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A new approach to the mechanics of DNA

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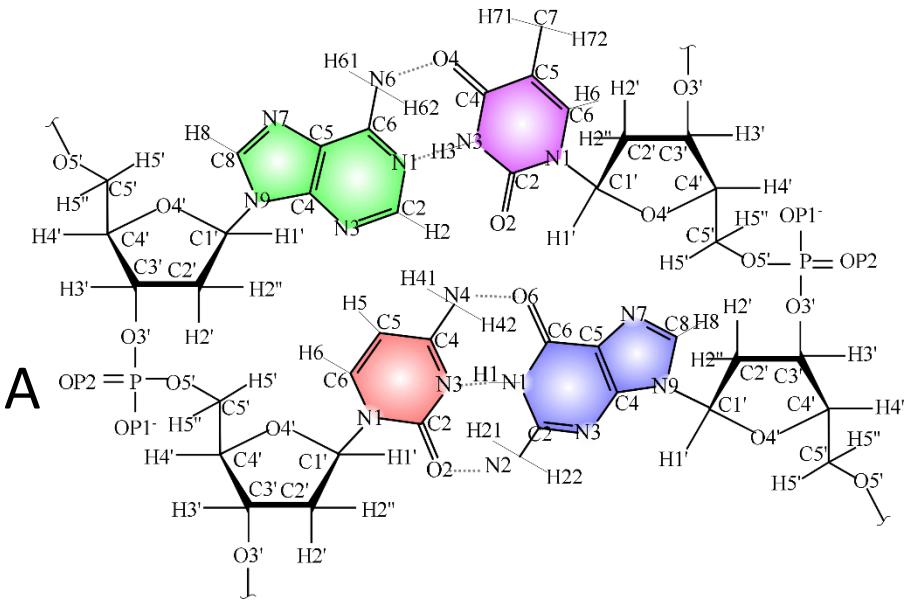
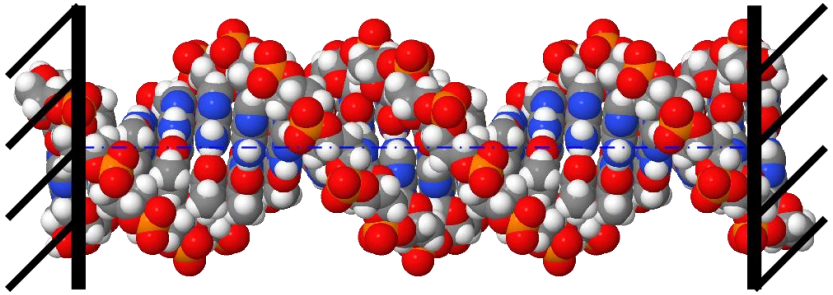
DNA

- stores all genetic information of humans, animals, plants and bacteria

- mechanics important for:
  - replication
  - gene expression
  - folding and packing of DNA

- knowing properties
  → better understanding diseases
  (e.g. cancer, genetic disorders)





