Charged Particle Track Simulation in Cells: A Tool for Testing Radiation Action Working Hypotheses

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Overview

Track structure simulation

- Cross sections
- Tracks

Target modelling

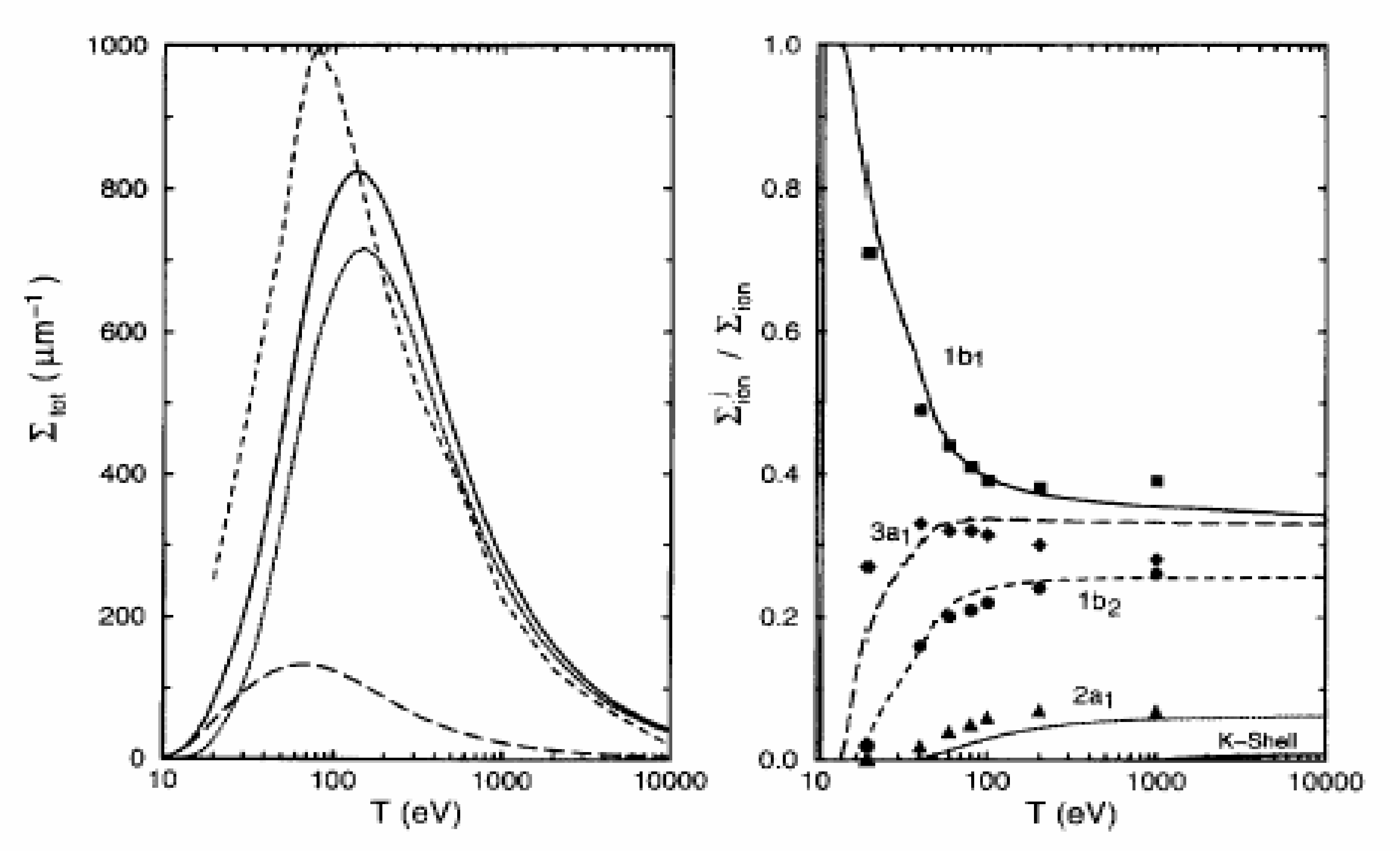
- DNA
- Structures in cells and tissues

Simulations of biological end points

- DSB induction
- DSB fragment distributions
- $HPRT^-$ mutations
- Multiple DNA damage

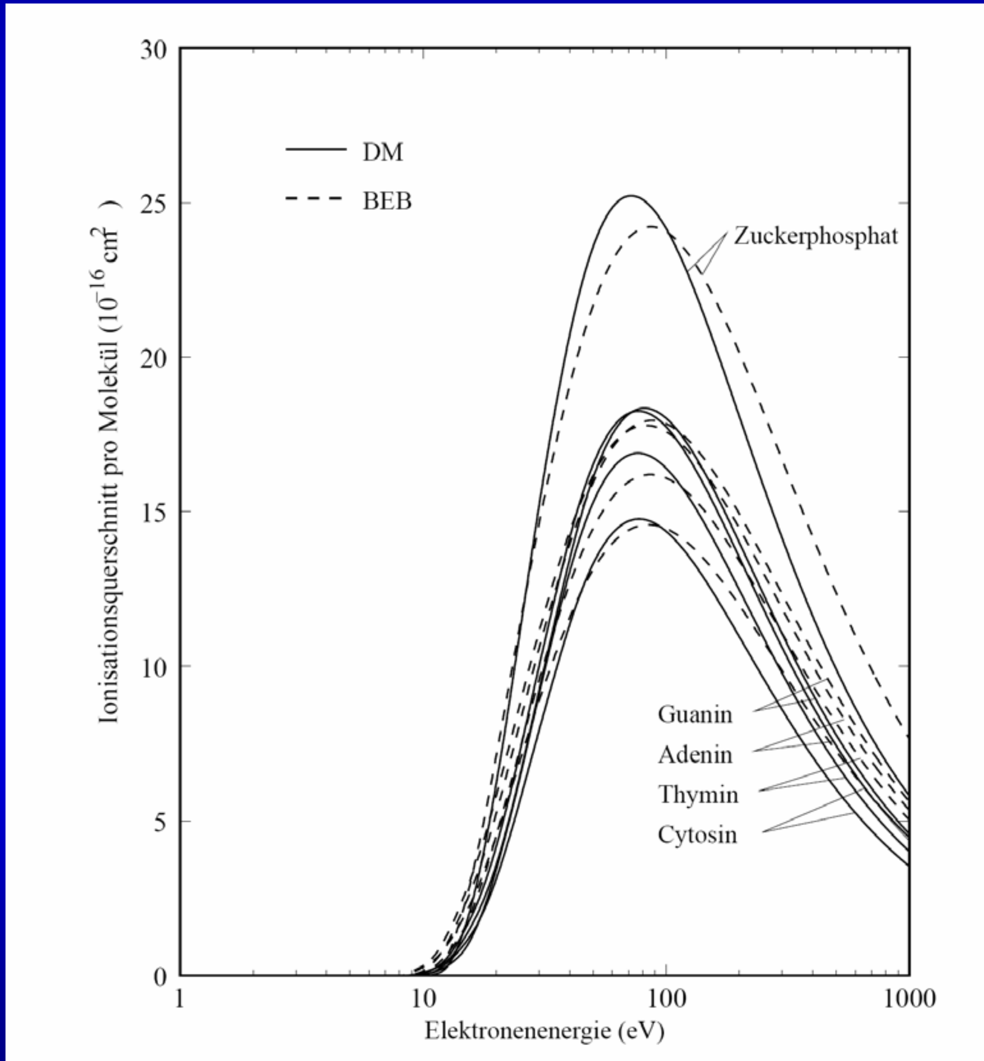
Inelastic scattering cross sections of electrons in liquid water

Dingfelder et al., Rad. Phys. Chem. 53, 1-18 (1998)

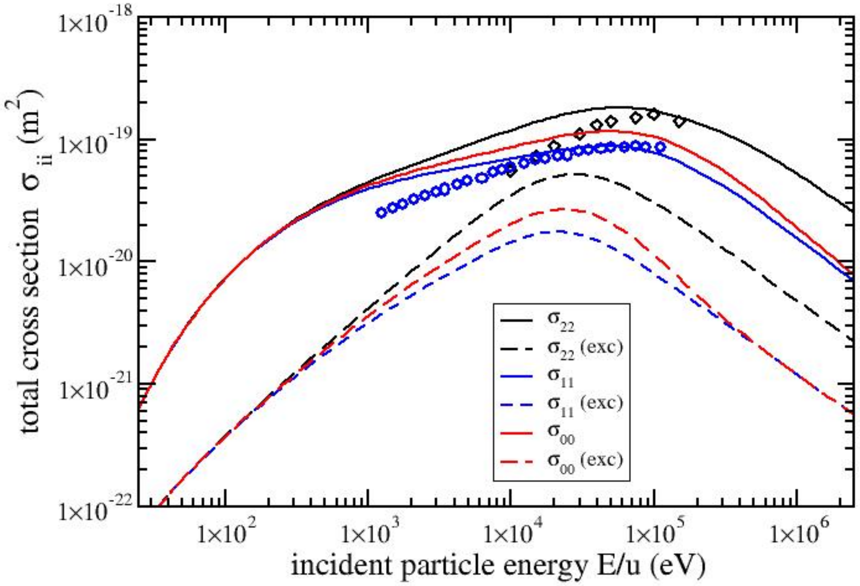


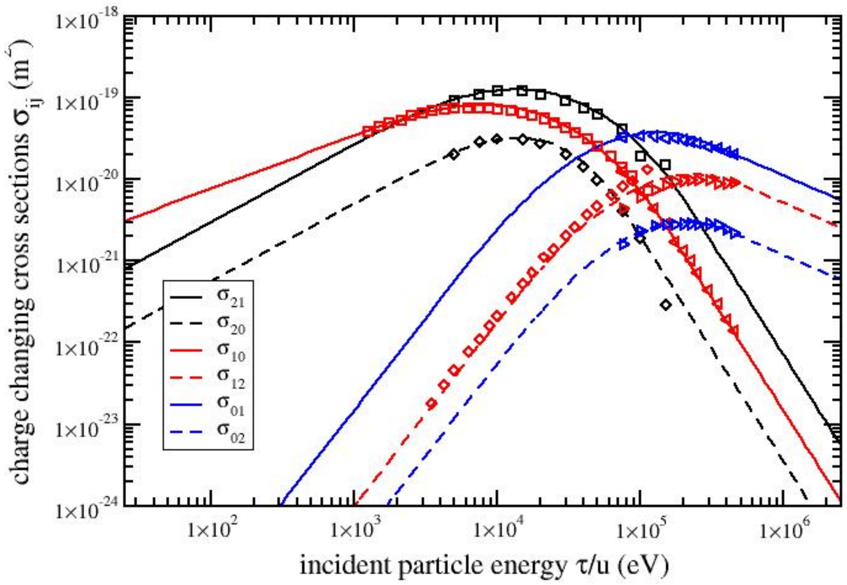
Ionisation cross section of DNA constituents

Bernhardt et al., Int. J. Mass Spectr. 223-224, 599-611 (2003)



Cross sections for ionisations, excitations and charge changing processes of He^{++}, He^{+} and He^{o}

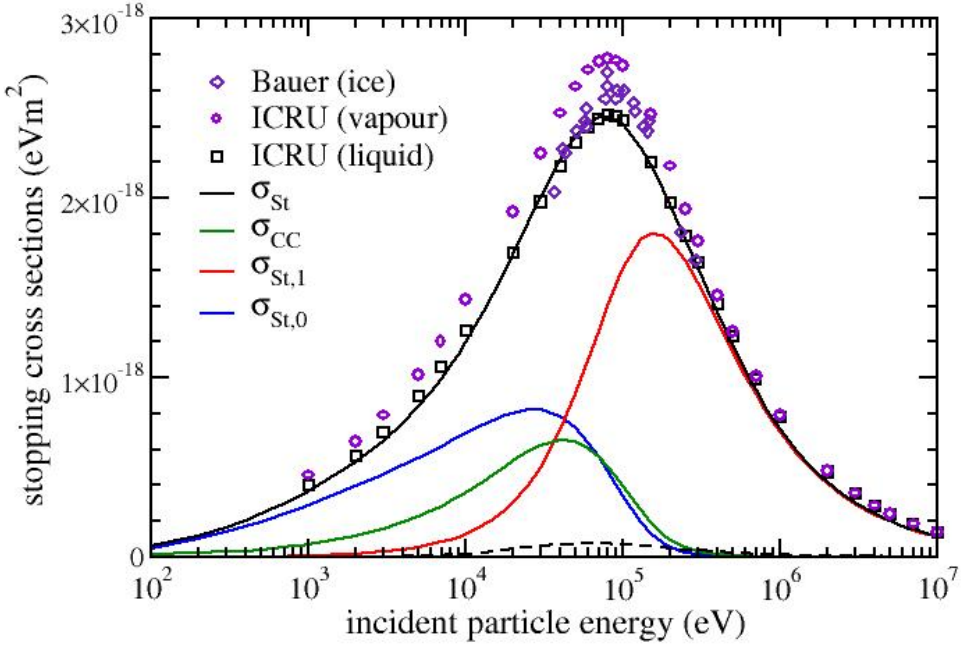


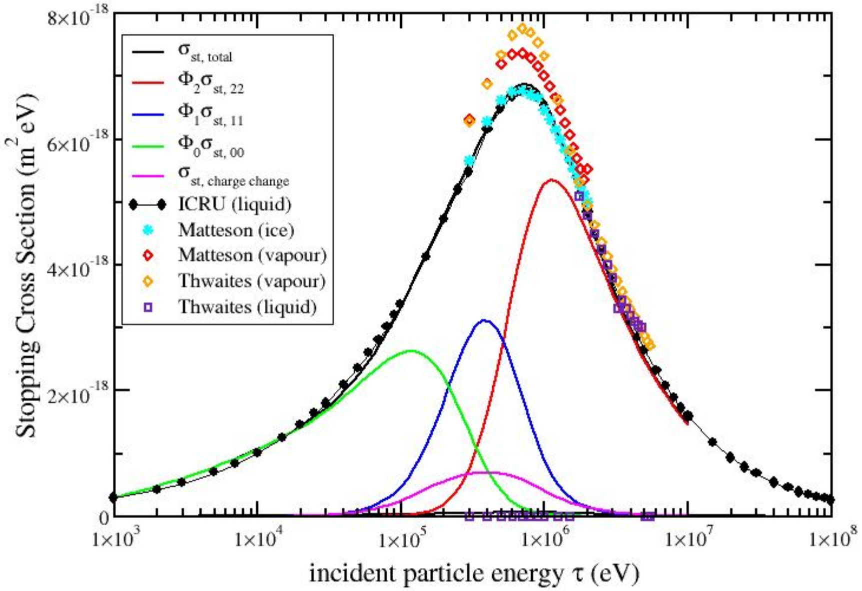


Stopping cross section for H and He

Dingfelder et al., Rad. Phys. Chem. 59, 255-275 (2000)

