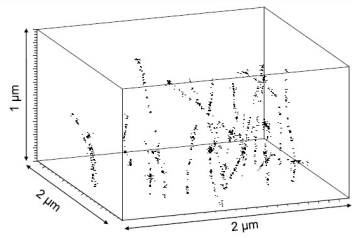
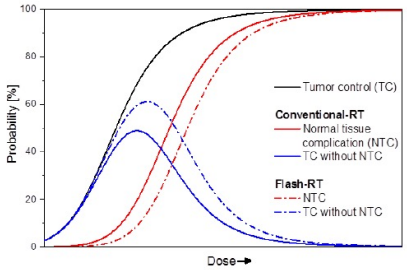
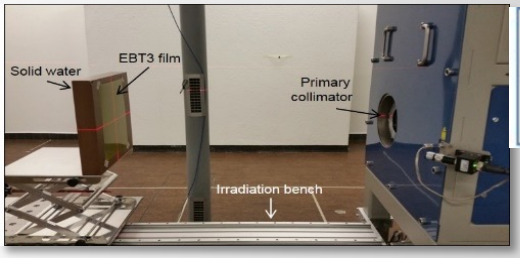
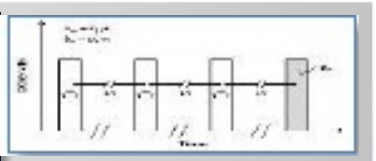
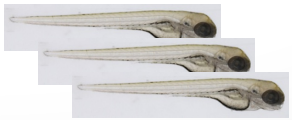










Geant4 Annual Collaboration Meeting

Ngoc Hoang Tran, CENBG

Mesoscopic model of Water Radiolysis in Geant4-DNA

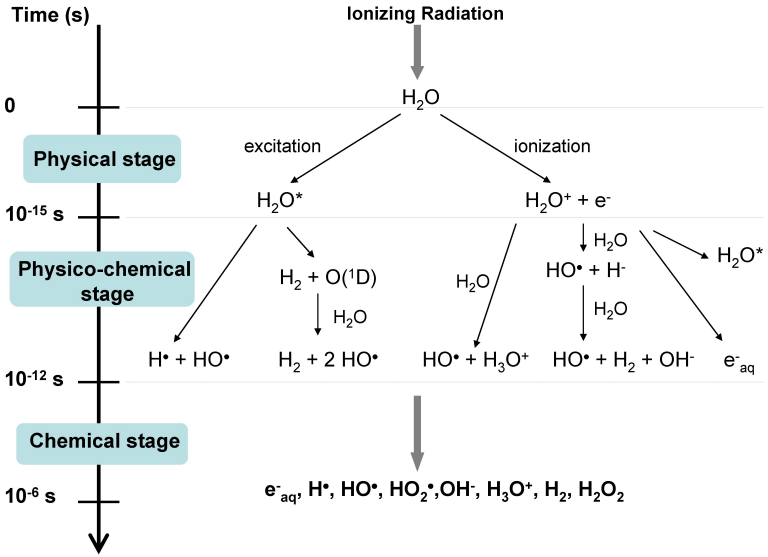
in collaboration with Laurent Desorgher, Flore Chappuis and Sébastien Incerti

FLASH Radiotherapy

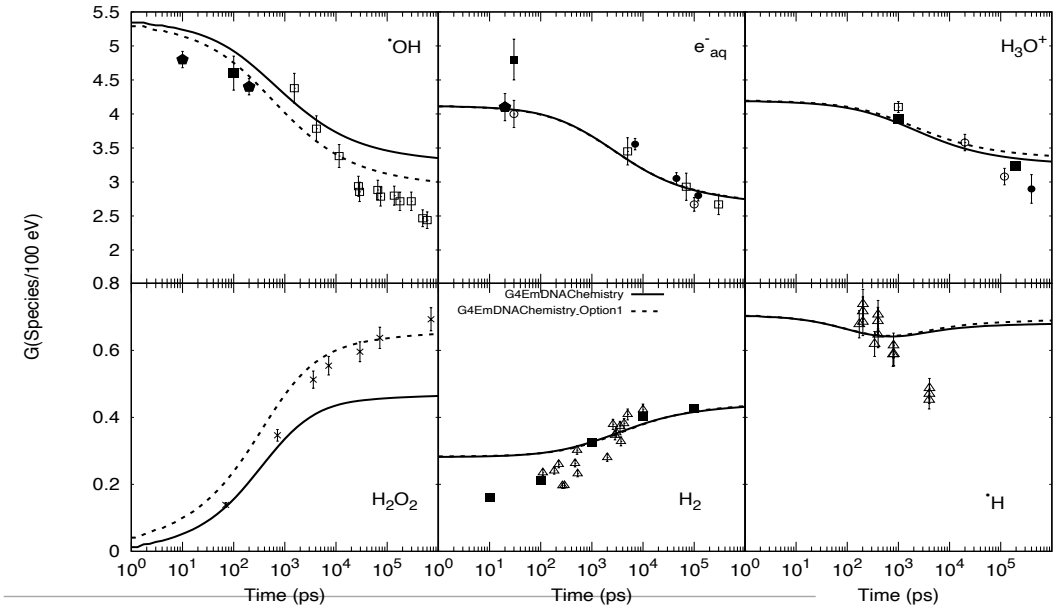
Modeling ultra-high dose rate irradiation requires

