# Calculation of Absorbed Dose Coefficients for Internal Ex Vivo Irradiation of Lymphocytes Using GATE and Geant4-DNA

M. Salas-Ramirez[1], L. Maigne[2], M. Lassmann[1], U. Eberlein[1]
[1]University of Würzburg, Department of Nuclear Medicine, Würzburg, Germany
[2]Laboratoire de Physique de Clermont, CNRS/IN2P3, Université Clermont Auvergne, Aubière, France

**Klinik und Poliklinik für Nuklearmedizin**
Direktor: Prof. Dr. A. Buck

# Background

## From Activity to Absorbed Dose
## Experimental Setup

Activity (MBq) → **Absorbed dose coefficient**

$$d_{Blood}(mGy \cdot ml \cdot MBq^{-1})$$
$$d_{Lymphocyte}(mGy \cdot ml \cdot MBq^{-1})$$

→ Absorbed Dose (Gy)

**Blood Irradiation**

1ml radioactive solution + 7 ml blood

Before centrifugation



Irradiated blood (1h, variable activity)

Yellow barrier

Density Gradient Media

centrifugation

After centrifugation

Plasma

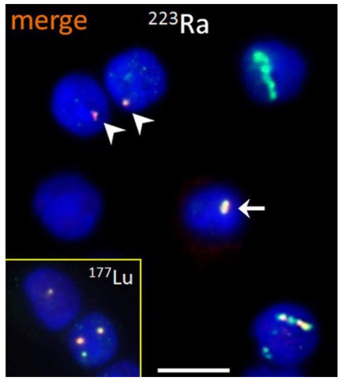
Lymphocytes Monocytes

Yellow barrier

Erythrocytes Neutrophils




**Quantification of DSB in lymphocytes**



# Aim

- The aim of this study is to establish a relationship between activity and absorbed doses in the nucleus of lymphocytes using GATE[2] (v9.1) at the macroscopic level and Geant4-DNA[3] (v10.7) at the cellular level

  - Reproduce the spatial distribution of lymphocytes in the irradiation vial

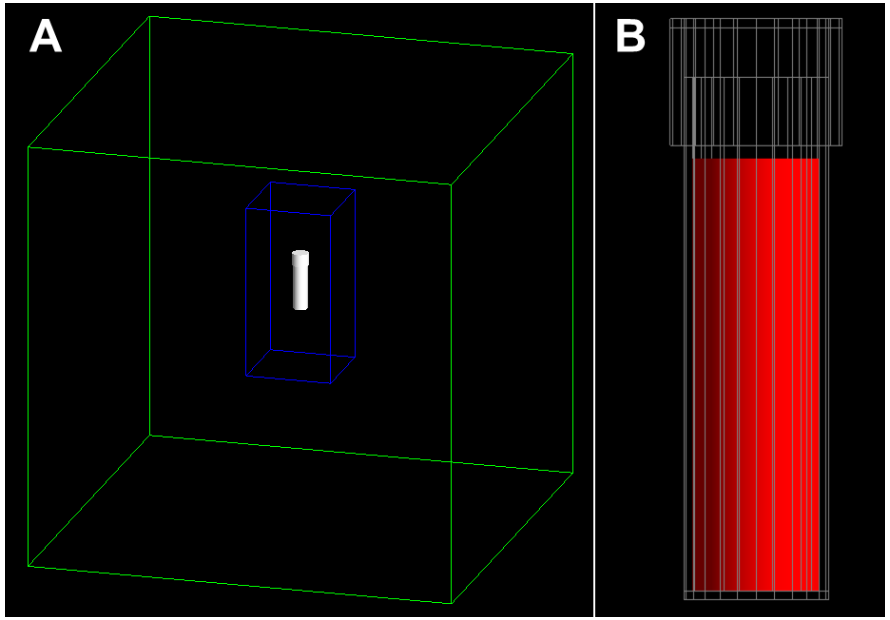
  - Determine the absorbed dose coefficient to lymphocytes per milliliter of blood ($\boldsymbol{d_{Lymphocyte}}$) for 1 h of internal ex vivo irradiation of whole blood :
    - Blood (vial) – **Source and Target (macroscopic simulation)**
    - Lymphocyte nuclei – **Target (microscopic simulation)**

[2] Jan, S., et al. Phys Med Biol, 2004. 49(19): p. 4543-61
[3] Incerti, S., et al. Int. J. Model. Simul. 2010 01:02, 157-178

# Methodology

- Macroscopic and microscopic geometries:

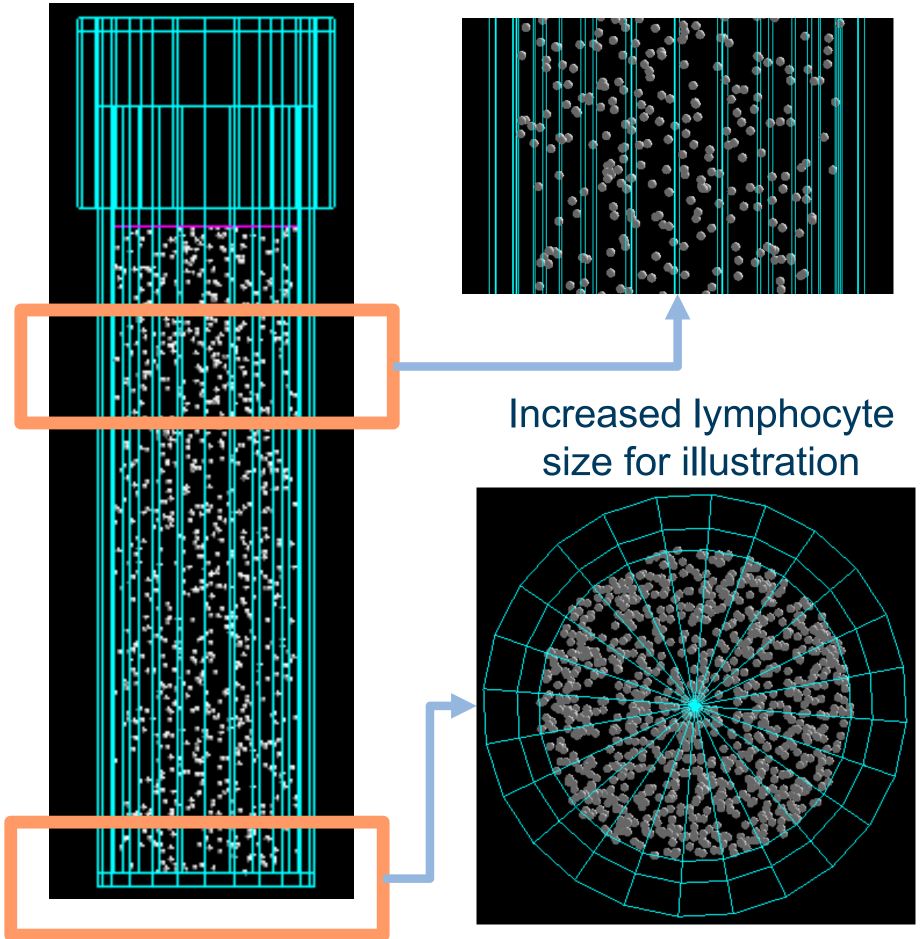
## Blood (8 ml vial) [4]




A)- Whole simulation space
B)- Whole Blood (red volume)

## Lymphocyte model

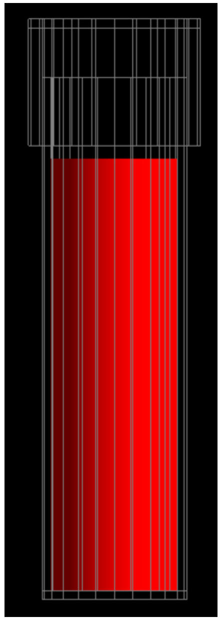
1000 spheres of 3.75 $\mu$m radius



# Methodology:

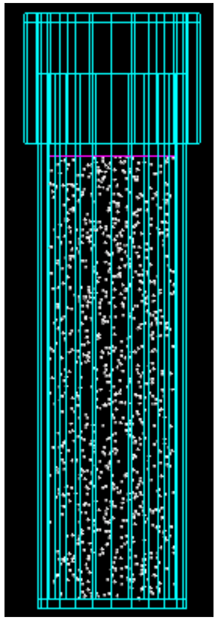
- Macroscopic and microscopic geometries:

## Blood (8 ml vial) [4]



- The source was distributed randomly in the vial (blood, water material)
- GATE/Geant4 *ion source* definition
- QGSP_BIC_EMZ physics
- 10 radionuclides were simulated: $^{18}F$, $^{68}Ga$, $^{90}Y$, $^{99m}Tc$, $^{123}I$, $^{124}I$, $^{131}I$, $^{177}Lu$, $^{223}Ra$, and $^{225}Ac$
- Full decay chain for $^{223}Ra$, and $^{225}Ac$

## Lymphocyte model



Lymphocyte mass fraction **2.8E-08**

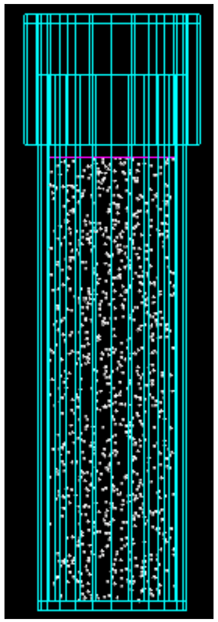
- The source was distributed randomly in the space non-occupied by the lymphocytes (blood, water material)
- GATE/Geant4 *ion source* definition. Same 10 radionuclides
- A phase space attached to each sphere
- Each sphere as a cold source

