Biophysical Modeling of the Ionizing Radiation Influence on Cells

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LABORATÓRIO DE INSTRUMENTAÇÃO
E FÍSICA EXPERIMENTAL DE PARTÍCULAS
partículas e tecnologia

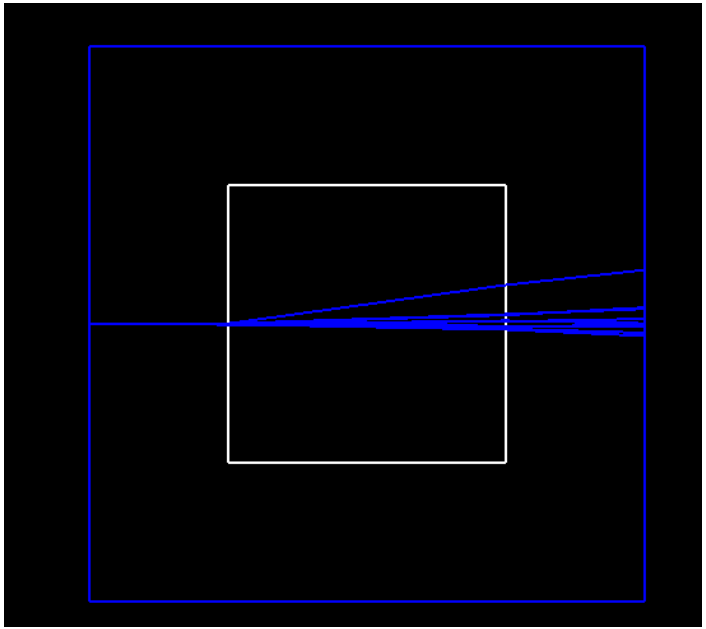
Motivation

- Physics processes and models of Topas nBio use only **water** as **biological material**
- However, only modelling the physics process in water has its limitations:
  - Does not capture **all elements** that are present in cells.
  - Does not fully account for varied **radiation reactions** of the other elements

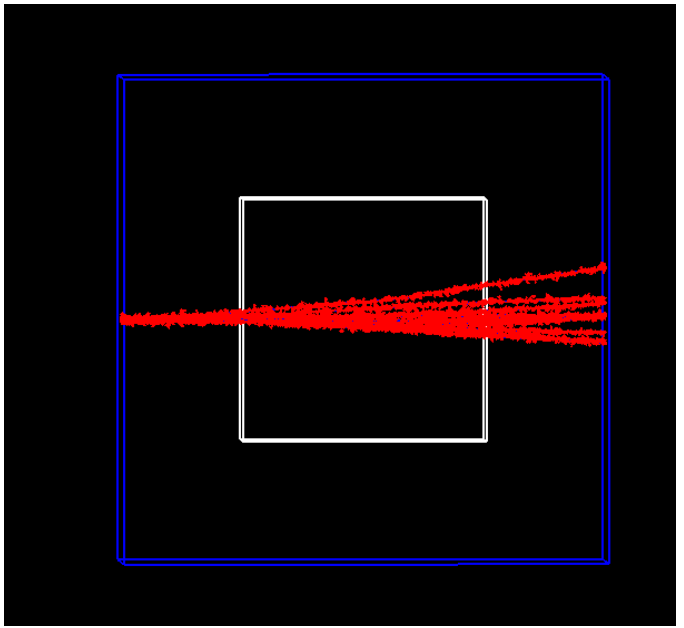
Objectives

- Simulate the influence of ionizing radiation in the cells using different elements found in the biological matter
- Understand the influence of those elements in the simulated dose

Impact of different physics list in the simulation



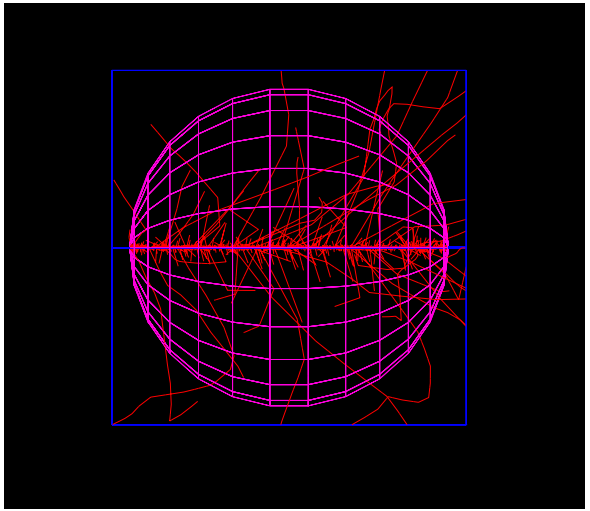
Simulation with proton beam irradiating water using the “g4em-standard_opt4” physics lists



