehr, R., Wedemann, G. & Rippe, K. Dissecting DNA-histone interactions by molecular dynamics simulations of unwrapping DNA from the nucleosome, *Biophys. J.*, in press.
3. Felle, M., Hofmeister, H., Rothammer, J., Fuchs, A., Exler, J., & Längst, G. Nucleosomes protect DNA from DNA methylation in vivo and in vitro. Nucleic Acids Res. DOI: 10.1093/nar/gkr263, 2011.
4. Teif, V. & Rippe, K. Nucleosome mediated cross-talk between transcription factors, Phys. Biol. 8, 044001, DOI: 10.1088/1478-3975/8/4/044001, 2011.
5. Kepper, N., Ettig, R., Stehr, R., Wedemann, G., & Rippe, K. Force spectroscopy of chromatin fibers: extracting energetics and structural information from Monte Carlo simulations. Biopolymers 95, 435-447, 2011.
6. Skrowny, D., Dickmann, F., Löhnhardt, B., Knoch, T. A., & Sax, U. Development of an information platform for new grid users in the biomedical field. Stud. Health Techno. Inform. 159, 277-282, 2010.
7. Kepper, N., Ettig, R., Dickmann, F., Stehr, R., Grosveld, F. G., Wedemann, G., & Knoch, T. A. Parallel high-performance grid computing: capabilities and opportunities of a novel demanding service and business class allowing highest resource efficiency. Stud. Health Techno. Inform. 159, 264-271, 2010.
8. Kepper, N., Schmitt, E., Lesnussa, M., Weiland, Y., Eussen, H. B., Grosveld, F. G., Hausmann, M., & Knoch, T. A. Visualization, analysis, and design of COMBO-FISH probes in the grid-based GLOBE 3D genome platform. Stud. Health Techno. Inform. 159, 159-171, 2010.

Reviews:

1. Papantonis, A. & Cook, P.R. Fixing the model for transcription: the DNA moves, not the polymerase. *Transcription*, 2, 41-44.
2. Teif, V. & Rippe, K. Calculating transcription factor binding to nucleosomal DNA for large genomic regions, Briefings Bioinf. 12, DOI: 10.1093/bib/bbr037, 2011.
3. Längst, G., Teif, V. B., & Rippe, K. Chromatin remodeling and nucleosome positioning. In *Genome organization and function in the cell nucleus*, Rippe, K., ed., pp. 111-139, Wiley-VCH, Weinheim, 2011.
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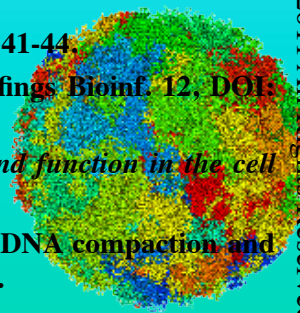

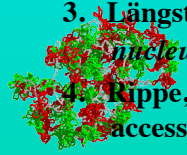

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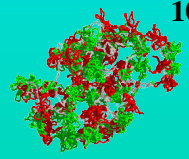
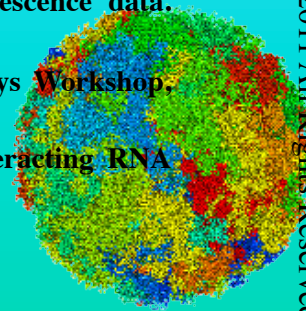
The Dissemination of Results of EpiGenSys is Underway and Taking Up Speed!

Presentations of EpiGenSys (before Holidays)

A major aim of the EpiGenSys consortium is to considerable contribute to systems biology in the genomic sector and increase the awareness and understanding of genomic complexity within society. Scientifically that means presenting our work at conferences. The list shown has increased over the holiday period tremendously.

