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Calculation of dose deposition in nanovolumes and simulation of γ-H2AX experiments

By

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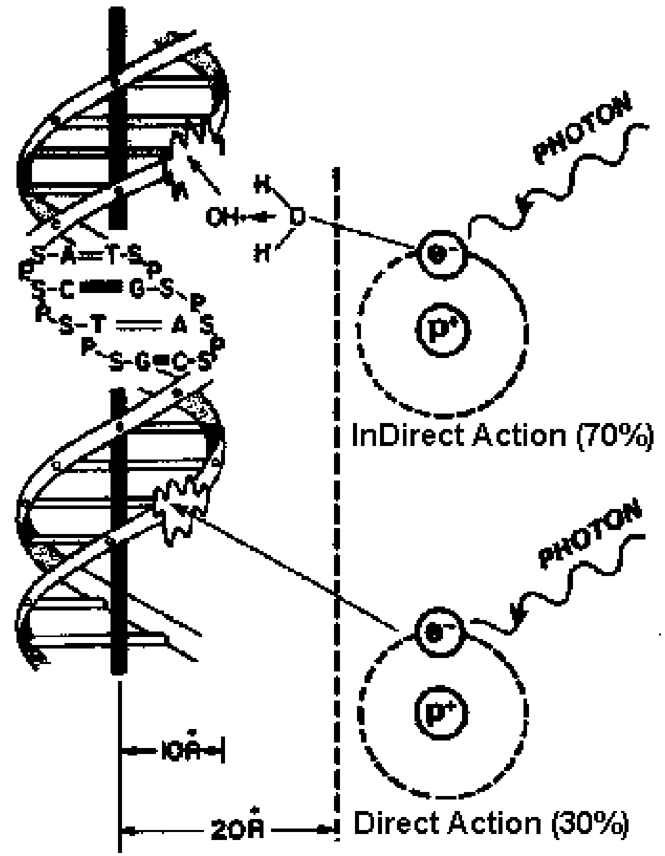
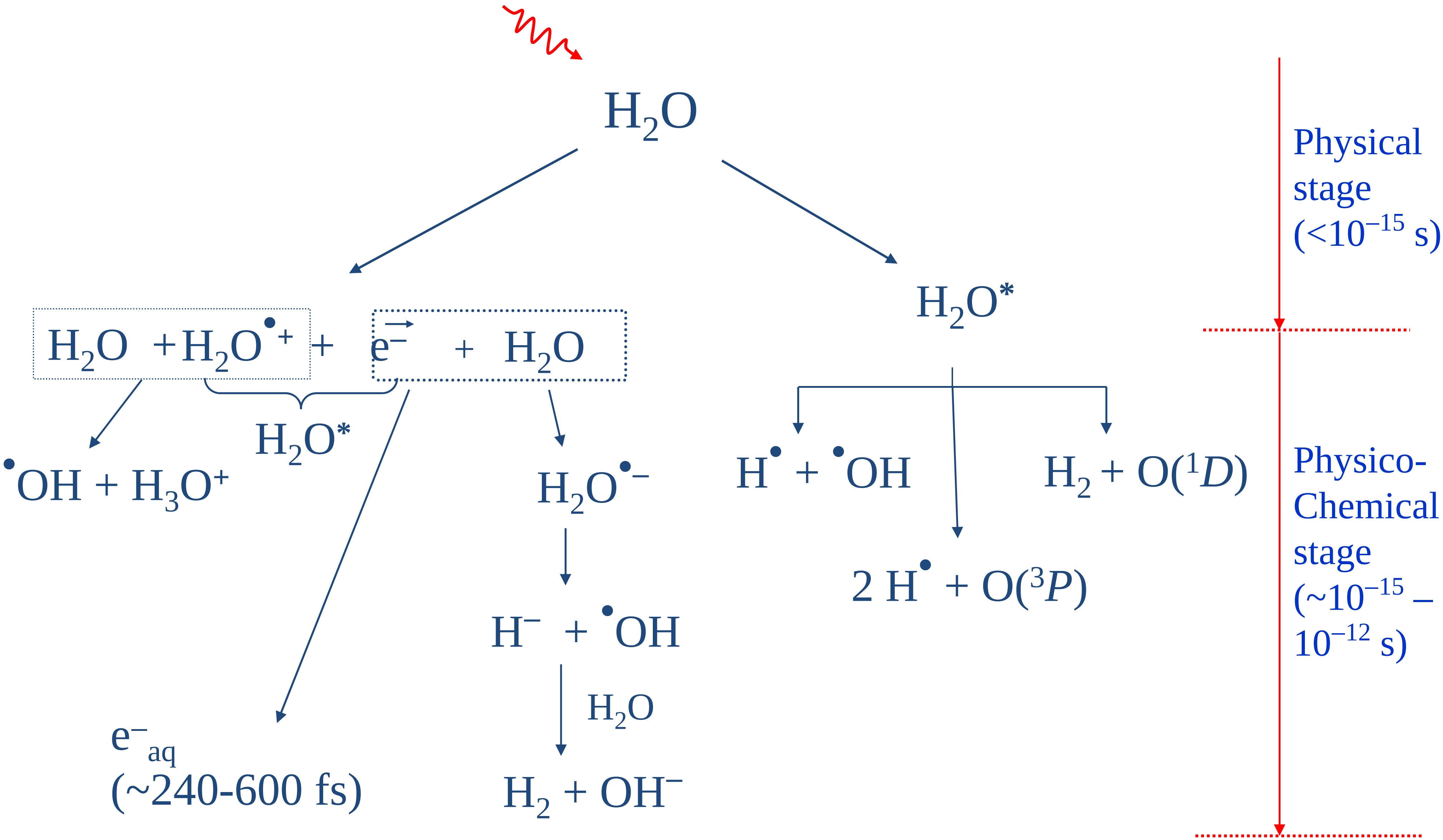
Why study the radiation track structure?

- The cross sections for some phenomenon in liquid water are not well known
- The radiation track structure is essential to understand the induction of DNA damage
- Multiple lesions in a localized region of DNA leads to complex damage, notably Double-Strand Breaks (DSB)
- DSB are considered the most important for long term effects of ionizing radiation



Hall, Lippincott, Williams & Wilkins, Philadelphia, PA, 2000.

Physical and physico-chemical stages

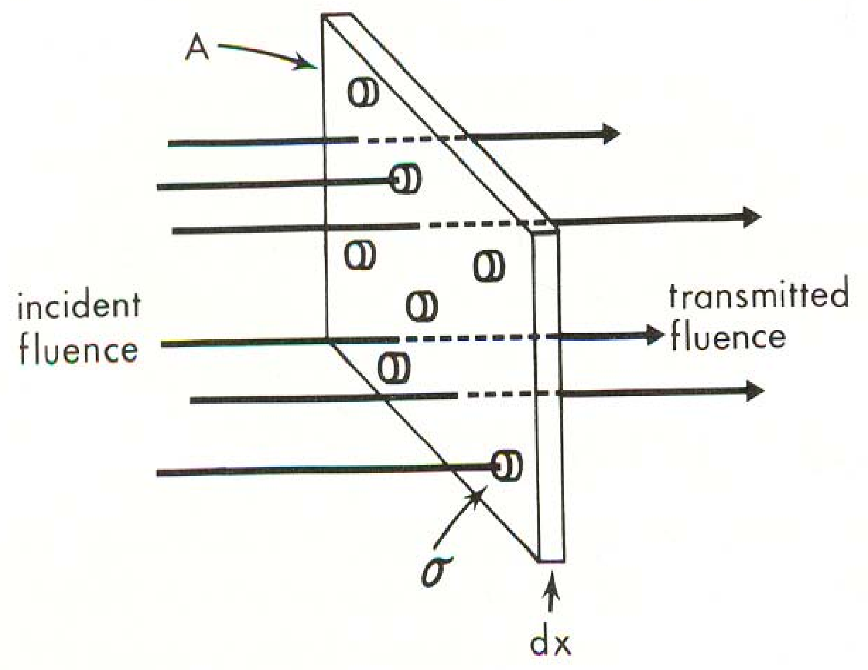


Cross sections

- Interaction between radiation and matter

$$dI = -In\sigma dx$$

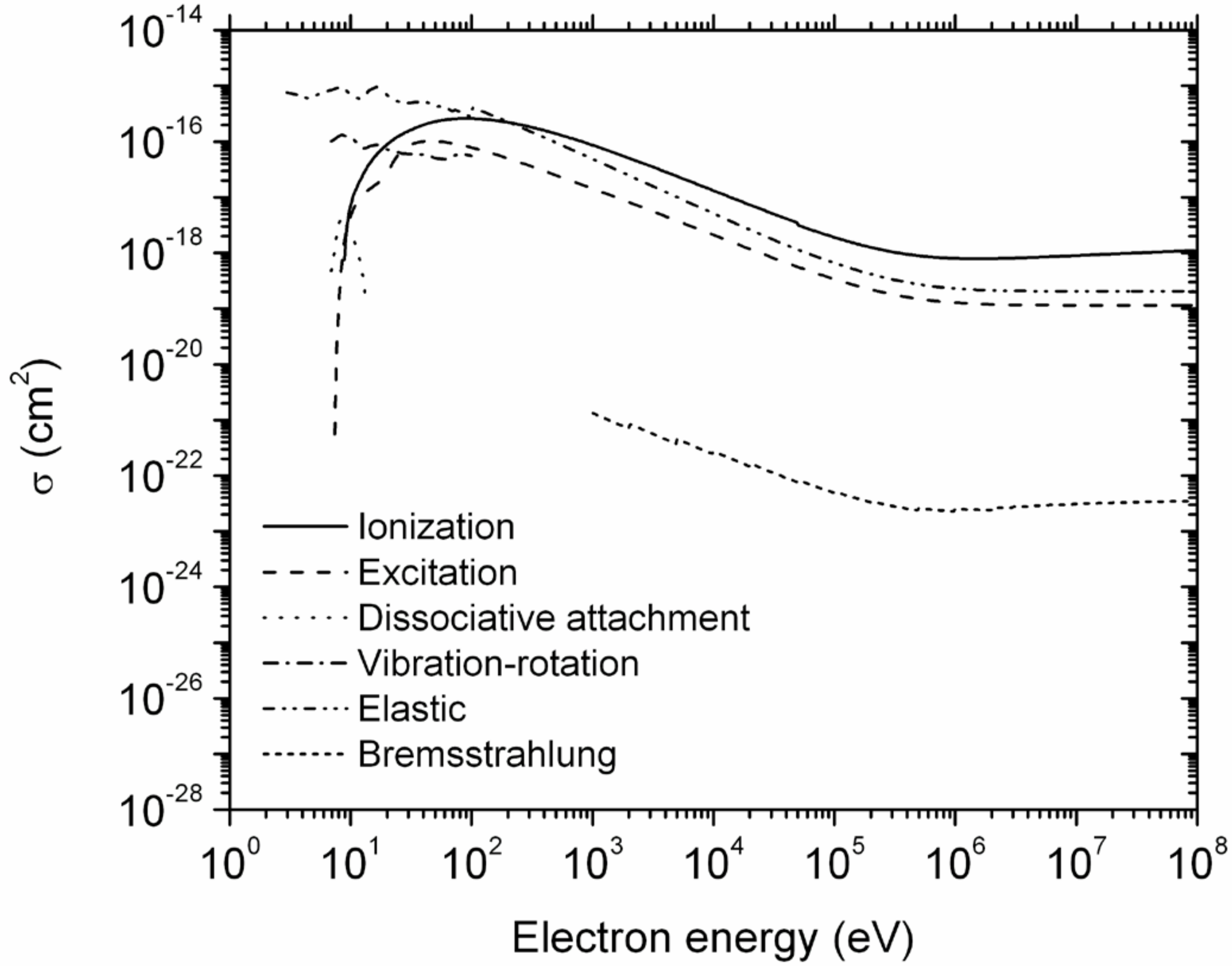
I: Incident fluence
n: Density of targets
dx: Width
σ: Cross section



- Cross sections (units: cm^2)

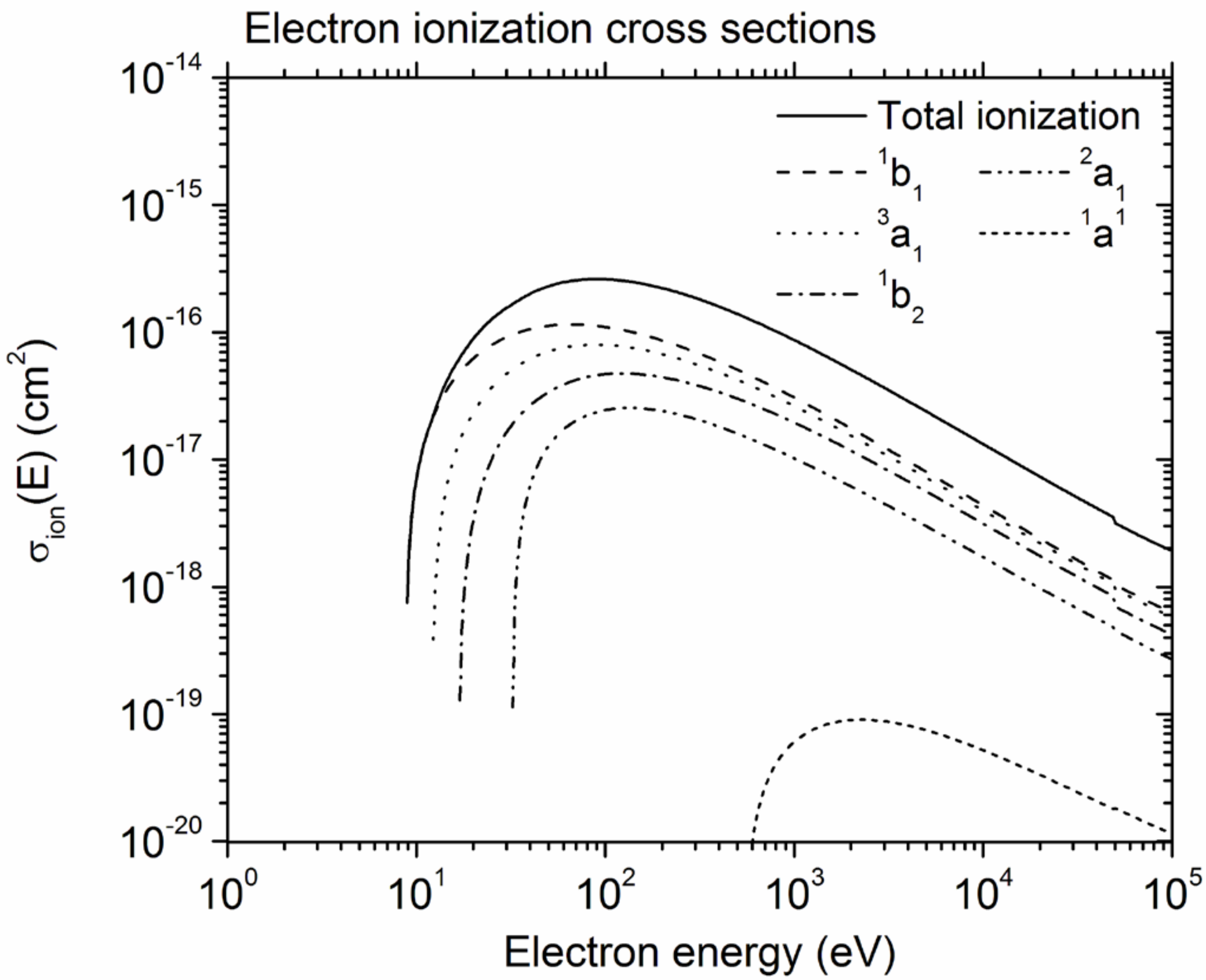
Anderson, D.W. (1984), University Park Press, Baltimore, MD

