

Towards the integration of fermentation and crystallisation

PhD-student: Maria C. Cuéllar

Promotor: Prof.Dr.Ir. Luuk A.M. van der Wielen, Prof.Dr.Ir. J.J. Heijnen

Supervisor: Dr.Ir. Adrie J.J. Straathof

Institute: Delft University of Technology, Department of Biotechnology, Bioseparation Technology section

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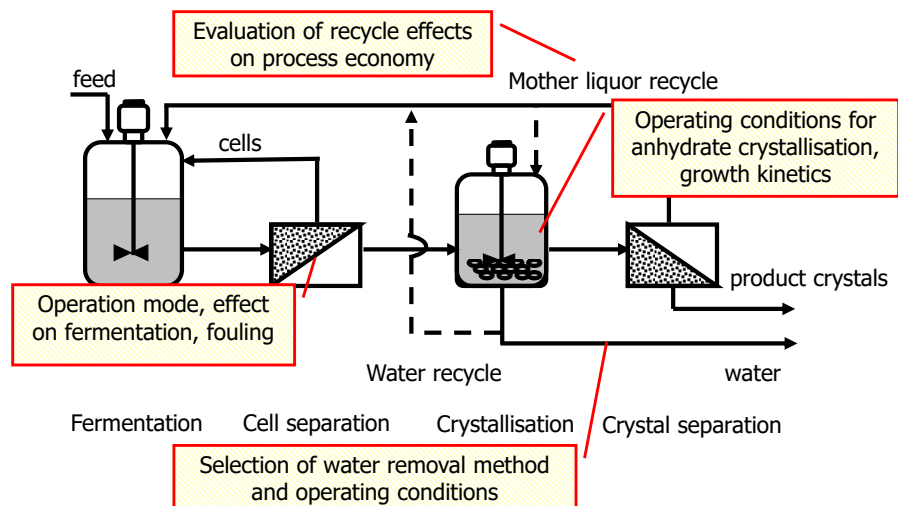
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Description

In this study, in situ crystallisation was studied, since most chemicals produced by fermentation are commercialised as solids. In this way, the resulting integrated process should lead to higher fermentation productivities (by removing product toxicity and/or degradation) and reduced downstream operations (by recovering the product already in crystal form), without requiring the use of auxiliary materials.

As a case study we chose the production of the amino acid L-Phenylalanine (Phe) by an engineered strain of *Escherichia coli*. Phe synthesis suffers from feedback inhibition, which limits the productivity of the system. Since Phe is still soluble at fermentation conditions, removal of product crystals might be possible by means of an external loop. The development of the concept for this model system is discussed, considering the metabolic capabilities of the microorganism, the crystallisation requirements (product specifications) and the integration of operations. The process performance is compared with that of the process without in situ product crystallisation.



Dissertation

M.C. Cuéllar Soares, Towards the integration of fermentation and crystallisation, PhD thesis, Delft University of Technology, 2008

Publications from the dissertation

1. M.C. Cuellar, D. Sanchez Garcia, A.J.J. Straathof, J.J. Heijnen and L.A.M. van der Wielen, Crystallization of L-phenylalanine anhydrate for product recovery during fermentation. In: P.J. Jansens, J.H. Ter Horst and S. Jiang, BIWIC 2006 13th International Workshop on Industrial Crystallization, IOS Press, Amsterdam (2006).
 2. M.C. Cuellar, T.W. Zijlmans, A.J.J. Straathof, J.J. Heijnen, L.A.M. van der Wielen, Model-based evaluation of cell retention by crossflow ultrafiltration during fed-batch fermentations with *Escherichia coli*, [Biochem. Eng. J. 44 \(2009\) 280-288](#).
 3. M.C. Cuellar, S.N. Herreilers, A.J.J. Straathof, J.J. Heijnen and L.A.M. van der Wielen, Limits of operation for the integration of water removal by membranes and crystallization of L-phenylalanine, [Ind. Eng. Chem. Res. 48 \(2009\)1566-1573](#).
 4. M.C. Cuellar, A.J.J. Straathof, E.J.A.X van de Sandt, J.J. Heijnen, L.A.M. van der Wielen, Conceptual evaluation of integrated process configurations for the recovery of L-phenylalanine product crystals during fermentation, [Ind. Eng. Chem. Res. 49 \(2010\) 682-689](#).
 5. M.C. Cuellar Soares, A.J.J. Straathof,, L.A.M. van der Wielen, E.J. van de Sandt, J.J. Heijnen, Process for in situ crystallisation of a product in a bioconversion process, [WO 2008022852](#)
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