Polymer physics of the genome: from chromosome territories to melts of rings

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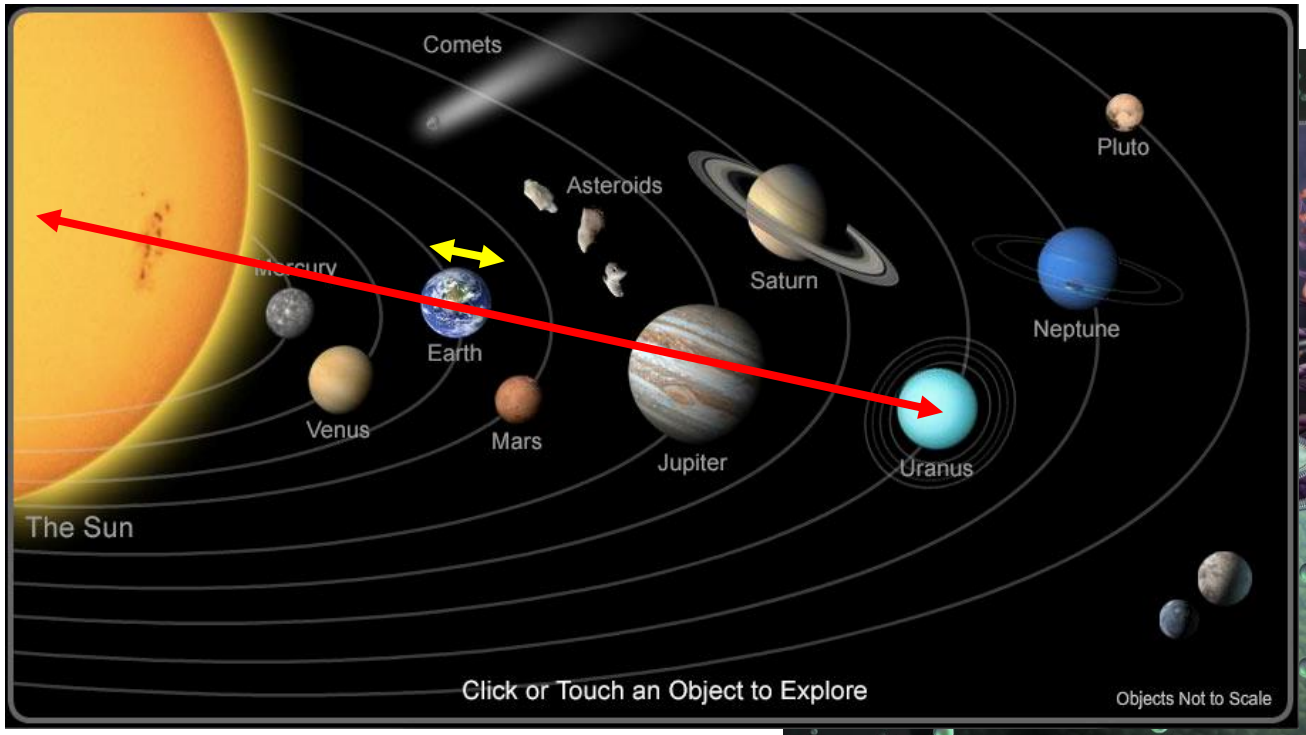
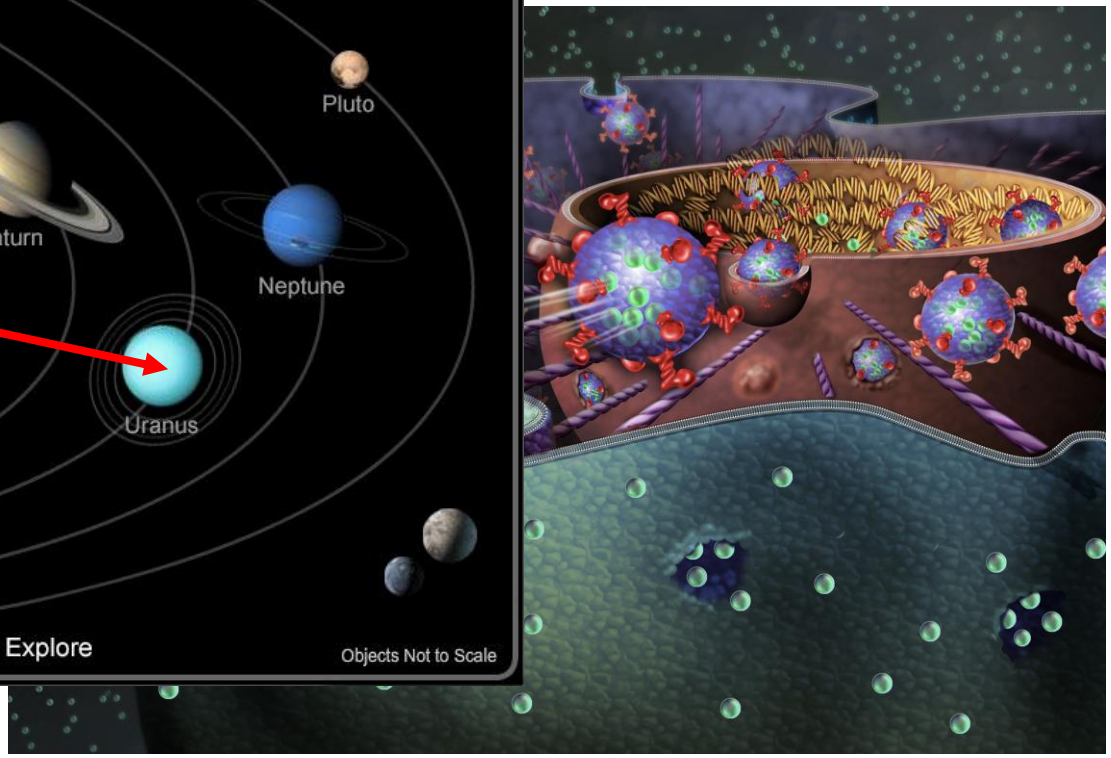
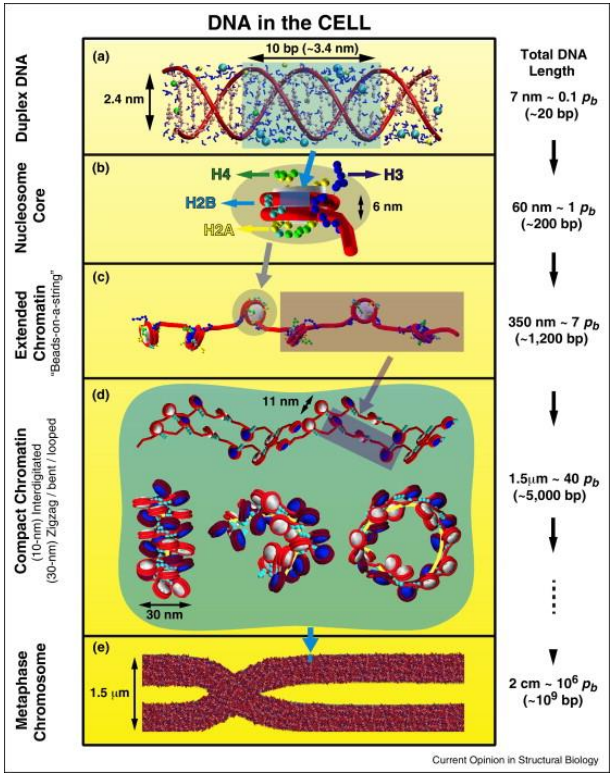
The problem of chromosome folding

- Each human cell contains ~6.5*10^9 basepairs of DNA => ~2m DNA
- DNA is hosted within the nucleus (~10microns=10^{-5}m)
- Like a rope of ~100km into a backpack





Spatial organization of DNA and chromosomes



Ozer et al., Curr. Opin. Struct. Biol. (2015)

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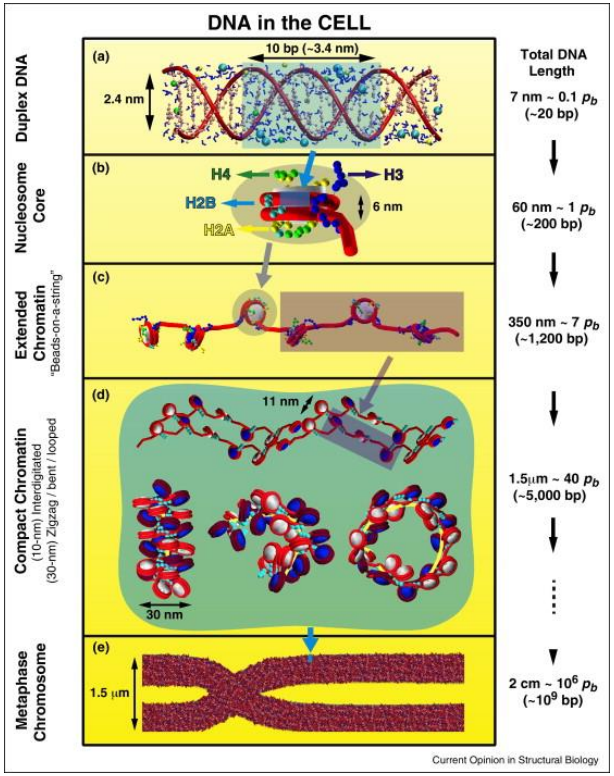

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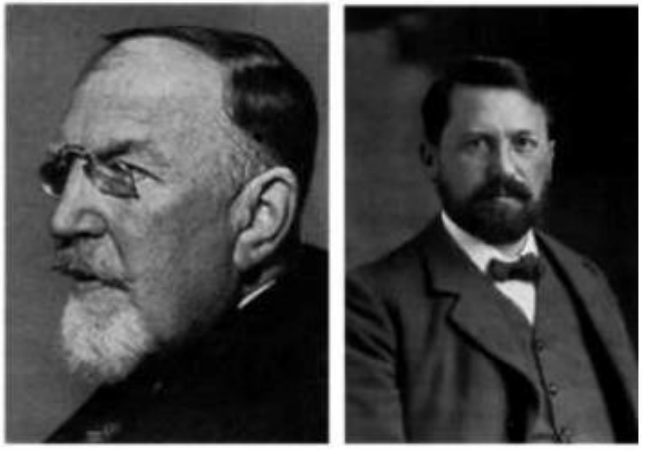

Carl Rabl (1853-1917) and Theodor Boveri (1862-1915).

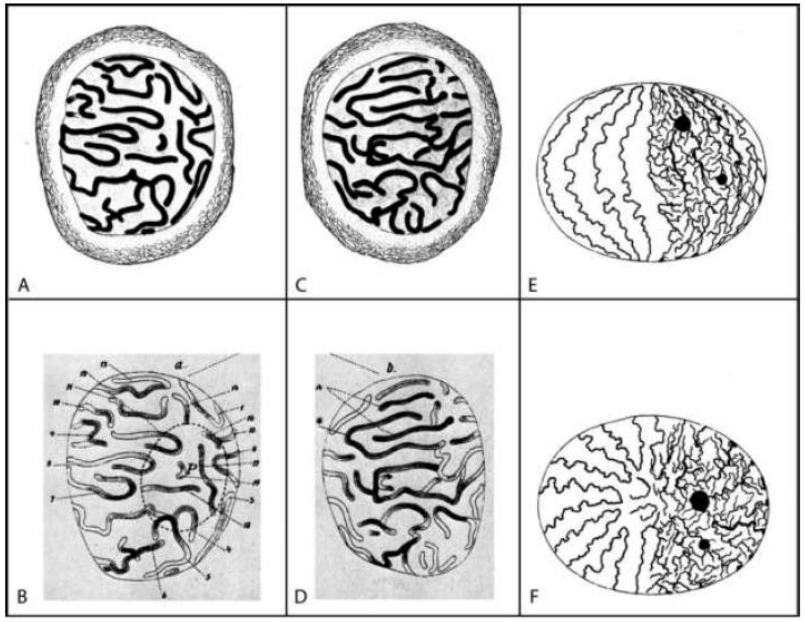

Figure 6. A-D. Drawings (A,C) and more schematic representations (B,D) of prophase chromosomes from an epidermal prophase nucleus of *Salamandra maculata* (Rabl, 1885). P: Polfeld. Rabl embedded sections from Salamandra larvae between two thin cover glasses. This approach allowed him to view individual cells from both sides. With the help of a camera lucida he documented the three-dimensional course of chromosomes and counted chromosome numbers. E and F) Rabl's model of interphase chromosome arrangements (Rabl, 1885); E. shows a lateral view, F. a view on the same model nucleus from above. In (E) Rabl's *Pol-Feld* (comprising the regions where chromosomes become attached to the spindle) is depicted at the top, the *Gegenpol-Feld* (comprising chromosome ends) at the bottom; the model nucleus shown in F. is turned around by 90° compared to (E) allowing a direct view on the Pol-Feld in the middle (for further details see text).

T. Cremer & C. Cremer, Eur. J. Histochem. (2006)

a) Rise, fall and resurrection of chromosome territories: a historical perspective. Part I. The rise of chromosome territories.

b) Rise, fall and resurrection of chromosome territories: a historical perspective. Part II. Fall and resurrection of chromosome territories during the 1950s to 1980s. Part III. Chromosome territories and the functional nuclear architecture: experiments and models from the 1990s to the present.

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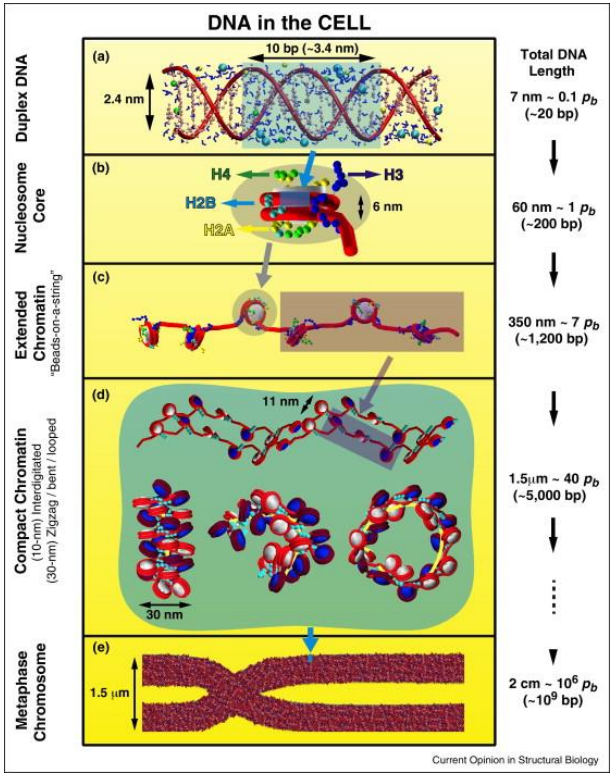

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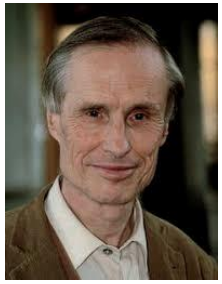
T. Cremer LMU-Munich (DE)



C. Cremer IMB-Mainz (DE)

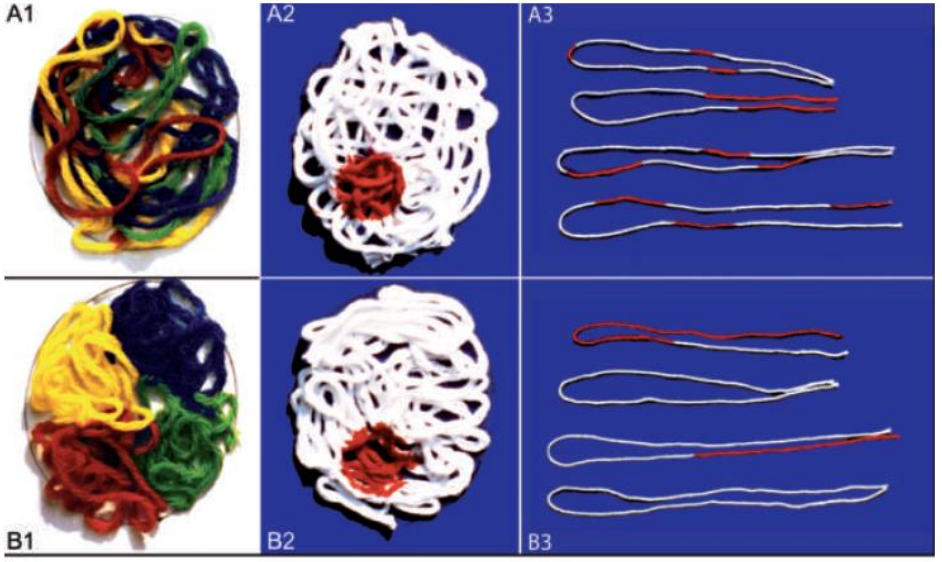


Figure 5. Experimental rationale of microirradiation experiments. (T. Cremer and C. Cremer, unpublished scheme from 1982, compare Figure 3 in Cremer T. , Cremer C. *et al.* 1982). The higher order chromatin arrangement in the interphase nucleus is compared with a coil composed of a number of threads (chromosomes). The examples shown do not refer to an actual chromosome arrangement of any particular cell type. For further details see text. A1) The threads are extended and intermingled B1) Each thread forms a distinct territory. A2 and B2) The arrangements of threads shown in A1 and A2 cannot be distinguished, when all threads bear the same colour. A small part of the coil is marked by red colour. A3 and B3) Threads show red marks after disassembling of the two coils. The distribution of these marks shows the regions of the threads located together in the two coils.

