International Student Practice, 2023, Egypt Stage 1.

Laboratory of Radiation Biology (LRB)

# Computer Modeling of Radiation Biophysics using the Geant4.

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Sector of Mathematical Modeling of Radiation-Induced Effects.

# Outlines

1- Purpose of the project

2- Introduction.

- Radiation
- Computational toolkit (Geant4)
- DNA damage and ionization.

3- Computational methodology.

4- Results.

5- Conclusion.

# Purpose of the project.

1. Radiation Biophysics: is the study of the effects of radiation on cells, tissues, biomolecules, and living organisms.

2. To know radiation types especially the ionizing radiation particles and predict their efficacy on DNA damage by using Geant4 toolkit.

3. To estimate the contribution of different physical interactions to DNA damage.

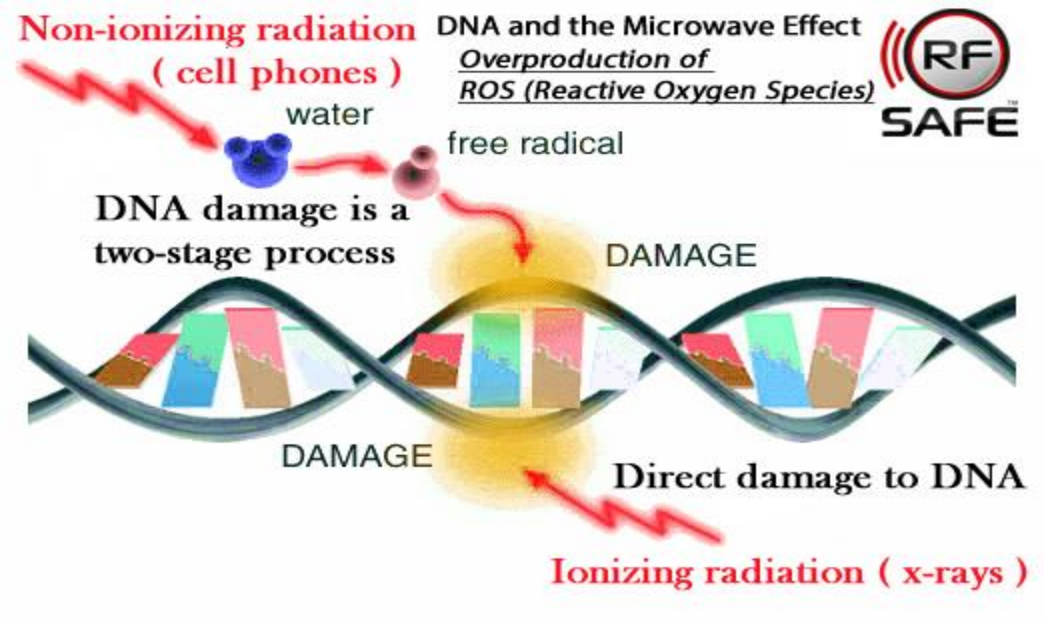
4. To prove that estimation of initial DNA damage is useful for cancer treatment, as well as for radiation protection, especially for astronauts in deep space missions.

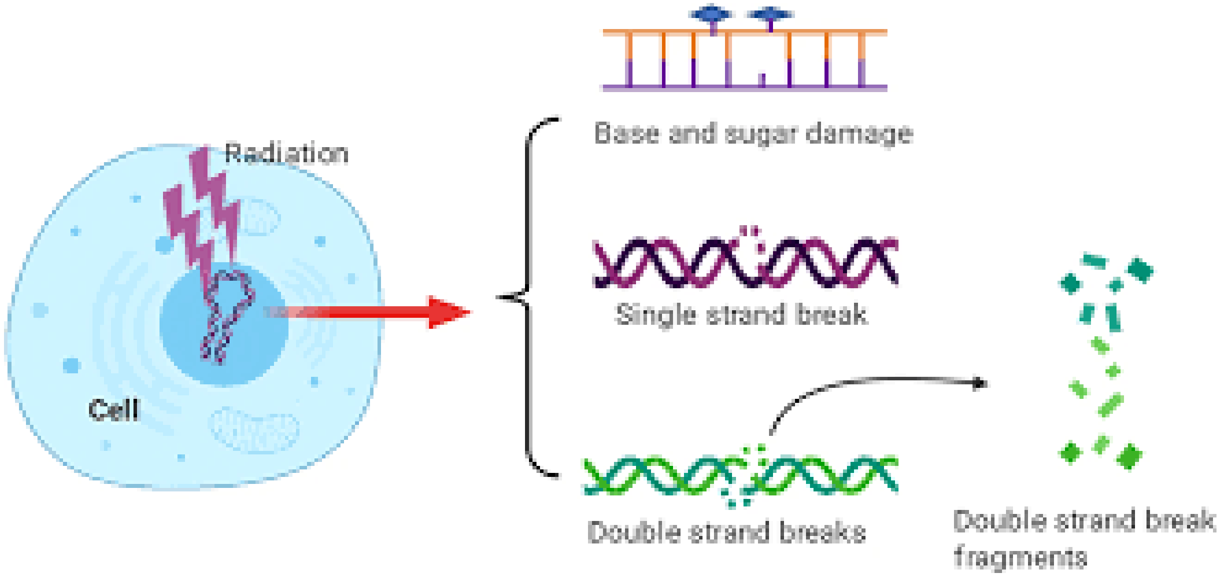
5. To construct 3D geometry of biomolecular structures.

➡ Visit Protein Data Bank website: http//www.rcsb.org/

# Introduction

- Radiation (X-rays, electrons, ions) causes lesions to biomolecules (DNA, proteins).
- The most sensitive target to radiation is the DNA molecule.
- Radiation damage to DNA plays a central role in radiation therapy to cure cancer.



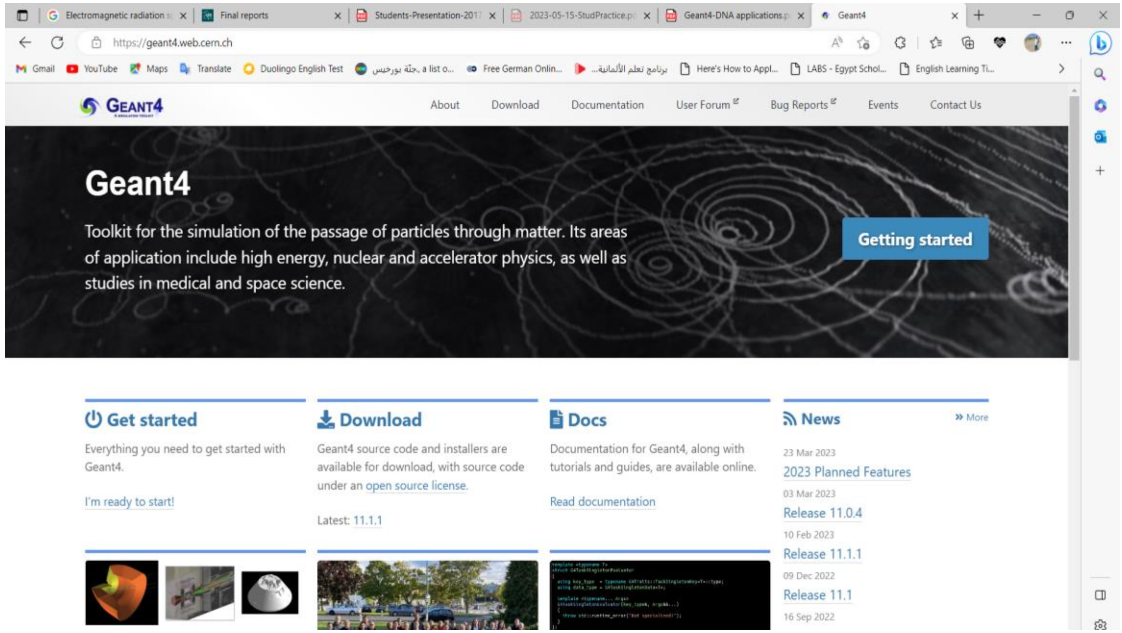



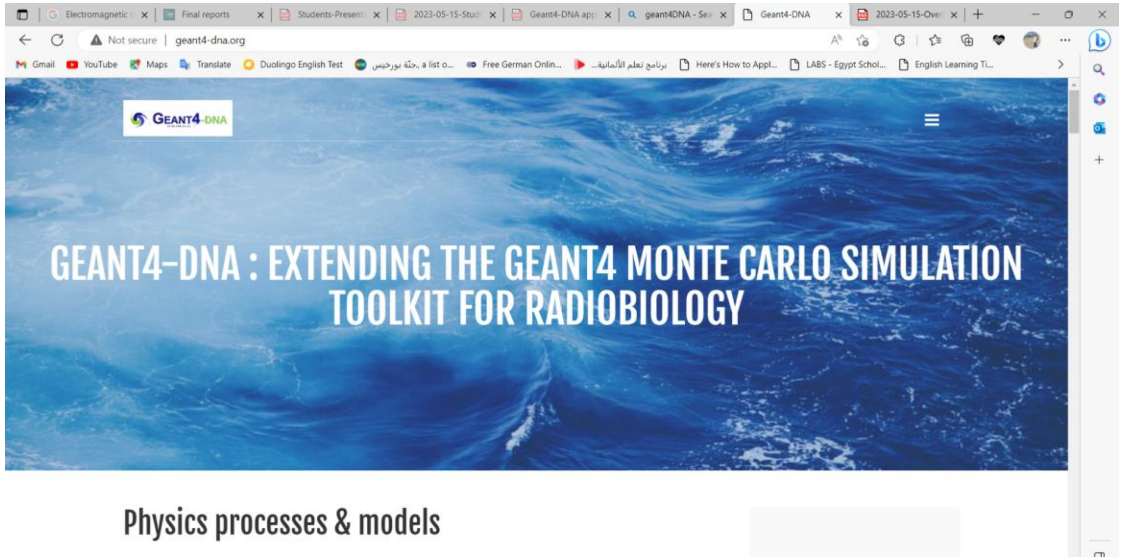

https://www.nature.com/articles/s41392-020-0150-x

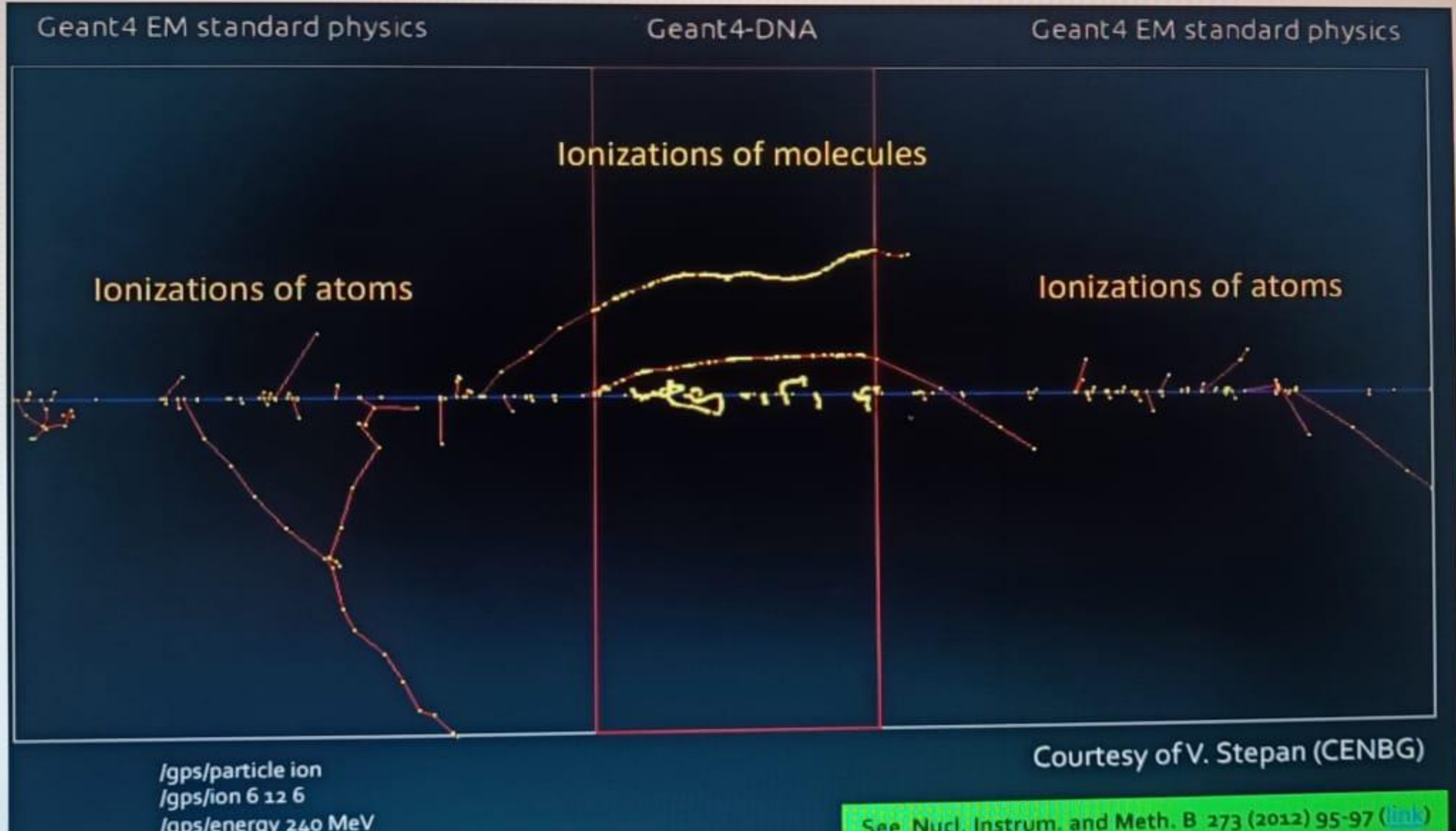
# Geant4 Toolkit.

