



Monte Carlo Simulation of Damage in DNA Produced by Direct Radiation Impact

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1. Introduction

When ionizing radiation interacts with the cell nucleus, it produces damage or a cluster of strand breaks as a consequence of a complicated set of physical, chemical and biological processes that can result in a single strand break (SSB), clusters of DNA strand breaks or changes in nitrogenous bases. The in-depth study of these effects is necessary, because even if they happen at distant points in the DNA chain, they can cause deleterious effects in the cell. As examples of the latter, we can mention mutations, chromosomal aberrations, cell inactivation and alteration of genome integrity. In recent years, important advances have been made in the development of biophysical models that facilitate the ability to predict the relationship between the intensity of irradiation measured by dose and the biological response observed, more specifically, in the case of the effects of low doses on DNA and the subsequent processes that can trigger the onset of cancer. The objective of this work is to simulate the size distribution of fragments and clusters in the DNA originated by the direct interaction of ionizing radiation through the microscopic calculation of traces, implementing routines using the Monte Carlo method[1].

2. Methodology

The spectrum of all possible radiation-induced DNA damage (on the order of 360 if we consider the different configurations of base damage, strand breaks, etc.[1]) can be divided into two large sets: simple lesions and complex lesions. The first group includes those DNA damage that can be repaired, regardless of the existence or not of other injuries: single strand breaks (SSB), damage to single bases and some damage that generates clusters in certain regions of the DNA. Complex injuries, on the other hand, can generate irreparable or potentially repairable damage, whether lethal or not. DSBs are typical cases of this type of lesion: two ends of two different DSBs can recombine and generate a chromosomal aberration that may or may not be lethal. Alternatively, a DSB can misconnect to another non-homologous endpoint, generating a point mutation.

The calculation was implemented by combining the results obtained from the dielectric formulation for the mean free path [2] with the fast Monte Carlo simulation algorithm (MCDS) proposed by Semenenko and Stewart [3], which allows a simple determination of a map of DNA lesions, including SSBs and DSBs.

3. Results and Discussion

The fitting of the model parameters was carried out from measurement data available in the literature [4]. As an example, in Figure 1 we present some calculated magnitudes for incident protons between 10 keV and 1 MeV: % of SSBs, % of two SSBs on the same strand, % of two or more SSBs on opposite strands separated by 10 p. B. and for less than 10 p.p.

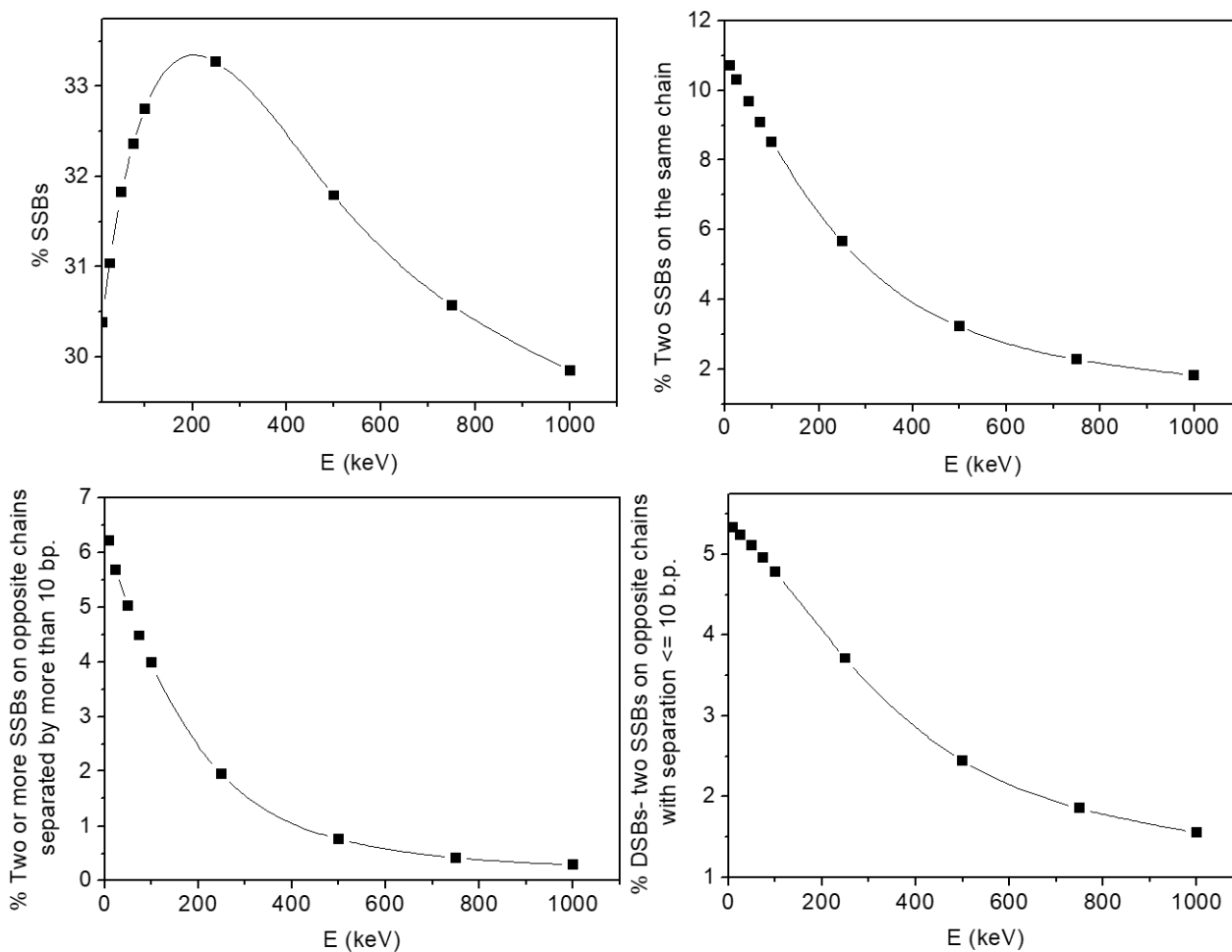


Figure 1 - % of DNA damage cluster distributions for protons between 10 keV and 1 MeV.

The calculation was implemented by combining the results obtained from the dielectric formulation for the mean free path[2] with the fast Monte Carlo simulation algorithm (MCDS) proposed by Semenenko and Stewart [1], which allows a simple determination of a map of DNA lesions, including single breaks (SSBs) and double breaks (DSBs). The size of the adopted DNA (10^9 bp) and the separation of 10 bp as criteria to consider SSB on different strands as a DSB are arbitrary. Even so, the decreasing behavior as a function of energy obtained for the percentages of DSBs, for the appearance of two SSBs on the same strand and for the occurrence of two or more SSBs on opposite strands separated by more than 10 bp is compatible with what is expected, since we are talking about direct damage. In this sense, the increase in energy is related to an increase in the mean free path.

4. Conclusions

The MCDS algorithm was successfully implemented. The obtained results, even in preliminary character and with parameters adopted without connection with experimental results, present a plausible behavior. New simulations will be needed, considering other particles and energy deposition models based on the dielectric formulation and the Monte Carlo method.

References

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