1. **Papantonis A., & Cook P. R. Active RNA polymerases are immobile molecular machines tethering dynamic intra- and inter-genic loops. 9th EMBL Conference "Chromatin and Transcription", EMBL, Heidelberg, Germany, 28th to 31th August 2010.**
2. **Cook, P.R. Active RNA polymerases are immobile molecular machines. The 69th Harden Conference ("RNAP2010 - Structure, function and evolution of RNA polymerases. A joint Biochemical Society / Wellcome Trust conference"), The Wellcome Trust, Hinxton, Cambridge, UK, 22th to 25th September 2010.**
3. **Cook, P. R. A model for all genomes: the role of RNA polymerases fixed in factories. GENOFIELD2011 ("International Symposium on the Physicochemical Field for Genetic Activities"), Awaji Island, Japan from 24th to 26th January 2011.**
4. **Cook, P. R. Active RNA polymerases are immobilized molecular machines. at 'The 46th WINTERSEMINAR ("Biophysical Chemistry, Molecular Biology and Cybernetics of Cell Functions"), Klosters, Switzerland, 15th to 29th January 2011.**
5. **Kepper, N., & Knoch, T. A. Parallel high-performance grid computing: capabilities and opportunities of a novel demanding service and business class allowing highest resource efficiency. HealthGrid 2010 ("Healthgrid Applications and core Technolgies"), University XI, Orsay, France, 28th to 30th June 2010.**
6. **Kepper, N., & Knoch, T. A. Visualization, analysis, and design of COMBO-FISH probes in the grid-based GLOBE 3D genome platform. HealthGrid 2010 ("Healthgrid Applications and core Technolgies"), University XI, Orsay, France, 28th to 30th June 2010.**
7. **Müller, O., Stehr, R., Schöpflin, R., Ettig, R., Kepper, N., Rippe, K., & Wedemann, G.: Computer simulation of chromatin: Modeling the influence of nucleosome repositioning. DPG conference, Verhandl. DPG(VI) 46, 1/2011, p. 231, Dresden., 14th March 2011.**
8. **Rippe, K. Dissecting epigenetic networks. Workshop: Spatio-temporal dynamics challenges from fluorescence data. Symposium series Complexity and Systems Biology. Warwick University, UK, July 13-16th 2010.**
9. **Rippe, K. Chromatin remodelers - from in vitro measurements to studies in living cells. Chromatin Days Workshop. Interdisciplinary Research Institute USR 3078 CNRS, Lille, France, October 7-8th 2010.**
10. **Schubert, T., Pusch, M., Diermeier, S., Gröbner-Ferreira, R., Imhof, A. and Längst, G. Chromatin interacting RNA maintains accessible higher order structures of chromatin, EMBL Transcription Meeting, Heidelberg 2010.**





Presentations of EpiGenSys (before Holidays)

A major aim of the EpiGenSys consortium is to considerable contribute to systems biology in the genomic sector and increase the awareness and understanding of genomic complexity within society. Scientifically that means presenting our work at conferences. The list shown has increased over the holiday period tremendously

1. Papantonis A., & Cook P. R. Active RNA polymerases are immobile molecular … and inter-genic loops. 9th EMBL Conference "Chromatin and Transcription", … to 31th August 2010.
2. Cook, P.R. Active RNA polymerases are immobile molecular mach… ce ("RNAP2010 - Structure, function and evolution of RNA polymerases. A joint … ust conference"), The Wellcome Trust, Hinxton, Cambridge, UK, 22th to 25th Sept…
3. Cook, P. R. A model for all genomes: the role of RNA … NOFIELD2011 ("International Symposium on the Physicochemical Field for Geneti… from 24th to 26th January 2011.
4. Cook, P. R. Active RNA polymerases are immo… 46th WINTERSEMINAR ("Biophysical Chemistry, Molecular Biology and Cybern… Switzerland, 15th to 29th January 2011.
5. Kepper, N., & Knoch, T. A. Parall… ing: capabilities and opportunities of a novel demanding service and business … iency. HealthGrid 2010 ("Healthgrid Applications and core Technolgies"), Universit… e 2010.
6. Kepper, N., & Knoch, T… esign of COMBO-FISH probes in the grid-based GLOBE 3D genome platform. H… ications and core Technolgies"), University XI, Orsay, France, 28th to 30th June 201…
7. Müller, O… Kepper, N., Rippe, K., & Wedemann, G.: Computer simulation of chromatin: Modeli… positioning. DPG conference, Verhandl. DPG(VI) 46, 1/2011, p. 231, Dresden., 14th M…
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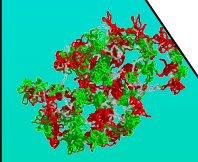
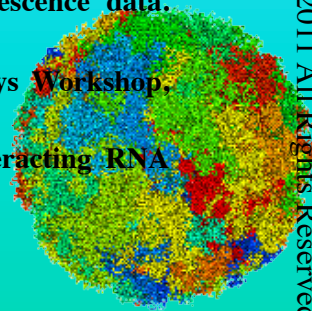
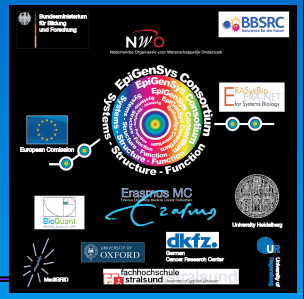
The EpiGenSys and EraSysBio+ is very well Disseminated via Presentations!





