

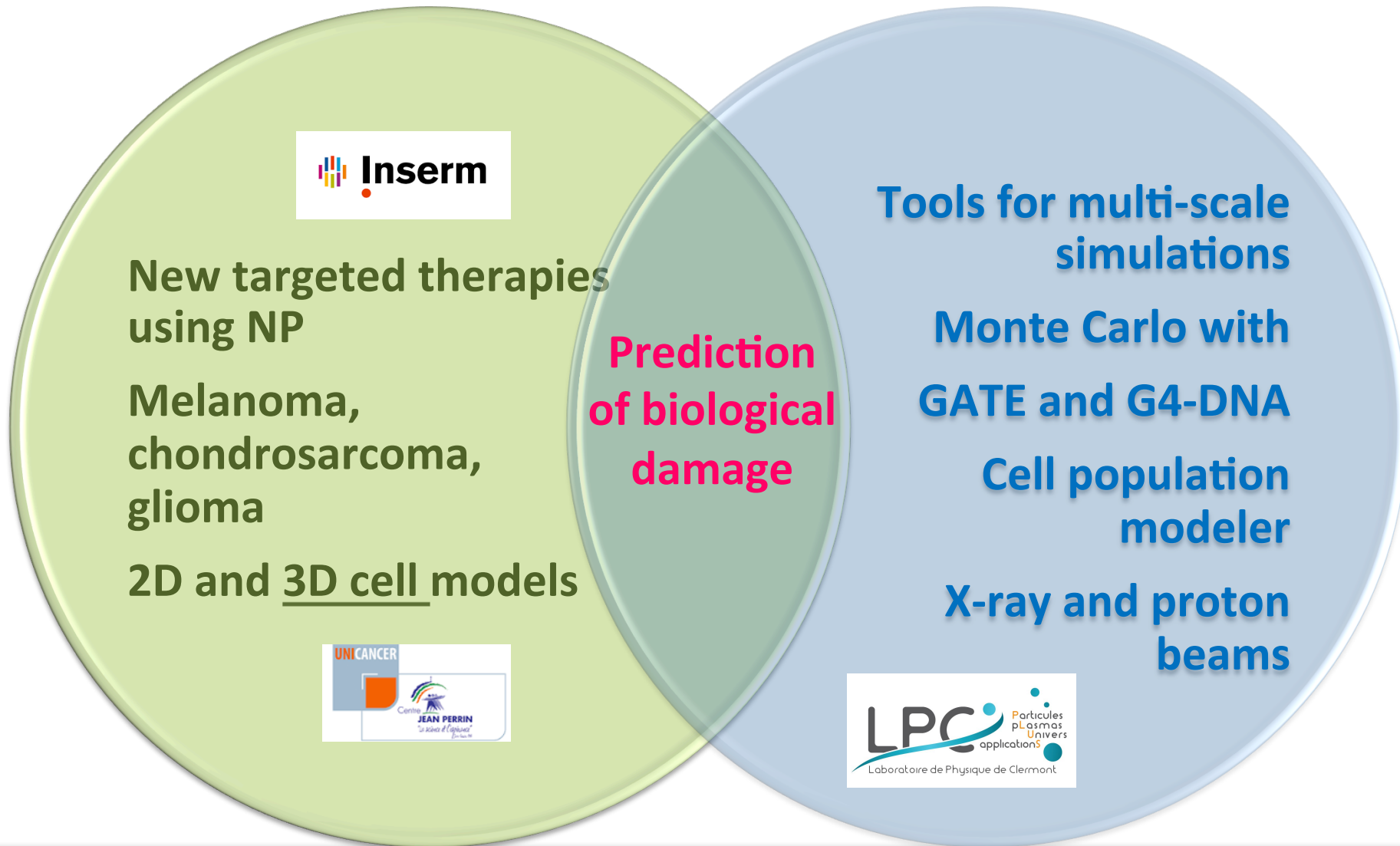
CPOP: an opensource C++ Cell POPulation modeler for radiation biology

