Guanine-Cytosine Dynamics During DNA Strand Separation

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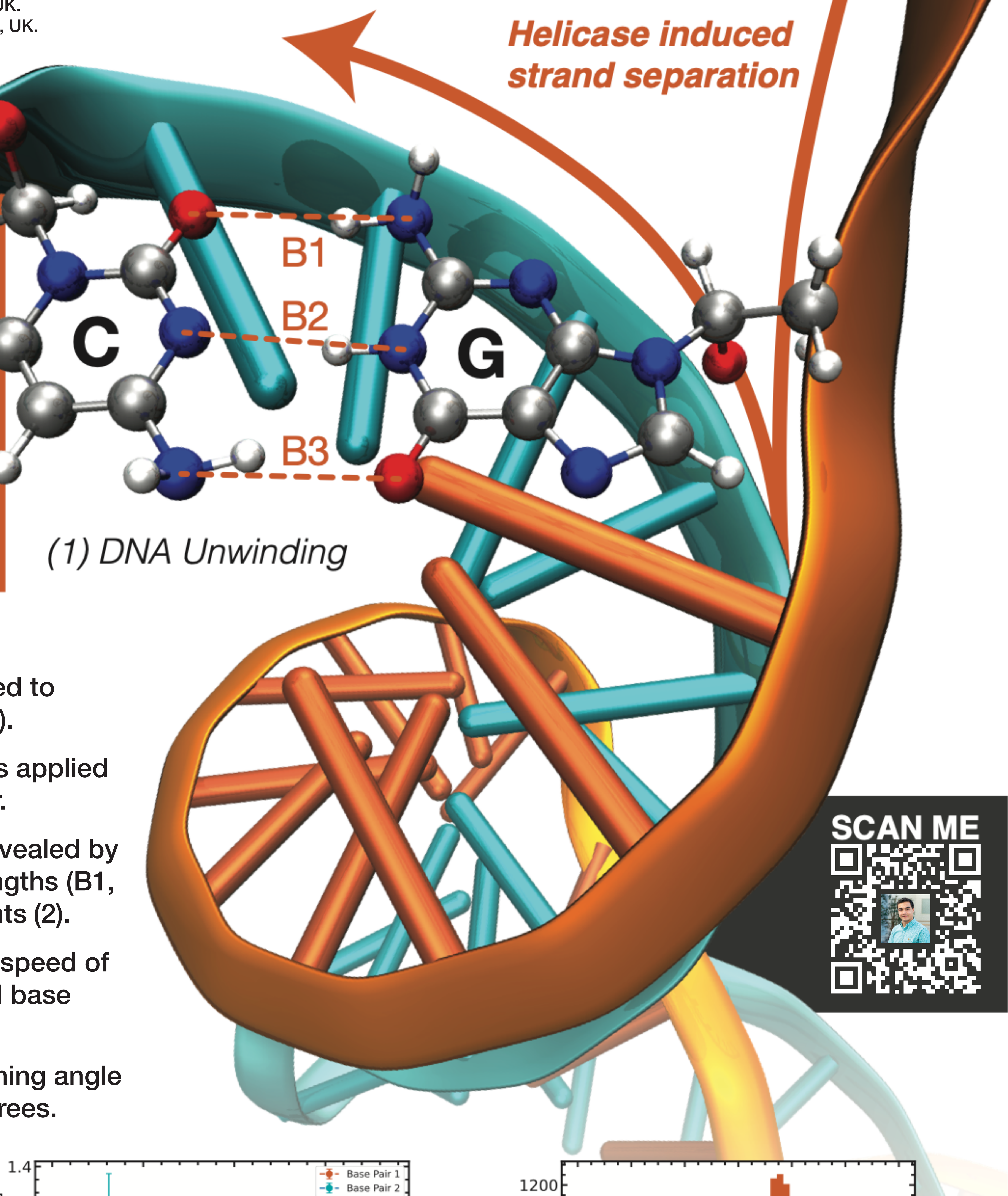