[4] M. Salas-Ramirez, et al. Z Med Phys. 2022

# Methodology:

- Microscopic geometry:

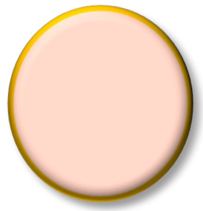
Lymphocyte model
One cell simplyfication



- 1000 spheres of 3.75 $\mu$m radius (water material)
- 1000 phase spaces

The 1000 phase spaces were translated to the position (0,0,0) and summed in one single phase space

Python code[5]

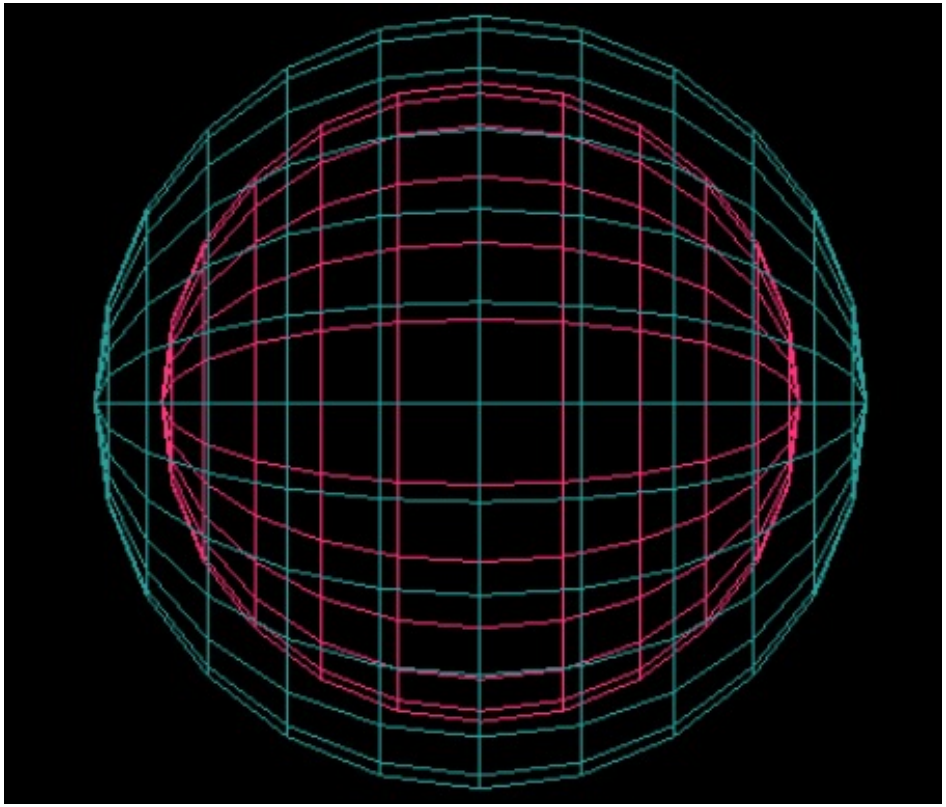


Higher statistics (number of particles x 1000)
Sampling of the center and periphery of the vial

[5] Laboratoire de Physique de Clermont, Université Clermont Auvergne, France

# Methodology

Lymphocyte model
Geant4-DNA



CELL
NUCLEUS

- *World*: Sphere of 3.76 $\mu$m radius filled with the G4Galactic material.
- Cell: Sphere of 3.75 $\mu$m radius[7] filled with the G4Water material.
- Nucleus: Sphere of 3.1 $\mu$m radius[7] filled with the G4Water material
- Change in the SteppingAction:
  - The **clustering algorithm**[6] and scoring of the deposited energy **ONLY in the nucleus**
  - Excludes transportation processes as in the **dnaphysics** example
  - Use of a modified "G4EmDNAPhysicsActivator" to simulate Beta particles with energies > $E_{max}$

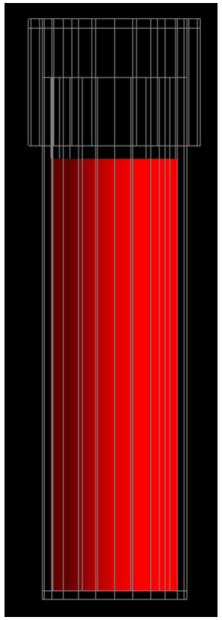
[6] Francis, Z., et al., Comput. Meth. Programs. Biomed. 2011 101(3)
[7] V. Loiko et al. J. Quant. Spectrosc. Radiat. 2006

# Methodology:

- Blood (8 ml vial) [4]

- Absorbed dose coefficient per milliliter for 1 h internal ex vivo irradiation of blood ($\boldsymbol{d_{Blodd}(mGy \cdot ml \cdot MBq^{-1})}$)

$$d_{Blood,8ml}\left[\frac{mGy \cdot ml}{MBq}\right] = \frac{E_{Deposited}\left[\frac{J}{nt}\right] \cdot N(1h)\left[\frac{nt}{Bq}\right]}{Mass_{Blood}[kg]} \times 10^{9}\left[\frac{mGy}{Gy}\right]\left[\frac{Bq}{MBq}\right] \times 8[ml]$$



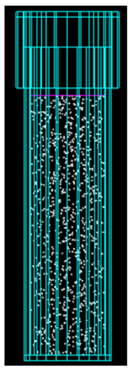
$N(1h)$: number of nuclear transformations occurring in 1 h of blood irradiation

# Methodology:

- Lymphocyte model
  - Absorbed dose coefficient to lymphocytes per milliliter of blood ($\boldsymbol{d_{Lymphocyte}(mGy \cdot ml \cdot MBq^{-1})}$) for 1 h of internal ex vivo irradiation of whole blood

$$\boldsymbol{d_{Lymphocyte,8ml}}\left[\frac{mGy \cdot ml}{MBq}\right] = \frac{E_{Deposited}\left[\frac{J}{nt}\right] \cdot N(1h)\left[\frac{nt}{Bq}\right]}{Mass_{Nucleus}[kg] \cdot 1000\ cells} \times 10^{9}\left[\frac{mGy}{Gy}\right]\left[\frac{Bq}{MBq}\right] \times 8[ml]$$

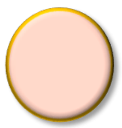
$N(1h)$: number of nuclear transformations occurring in 1 h of blood irradiation



- 1000 spheres of 3.75 $\mu$m radius (water material)
- 1000 phase spaces

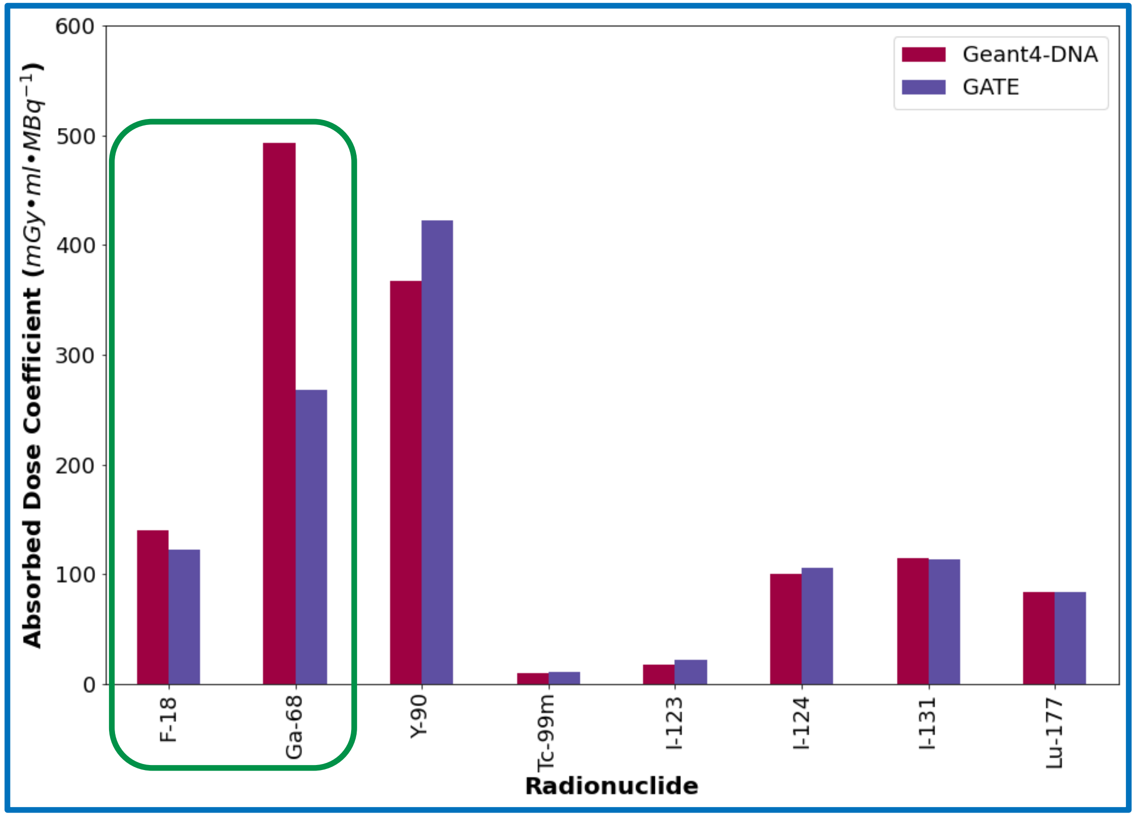
The 1000 phase spaces were translated to the position (0,0,0) and summed in one single phase space

