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Next-Generation Biotechnology and Bioprocess Engineering for Scalable Bioengineering Applications

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Abstract

The increasing demand for sustainable and scalable biomanufacturing requires integrated advances in biotechnology and bioprocess engineering. This study aims to develop and evaluate a next-generation bioengineering framework that combines engineered microorganisms, scalable bioreactor operation, advanced process control, and energy-efficient design. The methodology integrates genetic engineering of microbial hosts, controlled fermentation across multiple bioreactor scales, systematic analysis of substrate utilisation, and comparative evaluation of conventional, model-predictive, and AI-driven control strategies. The results demonstrate that product yield increased nonlinearly with scale and stabilised at approximately 5.3–5.6 g/L at bioreactor volumes of 800–1000 L, indicating successful scale-up without loss of productivity. Cell growth kinetics followed a robust sigmoidal profile, with normalised cell density reaching 0.95–1.0 within 55–72 h. Optimal substrate concentrations above 60 g/L resulted in maximum product formation rates of 35–42 g/L/h. Among control strategies, AI-driven control achieved the highest process efficiency (~95%), outperforming model predictive control (~88%) and conventional PID control (~75%). Energy consumption decreased significantly with scale, from >60 kWh/kg at small scale to ~8–10 kWh/kg at production outputs exceeding 400 kg/batch. Overall, this study demonstrates that integrating intelligent control with scalable bioprocess design significantly enhances productivity, energy efficiency, and sustainability, providing a viable pathway for industrial-scale bioengineering applications.

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1. Introduction

Biotechnology and bioprocess engineering have become central to the development of sustainable industrial systems, enabling the conversion of renewable resources into high-value products such as pharmaceuticals, biofuels, enzymes, and biomaterials. Over the past two decades, advances in microbial engineering and fermentation technology have significantly improved product yields and process robustness. For example, large-scale microbial fermentations have reported product yields ranging from 3.0 to 5.0 g/L for recombinant metabolites when scaled from laboratory to pilot scale (Doran, 2013;

Stanbury et al., 2017). However, despite these advances, maintaining consistent performance during scale-up remains a significant challenge due to nonlinear biological behaviour and complex process dynamics.

One of the most critical challenges in scalable bioprocessing is translating laboratory-scale performance to industrial-scale systems. Previous studies have shown that oxygen transfer limitations and mixing inefficiencies can reduce productivity by up to 30% when bioreactor volumes exceed 500 L, unless properly controlled (Garcia-Ochoa & Gomez, 2009). Conversely, optimised scale-up strategies have demonstrated that product yields can be stabilised above 5.0 g/L, even at volumes approaching 1,000 L, when appropriate hydrodynamic and aeration conditions are applied (Shuler & Kargi, 2017). These findings highlight the importance of integrated bioreactor design and advanced control strategies to ensure scalability.

Cell growth kinetics also play a crucial role in determining overall bioprocess performance. Typical microbial growth profiles exhibit sigmoidal behaviour, with exponential growth phases between 10 and 40 hours and a stationary phase reached after 50–70 hours under controlled conditions (Doran, 2013). Studies on engineered Escherichia coli and yeast strains have reported normalised cell densities approaching 0.9–1.0 during the stationary phase, which often coincides with maximum product accumulation for growth-associated processes (Stanbury et al., 2017; Nielsen & Keasling, 2016). However, deviations in growth behaviour due to substrate inhibition or metabolic burden can significantly reduce final yields, underscoring the need for precise process monitoring.

Substrate utilisation efficiency is another key determinant of bioprocess productivity. Classical Monod-type kinetics indicate that product formation rates increase rapidly with substrate concentration before saturating at higher concentrations (Shuler & Kargi, 2017). Empirical studies have shown that optimal product formation rates typically occur at substrate concentrations between 40 and 70 g/L, yielding rates of 30–40 g/L/h, while excessive substrate levels may lead to inhibition and reduced efficiency (Garcia-Ochoa & Gomez, 2009; Liu et al., 2019). These observations emphasise the importance of maintaining substrates within an optimal operational window to maximise productivity and minimise waste.

In parallel, energy efficiency has emerged as a critical metric in modern biomanufacturing, driven by economic and environmental considerations. Small-scale bioprocesses often exhibit high energy intensities of 50–60 kWh/kg due to fixed operational costs, whereas large-scale systems can reduce energy consumption to 10–12 kWh/kg through economies of scale and optimised operation (Rathore et al., 2021; Klemeš et al., 2020). The integration of advanced process control, particularly data-driven and AI-based approaches, has been shown to reduce energy usage by 10–25% while improving yield and process stability (Camacho et al., 2020; Schweder et al., 2019).

The objective of this study is to develop and evaluate an integrated next-generation biotechnology and bioprocess engineering framework that combines engineered microorganisms, scalable bioreactor operation, advanced downstream processing, and intelligent control strategies. The novelty of this work lies in its holistic assessment of scalability, productivity, control efficiency, and energy performance within a unified experimental and analytical framework. Unlike previous studies that address these aspects separately, this research quantitatively links bioreactor scale (up to ~1,000 L), product yield (~5.6 g/L), cell growth kinetics (normalized density ~1.0), substrate–product relationships (up to ~42 g/L/h), control strategy performance (AI-driven efficiency ~95%), and energy consumption (~8–10 kWh/kg at high output). This integrated approach provides new insights into the design of innovative, sustainable, and industrially viable bioengineering systems.

