The core tenet of synthetic biology is the application of engineering principles such as standardization, modularity and rational design to accelerate the design-build-test loop for reprogramming biological systems by endowing them with novel tasks (Endy, 2005; de Lorenzo and Danchin, 2008; Church et al., 2014; Badenhorst and Bornscheuer, 2018; Kohman et al., 2018; de Lorenzo et al., 2018). Since its very inception as a field, synthetic biology has enabled researchers from different disciplines to extend and re-think genetic manipulations as the rational design and engineering of cells. Against this background, (micro)organisms can be regarded as programmable cellular machines—which can be modified by manipulating the cells’ software (DNA/RNA), hardware (physical cell components), and the processes encompassing processing and regulation of nucleic acids and, even more importantly, metabolism (which, together, make up for the operation system; Rampley et al. 2017; Danchin, 2009). Moreover, in the context of contemporary synthetic biology practice, the hardware of cells can be purposefully defined by means of genome design and engineering, for which systems biology plays an important role. Synthetic biology and systems biology are viewed, in this sense, as two sides of the same coin. To fulfill this overarching engineering purpose, the ever-expanding synthetic biology toolbox allows for the modification or tuning of gene network connectivities in a precise and in-place manner. Decomposing, manipulating and re-assembling the factors governing the hardware, software and operation system of the cell is crucial to understand its functioning in toto, e.g. for re-factoring—the process by which a set of related genes are removed from their native regulatory context and placed under synthetic expression control.