Python code[5]



# Results

- Evaluation of the Lymphocyte model – Beta and Gamma emitters

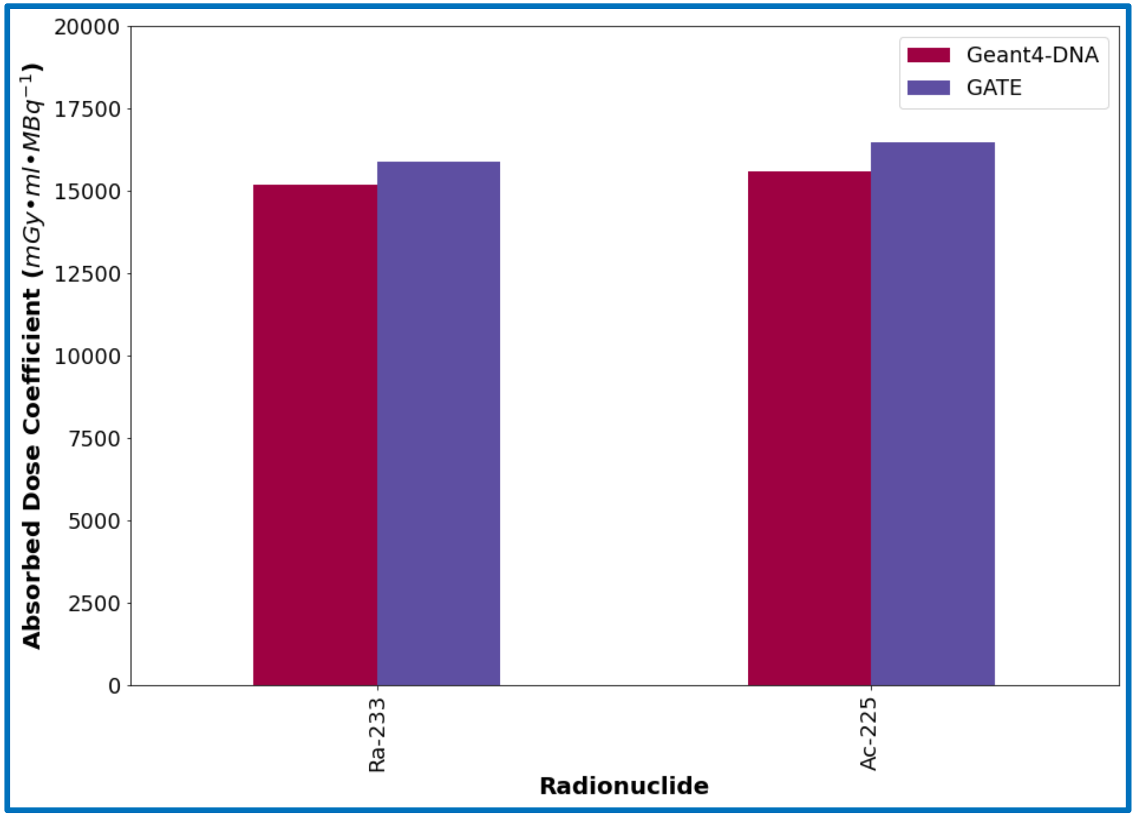



- $^{68}$Ga and $^{18}$F presented the largest errors
  - Geant4-DNA does not have specific processes to simulate positron at low energies.
- For all others the relative error stay below -13%
- Physics :
  - $^{18}$F, $^{90}$Y, $^{131}$I, and $^{177}$Lu: DNAOpt4 + Activator
  - $^{68}$Ga and $^{124}$I: DNAOpt6 + Activator
  - $^{99m}$Tc: DNAOpt6
  - $^{123}$I: DNAOpt2 + Activator

G4EmDNAPhysicsActivator = Activator

# Results

- Evaluation of the Lymphocyte model – Alpha emitters



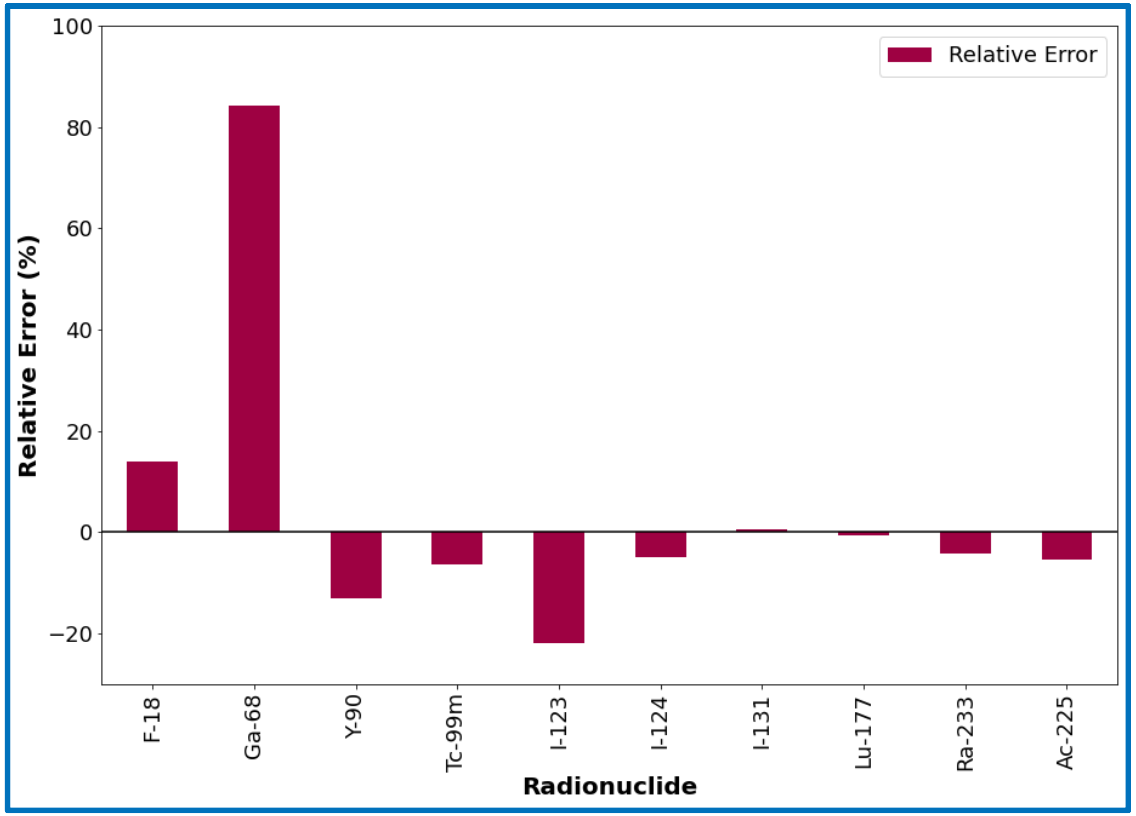

- $^{223}$Ra and $^{225}$Ac presented a good agreement. The relative error stay below -6%

- Physics:
  - DNAOpt2 + Activator

G4EmDNAPhysicsActivator = Activator

# Results

- Relative error between macroscopic and microscopic simulation




- Negative relative errors are expected → **Cell nucleus does not have self-irradiation**

- Further evaluation are required to simulate the **$^{68}$Ga and $^{18}$F sources**

# Conclusions

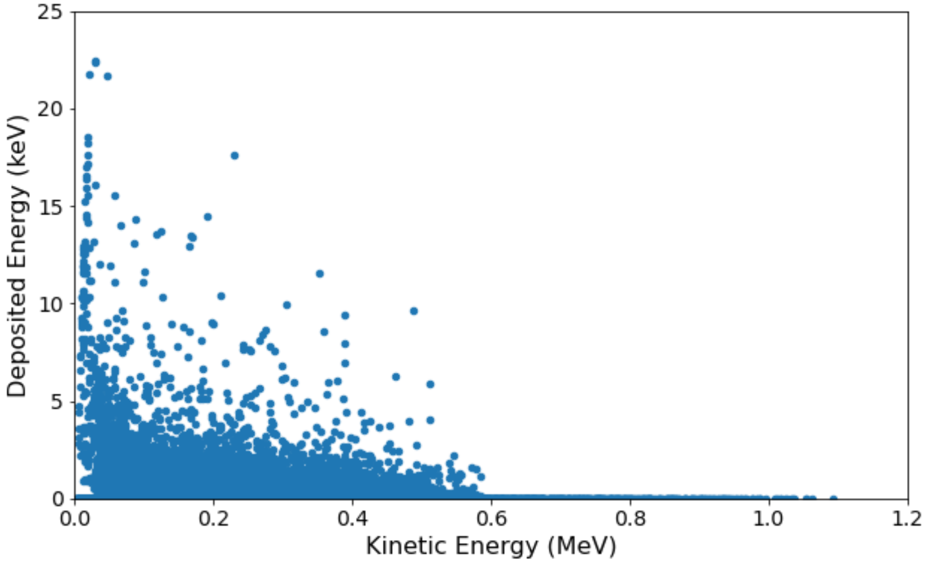
- Except for positron emitters, the lymphocyte model adequately reproduces the whole blood absorbed dose coefficients ($\boldsymbol{d_{Blood}}(\boldsymbol{mGy \cdot ml \cdot MBq^{-1}})$)

