Nucleosome with GFP randomly attached.

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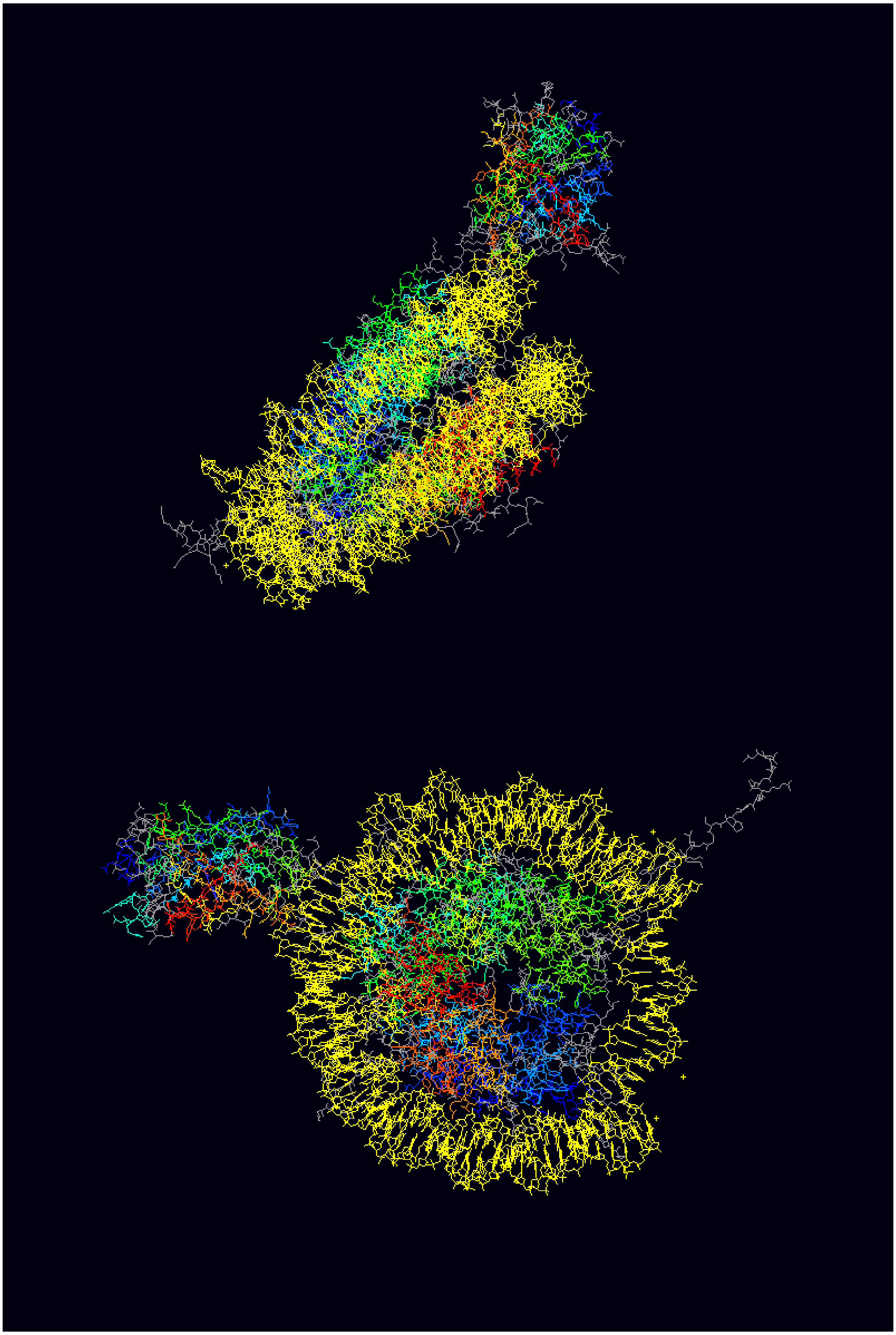

Determination of the Fractal Dimensions in Cells expressing Hx-XFP Fusionproteins

YFP:	HX-YFP-Mass distribution	t:	time
$D_{F/L}$:	Fractal/Lacunarity Dimension	r:	space vector
s:	equilibrium step		

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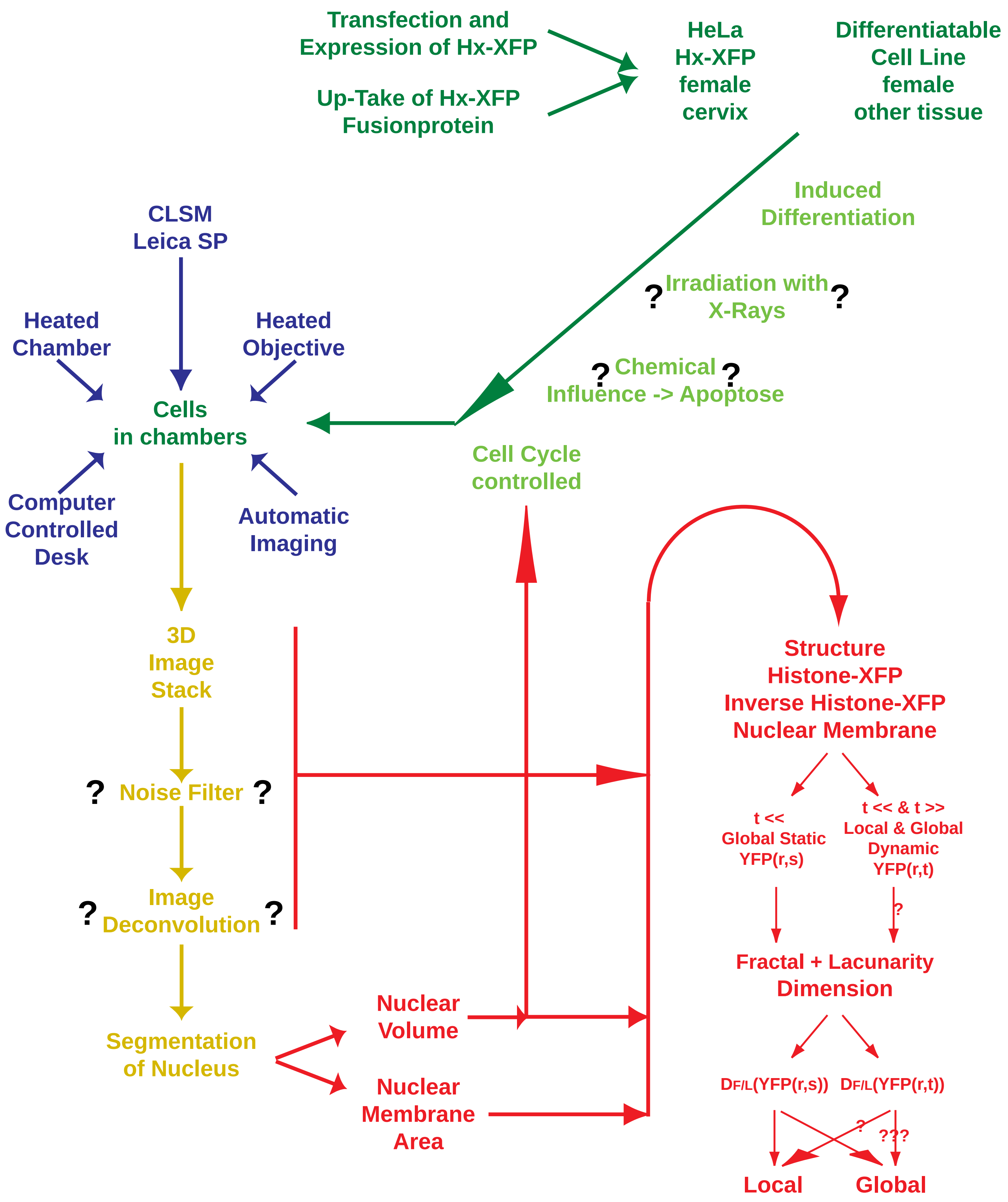

