

Francesco Gervasio (ETH Zurich) Charge transfer and oxidative damage in DNA fibers.

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Guanine radical cation is the initial product of DNA oxidation by a wide variety of reagents: pulse radiolysis, photo-oxidants, transition metal complexes, UV. G^+ can be formed directly or via charge transfer. Charge transfer: the nature of DNA is a stack of aromatic molecules, possible conduction, highly insulating or superconducting depending on length. DNA is soft segmented, not a coherent long-range transfer. Charge hopping via tunneling (few bases) but is more likely polaron-like because of the tilt of the bases due to local distortion, or possibility of fluctuation of counter-ions, or deprotonation of G . Model system is the $G:C$ decamer in the Z conformation. X-ray structure available, self-complementary. Crystal structure has few water molecules but is closely packed, no conformational changes, but possible loss of biological significance. Uses linear scaling methods to simplify calculations to laptop. From 300K to 0K polarons appear due to tilt of guanines. Third possibility is the G deprotonation: spin trapping. Simulations suggest that tilt of bases is not likely. H/D isotope effects. If the deprotonation was a parasite event an increase in the charge transfer is expected upon deuteration. In deuterated DNA the hole transfer is three times less efficient! At least the $G:C$ couples the charge transfer is coupled to proton transfer. Reactions: Protonation State of the $G:C$ couple, $\Delta E \approx 3.6$ kcal/mole, fate of G^+ in DNA. In duplex DNA the initial product is 8-oxo G . First step in oxidation reaction using ab-initio molecular dynamics. Rate limited by water autoprotolysis, catalyzed by phosphate backbone. Stabilization of the intermediate is achieved by proton transfer from the cytosine.