The Abdus Salam
International Centre for Theoretical Physics

United Nations
Educational, Scientific and
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IAEA
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Conference: From DNA-Inspired Physics to Physics-Inspired Biology

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Electrostatic Interactions between DNA Double Helices

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Electrostatic interactions between DNA double helices

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In collaboration with:

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Kornyshev, Lee, Leikin, and Wynveen (2007). *Rev Mod Phys* **79**, 943-996

Electrostatic interactions between DNA double helices

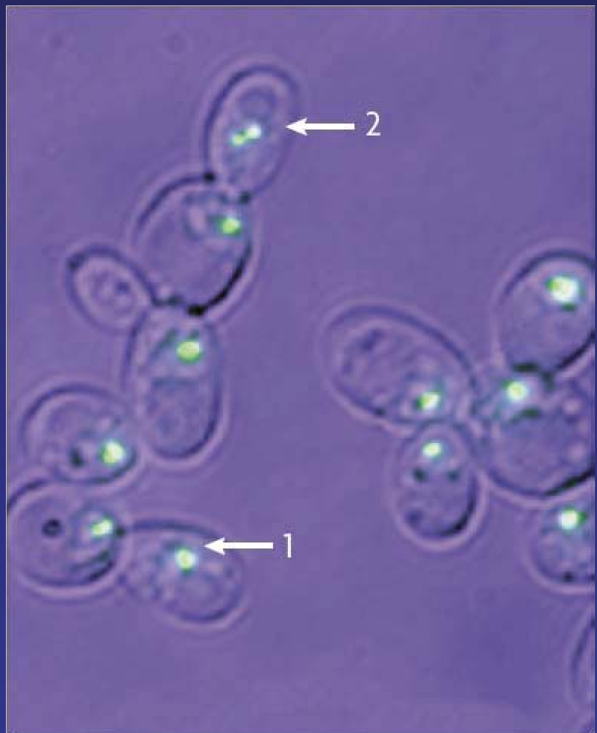
Predatory adaptation and evolution

Animals - speed

Humans - endurance

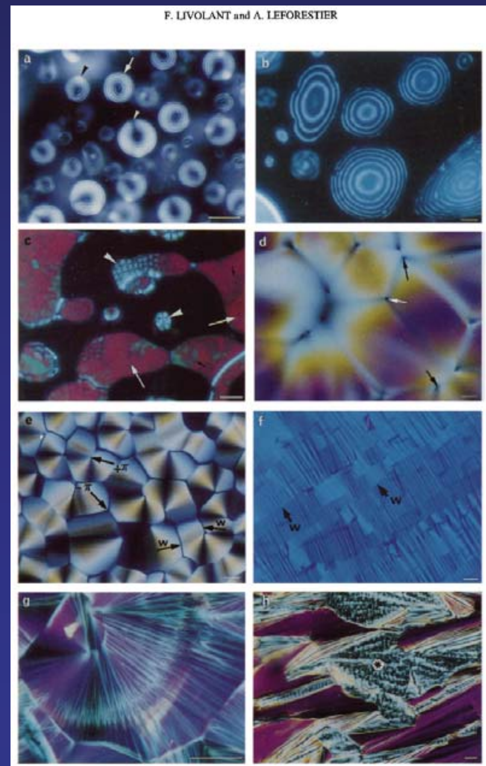
Electrostatic interactions between DNA double helices

