## Laboratory Evolution to Alternating Substrate Environments Yields Distinct Phenotypic and Genetic Adaptive Strategies - DTU Orbit (09/11/2017)

Laboratory Evolution to Alternating Substrate Environments Yields Distinct Phenotypic and Genetic Adaptive Strategies Adaptive laboratory evolution (ALE) experiments are often designed to maintain a static culturing environment to minimize confounding variables that could influence the adaptive process, but dynamic nutrient conditions occur frequently in natural and bioprocessing settings. To study the nature of carbon substrate fitness tradeoffs, we evolved batch cultures of Escherichia coli via serial propagation into tubes alternating between glucose and either xylose, glycerol, or acetate. Genome sequencing of evolved cultures revealed several genetic changes preferentially selected for under dynamic conditions and different adaptation strategies depending on the substrates being switched between; in some environments, a persistent "generalist" strain developed, while in another, two "specialist" subpopulations arose that alternated dominance. Diauxic lag phenotype varied across the generalists and specialists, in one case being completely abolished, while gene expression data distinguished the transcriptional strategies implemented by strains in pursuit of growth optimality. Genome-scale metabolic modeling techniques were then used to help explain the inherent substrate differences giving rise to the observed distinct adaptive strategies. This study gives insight into the population dynamics of adaptation in an alternating environment and into the underlying metabolic and genetic mechanisms. Furthermore, ALEgenerated optimized strains have phenotypes with potential industrial bioprocessing applications.IMPORTANCE Evolution and natural selection inexorably lead to an organism's improved fitness in a given environment, whether in a laboratory or natural setting. However, despite the frequent natural occurrence of complex and dynamic growth environments, laboratory evolution experiments typically maintain simple, static culturing environments so as to reduce selection pressure complexity. In this study, we investigated the adaptive strategies underlying evolution to fluctuating environments by evolving Escherichia coli to conditions of frequently switching growth substrate. Characterization of evolved strains via a number of different data types revealed the various genetic and phenotypic changes implemented in pursuit of growth optimality and how these differed across the different growth substrates and switching protocols. This work not only helps to establish general principles of adaptation to complex environments but also suggests strategies for experimental design to achieve desired evolutionary outcomes.

## **General information**

## State: Published

Organisations: Novo Nordisk Foundation Center for Biosustainability, Big Data 2 Knowledge, Network Reconstruction in Silico Biology, ALE Technology & Software Development, University of California, San Diego, University of Tartu Authors: Sandberg, T. E. (Ekstern), Lloyd, C. J. (Ekstern), Palsson, B. O. (Intern), Feist, A. M. (Intern), Kivisaar, M. (ed.) (Ekstern)

Number of pages: 15 Publication date: 2017 Main Research Area: Technical/natural sciences

## **Publication information**

Journal: Applied and Environmental Microbiology Volume: 83 Issue number: 13 Article number: e00410-17 ISSN (Print): 0099-2240 Ratings: BFI (2017): BFI-level 2 Web of Science (2017): Indexed yes BFI (2016): BFI-level 2 Scopus rating (2016): CiteScore 4.08 Web of Science (2016): Indexed yes BFI (2015): BFI-level 2 Scopus rating (2015): SJR 1.891 SNIP 1.308 CiteScore 4.14 Web of Science (2015): Indexed yes BFI (2014): BFI-level 2 Scopus rating (2014): SJR 1.857 SNIP 1.384 CiteScore 4.02 Web of Science (2014): Indexed yes BFI (2013): BFI-level 2 Scopus rating (2013): SJR 1.899 SNIP 1.414 CiteScore 4.25 ISI indexed (2013): ISI indexed yes Web of Science (2013): Indexed yes BFI (2012): BFI-level 2 Scopus rating (2012): SJR 1.975 SNIP 1.429 CiteScore 4.29 ISI indexed (2012): ISI indexed yes

Web of Science (2012): Indexed yes BFI (2011): BFI-level 2 Scopus rating (2011): SJR 1.914 SNIP 1.455 CiteScore 4.12 ISI indexed (2011): ISI indexed yes Web of Science (2011): Indexed yes BFI (2010): BFI-level 2 Scopus rating (2010): SJR 1.887 SNIP 1.436 Web of Science (2010): Indexed yes BFI (2009): BFI-level 2 Scopus rating (2009): SJR 1.972 SNIP 1.528 Web of Science (2009): Indexed yes BFI (2008): BFI-level 2 Scopus rating (2008): SJR 2.156 SNIP 1.572 Web of Science (2008): Indexed yes Scopus rating (2007): SJR 2.043 SNIP 1.647 Web of Science (2007): Indexed yes Scopus rating (2006): SJR 2.054 SNIP 1.602 Web of Science (2006): Indexed yes Scopus rating (2005): SJR 2.074 SNIP 1.653 Web of Science (2005): Indexed yes Scopus rating (2004): SJR 2.108 SNIP 1.648 Web of Science (2004): Indexed yes Scopus rating (2003): SJR 2.097 SNIP 1.821 Web of Science (2003): Indexed yes Scopus rating (2002): SJR 2.046 SNIP 1.754 Web of Science (2002): Indexed yes Scopus rating (2001): SJR 1.989 SNIP 1.736 Web of Science (2001): Indexed yes Scopus rating (2000): SJR 1.957 SNIP 1.758 Web of Science (2000): Indexed yes Scopus rating (1999): SJR 2.3 SNIP 1.732 Original language: English Adaptive laboratory evolution, Escherichia coli, Adaptive mutations, Phenotypic variation DOIs: 10.1128/AEM.00410-17 Source: FindIt Source-ID: 2358105263 Publication: Research - peer-review > Journal article - Annual report year: 2017