Measurement and Simulation of the Microscopic Energy Deposit: A general approach applicable to Ionizing Radiation Sources of varying Linear Energy Transfer.

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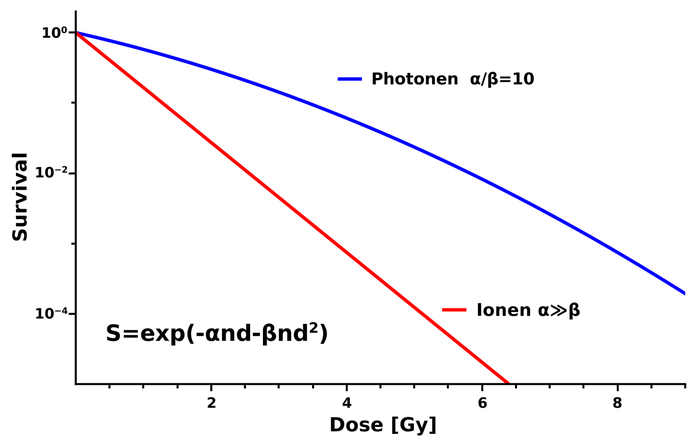
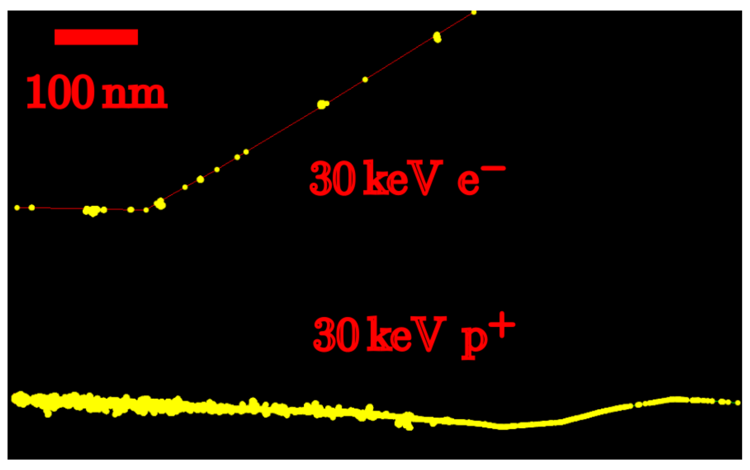
Motivation

Damage to DNA: one of the main causes for cancer. Radiation therapy is main tool to cure cancer. Obtain a better understanding of the relation between tumor survival and radiation interactions to improve therapies
In radiation therapy cell survival is estimated by an empirical model:



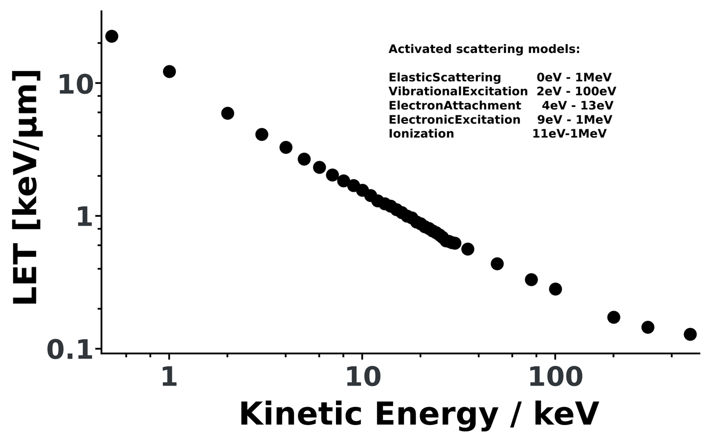
How is this model connected to the scattering events at the microscopic level?