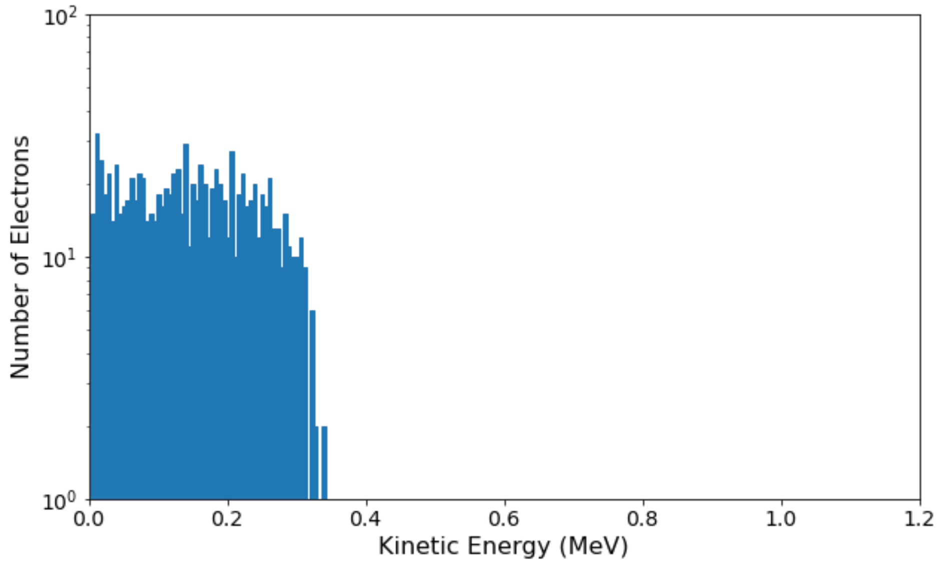
- The lymphocyte model provides a large statistics (1000 cells) and sampled the vial in the center and periphery (different irradiation conditions)

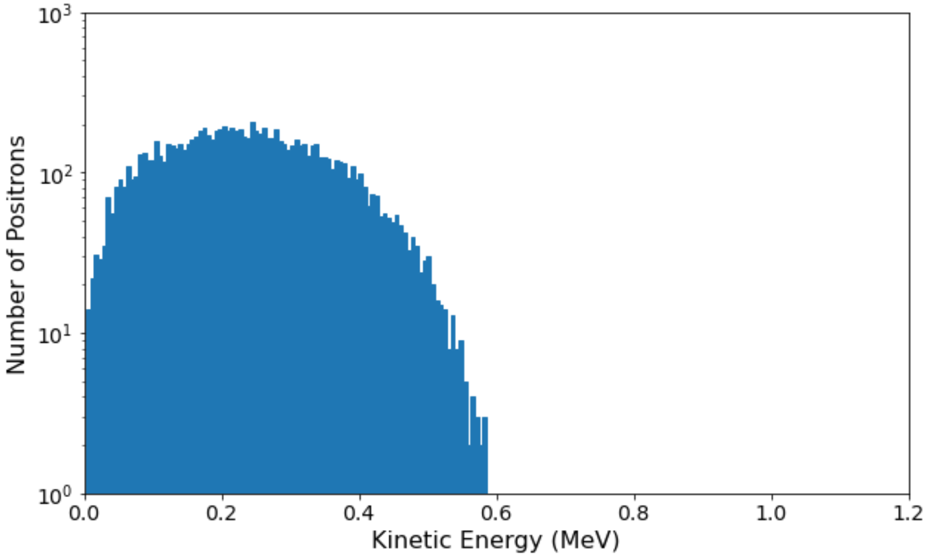
- This study proposes a radiation transport model for further studies on DNA damage (DSB quantification) using Geant4-DNA

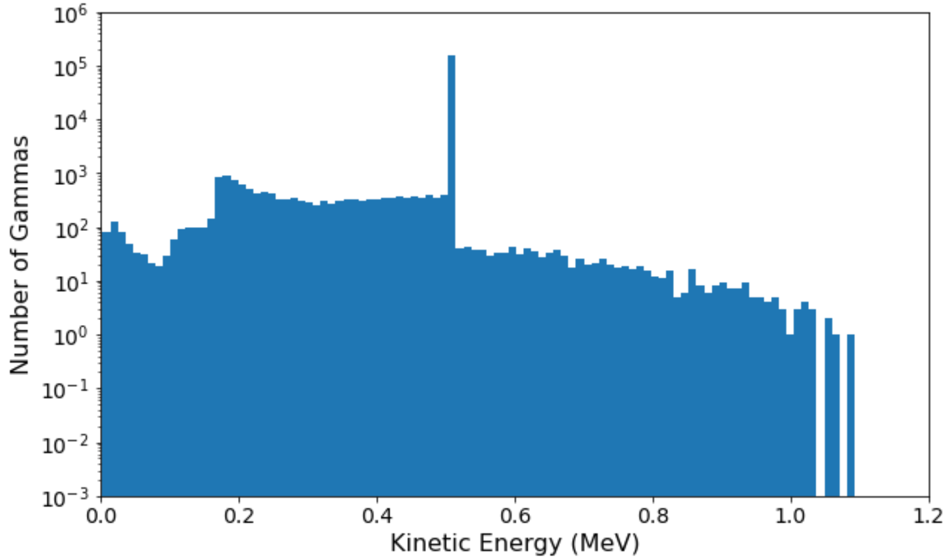
Thank you very much for your attention!

