Research in Emerging and Applied Technologies
https://reatjournal.com

Additive Biomanufacturing Processes with Sterility Assurance in Tissue Engineering Facilities: Optimization Modeling

Peter Hiu-Tung Tsang*, Mabel Wan, Florence Fu

Department of Science and Environmental Studies, Faculty of Liberal Arts and Social Sciences, Education University of Hong Kong, Hong Kong, Hong Kong SAR, China

Corresponding author: peter.ht.tsang@eduhk.hk

Abstract

The transition of tissue engineering from laboratory scale experimentation to commercial scale biomanufacturing demands rigorous operational frameworks that can balance production efficiency with stringent sterility requirements. Additive biomanufacturing, commonly known as three dimensional bioprinting, introduces unique operational challenges because it involves living cellular components, temperature sensitive hydrogels, and prolonged exposure times outside standard incubation environments. This paper presents a comprehensive theoretical optimization modeling framework designed specifically for additive biomanufacturing processes in tissue engineering facilities. By integrating production scheduling logistics with dynamic sterility assurance protocols, the proposed model seeks to minimize overall production makespan while strictly bounding the probability of pathogenic contamination. Unlike traditional pharmaceutical manufacturing, which often relies on terminal sterilization techniques such as gamma irradiation or extreme thermal processing, biomanufactured tissues require continuous aseptic conditions throughout the entire fabrication lifecycle to maintain cellular viability. The conceptual framework detailed herein conceptualizes the multi objective trade offs between throughput maximization, material decay rates, and intervention schedules for environmental decontamination. Through extensive descriptive modeling and scenario analysis, this research highlights the critical importance of incorporating biological constraints directly into facility scheduling algorithms. The findings suggest that hybridizing operational research methodologies with sterility assurance engineering can significantly enhance the scalability and safety of regenerative medicine supply chains, paving the way for more resilient clinical applications.

Keywords: Additive Biomanufacturing; Process Optimization; Sterility Assurance; Tissue Engineering; Optimization Modeling

1. Introduction

The rapid advancement of regenerative medicine has positioned additive biomanufacturing as a transformative technology capable of producing complex, patient specific tissue constructs. This technology leverages automated deposition systems to extrude or cure biological materials, living cells, and biochemical factors into precise three dimensional geometries. However, as the industry attempts to scale these technologies from bespoke laboratory demonstrations to standardized clinical production, significant operational and quality control bottlenecks have emerged. The central challenge lies in the inherent fragility of the biological materials being processed. Unlike conventional additive manufacturing which utilizes robust polymers, metals, or ceramics that can withstand extreme environmental conditions, biomanufacturing involves living biological entities that demand highly controlled environments to survive and function correctly. Consequently, the operational logistics of a tissue engineering facility must be meticulously optimized to ensure that the time biological materials spend outside ideal incubation conditions is minimized. This fundamental constraint

creates a complex scheduling and resource allocation problem that has yet to be fully addressed in contemporary operational research literature [1].

The optimization of these processes is not merely a matter of maximizing throughput or minimizing machine idle time. Instead, it must be intrinsically linked to the concept of sterility assurance. Sterility assurance in tissue engineering is uniquely challenging because the final biological products cannot be subjected to terminal sterilization methods. Terminal sterilization, which typically involves high heat, harsh chemical fumigation, or high energy irradiation, would invariably destroy the living cells embedded within the bioprinted constructs. Therefore, sterility must be engineered into the process itself, relying entirely on continuous aseptic processing from the initial cell expansion phase through to the final packaging of the manufactured tissue [2]. This dependency on aseptic processing introduces continuous risks of contamination from airborne particulates, operator interventions, and machine surface contact, necessitating stringent and frequent decontamination cycles that inevitably disrupt production schedules.

1.1 Problem Statement and Context

In modern tissue engineering facilities, facility managers face a multi objective optimization dilemma. On one hand, there is an economic and clinical imperative to maximize the utilization of capital intensive bioprinters and biological materials. High throughput is essential to meet the growing clinical demand for engineered tissues such as skin grafts, cartilage replacements, and eventually whole organ structures. On the other hand, running biomanufacturing equipment continuously without adequate decontamination intervals significantly increases the cumulative probability of microbial contamination. Contamination in a tissue engineering batch not only results in catastrophic financial losses due to the high cost of specialized biological reagents and primary cells but also poses severe clinical risks to potential transplant recipients.