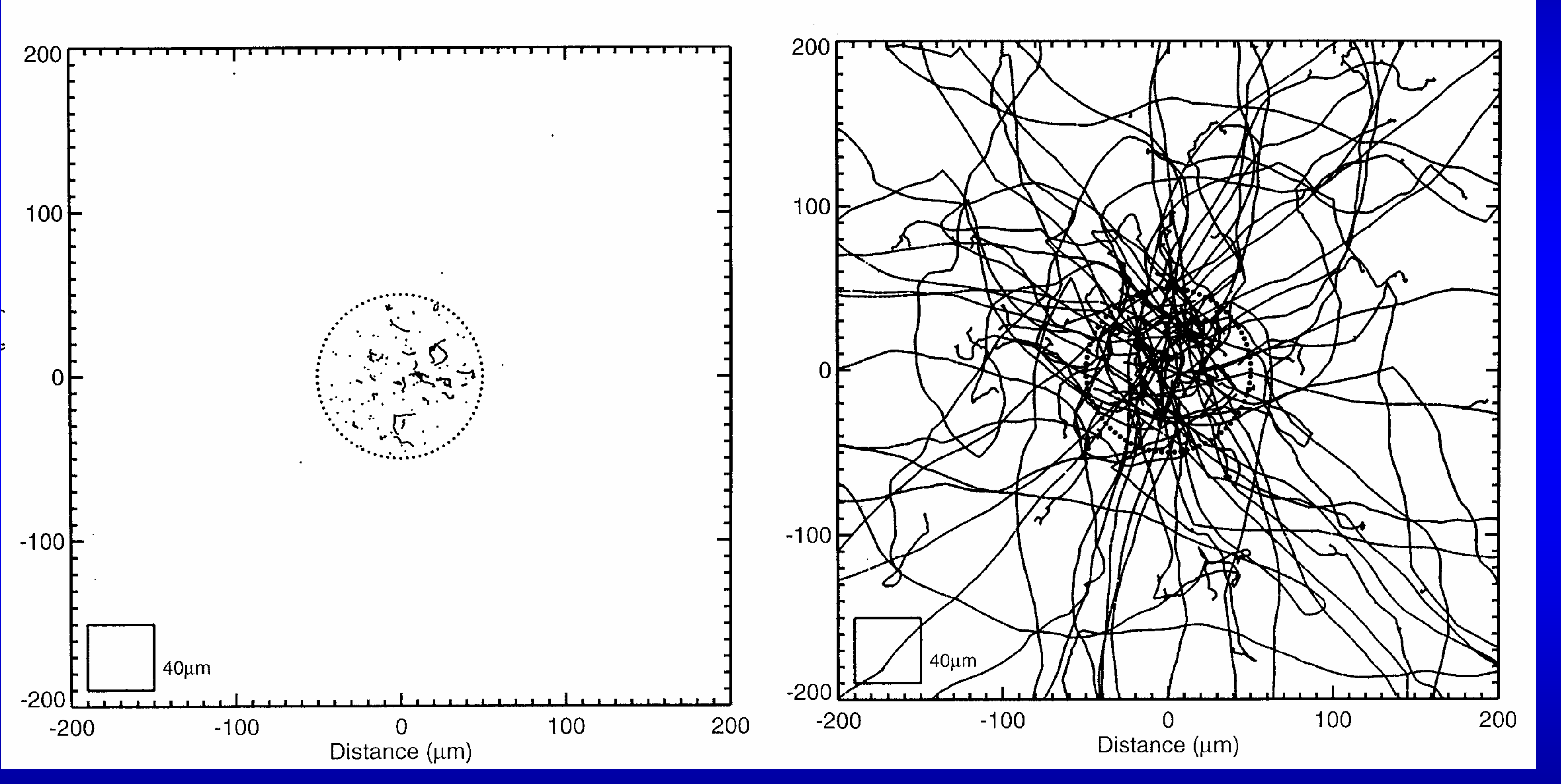
Friedland et al, Rad. Phys. Chem. accepted (2004)



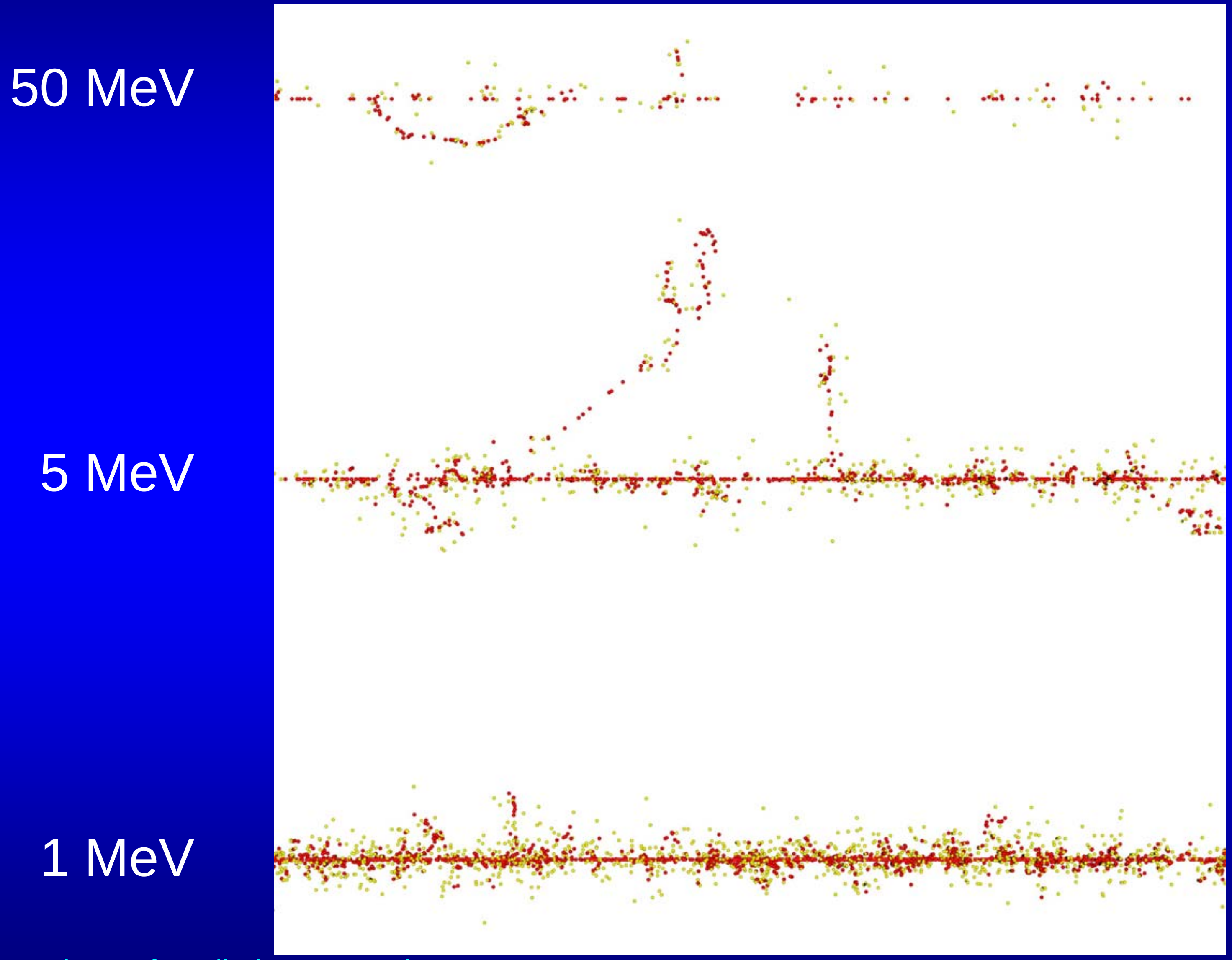


Tracks from I-125 and I-131 decays

Li et al., Radiat Res. 156, 419-429 (2001)



