Contribution of growth rate fluctuations to gene expression noise

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***Short Abstract* — We study the temporal fluctuations of protein concentrations, growth rate and its correlation within *E.coli* bacteria. While noise in protein concentrations and its propagation within regulatory networks has been investigated, we additionally consider the role of the growth rate. Even during steady exponential phase growth rates fluctuate significantly within single cells and thus can reflect the current state of the cell. We investigate to what extent these fluctuations account for extrinsic noise. To address this question we use fluorescent proteins and time lapse microscopy and extract growth rates and protein production rates of single cells on a sub-cell-cycle resolution.**

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

I. Purpose

ABUNDANCE of components within a bacterial cell, such as proteins, is subject to substantial stochastic fluctuations [1,2]. Noise in protein level affects cellular behavior and leads to cell-to-cell variability. Whether that is beneficial or detrimental depends on the specific context [2].

Randomness in protein content is caused in part by the inherent stochasticity of chemical reactions involved in gene expression [1] (“intrinsic noise”). Additionally, fluctuations in global components that are necessary for gene expression, such as ribosomes or RNA-polymerases, affect protein production from all genes within a cell in a coordinated manner and have been named “extrinsic noise” [1]. While the first type of fluctuation is very rapid, the latter one has decay times of the order of a cell cycle [3] and thus can substantially influence cellular behavior and might affect fitness.

So far uninvestigated has been the role of cellular growth rate within this framework of dynamic fluctuations. While an interdependence between protein content and growth rate in steady state exponential growth has been examined [4], time resolved data is lacking.

Bacteria will optimally seek to balance its components well and grow constantly at a maximum rate, yet in reality also growth rate is noisy. It varies between clonal cells as well as within one individual cell over time. The growth rate might fluctuate due to varying cellular parameters such as metabolic activity, protein content or availability of building blocks. Thus, it can reflect or parameterize the current state of a cell.

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We aim to quantify what part of gene expression noise can be explained by growth rate fluctuations. Therefore, we separate fluctuations in protein production into extrinsic and intrinsic noise and examine the noise contribution of the growth rate by applying the law of total covariance.

Experimentally, we record time lapse phase contrast and fluorescence images during the growth of single *E.coli* cells into microcolonies. The strain contains two different fluorescent proteins under the control of the *lac* promoter [1], thus the measured intensity reflects protein concentration. Segmentation and tracking of the cells result in time resolved information on protein production and growth rate [5] for which noise and correlations (following [6],[7]) can be calculated.

II. Conclusion

We find that protein production correlates positively with growth rate, showing that growth rate can serve as a description of (part of) the cellular state. As expected, fluctuations in growth rate explain almost nothing of intrinsic noise and the remaining contribution is presumably due to measurement errors. Contribution to the extrinsic noise can be significant and the magnitude depends on the specific growth conditions.

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