- **High radical species concentration**
- **Long time chemical yield evolution (beyond 1 us)**

GEANT4-DNA chemistry



Electronic state	Decay channel	Fraction
All ionization states	$H_2O^+ + H_2O \rightarrow H_3O^+ + {}^\bullet OH$ (through proton transfer)	100 %
Excitation state A1B1: (1b1) → (4a1/3s)	$H_2O^* \rightarrow {}^\bullet OH + H^\bullet$ $H_2O^* \rightarrow H_2O + \Delta E$	65 % 35 %
Excitation state B1A1: (3a1) → (4a1/3s)	$H_2O^* \rightarrow HO^+ + {}^\bullet OH + e^-_{aq}$ $H_2O^* \rightarrow {}^\bullet OH + {}^\bullet OH + H_2$ $H_2O^* \rightarrow H_2O + \Delta E$	55 % 15 % 30 %
Excitation state : Rydberg, diffusion bands	$H_2O^* \rightarrow HO^+ + {}^\bullet OH + e^-_{aq}$ $H_2O^* \rightarrow H_2O + \Delta E$	50 % 50 %

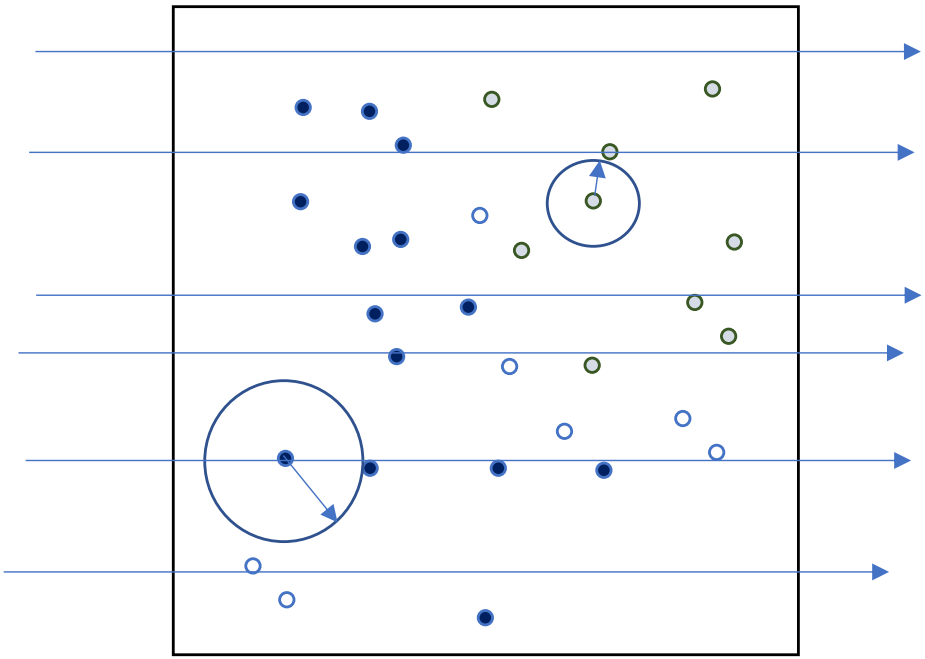


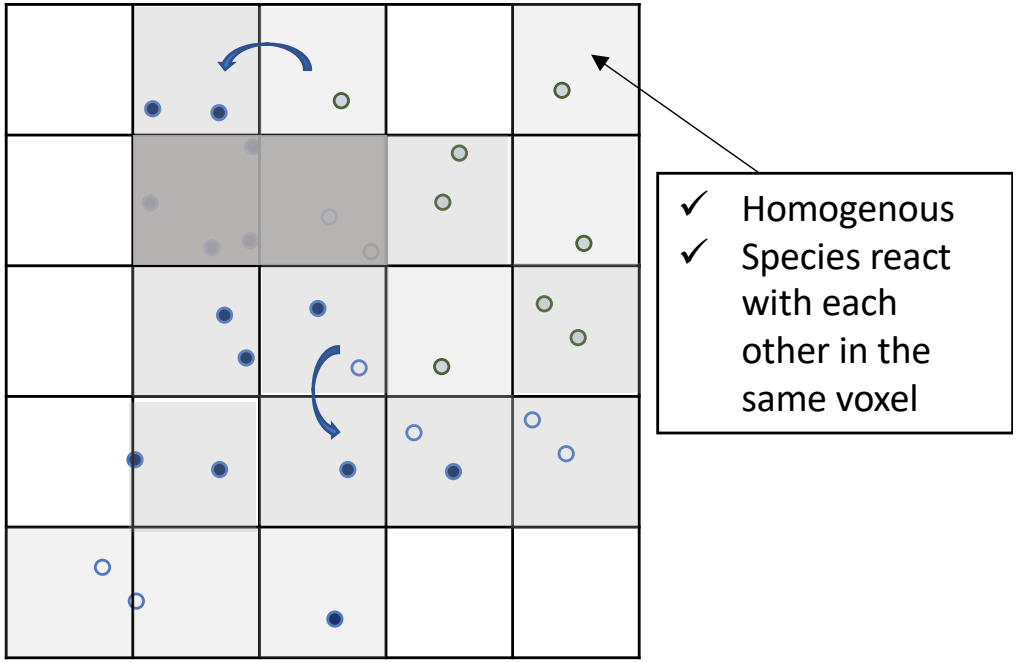
Geant4-DNA: Step by Step (SBS) and Independent Reaction Time (IRT) methods

- Using the dynamic time step model
- Describing the diffusion process corresponding to the Brownian motion (SBS)