Electron cross sections for RITRACKS



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

Electron cross sections for RITRACKS



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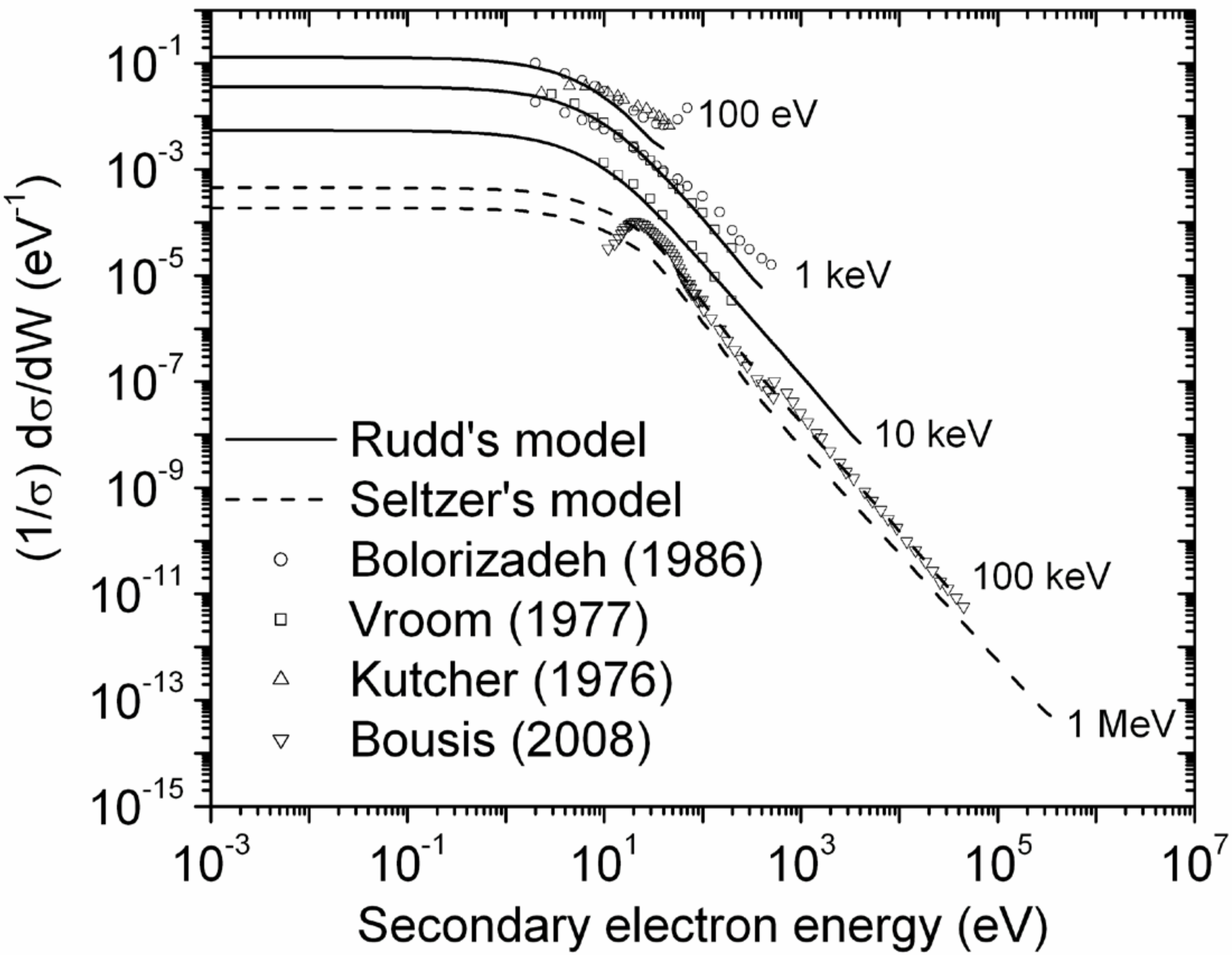
Electron cross sections for RITRACKS

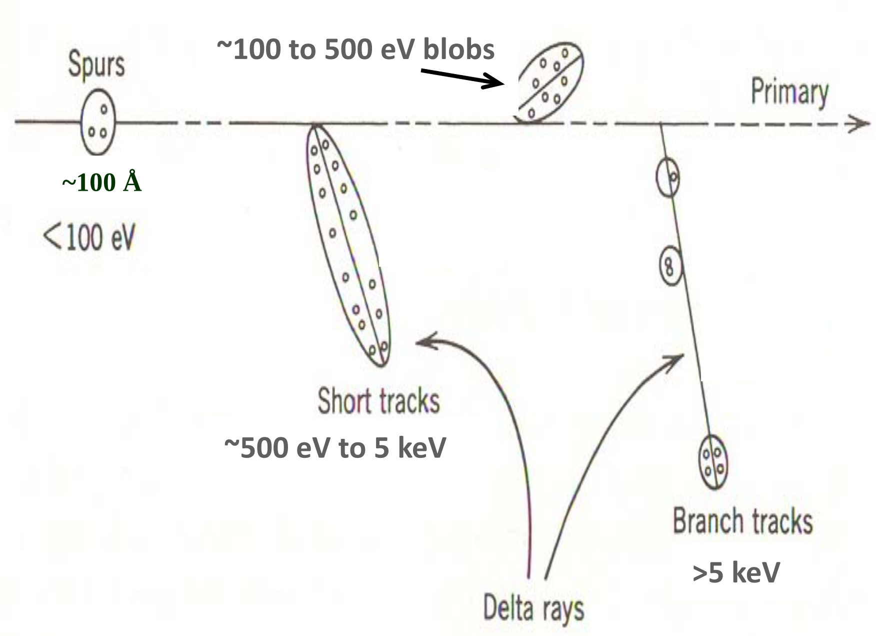


Plante, I. and Cucinotta, F. A. (2009). *New J. Phys.* **11**, 063047

Physical and physicochemical stages

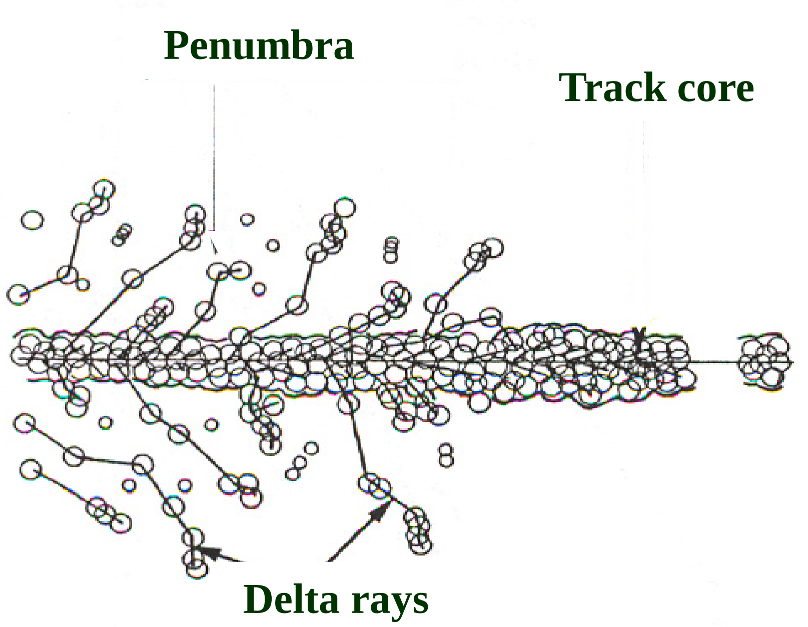
- The nonhomogeneous deposition of energy is called “radiation track structure”

Primary energy loss events in low-LET tracks



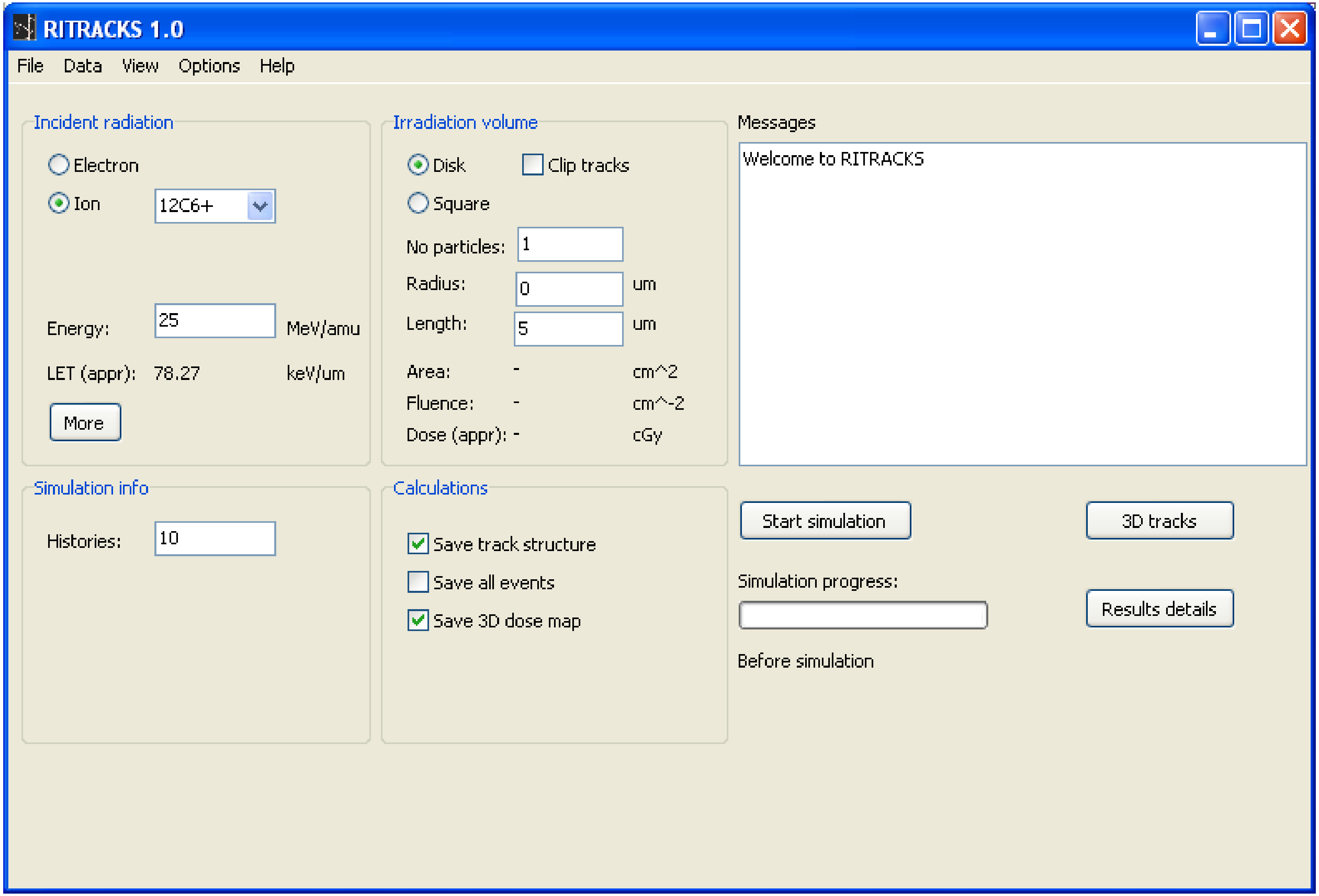
A. Mozumder and J.L. Magee (1966) *Radiat. Res.* **28**, 203

