

How soft is DNA?

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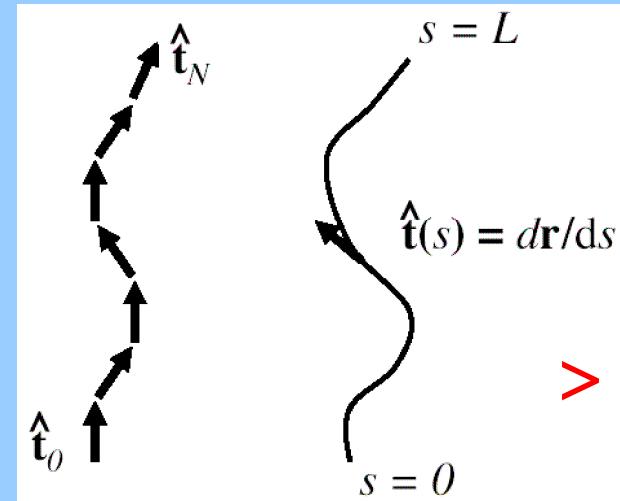
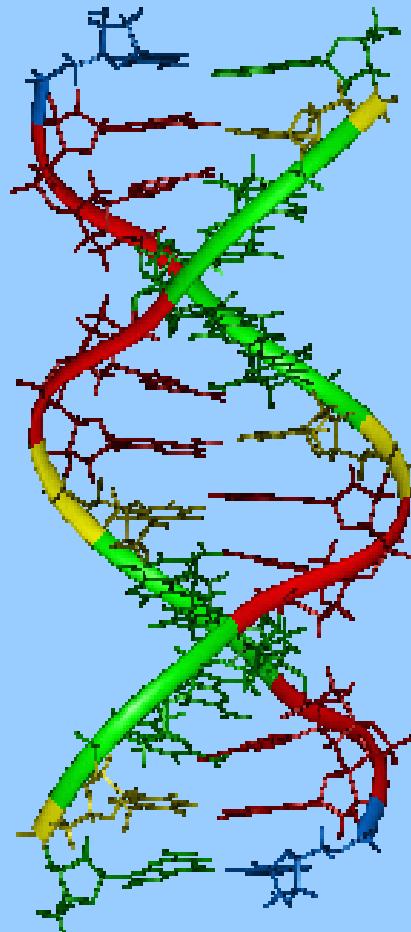
**ENS-Lyon

109th Statistical Mechanics Conference
Rutgers University, May 12-14, 2013



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Reduced complexity ...



averages over genomic content

Kratky – Porod (WLC)

$$H = -\frac{B}{l} \sum_{n=1}^N \hat{\mathbf{t}}_n \cdot \hat{\mathbf{t}}_{n+1}$$

Bending stiffness
(twist, stretch ...)

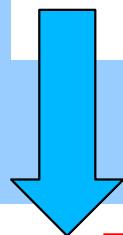
Stiff at the nanoscale

$$\langle \hat{t}_n \cdot \hat{t}_m \rangle = e^{-|m-n|l/\lambda}$$

$$\lambda = \frac{B}{k_B T}$$

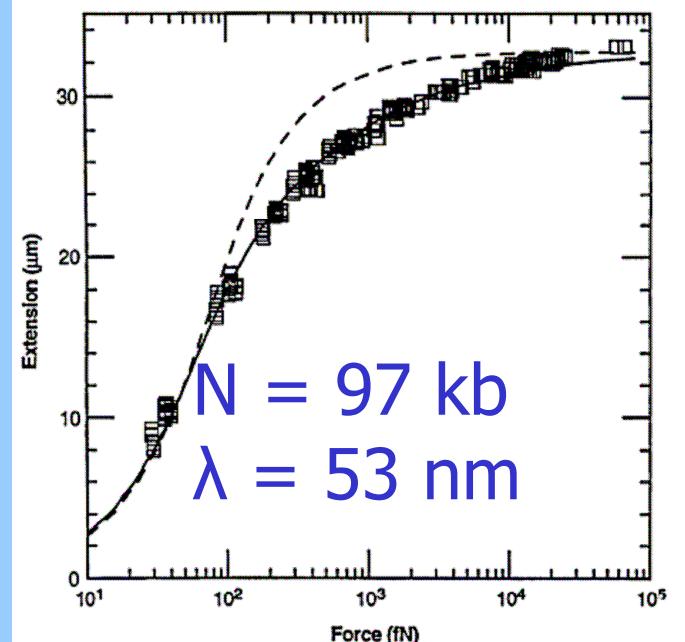
persistence length

or: indirect, e.g. light scattering,
end-to-end distance, R_g



$\lambda \sim 50 \text{ nm (d-s DNA)} \sim 150 \text{ bps}$
cf. $\sim 1 \text{ nm (s-s DNA)}$

force – extension



Bustamante, Marko, Siggia,
Smith (Science, 1994)

→ d-s binding forces !

