Implementation and benchmarking of radiobiological models for the prediction of biological dose in hadrontherapy

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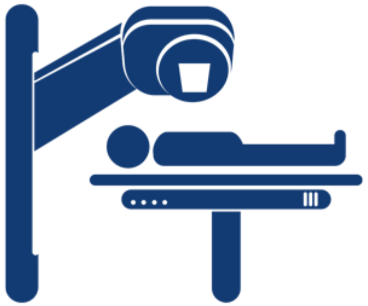
Context

Biophysical models implementation in Gate

For hadrontherapy applications, biological dose prediction will enhance treatments optimization.



Why using an approximative RBE value for ions isn't relevant?

What would be the tools for an accurate RBE estimation?

In which ways our work contribute to this purpose?

Biophysical Models

The biophysical models requires several types of data to lead to the relative biological effectiveness

Microkinetic model

Cell survival fraction

$$S = e^{-\langle L_n \rangle}$$

Number of damages in the nucleus

$$\langle L_n \rangle = (\alpha + \beta z)D + \beta D^2$$

Inaniwa T. et al. (2010)

NanOx

Cell survival fraction

$$S = S_{local\ events} \cdot S_{non\ local\ events}$$

LOCAL EVENTS

Effective lethal function

$$F(z) = -N \ln(1-f(z))$$

NON LOCAL EVENTS

Oxidative stress

$$F(Y) = e^{(-\langle \alpha Y + \beta Y^2 \rangle)}$$

C. Monini et al. (2017)

Biological data

α, β : constants of the linear and quadratic components of cell killing

Physical data

z: specific energy deposited in a target

N : targets distributed in sensitive volume

Chemical data

Y : yield of OH· the sensitive volume

Models implementation

Our methodology

To estimate the biological effectiveness, Monte Carlo simulations go hand in hand with biological, physical, chemical data.

GEANT4

LPCHEM

Databases

Biological, physical and chemical data are stored under databases.

Physical data

Specific energy for micrometric and nanometric targets.

Chemical data

Radiochemical species yields.

GATE

opengatecollaboration.org

Databases

Biological, physical and chemical data.

Biophysics Models

The models use the data tables data to then estimate the RBE.

RBE

RBE estimation by a Gate actor

G4DNA vs. LPCHEM

Differences between the codes

We use simular simulation parameters for both LPCHEM and GEANT4DNA, however a few differences can be noted between the codes.

	Physics Models	Simulated interactions		Stored interactions	Energies	
		Electrons	Protons		Electrons	Protons
LPCHEM 1.11	CDW-EIS calculations	Ionizations Electronic excitation Vibrational excitation Attachment	Ionization Excitation	80% of deposited energy, events relevant for the biological effect of radiation	10 keV to 100 keV	10 MeV to 250 MeV
G4DNA 10.5	G4DNA_Option 0 G4DNA_Option 2 G4DNA_Option 6	Ionizations Electronic excitation Vibrational excitation Attachment	Ionization Excitation Capture	100% of deposited energy	10 keV to 100 keV	10 MeV to 100 MeV

