Discrete topological solitons & 1D thermodynamic instabilities: application to DNA melting & unzipping

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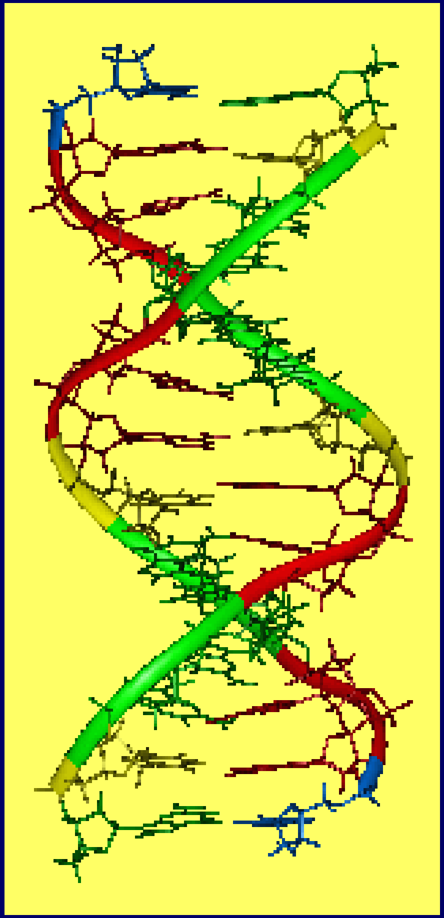
Outline

- expt. review (DNA „melting“)
- modeling I (Helices & loops, Ising)
- micromanipulation (DNA „unzipping“)
- modeling II (Hamiltonian)
- nonlinear equilibrium structures (DWs)
- DW thermodynamics (1D phase trans.)

DNA Denaturation („melting")



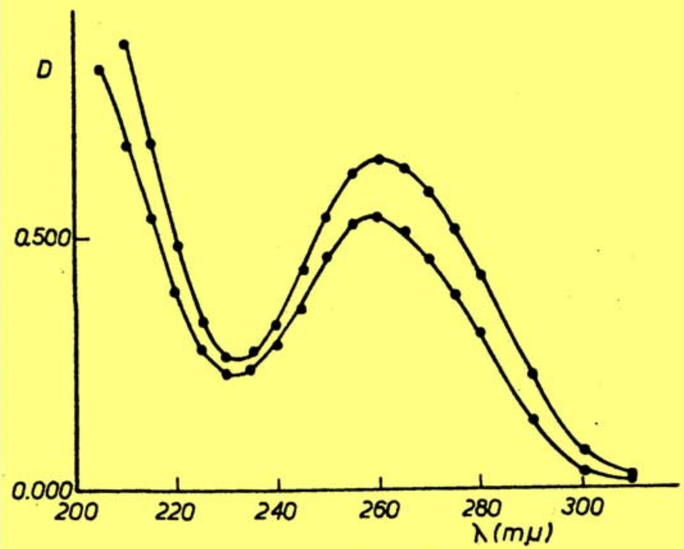


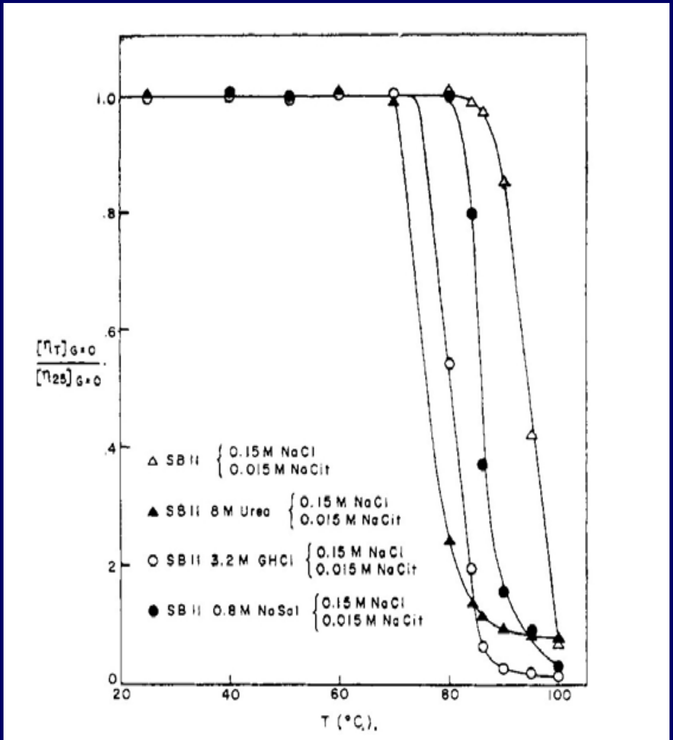
Fig. I. ADN de testicules d'étoile de mer. Accroissement de l'absorption UV par diminution de la concentration en sels: (a) NaCl 10^{-2} M; (B) NaCl $10^{-4.4}$ M.

R. Thomas, Biochim. Bioph. Acta **14**, 231 (1954)

D-H conditionally stable (pH, T)

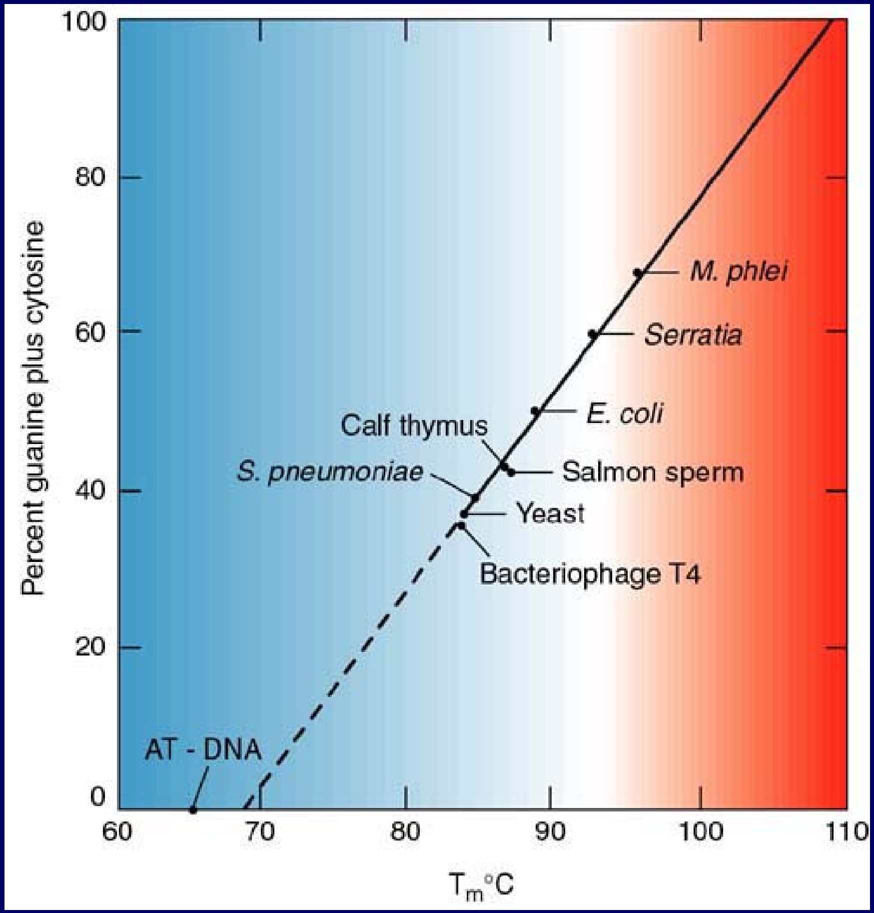
macroscopic evidence

- viscosity
- UV-absorption
- high T: ss-DNA
- (only) H-bonds break
- reversible
- T_m def. as 50% helical
- $\Delta T \sim$ 10-20 K (heterog.)



