Additive scaling law for organization of the chromatin

(SESANS for investigation of the structure organization of chromatin in biological cell)

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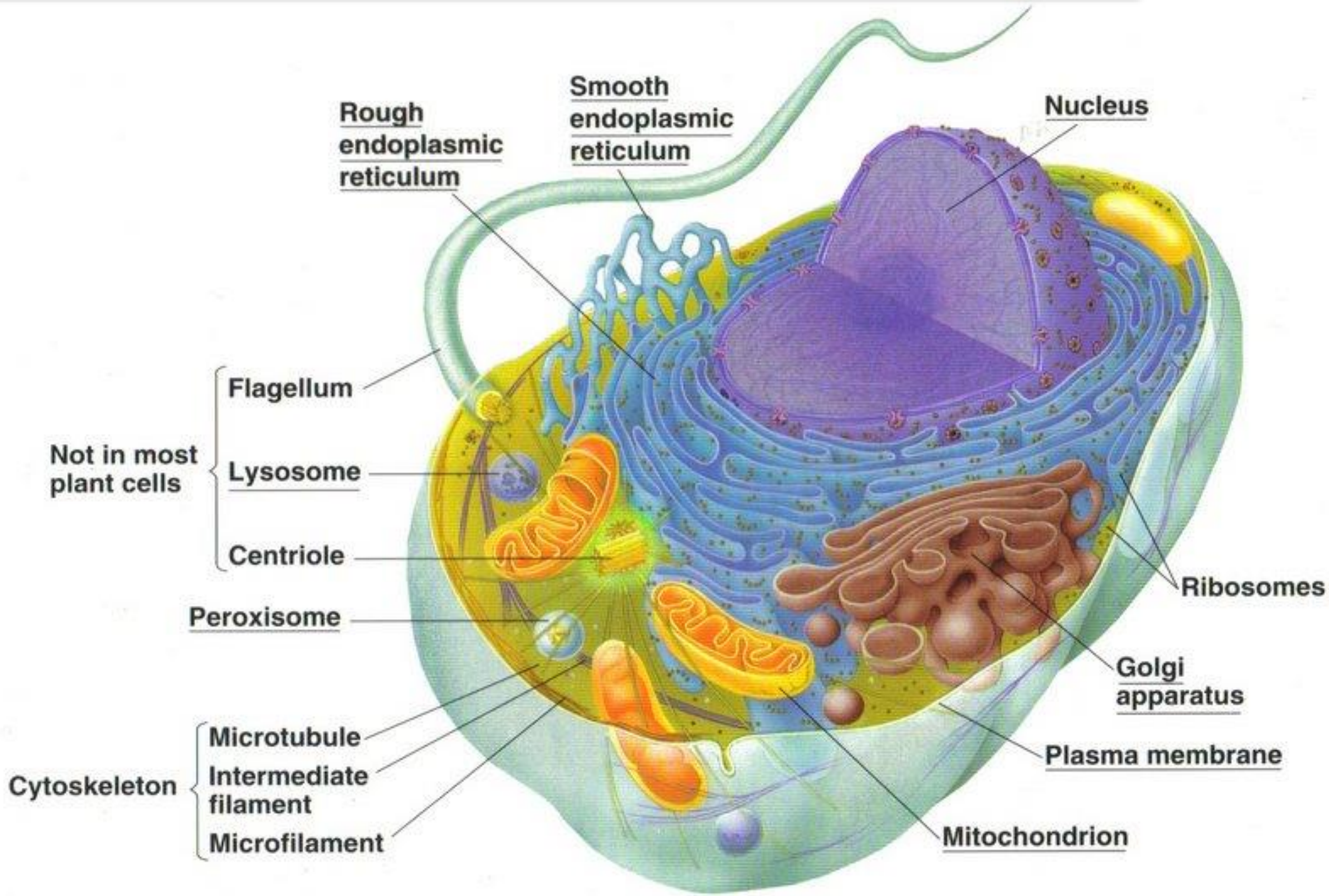
The cell is the basic structural, functional, and biological unit of all known living organisms.



Chromatin at interphase

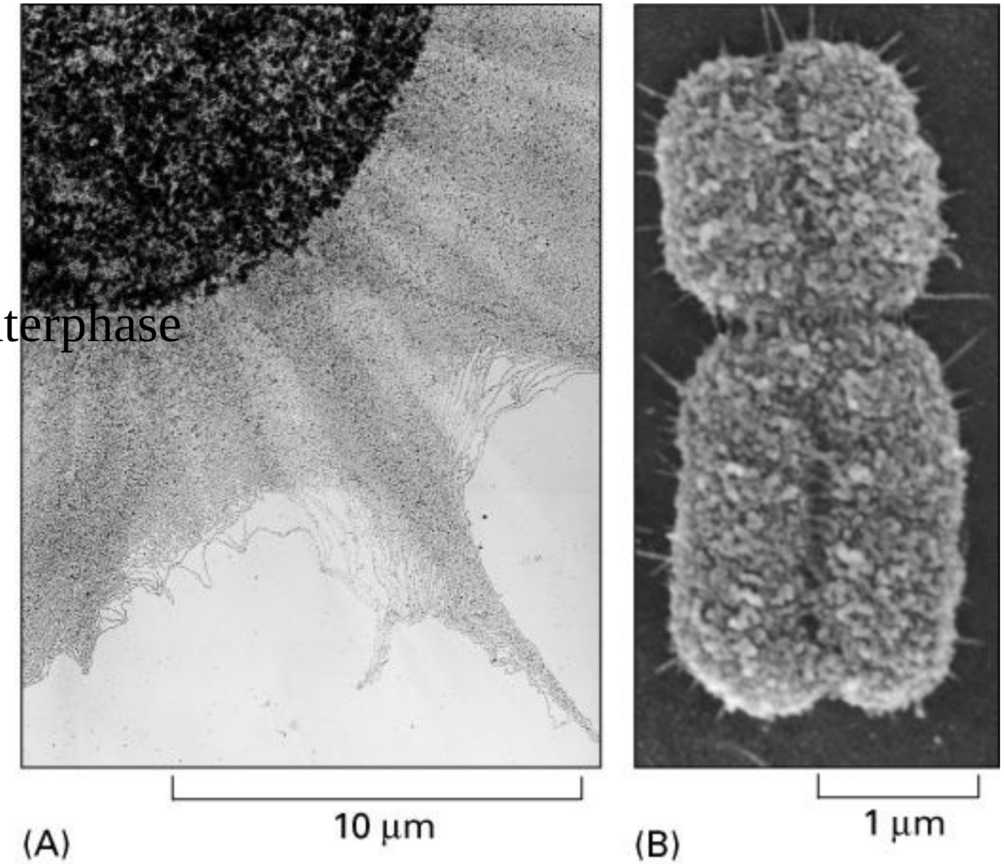
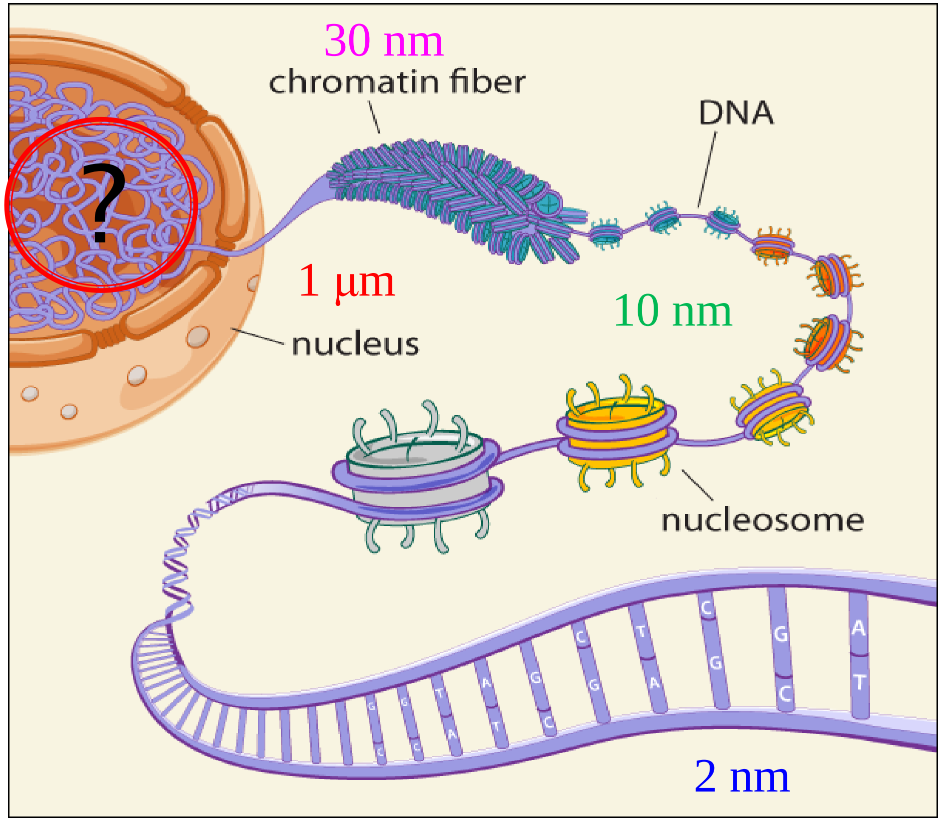


Figure 4–21. Molecular Biology of the Cell, 4th Edition.