Prophase

Two HeLa cells expressing H2A-YFP:
Left: cell in prophase, H2A-YFP is found also in the cytoplasma.
Right: cell in G1, H2A-YFP is mostly in the nucleus.

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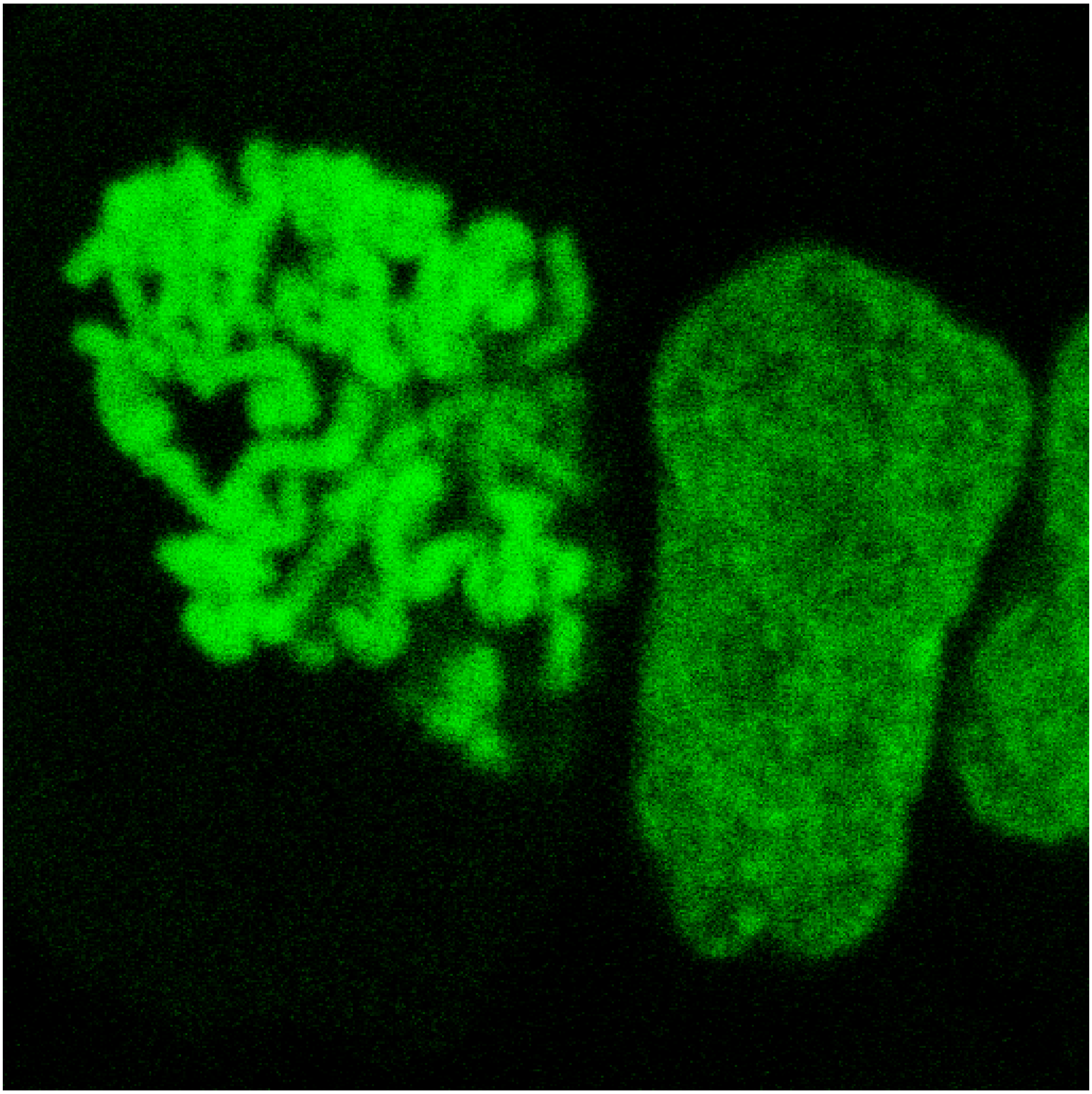

Excitation and Emission Spectra of
EBFP ECFP EGFP EYFP DsRed
from Aequorea victoria from Discosoma striata

(data from Clontech)