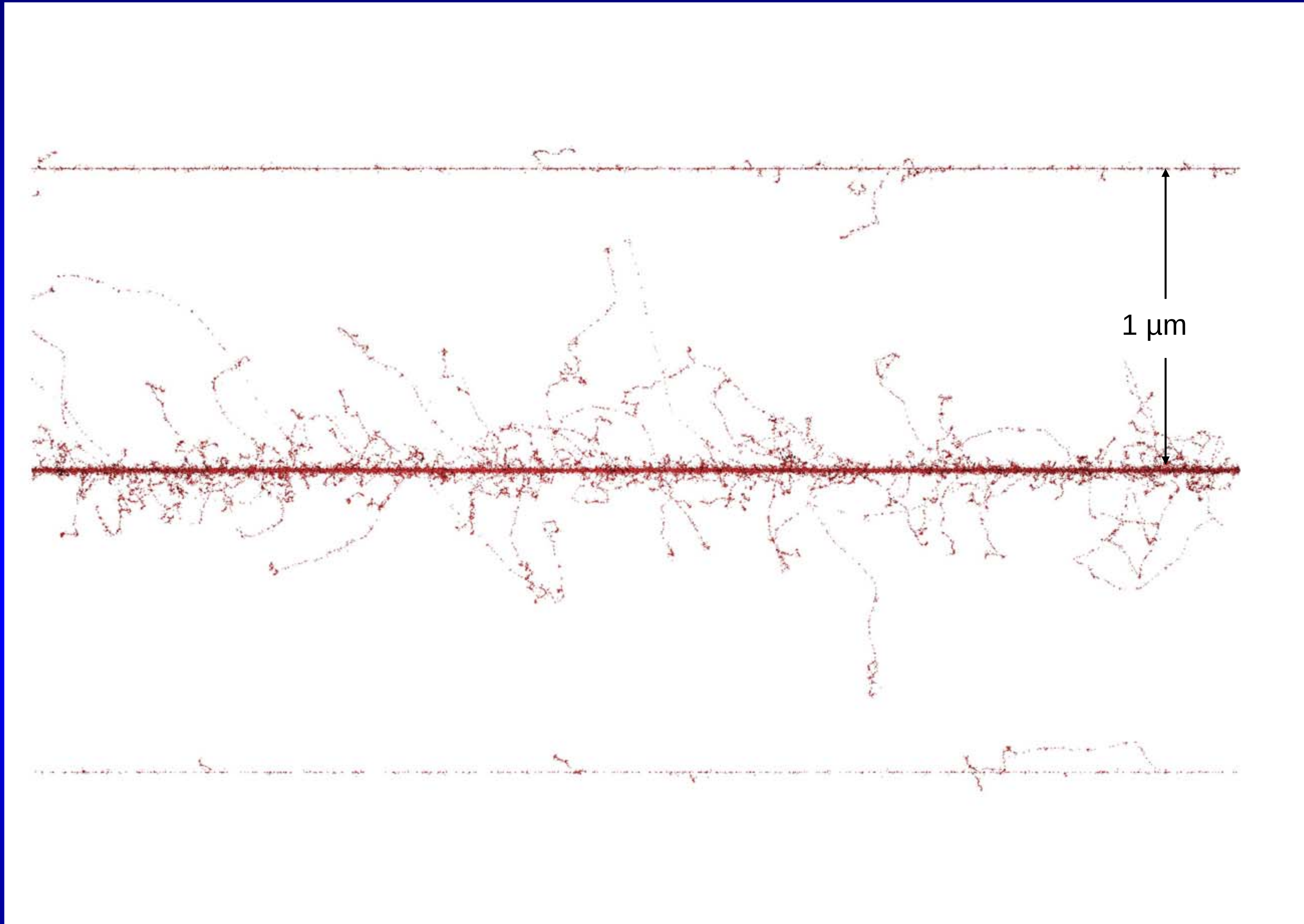
Tracks of He ions



^{4}He
25 MeV

^{16}O
40 MeV

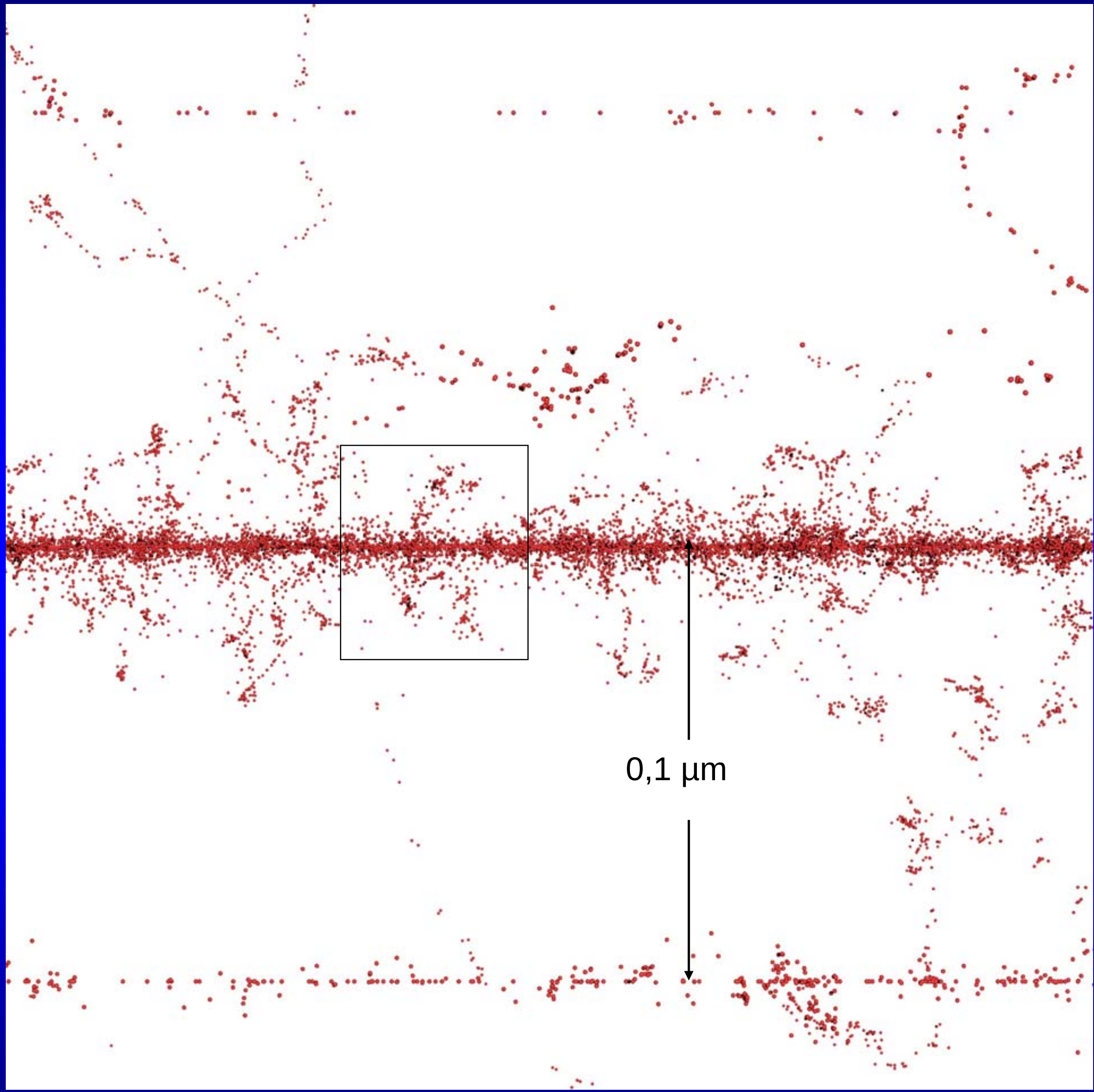
6 MeV
p



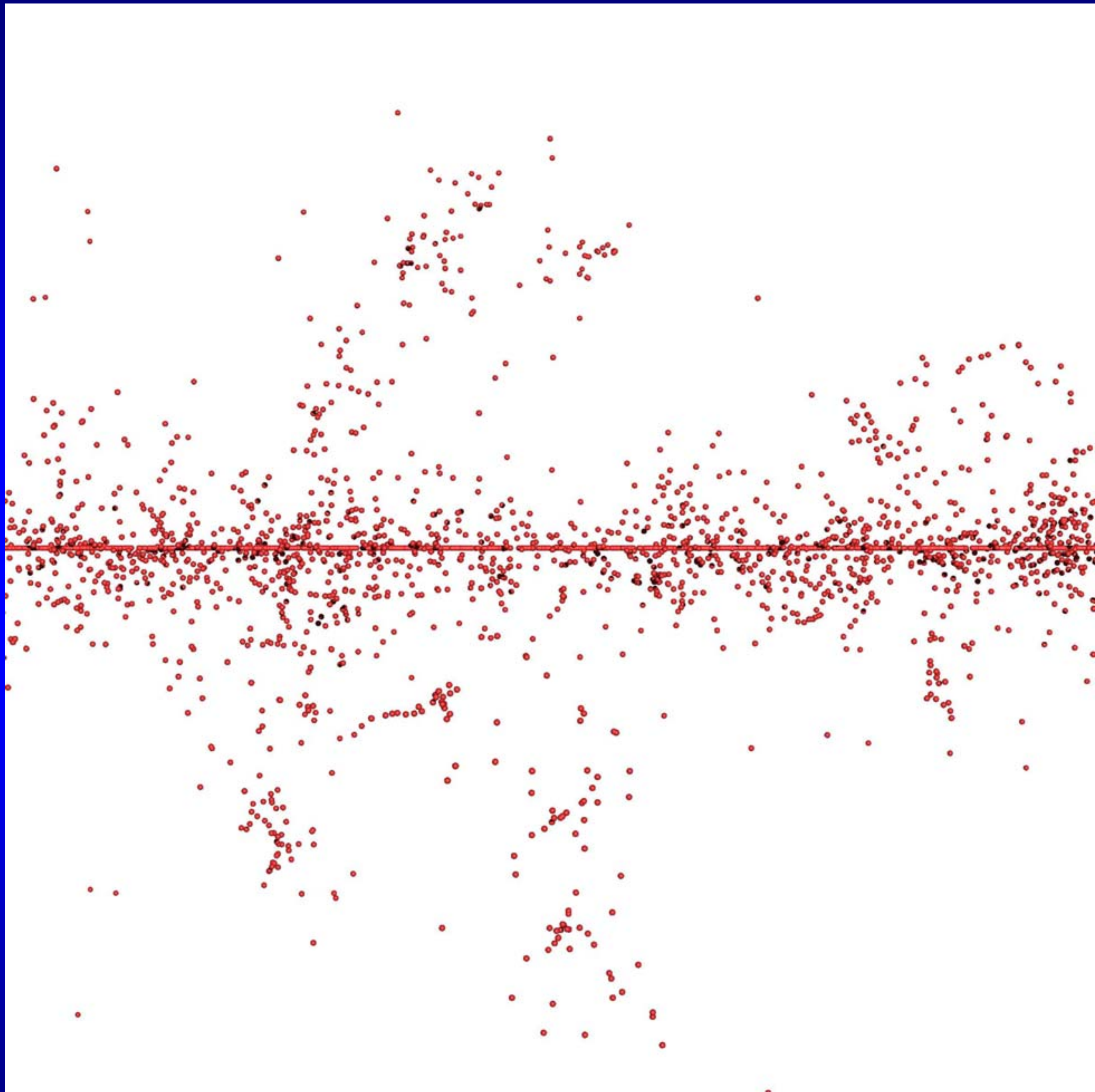
6 MeV p

40 MeV ^{16}O

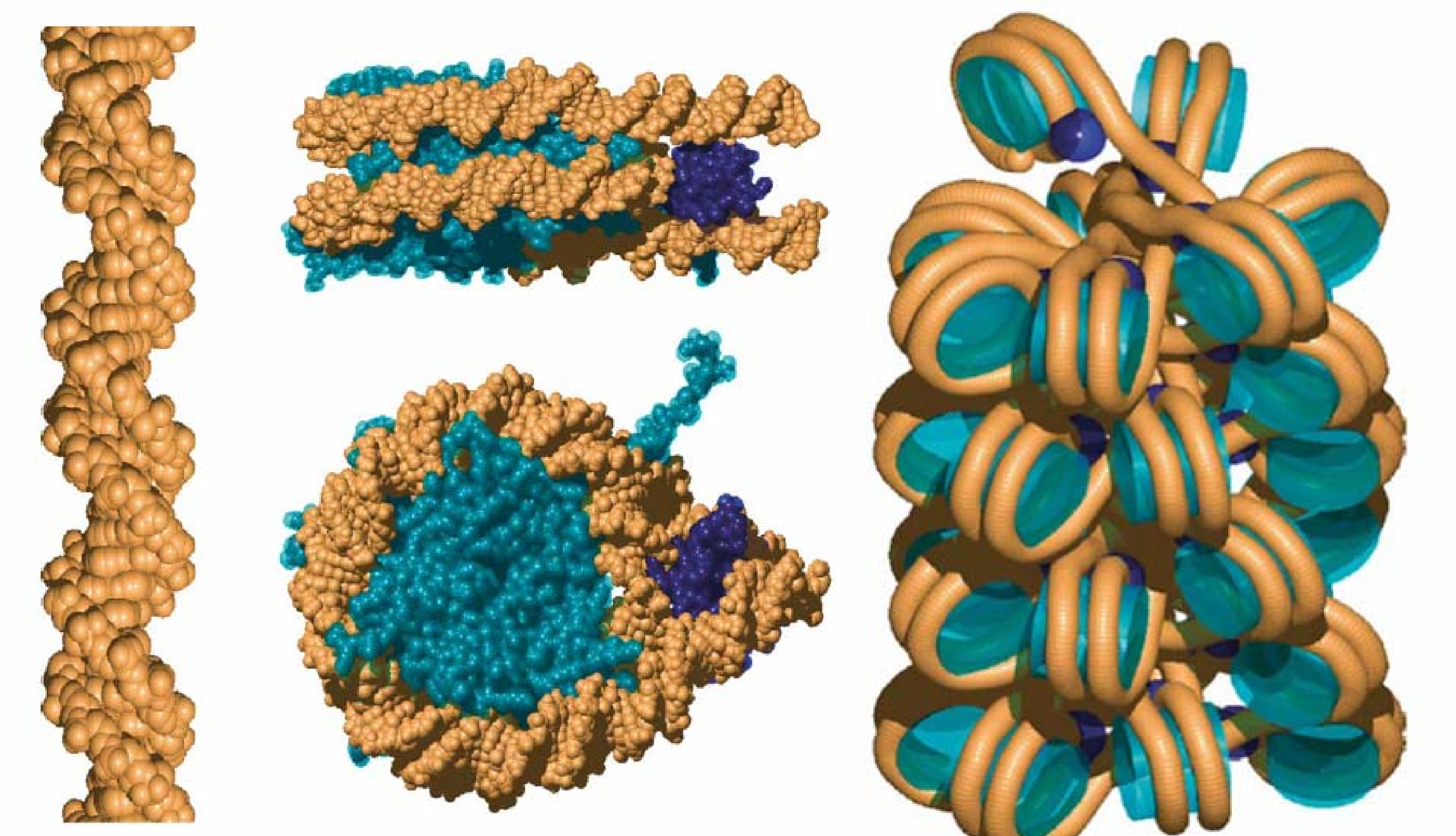
25 MeV ^{4}He



40 MeV ^{16}O



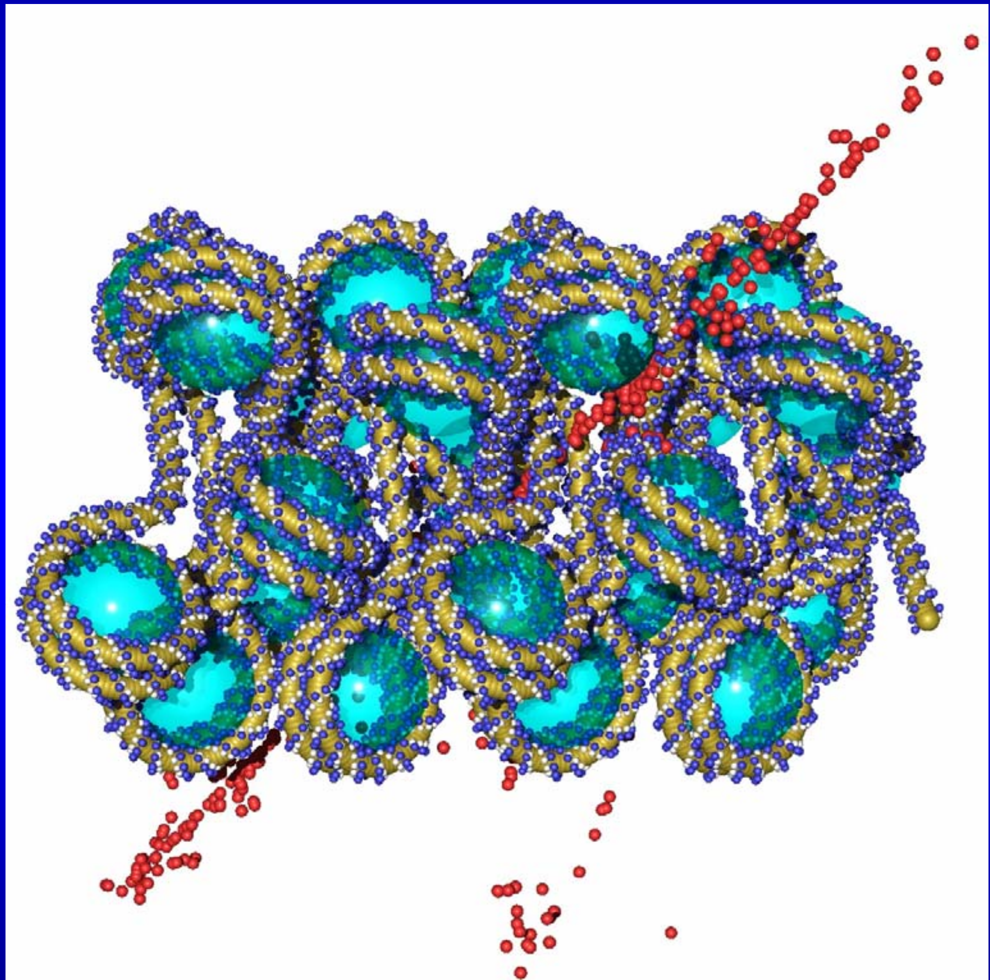
Linear DNA - Nucleosome - Chromatin fiber