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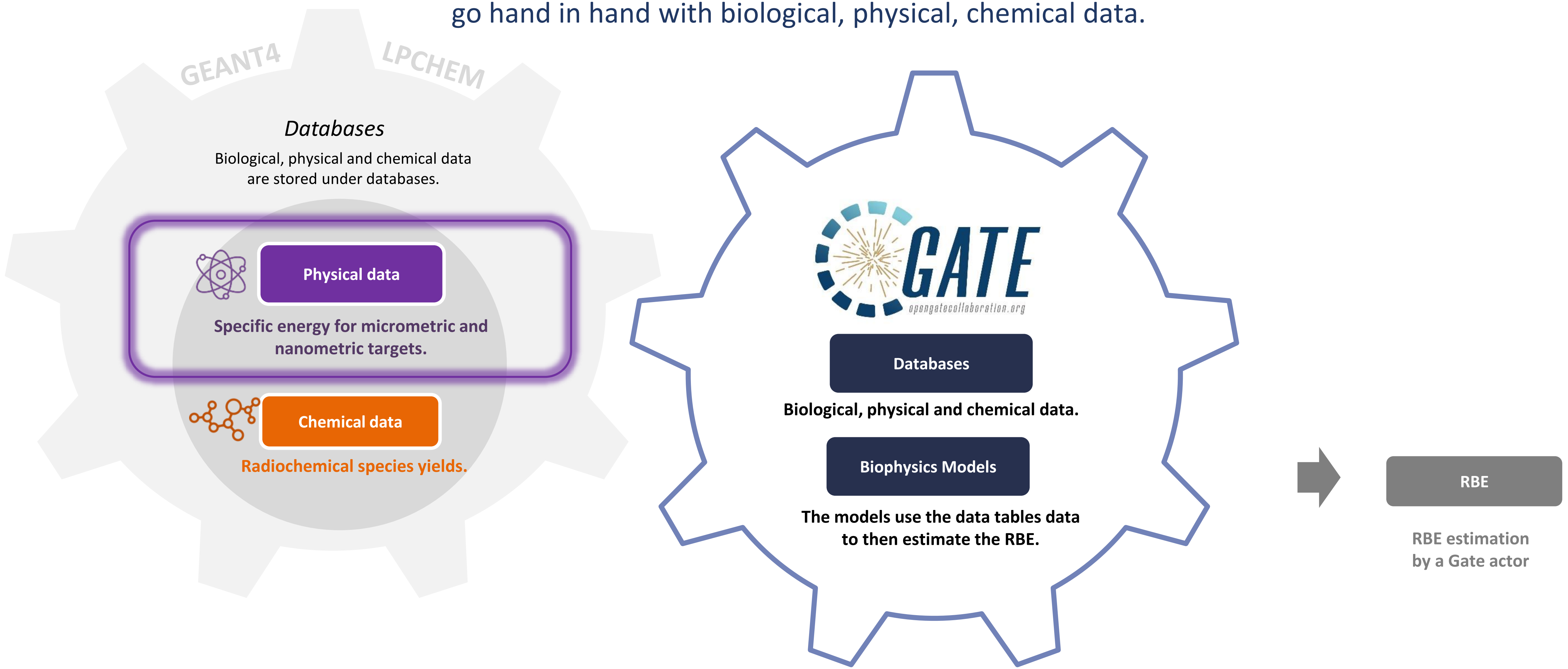
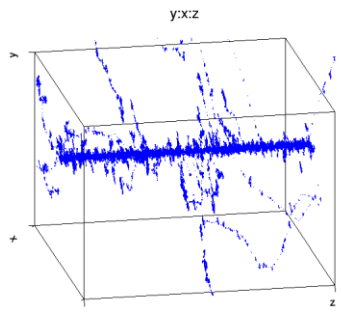


Physical data simulation

From energy transfer points to the specific energy distributions in micrometric and nanometric targets

ENERGY TRANSFER POINTS

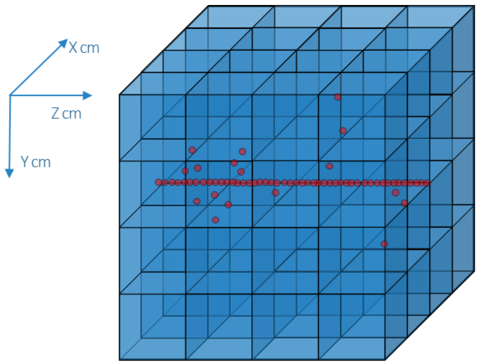
From LPCHEM or G4DNA



The LPCHEM and G4DNA physical modules simulate the energy transfer points.

THE MESH AND 3D MATRIX

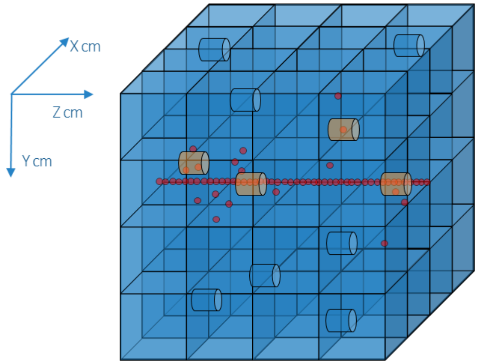
Calculation time saving biased method



The track volume is devided into voxels.

