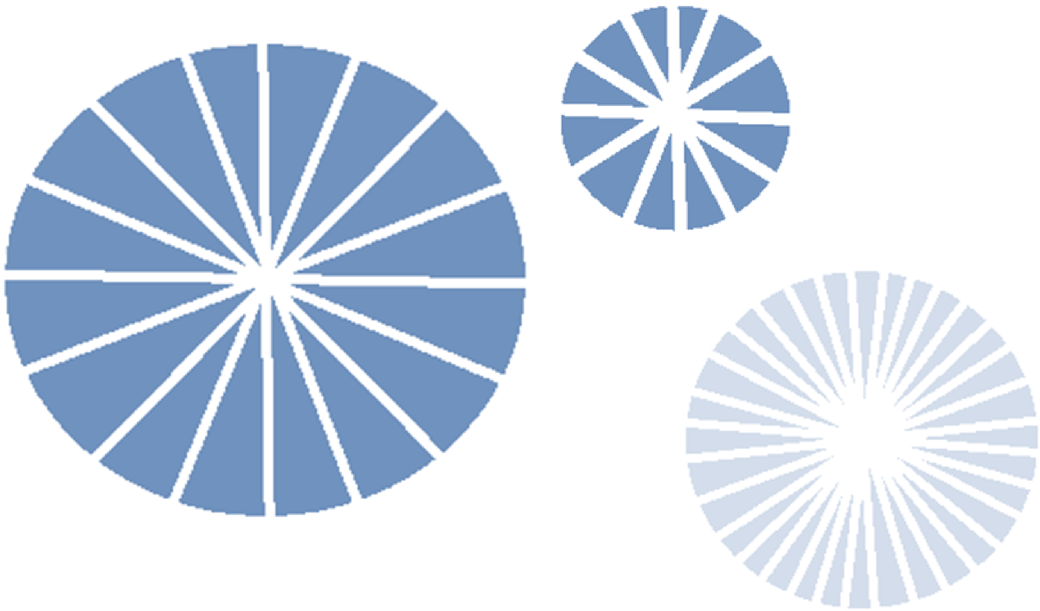

Introduction to MIKROdosimetry

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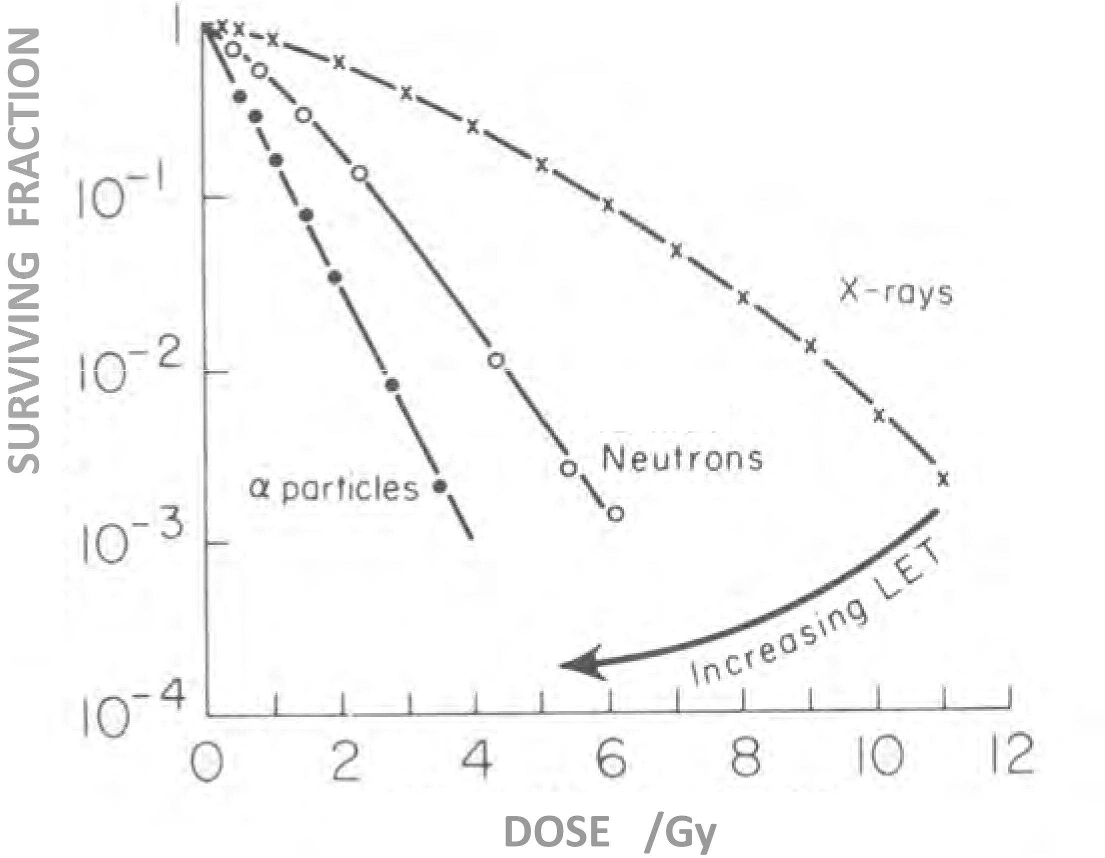
Faculty of Nuclear Sciences and Physical Engineering, CTU Prague, CR

Biological effects of radiation

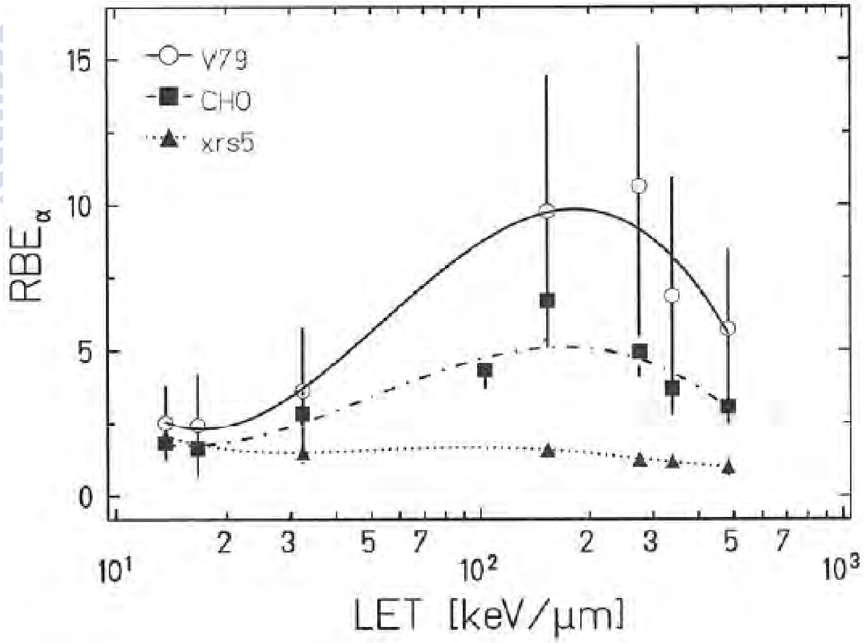


According to Hall 1988

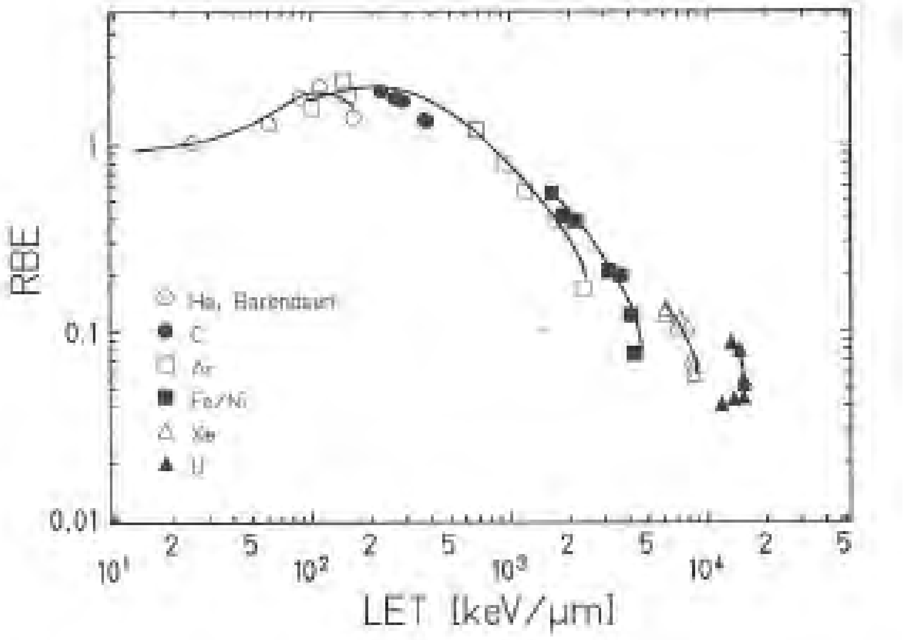
Biological effects of radiation

Radiobiological efficiency

$\mathrm{RBE} = [D_{60Co} / D_{radiation}]_{isoeffect}$



Weyrather W.K. et al, Int. J. Radiat. Biol. 75, 1357-1364, 1999:
All cells from Chinese hamster, V79 lung fibroblasts, CHO ovary cells, XRS genetic variant of CHO, but DSB repair deficient



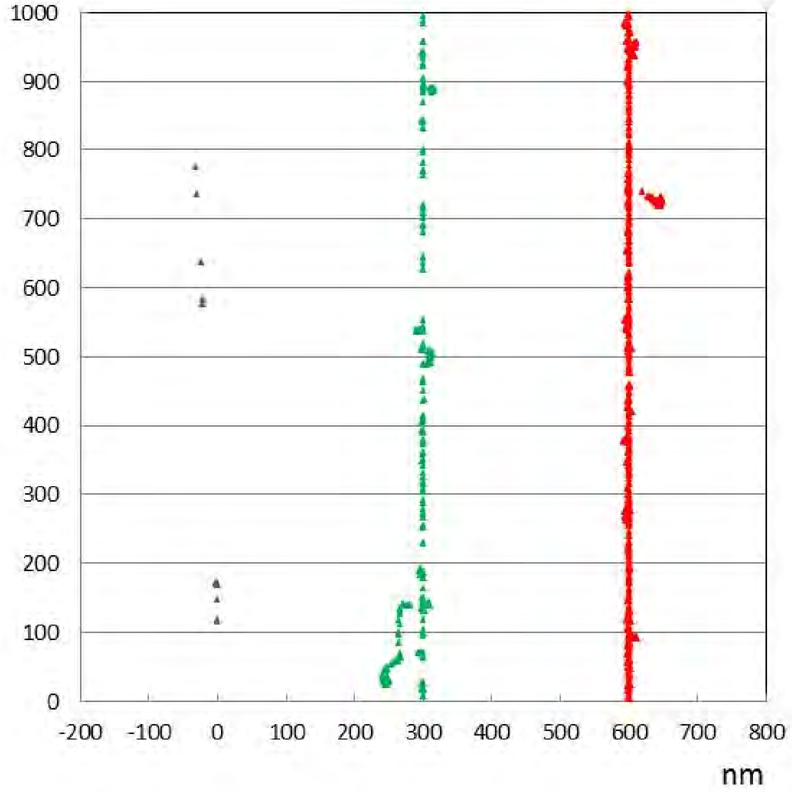
Kraft G., Nucl. Sci. Appl. 3, 1-28, 1987

Particle track

- indicates inchoate distribution of transfer points resulting from the passage of a single primary charged particle, the aggregate of electrons, ions, and excited atoms and molecules, etc. immediately after the ending of all secondary electron interactions, and to the related aggregate of energy deposits which is the energy expended at an individual transfer point (ICRU 36, 1983)

Electron 100keV	~1,5keV/μm
Carbon 480MeV/u	14 keV/μm
Proton 1MeV	24 keV/μm

Absorbed energy 100 keV



LET linear energy transfer, $L_\Delta = (dE/dx)_\Delta$

dx – length of particle trajectory

dE – energy transfered to matter in quantities lower then Δ

Particle track

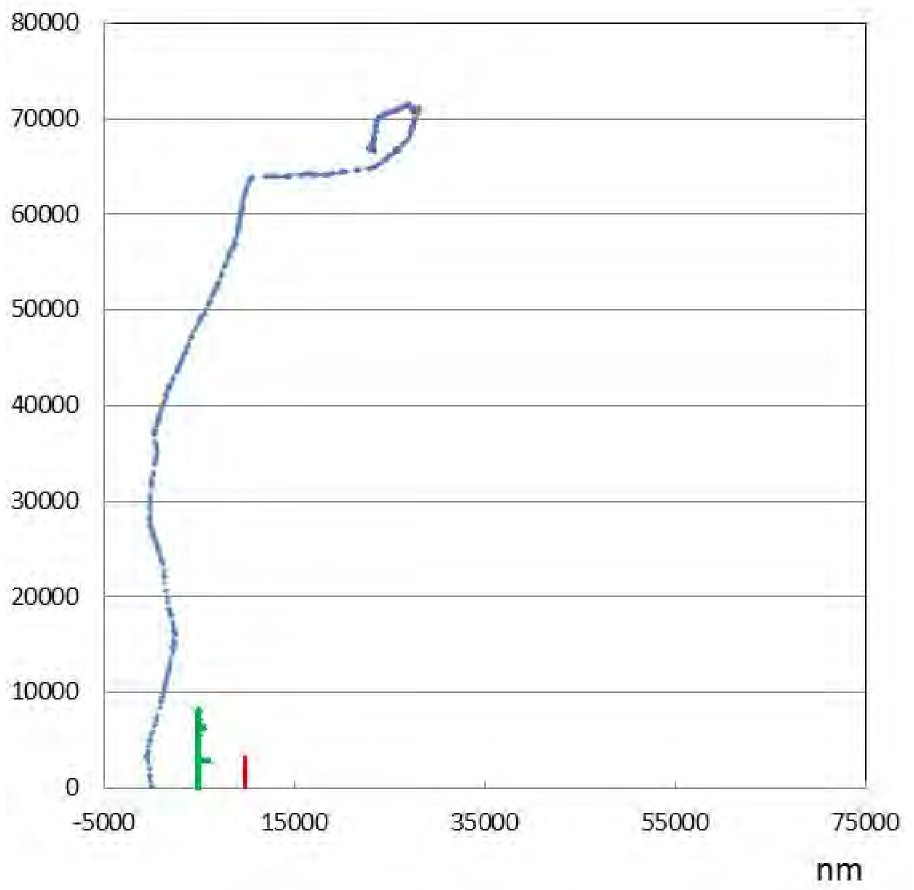
To deliver 1 Gy to cell nucleus (diameter 6 μm):