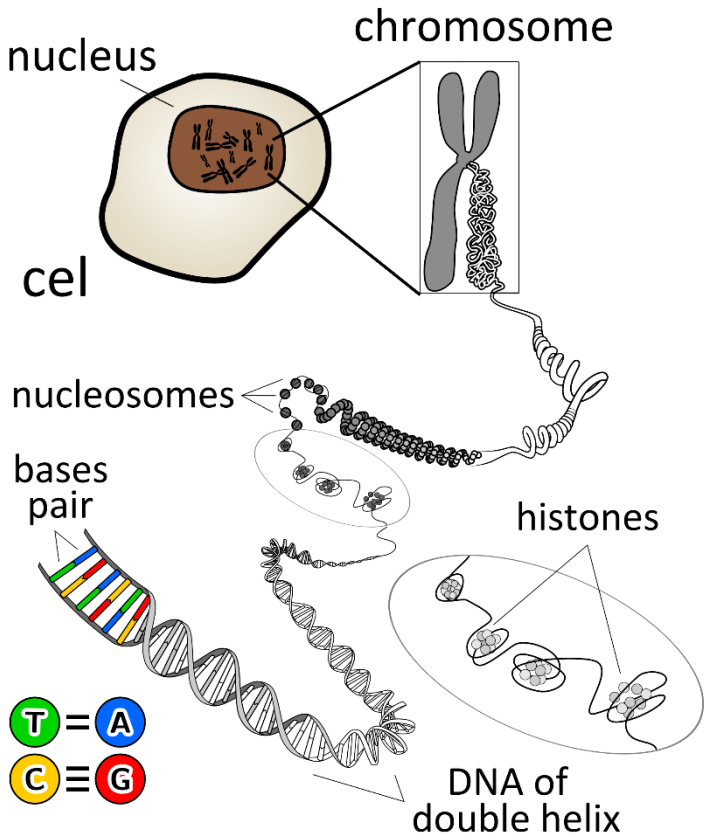
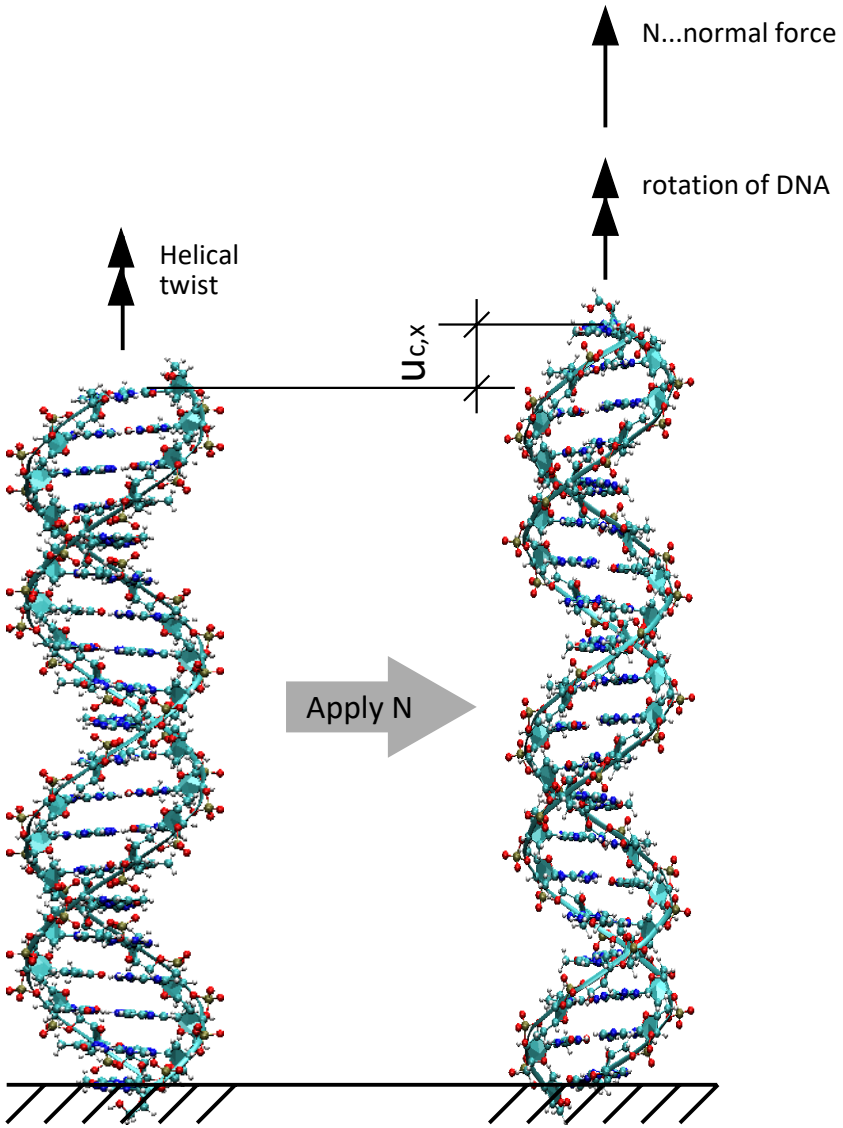


image: CC-BY-SA 3.0 KES47
https://commons.wikimedia.org/wiki/File:Chromosome_en.svg

Force-moment interaction



[Gore et al., Nature , 2006]

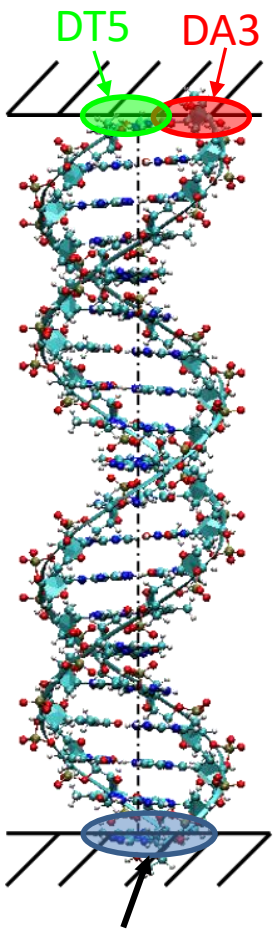
- coupling between stretch and torsion shown experimentally
- state of the art (so far): modeling DNA as **homogeneous, isotropic, cylindrical rod** → coupling not reproducible
- molecular dynamics to beam

Molecular dynamics model

- 20 polyadenine-polythymine-base pairs (two full turns)
  - helical twist of 36° per base-pair
  - helical rise of 3.38 Å per base-pair
- initial displacement field
  - beam-related homogeneous stretches and twists
  - rigid body cross sections