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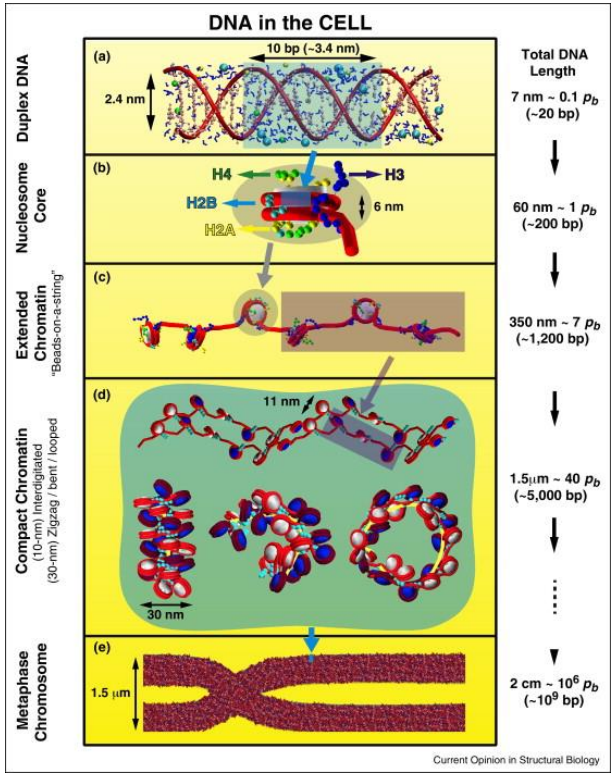

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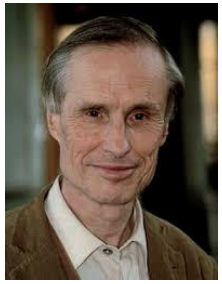
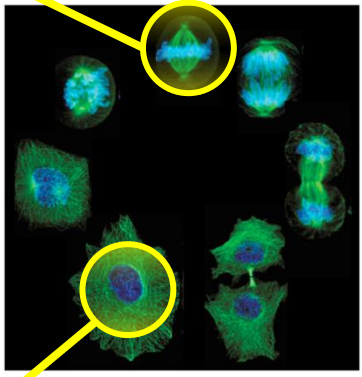
LMU-Munich (DE)

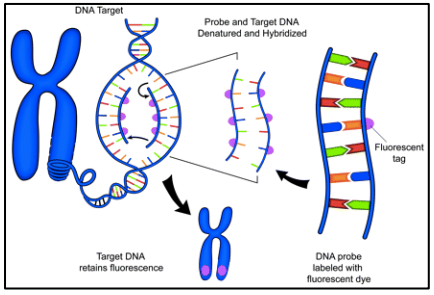


C. Cremer
IMB-Mainz (DE)

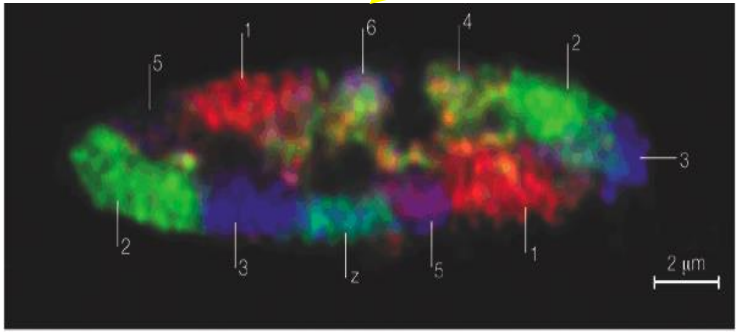
MITOSIS



Fluorescence in-situ hybridization (FISH)



INTERPHASE



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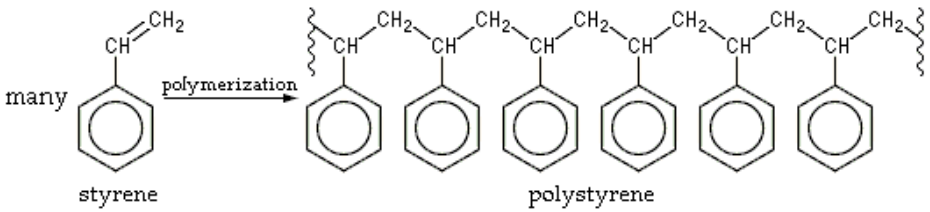
A digression on polymers

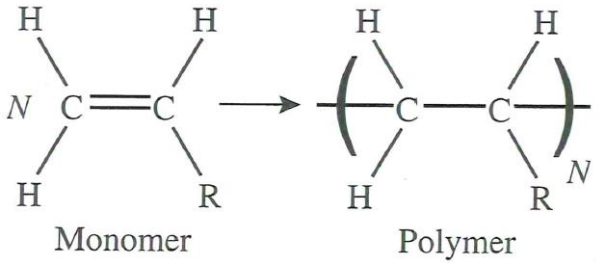
- https://boulderschool.yale.edu/2012/boulder-school-2012-lecture-notes
  - See lectures by **AY Grosberg** and M Rubinstein

- Wang, Z-G, *50th Anniversary Perspective: Polymer Conformation - A Pedagogical Review*, Macromolecules (2017); 10.1021/acs.macromol.7b01518

Definition. Polymers (from Greek, poly="many" + meros="parts") are chain molecules consisting of 10^2-10^9 monomeric units joined together by chemical reaction.

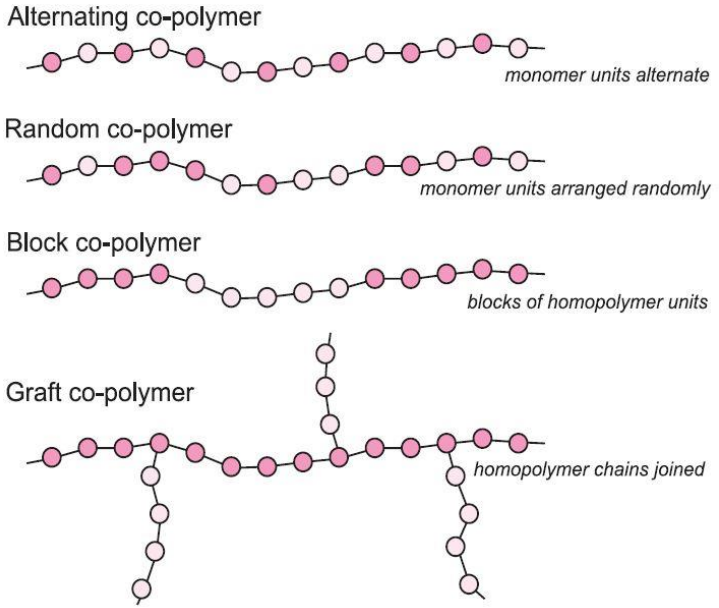
Polymerization. Chain-reaction process of covalent bonding of elementary units:





- R = H => Polyethylene
- R = Cl => Polyvinylchloride (PVC)
- R = Benzene => Polystyrene

Polymer architectures



Aggregate states / dilution

1. Gas: dilute solutions
2. Liquid: semi-dilute solutions / melts
3. Solid: rubber-elastic networks, polymer glasses, semi-crystalline polymers

Scales:

- $k_B T$=4.1 pN*nm at room temperature (24°C)
- Breaking covalent bond: ~10000 K; bonds are NOT in equilibrium.
- "Bending" and non-covalent bonds compete with $k_B T$
- Monomer size b~Å;
- Monomer mass m - from 14 to ca 1000;
- Polymerization degree N~10 to 10^9;
- Contour length L~10 nm to 1 m.

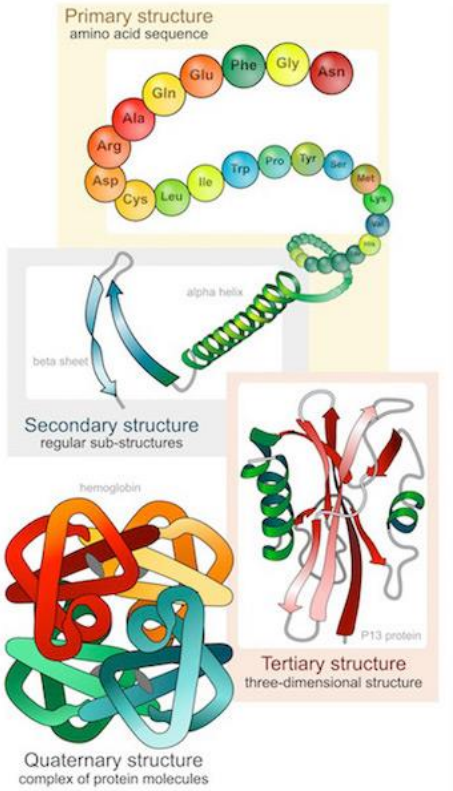
Polymers in materials science

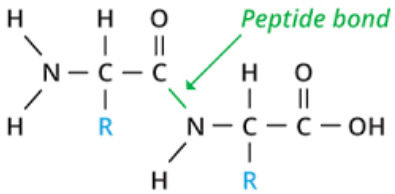
(e.g., alkane hydrocarbons $-(CH_2)-$)

# C atoms	1-5	6-15	16-25	20-50	1000 or more
@ 25°C and 1 atm	Gas	Low viscosity liquid	Very viscous liquid	Soft solid	Tough solid
Uses	Gaseous fuels	Liquid fuels and solvents	Oils and greases	Candles and coatings	Bottles...
Examples	Propane	Gasoline	Motor oil	Paraffin wax	Polyethylene
					

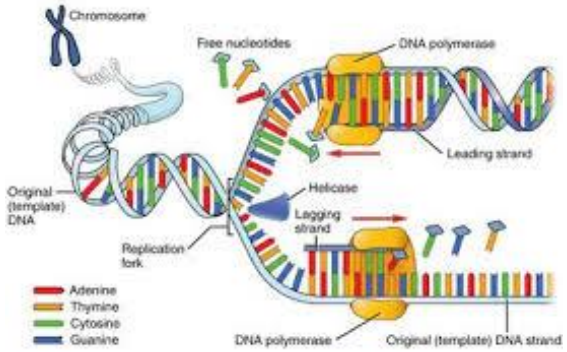
Biopolymers

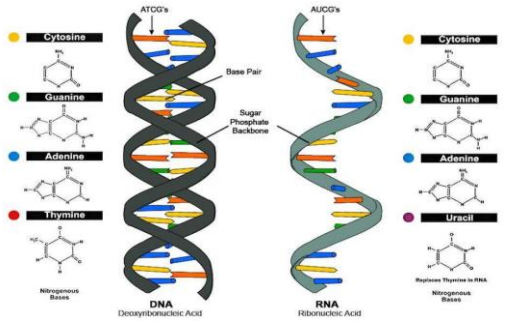
Proteins

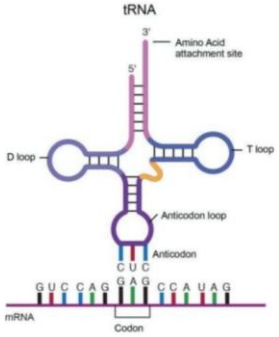




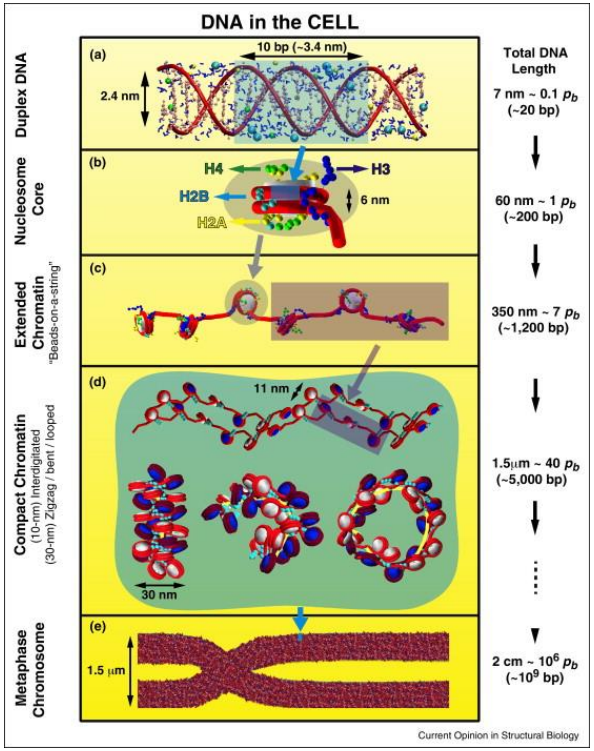
Nucleic acids: DNA, RNA



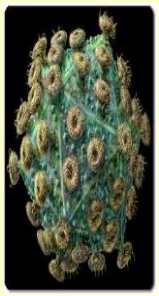
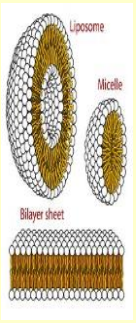
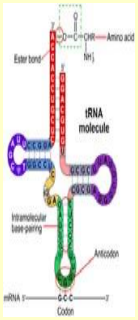
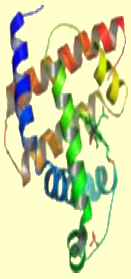
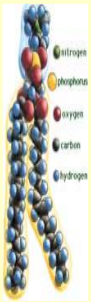




