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Correlations and Helical Coherence in DNA Structure: "Straightening" out the Helix upon Crystal Packing

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Correlations and helical coherence in DNA structure: “straightening” out the helix upon crystal packing

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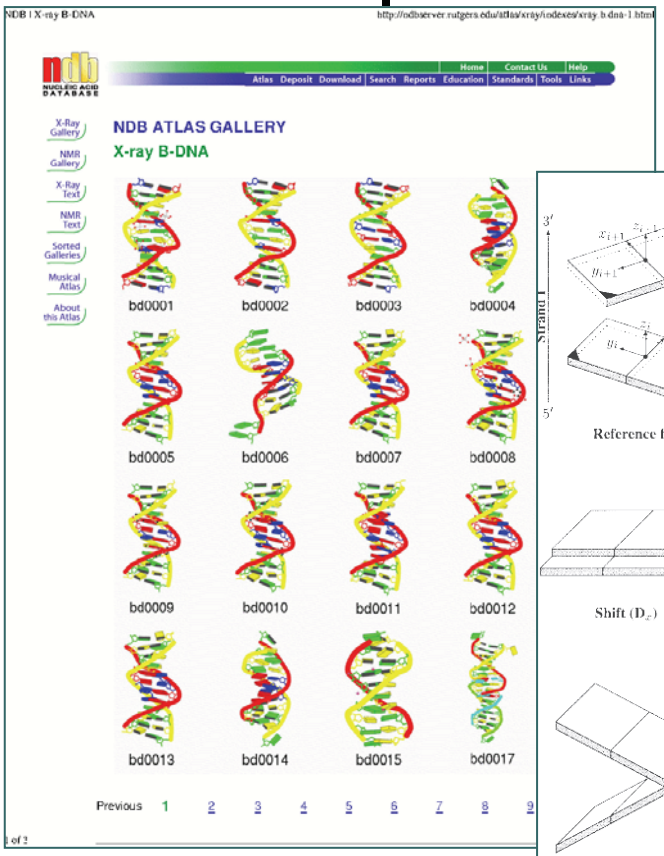
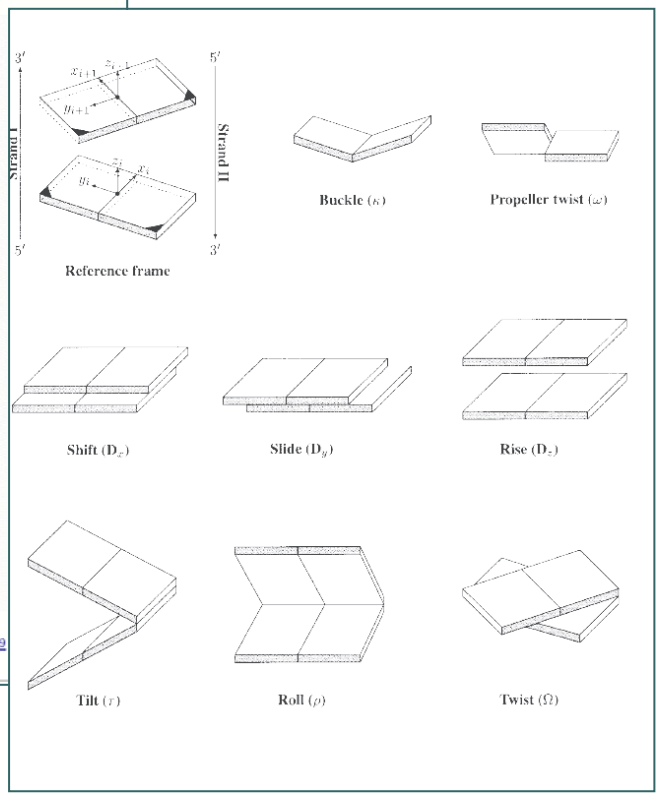
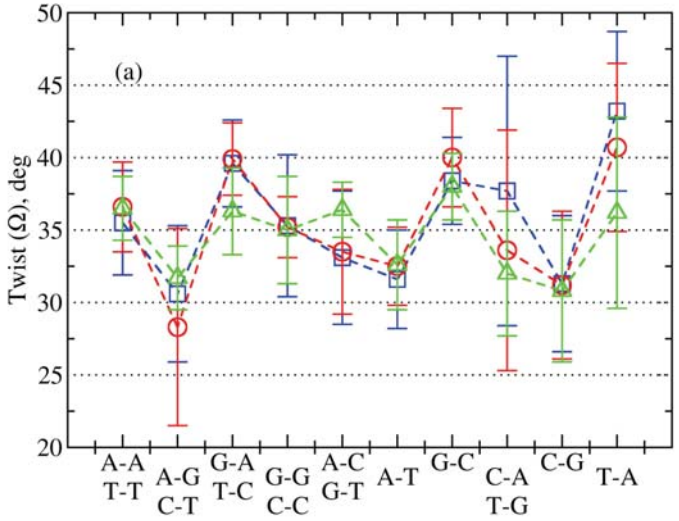
Introduction

