GATE for radiation biology applications

CPOP & water radiolysis chemistry

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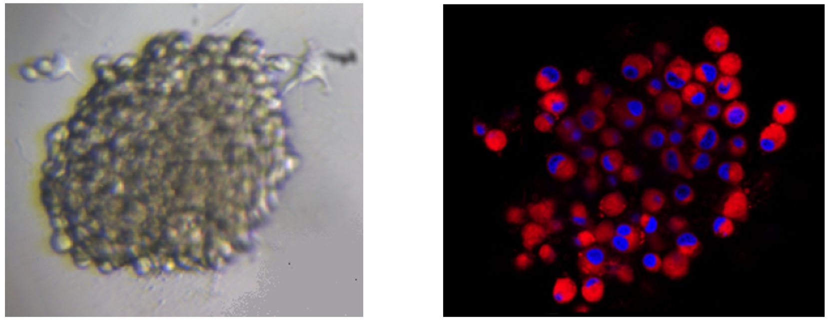
CPOP: a C++ cell population modeler coupled with Geant4

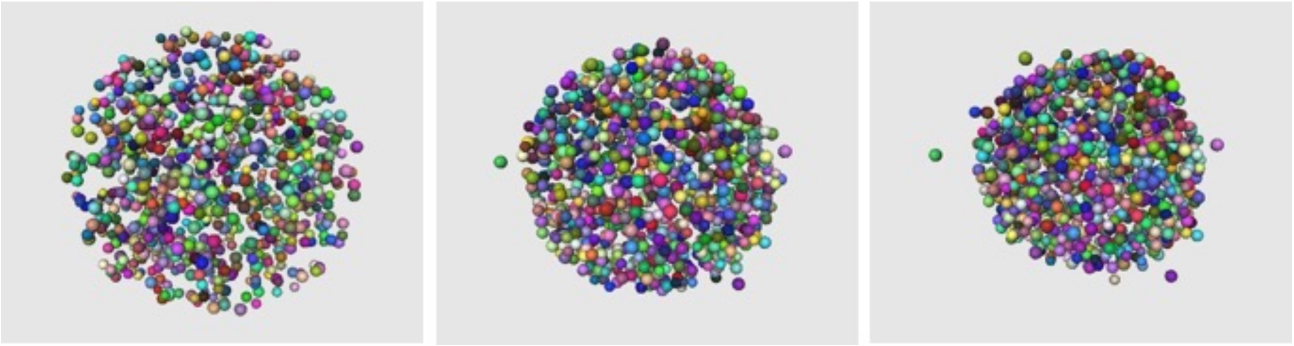
L. Maigne, et al. 2021, https://doi.org/10.1016/j.ejmp.2021.07.016

https://github.com/lpc-umr6533/cpop

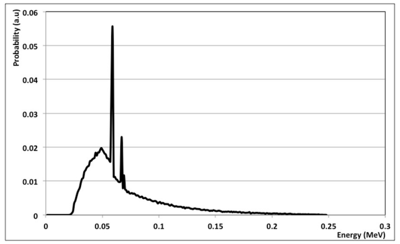


(a) (b)

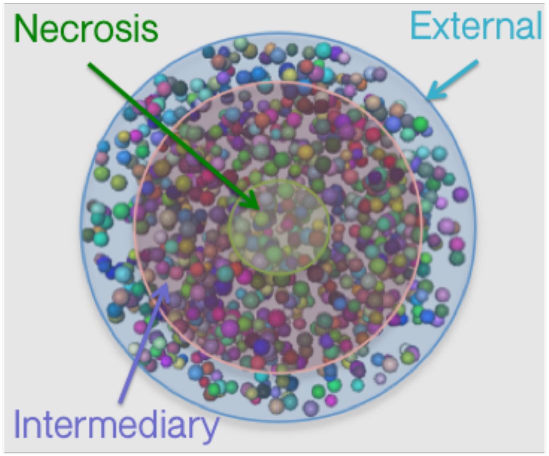
(a) Reverse-phased microscopy imaging of a spheroid (SK-MEL 28 type) of 550±40 µm in diameter (b) Fluorescent confocal microscopy of a spheroid (SK-MEL 28 type)