Simulation with proton beam irradiating water using the “g4em-dna” physics lists

Adding a cell

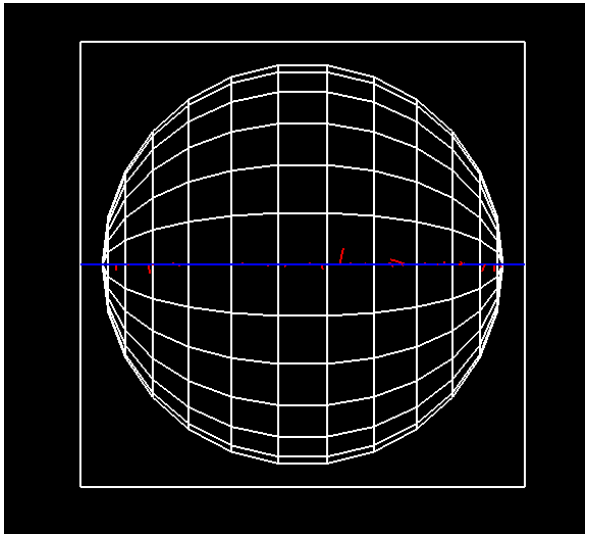
- Box size: 1000 Å x 1000 Å x 1000 Å
- Cell size : 900 Å x 900 Å x 900 Å
- Cell type : TsEllipsoidCell
- World : “g4em-standard_opt4”
- Cell : “g4em-dna”



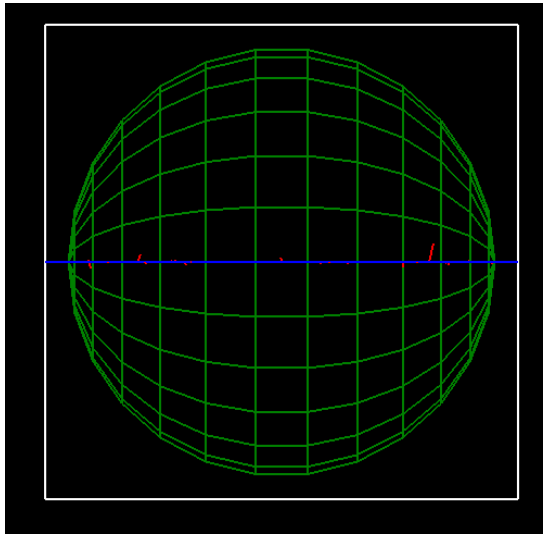
Topas nBio simulation with proton beam irradiating a cell

Simulation of different elements in the cell

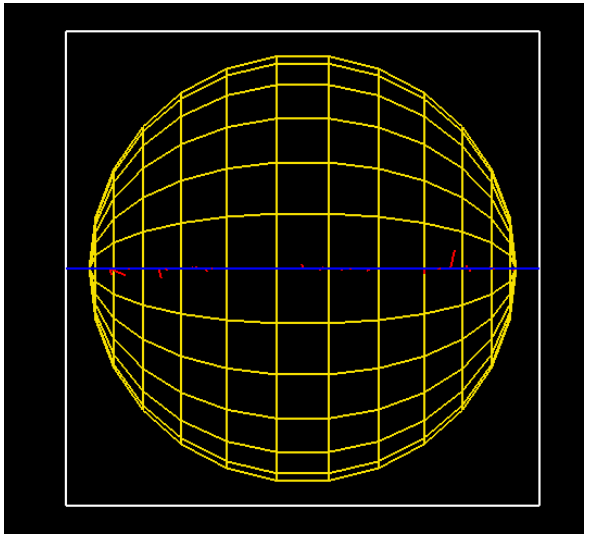
- Simulation using two different particle beams : **proton** and **electron**



Topas nBio simulation of a cell using **water** as material



Topas nBio simulation of a cell using **70% water and 30% phosphorus** as material

