Simulation of water radiolysis from conventional dose rate to ultra high dose rate

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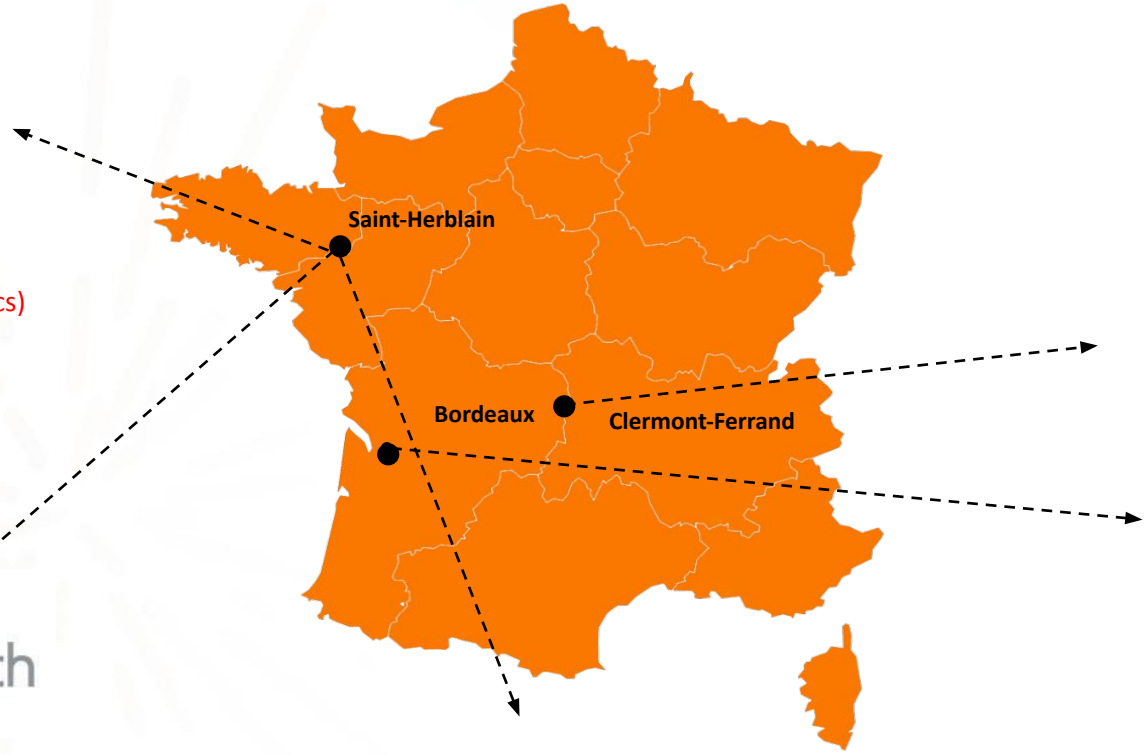

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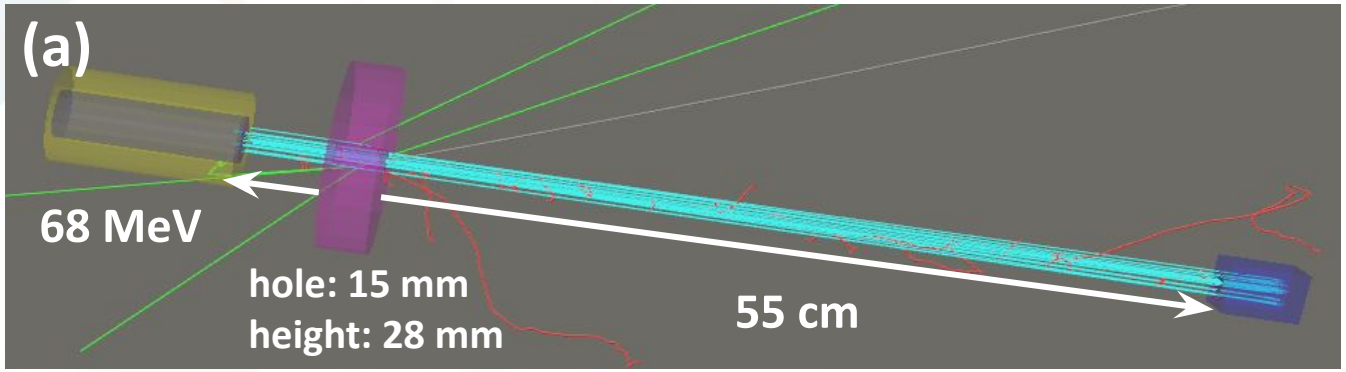
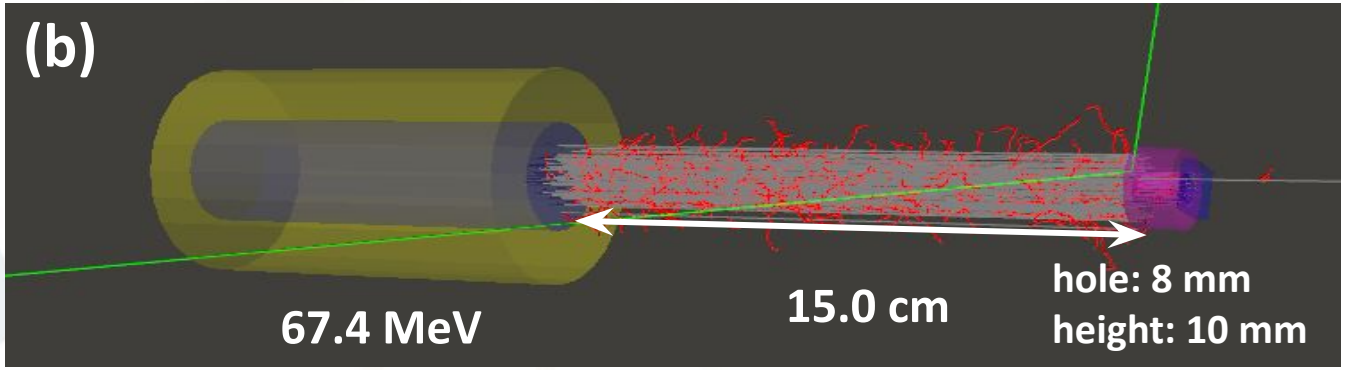
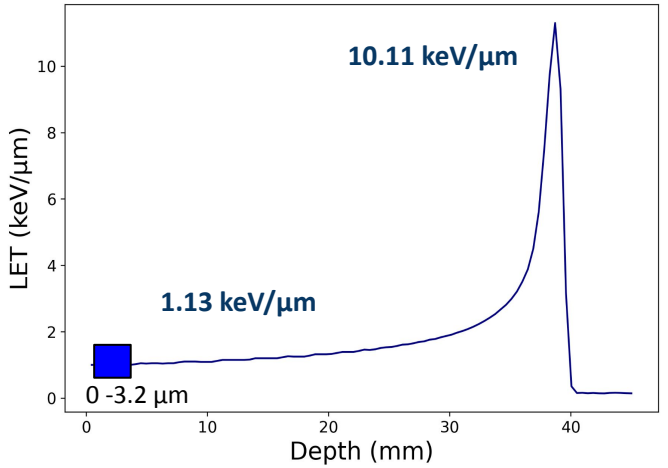
Beamlines modeling with GATE 10