(1) DNA Unwinding

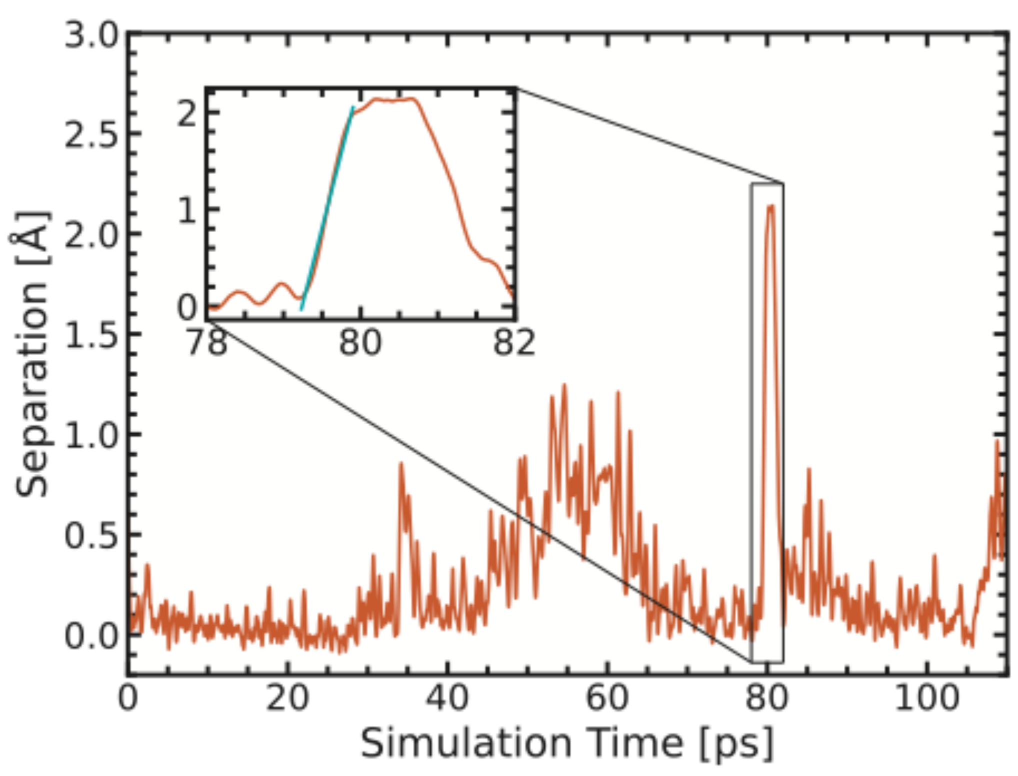
Background

Double proton transfer in static G-C has been described by density functional theory.[1] Literature has dismissed the plausibility of tautomers surviving DNA replication (and thus contributing to mutations) due to their short lifetime.[2]

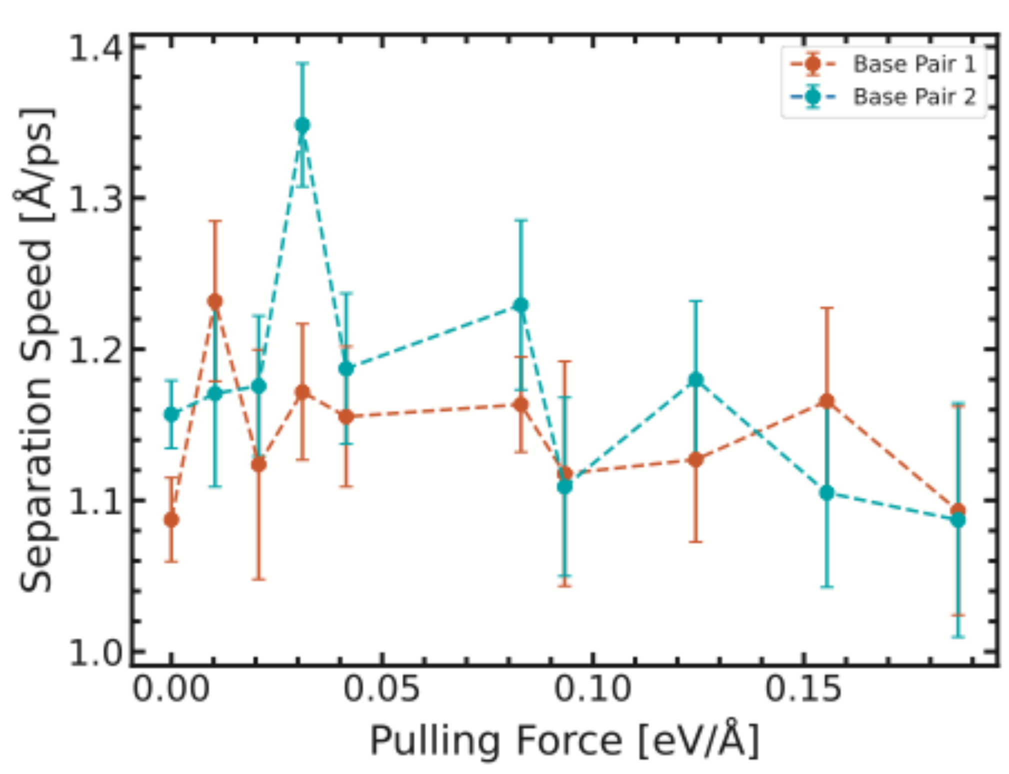
Methodology & Results

- Steered molecular dynamics (SMD) is used to simulate aqeous double stranded DNA (1).
- To model the action of Helicase, a force is applied to the backbone of the terminal base pair.
- The dynamics of strand separation are revealed by measuring variation in hydrogen bond lengths (B1, B2, B3). An algorithm fits separation events (2).
- Figure (3) provides novel insight in to the speed of separation, largely unbiased by force and base pair choice, centering on 1.2 Å/ps.
- We find a bimodal distribution in the opening angle (4) peaked at 18.9±0.1 and -17.4±0.1 degrees.

