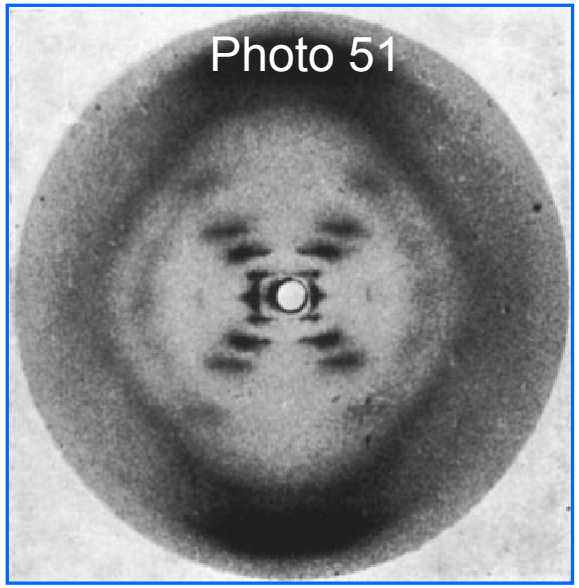
DNA: structure, dense phases, charges, interactions

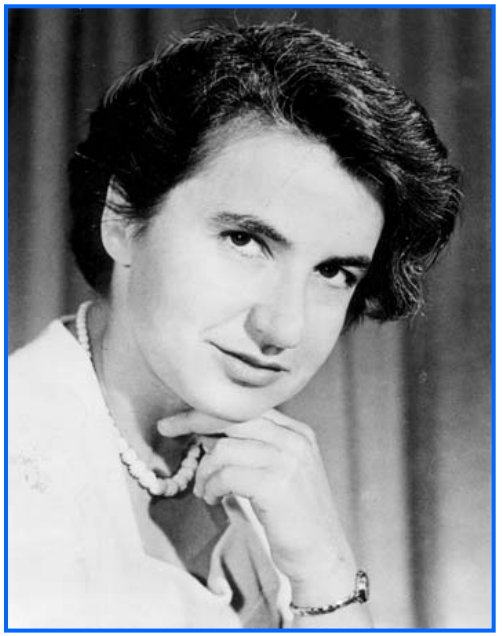
Outline

1. DNA: structure, charges, dense phases
2. Counterion and DNA condensation
3. ES DNA-DNA interactions
4. DNA toroidal structures
5. Interactions of real DNA helices
6. DNA-DNA ES recognition
7. DNA melting in aggregates
8. Azimuthal frustrations on DNA lattices
9. Dense phases of nucleosomes
10. PE model of *B*-*Z* DNA transition
11. DNA chiral phases
12. DNA-DNA ES friction

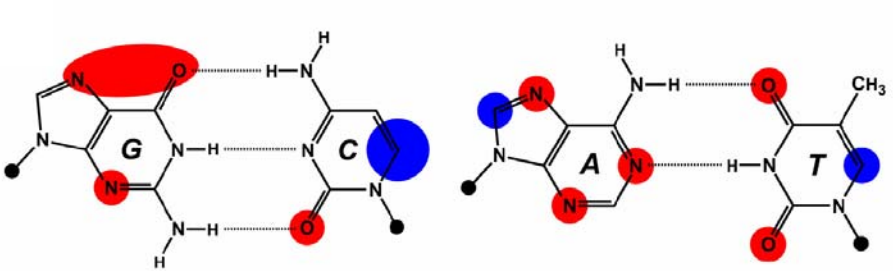
13. DNA-proteins: facilitated diffusion
14. DNA-proteins: ES complementarity
15. DNA-protein: ES PDB analysis

B-DNA is a double helix: Franklin → Crick+Watson+Wilkins





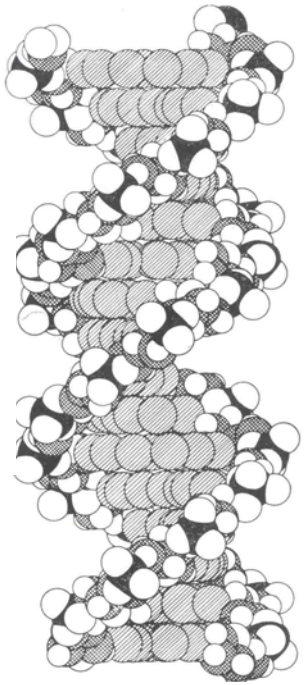
R. Franklin and R.G. Gosling,
Nature, 171 740 (1953)



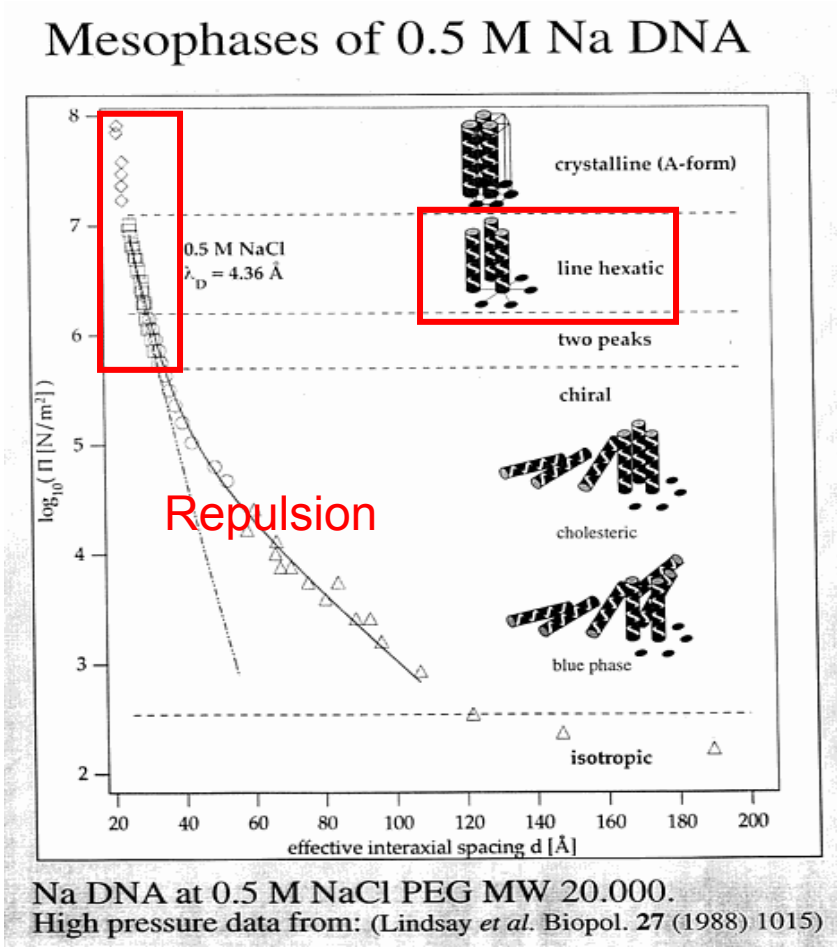
Helices in Biology

- DNA, collagen, guanosine, myosin, α-helices;
Tobacco Mosaic Virus, fd-virus, ...
- DNA: genetic code and storage
- Collagen: tissues (tendons, bones, skin, cornea)

Dense hydrated phases of B-DNA



Cations bind to DNA and compensate 70-90% (θ=0.7-0.9) of its charge. f is the fraction of cations in the *minor* groove.

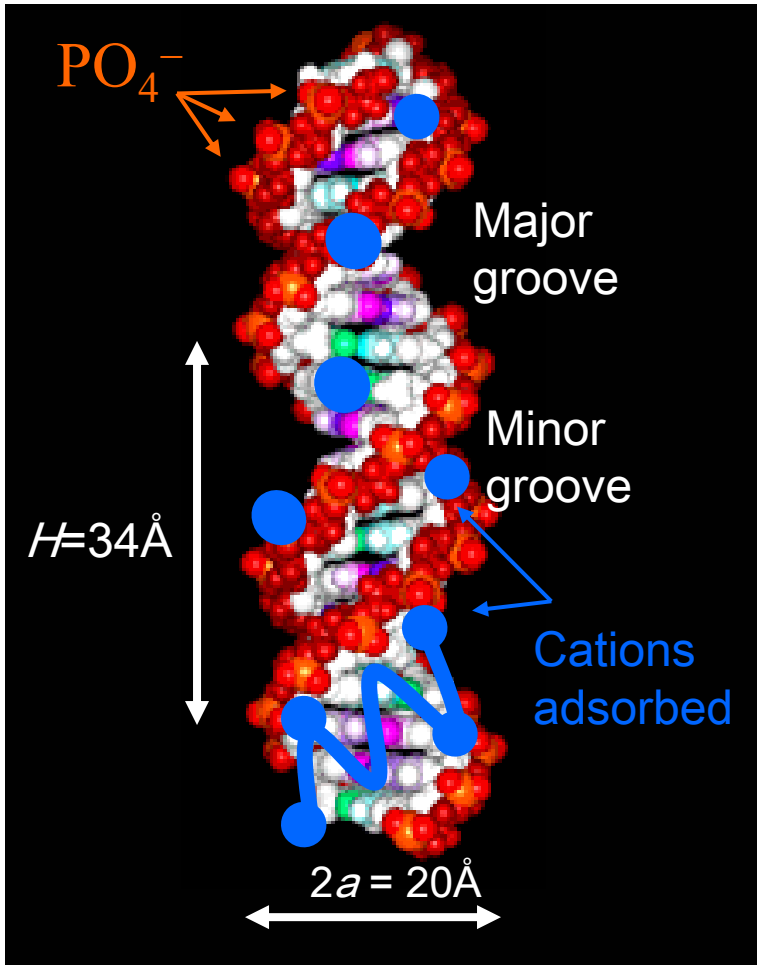


Osmotic stress experiments allow to measure DNA-DNA forces

B-DNA charge and non-ideality of its structure

$-1e_0$ per b=1.7 Å along DNA axis

$\sigma=-1e_0/nm^2$ on DNA surface



z=1:θ=76% 2:88% 3:92% 4:94%

The 10 Twist Angles of B-DNA

Dinucleotide	Twist Angle (h)
(AA) · (TT)	35.6 ± 0.1
(AC) · (GT)	34.4 ± 1.3
(AG) · (CT)	27.7 ± 1.5
(AT) · (AT)	31.5 ± 1.1
(CA) · (TG)	34.5 ± 0.9
(CC) · (GG)	33.7 ± 0.1
(CG) · (CG)	29.8 ± 1.1
(GA) · (TC)	36.9 ± 0.9
(GC) · (GC)	40.0 ± 1.2
(TA) · (TA)	36.0 ± 1.0

W. Kabsch et al., NAR, 10 1097 (1982)
W. K. Olson et al., PNAS, 95 11163 (1998)

Manning's theory of counterion condensation: dsDNA

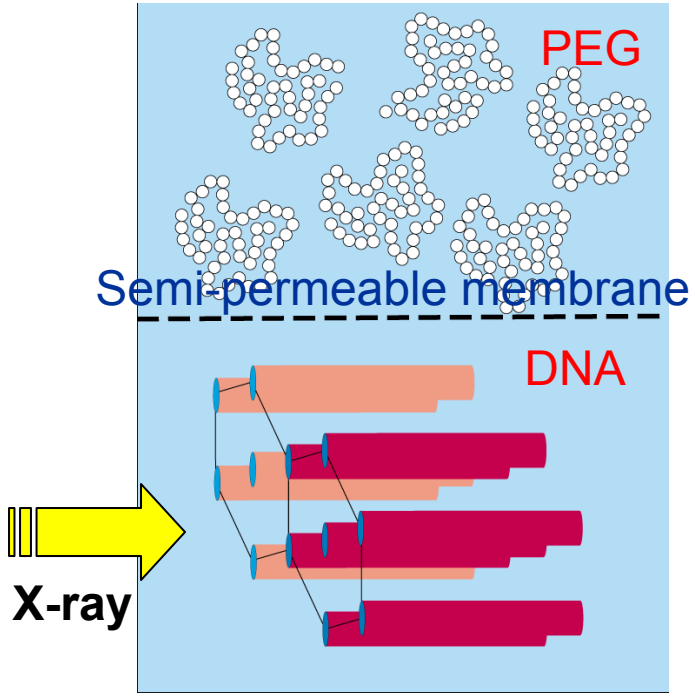
$\theta = 1 - 1/(z\xi)$, $\xi = l_B/b \approx 4.2$, $l_B = 7.1$ Å

- No salt
- Thin PE
- Only ES

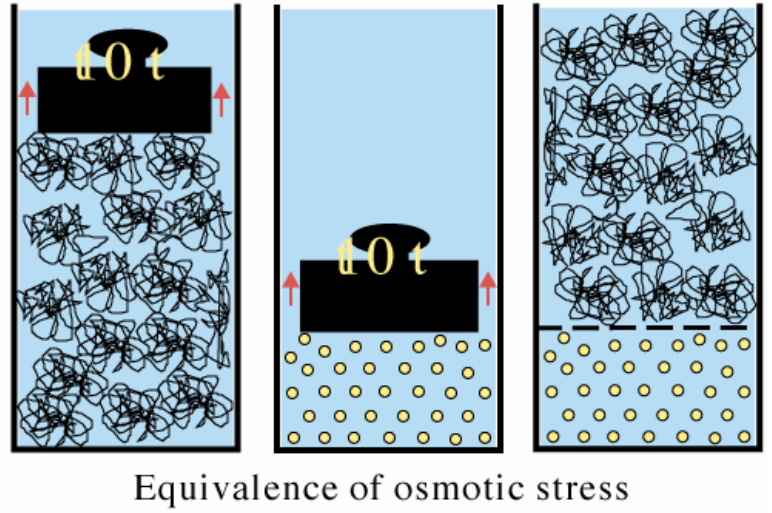
G. S. Manning, Q. Rev. Biophys.11, 179 (1978)

Osmotic stress for measuring DNA-DNA forces

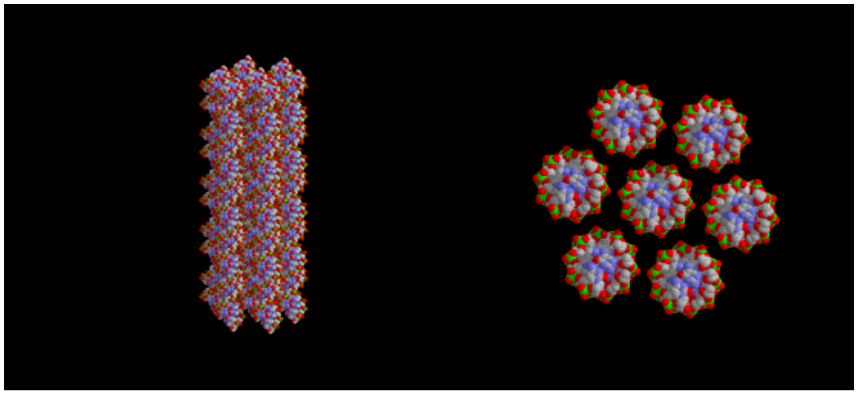
PEG exerts osmotic stress on DNA phase



Small ions can penetrate through the membrane. X-ray measures DNA-DNA separation

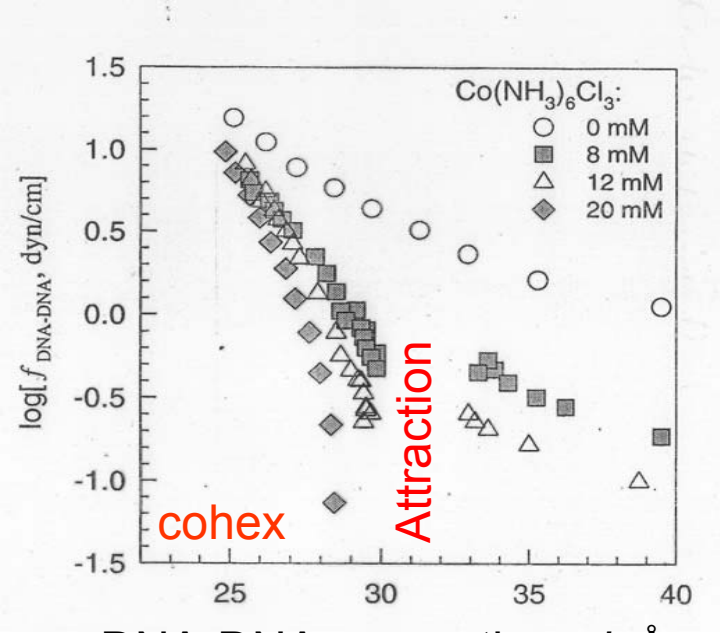


V. A. Parsegian, PNAS 1984

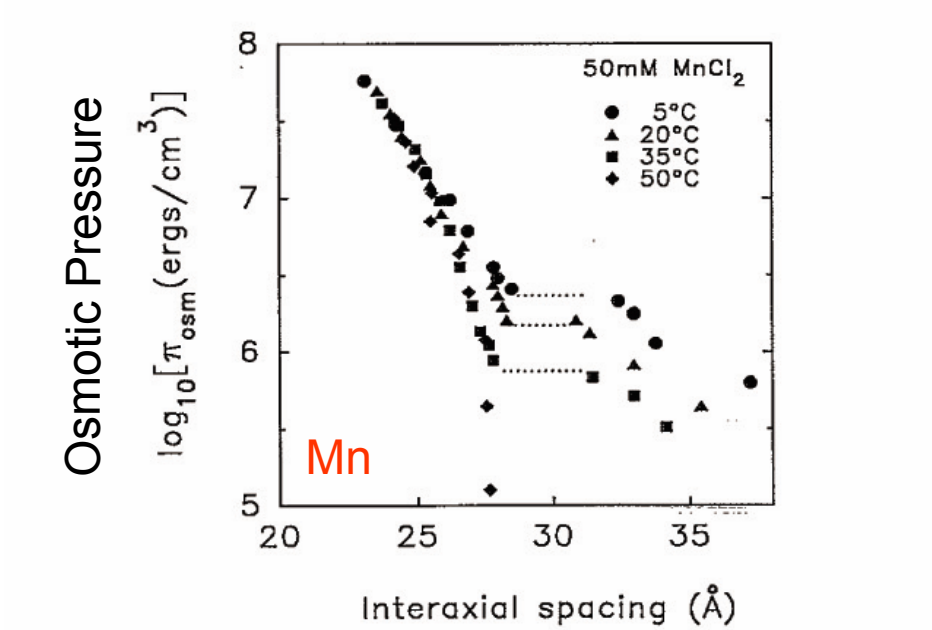


Structure of dense columnar DNA phases: last 20 Å before the contact

Multivalent cations condense B-DNA in dense assemblies: Osmotic Stress measurements *in vitro*



