

The GLOBE-Consortium
The Erasmus Computing Grid
&
The Next Generation Genome Viewer

by

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Clinical Genetics
Virology/Bioinformatics
Cell Biology & Genetics

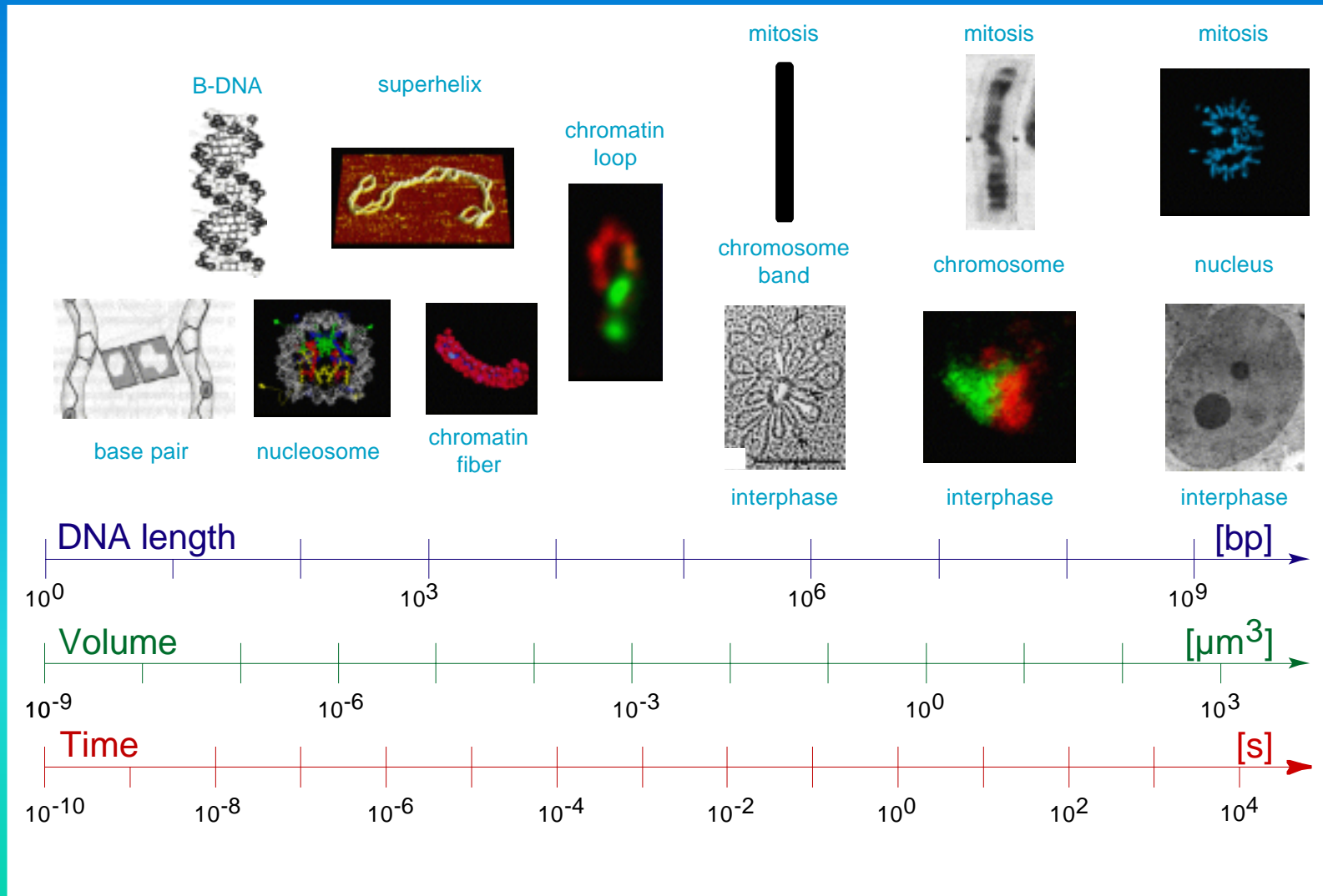
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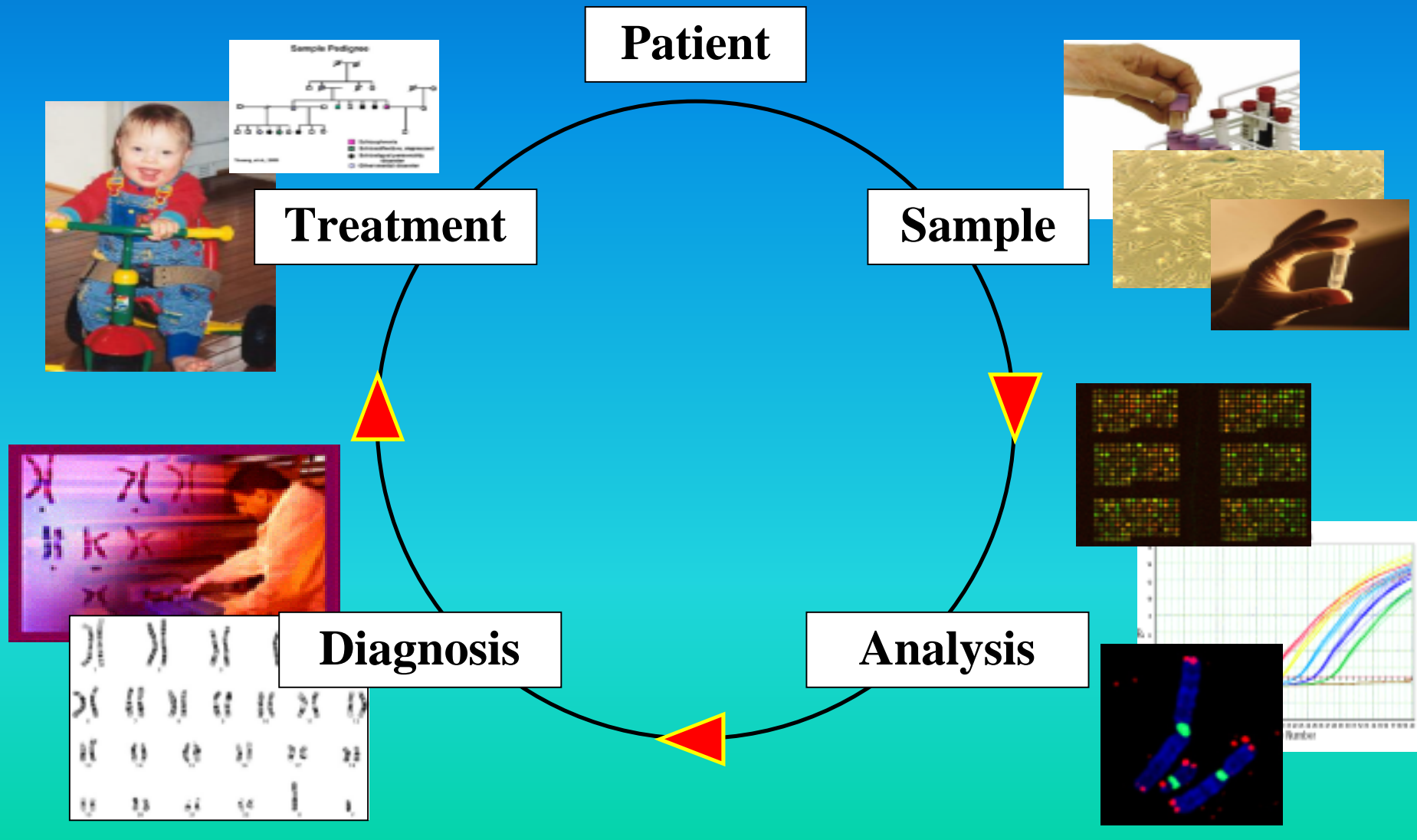
Dynamic and Hierarchical Genome Organization

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?



