

Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (71): I-motif stability prediction under molecular crowding condition

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Quantifying and predicting the stability of nucleic acid structures are vital for analyzing their biological functions and designing novel materials. The prediction methods for the stability of canonical duplexes of nucleic acids have been well established and known as nearest-neighbor (NN) model, which is now expanded to apply for the intracellular condition molecularly crowded.¹ On the other hand, the stability prediction for non-canonical structures is still in progress. The i-motif is one of the non-canonical structures formed by cytosine-hemi protonated base pairs (denoted as C-C⁺) in cytosine-rich nucleic acid sequences clustered at the promoter regions, which controls replication and transcription.² As i-motif forming sequences have a different number of C-C⁺ base pairs and different length of loop regions (Figure 1), the establishment of stability prediction of i-motif from the sequence information is highly required to understand and regulate i-motif formations in cells. In this study, we systematically analyzed thermodynamic parameters (ΔH° , ΔS° , ΔG°_{37} , and T_m) of the formation of i-motif DNAs having a different number of C-C⁺ base pairs and thymine bases within loop regions. We found that the increase in the number of C-C⁺ base pairs increased the stability due to enthalpic gain, whereas that of loop regions decreased the stability due to entropic contribution. These systematic results enabled us to determine the quantitative relationship between the number of cytosines and loop length, which could predict the stability of the i-motif DNA of interest. Furthermore, we found the linear correlations between the stabilities in the absence and presence of the molecular crowder. The combination of these treatments provides an insight for the prediction of i-motif stability under a certain crowding condition from the information of the DNA sequence that forms i-motif.

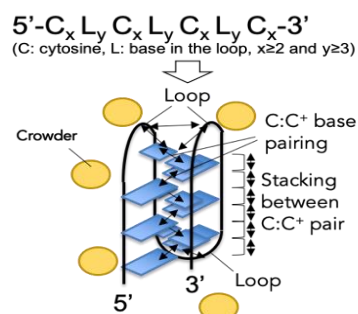


Figure 1. The schematic illustration of the formation of i-motif and factors determining the stability of i-motif.

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