A predictive model for the thermomechanical melting transition of double stranded DNA

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DIPARTIMENTO DI INGEGNERIA CIVILE, AMBIENTALE, DEL TERRITORIO, EDILE E DI CHIMICA

In collaboration with
- G. Puglisi, PoliBA

Related research activity in progress with
- L. Bellino, PoliBa
- N. M. Pugno, Trento
- S. Giordano, CNRS-Lille
- A. Goriely, Oxford
- M. J. Buehler, MIT

SM&FT 2022 - The XIX Workshop on Statistical Mechanics and non pertubative Field Theory

December 19-21, 2022, Bari

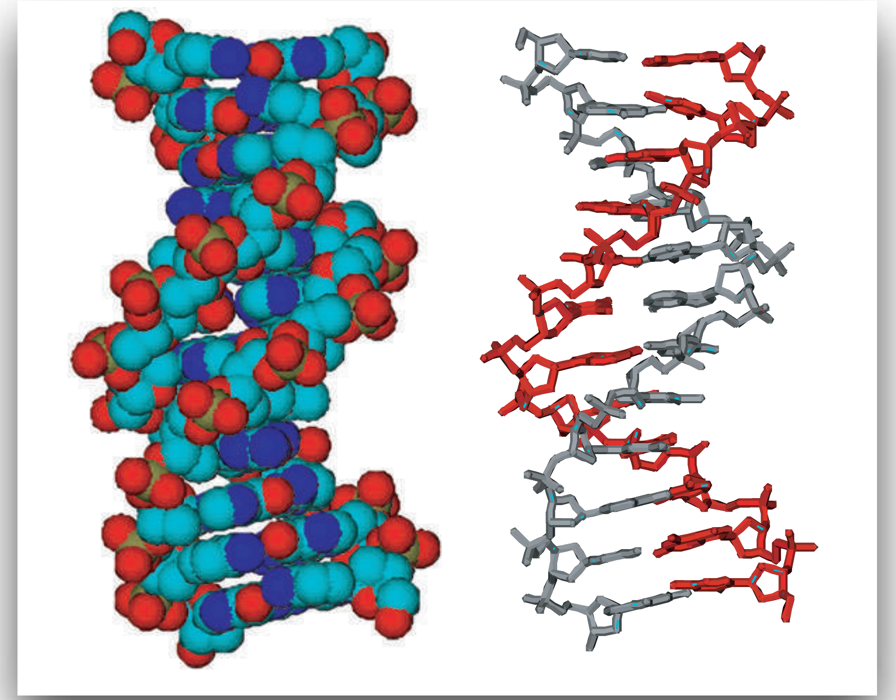
MOTIVATIONS AND OUTLINE OF THE TALK

- Modelling DNA
- Analytical results for predicting properties and designing bio-inspired materials
- Extending the models to different systems

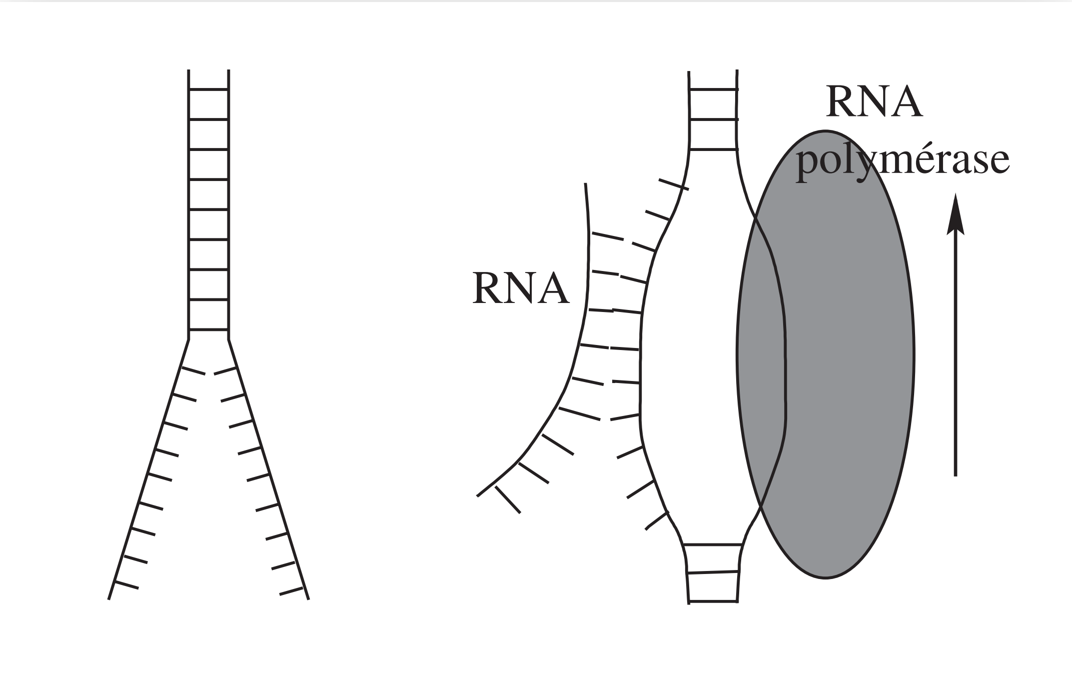
- Models at the micro-scale for DNA
- Effects of temperature
- Comparison with experimental data

