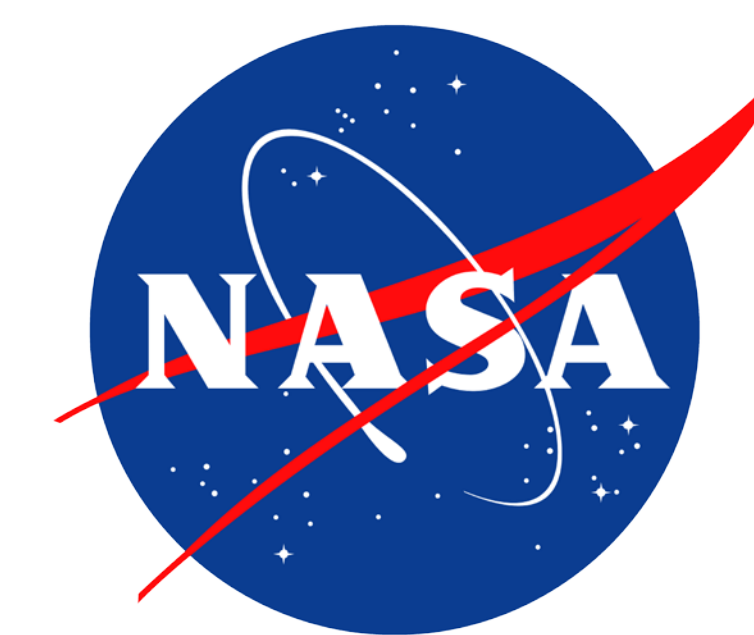


A bi-exponential repair algorithm for radiation-induced double-strand breaks: application to chromosome aberrations

National Aeronautics and
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Introduction

- Chromosome aberrations (CAs) are one of the effects of radiation exposure and are used as a biomarker.
- A new simulation program, named RITCARD (Radiation induced tracks, chromosome aberrations, repair, and damage) was developed to simulate radiation-induced CA [1].
- RITCARD is used with the program RITRACKS (Relativistic Ion Tracks), which simulates the radiation tracks
- The restitution kinetics algorithm presented here [2] is a significant improvement over the one used in the first version.
- Simulations of radiation-induced CA were performed for several ion types and mixed irradiation fields.
- These simulations will be useful to help interpreting experiments of galactic cosmic rays (GCR) simulator.