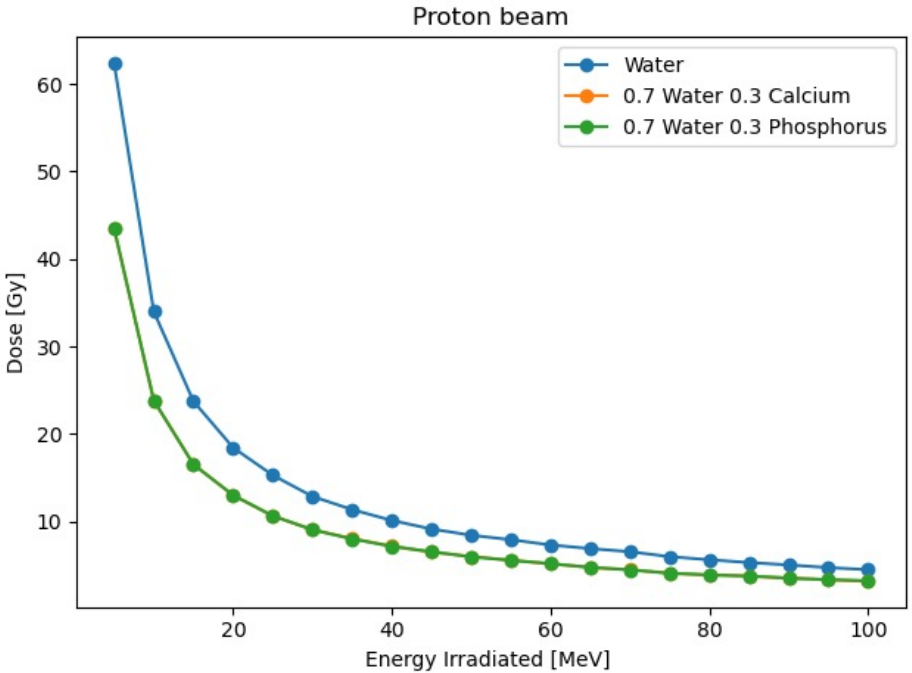


Topas nBio simulation of a cell using **70% water and 30% calcium** as material

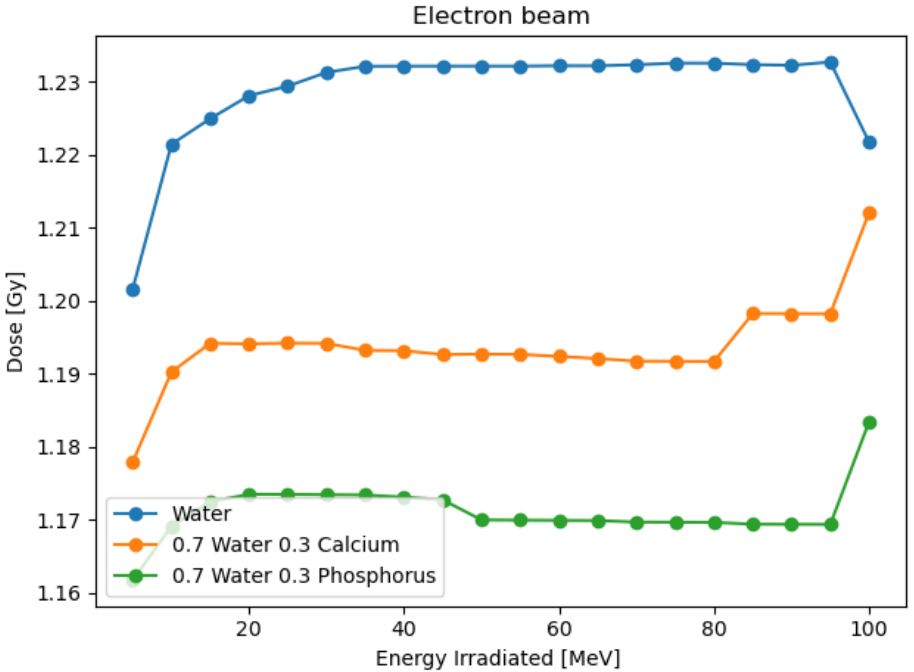
Results

Dose to the medium

- Number of events: 10000
- Energy ranges: 5-100 MeV

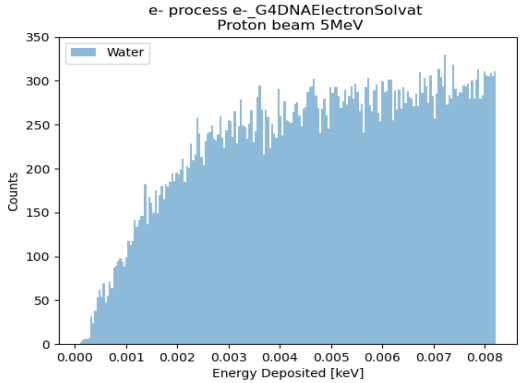


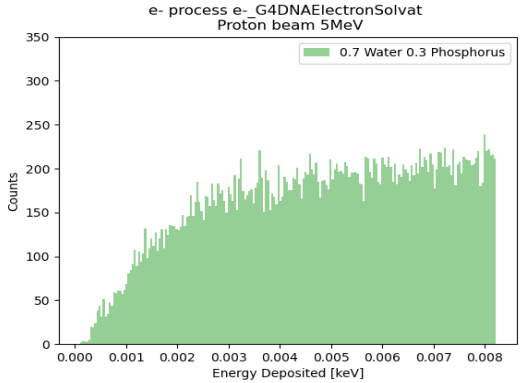
