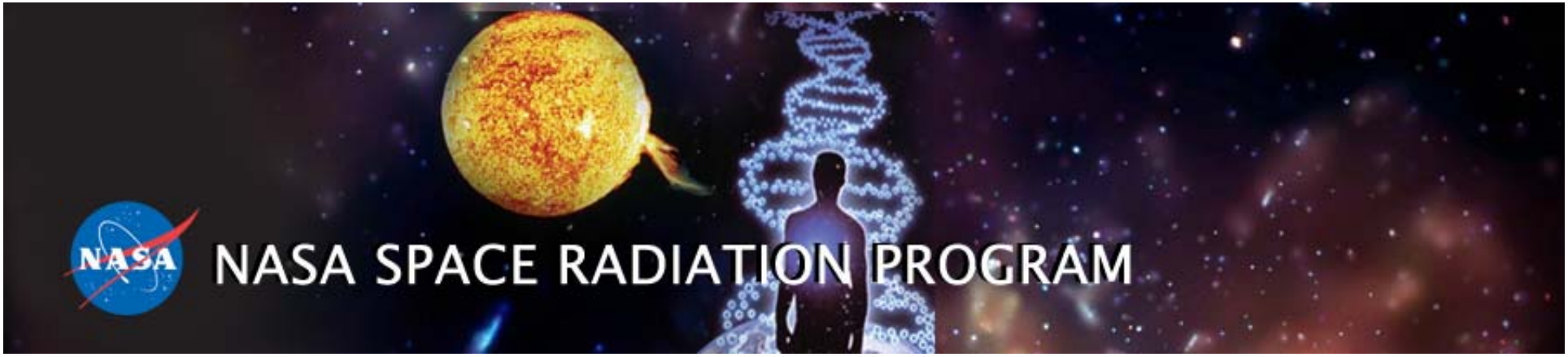


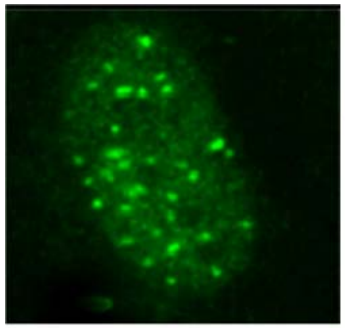
A radiation chemistry code based on the Green's functions of the Diffusion Equation

Ianik Plante
Universities Space Research Association
Division of Space Life Sciences
NASA Johnson Space Center, Houston TX

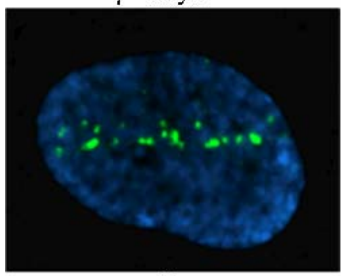
NASA Human Research Program Investigators' Workshop
February 11-13, 2014

The space radiation problem

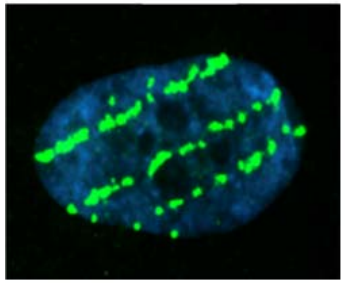
- Space radiation is comprised of high-energy protons and heavy ions (HZE's) and secondary protons, neutrons, and heavy ions produced in shielding
- Unique damage to bio-molecules, cells, and tissues occurs from HZE ions that is qualitatively distinct from X-rays and gamma-rays on Earth
- No human data 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)



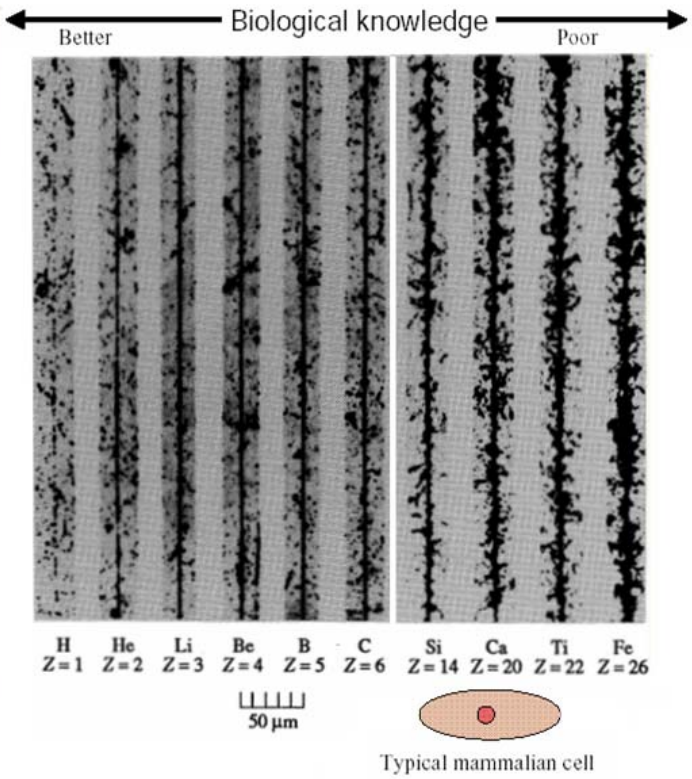
γ – rays



silicon



iron

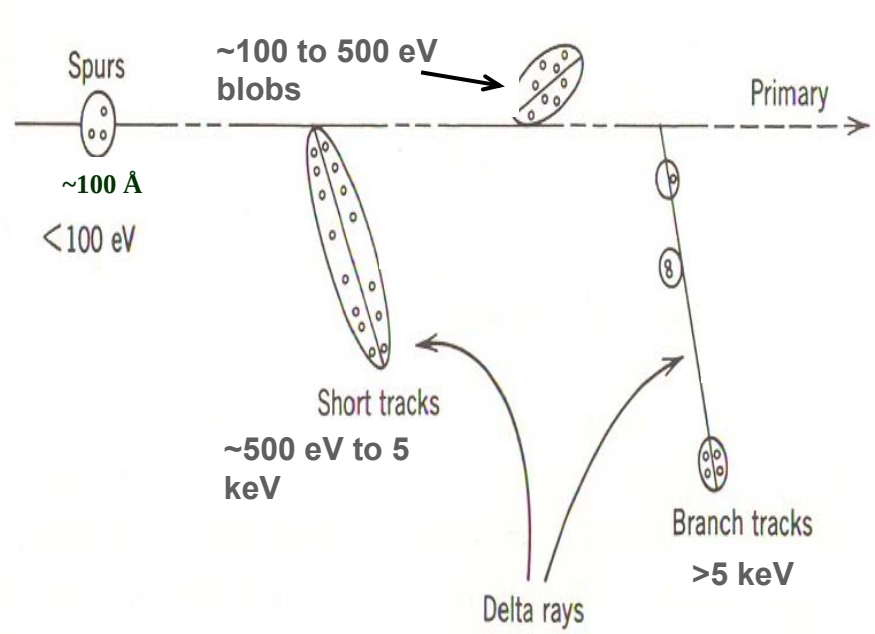


Cucinotta and Durante, *Lancet Oncology (2006)*

Radiation tracks and energy deposition

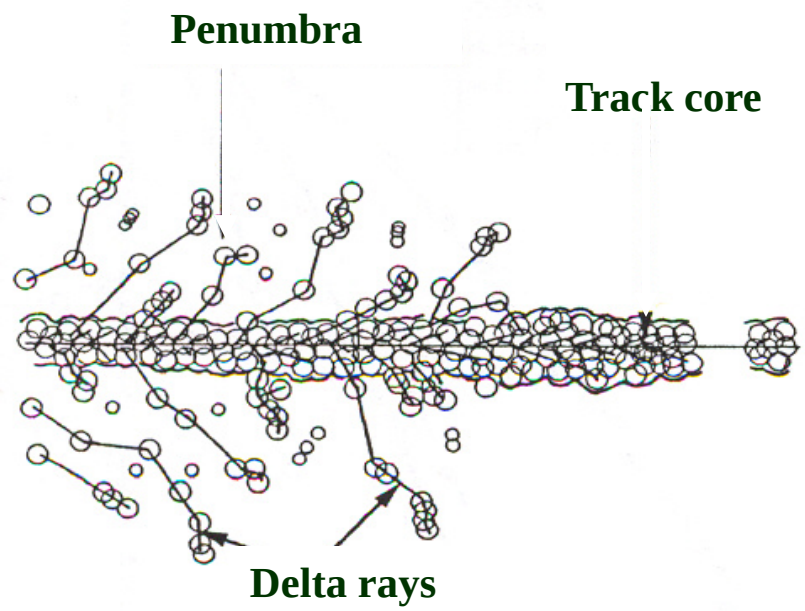
- The energy deposition by heavy ions is highly heterogeneous and dependent on the type and energy of the ion
- The interactions of radiation with matter are stochastic in nature and therefore often studied by Monte-Carlo simulations

Primary energy loss events in low-LET tracks



A. Mozumder and J.L. Magee (1966) *Radiat. Res.* **28**, 203

Primary energy loss events in high-LET tracks

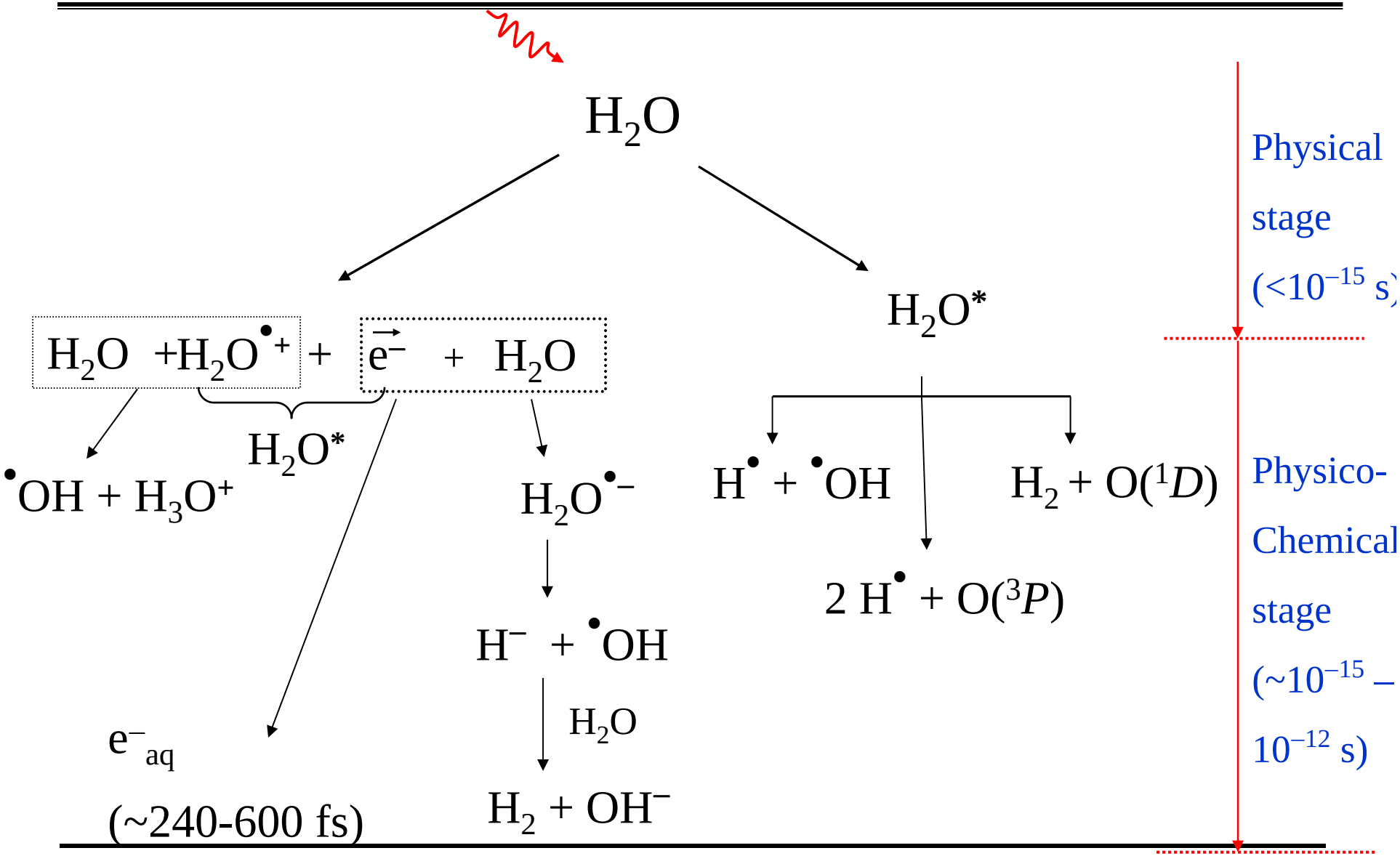


C. Ferradini (1979) *J. Chim. Phys.* **76,** 636

Radiation effects: time sequence of events

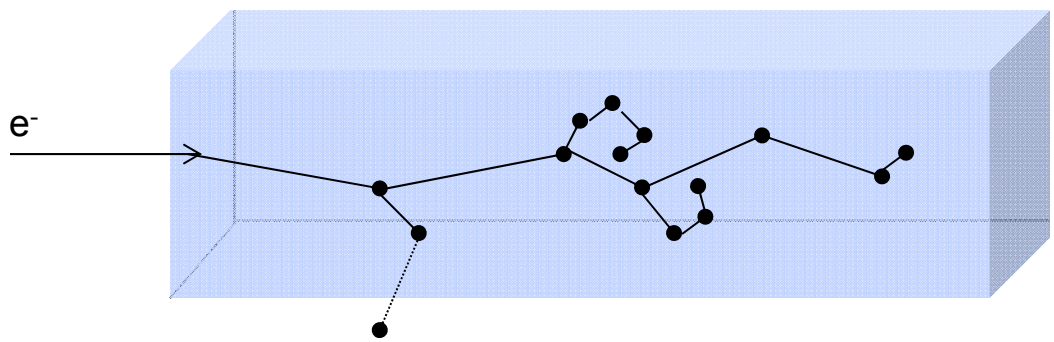
Time (s)	Stage	Events	Modeling
10^{-15}	Physical	Energy absorption	Particle transport Cross sections
10^{-12}	Physico-chemical	Reorganization Electron thermalization	
10^{-9}	Chemical	Radical diffusion Chemical reactions	Green's functions
10^{-6}			
10^{-3}	Biological	DNA repair	Kinetics models Molecular dynamics

Radiation effects: time sequence of events



Particle transport basics

- **The trajectory of a particle and all its interactions is followed in the medium**
- **Many other particles are generated by the interactions of the "primary" particle. The trajectories of these secondary particles should also be followed.**
- **A particle is followed until**
  - Its energy decrease below a threshold
  - It disappears by a physical process (e.g. absorption of a photon during a photo-electric effect
  - It leaves the volume of interest



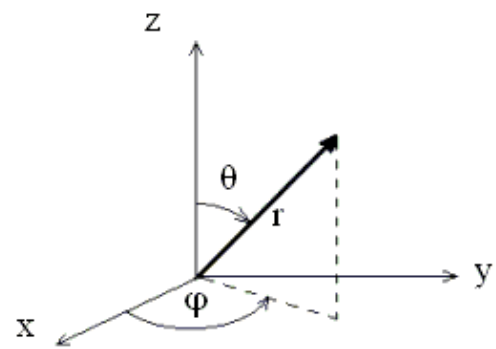
Plante, I. and Cucinotta, F.A. (2011) Monte-Carlo Simulation of Ionizing Radiation Tracks. In: Mode, C.J. (Ed.) Applications of Monte Carlo Methods in Biology, Medicine and Other Fields of Science. InTech, Rijeka, Croatia. www.intechopen.com

Particle transport basics

❑ Particles

- Position (x,y,z)
- Energy (E)
- Direction (θ,φ)

$$\vec{v} = \begin{bmatrix} \sin(\theta)\cos(\varphi) \\ \sin(\theta)\sin(\varphi) \\ \cos(\theta) \end{bmatrix}$$



❑ Cross sections

- Probability of interaction between radiation and matter

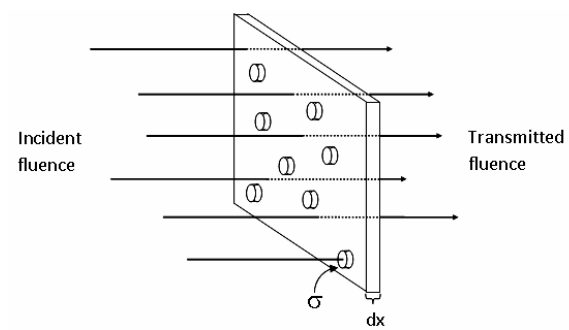
$$dI = -In\sigma dx$$

I: Incident fluence

n: Density of targets

dx: Width

σ: Cross section



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

$$I(x) = I(0)\exp(-x/\lambda(E))$$

$$\lambda(E) = 1/(N\sigma(E))$$

Plante, I. and Cucinotta, F.A. (2011) Monte-Carlo Simulation of Ionizing Radiation Tracks. In: Mode, C.J. (Ed.) Applications of Monte Carlo Methods in Biology, Medicine and Other Fields of Science. InTech, Rijeka, Croatia. www.intechopen.com