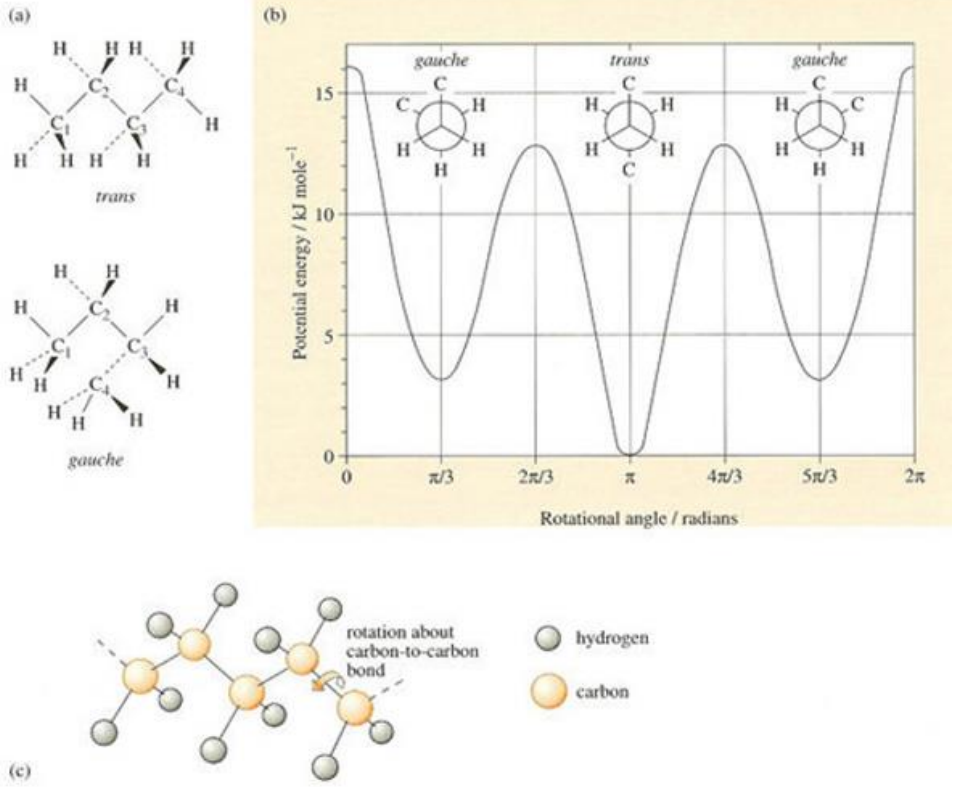
Chromatin



Polymers in living nature

	DNA	RNA	Proteins	Lipids	Polysaccharides
N	Up to 10^{10}	10 to 1000	20 to 1000	5 to 100	gigantic
Nice physics models	Bioinformatics, elastic rod, charged rod, helix-coil	Secondary structure, annealed branched, folding	Proteomics, random/designed heteropolymer, HP, funnels, ratchets, active brushes	Bilayers, liposomes, membranes	??? Someone has to start
Uses					
Molecule					

Polymer Physics is the study of polymer conformations



Total number of polymer conformations

$\Omega(N) \sim 10^N$

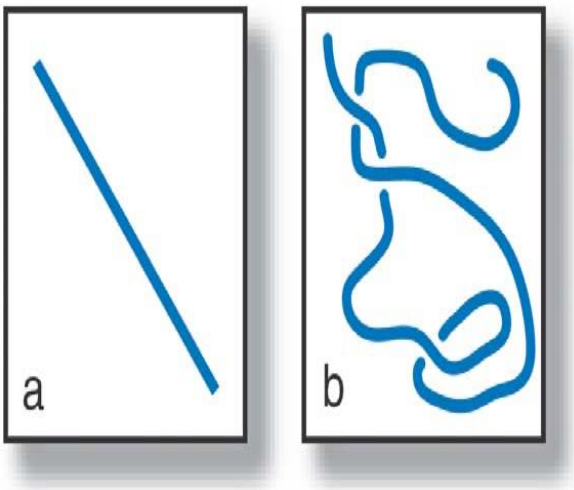
Statistical physics problem

Basic ideas (1930-60): Kuhn, Flory, Huggins, Stockmayer, James, Guth, Zimm, Rouse

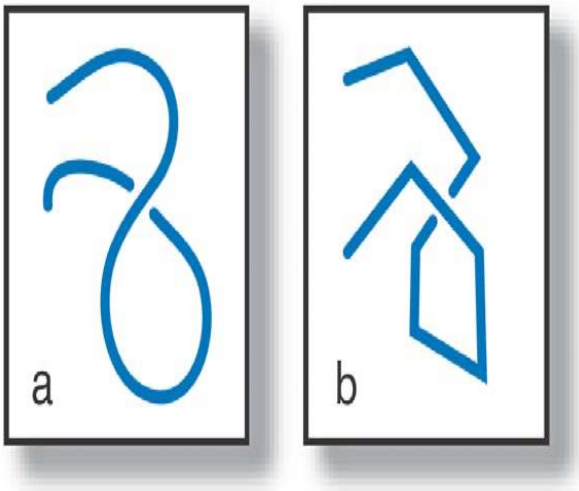
Correlations / entanglements (1960-90): Edwards, de Gennes, des Cloizeaux

Flexibility

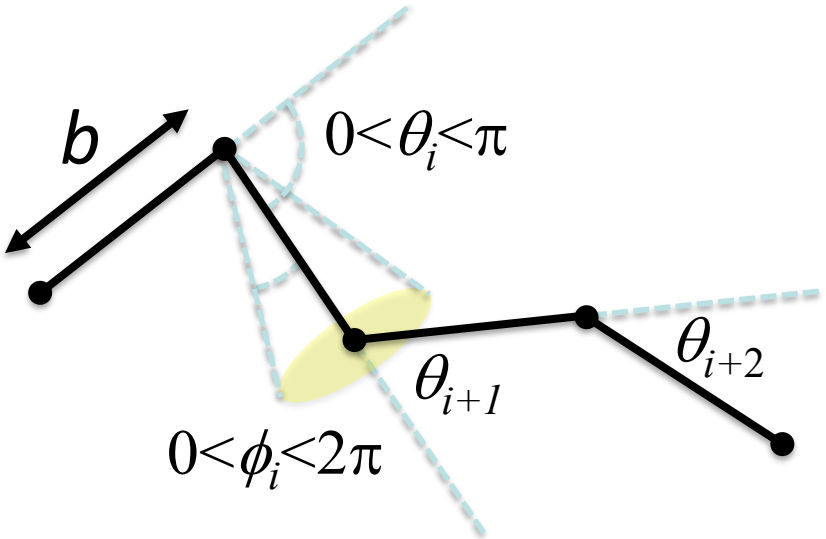
- Sufficiently long polymer is never straight

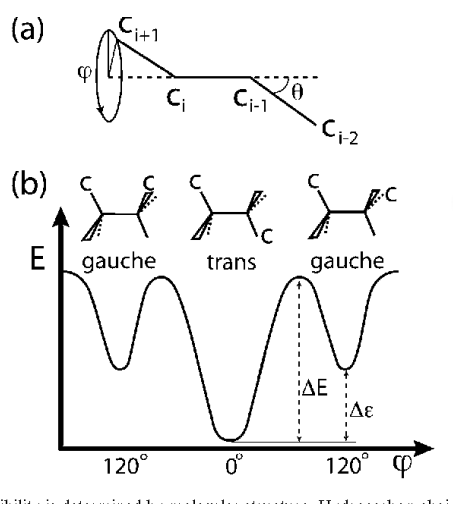


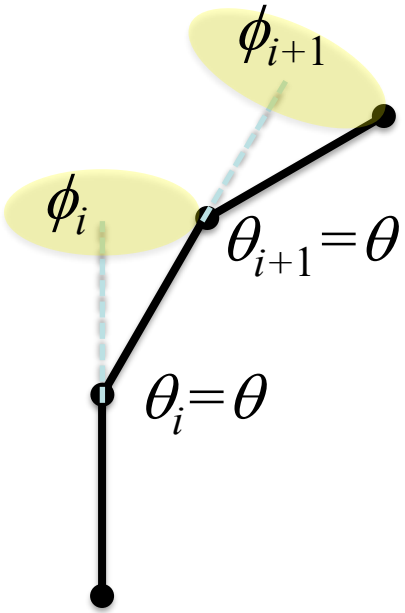
- Different polymers bend differently:



Physical models for ideal chains







> Freely-*jointed* chain: (θ_i, ϕ_i) unrestricted

$$\langle \vec{R}_{ee}^2 \rangle = b^2 N$$

$$\ell_K = b$$

$$\langle \vec{R}_{ee}^2 \rangle \equiv \ell_K L_c = \ell_K^2 \left(\frac{L_c}{\ell_K} \right) \equiv \ell_K^2 N_K$$

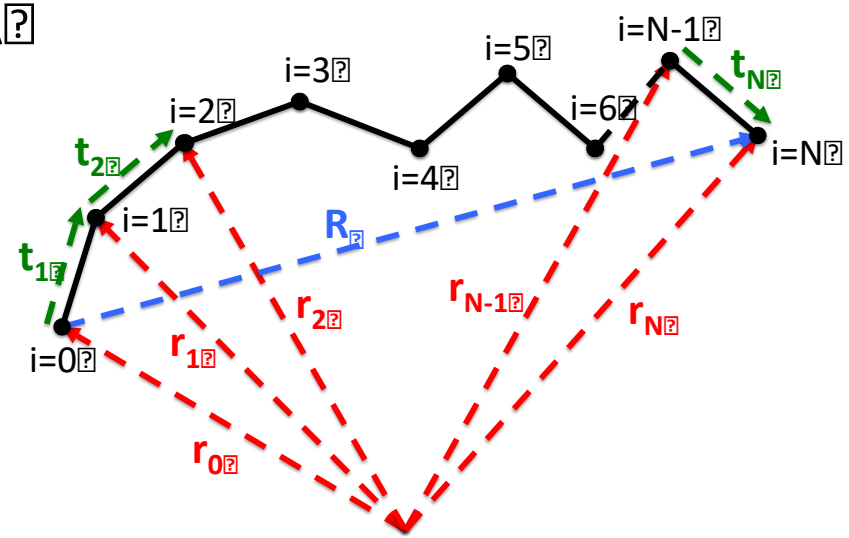
$$\ell_K = b \frac{1+\cos\theta}{1-\cos\theta}$$

$$\langle \vec{R}_{ee}^2 \rangle = b^2 \frac{1+\cos\theta}{1-\cos\theta} N$$

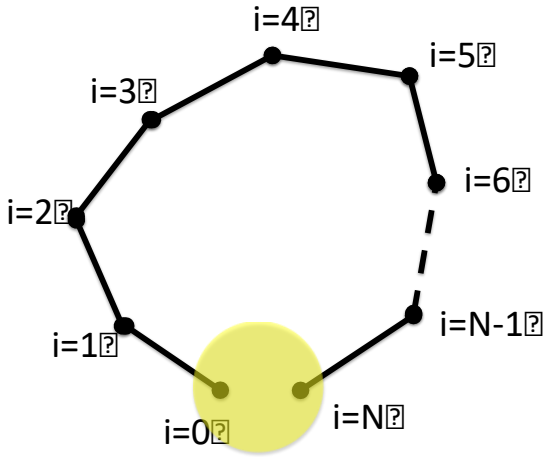
> Freely-*rotating* chain: ($\theta_i=\theta$, ϕ_i unrestricted)

Physical models for ideal chains

A



B



Relevant observables to characterise polymers:

1. Average-square end-to-end distance:
   $\langle R_{ee}^2 \rangle \equiv (\vec{r}_N - \vec{r}_0)^2$
2. Average-square gyration radius:
   $\langle R_g^2 \rangle \equiv \frac{1}{N+1} \left\langle \sum_{i=0}^{N} (\vec{r}_i - \vec{R}_{cm})^2 \right\rangle$, $\vec{R}_{cm} \equiv \frac{1}{N+1} \sum_{i=0}^{N} \vec{r}_i$
3. Average end-to-end contact probability:
   $\langle p_c(N) \rangle$

Physical models for ideal chains

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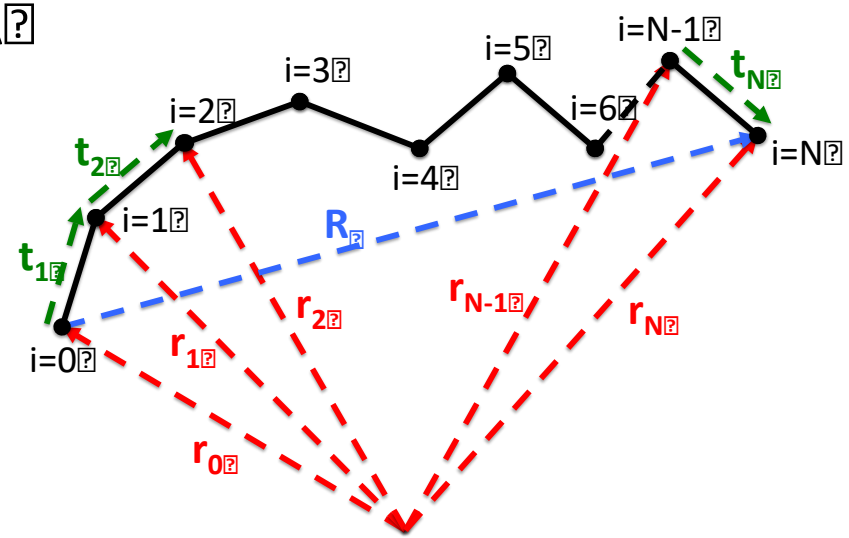

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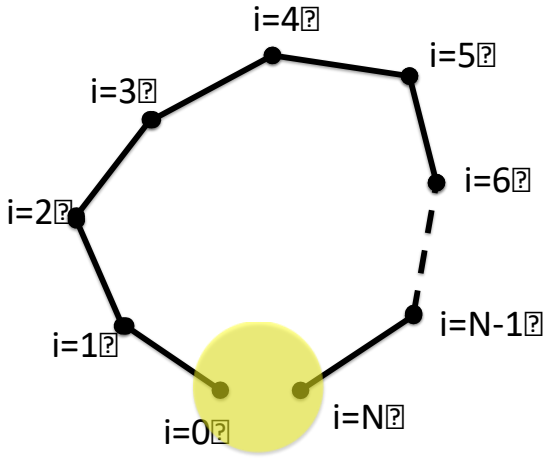
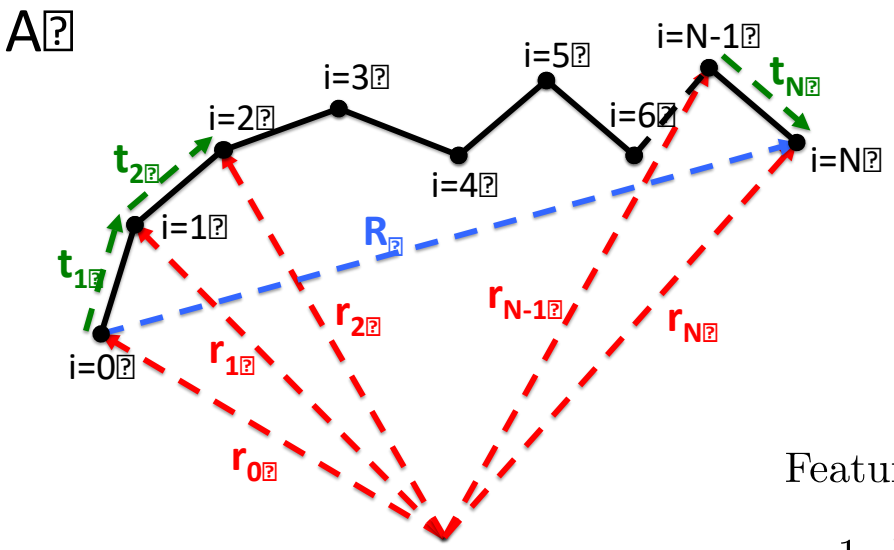


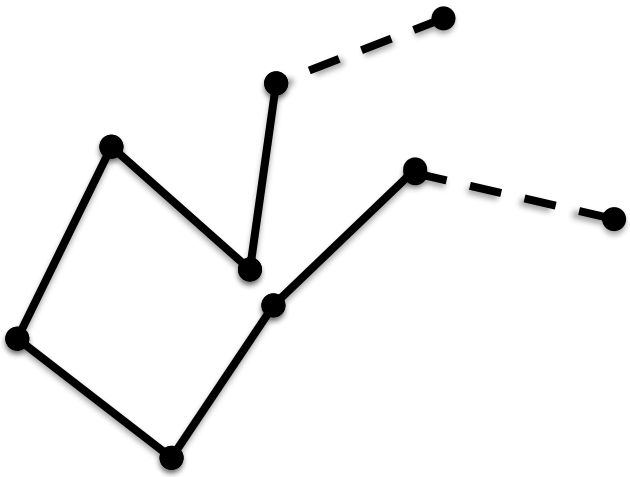
Scaling relationships:

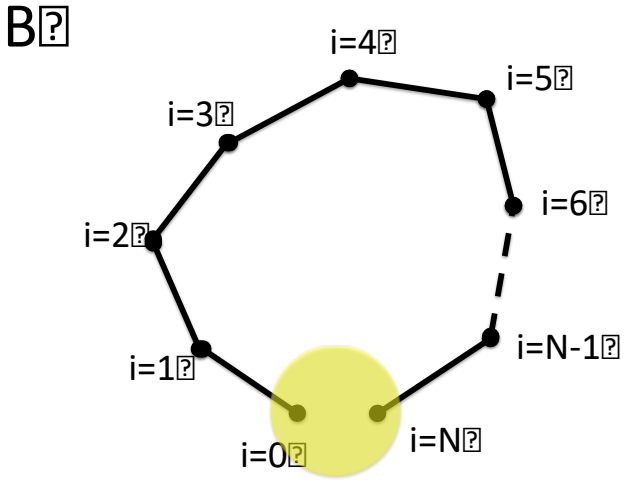
1. $\sqrt{\langle R_{ee}^2 \rangle} \sim \sqrt{\langle R_g^2 \rangle} \sim N^{\nu}$
2. $\langle p_c(N) \rangle \sim N^{-\gamma}$

ν and γ depend on the *universality class* of the chosen polymer model!!