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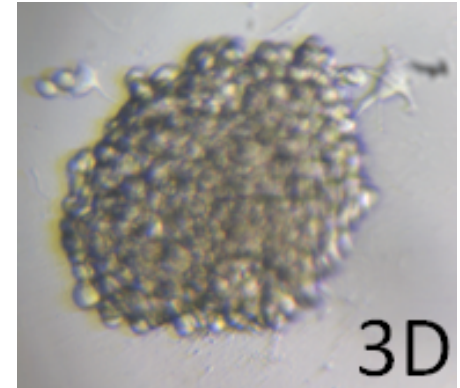
Improve radiation therapy treatments for resistant cancer cells



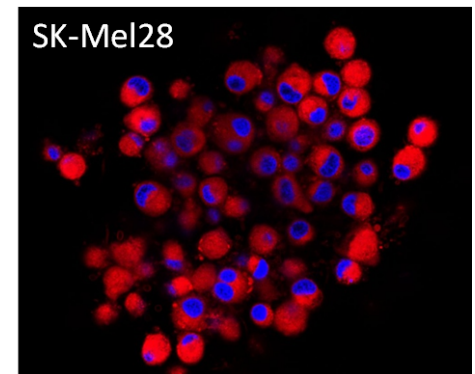
3D cell models

- Melanoma spheroid

- Obtained from 0.5% methylcellulose added to the culture medium
- Resistant
- At day 4 :
 - Spheroid diameter 550 μm
 - Cell diameter 17,2 \pm 2,5 μm
 - Nucleus diameter 11,2 \pm 2,0 μm
 - Around 1000 cells
 - Cultured in 96-well polystyrene conical plates



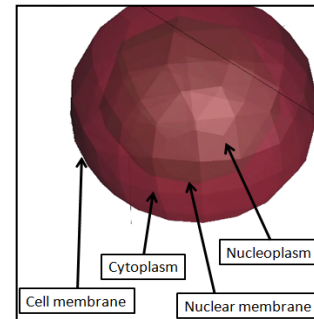
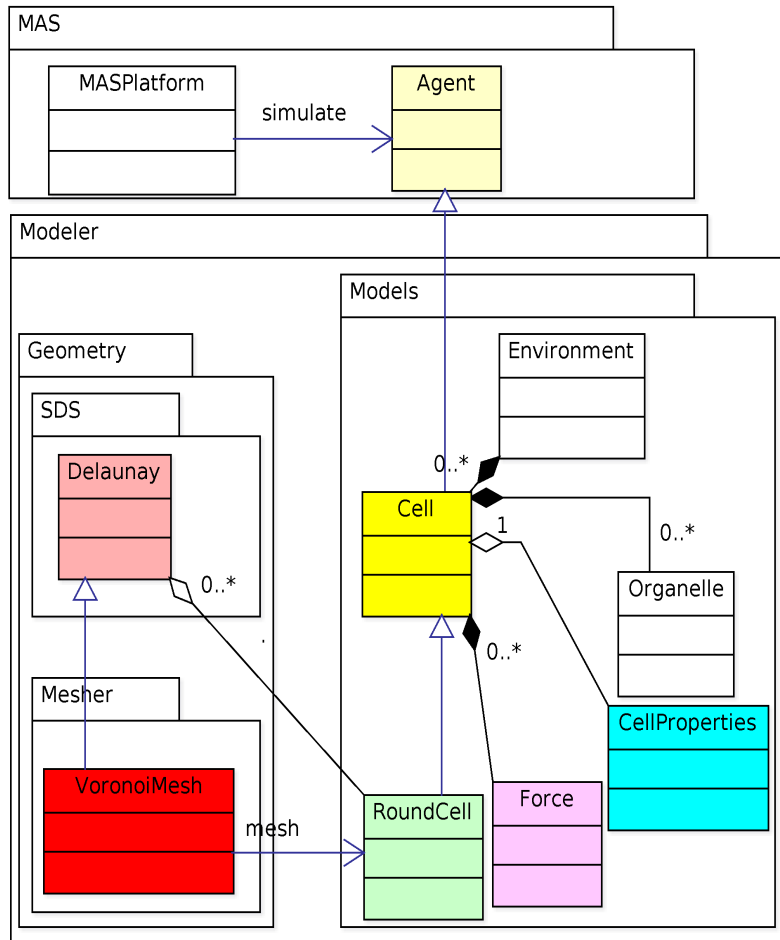
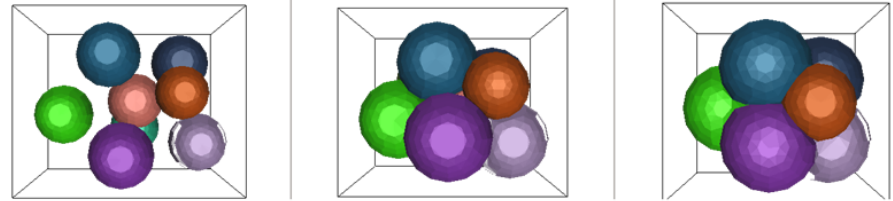
Day 6 \varnothing 570 μm



