Gene expression noise – How much is explained by growth fluctuations?

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Short Abstract — **Noise in gene expression can lead to a loss of signal transmission fidelity and cell-to-cell variability. Two elementary categories of expression noise are intrinsic noise that affects individual genes only and extrinsic noise that affects multiple genes simultaneously. Recently it has been shown that also growth rate of individual cells fluctuates and that fluctuations couple to gene expression. This raises the question whether variations in growth can explain expression noise. Using time lapse microscopy and an *E. coli* strain containing fluorescent protein reporters we show that fluctuations in growth rate can explain extrinsic noise and are uncoupled to intrinsic noise.**

Keywords — **Single cell, fluctuation, noise, growth rate, gene expression, time lapse, e coli.**

I. Introduction

BACTERIAL gene expression is noisy and leads to time dependent fluctuations of protein concentration within a cell and cell-to-cell variability [1]. Consequences of expression noise can be beneficial or detrimental, depending on the context. Noise reduces for example fidelity of signal transmission within gene networks but phenotypic variability among cells can also be a beneficial bet-hedging strategy in fluctuating environments [1,2]. Fluctuations in expression can be divided into the two main categories "intrinsic" and "extrinsic" noise [3,4]. Intrinsic noise affects individual genes only and describes stochasticity due to low molecular copy numbers within the biochemical reactions transcription and translation. Extrinsic noise denotes global fluctuations of the cellular state that affect many genes simultaneously and includes for example variations in amount of ribosomes, ATP or the stage in the cell cycle.

Recently it has been shown that also growth rate of individual cells within an exponentially growing culture fluctuates around a constant population mean [5]. Fluctuations in growth rate are connected to a time-varying metabolic efficiency and therefore coupled to gene expression. In this study we address the question whether variations in growth can explain extrinsic noise, intrinsic noise or both of them.

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II. Methods

For experimental distinction between noise categories we use an E. coli strain expressing two different fluorescent proteins under control of identical promoters [3]. Correlation resp. difference of the two fluorescent signals describes common extrinsic resp. local intrinsic noise. By acquiring time lapse movies over many hours we obtain protein expression rate and instantaneous growth rate at sub-cell-cycle resolution. Contribution of growth fluctuations to protein noise is then calculated by applying noise decomposition methods such as the law of total covariance to protein expression data [6,7].

III. Conclusion

Our results show that part of the extrinsic noise can be explained by growth rate fluctuations while intrinsic noise is uncoupled to growth. The fraction of extrinsic noise that is explained by growth fluctuations depends on the growth conditions and increases with decreasing average growth rate. Thus, at slow growth a significant part of expression noise can be captured by growth fluctuations and coupling between growth and expression could be due to common limiting factors such as ribosomes or ATP. At fast growth, however, independent noise sources of protein expression and growth rate dominate. Our results could be a next step towards a better understanding and characterization of the sources of gene expression noise.

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