In silico RECONSTRUCTION OF PROTEIN-PROTEIN INTERACTION NETWORKS OF BACTERIA USED IN SYNTHETIC BIOLOGY APPLICATIONS

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ABSTRACT

The genetic and physiological characterization of bacteria that are metabolic engineering and synthetic biology resources is essential for the identification of appropriate targets for genetic modification towards the development of more efficient strains and the optimization of their fermentation processes. The number of fully sequenced bacteria has dramatically increased in recent years, providing a valuable basis for the design of high-throughput biomolecular (omic) analyses that can help elucidate the regulatory machinery connecting genotype to phenotype. The interpretation of physiological and omic measurement datasets could be greatly assisted by the accurate reconstruction and integrated analysis of the metabolic and protein-protein interaction (PPI) networks of the investigated bacteria. While a lot of effort has been placed in the genome-scale metabolic network reconstruction in bacteria, being a focal area of research in metabolic engineering for many years, this is not the case with the bacterial PPI networks. To-date, experimentally reconstructed PPI networks based on high-throughput experiments exist for very few bacterial systems[1]. Thus, for most of the bacteria, there is a need to *in silico* reconstruct their potential PPI network based on any available experimental data and bioinformatic resources using predictive models.

In light of this limited experimental PPI data availability for microbial systems, we designed and applied a workflow for the *in silico* reconstruction of the PPI network of two bacteria, *Streptomyces lividans* and *Moorella thermoacetica*, which have been used in synthetic biology applications in the recent years. *S. lividans* is a preferred host for the overproduction of secretory proteins and secondary metabolites of industrial and pharmaceutical interest[2], however, it has a very small number of experimentally determined PPIs reported in source databases. Through the applied workflow, we were able to identify more than a thousand experimentally supported PPIs based on comparative genomic analysis with evolutionarily adjacent bacterial systems. *M. thermoacetica* is a thermophilic Gram-positive acetogen that has been used for the non-photosynthetic CO_2 fixation for the production of useful chemicals[3]. While there is a limited number of experimentally determined PPIs for this bacterium too, a larger than for *S. lividans* number of multi-omic datasets are available, supporting a more reliable application of bioinformatics predictive algorithms. Our analysis so far has identified ~100 experimentally supported PPIs, which can be used to enrich our understanding of the molecular physiology of this microorganism. The reconstructed PPI networks of both microbes can form the basis for validation studies of key PPIs and be used in the design of synthetic biology experiments.

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