

# Quantitative mass spectrometry reveals simple patterns of proteome-wide responses to different modes of growth limitation in *E. coli*

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**Short Abstract** — Gene expression may generally exhibit complex growth rate dependences. Here with quantitative mass spectrometry, we probe the responses of the proteome to different modes of growth limitation in *E. coli*. We found the proteome to be partitioned into a few sectors whose proteome fractions obey simple linear growth rate dependences, either decreasing or increasing depending on the specific limitation imposed. The up-regulated proteins largely correspond to those involved in the metabolic section targeted by the applied limitation. The growth-rate dependent fractions of the proteome comprise about half the proteome.

## I. INTRODUCTION

ALTHOUGH bacterial gene expression can in general exhibit complex growth rate dependences, depending on the regulatory mechanisms and the ways that growth is limited [1,2], recent studies suggest that exponentially growing cells carefully counterbalance the expression of various metabolic proteins with ribosome biosynthesis [3]. The expression levels of exemplary catabolic and anabolic proteins revealed striking, distinct linear growth-rate dependences upon various modes of growth limitation [4]. Based on these results it was hypothesized that the proteome of the cell is partitioned into a few proteome sectors, each of which comprises of a group of proteins with similar growth rate dependences [3,4]. Extending a recently developed method of quantitative mass spectrometry [5], we directly characterized the responses of protein expression to different modes of growth limitation at the proteome-wide scale to examine the existence and dynamics of the proteome sectors.

## II. RESULTS & DISCUSSION

High-coverage protein expression data were generated for 14 growth conditions providing three distinct series of growth limitation: catabolic, anabolic, and translational limitation, referred to as C-, A-, and R- limitation respectively. Based on the highly quantitative relative expression levels, proteins with similar growth-rate dependences were grouped together. Then coarse-graining was done by summing the mass of individual proteins in a

group based on the method of spectral counting [6].

The coarse-graining results show that the proteome can be partitioned into a growth-rate independent sector (Q) which comprise ~45% of the proteome as previously predicted [3,4], and 5 additional major sectors (comprising >5% of the proteome). The proteome fractions of these 5 sectors exhibit striking linear dependence on the growth rate, either increasing or decreasing depending on the applied mode of growth limitation. Three sectors (C, A, R) each increases upon one mode of growth limitation and decreases upon the other two modes of growth limitation. E.g., the C-sector increases upon C-limitation but decreases upon A- and R-limitation. One sector (S) increases upon either C- or A-limitation, but decreases with R-limitation. Finally, the sector O decreases upon all 3 modes of growth limitation.

A gene ontology enrichment analysis shows that the C-, A-, and R- sectors comprise largely of catabolic, anabolic, and ribosomal proteins, respectively. They are the proteins induced by the corresponding mode of growth limitation. The S-sector is enriched of proteins expressed in stationary phase and corresponds to the general starvation response. The O-sector comprises of other sections of metabolism (e.g., nucleotide synthesis, sulfate metabolism) not probed specifically by the 3 modes of growth limitations applied.

At this coarse-grained level, the responses of the proteome to the basic modes of growth limitations are surprisingly simple, and can be characterized by a handful of parameters as suggested from previous studies based on a few reporters [3,4].

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