Step-by-step simulation of radiation of radiation chemistry using Green Functions for diffusion-influenced reactions

Ianik Plante[1,2] and Francis A. Cucinotta[1]

[1]NASA/JSC, Houston, TX; [2]Division of Space Life Sciences, Universities Space Research Association, Houston, TX

Introduction

- The irradiation of biological systems leads to the formation of radiolytic species such as H·, ·OH, H_2, H_2O_2, e^-_{aq}, etc. [1]
- These species react with neighboring molecules, which result in damage in biological molecules such as DNA.
- Radiation chemistry is therefore very important to understand the radiobiological consequences of radiation [2].
- In this work, we discuss an approach based on the exact Green Functions for diffusion-influenced reactions which may be used to simulate radiation chemistry and eventually extended to study more complex systems, including DNA.

Green functions

- The exact Green functions for an isolated pair are known analytically [3-4]:

$$4\pi r r_0 p(r,t|r_0)=\frac{1}{\sqrt{4\pi Dt}}\left\{\exp\left[-\frac{(r-r_0)^2}{4Dt}\right]+\exp\left[-\frac{(r+r_0-2R)^2}{4Dt}\right]\right\}+\frac{\alpha(\beta+\alpha)(\gamma+\alpha)}{(\beta-\alpha)(\gamma-\alpha)}W\left(\frac{r+r_0-2R}{\sqrt{4Dt}},-\alpha\sqrt{Dt}\right)+\frac{\beta(\gamma+\beta)(\alpha+\beta)}{(\gamma-\beta)(\alpha-\beta)}W\left(\frac{r+r_0-2R}{\sqrt{4Dt}},-\beta\sqrt{Dt}\right)+\frac{\gamma(\alpha+\gamma)(\beta+\gamma)}{(\alpha-\gamma)(\beta-\gamma)}W\left(\frac{r+r_0-2R}{\sqrt{4Dt}},-\gamma\sqrt{Dt}\right)$$

$$Q(t|r_0)=1+\frac{(R\alpha+1)(\beta+\alpha)(\gamma+\alpha)}{r_0\alpha(\beta-\alpha)(\gamma-\alpha)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\alpha\sqrt{Dt}\right)+\frac{(R\beta+1)(\gamma+\beta)(\alpha+\beta)}{r_0\beta(\gamma-\beta)(\alpha-\beta)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\beta\sqrt{Dt}\right)+\frac{(R\gamma+1)(\alpha+\gamma)(\beta+\gamma)}{r_0\gamma(\alpha-\gamma)(\beta-\gamma)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\gamma\sqrt{Dt}\right)-\left(\frac{1}{r_0}\right)\left(\frac{\alpha\beta+\beta\gamma+\gamma\alpha}{\alpha\beta\gamma}+R\right)\mathrm{Erfc}\left(\frac{r_0-R}{\sqrt{4Dt}}\right)$$

$$p(*,t|r_0)=\frac{k_a}{k_D r_0}\left[\frac{\alpha}{(\beta-\alpha)(\gamma-\alpha)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\alpha\sqrt{Dt}\right)+\frac{\beta}{(\gamma-\beta)(\alpha-\beta)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\beta\sqrt{Dt}\right)+\frac{\gamma}{(\alpha-\gamma)(\beta-\gamma)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\gamma\sqrt{Dt}\right)\right]$$

$$p(**,t|r_0)=\frac{k_a k_e}{r_0 D k_D\alpha\beta\gamma}\left[\frac{\beta\gamma}{(\beta-\alpha)(\gamma-\alpha)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\alpha\sqrt{Dt}\right)+\frac{\alpha\gamma}{(\gamma-\beta)(\alpha-\beta)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\beta\sqrt{Dt}\right)+\frac{\alpha\beta}{(\alpha-\gamma)(\beta-\gamma)}W\left(\frac{r_0-R}{\sqrt{4Dt}},-\gamma\sqrt{Dt}\right)-\mathrm{Erfc}\left(\frac{r_0-R}{\sqrt{4Dt}}\right)\right]$$

$$p(r,t|*)=\frac{k_d}{4\pi rRD}\left[\frac{\alpha}{(\beta-\alpha)(\gamma-\alpha)}W\left(\frac{r-R}{\sqrt{4Dt}},-\alpha\sqrt{Dt}\right)+\frac{\beta}{(\gamma-\beta)(\alpha-\beta)}W\left(\frac{r-R}{\sqrt{4Dt}},-\beta\sqrt{Dt}\right)+\frac{\gamma}{(\alpha-\gamma)(\beta-\gamma)}W\left(\frac{r-R}{\sqrt{4Dt}},-\gamma\sqrt{Dt}\right)\right]$$

