From Macro to Nanodosimetry:

Limits of the Absorbed Dose Concept and Definition of New Quantities

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The "Golden Rule" of Conventional Applied Radiation Physics

Radiation effects in matter can be described by macroscopic quan-tities like absorbed dose or *LET*

- *Radiation Biology*
- *Radiation Therapy*
- *Radiation Protection*

Experimental Tools:

Ionization chambers, solid state detectors,

Numerical Tools:

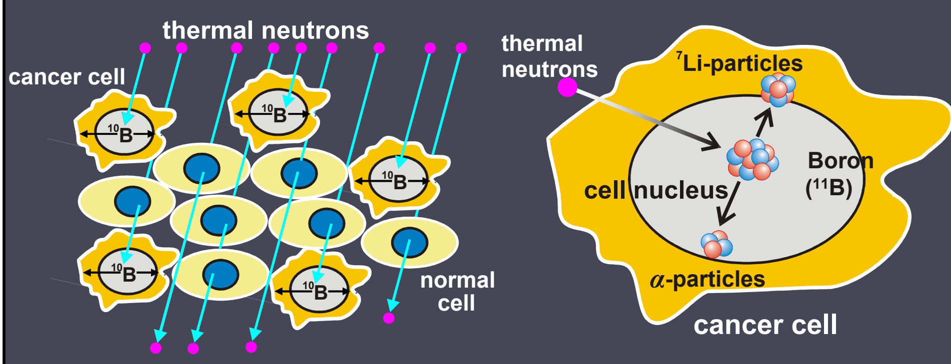
Condensed history MC-models

One Weakness of Absorbed Dose:

Creation and stopping of short-range particles in the cell nucleus

A typical example:

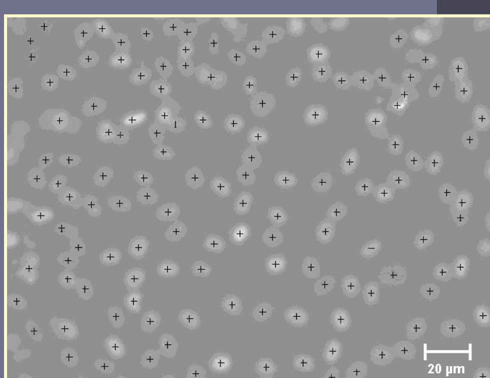
Boron Neutron Capture Therapy **(BNCT) with thermal neutrons**



The stopping of the particles in the cell nucleus leads to a very high energy density which cannot be described by conventional dosimetric procedures.

Radiobiological Experiments Using a Microbeam Facility

Radiobiological experiments are interpreted conventionally in terms of absorbed dose:



$$D = \frac{\Delta E_{cell}}{m_{cell}}$$

here, Δ*E* is calculated and *m* is estimated

The "True" Target Volume of Radiation Physics

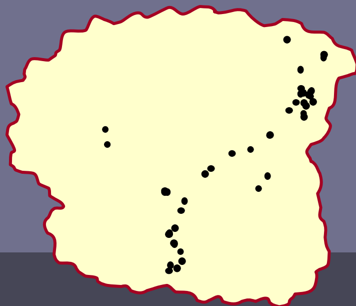
The real target volumes of radiobiology and, therefore, also of radiation physics are the volumes of sub-cellular structures

Radiation Damage to Genes or Cells Starts with the Initial Damage to Segments of the DNA

Radiation damage strongly depends on particle track structure

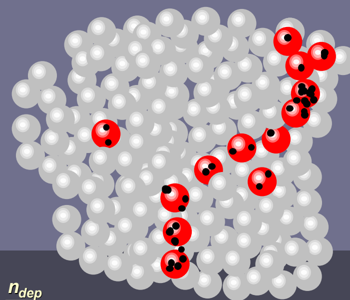
The Breakdown of the Absorbed Dose Concept in Nanometric Target Volumes

