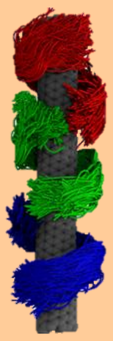
2014

Coarse-Grained DNA Modeling

Mathew Boyer

Development of a Coarse-Grained DNA Model for Bio-Nano-Interfaces



Mathew Boyer, Yajun Ding, and Jeetain Mittal

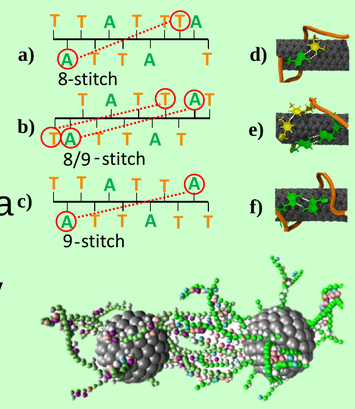
Department of Chemical Engineering, Lehigh University, Bethlehem, PA

Background

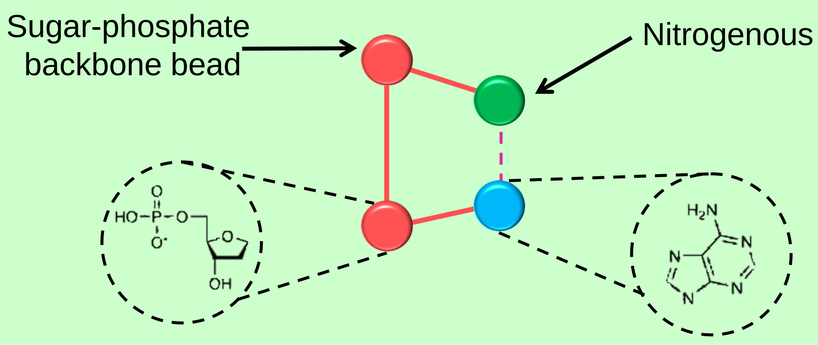
- DNA is used in a wide variety of applications and technologies including: DNA-based nanomaterials, recognition and separation of carbon nanotubes, biosensors and microarrays, and gene delivery.
- Fundamental understanding at the molecular level of the underlying phenomena is lacking, which negatively impacts our ability to control the outcome thus leaving potential for improvement which can be achieved by modeling.
- In terms of accuracy, all-atom force fields would be most appropriate, but they are not feasible for the length- and time-scales of interest for this system involving large intra- and inter-strand structural rearrangements and involving a large number of components (several DNA strands, SWCNT, solvent, and ions).
- Coarse-grained (CG) DNA models (with fewer degrees of freedom) can provide an alternative representation capable of simplifying the system.

Motivation

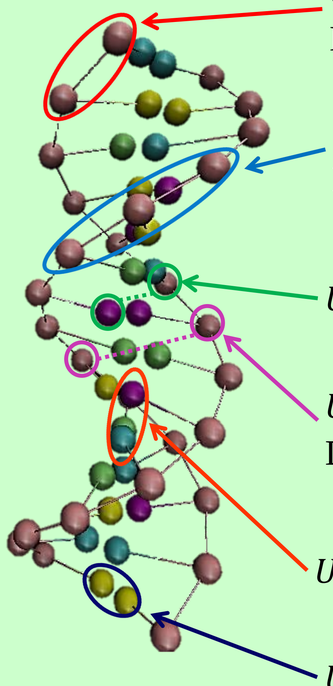
- Current models lack necessary properties to model DNA interactions at an interface.
- It is necessary to capture the effect of non-Watson-Crick base pair interactions which play a dominant role in interactions at surfaces.
- Current models lack the ability to simulate many strands.
- Fundamental understanding leads to predictive modeling to better technologies.



Model Outline



$$U_{total} = U_{bond} + U_{angle} + U_{ex} + U_{qq} + U_{st} + U_{hb}$$



$U_{bond} = K_{bond}[r - r_{eq}]^2$
Harmonic bonds

$U_{angle} = K_{angle}[\cos(\theta) - \cos(\theta_{eq})]^2$
Harmonic angle

$$U_{ex} = \begin{cases} 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] + \varepsilon, & if\ r \le r_{cut} \\ 0, & if\ r > r_{cut} \end{cases}$$

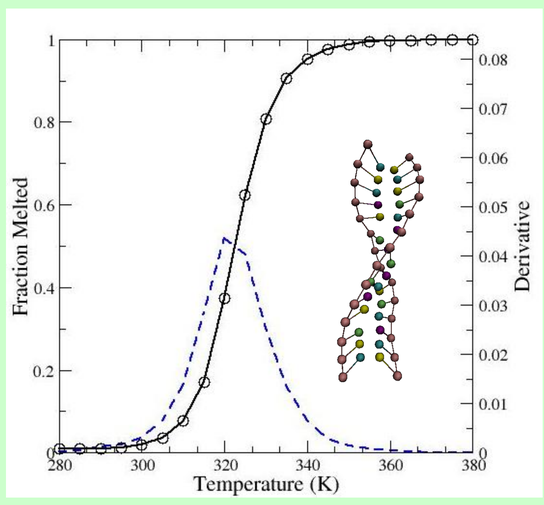
$U_{qq} = Ae^{\frac{-r}{\kappa}}$
Debye screened electrostatics

$$U_{st} = \delta_{st}\left[5\left(\frac{\sigma_{st}}{r}\right)^{12} - 6\left(\frac{\sigma_{st}}{r}\right)^{10}\right]$$

$$U_{hb} = \delta_{hb}\left[5\left(\frac{\sigma_{hb}}{r}\right)^{12} - 6\left(\frac{\sigma_{hb}}{r}\right)^{10}\right]$$