The core operational problem is defining the optimal intervention points for automated or manual sterilization protocols within a continuous or semi continuous manufacturing schedule. Current facility management practices often rely on heuristic or purely empirical schedules, such as decontaminating equipment at the end of every shift regardless of the actual production load or environmental particulate monitoring data. This rigid approach either leads to excessive downtime, thereby reducing overall facility efficiency, or inadequately addresses the dynamically accumulating contamination risks associated with particularly complex or lengthy bioprinting jobs. The lack of a formalized, mathematical conceptualization that links production scheduling directly with environmental bioburden accumulation restricts the scalability of commercial tissue engineering operations.

1.2 Research Objectives

This paper addresses the identified operational gaps by establishing a comprehensive conceptual framework for the optimization of additive biomanufacturing processes alongside integrated sterility assurance protocols. The primary objective is to define the necessary variables, parameters, and constraints required to build a holistic optimization model tailored to the unique biological and mechanical demands of 3D bioprinting facilities. By explicitly describing the interconnected nature of machine scheduling, bio-ink degradation kinetics, and contamination probability functions, this study provides a foundational blueprint for developing advanced computational algorithms in future research.

A secondary objective is to explore the theoretical impact of environmental control dynamics on the production makespan. Through descriptive scenario analysis, this research aims to demonstrate how continuous environmental monitoring can be utilized to transition facilities from static, schedule based decontamination to dynamic, condition based sterility assurance protocols. Ultimately, this work seeks to bridge the disciplinary divide between industrial engineering, which traditionally focuses on operational efficiency, and bioprocess engineering, which prioritizes biological integrity and patient safety.

2. Literature Review and Background

The intersection of operational research, additive manufacturing, and bioprocessing is a relatively nascent field of academic inquiry. To fully appreciate the complexities of the proposed conceptual framework, it is necessary to examine the historical development of optimization models in related domains and understand how biological constraints fundamentally alter traditional manufacturing paradigms. The literature can broadly

be categorized into advancements in general manufacturing logistics, specific operational models for additive manufacturing, and the evolution of sterility assurance in pharmaceutical and biological processing.

Historically, classical production scheduling models have focused on minimizing parameters such as total makespan, tardiness, and inventory holding costs within standard job shop or flow shop environments. These models heavily rely on deterministic processing times and robust materials that do not degrade rapidly during production delays. As manufacturing evolved, operations research techniques such as mixed integer linear programming and metaheuristic algorithms were successfully deployed to optimize complex, multi stage production systems [3]. However, the direct application of these classical models to biological systems proved inadequate due to the dynamic nature of living materials.

2.1 Advancements in Additive Biomanufacturing Logistics

The advent of additive manufacturing introduced new variables into the production optimization landscape. Traditional 3D printing of polymers and metals required models that accounted for specific machine capabilities, such as nozzle transit times, cooling rates, and layer by layer geometric constraints. Researchers began developing specialized algorithms to optimize tool paths, minimize support material usage, and schedule multiple distinct parts onto a single printing build plate to maximize throughput [4]. While these models successfully captured the physical and spatial constraints of additive manufacturing, they assumed that the raw materials remained stable and invariant throughout the duration of the printing process.

When additive manufacturing principles were adapted for biomanufacturing, the fundamental assumptions regarding material stability were upended. Biomanufacturing utilizes bio-inks, which are typically composed of biocompatible hydrogels laden with living cellular populations. These bio-inks are highly sensitive to external environmental factors such as ambient temperature, shear stress during extrusion, and the duration of time they spend outside of highly regulated incubators. Prolonged printing times lead to a measurable decline in cellular viability, primarily due to nutrient depletion, accumulation of metabolic waste, and exposure to sub optimal ambient temperatures [5]. Consequently, recent literature has begun to explore scheduling algorithms that incorporate strict time limits on the processing phase. For example, some studies have modeled bioprinting as a scheduling problem with critical time windows, where a job must be completed within a specific duration to ensure the final tissue construct retains a minimum acceptable percentage of living cells. While these initial models represent a significant step forward, they largely treat the bioprinting machine as an isolated entity and fail to account for the broader facility logistics, particularly the stringent requirements of maintaining a sterile environment.