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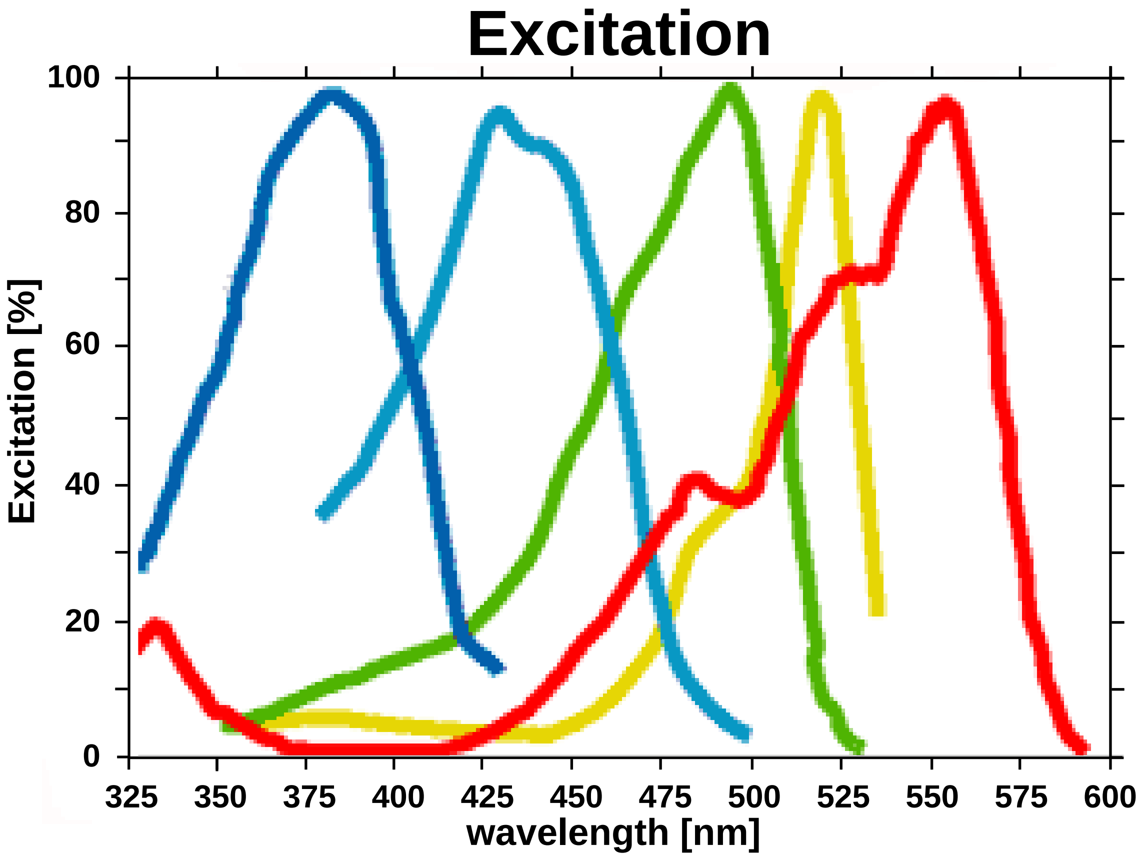

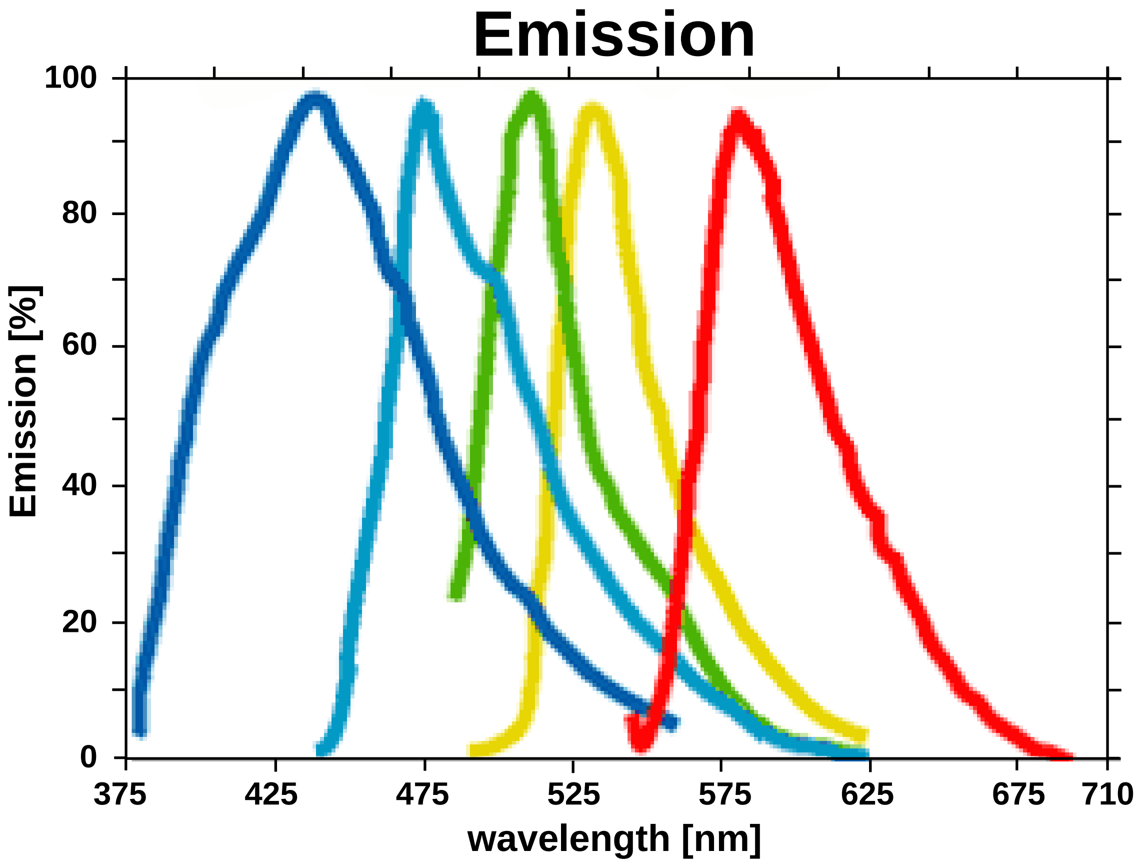

The volume fraction of chromatin in average and active cell nuclei lies under 10%.