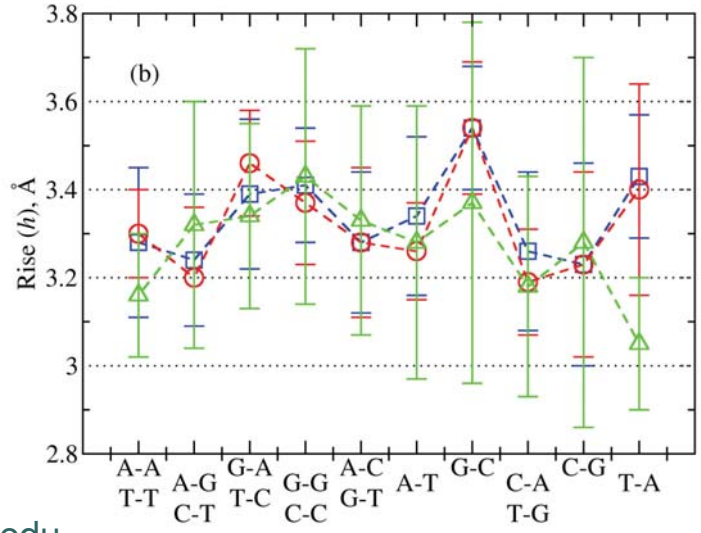
- Structural parameters (twist, rise, slide, etc.) of adjoining DNA base pairs depend on the text of the constituent bases.
- This structural dependence on the sequence (providing the specific DNA conformation) may have consequences, e.g., for nucleosome binding, recognition of DNA by regulatory proteins, DNA-DNA interactions and synthesis of RNA on DNA templates.
- However, parameters for a specific dinucleotide step, e.g., AC•GT, are further influenced by the surrounding sequence text as well as the DNA environment.
- Introduce a quantity, the helical coherence length, that takes into account, and thus reflects, the intrinsic (auto- and cross-) correlations of the step parameters along a sequence.

