Predicting melting temperatures and deriving hydrogen bonds using the Peyrard-Bishop model for LNA+DNA:DNA sequences

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Abstract

Locked nucleic acids are nucleic acids modified by introducing a 2'-O-, 4'-C methylene bridge. This modification induces a conformation change in the backbone, locking the ribose ring in a C3-endo conformation. Thus inducing a favorable entropic variation in its vicinity increasing the overall helix stability. It has been shown to improve mismatch discrimination, compatibility, and specificity toward complementary DNA and RNA strands. Several applications have been described in nucleic acid-based therapeutic strategies both in vitro and in vivo. Even so, there are not many accurate temperature prediction methods applicable to LNA probes. Such temperature predictions are important, as an example, for probe design and PCR applications since both rely on the melting temperature. For instance, it is not yet fully established how much of the improvement in affinity and specificity is actually due to stacking interactions or hydrogen bonds. Here, we use the Peyrard-Bishop mesoscopic model that was successfully used for describing DNA, RNA, and more recently DNA/RNA hybrids, to characterize the thermodynamic properties of LNA. We use existing melting temperatures of LNA/DNA hybrids, to extract model parameters which can be interpreted in terms of hydrogen bonding and stacking interaction. Our results show a considerable increase in the hydrogen bonds of the modified nucleotides and also an instability on some stacking potentials, which is relatable to the destabilizing effect in some LNA modified probes.

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Link to Video: