New approaches for improving strain design methodologies

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The field of Metabolic Engineering (ME) allows the design of improved microorganisms for industrial applications. The ultimate aim of ME is to identify genetic manipulations in silico leading to improved microbial strains that can be implemented using novel molecular biology techniques. This task, however, is a complex one, requiring the existence of reliable models and strain design tools. In this talk, several contributions to the field of ME will be presented.

Although the search for gene knock-outs is fairly established with in silico methodologies, most computational strain design methods fail to predict the effects of gene up/down-regulations and the addition of heterologous genes. In this scope, we have developed a new simulation method, Turnover Dependent Phenotypic Simulation (TDPS), which was designed with the goal of simulating quantitatively the phenotype of strains with diverse genetic modifications in a resource conscious manner. Besides gene deletions and down-regulations, TDPS can also simulate the up-regulation of metabolic reactions as well as the introduction of heterologous genes or the activation of "dormant" reactions. TDPS was validated using metabolically engineered S. cerevisiae strains available in the literature by comparing the simulated and experimental production yields of the target metabolite.

Another important aspect associated with model predictions is the influence of the biomass equation added to the model. Since most simulation tools require directly or indirectly the computation of maximal biomass formation, this composition has a great impact in the predictive power of these models. Moreover, biomass composition is intrinsically related with essentiality predictions. Within this scope, we have developed a framework to determine the soluble biomass components to be included in Genome-scale metabolic models.

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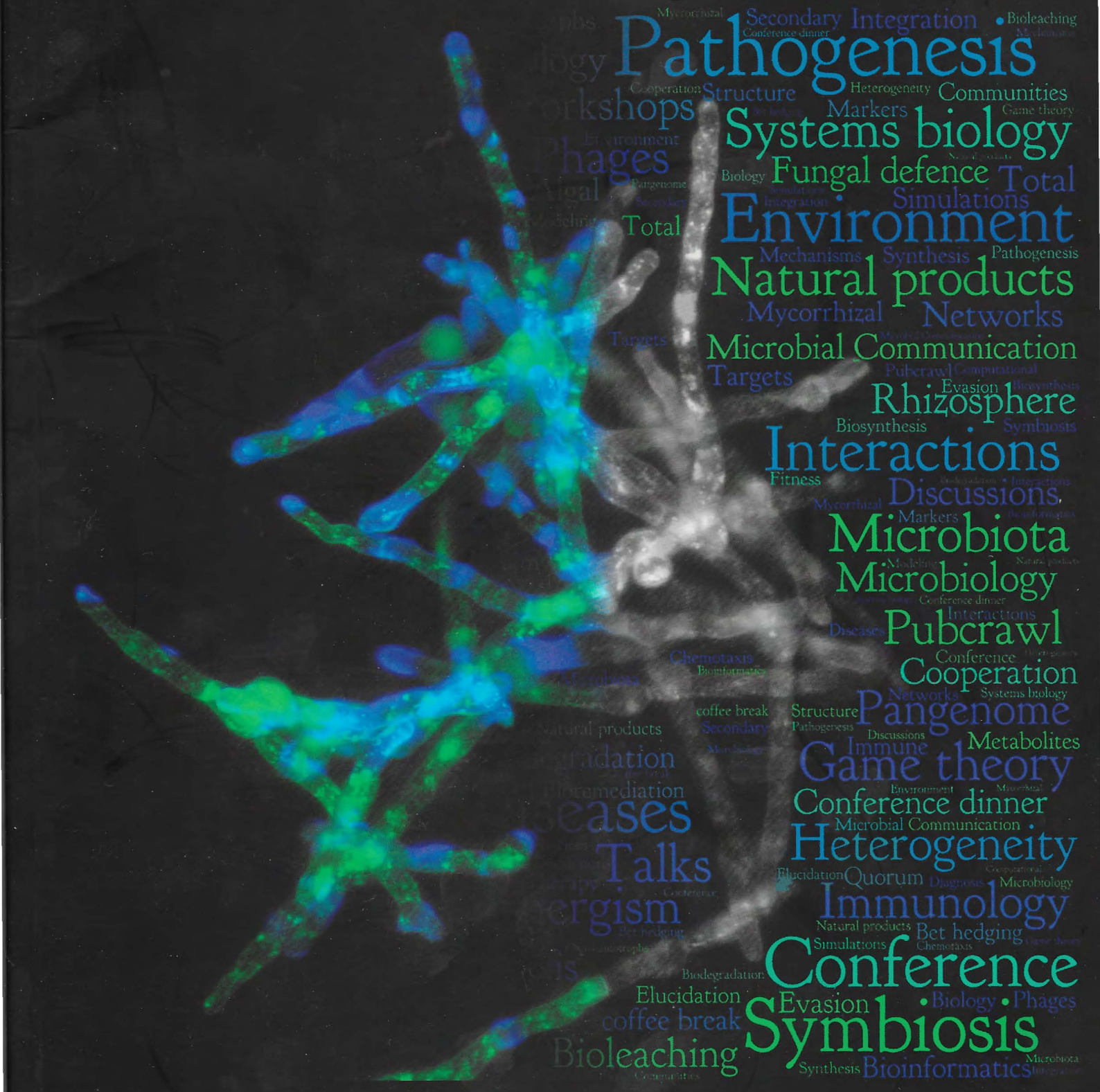

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