Simulation of ionizing radiation tracks and its applications

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NASA Space Radiation Summer School 2014
Brookhaven National Laboratory
May 30 – June 20, 2014
The space radiation problem

- Space radiation is comprised of high-energy protons and heavy ions (HZE’s) and secondary protons, neutrons, and heavy ions produced in shielding.

- Unique damage to biomolecules, cells, and tissues occurs from HZE ions that is qualitatively distinct from X-rays and gamma-rays on Earth.

- No human data to estimate risk from heavy ions, thus requiring use of biological models and theoretical understanding to assess and mitigate risks.

- Shielding has excessive costs and will not eliminate galactic cosmic rays (GCR).
The energy deposition by heavy ions is highly heterogeneous and dependent on the type and energy of the ion

The interactions of radiation with matter are stochastic in nature and therefore often studied by Monte-Carlo simulations

Primary energy loss events in low-LET tracks

Primary energy loss events in high-LET tracks


## Radiation effects: time sequence of events

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>Stage</th>
<th>Events</th>
<th>Modeling</th>
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<tbody>
<tr>
<td>$10^{-15}$</td>
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<td>Energy absorption</td>
<td>Particle transport</td>
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<td>$10^{-6}$</td>
<td>Biological</td>
<td>DNA repair</td>
<td>Kinetics models</td>
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<td>Molecular dynamics</td>
</tr>
</tbody>
</table>
Radiation effects: time sequence of events

H₂O + H₂O⁺ + e⁻ → H₂O + H₂O

•OH + H₃O⁺

H₂O⁺

H₂O⁻

H⁻ + •OH

H₂O

H₂ + OH⁻

H₂O⁺ → H⁺ + •OH

H₂ + O(¹D)

2 H⁺ + O(³P)

Physical stage (<10⁻¹⁵ s)

Physico-Chemical stage (~10⁻¹⁵ – 10⁻¹² s)

(~240-600 fs)
The trajectory of a particle and all its interactions is followed in the medium

A particle is followed until
- It leaves the volume of interest
- Its energy decrease below a threshold
- It disappears by a physical process (e.g. absorption of a photon during a photo-electric effect)

Many other particles are generated by the interactions of the “primary” particle. The trajectories of these secondary particles should also be followed.
Particle transport basics

Particles

- Position \((x, y, z)\)
- Energy \((E)\)
- Direction \((\theta, \phi)\)

Cross sections

- Probability of interaction between radiation and matter

\[
dI = -I n \sigma dx
\]

- Cross sections (units: \(cm^2\))
- Mean free path \(\lambda\) (units: \(cm\))

\[
\lambda(E) = 1/(N\sigma(E))
\]

\[
I(x) = I(0) \exp(-x / \lambda(E))
\]
Particle transport basics

- Cross sections (total and differential in energy, angle, ... i.e. $d\sigma/dW$, $d\sigma/d\theta$, $d^2\sigma/dWd\sigma$, ...) are needed for particle transport.

- The total cross section is the sum of the cross sections for each interaction.

- A distance to the next interaction ($s$) is sampled from the exponential distribution:
  \[ s = -\lambda \log(U) \]
  \[ \lambda(E) = 1/(N\sigma(E)) \]

- The particle is moved to the next interaction site:
  \[ x' = x + s \sin(\theta) \cos(\varphi) \]
  \[ y' = y + s \sin(\theta) \sin(\varphi) \]
  \[ z' = z + s \cos(\theta) \]

- The phenomenon (e.g. ionization) is determined by the ratio of the cross section a phenomenon over the total cross section.

- The energy loss and change of direction are determined by sampling the differential cross sections.
Cross sections

- RITRACKS includes accurate cross section models for all ions and secondary electrons or photons

- **For electrons:**
  - Ionization
  - Excitation
  - Elastic collisions
  - Dissociative electron attachment
  - Bremsstrahlung

- **For ions:**
  - Ionization
  - Excitation

- **For photons:**
  - Compton effect
  - Coherent diffusion
  - Photoelectric effect
  - Pair production

Cross sections

- Cross sections used in RITRACKS

The cross sections for ions are scaled with $Z_{\text{eff}}$:

$$\frac{d\sigma_{\text{ion}}(v)}{dW} = Z_{\text{eff}}^2 \frac{d\sigma_{\text{proton}}(v)}{dW}$$

$$Z_{\text{eff}} / Z = 1 - \exp(-125\beta^2 / Z^{2/3})$$

$v$: velocity of the ion

$\beta$: relativistic $v/c$
Monte-Carlo simulations

- Used to simulate stochastic systems

Example: Calculation of $\pi$

$$N=10000; N_c = 7863; \pi = 4 \times N_c / N = 3.1452$$

By increasing the number of random points, $4N_c/N$ converges to the value of $\pi$. 
Monte-Carlo simulations

- Random numbers
- Probability distributions
- Normalization

\[ \sum_{i=1}^{N} p_i = 1 \] \hspace{1cm} \text{Discrete}

\[ \int_{-\infty}^{\infty} f(x')dx' = 1 \] \hspace{1cm} \text{Continuous}

Poisson distribution
\[ P(x=k) = \frac{\lambda^k e^{-\lambda}}{k!} \]

Uniform distribution
\[ \frac{1}{b-a} \]