# F-18 (DNAOpt4 + Activator)

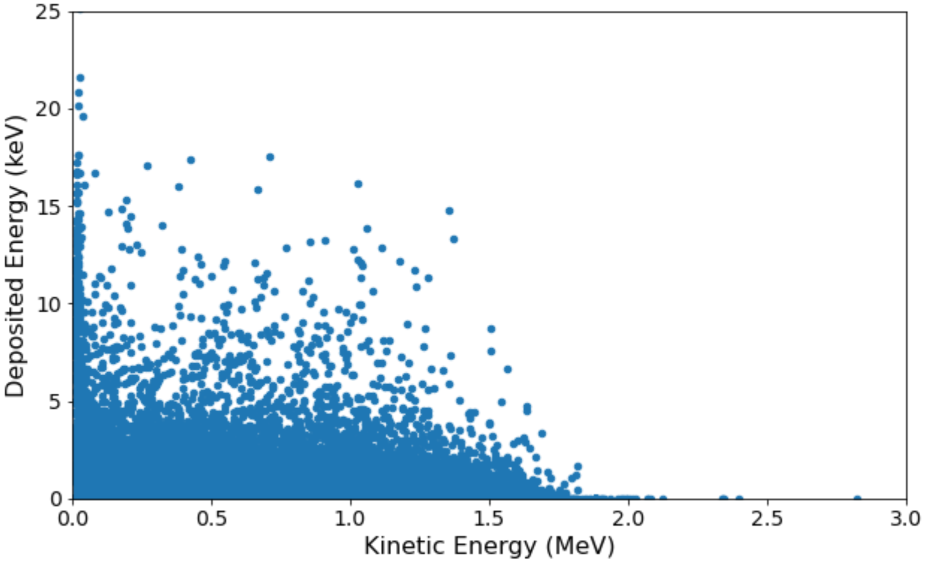


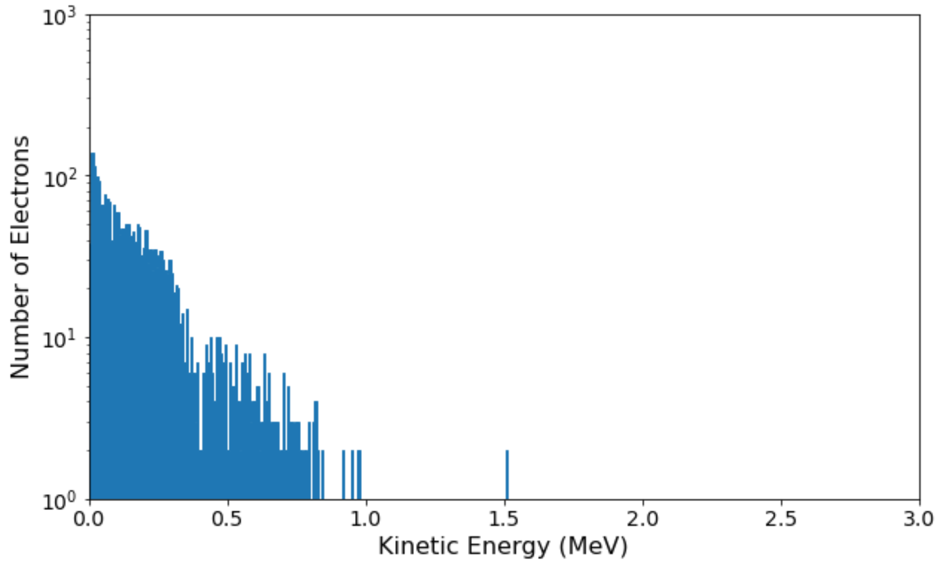



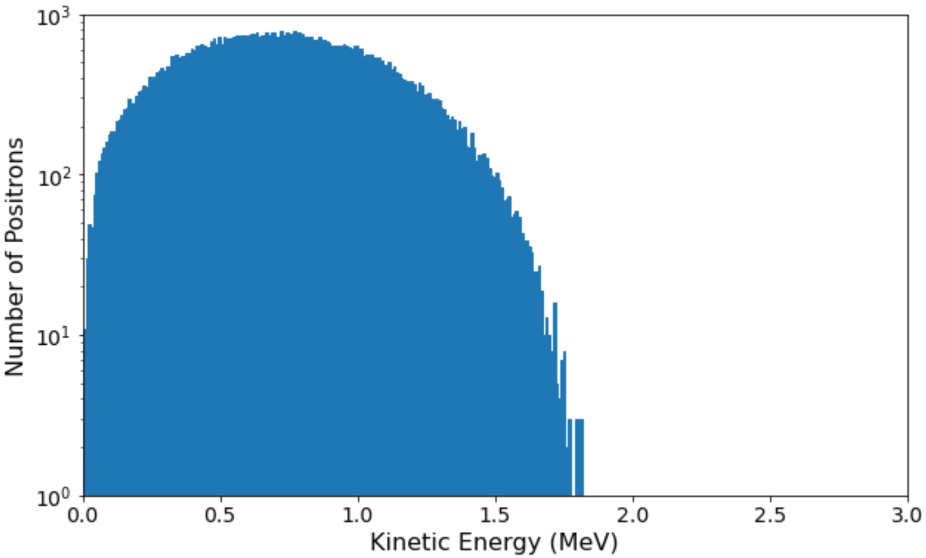



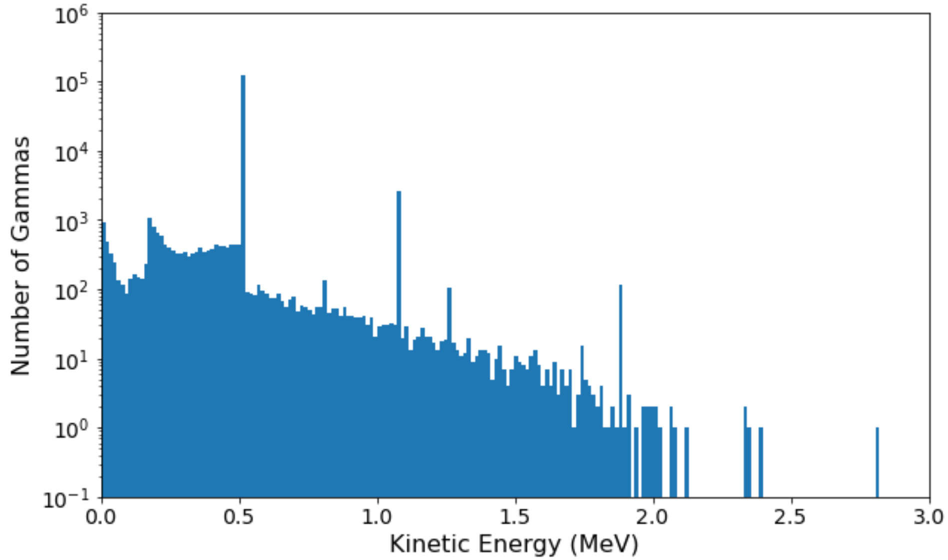



# Ga-68 (DNAOpt6 + Activator)

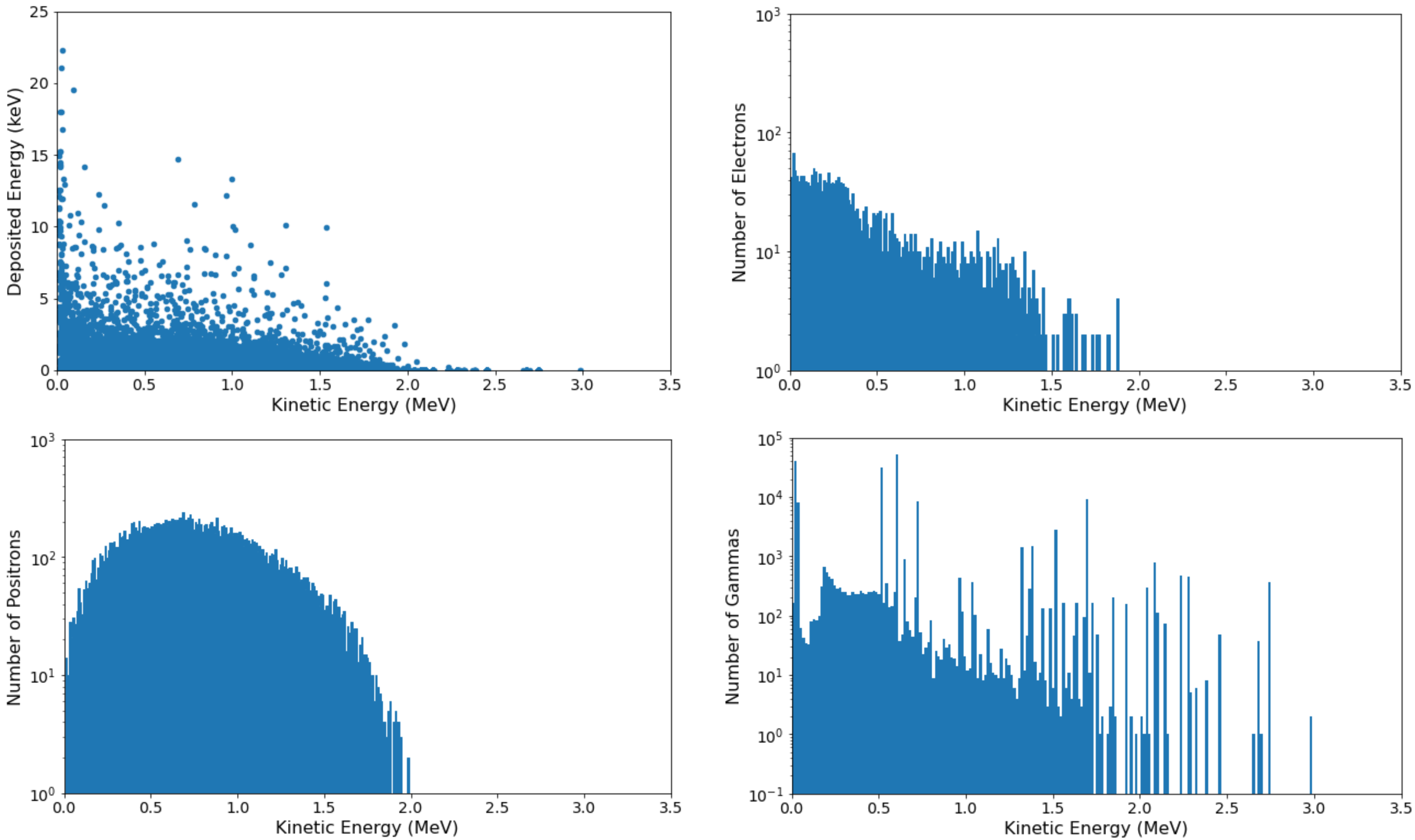


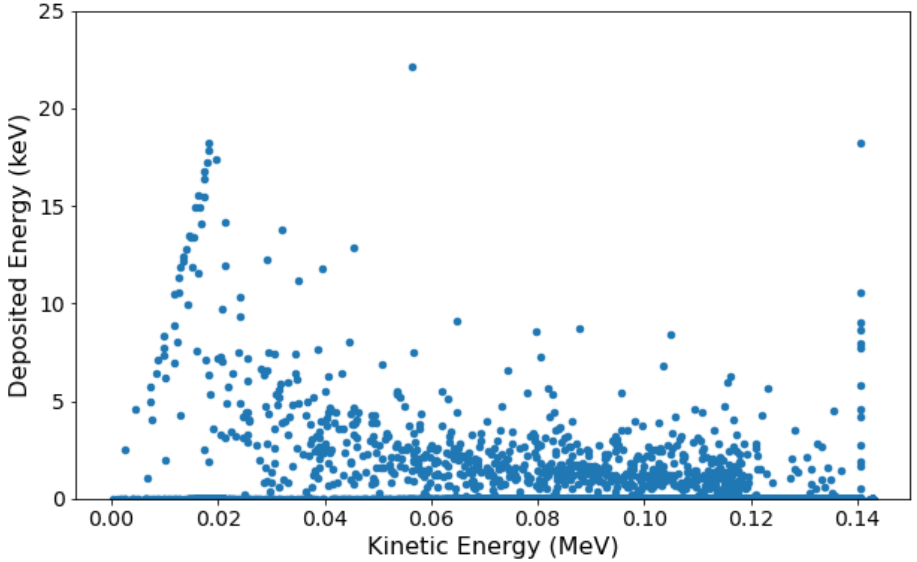