Cross sections

- **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**
- **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

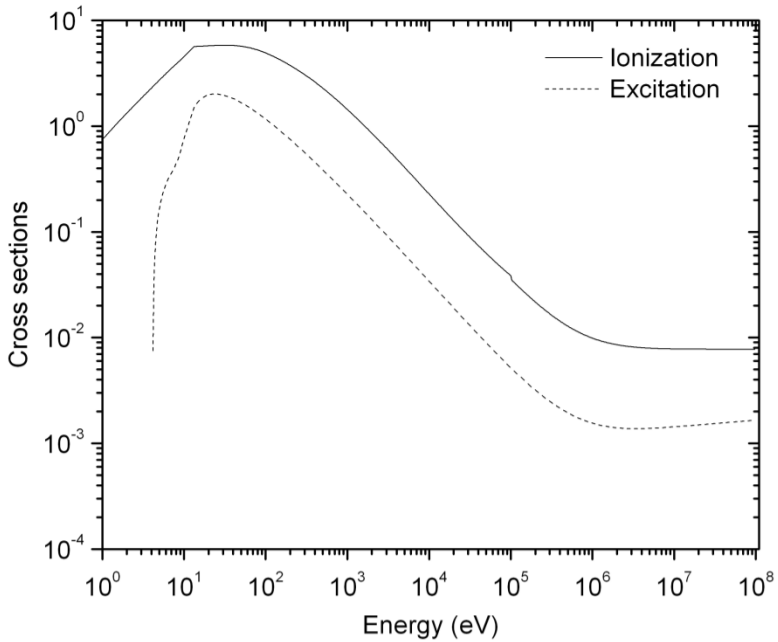
- **For photons:**
  - Compton effect
  - Coherent diffusion
  - Photoelectric effect
  - Pair production

Plante, I. and Cucinotta, F.A. (2011) Monte-Carlo Simulation of Ionizing Radiation Tracks. In: Mode, C.J. (Ed.) Applications of Monte Carlo Methods in Biology, Medicine and Other Fields of Science. InTech, Rijeka, Croatia. www.intechopen.com

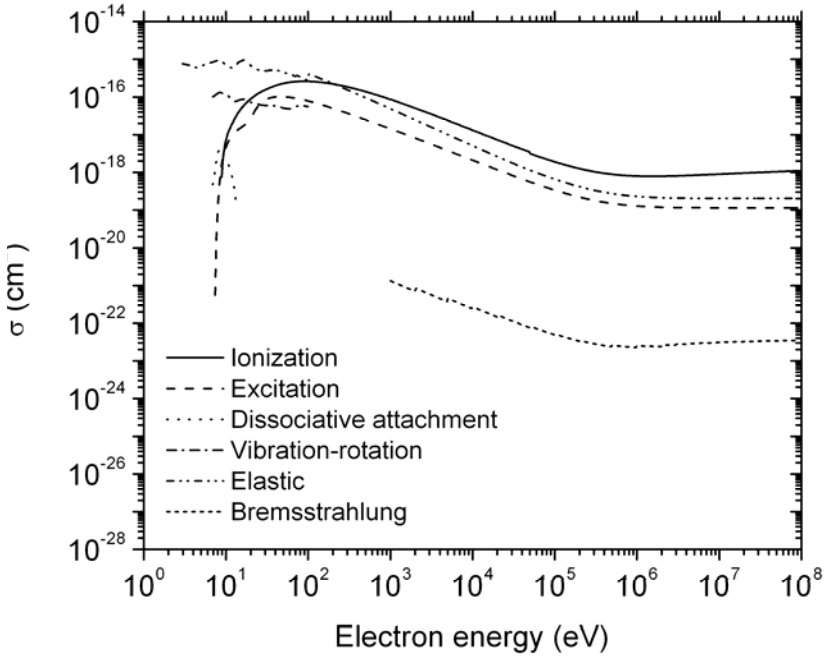
Cross sections

❑ Cross sections used in RITRACKS

Ions



Electrons



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

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

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

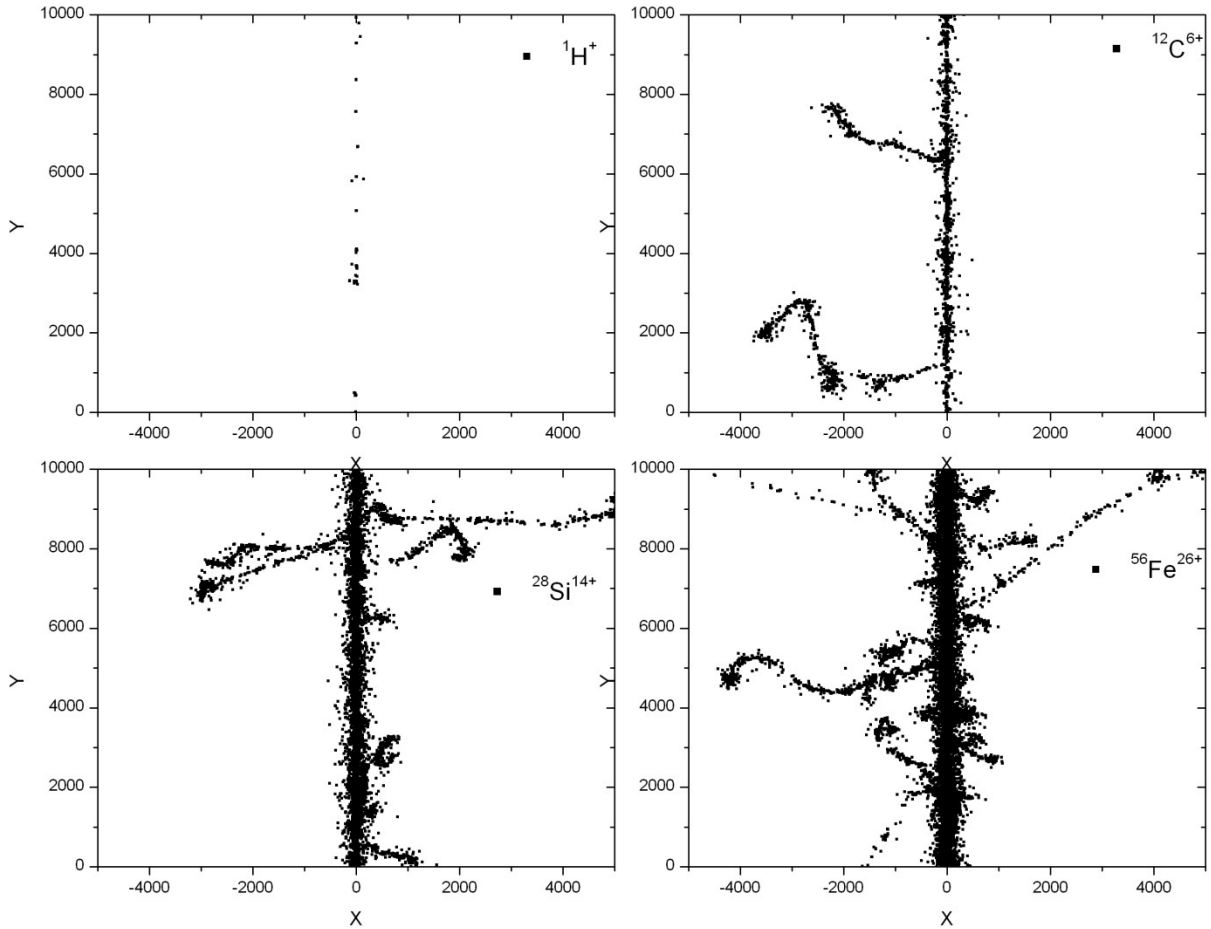
v: velocity of the ion

β: relativistic v/c

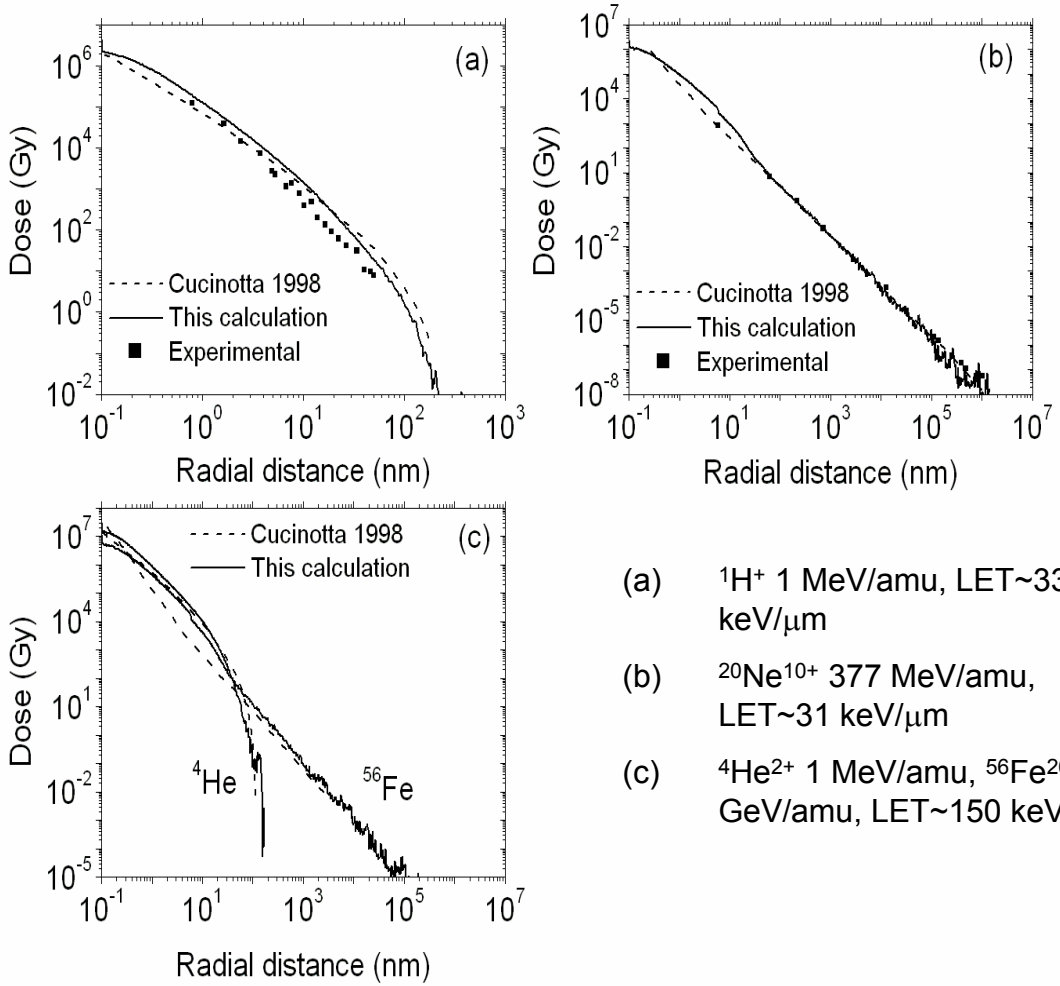
Plante, I. and Cucinotta, F. A. (2009). *New J. Phys.* **11**, 063047

Heavy ion track structure simulation

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



Radial dosimetry



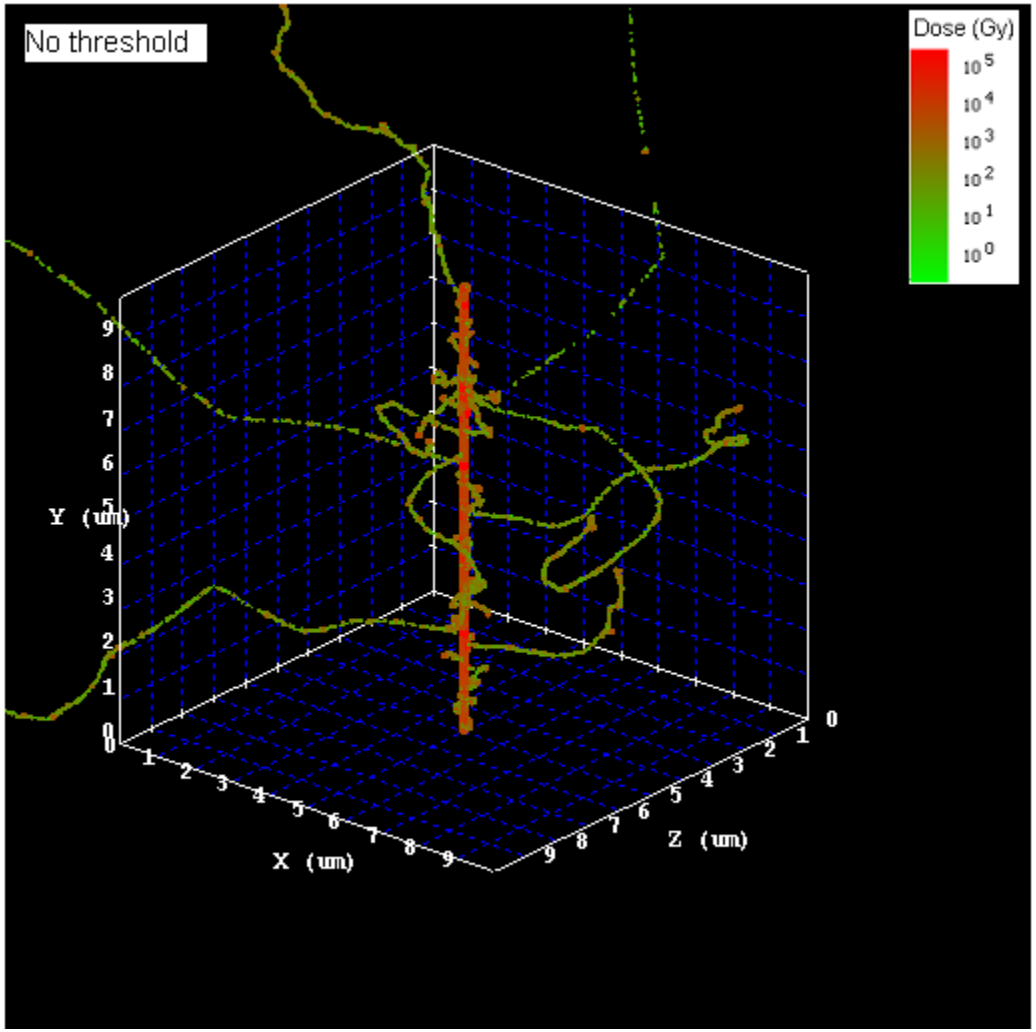
(a) $^{1}H^{+}$ 1 MeV/amu, LET~33 keV/μm

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

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

Plante, I. and Cucinotta, F.A. (2008), *New J. Phys.* **10**, 125020

Voxel dosimetry



1 GeV/amu $^{56}Fe^{26+}$ ion

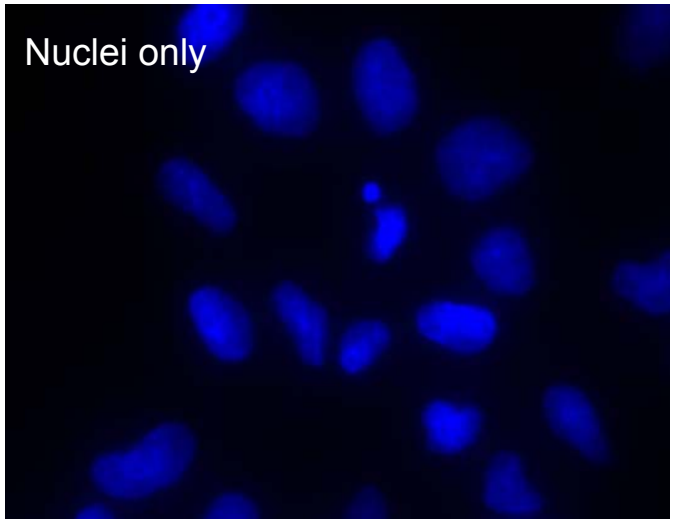
LET~150 keV/μm

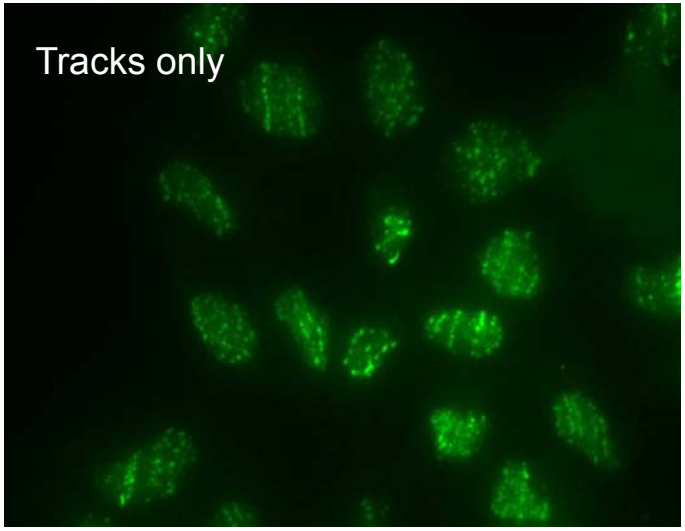
Voxels: 40 nm x 40 nm x 40 nm

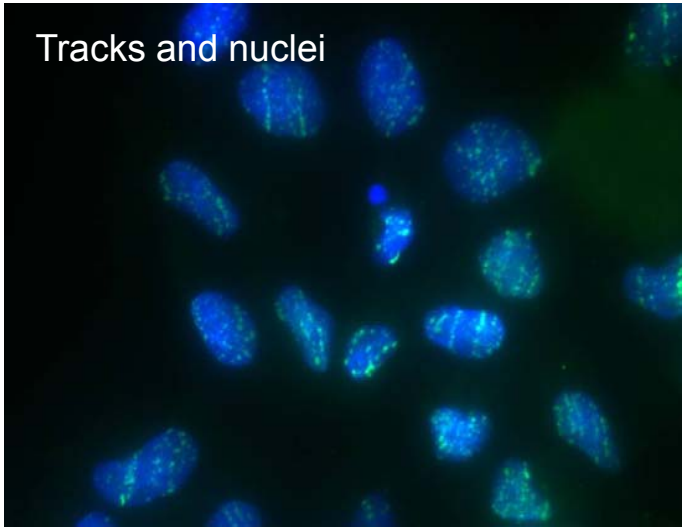
Plante I. et al. (2011). *Radiat. Prot. Dosim.* **143**, 156-161.