Homologous pairing

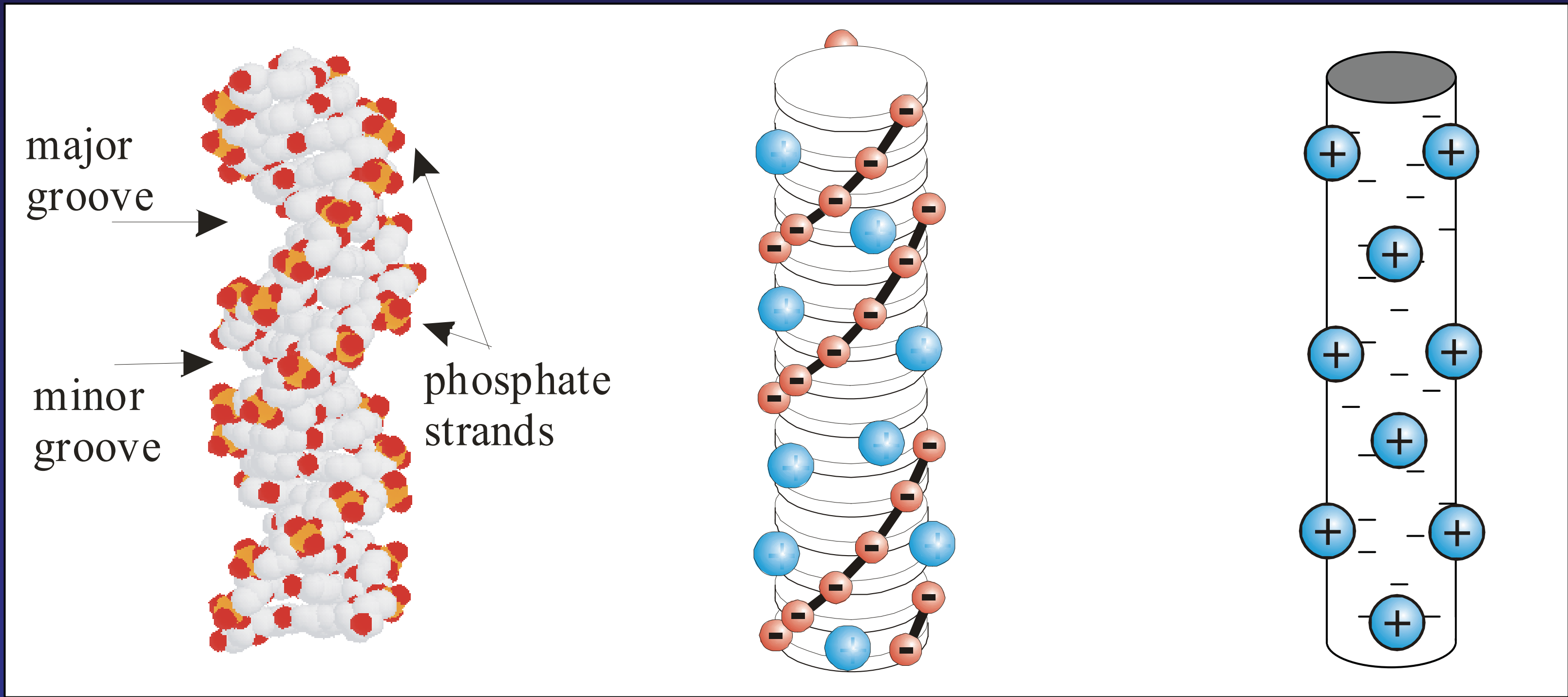


DNA packing

Poly- and meso-morphism



Surface charge pattern



DNA

charged helix

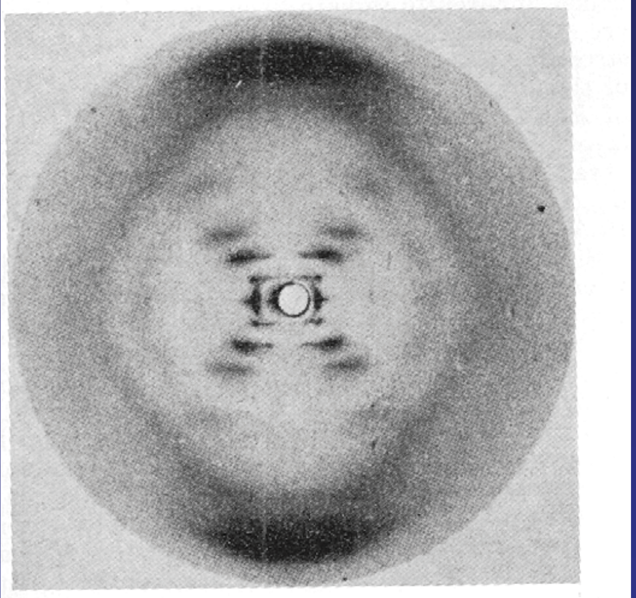
charged cylinder
with counterions

DNA structure and interactions

$$I(\mathbf{k}) = \sum_{\nu,\mu} \sum_{i,j} f_i f_j \left\langle F_i^{\nu}(\mathbf{k}) F_j^{\mu}(-\mathbf{k}) \right\rangle$$

$$F_i^{\nu}(\mathbf{k}) = \frac{1}{(2\pi)^{3/2}} \int n_i^{\nu}(\mathbf{r}) \exp(i\mathbf{kr})\, d^3\mathbf{r}$$

$$\mathcal{E} \approx \frac{2\pi e^2}{\varepsilon} \sum_{\nu,\mu=1}^{2} \sum_{i,j} q_i q_j \int \frac{F_i^{T,\nu}(\mathbf{k}) F_j^{\mu}(-\mathbf{k})}{k^2 + \kappa_D^2} d^3\mathbf{k}$$