Chromatin at mitotic
M phase.
Chromosome – condensed chromatin

All the information about biological organism is written in the double-helix DNA consequence. Although DNA macromolecules extend up to few meters in unraveled condition, they are packed really tight in the nucleus.

Multiple levels of chromatin folding



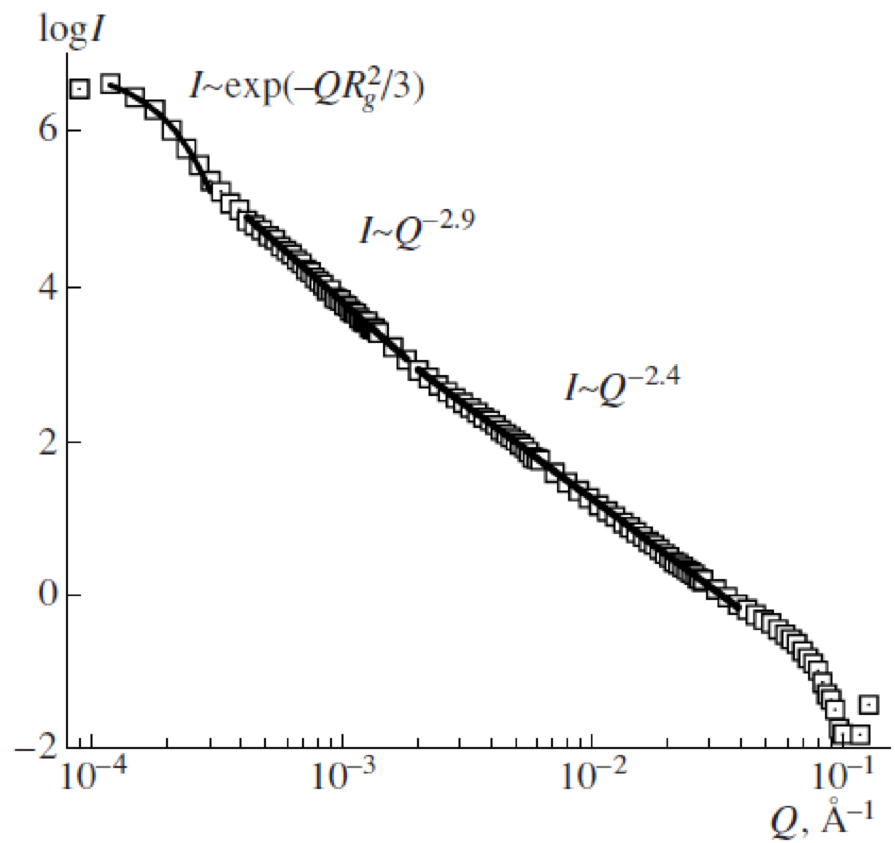
1) At the simplest level, chromatin is a double-stranded helical structure of DNA.
2) DNA is complexed with histones to from nucleosomes. Each nucleosome consist of eight histone proteins around which the DNA wraps 1.65 times.
3) The nucleosomes fold up to produce a 30-nm fiber.

Structural Hierarchy of Chromatin in Chicken Erythrocyte Nuclei Based on Small-Angle Neutron Scattering: Fractal Nature of the Large-Scale Chromatin Organization

D. V. Lebedev[a, b], M. V. Filatov[a], A. I. Kuklin[c], A. Kh. Islamov[c], J. Stellbrink[d],
R. A. Pantina[a], Yu. Yu. Denisov[a], B. P. Toperverg[a], and V. V. Isaev-Ivanov[a, b]

Chromatin exhibits properties that are characteristic of a mass fractal with fractal dimension D_m=2.4 on the scale between 15–20 nm and 400 nm.

The DNA organization was **biphasic**, with the fractal dimension slightly higher than 2 on the scales smaller than 300 nm and approaching 3 on the larger scales.

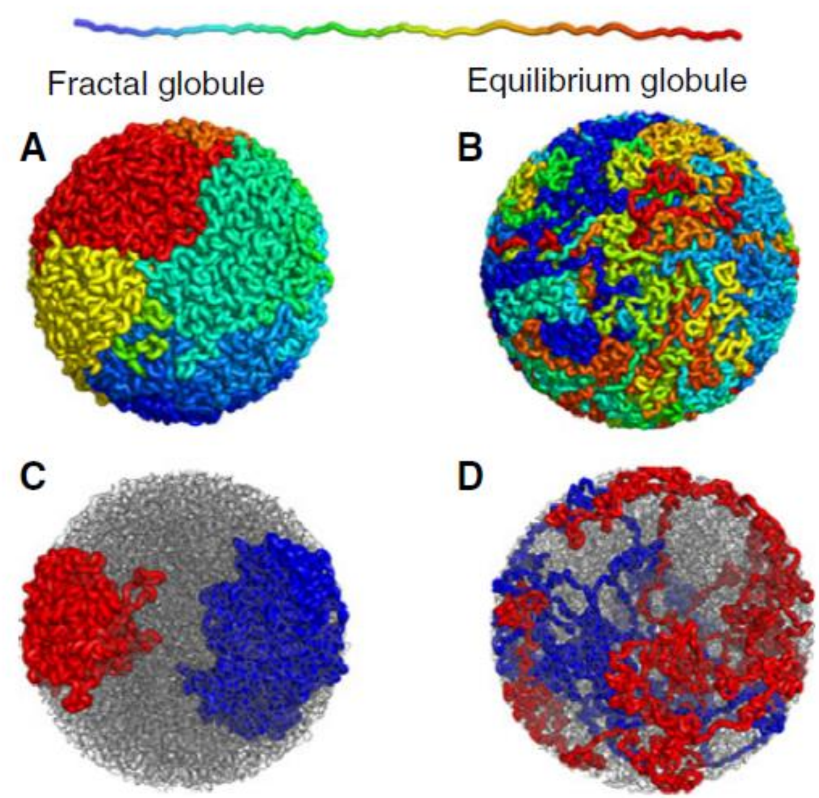


Fractal globule

The fractal globule as a model of chromatin architecture in the cell

Leonid A. Mirny

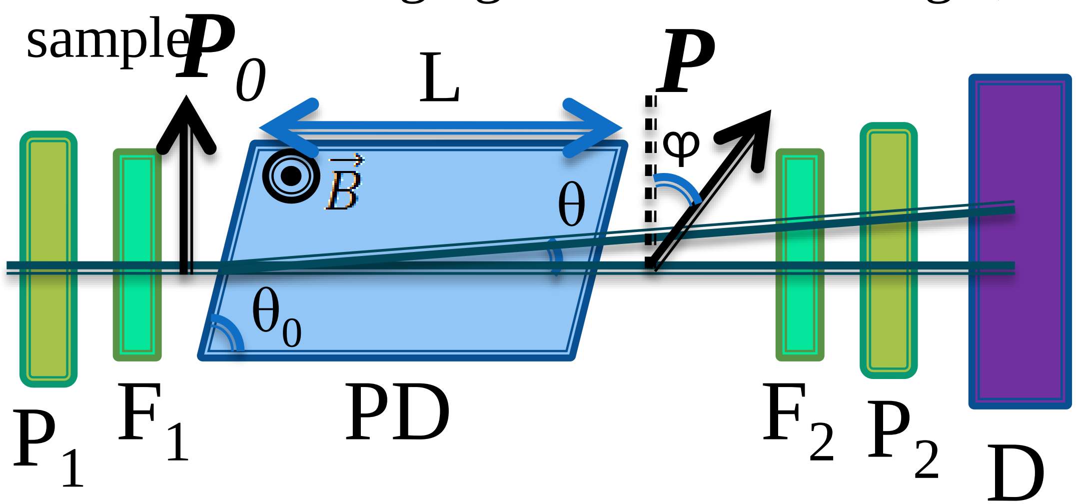
The fractal globule is a compact polymer state that emerges during polymer condensation as a result of topological constraints which prevent one region of the chain from passing across another one.



