MA402 Paper Review

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Queueing Models of Potentially Lethal Damage Repair in Irradiated Cells

Radiation is a very effective method used to destroy cells. It is very useful in treating diseases like cancer. Radiation randomly mutates DNA of the cells, which leads to death of cells. However, cells can also repair the damage caused to DNA by its own repair mechanism. There are several enzymes involved in damage repair, each one acts like a server, and the damaged DNA is the customer in this queueing model and service is done in a random order. The number of lesions (N) in a single cell is dependent on the radiation dose:

$$\Pr(\nu_0 = N) = \frac{(\theta D)^N}{N!} e^{-\theta D}$$

Where, theta is the mean number of lesions in a cell that depends on the radiosensitivity of the cell to the radiation dose D. Also, we assume number of servers as m and service is exponential with intensity µ.

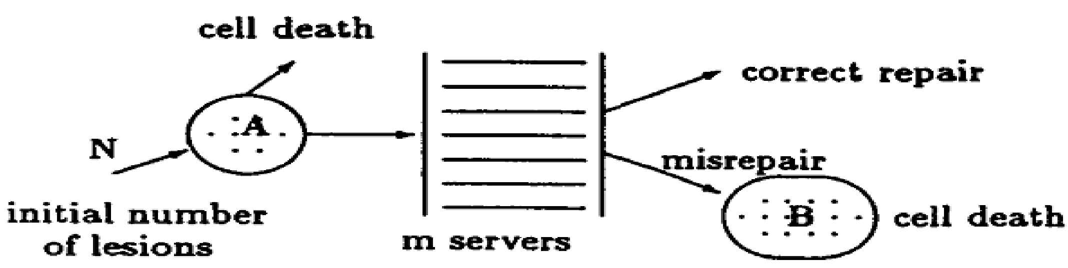
Cells are irradiated *in vitro* and then subcultured after certain time. Now, the numbers of cells that survive is measured. The paper is concerned about giving an expression for the cell survival probability S (D; t) as function of the irradiation dose D and the time of subculturing t, provided the cell is exposed to radiation at time t = 0.

$$S(D;t) = \sum_{N=0}^{\infty} \frac{(\theta D)^N}{N!} e^{-\theta D} F(N,t)$$

Where, F (N, t) gives conditional cell survival probability when number of lesions is N.

Model 1:

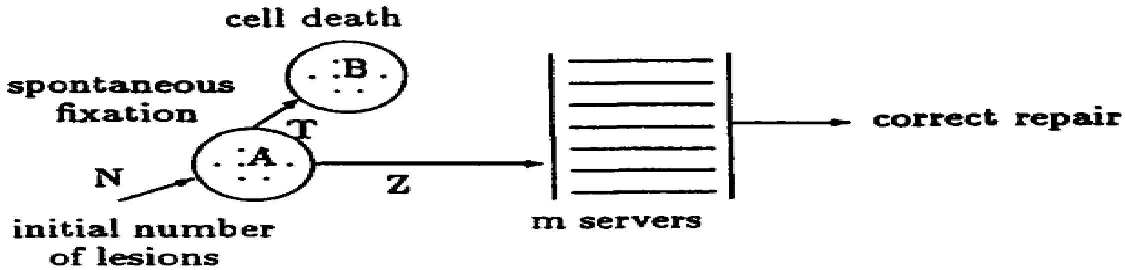
In this model, error in DNA repair is taken into account. So, cell death can happen in two ways. The process of repair is considered as a pure death process, with m channel service. In the act of serving a lesion an error may occur with probability ß. So, we have unrepaired lesions that are waiting in the queue, and also misrepaired lesions.



Using this model, the probability that K customers are waiting in the queue is calculated. Also, two sub-cases are made. It is assumed that subculture does not stop the repair process in one case and it is assumed that subculture stops the repair mechanism in another case. The cell survival probability is calculated in each case, after calculating the conditional survival probability using the pure death model.

Model 2:

In this model, error in DNA repair is not taken into account. A concept of spontaneous fixation is introduced. It is assumed that the radiation-induced lesions can be fixed spontaneously to form the flow of lesions fixed before entering the service system.



Here, two cases are made based on state of the cells not undergoing spontaneous fixation (type A). First case assumes that these cells are not in service at the time of subculturing while second case assumes that they are in service when subculturing takes place.
The cell survival probability is calculated in both the cases.

The problem with both the models is that we get an exponential survival curve when time of subculturing is taken as zero. This however is inconsistent with experimental data. Hence, a new model is proposed which allows for both misrepair of the lesions and also spontaneous fixation.

These models are then used for analyzing some of the experimentally available data. The experimental data is found consistent with the models proposed.

References:

"Queueing Models of Potentially Lethal Damage Repair in Irradiated Cells" E.M.Myasnokova, S.T.Rachev, A.Y. Yakovlev