Exponential distribution
\[ p(x) = \lambda e^{-\lambda x} \]

From http://en.wikipedia.org/wiki/List_of_probability_distributions
Monte-Carlo simulations

Generating probability distributions

Example: Exponential distribution

\[ f(x) = \lambda e^{-\lambda x}, \quad \lambda > 0, \quad x \geq 0 \]

\[ F(x) = 1 - e^{-\lambda x} = U \]

\[ X = \frac{-\ln(1-U)}{\lambda} \text{ or } X = \frac{-\ln(U)}{\lambda} \]

U is a random number between 0 and 1

F(x) is the cumulative probability distribution

\[ F(x) = \int_{-\infty}^{x} f(x')dx' \]

\[ P_k = \sum_{i=1}^{k} p_i \]
Monte-Carlo simulations

Generating the exponential distribution

Sampling of the exponential distribution

- N=100
- N=1000
- N=10000
- N=100000

$\rho(x)$
The software RITRACKS

- **The software RITRACKS comprises several parts**
  - The calculation part includes:
    - The cross sections, which are necessary for particle transport
    - The particle transport routines
    - Post-simulation data management
  - The Graphic User Interface (GUI), comprises several windows:
    - The main window
    - Incident radiation window
    - Cross sections windows (electrons and ions)
    - Results (events) details
  - The 3D visualization window
  - The help file

- **All necessary files are included in an installer for Windows**
The software RITRACKS

- Multiple CPU computing

Begin

Input
- Simulation parameters
- No of histories (N)
- No of CPU (N_CPU)

Create directory 1
- Copy files in dir 1
  - program
  - input files
  - 1st seed
- Execute program in dir 1 on CPU 1

Create directory 2
- Copy files in dir 2
  - program
  - input files
  - 2nd seed
- Execute program in dir 2 on CPU 2

Create directory i
- Copy files in dir i
  - program
  - input files
  - i-th seed
- Execute program in dir i on CPU i mod N_CPU

Create directory N
- Copy files in dir N
  - program
  - input files
  - N-th seed
- Execute program in dir N on CPU N mod N_CPU

Collect results when all simulations are done

End

The software RITRACKS

- Multiple CPU computing (Windows)

Heavy ion track structure simulation

Simulation for $^1\text{H}^+$, $^{12}\text{C}^{6+}$, $^{28}\text{Si}^{14+}$ and $^{56}\text{Fe}^{26+}$ tracks, 100 MeV/amu
Radial dosimetry

(a) $^{1}\text{H}^{+}$ 1 MeV/amu, LET~33 keV/μm

(b) $^{20}\text{Ne}^{10+}$ 377 MeV/amu, LET~31 keV/μm

(c) $^{4}\text{He}^{2+}$ 1 MeV/amu, $^{56}\text{Fe}^{26+}$ 1 GeV/amu, LET~150 keV/μm

Voxel dosimetry

1 GeV/amu $^{56}\text{Fe}^{26+}$ ion
LET~150 keV/μm
Voxels: 40 nm x 40 nm x 40 nm

Target dosimetry

(a) $^{16}$O$^{3+}$, 21.2 MeV/amu, LET~168 keV/μm
(b) $^{12}$C$^{6+}$, 25 MeV/amu, LET~76 keV/μm
(c) $^4$He$^{2+}$, 25 MeV/amu, LET~9.5 keV/μm
Target dosimetry

Target size: 150 nm
- This calculation
- Schmollack 2000 (exp)
- Schmollack 2000 (fit)
- Kiefer 1986 (calc)
DNA damage / $\gamma$H2AX foci studies

- Irradiation by 1 GeV/amu Fe ions
- 100 cGy
- LET $\sim$ 149 keV/µm

Experiments performed at the NASA Space Radiation Laboratory (2007)
DNA damage

2700 x $^{1}\text{H}^+$, 300 MeV (1 Gy)
Dose in voxels (20 nm)
Chromosomes (RW model)
Intersection voxels
H2AX foci experiments
Application of DSB probability
DNA damage

6 x \( ^{56}\text{Fe}^{26+} \), 1 GeV/u (1 Gy)

Dose in voxels (20 nm)

Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

Application of DSB probability

DNA damage / γH2AX foci studies

• Calculation of DSBs by low- and high-LET radiation

DNA damage / $\gamma$H2AX foci studies

- Calculation of DSBs by $^1$H$^+$, $^{12}$C$^{6+}$ and $^{56}$Fe$^{26+}$ ions

DNA damage / $\gamma$H2AX foci studies

- Calculation of DSBs vs LET by $^1$H$^+$, $^{12}$C$^{6+}$ and $^{56}$Fe$^{26+}$ ions

DNA damage / $\gamma$H2AX foci studies

- DSBs per cell vs dose is linear
- Exchanges per cell vs dose is linear-quadratic
To better understand the formation of DSBs, a chromatin fiber is built from nucleosome units and linker DNA.
DNA damage simulations

- The Binary-Encounter-Bethe (BEB) model of ionization cross section

\[
\frac{d\sigma}{dw} = \frac{s}{t + u + 1} \left\{ \frac{1}{(t-w)^2} + \frac{1}{(1+w)^2} - \frac{1}{1+t} \left[ \frac{1}{t-w} + \frac{1}{1+w} \right] + \left[ \frac{1}{(t-w)^3} + \frac{1}{(1+w)^3} \right] \log(t) \right\}
\]

