

# Growth-rate dependent effects on bacterial gene expression

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**Short Abstract** — The composition of bacteria varies greatly for different bacterial growth rates. Therefore significant changes in gene expression are expected to arise “passively” from changes in growth rate alone. We performed a joint theoretical/experimental study for *E. coli* to obtain a quantitative understanding of these effects. We characterized the growth-rate dependent expression of “constitutively expressed” genes and of several simple genetic circuits and explored regulatory strategies to make gene expression robust against growth-rate dependent effects.

**Keywords** — Gene expression, growth rate, constitutive promoter, genetic circuits, autorepression.

## I. OBJECTIVE

FOR fast growing bacteria which can adapt to wildly different growth conditions, changes in gene expression are often accompanied by changes in growth rates. Because the macroscopic composition of bacteria (e.g., cell size, ribosome concentration, gene copy number) is known to vary greatly for bacteria grown at different rates [1], significant changes in gene expression may arise “passively” just due to the growth rate change alone [2,3]. Therefore, quantitative understanding of gene regulation and the robust operation of genetic circuits require, first and foremost, a quantitative understanding of these passive growth rate dependent effects. Towards this end, we performed a joint theoretical/experimental study for *E. coli*. Specifically, we aimed to characterize the growth-rate dependent expression of genes driven by “constitutive” promoters, and explore regulatory strategies to make gene expression independent of changes in growth rates.

## II. RESULTS

We analyzed quantitatively available data for the growth rate dependence of various macroscopic parameters affecting gene expression in *E. coli*, and predicted the growth-rate dependence of gene expression for various simple genetic circuits. We tested these predictions by driving the expression of several exemplary genes by various promoters, for several strains of *E. coli* grown in a variety of media. For

each strain and growth medium, mRNA levels were measured by qPCR and protein levels by activity assays or quantitative Western blotting. For a constitutively expressed gene, the mRNA level (relative to ribosomal RNA) was found to be weakly dependent on the growth rate while the expressed protein concentration decreased nearly inversely with the growth rate, in accordance with predictions of our model. Weak growth-rate dependence was predicted and observed also for autorepressing genes and for genes under negative control by an autorepressor. Other growth-rate dependent effects due to the location of genes and their regulators at different parts of the chromosome were also investigated.

## III. CONCLUSION

Our studies demonstrate that growth rate has important and substantial effects on gene expression of fast growing bacteria. These effects must be taken into account when analyzing gene expression data under different condition. Buffering against these growth rate dependent effects may be an important requirement underlying the robust operation of endogenous genetic circuits in these bacteria, and should be a prime factor to consider in the design of robust, synthetic circuits.

## REFERENCES

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