Principle of SESANS

[1] M.Th. Rekveldt, J.Nucl.Instr.Meth. B 114, (1996) 366

The principle is based on the difference in Larmor precession angle in a coil with changing transmission angle, caused by scattering from a sample[1]



$P_{1,2}$ – polarizer,
$F_{1,2}$ – analyzer,
PD – precession devise,
D - detector

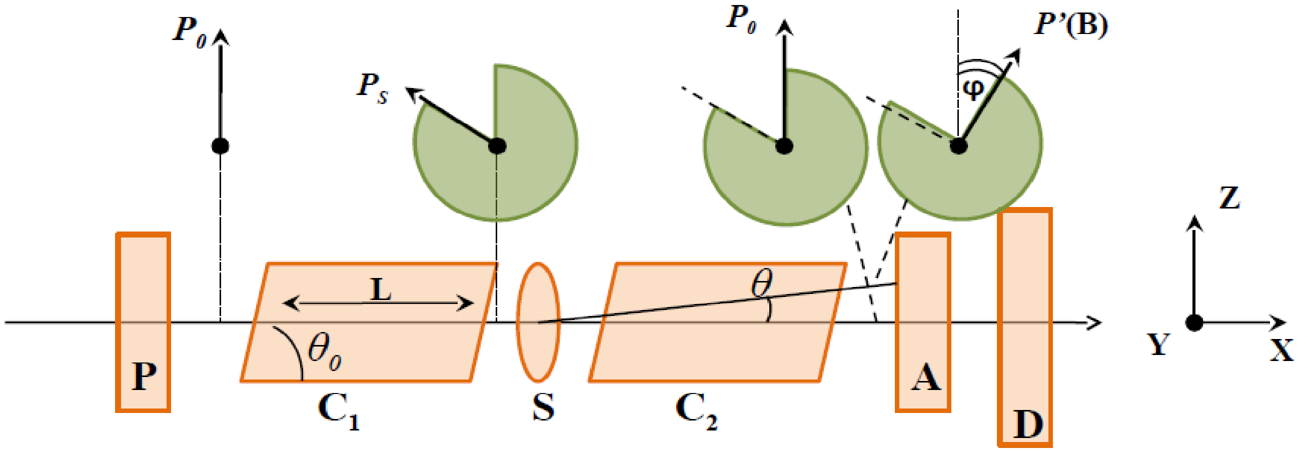
$$P(\varphi) = P_0 \cos(\varphi)$$

Their z-component of the polarization has changed due to the path difference in PD

$$\varphi = c\lambda BL \frac{\sin\theta_0}{\sin(\theta_0 - \theta)} \simeq c\lambda BL(1 + \theta\cot\theta_0)$$

$$z = \frac{c\lambda^2 BL\cot\theta_0}{2\pi}$$ -spin-echo length

SESANS instrument with 2 precession devices



$$Q_z = \frac{2\pi}{\lambda}(\theta_2 - \theta_1)$$

z-component of the momentum transfer of the neutron at the sample

$$z = \frac{c\lambda^2 BL\cot\theta_0}{2\pi}$$

spin-echo length

[] Sergey V. Grigoriev, Theo M. Rekveldt, Timofey V. Krouglov, Wicher H.Kraan, Wim G. Bouwman, J. Appl.Cryst., 39 (2006) 252-258.

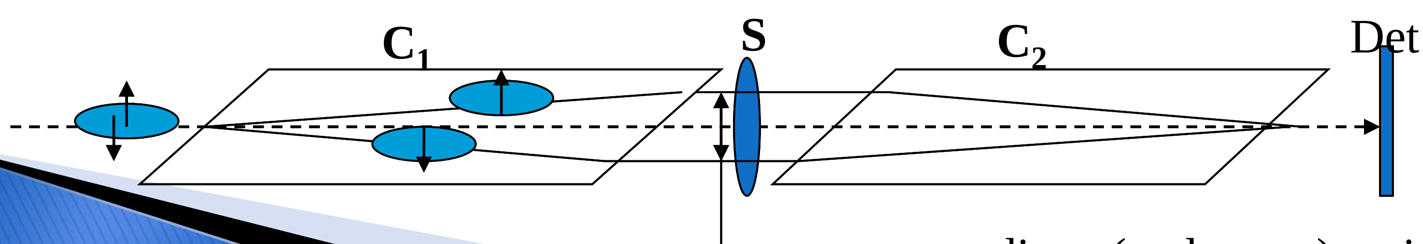
SESANS function

$$G(z) = \frac{1}{\sigma k_0^2}\int_{\mathbb{R}^2} \cos(zQ_z)\frac{d\sigma}{d\Omega}(Q)dQ_y dQ_z$$

Polarization as a function of spin-echo length

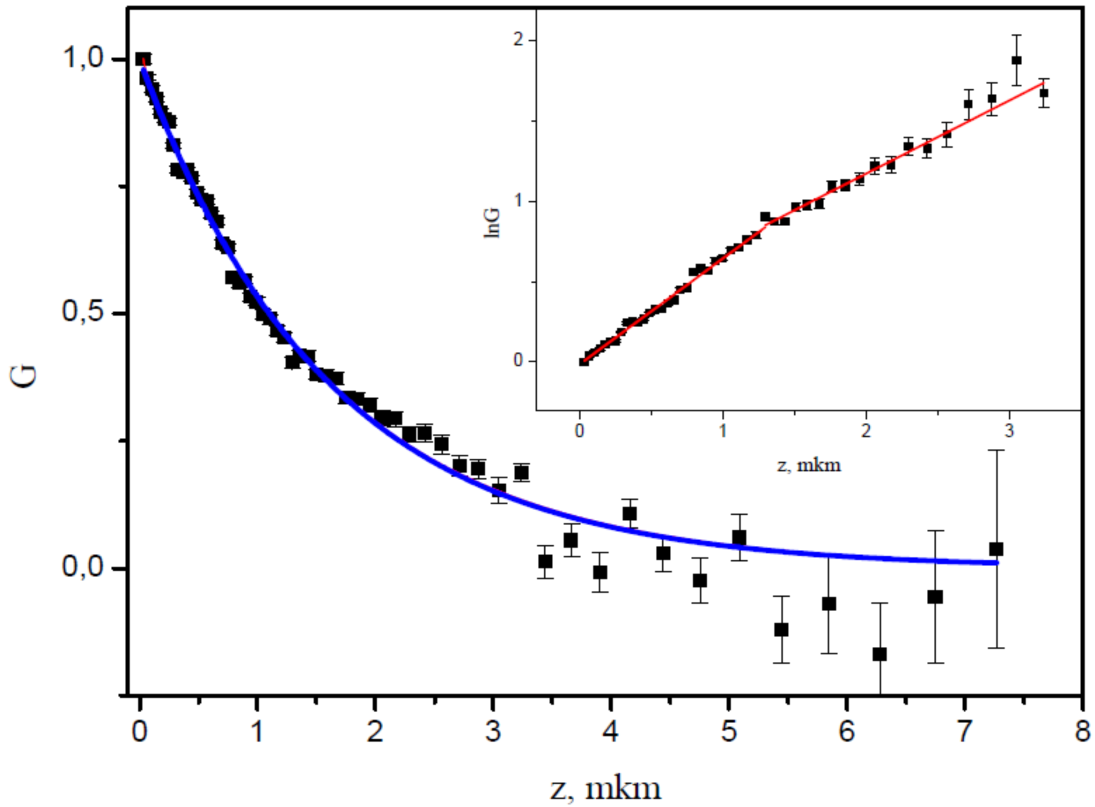
$$P(z) = \exp(l\sigma(G(z)-1))$$

Let one neutron goes to SESANS setup



z - space coordinate(real space)=spin-echo length

SESANS measurements **form chicken erythrocyte nuclei**



SESANS function from isolated chicken erythrocyte nuclei

(SESANS, TU, Delft, Netherlands)

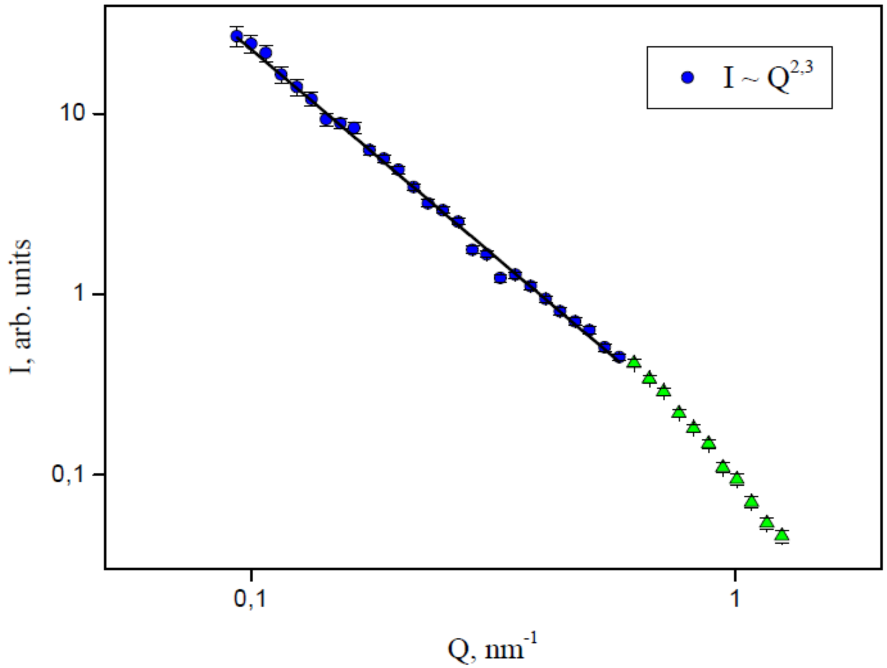
Solid curve is the result of approximation of experimental data by an exponential function

