How can GATE Simulation Unravel the Mysteries of the FLASH Effect in Ultra-High Dose Rate Radiotherapy?

1 April 2026, GATE scientific meeting, IPHC Strasbourg

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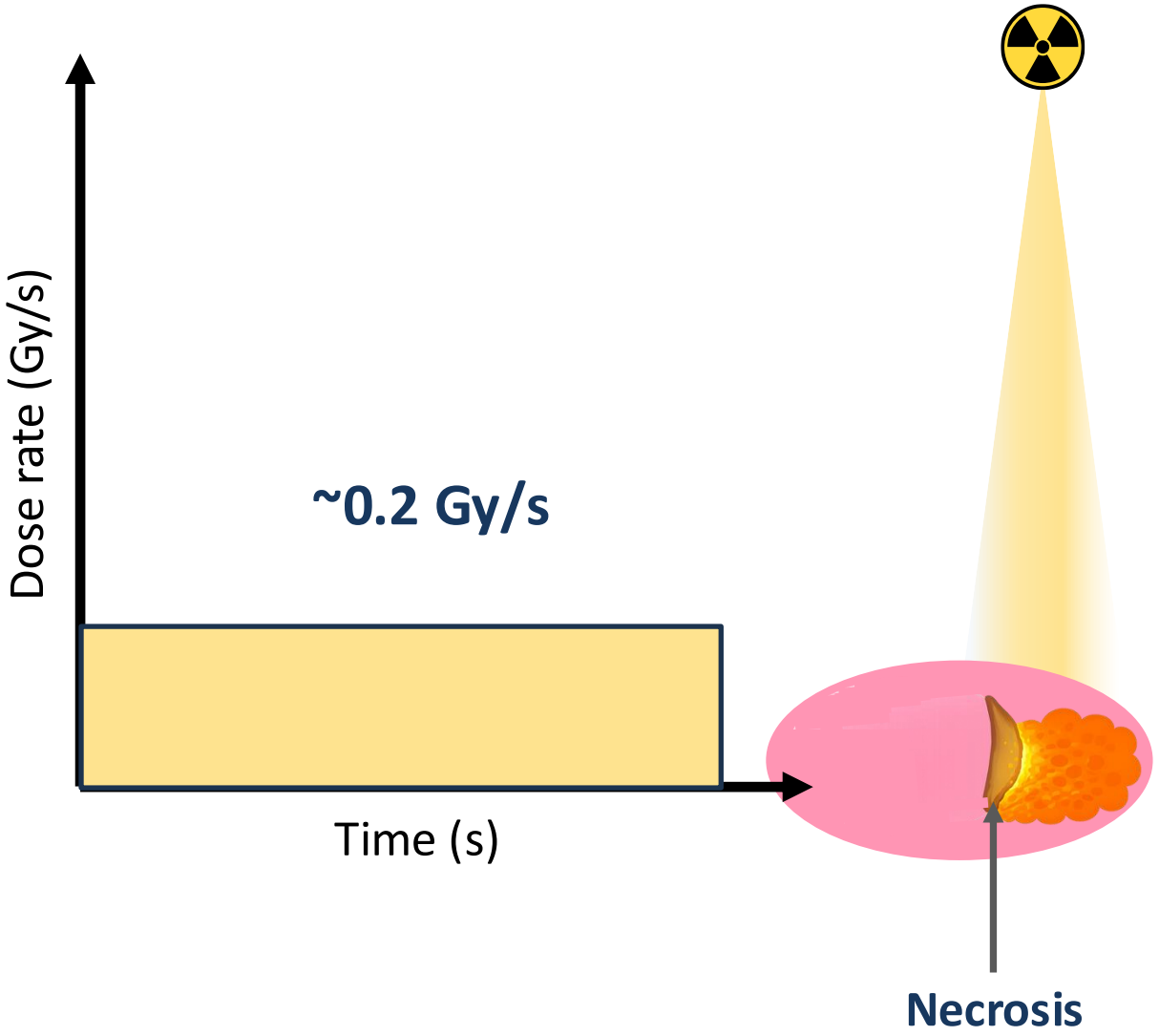
What is FLASH Radiotherapy ?

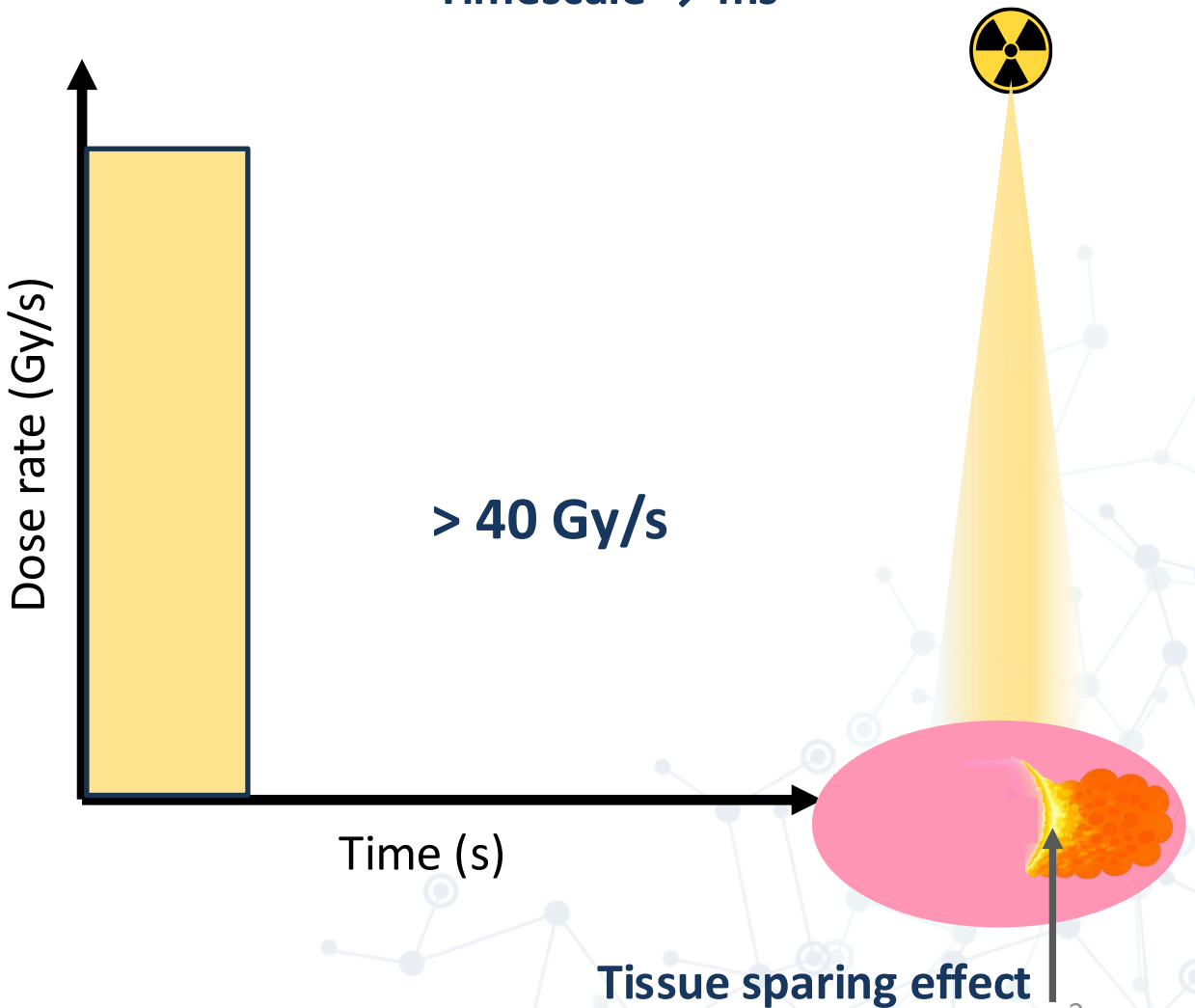
Conventional (Lower intensity of beam)

Timescale → min



FLASH (Higher intensity of beam)

Timescale → ms



Accelerator system for FLASH irradiation

Arronax Nantes

IBA Cyclotrone70
for H^+, He^{2+}, D^+

Sumitomo Heavy Industries, Ltd.

PROBEAT-RT for H^+

institut Curie

FRATHEA for e^-

CHUV

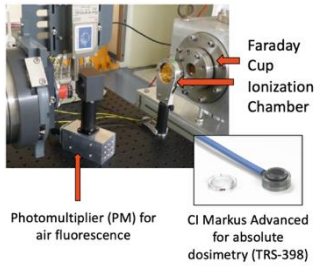
Oriatron 6e for e^-

A multidisciplinary project

Arronax Nantes

Subatech

^{12}C (95 MeV) [0,01 Gy/s – 100 Gy/s]

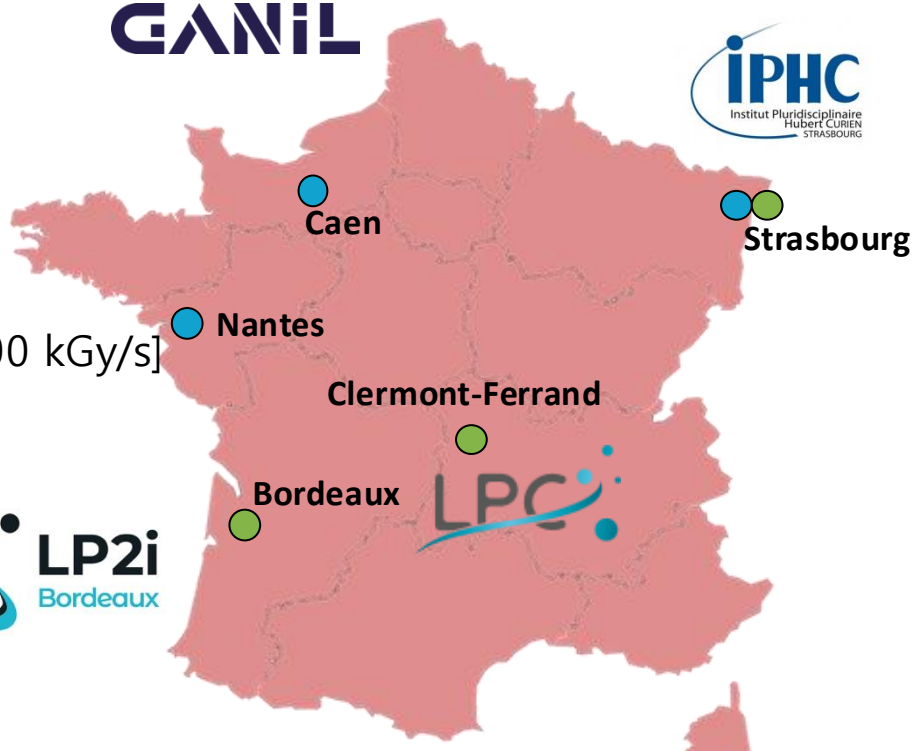


GANIL

H^+ (68 MeV), He^{2+} (70 MeV) [0,1 Gy/s – 300 kGy/s]