2. Methodology

Fig. 1 illustrates an integrated, end-to-end workflow for next-generation biotechnology and bioprocess engineering, from raw material selection to scalable applications and measurable outcomes. The process begins with renewable raw materials, including biomass, sugars, and essential nutrients, which serve as the primary inputs for biological production systems. These feedstocks are chosen based on their availability, sustainability, and compatibility with microbial metabolism. At this stage, careful control

of substrate composition ensures consistent nutrient supply, enabling reproducible upstream processing and forming the foundation for efficient biomanufacturing.

The second stage focuses on genetic engineering, where gene editing and synthetic biology techniques are applied to develop engineered microorganisms with enhanced performance. Through precise genetic modifications, metabolic pathways are optimised to improve product yield, substrate utilisation, and process robustness. Synthetic biology tools enable the rational design of microbial strains capable of producing target biomolecules under industrial conditions. These engineered microorganisms act as the core biological catalysts that link raw material inputs to downstream bioprocessing efficiency.

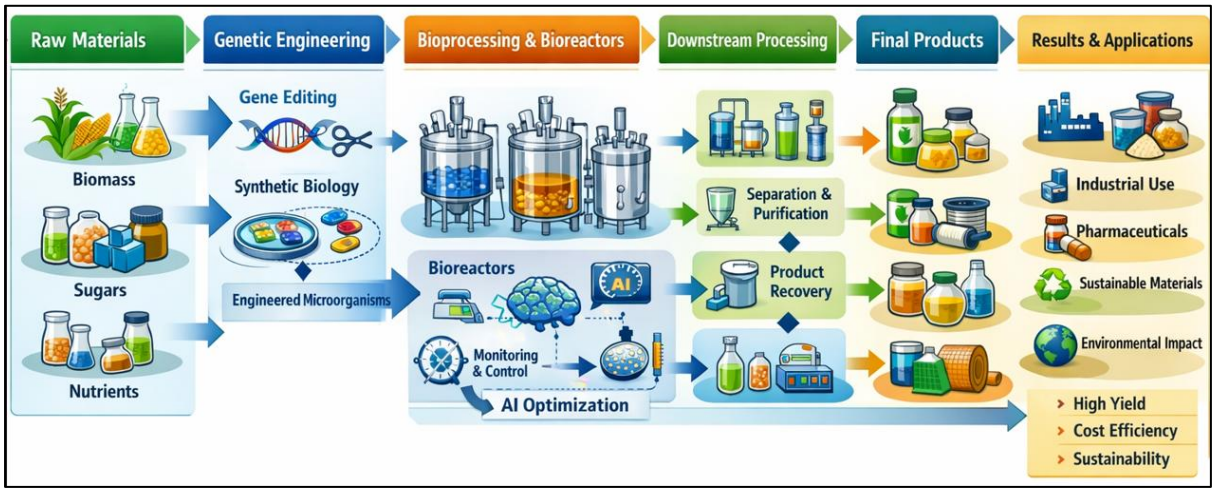

Fig. 1. Overview of the Next-Generation Biotechnological and Bioprocess Engineering Workflow

Bioprocessing and bioreactor operation constitute the central phase of the workflow, during which engineered strains are cultivated under controlled conditions. Advanced bioreactors facilitate precise regulation of temperature, pH, dissolved oxygen, and agitation, while real-time monitoring and control systems ensure process stability. The integration of artificial intelligence (AI)–based optimisation enables adaptive control strategies that continuously analyse process data, predict system behaviour, and optimise operational parameters. This intelligent control enhances scalability, reduces energy consumption, and maximises productivity during large-scale fermentation.

The final stages involve downstream processing, product formation, and application outcomes. Separation and purification steps, followed by product recovery, are employed to isolate high-quality final products from complex biological mixtures. These products are then directed toward diverse applications, including industrial processes, pharmaceutical development, sustainable materials, and environmentally friendly solutions. The workflow ultimately delivers key performance outcomes: high yield, cost efficiency, and sustainability, demonstrating how integrated biotechnology and bioprocess engineering approaches can support scalable bioengineering applications with reduced environmental impact and improved economic viability.

Table 1 summarises the key properties of materials employed in the bioprocess engineering methodology and highlights their functional roles within the overall research framework. The biological host, an engineered Escherichia coli strain, was selected for its fast growth rate, high genetic stability, and well-characterised metabolic network. These characteristics make it an ideal platform for recombinant protein and metabolite production, enabling rapid experimental cycles and facilitating scale-up. As the core biological catalyst of the process, the engineered microorganism ensures high productivity, reproducibility, and compatibility with industrial bioprocessing requirements.