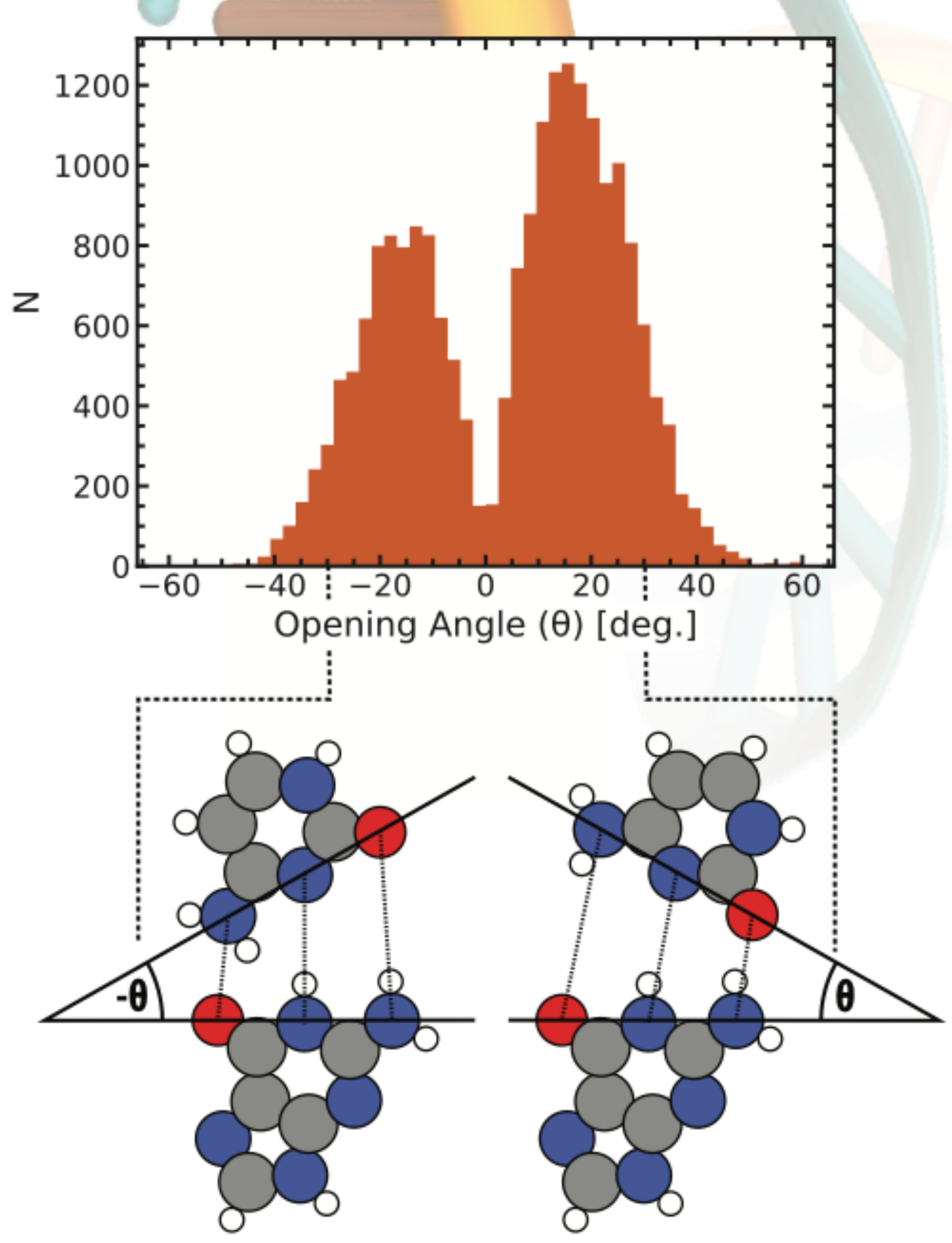
SCAN ME



(2) H-bonds breaking in MD



(3) Speed of GC separation



(4) Asymmetry of separation

Conclusion

Our SMD results show that, at the atomistic level, DNA strand separation occurs at two magnitudes faster than experimental Helicase translocation speed, and that a wide variety of dynamics both in speed and opening angle are observed. Future work in G-C tautomerism must include such dynamics. Fundamental physics can offer insight into the nature of the Life Code and cellular biology.

[1] Slocombe, L.; Al-Khalili, J. S.; Sacchi, M. Quantum and classical effects in DNA point mutations: Watson–Crick tautomerism in AT and GC base pairs. *Phys. Chem. Chem. Phys.* **2021**, *23*, 4141–4150.
[2] Brovarets', O. O.; Hovorun, D. M. Atomistic mechanisms of the double proton transfer in the H-bonded nucleobase pairs: QM/QTAIM computational lessons. *J. Biomol. Struct* **2019**, *37*, 1880–1907.

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