Primary energy loss events in high-LET tracks



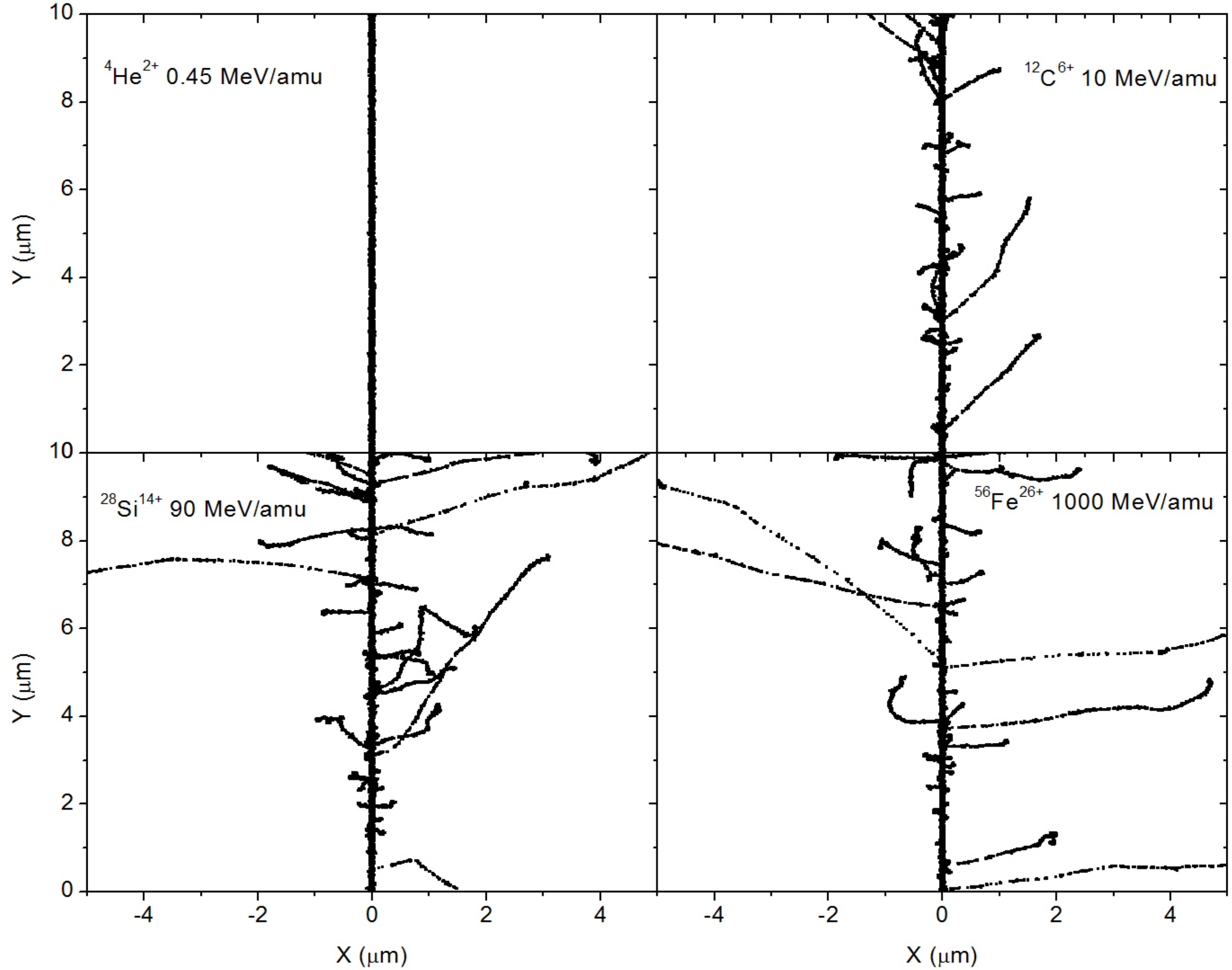
C. Ferradini (1979) *J. Chim. Phys.* **76,** 636

RITRACKS main screen



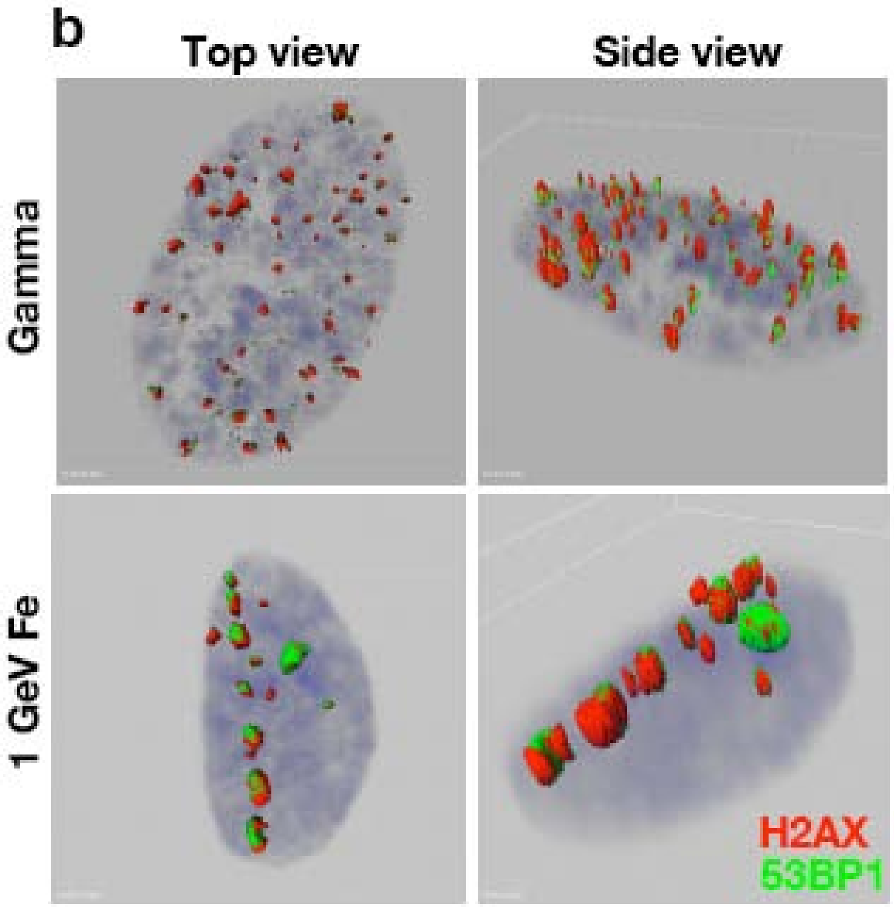
Heavy ions track structure simulations

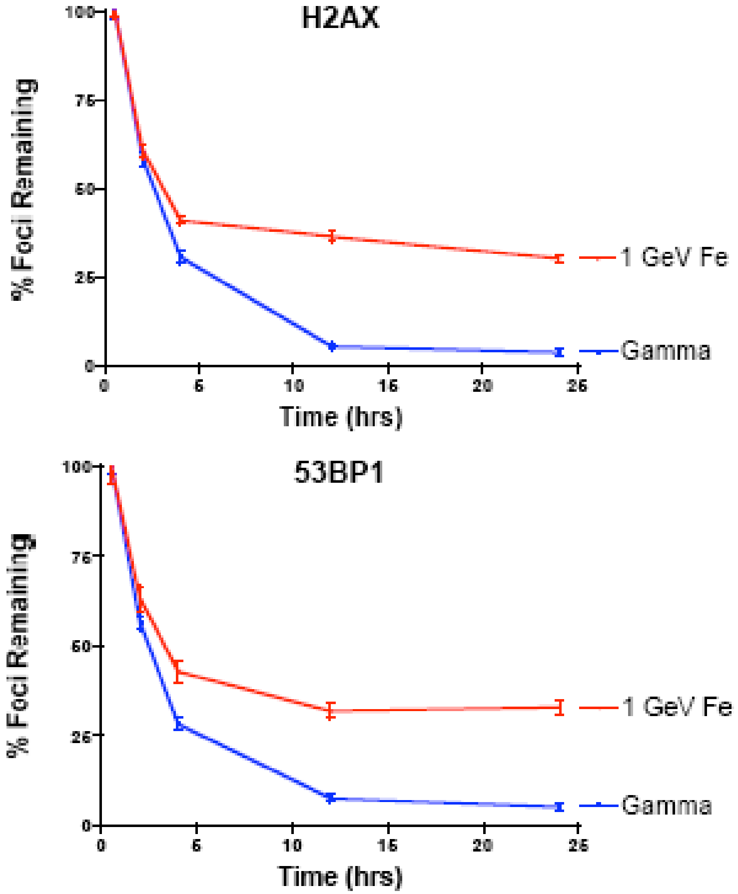
LET~150 keV/μm



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

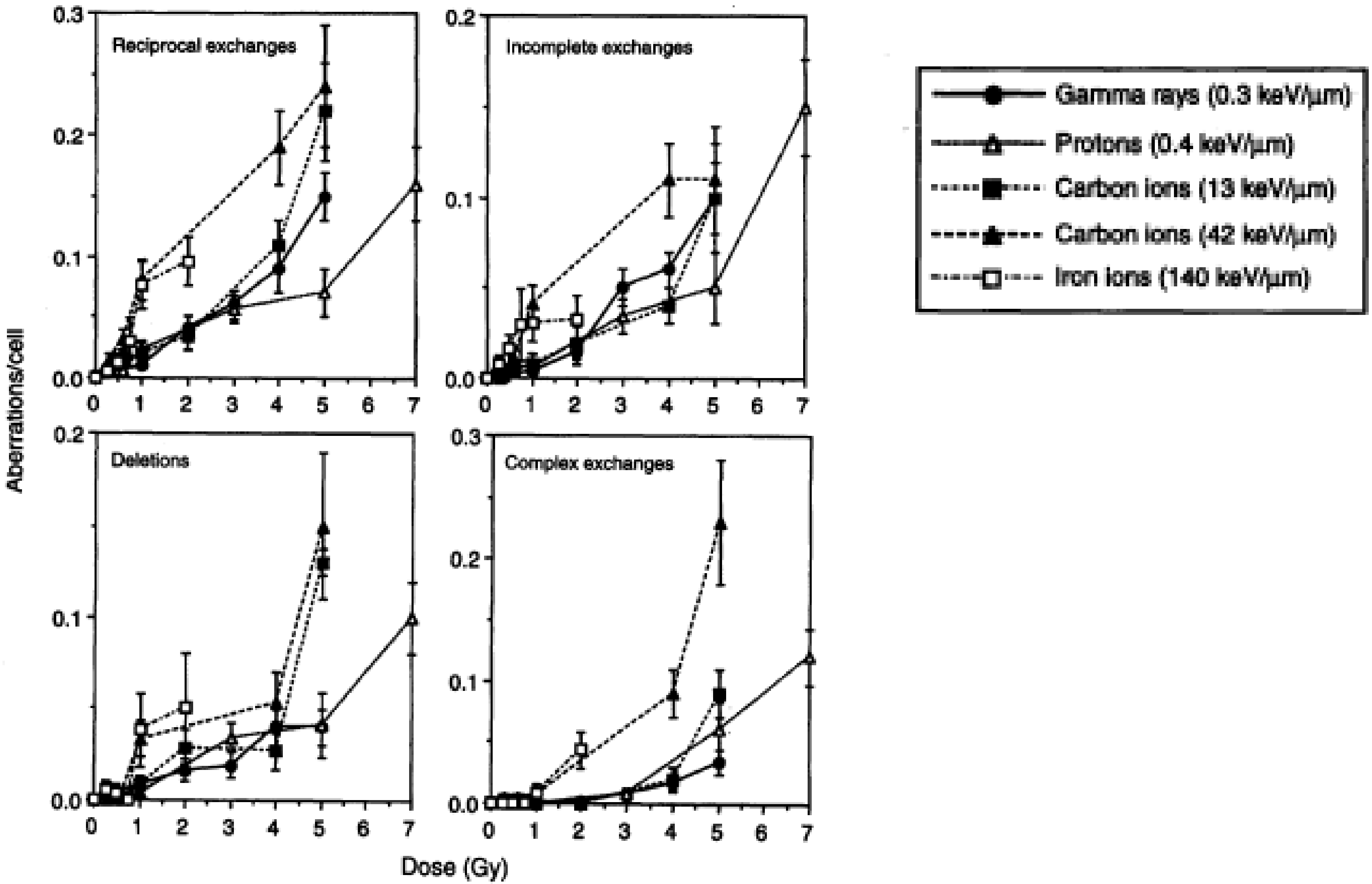
DNA damage





Mukherjee, B. et al. (2008), *DNA repair* **7**, 1717-1730

DNA damage



Wu, H. et al. (1997) *Radiat. Res.* **148**, S102-S107

DNA damage models

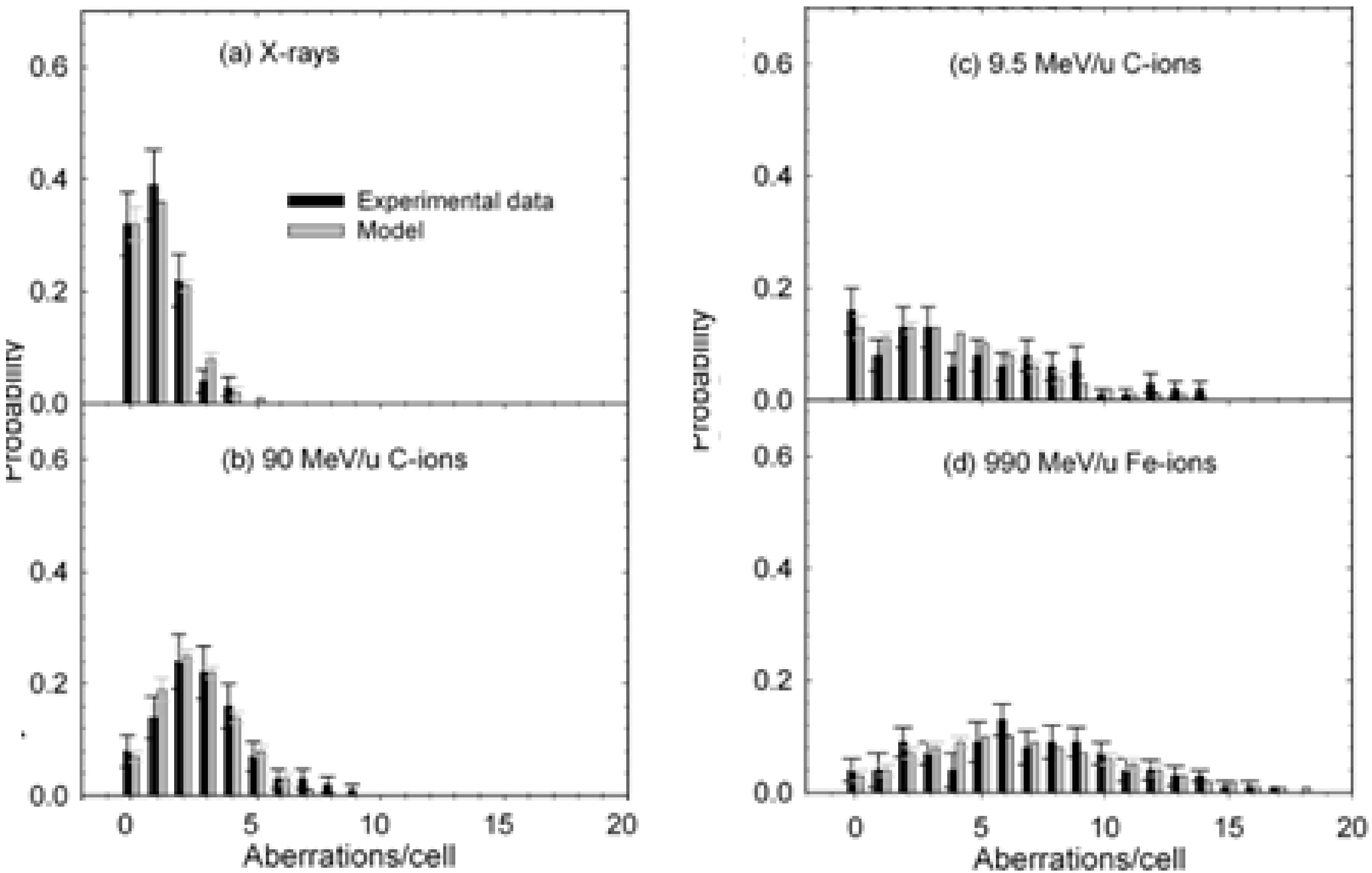
- Chromosomes simulated by random walk models
- The whole chromosome is located randomly with respect to the track center
- The radial dose is used to obtain the local dose
- The probability of having a double-strand break (DSB) is given by:

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

D(t): Radial dose at the distance t (Gy)
Q: Track efficiency parameter (Gy^{-1})

Ponomarev, A. L. et al. *Radiat. Res.* **156**, 594-597 (2001)

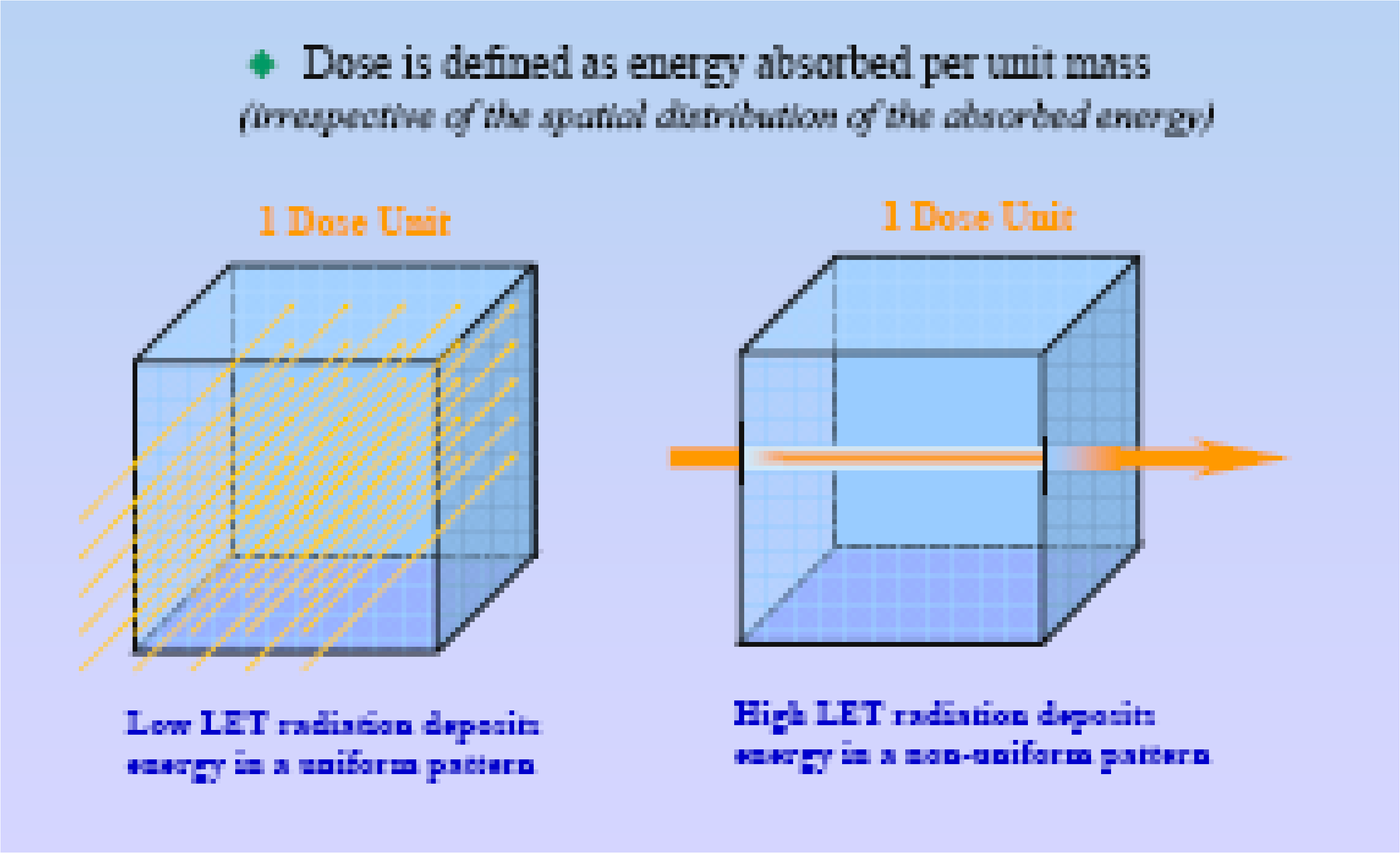
DNA damage models



Deperas-Standylo et al. *Eur. J. Phys. D* **60**, 93-99(2010)

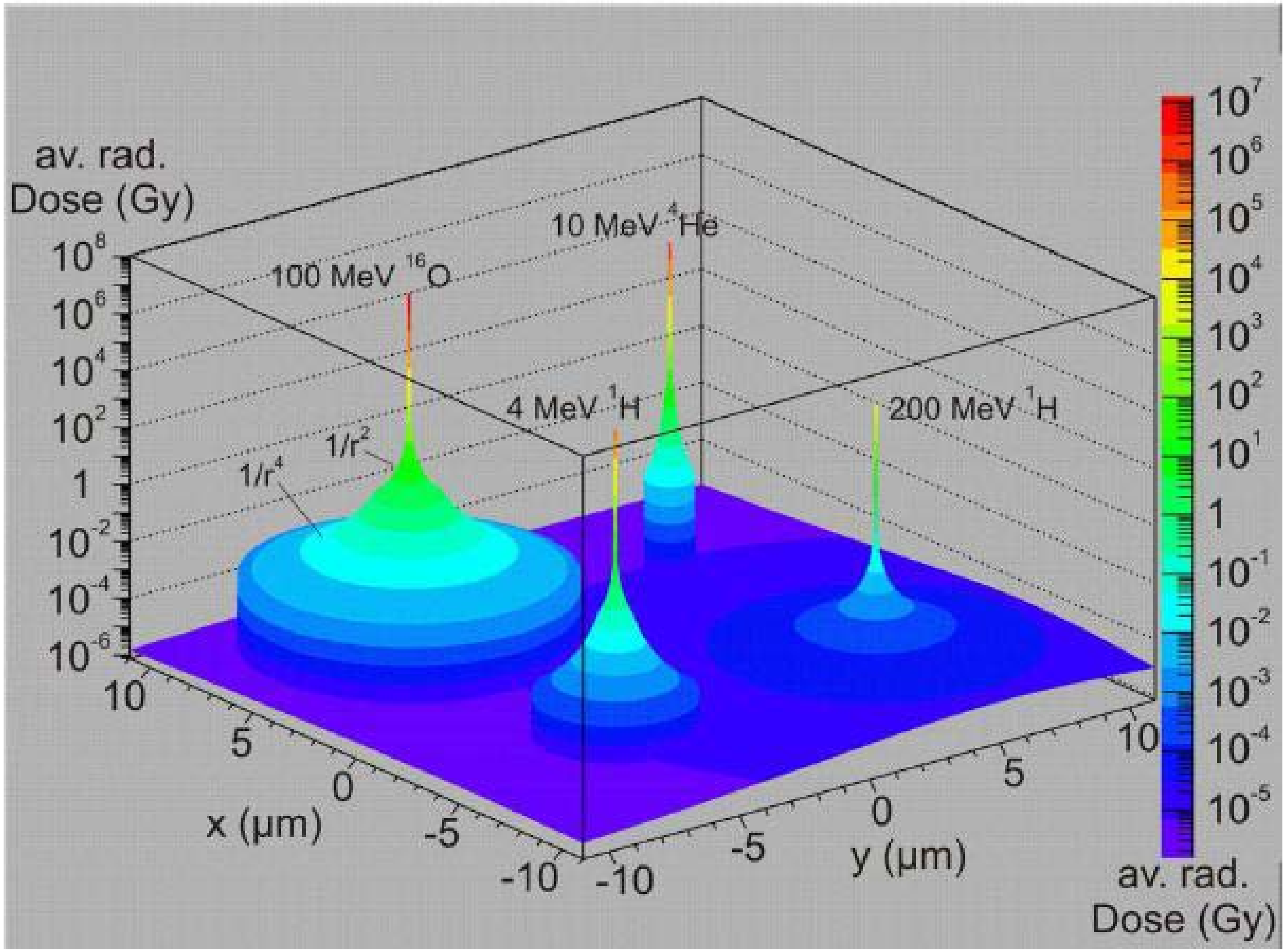
Definition of dose

- Dose: energy absorbed/unit mass



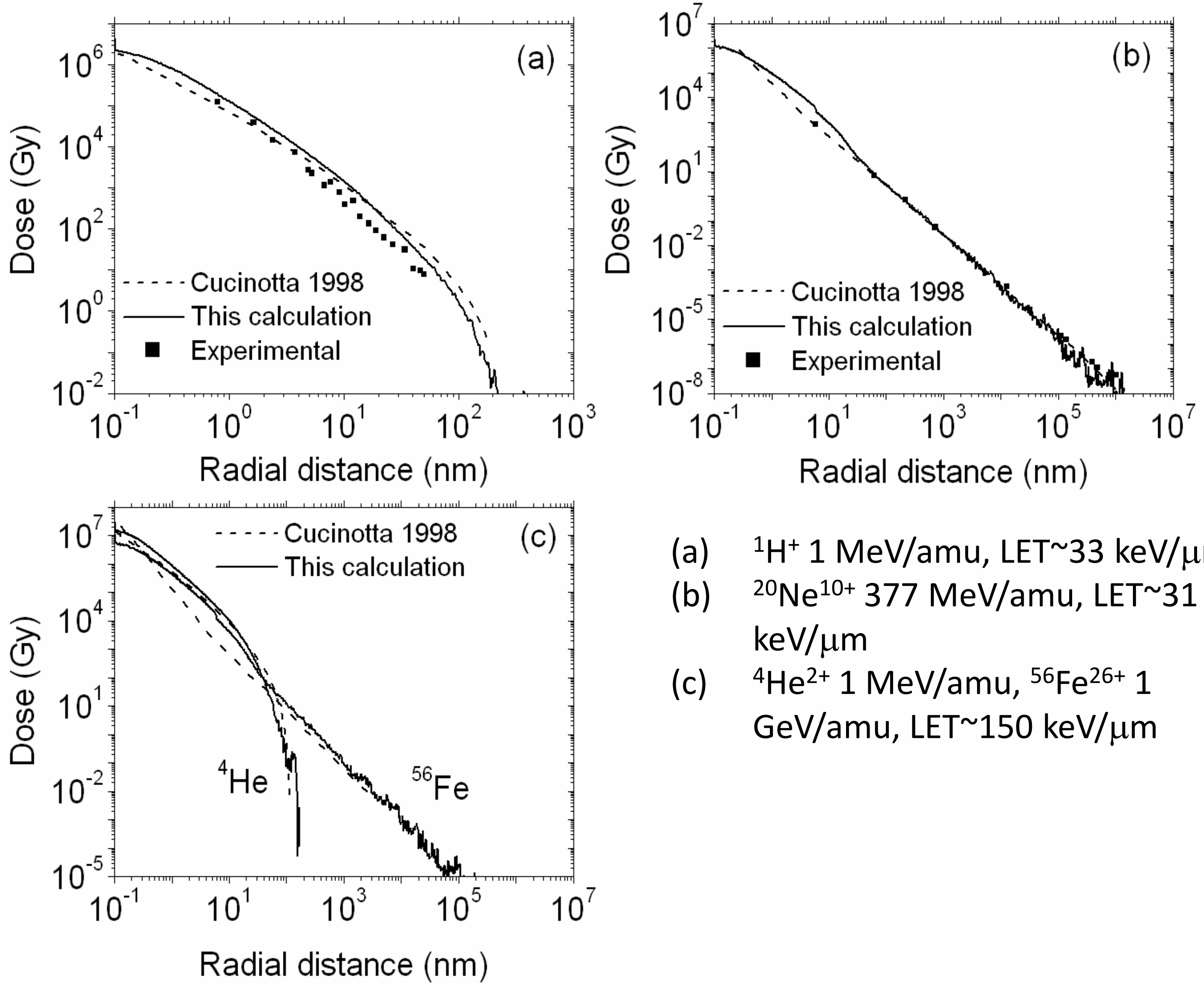
Unknown source

Dosimetry: 3D



Hauptner, A. et al. *MfM* **52**, 59-85(2006)

