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TOPAS-nBio for water radiolysis simulation

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8/14/18

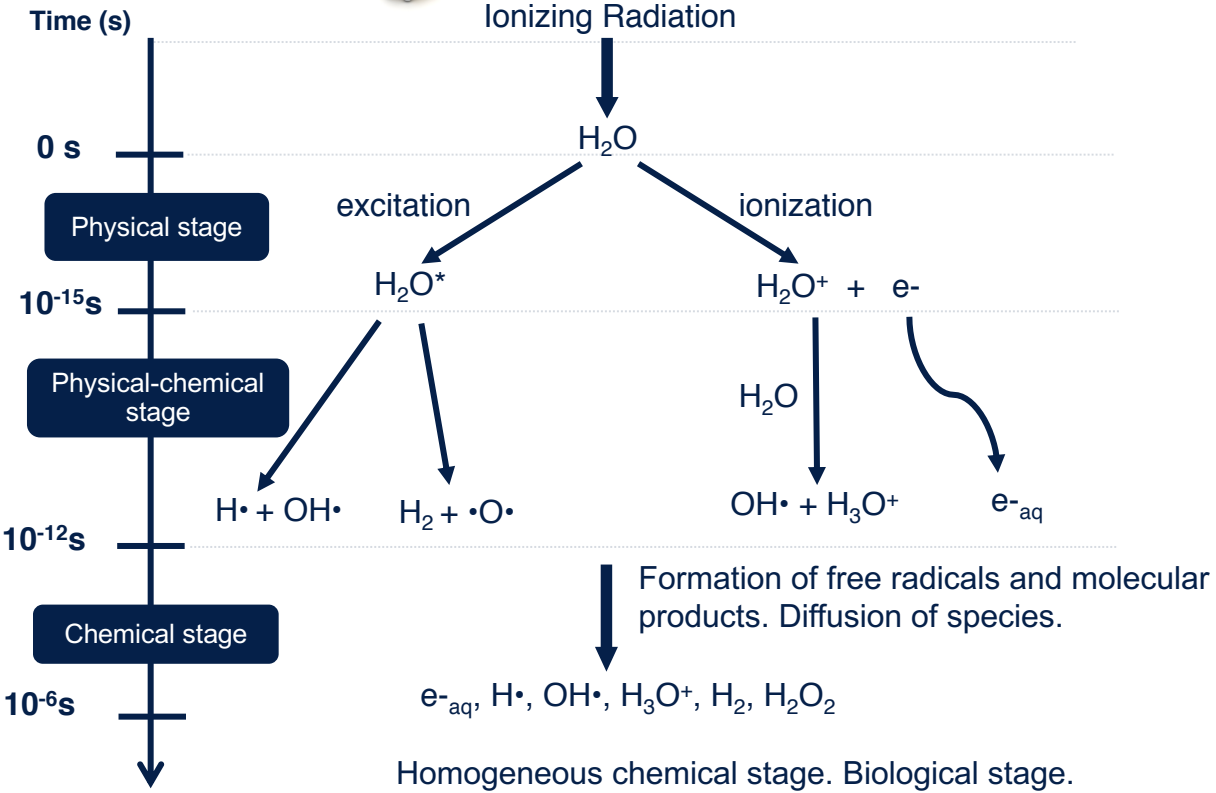
TOPAS nBio

Outline

What?

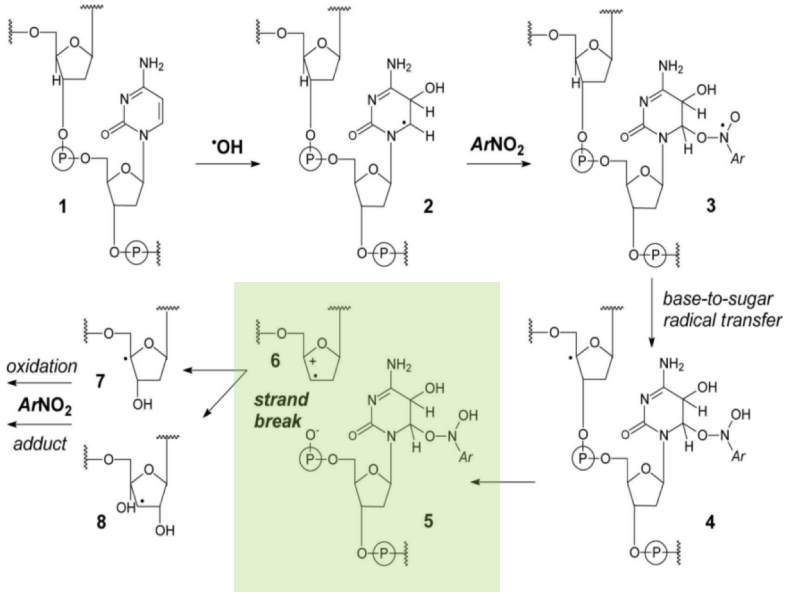
Why?