- Simplifying the multiple particle problem to the two-particle problem in an approximation (IRT)
- Until 1 us

Computation time is the main drawback

Particle-based model → Compartment-based model





Using Brownian dynamics and Smoluchowski theory

Using Reaction-Diffusion Master Equation (RDME)

Reaction-Diffusion Master Equation

$$\frac{\partial}{\partial t}\mathbb{P}(\boldsymbol{u},t) = \sum_{i=1}^{I}\sum_{r=1}^{R}\left[a_i^r(\mathbf{u}-\boldsymbol{\nu}_{i,r})\,\mathbb{P}(\boldsymbol{u}-\boldsymbol{\nu}_{i,r},t) - a_i^r(\mathbf{u})\,\mathbb{P}(\boldsymbol{u},t)\right] + \sum_{i=1}^{I}\sum_{\substack{j=1\\ j\neq i}}^{I}\sum_{\ell=1}^{L}\left[\lambda_{i,j}^{\ell}\left(u_i^{\ell}(t)+1\right)\mathbb{P}\left(\boldsymbol{u}-\boldsymbol{e}_{i,j}^{\ell},t\right) - \lambda_{i,j}^{\ell}u_i^{\ell}(t)\mathbb{P}(\boldsymbol{u},t)\right],$$

Event-driven simulation using the "Next-Subvolume Method" (NSM):

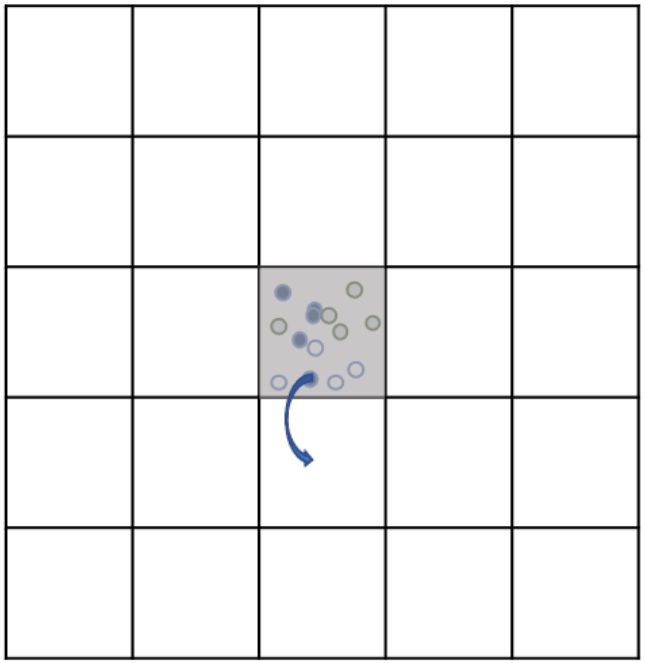
- Calculation of the propensity functions a_i for all voxels
- Sampling of the time when the next event occurs

