Proton transport in water and DNA components: A Geant4 Monte Carlo simulation

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ABSTRACT

Accurate modeling of DNA damages resulting from ionizing radiation remains a challenge of today's radiobiology research. An original set of physics processes has been recently developed for modeling the detailed transport of protons and neutral hydrogen atoms in liquid water and in DNA nucleobases using the Geant4-DNA extension of the open source Geant4 Monte Carlo simulation toolkit. The theoretical cross sections as well as the mean energy transfers during the different ionizing processes were taken from recent works based on classical as well as quantum mechanical predictions. Furthermore, in order to compare energy deposition patterns in liquid water and DNA material, we here propose a simplified cellular nucleus model made of spherical voxels, each containing randomly oriented nanometer-size cylindrical targets filled with either liquid water or DNA material (DNA nucleobases) both with a density of 1 g/cm^3. These cylindrical volumes have dimensions comparable to genetic material units of mammalian cells, namely, 25 nm (diameter) × 25 nm (height) for chromatin fiber segments, 10 nm (d) × 5 nm (h) for nucleosomes and 2 nm (d) × 2 nm (h) for DNA segments. Frequencies of energy deposition in the cylindrical targets are presented and discussed.

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1. Introduction

The Geant4 Monte Carlo simulation toolkit [1] provides an open source and flexible framework for the modeling of particle interactions with matter. Within the Geant4-DNA project, Geant4 is being extended to allow for the simulation of biological effects of ionizing radiation at the DNA scale [2], an activity of the Geant4 collaboration initiated by the European Space Agency aimed at modeling radiobiological damages during long duration manned exploration missions. This extension is able to model detailed physics interactions for nanodosimetry using a set of physics processes for electrons, protons, neutral hydrogen atoms, alpha particles and their different charged states and for C, N, O and Fe ions, but it is currently limited to liquid water targets only [3]. We present in this work the first implementation of physics processes using the Geant4-DNA extension for the modeling of proton and neutral hydrogen atom interactions with liquid water and the four DNA

nucleobases, namely, Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). The corresponding physics models developed within a Classical Trajectory Monte Carlo (CTMC) approach are briefly presented, as well as their implementation into the Geant4-DNA extension. Comparisons between energy deposit distributions in nanometer size targets made of either liquid water or DNA nucleobases are shown and discussed.

2. Physics models in liquid water and in DNA following a classical approach

The physics models adopted in this work follow the CTMC approach fully described in [4,5]. In brief, it consists in modeling a large number of ion trajectories within the impact parameter framework in which all particle movements are described by means of Newtonian laws. For each trajectory, the occurrence of the ionizing processes – including single processes (ionization and electron capture) as well as multiple processes like double ionization and transfer ionization – depends on specific energetic criteria – called Classical Over-Barrier (COB) criteria – linked to the position of the binding energy of the "impacted" target electron

relatively to the maximum of the Coulomb potential barrier existing between the ion projectile and the molecular target. This CTMC-COB approach is an interesting alternative since it can be applied to colliding systems which are difficult to model using quantum mechanics such as the ones involving large molecules.

3. Implementation of CTMC-COB physics models using the Geant4-DNA extension

In a private version of the Geant4-DNA extension, ionizing processes for protons and neutral hydrogen atoms in liquid water and DNA nucleobases were implemented. These processes include single electron capture, single ionization, double ionization and transfer ionization for protons as well as single ionization and stripping for hydrogen atoms. Each process computes the total cross section of the corresponding physical interaction and fully describes the final state of the system (incident projectile energy loss, production of secondary electrons...) according to the CTMC-COB approach described above. Molecular binding energies for DNA bases have been extracted from [4,5]. CTMC-COB cross sections have been pre-tabulated and are directly interpolated – step by step – by the Geant4-DNA software for projectile energies ranging from 10 keV up to 1 MeV. Below 10 keV, *i.e.* below the validity range of the CTMC-COB approach, the tracking of incident particles is stopped, the remaining kinetic energy being assumed as released into the medium. The corresponding Geant4-DNA process and model C++ classes adopt the most recent software design of the electromagnetic physics category available in the Geant4 toolkit as explained in [3,6].

Besides, singly differential cross sections, namely, differential in the energy transfer, are not yet available in the current CTMC-COB approach in particular to describe the secondary electron energy spectra. To overcome this limitation, we have here adopted a simplified approach which consists in using the mean energy transfers (potential as well as kinematical) provided by the quantum mechanical description recently reported by Champion and co-workers to describe the proton-induced ionization and capture processes on DNA components [9–11].

Finally, note that the hydrogen-induced interactions (ionization and stripping processes) are described by means of semi-phenomenological cross sections (for more details, we refer the reader to [3]). Furthermore, we have here assumed identical cross sections for the four nucleobases A, T, G and C.