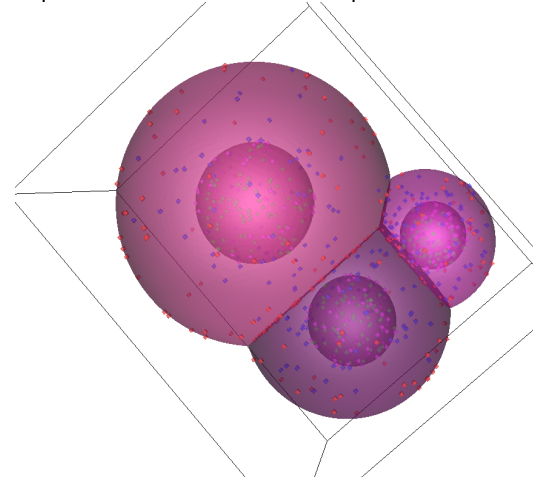
- Development of a 3D cell population platform from biological inputs
 - C++
 - Able to deal with large cell populations (more than 1 million cells).
 - **Each cell can be distorted in function of the environment with variable cell radius**
 - **Open-source and cross-platform**
 - For 2D and 3D cell modeling
 - Mesh
 - Famous mesh library: **CGAL**
 - Compilation with Geant4 (10.0 and further) and ROOT, 2 ways to run it:
 - Export to **Geant4** / GATE (geometry and material compatibility) through xml files
 - Autorun Geant4 simulations
 - I/O files

