UHDR example

geant4-dna.org

Serena Fattori
INFN - LNS, Catania, Italy
serena.fattori@lns.infn.it

Euntaek Yoon
SNUH, South Korea
xmfla0803@gmail.com

Hoang TRAN
LP2i/In2p3/CNRS, Bordeaux, France
tran@lp2ib.in2p3.fr

Geant4-DNA tutorial
Pohang Accelerator Laboratory, Republic of Korea
07/02/2025

Geant4 version 11.3
Released in December 2024

UHDR Example

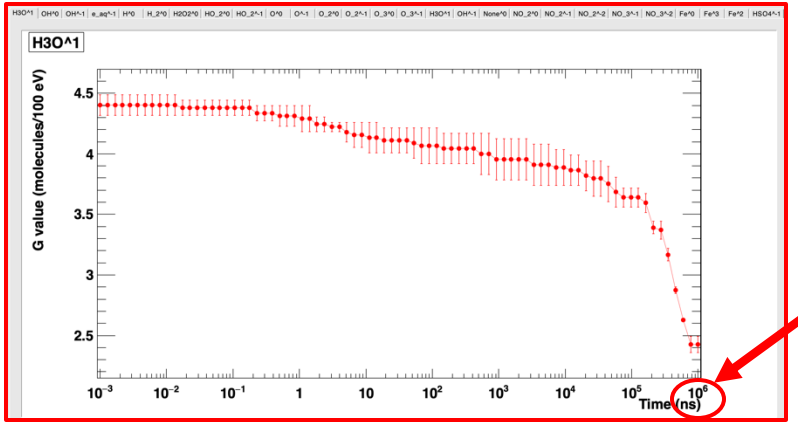
Tran, H. N. et al. (**2021**) Geant4-DNA Modeling of Water Radiolysis beyond the Microsecond: An On-Lattice Stochastic Approach. International Journal of Molecular Sciences, 22(11), 6023. https://doi.org/10.3390/ijms22116023

- ✅ The world is a water box with two possible optimized dimensions
- ✅ The example implements the mesoscopic approach (SBS-RDME)
- ✅ Chemical reactions implemented by builders for specific applications)
- ✅ Scavenger molecules
- ✅ Chemical evolution vs. ph
- ✅ Each event consists of multiple incident particles

As chem6 provides scoring of the radiochemical yield G:

$$G = \frac{\text{Number of species X}}{\text{100 eV of deposited energy}}$$

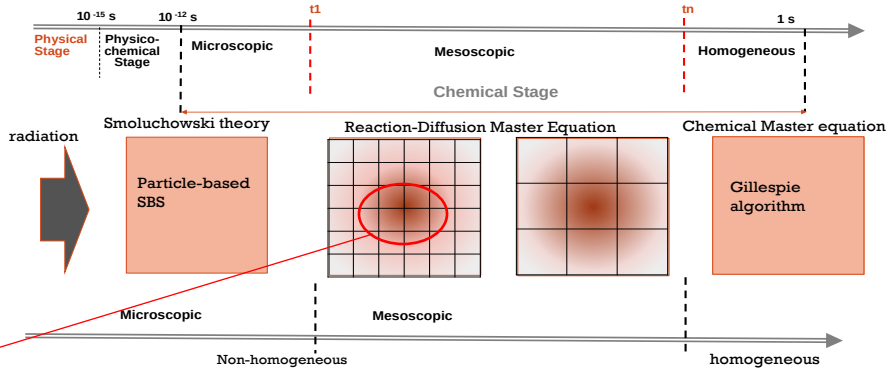
as a function of time.

