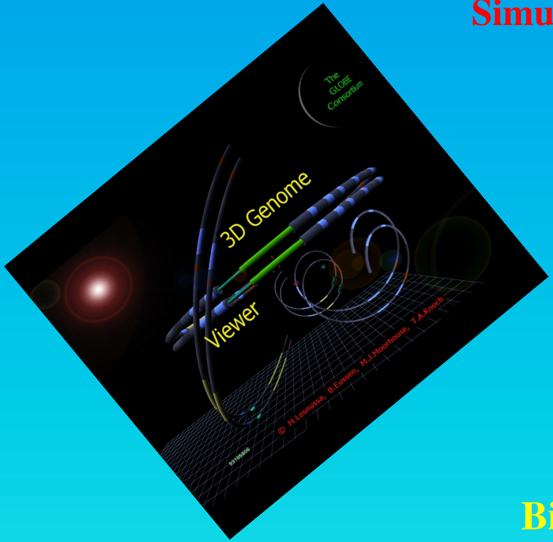
Erasmus Computing Grid

Erasmus MC
University Medical Center Rotterdam

From Sequence to Morphology

-

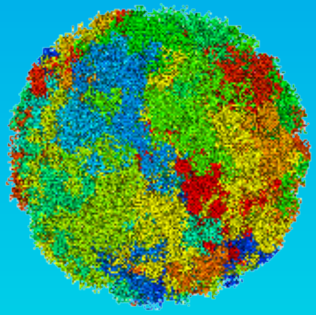
Approaching the Three-Dimensional Organization of the Human Genome



Simulation of Structural-, Scaling and Dynamic-Properties

The Erasmus Computing Grid

The Next Generation Genome Viewer



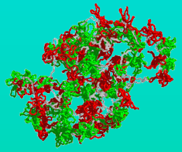
by

Tobias A. Knoch

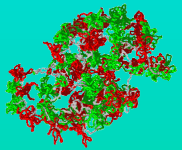
Biophysical Genomics in Cell Biology & Genetics

Bert Eussen, Michael Moorhouse, Annelies de Klein, & Frank Grosveld

Cell Biology & Genetics, Clinical Genetics, & Virology



Erasmus MC, Rotterdam,The Netherlands



Erasmus Computing Grid

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From Sequence to Morphology

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Simulation of Structural-, Scalin

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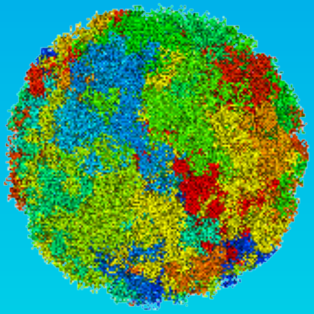


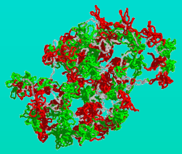
From Sequence to Morphology:
Towards a Holistic Understanding of Genomes!