Cell nucleus with 5 m radius:	$V_c = 523\ m^3$
Fibroblast in G_1:	$V_c = 450\ m^3$
Hela:	$V_c = 1100\ m^3$

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30 nm chromatin fiber as cylinder - volume approach

Length of 30 nm chromatin fiber in an average cell nucleus

$$7 * 10^9\ bp \Big/ \frac{1.04\ 10^4 bp}{100\ nm} = 6.73 * 10^5 * 100\ nm = 6.73 * 10^4\ m = 6.73\ cm$$

Volume of the 30nm chromatin fiber in an average cell nucleus

$$V_c = * (0.015\ m)^2 * 6.73 * 10^4\ m = 47\ m^3$$

Mass, density - volume approach

H10	21 kDa
H2A	2 * 13.9 kDa
H2B	2 * 13.7 kDa
H3	2 * 15.2 kDa
H4	2 * 11.2 kDa
	+ ============
nucleocomplex	128.0 kDa

$$\frac{7 * 10^9\ bp}{200\ bp/nucleosome} = 3.5 * 10^7\ nucleosomes$$

146 bp direct on Nucleosome 146 bp * 660 Da	96.3 kDa
	+ ============
nucleosome	224.3 kDa

volume of one nucleosome

$$*(5.5\ nm)^2 * 6\ nm = 568\ nm^3$$

density of the nucleosome

$$224.3\ kDa / 568\ nm^3 = 0,39 \frac{kDa}{nm^3}$$

nuclesomal mass in one average cell nucleus $4.5 * 10^{12}\ Da = 7.2\ pg$

DNA mass in one average cell nucleus

$$7 * 10^9\ bp * 6.6 * 10^2\ Da = 4.6 * 10^{12}\ Da = 7.3\ pg$$

+ ==================

$$9.1 * 10^{12}\ Da = 14.5\ pg$$

Volume of the 30nm chromatin fiber in an average cell nucleus

$$V_c = \frac{4.5 * 10^{12} Da}{0.39 \frac{kDa}{nm^3}} + \frac{4.6 * 10^{12} Da}{0.39 \frac{kDa}{nm^3}} = 23.6\ m^3$$

Anomalous Diffusion in Fractal Systems

The dimension of a random walk D_w and the Fractal Dimension D_f are connected by the super universal Fracton Dimension D_s.

r:	diffusion displacement	D_F:	Fraktal Dimension	d:	Euclidian dimensiontime
s:	visited sites	D_w:	Walk Dimension	p_c:	Percolation threshold
t:	time	D_s:	Fracton Dimension		

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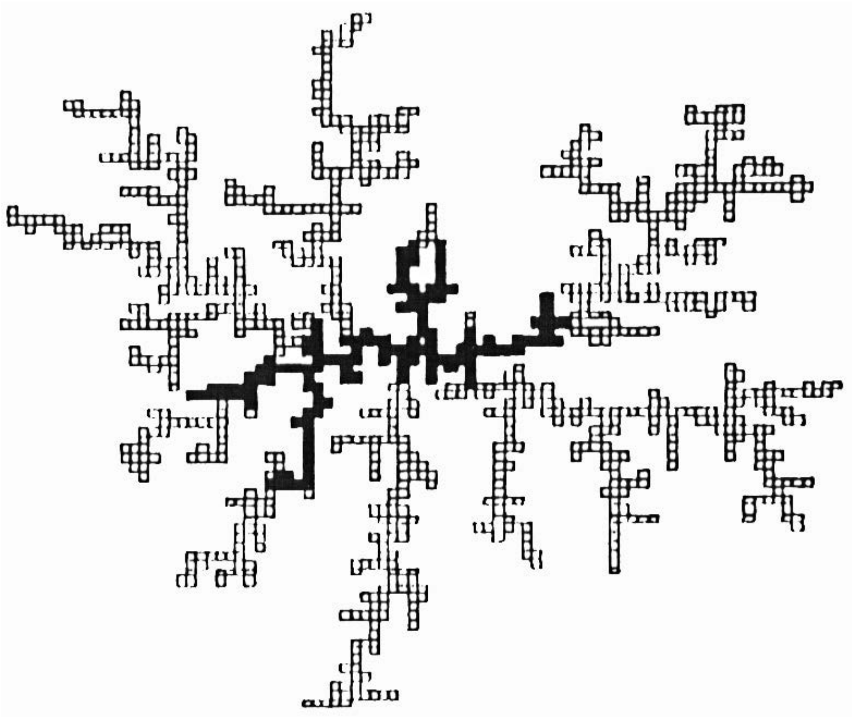

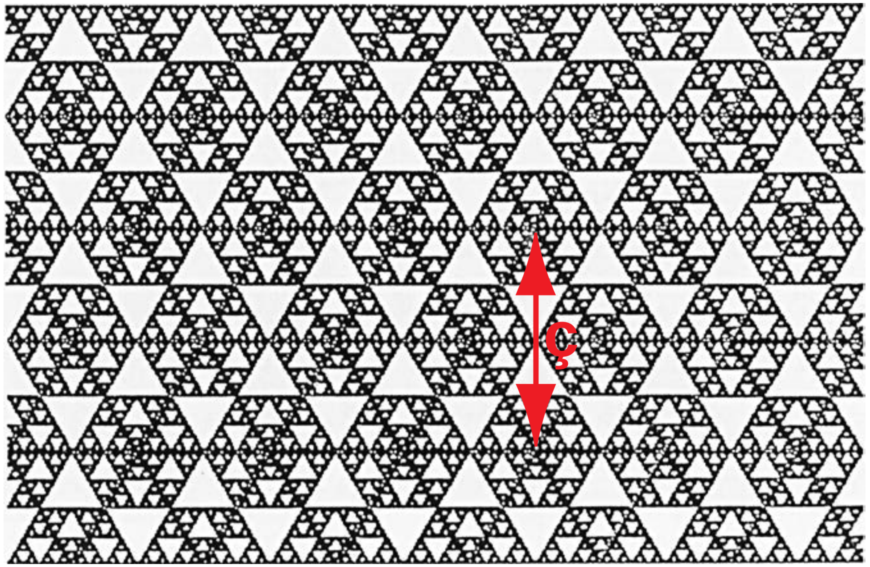

Left: 2500 random walk steps on a DLA cluster of 1000 sites.
(P. Meakin, H. E. Stanley, Phys. Rev. Lett. 51, p 1457, 1983.)
Right: Latice composed of Sierpinski gasket cells of sice ç.
(Bunde, Havlin, Fractals and Disordered Systems, Springer 1995.)

Mean square displacement: $< r^2 > = t^{2/D_w}$

Mean number of visited sites: $< s^2 > = t^{2D_f/D_w} \equiv t^{D_s}$

Alexander and Orbach Conjecture:
Fracton Dimension Ds = 4/3
[2 d 6]
for percolating systems at p_c

Percolating Systems can be described with different Fractal Dimensions

The pictures show large percolation clusters at the critical concentration pc. The colours of the sites characterice their Euclidean distance (left) and their chemical distance (right) from a site chosen as the origing of the cluster. The distances lead to the fractal Dimension D_f and the chemical dimension D_l.