Institut de Cancérologie de l'Ouest

unicancer PAYS DE LA LOIRE



IPHC Institut Pluridisciplinaire Hubert CURIEN STRASBOURG

LP2i Bordeaux

H^+ (16–25 MeV) [0,1 Gy/s – 300 Gy/s]

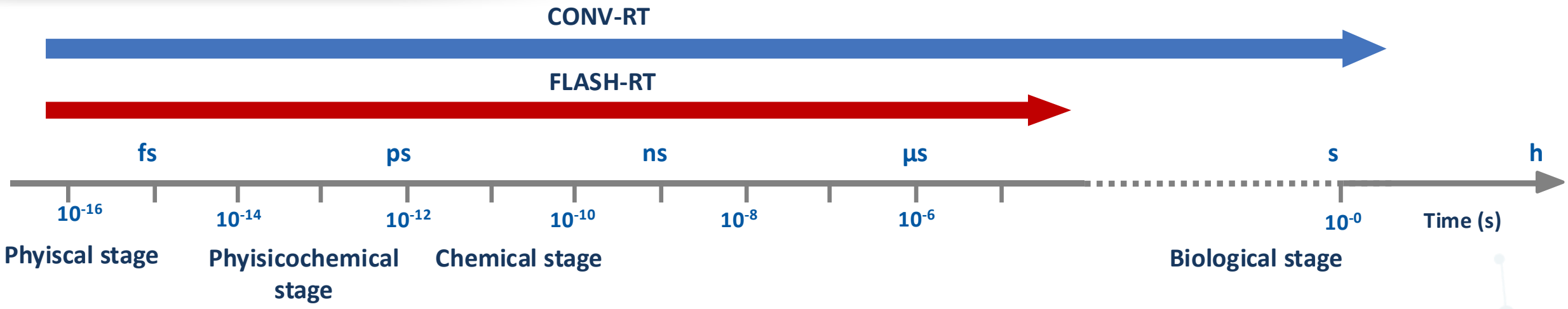
CYRCé

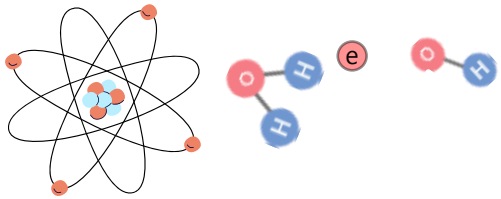
DB gathering GATE digital twins of the beam lines

Experiment + **Simulation**

Mechanistic understanding of the FLASH effect

Water radiolysis





H_2O

H_2O^* Excitation → $^{\bullet}OH + H^{\bullet}$; $H_2O + \Delta E$

$H_2O^+ + e^-$ Ionization → $H_2 + {}^{\bullet}OH + {}^{\bullet}OH$; $^{\bullet}OH + H_3O^+$; e^-_{aq}

e^-_{aq}, $H^{\bullet}$, H_2, $^{\bullet}OH$, OH^-, H_3O^+, H_2, H_2O_2

H_2O_2 as sense of $^{\bullet}OH$

Oxygen depletion

$e^-_{aq} + O_2 \rightarrow O_2^{\bullet-}$

$H^{\bullet} + O_2 \rightarrow HO_2^{\bullet}$

ROS scavenging

$RH + {}^{\bullet}OH \rightarrow R^{\bullet} + H_2O$

Radical recombination

$^{\bullet}OH + {}^{\bullet}OH \rightarrow H_2O_2$

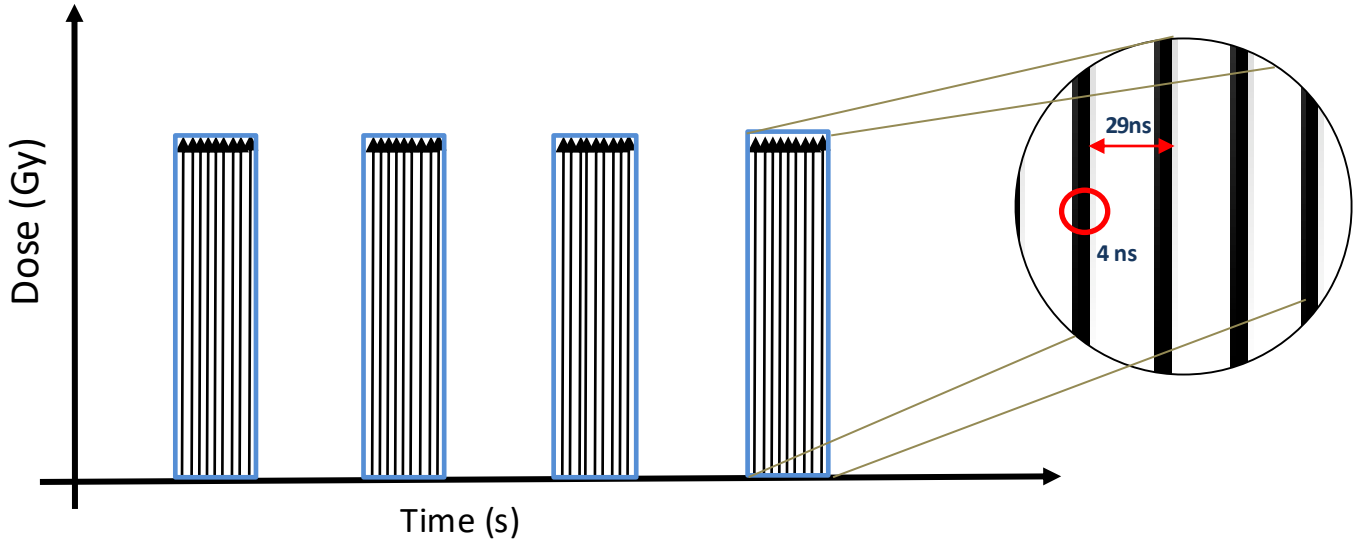
$H^{\bullet} + H^{\bullet} \rightarrow H_2$