Electron 100keV ~1,5keV/μm
~10^5 particles

Carbon 480MeV/u 14 keV/μm
~1.3×10^4 particles

Proton 1MeV 24 keV/μm
~7.4×10^3 particles

Absorbed energy 100 keV



LET linear energy transfer, $L_\Delta = (dE/dx)_\Delta$
dx – length of particle trajectory
dE – energy transfered to matter in quantities lower then Δ

Energy deposit ε_i

ICRU Report 36 (1983)

energy deposited in a single interaction

$$\varepsilon_i = T_{in} - T_{out} + Q_{\Delta m} \qquad [\varepsilon_i] = J$$

T_{in} - energy of the incident ionizing particle (exclusive of rest mass energy)

T_{out} - sum of energies of all ionizing particles energing from the interaction (exclusive of rest mass energy)

Q - changes of rest mass energy of the atom and all particles involved in the interaction ($Q > 0$ decrease of rest mass, $Q < 0$ increase of rest mass)

a) ε_i is a stochastic quantity
b) ε_i is the energy deposited at the point of interaction $\Rightarrow$ “transfer point”

Energy imparted in a volume

$$\varepsilon = \sum_i \varepsilon_i \qquad [\varepsilon] = J$$

a) ε is a stochastic quantity
b) summation independent of the origin

Proximity function

Energy imparted related to integral proximity functions T(x);

for j-track $T_j(x) = \sum i \sum k\, \varepsilon_i . \varepsilon_k / \sum i\, \varepsilon_l$

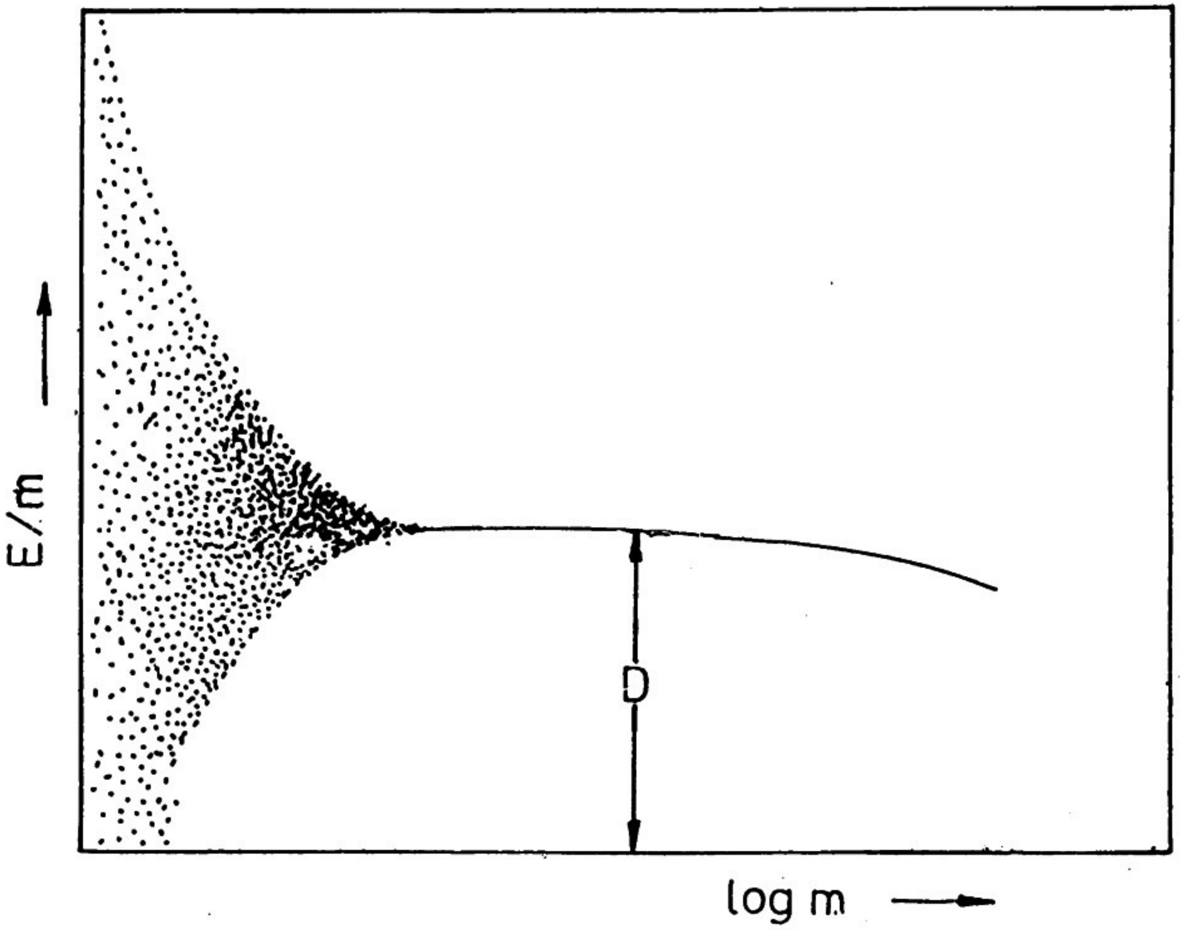
$$T(x) = \lim_{n \to \infty} \frac{1}{n} \sum_{j=1}^{n} \tilde{T}_j(x)$$

T(x) weighted mean energy imparted to a spherical volume of radius x, centred at an arbitrary transfer point of an arbitrary track

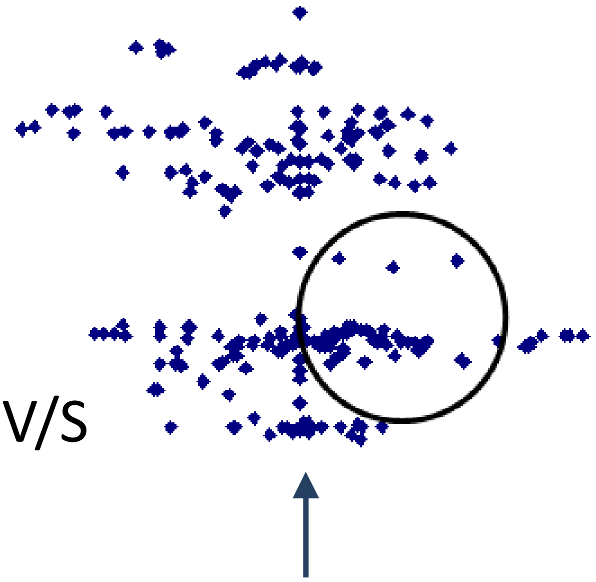
- The integral energy proximity function is an average over a large number of tracks

Differential proximity function t(x) = dT(x)/dx

Hypothetical measurements of E/m



Lineal energy, y



$y = \varepsilon / l$ $[y] = J/m$; often keV/µm

Mean chord length - l; for convex body $l = 4V/S$

e.g. sphere $l = 4/3\ r$

- stochastic quantity

Distribution functions:

Integral: F(y) – probability that linear energy is less than y

Differential: f(y) - probability density $f(y) = dF(y)/dy$

Lineal energy - remarks

- f(y) frequency distribution of lineal energy

  $Y_F = \int y.f(y).dy$ frequency-mean lineal energy

- d(y) dose distribution of lineal energy

  $d(y) = dD(y)/dy$

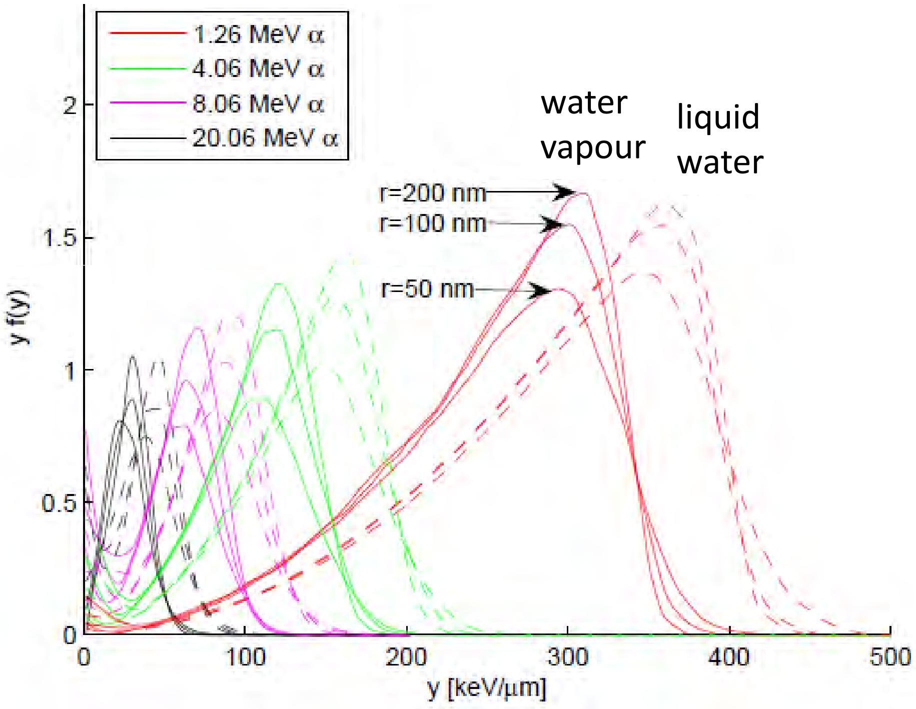
  $Y_D = \int yD(y)\, dy$ dose-mean lineal energy

