Redox-Based Defect Detection in Packed DNA: Insights from Hybrid Quantum Mechanical/Molecular Mechanics Molecular Dynamics and Feature Selection Studies

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A hybrid quantum mechanics/molecular mechanics molecular dynamics (QM/MM MD) study explored the effect of oxidative damage on DNA redox properties in both unraveled and packed (nucleosome core particle, NCP) DNA systems under biological conditions. From the QM/MM MD studies, we applied a correlation-based feature selection machine learning algorithm to the packed DNA simulation data revealing the electrostatic and structural features which most directly influence the redox properties of a packed DNA system. Furthermore, our work to date shows that DNA lesions caused by oxidative damage yield subtle structural effects, but notable redox changes in guanine-rich regions of both unraveled and packed DNA. In addition to providing quantum-level accuracy of redox properties in DNA affected by oxidation, the findings support the proposed charge transfer (CT) mechanism for DNA damage recognition in guanine-rich DNA sites, regardless of DNA structure [1]. We aim to be able to identify potential oxidative damage “hotspots” in any nucleosome core particle in the future utilizing the data generated from ongoing QM/MM MD studies and the following feature selection analysis.

[1] Amie K Boal, Jacqueline K Barton, *Bioconjugate Chemistry*, **2005**, 16, 312–321.