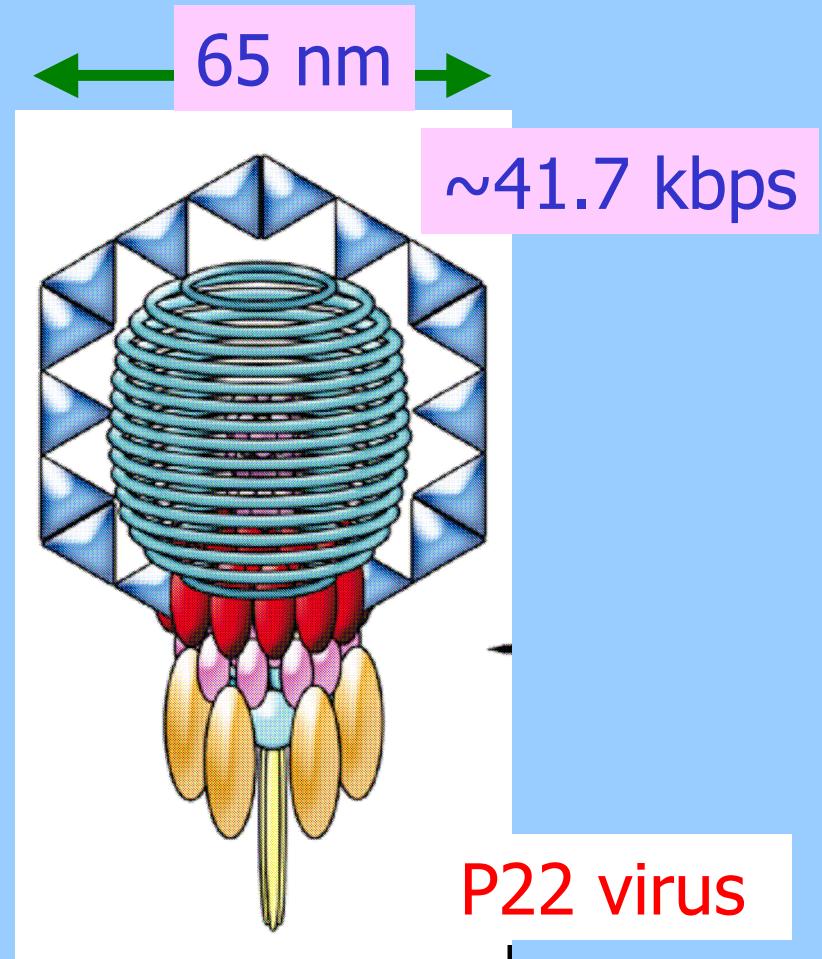
< 100 bps: “rigid rods” ?

Key processes depend on flexibility

< 100 bps: “rigid rods” ?

Viral DNA packaging

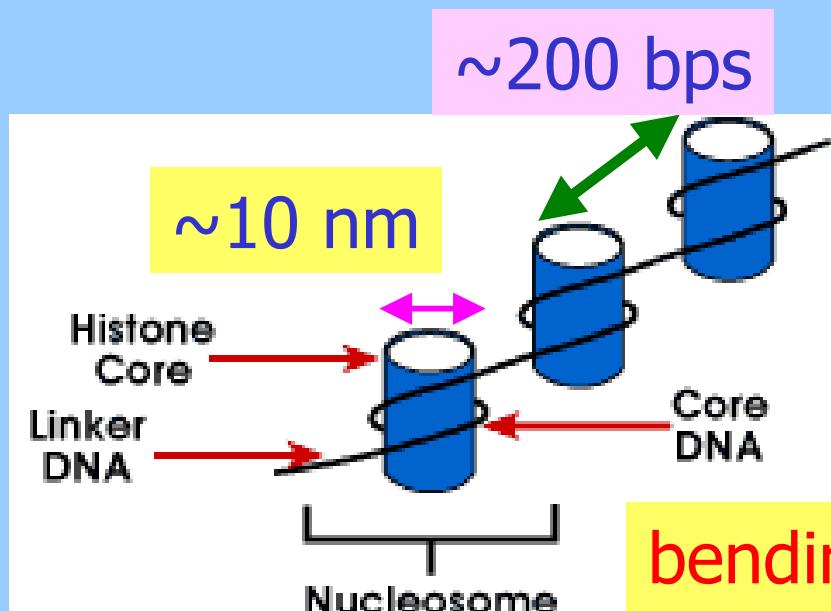
Lots of bending energy!
pressure on capsid
wall O(50 at)



Johnson & Chiu,
Curr. Op. Str. Bio. (2007)

evolution demands more flex!

< 100 bps: “rigid rods” ?