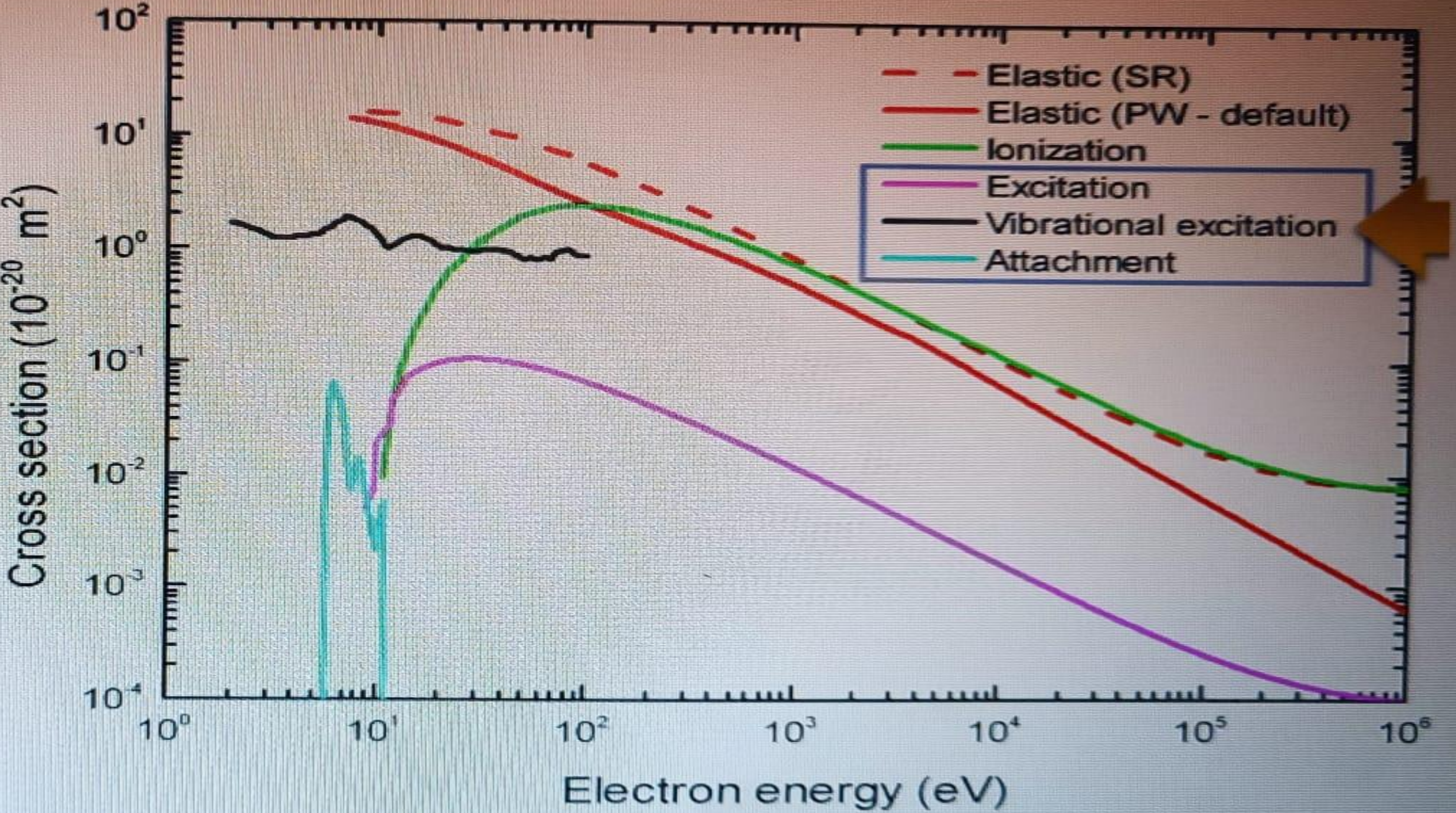
- The Geant4 is a general particle-matter Monte Carlo simulation toolkit, which includes the Geant4-DNA models for micro-dosimetry simulations of stochastic nature of particle track structure in small targets.
  http://geant4.cern.ch/
  http://geant4-dna.org/

- Monte Carlo virtual-experiment applications of radiation biophysics developed in the Geant4 toolkit is used in this project.



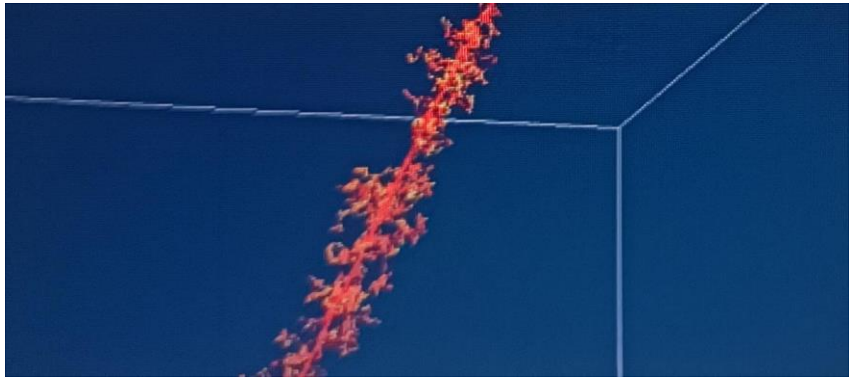

Geant4 EM standard physics
Geant4-DNA
Geant4 EM standard physics
Ionizations of molecules
Ionizations of atoms
Ionizations of atoms
Courtesy of V. Stepan (CENBG)
/gps/particle ion
/gps/ion 6 12 6
/gps/energy 240 MeV
See Nucl. Instrum. and Meth. B 273 (2012) 95-97 (link)



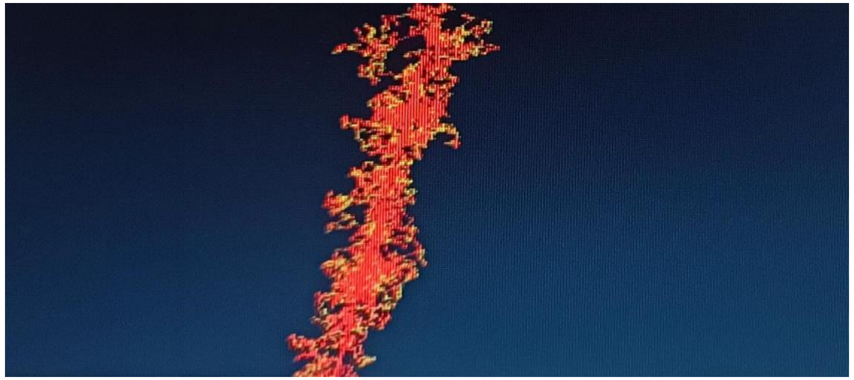

Med. Phys. 37 (2010) 4692-4708

# Track structure for different particles.

Electron , 10 keV



Proton, 100 keV



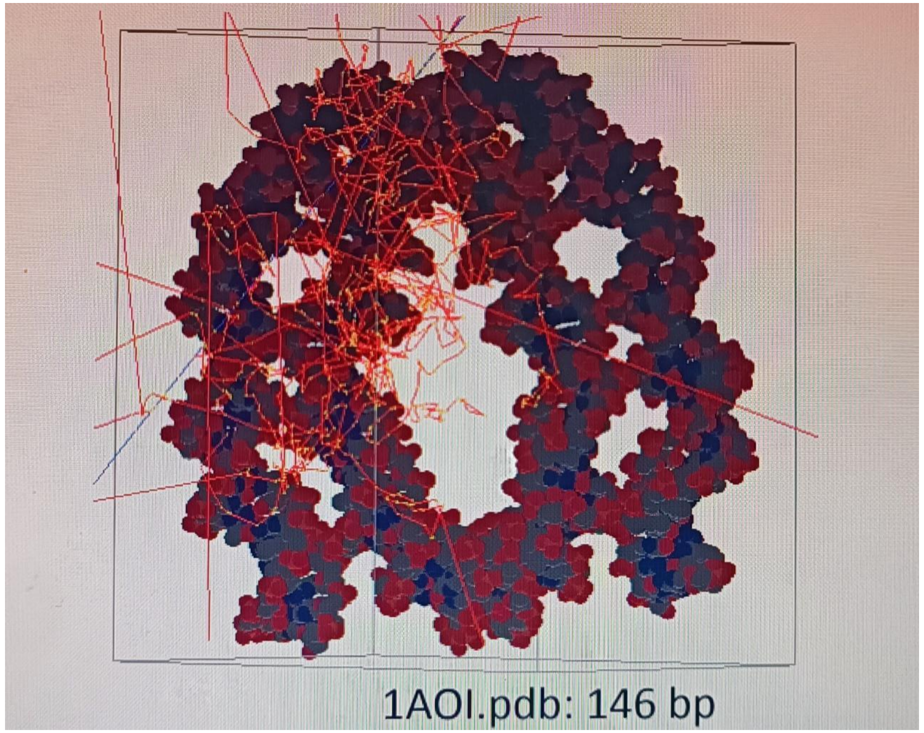
Alpha, 1000 keV

# Computational Simulation

## Modeling & Scoring of E. deposition in DNA nucleosome

- After simulation of the incoming particle around the DNA nucleosome, the atoms are represented by spheres and when the particle energy is deposited in the molecule as shown, it will be scored.

| Atoms | Van der Waals radius (nm) | Simulted Color |
|---|---|---|
| H | 0.12 | White |
| C | 0.17 | Gray |
| N | 0.155 | Blue |
| P | 0.18 | Orange |
| O | 0.152 | Red |



# Results

- We will see the results of energy deposition plotting for different particles (electrons, protons and alpha particles).

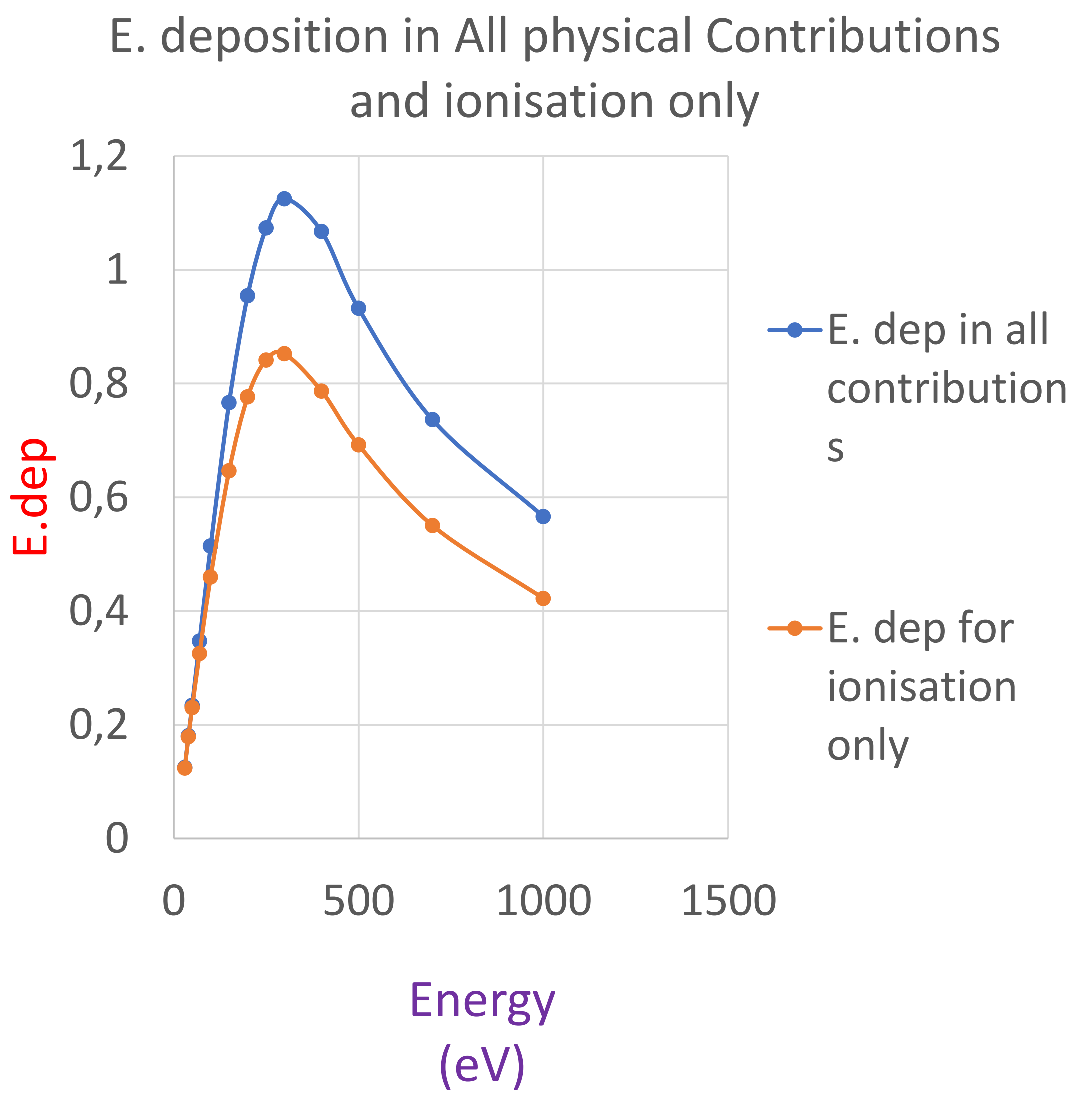
- DNA damage ( SSB and DSB) also for different used particles (e-, p, alpha)
- SSB/DSB Ratio for Protons and Alpha Particles.

# Analysis of Energy Deposition (E. dep) in DNA nucleosome for electrons in the case of all physical interactions and only ionisation

- Electron energy: 30,40, 50, 70,100, 200, 250,300, 400, 500,700, 1000 [eV]

- In case of  All physical interactions (the blue curve); energy deposition reached the peak when the electron energy was about 300 eV.