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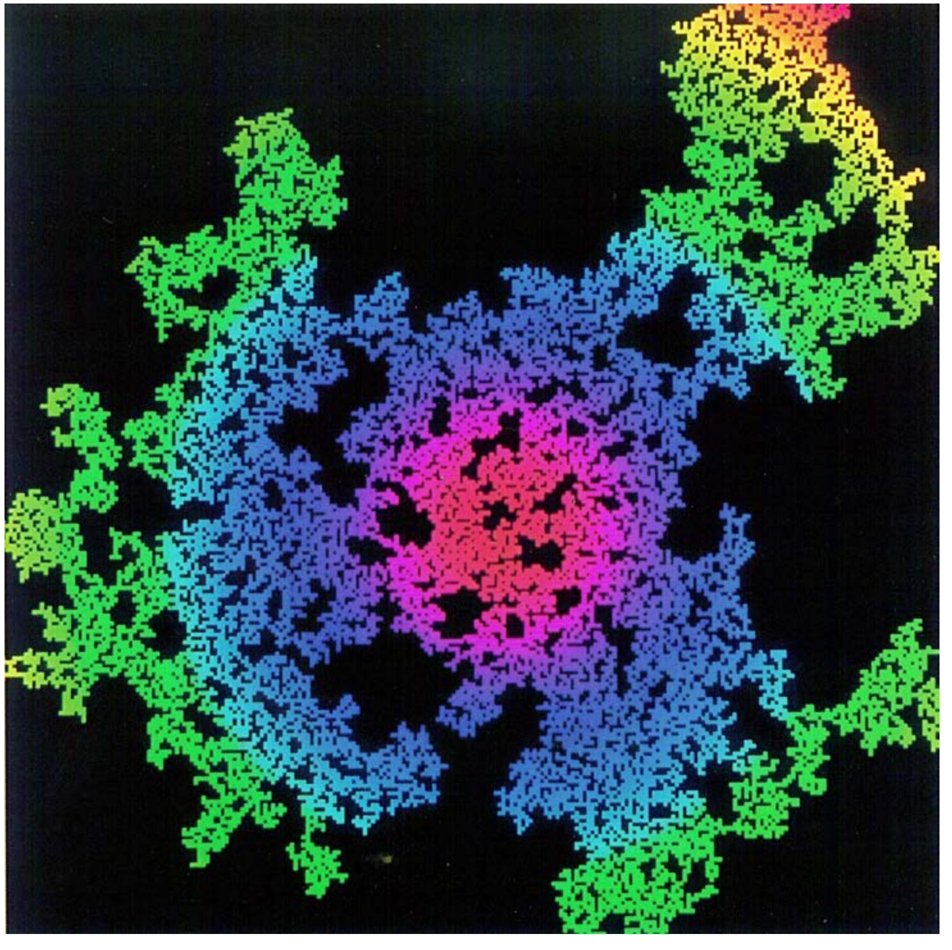

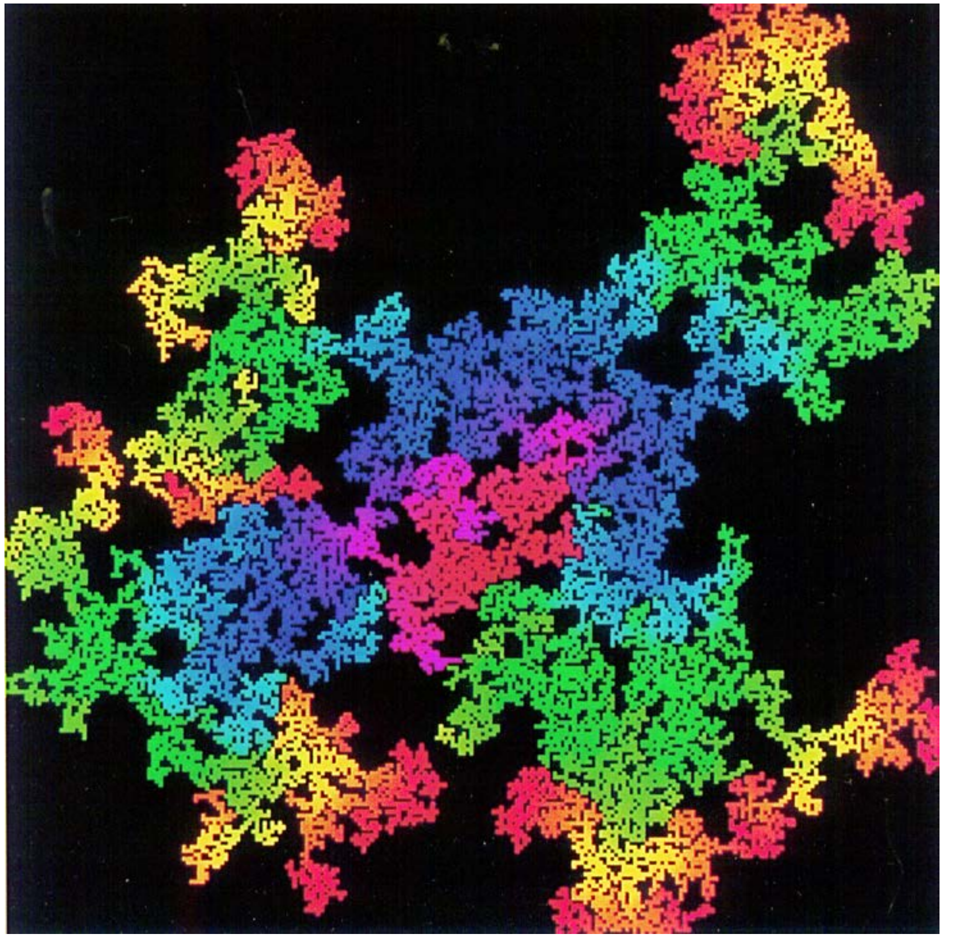

(B. L. Trus in A. Bunde, S. Havlin, Fractals and Disordered Systems, Springer 1995)

Diffusion Limited Aggregation (DLA)

DLA is a model for random structure formation and the accesability of cluster sites by diffusing particles. Thus DLA describes the conditions for diffusing proteins from the nuclear membrane to its target side on the genome.