bias A. Knoch

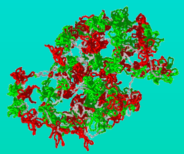
al Genomics in Cell Biology & Genetics

, Michael Moorhouse, Annelies de Klein, & Frank Grosveld

Cell Biology & Genetics, Clinical Genetics, & Virology

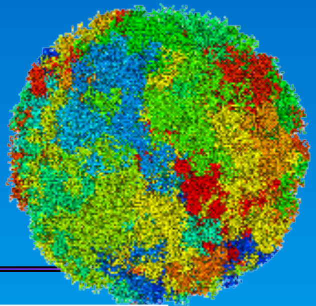


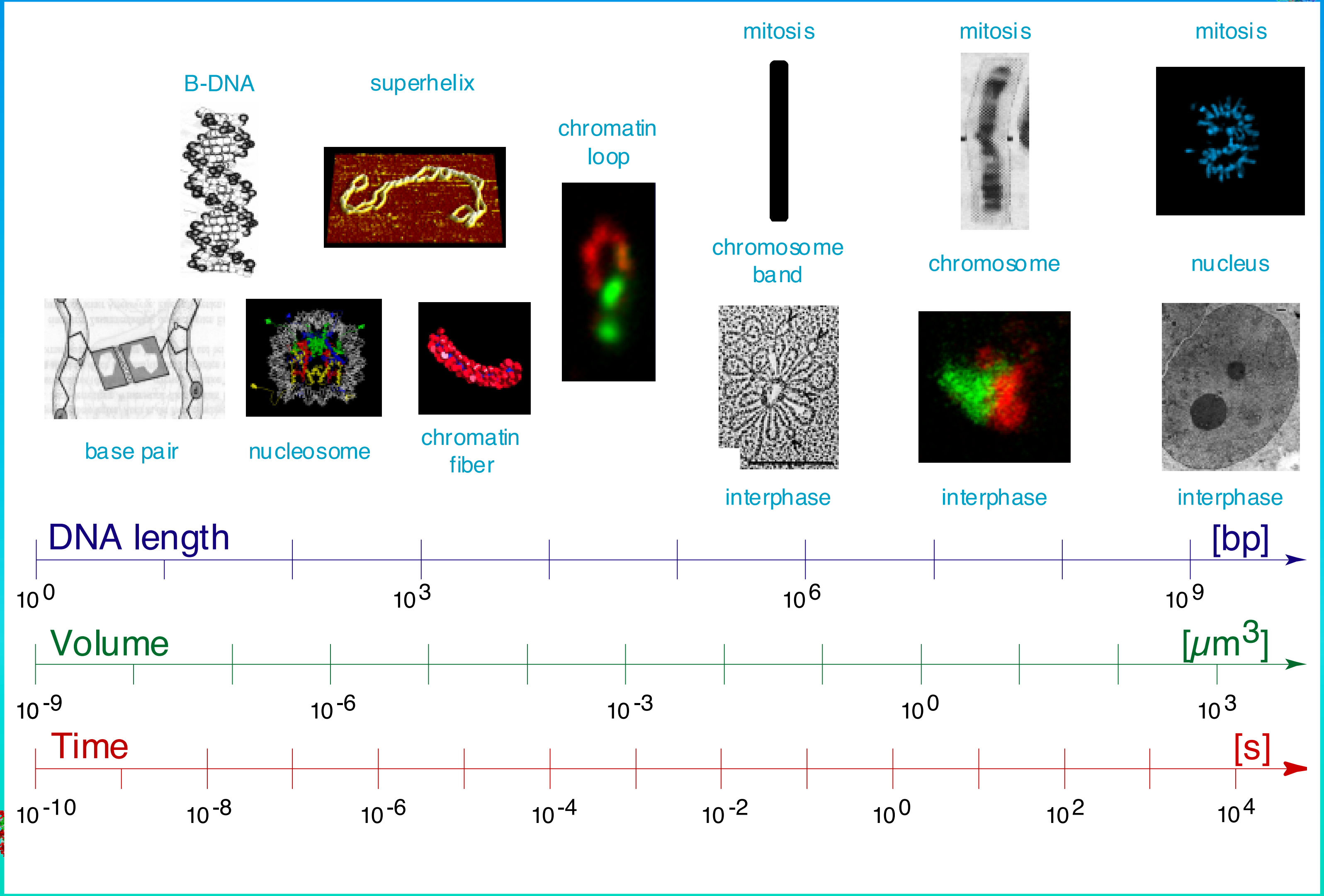
Erasmus MC, Rotterdam,The Netherlands

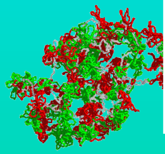


Dynamic and Hierarchical Genome Organization

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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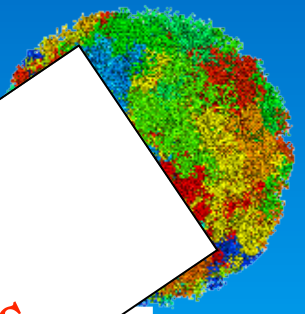
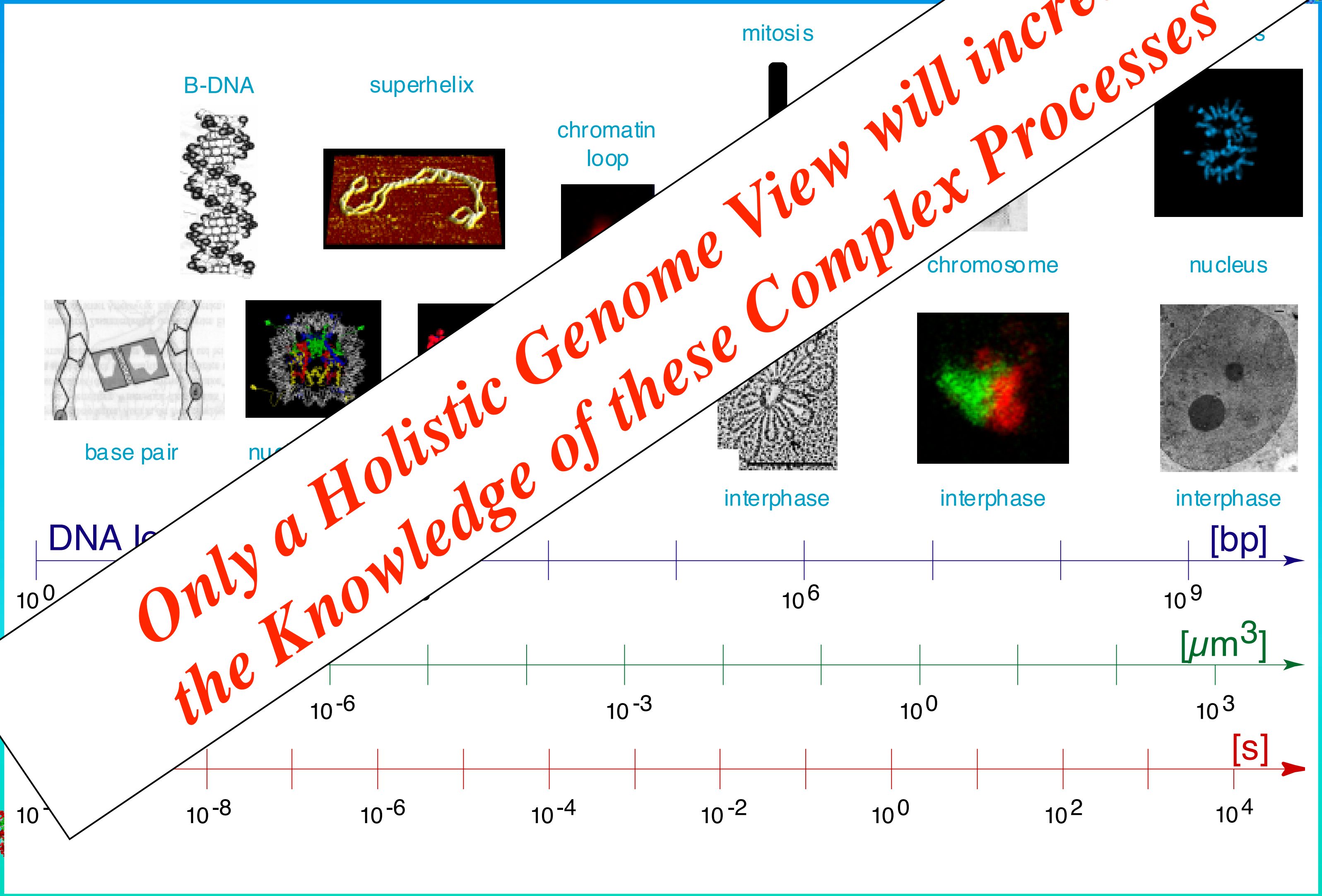
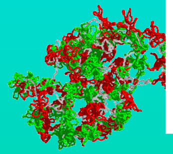


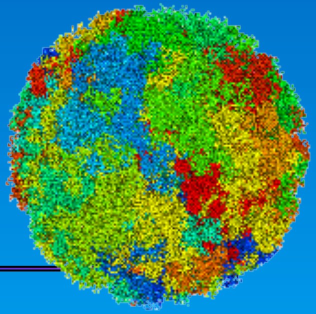


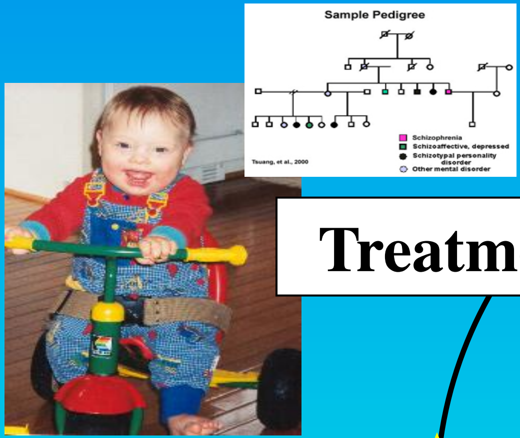
Only a Holistic Genome View will increase the Knowledge of these Complex Processes

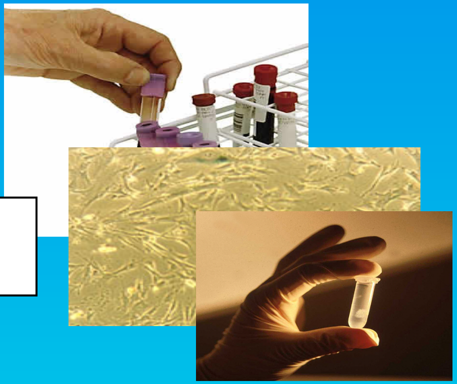


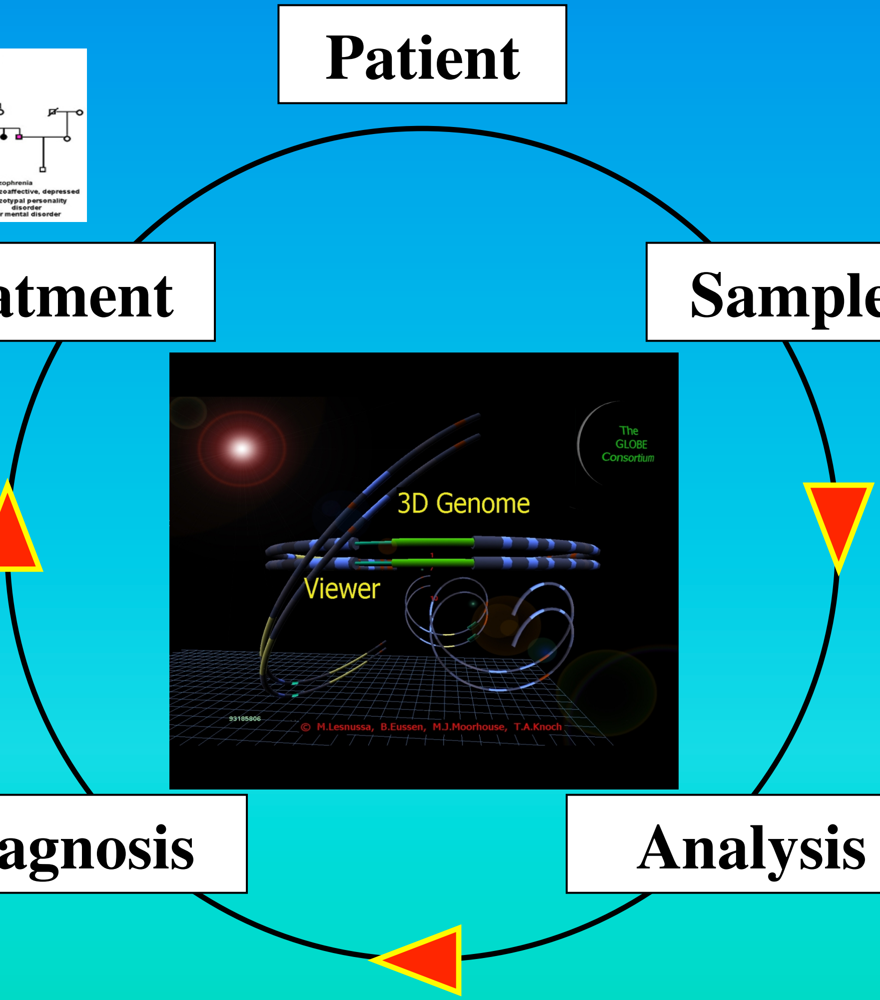
The Complexity of Cytogenetic Diagnostics