Base pair step parameters







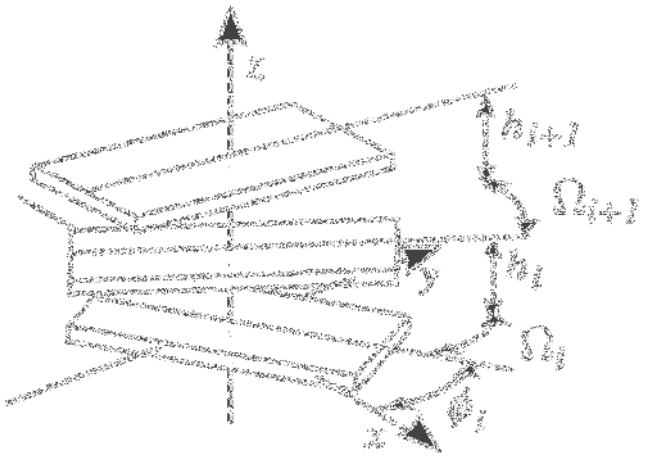


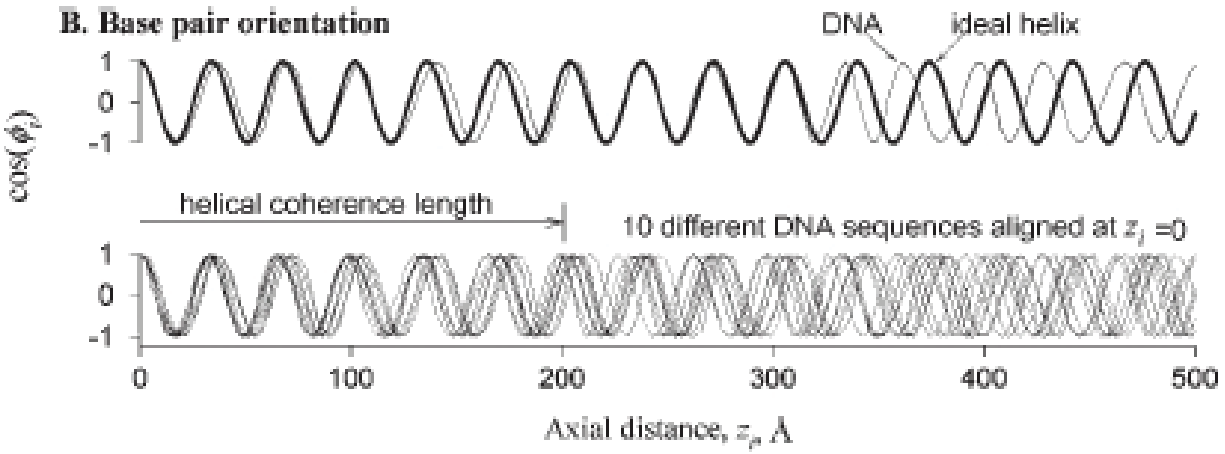
□ = published results*

○ = x-ray △ = nmr

*Gorin et al., J. Mol. Biol. 247 (1995); NDB: http://ndbserver.rutgers.edu

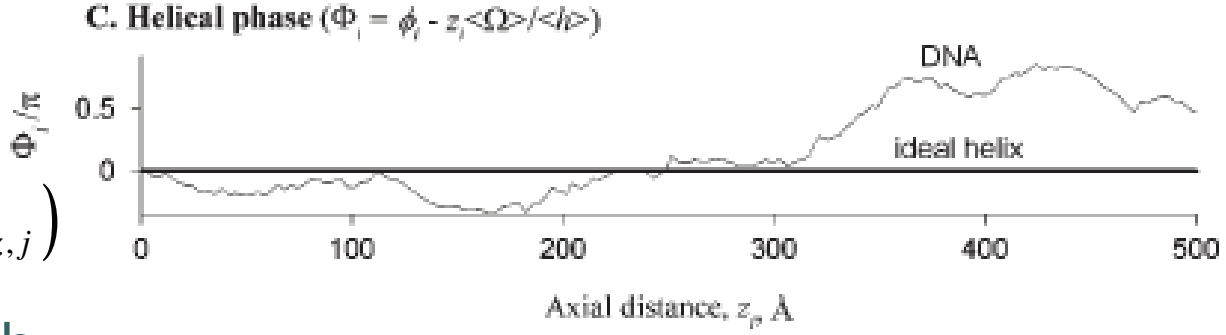
Helical Coherence Length (λ_c)





Helical phase:

$$\Phi_z(z_i) = \Phi_0 + \sum_{j=1}^{i}\left(\Omega_{z,j} - g_0 h_{z,j}\right)$$



Average (inverse) pitch:

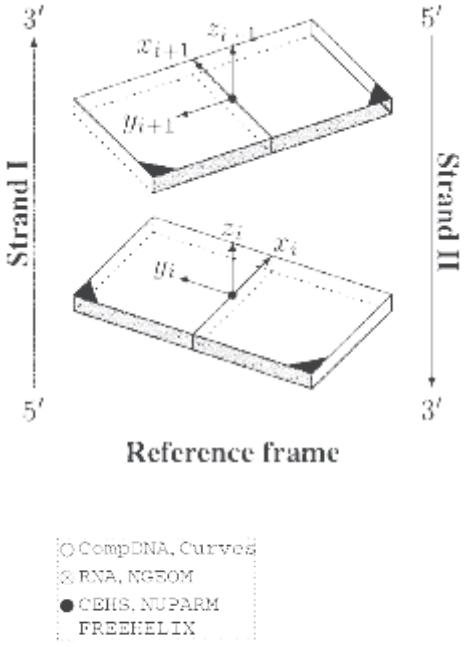
$$g_0 = \left\langle \Omega_{z,i} \right\rangle \Big/ \left\langle h_{z,i} \right\rangle$$

