Automated In-Situ Monitoring of Cell Health in Monoclonal Antibody Production

We present fully automated in-situ monitoring of a CHO fed-batch culture using the CellQuant, a flow cytometer specialized for hands-free tracking of biological parameters. Connected via onCyt's proprietary aseptic sampling, the system enables round-the-clock monitoring with zero manual input. The CellQuant detects rising levels of damaged (apoptotic) cells early in the process—well before dead cell concentrations increases. This early warning allows timely intervention to optimize the process, reduce cell death, improve yields, and shorten downstream processing time.

Context

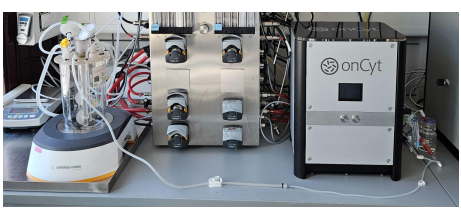
Monoclonal antibody (mAb) production - typically using Chinese Hamster Ovary (CHO) cell cultures - is a cornerstone of modern biopharmaceutical manufacturing. To scale and optimize production, manufacturers seek greater efficiency and control. However, progress is hindered by limited process analytics. While physical and chemical parameters like pH are routinely monitored in real time, key biological indicators still require offline sampling. This manual approach demands expert handling, introduces contamination risk, and delivers only sparse data - slowing process development and hindering real-time optimization. Here, we describe the fully automated monitoring of a ExpiCHO-S cell culture operated in fed-batch mode.

Highlights

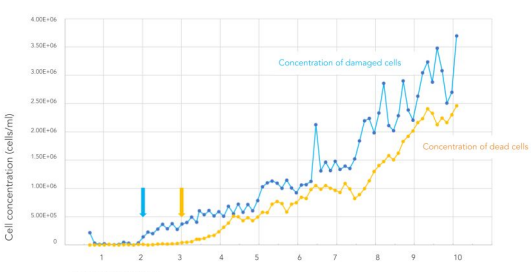
- CellQuant enabled fully automated in-situ monitoring of CHO fed-batch cultures.
- Dead and damaged cells measured every 3 hours over 10 days — 80 data points, no manual input.
- 20-minute time-to-result supports timely process decisions.
- Cell damage was detected ~35 hours before cell death rise, allowing yield-boosting interventions.

Experiment Description

The CellQuant automated flow cytometer was connected to a single-use bioreactor (2 L UniVessel SU, Sartorius) through an aseptic sampling system that ensures a contamination-free environment through a defined sterile interface and flow control via check valves. The CellQuant automated workflow included sampling, dilution, marker addition, incubation, measurement, data analysis and cleaning. Damaged (apoptotic) and dead cell concentration were measured using staining with Annexin V-FITC and Propidium Iodide. Cell health of the CHO fed-batch culture was followed through fully automated measurements collected every three hours.



The CellQuant connected to the bioreactor.



Results

The graph (lower left) displays the cell concentration as a function of cultivation days, showing the progression of damaged (blue) and dead (yellow) cell populations as tracked by the CellQuant throughout the 10-day fed-batch process. Compared to offline measurements, typically collected only once a day, the CellQuant gives insight into critical process dynamics without requiring additional resources.

As expected in fed-batch cultures, both populations increase over time. Arrows indicate the time point when the first increase in the damaged and dead cell population are detected. We note that the CellQuant detected a rise in the damaged cell population approximately 35 hours before a measurable increase in dead cells. This early signal is critical: the ability to detect declining cell health before irreversible cell death allows operators to intervene sooner, potentially adjusting feeding strategies, process conditions, or harvest timing to preserve culture viability and maximize yield.

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