Beneficial effects of pyruvate for a high-density perfusion process

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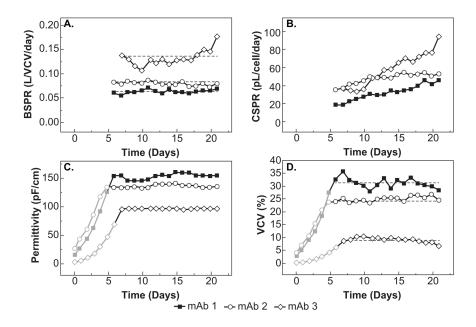
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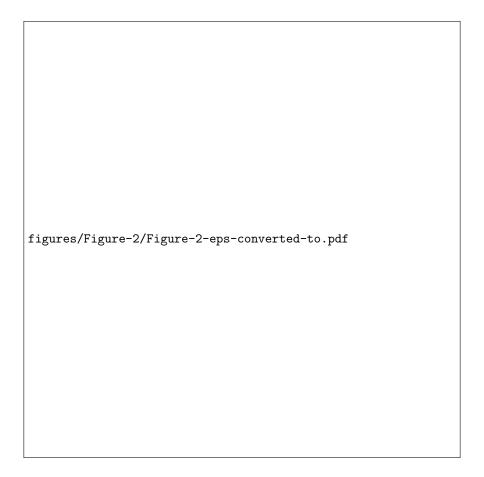
Abstract

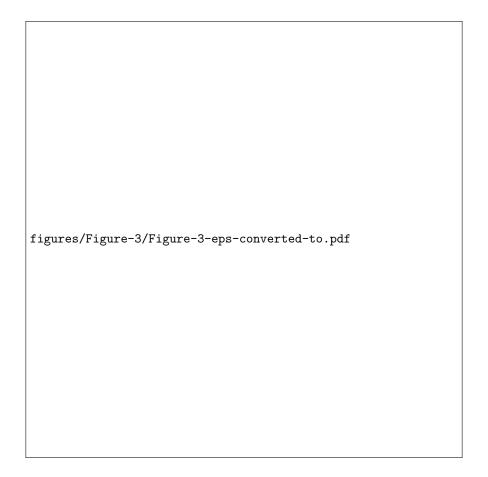
High volumetric productivities can be achieved when perfusion processes are operated at high cell densities. Yet it is fairly challenging to keep high cell density cultures in a steady state over an extended period. Aiming for robust processes, in this study cultures were operated at a constant biomass 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.

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