ADENINE-THYMINE BASE-PAIR STEP FOUR-BODY NON-ADDITIVITY CONTRIBUTION TO B-DNA: A QUANTUM MONTE CARLO STUDY

BAKASA NAMAROME CAROLYNE

S. T. Lutta, G. O. Amolo, N. W. Makau, K. Hongo & R. Maezono

University of Eldoret
flame of knowledge and innovation

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Outline

1. Inspiration
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3. Target system
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6. References
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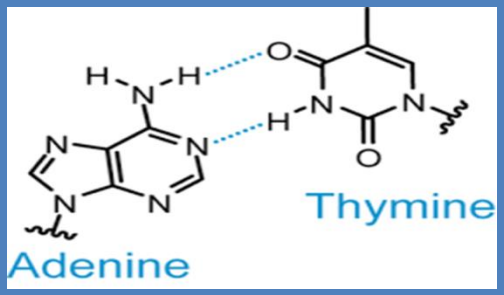
INSPIRATION

- **Watson-Crick base-pairs**

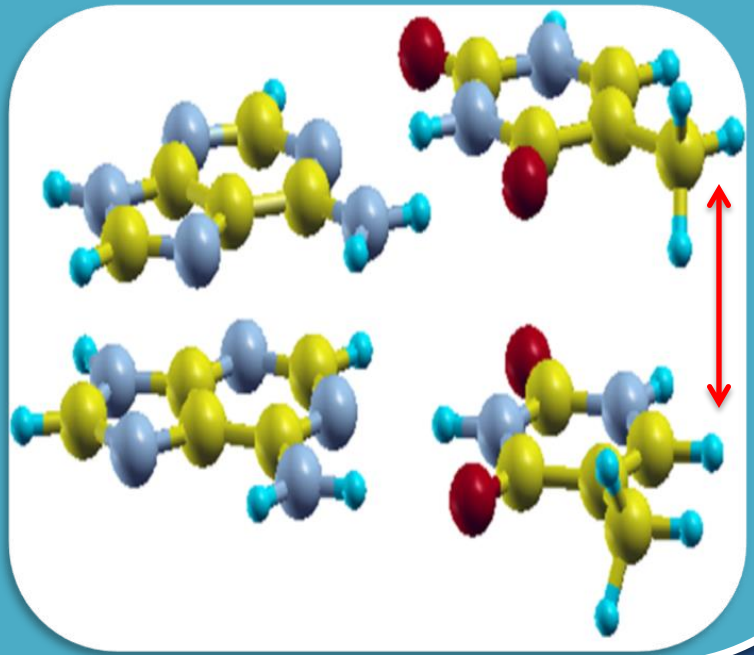


- **Base- pairs are stacked by dispersion effects.**

http://www.Structural_Biochemistry/Nucleic_Acid/DNA/DNA_structure

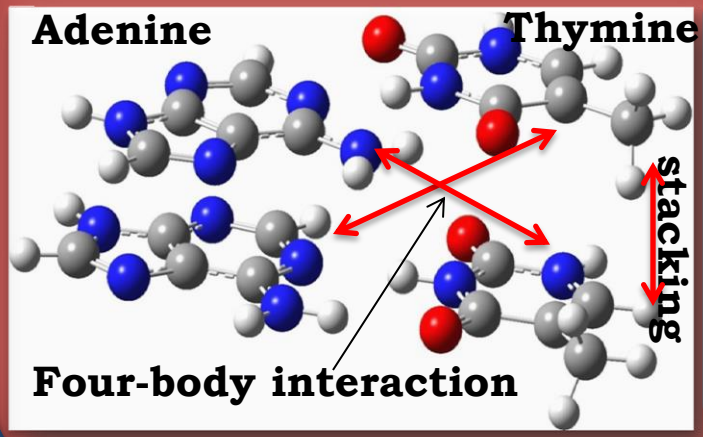
Hong *et al.*, (2013)

- **QMC can simulate correlation effects in molecules**
- **Vertical separation 3.24Å**
- **Potential Energy Graphs**