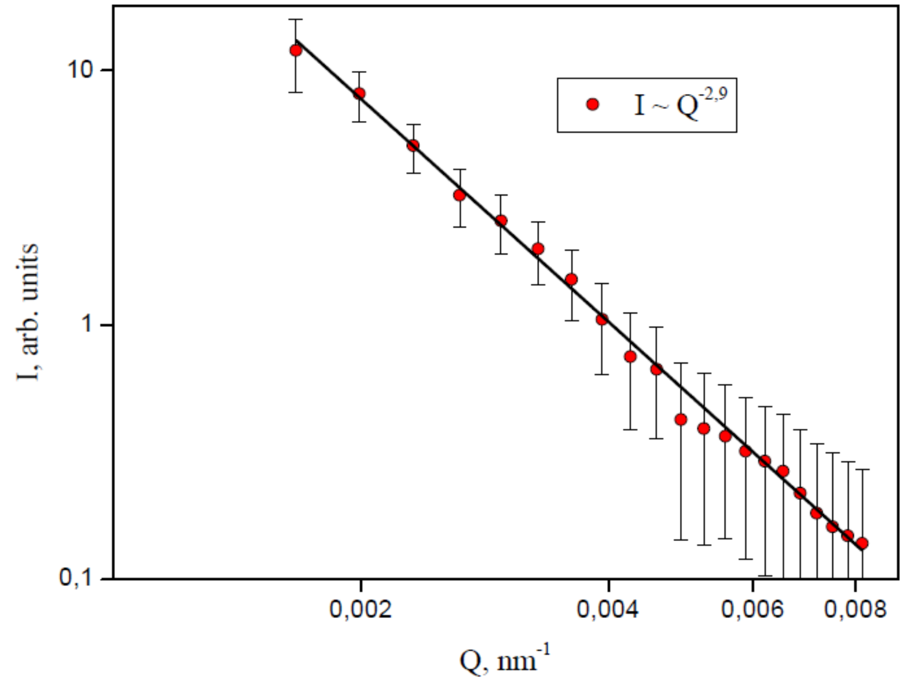
$\exp(-z/\xi)$, $\xi = 1.6,\ \chi^2 = 4$

SANS form chicken erythrocyte nuclei

Spectrometer UMO,
JINR, Dubna

MAUD (DCD), NPI
ASCR, Czech Republic





Mass fractal

$\gamma(r) \sim r^{D_F-3}$, $D_F = 2.3$,

$V \sim r^{D_F}$

6–60 нм

The power-law character of the neutron scattering intensity versus the scattering vector with parameter D = 3 or close.

0.6–1 мкм

Chromatin organization in interphase chicken erythrocytes nuclei (0.1–5.0mkm)

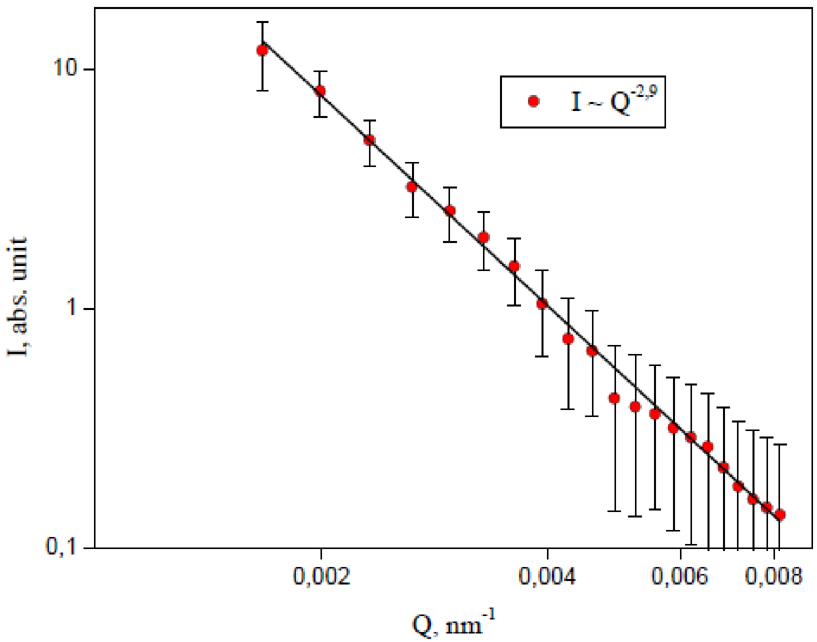
MAUD (DCD), NPI ASCR, Czech Republic

SANS

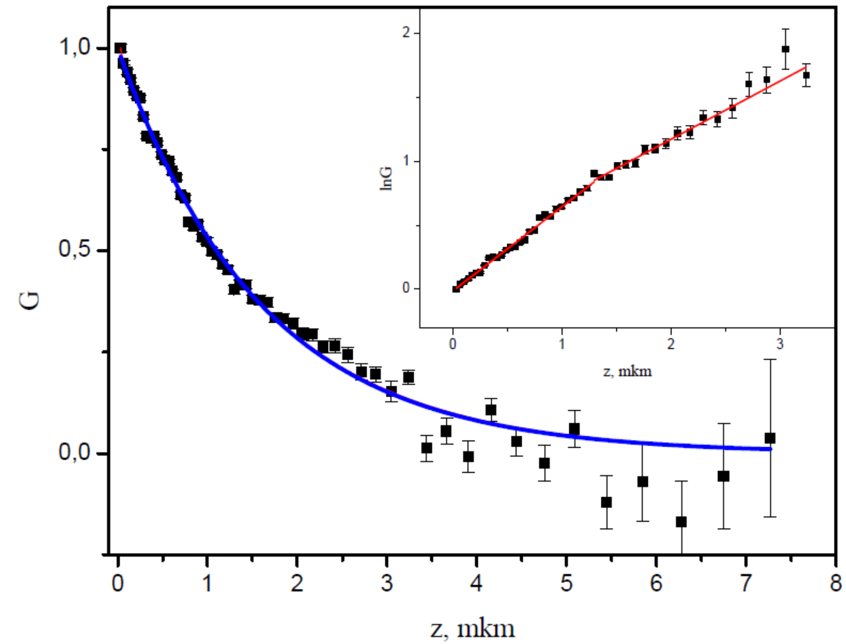
+

SESANS

(SESANS, TU, Delft, Netherlands)



Small-angle neutron scattering from isolated chicken erythrocyte nuclei



SESANS function from isolated chicken erythrocyte nuclei

$$I(Q) = \frac{1}{(1+(Q\xi)^2)^{3/2}}$$

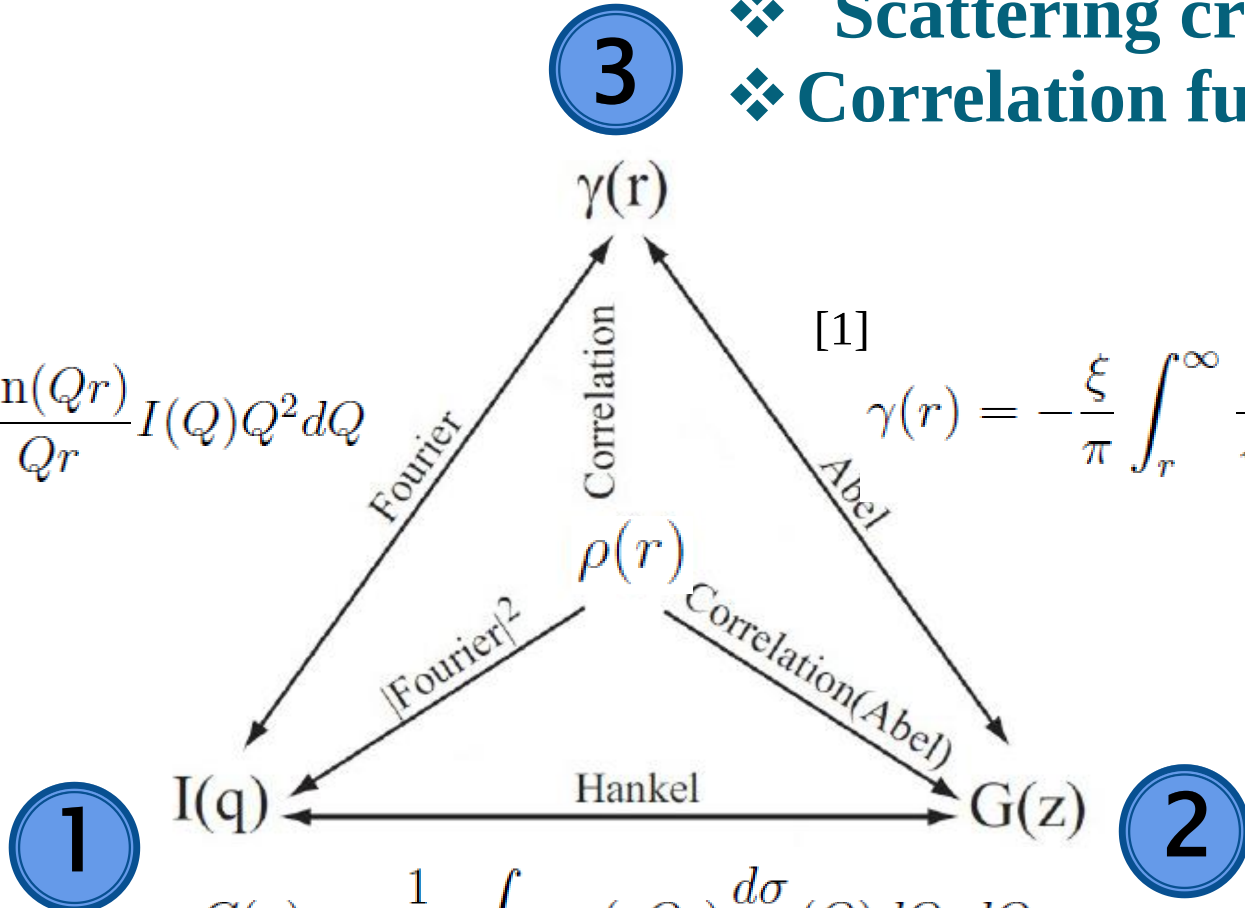
0.6–1 мкм

$$G(z) = \exp(-z/\xi)$$

The power-law character of the neutron scattering intensity versus the scattering vector with parameter D = 3 or close to corresponds to the exponential law of the SESANS function.