DNA-DNA separation, *d*, Å

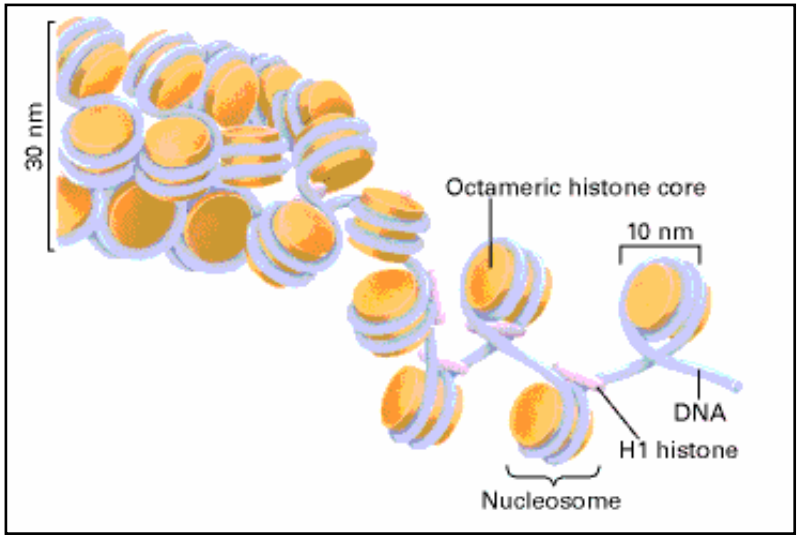


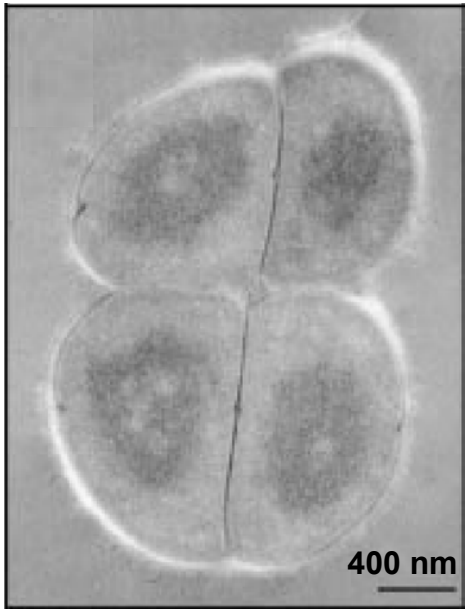
Attraction at ~30 Å
between DNA axes

Entropy-driven aggregation is also observed for collagen, myosin, HP-Cellulose

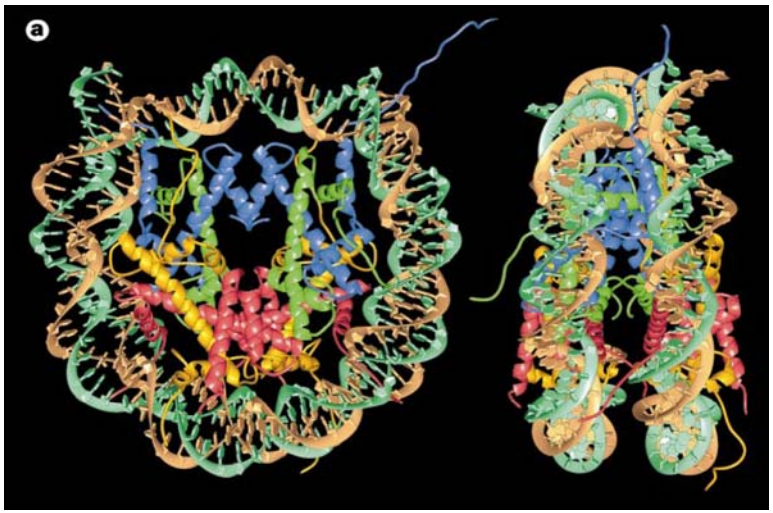
S. Leikin et al., Phys. Rev. A, 44 5272 (1991)

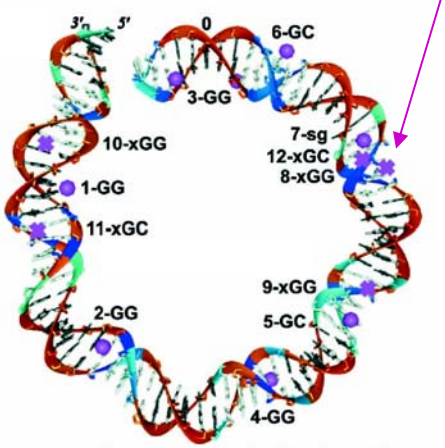
Dense DNA phases and packing in vivo

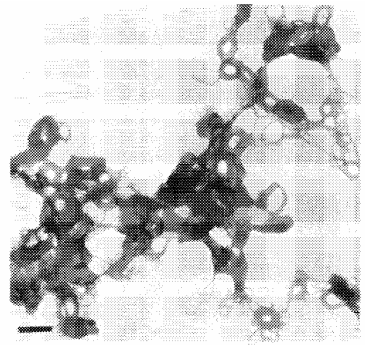




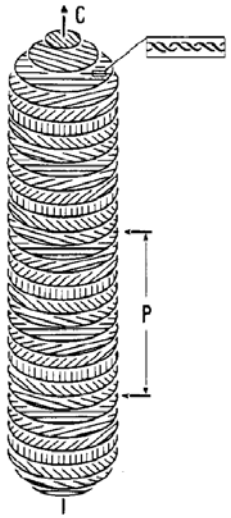
Deinococcus radiodurans:
DNA toroids + Mn2+







DNA in sperm:
protamines



Dinoflagellate (algae)

Screening in electrolyte solution: DH and Linear PB

$$\varphi(r) = \frac{e_0}{\varepsilon_0 r} \rightarrow \frac{e_0}{\varepsilon_0 r} e^{-\kappa r}$$

$$\kappa = \sqrt{8\pi l_B n_0} = \frac{\sqrt{I(M)}}{3\text{Å}} \qquad \kappa_{phys} = 1/7\text{Å}$$

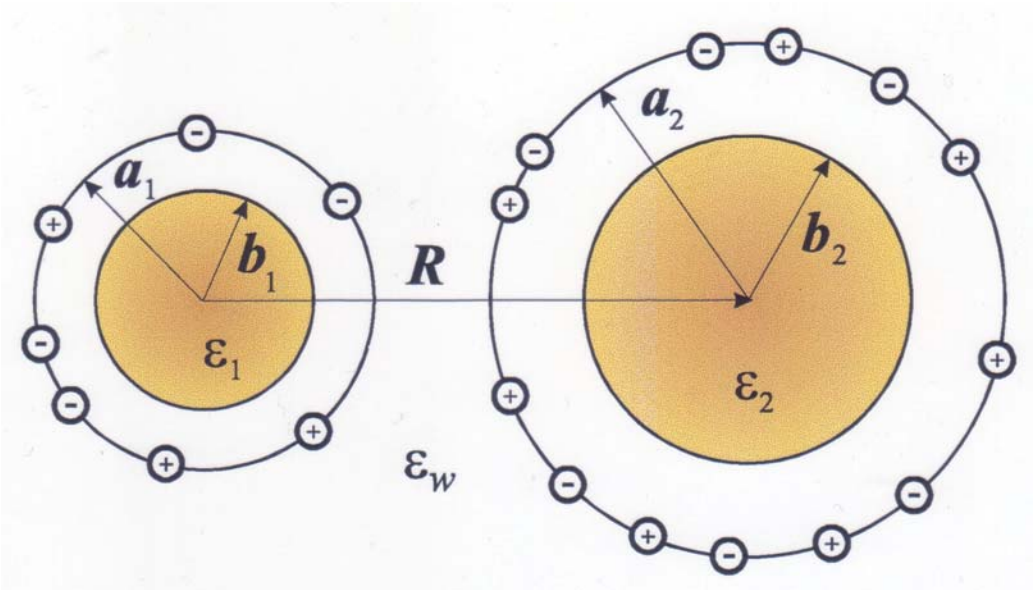
$$\psi = \frac{e_0 \varphi}{k_B T} \qquad \Delta\psi = 0 \rightarrow \Delta\psi = \kappa^2 \psi$$

$$dsDNA : -e_0 / 1.7\text{Å}$$

$$\sigma \sim e_0 / nm^2$$

Strong ES interactions

Theory of DNA-DNA ES interactions



- Debye-Hückel-Bjerrum approx.
- Ideal helices at *T*=0
- Continuous spiral of charges
- Linear PB equation

Solution

$$\Delta\varphi(\mathbf{r})-\kappa^2\varphi(\mathbf{r})=-4\pi\rho(\mathbf{r})/\varepsilon_w,$$

Low-dielectric Core

$$\Delta\varphi(\mathbf{r})=0$$

Boundary conditions

$$\varphi(b_\nu)=\varphi(b_\nu),\qquad \varepsilon_w\nabla_n\varphi(\mathbf{r})\Big|_{r=b_\nu}=\varepsilon_\nu\nabla_n\varphi(\mathbf{r})\Big|_{r=b_\nu}$$

A. A. Kornyshev and S. Leikin, J. Chem. Phys., 107 3656 (1997)

Exact solution for pair ES energy of B-DNA ideal spirals

System ES energy

$$E=\frac{1}{2}\int d\mathbf{r}\varphi(\mathbf{r})\rho(\mathbf{r})$$

Interaction energy

$$E_{\text{int}}(R)=E(R)-E(\infty)$$

Force

$$f=-\frac{\partial E_{\text{int}}(R)}{\partial R}$$

$$E\left(\delta\phi,R\right)=\frac{\left(4\pi\sigma_0\right)^2}{\varepsilon}\left[u_{cyl}\left(R\right)+u_{self}\left(R\right)+u_{cross}\left(\delta\phi,R\right)\right]$$

$$u_{cyl}\left(R\right)=\frac{\left(1-\theta\right)^2}{2\kappa^2}\frac{K_0\left(\kappa R\right)}{K_1^2\left(\kappa a\right)}$$

$$u_{cross}\left(\delta\phi,R\right)=\sum_{n=1}^{\infty}\left(-1\right)^n\cos^2\left[\frac{n\tilde{\phi}_s}{2}\right]\frac{\cos\left[n\delta\phi\right]K_0\left(\kappa_n R\right)}{\left[\kappa_n K_n^{'}\left(\kappa_n a\right)\right]^2}$$

$$u_{self}\left(R\right)=\sum_{n=1}^{\infty}\cos^2\left[\frac{n\tilde{\phi}_s}{2}\right]\frac{\sum_{j=-\infty}^{j=\infty}\left[K_{j-n}\left(\kappa_n R\right)\right]^2\frac{I_j^{'}\left(\kappa_n a\right)}{K_j^{'}\left(\kappa_n a\right)}}{\left[\kappa_n K_n^{'}\left(\kappa_n a\right)\right]^2}$$

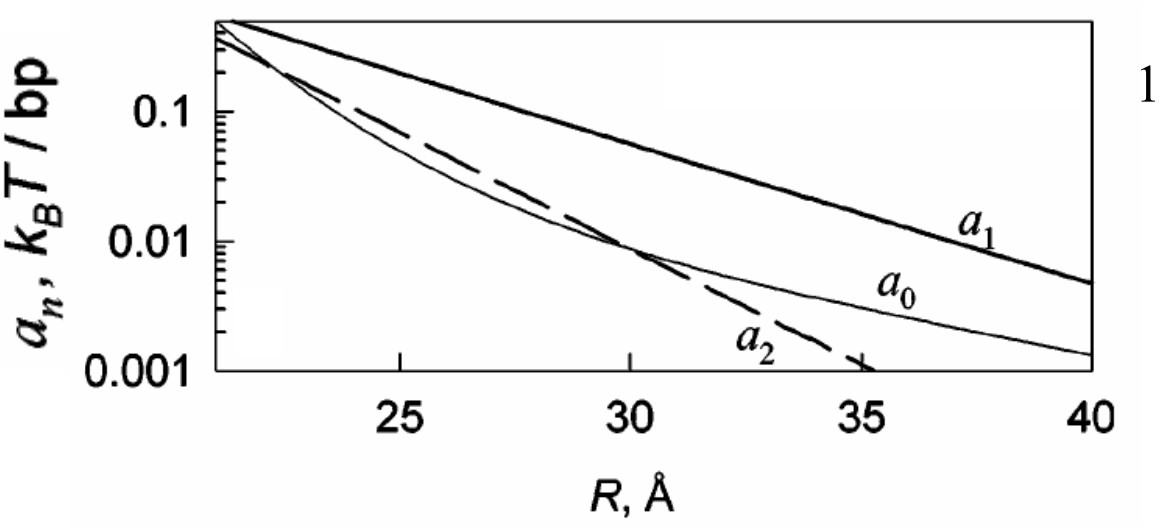
$\kappa_n=\sqrt{\kappa^2+n^2g^2},\ g=2\pi/H$ effective screening lengths

$\sigma=\sigma_0(1-\theta)$ Mean surface charge density

Strength of DNA-DNA ES interactions: axial shift $\delta z = \delta\phi H/(2\pi)$

attraction

$$E_{\text{int}}(\delta\phi, R) \approx \underbrace{a_0(R)}_{\text{cylinders}} \underbrace{- a_1(R)\cos[\delta\phi] + a_2(R)\cos[2\delta\phi]}_{\text{helices}}$$



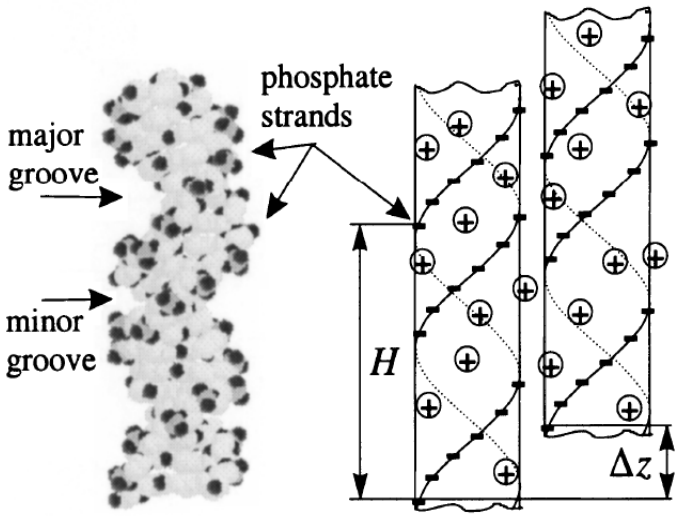
$$1/\kappa_D = 1/\sqrt{8\pi l_B n_0} \approx 7\,\text{Å}$$

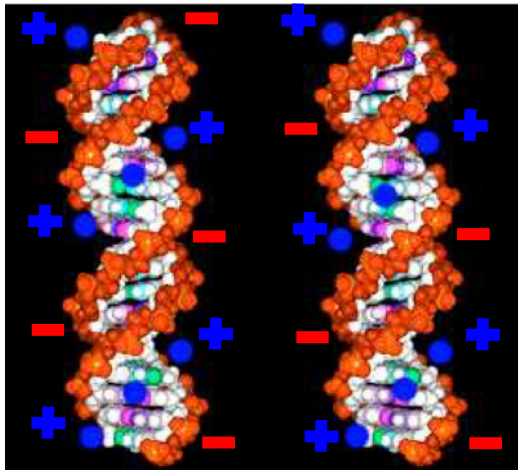
θ=90%

f=30%

- Nearly exponential decay of $a_n(R)$
- a_1 term dominates for large θ and small f

Zipper-like motif of DNA-DNA attraction: register of ideal helices





Positive
Negative

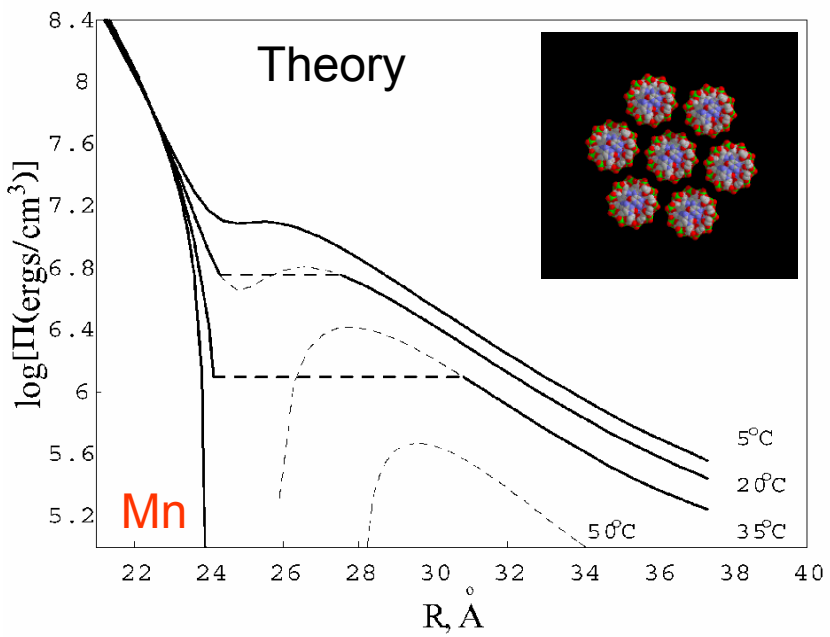
Charge zipper established along *homologous* DNAs

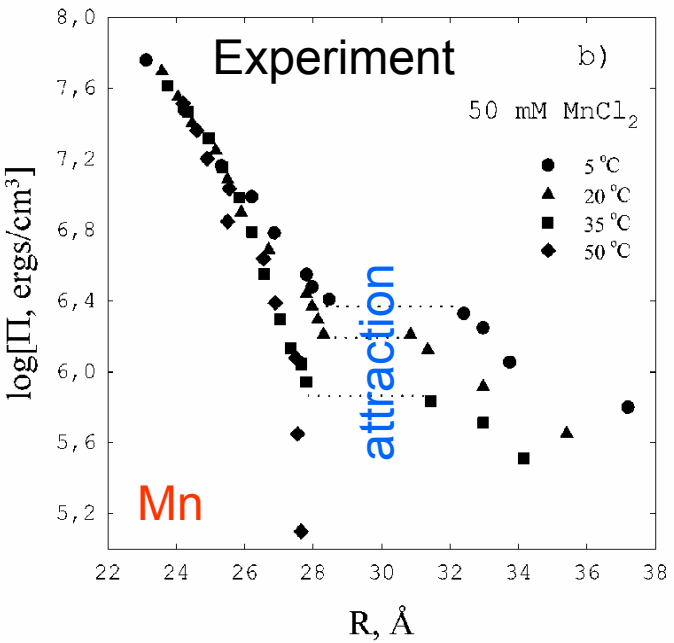
- Axial separation of +/- charges: closest charges are of opposite sign
- ES Attraction: Phosphate strands of one DNA are in *register* with adsorbed cations in grooves of another DNA. Charge density waves
- Cations in *major* groove - stronger attraction - better charge separation along DNA
- Experiments: DNA-condensing cations do prefer DNA major groove (Mn 2+, cohex 3+, spermine 4+, etc.)

A. A. Kornyshev and S. Leikin, PRL 82, 4138 (1999)

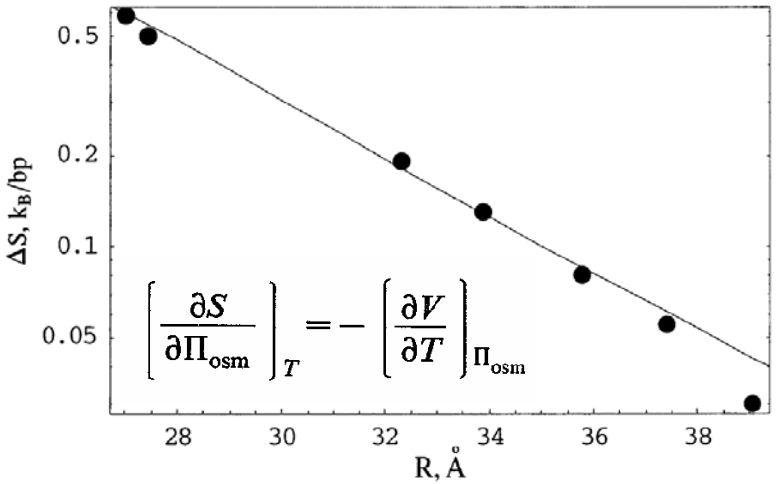
T-induced DNA-DNA attraction: cations' repartitioning

Osmotic Pressure





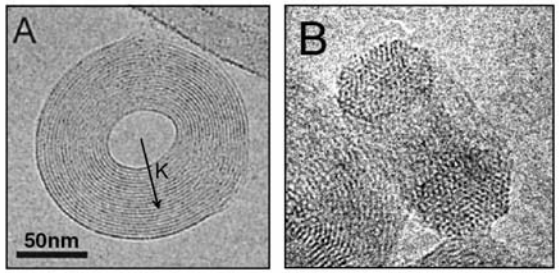
Entropy Difference



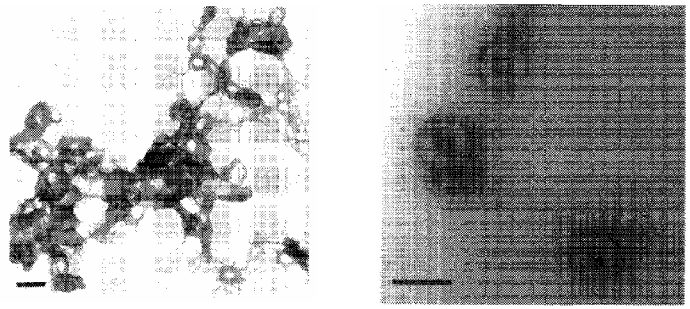
- Mn can bind in both DNA grooves
- In major groove Mn has larger entropy and such DNAs ES attract better
- With T and lattice compression Mn prefer major groove
- Exponential entropy increase: 3-5 Mn2+ per pitch H go from DNA minor to major groove

A.G.C., S.L., A.A.K., J. Phys. Chem. B, 106 13362 (2002)

DNA toroids in 3D: *in vitro* and *in vivo*



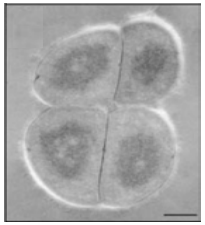
Bar = 100 nm



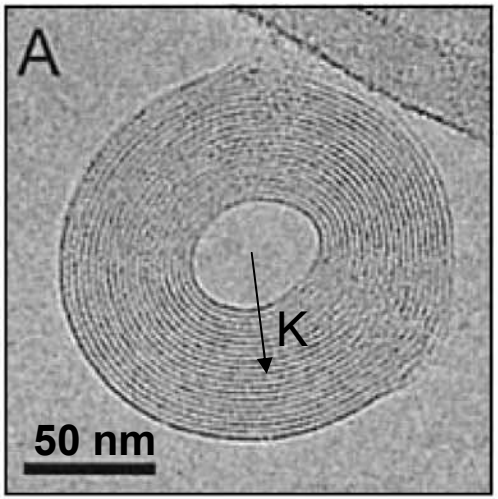
- Cryo-EM imaging
- Multivalent cations (spermine^{4+}, spermidine^{3+}, cohex^{3+}, etc.)
- Optimal toroid: 2-3 λ-DNAs
- Resolubilization by simple salt
- PEG + Mn^{2+} condenses DNA
- DNA+ cation^{1+}: never does!

