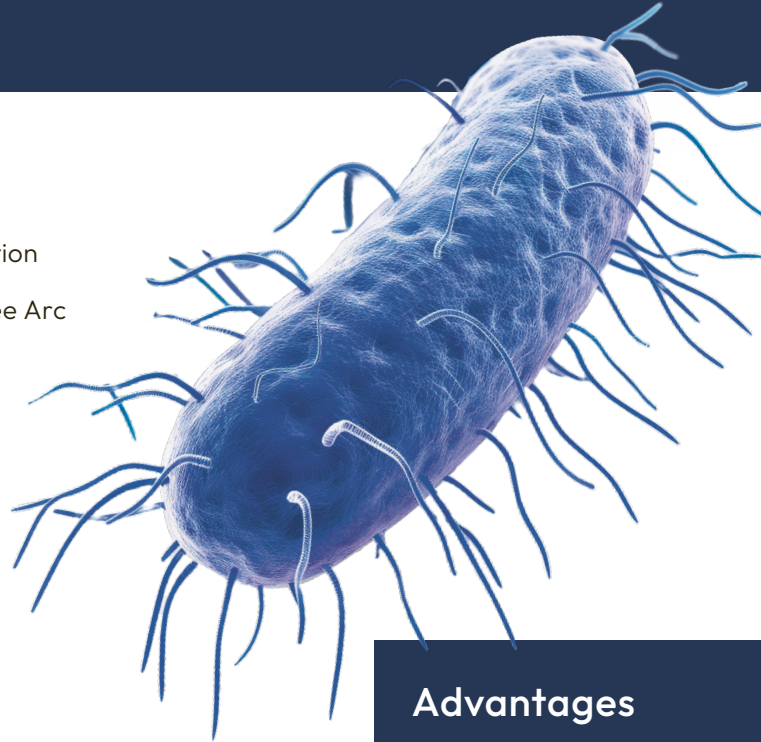


Automated Induction Piloted by Dencytee Probe Signal for Recombinant *E. coli* Production

Industry: Biopharma

Application field: Fermentation

Hamilton products: Dencytee Arc



Introduction

The cultivation of *Escherichia coli* (*E. coli*) is a fundamental process in vaccine drug substance development. Within Sanofi's upstream development workflows, *E. coli* cultures progress through multiple phases, each requiring precise control and monitoring of critical process parameters such as dissolved oxygen and optical density at 600 nm (OD600). Automation of these transitions is essential for process robustness, reducing manual intervention, and minimizing the need for frequent sampling. Furthermore, continuous data collection is a cornerstone for advancing process modeling and digitalization.

The Dencytee probe provides real-time, continuous monitoring of bacterial growth, enabling fully automated phase transitions – even in the absence of an operator at the bioreactor. This application note details the implementation and benefits of automated induction in *E. coli* cultures using the Dencytee probe.

Advantages

- **Seamless Integration:** Direct OPC integration with the Lucullus process control system.
- **Continuous Data Collection:** Enables real-time monitoring and documentation of cell growth.
- **Reduced Manual Intervention:** Once the correlation model is established, manual sampling is minimized or eliminated.
- **Flexible Modeling:** High-quality transmission and reflection signals support the development of custom models tailored to specific process needs.
- **Scalability:** The probe is available in a range of sizes, allowing the same measurement principles and models to be applied across laboratory and pilot scales.
- **User-Friendly Operation:** The probe is easy to use; Arc Air software is employed solely for signal quality control, not for data capture or model generation.

Principle of Measurement

The Dencytee probe utilizes two optical measurement principles to monitor cell density throughout the culture:

- Transmission: Primarily used for low cell densities, measuring the amount of light passing through the sample.
- Reflection: Used for high cell concentrations, measuring the light reflected back from the sample.

By combining these two signals (Figure 1), a robust and broad-range detection of cell growth is achieved. Based on data collected across multiple *E. coli* cultures, a custom correlation model was developed at Sanofi to predict OD600 values from the Dencytee probe signals (Figure 2).

Automated Process Control

The continuous generation of predicted OD600 data eliminates the need for manual sampling and enables automated control of critical process steps. In the example shown in Figure 2, when the predicted OD600 reaches a set threshold (e.g., OD600 = 60), the system automatically starts the induction phase by activating the induction pump at 100% for five minutes. The precise inducer dose is delivered at the optimum time for recombinant protein expression.

This automated approach ensures highly reproducible process transitions, supports round-the-clock operation, and provides comprehensive datasets for further process analysis and modeling.

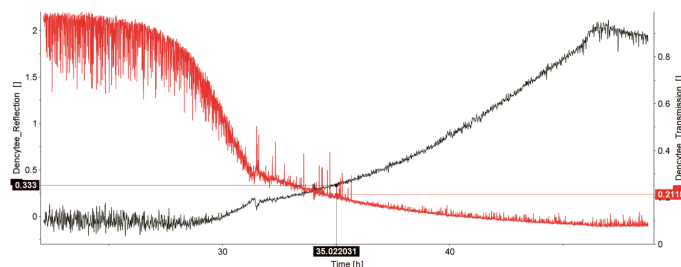


Figure 1: Transmission and Reflection signals from the Dencytee probe during *E. coli* culture.

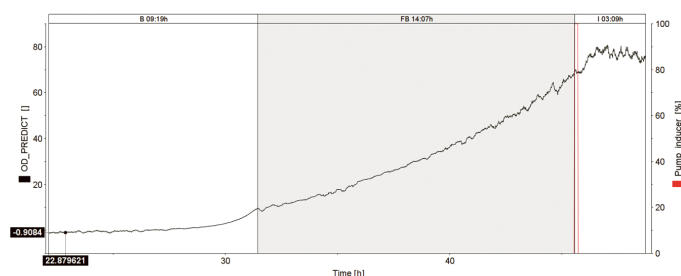


Figure 2: Predicted OD600 and automated induction trigger during *E. coli* culture.

Conclusion

Implementing the Dencytee probe for automated induction in recombinant *E. coli* production represents a significant step forward in bioprocess automation. The technology delivers robust, scalable, and operator-independent process control, while continuous data collection paves the way for advanced process modeling and digitalization. This approach not only enhances process reliability and reproducibility but also supports the evolving demands of modern biopharmaceutical development.

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