Relationship between

- ❖ SESANS function
- ❖ Scattering cross section
- ❖ Correlation function



[1]

$$\gamma(r) = -\frac{\xi}{\pi}\int_r^\infty \frac{G'(z)}{\sqrt{z^2 - r^2}}dz$$

$$\gamma(r) = \int_0^\infty \frac{\sin(Qr)}{Qr} I(Q)Q^2 dQ$$

$$G(z) = \frac{1}{\sigma k_0^2}\int_{\mathbb{R}^2} \cos(zQ_z)\frac{d\sigma}{d\Omega}(Q)dQ_y dQ_z$$

[1] Krouglov, T., de Schepper, I. M., Bouwman, W. G. & Rekveldt, M. Th.(2003a). J. Appl. Cryst. 36, 117–124

Scattering on a fractal sample

Unlimited mass fractal

$I(Q) \sim Q^{-D}$,

where $1<D<3$, and $D=D_m$ – fractal dimension

Volume

$V(r) \sim r^{Dm}$

Unlimited surface fractal

$I(Q) \sim Q^{D-6}$,

where $3<D<4$, and $D=D_s$ – fractal dimension of surface

Surface

$S(r) \sim r^{Ds}$

But what means D=3?

Scattering cross section - $\frac{d\sigma}{d\Omega}(Q) = \frac{N}{V}P(Q)S(Q)$

Mass fractal	Surface fractal

Main contribution to scattering cross section

$S(Q)$	$P(Q)$

J. Teixeira, J. Appl. Cryst. (1988). 21,781-785

Mass fractal

$$S(Q) = 1 + \frac{D\Gamma(D-1)\sin[(D-1)\arctan(Q\xi)]}{(Qr_0)^D(1+\frac{1}{(Q\xi)^2})^{(D-1)/2}}$$

$Q \ll 1/\xi$

$$\sin[(D-1)\arctan(Q\xi)] \sim Q\xi$$

$$\sqrt{1+(Q\xi)^2} \sim 1$$

$1/\xi \ll Q \ll 1/r_0$

$$\arctan(Q\xi) \sim 1$$

$$\sqrt{1+(Q\xi)^2} \sim Q\xi$$

$$S(Q) \approx \frac{1}{(1+(Q\xi)^2)^{D/2}}$$

Surface fractal

$$P(Q) \sim \frac{1}{Q^{6-D_s}}$$

$Q \gg 1/r_0$

$$P(Q) \sim \frac{1}{(1+(Q\xi)^2)^{\frac{6-D_s}{2}}}$$

ξ – correlation length

$$\boxed{\frac{d\sigma}{d\Omega}(Q) = \frac{A}{(1+(Q\xi)^2)^{D/2}}}$$

$$\boxed{\frac{d\sigma}{d\Omega}(Q) = \frac{A}{\left(1+(Q\xi)^2\right)^{D/2}}} \quad + \quad G(z) = \frac{1}{\sigma k_0^2}\int\limits_{\mathbb{R}^2} \cos(zQ_z)\frac{d\sigma}{d\Omega}(Q)\,dQ_y\,dQ_z$$

$$\boxed{G(z) = \frac{2}{\Gamma(\frac{D}{2}-1)}\left(\frac{z}{2\xi}\right)^{\frac{D}{2}-1} K_{\frac{D}{2}-1}\left(\frac{z}{\xi}\right)}$$

$K_\nu(x)$ is Macdonald's (Modified Bessel) function of ν kind, $\Gamma(x)$ is gamma function, ξ is correlation function, D is a parameter which is associated with fractal dimension .

$\nu = D/2-1$

$$\gamma(r) = -\frac{\xi}{\pi}\int_r^\infty \frac{G'(z)}{\sqrt{z^2-r^2}}dz$$

$$\boxed{\gamma(r) = \frac{2}{\sqrt{\pi}\,\Gamma(\frac{D}{2}-1)}\left(\frac{r}{2\xi}\right)^{\frac{D-3}{2}} K_{\frac{D-3}{2}}\left(\frac{r}{\xi}\right)}$$

Approximation by elementary function

$$K_n(x) = \sqrt{\frac{\pi}{2x}} \frac{\exp(-x)}{\Gamma(n+1/2)} \int_0^\infty \exp(-t) t^{n-1/2} (1 + \frac{t}{2x})^{n-1/2} dt$$

$x > 1/2$

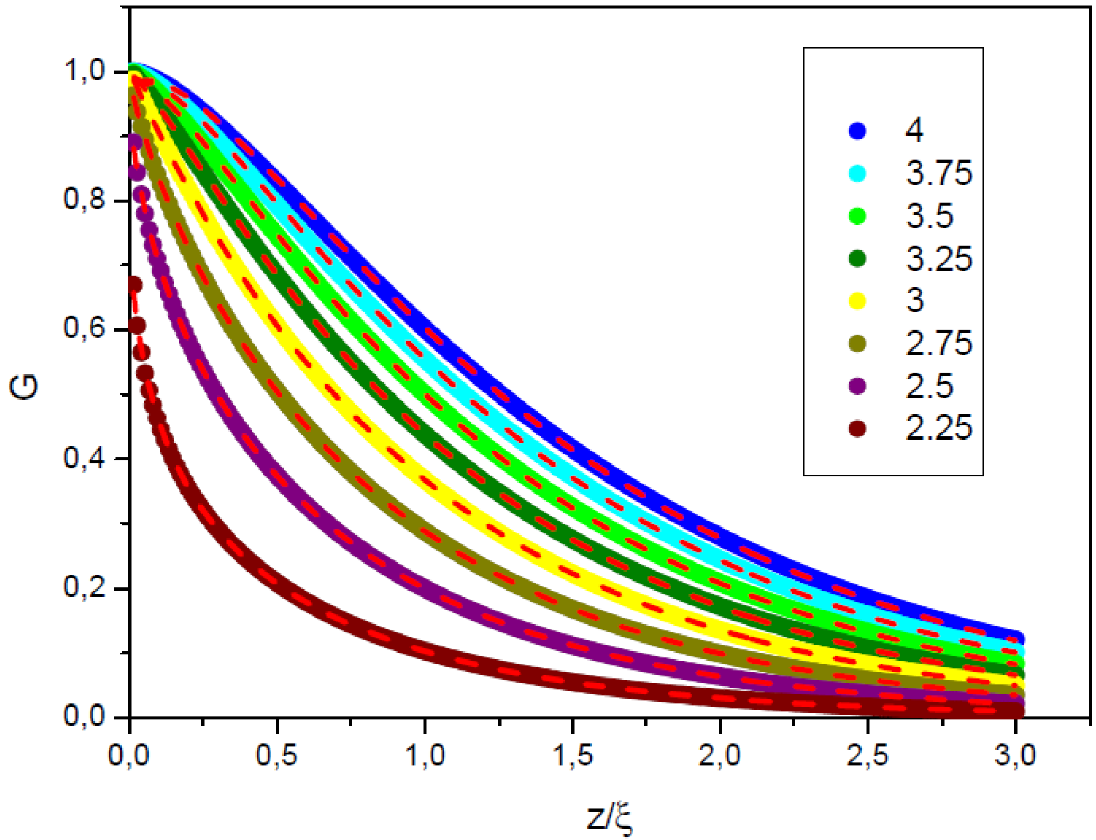
$$K_n(x) = \sqrt{\frac{\pi}{2x}} \exp(-x) \left(1 + \sum_{r=1}^{\infty} \frac{\Gamma(n+1/2-r)}{\Gamma(n+1/2)} \frac{(n-1/2)...(n-r+1/2)}{r!} (2x)^{-r} \right)$$

$$K_n(x) \simeq \sqrt{\frac{\pi}{2x}} \exp(-x) \left(1 + 1/x\right)^{\frac{(D-3)(D-1)}{8}}$$

$z/\xi > 1/2$

$$G(z) = \frac{\sqrt{\pi}}{\Gamma(\frac{D}{2}-1)} \left(\frac{z}{2\xi}\right)^{\frac{D-3}{2}} \exp(-z/\xi) \left(1 + \xi/z\right)^{\frac{(D-3)(D-1)}{8}}$$