The Complexity of Cytogenetic Diagnostics

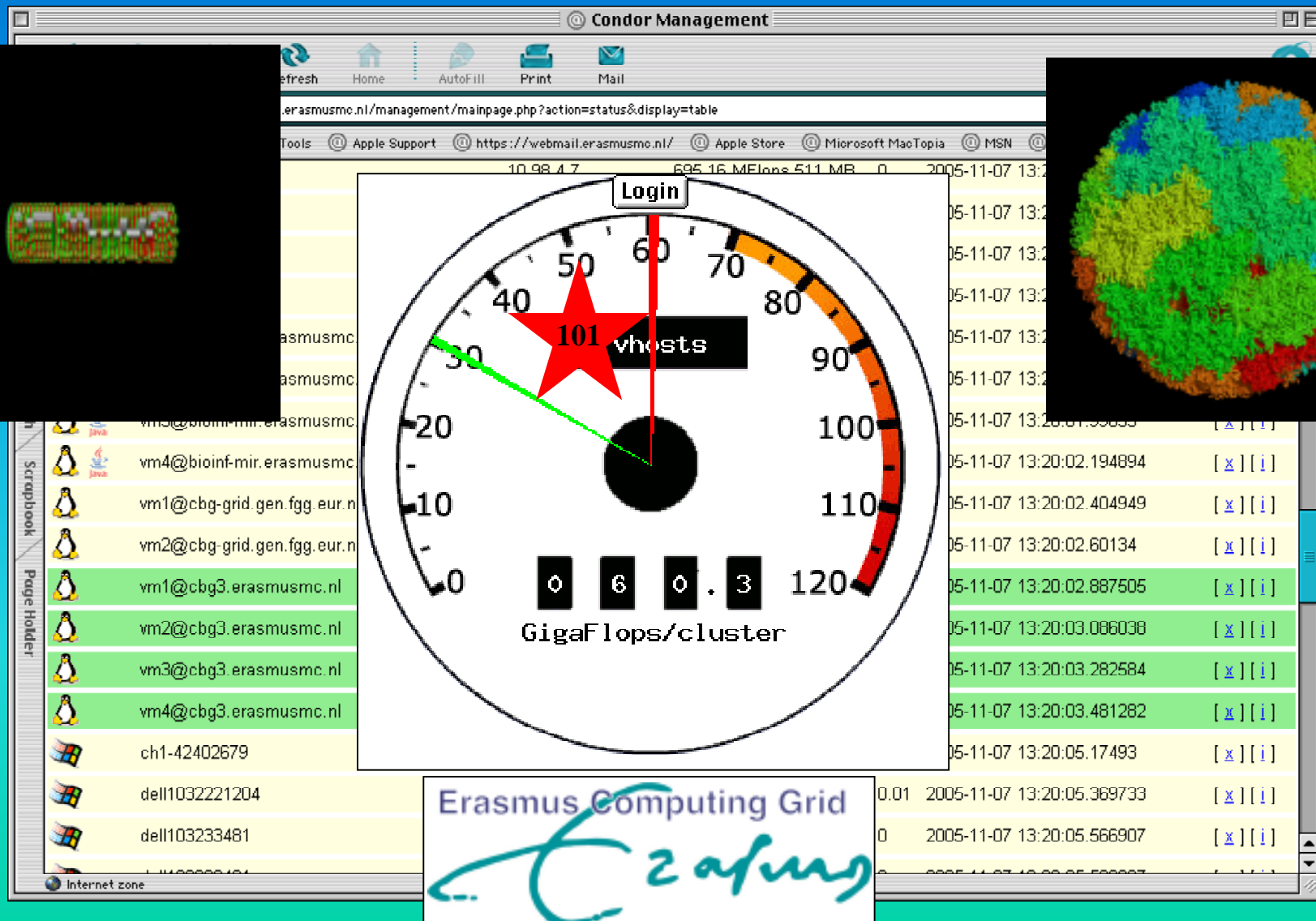
The process of cytogenetic analysis requires proper patient and sample analysis as well as a comprehensive evaluation of the results.