CPOP structuration

Elastic forces applied to cells

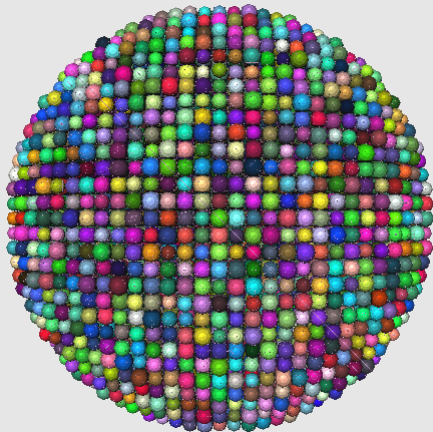


Each cell can be distorted keeping a round nucleus

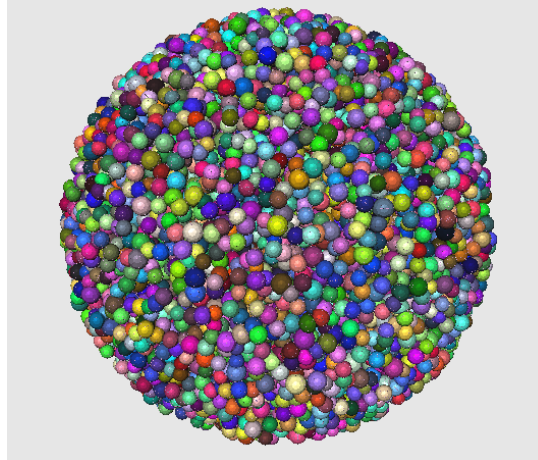


Influence of NP

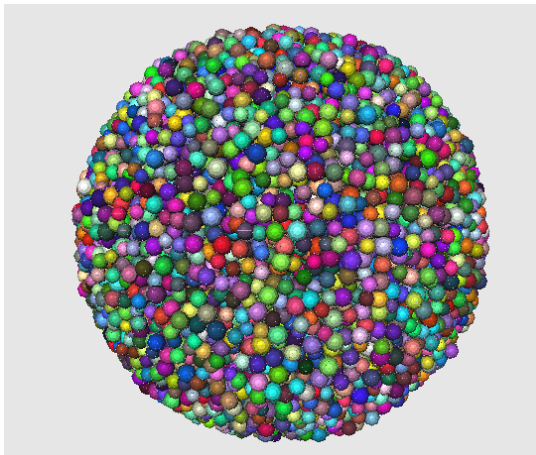
Spheroid modeling



Using a grid, no forces



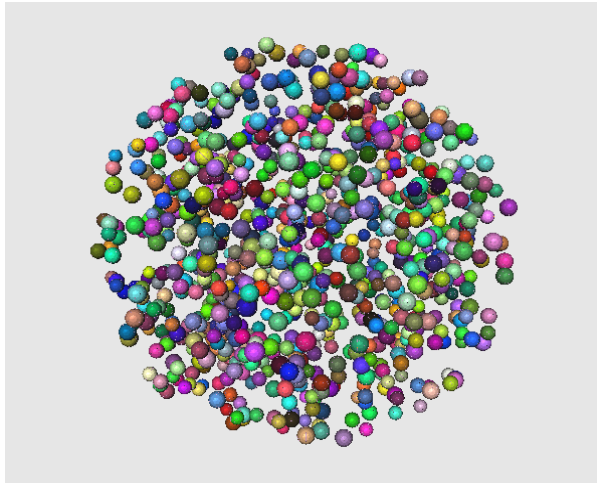
Without grid, no forces



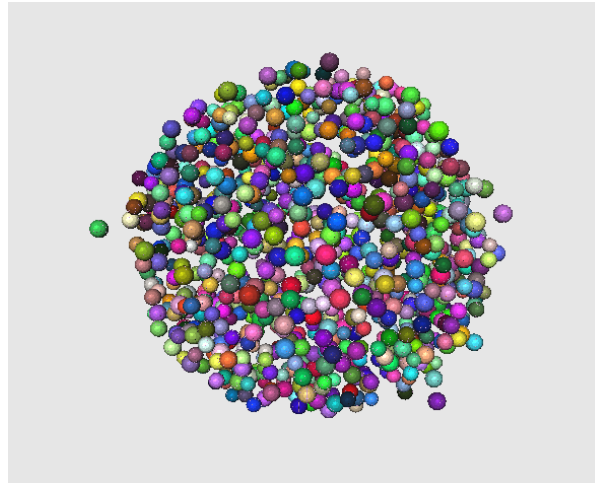
*Without grid, with forces (rigidity=0.002;
ratioToStableLength=0.7*

Parameter name	Description	Value or range values
Cell properties		
nucleusRadius	Radius of the nucleus (μm)	4.6 – 6.6
membraneRadius	Radius of the cell (μm)	7.35 – 9.85
cytoplasmMaterials	Material composing the cytoplasm	
nucleusMaterials	Material composing the nucleus	
Spheroid properties		
internalRadius	Internal radius of the spheroid (μm)	0
externalRadius	External radius of the spheroid (μm)	225
nbCell	Number of cells composing the spheroid	18124
Mesh properties		
maxNumberOfFacetPerCell	Maximum number of facets to represent round cells	300
Force properties		
ratioToStableLength	Ratio of elastic length	0.7
rigidity	Intensity of the force	0.002
Simulation properties		
Duration	Total duration of the simulation in seconds (s)	600
numberOfAgentToExecute	Number of agents to execute per step	100
displacementThreshold	Maximum displacement of cells for each step simulation (μm)	0.5
stepDuration	Duration of a step in second (s)	1

