Why is Baker's yeast only *partially* starving on xylose?

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In the process of making biochemicals from lignocellulose—a feedstock rich in pentose sugars—*Saccharomyces cerevisiae* strains engineered for pentose utilization struggle with efficient xylose fermentation [1]. It is well known that when present, *S. cerevisiae* will prioritize the use of glucose over other sugars. This prioritization is controlled by complex regulatory pathways that depend on both intra– and extracellular stimuli, for instance via allosteric interactions and membrane receptors [1]. When the cells are completely starved of glucose and other natively consumed hexoses, the regulatory systems are expected to trigger a lowered protein kinase A (PKA) activity and a decreased expression of sugar transporters and extracellular invertase.

When xylose is supplied, we indeed observe a decrease in PKA activity and transporter expression; however, the extracellular invertase expression increased instead [2]. This regulatory state usually only occurs when very low levels of glucose are supplied (~1g/L), and results in increased respiratory and gluconeogenesis activity—the opposite of the desired fermentation. Could it be that the inefficient xylose utilization is caused by dysregulation in the nutrient starvation pathways? And if so, what causes xylose to elicit this regulatory response?

This poster summarizes our findings over the past five years on *S. cerevisiae*'s response to xylose. In short, we have found evidence that the dysregulation primarily stems from the formation of glycolytic intermediates used to control key regulatory enzymes [3]. In addition to this, xylose itself appears to be detected by extracellular receptors responsible for sensing low glucose concentrations, and pathway-specific redox imbalances do not appear to be pivotal.

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References:
[1] Brink, D.P., et al., *D-xylose sensing in Saccharomyces cerevisiae: Insights from d-glucose signaling and native d-xylose utilizers.* International Journal of Molecular Sciences, 2021.
[2] Osiro, K.O., et al., *Assessing the effect of d-xylose on the sugar signaling pathways of Saccharomyces cerevisiae in strains engineered for xylose transport and assimilation.* FEMS Yeast, 2018.
[3] Borgström, C., et al., *Using phosphoglucose isomerase-deficient (pgi1Δ) Saccharomyces cerevisiae to map the impact of sugar phosphate levels on d-glucose and d-xylose sensing.* Microbial Cell Factories, 2022.