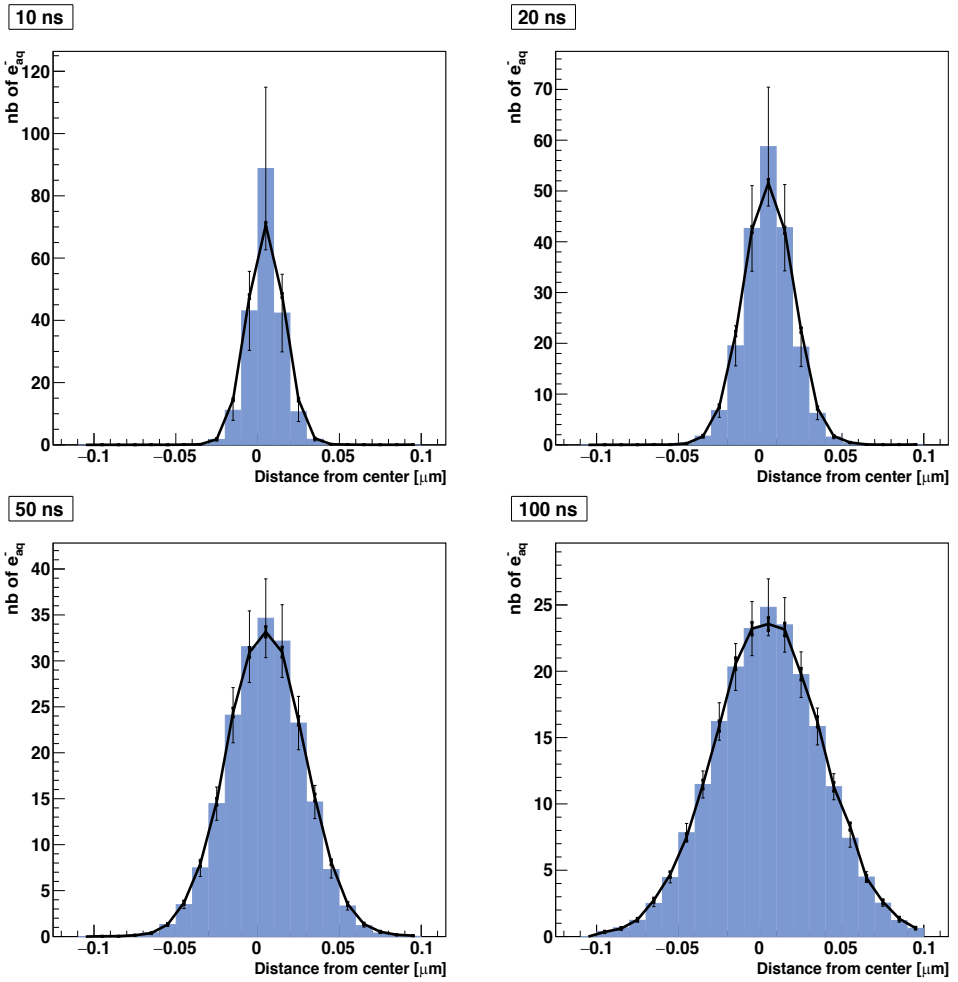
$$\tau_i = \frac{-\ln(\xi)}{a_i}$$

- Sampling which reaction or diffusion will take place according to the propensity function a_i
- Processing the first event in the queue and changing the concentrations in the voxels involved in the event
  - ✓ If the event is a reaction, we eliminate reactants and create products.
  - ✓ If the event is a diffusion, we remove the particle in the voxel where it was located and add the particle in the voxel where it goes.

RDME method (blue histogram) and the SBS (line)

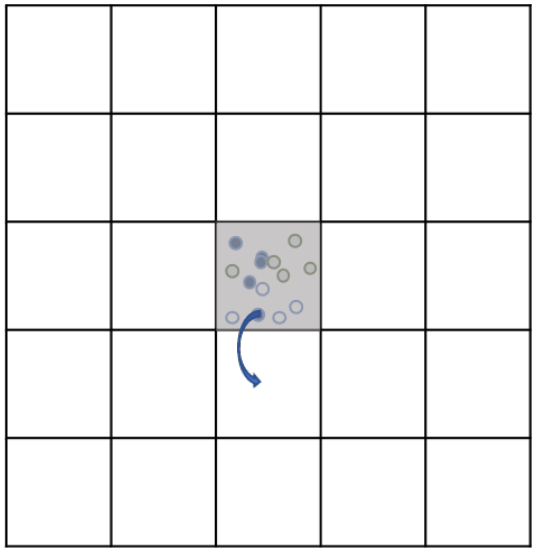
Test 1 : Spatial (radial) distributions of solvated electrons

