Inferring metabolic dynamics using optimal control: the role of constraints and trade-offs

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Evolution can be considered as a natural process of trait optimization. Several researchers have exploited this idea by using optimality principles to explain the dynamic behavior of biological systems. The majority of these studies have considered single-objective criteria, leaving the identification of the underlying optimality principles as an open question. In parallel, the existence of functional biological trade-offs has been extensively discussed, mostly in terms of conflicting constraints. However, until recently, researchers have failed to make a connection between these two perspectives.

Here, we consider a unifying framework that integrates all these aspects by using a multicriteria optimal control formulation. For a given dynamic model of a biosystem and a set of possible cost functions, this method produces a set of Pareto optimal solutions (i.e. optimal trade-offs) which can be reconciled with experimental evidence to infer the optimality principle. This methodology also allow us to investigate how different balances in these trade-offs affect the dynamics. Further, we also show how it can be used to study the effect of constraints on the Pareto optimal predictions, highlighting their importance and the possible implications of associated uncertainties. We illustrate the capabilities of this approach with two case studies regarding the central carbon metabolism of *S. cerevisiae* and *B. subtilis*.