# Biophysical modeling for radiosensitizing effect of gold nanoparticles

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**Introduction**

One of the challenge of external radiotherapy is to focus the dose effects in cancer cells while limiting it to healthy cells around. Among the possible techniques, radiosensitizers aim to emphasis the destructive effect of the dose inside the tumor. Made of high-Z elements (gold, gadolinium ..), nanoparticles (NPs) have experimentally shown to be part of this category (1). When injected in the cancer, NPs increase the radiation exposure efficiency.

**Context**

Although this effect has been observed for decades, its origin is not yet fully understood. Physics mechanisms have been proposed. When photons interact with gold NPs, photoelectric effect followed by Auger cascade occur, leading to an increase of secondary electrons production. These electrons can leave the NPs to spread in the cell, locally increasing the dose and boosting the production of free radicals. Both are toxic to the cells and will therefore increase cell killing.

These mechanisms occur at very short time scale ($10^{-15}$ to $10^{-12}$ second) and at nanoscale, which make it impossible to directly observe it. Simulations are therefore required to model the mechanisms, and compare results to experimental data – such as cell-surviving curves – to validate hypothesis.

**Goal**

The aim is to reproduce experimental cell-surviving data to validate the mechanisms proposed. It requires to validate, step by step, the different models used. The global aim of this work is develop a toolkit to investigate the radiosenzitising effects of NPs in view of a clinical application of anti-cancer treatments.

**Method**

Such a toolkit was designed using a physics and chemistry simulation, MDM, and a biophysical model, Nanox.

1. *MDM*

MDM is a Monte Carlo simulation modeling interaction of electrons, photons and ions with water and gold, down to thermalization energy (2). The simulation will enable to quantify nanodose deposition and a free radical distribution induced by nanoparticles. These data will be then injected in a biophysical model : Nanox.

2. *Nanox*

Using dose and chemical species distribution, Nanox relies on statistical mathematical models to calculate cell-survival curves for a given dose. It will be used to reproduce radiosensitizing effect of gold NPs by predicting increase of cell-killing.

Nanox was originally designed for hadrontherapy (3). It has shown good results for various ion irradiations with various energies. Ions – such as carbon ion – are well known for their cell-killing efficiency, compared to photon irradiation. This efficiency comes from the specificity of ion tracks, which deposit their energy along their path, generating locally a high dose concentration. The probability of generating lethal events is increased, leading to a higher chance of killing the cell. As shown in Fig. 1, this track is very similar to the one observed when a photon is interacting with a gold NP. Therefore, when injecting data from NP X-ray irradiation, an increase of cell killing efficiency is expected, similar to the one observed for ion irradiation.

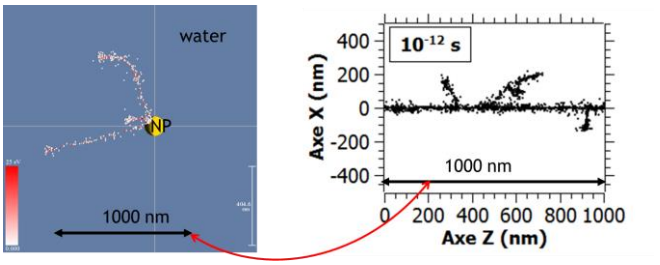


*Fig. 1 : Track for 20 keV photon irradiation (left) and 65 MeV carbon ion irradiation (right, (2))*

One challenge is also to optimize computing time, Monte Carlo simulation being usually very time consuming.

**Preliminary results: benchmarking of MDM**

The aim is to validate, step by step, the different models used to describe the interactions implemented in MDM with experimental data. Preliminary results are shown for an electron beam impinging on thin gold films. In Fig. 2 the number of backscattered (left) and transmitted electrons (right) are simulated and compared to measurements.

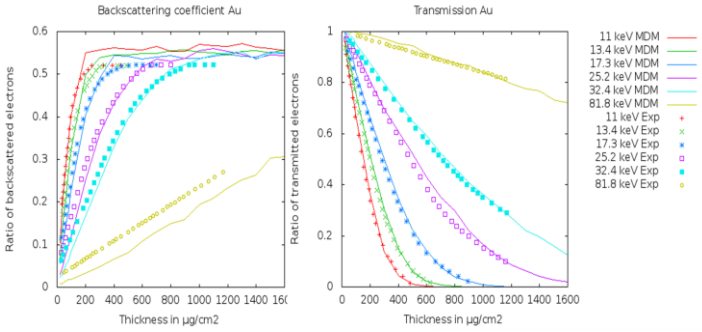


**Fig. 2 :** MDM vs experimental (4) results

**References**


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