How?


Time (s)
Ionizing Radiation
0 s
H_2O
Physical stage
excitation
ionization
10^{-15}s
H_2O^*
H_2O^+ + e-
Physical-chemical stage
H_2O
$H^\bullet + OH^\bullet$
$H_2 + {}^\bullet O^\bullet$
$OH^\bullet + H_3O^+$
e^-_{aq}
10^{-12}s
Formation of free radicals and molecular products. Diffusion of species.
Chemical stage
10^{-6}s
e^-_{aq}, $H^\bullet$, $OH^\bullet$, H_3O^+, H_2, H_2O_2
Homogeneous chemical stage. Biological stage.

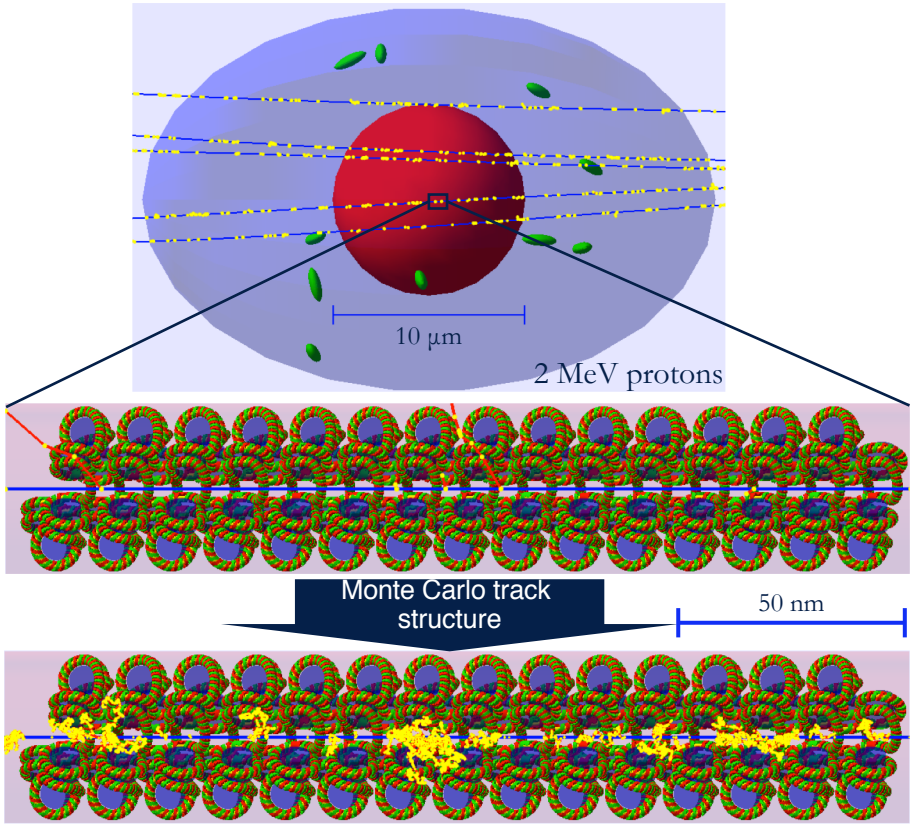
Radiolysis of water

- DNA damage.
  - Formation of single-strand breaks.
  - Identification of clustered damage.
- Free radicals in radiation biology
  - Reactive oxygen
  - Radical repair by thiols
  - Cell signaling and bystander response
- Cancer treatment and diagnosis
  - Radiosensitizers –nitric oxide
  - Hypoxia
  - Radiation detector – Fricke dosimeter

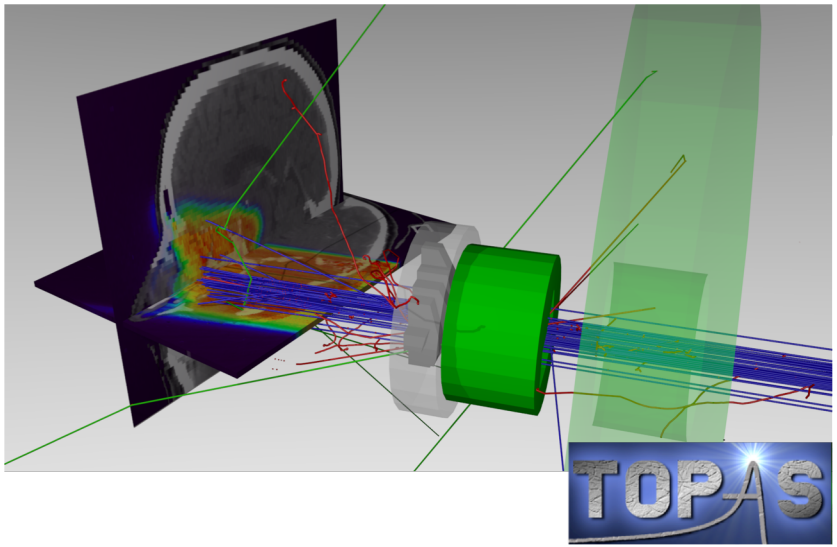


Formation of single-strand breaks by reaction of hydroxyl radical adducts of DNA bases with nitroimidazoles. From O'Nell and Wardman 2009, based on extensive search survey by von Sonntag (2006), *cf.* (Bamatraf et al. 1998, Wardman 2007a, 2009b)