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









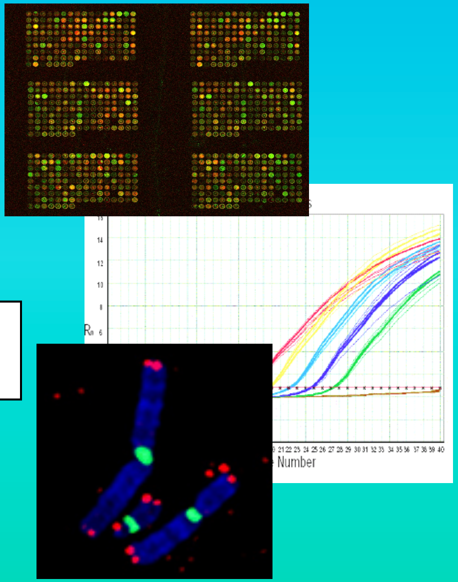
Patient

Sample

Analysis

Diagnosis

Treatment



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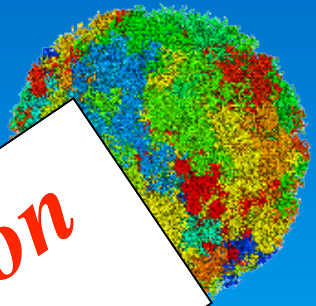

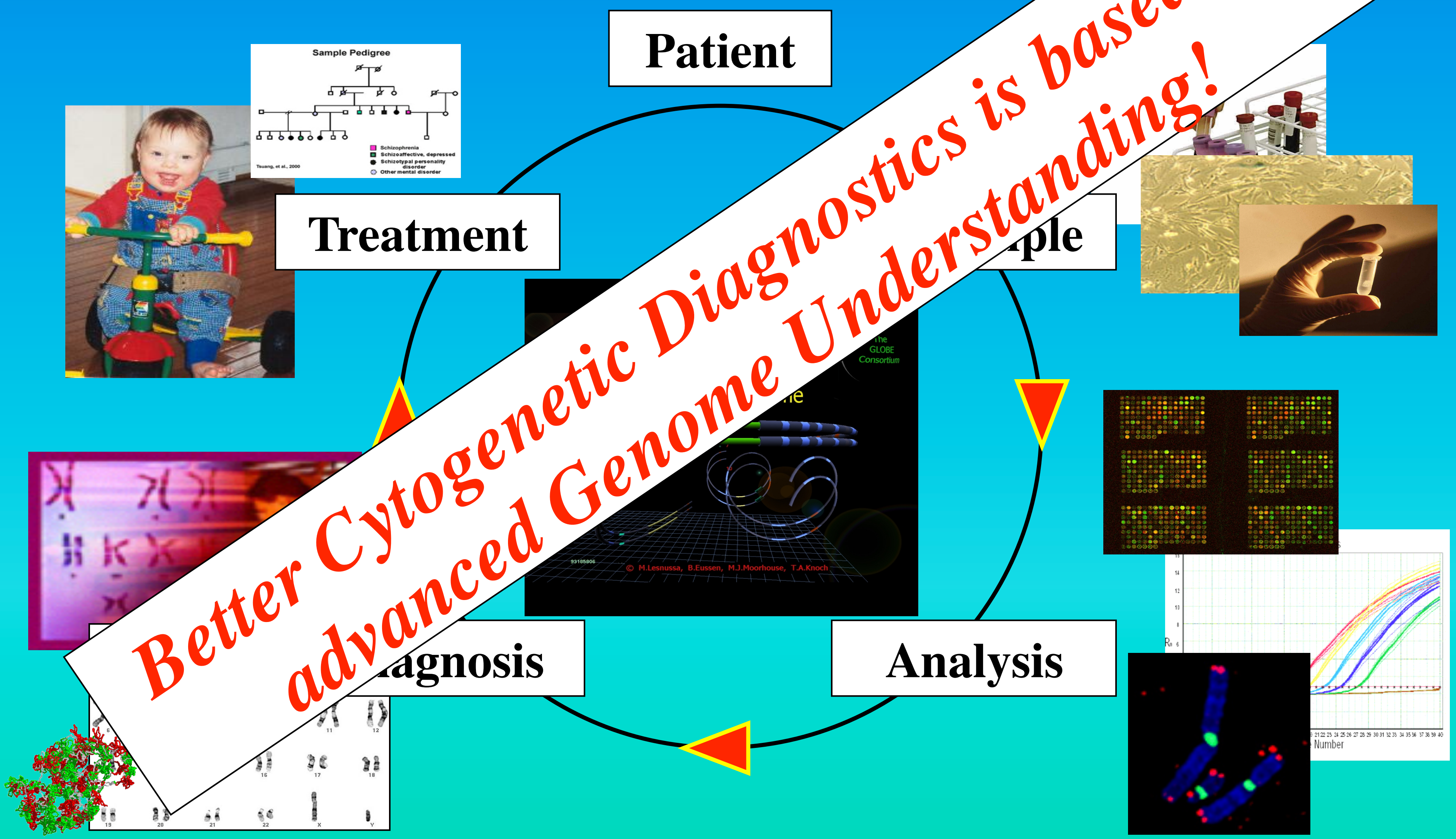

Patient

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Analysis

agnosis

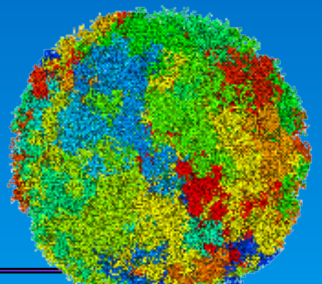
Treatment

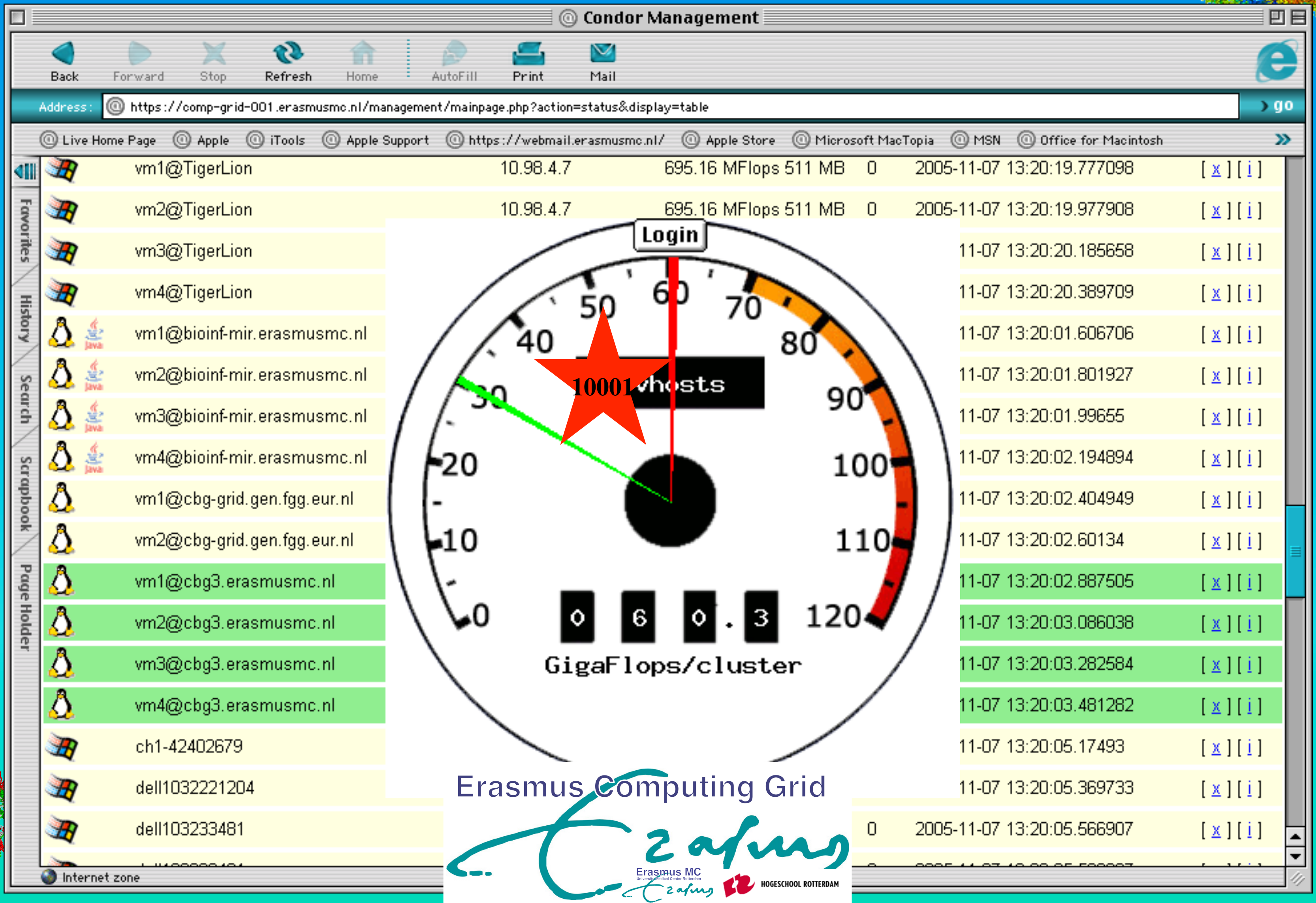
Better Cytogenetic Diagnostics is based on advanced Genome Understanding!