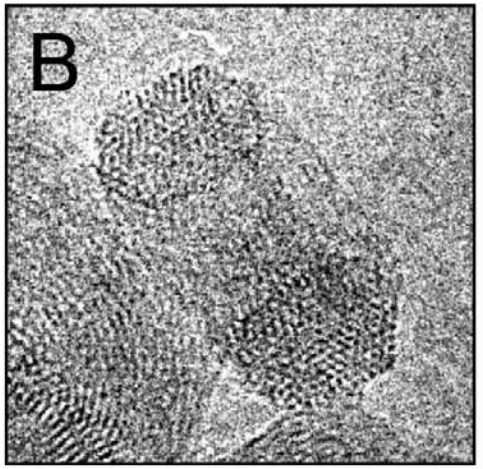
- AFM and TEM of DNA in mammalian sperm
- Native and reconstituted chromatin
- Protamine is >95% of nuclear proteins
- 20(!) Arg^{+} out of 30 protein residues
- Toroidal unit is 60 kbp of DNA
- Full man genome: ~50000 packed tori

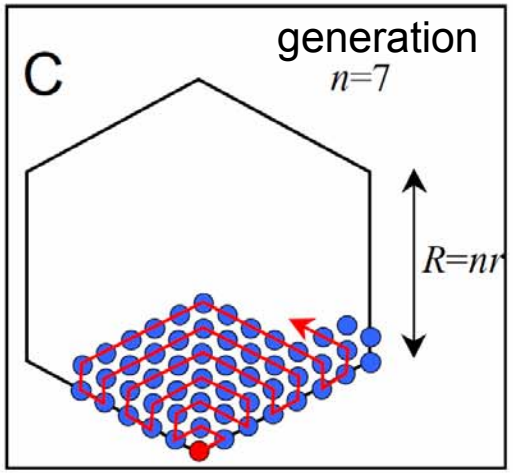
N. Hud et al., PNAS, 98 14925 (2001)
N. Hud et al., Biochem. Biophys. Res., 193 1347 (1993)
A. Cherstvy, J. Phys.: Cond. Matt., 17 1363 (2005)



DNA toroids and DNA-DNA attraction



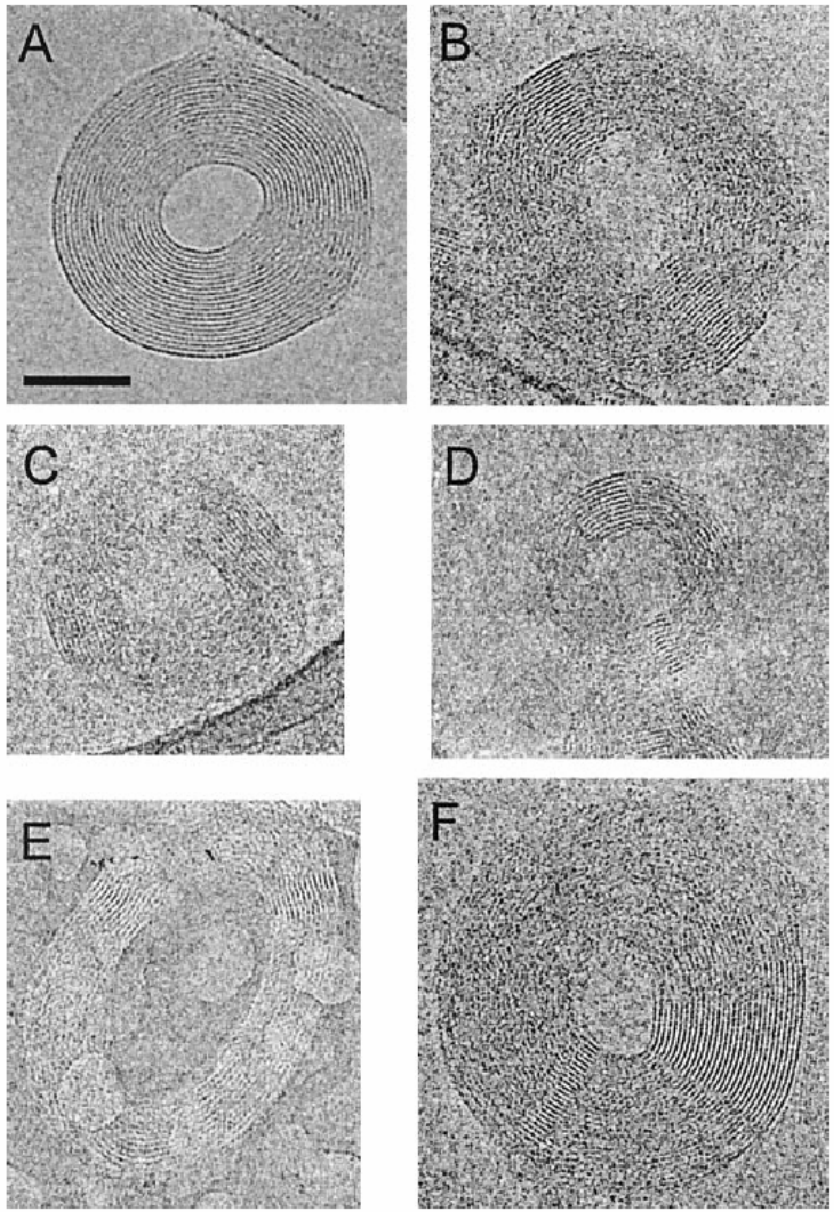


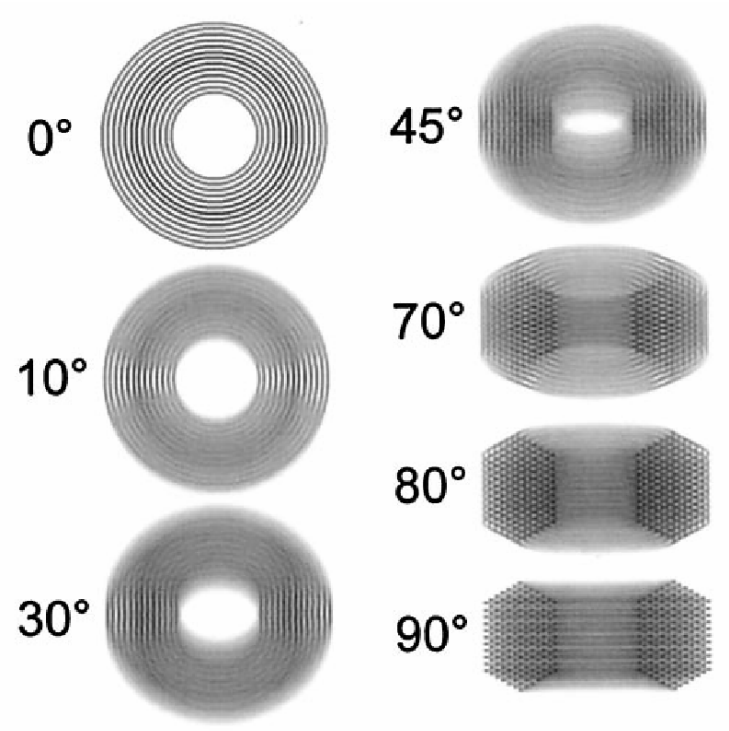


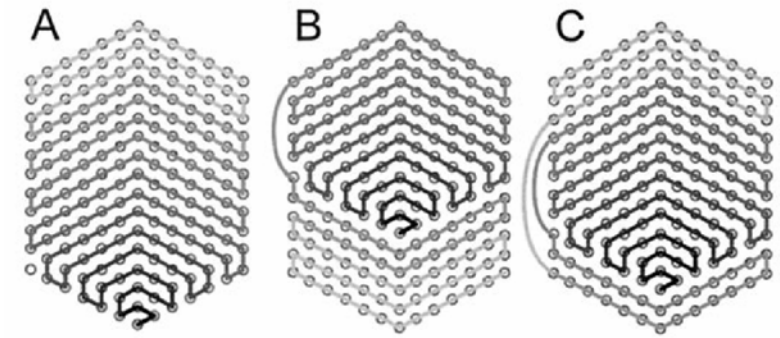
- λ phage DNA: 48 kbp
- 0.2 mM of cohex 3+

• Hexagonal cross-section maximizes the # of inner DNA turns with 6 neighbors (outer turns: 3-4 neighbors)
• DNA-DNA separation in toroids r = 28Å: attraction in aggregates
• More salt ⇒ weaker ES attraction ⇒ larger toroids
• Persistent chains ⇒ Larger E bending ⇒ larger toroids

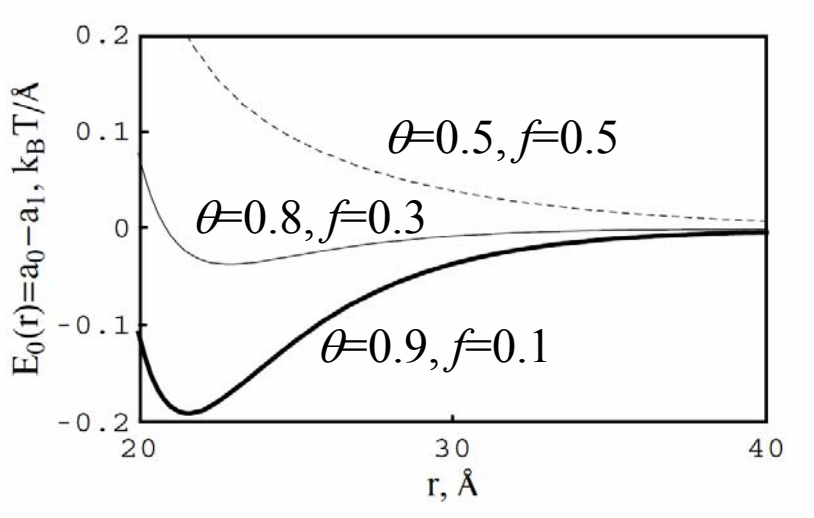
N. V. Hud et. al., PNAS, 98 14925 (2001)


A
B
C
D
E
F


0°
10°
30°
45°
70°
80°
90°


A
B
C

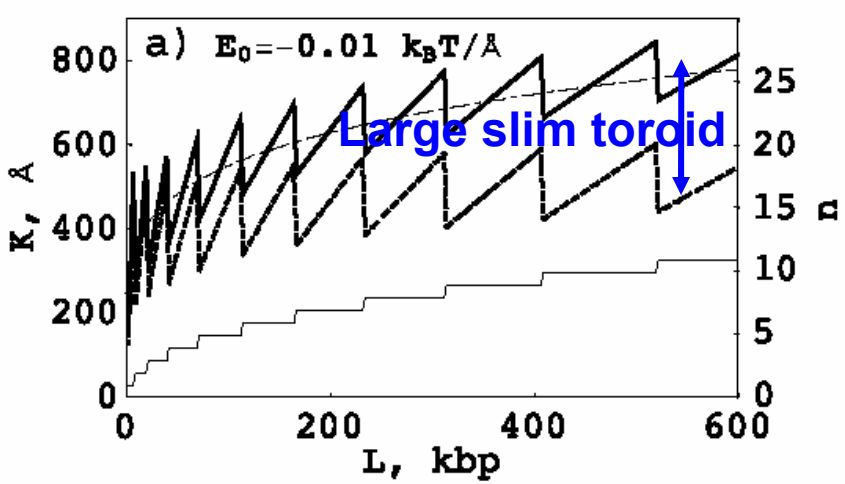
Strength of DNA attraction E_0 controls toroidal size

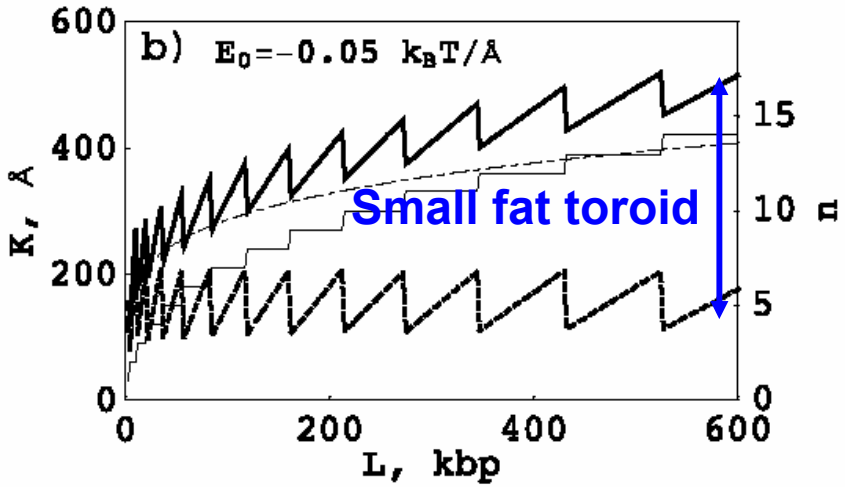


$$n \propto |E_0|^{1/5} L^{2/5} l_p^{-1/5}$$

$$K \propto |E_0|^{-2/5} L^{1/5} l_p^{2/5}$$

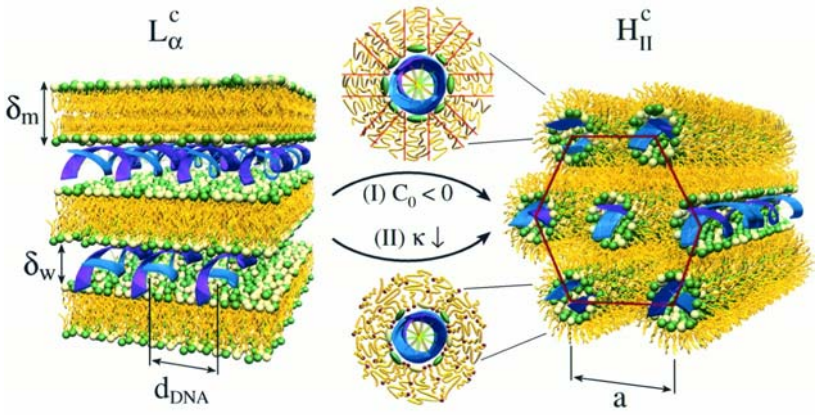
Consistent with experiments!

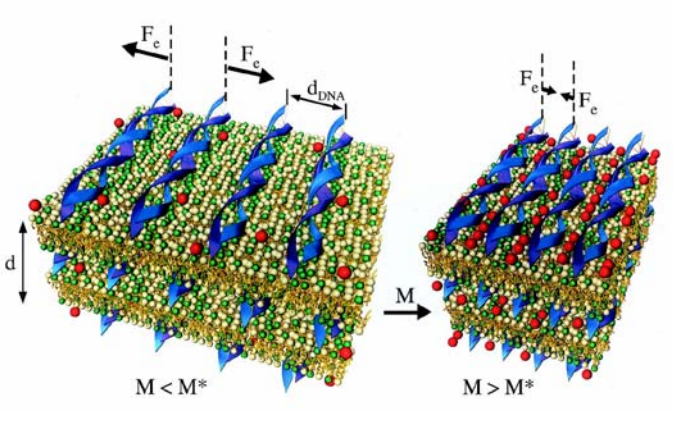


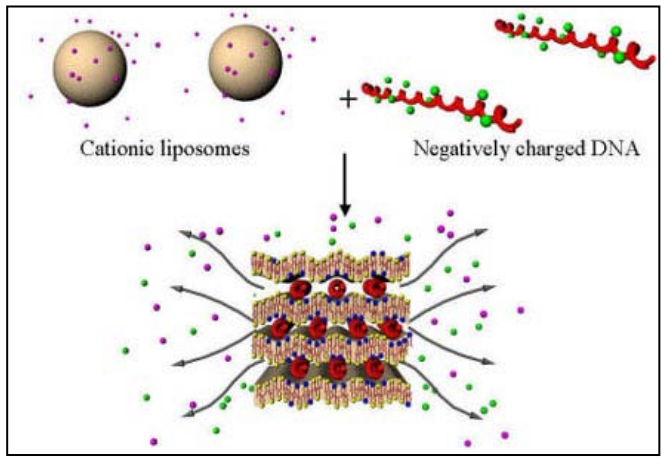


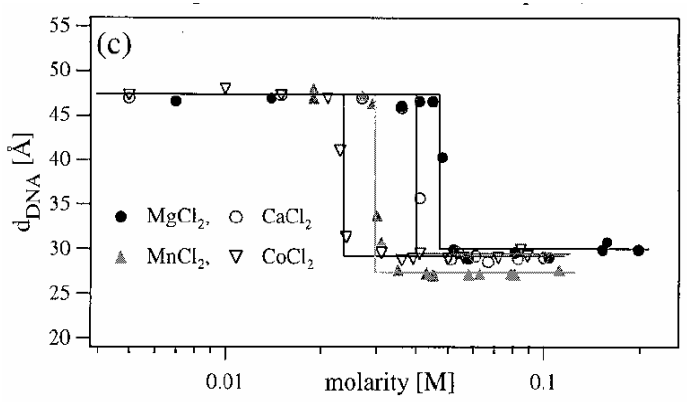
A. G. C., J. Phys.: Cond. Matt., 17 1363 (2005)

DNA assembly with cationic lipid membranes









I. Koltover et al., PNAS 97, 14046 (2000)

- Electro-neutrality + counterion release are the driving forces for assembly
- CL + {DNA, actin, microtubuli, filamentous viruses (fd, M13)}
- DNA-(CL membrane) complexes are gene therapy vectors (lung cancer)

A. G. Cherstvy, J. Phys. Chem. B, 111 7914 (2007)

Interaction of *non-ideal* and torsionally *soft* DNA

The 10 Twist Angles of B-DNA

Dinucleotide	Twist Angle (h)
(AA) · (TT)	35.6 ± 0.1
(AC) · (GT)	34.4 ± 1.3
(AG) · (CT)	27.7 ± 1.5
(AT) · (AT)	31.5 ± 1.1
(CA) · (TG)	34.5 ± 0.9
(CC) · (GG)	33.7 ± 0.1
(CG) · (CG)	29.8 ± 1.1
(GA) · (TC)	36.9 ± 0.9
(GC) · (GC)	40.0 ± 1.2
(TA) · (TA)	36.0 ± 1.0

Real DNA is not an ideal duplex: local DNA twist angles depend on DNA sequence and affect DNA-DNA ES forces

DNA torsional elasticity modulus: $C \approx 3 \times 10^{-19}$ erg cm or $\lambda_{tw} \approx 750$ Å.
[D.S. Horowitz *et al.*, J. Mol. Biol., 173 75 (1984)]

Challenge: Will realistic DNAs still attract one another?

