On the thermodynamics of folding of an i-motif DNA in solution under favorable conditions

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Under slightly acidic conditions, cytosine-rich DNA sequences can form non-canonical secondary structures called i-motifs (iMs), which occur as four stretches of cytosine repeats form hemi-protonated $C{\cdot}C^+$ base pairs [1]. The growing interest in the i-motif structures as important components in functional DNA-based nanotechnology [2] or as potential targets of anticancer drugs [3], increases the need for a deep understanding of the energetics of their structural transitions.

In this work, a full thermodynamic characterization of an iM formation, at different pH values and in the presence of two different cations (Na^+ or K^+), was obtained through a combination of spectroscopic and calorimetric techniques. Indeed, circular dichroism (CD) spectroscopy and differential scanning calorimetry (DSC) data described a reversible folding/unfolding process for the iM-forming oligonucleotide investigated. The close correspondence between the calorimetric and van't Hoff enthalpies, calculated from DSC and CD experiments respectively, was consistent with a two-state equilibrium. In order to confirm the two-state transition assumption, 3D melting curves were submitted to principal component analysis (PCA). Moreover, native PAGE experiments excluded the presence of a conformational heterogeneity.

References

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