Extending a shadow price-based definition of nutrient limitation to genome-scaled metabolic netwotks in complex mediums

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Abstract

Nutrient limitation is a culture condition that experimentalists can easily identify, particularly in continuous culture steady states, where the biomass may stabilize due to depletion of a critical nutrient supply. However, reproducing this property in genome-scaled metabolic models is difficult, as its emergent nature lacks a clear mechanism of how such a condition can arise from the state distribution of cells in the culture. In this work, we use a particular, well-defined single-cell definition of nutrient limitation based on the shadow price of the boundary constraints over biomass production. This definition has been proven to work with networks constrained by simple medium compositions and is well supported by experimental data. We aim to extend this procedure to networks constrained by complex mediums, which is the case of mammalian cells cultures. Our results show that we can easily find minimal contraint modifications that produce nutrient-limited subnetworks. In particular, for HEK and CHO networks, there are only a few such minimal sets. This procedure can be used to contextualize metabolic networks to include the nutrient limitation phenotype before further analysis.