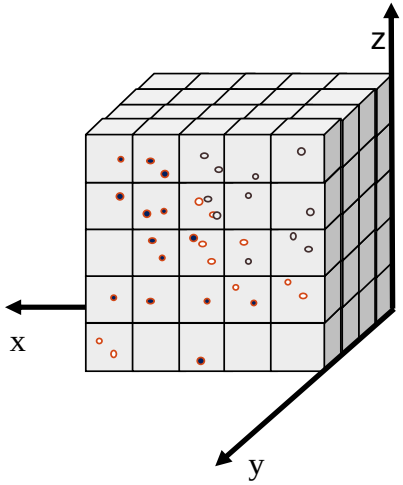


New « UHDR » example

Tran et al., Int. J. Mol. Sci. (2021) 22 (link)

- Use new « mesoscopic » approach
- Coarse-grained model: compartment based ("on-lattice")
- Simulation from heterogeneous to homogeneous states
- pH-dependence of $HO_2^{\bullet}/O_2^{\bullet-}$ kinetics in water
- Developed in Geant4-DNA by the MAGIC Collaboration (CHUV, Switzerland & CNRS/LP2i, France)

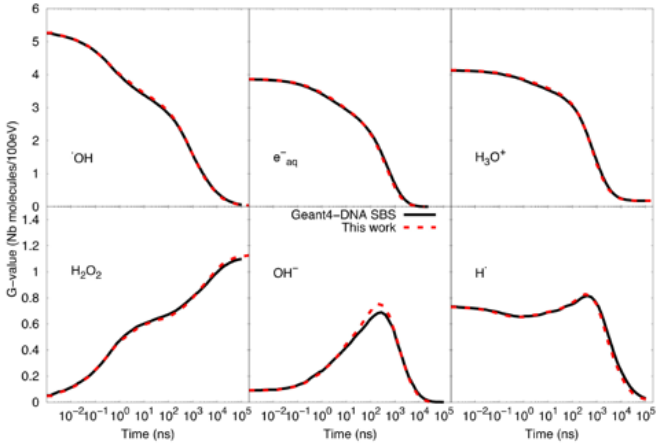




1. *Well mixed species in voxels*
2. *Species can react with each other in the voxels*
3. *Diffusion is modelled by jumps between adjacent voxels*

- Next sub-volume algorithm
- Hierarchical algorithm for the RDME ("hRDME")
- Spatial distributions are simulated at voxel level.
- Coarser meshes over time until we reached the coarsest mesh.

Principle of the combination of the particle-based SBS model with the compartment-based model



User interface

UHDR example provides a user interface to control the simulation :

- Irradiated geometries
- pH control
- Oxygen concentration
- cut-off dose

```
#/run/numberOfThreads 10
/process/dna/e-SolvationSubType Meesungnoen2002
#/process/dna/e-SolvationSubType Ritchie1994
#/process/dna/e-SolvationSubType Terrisol1990

# Set the simulation volume (half Side Length)
#/UHDR/env/volume 0.8 um # for UHDR
/UHDR/env/volume 1.6 um # for CONV

/run/initialize

# time structure (not available)
#/UHDR/pulse/activate true

# pH and Scavenger
/UHDR/env/pH 5.5

# Oxygen concentration
/UHDR/env/scavenger O2 19 %

/chem/reaction/print

#/run/verbose 1
/tracking/verbose 0
/scheduler/verbose 0
/scheduler/endTime 1 ms

# set false if many beamOn in medium
/scheduler/ResetScavengerForEachBeamOn true

/scorer/Gvalues/nOfTimeBins 80

/run/printProgress 10

/scorer/Dose/cutoff 0.01 Gy
/UHDR/source/particle e-
/UHDR/source/energy 0.999 MeV
/run/beamOn 2
```

Irradiated geometries

pH control

oxygen control

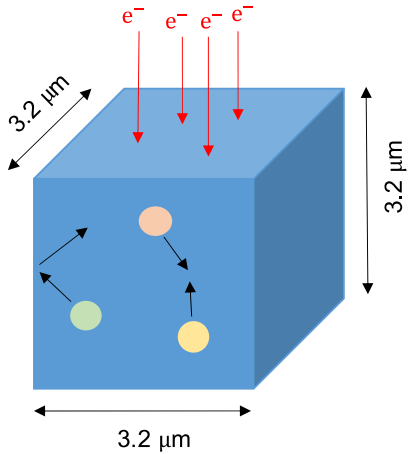
Chemistry simulation controls

Cut-off Dose

Geometry

- Two cubic water volumes of 3.2 x 3.2 x 3.2 µm3 and 1.6 x 1.6 x 1.6 µm3 are used for UHDR and CONV simulations
- Chemical molecules diffuse and react in a bound volume that is, the diffusion is limited by geometrical boundaries.
- The bouncing of chemical molecules on the volume border is applied for both microscopic and mesoscopic sub-stages, depicting a closed system of test cells for in vitro measurements