RITRACKS: simulation of the radiation track structure

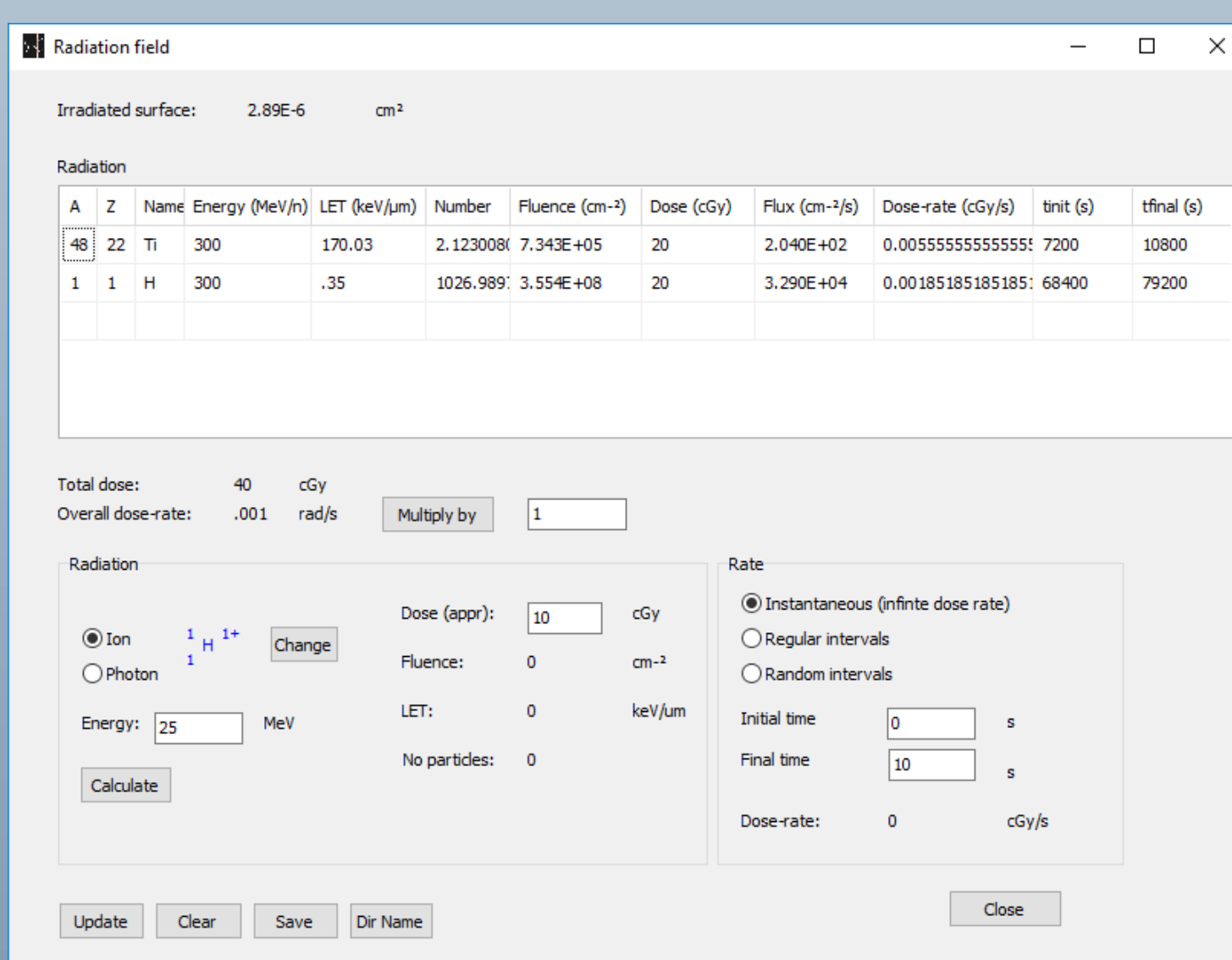
- Radiation interaction with water produces radiolytic species such as H[•], •OH, H₂, H₂O₂, e⁻_{aq}, etc.
- The code RITRACKS (Relativistic Ion Tracks) was developed to simulate detailed stochastic radiation track structures of ions of different types and energies [3].
- Many new simulation capabilities were added to RITRACKS during the recent years, notably the simulation of mixed field of ion types at different dose-rate or a GCR field environment
- Time-dependent 3D voxel dose maps (differential and integral) can be calculated from energy deposition.

RITCARD: simulation of CAs

- The program RITCARD is composed by three parts.
- Calculation of chromosome breaks. This part requires pre-calculated simulation results:
 - Simulation of chromosomes by random walk (RW). This is based on the NASARTI algorithm [4].
 - Time-dependent 3D voxel dose map in irradiated volume, calculated by RITRACKS.
 - Breaks occurs at intersections between RW and voxels, with probability $p=1-\exp(-QD)$, where Q is a parameter and D is the voxel dose.
 - Each break leads to two free end pairs.
- Repair of breaks (restitution kinetics algorithm).
 - Breaks can be repaired properly.
 - This generates fragment sequences.
- Classification of aberrations.
 - Fragment sequences are grouped by chromosome material composition.
 - The program assesses several types of aberrations: simple and complex exchanges, dicentric, rings, deletions, terminal deletions, color junctions, and inversions.