Radial Dosimetry



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

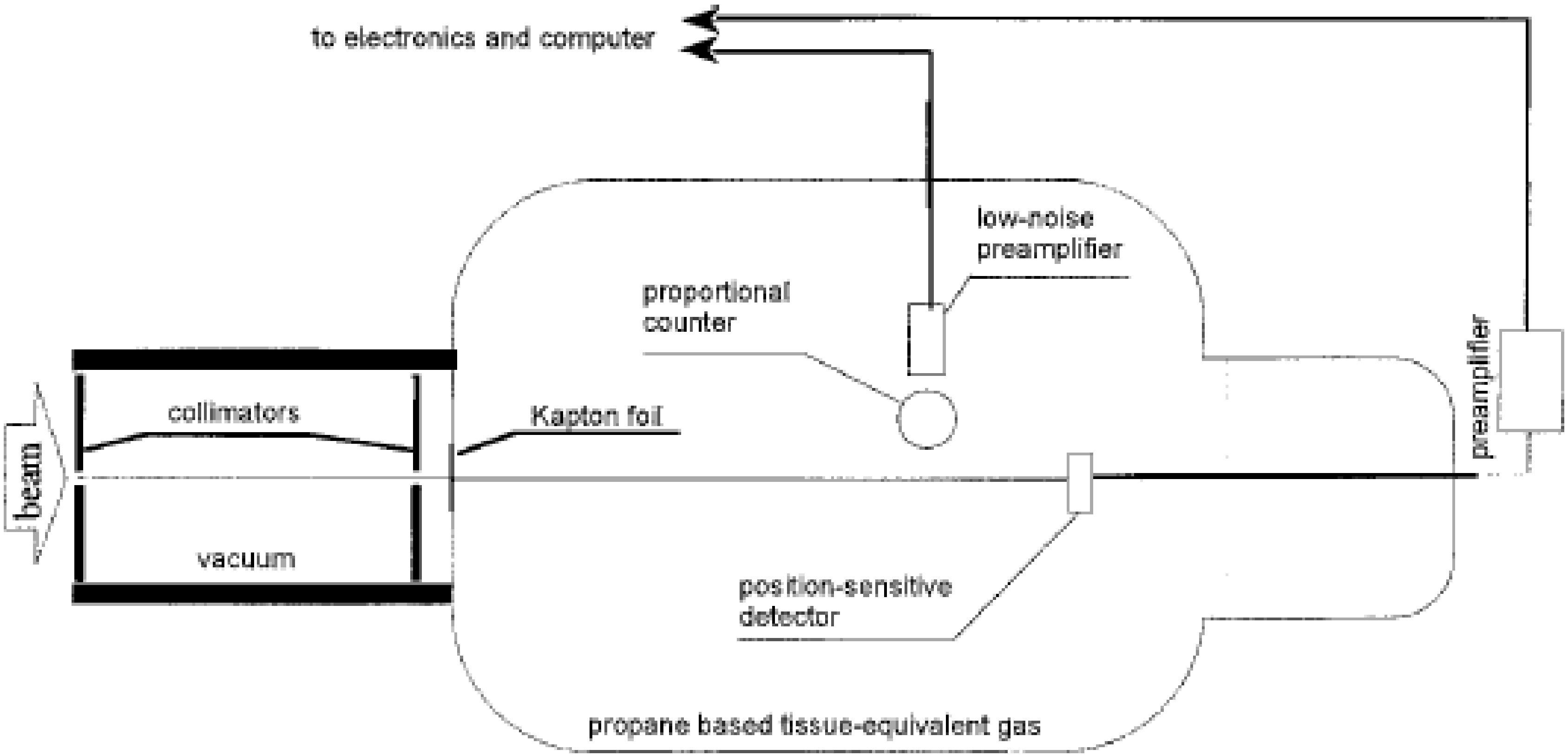
(b) $^{20}Ne^{10+}$ 377 MeV/amu, LET~31 keV/μm

(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

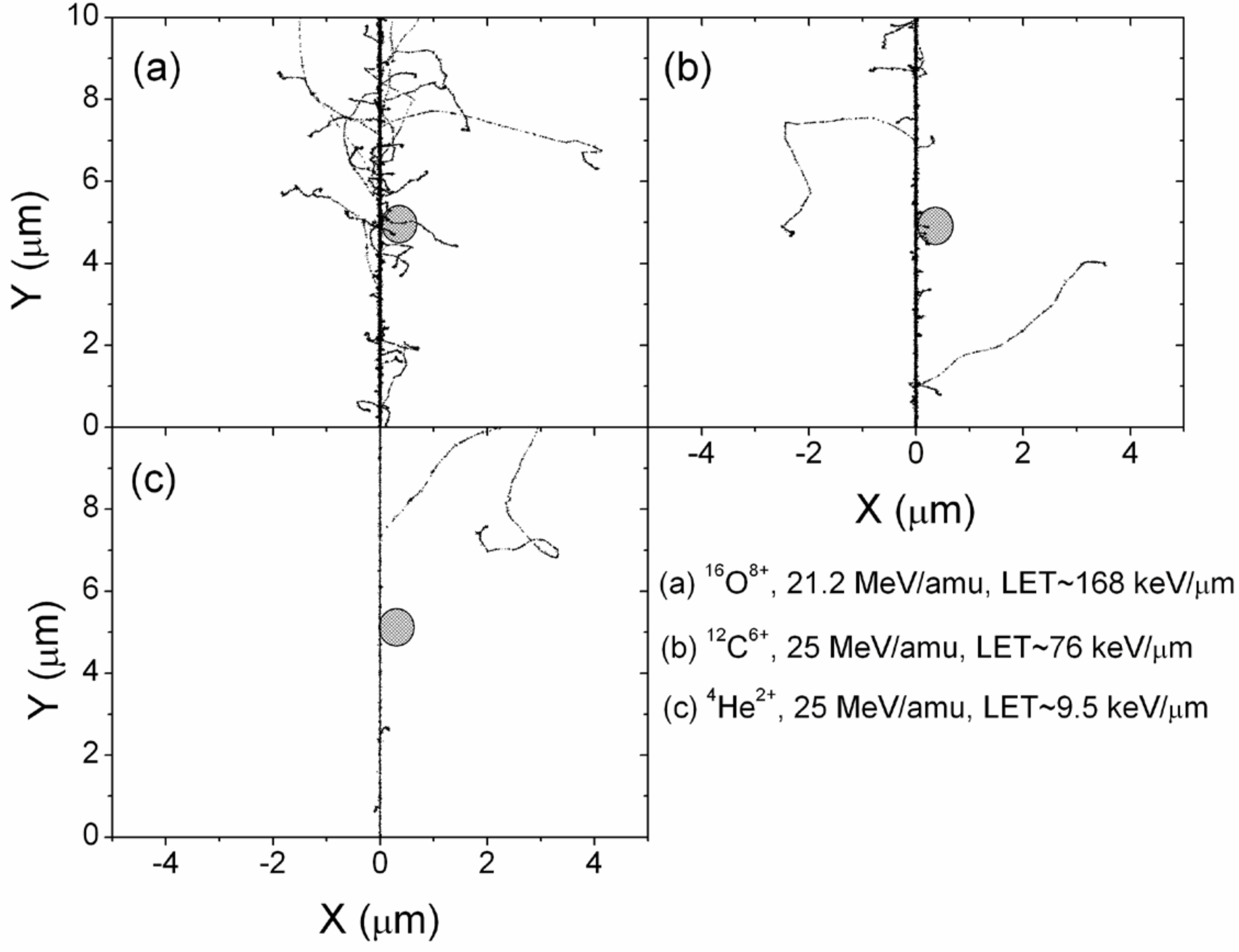
Dosimetry

- Experimental setup



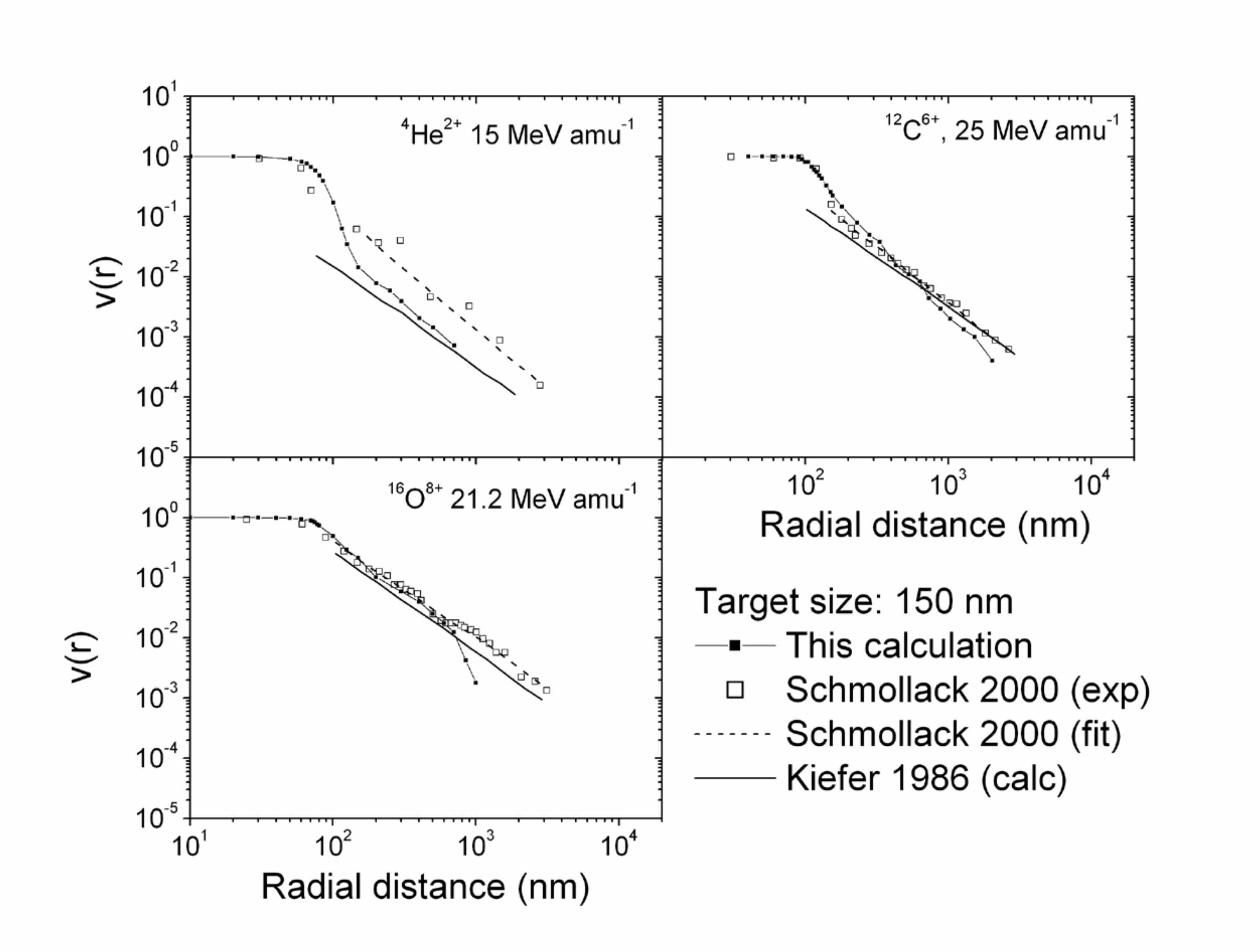
Schmollack, J. U. et al. (2000), *Radiat. Res.* **153**, 469-478

Simulation



Plante, I. and Cucinotta, F.A. (2009), *Radiat. Env. Biophys.* **49**, 5-13

Frequency of site hits



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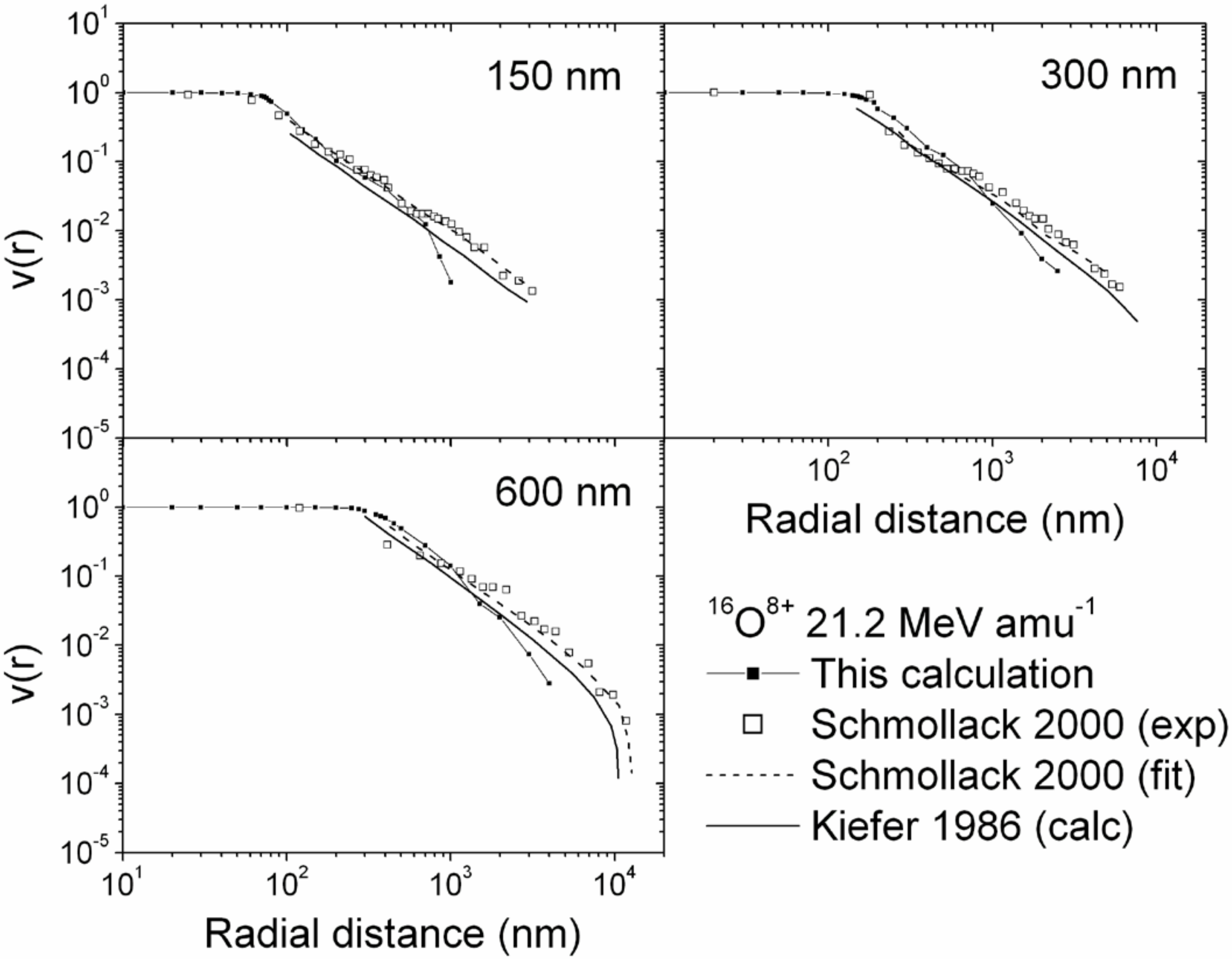
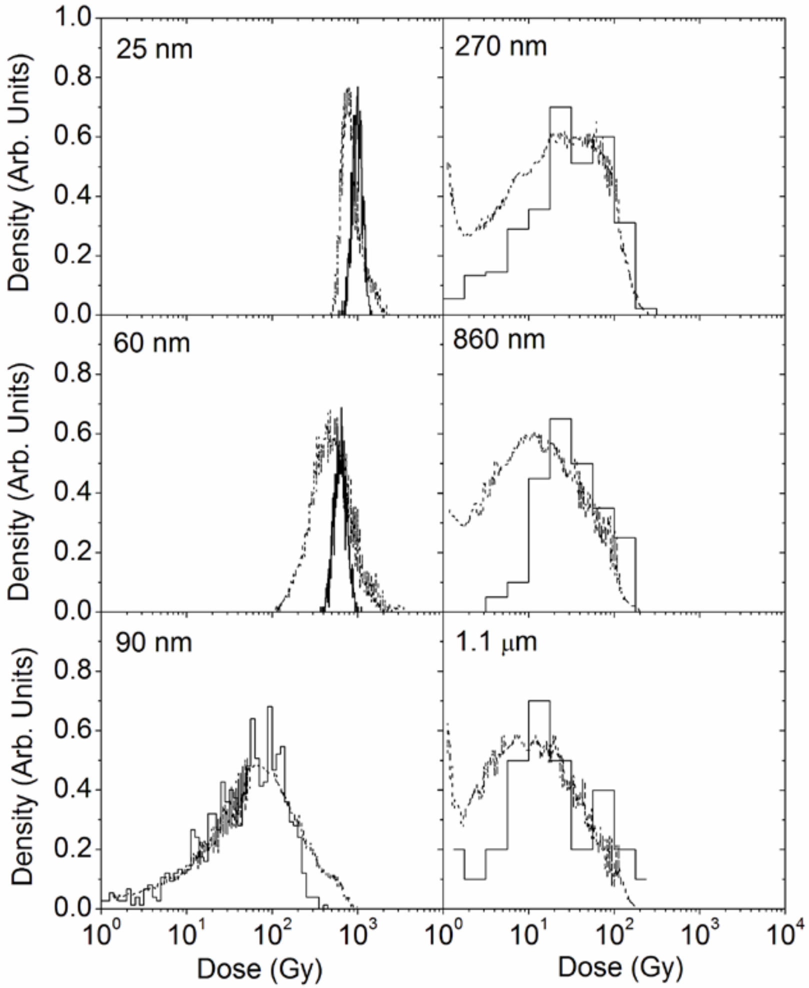


