
The Transcriptional Landscape of the Cyanobacterium *Synechocystis*

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Cyanobacteria form a highly versatile group of microorganisms which have successfully adapted to various environmental conditions on Earth. Cyanobacteria have to respond to many environmental cues, integrating various external and internal stimuli to 'select the proper response'. Especially, their capacity for adaptation makes cyanobacteria an attractive paradigm for the study of regulatory mechanisms. Despite considerable progress, however, the knowledge of these mechanisms remains limited.

In striking contrast to the limited knowledge of regulatory interactions, considerable amounts of expression data has been accumulated for cyanobacteria over the recent decade. These data were produced by microarray experiments studying cyanobacteria in a large variety of conditions. Especially for *Synechocystis*, the first cyanobacterium sequenced and so far the best studied, a large number of microarray experiments have been performed. The experiments gave not only us the expression response of single genes, but have allowed the study of coordinated transcriptional responses to internal or external perturbations. It should be noted, however, the vast majority microarray analyses for *Synechocystis* have focused on a narrow range of mutations or environmental changes.

To obtain a more holistic picture of the transcriptional responses of *Synechocystis*, we have conducted a comprehensive meta-analysis of over 600 single microarrays measurements for more than 160 environmental conditions or genetic perturbations. Since these datasets are generated on different platforms, we took special care in the curation and pre-processing of the microarray data. This allowed us to avoid several pitfalls and to detect a large set of distinct expression patterns. Using an iterative two-way clustering approach, we identified characteristic expression patterns for photosynthesis, transcription, iron homeostasis and various other processes. Besides known and expected patterns for co-regulation, we detected a series of surprising co-expression patterns that pointing to novel co-regulatory mechanisms. This allowed us to study in detail the dynamic coupling of different biological processes as well as the influence of external and internal perturbations on this coupling.

Our approach does not only help to elucidate the response of gene clusters to a large set of perturbations, but also will assist in the annotation of a large set of genes whose functions are still not known. As two exemplary applications, we utilize the expression compendium to predict functions of uncharacterized genes as well as to elucidate the operon structure in *Synechocystis*.