



Evaluating Clone Performance and Cell-Specific Productivity: Comparing the Cydem VT System and 10 L Bioreactor Cultivations

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Introduction

In cell line development, consistent and reliable top clone screening is paramount for confidently selecting superior clones. Continuous online monitoring of critical parameters such as pH, dissolved oxygen (DO) and biomass provides essential online control. This is complemented by automated, at-line analysis yielding total cell density (TCD) and viable cell density (VCD), viability and IgG titer data, which are key to selecting the top performers. The combined information on pH, DO, VCD, viability and IgG titer are highly beneficial for a successful scale-up to higher-volume bioreactors regarding top clones and their ranking.

The Cydem VT Automated Clone Screening System's bioreactor module features fine-tuned delivery of O₂, CO₂ and N₂ gases via micro-channeled gassing chips to individual microplate cultivation wells, which creates a stable environment for mammalian cell growth and antibody production. This is done with proportional-integral-derivative (PID) controlled feedback looping using real-time pH and DO data from calibrated optical sensors attached to the bottom of the microbioreactors. Scheduled feeds, base additions, and analytical tests also ensure consistent nutrient delivery and testing times.

This application note describes a comparative study conducted using the Cydem VT Automated Clone Screening System in conjunction with a 10 L bioreactor. To determine clone ranking, five CHO cell line clones were evaluated based on selected performance parameters.

Method

The experimental study using the Cydem VT Automated Clone Screening System was conducted at a Beckman Coulter Life Sciences laboratory, while the 10 L bioreactor experiments were carried out by a collaborating partner. Five CHO clones were selected and divided into two groups, with each group expressing a different IgG antibody gene. Group 1 consisted of clones 1-1 and 1-2, whereas Group 2 included clones 2-1, 2-2, and 2-3.

The following method description refers to the cultivation in the Cydem VT system, aligning with the process conditions in the 10 L bioreactor as closely as possible. All clones were cultivated in 16-fold replicate under fed-batch conditions using HyClone™ ActiPro™ cell culture medium, supplemented with 6 mM L-glutamine. Feeding commenced on the third day and continued thereafter with a proprietary feed solution and glucose, maintaining a target concentration between 2 and 7 g/L of the latter. The initial seeding density was 0.5×10^6 cells/mL in a starting volume of 5 mL in the microplate-based bioreactors. Cultivation parameters were controlled, with DO set at $50\% \pm 10\%$. The control parameters for pH were set to 7.0 ± 0.1 through CO₂ and 0.5 M NaOH regulation, with the latter being added two times per day, and temperature held constant at 36.5°C. Shaking of the bioreactor microplates was maintained at 800 RPM using a shaking diameter of 3 mm to ensure optimal mixing and gas transfer throughout the cultivation process.

Results

The performance of the various clones was evaluated by comparing key parameters, including cell-specific productivity (qP), product titer, pH, DO levels and viable cell density. On the Cydem VT Automated Clone Screening System, these parameters were continuously monitored and recorded at-line/online. The results were analyzed to assess the comparability of clone behavior between the Cydem VT system and the 10 L bioreactor.

Performance Evaluation of the Cydem VT System - Online Monitoring of pH and DO

Data for pH and DO were collected online for all clones using the Cydem VT system. Analysis of the data demonstrated consistent DO control (setpoint 50%) and maintenance of an approximately neutral pH (setpoints of 7.1, later 7.0) across all clones. The Cydem VT system exhibited precise regulation of both pH and DO, significantly outperforming conventional platforms such as deep-well plates and spin tubes in terms of environmental control and process stability. This enhanced control can be attributed to the system's PID-controlled sensors and real-time feedback mechanisms, which enable dynamic adjustments to culture conditions. Such capabilities are critical for maintaining optimal environments, thereby improving the reliability of early-stage clone screening and translation of top clone ranking to larger-scale optimization where process parameters are equally tightly controlled.

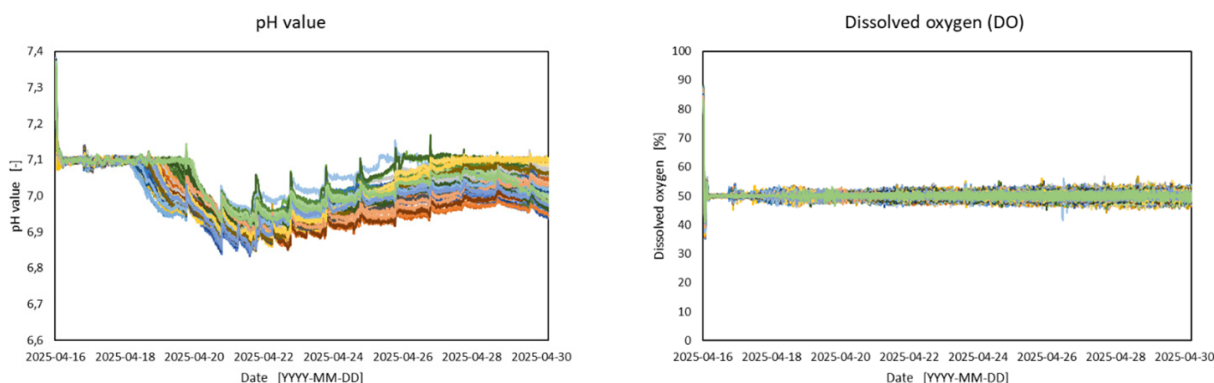


Figure 1: pH and DO values for all five clones in the Cydem VT system, each clone in 16-fold replicate.

