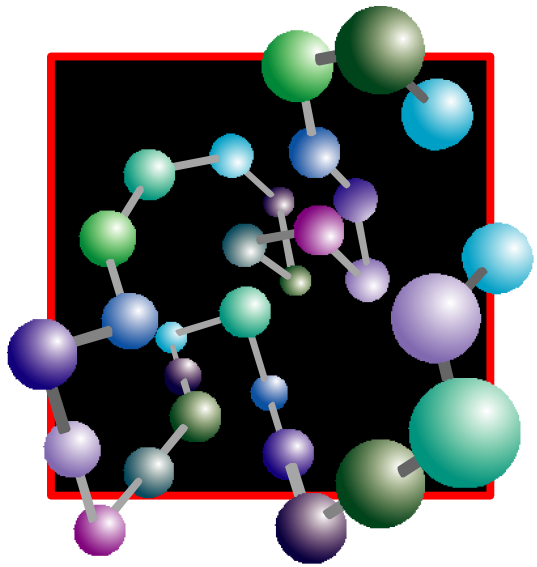
Introduction to polymer physics
Lecture 5: Biopolymers

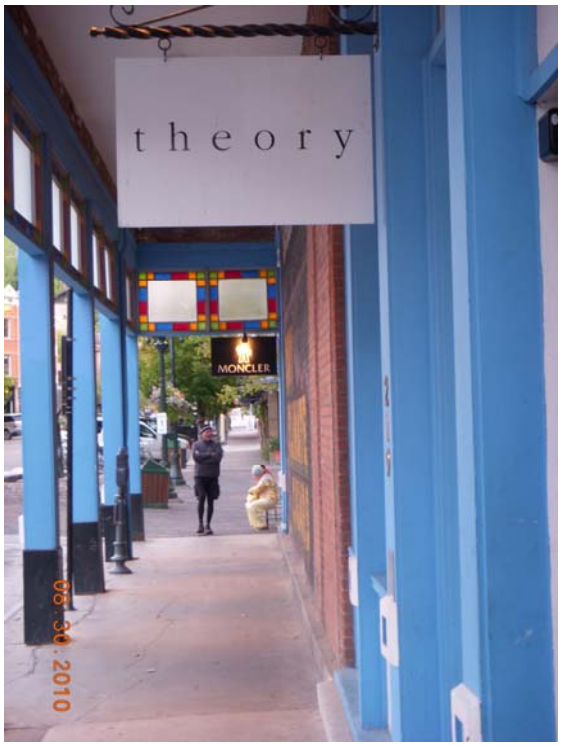
Boulder Summer School
July 9 – August 3, 2012



A.Grosberg
New York University

Colorado - paradise for scientists:

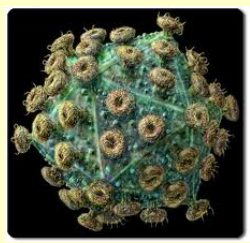
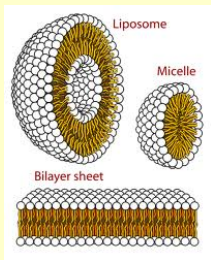
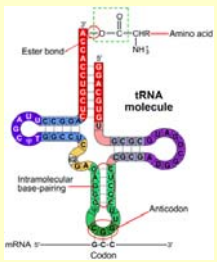
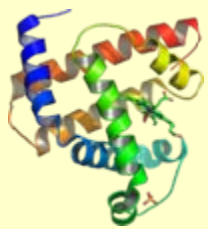
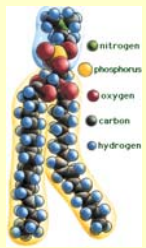
If you need a theory…



If your experiment does not work, and your data is so-so…

- **Theory Return & Exchange Policies:**
  We will happily accept your return or exchange of … when accompanied by a receipt within 14 days … if it does not fit

Polymers in living nature

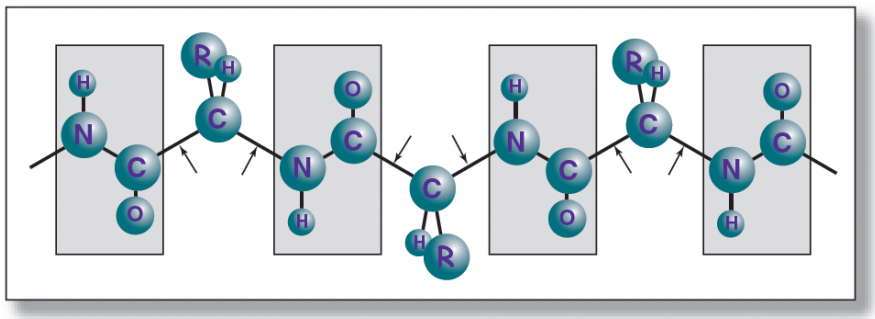
	DNA	RNA	Proteins	Lipids	Polysaccharides
N	Up to 10^{10}	10 to 1000	20 to 1000	5 to 100	gigantic
Nice physics models	Bioinformatics, elastic rod, ribbon, charged rod, helix-coil	Secondary structure, annealed branched, folding	Proteomics, random/designed heteropolymer, HP, funnels, ratchets, active brushes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

Polysaccharides

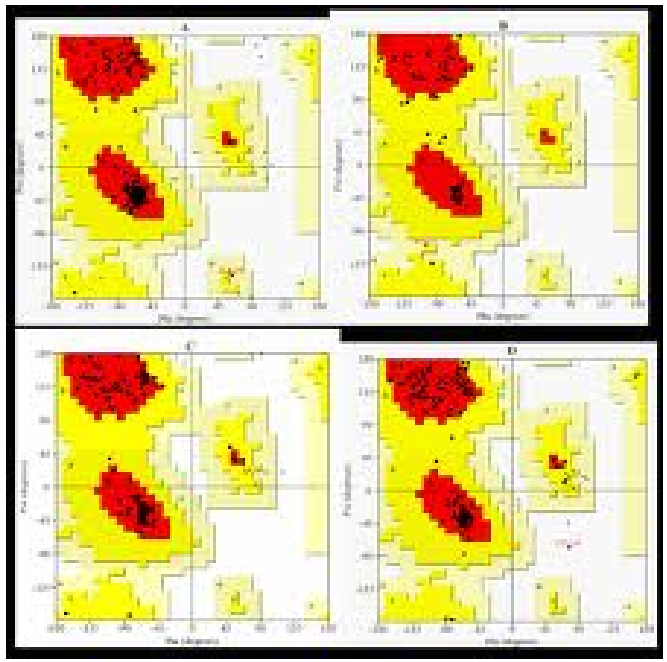
Lipids

- See lectures by Sam Safran

Proteins

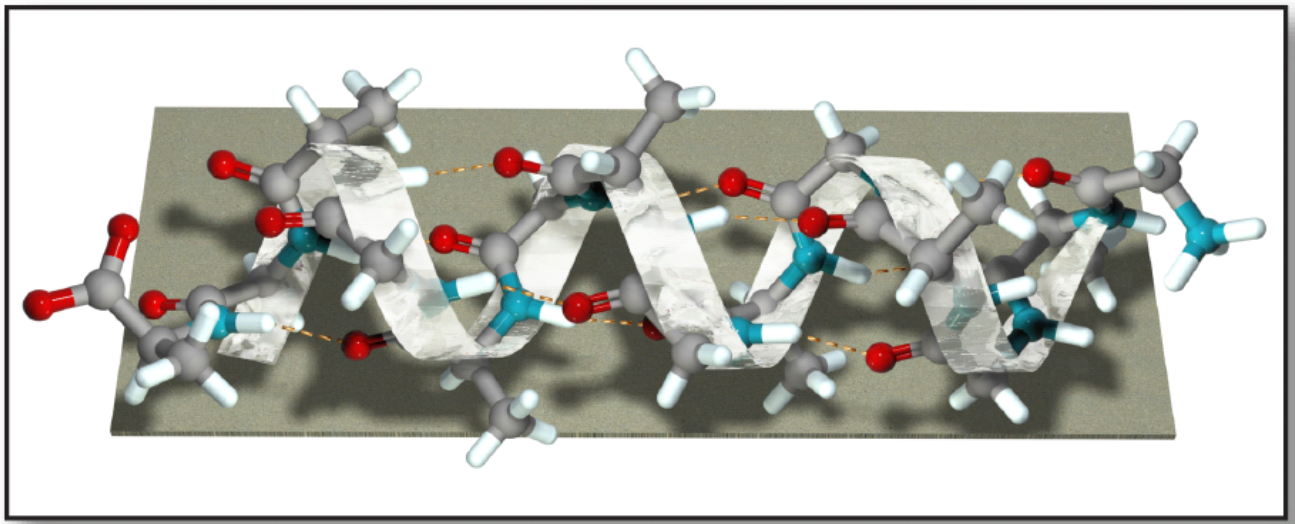


Ramachandran map



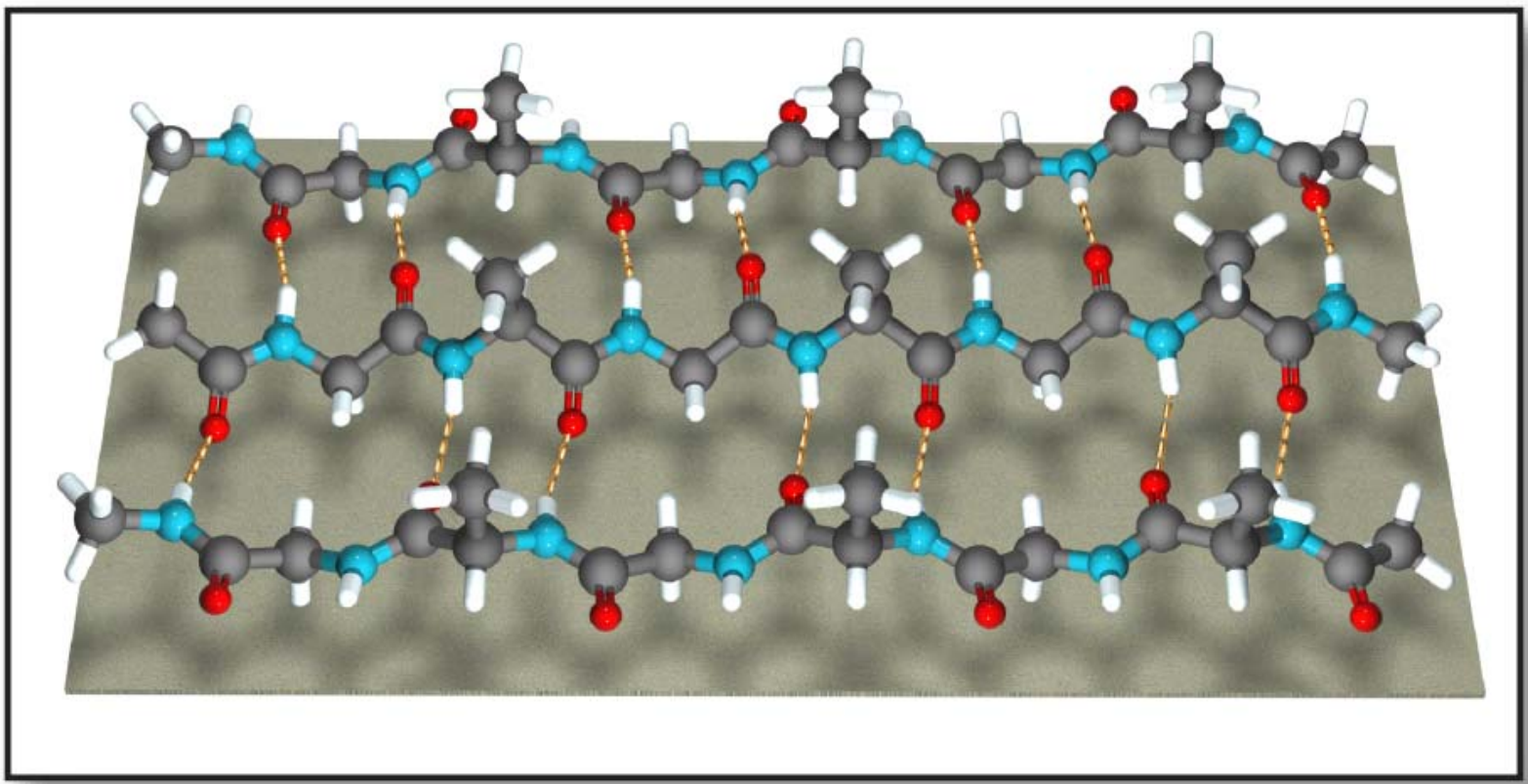
Rotational isomer (not worm-like) flexibility

Secondary structures: α

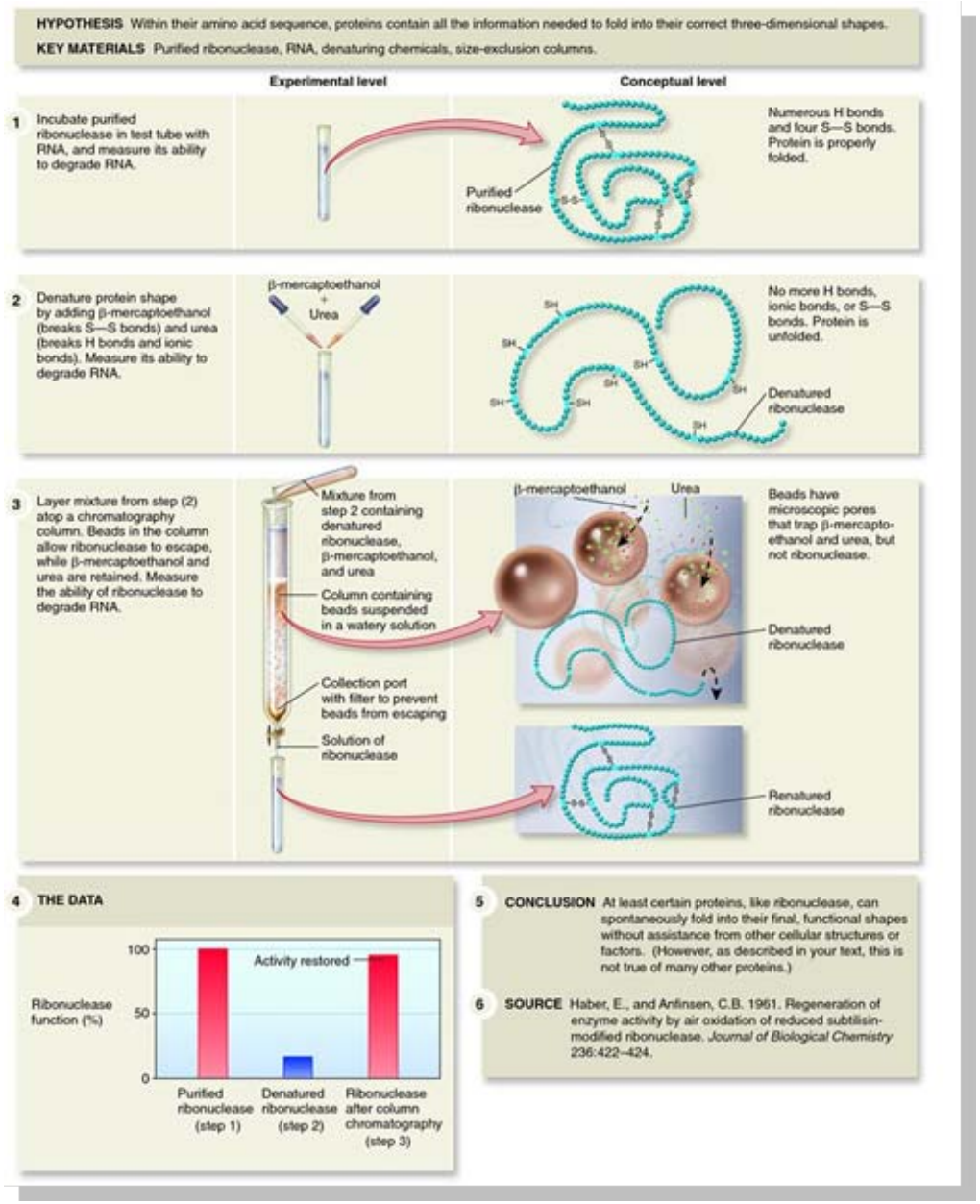


While main chain is of helical shape, the side groups of aminoacid residues extend outward from the helix, which is why the geometry of α-helix is relatively universal, it is only weakly dependent on the sequence. In this illustration, for simplicity, only the least bulky side groups (glycine, side group H, and alanine, side group CH_3) are used. The geometry of α-helix is such that the advance per one amino-acid residue along the helix axes is 0.15 nm, while the pitch (or advance along the axes per one full turn of the helix) is 0.54 nm. That means, the turn around the axes per one monomer equals $360^0 * 0.15/0.54 = 100^0$; in other words, there are $360^0/100^0 = 3.6$ monomers per one helical turn. Accordingly, hydrogen bonds CO…HN (shown in the figure as dotted lines) connect residues k and k+3 for every k.

