Content

1 Introduction, objectives and thesis outline 1

2 Theoretical background 5

2.1 State of the art of microfluidics and microbioreactors 5

2.1.1 State of the art of microbioreactors for bacterial and yeast cell cultivations 8

2.1.2 Microreactors for biocatalysis 17

2.2 Sensor integration in microbioreactors for monitoring biotechnological process variables 17

2.3 Fluid dynamic characterization of microbioreactors 18

2.4 Cultivation of microorganisms 24

2.4.1 Batch cultivation 24

2.4.2 Continuous cultivation 25

3 Materials and methods 27

3.1 Materials 27

3.1.1 Microbioreactor designs and manufacturing 27

3.1.2 Strains, enzymes and carriers 30

3.2 Methods 34

3.2.1 Characterization of a multiphase microbioreactor 34

3.2.2 Computational fluid dynamics simulations 37

3.2.3 Cultivation of *Saccharomyces cerevisiae* 39

3.2.4 Cultivation of *Staphylococcus carnosus* 40

3.2.5 Heterogeneous biocatalysis 41

3.2.6 Sensors 43

4 Characterization of a multiphase microbioreactor 51

4.1 Fluid dynamics 51

4.1.1 Airflow rate 51

4.1.2 Bubble characterization and gas hold-up 52

Dieses Werk ist copyrightgeschützt und darf in keiner Form vervielfältigt werden noch an Dritte weitergegeben werden.
Es gilt nur für den persönlichen Gebrauch.

4.1.3 Reynolds number of the rising bubbles and volumetric power input 54
4.1.4 Steady-state computational fluid dynamics simulations, superficial liquid velocity, and the Reynolds number of the liquid 56
4.2 Mixing time and transient computational fluid dynamics simulations 57
4.3 Oxygen transfer 60
4.4 Cultivation of *Saccharomyces cerevisiae* 62
5 Online sensor integration of a multiphase microbioreactor 65
5.1 Microbioreactor characterization 65
5.2 Sensor integration and calibration 67
5.3 Cultivation of *Saccharomyces cerevisiae* 68
6 Application of microbioreactors 75
6.1 Cultivation in batch and continuous mode of *Staphylococcus carnosus* 76
6.2 Biotransformation in batch and continuous mode in a microfluidised bed bioreactor 82
7 Conclusions and outlook 93
8 References 97

Dieses Werk ist copyrightgeschützt und darf in keiner Form vervielfältigt werden noch an Dritte weitergegeben werden.
Es gilt nur für den persönlichen Gebrauch.