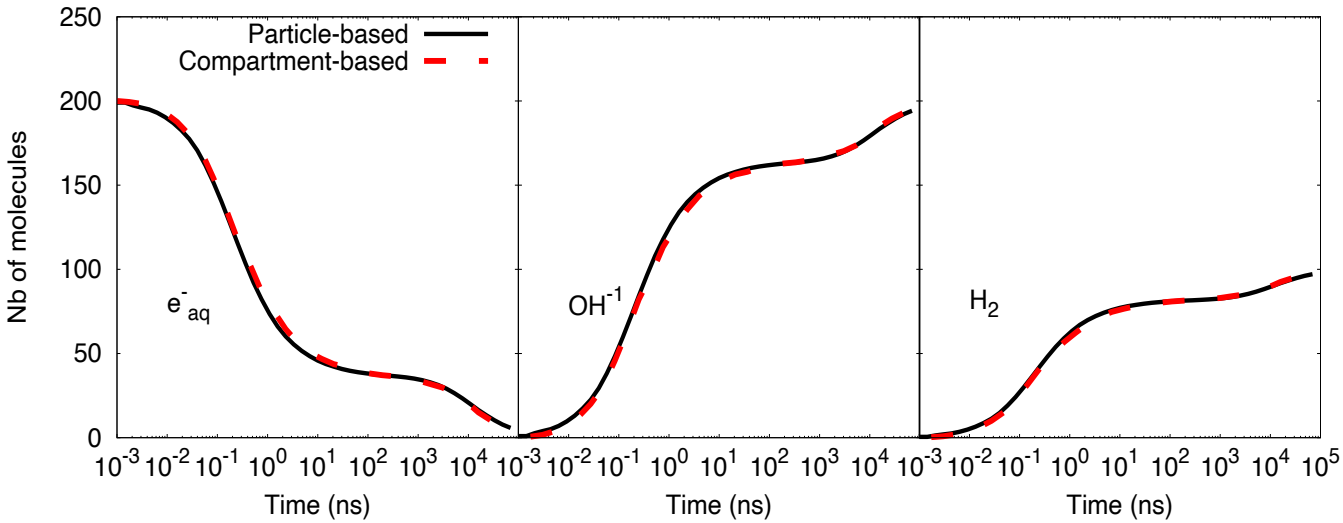




Test 2 : Spatial (radial) distribution and reaction of solvated electrons

$$e^-_{aq} + e^-_{aq} + 2H_2O \rightarrow 2OH^- + H_2$$

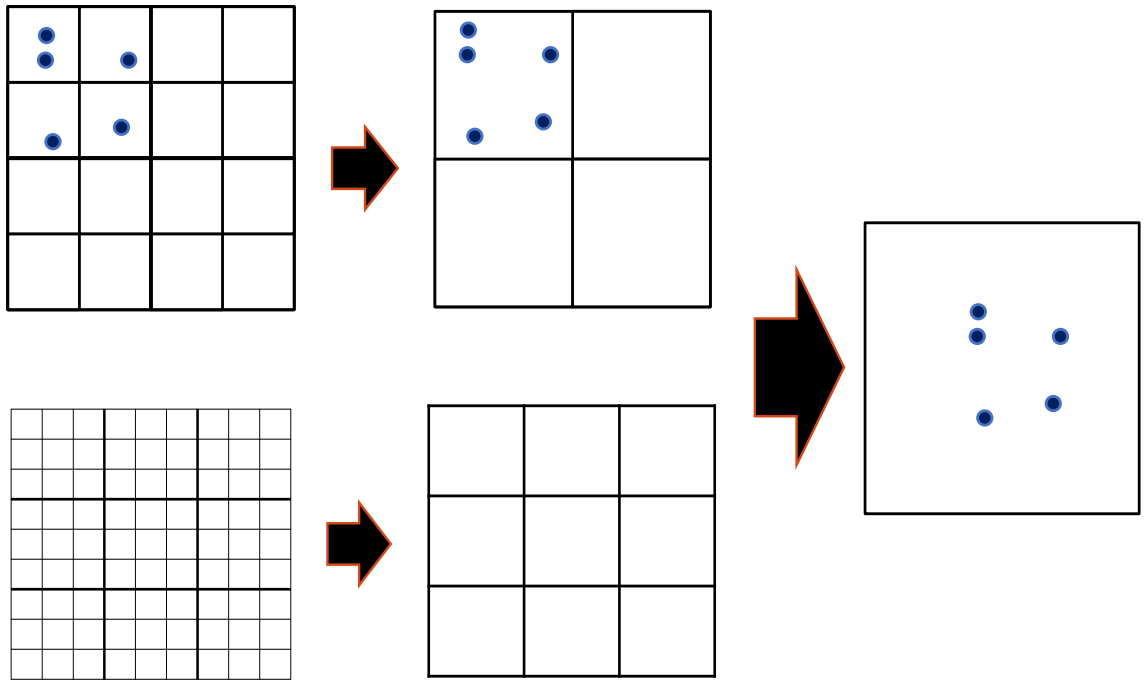




Two main drawbacks of the compartment-based model :

- "Well-mixed" condition
- Computational efficiency and physical validity of the model