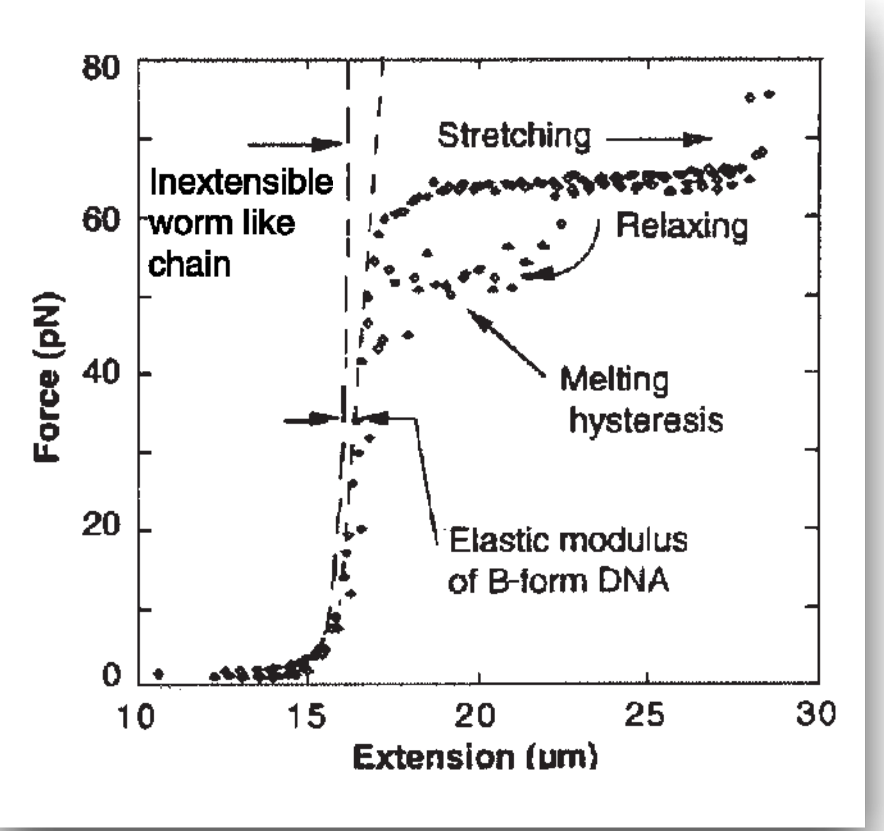
MOTIVATION: DNA MECHANICS

Double helix structure of DNA



Replication and transcription

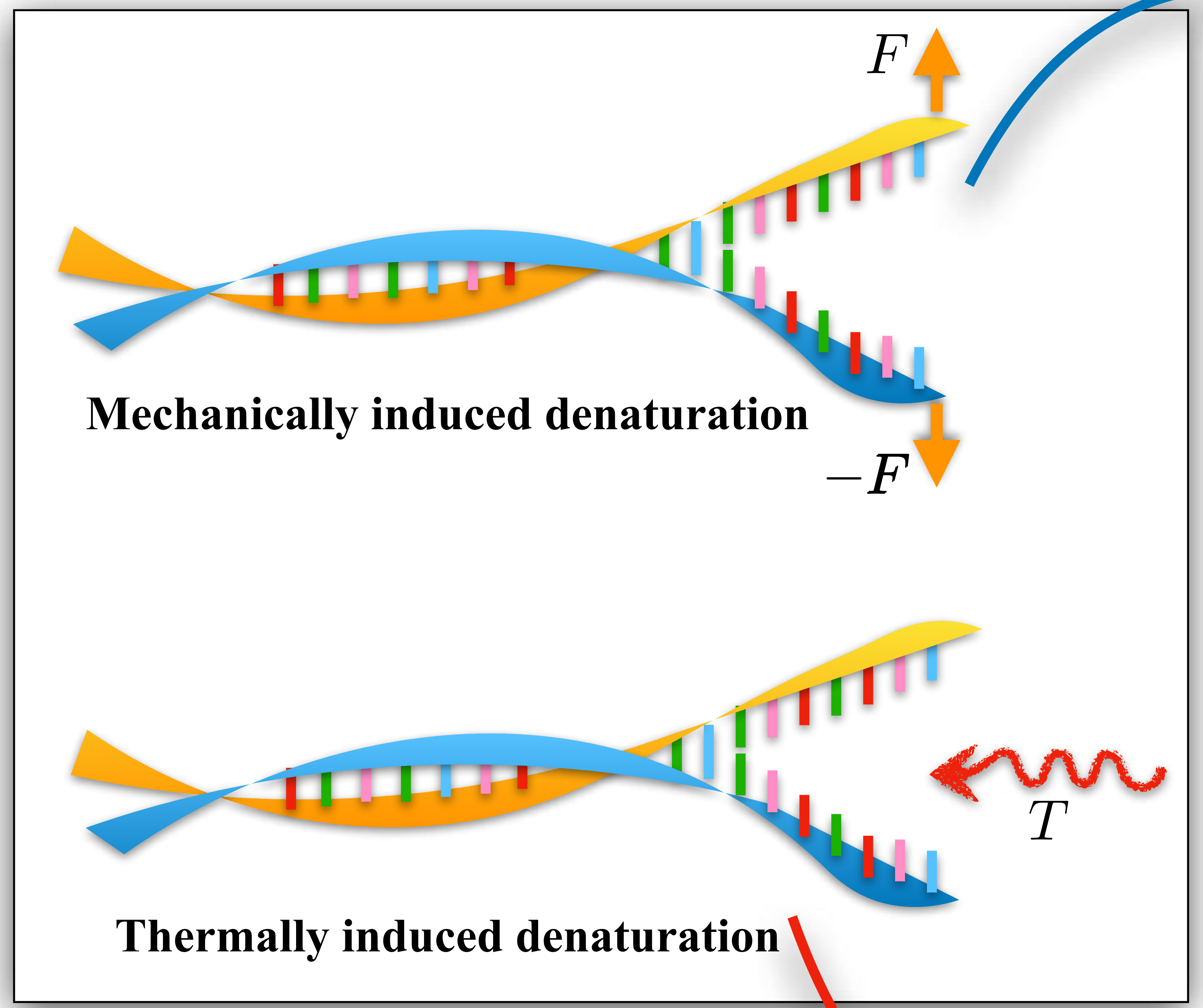


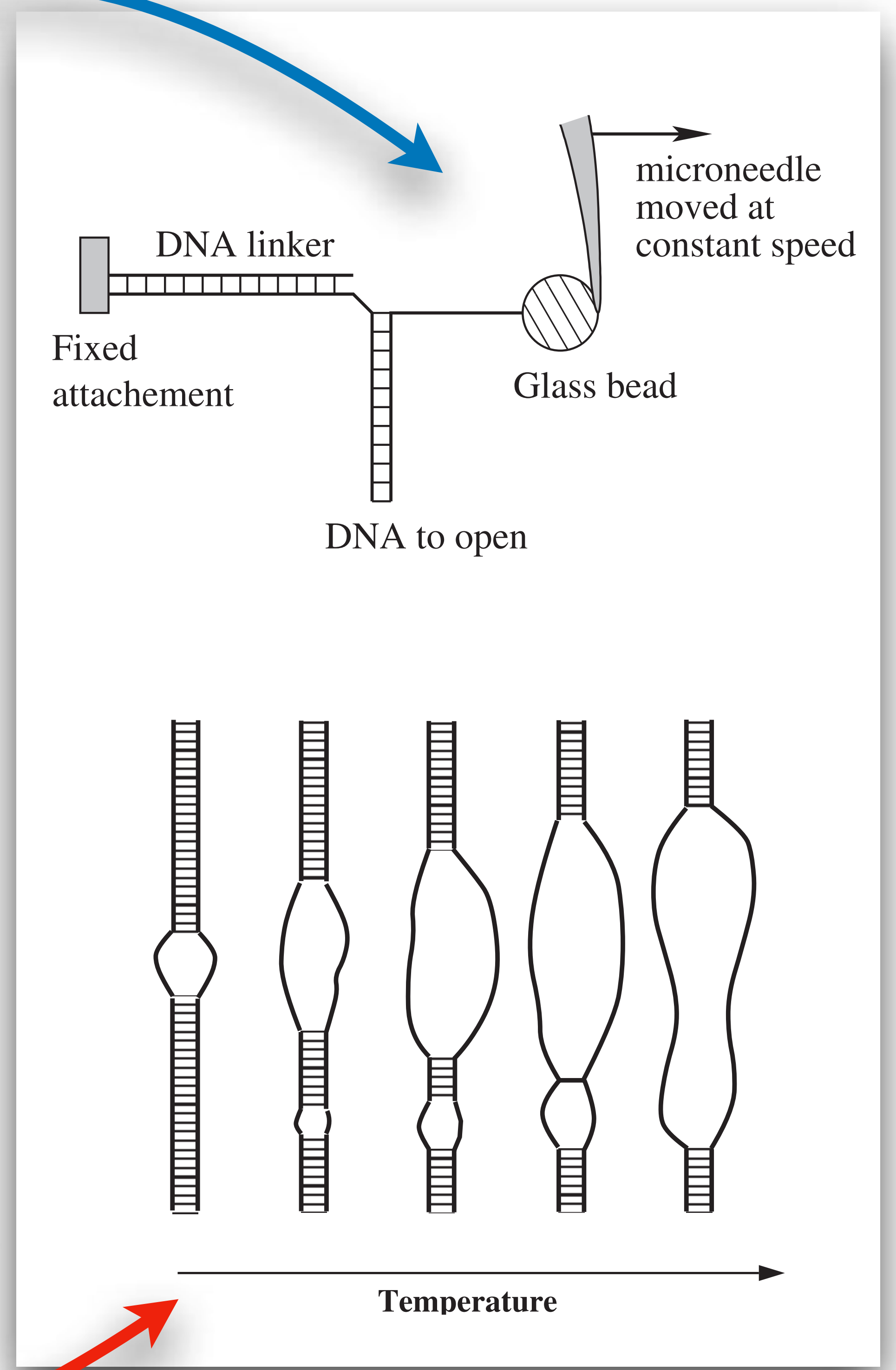


Peyrard, *Nonlinear dynamics and statistical physics of DNA*, Nonlinearity 2004

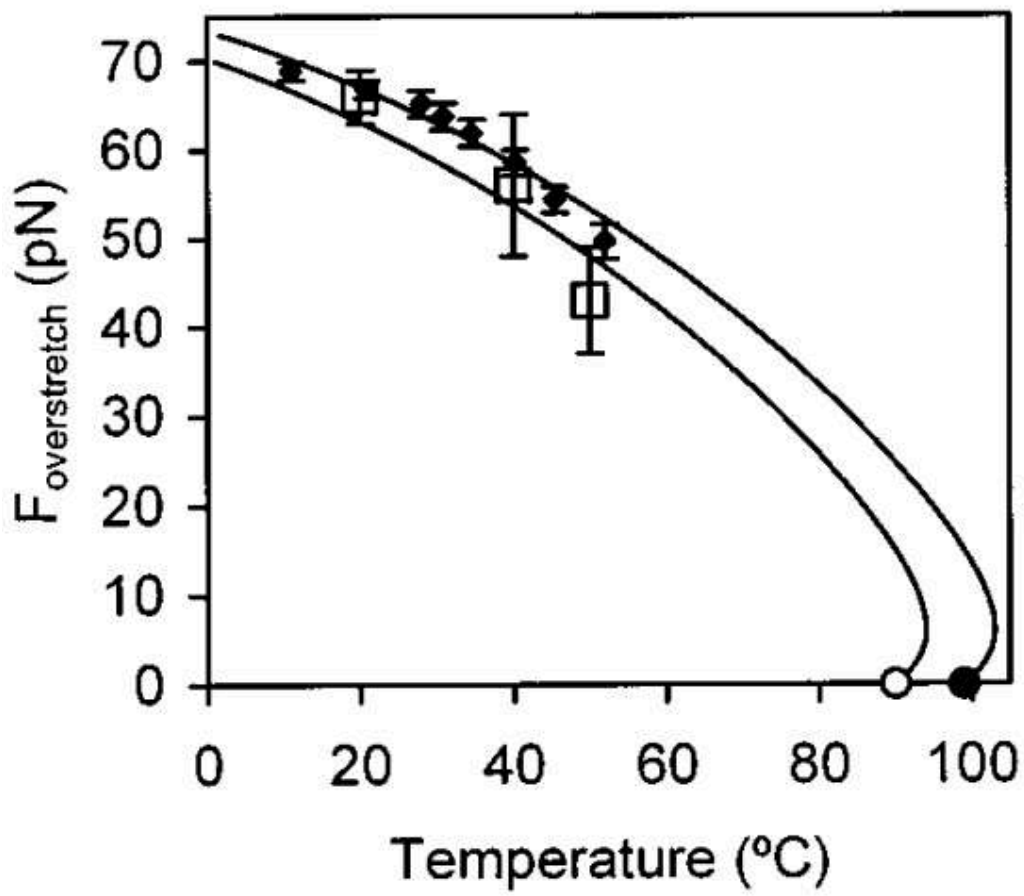