DNA damage / γH2AX foci studies

- Irradiation by 1 GeV/amu Fe ions
- 100 cGy
- LET ~ 149 keV/µm

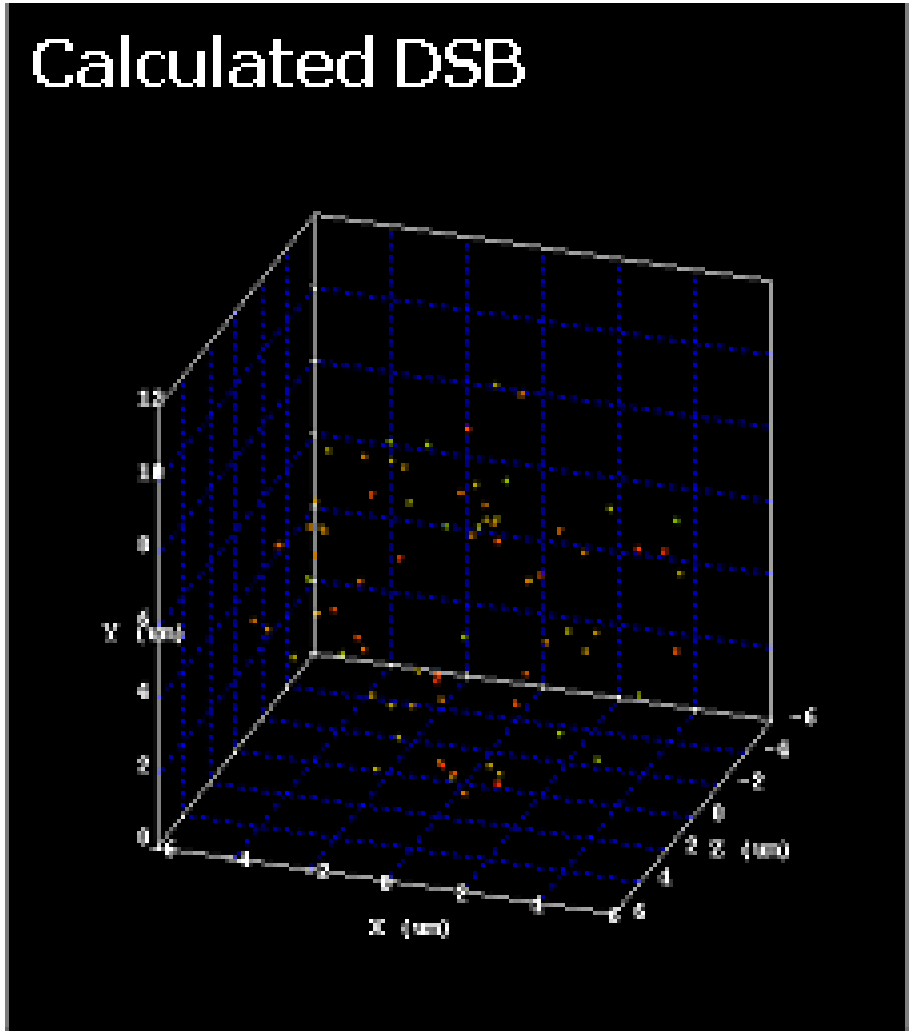






Experiments performed at the NASA Space Radiation Laboratory (2007)

DNA damage



2700 x $^{1}H^{+}$, 300 MeV (1 Gy)

Dose in voxels (20 nm)

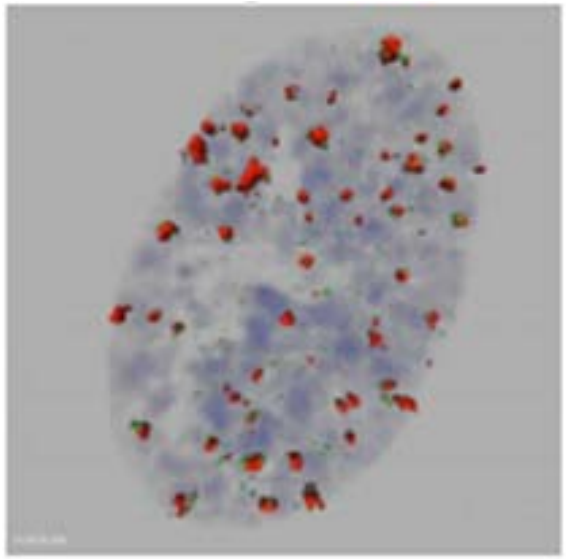
Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

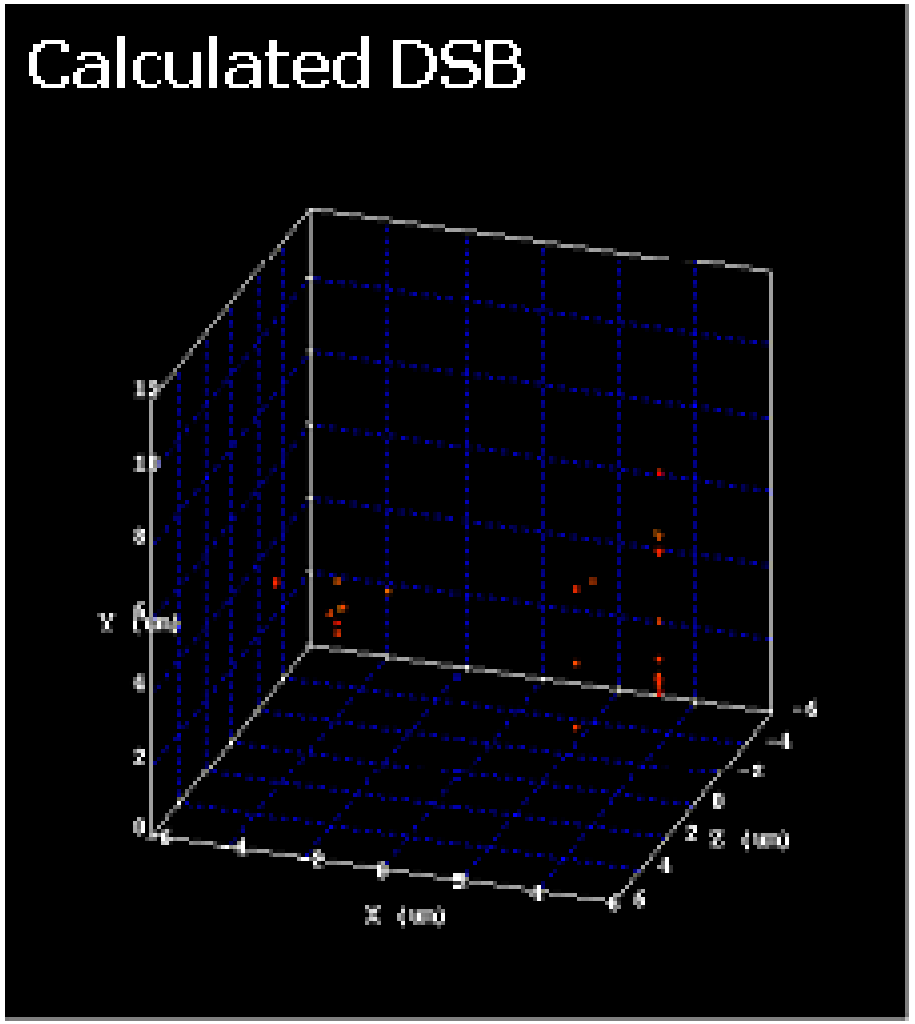
Application of DSB probability

$$\psi = 1 - e^{-QD(t)}$$



Mukherjee, B. et al. (2008), *DNA repair* **7** 1717-1730; Plante, I. et al. (2013), *Phys. Med. Biol.* ***58****, 6393-6405*

DNA damage



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

Dose in voxels (20 nm)

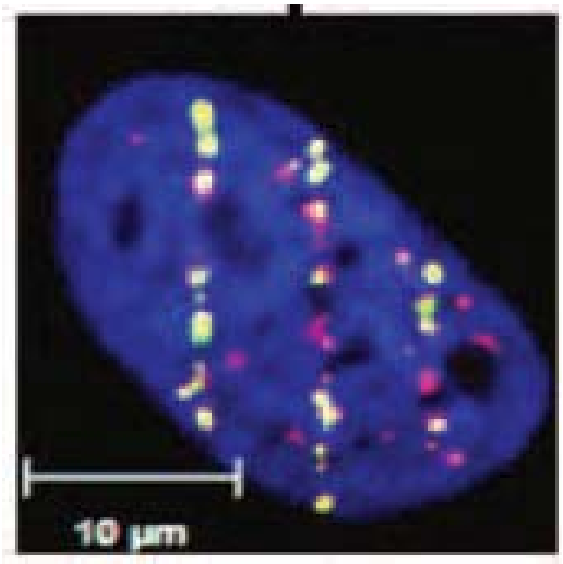
Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

Application of DSB probability

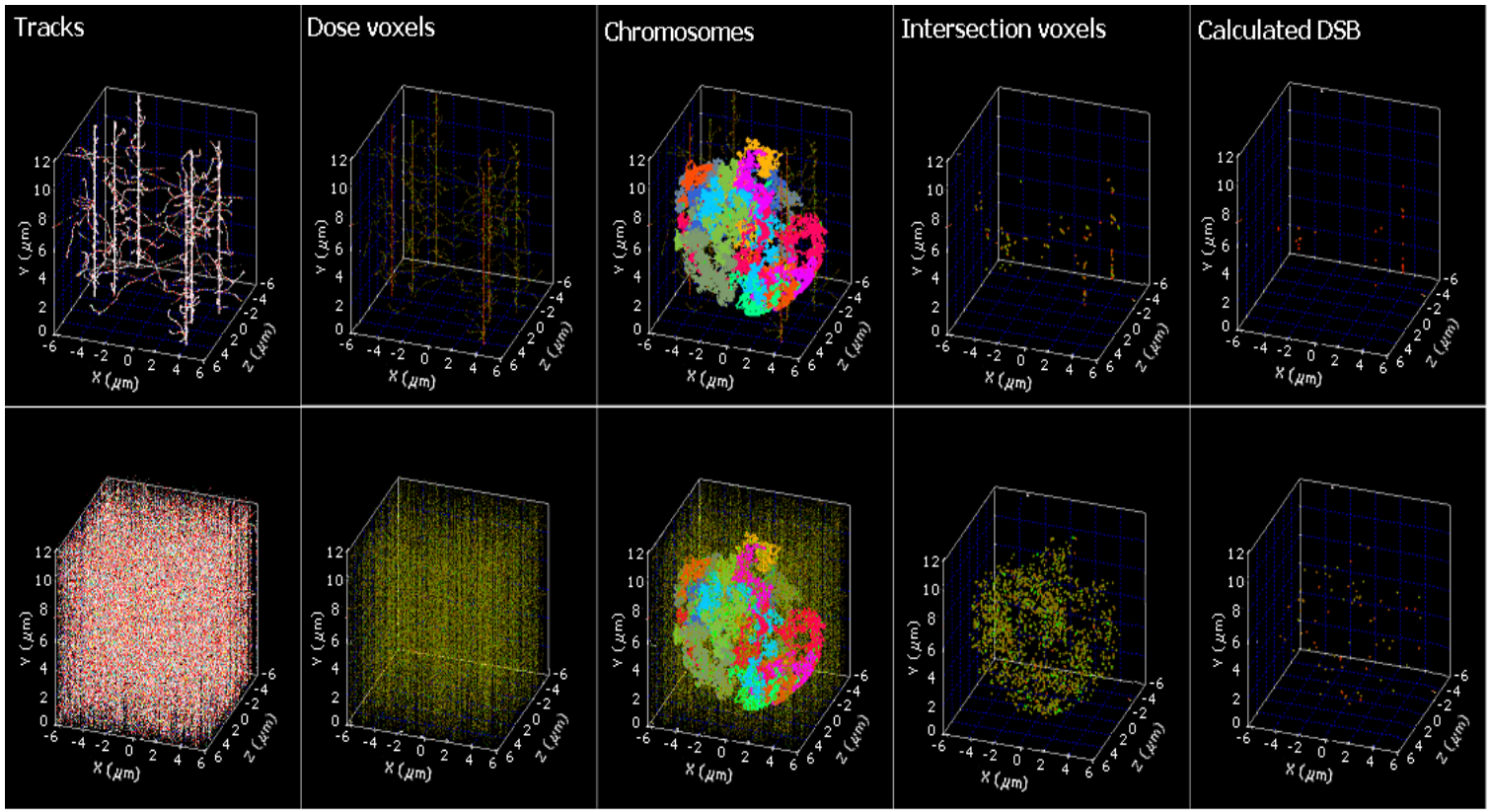
$$\psi = 1 - e^{-QD(t)}$$



Asaithamby, A. et al. (2008) *Radiat. Res.* **169**, 437-446; Plante, I. et al. (2013), *Phys. Med. Biol.* ***58***, *6393-6405*

DNA damage / γH2AX foci studies

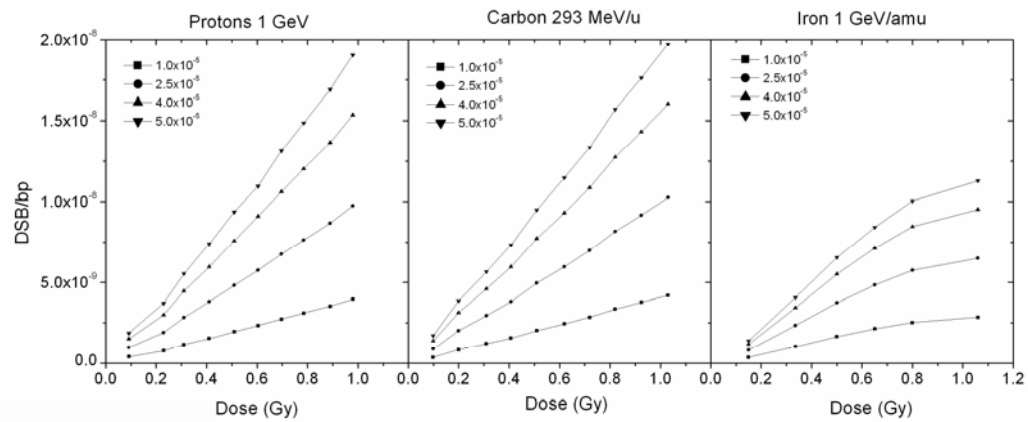
- Calculation of DSBs by low- and high-LET radiation