DNA packaging in chromosomes

Folding around histones:
 $\sim 127 \text{ bps}$ 1.65 folds

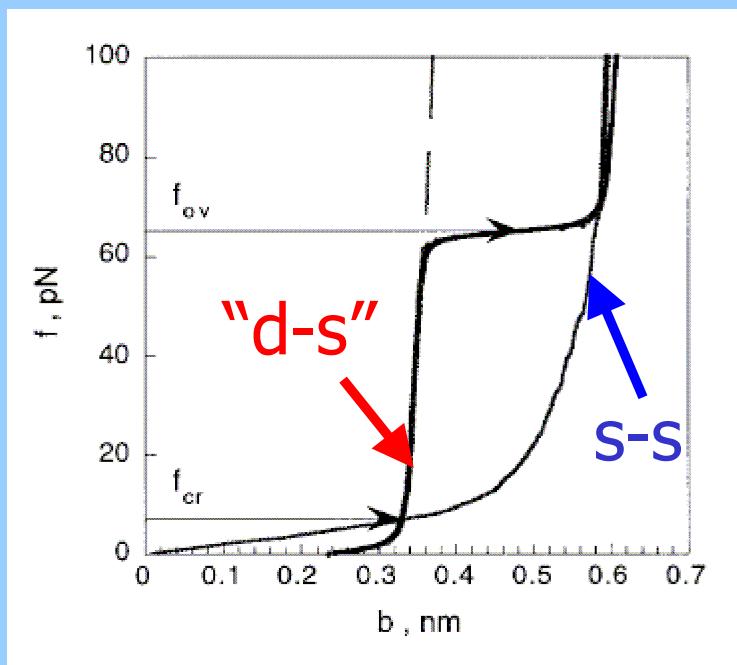
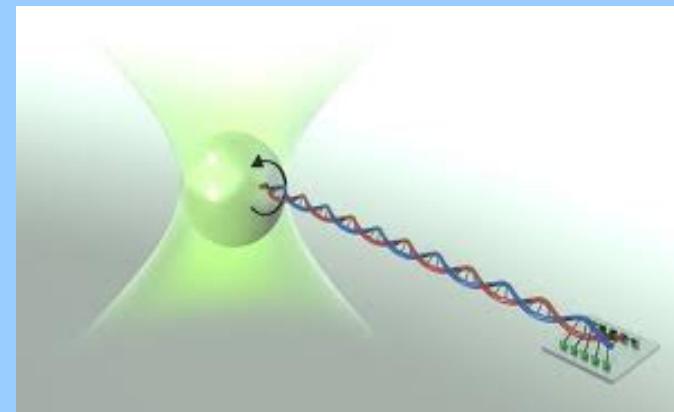
bending sites
specificity (large adsorption energies)

variations in (local) flexibility – functionally significant

mechanical unbinding, (I)

overstretching

(longitudinal) force vs. extension

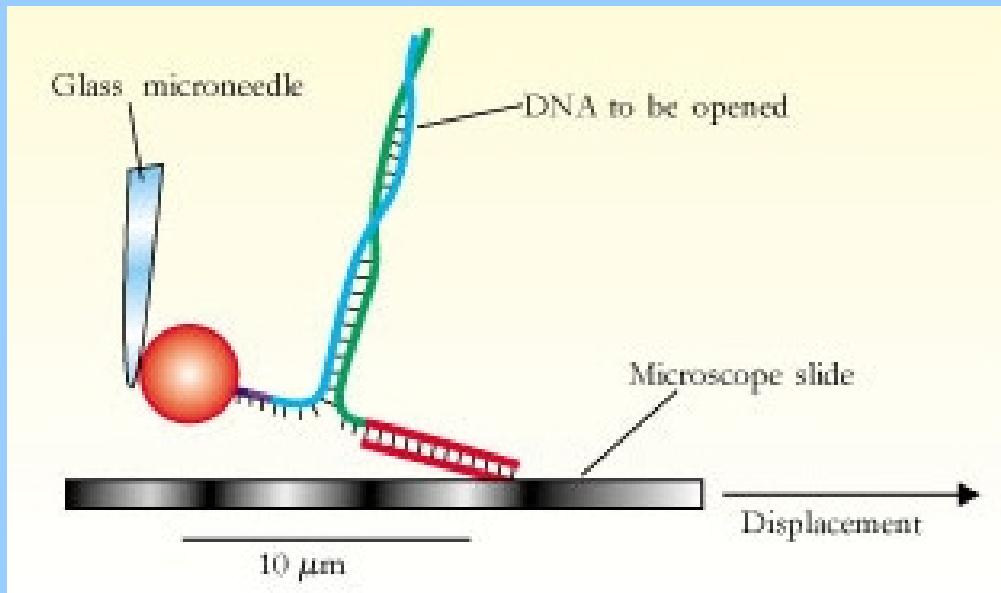


$$F_{\text{overstretching}} = 65 \text{ pN}$$

$$\frac{\Delta \ell}{\ell} = 1.7$$

Smith et al., Science (1996)

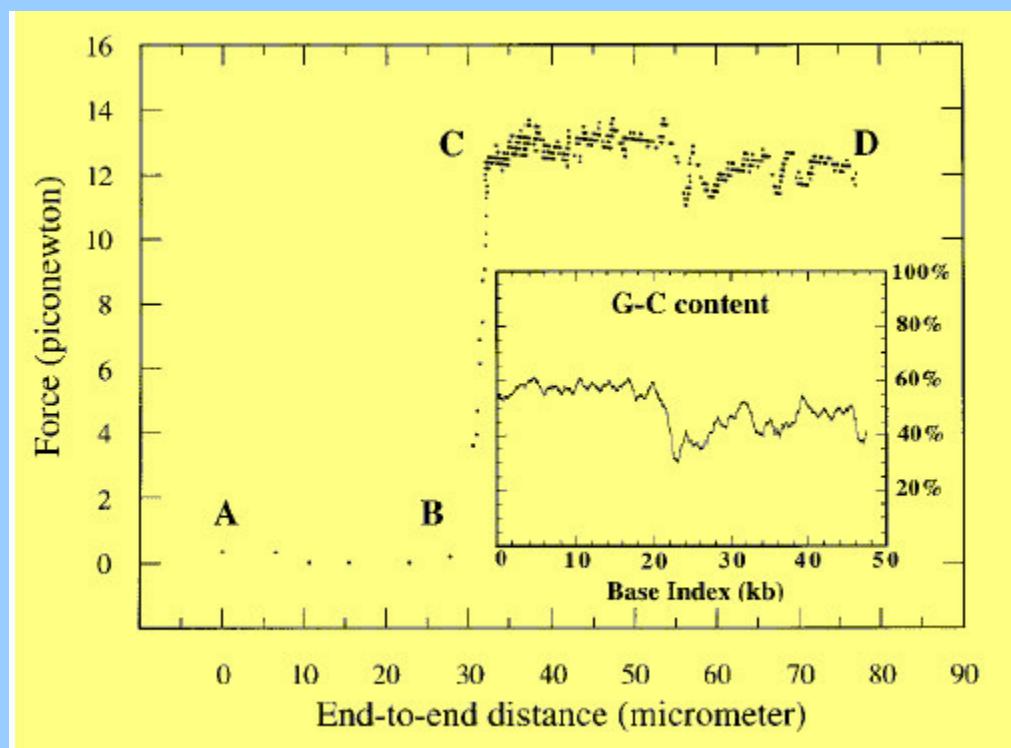
mechanical unbinding (II)