THE TARGETS

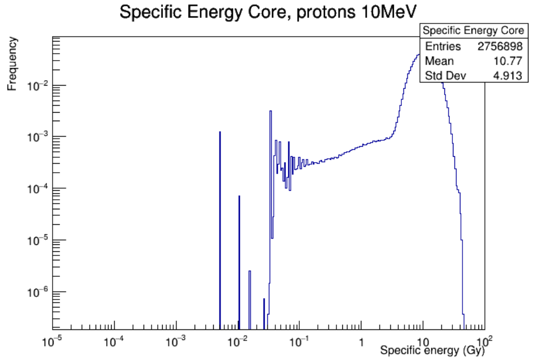
1µm micrometric and 10nm nanometric targets



Targets are generated in the voxels containing energy transfer points.

PROBABILITY DISTRIBUTIONS

Specific energy



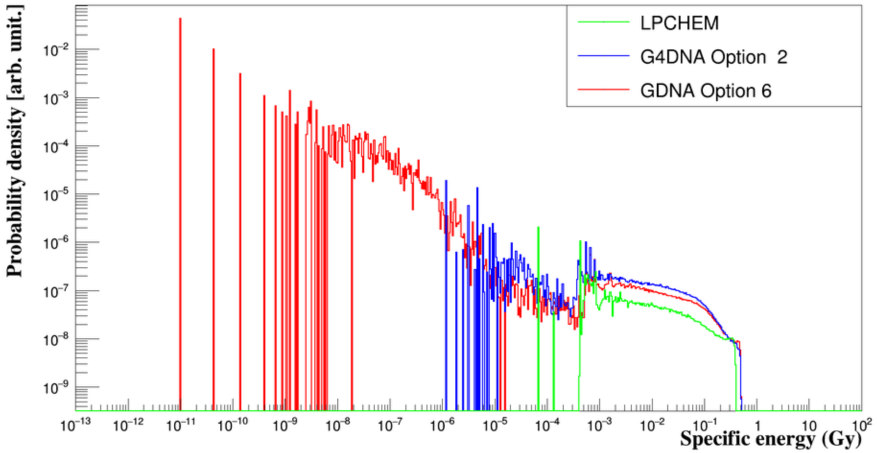
The probability distributions of specific energy are calculated.

Specific energy probability distribution

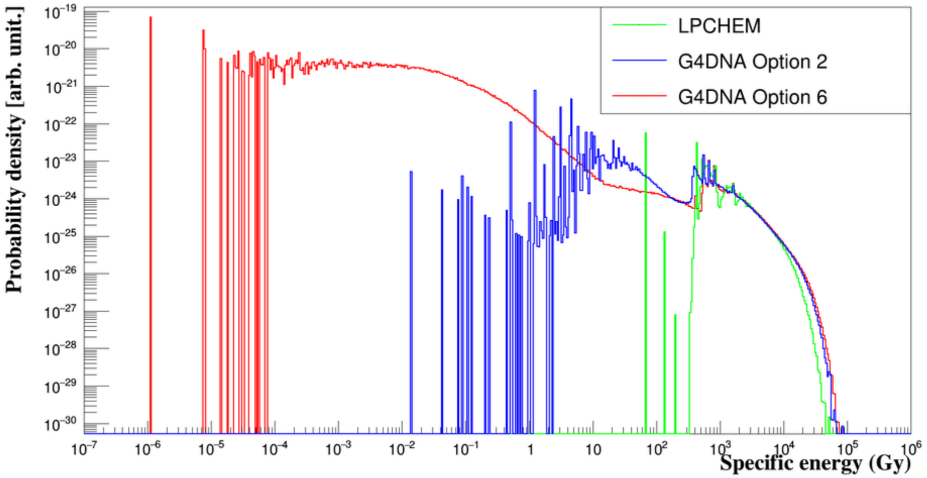
for 1µm micrometric and 10nm nanometric targets