Secondary structures: β



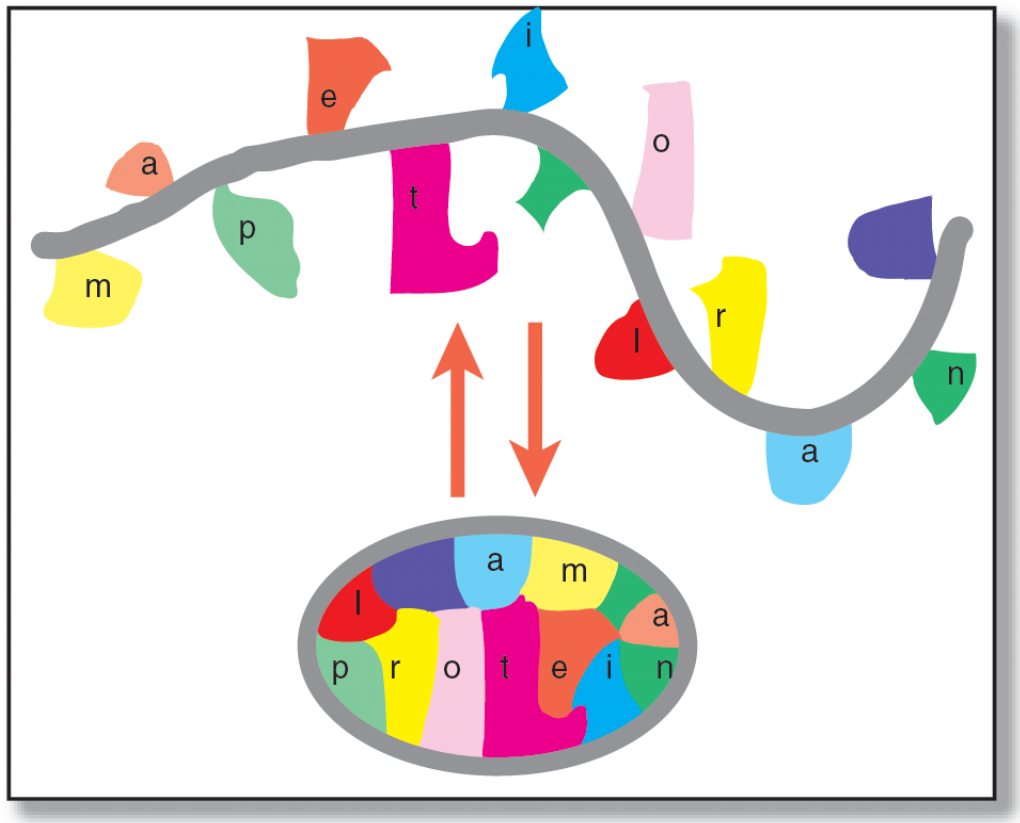
Anfinsen's experiment (1962)



C.Anfinsen

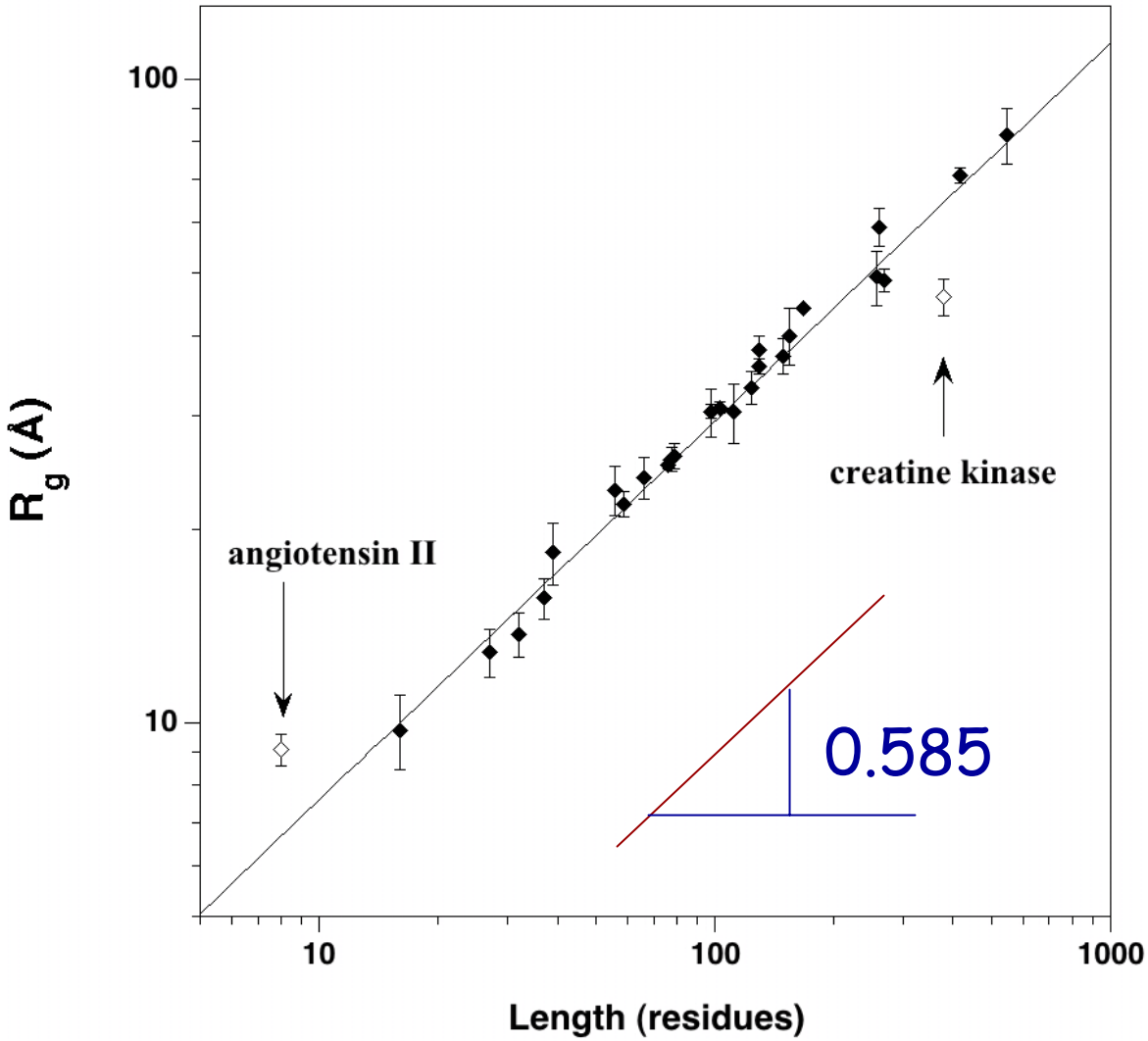
http://biology-forums.com/index.php?action=gallery;sa=view;id=173#download

All the information is in the sequence



Denatured proteins

- Kevin Plaxco (2004):



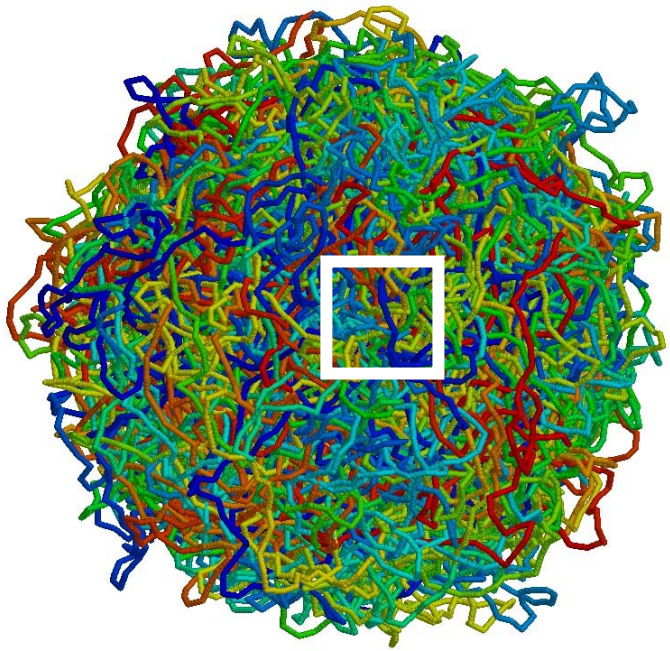
Denatured proteins behave just like polymers with excluded volume…

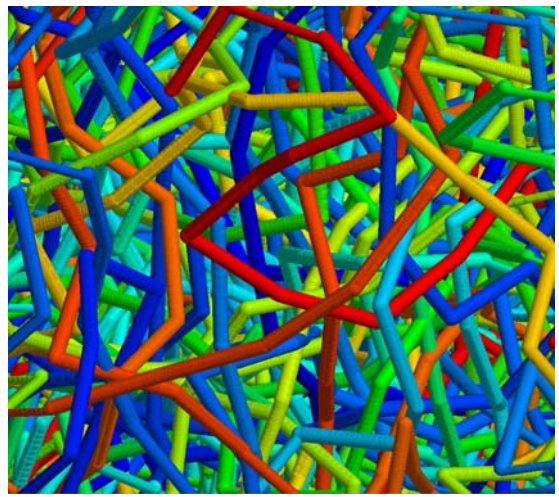
If it looks like a duck, and walks like a duck, and quacks like a duck – then it is probably a duck

All-or-none (1st order)

- Calorimetry heat vs. Van't Hoff heat

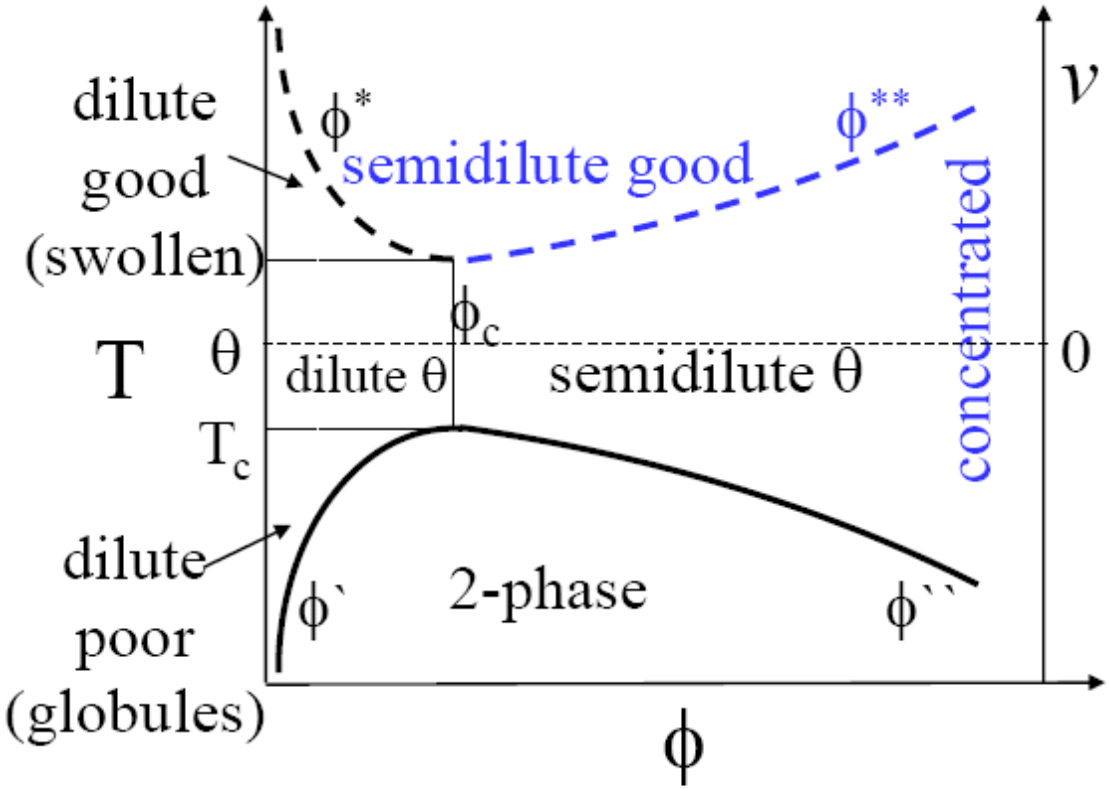
Digression: homopolymer globule





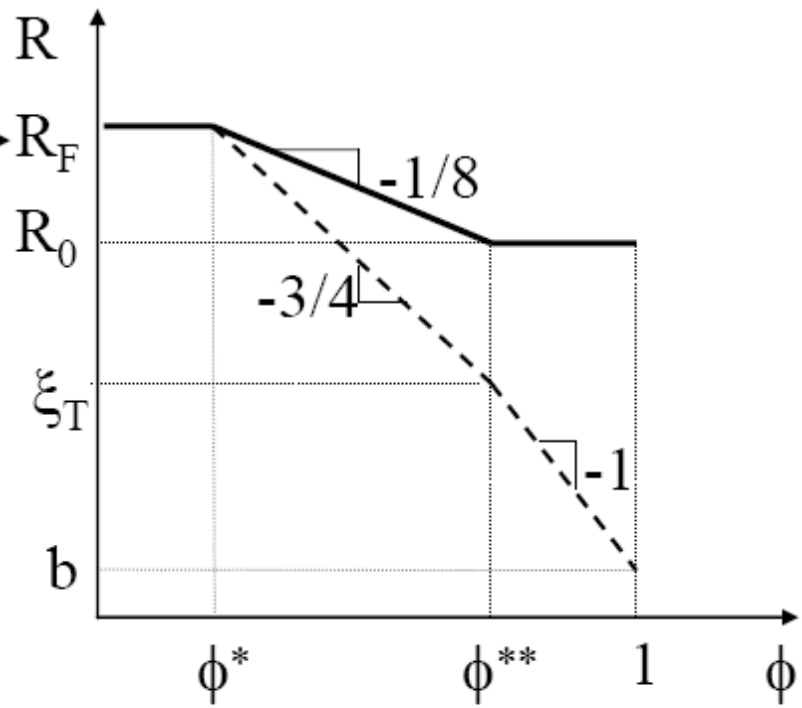
Images: M.Imakaev

Polymer Solutions



$$R \approx R_0 \left(\frac{\phi}{\phi^{**}} \right)^{-1/8}$$

for $\phi^* < \phi < \phi^{**}$



In athermal solvent $v \approx b^3$ $\quad \xi_T \approx b$

$$\xi \approx \frac{b}{\phi^{3/4}} \qquad R \approx \frac{bN^{1/2}}{\phi^{1/8}}$$

$$\phi^{**} \approx 1$$

Coil-globule transition

- Globule density: $p^*(n_0)=0$ ->

$$p^*(n) = Bn^2 + 2Cn^3 \implies n_0 = -B/2C$$

- Free energy $F=F_{vol}+F_{surf}$

$$F_{\rm vol} = \frac{N}{n_0} f^*(n_0) = -NT\frac{B^2}{4C}$$

$$F_{\rm surf} = a^2(\psi, \Delta\psi) = TN^{2/3} a \frac{(-B)^{4/3}}{C^{5/6}}$$

- Assuming $B=v\tau$ and $C=v^2$, the transition point (F=0) and transition width (F~T) are found

$$\tau_{\rm tr} = -\left(\frac{a^3}{Nv}\right)^{1/2}$$

$$\frac{\Delta T}{\theta} = \left(\frac{v}{Na^3}\right)^{1/2} = |\tau_{\rm tr}|\,\frac{v}{a^3}$$

Challenge problem

- Derive all equations given in the previous slide

Reminder

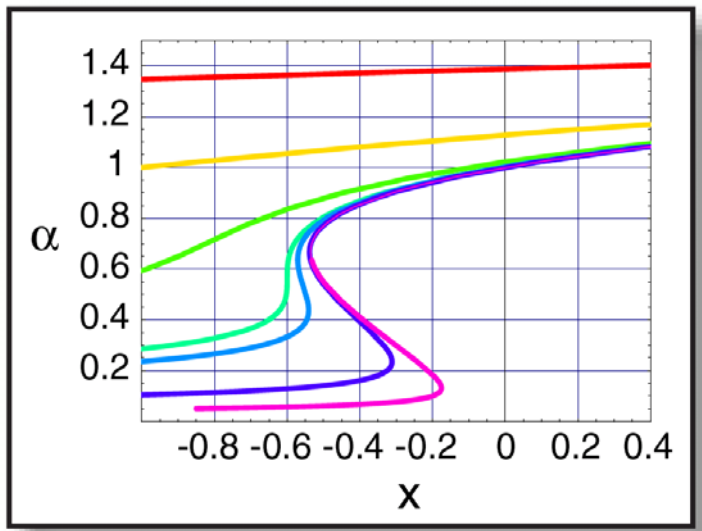
- For rods, $v \sim l^2 d$ and $a \sim l$, so $v/a^3 \sim d/l < 1$

