SIMULTANEOUS DYNAMIC OPTIMIZATION OF PROCESS OPERATION AND PRODUCT QUALITY IN THE PRODUCTION OF MONOCLONAL ANTIBODIES

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ABSTRACT

Monoclonal antibodies (mAbs) constitute a rapidly-evolving high-value biopharmaceutical product with both therapeutic and diagnostic applications. Recent progress in mathematical modeling of biopharmaceutics has enabled the use of model-based approaches for optimization and control of mAb-producing processes [1-4]. Nowadays, one of the major challenges in the biopharmaceutical industry is the incorporation of quality by design (QbD) principles [5]. Among the major quality attributes in the mAb production process, glycosylation stands out.

The present work aims at optimizing the mAb production, taking into account product quality that is derived from the glycosylation mechanism within the cells. For this purpose, we utilize a mechanistic dynamic model for the production of mAbs in mammalian cell cultures presented in Ehsani et al. (2017) [6]. We formulate an optimization problem that derives optimal feeding profile of nutrients and/or nucleotide sugars for maximum product formation in semi-batch mode of operation, with simultaneous control of the glycoprotein distribution in the final product.

In the considered case study, the optimization results in an increased production of mAbs, while complying with the imposed quality constraints. This work shows an effective way, with which quality attributes can be incorporated into the optimization problem for the intensification of mAb-producing processes. It additionally highlights the multiple benefits of utilizing mathematical models for process optimization in biopharmaceutics, within the broader concept of QbD approach.

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