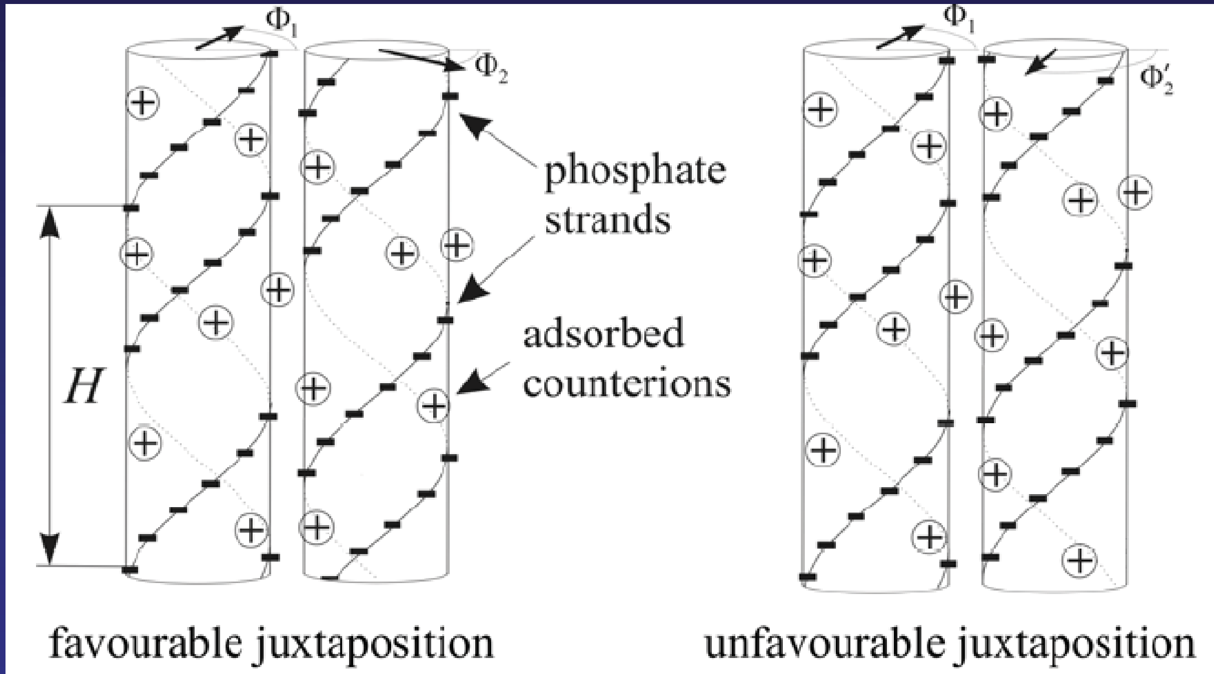
Sodium deoxyribose nucleate from calf thymus. Structure *B*

Franklin & Gosling,
Nature 171 (1953) 740

- **ideal, parallel helices** (1997)
- **ideal, crossed helices** (2000)
- **straight, non-ideal helices** (2004)
- **fluctuating helices** (ongoing)
(*static and dynamic torsional, stretching and bending fluctuations*)
- **counterion correlations** (ongoing)
(*ideal helices, point counterions, no hydrogen bonding, simple limiting cases*)

Helix-helix alignment

Prediction: Electrostatic interactions cause alignment of DNA backbones in hydrated aggregates

