# The Nature and Characterization of Order in High Density DNA Mesophases

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- DNA and the phenomenology of DNA mesophases
- salient features of DNA mesophases
- unusual features of DNA mesophases
- the screw-like order and molecular pitch
- DNA-DNA azimuthal correlations
- angular frustrations and the orthorhombic phase
- organization of eucaryotic genome
- nucleosomes and nucleosomal core particles (NCP)
- NCP mesophases

V. A. Parsegian (NIH, USA)

D. C. Rau (NIH, USA)

V. Lorman (U MONTPELLIER, FR)

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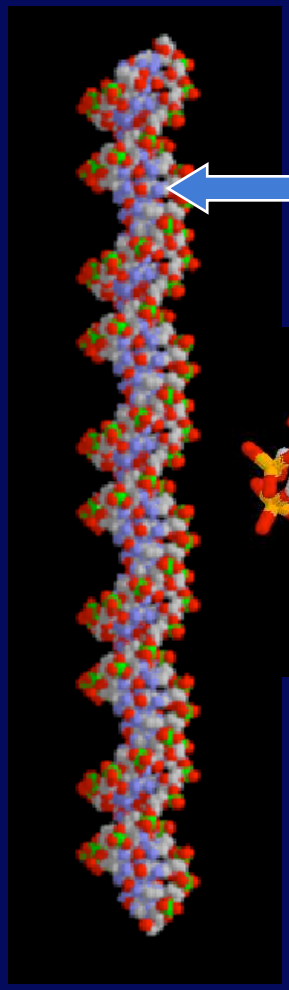
B. Žekš (U LJUBLJANA, SLO)

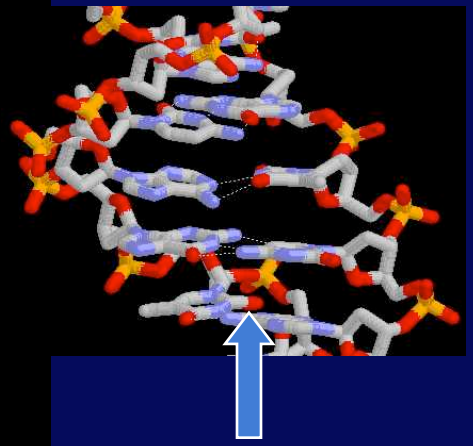
M. Kanduč (U LJUBLJANA, SLO)

# DNA



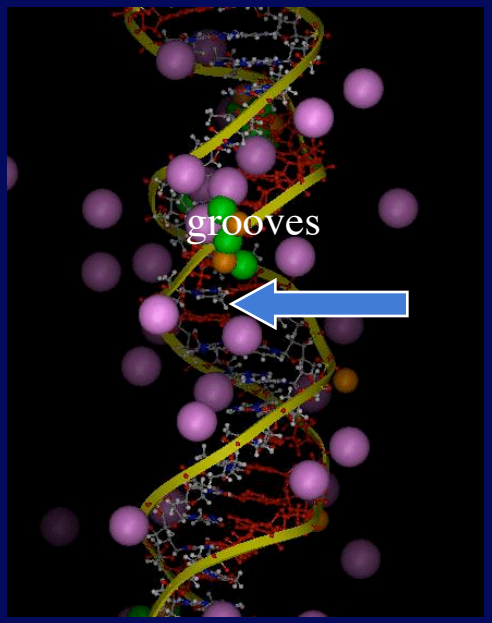
helix

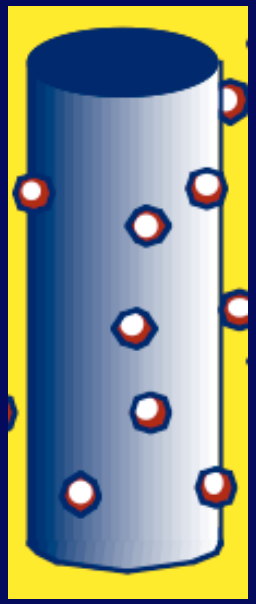
Structure
(B-form double-helix)



discrete charges

Charge:
2 $e_0$ / 3.4 Å
~ $e_0$ / $nm^2$



Polipeptides: 0.6 $e_0$ / nm

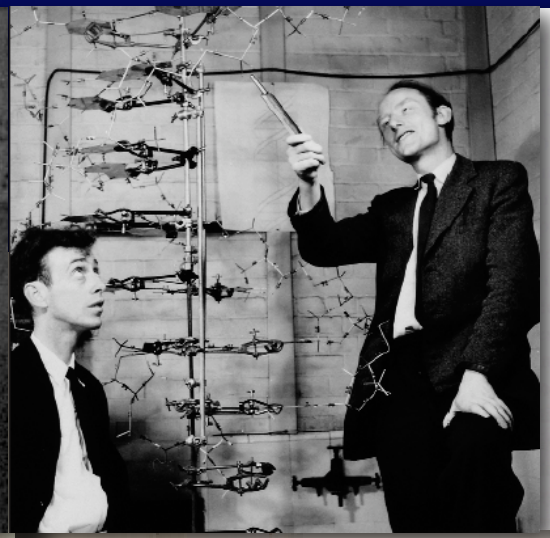
Membranes: 0.1 - 1 $e_0$ / $nm^2$

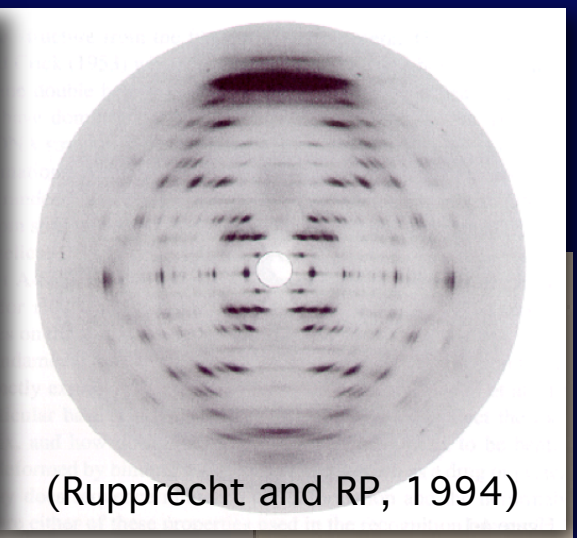
- a ~ 1 nm
- h ~ 0.17 nm
- DNA pitch p ~ 3.4 nm
- DNA length L ~ 50 nm to ~ μm
- DNA persistence length $L_p$ ~ 50 nm

- it is a RH double helix
- it has lots of discrete structural (phosphate) charges (pH > 1)
- it has lots of room to accommodate small counterions

# Discovery of the double helix structure of DNA

Nature, april 25, 1953.





(Rupprecht and RP, 1994)

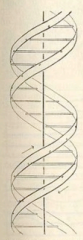
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

**A Structure for Deoxyribose Nucleic Acid**

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three inter-twined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate–sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate di-ester groups joining β-D-deoxy-ribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

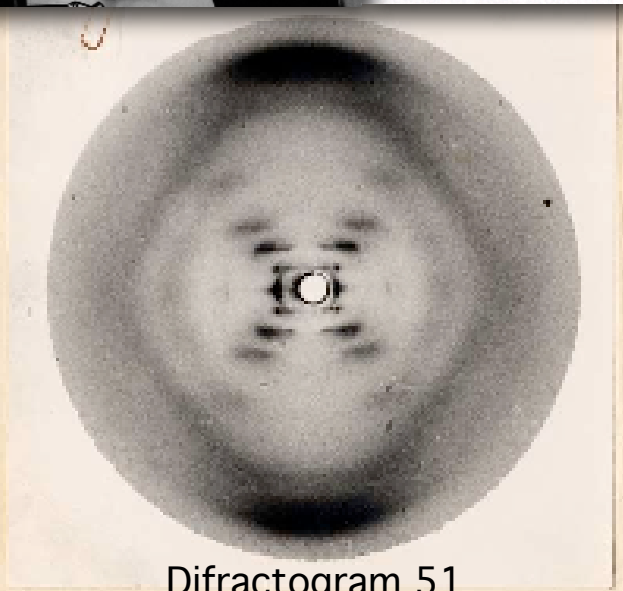
It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxy-ribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereo-chemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on inter-atomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

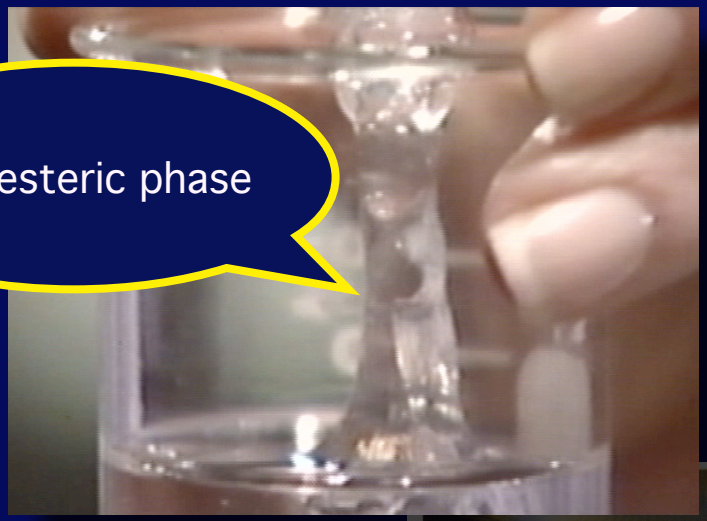


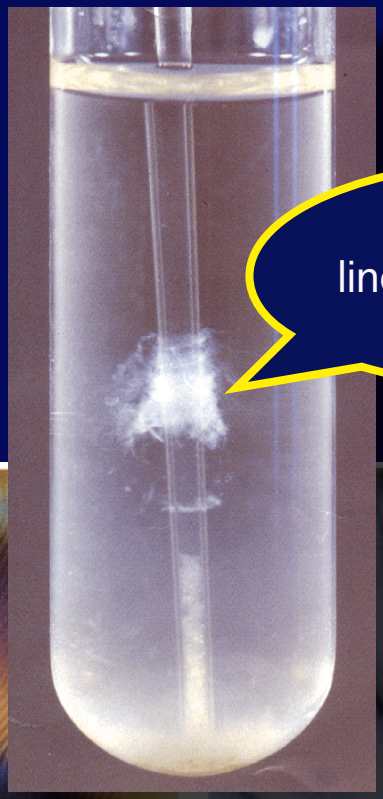
Difractogram 51
(Franklin and Gosling, 1952).

Based on the CCV theory of diffraction by helical molecules and X-ray diffraction experiment.

# Discovery of DNA mesophases

DNA in concentrated solutions makes ordered phases. Not that difficult to observe.

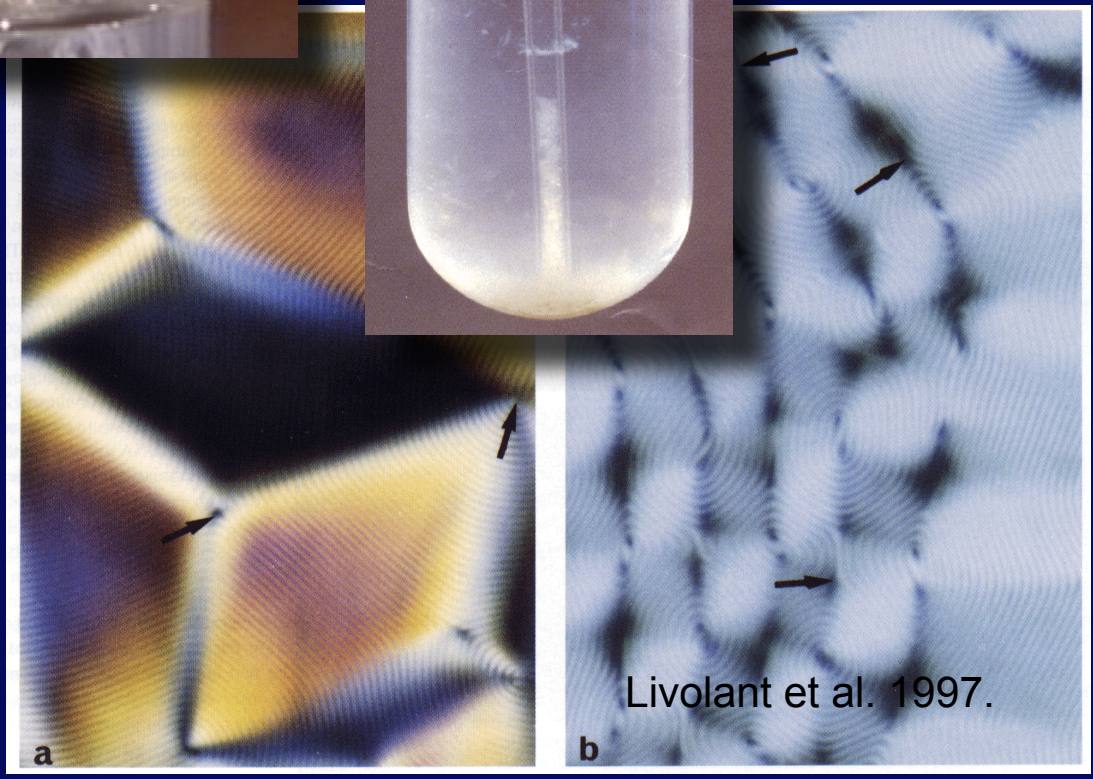



Conmar Robinson in 1958 described the cholesteric phase of poly(benzyl-L-glutamate) in dimethylformamide and in 1961 of DNA.

V. Luzzati et al. in 1961 observed indications of ordered phases of DNA in SAXS (small angle X-ray scattering)

R. Rill et a. in 1981 saw ordered phases with short fragment DNA (146 bp about 50 nm)

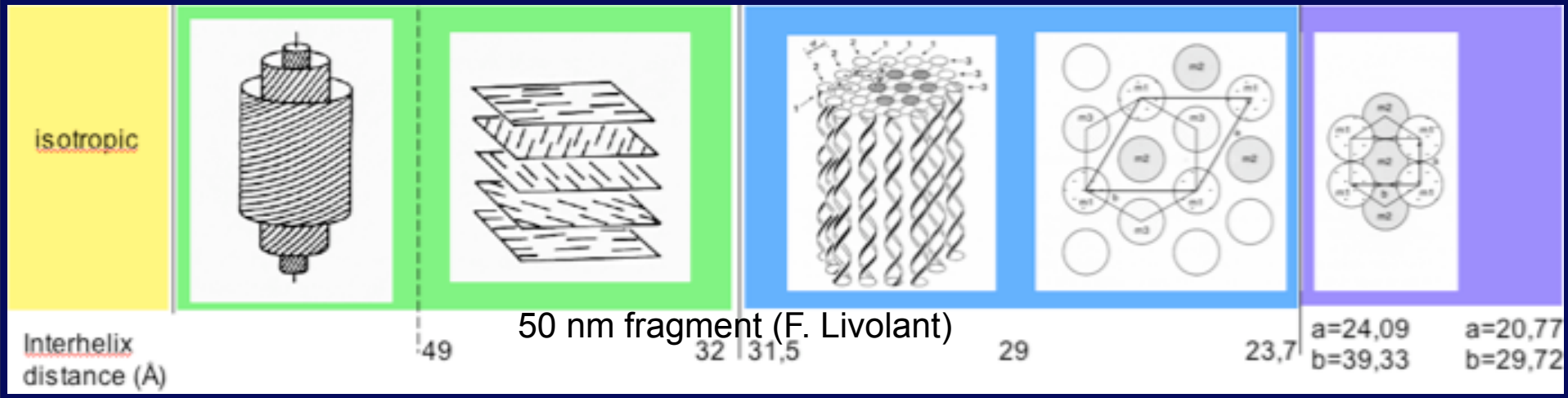



Livolant et al. 1997.

# DNA mesophase zoo

Mesophases at different DNA density.

mg/ml 15 160 380 440 670 1055




50 nm fragment (F. Livolant)

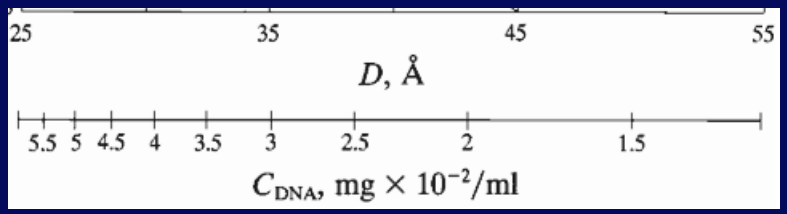
blue phases

cholesteric

hexatic - deformed hexatic

orthorhombic

columnar hexagonal - hexagonal

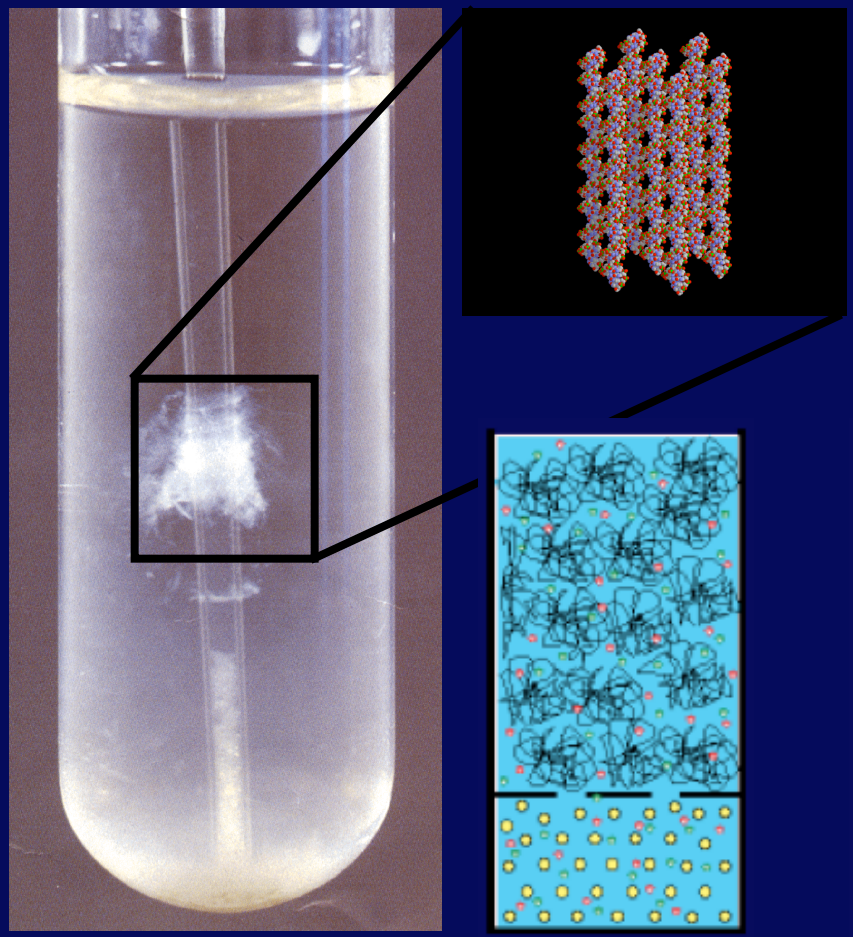



The exact positions of the phase boundaries do depend on the method of preparation (osmotic stress, controlled drying, condensation ) and the length of the DNA.


Durand, Doucet, Livolant (1992) J. Physique 2, 1769.
Pelta, Durand, Doucet, Livolant (1996) Biophys. J., 71, 48
RP et al. COSB. 8 (1998) 309. COCIS. 3 (1998) 534.

# Methods of preparation

The question is how to control and change the DNA density in solution.



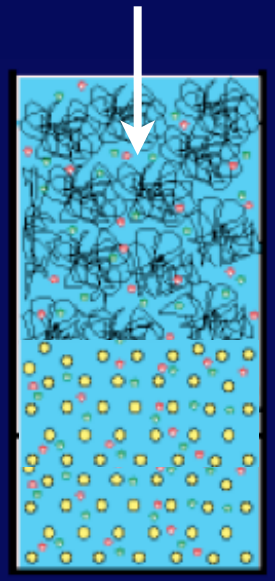


Dense ordered phases of DNA can be prepared by a variety of methods used in different experimental setups.