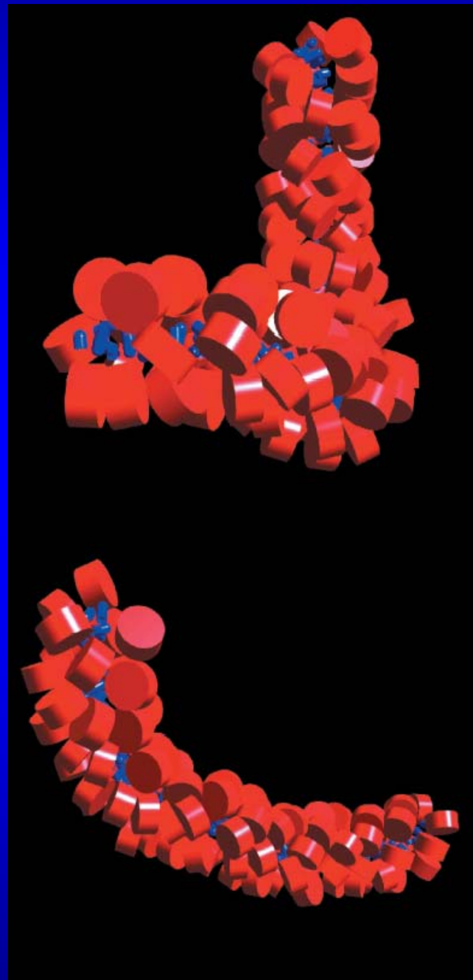


(a) linear DNA

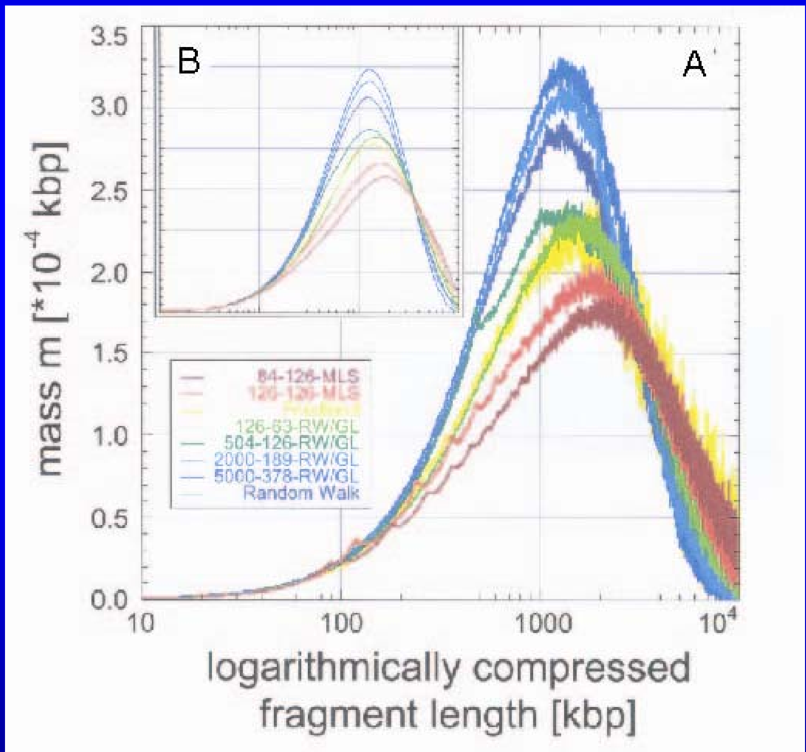
(b) nucleosome core particle

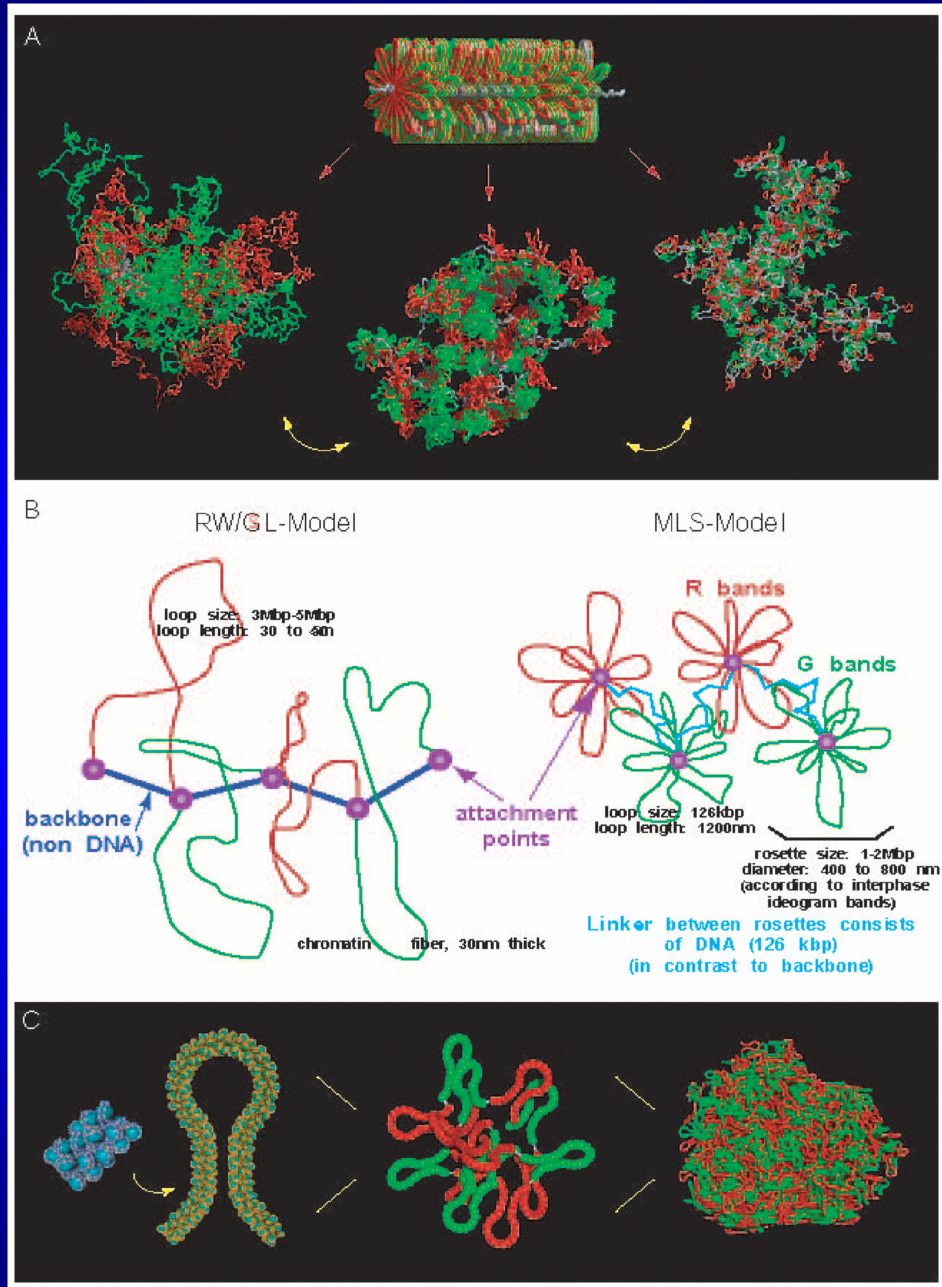
Simulated stochastic crossed-linker chromatin fibers (GSF and DKFZ)



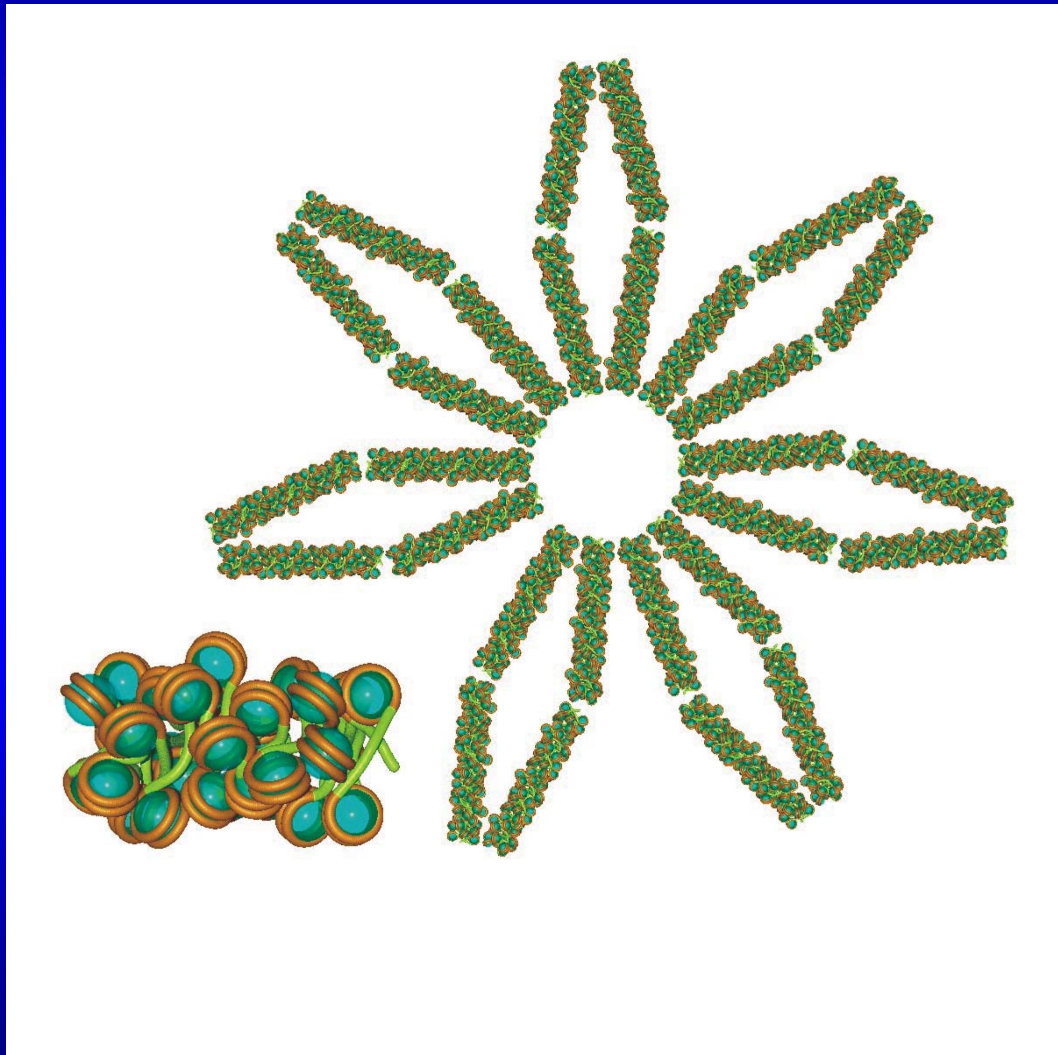


Models of Chromosomes by KIP+DKFZ (A+MLS) UCB (RW/GL) GSF (C)