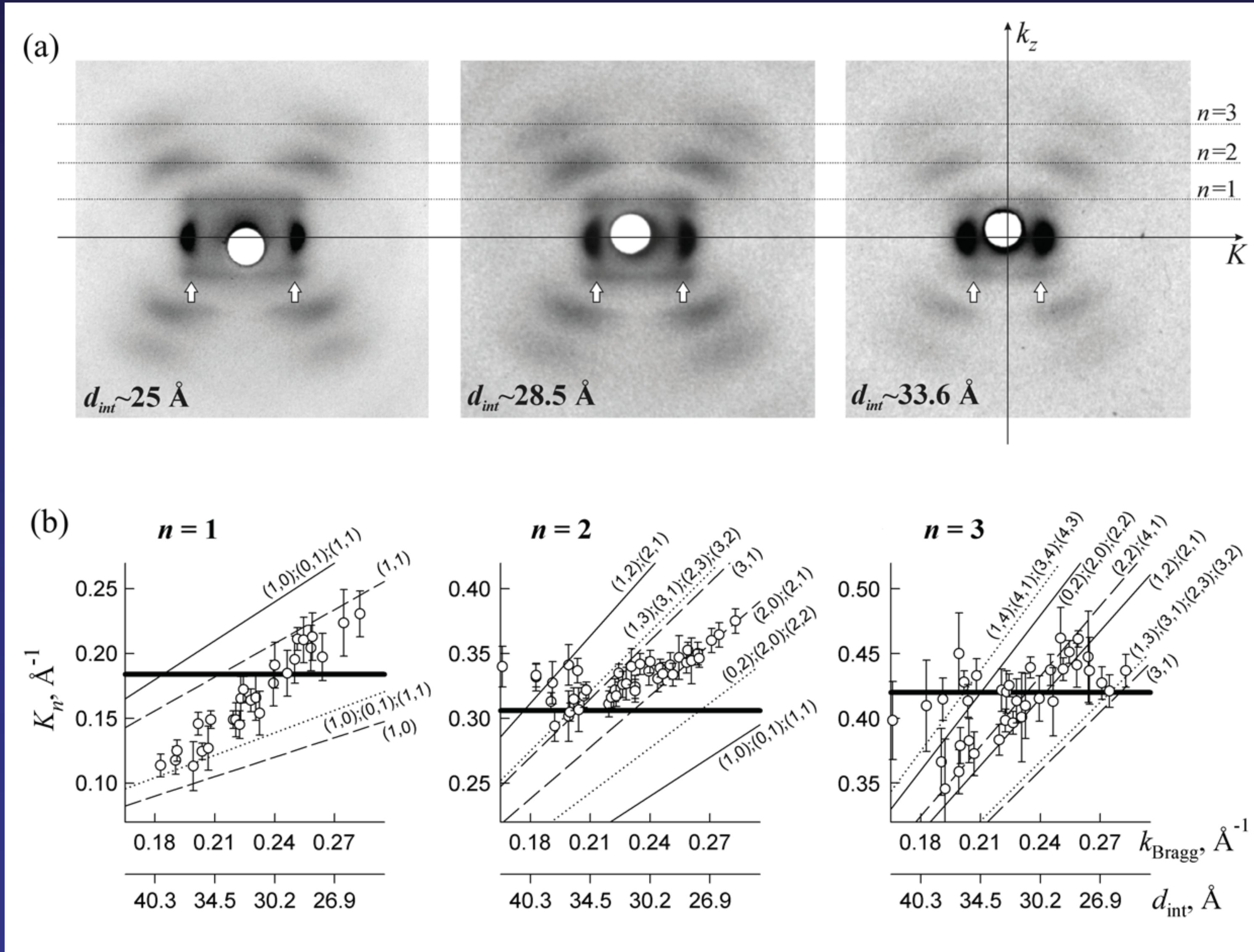


Kornyshev & Leikin, J. Chem. Phys. (1997)

"It therefore seems reasonable to suppose that in structure B the structural units [...] are relatively free from the influence of neighboring molecules, each unit being shielded by a sheath of water."

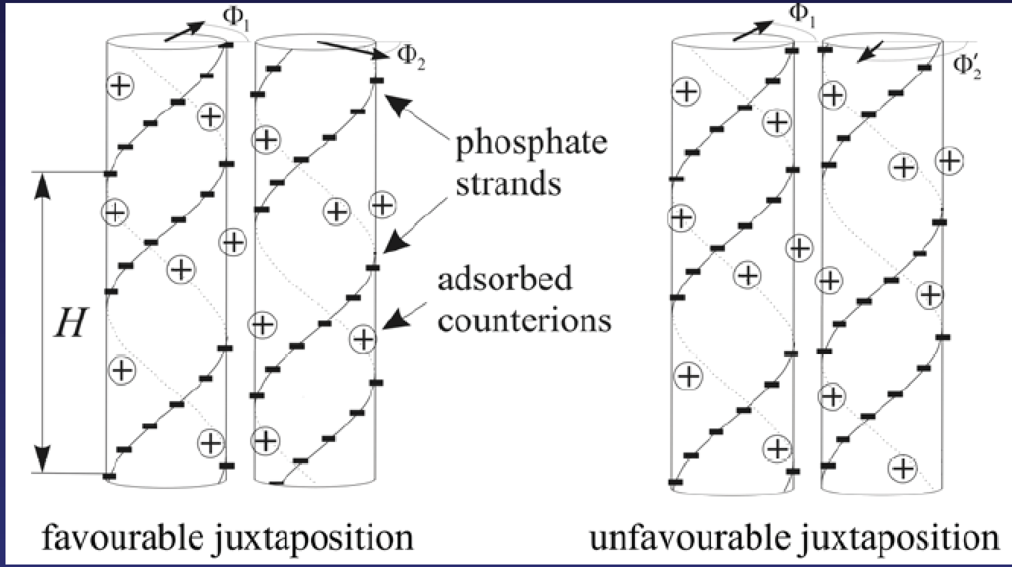
Franklin & Gosling, Nature (1953)