Graph of the dose deposited to the medium per energy irradiated of proton beam

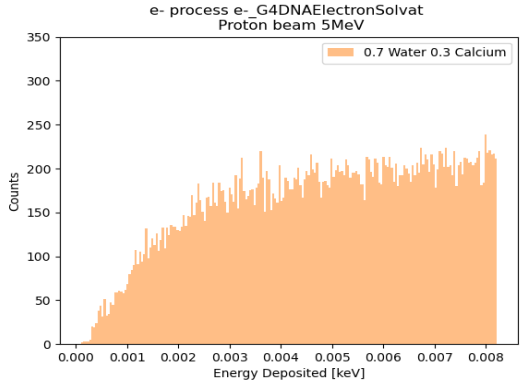


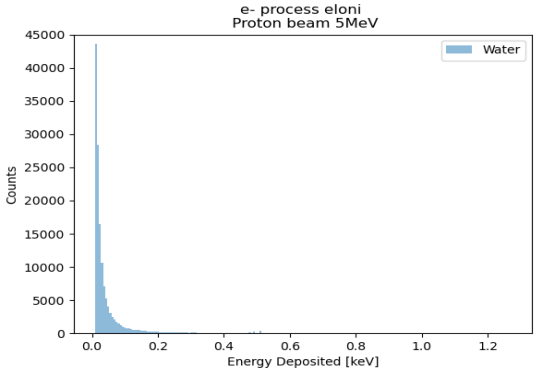
Graph of the dose deposited to the medium per energy irradiated of electron beam

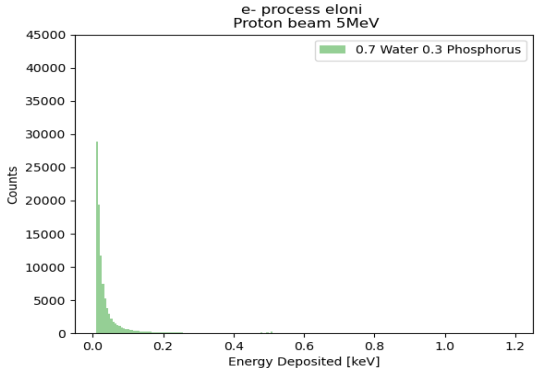
Processes per particle of proton beam at 5 MeV