The Erasmus Computing Grid

Building a Super-Computer at Erasmus MC for Free!

Applications at Erasmus MC: E.g. genome sequence analysis, protein structure simulations, chip/array analysis, epidemiology of viral infections, patient diagnostic image analysis (AMI).





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vm2@TigerLion	10.98.4.7	695.16 MFlops 511 MB	0	2005-11-07 13:20:19.977908	[x] [i]
vm3@TigerLion				11-07 13:20:20.185658	[x] [i]
vm4@TigerLion				11-07 13:20:20.389709	[x] [i]
vm1@bioinf-mir.erasmusmc.nl				11-07 13:20:01.606706	[x] [i]
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vm3@cbg3.erasmusmc.nl				11-07 13:20:03.282584	[x] [i]
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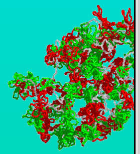

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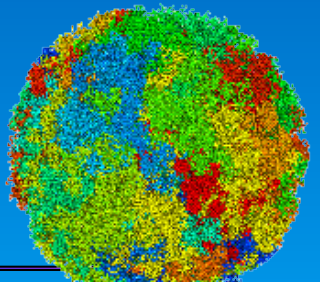

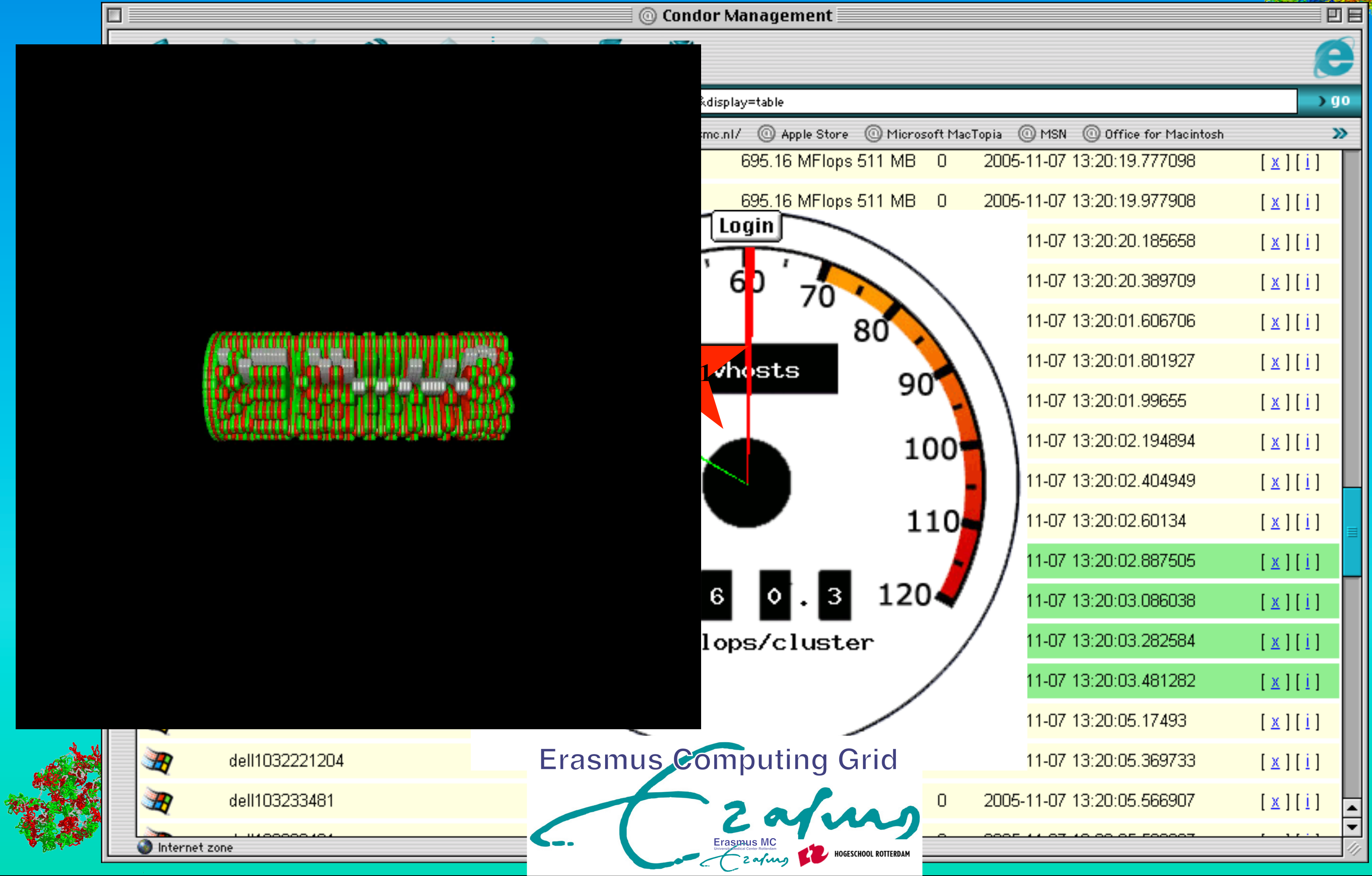

695.16 MFlops 511 MB 0 2005-11-07 13:20:19.777098 [x] [i]
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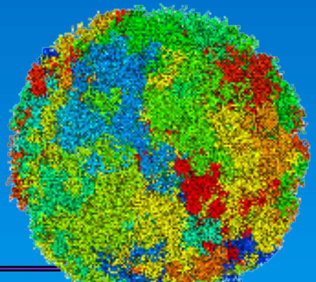