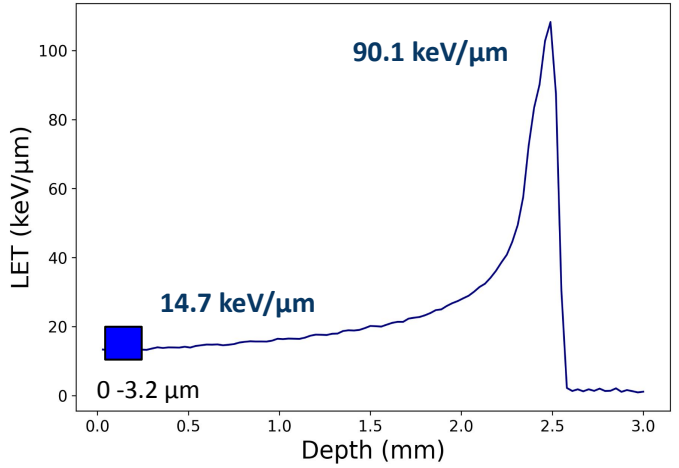
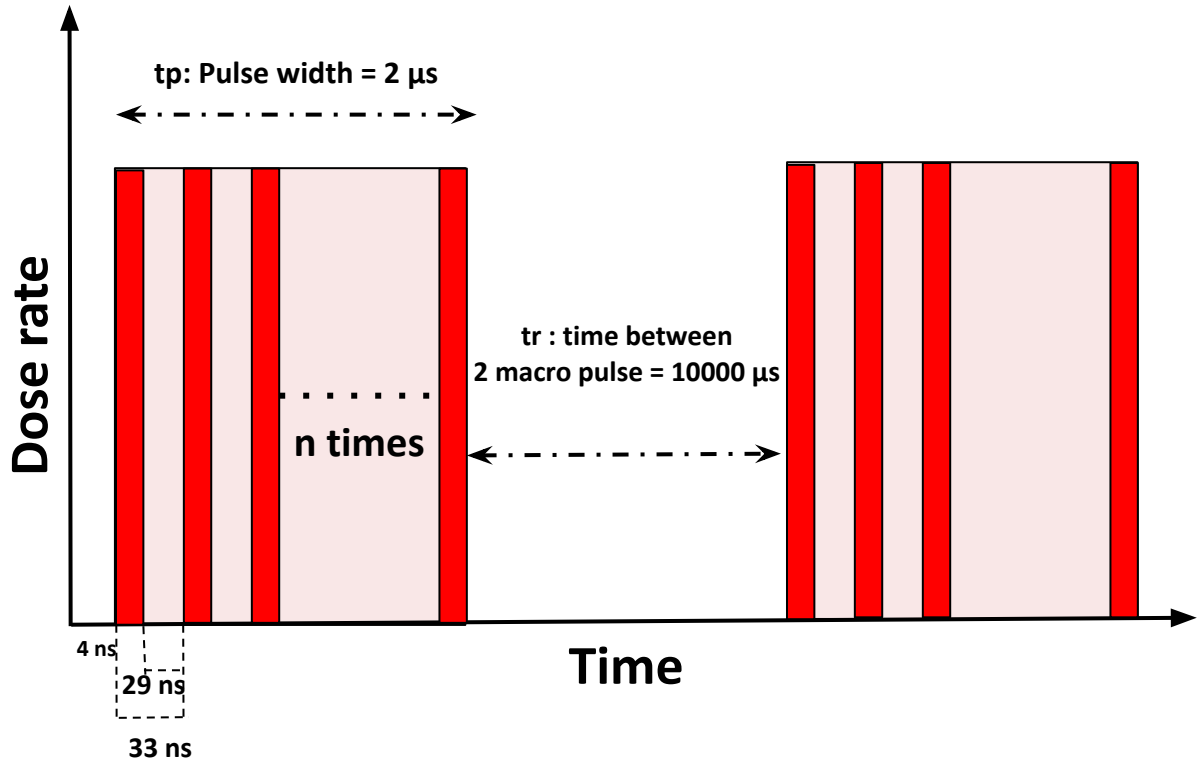


Figure 1. Simulation of ARRONAX (a) proton and (b) alpha beamlines modeling using GATE. beampipe + kapton window (yellow), collimation (pink), water target (blue)

Dose rate - experimental condition

ARRONAX (IBA Cyclone 70 XP)

- Protons: 68 MeV (range in water 39 mm)
- Alphas: 57 MeV (range in water 3 mm)
- Dose rates: from 0.02 Gy/s to 350 kGy/s



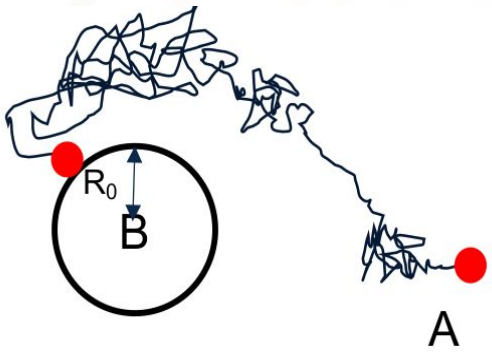
Computational chemistry models

- SBS (step by step)

Debye-Smoluchowski Brownian diffusion model from which encounters between reactants are dynamically sampled.

Reactions happen when A diffuse close to B within a distance R_0 **(Diffusion-controlled reactions)**

Simulation time needed for calculating the distance between species at every time step is a *huge computational burden.*

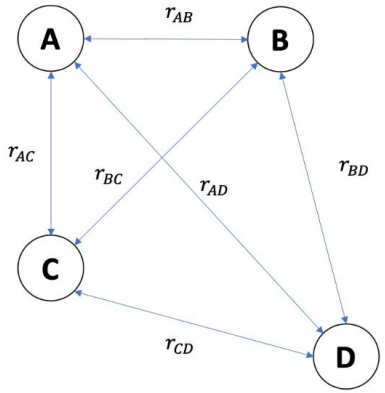


- IRT (Independent Reaction Times)

An event table is constructed with the **initial chemical species positions and reaction times** for each reactant pair of interest

Reaction product positions are **randomly sampled within a sphere centred at the reaction site**.

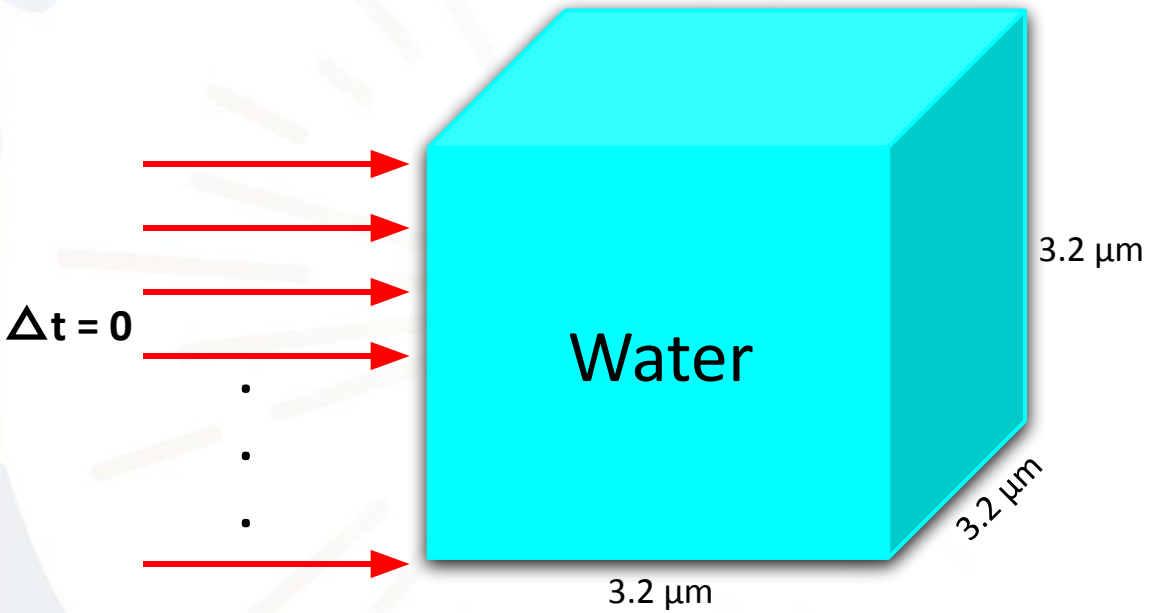
No spatial information



Reaction	Time (ps)	Order of reactions
A+B	63	X
A+C	3	1
A+D	111	X
B+C	192	X
B+D	15	2
C+D	90	X