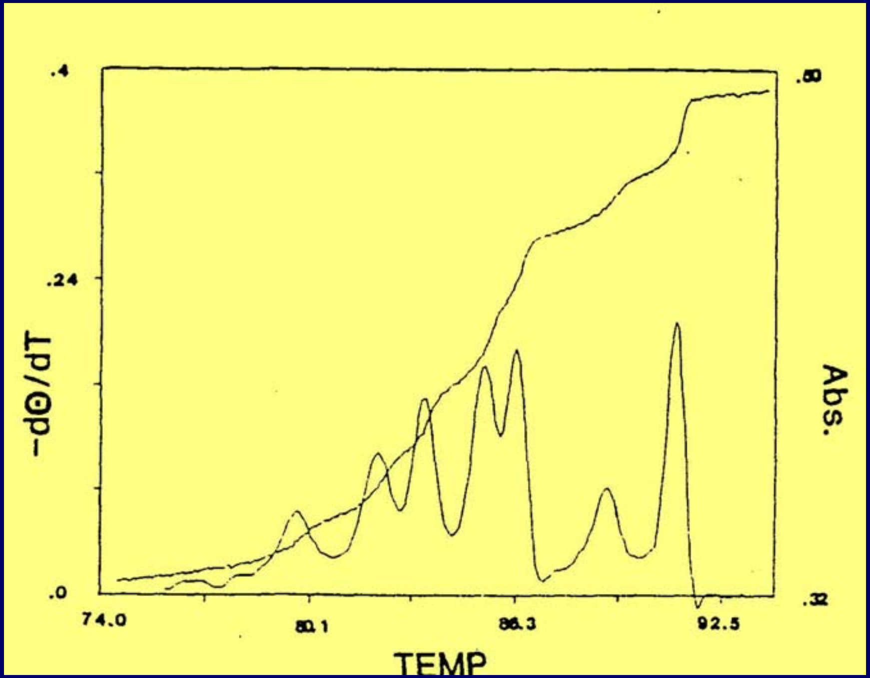
Rice & Doty, JACS **79**, 3937 (1957)

T_m grows with G-C %



- G-C: 3 H-Bonds
- A-T: 2 H-Bonds

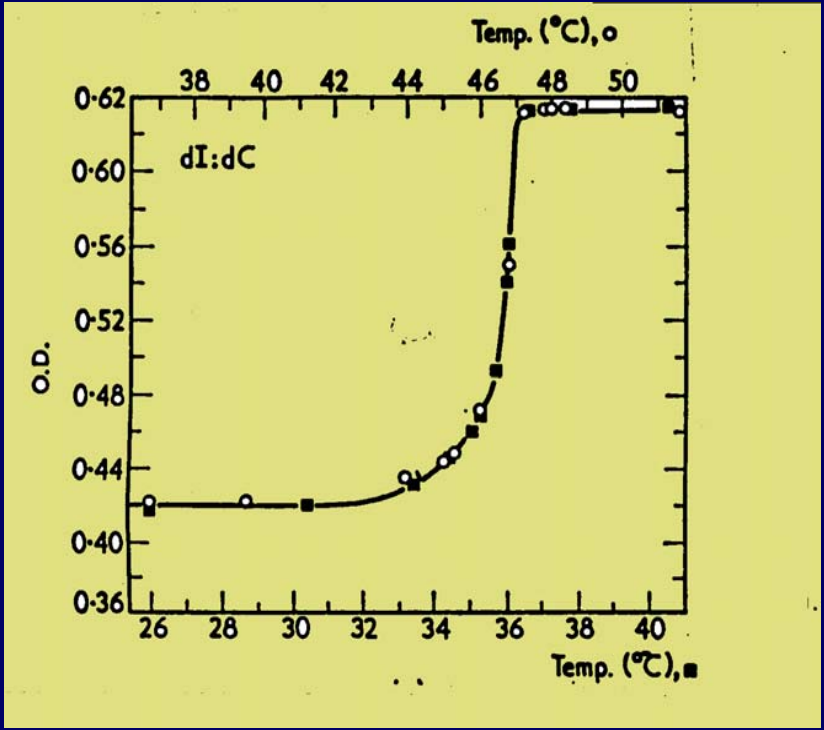
fine structure of melting curve



1630 bp Hinf I Restriction Endonuclease DNA fragment of the plasmid pBR322

- multistep melting
- fragment-specific peaks („fingerprinting“)

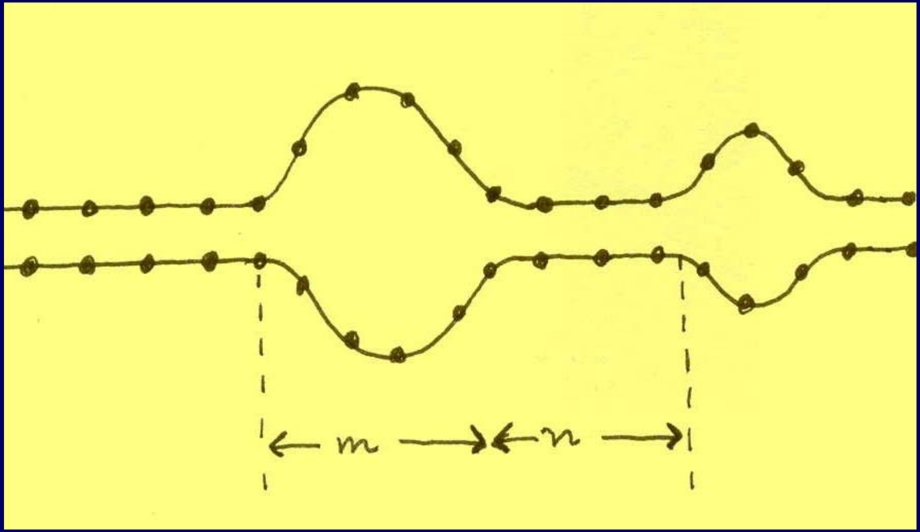
Denaturation of polynucleotides



- „homogeneous“ DNA (identical bp´s)
- $\Delta T/T_m = O(10^{-3})$
- still not $N \to \infty$!