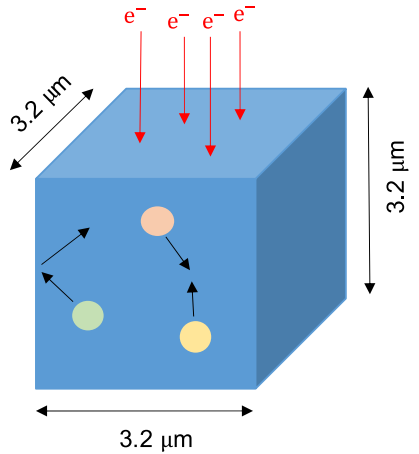
```
# Set the simulation volume (half Side Length)
#/UHDR/env/volume 0.8 um # for UHDR
/UHDR/env/volume 1.6 um # for CONV
```



Particle source

Modelling of ultra-high dose rate (UHDR) electron beams

- Source: 1 MeV electron beam
- Primary electrons are shot at the same time until the sum of all energy deposits in the volume reaches a given absorbed dose ("instantaneous pulse").
- By cumulating the dose until 0.01 Gy (cut-off dose), we define a conventional irradiation (or CONV) and from 1-10 Gy, we define a higher dose rate (or UHDR).
- Electron irradiation until the total energy deposition reaches 1-10 Gy (UHDR) or ~ 0.01 Gy (conventional)
- Instantaneous pulse (all species are produced simultaneously). Pulse duration is not considered. All species are produced simultaneously at 1 ps.



Modalities	Volume (µm³)	Dose rates (Gy/pulse)	Incident electrons (tracks)	deposit energy (keV)
CONV	3.2 x 3.2 x 3.2	0.0109812	6	2.246
UHDR	1.6 x 1.6 x 1.6	1.00273	110	25.637
		5.01636	562	128.254
		10.0076	1063	255.866

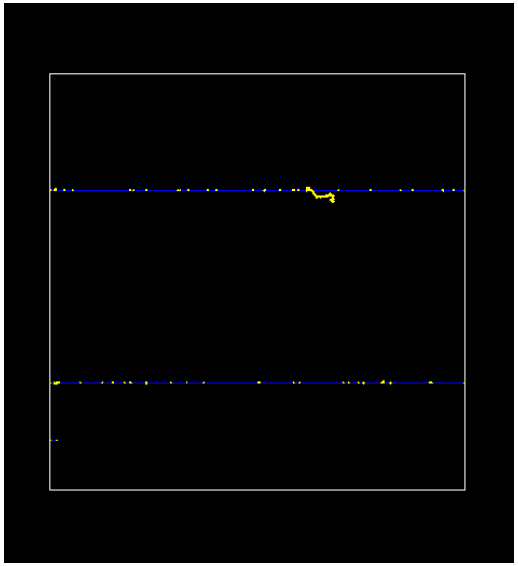
Table 1. An example of simulation setup at different irradiations where the deposit energy and incident electrons are recorded until the dose per pulse corresponding with the irradiated volumes.

