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Harnessing Microbial Potential for Sustainable Biomanufacturing and Bioeconomic Growth

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Abstract: Biomanufacturing relies on microorganisms as production platforms due to their inherent metabolic versatility, rapid growth, and suitability for scalable biological processes. Compared to plant and mammalian systems, microbial platforms are preferred because they enable efficient process control, flexible substrate utilization, and straightforward translation from laboratory to industrial scale. Central to the success of microbial biomanufacturing is strain engineering, which allows the redirection of metabolic fluxes, enhancement of product yields, and improvement of robustness under industrial operating conditions. Despite advances in molecular and systems level tools, strain improvement remains a major bottleneck, particularly when transitioning from proof-of-concept to large-scale production. Additional challenges include process scale-up, infrastructure availability, regulatory harmonization, and workforce capacity. In the Indian context, national initiatives such as Make in India and the BioE3 policy are supporting the development of domestic biomanufacturing capabilities, however, continued dependence on imported single-use components and high capital and operational costs limit broader adoption. Future progress is expected to be driven by systematic strain engineering, data-driven design–build-test cycles, and integrated biofoundry models, enabling the establishment of a resilient and competitive biomanufacturing ecosystem.

Key words: Biomanufacturing, sustainable future, bio-based processes, industrial applications, bioeconomy.

The pivotal role of microorganisms in shaping modern biomanufacturing and industrial biotechnology is now firmly acknowledged by both the scientific community and industry. Over time, manufacturing strategies have transitioned from conventional chemical synthesis to bio-based processes that harness microbial metabolism. Here we highlight the central importance of microorganisms in advancing biomanufacturing, drawing on recent research insights, technological breakthroughs, and current industrial practices, while also addressing the key gaps and challenges that continue to limit broader adoption. The discussion emphasizes how microbial platforms drive the bioeconomy through their unique characteristics, diverse applications, rapid development cycles, and the integration of cutting-edge tools

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such as CRISPR-Cas9, which are transforming the scope and efficiency of strain engineering.

Biomanufacturing involves harnessing the metabolic ability of living organisms to produce therapeutics, chemicals, materials, and foods. Bacteria, yeasts, and filamentous fungi possess characteristics that make them ideal for these applications, including rapid proliferation, high metabolic flexibility, and exceptional genetic accessibility. Model strains such as *Escherichia coli*, *Bacillus subtilis*, *Leuconostoc* sp. and *Saccharomyces cerevisiae* remain mainstays in industrial manufacturing thanks to decades of optimization and the availability of robust genetic and process engineering toolkits (Xie, 2022). The emergence of engineered non-conventional microbes like *Yarrowia lipolytica*, *Corynebacterium glutamicum*, *Sphingomonas* sp. and *Pseudomonas putida* has significantly expanded the range of biomolecules accessible through biological routes (Cho *et al.,* 2022)

With recent advances in molecular biology, alterations to pathways and strain improvements are now possible in accelerated timeframes when compared with plant and mammalian systems. By reducing development timelines from years to weeks, this efficiency redefines innovation cycles in research and commercial bioprocess development. Under the right conditions, the metabolic diversity among microorganisms makes it possible to redirect carbon flux and cellular resources towards the accumulation of targeted products with yields that often surpass those of higher organisms or synthetic routes.

Microbial cell factories now support diverse industrial segments, ranging from legacy applications in food and beverage production to contemporary roles in pharmaceuticals, sustainable chemicals, and biomaterials (Arshad *et al.,* 2025). In the food industry, *S. cerevisiae*, *Lactobacillus* sp., and *Aspergillus niger* are essential for bread, dairy, and organic acid production, respectively (Que *et al.,* 2024; Upton *et al.,* 2020; Ngamsomchat *et al.,* 2022). The microbial synthesis of complex molecules, such as the production of recombinant human insulin in *E. coli* and the microbial biosynthesis of antibiotics, vitamins, and therapeutic enzymes, has driven pharmaceutical innovation (Sharma *et al.,* 2024).

Emerging applications focus on environmentally sustainable alternatives to petroleum-based manufacturing, including the production of biodegradable polymers (polyhydroxyalkanoates), a fructose-based polymer (Levan), advanced biofuels, and platform chemicals such as succinic acid and 1,4-butanediol (Cho *et al.,* 2022). Microbial hosts allow the efficient conversion of waste into valuable products by generating “cell factories” that convert waste into compounds like bioplastics, biofuels, and biofertilizers.