Radiolysis of water



Condensed-history Monte Carlo



Radiolysis of water

- Track structure Monte Carlo codes are usually difficult to obtain.
- Geant4 Collaboration's[1] project: Geant4-DNA[2,3].
  - Steep learning curve.
- University of California San Francisco, Massachusetts General Hospital & SLAC National Laboratory developed TOPAS[3] to facilitate MC for radiotherapy.
- TOPAS-nBio[4,5,6] to facilitate MC track-structure simulations.

[1]Agostinelli, S. *et al.* (2003) *Nucl. Inst. and Methods in Phys. Res. A,* 506(3), 250–303.
[2]Incerti, S. *et al.* (2010) *Med. Phys.*, 37(9), 4692–4708.
[3]Bernal, M. A. *et al.* (2015) *Physica Medica*, 31(8), 861–74.
[4]Perl, J. *et al.* (2012) *Med. Phys.*, 39, 6818–6837.
[5]McNamara, A. *et al.* (2017) '', *Physica Medica*, 33, 207–215.
[6]Ramos-Mendez, J. *et al.* (2018) *Phys. Med. Biol.*. doi:10.1088/1361-6560/aac04c.

TOPAS-nBio Monte Carlo track structure simulations

Physics Stage
step-by-step modeling of **physics interactions** of incoming & secondary radiation with biological medium

- Excited **water molecules**
- Ionized **water molecules**
- Solvated **electrons**

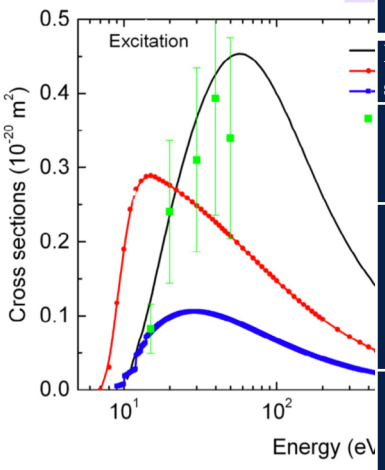
Physicochemical/chemistry Stage
- Radical species production
- Diffusion
- Mutual interaction

Karamitros M. *et al.* (2014) *J. Comput. Phys.* 272, 686–703

Karamitros M. *et al.* (2011) *Phys. Med. Biol.* 56, 7475–7487

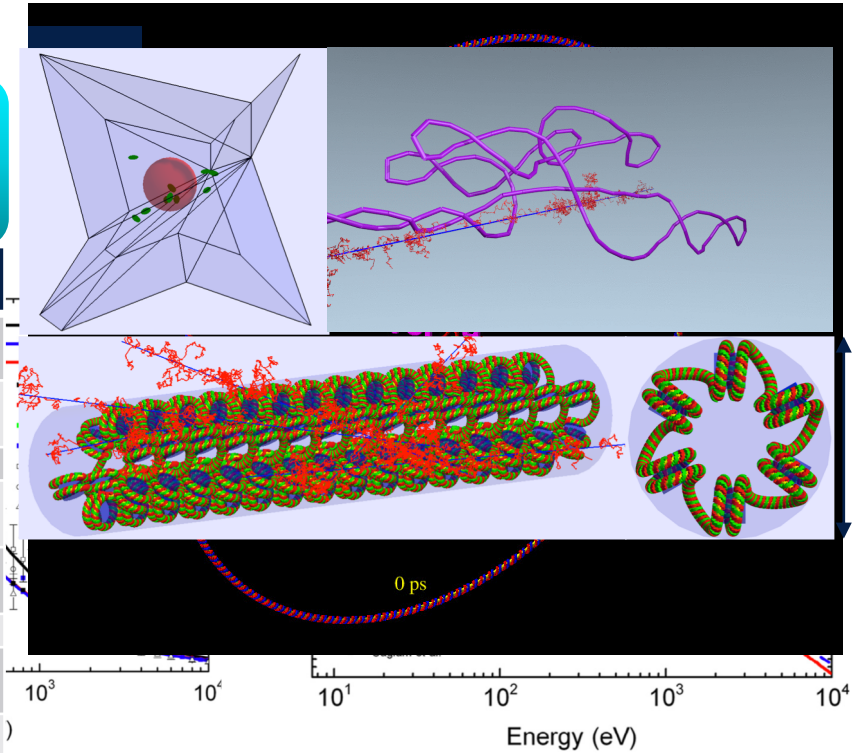
Incerti S. *et al.* (2010) *Med. Phys.* 37, 4692–4708