- The energies are expressed in units of ionization potential of the orbital (B):
  - \(t=T/B\) is the kinetic energy of the incident electron
  - \(w=W/B\) is the kinetic energy of the ejected electron
  - \(u=U/B\) is the kinetic energy of the electron in the orbital

- The total cross section is obtained by integration

\[
\sigma = \int_0^{(t-1)^2} \frac{d\sigma}{dw} dw = \frac{s}{t + u + 1} \left\{ 1 - \frac{1}{t} + \frac{1}{2} \left[ 1 - \frac{1}{t^2} \right] \log(t) - \frac{\log(t)}{t+1} \right\}
\]

In the DNA bases, there are many internal and valence electrons. The BEB model allows to model the ionization for each electron of the molecule.

### Thymine

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Calculations of MO from the site www.chemeddl.org
The BEB cross section can be written in a form suitable for sampling by a composition method:

\[
\frac{d\sigma}{dw} = \frac{s}{t+u+1} \left\{ \frac{1}{(t-w)^2} + \frac{1}{(1+w)^2} - \frac{1}{1+t} \left[ \frac{1}{t-w} + \frac{1}{1+w} \right] + \left[ \frac{1}{(t-w)^3} + \frac{1}{(1+w)^3} \right] \log(t) \right\}
\]

\[
\frac{d\sigma}{dw} = \sum_{i=1}^{3} k_i(w) = \sum_{i=1}^{3} A_i g_i(w) h_i(w)
\]

where

\[
A_i = \frac{s}{t+u+1} \left( \frac{t}{t+1} \right) \left( \frac{t-1}{t+1} \right)
\]

\[
h_i(w) = \frac{t+1}{t} \left[ \frac{1}{1+w} \right]^{1/2}
\]

\[
g_i(w) = \frac{t+1}{t-1} \left( \frac{1}{w+1} \right)^{1/2}
\]

\[
\int_{0}^{(t-1)/2} g_i(w) dw = 1
\]

\[
0 \leq h_i(w) \leq 1
\]

\[
A_i \geq 0
\]

Adapted from S. Edel, PhD thesis, Université de Toulouse
DNA damage simulations

Sampling algorithm and results

Algorithm to sample the energy of the ionized electron \( w_e \) from the BEB model of ionization cross sections

\[
\text{CALCULATE } A_1, A_2, A_3 \text{ and } A_{123} = A_1 + A_2 + A_3
\]

\[
\text{REPEAT} \{
\begin{align*}
\text{GENERATE random numbers } & R_1, R_2, \text{ and } R_3 \\
\text{IF } & (R_1 < A_1/A_{123}) \{ \\
& \quad \omega_x = \frac{R_2(t-1)}{(t+1) - R_3(t-1)} \\
& \quad \text{IF } (R_3 \leq \frac{t - \omega_x}{t}) \text{ EXIT loop} \\
\} \\
\text{IF } & (A_1/A_{123} < R_1 < A_1 + A_2/A_{123}) \{ \\
& \quad \omega_x = \frac{R_2(t-1)}{(t+1) + R_3(t-1)} \\
& \quad \text{IF } (R_3 \leq 2\left(1 - \frac{t - \omega_x}{t+1}\right)) \text{ EXIT loop} \\
\} \\
\text{IF } & (R_2 < (A_1 + A_2)/A_{123}) \{ \\
& \quad \omega_x = \frac{i + 1}{\sqrt{4 + (R_2 - 1)(t + 1)^2 - 4}} - 1 \\
& \quad \text{IF } (R_3 \leq \frac{1}{2}\left[1 + \left(\frac{\omega_x + 1}{t - \omega_x}\right)^2\right]) \text{ EXIT loop} \\
\} \\
\} \\
\text{RETURN } w_e.
\]

Adapted from S. Edel, PhD thesis, Université de Toulouse
DNA damage studies

- Cross sections can be calculated for the bases, sugars and phosphates.
- In this case, the medium is considered a succession of homogeneous media.

\[
dI = -\ln \sigma dx
\]

\[
\ln(I / I_0) = -\int_0^x \sigma(u) N du
\]

\[
I = I_0 \exp \left\{ -N \sum_{j=1}^{i-1} (\sigma_j - \sigma_i) W_j + \sigma_i x \right\}
\]

Relative weight

\[
\exp(-N \sum_{j=1}^{i-1} W_j \sigma_j)(1 - \exp(-NW_i \sigma_i))
\]

\[
p_i = I_0 \frac{1}{N \sigma_i}
\]

Sampling of \( W_s \)

\[
W_s = \sum_{j=1}^{i-1} W_j - \frac{1}{N \sigma_i} \log[1 - V(1 - e^{-\sigma_j NW_i})]
\]

Radiation chemistry

- \( \sim 10^{-12} - 10^{-6} \) s
  - Particles diffusion
  - Chemical reactions

- The radiolytic species are not uniformly distributed. Therefore, an approach based on Green’s functions of the diffusion equation (DE) is used.

