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ASIA EDITION

# AI: Tremendous Potential to Transform Bioprocessing Efficiencies

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**The biopharma manufacturing industry has started embracing Bioprocessing 4.0 solutions that incorporate intelligent automation and advanced process control and optimisation tools**

The biopharmaceutical industry is witnessing unprecedented growth, with a surge in demand for vaccines, monoclonal antibodies (mAbs), and advanced modalities including RNA therapeutics, mRNA vaccines, and cell and gene therapies (CGTs). Bioprocessing requirements for advanced modalities are increasingly complex, time-consuming, and expensive, with challenges associated with scaling up and reproducibility. Manufacturing of these advanced biopharma products using microbial, or mammalian cell lines needs to be safe, reliable, and cost-effective to enable the production of industrial levels of therapeutics with the desired quality.

While bioprocessing technologies have advanced exponentially over the years, with a shift to digitisation, single-use systems, robust analytics, and near real-time product release (enabled by in-line or at-line monitoring), enabling continuous manufacturing for traditional vaccines and mAbs, there is still a huge unmet need to replicate this for advanced modalities. It is therefore critical to optimise the cell culture conditions, upstream and downstream processes, and monitor and control the processes and product characteristics to improve yield, quality, and overall process efficiency.

The COVID-19 pandemic has created a huge demand for scalable and rapid manufacture of mRNA vaccines and other vaccine formats, making it a strategic imperative to focus on high throughput, scalable, and cost-effective manufacture of such biomolecules.

Artificial intelligence (AI) has already made a huge impact on the healthcare industry with multiple stakeholders across the healthcare continuum leveraging data-driven tools and AI in their workflows, with the highest impact in drug discovery and diagnostics. The biopharma manufacturing industry has also started embracing Bioprocessing 4.0 solutions that incorporate intelligent automation and advanced process control and optimisation tools using machine learning (ML) and AI.

Advanced ML algorithms and AI-based tools, along with automation can play a key role in improving the manufacturing efficiency of these modalities. On a global scale, multiple Tier 1 biopharma companies and large Contract Development and Manufacturing Organisations (CDMOs) such as GSK, Merck, Takeda, Roche, Pfizer, Cytiva, GE Healthcare, Fujifilm Diosynth, and Catalent have adopted AI-augmented software and tools to optimise and control their manufacturing processes.

Several technology startups focused on biomanufacturing targeted AI-based solutions have emerged to improve process analytics, process control, product characterisation, supply chain management, and factory operations. Companies such as Nucleus Biologics, Culture Biosciences, Valitacell, BiologIC Technologies, and Trakcel have developed innovative platforms and solutions for biopharma companies and CDMOs that can be adopted in their workflows. US-based Nucleus Biologics' AI-enabled NB-AIR (first of its kind globally) and NB-Lux are AI platforms that help select optimal cell culture conditions and identify precision formulations suitable for CGTs.

On a similar note, Hong Kong-based Great Bay Bio (GBB) has also launched AI-powered platforms for cell line development and media design, known as AlfaCell and AlfaMedX respectively. It aims to develop AI-based end-to-end solutions for biomanufacturing. Similarly, Culture Biosciences has a cloud-based platform that helps in scaling up bioprocesses, designing optimal bioreactor conditions to translate from bench to the bioreactor, and achieving desired manufacturing efficiency.

**Unravelling "Unknown" Patterns**

A key bottleneck in biopharma manufacturing is to achieve the desired critical quality attribute (CQAs) by optimising process variables known as critical process parameters (CPPs) based on conventional multivariate data analysis (MVDA). With an improved understanding of the non-linear, complex relation between CPPs and CQAs, and the growing number of CPPs, the adoption of advanced modelling solutions and ML algorithms can support the development of a QbD (quality by design) approach for biopharma manufacturing.

The use of soft sensors based on advanced neural networks such as ANNs (artificial neural networks), DNNs (deep neural networks), and RNNs (recurrent neural networks), can boost upstream processes by predicting the impact of different CPPs on CQAs, and pave the way for the development of robust models, which can be used to standardise GMP for biologics and develop a DoE (design of experiment) approach.

Augmenting bioprocess monitoring with AI can be useful for analysing large amounts of data generated by the manufacturing processes, which are used to develop predictive models and build in silico Digital Twins to guide process optimisation.

The seamless integration of AI and advanced deep learning algorithms across the bioprocessing value chain right from cell culture and media optimisation to upstream processing, downstream processing, and overall operations would improve the efficiency and robustness of bioprocessing. It can simplify the integration and analysis of siloed, multimodal data and decipher "hidden" patterns and develop predictive models for process optimisation. Deep learning-based soft sensors that use DNNs have been shown to be accurate even without extensive training data sets.

**Poised to grow further**

The potential for growth of biopharma manufacturing is picking up in Asia and is poised to grow over the next decade. Many of the new bioprocessing facilities are being built in the region, with advanced digitisation and AI capabilities. Some of the key players such as Wuxi Biologics, Samsung Biologics, Yokogawa, Celltrion, Beigene, and Dr. Reddys are making enormous investments in capacity building as well as strengthening infrastructure and data-enabled platforms, presenting a potential market opportunity for AI-augmented bioprocessing.

Within Asia, China, Japan, and Singapore lead in terms of initiatives, innovations and partnerships in the data and AI-powered bioprocessing space. China-headquartered Beigene has made rapid strides in the digital biomanufacturing space and was the first company to launch a digitised “paperless” biological manufacturing facility in China in its Guangzhou site.

In addition, manufacturing efficiencies are also being improved with the integration of 3D modelling, digital twin, augmented interfaces, and AI in the plant. On a similar note, China-based WuXi Biologics leverages AI in its WuXia Cell line Development Platform and is leveraging big data analytics and AI in its bioprocessing workflow. Samsung Biologics (South Korea) has also been quick to adopt AI and advanced data-driven analytics in its biologics manufacturing units.

Globally renowned bioprocess software developers have also partnered with Asian entities. For instance, one of the key innovators in the biomanufacturing software and digital twin solutions space – Insilico Biotechnology (headquartered in Germany) – had partnered with several companies in Asia before being acquired by Yokogawa Electric Corp (Japan) in November 2021.

Insilico’s AI solutions include digital twin models and real-time process monitoring to improve the cell culture environment. In October 2021, Insilico Biotechnology, had entered into an agreement with Ajinomoto and its subsidiary Ajinomoto Genexine Co. Ltd., to leverage Digital twin technology to improve process development and production of biologics.

The collaborative landscape is also evolving with many established CDMOs leveraging partnerships with AI platform developers such as the one between Swiss-based Securecell and Japanese company Yokogawa Life Science which uses advanced process information management systems to optimise mAb productivity. Product characterisation using AI is a lesser traversed area, especially for complex biomolecules and their visualisation remains a key bottleneck in novel therapeutics and vaccine manufacturing. Waters Corporation, a reputed US-based instrumentation company partnered with A*STAR’s Bioprocessing Technology Institute (BTI) in 2021 to advance structural analysis and annotation of complex biomolecules using advanced bioinformatics and ML.

Though the overall AI-based bioprocessing ecosystem is still nascent in Asia, and the innovation index is lower compared to the US and Europe, recent investments, and the proactive approach of the biomanufacturing companies operating in the region will spur further innovations and developments.

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