1.74 Fed-batch Cultivation of *Saccharomyces cerevisiae* in a Hyperbaric Bioreactor

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Fed-batch cultivation of *Saccharomyces cerevisae* is the dominating technique in high cell density cultures of processes such as the production of Baker's yeast [1] and recombinant proteins [2]. Due to the high oxygen demand of these cultures, the oxygen supply to the culture is an important and difficult task.

The aim of this work was to study the use of hyperbaric air for oxygen mass transfer improvement on *S. cerevisiae* fed-batch cultivation. Thus, the effects of increased air pressure up to 1.5 MPa on cell behaviour were investigated. The effects of oxygen and carbon dioxide were dissociated from the effects of total pressure by the use of pure oxygen and gas mixtures enriched with CO_2.

Fed-batch experiments were performed in a stirred tank reactor with a 600 mL stainless steel vessel. Exponential feeding at dilution rates up to 0.1 h^{-1} was used, in order to ensure full respiratory metabolism [3]. The ethanol production observed at atmospheric pressure was reduced by the bioreactor pressurization up to 1.0 MPa. Best results were obtained for experiments where pressure was increased gradually throughout time. In this case, the experimental cell mass yield attained the predicted value. This result indicates the existence of an adaptation period of the cells to hyperbaric conditions. This work proved that hyperbaric air up to 1.0 MPa could be applied on *S. cerevisiae* cultivation under low glucose flux. According with previous work, the effect of pressure on yeast behaviour strongly depends on other conditions of operation [4].

Inhibition of cell growth and product formation was observed for the operation at 1.5 MPa total air pressure. This effect was due to the increase on the oxygen partial pressure because similar cell behaviour was obtained using pure oxygen at the same partial pressure (0.32 MPa). Oxygen toxicity resulted in a drastic loss of cell viability, inhibition of ATP synthesis and morphologic changes. The increase of carbon dioxide partial pressure in the gas mixture up to 48 kPa slightly decreased the cell mass yield, but had no significative effects on cell viability.

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