Simulation of a mixed field radiation field

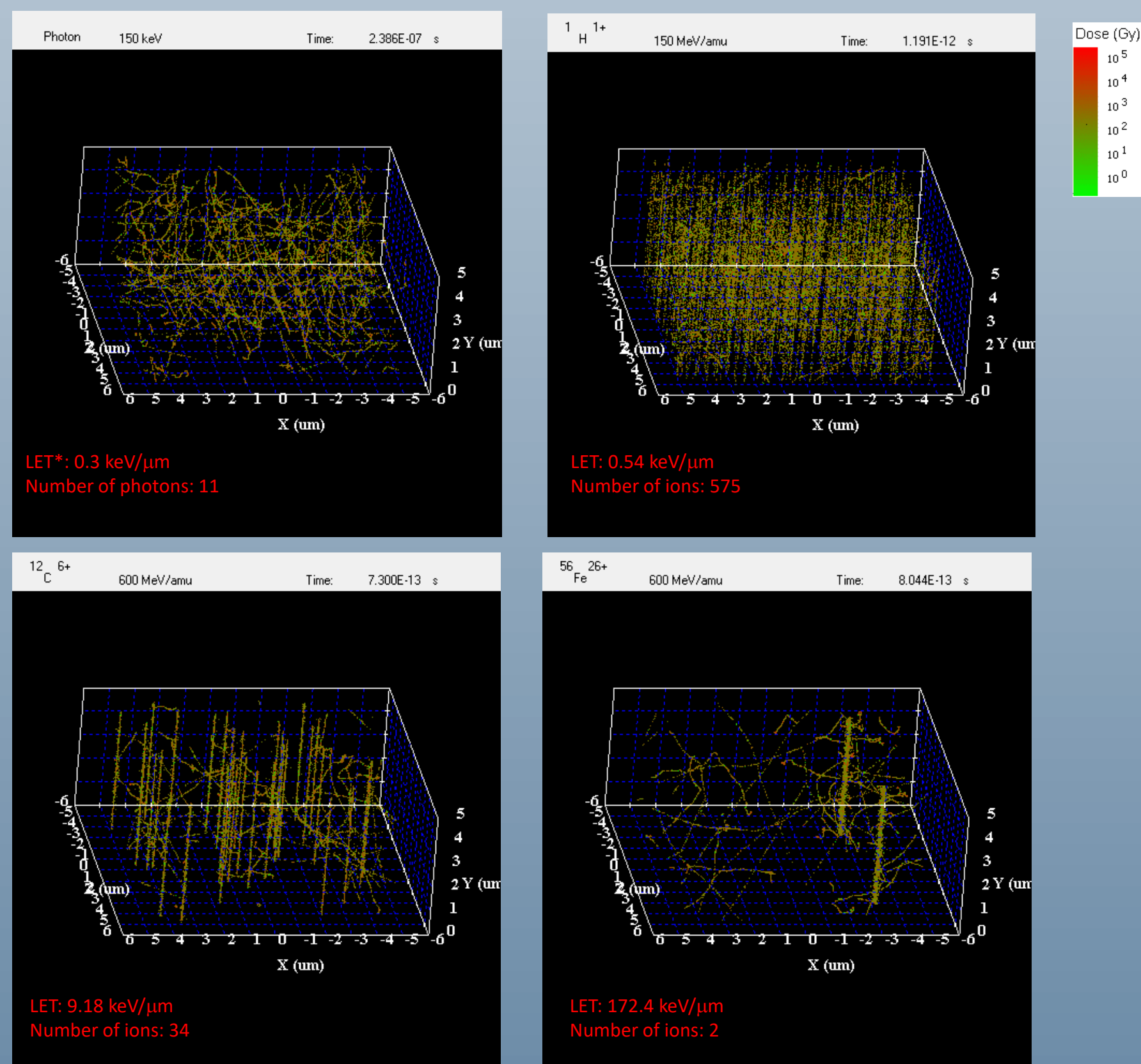
- Mixed field



- Enter the ion type, energy, dose contribution, initial and final irradiation time for each ion.
- Quantities such as flux, fluence and dose-rate are calculated.