Comparison of Viable Cell Density

VCD data were collected in the Cydem VT system (automated at-line measurement) and the 10 L bioreactor. The growth profiles observed in the Cydem VT system closely mirrored those seen in the 10 L bioreactor, indicating a high degree of process fidelity. The observed similarity in growth kinetics indicates that the Cydem VT system closely emulates the physiological conditions of larger-scale bioreactor environments. This alignment reinforces its value as a predictive platform for early-stage top clone screening and supports its applicability in guiding scale-up strategies with greater confidence.

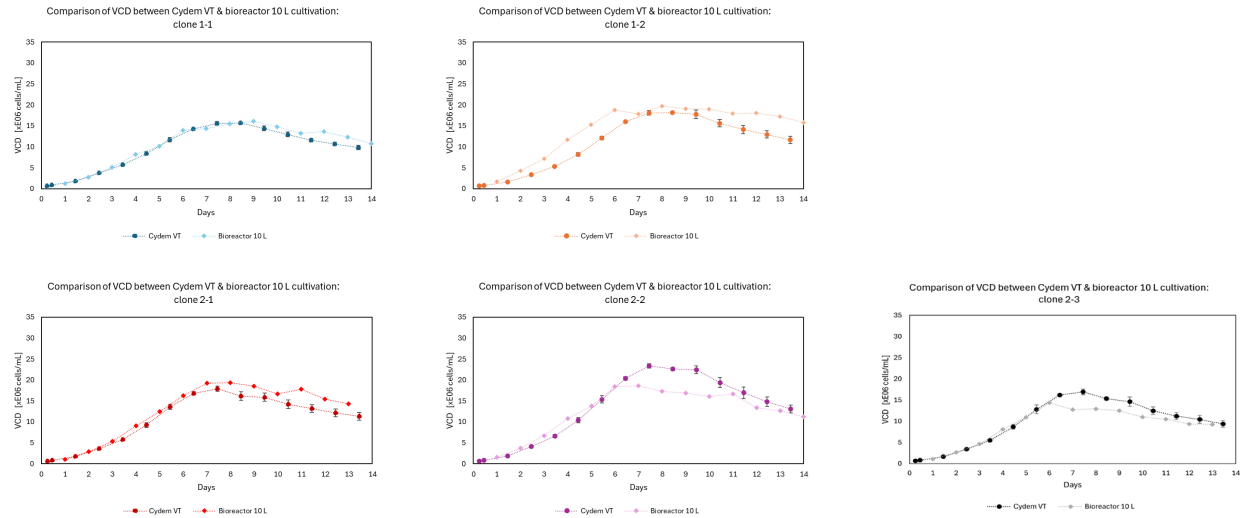


Figure 2: Comparison of VCD in the Cydem VT system and 10 L bioreactor for all five clones.

Comparison of the Product Titer

IgG titers for all five clones—split into two groups each expressing a different IgG coding gene—were measured on day 6 of the cultivation and going forward compared between both the Cydem VT system and the 10 L bioreactor. The data demonstrate a high degree of concordance in IgG titers across both systems. The observed alignment in results underscores the system's practical effectiveness in simulating bioreactor environments, facilitating accurate clone productivity evaluation and informed scale-up forecasting.

