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Path Sampling Simulations of the Mechanisms and Rates of Transitions between Watson-Crick and Hoogsteen Base Pairing in DNA

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DNA duplexes predominantly contain Watson-Crick (WC) base pairs. However, at any time, a non-negligible fraction of base pairs exhibit a different interaction pattern, called Hoogsteen (HG) where the purine base is rotated approximately 180^{o} relative to its orientation in the WC pairing. The conversion from WC to HG alters the conformation of DNA, and may play a role in several processes, including recognition and replication. The transient nature of these transitions hamper thorough experimental investigation. Molecular dynamics simulations complement experimental work by providing insights at very high spatial and temporal resolution. Path sampling methods focus the molecular dynamics effort on the dynamics during a transition, thus avoiding the long waiting times in stable states. We apply two different path sampling techniques to study the transitions between the WC and HG base pairing motifs. By using transition path sampling we observed that the WC to HG conversion can proceed along several mechanistic routes with varying degrees of exposure of the purine. We computed the rate for each process by employing transition interface sampling.