MASTER'S THESIS

P53 dynamics: single-cell imaging data analysis and modeling

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Date of Award:
2014

ABSTRACT

The p53 protein plays a central role in controlling the fate of cancer cells. At moderate levels of DNA damage, the concentration of the phosphorylated form of p53 undergoes temporal oscillation with a period of a few hours. In Dr. Shi's lab, single-cell measurements were carried out using the p53-YFP fusion proteins and time-lapse fluorescence microscopy. We report here a detailed study of the image data. From the time series of the p53 concentration in individual cells, we deduce the amplitude and period of the oscillation. The pulse-to-pulse and cell-to-cell variability of the oscillation is characterized. We then carry out a computational study of a mathematical model that involves a negative feedback loop between p53 and Mdm2 proteins. We have determined the phase diagram of the model, and studied the sensitivity of the properties of the oscillating state against the model parameters. Although only p53 concentration is measured in the experiment, we show that careful analysis of the pulse shape can nevertheless yield valuable information on the underlying molecular processes, and shed light on the possible origin of the observed cell-to-cell variations.

ACKNOWLEDGEMENTS

First and foremost, I would like to express my greatest appreciation to my supervisor, Prof. Lei-Han Tang, who patiently taught me lots of methods and spirits to do scientific research. Besides, his broad and profound knowledge as well as rigorous logical thinking is of great value for me.

Secondly, I am really grateful for the discussions with Dr. Li Xuefei, his kindly help and suggestions are significant for my research. Besides, I am also very grateful for the kindly help from other group members Mr. Moritz Zehl, Mr. Durga Datta Kandel, Ms. He Xiaojuan, Mr. Qi Fei and the discussions with them inspired me a lot.

Thirdly, I would like to give my special thanks to Dr. Jue Shi from the Department of Physics for her selfless sharing experimental data with me as well as many discussions.

Last but not least, I would like to owe my loving thanks to my family and my friends for every thing they have done for me.

My study is partially supported by the Research Grants Council under the project " Noise and Transient Dynamics in Intracellular Biochemical Networks ", Grant code N_HKBU 213/10.

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