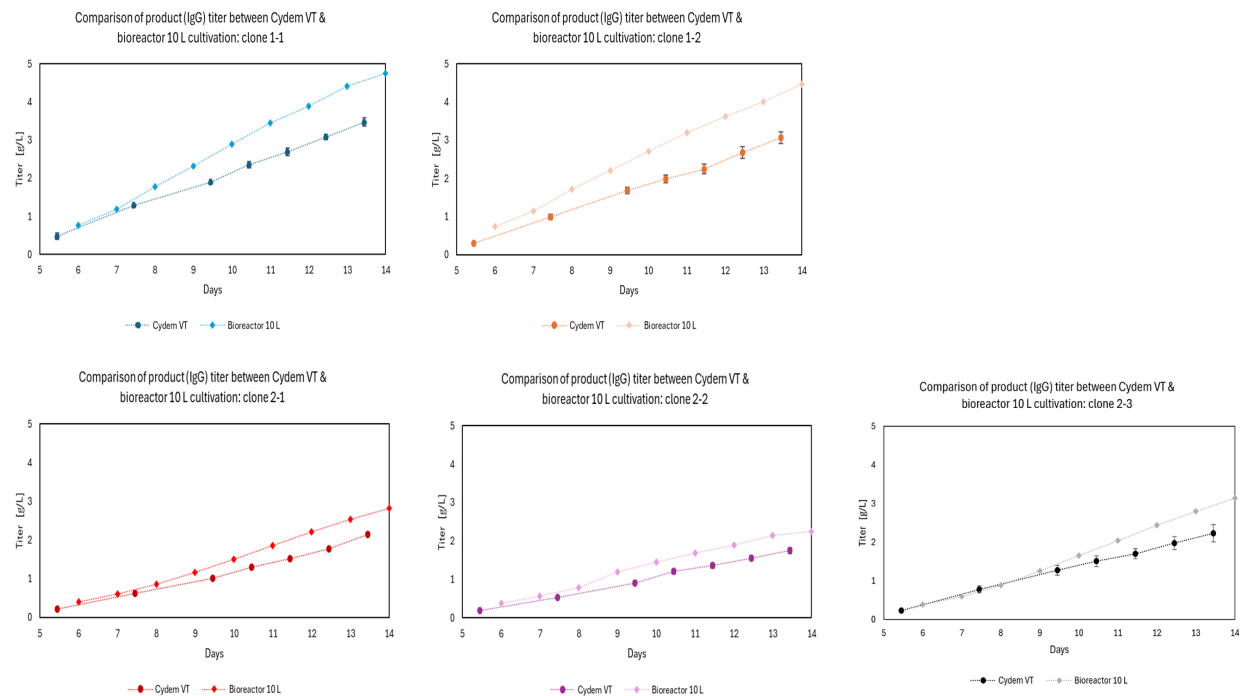


Figure 3: Comparison of product titer (IgG) between the Cydem VT system and 10 L bioreactor across all five clones.

Comparison of Cell-Specific Productivity

Throughout the cultivations, the cell-specific productivity regarding IgG formation was evaluated for all five clones. The data demonstrated a strong correlation in qP outcomes between the two systems. This alignment highlights the Cydem VT system's utility in enabling the early and accurate identification of top clones with superior productivity, under conditions closely matching larger scale. Consequently, the Cydem VT system facilitates reproducible and reliable clone ranking, matching data from 10 L bioreactors.

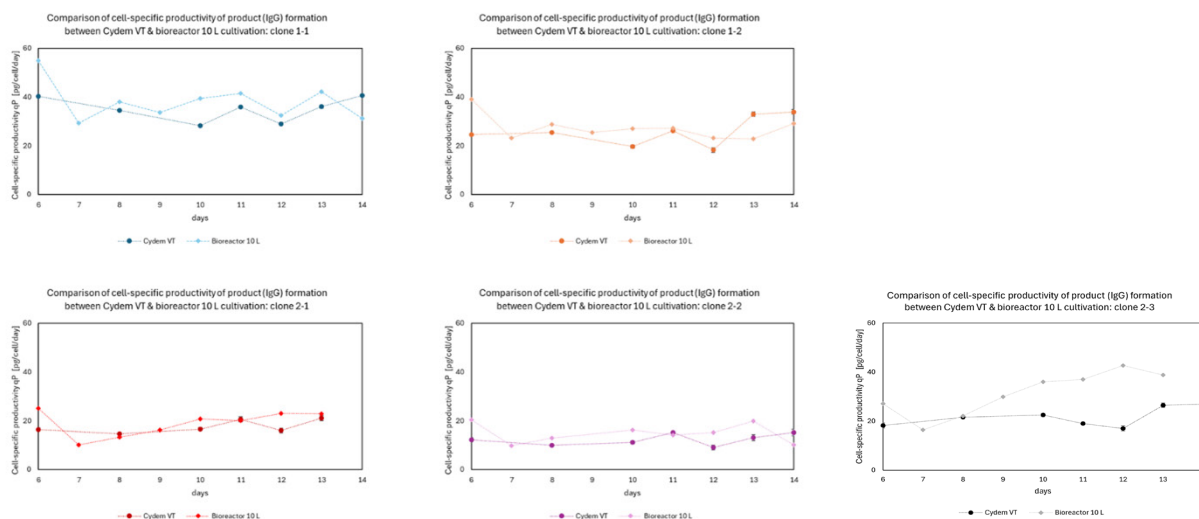


Figure 4: Comparison of cell-specific productivity in the Cydem VT system and 10 L bioreactor across all five clones.

Conclusion

This study demonstrates the effectiveness of the Cydem VT Automated Clone Screening System as a reliable and predictive platform for early-stage top clone screening and ranking, with results translating well to the 10 L bioreactor scale and hence increasing confidence in clone choice. By enabling online/at-line monitoring of critical parameters such as pH, DO, VCD and IgG titer, the Cydem VT system provides a comprehensive and high-resolution understanding of clone performance. The strong correlation observed between data generated in the Cydem VT system and the 10 L bioreactor underscores the system's utility in data-driven decision making in top clone screening and reduces the risk of scale-up failures or misses of high-performance clones.

References

1. [Introducing the Cydem VT Automated Cell Culture System: A high-throughput platform for fast and reliable clone screening experiments.](#)
2. [Cultivation of Mammalian Cells in the Cydem VT System Bioreactor Module.](#)
3. [Efficient clone screening with increased process control and integrated cell health and titer measurements with the Cydem VT Automated Clone Screening System.](#)

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