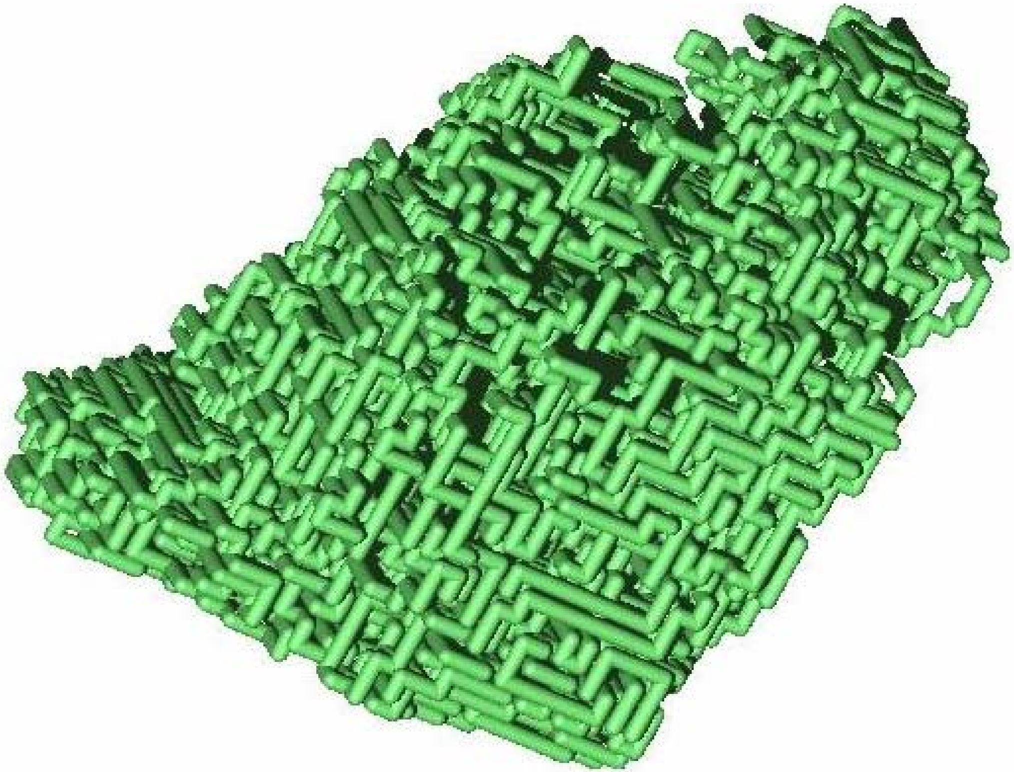




Model of 0.5 Mbp chromatin domain

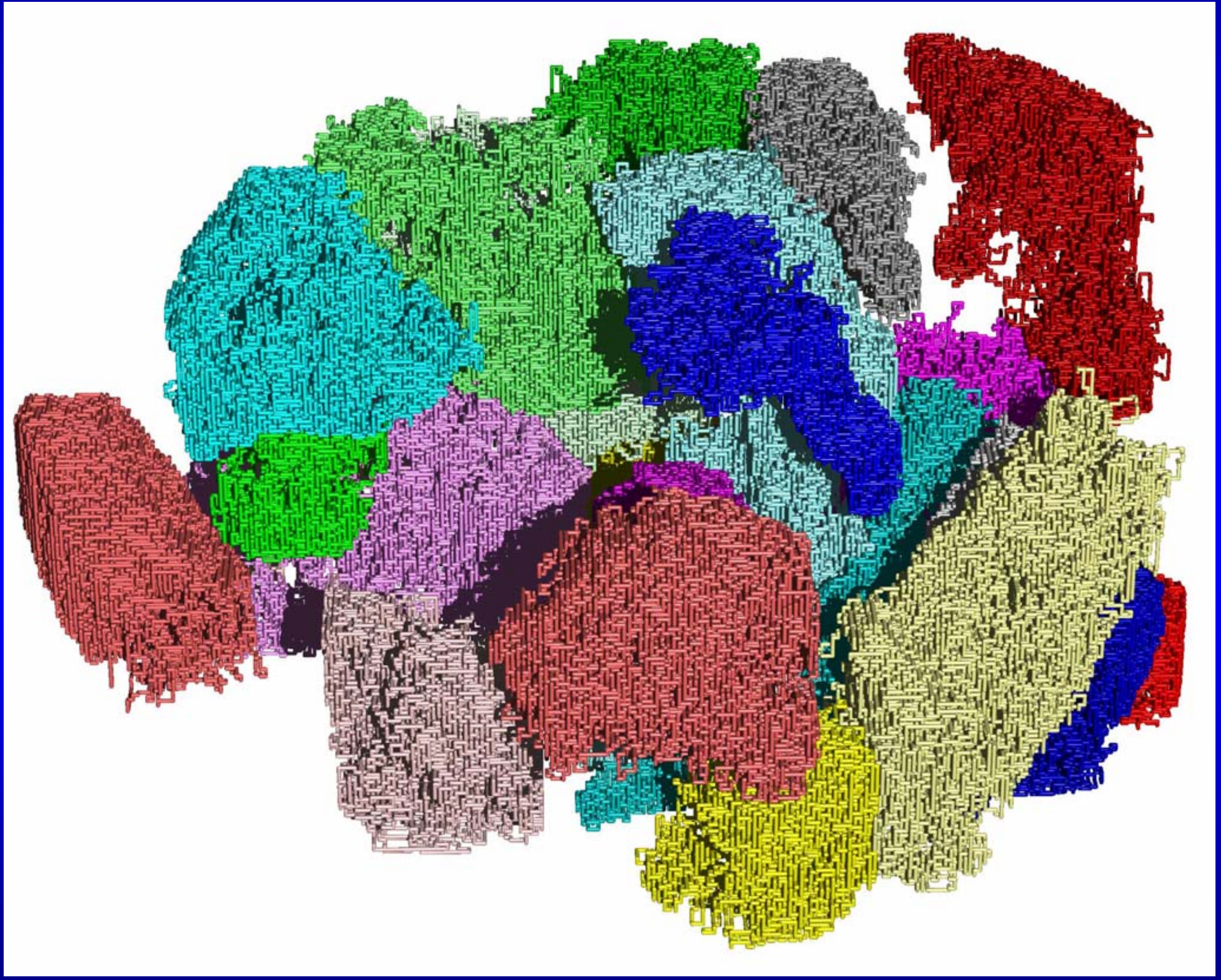


Chromatin fiber on voxel grid



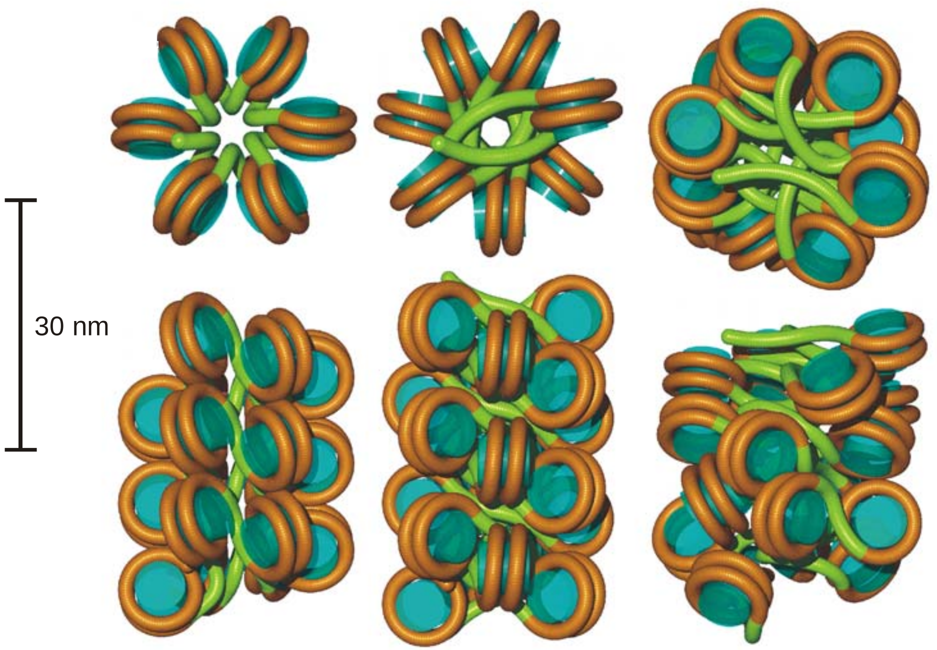
DNA target model: Human fibroblast cell

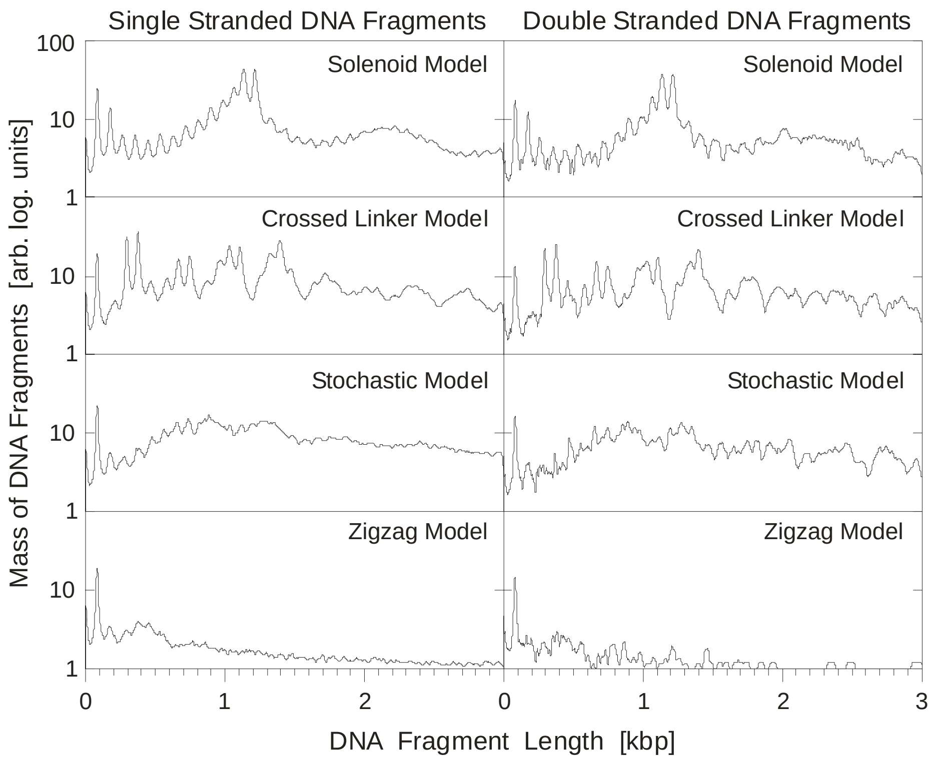
23 out of 46 human chromosomes in cylindrical nucleus



Models of chromatin fiber structures

Friedland et al., Radiat. Res. 150, 170-182 (1998)

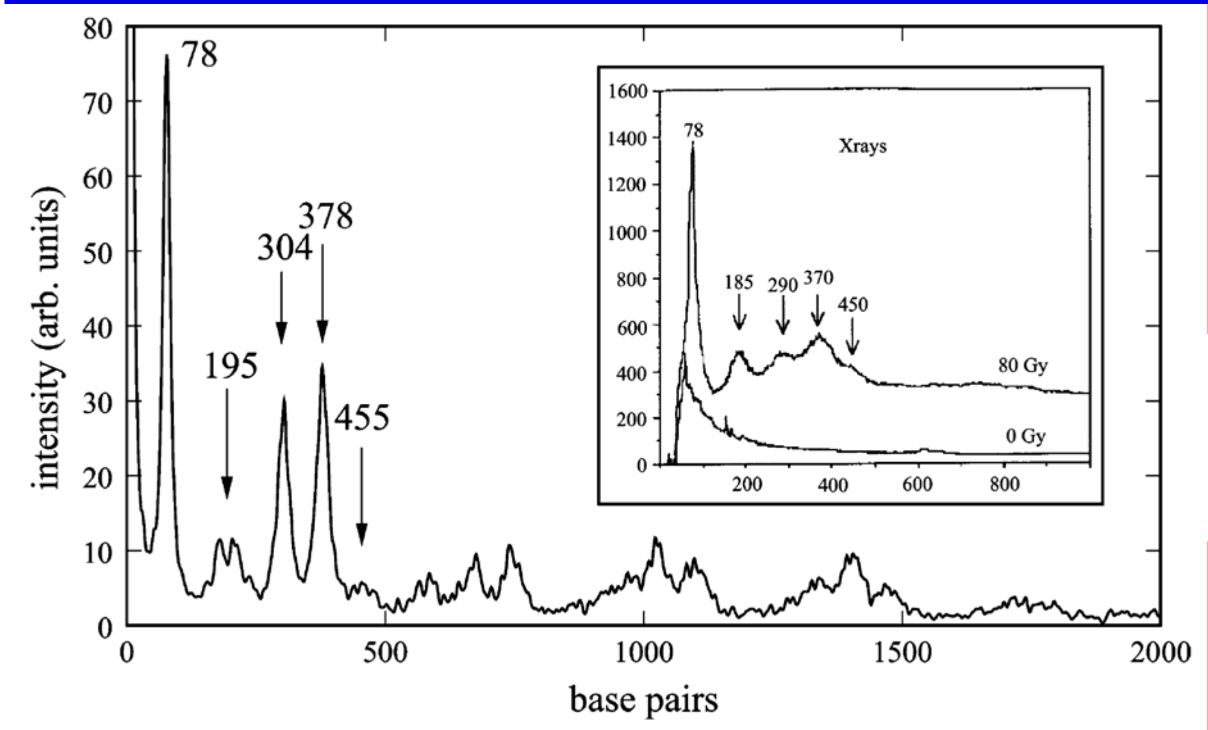


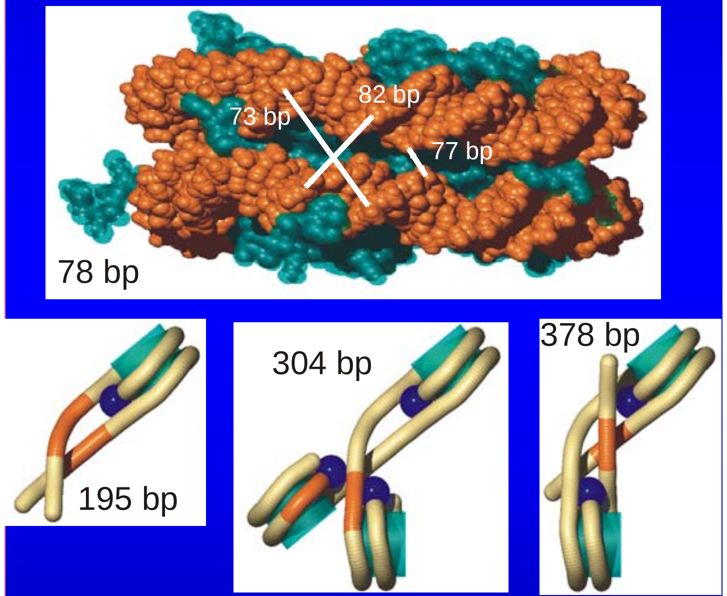


Size distribution of small DNA fragments

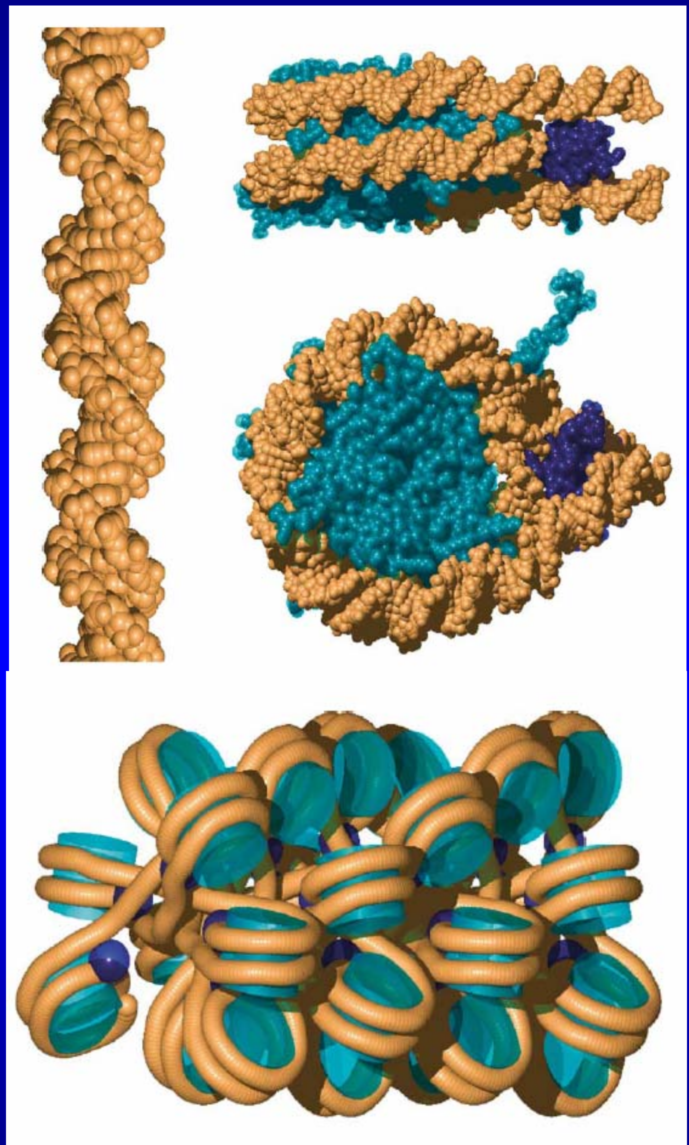
Bernhardt et al., Int. J. Mass Spectr. 223-224, 579-597 (2003)

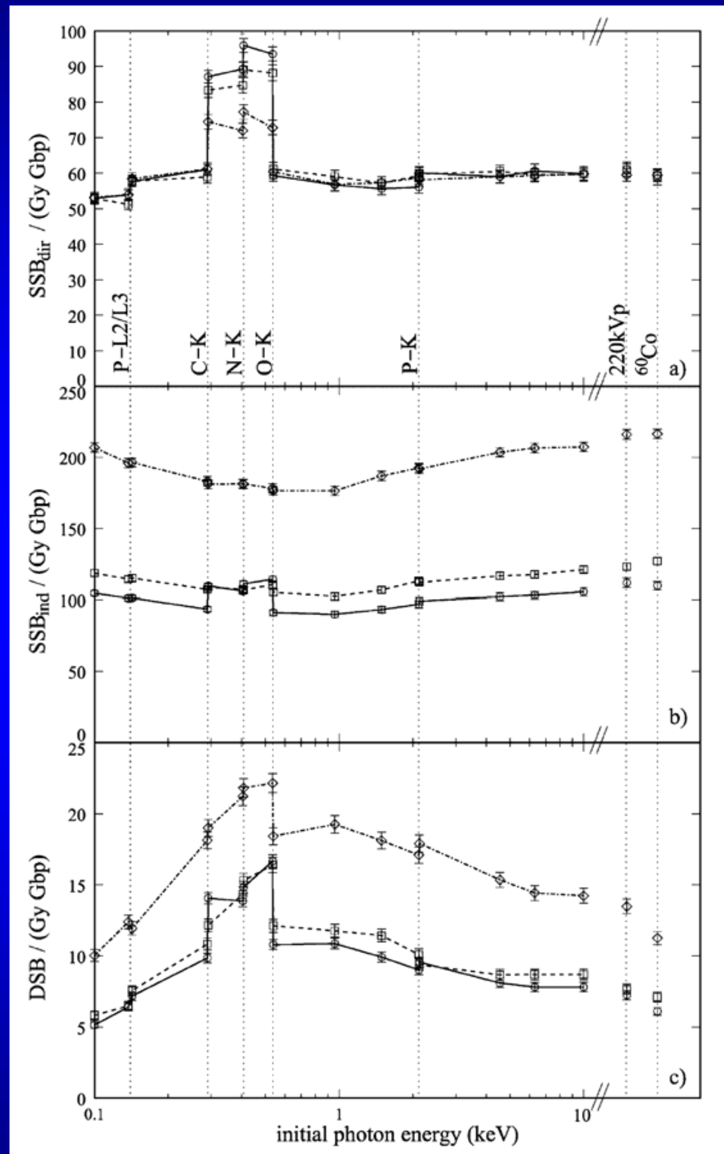
Exp.: Rydberg et al., J. Mol. Biol. 284, 71-84 (1998)