Examples of chemical reactions:

\[
\begin{align*}
e^{-}_{aq} + e^{-}_{aq} & \rightarrow \text{H}_2 + 2 \text{OH}^- \\
\cdot\text{OH} + e^{-}_{aq} & \rightarrow \text{OH}^- \\
\cdot\text{OH} + \cdot\text{OH} & \rightarrow \text{H}_2\text{O}_2 \\
\cdot\text{OH} + \text{H}_2\text{O}_2 & \rightarrow \text{HO}_2\cdot + \text{H}_2\text{O} \\
\text{H}^+ + \text{O}_2\cdot & \leftrightarrow \text{HO}_2\cdot \\
\text{H}^+ + \text{H}_2\text{O}_2 & \rightarrow \cdot\text{OH} + \text{H}_2\text{O}
\end{align*}
\]

(More than 60 reactions...)

\[ G(X) = \frac{\text{Number of chemical species created}}{100 \text{ eV deposited energy}} \]
Bimolecular reactions

- DE for the propagation of particles A and B

\[
\frac{\partial p(r_A, r_B, t | r_{A0}, r_{B0}, t_0)}{\partial t} = \left[ D_A \nabla^2_{r_A} + D_B \nabla^2_{r_B} \right] p(r_A, r_B, t | r_{A0}, r_{B0}, t_0)
\]

- Transformation of variables

\[
R = \left( D_B r_A + D_A r_B \right) / (D_A + D_B) \\
r = r_B - r_A
\]

\[
\frac{\partial p(R, r, t | R_0, r_0, t_0)}{\partial t} = (D_A + D_B) \left[ \nabla_R^2 + \nabla_r^2 \right] p(R, r, t | R_0, r_0, t_0)
\]

\[
p(R, r, t | R_0, r_0, t_0) = p^R(R, t | R_0, t_0) p^r(r, t | r_0, t_0)
\]

\[
\frac{\partial p^R(R, t | R_0, t_0)}{\partial t} = (D_A + D_B) \nabla_R^2 p^R(R, t | R_0, t_0)
\]

\[
\frac{\partial p^r(r, t | r_0, t_0)}{\partial t} = (D_A + D_B) \nabla_r^2 p^r(r, t | r_0, t_0)
\]

Uncoupled equations in \( r \) and \( R \)

Free diffusive motion of the coordinate $\mathbf{R}$

$$\frac{\partial p^R(\mathbf{R}, t \mid \mathbf{R}_0, t_0)}{\partial t} = D \nabla_R^2 p^R(\mathbf{R}, t \mid \mathbf{R}_0, t_0)$$  \hspace{1cm} \text{(DE)}$$

$p^R(\mathbf{R}, t \mid \mathbf{R}_0, t_0) = \delta(\mathbf{R} - \mathbf{R}_0)$  \hspace{1cm} \text{(Initial condition)}$

$p^R(|\mathbf{R}| \to \infty, t \mid \mathbf{R}_0, t_0) = 0$  \hspace{1cm} \text{(Boundary condition)}$

$$p^R(\mathbf{R}, t \mid \mathbf{R}_0, t_0) = \frac{1}{[4\pi D(t - t_0)]^{3/2}} \exp \left[ \frac{(\mathbf{R} - \mathbf{R}_0)^2}{4D(t - t_0)} \right]$$  \hspace{1cm} \text{(Solution)}$

$p^R(\mathbf{R}, t \mid \mathbf{R}_0, t_0)$: probability distribution of the vector $\mathbf{R}$ at time $t$, given that it was located at position $\mathbf{R}_0$ at time $t_0$

$D = D_A + D_B$: Sum of the diffusion coefficients

Bimolecular reactions

- Free diffusive motion* of the inter-particle separation vector \( r \)

\[
\frac{\partial p^r(r, t \mid r_0, t_0)}{\partial t} = D \nabla_r^2 p^r(r, t \mid r_0, t_0)
\]  
\( p^r(r, t \mid r_0, t_0) = \delta(r - r_0) \)

- For chemical reactions, we need the inter-particle distance \( r \).
  - Therefore, the DE is written in spherical coordinates.
  - Only the radial component will be considered (angular dependency terms are neglected). This considerably simplifies the analytical solution.

\[
\frac{\partial p(r, t \mid r_0)}{\partial t} = \frac{D}{r^2} \frac{\partial}{\partial r} \left[ r^2 \frac{\partial}{\partial r} p(r, t \mid r_0) \right]
\]  
\( 4\pi r_0^2 p(r, t \mid r_0) = \delta(r - r_0), r \geq R \)

\( p(r,t\mid r_0,t_0) \): probability distribution of the separation distance \( r \) at time \( t \), given that it was \( r_0 \) at time \( t_0 \)

*We assume that there is no force interacting between particles. This is the case for most of the chemical reactions that we are interested in.
Bimolecular reactions

- Simple case: partially diffusion-controlled reaction with rate $k_a$ and reaction radius $R$

\[ A + B \rightarrow C \]

\[ 4\pi R^2 D \frac{\partial p(r, t | r_0)}{\partial r} \bigg|_{r=R} = k_a p(R, t | r_0) \]

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

\[ Q(t | r_0) = \int_0^\infty 4\pi r^2 p(r, t | r_0) dr = 1 + \frac{R \alpha + 1}{r_0 \alpha} \left[ W \left( \frac{r_0 - R}{\sqrt{4Dt}}, \alpha \sqrt{Dt} \right) - \text{Erfc} \left( \frac{r_0 - R}{\sqrt{4Dt}} \right) \right] \]

\[ \alpha = -\frac{k_a + 4\pi RD}{4\pi R^2 D} \]

The probability of reaction $P(t|r_0) = 1 - Q(t|r_0)$. At each time step, the probability of reaction is assessed. If the particles have not reacted, their relative distance is obtained by sampling the Green’s function using the algorithm described in Plante et al. (2013).