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

Helices & Loops



- each bp: helical / unbound
- Nucleation, $\sigma << 1$
- Helix growth

  $s = s_0 \exp(-\varepsilon / T) \sim 1$
- Loop Entropy

$$p_n = \sigma s^n$$

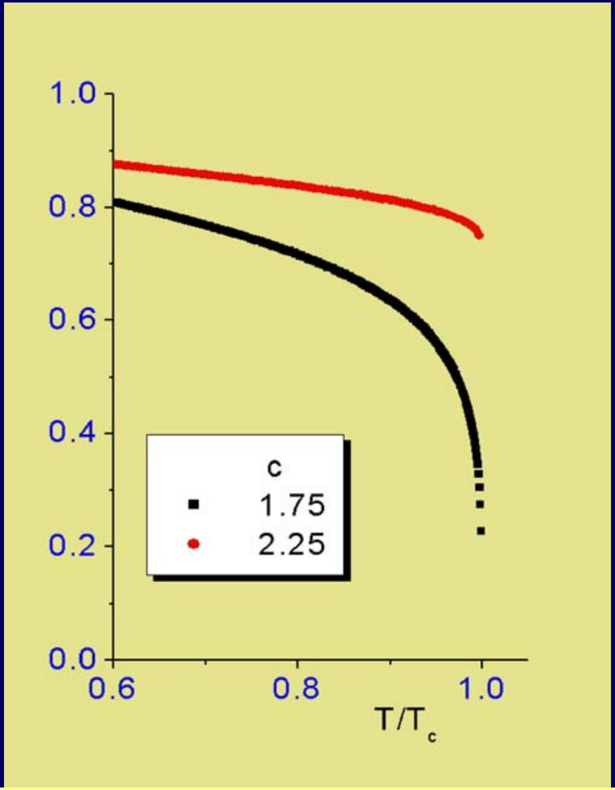
$$q_m = \frac{b^m}{m^c}$$

$$P_{n,m} = z\, p_n q_m$$

$$\sum_{n,m} P_{n,m} = 1$$

Poland & Scheraga, JCP **45,** 1464 (1966)

Order parameter: Helix%



helix fraction vs. T

- c<1 no ph-trans.
  1<c<2 2. Order
- c>2 1. Order

$c = d/2\ (=1.5)$ RW

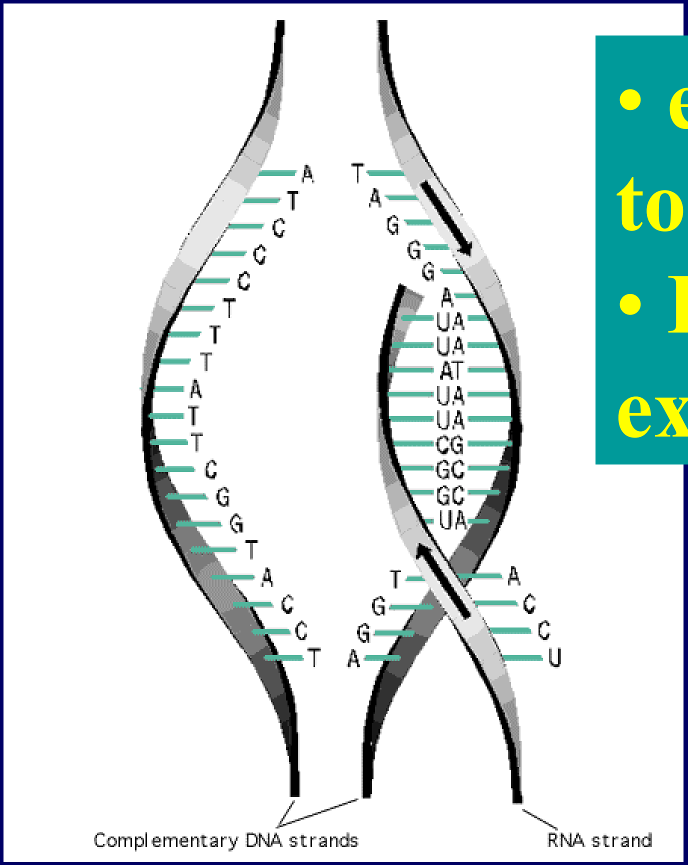
$c = 1.75$ SAW[1]

$c = 2.1$[2]

[1] Fisher , JCP (1966)

[2] Kafri et al, PRL (2000)

Denaturation loop

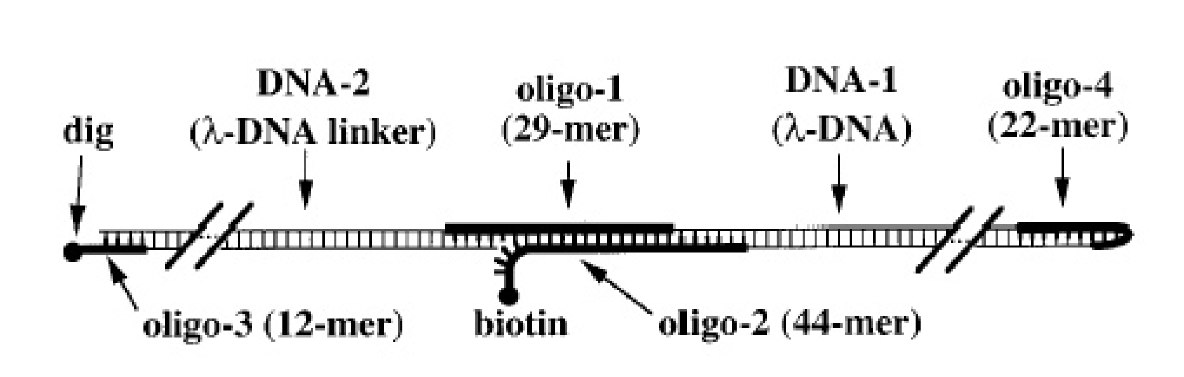


- **essential for transcription to mRNA**
- **BP- lifetime (Imino-p exchange) : $\tau_{BP} \approx 10$ msec**

PS model:

- **> 0 probability**
- **no dynamics!**

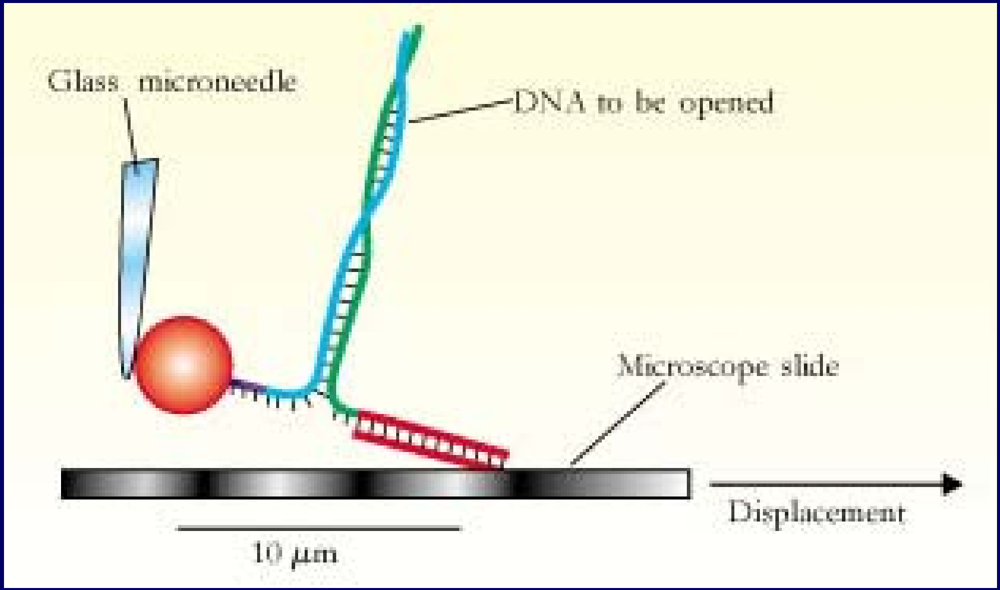
„unzipping“ DNA



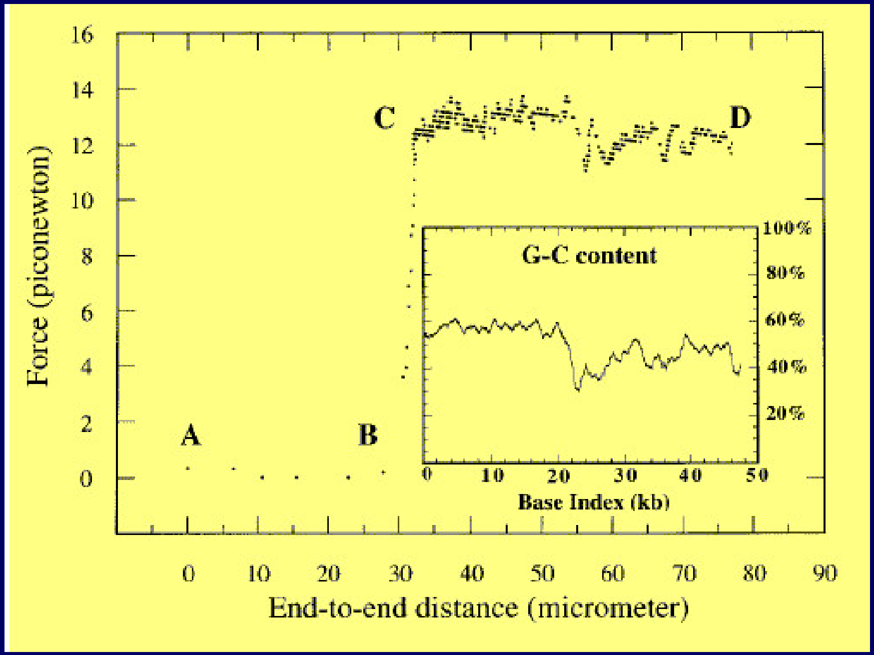
Essevat-Roulet, Bockelmann & Heslot, PNAS **94**, 11935 (1997)

molecular construction

Force measurement during mechanical DNA separation (principle)

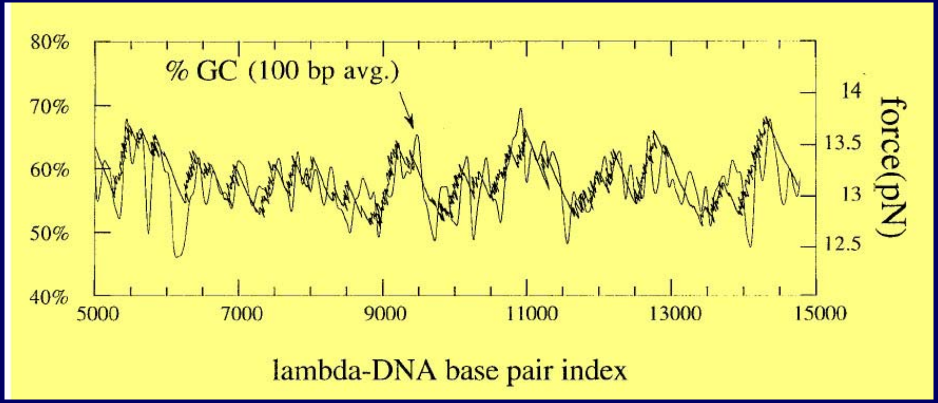


How hard must one pull?



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

F_{break} = 13 pN



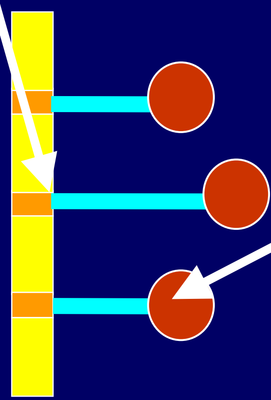
F vs. G-C % ave. over 100 BP

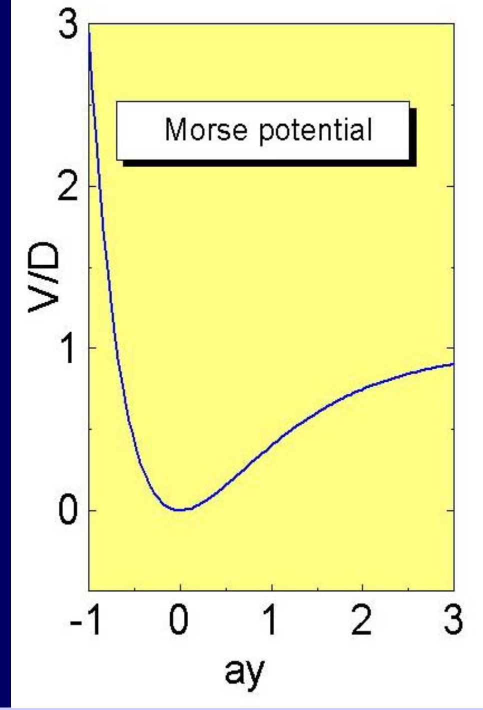
A lattice model

$$W(y_n, y_{n-1}) = \frac{1}{2}k\left[1+\rho e^{-\beta(y_n+y_{n-1})}\right](y_n - y_{n-1})^2$$

stacking-int (ρ=0, linear)

continuum-generaliz. y_n
1 d.o.f / bp





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

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

Peyrard & Bishop PRL **62,** 2755 (1989)
Dauxois, Peyrard & Bishop PRE (1991)

Exact Thermodynamics (TI)

partition fn.

$$Z_P = \int dy_1 \ldots dy_n \; e^{-H_P(\{y\})/T}$$

$$= \int dy_1 \ldots dy_n \; K(y_1, y_2) \ldots K(y_{N-1}, y_N)$$

kernel

$$K(x,y) = e^{-W(x,y)/T} \; e^{-V(x)/T}$$

Transfer Integral Eq. (singular!)

$$\int_{-\infty}^{+\infty} dy \, K(x,y) \, \phi_\nu(y) = e^{-\varepsilon_\nu/T} \phi_\nu(x)$$