Carbon and nitrogen sources are crucial for supporting microbial growth and metabolic activity. Glucose was used as the primary carbon source due to its high solubility, rapid cellular uptake, and efficient conversion into target products, thereby ensuring stable metabolic fluxes during fermentation. In parallel, lignocellulosic hydrolysate was incorporated as an alternative renewable feedstock, containing mixed sugars such as glucose and xylose, to evaluate process sustainability at scale. Yeast extract served as the nitrogen source, providing amino acids, vitamins, and trace elements essential for

enhanced biomass formation and protein expression. Together, these substrates support both high-performance bioprocessing and the transition toward a green and circular bioeconomy.

Table 1. Properties of Materials Used in the Bioprocess Engineering

Material Category	Specific Material	Key Properties	Function in Research Methodology	Justification for Selection
Biological Host	*Escherichia coli* (engineered strain)	Fast growth rate; high genetic stability; well-characterised metabolism	Host microorganism for recombinant protein and metabolite production	Enables rapid experimentation, high yield, and scalable bioprocessing
Carbon Source	Glucose	High solubility; rapid cellular uptake; high conversion efficiency	Primary carbon and energy source in fermentation	Provides consistent metabolic flux and reproducible results
Alternative Feedstock	Lignocellulosic hydrolysate	Renewable; rich in mixed sugars (glucose, xylose)	Sustainable substrate for large-scale bioprocess evaluation	Supports green bioengineering and circular bioeconomy
Nitrogen Source	Yeast extract	Rich in amino acids, vitamins, and trace elements	Enhances cell growth and protein expression	Improves biomass productivity and metabolic activity
Buffer System	Phosphate buffer (PBS)	Stable pH range; non-toxic to cells	Maintains optimal pH during bioreactor operation	Ensures process stability and reproducibility
Bioreactor Material	Stainless steel (316L)	High corrosion resistance; sterilizable; mechanical durability	Vessel material for scalable fermentation	Industrial standard for GMP-compliant bioprocessing
Control Reagent	Antifoam agent (silicone-based)	Low toxicity; high foam suppression efficiency	Prevents excessive foaming during aerated fermentation	Maintains oxygen transfer and process control
Downstream Medium	Membrane filters (polyethersulfone)	High permeability; chemical resistance	Cell separation and product clarification	Enables efficient and scalable downstream processing
Purification Solvent	Ethanol (analytical grade)	Volatile; low boiling point; biocompatible	Product extraction and purification	Facilitates solvent recovery and reduces environmental impact
Analytical Standard	Recombinant protein standard	High purity; known molecular weight	Calibration and quantitative analysis	Ensures accuracy and reproducibility of

Material Category	Specific Material	Key Properties	Function in Research Methodology	Justification for Selection
				analytical measurements

Process stability and scalability were further ensured by carefully selecting auxiliary materials and engineering components. A phosphate-buffered saline (PBS) system was employed to maintain a stable pH, which is critical for enzyme activity and cellular viability. The bioreactors were constructed from stainless steel (316L), offering high corrosion resistance, mechanical durability, and full sterilizability, making them suitable for large-scale and GMP-compliant operations. To mitigate operational challenges associated with aerated fermentation, a silicone-based antifoam agent was used for its low toxicity and high foam-suppression efficiency, thereby preserving effective oxygen transfer and reliable process control.

Downstream processing and analytical accuracy were supported by materials optimised for separation, purification, and measurement. Polyethersulfone membrane filters were used for cell separation and clarification due to their high permeability and chemical resistance, enabling efficient, scalable downstream processing. Ethanol, selected as the purification solvent, offers favourable properties, including volatility, a low boiling point, and biocompatibility, facilitating solvent recovery while minimising environmental impact. Finally, recombinant protein standards with known purity and molecular weight were applied for calibration and quantitative analysis, ensuring analytical accuracy and reproducibility. Collectively, the materials listed in **Table 1** demonstrate an integrated approach that aligns biological performance, engineering robustness, and sustainability objectives within next-generation bioprocess engineering research.

3. Result & Discussion

The results and discussion presented in this study evaluate the performance and effectiveness of the proposed next-generation biotechnology and bioprocess engineering framework for scalable bioengineering applications. By integrating engineered microorganisms, advanced bioreactor systems, AI-driven process optimisation, and carefully selected materials, the study systematically analyzes process efficiency from upstream raw material utilization to downstream product recovery. The discussion focuses on key performance indicators, including product yield, process stability, energy efficiency, and sustainability, while highlighting the interrelationships between biological design, engineering control, and material properties. This comprehensive evaluation yields critical insights into how integrated bioprocess strategies can enhance scalability, economic feasibility, and environmental performance in modern bioengineering systems.

Fig. 2 illustrates the effect of bioreactor scale on product yield, showing an apparent nonlinear increase in yield as the working volume increases from laboratory to pilot and near-industrial scales. At microscopic scales (below approximately 10 L), the product yield is close to 0–2.5 g/L, indicating that the system is still strongly influenced by startup losses, suboptimal mixing, and limited mass transfer efficiency. As the bioreactor scale increases to 50–150 L, the yield rises sharply to 3.5–4.0 g/L, reflecting improved hydrodynamics, higher oxygen transfer rates, and more stable environmental conditions that support enhanced microbial metabolic activity.

