The Abdus Salam
International Centre for Theoretical Physics

United Nations
Educational, Scientific and
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IAEA
International Atomic Energy Agency

2038-16

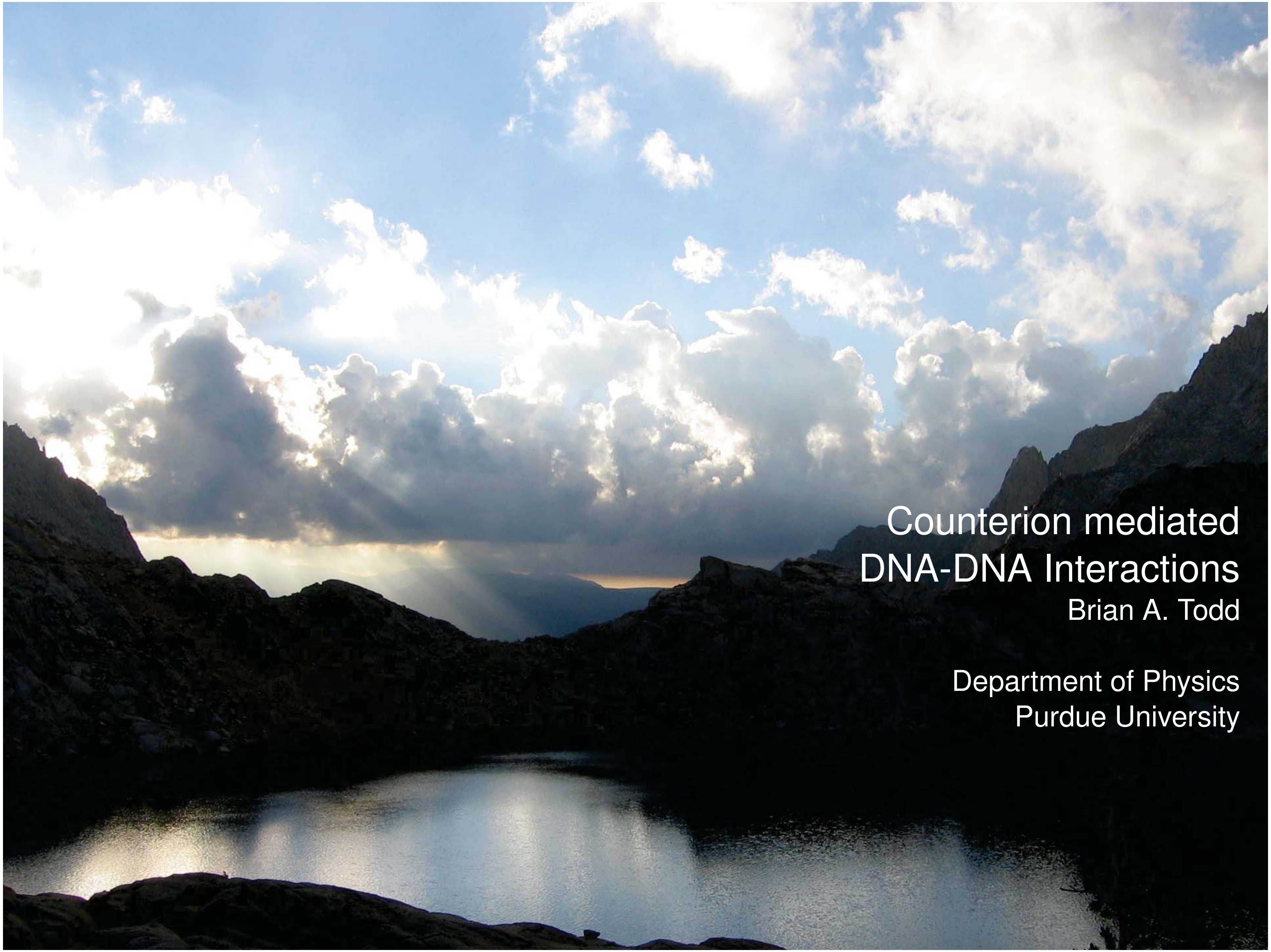
Conference: From DNA-Inspired Physics to Physics-Inspired Biology

1 - 5 June 2009

Counterion Mediated DNA-DNA Interactions

Brian A. TODD

Department of Physics, Purdue University
525 Northwestern Ave. West Lafayette
IN 47907-0706
USA



Counterion mediated DNA-DNA Interactions

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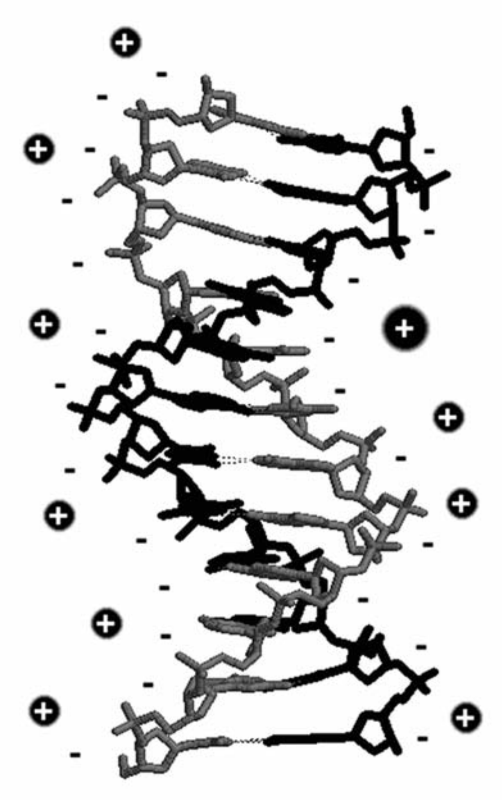
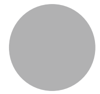
DNA Interactions are Mediated by Counterions



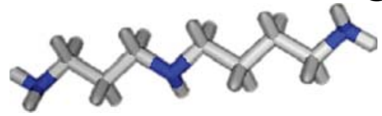
Kurtz, 2008

1+



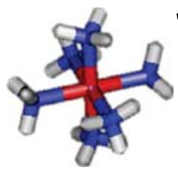
sodium

3+



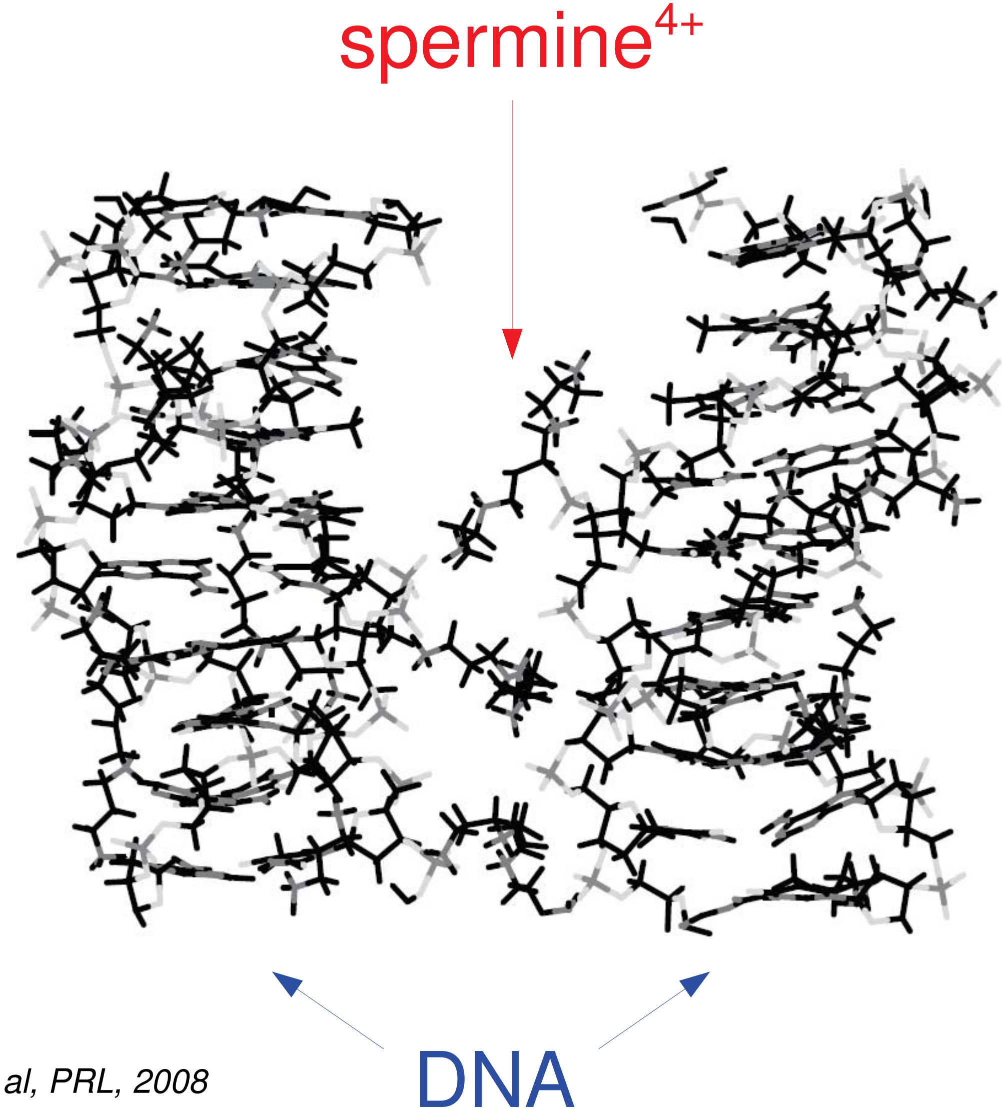
spermidine

3+



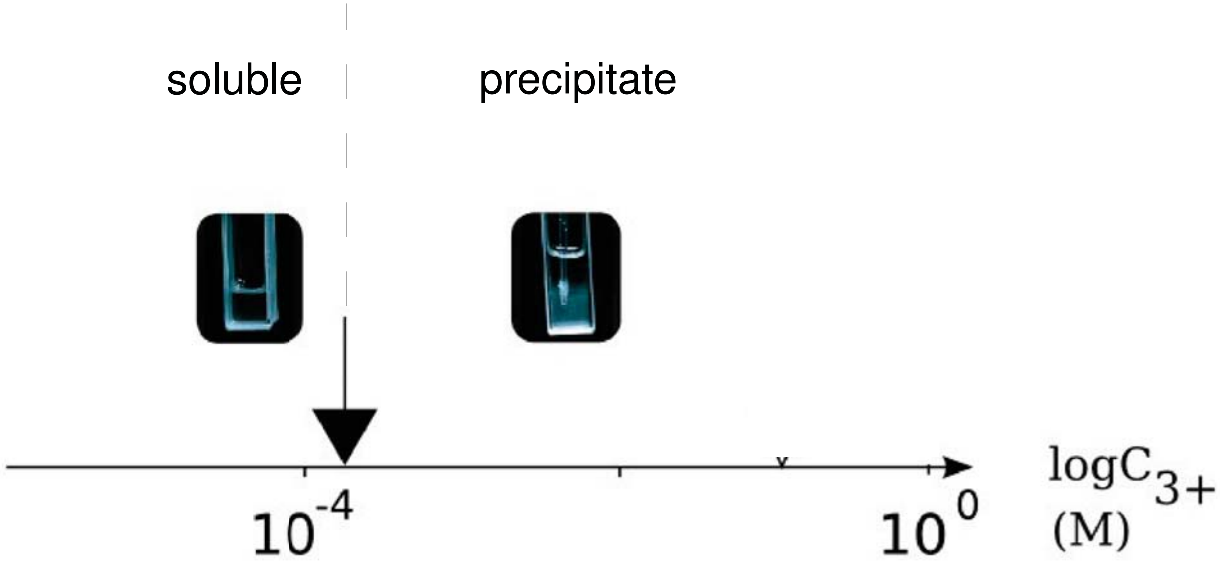
cobalt hexammine

Multivalent Ions Cause Attractions



picture from Dai et al, PRL, 2008

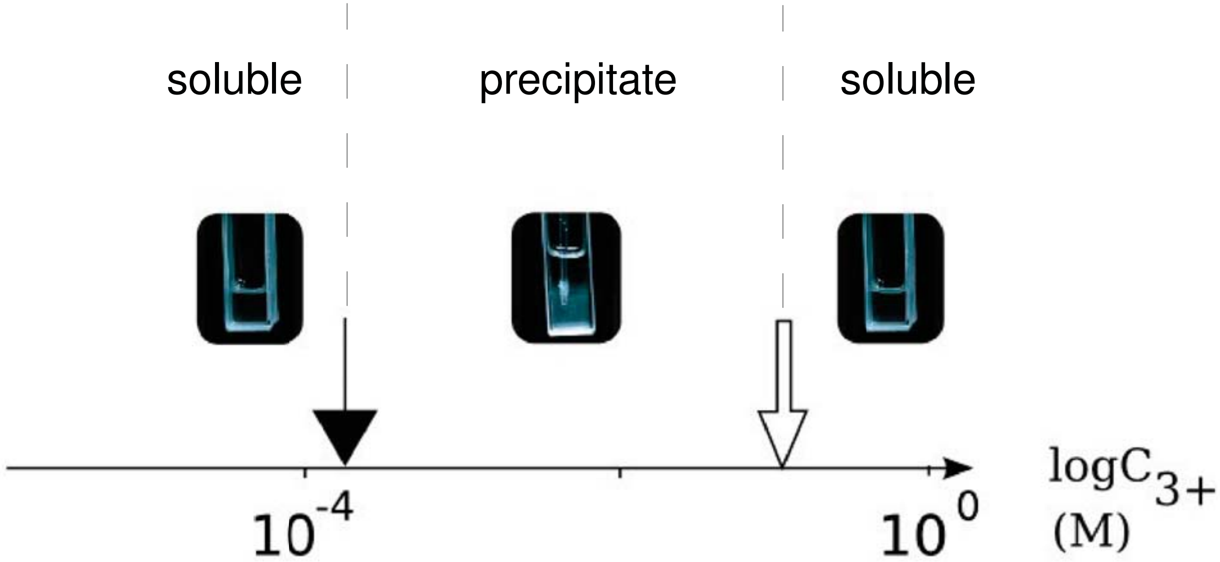
Precipitation of DNA by Multivalent Cations



$$d \bigtriangleup G = - \bigtriangleup n_{3+} d\mu_{3+}$$

Pelta et al, Biophys. J., 1997; Raspaud et al., Biophys. J., 1998

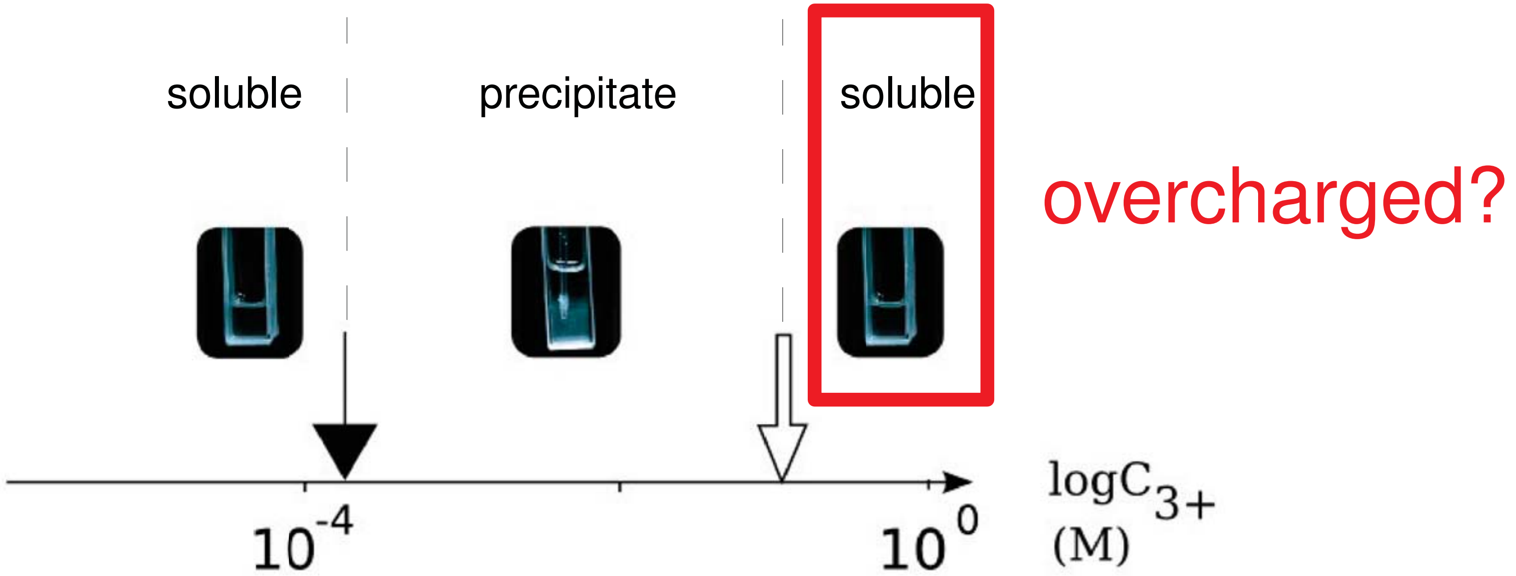
Resolubilization of DNA by Multivalent Cations



