

# DNA Mediated Charge Transport: Characterization of a DNA Radical Localized at an Artificial Nucleic Acid Base

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## Abstract:

DNA assemblies containing 4-methylindole incorporated as an artificial base provide a chemically well-defined system in which to explore the oxidative charge transport process in DNA. Using this artificial base, we have combined transient absorption and EPR spectroscopies as well as biochemical methods to test experimentally current mechanisms for DNA charge transport. The 4-methylindole radical cation intermediate has been identified using both EPR and transient absorption spectroscopies in oxidative flash-quench studies using a dipyridophenazine complex of ruthenium as the intercalating oxidant. The 4-methylindole radical cation intermediate is particularly amenable to study given its strong absorptivity at 600 nm and EPR signal measured at 77 K with  $g = 2.0065$ . Both transient absorption and EPR spectroscopies show that the 4-methylindole is well incorporated in the duplex; the data also indicate no evidence of guanine radicals, given the low oxidation potential of 4-methylindole relative to the nucleic acid bases. Biochemical studies further support the irreversible oxidation of the indole moiety and allow the determination of yields of irreversible product formation. The construction of these assemblies containing 4-methylindole as an artificial base is also applied in examining long-range charge transport mediated by the DNA base pair stack as a function of intervening distance and sequence. The rate of formation of the indole radical cation is  $\geq 10^7 \text{ s}^{-1}$  for different assemblies with the ruthenium positioned 17-37 Å away from the methylindole and with intervening A-T base pairs primarily composing the bridge. In these assemblies, methylindole radical formation at a distance is essentially coincident with quenching of the ruthenium excited state to form the Ru(III) oxidant; charge transport is not rate limiting over this distance regime. The measurements here of rates of radical cation formation establish that a model of G-hopping and AT-tunneling is not sufficient to account for DNA charge transport. Instead, these data are viewed mechanistically as charge transport through the DNA duplex primarily through hopping among well stacked domains of the helix defined by DNA sequence and dynamics.

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