Macroscopic Targets:



$$D_{macros} = \frac{\sum_{i=1}^{n_{dep}} \varepsilon_i}{m}$$

Nanometric Targets:

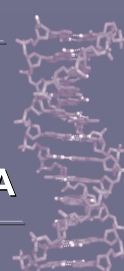


$$D_{micros} = \frac{\sum_{i=1}^{n_{dep}} \varepsilon_i}{n_{hit} \Delta m} : \quad \text{If} \quad m = N \times \Delta m,$$

$$D_{micros} = \frac{N}{n_{hit}} \times \frac{\sum_{i=1}^{n_{dep}} \varepsilon_i}{m}$$

Nanometric Target Volumes, a Challenge to Current Radiation Dosimetry

The greater part of radiation damage to genes or cells starts with the initial damage to segments of the DNA



The Problem: A transition from macroscopic target volumes to those of sub-cellular structures requires a change of physical quantities!

The Hypothesis: The damage to DNA segments is determined to the greater part by ionizing processes

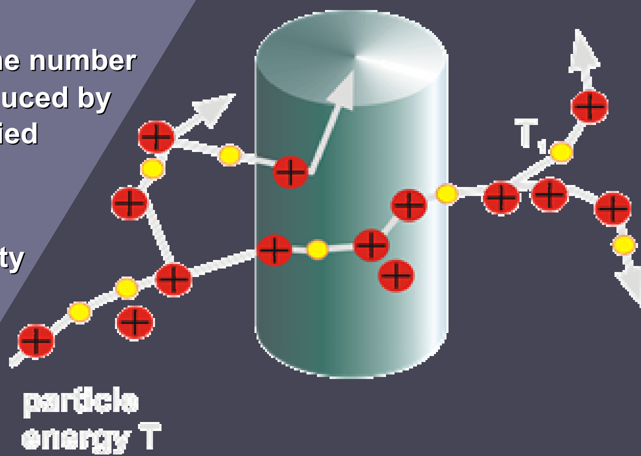
The Idea of Experimental Nanodosimetry

- ► Ionization cluster-size formation in nanometric cylindrical volumes of liquid water is represen

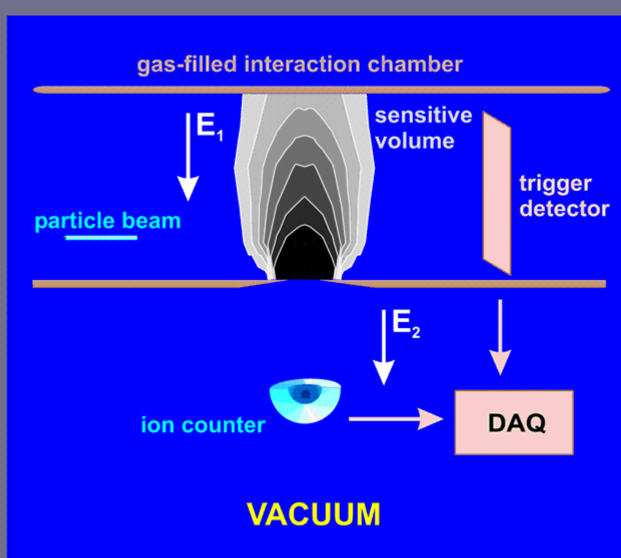
__Definitions:__

The cluster size is the number ν of ionizations produced by a particle in a specified piece of matter.