INTRODUCTION

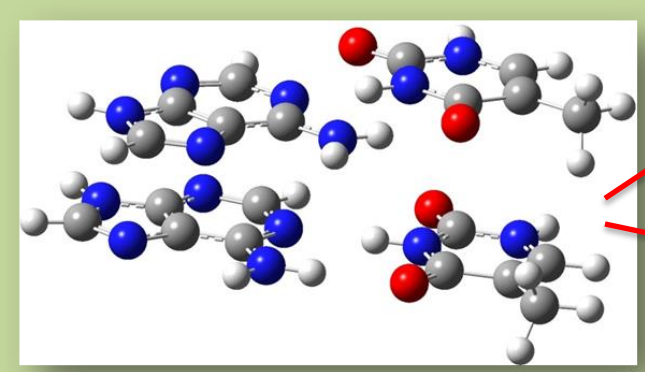
- Stacking is a non-covalent interaction
- Four-body is rarely considered in Deoxyribonucleic Acid (DNA) bases in a lot of research, yet it influences DNA dynamism Ŝponer *et al.*, (1997).

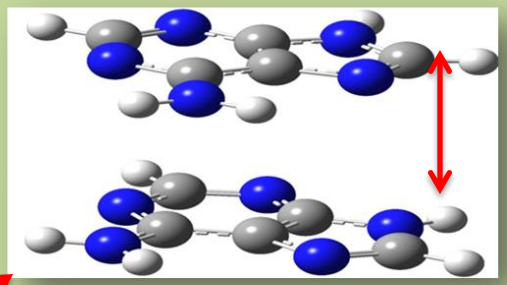


- Quantum Monte Carlo (QMC) approach can simulate correlation effects unlike Hatree-Fock and convectional function Density Functional Theory (DFT) Hong *et al.*, 2013.

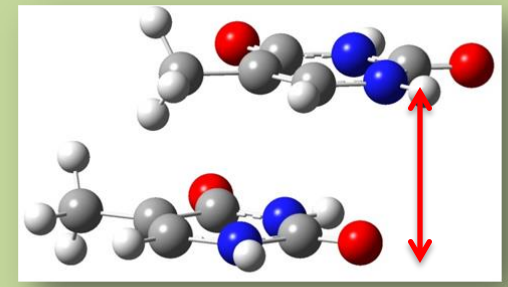
TARGET SYSTEM

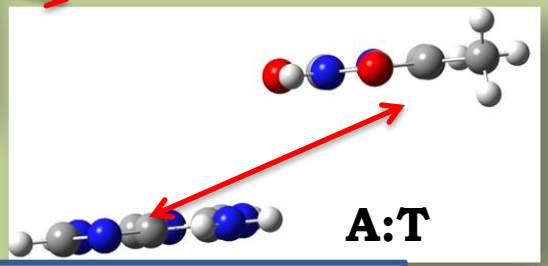
- Stacked Adenine-Thymine (AA:TT) geometries