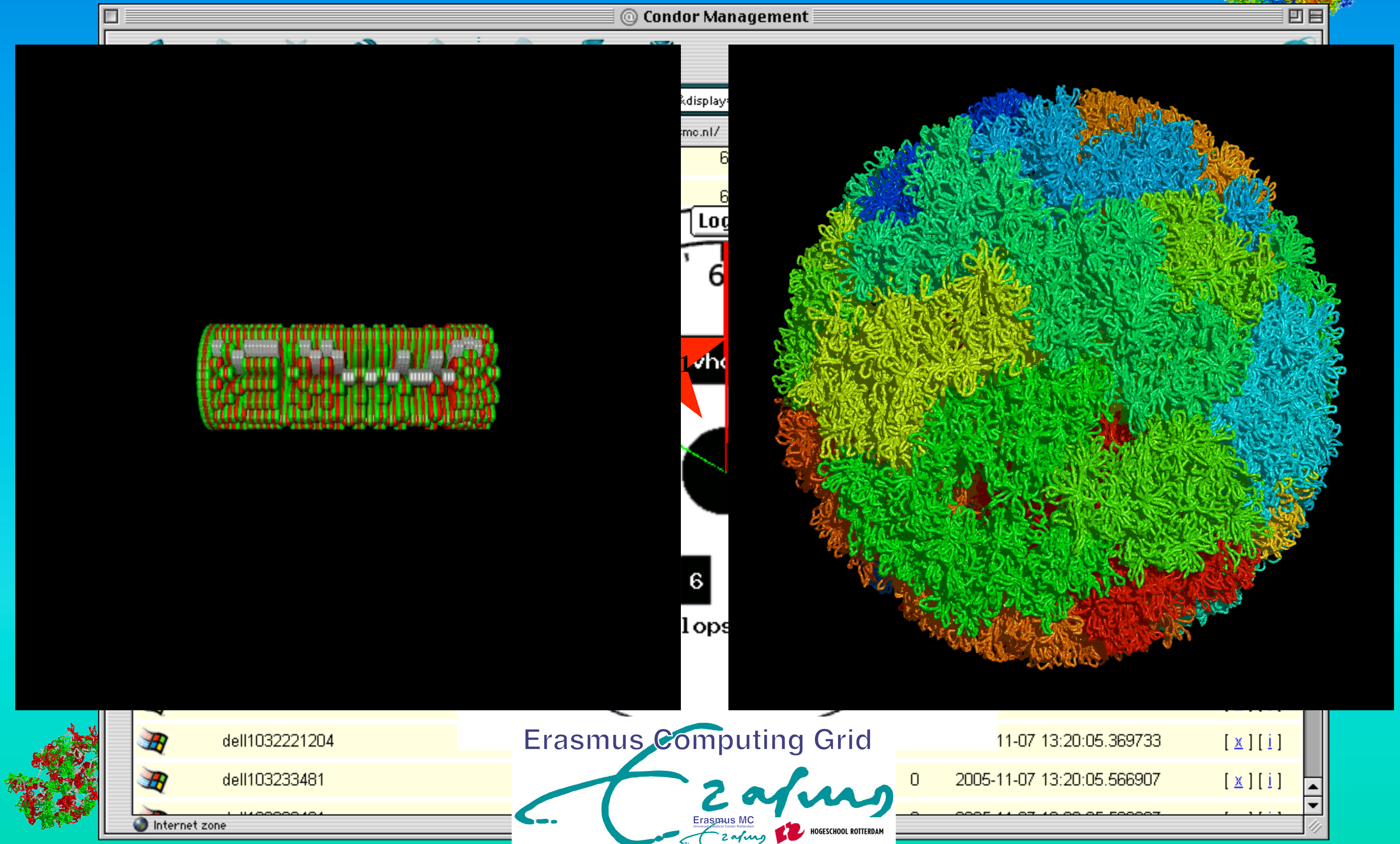

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Erasmus Computing Grid

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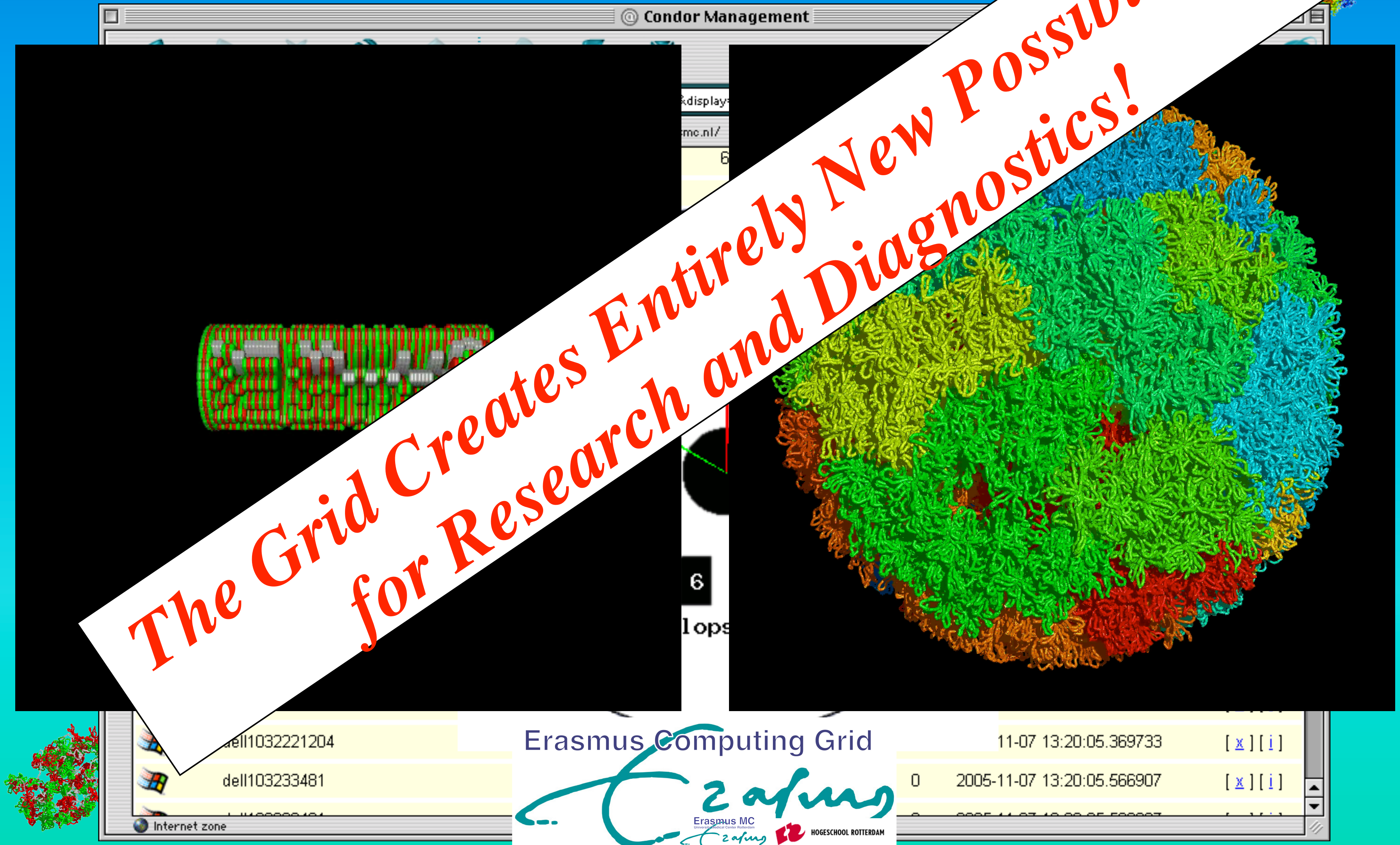

The Grid Creates Entirely New Possibilities for Research and Diagnostics!

Erasmus Computing Grid

Erasmus MC

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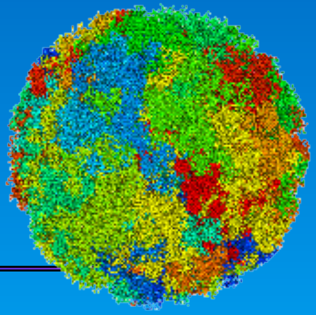
The 3D Genome Viewer

To develop an entire novel system-biology oriented genome browser, i.e. integrating the holistic complexity of genome organization in a single easy comprehensible platform has required completely new approaches to represent the genome architecture realistically in combination with the various types experimental data or instant analysis capabilities and annotation.