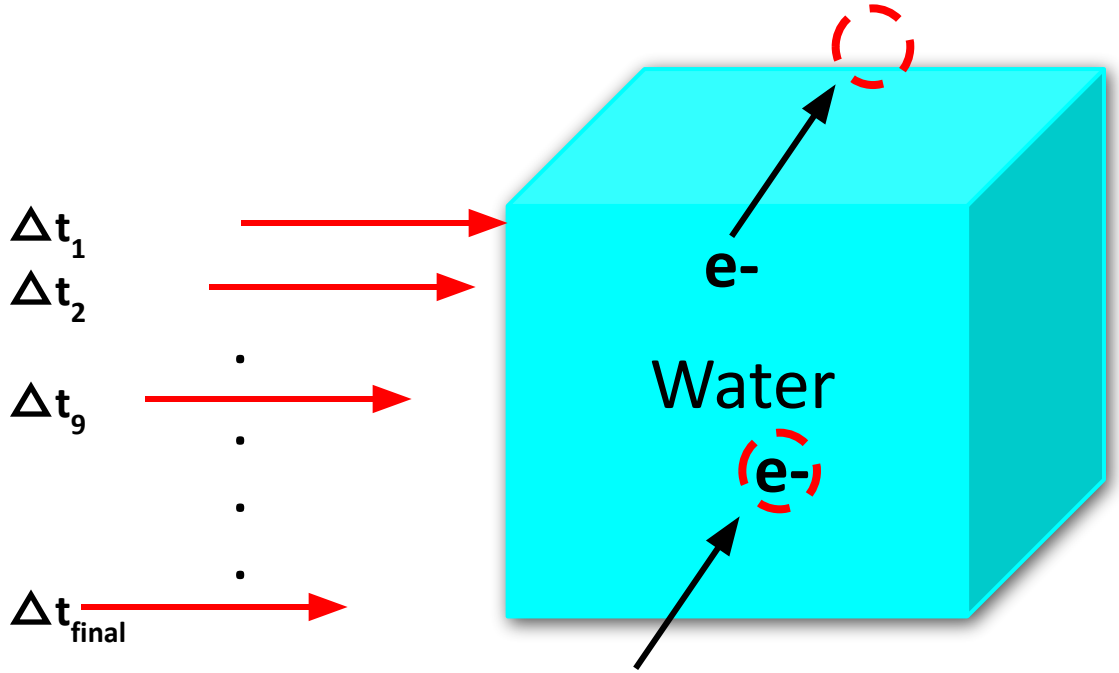
Physical stage - incident particles

- Version Geant4 - 11.2



Dose (Gy)	0.01	1	5	10
Simultaneous number of particles (#)	1.2	81	400	800

- Upcoming version



PBC (Periodic Boundary Condition - A maximum dose (xxx) to terminate the event to avoid the high energy of secondary electrons deposit a large energy inside the micro volume.)

/UHDR/Detector/PBC true

/scorer/Dose/abortedDose 0.05 Gy

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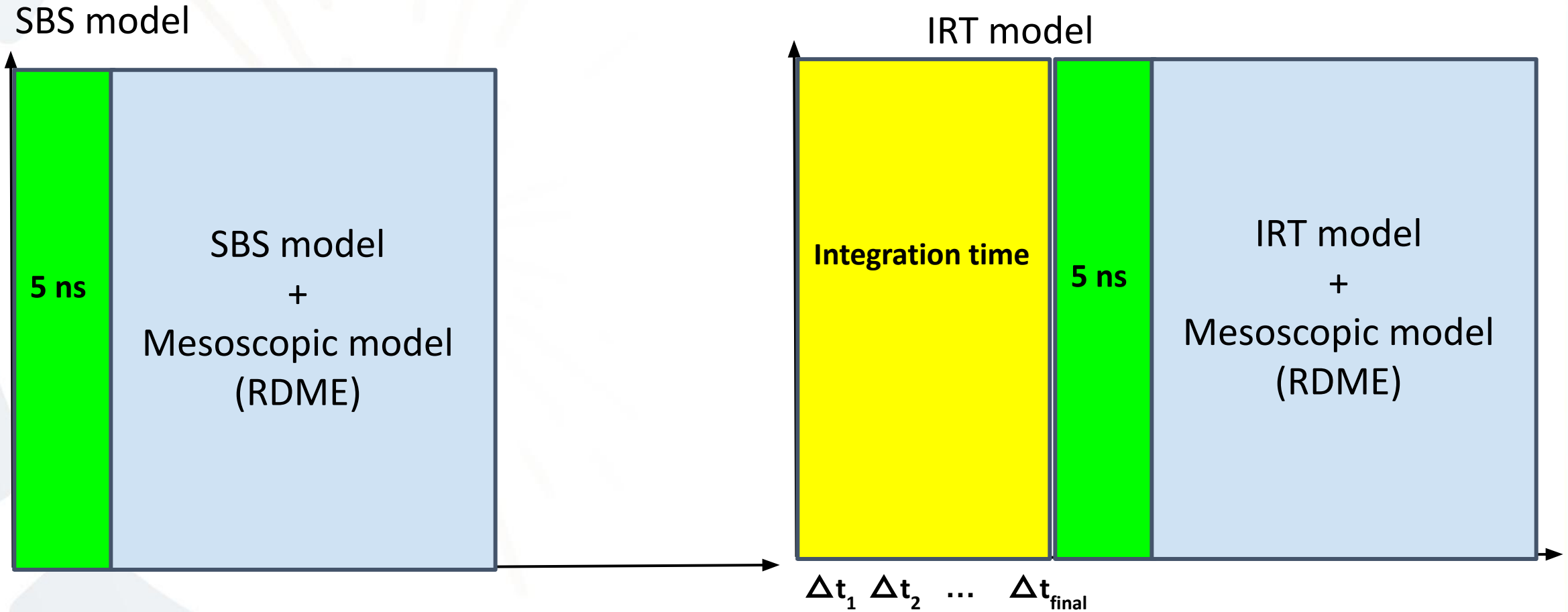
Chemical stage