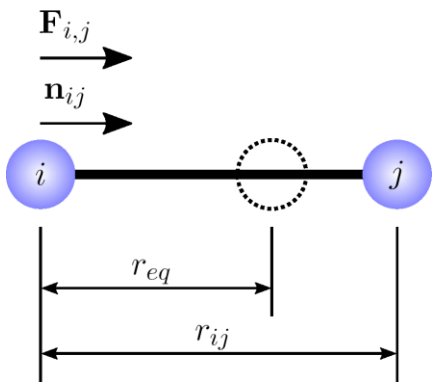
$$\mathbf{u}(x,y,z) = \epsilon_x\, x\, \mathbf{e}_x - \sin\left(\arctan\left(\frac{z}{y}\right) + \vartheta_x\, x\right) \sqrt{y^2+z^2}\, \mathbf{e}_y + \cos\left(\arctan\left(\frac{z}{y}\right) + \vartheta_x\, x\right) \sqrt{y^2+z^2}\, \mathbf{e}_z$$

- fixed upper end:
  3end adenine(DA3) and 5end thymine (DT5)
- fixed lower end:
  5end adenine (DA5) and 3end thymine (DT3)



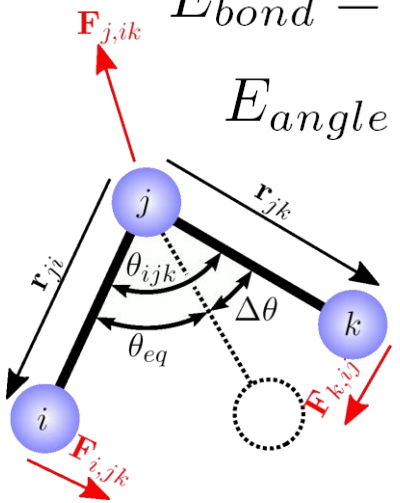
back: DA5
front: DT3

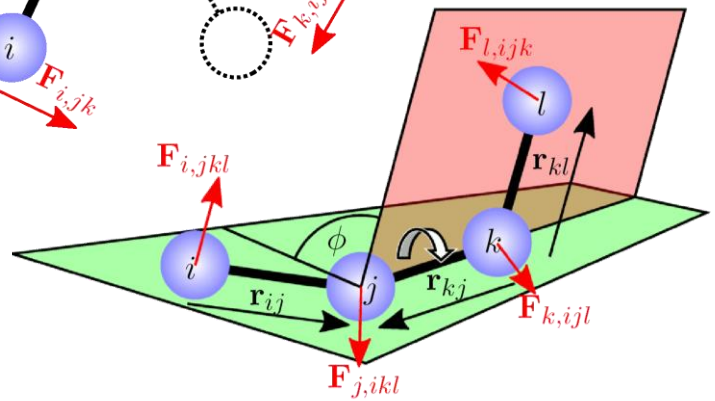
Interatomic potentials with DNA



$$E_{bond} = k\,(r - r_{eq})^2$$

$$E_{angle} = k_\theta\,(\theta - \theta_{eq})^2$$





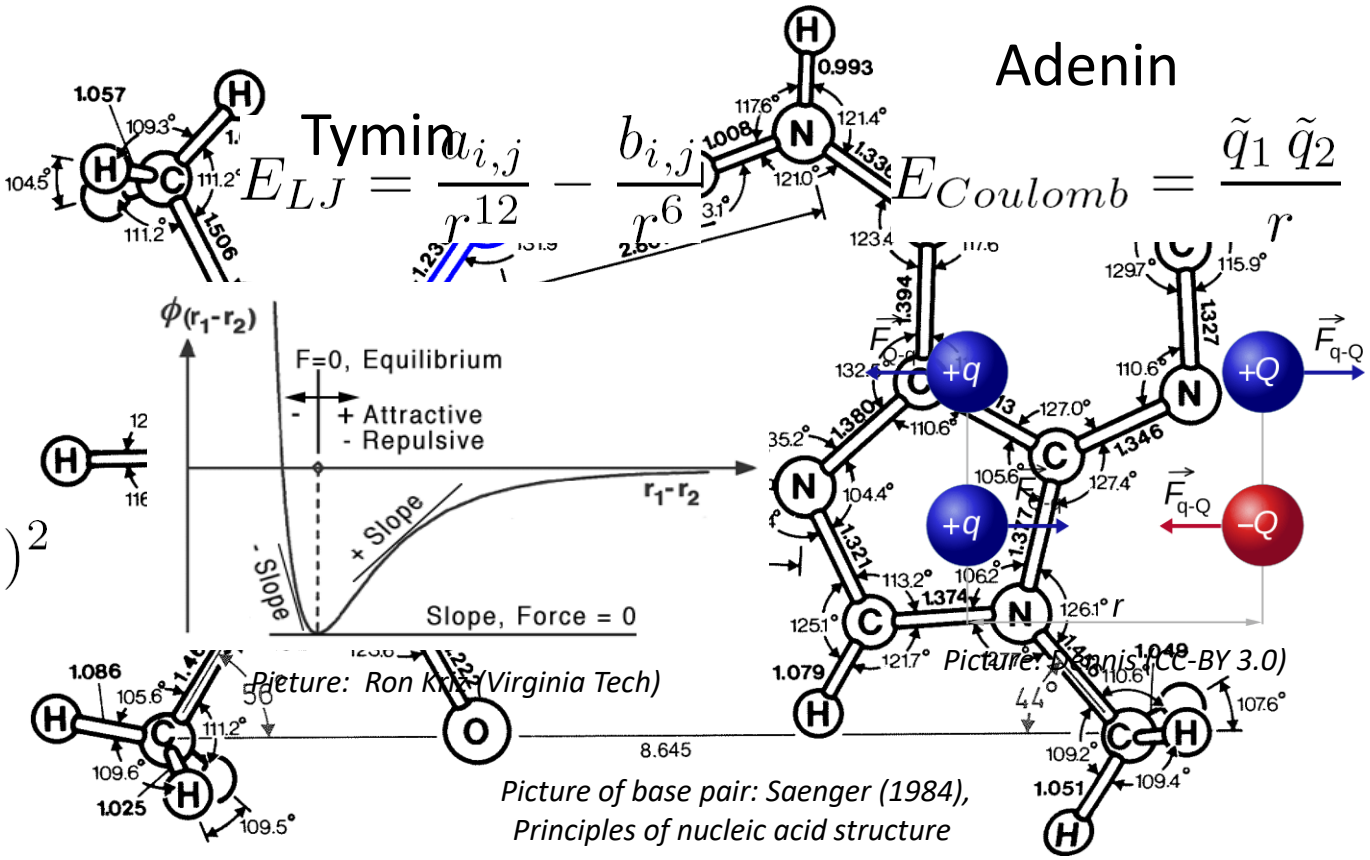
Tymin

Adenin

$$E_{LJ} = \frac{a_{i,j}}{r^{12}} - \frac{b_{i,j}}{r^6}$$

$$E_{Coulomb} = \frac{\tilde{q}_1\,\tilde{q}_2}{r}$$

Picture: Ron Knott (Virginia Tech)



Picture: Dennis (CC-BY 3.0)

Picture of base pair: Saenger (1984), Principles of nucleic acid structure