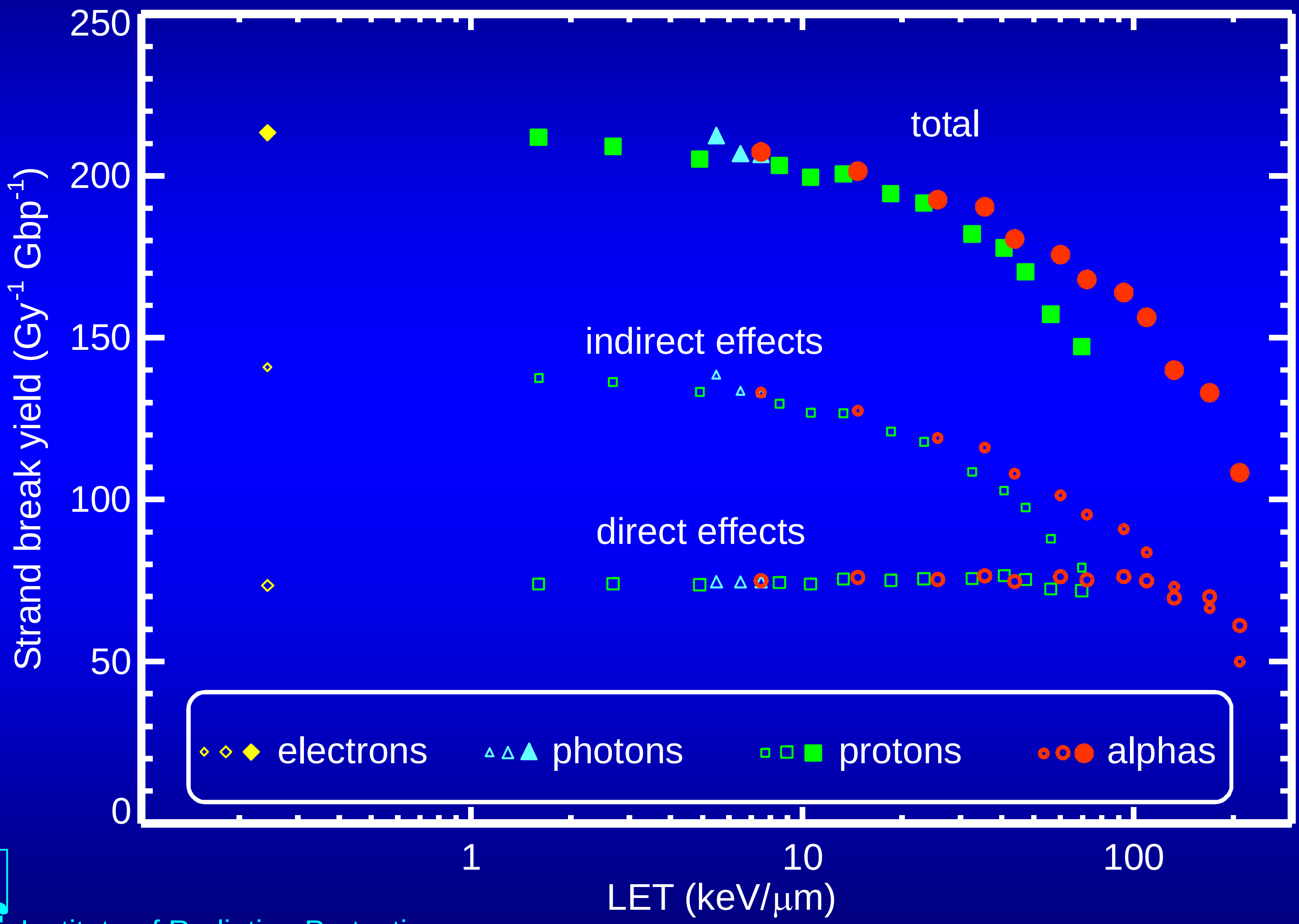


SSB and DSB yield for different DNA target models

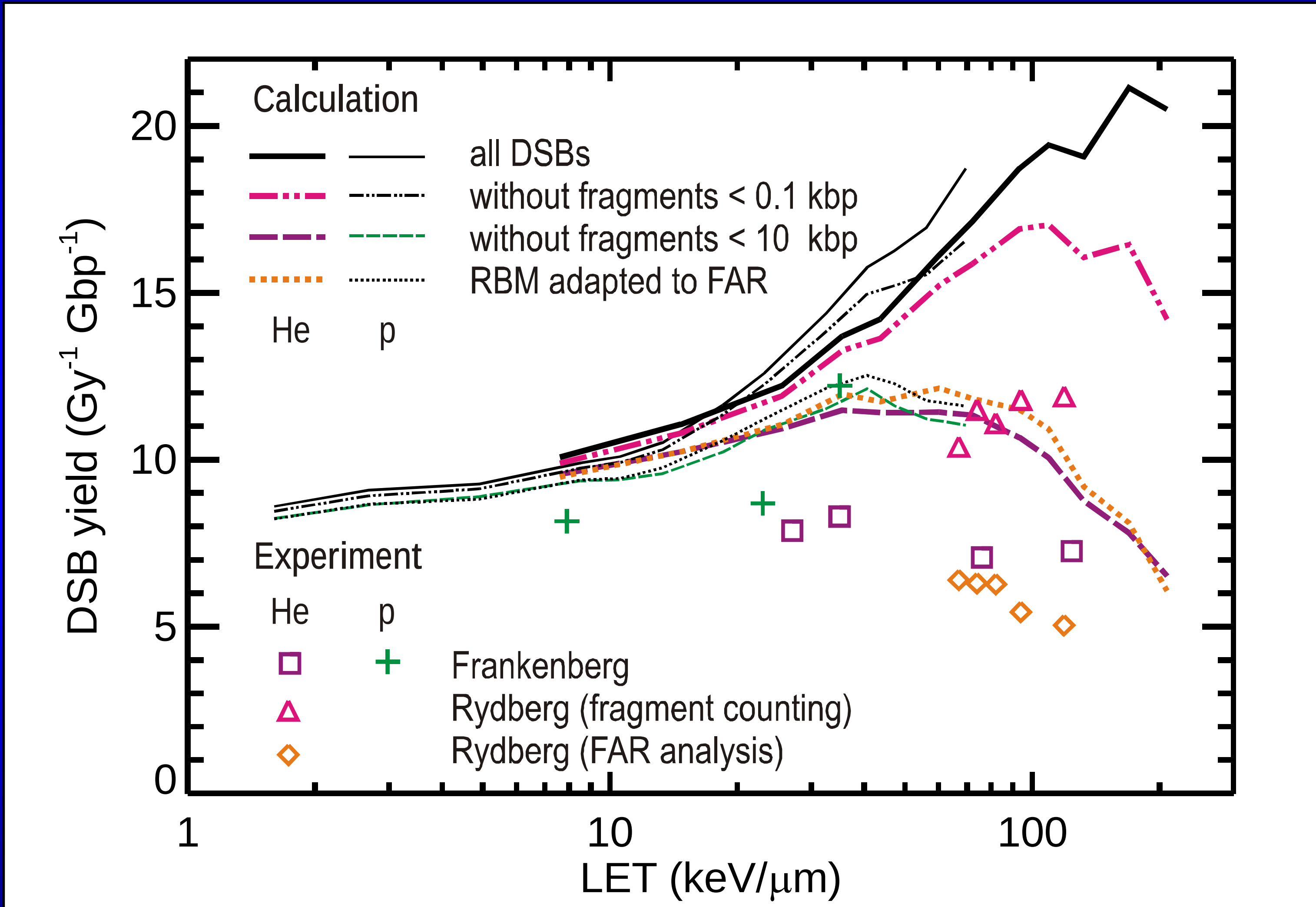




Induction of DNA strand breaks

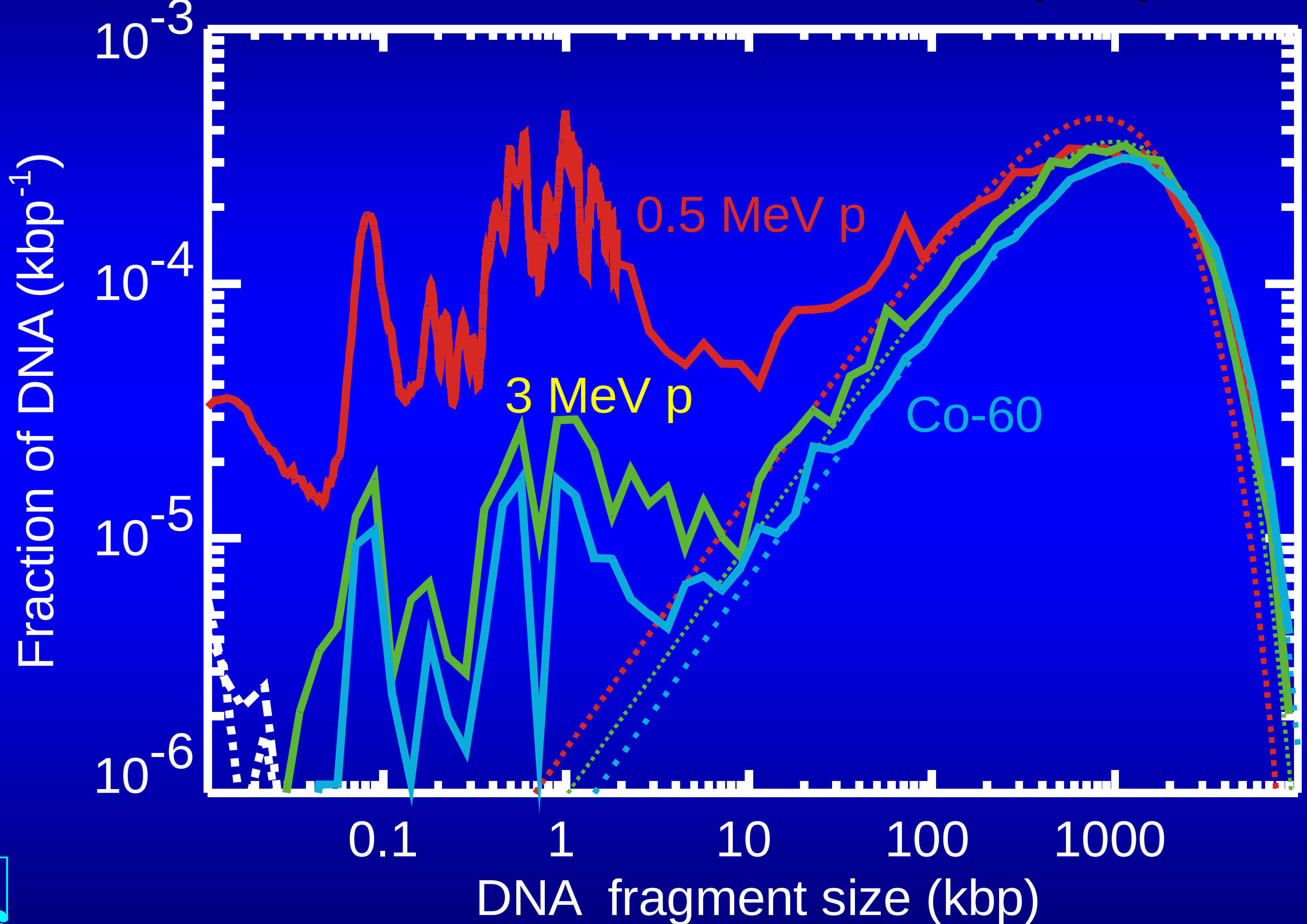


DSB induction from p and He ion irradiation

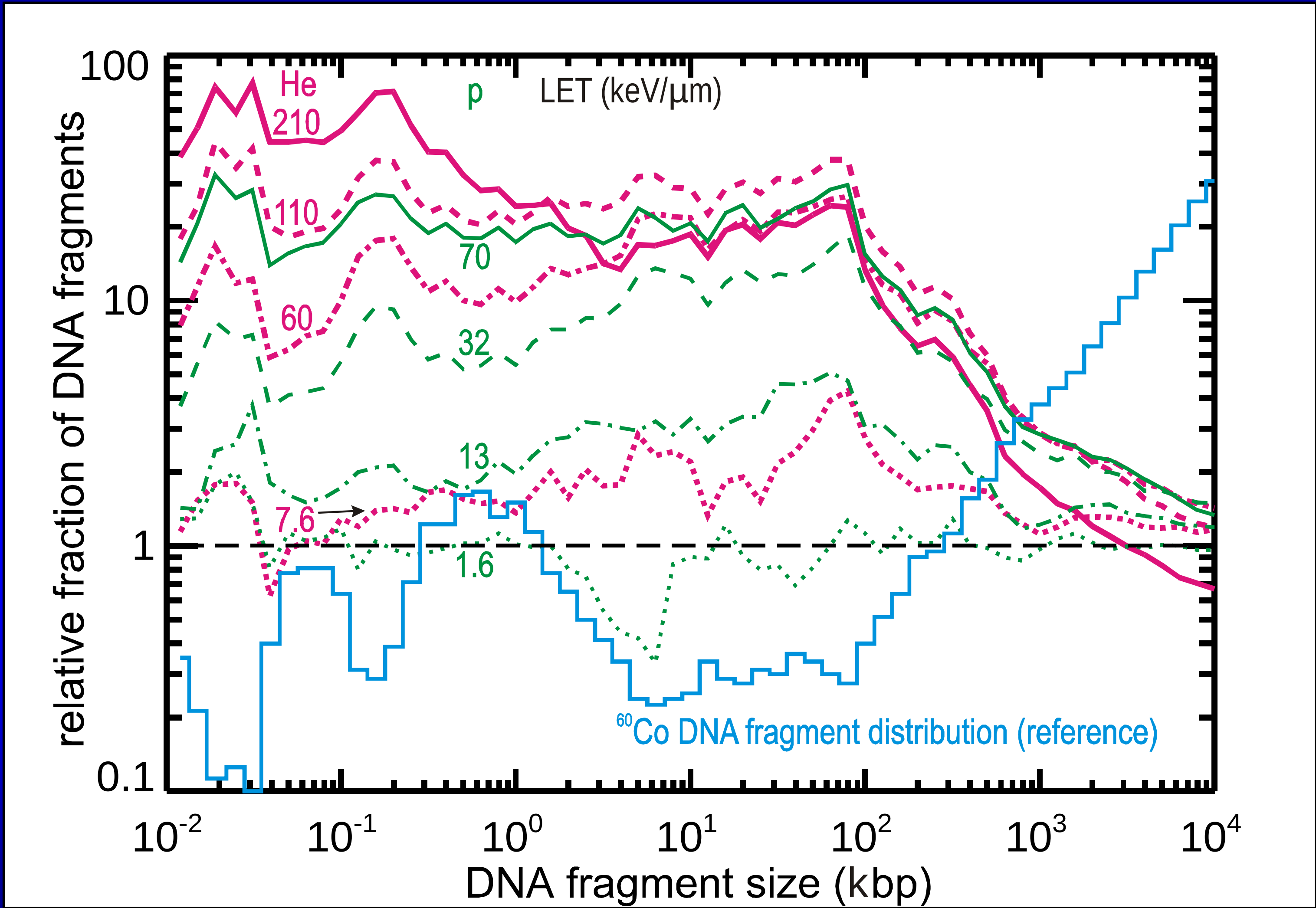


DNA Fragments: Fraction of DNA

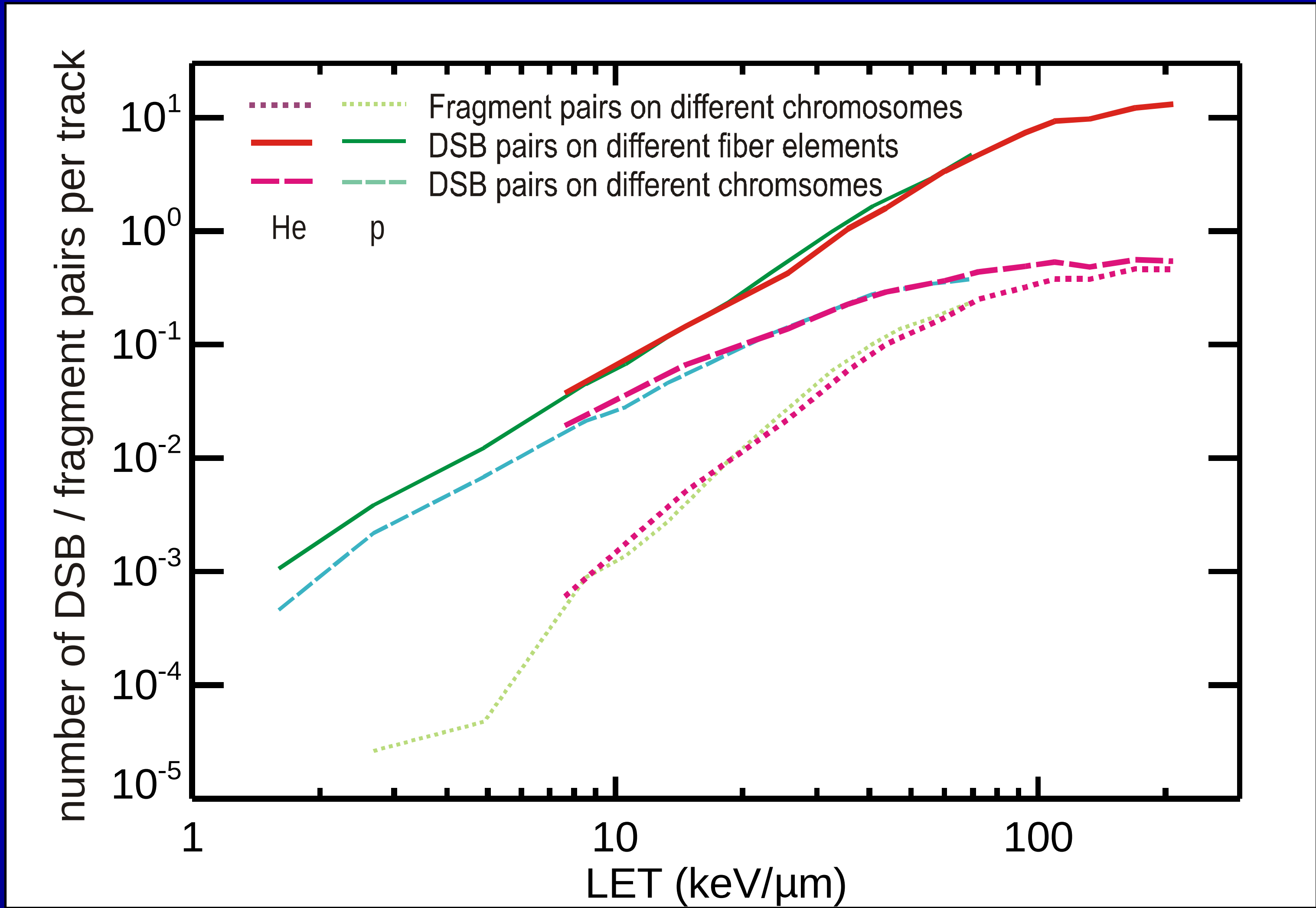
Friedland et al., Radiat Res. 159, 401-410 (2003)



