

# Testing plasmid stability of Escherichia coli using the Continuously Operated Shaken BIOreactor System.

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## Abstract

Plasmids are common vectors to genetically manipulate Escherichia coli or other microorganisms. They are easy to use and considerable experience has accumulated on their application in heterologous protein production. However, plasmids can be lost during cell growth, if no selection pressure like, e.g., antibiotics is used, hampering the production of the desired protein and endangering the economic success of a biotechnological production process. Thus, in this study the Continuously Operated Shaken BIOreactor System (COSBIOS) is applied as a tool for fast parallel testing of strain stability and operation conditions and to evaluate measures to counter such plasmid loss. In specific, by applying various ampicillin concentrations, the lowest effective ampicillin dosage is investigated to secure plasmid stability while lowering adverse ecological effects. A significant difference was found in the growth rates of plasmid-bearing and plasmid-free cells. The undesired plasmid-free cells grew 30% faster than the desired plasmid-bearing cells. During the testing of plasmid stability without antibiotics, the population fraction of plasmid-bearing cells rapidly decreased in continuous culture to zero within the first 48 h. An initial single dosage of

ampicillin did not prevent plasmid loss. By contrast, a continuous application of a low dosage of 10 µg/mL ampicillin in the feed medium maintained plasmid stability in the culture. Consequently, the COSBIOS is an apt reactor system for measuring plasmid stability and evaluating methods to enhance this stability. Hence, decreased production of heterologous protein can be prevented. © 2016 American Institute of Chemical Engineers Biotechnol. Prog., 32:1418-1425, 2016.

## Involved units

[Bio Pilot Plant](#) [Miriam Agler-Rosenbaum](#) [Read more](#)

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## Identifier

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