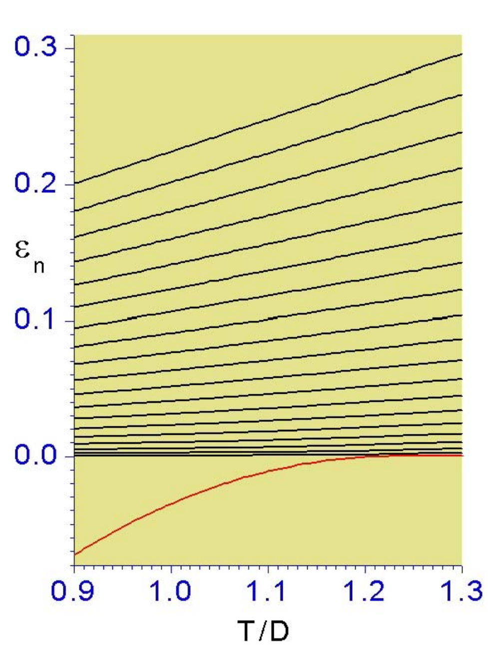
$$\varepsilon_0 \le \varepsilon_1 \le \ldots$$

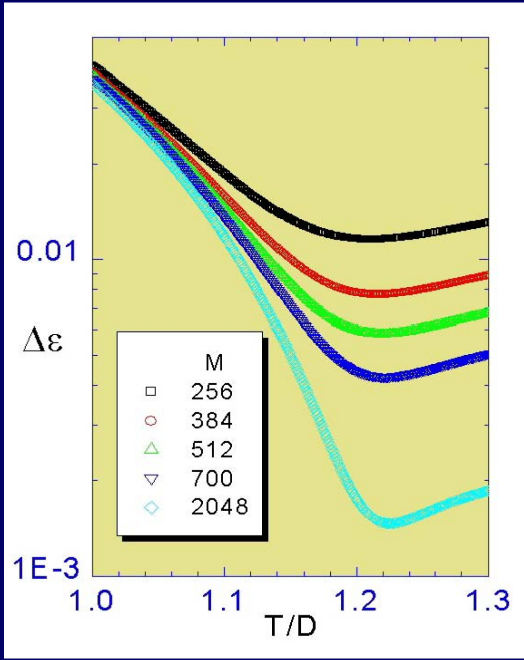
free energy

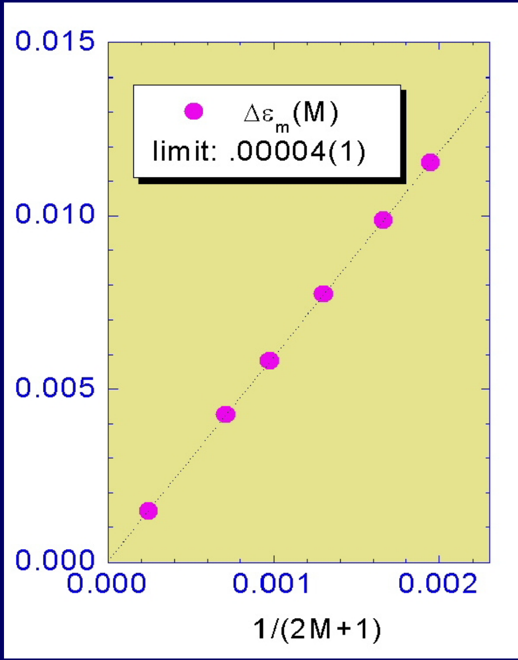
$$Z_P \approx e^{-N\varepsilon_0/T}$$

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

Spectrum of TI-eq. (ρ=0, num.)







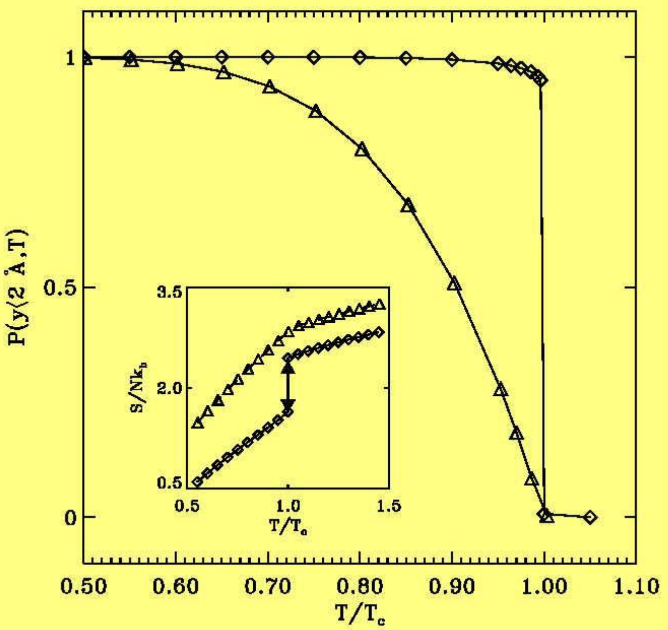
Th., PR E **68**, 026109 (2003)

$$\Delta\varepsilon \equiv \varepsilon_1 - \varepsilon_0 \propto \xi^{-1} \to 0$$

$$\propto (T_c - T)^2$$

long-range correlations
(scaling theory of phase transitions)
here: finite-size scaling

Order of Phase Transition?



