Chapter 7

Summary and Conclusions

Double helical DNA, containing a π-stacked array of base pairs within its interior, represents a unique medium for electron transfer. The structural and electronic properties of the DNA π stack have fueled research into the nature of DNA-mediated charge transfer since the structure of DNA was solved several decades ago. Numerous biochemical, photophysical, and electrochemical experiments aimed at uncovering the true nature of charge migration through the double helix have produced an adequate understanding of the phenomenon. Charge transfer proceeds rapidly and efficiently between donors and acceptors which are well coupled to the DNA base stack.

As described in this thesis, we focused on spectroscopy experiments in which electron transfer probes were intimately intercalated or stacked within the DNA double helix. The stacking of these reactants and the intervening base pairs, both statically and dynamically, is the key parameter that ties together this body of work and the phenomenon of DNA-mediated charge transfer as a whole. The following is a summary of the results that further underscore the sensitive nature of DNA-mediated charge transfer to static and dynamic stacking and structural perturbations.

The classic intercalator ethidium (Et) was tethered to the end of a DNA duplex, and the dynamics of photoinduced charge transfer between Et and the modified base 7-deazaguanine (Z) were studied as a function of distance. As expected, charge transfer was rapid and efficient. However, the rates corresponding to charge transfer did not decrease with increasing donor-acceptor separation. Two main charge transfer decays were observed: (1) a 5-picosecond component, consistent with charge injection into the base stack and (2) a 75-picosecond component found to correspond to ethidium reorientational motion within the DNA duplex. This orientation-dependent charge transfer rate was the first conclusive demonstration of the significant role structural dynamics can play in DNA-mediated charge transfer. Introduction of a mismatch between Et and Z attenuated the luminescence quenching yield depending on how well

the intervening bases were stacked within the DNA, once again demonstrating the importance of stacking to DNA-mediated charge transfer.

Ultrafast dynamics were also measured for the intrastrand DNA-mediated charge transfer reaction between two modified DNA bases. The photooxidation of guanine (G) and Z by 2-aminopurine (Ap) proceeds on the picosecond timescale. Charge transfer rates were found to depend on the driving force of the reaction, and luminescence quenching efficiencies were greatly affected by the stacking and redox potential of the intervening base pair medium.

The photooxidation of Z at a distance through DNA by a ruthenium(II) intercalator was found to be exquisitely sensitive to how well the ruthenium complex was stacked within the DNA double helix. The Δ isomers of the metal complex, which bind more deeply into the DNA base stack, exhibited fast (subnanosecond) charge transfer kinetics. The Λ isomers, which are not able to intercalate as deeply within the DNA base stack, showed photoinduced charge transfer times with Z on the order of 100 nanoseconds. Clearly, the structure and stacking of reactants have a profound effect on DNA-mediated charge transfer.

To probe the effect of redox potential on reactivity with DNA, several dipyrido-phenazine-based ruthenium intercalators with high redox potentials were synthesized. The reactivity of these compounds with the DNA base stack did not depend directly on redox potential. Rather, reactivity was controlled by how well the complexes intercalated into the double helix. Structure and binding must, therefore, be considered when examining the behavior of reactants with DNA. Using redox potential as the sole predictor of reactivity is not a viable option.

Finally, the interactions of ruthenium(II) and rhodium(III) intercalators along the DNA double helix were examined using circular dichroism and NMR spectroscopy. It was conclusively shown that the positively charged metallointercalators preferred to bind away from each other at sites on the DNA. The data proved that direct contact between

reactants cannot be used to explain fast and efficient charge transfer between intercalators bound noncovalently to the DNA double helix.

The experiments described here paint a clear picture regarding the main factors controlling the migration of charge through DNA. The integral parameters for DNA-mediated charge transfer are the stacking and dynamics of the reactants and the DNA bases. As researchers develop new methods to describe and explore these parameters, the already burgeoning field of charge transfer through DNA may be propelled into the spotlight. Many crucial questions, including the relevance of the phenomenon to living systems and biological implications, remain to be answered. The conversion of basic charge transfer parameters into biologically relevant information represents an important challenge for the future.