$$F_{\text{break}} = 13 \text{ pN}$$

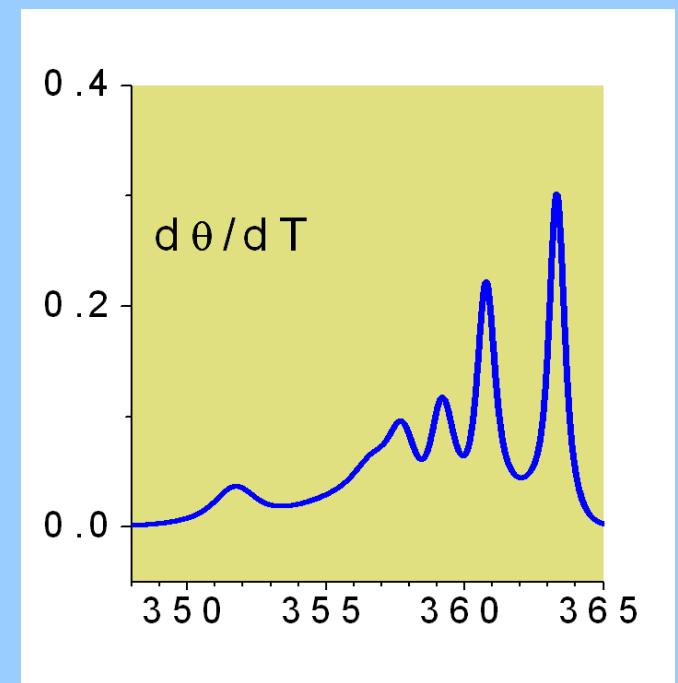
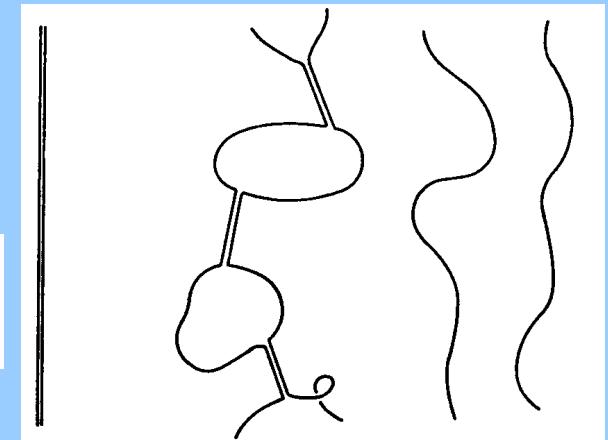
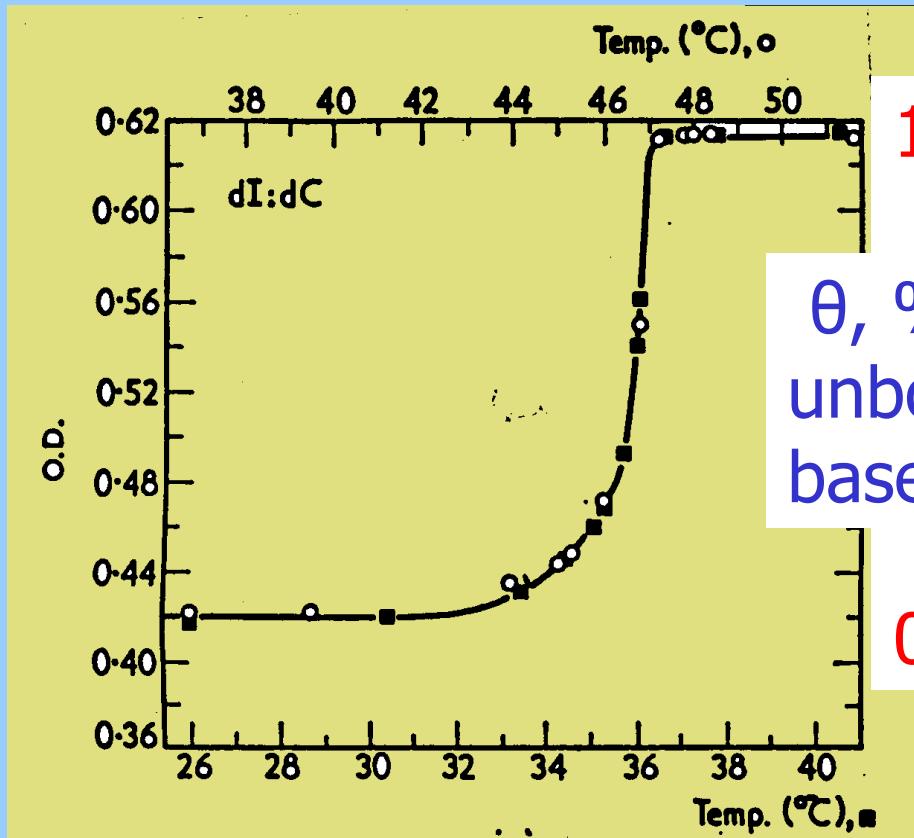
Essevat-Roulet, Bockelmann & Heslot, PNAS **94**, 11935 (1997)

