Product design / development / engineering | Healthcare / Pharmaceuticals | Improved process performance | Dimensionality reduction

Preemptive variation reduction in biologic drug substance manufacturing

BUSINESS PROBLEM

Biomanufacturing processes are inherently complex and subject to variability, leading to significant challenges in maintaining product consistency and efficiency.

APPROACH

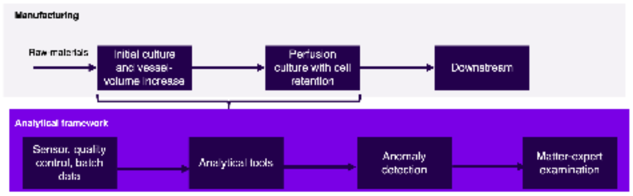
The core hypothesis in this thesis is that the decision-making workflow can be significantly improved by integrating a digital twin (a dynamic, data-driven model that simulates the biomanufacturing process), and soft sensors for real-time monitoring and estimating critical parameters.

DATA SOURCES

Time series data was collected from sensors across the four reactors, focusing on critical variables typically monitored in bioprocesses from 20 batches spanning from 2020 to 2023.

Data Types and Format

Five-minute interval data from PI Datalink 2018, which employed interpolation to align timestamps across variables. Data was saved as comma-separated values (.csv) to facilitate modeling.



Author: Ismael Guereca Valdivia

IMPACT

A digital twin such as the one developed for this thesis presents the company with greater process insight and control than previously. By constructing a dynamic and accurate digital replica of the bioreactor environment, the digital twin has the potential to facilitate an in-depth, real-time monitoring of the process. This advanced level of monitoring can enable the preemptive identification and mitigation of potential process variations before they are significant, therefore reducing the overall variation in the manufacturing process. By enabling the capability to monitor cell growth through a calculation, the soft sensor for biomass concentration can validate the measurements of current physical sensors. Within the broader biomanufacturing industry, such biomass measurements are validated through offline laboratory tests. An online validation allows the company to adjust to cultivation conditions immediately, ensuring that the bioreactor operates with in optimal conditions. This possibility of control allows the company to maintain product quality, maximize yield, and ensure regulatory compliance. This can be done by detecting deviations from expected patterns early, potentially flagging issues before they impact product quality or yield.

DRIVERS

In a highly regulated industry such as biomanufacturing precise control of process variables during manufacturing is not just nice to have – it is imperative. Keeping process and quality variables within pre-established control limits is crucial. As such, technologies such as digital twins and soft sensors can provide a solution to reduce process variation and allow the potential of process improvement.

BARRIERS

One important barrier while implementing technologies such as the ones presented in this project is the need for multidisciplinary skills. The modeling requires knowledge about the information systems, the business drivers, and process knowledge. There was a learning curve in getting sufficiency to drive the project.

ENABLERS

The management team of the MSAT group was supportive in driving digital initiatives.

ACTIONS

The general approach was taken: speak with stakeholders to gain process knowledge, gather data, build the models, validate the models with real-world data, and then engage with experts within the company to gather their feedback.

INNOVATION

The proposed solution leverages such tools to drive process knowledge and improvement using the process data from the company. Building such tools can help the decision-makers to make better business decisions.

IMPROVEMENT

The improvement my solution provided was a proof of concept of the performance of the tools. They would still would need to be further refined and implemented. Nevertheless they proved that important process parameters can be estimated using process data, and that digital representation of the manufacturing process can be developed to drive continuous improvement.

BEST PRACTICES

A best practice is engaging with technical experts early in the process and often while developing the solution. Furthermore building simple tools as a proof of concept is useful to validate their applicability. If validated then more resources can be used to improve and expand the scope of digital tools with applications on manufacturing.

OTHER APPLICATIONS

My solution focused on a specific part of the biomanufacturing process. Similar approaches can be applied to other steps of the large scale drug manufacturing process.