**479a A Structured Model to Represent Sequential Substrate Uptake during Rifamycin B Fermentation in Complex Media**

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Modeling of growth and product formation on complex media containing multiple substitutable substrates is a challenge. Complex media offers the organism multiple choices of carbon and nitrogen substrates including free amino acids, peptides, soluble and insoluble proteins in addition to the defined sources such as glucose and ammonium sulfate. We present a structured model that accounts for growth and product formation kinetics of rifamycin B fermentation in a multi-substrate complex medium. The model considers the organism to be an optimal strategist with a mechanism to regulate the uptake of the substrate combinations. Further, we assume that the uptake of a substrate depends on the level of a key enzyme, which may be inducible. The model also considers control parameters as fraction of flux through a given metabolic branch. The control parameters are obtained using a simple multi-variable constrained optimization. The model parameters were rigorously estimated via a specifically designed experimental plan.

The model correctly predicts the experimentally observed growth and product formation kinetics and the regulated sequential / simultaneous uptake of the substitutable substrates under different fermentation conditions. We experimentally verified the sequence of uptake of over a dozen substrates including individual amino acids. This presentation will describe the experimental results, the model development and the relevant model parameters for A. mediterranei S699.