$$Q(t|*)=\frac{k_d}{RD}\left[-\frac{1}{\alpha\beta\gamma}+\frac{(R\alpha+1)}{\alpha(\beta-\alpha)(\gamma-\alpha)}\Omega\left(-\alpha\sqrt{Dt}\right)+\frac{(R\beta+1)}{\beta(\gamma-\beta)(\alpha-\beta)}\Omega\left(-\beta\sqrt{Dt}\right)+\frac{(R\gamma+1)}{\gamma(\alpha-\gamma)(\beta-\gamma)}\Omega\left(-\gamma\sqrt{Dt}\right)\right]$$

$$p(*,t|*)=-\frac{\alpha(\beta+\gamma)}{(\beta-\alpha)(\gamma-\alpha)}\Omega\left(-\alpha\sqrt{Dt}\right)-\frac{\beta(\alpha+\gamma)}{(\gamma-\beta)(\alpha-\beta)}\Omega\left(-\beta\sqrt{Dt}\right)-\frac{\gamma(\alpha+\beta)}{(\alpha-\gamma)(\beta-\gamma)}\Omega\left(-\gamma\sqrt{Dt}\right)$$

$$p(**,t|*)=\frac{k_e}{D}\left[\frac{\alpha+\beta+\gamma}{\alpha\beta\gamma}-\frac{(\beta+\gamma)}{\alpha(\beta-\alpha)(\gamma-\alpha)}\Omega\left(-\alpha\sqrt{Dt}\right)-\frac{(\alpha+\gamma)}{\beta(\gamma-\beta)(\alpha-\beta)}\Omega\left(-\beta\sqrt{Dt}\right)-\frac{(\alpha+\beta)}{\gamma(\alpha-\gamma)(\beta-\gamma)}\Omega\left(-\gamma\sqrt{Dt}\right)\right]$$

- The coefficients α,β and γ are related to the reaction rate constants ($k_D=4\pi RD$):

$$\alpha+\beta+\gamma=-(1+k_a/k_D)/R$$
$$\alpha\beta+\beta\gamma+\gamma\alpha=(k_e+k_d)/D$$
$$\alpha\beta\gamma=-[(1+k_a/k_D)k_e+k_d]/DR$$

$$\mathrm{Erfc}(x)\equiv\frac{2}{\sqrt{\pi}}\int_x^\infty e^{-\xi^2}d\xi$$
$$W(x,y)\equiv\exp(2xy+y^2)\mathrm{Erfc}(x+y)$$
$$\Omega(x)\equiv\exp(x^2)\mathrm{Erfc}(x)$$

Chemical reactions and radiolytic yields

- The chemical reactions between radiolytic species with no electrostatic interaction (i.e. their charge product is 0) can be simulated by using the Green Functions described above.
- The radiation chemistry code can be used to simulate the time evolution of the radiolytic species (radiation chemistry) and radiochemical yields [5,6].