Modern biomanufacturing predominantly relies on genetically characterized or domesticated strains instead of environmental or wild-type microorganisms. This is due to process stability, genetic containment, regulatory compliance, and the risks associated with unpredictable environmental isolates (Pantoja Angles *et al.,* 2022). The continuous improvement of established microbial platforms remains the competitive strategy for most commercial bioprocessing operations.

Microbial growth kinetics surpass those of plant or animal cells by orders of magnitude, a fact of both biological consequence and fundamental economic significance. Bacterial species such as *Vibrio natriegens* exhibit unparalleled population-doubling times of less than ten minutes in laboratory settings, while the classic *E. coli* and yeast platforms maintain doubling times of 20 minutes to a few hours. In contrast, mammalian cultures and plant cell lines are limited to doubling intervals measured in days.

This acceleration cascades through process development and manufacturing, enabling higher productivity, more rapid scale-up, and iterative optimization in research and industry. Time-to-market for novel bioproducts is thus frequently dictated by microbial growth rates, supporting strategic deployment of these platforms for competitive advantage. High cell density and continuous bioprocessing, enabled by robust microbial hosts and controlled bioreactor environments, further augment the intrinsic speed advantage and maximize volumetric yields. The capacity to efficiently upgrade strains through adaptive laboratory evolution, pathway editing, and high-throughput screening is directly facilitated by these rapid cell cycles.

The introduction of CRISPR-Cas9 marked a profound transformation in genetic engineering, unlocking precise, multiplex, and efficient genome editing for microorganisms. CRISPR systems provide programmable nucleases capable of targeted, markerless modifications, pathway construction, and genetic circuit implementation at large scale. Novel toolkits such as YaliCraft for non-conventional hosts, and the development of modular, high-throughput engineering platforms, have streamlined the insertion, deletion, or regulation of genes in both model and emerging organisms (Yuzbashev *et al.,* 2023).

Beyond genome editing, CRISPR technologies enable dynamic gene regulation (CRISPRi and CRISPRa), base editing without double-stranded breaks, and epigenetic control, all of which facilitate rational strain optimization and investigation of complex metabolic systems. The convergence of these molecular technologies with computational tools, AI-driven design, and high-throughput phenotyping accelerates the transition from concept to functional bioprocess. The breadth of CRISPR-enabled engineering extends the microbial toolbox to previously recalcitrant hosts, expanding the repertoire of bio-manufacturable products and enabling unique metabolic traits to be exploited efficiently (Cetin *et al.,* 2025).

Biomanufacturing holds immense potential for sustainable, scalable production of biopharmaceuticals, biofuels, chemicals, and more. However, several critical gaps hinder its broader adoption and economic viability. Despite rapid progress in genome editing, synthetic biology, and automation, accurately engineering microbial strains for high performance remains a major challenge. Biological systems are inherently complex and unpredictable, which limits the modularity and transferability of engineered traits across different chassis organisms. High-throughput screening has accelerated strain discovery, but integration of these tools into industrial workflows is still limited, creating a gap between laboratory innovation and real-world application. Furthermore, laboratory-scale processes frequently fail to translate to industrial settings due to heterogeneous mixing, nutrient gradients, and unexpected stress responses in larger bioreactors. Tools such as scale-down simulators and lifeline tracking can help identify more robust strains, but the lack of standardized workflows and insufficient collaboration between academia and industry continue to exacerbate the strain engineering to scale-up gap (Takors, 2025).

Establishing biomanufacturing facilities demands substantial infrastructure investment. Biofoundries, while offering multi-product versatility and potential cost efficiencies, require capital investments of $ 300-400 m and typically take 3 to 5 years for planning and construction (Bobier *et al.,* 2024). Single-use technologies, which enable modular and rapid facility deployment, can lower capital expenditure (CAPEX), but also come with trade-offs such as scalability limits and long lead times for consumables. Moreover, operational expenditure (OPEX) remains significant due to high-cost single-use materials, energy consumption, and maintenance needs, with downstream processing alone contributing to over 50% of total manufacturing costs (Takors, 2025). Though transitioning toward continuous bioprocessing offers opportunities to reduce OPEX and improve efficiency, broad adoption of this model remains a considerable challenge (Drobnjakovic *et al.,* 2023). In the Indian context, these challenges are more acute. India is actively pursuing self-reliance in biopharmaceutical manufacturing but continues to rely heavily on imported bioprocessing systems and consumables, especially for single-use technologies. This creates vulnerability in supply chains and inflates both CAPEX and OPEX for startups and firms scaling up.