- Version Geant4 - 11.2
- Upcoming version



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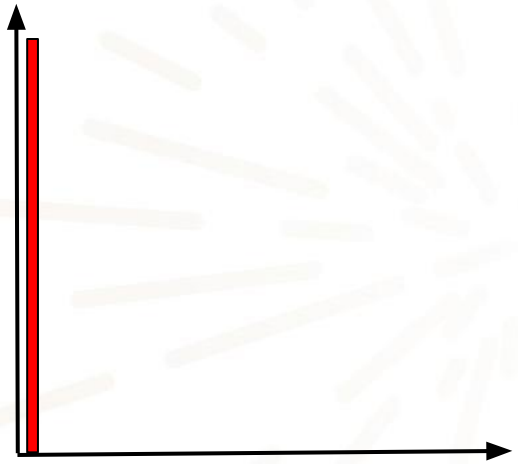
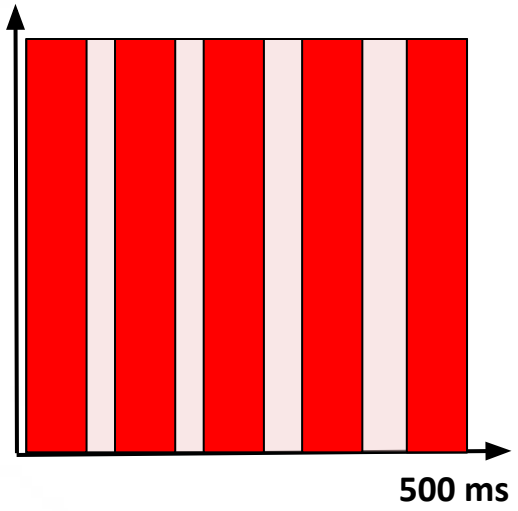
Time structure pulse

- Version Geant4 - 11.2



infinite pulse (= instantaneous) :
all incident particles are shot at the same time

- Upcoming version



pulse duration (500 ms)
÷
[single pulse (90 ms - red) + Pause (10 ms - pink)]
=
number of pulse (5)

```
# time structure
/UHDR/pulse/On true
/UHDR/pulse/multiPulse true
/UHDR/pulse/pulsePeriod 500 ms
/UHDR/pulse/NumberOfPulse 5
/UHDR/pulse/pulseFile 90 us
```

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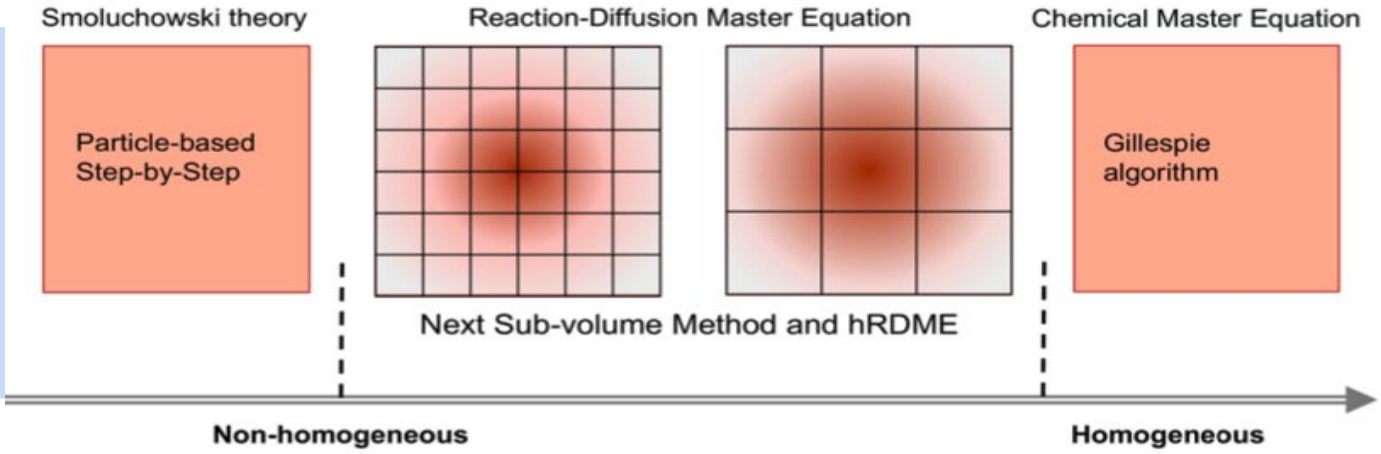
Water radiolysis chemistry in Geant4-DNA (version 11.2)

Parameters

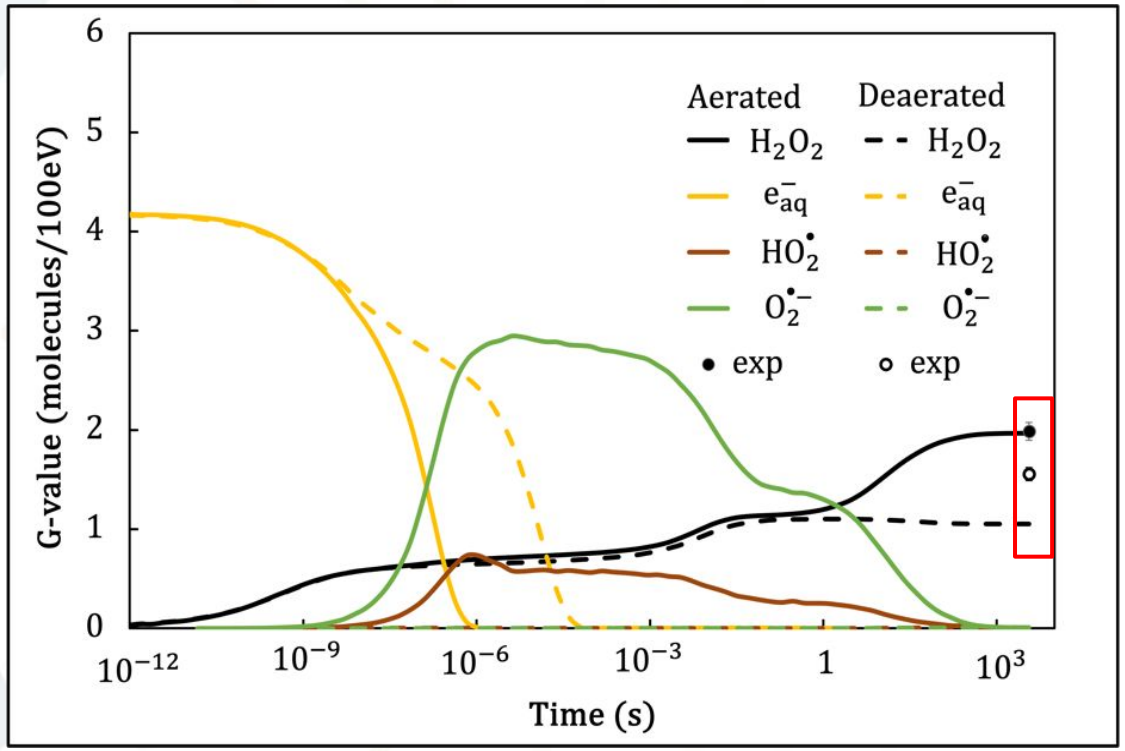
- Oxygen level (%): 0 - 19
- pH 5.5
- Dose to the target: 0.01 Gy (conv) , 1 Gy (UHDR)
- G4EmDNAPhysics_option2
- G4EmDNAChemistry_option1
- SBS model



Tran,H.N.;Chappuis,F.; Incerti, S.; Bochud, F.; Desorgher, L. **Geant4-DNA Modeling of Water Radiolysis beyond the Microsecond: An On-Lattice Stochastic Approach.***Int. J. Mol. Sci.* **2021**, *22*, 6023. https://doi.org/10.3390/ ijms22116023 *