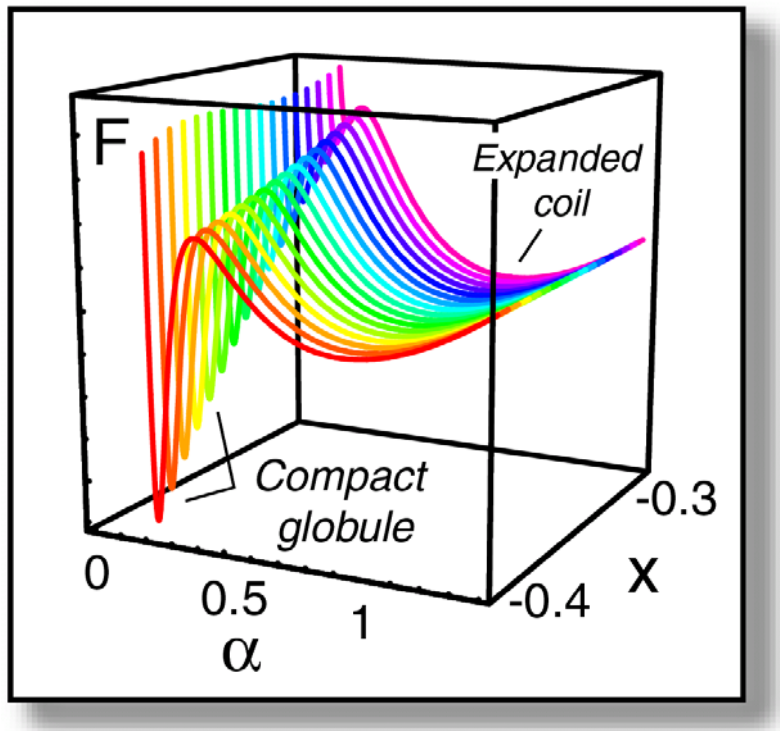
$$\frac{\Delta T}{\theta} = \left(\frac{v}{Na^3}\right)^{1/2} = |\tau_{\rm tr}|\,\frac{v}{a^3} = |\tau_{\rm tr}|\,\frac{d}{\ell} \ll |\tau_{\rm tr}|$$

- The transition is separated from θ-point
- Although the transition is somewhat sharp, its latent heat is still only $\sim N^{1/2}$

Challenge problem

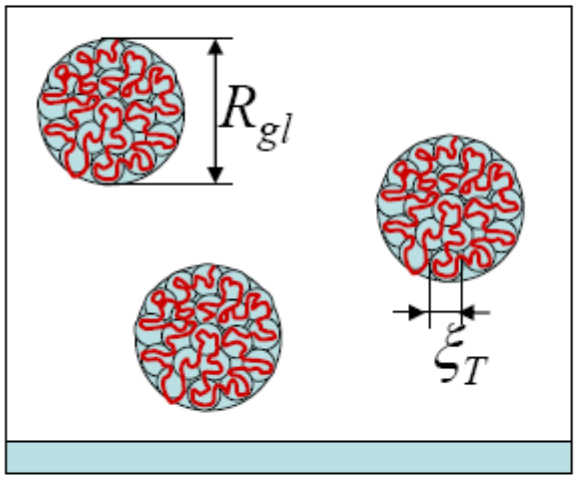
- Re-derive (all or some) results from Flory theory.





Aggregation of globules

Dilute Supernatant of Globules



Globules behave as liquid droplets with size

$$R_{gl} \approx \frac{b^2 N^{1/3}}{|v|^{1/3}} \qquad \xi_T \approx \frac{b^4}{|v|}$$

Surface tension is of order kT per thermal blob

$$\gamma \approx \frac{kT}{\xi_T^2} \approx \frac{kT}{b^8} v^2 \approx \frac{kT}{b^2}(2\chi - 1)^2$$

Total surface energy of a globule $\gamma R_{gl}^2 \approx \frac{kTR_{gl}^2}{\xi_T^2} \approx \frac{kT|v|^{4/3}}{b^4} N^{2/3}$ is balanced by its translational entropy $kT \ln \phi'$

Concentration of a dilute supernatant

$$\phi' = \phi'' \exp\left(-\frac{\gamma R_{gl}^2}{kT}\right) \approx \frac{|v|}{b^3} \exp\left(-\frac{|v|^{4/3}}{b^4} N^{2/3}\right)$$

is different from the mean field prediction.

Proteins are quite special:

1. Sharp first order transition;
2. No aggregation at appreciable concentrations.

Knots in proteins

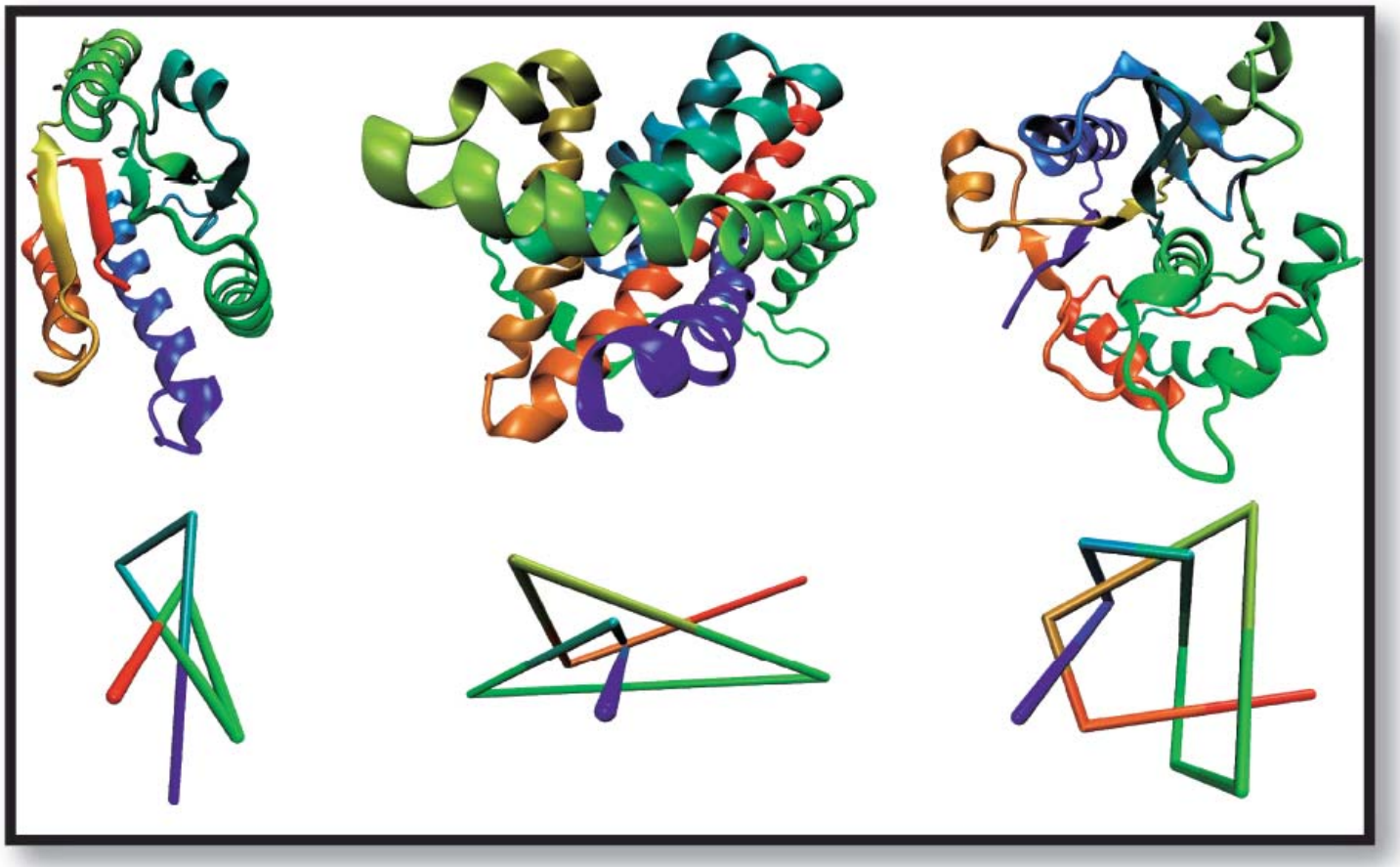
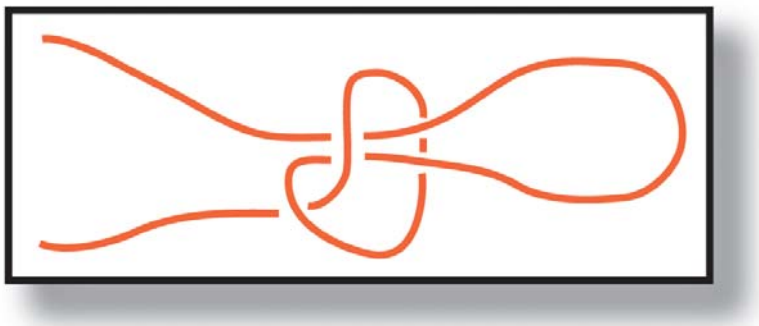


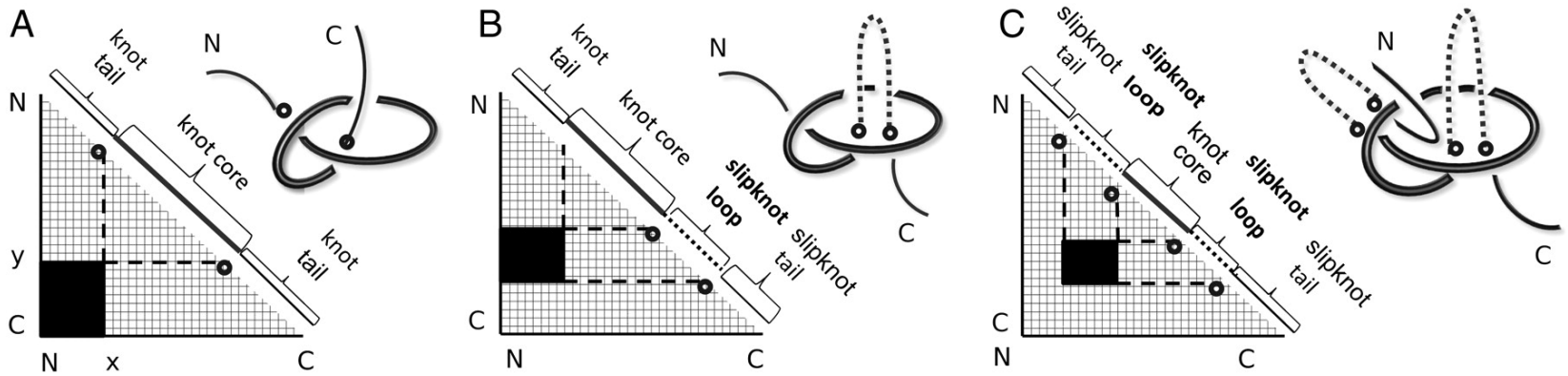
Image: Peter Virnau

Slip-knots



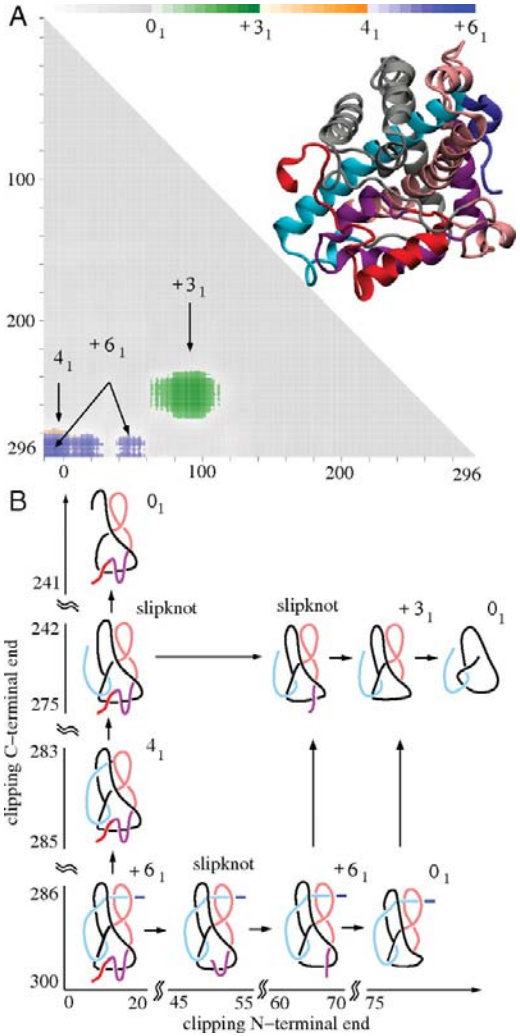
Joanna I. Sułkowska, Eric J. Rawdon, Kenneth C. Millett, Jose N. Onuchic, Andrzej Stasiak "Conservation of complex knotting and slipknotting patterns in proteins", PNAS, v. 109 no. 26, p. E1715-E1723, 2012

Matrix presentations of protein knotting.



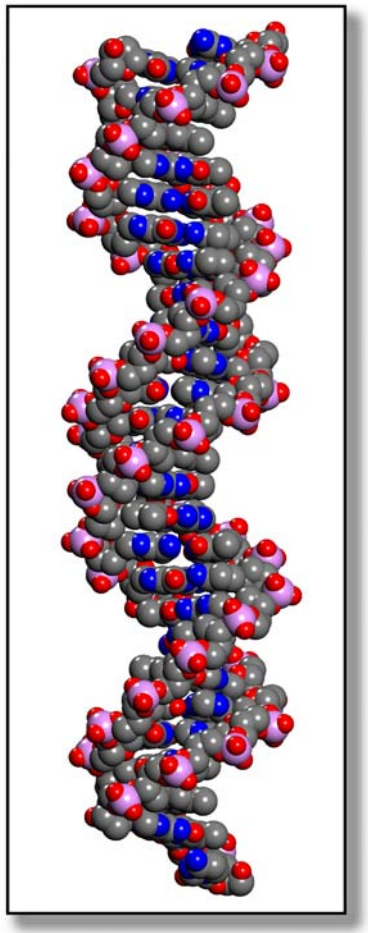
Sułkowska J I et al. PNAS 2012;109:E1715-E1723

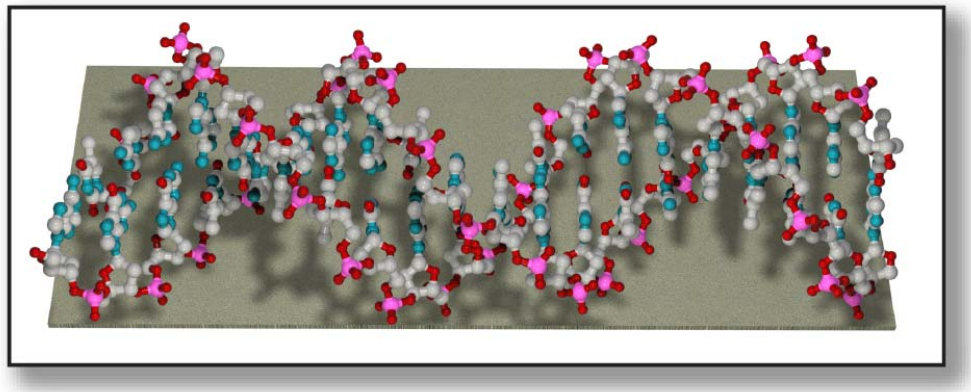
The Dehl protein forms the Stevedore's knot as a whole but some of its subchains form 41 and 31 knots or form Stevedore's and trefoil slipknots.