Incerti S. *et al.* (2010) *Int. J. Model. Simul. Sci. Comput.* 1, 157–178

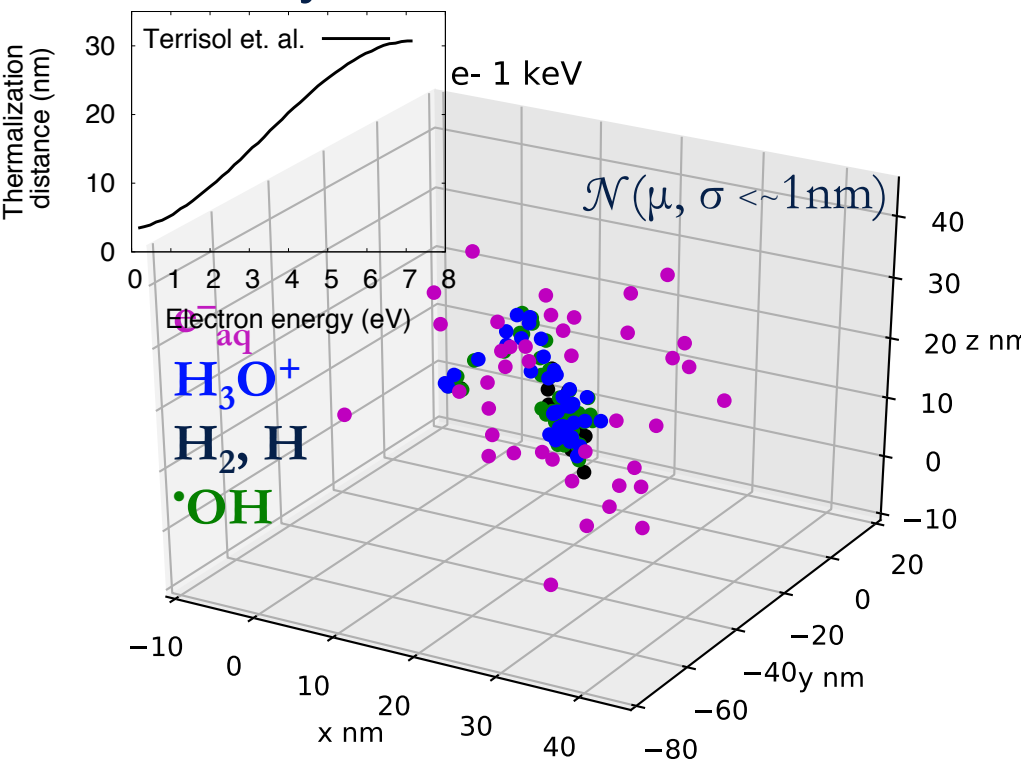


Process		Decay channel	Prob (%)
Ionization state	Dissociative decay	$H_3O^+ + {}^{\bullet}OH$	100
A^1B_1	Dissociative decay	${}^{\bullet}OH + H^{\bullet}$	65
	Relaxation	$H_2O + \Delta E$	35
B^1A_1	Auto-ionization	$H_3O^+ + {}^{\bullet}OH + e^-_{aq}$	55
	Auto-ionization	${}^{\bullet}OH + {}^{\bullet}OH + H_2$	15
	Relaxation	$H_2O + \Delta E$	30
Rydberg, diffuse bands	Auto-ionization	$H_3O^+ + {}^{\bullet}OH + e^-_{aq}$	50
	Relaxation	$H_2O + \Delta E$	50

Mechanistic Biological modeling



Radiolysis of water – *Pre-chemical stage (10^{-15}-10^{-12}s)*



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A^1B_1	Dissociative decay	${}^\bullet OH + H^\bullet$	65
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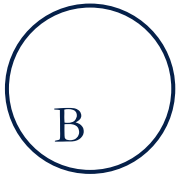
	Auto-ionization	${}^\bullet OH + {}^\bullet OH + H_2$	15
	Relaxation	$H_2O + \Delta E$	30
Rydberg, diffuse bands	Auto-ionization	$H_3O^+ + {}^\bullet OH + e^-_{aq}$	50
	Relaxation	$H_2O + \Delta E$	50

