

In-situ removal of solid products during whole-cell biocatalysis

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Project term: September 2001 – September 2004

Financed by: MHO-USC-DUT Project in Chemical Engineering



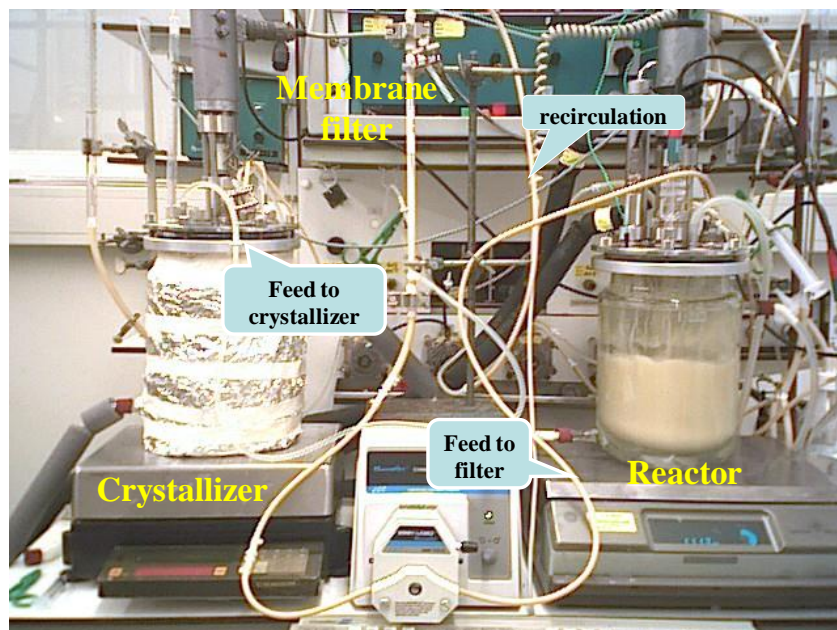
Description

In-situ product crystallization was considered in this project, as most products that are produced by fermentation are solids, and many inhibit the fermentation or are degraded during fermentation. In-situ crystallization may directly provide the desired product (in already pure form) without the need for an auxiliary phase. The combination of fermentation and product crystallization could be a route to sustainable processes.

If the crystals could be separated directly from the cells during fermentation, production costs might be reduced as:

- the number of unit operations is reduced,
- the amounts of solvent and waste streams are minimized, if not eliminated; and
- fed-batch fermentation might become more productive, either if high hold-ups of crystals in the medium are limiting the length of the process, or if crystallization reduces product inhibition and degradation, by lowering the extracellular product concentration.

We considered aerobic fed-batch operation, which is the usual fermentation operation, in our study of coupled fermentation-crystallization processes. The model microorganism was *Saccharomyces cerevisiae* and it was used for enantioselective reductions of precursors.



Dissertation

E.M. Buque, In-situ removal of solid products during whole-cell biocatalysis. PhD thesis, Delft University of Technology, 2005. <http://resolver.tudelft.nl/uuid:02f16872-c4b3-41c8-9b47-9c5301bf3957>

Publications from the dissertation

1. E.M. Buque, I. Chin-Joe, A.J.J. Straathof, J.A. Jongejan, and J.J. Heijnen, Immobilization affects the rate and enantioselectivity of 3-oxo-ester reduction by baker's yeast [Enzyme Microb. Technol.](#), **31** (2002) 656-664.
 2. E.M. Buque, A.J.J. Straathof, J.J. Heijnen and L.A.M. van der Wielen, In situ product removal using a crystallization loop in asymmetric reduction of 4-oxoisophorone by *Saccharomyces cerevisiae*, [Biotechnol. Bioeng.](#) **86** (2004) 795-800 .
 3. E.M. Buque-Taboada, A.J.J. Straathof, J.J. Heijnen, and L.A.M. van der Wielen, Substrate inhibition and product degradation during the reduction of 4-oxoisophorone by *Saccharomyces cerevisiae*, [Enzyme Microb. Technol.](#) **37** (2005) 625-633.
 4. E.M. Buque-Taboada, A.J.J. Straathof, J.J. Heijnen, and L.A.M. van der Wielen, Microbial reduction and in-situ product crystallization coupled with biocatalyst cultivation during the synthesis of 6R-dihydro-oxoisophorone, [Adv. Synth. Catal.](#) **347** (2005) 1147-1154.
 5. E.M. Buque-Taboada, A.J.J. Straathof, J.J. Heijnen, and L.A.M. van der Wielen, In Situ Product Recovery by Crystallization: basic principles, design, and potential applications in whole-cell biocatalysis. [Appl. Microbiol. Biotechnol.](#) **71** (2006) 1-12.
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