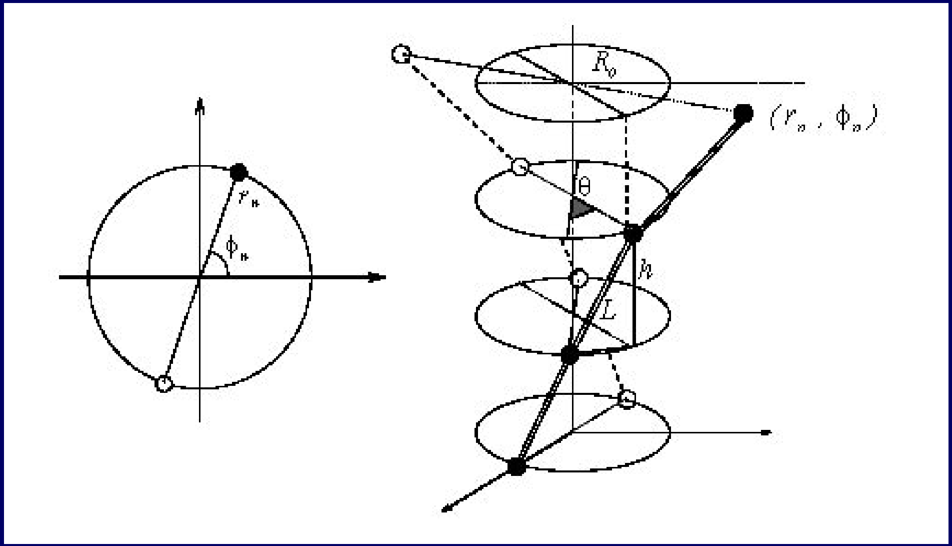
helix fraction vs. T/T_c
inset: entropy

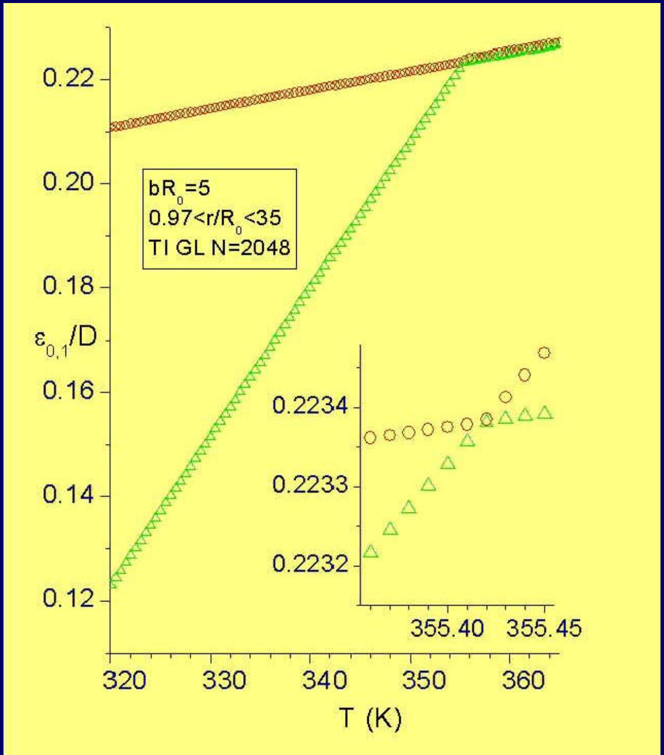
$$P(y < y_0 \ , T) \propto (T_c - T) \ \ , \ \rho = 0$$
$$\rightarrow const \ , \ \rho = 1$$

nonlinear stacking int.
$\Rightarrow$ *effectively* 1st order

Th., Dauxois & Peyrard, PRL **85**, 26 (2000)

Helicoidal version





bp´s on fixed planes, 2 DoF / bp

Barbi, Cocco & Peyrard, PL A (1999)

- **also *effectively* 1st order**
- **$\Delta T_{crossover} < 0.003$ K**

$$\Delta\varepsilon \propto e^{-const/(T_c - T)} \quad , \quad \rho = 0$$

$$\approx (T_c - T) \quad , \quad \rho = 1$$

Barbi, Lepri, Peyrard & Th., PR E (2003)

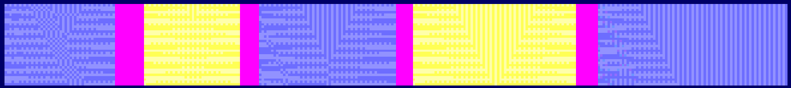
Lattice models (up to now)

- **exact ph-tr for homogeneous DNA**
- ***effective* order of ph-tr: stacking int.**
- **heterogeneity (disordered D_n – Morse-depth): multistep melting**
- **critical dynamics ($\omega \rightarrow 0$)**
- **fluctuational opening (nonlinear localization phenomenon)**

Phase transitions in 1D?

- general prohibition: *myth**
- proh. for short-range interactions: *half-truth*
- proh. for short-range *pair* interactions (lattice): *theorem by van Hove* [not applicable here, nor in case of φ^4 (or 1D-Ising)!]

**Landau:* Energy cost of DW vs. Entropy gain



$$N_{DW} = N\, e^{-\varepsilon/T}$$

n.l. equilibrium structures

$$H_P = \sum_{n=0}^{N} \frac{1}{2R}\left(y_{n+1} - y_n\right)^2 + V(y_n)$$

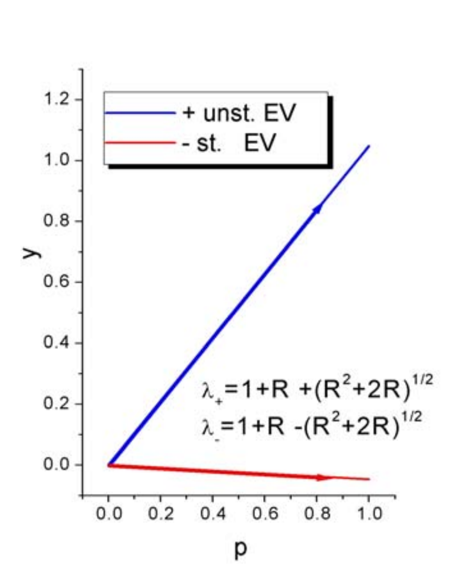
$$\left.\frac{\delta H}{\delta y_n}\right|_{\{\dot{y}_j = 0\}} = 0 \quad \forall n$$

$$\left.\begin{aligned} p_{n+1}^{(\alpha)} &= p_n^{(\alpha)} + RV'(y_n^{(\alpha)}) \\ y_{n+1}^{(\alpha)} &= y_n^{(\alpha)} + p_{n+1}^{(\alpha)} \end{aligned}\right|$$

hyperbol. FP

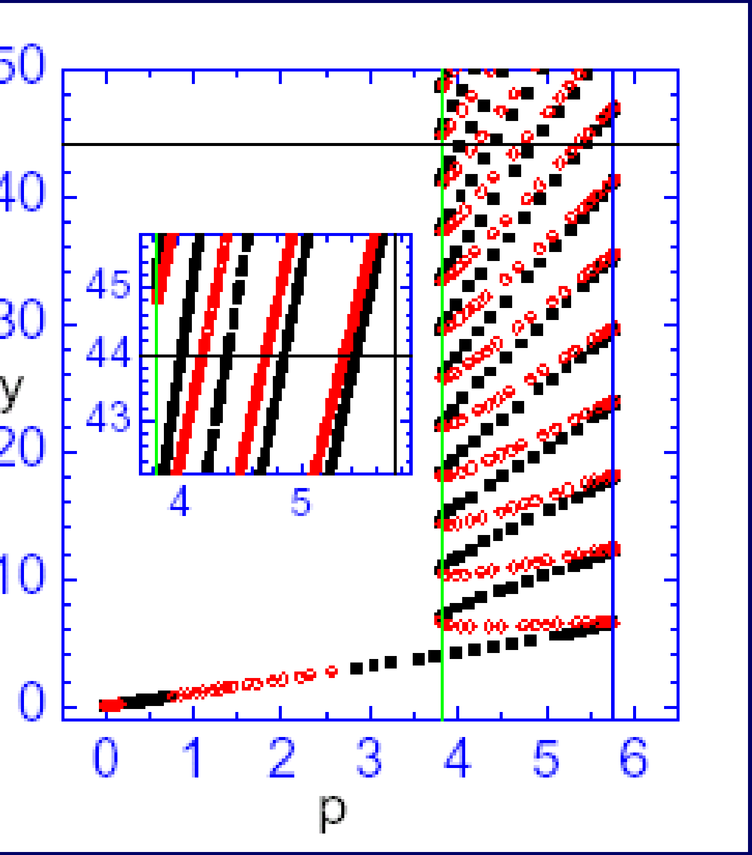
$$y^{(0)} = p^{(0)} = 0$$

$$R >> 1 \quad (10.1)$$



Th., Peyrard & MacKay (2004)