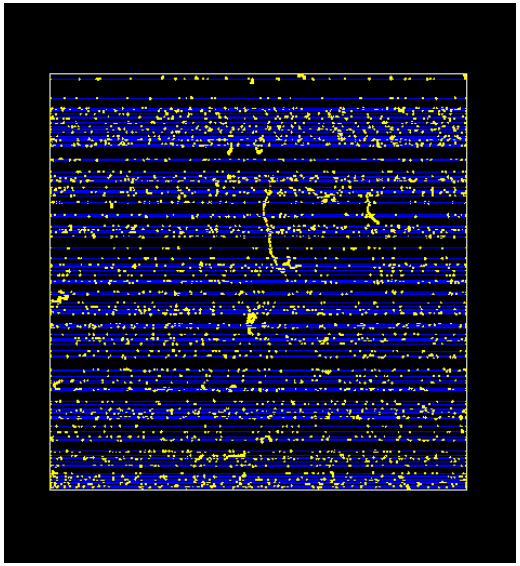
Visualisation

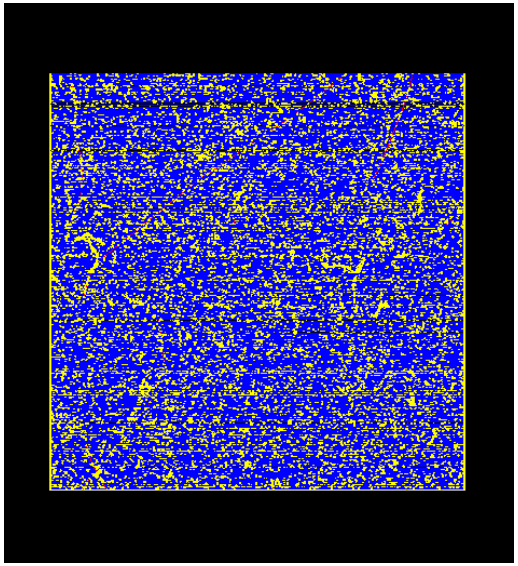
- Proton,100 MeV: 0.01 Gy, 1 Gy, 10 Gy

```
/scorer/Dose/abortedDose 0.05 Gy

/scorer/Dose/cutoff 0.01 Gy
/UHDR/source/particle proton
/UHDR/source/energy 100 MeV
```