$$d \triangle G = - \triangle n_{3+} d\mu_{3+}$$

Pelta et al, Biophys. J., 1997; Raspaud et al., Biophys. J., 1998

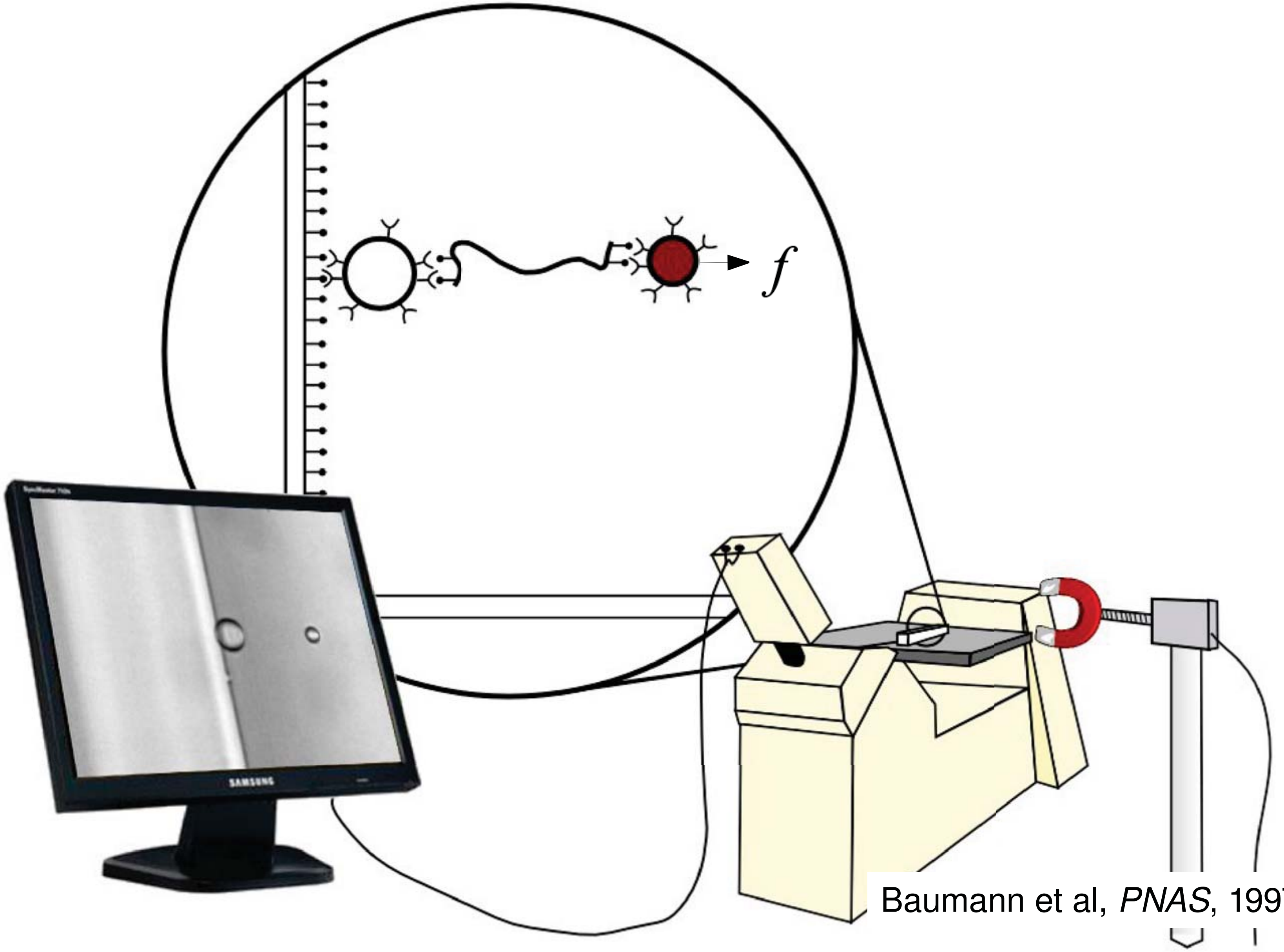
Resolubilization of DNA by Multivalent Cations



$$d \triangle G = - \triangle n_{3+} d\mu_{3+}$$

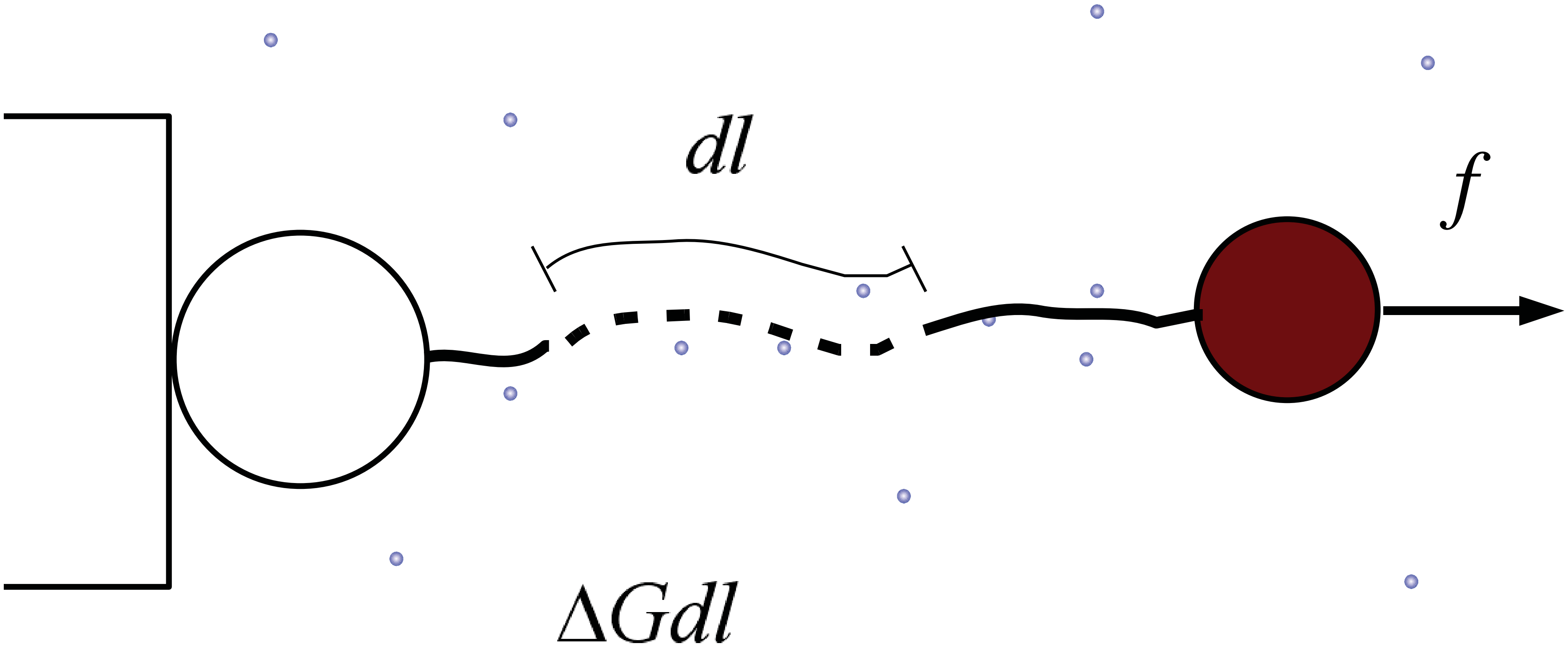
Pelta et al, Biophys. J., 1997; Raspaud et al., Biophys. J., 1998