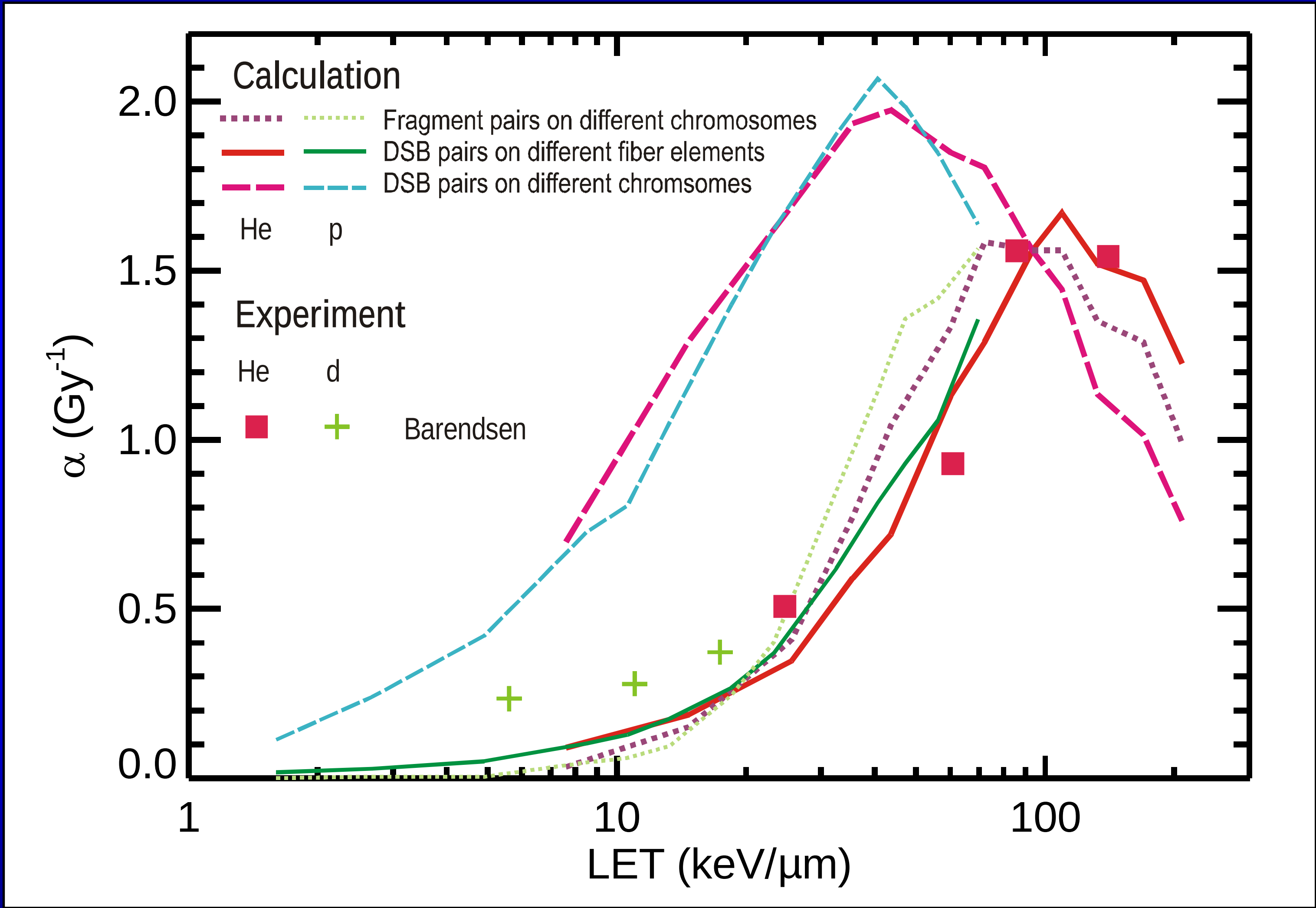
Relative distribution of DNA fragments due to 1 Gy irradiation with p and He ions



Frequency of multiple DNA damage from p and He ion irradiation

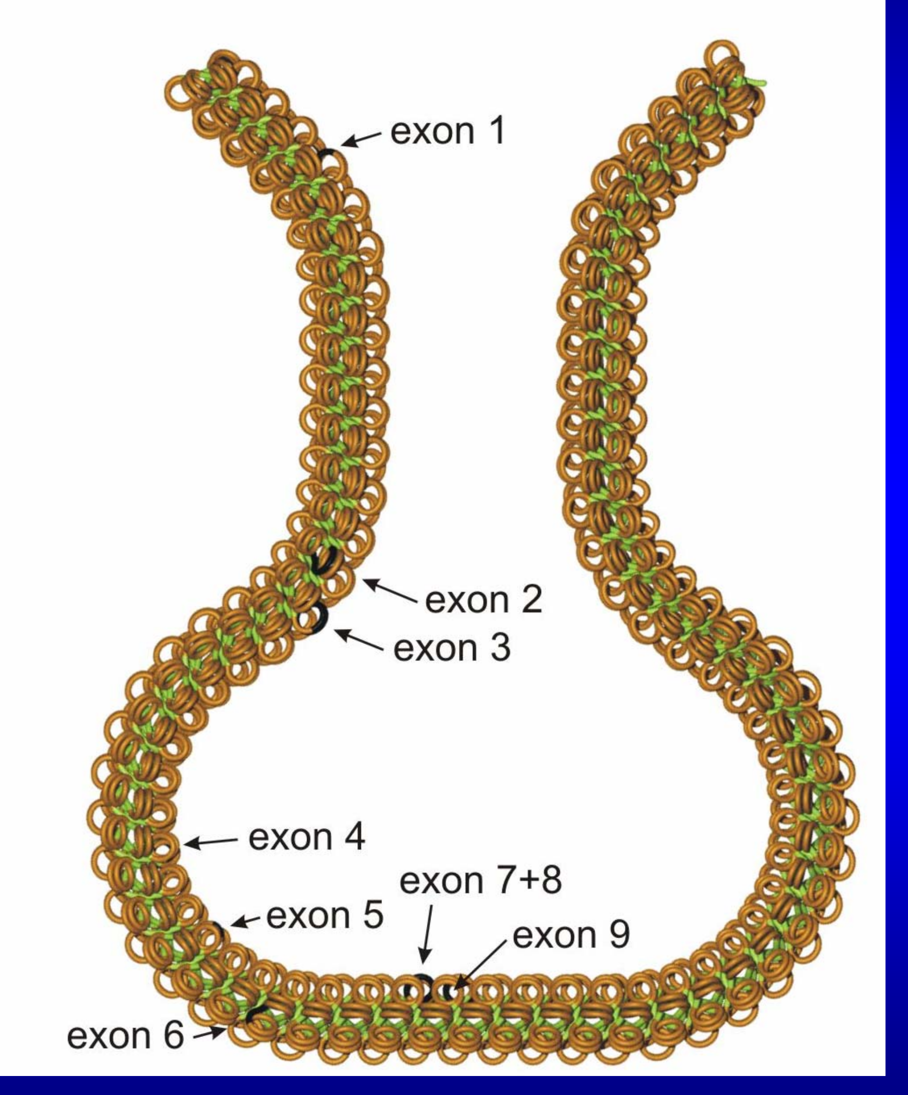


Frequency of multiple DNA damage and cell inactivation for H and He ion irradiation



Chromatin fiber loop with HPRT gene

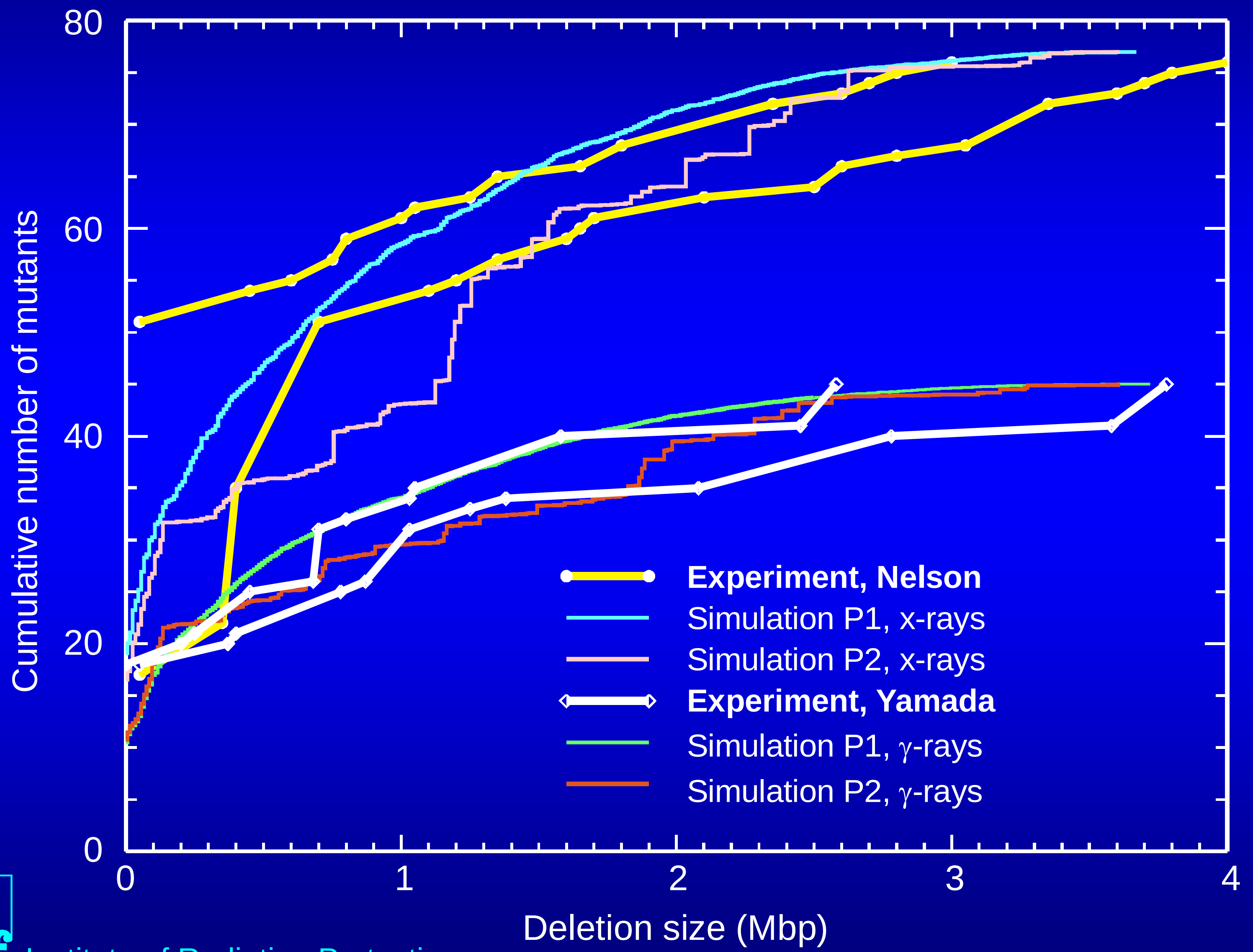
Friedland et al., Radiat. Res. 155, 703-715 (2001)