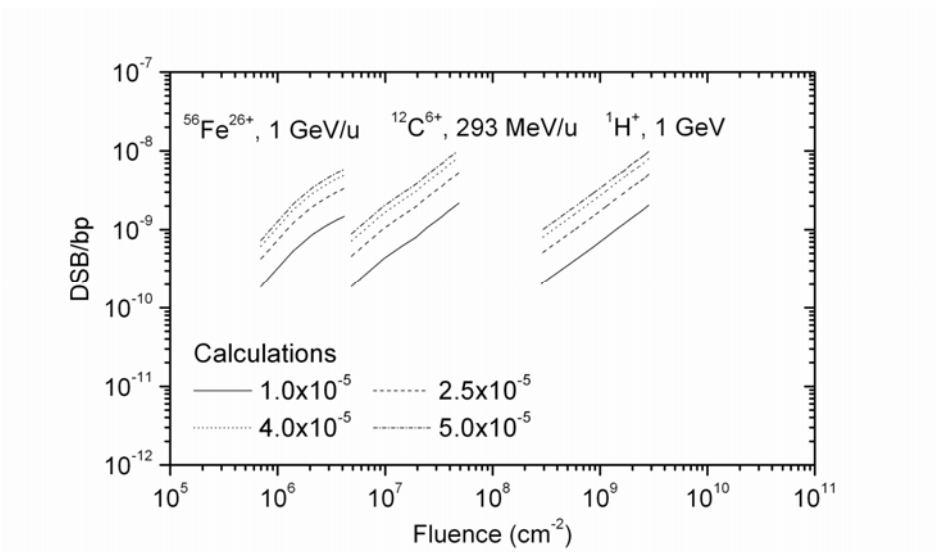


Plante, I. et al. (2013), *Phys. Med. Biol.* ***58****, 6393-6405*

DNA damage / γH2AX foci studies

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

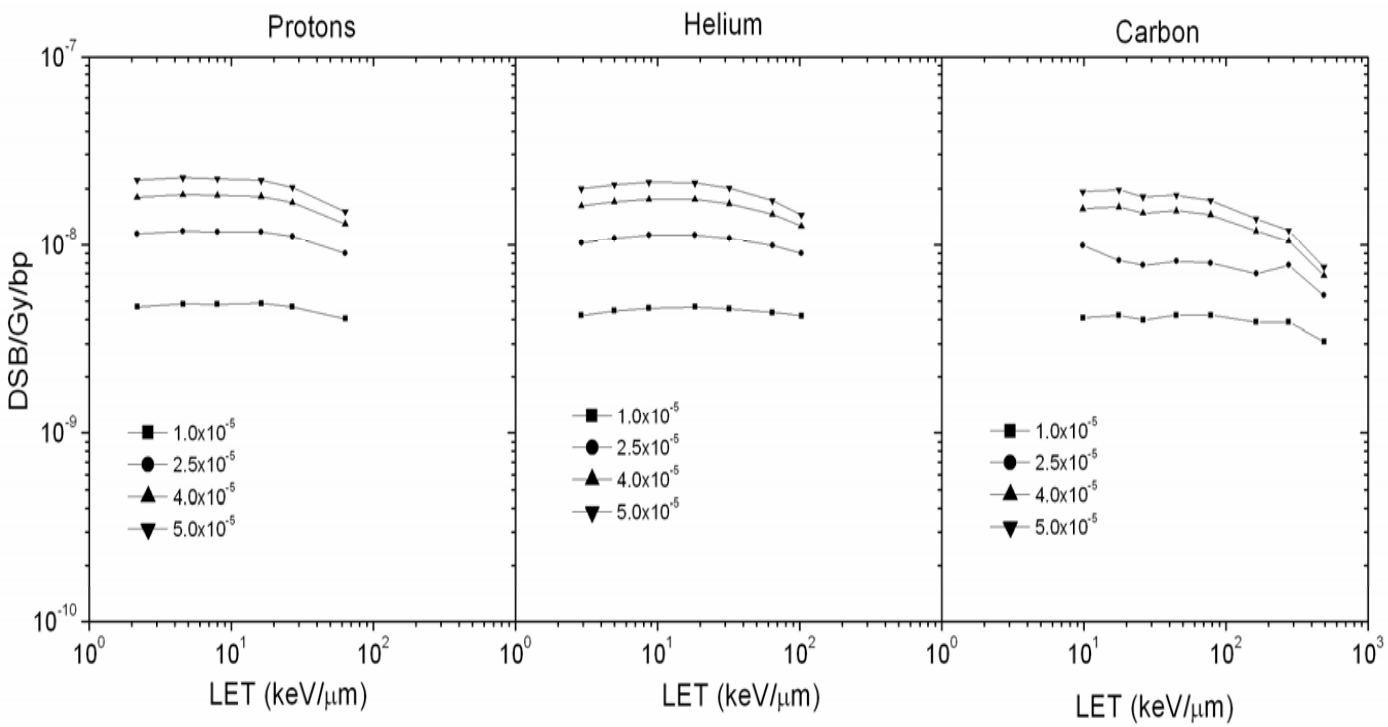




Plante, I. et al. (2013), *Phys. Med. Biol.* ***58****, 6393-6405*

DNA damage / γH2AX foci studies

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

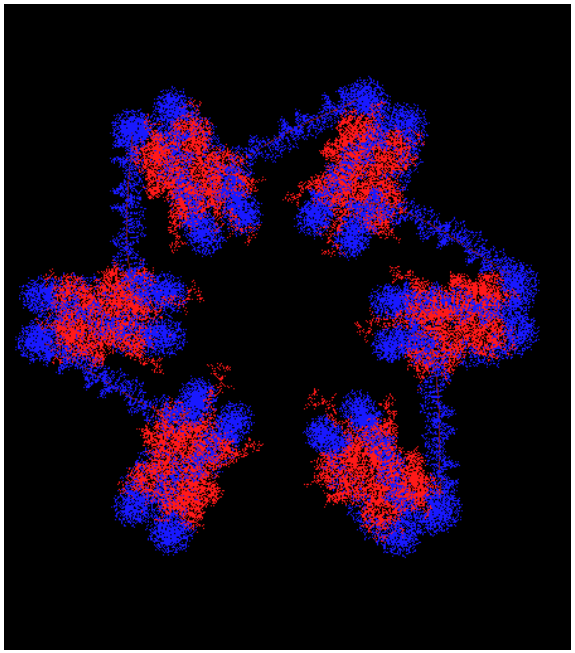


Plante, I. et al. (2013), *Phys. Med. Biol.* ***58****, 6393-6405*

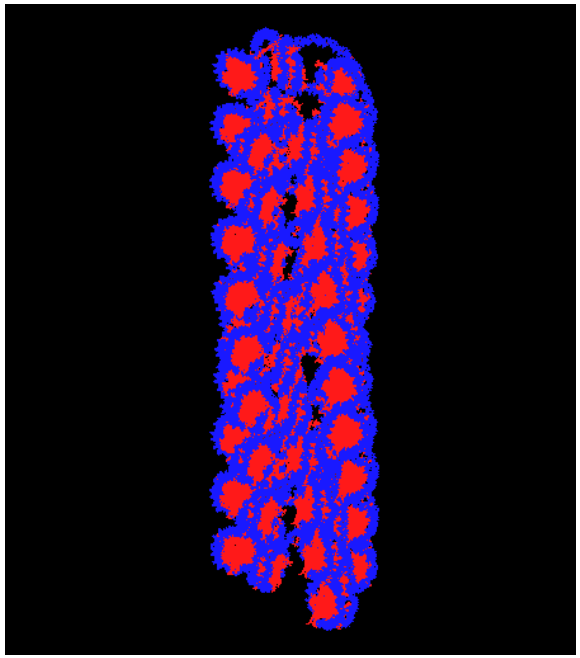
DNA damage simulations

- **To better understand the formation of DSBs, a chromatin fiber is build from nucleosome units and linker DNA**

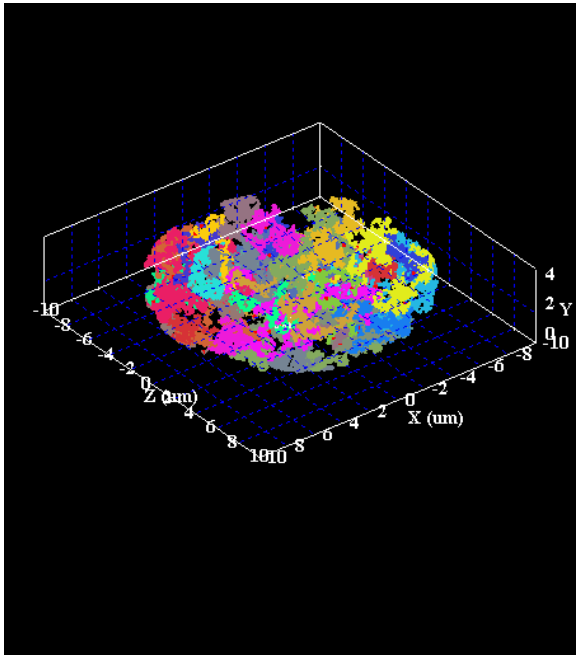
Nucleosome (DNA fragments)



Chromatin fiber



Nuclei



Nuclei simulations courtesy of Dr. Artem Ponomarev

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**

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

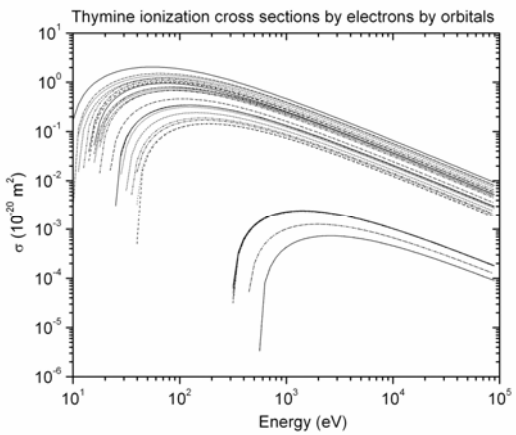
Adapted from S. Edel, PhD Thesis, Université de Toulouse (2006)

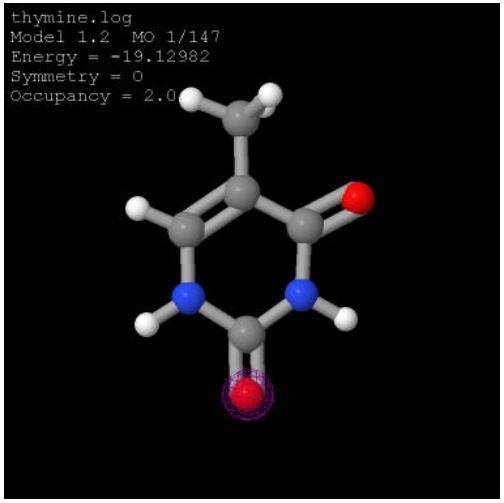
DNA damage simulations

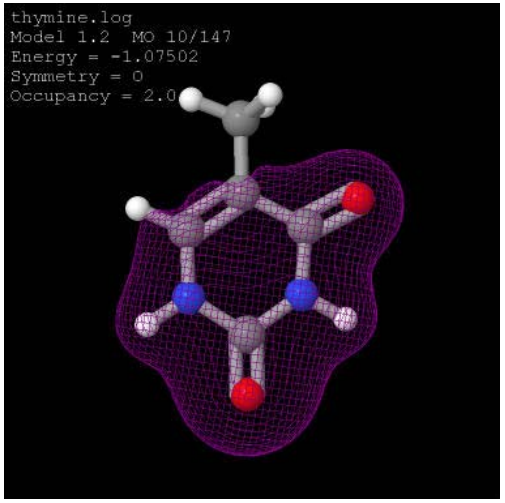
- **In the DNA bases, there are many internal and valence electrons. The BEB model allows to model the ionization for each electron of the molecule.**

Thymine

	No	U (eV)	B (eV)	N
Internal electrons (18)	1	794.1	559.41	2
	2	794.1	559.18	2
	3	601.5	425.6	2
	4	601.5	425.48	2
	5	435.9	311.36	2
	6	435.9	310.43	2
	7	435.8	308	2
	8	435.7	306.41	2
	9	435.8	305.8	2
Valence electrons (44)	10	66.26	40.06	2
	11	71.74	39.14	2.04
	12	63.05	36.16	1.86
	13	57.89	34.56	1.85
	14	44.95	30	2.3
	15	43.96	26.22	2.35
	16	47.64	25.14	2.11
	17	40.64	24.85	2.15
	18	41.92	21.32	2.18
	19	39.28	20.94	2.02
	20	36.32	19.4	1.86
	21	44.53	18.7	2.05
	22	55.89	18.56	1.92
	23	54.72	17.59	1.99
	24	39.88	16.62	2.01
	25	46.93	16.15	2.03
	26	39.89	15.44	1.78
	27	47.3	13.96	1.83
	28	59.96	13.15	1.86
	29	54.12	12.31	2.07
	30	60.23	12.10	1.78
	31	40.38	9.27	1.97







Calculations of MO from the site www.chemeddl.org

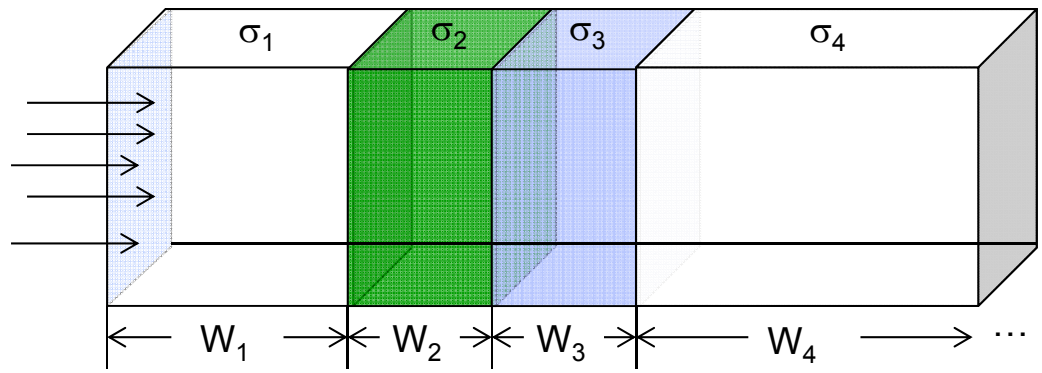
DNA damage studies

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

$$dI = -IN\sigma dx$$

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

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

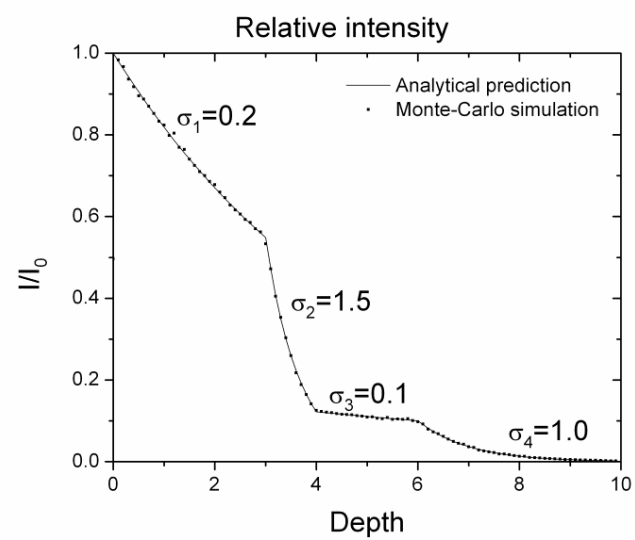


Relative weight

$$p_i = I_0 \frac{\exp(-N\sum_{j=1}^{i-1} W_j \sigma_j)(1-\exp(-NW_i\sigma_i))}{N\sigma_i}$$

Sampling of W_s

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



Adapted from S. Edel, PhD Thesis, Université de Toulouse (2006)

Radiation chemistry

- ~10^{-12} – 10^{-6} s
  - Particles diffusion
  - Chemical reactions

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

- **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:

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

$$^{\bullet}OH + e^-_{aq} \longrightarrow OH^-$$

$$^{\bullet}OH + {}^{\bullet}OH \longrightarrow H_2O_2$$

$$^{\bullet}OH + H_2O_2 \longrightarrow HO_2^{\bullet} + H_2O$$

$$H^+ + O_2^{\bullet -} \rightleftharpoons HO_2^{\bullet}$$

$$H^{\bullet} + H_2O_2 \longrightarrow {}^{\bullet}OH + H_2O$$

(More than 60 reactions...)