Green’s function for radiation chemistry

- Simple case: partially diffusion-controlled reaction with rate $k_a$ and reaction radius $R$

$$k_a$$
$$A + B \rightarrow C$$

Green’s functions (3D) for radiation chemistry

Green’s function with angular dependency (exact)

\[ p(r, \theta, \phi, t | r_0, \theta_0, \phi_0) = \frac{1}{4\pi\sqrt{rr_0}} \sum_{n=0}^{\infty} (2n+1)P_n(\cos(\gamma)) \int_{0}^{\infty} e^{-u^2Dt} uF_{n+1/2}(u, r)F_{n+1/2}(u, r_0) du \]

\[ F_v(u, r) = \frac{(2Rk_a + 1)[J_v(uR)Y_v(uR) - Y_v(uR)J_v(uR)] - 2uR[J_v(uR)Y'_v(uR) - Y_v(uR)J'_v(uR)]}{\sqrt{[(2Rk_a + 1)J_v(uR) - 2uRJ'_v(uR)]^2 + [(2Rk_a + 1)Y_v(uR) - 2uRY'_v(uR)]^2}} \]

\[ \cos(\gamma) \equiv \cos(\theta)\cos(\theta_0) + \sin(\theta)\sin(\theta_0)\cos(\phi - \phi_0) \]

\[ P_n(x) \quad n^{th} \text{Legendre polynomial} \]

\[ J_n(x) \quad \text{Bessel function of the first kind} \]

\[ Y_n(x) \quad \text{Bessel function of the second kind} \]

=> Even though this distribution is very complex, it is possible to generate the exact length and the approximate angles of the inter-particle vector from this Green’s function.

Green’s functions (3D) for radiation chemistry

- Limiting case: \(R\to 0, \ k_a=0\)
- In principle, this should be equivalent to free diffusion

\[
p(r, \theta, \phi, t \mid r_0, \theta_0, \phi_0) = \frac{1}{4\pi\sqrt{rr_0}} \sum_{n=0}^{\infty} (2n+1)P_n(\cos(\gamma)) \int_0^\infty e^{-u^2Dt} u F_{n+1/2}(u, r) F_{n+1/2}(u, r_0) du
\]

\[
F_v(u, r) = \left[ J_v(\nu r) Y_v(\nu r) - Y_v(\nu r) J_v(\nu r) \right] - 2uR \left[ J_v(\nu r) Y_v'(\nu r) - Y_v(\nu r) J_v'(\nu r) \right]
\]

\[
\sqrt{\left[ J_v(\nu r) - 2uR J_v'(\nu r) \right]^2 + \left[ Y_v(\nu r) - 2uR Y_v'(\nu r) \right]^2}
\]

\[
\lim_{R \to 0} F_v(u, r) = J_v(\nu r)
\]

\[
p(r, \theta, \phi, t \mid r_0, \theta_0, \phi_0) = \frac{1}{4\pi\sqrt{rr_0}} \frac{1}{2Dt} e^{-\left(r^2+r_0^2\right)/4Dt} \sum_{n=0}^{\infty} (2n+1)P_n(\cos(\gamma)) I_{n+1/2}\left(\frac{rr_0}{2Dt}\right)
\]

Weber’s formula

\[
\sqrt{\frac{\pi}{2z}} \sum_{k=0}^{\infty} (2k+1) I_{k+1/2}(z) P_k(\cos \gamma) = e^{z\cos \gamma}
\]

\[
p(r, \theta, \phi, t \mid r_0, \theta_0, \phi_0) = \frac{1}{(4\pi Dt)^{3/2}} e^{-\left(r^2+r_0^2-2rr_0\cos \gamma\right)/4Dt}
\]

≡ Free diffusion!
Green’s functions (3D) for radiation chemistry

- Radial distribution of the exact Green’s function
- The radial distribution is not function of $\theta_0$ and $\phi_0$, so we use $\theta_0=0$ and $\phi_0=0$, for which $\cos(\gamma) = \cos(\theta)$

\[
p(r, t \mid r_0, 0, 0) = \int_0^\pi \int_0^\pi r^2 p(r, \theta, \phi, t \mid r_0, 0, 0) \sin \theta d\theta d\phi = \int_0^\pi 2\pi r^2 p(r, \theta, \phi, t \mid r_0, 0, 0) \sin \theta d\theta
\]

\[
\int_0^{\pi} (2n + 1) P_n(\cos \theta) \sin(\theta) d\theta = 2\delta_{n0}
\]

\[
p(r, t \mid r_0, 0, 0) = \frac{r^2}{\sqrt{r_0}} \sum_{n=0}^\infty \delta_{n0} \int_0^\infty e^{-u^2Dt} uF_{n+1/2}(u, r)F_{n+1/2}(u, r_0) du = \frac{r^2}{\sqrt{r_0}} \int_0^\infty e^{-u^2Dt} uF_{1/2}(u, r)F_{1/2}(u, r_0) du
\]

\[
J_{n+1/2}(z) = \sqrt{2z / \pi} j_n(z) \quad j_0(z) = \frac{\sin z}{z} \quad Y_{n+1/2}(z) = \sqrt{2z / \pi} y_n(z) \quad y_0(z) = -\frac{\cos z}{z}
\]