Force–extension curve of a single DNA molecule

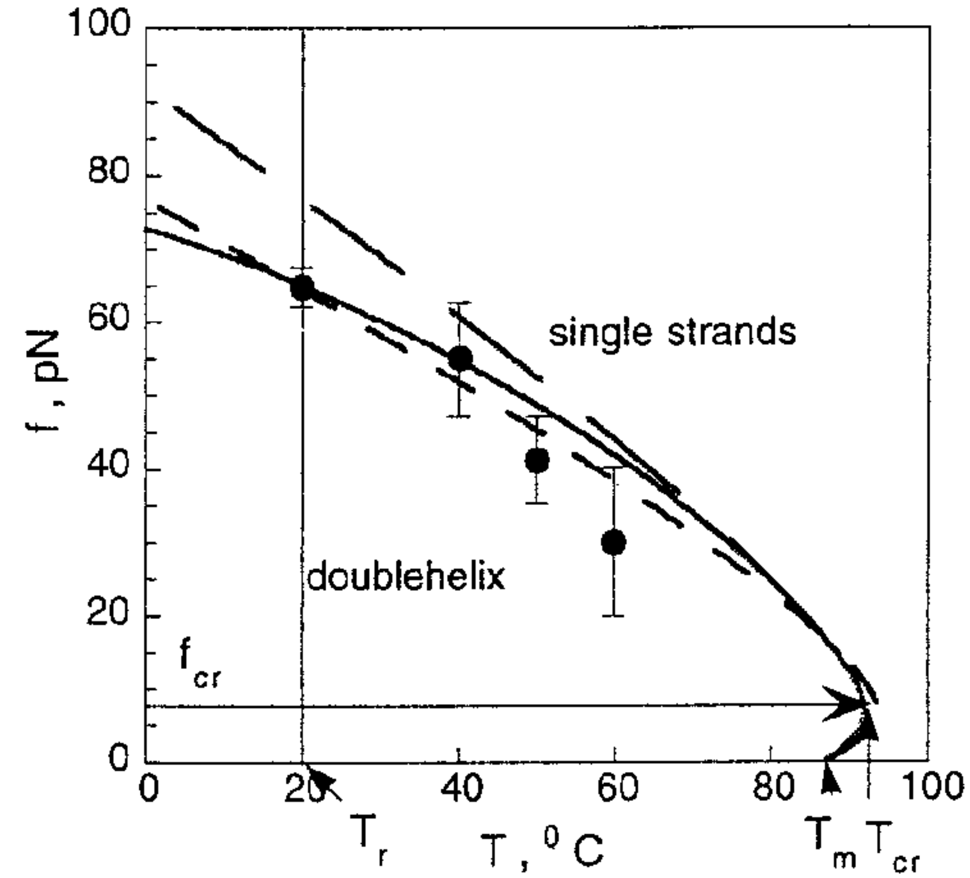
MOTIVATION: DNA MECHANICS





TEMPERATURE EFFECTS



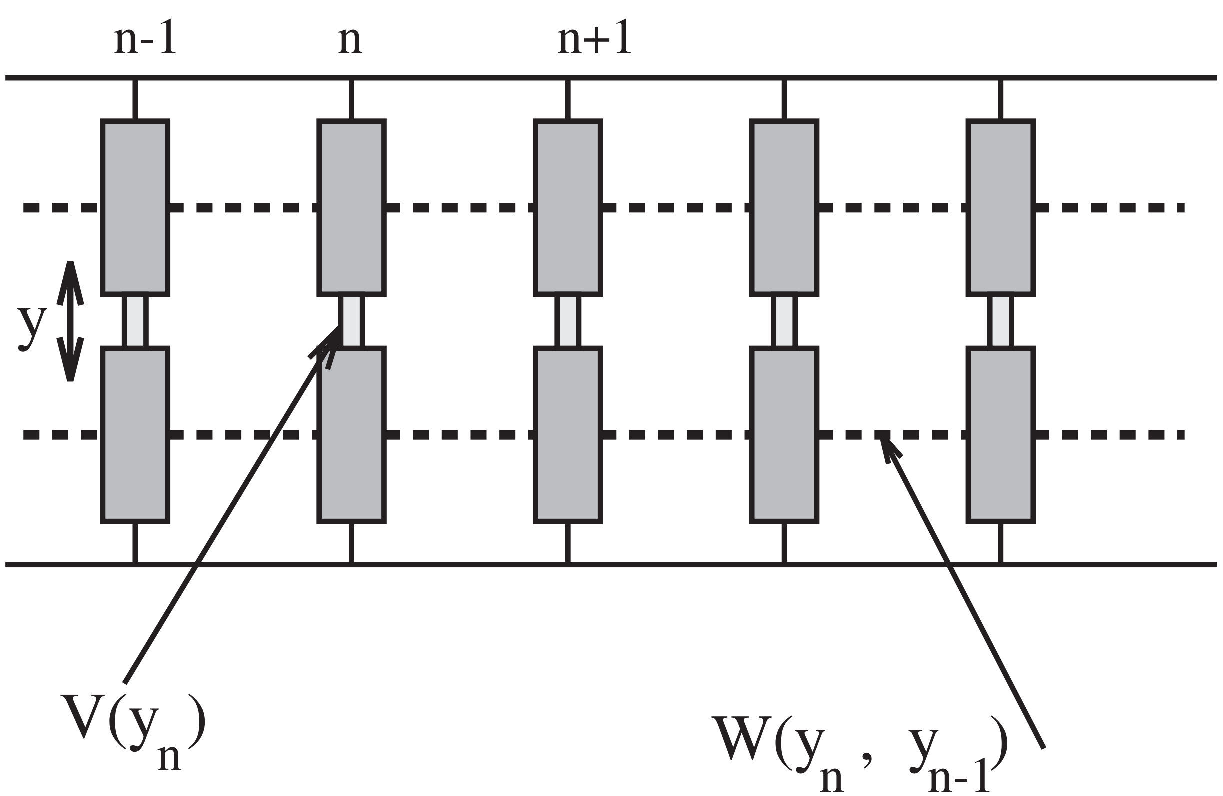


C. Williams, I. Rouzina, A. Bloomfield, *Thermodynamics of DNA Interactions from Single Molecule Stretching Experiments*, Acc. Chem. Res.**35**, 159–166, 2002