Water radiolysis at conventional dose rate

Conv. - Comparison with experiments - impact on O_2



- **H_2O_2 Formation reaction**

$$HO^\cdot + HO^\cdot \rightarrow H_2O_2$$

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

$$H^\cdot + O_2 \rightarrow HO_2^\cdot$$

$$O^{\cdot -} + H^+ \leftrightarrows HO_2^\cdot$$

$$HO_2^\cdot + O_2^{\cdot -} \rightarrow HO_2^{\cdot -} + O_2$$

$$HO_2^{\cdot -} + H_2O \rightarrow H_2O_2 + HO^-$$

$$H_3O^+ + HO_2^{\cdot -} \rightarrow H_2O_2$$

- **H_2O_2 consuming reaction**

$$H_2O_2 + e^-_{aq} \rightarrow HO^\cdot$$

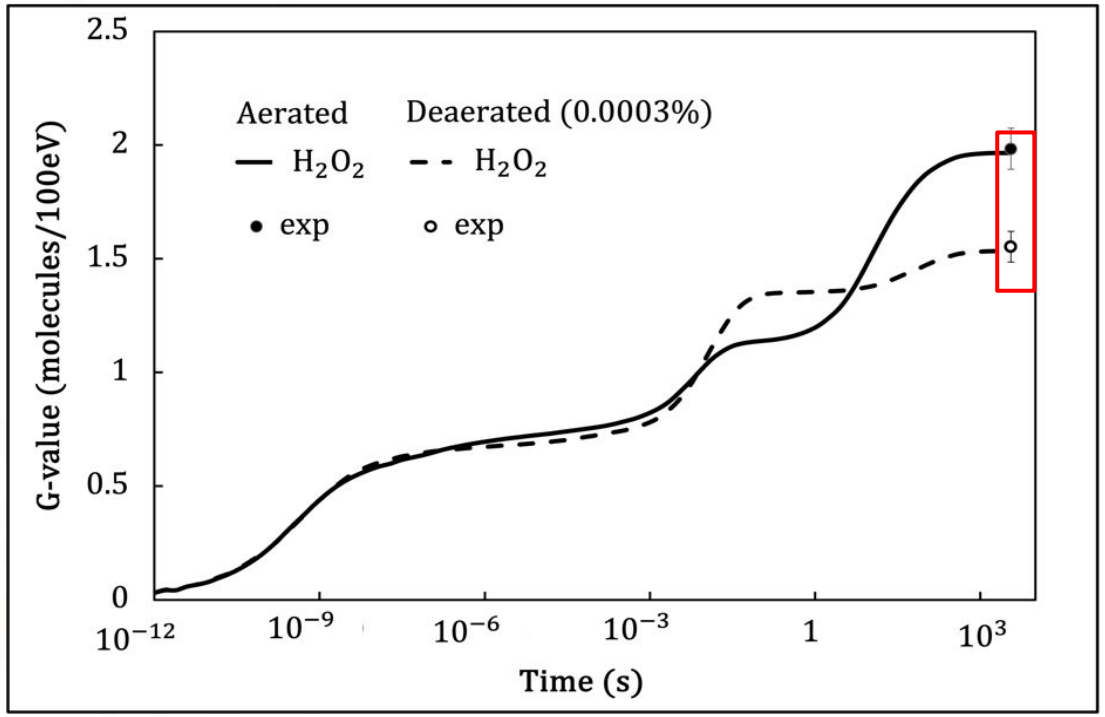
$$H_2O_2 + H^\cdot \rightarrow HO^\cdot + H_2O$$

$$H_2O_2 + H^\cdot \rightarrow HO_2^\cdot + H_2O$$

$$H_2O_2 + HO^- \rightarrow HO_2^{\cdot -}$$

Fois, G.R.; Tran, H.N.; Fiegel, V.; Blain, G.; Chiavassa, S.; Craff, E.; Delpon, G.; Evin, M.; Haddad, F.; Incerti, S.; et al. Monte Carlo Simulations of Microdosimetry and Radiolytic Species Production at Long Time Post Proton Irradiation Using GATE and Geant4-DNA. *Med. Phys.* 2024

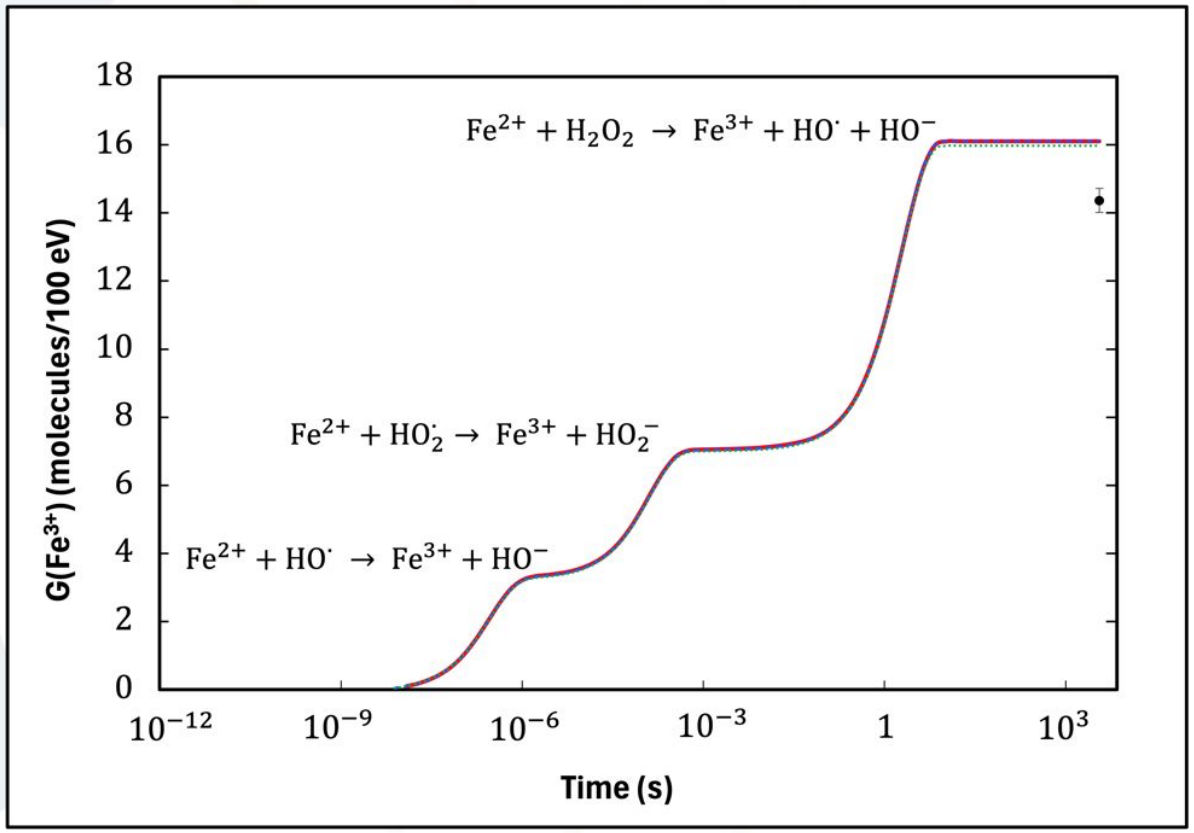
Conv. - Comparison with experiments - impact of O_2

