Determining the stability of DNA/RNA hybrid duplexes

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We study the stability of secondary structures in DNA/RNA hybrid duplexes by a nearest neighbor (NN) thermodynamic model. DNA/RNA hybridization has important role in biotechnological applications such as in CRISPR/Cas9 genome editing. Differently from double helices like a DNA/DNA or RNA/RNA which can be self-complementary, sequences of DNA/RNA hybrids constitute a strongly asymmetrical structure due the different compositions the backbone. Nevertheless, it is possible to use a NN model to describe and quantify these interactions for short hybrid sequences with different configurations. Here, we use a set of published experimental sequences of DNA/RNA hybrids and their corresponding melting temperatures measured by UV spectroscopy (Sugimoto et al, Biochemistry, 34, 1995) to determine thermodynamic parameters like free energies formation (ΔG°) and entropic effects (ΔS°) these hybrids. We use a minimization procedure which was recently developed by our group (Weber, Bioinformatics, 31(6), 2015) which bypasses the linear regression of the Van't Hoff plot. This method has the advantage of reducing the uncertainty of the calculated parameters. We also determine the initial free energy factors and an initial entropy factors associated to the formation of the double helix. Such initiation factors are commonly used for DNA/DNA and RNA/RNA, but are currently missing for DNA/RNA hybrids. They are important to supply the necessary energy to form the state of a duplex and are directly associated to the molecular stability of these sequences. Another important factor is the calculation of free energy corrections for terminal base pairs. Our results show that these terminal corrections are very similar to each other for dTrA, dCrG and dGrC base pairs. Finally, we describe physical properties and we discuss the stability of these sequences using the newly calculated parameters. We acknowledge financial support by Capes, CNPq and Fapemig.