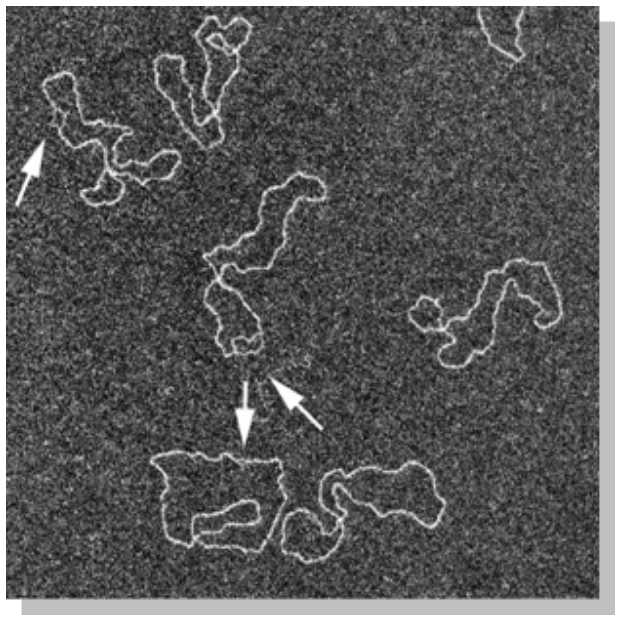


Sułkowska J I et al. PNAS 2012;109:E1715-E1723

"Usual" double helix



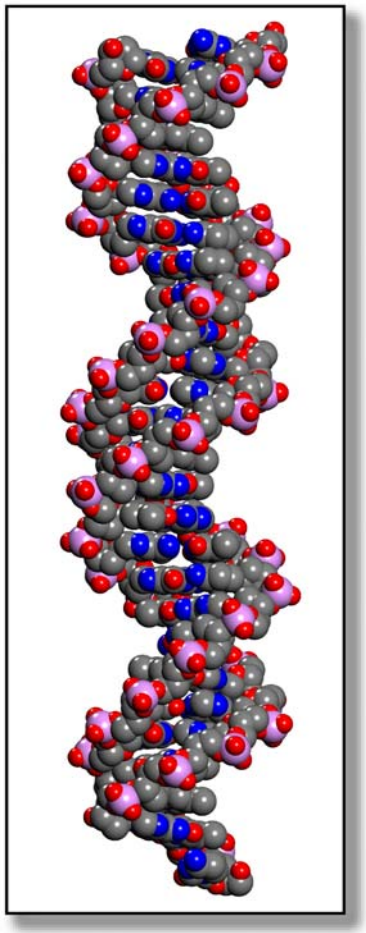


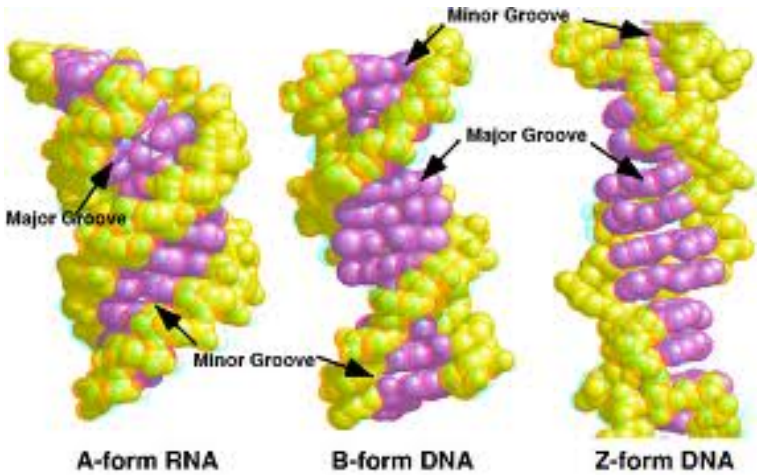


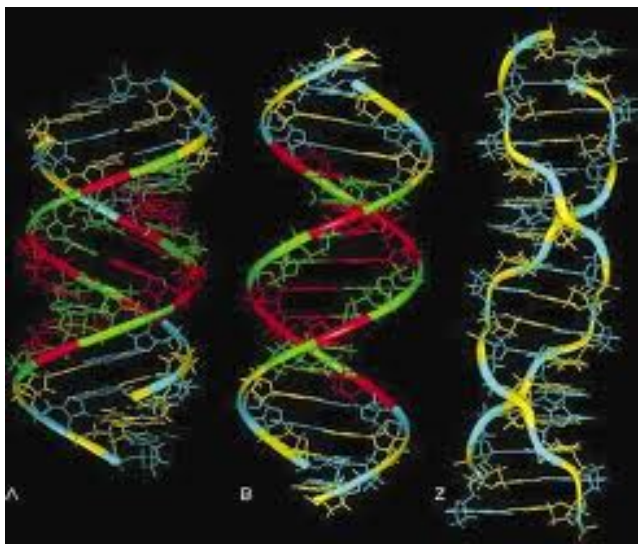
- Elastic rod;
- Charged rod;
- Helix-coil;
- Lk=Tw+Wr

Images: P.Khalatur,
A.Cherny

Unusual forms of helix

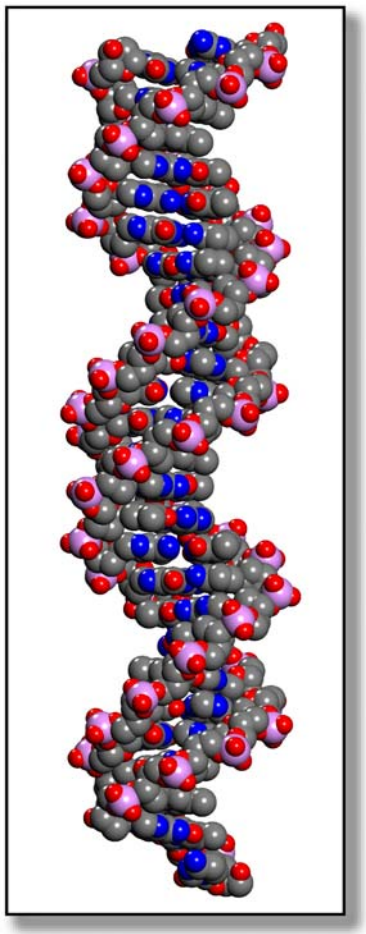


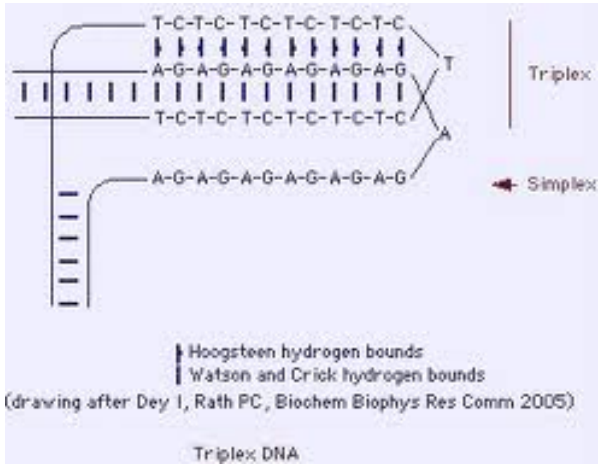




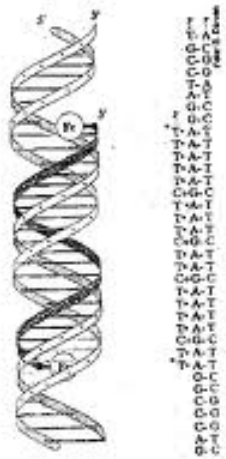
Alex Rich (MIT)

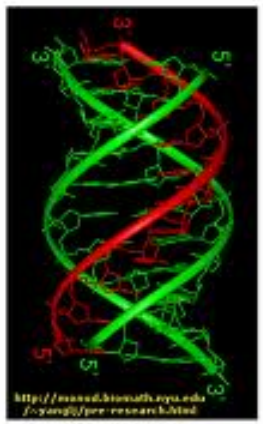
One more: H-form





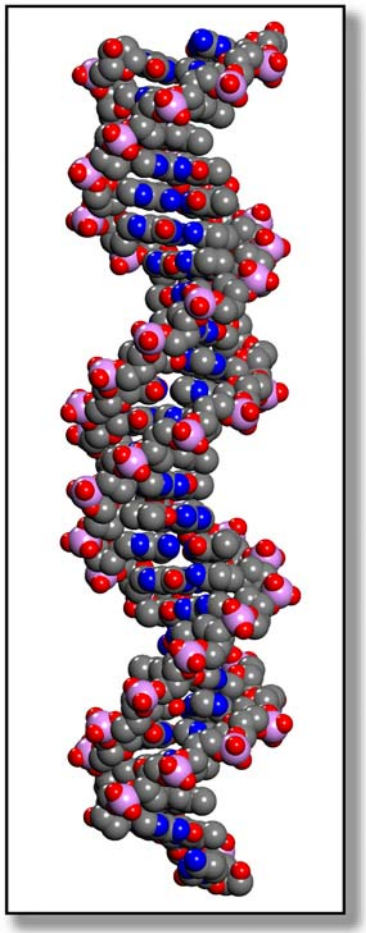
Triplex DNA

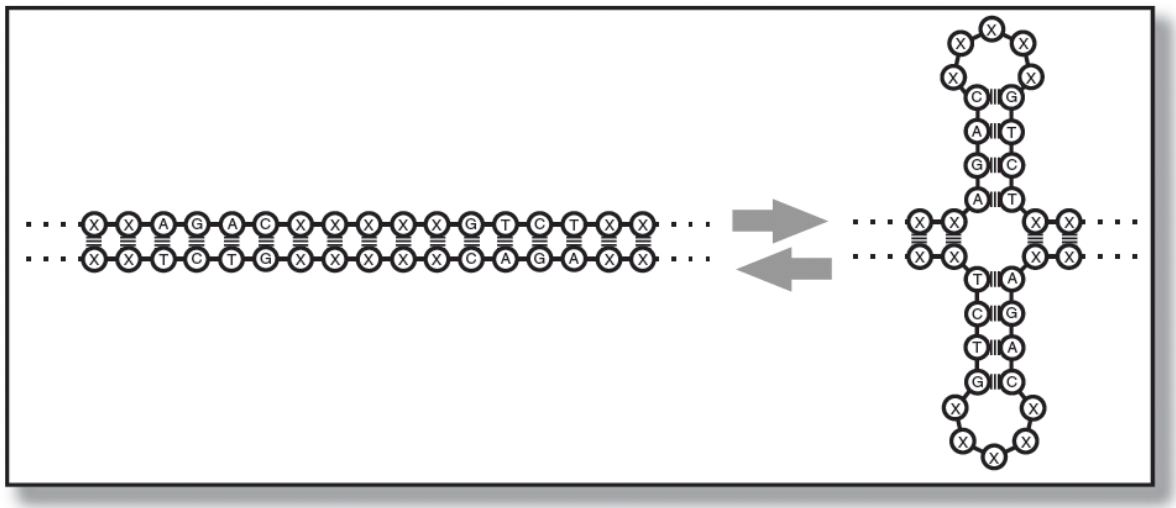




Maxim Frank-Kamenetskii

And one more …



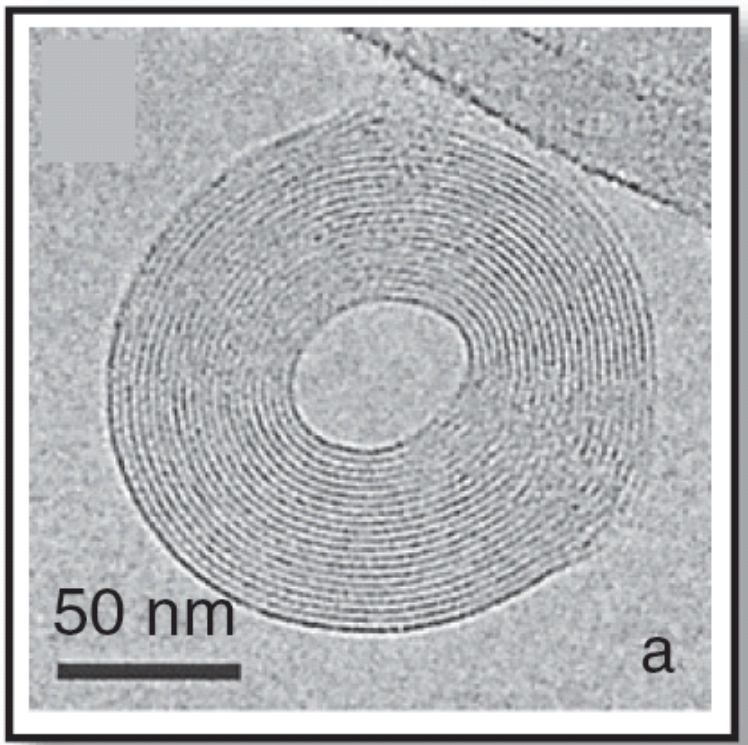


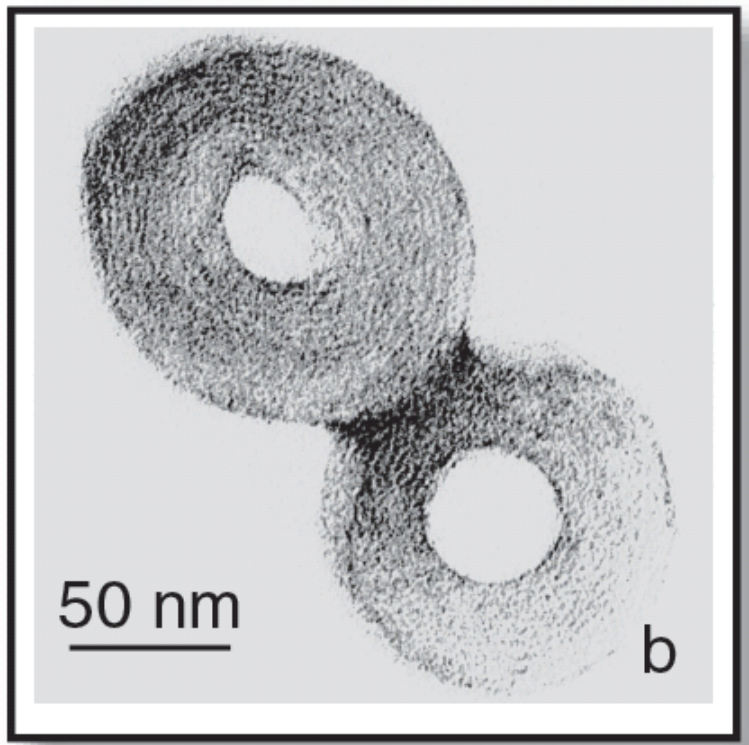
… palindrome sequences

Challenge problems:

1. Develop theory of B-Z transition in DNA
2. Develop theory of B-H transition in DNA
3. Develop theory of cross-structure

DNA condensation





Images by N.Hud (left) and J.-L.Sikorav (right)

DNA condensation (cont'd)

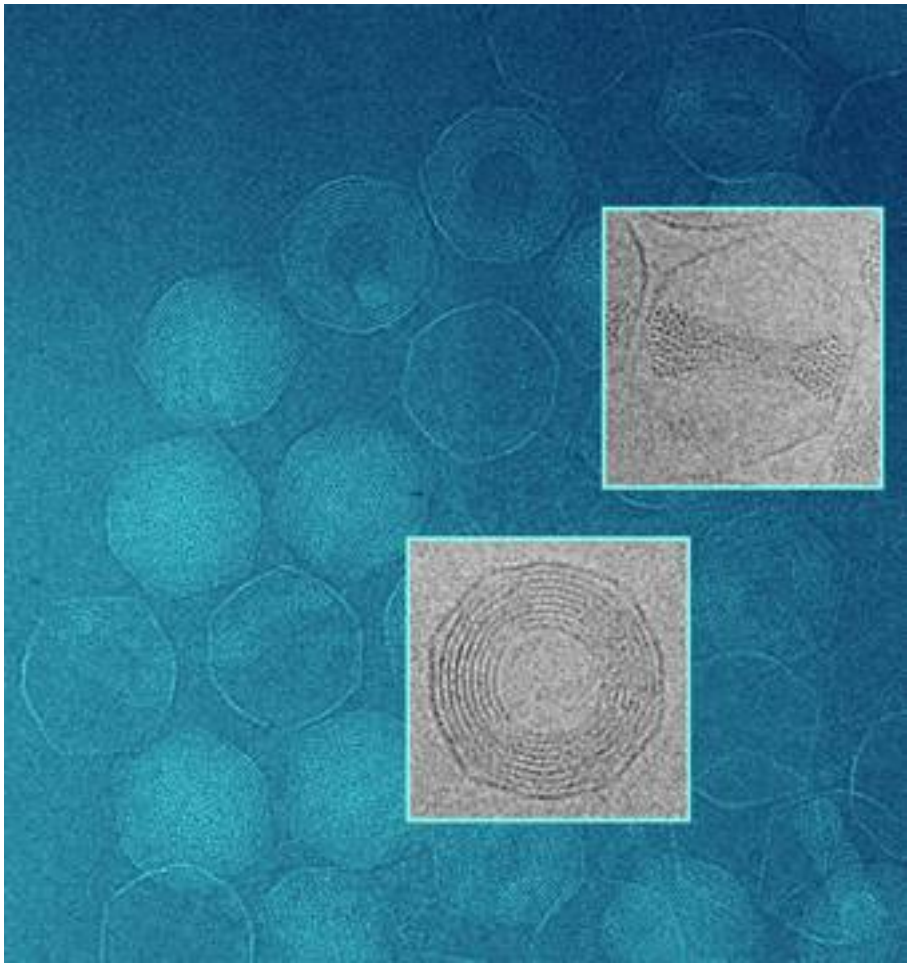
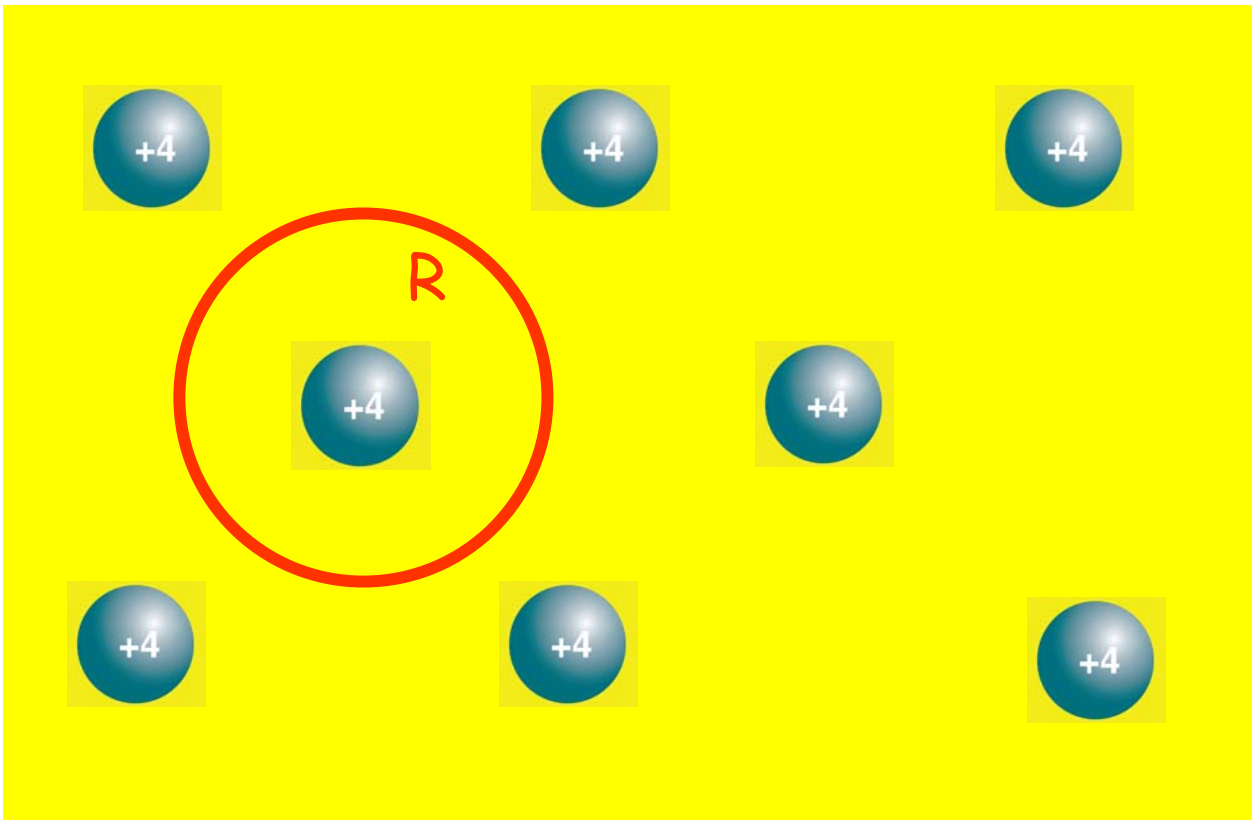


Image: F.Livolant

How does one beat Coulomb repulsion?