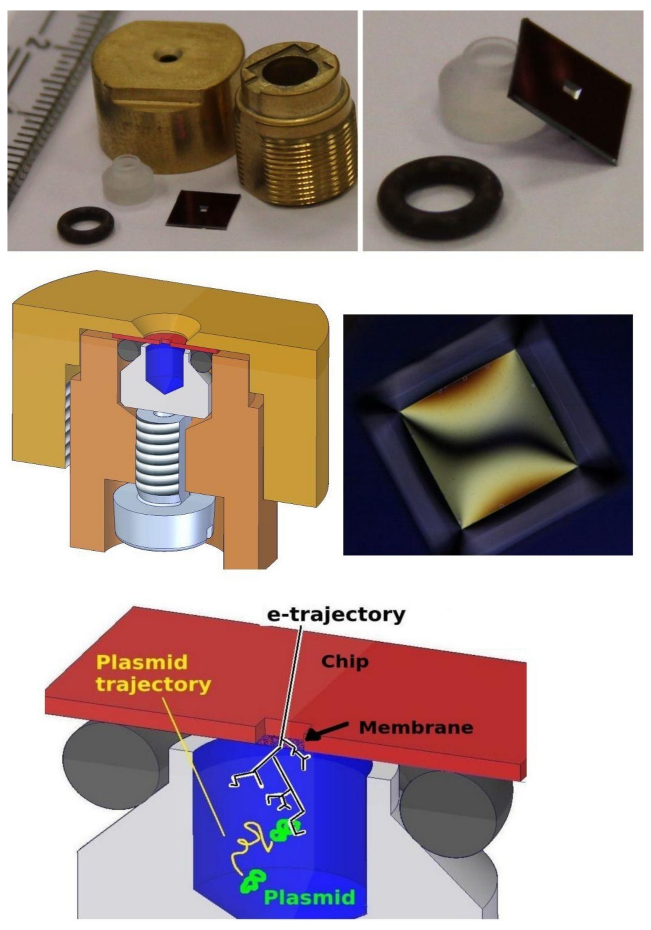
The linear energy transfer (LET) of radiations depens on type and kinetic energy of the particles.

Electron irradiation of liquids

Electron microscopes provide a unique possibility to irradiation a sample within the same experimental setup with radiation of different linear energy transfer:



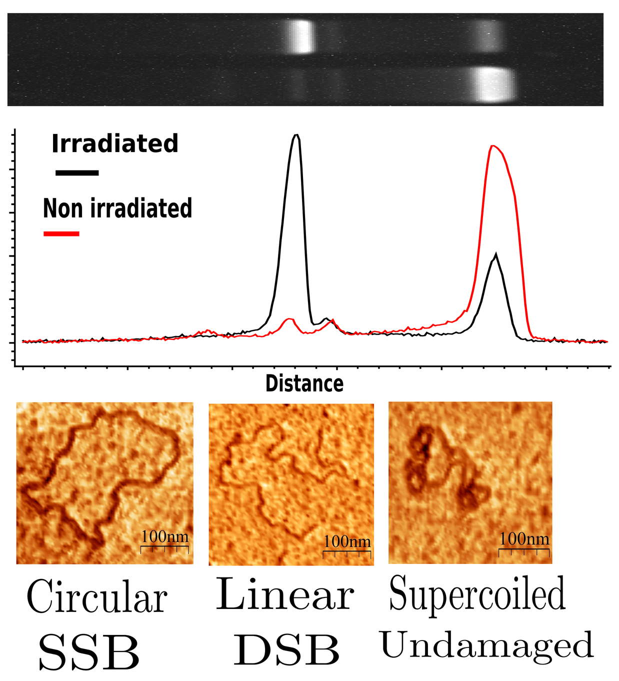
Therefore a sample holder including a 100 nm thick silicon nitride membrane was constructed which is transparent for keV electrons and separates water and vacuum.[2]



Plasmid DNA (pUC19) in water and PBS was directly irradiated by electrons.