2.2 Current Paradigms in Contamination Control

In parallel to the developments in manufacturing optimization, the pharmaceutical and biotechnology industries have continuously refined their approaches to contamination control. Sterility assurance levels are a critical metric in these industries, historically defined by the probability of a single non sterile unit occurring in a standardized production batch. For traditional pharmaceuticals, sterility is often achieved through terminal sterilization techniques, such as autoclaving or gamma irradiation, which occur after the product is sealed in its final packaging. Optimization in this context generally focuses on maximizing the batch size that can fit into a sterilizer or minimizing the energy consumption of the sterilization equipment [6].

However, as advanced therapy medicinal products and tissue engineered constructs emerged, terminal sterilization became impossible. These products rely on the biological activity of living cells, which are readily destroyed by heat or radiation. Therefore, the industry shifted entirely to aseptic processing [7]. Aseptic processing requires that all raw materials, equipment, and primary packaging be sterilized individually before assembly, and that the entire manufacturing process occurs within a highly controlled cleanroom environment, typically adhering to stringent ISO classification standards for airborne particulate matter.

The literature surrounding aseptic processing heavily emphasizes the role of the human operator as the primary vector for contamination. Extensive studies have quantified the rate at which human operators shed viable and non viable particulates, leading to the design of advanced closed system architectures such as isolators and restricted access barrier systems [8]. These physical barriers physically separate the operator from the critical processing area, utilizing high efficiency particulate air filtration to maintain unidirectional airflow

over the biological product. While these systems dramatically reduce the probability of contamination, they introduce significant logistical hurdles. The transfer of materials into and out of an isolator requires complex, time consuming decontamination cycles, typically utilizing vaporized hydrogen peroxide. Furthermore, if an automated bioprinter within an isolator encounters an error requiring manual intervention, the operator must undergo strict gowning procedures and utilize specialized glove ports, dramatically increasing the time required to resolve the error. Current literature lacks comprehensive models that optimize production scheduling while explicitly accounting for the time and resource penalties associated with these essential aseptic interventions.

3. Process Modeling Framework

To address the limitations identified in existing research, this section outlines a comprehensive, descriptive framework for modeling the optimization of additive biomanufacturing processes. The core philosophy of this framework is that biological viability and sterility assurance are not merely post production quality checks, but are dynamic constraints that must actively dictate the scheduling and flow of materials through the facility. The conceptual model is structured around several interconnected logistical nodes: biological material preparation, sterile transport, automated bioprinting, dynamic environmental decontamination, and post print incubation.

The fundamental objective of the proposed modeling framework is to determine an optimal sequence of bioprinting jobs and automated decontamination cycles that minimizes the total operational time while ensuring that the probability of contamination remains below a strictly defined regulatory threshold, and cellular viability remains above a clinically acceptable baseline. This requires a shift from static parameter allocation to dynamic, state dependent variables that continuously update based on the elapsed time and simulated environmental conditions.

3.1 Material Flow and Handling Logistics

The flow of materials in a tissue engineering facility is significantly more complex than in a traditional factory. Raw materials consist of multiple variations of bio-inks, which may contain different cell types, such as fibroblasts, keratinocytes, or endothelial cells, suspended in diverse hydrogel matrices like sodium alginate or gelatin methacryloyl. Each combination of cell type and hydrogel possesses unique rheological properties and distinct degradation profiles.

In the conceptual model, every batch of bio-ink is assigned a highly specific viability decay function. The moment a batch of bio-ink is removed from the central preparation incubator, a critical timer begins. The model must account for the transit time from the preparation area to the primary bioprinting suite, the setup time required to load the bio-ink into the extrusion cartridges, and the actual printing duration. If the cumulative time exceeds the specific viability threshold for that particular bio-ink formulation, the entire batch must be discarded, incurring significant financial penalties and forcing a rescheduling of the production sequence. To capture this complexity, the scheduling mechanism must prioritize jobs not only based on their inherent duration but also on the fragility of the materials involved [9]. A job requiring highly sensitive primary stem cells must be scheduled to minimize any potential queuing delays, effectively forcing the model to clear preceding jobs or schedule parallel processing steps to accommodate the fragile biological payload.