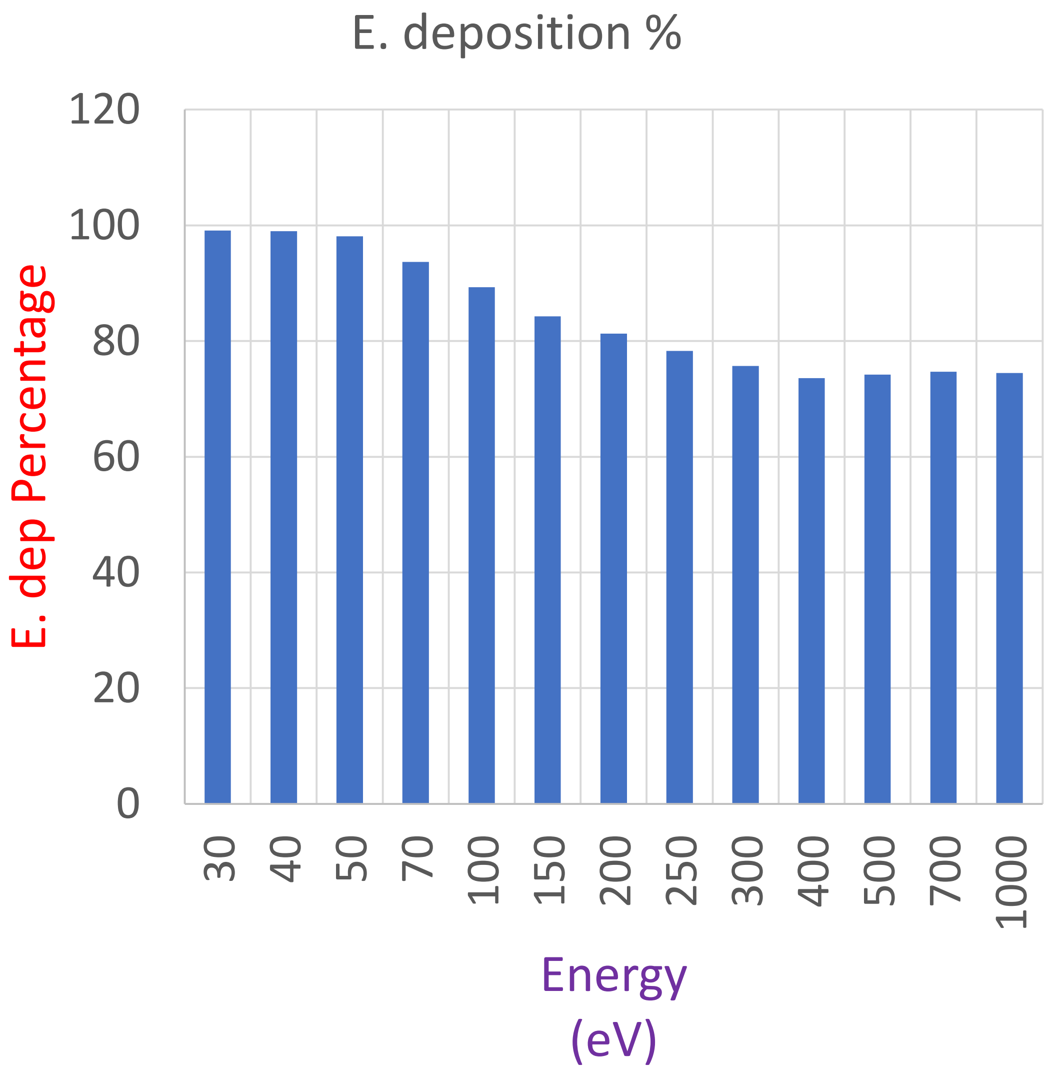
- In case of Ionisation only (the orange curve); energy deposition also reached the peak when the electron energy was about 300eV.



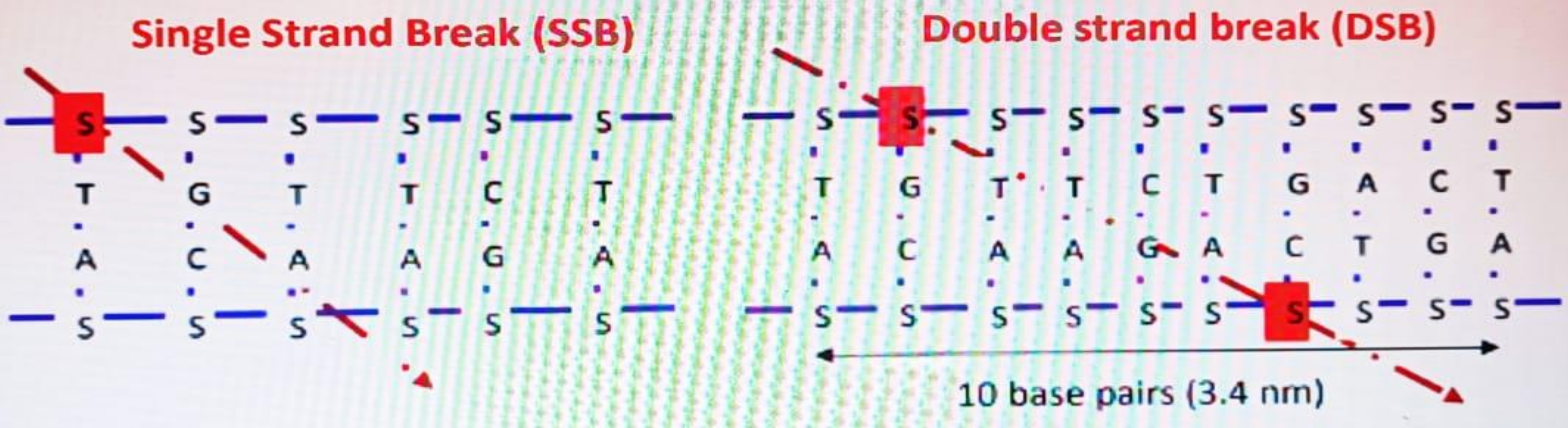
# Contribution of ionization only to all Energy Deposition in DNA nucleosome

- The highest energy deposition for only ionization process reached 99% when the electron energy was 30 eV.

- It became 78% when the electron energy was 1000 eV, then it started to decrease due to the physical interactions happened especially ionization.



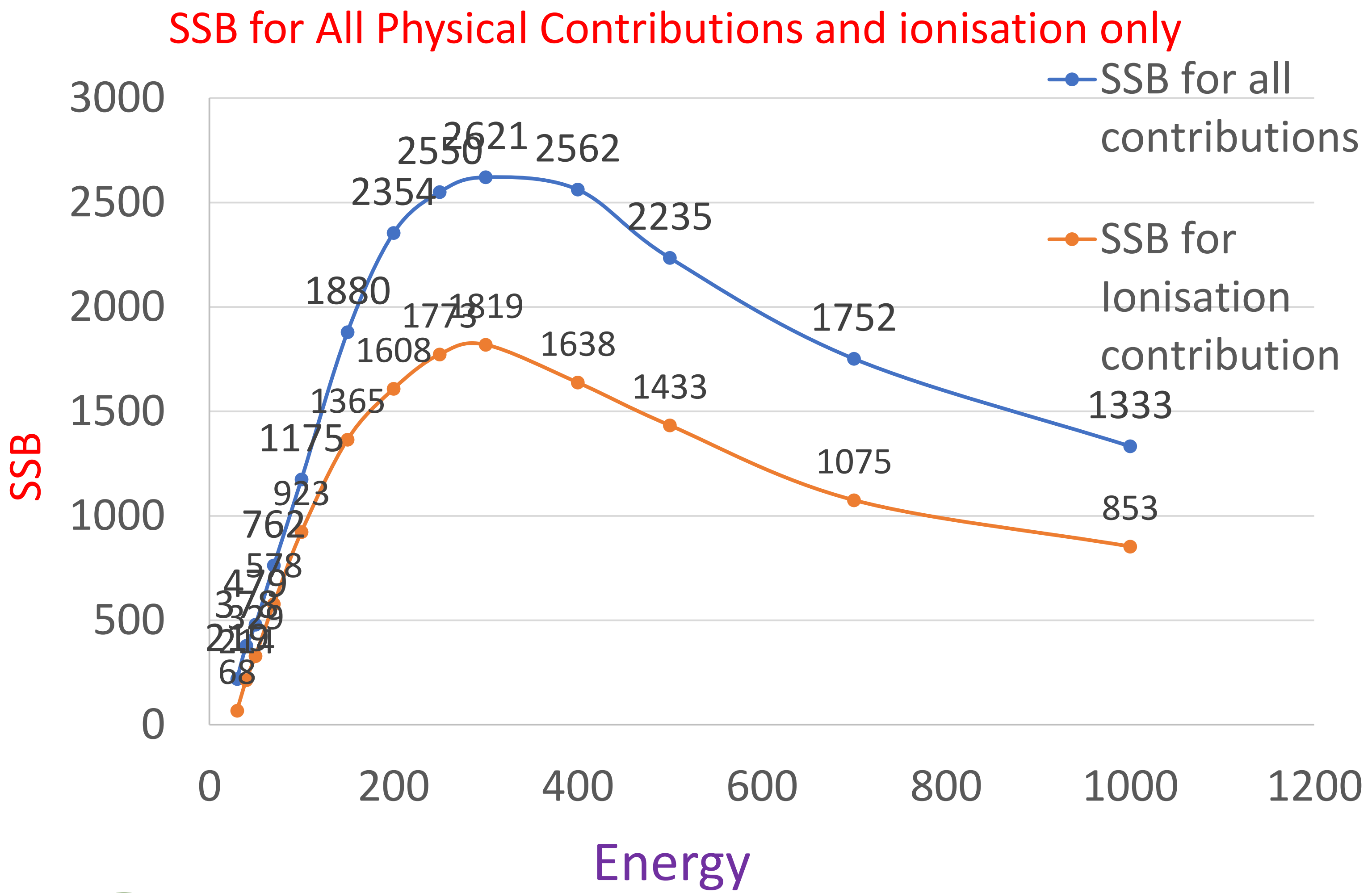
# Counting DNA Breaks




The counting of breaks was done like so:

- If energy deposition in the single strand of DNA > 8 eV then we have a SSB
- If there is a SSB on each strand and the distance between them < 10 base pairs (3.4 nm) then we have a DSB

## Calculating SSB for all contributions and in ionization only in case of using for electrons.




In case of All physical contributions (the blue curve); Single Strand Breaks (SSB) reached the peak when the electrons' energy was about 300 eV.

In case of Ionization only (the orange curve); SSB also reached the peak when the electrons' energy (e-) was about 300eV.

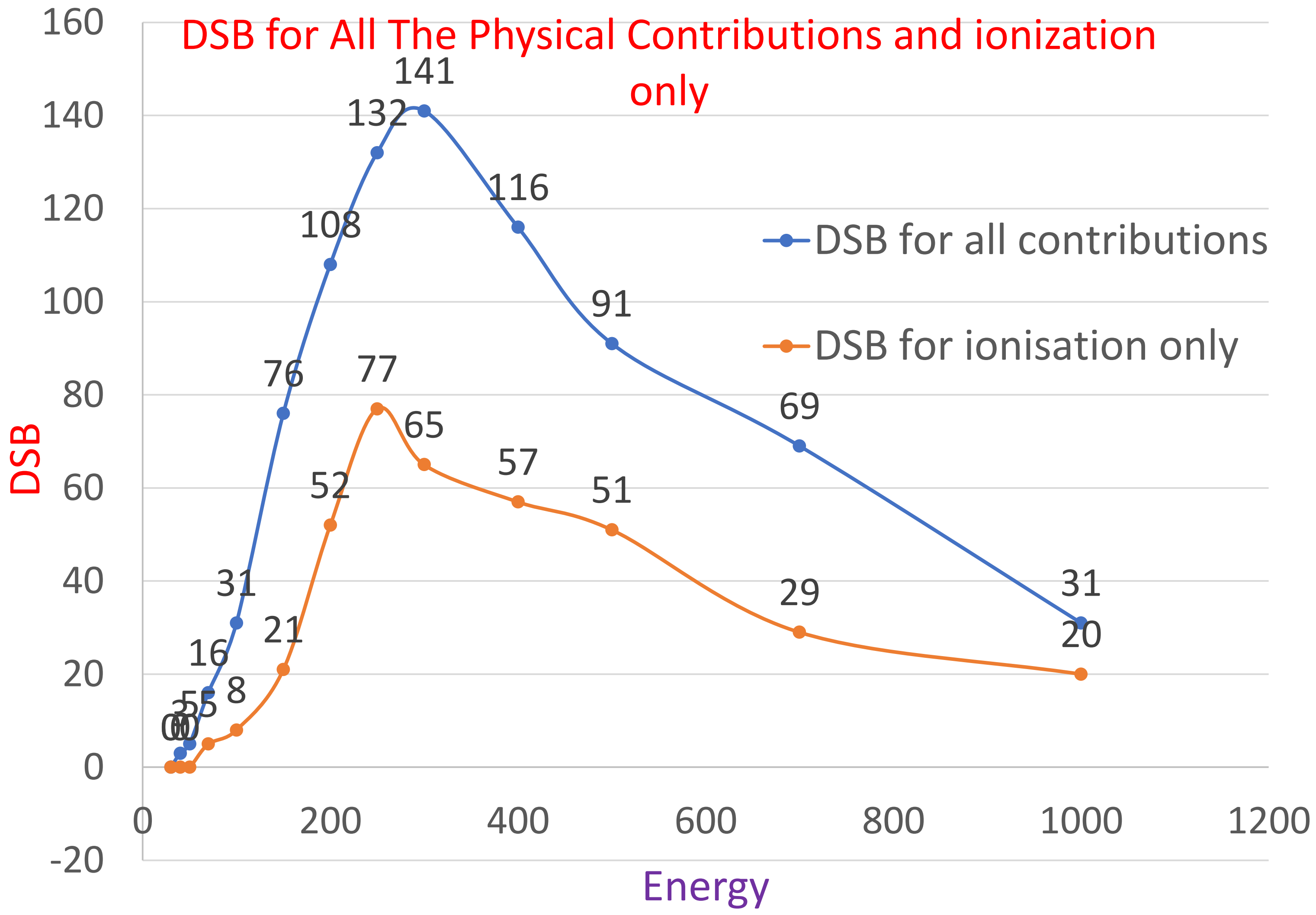
Why ?