Bimolecular reactions

❑ DE for the propagation of particles A and B

$$\partial p(\mathbf{r_A},\mathbf{r_B},t\,|\,\mathbf{r_{A0}},\mathbf{r_{B0}},t_0)/\partial t$$
$$=\left[D_A\nabla_{\mathbf{A}}{}^2+D_B\nabla_{\mathbf{B}}{}^2\right]p(\mathbf{r_A},\mathbf{r_B},t\,|\,\mathbf{r_{A0}},\mathbf{r_{B0}},t_0)$$

$p(\mathbf{r_A},\mathbf{r_B},t|\mathbf{r_{A0}},\mathbf{r_{B0}},t_0)$: probability of particles A and B to be at positions $\mathbf{r_A}$ and $\mathbf{r_B}$ at time t, given that they were at $\mathbf{r_{A0}}$ and $\mathbf{r_{B0}}$ at t_0

D_A, D_B: Diffusion coefficients

❑ Transformation

$$\mathbf{R}=\sqrt{D_B/D_A}\,\mathbf{r_A}+\sqrt{D_A/D_B}\,\mathbf{r_B}$$
$$\mathbf{r}=\mathbf{r_B}-\mathbf{r_A}$$

$$\nabla_{\mathbf{R}}=\partial/\partial\mathbf{R}$$
$$\nabla_{\mathbf{r}}=\partial/\partial\mathbf{r}$$

$$\partial p(\mathbf{R},\mathbf{r},t\,|\,\mathbf{R_0},\mathbf{r_0},t_0)/\partial t=(D_A+D_B)\left[\nabla_{\mathbf{R}}{}^2+\nabla_{\mathbf{r}}^2\right]p(\mathbf{R},\mathbf{r},t\,|\,\mathbf{R_0},\mathbf{r_0},t_0)$$

$$p(\mathbf{R},\mathbf{r},t\,|\,\mathbf{R_0},\mathbf{r_0},t_0)=p^{\mathbf{R}}(\mathbf{R},t\,|\,\mathbf{R_0},t_0)\,p^{\mathbf{r}}(\mathbf{r},t\,|,\mathbf{r_0},t_0)$$

$$\partial p^{\mathbf{R}}(\mathbf{R},t\,|\,\mathbf{R_0},t_0)/\partial t=(D_A+D_B)\nabla_{\mathbf{R}}{}^2p^{\mathbf{R}}(\mathbf{R},t\,|\,\mathbf{R_0},t_0)$$

$$\partial p^{\mathbf{r}}(\mathbf{r},t\,|\,\mathbf{r_0},t_0)/\partial t=(D_A+D_B)\nabla_{\mathbf{r}}^2p^{\mathbf{r}}(\mathbf{r},t\,|\,\mathbf{r_0},t_0)$$

Uncoupled equations

in **r** and **R**

Van Zon, J. S. et al. (2005) *J. Chem. Phys.* **123**, 234910

Bimolecular reactions

❑ Free diffusive motion of the coordinate R

$$\partial p^{\mathbf{R}}(\mathbf{R}, t \mid \mathbf{R_0}, t_0)/\partial t = D\nabla_{\mathbf{R}}{}^2 p^{\mathbf{R}}(\mathbf{R}, t \mid \mathbf{R_0}, t_0)$$ (DE)

$$p^{\mathbf{R}}(\mathbf{R}, t \mid \mathbf{R_0}, t_0) = \delta(\mathbf{R} - \mathbf{R_0})$$ (Initial condition)

$$p^{\mathbf{R}}(|\mathbf{R}| \to \infty, t \mid \mathbf{R_0}, t_0) = 0$$ (Boundary condition)

$$p^{\mathbf{R}}(\mathbf{R}, t \mid \mathbf{R_0}, t_0) = \frac{1}{[4\pi D(t - t_0)]^{3/2}} \exp\left[\frac{(\mathbf{R} - \mathbf{R}_0)^2}{4D(t - t_0)}\right]$$ (Solution)

$p^{\mathbf{R}}(\mathbf{R},t|\mathbf{R_0},t_0)$: probability distribution of the vector **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

Van Zon, J. S. et al. (2005) *J. Chem. Phys.* **123**, 234910

Bimolecular reactions

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

$$\frac{\partial p^{\mathbf{r}}(\mathbf{r}, t \mid \mathbf{r_0}, t_0)}{\partial t} = D\nabla_{\mathbf{r}}^2 p^{\mathbf{r}}(\mathbf{r}, t \mid \mathbf{r_0}, t_0)$$ (DE)

$$p^{\mathbf{r}}(\mathbf{r}, t \mid \mathbf{r_0}, t_0) = \delta(\mathbf{r} - \mathbf{r_0})$$ (Initial condition)

- **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.

$$\frac{\partial p(r, t \mid r_0)}{\partial t} = \frac{D}{r^2}\frac{\partial}{\partial r}\left[r^2 \frac{\partial}{\partial r} p(r, t \mid r_0)\right]$$ (Radial part of the DE)

$$4\pi r_0^2 p(r, t \mid r_0) = \delta(r - r_0), r \geq R$$ (Initial condition; R=reaction radius)

$p(r,t|r_0,t_0)$: 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: reaction with rate k_a

$$A + B \overset{k_a}{\rightarrow} C$$ (Reaction)

$$4\pi R^2 D \left.\frac{\partial \mathrm{p}(\mathrm{r},\mathrm{t}\,|\,\mathrm{r}_0)}{\partial \mathrm{r}}\right|_{r=R} = k_a\, p(R,t\,|\,\mathrm{r}_0)$$ (Boundary condition)

$$4\pi \mathrm{r}\mathrm{r}_0 \mathrm{p}(\mathrm{r},\mathrm{t}\,|\,\mathrm{r}_0) = \frac{1}{\sqrt{4\pi Dt}}\left\{\exp\left[-\frac{(r-r_0)^2}{4Dt}\right] + \exp\left[-\frac{(r+r_0-2R)^2}{4Dt}\right]\right\} + \alpha W\left(\frac{r+r_0-2R}{\sqrt{4Dt}}, -\alpha\sqrt{Dt}\right)$$ (Green's function)

$$\mathrm{Q}(\mathrm{t}\,|\,\mathrm{r}_0) = \int_R^\infty 4\pi r^2 \mathrm{p}(\mathrm{r},\mathrm{t}\,|\,\mathrm{r}_0)\mathrm{dr} = 1 + \frac{R\alpha+1}{r_0\alpha}\left[W\left(\frac{r_0-R}{\sqrt{4Dt}}, \alpha\sqrt{Dt}\right) - Erfc\left(\frac{r_0-R}{\sqrt{4Dt}}\right)\right]$$ (Survival probability)

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

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.

Plante, I. et al. (2013) *J. Comput. Phys.* **242**, 531-543

Green's function for radiation chemistry

❑ Partially diffusion-controlled ABC reaction

$$A + B \underset{k_d}{\overset{k_a}{\rightleftarrows}} C \xrightarrow{k_e} \text{Products}$$

System

k_a, k_d and k_e: reaction rate constants

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

Diffusion equation (radial)

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

Initial condition

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

Green's function

$$\alpha + \beta + \gamma = -(1 + k_a / k_D)/R$$

$$\alpha\beta + \beta\gamma + \gamma\alpha = (k_e + k_d)/D$$

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

Coefficients

Plante, I. et al. (2013) *J. Comput. Phys.* **242**, 531-543

Green's functions for radiation chemistry

❑ Partially diffusion-controlled reversible ABC reaction

- Time discretization equations for $p(r,t|r_0)$ and $p(*,t|r_0)$

$$p(r,\Delta t_1+\Delta t_2\,|\,r_0)=\int_R^\infty 4\pi r_1^2 p(r,\Delta t_2\,|\,r_1)p(r_1,\Delta t_1\,|\,r_0)dr_1+p(r,\Delta t_2\,|\,*)p(*,\Delta t_1\,|\,r_0)$$

$$p(*,\Delta t_1+\Delta t_2\,|\,r_0)=\int_R^\infty 4\pi r_1^2 p(*,\Delta t_2\,|\,r_1)p(r_1,\Delta t_1\,|\,r_0)dr_1+p(*,\Delta t_2\,|\,*)p(*,\Delta t_1\,|\,r_0)$$

- Time discretization equations for $p(r,t|*)$ and $p(*,t|*)$

$$p(r,\Delta t_1+\Delta t_2\,|\,*)=\int_R^\infty 4\pi r_1^2 p(r,\Delta t_2\,|\,r_1)p(r_1,\Delta t_1\,|\,*)dr_1+p(r,\Delta t_2\,|\,*)p(*,\Delta t_1\,|\,*)$$

$$p(*,\Delta t_1+\Delta t_2\,|\,*)=\int_R^\infty 4\pi r_1^2 p(*,\Delta t_2\,|\,r_1)p(r_1,\Delta t_1\,|\,*)dr_1+p(*,\Delta t_2\,|\,*)p(*,\Delta t_1\,|\,*)$$

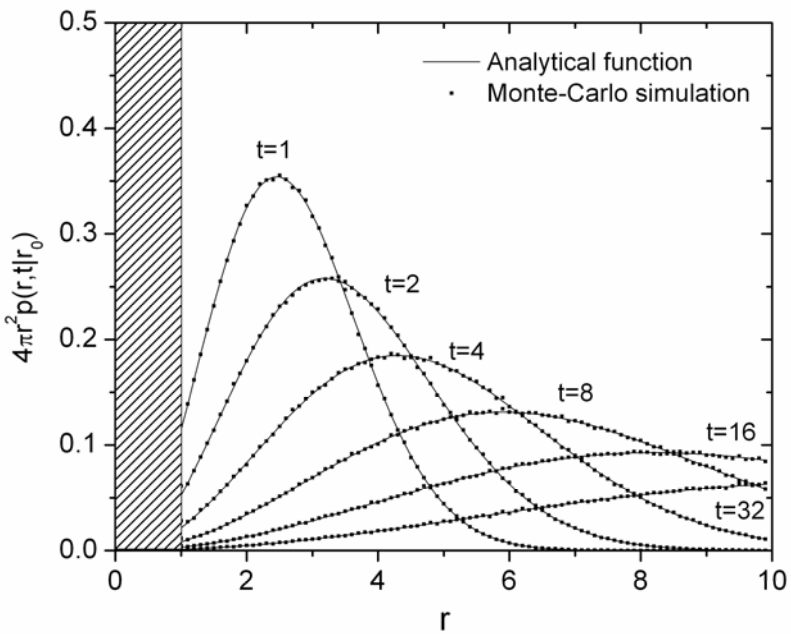
❑ Proven numerically in Mathematica for all tested values of the parameters

Plante, I. et al. (2013) *J. Comput. Phys.* **242**, 531-543

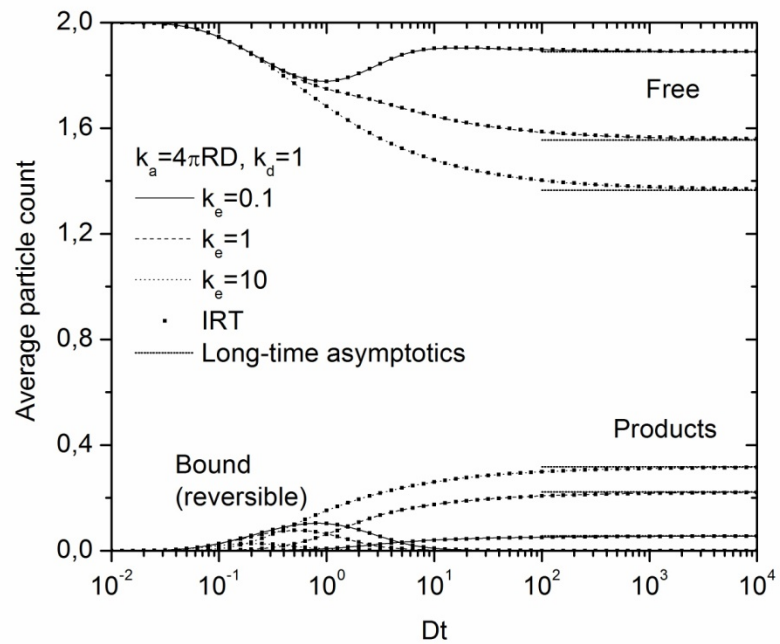
Green's function for radiation chemistry

$$A + B \underset{k_d}{\overset{k_a}{\rightleftarrows}} C \xrightarrow{k_e} \text{Products}$$

Green's functions



Survival and binding probabilities



Plante, I. et al. (2013) *J. Comput. Phys.* **242**, 531-543

Green's functions for radiation chemistry

❑ Partially diffusion-controlled ABCD reaction

$$A + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} C + D$$

Boundary conditions

$$4\pi a_1^2 D_1 \left.\frac{\partial p_1(x_1,t\,|\,x_0)}{\partial x_1}\right|_{x_1=a_1} = k_1 p_1(a_1,t\,|\,x_0) - k_2 p_2(a_2,t\,|\,x_0)$$

Green's function $x_0 \rightarrow x_1$ (AB→AB)

$$p_1(x_1,t\,|\,x_0) = \mathrm{p}_{\mathrm{ref}_1}(x_1,t\,|\,x_0) - \frac{k_1 a_1^2}{\sqrt{\tau_1\tau_2}\,k_{D_1}^2 x_1 x_0}\left[\frac{\sigma_+}{\sigma_+-\sigma_-}\frac{1-\sigma_+\sqrt{\tau_2}}{1-\sigma_+\sqrt{\tau_1}}W\left(\chi_1+\chi_0,\sigma_+\sqrt{t}\right)\right.$$

$$\left. -\frac{\sigma_-}{\sigma_+-\sigma_-}\frac{1-\sigma_-\sqrt{\tau_2}}{1-\sigma_-\sqrt{\tau_1}}W\left(\chi_1+\chi_0,\sigma_-\sqrt{t}\right) - \left(1-\sqrt{\frac{\tau_2}{\tau_1}}\right)\frac{W(\chi_1+\chi_0,\sigma_+\sqrt{t/\tau_1})}{(1-\sigma_+\sqrt{\tau_1})(1-\sigma_-\sqrt{\tau_1})}\right]$$

$$\mathrm{p}_{\mathrm{ref}_1}(x_1,t\,|\,x_0) = \frac{1}{4\pi x_1 x_0 a_1}\left[\sqrt{\frac{\tau_1}{4\pi t}}\left(e^{-(\chi_1-\chi_0)^2} + e^{-(\chi_1+\chi_0)^2}\right) - W\left(\chi_1+\chi_0,\sqrt{\frac{t}{\tau_1}}\right)\right]$$

Green's function $x_0 \rightarrow y_1$ (AB→CD)

$$p_2(y_1,t\,|\,x_0) = \frac{k_1 a_1 a_2}{\sqrt{\tau_1\tau_2}\,k_{D_1}k_{D_2}y_1 x_0(\sigma_+-\sigma_-)}\left[\sigma_+ W\left(\chi_0+\gamma_1,\sigma_+\sqrt{t}\right) - \sigma_- W\left(\chi_0+\gamma_1,\sigma_-\sqrt{t}\right)\right]$$

Probability of reaction AB→CD

$$P_{AB\rightarrow CD}(t\,|\,x_0) = \frac{a_1}{x_0}\frac{k_1/k_{D_1}}{1+k_1/k_{D_1}+k_2/k_{D_2}}\left[Erfc\,\chi_0 + \frac{\sigma_-(1-\sigma_+\sqrt{\tau_2})}{\sigma_+-\sigma_-}W\left(\chi_0,\sigma_+\sqrt{t}\right) - \frac{\sigma_+(1-\sigma_-\sqrt{\tau_2})}{\sigma_+-\sigma_-}W\left(\chi_0,\sigma_-\sqrt{t}\right)\right]$$

$$\sigma_\pm = \frac{1}{2}\left[\mu_1+\mu_2 \pm \sqrt{(\mu_1-\mu_2)^2+\lambda}\right]$$

$$\mu_i = (1+k_i/k_{D_i})/\sqrt{\tau_i}$$

$$\lambda = \frac{4k_1k_2}{k_{D_1}k_{D_2}\sqrt{\tau_1\tau_2}}$$

$$\chi_i = (x_i-a_1)/\sqrt{4D_1t}$$

$$\gamma_i = (y_i-a_2)/\sqrt{4D_2t}$$

x_i: distance between A and B

y_i: distance between C and D

$D_1 = D_A + D_B$

$D_2 = D_C + D_D$

Popov, A.V. and Agmon, N. (2002). *J. Chem. Phys.* **117**, 5770-5779

Green's functions for radiation chemistry

- **Partially diffusion-controlled reversible ABCD reaction**
  - Time discretization equations for p_1 and p_2

$$p_1(x_2,t_1+t_2 \mid x_0) = \int_{a_1}^{\infty} p_1(x_2,t_2 \mid x_1)p_1(x_1,t_1 \mid x_0)4\pi x_1^2 dx_1 + \int_{a_2}^{\infty} p_4(x_2,t_2 \mid y_1)p_2(y_1,t_1 \mid x_0)4\pi y_1^2 dy_1$$

$$p_2(y_2,t_1+t_2 \mid x_0) = \int_{a_1}^{\infty} p_2(y_2,t_2 \mid x_1)p_1(x_1,t_1 \mid x_0)4\pi x_1^2 dx_1 + \int_{a_2}^{\infty} p_3(y_2,t_2 \mid y_1)p_2(y_1,t_1 \mid x_0)4\pi y_1^2 dy_1$$