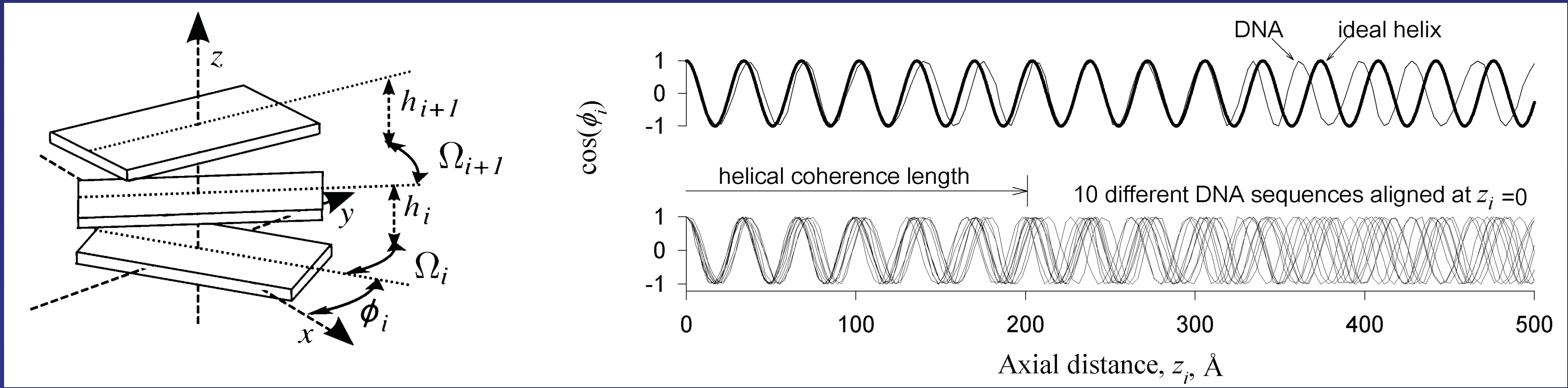
Franklin & Gosling were wrong.



Kornyshev, Lee, Leikin, Wynveen & Zimmerman, Phys. Rev. Lett. (2005)

But, how do non-ideal, fluctuating helices align?

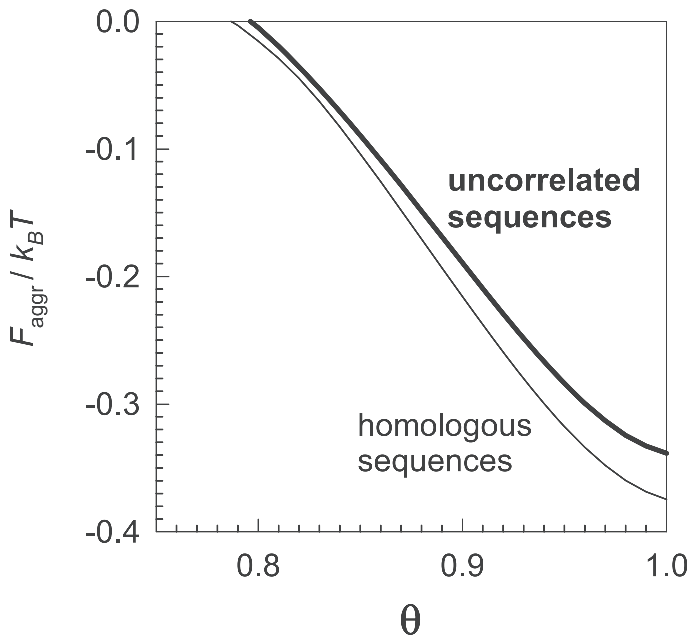


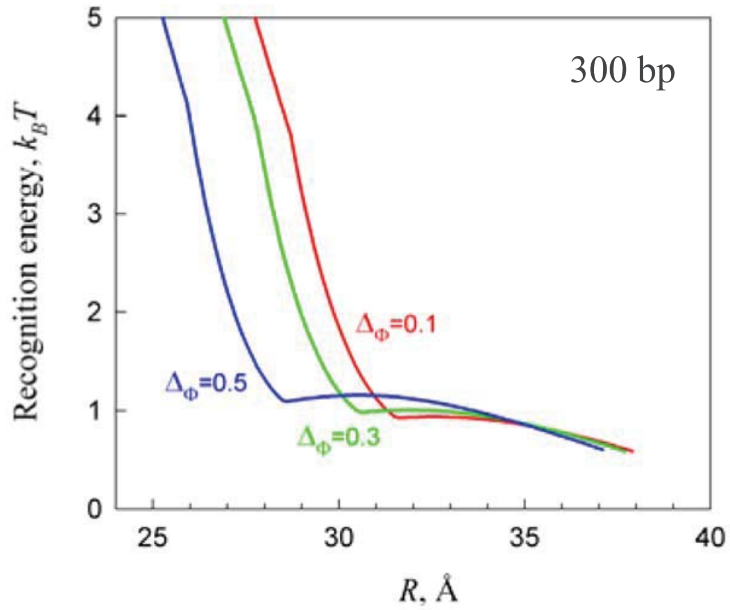


Cherstvy, Kornyshev, and Leikin, J. Phys. Chem., 2004
Wynveen, Lee, Kornyshev, and Leikin, Nucl. Acids Res., 2008