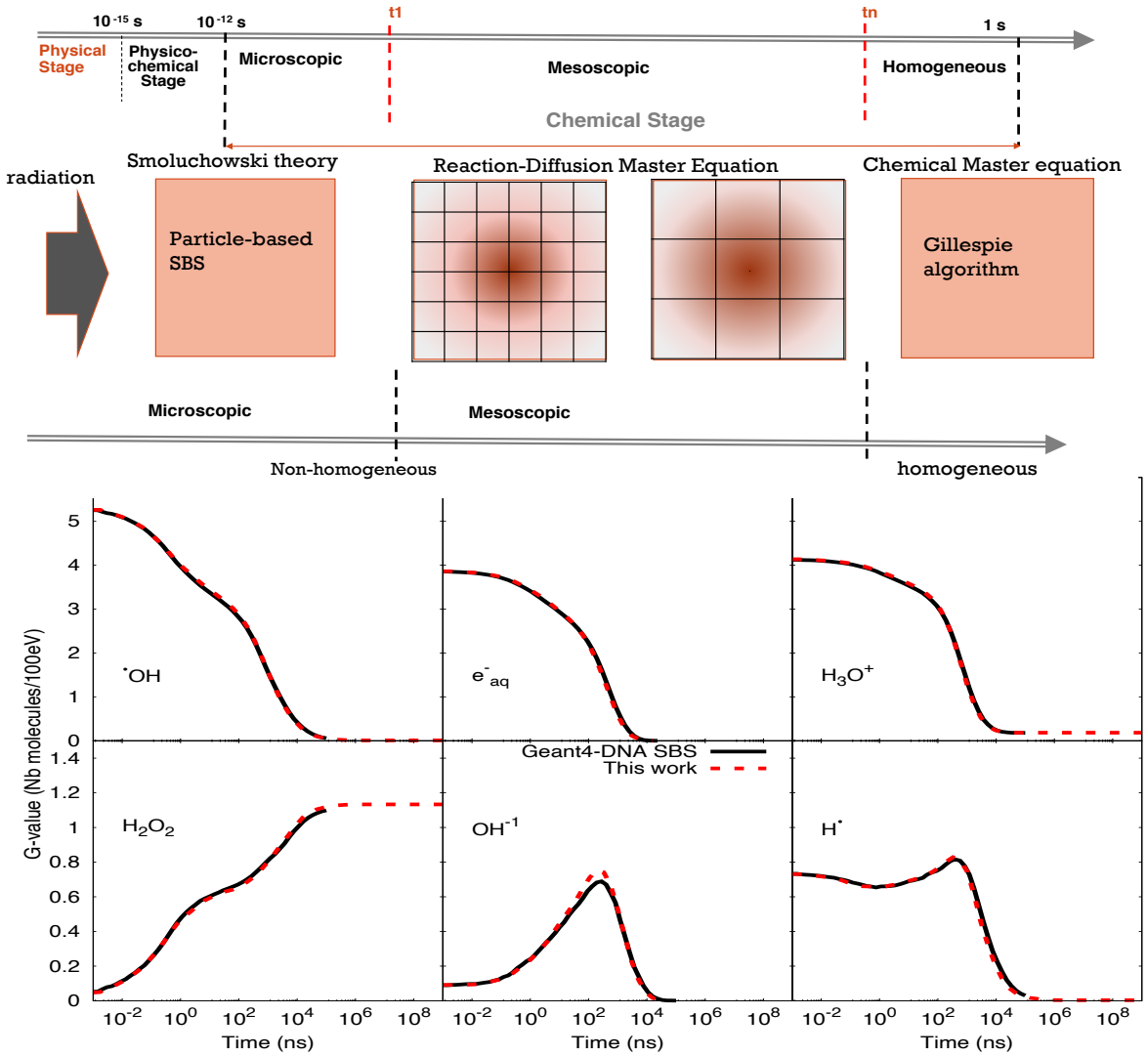
Adaptation of voxel sizes during the evolution time



All species of finer voxels are moved to a larger voxel of a coarser mesh after each "transfer time"

End time	1 ns	10 ns	100 ns	1 µs	10 µs	100 µs
Speedup factor	1.3×10^{1}	1.57×10^{1}	1.65×10^{1}	2.5×10^{2}	2.3×10^{3}	2.3×10^{4}