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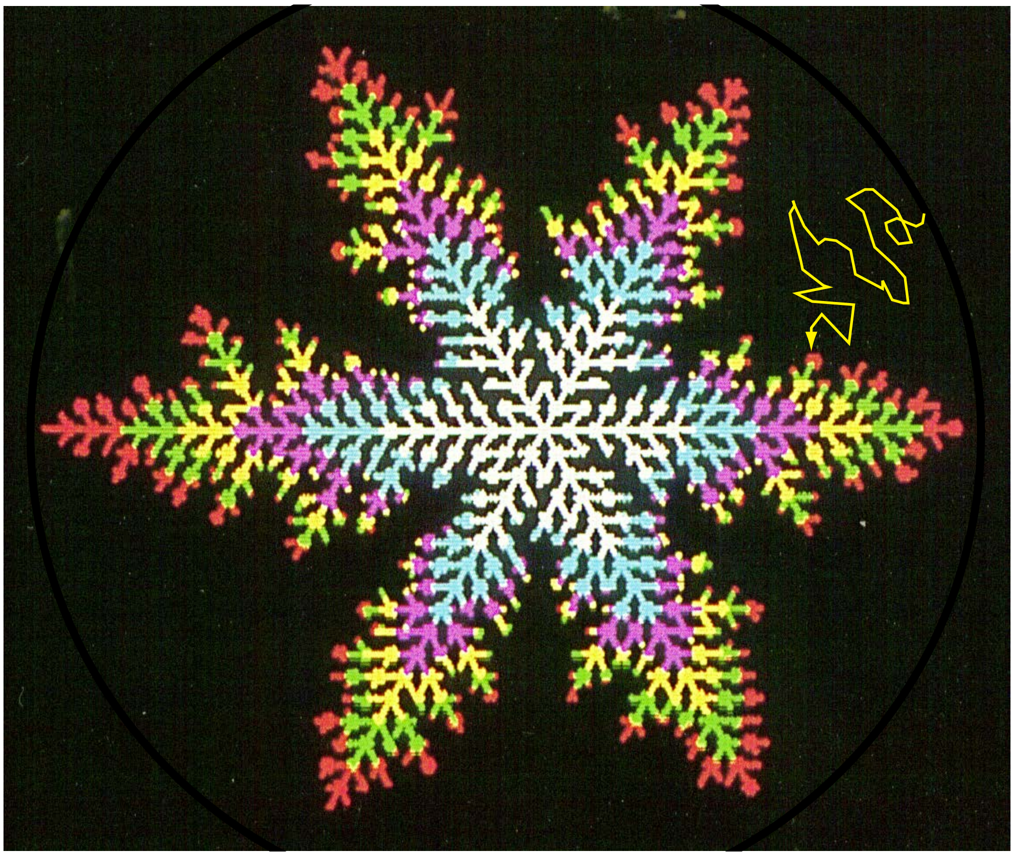

DLA cluster on a triangular latice, with noise reduction and lattice anisotropy. Colour coding according to the time of arrival. (after J. Nittmann, H. E. Stanley, Nature 321, p. 663f, 1986.)

"Rosetta Stone" connecting the underlying Physics

Electric	Fluid Mechanics	Dendritic Solidification
Electrostatic Potential	Pressure	Concentration
ø(r,t)	P(r,t)	c(r,t)
Electric Field	Velocity	Growth rate
E α - ø(r,t)	v α - P(r,t)	v α - c(r,t)
Conservation		
· E = 0	· v = 0	· v = 0
Laplace Equation		
^{2}ø = 0	^{2}P = 0	^{2}c = 0

Viscous Fingering

The picture shows the a metalic moulding of the penetration space of water injected into plaster. Hight 6cm, smallest branching 20 m. (G. Daccord, R. Lenormand, Nature 325, p 41, 1987.)

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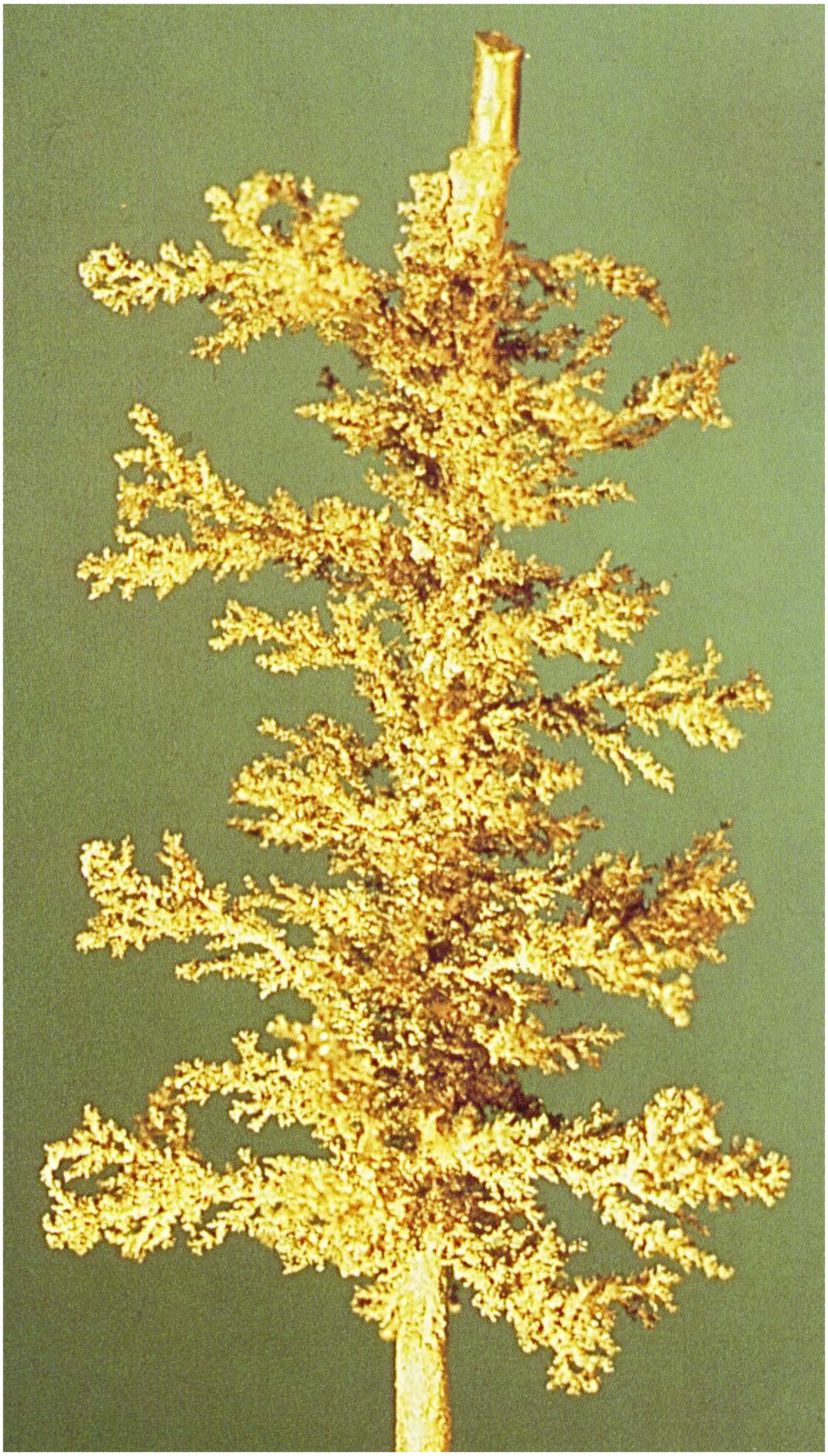

Structure/Fractal Dimension correlates with Anomalous Diffusion.