Plante, I. and Cucinotta, F.A. (2009), *Radiat. Env. Biophys.* **49**, 5-13

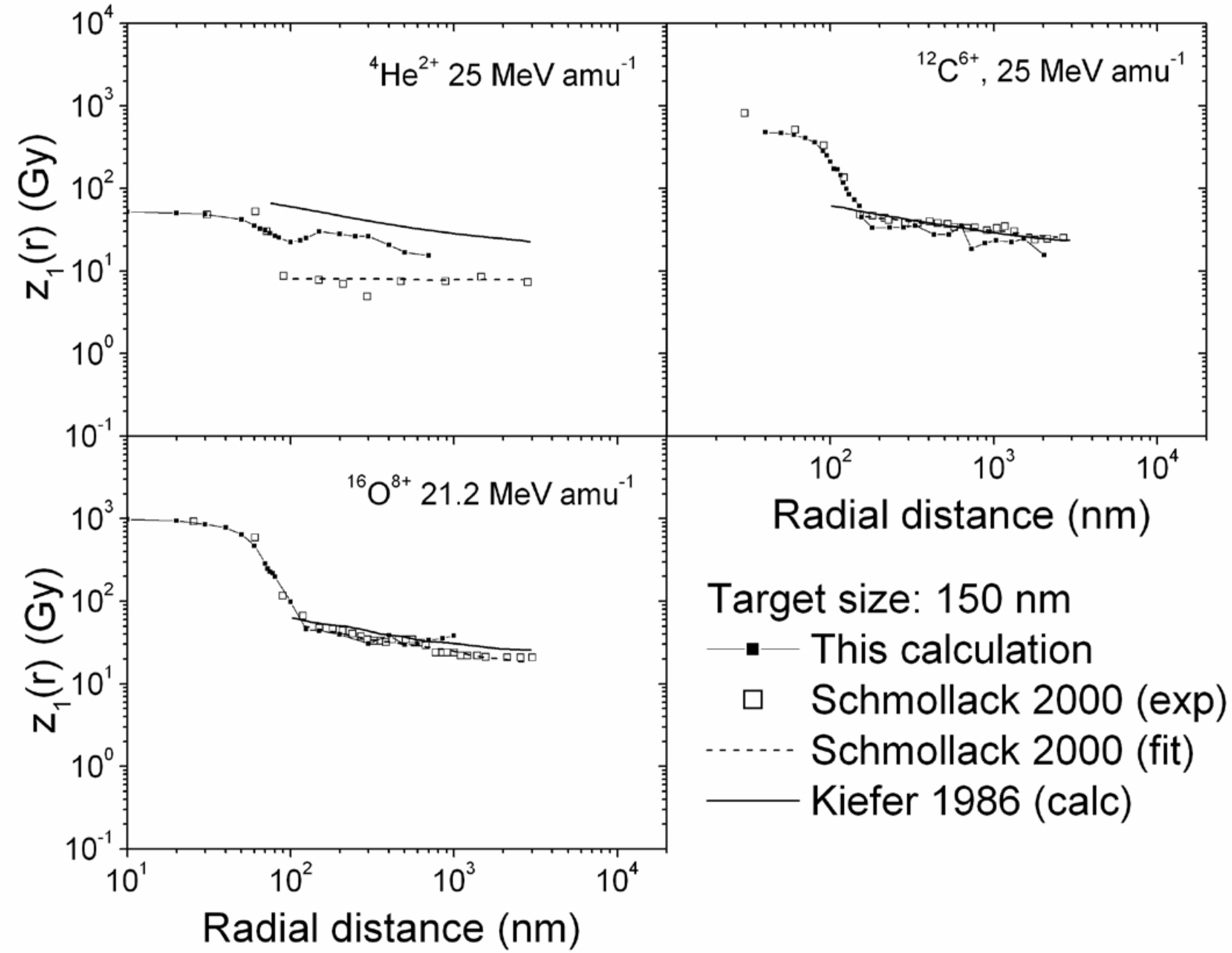
Dose distribution in target



$^{16}O^{8+}$, 21.2 MeV amu^{-1}

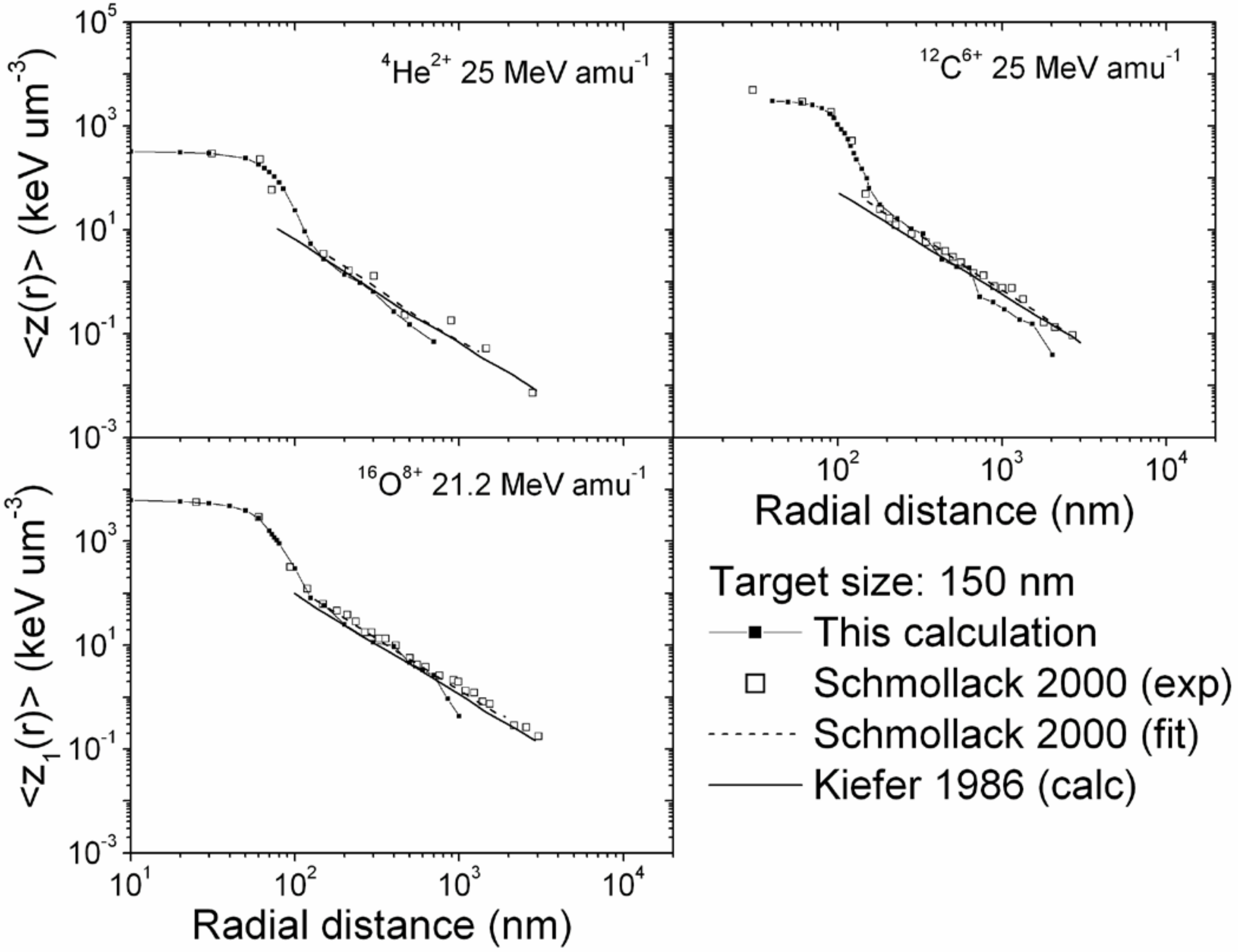
Plante, I. and Cucinotta, F.A. (2009), *Radiat. Env. Biophys.* **49**, 5-13

Specific energy per event



Plante, I. and Cucinotta, F.A. (2009), *Radiat. Env. Biophys.* **49**, 5-13

Specific energy per ion

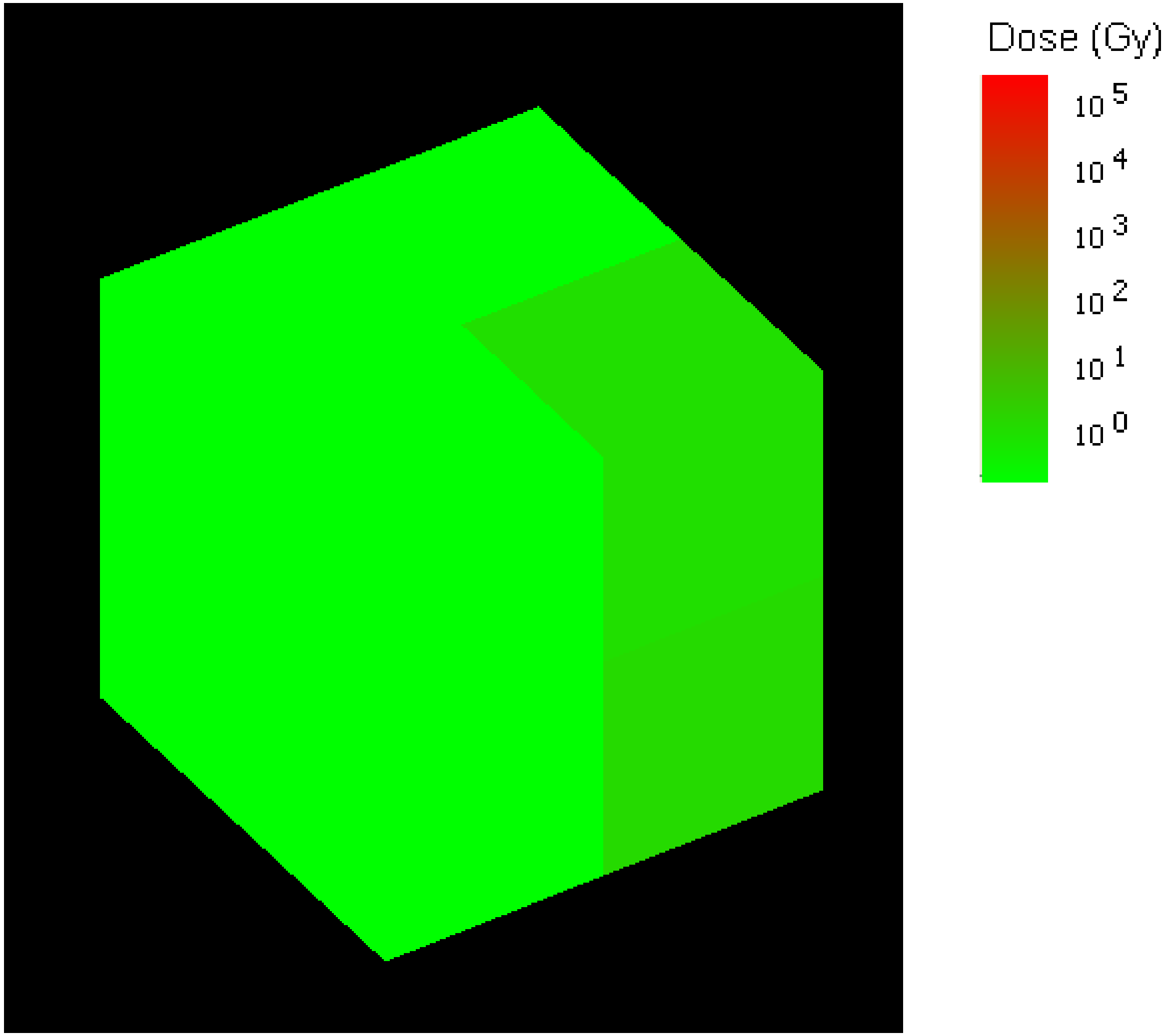


Plante, I. and Cucinotta, F.A. (2009), *Radiat. Env. Biophys.* **49**, 5-13

Calculation of dose in voxels

- Irradiated volume: 5 μm x 5 μm x 5 μm
- Dose: ~1 Gy
- Radiations:
  - 450 $^{1}H^{+}$ ions, 300 MeV, LET: ~0.3 keV/μm
  - 1 $^{56}Fe^{26+}$ ions, 1 GeV/amu, LET: ~150 keV/μm
- Calculation of the track structure(s) with RITRACKS
- All energy deposition events are recorded
- Dose recalculated in voxels