- 3 shells: Necrosis, Intermediary, External
- Cells sampled per zone
- NPs positionning: membrane, cytoplasm, nucleoplasm or nuclear membrane
- Energy spectra of particles:
  - With and without Gd NP
  - Different levels
- G4 PhysicsList: Penelope, Geant4-DNA…
- Energy deposited to cells and sub-cellular compartment
- Tested in targeted alpha therapy



Photon energy spectrum entering a water sphere of 550 µm at 2 cm depth.



How to use the platform

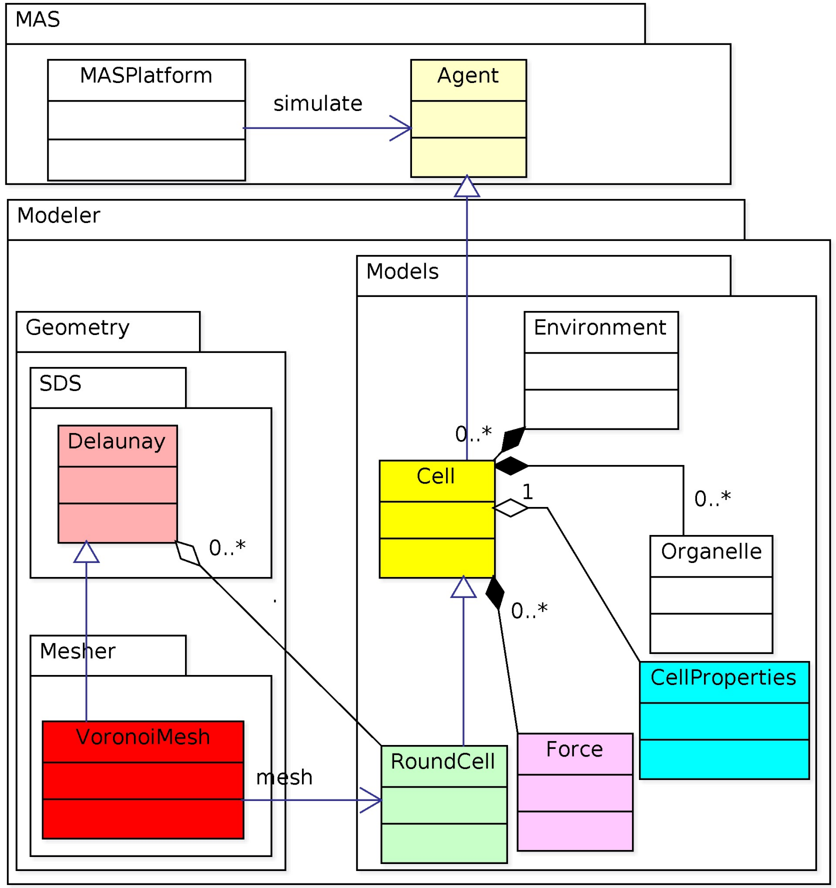
Mandatory libraries:

- Geant4 (11.1)
- Qt5
- CGAL 5.5.1 (=> Boost, Mpfr, Xerces)
- CLHEP (2.4.6.1)
- Root (6.26.10)