Patents and Additional Funding

Each of the technologies used (and their future developments), plus the synergies that might arise from their combined use, have potential for commercialization due to their uniqueness, novelty, and frontier position, e.g. concerning academic, diagnostic and commercial aspects. These successes also generates new funding opportunities.



Patens:

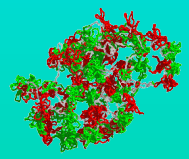
1. **Patent 1 by the Knoch/Grosveld group. WP 2.**

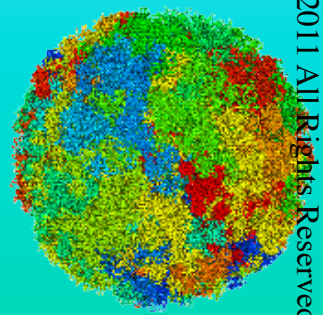
2. **Patent 2 by the Knoch/Grosveld group. WP 2.**

Funding due to EpiGenSys:

1. **1,000,000 Euros on funding the Erasmus Computing Grid over 5 years in end 2009 due to the EpiGenSys expected granting. WP 1 to WP 5.**

2. **Computer time at the supercomputer center in Hannover twice: i) 24,500 Euros for computation time 2008/2009, and ii) 42,000 Euros for computation time in 2009/2010. WP 1 and WP 2.**





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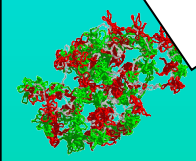
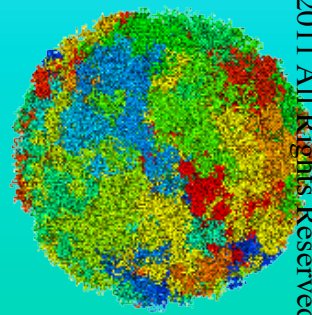
Exploitation and Refunding is Underway!





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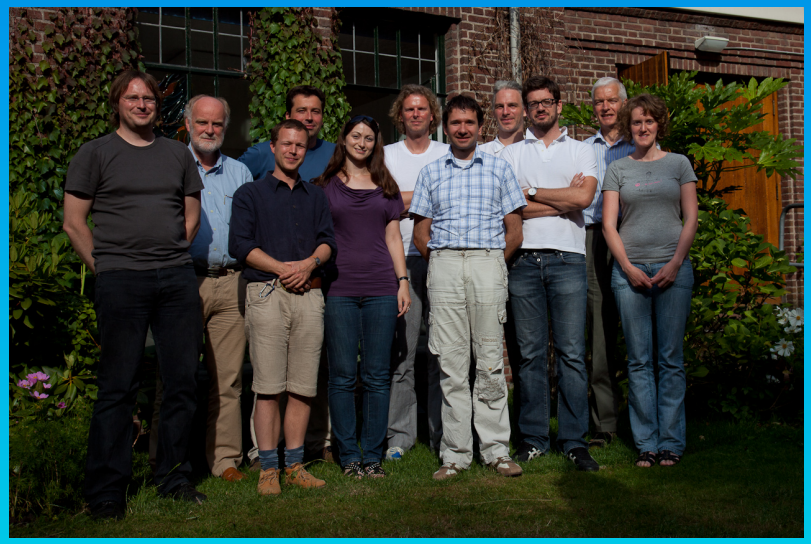
Thanks go to all the lab local lab members, those people who supported this work in the last decades, the institutions providing their infrastructure, and the national and international computing infrastructures.

Special thanks go to the reviewers, the EraSysBio Plus initiative and the national and EU funding bodies.



