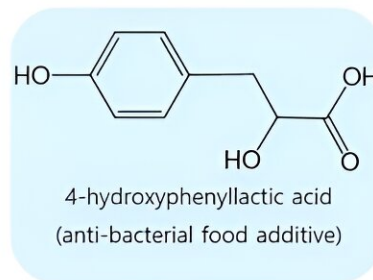
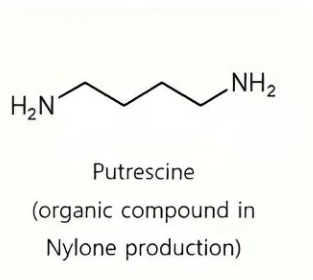
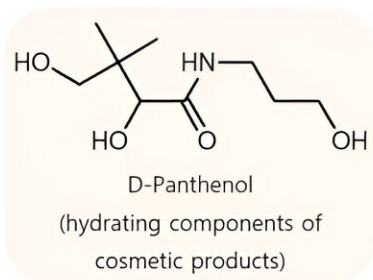
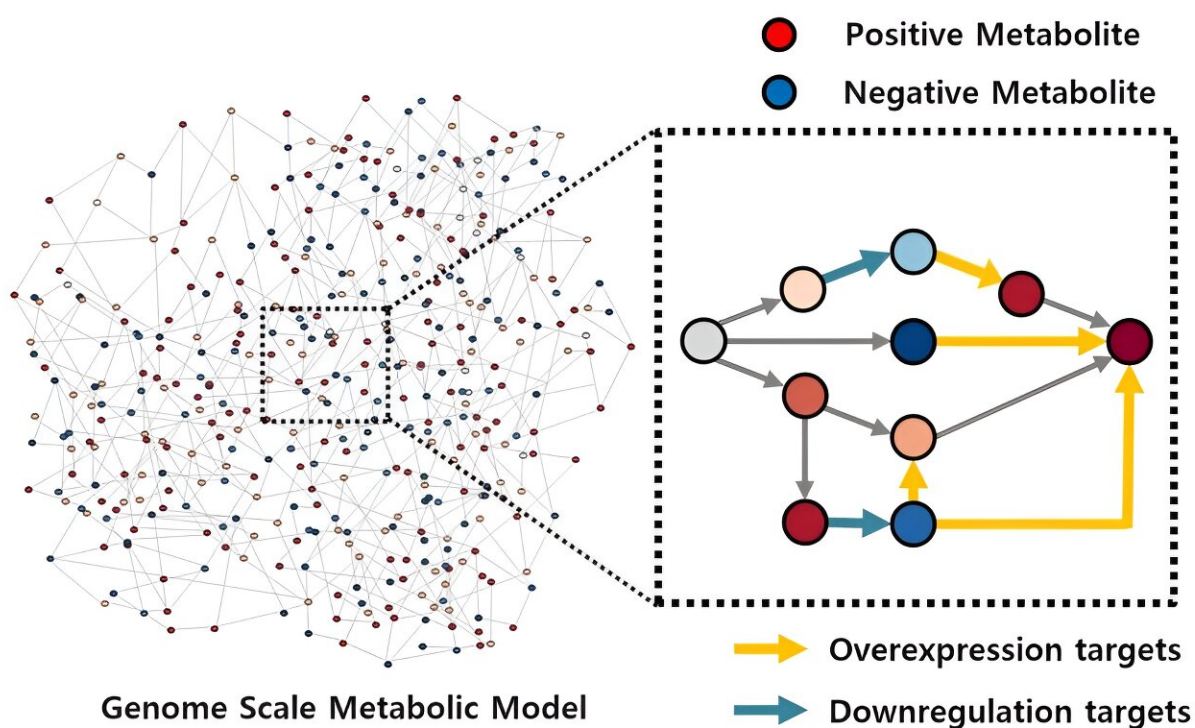


# New simulation program offers way to build microbial cell factories quickly and efficiently

November 9 2023



Conceptual diagram of the flow of iBridge simulation. Credit: KAIST Metabolic & Biomolecular Engineering National Research Laboratory

As climate change and environmental concerns intensify, sustainable microbial cell factories garner significant attention as candidates to replace chemical plants. To develop microorganisms to be used in the microbial cell factories, it is crucial to modify their metabolic processes to induce efficient target chemical production by modulating its gene expressions.