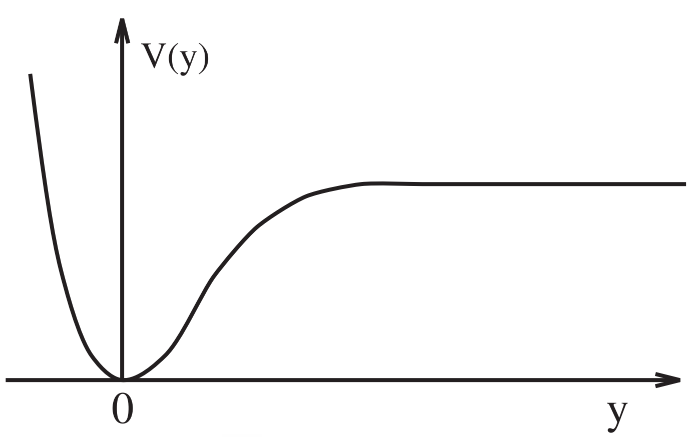
I. Rouzina, A. Bloomfield, *Force-Induced Melting of the DNA Double Helix. 2. Effect of Solution Conditions*, Biophysical Journal 80(2):894-900, 2001

PEYRARD-BISHOP MODEL

M. Peyrard, A. R. Bishop, *Statistical Mechanics of a Nonlinear Model for DNA Denaturation*, PRL 1989



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



Morse potential

$$H = \sum_n \frac{p_n^2}{2m} + W(y_n, y_{n-1}) + V(y_n)$$

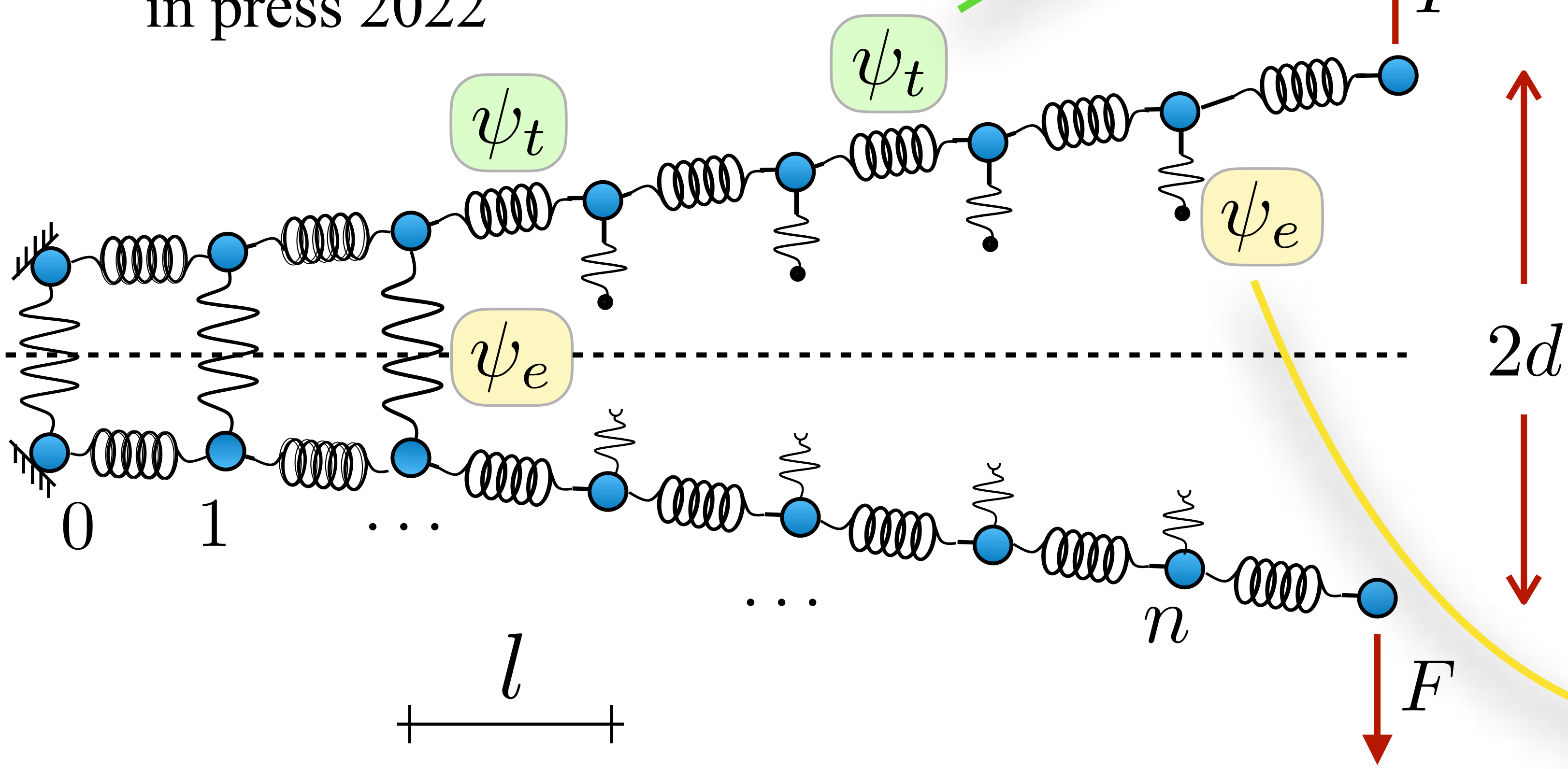
$$W(y_n, y_{n-1}) = \frac{1}{2} K (y_n - y_{n-1})^2$$

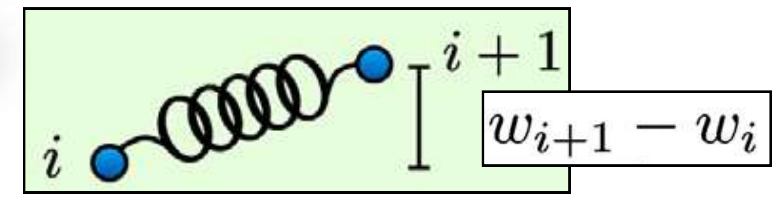
Elastic potential

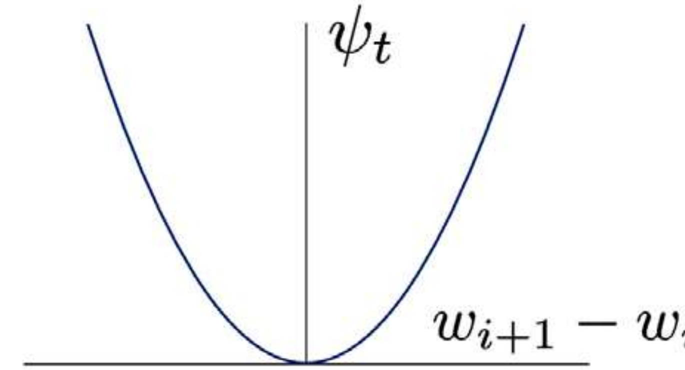
MODEL: SUBSTITUTE THE MORSE POTENTIAL

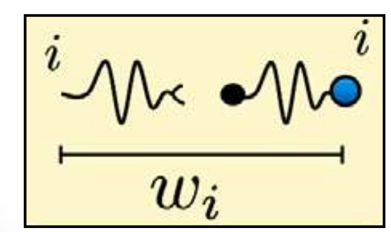
We substitute the Morse potential with a piece-wise potential energy.