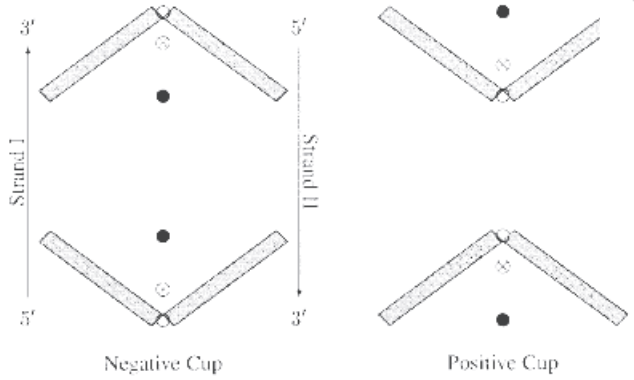
$$\left\langle \left[\Phi_z(z_i) - \Phi_z(z_j)\right]^2 \right\rangle = \frac{|z_i - z_j|}{\lambda_c}$$

Helical Coherence Length: Complication 1

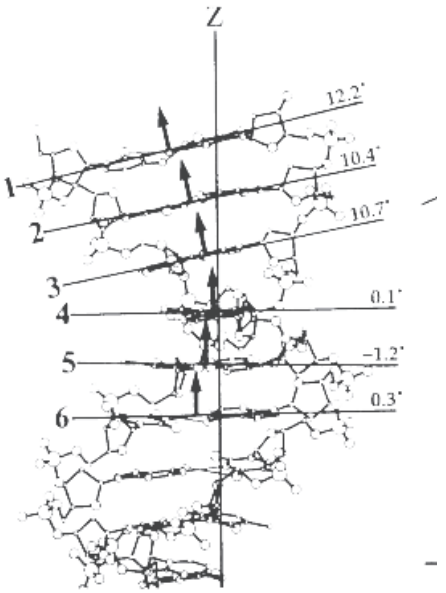
How does one definite twist, rise and other base pair step parameters?
For example, depending on the reference frame, the twist-rise (cross-correlation) may be either negative or positive.

"Local" base pair step parameters: intermediate reference frame.





"Global" base pair step parameters: project bases on planes defined by a best-fit long molecular axis.