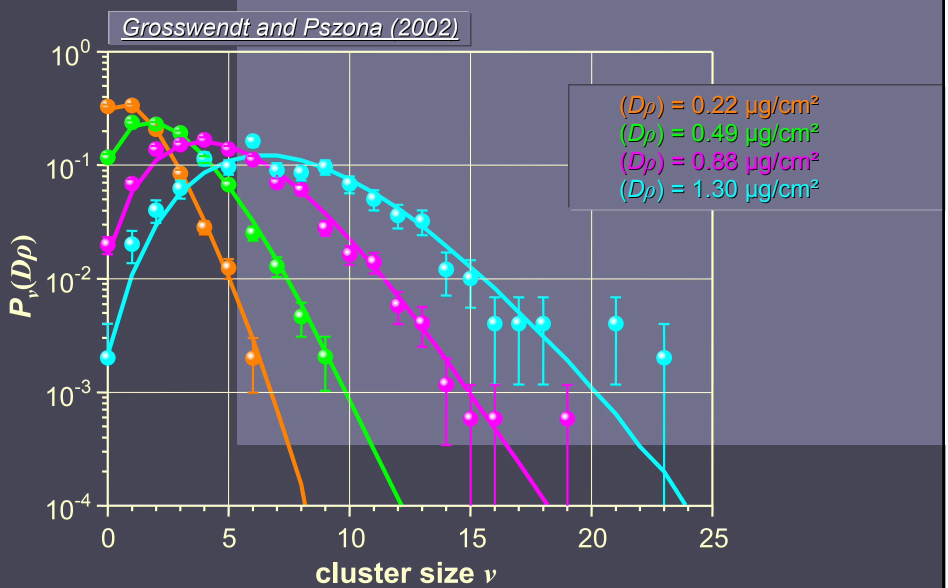
$P_\nu(T)$ is the probability of producing an ionization cluster of size ν.



Principle of a Nanodosimetric Measuring Device Based on Single-ion Counting

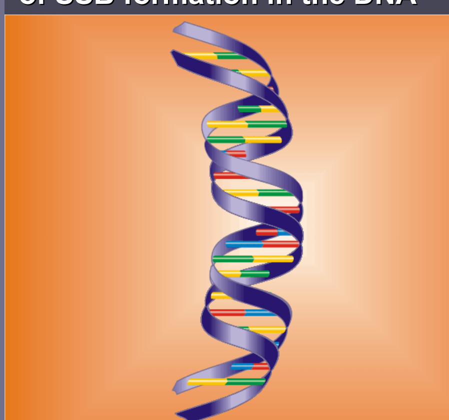


Ionization Cluster-size Distributions of 4.6 MeV α-Particles in Nitrogen



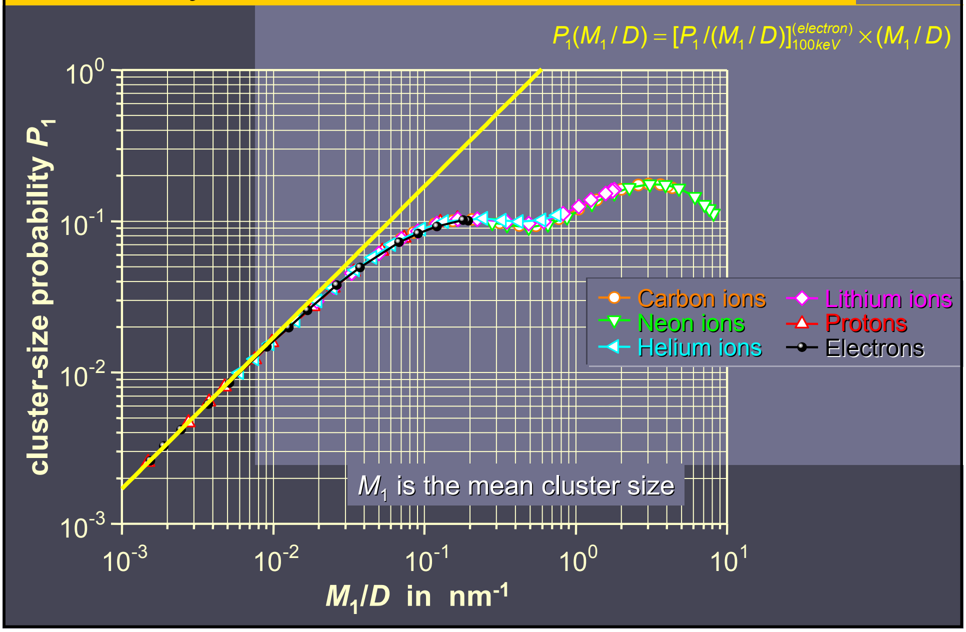
The Relation Between Ionization Cluster-size Formation and Radiation Biology

