Integration of the Vi-CELL BLU Cell Viability Analyzer into the Sartorius Ambr® 250 High Throughput for automated determination of cell concentration and viability

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Introduction

The Sartorius Ambr® 250 High Throughput system is a high-throughput, automated bioreactor system for process development with 12 or 24 parallel 100 to 250 mL mini bioreactors designed for both cell culture and microbial fermentation experiments. The system can be further upgraded with several integrated analyzers to add additional value to your cultivation results. Previously, the Vi-CELL XR analyzer could already be fully integrated into the Ambr® 15 Cell Culture and Ambr® 250 High Throughput Bioreactors to provide automated viable cell density and viability data during cultivation experiments. These results allow for additional process control without operator attendance.

Now, the integrated cell count and viability measurement capabilities can be further enhanced by integrating the Vi-CELL BLU Cell Viability Analyzer into the Sartorius Ambr® 250 High Throughput system. The Vi-CELL BLU analyzer provides all the advantages of the Vi-CELL XR analyzer, but with shorter sampling times and lower sampling volumes. In addition, the integrated Vi-CELL BLU device can be used for standalone measurements as well, allowing for easy quality control checks and resulting in better reproducibility between the Sartorius Ambr ®250 High Throughput bioreactor data compared to other (seeding) cultures in your lab.

A Vi-CELL BLU cell viability analyzer integrated into a Sartorius Ambr® 250 High Throughput system leverages the strengths of both instruments and provides users with the advantages of automated cell culture handling and analysis. The combination of these technologies provides researchers and bioprocess engineers with many benefits, such as real-time culture monitoring and enhanced data analysis, while saving valuable time and resources. Automated cell culture analysis helps optimize workflows and could improve scalability.

In this application note, we provide data from cultivations performed in a Sartorius Ambr® 250 High Throughput system which were sampled daily on an integrated Vi-CELL BLU analyzer to determine cell concentration and viability online. These results are compared with offline values. The integrated Vi-CELL BLU Cell Viability Analyzer was installed at Boehringer Ingelheim Pharma GmbH & Co. KG (Biberach, Germany); the data shown in this application note was obtained during beta testing of the integration at their facilities. We would like to thank Boehringer Ingelheim GmbH & Co. KG and its respective employees for the successful collaboration.

Methods

During beta testing, 12 bioreactors in the Sartorius Ambr® 250 High Throughput were inoculated with cells from distinct pre-cultures. The cultivations were run for up to 13 days – in a continuous fed-batch – and samples were taken daily to determine cell concentration and viability. First, the scheduled integrated cell viability determination was performed with the full system; the Sartorius Ambr® 250 High Throughput would take a sample and add it to the sample cup on the deck allowing the Vi-CELL BLU analyzer to measure it. Afterwards, the network connection between the Vi-CELL BLU analyzer and the Sartorius Ambr® 250 High Throughput was separated, and the Vi-CELL BLU was used as a standalone device to determine cell concentration and viability of all 12 cultures. The integrated and standalone values were compared to determine how well they correlated.

All measurements were run in *Normal Wash* mode (200 µL sample volume), with a custom *Cell Type* optimized for the cells used. Throughout the experiment, cell concentration and viability were determined as single measurements (N=1) for both the integrated and standalone method. Later samples were 2- or 4-fold diluted to accommodate the analysis of high-concentration samples. For the integrated Vi-CELL BLU analyzer, these dilutions were performed with the Sartorius Ambr® 250 High Throughput prior to adding the cell suspension to the sample cup. Afterwards, cultivation graphs were made for each bioreactor comparing the viable cell density (VCD) and viability measured online with the results on the standalone Vi-CELL BLU cell viability analyzer. The performance of the Vi-CELL BLU analyzer in standalone mode was validated using concentration control beads at a 0.5 and 10 million/mL concentration.

Results

The performance of the Vi-CELL BLU analyzer was validated before experiment start with a single measurement of a 0.5M and 10M single-use Concentration Control vial. The measured Total Cell Densities (0.51*10^6 cells/mL and 10.19*10^6 cells/mL, respectively) were within range and showed a perfect linear correlation (Figure 1, trend line forced through (0,0)).

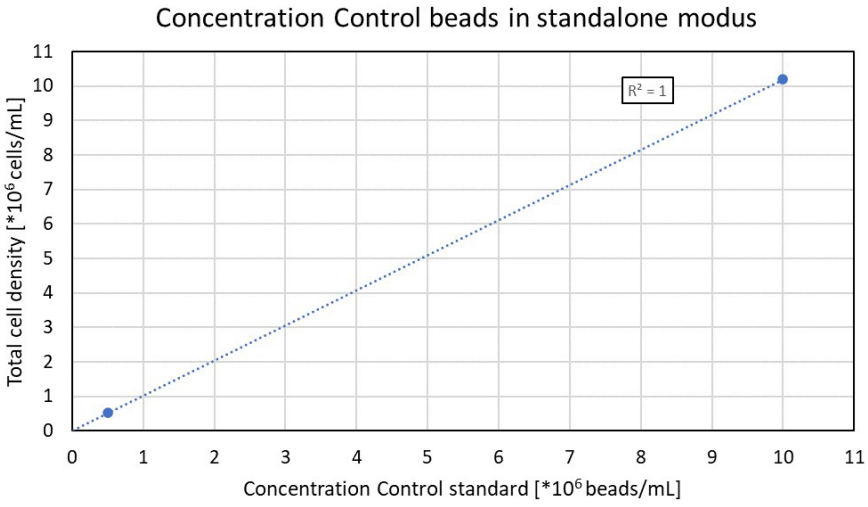

Figure 1. Concentration control beads run on the Vi-CELL BLU cell viability analyzer in standalone modus. A perfect linear correlation is observed. Trend line forced through (0,0).