Bessel functions

Substituting

\[
p(r, t \mid r_0, 0, 0) = \int_0^\pi e^{-u^2Dt} \left( \frac{2(u \sigma \cos[u(r - \sigma)] + (1 + k_a^2) \sin[u(r_0 - \sigma)](u \sigma \cos[u(r_0 - \sigma)] + (1 + k_a^2) \sin[u(r_0 - \sigma)]]}{\pi u(1 + k_a^2 + u^2)\sigma^2} du
\]

\[
p(r, t \mid r_0, 0, 0) = \frac{r}{r_0 \sqrt{4\pi Dt}} \left\{ \exp\left[ -\frac{(r-r_0)^2}{4Dt} \right] + \exp\left[ -\frac{(r+r_0-2\sigma)^2}{4Dt} \right] \right\} + \alpha \frac{r + r_0 - 2\sigma}{\sqrt{4Dt}} W\left( \frac{r + r_0 - 2\sigma}{\sqrt{4Dt}}, -\alpha \sqrt{Dt} \right) \equiv 4\pi r^2 p_{rad}(r, t \mid r_0)
\]

\[\equiv \text{Radial GF!}\]
Green’s functions (3D) for radiation chemistry

• The sampling algorithms for chemical reactions yields values of \( r, \theta \) and \( \phi \)

• Therefore, we need to work with the distributions \( p(r,t| r_0, \theta_0, \phi_0) \), \( p(\theta,t| r_0, \theta_0, \phi_0) \) and \( p(\phi,t| r_0, \theta_0, \phi_0) \).

• These distributions are difficult to obtain for the general case \( (\theta_0 \neq 0, \phi_0 \neq 0) \) even for simple free 3D diffusion

\[
p_{fr}(r, t | r_0, \theta_0, \phi_0) = \int_0^\pi \int_0^{2\pi} p_{fr}(r, \theta, \phi, t | r_0, \theta_0, \phi_0) \sin \theta d\theta d\phi = \frac{r}{\sqrt{\piDt}} \exp \left( -\frac{r^2 + r_0^2}{4Dt} \right) \sinh \left( \frac{rr_0}{2Dt} \right)
\]

\[
p_{fr}(\theta, t | r_0, \theta_0, \phi_0) = \int_0^\infty \int_0^{2\pi} p_{fr}(r, \theta, \phi, t | r_0, \theta_0, \phi_0) \sin(\theta) d\phi dr
\]

\[
= \sum_{n=0}^{\infty} \frac{(2n+2)!}{(n!)^2} e^{-r_0^2 (1-\cos^2 \theta \cos^2 \theta_0) / 4Dt} i^{2(n+1)} Erfc \left( \frac{-r_0 \cos \theta \cos \theta_0}{\sqrt{4Dt}} \right) \left( \frac{r_0 \sin \theta \sin \theta_0}{\sqrt{4Dt}} \right)^{2n} \sin \theta
\]

\[
p_{fr}(\phi, t | r_0, \theta_0, \phi_0) = \int_0^\pi \int_0^{2\pi} p_{fr}(r, \theta, \phi, t | r_0, \theta_0, \phi_0) \sin(\theta) d\theta d\phi = \frac{1}{2\sqrt{\pi}} e^{-\phi_0^2 \sin^2(\phi-\phi_0) \sin^2 \theta_0 / 4Dt} iErfc \left( -\frac{r_0 \cos(\phi-\phi_0) \sin \theta_0}{\sqrt{4Dt}} \right)
\]

\[
i^n Ercf(z) = \int_z^\infty i^{n-1} Ercf(t) dt
\]
Green’s functions (3D) for radiation chemistry

- The sampling algorithms for chemical reactions yields distributions of $r$, $\theta$ and $\phi$
- The analytical distributions $p(r,t|r_0,\theta_0,\phi_0)$, $p(\theta,t|r_0,\theta_0,\phi_0)$ and $p(\phi,t|r_0,\theta_0,\phi_0)$ are difficult to obtain for the general case ($\theta_0 \neq 0$, $\phi_0 \neq 0$) even for simple free diffusion
- The case $\theta_0=0$, $\phi_0=0$ is much simpler since $\phi$ is uniformly distributed between 0 and $2\pi$.
- It is possible to sample the distributions in a referential aligned with the z axis and then perform two rotations to get the sampled values for the general case

\[
\begin{bmatrix}
 x' \\
 y' \\
 z'
\end{bmatrix} = \begin{bmatrix}
 \cos \phi_0 & -\sin \phi_0 & 0 \\
 \sin \phi_0 & \cos \phi_0 & 0 \\
 0 & 0 & 1
\end{bmatrix} \begin{bmatrix}
 \cos \theta_0 & 0 & \sin \theta_0 \\
 0 & 1 & 0 \\
 -\sin \theta_0 & 0 & \cos \theta_0
\end{bmatrix} \begin{bmatrix}
 x'' \\
 y'' \\
 z''
\end{bmatrix}
\]
Green’s functions (3D) for radiation chemistry