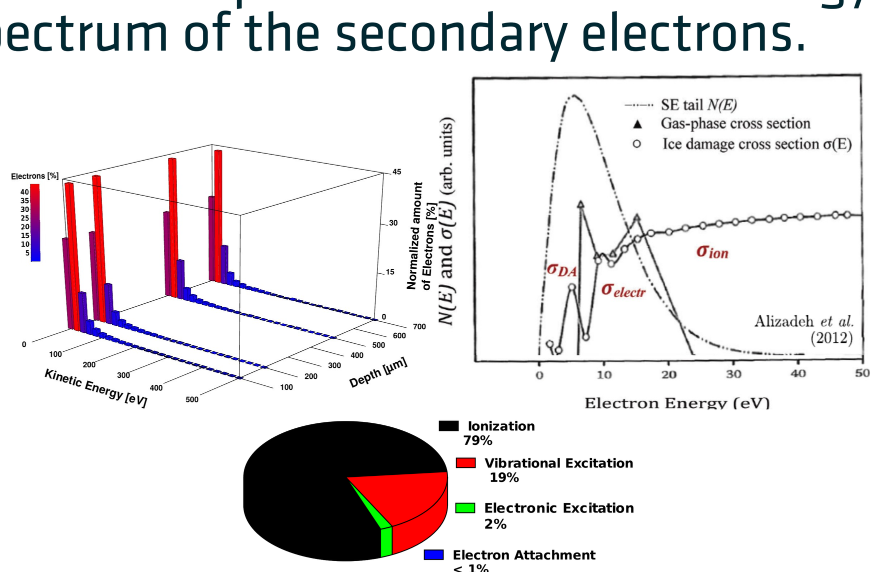
Damage determination

Agarose gel electrophoresis separates plasmid DNA in dependence of its conformation which is related to DNA strand breaks.



Secondary species

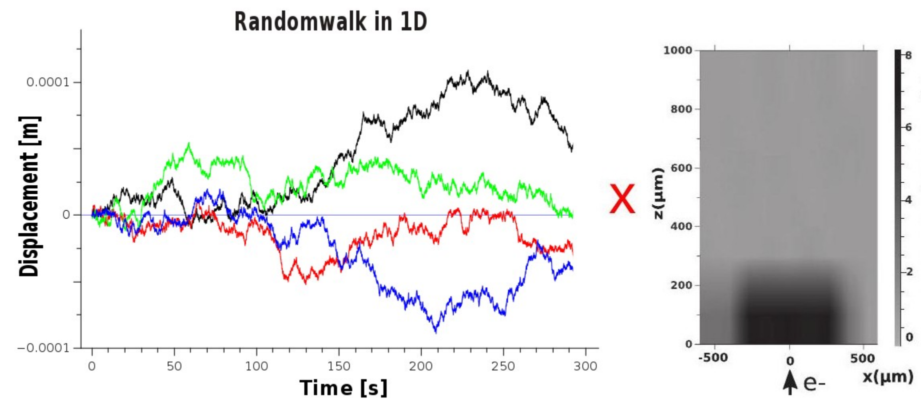
The production of OH-radicals and electrons depends on the kinetic energy spectrum of the secondary electrons.



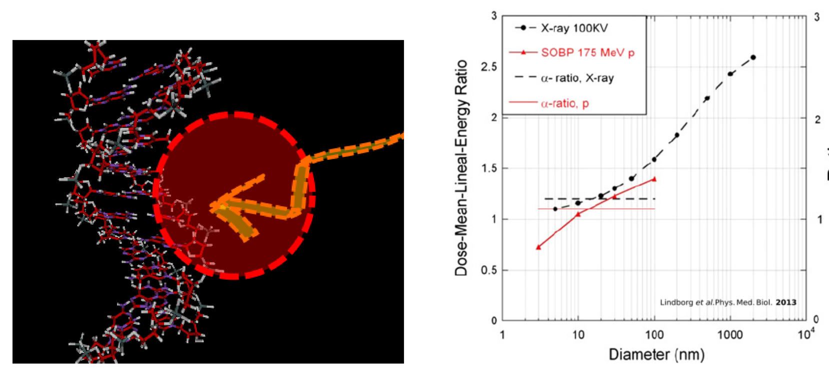
For low LET 30 keV electrons the production ratio of $OH:e^-$ becomes 1:1.

