Impact of geometry optimization on base-base stacking interactions:

An energy decomposition analysis

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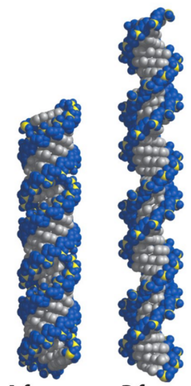
Introduction

Deoxyribonucleic acid (DNA) exists in multiple conformations, including A- and B-forms. Although both A- and B-form DNA structures are right-handed double helixes, they have obvious differences in their conformations, which changes the energetics of the helix.



A- and B-form DNA structures.[3]

(i) Energies associated with the DNA backbone and glycosidic linkage

(ii) Environmental interactions

(iii) Energies associated with base stacking.[1]

This study aimed to provide insight into the energetics of base stacking in A and B form DNA. Correlated electronic structure techniques were utilized to compute and analyze the types of energies contributions to overall stacking energy.

Computational Details

The sixteen DNA stacked dimers of both A- and B-form conformations were analyzed using symmetry-adpated perturbation theory (SAPT) in conjunction with the jun-cc-pVDZ basis set. SAPT decomposes the total interaction energy into its physically relevant components:

1. **Electrostatics**
2. **Exchange**
3. **Induction**
4. **Dispersion**

The **Net dispersion** energy was calculated as the sum of the dispersion and exchange energies.[2] PSI4 software was utilized for all SAPT computations.

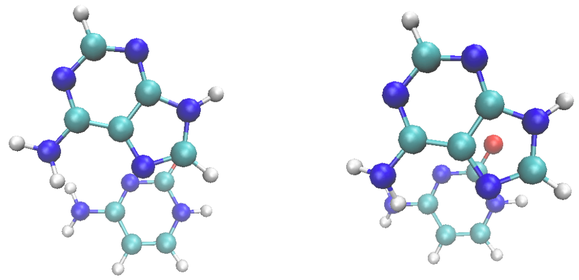
Project Goals

The analysis of the SAPT results provides insight into **why A- and B-form conformations are favored in various environments**. Evidence to support previous predictions[1] regarding dimer stability was examined, namely

I. Most A-form favorable stacked dimers will have a cytosine base present in the dimer

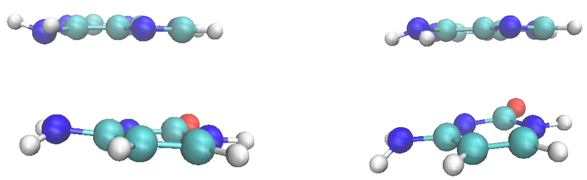
II. B-form DNA is more common on average due to favorable π-stacking interactions.

Top view of CA stacked dimer



A-form **B-form**

Side view of CA stacked dime



A-form **B-form**

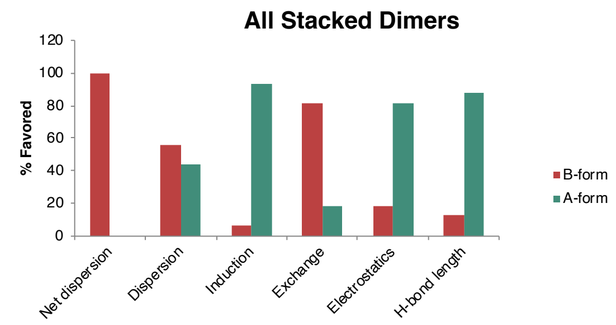
References

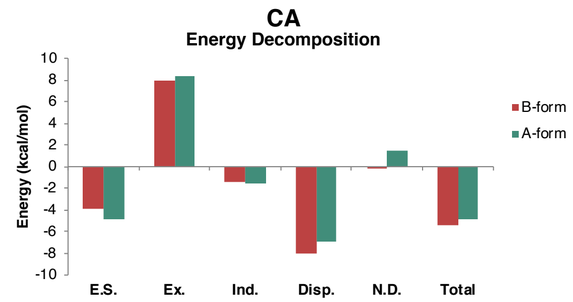
1. **Impact of Geometry Optimization on Base–Base Stacking Interaction Energies in the Canonical A- and B-Forms of DNA.** Ashley Ringer McDonald, Elizabeth J. Denning, and Alexander D. MacKerell, Jr.*The Journal of Physical Chemistry A* **2013** *117* (7), 1560-1568
2. **Effects of Heteroatoms on Aromatic π–π Interactions: Benzene–Pyridine and Pyridine Dimer.** Edward G. Hohenstein and C. David Sherrill. *The Journal of Physical Chemistry A* **2009** *113* (5), 878-88
3. **Nucleotides and Nucleic Acids.** *Breaking Biochem.* WordPress.com, 05 Apr. 2014. Web. 04 Mar. 2016.

Acknowledgements

1. Cal Poly San Luis Obispo Department of Chemistry and Biochemistry
2. Bill Frost Summer Research Program

Results





SAPT0/jun-cc-pVDZ interaction energy computed with PSI4.

Conclusions

- Net Dispersion always favors B-form, which suggested more favorable π-stacking.
  - This is consistent with π-stacking in other aromatic compounds, where parallel-displaced configurations are more favorable than sandwich configurations.[2]
- Electrostatics typically favor A-form due to more favorable hydrogen-bonding ability.
  - H-bond length in A-form is less than the H-bond length in B-form in all but one stacked dimer.
- A number of stacked dimers are more stable in the A-form all of which include a C base, with the exception of TA.[1]
  - This is consistent with previous studies showing C intrinsically favors the A-form due to stacking interactions.[1]