Investigation of Mismatch Base Pairing in DNA Polymerase

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DNA polymerase is the primary enzyme responsible for DNA replication in living organisms. The high fidelity of DNA polymerase for Watson-Crick nucleotide pairs complicates investigation of nucleotide mismatches using traditional experimental methods. Modern computational methods allow for study of such mismatches at the atomic level. Using three solved crystal structures of *Bacillus sterothermophilus* DNA polymerase I, all twelve possible template-primer DNA nucleotide mismatches were propagated using the molecular dynamics software package AMBER, by *in silico* mutating the nascent base pair. Simulations were analyzed to characterize the behavior of residues in and around the active site to help discern methods of nucleotide discrimination in mismatches. In particular, a tyrosine (Tyr 714) and phenylalanine (Phe 710) located within the active site help directly determine the behavior of the nascent base pair.