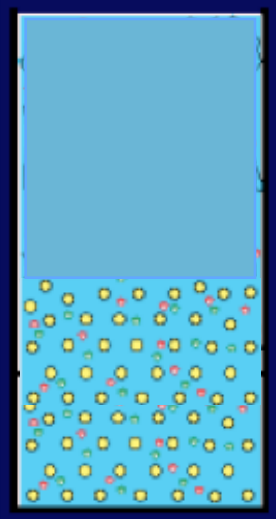


Osmotic stress (membrane)

osmoticant

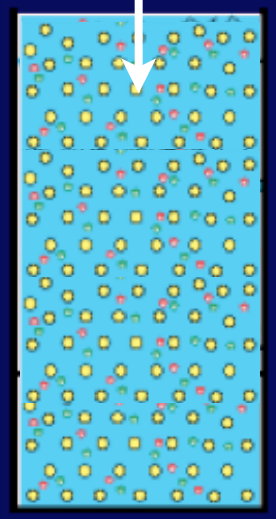


Osmotic stress (PEG...PSI DNA)



Controlled drying

condensing agents



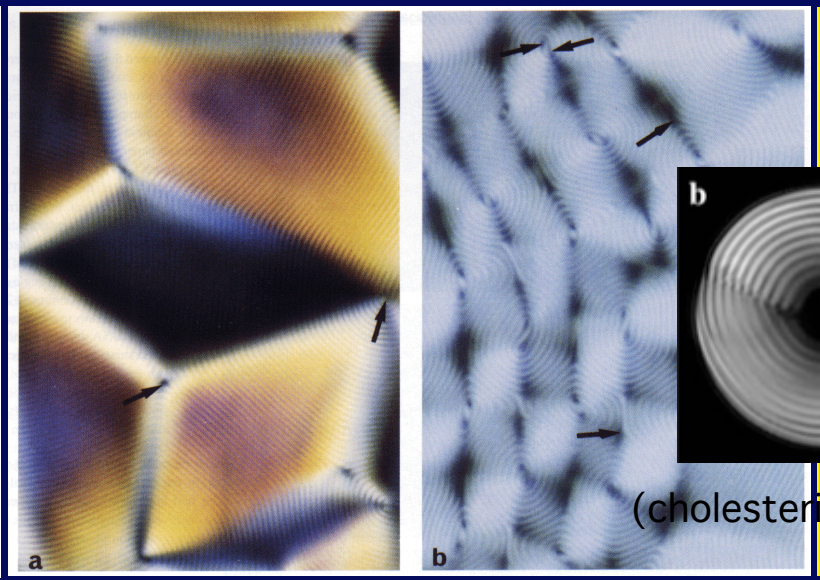
Condensation (polyamines...)

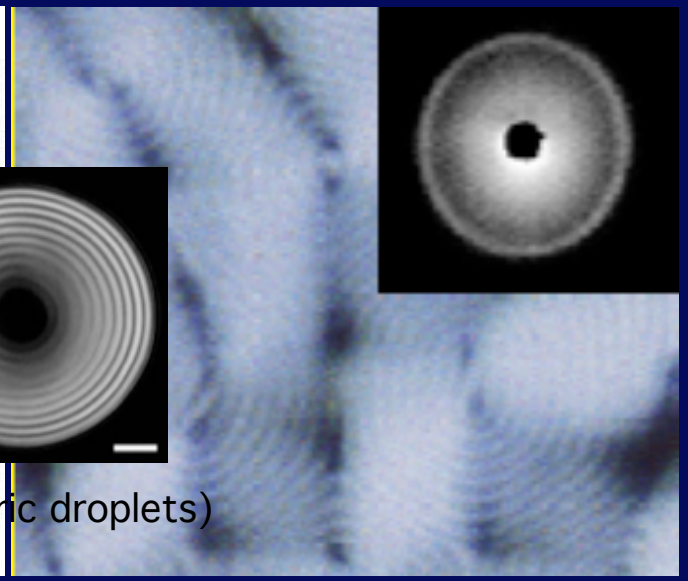
While there are no qualitative differences between the nature of the phases and their boundaries, they have not been studied systematically.

# Cholesteric phase

160 - 380 mg/ml

C. J. Barrett



(cholesteric droplets)

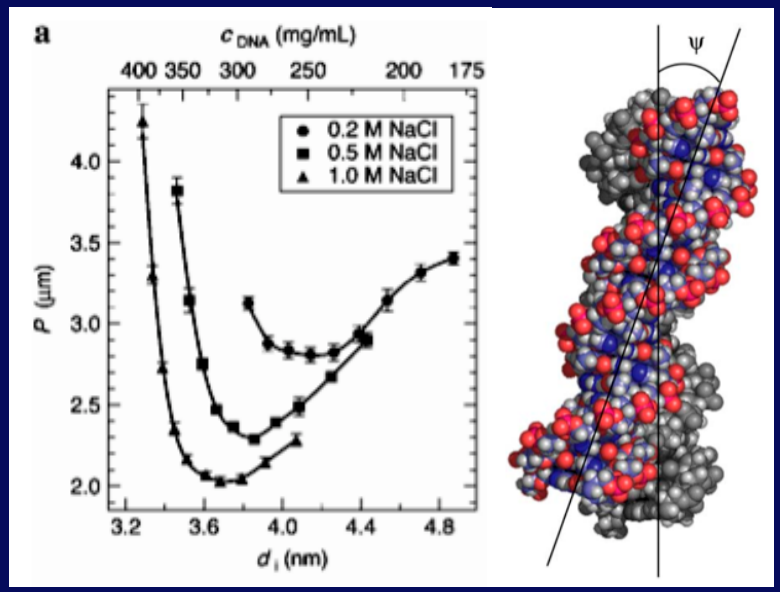
Durand, Doucet, Livolant (1992) J. Physique 2, 1769.

The pitch of the cholesteric phase ~ μm.

**TABLE 1 Ionic-strength dependence of the pitch minimum and twist-angle maximum**

| $I$ (M NaCl) | $P_{min}$ (μm) | $d_i$ (nm) | $c_{DNA}$* (mg/mL) | $\psi_{max}$ (deg) | $d_i$ (nm) | $c_{DNA}$* (mg/mL) |
|---|---|---|---|---|---|---|
| 0.2 | 2.81 ± 0.05 | 4.14 | 249 | 0.54 ± 0.02 | 4.26 | 235 |
| 0.5 | 2.29 ± 0.02 | 3.86 | 286 | 0.61 ± 0.01 | 3.86 | 286 |
| 1.0 | 2.03 ± 0.03 | 3.68 | 315 | 0.67 ± 0.02 | 3.79 | 297 |

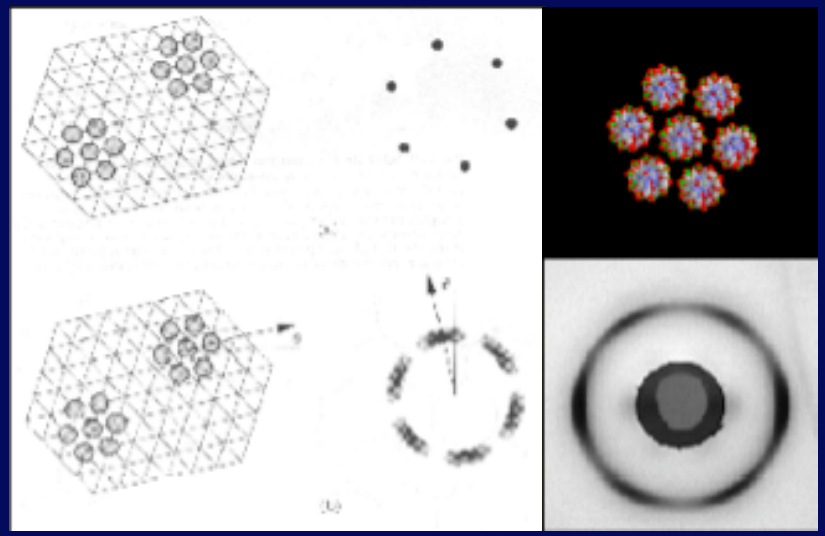
Cholesteric pitch:
(Stanley et al. BJ 89 (2005))



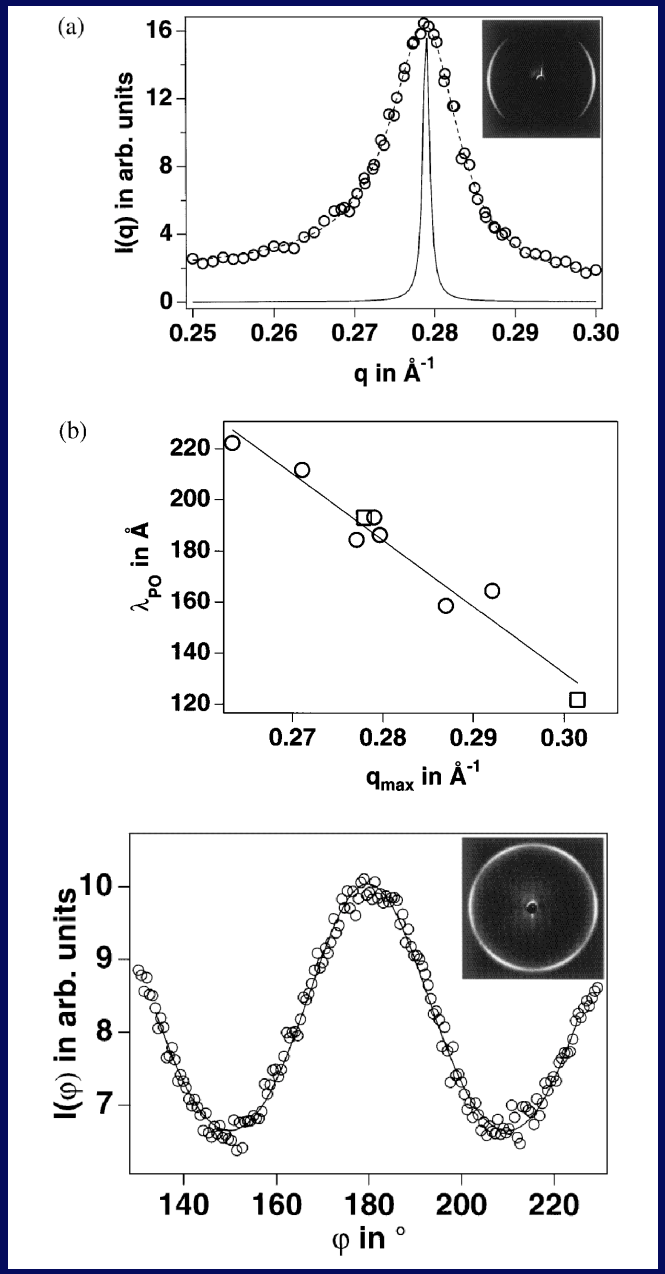
# Hexatic - deformed hexatic

380 - 440 mg/ml

A most “mysterious” phase!

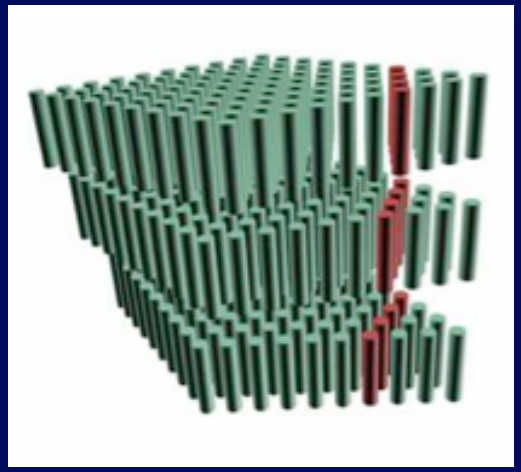


(Predicted by Toner, 1983 observed by RP et al. 1996.)




- Long range BO order ~ 0.6 mm
- Long range nematic order
- Liquid like positional order, $\lambda_{PO}$
- No twisting of the hexatic order

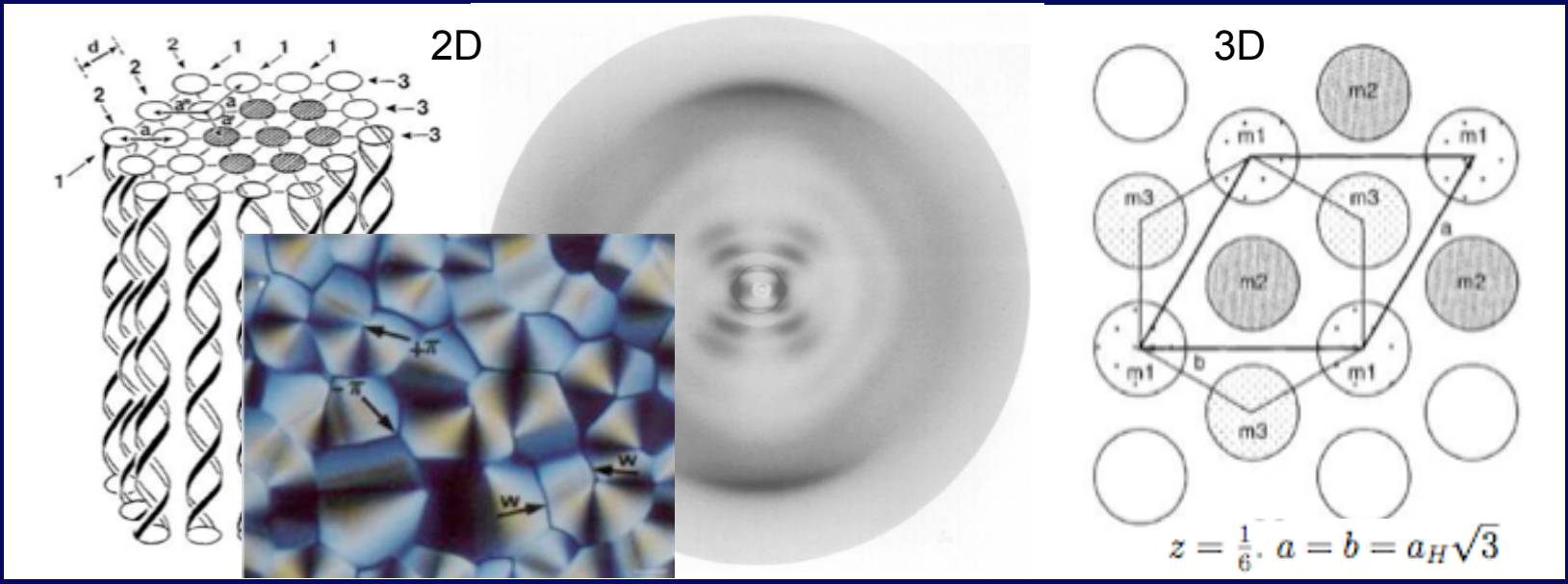
(cholesteric-hexatic coupling)



Kamien and Levine, PRL (2000).

# Columnar hexagonal - hexagonal

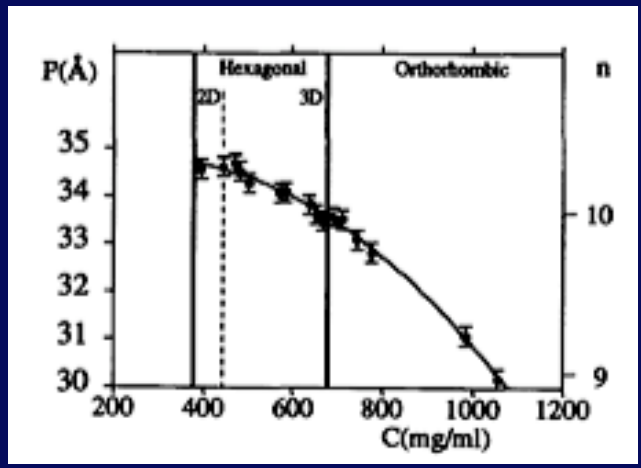
440 - 670 mg/ml




A 2D crystal. Scattering from a columnar hexagonal phase reveals hexagonal order in the equatorial reflections. Hexagonal phase is a real 3D crystal, order in all directions. Relative displacements of 1/6 DNA pitch along z-axis. Livolant et al., Nature (1989).

Changes in DNA pitch as a function of density.

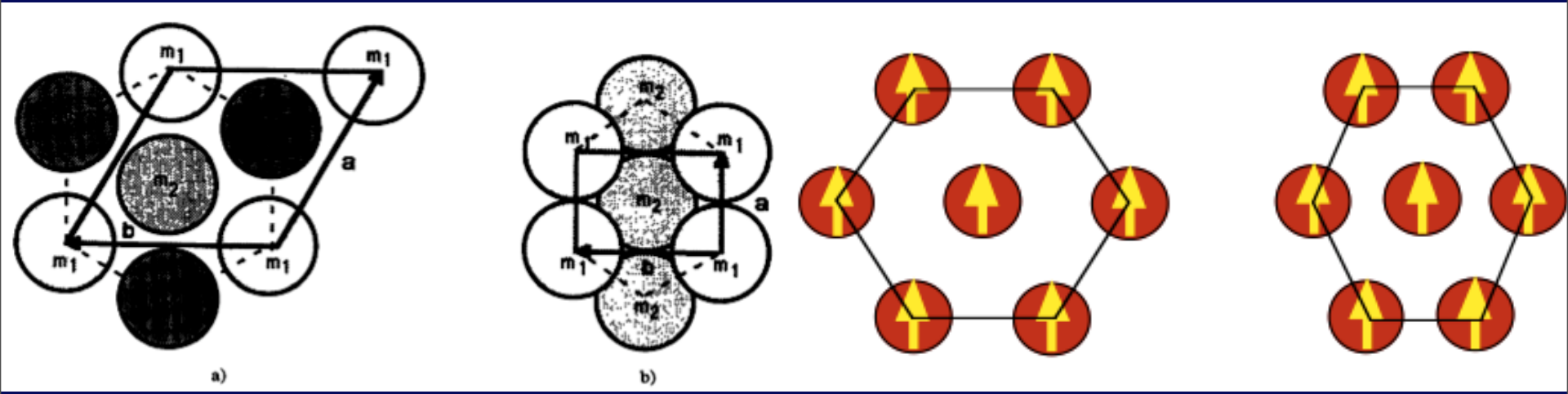
This is the range of densities of the Franklin-Gosling experiment.



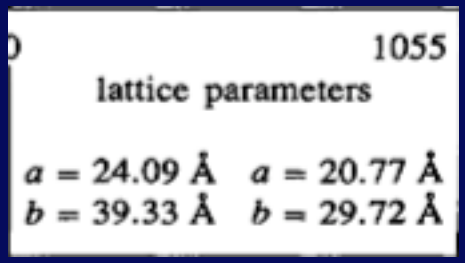

Livolant and Leforestier, Prog. Pol. Sci. (1996).

# Orthorhombic

670 → mg/ml

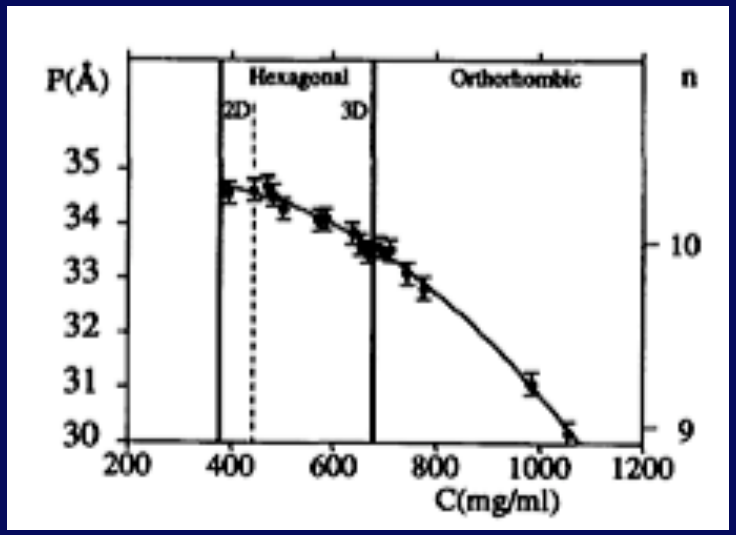



Orthorhombic phase is also a real 3D crystal. A distorted hexagonal lattice.
Relative displacement of m1 and m2 is ~ 1/3 DNA pitch along z-axis.
A (volume) discontinuous transition from the hexagonal to orthorhombic.



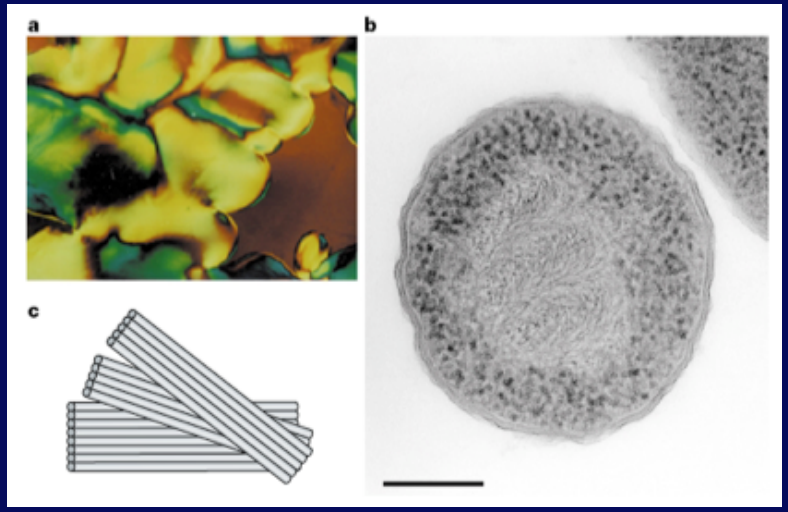

The orthorhombic lattice parameters also change as a function of the DNA density.

Durand, Doucet, Livolant, J. Phys. France II (1992).