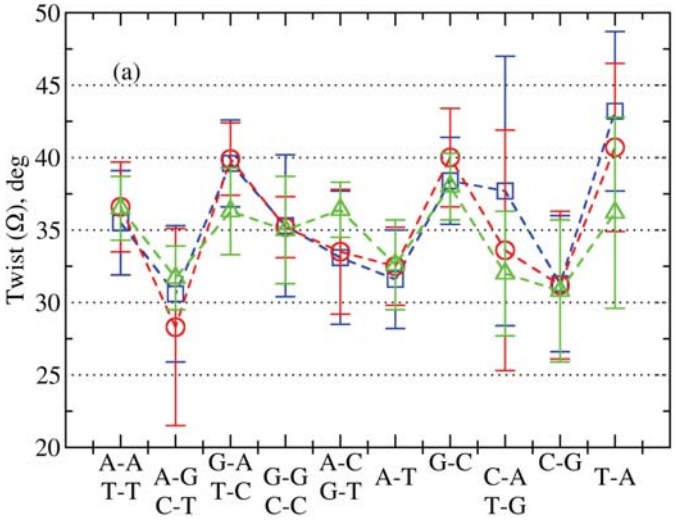


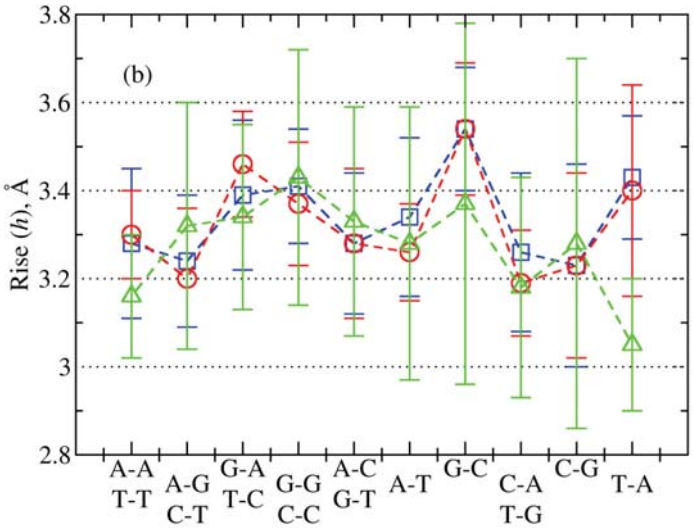
Lu & Olson, J. Mol. Biol. 285 (1999)

Helical Coherence Length: Complication 2

How would correlations of adjacent base pair steps along a sequence affect helical coherence?

Assuming base pair step parameters are uncorrelated with their surrounding sequence, the coherence lengths for crystallized DNA (-cry) and isolated DNA in solution (-nmr) would roughly be the same.





□ = total

○ = x-ray △ = nmr

Helical Coherence Length: Solution

- Compare algorithms that use different definitions for the reference frames to calculate “local” as well as “global” base-pair step parameters from PDB files.
→ 3DNA (Lu & Olson) and FreeHelix98 (Dickerson) *
- Construct long artificial molecules from many multi-base-pair fragments for crystalline DNA (50 oligomers) and isolated DNA in solution (26 oligomers).

Reformulation of helical coherence length in terms of step correlations.

$$\Phi_z(z_i) = \Phi_0 + \sum_{j=1}^{i}\left(\Omega_{z,j} - g_0 h_{z,j}\right) \longrightarrow \; 1/\lambda_c^{(0)} = 1/\lambda_{\Omega,\Omega} + 1/\lambda_{h,h} - 2/\lambda_{\Omega,h}$$

$$\left\langle \left[\Phi_z(z_i) - \Phi_z(z_j)\right]^2 \right\rangle = \frac{|z_i - z_j|}{\lambda_c}$$

