Optimized RNA nearest-neighbor enthalpy and entropy parameters as function of salt concentration

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Nearest-neighbor (NN) method using enthalpy and entropy parameters is the most common method used to predict melting temperatures for oligonucleotides. The application of those parameters goes well beyond melting temperature prediction, for instance they are crucial for predicting RNA secondary structures. The NN parameters are usually derived from a small set of melting temperatures measured over a range of oligonucleotide concentrations. To obtain the parameters one would typically first obtain the total enthalpies and entropies from a Van't Hoff plot linear regression and afterward extract the detailed NN parameters with linear algebra methods. Here, we use a recently developed optimization method which bypasses the linear regression, the NN parameters are instead obtained directly from the melting temperatures. The advantage of this method is that it avoids the increased uncertainty induced by the linear regression of the Van't Hoff plot and as a result the predicted temperatures are much closer to the experimental data especially at higher temperatures and long sequences. We apply this technique to obtain the parameters for RNA over a range of different sodium concentrations. The parameter optimization were performed on 18 different RNA sequences at 5 different sodium concentration and 9 to 11 different oligonucleotide concentrations. Our results show that in particular CG-CG NN parameters show very little dependence with sodium concentration. On the other hand NN parameters containing AT base pairs show a quadratic dependence with salt concentration which opens the possibility of deriving salt corrections for enthalpy and entropy parameters specifically for those nearest-neighbor configurations.

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