Y_F and Y_D are nonstochastic quantities

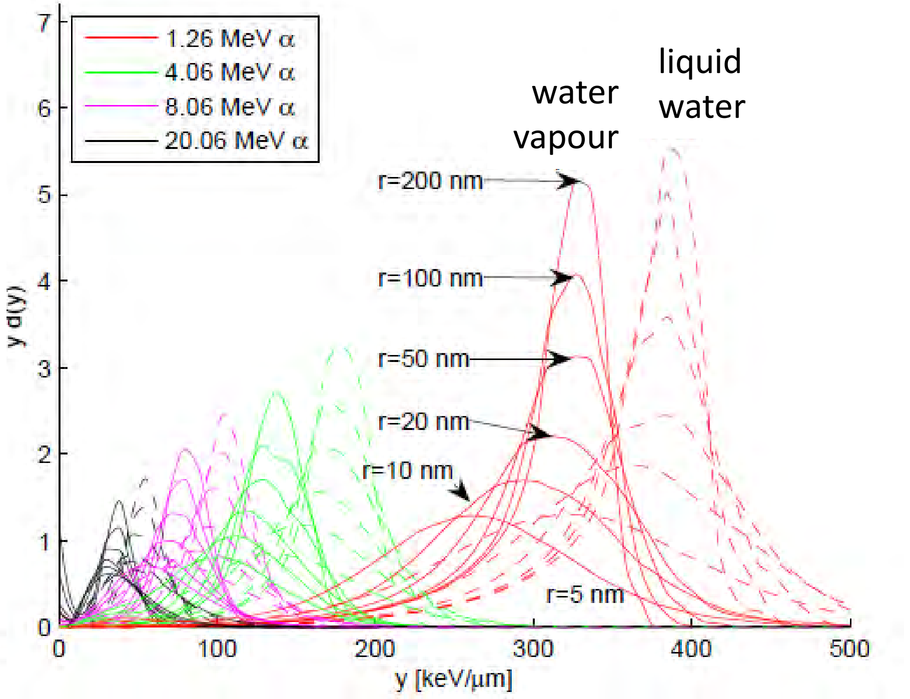
$Y_D = 1/Y_F \int Y^2 f(y)\, dy$

Lineal energy distributions

y.f(y) frequence distribution

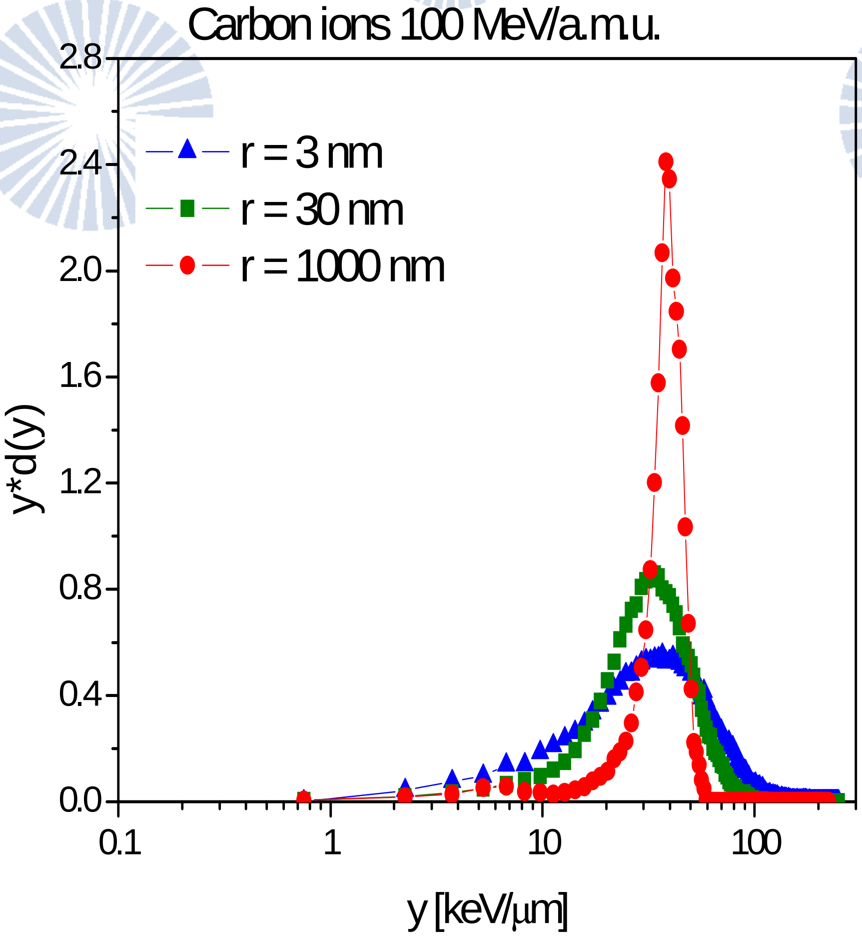


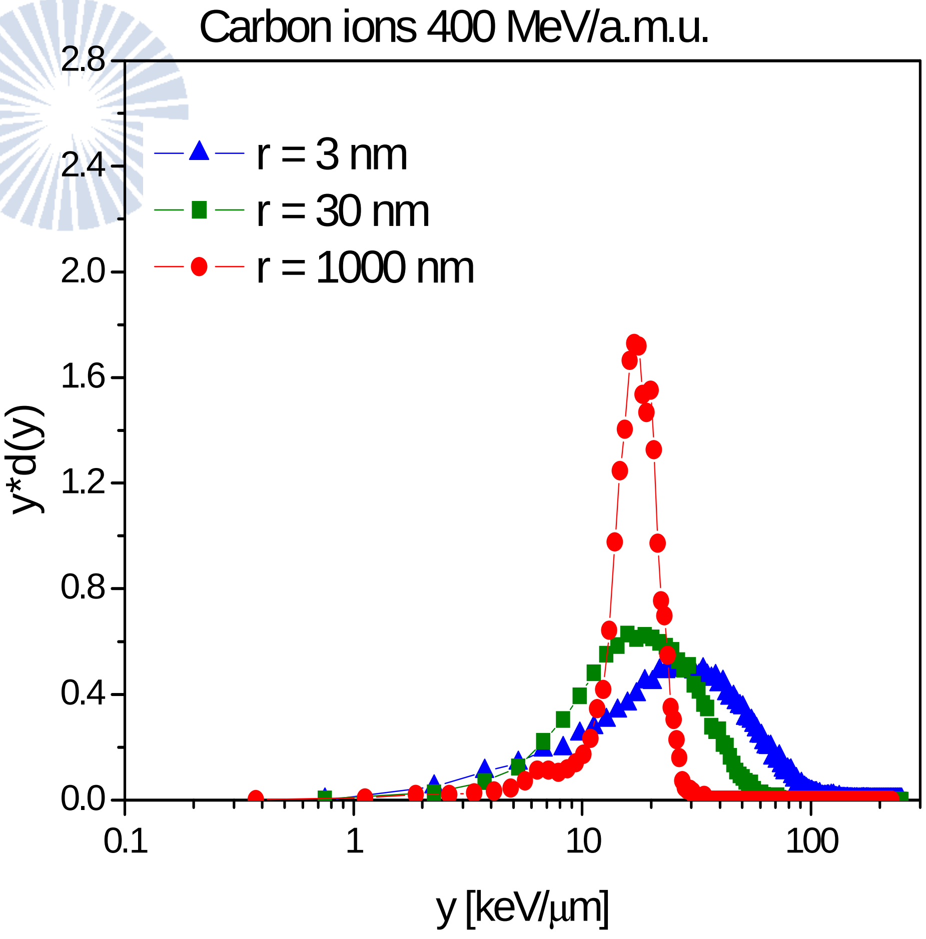
y.d(y) dose distribution



TRIOL and TRION track structure codes

Lineal energy distributions


Carbon ions 100 MeV/a.m.u.


Carbon ions 400 MeV/a.m.u.

TRIOL code

Lineal energy – remarks

Relation y x LET:

- LET – nonstochastic, energetically restricted, used only for dx < range
- y – stochastic, geometrically restricted, single event; valid also for l > range

Specific (imparted) energy, z

Specific energy

$z = \varepsilon/m \qquad [z]=\mathrm{Gy}$

Notes:

- stochastic quantity
- $F(z)$ – integral distribution function – probability that specific energy is equal or less than z
- $f(z) = dF(z)/dz$ differential distribution function (probability density)

- Mean specific energy $\bar{z} = \int z.f(z)\, dz \approx D$ is nonstochastic quantity

DISTRIBUTIONS $f(z;D)$

Analogy:

$$F(z;D) = \int f(z'; D)\, dz'$$

$$D(z;D) = \int z' . f(z'; D)\, dz'$$

- i.e. probability that, at the dose D, specific energy is not higher than z (or the contribution of dose below z)
- $f(z;D)$: at low doses – similar to $f_1(z)$
- for large sensitive volumes – $f(z;D)$ approaches to normal distribution with average value ~ D; its width diminishes

Dosimetry versus microdosimetry

There are fundamental differences in the character of quantities:

1. Dosimetry – nonstochastic; their values:

- anticipated;
- continuous in the space and time

2. Microdosimetry – stochastic; their values:

- non-anticipated
- not continuous in the space and time

Dosimetry versus microdosimetry

LET

- transition between dosimetry and microdosimetry
- nonstochastic but locally imparted

Of course – even for monoenergetic charged particle – whole spectrum of LET

Two possibilities how to express theirs average values:

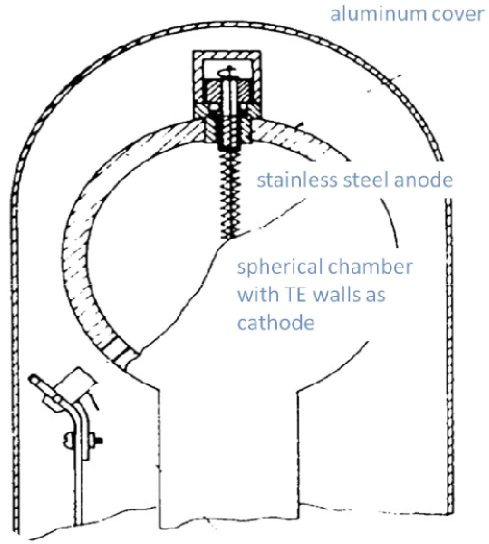
Spectrum of track lengths at which there is L – T(L): $L_T = \int T(L)\, L\, dL$
"track averaged LET"

Spectrum of absorbed doses at given L- values – D(L): $L_D = \int D(L)\, L\, dL$
"dose averaged LET"

$L_T < L_D$
Generally – when L smaller – range large

TEPC – Tissue Equivalent Proportional Counter

Harald H. Rossi (1917-2000)
Columbia University, NY, USA
Center for Radiological Research



Principle (about 1955):
Height of an impulsion (IH)– proportional to energy absorbed in the sensitive volume: f(IH) ≈ f(z)

TISSUE EQUIVALENCY

(ICRU 36, 1983)

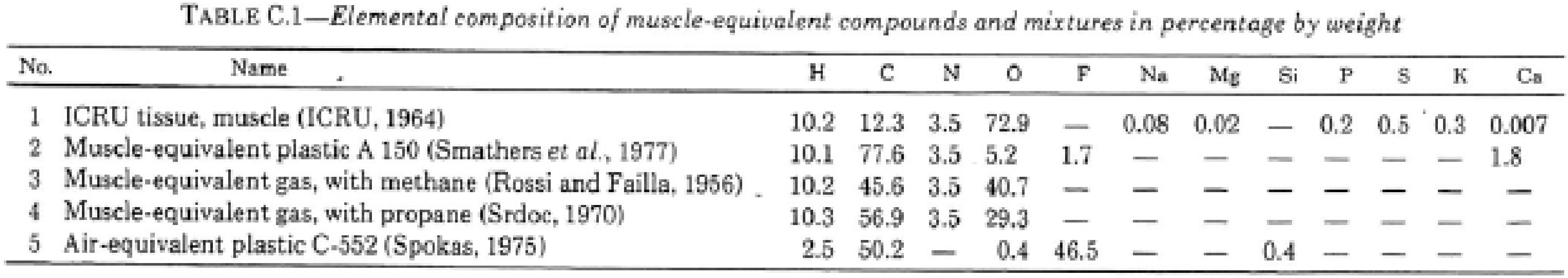


TABLE C.1—*Elemental composition of muscle-equivalent compounds and mixtures in percentage by weight*

No.	Name	H	C	N	O	F	Na	Mg	Si	P	S	K	Ca
1	ICRU tissue, muscle (ICRU, 1964)	10.2	12.3	3.5	72.9	—	0.08	0.02	—	0.2	0.5	0.3	0.007
2	Muscle-equivalent plastic A 150 (Smathers *et al.*, 1977)	10.1	77.6	3.5	5.2	1.7	—	—	—	—	—	—	1.8
3	Muscle-equivalent gas, with methane (Rossi and Failla, 1956)	10.2	45.6	3.5	40.7	—	—	—	—	—	—	—	—
4	Muscle-equivalent gas, with propane (Srdoc, 1970)	10.3	56.9	3.5	29.3	—	—	—	—	—	—	—	—
5	Air-equivalent plastic C-552 (Spokas, 1975)	2.5	50.2	—	0.4	46.5	—	—	0.4	—	—	—	—

- TE gas fill: 64.4% methane, 32.4% carbon dioxide and 3.2% nitrogen
- not TE gas fill: noble gases, hydrocarbon gases (methane, propane, ethylene), or a mixture of noble and hydrocarbon gases, helium-3 or BF_3 for neutron detection, air for alphas

Typical characteristics:

Diameter: 2.5 – 10 cm, pressure: ~ mm Hg

For diameter ~ 10 cm, and 10 mm Hg (13 kPa) – simulated volume with d~ 1.5 µm

Limitations:

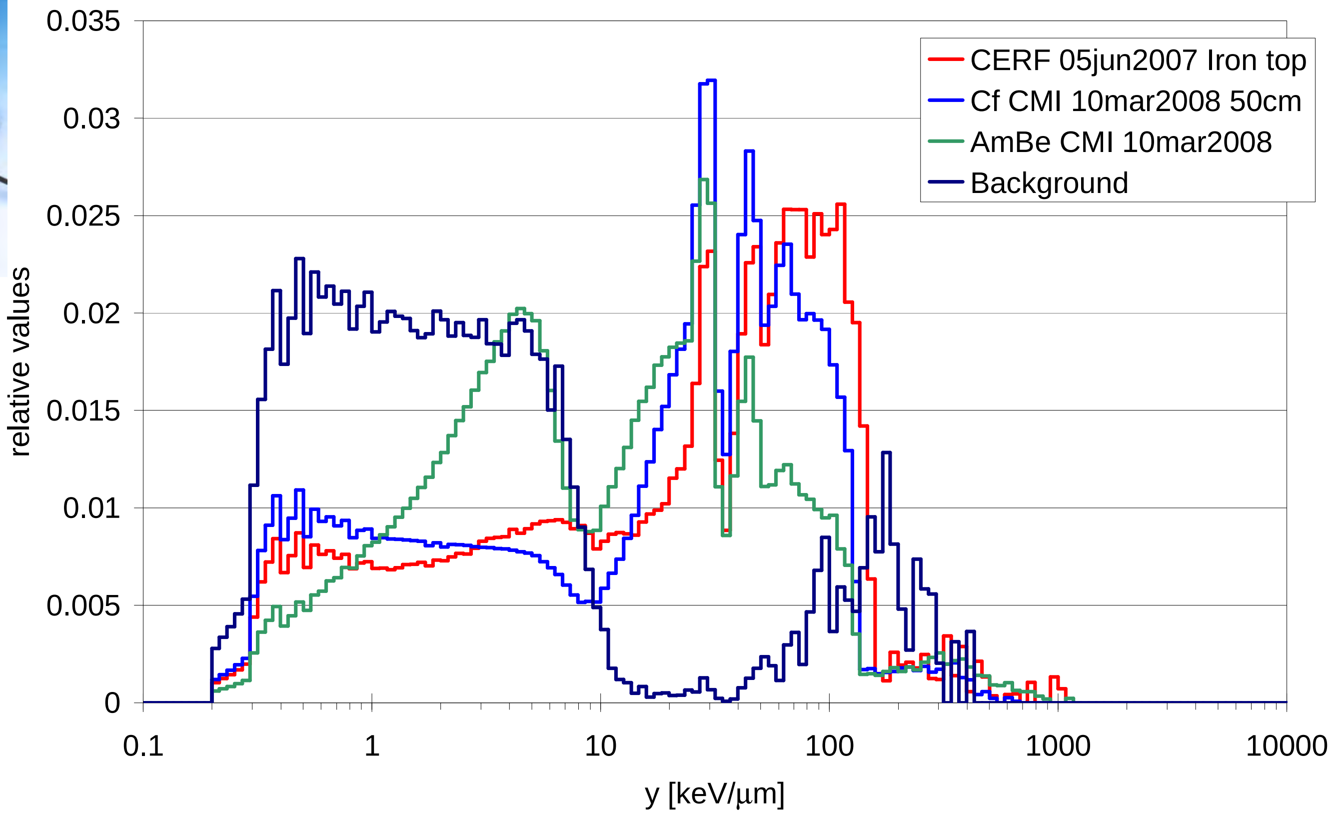
gas pressure sufficient to assure constant magnification factor (proportionality)

at least one ionization had to take place → dmin about 50 nm

Examples of TEPC measured spectra

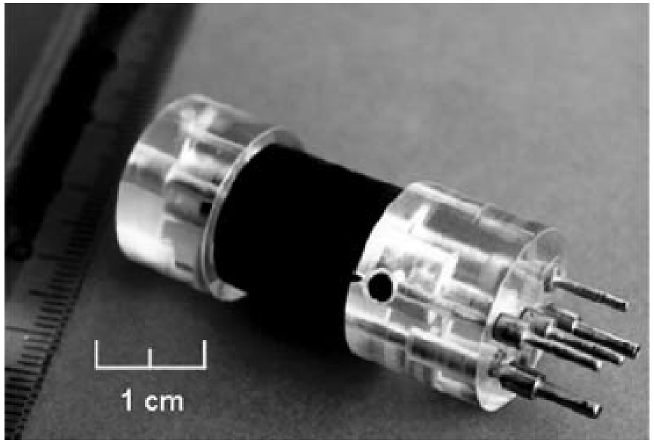
Relative y*d(y) distributions (own NPI results – O. Ploc)