Physical models for ideal chains



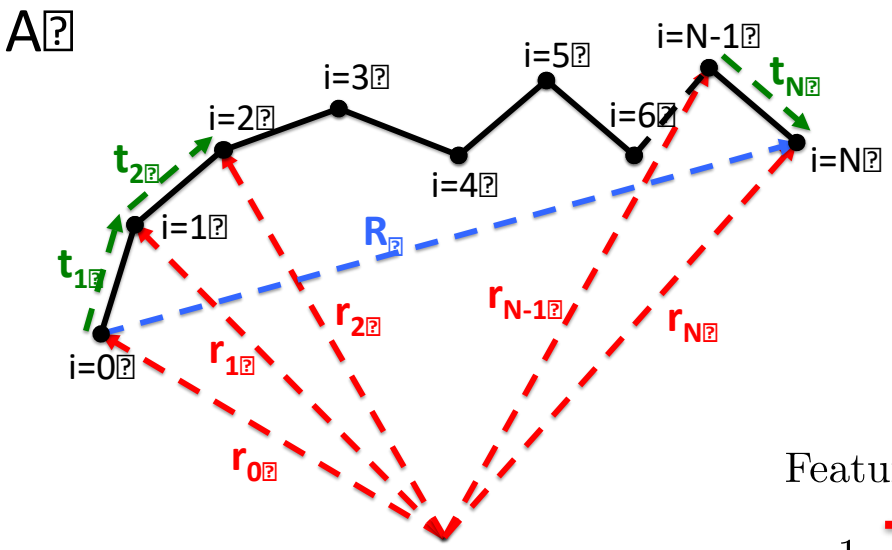


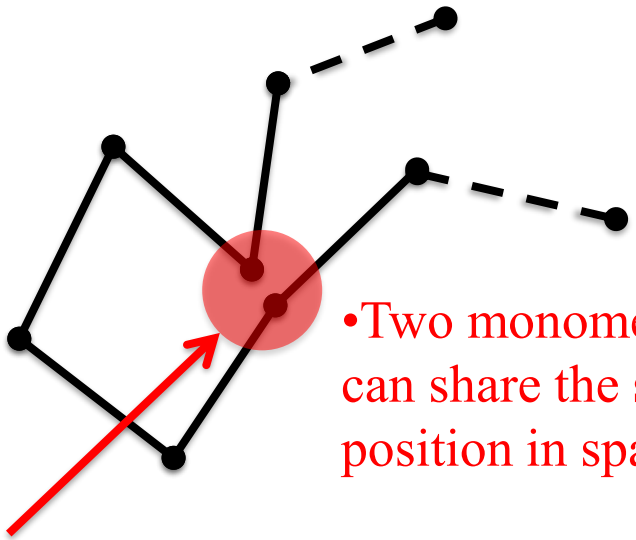


Features:

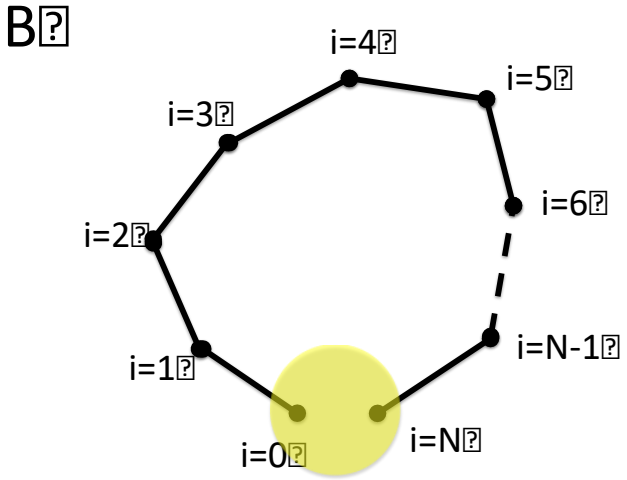
1. No excluded-volume interactions between monomers;
   Random orientations of the bonds;
   No *sequence* correlations for the bonds.
2. $\sqrt{\langle R_{ee}^2 \rangle} \sim \sqrt{\langle R_g^2 \rangle} \sim bN^{1/2} \rightarrow \nu = 1/2$
3. End-to-end distribution function is Gaussian:
   $p(\vec{R}_{ee} = \vec{R}) = \left(\frac{3}{2\pi N b^2}\right)^{3/2} e^{-\frac{3R^2}{2Nb^2}}$
4. $\langle p_c(N) \rangle \sim p(\vec{R}_{ee} = \vec{R} = 0) \sim N^{-3/2} \rightarrow \gamma = 3/2$

Physical models for ideal chains





•Two monomers can share the same position in space!



Features:

1. No excluded-volume interactions between monomers;
   Random orientations of the bonds;
   No *sequence* correlations for the bonds.

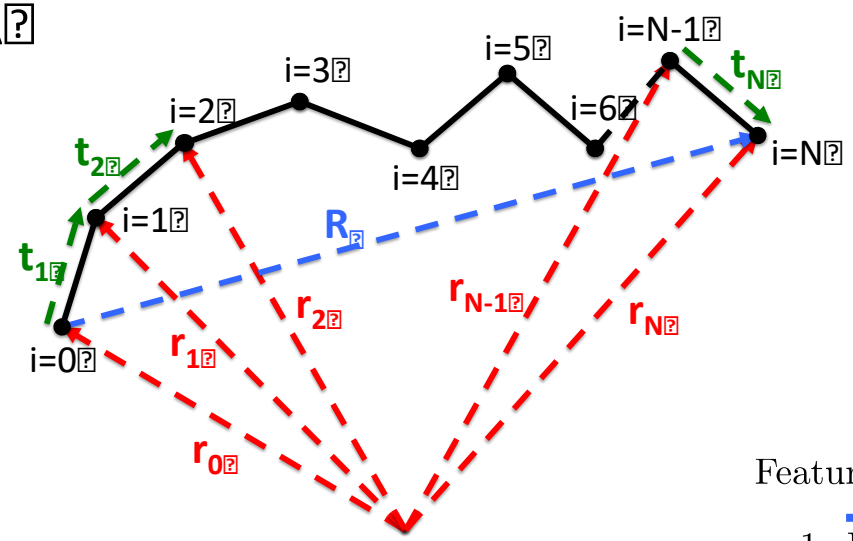
2. $\sqrt{\langle R_{ee}^2 \rangle} \sim \sqrt{\langle R_g^2 \rangle} \sim bN^{1/2} \rightarrow \nu = 1/2$

3. End-to-end distribution function is Gaussian:
   $p(\vec{R}_{ee} = \vec{R}) = \left(\frac{3}{2\pi N b^2}\right)^{3/2} e^{-\frac{3R^2}{2Nb^2}}$

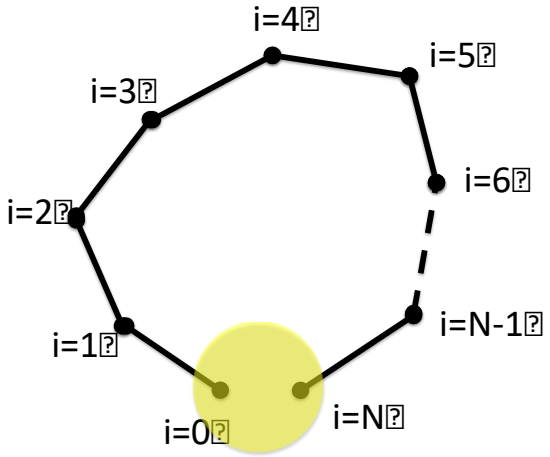
4. $\langle p_c(N) \rangle \sim p(\vec{R}_{ee} = \vec{R} = 0) \sim N^{-3/2} \rightarrow \gamma = 3/2$

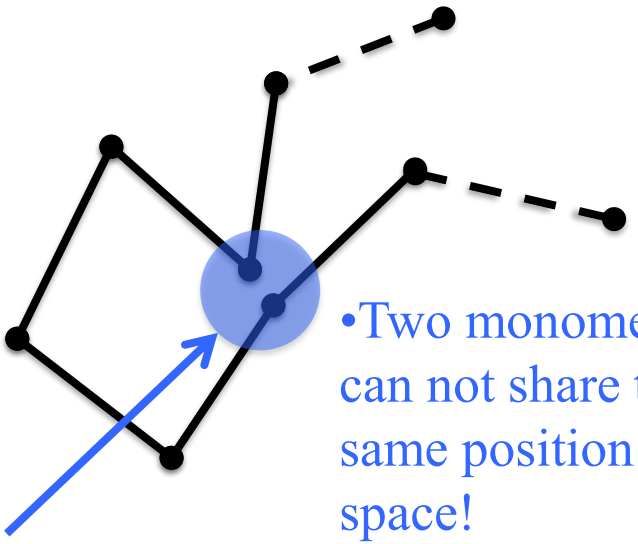
Physical models for real chains

A



B





- Two monomers can not share the same position in space!

Features:

1. Excluded-volume interactions between monomers;
   Random orientations of the bonds;
   No *sequence* correlations for the bonds.

2. $\sqrt{\langle R_{ee}^2 \rangle} \sim \sqrt{\langle R_g^2 \rangle} \sim bN^{3/5} \rightarrow \nu = 3/5 > 1/2$

3. End-to-end distribution function is not Gaussian
   $\rightarrow$ Redner-Des Cloizeaux function:
   $$p(\vec{R}_{ee} = \vec{R}) = C \left(\frac{R}{\sqrt{\langle R_{ee}^2 \rangle}} \right)^{3+\theta} \exp\left(- \left(K \frac{R}{\sqrt{\langle R_{ee}^2 \rangle}} \right)^t \right)$$
   $\theta \approx 0.27$ and $t \approx 2.45$

4. $\langle p_c(N) \rangle \sim p(\vec{R}_{ee} = \vec{R} = 0) \sim N^{-\nu(3+\theta)} \rightarrow \gamma = 3(\nu + \theta) \approx 2.58$
   i.e. much steeper than the prediction for the Gaussian chain

The problem of chromosome folding: topological effects

J. Phys. France **49** (1988) 2095-2100

The role of topological constraints in the kinetics of collapse of macromolecules

A. Yu. Grosberg (1), S. K. Nechaev (1) and E. I. Shakhnovich (2)

(1) Institute of Chemical Physics, U.S.S.R. Academy of Sciences, Moscow, U.S.S.R.
(2) Institute of Protein Research U.S.S.R. Academy of Sciences, Pouschino, Moscow Region, U.S.S.R.

Abstract. — It is shown that the kinetics of collapse of a polymer coil consisting of N segments after an abrupt decrease of temperature is a two-stage process if $N \gg N_c$. The first stage takes a time $\sim N^2$ and leads to the peculiar state — crumpled, or fractal, globule. Any part of a chain of any scale is itself a globule in this state ; these parts are segregated from each other in space due to the non-phantomness of a chain. The chain fold in the crumpled globule is a fractal line with fractal dimension 3, equal to the space dimension. The second stage is a chain knotting ; it is realized by means of reptation-like mechanism of motion, takes a time $\sim N^3$ and is accompanied by an increase of globule density.

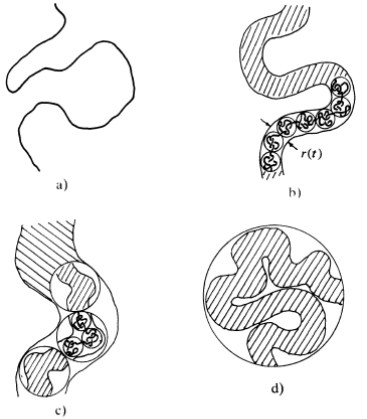


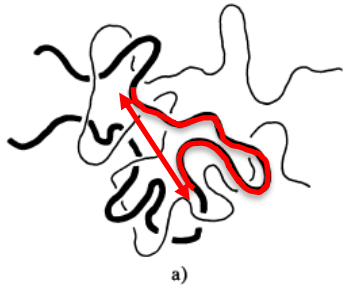
Fig. 1. — The sequential stages of collapse. (a) Initial state ; (b), (c) Intermediate stages ; (d) Final state — crumpled globule.

Europhys. Lett., **23** (5), pp. 373-378 (1993)

Crumpled Globule Model of the Three-Dimensional Structure of DNA.

A. Grosberg (*) (§), Y. Rabin (**), S. Havlin (**) and A. Neer (***)

Abstract. – We argue that in order to maintain the biological function of DNA confined inside the cell nucleus, its spatial structure has to be unknotted, of the so-called «crumpled globule» type. The fixation of a particular realization of this non-equilibrium structure by attractive interactions between specific units imposes a connection between the spatial structure of DNA and the statistical distribution of these units along the chain contour. This suggests that both primary sequence and spatial structure of native DNA were formed simultaneously by a self-similar evolution process. The predictions of our model are compared with recent observations of long-range correlations in intron-containing genes and non-transcribed regulatory elements and further experimental tests are proposed.



$$R(d;L) \sim \begin{cases} L^{1/2} \text{ (equilibrium globule)} \\ L^{1/d} \text{ (crumpled globule)} \end{cases}$$

Fig. 2. — (a) The interpenetration of two different parts of a chain in the crumpled globule ; (b) The chain plays role of an array of obstacles for its part denoted by thick line.