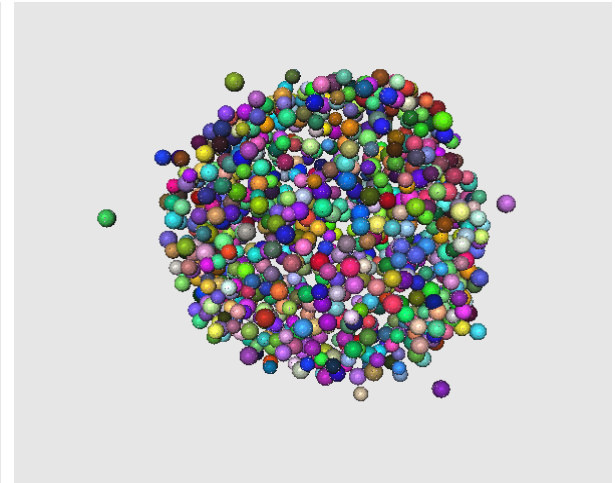
Melanoma spheroids



(a)



(b)



(c)

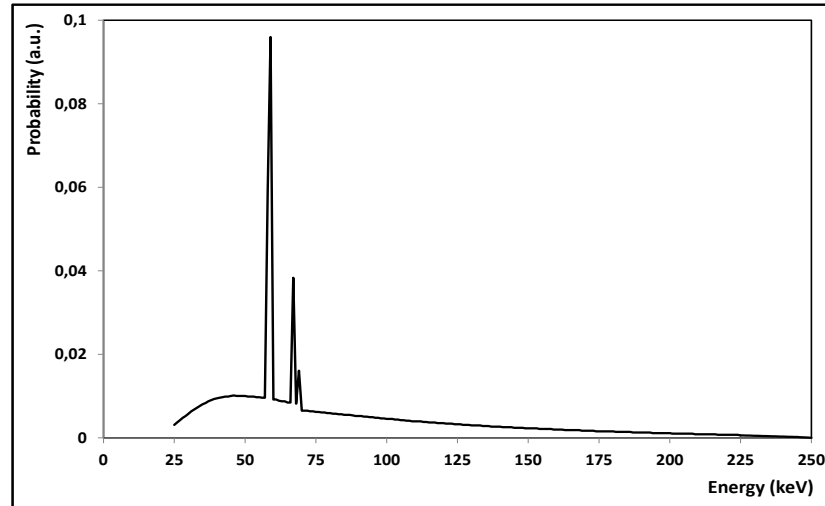
Spheroids corresponding to SkMel28 cell populations.

(a) 962 cells generated without forces,

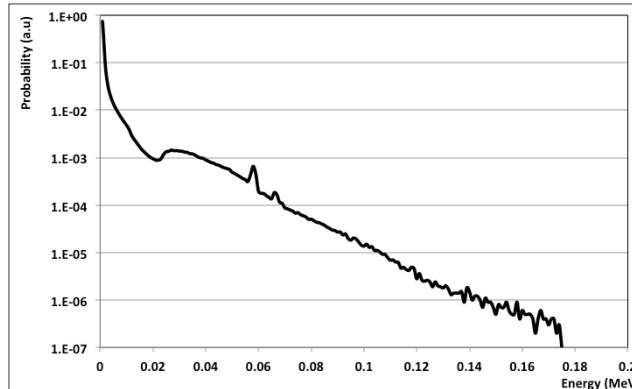
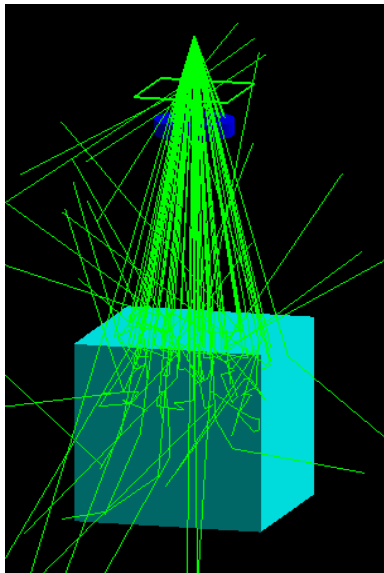
(b) 989 cells generated with a force rigidity=0.0007,

(c) 989 cells generated with a force rigidity=0.002.