applied method:

generalized Born Implicit Solvent

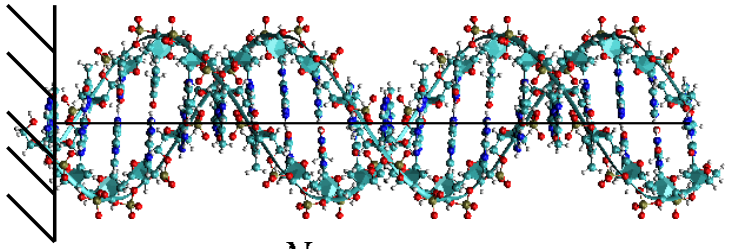
$$E_{torsion} = k_{tor}\,(1 + \cos(n\,\phi + \psi))$$

[Kalliauer et al., JMPS , 2020]

Molecules-to-beam-element homogenization

[Kalliauer et al., JMPS , 2020]

molecular system



$$p^{\text{int}} = \frac{1}{\ell_{\text{RLE}}} \sum_{i=1}^{N_{\text{atom}}} \mathbf{F}_i^{\text{int}}(\mathbf{x}_i) \cdot \hat{\mathbf{v}}^{\text{int}}(\mathbf{x}_i)$$

$\mathbf{F}_i$ ... atom-specific internal force vector
$\mathbf{x}_i$ ... atom-specific location vector
$\mathbf{v}_i$ ... atom-specific virtual velocity vector
ℓ_{RLE} ... length of representative beam element

with beam-informed molecular virtual velocity field:

$$\hat{\mathbf{v}}^{\text{int}}(\mathbf{x}) = x_i \left(\frac{\partial \hat{V}(X)}{\partial X} \mathbf{e}_x + \frac{\partial \hat{\Omega}(X)}{\partial X} (-z_i \, \mathbf{e}_y + y_i \, \mathbf{e}_z) \right)$$

continuum beam system (element)

