

Microdosimetry in High-Resolution Cellular Phantoms Using the Very Low Energy Electromagnetic Extension of the Geant4 Toolkit

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Abstract—This study presents the simulation of ionizing track structures in single biological cells modeled as high resolution cellular phantoms using the new “Geant4 DNA” very low energy extension of the Geant4 Monte Carlo simulation toolkit.

I. INTRODUCTION

UNDERSTANDING the health effects of low doses of ionizing radiation is the challenge of today’s radiobiology research. Recent results include the observation of bystander effects, adaptive response, gene expression changes, genomic instability and genetic susceptibility, which may question the validity of health risk estimation at low doses [1].

Dedicated experimental facilities have been developed in order to investigate the interaction of ionizing radiation with living cells, making use for example of radioactive sources, classical beams or microbeams [2]. The latter allows a perfect control of the deposited dose in the targeted cell with a beam spatial resolution of a few microns in air. Such a facility is available for routine irradiation of single living cells in single ion mode at the Centre d’Etudes Nucléaires de Bordeaux Gradignan (CENBG), a Bordeaux 1 University – CNRS / IN2P3 located in France [3].

In support to the experimental activity, modeling of the radiation interactions at the cellular scale is an important activity in this field. Modeling biological systems and physics processes down to the nanometer / electronVolt scale is a challenge.

Several specialized Monte Carlo codes have been developed so far for radiobiology and microdosimetry. However, this is the first time that a general-purpose Monte Carlo system – the Geant4 [4], [5] toolkit – is equipped with functionality specific to the simulation of biological effects of radiation: the Geant4 DNA package [6]. In the following sections, this very low energy extension is briefly introduced, the modeling of realistic cellular models in Geant4 is presented and a track structure sample in a high resolution cell geometry model is shown.

II. THE GEANT4 DNA PROJECT

The Geant4 DNA extension of the Geant4 toolkit is valid in liquid water down to very low energies (electronVolt scale) and it covers the interactions of electrons, protons, hydrogen, alpha particles and their charge states. The physics processes available in this package are presented in Table 1.

TABLE I
PHYSICS PROCESSES AVAILABLE IN GEANT4 DNA

Incident particle	Processes
Electron	Elastic scattering Excitation Ionization
Proton	Charge decrease Excitation Ionization
H	Charge increase Ionization
He ⁺⁺	Charge decrease Excitation Ionization
He ⁺	Charge decrease Charge increase Excitation Ionization
He	Charge increase Excitation Ionization

For the first time in Monte Carlo simulation technology, the Geant4 DNA extension uses a policy-based class design [7], where physics processes are configurable with a variety of model options for cross section and final states computation. Physics processes can be handled transparently by the Geant4 kernel and can be configured by template specialization to acquire physics properties.

The Geant4 DNA extension will be part of the low energy electromagnetic package of the Geant4 9.1 public release.

III. HIGH RESOLUTION CELLULAR PHANTOMS

Microdosimetry calculations at the individual cell scale for the CENBG microbeam line and for other classical cellular irradiation facilities have been previously presented, using the Geant4 toolkit and simple cell geometries, like parallelepiped or embedded ellipsoid models for the nucleus and for the cytoplasm [2].

More detailed cell geometries become available thanks to high-resolution imaging techniques, like confocal microscopy, allowing the design of realistic 3D geometries with a voxel

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structure. Such geometries can be implemented in Geant4. A single cell can be modeled in Geant4 using “phantoms” made of parallelepiped voxels.

Phantoms containing a large number of voxels (slices with a resolution up to 512×512) have been implemented in the presented simulation application. Each individual voxel contains information on its absolute position within the whole cellular phantom as well as information on local chemical composition and density. The whole cell phantom is implemented using the Geant4 *G4PVParameterised* class. In this implementation each voxel position and material is parameterized in function of the voxel copy number.

Single-cell targeted irradiation is routinely performed at CENBG with 3 MeV incident alpha particles on human keratinocyte cells of the HaCaT line (Human adult Calcium and Temperature). A specific HaCaT cell line, expressing the chimeric recombinant histone GFP-H2B and identified as HaCaT/(GFP-H2B)Tg, has been developed at CENBG for in vivo staining of the cells’ nuclei, allowing safe automated cell recognition during the irradiation phase.

The cell phantoms were originally created from actual confocal microscopy images of HaCaT/(GFP-H2B)Tg cells. 2D images of the stained cells were acquired every 163 nm with a Leica® DMR TCS SP2 confocal microscope for several 2D resolutions, up to 512×512 pixels. The full sets of images were reconstructed in three dimensions using the Leica Confocal Software®. These images were transferred into the Mercury® Computer Systems, Inc. Amira® suite for filtering and geometry reconstruction.

The cell nucleus and cytoplasm could be extracted into individual files which were merged into a single phantom file. This file contains information about the total number of voxels for each cellular region, the voxel size along the three dimensions, a position shift in order to centre the cell in the simulated irradiation dish and the list of each voxel’s position and material composition, as well as the intensity fluorescence content of the voxel. The phantom could then be imported directly into the Geant4-based simulation. Figure 1 shows the graphical visualization of the 3D HaCaT phantom which can be displayed by the simulation application.