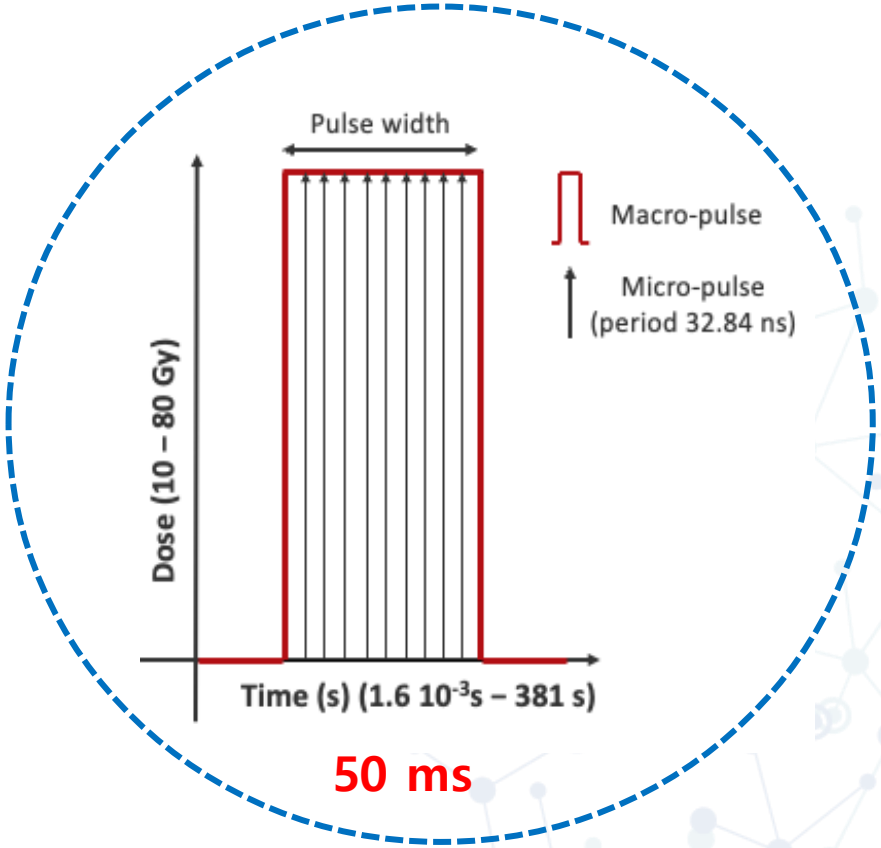
Fenton reaction

$Fe^{2+} + H_2O_2 \rightarrow {}^{\bullet}OH + OH + Fe^{3+}$

Beam Production @ ARRONAX

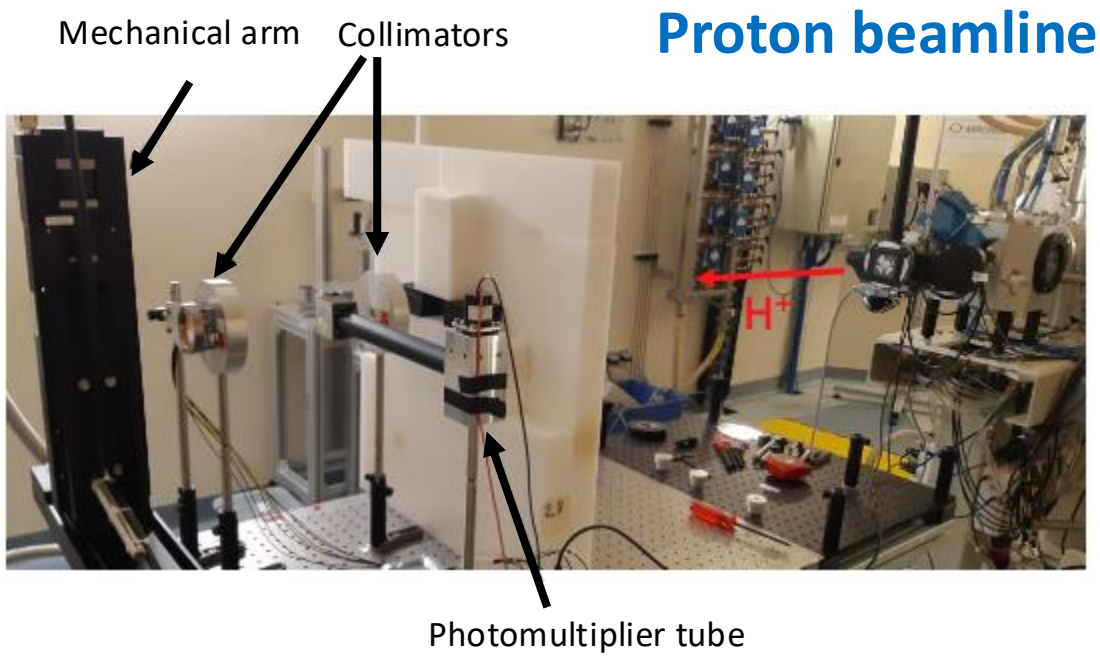
The time pulse structure



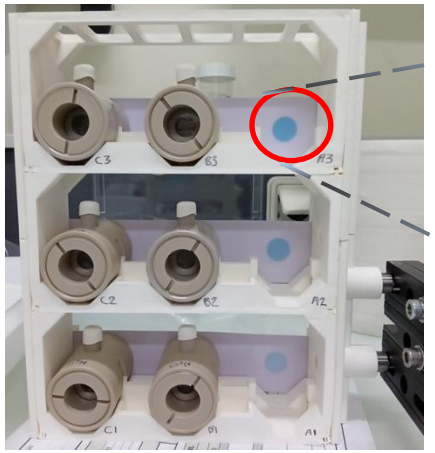


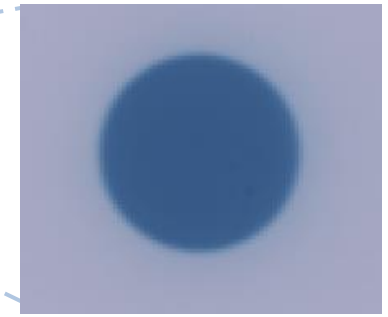
Measurement of Hydrogen Peroxide

Proton beamline



3D-printed cellholder





Film Orthochromic OC-1 (Confirmation dose)

Beamline production

67.5 MeV proton beam

Intensity: 1 pA ~ 350 µA

Dose rate: 0.2 ~6000 Gy/s

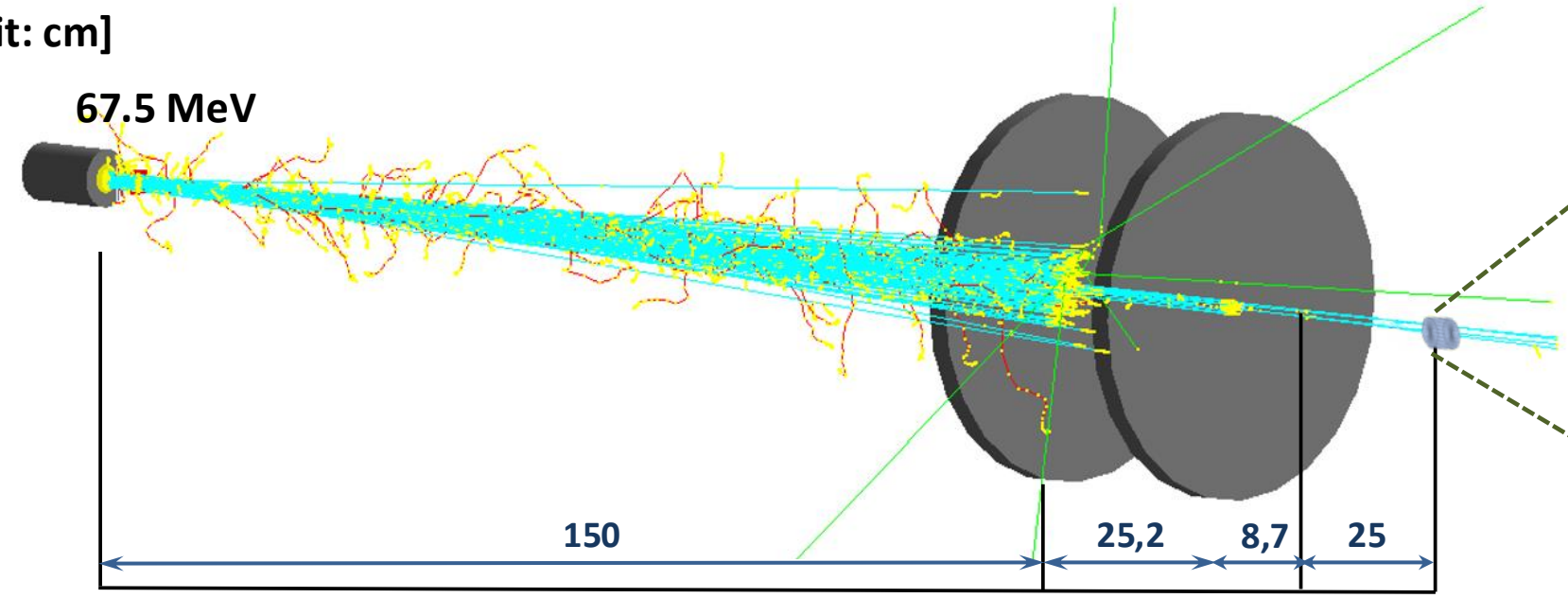
Parameters in measurement

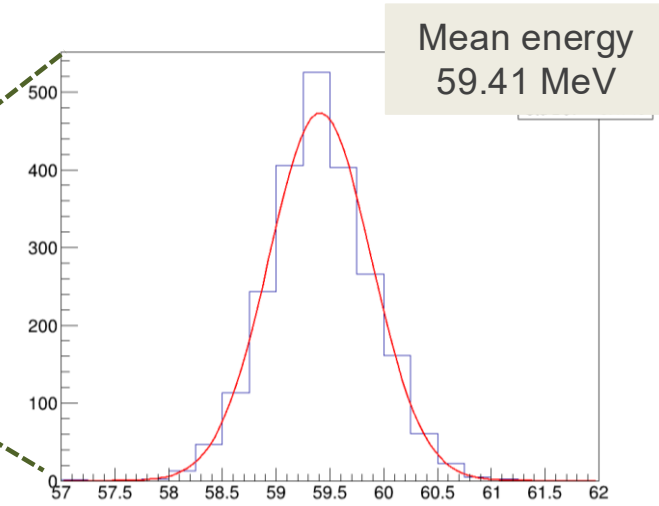
O_2 levels: Air (1%±0.6% and 21%)

pH : 5.5±0.3 (pure water condition)

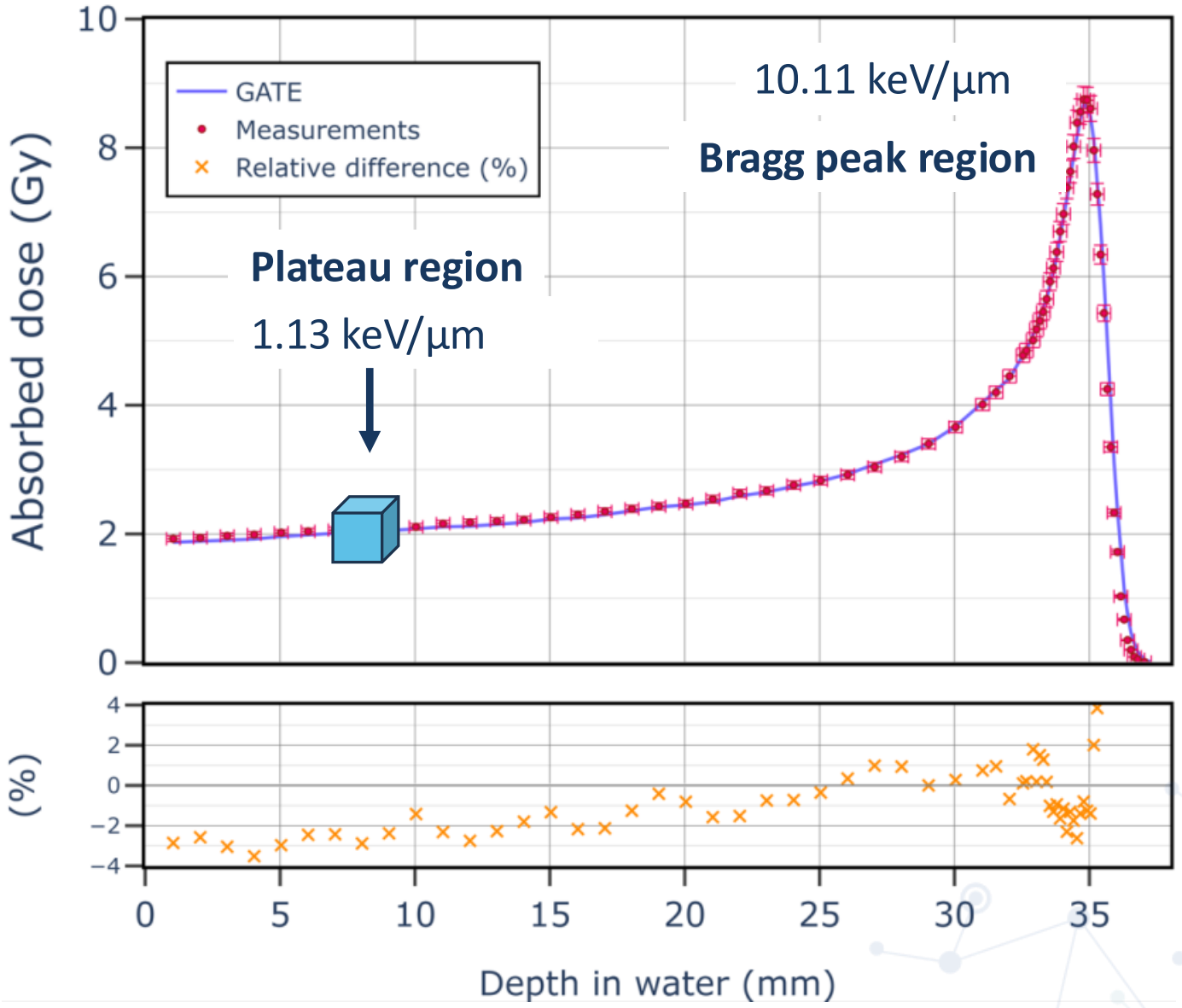
A macro – level digital twin of ARRONAX proton beamline