unzipping



thermal unbinding

melting



"homogeneous" DNA (10^3 - 10^4 identical bps)

natural DNA

Inman & Baldwin, J. Mol. Biol. 8, 452 (1964)

$T_m(GC) > T_m(AT)$

Energy / Entropy balance in unbinding

Melting entropy

$$\Delta S \sim 12.5 k_B$$

enthalpy

$$\Delta H = T_m \Delta S$$

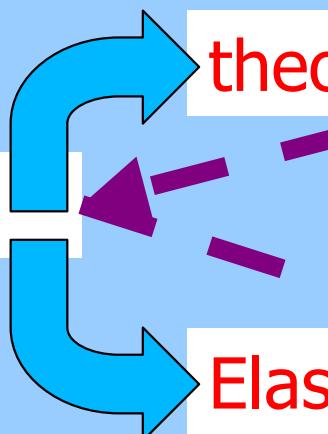
$$\Delta H - T\Delta S \sim F_{unzip} R$$

$$T < T_m$$

$$\Delta H - T\Delta S^* \sim F_{overstr} \Delta l$$

Mechanical transitions
(common energetics)

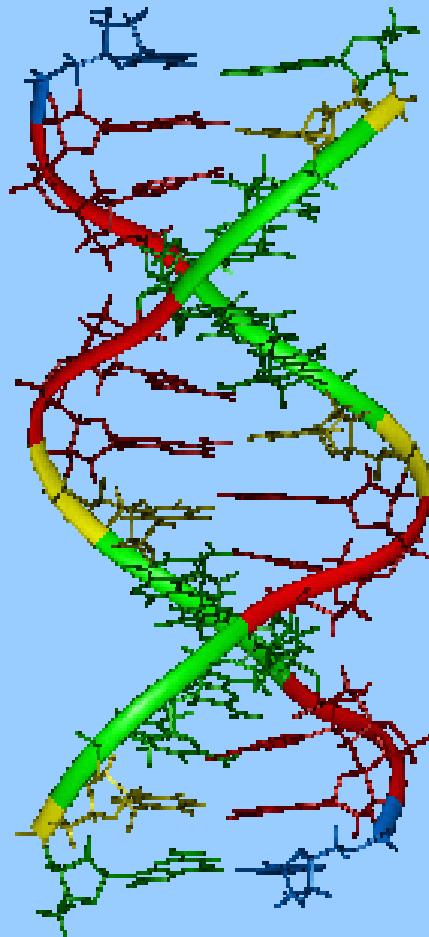
Binding forces



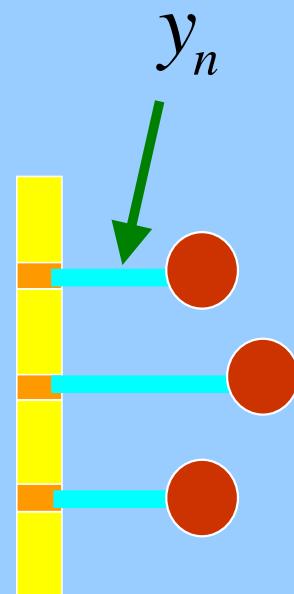
theory of melting

Elastic properties

Mesoscopic modeling of DNA melting, I



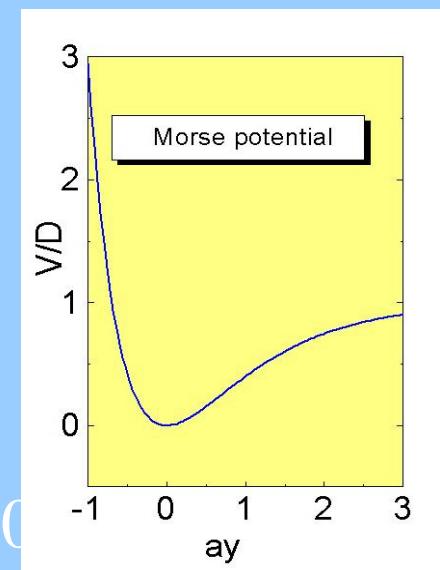
O(1) d.o.f. / base pair
1: Transverse displacement (bp separation)



H-bonding (eff.)
(Morse)

$$V(y) = D \left(1 - e^{-ay}\right)^2$$

$$V'(0) = 0$$
$$V'(\infty) = 0$$



Peyrard & Bishop PRL **62**, 2755 (1989)
Dauxois, Peyrard & Bishop PRE **47**, R44 (1993)