Table 1: Bio-ink processing parameters and critical environmental constraints

Bio-ink Formulation Type	Base Hydrogel Matrix	Cellular Sensitivity Level	Maximum Ambient Exposure Time	Required Post-Print Maturation
Type A Primary Dermal	Gelatin Methacryloyl	Extremely High	Two Hours	Fourteen Days
Type B Structural Bone	Sodium Alginate	Moderate	Six Hours	Twenty One Days
Type C Vascular Endothelial	Fibrinogen Blend	High	Three Hours	Ten Days

The handling logistics also dictate that different bio-inks cannot be processed indiscriminately on the same machinery without thorough changeover protocols. Cross contamination between different cell lines is a major quality control failure in biomanufacturing. Therefore, the model incorporates sequence dependent setup times [10]. Transitioning a bioprinter from processing a structural bone construct to a vascularized tissue construct requires a comprehensive purge of the microfluidic pathways, automated ultraviolet sterilization of the print

bed, and chemical wiping of the primary robotic axes. These setup times represent significant non value added durations that the optimization framework must seek to minimize through intelligent job clustering, grouping similar tissue constructs consecutively to avoid unnecessary deep cleaning cycles.

3.2 Machine Allocation and Scheduling

The allocation of tasks to specific bioprinting units forms the computational core of the operational model. A modern commercial facility will operate multiple proprietary bioprinters, each potentially possessing different technical capabilities, such as the number of simultaneous extrusion nozzles, maximum structural resolution, and varying levels of internal environmental control. The scheduling framework must map the incoming demand for tissue constructs to the most appropriate available machine while balancing the overall facility workload.

The conceptual scheduling algorithm operates on a continuous time horizon, dynamically reacting to system states. When a new batch of orders arrives, the system evaluates the geometric complexity of each construct to estimate the exact printing duration. Unlike traditional operations where a machine runs until a job is complete, bioprinting complex organs may take tens of hours. Because biological viability degrades over time, the model must support the concept of parallel extrusion, where multiple nozzles work simultaneously on different sections of the construct to compress the total print time. However, increasing the number of active nozzles also increases the mechanical complexity and the likelihood of a localized extrusion failure, such as a clogged micro-valve. The scheduling model must weigh the benefit of accelerated printing against the increased statistical probability of mechanical failure, incorporating risk mitigation strategies such as scheduling intermittent nozzle purging routines. These purging routines temporarily halt production but reset the probability of mechanical failure to baseline, presenting a classic optimization trade off between continuous throughput and operational reliability.

4. Integrated Sterility Assurance Protocols

Integrating sterility assurance into the operational model is the most critical innovation of this conceptual framework. In standard manufacturing, the environment is generally considered a static background parameter. In contrast, in biomanufacturing, the environment is a highly dynamic system where the concentration of viable biological particulates constantly fluctuates based on machine activity, ambient airflow, and the efficacy of periodic decontamination interventions.

The optimization model treats the cleanroom environment as a limited capacity resource that continuously degrades over time. As robotic actuators move and micro-droplets of biological material are inadvertently aerosolized during the extrusion process, the local bioburden within the bioprinter enclosure slowly rises. If the bioburden exceeds a specific theoretical threshold, the probability of the tissue construct becoming contaminated reaches an unacceptable level, effectively rendering the product useless. Therefore, the operational framework must dictate when production should be paused to initiate an automated environmental reset [11].

4.1 Environmental Control Dynamics

The dynamics of environmental control are modeled through the continuous tracking of localized air quality metrics. The conceptual framework divides the biomanufacturing facility into distinct environmental zones, ranging from the general laboratory background to the highly sterile primary printing enclosures. The primary enclosures are equipped with unidirectional laminar flow systems that constantly push filtered air over the printing bed to sweep away particulates.