J. Dekker (UMass, USA)

Comprehensive Mapping of Long-Range Interactions Reveals Folding Principles of the Human Genome

Erez Lieberman-Aiden,[1,2,3,4]* Nynke L. van Berkum,[5]* Louise Williams,[1] Maxim Imakaev,[2] Tobias Ragoczy,[6,7] Agnes Telling,[6,7] Ido Amit,[1] Bryan R. Lajoie,[5] Peter J. Sabo,[8] Michael O. Dorschner,[8] Richard Sandstrom,[8] Bradley Bernstein,[1,9] M. A. Bender,[10] Mark Groudine,[6,7] Andreas Gnirke,[1] John Stamatoyannopoulos,[8] Leonid A. Mirny,[2,11] Eric S. Lander,[1,12,13]† Job Dekker[5]†

We describe Hi-C, a method that probes the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing. We constructed spatial proximity maps of the human genome with Hi-C at a resolution of 1 megabase. These maps confirm the presence of chromosome territories and the spatial proximity of small, gene-rich chromosomes. We identified an additional level of genome organization that is characterized by the spatial segregation of open and closed chromatin to form two genome-wide compartments. At the megabase scale, the chromatin conformation is consistent with a fractal globule, a knot-free, polymer conformation that enables maximally dense packing while preserving the ability to easily fold and unfold any genomic locus. The fractal globule is distinct from the more commonly used globular equilibrium model. Our results demonstrate the power of Hi-C to map the dynamic conformations of whole genomes.

The three-dimensional (3D) conformation of chromosomes is involved in compartmentalizing the nucleus and bringing widely separated functional elements into close spatial proximity (*1*–*5*). Understanding how chromosomes fold can provide insight into the complex relationships between chromatin structure, gene activity, and the functional state of the cell. Yet beyond the scale of nucleosomes, little is known about chromatin organization.

Long-range interactions between specific pairs of loci can be evaluated with chromosome conformation capture (3C), using spatially constrained ligation followed by locus-specific polymerase chain reaction (PCR) (*6*). Adaptations of 3C have extended the process with the use of inverse PCR (4C) (*7*, *8*) or multiplexed ligation-mediated amplification (5C) (*9*). Still, these techniques require choosing a set of target loci and do not allow unbiased genomewide analysis.

Here, we report a method called Hi-C that adapts the above approach to enable purification of ligation products followed by massively parallel sequencing. Hi-C allows unbiased identification of chromatin interactions across an entire genome. We briefly summarize the process: cells are crosslinked with formaldehyde; DNA is digested with a restriction enzyme that leaves a 5′ overhang; the 5′ overhang is filled, including a biotinylated residue; and the resulting blunt-end fragments are ligated under dilute conditions that favor ligation events between the cross-linked DNA fragments. The resulting DNA sample contains ligation products consisting of fragments that were originally in close spatial proximity in the nucleus, marked with biotin at the junction. A Hi-C library is created by shearing the DNA and selecting the biotin-containing fragments with streptavidin beads. The library is then analyzed by using massively parallel DNA sequencing, producing a catalog of interacting fragments (Fig. 1A) (*10*).

We created a Hi-C library from a karyotypically normal human lymphoblastoid cell line (GM06990) and sequenced it on two lanes of an Illumina Genome Analyzer (Illumina, San Diego, CA), generating 8.4 million read pairs that could be uniquely aligned to the human genome reference sequence; of these, 6.7 million corresponded to long-range contacts between segments >20 kb apart.

We constructed a genome-wide contact matrix M by dividing the genome into 1-Mb regions ("loci") and defining the matrix entry m_{ij} to be the number of ligation products between locus i and locus j (*10*). This matrix reflects an ensemble average of the interactions present in the original sample of cells; it can be visually represented as a heatmap, with intensity indicating contact frequency (Fig. 1B).

We tested whether Hi-C results were reproducible by repeating the experiment with the same restriction enzyme (HindIII) and with a different one (NcoI). We observed that contact matrices for these new libraries (Fig. 1, C and D) were extremely similar to the original contact matrix [Pearson's $r = 0.990$ (HindIII) and $r = 0.814$ (NcoI); P was negligible ($<10^{-300}$) in both cases]. We therefore combined the three data sets in subsequent analyses.

We first tested whether our data are consistent with known features of genome organization (*1*): specifically, chromosome territories (the tendency of distant loci on the same chromosome to be near one another in space) and patterns in submuclear positioning (the tendency of certain chromosome pairs to be near one another).

We calculated the average intrachromosomal contact probability, $I_n(s)$, for pairs of loci separated by a genomic distance s (distance in base pairs along the nucleotide sequence) on chromosome n. $I_n(s)$ decreases monotonically on every chromosome, suggesting polymer-like behavior in which the 3D distance between loci increases with increasing genomic distance; these findings are in agreement with 3C and fluorescence in situ hybridization (FISH) (*6*, *11*). Even at distances greater than 200 Mb, $I_n(s)$ is always much greater than the average contact probability between different chromosomes (Fig. 2A). This implies the existence of chromosome territories.

Interchromosomal contact probabilities between pairs of chromosomes (Fig. 2B) show that small, gene-rich chromosomes (chromosomes 16, 17, 19, 20, 21, and 22) preferentially interact with each other. This is consistent with FISH studies showing that these chromosomes frequently colocalize in the center of the nucleus

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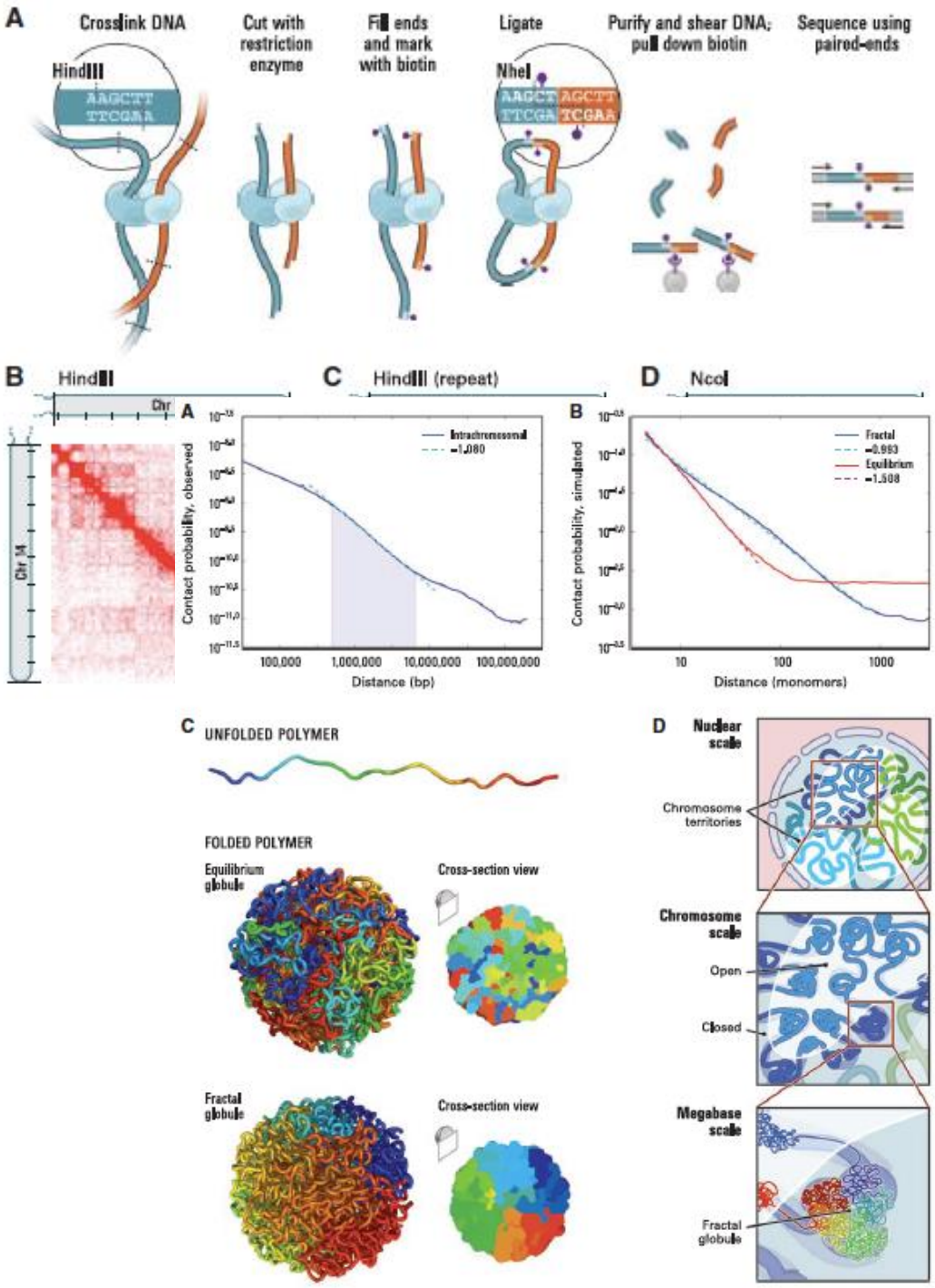
*These authors contributed equally to this work.
†To whom correspondence should be addressed. E-mail: lander@broadinstitute.org (E.S.L.); job.dekker@umassmed.edu (J.D.)

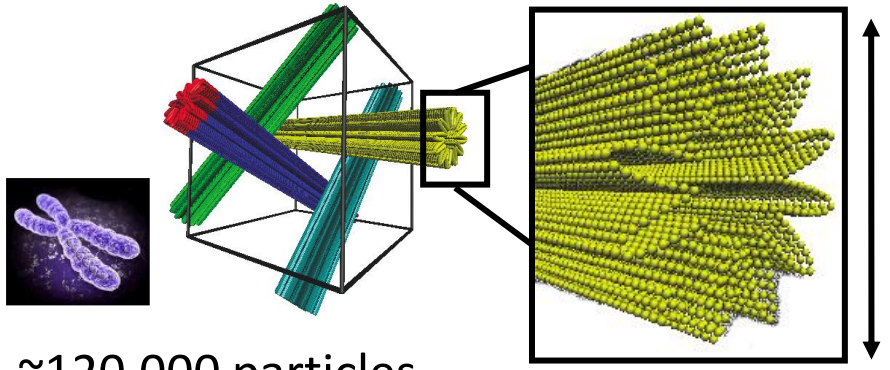


Structure and Dynamics of Interphase Chromosomes

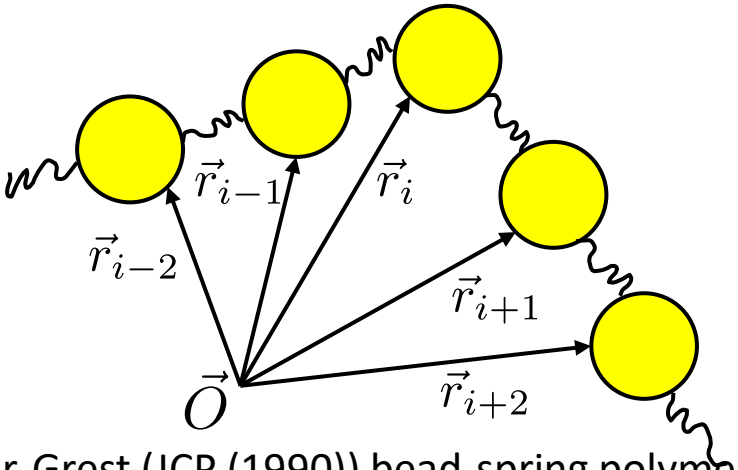
Angelo Rosa[1,2]*, Ralf Everaers[1,3]
PLoS Computational Biology | www.ploscompbiol.org 1 August 2008 | Volume 4 | Issue 8 | e1000153

Looping Probabilities in Model Interphase Chromosomes

Angelo Rosa,[†*] Nils B. Becker,[‡] and Ralf Everaers[‡]
Biophysical Journal Volume 98 June 2010 2410–2419



~120,000 particles



Brownian Dynamics computer simulations of a generic Kremer-Grest (JCP (1990)) bead-spring polymer model:

$$m\,\ddot{\vec{r}}_i(t) = -\gamma\,\dot{\vec{r}}_i(t) - \nabla_{\vec{r}_i} V(\ldots, \vec{r}_{i-1}, \vec{r}_i, \vec{r}_{i+1}, \ldots) + \vec{\eta}_i(t)$$

$$\langle \vec{\eta}_i(t) \rangle = 0$$

$$\langle \vec{\eta}_i(t) \cdot \vec{\eta}_j(t') \rangle = 6\,\kappa_B T\,\gamma\,\delta_{ij}\,\delta(t-t')$$

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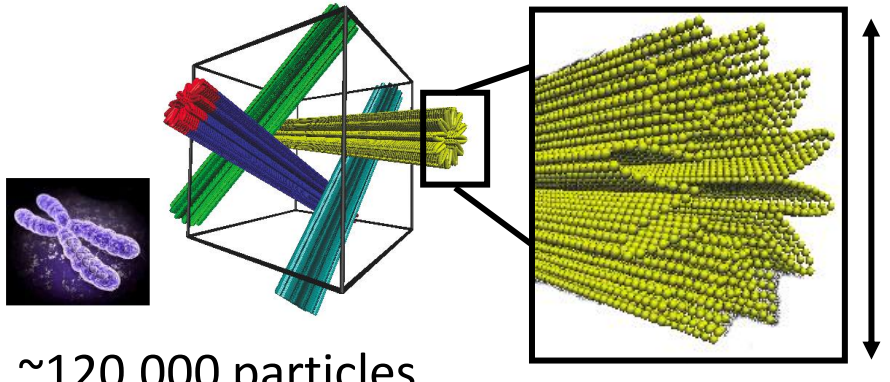
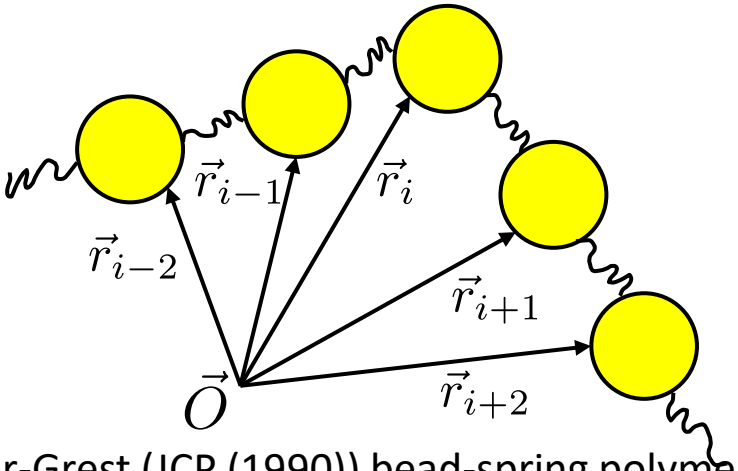


~120,000 particles



Brownian Dynamics computer simulations of a generic Kremer-Grest (JCP (1990)) bead-spring polymer model:

1) Chain connectivity =>
$$V_{\rm FENE}(\vec{r}_i,\vec{r}_{i+1}) = -\frac{1}{2}\kappa_{\rm FENE}\,R_0^2\,\ln\left[1-\left(\frac{|\vec{r}_{i+1}-\vec{r}_i|}{R_0}\right)^2\right]\Theta\left(1-\frac{|\vec{r}_{i+1}-\vec{r}_i|}{R_0}\right)+V_{\rm hc}(\vec{r}_i,\vec{r}_{i+1})$$

2) Chromatin stiffness =>
$$V_{\rm bend}(\vec{r}_{i-1},\vec{r}_i,\vec{r}_{i+1}) = -\kappa_\theta\,\frac{\vec{r}_{i+1}-\vec{r}_i}{|\vec{r}_{i+1}-\vec{r}_i|}\cdot\frac{\vec{r}_i-\vec{r}_{i-1}}{|\vec{r}_i-\vec{r}_{i-1}|}$$

3) “Natural” DNA/chromatin density =>
$$\rho_{\rm DNA}\approx 0.012\,{\rm bp/nm^3}$$

