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Biochemical reaction networks meet Coalitional Game Theory: The importance of not being single

A fundamental question in the analysis of complex biological networks is how to determine which components (e.g. reactions) are most important regarding specific function. Virtually all existing approaches for establishing the importance of a reaction in a biological network are based on vitality-like indices. The importance of a reaction is then specified by the effect of its removal, emulating single knockout experiments in biology. However, such technique neglects topological features, like bypassing pathways, which are crucial for network robustness. Coalitional game theory provides a framework for extending the vitality-like indices by considering the contribution of single network elements with respect to all of its interactions in the network, based purely on the network topology. Here we propose a method combining cooperative game theory with flux balance analysis, a standard technique in the investigation of metabolic networks. We employ the method to rank reactions in metabolic networks with respect to a biologic function, in particular biomass production. Furthermore, our method is used in the design of a novel approach for determining network robustness to changes imposed by gene knock-outs.