Compilation and installation

Using cmake and make

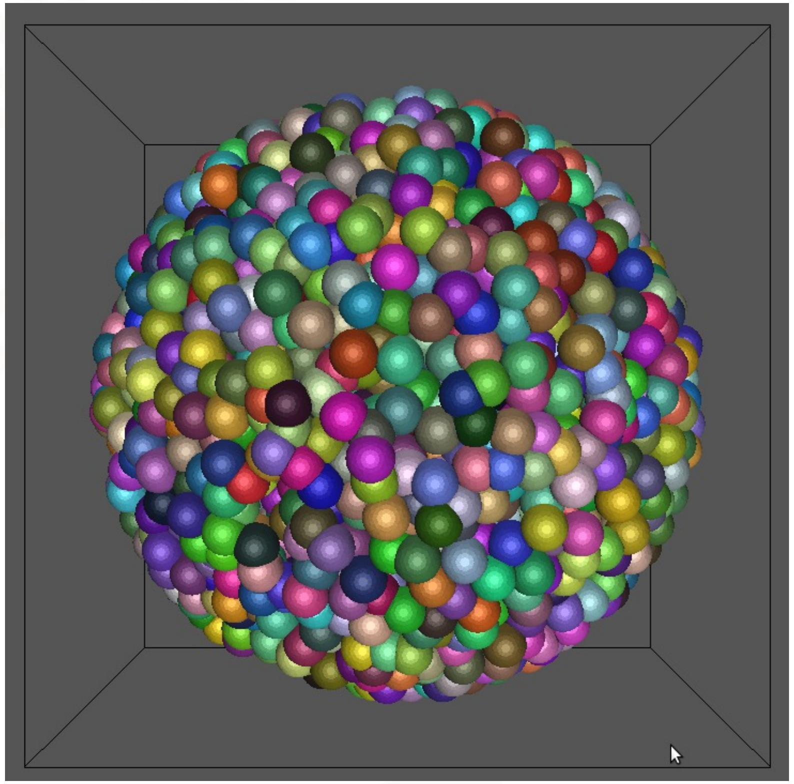
4 examples to test



https://github.com/lpc-umr6533/cpop

Example 1: Generate a cell population

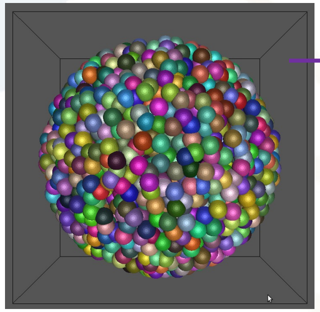
```
./generatePopulation -f data/exampleConfig.cfg -vis

geomview data/exampleConfig.cfg.off &
```

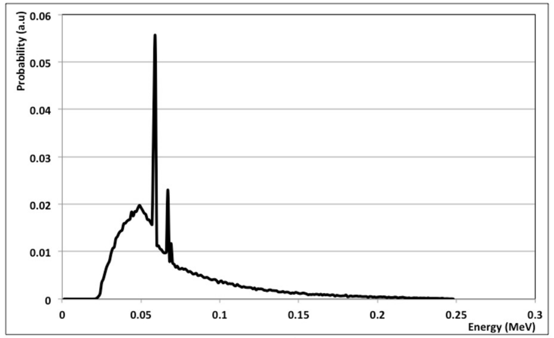


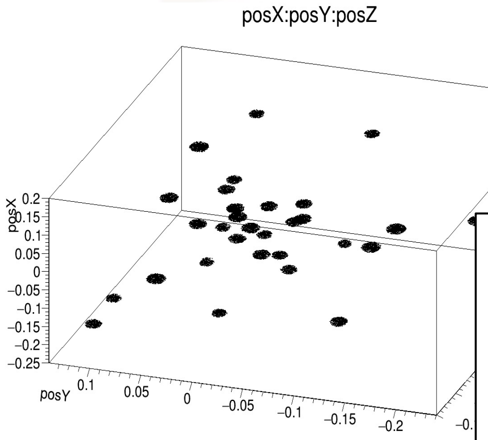
```
[UnitProperties]
metricSystem = Micrometer

[CellProperties]
nucleusRadius      = 5.5 5.5
membraneRadius     = 6.9 6.9
cytoplasmMaterials = G4_WATER
nucleusMaterials   = G4_WATER

[SpheroidProperties]
internalRadius = 0
externalRadius = 95
nbCell         = 60000
#18124
[MeshProperties]
maxNumberOfFacetPerCell = 1000

[ForceProperties]
ratioToStableLength = 0.7
rigidity            = 0.002

# Time is given in second
[SimulationProperties]
duration                = 0
numberOfAgentToExecute  = 100
displacementThreshold   = 0.5
stepDuration            = 1
```