Electrons 10 keV

Micrometric

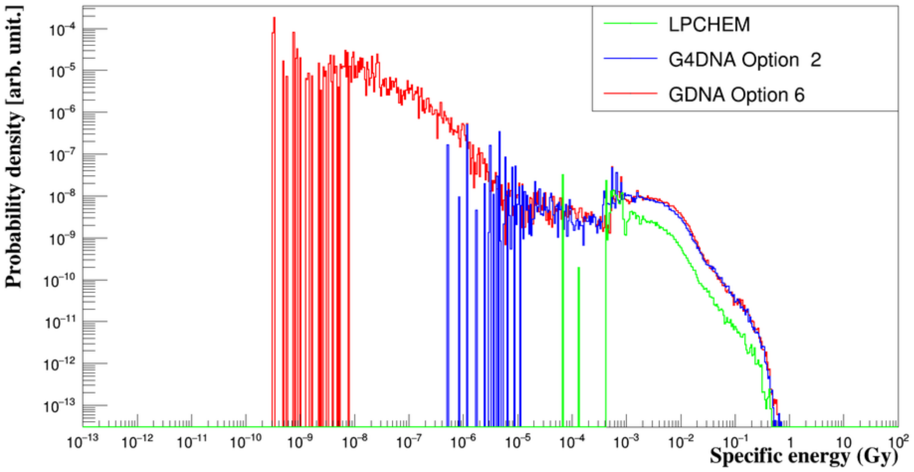


Nanometric



Electrons 100 keV

Micrometric



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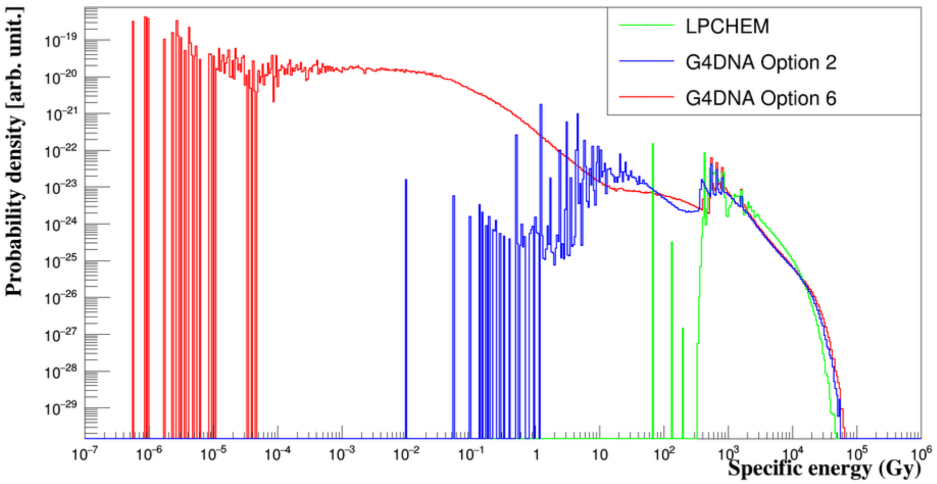
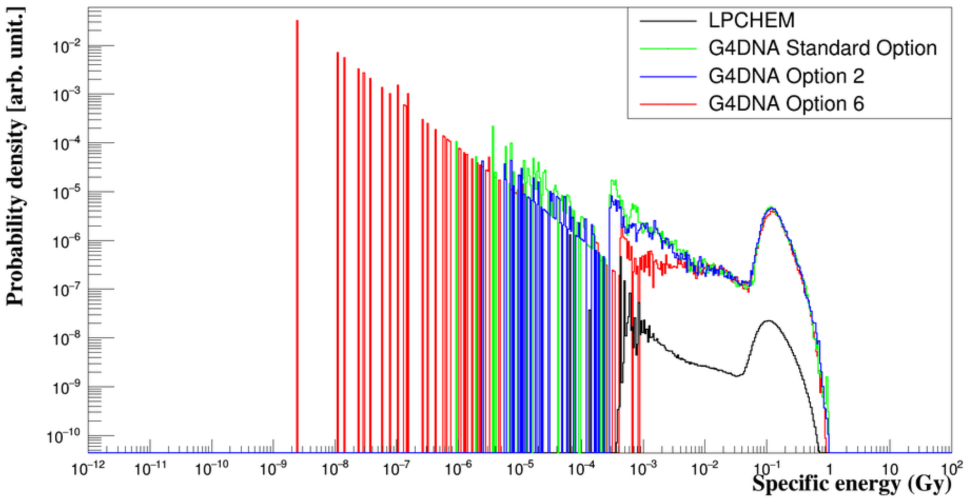


