Under the Placid Surface of Exponential Cell Growth

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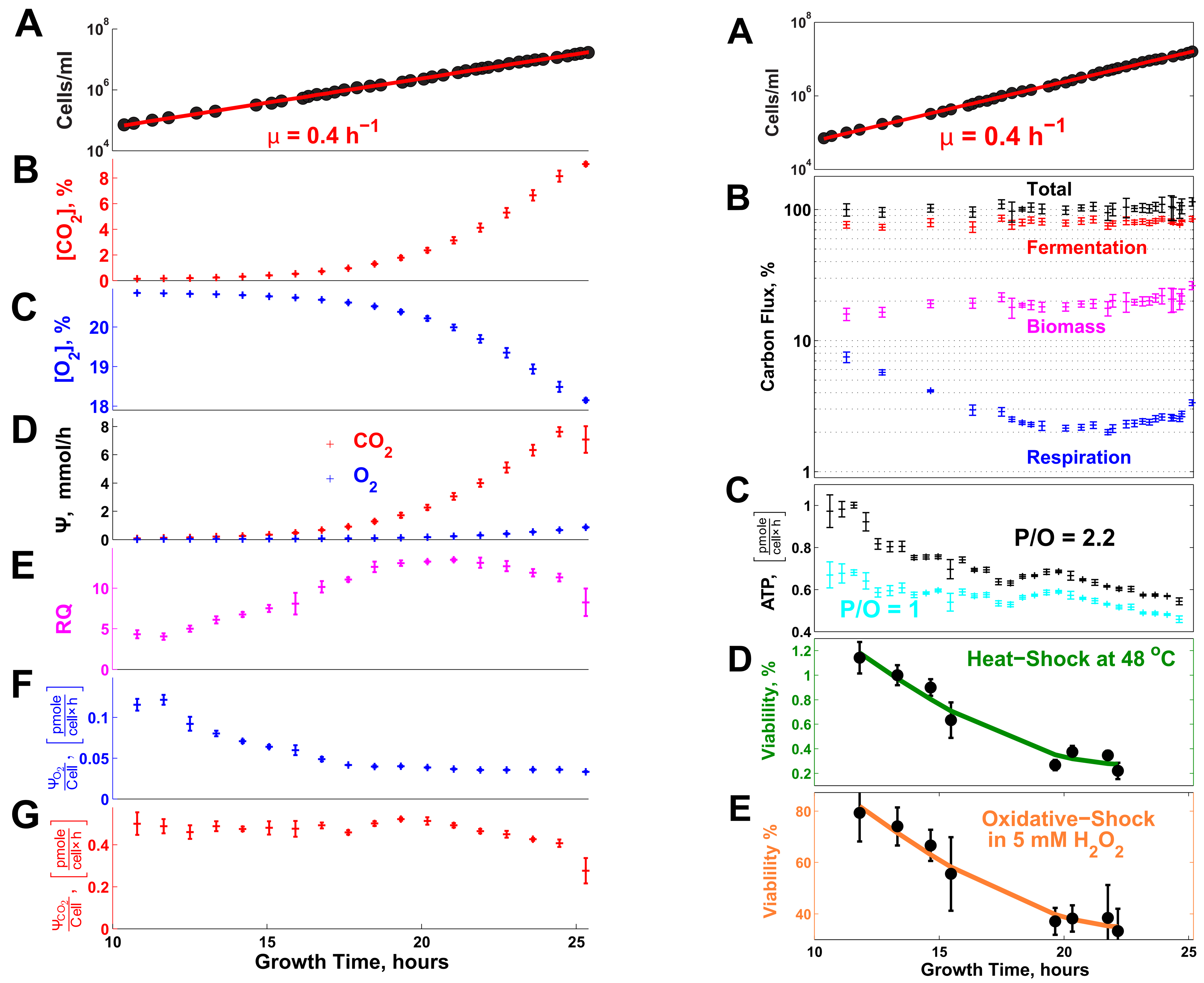
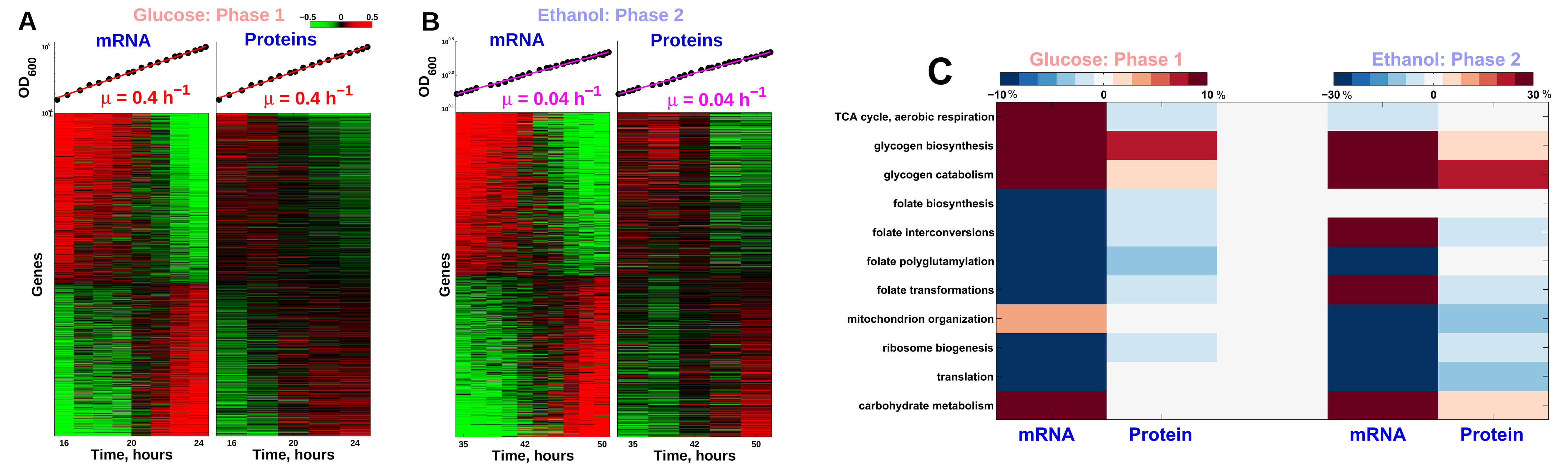
Abstract

