A model-based framework for design of intensified enzyme-based processes

This thesis presents a generic and systematic model-based framework to design intensified enzyme-based processes. The development of the presented methodology was motivated by the needs of the bio-based industry for a more systematic approach to achieve intensification in its production plants without an excessive investment in experimental resources. Process intensification has recently gained a lot of attention since it is a holistic approach to design safer, cleaner, smaller, cheaper and more efficient processes. This dissertation proposes a methodological approach to achieve intensification in enzyme-based processes which have found significant application in the pharmaceutical, food, and renewable fuels sector. The framework uses model-based strategies for (bio)-chemical process design and optimization, including the use of a superstructure to generate all potential reaction(s)-separation(s) options according to a desired performance criteria and a generic mathematical model represented by the superstructure to derive the specific models corresponding to a specific process option. In principle, three methods of intensification of bioprocess are considered in this thesis: 1. enzymatic one-pot synthesis, where, for example, the combination of two enzymatic reactions in one single reactor is examined; 2. chemo-enzymatic one pot synthesis, where, for example, one enzymatic reaction and one alkaline catalytic reaction occur simultaneously in a single reactor; and 3. in-situ product recovery/removal (ISPR), where, for example, a separation step is integrated with the reaction step. Often, enzyme-based processes have limited productivity and yield, which may be due to the unfavorable reaction equilibrium, product inhibition to the enzyme and/or product degradation. Additionally, downstream processing for enzyme-based processes is difficult and a way to simplify it is by reducing the reaction and separation steps by for example, combining the reaction and separation in a single processing step. The implementation of intensification methods usually involves experiment-based investigation which causes limitations in the search space of process options leading to a high risk of implementing sub-optimal processes. Therefore, applying the framework presented in this thesis, all possible process options can be considered, and using a hierarchical decomposition approach for optimization, the search space is reduced to locate the candidate process options, giving an optimal design where further experimental efforts can be focused on. The application of a generic and systematic model-based framework is illustrated through a case study involving the production of an important intermediate pharmaceutical: N-acetyl-D-neuraminic acid (Neu5Ac). A second case study is added and deals with the enzymatic production of biodiesel.