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TOPAS-nBio –a Monte Carlo approach to mechanistic modeling at the cell-scale, connecting physics and biology

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Purpose: TOPAS-nBio brings a track-structure Monte Carlo (MC) simulation framework to the research community to test hypotheses of radiation effects at the nanometer/cell scale. Here, I present the developments and progress made over the last decade of the TOPAS-nBio project.

Methods: TOPAS-nBio1 extends the TOPAS2 MC application to the nanoscopic scale, and is built on the Geant4 MC toolkit, an open-source MC framework for radiation transport. The TOPAS-nBio project links detailed MC track-structure simulations with geometrical representations of (sub-) cellular components, including initial chemical processes and likely biological outcomes via mechanistic models of DNA repair. The DNA is modeled as a chain of molecules with a resolution of single base (~0.34 nm).

Results: The latest TOPAS-nBio release v4.0 (https://github.com/topas-nbio) provides a simulation framework for nanometer scale radiobiology research. We have developed a variety of geometries, including multiple cell topologies and different representations of DNA geometries, including cell-line specific DNA representations using Hi-C data. Energy depositions can be scored to obtain induction of direct DNA damage after irradiation or indirect DNA damage following chemical reactions after radiolysis. Special emphasis was given to the chemistry framework, improving simulation speed using the independent reaction time method, expanding the simulated time to include long-term (seconds to hours) reactions by merging non-homogeneous and homogeneous chemistry stages, adding chemistry processes mimicking cell environments, including reactions with DNA constituents, and the capability to simulate ultra-high dose-rate irradiation. Two models of DNA repair kinetics have been linked to predict final biological effects and cell fate.

Conclusion: TOPAS-nBio offers cross-disciplinary simulations aiming to understand cell-level radiobiology, and has been applied internationally by multiple groups, providing insights into mechanisms of cell responses for different radiation modalities or when investigating new technologies (e.g., radiosensitization with nanoparticle or healthy tissue protection with ultra-high dose rate irradiations).

References:

1 B. Faddegon et al., Phis. Med., 72, 114-121 (2020).

2 J. Schuemann et al., Radiat. Res., 191(1), 125-138 (2019).

Author: SCHUEMANN, Jan (Massachusetts General Hospital & Harvard Medical School)

Co-author: Dr RAMOS-MÉNDEZ, Jose (UCSF)

Presenter: SCHUEMANN, Jan (Massachusetts General Hospital & Harvard Medical School)