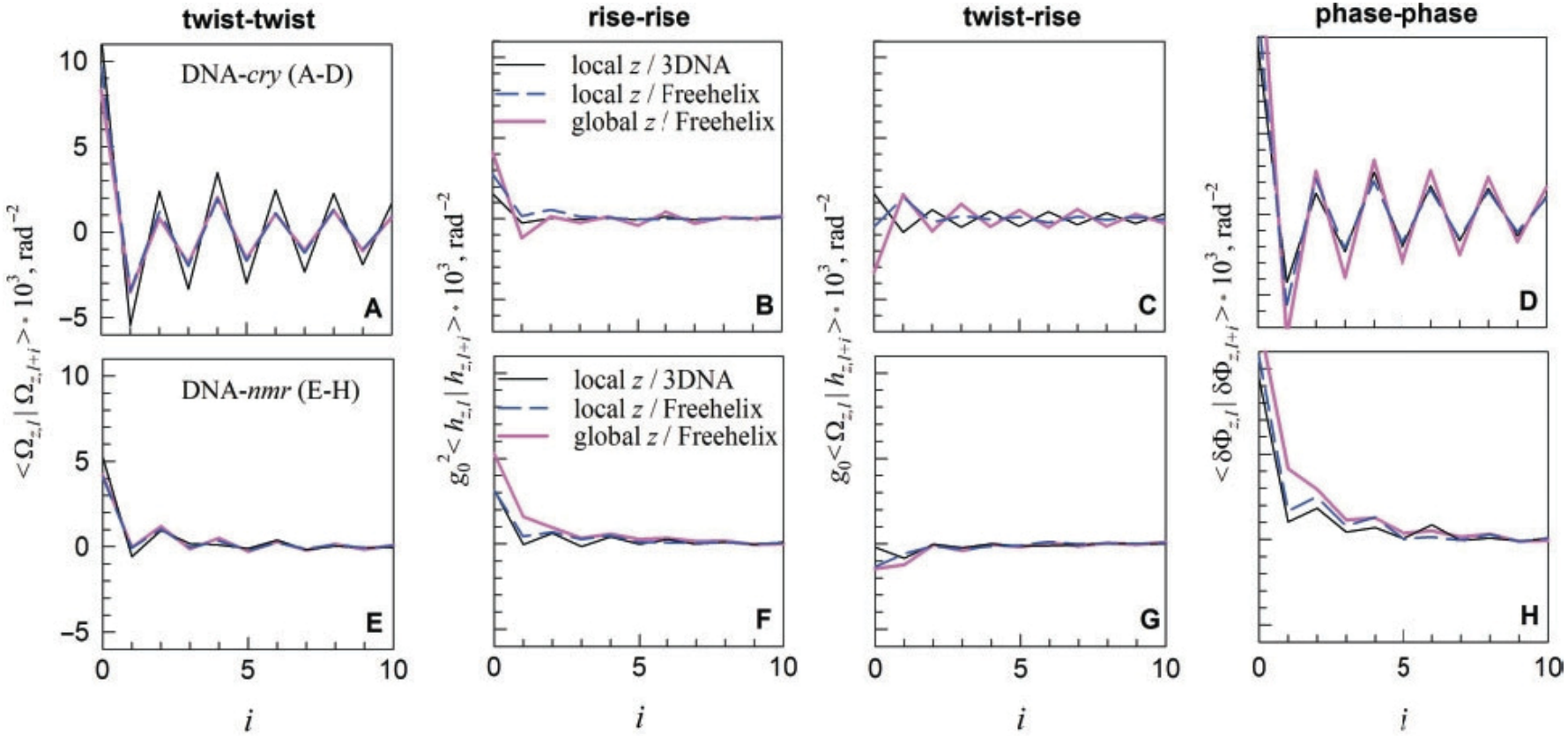
Twist-twist $$\lambda_{\Omega,\Omega} = \langle h_{z,l}\rangle_l \Big/ \sum_i \left\langle \left(\Omega_{z,l} - \langle\Omega_{z,l}\rangle_l\right)\left(\Omega_{z,l+i} - \langle\Omega_{z,l}\rangle_l\right)\right\rangle_l$$

Rise-rise $$\lambda_{h,h} = \langle h_{z,l}\rangle_l \Big/ g_0^2 \sum_i \left\langle \left(h_{z,l} - \langle h_{z,l}\rangle_l\right)\left(h_{z,l+i} - \langle h_{z,l}\rangle_l\right)\right\rangle_l$$

Twist-rise $$\lambda_{\Omega,h} = \langle h_{z,l}\rangle_l \Big/ g_0 \sum_i \left\langle \left(\Omega_{z,l} - \langle\Omega_{z,l}\rangle_l\right)\left(h_{z,l+i} - \langle h_{z,l}\rangle_l\right)\right\rangle_l$$

3DNA: Lu & Olson, Nucleic Acids Res. 31 (2003); FreeHelix98: Dickerson, Nucleic Acids Res. 26 (1998)