« mesoscopic » approach

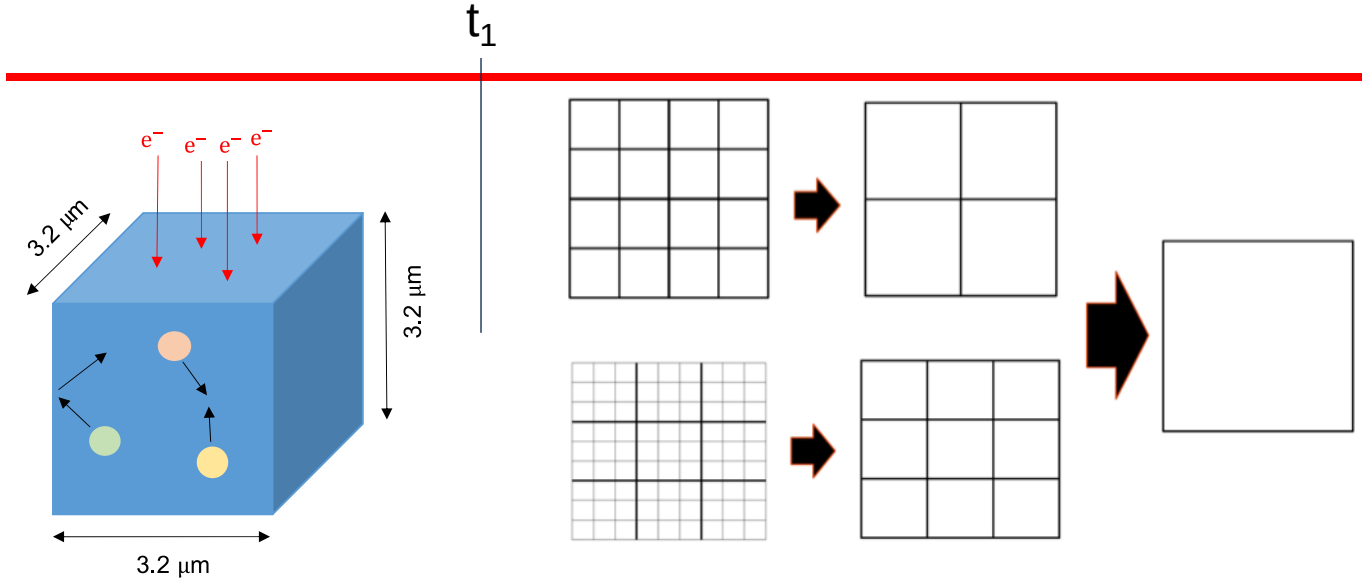


Figure 4. The hRDME approach, here represented in 2D. The mesh of 4^3 voxels (**top**) is moved to 2^3, and then to one voxel. The mesh of 9^3 voxels (**bottom**) is moved to 3^3 and then to one voxel.