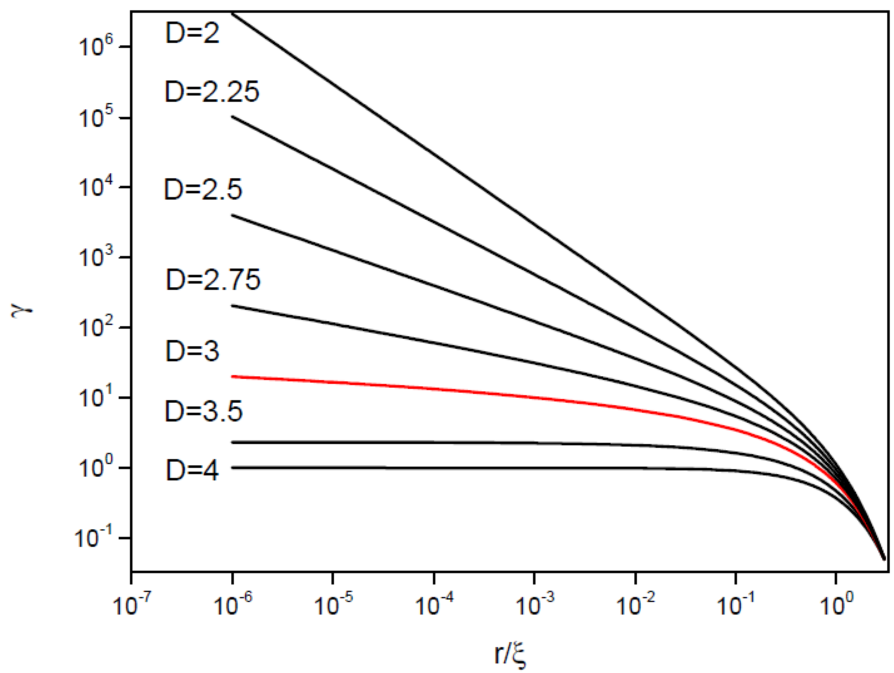
$$\boxed{\tilde{G}(z) = \frac{\sqrt{\pi}}{\Gamma(\frac{D}{2}-1)} \left(\frac{z+a_0}{2\xi}\right)^{\frac{D-3}{2}} \exp(-z/\xi) \left(1 + \xi/(z+a_0)\right)^{\frac{(D-3)(D-1)}{8}}}$$

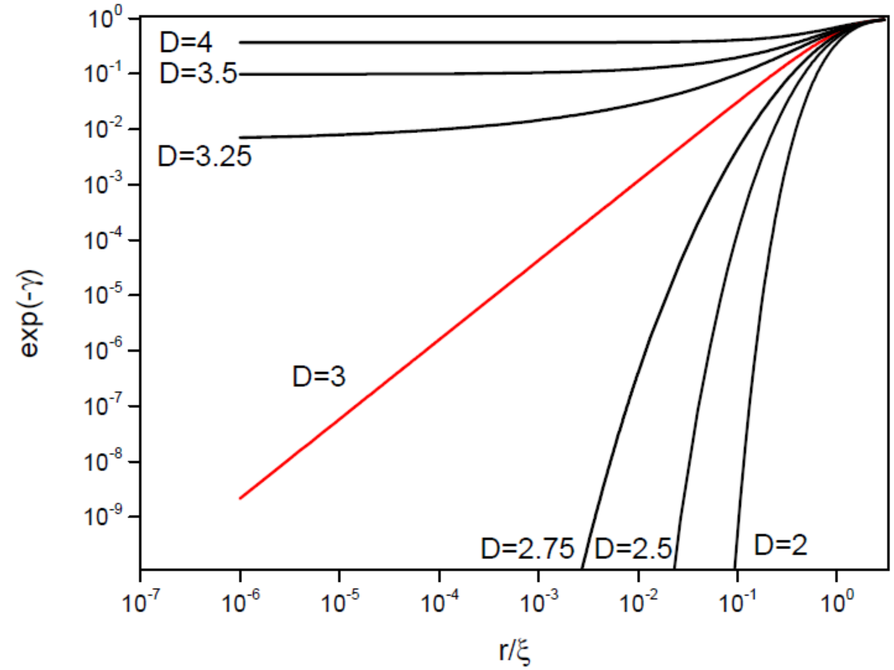


$$G(z) = \frac{2}{\Gamma(\frac{D}{2}-1)} \left(\frac{z}{2\xi}\right)^{\frac{D}{2}-1} K_{\frac{D}{2}-1}\left(\frac{z}{\xi}\right)$$

$$G(z) = \frac{\sqrt{\pi}}{\Gamma(\frac{D}{2}-1)} \left(\frac{z+a_0}{2\xi}\right)^{\frac{D-3}{2}} \exp(-z/\xi)\left(1+\xi/(z+a_0)\right)^{\frac{(D-3)(D-1)}{8}}$$

Correlation function





$$\gamma(r) = \frac{2}{\sqrt{\pi}\,\Gamma(\frac{D}{2}-1)} \left(\frac{r}{2\xi}\right)^{\frac{D-3}{2}} K_{\frac{D-3}{2}}\left(\frac{r}{\xi}\right)$$

$$r/\xi < 1$$

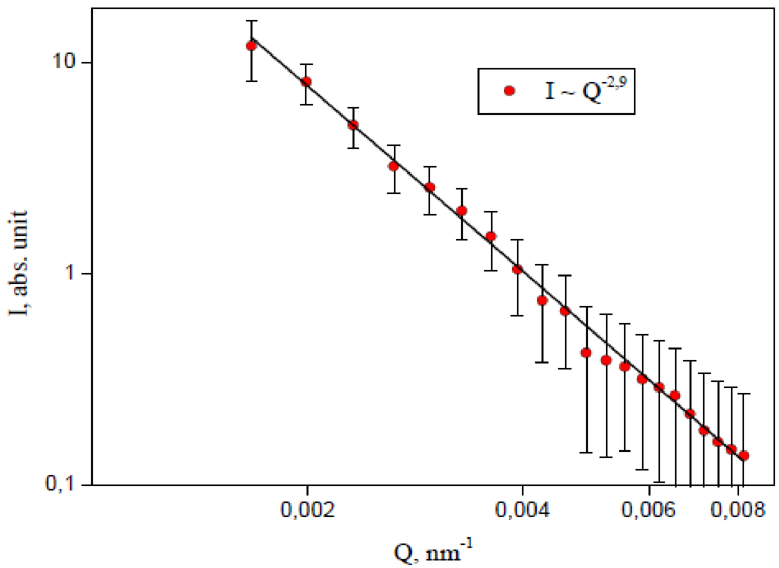
D<3 – power function r^{3-D}

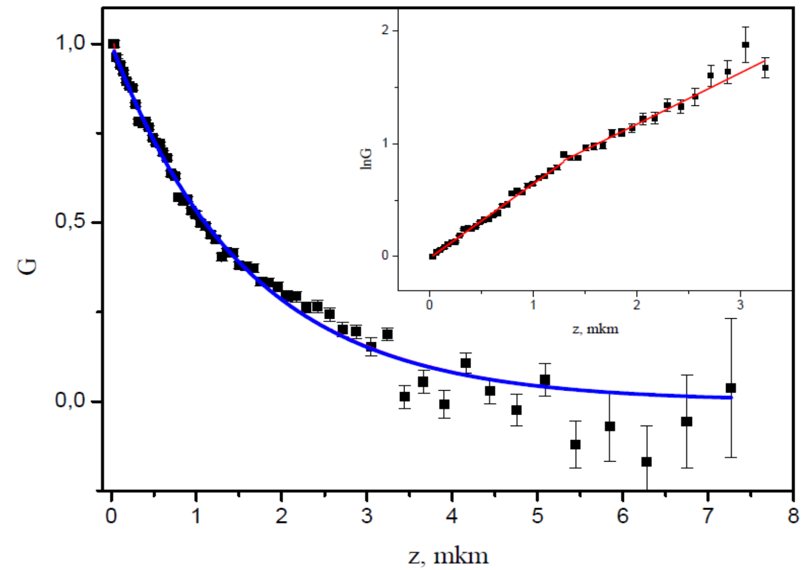
D=3 – logarithm ln(1/r)

D>3 – constant

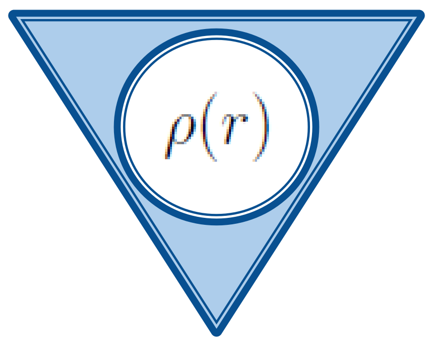
SANS

SESANS





$$I(Q) = \frac{1}{(1+(Q\xi)^2)^{3/2}}$$



$$G(z) = \frac{2}{\Gamma(½)}\left(\frac{z}{2\xi}\right)^{1/2} K_{1/2}\left(\frac{z}{\xi}\right)$$

$$G(z) = \exp(-z/\xi)$$

$$\gamma(r) = \frac{1}{\pi}K_0(r/\xi)$$

Correlation function

If $r/\xi < 1$

then $\gamma(r) \sim \ln(\xi/r)$

What means γ(r)~ln(ξ/r)?

correlation function

$$\gamma(r) \sim \ln(\xi/r)$$

scaling law

$$\gamma(r/a) = \gamma(r) + \ln(a)$$

$\ln(a)$ - additive constant

It has an unusual scaling law. The correlation function increases with an additive rather than multiplicative constant, upon reducing the ruler length by a fixed rescaling factor. This leads to a logarithmic law instead of the usual power law for fractals.