The probability P_1 to create a cluster size $\nu = 1$ should be proportional to the probability of SSB formation in the DNA

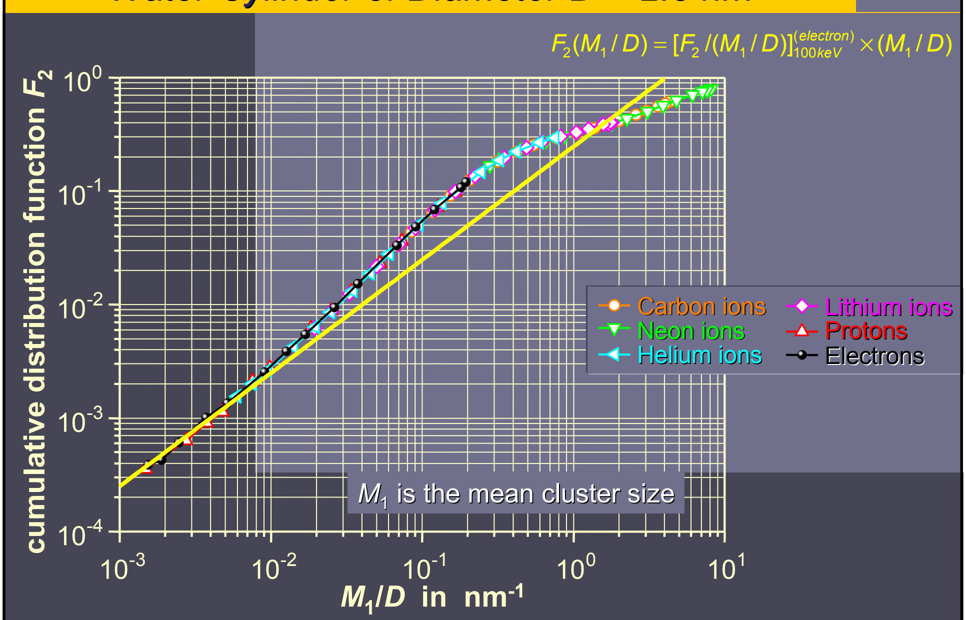


The probability F_2 to create a cluster size $\nu \geq 2$ should be proportional to the probability of DSB formation in the DNA

Cluster-size Probability P_1 in a Liquid Water Cylinder of Diameter D = 2.3 nm



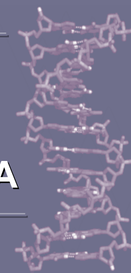
Cumulative Distribution Function F_2 in a Liquid Water Cylinder of Diameter D = 2.3 nm



Nanodosimetry, the Missing Link Between Radiation Physics and Radiation Biology ?

PTB

The greater part of radiation damage to genes or cells starts with the initial damage to segments of the DNA

