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3D Printed, Single-Use Bioreactor with Integrated Inline Sensors for Microbial and Mammalian Cell Cultivation – A Case Study

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Abstract:

The development of upstream bioprocesses necessitates small, instrumented bioreactors for investigating and optimizing production processes in a cost-effective manner. Due to advances in both the equipment and the materials used in additive manufacturing, 3D printing of customized bioreactors is now in the realm of possibilities. In this study, a small-scale 3D printed bioreactor suitable for mammalian and microbial cultivations was developed, featuring a working volume of 90 mL, inline pH and dissolved oxygen probes and a levitating magnetic stirrer. Aeration channels and a sampling port were printed directly into the vessel walls. Additionally, the vessel was equipped with a 3D printed customizable optical biomass-sensor. The bioreactor's performance was evaluated through technical characterization and proof of concept cultivations, demonstrating that mixing time and oxygen mass transfer were sufficient for cultivating mammalian as well as microbial cells at high cell densities. Specifically, an Escherichia coli fed-batch cultivation achieved a maximum OD_{600} of 204. Furthermore, a fed-batch cultivation of an IgG antibody-producing Chinese hamster ovary cell line reached a peak viable cell density of 10.2 x 10^6 cells mL^{-1} and a maximum product titer of 2.75 g L^{-1}. Using a three-parameter fit, the inline biomass signal could be correlated to the corresponding offline values with satisfactory accuracy, making it possible to monitor cell growth in real-time.

Keywords: additive manufacturing; Chinese hamster ovary cells; Escherichia coli; inline biomass sensor; inline optical density; online sensors; single-use bioreactor development; 3D printing