A.G.C., A.A.K, S.L., J. Phys. Chem. B, 108 6508 (2004)

ES interaction of randomly sequenced DNAs

Model: twist angles $\delta\Omega$ build a *random walk* on DNA, twist softness relaxes mutual twist mismatch and restores the ideality of helical patterns

$$\Omega_i(z) = \langle\Omega\rangle \pm \Delta\Omega,\ \langle\Omega\rangle = 36^\circ,\ \Delta\Omega \approx 4 \div 6^\circ$$

is the fingerprint of the sequence

$$\delta\Omega = \Omega_1 - \Omega_2$$

Total energy $$E(L) = E_{\text{int}}(L) + E_{t,1}(L) + E_{t,2}(L)$$

z-local Interaction energy $$E_{\text{int}}(R,L) \approx \int_0^L dz\left\{a_0(R) - a_1(R)\cos\left[\delta\phi(z)\right] + a_2(R)\cos\left[2\delta\phi(z)\right]\right\}$$

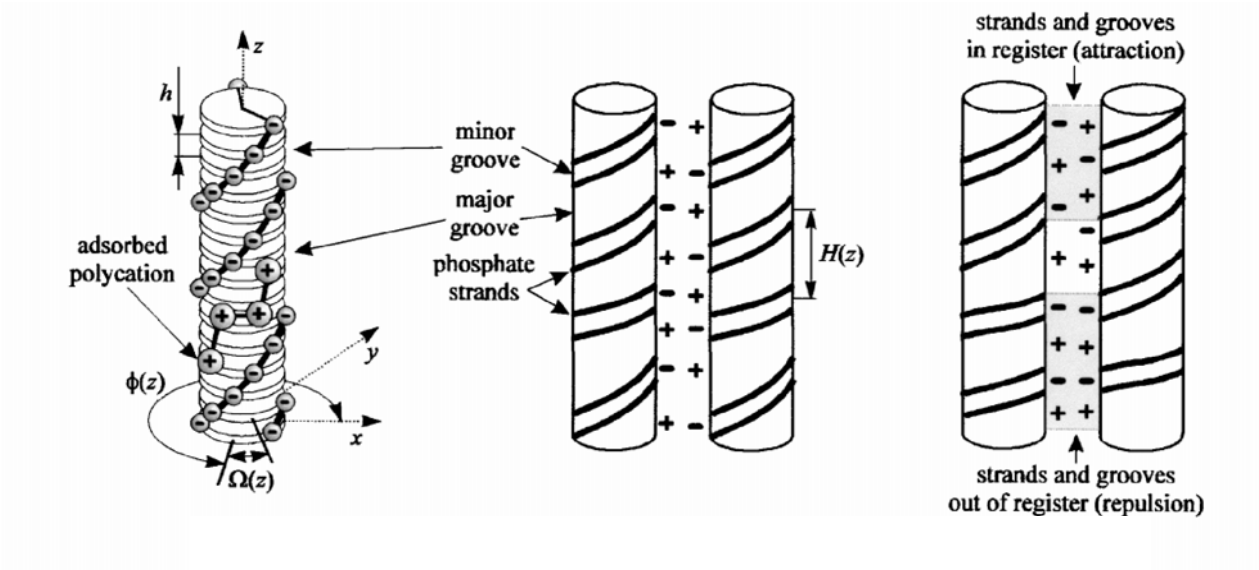
Torsional energy $$E_{t(i=1,2)} = \frac{C}{2}\int_0^L dz\left(\frac{d\Phi_i(z)}{dz} - \frac{\Omega_i(z)}{h}\right)^2$$

Euler Equation $$\lambda_t^{\,2}\frac{d^2(\delta\phi)}{dz^2} - \sin(\delta\phi)\left\{1 + \frac{8a_2}{a_1 - 4a_2}\sin^2(\delta\phi/2)\right\} = \frac{\lambda_t^2}{h}\frac{d(\delta\Omega)}{dz}$$

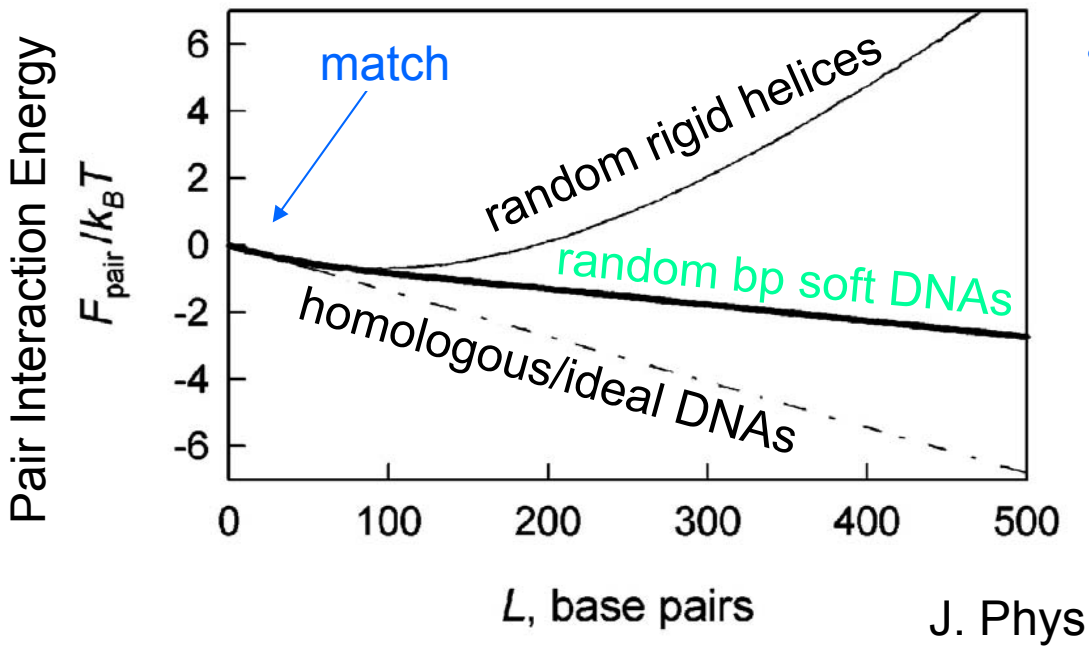
$$\delta\phi(\delta\Omega) \Rightarrow \left\langle E_{\text{int}}(\delta\phi) + E_t(\delta\phi)\right\rangle_{\delta\Omega}$$

$$\lambda_t = \sqrt{\frac{C}{2(a_1 - 4a_2)}}$$

Interaction of non-ideal and torsionally soft helices



$$\lambda_c = h/\Delta\Omega^2 \approx 300-700 \text{ Å}$$



- Homology exists for DNA lengths $L \leq \lambda_c \approx$ 300-700 Å
- DNA torsional adaptation restores ES attraction for non-ideal DNAs

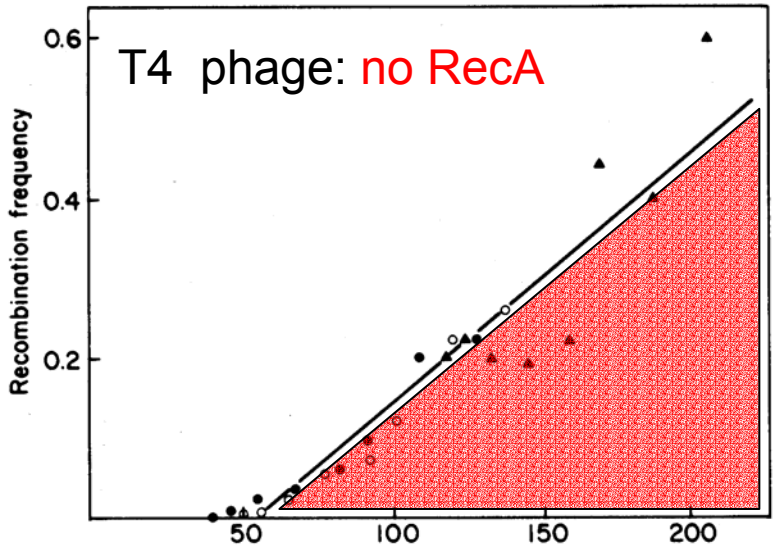
PRL, 86 3666 (2001)
J. Phys. Chem. B, 108 6508 (2004)

ES mechanism of dsDNA-dsDNA recognition

Juxtaposition of homologous DNA sequences is a precursor stage of homologous recombination.
How DNA find each other in solution and align, to repair breaks of strands?

Dogma: “We know only one mechanism for nucleic acids to recognize one another on the basis of sequence: complementarity between single strands” [B. Lewin, *Genes*, 1997]

A mystery of DNA homologous recombination

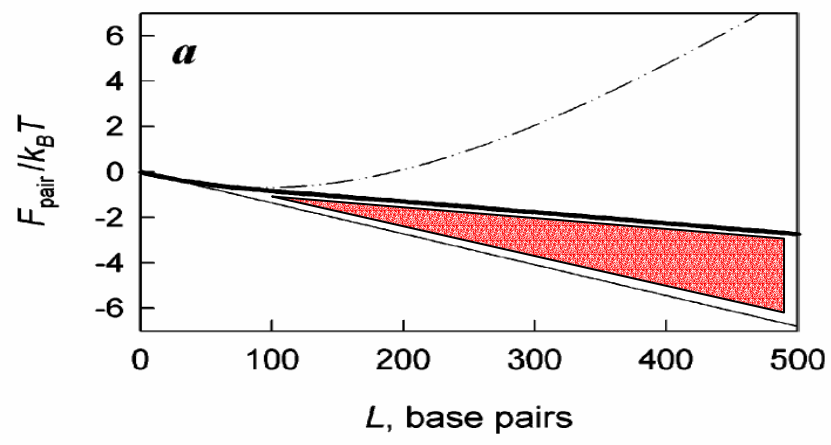


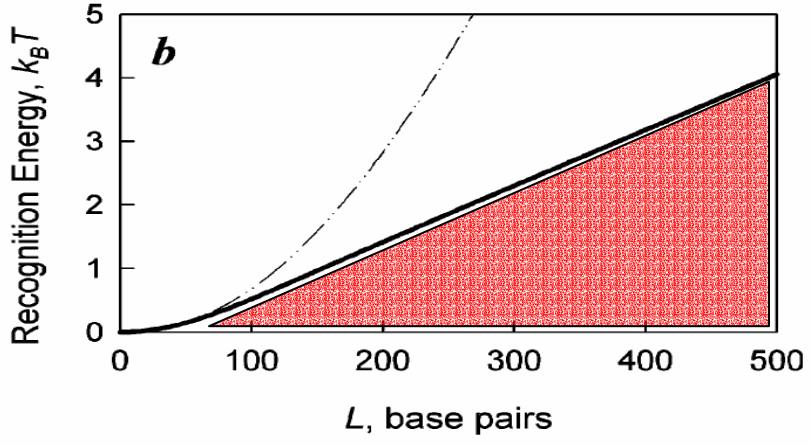
Homologous recombination in *E.coli*, T4 phage, and in mammalian cells occurs more frequently for longer lengths of DNA homology

Can intact homologous DNA duplexes recognize each other from a distance?

B.S. Singer et al., Cell, 31 25 (1982)

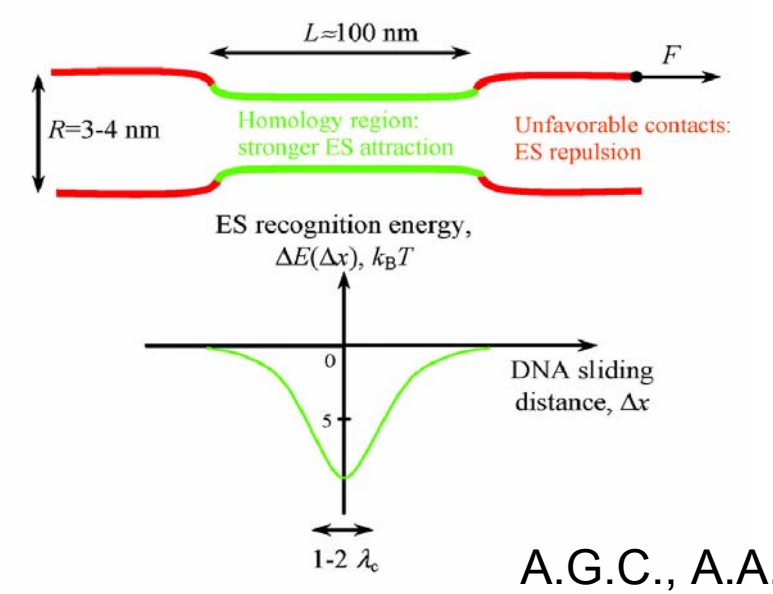
“Snap-shot” gene-gene ES recognition from a distance





Interaction energy depends nonlinearly on the length of DNA sequences, *L*.

Longer helices recognize each other better

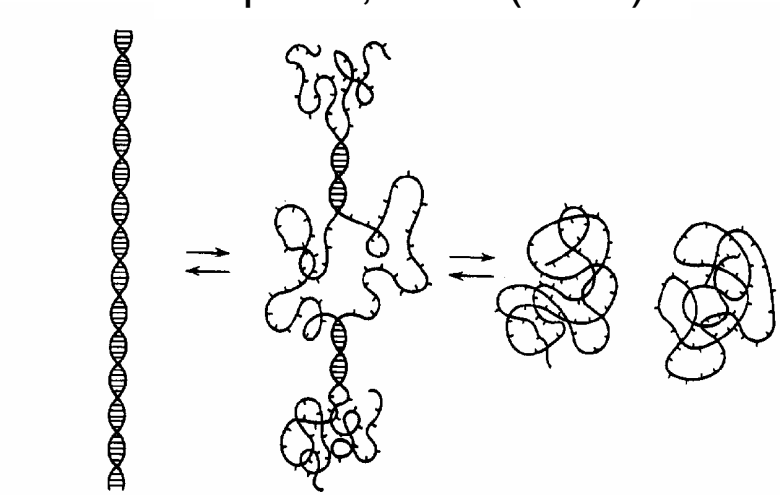


Direct experimental verifications are needed!

A.G.C., A.A.K, and S.L, J. Phys. Chem. B, 108 6508 (2004)
A. G. C., Phys. Chem. Chem. Phys., 13 9942 (2011)

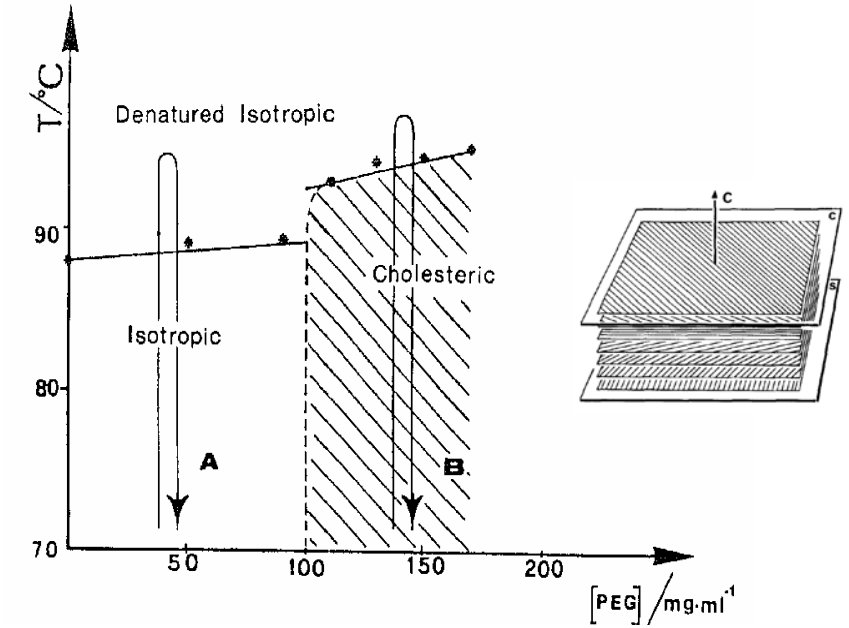
DNA melting in dense assemblies: fibers like in 1953

Y.S. Lasurkin et. al.,
Biopol. 9, 1253 (1970)



At elevated T, partially melted DNA in solution is the sequence of alternating melted and helical regions.

D. Grasso et al.,
Liquid Cryst, 9 299 (1991)



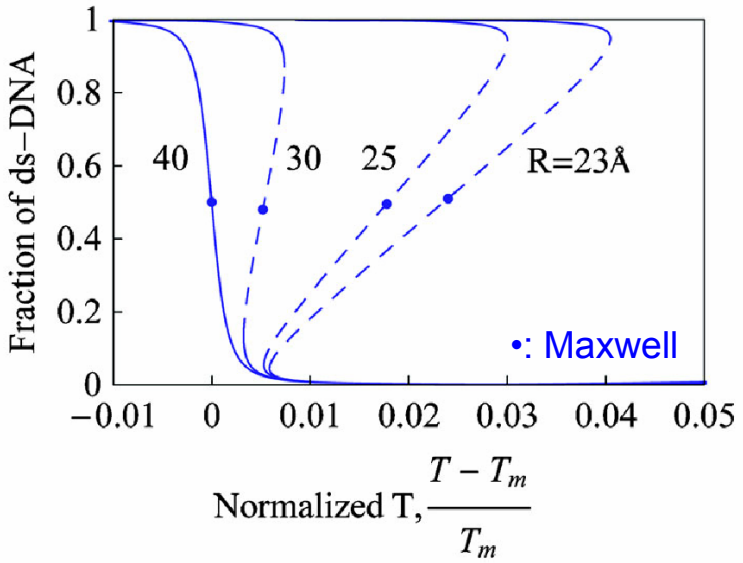
DNAs melt at higher T in dense liquid-crystalline state

- How intermolecular interactions affect DNA melting in aggregates?
- Do homologous and unrelated DNA fragments melt differently?