TEPC HAWK in the flight case

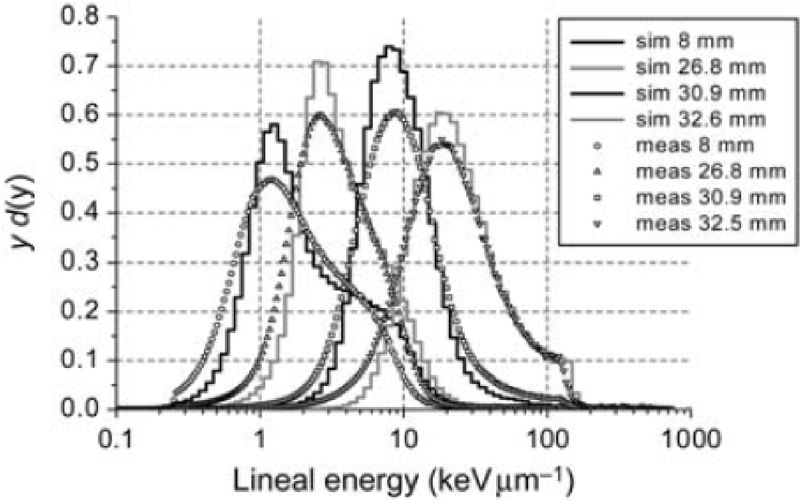


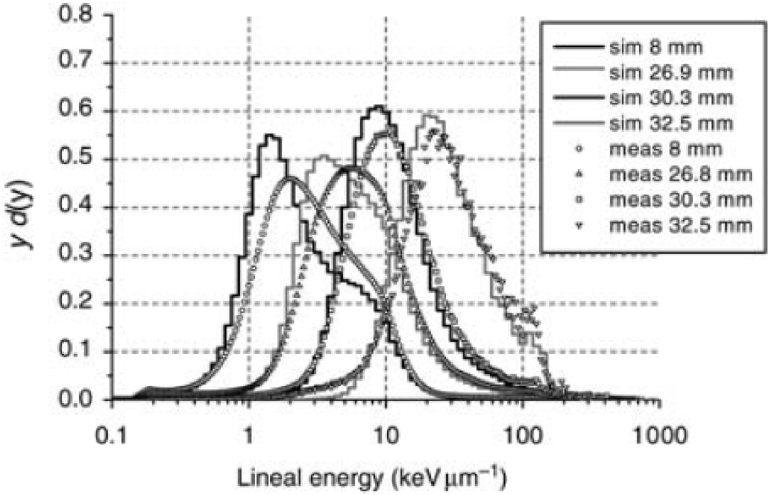
MINITEPC in RADIOTHERAPY

Rollet et al. 2011, Radiation Protection Dosimetry 143, 445



MINITEPC measurements
FLUKA calculations





Irradiation by nonmodulated beam and SOBP of 62 MeV protons (therapeutic proton beam at the Centre Antoine Lacassagne in Nice, France

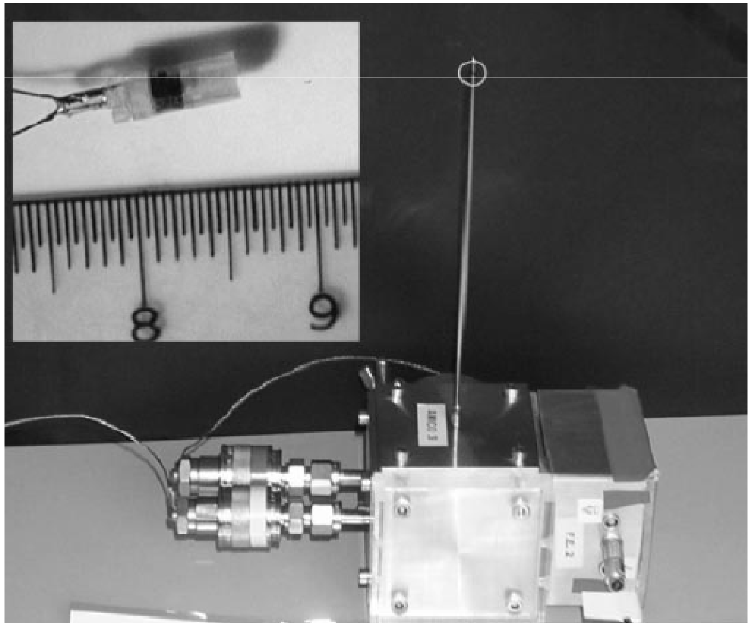
MICRO DOSIMETRY in RADIOTHERAPY

De Nardo et al. 2004, Radiation Protection Dosimetry 110, 681

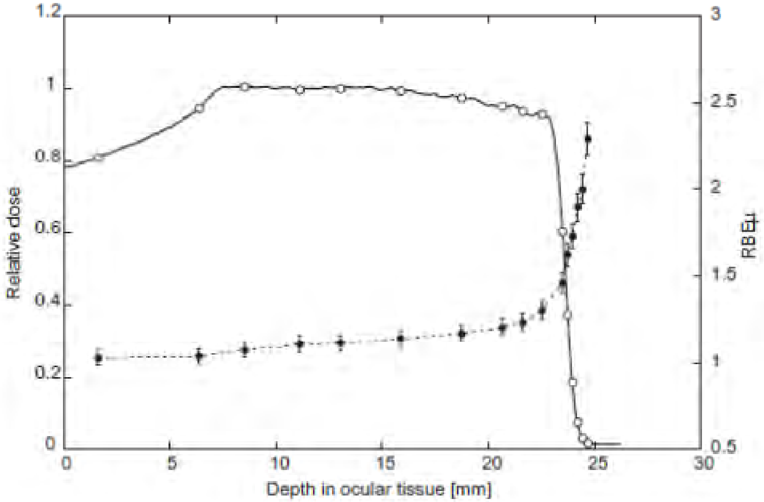
$$\mathrm{RBE}_{\mu} = \int r(y)d(y)\mathrm{d}y$$

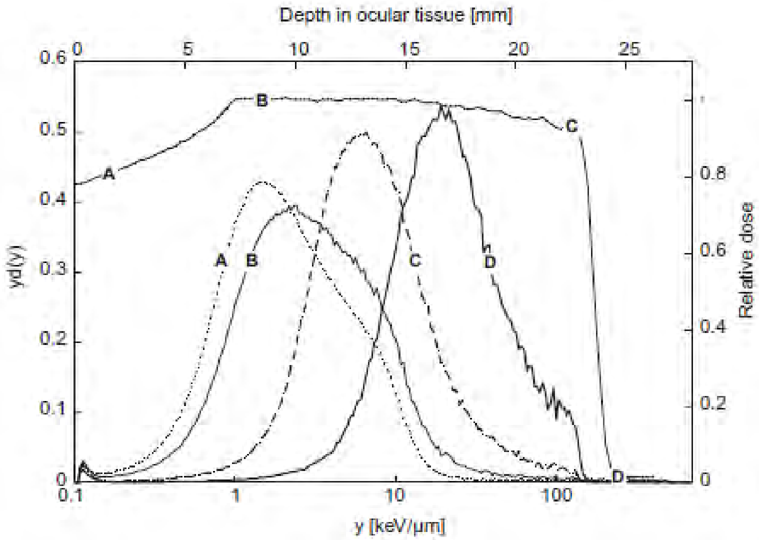
Loncol et al., Rad.Prot.Dosim. 52, 1994

MINI TEPC measurements



CATANA facility, proton SOBP





SILICON DETECTORS

- Alternative to TEPC for applications in medical physics and radiation protection

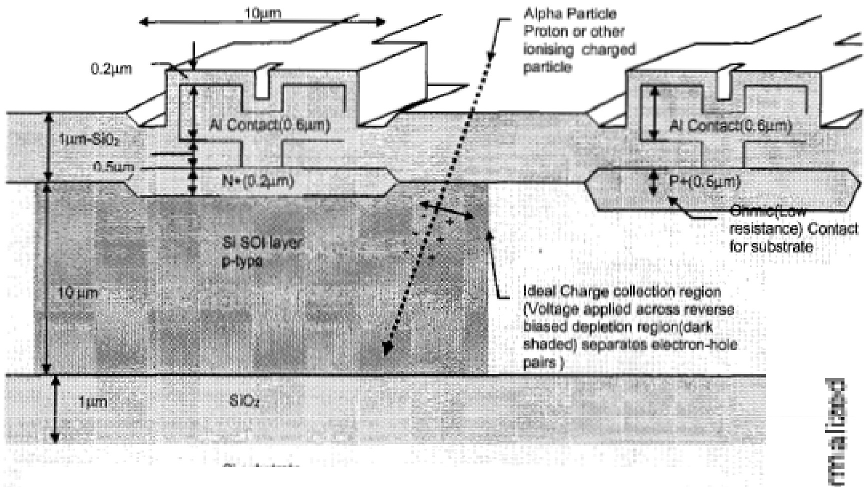
- silicon detectors: W-value about 3 eV (for TEPC it is about 10 times higher)

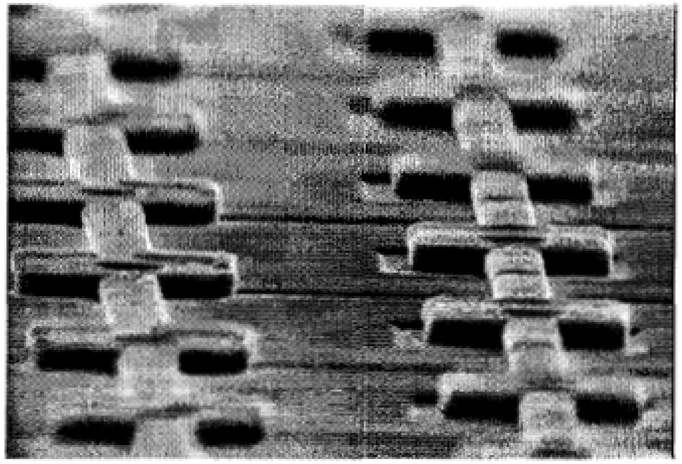
- measuring of lineal energy
    - very low voltage to simulate small volume
    - plastic convertor for tissue equivalency

- measuring of LET with semiconductors (differential methods):
    - Liulin
    - Medipix

Silicon detectors in radiotherapy

Rosenfeld et al. 2000, IEEE Transactions on Nuclear Science 47, 1386





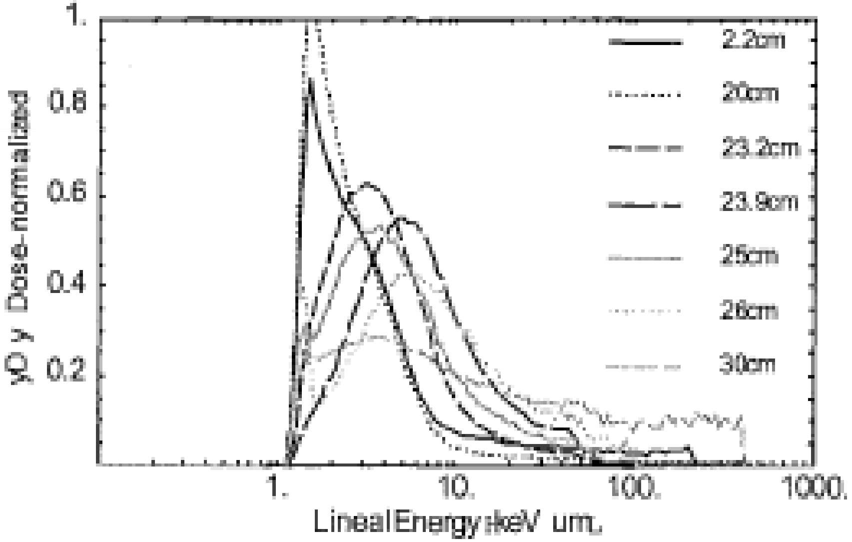


Figure 10: Microdosimetric spectra of 191.5 MeV proton beam at various depths in a water phantom. Range of proton is approximately 23.7 cm.

