Thermodynamics and kinetics of folding in nucleic acids investigated by mechanically unzipping single DNA molecules

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Abstract:

Single molecule manipulation makes possible to disrupt molecular bonds that hold native structures in nucleic acids and proteins. By exerting tiny forces in the piconewton range single molecule techniques allow scientists to monitor molecular reactions in real time (e.g. molecular folding) and characterize thermodynamics and kinetics of individual molecules (e.g. nucleic acids and proteins) with unprecedented energy accuracy within tenths of a kcal/mol.

In this talk I will show experimental results on thermodynamics and kinetics of folding in nucleic acid hairpins that are mechanically unzipped using optical tweezers. First I will report measurements of the DNA base-pair free energies based on the mechanical unzipping of single DNA molecules. By combining experimental data with a physical model and an optimization algorithm for analysis, we measure the 10 unique nearest-neighbor base-pair (NNBP) free energies with 0.1 kcal/mol accuracy over two orders of magnitude of monovalent salt concentration. We find an improved set of standard energy values compared with the unified oligonucleotide set of parameters and a new set of 10 base-pair-specific salt-correction values. Then I will present results of specifically designed DNA hairpins that exhibit molecular misfolding to investigate the role of irreversibility and dissipation during the folding process. Our results suggest the existence of a widespread mechanism that might be used by chaperones to assist molecular folding of RNAs and proteins.

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