It's Proportional relation. When the energy deposition in DNA increases, the SSB increases!

# Calculating DSB for all contributions and in ionization only in case of using for electrons.

- In case of All physical contributions (the blue curve); Double Strand Breaks (DSB) reached the peak when the electrons energy was about 300 eV.

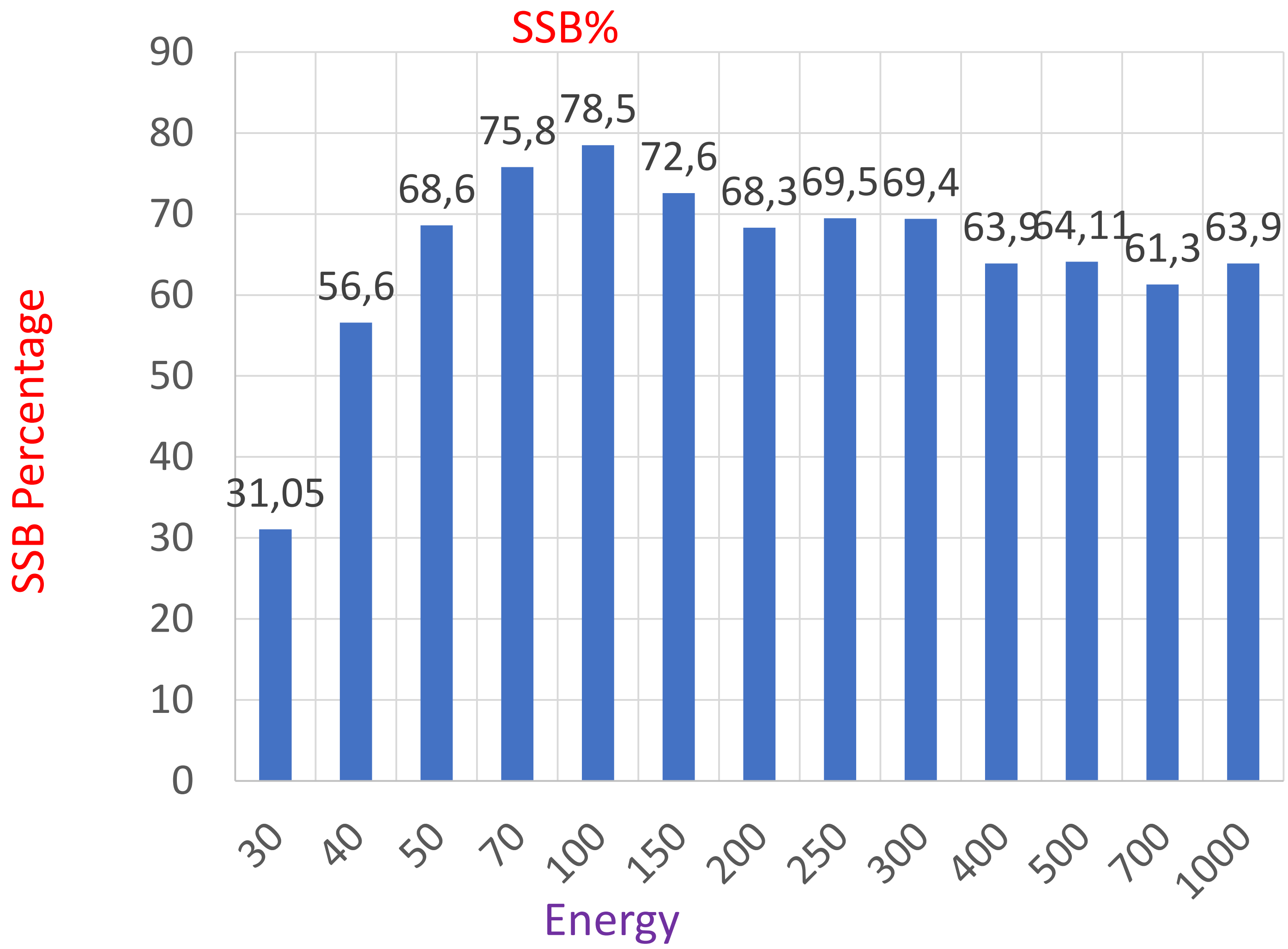
- In case of Ionization only (the orange curve); DSB also reached the peak when the particle energy (e-) was about 250eV.

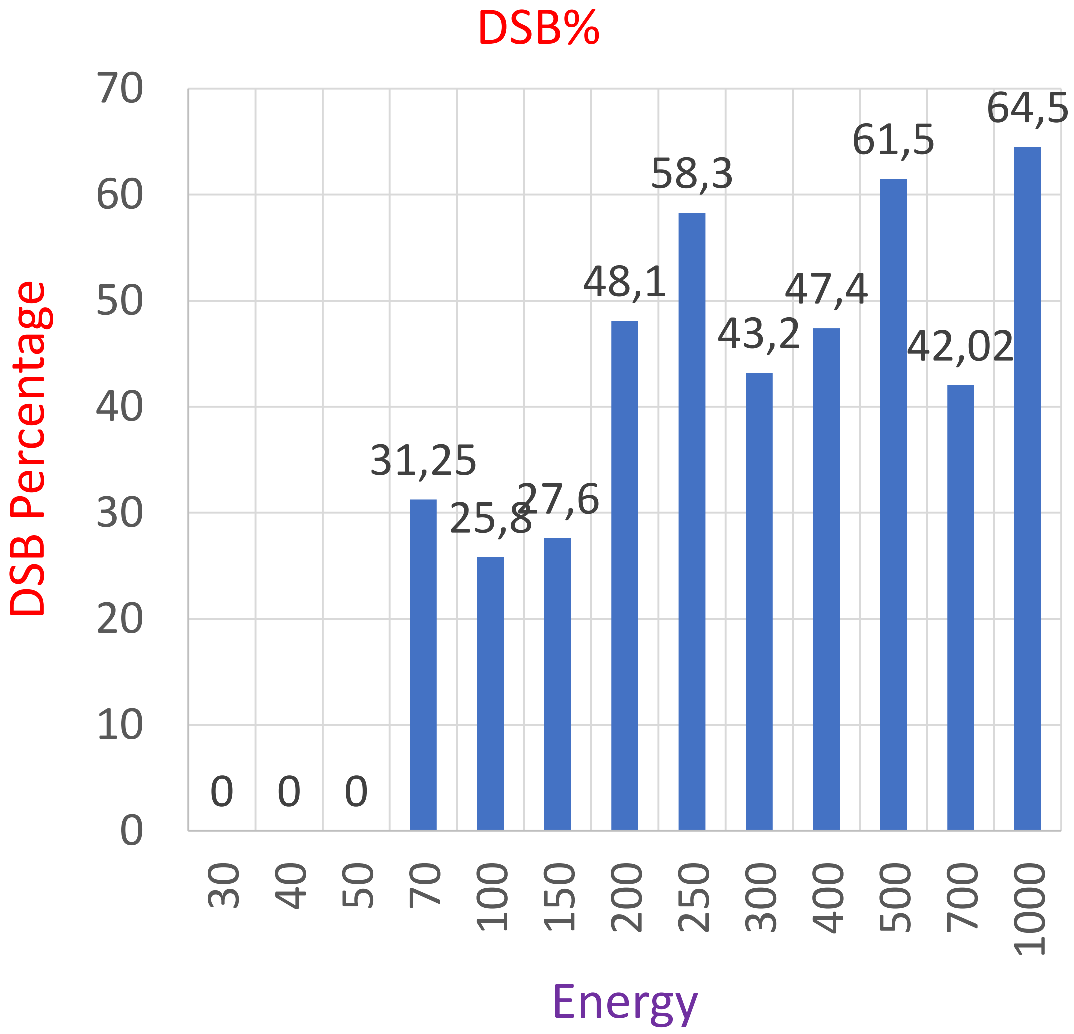



Why ?

Due to physical interaction steps closer DNA width (2.4 nm). That's why the geometrical interactions are important for calculating DNA damage.

# Calculation of SSB% and DSB% for all physical contributions and ionization only in case of electrons.

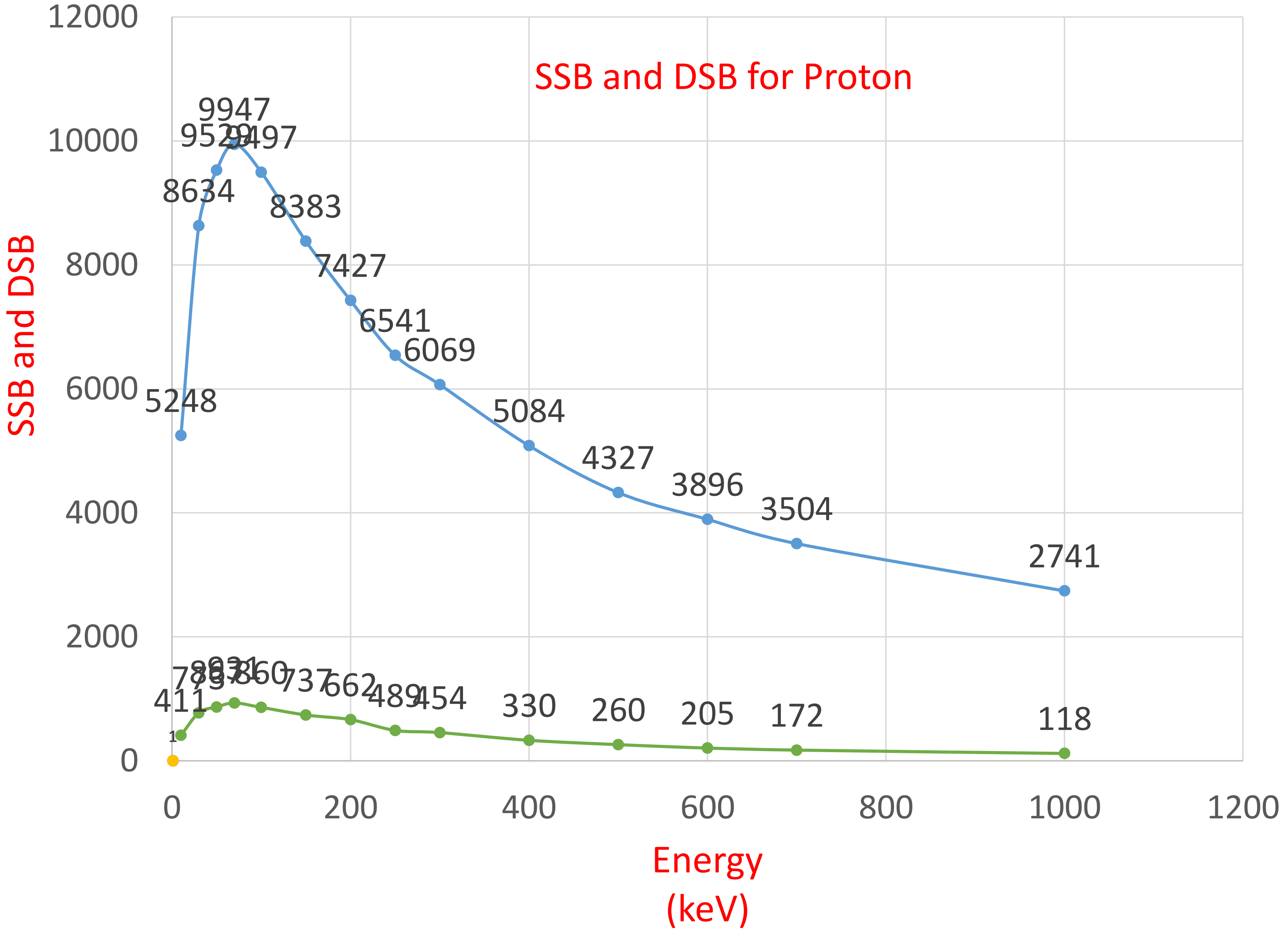



- ➢ The highest percentage of SSB% was 78.5% when the energy of the electron was 100ev.
- ➢ The highest Percentage of DSB% was 64.5% when the energy of the electron was 1000eV.