Paradigm:

- **simplicity, flexibility, customisability, expandability and open-source sustainability**

concerning

- **user accessibility and needs, the in-/output of data sources, system modularity, and integration of future developments**

Content:

- **all spatial scales from the base-pair to nuclear morphology including all other system composites**
- **every type of even large multi-dimensional datasets**

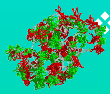
User Handling:

- **intuitive navigation with dynamical semantic resolution and relational arrangement**

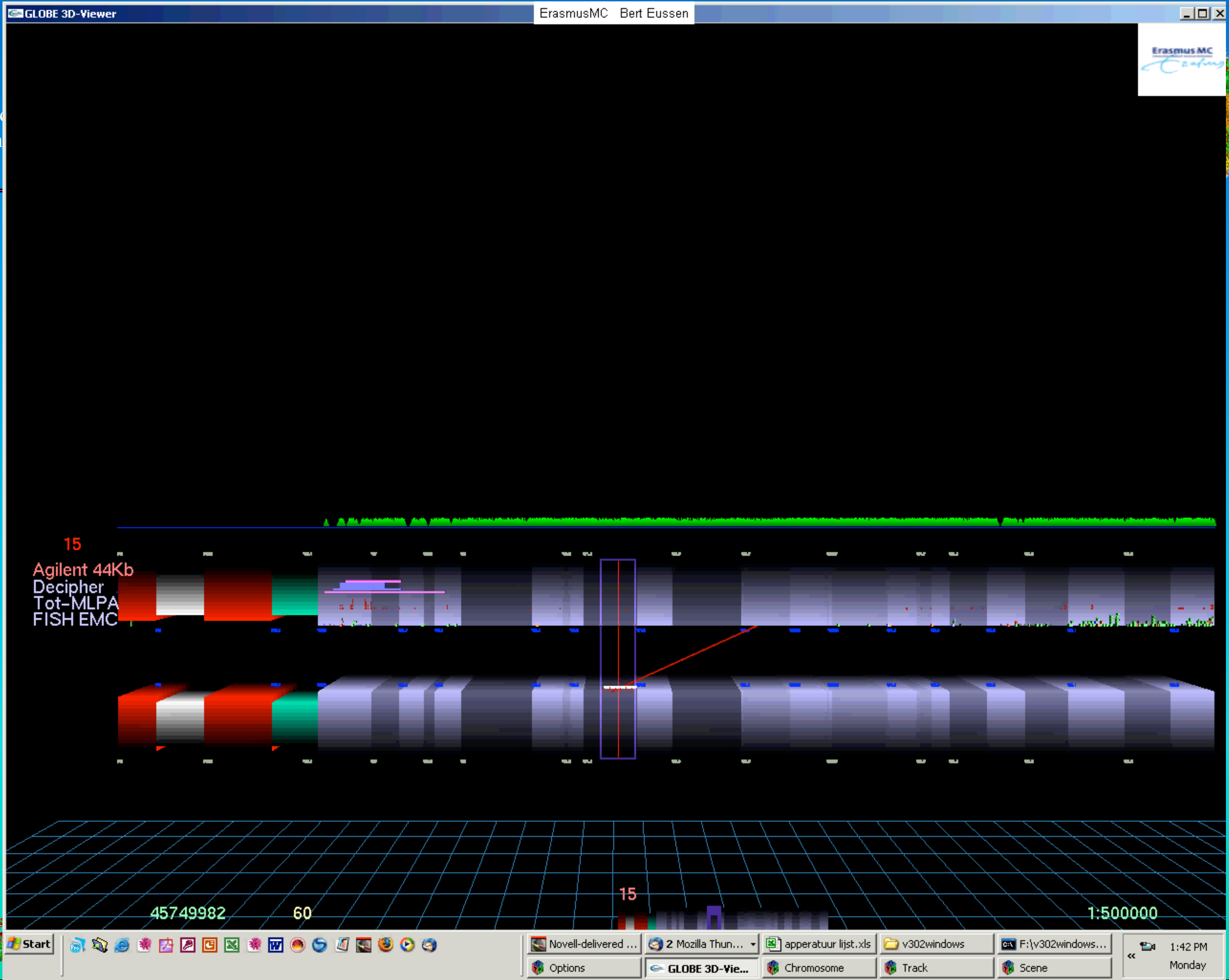
Data Handling:

- **real-time interaction with data manipulation or annotation**
- **simple relational or complex correlative multi-dimensional analysis and planning capabilities**

Control Options:



- **front-end access and control of virtual system biological genome simulations**


GLOBE 3D-Viewer
ErasmusMC Bert Eussen
Erasmus MC
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Agilent 44Kb
Decipher
Tot-MLPA
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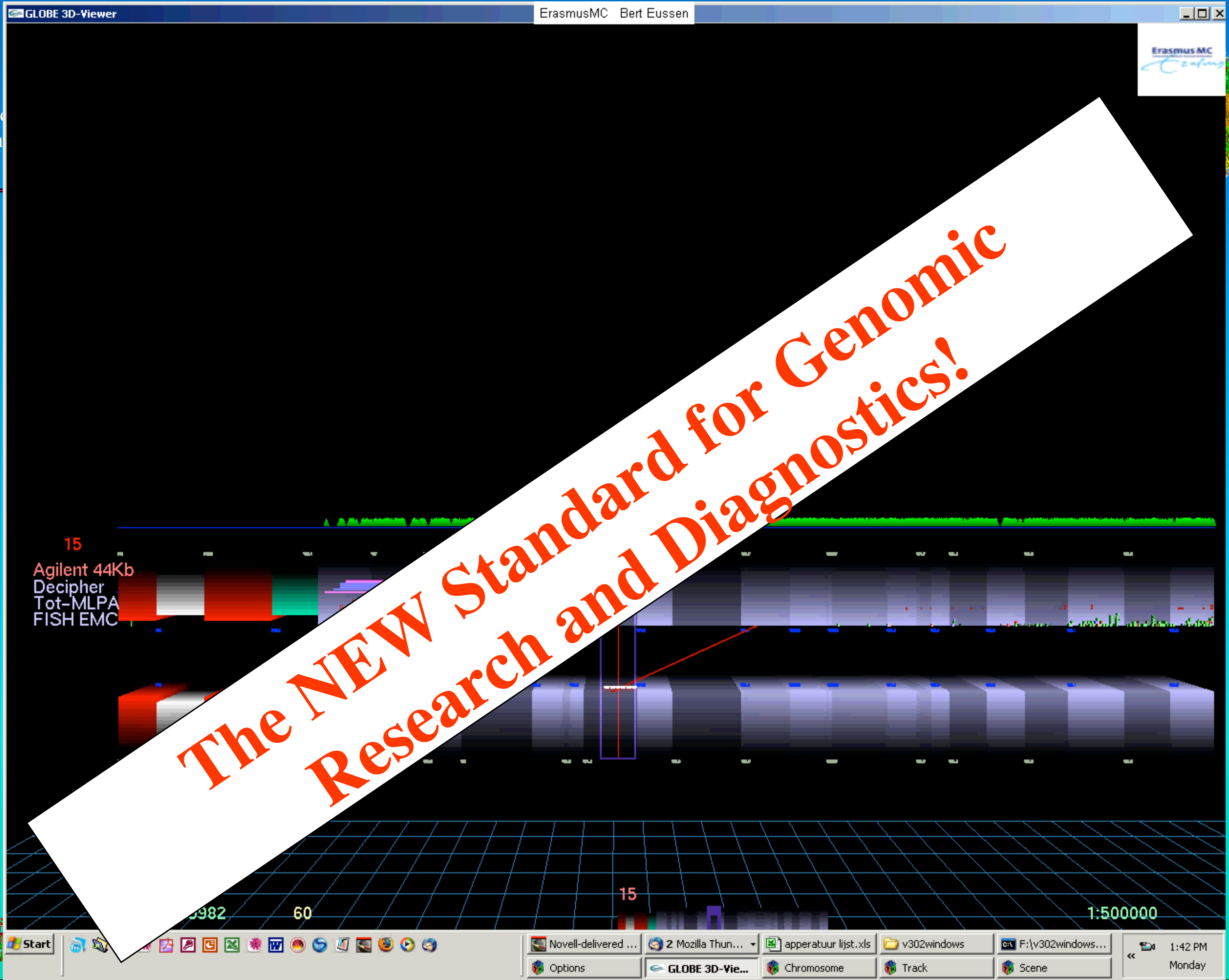
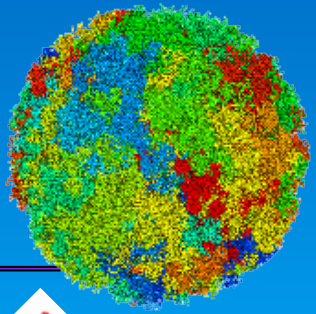


The NEW Standard for Genomic Research and Diagnostics!

