Balancing & Re-routing: Distinctive control principles and synthetic biology applications of cyanobacterial metabolism

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Within a cell, all metabolic routes are closely connected. Therefore, cells have to manage the distribution of resources, i.e. the overall metabolism is coordinated and balanced according to the availability of energy equivalents as well as nutrients. As bacteria have a high surface to volume ratio they are even more challenged by constant changes of environmental as well as biochemical parameters. To maintain homeostasis and to adjust metabolism bacterial cells therefore require a plethora of sophisticated regulatory mechanisms that continuously process external or internal signals to determine in a situation-dependent way whether metabolic fluxes are finally directed into one or another route. However, it is scarcely understood how all these processes are regulated and coordinated in cyanobacteria. It turned out that data from typical model bacteria like *E. coli* or *Bacillus subtilis* can regularly not be applied because even for ubiquitous pathways cyanobacteria evolved unique regulatory mechanisms (as exemplified by the regulation of glutamine synthetase, BIOspektrum 25, p.610–613). However, to rationally engineer cyanobacteria for biotechnological or pharmaceutical applications, e.g. by channeling metabolic fluxes to obtain the maximum yield of a desired chemical product, it is of paramount importance to fully comprehend underlying molecular processes that control primary metabolism. Our research tackles these problems and aims at the basic understanding of key regulatory switches as well as their utilization to engineer synthetic cyanobacterial cell factories. Our investigation is targeting all regulatory levels: sensing and signaling (via sensory proteins or RNAs), transcriptional regulation of genes (via transcriptional regulators), RNA-based mechanisms targeting the posttranscriptional level (small regulatory RNAs and riboswitches) as well as the modulation of enzyme activities by molecular effectors (small regulatory proteins). In addition, we also make use of these intrinsic regulators to enable inducible expression of heterologous genes (for enzymes or entire pathways) or to direct metabolic fluxes towards specific products. The obtained knowledge will provide a scientific fundament for the rational design of photosynthesis-driven applications.