Specific energy probability distribution

for 1µm micrometric and 10nm nanometric targets

Protons 10 MeV

Micrometric



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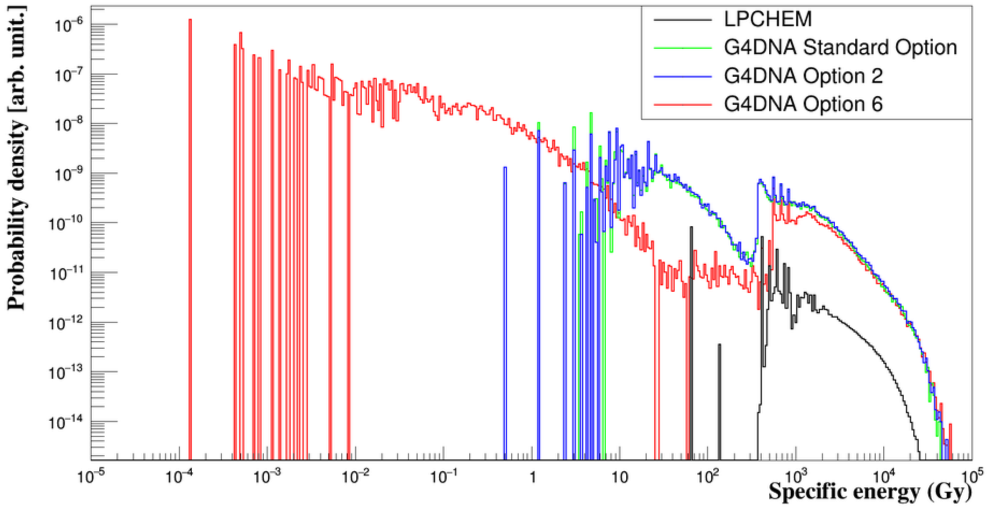
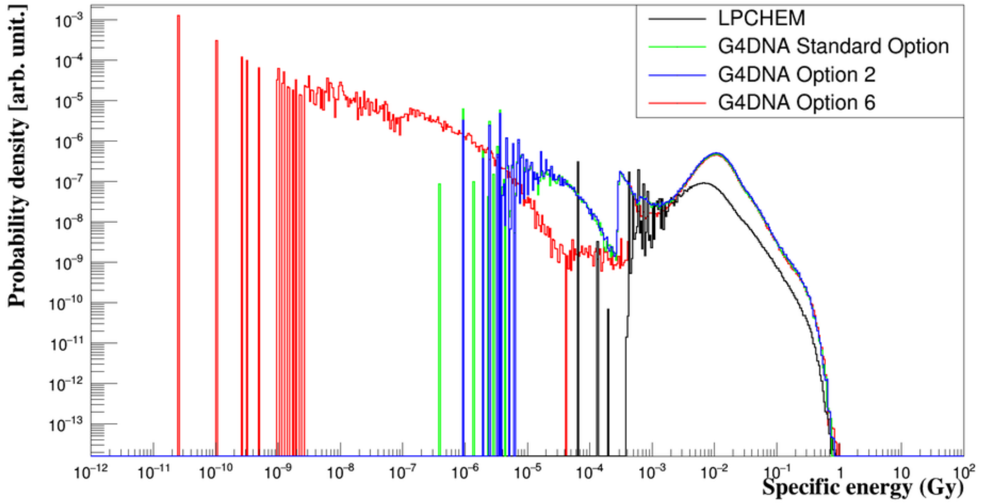
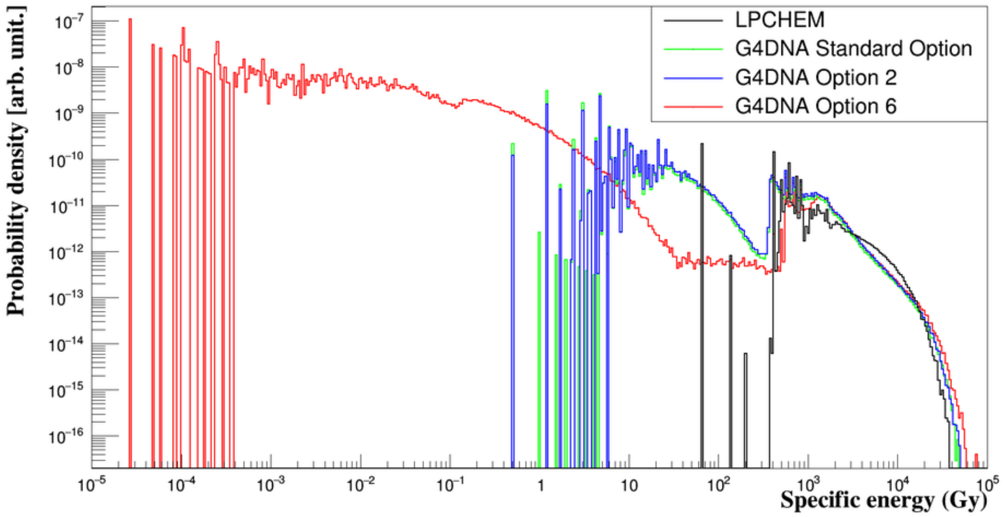


