

**Table S2.** Extended free energy rules for quadruplets of nucleotide pairs in a DNA duplex.

Class	Quadruplet <sup>a</sup>	$\Delta G^{\circ b}$	Description
1	●●**	Table S1A	Nearest neighbor in the first two positions.
2	●^●●	Table S1B	Mismatch loop based on the triplet in the first three positions.
3	●-●●	Table S1C	Bulged mismatch loop based on the triplet in the first three positions.
4	●^^●	Table S1D	Tandem mismatch.
5	●^ - ● ●-^● ●--●	1.0	Bulged tandem mismatch loop.
6	###●	1.0	End of a mismatch series with at least three mismatches.
7	●#●#	1.0	Adjacent mismatch loops interfering with at least four nearest neighbors.
8	#**#	0.0	No additional penalty since used mismatch loop information is contained in neighboring quadruplets.
9	#●●●	0.0	No additional penalty since used mismatch loop information is contained in neighboring quadruplets.
10	##●●	0.0	No additional penalty since used mismatch loop information is contained in neighboring quadruplets.
11	#●#●	0.0	No additional penalty since used mismatch loop information is contained in neighboring quadruplets.
12	●###	0.0	Beginning of a mismatch series with at least three mismatches. Penalty is placed at the end of the mismatch series (see Type 6).

<sup>a</sup> ●, matching pair; ^, base to base mismatched pair; -, gap to base mismatch (bulged mismatch); #, any mismatch; \*, any pair.

<sup>b</sup> For studied conformations, corresponding table of parameters is indicated. For others, approximations are provided in kcal/mol.