M: Mass distribution
YFP: HX-YFP-Mass distribution
$D_{F/L}$: Fractal/Lacunarity Dimension
R: Diffusion: displacement
D_W: Walk Dimension $\langle r^2 \rangle \sim t^{2/D_W}$

p: Effective potential between structure and diffusing particle
EV: Excluded Volume potential
B: Effective Binding potential
s: equilibrium step

t: time
r: space vector

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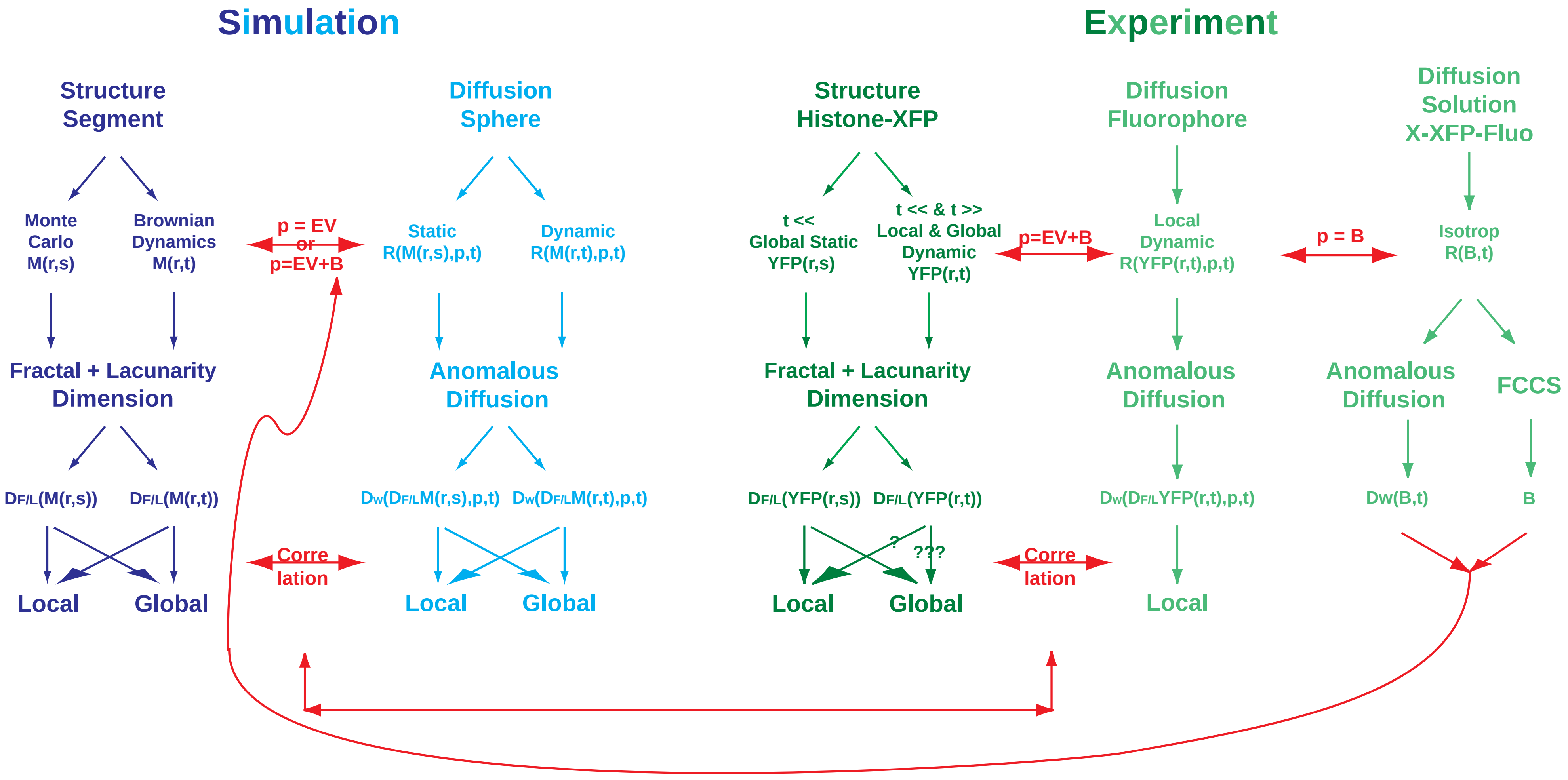

Simulated Diffusion of Particles

The diffusion of spheres with 1nm and 50 nm in a nucleus with all 46 chromosomes and 5 m radius. The diffusion constant shows characteristic peaks as function of time which could be due to different fractal dimensions on different scales.