4) Hard-core repulsion between monomers =>
$$V_{\rm hc}(\vec{r}_i,\vec{r}_j) = 4\epsilon\left[\left(\frac{\sigma}{|\vec{r}_i-\vec{r}_j|}\right)^{12}-\left(\frac{\sigma}{|\vec{r}_i-\vec{r}_j|}\right)^{6}\right]\Theta\left(1-\frac{|\vec{r}_i-\vec{r}_j|}{2^{1/6}\sigma}\right)$$

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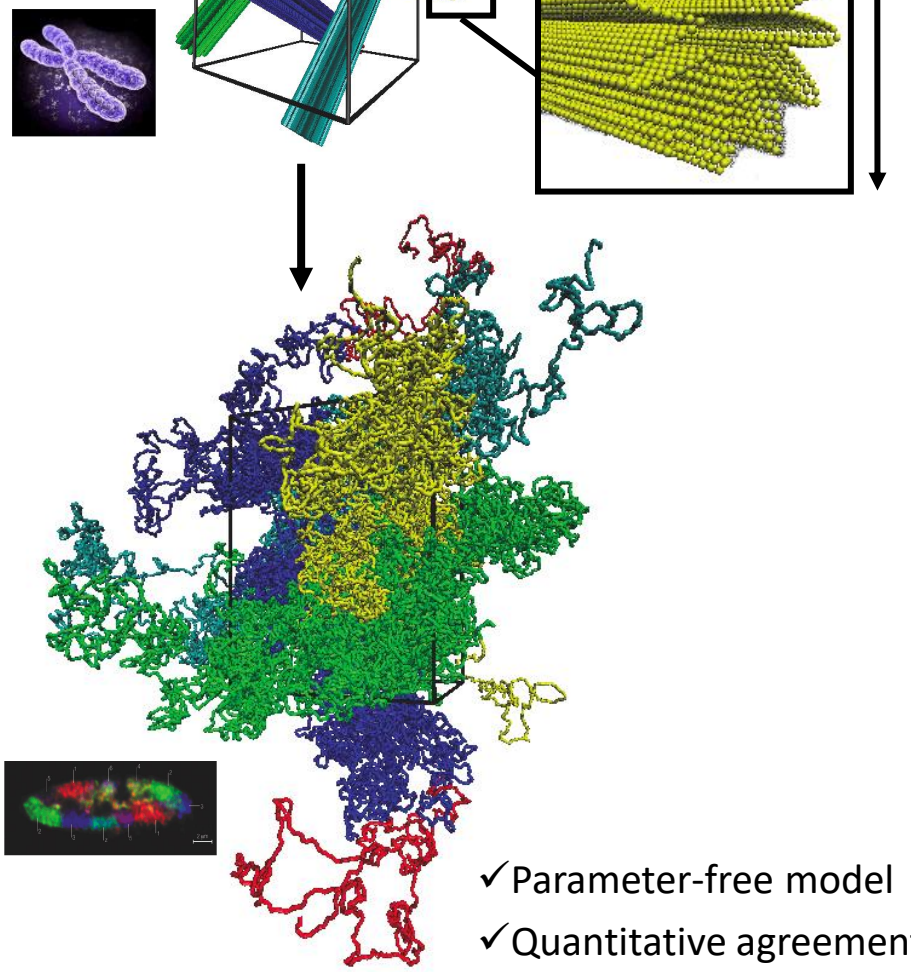
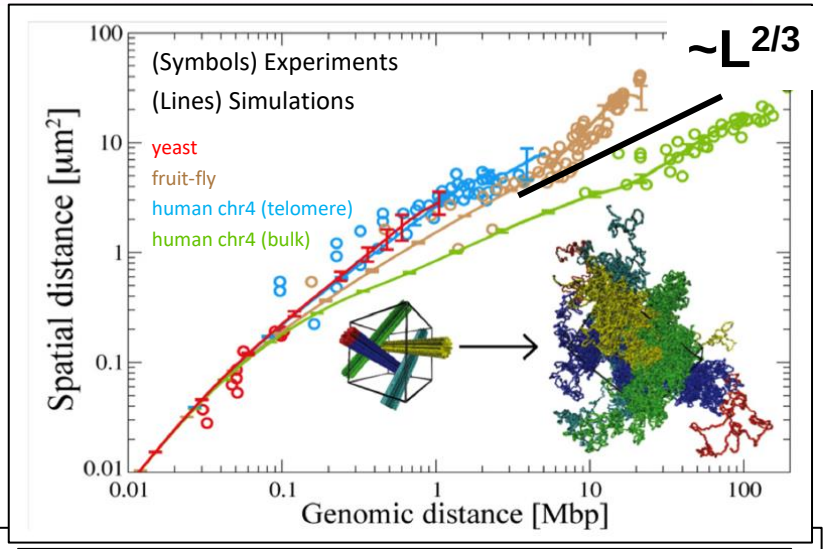
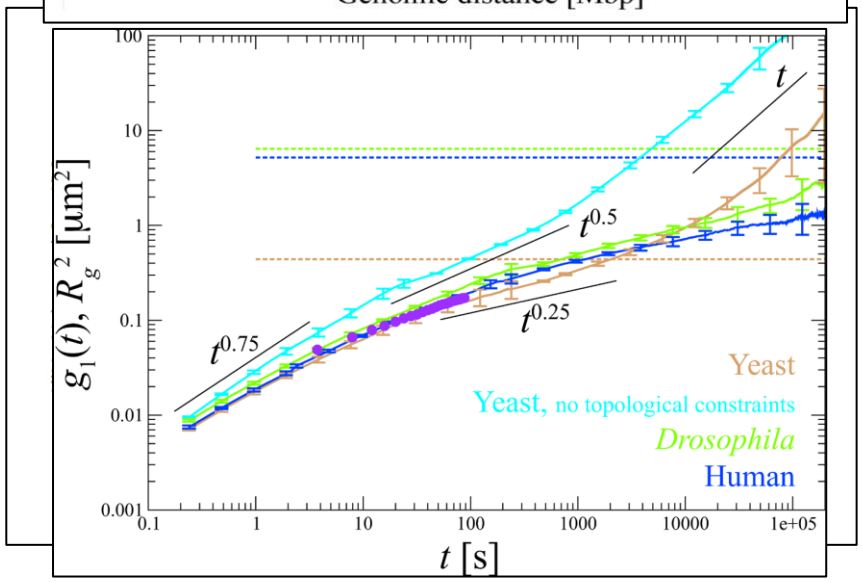


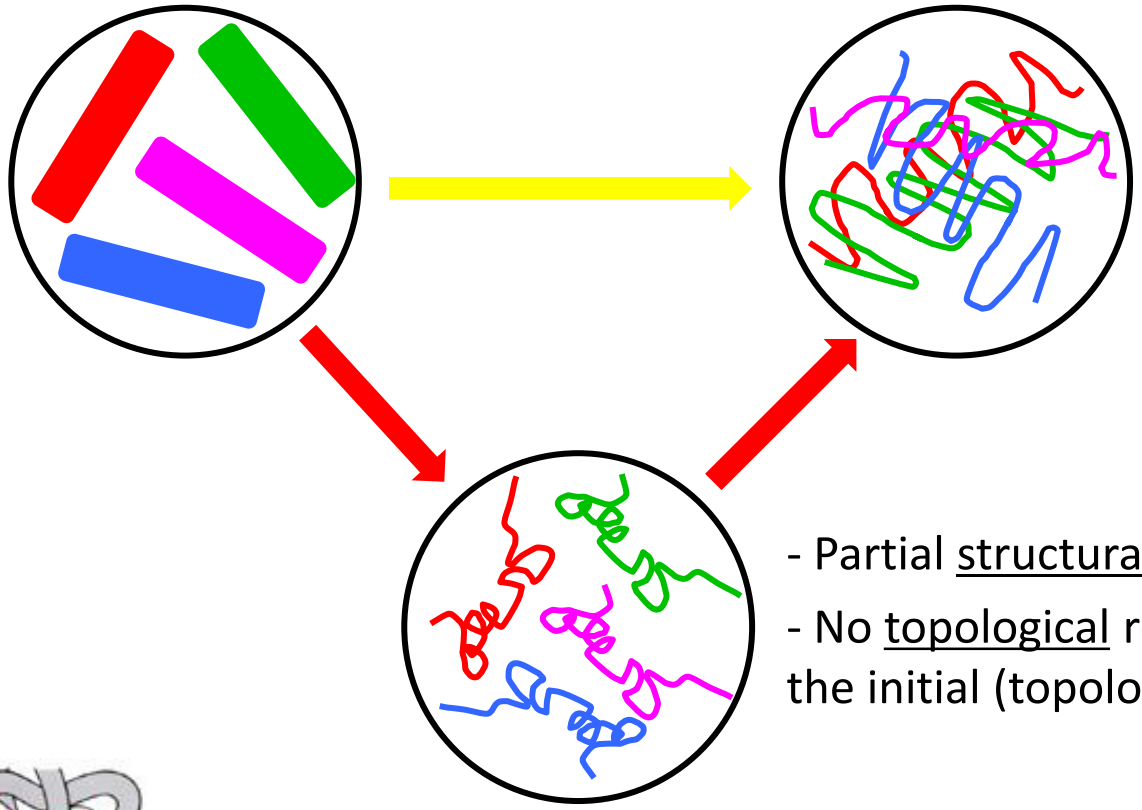




✓Parameter-free model

✓Quantitative agreement with FISH and HiC experimental data

Do chromosomes behave like equilibrated *linear* polymers?



- Partial structural relaxation
- No topological relaxation → Memory of the initial (topological) state, preserved!!

$$\tau_{\mathrm{mix}} = \tau_{\mathrm{relax}} = \tau_e \left(\frac{L_{\mathrm{chain}}}{L_e} \right)^3$$

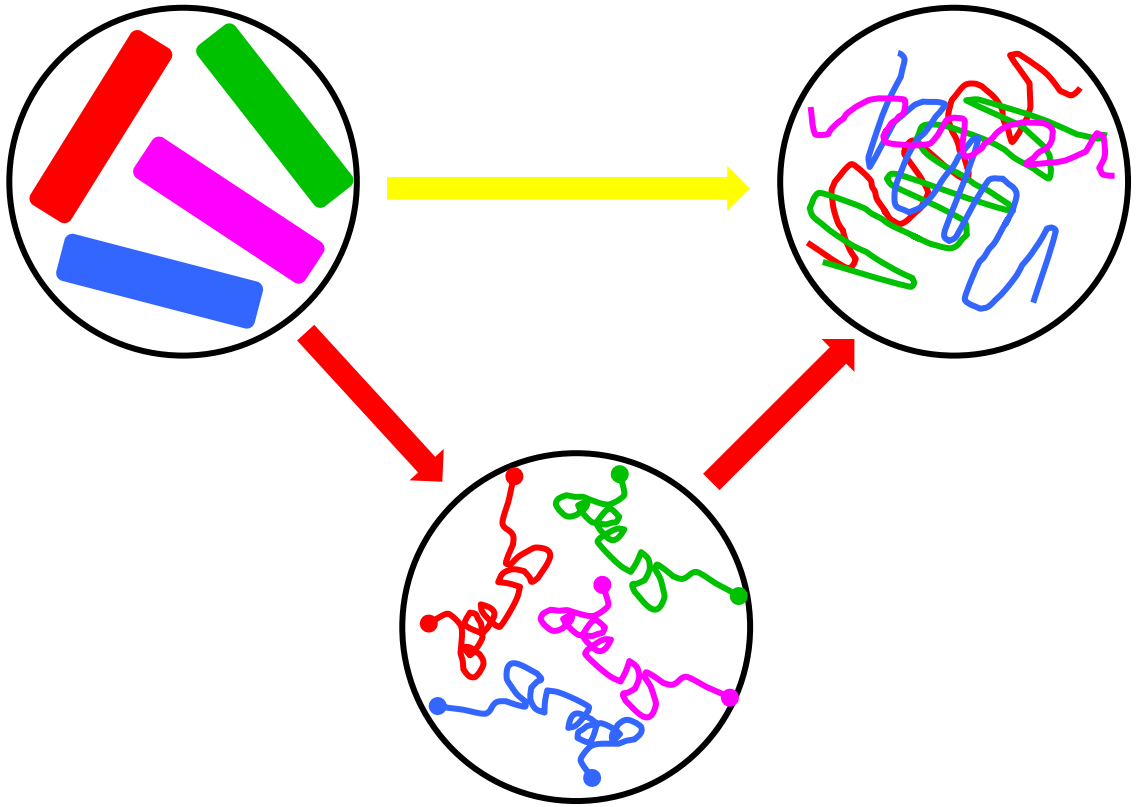
De Gennes, J Chem Phys (1971)

Doi & Edwards, The Theory of Polymer Dynamics

Species	Chromos. length, L_{chain}	Mixing time, t_{mix}
S. cerevisiae	≈ 1Mbp	≈ 1hrs
D. melanogaster	≈ 10Mbp	≈ 1years
H. sapiens	≈ 100Mbp	≈ 100years

AR & Everaers, PLoS Comput Biol (2008)

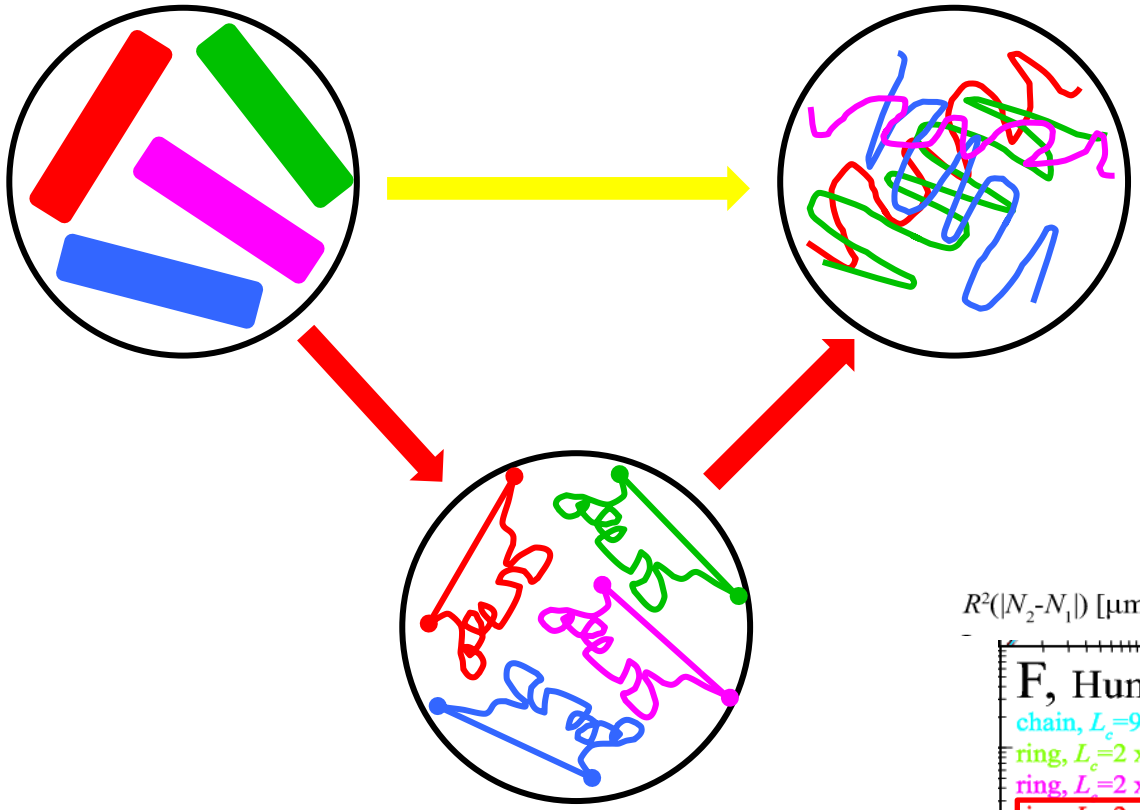
Do chromosomes behave like equilibrated *linear* polymers?