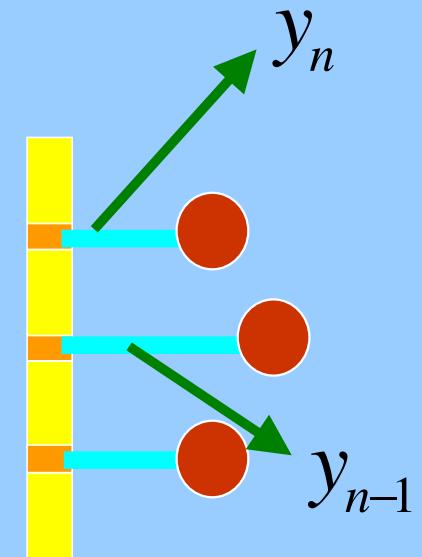
mesoscopic modeling, II

base stacking

nonlinear

$$W(y_n, y_{n-1}) = \frac{1}{2} K (y_n - y_{n-1})^2$$

$$K \rightarrow k \left\{ 1 + \rho e^{-b(y_n + y_{n-1})} \right\}$$



relative stiffness of ds- vs. ss-DNA ?

$$H_P = \sum_n W(y_n, y_{n-1}) + V(y_n)$$

Peyrard & Bishop PRL **62**, 2755 (1989)

Dauxois, Peyrard & Bishop PRE **47**, R44 (1993)

Exact Thermodynamics (TI, homog.)

$$Z_P = \int dy_1 \dots dy_n \underbrace{K(y_1, y_2) \dots K(y_{N-1}, y_N)}_{e^{-W(y_1, y_2)/T} e^{-V(y_1)/T}}$$

$$\int_{-\infty}^{+\infty} dy K(x, y) \phi_\nu(y) = \Lambda_\nu \phi_\nu(x)$$

$$\Lambda_0 \geq \Lambda_1 \geq \dots$$

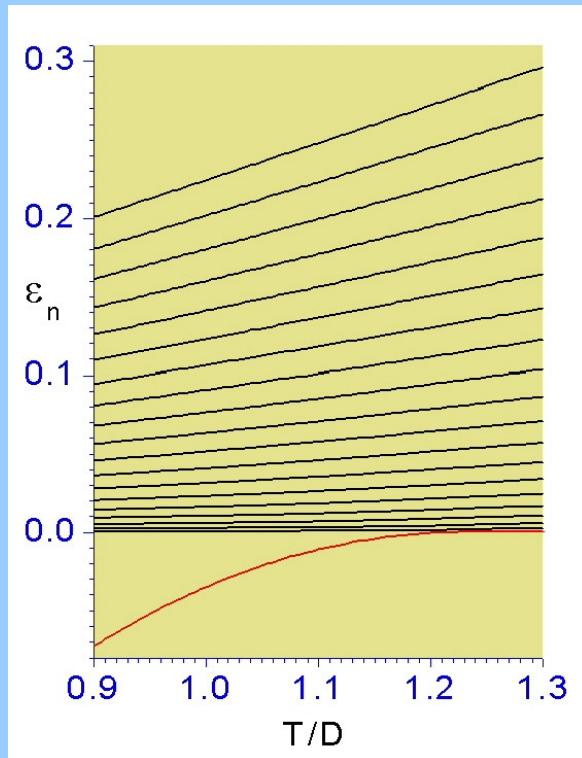
$$Z_P = \sum_\nu \Lambda_\nu^N \approx \Lambda_0^N$$