Fig. 1 shows the total CTMC-COB cross sections for protons and neutral hydrogen atoms as a function of the incident kinetic energy obtained using the new Geant4-DNA processes for liquid water (left side) and Adenine (right side) targets, respectively. It clearly appears that the Adenine cross sections are of about one order of magnitude greater than their homologous in liquid water over the whole energy range and for all the ionizing processes here studied (except for the double ionization which exhibits a 2 orders of magnitude ratio and for the transfer ionization which has a similar magnitude). Such differences obviously arise from the size of the DNA nucleobases compared to the water molecule as well as from the large number of molecular subshell contributions (25 for A versus 5 for water). Besides, let us note that Adenine has been here used as an example among the four DNA bases. Under these conditions, the results hereafter reported in terms of energy deposition frequencies could be obviously generalized to the other DNA bases, the interaction cross sections being of the same order of magnitude for each of them.

4. Geant4-DNA track structure simulation in liquid water and in DNA

4.1. Method

A Geant4-based user application was then developed to simulate proton tracks in liquid water and in DNA. Protons are shot randomly onto a sphere of liquid water of 1 micrometer-diameter filled with randomly oriented spherical voxels. We developed a similar geometrical approach a few years ago for the Monte Carlo estimation of specific energy for targeted irradiation of biological cells [7]. Each spherical voxel contains a cylindrical target which is filled exclusively either with liquid water or with DNA material (A, T, G or C). Material density is set to 1 g/cm³. Cylindrical targets
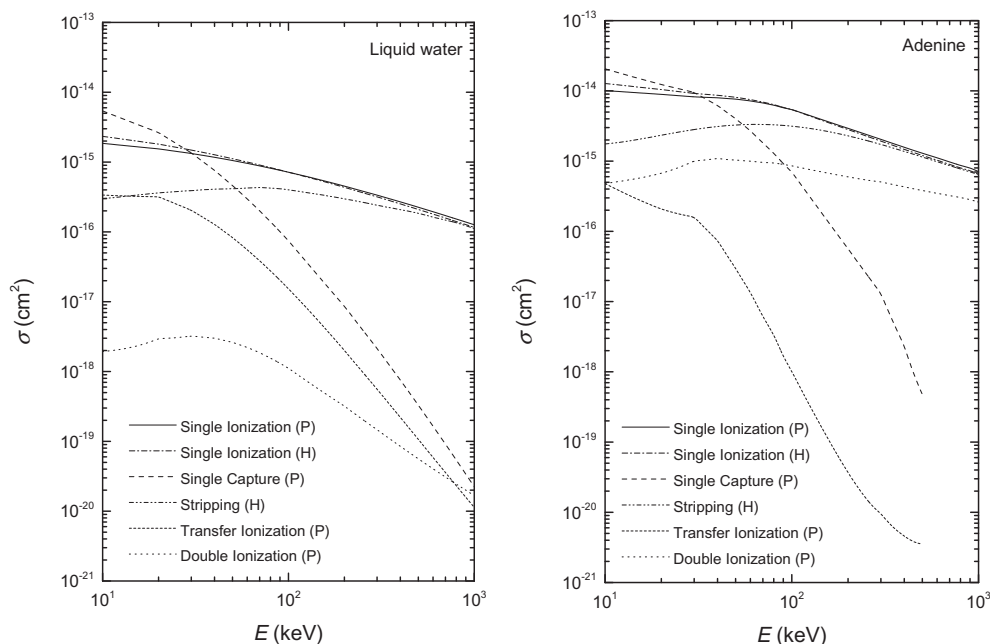

Fig. 1. CTMC-COB cross sections of the ionizing processes induced by proton (P) and neutral hydrogen atom (H) impact as a function of the incident kinetic energy in liquid water (left panel) and in Adenine (right panel).
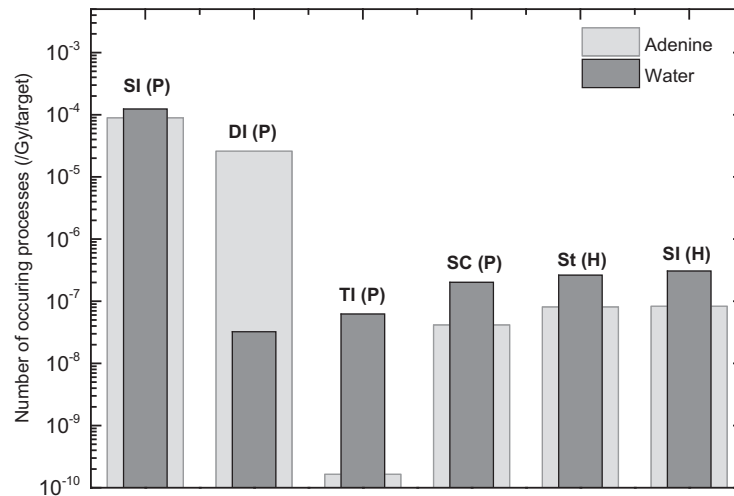
Fig. 2. Number of physical processes occurring in 10 nm (d) × 5 nm (h) cylindrical targets containing either liquid water or Adenine, expressed per Gray deposited in the liquid water sphere and per cylinder target. The statistics was obtained using 10^4 incident 500 keV-protons randomly shot onto the spherical phantom (SI: single ionization, DI: double ionization, TI: transfer ionization, SC: single capture, St: stripping). The label P and H refers to the proton and the Hydrogen processes, respectively.