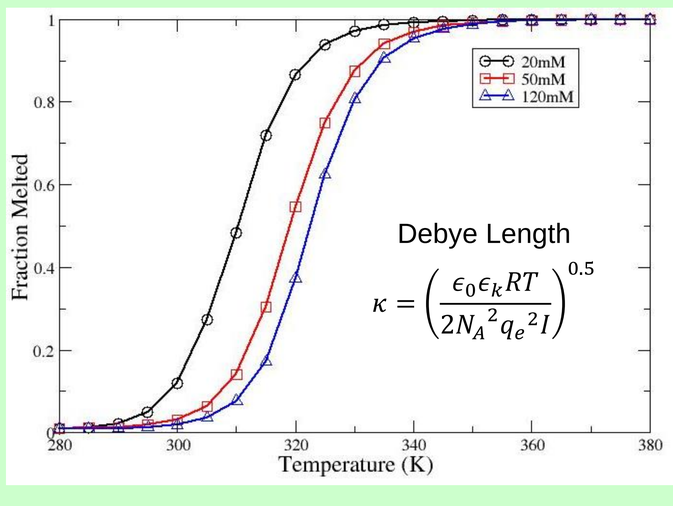
Results

DNA Hybridization



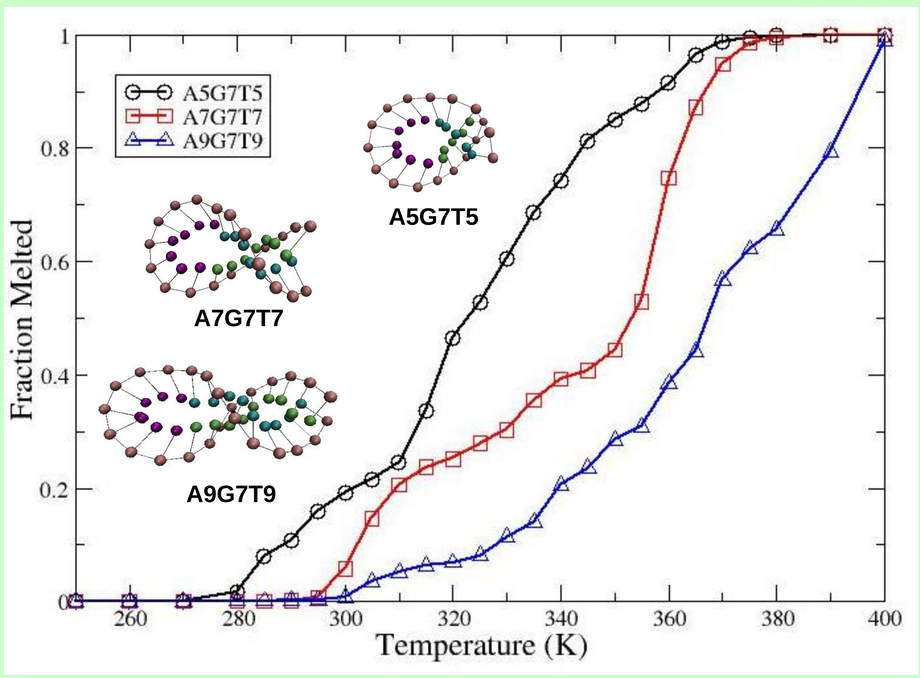
- S1:S2 (5-GCGTCATACAGTGC-3 and its compliment) form the duplex shown to the right at low temperatures.
- At high temperatures, the duplex melts.
- The melting behavior exhibits a sigmoidal shape where the inflection point represents the melting temperature.
- The maximum of the dashed derivative curve shows this point.

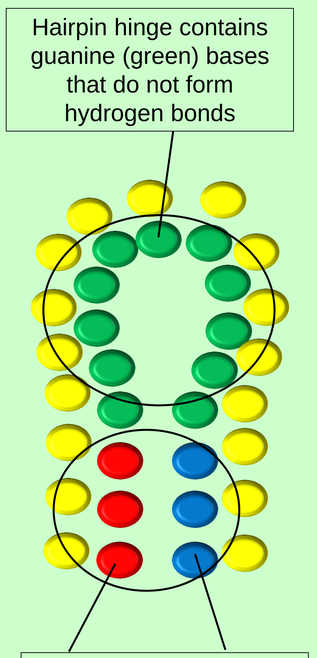
Salt Dependence of DNA Hybridization



- The plot shows the effect of salt concentration on the melting of S1:S2 dsDNA.
- The model shows the melt behavior over the $[Na]^+$ range of 20, 50, and 120mM.
- The effect of salt concentration is represented through the Debye length in the electrostatics potential applied to the backbone beads.

DNA Hairpin Melting





The plot on the left shows how melting behavior for a DNA hairpin with a hinge size of 7 bases and varying stem size. All the hairpins melt at higher temperatures than expected, but the qualitative behavior and structures are reasonable. The higher melting temperature can be explained by the isotropic nature of the hydrogen bonds which allow for one base to form up to three simultaneous bonds in a sequence that is not specific like the S1:S2 duplex tested above.

Conclusions and Future Work

The data shows that the model captures the thermodynamic properties of the duplexes, but not of the hairpins. For future applications, anisotropic hydrogen bonds must be implemented to prevent strand aggregation which should improve the thermodynamics of the hairpins. For the surface interactions of interest, non-Watson-Crick hydrogen bonds play a significant role and must be included as well.

References

1. ***Shankar, Jagota, and Mittal. Journal of Physical Chemistry B 116.40 (2012): 12088-12094***.
2. ***Boyer, Ding, and Mittal. Journal of Chemical Physics (To Be Submitted)***.