Timing and variability of metabolic gene activation depend on the rate of environmental change

Truong Nguyen[1], Bo Ma[1], Yu-Yu Cheng[1] & Matthew R. Bennett[1]

***Short Abstract* — Activity of a genetic network depends on environmental signal. We subjected the Galactose metabolic network to different time periods of glucose depletion and measured the induction time of the Gal network at single cell level. Our data indicates that the dynamics of environmental factors can determine the phenotypic outcome at single cell and population level**

***Keywords* — Gal network, glucose depletion, single cell**

I. Purpose

Modulation of gene network activity allows cells respond to changes in environmental conditions. For instance, activation of the galactose-metabolic pathway (the GAL network) allows *Saccharomyces cerevisiae* to metabolize galactose in the absence of glucose. In contrast, this network is strictly repressed when both glucose and galactose are available and thus, is only activated when glucose is completely depleted from the environment. In this project, we examined how the time rate of change of the environmental glucose level affects induction of the GAL network. We use custom-design microfluidic chips to change glucose level at different time-dependent rates, and combined with fluorescent microscopy at single cell level to track the expression of the fluorescent-tagged *gal1*, encoding galactose kinase [1, 2]. Our data show that the time it takes to induce *gal1* expression is in inverse relationship with the glucose-depletion rate. In fact, this induction time was largest when glucose was withdrawn instantaneously from the environment. Furthermore, we show that the variability of the induction time depends non-monotonically on the rate of glucose depletion and exhibits a minimum at intermediated rates. Thus, the time-scales over which environmental factors change can affect single cells differently within the isogenic population. Our mathematical modeling suggests that pleiotropic effects of the metabolic transition from glucose to galactose are likely responsible for the variations of the GAL network's activation. These findings shown the dynamics of environmental factors can determine the phenotypic outcome at single cell and population level.

[1]Department of Biochemistry and Cell Biology, Rice University, Houston, Texas (USA)

II. Results

A. The time length of the induction of the Gal network is longest when glucose was withdrawn instantaneously

When glucose was removed instantaneously (1 min) from the environment, the time it take for activating the Gal network is the longest (~3.5h). This induction time is decreased when the glucose depletion time is increased. At the longest depletion time (8h), most of the cell population turn on the Gal network before glucose is completely removed.

B. The variability of the induction time is minimal at intermediate rate of glucose depletion

The variability of the induction time of the Gal network among individual cells depends non-monotonically on the time interval of glucose depletion. The variable value is largest at the two extreme glucose-depletion times (1 min and 8h). This variability reaches minimum at the intermediate rate of 3h.

III. Conclusion

The dynamic modulation of the Gal network regulated by the signal of glucose concentration can be attributed to the dual roles of glucose and galactose; as both serve as metabolites and signaling molecules. Our data provides a new aspect of genetic response to environmental signal at single cell and population level.

References

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