[unit: cm]



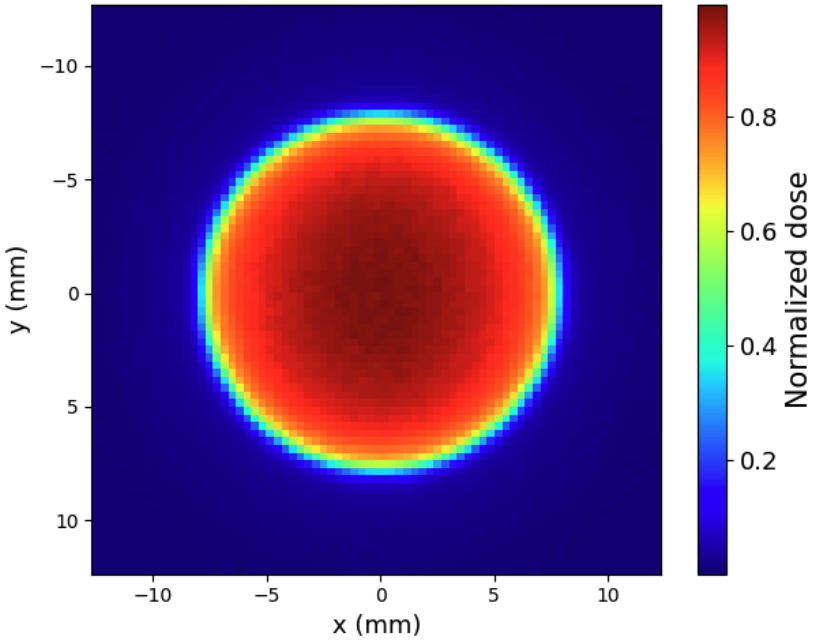


ARRONAX Proton beamlines using GATE 10

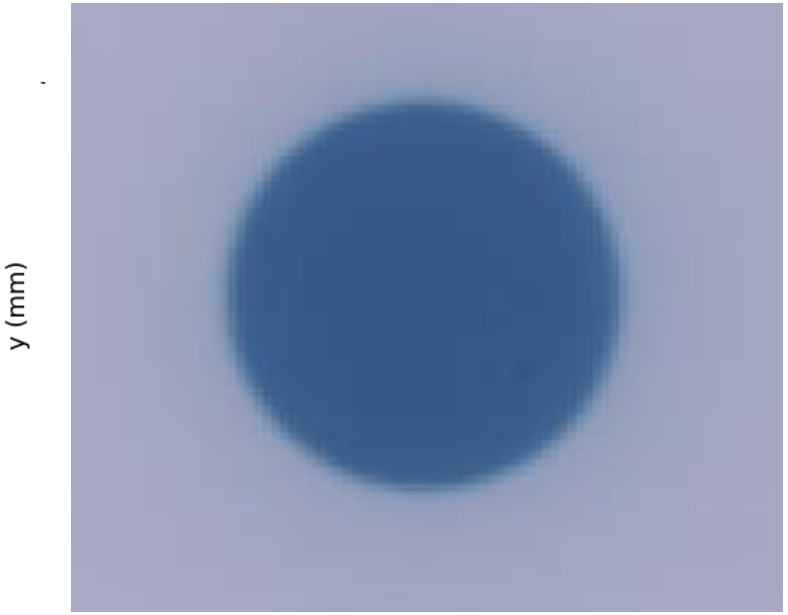


Film dosimetry validation: simulation vs Experiment

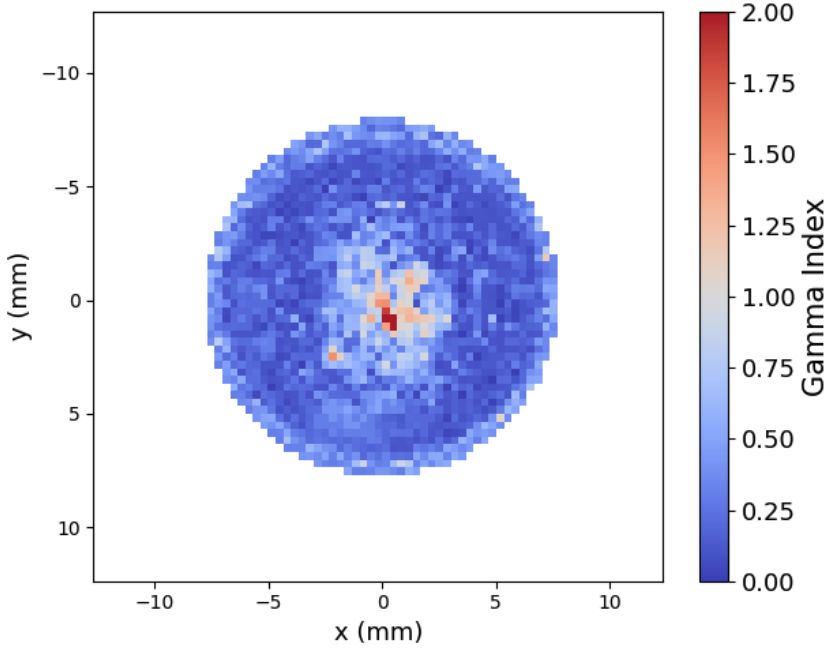
Simulated film



Film measurement



Comparision (97.43%)



Film resolution: 75 x 75

Pixel size (mm): 0.34 x 0.34

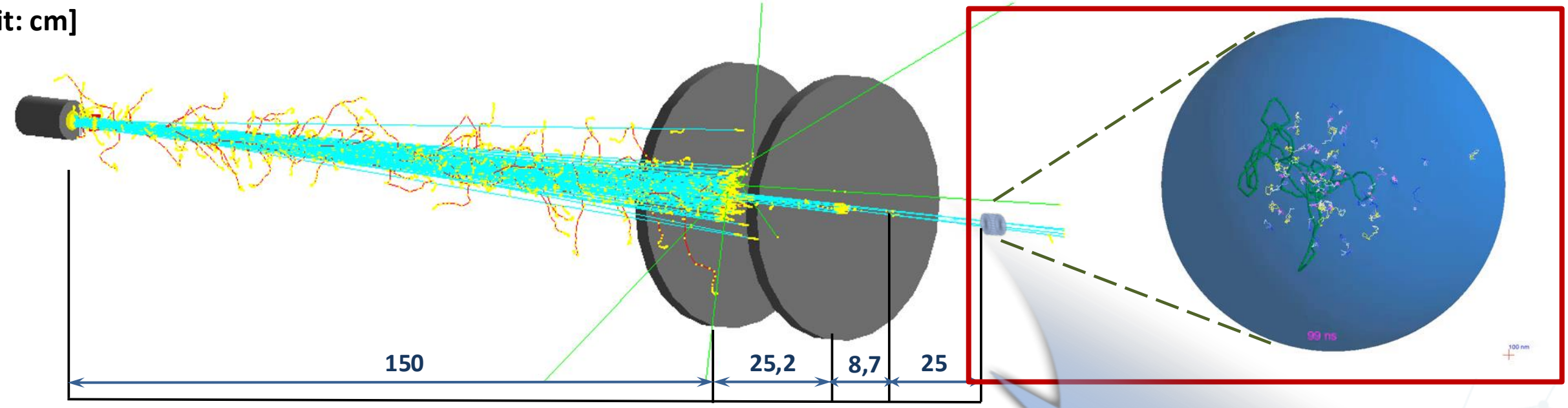
Gamma-index analysis

Dose/distance: 2%/2mm

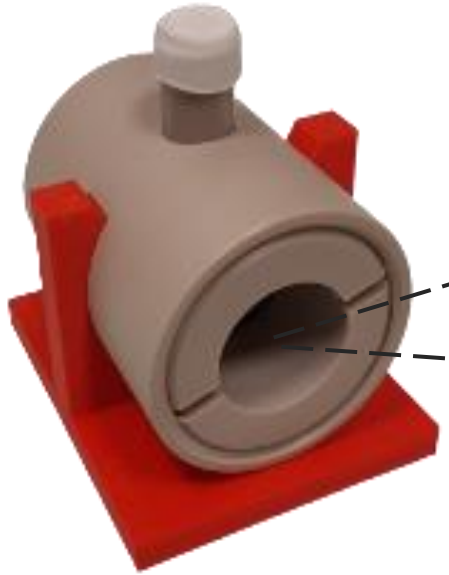
Dose threshold: 10%

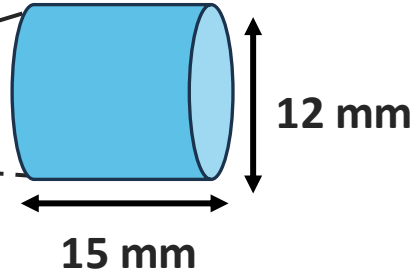
A micro – level digital twin of water radiolysis

[unit: cm]

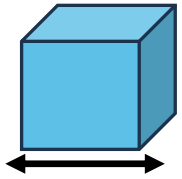


GEANT4-DNA
A SIMULATION TOOLKIT





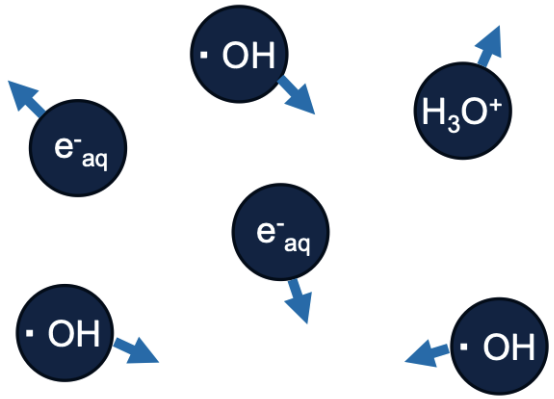
Experimental radiolysis cell



Simulation

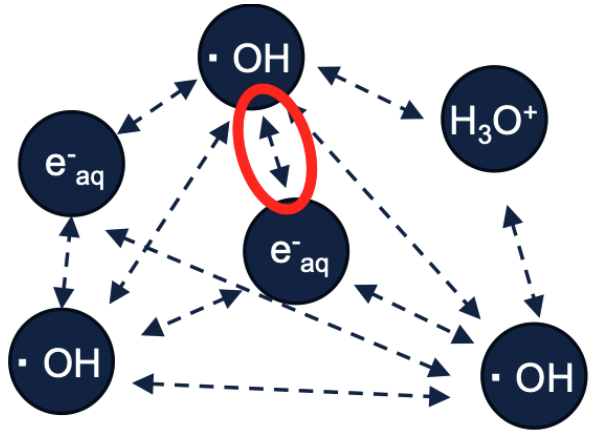
Geant4-DNA: Chemical stage

SBS (Step by step)