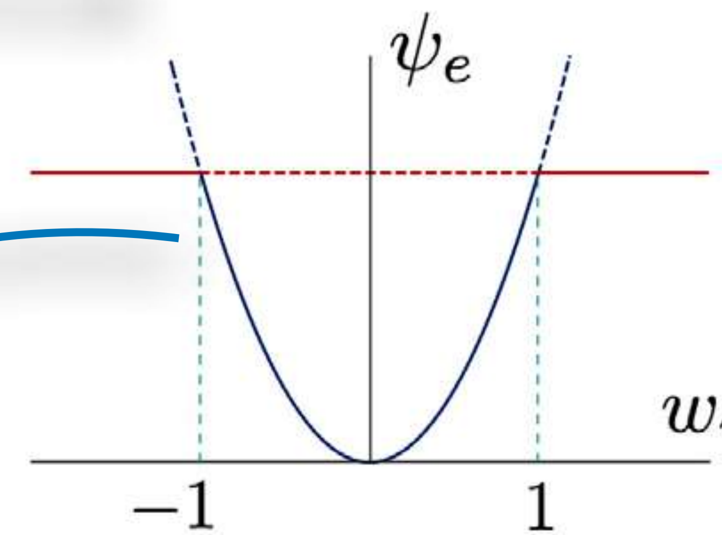
GF, Puglisi, Acta Biomaterialia, in press 2022











u_i transverse displacement

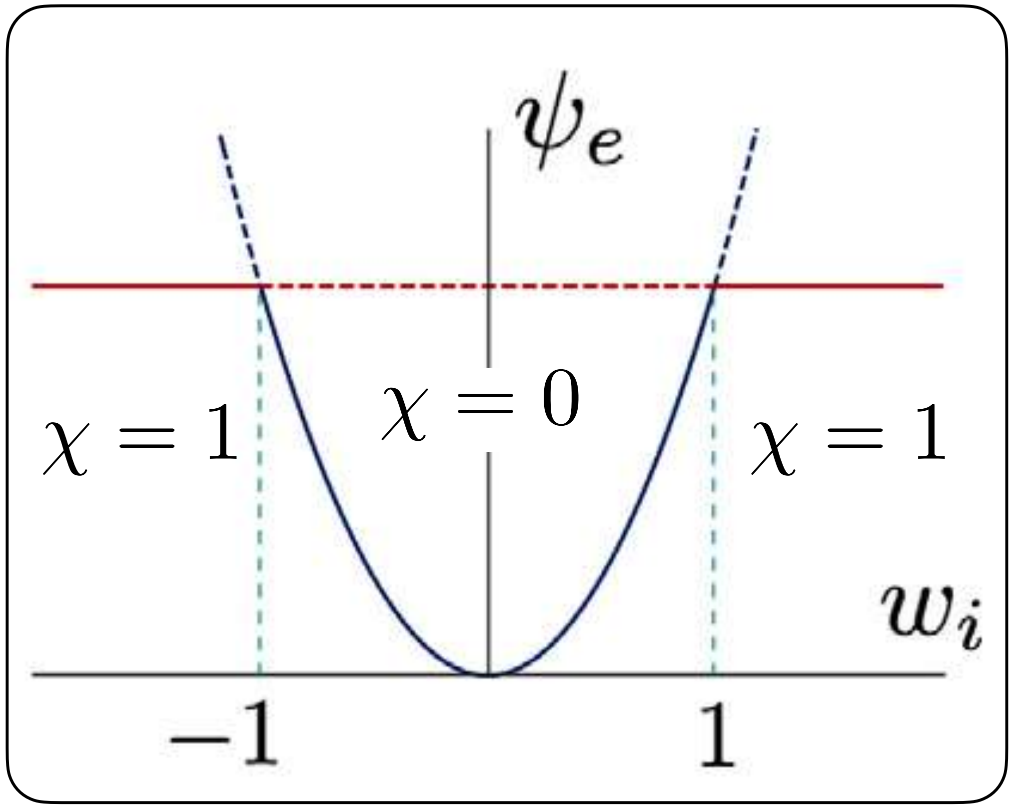
u_d debonding threshold

$w_i = u_i/u_d$ rescaled displacement

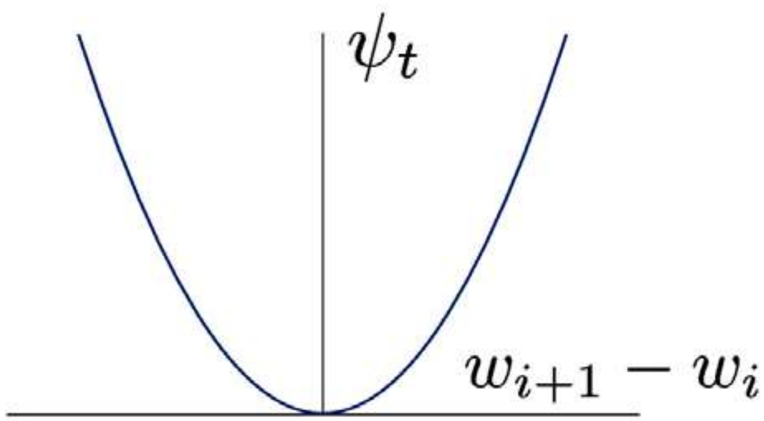
$$\psi_e(u_i) = \frac{k_e l}{2} \begin{cases} (u_i/u_d)^2, & \text{if } |u_i/u_d| \le 1 \\ 1 & \text{if } |u_i/u_d| > 1 \end{cases}$$

MODEL: SUBSTITUTE THE MORSE POTENTIAL

Introduce an internal (spin) variable: $\chi = \begin{cases} 0, & \text{if } |u| \leq u_d, \\ 1, & \text{if } |u| > u_d, \end{cases}$ unbroken link / broken link



$$= \frac{lk_e}{2}\left[(1-\chi_i)w_i^2 + \chi_i\right]$$



$$\psi_t(u_{i+1}, u_i) = \frac{k_t l}{2}\left(\frac{u_{i+1} - u_i}{l}\right)^2$$

ENERGY AND MECHANICAL LIMIT

$$n\,\phi = \frac{\Phi}{k_e l} = \frac{\nu^2}{2}\sum_{i=0}^{n}(w_{i+1}-w_i)^2 + \frac{1}{2}\sum_{i=1}^{n}\left[(1-\chi_i)w_i^2+\chi_i\right]$$

Strand elastic energy

Energy of the breakable bonds

$$\nu = \sqrt{\frac{k_t}{k_e}\frac{u_d}{l}}$$

Main non-dimensional parameter

Equilibrium configurations from the minimization of

$$n\,g = n\,\phi - f\,\delta$$

with

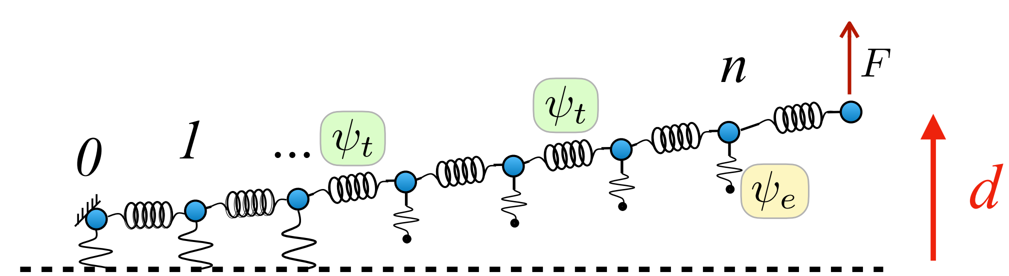
$\delta = d/u_d$ rescaled end-point displacement