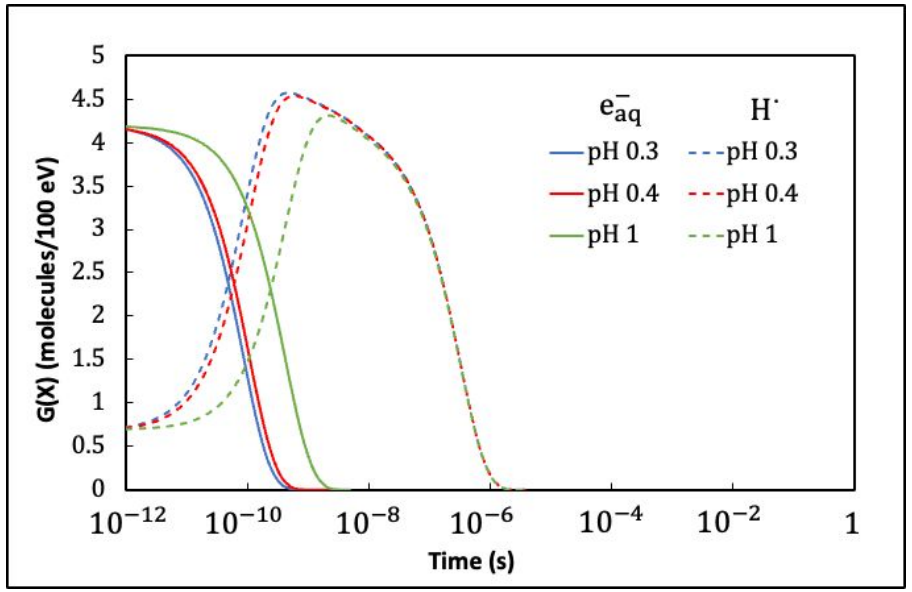


O_2 concentration (%)	0	4 10^{-4}	2	3	19
O_2 concentration (mol.L^{-1})	0	3.9 10^{-4}	2.6 10^{-5}	3.9 10^{-5}	2.5 10^{-4}
G(H_2O_2) at 1 hour post-irradiation (molecules/100 eV)	1.05	1.53	1.89	1.92	1.96

Fois, G.R.; Tran, H.N.; Fiegel, V.; Blain, G.; Chiavassa, S.; Craff, E.; Delpon, G.; Evin, M.; Haddad, F.; Incerti, S.; et al. Monte Carlo Simulations of Microdosimetry and Radiolytic Species Production at Long Time Post Proton Irradiation Using GATE and Geant4-DNA. *Med. Phys.* 2024

Conv. - Fricke dosimetry and impact of pH



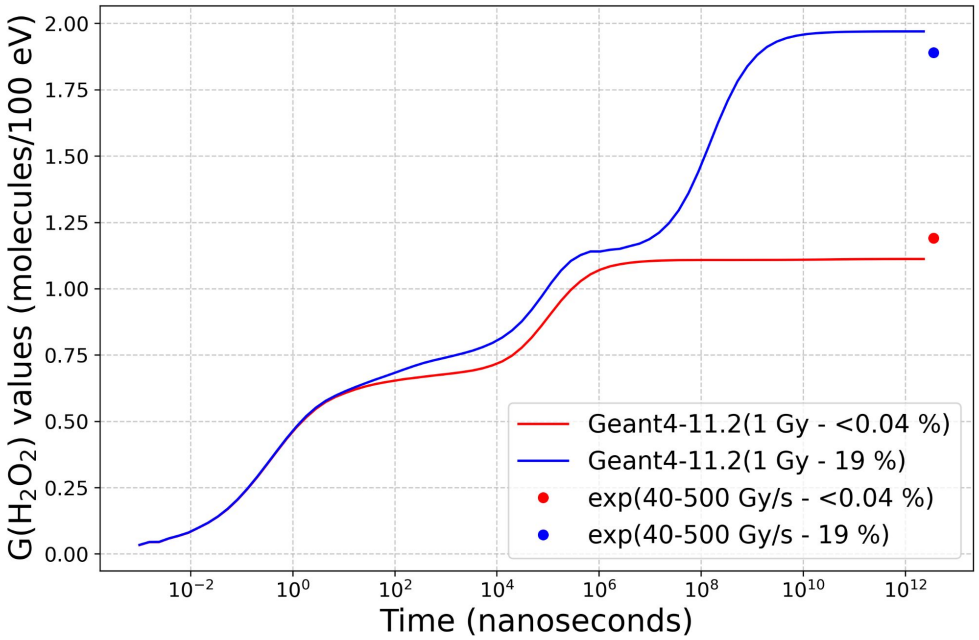


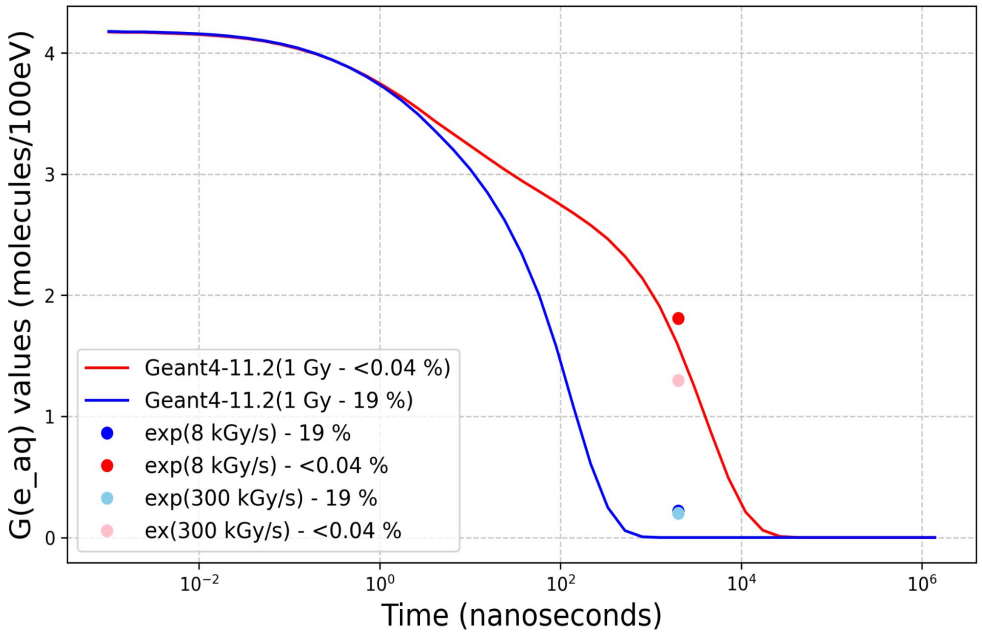
The more pH is acid, the more react faster with H^+ and then more species are produced to faster the oxidation of Fe^{2+}

Fois, G.R.; Tran, H.N.; Fiegel, V.; Blain, G.; Chiavassa, S.; Craff, E.; Delpon, G.; Evin, M.; Haddad, F.; Incerti, S.; et al. Monte Carlo Simulations of Microdosimetry and Radiolytic Species Production at Long Time Post Proton Irradiation Using GATE and Geant4-DNA. *Med. Phys.* 2024