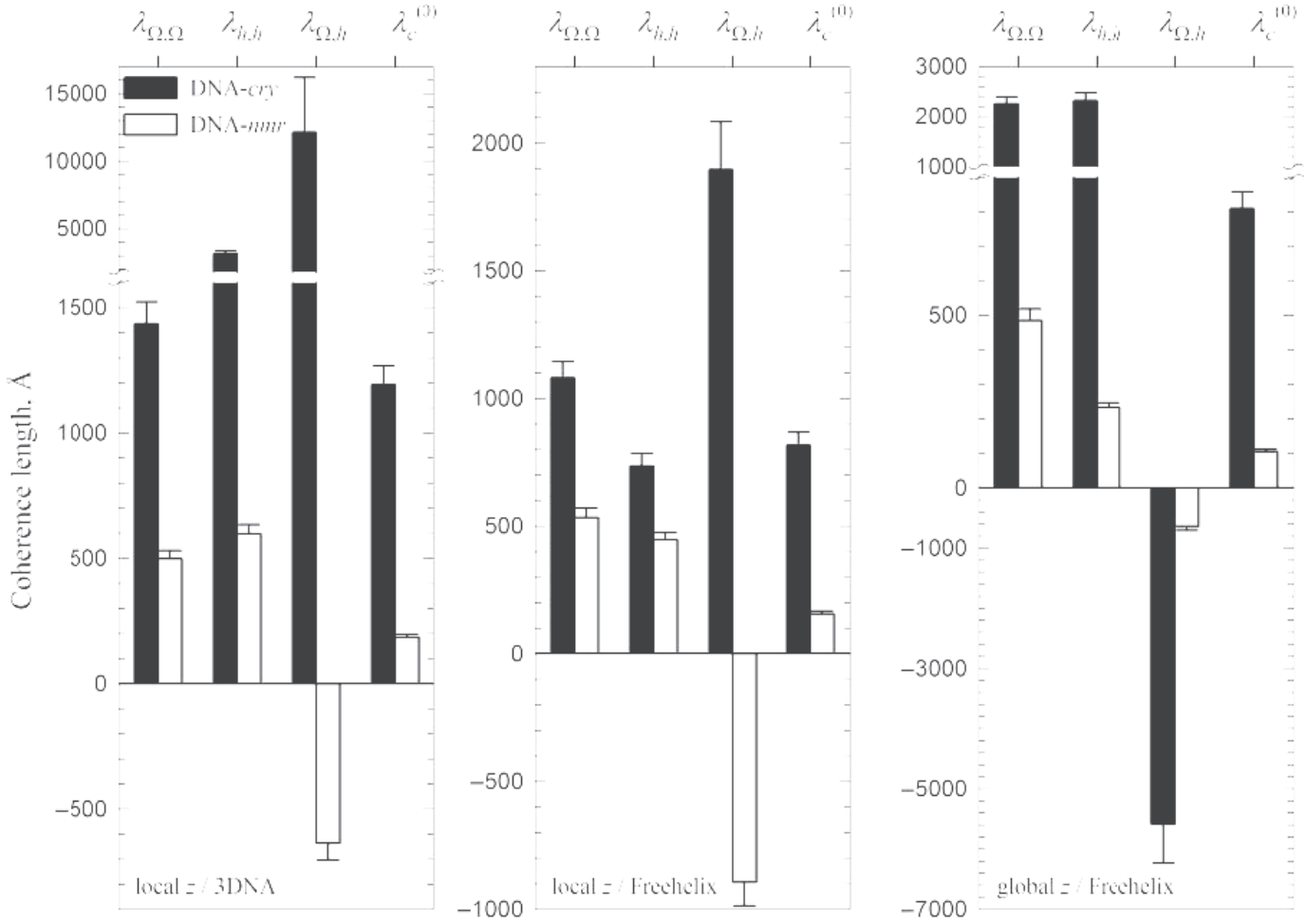
Helical Coherence Length: Correlations



Short range correlations of base pair step parameters.
Correlations depend on algorithm used and DNA environment.

3DNA: Lu & Olson, Nucleic Acids Res. 31 (2003); FreeHelix98: Dickerson, Nucleic Acids Res. 26 (1998)

Helical Coherence Length: Individual and total



- Coherence lengths (esp. twist-rise) very much depend on algorithm.
- Yet total coherence length nearly same for any choice of algorithm.
- Twist-rise correlation and short-range correlations of adjacent base pair steps give very different results for the two cases:

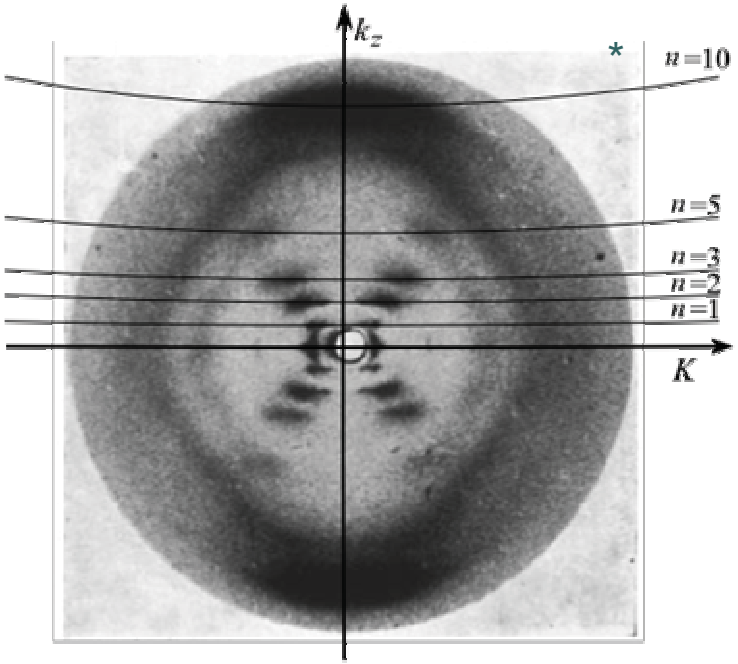
Crystal $\lambda_c^{(0)} \sim 1000\text{Å}$

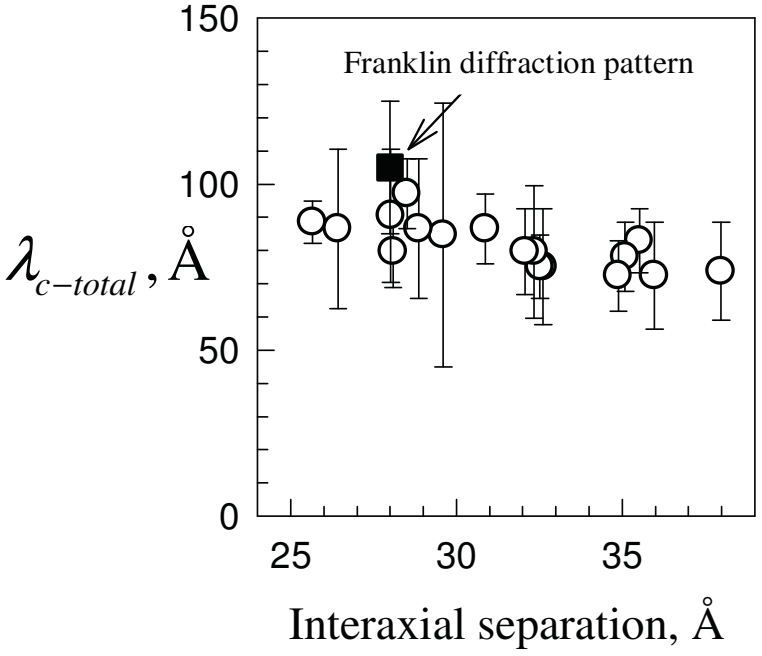
Isolated $\lambda_c^{(0)} \sim 150\text{Å}$

Helical Coherence Length: X-ray Diffraction of Fiber DNA

coherence length extracted from k_z-width of diffraction layer lines

$$\tilde{I}_n(K,k_z) \propto \frac{J_n^2(Ka)}{(k_z+ng_0)^2+n^4/4\lambda_c^2}$$ #





$$\frac{1}{\lambda_c} = \frac{1}{\lambda_c^{(0)}} + \frac{1}{l_p} \qquad l_p \sim 700\text{Å} \rightarrow \lambda_c^{(0)} \sim 120-160\text{Å}$$

(consistent with NMR results for isolated DNA)

* Franklin and Gosling, Nature 171 (1953)

D. J. Lee et al., to be published

Conclusions

- The helical coherence length is relatively independent of how base pair step parameters are defined.

- The coherence length for crystallized DNA and isolated DNA in solution differ roughly by an order of magnitude.

  → results from different correlations between twist and rise as well as short-range (auto-)correlations of the base pair step parameters themselves.

  → crystal packing of DNA effectively “straightens” (becoming a more ideal helix) due to interactions between the molecules.

- The coherence length of fiber DNA (most closely related to what is in cell nuclei) is roughly 150 Å, in agreement with the NMR-derived values.

- The coherence length for DNA in solution is much smaller than what had been previously calculated, suggesting that structurally-dependent DNA interactions, e.g., homologous recognition, may be larger than anticipated.

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