A novel model-based control strategy for aerobic filamentous fungal fed-batch fermentation processes - DTU Orbit (16/12/2018)

A novel model-based control strategy has been developed for filamentous fungal fed-batch fermentation processes. The system of interest is a pilot scale (550L) filamentous fungus process operating at Novozymes A/S. In such processes, it is desirable to maximize the total product achieved in a batch in a defined process time. In order to achieve this goal, it is important to maximize both the product concentration, and also the total final mass in the fed-batch system. To this end, we describe the development of a control strategy which aims to achieve maximum tank fill, while avoiding oxygen limited conditions. This requires a two stage approach: (i) calculation of the tank start fill; and (ii) on-line control in order to maximize fill subject to oxygen transfer limitations. First, a mechanistic model was applied off-line in order to determine the appropriate start fill for processes with four different sets of process operating conditions for the stirrer speed, headspace pressure, and aeration rate. The start fills were tested with eight pilot scale experiments using a reference process operation. An on-line control strategy was then developed, utilizing the mechanistic model which is recursively updated using on-line measurements. The model was applied in order to predict the current system states, including the biomass concentration, and to simulate the expected future trajectory of the system until a specified end time. In this way, the desired feed rate is updated along the progress of the batch taking into account the oxygen mass transfer conditions and the expected future trajectory of the mass. The final results show that the target fill was achieved to within 5% under the maximum fill when tested using eight pilot scale batches, and over filling was avoided. The results were reproducible, unlike the reference experiments which show over 10% variation in the final tank fill, and this also includes over filling. The variance of the final tank fill is reduced by over 74%, meaning that it is possible to target the final maximum fill reproducibly. The product concentration achieved at a given set of process conditions was unaffected by the control strategy. Biotechnol. Bioeng. 2017;9999: 1–10. © 2017 Wiley Periodicals, Inc.