- DNA charge: -1e per 0.17nm, or -1e per nm^2, all negative…
- Add salt, screen it – not enough…
- Add multivalent salt, or
- Add PEG (in addition to salt) – Ψ condensation

Attraction of like charges in the presence of multivalent salt



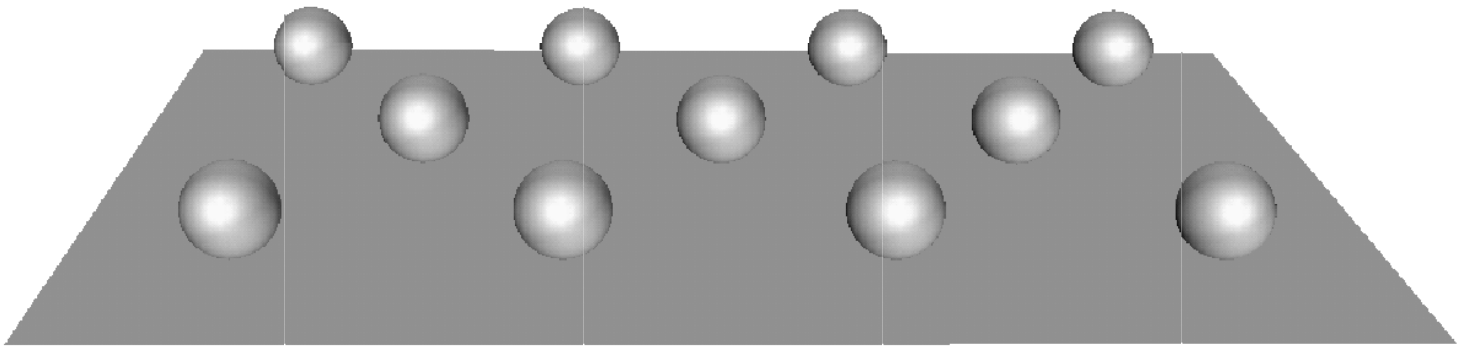
In neutral system, each ion owns a plot of land of the size R such that $\sigma R^2=Q$

Energy per ion is then

$\varepsilon=Q^2/R=$

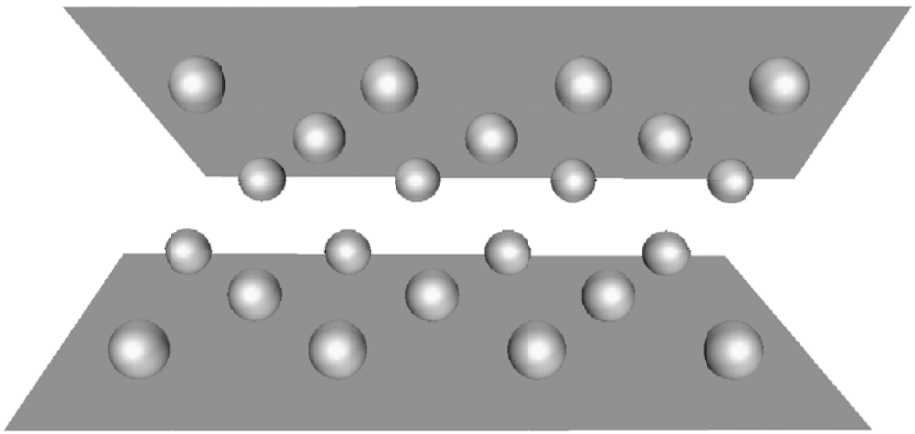
$=Q^{3/2}\sigma^{1/2}$

An image to take home:



Challenging problem: estimate energy of Coulomb repulsion between Z=4 ions in water and show that it is sufficiently strong to maintain somewhat orderly arrangement. What would be your conclusions for Z=3,2,1?

Two like-charged surfaces: short-range attraction



Idea: I.Rouzina, V.Bloomfield (1996)

Theory: B.Shklovskii (1999)

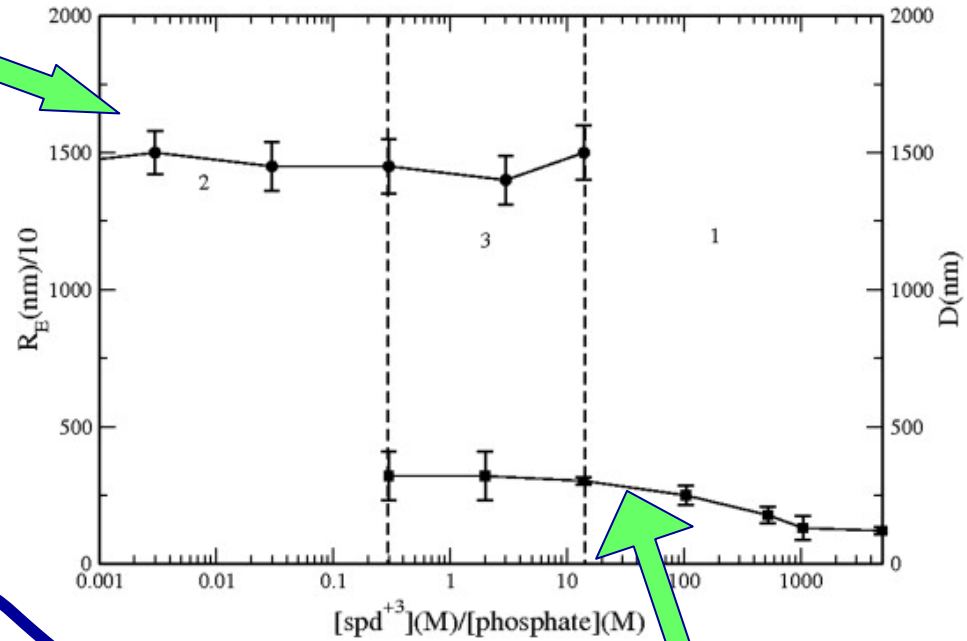
Several equivalent ways to express the same idea, many common errors…

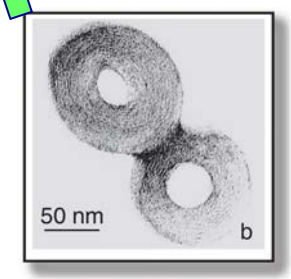
Review: Rev. Mod. Phys., 2002

Now each ion owns two "plots of land", one on the floor and one on the ceiling. Total area is the same Q/σ, but radius is smaller!!! In other words, $\sigma \to 2\sigma$, and energy per ion is more favorable:

$$\varepsilon(2\sigma) \sim -Q^{3/2}(2\sigma)^{1/2} < \varepsilon(\sigma)$$

Looks like 1st order…





- I.S.S. Carrasco, F.M. Bastos, M.L. Munford, E.B. Ramos, M.S. Rocha "Atomic Force Microscopy of spermidine-induced DNA condensates on silicon surfaces" Materials Science and Egineering: C, v. 32, n. 1, Pages 36-39, 2012

Challenging problems:

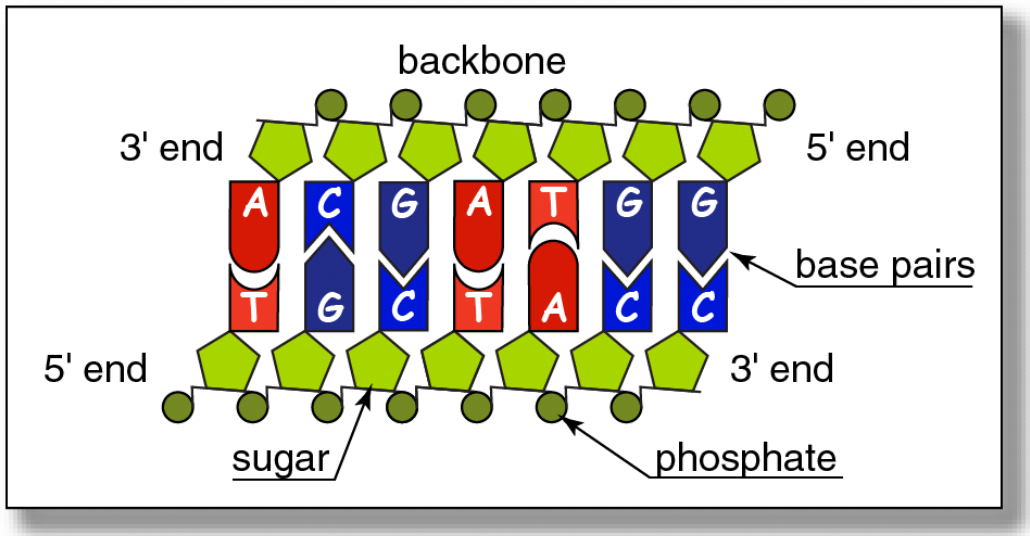
- *Find internal and external radii of a "torus globule".
- *Consider a solution of DNA of some finite concentration. Address the possibility of toroidal particles involving more than one DNA.

When is coil-globule first order?

- Polymer chains with peculiar interactions, in which third (or higher) virial coecient becomes negative at a temperature (or solvent conditions) where second virial coecient is still positive. An example is the system in which monomers can form complexes, similar to micells, with a dened number of participants. Following de Gennes, this is sometimes called p-cluster model.
- Macromolecules capable of internal local orientational ordering, usually of nematic type, in the globular state, like in toroid DNA case.
- Polymers in which monomers can have two dierent states, such as helical or non-helical, when globule can be formed due to the jump in, e.g., the degree of helicity.
- Polymers in which monomers can absorb ligands from the solvent, such that globule can be formed due to a jump in the number of absorbed ligands.
- Polymer chains in multicomponent solvents, when globule formation can be achieved by the re-distribution of solvent components between the globule interior and the outer solution.
- Polymer chain or network with ionizable groups and in a poor solvent (e.g., with hydrophobic monomers), when osmotic pressure of counterions is responsible for the sharpness of the transition.
- Last but not least, the heteropolymers with properly selected sequences.

Challenge: derive all of the above

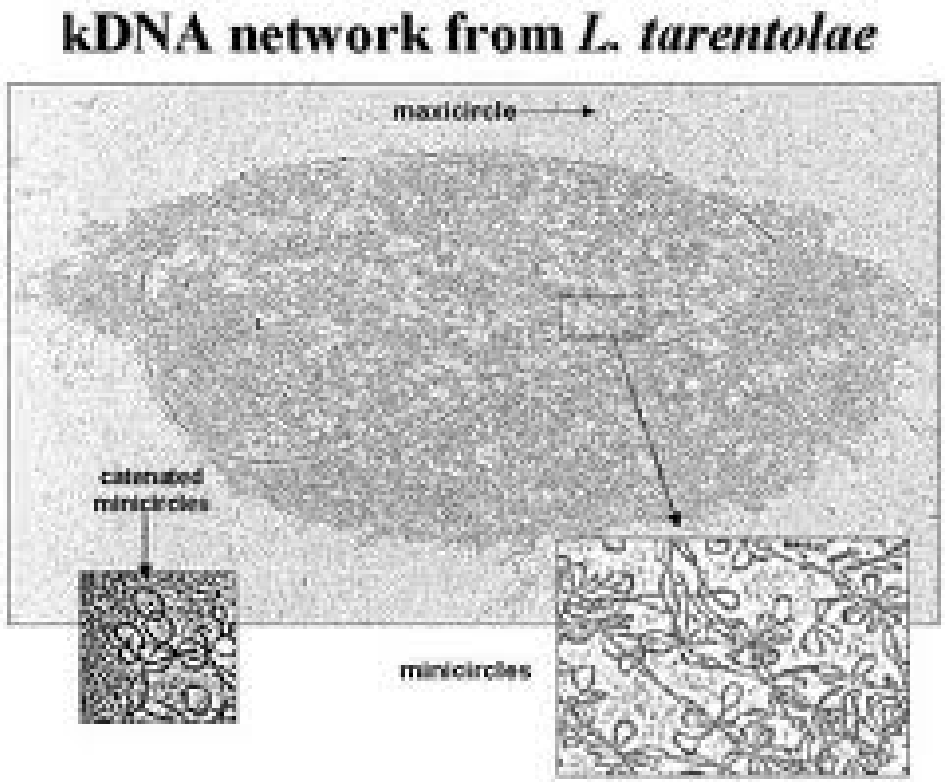
Rings



Each strand can connect to its own end, but not to one another

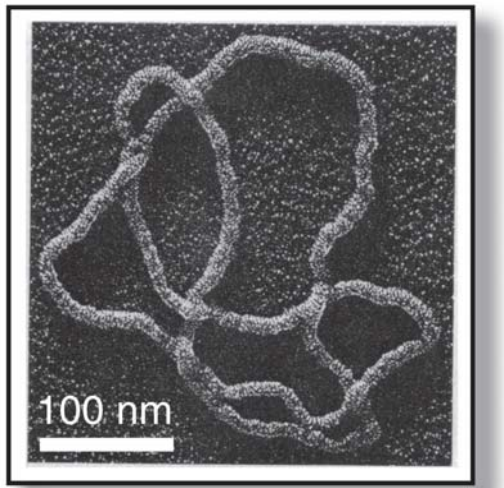
Kinetoplast

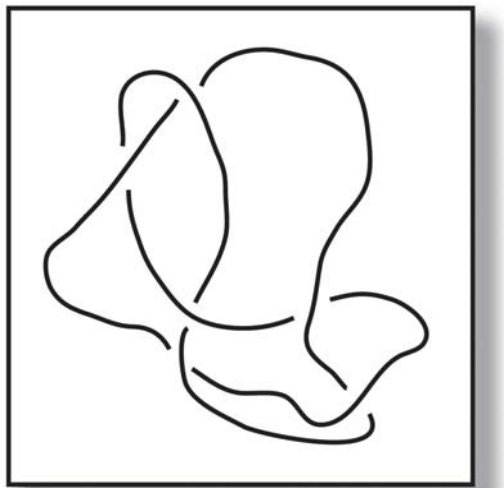
- Leishmania and other trypanosomatids
- There are approximately 10,000 minicircles and 50 maxicircles in the network.
- Question: how does it reproduce its topology? Answer: it does not…