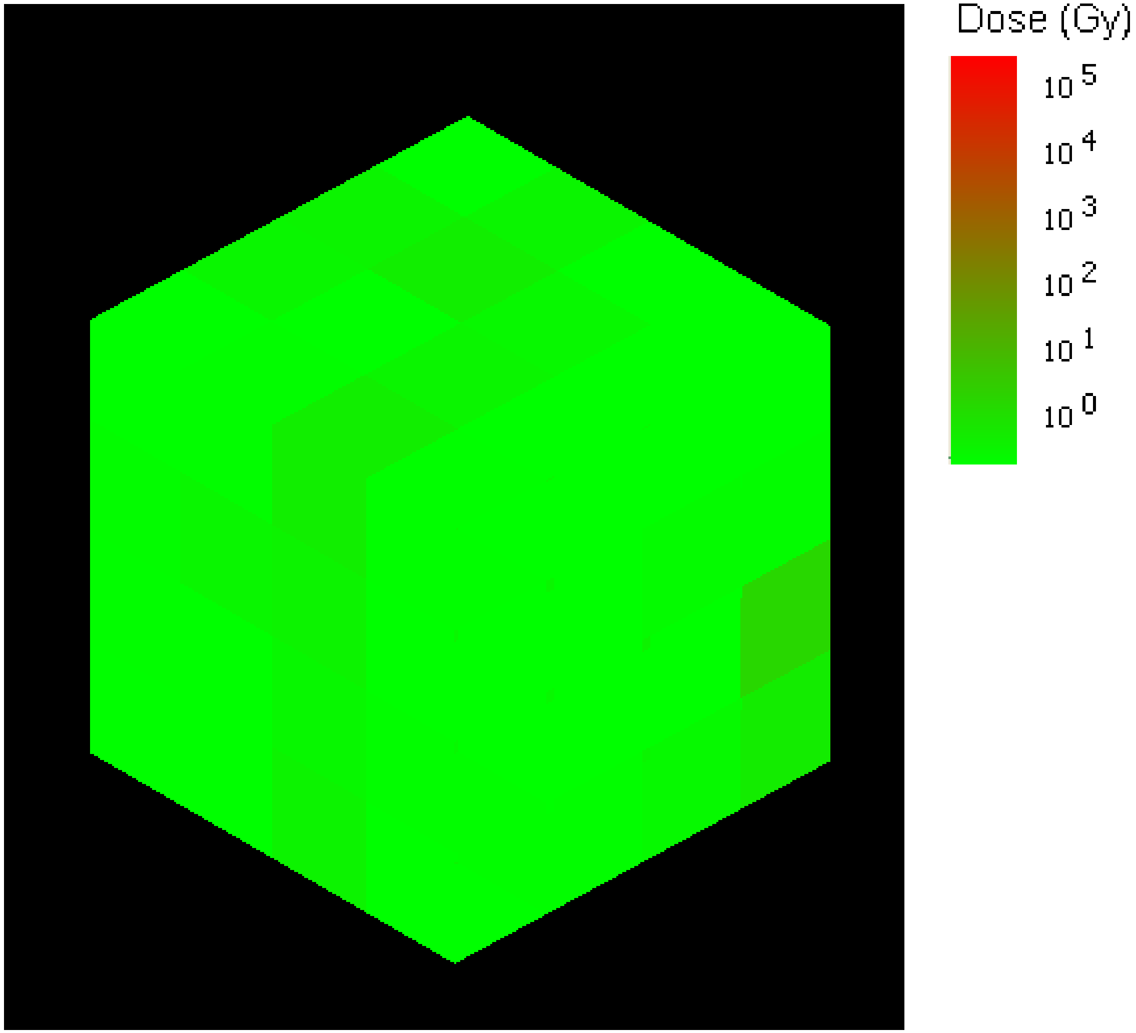
Calculation of dose in voxels



Voxels size: 2560 nm

- Calculations with RITRACKS
- 1 $^{56}Fe^{26+}$ ions, 1 GeV/amu
- LET: ~150 keV/μm
- Irradiated volume: 5 μm x 5 μm x 5 μm
- Voxels: 20 nm, 40 nm, 80 nm, 160, 320 nm, 640 nm, 1280 nm, 2560 nm

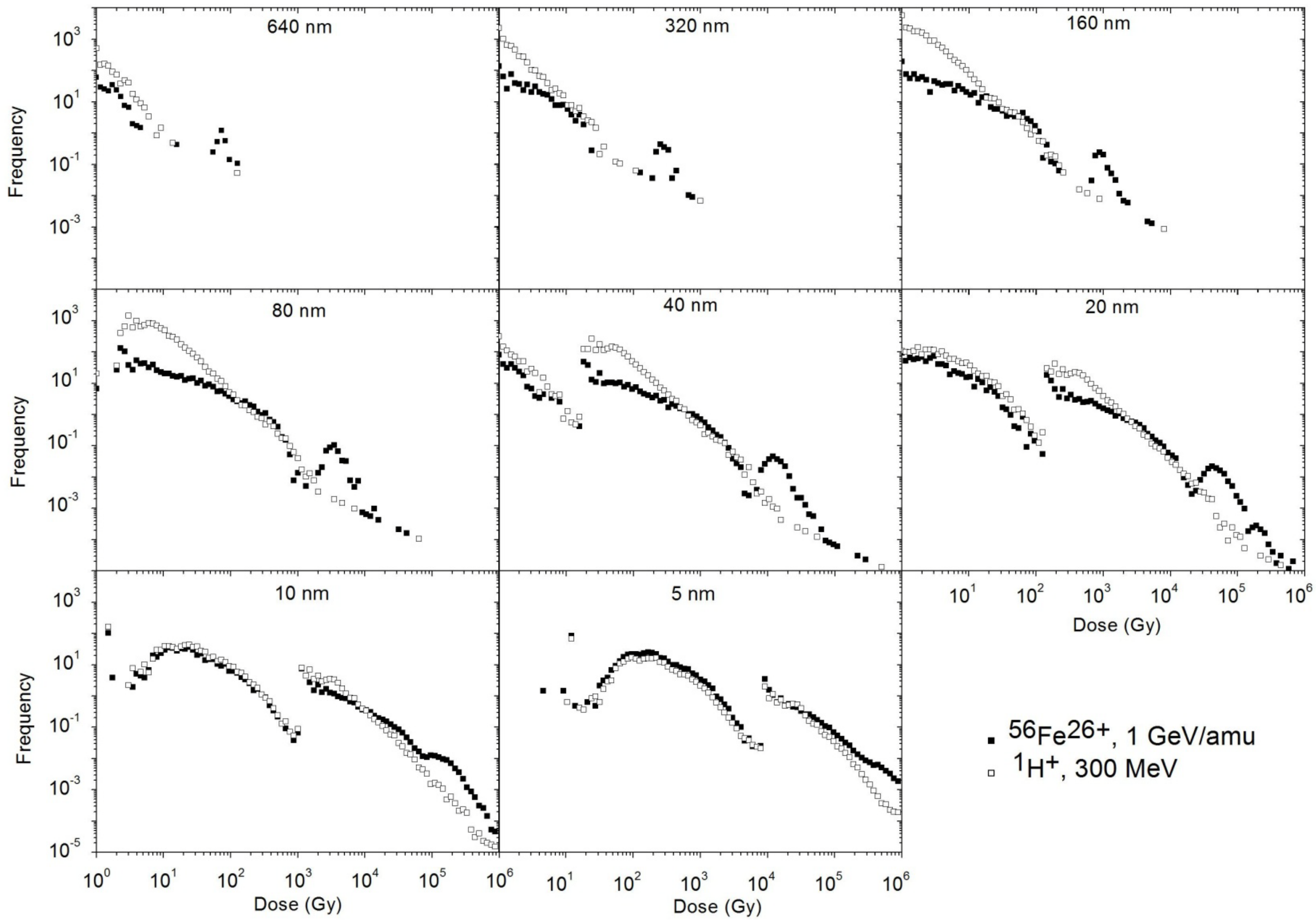
Calculation of dose in voxels



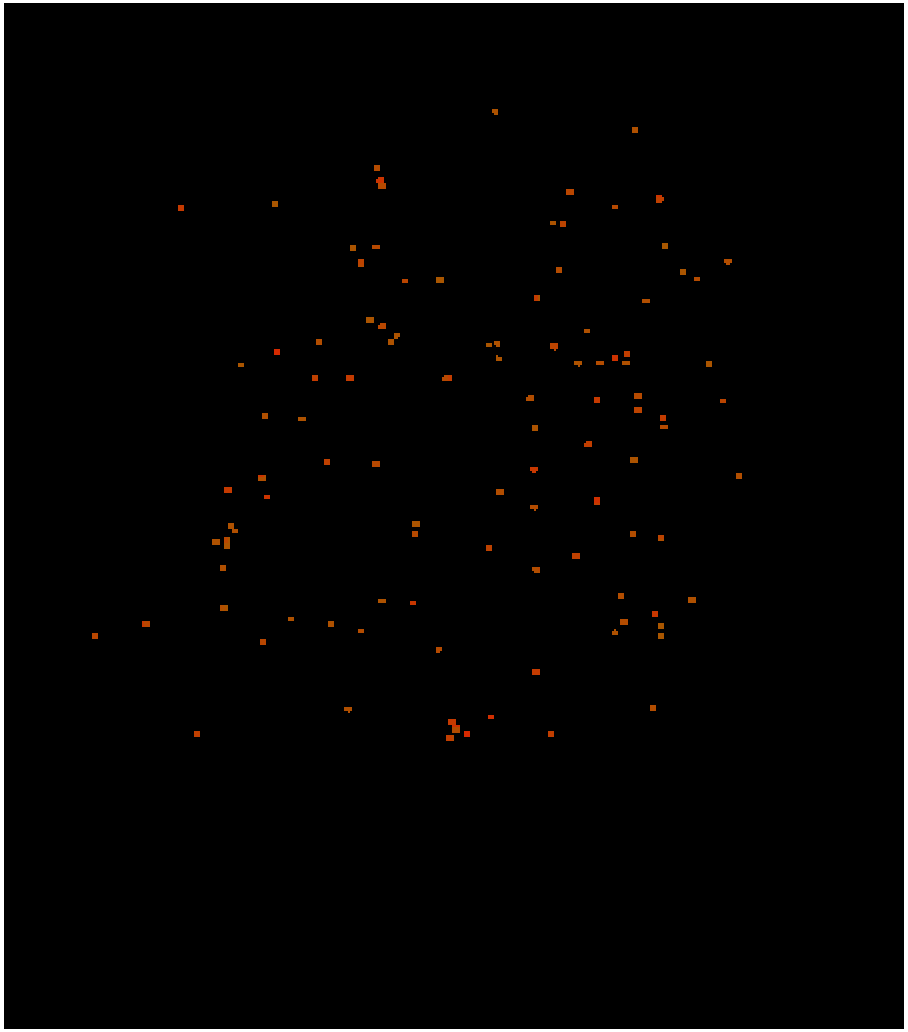
- Calculations with RITRACKS
- 450 $^{1}H^{+}$ ions, 300 MeV
- LET: ~0.3 keV/μm
- Irradiated volume: 5 μm x 5 μm x 5 μm
- Voxels: 20 nm, 40 nm, 80 nm, 160 nm, 320 nm, 640 nm, 1280 nm