$F = \dfrac{k_e l}{u_d} f$ rescaled force

We find $\delta = \dfrac{f}{k(p)}$

$p = 0, \ldots, n,$ global stiffness

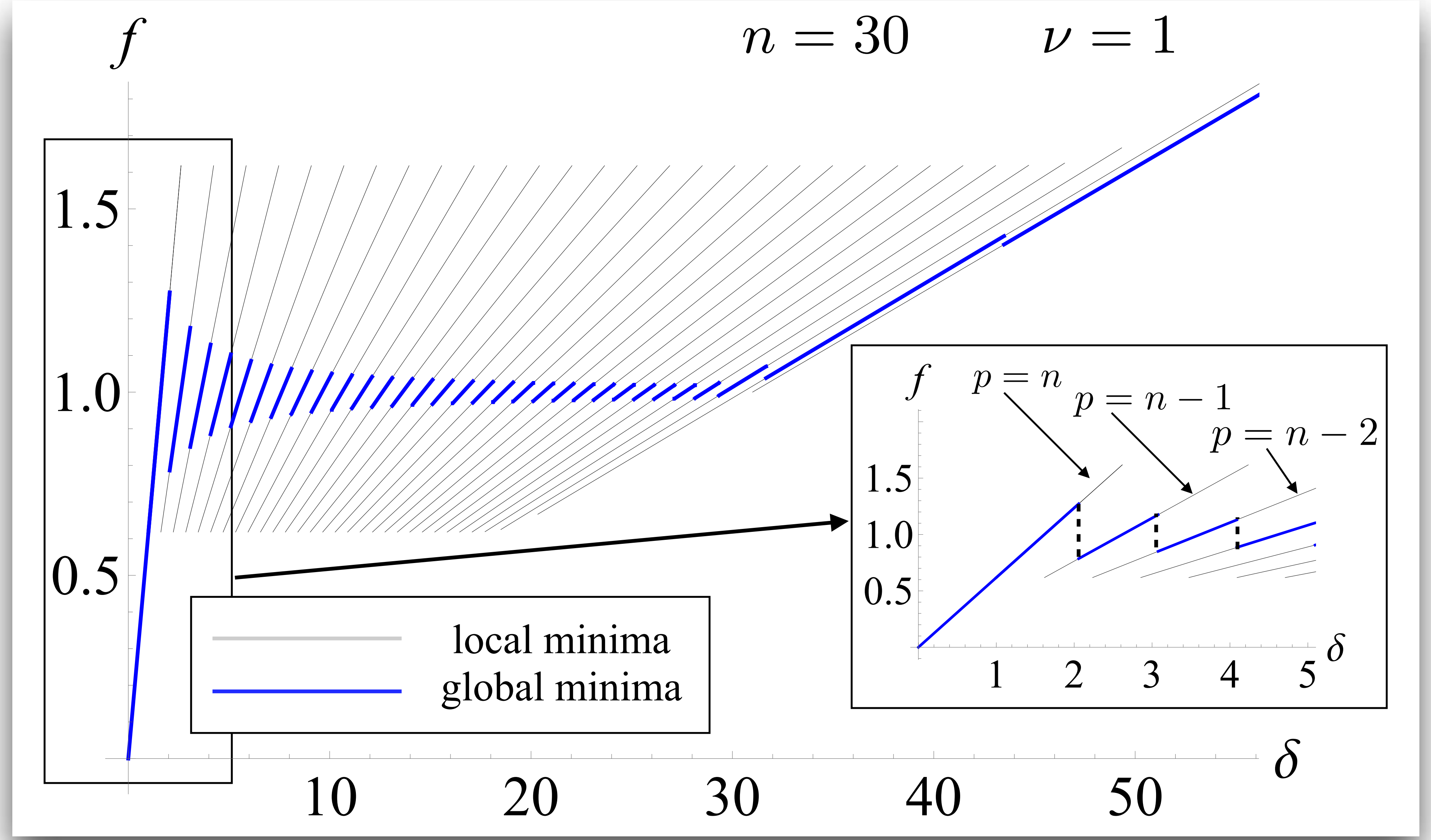
attached links (single domain wall solutions)



MECHANICAL LIMIT (ZERO TEMPERATURE)

Force-displacement relation

Jumps in the force each time a link is broken (sequential breaking of base pairs)



TEMPERATURE EFFECTS

Partition function $$\mathcal{Z} = \sum_{\{\chi_i\}} \int_{\mathbb{R}^n} e^{-\beta n \phi(\boldsymbol{w},\delta)}\, d\boldsymbol{w}$$

$$\beta = \frac{k_e l}{k_B T}$$

Rescaled inverse temperature

Average Force $$\bar{f}(\beta,\delta) \simeq \frac{\sum_{p=0}^{n} k(p)\Gamma_p(\beta,\delta)}{\sum_{p=0}^{n} \Gamma_p(\beta,\delta)}\,\delta$$

(single domain wall solutions)

with

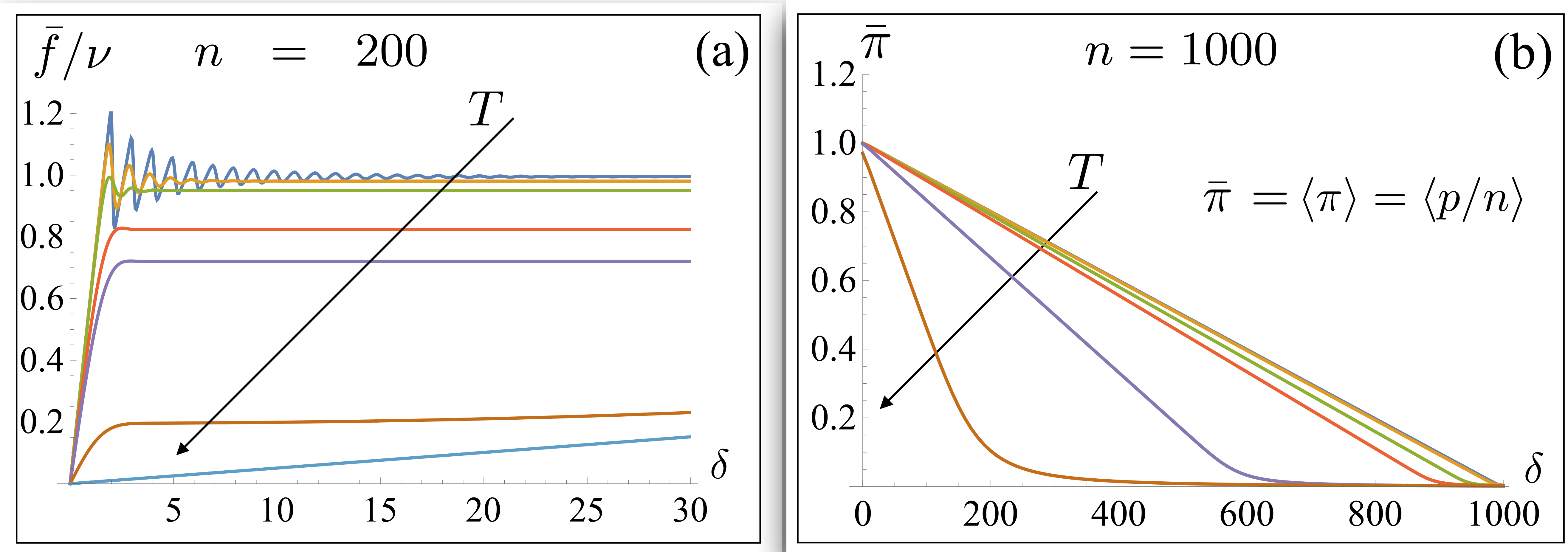
$$\Gamma_p(\beta,\delta) = \frac{1}{\sqrt{\det \boldsymbol{B}(p)}} e^{-\frac{\beta}{2}(n-p)} e^{-\frac{\beta}{2}k(p)\delta^2}$$

$$\det \boldsymbol{B} = \frac{\nu^{2n}}{\sinh\lambda}\left[(n-p+1)\sinh[(p+1)\lambda] - (n-p)\sinh(p\lambda)\right]$$

