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DO AND pH MONITORING IN PROCESS SCOUTING DEVICES AT THE mL-SCALE AND ITS BIOPROCESS DESIGN IMPLICATIONS FOR MAMMALIAN CELL CULTURES

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Abstract

Despite their wide use in bioprocess development (i.e. process optimization and process validation), miniature process scouting devices (0.1mL to 100mL, PSDs) are considered “black boxes” because they are generally not equipped with sensors.

In this study, we show that on-line monitoring of dissolved oxygen (DO) and pH in a T-75 flask-based PSD can be achieved during cell cultures and that this information can be linked to the physiological activity of the cells. In this case, we were able to monitor specific oxygen uptake rate fluctuations between 7.3 and 3.3 ($x10^{-10}$mmol/cells·h) as a hybridoma cell line evolved from thaw and subculturing up to 28 passages (84 days). The lowest pH reached per passage was on average 6.73, but with a decreasing trend as the number of passages increased. The change in pH oscillated between 0.42 and 0.6 from the initial pH value with an average per passage of 0.49. These findings are particularly useful because real time monitoring of environmental conditions during cell culture shows that cells may be exposed to adverse conditions even under a controlled environment.

As very early pre-culture in commercial settings is often performed in unmonitored T-flasks prior to scaling-up to spinner vessels and/or bench-scale bioreactors, the present work shows the importance of monitoring critical process parameters such as DO and pH as it could help design control strategies that would integrate unmonitored PSDs with fully instrumented lab scale devices.