Radiolysis of water – *Chemical stage (10^{-12}-10^{-6}s)*

- Species move under Brownian motion
- Totally diffusion-controlled reactions

$$A + B \xrightarrow{k} \text{Products}$$



$d < 2\,k/4\pi(D_A+D_B)$

$$p(\mathbf{r},t|\mathbf{r_0}) = \frac{1}{(4\pi Dt)^{n/2}}\exp\left[-\frac{(\mathbf{r}-\mathbf{r_0})^2}{4Dt}\right]$$

Radiolysis of water – *Chemical stage (10^{-12}-10^{-6}s)*

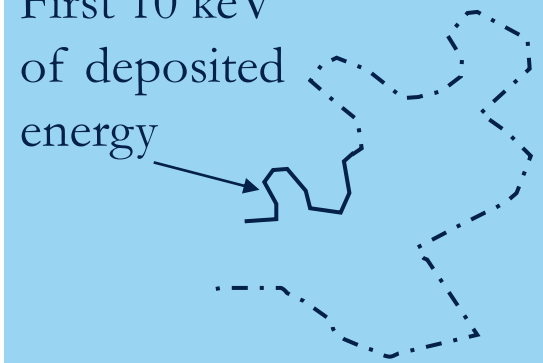
Reaction	Reaction rate constant k_{obs} (10^{10} $M^{-1}s^{-1}$)	
	Geant4-DNA Default	TOPAS-nBio
$e^-_{aq} + e^-_{aq} \rightarrow H_2 + 2OH^-$	0.5	0.647
$e^-_{aq} + {}^{\bullet}OH \rightarrow OH^-$	2.95	2.95
$e^-_{aq} + H^{\bullet} \rightarrow H_2 + OH^-$	2.65	2.65
$e^-_{aq} + H_3O^+ \rightarrow H^{\bullet}$	2.11	2.11
$e^-_{aq} + H_2O_2 \rightarrow OH^- + {}^{\bullet}OH$	1.41	1.41
${}^{\bullet}OH + {}^{\bullet}OH \rightarrow H_2O_2$	0.44	0.475
${}^{\bullet}OH + H^{\bullet} \rightarrow H_2O$	1.44	1.44
$H^{\bullet} + H^{\bullet} \rightarrow H_2$	1.2	0.503
$H_3O^+ + OH^- \rightarrow H_2O$	14.3	11.0
${}^{\bullet}OH + H_2 \rightarrow H$	–	0.0045
${}^{\bullet}OH + H_2O_2 \rightarrow HO_2$	–	0.0023
${}^{\bullet}OH + HO_2 \rightarrow O_2$	–	1.0
${}^{\bullet}OH + O_2^- \rightarrow O_2 + OH^-$	–	0.9
${}^{\bullet}OH + HO_2^- \rightarrow HO_2 + OH^-$	–	0.5
$e^-_{aq} + HO_2 \rightarrow HO_2-$	–	2.0
$e^-_{aq} + O_2 \rightarrow O_2^-$	–	1.9
$e^-_{aq} + O_2^- \rightarrow OH^- + HO_2^-$	–	1.3
${}^{\bullet}H + H_2O_2 \rightarrow {}^{\bullet}OH$	–	0.01
${}^{\bullet}H + HO_2 \rightarrow H_2O_2$	–	2.0
${}^{\bullet}H + O_2 \rightarrow HO_2$	–	2.0
$H + OH- \rightarrow e^-_{aq}$	–	0.002
$H + O_2^- \rightarrow HO_2^-$	–	2.0
$H_3O^+ + O_2- \rightarrow HO_2$	–	3.0
$H_3O^+ + HO_2- \rightarrow H_2O_2$	–	2.0
$HO_2 + HO_2 \rightarrow H_2O_2 + O_2$	–	0.000076
$HO_2 + O_2- \rightarrow O2 + HO_2^-$	–	0.00274