Magnetic Tweezing of Condensed DNA

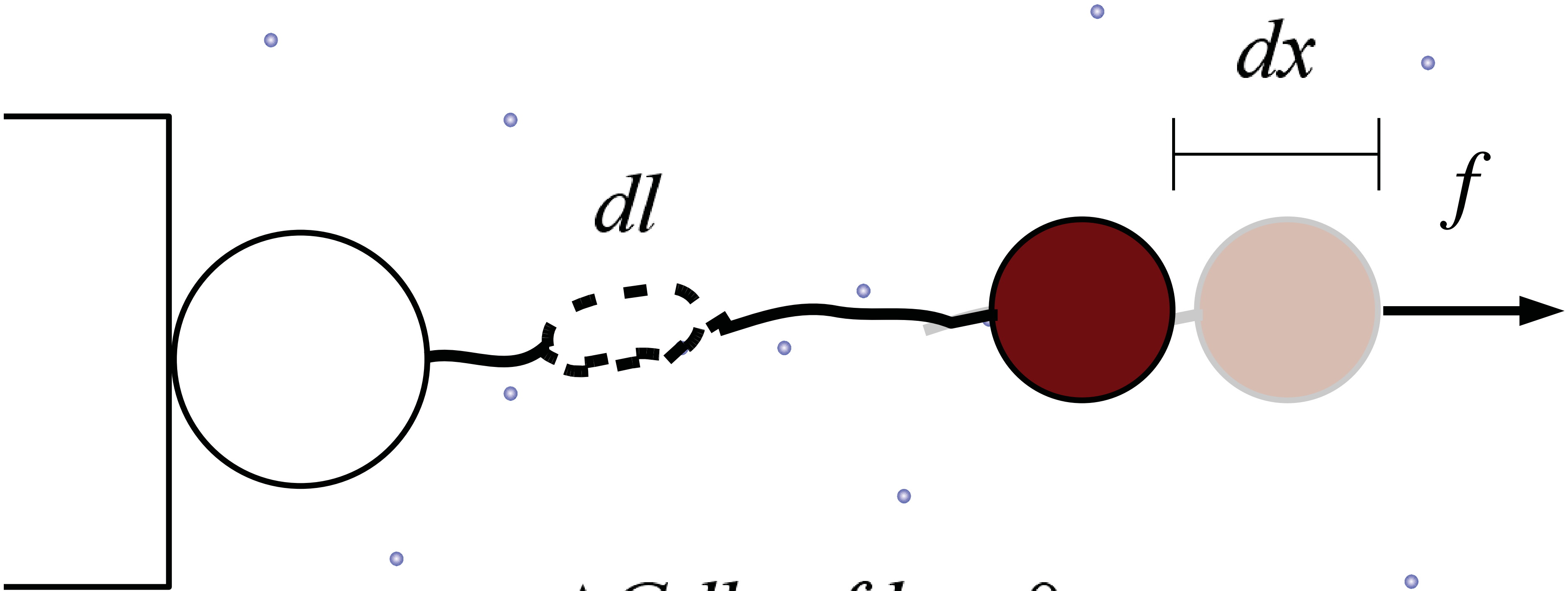


Baumann et al, *PNAS*, 1997

Compaction Against a Force

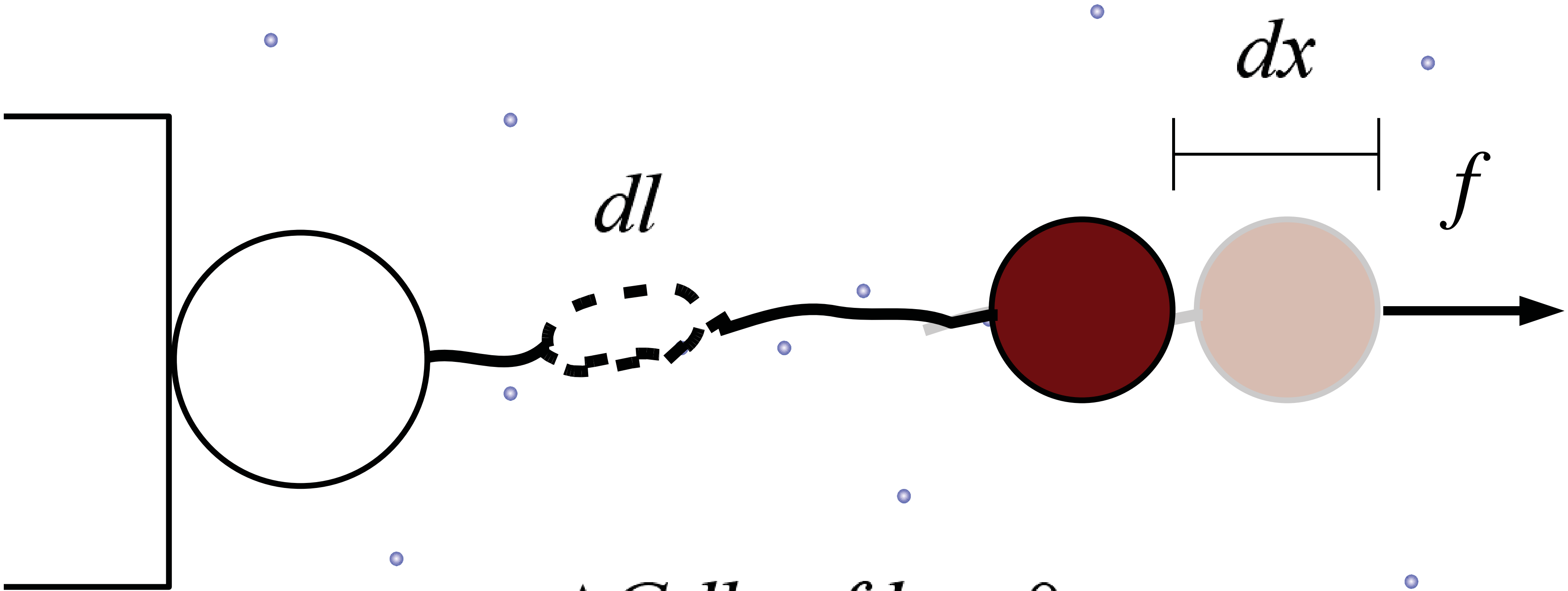


Compaction Against a Force



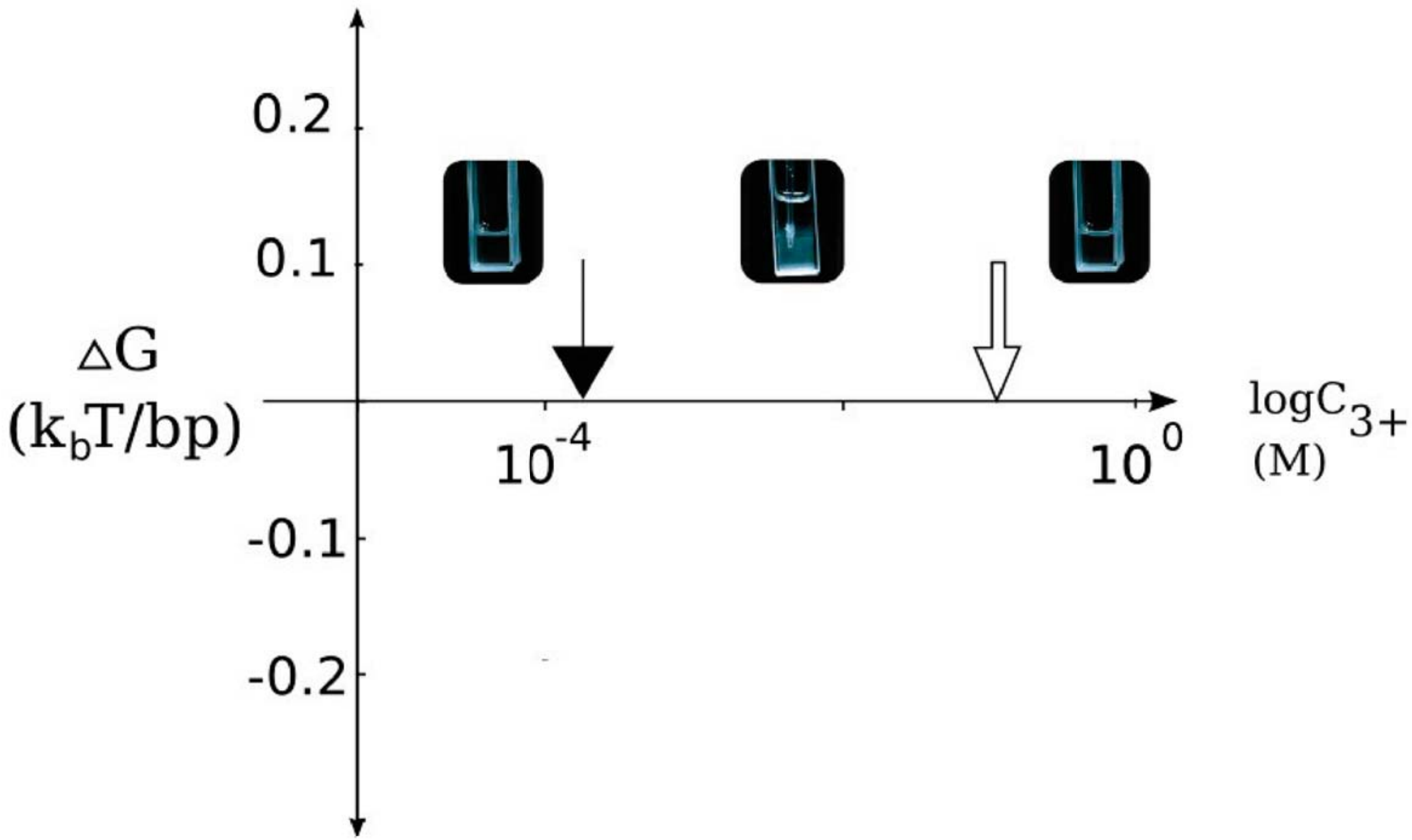
$$\Delta G dl + f dx = 0$$

Force ~ Free Energy/Length

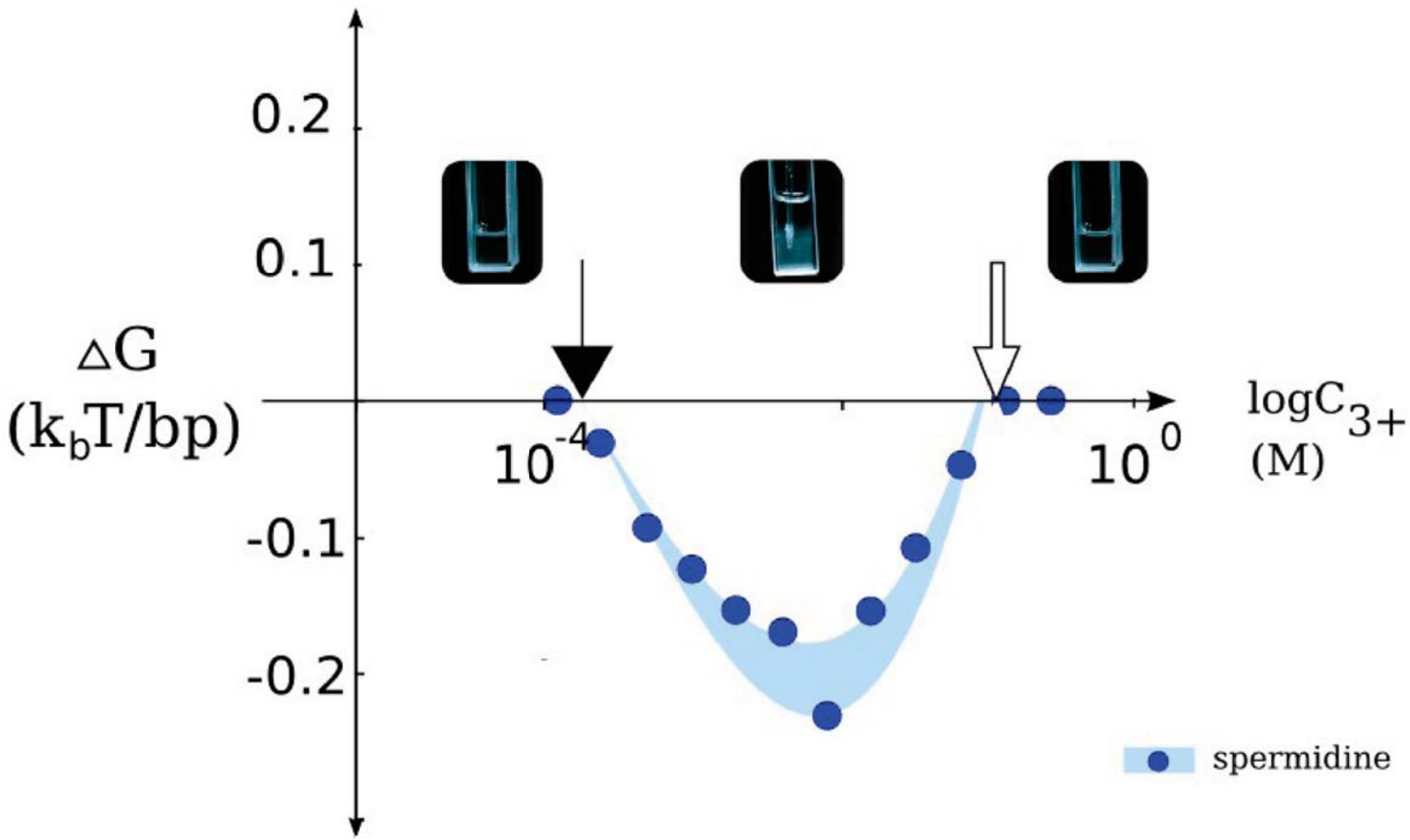


$$\Delta G dl + f dx = 0$$

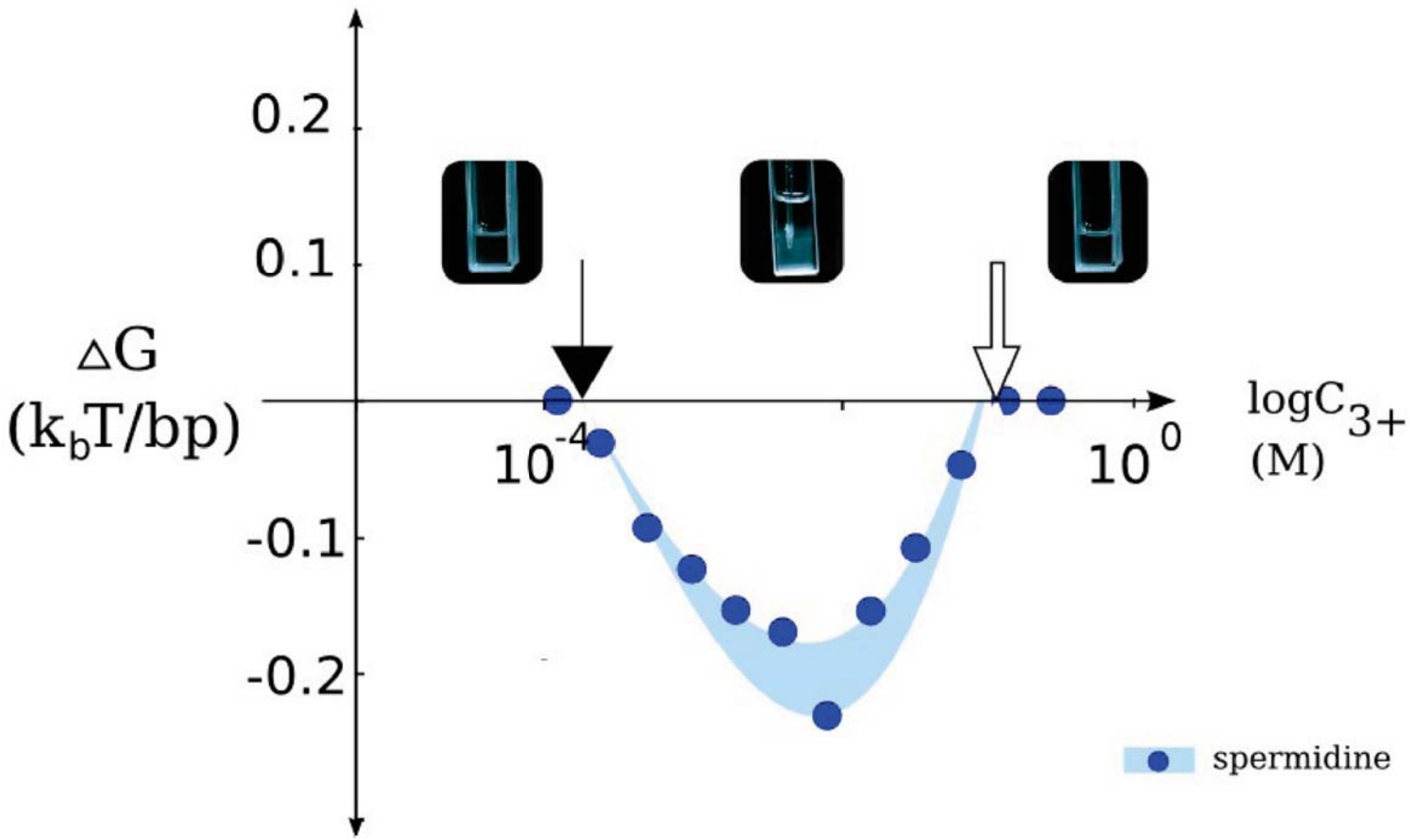
$$\Delta G \sim -f$$


0.2
0.1
-0.1
-0.2
△G
(k_bT/bp)
10^-4
10^0
logC_3+
(M)