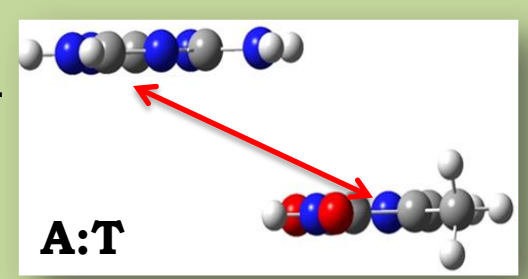


Intra-





Inter-



Tetramer → Dimers → Monomers

METHODOLOGY

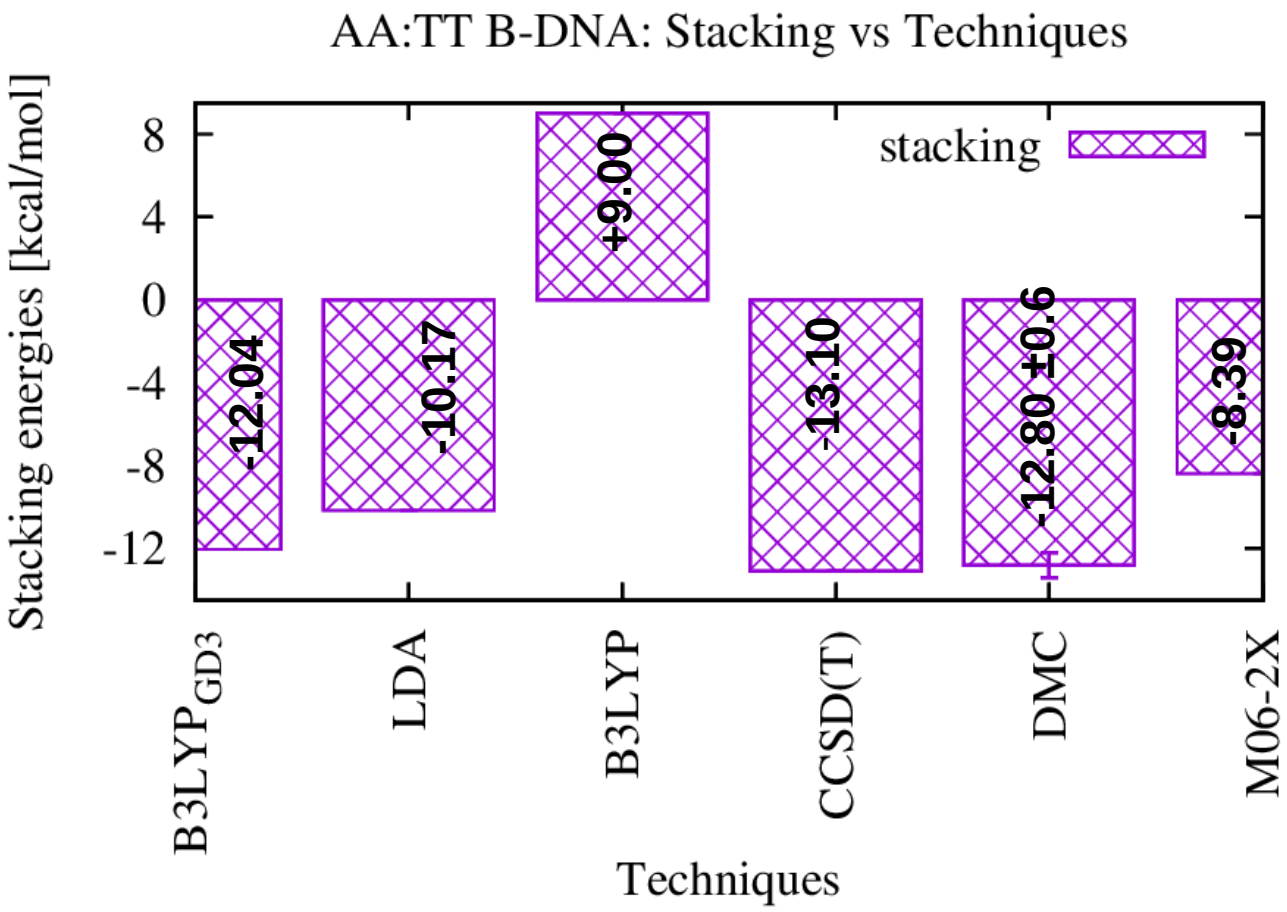
- Computation Approach
  - Gaussian 09
  - CASINO code for Quantum Monte Carlo (QMC)

- **Wavefunction**: generation of single particle orbital wave-function via the LDA/SVWN with BFD-PPs can read molecular orbitals
- **Optimization:** Variance Minimization by Jastrow factor. This is done repeatedly to find the best possible solution. One with the least possible error

- **Variational Monte Carlo:** The optimized wavefunction is used to attain the ground state total energies
- **Diffusion Monte Carlo**
  - **Configuration generation: by variance minimization ”vmc-dmc.”**
  - **DMC equilibration: period of configuration the distribution chang until all walkers are distributed based on the ground state wave-function of the molecular system.**
  - **Statistical accumulation: by propagation for a longer period of time allowing the collection of enough energy, E, having a sufficiently lower error bar**