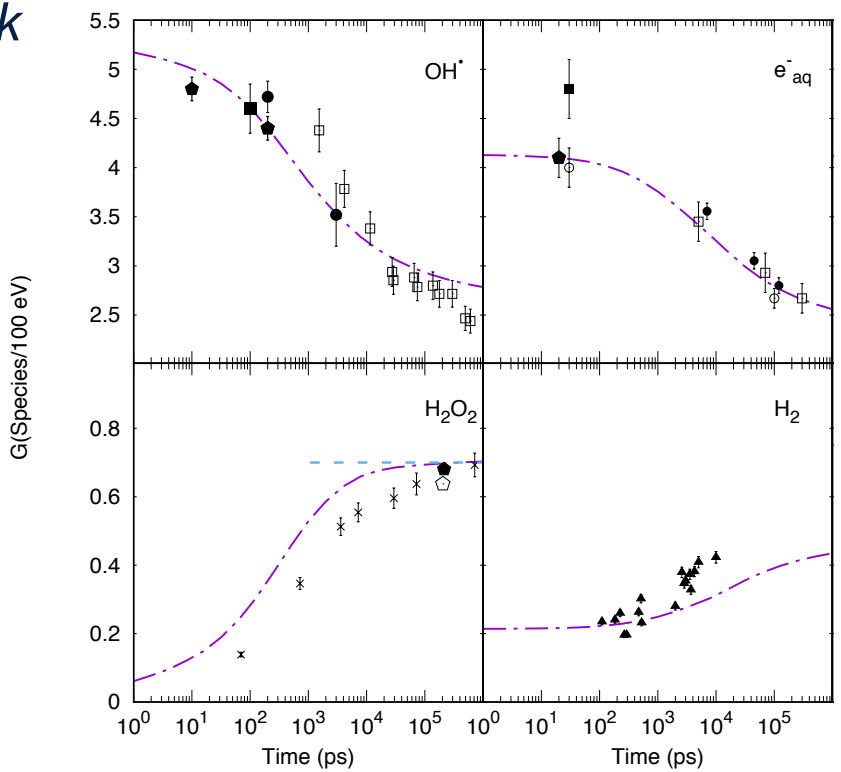
Chemical species	Name in TOPAS-nBio	Diffusion coefficients D ($10^{-9}m^2s^{-1}$) at 25°C		Reaction radius (nm)
		Geant4-DNA Default	TOPAS-nBio	
e^-_{aq}	SolvatedElectron	4.9	4.9	0.5
${}^{\bullet}OH$	Hydroxyl	2.8	2.2	0.22
$H^{\bullet}$	Hydrogen	7.0	7.0	0.19
H_3O^+	Hydronium	9.0	9.46	0.25
H_2	Dihydrogen	5.0	4.8	0.14
OH^-	Hydroxide	5.0	5.3	0.33
H_2O_2	HydrogenPeroxide	1.4	2.3	0.21
O_2	Oxygen	–	2.1	0.17
O_2^-	SuperoxideAnion	–	2.1	0.22
HO_2	HydroPeroxide	–	2.0	0.21
HO_2^-	Dioxidanide	–	2.0	0.25

[1] M. S. Kreipl, W. Friedland, and H. G. Paretzke, "Time- and space-resolved Monte Carlo study of water radiolysis for photon, electron and ion irradiation," *Radiat. Environ. Biophys.*, vol. 48, no. 1, pp. 11–20, 2009.
[2] J. Ramos-Mendez, J. Perl, J. Schuemann, A. McNamara, H. Paganetti and B. Faddegon "Monte Carlo simulation of chemistry following radiolysis with TOPAS-nBio" *Phys Med Biol.* 64, 105104-12pp (2018)
[3] S. Uehara and H. Nikjoo, "Monte Carlo simulation of water radiolysis for low-energy charged particles.," *J. Radiat. Res.*, vol. 47, no. 1, pp. 69–81, 2006.

Radiolysis of water – *Ongoing work*

G-values: Yield of chemical species per 100 eV of deposited energy.

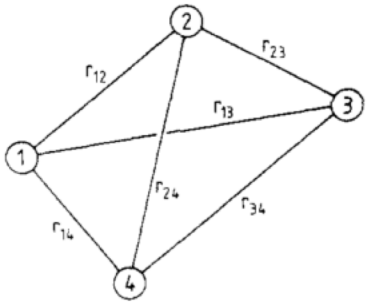




Ramos-Mendez J, et. al., Phys Med Biol. 64, 105104-12pp (2018)

Independent reaction times.

- Alternative to the step-by-step Monte Carlo for the chemistry stage.
- It is an stochastic method developed more than 30 years ago[1].



Pair	r_{ij}/nm	t_{ij}/ps	Reaction
1+2	1·3	12	x
1+3	2·1	27	x
1+4	1·0	40	2
2+3	1·1	8	1
2+4	1·7	125	x
3+4	1·8	∞	x

From Green et. al. J. Phys. Chem. 1990

Totally diffusion-controlled reactions

$$W(r,t) = \frac{R_{eff}}{r_{eff}} = \operatorname{erfc}\left(\frac{r_{eff} - R_{eff}}{\sqrt{4D't}}\right)$$

Partially diffusion-controlled reactions

$$W(r,t) = \frac{R_{eff}\alpha + 1}{r_{eff}\alpha}\left[-F\left(\frac{r_{eff} - R_{eff}}{\sqrt{4D't}}, -\alpha\sqrt{D't}\right) + \operatorname{erfc}\left(\frac{r_{eff} - R_{eff}}{\sqrt{4D't}}\right)\right]$$

$$F(x,y) = \exp\left(2xy + y^2\right)\operatorname{erfc}\left(x + y\right)$$

[1]Clifford et. al. J. Chem. Soc., Faraday Trans 1, 1986

IRT

Independent Reaction Times
(71 reactions, 15 species)

Totally diffusion controlled (10 reactions)