Larry Simpson (UCLA) web site http://dna.kdna.ucla.edu/simpsonlab/ls/lps1.htm

DNA knots



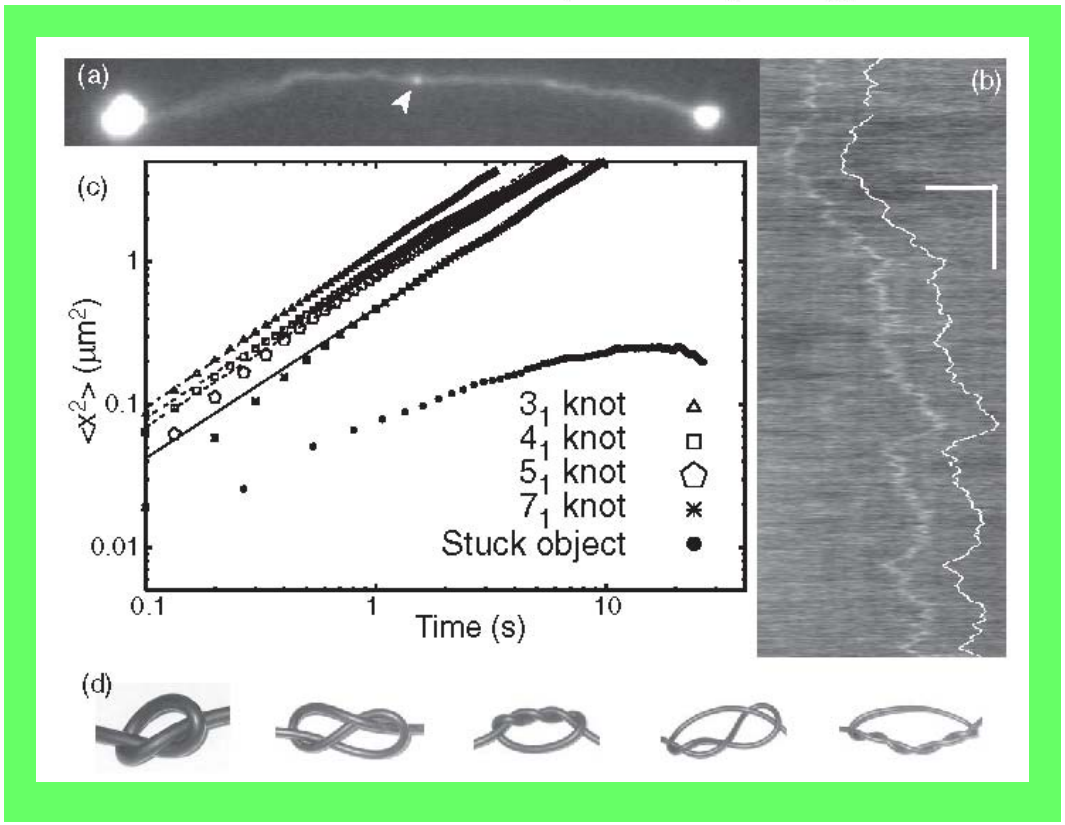


Let us tie a knot on a long dsDNA

VOLUME 91, NUMBER 26 PHYSICAL REVIEW LETTERS week ending 31 DECEMBER 2003

Behavior of Complex Knots in Single DNA Molecules

Xiaoyan R. Bao, Heun Jin Lee, and Stephen R. Quake
Department of Applied Physics, California Institute of Technology, Pasadena, California 91125, USA
(Received 1 August 2003; published 31 December 2003)

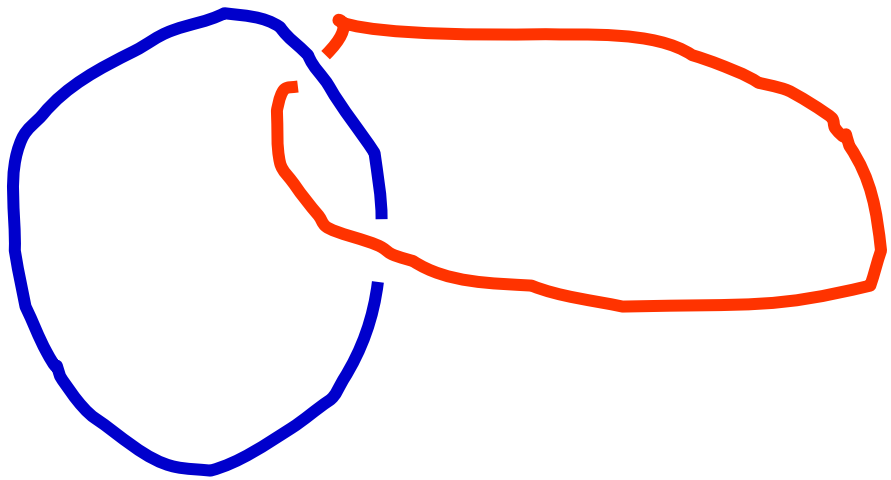


The knots were produced on purpose, by artfully manipulating optical tweezers.

Gauss (1834)

$$Lk = \frac{1}{4\pi} \oint_C \oint_D \frac{(\mathbf{x}-\mathbf{y})\cdot\dot{\mathbf{x}}\times\dot{\mathbf{y}}}{|\mathbf{x}-\mathbf{y}|^3} dsdt$$

C: x(s)
D: y(t)



Calagareanu-Fuller-White:

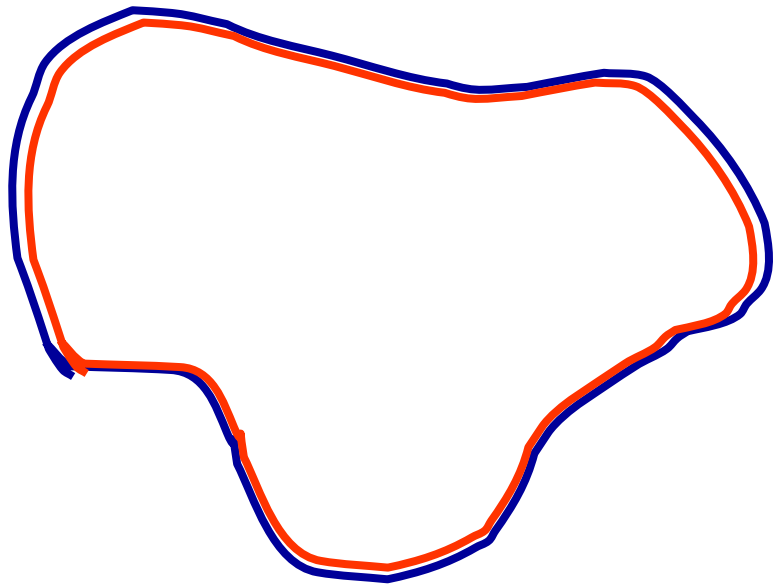
- Lk=Tw+Wr
- DNA is a two-sided ribbon.
- Diameter much smaller than persistence length: $d \ll l$

Writh:

$$Wr = \frac{1}{4\pi} \oint_C \oint_C \frac{(\mathbf{x}-\mathbf{y})\cdot\dot{\mathbf{x}}\times\dot{\mathbf{y}}}{|\mathbf{x}-\mathbf{y}|^3} dsdt$$

C: x(s) and y(t)

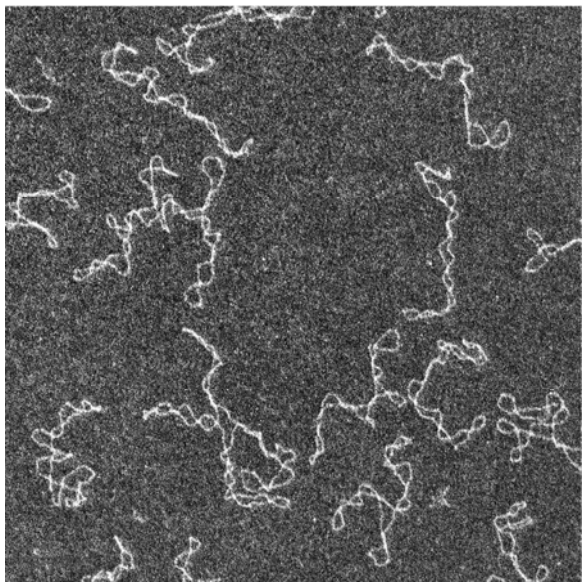
Equivalent definition: averaged number of signed crossings

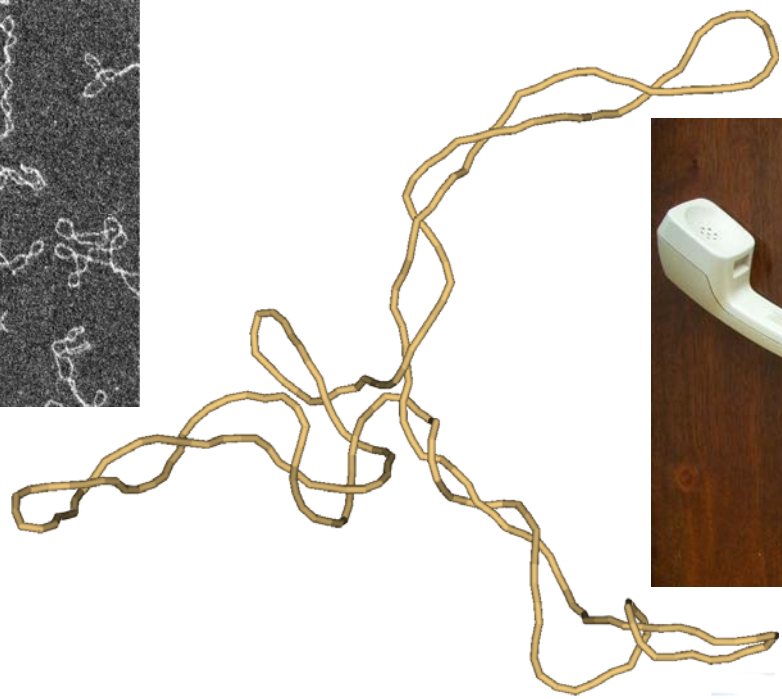


Plectonemes

$E=E_{bend}+E_{twist}$

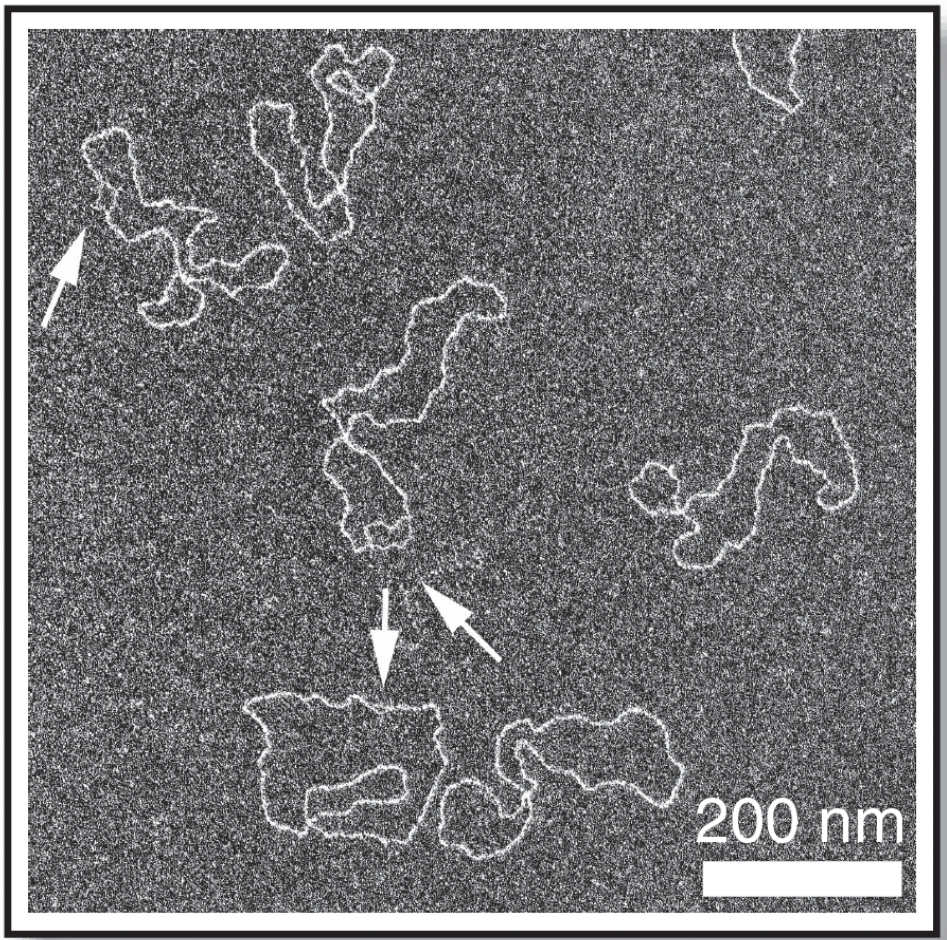
Minimization is restricted by Lk=Tw+Wr



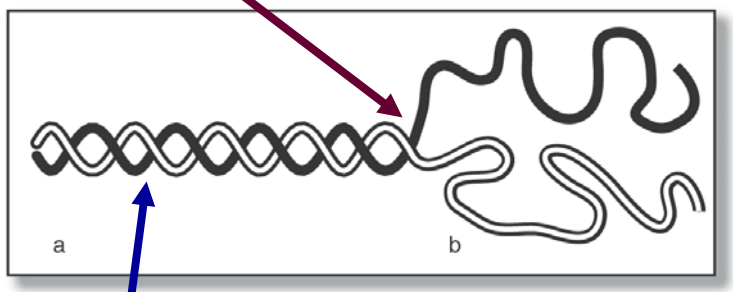


Images: A.Cherny, A.Vologodskii, Radio Shack

Helix-coil



(free) energy loss Δf_{surf}



(free) energy gain Δf per monomer

Main parameters: $s=\exp[-\Delta f]$, $\sigma=\exp[-2\Delta f_{surf}]<<1$

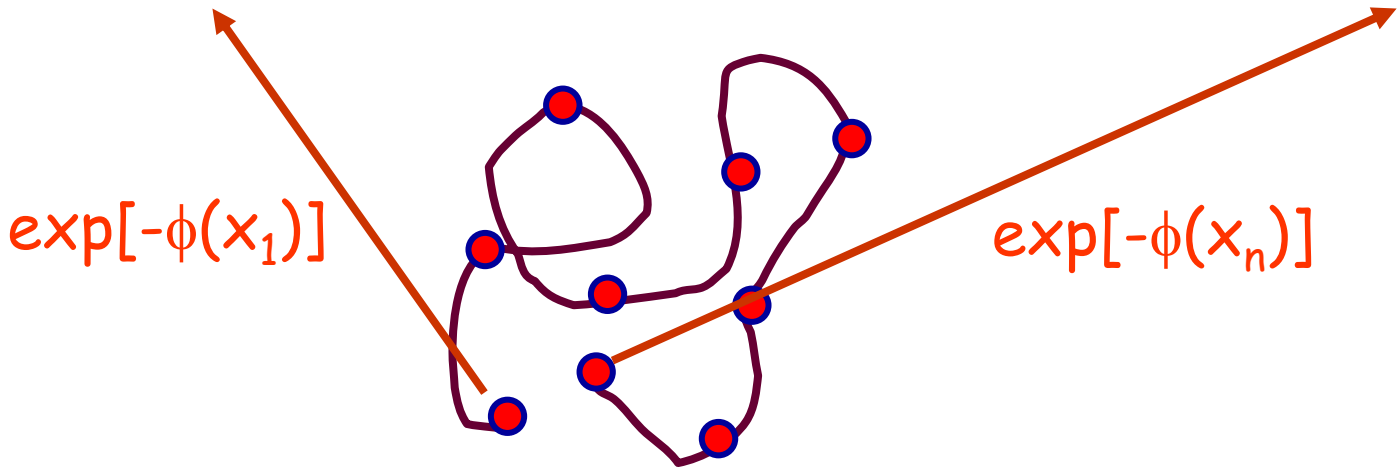
A bit more general: $\phi(x)$

- Still assume ideal polymer, but suppose each monomer (really -- representative point) carries energy $\phi(x)$ which depends on position (or in general on x). Instead of

$G(x_1,x_2,\ldots,x_n)=g(x_1,x_2)g(x_2,x_3)\ldots g(x_{n-1},x_n)$.

we now have (assuming $k_B T=1$)

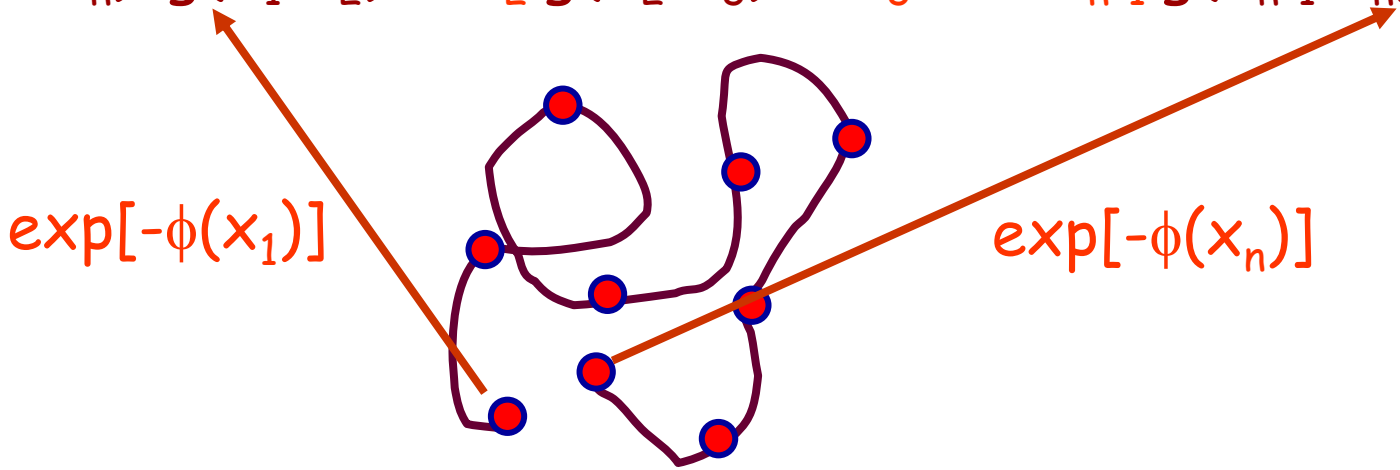
$G(x_1,x_2,\ldots,x_n)=g(x_1,x_2)e^{-\phi(x_2)}g(x_2,x_3)e^{-\phi(x_3)}\ldots e^{-\phi(x_{n-1})}g(x_{n-1},x_n)$.



