CSB team project

Predicting strain design for PHB overproduction based on genome-scale model of Yeast

Poly-(R)-3-hydroxybutyrate (PHB) is the most common type of poly hydroxyalkanoates (PHAs) synthesized and accumulated by microorganisms. PHB has features that are similar with artificial synthetic plastics both physically and chemically, besides, it also has excellent characteristic such as biodegradability, optical activity, biocompatibility, which make them being widely applied in material field. Here, the aim of this project is to identify feasible strategies (knockout/overexpression/downexpression of particular genes) to overproduce PHB in Yeast.

Basic requirement:

1. Get the genome-scale metabolic model **Yeast 7.6_PHB**, analyze the topological properties, and find the important enzymes and compounds.
2. Learn about the *in-silico* strain design methods from the literature [1] and the database: https://omictools.com/metabolic-engineering-databases-category
   Please select one method, such as **OptFlux(**http://www.optflux.org/**), OptGene(in COBRA)**, to identify potential strategies of **metabolic genes** for PHB overproduction based on Yeast metabolic model above.

Advanced requirement:

1. Learn about the integration of regulatory network and metabolic network, get the integrated model from IDREAM[2] paper, and run **OptRAM** method[3] to identify potential strategies including both modification (knockout/overexpression/downexpression) of **TFs** and **metabolic genes** for improving PHB production.

Note: The Yeast 7.6_PHB model, regulatory associated files of Yeast, and the OptRAM code will be provided by instructor.

Team:

1. Students are required to form a **six-person-group**, so there will be five groups in total.
2. All groups are assigned with **the same project** mentioned in this guide.
3. Please select a leader and report your **group information** to T.A. after class, students left with no group will be randomly organized into teams.

Scores:

Your score of this project will be evaluated on following three aspects:

1. Results (including final result and stepwise ones) and detailed procedure (how you obtain your results)
2. Presentation delivered by your group on week16
3. Report submitted by your group by the end of semester

*Note: You should **explicitly** state the role of each group member by describing the task each person have done. Score will be given based on the responsibility you took, so it can be different among the same group.*

Reference

[1] Maia P, Rocha M, Rocha I. 2016. In silico constraint-based strain optimization methods: the quest for optimal cell factories. Microbiol Mol Biol Rev 80:45-67. doi:10.1128/MMBR.00014-15.

[2] Wang Z, Danziger SA, Heavner BD, Ma S, Smith JJ, Li S, et al. (2017) Combining inferred regulatory and reconstructed metabolic networks enhances phenotype prediction in yeast. PLoS Comput Biol 13(5): e1005489.

[3] Shen F, Sun R, Yao J, Li J, Liu Q, Price ND, et al. (2019) *OptRAM*: *In-silico* strain design via integrative regulatory-metabolic network modeling. PLoS Comput Biol 15(3): e1006835. https://doi.org/10.1371/journal.pcbi.1006835