The 3D Genome Viewer



Due to its broad impact, the GLOBE 3D Genome Viewer addresses different markets and revenue streams in the areas of research, education, diagnostics and industry with different detailed business models and contracting patterns which will guaranty a constant high-profile valorization.

Basic Corporate License:

- 50% science
- 50% industry

White Label Products:

- special customer products

Content Sale

- specially defined data sets
- specially connected data sets

Advertising:

- sponsored free version
- content and user related

eCommerce:

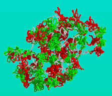
- community portal and referral fees

Companies/Organizations:

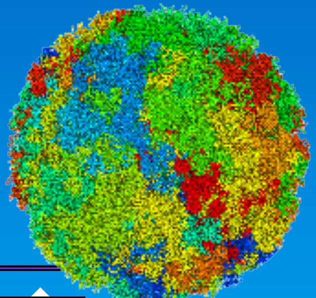
- Invitrogen (Karlsbad, CA, USA)
- Affimetrix (Santa Clara, CA, USA)
- Soft Genetics (State College, PA, USA)
- Combimatrix CMDX (San Antonio, CA, USA)
- Philips (The Netherlands)
- MediGRID (Goettingen, Germany)

Collaborators:

- Prof. Dr. Evan E. Eichler (Seatle, WA, USA)
- Prof. Dr. Stephen W. Scherer (Toronto, Canada)
- Prof. Dr. Michael Hausmann (Heidelberg, Germany)
- Dr. Malte Wachsmuth (Seoul, Korea)
- Dr. Gregory Cox (Karlsbad, CA, USA)
- Dr. Eberhard Schmitt (Jena, Germany)
- Dr. Sabine Baars (Leiden, The Netherlands)



The 3D Genome Viewer



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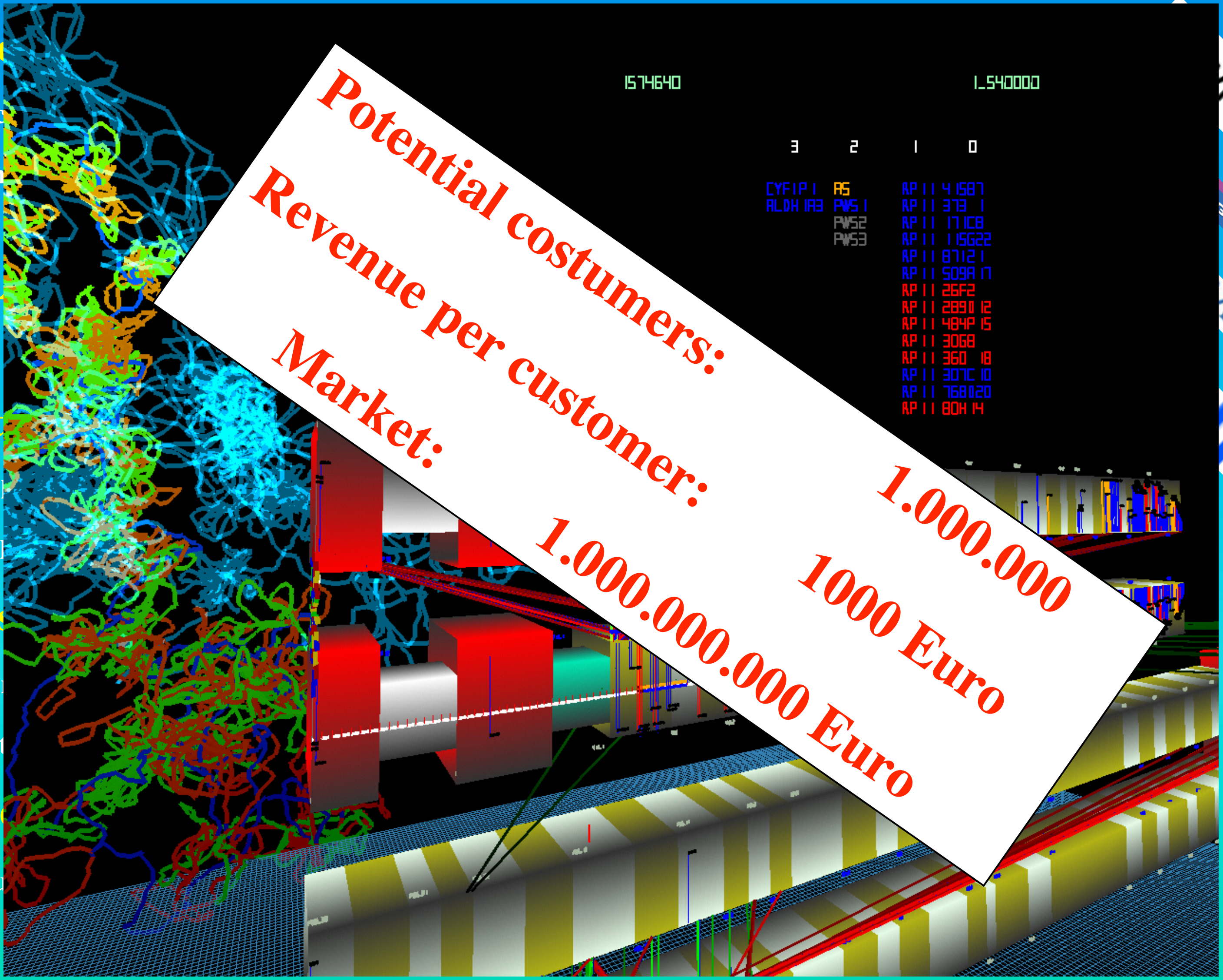
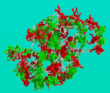


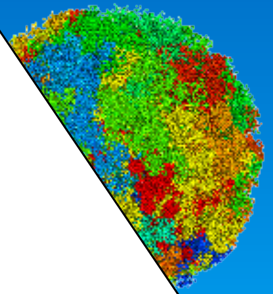
Potential costumers: 1.000.000

Revenue per customer: 1000 Euro

Market: 1.000.000.000 Euro



The 3D Genome Viewer



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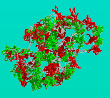
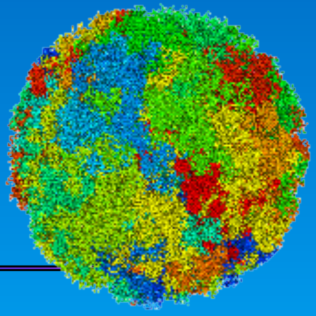
The 3D Genome Viewer allows a Holistic Genome View with Clear Benefits for Research, Diagnostics and Treatment!