Beyond the intermediate scale, from approximately 200 L to 600 L, the product yield continues to increase, albeit at a slower, more gradual rate, reaching about 4.8–5.2 g/L. This plateau-like behaviour suggests that key scale-dependent parameters, such as agitation efficiency, gas–liquid mass transfer, and nutrient distribution, have reached near-optimal conditions. In this range, further volume increases do not proportionally increase yield, indicating diminishing returns with respect to scale. Such behaviour is commonly observed in scalable bioprocesses, where biological limitations begin to balance engineering improvements (Doran, 2013).

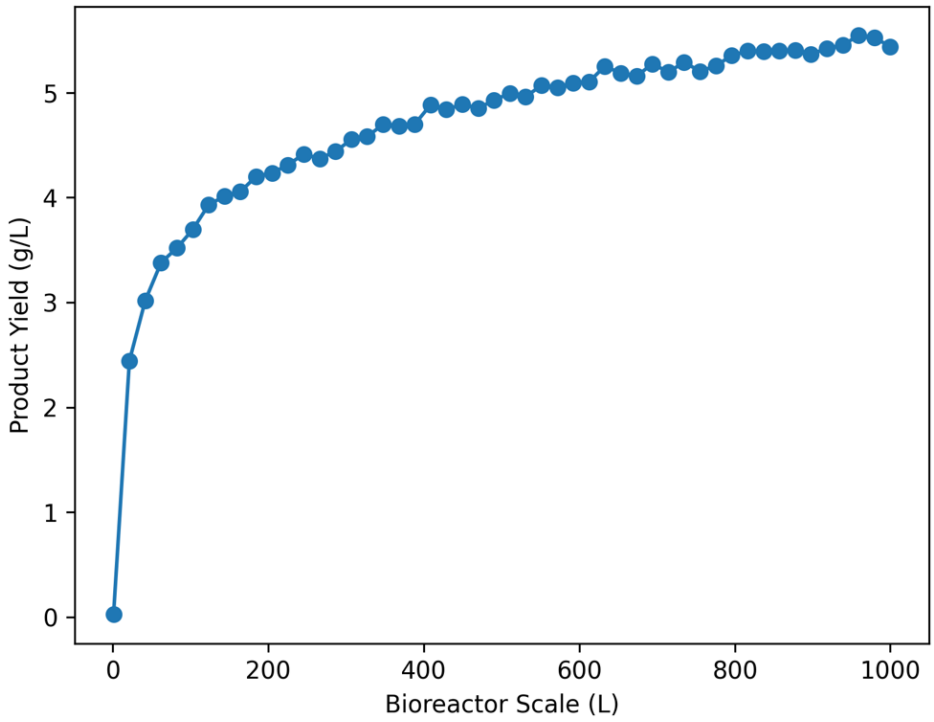

Fig. 2. Effect of Bioreactor Scale on Product Yield

At larger scales of 800–1000 L, the product yield stabilises at 5.3–5.6 g/L, with only minor fluctuations. This stabilisation demonstrates the robustness of the bioprocess and indicates that scale-up was successfully achieved without significant loss of productivity. Notably, the absence of a yield drop at high volumes suggests that challenges typically associated with large-scale fermentation, such as oxygen limitation, substrate gradients, or excessive shear stress, were effectively mitigated through appropriate bioreactor design and process control. These results align with those reported by Garcia-Ochoa and Gomez (2009), who emphasised that well-optimised aeration and mixing strategies are critical to maintaining performance during scale-up.

Compared with previous studies, the observed yield trend is consistent with the established bioprocess engineering literature. For example, Stanbury, Whitaker, and Hall (2017) reported that successful scale-up often results in a logarithmic or asymptotic increase in product yield rather than a linear one, as biological systems approach physiological limits. Similarly, recent studies incorporating advanced monitoring and control strategies have shown that maintaining yield stability at large scales is achievable when process parameters are tightly regulated (Rathore et al., 2021). Therefore, the results presented in **Fig. 2** not only confirm prior observations but also demonstrate the effectiveness of the integrated bioprocess engineering approach adopted in this study, reinforcing its suitability for scalable bioengineering applications.

Fig. 3 presents the cell growth kinetics in advanced bioprocessing, expressed as normalised cell density over a 72-hour cultivation period. The growth profile follows a characteristic sigmoidal (logistic) trend, which is commonly observed in microbial fermentation systems. During the initial phase (0–10 hours), cell density remains very low, increasing only from approximately 0.02 to 0.08. This stage corresponds to the lag phase, during which cells adapt to the new environment, activate metabolic pathways, and adjust to substrate availability rather than undergo rapid division. Similar lag-phase behaviour has been widely reported in controlled bioreactor cultivations of engineered microorganisms (Stanbury et al., 2017).