Combination of the SBS model with the compartment-based model

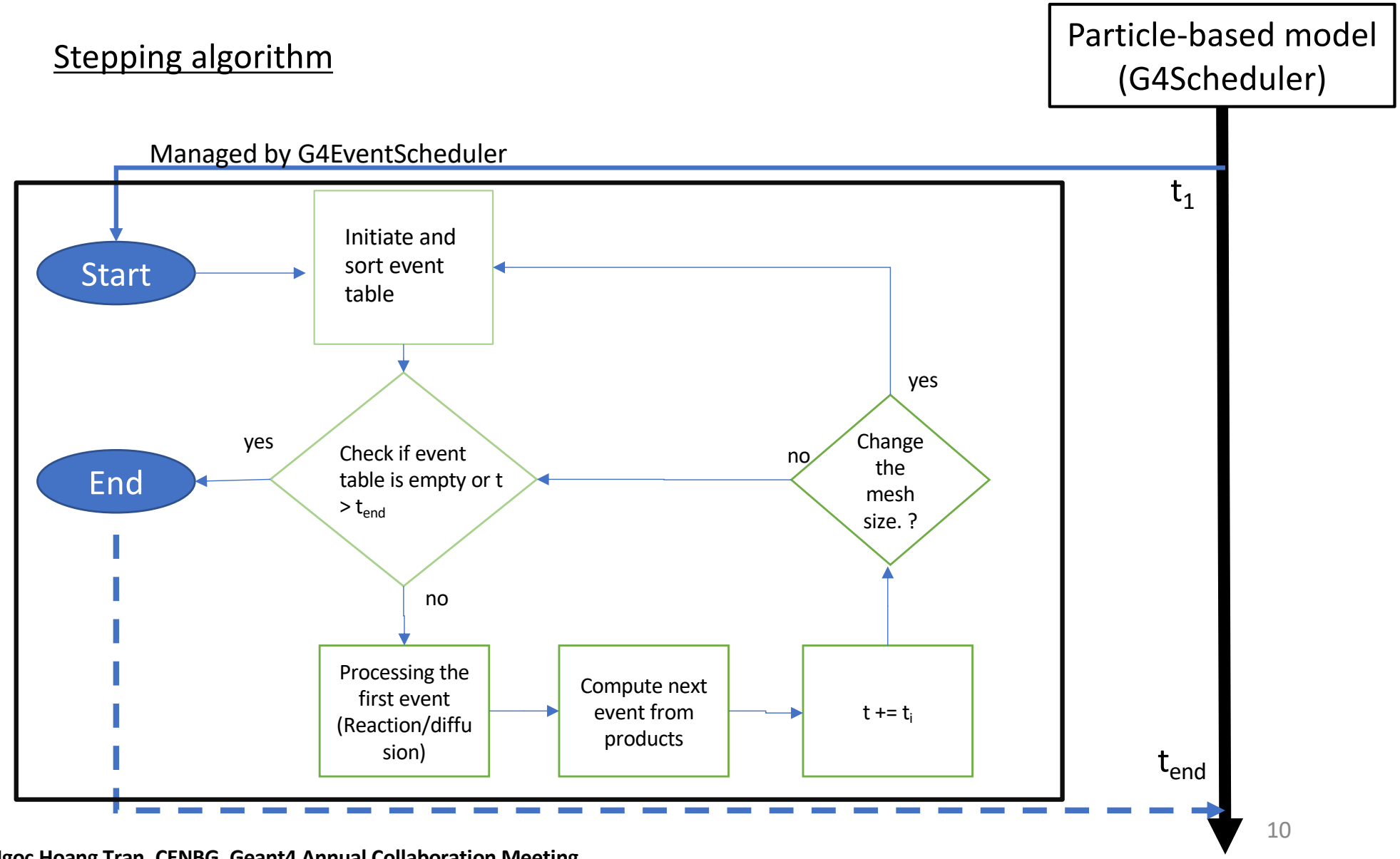


Reaction
$H^{\bullet} + e^-_{aq} + H_2O \rightarrow OH^- + H_2$
$H^{\bullet} + {}^{\bullet}OH \rightarrow H2O$
$H^{\bullet} + H^{\bullet} \rightarrow H2$
$H_2O_2 + e^-_{aq} \rightarrow OH^- + {}^{\bullet}OH$
$H_3O^+ + e^-_{aq} \rightarrow H^{\bullet} + H_2O$
$H_3O^+ + OH^- \rightarrow 2H_2O$
${}^{\bullet}OH + e^-_{aq} \rightarrow OH^-$
${}^{\bullet}OH + {}^{\bullet}OH \rightarrow H_2O_2$
$e^-_{aq} + e^-_{aq} + 2H_2O \rightarrow 2OH^- + H_2$