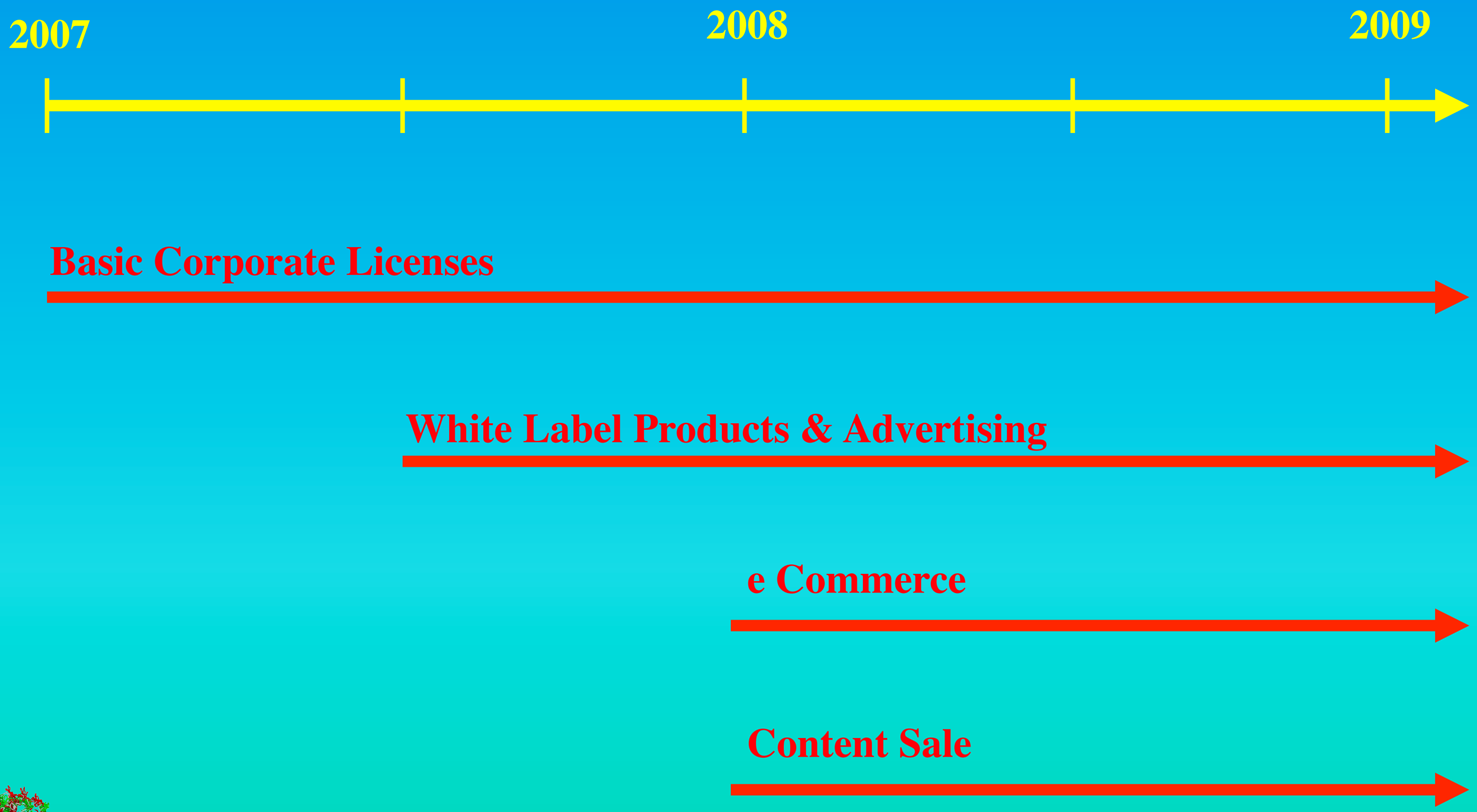


The 3D Genome Viewer

The NEW Standard for Genomic Research and Diagnostics!

Ready to be Valorized!!!





2007

2008

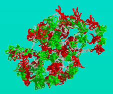
2009

Basic Corporate Licenses

White Label Products & Advertising

e Commerce

Content Sale



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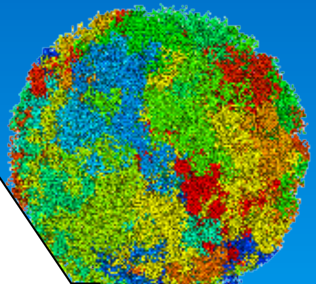

2007

Basic Co

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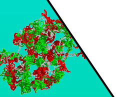


Opportunities

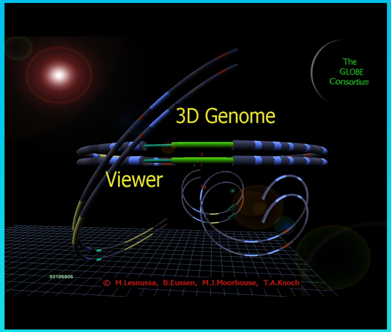
We have started to establish successfully a unique environment for genomic research and diagnostics leading to a holistic understanding of genomes necessary for the improvement of mankind!

The Erasmus Computing Grid:

The Erasmus Computing Grid greatly advances the computing capabilities of the Erasmus Mc, e.g. for:

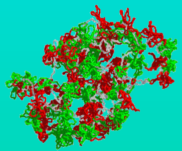
- genomic and proteomic analysis
- epidemiology
- clinical image analysis, e.g. Applied Molecular Imaging (AMI)

The 3D Genome Viewer:

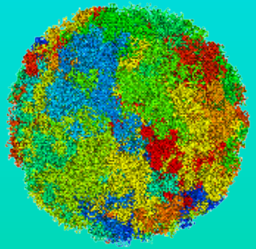


The 3D Genome Viewer greatly advances the integration of multi-dimensional data, e.g.:

- sequential genomic data
- structural genomic data
- clinical diagnosis data



Both the Erasmus Computing Grid and the 3D Genome Viewer have potential for commercialization!



Opportunities

We have started to establish successfully a unique environment for genomic research and diagnostics leading to a holistic understanding of genomes necessary for the improvement of mankind!

The Erasmus Computing Grid:

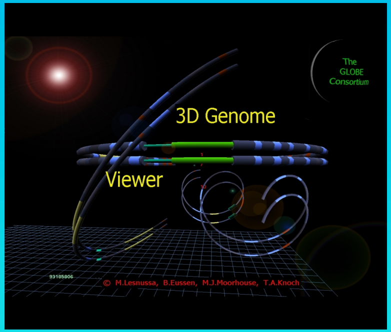
The Erasmus Computing Grid greatly advances the computi

- genomic and proteomic analysis
- epidemiology
- clinical image analysis, e.g. Appli

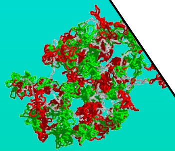
The 3D Genom

The 3D Genc ulti-dimensional data, e.g.:

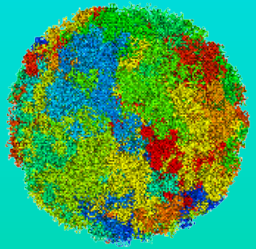
-



Both the Erasmus Computing Grid & the 3D Genome Viewer have great potential for commercialization!



asmus Computing Grid and the 3D Genome Viewer have potential for commercialization!



Approaching the Sequential and Three-Dimensional Organization

Of

Genomes

Knoch, T. A.

EuroBio 2006 - Tenth European Biotech Crossroads, Paris, France, 25th - 27 October, 2006.

Abstract

Genomes are one of the major foundations of life due to their role in information storage, process regulation and evolution. To achieve a deeper unterstanding of the human genome the three-dimensional organization of the human cell nucleus, the structural-, scaling- and dynamic properties of interphase chromosomes and cell nuclei were simulated and combined with the analysis of their sequential organization and (*in vivo*) experiments: The Multi-Loop-Subcompartment model is currently in best agreement with experiment concerning formation and overlap of chromosomes, -territories -arms and subcompartments. Even small model changes lead to pathological recognisable morphologic differences. Review and comparison of experimental to simulated spatial distances between genomic markers even lead to specifics as a chromatin loop size of 63 to 126 kbp. Correlation analyses on the DNA sequence level of completely sequenced Archaea, Bacteria and Eukarya revealed fine-structured positive multi-scaling long-range correlations being again in agreement. Simulations and experiments agree also in the diffusion behaviour of biologically relevant tracers being only moderately obstructed. Thus, the local, global and dynamic genome characteristics are tightly inter-connected and integrated holisticly to fulfill their function.

On this bases we also developed the first system-biology oriented genome browser - the ***GLOBE 3D Genome Viewer*** - necessary to access, present, annotate, and to simulate this holistic complexity in a unique gateway towards a real understanding, educative presentation and curative manipulation planning of genomes. Additionally, we currently set-up the ***Erasmus Computing Grid*** for the enormous computational needs of live-science research and diagnostics. With 3 Tera flops and reaching 20 Tera flops in the first set-up phase the ECG is one of the worlds largest desktop computing grids.

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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, 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.

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