ELECTRON NUCLEAR DYNAMICS INVESTIGATION OF WATER RADIOLYSIS AND DNA DAMAGE IN PROTON CANCER THERAPY

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Despite established clinical use, a deep understanding of proton cancer therapy (PCT) from its underlying physicochemical processes remains elusive[1]. This situation prevents a rational design of PCT that can maximize its therapeutic power and minimize its side effects[1].The poor characterization of PCT processes arises from the fact that current experimental and clinical techniques cannot reveal all the microscopic details of PCT, especially without putting human subjects at risk[1]. To overcome this situation, we are performing electron nuclear dynamics (END)[2] simulations of PCT reactions to elucidate all their microscopic details; these simulations are virtual tests that harm no patients. END is a time-dependent, variational, direct and non-adiabatic method to simulate chemical reactions. The simplest-level END (SLEND) employed herein adopts classical mechanics for the nuclei and a single-determinantal wavefunction for the electrons. SLEND can properly describe the numerous processes that occur simultaneously during PCT (e.g. scattering, fragmentations, and energy/electron transfers). Our SLEND code PACE[2] utilizes various advanced techniques in computer science, such as Python, FORTRAN and C^{++} languages, and intra- and internode parallelization. Because the healing power of PCT lies in its capacity to inflict nearly irreparable DNA damage in cancerous cells, we are simulating three types of PCT reactions leading to such damage: **(a)** high-energy proton collisions with the water clusters $(H_2O)_{1\text{-}6}$ as prototypes of water radiolysis reactions[1-3]—the initial PCT reactions in cell water that generate the radicals, ions, and electrons that damage DNA; **(b)** high-energy proton collisions with DNA bases and nucleotides as prototypes of proton-induced DNA damage[1, 2]; and **(c)** electron-induced single strand breaks (SSBs) in the cytosine nucleotide as a prototype of electron-induced DNA SSBs[1]. For **(a)** and **(b)**, SLEND simulations provide target-to-proton one-electron-transfer and projectile stopping-power integral cross sections in good agreement with experimental results and predict the formation of radicals and ions involved in DNA damage[1-3]. For **(c)**, our simulations provide a unique insight into electron-induced DNA SSB. Our END simulations of proton- and electron-induced SSBs in nucleotides are the first ever performed on those large biomolecules with an ab initio, non-adiabatic method [1].

References

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