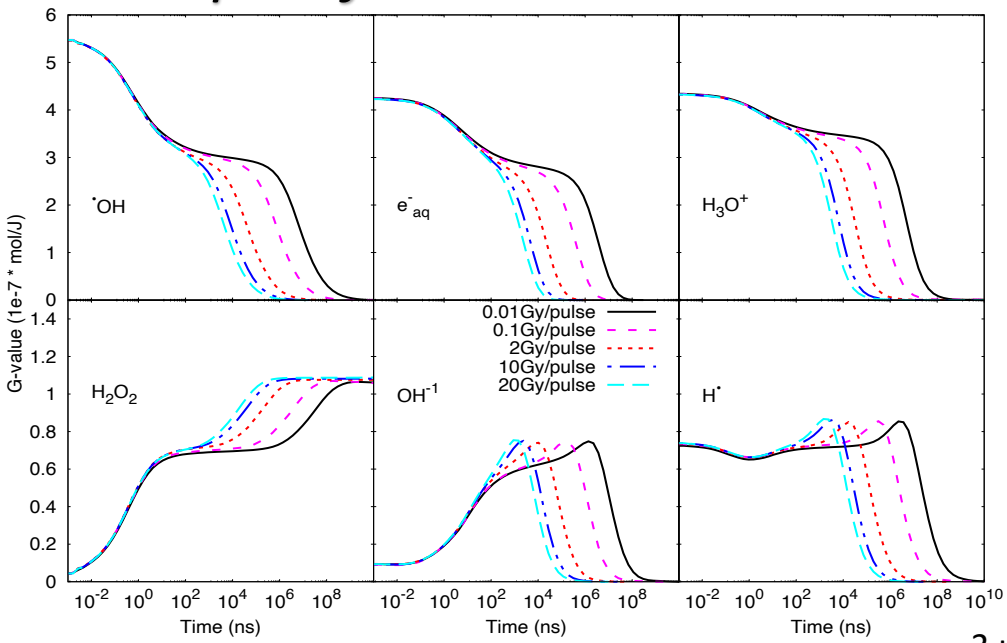
Just published :

Tran et al., Int. J. Mol. Sci. 2021, 22

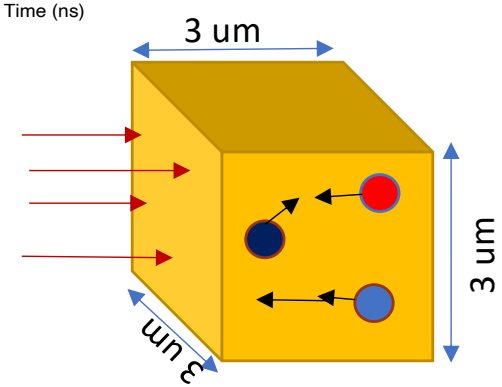
Stepping algorithm

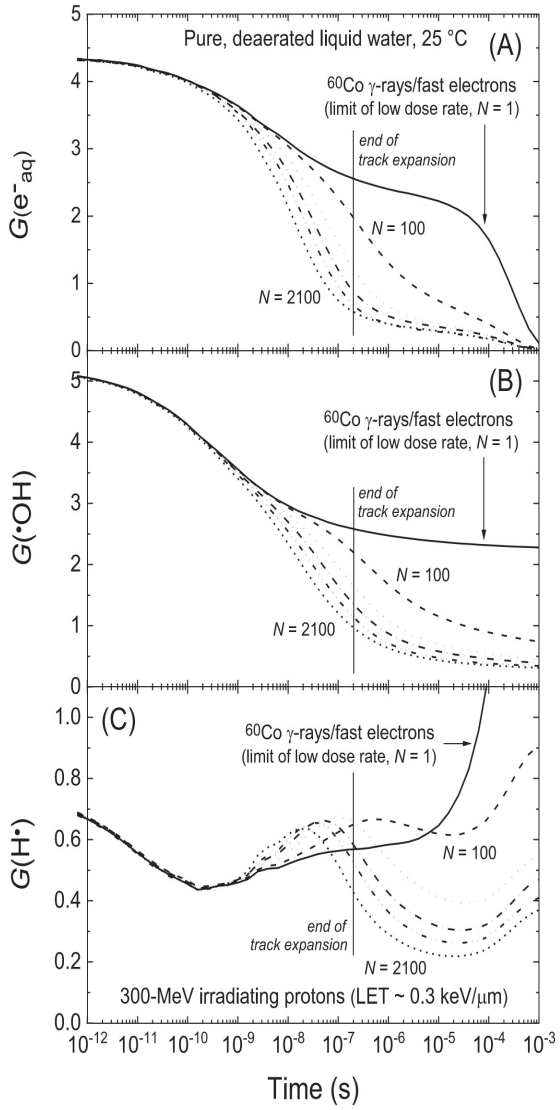


Example of deaerated water



- Electron beam of 1 MeV
- Incident electrons are shot onto the volume until total deposited energy reaches **1-20 Gy (FLASH) or about 0.01 Gy (CONV)**
- Produced species starts **simultaneously** (pulse length not taken into account)
- The results are normalized to the deposited energy using **G-value (mol/J) from 1 ps until reaching steady states**





Alanazi et al. Radiation Research,2021

Conclusion

- Coarse-grained model
- Simulating from heterogeneous -> homogeneous states
- Taking into account secondary reactions at long time (beyond 1 us)

The first prototype of model could be released from version Geant4 11 and feedback is welcome

Thank you very much