  - Time discretization equations for $P_{AB\rightarrow CD}$

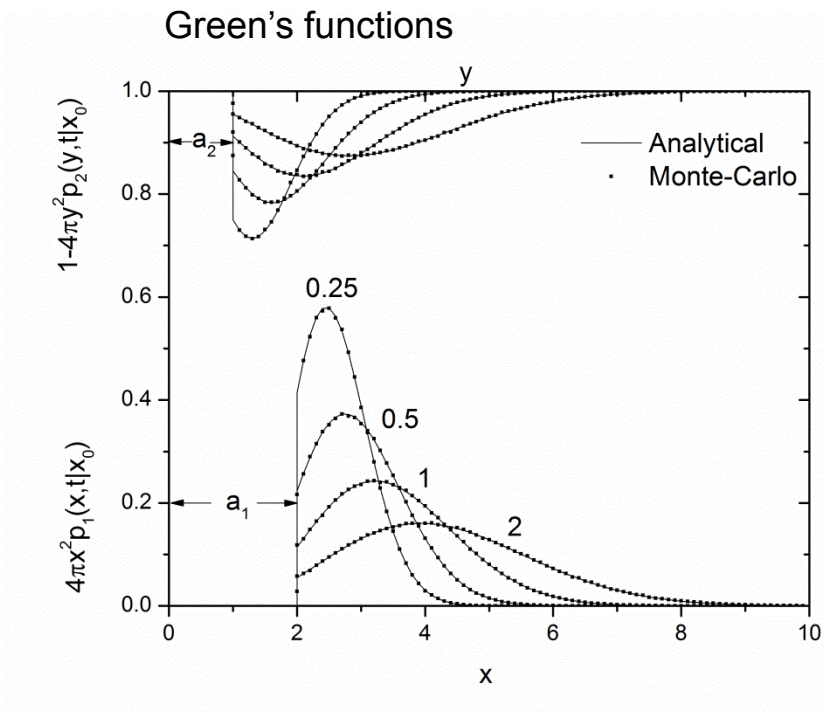
$$P_{AB\rightarrow CD}(t_1+t_2 \mid x_0) = \int_{a_1}^{\infty} P_{AB\rightarrow CD}(t_2 \mid x_1)p_1(x_1,t_1 \mid x_0)4\pi x_1^2 dx_1 + \int_{a_2}^{\infty} (1 - P_{CD\rightarrow AB}(t_2 \mid y_1))p_2(y_1,t_1 \mid x_0)4\pi y_1^2 dy_1$$

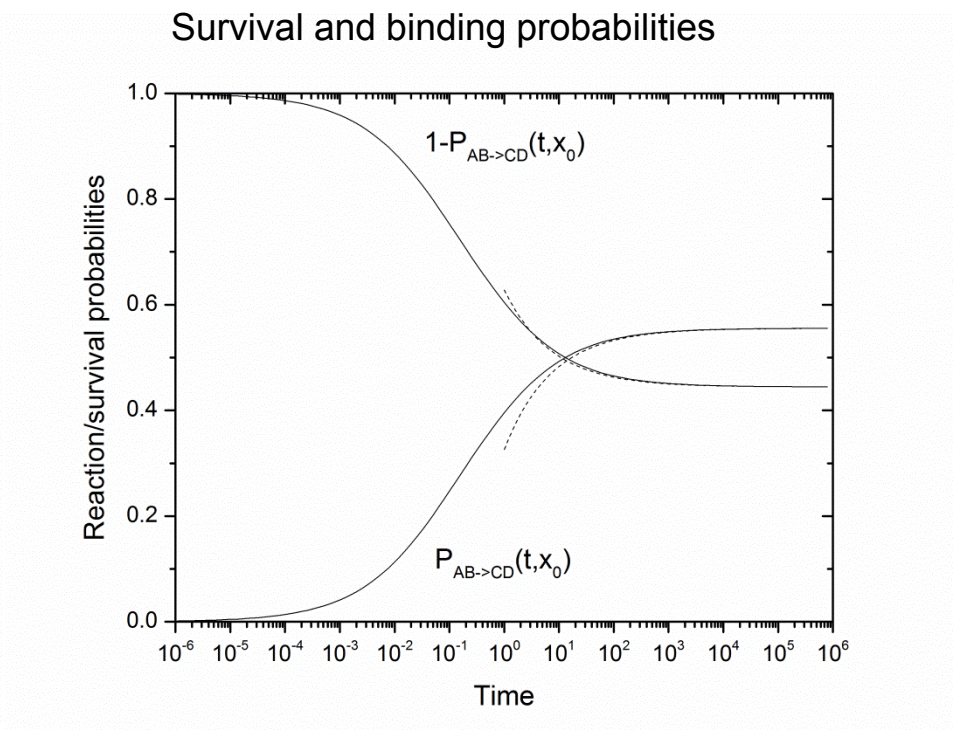
- **Similar equations for p_3,p_4 and $P_{CD\rightarrow AB}$**
- **Proven numerically in Mathematica for all tested values of the parameters**

Plante, I. et al. (2014), submitted to *J. Comput. Phys.*

Green's functions for radiation chemistry

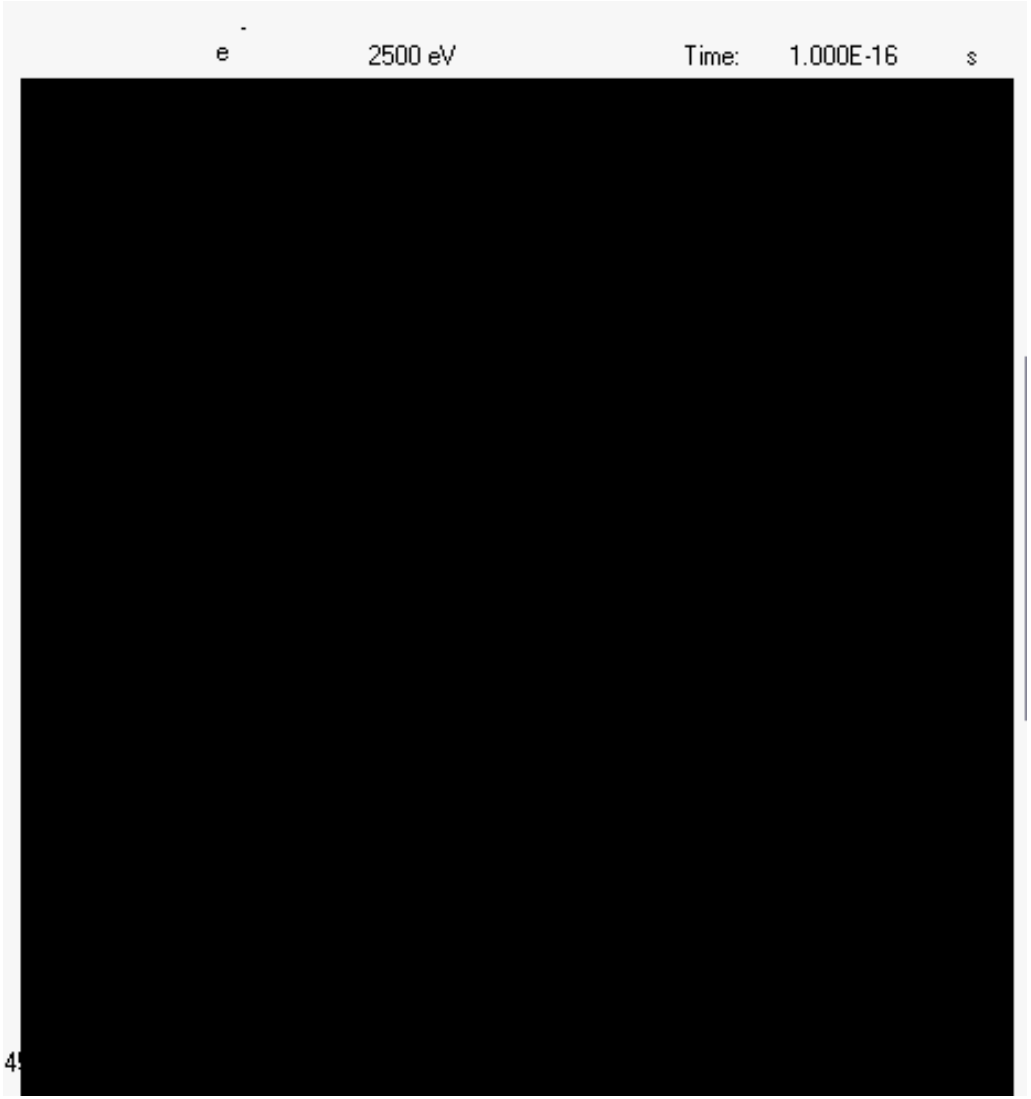
$$A + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} C + D$$





Plante, I. et al. (2014), submitted to *J. Comput. Phys.*

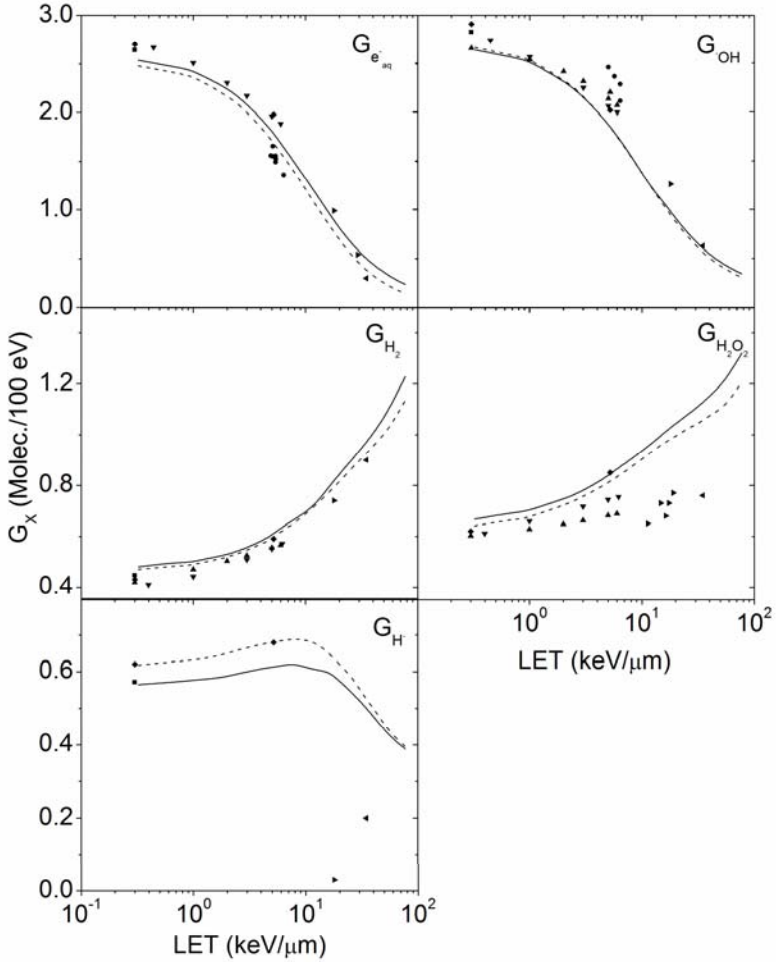
Radiation chemistry



See video at: http://youtu.be/If29Rs4fDO4

Radiation chemistry

Primary yields of e^-_{aq}, $^{\cdot}OH$, $H^{\cdot}$, H_2 and H_2O_2 as a function of the LET



Irradiation by 300-0.1 MeV protons

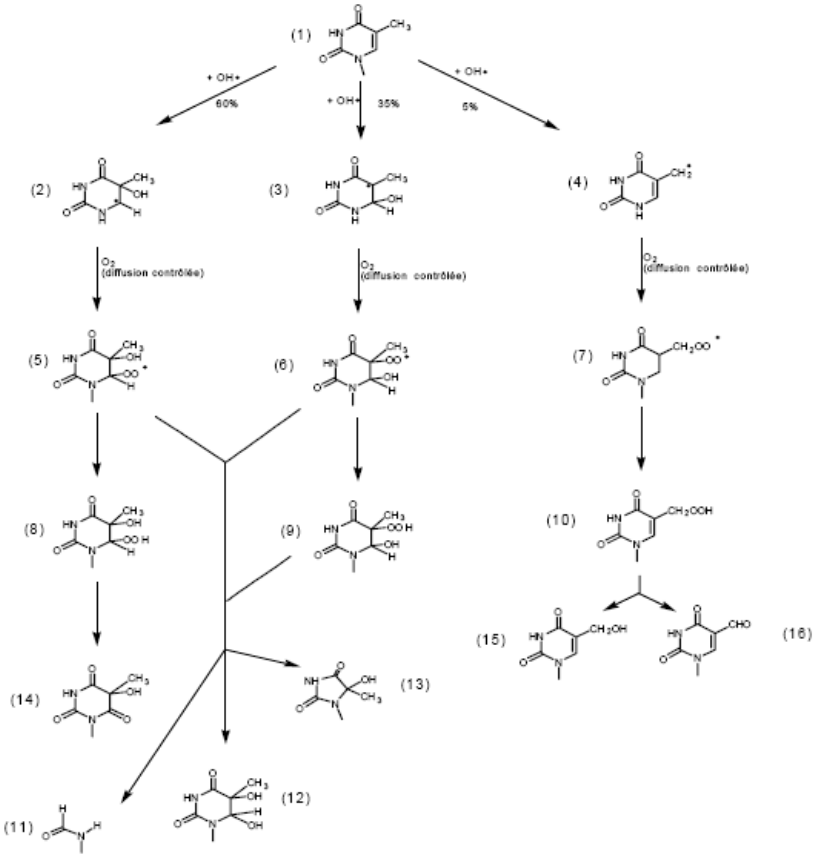
LET: ~0.3-85 keV/μm

Note: the *primary yields* (noted G_X) are the yields at the end of spur expansion (~10^{-6} s)

Plante, I. (2011), *Radiat. Env. Biophys.* **50**, 405-415

Radiation chemistry (DNA)

- The radiation chemistry of DNA is very complex
- Many reaction rate constants are known



Reaction	k ($dm^3.mol^{-1}.s^{-1}$)	Radius (Å)
e^-_{aq}+Thymine→Thy(+e)	1.79×10^{10}	5.287
·OH + Thymine → TC5OH·+TC6OH·+TUCH2·	6.4×10^{9}	3.02
H.+Thymine→Thymine*	5.7×10^{8}	0.11

Cadet, J. et al. (1997) *Reviews in Physiology, Biochemistry and Pharmacology* **31**, 1-87

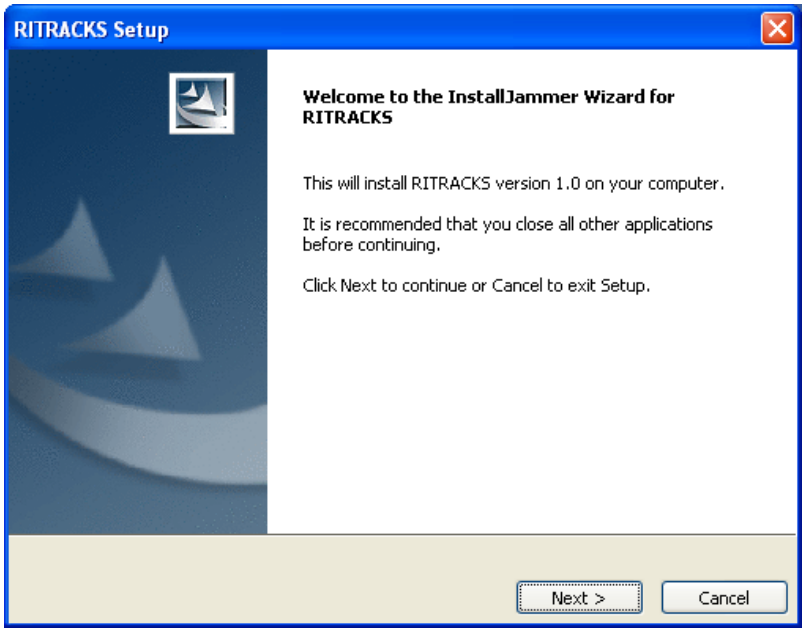
The software RITRACKS

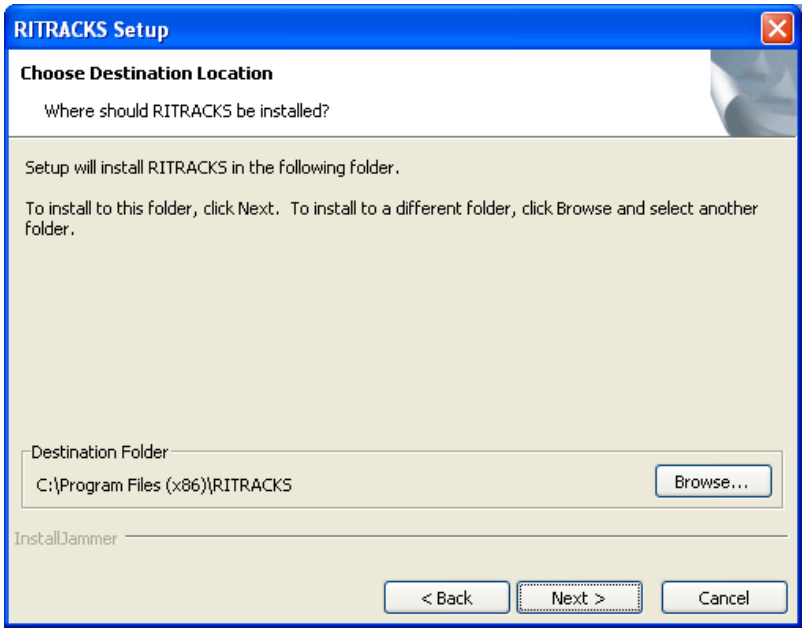
- **The software RITRACKS comprises several parts**
  - The calculation part includes:
    - ✓ The cross sections, which are necessary for particle transport
    - ✓ The particle transport routines
    - ✓ Post-simulation data management
  - The Graphic User Interface (GUI), comprises several windows:
    - ✓ The main window
    - ✓ Incident radiation window
    - ✓ Multi-CPU support
    - ✓ 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**