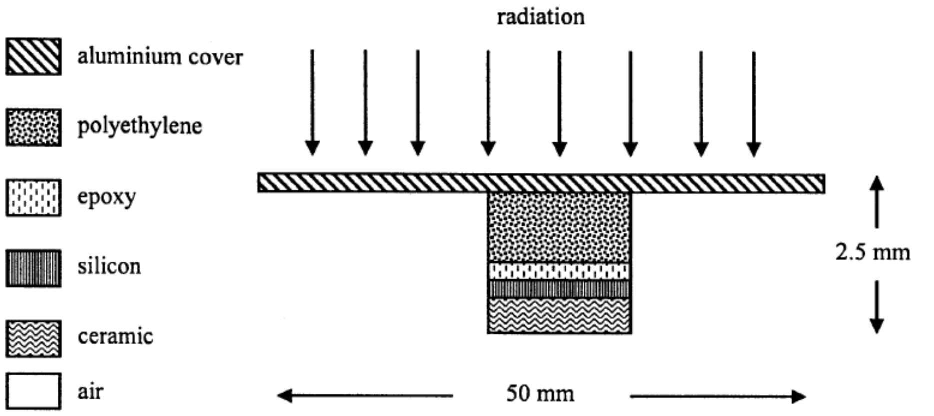
Irradiation by nonmodulated beam and NPTC Boston

LIULIN energy deposition spectrometer

- energy deposition in silicon
- active volume: small silicon diode $10 \times 20 \times 0.3\ \text{mm}^3$
- battery charged
- for perpendicular particles detector range in terms of LET in water up to 33 $\text{keV}.\mu\text{m}^{-1}$
- different designs

Specifications:

- Dose range: 0.093 – 1.56 mGy;
- Flux range: 0.01 – 1250 $\text{part/cm}^2\text{s}$;
- LET (Si) range: 0.27– 69.4 keV/µm;
- Temperature range: 0°C – 40°C;
- Operation time: 110 days



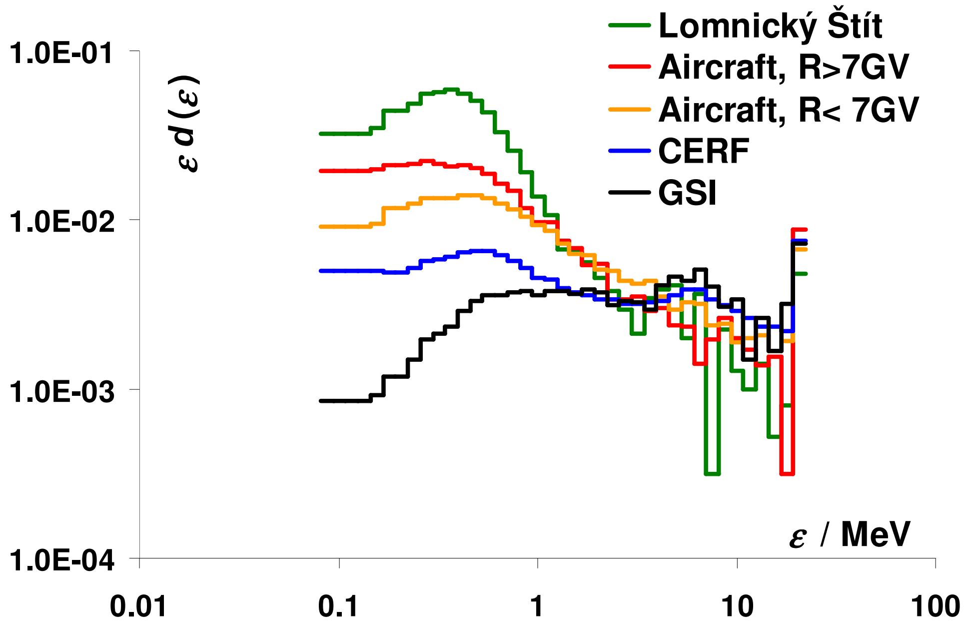
LIULIN

- dose calculation

$$D(Si) = \frac{1}{m}\sum_i \varepsilon_i N_i$$

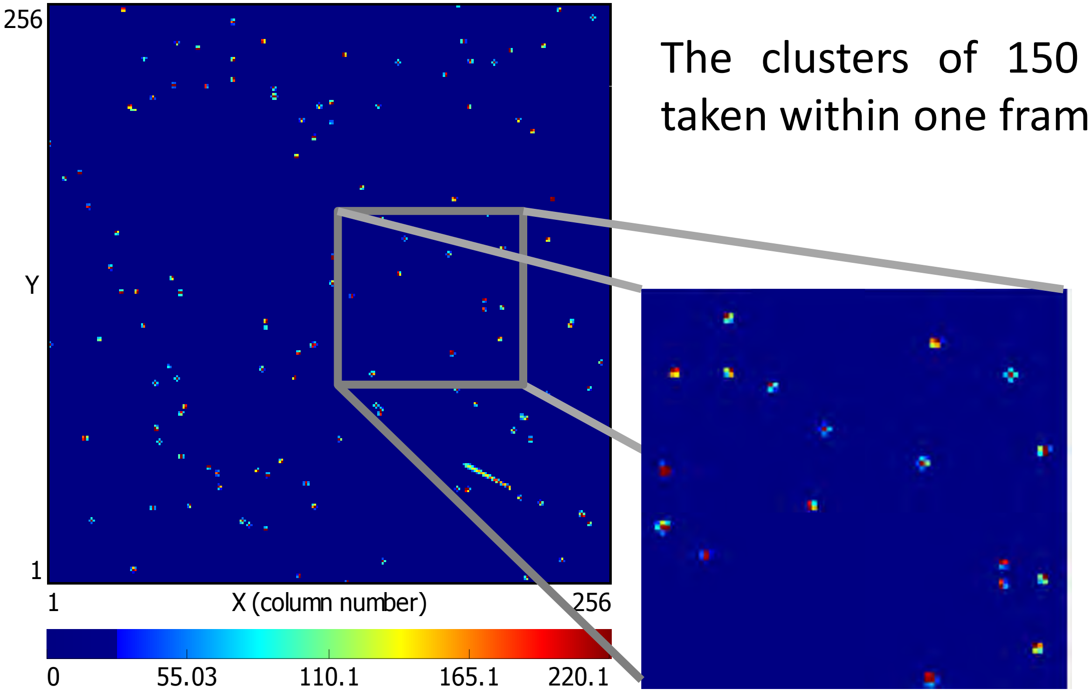
m is detector mass, E_i is energy loss for i channel, N_i is number of events in i channel

- dose equivalent calculation $H = Q(LET)D$



MEDIPIX

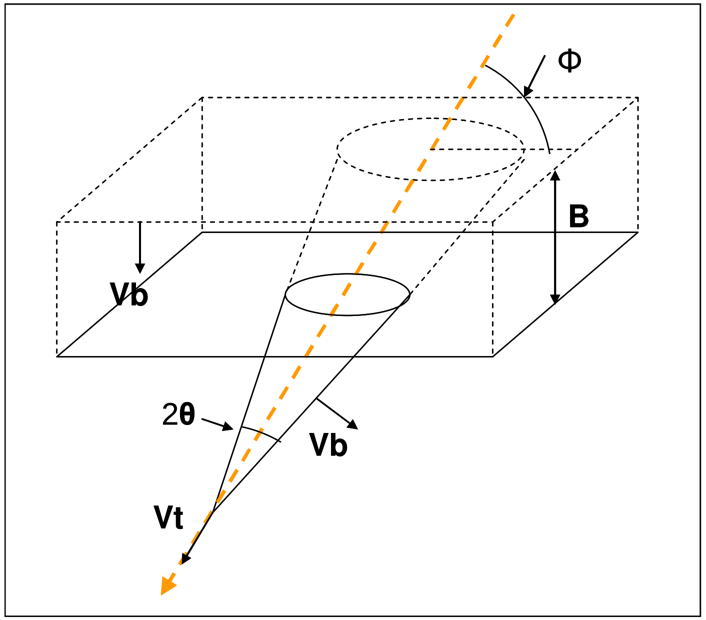
- silicon hybrid pixel detector
- works as active nuclear emulsion
- the group of pixels corresponding to one particle’s hit is called cluster



The clusters of 150 MeV protons taken within one frame in 5 ms

Track Etched Detectors (TED)

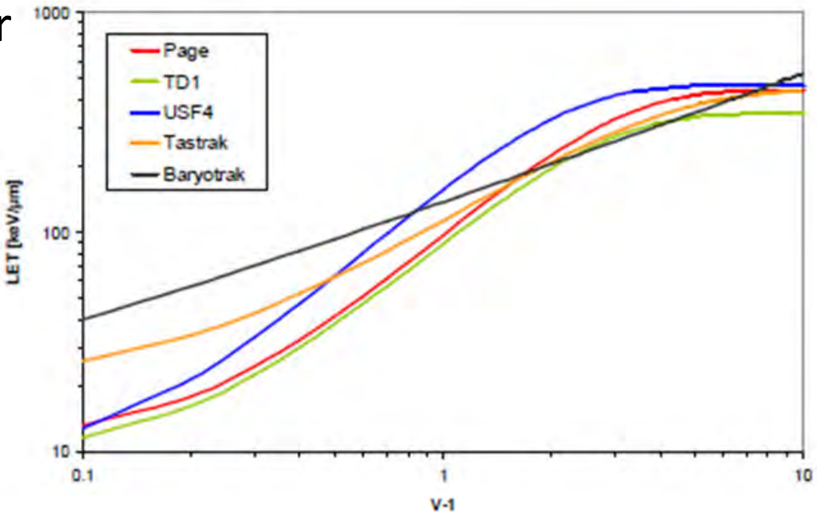
- etching out of sites damaged in plastic material by charged particle creates “track” visible by a microscope (SEIKO HSP-1000)
- relative track size = f(LET) → LET spectra



- material damaged along the charged particle track is etched out faster then surrounding material: Vt > Vb, V=Vt/Vb...”relative track size”
Vt=f(absolute track size), Vb=f(material etching velocity)

Track Etched Detectors

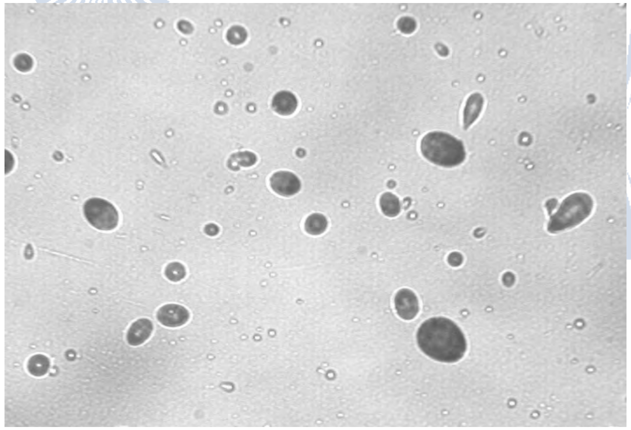
- thin plastic plates (possible cut to whatever sizes – circle, strip, …)
- “passive detectors” – integral information over time
- light, no built-in electronics, cheap, easy to evaluate



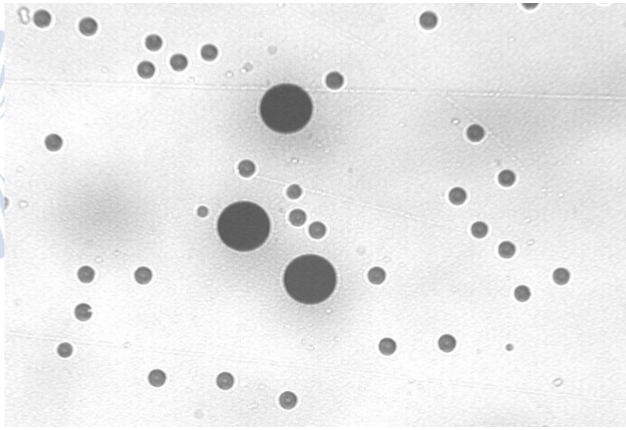
- applied as LET spectrometers:

- on board spacecraft and aircraft
- radon monitoring
- personal neutron dosimetry
- nuclear fragmentation studies in radiation therapy
- detection of particles with very short ranges

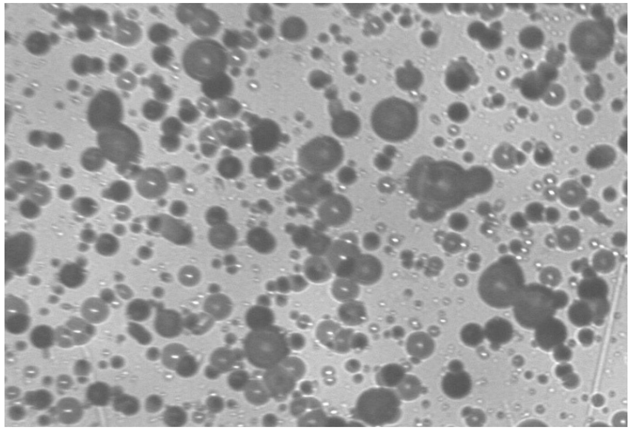
Examples of etched tracks



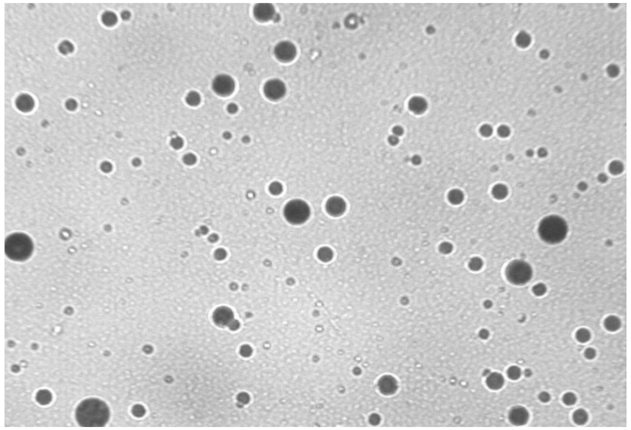
Matrjoshka – 9 months on ISS



^{16}O (20) and ^{56}Fe (402 keV/mm)