Simulation of volume irradiation

- Ions or photons

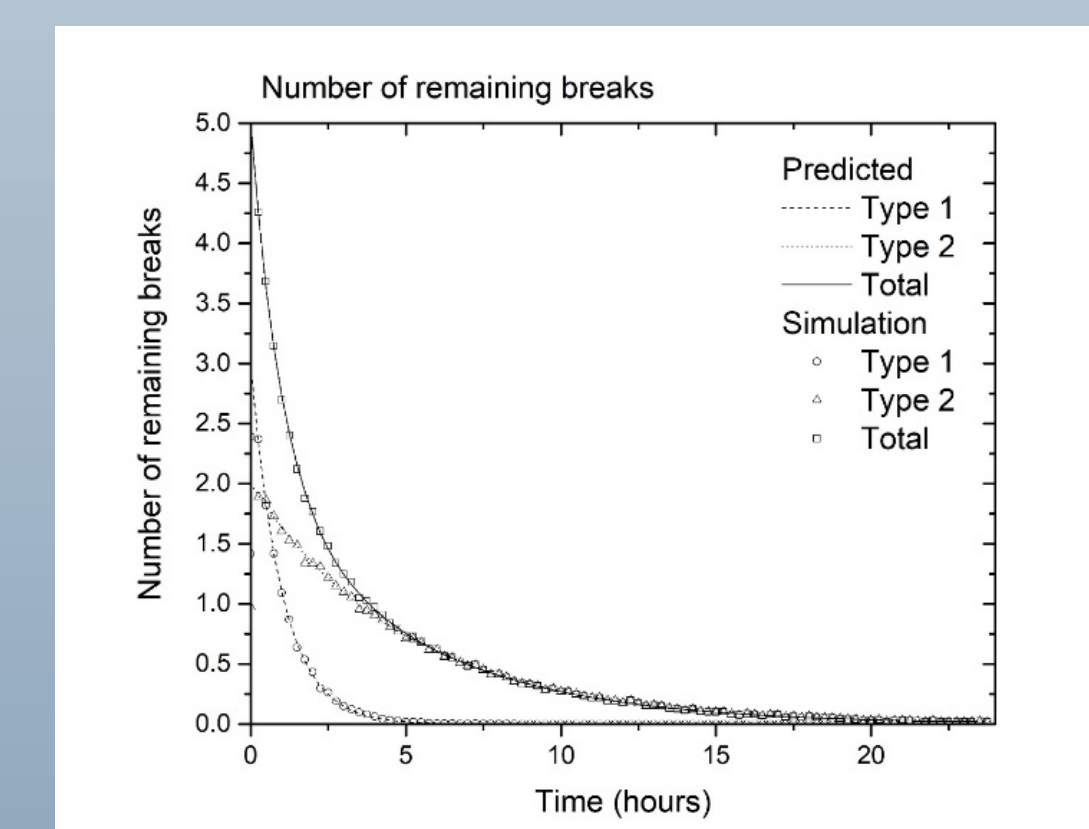


Dose voxels can be calculated for various types of ions and photons

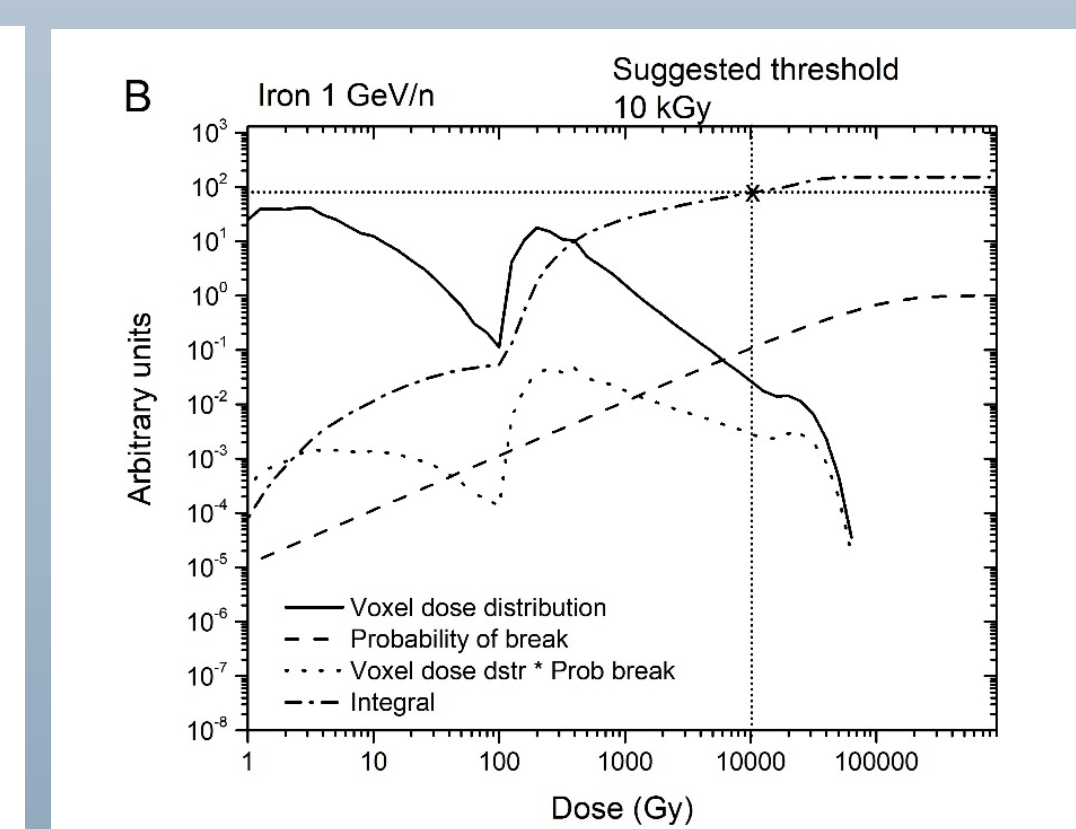
- Two types of breaks: simple (type 1) that repair quickly (τ_1) and complex (type 2) that repair slowly (τ_2).
- The overall repair kinetics is