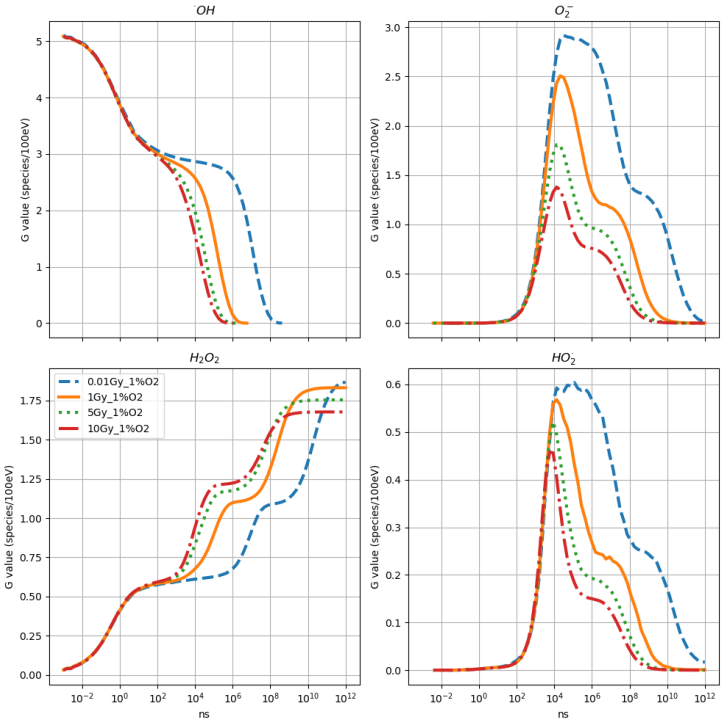
Int. J. Mol. Sci. 2021, 22, 6023

T_1 = 5 ns

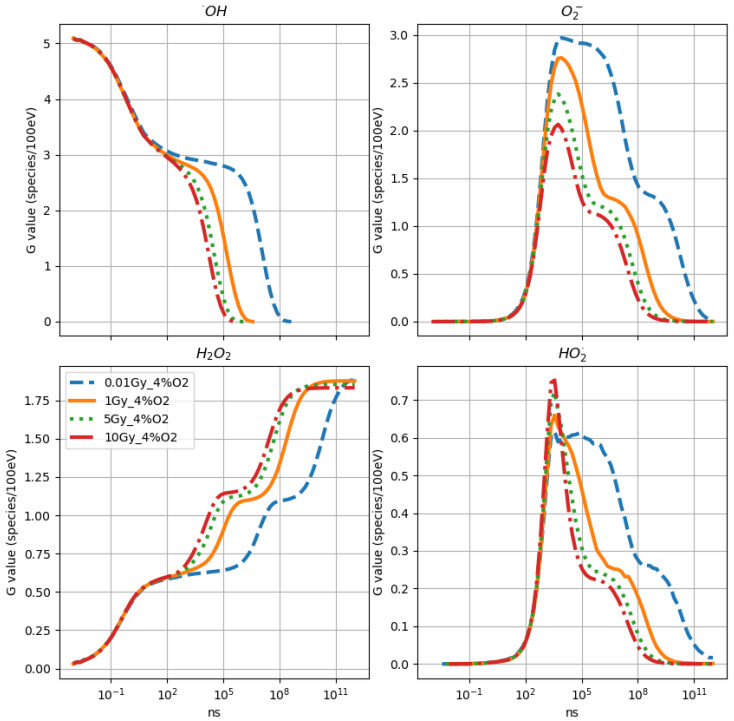
```
G4WT0 > At time :  4.1792 ns  Reaction : °OH^0 (-1964) + °OH^0 (-1804) -> H2O2^0 (-2672)
G4WT0 > At time :  4.2158 ns  Reaction : H3O^1 (-1429) + HO_2^-1 (-2578) -> H2O2^0 (-2673)
G4WT0 > At time :  4.2261 ns  Reaction : °OH^0 (-1922) + °OH^0 (-1896) -> H2O2^0 (-2674)
G4WT0 > At time :  4.2605 ns  Reaction : °OH^0 (-1874) + °OH^0 (-1328) -> H2O2^0 (-2675)
G4WT0 > At time :  4.2978 ns  Reaction : °OH^0 (-1356) + °OH^0 (-1268) -> H2O2^0 (-2678)
G4WT0 > At time :  4.3392 ns  Reaction : H2O2^0 (-2538) + OH^-1 (-2478) -> HO_2^-1 (-2679)
G4WT0 > At time :  4.6044 ns  Reaction : H3O^1 (-1673) + O^-1 (-2588) -> °OH^0 (-2680)
G4WT0 > At time :  4.7143 ns  Reaction : °OH^0 (-2034) + e_aq^-1 (-1213) -> OH^-1 (-2681)
G4WT0 > At time :  4.7683 ns  Reaction : °OH^0 (-1860) + e_aq^-1 (-426) -> OH^-1 (-2682)
G4WT0 > At time :  4.9583 ns  Reaction : H^0 (-2294) + e_aq^-1 (-1096) -> OH^-1 (-2684) + H_2^0 (-2685)
G4WT0 > At Time :  5.0025 ns  the Mesh has 512 x 512 x 512 voxels with Resolution 6.25 nm  during next 93.006 ns
G4WT0 > At time :  5.0641 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.1824 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.1916 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.2799 ns  Reaction : H3O^1 + OH^-1 -> No product
G4WT0 > At time :  5.3877 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.4311 ns  Reaction : e_aq^-1 + O_2^0 -> O_2^-1
G4WT0 > At time :   5.434 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.5869 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :   5.632 ns  Reaction : e_aq^-1 + e_aq^-1 -> OH^-1 + OH^-1 + H_2^0
G4WT0 > At time :  5.7071 ns  Reaction : e_aq^-1 + °OH^0 -> OH^-1
G4WT0 > At time :  5.7311 ns  Reaction : H3O^1 + OH^-1 -> No product
G4WT0 > At time :  5.7387 ns  Reaction : e_aq^-1 + H3O^1 -> H^0
```

Simulations

1% O2



4% O2



Dissolved Oxygen in Water

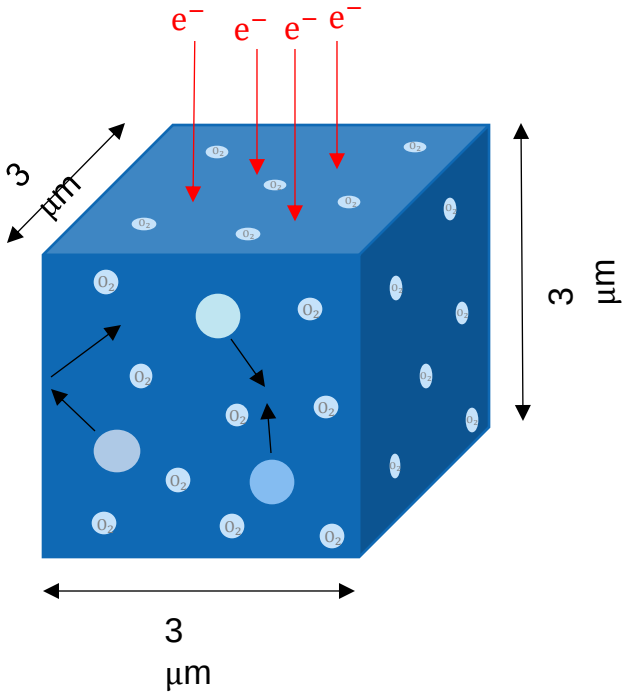
Modelling oxygen as a continuum

$$\frac{dX}{dt} = -k\,[O_2]\,X$$

X = concentration of species X [M]

k = reaction rate $[M^{-1}s^{-1}]$

$[O_2]$ = concentration of oxygen [M]