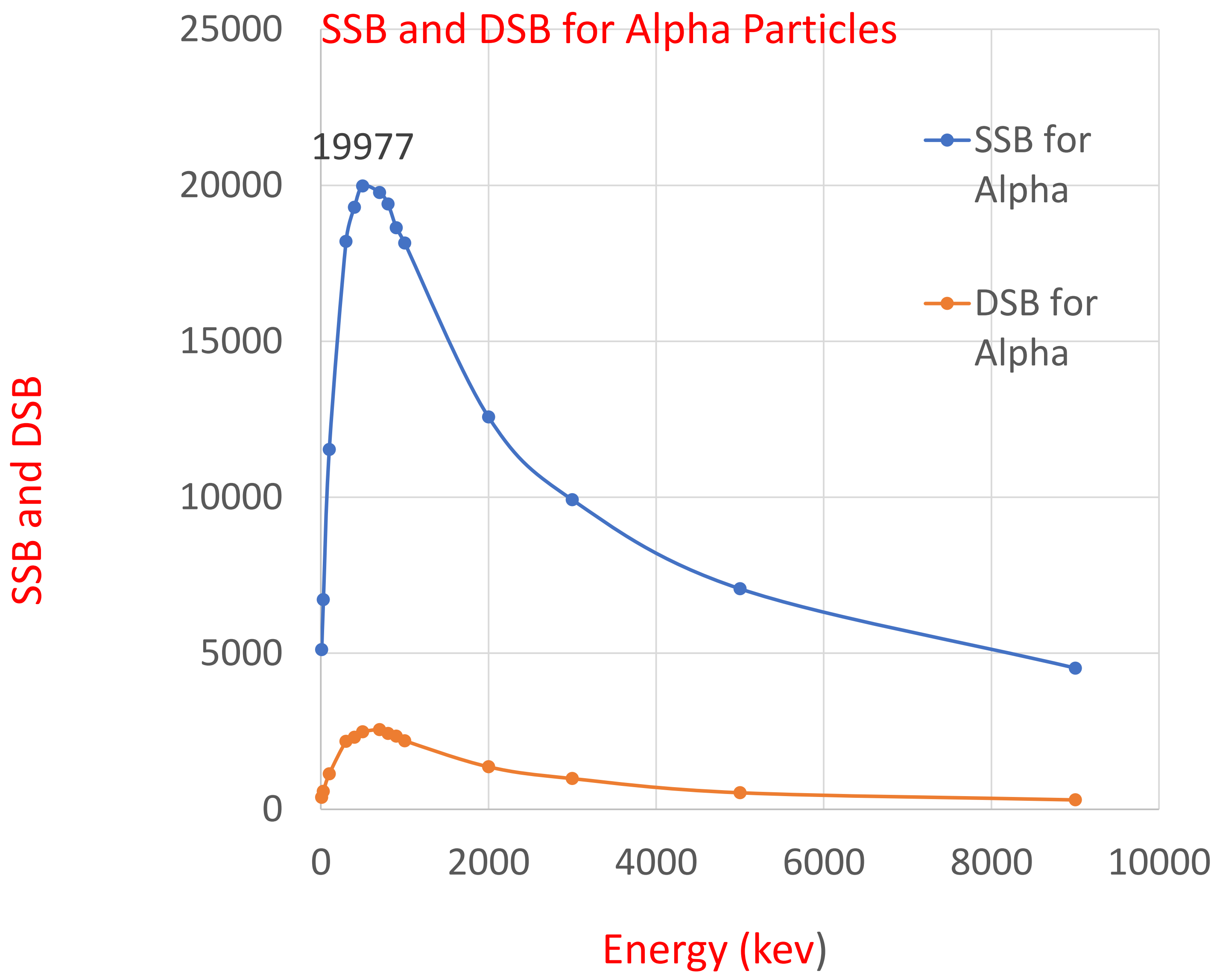
# Calculation of SSB and DSB when we used proton.

- SSB (the blue curve) reached 9947 when the proton beam was 70kev, then it started to decrease.
- DSB (the green curve) reached 931 when the proton beam was 70keV, then it started to decrease.

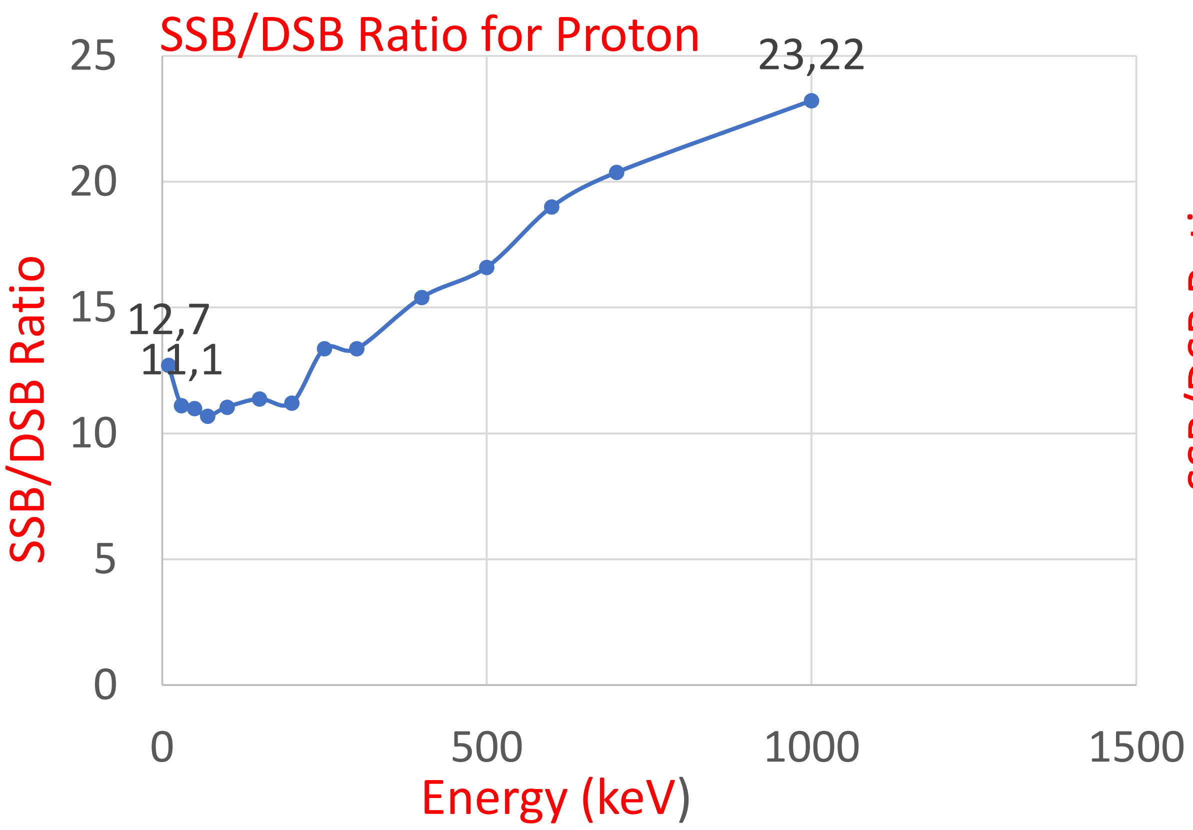


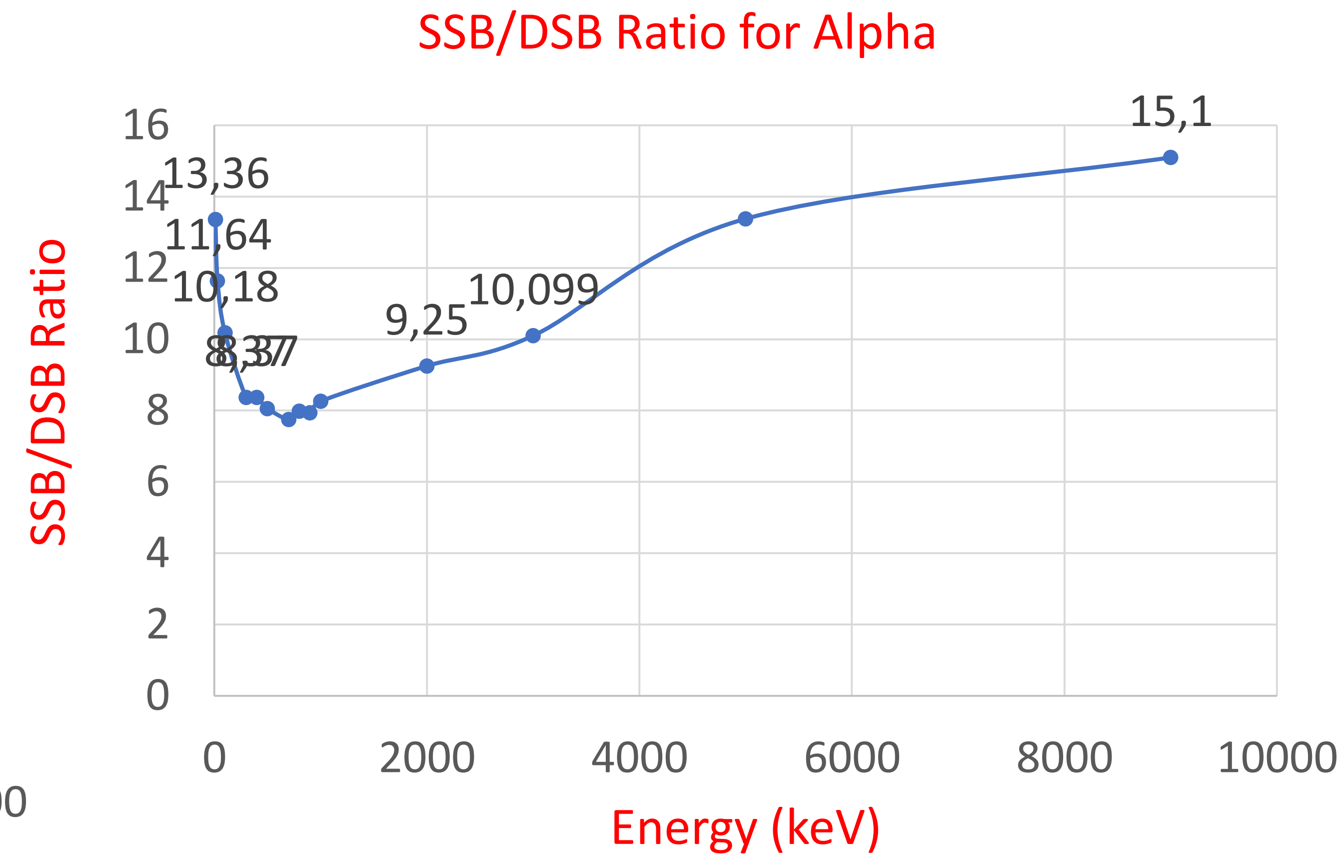
# Calculation of SSB and DSB when we used alpha particles.

- SSB reached 19977 when the alpha particles' energy was 500keV, then it started to decrease.
- DSB reached 2549 when the alpha particles' beam energy was 700keV, then it started to decrease.



# Comparison between SSB/DSB ratio when we used proton and SSB/DSB ratio when we used alpha particles.




- The highest ratio of SSB/DSB when we used protons was 23.22, when the Proton energy was 1000keV.
- The highest ratio of SSB/DSB when we used alpha particles was 15.1, when the alpha particles' energy was 9000keV.

# Conclusion

- By using GEANT4-DNA, we simulated the track of e-, p+, alpha with different energies (10 keV, 100 keV, 1000 keV) until the particles stop in water.
- We predicted the DNA damage happened by using different types of charged particles and calculated the SSB and DSB due to the Energy of the particles' used after the beams scattering.
- We have found that DNA SSBs and DSBs reached their peak at different energies of the particles.
- An interesting observation that ionization events play a major role in DNA damage (78% for SSB, 64% for DSB).
- It is observed that the effect of protons and alpha particles is larger than that of the electrons on DNA damage.
- We observed that alpha particles have the highest deposited energy (E.dep).
- Geant4 is an awesome outstanding computational toolkit that helps us to predict what the experimental research should prove.

# Context

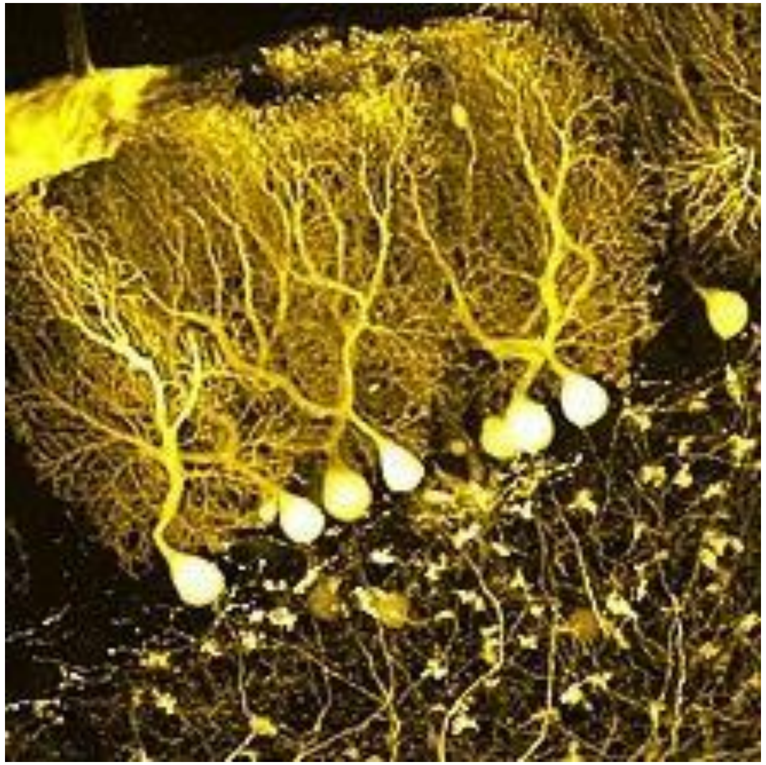
# Aim and objectivities of the project

| | |
|---|---|
| Learn | Learn modern methods of computer simulations in radiation  biophysics |
| Gain | Gain practical skills in using Geant4-DNA Monte Carlo simulation toolkit |
| Construct | Construct 3D geometry of neurons and glia for microdosimetry calculations |
| Calculate | Calculate radiation dose deposition in neurons and glia in mouse and human brain |