The Erasmus Computing Grid

Building a Super-Computer at Erasmus MC for Free!

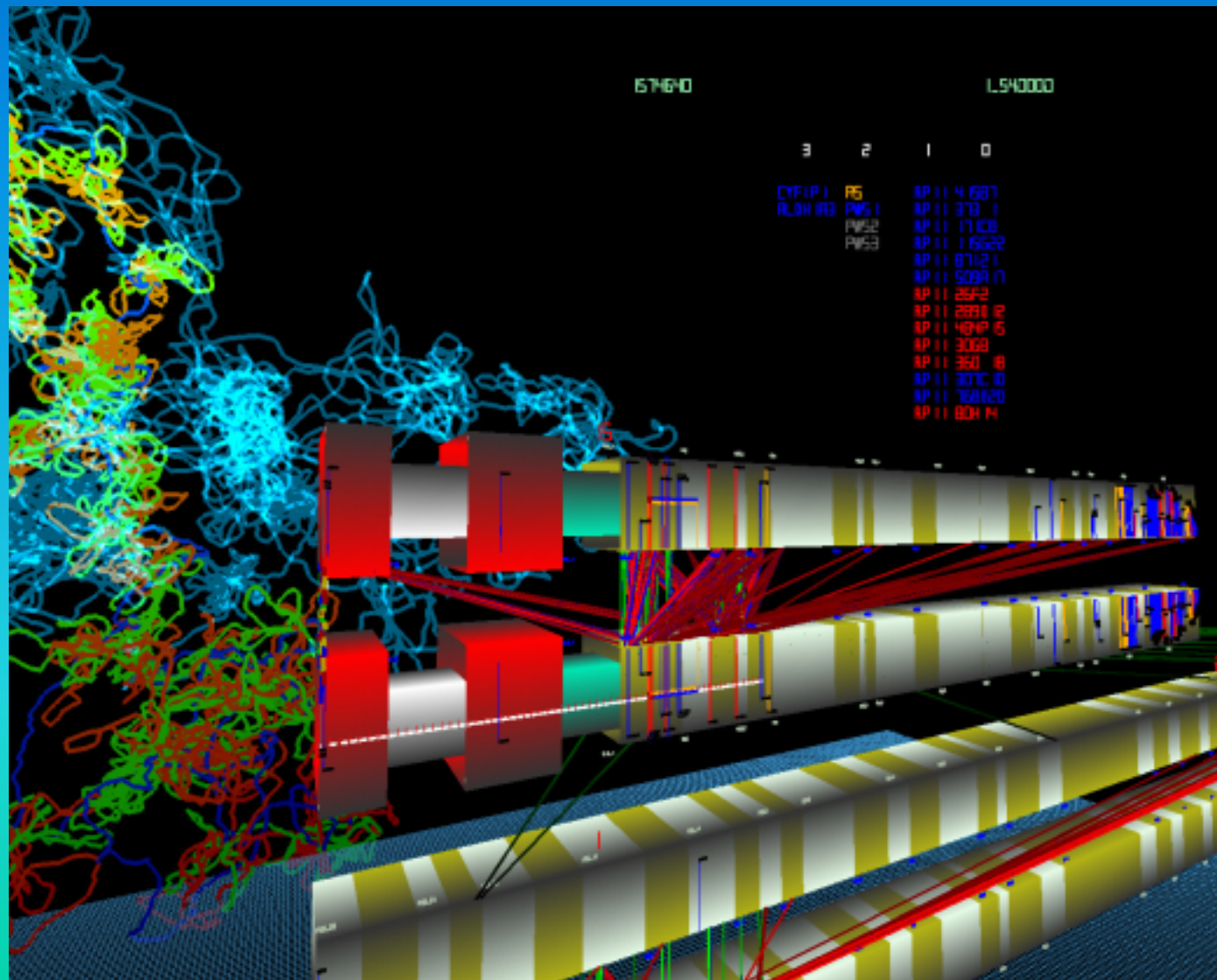
Applications at Erasmus MC: E.g. genome sequence analysis, protein structure simulations, chip/array analysis, epidemiology of viral infections, patient diagnostic image analysis (AMI).



