

Abstract Submitted
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Chiral pathways in DNA dinucleotides using gradient optimized refinement along metastable borders¹ PABLO ROMANO, MARINA GUENZA, University of Oregon Department of Chemistry and Biochemistry — We present a study of DNA breathing fluctuations using Markov state models (MSM) with our novel refinement procedure. MSM have become a favored method of building kinetic models, however their accuracy has always depended on using a significant number of microstates, making the method costly. We present a method which optimizes macrostates by refining borders with respect to the gradient along the free energy surface. As the separation between macrostates contains highest discretization errors, this method corrects for any errors produced by limited microstate sampling. Using our refined MSM methods, we investigate DNA breathing fluctuations, thermally induced conformational changes in native B-form DNA. Running several microsecond MD simulations of DNA dinucleotides of varying sequences, to include sequence and polarity effects, we've analyzed using our refined MSM to investigate conformational pathways inherent in the unstacking of DNA bases. Our kinetic analysis has shown preferential chirality in unstacking pathways that may be critical in how proteins interact with single stranded regions of DNA. These breathing dynamics can help elucidate the connection between conformational changes and key mechanisms within protein-DNA recognition.

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