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## Requirements of modelling tools for the understanding of radiation-induced biological damage at the cellular level.

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### Introduction:

Modelling the biological impact of the effect of ionizing radiation is of crucial importance for understanding the mechanisms involved but also for exploring the consequences of complex exposures. Our group at the French Institute for Radioprotection and Nuclear Safety (IRSN) is working on the development of a method in order to improve knowledge of the risks of complications during radiotherapy treatments. It combines a Track Structure Monte Carlo (TSMC) simulation tool of the interactions of ionizing radiation and radiolytic species [1] based on Geant4-DNA [2, 3, 4, 5] with a multi-scale modeling tool of the exposed cell population based on new functionalities implemented in the DNAFabric software [6]. The benchmarking with experimental data [7] and the integration of mathematical functions derived from experimental biological data on cell fate in a broad sense is ongoing. As with any modeling tool, continuous benchmarking is required to adapt to improvements in the simulation codes involved or to the availability of experimental data.

### Materials and Methods:

DNAFabric was first developed to generate geometrical models of nuclear DNA that can be exported to Geant4-DNA (TSMC) with the intention to be able to calculate the amount of early DNA damage (direct and indirect) within a particular nucleus for a given radiation quality. The parameterization of the simulation is carried out in accordance with the available experimental data. This tool was then extended to provide the essential framework for modeling the fate of a cell layer from the early simulated early DNA damage as well as other biological data that may be relevant.

### Results:

As a first step, we will show how our simulation could be benchmarked against experimental data for induction of early radiation-induced DNA damage up to some biological endpoints (survival, DSBs repair). Improvements under development will be presented: more refined target geometries, new methods for modelling the chemical stage (Independent Reaction Time method based), inclusion of the cellular layer. Each element being a source of uncertainty, it will make it possible to present the prerequisites for benchmarking in general terms. Nevertheless, we will see that a complete benchmark must be based on experimental data obtained under controlled conditions.

### Conclusion and perspectives:

Modeling tools of the risks for ionizing radiation effects are indispensable to better anticipate the effects of ionizing radiation on living organisms. With the example of DNAFabric new feature developments, we emphasize the indispensable and obvious complementarity of experimental and modelling activities. Developments of each activity must be linked. To achieve this, the standardization of experimental and simulation data should be the first prerequisite.

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