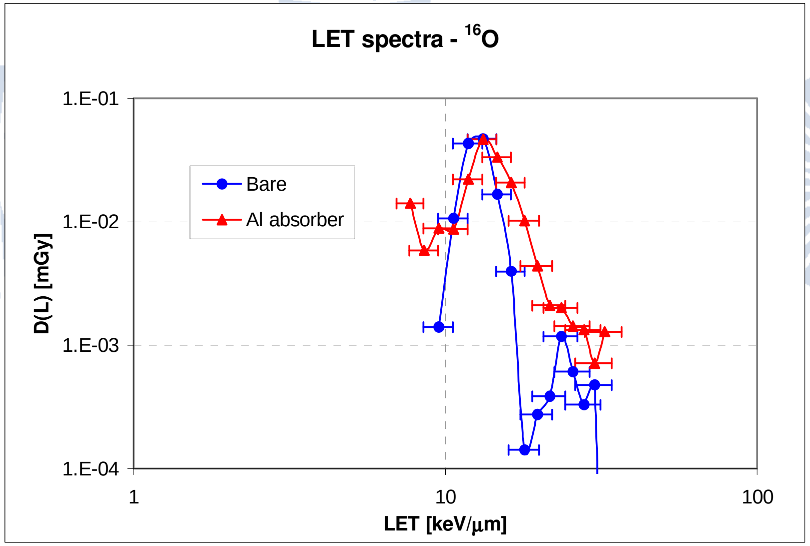


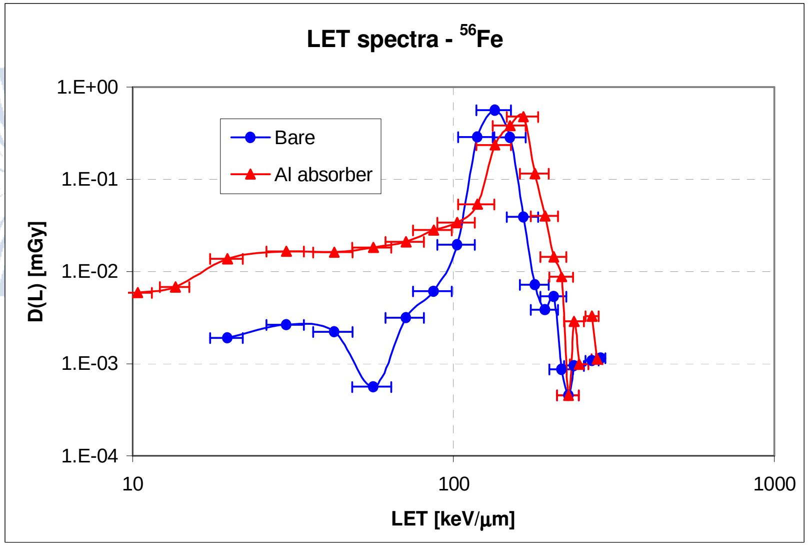
Blind exposure No.3 ICCHIBAN 8

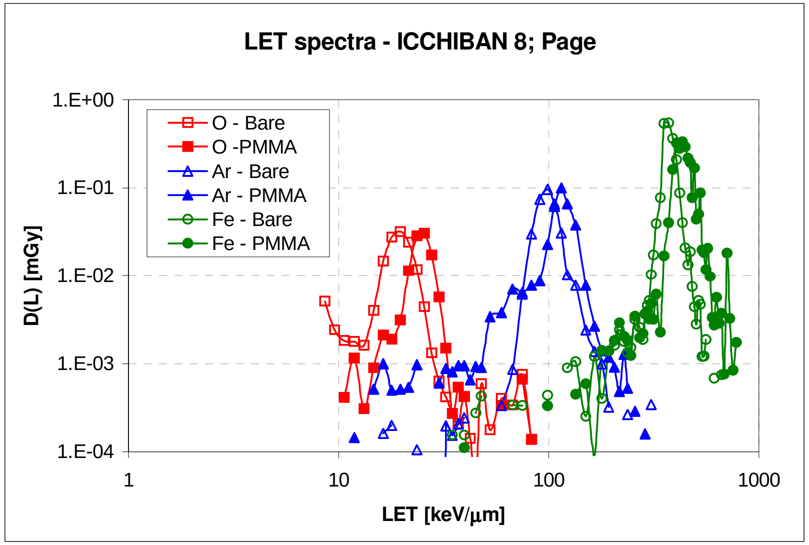


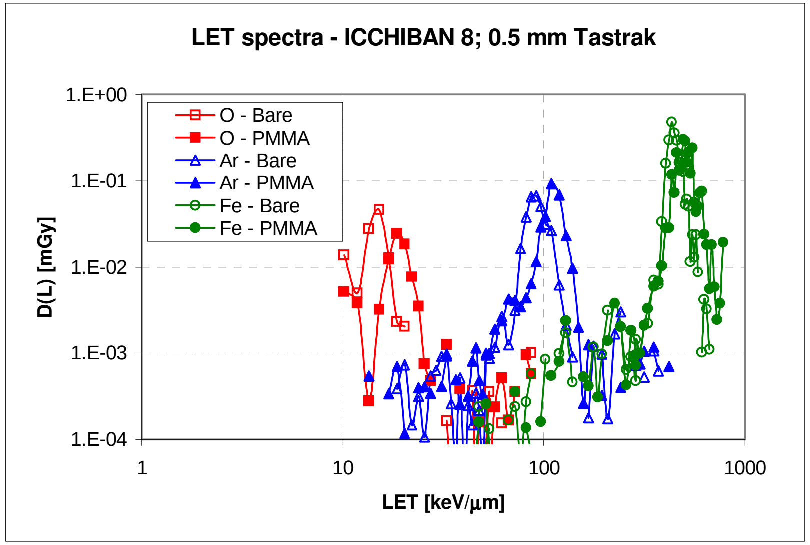
protons – Bragg peak

LET spectra for different ions: ICCHIBAN program at Brookhaven and/or Chiba



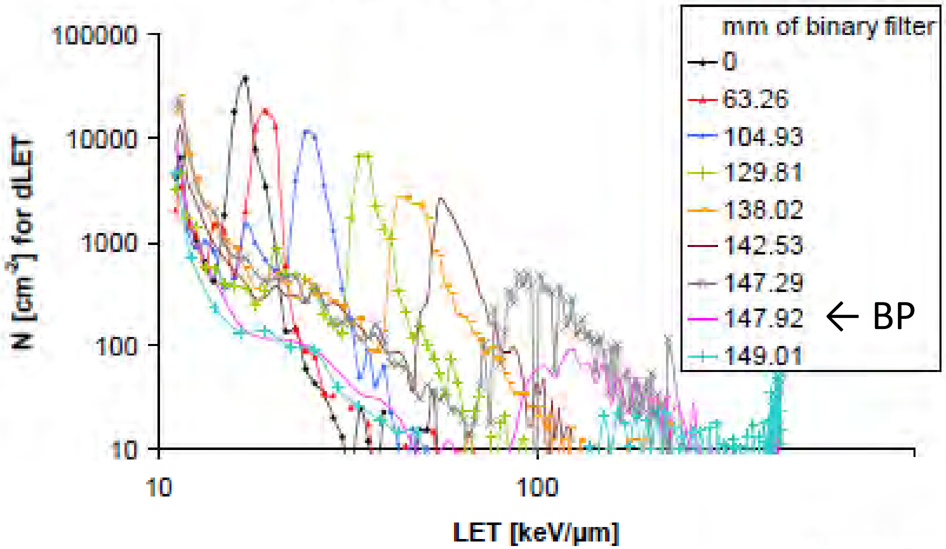




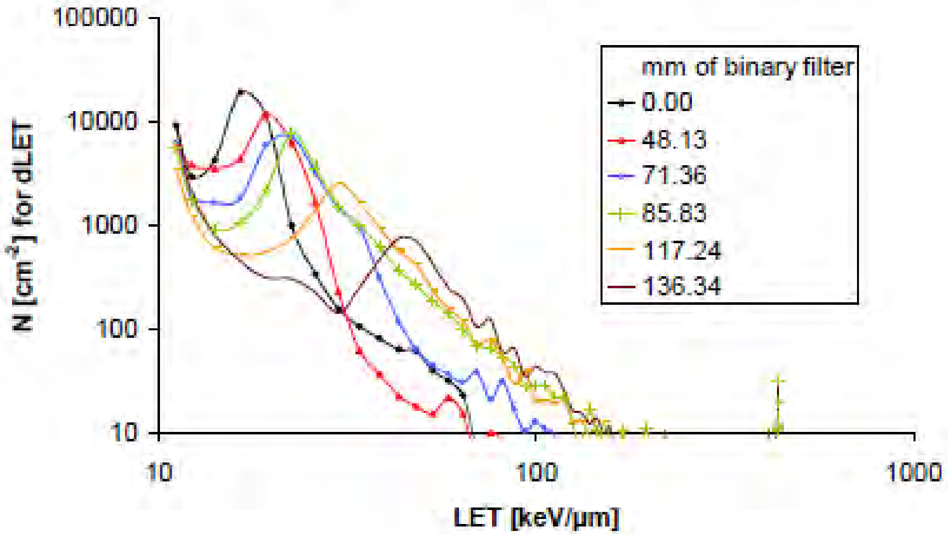


LET spectra for different positions in carbon beam at HIMAC, Chiba

C 290 MeV/amu: MONO



C 290 MeV/amu: SOBP



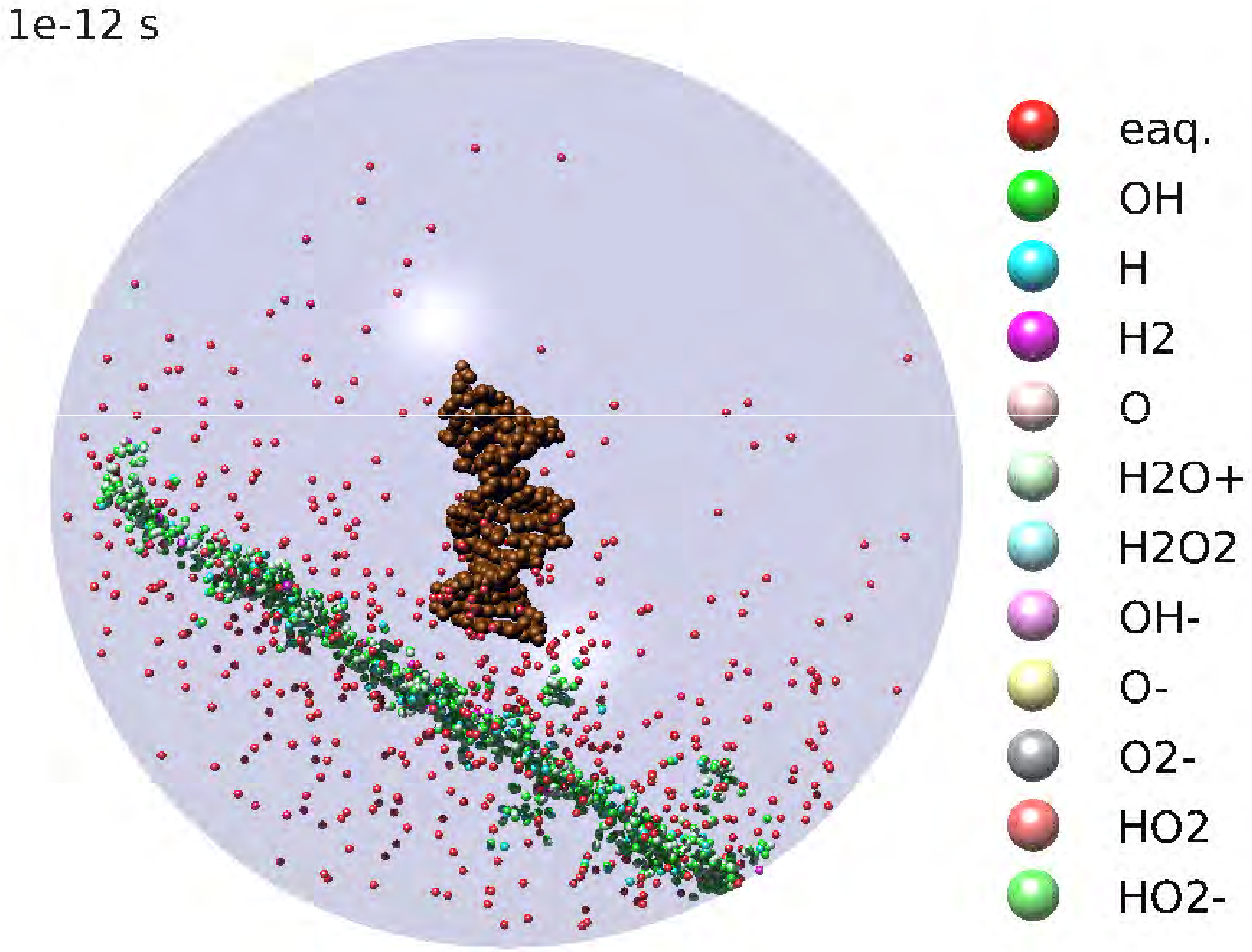
Theoretical MIKROdosimetry

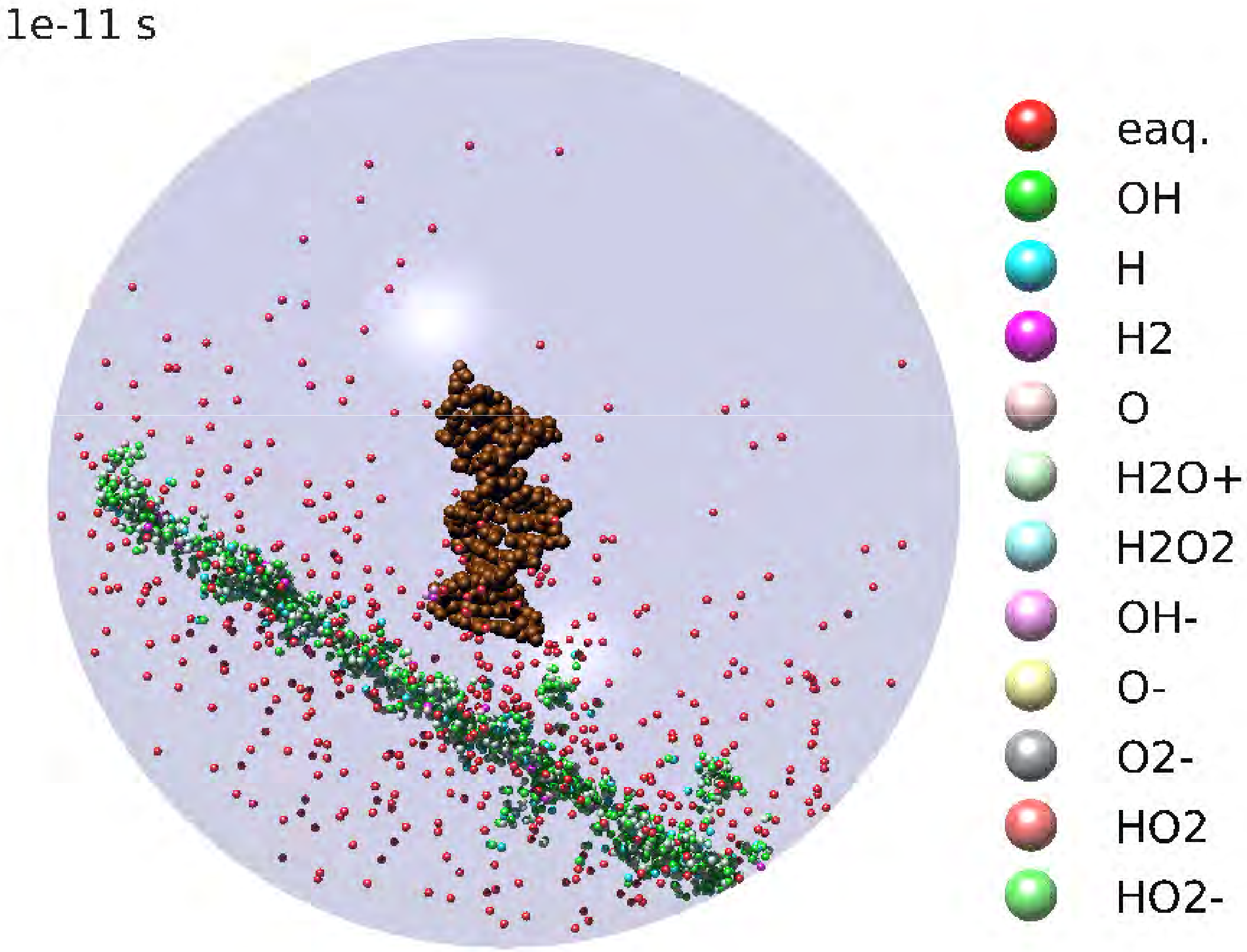
Standard method: generating particle tracks by Monte Carlo sampling using interaction cross sections