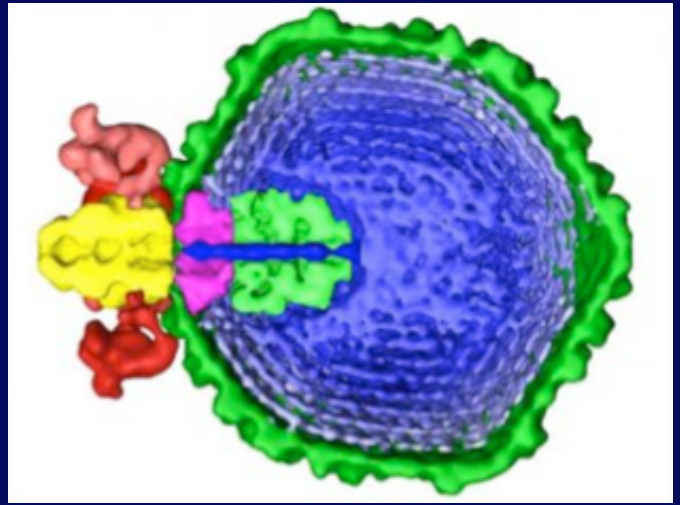



Here too the pitch of the molecule changes.

# The relevance of high density mesophases

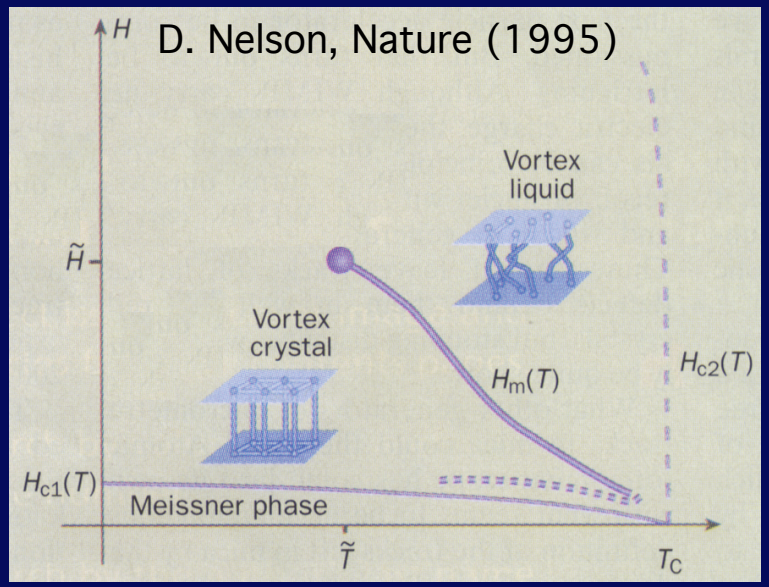



.. organisms exposed to prolonged stress can circumvent their fate through formation of highly ordered DNA assemblies... Minsky, Nature 2002.



Cryo-electron microscopy of ε15. The genome is (hexagonally) packed in coaxial coils in at least three outer layers. Jiang et al. 2006.

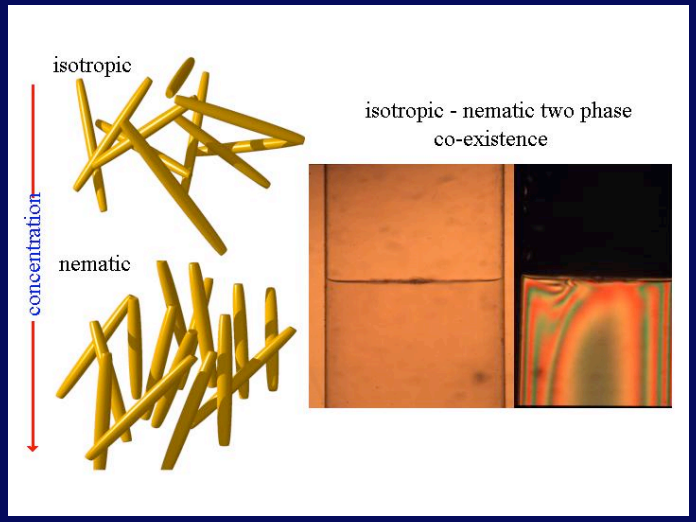
D. Nelson, Nature (1995)



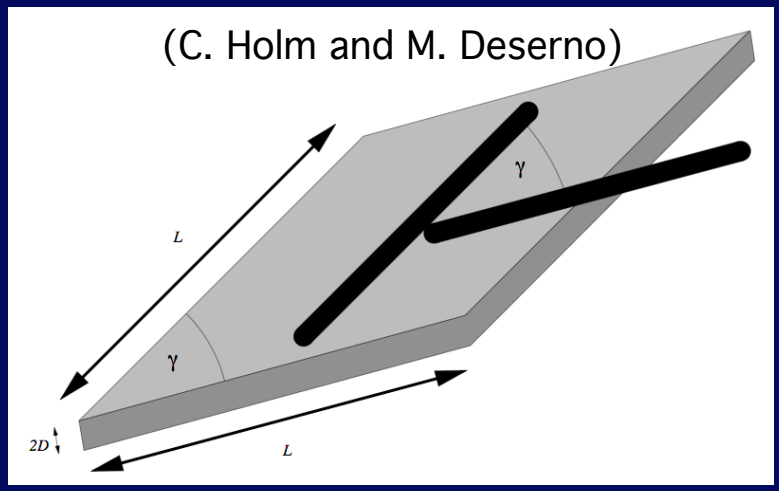

Type II SC:
Tension
Non-chiral
Magnetic field
Temperature
London repulsion

DNA:
Bending
Chiral
Density
Ionic strength
Debye-Huckel repulsion

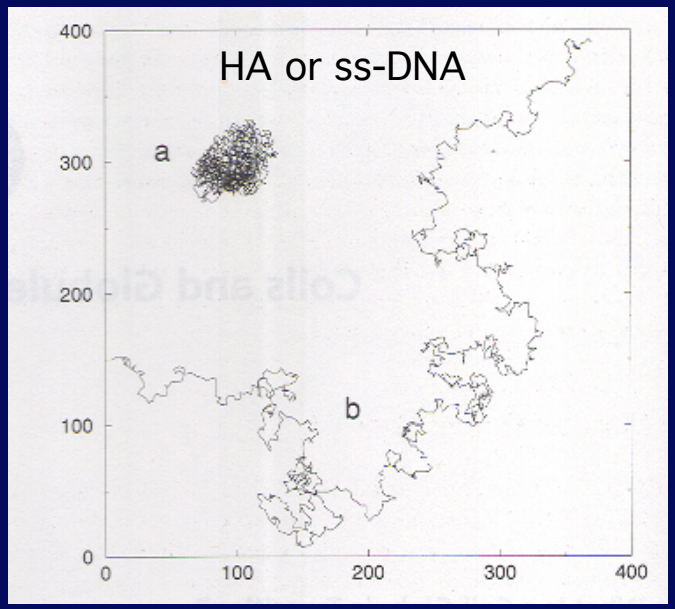
# Why does DNA make ordered phases?




S. Fraden, Purified TMV in aqueous buffer. Top phase is isotropic, bottom is nematic.




Onsager (1949) excluded volume interactions. Length to thickness ratio.




No order in flexible polymer solutions.

For stiff polymers the role of the length is played by the persistence length.

Khokhlov-Semenov et al. 1981

$$K_C = kT\ \ell_P^{(0)}$$

$$\mathcal{H} = \frac{k_B T \ell_p^{(0)}}{2} \int ds \left( \frac{\partial^2 \mathbf{r}}{\partial s^2} \right)^2$$

ds-DNA persistence length (0.2 M NaCl) 50nm
E~300 MPa (plexiglass)

# DNA persistence length

## Light Scattering by very Stiff Chain Molecules

VERY precise light-scattering measurements by B. H. Bunce[1] on several thymonucleic acid preparations have shown that the scattering function of these gigantic macromolecules—the molecular weights are between 2·6 and 6·7 millions—differ remarkably from that of a random coil. The angular dependence of the reciprocal reduced intensity $1/P = I(0)/I(\vartheta)$, for all samples, reveals that the molecules are not perfectly coiled. The experimental points are situated between the curves for a random coil and that for a stiff rod.

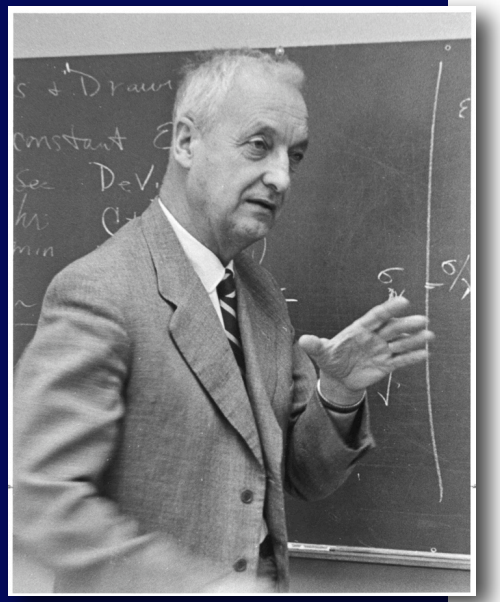
Therefore it seemed worth while to compute the shortening of the chain may be the consequence of an internal association of neighbouring chain segments. The additional linkages coupled with the increased density evidently stiffen the molecule and yield a more extended coil. Very careful preparation may prevent such an internal association, which takes place also on degradation in acid solutions.

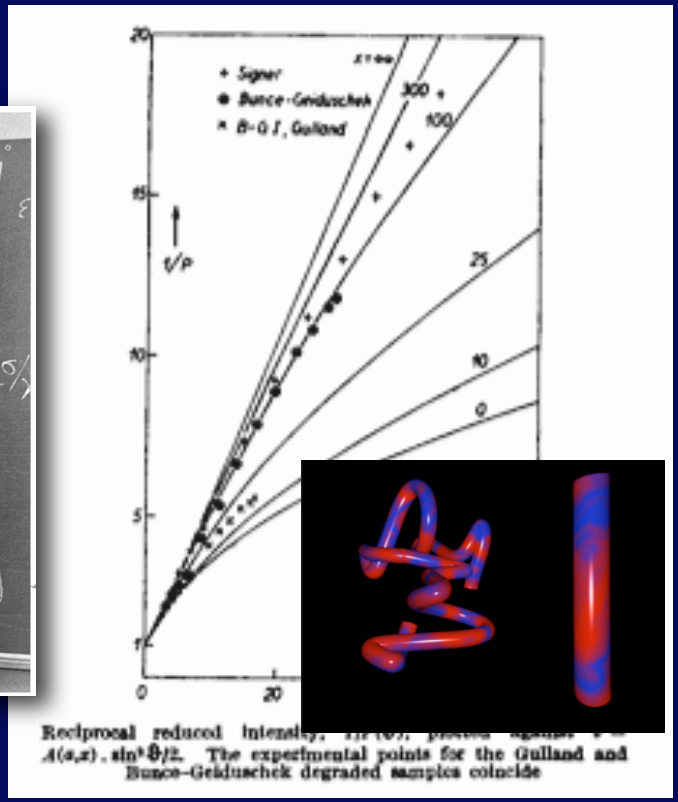
A. PETERLIN

"J. Stefan" Institute of Physics,
Ljubljana. June 5.

[1] Bunce, B. H., thesis, Cambridge, Mass. (1951).
[2] Peterlin, A., *J. chim. Phys.*, **47**, 669 (1950); **48**, 13 (1951); *J. Polymer Sci.*, **8**, 173 (1952).
[3] Porod, G., *Monatsh. Chem.*, **80**, 251 (1949). Kratky, O., and Porod, G., Proc. Int. Coll. Macromol. Amsterdam, 250 (1949).

Nature, february 7, 1953.






Reciprocal reduced intensity. $A(a,x)$, $\sin^2\vartheta/2$. The experimental points for the Gulland and Bunce-Geiduschek degraded samples coincide

Anton Peterlin (1908 – 1993)
Analysis of light scattering (Dotty and Bunce) on DNA solutions.

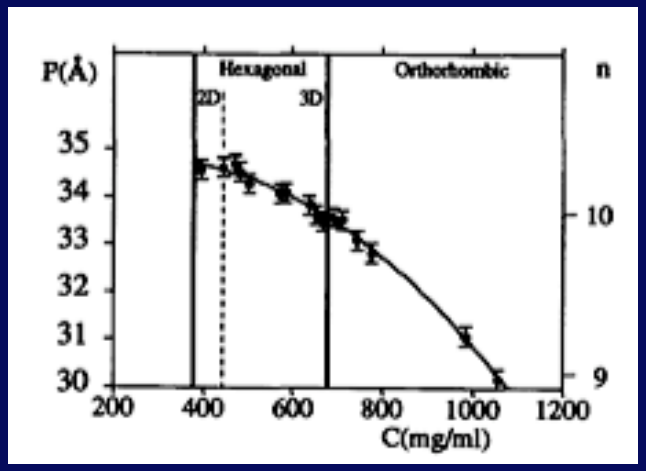
| DNA preparation | $M \times 10^{-6}$ | $a$[nm] | $L$[nm] |
|---|---|---|---|
| Signer | 6.7 | 28.5 | 4300 |
| Bunce-Geiduschek | 4 | 26 | 2600 |
| Gülland | 4 | 40 | 1000 |
| Bunce-Geiduschek I | 2.64 | 40 | 1000 |
| Bunce-Geiduschek II | 2.1 | 37 | 1100 |
| Bunce-Geiduschek III | 2.7 | 54 | 1080 |
| Varin I | 7.7 | 60.6 | 2100 |

Watson-Crick-Franklin double helix
Nature, april 25, 1953.

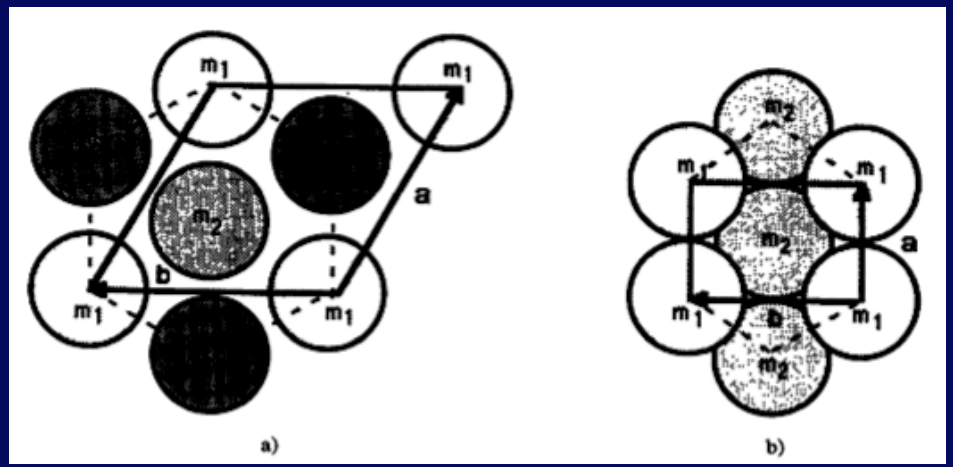
A. Peterlin was one of the founding fathers of the physics department of UNI-LJ and the first director of the J. Stefan Institute.

# What and why - the order of DNA mesophases

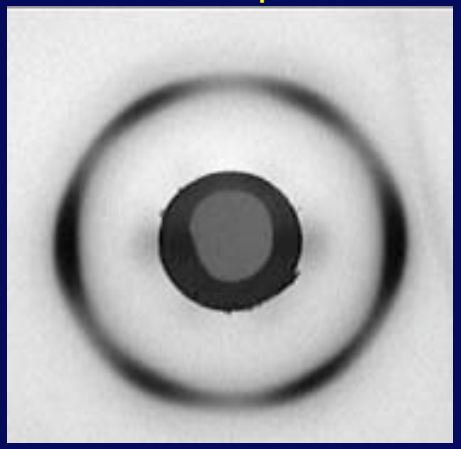
Why does the molecular pitch change?
Overwinding of DNA coupled to ordering.



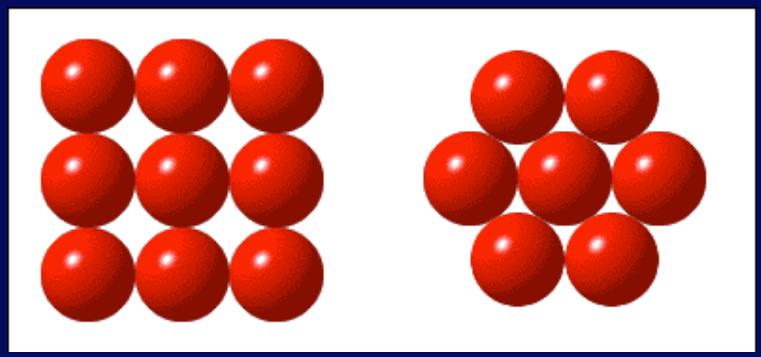

Why are there relative displacements in the z direction of nearest neighbors in hex and ortho phases?
DNAs do not behave like featureless cylinders.




Why is hexatic order not modified by the cholesteric order?
Hexatic order should rotate and give a circular diffraction pattern.



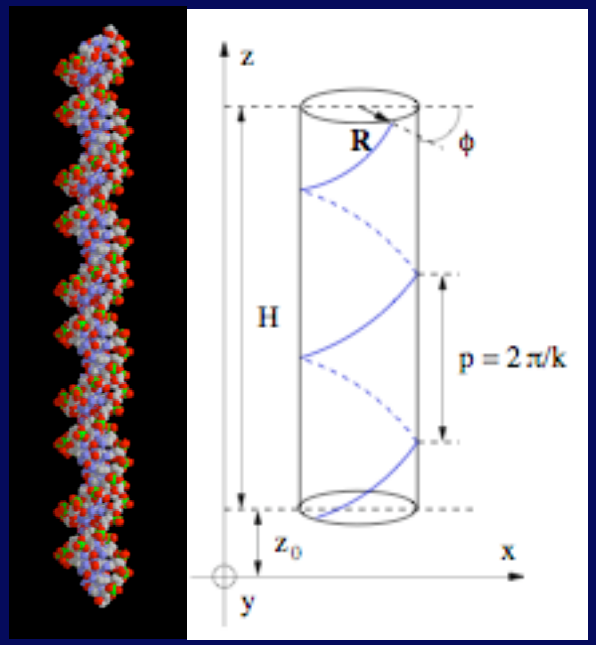
Why the orthorhombic symmetry?
If DNAs were cylinders, they would pack hexagonally.



IP = 78.5398163%  IP = 90.6899682%

# DNA - a helical molecule

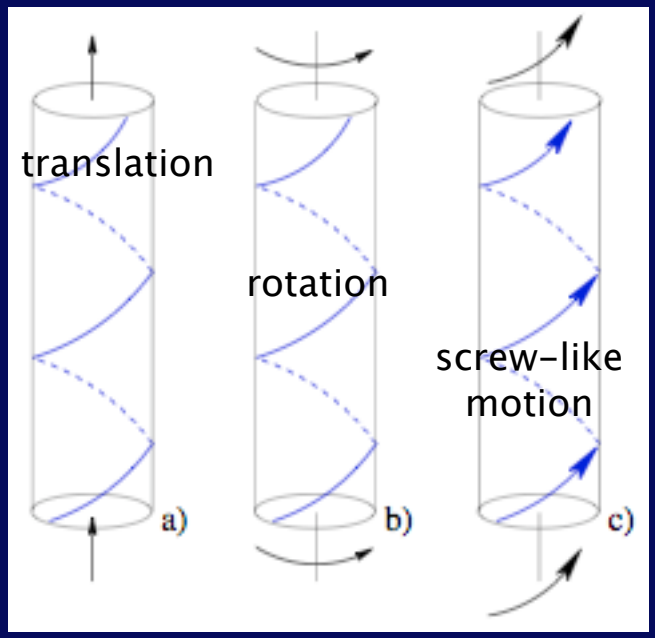
Description of the order in a parent nematic phase of DNA molecules.




The CCV theory (1952).

$$x = R\cos(\phi + k\zeta)$$
$$y = R\sin(\phi + k\zeta)$$
$$z = z_0 + \zeta$$

Initial position and initial phase.



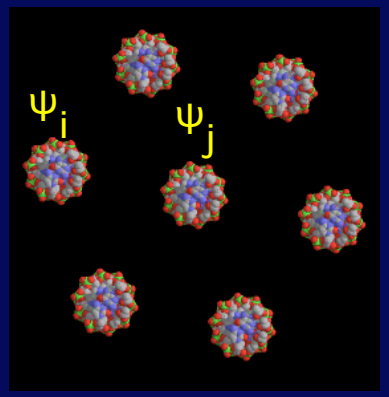

Three possible types of fluctuations in a nematic composed of helical molecules.