Reaction	k_{obs} ($M^{-1}s^{-1}$)	R (nm)	k_{dif} ($M^{-1}s^{-1}$)	k_{act} ($M^{-1}s^{-1}$)	P_{React}	α (nm^{-1})
H. + .OH → H_2O	1.55 x 10^{10}	0.41	2.86 x 10^{10}	3.40 x 10^{10}	0.33	5.34
H. + H_2O_2 → H_2O + .OH	3.50 x 10^{7}	0.40	2.82 x 10^{10}	3.50 x 10^{7}	0.00	2.50
H. + OH^- → H_2O + e^-_{aq}	2.51 x 10^{7}	0.52	4.84 x 10^{10}	2.51 x 10^{10}	0.00	1.92
H. + O_2 → HO_2.	2.10 x 10^{10}	0.36	2.56 x 10^{10}	1.17 x 10^{11}	0.67	15.4
H. + HO_2. → H_2O_2	1.00 x 10^{10}	0.40	2.82 x 10^{10}	1.55 x 10^{10}	0.19	3.88
H. + O_2.$^-$ → HO_2^-	1.00 x 10^{10}	0.41	2.72 x 10^{10}	1.58 x 10^{10}	0.20	3.86
.OH + .OH → H_2O_2	5.50 x 10^{9}	0.44	7.32 x 10^{9}	2.21 x 10^{10}	0.55	9.14
.OH + H_2O_2 → HO_2. + H_2O	2.88 x 10^{7}	0.43	1.46 x 10^{10}	2.88 x 10^{7}	0.00	2.33
.OH + H_2 → H. + H_2O	3.28 x 10^{7}	0.36	1.91 x 10^{10}	3.29 x 10^{7}	0.00	2.78
.OH + e^-_{aq} → OH^-	2.95 x 10^{10}	0.72	3.87 x 10^{10}	1.25 x 10^{11}	0.49	5.87
.OH + OH^- → O.$^-$ + H_2O	6.30 x 10^{9}	0.55	3.12 x 10^{10}	7.90 x 10^{9}	0.08	2.28
.OH + HO_2. → O_2 + H_2O	7.90 x 10^{9}	0.43	1.46 x 10^{10}	1.72 x 10^{10}	0.33	5.05
.OH + O_2.$^-$ → O_2 + OH^-	1.07 x 10^{10}	0.44	1.32 x 10^{10}	5.76 x 10^{10}	0.64	12.2
.OH + HO_2^- → HO_2. + OH^-	8.32 x 10^{9}	0.47	1.28 x 10^{10}	2.38 x 10^{10}	0.42	6.08
.OH + O.$^-$ → HO_2^-	1.00 x 10^{9}	0.47	1.49 x 10^{10}	1.07 x 10^{9}	0.03	2.28
.OH + O_3.$^-$ → O_2.$^-$ + HO_2.	8.50 x 10^{9}	0.42	1.34 x 10^{10}	2.34 x 10^{10}	0.42	6.55

Reaction rate constants (k_{obs}, k_{dif} and k_{act}), reaction radii (R), probability of geminate recombination, and α for reactions between radiolytic species [5].

Assumptions of the model

- The pair of particle may react as follow [3]:

$$A+B \underset{k_b}{\overset{k_a}{\rightleftarrows}} (AB)^* \xrightarrow{k_e} AB$$

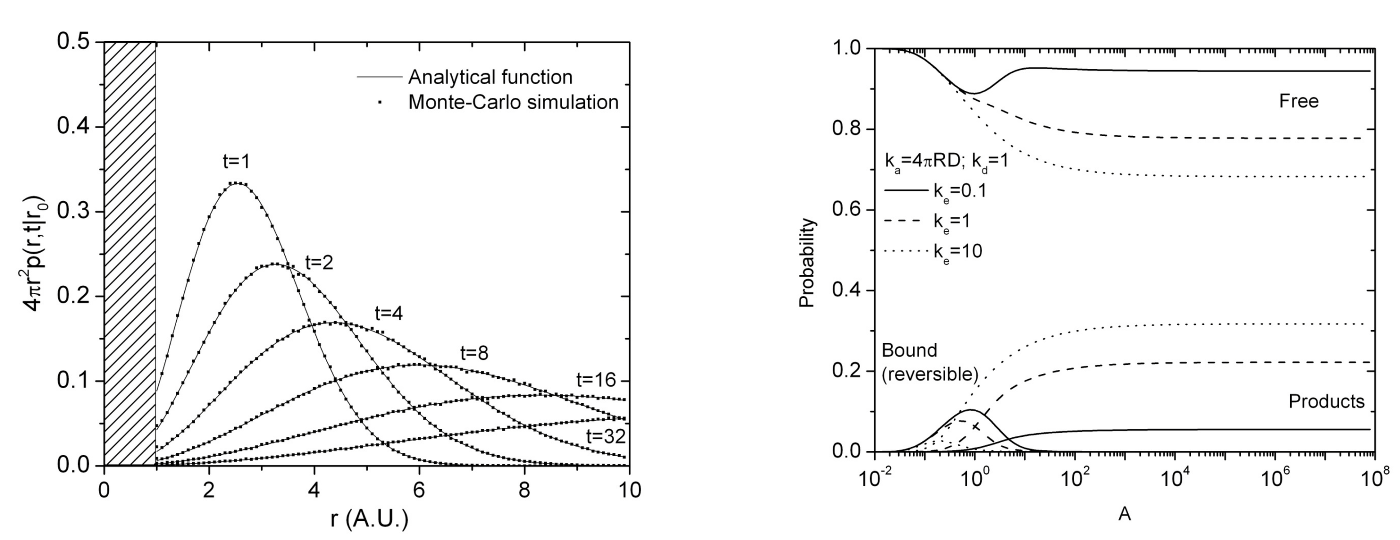
k_a: association rate constant
k_d: dissociation rate constant
k_e: product formation rate constant