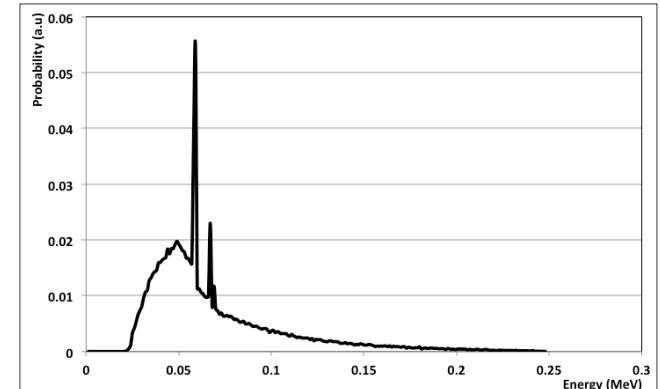
Simulate X-Ray beam using GATE



Energy spectrum of X-RAD 320 system derived from measurements



(a) Electron energy spectrum collected around a water sphere of 550 μm at 2 cm depth in a water box of $2.5 \times 2.5 \times 2.5 \text{ mm}^3$

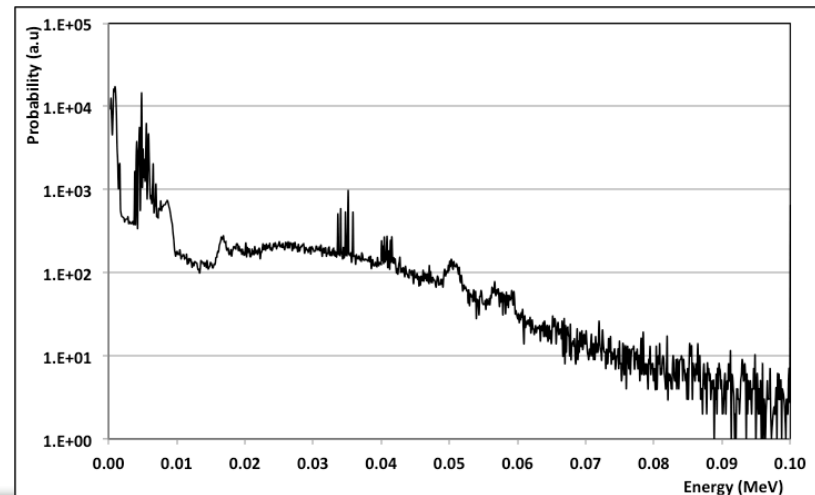
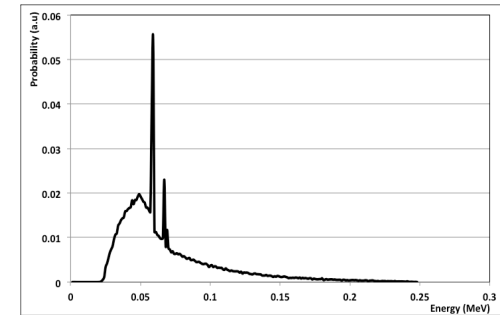
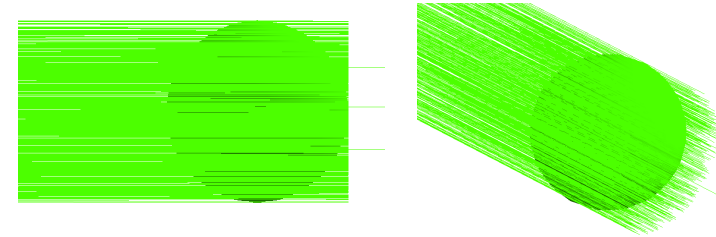


