Yeast as a ratio sensor: the ratio of glucose and galactose determines cell state

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To survive, cells must sense and respond to multiple signals from their environment. We studied how yeast responds to a mixture of preferred carbon source, glucose, and less preferred one, galactose. We found that cells determine whether to induce genes involved in galactose metabolism based on the ratio of glucose and galactose rather than glucose threshold concentration. We investigate the regulatory networks that can result in a ratio sensor and the scenarios in which decision making based on ratio sensing may provide fitness advantage. Our results suggest a novel sensing paradigm for the integration of signals from multiple nutrient sources.

***Keywords* — Gene-regulatory networks, Nutrient sensing, Cellular decision making**

I. Introduction

One of the main determinants of the cell fitness is its ability to integrate multiple cues about nutrient availability from the environment and coordinate its metabolism and regulatory networks accordingly. A classical example for the ability of cells to sense multiple signals and execute a regulatory program in response is that of catabolite repression and diauxic growth [1]. When cells are in an environment that contains both preferred and less preferred carbon sources, such as glucose and galactose, respectively, the pathway of the less preferred carbon source is inhibited by the preferred one. Previous studies of the genetic response of cells to multiple carbon sources suggested that the overall output could be described as a product of single carbon output function [2-4]. Here we characterize the integration of signals that occurs while yeast response to galactose, one of the best-studied Eukaryotic signaling pathways [5].

II. Results

We have found that instead of simply inhibiting galactose utilization when glucose is above a threshold concentration, individual cells respond to the ratio of glucose and galactose and based on this ratio determine whether to induce the galactose metabolic pathway. The ratio of glucose and galactose in which the induction occurs is strain dependent and varies between one and half. Using mathematical modeling, we analyzed the possible genetic circuits that could give rise to ratio sensing and found that negative interaction between binding sites plays a crucial role in such circuits. We also investigate, theoretically, the potential fitness advantage of ratio sensing over threshold sensing. We find that switching strategies in which cells prepare for galactose consumption, that is induce before glucose is fully depleted, may provide fitness advantage.

III. Conclusions

Our results suggest that the interaction between multiple nutrient sources is more complex than previously believed and involves a ratio sensing that may allow cells to respond in an efficient way to a dynamically changing environment.

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