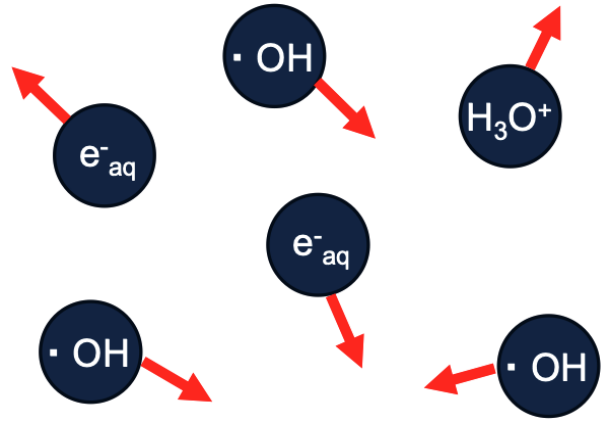


- Diffuse molecules with fixed T-step (time step)
- Time step must be always short enough

IRT (Independent Reaction time)



- Calculate the shortest T-step



- Diffuse with the shortest T-step

Digital twins in micro-scale simulation

Parameters in simulation

- G4 EmDNAPhysics_option2
- G4 EmDNAChemistry_option3
- Oxygen levels: 0.04% and 21%
- CO_2 contents: 0.042 %
- pH level: 5.5 ± 0.3 (pure water condition)
- Single pulse: 50 ms

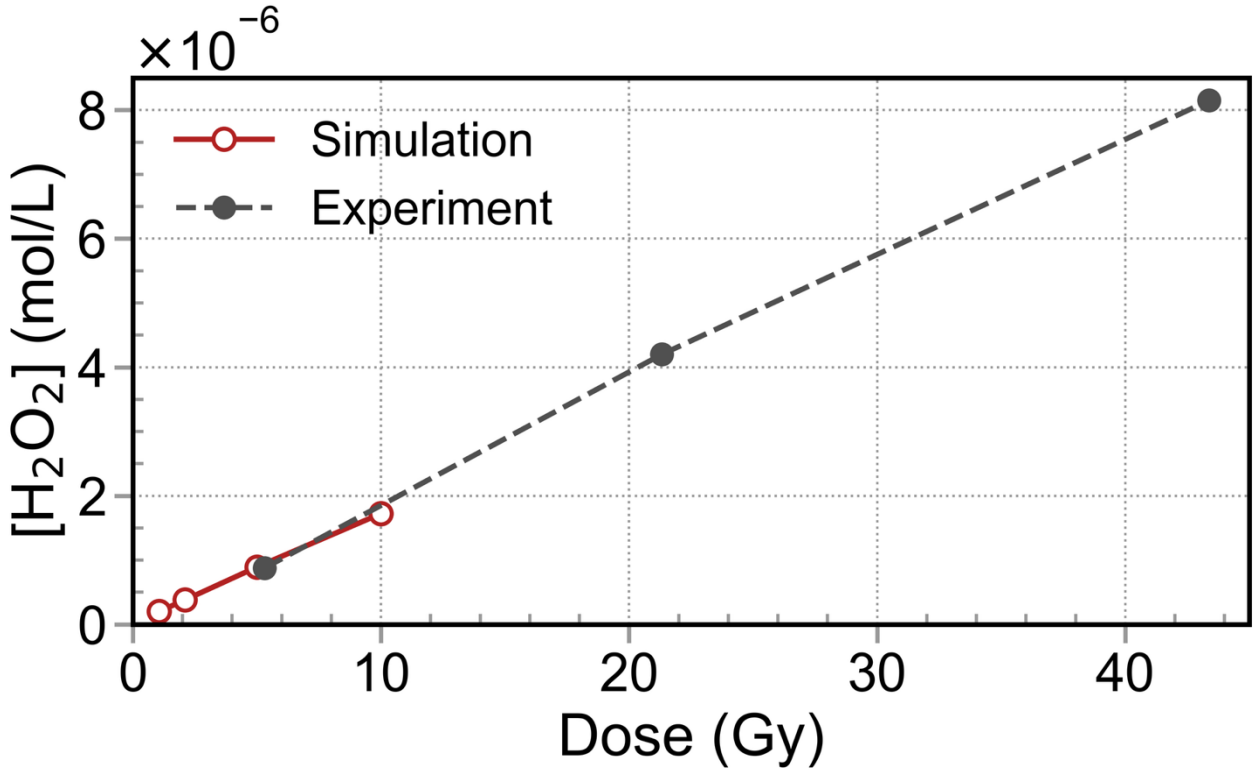
Experiment

Mean dose rate (Gy/s)	Pulse duration (s)	Dose to the target (Gy)
0.2	[6.3 10^{-3} – 1.9]	[10, 20, 30, 40, 60, 80]
8		
40		
100		
500		

Simulation

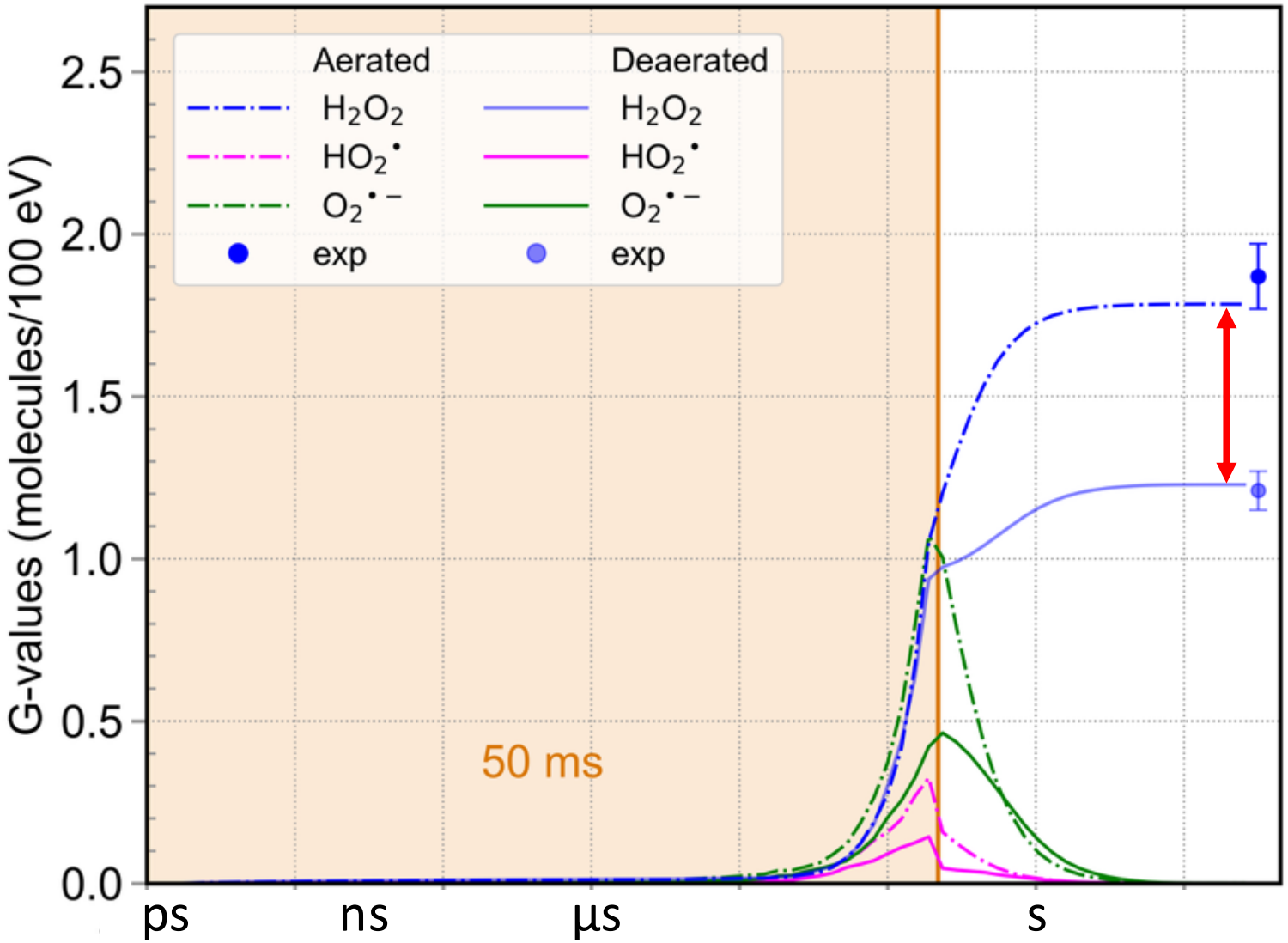
Mean dose rate (Gy/s)	Pulse duration (ms)	Dose to the target (Gy)
0.2	50	0.01
8		0.4
40		2
50		2.5
110		5.5