DNA melting in the presence of mutual ES interactions

$$F_0 = nF_s + N_m F_m + N_h F_h + k_B T\left\{ n\ln\frac{n}{N_m} + (N_m - n)\ln\frac{N_m - n}{N_m} + n\ln\frac{n}{N_h} + (N_h - n)\ln\frac{N_h - n}{N_h}\right\}.$$

$$E_{\text{int}}(N_h, n) = n a_0^{\,m}(R) l_m + n a_0(R) l_h - n a_1(R) \begin{cases} 2\lambda_c\left[1 - \exp\left(-\dfrac{l_h}{2\lambda_c}\right)\right], & \text{rigid sequences} \\ l_h\left[1 - \dfrac{\lambda_f}{2\lambda_c}\right] + \dfrac{\lambda_f^2}{2\lambda_c}\left[1 - \exp\left(-\dfrac{l_h}{\lambda_f}\right)\right], & \text{soft sequences} \\ l_h, & \text{ideal sequences} \end{cases}$$



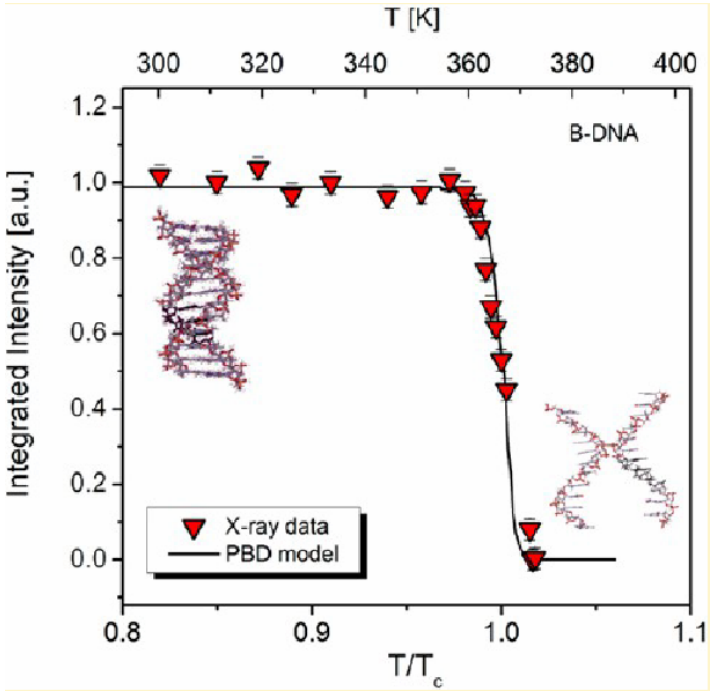
- Ideal DNAs attract each other that hampers their melting. Melting T rises by several degrees, $\Delta T_m \approx 3(a_0\text{-}a_1)h/12k_B > 0$

- Melting of non-ideal rigid DNA is strongly enhanced -- DNA nicking/cracking at room *T*

A. G. Cherstvy, Phys. Chem. Chem. Phys., 13 9942 (2011).

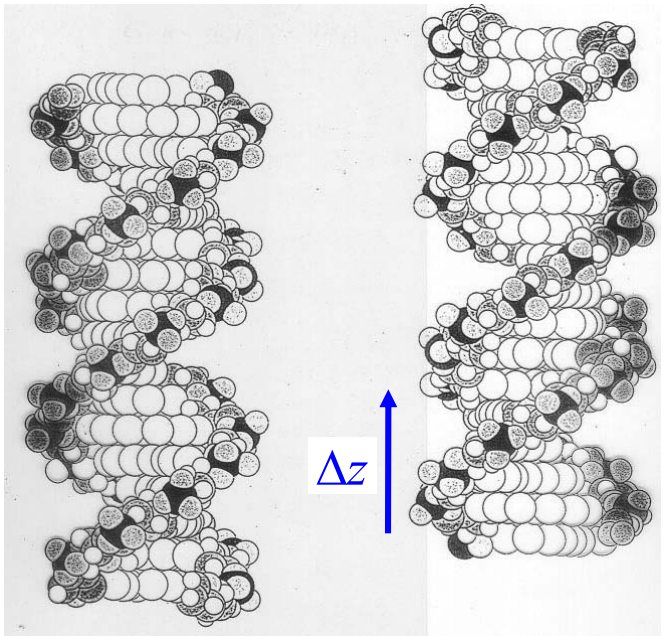
Experimental verification: T_m increases in dense fibers!

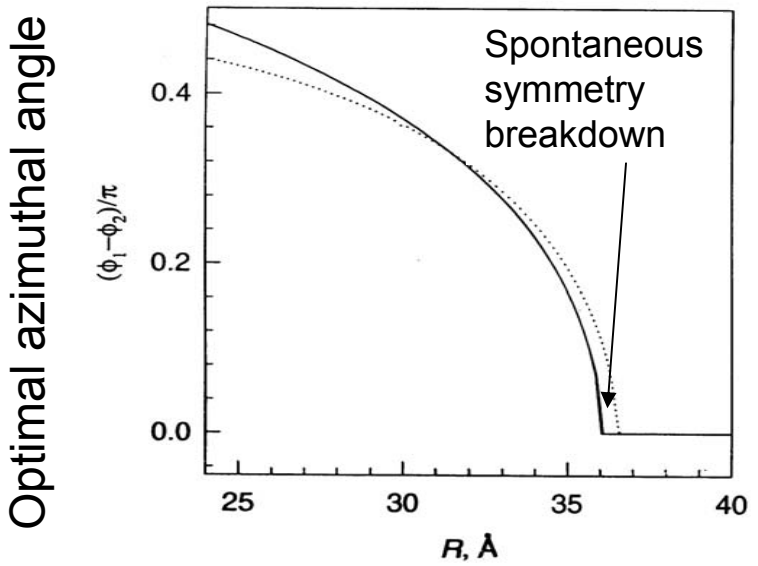
In this regard Cherstvy and Kornyshev predicted that intermolecular electrostatic interactions would possibly prevent DNA melting in dense aggregates.[41] In fact, in excellent agreement with their calculations for an interhelical distance of 25 Å we observe an upward shift of about 5.5 K (1.5%) in the melting temperature of B-DNA with respect to that measured in dilute solutions of DNA sodium salt from salmon testes (about 360.5 K), as reported by Sigma-Aldrich (St. Louis, MO).



F. Sebastiani et al., J. Phys. Chem. B 118, 3785 (2014).

Two parallel DNA: azimuthal alignment





$$\Delta z = \delta\phi \, H / (2\pi)$$

DNA axial shift = azimuthal rotation

$$E_{\text{int}}(\delta\phi, R) = E_{\text{int}}(R) + \delta E_{\text{int}}(\delta\phi, R)$$

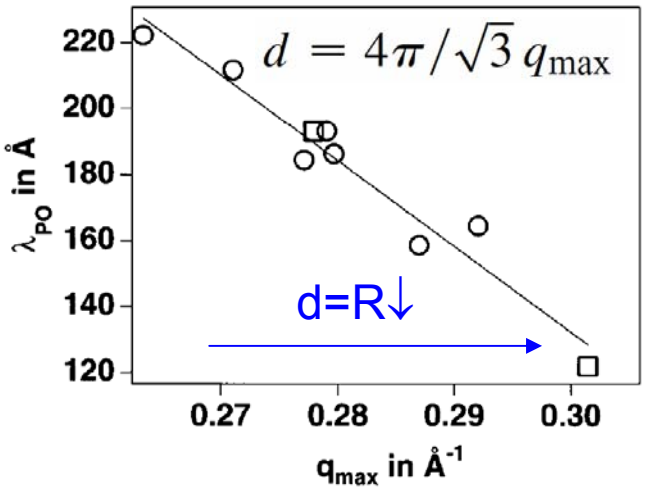
$$\delta E_{\text{int}}(\delta\phi, R) \approx -a_1(R)\cos[\delta\phi] + a_2(R)\cos[2\delta\phi]$$

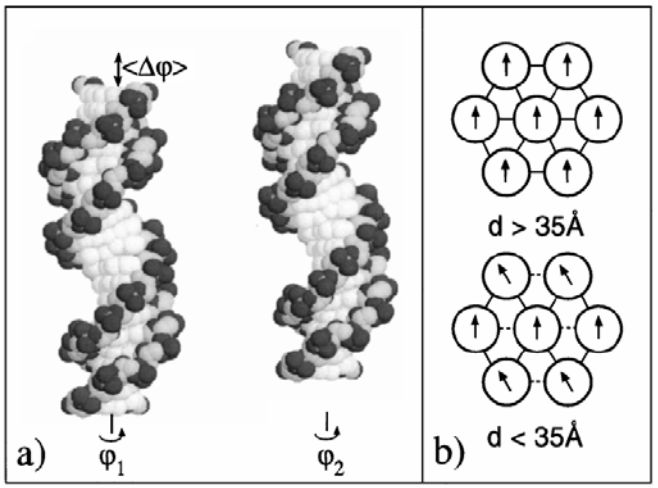
$$\delta\phi = \phi_1 - \phi_2$$

A.A.K and S.L, J. Chem. Phys., 107 3656 (1997)

DNA azimuthal frustrations on hexagonal lattice

H. H. Strey et al., PRL, 84 3105 (2000)



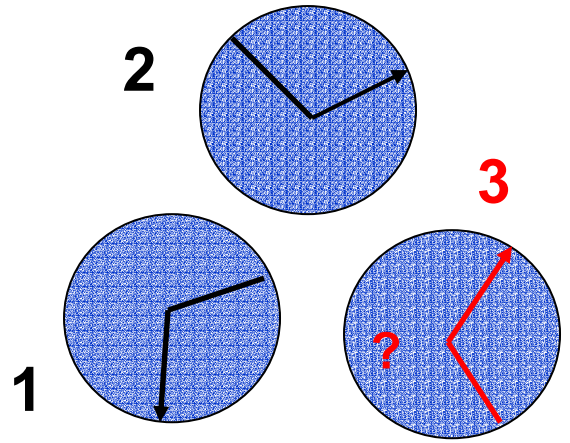


Why positional order becomes more liquid-like as DNA arrays get denser?

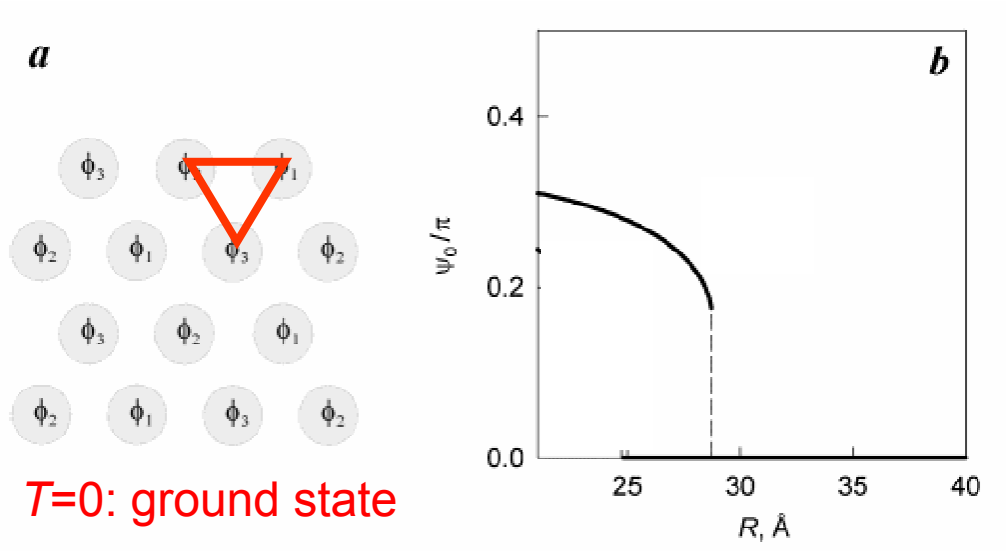
Why bond-orientation order is frustrated for dense DNA lattices?

Explanation: ES interaction couples DNA angular and positional degrees of freedom

$$\varepsilon_{int}(R,\delta\phi)=a_0(R)-a_1(R)\cos(\delta\phi)+a_2(R)\cos(2\delta\phi)$$



Potts Lattices and Spin models: optimal azimuthal angles

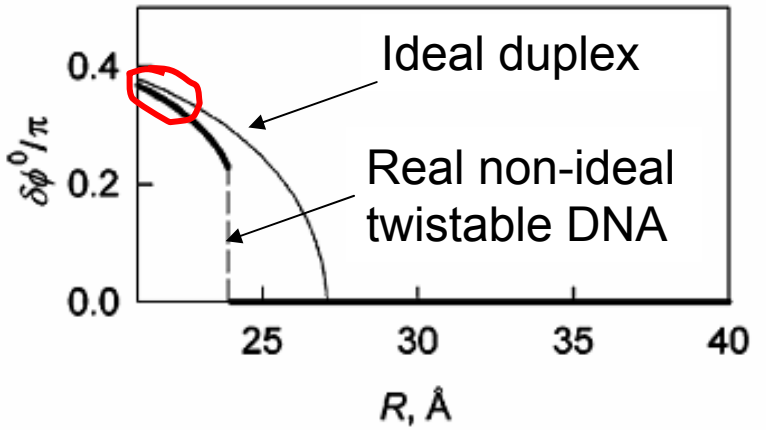


T=0: ground state

$$\cos(\psi_0) = \frac{1}{4}\left(1 + \sqrt{1 + \frac{2A_1(\lambda, R)}{A_2(\lambda, R)}}\right)$$

Energy minimization in elementary triangle

$$\psi_0 = |\phi_1 - \phi_2| = |\phi_1 - \phi_3| = 0.5|\phi_2 - \phi_3|$$

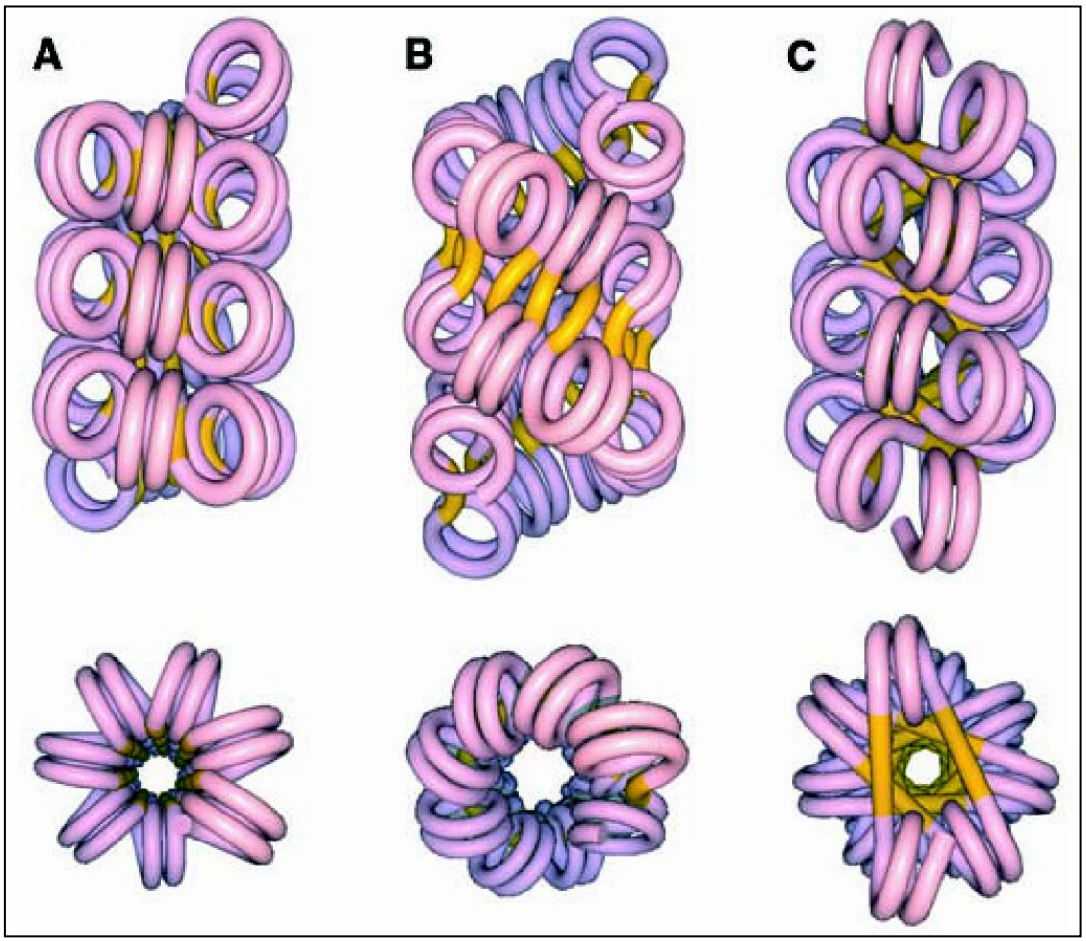


• ES wants DNA to be ideal helices in dense phases and "straighten" them

• Nearly ideal x-ray pictures in columnar lattices of randomly sequenced DNA [M.Wilkins et.al., J. Mol. Biol. 2. 19 (1960)]

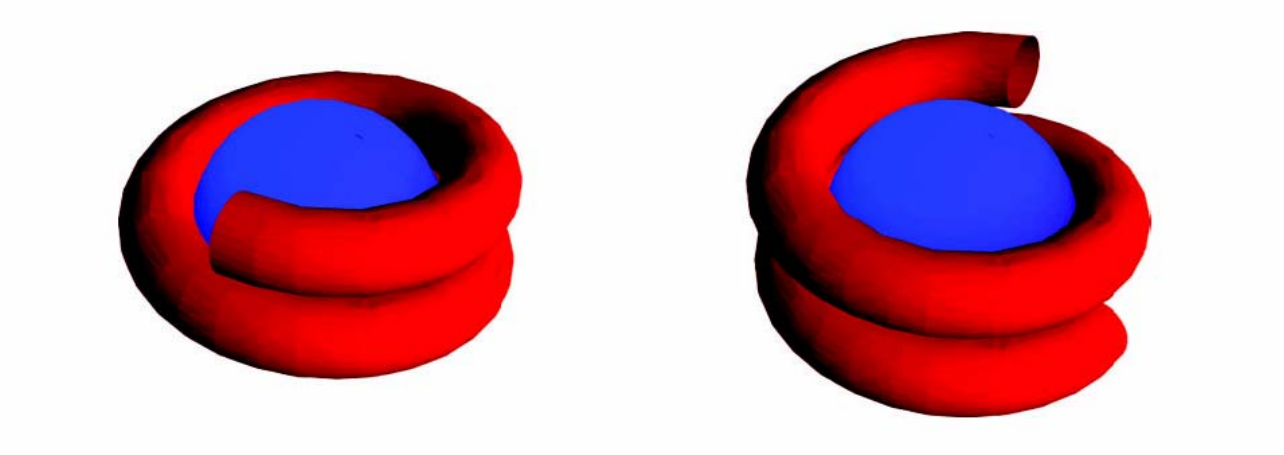
A.G.C., A.A.K, S.L, J. Phys. Chem. B, 108 6508 (2004)

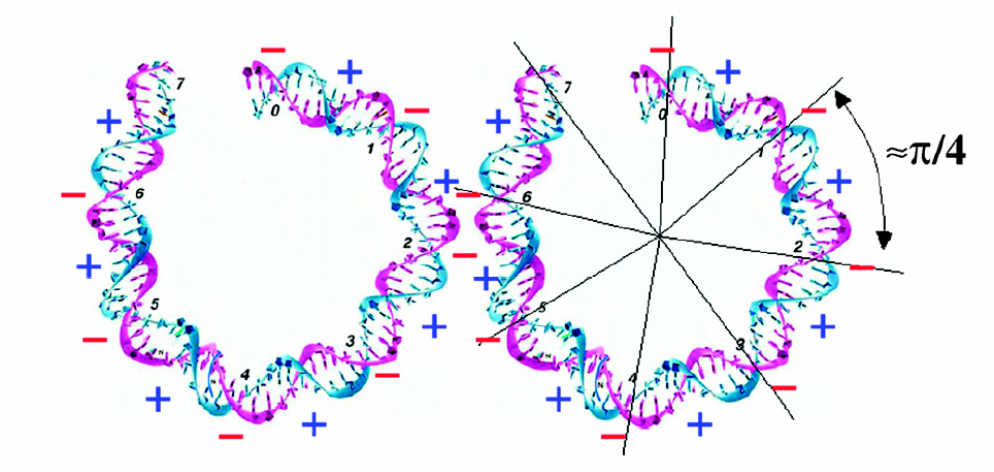
Chromatin 30 nm fibers: solenoid vs cross-linked



- Higher-order DNA structures in eukaryotes
- 3D structure of chromatin fibers is governed by (a) NCP-NCP interactions and (b) DNA bending