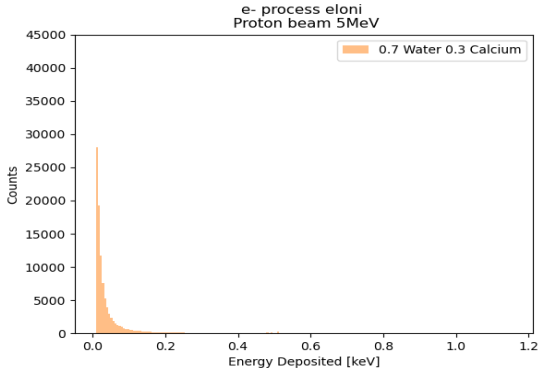




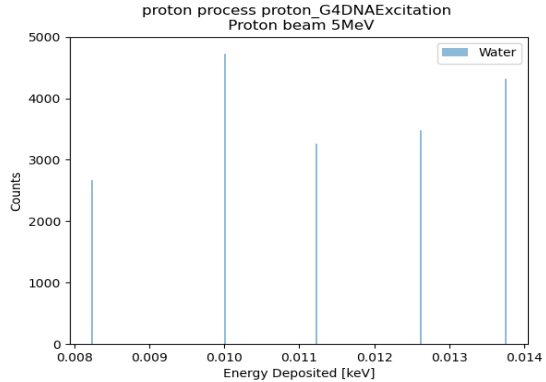


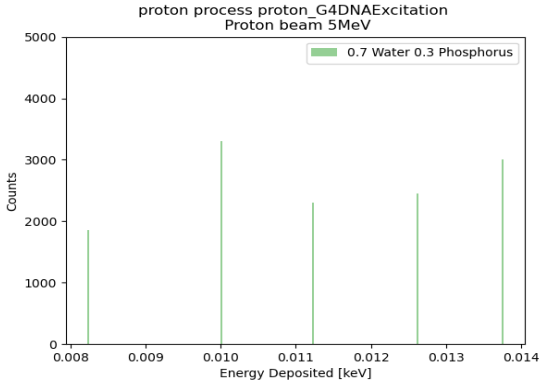


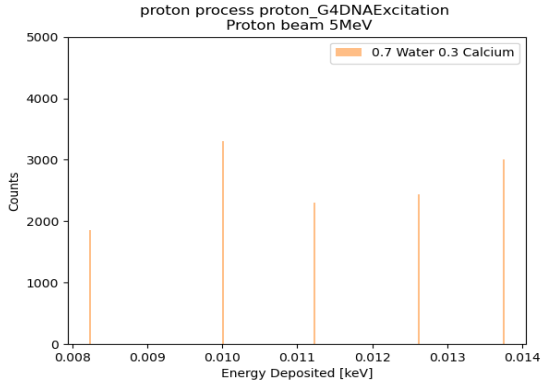


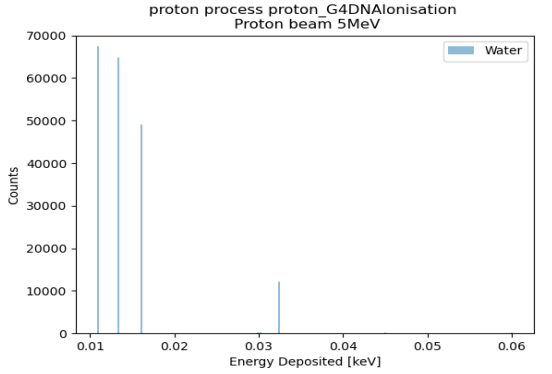


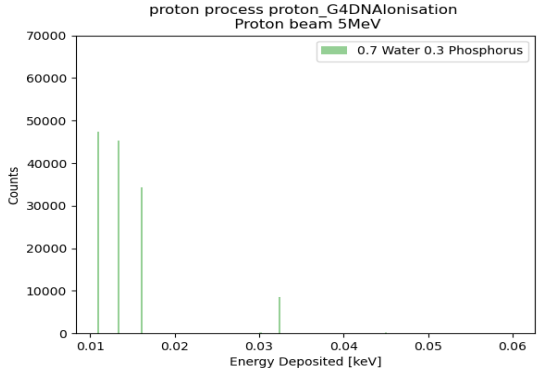
Processes per particle of proton beam at 5 MeV