Voxels size: 1280 nm

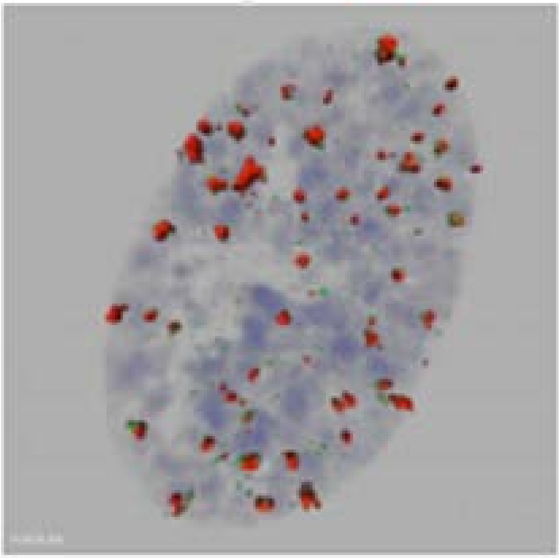
Dose distribution in voxels



DNA damage

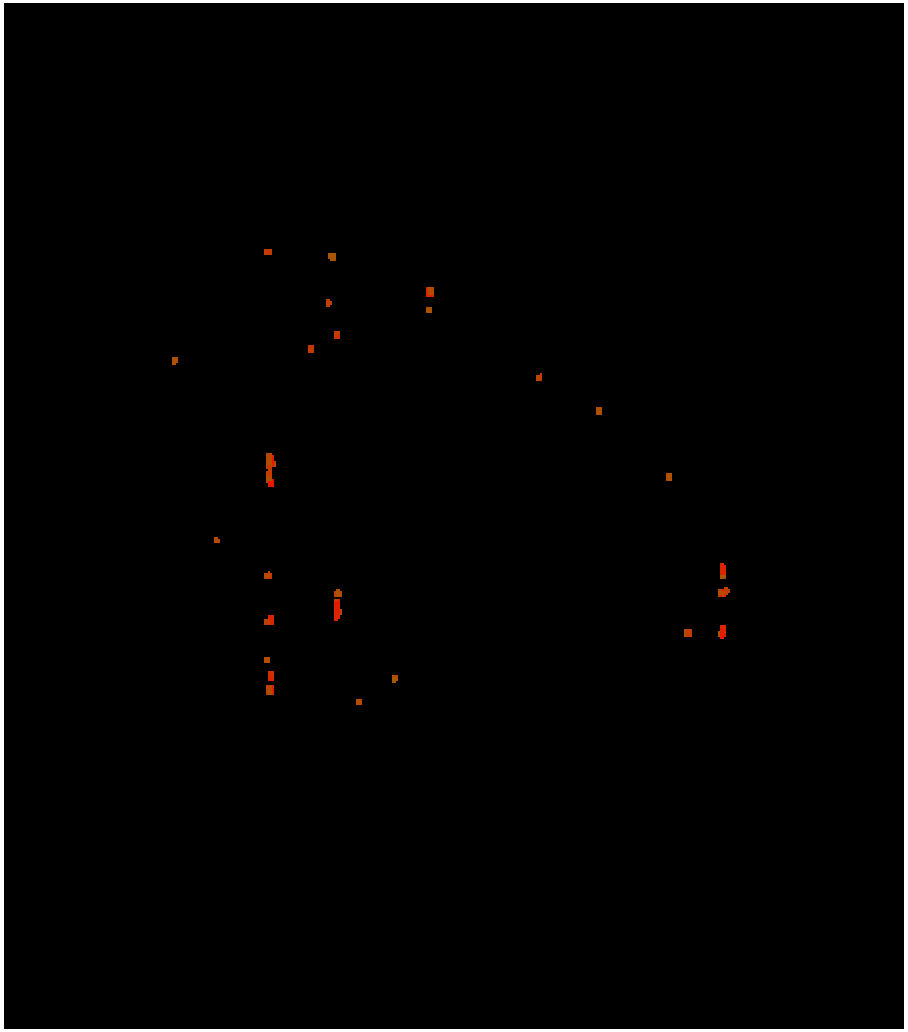


1800 x $^{1}H^{+}$, 300 MeV (1 Gy)
Dose in voxels (20 nm)
Chromosomes (RW model)
Intersection voxels
H2AX foci experiments
Threshold (2000 Gy)

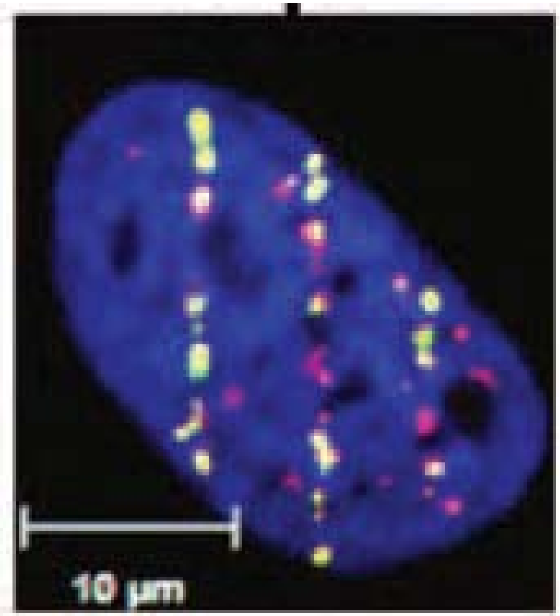


Mukherjee, B. et al. (2008), *DNA repair* **7** 1717-1730

DNA damage

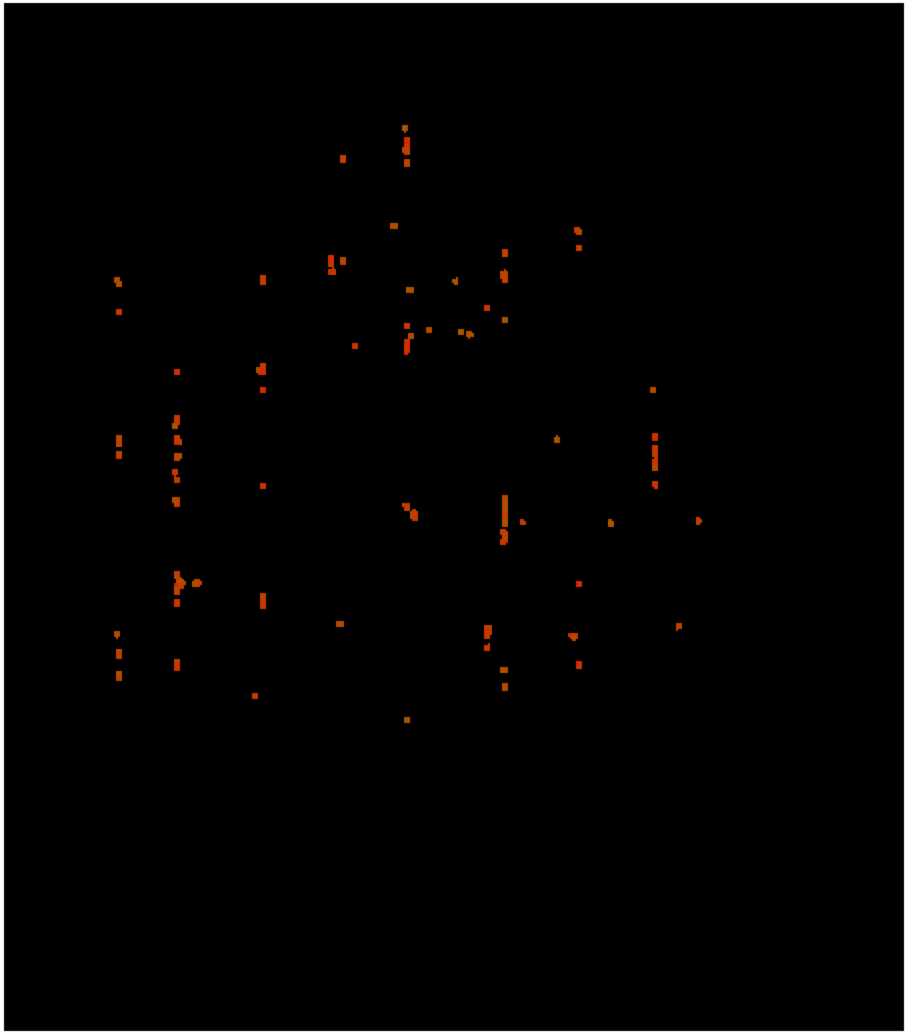


4 x $^{56}Fe^{26+}$, 1 GeV/u (1 Gy)
Dose in voxels (20 nm)
Chromosomes (RW model)
Intersection voxels
H2AX foci experiments
Threshold (2000 Gy)



Asaithamby, A. et al. (2008) *Radiat. Res.* **169**, 437-446

DNA damage



15 x $^{28}Si^{14+}$, 1 GeV/u (1 Gy)

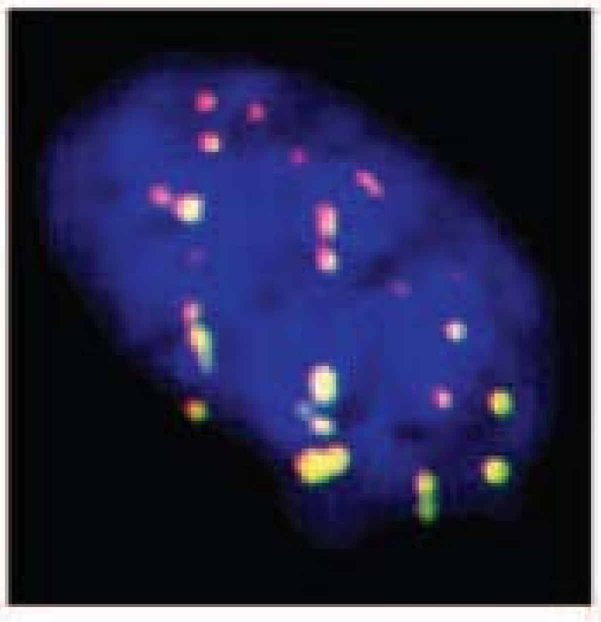
Dose in voxels (20 nm)

Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

Threshold (2000 Gy)



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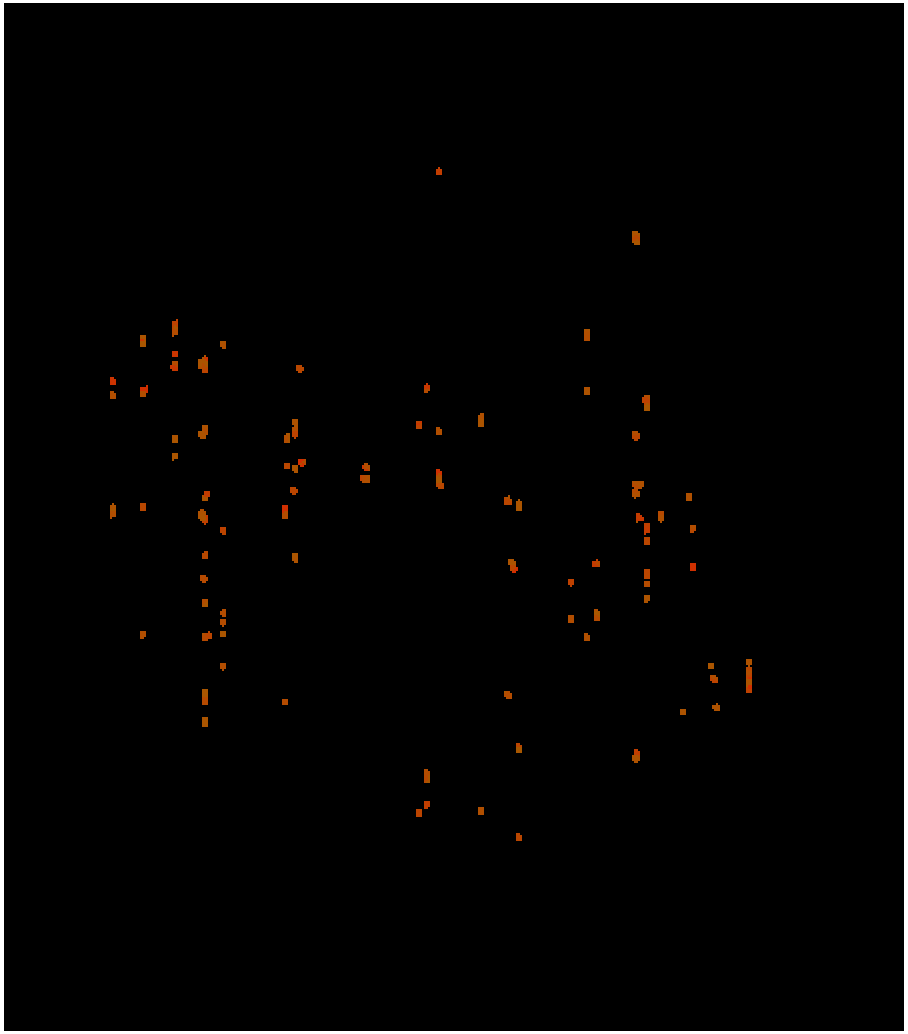
DNA damage



45 x $^{16}O^{8+}$, 1 GeV/u (1 Gy)

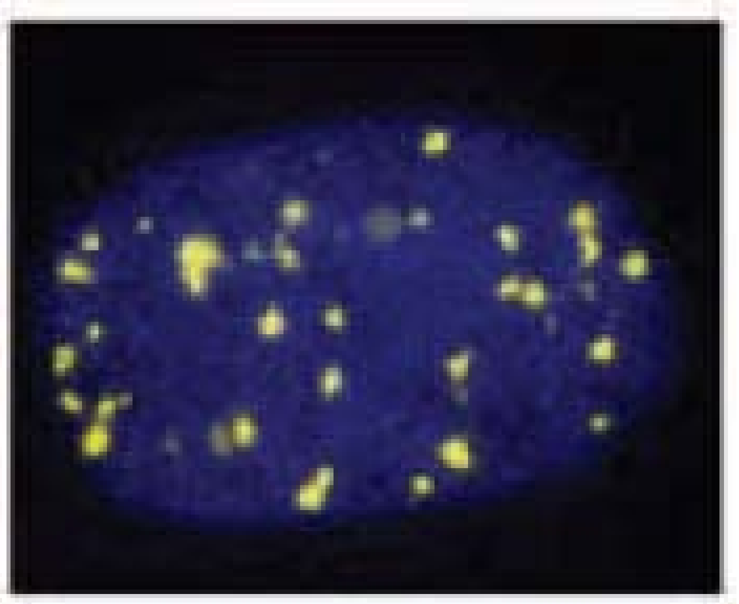
Dose in voxels (20 nm)

Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

Threshold (2000 Gy)



Asaithamby, A. et al. (2008) *Radiat. Res.* **169**, 437-446

Conclusion and perspectives

- Monte-Carlo track structure simulations can accurately simulate experimental data
  - Frequency of target hits
  - Dose per event
  - Dose per ion
  - Radial dose
- The dose is uniform in micrometers sized voxels; at the nanometer scale, the difference in energy deposition between high and low-LET radiations appears.
- The calculated 3D distribution of dose voxels, combined with chromosomes simulated by random walk is very similar to the distribution of DSB observed with γ-H2AX experiments. This is further evidenced by applying a visualization threshold on dose.

Conclusion and perspectives

- Since high-dose voxels are found mainly in high-LET radiation simulations and DSBs created by high-LET ions are more difficult to repair, we may hypothesis that complex DSB may be created in areas corresponding to high-dose voxels.
- Future work:
  - Parallelize RITRACKS (multi CPU or GPU)
  - Calculations of chromosome aberrations using the 3D dose distribution and chromosomes simulations
  - Include chemistry

Acknowledgments

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