Protons 100 MeV

Micrometric



Nanometric



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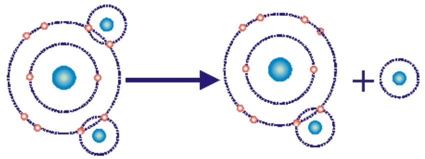
Chemical data simulation

To estimate the type, the quantity of free radicals with the chemistry modules

PHYSICOCHEMICAL STAGE

By LPCHEM and G4DNA



In the physicochemical stage of LPCHEM and G4DNA chemistry modules, the radiochemical products are generated.

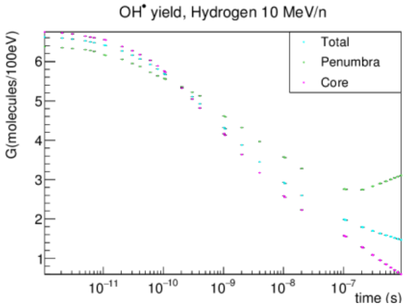
CHEMICAL STAGE

Radiochemical products

In the chemical stage, the radiochemical products interactions and their diffusion are simulated.

FREE RADICAL YIELDS

OH Yield



The average yield of OH molecules between 10^{-12} and 10^{-06} second for a 100eV deposited energy is estimated.

G4DNA vs. LPCHEM

Differences between the codes

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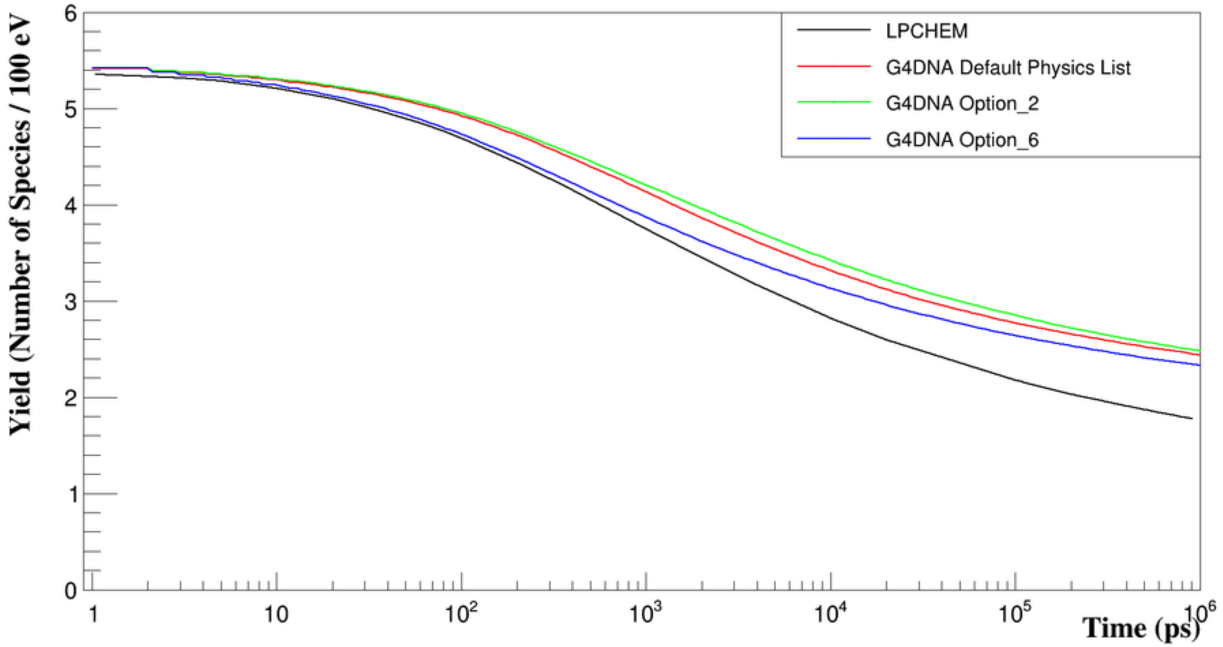
however a few differences can be noted between the codes.

