Improved provision of pure enantiomers by coupling separation, racemizaton and recycling processes

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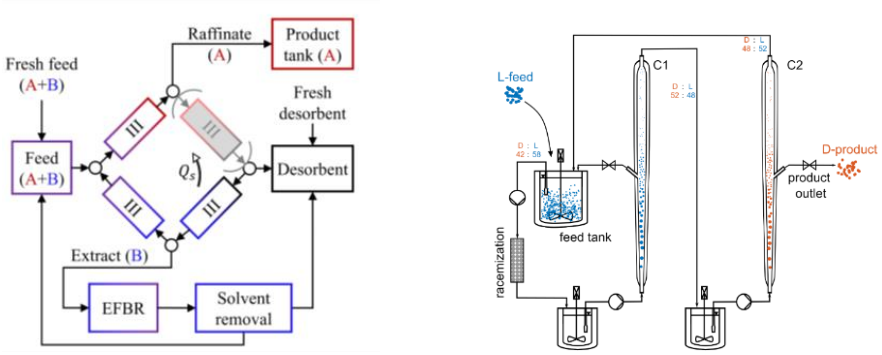
Abstract

Enantiomers are pairs of chemical compounds, which behave as image and mirror-image. Since the living world constitutes exclusively of the L-form of amino acids, two enantiomers generate different effects in biological systems. For this reason there is a need in efficient methods to provide pure enantiomers.
We will report about the development of processes based on applying enantioselective chromatography and preferential crystallization [1]. Besides discussing the separation of racemic feed mixtures we will also consider the transformation of an wanted into a target enantiomer. Essential ingredient of the corresponding continuous processes suggested is the exploitation of racemization reactions carried out in enzymatic fixed bed reactors (EFBR) which contain immobilized racemases.
As a first example we will discuss the continuous separation of racemic DL-methionine using Simulated Moving Bed (SMB) chromatography combined with an immobilized amino acid racemase originating from *Pseudomonas putida*. D-methionine could be produced with very high purity and yield using the configuration shown below (left). A second example exploits preferential crystallization (PC). This growth controlled process works in metastable solutions which contain both enantiomers. PC is initiated by seeding enantiopure crystals and must be terminated prior to the nucleation of the other enantiomer. The process suggested starts with enzymatically converting an available but "wrong" enantiomer (e.g. a L-amino acid) into a racemic mixture. To generate favorable driving forces the subsequent application of two sequential PC steps is attractive. After the second step pure target (e.g. a D-amino acid) can be collected. This will be demonstrated for transforming L- into D-asparagin monohydrate applying an EFBR jointly with two fluidized bed crystallizers (right part of figure).



Left: Coupling of SMB chromatography with an enzymatic fixed bed reactor (EFBR) for racemization to continuously provide an enantiomer A from a racemic feed mixture (A+B). **Right:** Coupling continuous enzymatic racemization with two-stage preferential crystallization (PC) performed in fluidized bed crystallizers to transfer a L-amino acid completely into the corresponding D-amino acid.

[1] Heike Lorenz and Andreas Seidel-Morgenstern, Processes to separate enantiomers, *Angewandte Chemie International Edition*, 53, 1218-1250 (2014)