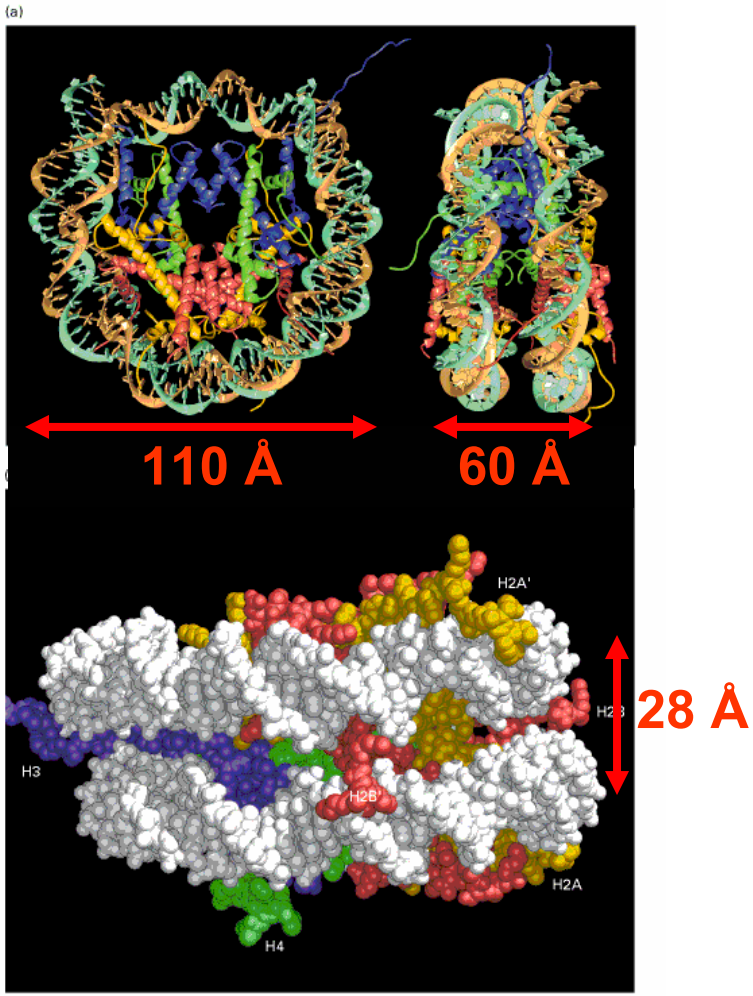
T. J. Richmond et al., Science, 306 1571 (2004)

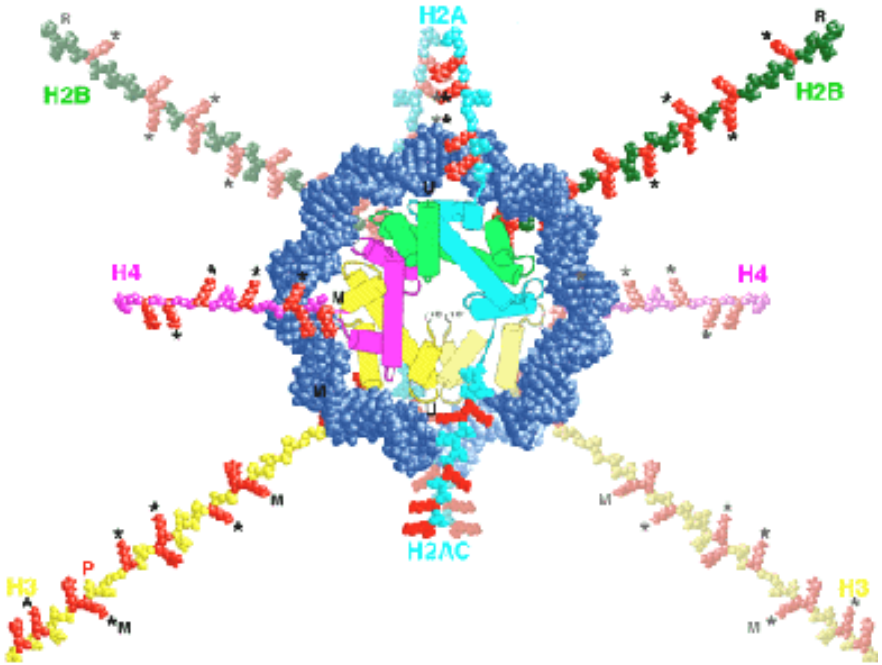




ES interactions of DNA can quantize
azimuthal orientations of NCPs in bilayers

Nucleosome core particle (NCP) structure and histone tails





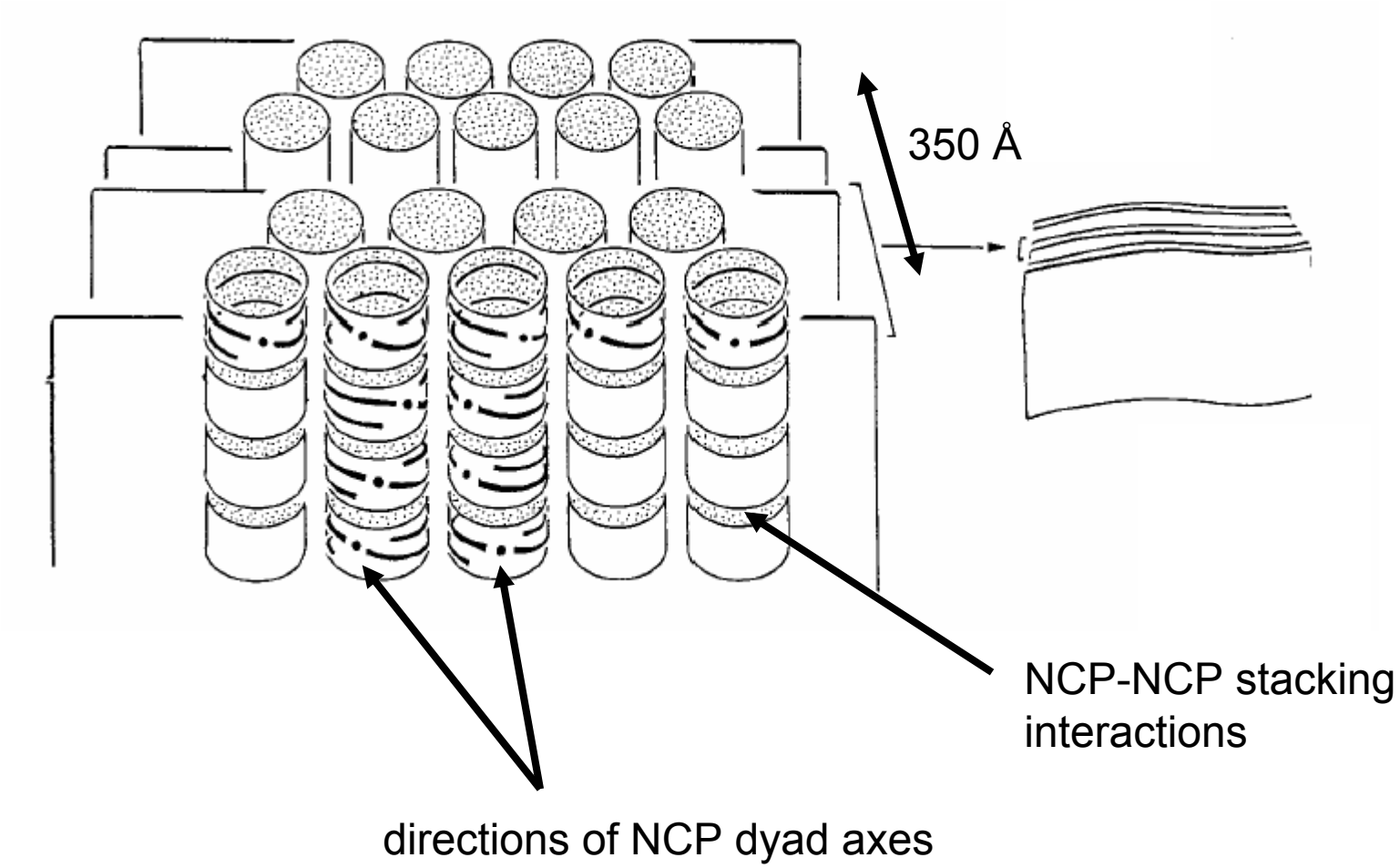
8 histone tails zip DNA turns in NCP and can affect NCP-NCP forces (bridging)

We consider below no-tail NCPs

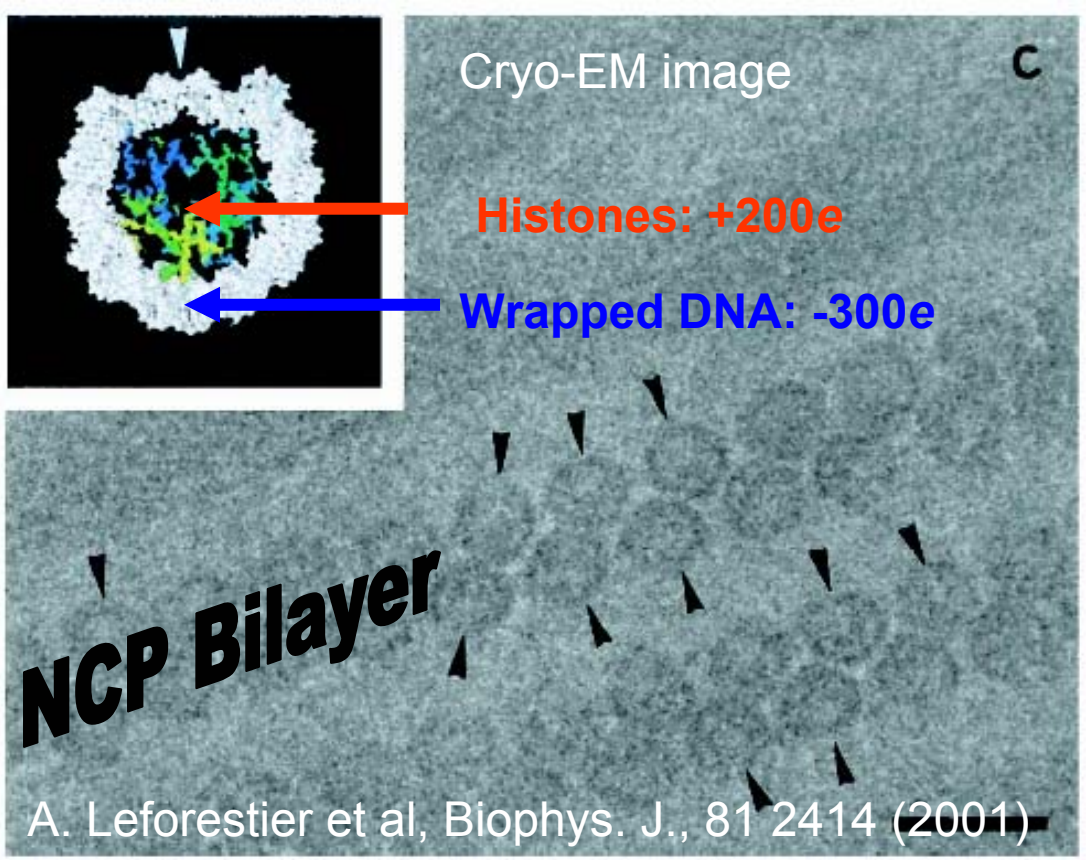
K. Luger et al., Science, 389 251 (1997)

Nucleosomal bilayers: no tails

[salt] + PEG outside

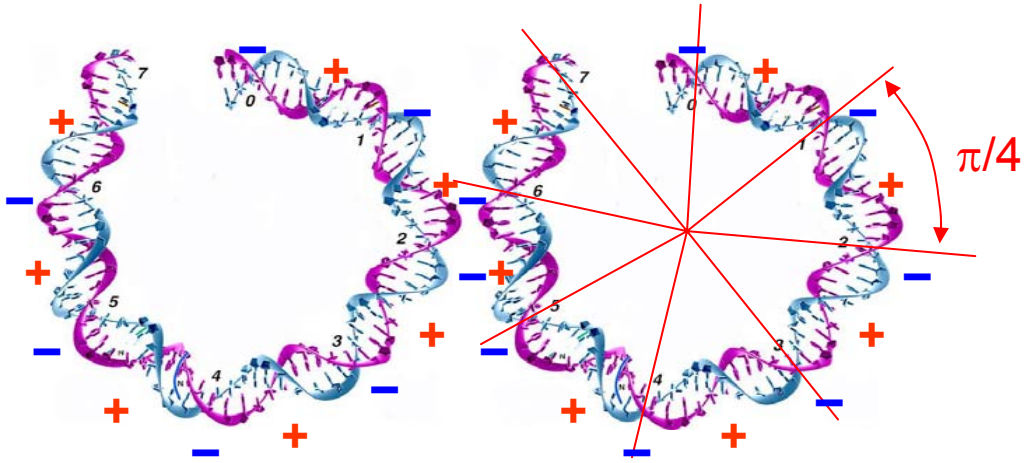


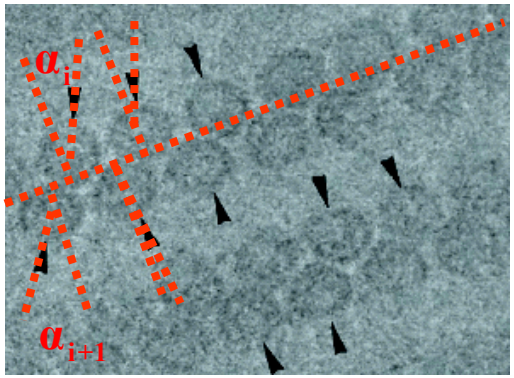
Experiments reveal azimuthal NCP frustrations in bilayers



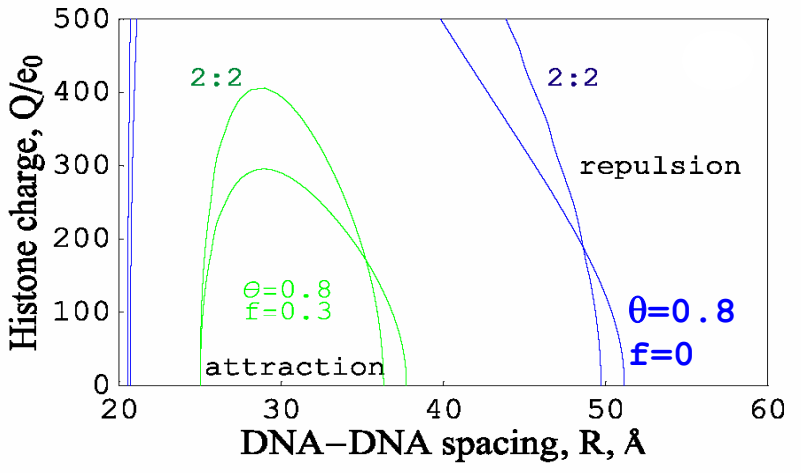
- NCP: highly charged structures
- NCP bilayers occur at 3-30 mM of NaCl; at larger [salt] NCP hexagonal phases
- NCP sides with two DNA turns are in contact
- DNA-DNA are at 5-15 Å on neighboring NCPs: strong ES interactions
- Dyad axes fluctuate within ±35 °

NCP-NCP azimuthal interactions are degenerate



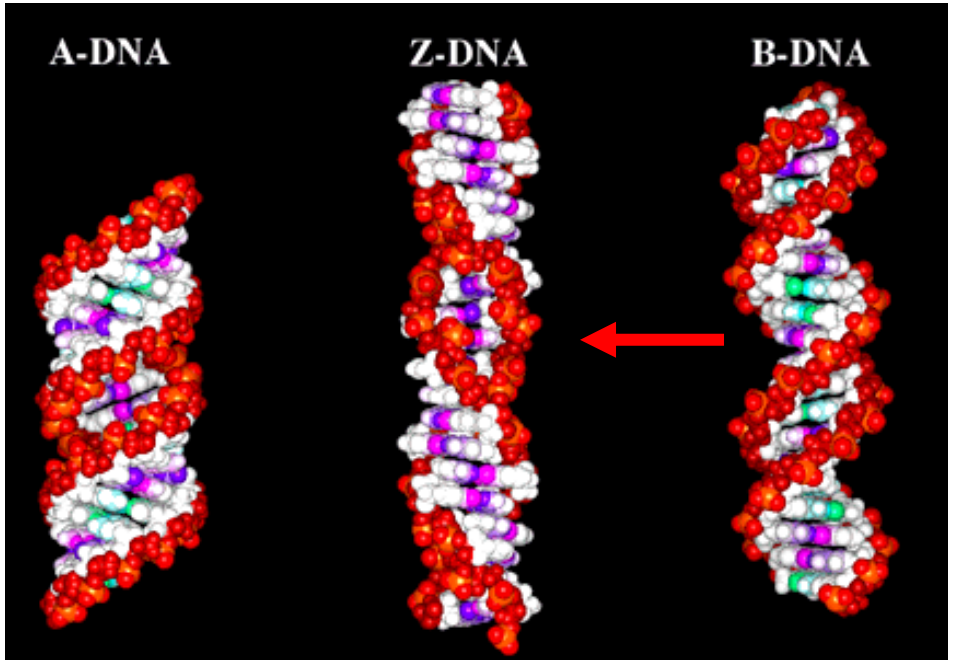


- Exact NCP-NCP ES theory is hopeless
- 8 DNA turns per DNA super-turn in NCP
- Azimuthal NCP rotations $\alpha_i = n\pi/4$ do not change ES forces
- This degeneracy affects statistics of azimuthal NCP frustrations in bilayers
- Statistics was not analyzed: low resolution!



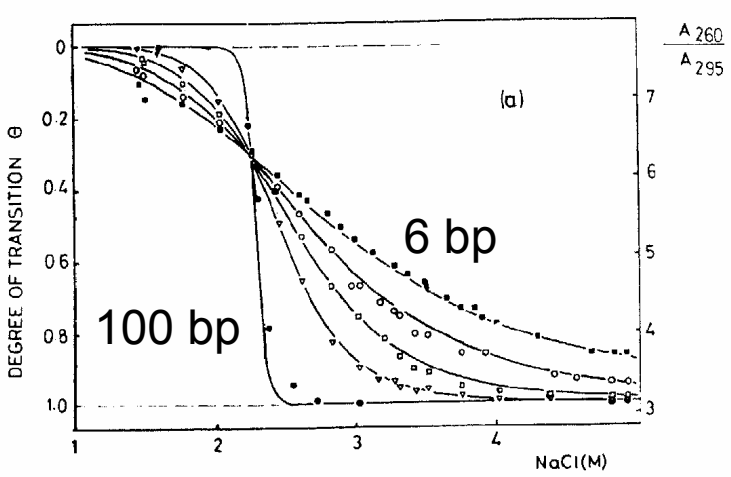
A. G. Cherstvy and R. Everaers, J. Phys.: Cond. Mat., 18 11429 (2006).

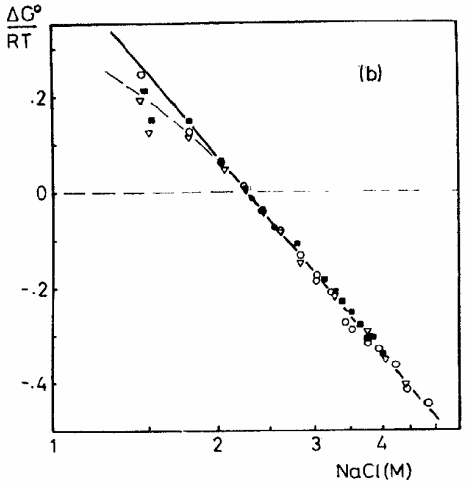
Polyelectrolyte model of *B*-*Z* DNA transition



- Franklin: low humidity DNA fibers feature *A*-DNA!

