

L-valine Production from *Escherichia coli* by Fed-batch Fermentation

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We have previously developed an *Escherichia coli* strain which is 100% genetically defined, producing high-yield L-valine in batch culture by targeted genome engineering combined with transcriptome analysis and gene knock-out simulation of the *in silico* genome-scale metabolic network. This engineered strain was able to produce 7.55 g/L L-valine with 20 g/L glucose, resulting in an impressively high yield of 0.378 g L-valine per g glucose. In this study, the remaining feedback inhibition was removed, and the development of a fed-batch fermentation process was performed. The results obtained here clearly demonstrate that the trade-off between L-valine and biomass formation should be optimized specifically towards L-valine production. Finally, the fed-batch culture of the further engineered strain allowed production of 32.3 g/L L-valine. To our knowledge, the L-valine concentration obtained here is the highest concentration ever reported in *E. coli*.

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