Homologous pairing of dsDNA

Double stranded DNA (dsDNA) have an innate homology recognition ability

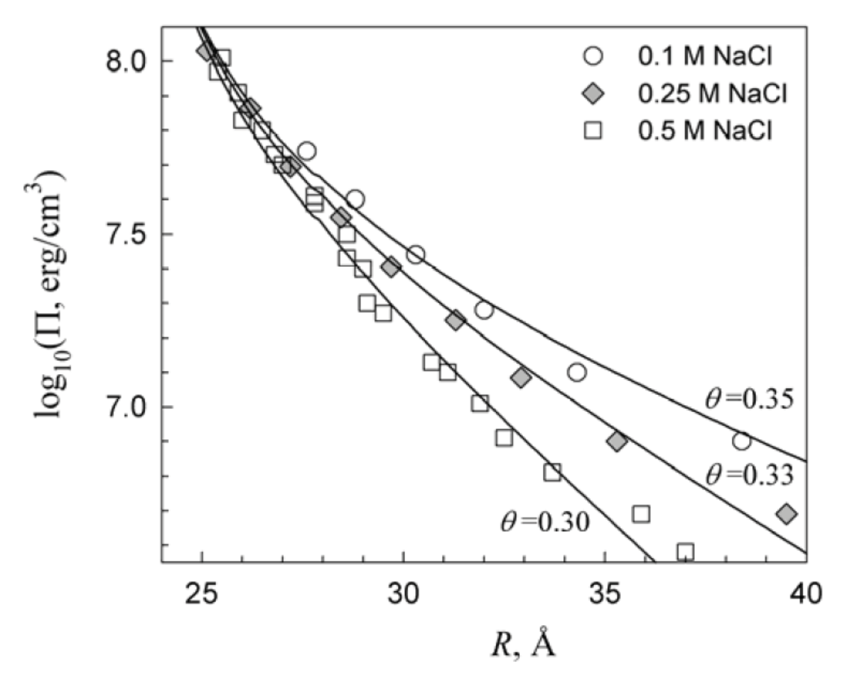


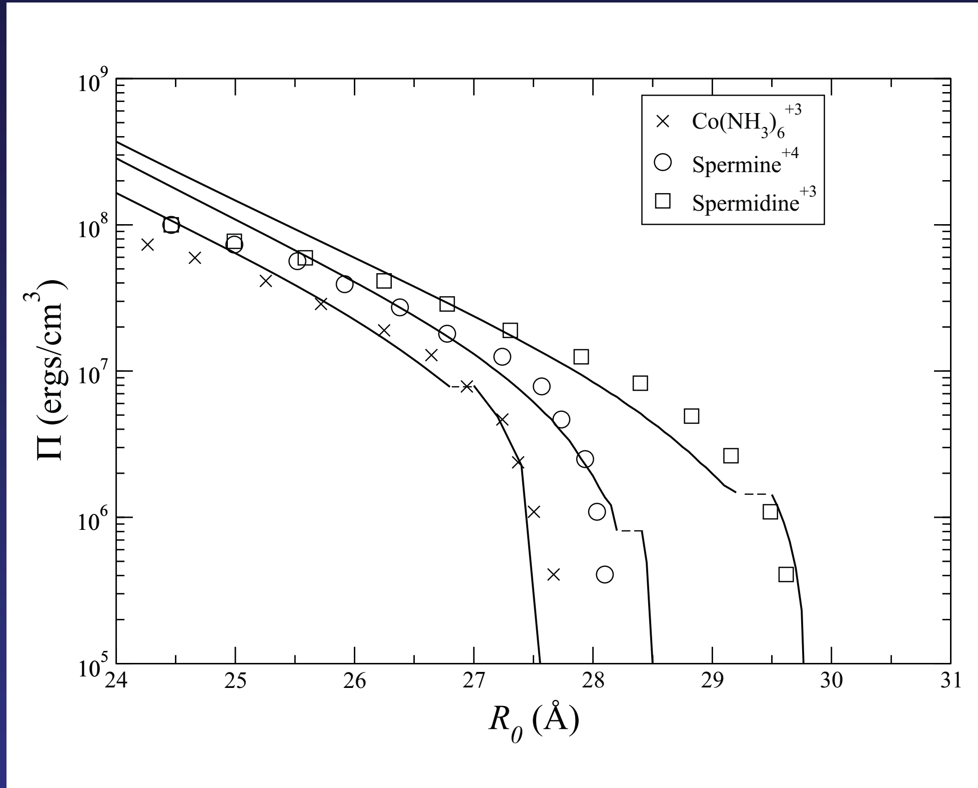


Theory: **Kornyshev & Leikin, Phys. Rev. Lett., 2001**
Cherstvy, Kornyshev & Leikin, J. Phys. Chem., 2004

Experiment: **Inoue, Sugiyama, Travers, Ohyama, Biochemistry, 2007**
Baldwin et. al, J. Phys. Chem., 2008
Prentiss et al. (this meeting)