- Transitions from a state to another are defined:

		State after one timestep		
		Free (x_1)	Rev bound (*)	Products(**)
Initial state	Free (x_0)	$p(x_1,t\|x_0)$	$p(*,t\|x_0)$	$p(**,t\|x_0)$
	Rev bound (*)	$p(x_1,t\|*)$	$p(*,t\|*)$	$p(**,t\|*)$
	Products (**)	0	0	1

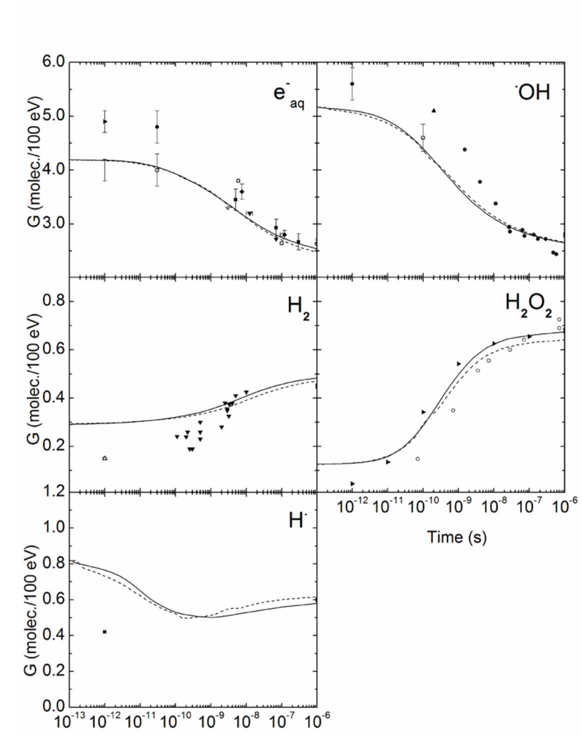
Sampling of the Green functions

- We have developed exact algorithms to sample the random variates r for $p(r,t|r_0)$ and $p(r,t|*)$ [4].
- The algorithm allow the simulation to be done in several timesteps (time discretization)