Fermenting glucose in the presence of enough oxygen to support respiration, known as aerobic glycolysis, is believed to maximize growth rate. We observed increasing aerobic glycolysis during exponential growth, suggesting additional physiological roles for aerobic glycolysis. We investigated such roles in yeast batch cultures by quantifying O2 consumption, CO2 production, amino acids, mRNAs, proteins, posttranslational modifications, and stress sensitivity in the course of nine doublings at constant rate. During this course, the cells support a constant biomass-production rate with decreasing rates of respiration and ATP production but also decrease their stress resistance. As the respiration rate decreases, so do the levels of enzymes catalyzing rate-determining reactions of the tricarboxylic-acid cycle (providing NADH for respiration) and of mitochondrial folate-mediated NADPH production (required for oxidative defense). The findings demonstrate that exponential growth can represent not a single metabolic/physiological state but a continuum of changing states and that aerobic glycolysis can reduce the energy demands associated with respiratory metabolism and stress survival.

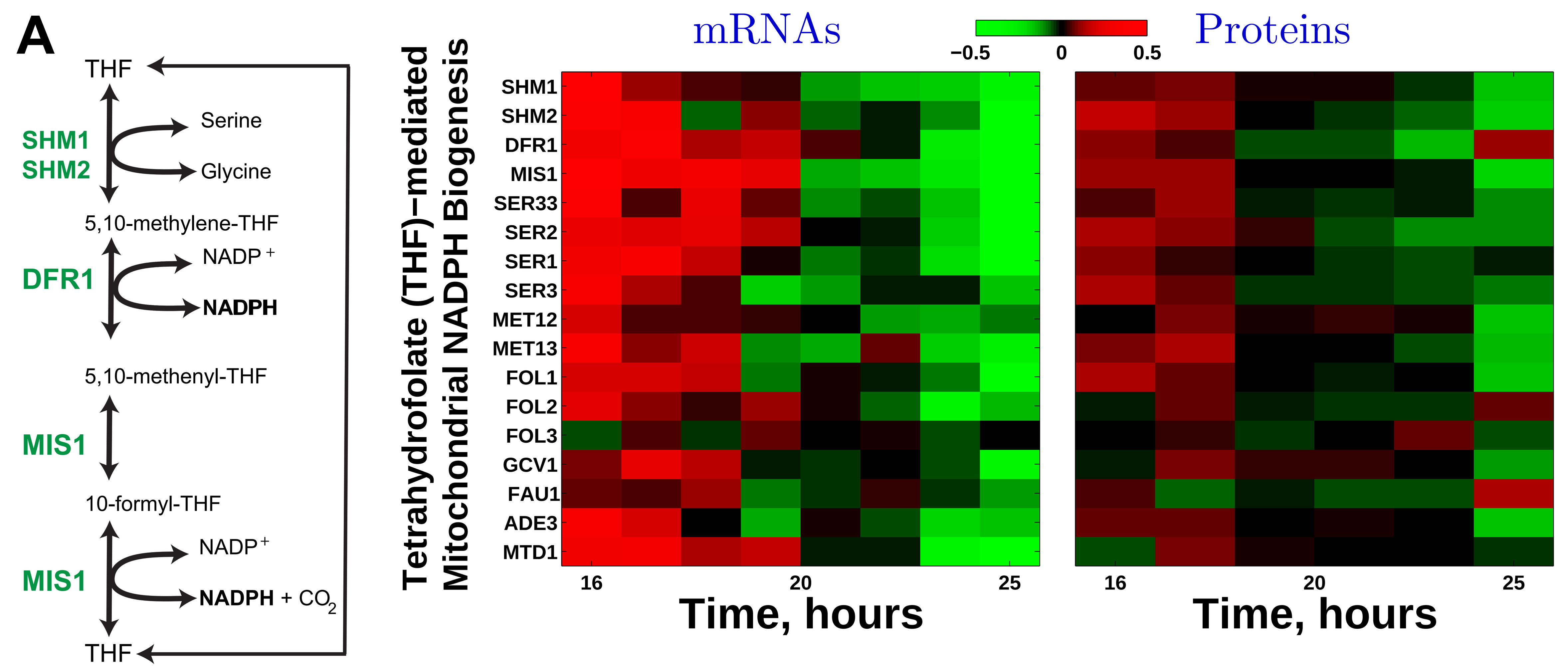
Metabolic and Physiological Dynamics



Global Gene Expression Dynamics



Mitochondrial Folate-mediated NADPH Production



The levels of enzymes (and their corresponding mRNAs) catalyzing the tetrahydrofolate (THF)-mediated mitochondrial NADPH biogenesis decline, parallel to the decreased oxygen consumption (Figure 2F), during the first exponential growth phase. These include all enzymes (Ser3p, Ser33p, Ser1p, Ser2p) catalyzing the serine biosynthesis from 3-phosphoglycerate, the hydroxymethyltransferases (Shm1p, Shm2p) and the mitochondrial NADPH synthetases: the dihydrofolate reductase (Dfr1p) and the mitochondrial C1–tetrahydrofolate synthase (Mis1p).

References

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