$$N(t) = N_1(t) + N_2(t) = N_1(0) \exp(-t/\tau_1) + N_2(0) \exp(-t/\tau_2)$$

- A voxel energy threshold of 500 eV (10 kGy) is used to determine whether breaks are of type 1 or 2.
- Free ends originating from type 1 breaks can only repair with their corresponding free ends (proper rejoins), whereas type 2 breaks can repair with others (improper rejoins).
- The algorithm is mathematically exact, and could be extended to include more than 2 types of breaks.



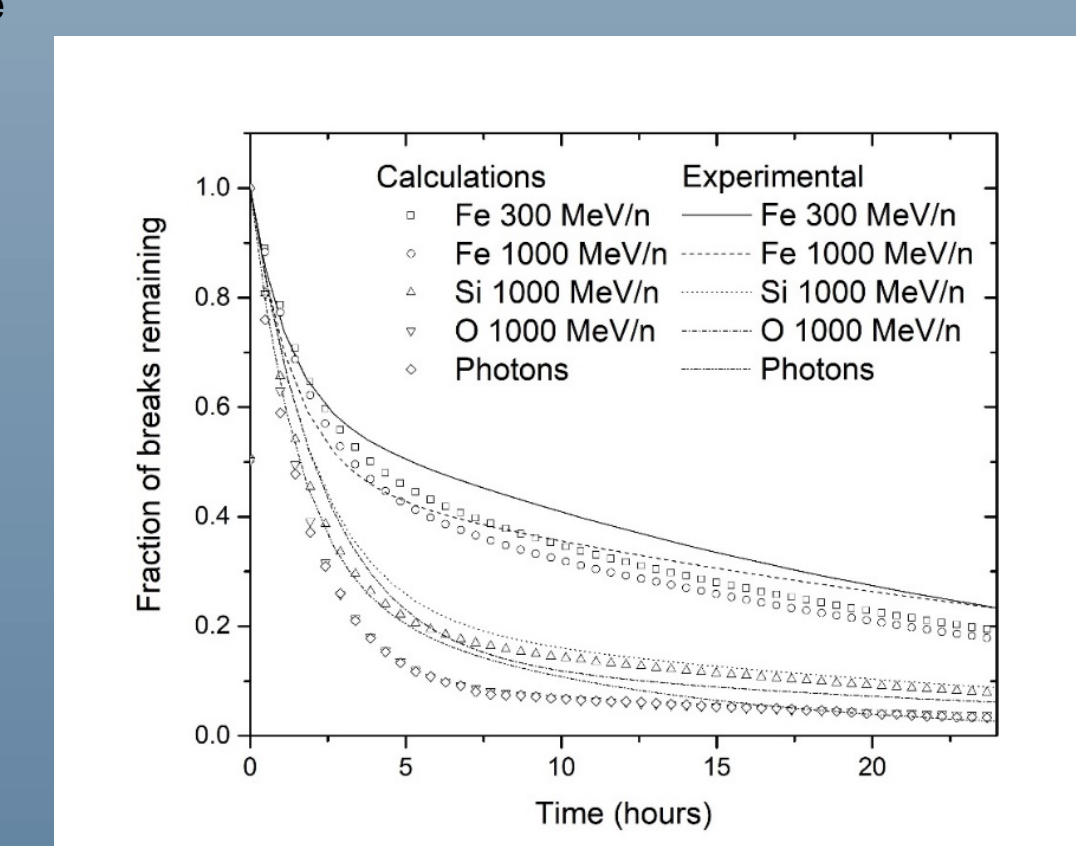
Repair kinetics of breaks of type 1 and 2, and the total number of breaks, as simulated with the algorithm, with parameters $N_1(0)=3$, $\tau_1=1$ h, $N_2(0)=2$, $\tau_2=5$ h. The number of simulation histories is 1,000,000. All simulation curves decay as predicted by the corresponding analytical curves.



