Counterion Mediated DNA-DNA Interactions

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DNA Interactions are Mediated by Counterions

Kurtz, 2008
Multivalent Ions Cause Attractions

spermine$^{4+}$

picture from Dai et al, PRL, 2008
Precipitation of DNA by Multivalent Cations

\[ d \Delta G = - \Delta n_{3+} d\mu_{3+} \]

Pelta et al., Biophys. J., 1997; Raspaud et al., Biophys. J., 1998
Resolubilization of DNA by Multivalent Cations

\[ d \Delta G = - \Delta n_{3+} d\mu_{3+} \]

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\[ d \Delta G = - \Delta n_{3^+} d \mu_{3^+} \]

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

\[ \Delta G \, dl \]

\[ dl \]

\[ f \]
Compaction Against a Force

\[ \Delta G dl + f dx = 0 \]
Force $\sim$ Free Energy/Length

\[ \Delta G \Delta l + f dx = 0 \]

\[ \Delta G \sim -f \]
Bulk (Arrows) vs. Single-molecule

\[ \Delta G \left( \frac{k_B T}{bp} \right) \]

\[ \log C_{3+} \ (M) \]

-0.2
-0.1
0.0
0.1
0.2

- $10^{-4}$
- $10^{0}$

spermidine
Bulk (Arrows) vs. Single-molecule

\[ \Delta G = - \Delta n_{3+} d\mu_{3+} \]
Modeling Concentration Dependence

extended/soluble \xleftrightarrow{\Delta n_{3^+}} \text{ compact/precipitate}
Condensate Neutralized by $+3$

$n = 1$ spermidine$^{3+}$ per 3 DNA phosphate$^{1-}$

$\Delta n_{3+}$

extended/soluble

compact/precipitate
Soluble Phase Modeled by Mean-field Theory

$n$ according to Manning – Oosawa theory

$n = 1$ spermidine$^{3+}$ per 3 DNA phosphate$^{1-}$

$\triangle n_{3+}$

extended/soluble

compact/precipitate
\[ d \triangle G = - \triangle n_{3+} d\mu_{3+} \]
Mean-field Prediction vs. Experiment

\[ \Delta G (k_B T/bp) \]

\[ \log C_{3+} (M) \]

- Red: Manning Model
- Blue dots: spermidine
Theories for Resolubilization

Besteman and Lemay, 2007
Shklovskii, PRL, 1999

Counterion correlations,
Wigner Crystals,
Overcharging

Golenstanian et al, PRL, 1999

Counterion fluctuations,
Debye screening

Olvera de la Cruz, 1995
Debye screening
The *anion* determines resolubilization

![Graph showing the relationship between spermidine concentration and a parameter D_average.](Image)

**Spd**\((SO_4)^{3/2}\)  
**SpdCl_3**  
**Spd(CH_3CO_2)_3**

*Yang and Rau, Biophys. J., 2005*
Trivalent Ions Not Ideal >1 mM

\[ \text{3+} + \text{Cl}^- \rightleftharpoons \text{Cl}^{2+} \]

\( K_d \sim 10-100 \text{ mM} \)

Treat Bjerrum Pair as $2^+$ Species

$3^+ + \text{Cl}^- \rightleftharpoons 2^+$

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

\[ d \, \triangle \, G = - \, \triangle \, n_{3+} \, d\mu_{3+} \]
\[ d \triangle G = - \triangle n_{3+} d\mu_{3+} - \triangle n_{2+} d\mu_{2+} \]
Precipitation of DNA by Nonideal Multivalent Cations

extended/soluble

compact/precipitate

3+  

2+  .Cl
Mean-field Prediction vs. Experiment

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 = − Δ n_3^+ dμ_3^+ − Δ n_2^+ dμ_2^+ − Δ n_1^+ dμ_1^+
Mean-field Prediction of Phase Diagram

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?
\[ \Delta G(C) = \Delta G_0 + \Delta G_{\text{ion-binding}}(C) \]
X-ray diffraction

D ~ 30 Å
Osmotic Stress

PEG

D ~ 30 Å
Osmotic Stress
Common 2.3 Å exponential repulsion

\( \langle \text{erg/cm}^3 \rangle \)

finite spacing at zero pressure --> repulsion and attraction

infinite spacing at zero pressure --> pure repulsion

\( D, \text{ interaxial spacing} \{\text{Å}\} \)
Common 2.3 Å exponential repulsion
So, for these polycations ...

... we introduced two constraints on possible theories.

\[ \lambda_{rep} \approx 2.3 \ \text{Å} \quad \frac{\Delta G_{att}}{\Delta G_{rep}} \approx 2 \]

Todd, Rau, Parsegian et al., Biophys. J., 2008
If we assume exponential attractions ...

\[
\frac{\Delta G_{\text{att}}}{\Delta G_{\text{rep}}} = \frac{\int_{D_{\text{eq}}}^{\infty} \Pi_{\text{att}} dD}{\int_{\infty}^{D_{\text{eq}}} \Pi_{\text{rep}} dD} = \frac{\int_{D_{\text{eq}}}^{\infty} Ae^{-D/\lambda_{\text{att}}} dD}{\int_{D_{\text{eq}}}^{\infty} Re^{-D/\lambda_{\text{rep}}} dD} = \frac{\Pi_{\text{att}} \lambda_{\text{att}}}{\Pi_{\text{rep}} \lambda_{\text{rep}}} = \frac{\lambda_{\text{att}}}{\lambda_{\text{rep}}}
\]

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

\[
\lambda_{\text{att}} = \frac{\Delta G_{\text{att}}}{\Delta G_{\text{rep}}} \lambda_{\text{rep}}
\]

\[
= 4.8 \pm 0.5 \text{ Å}
\]
Characteristic Length

Mean-field picture | Structured

\[ \lambda_{\text{att}} \]

### Counterion correlations

<table>
<thead>
<tr>
<th>ion valence</th>
<th>$\lambda_{\text{att}}, \ \text{Å}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>+3</td>
<td>2.8</td>
</tr>
<tr>
<td>+4</td>
<td>3.2</td>
</tr>
<tr>
<td>+6</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Helical Interactions

Kornyshev and Leikin, *PRL*, 1999

\[ \lambda_{att} = \frac{H}{2\pi} = 5.4 \text{ Å} \]
Hydration Forces

\[ \lambda_{\text{water}} = 3-4 \, \text{Å} \]

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.
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Thanks
Other Slides
Integrate over distance to get reversible work