- *Z*-DNA (*zigzag* DNA form): GC bps alternate + high salt= left-handed *Z*-DNA





oligo(dG-dC): F. M. Pohl, Cold Spring Harb. Symp., 47 113 (1983)

Solution of *linear* Poisson-Boltzmann equation

$$\frac{\partial^2\phi}{\partial r^2}+\frac{1}{r}\frac{\partial\phi}{\partial r}+\frac{1}{r^2}\frac{\partial^2\phi}{\partial\varphi^2}+\frac{\partial^2\phi}{\partial z^2}=\kappa^2\phi$$

$$\begin{Bmatrix}\phi(z,\varphi,r)\\ \sigma(z,\varphi)\end{Bmatrix}=\int_{-\infty}^{\infty}dke^{ikz}\sum_{n=-\infty}^{\infty}e^{in\varphi}\begin{Bmatrix}\tilde{\phi}(k,n,r)\\ \tilde{\sigma}(k,n)\end{Bmatrix}$$

$$\tilde{\phi}(k,n,r)=-\frac{4\pi a\tilde{\sigma}(k,n)}{\varepsilon}\frac{K_n(\tilde{\kappa}_k r)}{\tilde{\kappa}_k a K_n'(\tilde{\kappa}_k a)}$$

$$E_{el}=\frac{1}{2}\int d^3\vec{r}\,\phi(\vec{r})\rho(\vec{r})$$

$$E_{el}=-a(2\pi)^3\int_{-\infty}^{\infty}dk\sum_{n=-\infty}^{\infty}\frac{|\tilde{\sigma}(k,n)|^2}{\varepsilon\tilde{\kappa}_k}\frac{K_n(\tilde{\kappa}_k a)}{K_n'(\tilde{\kappa}_k a)}$$

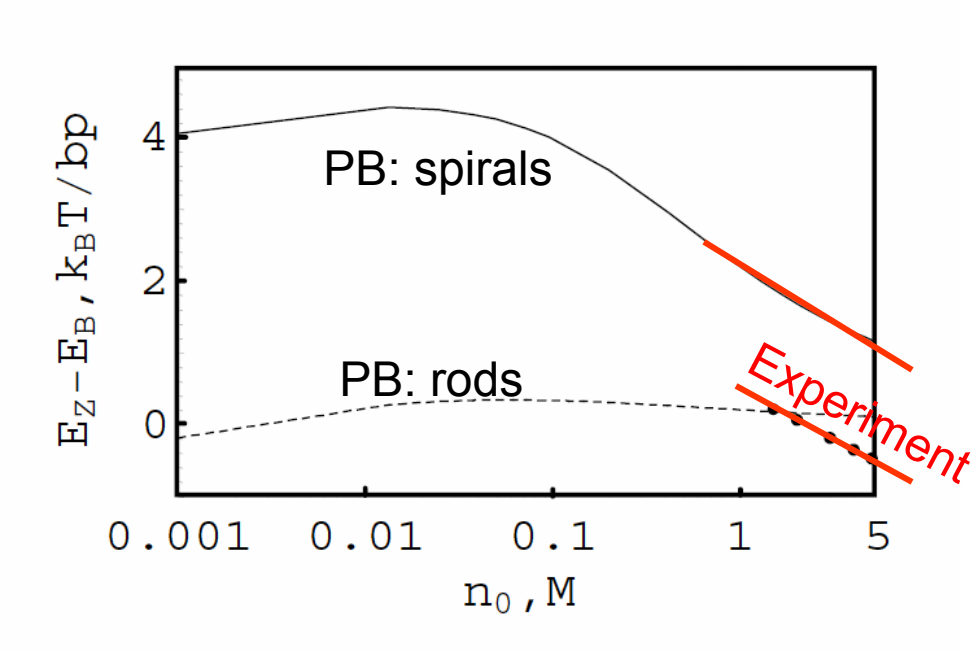
The energy of *any helical* charge distribution

$$E_{el}=\frac{4\pi^2\sigma_p^2a^2}{\varepsilon}\left\{\frac{K_0(\kappa a)}{\kappa a K_1(\kappa a)}\right.$$

$$\left.-\sum_{n=1}^{\infty}\frac{[1+\cos(ngh)]K_n(\kappa_n a)}{\kappa_n a K_n'(\kappa_n a)}\right\}>0.$$

ES energy of double stranded DNA-like helix

Z-DNA is stabilized at high salt



- Width of *Z*-DNA minor groove h controls ΔES([salt]) slope

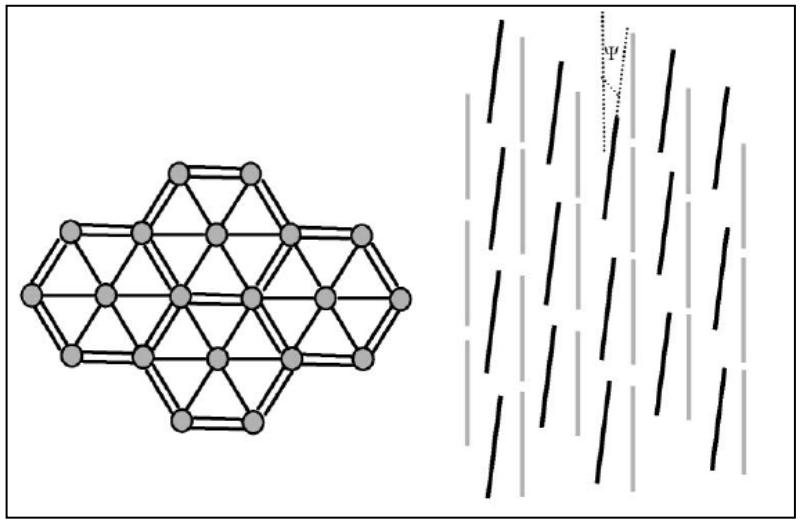
- Model of uniformly charged rods fails to predict the slope [M. D. Frank-Kamenetskii et al., J. Biom. Str. Dyn., 3 35 (1985)]

Energy of DNA phosphates only

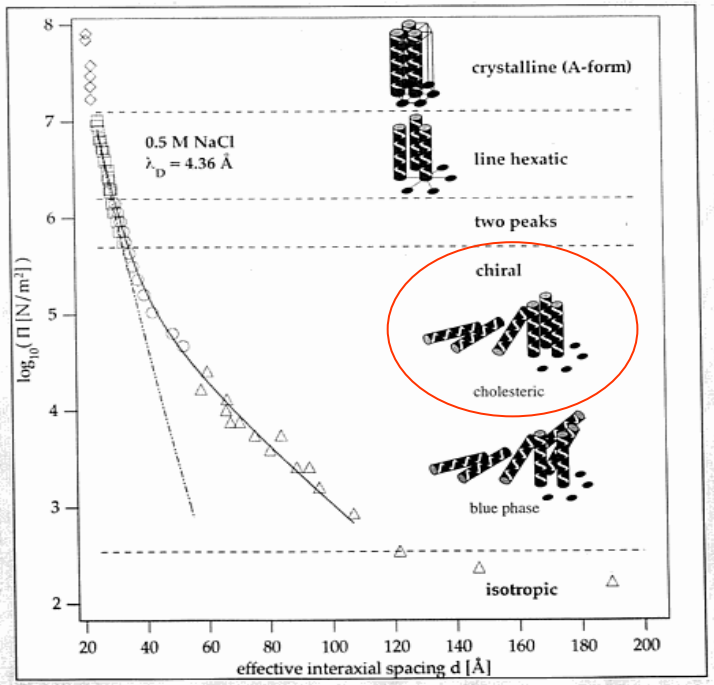
- *B*-DNA: *a*=9Å, *H*=34Å, *h*=13Å; 10 bp/*H*
- *Z*-DNA: *a*=7.5Å, *H*=44Å, *h*=8Å; 12 bp/*H*
- Pure DNA structure, no adjustable paramet

$$E_{el} = \frac{4\pi^2\sigma_p^2 a^2}{\varepsilon}\left\{\frac{K_0(\kappa a)}{\kappa a K_1(\kappa a)} - \sum_{n=1}^{\infty}\frac{[1+\cos(ngh)]K_n(\kappa_n a)}{\kappa_n a K_n'(\kappa_n a)}\right\} > 0.$$

A. G. C., J. Chem. Phys. 123, 116101 (2005)

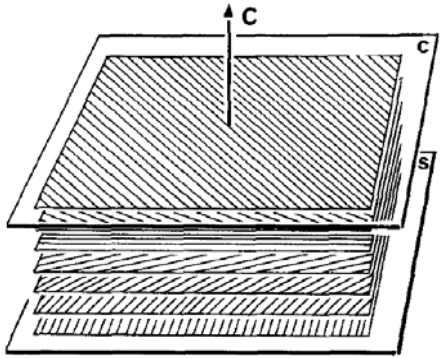


Mesophases of 0.5 M Na DNA

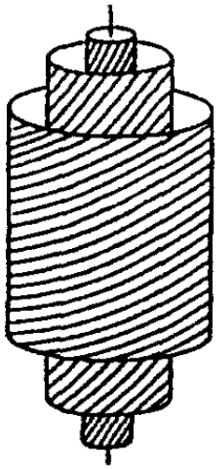


Na DNA at 0.5 M NaCl PEG MW 20.000.
High pressure data from: (Lindsay *et al.* Biopol. **27** (1988) 1015)

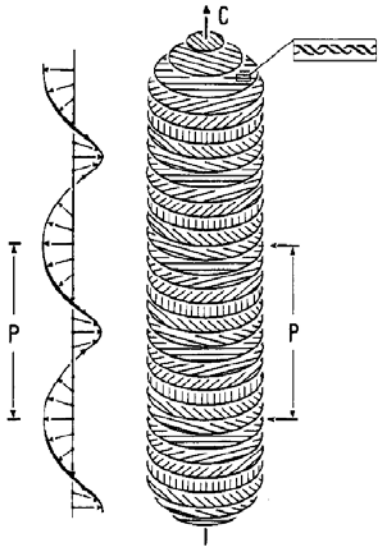
Left-handed chiral phases of right-handed DNA *in vivo* and *in vitro*



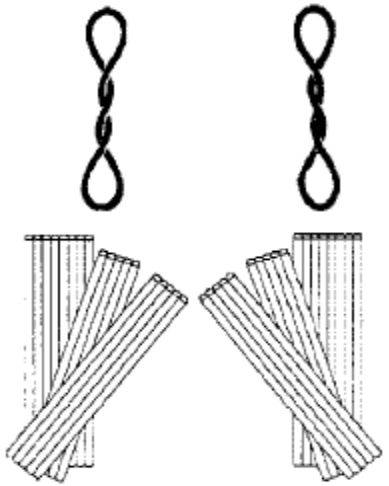
Left-handed cholesteric of 146 bp NCP DNA. Chol. Pitch *P*=2-4 μm



Double-twisted LH cholesteric phase

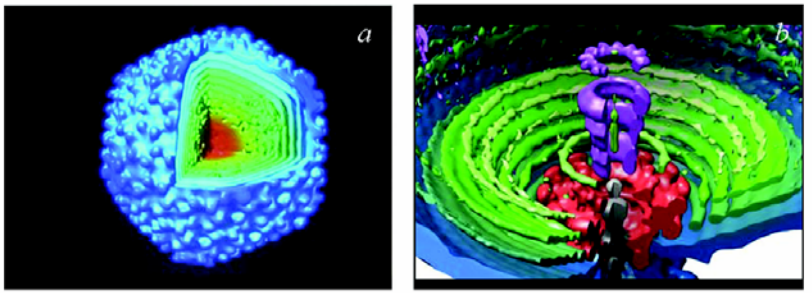


Dinoflagellate chromosome (unicellular algae): LH phase, *P*=0.2-0.4 μm

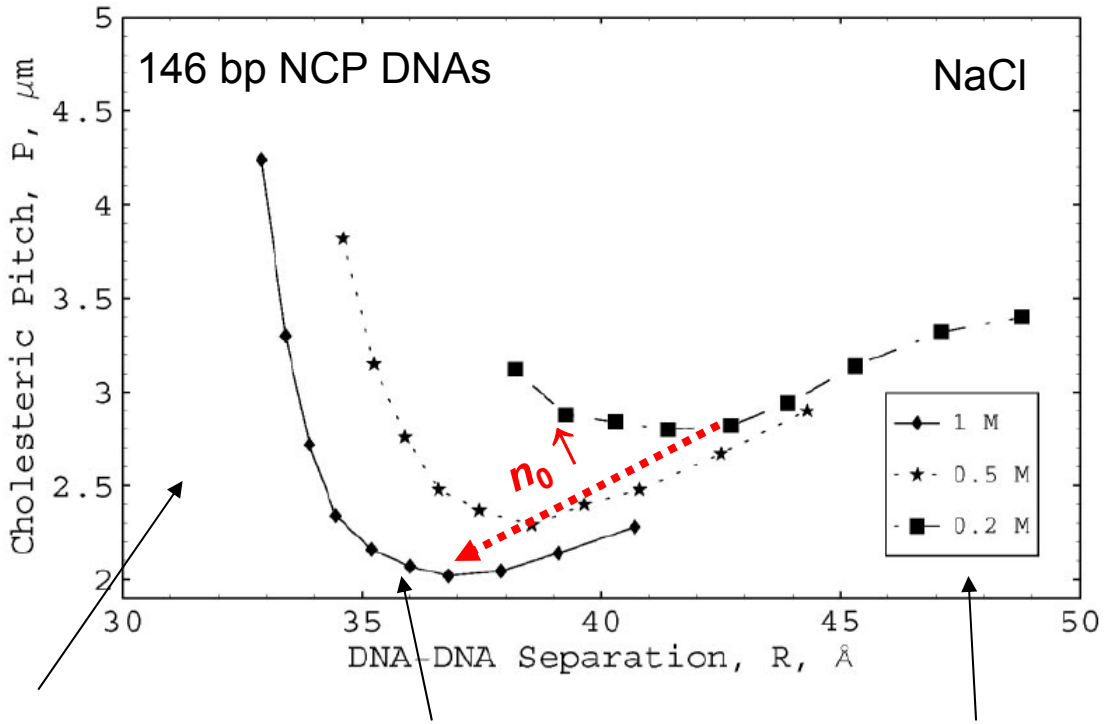


RH DNA supercoils form LH phases, as from steric fitting of ridged helices with α>45°

Some viruses and sperm cells of vertebrates also pack their DNA into dense chiral phases



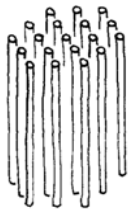
Experiments: non-monotonic LH cholesteric pitch is P=2-4 μm

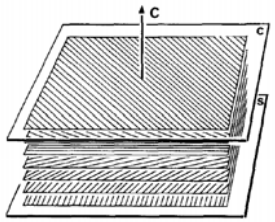


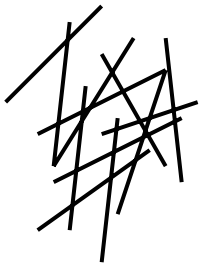
Columnar hexagonal: >350 mg/ml

Cholesteric Phase: 160<[DNA]<350 mg/ml

Isotropic



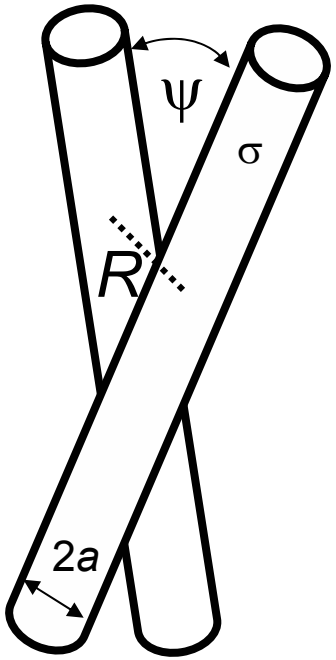




- P grows at boundaries of chol-hex and chol-iso phases
- Shift of stability regions to denser lattices at high [salt] is consistent with ES screening: smaller R ensure strong azimuthal correlations vital for existence of chiral phases
- Counter-intuitive: DNA: $n_0\uparrow P\downarrow$, fd-virus: $n_0\uparrow P\uparrow$
- NaCl: P=2-4 μm;
- spermidine^{3+}: P=22 μm and strongly T-dependent.
- DNA complexes with short positive cations (chitosan, poly-lysine) reveal inversion of P sign
- Complex systems!

C. B. Stanley et al., Biophys. J., 89 2552 (2005)

ES interaction of long skewed rods in electrolyte solution

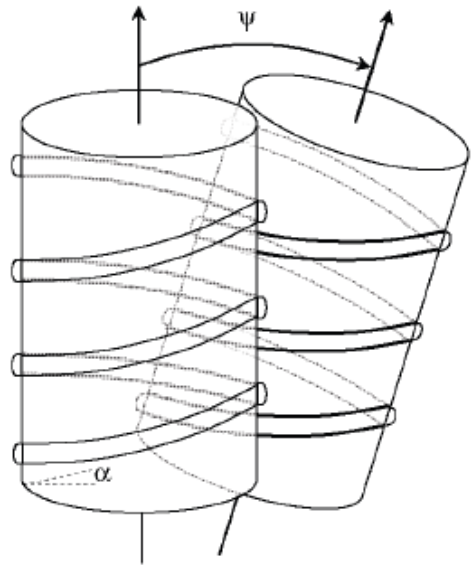


Energy is minimal at $\psi=\pi/2$ and it diverges as $\psi\to 0$

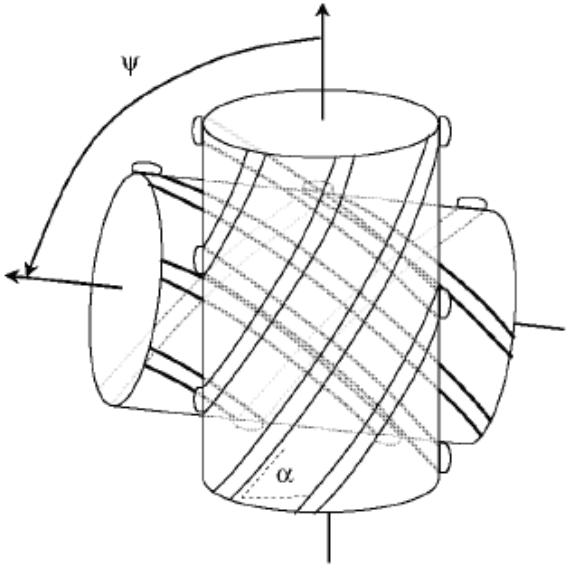
$$E(\Psi) = \frac{8\pi^3\sigma^2}{\varepsilon\kappa^3 K_1^{\,2}(\kappa a)} \frac{e^{-\kappa R}}{|\sin(\Psi)|}$$

S. L. Brenner and A. V. Parsegian,
Biophys. J., 14 327 (1974)

Steric + ES forces: favorable alignments of RH DNA-like helices

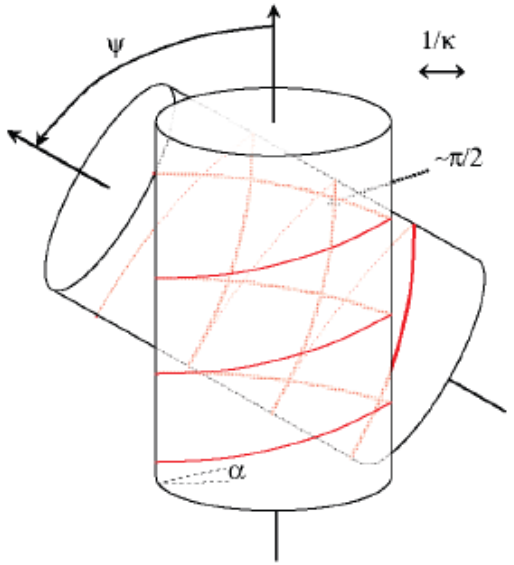


a) Steric interactions of uncharged helices:
α<45°, ψ>0, right-handed cholesteric twist

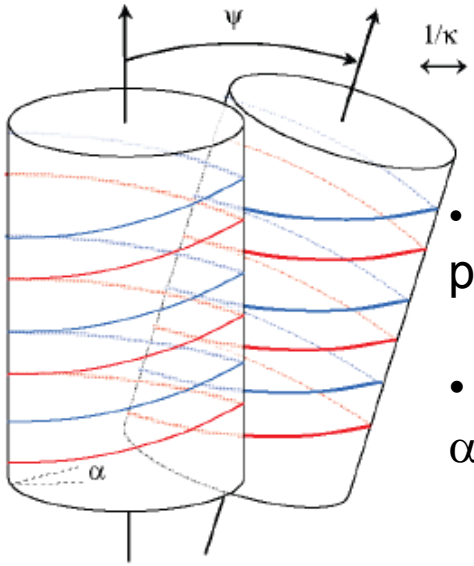


b) Steric interactions of uncharged helices:
α>45°, ψ<0, left-handed twist

Ridges: $\alpha > \pi/4$ vs $\alpha < \pi/4$



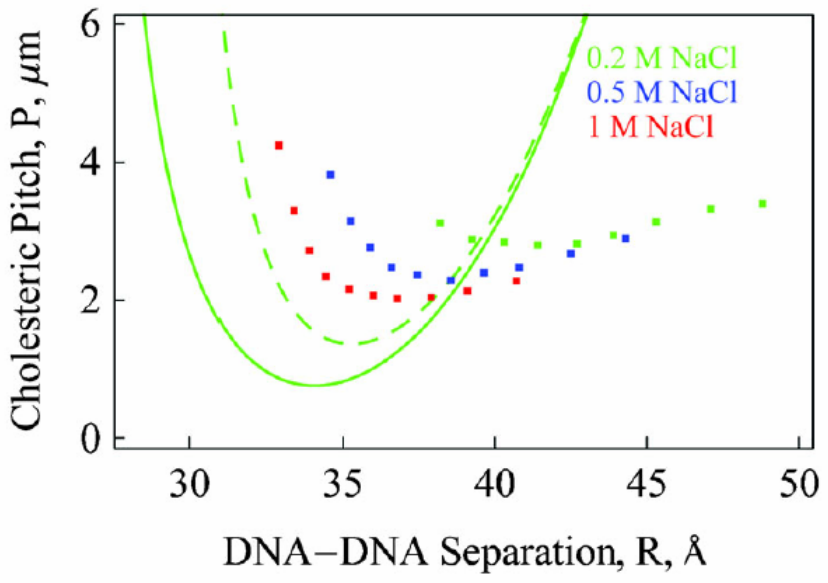
c) Electrostatic interactions of charged spirals:
α<45°, ψ<0, left-handed twist



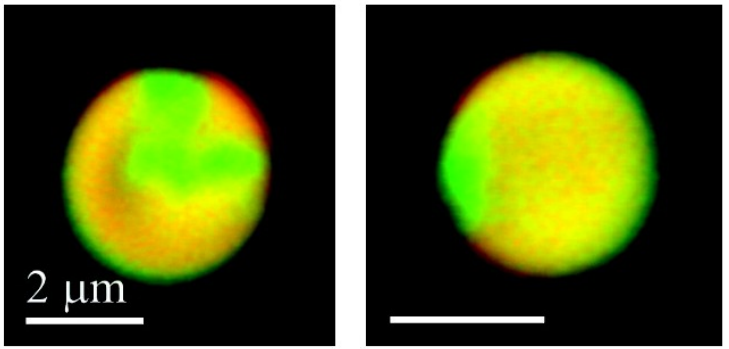
d) Electrostatic interactions of charged spirals with cations:
α<45°, ψ>0, right-handed twist

- Theory: predicts RH cholesteric phases for DNA+cations
- Exper: DNA are RH helices with $\alpha < 45°$, but form LH cholesterics!