Neutral species

$$P_I(t \mid r_0) = \frac{\sigma}{r_0}\mathrm{erfc}\left(\frac{r_0 - \sigma}{\sqrt{4Dt}}\right)$$

Charged species

$$P_{III} = \frac{\sigma_{eff}}{r_{eff}}\mathrm{erfc}\left(\frac{r_{eff} - \sigma_{eff}}{\sqrt{4Dt}}\right)$$

Partially diffusion controlled (42 reactions)

Neutral species

$$P_{II}(t \mid r_0) = \frac{\sigma\alpha + 1}{r_0\alpha}\left[\mathrm{erfc}\left(\frac{r_0 - \sigma}{\sqrt{4Dt}}\right) - W\left(\frac{r_0 - \sigma}{\sqrt{4Dt}}, -\alpha\sqrt{Dt}\right)\right]$$

Charged species

$$P_{IV} = \frac{\sigma''_{eff}}{r_{eff}}\left[\mathrm{erfc}(b) - W(a,b)\right]$$

$$W(x,y) = \exp(2xy + y^2)\mathrm{erfc}(x + y)$$

First order reactions (19 reactions)

All species

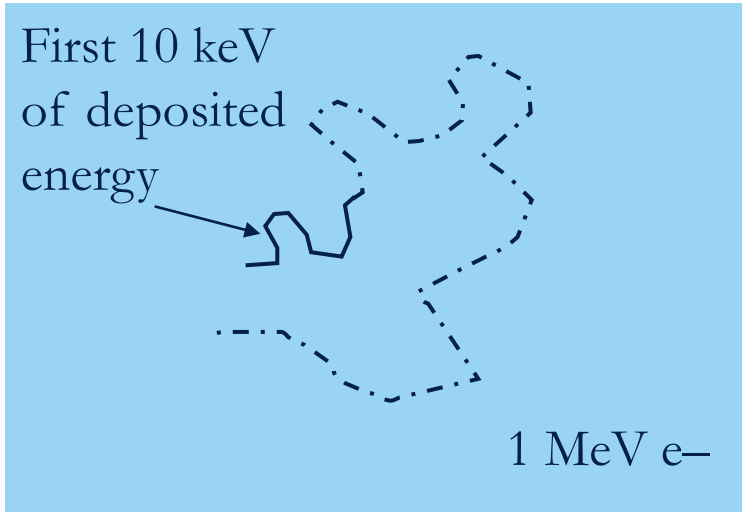
$$P_{VI} = 1 - \exp\left(-k[B]\Delta t\right)$$

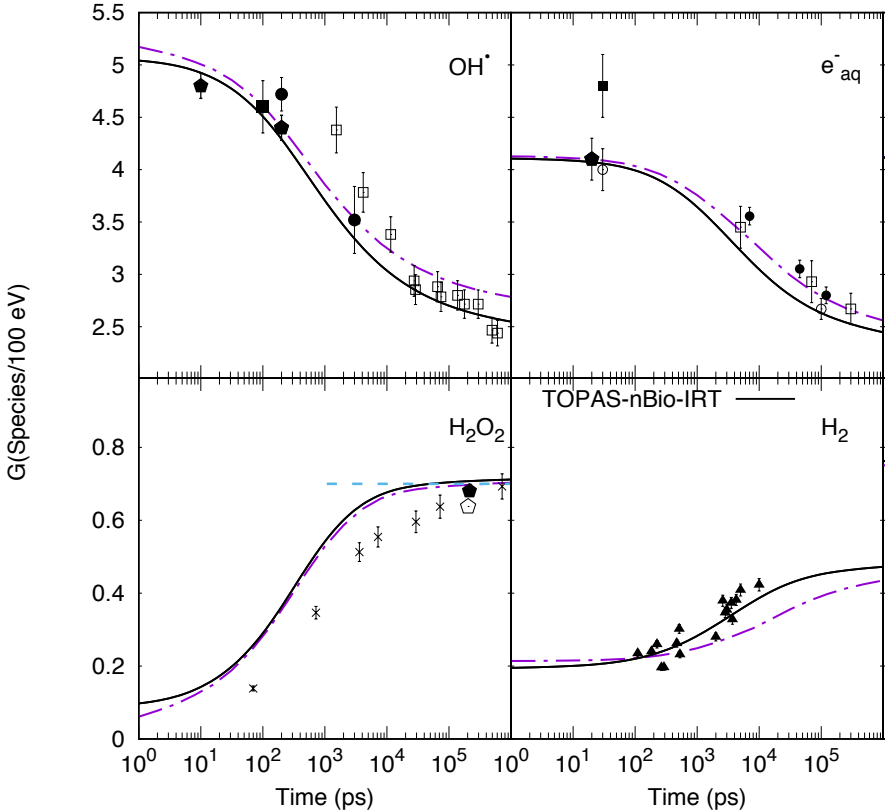
[B]: concentration of the specie
k: reaction rate
k[B]: scavenging power/capacity