Correlation function for ordinary fractal

correlation function

$$\gamma(r) \sim r^{D_m - 3}$$

D_m - fractal dimension

scaling law

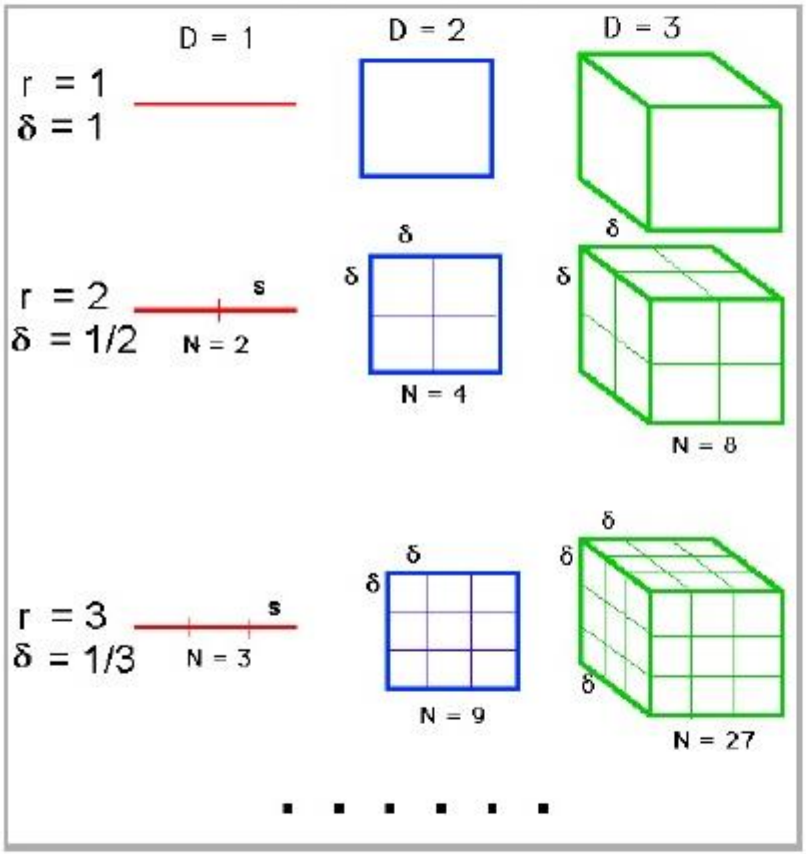
$$\gamma(r/a) = \frac{\gamma(r)}{a^{D_m}}$$

$\frac{1}{a^{D_m}}$ - multiplicative constant

Fractal geometry.

Ordinary fractal

$$N = r^{D} \qquad N = \delta^{-D}$$



Measure Hausdorff - Besicovitch

$$M_D = N(\delta) \cdot \delta^{D}$$

$$\begin{cases} M_D \xrightarrow[\delta \to 0]{} 0, & \text{при} \quad D > D_H \\ M_D \xrightarrow[\delta \to 0]{} const, & \text{при} \quad D = D_H \\ M_D \xrightarrow[\delta \to 0]{} \infty, & \text{при} \quad D < D_H \end{cases}$$

$$D_F > D_T \xRightarrow{\textbf{def}} \text{fractal subset}$$

Volume

$V(\delta) \sim \delta^{Dm}$

[] B. Mandelbrot, The Fractal Geometry of Nature, Freeman, New York, 1983.

Logarithmic fractal

A subject can be characterized by the fractal measure

$$\mu(r) = r^{D_f} \ln^{\Delta}(1/r)$$

where D_F is fractal dimension and
D_F equal to topological dimension (D_T =1, 2, 3)
Δ is subdimension

[] B. Mandelbrot, The Fractal Geometry of Nature, Freeman, New York, 1983.

For chromatin structure

$$\mu(r) = V(r) \sim M \sim r^3 \ln(1/r)$$

$$\text{thus } D_F = 3, \quad \Delta = 1$$

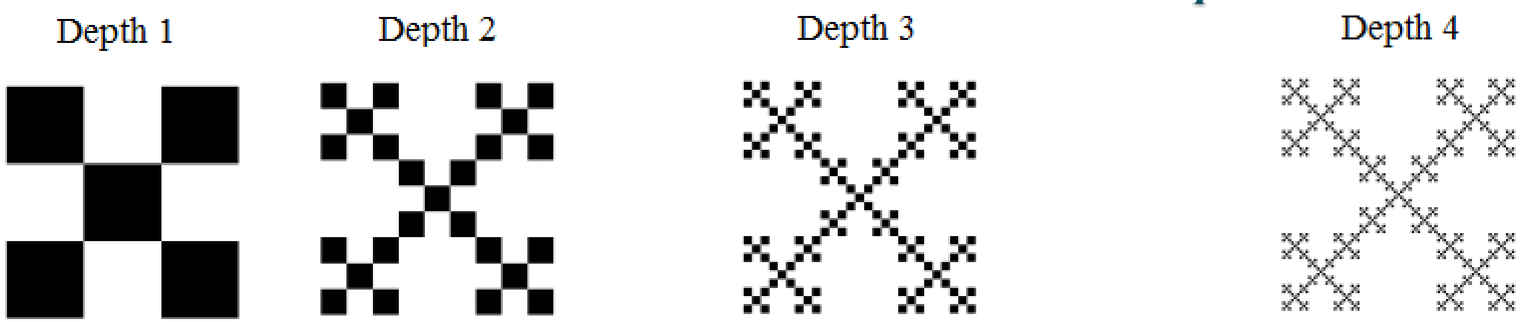
$$\lim_{r \to 0} N(r) \cdot \mu(r) = \text{const}$$

Covering the object with squares of linear size $r = 1, ½, ¼ \ldots (½)^n$ one finds that the number of squares ($N(r)$) times $r^3 \ln(1/r)$ tends to the value const in the limit $r \to 0$.

$$N(n) \sim 2^{3n}/n$$

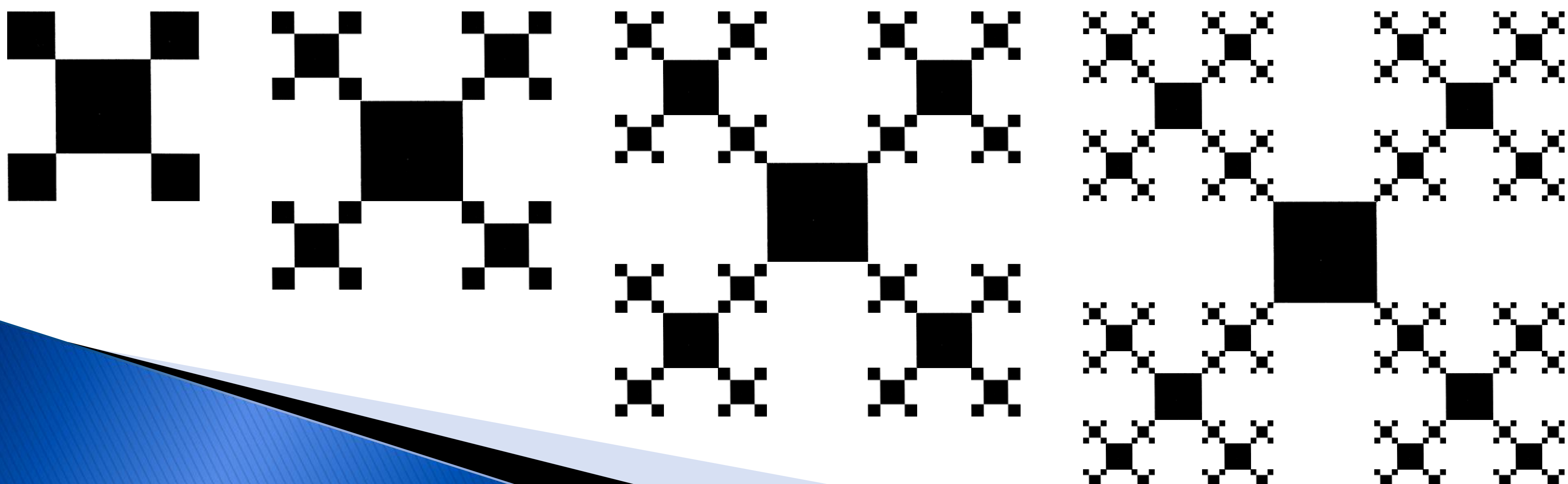
For example

The Hausdorff dimension of this fractal is $D_F \approx 1.46497$, $\mu(r)=r^{D_F}$



Logarithmic fractal, $\mu(r)=r^2/\ln(1/r)$, $D_F=2$, $\Delta=-1$

As a possible example we propose a graphical representation of the branching process of a botanical tree, according to the simple principle ascribed to Da Vinci.



Many thanks to SESANS team!

Sergey Grigoriev, PNPI, SPbSU

Vladimir Zabenkin, PNPI, SPbSU

Evgeny Velichko, SPbSU, TU Delft

Konstantin Pavlov, PNPI, SPbSU

Ekaterina Iashina, PNPI, SPSU

Many thanks to biologists!