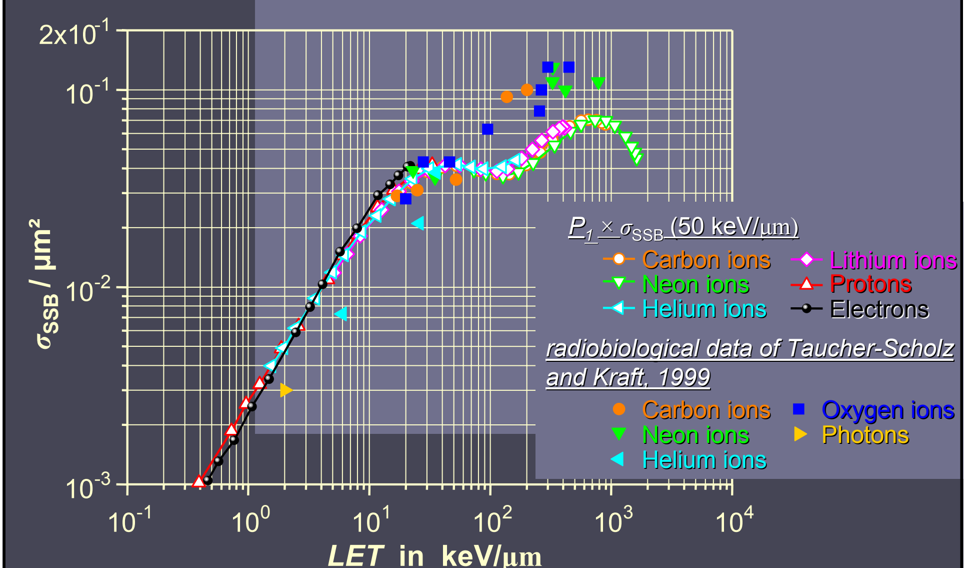


Radiation Quality: The natural nanodosimetric parameters to describe the radiation quality of ionizing particles are the probabilities P_1 and F_2

The Hypothesis: The cluster-size probabilities P_1 and F_2 are directly correlated with the damage to DNA