Rationalization of measured forces



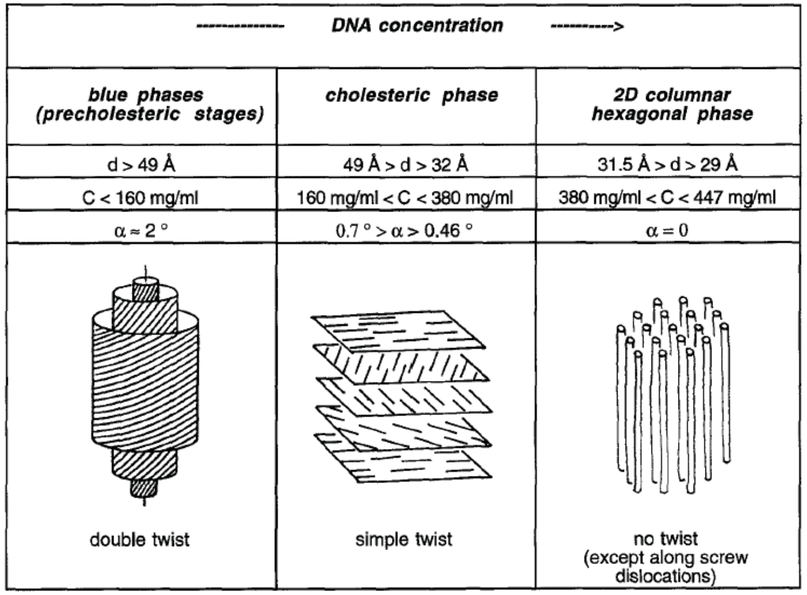


Undulations of DNA dramatically enhance and extend the range of structure-dependent forces.

$$E_{undulations} / E_0 \sim \exp\left(d^2 / \lambda^2\right)$$

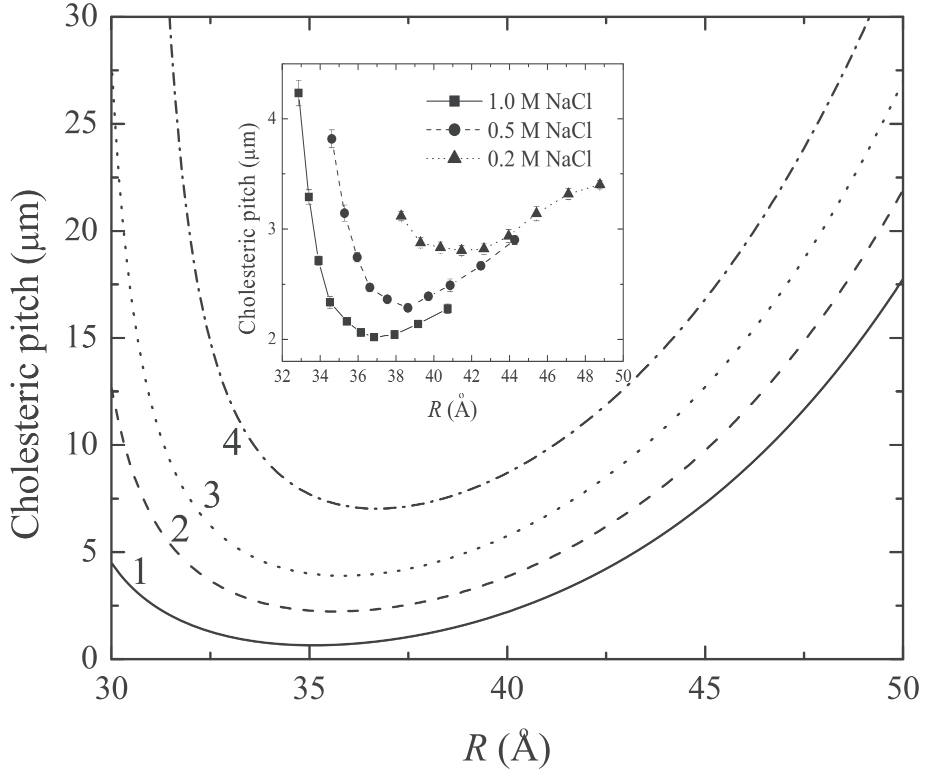
Force measurements: **Parsegian, Rau, et al., 1984-2008**
Theory: **Kornyshev, Lee, Leikin & Wynveen, 2007-2009**

Chiral interactions, cholesteric phase, poly- and meso-morphism



DNA concentration --------->		
blue phases (precholesteric stages)	cholesteric phase	2D columnar hexagonal phase
d > 49 Å	49 Å > d > 32 Å	31.5 Å > d > 29 Å
C < 160 mg/ml	160 mg/ml < C < 380 mg/ml	380 mg/ml < C < 447 mg/ml
α ≈ 2 °	0.7 ° > α > 0.46 °	α = 0
double twist	simple twist	no twist (except along screw dislocations)