Michael Filatov, PNPI

Dmitry Lebedev, PNPI

Thank you for attention and patience ☺

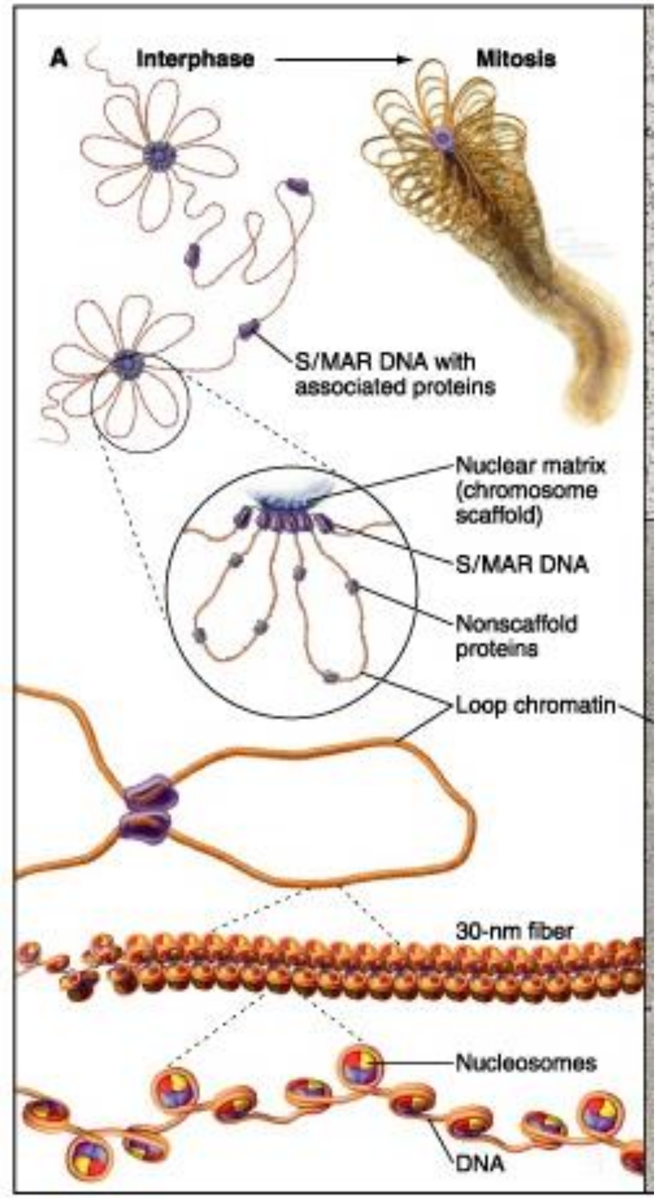
С ДНЁМ РОЖДЕНИЯ!

The Structure and Function of DNA

I. Genetic information is carried in the linear sequence of nucleotides in DNA
II. Genetic information contains instructions to synthesize proteins
III. DNA forms double helix with two complimentary strands holding together by hydrogen bonds between A-T (2 bonds) and G-C (3 bonds)
IV. DNA duplication occurs using one strand of parental DNA as template to form complimentary pairs with a new DNA strand.
V. DNA is in nucleus in eucaryotes

Overview of Chromosome Structure

- Nucleosomes
  - ~200 bp DNA in 120Å diameter coil
  - 3.4Å/bp x 200 = 680Å
  - 680/120 = 5X compaction
- 30nm fiber
  - Coil of nucleosomes w/ 6/turn
  - 1200bp/120Å vs 4080Å = 34X compaction
- Chromatin loops
  - 30nm fiber is looped into 15-100Kbp loops
  - 7-8 loops form rosette w/ bases of loops attached to central core of scaffold proteins
  - 300Å/rosette, 800Kbp/rosette = 800kbp/300Å vs 2720000Å ≈9000X compaction



Chromatin Packing
Condensin plays important roles

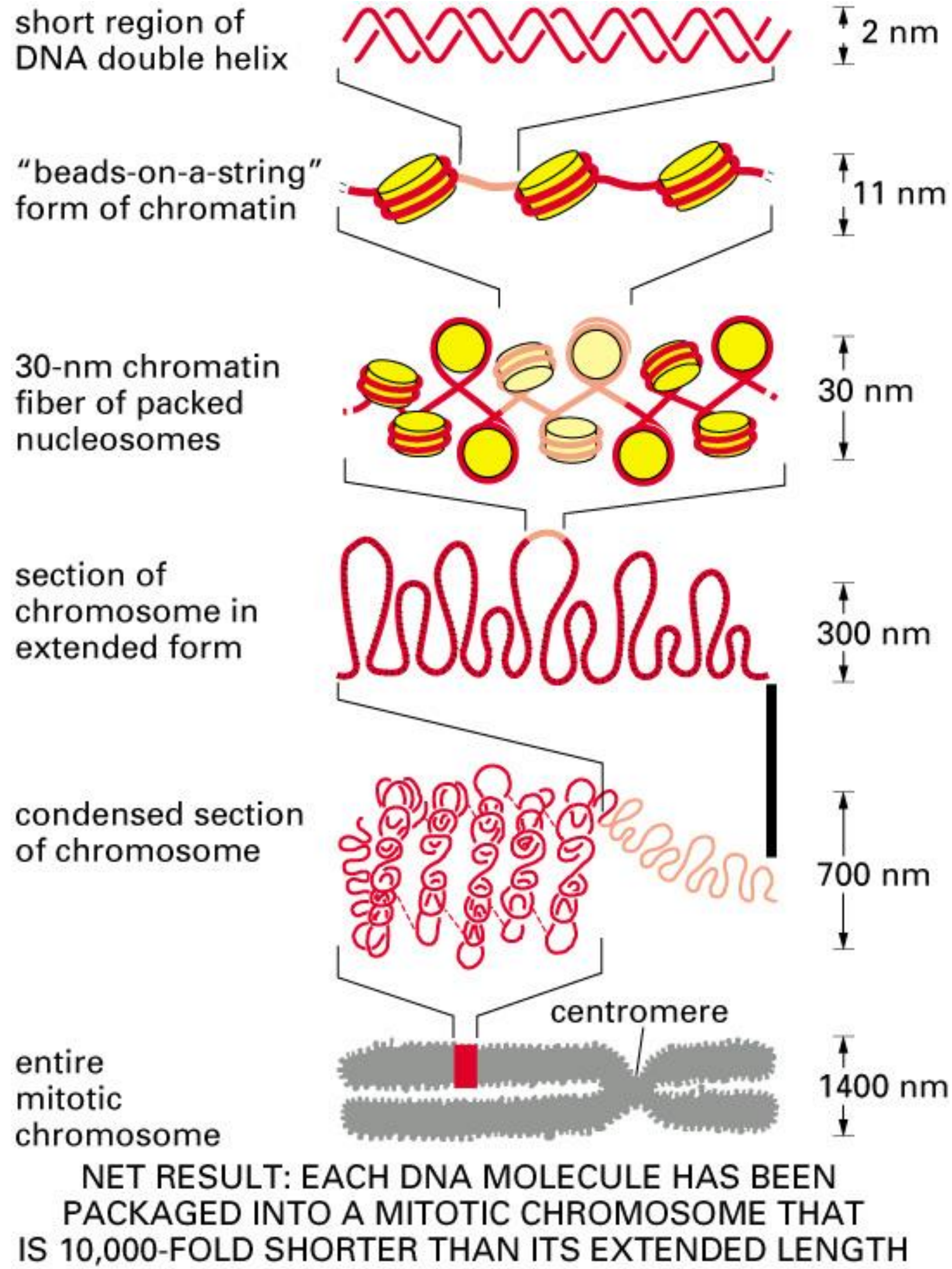
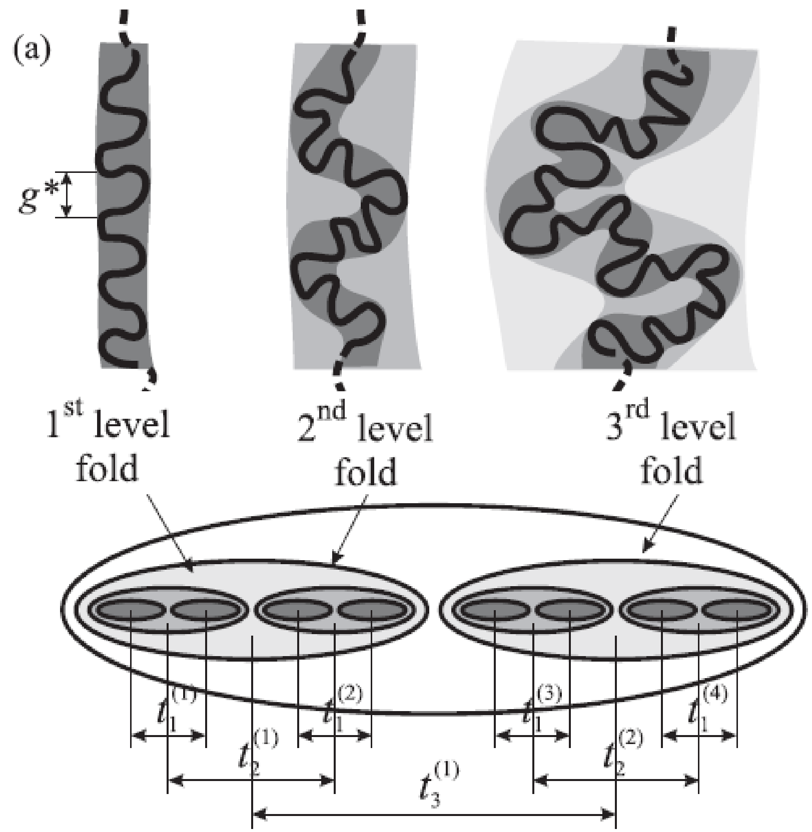


Figure 4–55. Molecular Biology of the Cell, 4th Edition.


(a)
g*
1st level fold
2nd level fold
3rd level fold
t1(1)
t1(2)
t1(3)
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t3(1)