Beneficial effects of pyruvate for a high-density perfusion process

Stefania Caso[1], Mathieu Aeby[1], Martin Jordan[1], Raphael Guillot[1], and Jean-Marc Bielser[1]

[1]Merck Serono SA

November 10, 2021

Abstract

High volumetric productivities can be achieved when perfusion processes are operated at high cell densities. Yet it is fairly challenging to keep high cell density cultures in a steady state over an extended period. Aiming for robust processes, in this study cultures were operated at a constant biomass specific perfusion rate (BSPR). The cell density was monitored with a capacitance probe and a continuous bleed maintained the cell density at the targeted viable cell volume (VCV). Despite our tightly controlled BSPR, a gradual accumulation of ammonium and changes in cell diameter were observed during the production phase for the three different monoclonal antibodies (mAbs). Although a lot of efforts in media optimization have been made to reduce ammonium in fed-batch process, less examples are known about how media components impact the cellular metabolism and thus the quality of monoclonal antibodies in continuous processes. In this work, we show that a continuous Na-pyruvate fed at 2 g/L/day strongly reduced ammonium production and stabilized fucosylation, sialylation and high mannose content for three different mAbs.

Hosted file

`Caso et al. - Beneficial effects of pyruvate for a high-density perfusion process.pdf` available at https://authorea.com/users/445383/articles/544923-beneficial-effects-of-pyruvate-for-a-high-density-perfusion-process