$$f = -\frac{1}{N} T \ln Z_P \approx -T \ln \Lambda_0 = \varepsilon_0$$

$$\Lambda_\nu \equiv e^{-\varepsilon_\nu/T}$$

$$\varepsilon_0 \leq \varepsilon_1 \leq \dots$$

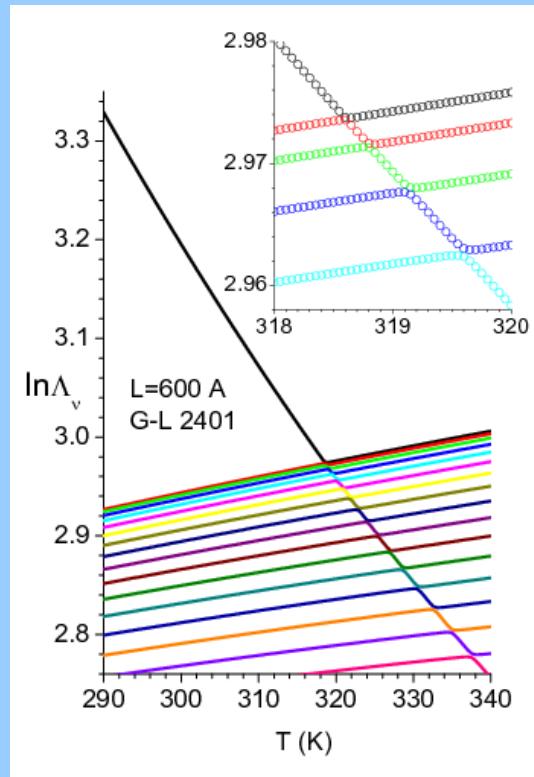
Critical behavior: spectral gap



$$\rho = 0 \Rightarrow \nu = 2$$

2nd order

cf. QM 0-d



$$\rho \neq 0 \Rightarrow \nu = 1$$

Eff. 1st order

$$\Delta\epsilon \propto (T_c - T)^\nu$$

Finite-size scaling

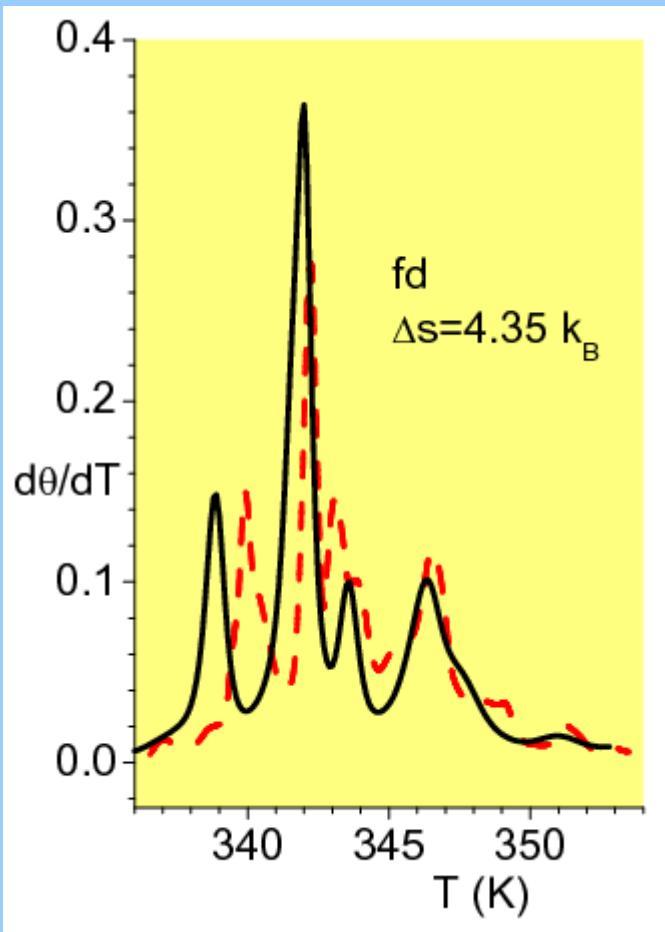
N. Th., PR E (2003)

Barbi, Lepri, Peyrard

& Th., PR E (2003)

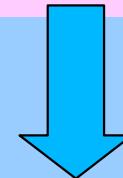
Heterogeneity
broadens phase
transition

Heterogeneous melting (multistep)



6408 bps, 40.9% GC,
[Na⁺]=0.0195M

Sequence & salt concentration



(any) melting profile

no adjustable parameters

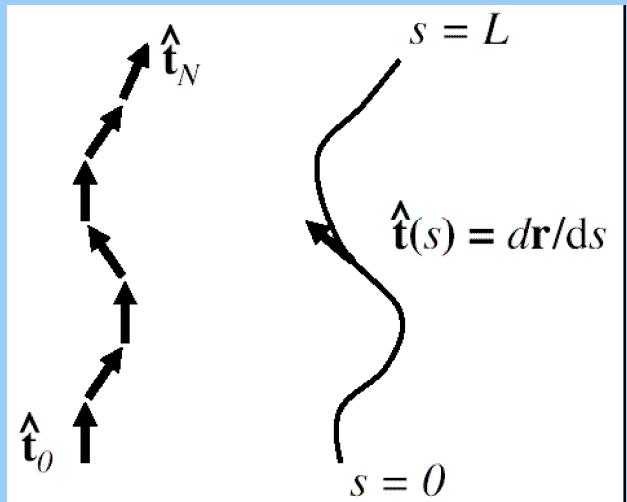
$$D_{AT,GC} = D_{AT,GC}^0 + \kappa_{AT,GC} \log\left(\frac{c}{c_0}\right)$$

- optimized „constants“
- rapid computation

Theory (solid line) N. Th. PRE (2010)

Expt (red dashed), Wada et al, Nature (1976)

Back to elasticity ...



Heterogeneous Kratky – Porod

$$H = - \sum_{n=1}^N B_{n,n+1} \hat{t}_n \cdot \hat{t}_{n+1}$$

$$B_{n,n+1} = (1 - P_{n,n+1})B + P_{n,n+1}B'$$



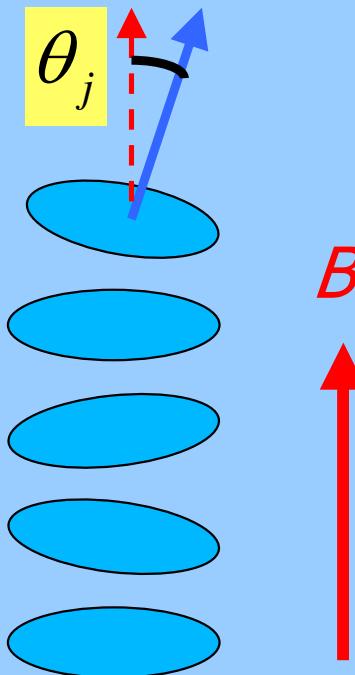
$$B' = B / 50$$

Probability that bps n & n+1 are “unbound”

computable from melting model

Bending flexibility, T-dependence ?