• Free diffusion for the case $\theta_0=0$, $\phi_0=0$

• The distributions in Cartesian coordinates are Gaussians. Their equivalents in spherical coordinates are given by

$$p_{fr}(r, t | r_0, 0, 0) = \frac{r}{\sqrt{\pi \sigma_0^2}Dt} \exp\left(-\frac{r^2 + r_0^2}{4Dt}\right) \sinh\left(\frac{rr_0}{2Dt}\right)$$

$$p_{fr}(\theta, t | r_0, 0, 0) = 2(\sin \theta)e^{-r_0^2 \sin^2 \theta / 4Dt}i^2\text{Erfc}\left(-\frac{r_0 \cos \theta}{2\sqrt{Dt}}\right)$$

$$p_{fr}(\phi, t | r_0, 0, 0) = \frac{1}{2\pi}$$
Green’s functions (3D) for radiation chemistry

- We know how to sample \( p(r, t| r_0, \theta_0, \phi_0) \).
- The exact Green’s function is difficult to evaluate numerically.
- To calculate it we write \( p(r, \theta, \phi, t| r_0, \theta_0, \phi_0) \) as the sum of free diffusion and correction terms (van Zon and ten Wolde, 2005)
- This approach reduces the number of terms necessary for convergence

\[
p_{\text{ex}} (r, \theta, \phi, t | r_0, \theta_0, \phi_0) = p_{\text{fr}} (r, \theta, \phi, t | r_0, \theta_0, \phi_0) + p_{\text{corr}} (r, \theta, \phi, t | r_0, \theta_0, \phi_0)
\]

\[
p_{\text{corr}} (r, \theta, \phi, t | r_0, \theta_0, \phi_0) = -\frac{1}{4\pi \sqrt{rr_0}} \sum_{n=0}^{n_{\text{max}}} (2n + 1)P_n (\cos \theta) \int_0^\infty e^{-u^2Dt} \frac{R_1}{R_1^2 + R_2^2} (R_1G_1 + R_2G_2) u dd
\]

\[
R_1 = (2\sigma k_a + 1)J_{n+1/2} (u\sigma) - 2u\sigma J'_{n+1/2} (u\sigma) \quad \quad \quad G_1 = J_{n+1/2} (ur)J_{n+1/2} (ur_0) - Y_{n+1/2} (ur)Y_{n+1/2} (ur_0)
\]

\[
R_2 = (2\sigma k_a + 1)Y_{n+1/2} (u\sigma) - 2u\sigma Y'_{n+1/2} (u\sigma) \quad \quad \quad G_2 = J_{n+1/2} (ur)Y_{n+1/2} (ur_0) + Y_{n+1/2} (ur)J_{n+1/2} (ur_0)
\]

Green’s functions (3D) for radiation chemistry

- To sample $\theta$ and $\phi$, we generate values for $\theta_0=0$, $\phi_0=0$ and perform the necessary rotations. In this system, $\phi$ is uniformly distributed between 0 and $2\pi$.
- Use the algorithm from Clifford et al. to generate the angle $\theta$ and $\phi$

$\vartheta = 2\pi U_1$

$\Theta = \cos^{-1}\left\{1 + \frac{1}{\alpha} \ln [1 - U_2 \left(1 - \exp(-2\alpha)\right)]\right\}$

where $U_1$ and $U_2$ are random numbers uniformly distributed $[0,1]$

$\alpha = r r_0 / 2 D t$

$r_0$ and $r$ are the inter-particle distances before and after the time step.
Radiation chemistry

Radiation chemistry
Primary yields of $e_{aq}^-$, ·OH, H, H₂ and H₂O₂ as a function of the LET

Irradiation by 300-0.1 MeV protons
LET: ~0.3-85 keV/μm

Note: the primary yields (noted $G_\chi$) are the yields at the end of spur expansion (~$10^{-6}$ s)

The radiation chemistry of DNA is very complex

Many reaction rate constants are known

\[
\begin{align*}
\text{Reaction} & \quad k \quad (\text{dm}^3\text{.mol}^{-1}\text{.s}^{-1}) & \quad \text{Radius} \\
\text{e}^-_{\text{aq}} + \text{Thymine} \rightarrow \text{Thy}(+e) & \quad 1.79 \times 10^{10} & \quad 5.287 \\
\cdot \text{OH} + \text{Thymine} \rightarrow & \quad 6.4 \times 10^{9} & \quad 3.02 \\
\text{TC5OH} + \text{TC6OH} + \text{TUCH2} \cdot & \quad & \\
\text{H.} + \text{Thymine} \rightarrow \text{Thymine}^* & \quad 5.7 \times 10^{8} & \quad 0.11 \\
\end{align*}
\]

Release history

- RITRACKS was used by the students at the NASA Space Radiation Summer School at the Brookhaven National Laboratory, Upton, New York (June 6-24, 2011, May 28 - June 15, 2012, MIT ICED June 2012)(over 40 users)
- The release to international partners was approved in 2011
- RITRACKS was released to NASA space radiation community with over 20 users
- The software is now available for download on the web site [http://spaceradiation.usra.edu/irModels/](http://spaceradiation.usra.edu/irModels/) (ITAR, authentication and password required)

http://spaceradiation.usra.edu
An online version of RITRACKS will be available soon!

