

# **<sup>1</sup>H NMR determination of base-pair lifetimes in oligonucleotides containing single base mismatches**

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Proton nuclear magnetic resonance (NMR) spectroscopy is employed to characterize the kinetics of base-pair opening in a series of 9mer duplexes containing different single base mismatches. The imino protons from the different mismatched, as well as fully matched, duplexes are assigned from the imino-imino region in the WATERGATE NOESY spectra. The exchange kinetics of the imino protons are measured from selective longitudinal relaxation times. In the limit of infinite exchange catalyst concentration, the exchange times of the mismatch imino protons extrapolate to much shorter lifetimes than are commonly observed for an isolated GC base pair. Different mismatches exhibit different orders of base-pair lifetimes, e.g. a TT mismatch has a shorter base-pair lifetime than a GG mismatch. The effect of the mismatch was observed up to a distance of two neighboring base pairs. This indicates that disruption in the duplex caused by the mismatch is quite localized. The overall order of base-pair lifetimes in the selected sequence context of the base pair is GC > GG > AA > CC > AT > TT. Interestingly, the fully matched AT base pair has a shorter base-pair lifetime relative to many of the mismatches. Thus, in any given base pair, the exchange lifetime can exhibit a strong dependence on sequence context. These findings may be relevant to the way mismatch recognition is accomplished by proteins and small molecules.

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