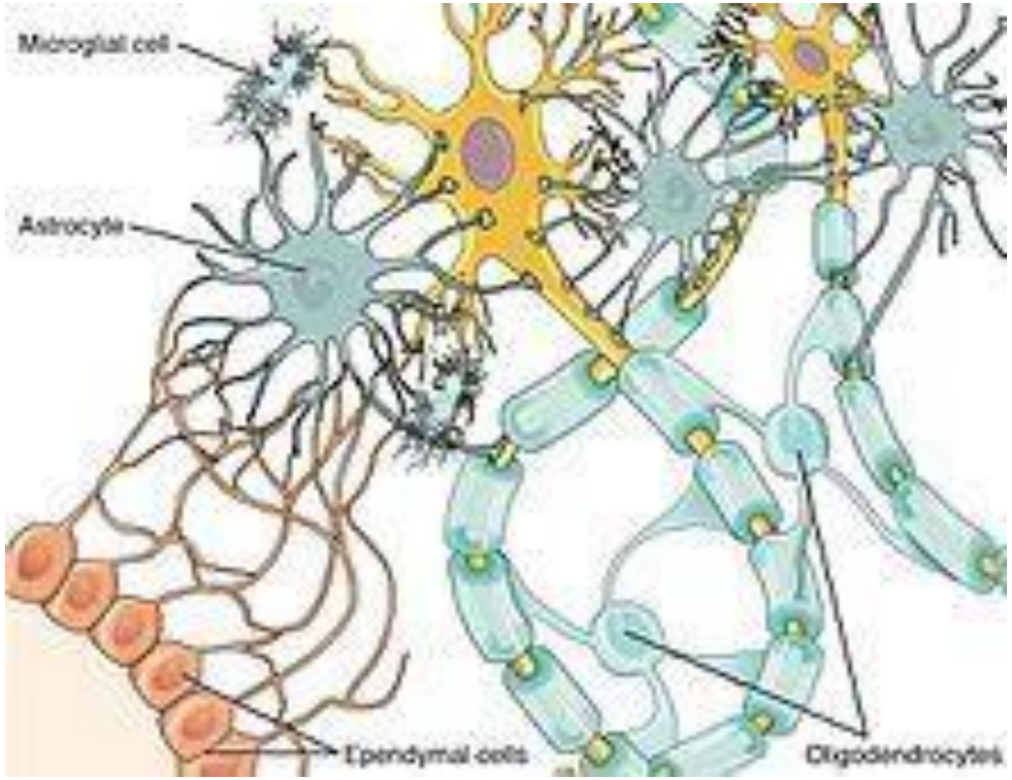
# Introduction

The two main types of cells in the brain are neurons, also known as nerve cells, and glial cells also known as neuroglia.[1]

Purkinje neurons

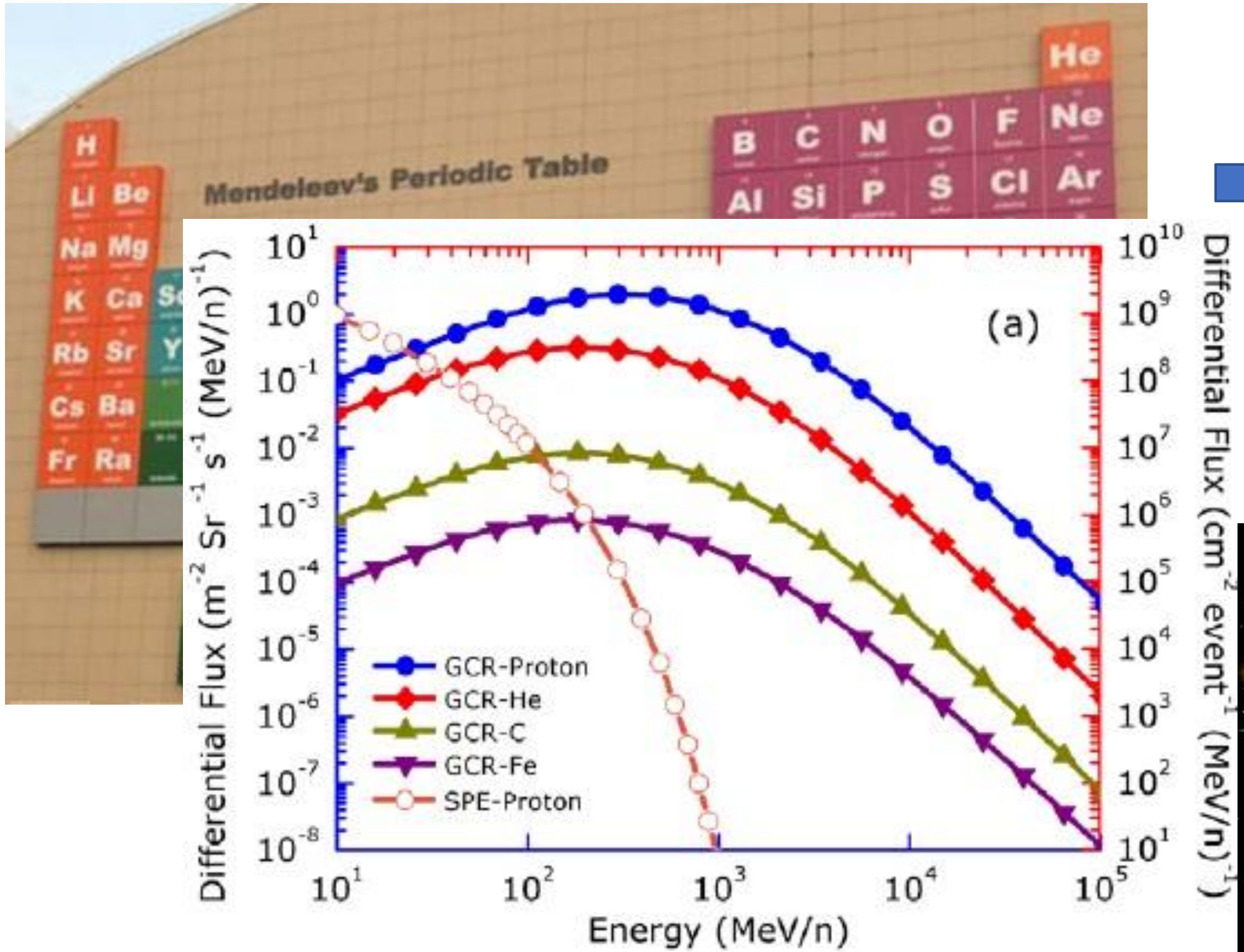


glial cells



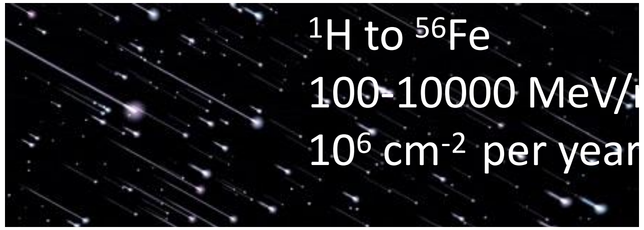

Wikipedia

# Why radiation damage to human brain is important?

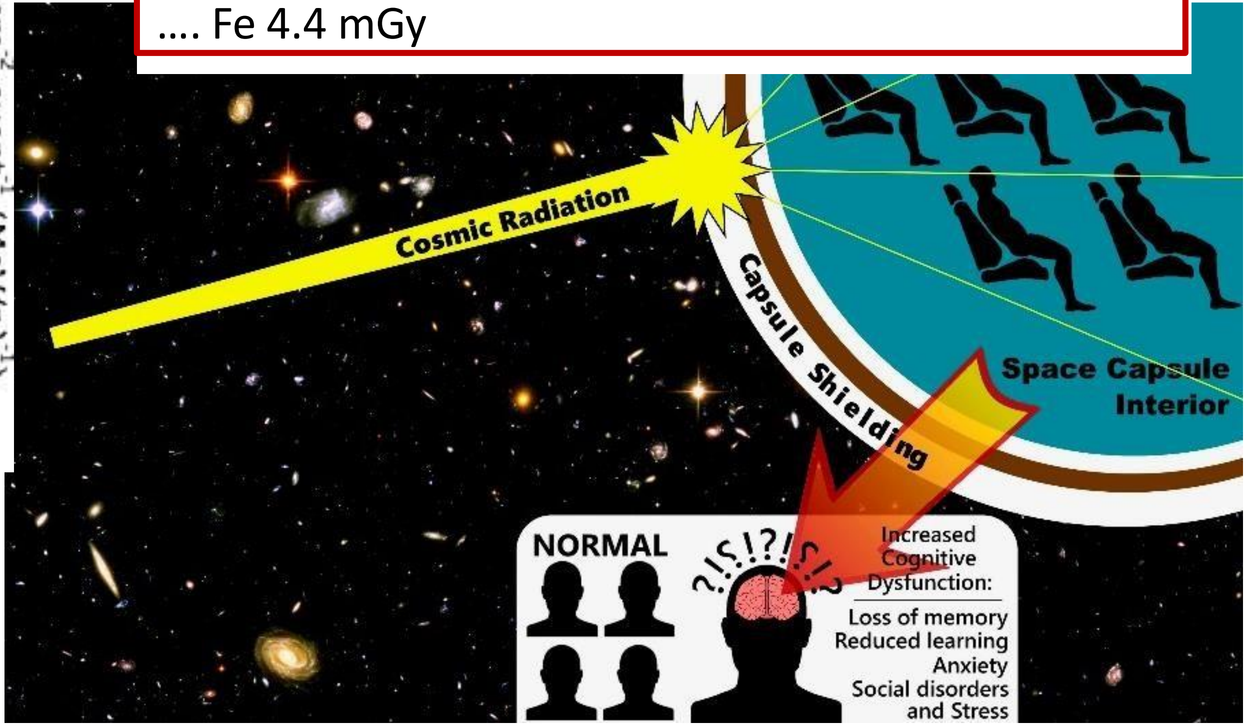



Journal of Radiological Protection 35(4):777-788

## Radiation risk in deep space

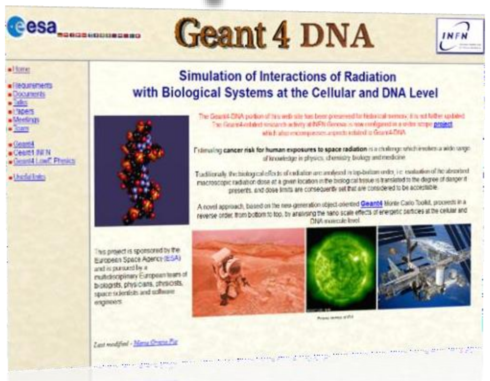


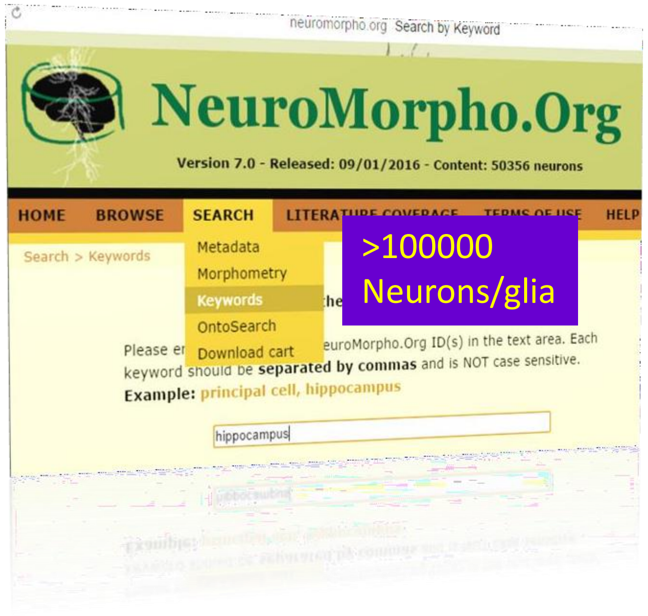

Annual space radiation dose 500-1000 mGy/y.
H 98 mGy; He 33 mGy; … C 4.7 mGy; …. Ar 0.3 mGy; …. Fe 4.4 mGy




It is connected with problems of predicting cosmic radiation risk to the organisms of astronauts during the deep space travel.

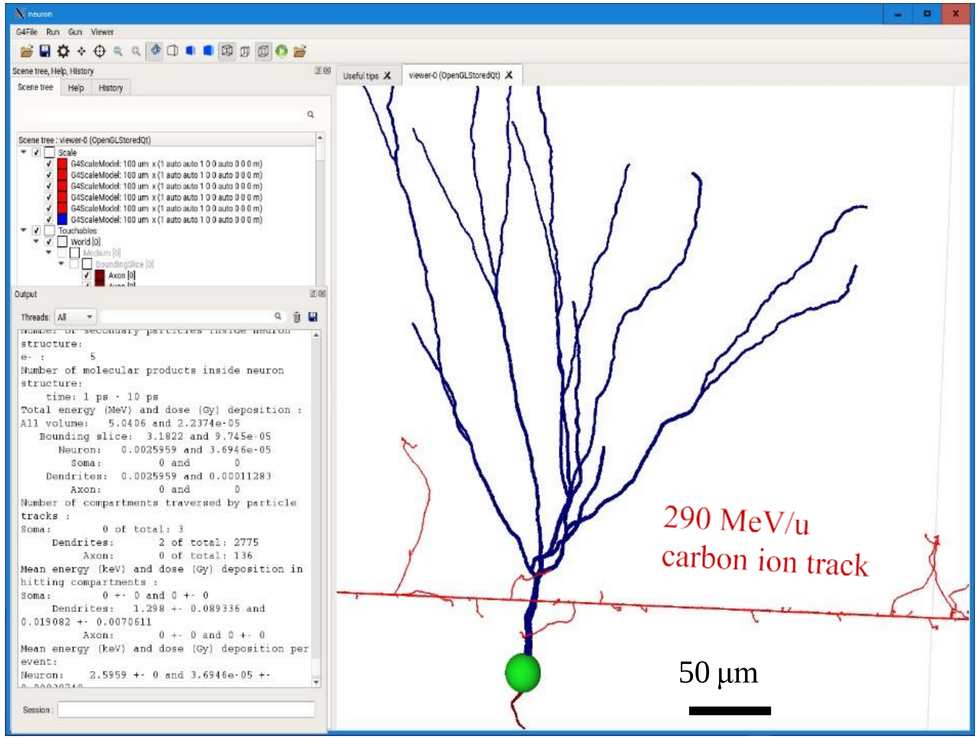
# "neuron" - radiobiology application of Geant4/Geant4-DNA

