Do *E. coli* cells care about metabolic noise?

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***Short Abstract* — Genetic circuits are subject to stochastic fluctuations in concentrations, also called noise. Using time lapse microscopy, we can quantify concentrations of fluorescently labeled enzymes and the growth rates of single *E. coli* cells. Earlier work has already shown direct correlations between these two quantities. We now set out to investigate the possible role of posttranslational regulation of metabolic enzymes in reducing the noise in metabolic networks.**

I. Introduction

Stochasticity leads to observable differences among bacterial cells. On the level of gene expression, randomness leads to temporal fluctuations that vary from cell to cell [1]. On the level of populations this can lead to different individual behavior [2]. This cell-to-cell variability offers cellular populations advantages such as bet-hedging and division of labor [3], [4]. Thus, observed dynamics in the biochemical network on the single cell level might be very different from the mean dynamics observed in populations. Hence, when investigating how cells function, it is important to not only look at population averages, but also investigate the behavior of single cells. Using such an approach, it has recently been observed that fluctuations in central metabolic enzyme expression can propagate to cellular growth [5]. Thus, remarkably, fluctuations on the level of single enzyme species can affect something as important for the competiveness of cells as its growth.

In general, we investigate how important biochemical noise is for cellular networks. Noise can be beneficial for cells, but might also hinder operation of biochemical networks. Here, we investigate whether cells might actively try to suppress fluctuations in metabolites – which can transmit to fluctuations in growth rate – by posttranslational regulation of enzymatic activity.

II. Methods and Outlook

We use time lapse microscopy to record the growth of single *E. coli* cells in a microcolony. Using Matlab software developed by Young et al. [6] and extended in our lab, we are able to segment and track cells (see Fig. 1). This allows us to determine the (fluctuating) growth rates of individual bacteria over multiple generations. Additionally, by using fluorescent labeling, enzyme concentrations can be determined in individual bacteria. Thus, correlations between enzyme expression and growth rate can be determined. These correlations can quantify noise transmission in the network. Key flux determining enzymes were identified using simulations [7]. The role of specific regulatory sites in enzymes can be investigated using novel techniques to generate mutants [8]. Using these methods, and mutants that lack posttranslational metabolic enzyme regulation, we aim to determine whether post translational regulation can play a role in reducing noise in biochemical networks.

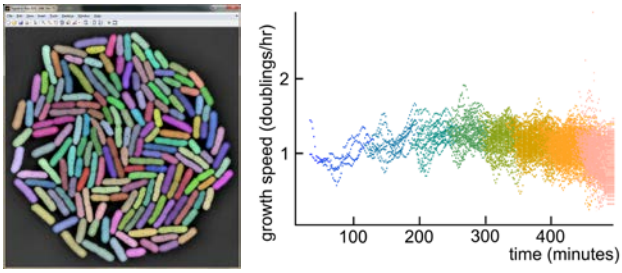

Figure 1. Left: Individual cells can be segmented and tracked. Right: Example of multiple obtained single cell growth curves.

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