IV. TRACK STRUCTURE MODELLING

A 2.4 MeV He+ particle, as typically delivered by the CENBG microbeam cellular irradiation facility, was shot on the cellular phantom filled with liquid water. The resulting full particle track structure is shown in Fig. 2. The figure color code illustrates the physics processes occurring along the track.

The simulation allows one to score the energy deposited in each voxel, and from it to evaluate the doses released to cellular structures, such as the nucleus. The features of the track structure, i.e. the evolution of the primary track itself and of its secondary products, can be studied in detail.

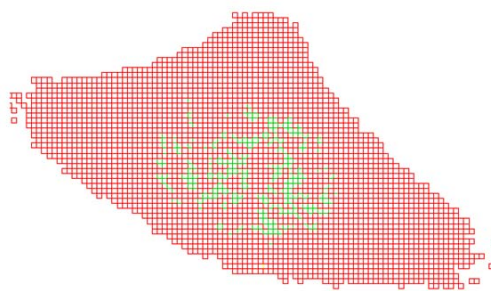


Fig. 1. Geant4 visualization of a 64×64 phantom of a HaCaT/(GFP-H2B)Tg cell (face view); the nucleus voxels are shown in green, the nucleus voxels in green. Each individual voxel has a volume of $0.36 \times 0.36 \times 0.16 \mu\text{m}^3$.

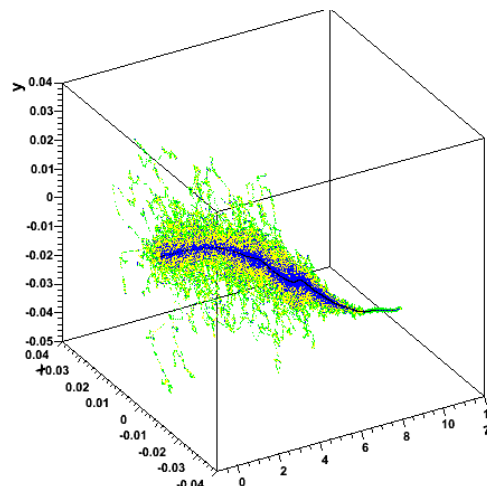


Fig. 2. Track structure of a 2.4 MeV He+ particle penetrating into the high resolution cellular phantom. Unit is micrometer. The primary particle propagates from left to right. Physics processes occurring are displayed with a color code: excitation in blue, elastic scattering for electrons in green, ionization in yellow, charge decrease in black and charge increase in red.

V. CONCLUSION

This work presents for the first time the simulation of track structures in high resolutions cellular phantoms using the Geant4 DNA extension of the Geant4 Monte Carlo toolkit. Thanks to this new Geant4 extension, it is now possible to study the energy deposits produced by a primary particle and its shower of secondary particles inside a high resolution biological cell model.

With the availability of biological dyes allowing the identification of specific cellular regions, as well as the future developments of the Geant4 DNA extension (additional physics processes, chemical phase production of radical species, DNA molecular modeling, ...), we expect to simulate in a more realistic way interactions of particles with biological cells, for interdisciplinary applications involving not only radiobiology, but also environmental exposure studies, microdosimetry for future manned space missions, etc...

REFERENCES

- [1] K. Prise, “New advances in radiation biology”, *Occup. Med.*, vol 56, no. 3, pp. 156-161, 2006
- [2] S. Incerti, N. Gault, C. Habchi, J. L. Lefaix, Ph. Moretto, J. L. Poncey, T. Pouthier and H. Seznec, “A comparison of cellular irradiation techniques

- with alpha particles using the Geant4 Monte Carlo simulation toolkit”, *Radiat. Prot. Dosim.*, vol. 122, pp. 327-329, 2006
- [3] Ph. Barberet, A. Balana, S. Incerti, C. Michelet-Habchi, Ph. Moretto and T. Pouthier, “Development of a focused charged particle microbeam for the irradiation of individual cells”, *Rev. Sci. Instr.*, vol 76, no. 015101, 2005
 - [4] S. Agostinelli et al., “Geant4 - a Simulation Toolkit”, *Nucl. Instrum. Methods A*, vol. 506 pp. 250-303, Jul. 2003.
 - [5] J. Allison, K. Amako, J. Apostolakis, H. Araujo, P. Arce Dubois, M. Asai, et al., “Geant4 developments and applications”, *IEEE Trans. Nucl. Sci.*, vol. 53, no. 1, pp. 270-278, Feb. 2006.
 - [6] S. Chauvie, Z. Francis, S. Guatelli, S. Incerti, B. Mascialino, P. Moretto, P. Nieminen and M. G. Pia, “Geant4 physics processes for microdosimetry simulation: design foundation and implementation of the first set of models”, to be published in *IEEE Trans. Nucl. Sci.*, Dec. 2007
 - [7] A. Alexandrescu, *Modern C++ Design*, Ed.: Addison-Wesley, 2001.