Bulk (Arrows) vs. Single-molecule

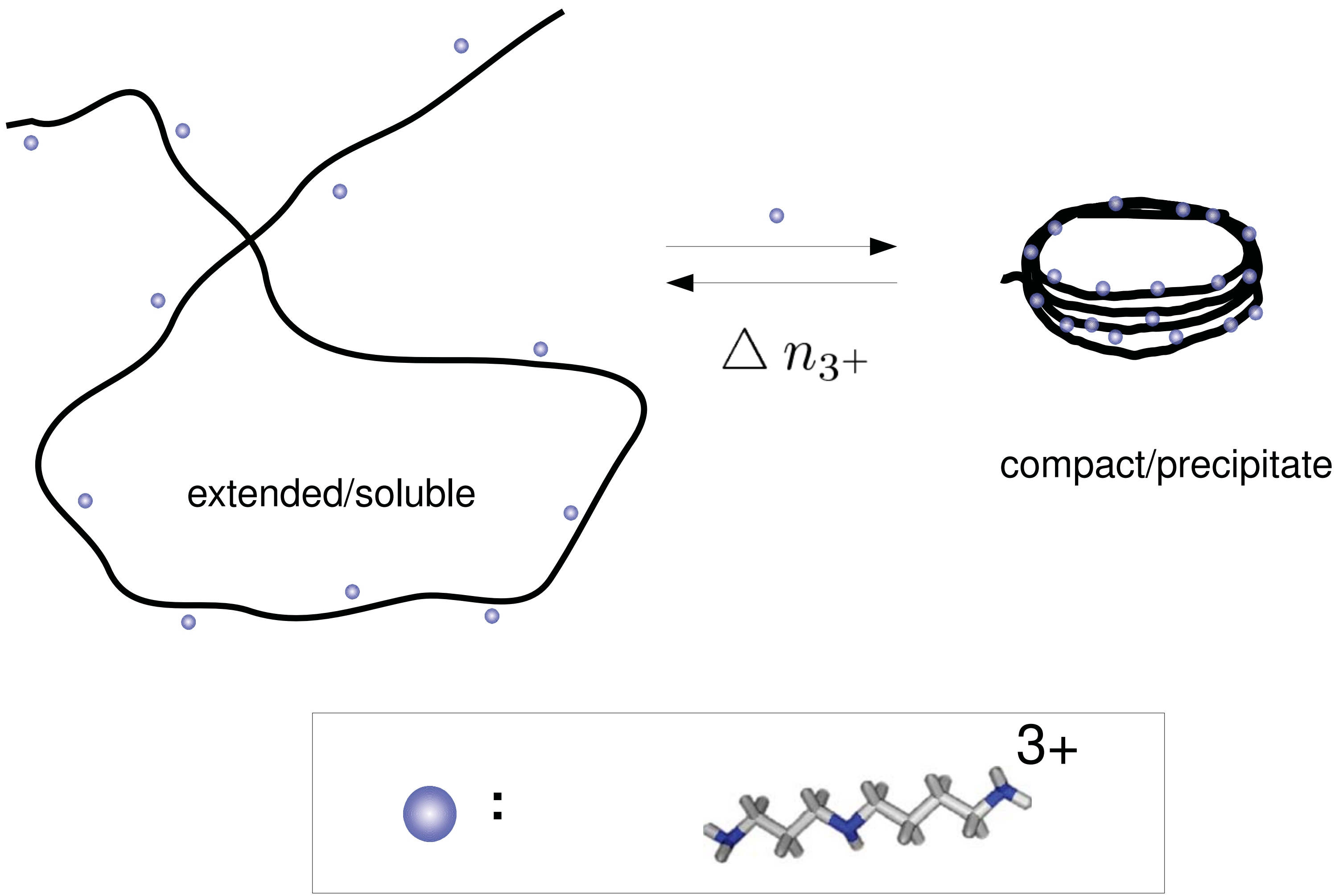


Bulk (Arrows) vs. Single-molecule

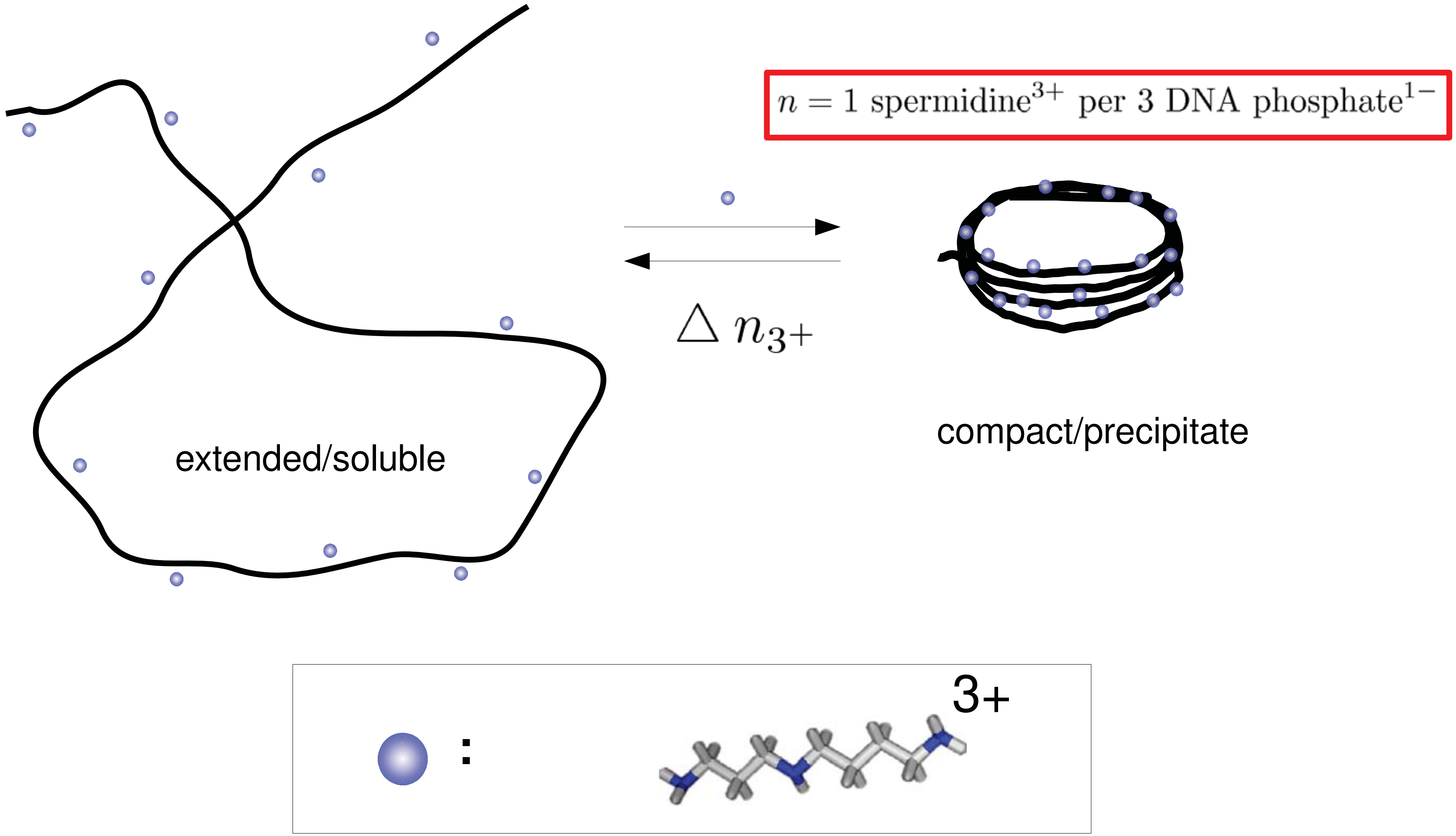


$$d \triangle G = - \triangle n_{3+} d\mu_{3+}$$

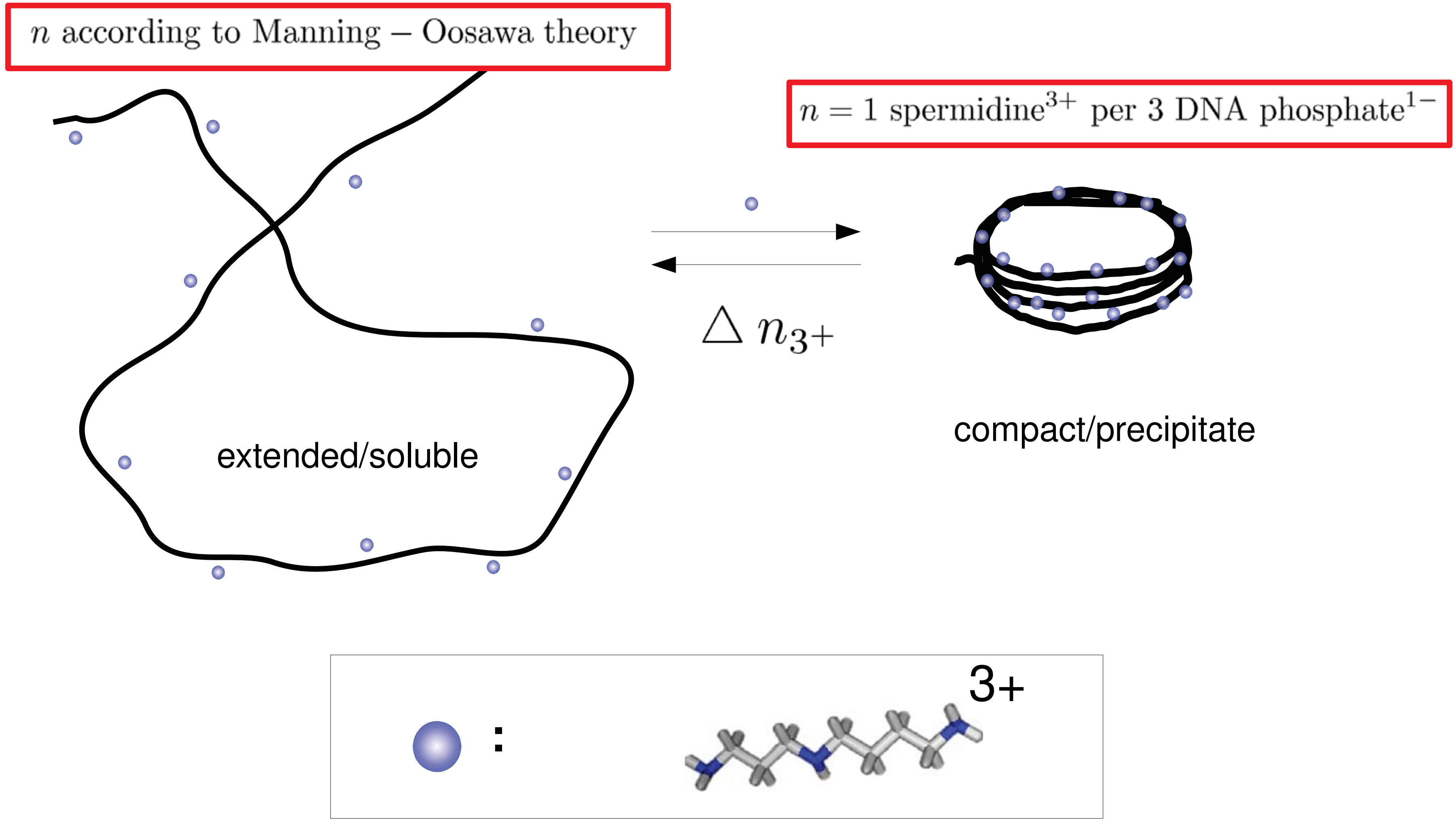
Modeling Concentration Dependence



Condensate Neutralized by +3

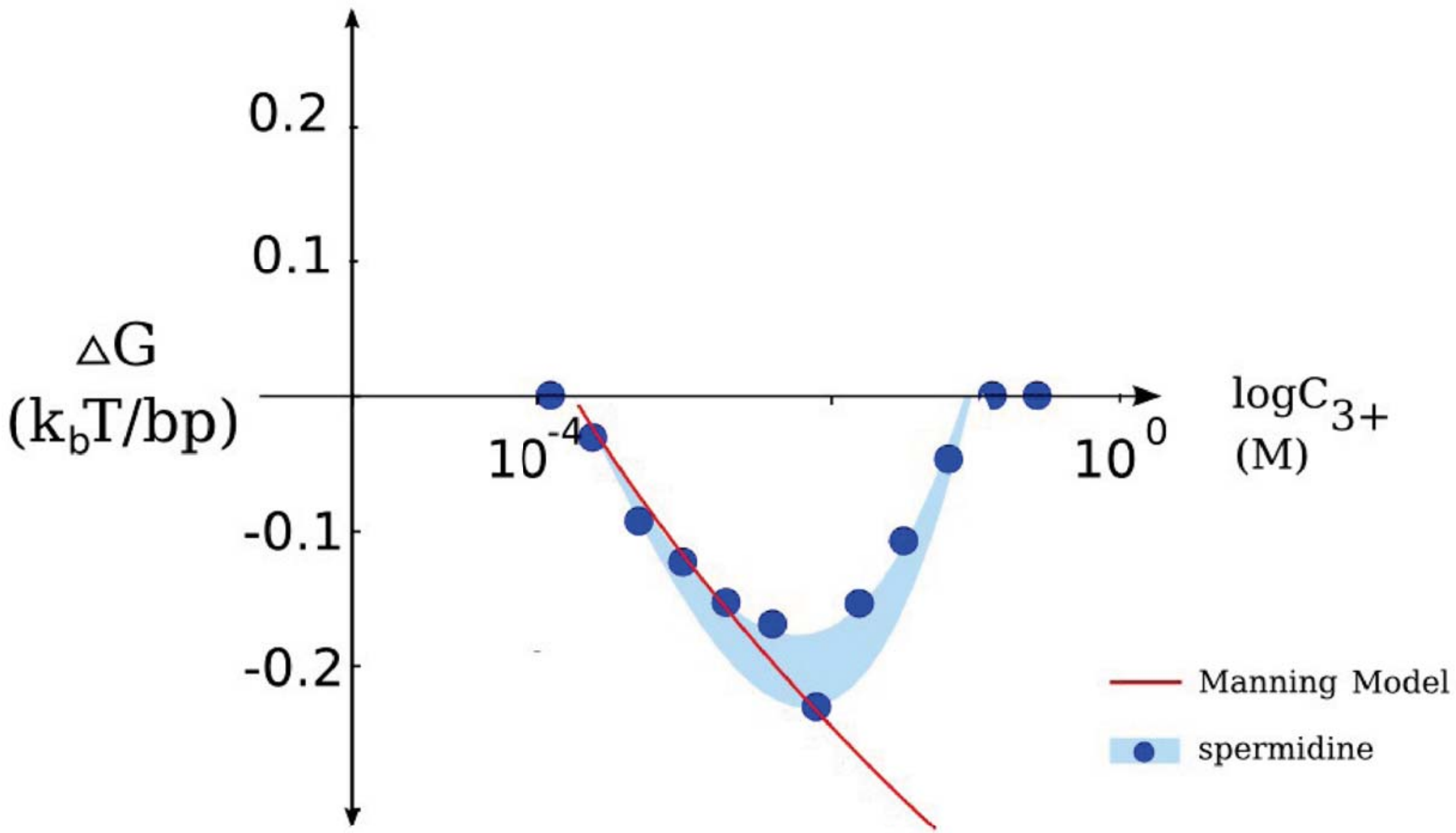


Soluble Phase Modeled by Mean-field Theory



$$d \triangle G = - \triangle n_{3+} d\mu_{3+}$$

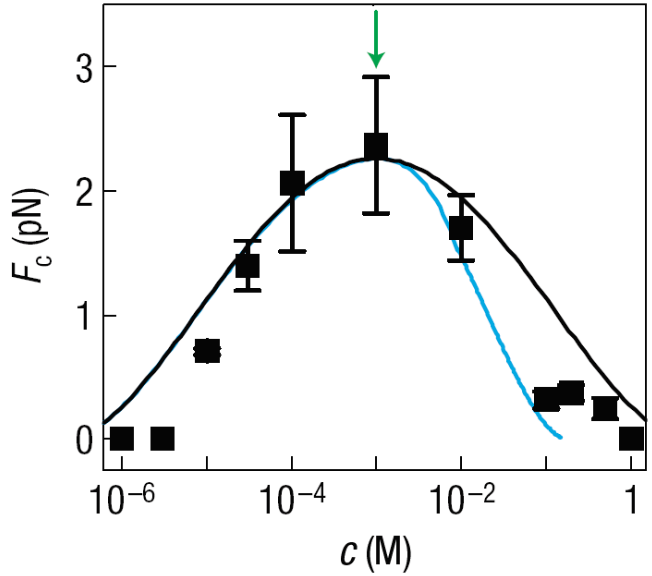
Mean-field Prediction vs. Experiment



Theories for Resolubilization

Besteman and Lemay, 2007
Shklovskii, PRL, 1999

Counterion correlations,
Wigner Crystals,
Overcharging



VOLUME 82, NUMBER 22 PHYSICAL REVIEW LETTERS 31 MAY 1999

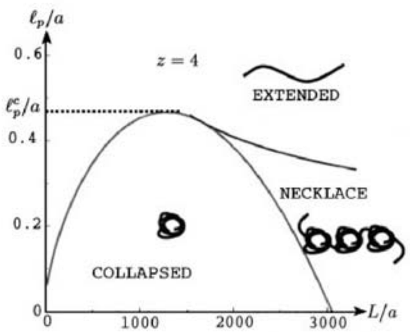


FIG. 2. Phase diagram for the salt-free case, for $z = 4$. The parameters $a = 1.7$ Å and $k_0 = 10^{-3}\pi/L$ are used.

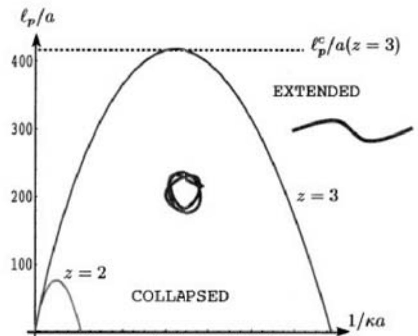


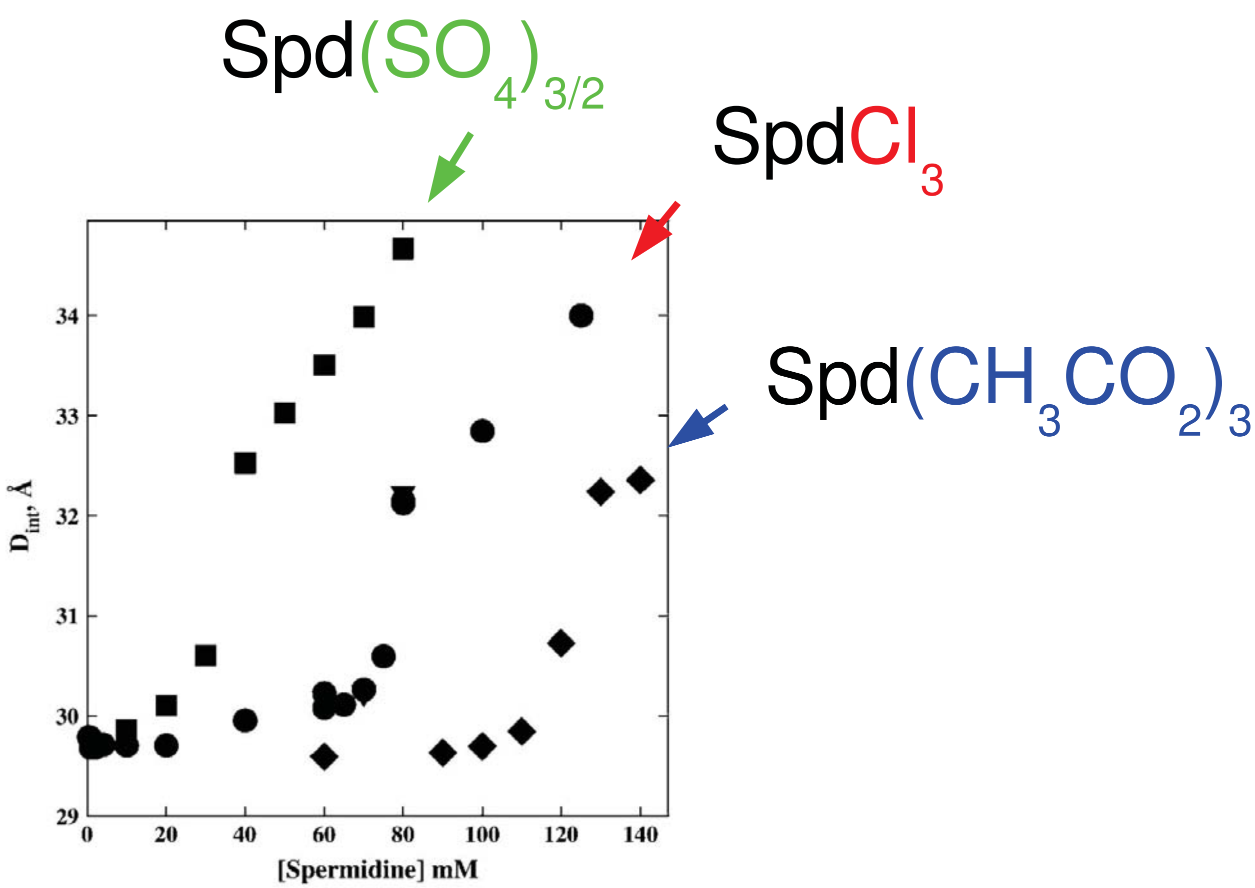
FIG. 3. Phase diagram for the added-salt case, for different values of the counterion valence z.

Golenstanian et al, PRL, 1999

Counterion fluctuations,
Debye screening

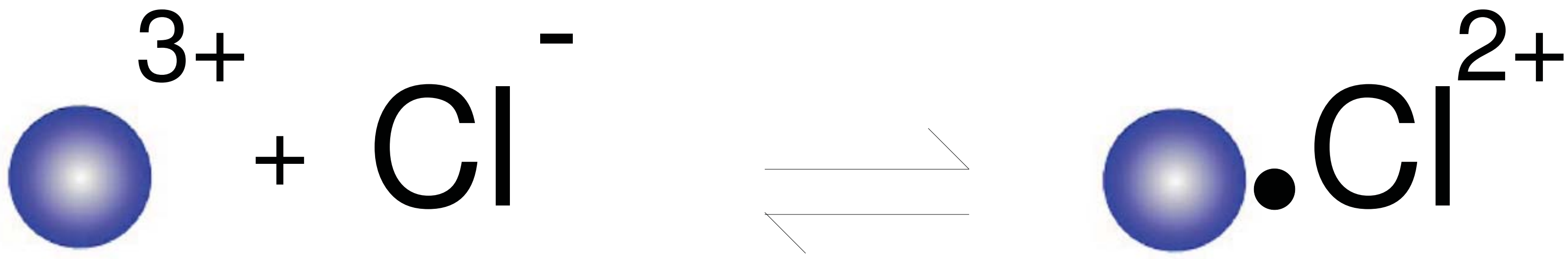
Olvera de la Cruz, 1995
Debye screening

The *anion* determines resolubilization



Yang and Rau, Biophys. J., 2005

Trivalent Ions Not Ideal >1 mM



$K_d \sim 10\text{-}100$ mM

Jenkins, J. Chem. Soc., 1953; Evans, Trans. Faraday Soc., 1951

Treat Bjerrum Pair as 2^{+} Species

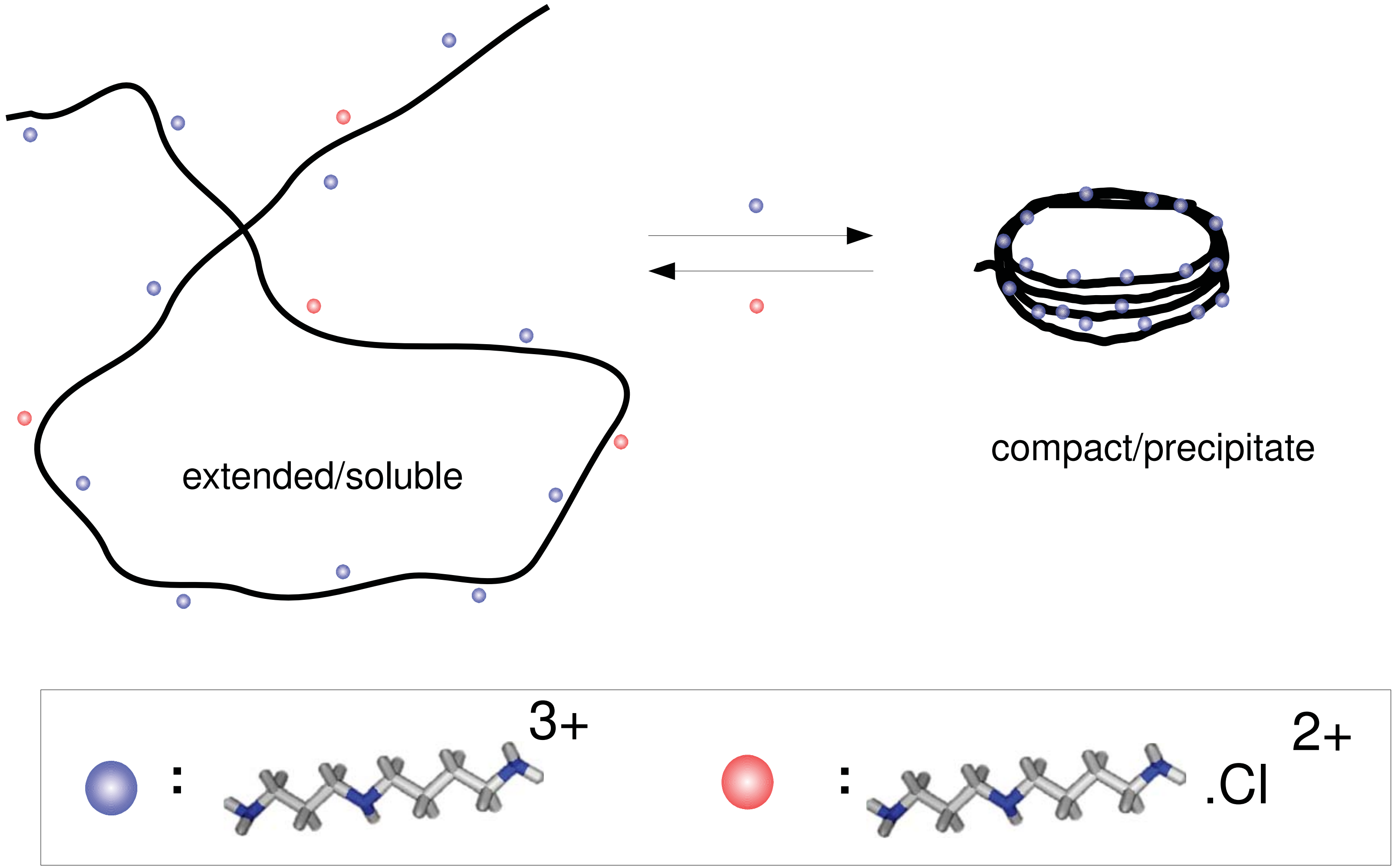
$K_d \sim$ 10-100 mM

Jenkins, J. Chem. Soc., 1953; Evans, Trans. Faraday Soc., 1951

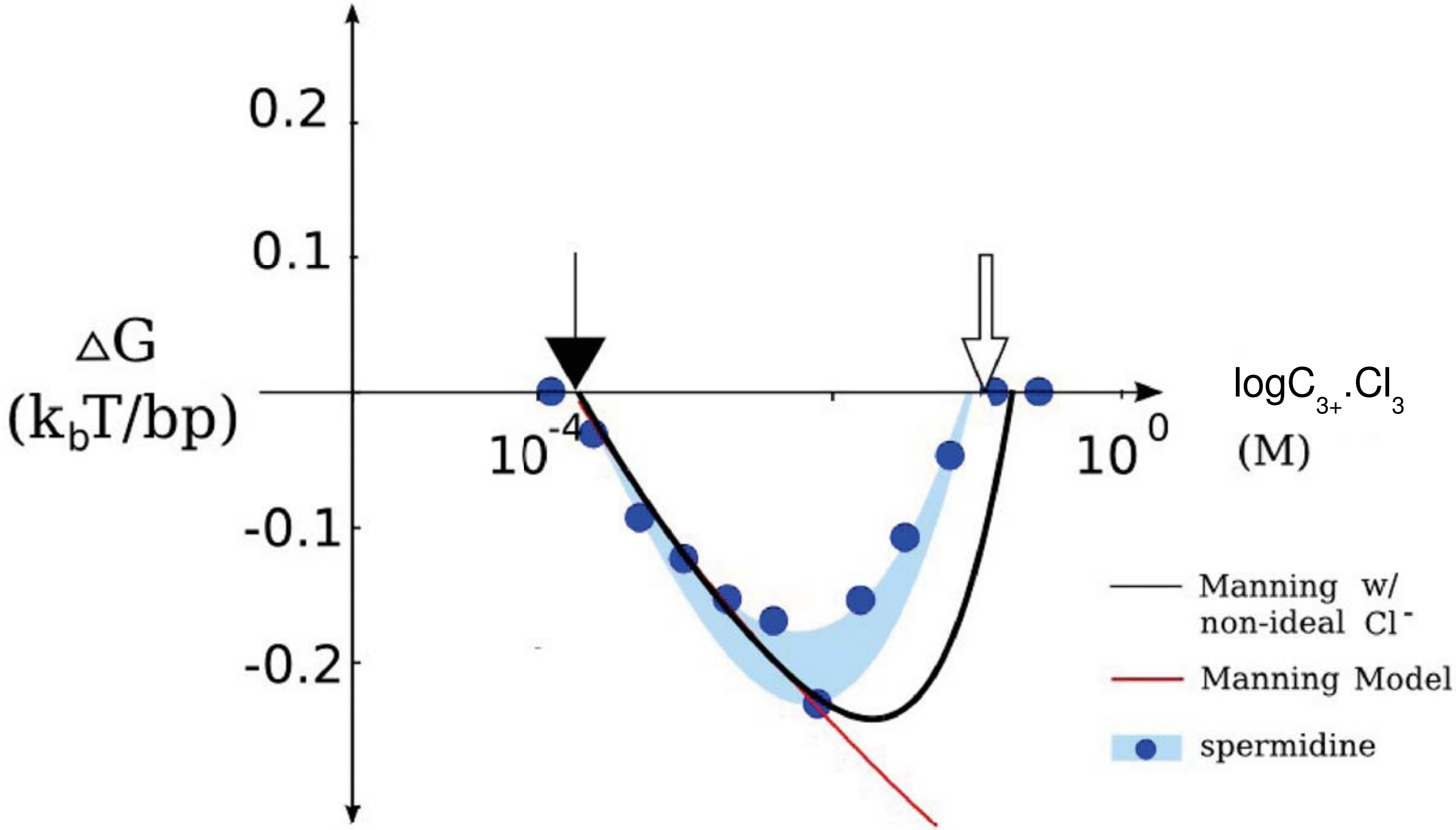
$$d \triangle G = - \triangle n_{3+} d\mu_{3+}$$

