# DNA Double Strand Breaks in Mammalian Cells Exposed to $\gamma$ Rays and Heavy Ions ◇

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The most commonly observed damage to cells following irradiation is the presence of base damage, single- and double-strand breaks (DSB) in the DNA. Cells react to these lesions in various ways, depending on the severeness of the damage. This includes complete repair of the damaged DNA, mutation resulting from misrepair, or the death of the cell.

In the view of the growing interest in the particular action of ions on cells in medicine and space research, the determination of the distribution of DNA fragments is an important tool to characterise the biological effects. The measurements employ the pulsed field gel electrophoresis (PFGE) technique. It has been shown earlier that exposure to $\gamma$-rays produces distributions of DNA fragment lengths that are in accord with a uniform statistically independent distribution of DSB, i.e. the distribution of DNA fragments resulting from sparsely ionising radiation such as $\gamma$-rays is predictable in terms of a random breakage model.

Exposure to heavy ions results in substantially overdispersed distributions, which indicates that the fragmentation of the DNA is not a statistically independent process. Heavy ions induce multiple, spatially correlated damage sites on the DNA strand. Various measurements were performed recently with densely ionising radiations by different authors, but there are very few data in the intermediate LET range.

To meet this lack of information human fibroblast were irradiated at the vertical beam-line facility using protons,alpha-particles and carbon ions. The calculated LETs were 2.5 keV/$\mu$m, 21 keV/$\mu$m and 251 keV/$\mu$m. The DNA is extracted out of these cells and put into a pulse field gel, in order to measure the length distribution of the DNA fragments after the irradiation. An extention of the range of measurable fragments sizes has been achieved by using a renormalisation technic: A known amount of unit length DNA was added to the DNA of the irradiated cell in order to create a artifical peak in the fragment size distribution which can be used to scale and normalise the distribution and different types of PFGE are linked. The measured range was extended from 50 kbp - 5 Mbp to 3 kbp - 5 Mbp.

Since the random breakage model (RBM) is not appropriate to describe fragment size distributions obtained at the vertical beam-line facility a new simulation technic was developed using analytical radial dose distribution models and a model of the DNA distribution in an interphase cell nucleus (fig. 1).

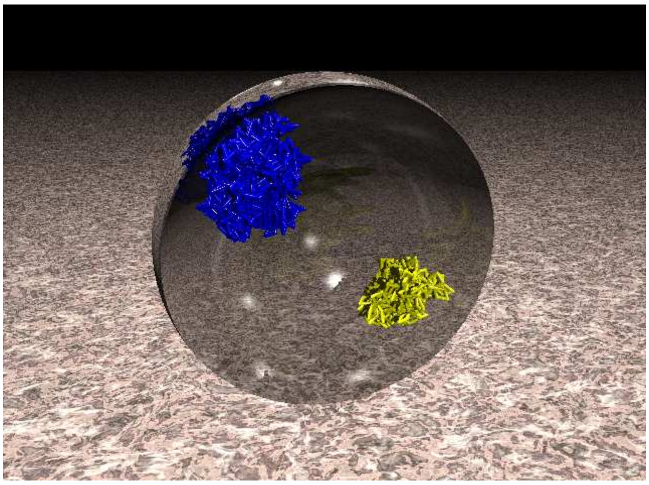

Fig. 1: Interphase cell nucleus - two chromosomes modelled by using the Multi Loop Sub-compartment Model(MLS)

By application of a dose dependent mixed Poisson process fragment size distribution were calculated and fitted to the measured data (fig. 2).

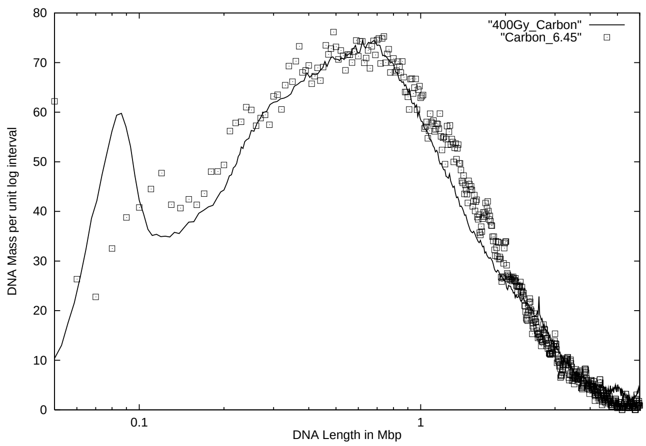


Fig. 2: Measured DNA-spectra (thick line) after irradiation of human fibroblasts with 5.9 Mev/amu Carbon ions. The dots represent the best fitted model using the radial dose distributions by Chatterjee and the MLS Model. The peak at small fragment sizes represents marker DNA.

The initial findings are presently beeing extended by further investigations and computations.

## References

[1] A. M. Kraxenberger, Verbesserungen der Methoden zur Pulsfeld-Gelelektrophorese und Anwendung der Technik auf de Analyse von DNA-Schäden durch dicht ionisierende Strahlung, Ph.D. thesis, 1995

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