Microscopic dose-damage relation

The electron trajectories, kinetic energy distribution, inelastic scattering events and the resulting energy deposit within water were simulated. The diffusion induced movement of the plasmids was simulated as a random walk within the boundaries of the sample holder geometry.
The combination of electron scattering and plasmid diffusion simulations leads to the determination of energy deposit in the vicinity of the individual irradiated molecule[1].

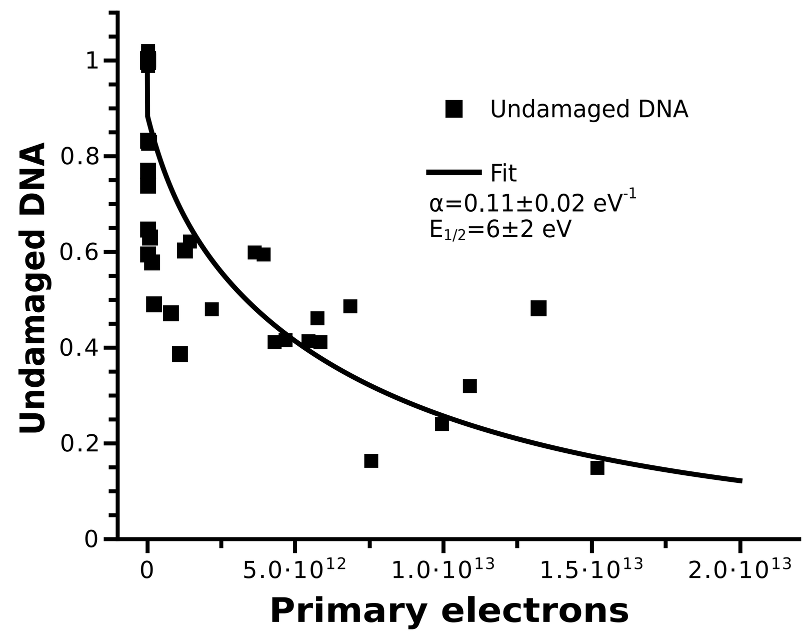


A microscopic target model for the plasmid DNA based on the relation of lineal energy and radiation quality was used to calculate the effective target volume.[2, 3]



In combination with the experimental results and a damage model based on target theory, the event-damage relation was calculated.[1]

$$S = \sum_{i=0} S_i = \sum_{i=0} N_i e^{-\alpha x E_i(V)} \quad (1)$$



The median lethal energy deposit for plasmid DNA pUC19 under electron irradiation in pure water becomes $E_{1/2}^{total} = 6 \pm 2\,eV$.

Results

- **Radiation of different LET can be produced by a single electron microscope**
- **Microscopic energy deposit and events can be determined for arbitay radiation sources**
- **For plasmid DNA in water median lethal dose was determined as 6±4 eV**
- **Arbitary experimental radiation sources and geometries can be simulated due to the fexibility of the Geant4 framework**
- **Low LET electrons: Production of $OH:e^-$=1:1**

[1] Marc Benjamin Hahn, Susann Meyer, Hans-Jörg Kunte, Tihomir Solomun, and Heinz Sturm. Measurements and simulations of microscopic damage to DNA in water by 30 keV electrons: A general approach applicable to other radiation sources and biological targets. *Physical Review E*, 95(5):052419, May 2017.

[2] Marc Benjamin Hahn, Susann Meyer, Maria-Astrid Schröter, Harald Seitz, Hans-Jörg Kunte, Tihomir Solomun, and Heinz Sturm. Direct electron irradiation of DNA in a fully aqueous environment. Damage determination in combination with Monte Carlo simulations. *Physical Chemistry Chemical Physics*, 19(3):1798–1805, January 2017.

[3] L. Lindborg, M. Hultqvist, Å Carlsson Tedgren, and H. Nikjoo. Lineal energy and radiation quality in radiation therapy: Model calculations and comparison with experiment. *Physics in Medicine and Biology*, 58(10):3089, 2013.