- Homogeneous distribution of oxygen
- Variation of $[O_2]$ over time
- partially oxygenated water is converted to concentration

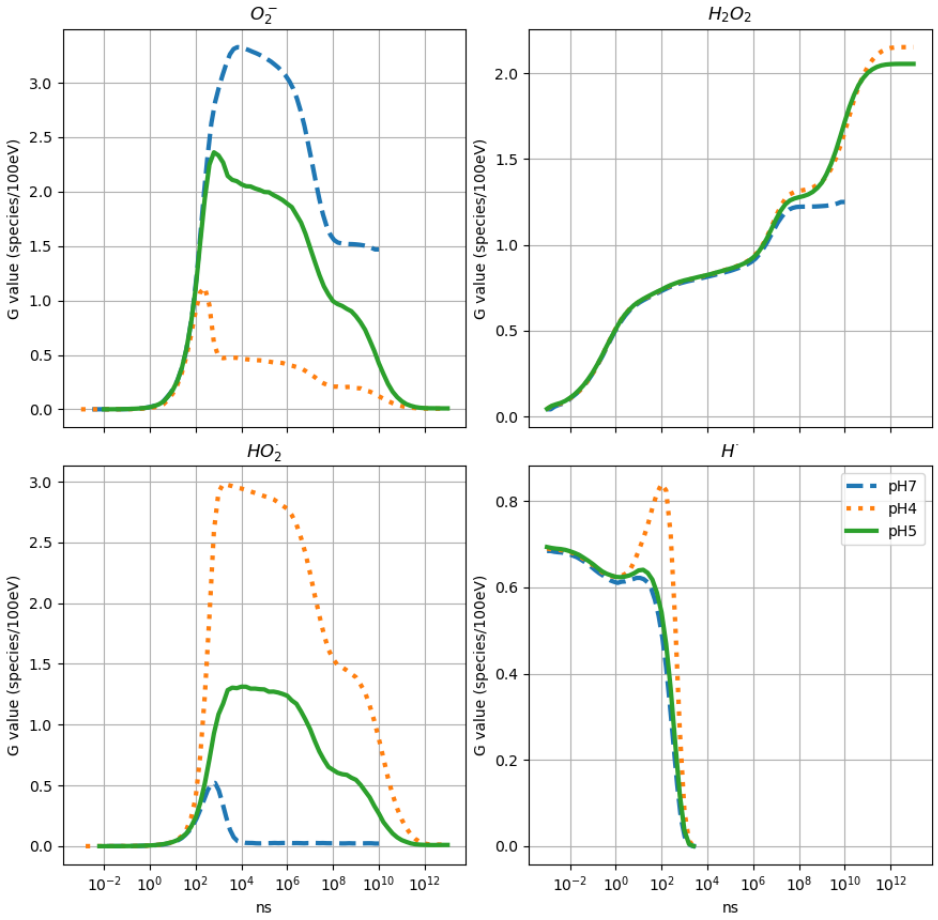
```
# Oxygen concentration
/UHDR/env/scavenger O2 19 %
```

pH simulation

#	Equilibrium	pKa
1	$2H_2O \leftrightarrow OH^- + H_3O^+$	13.999
2	$H_2O_2 + H_2O \leftrightarrow HO_2^- + H_3O^+$	11.65
3	$^{\bullet}OH + H_2O \leftrightarrow O^- + H_3O^+$	11.9
4	$HO_2 + H_2O \leftrightarrow O_2^- + H_3O^+$	4.57
5	$H + H_2O \leftrightarrow e^-_{aq} + H_3O^+$	9.77

