Two-dimensional Infrared Spectroscopy of RNA Folding

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Introduction

The phenomenon of RNA folding has been studied with a variety of methods, including MD simulations, temperature jump kinetics, and NMR spectroscopy. Despite this, many questions remain unanswered as to how intermolecular and intramolecular interactions influence folding and what mechanism the system follows. In particular, how do these signatures change at temperatures below, including, and above the strands' melting temperature could reveal structural details about the folding dynamics.

2D IR is a powerful method for addressing these issues; resolution is greatly improved by spreading the IR spectra in two dimensions, while cross-peak intensities and frequencies probe the fluctuations of the correlations among structural elements. In a 2D IR experiment, three incoming pulses with wavevectors \( k_1, k_2, \) and \( k_3 \) interact with the system to generate a coherent signal in one of the directions \( k_f = 2k_1 \pm k_2 \pm k_3 \). 2D correlation plots are created by plotting the Fourier transforms of the signals with respect to two of the delay periods \( (t_1, t_2, t_3) \). Additionally, by using polarized light pulses the contribution of the diagonal peak can be reduced, thus emphasizing the contributions from the cross-peaks.\(^2\)

RNA Tetraloop: ucUUCGgg

Stable RNA loop with a base-paired stem and four bases “looped out” where the strand turns back on itself.

Molecular Dynamics

- 10 ns trajectory at 200 K in NPT ensemble, using CHARMM27 force field. Snapshots saved every 10 ps.
- Ten 3 ns trajectories collected at 300 K, 400 K to create ensemble average. Snapshots saved every 10 ps.

Vibrational Modes\(^4\)

![Vibrational Modes](image)

While the linear IR and the 2DIR spectra with identical pulses (figures (b) and (c) at right) are similar for all temperatures examined, the cross-polarized spectra (figures (d) and (e)) probe how the base-pairing and base-stacking interactions change as the ucUUCGgg loop unfolds. At 200 K, when the loop is rigid, the diagonal peaks are greatly reduced, revealing detailed coupling information. As temperature is increased, the loop becomes less rigid and thus the diagonal peaks are no longer fully cancelled. Additionally, the evolving cross-peaks can be used to follow structural changes. Pulse shaping and coherent control techniques will be designed to further explore the folded and unfolded conformations of RNA strands.

References


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