Cross Section of Single-strand-break Formation of SV40 Viral DNA

PTB



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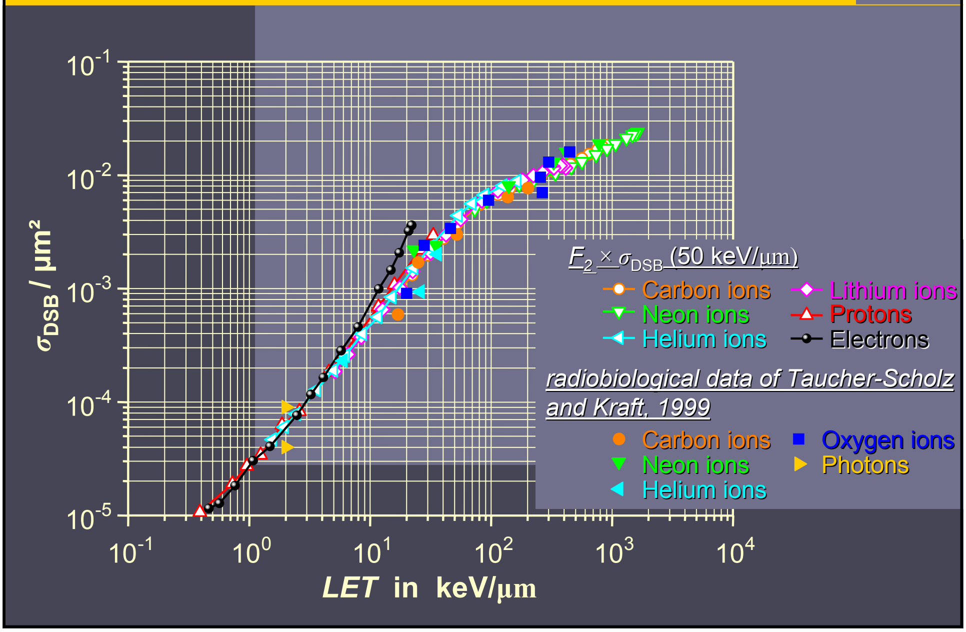
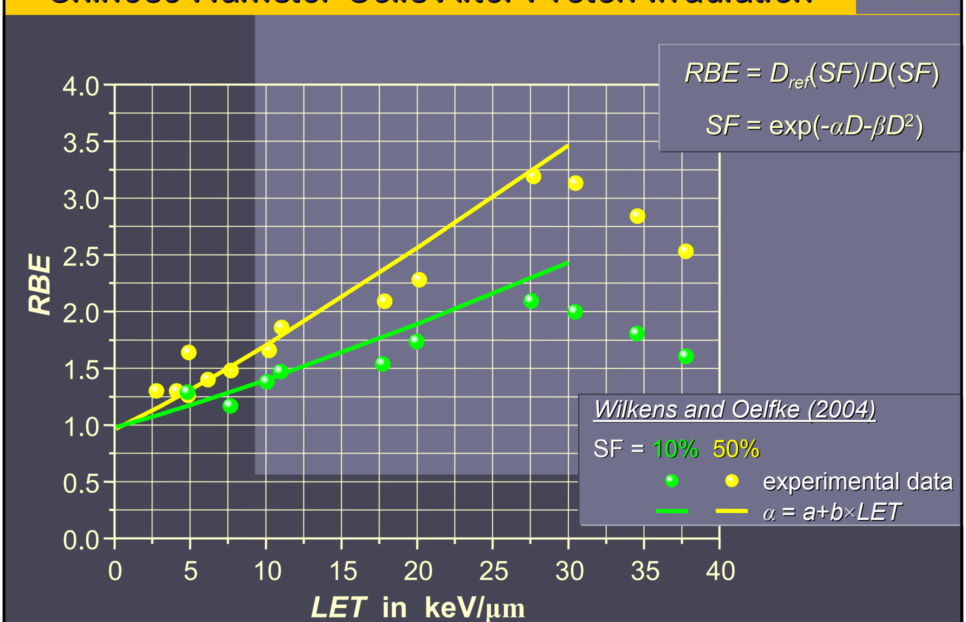
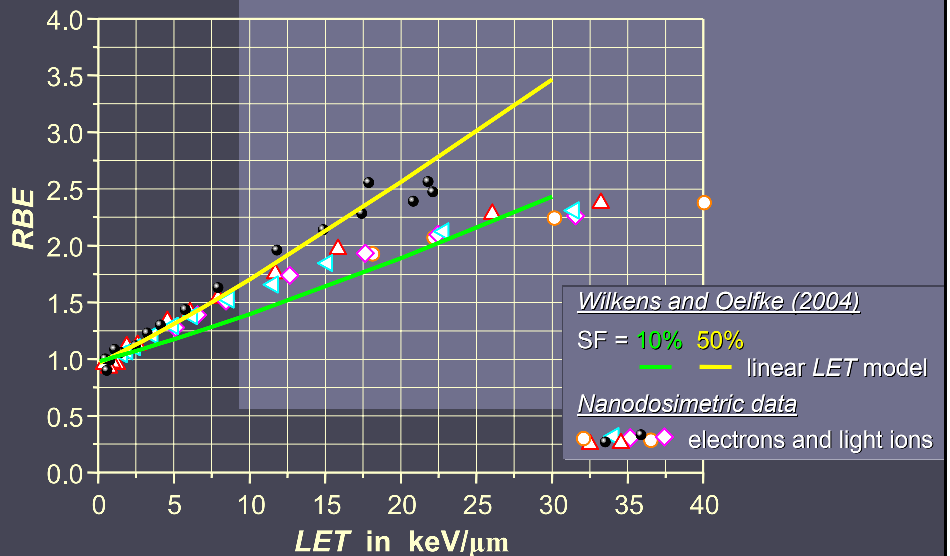


Radiobiological Effectiveness: Survival of V79 Chinese Hamster Cells After Proton Irradiation



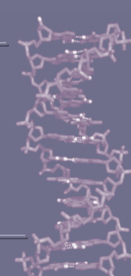
Radiobiological Effectiveness: Survival of V79 Chinese Hamster Cells After Proton Irradiation

$$RBE = \left[F_2^{(particle)}(T) / M_1^{(particle)}(T)\right] / \left[F_2^{(electron)}(100keV) / M_1^{(electron)}(100keV)\right]$$



From Macro to Nanodosimetry: The absorbed-dose concept breaks down in nanometric target volumes

The probabilities P_1 and F_2 of ionization cluster-size distributions are strongly related to the initiation of radiation damage to the DNA



Vision of the Future:

Absorbed dose will be exchanged or, at least, supplemented by nanodosimetric quantities