

Long-range oxidative damage to cytosines in duplex DNA

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Charge transport (CT) through DNA has been found to occur over long molecular distances in a reaction that is sensitive to intervening structure. The process has been described mechanistically as involving diffusive charge-hopping among low-energy guanine sites. Using a kinetically fast electron hole trap, *N*₄-cyclopropylcytosine (^{CP}C), here we show that hole migration must involve also the higher-energy pyrimidine bases. In DNA assemblies containing either [Rh(phi)₂(bpy')]³⁺ or an anthraquinone derivative, two highenergy photooxidants, appreciable oxidative damage at a distant ^{CP}C is observed. The damage yield is modulated by lower-energy guanine sites on the same or complementary strand. Significantly, the efficiency in trapping at ^{CP}C is equivalent to that at *N*₂-cyclopropylguanosine (^{CP}G). Indeed, even when ^{CP}G and ^{CP}C are incorporated as neighboring bases on the same strand, their efficiency of photodecomposition is comparable. Thus, CT is not simply a function of the relative energies of the isolated bases but instead may require orbital mixing among the bases. We propose that charge migration through DNA involves occupation of all of the DNA bases with radical delocalization within transient structure-dependent domains. These delocalized domains may form and break up transiently, facilitating and limiting CT. This dynamic delocalized model for DNA CT accounts for the sensitivity of the process to sequence-dependent DNA structure and provides a basis to reconcile and exploit DNA CT chemistry and physics.

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