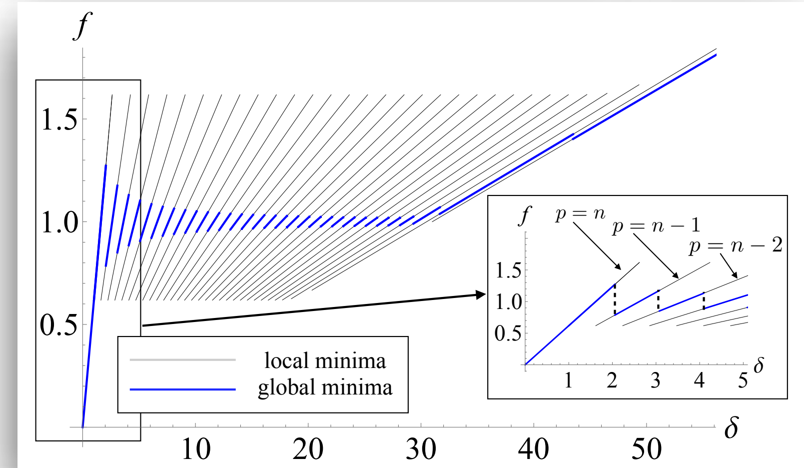
$$\cosh\lambda = 1 + \frac{1}{2\nu^2}$$

TEMPERATURE EFFECTS

Increasing temperature: the force of the plateau and the number of attached base pairs decrease



