Monitoring and external control of pH in microfluidic droplets during microbial culturing.

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Details

Abstract

Background: Cell-based experimentation in microfluidic droplets is becoming increasingly popular among biotechnologists
and microbiologists, since inherent characteristics of droplets allow high throughput at low cost and
space investment. The range of applications for droplet assays is expanding from single cell analysis toward complex
cell–cell incubation and interaction studies. As a result of cellular metabolism in these setups, relevant physicochemical
alterations frequently occur before functional assays are conducted. However, to use droplets as truly miniaturized
bioreactors, parameters like pH and oxygen availability should be controlled similar to large-scale

fermentation to
ensure reliable research.
Results: Here, we introduce a comprehensive strategy to monitor and control pH for large droplet populations during
long-term incubation. We show the correlation of fluorescence intensity of 6-carboxyfluorescein and pH in single
droplets and entire droplet populations. By taking advantage of inter-droplet transport of pH-mediating molecules,
the average pH value of several million droplets is simultaneously adjusted in an a priori defined direction. To demonstrate
the need of pH control in practice, we compared the fermentation profiles of two E. coli strains, a K12-strain
and a B-strain, in unbuffered medium with 5 g/L glucose for standard 1 L bioreactors and 180 pL droplets. In both
fermentation formats, the commonly used B-strain E. coli BL21 is able to consume glucose until depletion and prevent
a pH drop, while the growth of the K12-strain E. coli MG1655 is soon inhibited by a low pH caused by its own high
acetate production. By regulating the pH during fermentation in droplets with our suggested strategy, we were able
to prevent the growth arrest of E. coli MG1655 and obtained an equally high biomass yield as with E. coli BL21.
Conclusion: We demonstrated a comparable success of pH monitoring and regulation for fermentations in 1 L scale
and 180 pL scale for two E. coli strains. This strategy has the potential to improve cell-based experiments for various
microbial systems in microfluidic droplets and opens the possibility for new functional assay designs.

Involved units

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