

## Cooperation in yeast sucrose metabolism

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The conditions required for the initiation and maintenance of cooperation is a classic problem in evolutionary biology<sup>1</sup>. As a model system to quantitatively test models in evolutionary game theory we are studying the metabolism of sucrose in the yeast *S. cerevisiae*. Digesting sucrose requires that the disaccharide be hydrolyzed into glucose and fructose, a reaction which is catalyzed by the enzyme invertase in the periplasmic space between the plasma membrane and the cell wall<sup>2</sup>. We have shown both theoretically and experimentally that a majority of the resulting monosaccharides diffuse away before they can be imported into the cell. The hydrolysis of sucrose is therefore a cooperative activity<sup>3</sup> and we find that the growth rate increases with cell density.

The expression of invertase is potentially a complicated and dynamic function of the environmental conditions. The most straightforward strategy would be for yeast to secrete invertase only when sucrose is present and glucose is absent (as glucose is the preferred carbon source). Surprisingly, while yeast do indeed detect glucose, there is no evidence that they directly detect sucrose at all. Instead, yeast express invertase at a low basal level even in the absence of glucose or sucrose in the surrounding medium. Rather than suppressing the expression of invertase, low concentrations of glucose (~0.005%) actually increase expression by an order of magnitude<sup>4</sup>. If there is sucrose in the environment then the low basal level of invertase expression is sufficient to generate a small local concentration of glucose. The increase in invertase expression at low glucose concentrations thus acts as a simple and elegant sensor for sucrose.

We have competed the wild-type cooperator against a mutant “cheater” strain that is unable to produce invertase. We use a histidine auxotroph cooperator, thus allowing us to control the “cost of cooperation” by varying the concentration of histidine in the growth medium. In a well-mixed environment we find that cooperators and defectors coexist, consistent with the interaction being a snowdrift game, in which the optimal strategy is the opposite of what one’s opponent is doing. Finally, we probe the success of the cooperator in spatially-structured competition and find that the effect depends upon the precise nature of the spatial structure.

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