have dimensions (diameter × height) of genetic units of mammalian cells originally proposed by Charlton and colleagues [8], namely, 2 nm × 2 nm, 10 nm × 5 nm and 25 nm × 25 nm, representing DNA segments, nucleosomes and chromatin fibers, respectively. Frequency of energy deposition in the cylindrical targets was computed per target and per Gray deposited in the liquid sphere. The implementation of the whole geometry and the extraction of energy deposition frequency are further described in [12].
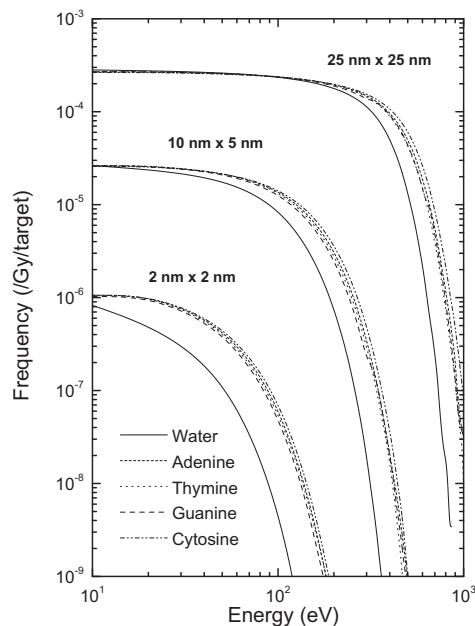

Fig. 3. Frequency distributions of the energy deposition per Gy deposited in the liquid water sphere and per cylinder target, obtained with 500 keV incident protons for the three geometries of cylinder targets (top curves: 25 nm (d) × 25 nm (h), middle curves: 10 nm (d) × 5 nm (h), bottom curves: 2 nm (d) × 2 nm (h)). Results obtained with liquid water or DNA material (A, T, G, C) are shown.

4.2. Results

Fig. 2 shows the number of physical processes occurring in the 10 nm × 5 nm (diameter × height) cylindrical targets, containing either liquid water or Adenine, per target and per Gray deposited in the liquid phantom. This statistics was obtained using 10^4 incident protons of 500 keV randomly shot onto the spherical phantom. The largest differences appear for the double ionization and transfer ionizing processes. The former occurs two orders of magnitude more in Adenine than in liquid water, while the later occurs at least two orders of magnitude more in liquid water than in Adenine. Let us note that a similar statistics has been observed for the two other geometries (not shown here), namely, the 25 nm × 25 nm and 2 nm × 2 nm cylinders. In fact, this observation is directly related to the magnitude of the corresponding cross sections shown in Fig. 1.

In Fig. 3, frequency distributions of the energy deposition by protons and hydrogen atoms are presented per cylinder target and per Gy deposited in the liquid water sphere. Like previously, they have been simulated by shooting 10^4 incident protons of 500 keV randomly onto the sphere. Three geometries of cylinder targets are considered (top curves: 25 nm (d) × 25 nm (h), middle curves: 10 nm (d) × 5 nm (h), bottom curves: 2 nm (d) × 2 nm (h)). These cylinders contain either liquid water or DNA material (A, T, G, and C). The results show a non-negligible increase in frequencies of energy deposition when switching from liquid water to DNA material. While distributions obtained for A, T, G and C materials are similar, the increase of frequency values from water to DNA material reaches one order of magnitude at ~100 eV for the smallest cylinders, at ~300 eV for medium size cylinders and at ~600 eV for the largest cylinders. As a consequence, the dose absorbed in cylindrical targets containing exclusively DNA material is larger than the dose absorbed in liquid water cylinders. The absorbed dose increase when replacing liquid water material in the cylindrical targets by DNA material (DNA nucleobases) varies from about 20% for Thymine up to 34% for Cytosine, for the three geometries considered in this work.

5. Conclusions

We have recently implemented a set of processes dedicated to the detailed Monte Carlo modeling of proton and neutral hydrogen

interactions with liquid water and DNA material following the CTMC-COB approach and covering the 10 keV–1 MeV kinetic energy range. These processes are currently included in a private version of the Geant4-DNA extension of the Geant4 Monte Carlo simulation toolkit. First results show a non negligible influence of the material (liquid water versus DNA nucleobases for a 1 g/cm^3 medium density) on the energy deposit distributions in nanometer-size targets. To our knowledge, no other Monte Carlo software currently allows the modelling of the transport of protons and neutral hydrogen atoms through liquid water and DNA nucleobases. More thorough studies are planned in this direction and we expect to deliver these developments in a forthcoming public release of the Geant4 toolkit.

Acknowledgments

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