Left: Simulation of a $^{12}$C$^{6+}$, 60 MeV/amu, on the projected RRAW site.
Right: Calculation of the radial dose for the track depicted on the left.

The track structure data and the radial dose are available for download after calculation.
Future plans for development and use

- Implementation of the non-homogeneous chemistry
- Predictions of clustered and complex DNA damage yields in human cells for improving the understanding of DNA repair and signal transduction
- Use with chromosome models to study double-strand breaks (DSB) in relation to cancer risks from space radiation
- Web-based version
- New GPU-CPU version to improve computational speeds by several orders of magnitude.
Future plans for development and use

- Android/iPhone version

- For ions:
  - LET
  - Relativistic $\beta$ and $\gamma$
  - $Z_{\text{eff}}$ and $Z_{\text{eff}}^2/\beta^2$
  - Maximum energy transfer to an electron
  - Dose and fluence
  - Radial dose
  - Number of hits per cell in a cell culture

- For electrons:
  - Relativistic $\beta$ and $\gamma$
  - Range
Future plans for development and use

- **Android/iPhone version**

- **For ions:**
  - LET
  - Relativistic $\beta$ and $\gamma$
  - $Z_{\text{eff}}$ and $Z_{\text{eff}}^2/\beta^2$
  - Maximum energy transfer to an electron
  - Dose and fluence
  - Radial dose
  - Number of hits per cell
  - in a cell culture

- **For electrons:**
  - Relativistic $\beta$ and $\gamma$
  - Range
Using RITRACKS

The installer

- The necessary files are included in an installer created by the freeware InstallJammer
- The program is installed in the folder C:\Program Files (x86)\RITRACKS
- Simulations are stored the subfolder RITRACKS Simulations in the My Documents folder
RITRACKS main window
Radiation info window

The following information is given in this window

Rest mass energy: \( Mc^2 \)

Total energy: \( \gamma Mc^2 \)

Relativistic \( \gamma \): \( \gamma = \frac{T}{Mc^2} + 1 \)

Relativistic \( \beta \): \( \beta^2 = 1 - \frac{1}{\gamma^2} \)

Momentum: \( p = \gamma Mv \)

Maximum energy transfer to e\(^{-}\): \( E_{\text{max}} = \frac{2mc^2(\gamma^2 - 1)}{1 + 2\gamma(m/M) + (m/M)^2} \)

\( \text{LET (MeV/cm): } \frac{-dE}{dx} = \frac{0.170}{\beta^2} [F(\beta) - 4.31] \quad \text{F(\beta) = } \ln \frac{1.02 \times 10^6 \beta^2}{1 - \beta^2} - \beta^2 \)
Electron cross sections window
Visualization window

Tools:
- Rotation
- Translation
- Zoom
- Save to file
- Copy to clipboard
- Create a .avi file
- Open data folder

Visualization:
- Radiolytic species
- Events
- Dose (voxels)

Time evolution
RITRACKS tools

- Calculation of tracks per cell in a cell culture for a given ion, energy and dose
Homework

- Install RITRACKS
- Max the number of CPUs
- Click on the More button for the Radiation Info window
Homework

- **Simulations:**
  - 1 ion $^{12}\text{C}^{6+}$, 25 MeV/amu, of length 5 μm. Use the following parameters:
    - #Copy = 1 and #Histories/Copy = 20
    - #Copy = 10 and #Histories/Copy = 2
    - Notice the difference in the progress window and calculation time

- **Visualize the tracks with the 3D interface**
  - Use visualization tools (displace, rotate, zoom, copy to clipboard, save to file, reset parameters, open folder).
  - Zoom and un-zoom (to un-zoom, draw a zoom box from the bottom right to upper left)
  - Use the time evolution bar.
  - Change the simulation number and click Draw.
  - Create an avi file of the track. Click on the movie icon, click on Create AVI, enter a name (test.avi).
Homework

- **Visualize the tracks with the 3D interface**
  - Switch between voxel dose and track. In the voxel dose representation, vary the threshold scale (the slider located at the left of the dose scale).
  - Display the axis (go to Options->Visualization, select the tab Axis and check the boxes).

- **Display the radial dose and voxel dose (from the main interface window).**

- **Repeat the simulations with the following ions**
  - 1 ion $^{56}\text{Fe}^{26+}$, 1000 MeV/amu, of length 5 μm (10 histories)
  - Irradiation of a cube of 5 μm x 5 μm x 5 μm with 450 x 300 MeV protons (1 history)
  - Irradiation of a cube of 5 μm x 5 μm x 5 μm with 1 1000 MeV/amu $^{56}\text{Fe}^{26+}$ ions (1 history)
References

Acknowledgements

- Dr. Luc Devroye (McGill University)
- Brian Fessler (USRA-Houston)
- Dr. Francis Cucinotta
- Radiation Biophysics group
- USRA
- NASA
- Dr. John Norbury