- The products of primary and secondary reactions can participate in equilibrium reactions which are associated with pKa (see the table)
- Based on the H3O+ and OH- ion concentrations determined by the pH, acid-base reactions associated with these pKa are simulated

```
# pH and Scavenger
/UHDR/env/pH 5.5
```



Acid-base reactions

Acid-base reactions associated with pKa at 25 °C. $[H_2O]$ = 55.3 M. k_{-1} and k_1 represent opposite directions in the first equilibrium process.

#	Acid-Base reactions	Rate coefficients and corresponding references	
1	$HO_2 \rightarrow H_3O^+ + O_2^-$	$k_{-1} * K_4$	7.58e5 s^{-1}
–1	$H_3O^+ + O_2^- \rightarrow HO_2$	[Elliot, 1994]	4.78e10 $M^{-1}s^{-1}$
2	$H \rightarrow e^-_{aq} + H_3O^+$	$k_{-2} * K_5$	6.32 s^{-1}
–2	$e^-_{aq} + H_3O^+ \rightarrow H^\bullet$	[Elliot, 1994]	2.25e10 $M^{-1}s^{-1}$
3	$e^-_{aq} + H_2O \rightarrow H^\bullet + OH^-$	$k_{-3} * K_1 / (K_5 * [H_2O])]$	1.57e1 $M^{-1}s^{-1}$
–3	$H^\bullet + OH^- \rightarrow H_2O + e^-_{aq}$	[Elliot, 1994]	2.49e7 $M^{-1}s^{-1}$
4	$O_2^- + H_2O \rightarrow HO_2 + OH^-$	$k_{-4} * K_1 / (K_4 * [H_2O])]$	0.15 $M^{-1}s^{-1}$
–4	$HO_2 + OH^- \rightarrow O_2^- + H_2O$	[Elliot, 1994]	1.27e10 $M^{-1}s^{-1}$
5	$HO_2^- + H_2O \rightarrow H_2O_2 + OH^-$	$k_{-5} * K_1 / (K_2 * [H_2O])]$	1.36e6 $M^{-1}s^{-1}$
–5	$H_2O_2 + OH^- \rightarrow HO_2^- + H_2O$	[Elliot, 1994]	1.27e10 $M^{-1}s^{-1}$
6	$O^- + H_2O \rightarrow OH + OH^-$	$k_{-6} * K_1 / (K_3 * [H_2O])]$	1.8e6 $M^{-1}s^{-1}$
–6	$OH + OH^- \rightarrow O^- + H_2O$	[Elliot, 1994]	1.27e10 $M^{-1}s^{-1}$
7	$H_2O_2 \rightarrow H_3O^+ + HO_2^-$	$k_{-7} * K_2$	7.86e-2 s^{-1}
–7	$HO_2^- + H_3O^+ \rightarrow H2O2$	[Elliot, 1994]	4.78e10 $M^{-1}s^{-1}$
8	$^\bullet OH \rightarrow O^- + H_3O^+$	$k_{-8} * K_3$	0.0602 s^{-1}
–8	$O^- + H_3O^+ \rightarrow OH$	[Elliot, 1994]	9.56e10 $M^{-1}s^{-1}$

Chemistry Builders

Chemical reactions can be grouped by different chemistry builders. Depend on user application, these builder can be used. UHDR provides 5 default builders.

- ChemPureWaterBuilder::WaterScavengerReaction to simulate acid-base reactions associated with pH
- ChemOxygenWaterBuilder::OxygenScavengerReaction to simulate the reactions with oxygen.
- ChemOxygenWaterBuilder:: SecondOrderReactionExtended to simulate secondary reaction
- ChemNO2_NO3ScavengerBuilder::NO2_NO3ScavengerReaction to simulate NO2+/NO3+
- ChemFrickeReactionBuilder::FrickeDosimeterReaction to simulate Fricke dosimeter