Optimal resource allocation or greed, what determines a winning strategy for nutrient sensing?

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Short Abstract — **Bistability is key to a wide range of cellular processes such as differentiation and neuronal memory. The evolutionary advantages for such processes seem clear; once a cell has obtained a certain property it should maintain it. For processes like nutrient sensing, however, it is less obvious why or when cells should respond in an all or nothing fashion instead of gradually adapting their response to the amount of nutrient available. We hypothesized that bistable nutrient responses are an adaptation to competition.**

Keywords — **Nutrient sensing, bistability, fitness, population growth.**

I. Bistability in Nutrient Sensing

THE essential feature of a bistable response is that genetically identical cells can respond in two different ways to the same stimulus. In bistable nutrient-sensing networks, cells express the enzymes needed to take up and metabolize the nutrient at either a maximal or a basal (almost inactive) rate. One such bistable nutrient response is the galactose-sensing network of *S. cerevisiae* [1, 2]. More commonly, cells respond to nutrients in a graded fashion, gradually adapting their enzyme expression to the amount of nutrient available. Graded responses not only differ in the amount of enzymes expressed, they are also less sensitive to stochasticity than bistable ones, which can randomly switch between the two stable states [3]. An example of a graded nutrient-sensing network is the *Lac*-operon of *E. coli* in response to its natural inducer lactose, which was shown to be optimal with respect to the costs of producing the enzymes and the benefits of taking up the sugar [4]. If graded nutrient responses evolved to optimize resource allocation, then what was the selective pressure for bistable nutrient responses?

Conventionally, a bistable response is considered advantageous because it allows a population of related cells to hedge their bets with some cells being in one of the bistable states and other cells in the other. This phenotypic variation increases the fitness of the population at the possible cost of reduced fitness for some individuals [5]. Phenotypic variation is, however, an argument for a stochastic response, which need not be bistable.

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II. Modeling Nutrient Competition

We hypothesize that competitive environments favor bistable nutrient responses, and test this hypothesis combining a population dynamical approach with a nutrient-uptake and response model.

A. Population dynamical model

The stochastic Price equation [6] describes the expected change of average phenotype of a population of cells within one generation. It is a simple yet general framework that links the individual fitness of each cell type to its contribution to population growth.

B. Nutrient-uptake and response model

We compute the amount of nutrient absorbed by each cell type using a simple ODE model for nutrient-uptake and regulation. Via the individual fitness function, the resulting absorbed amounts then feed into the Price equation telling us under which circumstances the bistable or graded strategy is expected to be more successful.

III. Conclusion

Our results suggest that highly competitive environments favor bistability. In particular, stochastic bistable responses, where cells randomly choose the on or off state with a probability different from 0 and 1, are only favored when the amount of nutrient available per cell is low.

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