In our case, either x=c or x=h

$$\hat{g} = \begin{pmatrix} 1 & \sigma^{1/2} \\ \sigma^{1/2} & 1 \end{pmatrix} \qquad e^{-\phi}\hat{g} = \hat{g} = \begin{pmatrix} 1 & \sigma^{1/2} \\ s\sigma^{1/2} & s \end{pmatrix}$$

$G(x_1,x_2,\ldots,x_n)=g(x_1,x_2)e^{-\phi(x_2)}g(x_2,x_3)e^{-\phi(x_3)}\ldots e^{-\phi(x_{n-1})}g(x_{n-1},x_n).$



Green's function:

$$G\left(\begin{array}{c|c} 1 & N \\ x & x' \end{array}\right) = \sum_{x_2,x_3,\ldots,x_{N-1}} \cdots = \left[\hat{Q}^N\right]_{xx'}$$

Partition sum: $Z=\mathrm{Tr}[(e^{-\phi}g)^N]$; free energy $F=-N\ln\Lambda_{max}$

$$e^{-\phi}\hat{g} = \hat{Q}; \quad \hat{Q}\psi = \Lambda\psi$$

"Densities":

$$\left(\begin{array}{c} n_c \\ n_h \end{array}\right) = \left(\begin{array}{c} \psi_c^2 \\ \psi_h^2/s \end{array}\right)$$

Home work: solve for the maximal eigenvalue

Challenging problem:

- Prove that the average length of continuous helical segment is

$$k_h = \frac{1+s+\sqrt{(s-1)^2+4s\sigma}}{1-s+\sqrt{(s-1)^2+4s\sigma}}$$

- Find also averaged fraction of helical parts, and averaged number of helix-coil boundaries.

Another method: generating function

$$\rho(\{h,c\}) = \prod_{i=1}^{k} \rho(h_i, c_i) \; ; \quad \rho(h,c) = \sigma s^h$$

$$Z(p) = \sum_{N=1}^{\infty} p^N \underbrace{\sum_{\{h,c\}} \rho(\{h,c\}) \delta(\sum_{i=1}^{k}(h_i + c_i) - N)}_{\text{partition sum}} =$$

$$= \sum_{k=1}^{N} \zeta(p)^k = \frac{\zeta(p)}{1-\zeta(p)}$$

$$\zeta(p) = \textstyle\sum_{h,c} \rho(h,c) p^{h+c} = \sigma \sum_{h=1}^{\infty} (sp)^h \sum_{c=1}^{\infty} p^c = \sigma \frac{sp}{1-sp} \frac{p}{1-p}$$

To find partition sum from Z(p), look for singularities: $\zeta(p)=1$ yields the same quadratic equation as before, with $\Lambda=1/p$

Complication 1: double helix

$$\rho(\{h,c\}) = \prod_{i=1}^{k} \rho(h_i, c_i) \; ; \quad \rho(h,c) = \sigma s^h c^{-\alpha}$$

$$Z(p) = \sum_{N=1}^{\infty} p^N \underbrace{\sum_{\{h,c\}} \rho(\{h,c\}) \delta(\sum_{i=1}^{k}(h_i + c_i) - N)}_{\text{partition sum}} =$$

$$= \sum_{k=1}^{N} \zeta(p)^k = \frac{\zeta(p)}{1-\zeta(p)}$$

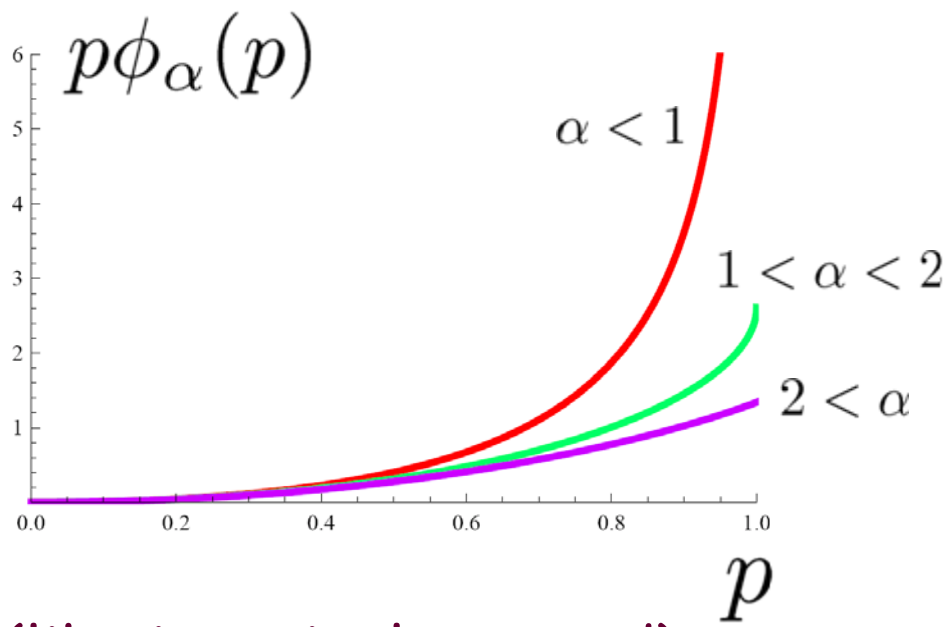
$$\zeta(p) = \textstyle\sum_{h,c} \rho(h,c) p^{h+c} = \sigma \sum_{h=1}^{\infty} (sp)^h \sum_{c=1}^{\infty} p^c c^{-\alpha} = \sigma \frac{sp}{1-sp} \phi_\alpha(p)$$

To find partition sum from Z(p), look for singularities: ζ(p)=1 yields a **new non-quadratic** equation, still F=-N ln(p)

Double helix (cont'd)

Equation for p at singularity (essentially – for free energy)

$$\frac{1}{s} - p = \sigma p \phi_\alpha(p)$$



Conclusions:

- α<1: no phase transition (like in a single strand);
- 1<α<2: phase transition, but smooth (2nd order);
- 2<α: sharp phase transition (1st order)

Challenging problems

- Prove the above statements
- Find latent heat when it is 1st order transition.
- Find the order of transition at every α.
- *Find a taking into account excluded volume interactions of helical parts with coiled ones

Complication 2: heteropolymer

Instead of

$$G\left(\begin{array}{c|c} 1 & N \\ x & x' \end{array}\right) = \sum_{x_2, x_3, \ldots, x_{N-1}} \cdots = \left[\hat{Q}^N\right]_{xx'}$$

We now have

$$G\left(\begin{array}{c|c} 1 & N \\ x & x' \end{array}\right) = \left[\hat{Q}_{s(1)}\hat{Q}_{s(2)}\cdots\hat{Q}_{s(N)}\right]_{xx'}$$

Each s(i) is either A or B, …
but Q_A and Q_B do not commute…

Can we take an average?

$$G\left(\begin{array}{c|c} 1 & N \\ x & x' \end{array}\right) = \left[\hat{Q}_{s(1)}\hat{Q}_{s(2)}\cdots\hat{Q}_{s(N)}\right]_{xx'}$$

$$\left\langle G\left(\begin{array}{c|c} 1 & N \\ x & x' \end{array}\right)\right\rangle = \left[\left\langle\hat{Q}\right\rangle^{N}\right]_{xx'}$$

$$\left\langle\hat{Q}\right\rangle = x_A\hat{Q}_A + x_B\hat{Q}_B$$

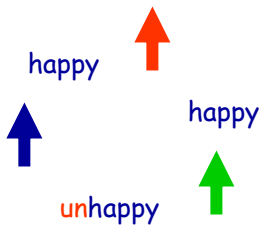
Which object does it describe?

Naïve example

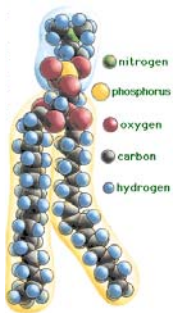
- Suppose Q may have two values, Q=0 or Q=2 with probability $\frac{1}{2}$ each.
- $Q_1 Q_2 \ldots Q_N$ equals on average $\langle Q \rangle^N = 1/2^N$, but
- Typical sequence yields just zero.

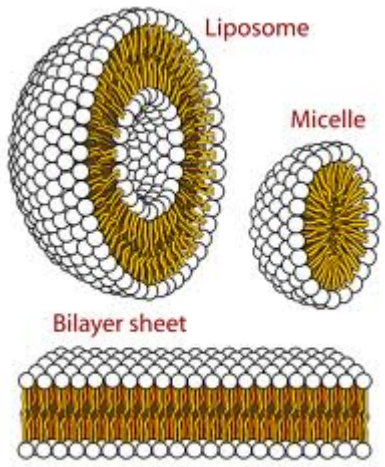
Quenched disorder and annealed disorder

- Frustration: $H=-J\sigma_1\sigma_2-J\sigma_2\sigma_3+J\sigma_3\sigma_1$



- Frustration in a polymer (examle):

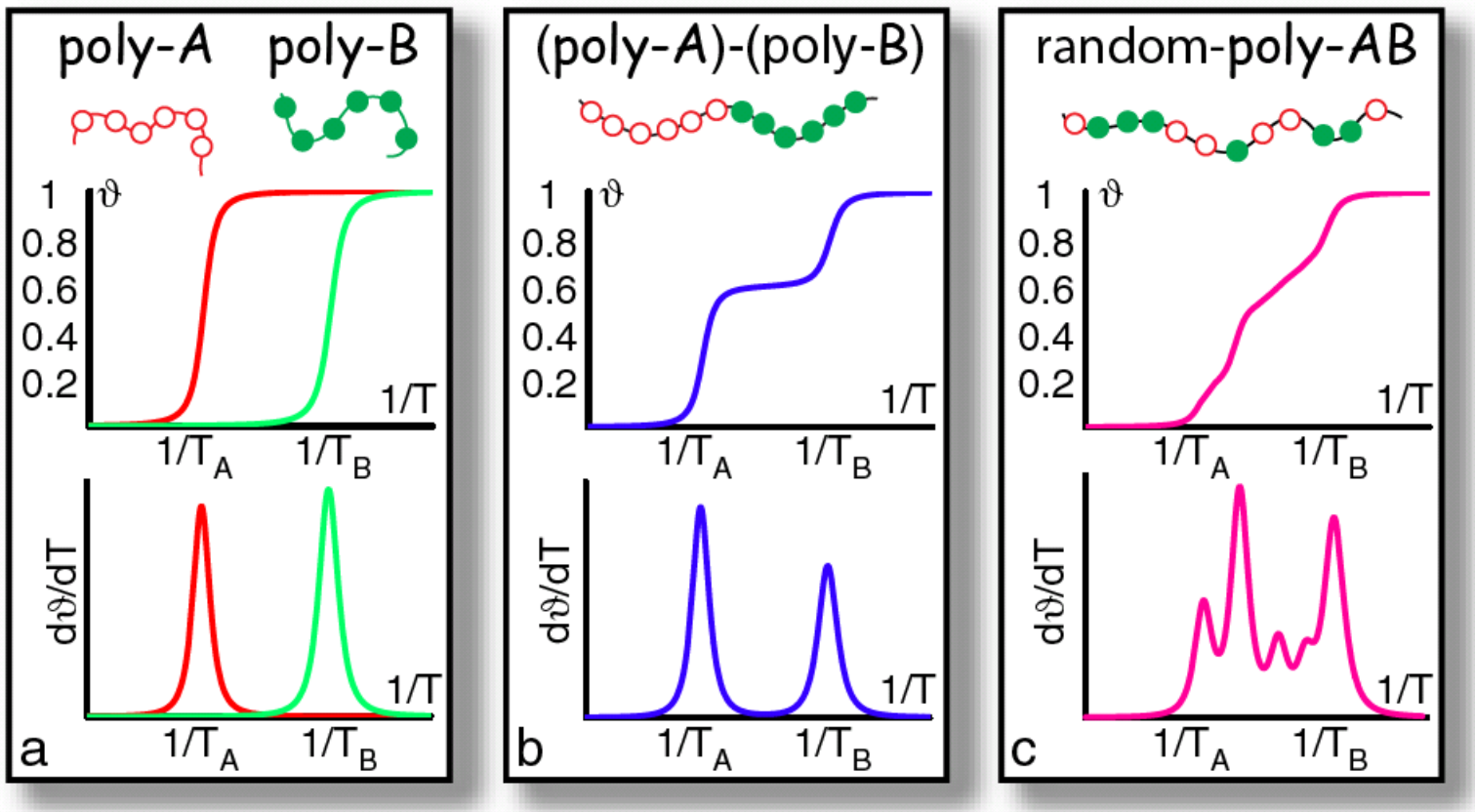




Physics preparation and biological preparation

- No two sample of a gel, even prepared in exactly the same way, are the same in microscopic details.
- Two molecules of the same protein are the same down to microscopic details (have the same sequence)
- Cells provide an unparalleled possibility of physics experiments completely imposible otherwise

Physical outlook



Simple theory

$$\Delta f_\mu = \Delta S(T - T_\mu) \text{ , where } \mu \text{ is either A or B}$$

"Concentrations" $x_A = x + \xi(t)$, $\quad x_B = 1 - x - \xi(t)$

$$\begin{aligned}
F(n) &= \sum_{i=1}^{n} \left[\Delta f_A x_A(i) + \Delta f_B x_B(i)\right] \\
&= \Delta S \sum_{i=1}^{n} \left[(T - T_A)\,(x + \xi(i)) + (T - T_B)\,(1 - x - \xi(i))\right] \\
&= \Delta S \sum_{i=1}^{n} \left[(T - xT_A - (1-x)T_B) - \xi(i)\,(T_A - T_B)\right] \\
&= n\Delta S \left[(T - T_x) - (T_A - T_B)\frac{\sum_{i=1}^{n} \xi(i)}{n}\right]
\end{aligned}$$

A.M.Dykhne et al, ca. 1975

Assume random sequence

$$F(n) = n\Delta S \left[(T - T_x) + (T_B - T_A) \frac{\sum_{i=1}^{n} \xi(i)}{n} \right]$$

Self-averaging

Suppose $T<T_x$, so "on average" system is helical, but $T_A<T_B$, so sufficiently long group of A can melt. A piece of length n melts out if F(n) is larger than $2\Delta f_{surf}$ ...