The relative azimuthal orientation:

$$\theta^i - \theta^j = \phi^i - \phi^j - k(z_0{}^i - z_0{}^j)$$

The phase ψ is a characteristic of each molecule.

$$\psi^i = \phi^i - kz_0{}^i$$




$$P = \langle \cos\psi \rangle = \int_0^{2\pi} \cos\psi f(\psi, \phi, z_0) d\psi$$

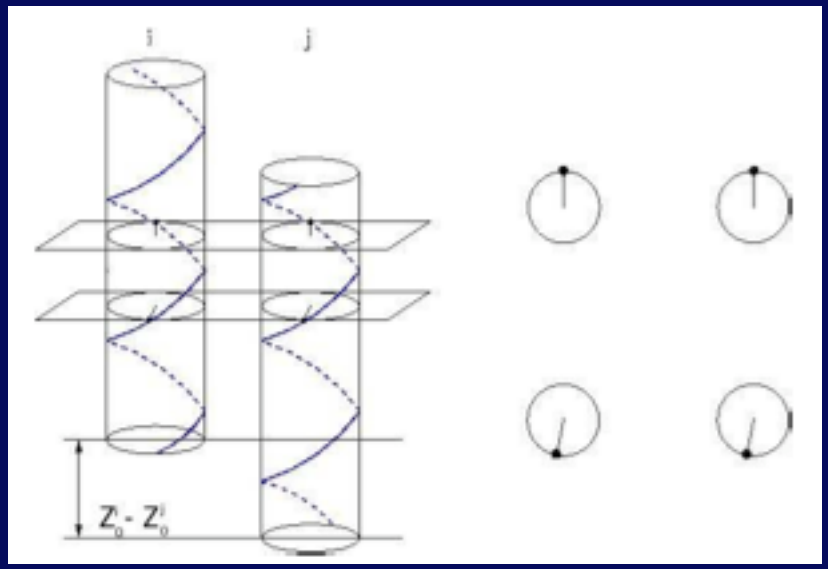
de Gennes macroscopic order parameter.

P=0 parent nematic phase
P=1 corresponds to a screw-like phase

(Manna, Lorman, RP and Zeks, 2007)

# Screw-like phase

The order of this phase can be described by a helical polar vector field.
The molecules are chiral and helical.




$$\vec{P}(z) = \eta\xi + \eta^*\xi^* = P\cos(Kz+\Phi)\hat{\mathbf{e}}_x + P\sin(Kz+\Phi)\hat{\mathbf{e}}_y$$

with

$$P = \langle\cos\psi\rangle$$

An appropriate order parameter for the transition into this phase is

$$\eta = P\exp(i\Phi)$$
$$\eta^* = P\exp(-i\Phi)$$

$$K = k = 2\pi/p$$

The Landau free energy with the chiral (Lifshiz) term comes out as:

$$F = \frac{1}{L}\int\left[\frac{a}{2}\eta\eta^* + \frac{b}{4}(\eta\eta^*)^2 - \lambda(\eta\frac{\partial\eta^*}{\partial z} - \eta^*\frac{\partial\eta}{\partial z}) + \frac{g}{2}\frac{\partial\eta}{\partial z}\frac{\partial\eta^*}{\partial z}\right]dz$$

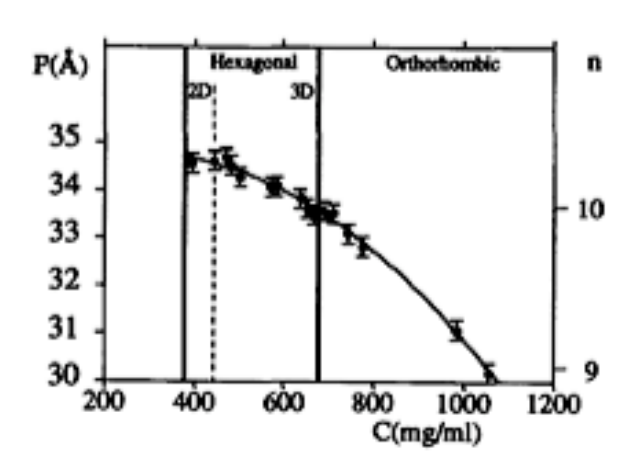
The minimum of this free energy close to the transition point (P=0) is obtained as:

$$\Phi = qz + \Phi_0 \longrightarrow \vec{P}(z) = P\cos((K+q)z+\Phi_0)\hat{\mathbf{e}}_x + P\sin((K+q)z+\Phi_0)\hat{\mathbf{e}}_x$$

The chiral term introduces a renormalization of the phase of the order parameter. Since it describes the helical molecule this means that its pitch is changed! Instead of twisting the hexatic order, the screw phase overwinds the molecule. The solution of the puzzle.

# Modulation of the molecular pitch

Remember this? Overwinding of DNA. So the screw-like order can induce a change in the pitch of the molecules.




$$p' = \frac{2\pi}{K+q}$$

Renormalization of the phase of the order parameter of drives the renormalization of molecular pitch.

$K = k = 2\pi/p$ with p given by the B-DNA value (3.4 nm).

Of course if DNA would not be soft an enormous energy would be needed to accomplish this. What is actually the energy needed to change the pitch of DNA? The twist energy is given by

$$\frac{E_{sur}}{k_B T} = \int_0^{l_0} \frac{C}{2} \Omega^2 \, ds$$

C is the twist persistence length ~ 75 nm.

Taking the above experimental data of F. Livolant one obtains the torque needed to get these changes in pitch of

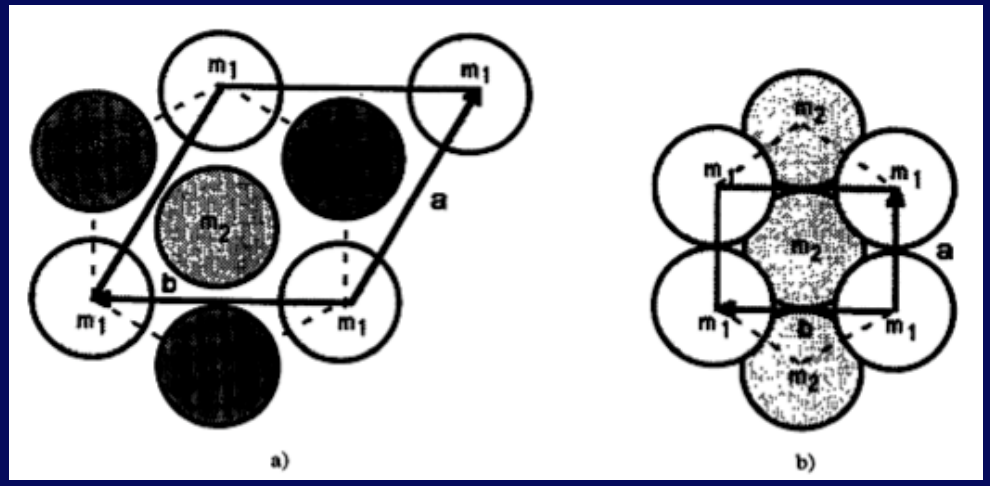
$$M \approx 15 \; pN.nm$$

The measured energies of DNA twisting and bending are ~ 10-100 pN nm and the measured overwinding torques are indeed of this magnitude (30 pN nm). DNA is fortunately soft enough.

# A side benefit of the screw-like phase

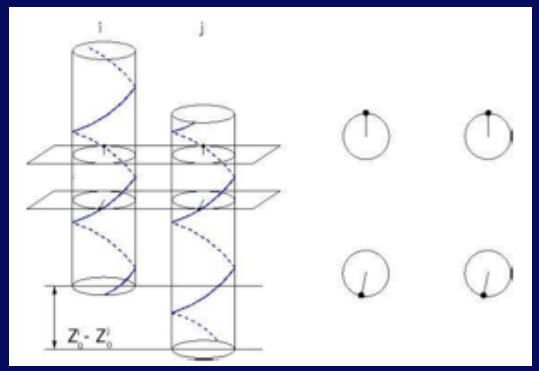
Experimentally seen displacement in the z-direction for 1/3 or 1/6 of the pitch.

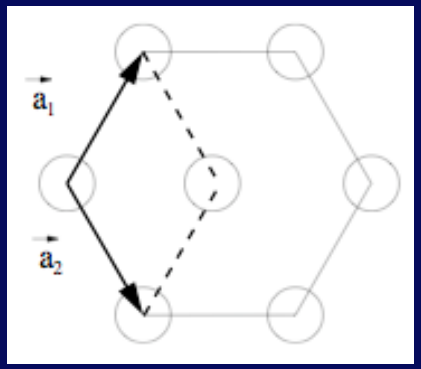
Hexagonal →

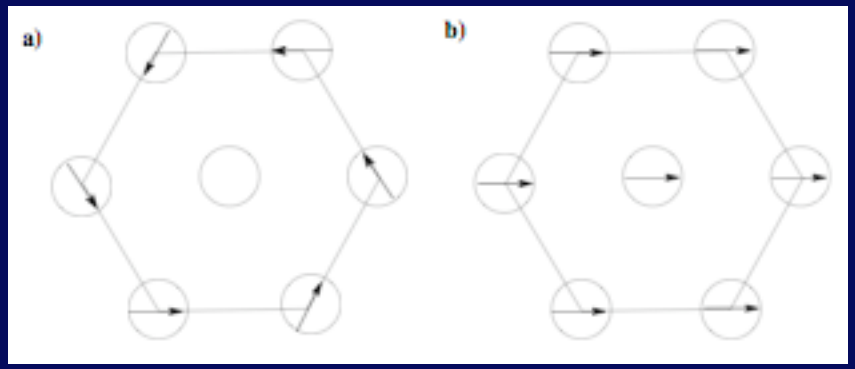



← Orthorhombic

There exists a coupling between the order parameter of the screw-like order and the symmetry of the lattice.



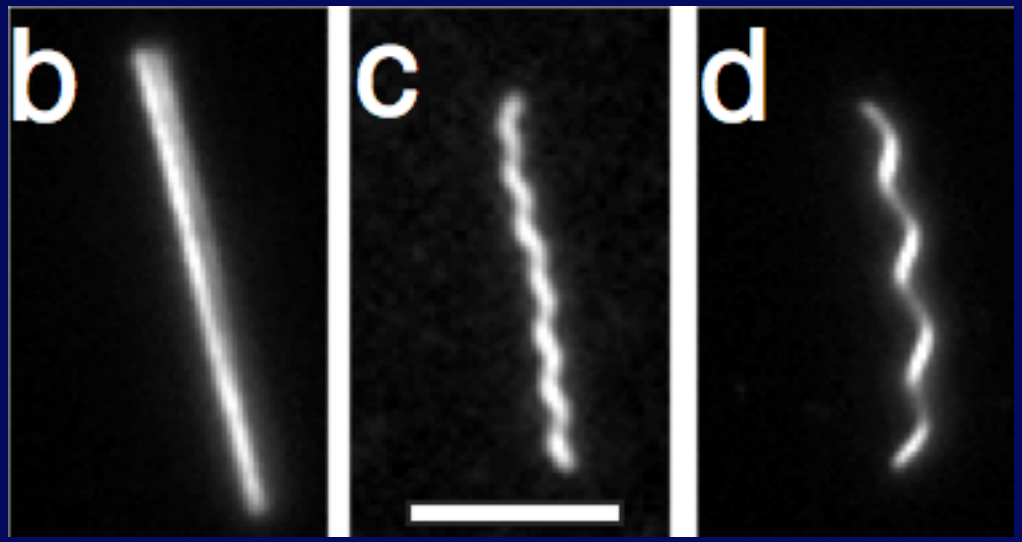



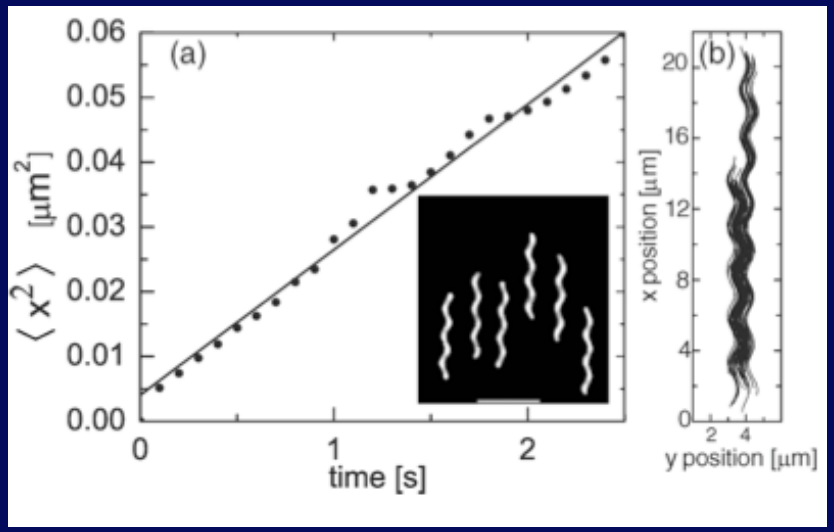

Too technical to derive here, but displacements of both p/6 and p/3 can be derived for hexagonal and orthorhombic symmetries. Exactly as seen in experiments!

# Direct visualization of the screw-like phase

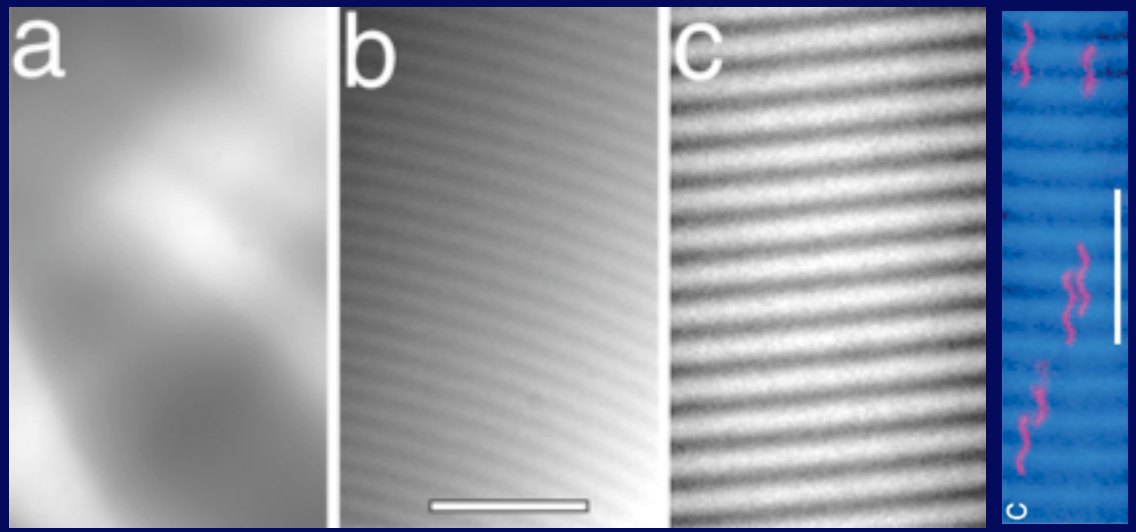
Ordered phases of bacterial flagella (Barry et al. PRL 2006).




Three pitches: zero, 1.1 μm and 3.6 μm.




Screw-like fluctuations observed directly.




Corresponding order under Xed polarizers and fluorescent labeling.

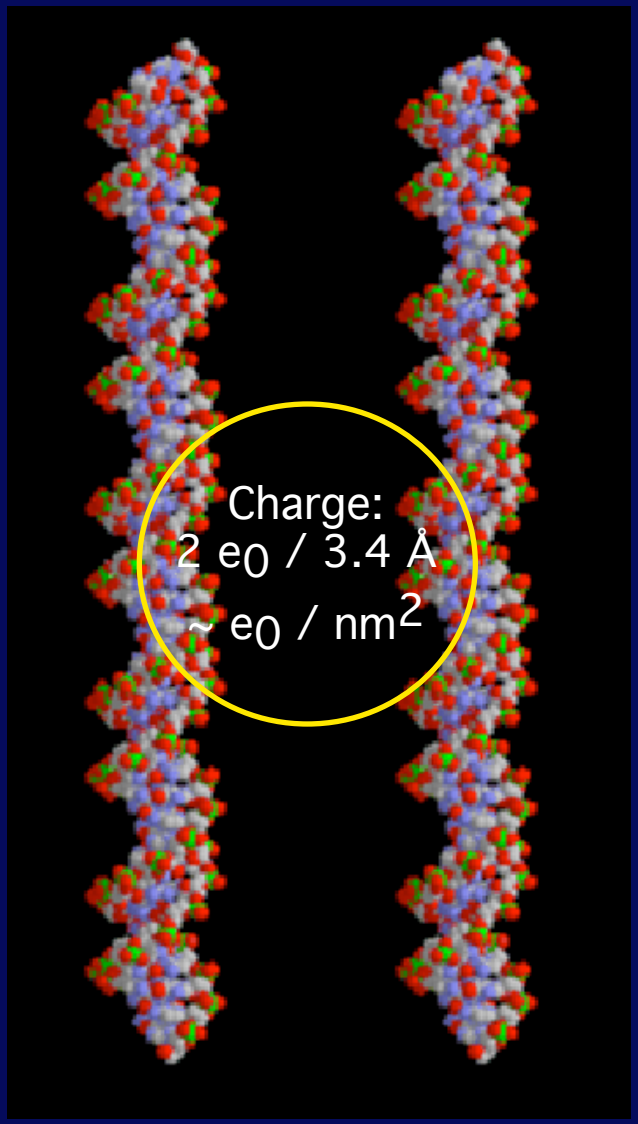
- periodicity
- direction of molecular axis
- nature of fluctuations
- modulation of the density

For DNA (because of the difference of scale) this experiment is not feasible.

Resonant X-ray scattering?

# The nature of DNA-DNA interactions

DNA as a cylindrical cow. No molecular details! Not good at large densities.



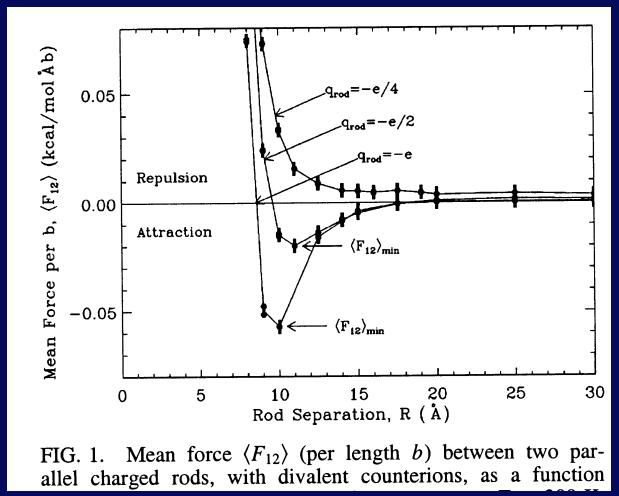
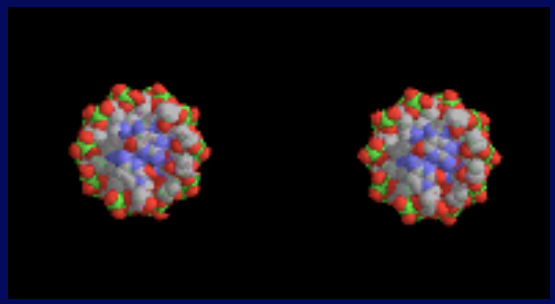




FIG. 1. Mean force $\langle F_{12} \rangle$ (per length $b$) between two parallel charged rods, with divalent counterions, as a function

A pair of DNAs with poly-counterions. Gronbech - Jensen et al. 1997.



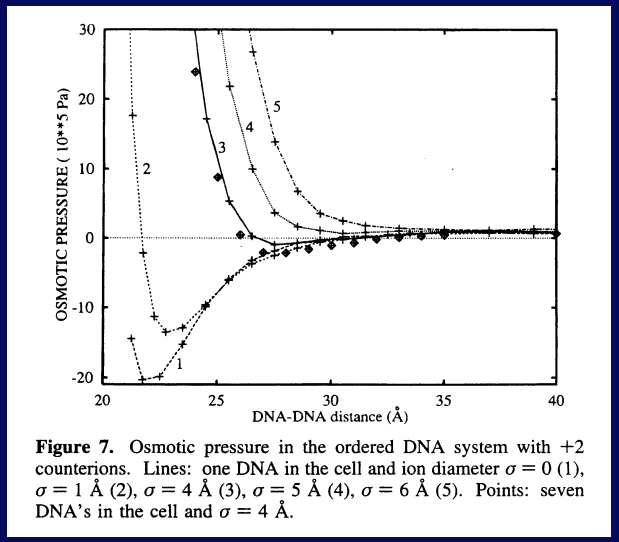
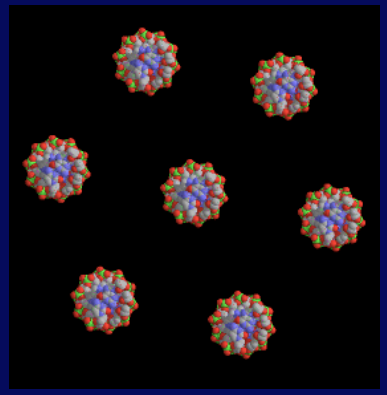



**Figure 7.** Osmotic pressure in the ordered DNA system with +2 counterions. Lines: one DNA in the cell and ion diameter $\sigma = 0$ (1), $\sigma = 1$ Å (2), $\sigma = 4$ Å (3), $\sigma = 5$ Å (4), $\sigma = 6$ Å (5). Points: seven DNA's in the cell and $\sigma = 4$ Å.

Hexagonal array of DNA with poly-counterions. Lyubartsev and Nordenskiold, 1995.



DNA is a very charged up molecule. Huge electrostatic interactions in salt solutions.

# The great electrostatic divide

A correct description of electrostatic interactions between DNAs is quite complicated.