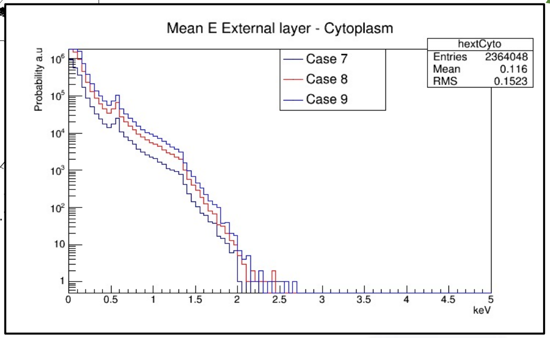
Example 2: uniform radiation

```
./homogeneousRadiation -m data/run.mac -t 4
```





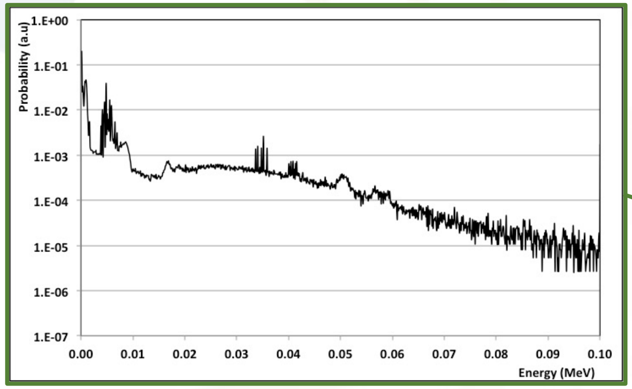




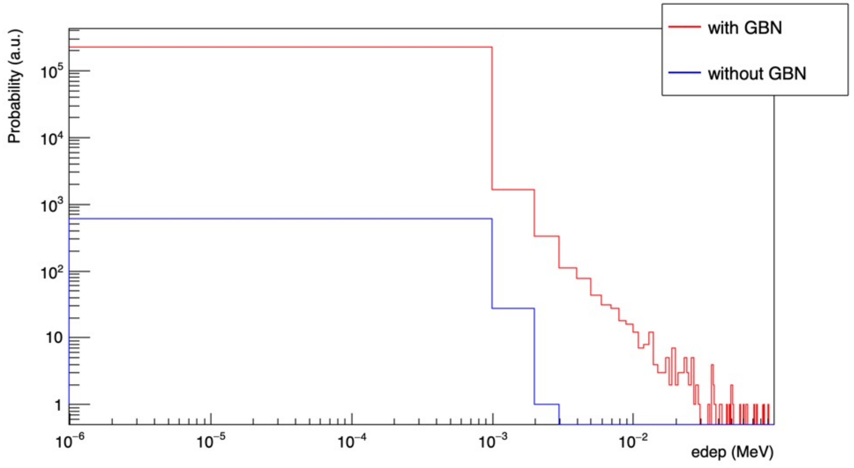

```
/cpop/population/input data/population.xml

/cpop/population/numberFacet 100
/cpop/population/internalRatio 0.25
/cpop/population/intermediaryRatio 0.75

/cpop/population/sampling !

/cpop/population/init
/run/initialize
# add a gamma source using a user defined spectrum
/cpop/source/addUniform gamma
/cpop/source/gamma/particle gamma
/cpop/source/gamma/spectrum data/phspectrum_spheroid.txt

/cpop/source/gamma/totalParticle 10000

/analysis/setFileName output.root

/run/beamOn 10000
```