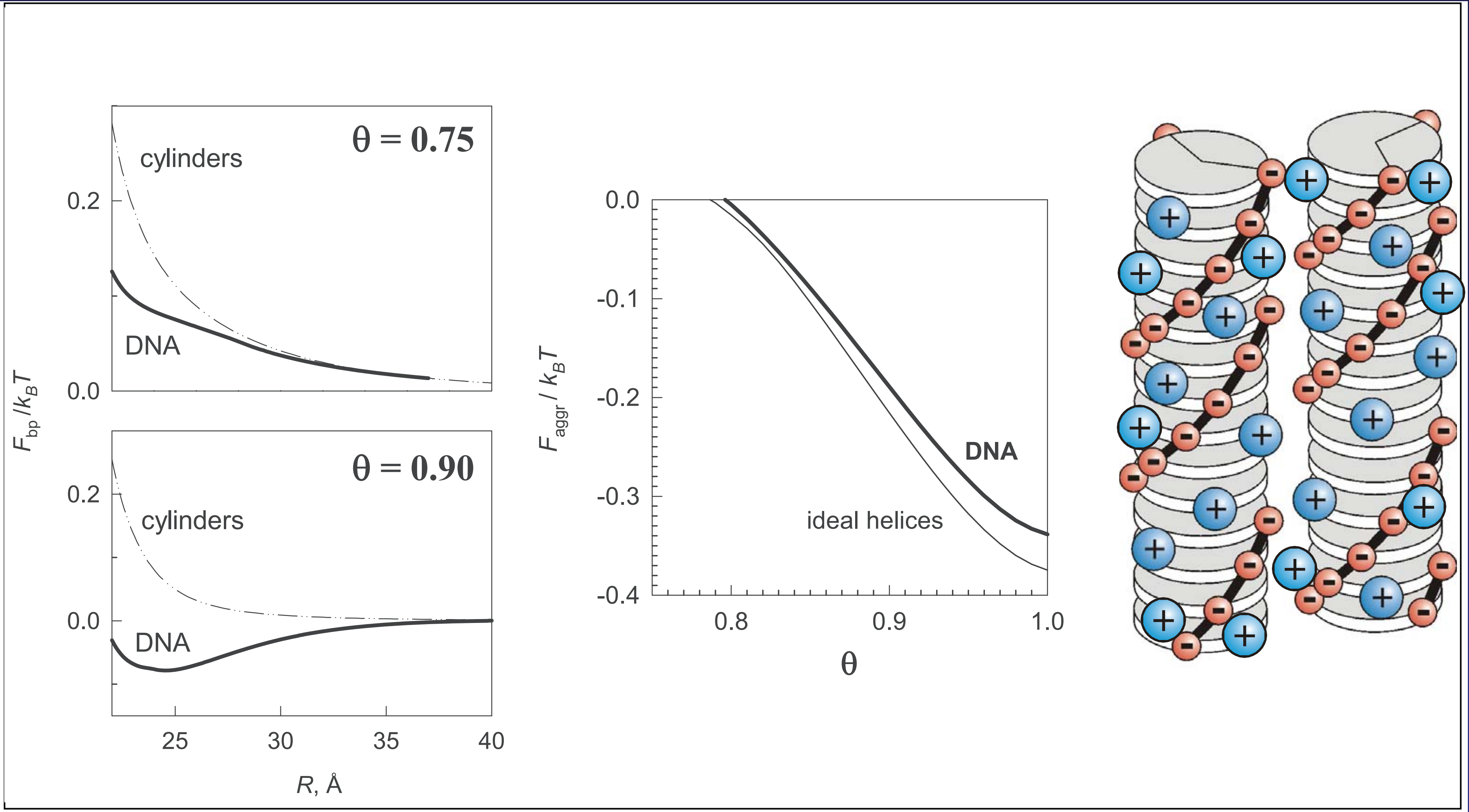
Fig. 25. Geometrical configurations as a function of DNA concentration in the different liquid crystalline phases. The concentration C was calculated from the interhelix distances d measured by X-ray diffraction experiments (Durand *et al.* 1992[32]). The twist angle α was deduced from the cholesteric pitch P (0.8 μm in blue phases and 2.5 μm in the cholesteric) and the interhelix distance d.



Theory: **Kornyshev, Leikin & Malinin, Eur. Phys. J. E, 2002**

Experiment: **Stanley, Hong & Strey, Biophys. J., 2005**

Counter-Ion Specific Aggregation



Kornyshev & Leikin, Phys. Rev. Lett., 1999
Cherstvy, Kornyshev & Leikin, J. Phys. Chem., 2004

Main conclusions

Helical structure of sugar-phosphate backbone strongly affects interactions between DNA. Conversely, interactions affect the structure of DNA in assemblies.

Static and dynamic undulations strongly enhance and extend the range of the structure-dependent forces Torsional and stretching fluctuations affect these forces relatively weakly.

dsDNA have an innate ability to recognize sequence homology through electrostatic interactions due to sequence dependence of the DNA backbone structure

Does direct sequence homology recognition between *ds*DNA occur *in vivo* and what is its role in homologous recombination?