Bjerrum length

$$\ell_B = e_0^2/4\pi\epsilon\epsilon_0 kT.$$

$$V(\mathbf{r}_1, \mathbf{r}_2) = \frac{e_1\ e_2}{4\pi\epsilon\epsilon_0|\mathbf{r}_1 - \mathbf{r}_2|},$$

Coulomb's law and kT

Gouy - Chapman length

$$\lambda_{GC} = \frac{2\ kT\ \epsilon\epsilon_0}{e_0\ \sigma}.$$

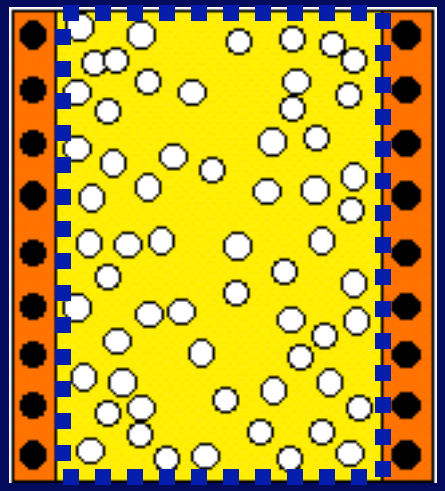
Ratio between the Bjerrum and the Gouy - Chapman lengths. Bulk versus surface interactions.

Weak coupling (WC) limit
(Poisson - Boltzmann)
$\Xi \rightarrow 0$

Coupling parameter

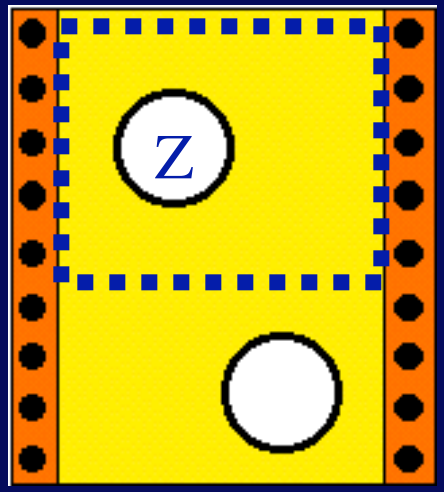
$$\Xi = 2\pi Z^3 \ell_B^2 \sigma$$

Strong coupling (SC) limit
(Netz - Moreira)
$\Xi \rightarrow \infty$



Collective description
("N" description)
vs.
Single particle description
("1" description)

Experimental confirmation?



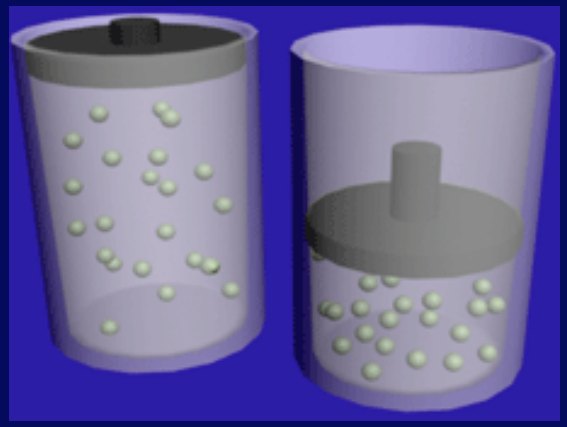

REPULSION

ATTRACTION

Fundamental difference between monovalent counterions and polyvalent counterions!

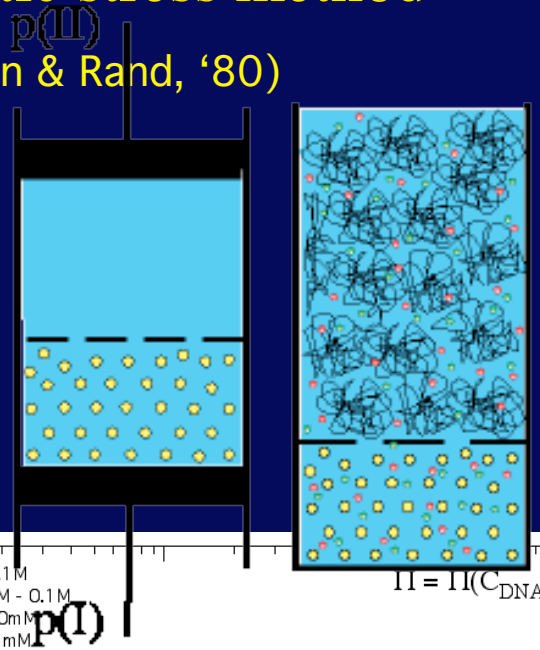
# The Boyle experiment - osmotic stress method

Osmotic stress method (Parsegian & Rand, '80)

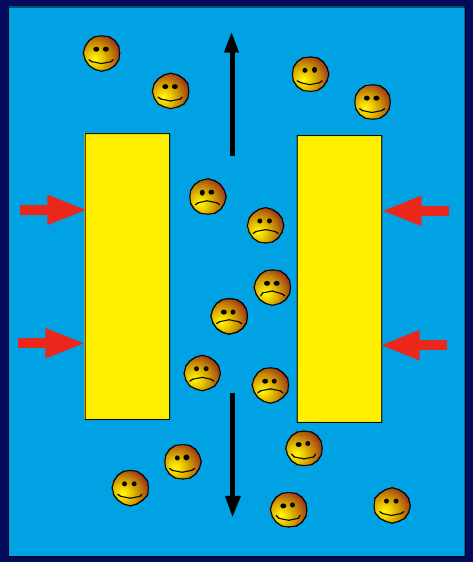


pressure

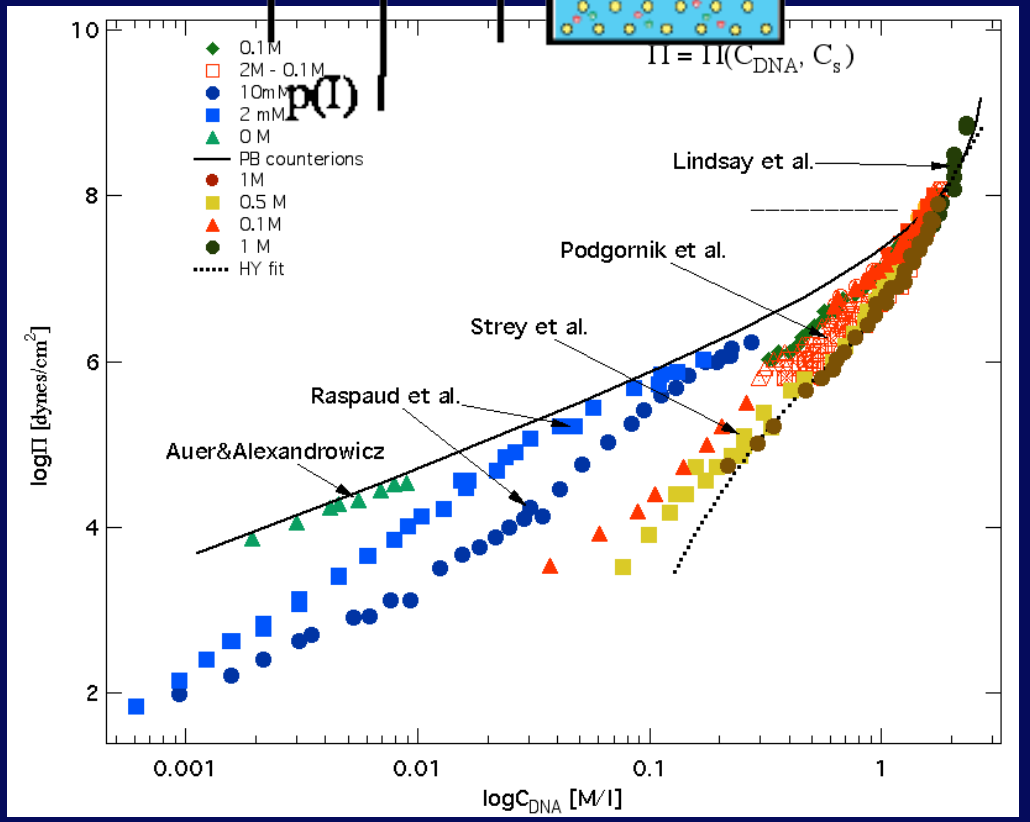
osmotic pressure




$\Pi\, dV$



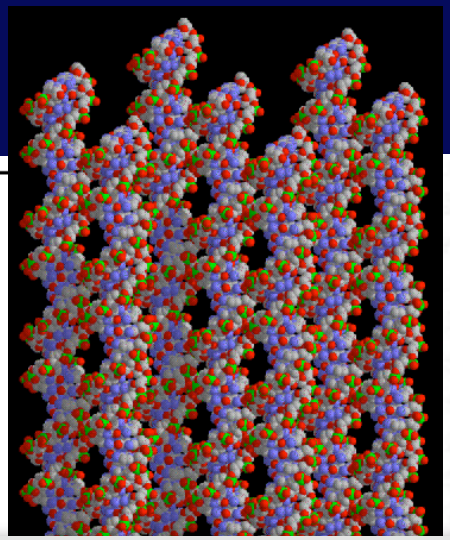
$-\mu dN$

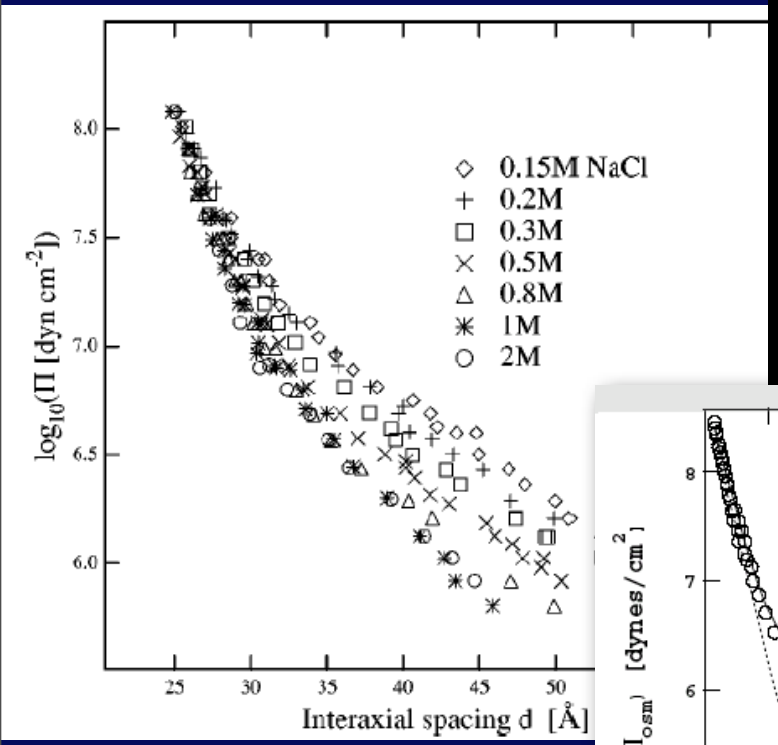


# Experimental evidence for the great electrostatic divide

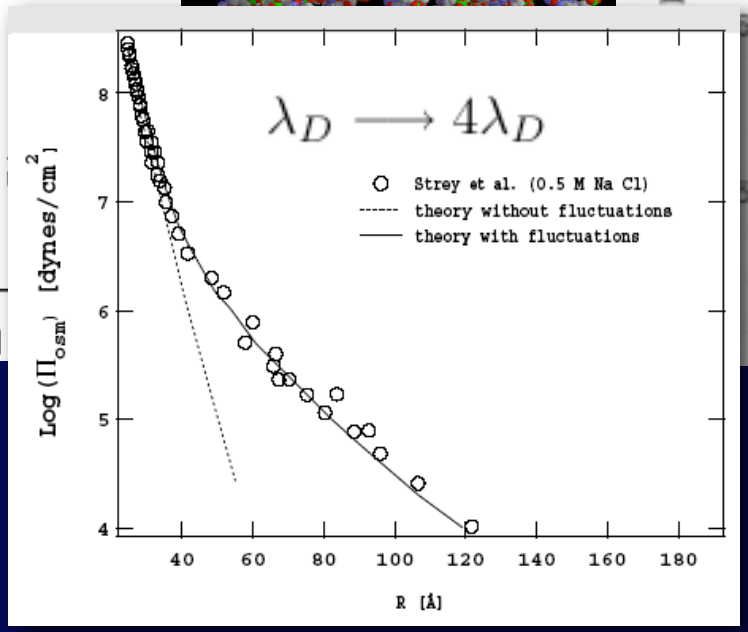
Electrostatic repulsion:
not eactly PB but
a lot stronger.

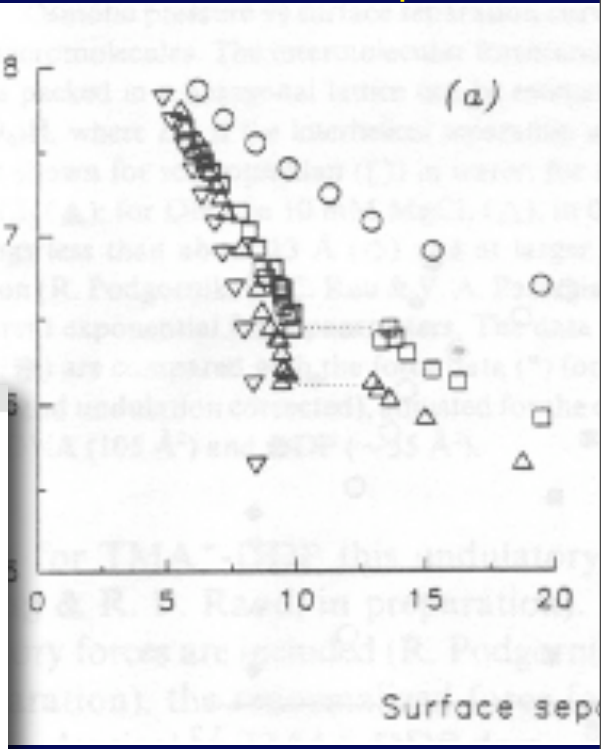
Correlation attractions.
Hydration attractions.
~ 0.1 kT/ base pair.






Podgornik et al. 2000




Rau et al., 1997.

Monovalent counterions

Polyvalent counterions

Electrostatics can only be seen indirectly, as modified by the presence of conformational fluctuations. Renormalized value of λ.

# Detailed nature of ES interactions

Non-monotonic interactions (Kornyshev-Leikin, 1997).
Theory based on the linearized PB equation!

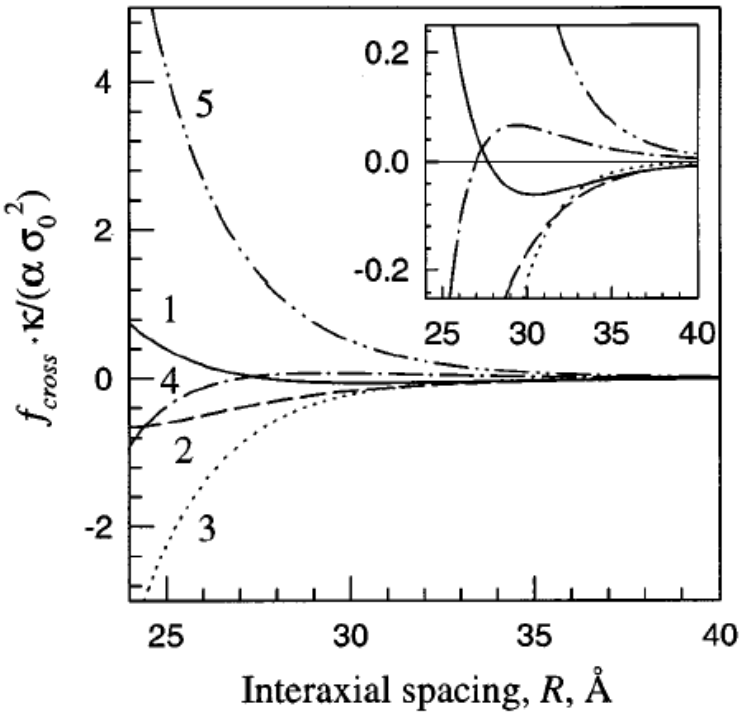
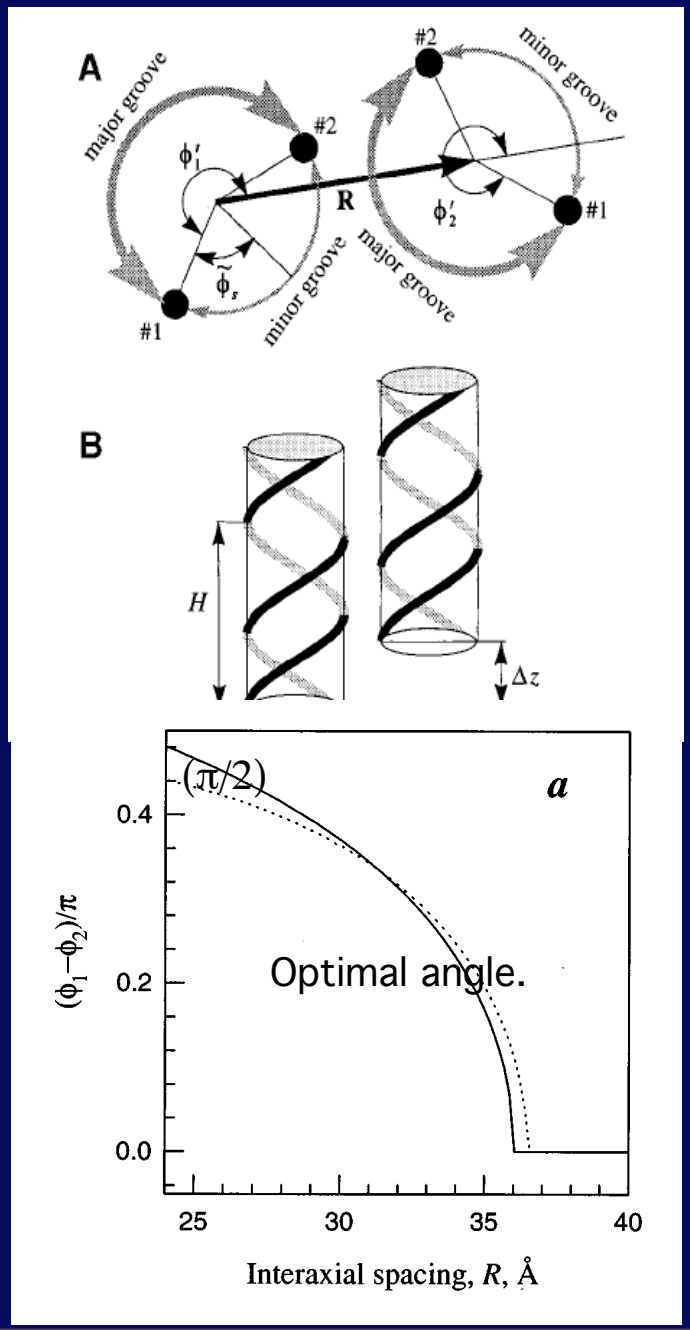



FIG. 5. The force–distance curves between two $B$-DNA-type double helices ($a = 10$ Å, $H = 34$ Å, $\phi_s = 0.8\pi$) at different fixed mutual rotation angles, $\phi_1 - \phi_2 =$: (1) 0; (2) $\pi/4$; (3) $\pi/2$; (4) $0.7\pi$; (5) $\pi$. The insert shows the sign of the forces and the crossover from repulsion to attraction at higher amplitude resolution.

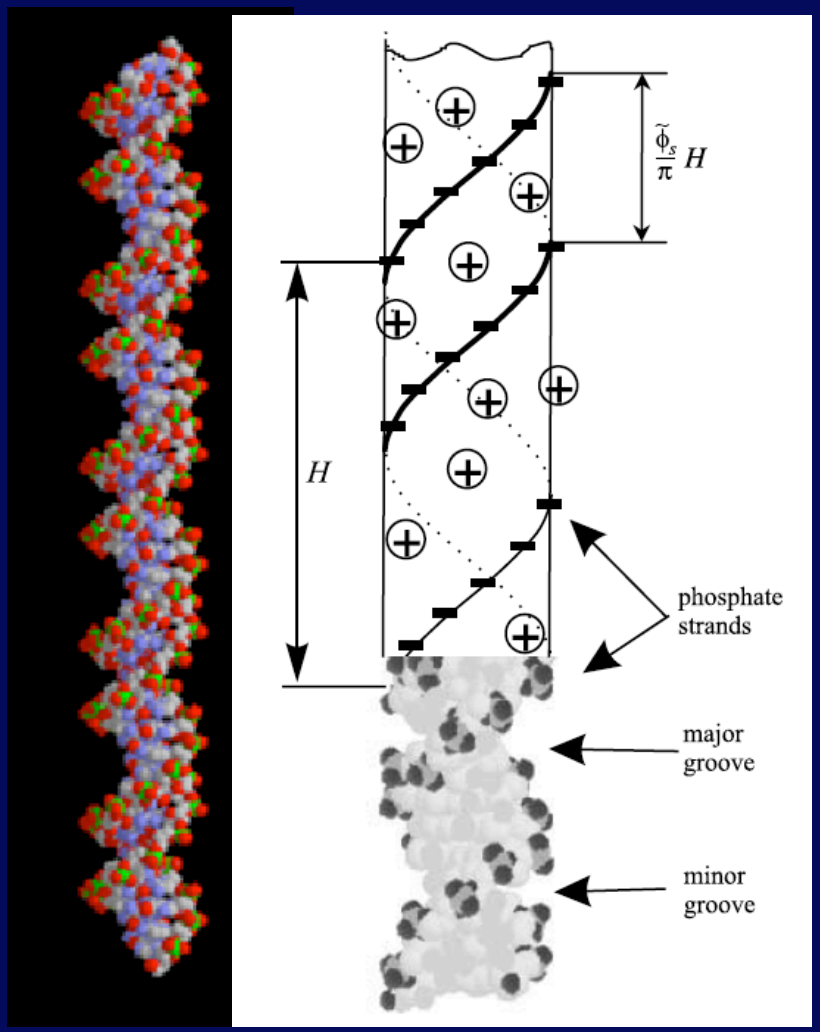
Orientational dependence.