$$d \triangle G = - \triangle n_{3+} d\mu_{3+} - \triangle n_{2+} d\mu_{2+}$$

Precipitation of DNA by Nonideal Multivalent Cations

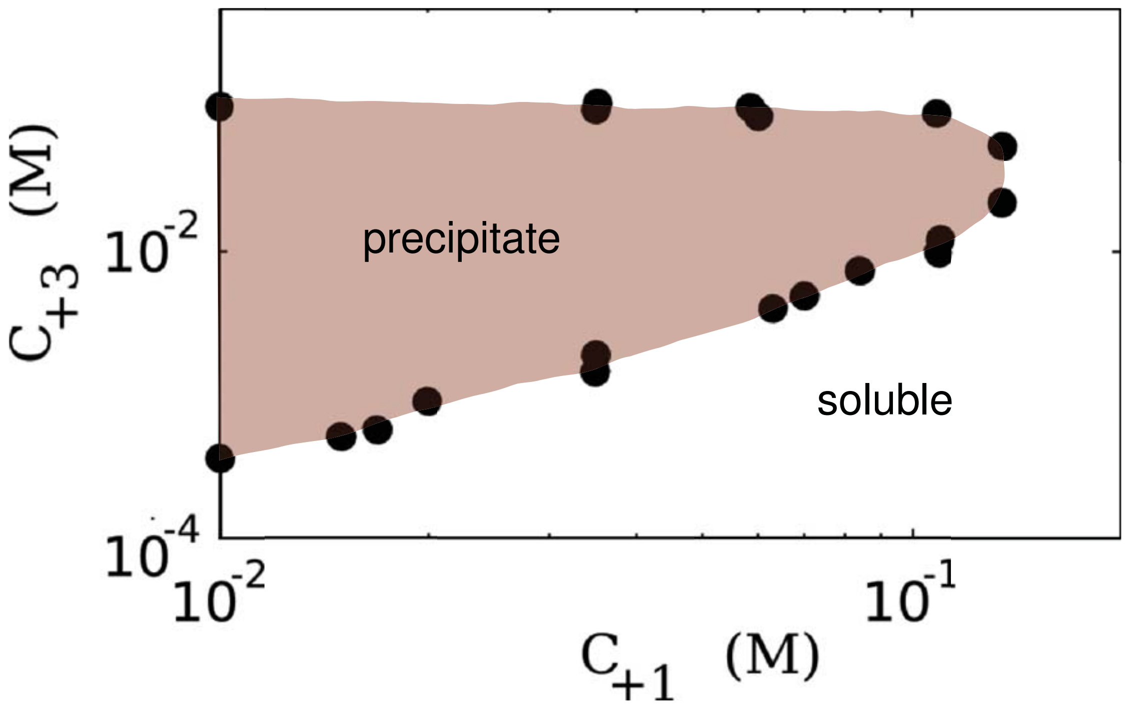


Mean-field Prediction vs. Experiment



Todd and Rau, Nuc. Acids Res., 2008

Modeling Previously Measured Phase Diagrams

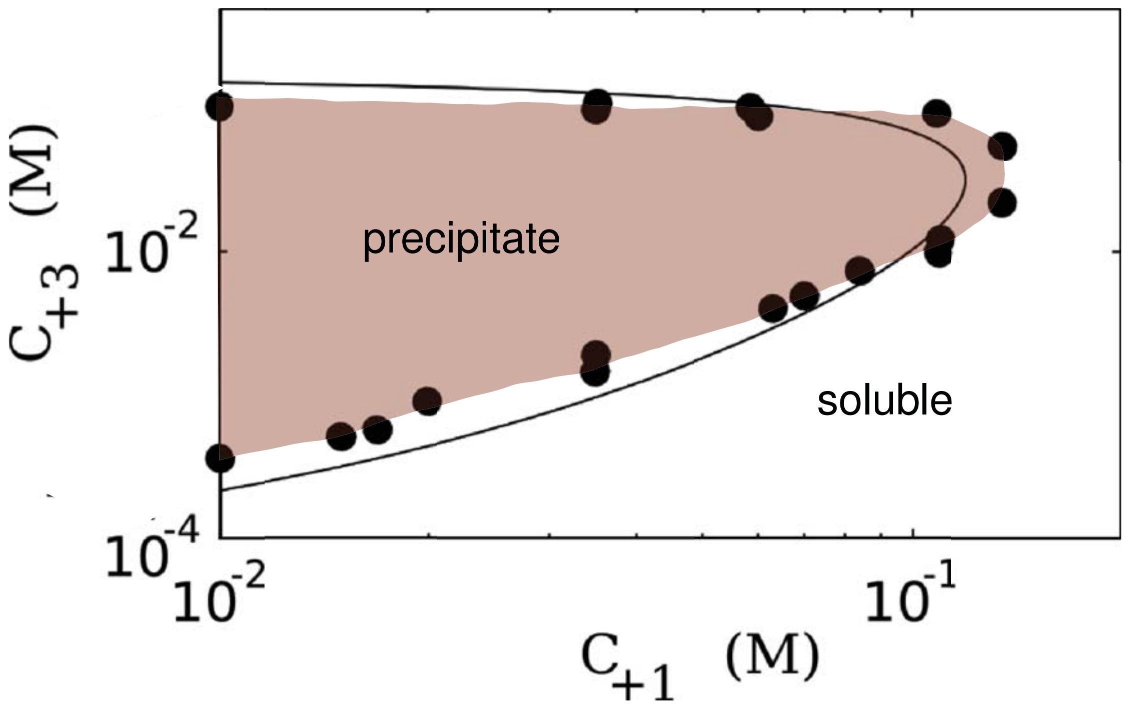


Raspaud et al., Biophys. J., 1998

$$d \triangle G = - \triangle n_{3+} d\mu_{3+} - \triangle n_{2+} d\mu_{2+} - \triangle n_{1+} d\mu_{1+}$$

$$0 = -\triangle n_{3+} d\mu_{3+} - \triangle n_{2+} d\mu_{2+} - \triangle n_{1+} d\mu_{1+}$$

Mean-field Prediction of Phase Diagram



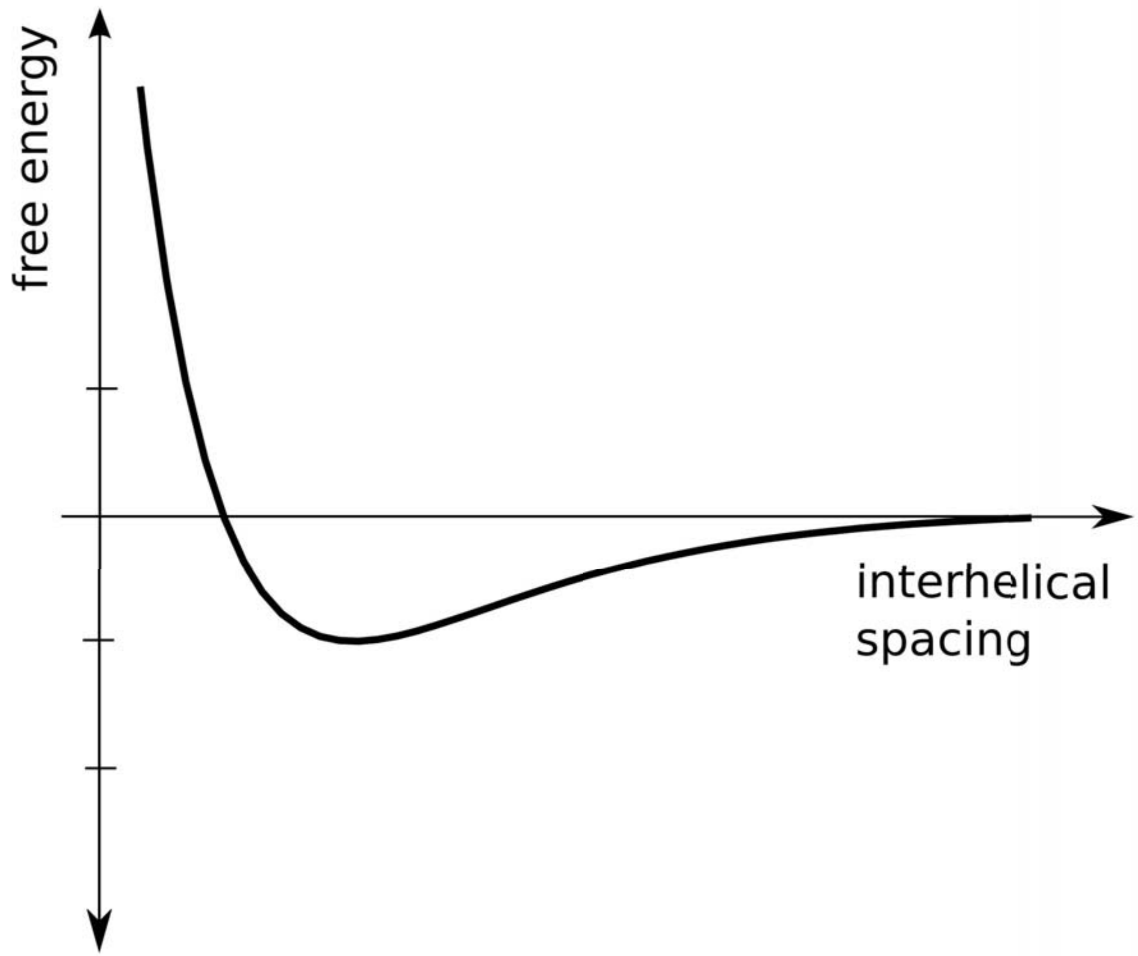
Raspaud et al., Biophys. J., 1998; Todd and Rau, Nuc. Acids Res., 2008

Part I - Conclusion

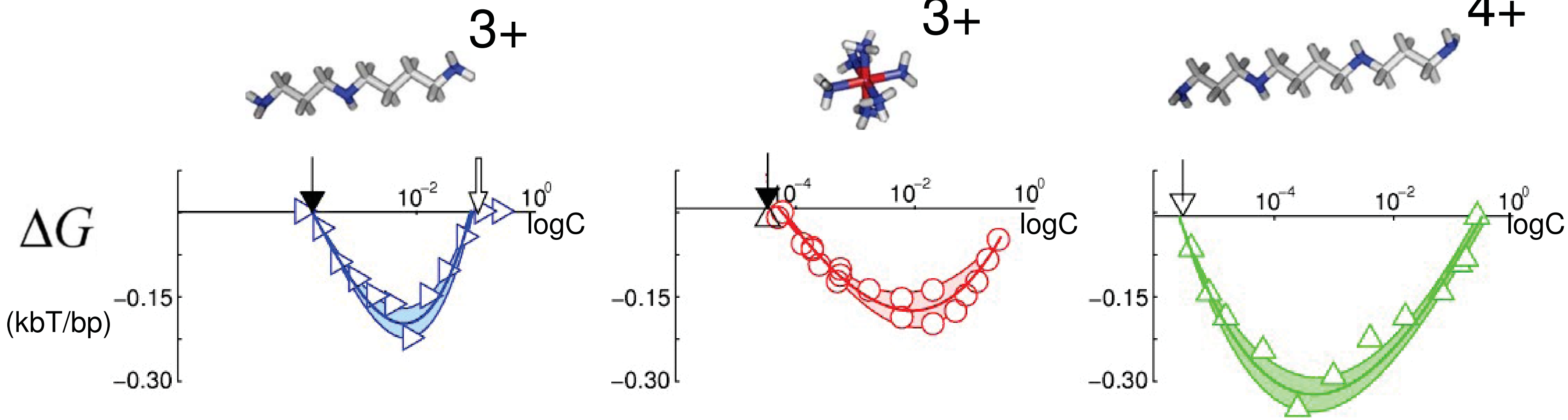
Resolubilization of DNA is caused by Bjerrum pairing.

The effect can be described quantitatively using traditional mean-field polyelectrolyte models (e.g. Manning condensation).

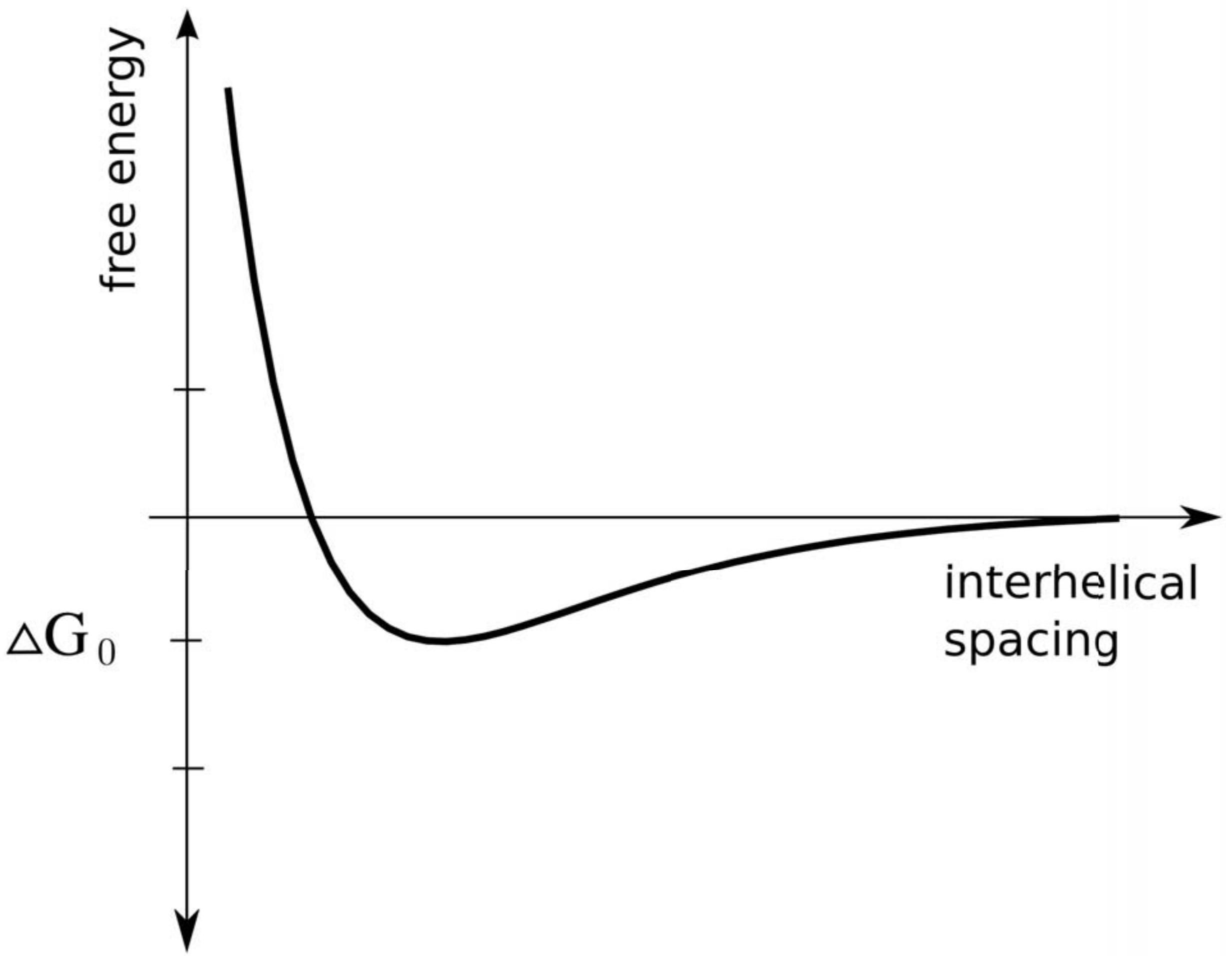
What are the interactions that drive condensation?