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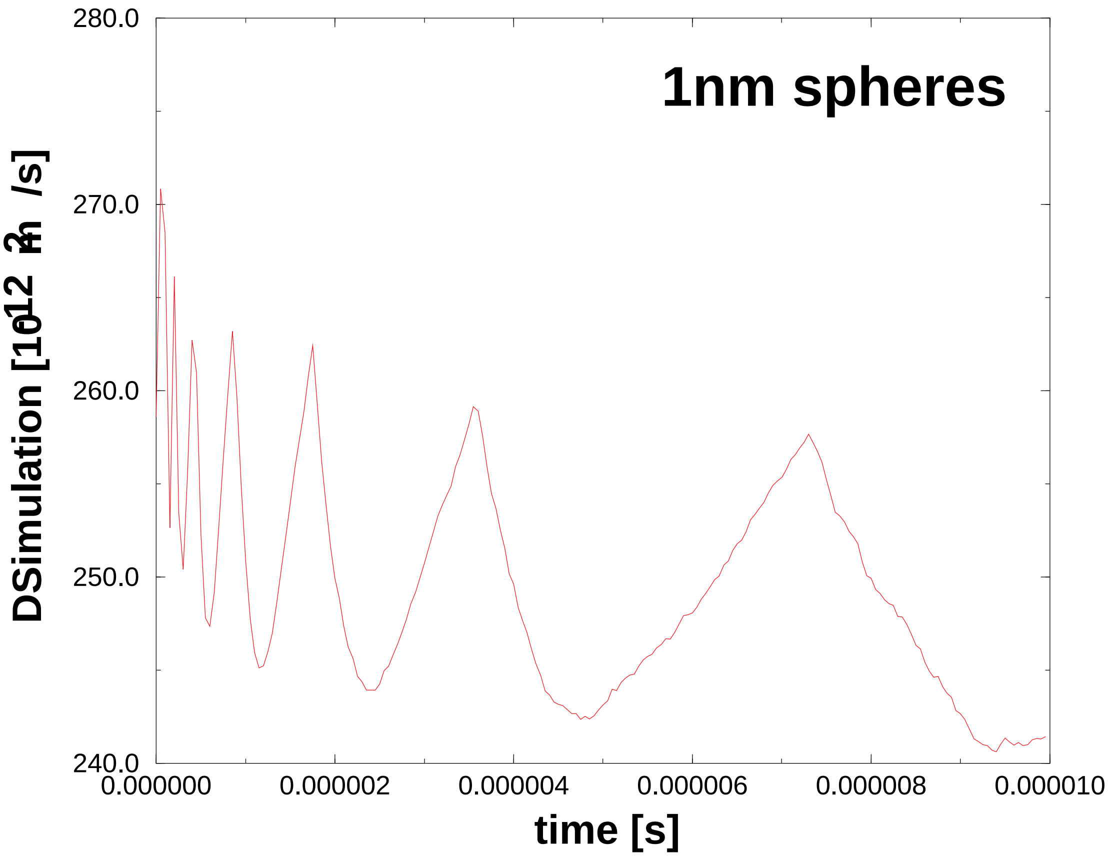

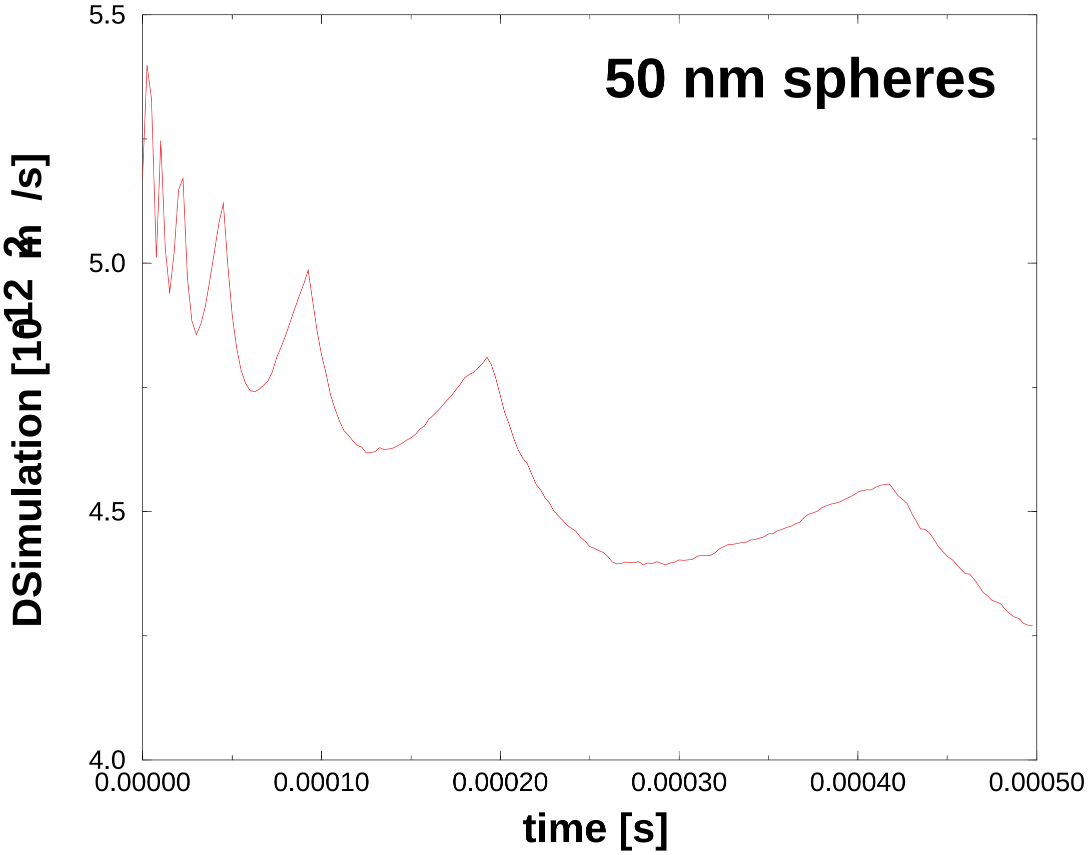

Fractal Organization, Dynamics, and Diffusion of Particles in Cell Nuclei using Histone-GFP Fusion-Protein Expressing Cells

Knoch, T. A.

Biophysics of Macromolecules Seminar, German Cancer Research Centre (DKFZ), Heidelberg, Germany, November, 1999.

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Keywords:

Genome, genomics, genome organization, genome architecture, structural sequencing, architectural sequencing, systems genomics, coevolution, holistic genetics, genome mechanics, genome function, genetics, gene regulation, replication, transcription, repair, homologous recombination, simultaneous co-transfection, cell division, mitosis, metaphase, interphase, cell nucleus, nuclear structure, nuclear organization, chromatin density distribution, nuclear morphology, chromosome territories, subchromosomal domains, chromatin loop aggregates, chromatin rosettes, chromatin loops, chromatin fibre, chromatin density, persistence length, spatial distance measurement, histones, H1.0, H2A, H2B, H3, H4, mH2A1.2, DNA sequence, complete sequenced genomes, molecular transport, obstructed diffusion, anomalous diffusion, percolation, long-range correlations, fractal analysis, scaling analysis, exact yard-stick dimension, box-counting dimension, lacunarity dimension, local nuclear dimension, nuclear diffuseness, parallel super computing, grid computing, volunteer computing, Brownian Dynamics, Monte Carlo, fluorescence in situ hybridization, confocal laser scanning microscopy, fluorescence correlation spectroscopy, super resolution microscopy, spatial precision distance microscopy, autofluorescent proteins, CFP, GFP, YFP, DsRed, fusionprotein, in vivo labelling.

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