OptimModels: a framework for strain optimization using kinetic models

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Mathematical models have been applied to represent the complexity of cellular metabolism over the last decades. Two types of mathematical models are used for this purpose: kinetic and stoichiometric models. The reconstruction of kinetic metabolic models, however, is a complex task due to the difficulty in obtaining detailed information of enzyme kinetics.
Despite the early stage of their development, when compared with the stoichiometric metabolic models, kinetic models have already proven their capability to improve phenotype predictions and consequently more precise *in silico* strain design approaches [1].

One of the goals of Metabolic Engineering is the identification of genetic manipulations that will result in a microbial strain with a high yield/productivity of the desirable compound. This task can be reached using optimization algorithms based on metaheuristic approaches, such as Evolutionary Algorithms [2]. Although they do not guarantee the convergence to the best solution, these algorithms require relatively low computational time and provide a family of optimal or sub-optimal solutions that can be further inspected to select the most promising ones. Moreover, they allow the implementation of flexible objective functions and multi-objective design, and are easily parallelizable.

In this work, we developed a python package, named *optimModels*, which implements strain design methods based on Evolutionary Algorithms, using large-scale kinetic models as input.
Our case study uses two of the published kinetic metabolic models for *Escherichia coli*, proposed by Chassagnole and co-workers in 2002, and Jahan and co-workers in 2016.
We selected the maximization of serine and succinate production as objective functions and applied two different approaches, knockouts and under/over expression of enzymes, for strain design.

Preliminary results show that the framework presented here can be used for *in silico* strain design with kinetic metabolic models by finding the combination of genes to be knockout or/and their optimal levels of up/down-regulation.

References

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