Radiolysis of water – *Ongoing work*

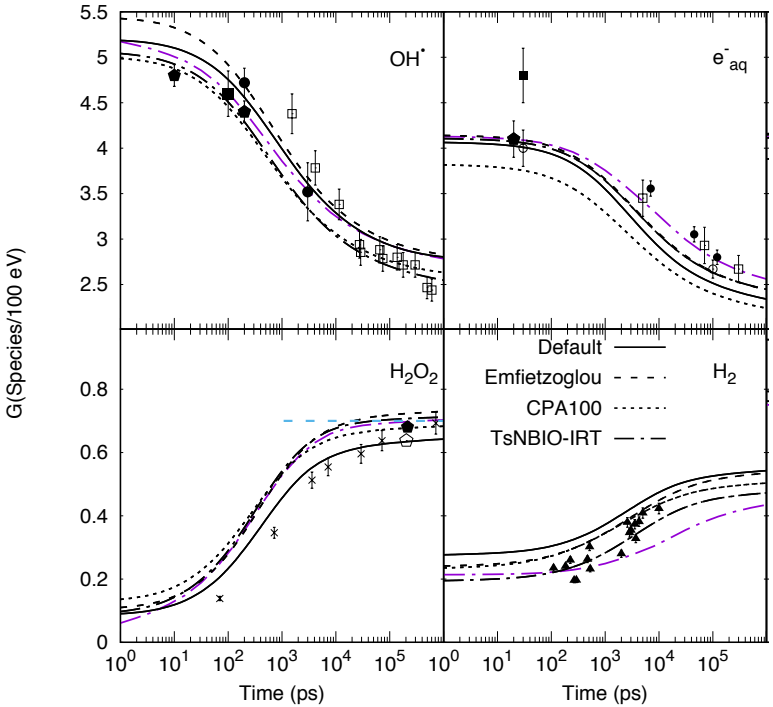
~150x faster

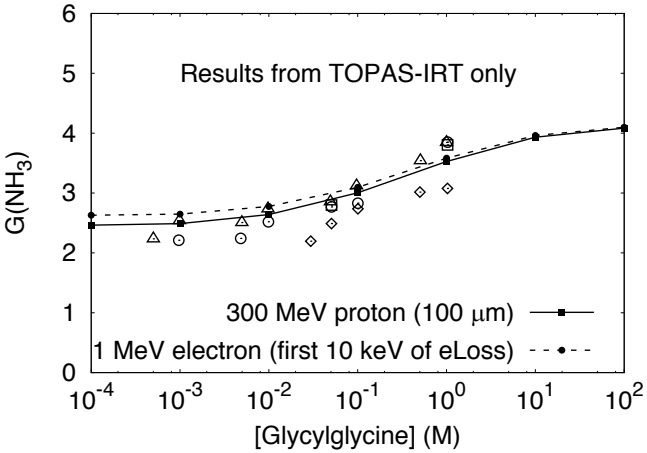
G-values: Yield of chemical species per 100 eV of deposited energy.

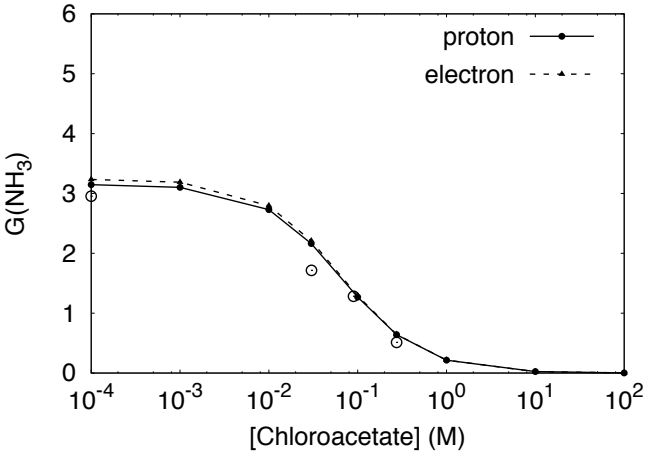




Radiolysis of water – *Ongoing work*







Conclusion

- TOPAS-nBio wraps and extends Geant4-DNA for track-structure simulations.
- It provides with high flexibility to combine complex geometry volumes with sophisticated scoring routines.
- It facilitates the validation of Geant4-DNA.
- Still an alpha version, so new users are welcome.

Acknowledges

- NIH grants 1R01CA187003 and 1P20CA183640.
- TOPAS and TOPAS-nBio Collaboration.
- Naoki Dominguez from Benemérita Universidad Autónoma de Puebla, México.
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- Dr. Eduardo Moreno from Benemérita Universidad Autónoma de Puebla, México.


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