Determination of the dose threshold using the voxel dose distribution and the probability of creating at least one break

Table 1. Bi-exponential parameters given in ref. [5]

Ion	a_1	a_2	$1/\tau_1$	$1/\tau_2$	τ_1	τ_2
Iron 300 MeV/n	46.0	0.85	1.18	71.1	0.04	25.0
Iron 1 GeV/n	62.8	0.72	1.39	57.0	0.03	33.3
Silicon 1 GeV/n	93.0	0.48	2.08	28.0	0.04	25.0
Oxygen 1 GeV/n	103.6	0.47	2.33	20.1	0.04	25.0
γ ray	90.4	0.65	1.54	36.8	0.10	10.0



Calculations of repair kinetics curve using the new restitution algorithm with a dose threshold set at 500 eV. The experimental data are the bi-exponentials from ref. [5]

Calculation of chromosome aberrations

- Chromosome aberrations

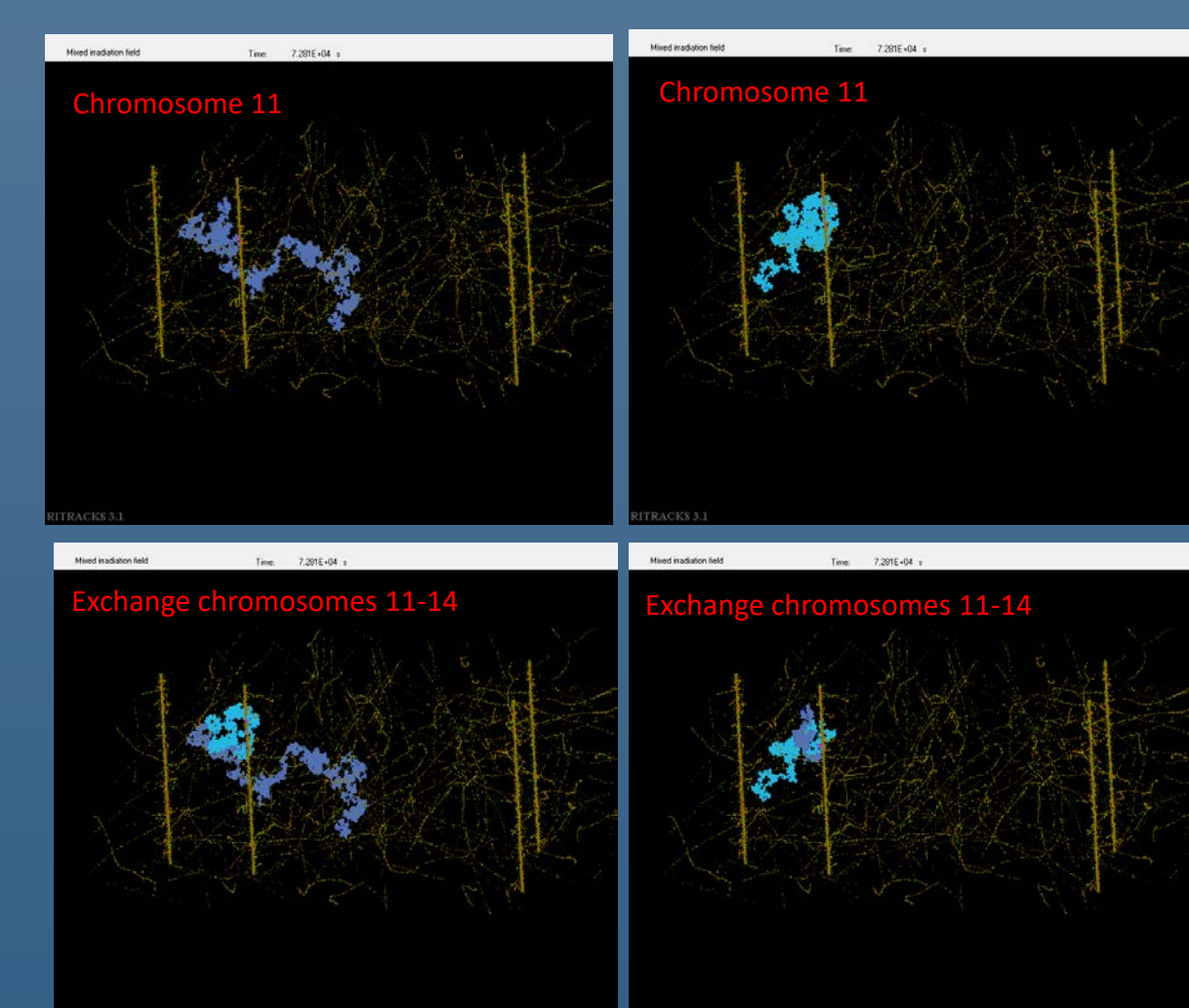
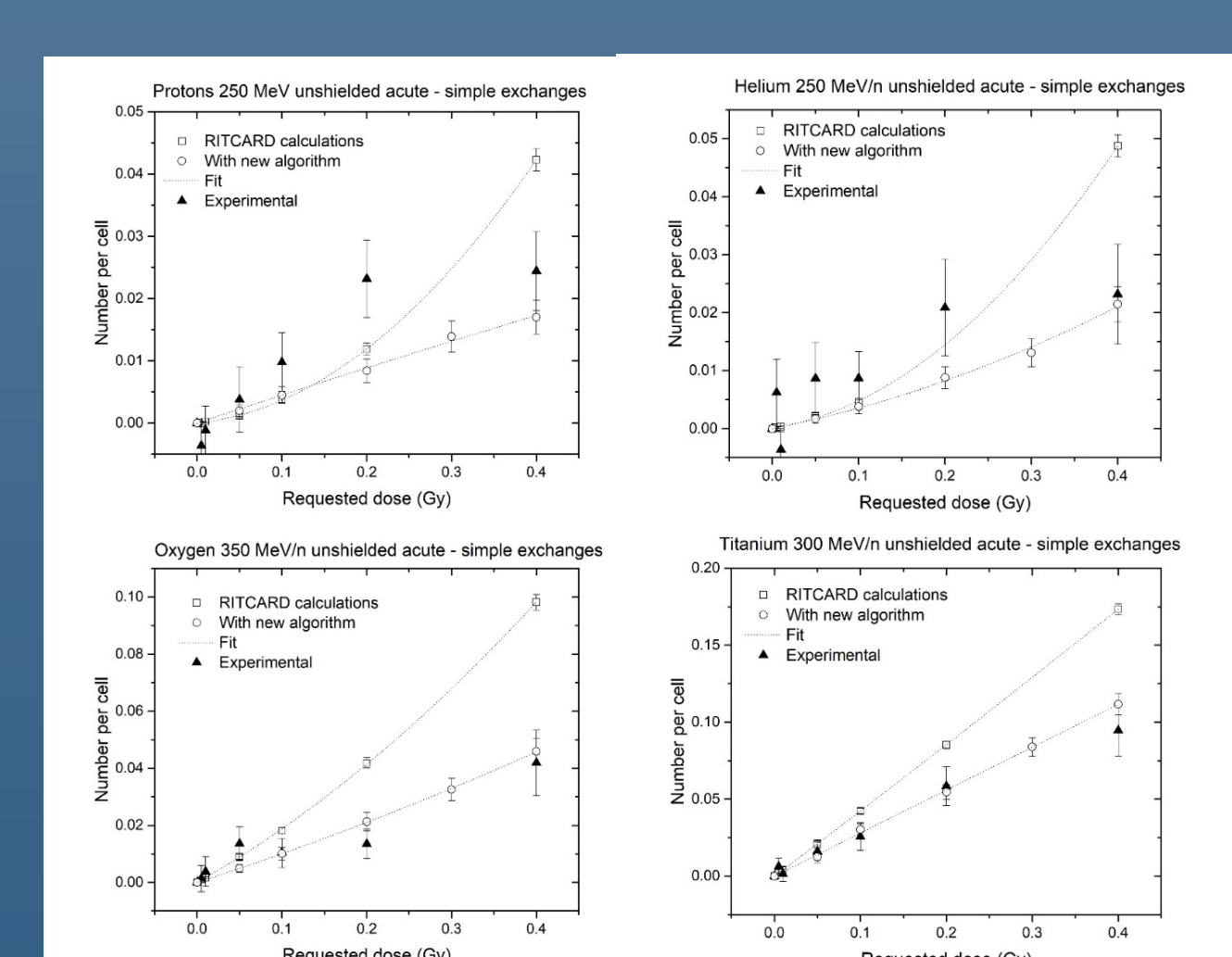