H_2O_2 linearity with dose at 100 Gy/s

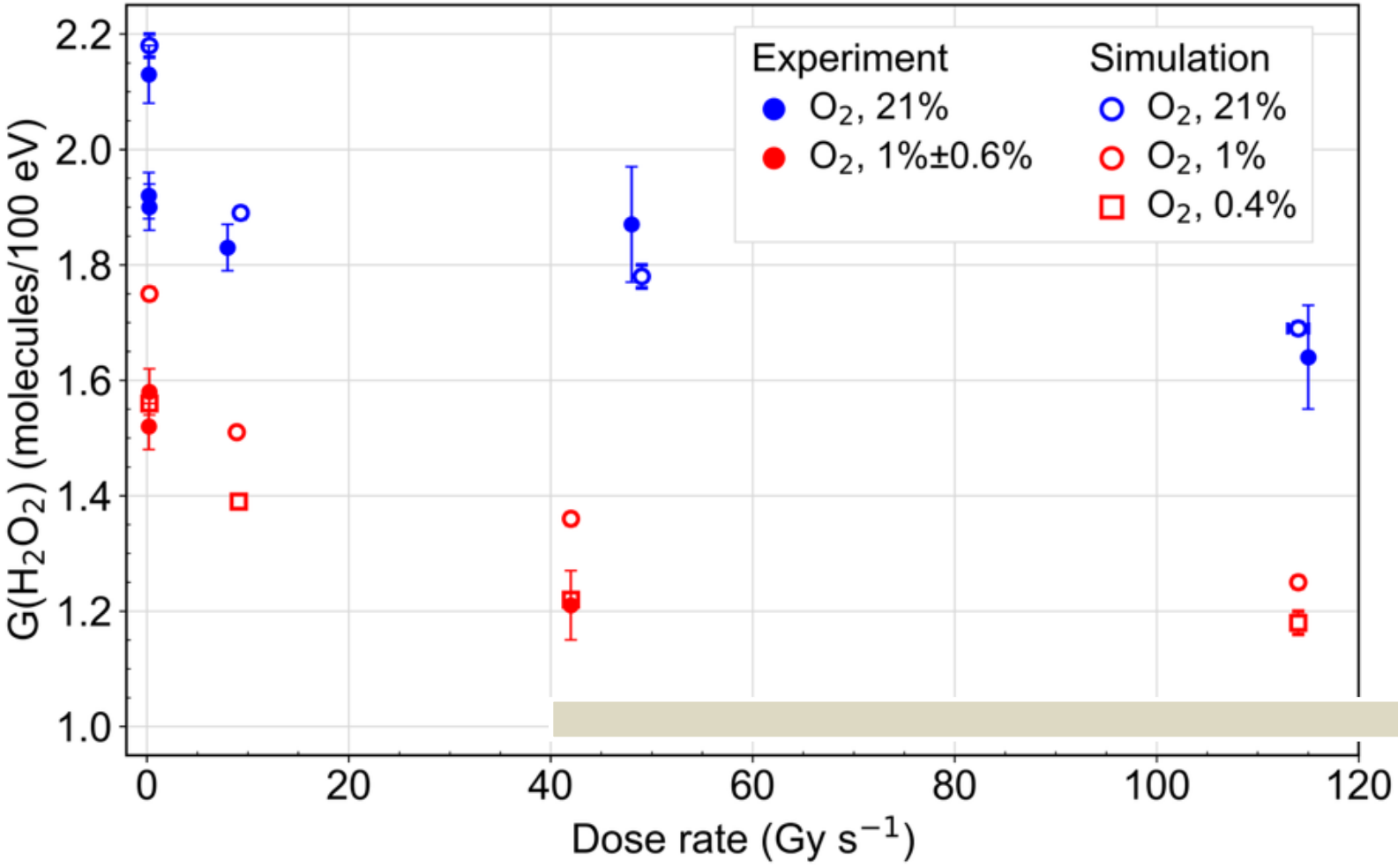


→ Simulated data (red open circles) are shown at 1.1, 2.1, 5 and 10 Gy (R^2=0.9997) and experimental data (grey filled circles) at 5.3, 21.3 and 43.4 Gy (R^2=0.9994).

Impact of O_2 on the radical formation at 42 Gy/s



Comparison of simulated and experimental $G(H_2O_2)$

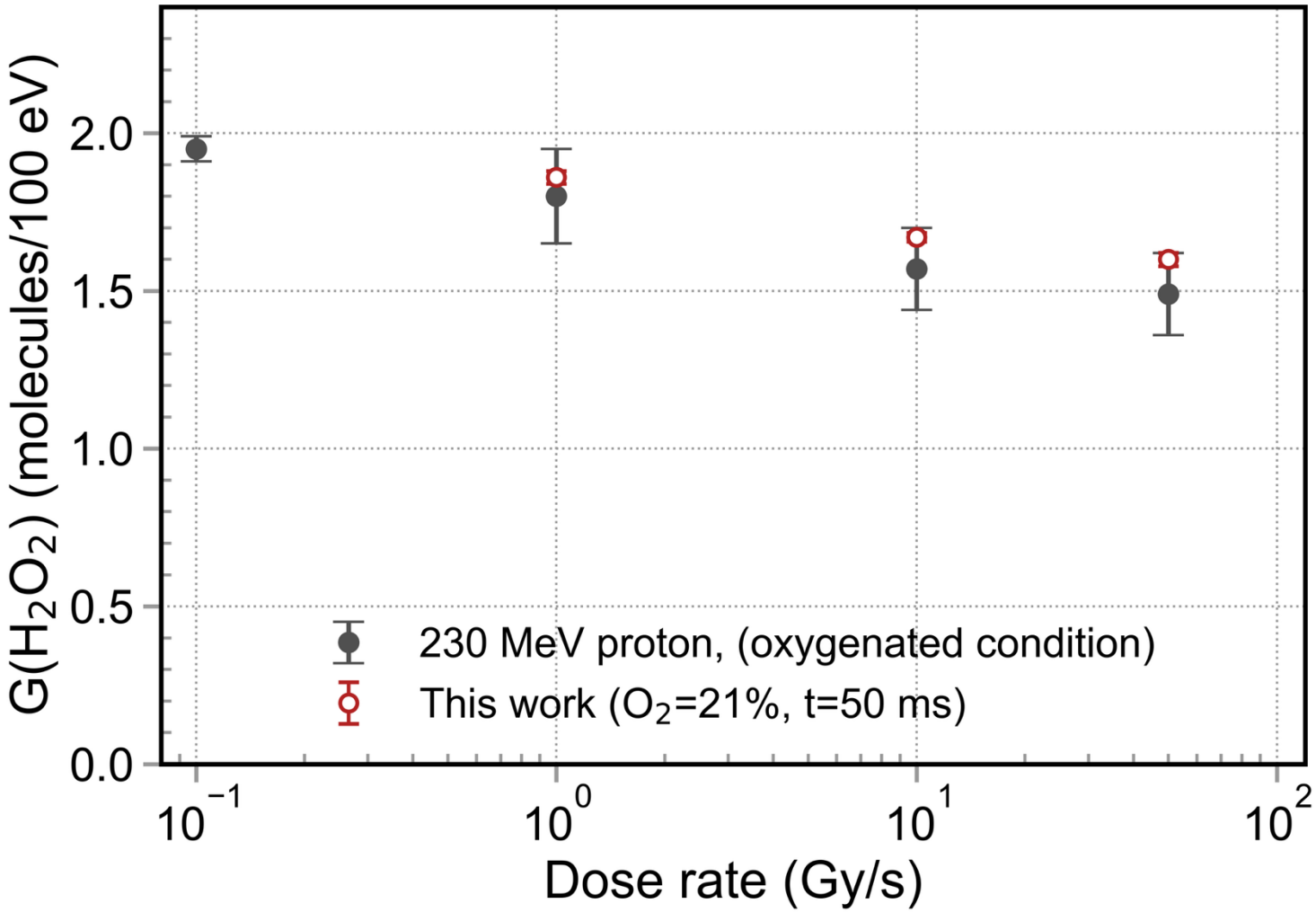


FLASH condition

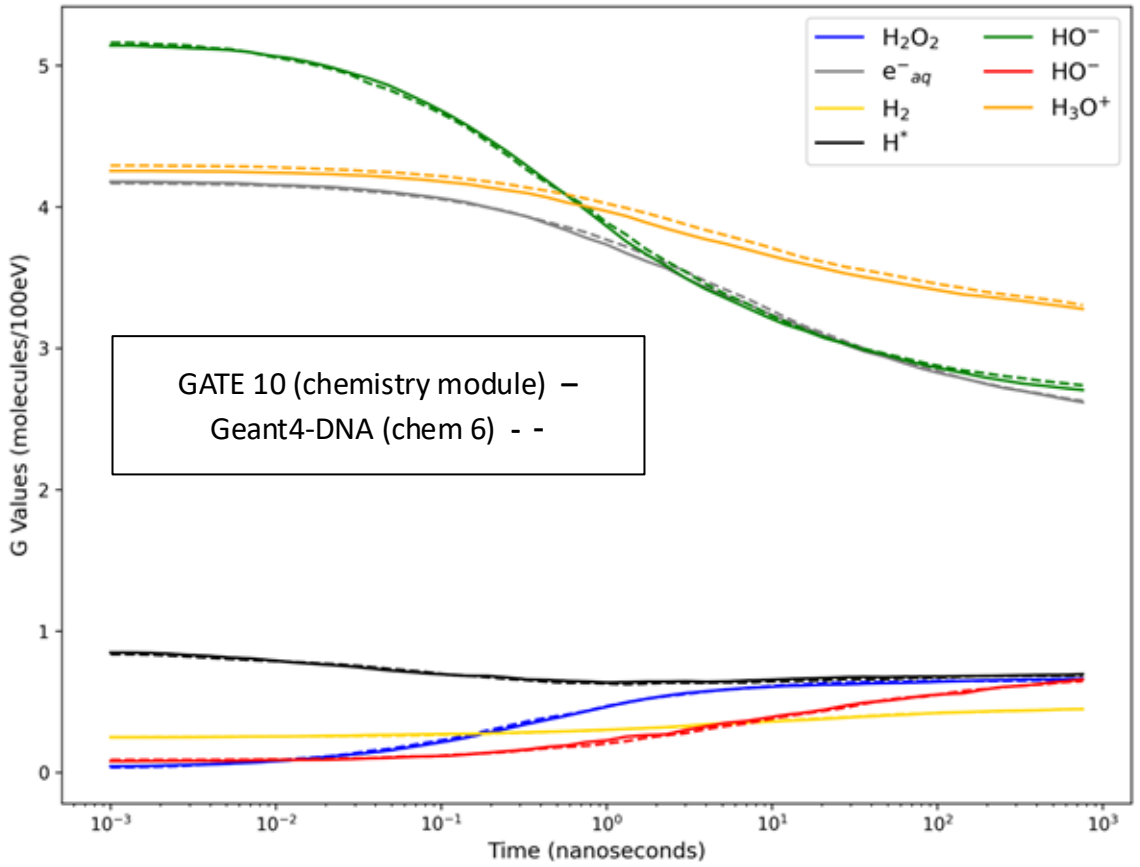
Digital twin with other experimental data

Sumitomo Heavy Industries, Ltd.