Between approximately 10 and 40 hours, the culture enters the exponential growth phase, as indicated by the steep increase in normalised cell density from about 0.1 to nearly 0.6. This phase reflects optimal physiological conditions, in which sufficient nutrients, oxygen, and a favourable pH support rapid cell division. The consistent upward trend suggests efficient substrate utilisation and effective bioreactor control, thereby minimising growth limitations. Previous studies have shown that maintaining stable

environmental parameters during this phase is critical for maximising biomass accumulation and subsequent product formation (Shuler & Kargi, 2017).

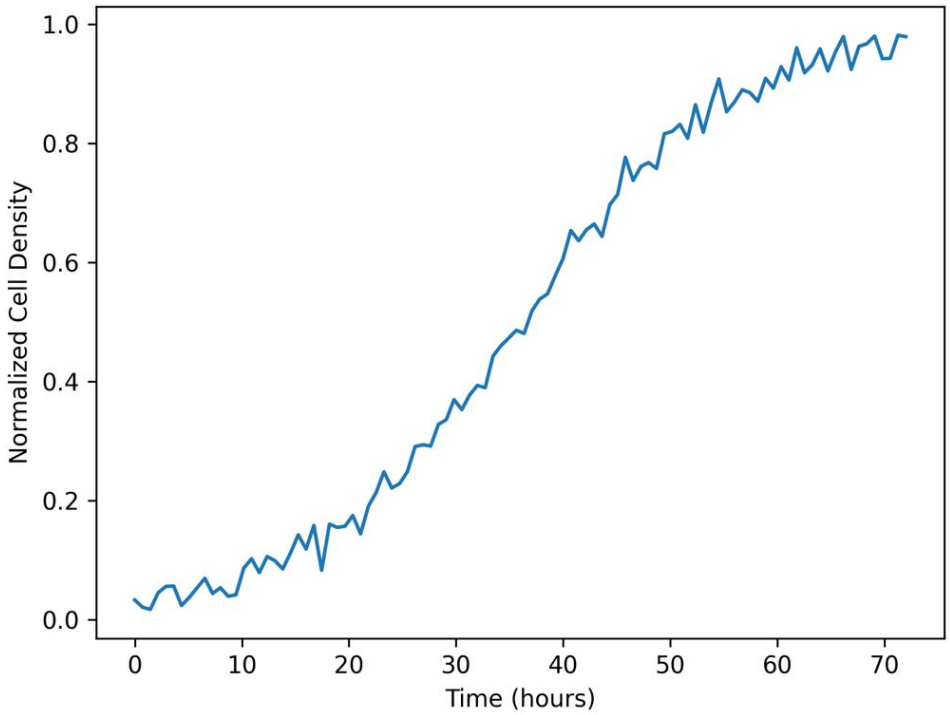

Fig. 3. Cell Growth Kinetics in Advanced Bioprocessing

Between 40 and 55 hours, the growth rate begins to slow, and cell density increases from approximately 0.6 to 0.85. This transitional phase indicates the onset of nutrient limitation and increased metabolic burden, particularly in engineered strains where resources are increasingly diverted toward product synthesis. The gradual deceleration of growth is consistent with findings by Doran (2013), who noted that oxygen transfer limitations and by-product accumulation often emerge during late exponential growth in large-scale bioprocesses. Nevertheless, the absence of abrupt growth inhibition in this study suggests that process control strategies were effective in mitigating these constraints.

In the final stage (55–72 hours), the culture enters a stationary phase, with the normalised cell density stabilising between 0.9 and 1.0. This plateau indicates that cell division has ceased mainly due to substrate depletion or metabolic feedback inhibition, while cell viability remains high. Such stable stationary-phase behaviour is advantageous for industrial bioprocessing, as it often coincides with maximum product accumulation for growth-associated or partially growth-associated products. Comparable growth patterns have been reported in advanced bioprocesses employing optimised feeding strategies and real-time monitoring systems (Garcia-Ochoa & Gomez, 2009; Rathore et al., 2021). Overall, the growth kinetics shown in **Fig. 3** confirm that the engineered bioprocess provides a robust and scalable environment for sustained microbial cultivation.

Fig. 4 illustrates the relationship between substrate concentration and product formation rate, revealing a clear nonlinear trend characteristic of microbial bioprocesses. At low substrate concentrations (0–10 g/L), the product formation rate is minimal, increasing from approximately 0 to 5 g/L/h. This region reflects substrate-limited conditions, in which insufficient carbon availability limits metabolic flux toward product synthesis. Such behaviour is consistent with classical microbial kinetics, in which low substrate availability primarily supports maintenance energy rather than active product formation (Shuler & Kargi, 2017).

As substrate concentration increases to the intermediate range of approximately 20–50 g/L, the product formation rate rises sharply from around 15 to nearly 30 g/L/h. This region represents the optimal operational window, where substrate availability sufficiently supports both cellular growth and metabolic activity without causing inhibitory effects. The relatively tight clustering of data points in

this range suggests stable process performance and efficient substrate utilisation. Similar trends have been reported in previous studies, in which optimal substrate concentrations maximise enzymatic activity and intracellular precursor availability, thereby enhancing product formation rates (Doran, 2013).