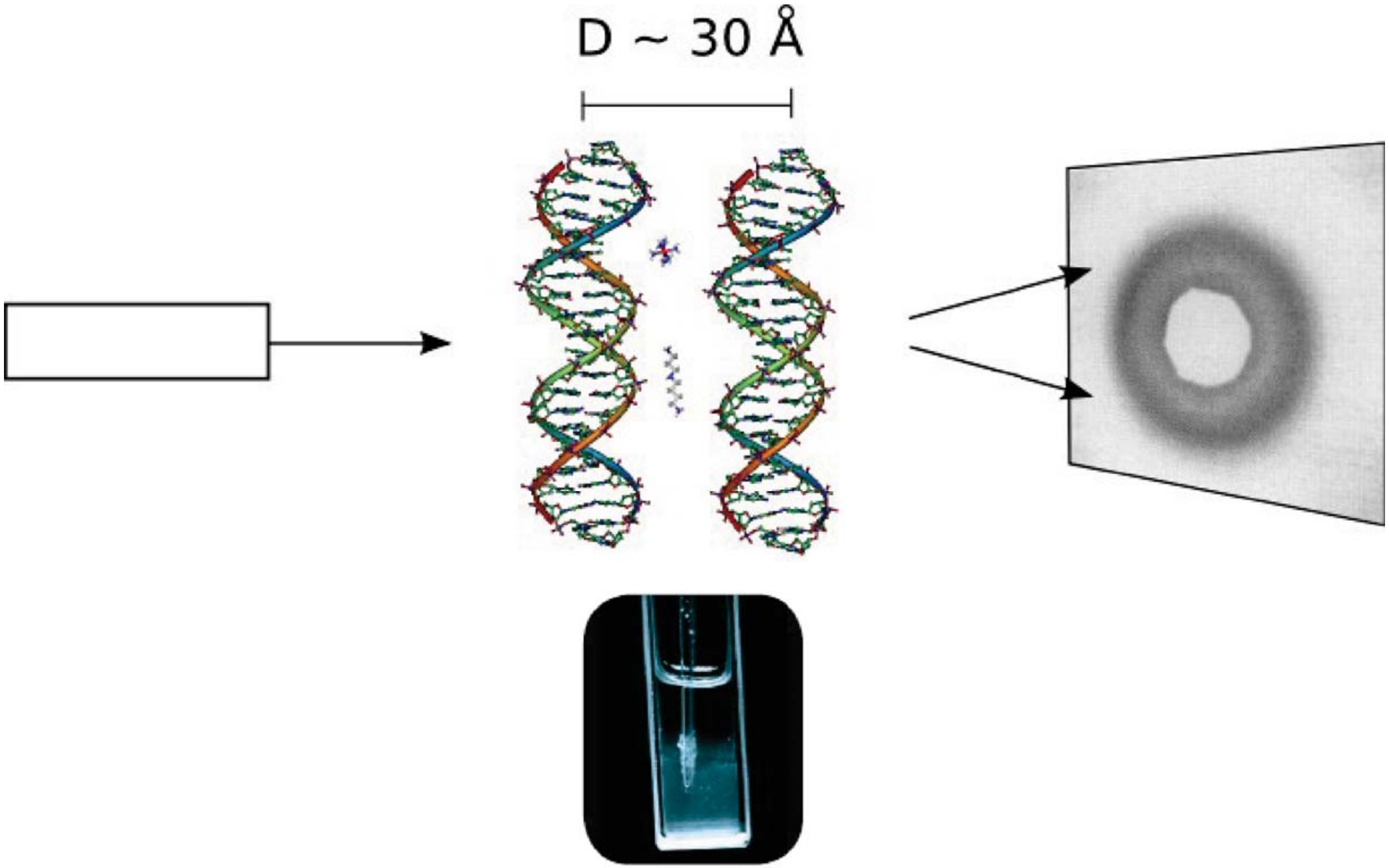
$$\Delta G(C) = \Delta G_0 + \Delta G_{ion-binding}(C)$$

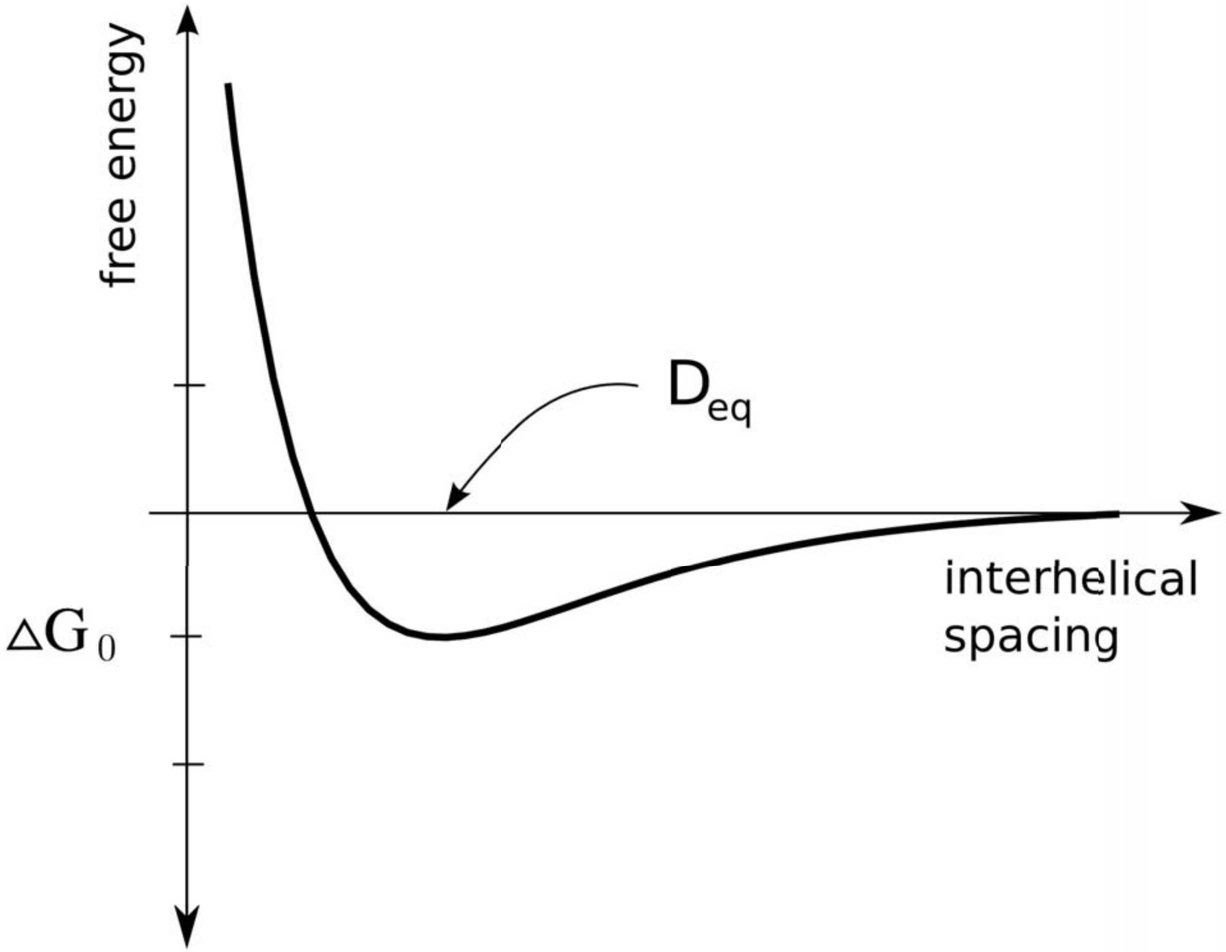


	ΔG_0, k_bT/bp
$Co(NH_3)_6Cl_3$	-0.21 ± 0.02
Spermidine	-0.20 ± 0.02
Spermine	-0.33 ± 0.03
sp^{6+}	-0.38 ± 0.04