Kusumoto et al., 2024

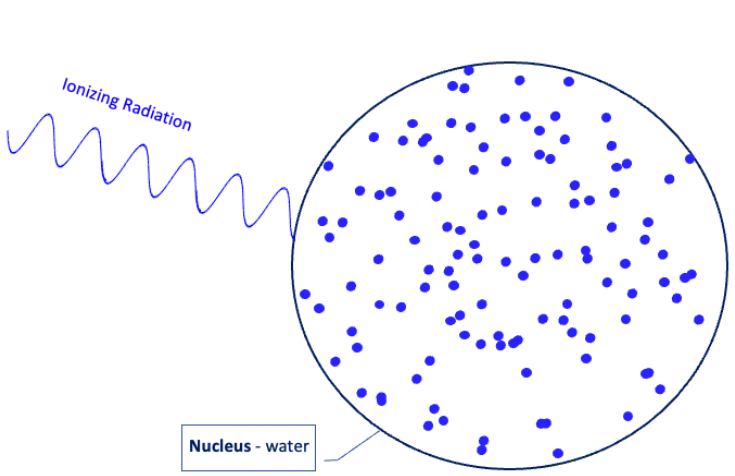


Soon a Chemistry Actor

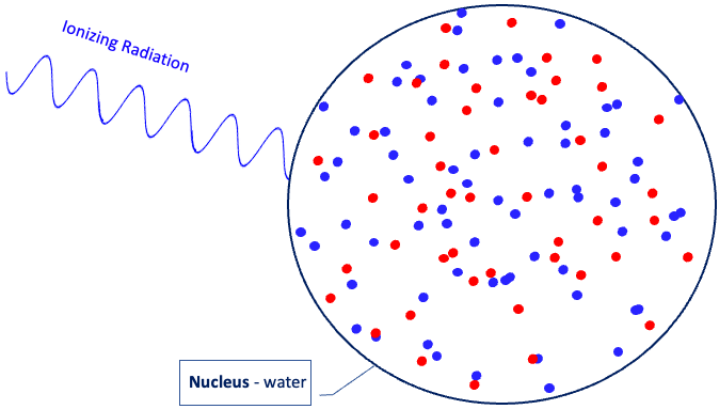



```
# Geometry Definition
world = sim.world
world.size = [3.2 * um, 3.2 * um, 3.2 * um]
world.material = "G4_WATER"

# physics
sim.physics_manager.special_physics_constructors.G4EmDNAChemistry_option3 = True

# chemistry actor
chem = sim.add_actor("ChemistryActor", "Chem")
chem.timestep_model = "IRT"
chem.end_time = 1 * us
chem.time_bins_count = 50
chem.reactions = [
                # totally diffusion-controlled (TDC)
                [["H", "H"], ["H2"], "Fix", 0.5e10, 0],
                [["e_aq", "H"], ["H2", "OHm"], "Fix", 2.5e10, 0],
                [["e_aq", "e_aq"], ["H2", "OHm", "OHm"], "Fix", 0.636e10, 0],
                [["H3Op", "OHm"], ["H2O"], "Fix", 1.13e11, 0]

def analysis(chem):
  times = chem.get_times()
  data = chem.get_data()

  for key in {'H2O2^0', 'e_aq^-1', 'OH^0', 'H3O^1', 'OH^-1', 'H^0', 'H_2^0', 'O^0'}:
                fig, ax = plt.subplots(figsize=(6.5, 5), dpi=300)
                ax.set_xlabel('time (ns)')
                ax.set_ylabel(r'G value (molecules / 100 eV)')
```

Clustering algorithm in GATE 10 (DBscan)

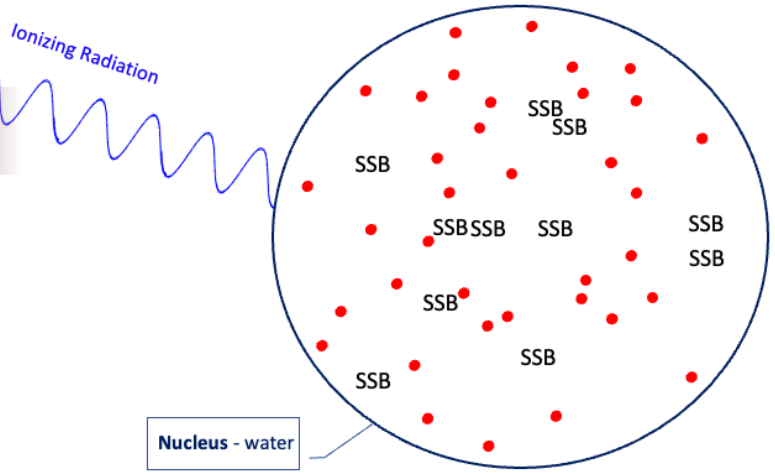


- Energy depositions

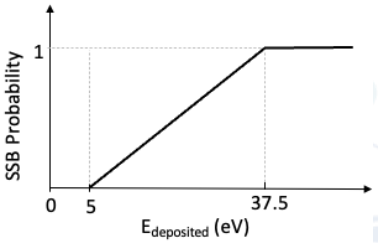


- Energy depositions
- Example: energy depositions in sensitive areas for SpointProb = 50%

$$\frac{V_{DNA}}{V_{nucleus}}$$



- Energy depositions
- Example: energy depositions in sensitive areas for SpointProb = 50%