Cholesteric pitch *vs.* DNA lattice density



G. S. Baldwin et al.,
J. Phys. Chem. B, 112 1060 (2008).

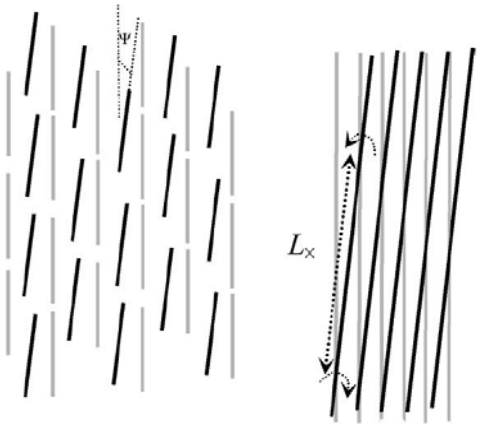


Different DNA sequences segregate into separate populations in cholesteric spherullites indicating sequence-specific chiral DNA-DNA interactions and **DNA-DNA recognition**

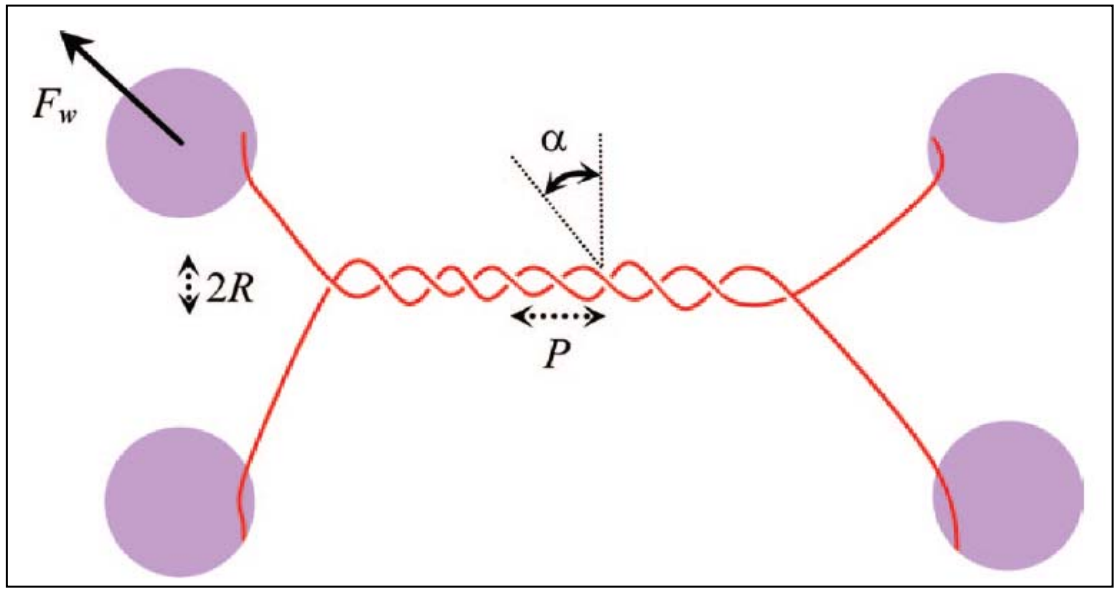
- Pitch magnitude and *R*-dependence agree with experiments.

- As $n_0 \uparrow$, chol. phases shift to larger *R* and *P* grows, contrary to experiments.

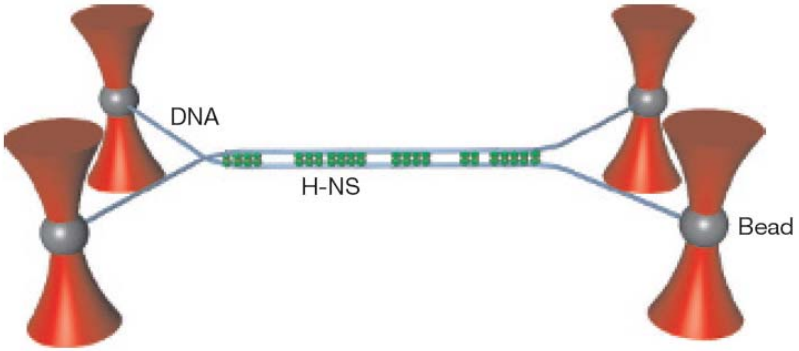
- With Donnan equilibrium, DNA chiral phases are stable also at low [salt].



A. G. C, J. Phys. Chem. B, 112 12585 (2008)

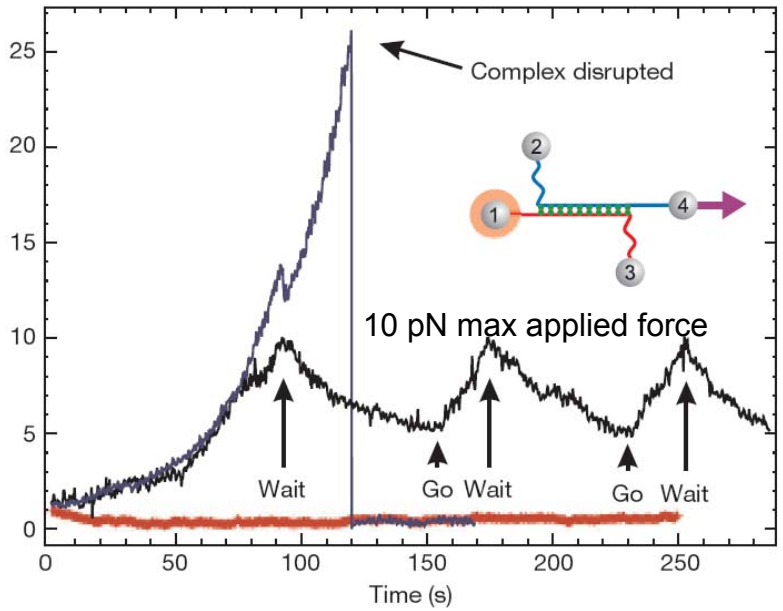

F_w
α
$2R$
P

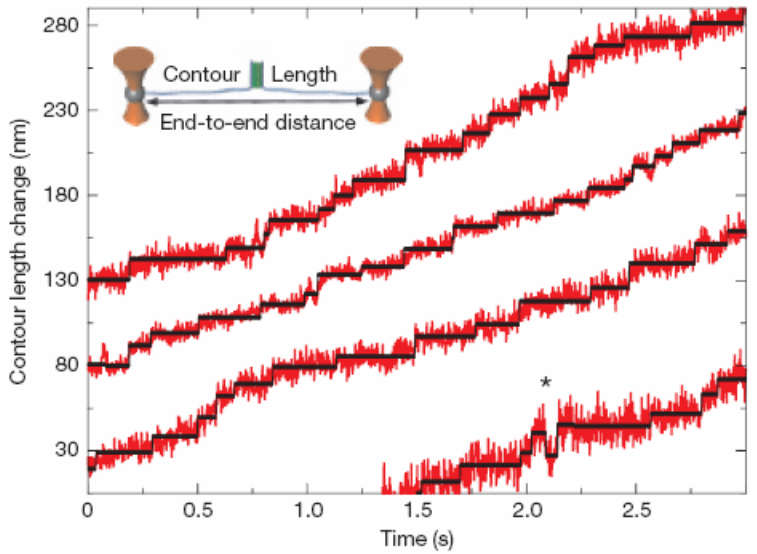
Dual optical trap experiments: DNA ply + H-NS proteins



R. T. Dame et al., Nature, 444 387 (2006)

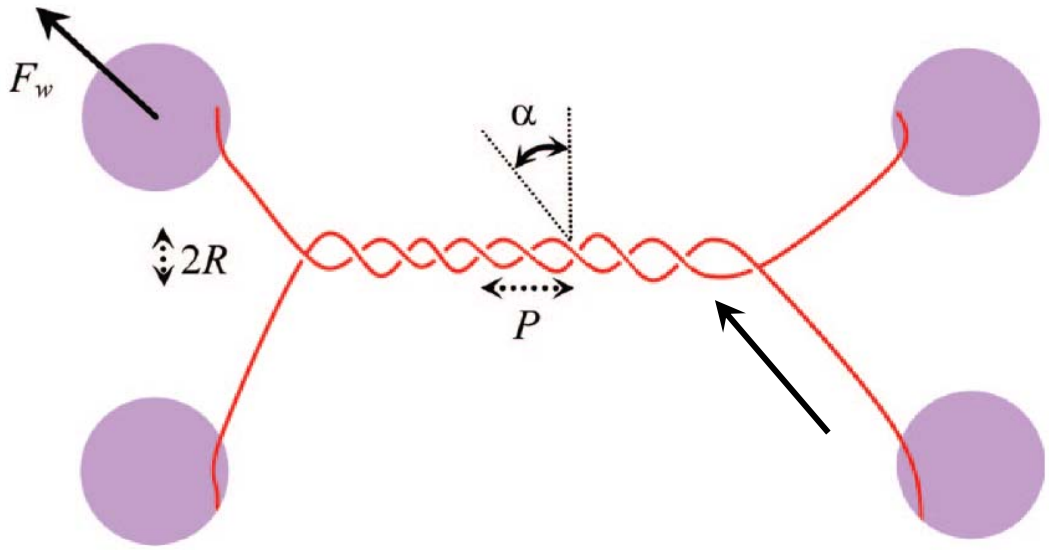
Non-specific DNA bridging by histone-like nucleoid structuring protein (H-NS)





- Ply disruption by shearing (25 pN at 22 nm/s) and unzipping
- Distribution of ply rupture events: multiples of 3.6 ±0.4 nm
- Rupture of DNA-(H-NS)-DNA links every 2-6 DNA repeats

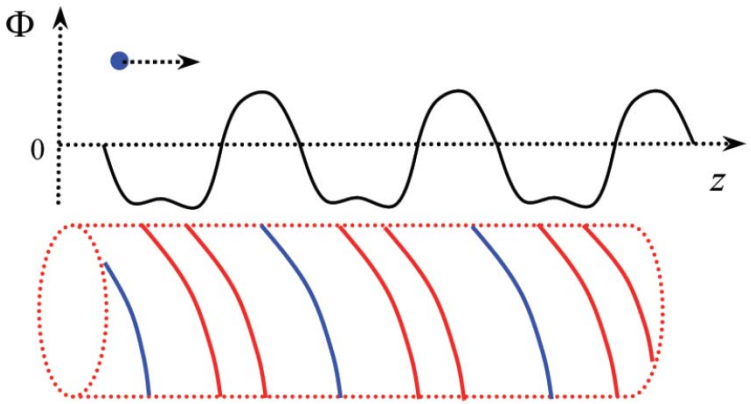
Dual optical trap experiments: DNA ply only

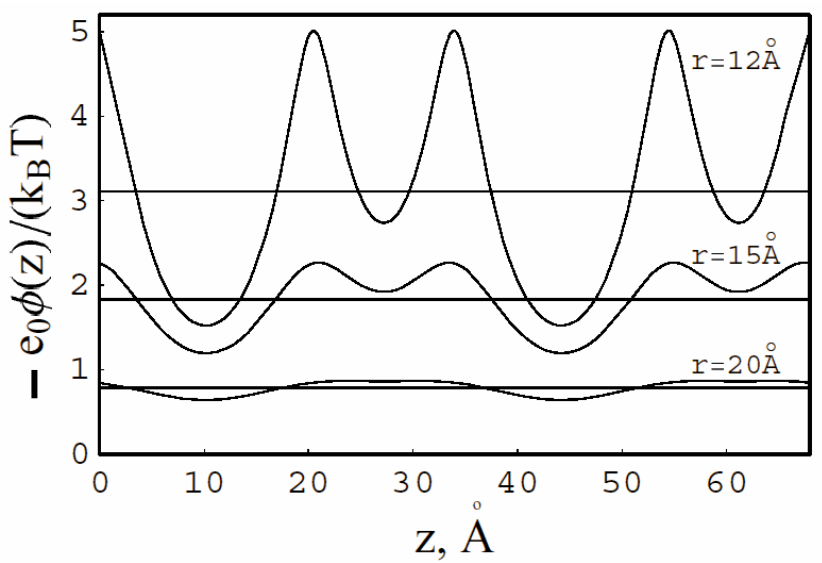


- No DNA-DNA friction detected: pulling forces < 1 pN !
- Mono- and multi-valent salt, different # of DNA turns, pulling speed, etc.
- DNA Ply Diameter 2R =50-100 Å
- Spatial resolution ≈50 bp

M. C. Noom et al., Nature Meth., 4 1031 (2007)

Electrostatic (ES) helix-mediated barriers around DNA





Sequence-specific ES barriers affect DNA-DNA interactions

A.G.C. and R.G.W. JCP,120 9394 (2004)

Friction of ideal rigid DNAs

$$E_{\text{int}}(R, \delta z) \approx L[a_0(R) - a_1(R)\cos(2\pi\delta z/H)]$$

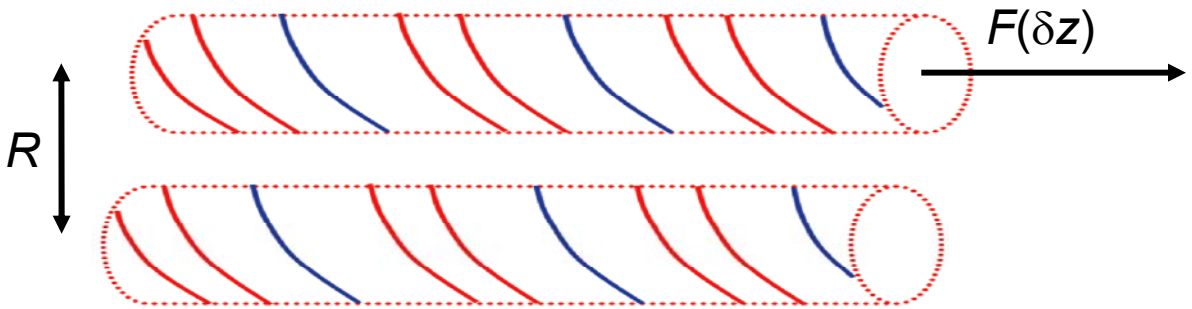
$$F_{\text{fr,rigid,ideal}}(\delta z) = -\frac{\partial E_{int}(\delta z)}{\partial \delta z} = -La_1\frac{2\pi}{H}\sin\frac{2\pi\delta z}{H}$$

$$F_{static} = [F]_{\max} = 2\pi a_1 N \approx$$

$$N \cdot 0.1 k_B T / \text{Å} \text{ at } R = 30\,\text{Å}$$

$$N \cdot 0.01 k_B T / \text{Å} \text{ at } R = 40\,\text{Å}$$

$$k_B T / \text{Å} \approx 41\,\text{pN}$$



- Friction force scales with DNA length: $F \propto N$, $N=L/H$
- DNA-DNA stick-slip motion at nano-scale, H=3.4 nm
- Friction is measurable at R-2a=10-20 Å
- Ideal ply with no fluctuations – they reduce friction

Friction of non-ideal rigid DNAs

$$E_{\text{int}}(R) = \int_0^L [a_0(R) - a_1(R)\cos\delta\phi(z)]\,\mathrm{d}z$$

$$\delta\phi(z) = \frac{1}{h}\int_0^z \delta\Omega(z)\,\mathrm{d}z \qquad \langle\Omega\rangle + \delta\Omega$$

$$\langle\delta\Omega(z')\delta\Omega(z'')\rangle = 2\Delta\Omega^2 h\delta(z'-z'') \qquad \Delta\Omega \approx 3-6^\circ \qquad \langle\Omega\rangle \approx 34-36^\circ$$

$$\left\langle F_{fr,rigid,random}(\delta z)\right\rangle \approx -a_1\left(1-e^{-L/\lambda_c}\right)e^{-\delta z/\lambda_c}$$

- *F* is averaged over many helix/(random field) realizations
- Exponential decay with pulling distance δz

Friction of non-ideal non-rigid/soft DNAs

$$C = k_B T l_{tw} \approx 3 \cdot 10^{-19}\,\mathrm{erg \cdot cm}$$

$$E_{\mathrm{int}}(R, \delta z) \approx L\left[a_0 - a_1\left(1 - \frac{\lambda_t}{4\lambda_c}\left(1 + \cos\frac{2\pi\delta z}{H}\right)\right)\right]$$

$$\lambda_t(R) = \sqrt{\frac{C}{2a_1(R)}}$$

$$F^{\max}{}_{fr,soft,random} = \frac{\lambda_t}{4\lambda_c} a_1 L \frac{2\pi}{H} \qquad \frac{\lambda_t}{4\lambda_c} << 1$$

- Register is restored due to DNA torsional flexibility
- Friction force scales with *L*, similar to ideal DNA
- The magnitude is however much lower

A.G.C., J. Phys. Chem. B, 113 5350 (2009)

Friction: conclusions

• Three regimes of DNA-DNA static ES friction:
ideal rigid, non-ideal rigid, non-ideal soft helices

• Real DNAs are between case 2 and 3

• Strong friction scales with a_1 and thus gets amplified by DNA-DNA attraction

• It is not surprising that Wuite observed no friction: thick fluctuating plies with no helix-specific features of DNA

• Resolution of $H/2$ needed at least – not the case