Magnetically induced optical birefringence*



Base planes: anisotropically diamagnetic

orient in external magnetic field

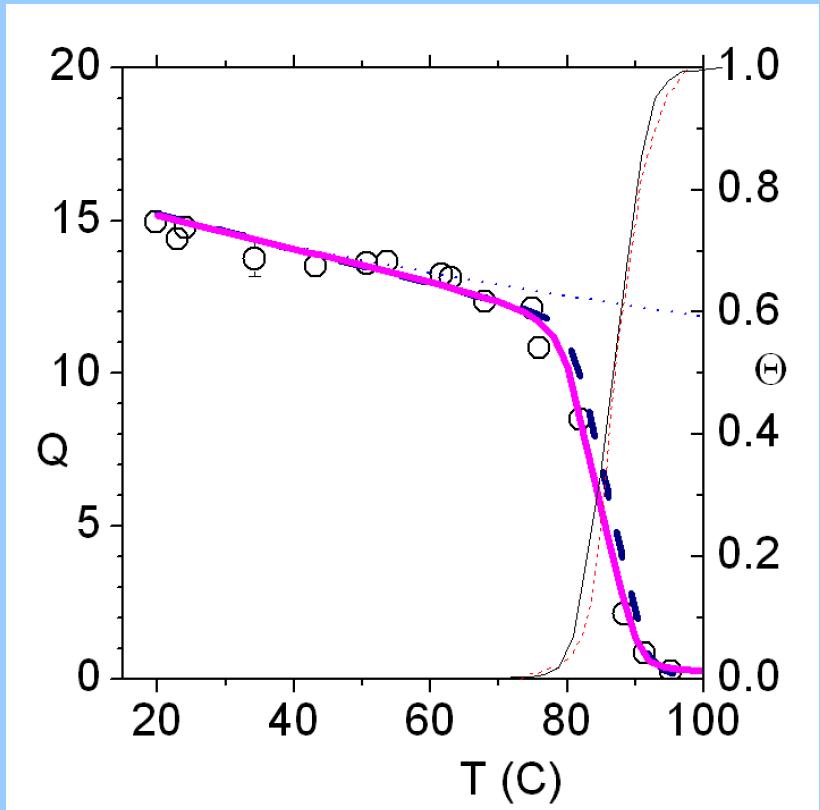
$$\Delta n = \frac{2\pi}{n} \rho \Delta\alpha \Delta\chi \frac{B^2}{k_B T} \underbrace{Q}_{\text{Q}}$$

$$\frac{1}{N} \sum_{i,j=1}^N \left\langle \frac{1}{2} (3 \cos^2 \theta_j - 1) \cos^2 \theta_i \right\rangle_0$$

* Maret et al, PRL 1975

Bending flexibility, T-dependence

Magnetically induced optical birefringence*



Birifringence:
property of intact clusters of
(oriented, diamagnetic) bps
Xtra flexibility: „bubbles“
Premelting !

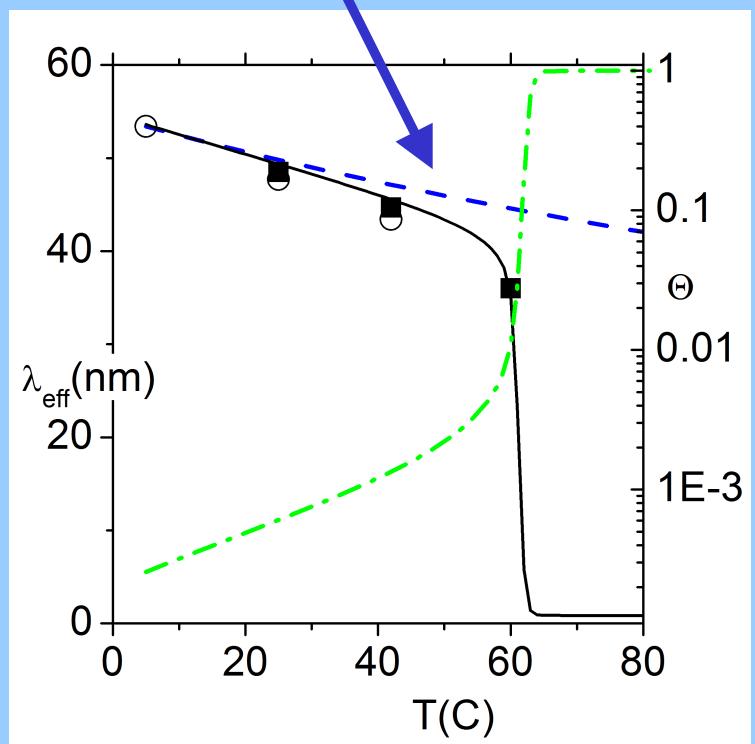
* Maret et al, PRL 1975 (bovine sample)

Theory: Th. & Peyrard, PRL 2012

Bending flexibility, T-dependence

Cyclization* (shorter chains, ca. 200 bps)

constant stiffness, $1/T$



„bubbles“ → Xtra flexibility

premelting (biologically relevant!)
nonlinear dependence
 $40\text{C} : \Theta = .001 , \Delta\lambda/\lambda(5\text{C}) \gg \Theta$

* Geggier, Kotlyat, Vologodskii, Nucl. Acids 2011

Theory: Th. & Peyrard, PRL 2012

Local openings & flexibility

(v. Hippel & coworkers, 1965-)