Using RITRACKS

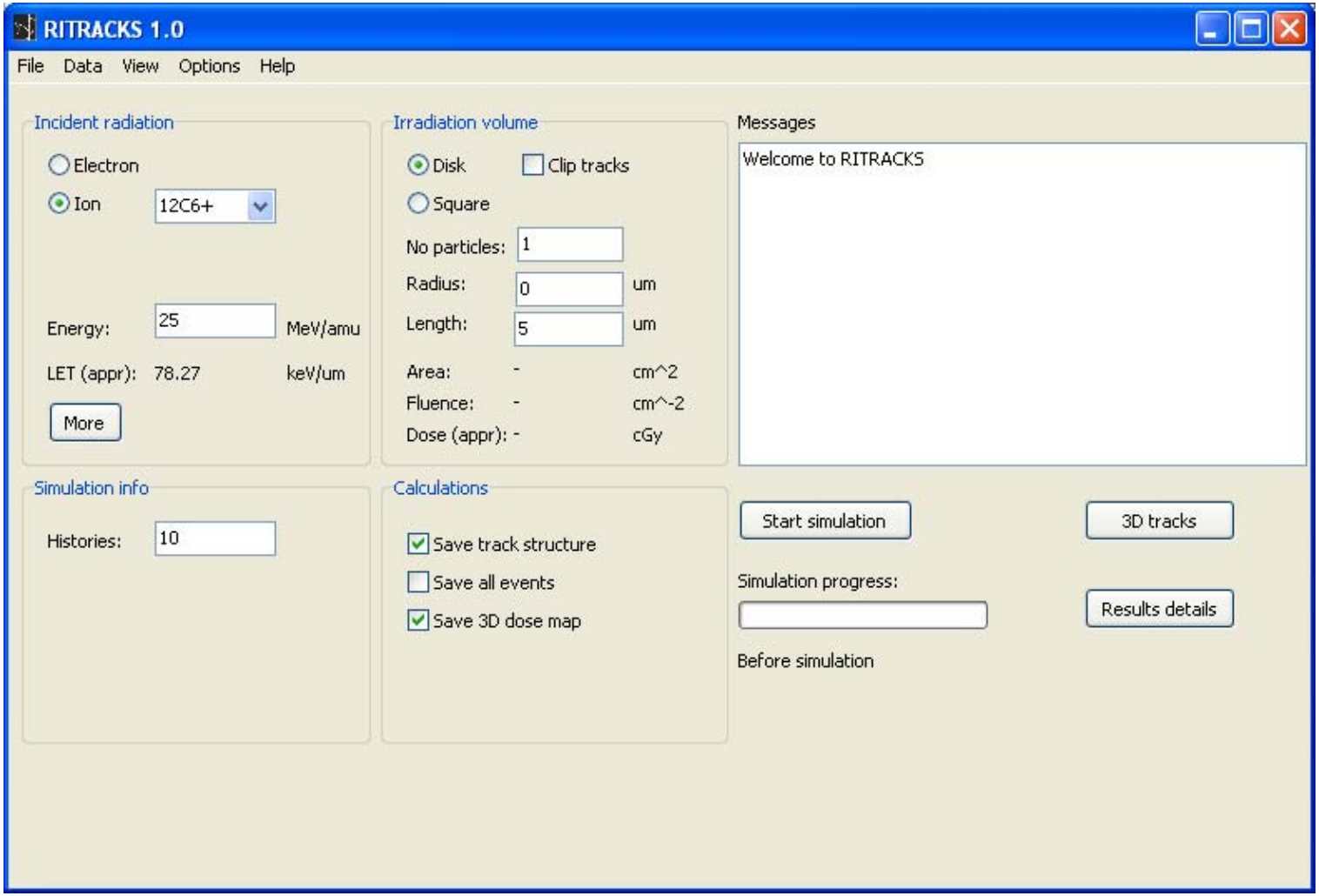
❑ The installer

- 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: γMc^2

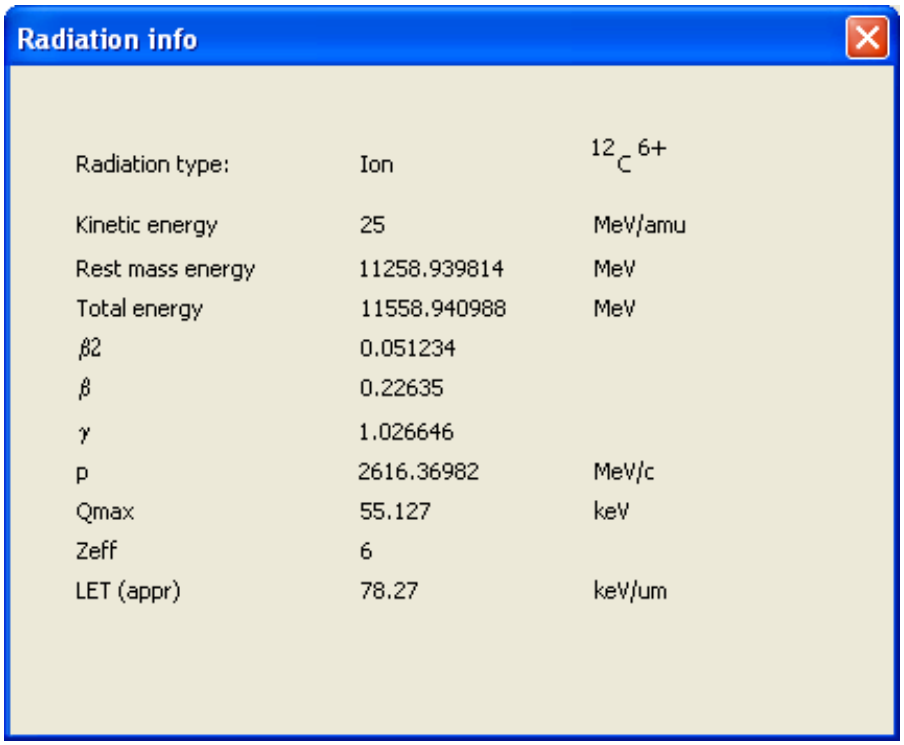
Relativistic γ: $\gamma = T / Mc^2 + 1$

Relativistic β: $\beta^2 = 1 - 1/\gamma^2$

Momentum: $p = \gamma M v$

Maximum energy Transfer to e^-: $E_{max} = \dfrac{2mc^2(\gamma^2 - 1)}{1 + 2\gamma(m/M) + (m/M)^2}$

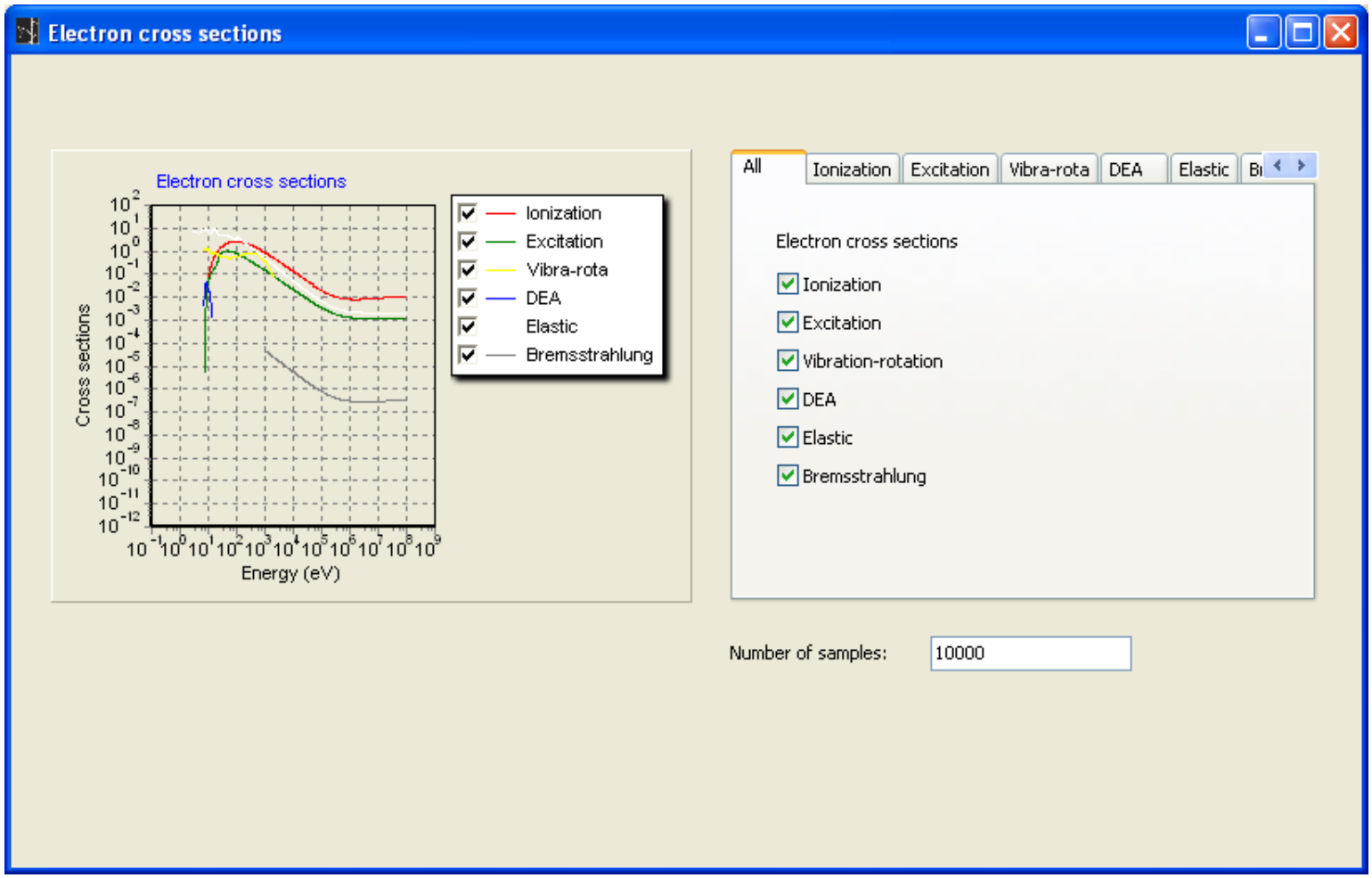
LET (MeV/cm): (Bethe) $-\dfrac{dE}{dx} = \dfrac{0.170}{\beta^2}[F(\beta) - 4.31]$ $\quad F(\beta) = \ln\dfrac{1.02x10^6\beta^2}{1-\beta^2} - \beta^2$



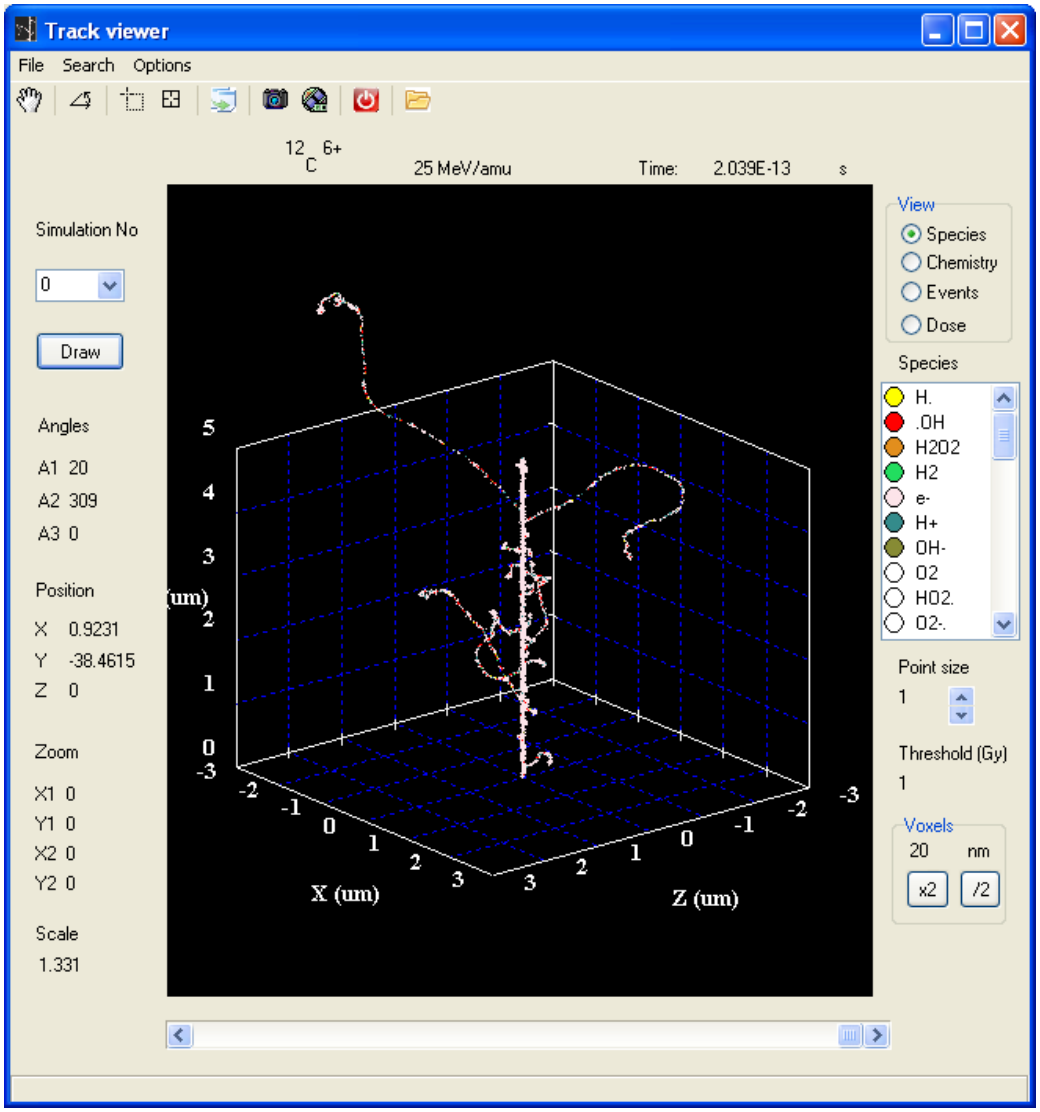
Radiation info

Radiation type:	Ion	$^{12}C^{6+}$
Kinetic energy	25	MeV/amu
Rest mass energy	11258.939814	MeV
Total energy	11558.940988	MeV
$\beta 2$	0.051234	
β	0.22635	
γ	1.026646	
p	2616.36982	MeV/c
Qmax	55.127	keV
Zeff	6	
LET (appr)	78.27	keV/um

Electron cross sections window



Visualization window



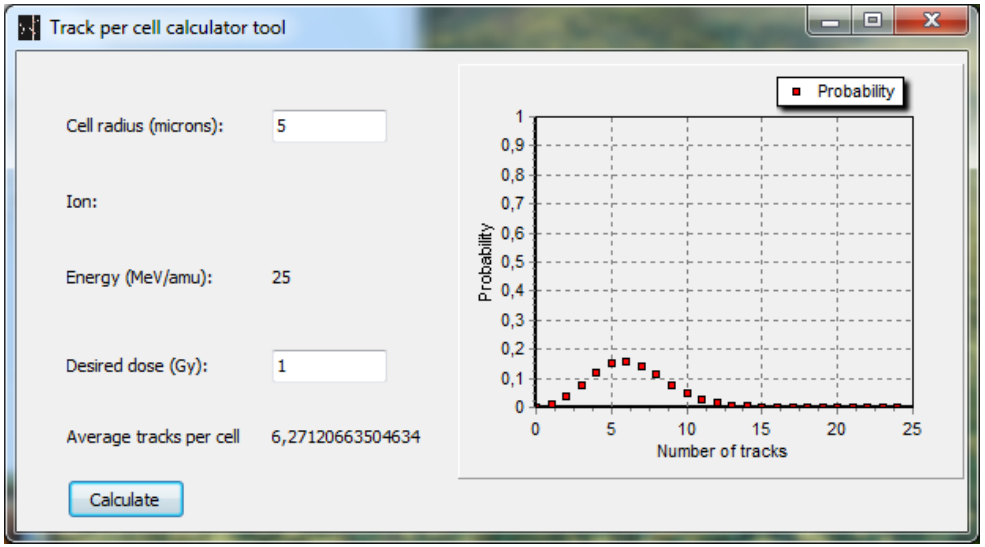
Tools:
- Rotation
- Translation
- Zoom
- Save to file
- Copy to clipboard
- Create a .avi file
- Open data folder