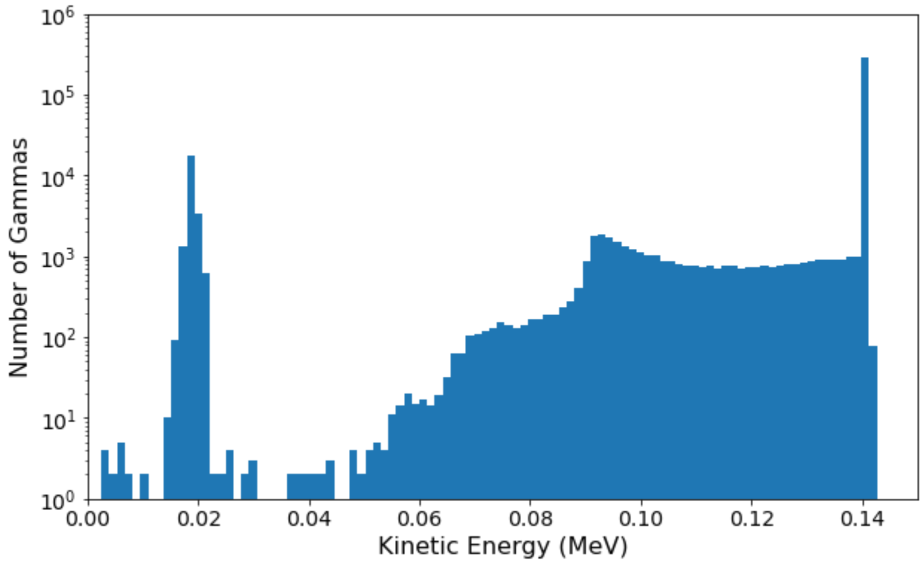



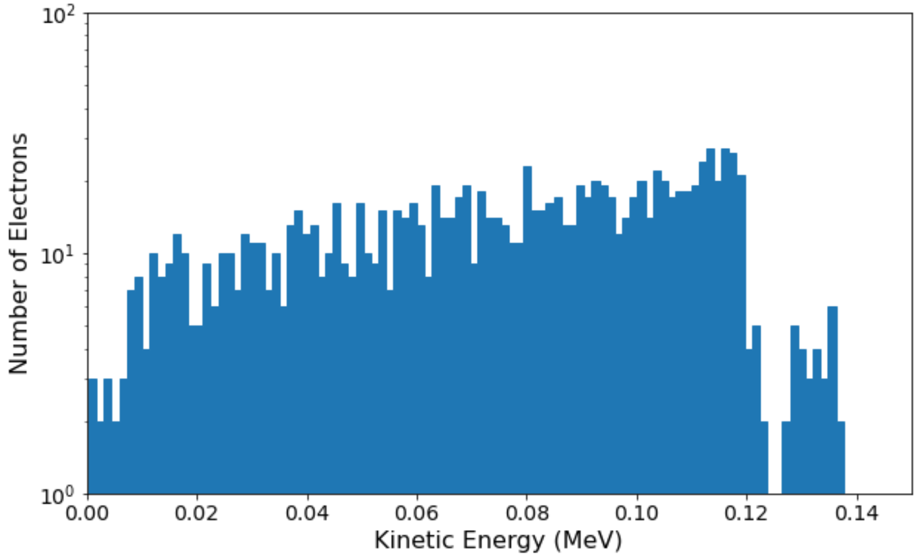
# I-124 (DNAOpt6 + Activator)



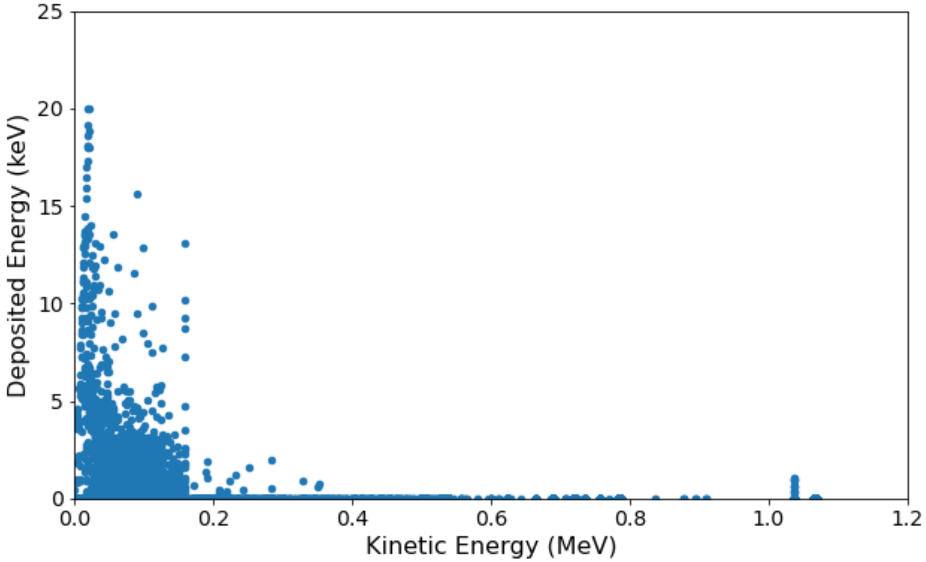
# Tc-99m (DNAOpt6)

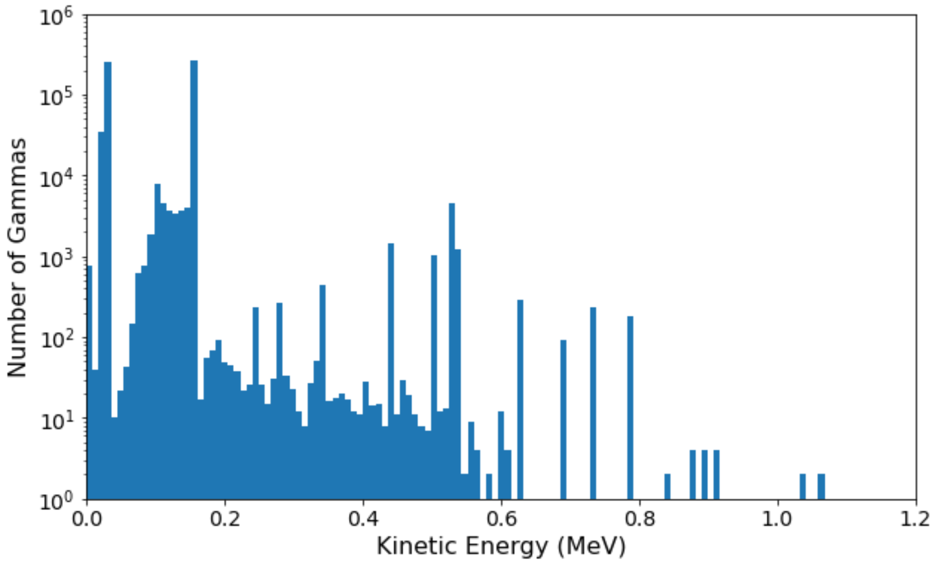


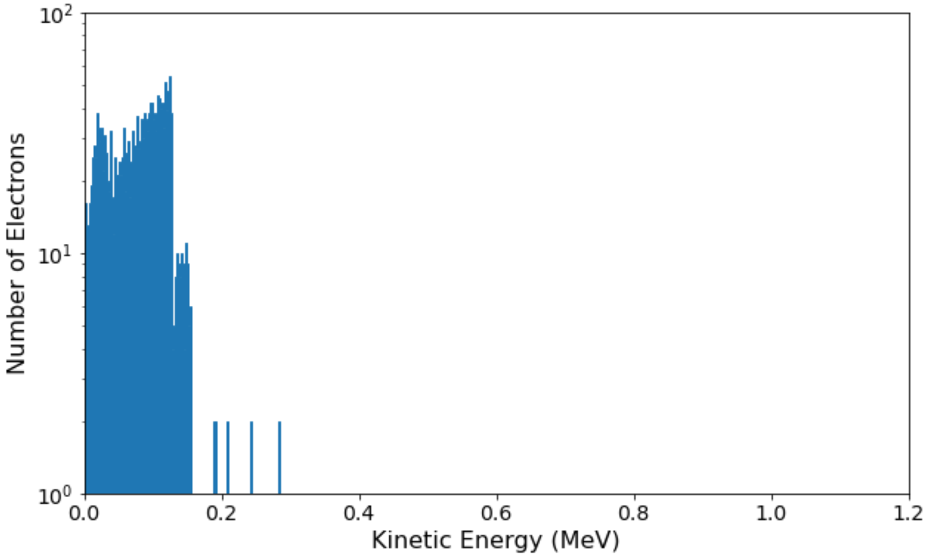



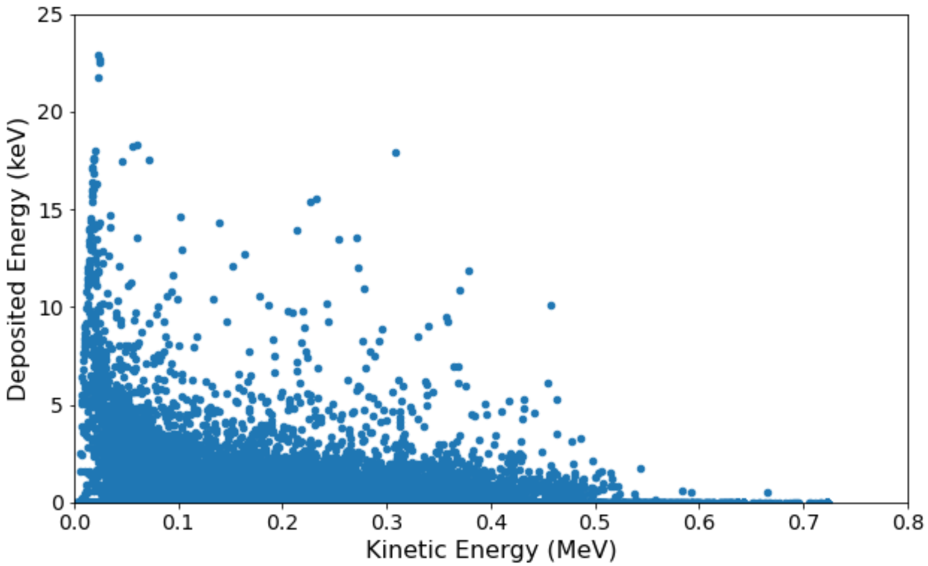
# I-123 (DNAOpt2 + Activator)