The results obtained during the cultivation experiment are shown in Figure 2. All twelve bioreactors show a similar growth profile, with fast growth observed up to day 4, followed by a plateau phase with high viability (>90%) up to day 10 for most cultures. In the final days of the experiment, the viability starts to decline.

Overall, the online data looks very comparable to the values obtained in standalone modus. Replicate measurements would potentially help excluding random outliers, caused by e.g., inaccurate diluting, pipetting, or mixing. The average deviation in the integrated viable cell densities across all measurements was -5.2% compared to the standalone values, and only 0.8% was observed for the viability.

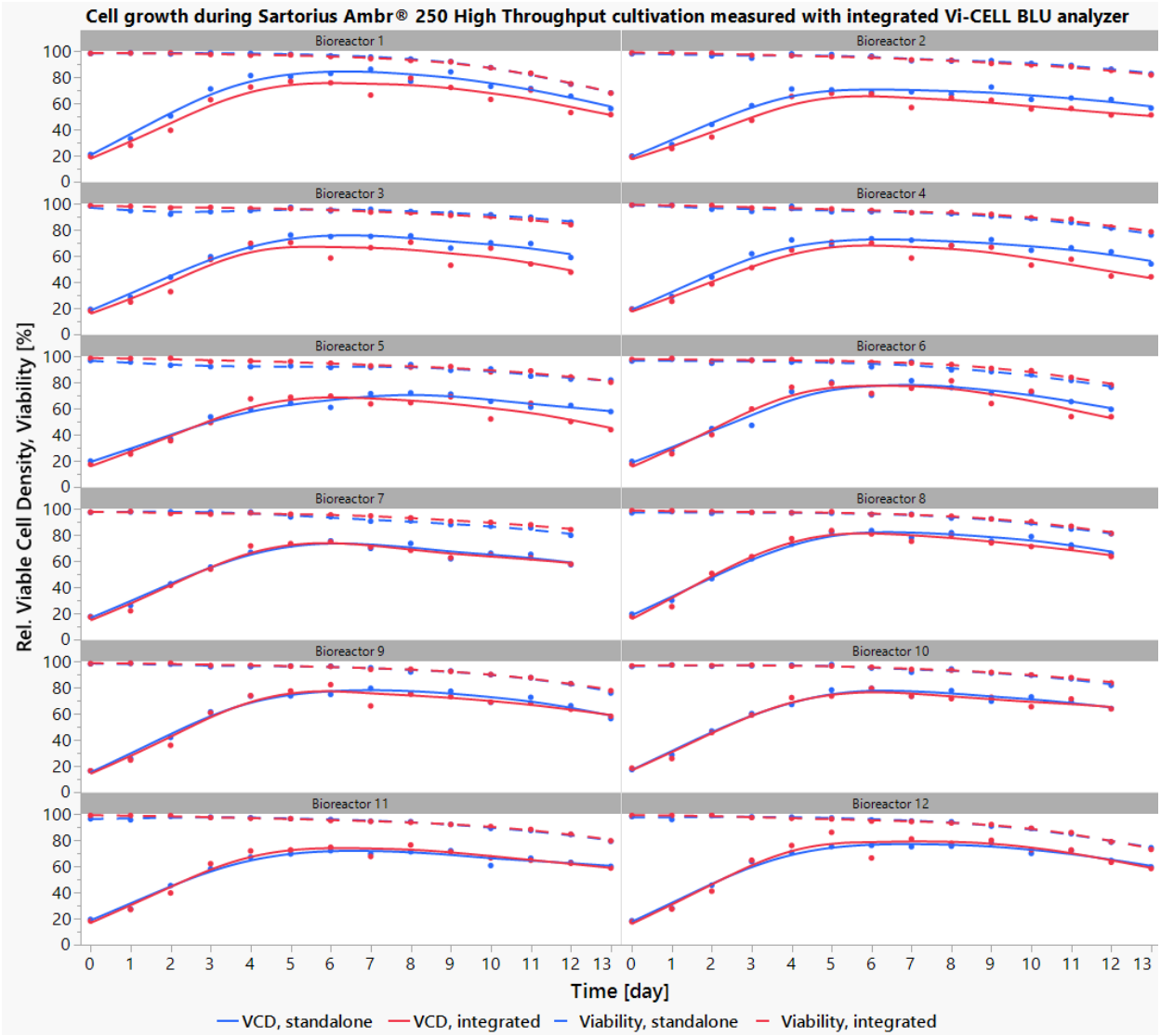

Figure 2. Comparison of integrated (red) and standalone (blue) values on the Vi-CELL BLU cell viability analyzer. The VCD (solid line) and viability (dotted line) are shown during the 12- or 13-day cultivation.

Conclusion

The results from the beta testing show strong comparability within a 5.2% deviation between automated cell concentration and viability measurements with an integrated Vi-CELL BLU analyzer. The growth curves of all 12 bioreactors show a very similar profile for both methods. The ease of switching between a connected and standalone system allows for regular performance checks with Vi-CELL BLU Quality Control products.

Overall, the integration of the Vi-CELL BLU analyzer and Sartorius Ambr® 250 High Throughput system opens new avenues for efficient and reliable cell culture analysis. Researchers and bioprocess engineers can now confidently utilize this automated platform to streamline their process development, optimize workflows, and make data-driven decisions, ultimately accelerating bioprocess development and ensuring high-quality results. The combination of these advanced technologies represents a significant advancement in cell culture analysis, benefiting biopharmaceutical research and production industries alike.

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