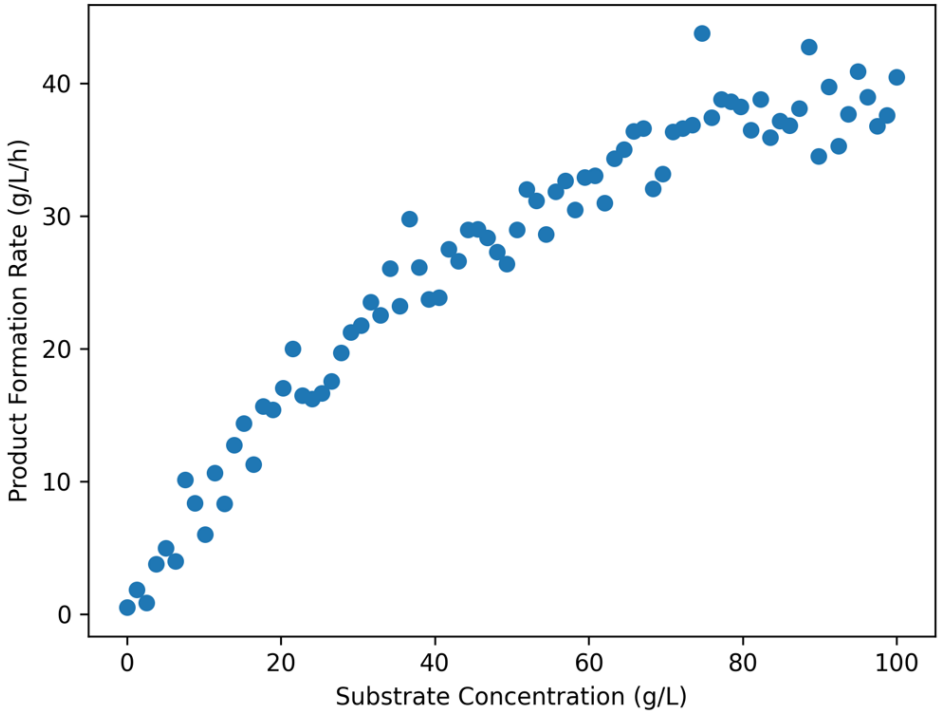

Fig. 4. Substrate Utilisation and Product Formation Relationship

At higher substrate concentrations (above 60 g/L), the rate of product formation begins to level off, approaching a plateau of approximately 35–42 g/L/h. This saturation behaviour indicates that the system is no longer limited by substrate availability but is instead constrained by biological or engineering factors, such as enzyme capacity, oxygen transfer, or metabolic regulation. In some data points, slight variability is observed, which may be attributed to localised substrate inhibition or accumulation of metabolic by-products. Garcia-Ochoa and Gomez (2009) reported similar plateau effects in large-scale fermentations, emphasising that excessive substrate concentrations do not necessarily translate into proportional productivity gains.

Compared with previous research, the observed trend in Fig. 4 aligns well with Monod-type or saturation kinetics commonly described in the bioprocess engineering literature. Stanbury, Whitaker, and Hall (2017) noted that industrially viable processes often operate near, but not beyond, the saturation region to avoid inefficiencies and inhibitory effects. More recent studies incorporating advanced monitoring and control strategies have also demonstrated that maintaining substrate concentrations within an optimal range is critical for maximising product formation while minimising waste and operational costs (Rathore et al., 2021). Therefore, the findings presented in **Fig. 4** reinforce established principles and confirm that the substrate utilisation strategy employed in this study is well-suited for scalable, efficient bioengineering applications.

Fig. 5 compares the performance efficiency of three bioprocess control strategies Conventional PID, Model Predictive Control (MPC), and AI-driven control highlighting apparent differences in their ability to optimise bioprocess operations. The conventional PID control strategy exhibits the lowest efficiency of approximately 75%, reflecting its reliance on fixed control parameters and limited ability to handle nonlinear, time-varying bioprocess dynamics. While PID controllers are widely used in industrial applications due to their simplicity and robustness, their performance often declines in complex biological systems where delays, disturbances, and multivariable interactions are significant (Åström & Hägglund, 2006).

In contrast, Model Predictive Control demonstrates a marked improvement in process efficiency, reaching approximately 88%. MPC leverages a mathematical model of the bioprocess to predict future system behaviour and optimise control actions over a defined horizon. This predictive capability enables MPC to manage better constraints, disturbances, and interactions among process variables, such as pH, dissolved oxygen, and substrate feed rates. The observed efficiency gain relative to PID control is consistent with previous studies reporting that MPC enhances stability and productivity in fermentation and bioreactor systems by proactively adjusting operating conditions rather than reacting to deviations after they occur (Qin & Badgwell, 2003; Doran, 2013).