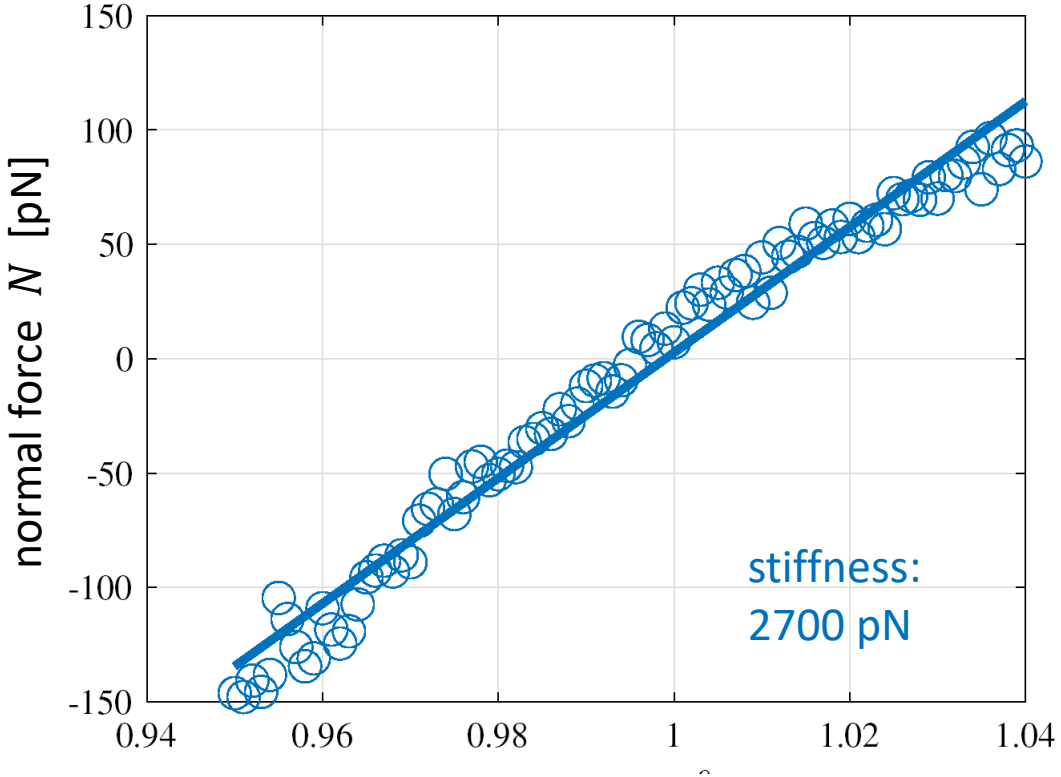
$$p_{\text{int}}(X) = -N(X) \frac{\partial \hat{V}(X)}{\partial X} - M_x(X) \frac{\partial \hat{\Omega}(X)}{\partial X}$$

N ... normal force
V ... virtual axial velocity
X ... beam element-specific location vector
M_x ... torsional moment
Ω ... virtual twisting velocity

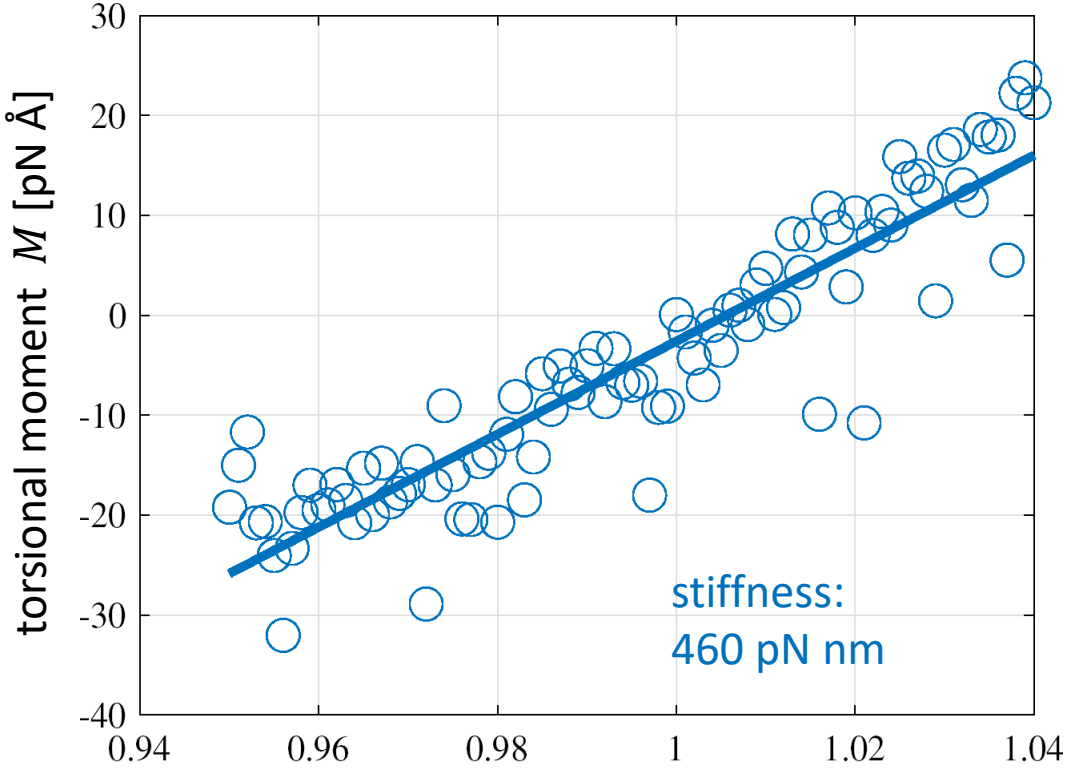
$$N(X) = \frac{-1}{\ell_{\text{RLE}}} \sum_{i=1}^{N_{\text{atom}}} x_i \, F_{i,x}^{\text{int}}$$

$$M_x(X) = \frac{-1}{\ell_{\text{RLE}}} \sum_{i=1}^{N_{\text{atom}}} x_i \left(-z \, F_{i,y}^{\text{int}} + y \, F_{i,z}^{\text{int}} \right)$$

