Editor's pick

Evaluation of early radiation DNA damage in a fractal cell nucleus model using Geant4-DNA

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What was your motivation for initiating this study?

Understanding the mechanism by which ionising radiation affects biological entities at the scale of DNA remains a challenge of today's radiobiology. The Geant4-DNA collaboration (http://geant4-dna.org) [1-4] is an international initiative that aims to extend the general purpose Geant4 Monte Carlo simulation toolkit (http://geant4.org) [5-7] in order to provide the scientific community with the first fully open-source simulation platform to study physical track structures as well as the effects of water radiolysis in biological media under irradiation. The Geant4-DNA initiative was spearheaded in 2001 by Dr Petteri Nieminen of the European Space Agency. In addition, Geant4-DNA can be used to combine various simplified geometries of biological targets (from a DNA strand to bacteria and cell nuclei) in order to predict early radiation-induced biological damage (such as DNA double-strand breaks). The paper presents the first combination of physical and chemical simulations of radiation effects (the latter adopts for the first time the efficient method named independent reaction time) with a fractal chromatin-based geometry of a cell nucleus in order to predict early direct (induced by physical interactions) and non-direct (induced by chemical interactions) DNA damage.

What were the main challenges to be overcome during the work?

This is not the first time that Geant4-DNA has been used to demonstrate that it is possible to combine physical track structure and radiolysis modelling in simplified geometries of biological targets for prediction of early DNA damage (see our list of publications at http://geant4-dna.org and particularly: Meylan et al., 2017 [8]; Lampe et al., 2018 [9]; de la Fuente Rosales et al., 2018 [10]; Tang et al. [11]). However, this work demonstrates the combination of the efficient independent reaction time approach for the simulation of water radiolysis (initiated by Dr M. Karamitros of the Geant4-DNA collaboration) with simplified geometries of cell nuclei that can be constructed quickly using an efficient fractal approach (developed by Dr N. Lampe of the Geant4-DNA collaboration to model induction of DNA damage in E. coli bacteria [9]). This combination enables in particular the calculation of the amount of DNA damage produced in a cell nucleus within a few hours, which is significantly faster than the use of step-by-step simulation of water radiolysis, already available in Geant4-DNA [12, 13].

What is the most important finding of your study?

This study allowed us to quantify early direct and non-direct damage to DNA in the form of single and double DNA strand breaks as well as DNA fragments. We could reproduce results in close agreement with "PARTRAC", which is a reference code in the track structure community for the prediction of early and late DNA damage under irradiation. Importantly, a good agreement with experimental data on the number of double-strand breaks and DNA fragments was also observed. This clearly underlines the capabilities and potential of Geant4-DNA for radiobiological research.

What are the implications of this research?

Geant4-DNA is a component of Geant4. The functionalities presented in this work will soon be integrated into Geant4 and released to the community (open source). The first Geant4-DNA physics models for track structure simulations in liquid water based on the dielectric response theory were delivered to the community in December 2007 [2]. Since then, step-by-step, we have added new functionalities in Geant4-DNA: improvement of physics models [14, 15]; addition of liquid water radiolysis simulation capabilities [12, 13]; and development of various simplified geometries of biological targets that enable DNA damage scoring [9, 11, 16-18]. We have always benefited from the constant support of the community. Our main motivation is the necessity to make such developments available to all, at no cost. Over time, Geant4-DNA improves in accuracy and extends its functionalities, and we welcome anyone interested in joining this global effort. There is still a lot more to do. For example, we are now developing Geant4-DNA models for the transport of electrons in gold, for the study of radiosensitisation using gold nanoparticles [19-21].

In the same spirit of making developments accessible to all, since 2004 we have provided freely a "virtual machine" (http://geant4.in2p3.fr/spip.php?rubrique8&lang=en) [1] to all Geant4 and Geant4-DNA users. This machine is regularly updated and emulates a functional workstation to develop and run Geant4/Geant4-DNA-based user applications, without the need to install any other software, which eases access to our developments. It is also used regularly during Geant4 and Geant4-DNA tutorials.

Through all the above efforts we strive to contribute to making science open and accessible to all.

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