Two DNA molecules with separated + and - charges along the length can attract each other at preferred mutual orientation.



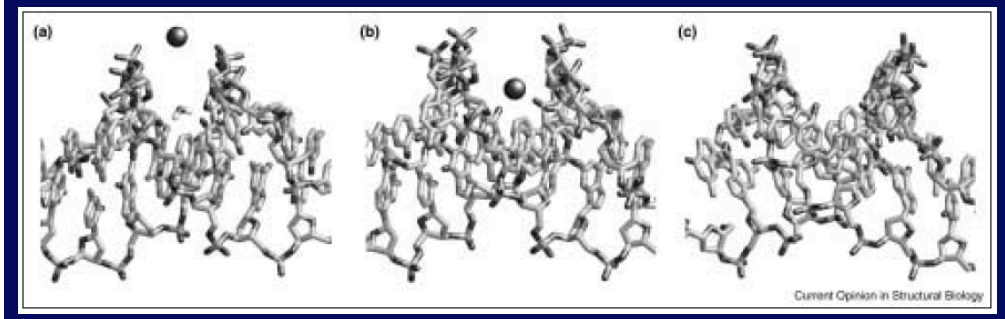
# Assumptions of the KL theory

Detailed charge distribution on the DNA helices - SC approach.
The grooves act as flexible ionophores that coordinate counterions in the duplex. Kornyshev - Leikin, 1998-2007.




Debye-Hueckel interaction:
- smeared charge
- smeared counterions
- Manning condensation

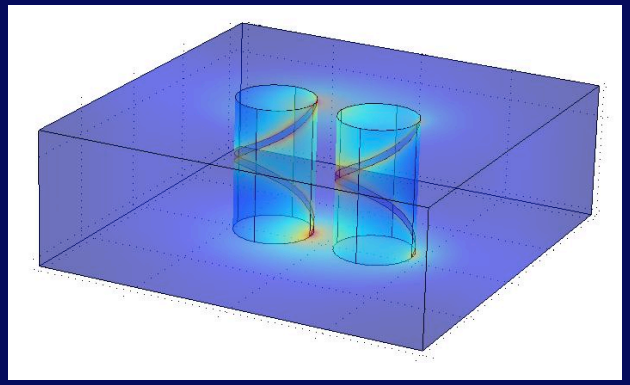
Kornyshev-Leikin interaction:
- explicit charge
- explicit counterions
- linearized PB




Hud and Plavec, 2004.

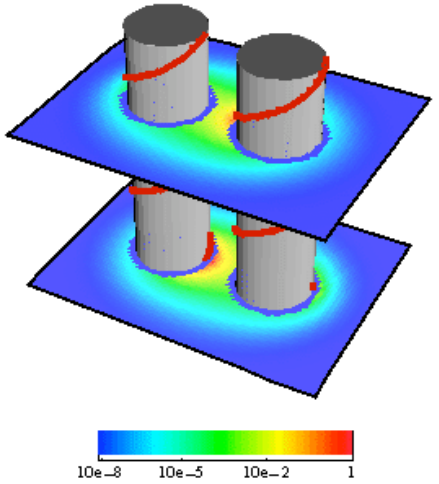
$Na^+$ in the minor groove of helix. But this preference is not universal and is stronger for polyvalent counterions.
Non-electrostatic interactions.

# WC (PB) and SC calculations

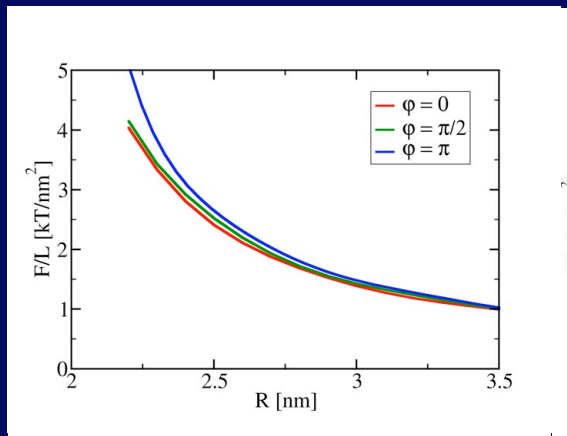


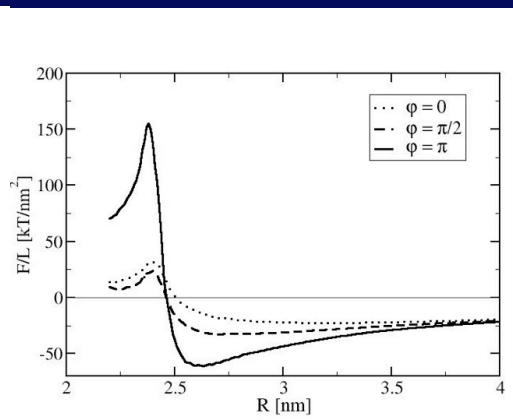
An “ab initio” calculation.

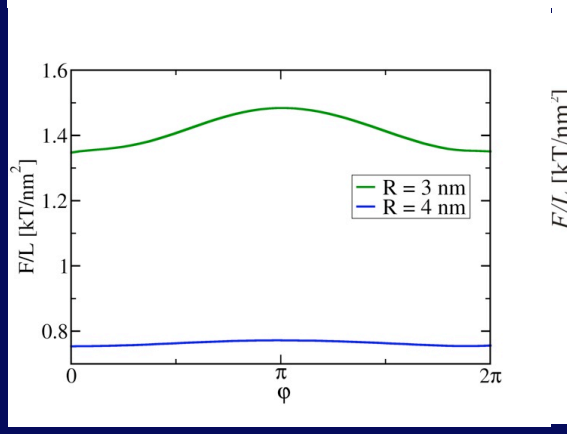
Poisson-Boltzmann
vs.
strong coupling limit

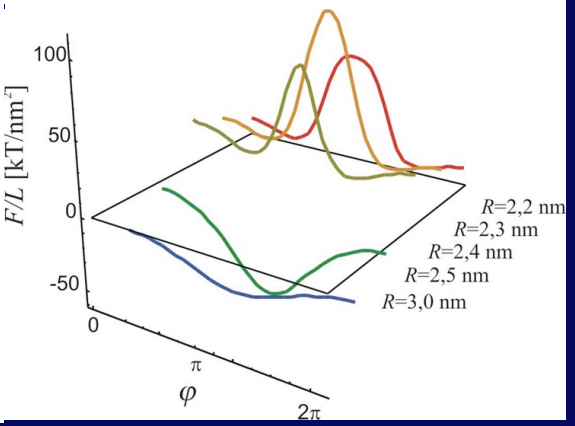



Strongly coupled counterion spatial distribution.



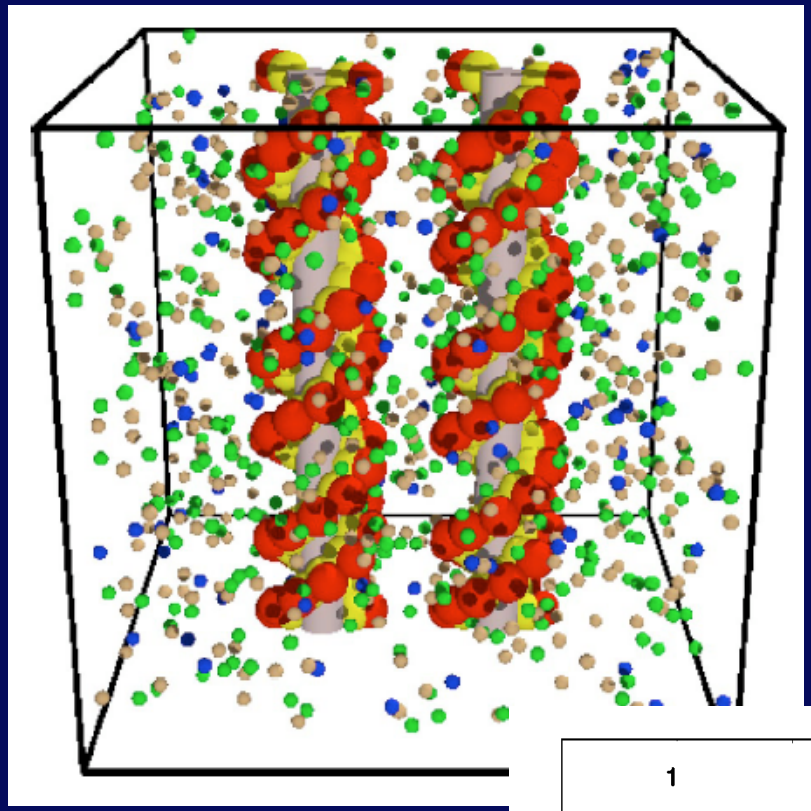

Whereas in the KL theory the strongly coupled counterions are put in “by hand”, here all interactions are electrostatic.

Qualitatively the results are the same.

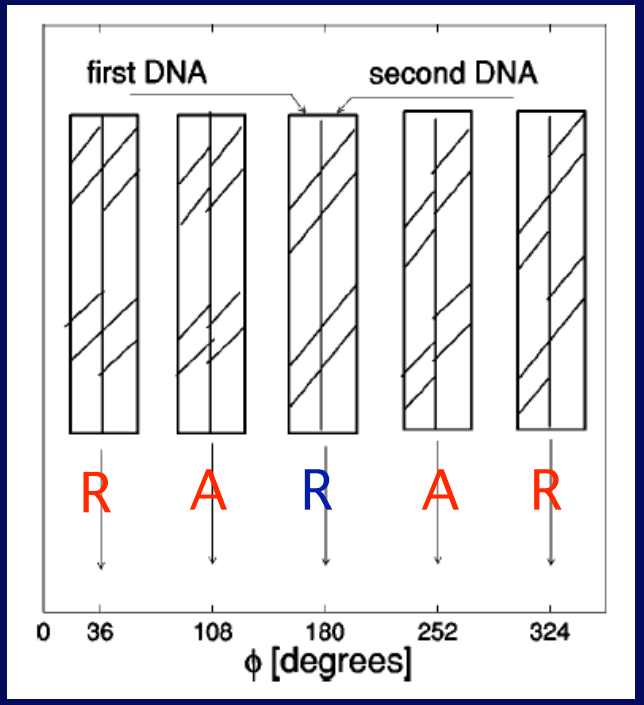
M. Kanduč (2007)

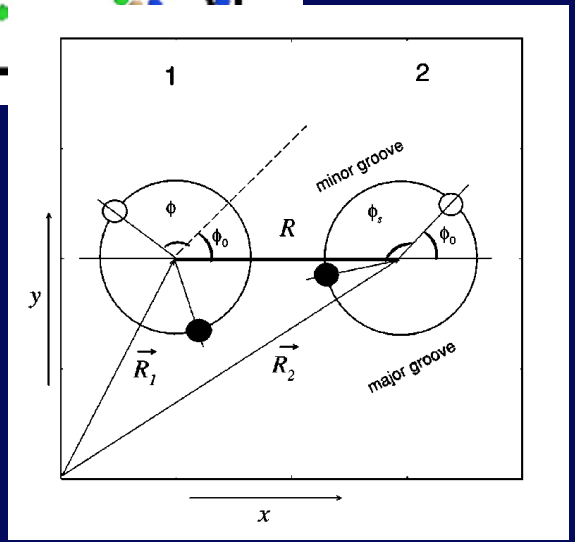
# Simulations

Realistic geometric models of DNA. Similar (but not exactly the same) conclusions.



Allahyarov et al., 2000 - 2004



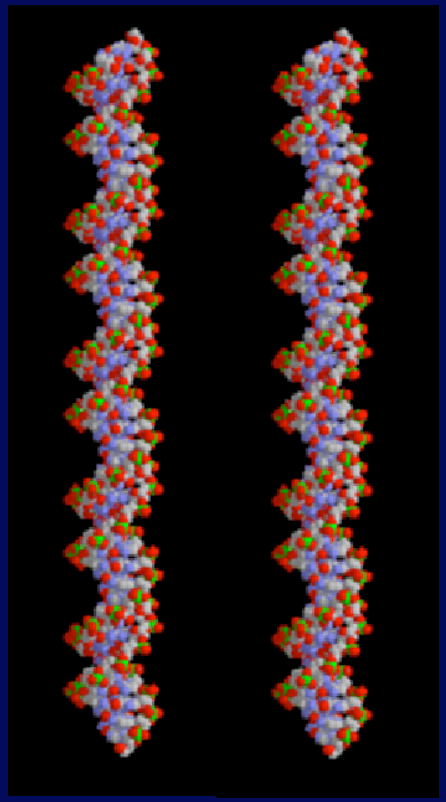




Schematics of the orientational effect. Strand opposition.

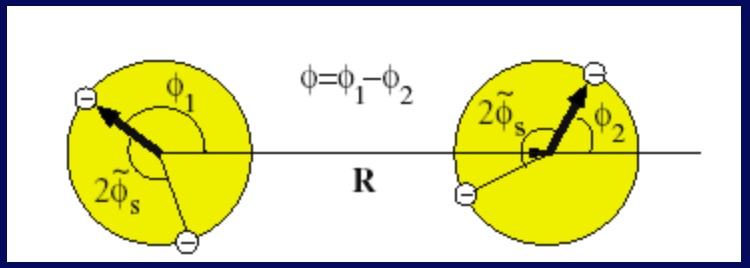
Dubious validity for large DNA density. No explicit water.

- explicit DNA structure
- explicit counterions
- explicit salt ions
- different salt concentrations

# A two-state KL model



The interaction potential between two helices is not a monotonic function of separation any more.




φ – mutual azimuthal orientation of the DNAs

The vectors joining axes with the points where 5'- 3' strand hits the plane are conventionally called « transverse polarization » vectors p

Simplified Form of the Interaction Potential
(Harreis et al. 2002)

$$u(R,\phi) \approx C(R) - A(R)\cos\phi + B(R)\cos^2\phi$$

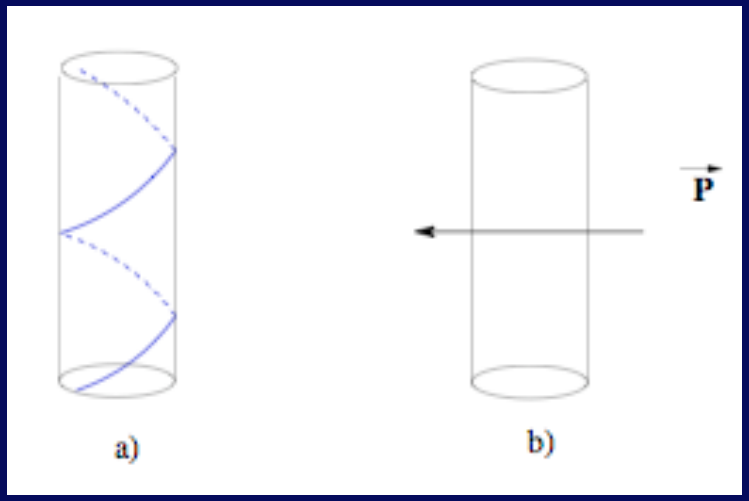
Critical distance $R_0$; for $R > R_0$ (large interaxial distances): $\varphi = 0$ (parallel orientation)
for $R < R_0$ (small interaxial distances) $\varphi \neq 0$ (equilibrium nonzero angle orientation)

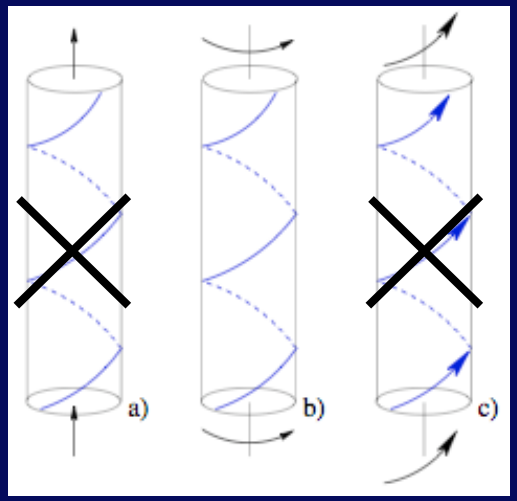
A two state model:

I. Intermediate densities : Parallel alignment of transverse polarization vectors
II. High densities : Preferred angle between transverse polarization vectors

# Azimutal interactions in constrained DNA nematics

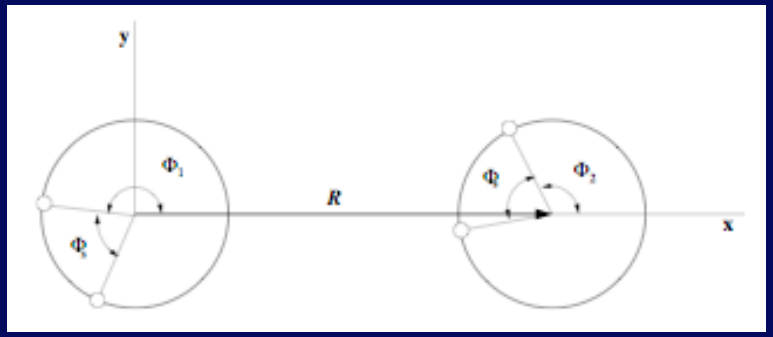
Assume a DNA fiber where molecules are not allowed to fluctuate translationally.



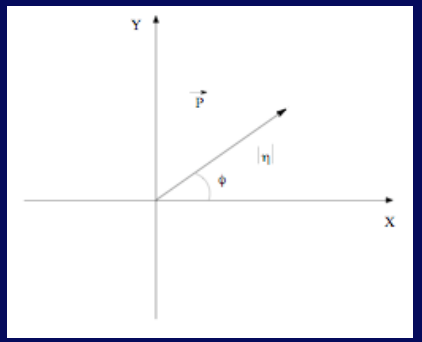




Only azimutal fluctuations are allowed.

A proper structural description of DNA on this level is:




The origin of the azimutal angle can be chosen arbitrarily, as the KL interaction depends only on the difference!




This description induces a macroscopic order parameter:

$$\eta = P_x - iP_y$$
$$\eta^* = P_x + iP_y$$

$$\eta = |\eta| e^{i\phi}$$
$$\eta^* = |\eta| e^{-i\phi}$$

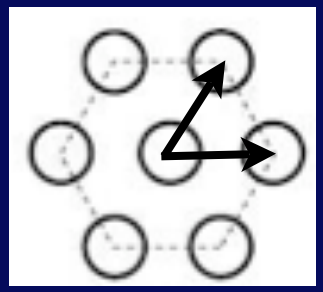
Transverze polarization (TP) vector. Lorman, RP and Zeks, PRL 2005.

# Intermediate density hexatic - TP coupling $\varphi = 0$

Line hexatic phase as the parent phase. Three order parameters:

Transverze polarization:

$$\eta = |\eta| e^{i\phi}$$
$$\eta^* = |\eta| e^{-i\phi}$$



Hexatic order:

$$\mu = |\mu| e^{-i6\theta}$$
$$\mu^* = |\mu| e^{i6\theta}$$

Bond angle Θ.

Deformation vector:

$$\epsilon = \epsilon_{xx} - \epsilon_{yy} + 2i\epsilon_{xy}$$
$$\epsilon^* = \epsilon_{xx} - \epsilon_{yy} - 2i\epsilon_{xy}$$

Follows polarization. Curie principle.