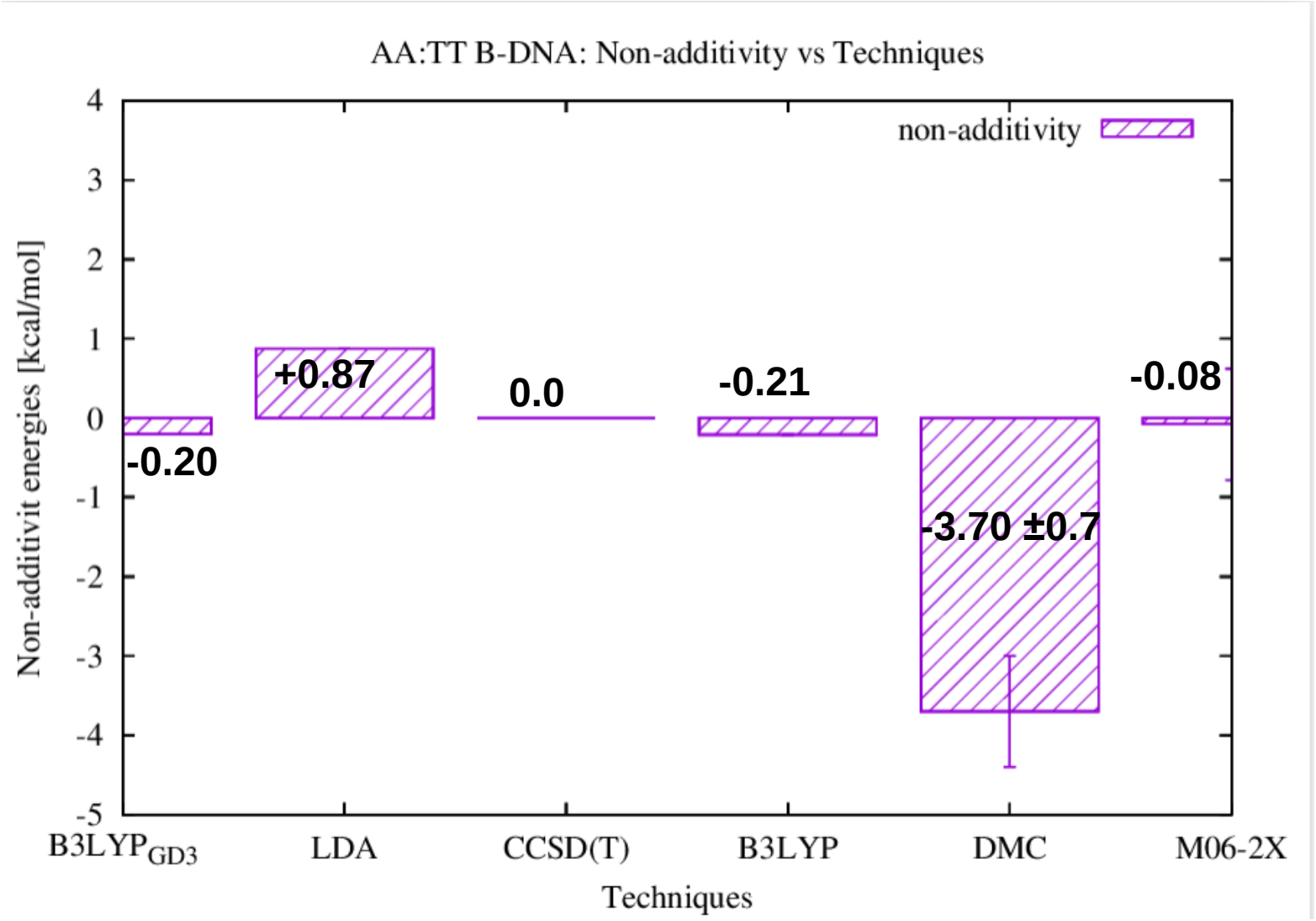
RESULTS AND DISCUSSION

Stacking



- B3LYP cannot describe correlation effects Hongo et al., (2013).
- LDA reproduces the binding energy of -10.17kcal/mol, due to not dispersion, but spurious chemical bindings (Hongo et al., 2013).
- M06-2X works with noncovalent effects, it treats the exchange term, though without dispersion correlation terms
- The B3LYP-GD3 provides for empirical dispersion of -12.04 kcal/mol and is in agreement with the CCSD(T).
- DMC approach is very close to the CCSD(T) value and provides for -12.80 kcal/mol and it includes correlation effects.