compare with
mechanical limit



THERMODYNAMIC LIMIT

l fixed

$n \to +\infty$

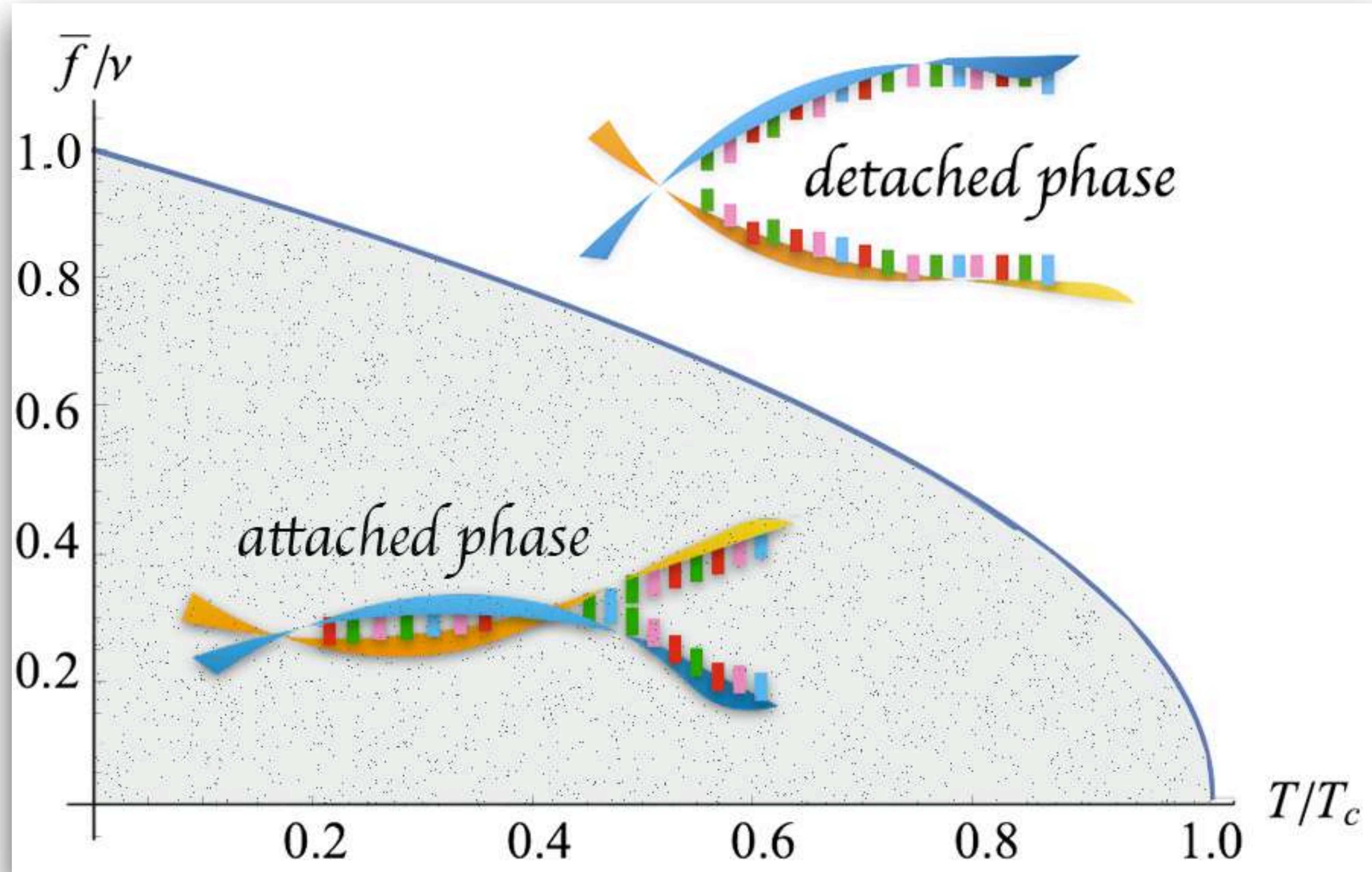
$L = nl \to +\infty$

$$\bar{f} \simeq \nu\sqrt{1 - \frac{T}{T_c}}$$

Force-temperature relation

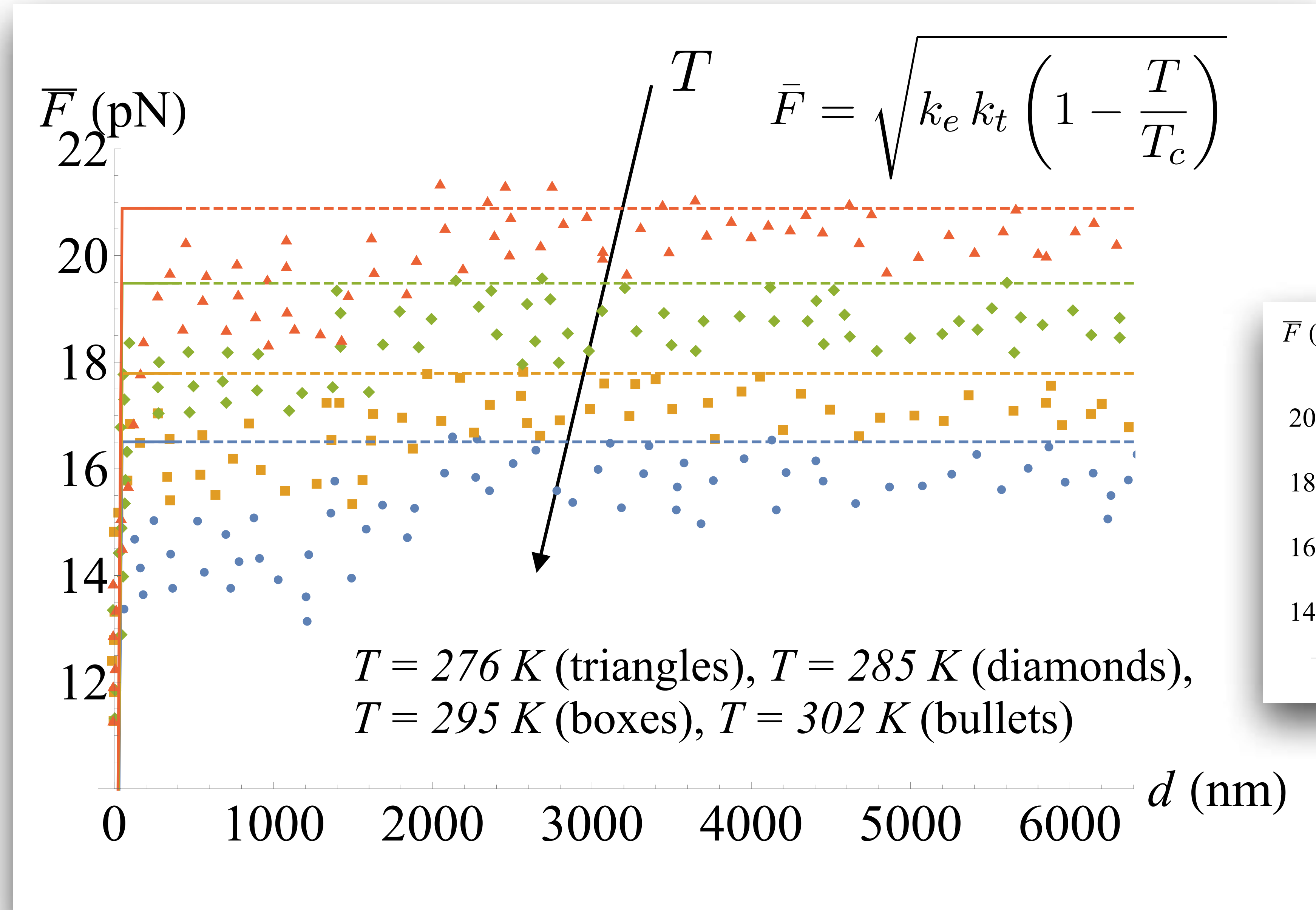
$$T_c = \frac{k_e\, l}{k_B\, \lambda}$$

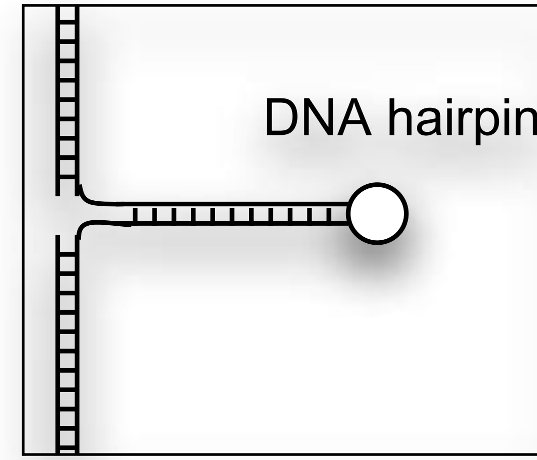
Critical temperature

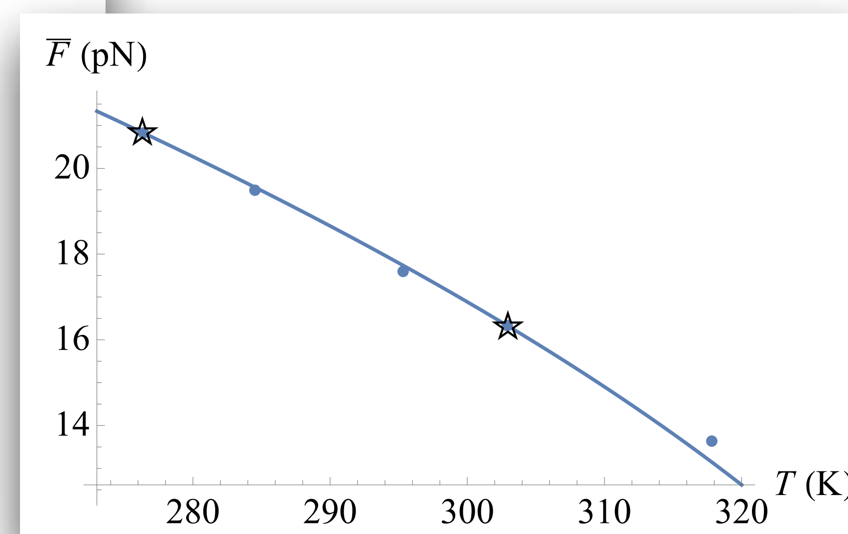


COMPARISON WITH EXPERIMENTS

Unzipping experiments with DNA hairpins:







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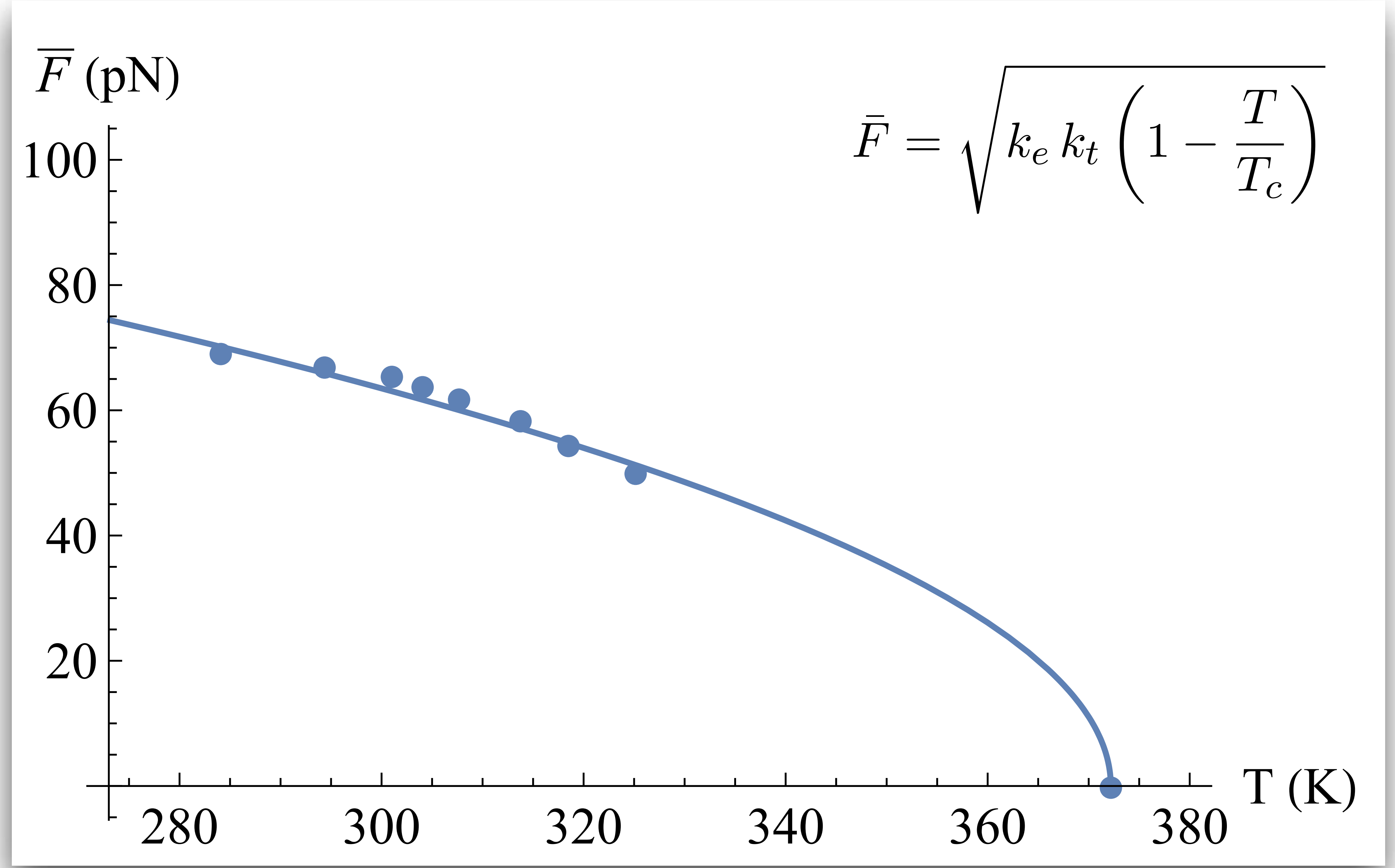
COMPARISON WITH EXPERIMENTS

Overstretching experiments in DNA



Data from: Williams, M. C.; Rouzina, I.; Bloomfield, V. A., Thermodynamics of DNA Interactions from Single Molecule Stretching Experiments, Acc. Chem. Res. 2002, 35, 159-166

CONCLUSIONS AND PERSPECTIVES

- We obtain a model allowing to deduce analytical formulas describing the (temperature-dependent) features observed in DNA

- The model is general and based on simple assumptions (use of spin variables): ion can be applied in more general contexts such as material science, biology, medicine, engineering (natural and artificial bio-inspired materials)

- Applications to phenomena in biological processes such as cell adhesion where cells interact with each other or with their substrate using specialized proteins, or mechanics of axonal damage in traumatic brain injuries

- Related works with softening and fracture

REFERENCES AND RELATED WORKS

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Thank you for your attention!!!