Construct the Landau free energy with appropriate invariants of this two order parameters:

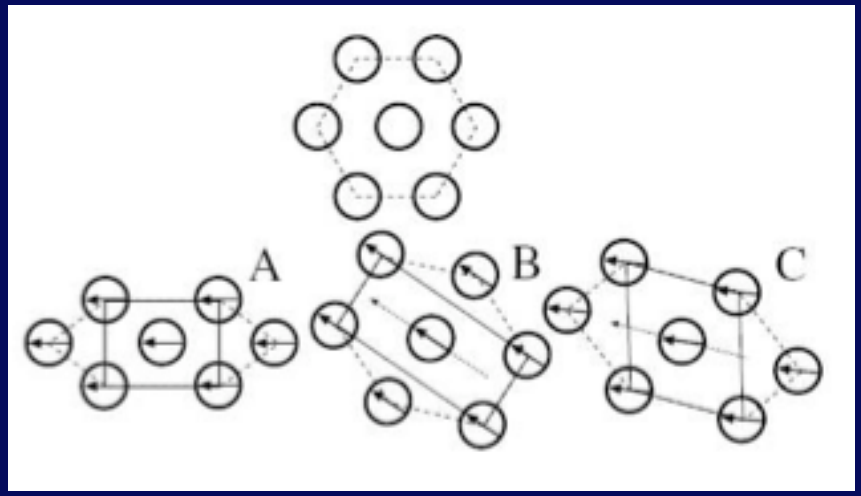
$$F = a_1|\eta|^2 + a_2|\eta|^4 + b_1|\mu|^2 + b_2|\mu|^4 +$$
$$+ c_1|\mu||\eta|^6 \cos 6(\phi - \theta) + c_2|\mu|^2|\eta|^{12} \cos^2 6(\phi - \theta)$$

← TP + hexatic

← coupling

Three types of phases from the minimization of FE:

A. deformed hexatic in the direction of first neighbors (excluding the central) ϕ = 0
B. deformed hexatic in the direction of second neighbors (excluding the central) ϕ = π/6
C. deformed hexatic in general direction 0 < ϕ < π/6.

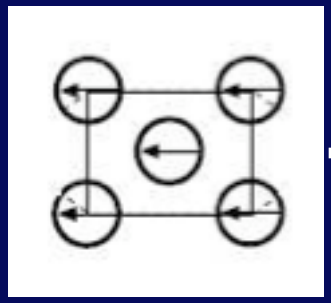


# High density hexagonal - TP coupling $\varphi \neq 0$

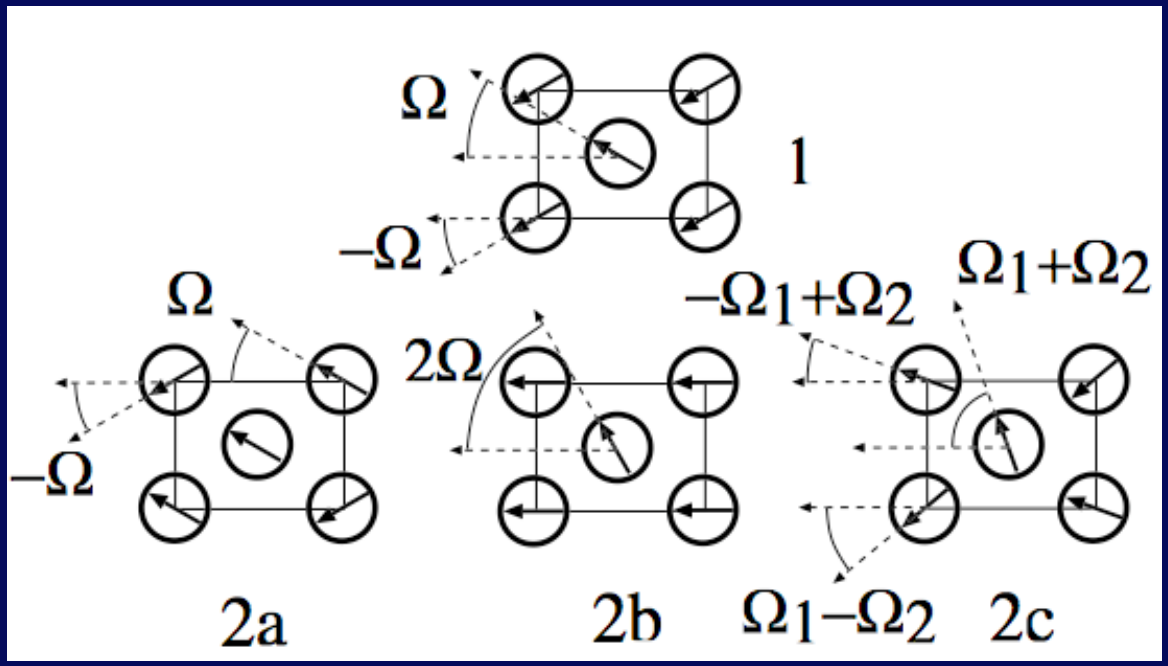
Again line hexatic phase as the parent phase. But a bit more complicated.
The nearest neighbor TP vector are at a finite angle!

This is possible only in periodic systems in terms of TP. Crystalline order is thus a consequence!

Azimutal frustrations of the lattice.



Start with e.g. A. structure deformed hexatic




a. one dimensional crystal in e.g. x-direction, one angle of reorientation
b. one dimensional crystal in general direction, one angle of reorientation
c. two dimensional crystal in, two angles of reorientation

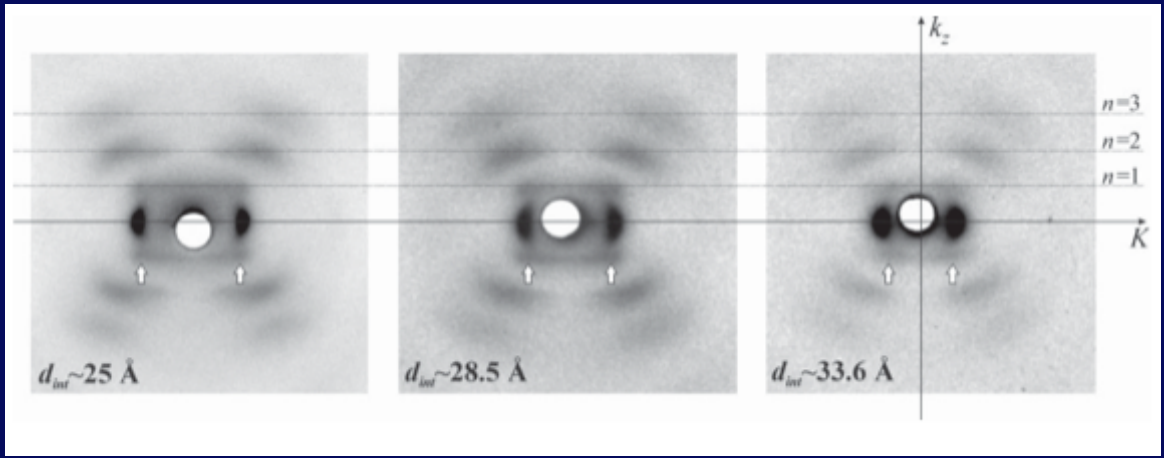
Freezing of the bond orientational order at higher densities. Angular correlations.

Observed already by Franklin in 1952, but not understood until now!

# Is this real?

Can one observe azimutal correlations predicted on the theory that is based on the two-state KL model?

Kornyshev and Leikin (PRL, 2005) reanalyzed the old diffraction data by S.B. Zimmerman. From almost contact to 40 Å separation.

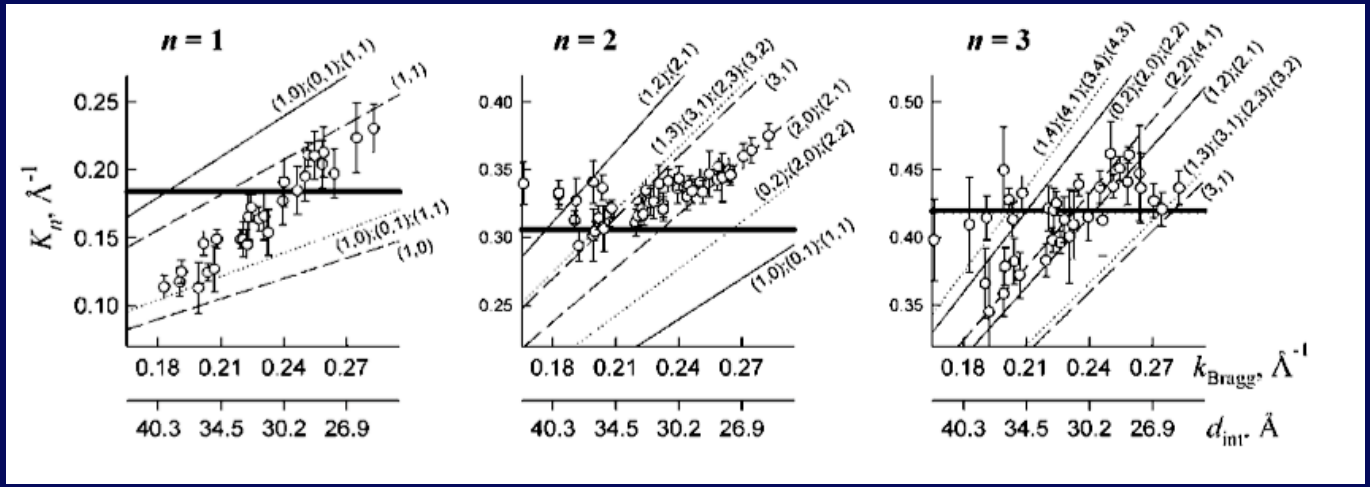



- equatorial n=0 peaks change with DNA density, positional order

- for small inter-chain correlations n ≠ 0 peaks should show no density variation

Equatorial lines remain the same - B-DNA for all densities.

Strong azimutal correlations of the type A, 2a or 2c.

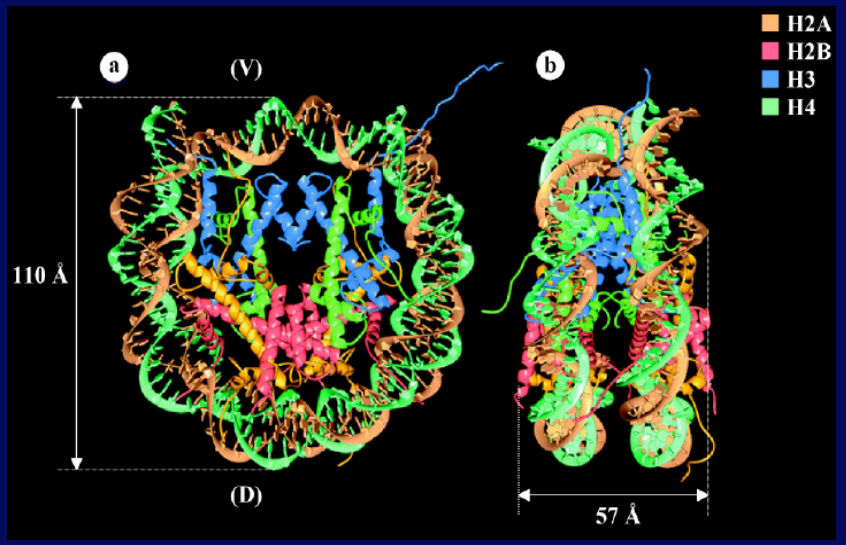


# A related problem of azimutal correlations

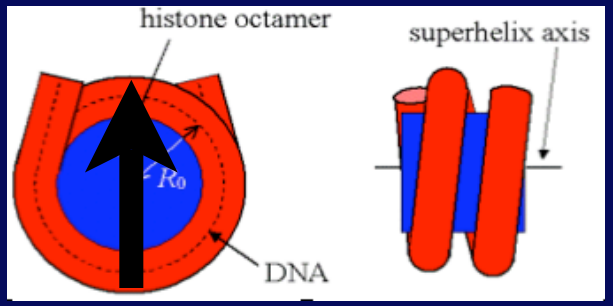
The structural cascade of chromatin in eucaryots starts with the nucleosomal particle.

From DNA to chromosomes. Many levels of as yet poorly understood organization but with interesting physics (Schiessel, 2002).

Viruses: toroidal packing just as in DNA collapse in vitro.
Bacteria (prokariotes): nucleoid, a loose DNA - protein gel



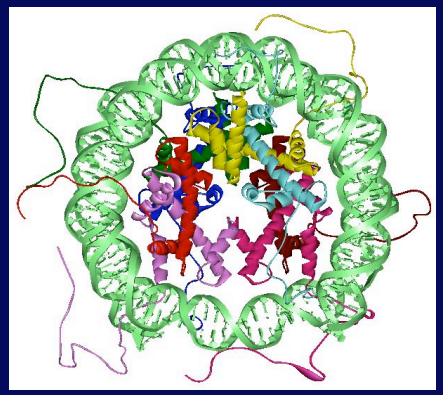

Existence of a polar dyadic axis.




A histone octamer (4 X 2) of 4 core histones:
H2A, H2B, H3 and H4
147 bp DNA wrapped 1.75 times in a left-handed helix, stable up to 0.75 M salt

# The nucleosomal core particle (NCP)

The “elementary particle” of chromatin organization. Missing just linker DNA and H1 histone.

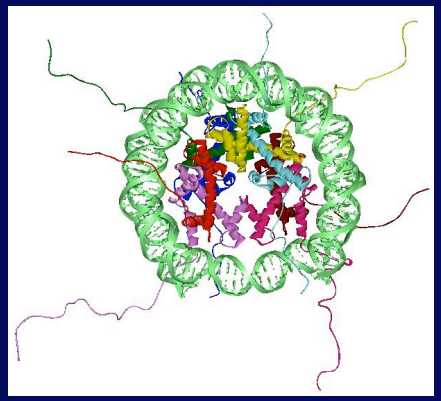


Folded N-tails

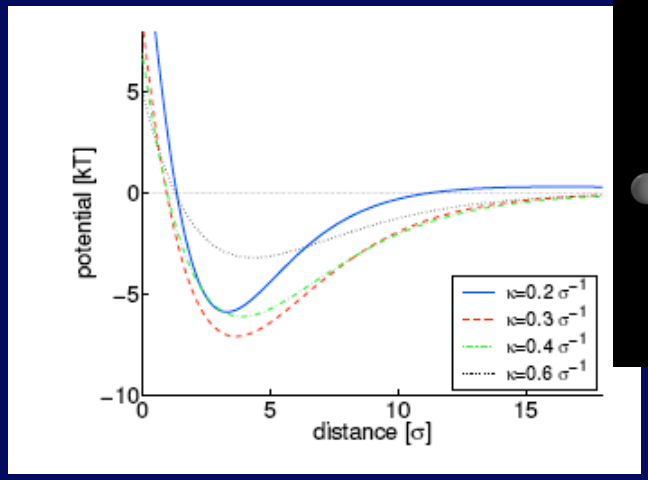
Folded vs. expanded N-tails
(N-terminals of histone core proteins)

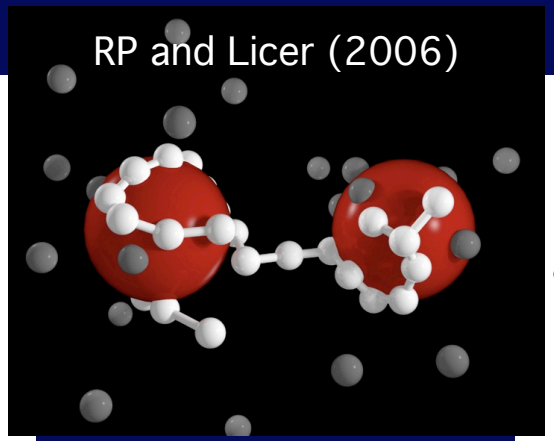
Folded tails below 50 mM
and expanded from 50
mM and above.

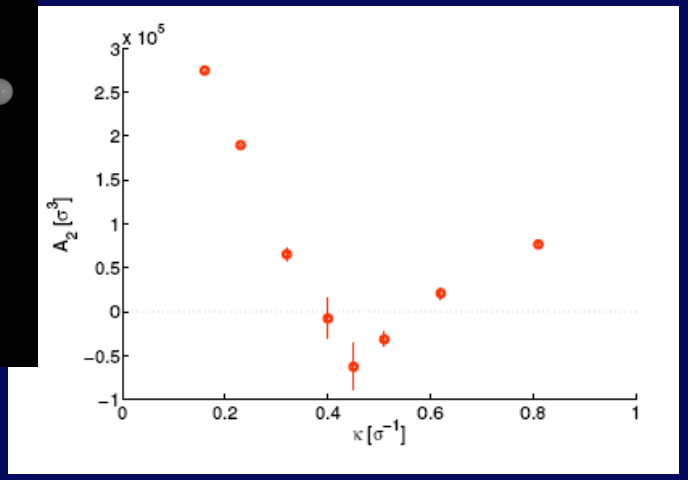
(Mangenot et al. 2002)



Expanded N-tails



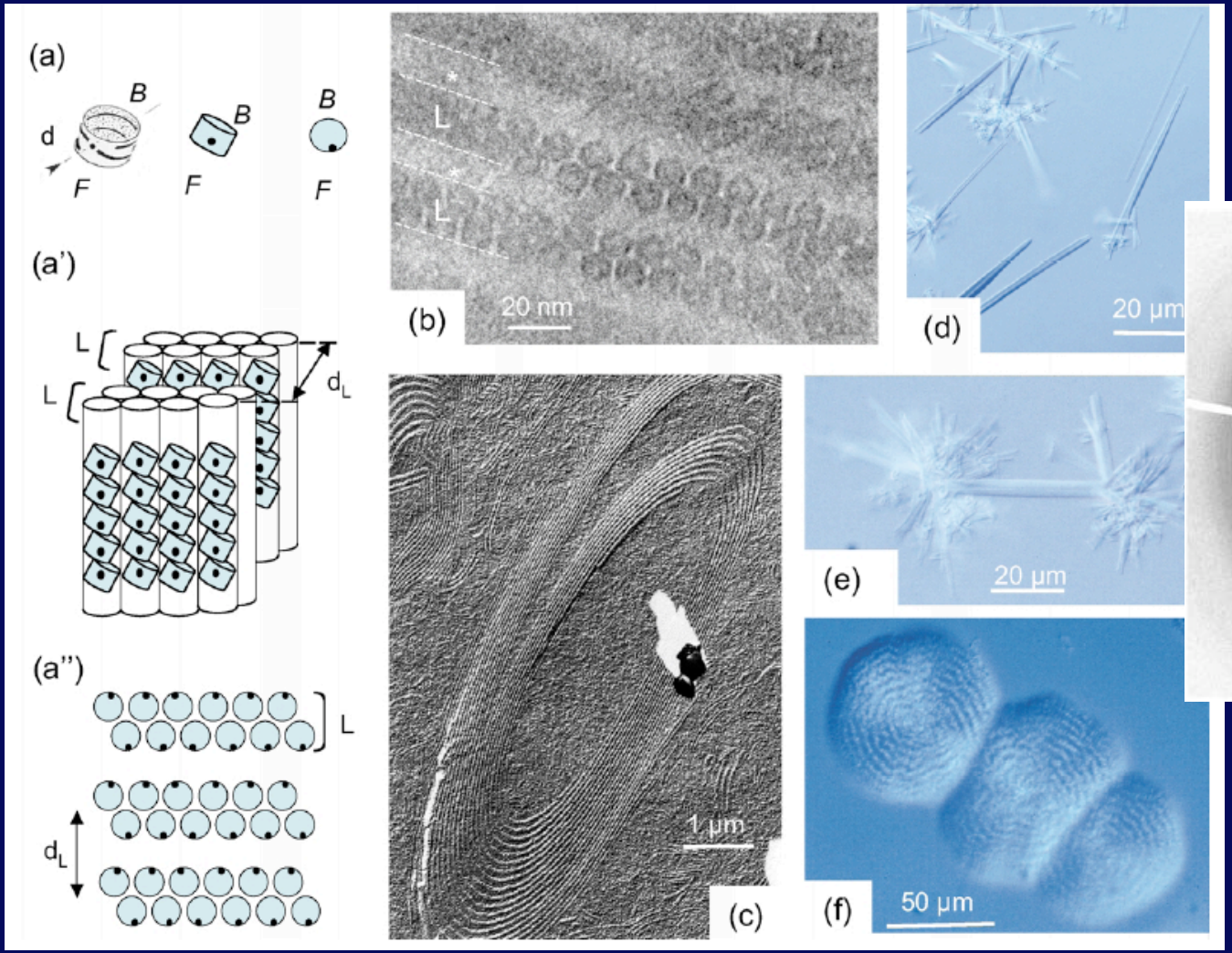



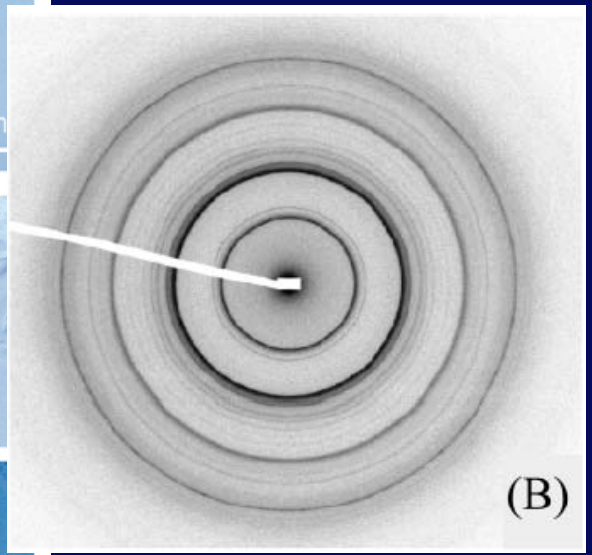

Bridging interactions can lead to association of nominally equally charged colloids.
Important also at large densities of NCPs where they make condensed mesophases...
Muehlbacher, Schiessel and Holm, (2005).