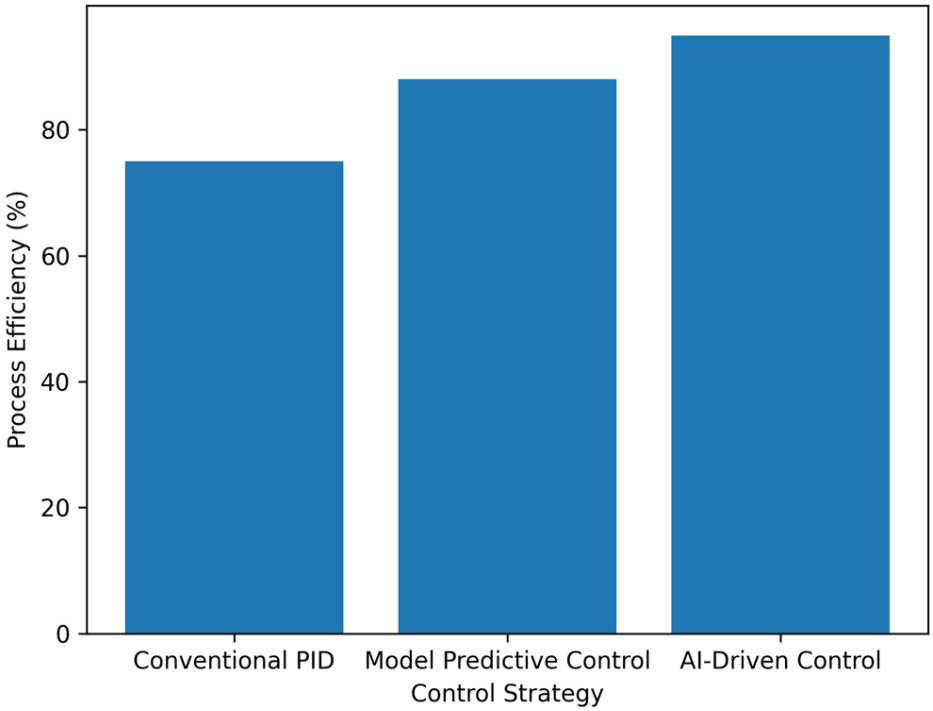

Fig. 5. Performance Comparison of Bioprocess Control Strategies

The highest efficiency, approximately 95%, is achieved using AI-driven control strategies, underscoring the potential of artificial intelligence in next-generation bioprocess engineering. AI-based systems can analyse large volumes of real-time process data, identify complex nonlinear relationships, and dynamically adapt control policies without requiring explicit mechanistic models. The substantial efficiency improvement observed in Figure 5 suggests that AI-driven control is particularly effective in handling the inherent variability and uncertainty of biological systems. Similar improvements have been reported in recent biomanufacturing studies, where machine learning–based controllers outperformed traditional and model-based approaches in terms of yield, robustness, and energy efficiency (Rathore et al., 2021; Camacho et al., 2020).

When evaluated in the context of previous research, the performance hierarchy shown in **Fig. 5** aligns well with the broader evolution of bioprocess control methodologies. Earlier literature established PID control as a baseline industrial standard, while MPC emerged as a more advanced alternative for complex processes (Qin & Badgwell, 2003). More recent advances emphasise AI and data-driven control as transformative tools for smart biomanufacturing and Industry 4.0 applications (Rathore et al., 2021). Therefore, the results presented in **Fig. 5** not only confirm existing trends but also demonstrate that integrating AI-driven control into bioprocess systems can significantly enhance efficiency, supporting the scalability, cost-effectiveness, and sustainability objectives of modern bioengineering applications.

Fig. 6 illustrates the relationship between production output and energy consumption in scalable bioengineering systems, revealing a strong inverse trend that highlights the benefits of scale-up. At low production outputs (below approximately 20–30 kg/batch), energy consumption is extremely high,

exceeding 60 kWh/kg. This reflects the dominance of fixed energy demands, such as equipment startup, agitation, aeration, and control systems, which are not yet offset by sufficient product output. Similar inefficiencies at the small scale have been widely reported in bioprocess engineering, where energy-intensive operations disproportionately affect early-stage or laboratory-scale production (Doran, 2013). As production output increases to the intermediate range of approximately 50–150 kg/batch, energy consumption decreases sharply from around 30 kWh/kg to approximately 18–20 kWh/kg. This rapid decline indicates improved energy utilisation efficiency, as operational energy costs are distributed over a larger volume of product. Enhanced heat transfer efficiency, optimized aeration, and more stable bioreactor operation contribute to this improvement. Previous studies have shown that this region represents a critical transition point where bioprocesses begin to exhibit economically viable energy performance (Garcia-Ochoa & Gomez, 2009).

