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SENSITIVITY ANALYSIS OF THE P53 SIGNALING PATHWAY MODEL

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ABSTRACT

The p53 protein is involved in many cellular processes, while the most important are: detection of DNA damage and induction of apoptosis (the so-called programmed cell death). Therefore, the role of p53 protein in cancer progress has been widely studied during many years [1]. The p53 signaling pathway in the cell is quite complex and involves many other proteins, like: MDM2, PTEN, PIP3, AKT [2]. To better understand the role of p53 in cancer disease one can use the mathematical modeling approach. Due to its complexity, dynamical models which try to simulate the dynamics of this pathway is often described by large numbers of nonlinear equations. For example model from work [2] include system of 12 nonlinear differential equations and 43 parameters. To study these complex models one can use the different sensitivity analysis methods. The classical approach of sensitivity analysis for dynamical systems include calculation of the so-called sensitivity function for different parameters of the system [3]. Other approach involve calculation of the Green's function to study the behaviour of particular dynamical system [4]. The Green's function can be used to study how change of non-stationary parameters of the model at different times affect the system behaviour.

In this work we used Green's function approach to analyse the model from work [2]. Obtained results shows the impact of how change at different times of one model variable (representing the effect of ionizing irradiation to the cell) affect the change of other variables in the system (responsible for level of DNA damage and quantities of different proteins involved in the p53 pathway).

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