(b) Photon energy spectrum

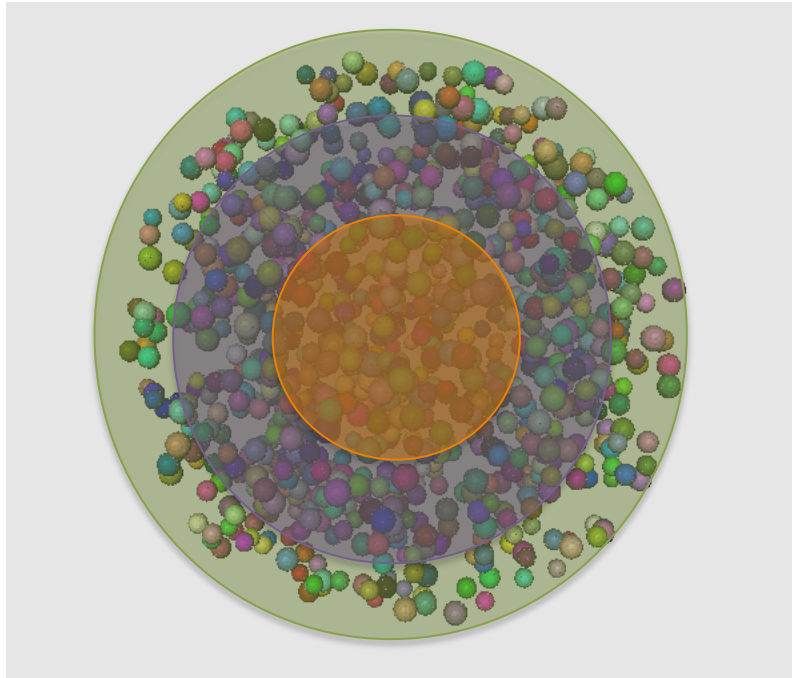
Gadolinium based NP (GBN) under X-Ray radiation

- Characteristics of AGuIX AC13 GBN

- Diameter 3.5 nm
- Mass: 8.5 kDa
- Chemical formula: $\text{Gd}_{10}\text{Si}_{30}\text{C}_{200}\text{N}_{50}\text{O}_{150}\text{H}_{577}$
- Cells incubated with GBN concentration of 4mM
($d=0.034 \text{ g.cm}^{-3}$) \rightarrow GBN density= 1.034 g.cm^{-3}
- Penelope physics down to 100 eV
- Energy spectrum actor to collect energy of secondary electrons exiting the GBN
- 300 billions of photons generated using the photon energy spectrum (User spectrum)

