PDA Parenteral Drug Association

UAB Universitat Autònoma de Barcelona

aizon

CPV-enabled Refinement of Biotechnological Manufacturing Recipe

Continued Improvement of Upstream Fermentation Manufacturing Through Dynamic Recipe Upgrades and Adaptive Process Control

After the development of a pharmaceutical product in an R&D environment, the regulatory approval procedures that follow result in industrial-scale manufacturing production recipes. For the biotechnology industry, in particular, such process operating conditions specifications cause considerable difficulties due to the high volatility that is natural in biological processes like upstream manufacturing.

Although manufacturers can use in-line and on-line sensors to directly measure Critical Process Parameter (CPP) variability, this will only help to identify an out-of-control process that risks entire batch rejection upon reaching out-ofspecification (OOS) conditions. A subsequent major challenge is how to leverage such information to directly interact with a pre-approved recipe, and maintain a state of control while driving process deviations within established conditions (ECs) for successful drug manufacturing according to GxP guidelines.

aizon

The Solution, Applying Advanced Analytics and Artificial Intelligence to Support Decision-Making While Maintaining Regulatory Compliance

Continued Process Verification (CPV) is an FDA-approved mechanism to ensure the verification and improvement of a manufacturing process after the initial stages of process qualification and validation (ICH Q13, 2021; FDA Process Validation Guidance, 2011). It provides the process manager a degree of flexibility defined in the control strategy to govern the production unit and adapt a product recipe according to inherent process variability.

A crucial step in this manufacturing governance is real-time access to sensor data that captures the quality and progress of an ongoing process according to Process Analytical Technology (PAT; ICH Q8, 2009). Aizon's award-winning platform connects and unifies factory IoT devices to ingest and store production sensor data in an underlying data lake following GAMP 5 best practices in a certified Integrated Management System (IMS; ISO-9001, ISO-27017).

But how can you use this process data to your advantage? And how can you apply advanced analytics and artificial intelligence (AI) to support your decision-making and maintain regulatory compliance?

To answer these questions, Aizon is leading the "CPV of the Future" project, a PQRI-supported initiative under the Parenteral Drug Association's (PDA) Process Validation Interest Group that brings together industry leaders and academic experts to explore the power, as well as the associated risks, of an AI-based adaptive system used to control a manufacturing unit within a regulatory-grounded framework.

aizon

The Result

In the first phase of the project, a bio-manufacturing task force, in collaboration with Prof. Dr. Valero Barranco and his team at Universitat Autònoma de Barcelona (UAB), employed a Pichia pastoris fermentation process to study the production of Candida rugosa lipase (CRL) under different levels of oxygenation (normoxic and hypoxic conditions). The team at Aizon was able to use this data to develop a series of AI models that learned the relationship between Critical Process Parameters (CPPs) and Critical Quality Attributes (CQAs), which together identified the ideal operating conditions for producing optimal batches. This in turn enabled them to perform a multivariate outlier detection algorithm to isolate low-quality batches before the process had finished (2 out of 2 poor-performing batches detected at the 50% progress mark of the operation).