Stretching at zero twist



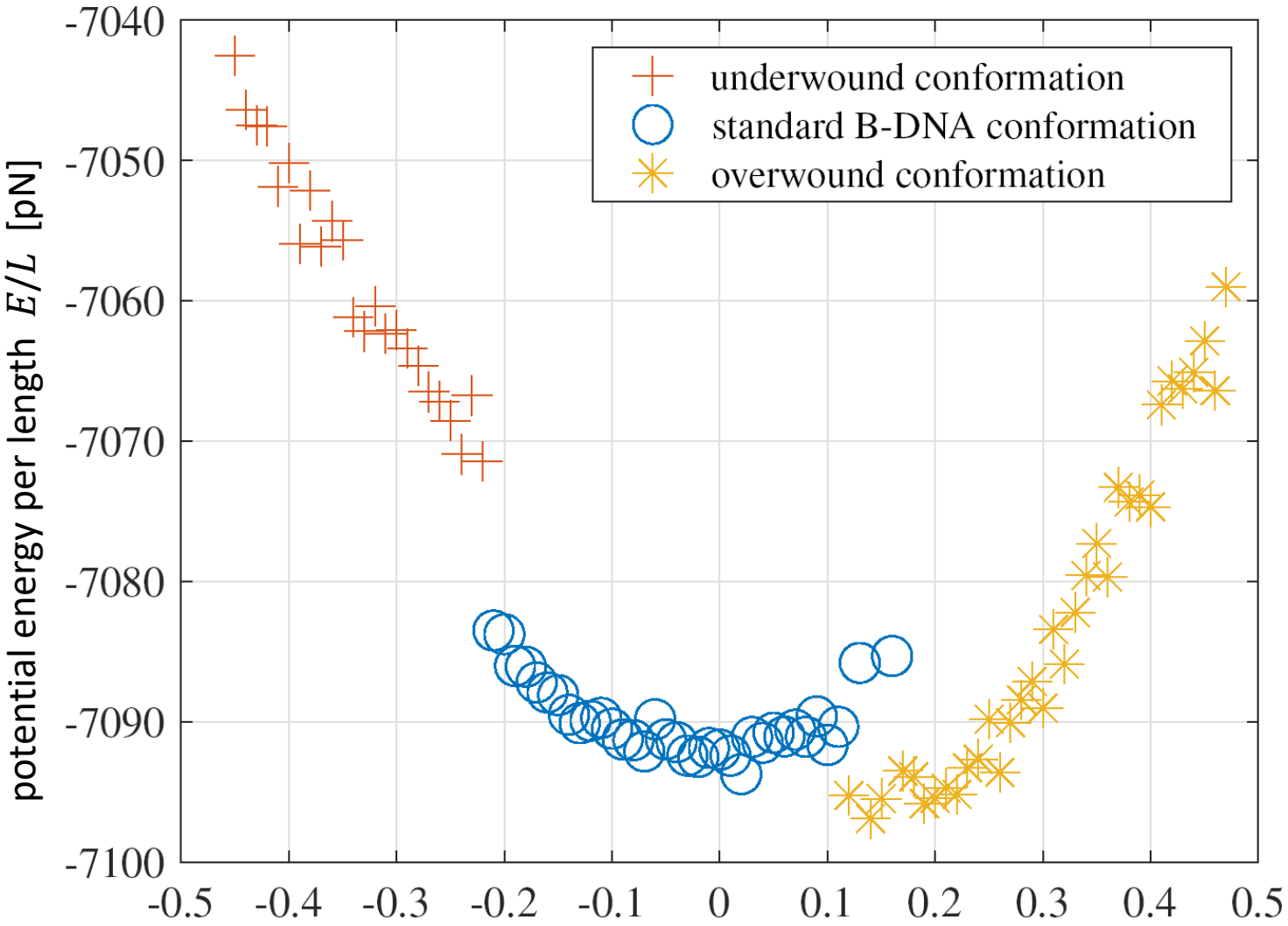
stretch $\lambda_x = \frac{L-L_0}{L_0}$ [-]



stretch $\lambda_x = \frac{L-L_0}{L_0}$ [-]

[Kalliauer et al., JMPS , 2020]