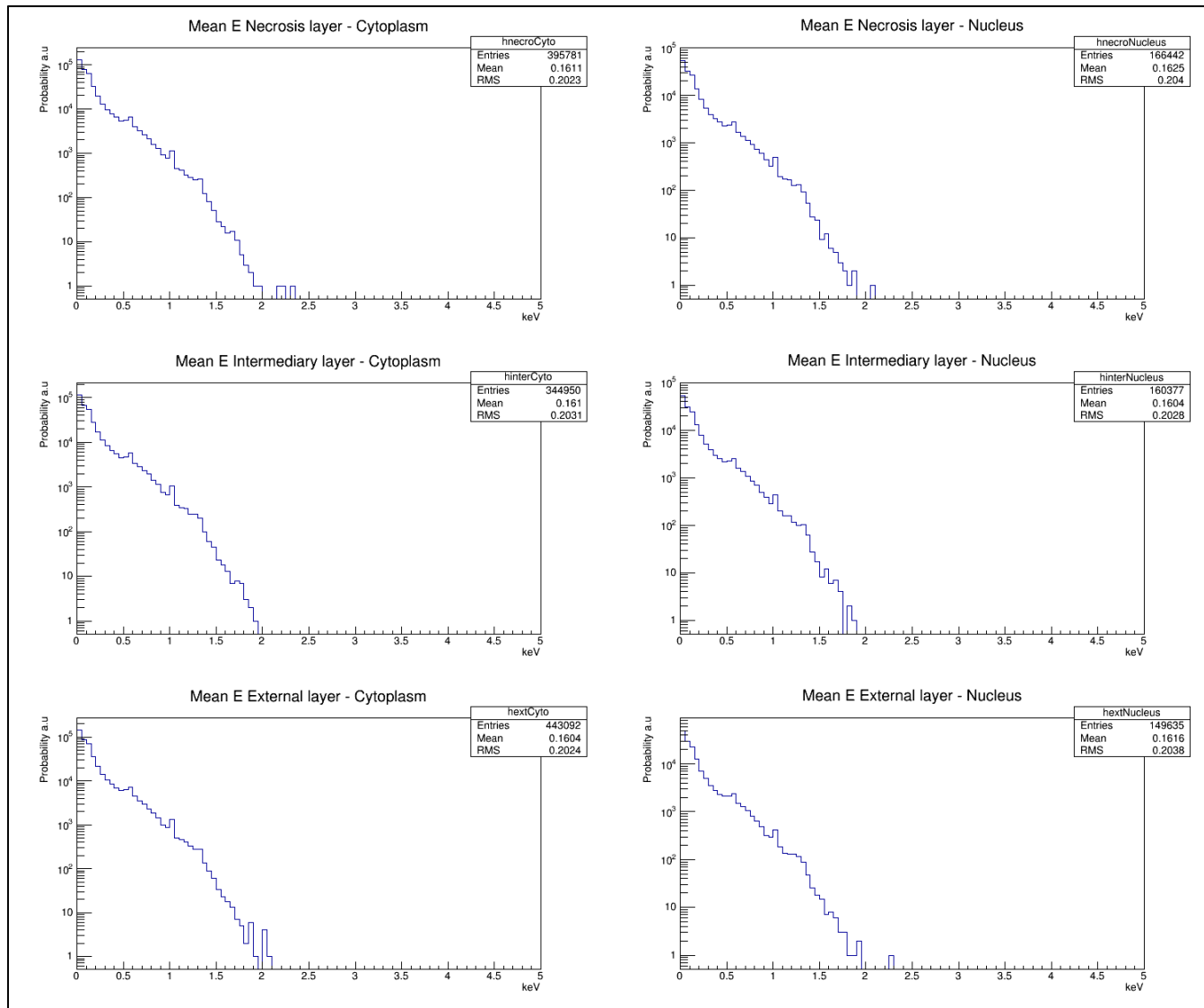


Results: Assessment of energy depositions to cells and organelles

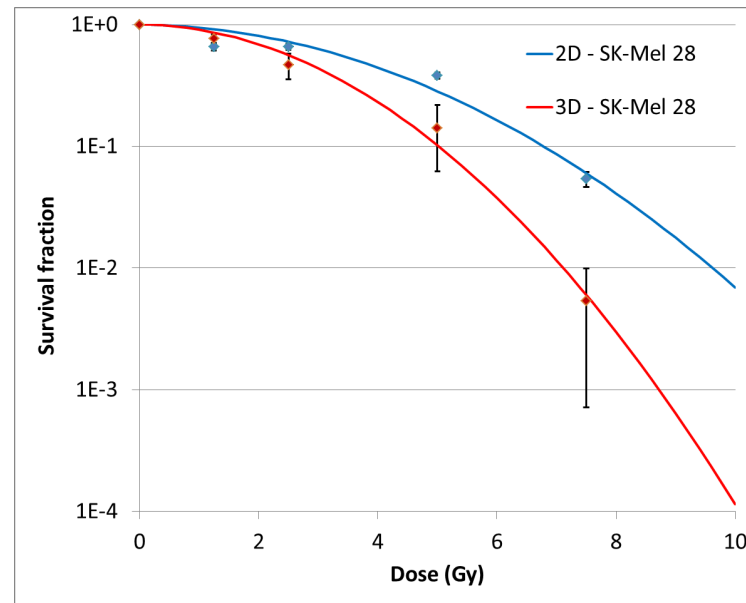


- 3 layers (thickness can be fixed by user):
 - Necrosis
 - Intermediary
 - External
- Sampling cells/region:10
- Location of GBN in cells: cell membrane, cytoplasm, nucleoplasm or nuclear membrane
- e- energy spectra:
 - e_spectrum and GBN_spectrum
 - Spectrum weight per region
- G4 PhysicsList: Penelope
- Mean energy spectra to organelles/region

Energy spectra obtained in 3 layers in nucleus and cytoplasm



- Ongoing simulations with GBN
- Correlate results with experiments and particularly cell survivals



- Collect energy spectrum in nucleus and go further with G4-DNA
- Poster AAPM 2017 in Denver
- Paper in preparation for Physics in Medicine and Biology
- ANR G4-ADN submitted