Four-body term



- QMC predicts -3.7 ±0.7kcal/mol. Provides for increased thermal stability compared to CCSD(T).
- LDA has a repulsive four-body term compared to other technique since it neglects the dispersion non-additivity.
- B3LYP, B3LYP-GD3 and M06-2X have four-body term that is agreeable with the reference CCSD(T)
- Non-additivity contributes to the total DNA stacking interactions and influences DNA dynamism.

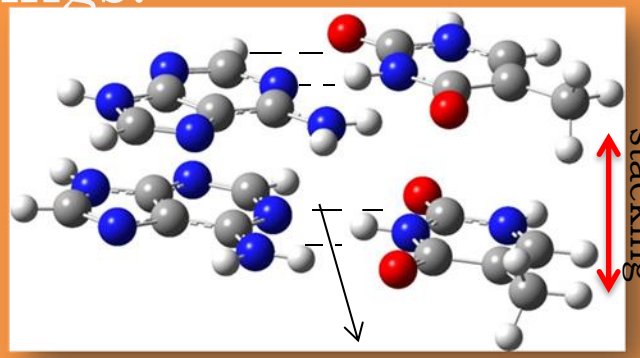
c) Binding Energies tetramer and dimers

	DFT-BSSE		QMC	
AA0/3.24	ΔE raw	ΔE corrected	ΔE	Err. bar
AA':TT'	-15.4	-12.0	-13.00	+/- 0.4
A//A'	-6.7	-4.9	-4.3	+/- 0.3
T//T'	-5.2	-3.8	-2.3	+/- 0.3

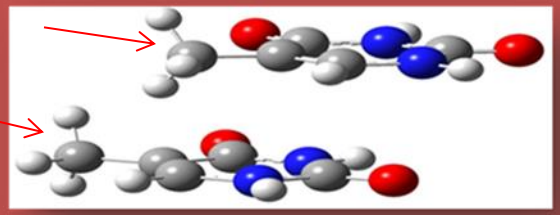
- Basis Set Superposition Error, BSSE –eliminated by counterpoise, CP method -it approximately estimates the BSSE size.
- QMC values are approximately half of the DFT simulations
- QMC approach includes the correlation effects thus improved the description of binding energies for the targeted systems

ii) Dimers A:A and T:T

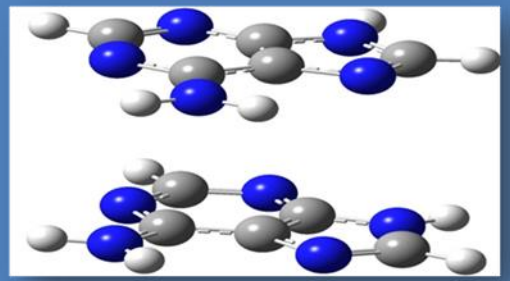
- AA':TT' most stable it experiences more interactions hence stronger bindings. -13.0 ±0.4
  - H-bonding
  - Stacking intra- & Inter-strand



- T//T less stable than A//A. The methyl group repulsion -2.3 ±0.3



- A//A binding is more stable -4.3 ±0.3



Conclusion

- ✓ QMC can provide for stacking interaction -12.80kcal/mol which agrees with the reference CCSD(T) -13.10kcal/mol
- ✓ QMC value of -3.7 ±0.7kcal/mol AA:TT four-body term predicts increased thermal stability.
- ✓ QMC also confirms that AA:TT binding energy is the most stable DNA form.

Recommendation

- ✓ Inclusion of the sugar-phosphate backbone in the study of stacking and four-body term.

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University of Eldoret

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Thank You