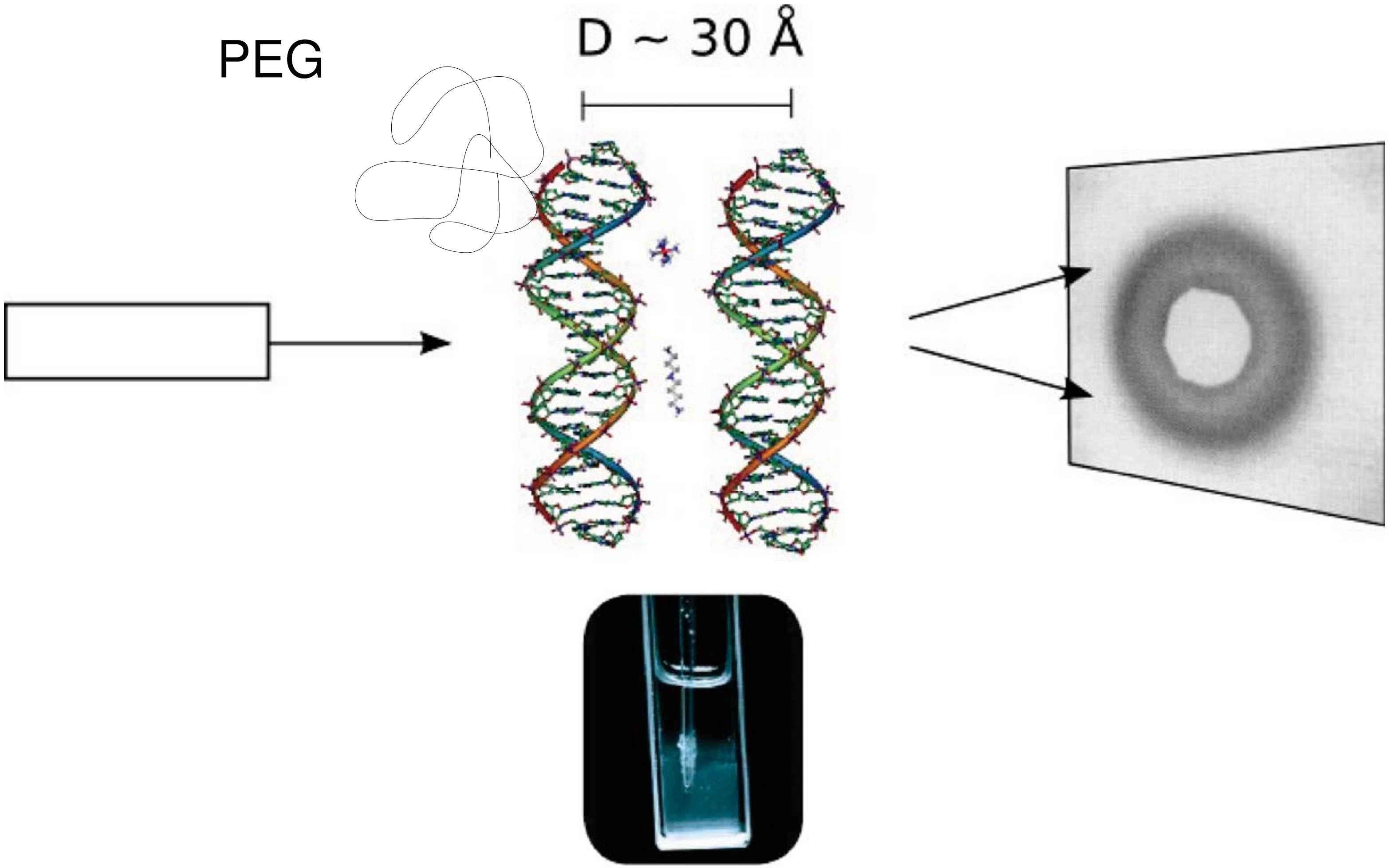

free energy
ΔG_0
interhelical
spacing

X-ray diffraction

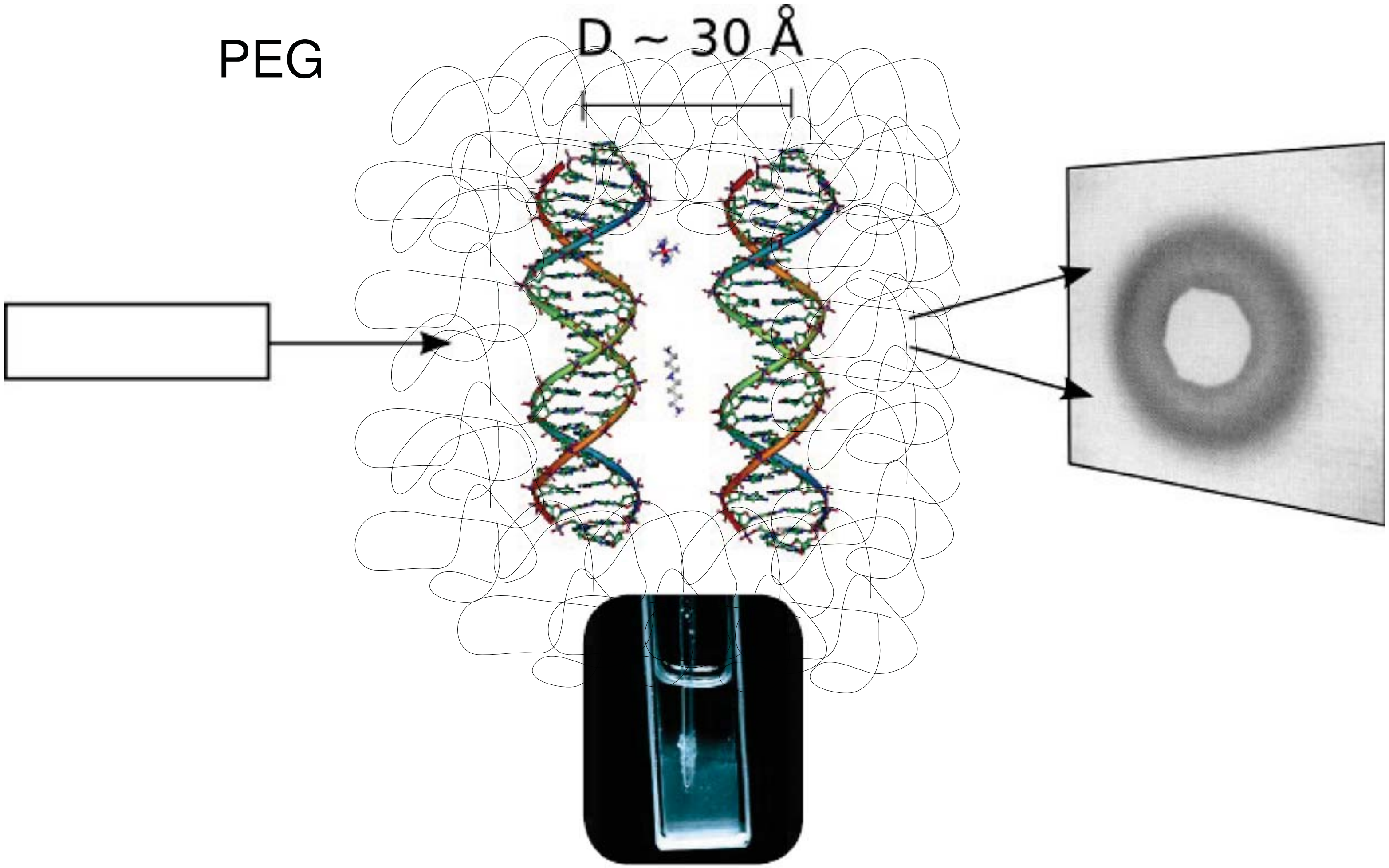


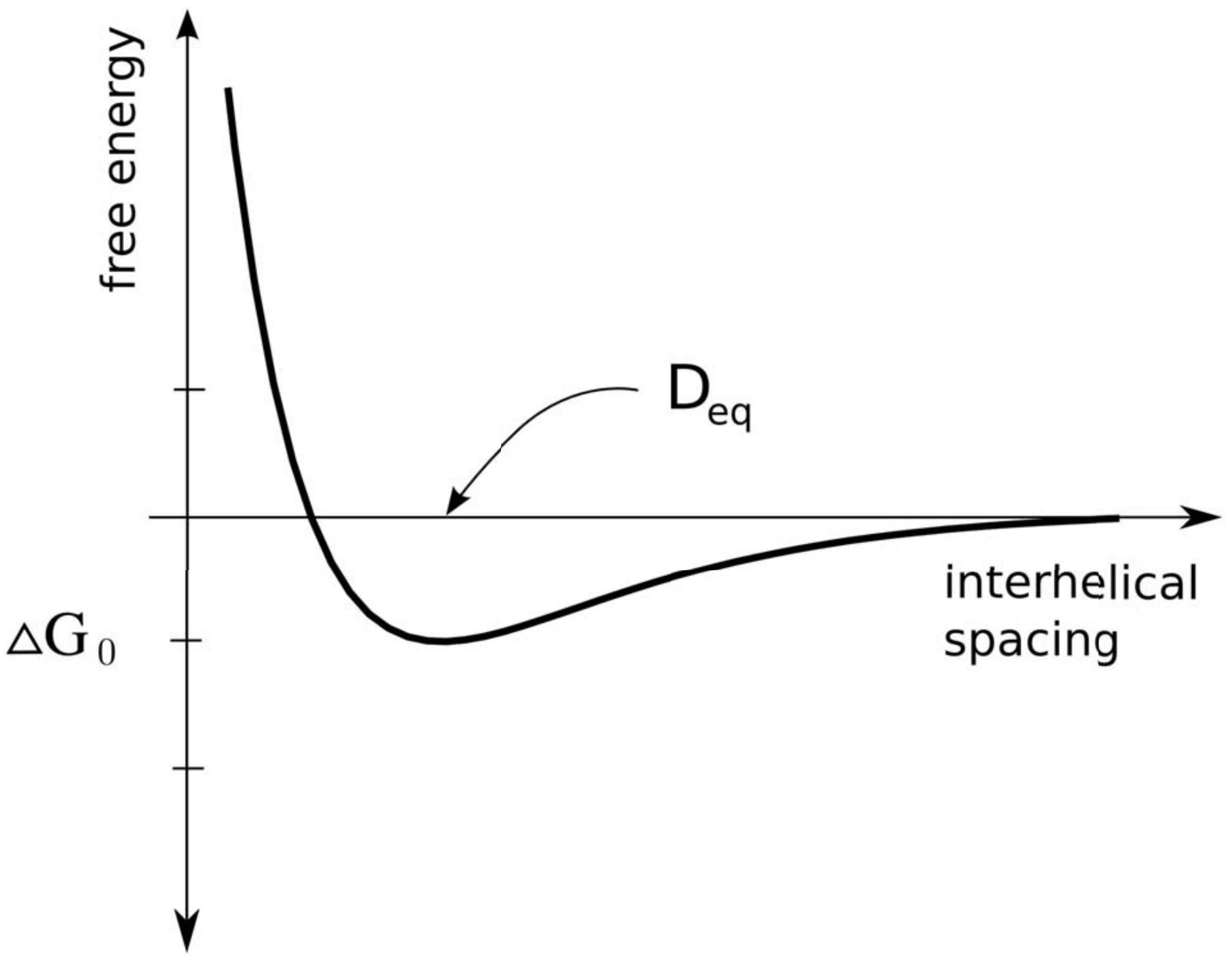

free energy
D_{eq}
interhelical
spacing
$\triangle G_0$

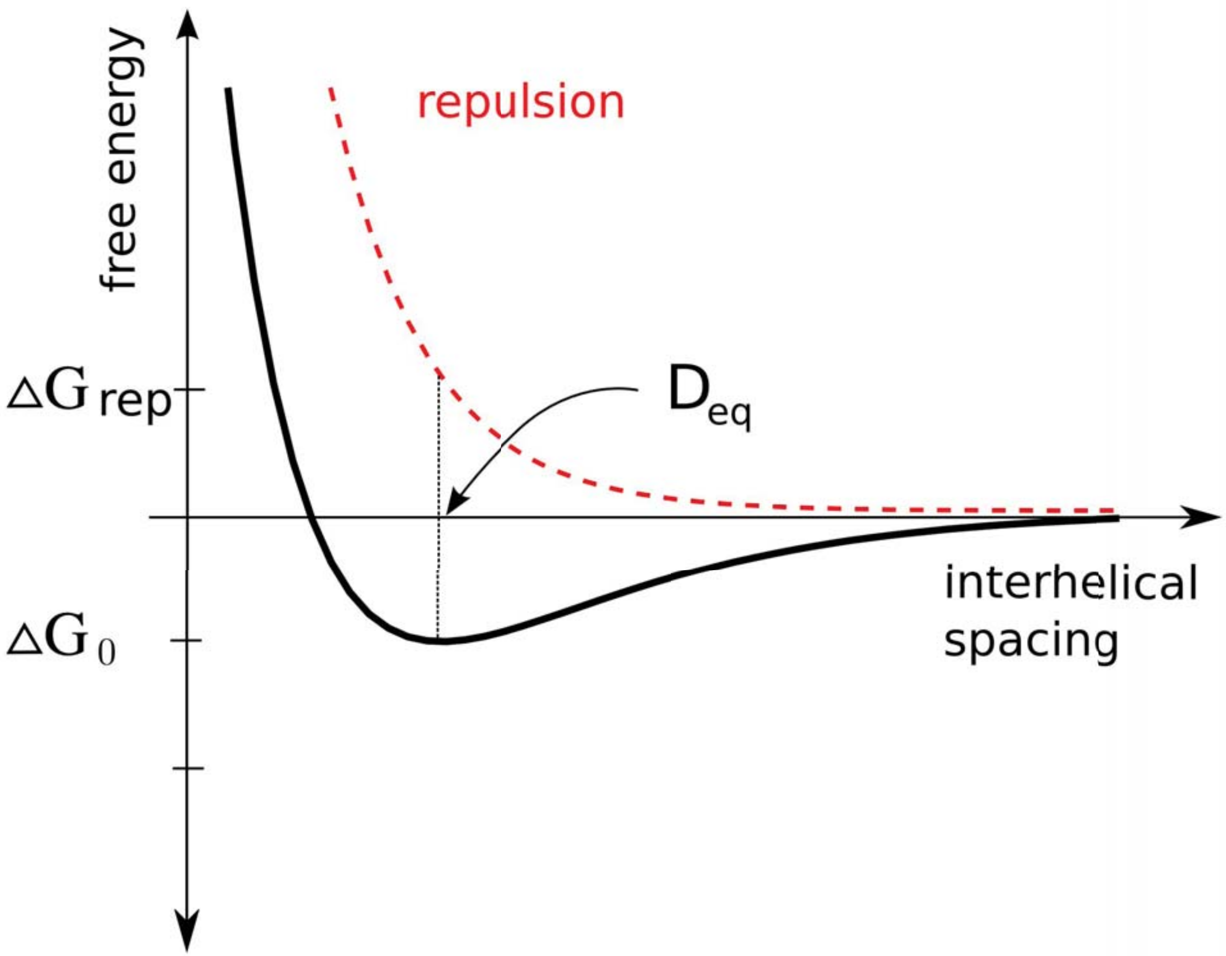
Osmotic Stress



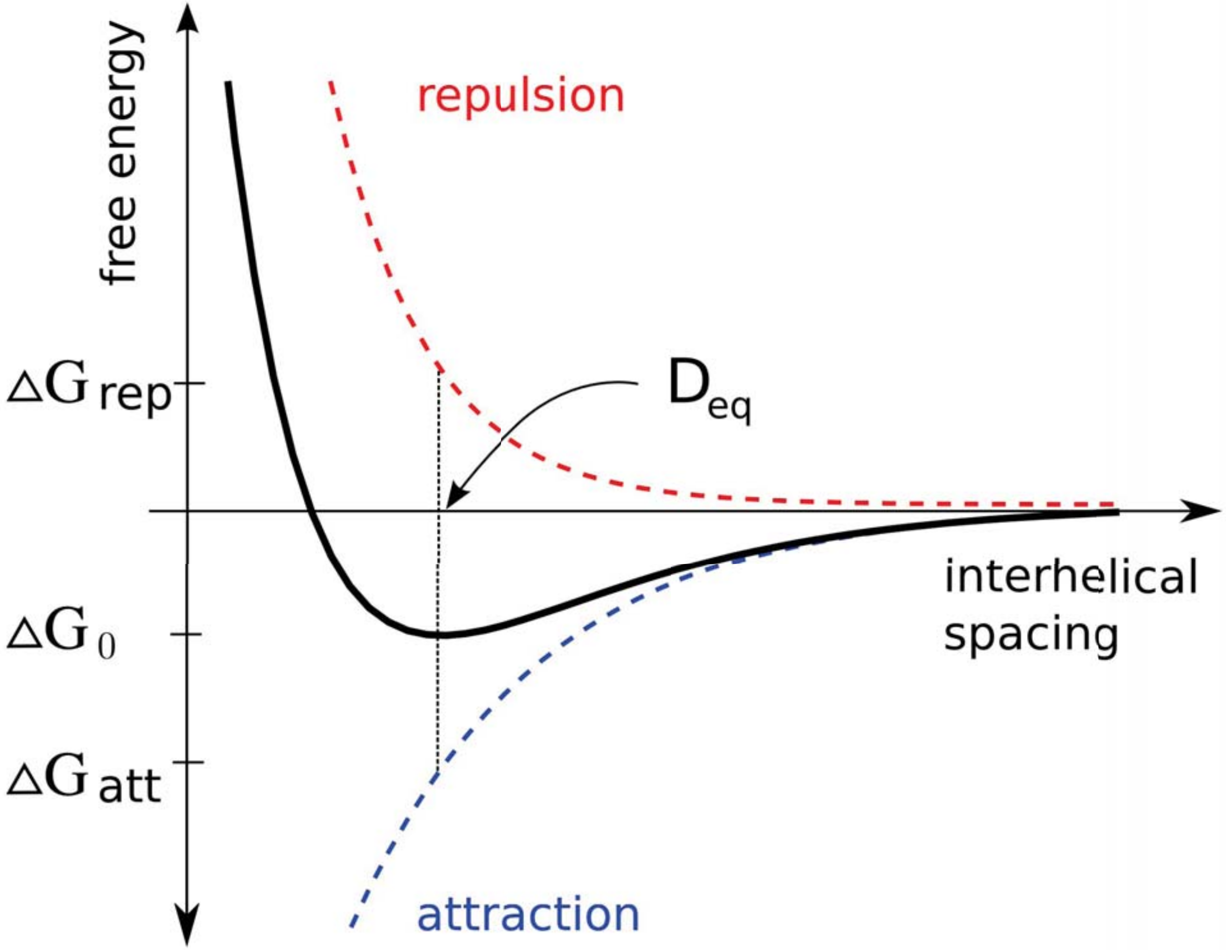
Osmotic Stress



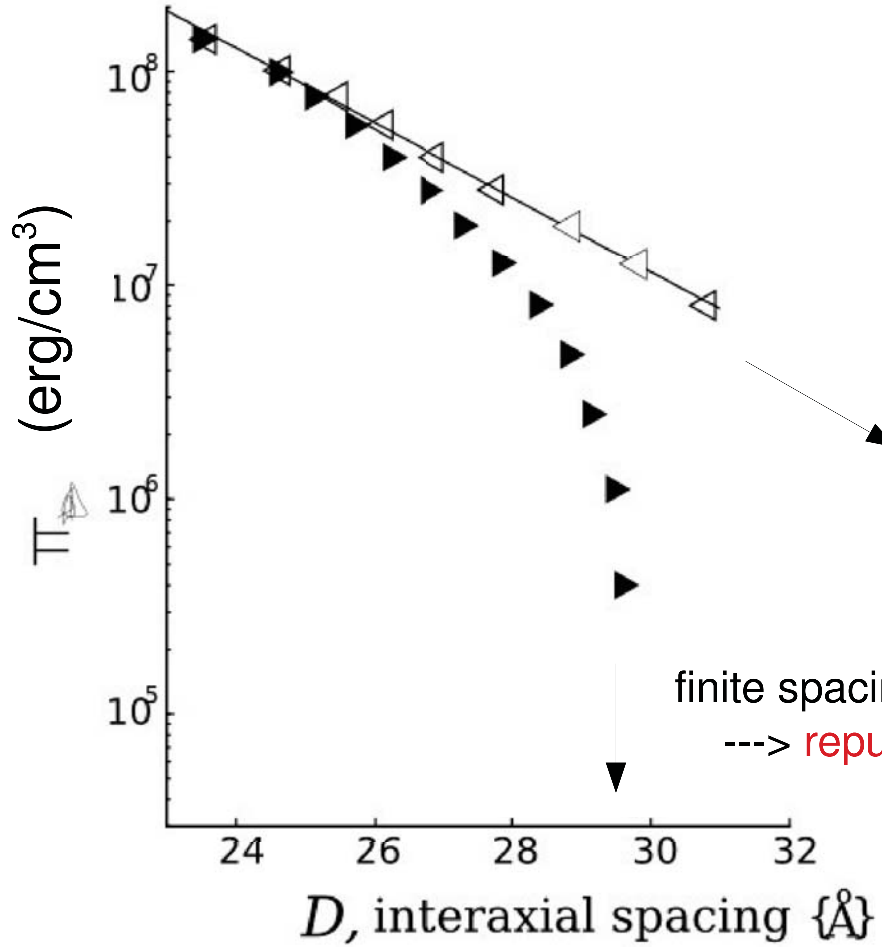

free energy
D_{eq}
$\triangle G_0$
interhelical spacing

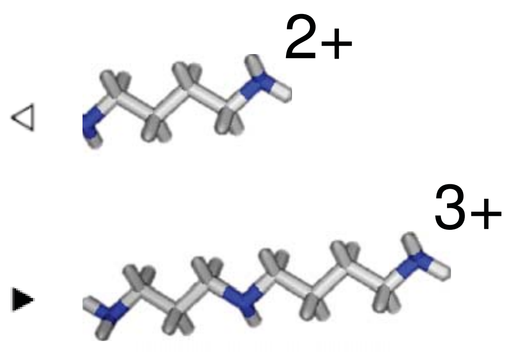


free energy
repulsion
ΔG_{rep}
D_{eq}
ΔG_0
interhelical
spacing


free energy
repulsion
ΔG_{rep}
D_{eq}
ΔG_0
interhelical spacing
ΔG_{att}
attraction