The HFP´s unstable manifold



$$A_{mn}^{(\alpha)} = \left.\frac{\partial^2 H}{\partial y_n \partial y_m}\right|_{\{y_i = y_i^{(\alpha)}\}}$$

$$A^{(\alpha)} b_\nu^{(\alpha)} = \Lambda_\nu^{(\alpha)} b_\nu^{(\alpha)}$$

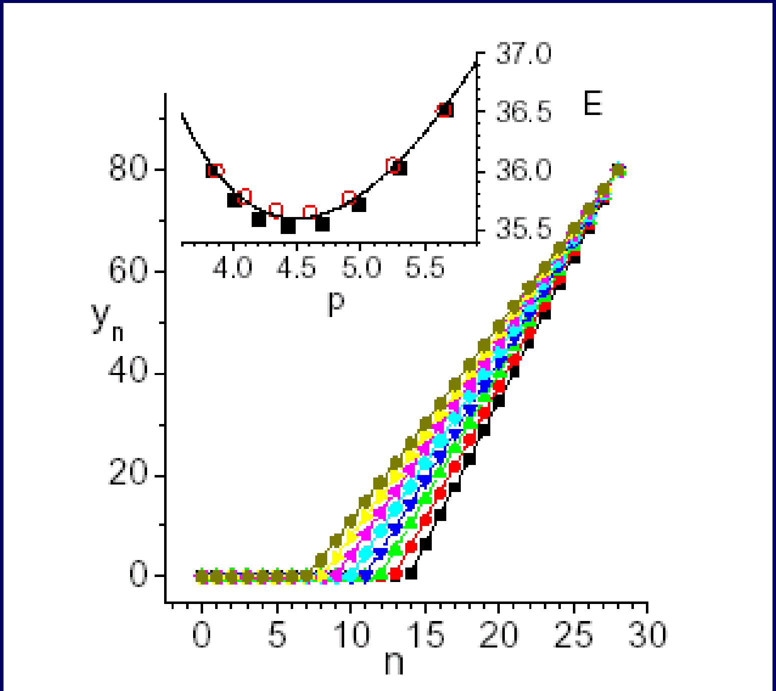
(i) $\Lambda_\nu^{(\alpha)} > 0$ $\nu = 1, 2, \cdots, N$ min(black)

(ii) $\Lambda_\nu^{(\alpha)} > 0$ $\nu = 2, \cdots, N$

$\Lambda_\nu^{(\alpha)} < 0$, $\nu = 1$, minmax (red)

$$y_0 = 0$$
$$y_{N+1} = L$$

Domain Walls (DW)



$$E(p,L) \approx N_{unbound}\left(1+\frac{p^2}{2R}\right)$$

$$N_{unbound} \approx L/p$$

global min at

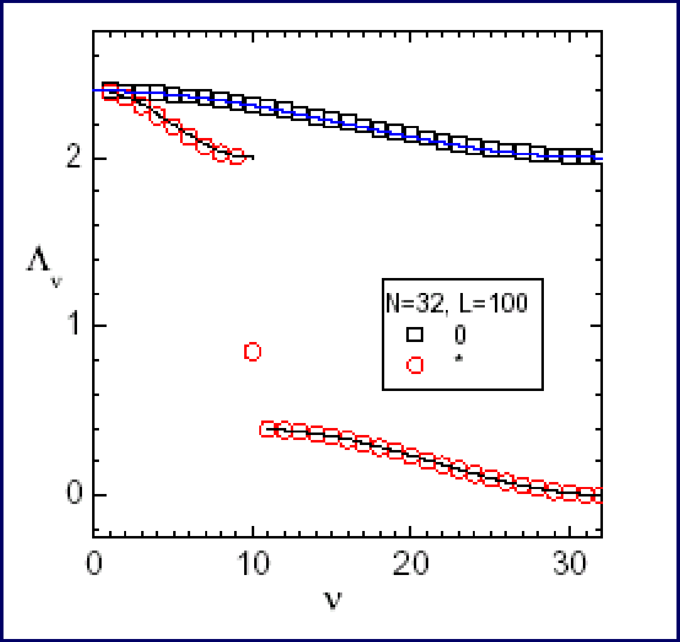
$$E^*(L) \approx 2L/p^*$$

$$p^* = (2R)^{1/2}$$

$$y_0 = 0$$

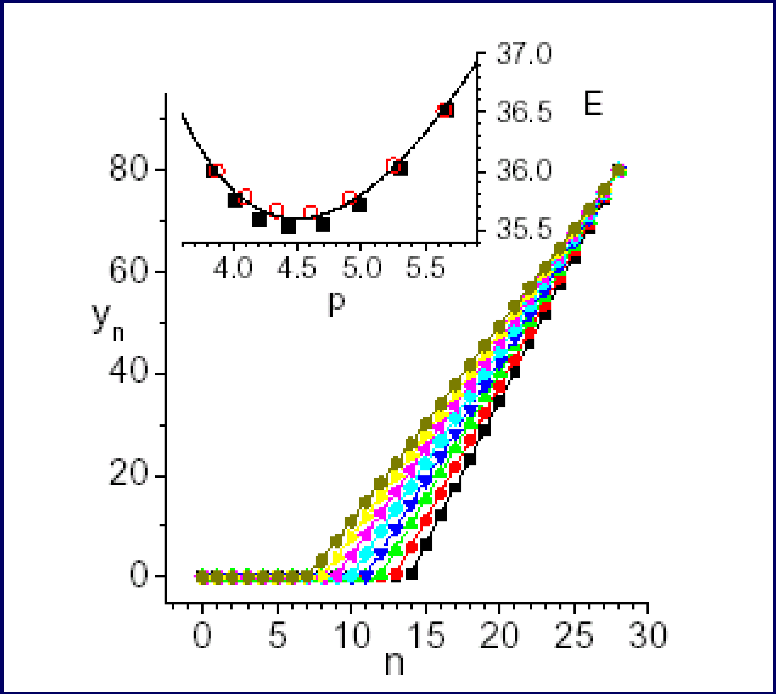
$$y_{N+1} = L$$

DW spectra



N_{unbound} **(R)**

N**-** N_{unbound} **(L)**



DW „interpolates“ between 2 equilibria

DW thermodynamics (I)

$$H^{(\alpha)}(\{\psi\}) = E^{(\alpha)} + \frac{1}{2}\sum_{m,n} A^{(\alpha)}_{mn}\psi_m\psi_n + \cdots$$

$$Z_N^{(\alpha)} = \int_{-\infty}^{\infty}\prod_{j=1}^{N} d\psi_j \, e^{-H^{(\alpha)}(\{\psi\})/T}$$

$$\approx e^{-E^{(\alpha)}/T}\prod_{\nu}\left\{\frac{2\pi T}{\Lambda_\nu^{(\alpha)}}\right\}^{1/2}$$

$$\Delta G(L,T) = -T\lim_{N\to\infty}\ln\left\{\frac{Z_N(L)}{Z_N(0)}\right\}$$

$$\frac{Z_N(L)}{Z_N(0)} \approx e^{-E^{*}/T}\prod_{\nu}\left\{\frac{\Lambda_\nu^{(0)}}{\Lambda_\nu^{(*)}}\right\}^{1/2}$$