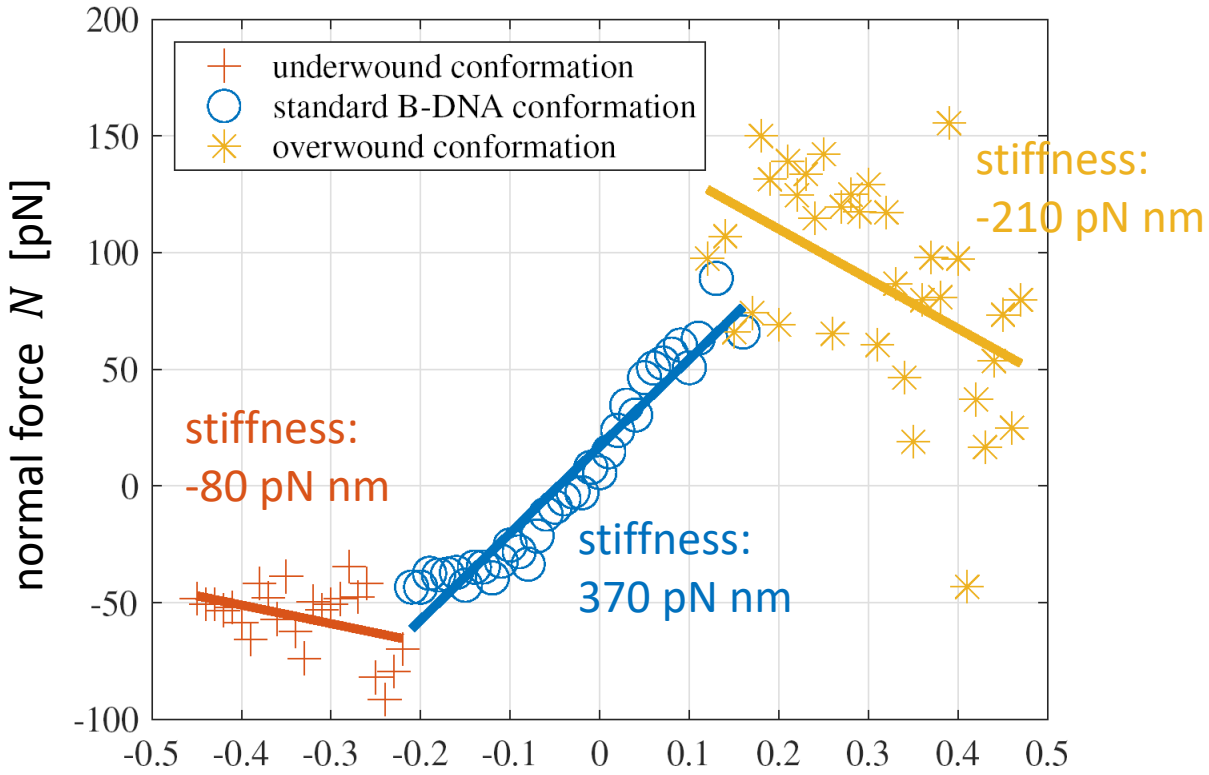
Twisting at constant length



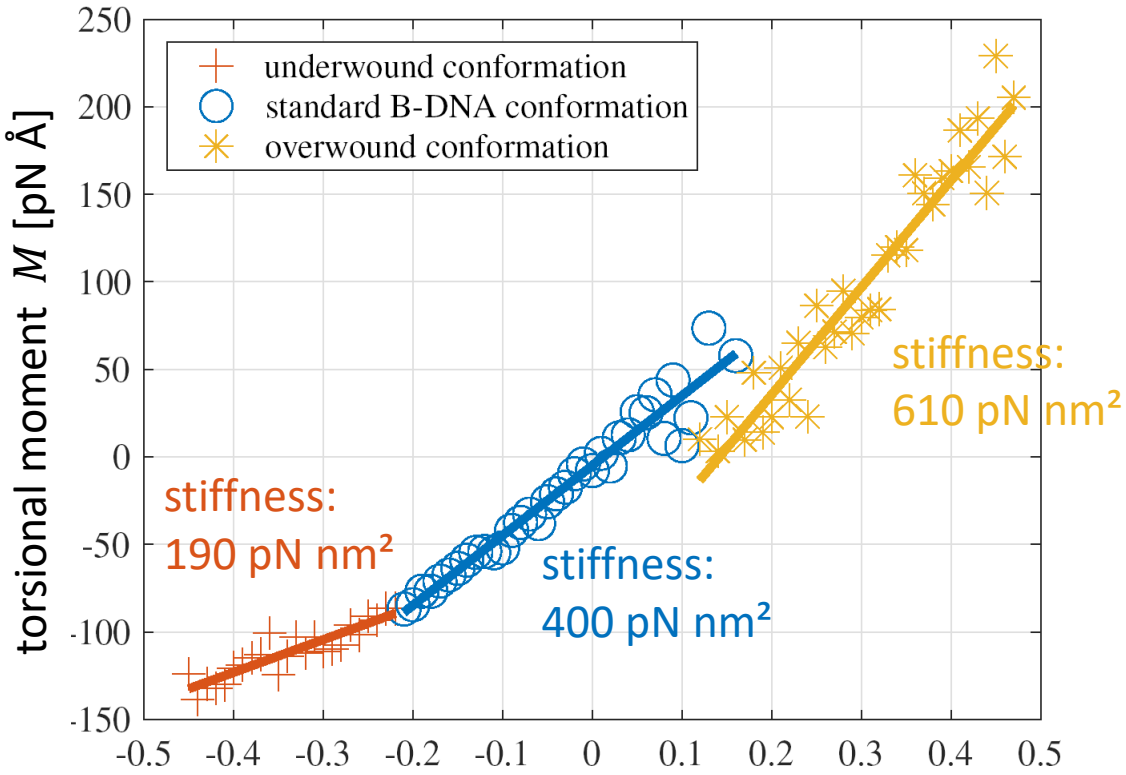
twist $\vartheta_x = \frac{\varphi}{L_0} \left[\frac{mrad}{\text{Å}}\right]$