Challenging problem: prove that the probability to find such piece in a long polymer reads

$$P_n \sim \exp\left[-\frac{\left[(T_x - T)\sqrt{n} + \frac{2}{\sqrt{n}} \frac{\Delta f_{\rm surf}}{\Delta S} \right]^2}{2(T_A - T_B)^2 x(1-x)} \right]$$

Melting curve of random sequence heteropolymer

$$P_n \sim \exp\left[-\frac{\left[(T_x-T)\sqrt{n}+\frac{2}{\sqrt{n}}\frac{\Delta f_{\rm surf}}{\Delta S}\right]^2}{2(T_A-T_B)^2x(1-x)}\right]$$

The most probable (optimal) length: $n_{\rm opt}(T)=\frac{2\Delta f_{\rm surf}/\Delta S}{T_x-T}$

Longer is improbable for length, shorter – for purity…

Challenging problem: show that the degree of helicity in a long polymer is self-averaging and is equal to

$$\vartheta=\frac{1}{2}-\frac{\sinh\frac{T-T_x}{\Delta T}-\frac{T-T_x}{\Delta T}}{4\sinh^2\frac{T-T_x}{2\Delta T}}$$

assuming $\Delta f_{surf} \gg \Delta S\,|T_A-T_B|$, where

$$\Delta T=(T_A-T_B)^2x(1-x)\frac{\Delta S}{\Delta f_{\rm surf}}$$

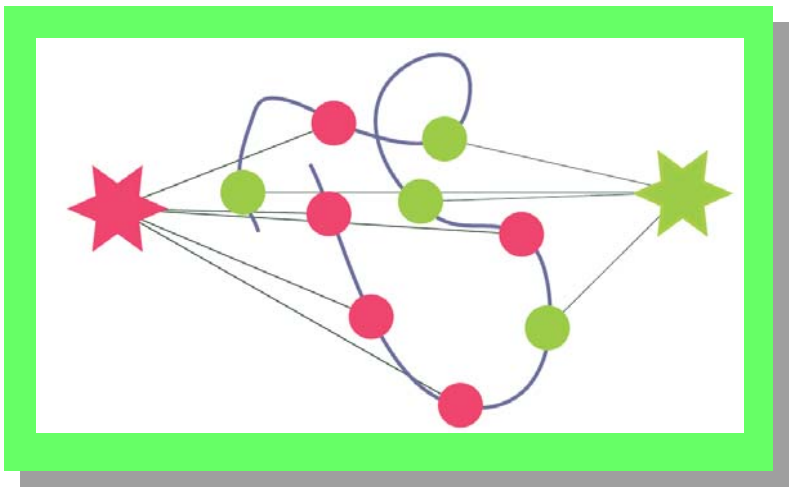
How to compute the melting curves

- Random Polymer Models, Giambattista Giacomin, Imperial College Press, 2007
- M.Fixman, J.J.Freire, Theory of DNA melting curves, Biopolymers, v. 16, pp. 2693-2704, 1977

Central idea of Freire algorithm: replace $c^{-\alpha}$ with $\exp[-\beta c]$ (or combination of several exponents). Why does it work? Consider mapping on "adsorption on a point" problem

Challenging problem

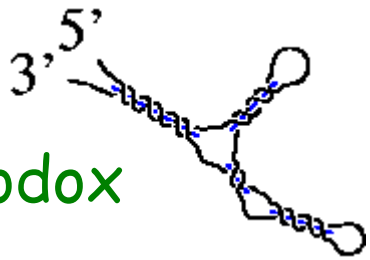
- Consider random heteropolymer with quenched sequence of two monomer species A and B, assuming no excluded volume and Gaussian bonds $g(\mathbf{y}) \sim \exp(-3\mathbf{y}^2/2a^2)$. Assume monomers feel harmonic potentials, with different centers for monomer species: $\phi_A(\mathbf{x})=k(\mathbf{x}-\mathbf{r}_A)^2/2$ and $\phi_B(\mathbf{x})=k(\mathbf{x}-\mathbf{r}_B)^2/2$. Find averaged spatial densities of all monomer species.



Generalizations: selective solvents, two walls, bacterial phenotypes…

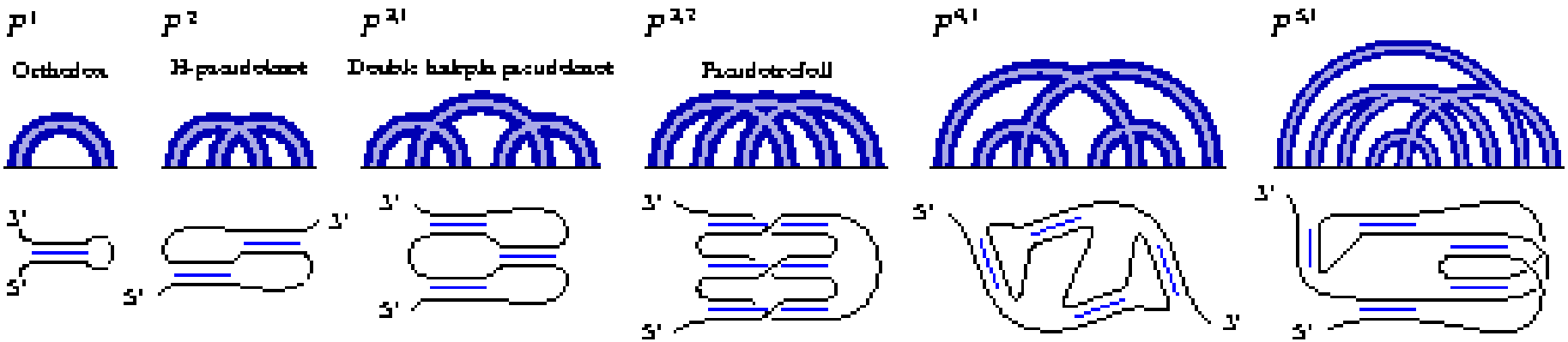
RNA: possible secondary structures

Orthodox

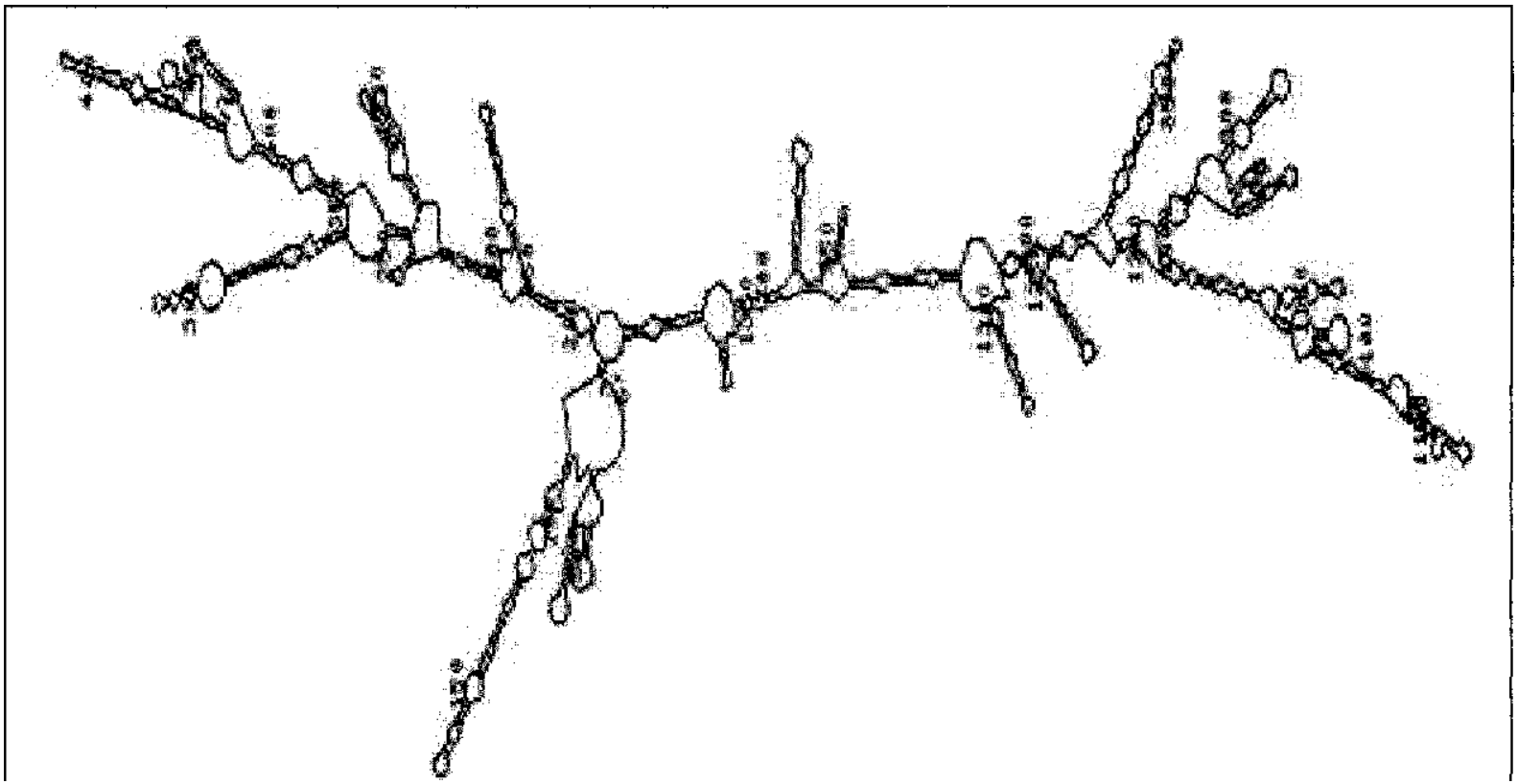


Pseudoknot

Diagrammatic representations:



Viral RNA: computed secondary structure



Can we treat it as a branched polymer?

De Gennes recurrence relation

- Let Green's function be the partition sum of a polymer with just one point fixed: $G_n(x)$
- For linear polymer, $G_{n+1}(x) = \hat{g} G_n(x')$
- For branched polymer, added monomer may be end or branch point:

$$G_{n+1}(x) = \Lambda_2 \hat{g} G_n(x') + \Lambda_3 \hat{g} \left[\sum_{i,j=2}^{\infty} G_i(x') G_j(x') \Delta(i+j-1-n) \right]$$

Generating function

- In terms of generating function, this produces branch point instead of the pole:

$$Z(p) = \sum_{n=2}^{\infty} p^{n-1} G_n$$

satisfies

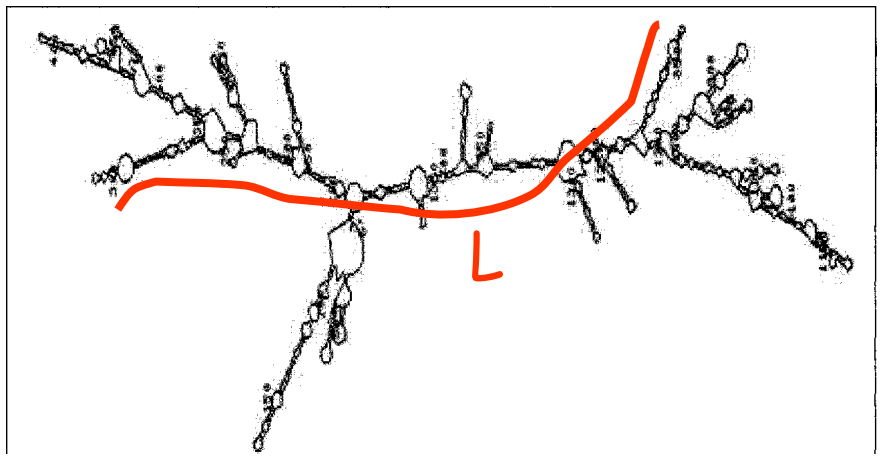
$$Z(p) = p\Lambda_1 + p\Lambda_3 Z^2(p)$$

1. Weakly challenging problem: solve quadratic equation and find Z(p)
2. More challenging: via proper integration in complex plane, reconstruct G_n from Z(p)
3. Find RNA free energy in this approximation.

P.-G. de Gennes, Biopolymers, v. 6, p. 715, 1968

Branched polymer: span is a new order parameter

Russian doll Flory theory



An old story: swelling of branched polymer

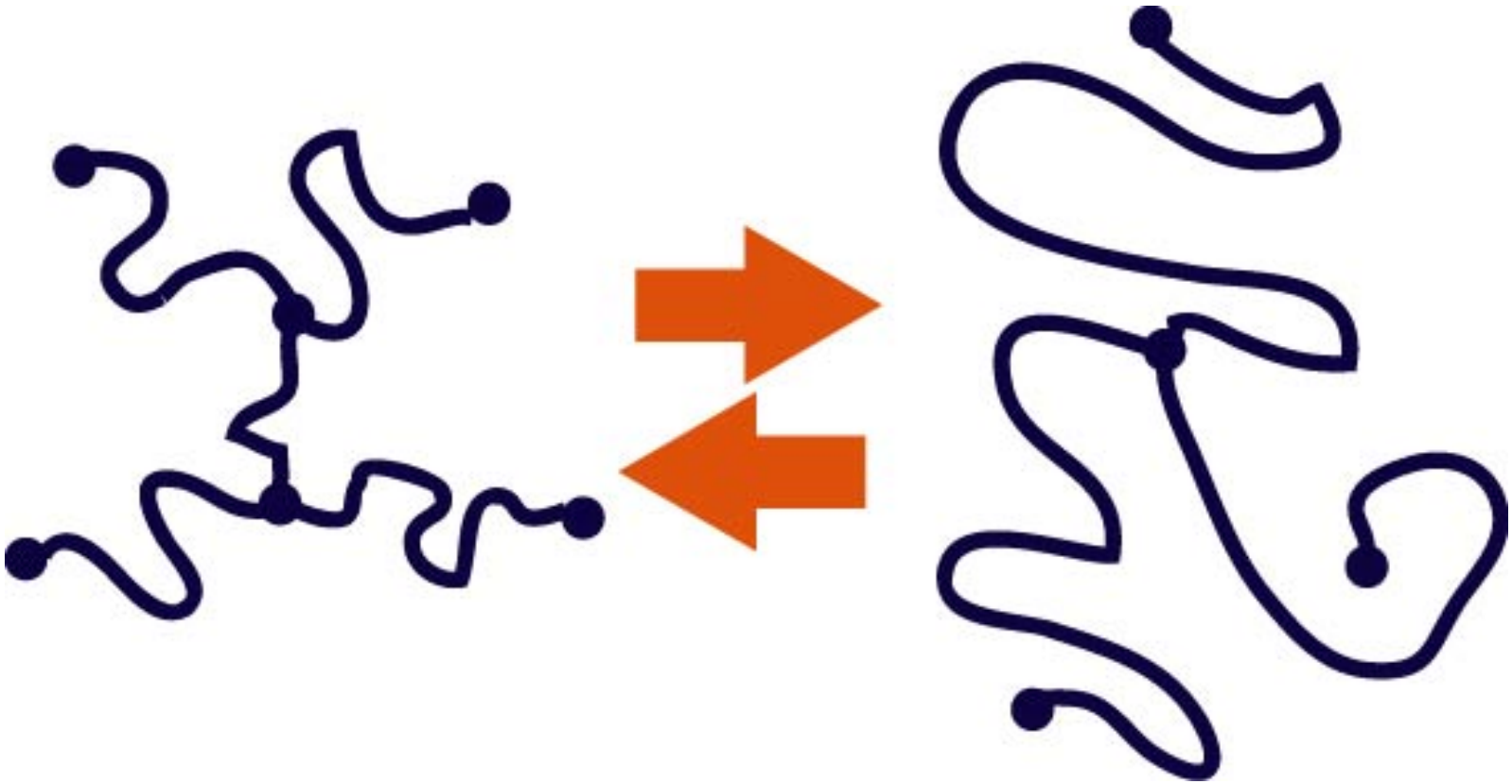
- Flory theory:

$$F/T = R^2/(a\,N^{1/4})^2 + v\,N^2/R^d$$

$R \sim N^{5/[2(d+2)]}$ $(R \sim N^{1/2}$ in 3D)

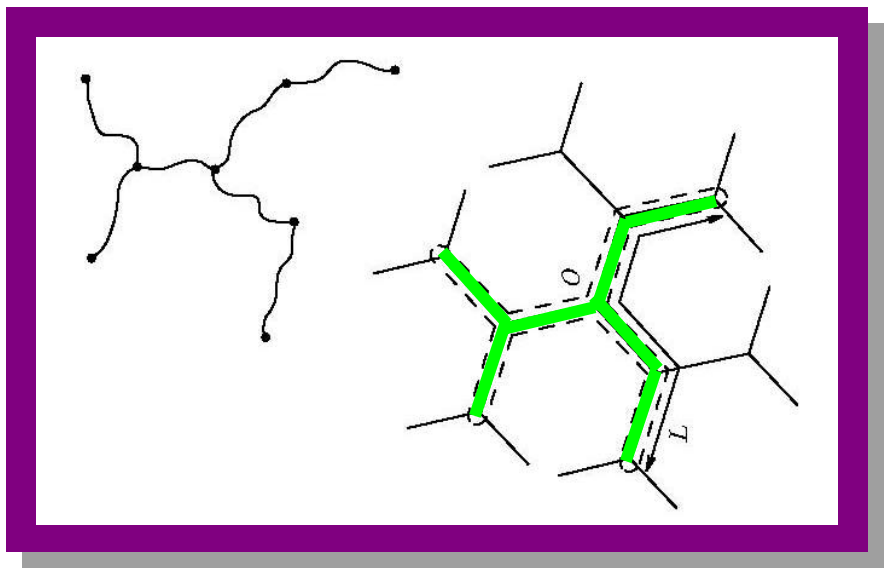
- Field theory: Parisi & Sourlas (1981)

A slightly newer story: annealed branched polymer



Annealed branched polymer

- Entropy has now TWO contributions:
  - Placement of polymer in space: $\sim R^2/L$ (span L plays the role of polymer length)
  - Re-distribution of branches = placement on Cayley tree: $\sim L^2/N$ (span L plays the role of spatial size)



Russian doll Flory theory

- Flory theory:

$$F/T = R^2/L + L^2/N + v\,N^2/R^d$$

$$L \sim R^{2/3} N^{1/3} \quad \text{and} \quad R \sim N^{7/[3d+4]}$$

- Span L does not depend on dimension;
- In 3D, $R \sim N^{7/13}$ compared at $N^{1/2}$ in quenched case. The difference is not so much in the power, but in principle and in a different outlook