Modelling of Gradients in Large Scale Bioreactors

The heart of biotechnology and the bio-based economy is microbial conversion of substrates to desired products in fermentation processes. The physiological machinery within the microorganism is able to synthesise a range of valuable molecules spanning the product portfolio from bulk chemicals, such as alcohols and organic acids to fine chemicals, such as vitamins and finally to complex molecules such as industrial enzymes and monoclonal antibodies. Common for the processes developed to produce the desired products is the need for large production tanks that compensate for the low productivity of fermentation processes compared to conventional chemical processes. The scale of the production tanks is generally in the range of ten cubic meters to several hundred cubic meters.

Maintaining optimal production conditions in these large vessels is often achieved by a configuration of several agitators inside the vessel. The agitation is not only responsible for maintaining homogeneous conditions inside the production vessels but also for providing a sufficient distribution of air in aerobic fermentation processes. In order to understand the performance and troubleshoot problems of the large-scale fermenters fundamental understanding of the mixing and mass transfer capabilities of these reactors is required. Computational fluid dynamics and spatial measurements of process variables are the most common theoretical and empirical ways to investigate the process gradients in large-scale fermenters resulting from insufficient homogenisation. The improvement of computational capabilities over the past few years has enabled simulations of these complex phenomena at full scale, but the modelling choices and assumptions required are yet to be thoroughly analysed. In this thesis, the role of mixing and mass transfer in relation to performance of large scale fermentation processes is outlined. The application of computational fluid dynamics in industrial fermentation processes is described at pilot and full scale for a Trichoderma reesei fermentation. A key input parameter in the numerical simulation of the aerobic fermentations is the size of air bubbles, which has been investigated at pilot scale using an endoscopic method. The oxygen concentration gradients of three impeller configurations of a full-scale fermenter have been characterised and compared with experimental data. Finally, a methodology for simplifying the complex mathematical models resulting from applying the finite element method to compartment models is described and applied to a pilot scale fermenter. The reduction of the model complexity enables a broader application of mathematical models for process optimization and control, but also introduces the possibility of including the understanding of hydrodynamics in process research and development at an early stage.