	Chemical stage	Simulated interactions
LPCHEM 1.11	IRT (Independant Reaction Times)	A maximum time step is chosen, only the couples requiring less time to interact are taken into account. The brownian movement isn't simulated for time saving purposes so the position of the species between the time steps isn't considered.
G4DNA 10.5	Step by Step	The distance between the radicals as well as their probability of interaction is estimated. The brownian movement is simulated for the particles, based on the Smoluchowski equation. Unlike LPCHEM, the position of the species can be known between the time steps.

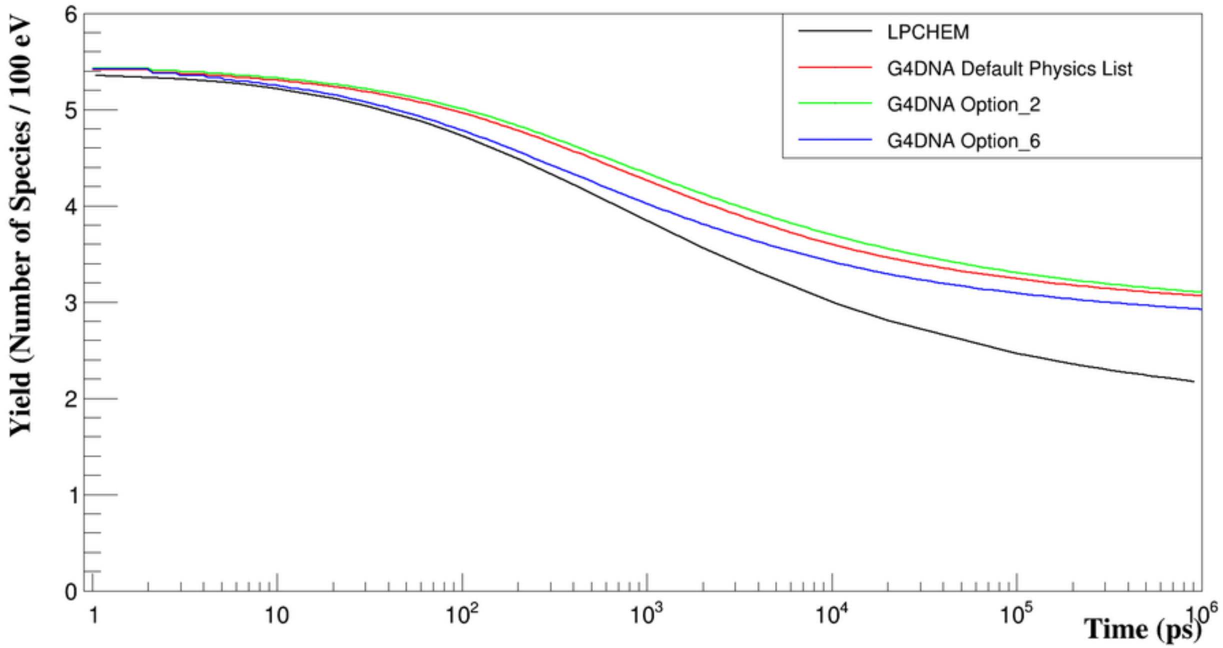
Hydroxyl radical yield

OH radical products yields for a 100 eV deposited energy

Protons 10 MeV



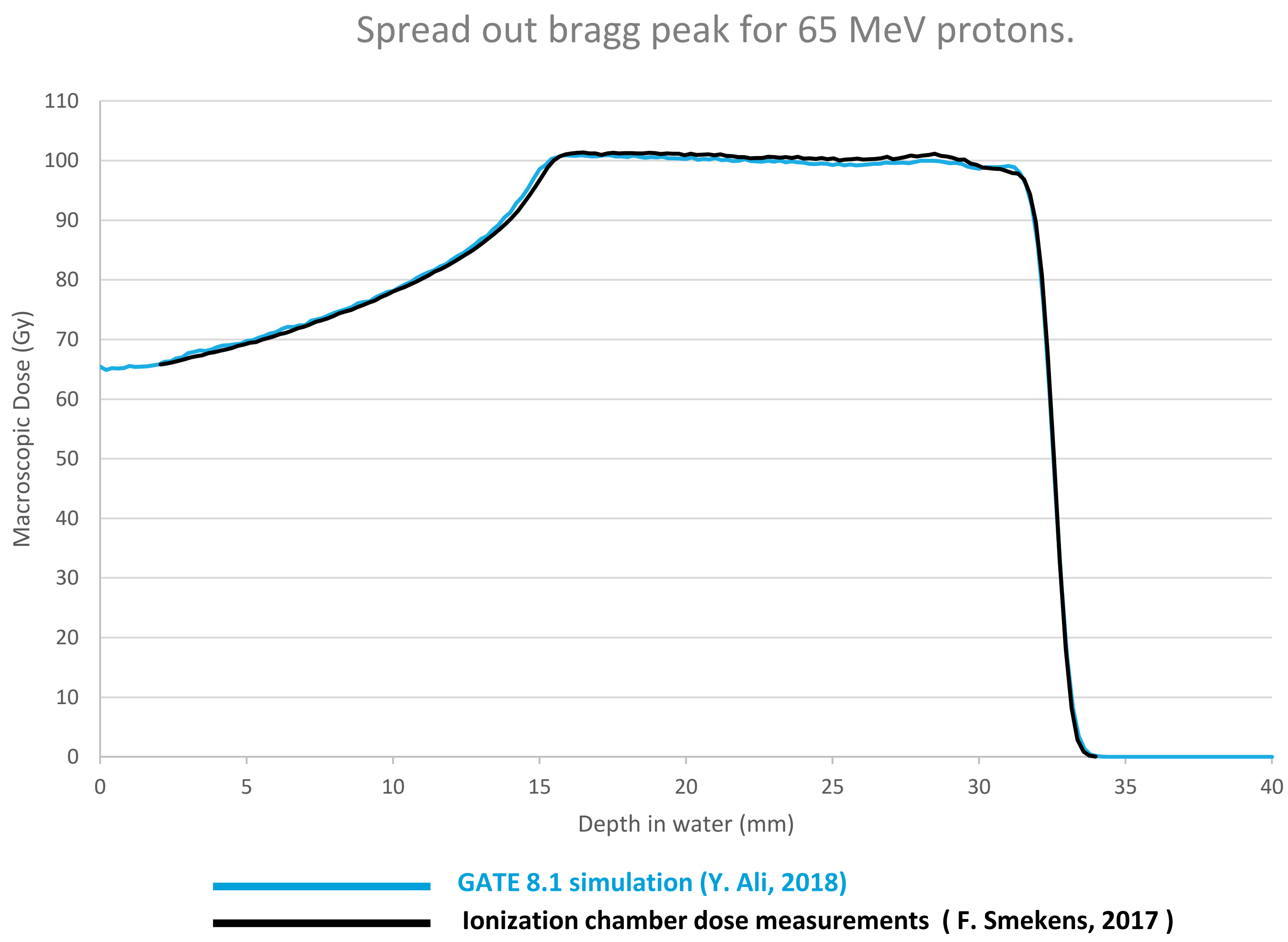
Protons 100 MeV



Spreak out bragg peak

Our methodology

Physical and chemical data have been simulated for monoenergetic beams, the next step will be to perform the same work for a clinical beam SOBP.



GATE ACTOR

The actor collects, for each voxel :

- the particles atomic number
- the deposited energy for each particle
- the proportion of each type of particles

DATA TABLES

We use data tables of biological, physical and chemical data calculated for monoenergetic beams, summed, to obtain the equivalent data for a SOBP.

Collaborations

We would like to thank

LPC – Laboratoire de Physique de Clermont: GATE & GEANT4

IPNL: NanOx, LQD, PHYCHEML

Antoine Lacassagne – Centre de Lutte contre le Cancer de Nice: Protons beam

CENBG: GEANT4DNA

GEANT4DNA
GATE

MedAustron: Carbon ions beam

LIDYL: Experimental Radiolysis products

fondazione CNAO: Carbon ions beam

THANK YOU.