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A Kinetic and Thermodynamic Perspective of RNA Folding Transition States JULIE FIORE, DAVID NESBITT, JILA, NIST and University of Colorado at Boulder — Structural assembly is critical to RNA biological functionality. However, an energetic and molecular description of how RNA folds pales in comparison to the understanding of protein folding. To gain molecular insight into the energetic barriers along RNA folding pathways, we explore the transition states for an elementary folding step by extracting the enthalpy and entropy changes associated with forming a single ubiquitous tertiary interaction. By combining single-molecule fluorescence resonance energy transfer methods with temperature variation, we measure the temperature-dependent docking and undocking rate constants of an intramolecular tetraloop–receptor motif. Tetraloop–receptor RNA folds through an early transition state with an entropic barrier. The net reaction is exothermic and entropically costly with a small favorable free energy change at 1 mM Mg^{2+}. Exploring the enthalpy and entropy changes along the reaction coordinate at varying [Mg^{2+}], reveals that Mg^{2+}-enhanced folding originates from a reduction in the entropic barrier and net cost of folding that outweighs unfavorable enthalpic effects.

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