Example 3: complex radiation

```
./complexRadiation -m data/run.mac -t 4
```

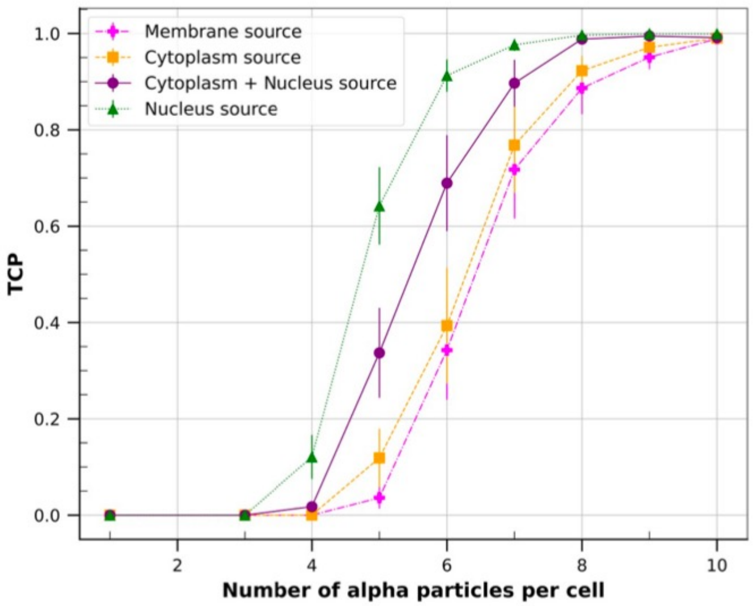



```
/cpop/source/addDistribution gadolinium

/cpop/source/gadolinium/particle e-
/cpop/source/gadolinium/spectrum data/eSpectrumGBN_550um.txt

/cpop/source/gadolinium/totalSource 30

/cpop/source/gadolinium/particlesPerSource 1

/cpop/source/gadolinium/distributionInRegion  10 10 10
```



Example 4: alpha targeted therapy

```
./targetedAlphaTherapy -m data/run.mac -t 4
```



Credit: Victor Levrague, PhD student, LPSC

```
/cpop/source/addDistribution radionuclide

/cpop/source/radionuclide/particle alpha

/cpop/source/radionuclide/spectrum data/At211.txt

/cpop/source/radionuclide/totalSource 2000

/cpop/source/radionuclide/particlesPerSource 1

# set to 1 to have all sources in a cell located in the same place
# set to 0 for a random distribution of sources in a cell
/cpop/source/radionuclide/only_one_position_for_all_particles_on_a_cell 0

# set the source distribution in each region
/cpop/source/radionuclide/distributionInRegion  0 0 2000

/cpop/source/radionuclide/distributionInCell 1 0 0 0

# Activate diffusion of radionuclide's daughter (for At-211 only)
/cpop/source/daughterDiffusion no


/cpop/source/radionuclide/maxSourcesPerCell 0 10000 10000
/cpop/source/radionuclide/cellLabelingPercentagePerRegion 100 100 100
```

Implementation in GATE 10

Generation of cell population geometry
opengate_lib/
GateCellPopulation.h GateCellPopulation.cpp