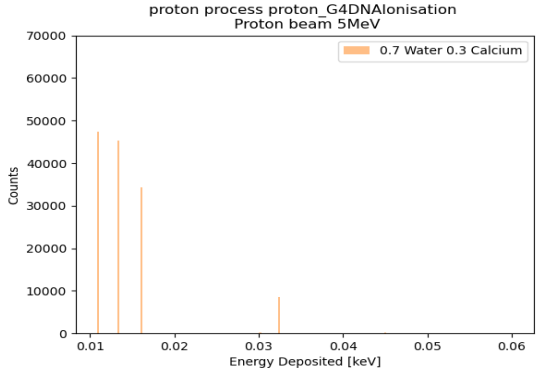




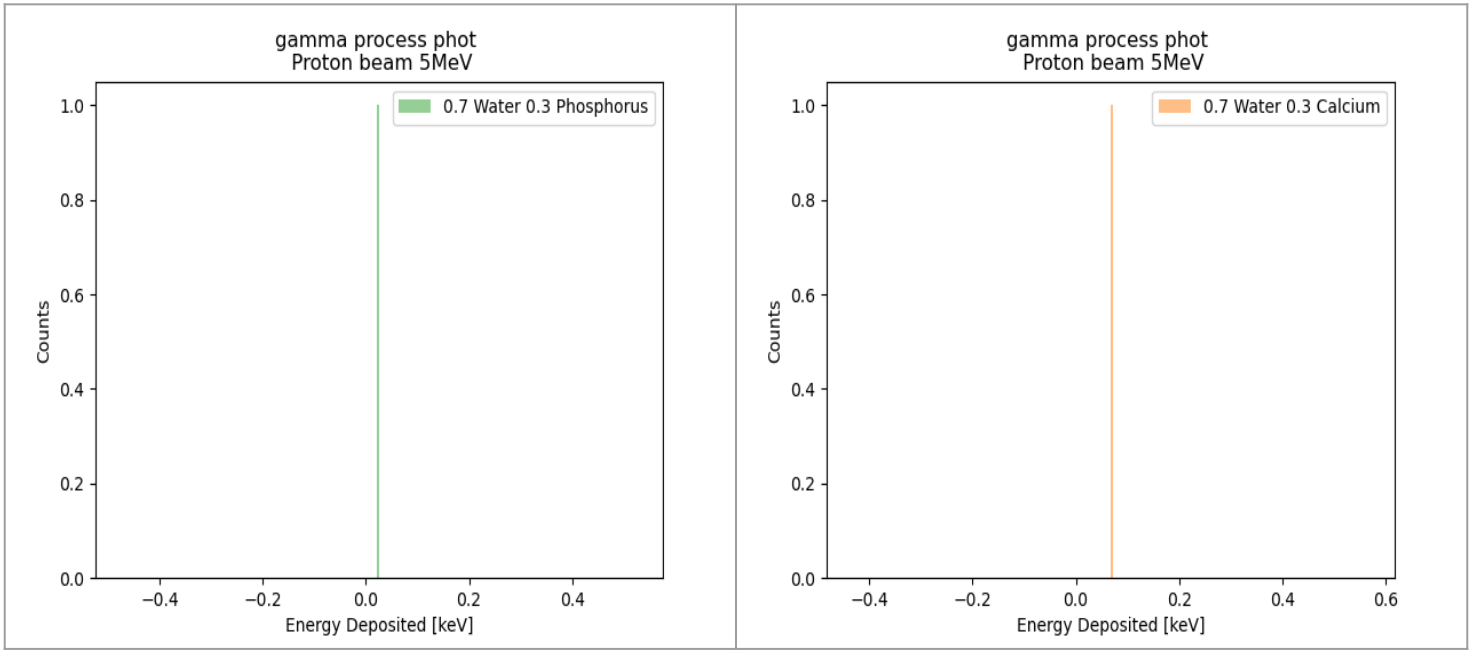




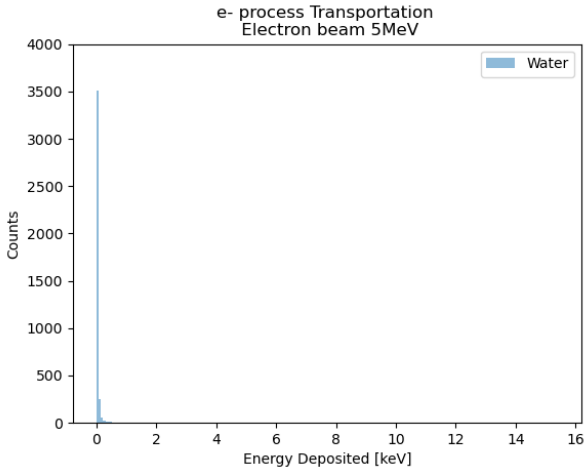


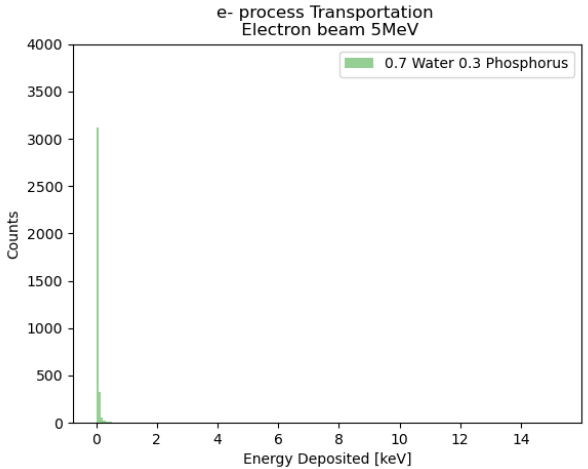


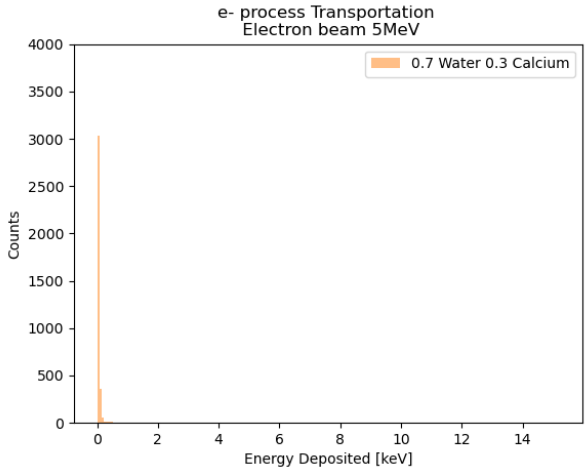
Processes per particle of proton beam at 5 MeV