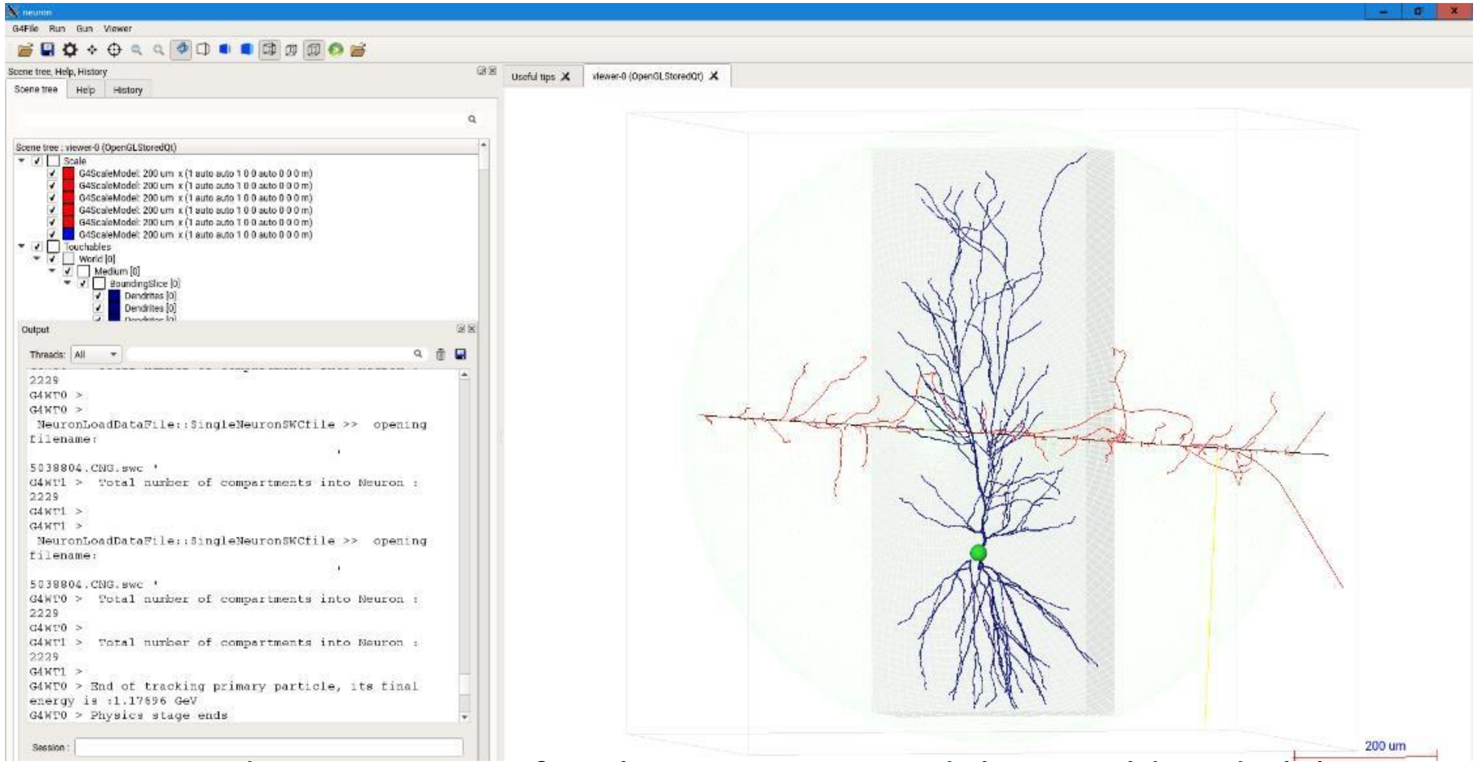


**G4examples/extended/medical/dna/NEURON** – reads standardized SWC file format representing the realistic neuron morphology and estimates the microscopic energy depositions and production of oxidative radiolytic species in the vicinity of neural cells.

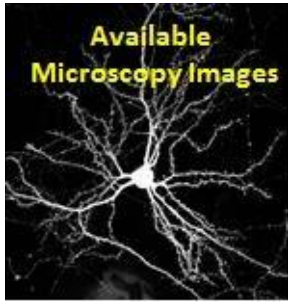


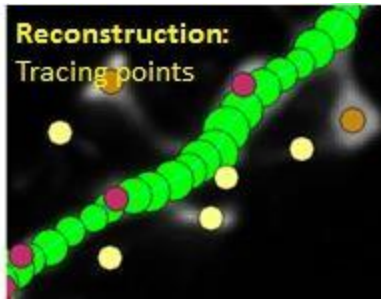

This application shows to users how to simulate neuron cell irradiation, in order to investigate cosmic radiation effects on nervous system.

# Simulation of particle traversing the neuronal cells




Construction and preparation of realistic neuron model in world-wide laboratories




**SWC File** – standardized neuromorphometric format:

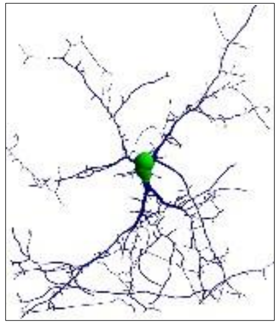
**n T x y z R P**

……………………,

51 3 -91.73 3.64 -2.25 0.24 50

52 3 -92.12 3.98 -1.91 0.29 51

……………………,



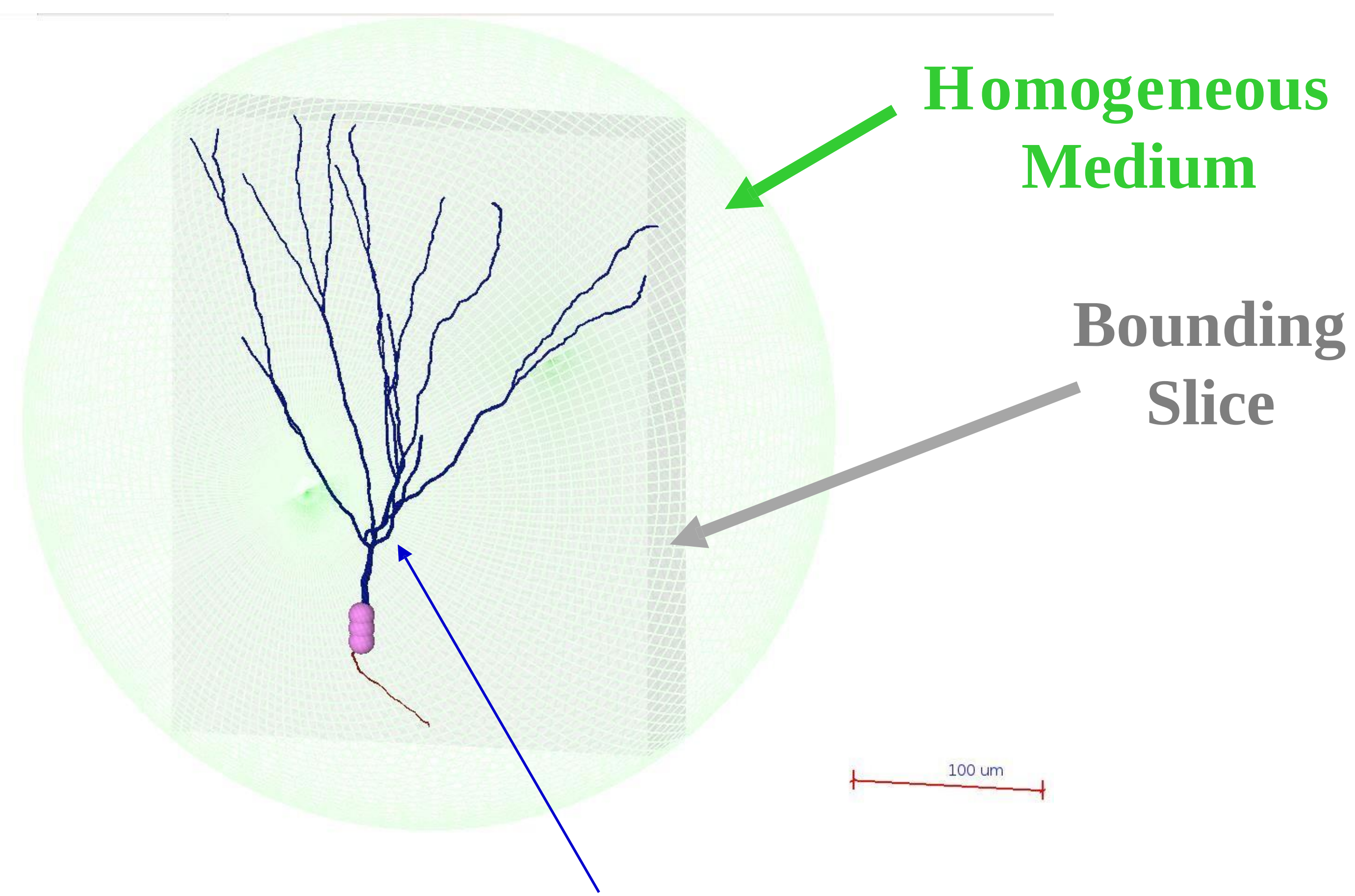
# Reconstruction of neuronal cell for radiation dosimetry

## DetectorConstruction.cc

```
class G4Sphere
class G4Tubs
class G4Ellipsoid
class G4Box
```

2914 compartments;

overall dimensions (X,Y,Z):
251, 316, 65 μm




Name: GranuleCell-Nr2.CNG.swc

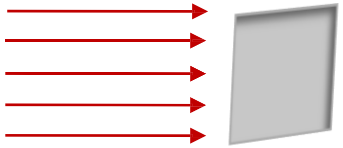
# Simulation of particle traversing the neuronal cells

## PrimaryGeneratorAction.cc

### Initial position and direction of particles beam

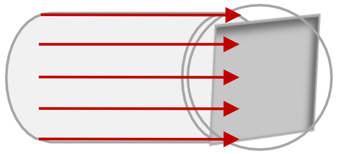
**Three options** for particle directions:

a) Partilces directed to "**square**" on the XY plane of bounding slice (or YZ, XZ)



./neuron -mac neuron.in -sXY

b)Partilces directed to "**disk**" on the XY plane of bounding slice (or YZ, XZ)

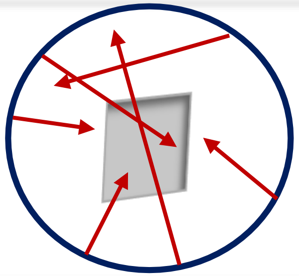


./neuron -mac neuron.in -dXY

Default:

c) Partilces directed as steradian toward the bounding slice (default option!)

./neuron -mac neuron.in



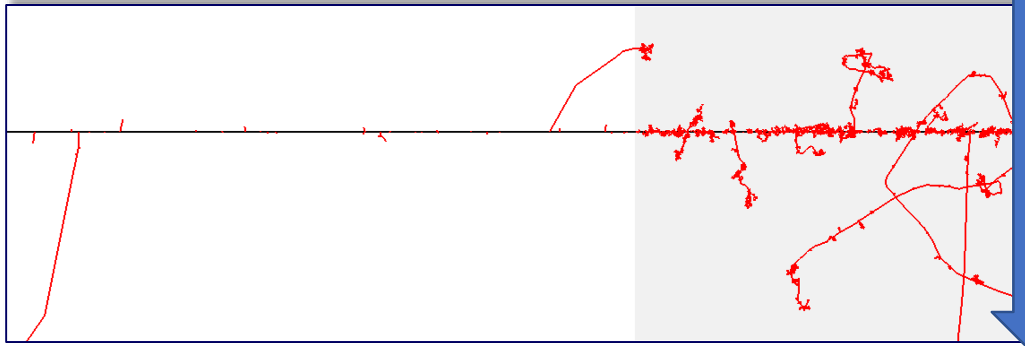
# Simulation of particle traversing the neuronal cells

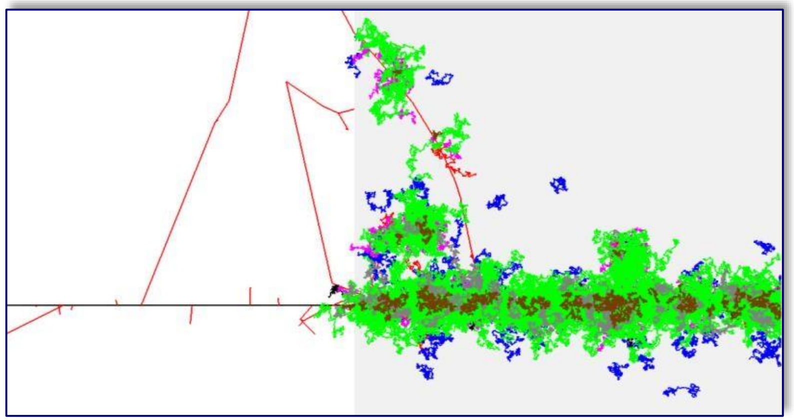
## PhysicsList.cc

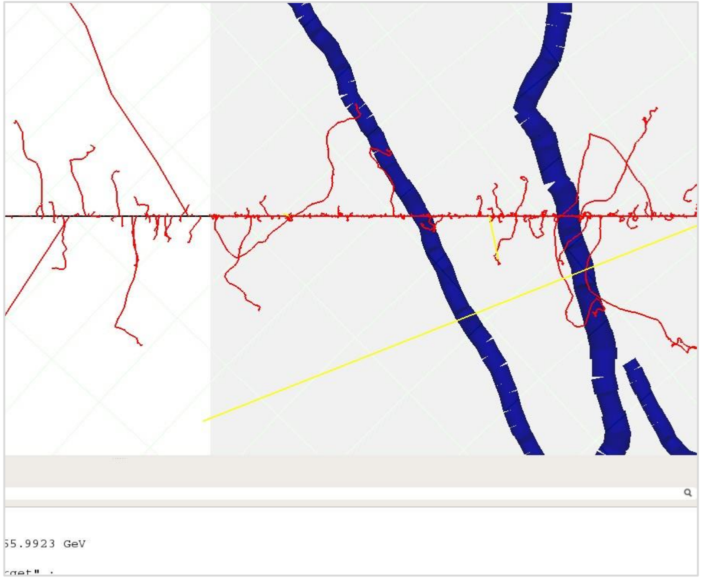
**Geant4 Standard Physics** outside target region