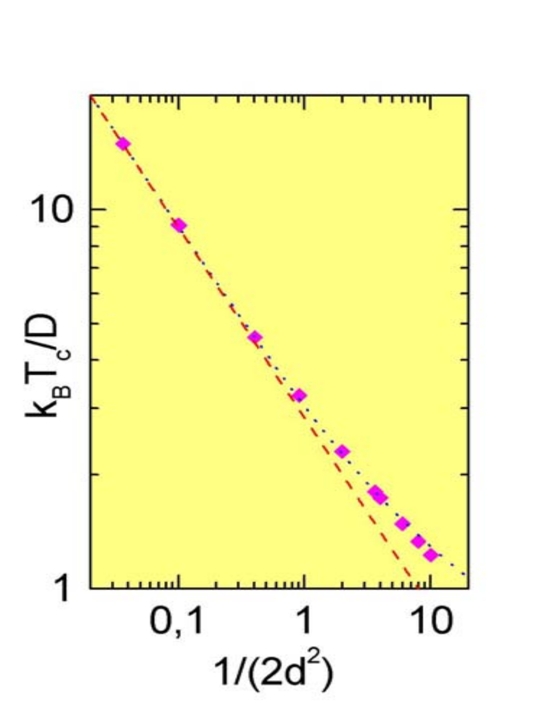
DW thermodynamics (II)

$$\Delta G \approx E^*(L) - T\Omega = (2 - T\sigma)\frac{L}{p^*}$$

*1<<N***unbound** *<N*

$$\Omega = \frac{1}{2}\sum_{\nu=1}^{N} \ln\left\{\frac{\Lambda_\nu^{(0)}}{\Lambda_\nu^{(*)}}\right\} = \frac{L}{p^*}\sigma + O(1)$$

$$\sigma = \ln\left[\left(1 + R/2\right)^{1/2} + \left(R/2\right)^{1/2}\right]$$



$$f(T) = \left(\frac{\partial \Delta G}{\partial L}\right)_T = \frac{2 - T\sigma}{p^*}$$

(unzipping force)

$$T_c^{DW,G} = \frac{2}{\sigma(R)}$$

Thermodynamic pert. theory (I)

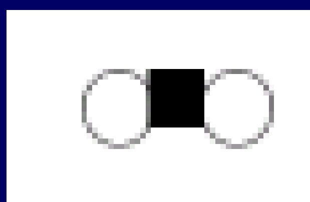
$$H^{(\alpha)}(\{\psi\}) = E^{(\alpha)} + \frac{1}{2}\sum_{m,n} A^{(\alpha)}_{mn}\psi_m\psi_n + \sum_m v^{(3)}_{m,\alpha}\psi^3_m + \sum_m v^{(4)}_{m,\alpha}\psi^4_m$$

$$v^{(j)}_{m,\alpha} = \frac{1}{j!}V^{(j)}\left(y^{(\alpha)}_m\right)$$

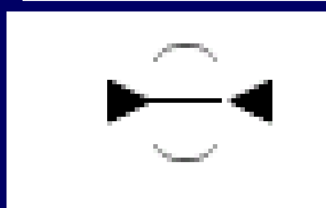
$$g^{\alpha}_{mk}A^{\alpha}_{kn} = \delta_{mn}$$

lowest order irreducible graphs

$\ln Z^{(\alpha)}_N$:



$$-3T\sum_m v^{(4)}_{m,\alpha}\left\{g^{\alpha}_{mm}\right\}^2$$

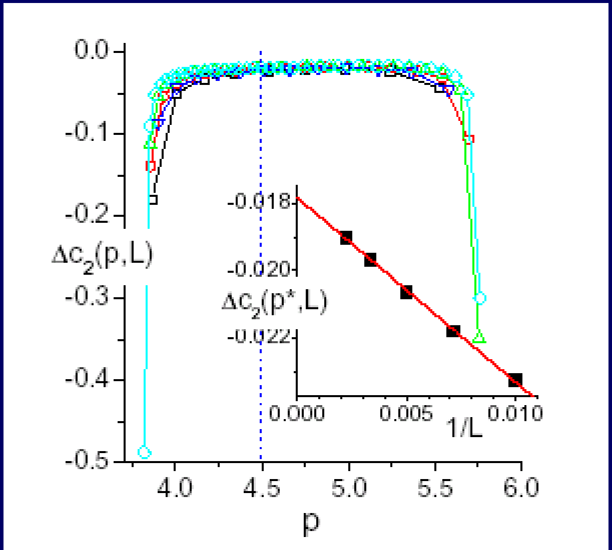


$$6T\frac{1}{2}\sum_m v^{(3)}_{m,\alpha}v^{(3)}_{n,\alpha}\left\{g^{\alpha}_{mn}\right\}^3$$

$$\equiv -TC^{\alpha}_2$$

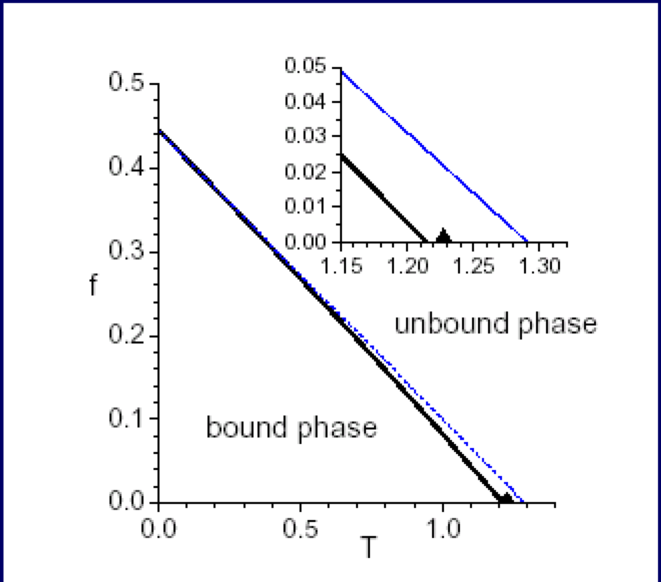
Thermodynamic pert. theory (II)

$$\Delta c_2(p_\alpha, L) \equiv \frac{C_2^{(\alpha)} - C_2^{(0)}}{L}$$



(unzipping force)

$$f(T) = \frac{2 - T\sigma}{p^*} + \Delta c_2^* T^2$$



Tc within 1% of TI (PBC) result

Conclusion

- formation of DW with energy O(L) „drives“ the 1D instability (phase transition)
- unzipping (mechanical, spontaneous thermal)