The pace of biomanufacturing innovation has outstripped regulatory frameworks, making compliance and product approval difficult. Agencies like the FDA and EMA face challenges in updating standards for gene editing, synthetic biology, and continuous processes, while fragmented regulations across regions further delay harmonization (Rikihisa, 2024). The adoption of process analytical technologies (PAT), real-time monitoring, and automation has created vast datasets, but ensuring data integrity, GMP compliance, and cross-platform harmonization remains a barrier to large scale implementation. In addition, a shortage of professionals with integrated skills in biology, engineering, automation, data science, and regulation continues to hinder innovation and deployment. Addressing this talent gap is essential to unlock the full potential of biomanufacturing.

Furthermore, skills and workforce are another challenge. Biomanufacturing requires multidisciplinary expertise spanning biology, chemical engineering, automation, data analytics, and regulatory affairs. However, the availability of professionals with this integrated knowledge base remains limited. This is compounded by the gap between academic research and industrial needs, where academic outputs are often not aligned with process scalability or regulatory requirements. Strengthening interdisciplinary collaboration between scientists, engineers, data scientists, and regulators as well as fostering academia industry partnerships will be essential to accelerate innovation and deployment.

As a cornerstone of the bioeconomy, biomanufacturing plays a critical role in producing medicines, fuels, materials, and chemicals in a more sustainable and scalable way. With its ability to reduce reliance on fossil resources, lower environmental impact, and enable precision production of high-value products, the field is now entering a new era, driven by the fusion of digital intelligence, sustainable biological resources, and globally connected infrastructure (Wohlgemuth, 2025). One of the most exciting opportunities lies in AI-driven strain design. By combining machine learning with digital twins, researchers can now predict microbial behaviour and design production strains with much greater accuracy. This shift reduces the reliance on trial and error approaches and speeds up the journey from lab discovery to large-scale industrial application (Helleckes *et al.,* 2023).

At the same time, marine bioresources are emerging as a sustainable alternative to traditional feedstocks. From protein-rich algae and complex polysaccharides to high-value marine collagen, these resources expand the range of inputs available for biomanufacturing while supporting circular bioeconomy principles and reducing dependence on fossil or crop-based raw materials.

Equally transformative are biofoundries for rapid prototyping. These highly automated, robotics driven facilities are changing how strains and processes are developed. By enabling faster design build test learn cycles, biofoundries shorten development timelines from years to months and create scalable solutions ready for industry (Watkins *et al.,* 2023). Importantly, when linked as collaborative networks, biofoundries can democratize access to advanced capabilities particularly for countries like India that are building biomanufacturing capacity.

Taken together, advances in AI-guided strain engineering, sustainable feedstocks from the ocean, and globally distributed biofoundries point toward a future where biomanufacturing is not only faster and more efficient, but also greener and more inclusive on a global scale.

Conclusions

Biomanufacturing is emerging as a cornerstone of the global bioeconomy, providing greener, faster, and more inclusive production routes for sustainable materials. While universal challenges persist-ranging from strain engineering to regulatory alignment-the Indian scenario presents unique opportunities. With strong governmental initiatives such as "Make in India" and the BioE3 policy, India is actively positioning itself to reduce dependency on imported technologies and build resilient, indigenous capacity in biomanufacturing. Leveraging its biodiversity, skilled scientific workforce, and growing innovation ecosystem, India is well placed to lead in biotechnology-driven areas such as continuous processing and distributed biofoundries. Future success will depend on strengthening academia industry partnerships, taking forward laboratory-based discoveries to real time applications, accelerating technology transfer, and embedding sustainability into process design. By promoting the collaborative biofoundry networks, India can address domestic needs while also positioning itself as a global leader in sustainable and competitive biomanufacturing.

Competing Interests

The authors declare no competing interests.

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