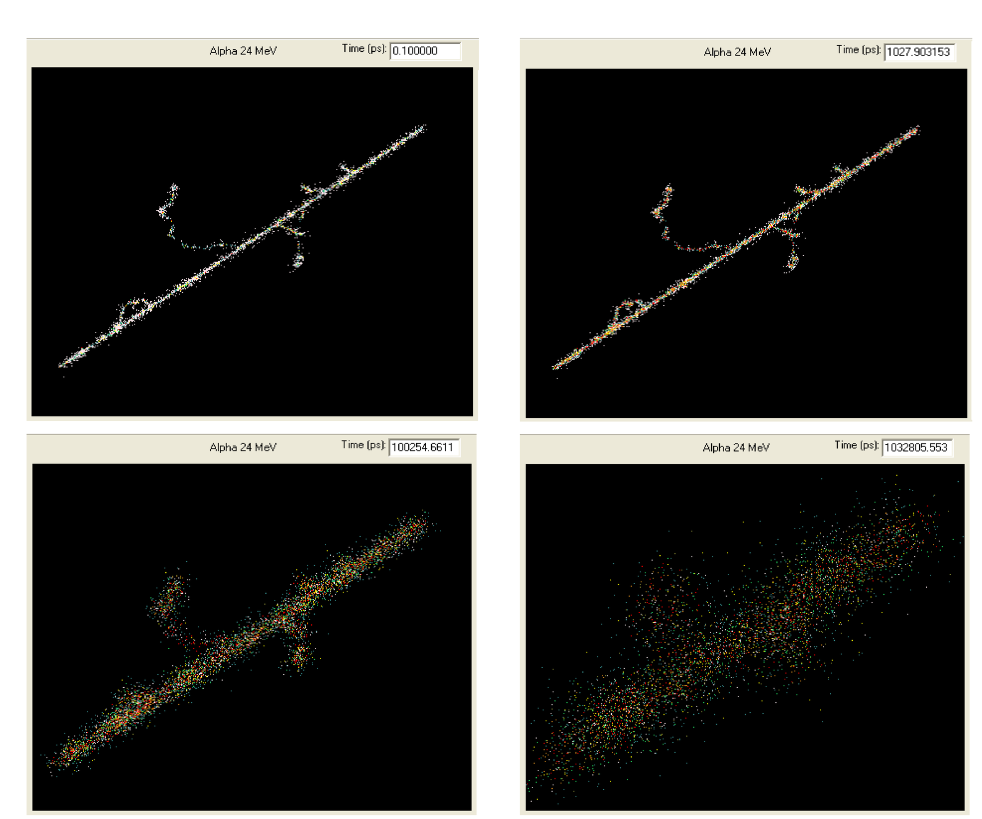


Left: Green function $4\pi r^2 p(r,t|r_0)$ for R=1, r_0=1.5, for k_a=4πRD, k_d=1 and k_e=1 at t=1, 2, 4, 8, 16 and 32. Analytical functions: (—); Result of sampling: (■). Right Survival probability $Q(t|r_0)$, binding probability $p(*,t|r_0)$ and reaction probability $p(**,t|r_0)$ as function of time for R=1, r_0=1.5, k_a=4πRD, k_d=1 and k_e=0.1 (—), k_e=1 (---) and k_e=10 (···).

Radiation track structure and evolution in time



Time-dependent yields of chemical species produced by 300 MeV protons (LET ~0.3 keV/μm) [6]. Calculations: IONLYS-IRT (---); SBS (___); The dots are experimental data.



Time evolution, in 3D, of a 24-MeV $^4He^{2+}$, LET~26 keV/μm, at 10^{-13}, 10^{-9}, 10^{-7} and 10^{-6} s. Each dot is a radiolytic species

Assumptions of the model

- The pair of particles is initially at a distance r_0 and at they are at the distance r at t:

$$4\pi r_0^2 p(r,t|r_0)=\delta(r-r_0)$$

- The distance between particle obeys a diffusion equation:

$$\frac{\partial p(r,t|r_0)}{\partial t}=D\frac{\partial^2}{\partial r^2}p(r,t|r_0)$$

- The material balance condition is:

$$k_a p(r,t|*)=k_d p(*,t|r)$$

- The boundary condition is

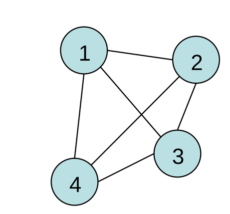
$$\frac{dp(*,t|r_0)}{dt}=k_a p(R,t|r_0)-(k_d+k_e)p(*,t|r_0)$$

- Survival and dissociation probabilities

$$Q(t|r_0)=\int_R^\infty 4\pi r^2 p(r,t|r_0)dr \qquad Q(t|*)=\int_R^\infty 4\pi r^2 p(r,t|*)dr$$

Many-particles system

- When more particles are added to the system, the number of interactions grow quickly
  - 2 Particles
    - -1-2 (1 interaction)
  - 3 Particles
    - -1-2,1-3, 2-3 (3 interactions)
  - 4 Particles
    - -1-2, 1-3, 1-4, 2-3, 2-4, 3-4 (6 interactions)
  - N Particles
    - -N(N-1)/2 interactions ➔ Grows as ~N^2!



- The Green Functions can be used to build a radiation chemistry code [4], by using average positions generated by sampling the inter-particle distance at each timestep

Conclusion

- This approach has been used successfully to simulate the time evolution of radiolytic species and to calculate radiochemical yields.
- The radiation track structure code RITRACKS [7] and the chemistry code will be of crucial importance in future models of DNA damage.

References

[1] Ferradini, C. and Jay-Gerin, J.-P. *Can J. Chem.* **77**, 1542-1575 (1999).
[2] O'Neill, P. and Wardman, P. *Int. J. Radiat. Biol.* **85**, 9-25 (2009).
[3] Park, S. and Agmon, N. *J. Phys. Chem. B* **112**, 5977-5987 (2008).
[4] Plante, I. et al. *Phys. Rev. E*, submitted.
[5] Plante, I. *Radiat. Env. Biophys.* **50**, 389-403 (2011).
[6] Plante, I. *Radiat. Env. Biophys.* **50**, 405-415 (2011).
[7] Plante, I. and Cucinotta, F.A. *New J. Phys.* **10**, 125020 (2008).