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Finding the ways for potential increasing of L-valine biosynthesis yield in *C. glutamicum* with mathematical modeling

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Motivation and Aim: Nowadays the industrial production of amino acids is mostly based on microbiological approaches. The main request of this industry is maximization of the products' yield and minimization of input resources and energy costs. The solution is to develop a new bacterial strain or to optimize metabolic pathways of the existing one. The flux balance analysis allows researchers to assess the potential of various metabolic pathway modifications and suggest the best ones. In this work, we are focused on finding the ways of improving *C. glutamicum* ACTT 14067 strain in L-valine production.

Methods and Algorithms: We have used newly published whole-genome model (iCGB21FR) [1] as the basis model. The model was built on the strain *C. glutamicum* ATCC 13032. We have used Python library CobraPy (https://cobrapy.readthedocs.io/) as a computational tool and Escher (escher.readthedocs.io/) for the visualization of results and subsequent analysis. We have fitted the model using the data on Russian National Collection of Industrial Microorganisms strain *C. glutamicum* ACTT 14067 (B-5212) (https://vkpm.genetika.ru/katalog-mikroorganizmov/show21916/).

Results: We adapted the recently published iCGB21FR full-genome model, which is based on the *C. glutamicum* strain ATCC 13032 - the parental strain for *C. glutamicum* ACTT 14067. A comparative analysis of the genomes of these two strains was performed. The analysis showed a difference in enzyme set including those involved in glycolysis, pentose phosphate pathway, tricarboxylic acid cycle, pantothenate and branched-chain amino acid biosynthesis pathways. The enzymes that had been knocked out were excluded from the original model. A series of computational experiments were performed with different environmental conditions, different carbon sources in order to obtain potential estimates of the productivity of the strain and its difference from the parental strain. To analyze the processes involved, the initial metabolic maps were extended to account for valine biosynthesis and additional carbon sources. A number of model scenarios were calculated and valine yields under aerobic and anaerobic conditions were shown. Varying the target function between biomass growth and valine yield produced upper and lower estimates for valine yield under different conditions. For each scenario, information on strain growth rate, valine yield, and the distribution of carbon across different products, including valine, is presented. The adapted model can be used for assessing the potential valine yield for particular cultivation medium conditions.

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References

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