Code	Particles	Energy range	Medium	Last use
CPA 100	e-		l. w.	1990
DELTA	e-	e-: 0.3–1.5 MeV	g.w.	1983
PROTON	p	p: 0.3–1 MeV	g.w.	1983
ETRACK	e-, p, ?		g. w.	1985
Geant4	e-, p, ?	e-: 0.025 eV+	l. w.	2012
KURBUC	e-	10 eV–10 MeV	g. w.	1993
LEEPS	e-, e+	0.1–100 keV	m. m.	1996
LEPHIST	protons	1 keV–1 MeV	g. w.	2001
Liamsuwan et al.	protons	1 keV–300 MeV	water	2012
LEAHIST	?	1 keV/u–2 MeV/u	g. w.	2002
MC4	e-, p, ?	e-: ? 10–10^4eV ions: ? 0.3–10 MeV/u	l.+g. w.	2010
Notre Dame	e-, ions		l.+g. w.	
OREC, NOREC	e-, ions		l.+g. w.	
PARTRAC	?, e-, ions	e-: 10 eV–10 MeV p/?: 1 keV–1 GeV ions: 1–103 MeV/u	l. w.	2012
PITS04	e-, ions		l. w.	2004
PITS99	e-, ions		g. w./others	2012
Sherbrooke	e-, ions		l.+g. w.	2004
STBRGEN	e-, ions		l.+g. w.	
TILDA	ions, e-		g. w.	2005
TRION	e-, ions		g. w.	1993
TRIOL	e-, ions		l. w.	2012
TRACEL	e-, ions		l.+g. w.	
Gervais/Beuve	ions	C: 1–65 MeV/u	l.w.	2009

Adapted and extended according to Nikjoo et al. Radiation Measurements 41, 1052, 2006