Processes per particle of electron beam at 5 MeV







Conclusions

- **Proton beam** :
  - The simulated dose around the Bragg's peak was higher in water than in the mixtures.
  - Gamma particles were found in the mixtures
- **Electron beam** : The results were similar
- In order to have a more accurate simulation, other cell elements may need to be simulated

Future Work

Adapt the PDB4DNA source code

- Protein Data Bank(PDB): international repository for 3D structural data of biological macromolecules, such as proteins and nucleic acids
- PDB4DNA is a source code of Topas nBio which reads the PDB files

```
ATOM      1  N   ASP A   1     -14.439 -56.597 103.986  1.00  0.00           N
ATOM      2  CA  ASP A   1     -15.582 -56.020 104.745  1.00  0.00           C
ATOM      3  C   ASP A   1     -15.885 -54.629 104.195  1.00  0.00           C
ATOM      4  O   ASP A   1     -15.323 -54.218 103.180  1.00  0.00           O
ATOM      5  CB  ASP A   1     -15.211 -55.945 106.236  1.00  0.00           C
ATOM      6  CG  ASP A   1     -14.903 -57.344 106.768  1.00  0.00           C
ATOM      7  OD1 ASP A   1     -15.840 -58.038 107.127  1.00  0.00           O
ATOM      8  OD2 ASP A   1     -13.736 -57.699 106.810  1.00  0.00           O1-
ATOM      9  H1  ASP A   1     -14.623 -57.601 103.789  1.00  0.00           H
ATOM     10  H2  ASP A   1     -13.569 -56.506 104.549  1.00  0.00           H
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ATOM     12  HA  ASP A   1     -16.453 -56.650 104.617  1.00  0.00           H
ATOM     13  HB2 ASP A   1     -14.338 -55.317 106.360  1.00  0.00           H
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ATOM     17  C   ALA A   2     -16.079 -51.557 104.834  1.00  0.00           C
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ATOM     19  CB  ALA A   2     -18.498 -52.168 105.131  1.00  0.00           C
ATOM     20  H   ALA A   2     -17.202 -54.290 105.667  1.00  0.00           H
ATOM     21  HA  ALA A   2     -17.311 -52.537 103.363  1.00  0.00           H
ATOM     22  HB1 ALA A   2     -18.386 -52.165 106.201  1.00  0.00           H
ATOM     23  HB2 ALA A   2     -19.256 -52.887 104.848  1.00  0.00           H
ATOM     24  HB3 ALA A   2     -18.801 -51.185 104.789  1.00  0.00           H
ATOM     25  N   GLU A   3     -15.640 -50.732 103.862  1.00  0.00           N
ATOM     26  CA  GLU A   3     -14.596 -49.712 104.093  1.00  0.00           C
ATOM     27  C   GLU A   3     -15.153 -48.303 103.804  1.00  0.00           C
ATOM     28  O   GLU A   3     -15.359 -47.942 102.647  1.00  0.00           O
ATOM     29  CB  GLU A   3     -13.394 -49.993 103.164  1.00  0.00           C
ATOM     30  CG  GLU A   3     -12.805 -51.398 103.436  1.00  0.00           C
ATOM     31  CD  GLU A   3     -11.587 -51.645 102.538  1.00  0.00           C
ATOM     32  OE1 GLU A   3     -11.780 -52.087 101.417  1.00  0.00           O
ATOM     33  OE2 GLU A   3     -10.482 -51.385 102.986  1.00  0.00           O1-
ATOM     34  H   GLU A   3     -16.034 -50.807 102.964  1.00  0.00           H
ATOM     35  HA  GLU A   3     -14.246 -49.741 105.124  1.00  0.00           H
ATOM     36  HB2 GLU A   3     -13.720 -49.939 102.133  1.00  0.00           H
```
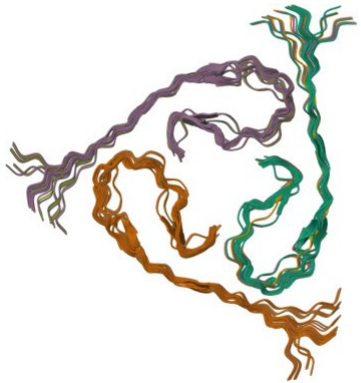