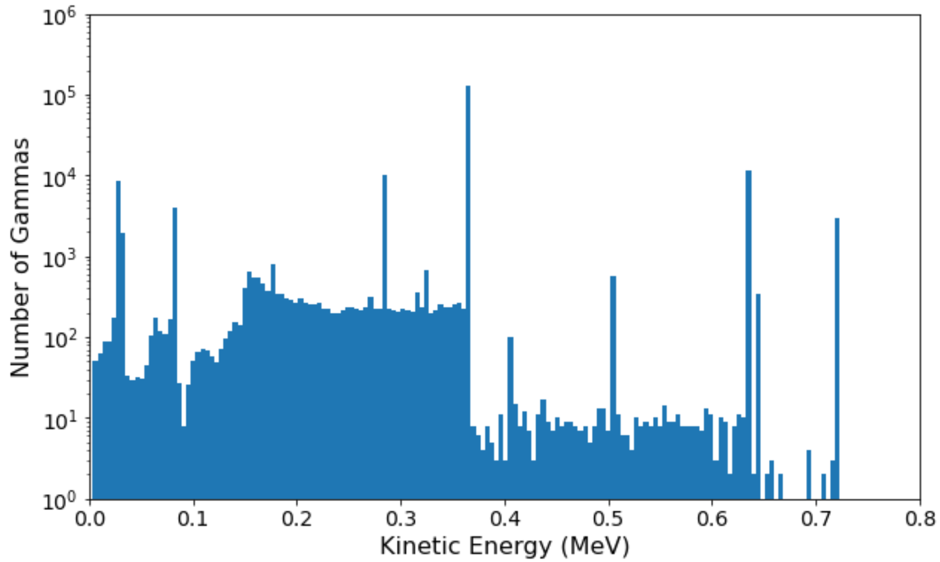


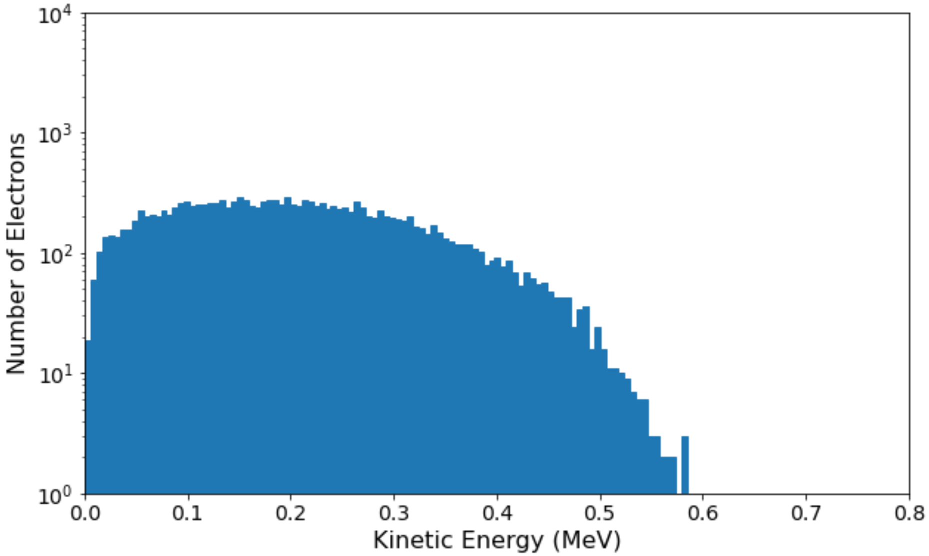



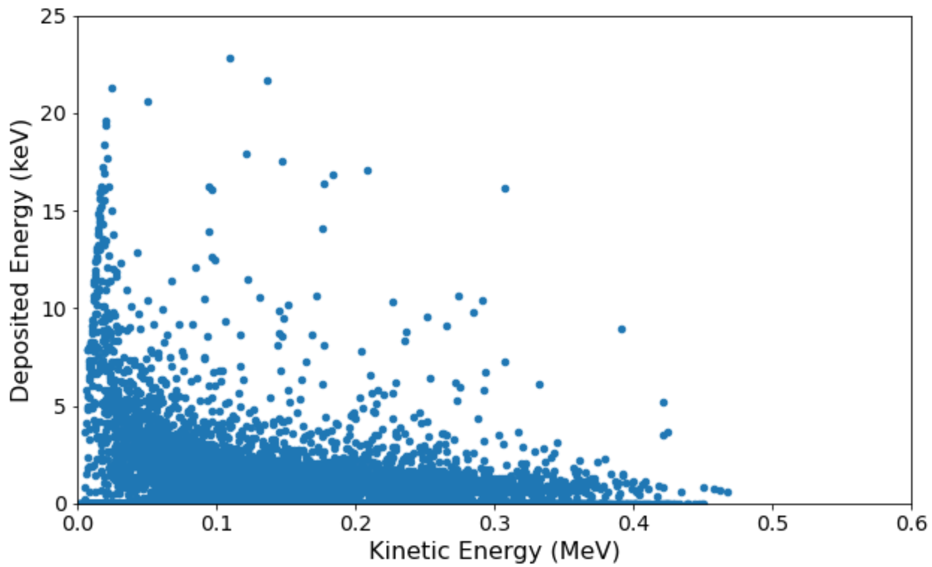
# I-131 (DNAOpt4 + Activator)