The 3D Genome Viewer

The NEW Standard for Genomic Research and Diagnostics!

Properties: flexible, customizable, and allows intuitive navigation. It provides dynamical resolution and object arrangement as well as real-time analysis of extremely large multi-dimensional data.



Opportunities

The GLOBE-Consortium has started to establish successfully a unique environment for genomic research and diagnostics!



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!

The GLOBE-Consortium:

The Erasmus Computing Grid and The Next Generation Genome Viewer

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Erasmus Medical Center, Erasmus University of Rotterdam, Rotterdam, The Netherlands, 9th November, 2005.

Abstract

The Set-Up of the 20 Teraflop Erasmus Computing Grid:

To meet the enormous computational needs of live-science research as well as clinical diagnostics and treatment the Hogeschool Rotterdam and the Erasmus Medical Center are currently setting up one of the largest desktop computing grids in the world – The Erasmus Computing Grid. Currently 3 Tera flops are operational and in early production, installation up to the today available maximum capacity of 20 Tera flops in both institutions is planned and partly underway. Thus the Erasmus Computing Grid transforms the existing and sustained huge computer capacity available into usable form via a reliable and secure installing and management system, so that the academic and industrial opportunities depending on such huge computing capacities can be realized for the benefit of society.

The Next Generation Genome Browser GLOBE 3D-Viewer:

The GLOBE 3D Genome Viewer is the novel system-biology oriented genome browser necessary to access, present, annotate, and to simulate the holistic genome complexity in a unique gateway towards a real understanding, educative presentation and curative manipulation planning of this tremendous evolutionary information grail – genomes. This has required completely new approaches to represent the genome architecture realistically in combination with the various types of informational annotation including experimental data or instant analysis capabilities. This creates unrivalled new opportunities for scientific researchers, diagnostic users, educators and publishers as well as PR and commercial applicants. Potential *BETA-TESTERS* of the GLOBE 3D Genome Viewer are asked to sign up now!

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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.