**Geant4-DNA Physics** inside target region

**Geant4-DNA Chemistry** inside target region







Results;

## Quantification of energy deposition in single granule neuron of mouse hippocampus irradiated by ion beams

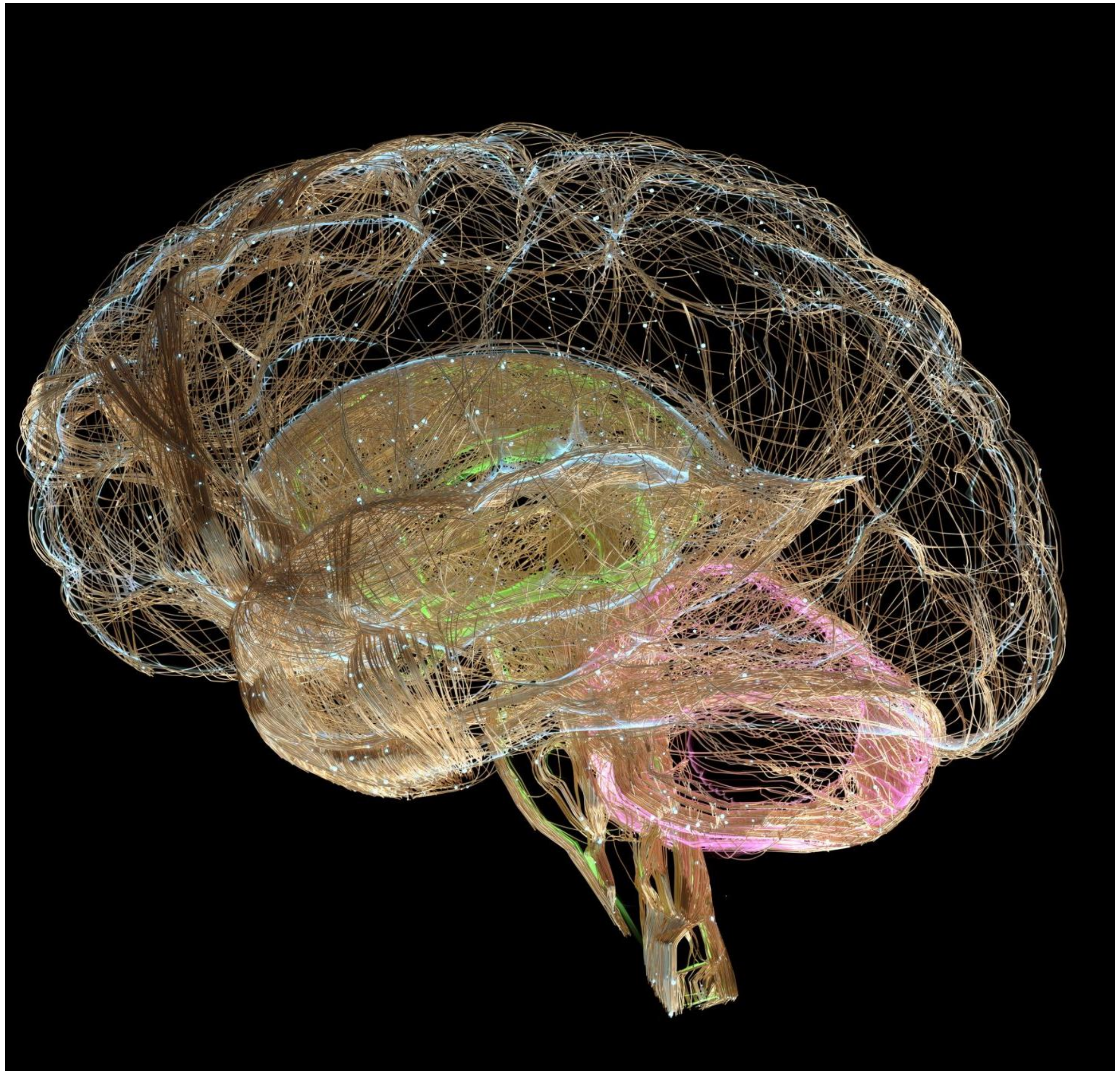
- Particle beam: Carbon ion
- Particle energy: 100 MeV/nucleon
- Neuron name: NMO_06177

| Ion beam | Fluence (particles/cm2) | Dose (mGy) | Edep in Neuron and only dendrites (MeV) | Edep in dendrites (%) | Hits of dendrites (%) |
|---|---|---|---|---|---|
| 200 | 38366 | 1.59 | 1.83 and 0.55 | 30% | 5% |
| 1000 | 1.9×105 | 7.99 | 6.34 and 2.35 | 37% | 17.6% |
| 3000 | 5.75×105 | 24 | 12.33 and 6.512 | 52% | 34.7% |
| 5000 | 9.59×105 | 40 | 20.79 and 11.15 | 54.4% | 56.3% |
| 7000 | 1.34×106 | 56 | 28.5 and 15.2 | 53.35% | 67% |
| 9000 | 1.73×106 | 72 | 37.7 and 19.85 | 53% | 76% |

More than 34.7% of neuronal dendrites are irradiated when radiation dose > 24 mGy.

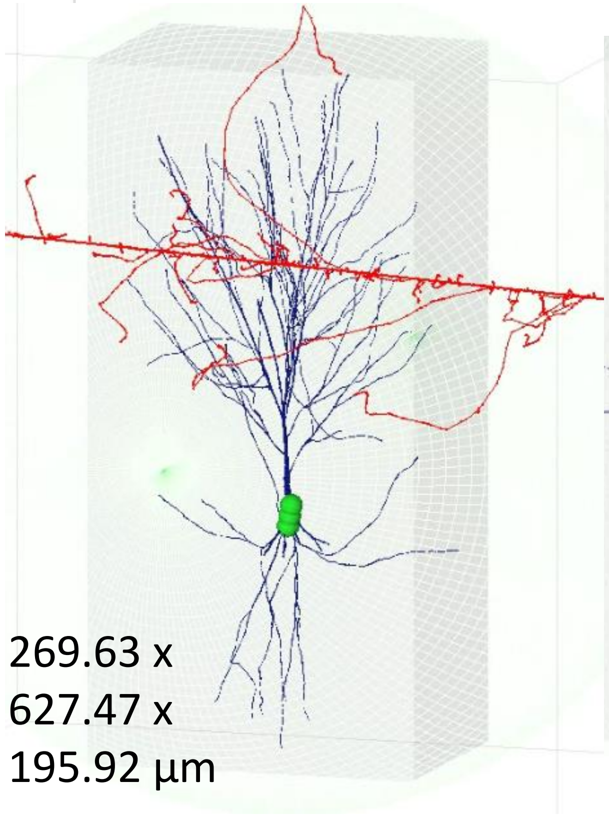
# Calculation of radiation energy deposition in different types of brain cells

- Particle beam: Carbon ion
- Particle energy: 100 MeV/nucleon



Results; **Irradiation of 3D neuron/astrocyte in mouse and human brain with Geant4**

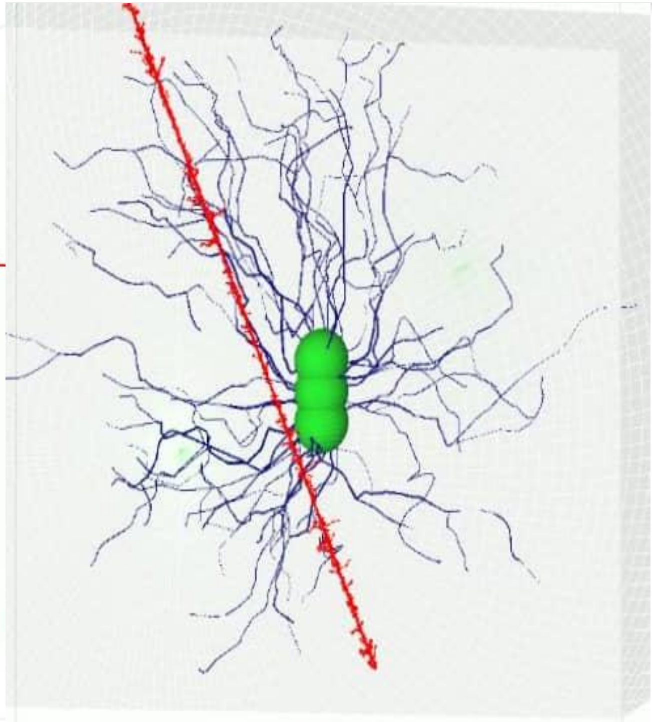
Human CA1 pyramidal neuron in hippocampus (NeuroMorpho ID: NMO_147145)



269.63 x 627.47 x 195.92 μm

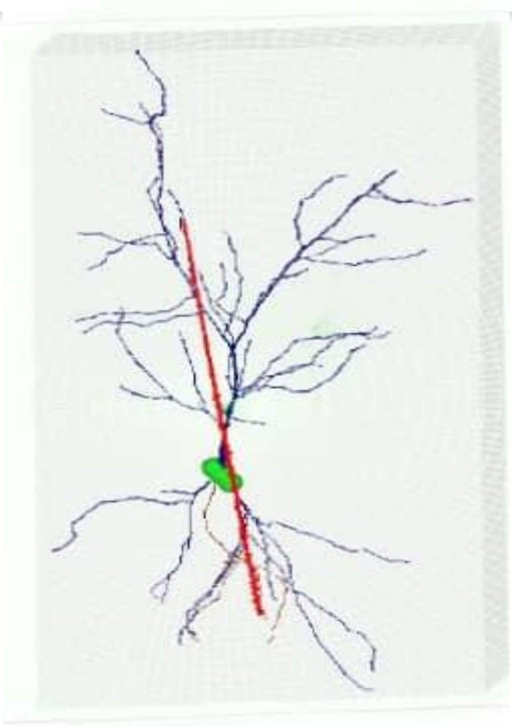
Soma Surface : 1750.6 $\mu m^2$
Dendrites Volume : 13848.6 $\mu m^3$
Average Diameter : 1.06 μm

Human **Glia (Astrocyte)** in neocortex (NeuroMorpho ID: NMO_189798)



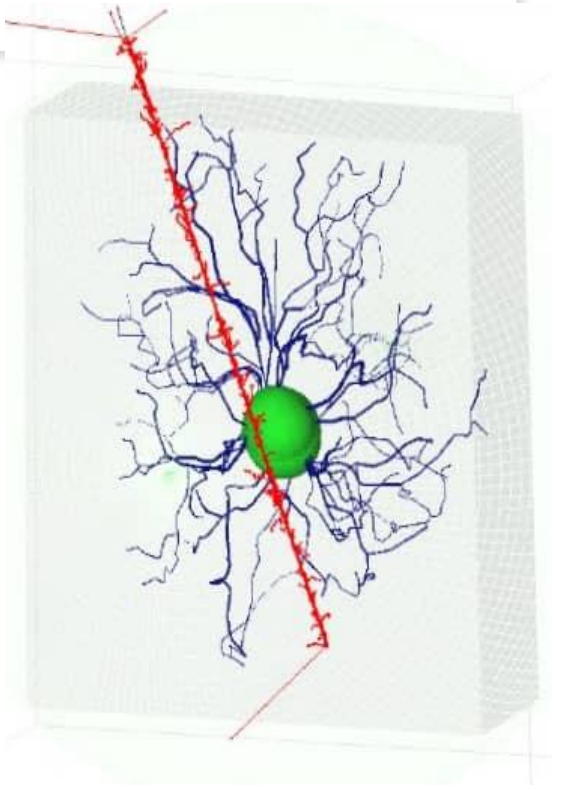
Soma Surface : 243.34 $\mu m^2$
Dendrites Volume : 89.87 $\mu m^3$
Average Diameter : 0.19 μm

Mouse CA1 pyramidal neuron in hippocampus (NeuroMorpho ID: NMO_147070)



Soma Surface : 596.15 $\mu m^2$
Dendrites Volume : 2819.03 $\mu m^3$
Average Diameter : 0.83 μm

Mouse **Glia (Astrocyte)** in neocortex (NeuroMorpho ID: NMO_189927)



Soma Surface : 176.43 $\mu m^2$
Dendrites Volume : 75.59 $\mu m^3$
Average Diameter : 0.21 μm

Results;

- Particle beam: Carbon ion
- Particle energy: 100 MeV/nucleon

| Species/Region of Brain | Cell type/ Neuromorpho ID | Fluence (particles/cm2) | Dose (mGy) | Edep in Neuron and only dendrites (MeV) | Edep in dendrites (%) |
|---|---|---|---|---|---|
| Human/hippocampus | CA1 Pyramidal neuron NMO_147145 | 3.5×105<br>8000 beams | 14.6 | 38.7 & 15.4 | 40% |
| Mouse/Hippocampus | CA1 Pyramidal neuron NMO_147070 | 3.4×105<br>3000 beams | 14.2 | 5.7 & 2.76 | 48% |
| Mouse/neocortex | Glia (Astrocyte)<br>NMO_189927 | 3.56×105<br>110 beams | 14.8 | 1 & .07 | 7% |
| Human/neocortex | Glia (Astrocyte)<br>NMO_189798 | 3.56×105<br>250 beams | 14.8 | 1.68 & .091 | 5% |

Human CA1 pyramidal neuron in hippocampus is received larger amount of energy deposition for 100 MeV/u carbon ions with similar radiation dose (~ 14 mGy).

# Aim and objectivities of the pr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| **Learn** | Learn modern methods of computer simulations in radiation biophysi |
| **Gain** | Gain practical skills in using Geant4-DNA Monte Carlo simulation toolkit |
| **Construct** | Construct 3D geometry of neurons and glia for microdosimetry calculations |
| **Calculate** | Calculate radiation dose deposition in neurons and glia in mouse and human brain |

# Thank you for your Attention!

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# Special thanks to our dedicating Supervisor!
## Dr. M. Batmunkh