# Balancing sensing and uptake of glucose in yeast

Hyun Youk[1], and Alexander van Oudenaarden[1,2]

**Executing diverse cellular activities while gathering enough energy to sustain them is an essential task for all organisms. Central to this task is consumption of a proper amount of carbohydrates. But what exactly constitutes a "proper amount"? We answered this question for the main carbohydrate glucose in budding yeast. We found that below a critical glucose uptake rate, increasing both glucose level and the cell's glucose uptake rate can result in decrease in cell's growth rate. This is due to glucose sensing. We showed that if the cell senses more glucose, it requires higher glucose uptake rate for growth.**

***Keywords* — metabolism, glucose, yeast, optimization.**

## I. Introduction

EXTRACTING energy from imported sugars, and using that energy to grow and maintain diverse cellular processes are fundamental tasks that all organisms must carry out. In the budding yeast *Saccharomyces cerevisiae*, the key carbohydrate glucose is imported by several types of passive transporters called hexose transporters that follow Michaelis-Menten transport kinetics and are essential for growth on glucose [1]. Six hexose transporters (Hxt1-4, 6 & 7), which are the main transporters responsible for glucose import, have each a different binding affinity for glucose [2]. The cell varies the expression levels of these six *HXT* genes depending on the concentration of extracellular glucose in the environment, presumably to achieve an uptake rate it considers "proper" for that environment. But what exactly is this "proper" amount?

## II. Results

A logical starting point to answer above question was to explore how fast a cell equipped with just one of the six main *HXT* genes grew as we freely controlled its expression level using an inducible promoter $P_{TET07}$. Five such "single-*HXT*" strains were constructed, one for each of *HXT1-4* and *HXT6*. By growing these "single-*HXT*" strains in a wide range of glucose concentrations, we found that the cell's growth rate did not increase monotonically with increasing extracellular glucose concentration. This is in stark contrast with the wild-type cell equipped with all the *HXT* genes. To explain this surprising observation, we measured the glucose uptake rates of each of the "single-*HXT*" strains and found that their glucose uptake rates increased monotonically with increasing glucose level. Therefore, we have found that yeast cell's growth rate does not always increase despite an increase in both the extracellular glucose and glucose uptake rate. Our growth experiments showed that glucose uptake rate alone is not sufficient for determining the cell's growth rate. Instead, we found that extracellular glucose concentration explicitly affects the cell's growth rate, independently of the cell's glucose uptake rate. We could describe this using a concise empirical equation for cell's growth rate as a function of just two variables: glucose and glucose uptake rate. Our experiments demonstrated for the first time that if more glucose is available to the cell in the environment, then the cell requires a higher glucose uptake rate for growth; any amount below this required minimum uptake rate results in the cell succumbing to growth arrest. We further showed that extracellular glucose affects cell's growth rate due to the cell's ability to measure the amount of glucose in its surrounding using two membrane-bound sensors Snf3 and Rgt2. By knocking out these two sensors, we found that the cell's growth rate had weaker dependence on extracellular glucose because the cell's ability to detect glucose was impaired. We found that this sensing mechanism affected growth rate only below a certain critical glucose uptake rate. Above this critical uptake rate, the cell's growth rate depended only on glucose uptake rate and not on glucose sensing. We found that the wild-type yeast overcame the possible detrimental effects of sensing by tuning its glucose uptake rate to be above this critical uptake rate value.

## III. Conclusion

Our study shows that yeast cell growth is an outcome of an intricate balance between sensing and uptake of glucose: Cell's perception of how much glucose is available to it affects its growth just as much as how much glucose is actually imported by the cell.

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[1]Department of Physics, Massachusetts Institute of Technology, Cambridge MA 02139, USA. E-mail: hyouk@mit.edu

[2]Department of Biology, Massachusetts Institute of Technology, Cambridge MA 02139, USA. E-mail: avano@mit.edu

## References

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