Yet, the challenge persists in determining which gene expressions to amplify and suppress, and the experimental verification of these modification targets is a time- and resource-intensive process even for experts. The challenges were addressed by a team of researchers at KAIST (President Kwang-Hyung Lee) led by Distinguished Professor Sang Yup Lee.

The school now has a method for building a microbial factory at low cost, quickly and efficiently, was presented by a novel computer simulation program developed by the team under Professor Lee's guidance, which is named "iBridge."

This innovative system is designed to predict gene targets to either overexpress or downregulate in the goal of producing a desired compound to enable the cost-effective and efficient construction of [microbial cell factories](#) specifically tailored for producing the [chemical compound](#) in demand from renewable biomass.

Systems [metabolic engineering](#) is a field of research and engineering pioneered by KAIST's Distinguished Professor Sang Yup Lee that seeks to produce valuable compounds in industrial demands using

microorganisms that are re-configured by a combination of methods including, but not limited to, metabolic engineering, [synthetic biology](#), systems biology, and fermentation engineering.

In order to improve microorganisms' capability to produce useful compounds, it is essential to delete, suppress, or overexpress microbial [genes](#). However, it is difficult even for the experts to identify the gene targets to modify without experimental confirmations for each of them, which can take up an immeasurable amount of time and resources.

The newly developed iBridge identifies positive and negative metabolites within [cells](#), which exert positive and/or negative impact on the formation of the products, by calculating the sum of covariances of their outgoing (consuming) reaction fluxes for a target chemical. Subsequently, it pinpoints "bridge" reactions responsible for converting negative metabolites into positive ones as candidates for overexpression, while identifying the opposites as targets for downregulation.

The research team successfully utilized the iBridge simulation to establish E. coli microbial cell factories each capable of producing three of the compounds that are in high demands at a production capacity that has not been reported around the world.

They developed E. coli strains that can each produce panthenol, a moisturizing agent found in many cosmetics, putrescine, which is one of the key components in nylon production, and 4-hydroxyphenyllactic acid, an anti-bacterial food additive. In addition to these three compounds, the study presents predictions for overexpression and suppression genes to construct microbial factories for 298 other industrially valuable compounds.

Dr. Youngjoon Lee, the co-first author of this paper from KAIST, emphasized the accelerated construction of various microbial factories

the newly developed simulation enabled. He stated, "With the use of this simulation, multiple microbial cell factories have been established significantly faster than it would have been using the conventional methods. Microbial cell factories producing a wider range of valuable compounds can now be constructed quickly using this technology."

Professor Sang Yup Lee said, "Systems metabolic engineering is a crucial technology for addressing the current [climate change](#) issues." He added, "This simulation could significantly expedite the transition from resorting to conventional chemical factories to utilizing environmentally friendly microbial factories."

The team's work on iBridge is described in a paper titled "Genome-Wide Identification of Overexpression and Downregulation Gene Targets Based on the Sum of Covariances of the Outgoing Reaction Fluxes" written by Dr. Won Jun Kim, and Dr. Youngjoon Lee of the Bioprocess Research Center and Professors Hyun Uk Kim and Sang Yup Lee of the Department of Chemical and Biomolecular Engineering of KAIST. The paper was [published](#) in *Cell Systems*.

**More information:** Won Jun Kim et al, Genome-wide identification of overexpression and downregulation gene targets based on the sum of covariances of the outgoing reaction fluxes, *Cell Systems* (2023). [DOI: 10.1016/j.cels.2023.10.005](#)

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