[Kalliauer et al., JMPS , 2020]

Twisting at constant length



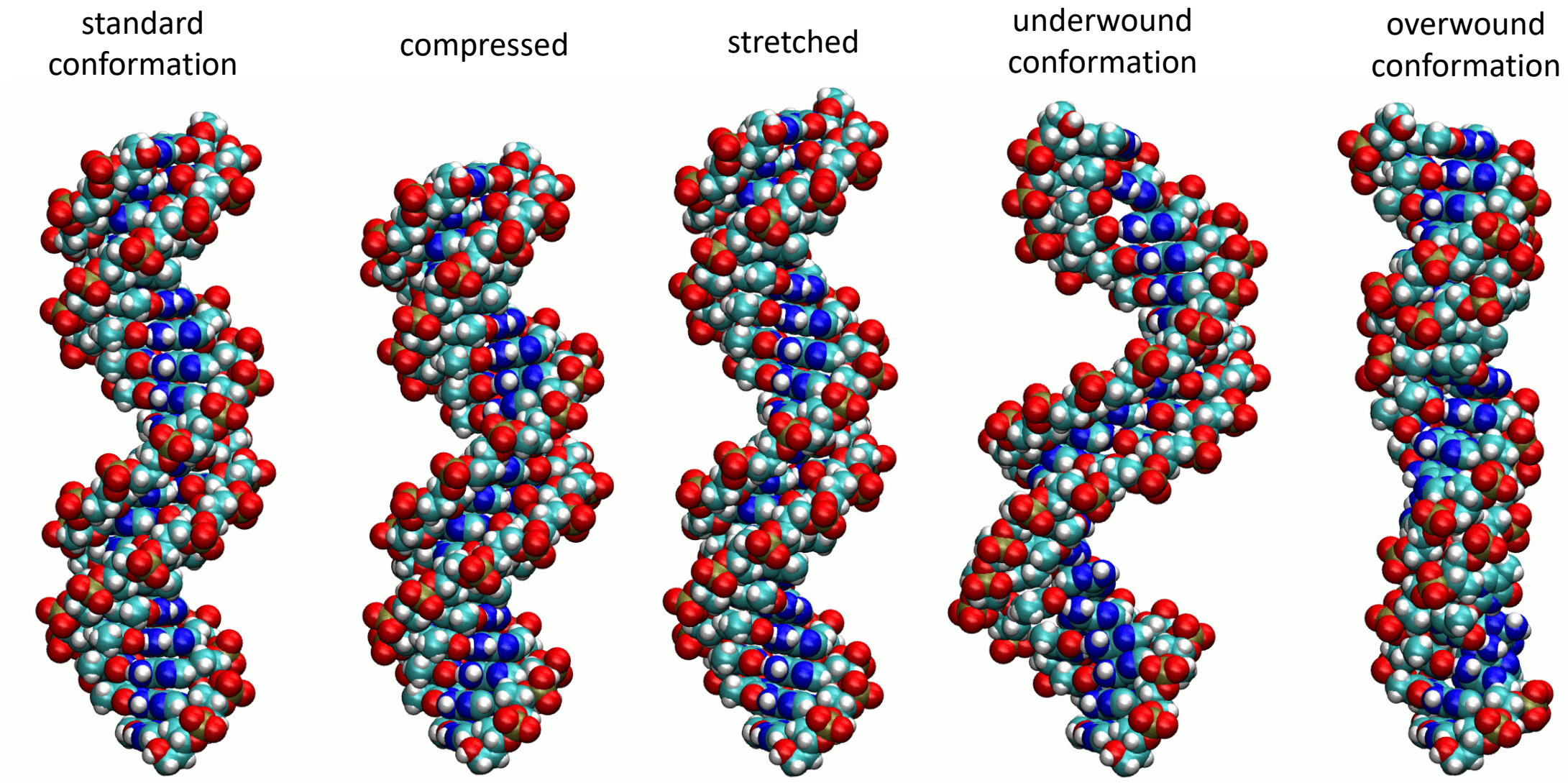
$$\text{twist } \vartheta_x = \frac{\varphi}{L_0} \left[\frac{mrad}{\text{Å}}\right]$$



$$\text{twist } \vartheta_x = \frac{\varphi}{L_0} \left[\frac{mrad}{\text{Å}}\right]$$

[Kalliauer et al., JMPS , 2020]

Snapshots of deformations



[Kalliauer et al., JMPS , 2020]

Conclusions and Outlook

- first ever beam model derived directly from molecular dynamics
- this model includes the stretch-to-torsion coupling known from DNA experiments
- stiffness below persistence length (~50nm)

- theory of large strains
- bending stiffness
- DNA origami
- other polymers (other sequences of DNA, RNA, collagen, …)

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