Radiation damage to DNA

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eaq.
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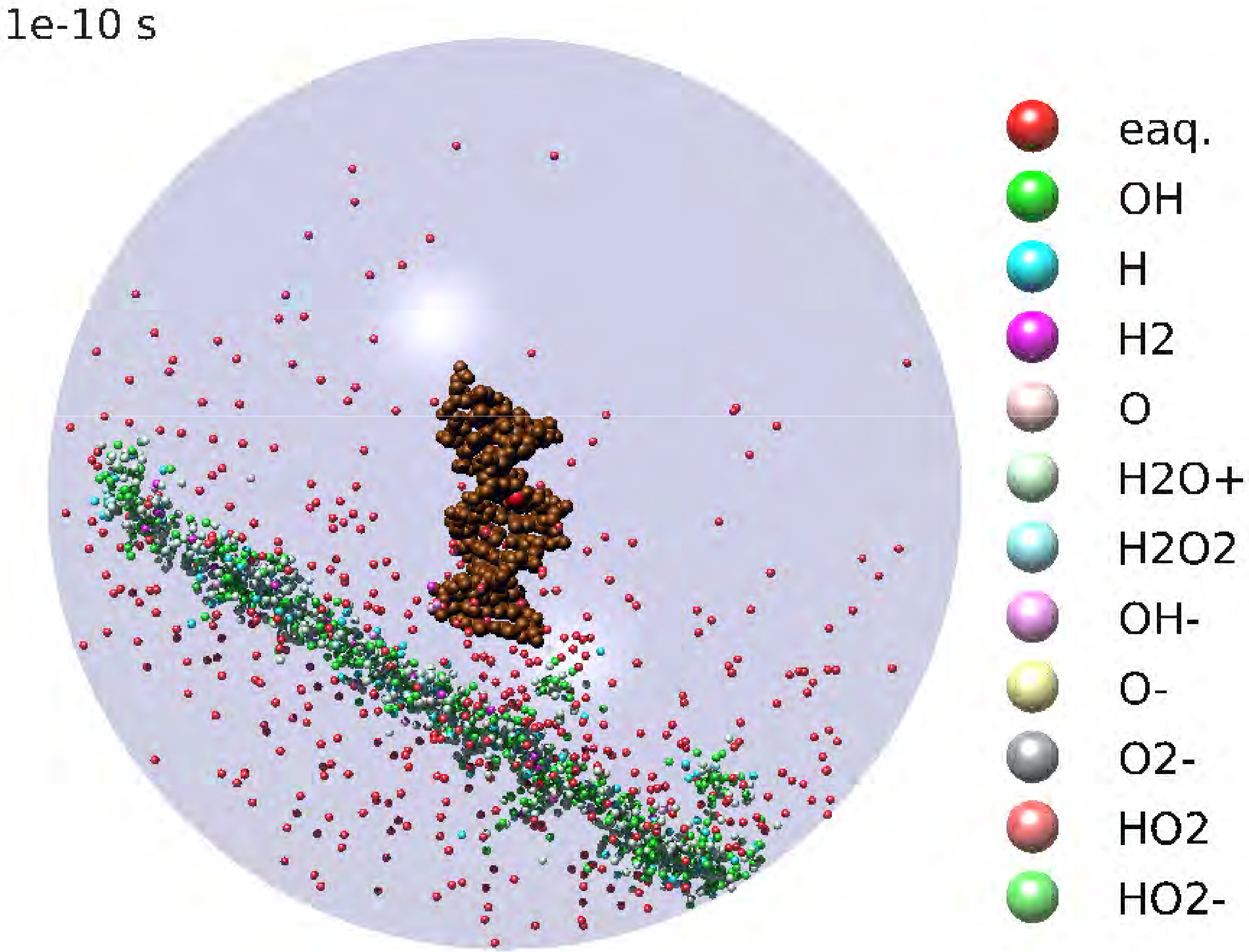
H
H2
O
H2O+
H2O2
OH-
O-
O2-
HO2
HO2-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O
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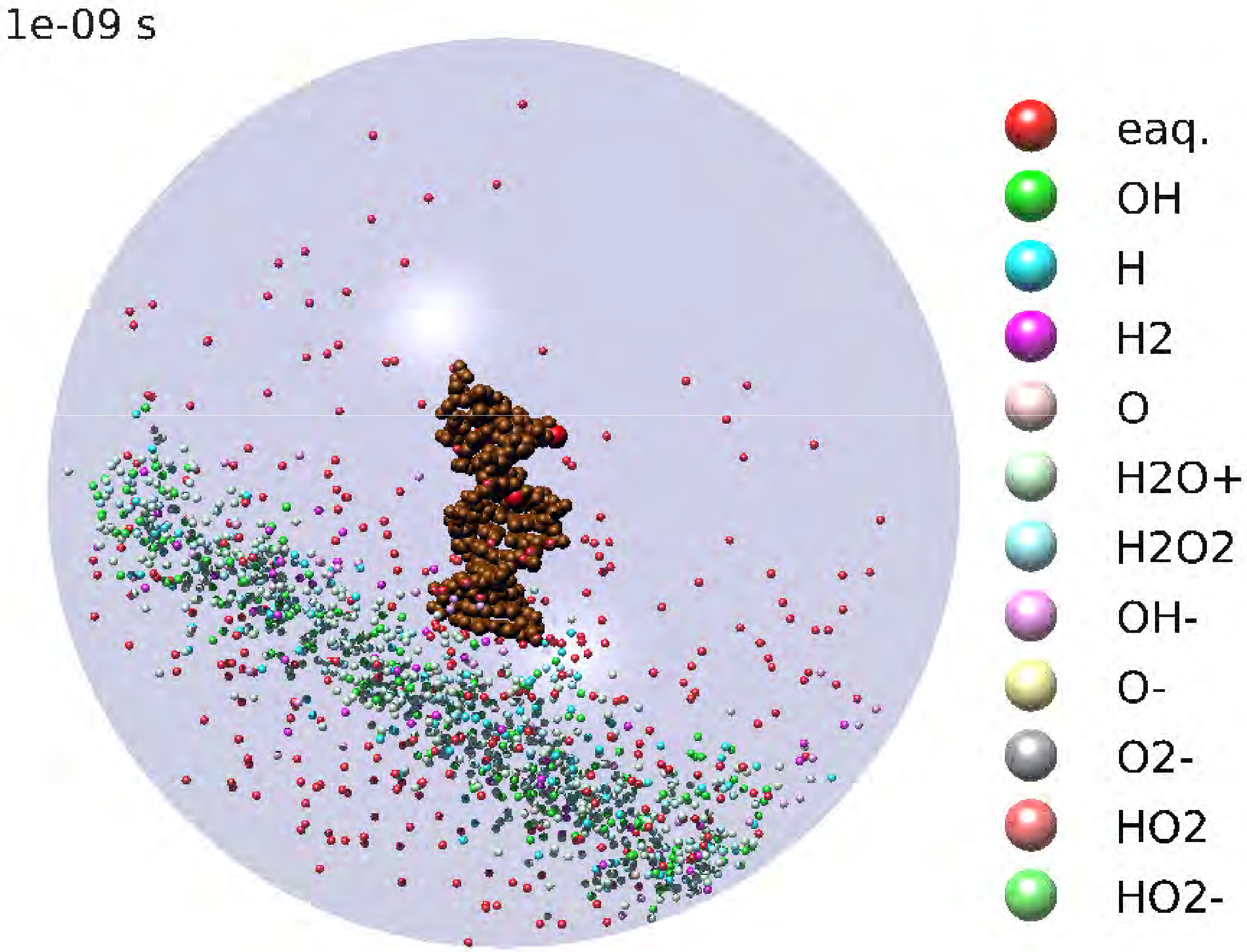
H2O2
OH-
O-
O2-
HO2
HO2-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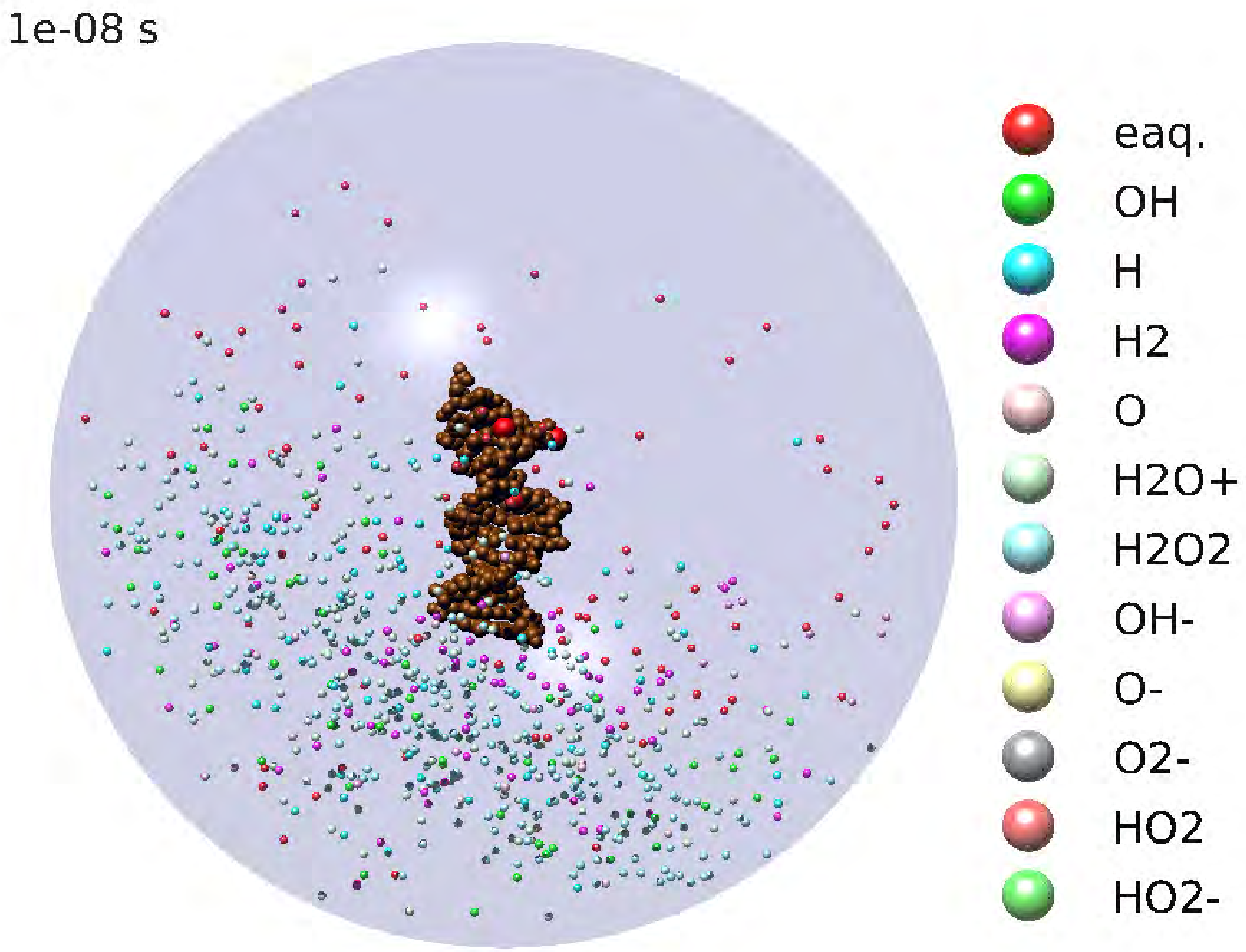
O
H2O+
H2O2
OH-
O-
O2-
HO2
HO2-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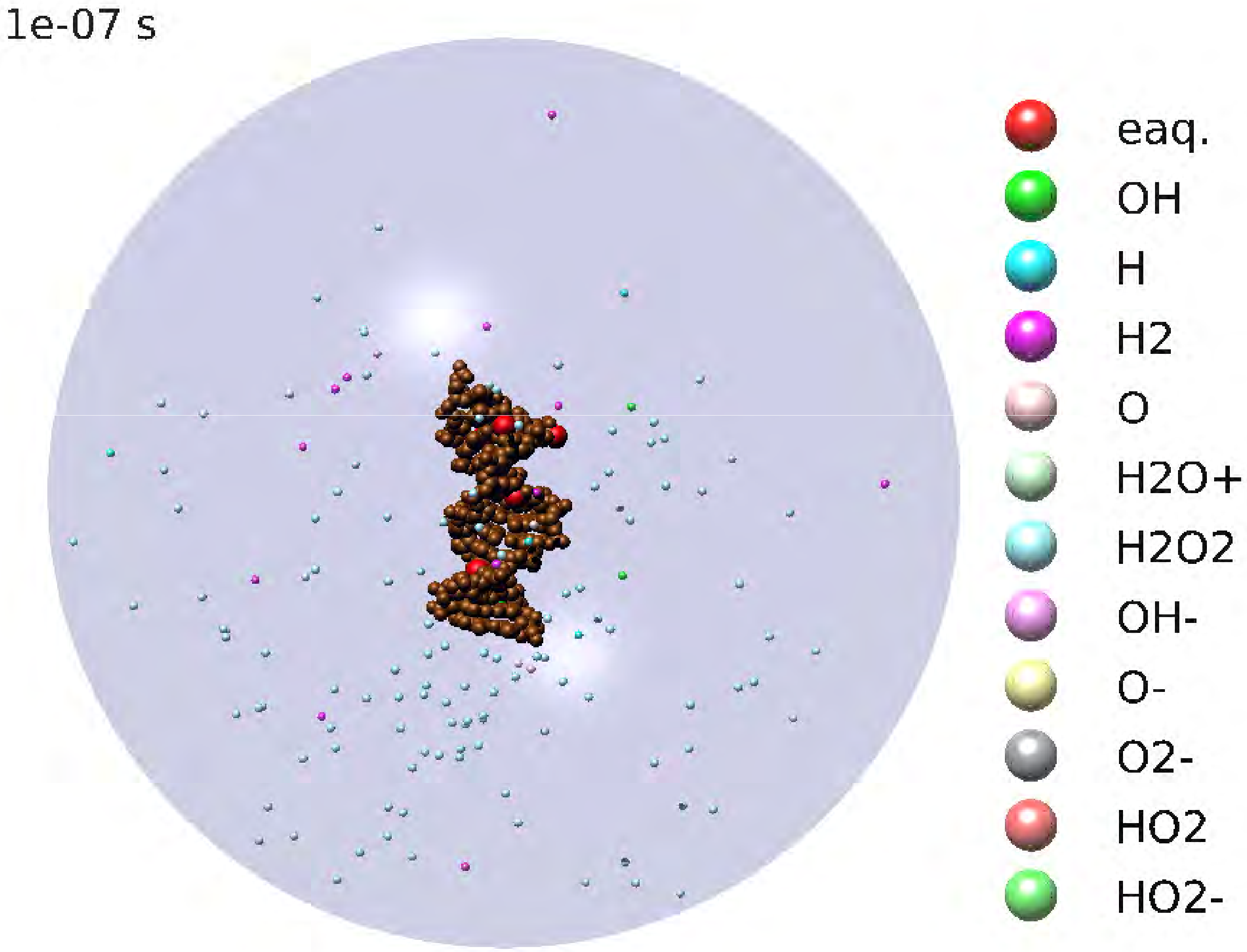
H2
O
H2O+
H2O2
OH-
O-
O2-
HO2
HO2-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H2
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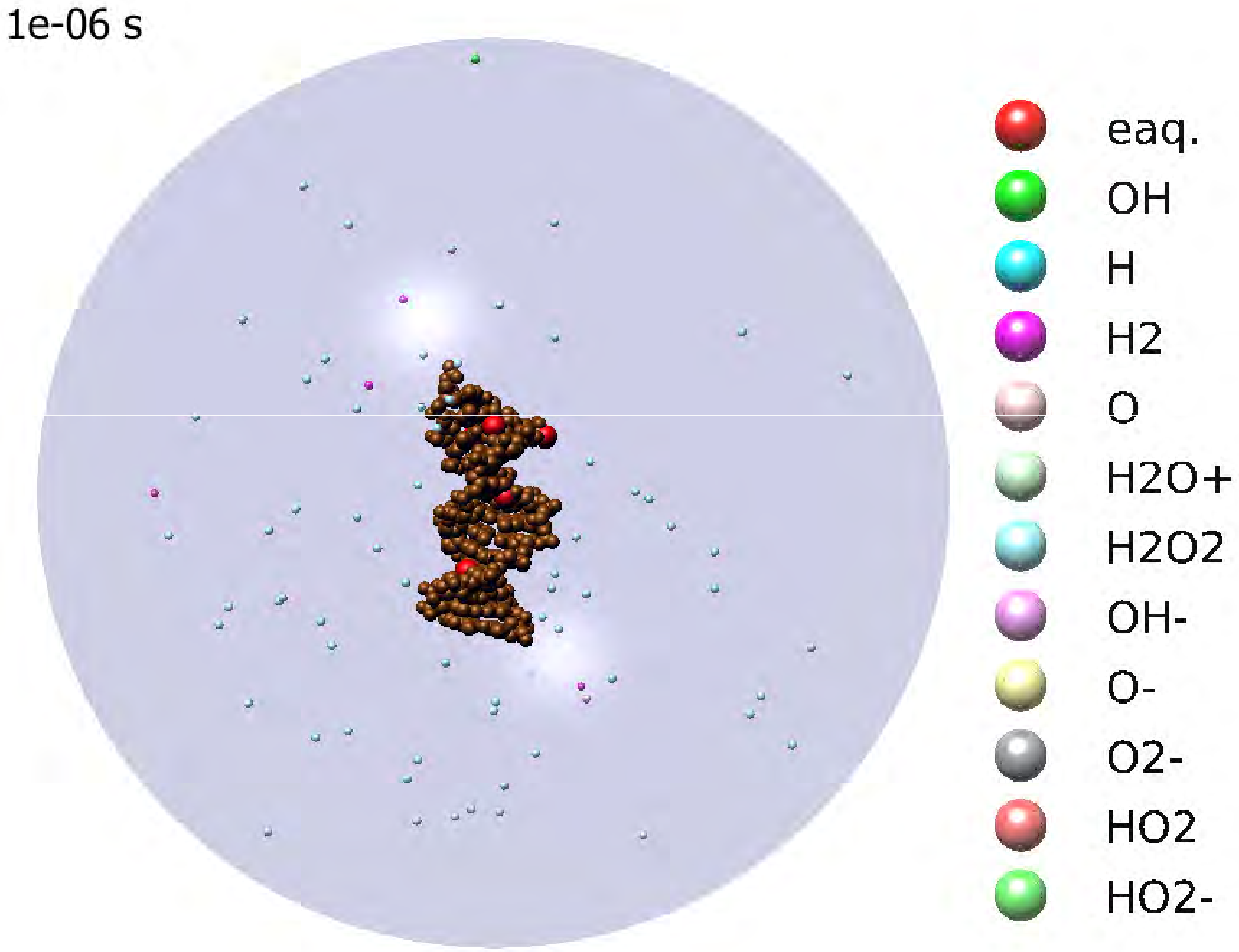
H2O+
H2O2
OH-
O-
O2-
HO2
HO2-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OH
H
H2
O
H2O+
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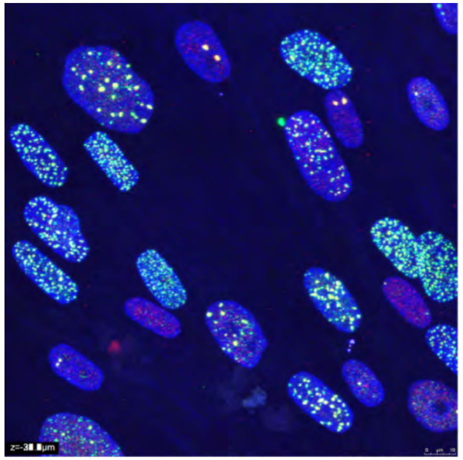
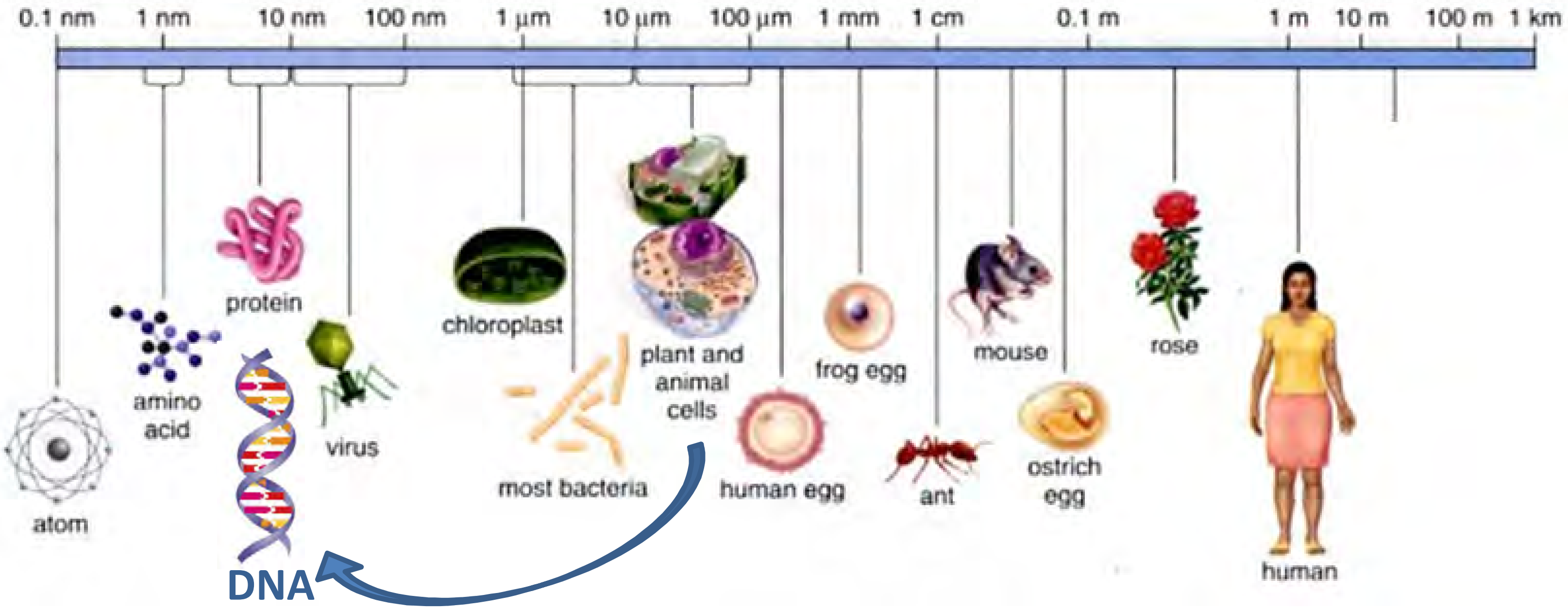
OH-
O-
O2-
HO2
HO2-

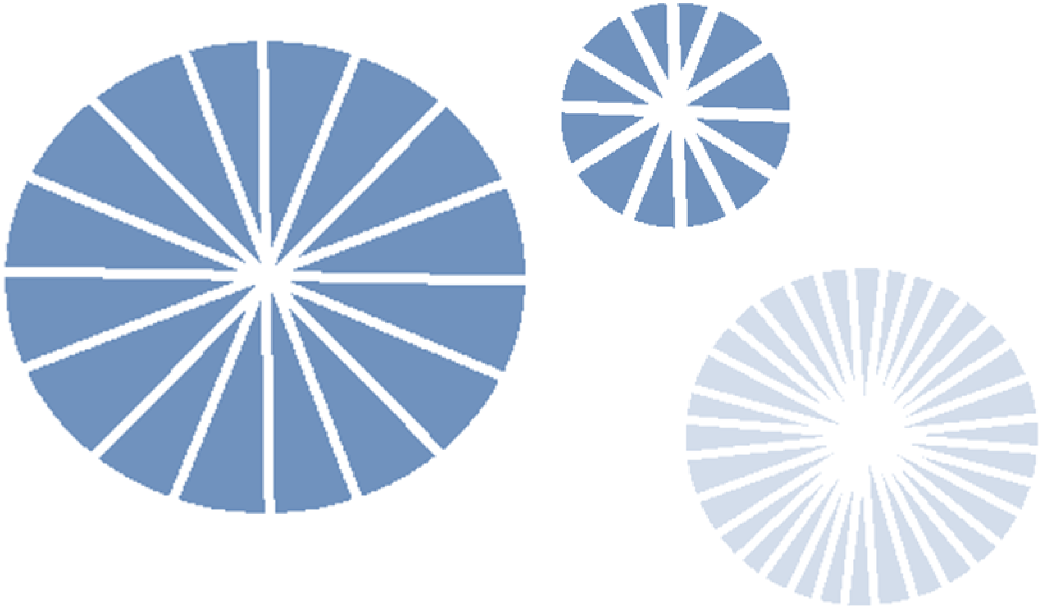
Perspectives in MIKROdosimetry

NANO

NANOdosimetry MIKROdosimetry







CONCLUSIONS

- MICRODOSIMETRY provides distributions of lineal energy, y, and specific energy, z, and thus detailed assessing of complex radiation environment such as:

- Therapeutic ion beams
- Radiation fields in accelerator proximity
- Radiation fields on board aircraft and spacecraft

- Focusing to nanometer region promise further applications of microdosimetry concepts → NANODOSIMETRY

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