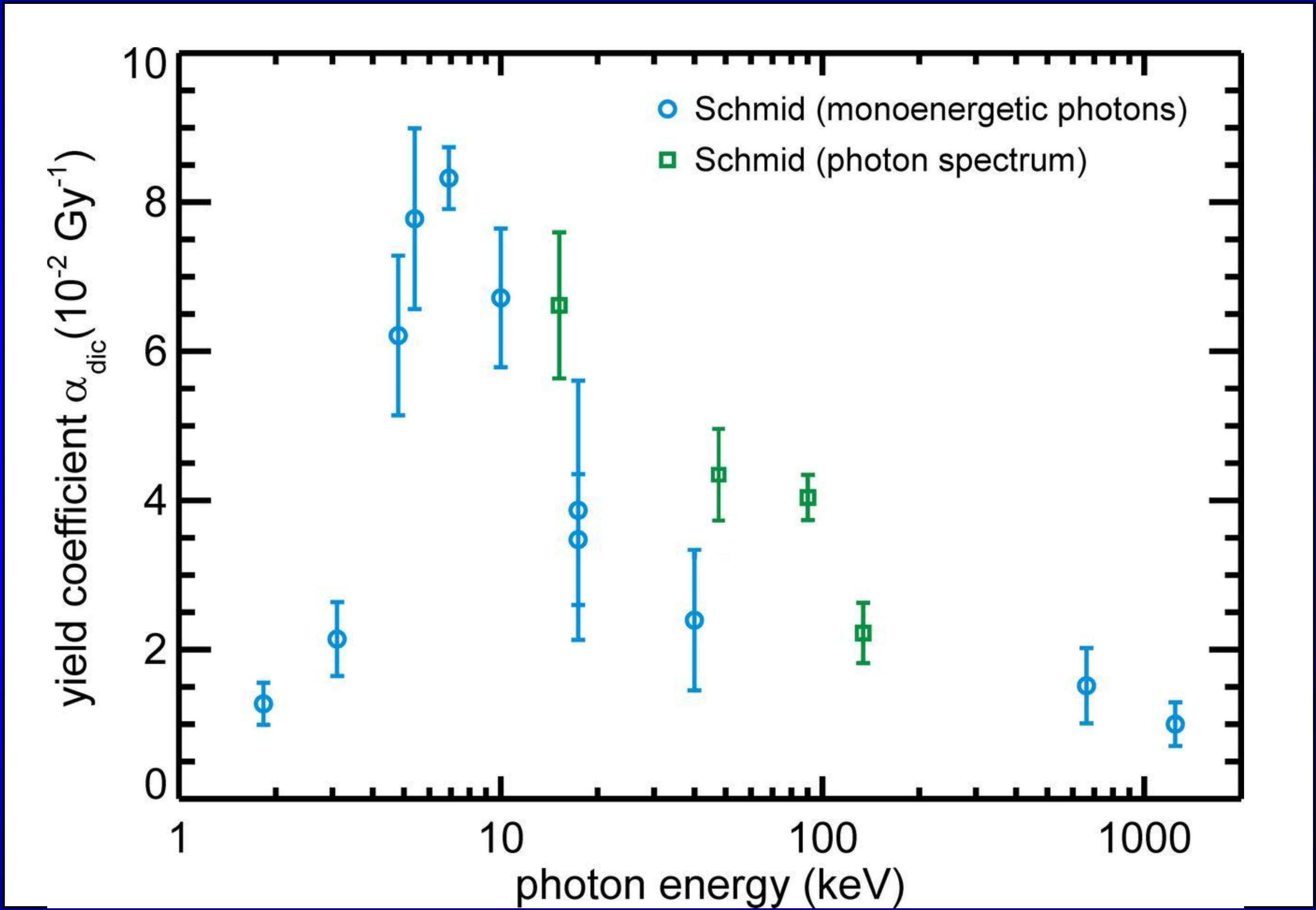
Patterns of exon deletions

Deleted exons								Number of mutants					
								Experiment ^{60}Co γ-rays 1 - 4 Gy	Simulation ^{60}Co γ-rays 2 Gy		Experiment 80 kV x-rays 2 Gy	Simulation 220 kV x-rays 2 Gy	
1	2	3	4	5	6	7 8	9	Yamada	P1	P2	Nelson	P1	P2
X								2	3.0	3.0	8	4.6	3.8
	X								1.3	1.3	1	2.1	1.8
		X						1	1.4	1.4	2	2.2	1.9
			X					3	1.4	1.4	2	2.6	2.2
				X					1.2	1.2	4	2.1	1.8
					X				1.3	1.3		2.3	2.0
						X		3	1.3	1.4	3	2.4	2.1
							X	3	1.2	1.2	2	2.2	1.9
X	X								0.22	0.21	1	0.4	0.23
	X	X						1	0.4	0.4		0.7	0.6
		X	X					1	0.014	0.004		0.015	0.013
			X	X					0.13	0.14	1	0.3	0.23
						X	X		0.9	0.9	2	1.6	1.4
X	X	X							1.2	1.1	4	2.1	1.4
					X	X	X		0.4	0.3	1	0.6	0.5
X	X	X	X					3	0.3	0.3		0.6	0.5
				X	X	X	X		0.4	0.4	1	0.8	0.7
X	X	X	X	X				3	0.3	0.24		0.7	0.5
			X	X	X	X	X		1.1	1.0	3	2.2	1.9
		X	X	X	X	X	X		0.19	0.17	1	0.4	0.3
	X	X	X	X	X	X	X		1.3	1.3	1	2.5	2.1
X	X	X	X	X	X	X	X	26	26.8	27.1	41	44.1	49.6

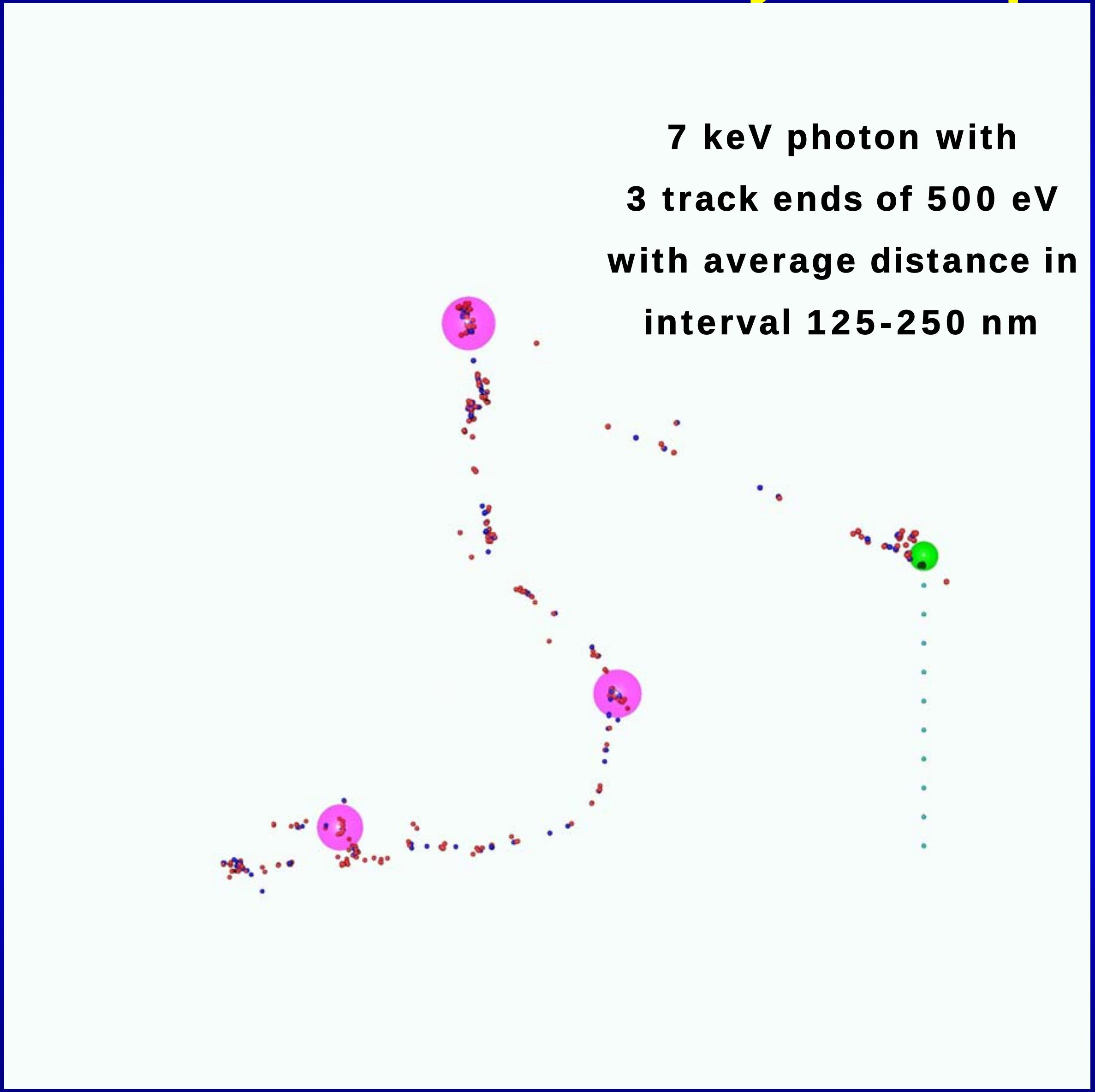
Deletion size distribution



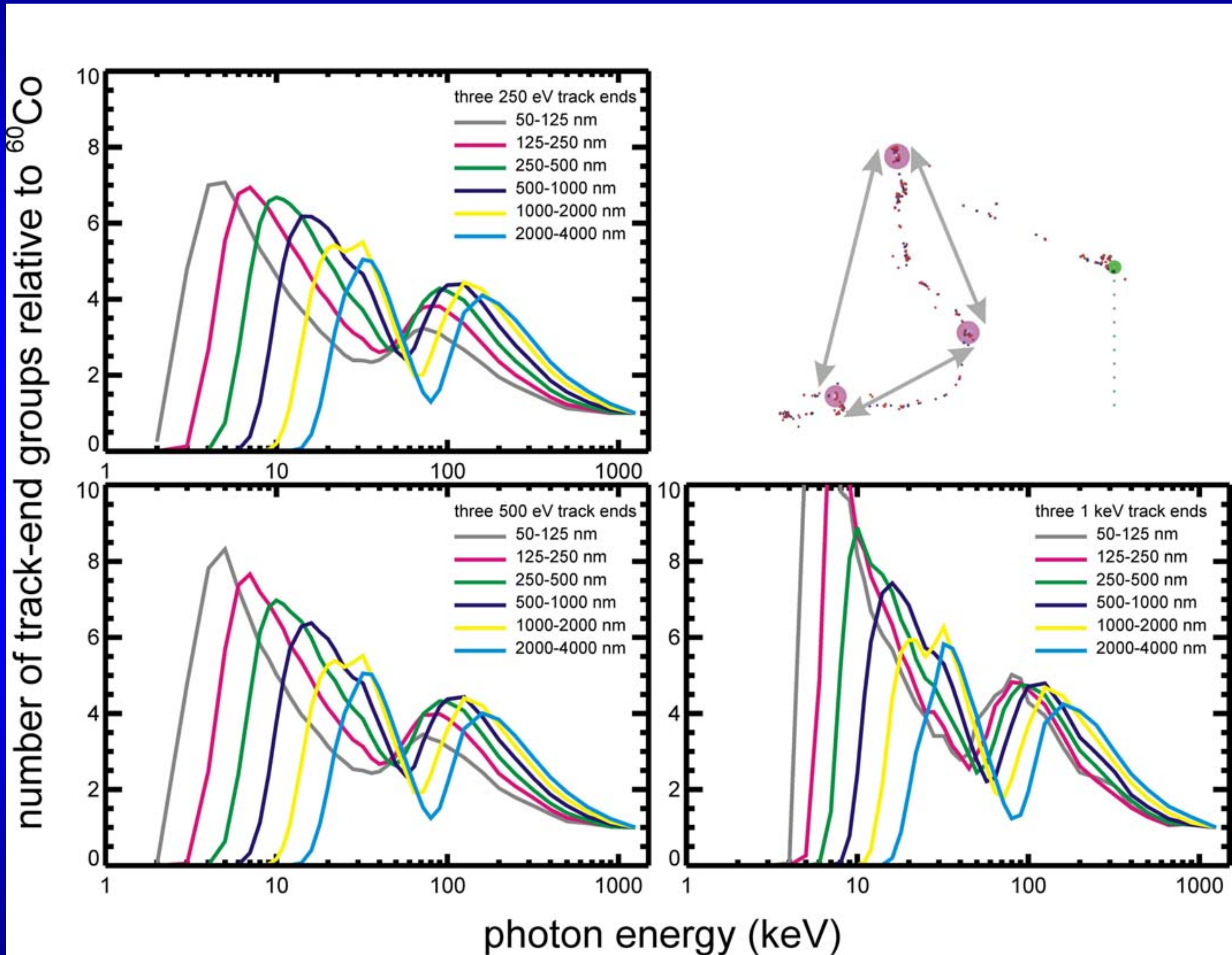
Yield of photon induced dicentrics



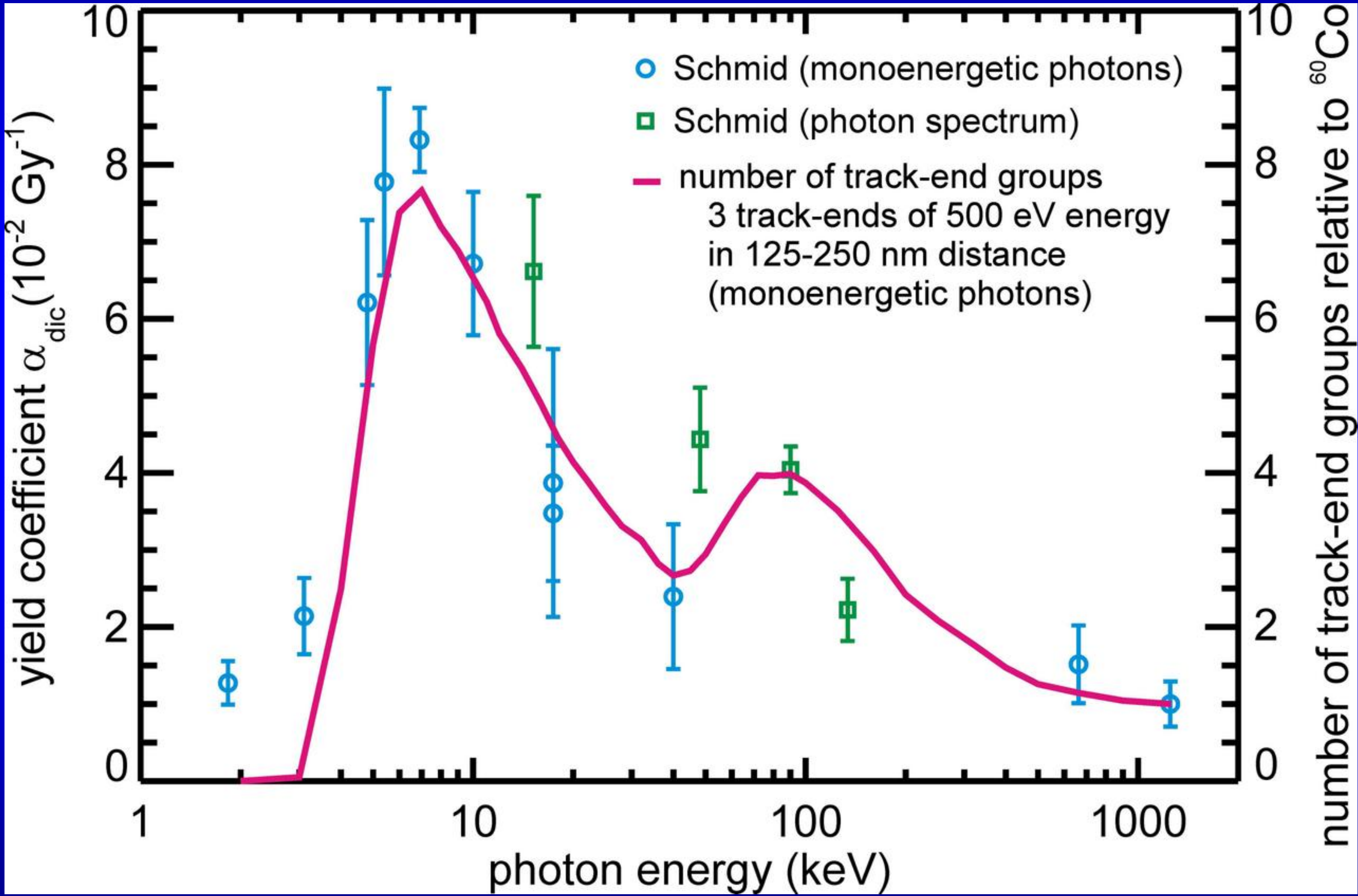
Electron track induced by 7 keV photon



Relative frequency of three track ends



Comparison between experiment and simulation



Hypothesis

Temporally coincident multiple DNA damage

- on different chromosomes
- in some ten kbp genomic distance
- in a few hundred nm spatial distance

may be of rather high importance for cellular radiation effects


Thank you for your attention !