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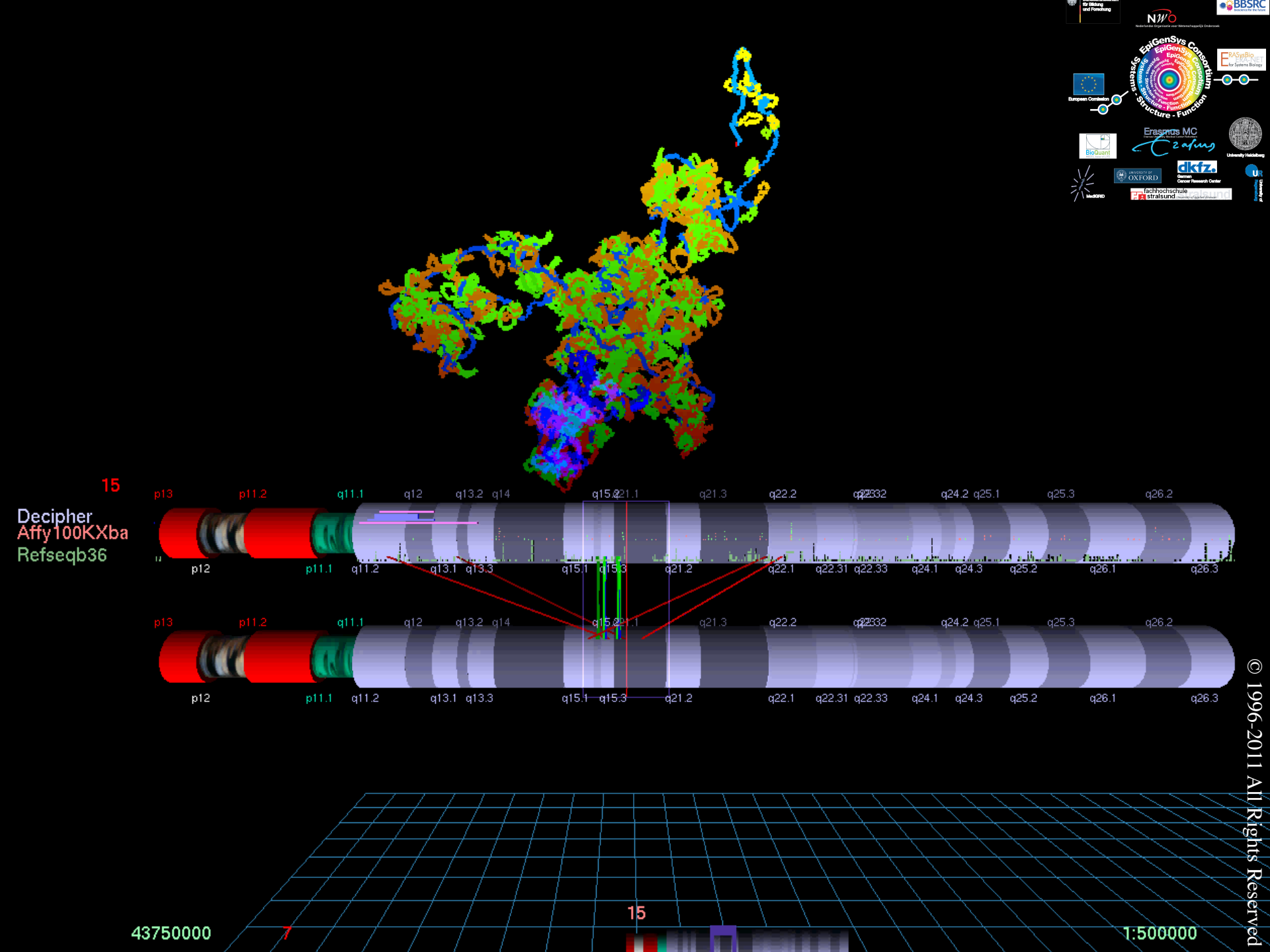
Towards a Holistic Genome Understanding by a Systems Biological/Medical Model for Research, Diagnostics and Treatment!



EpiGenSys

–

Systems Biological Determination of the Epigenomic Structure Function Relation: Nucleosomal Association Changes, Intra/Inter Chromosomal Architecture, Transcriptional Structure Relationship, Simulations of Nucleosomal/Chromatin Fiber/Chromosome Architecture and Dynamics, and Systems Biological/Medical Result Integration via the GLOBE 3D Genome Platform.

Knoch, T. A.

EpiGenSys Midterm Meeting and Evaluation Conference, Hotel Kaiserwasser, Vienna, 15th September, 2011.

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 Immunoglobin 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.

Corresponding author email contact: TA.Knoch@taknoch.org

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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