Illustration of a chromosome exchange

- Dose-response curves



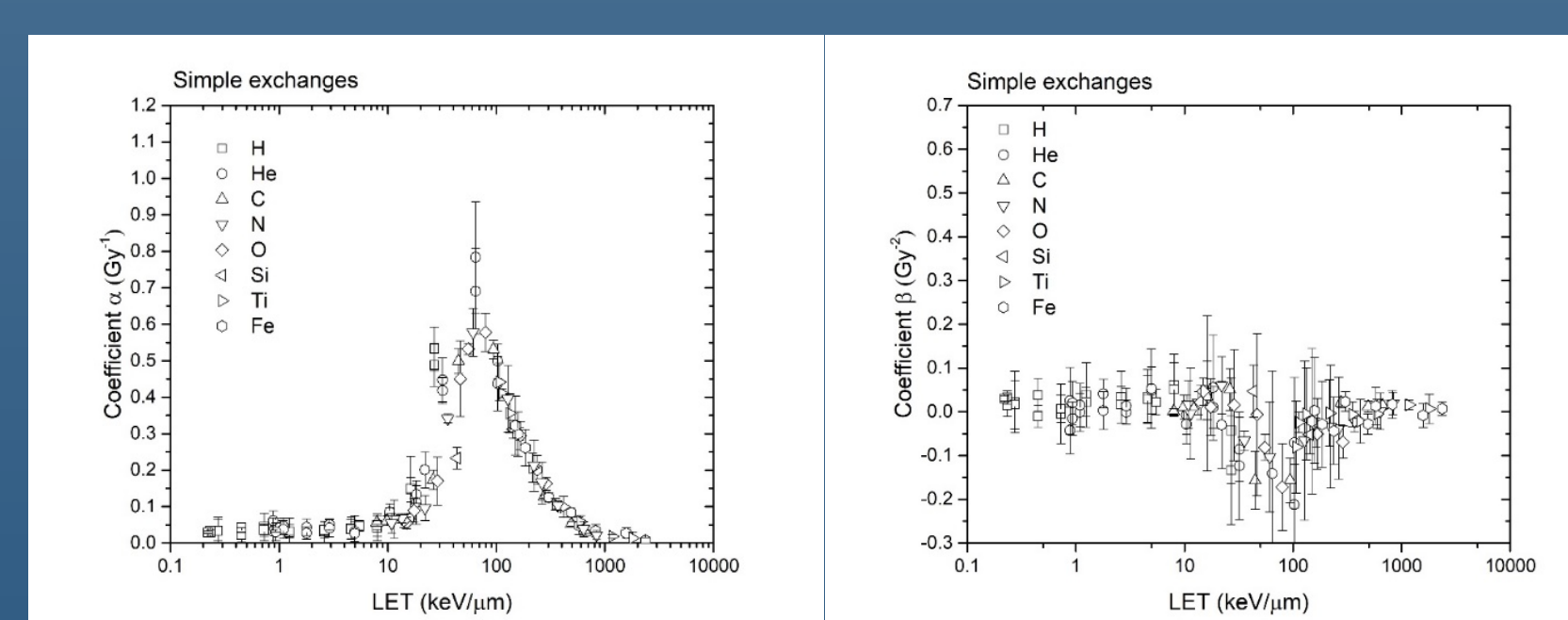
Simulated dose-response curves and experimental data using the old and new algorithms.

- Alpha and beta coefficients.

A linear-quadratic (LQ) model is used for the dose-response curves.

$$CA = \alpha D + \beta D^2$$

A peak is observed at a LET of about 100 keV/ μ m.



Coefficients α and β of the dose-response curves for simple exchange

Conclusion

- RITRACKS is now able to simulate time-dependent 3D voxel dose map for multiple ion beams and GCR.
- The new code RITCARD simulates CA yields in different irradiation conditions.
- The CA yield predicted by RITCARD follow a LQ model.
- The coefficient α in the LQ model peaks at a LET of ~ 100 keV/ μ m.
- Other types of repair kinetics are being investigated.

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