Components of PDB files, in this case 2m4j.pdb

Add the amyloid to the simulation



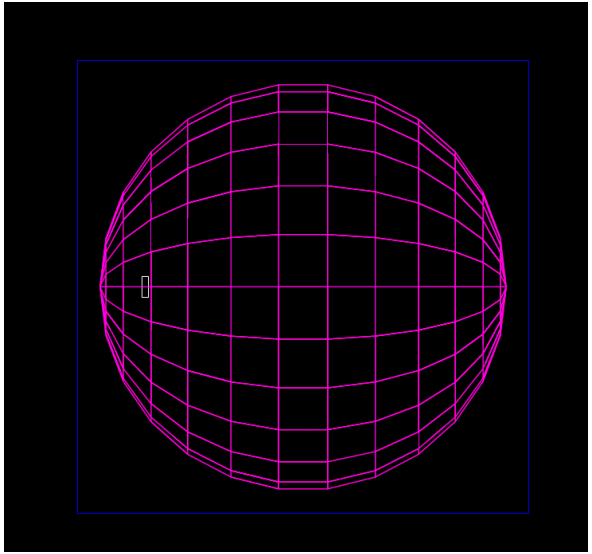
PDB file 2m4j [1]
40-residue beta-amyloid fibril derived from Alzheimer's disease brain from the PDB bank

- Amyloids are abnormal protein aggregates which adopt a fibrillary structure.
- Associated with various neurodegenerative diseases

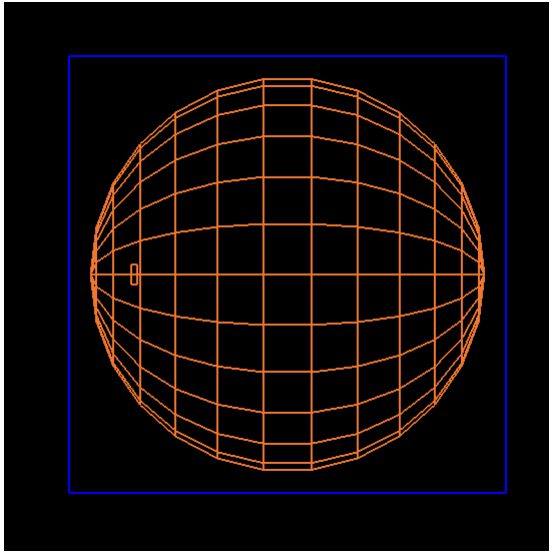
Simulate with different materials for the cell and amyloid

- World: “g4em-standard_opt4”
- Cell and amyloid: “g4em-dna”

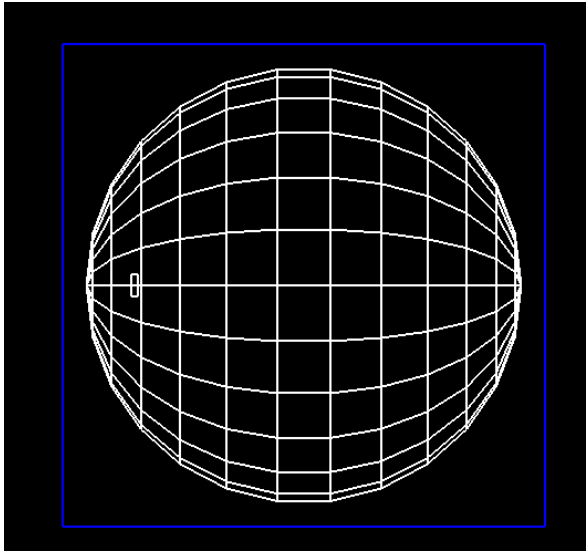
Amyloid size : 50 Å x 50 Å x 14 Å



Simulation with a proton beam irradiation cell and the amyloid using **water** as the material



Simulation with a proton beam irradiation cell and the amyloid using **lead** as the material



Simulation with a proton beam irradiation cell and the amyloid using **lead and water** as the material

THANK YOU!

References

- [1] 2M4J https://www.rcsb.org/structure/2M4J

Processes per particle of proton beam at 5 MeV