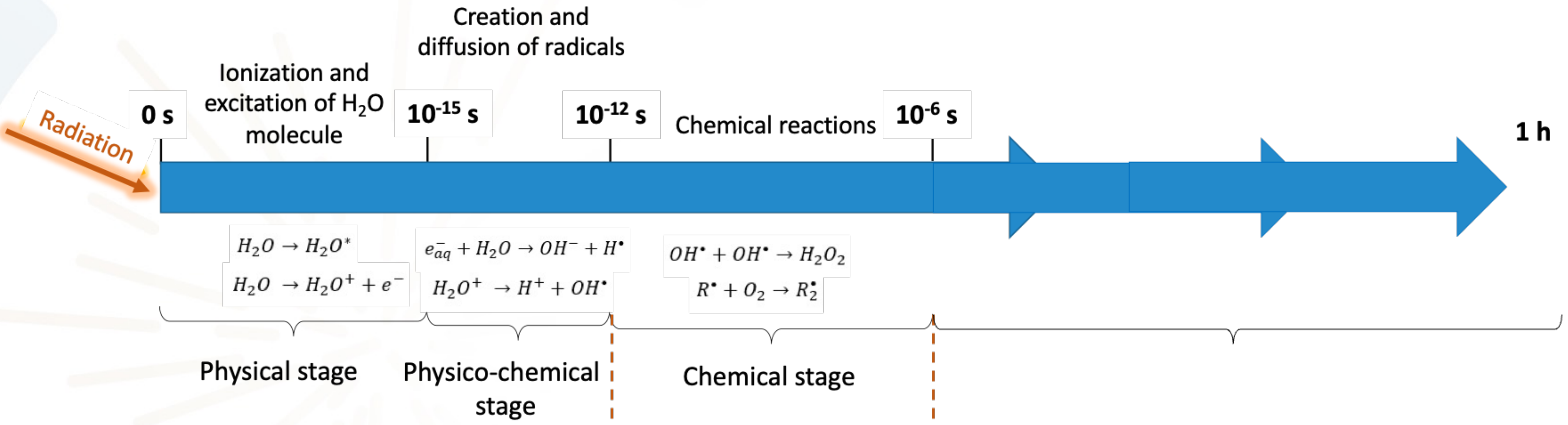
3 actors to analyze energy deposited in cell population
opengate_lib/
GateCellUniformActor.h GateCellUniformActor.cpp
GateCellNanoActor.h GateCellNanoActor.cpp
GateCellAlphaActor.h GateCellAlphaActor.cpp

Generation of cell population geometry
opengate/
CellPopulation.py

3 actors to analyze energy deposited in cell population
opengate/
CellUniformActor.py CellNanoActor.py CellAlphaActor.py

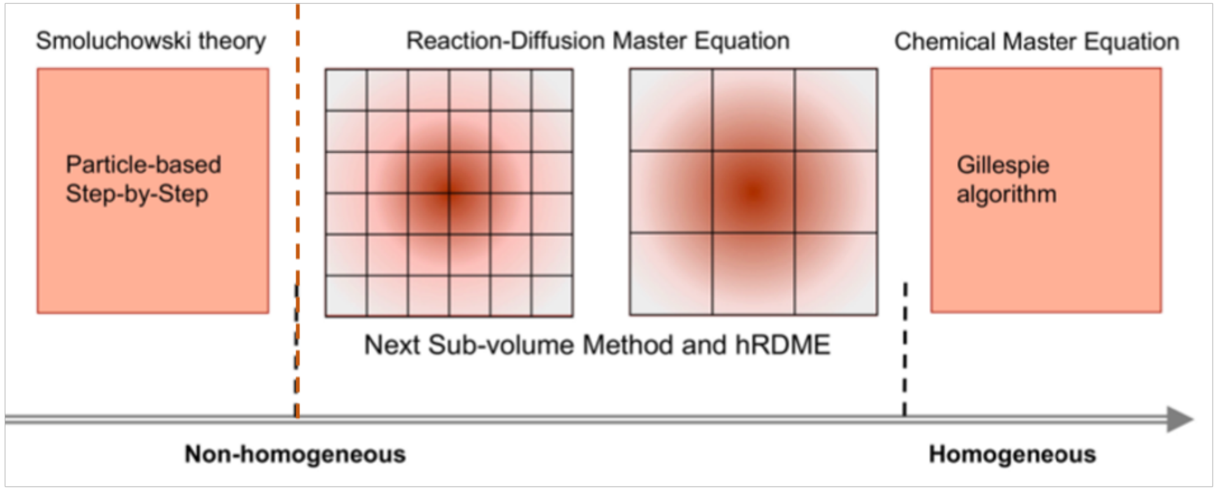
Geant4-DNA water radiolysis Chemistry module

Handle water radiolysis chemistry in Geant4-DNA



Beyond the µs

- Homogeneity within each voxel
- Diffusion of species between voxels
- Reaction between species within voxels
- Voxel size increases over time
  - (heterogeneous -> homogeneous)