# NCP mesophases in ionic solutions

S. Mangenot, A. Leforestier, D. Durand, and F. Livolant (2003-2005).




Intriguing texture and order of mesophases...



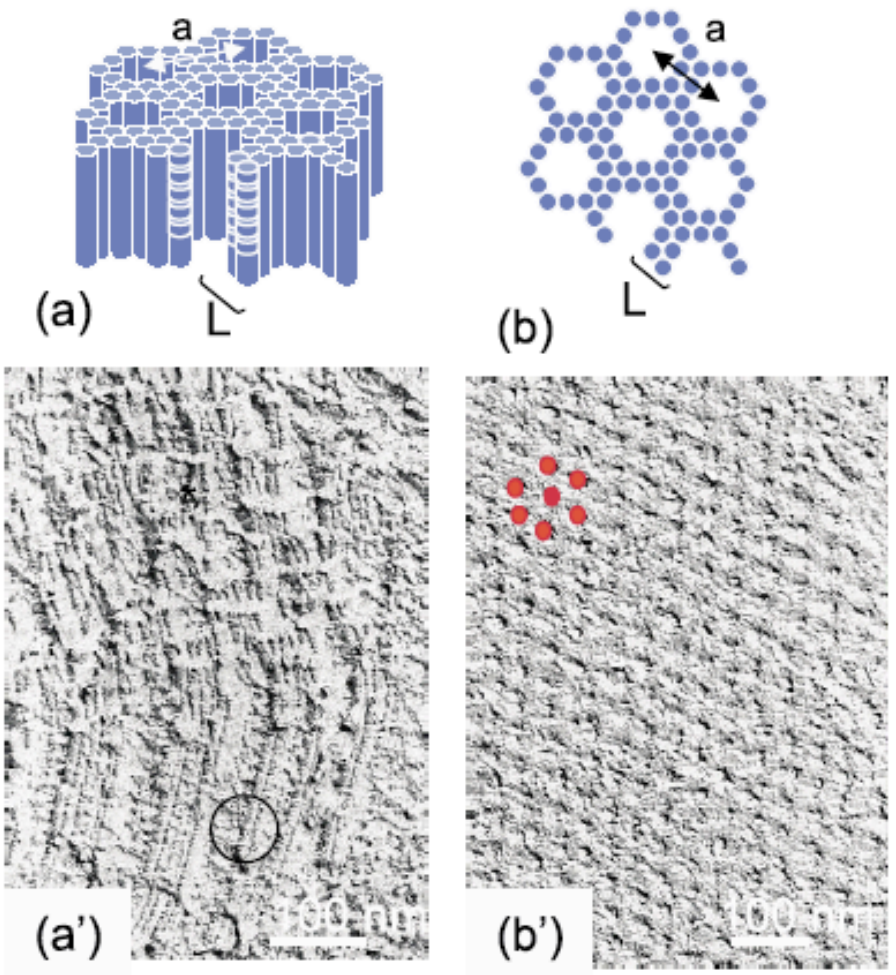

lamellar phase

inverted hexagonal phase
orthorhombic phase

X-ray scattering plus optical texture serve to identify the phases. They come in very exotic varieties....Superb work of F. Livolant et al.

# More NCP mesophases in ionic solutions

S. Mangenot, A. Leforestier, D. Durand, and F. Livolant (2003-2005).



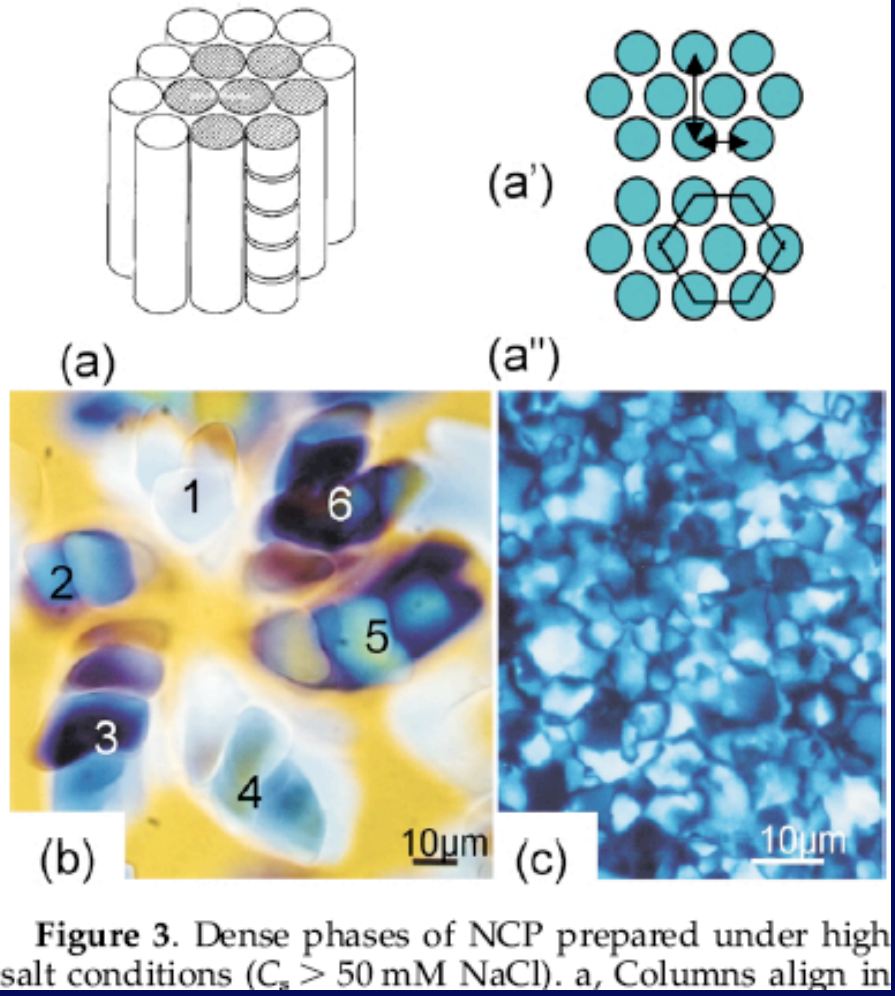




**Figure 3.** Dense phases of NCP prepared under high salt conditions ($C_s > 50$ mM NaCl). a, Columns align in

X-ray scattering plus optical texture serve to identify the phases. They come in different varieties: isotropic, lamellar, hexagonal, inverted hexagonal.

# NCP mesophase phase diagram

Changing the osmotic pressure (i.e. density) and ionic strength of the solution.

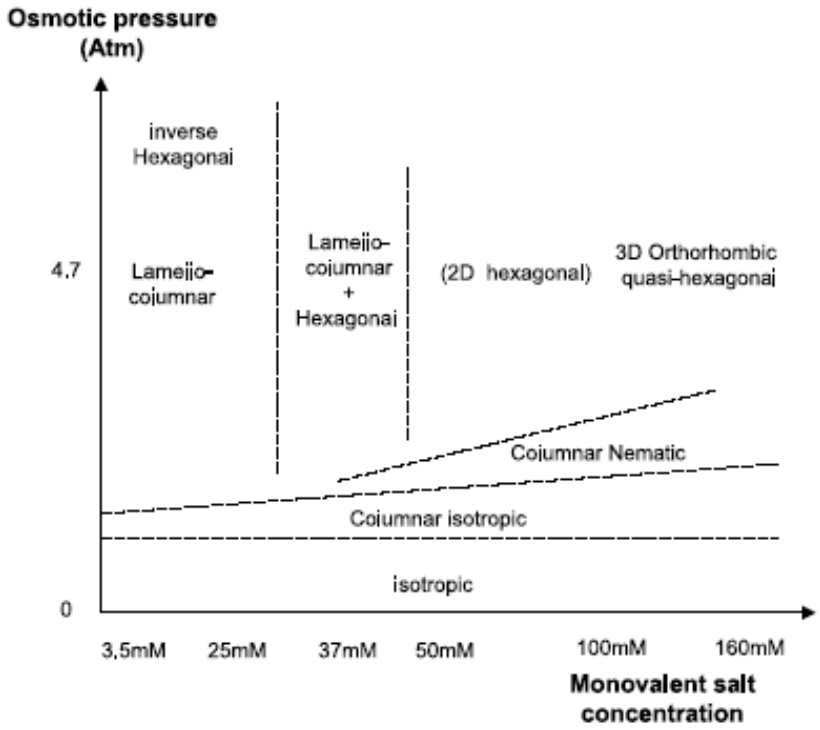
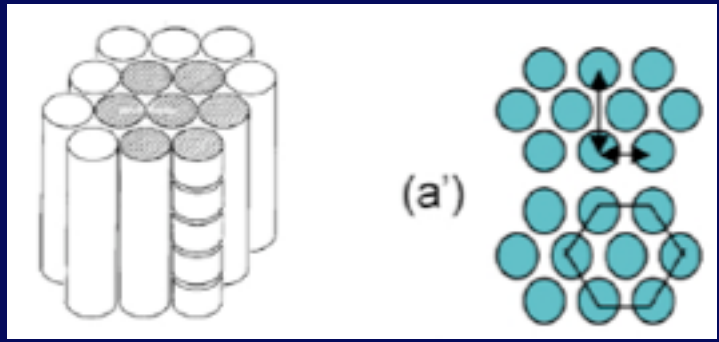
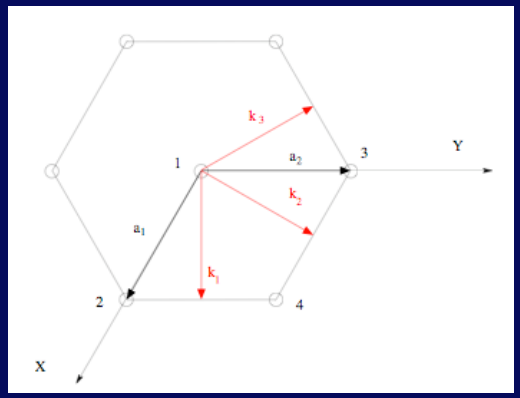



**Figure 7**. Tentative phase diagram of isolated NCP as a function of monovalent salt ($3 < C_s < 160$ mM) and applied osmotic pressure.

Here the parent phase is assumed to be columnar hexagonal.




Constructing the order parameter based on the existence of dyadic axis:




Three order parameters out of polarization vector:

$$\eta_1 = P_{x1} - P_{x2} + P_{x3} - P_{x4} + \frac{1}{2}(P_{y1} - P_{y2} + P_{y3} - P_{y4})$$

$$\eta_2 = \frac{1}{2}(P_{x1} + P_{x2} - P_{x3} - P_{x4}) + P_{y1} + P_{y2} - P_{y3} - P_{y4}$$

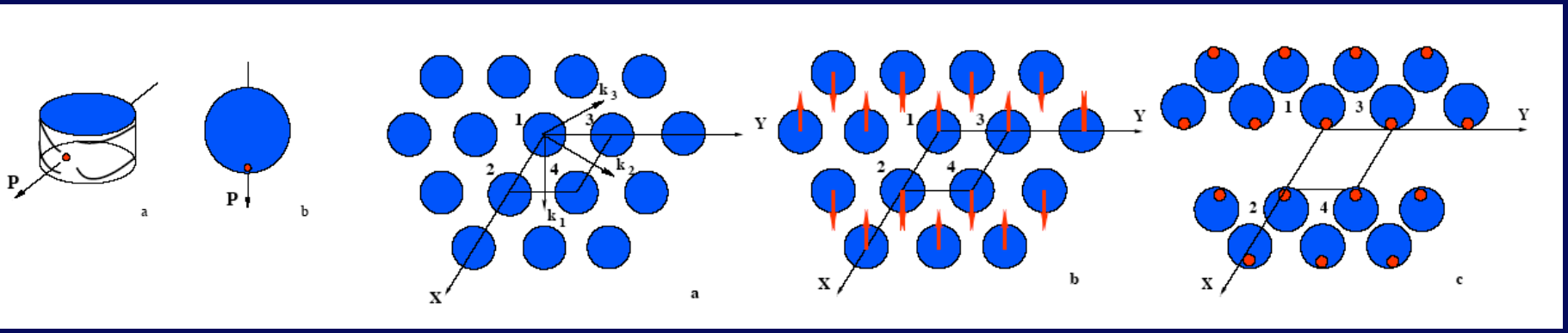
$$\eta_3 = \frac{1}{2}(-P_{x1} + P_{x2} + P_{x3} - P_{x4} + P_{y1} - P_{y2} - P_{y3} + P_{y4})$$

And the density variation:

$$\rho(x, y, z) = \rho_0 + \sum_{i=1}^{3} \eta_i \Psi_i(x, y, z)$$

# Lamellar phase of NCPs

Starting from a parent hexagonal phase transitions into several other phases of lower symmetry are possible, e.g. a lamellar phase (very technical).




Duality between the P ordering and the u displacement (plus chirality).

Curie's principle.

Writing down the free energy from invariants of the three order parameters that are defined via transverse polarization vector.

| $\eta_i$ | $V_{ord}/V_{hex}$ | Space Group |
|---|---|---|
| $\eta, 0, 0$ | 2 | $C^1_{2v}$ |
| $\eta, \eta, \eta$ | 4 | $D^1_{3h}$ |
| $\eta, \eta, 0$ | 4 | $D^1_{2h}$ |
| $\eta_1, \eta_2, 0$ | 4 | $C^1_{2h}$ |
| $\eta_1, \eta_1, \eta_2$ | 4 | $C^1_{2v}$ |
| $\eta_1, \eta_2, \eta_3$ | 4 | $C^1_S$ |

TABLE I – *Different solutions of the equation of state.*

lamellar phase

inverted hexagonal phase

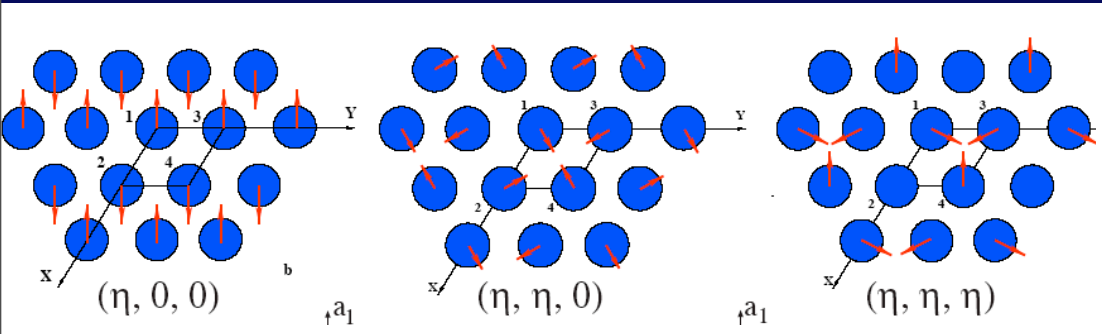
orthorhombic phase

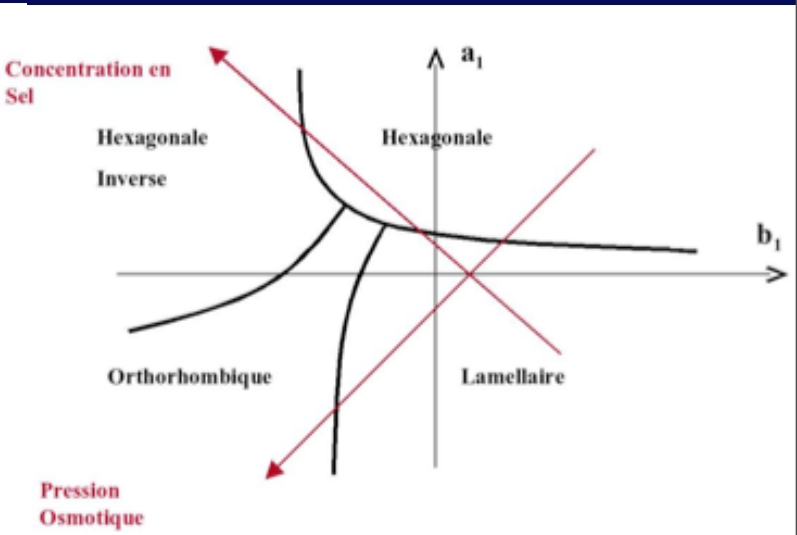
Free energy minimization. (Manna, RP, Lorman and Zeks, 2007)

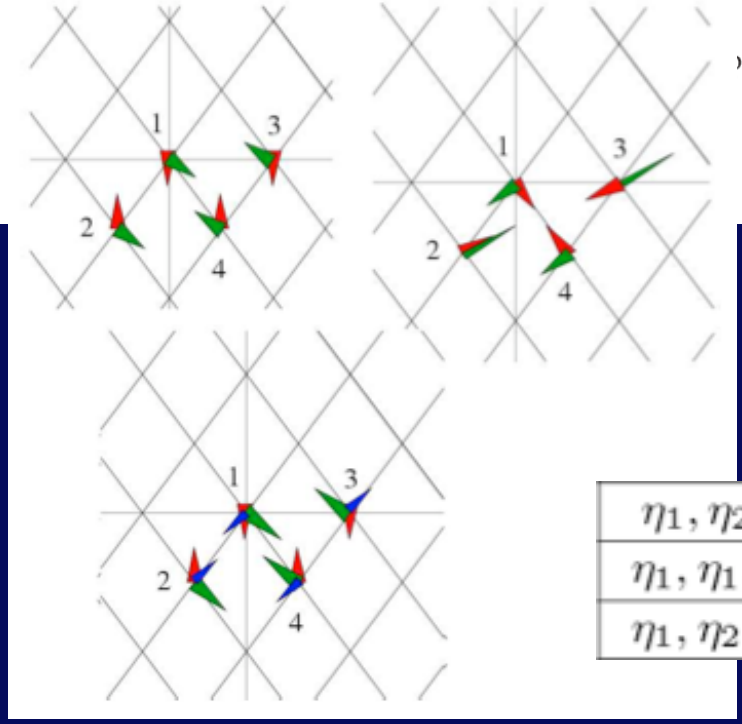
# Inverted hexagonal and orthorhombic lattice

Apart from the lamellar phase other phases and transitions between them are possible.

lamellar phase  inverted hexagonal  orthorhombic phase  Phase diagram.



These last three phases have not been observed (yet).

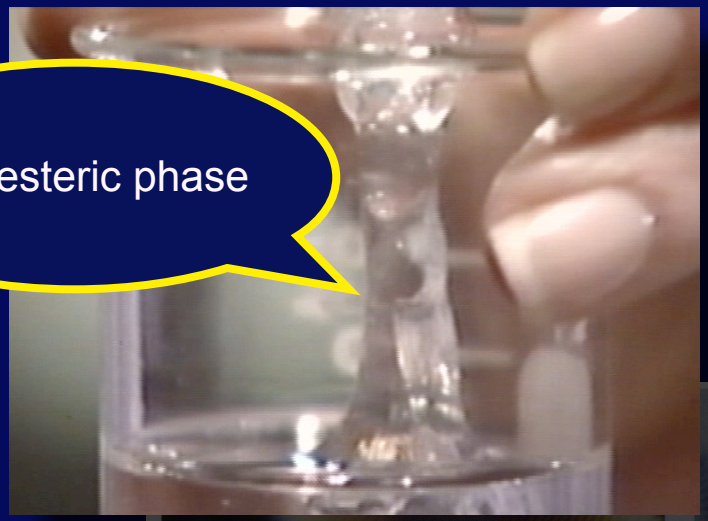
| | | |
|---|---|---|
| $\eta_1, \eta_2, 0$ | 4 | $C_{2h}^1$ |
| $\eta_1, \eta_1, \eta_2$ | 4 | $C_{2v}^1$ |
| $\eta_1, \eta_2, \eta_3$ | 4 | $C_S^1$ |

Nature of the 2D molecular displacement.

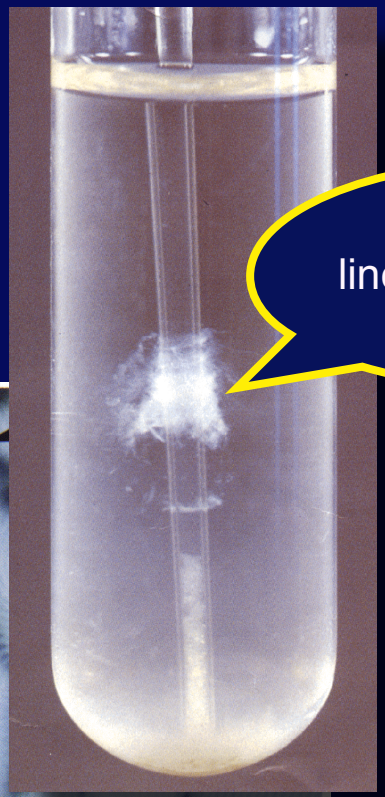
Lorman, RP, Zeks EPL (2005).

# From observing to understanding DNA mesophases

Not that difficult to observe, but not simple to understand.



cholesteric phase



line hexatic phase


Livolant et al. 1997.

Many details still need to be worked out, but the big picture is most probably correct.

FINIS