Effect of Cy3 and Cy5 dyes on the hydrogen bonds of oligonucleotides

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Cyanine dyes Cy3 and Cy5 exhibit intense visible florescence and when attached to the 5' ribose terminus of DNA stabilize the duplex. Oligonucleotides modified with cyanines are widely used in biotechnological techniques such as microarrays and real-time PCR. They also allow for nanoscale measurements by using Forster resonance energy transfer (FRET). Despite its importance little is known on how these dyes affect the intramolecular interactions of the base pairs they are attached to. A detailed knowledge of these interactions would allow for a better understanding and perhaps would lead to the optimization of experimental techniques. Here we use the Peyrard-Bishop (PB) mesoscopic model to obtain estimates of the hydrogen bonds and stacking parameters of DNA with attached Cy3 and Cy5 molecules. The PB model has the unique ability to consider separately the hydrogen bonds and the stacking interactions by using independent potentials. We applied the PB model successfully to predict the molecular interactions in DNA and RNA. In particular, we confirmed independent NMR measurements on AU in RNA showing a stronger hydrogen bond than AT in DNA. More recently we were able to correctly predict single hydrogen bonding in specific GU tandem base pairs. We also showed how the solvent affects the hydorgen bonds of terminal base pairs. Here, we use a recently published melting temperature data set of 35 DNA sequences with cyanine dyes and 10 control sequences. By combining the PB model and adjusting the parameters to provide a better fit to the experimental melting temperatures we are able to determine not only the interactions of the dyes with the DNA terminus but also how those affect the neighboring base pairs. In particular we show an enhanced thermal stability induced by the cyanine dyes. The method also allows a detailed map of the opening probabilities along the oligonucleotide sequence were we show how the dyes affect the stability at the base pair level.

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