ZENTRUM ANGEWANDTE CHEMIE

Institut für Technische Chemie

Institut für Technische Chemie, Callinstr. 5, 30167 Hannover

Partner in der Forschung

Leibniz Universität Hannover

Investigation of the productivity of a novel ceramic membrane bioreactor system for steady-state fermentations

Christian Endres[1], Sascha Beutel[1], Sheena Fraser[2], Wade Edwards[2] and Thomas Scheper[1]

1) Institut für Technische Chemie, Universität Hannover, Callinstr. 5, 30167 Hannover, Germany

2) Synexa Life Sciences, Cape Town, South Africa

Introduction

Compared to traditional fermenters an important advantage of membrane-based bioreactors is the provision of an artificial environment for an increased biomass density and enhanced productivity of immobilized shear stress-sensitive organisms.

The novel Quorus GLS and LS bioreactors investigated in this study consist of ceramic capillary membranes and therefore provide an ideal platform for the immobilization and cultivation of aerobic or anaerobic shear stress-sensitive microorganisms. Due to their design they are suited for steady-state or submerged and oxygen limited cultivation and continuous production of valuable secondary metabolites, recombinant products or toxic metabolites.

Quorus GLS

Mode of operation

- Biomass is grown in the aerated extracapillary space (ECS) with nutrient medium flowing unidirectional from the lumen of the capillary membranes towards the ECS.
- With a sufficient thickness of the biofilm radial nutrient and oxygen gradients are established across the biofilm.
- The nutrient gradient is controlled to support primary growth of the microorganism and to induce secondary metabolite production.
- Secreted products are collected with the medium stream passing the biofilm.

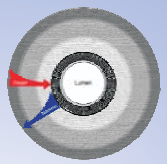

Fig. 1: Oxygen and nutrient gradients during biofilm formation around the ceramic membranes in the Quorus GLS bioprocess

Evaluation of productivity

- Cultivation of the fungus *A.niger* in a 50 membrane Quorus 2 L bioreactor and monitoring of the production of a secreted recombinant protein.
- Benchmarking in traditional fermentation vessels like shaking flasks, 3 L Biostat A plus, and 15 L Biostat C.
- Stable protein production in the Quorus GLS bioreactor for more than 40 days.
- Quorus GLS space-time-yield is significantly higher than in all other cultivation vessels.

Fig. 2: Growth of *A.niger* on the Quorus GLS ceramic membranes

- Best suited for steady-state cultivations of aerobic filamentous microorganisms
- Disposable and scalable ceramic membrane bioreactor
- Fully automated design
- Stable and continuous process
- Low shear stress environment
- Exploitation of steady-state biofilms for the production of secreted compounds such as recombinant proteins or secondary metabolites
- Cultivation controlled through rate of nutrient delivery

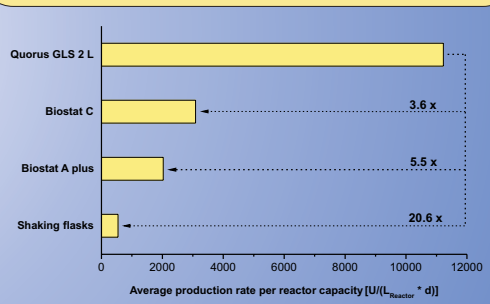

Fig. 3: Average production rate of a recombinant protein per reactor capacity in various cultivation vessels while cultivation of *A.niger*.

Quorus LS

Mode of operation

- Biomass is immobilized and established on the outer surface of the ceramic membranes in the ECS in a submerged and oxygen-limited environment.
- With a sufficient thickness of the biofilm a radial nutrient gradient is established across the biofilm.
- Nutrient supply is achieved through a continuous feed into the ECS.
- Secreted products and metabolic waste are continuously removed by transportation through the capillary wall into the intracapillary space.

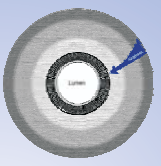

Fig. 4: Nutrient gradient during biofilm formation around the ceramic membranes in the Quorus LS bioprocess

Evaluation of productivity

- Cultivation of the facultative anaerobic bacterium *L.lactis* PRA290 in a Quorus LS 0.22 L bioreactor and monitoring of the production of recombinant β-lactamase.
- Benchmarking in traditional fermentation vessels like shaking flasks, stationary flask cultures and Biostat A plus.
- Quorus LS space-time-yield and total product output is significantly higher than in all other cultivation vessels.

Fig. 5: Quorus bioreactor compartment with one LS 0.22 L reactor chamber

- Best suited for cultivations of facultative anaerobic or microaerophillic microorganisms
- Low shear stress environment
- Disposable and scalable ceramic membrane bioreactor
- Fully automated design and product sampling
- Cell-free product stream and continuous removal of toxic metabolites and/or metabolic waste
- Exploitation of submerged biofilms for the production of secreted compounds, e.g. recombinant proteins
- Cultivation controlled through nutrient flux or pH

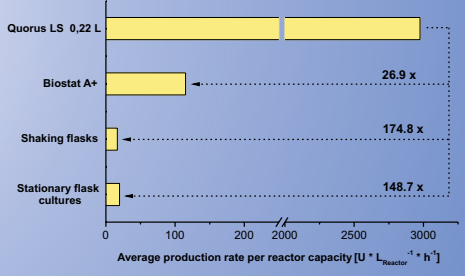

Fig. 6: Average production rate of a β-lactamase per reactor capacity in various cultivation vessels while cultivation of *L.lactis* PRA290.

This project was supported by Synexa Life Sciences

synexa LIFE SCIENCES www.synexagroup.com