A Filter for the Cooperative Kinase Network of Budding Yeast *Saccharomyces cerevisiae*

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Abstract. In the cooperative kinase network, a kinase interacts with other kinases for sustaining cellular signaling processes that greatly influence the major functions of cells. Here a key question is how the interacting kinases form a filtering network to estimate the original signal in the presence of stochastic fluctuation caused by the interactions. In this short paper, a filter is designed to estimate the concentration of the molecular signal Ste20 of the MAPK (mitogen-activated protein kinase) cascade in budding yeast based on the Ste20-Ste11-Ste7 pathway, in which kinases interact with each other. The filter is tested in simulations and the result shows that the estimated signal can be used to recognize the original signal. It is concluded that the Ste20-Ste11-Ste7 pathway can be regulated to analyze cell cycle processes through the interactions among kinases in the MAPK cascade.

Keywords: Signaling pathway, kinase, MAPK cascade, bioinformatics.

1 Introduction

Motivated by a recent report on a kinase and phosphatase interaction network which shows that cross-talks among kinases play an important role in cellular signaling [1,2], we have investigated filtering mechanisms of the MAPK (mitogen-activated protein kinase) cascade in budding yeast *Saccharomyces cerevisiae* – the Ste20-Set11-Ste7-Kss1/Fus3 pathway [3] where cross-talks act as the convolution factor of a layered filter. In this pathway, signaling is initiated from the top of the hierarchy of signaling processes involving Ste20 and streamed toward the bottom of the hierarchy where Kss1 or Fus3 is involved. Here MAPKKK (mitogen-activated protein kinase kinase kinase kinase) is Ste20; MAPKK (mitogen-activated protein kinase kinase kinase) is Ste11; MAPKK (mitogen-activated protein kinase kinase) is Ste7; MAPK (mitogen-activated protein kinase) has two types – Kss1 and Fus3 that have different effectors. This pathway determines the function of the cell cycle process of budding

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yeast where the kinases of the pathway interact with each other as well as other signaling molecules in the kinase interaction network. In the MAPK cascade, Ste20 also interacts with Cdc28, Cbk1 and Swe1; and Ste11 interacts with Pbs2 in addition to Ste7, Kss1, and Fus3.

In order to investigate the ability of the pathway to restore the original signal in the presence of stochastic effects, we have designed a filter based on the Ste20-Ste11-Ste7 pathway where Ste11 interacts with Pbs2, Ste11 with Kss1, and Ste11 with Fus3. The filter is designed based on four order derivatives to perform nonlinear filtering for random signals. Simulation experiments were conducted to understand the ability of the pathway to estimate the original signal level of Ste20 where the interactions of Ste20 with Cdc28, Cbk1, and Swe1 are formalized as a stochastic process.

2 Results

A simulation result is given in Figure 1 where the original signal level of Ste20 varies in the range of [2.57, 3.44] (nM) and the estimated result for the filter is stationary with the variation within [2.82,3.11] (nM). Owing to the stationary characteristic of the estimated result, the mean (expectation) of the original signal level is inferred as 3 nM with the error limitation ±0.2 nM. When the periodic and random influence on Ste20 is considered, the filter can also restore the original signal with the error limitation of ±0.2 nM. It is inferred that the filtering mechanism of budding yeast may help us to explain how the specificity of the MAPK cascade is sustained in the dynamic processes of cell division.

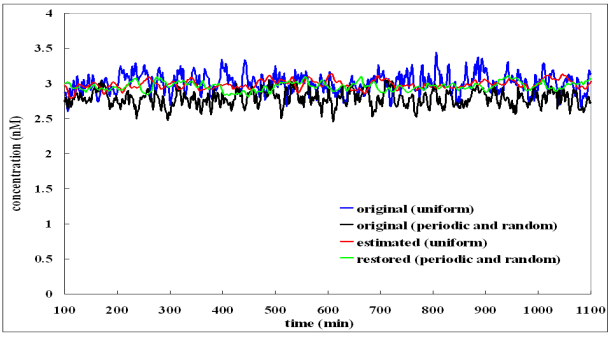

Fig. 1. Concentration-versus-time curve of the original signal (blue) under the uniform distribution; the original signal under the periodic and random influence (black); the estimated result of the filter (red) in the uniform case; the restored result of the filter (green) in the periodic random case

References

1. Breitkreutz, A., Choi, H., Sharom, J.R., et al.: A Global Protein Kinase and Phosphatase Interaction Network in Yeast. Science 328, 1043–1046 (2010)
2. Levy, E.D., Landry, C.R., Michnick, S.W.: Signaling Through Cooperation. Science 328, 983–984 (2010)
3. Elion, E.A., Qi, M., Chen, W.: Signaling Specificity in Yeast. Science 307, 687–688 (2005)