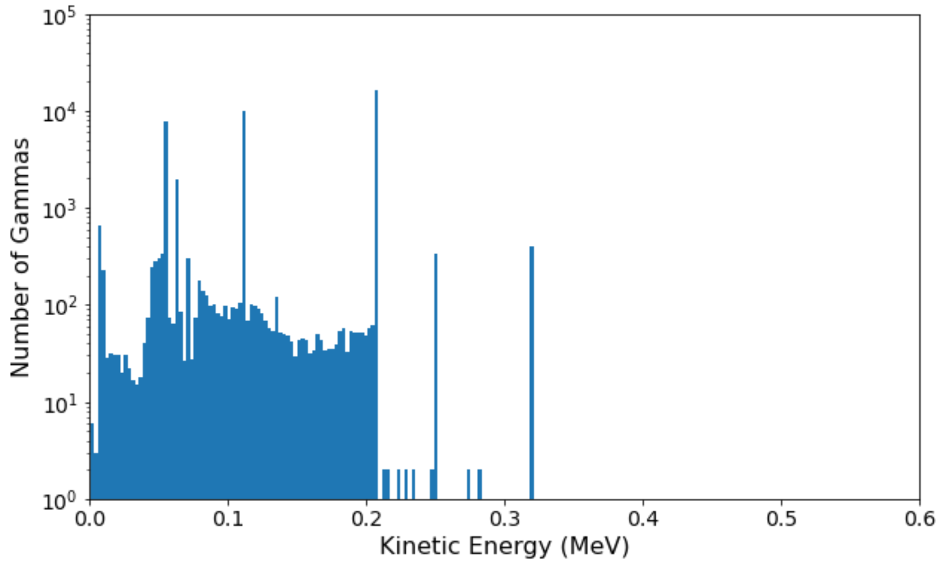


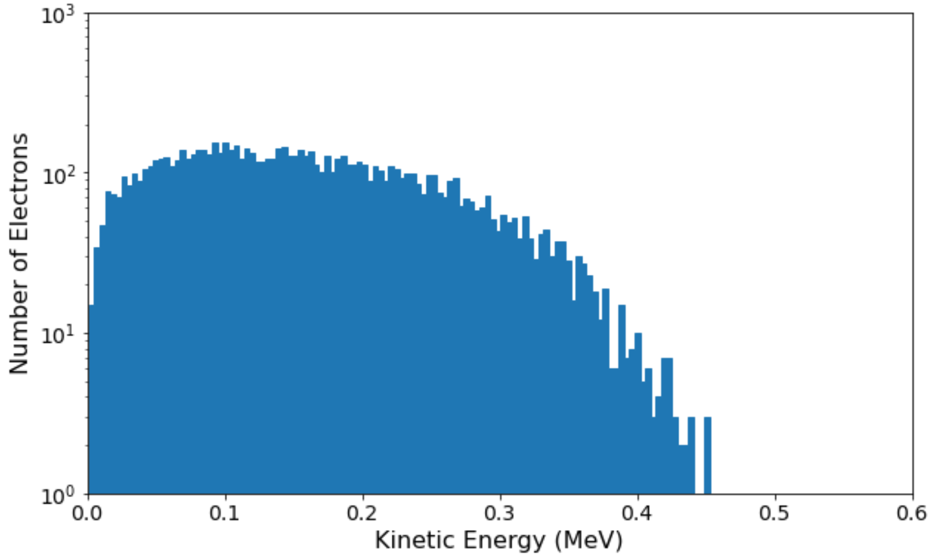



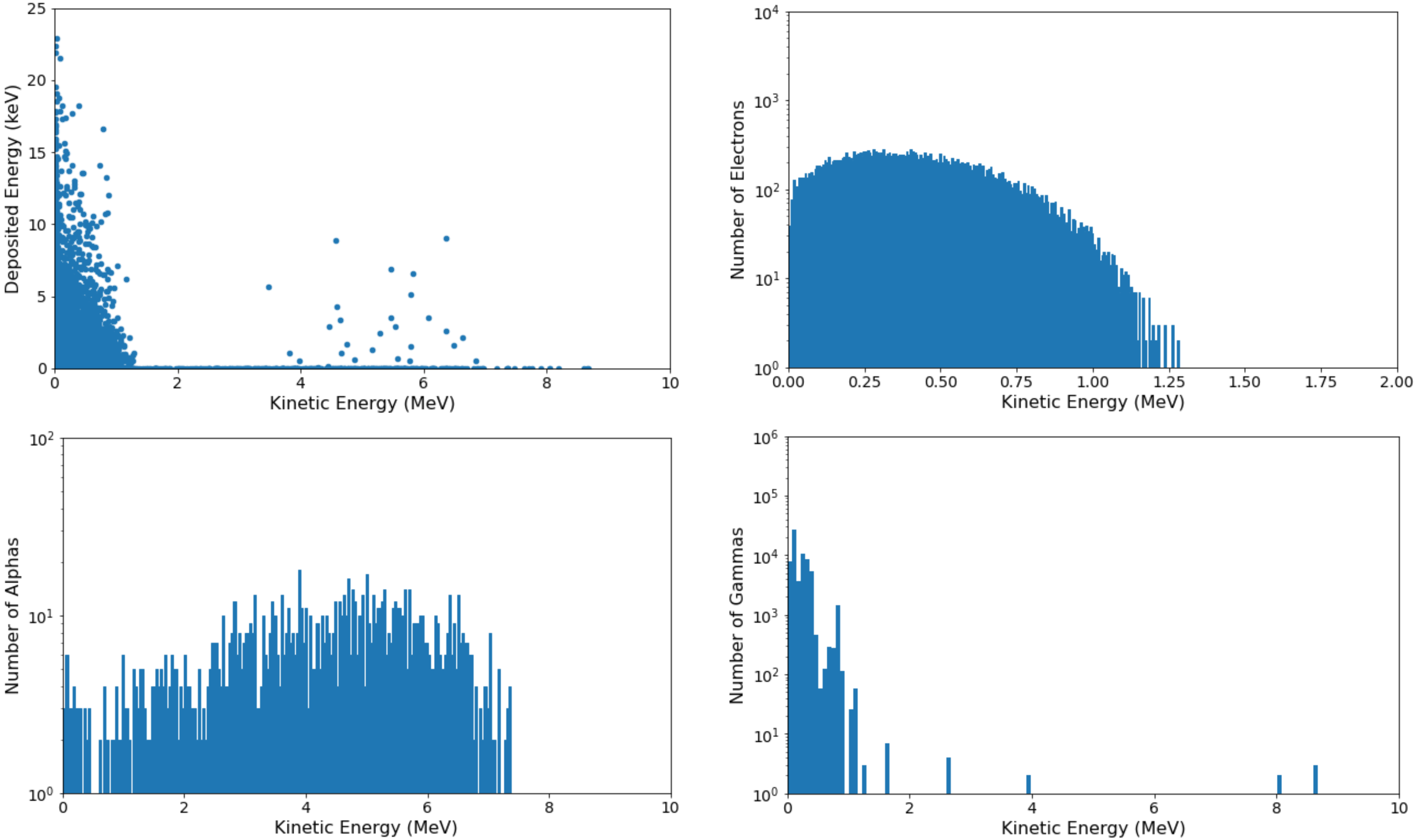
# Lu-177 (DNAOpt4 + Activator)



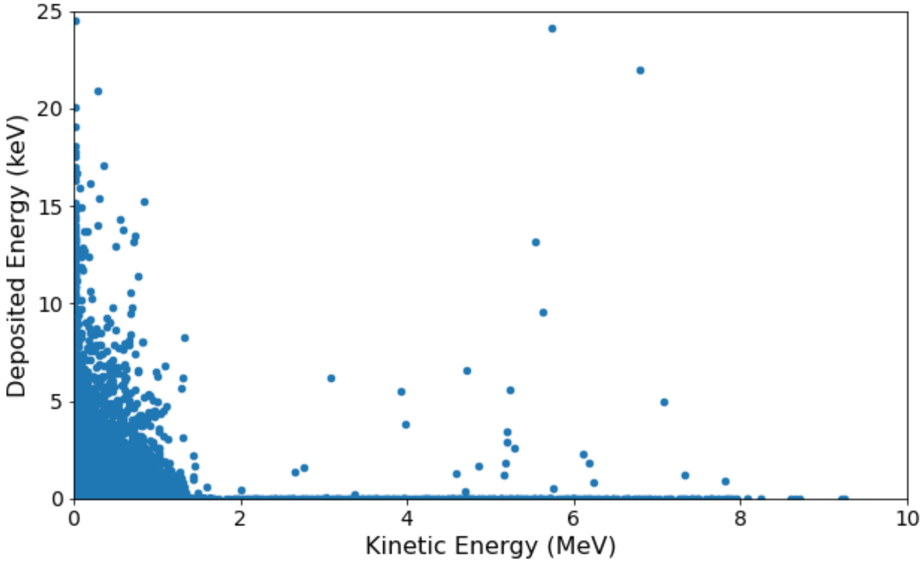



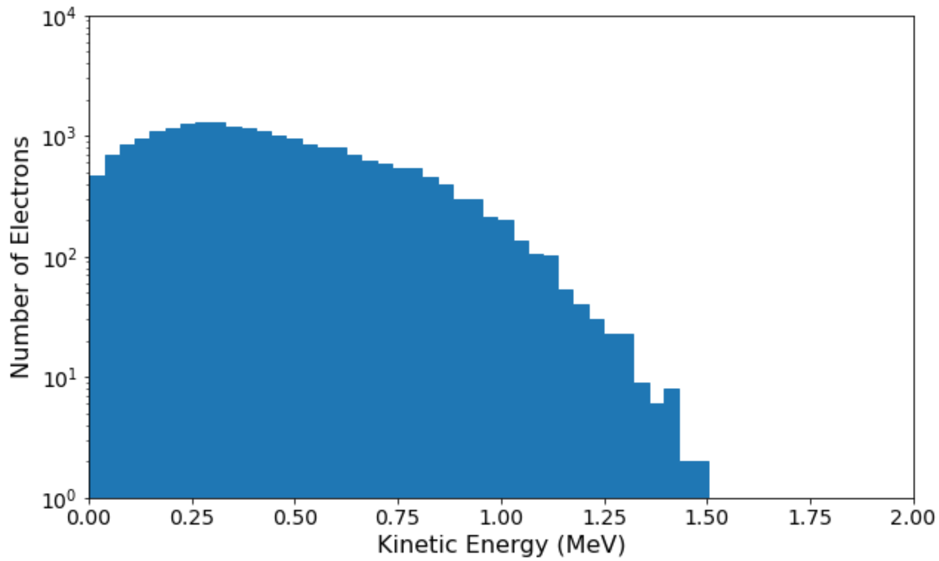



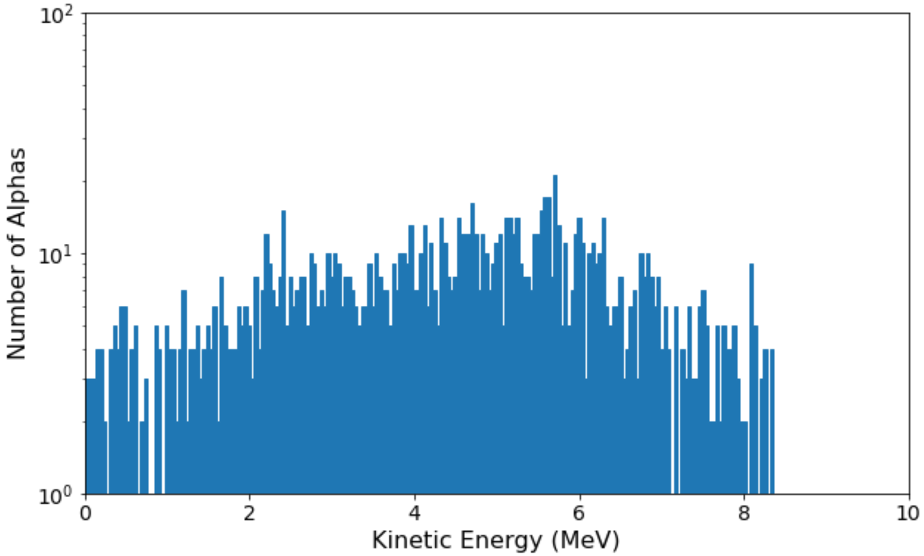
# Ra-223 (DNAOpt2 + Activator)

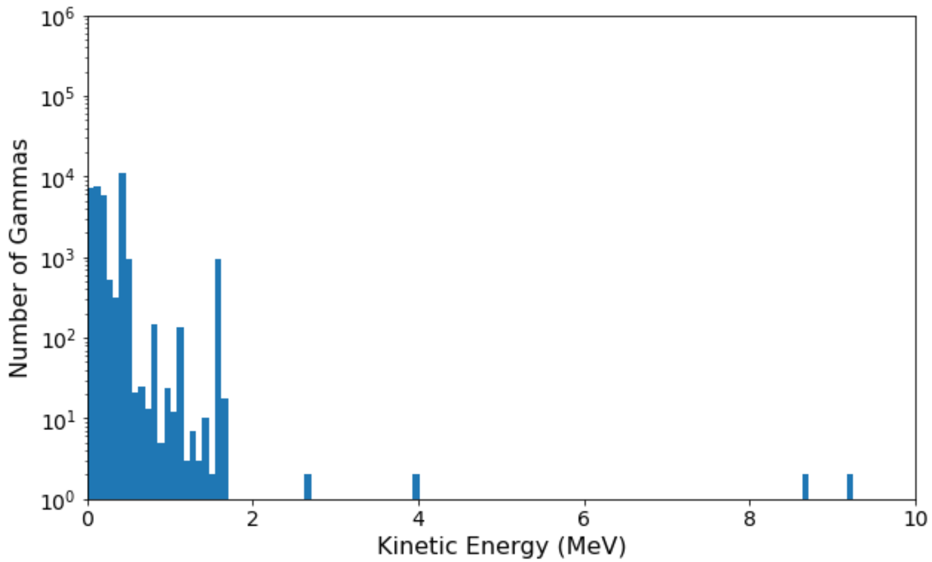


# Ac-225 (DNAOpt2 + Activator)



# Y-90 (DNAOpt4 + Activator)