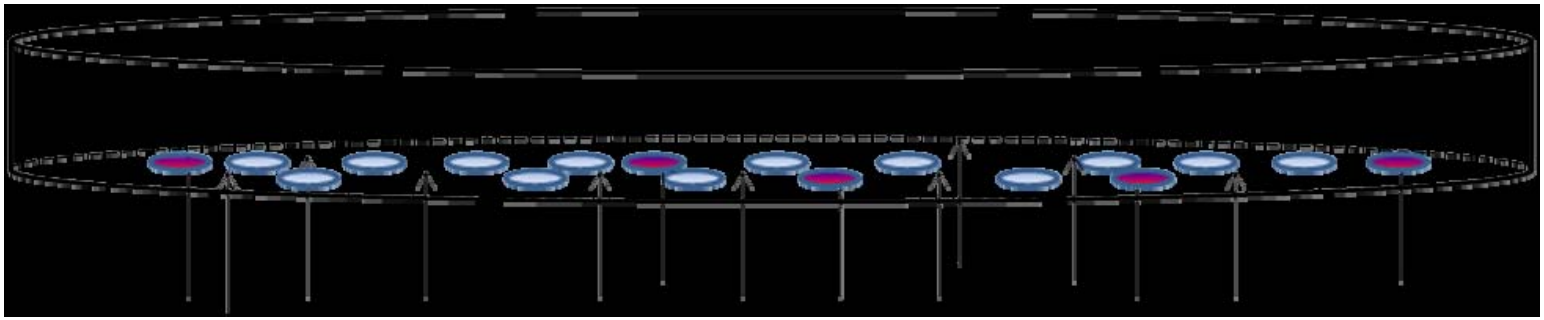
Visualization:
- Radiolytic species
- Events
- Dose (voxels)

Time evolution

RITRACKS tools

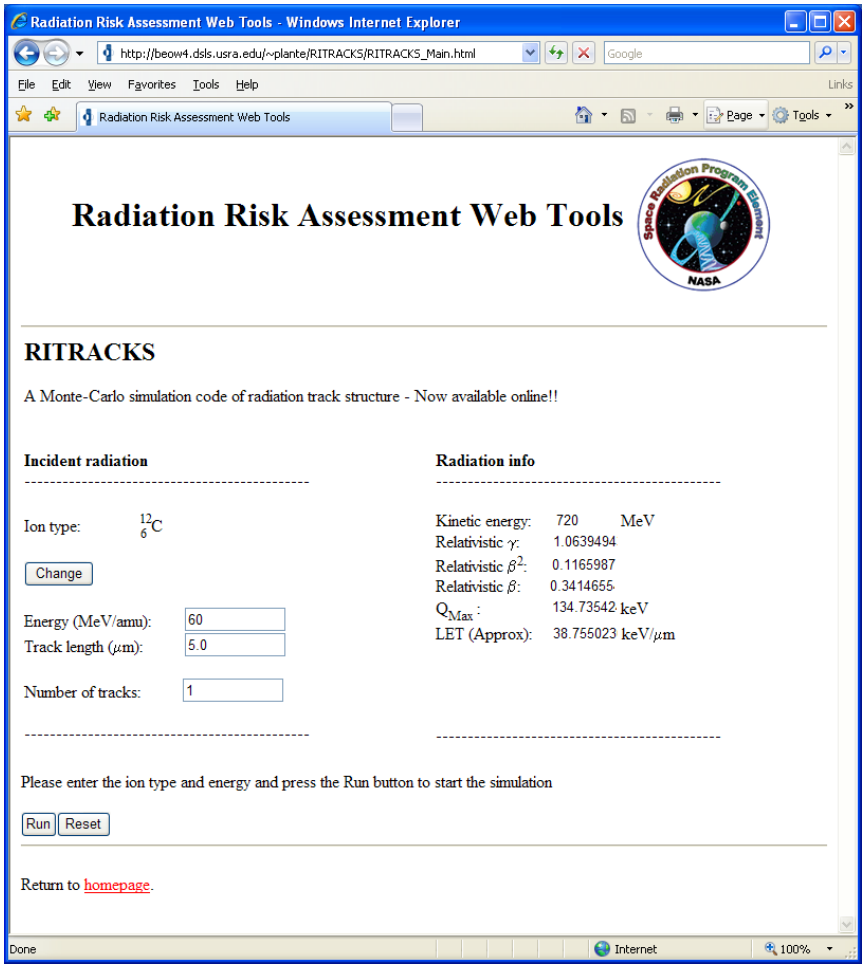
- **Calculation of tracks per cell in a cell culture for a given ion, energy and dose**





Release history

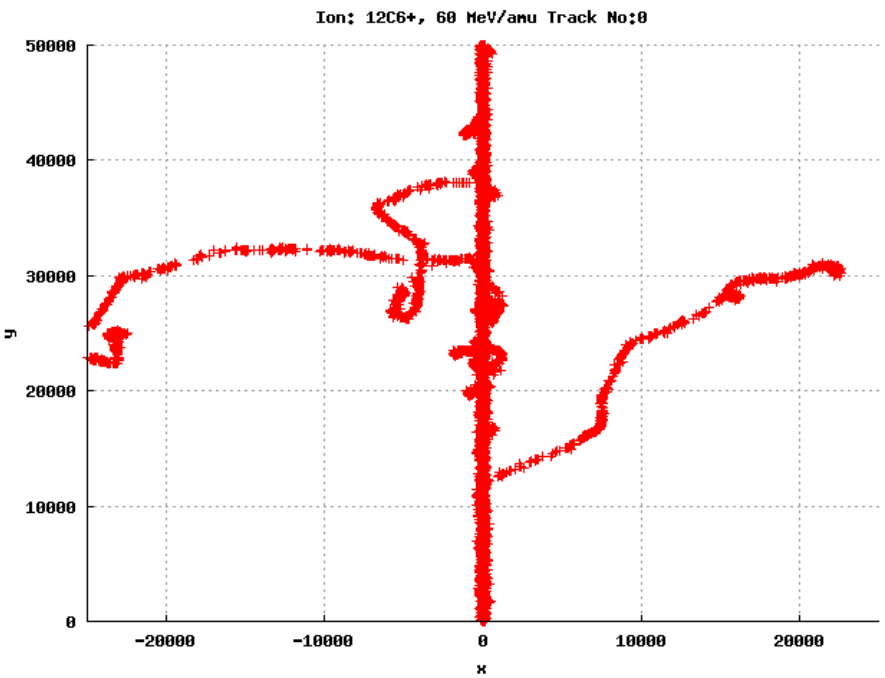
- RITRACKS was used by the students at the NASA Space Radiation Summer School at the Brookhaven National Laboratory, Upton, New York (June 6-24, 2011, May 28 - June 15, 2012, MIT ICED June 2012)(over 40 users)
- The release to international partners was approved in 2011
- RITRACKS was released to NASA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

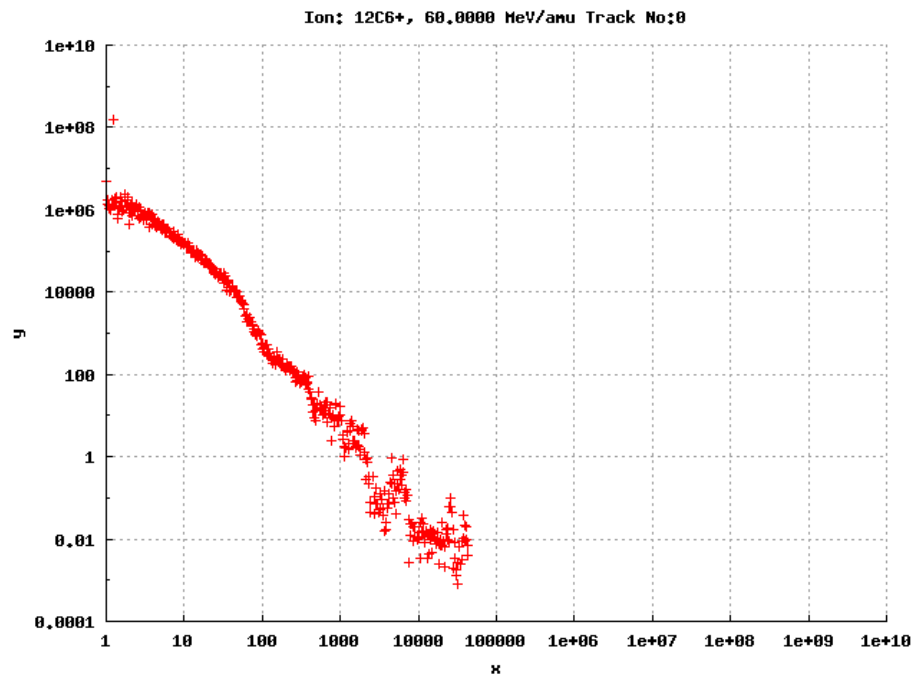


http://spaceradiation.usra.edu

Release history

- **An online version of RITRACKS will be available soon!**





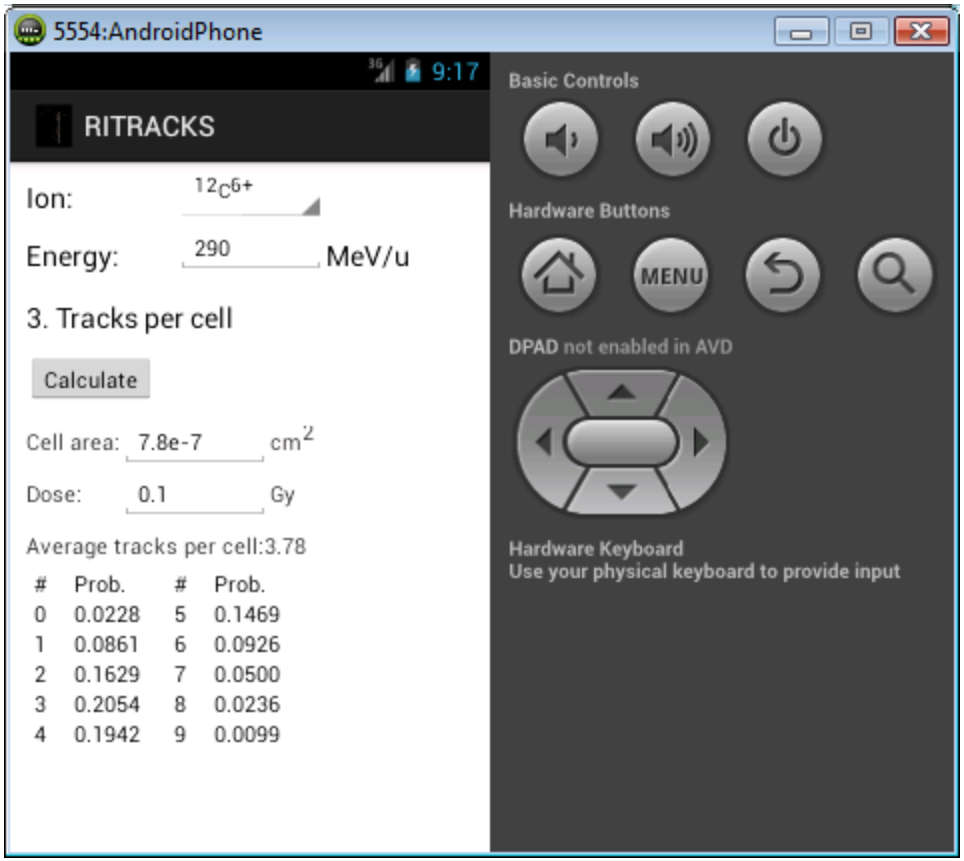
Left: Simulation of a $^{12}C^{6+}$, 60 MeV/amu, on the projected RRAW site.

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

- **Android/iPhone version**
- **For ions:**
  - LET
  - Relativistic β and γ
  - Z_{eff} and Z_{eff}^2/β^2
  - Maximum energy transfer to an electron
  - Dose and fluence
  - Radial dose
  - Number of hits per cell
  - in a cell culture
- **For electrons:**
  - Relativistic β and γ
  - Range



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.

Acknowledgements

- Dr. Oleg Belov (JINR)
- Dr. Luc Devroye (McGill University)
- Brian Fessler (USRA-Houston)
- Dr. Francis Cucinotta (UNLV)
- Dr. Tom Borak (Colorado State University)
- Radiation Biophysics group at JSC
- USRA
- NASA

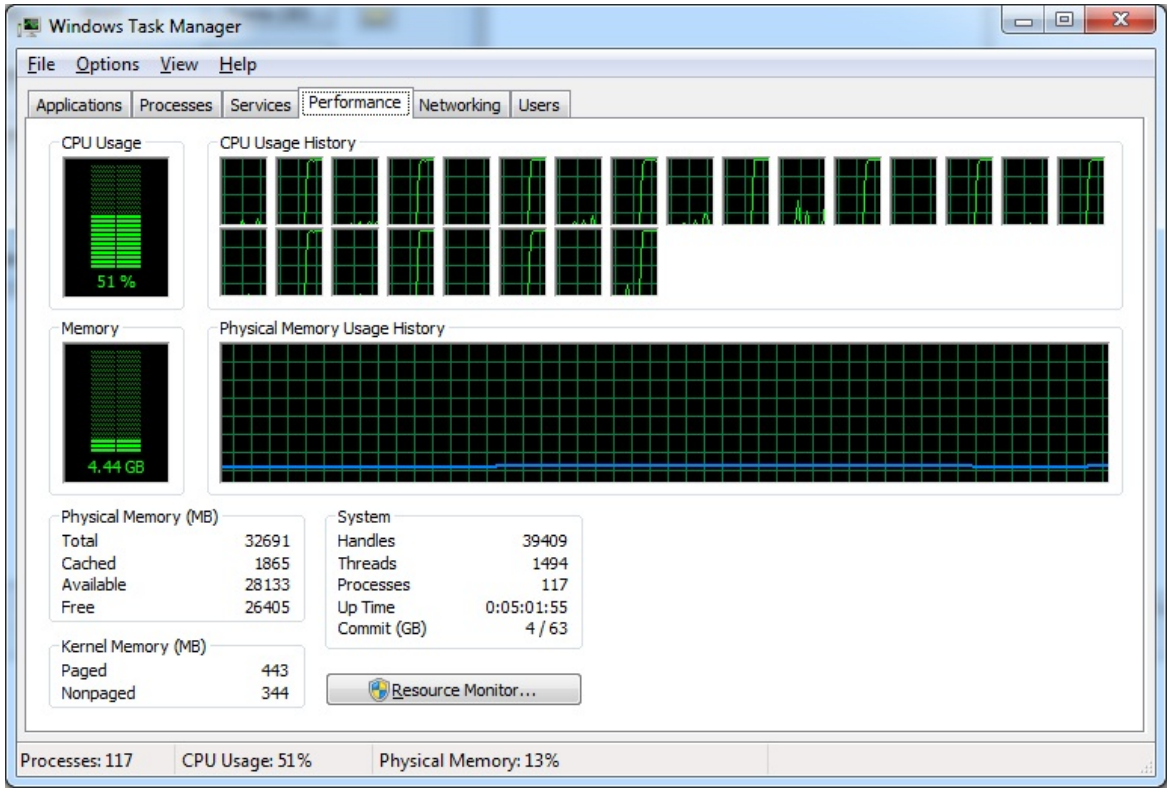
References

- Plante I and Cucinotta FA (2012). *Lecture Notes in Computer Sciences* 7845, 12-25
- Plante I, Ponomarev AL and Cucinotta FA (2011). *Radiat. Prot. Dosim.*, 143, 156-161.
- Plante I and Cucinotta FA (2011). Book chapter published in: Mode, CJ (Ed.) *Applications of Monte-Carlo Methods in Biology, Medicine and Other fields of Science.* InTech, Rijeka, Croatia.
- Durante M, and Cucinotta FA (2011), The Physical Basis for Radiation Protection in Space. *Reviews of Modern Physics* 83, 1245-1281.
- Plante I and Cucinotta FA (2010). *Radiat. Env. Biophys.* 49, 5-13.
- Plante I and Cucinotta FA (2008). *New J Phys* 10, 125020.
- Plante I and Cucinotta FA (2009). *New J Phys* 11, 063047.
- Cucinotta FA, and Durante M (2006). Cancer risk from exposure to galactic cosmic rays: implications for space exploration by human beings*The Lancet Oncology* 7, 431-435.
- Cucinotta FA, Nikjoo H, and Goodhead DT (2000). Model of The Radial Distribution of Energy Imparted in Nanometer Volumes From HZE Particle. *Radiat Res* 153, 459-468.
- Cucinotta FA, Nikjoo H, and Goodhead DT (1999), Applications of Amorphous Track Models in Radiobiology. *Radiat Environ Biophys* 38, 81-92.
- Cucinotta FA, Katz R, and Wilson JW (1998), Radial Distributions of Electron Spectra from High-Energy Ions. *Radiat Environ Biophys* 37, 259-265.

The software RITRACKS

❑ Multiple CPU computing (Windows)

RITRACKS V3



Select the CPUs you want to use

Plante, I. and Cucinotta, F. A. (2013). *Lecture Notes in Computer Sciences* **7845**, 12-25