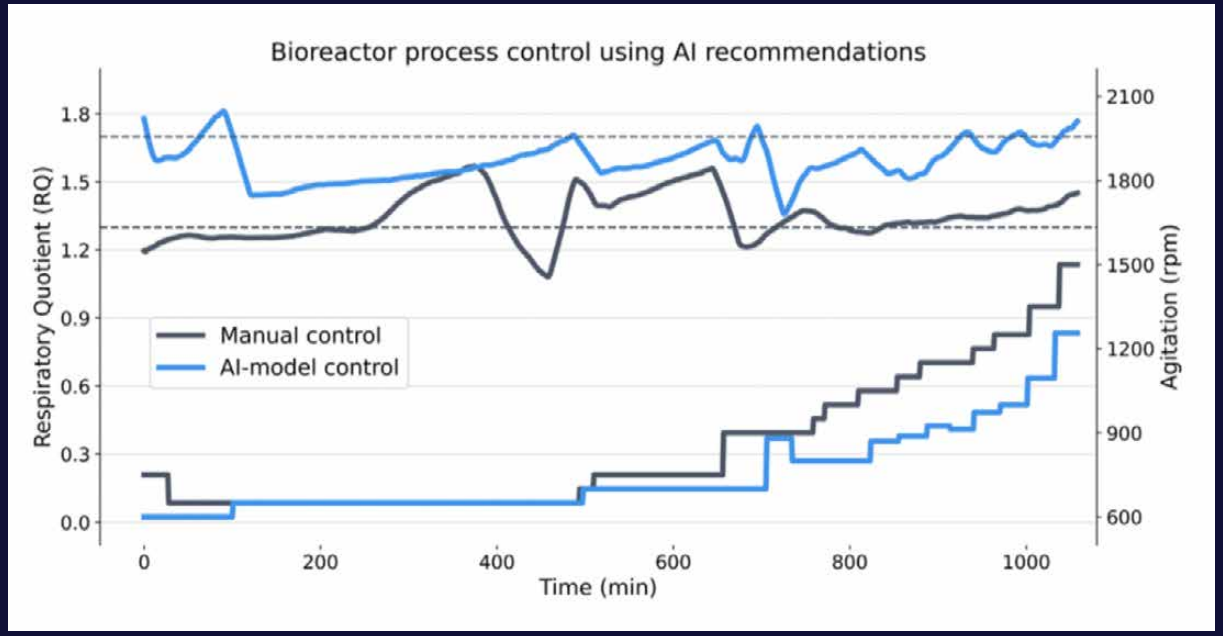
With this acquired understanding of process dynamics and product quality, the next step was to develop a control strategy for the bioreactor relative to changing process conditions. The team deployed an AI model to recommend operator control actions for the bioreactor's agitator during the semi-automated late fed- batch phase with rapidly increasing biomass. Several models were trained using data from 3 historical batches, each covering a different phase of the process, that jointly predicted optimal values for the agitator in the final batch to maintain the respiratory quotient (RQ) of the medium within a desired range with maximum production rates.

aizon

Professor Dr. Valero Barranco, Chemical, Biological and Environmental Engineering Department, UAB

Toni Manzano, PhD Co-founder & CSO, Aizon

These results demonstrate that AI can be a valuable tool for real-time monitoring and control of biopharma manufacturing processes to improve their efficiency and to assure product quality. Regulatory bodies, such as the FDA and ICH, are guiding the manufacturing industry to adopt 4.0 technologies, and Aizon is committed to continuing the digitalization and advancement of AI tools and cloud computing in the domains of biotechnology and drug manufacturing. Together with its partners, the “CPV of the Future” project will bring a better understanding of the strengths and challenges of AI implementation, and provide a roadmap with recommendations for the pharma industry operating under GMP guidelines.



AI-Powered Control of a Bioreactor
A graph showing that AI-based operator recommendations for agitation can maintain broth oxygenation levels (RQ) of late fed-batch fermentation within the desired range of 1.3–1.7 for ideal manufacturing conditions.

aizon

Unlock the Full Potential of Smart Pharma Manufacturing with Aizon

Talk to our Sales Team: sales@aizon.ai

Learn More: www.aizon.ai

About Aizon

Aizon is a software provider that transforms manufacturing operations with the use of IoT, cloud, advanced analytics, artificial intelligence, and Pharma 4.0 technologies focused on optimizing pharmaceutical and biotech companies. The Aizon analytics platform seamlessly integrates unlimited sources of structured and unstructured data to deliver actionable insights across all manufacturing sites. Aizon offers an intuitive way to gain meaningful operational intelligence with data by enabling real-time visibility and predictive insights in a GxP compliant manner with end-to-end data integrity. Aizon is based in San Francisco, California and also has a European office in Barcelona, Spain.

aizon

sales@aizon.ai
+1 628-243-2513

01.26.22