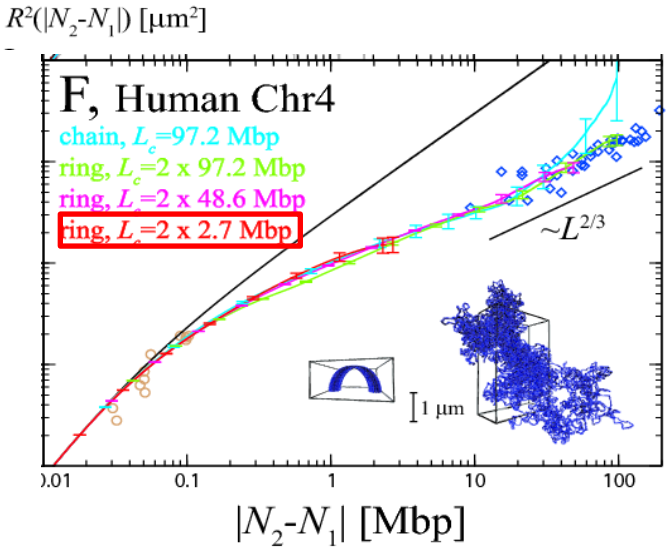


The motion of **chain ends** is irrelevant for the relaxation dynamics in the bulk of a (long) linear chain

AR & Everaers, PLoS Comput Biol (2008)

Do chromosomes behave like equilibrated *linear* polymers?



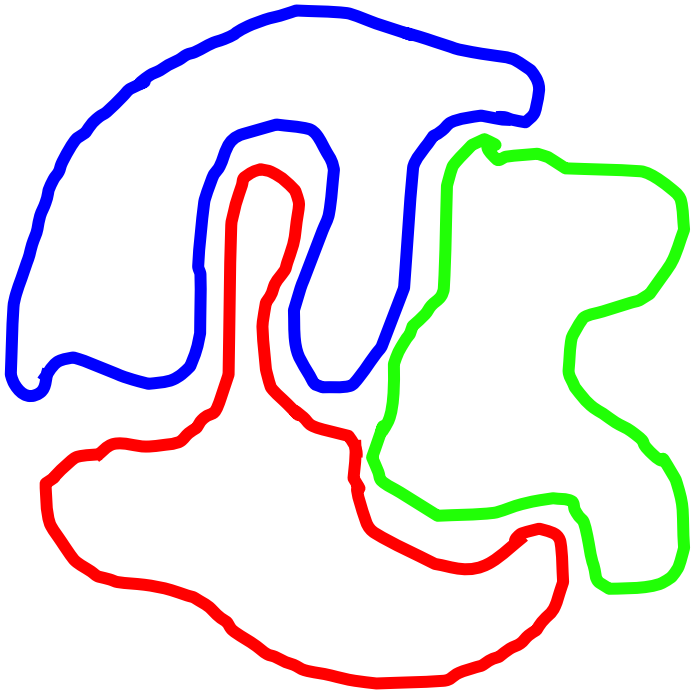


The motion of **chain ends** is irrelevant for the relaxation dynamics in the bulk of a (long) linear chain

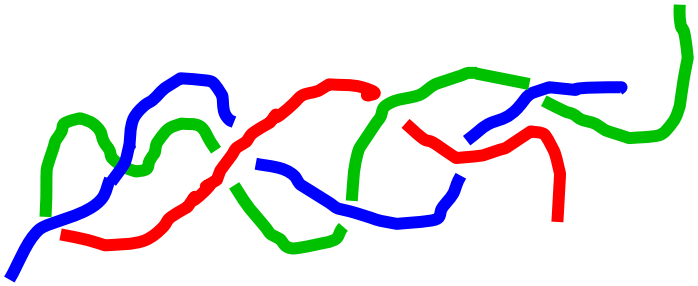
Same bulk behavior for (unknotted & non-concatenated) ring polymers and linear chains!

AR & Everaers, PLoS Comput Biol (2008)

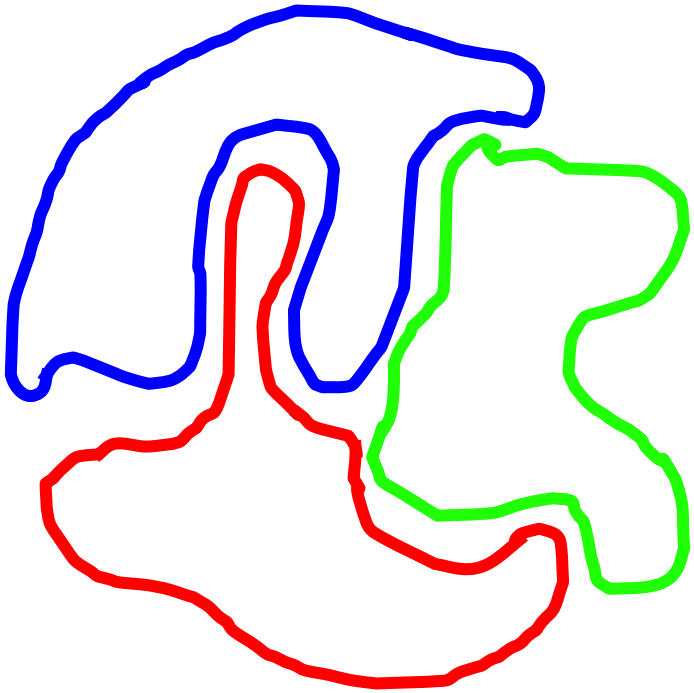
Melt of rings



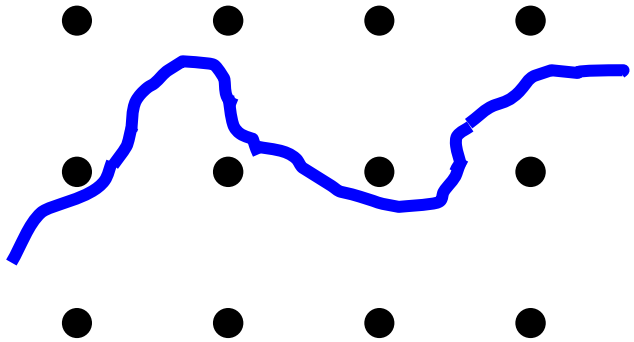
Melt of linear chains



Melt of rings



Melt of linear chains



$$R \sim N^{1/2}$$

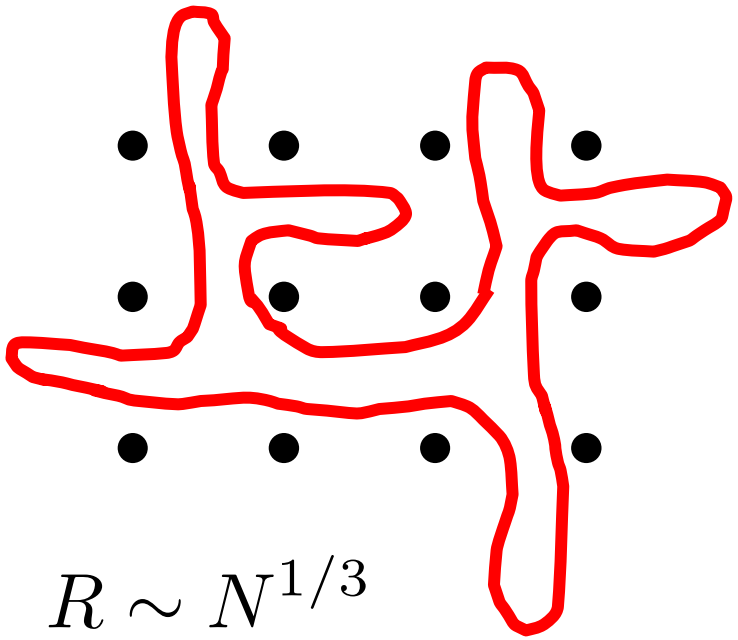
$$\tau_{eq} \sim N^{3}$$

THE JOURNAL OF CHEMICAL PHYSICS VOLUME 55, NUMBER 2 15 JULY 1971

Reptation of a Polymer Chain in the Presence of Fixed Obstacles

P. G. DE GENNES
Laboratoire de Physique des Solides, Faculté des Sciences, 91—Orsay, France
(Received 18 January 1971)

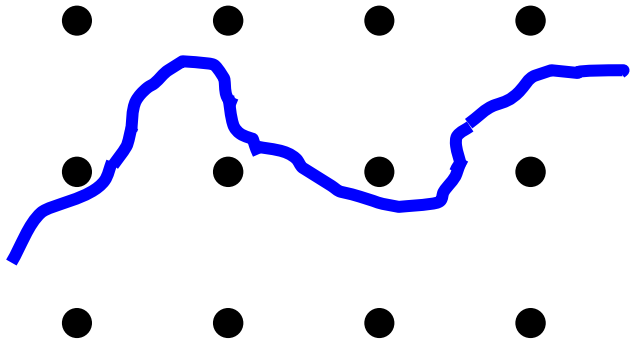
Melt of rings



$$R \sim N^{1/3}$$

$$\tau_{eq} \sim N^{2.5-2.6}$$

Melt of linear chains



$$R \sim N^{1/2}$$

$$\tau_{eq} \sim N^{3}$$

POLYMER CHAIN IN AN ARRAY OF OBSTACLES

A.R. KHOKHLOV and S.K. NECHAEV

Physics Department, Moscow State University, Moscow 119899, USSR

Physics Letters (1985)

THE JOURNAL OF CHEMICAL PHYSICS VOLUME 55, NUMBER 2 15 JULY 1971

Reptation of a Polymer Chain in the Presence of Fixed Obstacles

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VOLUME 57, NUMBER 24 PHYSICAL REVIEW LETTERS 15 DECEMBER 1986

Dynamics of Ring Polymers in the Presence of Fixed Obstacles

Michael Rubinstein

Corporate Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

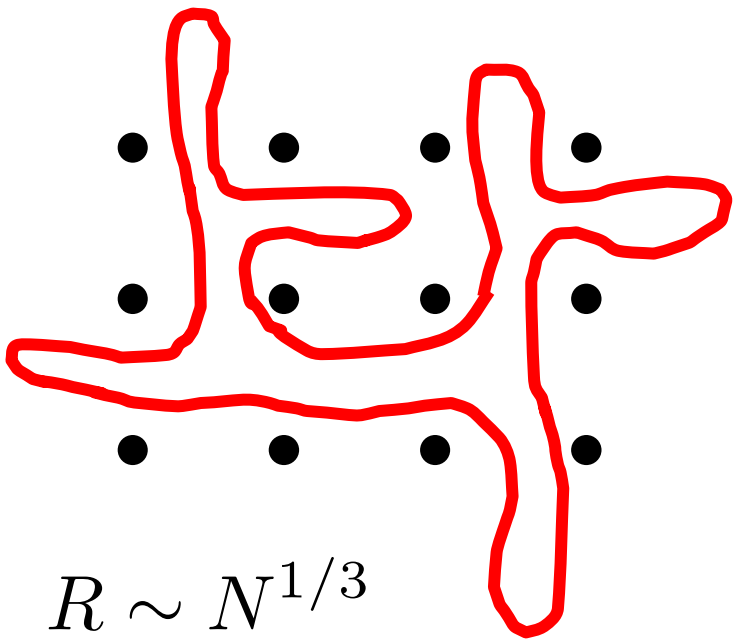
(Received 18 November 1985)

Grosberg, Soft Matter (2014)

Smrek & Grosberg, J. Phys.: Condens. Matter (2015)

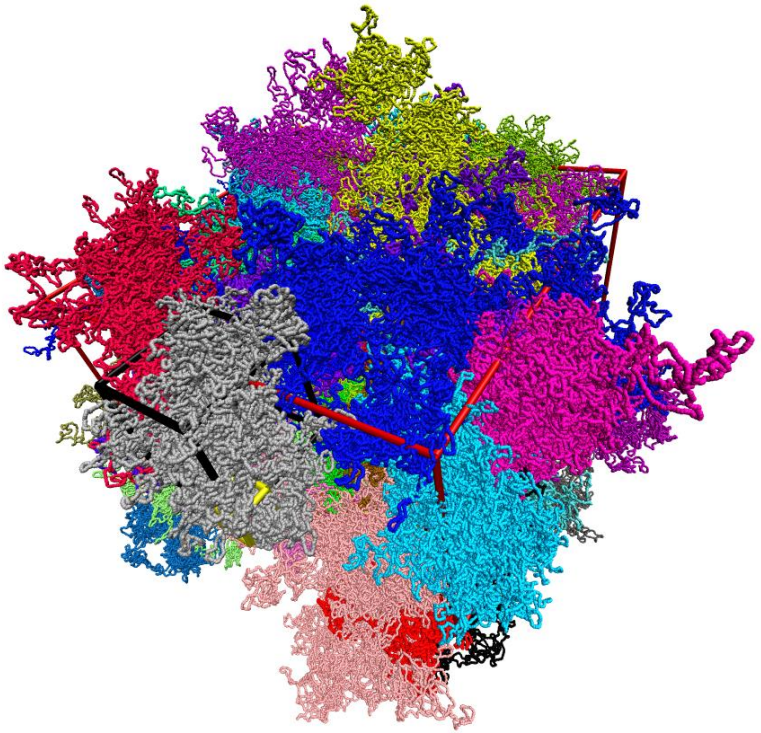
Everaers, Grosberg, Rubinstein, AR, Soft Matter (2017)

Melt of rings



$$R \sim N^{1/3}$$

$$\tau_{eq} \sim N^{2.5-2.6}$$



POLYMER CHAIN IN AN ARRAY OF OBSTACLES

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Physics Department, Moscow State University, Moscow 119899, USSR

Physics Letters (1985)

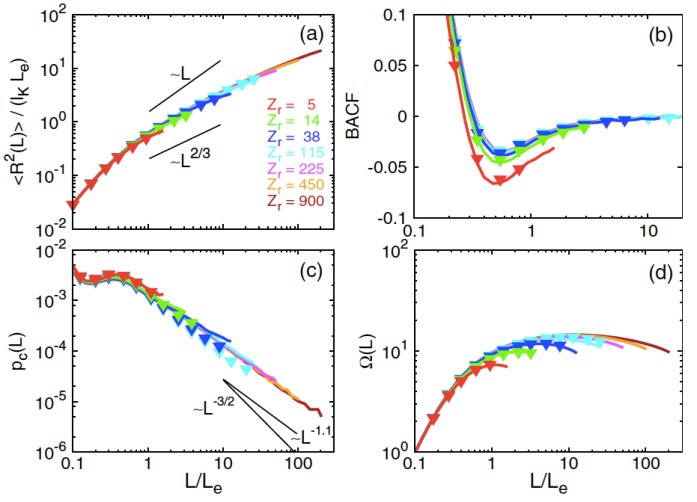
VOLUME 57, NUMBER 24 PHYSICAL REVIEW LETTERS 15 DECEMBER 1986

Dynamics of Ring Polymers in the Presence of Fixed Obstacles

Michael Rubinstein

Corporate Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

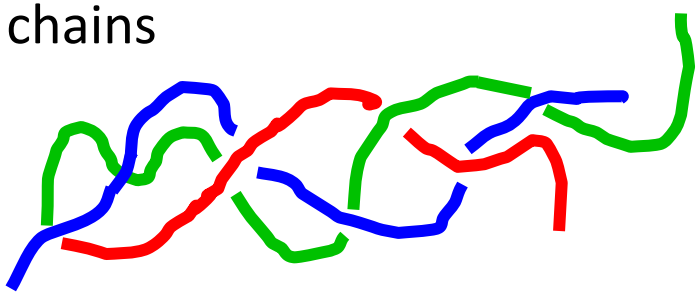
(Received 18 November 1985)