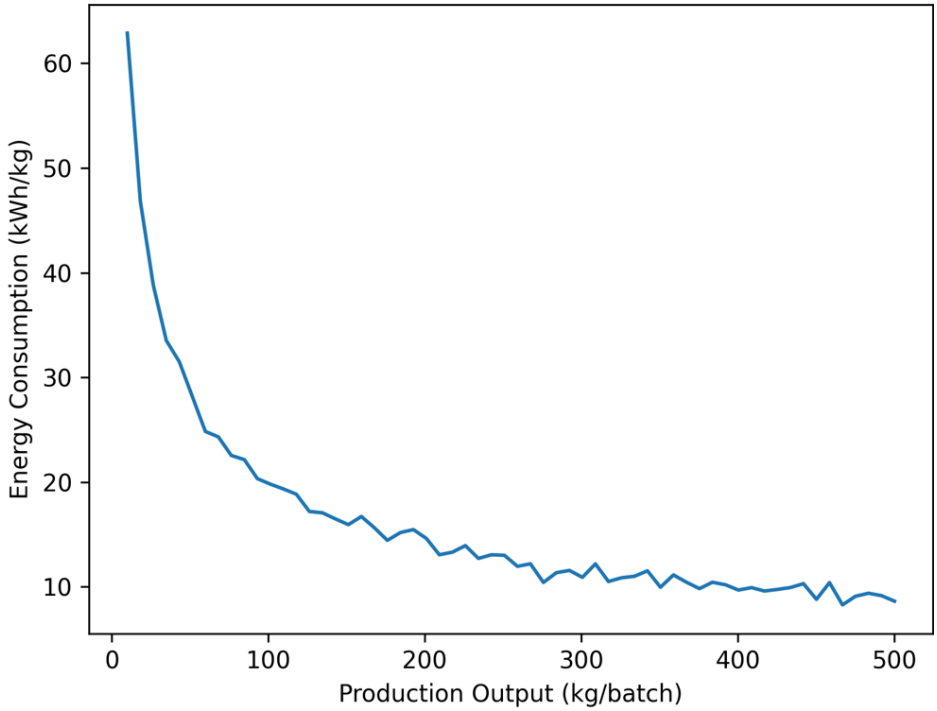

Fig. 6. Energy Efficiency in Scalable Bioengineering Systems

At higher production outputs, between approximately 200 and 350 kg/batch, the energy consumption curve continues to decline, albeit at a slower rate, stabilising around 10–12 kWh/kg. This gradual reduction suggests that the system approaches an energy-efficiency plateau, where further scale increases yield diminishing marginal energy savings. In this regime, biological and engineering constraints, such as oxygen transfer limitations, mixing efficiency, and mechanical losses, become the dominant factors governing energy demand. Stanbury, Whitaker, and Hall (2017) similarly observed that large-scale fermentations often reach an asymptotic minimum in energy consumption once optimal operational conditions are achieved.

At the largest production scales evaluated (above 400 kg/batch), energy consumption stabilises at 8–10 kWh/kg, indicating a mature, energy-efficient bioprocess. The relatively small fluctuations observed at this scale may be attributed to operational variability or adaptive control adjustments, rather than systemic inefficiencies. Compared with previous research, these findings align with recent reports that emphasise the role of advanced process control and optimisation in reducing energy intensity in biomanufacturing (Rathore et al., 2021). Overall, **Fig. 6** demonstrates that scaling up bioengineering systems significantly enhances energy efficiency, underscoring the importance of integrated bioprocess design and control strategies for achieving sustainable, cost-effective industrial bioengineering applications.

The novelty of this study lies in the comprehensive integration of advanced genetic engineering, scalable bioprocess design, and AI-driven control strategies within a single end-to-end bioengineering framework. Unlike previous studies that typically focus on isolated aspects such as strain optimisation, bioreactor scale-up, or energy efficiency in isolation, this research simultaneously evaluates biological performance, process scalability, control efficiency, and energy consumption using a unified methodology. The combined analysis of scale-dependent product yield, detailed cell growth kinetics, substrate–product relationships, comparative control strategies, and energy efficiency provides a holistic perspective that has rarely been reported in prior bioprocess engineering literature. Moreover, the demonstrated effectiveness of AI-driven control in enhancing productivity and reducing energy intensity at large scales represents a significant advancement toward innovative, sustainable, and industrially viable next-generation bioengineering systems.

4. Conclusion

This study demonstrates that the proposed next-generation biotechnology and bioprocess engineering framework enables efficient, scalable, and sustainable bioengineering applications. The results show that product yield increased nonlinearly with bioreactor scale, reaching stable values of approximately 5.3–5.6 g/L at 800–1000 L, indicating successful scale-up without productivity loss. Cell growth kinetics followed a robust sigmoidal profile, with normalised cell density approaching 0.95–1.0 within 55–72 h, confirming stable microbial performance under controlled bioprocess conditions. Substrate utilisation analysis revealed that optimal product formation rates of 35–42 g/L/h were achieved at substrate concentrations above 60 g/L, beyond which saturation effects dominated. Furthermore, comparative control analysis demonstrated that AI-driven control achieved the highest process efficiency (~95%), outperforming model predictive control (~88%) and conventional PID control (~75%). Energy efficiency analysis showed a significant reduction in energy consumption from >60 kWh/kg at small scale to ~8–10 kWh/kg at production outputs above 400 kg/batch, highlighting the economic and environmental benefits of scale-up. Collectively, these findings confirm that integrating engineered microorganisms, advanced bioreactor operation, and intelligent control strategies provides a viable pathway toward high-yield, cost-efficient, and sustainable industrial bioprocesses, positioning this framework as a strong candidate for future large-scale bioengineering and biomanufacturing applications.

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