Common 2.3 Å exponential repulsion

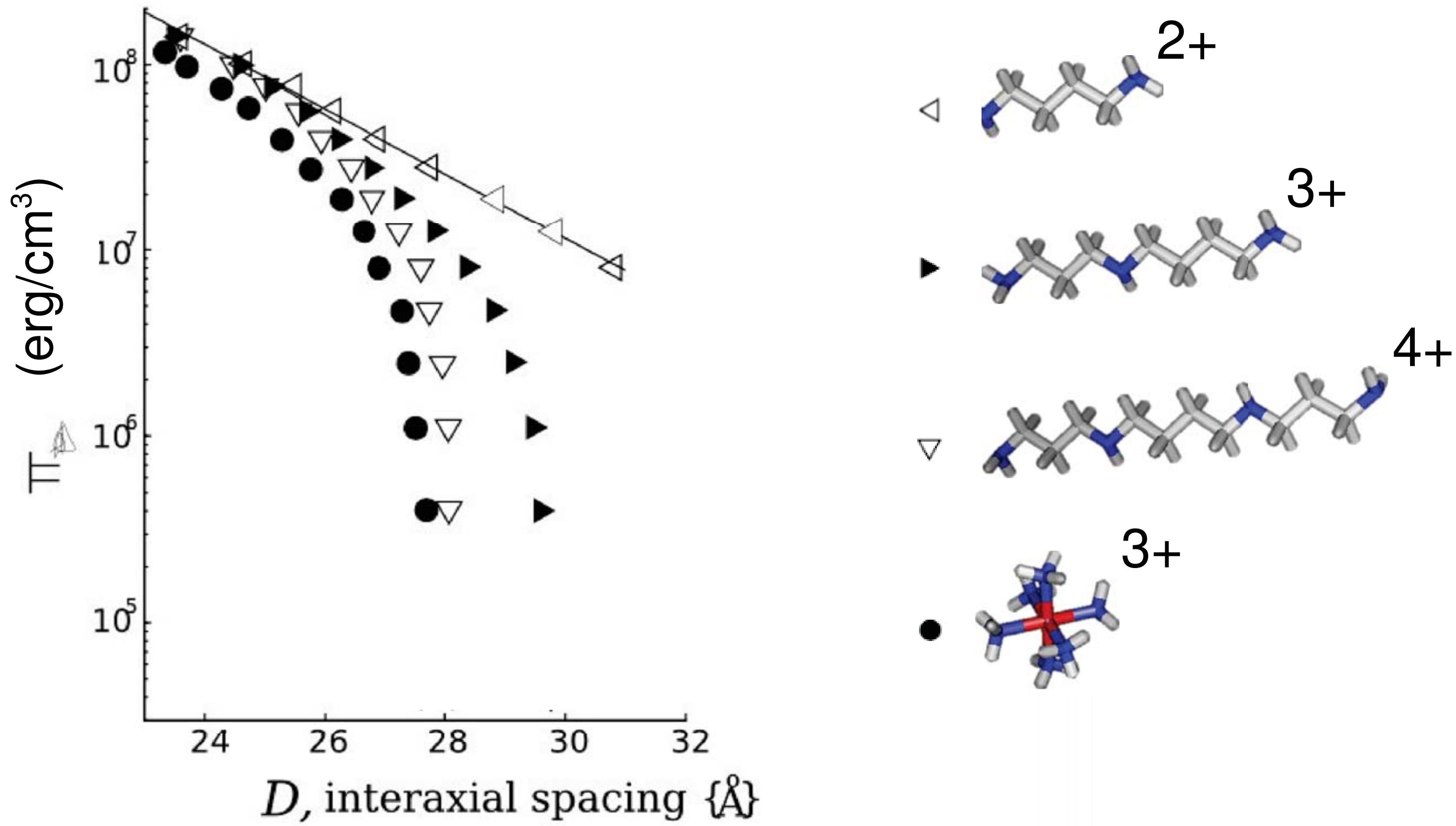


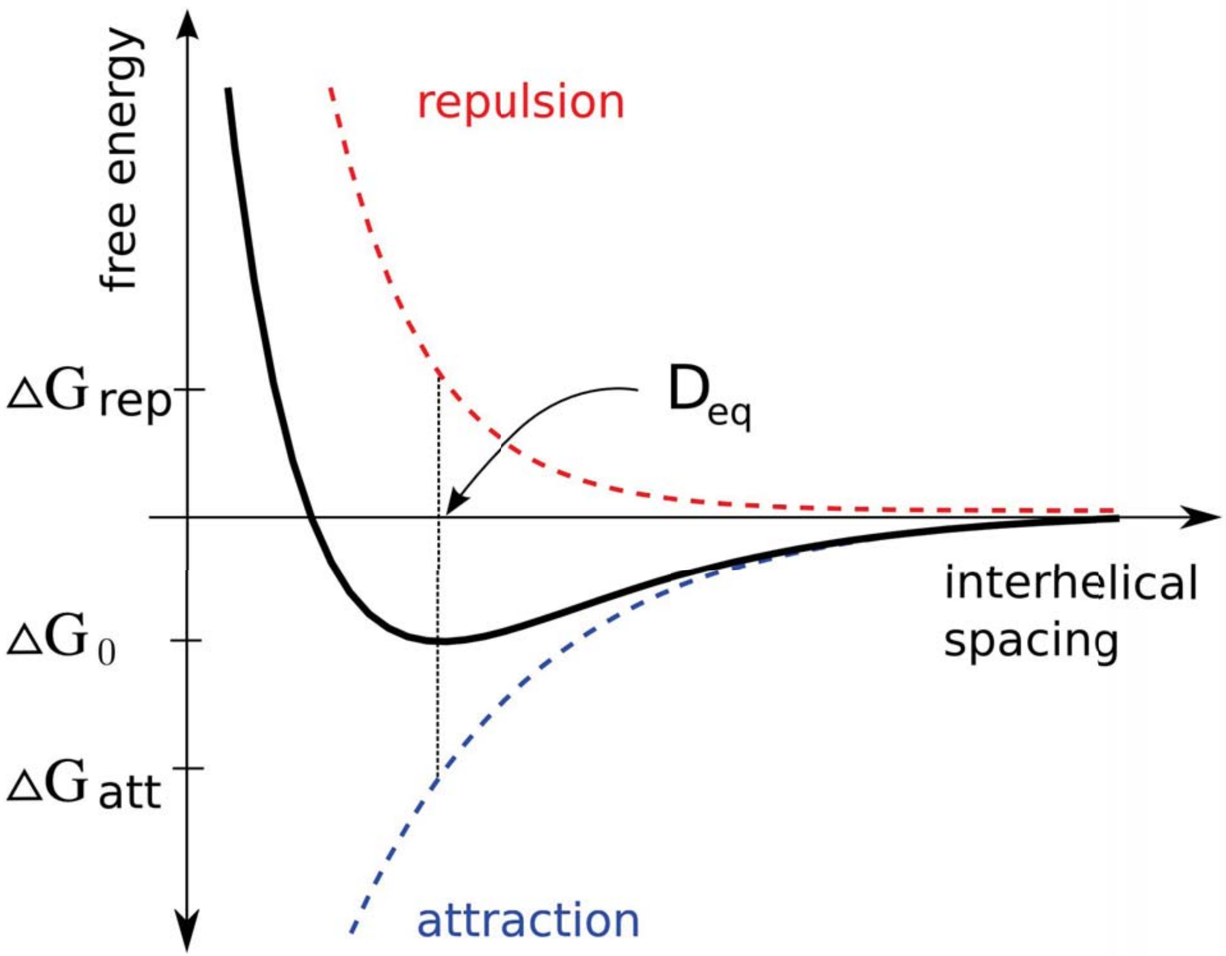


infinite spacing at zero pressure
---> pure repulsion

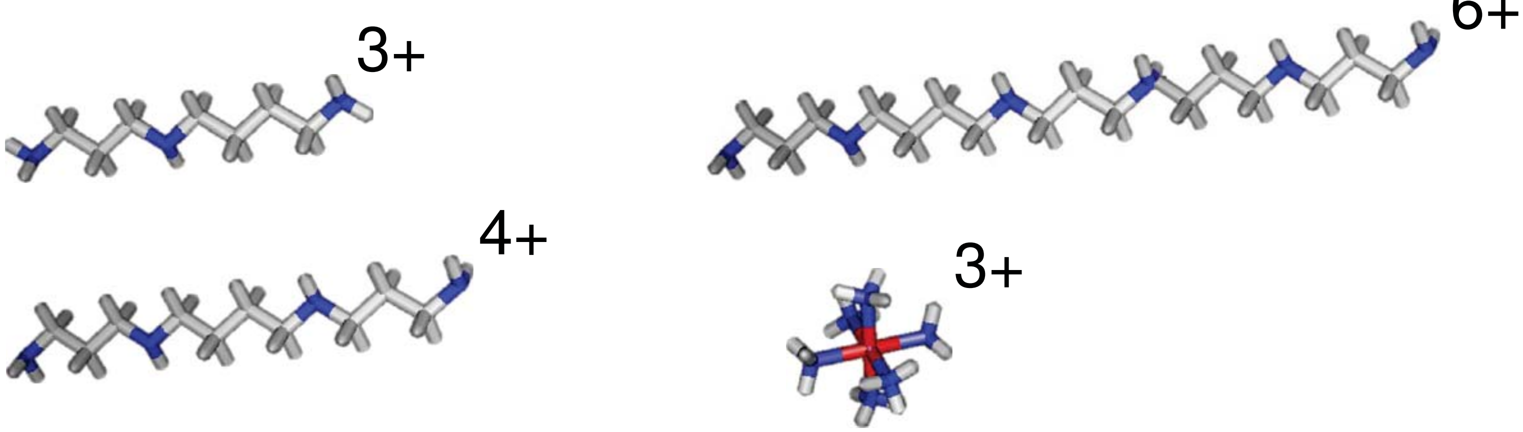
finite spacing at zero pressure
---> repulsion and attraction

Common 2.3 Å exponential repulsion




free energy
repulsion
ΔG rep
D eq
interhelical spacing
ΔG 0
ΔG att
attraction

So, for these polycations ...



... we introduced two constraints on possible theories.

$$\lambda_{rep} \approx 2.3 \text{ Å}$$

$$\frac{\Delta G_{att}}{\Delta G_{rep}} \approx 2$$

Todd, Rau, Parsegian et al., Biophys. J., 2008

If we assume exponential attractions ...

$$\frac{\Delta G_{att}}{\Delta G_{rep}} = \frac{\int_{\infty}^{D_{eq}} \Pi_{att}\, dD}{\int_{\infty}^{D_{eq}} \Pi_{rep}\, dD} = \frac{\int_{\infty}^{D_{eq}} A e^{-D/\lambda_{att}}\, dD}{\int_{\infty}^{D_{eq}} \mathrm{R} e^{-D/\lambda_{rep}}\, dD} = \frac{\Pi_{att}\lambda_{att}}{\Pi_{rep}\lambda_{rep}} = \frac{\lambda_{att}}{\lambda_{rep}}$$

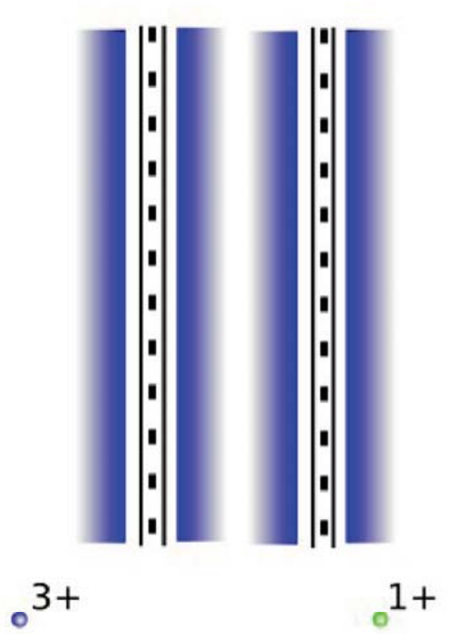
$$\lambda_{att} = \frac{\Delta G_{att}}{\Delta G_{rep}} \lambda_{rep}$$

$$= 4.8 \pm 0.5\ \text{Å}$$

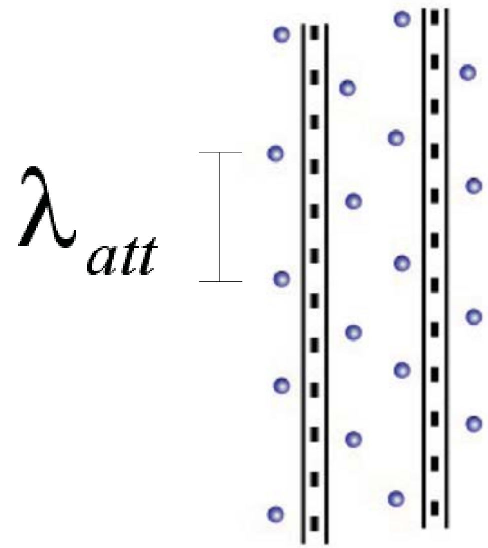
... we get a characteristic length-scale for attractions.

Characteristic Length

Mean-field picture



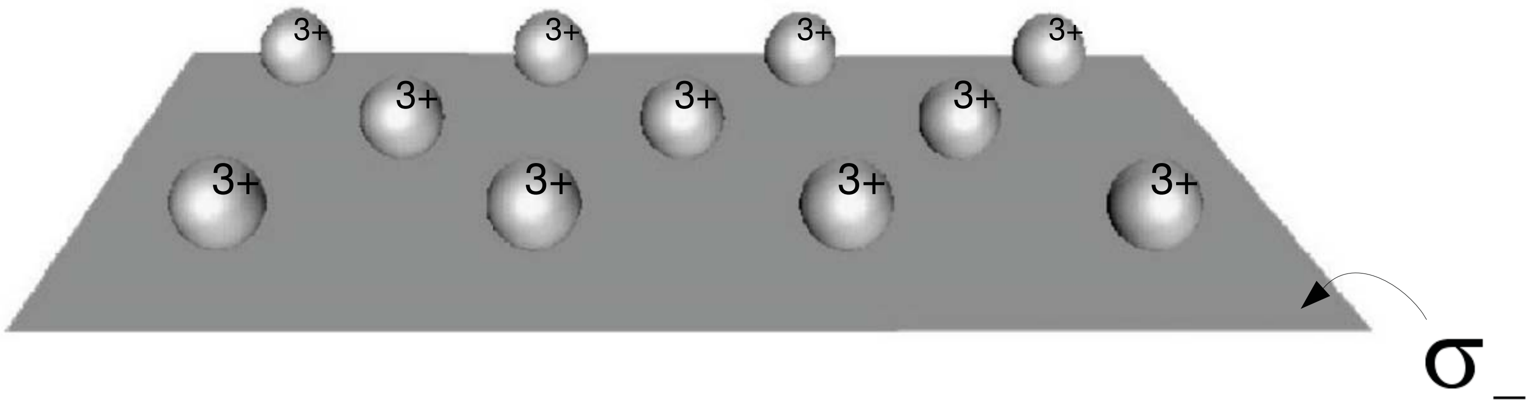
Structured



Guoy-Chapman (1910), Debye-Huckel (1923), Onsager-Manning-Oosawa (1969), Poisson-Boltzmann

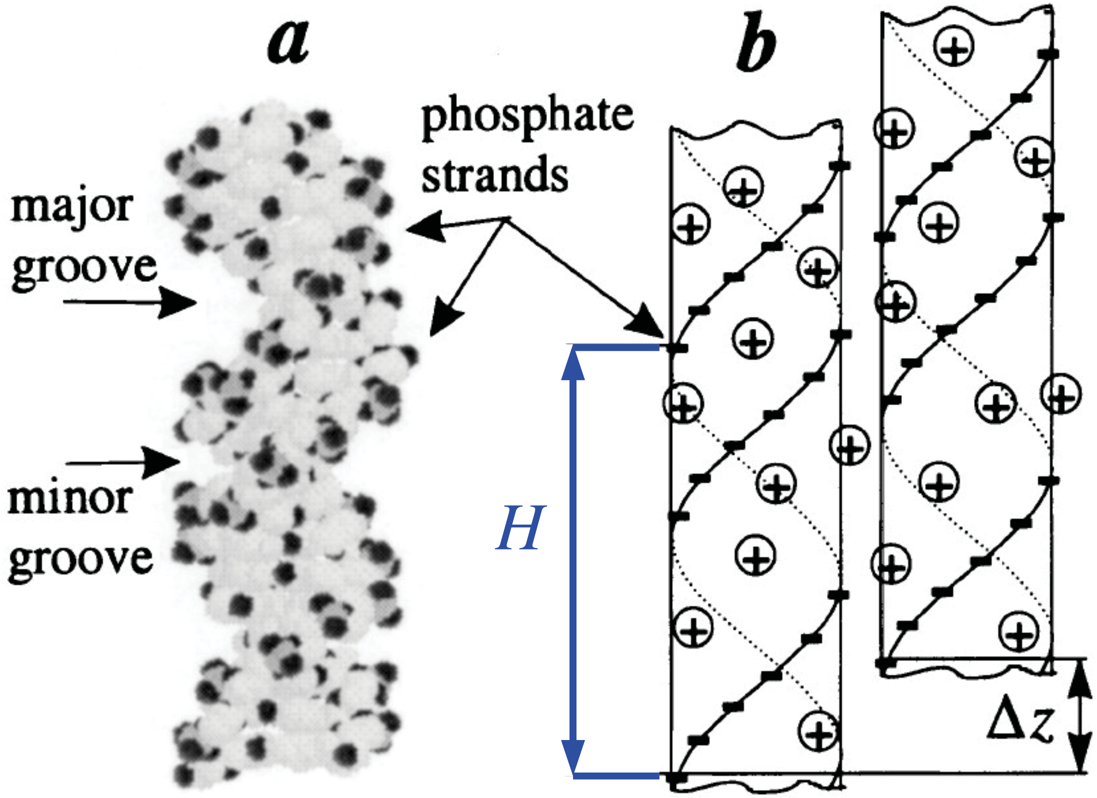
Counterion correlations

ion valence	λ_{att} , Å
+3	2.8
+4	3.2
+6	4.0



Shklovskii, *PRL*, 1999, Rouzina, *Biophys. J.* 1996, Grosberg, et al, *Rev. Mod. Phys.*, 2004

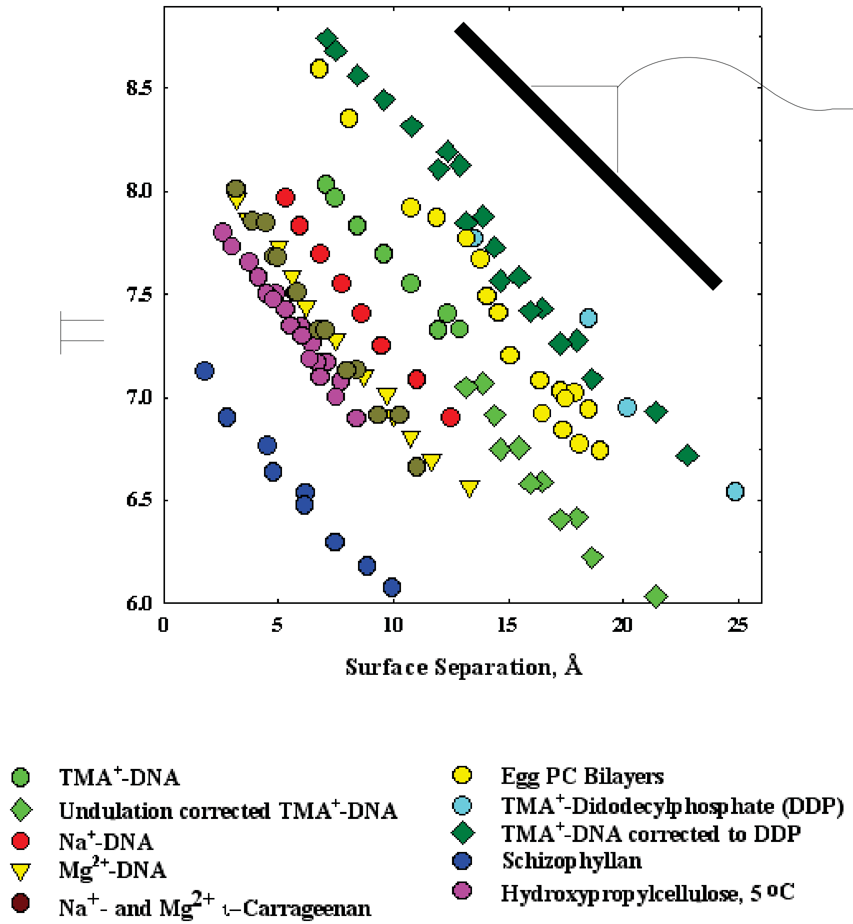
Helical Interactions



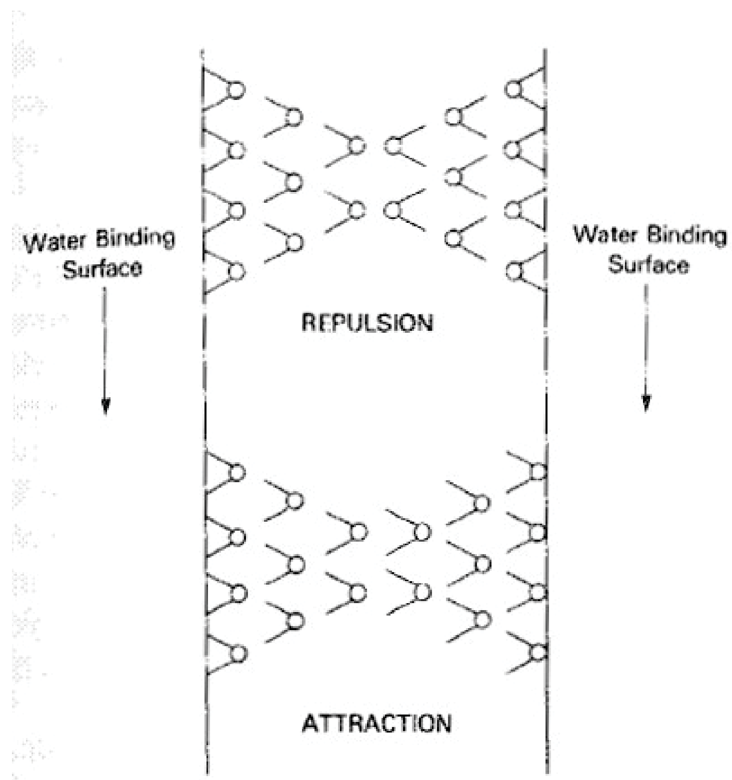
$$\lambda_{att} = \frac{H}{2\pi} = 5.4\ \text{Å}$$

Kornyshev and Leikin, *PRL*, 1999

Hydration Forces



λ_{water} = 3-4 Å



Parsegian, Rand, Rau, *Chemica Scripta*, 1985; Rau and Parsegian, *Biophys. J*, 1992.

Part II - Conclusions

2.3 Å characteristic length-scale for counterion-mediated repulsions.

Repulsive magnitude depends only on the chemical composition and not the valence of the counterion.

4.8 Å characteristic length-scale for counterion-mediated attractions.

Acknowledgments

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Daniel Harries
Nina Sidorova
Horia Petrache

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Thanks

Other Slides

Integrate over distance to get reversible work