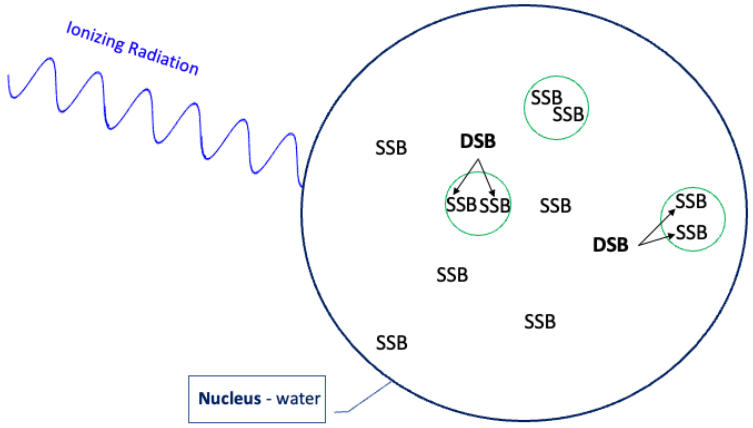


For minimum 2 SSB within a radial distance of 3.5 nm

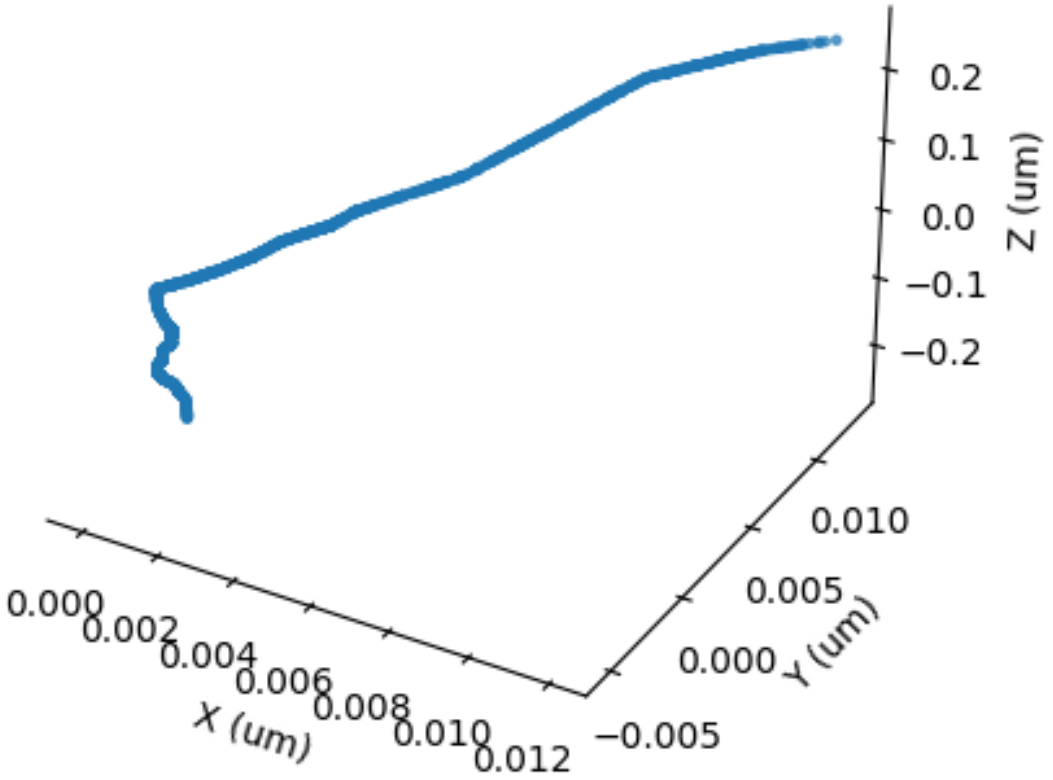
cluster

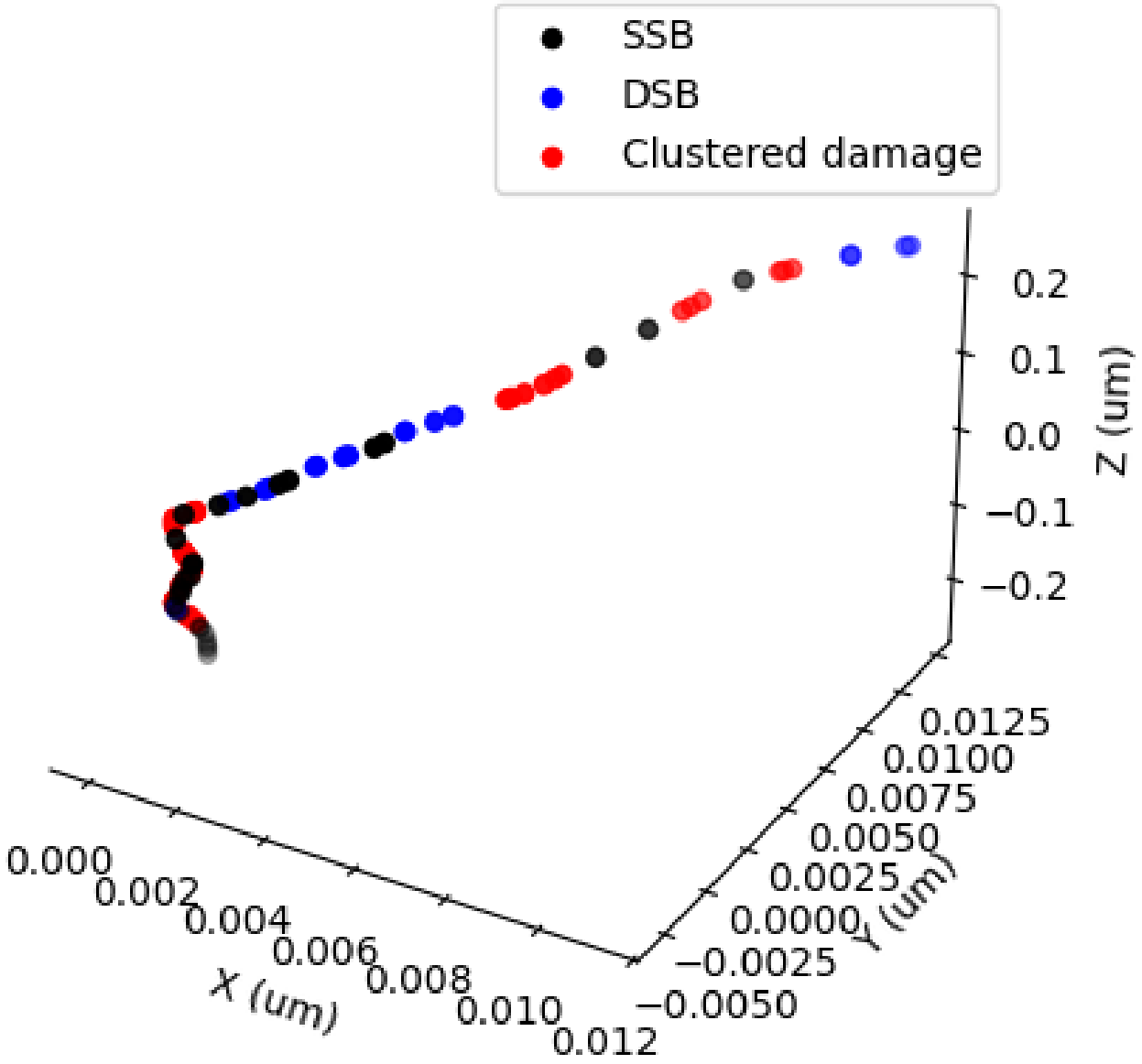
For minimum 2 SSB on opposite strands within a cluster

DSB

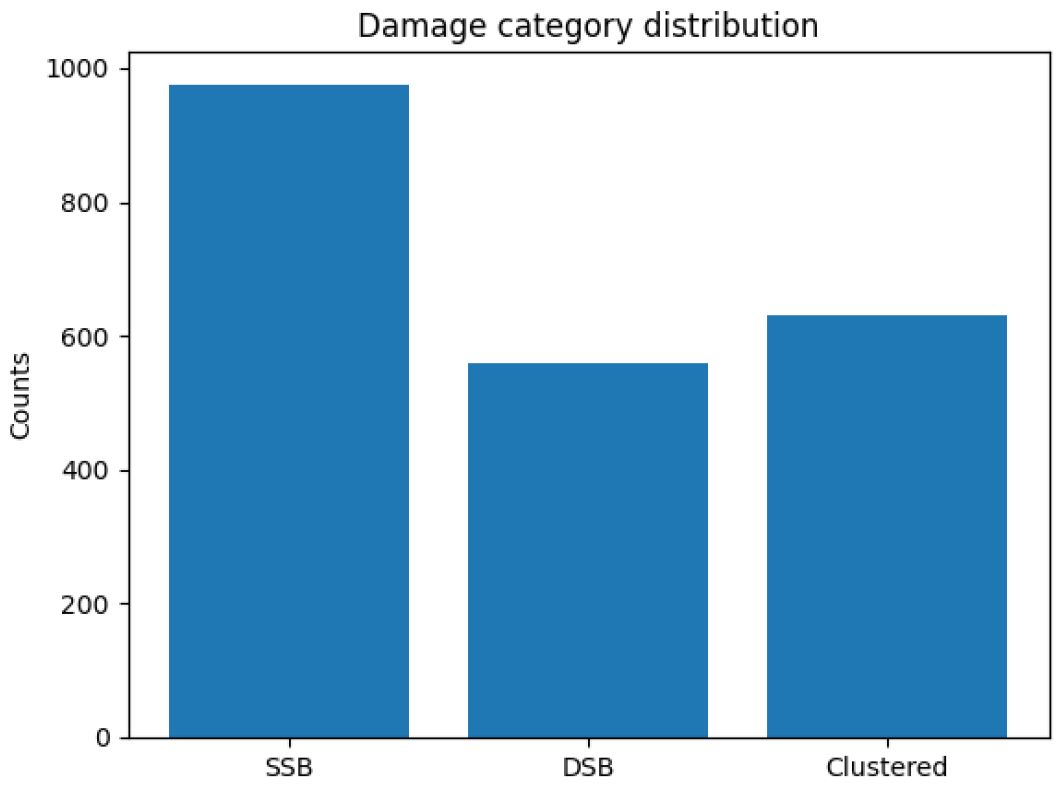


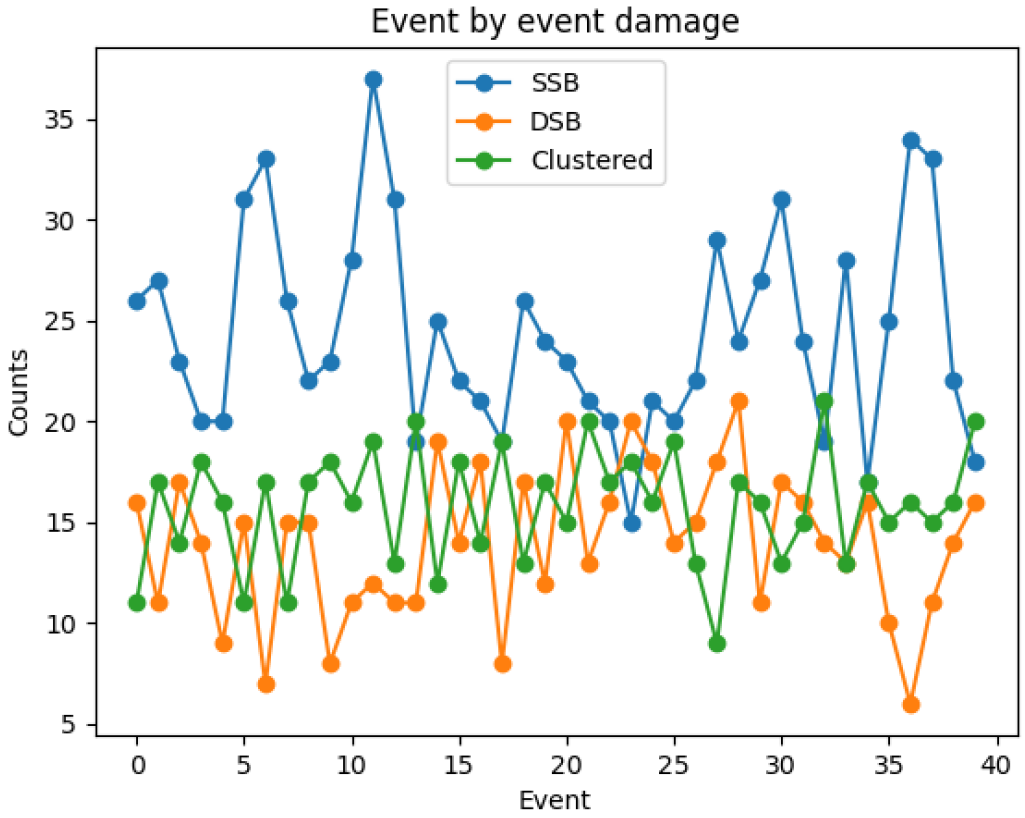
DNA damage with GATE 10





SSB & DSB estimation





Conclusion and Perspectives

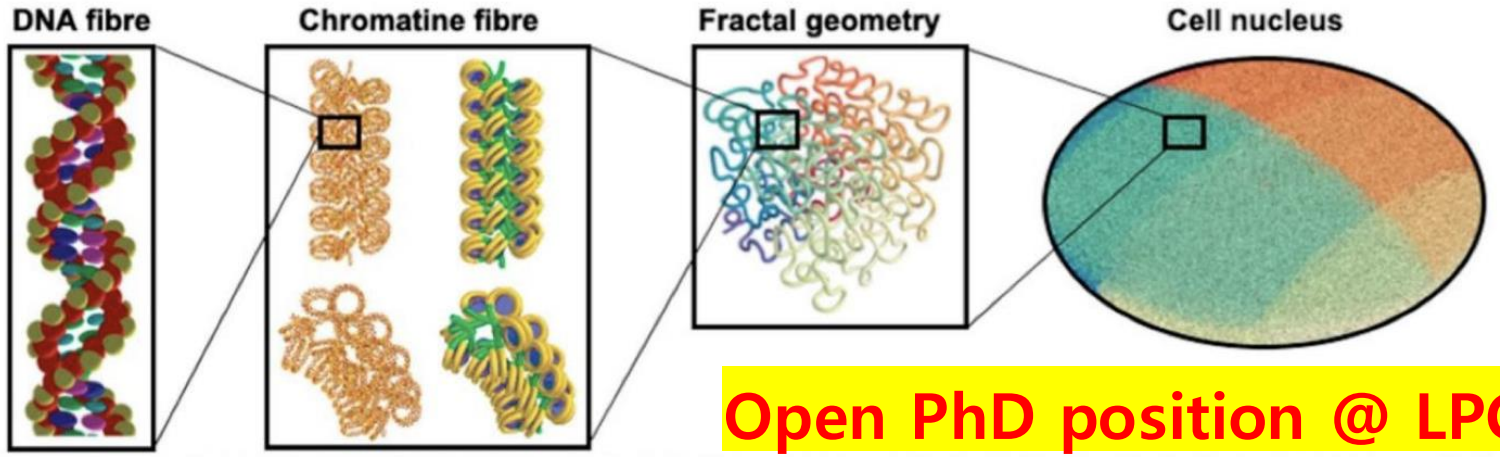
Validation of FLASH irradiations @ ARRONAX from Physics to Chemistry ✓

D. Kwon et al, accepted in Med. Phys., April 2026

- Scavenging e^-_{aq} and blocking $HO_2^\bullet$ / $O_2^{\bullet-}$ pathway to observe H_2O_2
- Extend the work to other French beam lines
  Other comparisons with HIMAC He^{2+} irradiations (IPHC)

GATE 10 to study biological endpoint using clustering algorithm ✓

- Integrating the DNA geometry using FractalDNA Python package



Open PhD position @ LPCA for Oct 2026