# Hybridization energy of native and modified DNA duplexes calculated using molecular dynamics approaches

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Development of new derivatives and analogues of nucleic acids (NA) is important both in practice and basic research. Molecular dynamics approach is a unique method for studying physico-chemical properties of nucleic acid and its derivatives complexes.

Recently we have shown the possibility of the calculation hybridization enthalpy of native DNA duplexes using MD simulation. It was found that hybridization enthalpies for complexes of various length (4-20 nt) and GC-content (0- 100%) can be calculated with accuracy comparable to experimental (12%). The results obtained show that MD modeling allows one to calculate enthalpy of matched DNA duplexes with surprisingly good accuracy.

At the next stage we have studied the possibility of calculation of stacking interaction energy using nicked DNA duplexes with various nucleotides in the nick. For this purpose we determine the error of MD simulation and the length of MD trajectory that would be enough to obtain reliable values of cooperative interaction energies. Then, the values of enthalpy for a series of cooperative contacts in the nick have been obtained experimentally (via DNA melting) and by MD simulation. The data from the two methods are in a good agreement, although the MD data are somewhat less sequence dependent than the experimental one.

At the third stage we have studied the influence of non-nucleotide insert based on diethеleneglycol phosphodiester ("bridged" oligonucleotides) [1,2] on conformational and

thermal stability. It was found, that local duplex structure perturbation leads to bending of the double helix as was observed experimentally. The thermodynamic effect of the DNA modification calculated from the melting data is also close to the value obtained via MD, again, with low sequence dependence in the case of MD.

Finally, we have studied complexes of morpholino nucleic acid analogues [3] of homonucleotidic sequence with non-modified RNA and DNA. The results of MD simulations show a good agreement of hybridization enthalpy for both such chimeric complexes with measured experimentally.

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