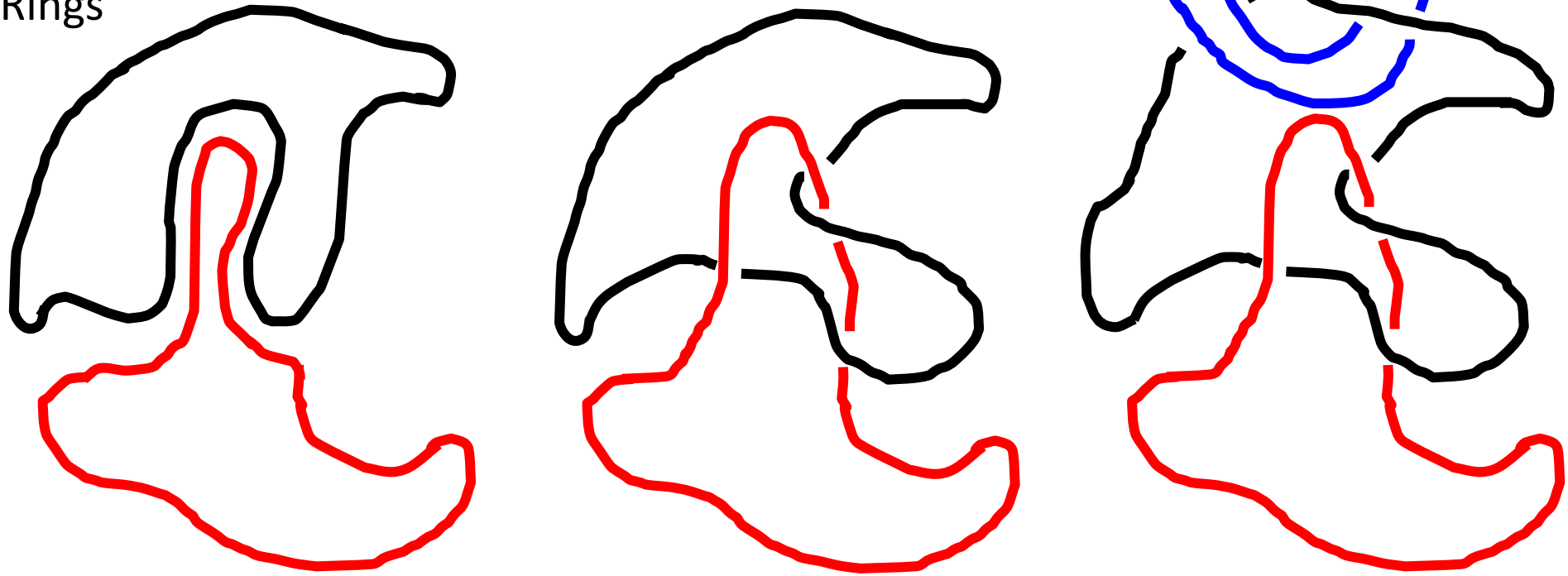
AR & Everaers, PRL (2014)

Open loops & threadings

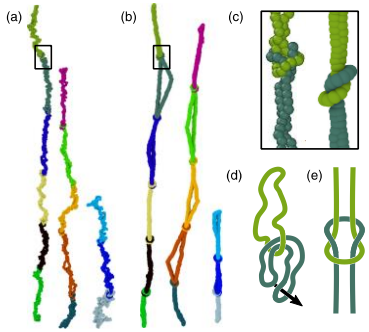
Linear chains



Rings

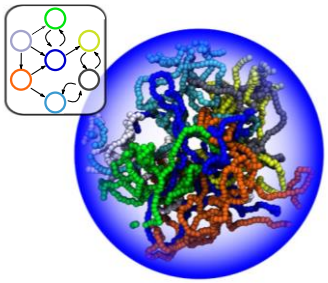


Open loops & threadings



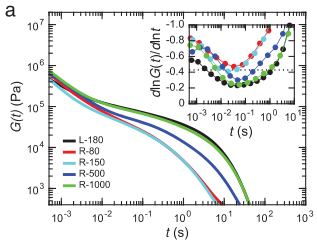
Rings in elongational flows

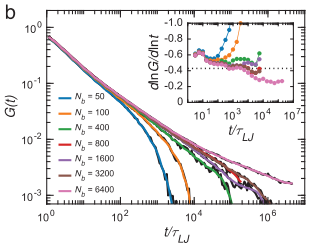
O'Connor et al., PRL (2020)



Topological glass

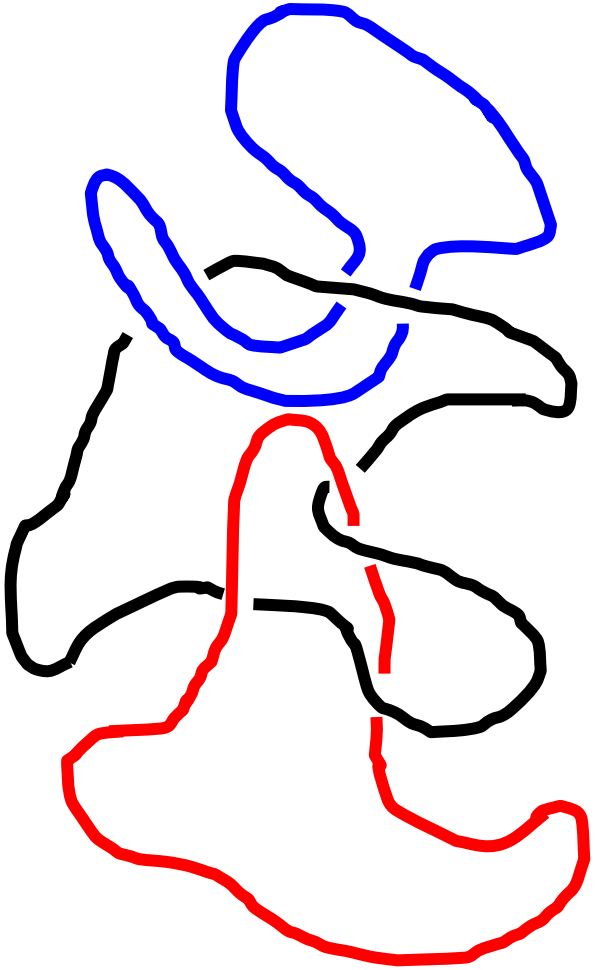
Michieletto & Turner, PNAS (2016)



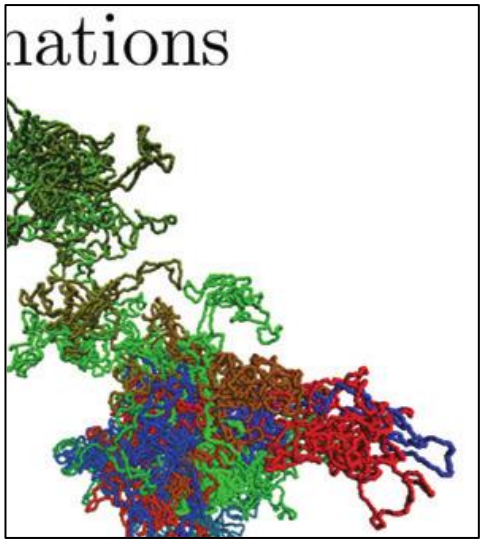


Slow relaxational dynamics

Tu et al., ACS Polymers Au (2023)



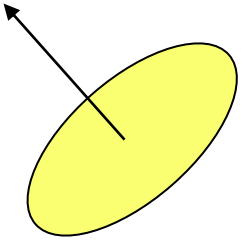
How do we quantify threadings?



Analogy to electrodynamics:

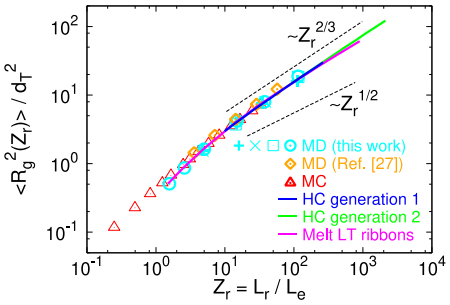
$$\vec{m} \equiv I\vec{A} = I\,\frac{1}{2}\int \vec{r}\times d\vec{r}$$

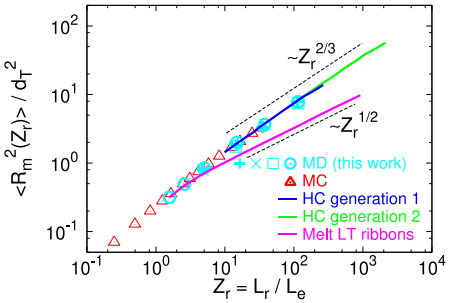
$$R_m^2 = \frac{1}{\pi}|\vec{A}|$$

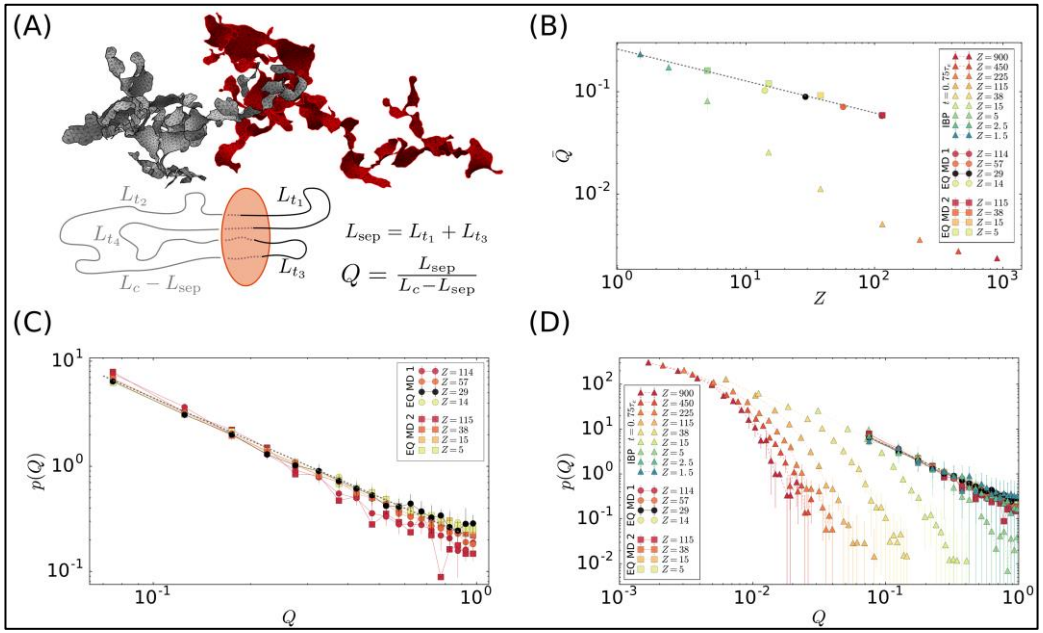


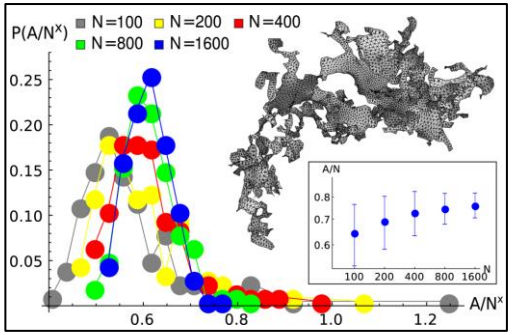
Schram, AR & Everaers

Soft Matter (2019)









Smrek & Grosberg

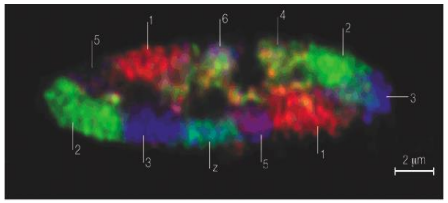
ACS Macro Letters (2016)

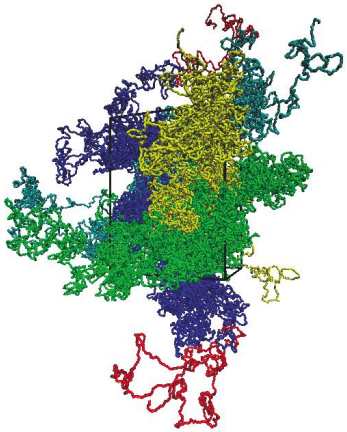
Smrek, Kremer & AR

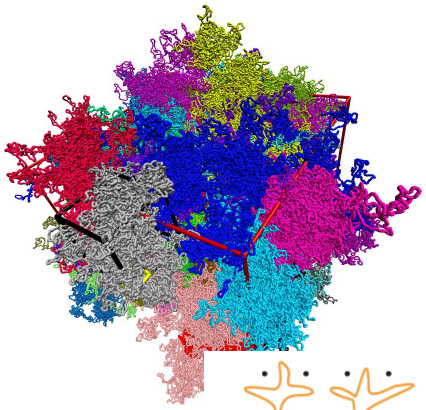
ACS Macro Letters (2019)

In a slide…

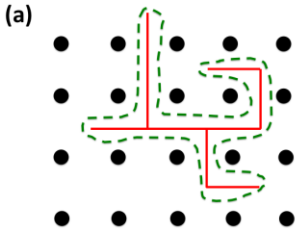
AR & Everaers, PlosCB (2008)
AR, Becker & Everaers, Biophys J (2010)
Di Stefano, AR, Belcastro, di Bernardo, Micheletti, PlosCB (2013)
Florescu, Thérizols & AR, PlosCB (2016)

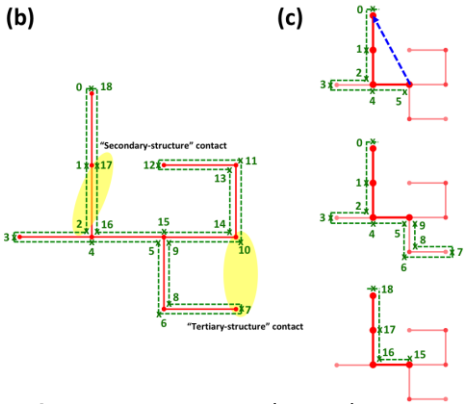




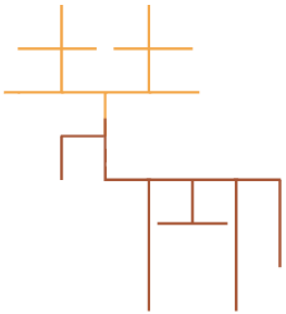


AR & Everaers, PRL (2014)
Michieletto, Nahali & AR, PRL (2017)
Nahali & AR, JCP (2018)
Smrek, Kremer & AR, ACS ML (2019)
Schram, AR & Everaers, Soft Matter (2019)
Ubertini, Smrek & AR, Macromolecules (2022)





AR & Everaers, JPhysA (2016)
AR & Everaers, JCP (2016)
AR & Everaers, PRE (2017)
Everaers et al., Soft Matter (2017)



AR & Everaers, EPJE (2019)

Credits

Chromosomes & rings

Ralf Everaers (ENS-Lyon, France)

Electrodynamics & enclosed surfaces of rings

Raoul D. Schram (ENS-Lyon, France)

Minimal surfaces

Jan Smrek (Uni-Vienna, Austria)

Kurt Kremer (MPI-Mainz, Germany)

HPC resources: PSMN (ENS-Lyon, FR); P2CHPD (UCB, Lyon 1, FR); CINECA (Bologna, IT); SISSA-cluster (Trieste, Italy)

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Thank you!