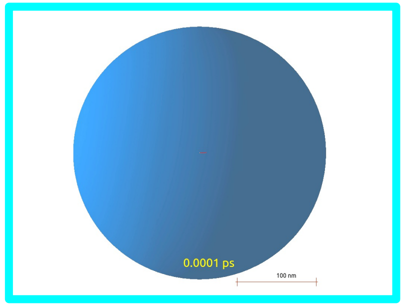
Chemical stage: 2 approaches

A collaborative
Geant4-DNA & TOPAS-nBio initiative

J. Comput. Phys. 274 (2014) 841 (link)
Phys. Med. 31 (2015) 861-874 (link)
J. Appl. Phys. 126 (2019) 114301 (link)
arXiv:2006.14225 (2020) (link)
Med. Phys. 47 (2020) 5920-5930 (link)
Phys. Med. 88 (2021) 86-90 (link)
Med. Phys. 48 (2021) 890-901 (link)

1. Step-by-step (« SBS ») « reference » approach

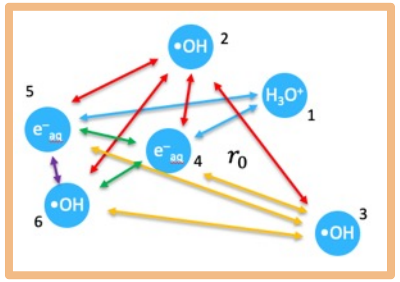
- Brownian transport of molecules from the Smoluchowski model.
- Chemical species are represented by point objects which diffuse in the liquid medium;
- Chemical reactions are « controlled by diffusion »
- 7 species, 9 chemical reactions



+: Tracking of species
-: Very slow & memory cons.

2. Independent Reaction Times (« IRT ») approach

- From the 1980's by Clifford, Green et al., widely used today.
- Iterative process where the approximation of « independent pairs » is assumed: calculates the reaction times between all possible pairs of reactive species, as if they were isolated. Then, reactions occur one by one, starting with the pairs having the shortest reaction times.
- No longer necessary to diffuse the molecular species and to calculate the possible reactions between the species at each time step.
- 15 species, 72 chemical reactions (totally & partially diff.controlled)
- A « synchronous » alternative hybrid version (« IRT-sync ») recently released by H. Tran et al. @ IRSN, which gives all spatio-temporal info. on radicals required for combination with geometries



Clifford et al. (1986)

+: Very fast
-: Tracking of species

The 4 Geant4-DNA « chemistry constructors »

Chemistry constructor	Description	Approach
G4EmDNAChemistry	**First constructor** implemented in Geant4-DNA for the chemistry processes with parameter values from Karamitros et al. (2014) – from PARTRAC	SBS
G4EmDNAChemistry_option1	Implements a **revisited set of chemistry parameters** from Shin et al. (2019) – from TRACs + Burns et al. (1981) + Rowe et al. (1988)	SBS
G4EmDNAChemistry_option2	Includes chemistry parameters for simulating **reactions with DNA components** – from Buxton et al. (1988)	SBS
G4EmDNAChemistry_option3	Implements the **IRT approach** from Ramos-Mendez et al. (2020) – from RITRACKS & Elliot et al. (1994)	**IRT**

The Geant4-DNA « chem » examples

- Six examples are available in Geant4-DNA in `extended examples/medical/dna`
  - CHEM1: activating chemistry
  - CHEM2: how to set minimum time-step limits
  - CHEM3: user interactivity and visualization
  - CHEM4: extraction of radiochemical yields (G) in a range of deposited energy
  - CHEM5: same with alternative physics and chemistry constructors
  - CHEM6: example for IRT approach

$$G(t) = \frac{N(t)}{E_{dep}}$$

Number of molecules at time t

Time-dependent radiochemical yield

Deposited energy scaling to 100 eV

- Note
  - Slow simulations: examples can be run in MultiThreading mode

Access in GATE 10

Chemistry constructors
g4_bindings/
pyPhysicsList.h pyPhysicsList.cpp

1 actor to score species along time
opengate_lib/
GateScoreSpecies.h GateScoreSpecies.cpp

1 actor to score species along time
opengate/
ScoreSpecies.py

THANK YOU

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