Water radiolysis at ultra high dose rate

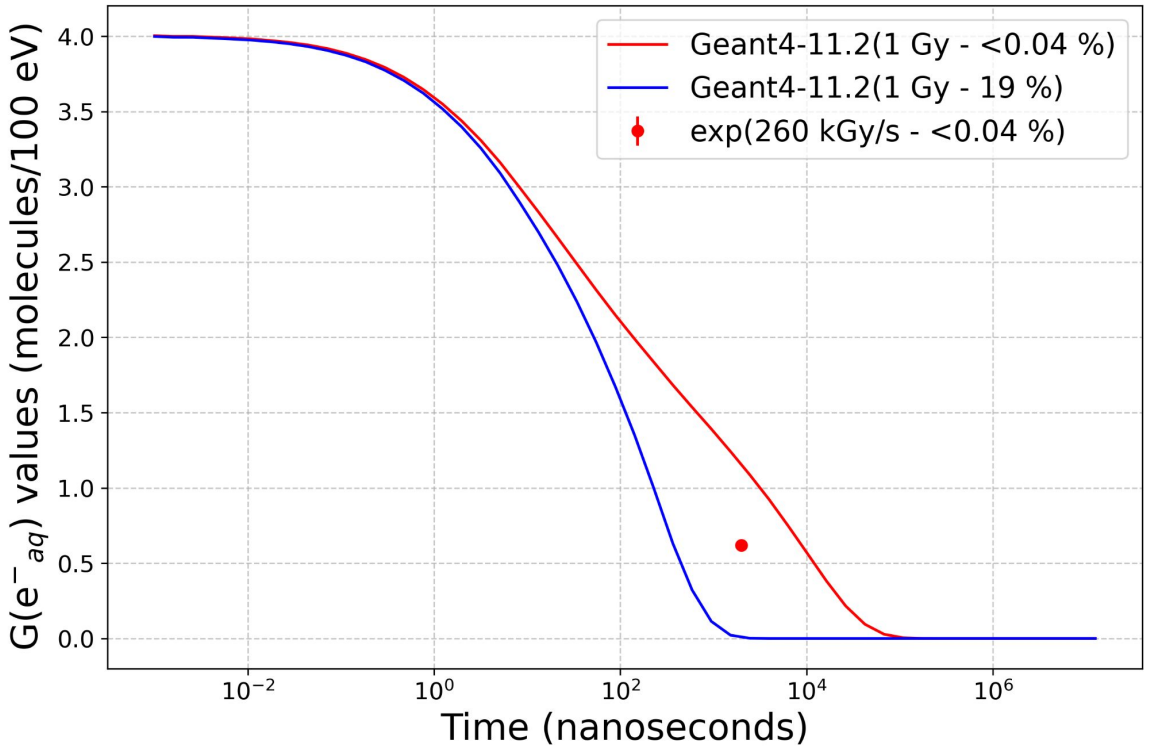
UHDR (proton) - Chemical species as function of O_2





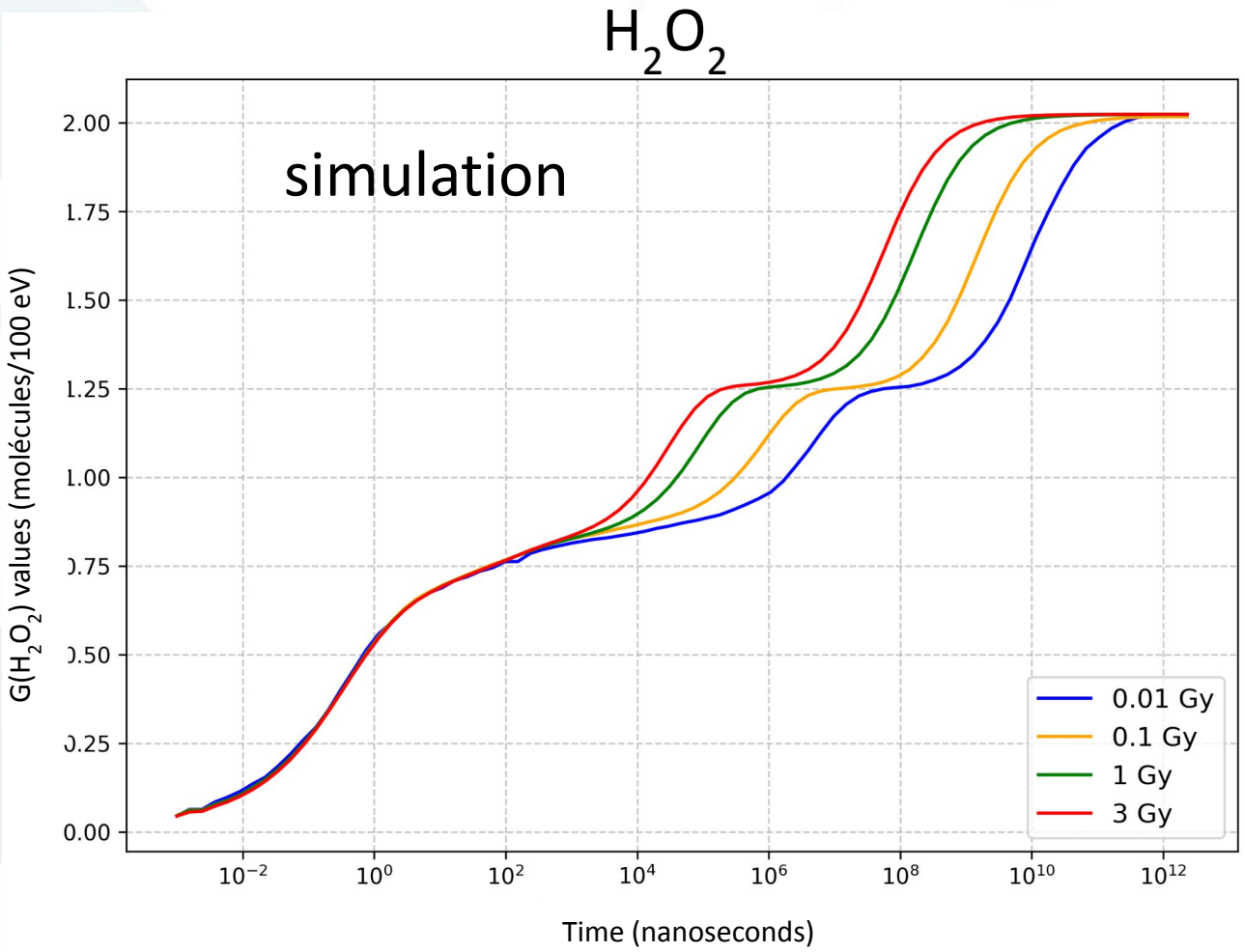
		H_2O_2	e^-_{aq}	
Dose rate (kGy/s)		0.04 ~ 0.5	8	300
Relative difference (%)	**Aerated**	5.08	- - -	- - -
	Deaerated	4.8	11.8	19.1

