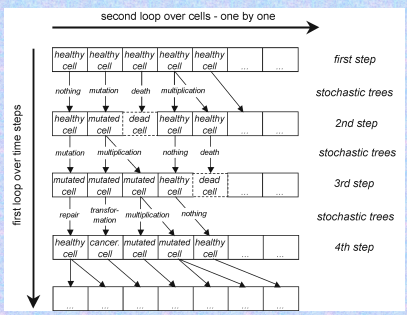
A Stochastic Markov Model of Cellular Response to Radiation

Krzysztof Wojciech Fornalski[a], Ludwik Dobrzyński[a,b], Marek Krzysztof Janiak[c]

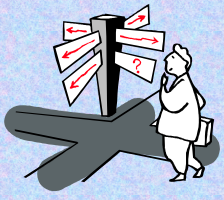
[a] The Andrzej Sołtan Institute for Nuclear Studies, 05-400 Otwock-Świerk, Poland; e-mail: krzysztof.fornalski@gmail.com
[b] Faculty of Physics, University of Białystok, Lipowa 41, 15-424 Białystok, Poland; e-mail: ludwik@ipj.gov.pl
[c] Department of Radiobiology and Radiation Protection, Military Institute of Hygiene and Epidemiology, Kozielska 4, 01-163 Warszawa, Poland; e-mail: mjaniak@wihe.waw.pl

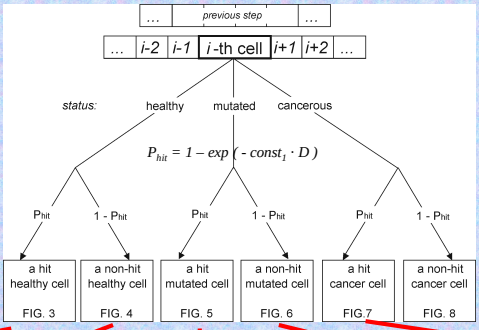
Abstract

A stochastic model based on the Markov Chain Monte Carlo process is used to describe responses to ionizing radiation of a group of cells. The results show that using in the input many relationships linearly depending on the dose the overall reaction shows a threshold, and, generally, a non-linear response. Such phenomena have been observed and reported in many papers. The presented model permits the inclusion of adaptive responses and bystander effects that can lead to hormetic effects. Essentially, all known biological effects can be reproduced by the model. In addition, the model allows for incorporation of various time-dependent phenomena.

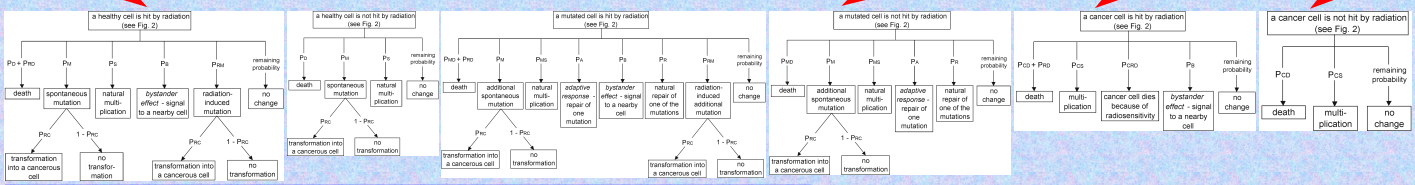


Algorithm





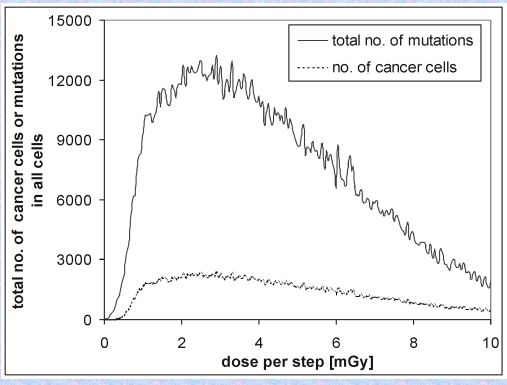
The reaction of a simulated simple organism (i.e., a group of cells) to ionizing radiation is analyzed in two numerical loops. Every step within the first loop one is a generation loop – each step represents the actual state of the cells. One can view the steps in this loop as the unit of time. At each step, the cells may exhibit possible changed states only or may be newly formed by the division of one or more progenitors. All those states are created in the second loop which inspects and acts on the set of cells delivered by the previous step. The second loop takes the cell one by one and uses a stochastic tree of probabilities which change the state of the cell depending on whether it was irradiated or not, became mutated, cancerous, dead, etc. This way a new state of cells is created and the process reiterates in the next step, i.e., returns to the first loop.



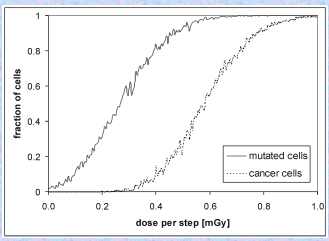
All the described rules work for the determined and constant value of a dose D per step D. A change of D means that the calculations must start from the beginning. The total absorbed dose is a product of D multiplied by the number of steps K. Consistently, the dose D shown in all the figures is the dose per unit time and not the total dose which led to the observed effect.

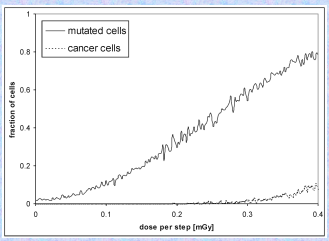
Construction of the stochastic tree of probabilities is the most important part of the used model's algorithm. The tree consists of a dozen of input parameters, eg., the values of probabilities or the usually assumed constants.

Results



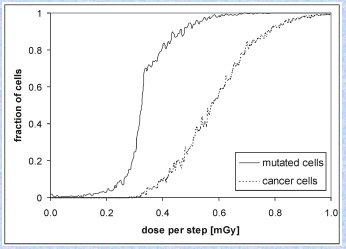
Results for high doses show, that the total number of cancer cells decreases (cell killing in high dose area)

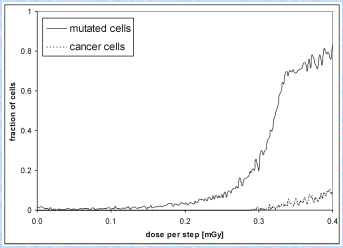




Final results of the simulation: with (below) and without (above) the adaptive response and bystander effect.

The results show the threshold among cancer cells and qualitative agreement with many experiments.





In the present simulation an undefined cell culture with no association to any specific tissue has been used. Indeed, the present model has no ambition to develop the algorithm for more complex tissue reactions. However, a potential user of the model can take their own values of input parameters specifying the type of cells or the tissue they may want to investigate.

The obtained results are consistent with many epidemiological and experimental data demonstrating or implicating a threshold. It must be stressed that the present model was not biased in any way towards a possibility of a threshold or hormesis. These effects seem to appear very naturally and, notably, the latter effect could be demonstrated only after taking the adaptive response into account.

Paper will be published in Dose Response journal (2011) and on conferences (as poster): 19th Nuclear Medical Defence Conference (Munich, Germany, 2011) and 14th International Congress of Radiation Research (Warsaw, Poland, 2011)