Temperature-Jump/Drop Infrared Spectroscopy Reveals RNA Tetraloop Refolding Dynamics

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The structural dynamics of RNA and DNA are essential to cellular function, but direct measurement of folding is challenging. We present a temperature-jump/drop method able to measure both melting and refolding dynamics, and apply it to a series of 12-nucleotide R/DNA sequences featuring the UNCG tetraloop commonly found in biological RNAs.

Stem-loop melting occurred an order of magnitude slower in RNA than DNA, while the refolding dynamics of both sequences required similar timescales. Both melting and refolding followed Arrhenius behaviour, though refolding was characterised by a negative activation energy, consistent with the complex energy landscape of folding initiation.

Placing a single AU pair at key points in the stem showed that RNA sequences begin melting from the loop while DNA hairpins begin melting from the terminal end of the stem. We thus conclude that conformational changes of analogous pairs of RNA and DNA tetraloops proceed by different mechanisms.

References:
J. Phys. Chem. Lett. 2022, 13, 39, 9171–9176
https://doi.org/10.1021/acs.jpclett.2c02338
J. Phys. Chem. B 2023, 127, 7, 1586–1597
https://doi.org/10.1021/acs.jpcb.2c08709

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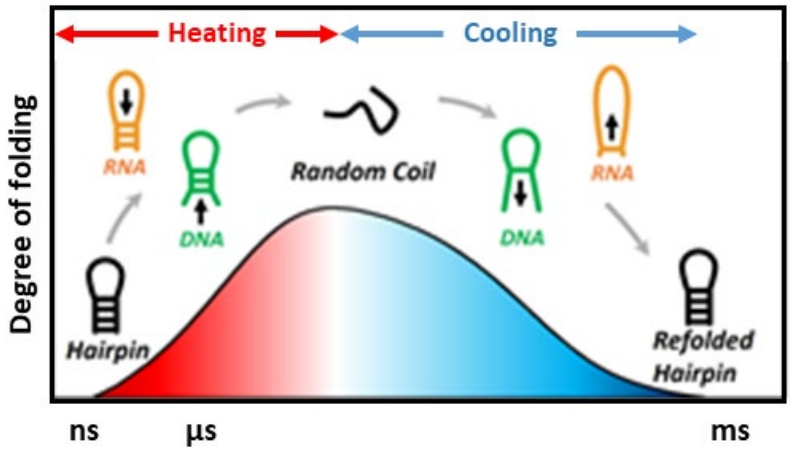

Schematic diagram of the T jump/drop experiment. A ns-duration laser-induced rise in temperature causes hairpin melting followed by fast sample cooling which enables measurement of refolding dynamics.