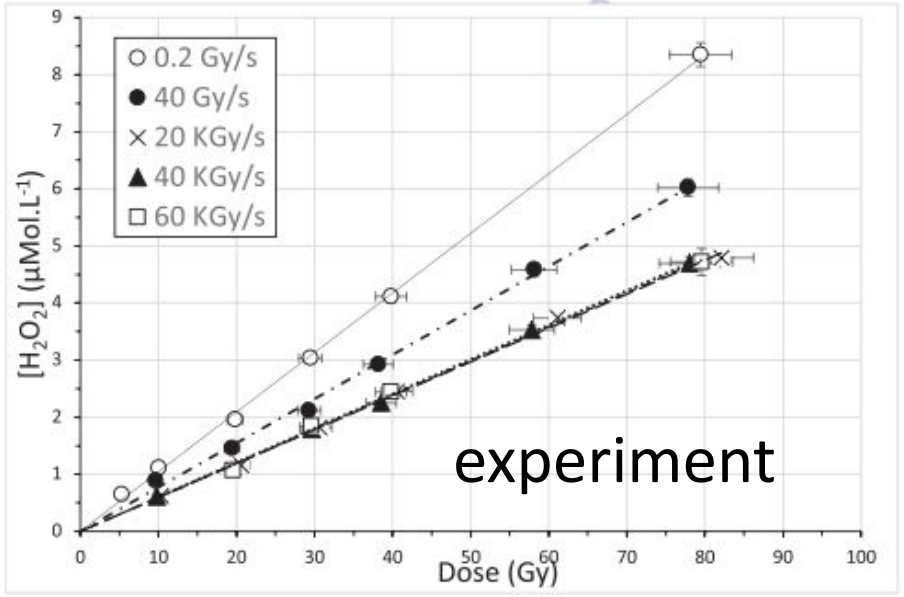
UHDR (alpha) - Chemical specie as function of O_2



		e^-_{aq}
Dose rate (kGy/s)		260
Relative difference (%)	Aerated	- - -
	Deaerated	19.4

UHDR example (version 11.2) - Limitation



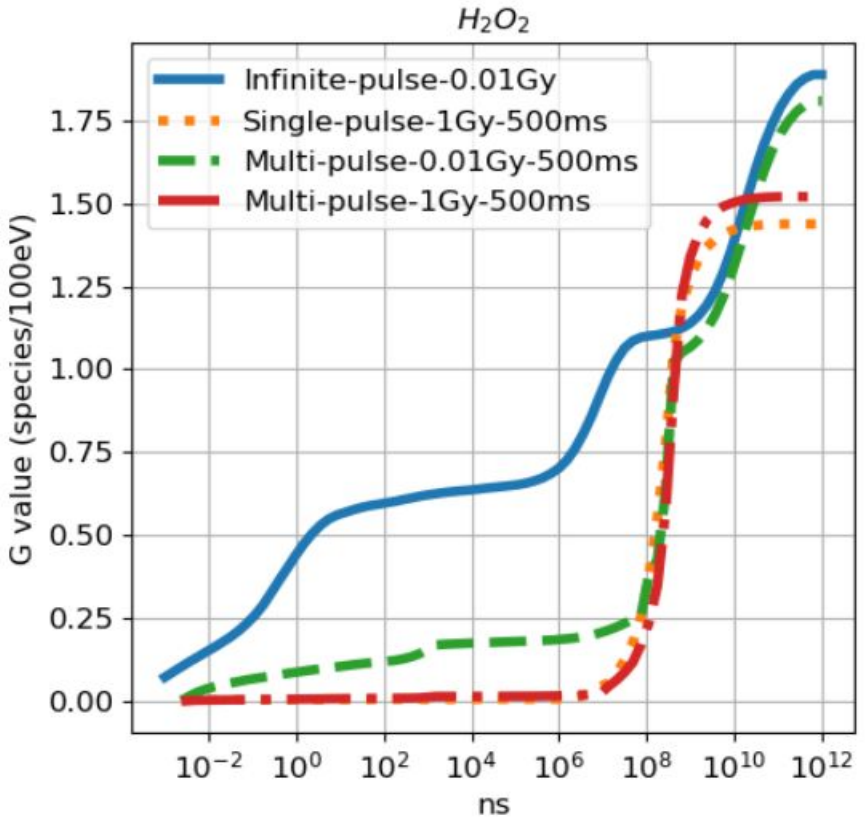


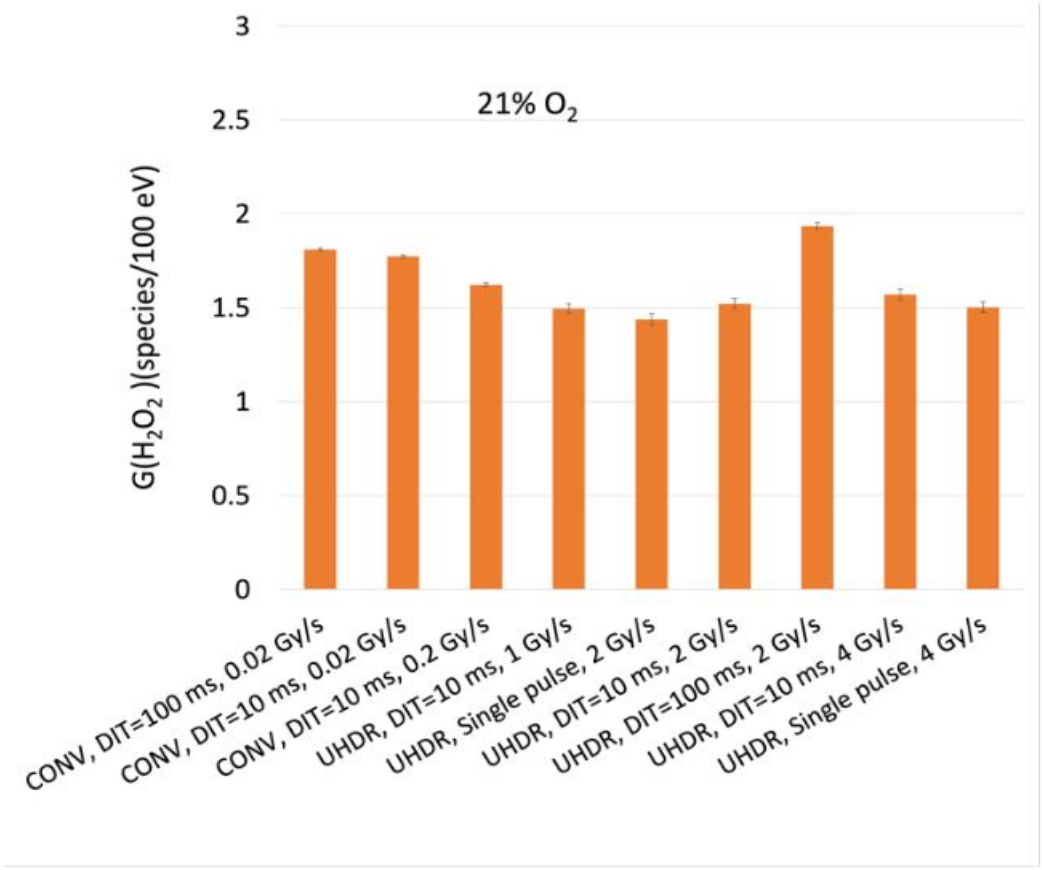
Therefore, dose rate and pulse intervals impact ROS generation; non-independent pulses may lead to different outcomes

Blain G et al. Radiation Research, 2022

Upcoming UHDR validation

Results - 1 MeV electron beam





TRANsportation effect **-> the chemical interaction and elimination of ROS ($O_2^{\cdot-}$/$HO_2^{\cdot}$) between tracks during longer pulse durations under <u>oxygen condition</u>**

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Conclusion and perspectives

- Geant4-DNA's chemistry module shows good performance in testing water radiolysis
- Discrepancies between Monte Carlo simulations and experimental measurements remain.
- non-independent pulses may lead to different outcomes.
- Time structure pulse is developed by Hoang (LP2i) - electron
- Further validation is needed for proton and alpha

Thank you