Literature References

- Knoch, T. A.** Dreidimensionale Organisation von Chromosomen-Domänen in Simulation und Experiment. (Three-dimensional organization of chromosome domains in simulation and experiment.) *Diploma Thesis*, Faculty for Physics and Astronomy, Ruperto-Carola University, Heidelberg, Germany, 1998, and TAK Press, Tobias A. Knoch, Mannheim, Germany, ISBN 3-00-010685-5 and ISBN 978-3-00-010685-9 (soft cover, 2nd ed.), ISBN 3-00-035857-9 and ISBN 978-3-00-0358857-0 (hard cover, 2nd ed.), ISBN 3-00-035858-7, and ISBN 978-3-00-035858-6 (DVD, 2nd ed.), 1998.
- Knoch, T. A.,** Munkel, C. & Langowski, J. Three-dimensional organization of chromosome territories and the human cell nucleus - about the structure of a self replicating nano fabrication site. *Foresight Institute - Article Archive*, Foresight Institute, Palo Alto, CA, USA, <http://www.foresight.org>, 1- 6, 1998.
- Knoch, T. A.,** Munkel, C. & Langowski, J. Three-Dimensional Organization of Chromosome Territories and the Human Interphase Nucleus. *High Performance Scientific Supercomputing*, editor Wilfried Juling, Scientific Supercomputing Center (SSC) Karlsruhe, University of Karlsruhe (TH), 27- 29, 1999.
- Knoch, T. A.,** Munkel, C. & Langowski, J. Three-dimensional organization of chromosome territories in the human interphase nucleus. *High Performance Computing in Science and Engineering 1999*, editors Krause, E. & Jäger, W., High-Performance Computing Center (HLRS) Stuttgart, University of Stuttgart, Springer Berlin-Heidelberg-New York, ISBN 3-540-66504-8, 229-238, 2000.
- Bestvater, F., **Knoch, T. A.,** Langowski, J. & Spiess, E. GFP-Walking: Artificial construct conversions caused by simultaneous cotransfection. *BioTechniques* 32(4), 844-854, 2002.
- Knoch, T. A. (editor),** Backes, M., Baumgärtner, V., Eysel, G., Fehrenbach, H., Göker, M., Hampl, J., Hampl, U., Hartmann, D., Hitzelberger, H., Nambena, J., Rehberg, U., Schmidt, S., Weber, A., & Weidemann, T. Humanökologische Perspektiven Wechsel - Festschrift zu Ehren des 70. Geburtstags von Prof. Dr. Kurt Egger. Human Ecology Working Group, Ruperto-Carola University of Heidelberg, Heidelberg, Germany, 2002.
- Knoch, T. A.** Approaching the three-dimensional organization of the human genome: structural-, scaling- and dynamic properties in the simulation of interphase chromosomes and cell nuclei, long- range correlations in complete genomes, *in vivo* quantification of the chromatin distribution, construct conversions in simultaneous co-transfections. *Dissertation*, Ruperto-Carola University, Heidelberg, Germany, and TAK†Press, Tobias A. Knoch, Mannheim, Germany, ISBN 3-00-009959-X and ISBN 978-3-00-009959-5 (soft cover, 3rd ed.), ISBN 3-00-009960-3 and ISBN 978-3-00-009960-1 (hard cover, 3rd ed.), ISBN 3-00-035856-9 and ISBN 978-3-00-010685-9 (DVD, 3rd ed.) 2002.
- Knoch, T. A.** Towards a holistic understanding of the human genome by determination and integration of its sequential and three-dimensional organization. *High Performance Computing in Science and Engineering 2003*, editors Krause, E., Jäger, W. & Resch, M., High-Performance Computing Center (HLRS) Stuttgart, University of Stuttgart, Springer Berlin-Heidelberg-New York, ISBN 3- 540-40850-9, 421-440, 2003.
- Wachsmuth, M., Weidemann, T., Müller, G., Urs W. Hoffmann-Rohrer, **Knoch, T. A.,** Waldeck, W. & Langowski, J. Analyzing intracellular binding and diffusion with continuous fluorescence photobleaching. *Biophys. J.* 84(5), 3353-3363, 2003.

- Weidemann, T., Wachsmuth, M., **Knoch, T. A.**, Müller, G., Waldeck, W. & Langowski, J. Counting nucleosomes in living cells with a combination of fluorescence correlation spectroscopy and confocal imaging. *J. Mol. Biol.* 334(2), 229-240, 2003.
- Fejes Tóth, K., **Knoch, T. A.**, Wachsmuth, M., Frank-Stöhr, M., Stöhr, M., Bacher, C. P., Müller, G. & Rippe, K. Trichostatin A induced histone acetylation causes decondensation of interphase chromatin. *J. Cell Science* 117, 4277-4287, 2004.
- Ermiler, S., Krunić, D., **Knoch, T. A.**, Moshir, S., Mai, S., Greulich-Bode, K. M. & Boukamp, P. Cell cycle-dependent 3D distribution of telomeres and telomere repeat-binding factor 2 (TRF2) in HaCaT and HaCaT-myc cells. *Europ. J. Cell Biol.* 83(11-12), 681-690, 2004.
- Kost, C., Gama de Oliveira, E., **Knoch, T. A.** & Wirth, R. Spatio-temporal permanence and plasticity of foraging trails in young and mature leaf-cutting ant colonies (*Atta spp.*). *J. Trop. Ecol.* 21(6), 677- 688, 2005.
- Winnefeld, M., Grewenig, A., Schnölzer, M., Spring, H., **Knoch, T. A.**, Gan, E. C., Rommelaere, J. & Cziepluch, C. Human SGT interacts with BAG-6/Bat-3/Scythe and cells with reduced levels of either protein display persistence of few misaligned chromosomes and mitotic arrest. *Exp. Cell Res.* 312, 2500-2514, 2006.