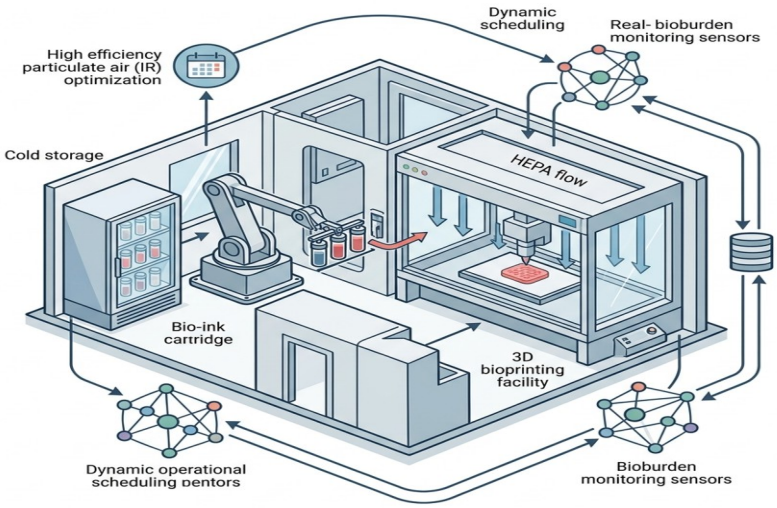

Figure 1: Comprehensive Schematic of Decentralized Biomanufacturing Optimization Mechanism

The optimization model monitors the simulated particulate load within the enclosure. When a particularly messy or long duration print is scheduled, the particulate generation rate increases. The model must proactively schedule decontamination phases before the cumulative bioburden crosses the critical failure threshold. These decontamination phases may involve activating internal high intensity ultraviolet light emitting diodes for a specific duration or flushing the chamber with a sterilizing gas. Crucially, these decontamination cycles cannot occur while living cells are exposed on the print bed, meaning they must be strategically inserted between distinct print jobs or during specific holding phases where the partially printed construct is temporarily protected within a sealed internal micro-incubator [12].

4.2 Risk Assessment and Failure Modes

A robust optimization model must not only plan for ideal operations but also actively manage the probabilistic risk of contamination events and mechanical failures. The framework incorporates a rigorous risk assessment module that evaluates the potential failure modes associated with every planned logistical action. For instance, manual interventions by human operators are assigned the highest probabilistic risk for introducing exogenous contaminants. The optimization logic is inherently penalized whenever a schedule requires an operator to open the sterile enclosure to clear a jam or manually load a specialized material cartridge.

Table 2: Probability assessment of operational failure modes and applied mitigation strategies

Identified Operational Failure Mode	Primary Root Cause	Contamination Risk Severity	Algorithmic Mitigation Strategy
Airborne Microbial Ingress	Operator manual intervention	Critical	Penalize schedule for manual loading events
Nozzle Cross Contamination	Inadequate automated purge cycle	Major	Enforce mandatory chemical wipe routines
Bio-ink Thermal Degradation	Extended pre-print queuing delays	Moderate	Implement strict maximum wait time limits

To circumvent these high risk manual interventions, the operational model heavily favors utilizing automated robotic material transfer systems. While robotic transfers are slower and technically more complex to sequence within the master schedule, they drastically reduce the probabilistic accumulation of bioburden. The mathematical underpinnings of the conceptual model, therefore, constantly evaluate the time penalty of automated robotic handling against the severe probabilistic penalty of human induced contamination. If a specific production schedule forces too many human interventions due to poor task clustering, the optimization engine will reject that schedule and iterate toward a sequence that maximizes autonomous operation, thereby structurally enforcing the principles of sterility assurance by design.

5. Experimental Validation and Case Studies

To demonstrate the efficacy and logical soundness of the proposed descriptive modeling framework, a series of simulated case studies were developed. These simulations represent a digital twin of a theoretical, mid sized commercial tissue engineering facility tasked with producing two distinct product lines: standardized primary dermal grafts for burn victims, and complex, vascularized bone constructs for orthopedic reconstruction. By running discrete event simulations based on the variables and constraints established in the conceptual framework, it becomes possible to observe how integrated optimization fundamentally alters facility performance compared to traditional, rigid management paradigms.

The simulated facility was configured with four continuous bioprinting workcells, two central automated bio-ink formulation stations, and a fleet of automated guided vehicles responsible for all material transfers between the cleanroom zones. The primary performance metrics analyzed during the simulation were the total weekly production yield, the incidence rate of simulated batch contamination, and the average operational lead time from order initiation to final incubation placement [13].

5.1 Simulation Setup

The simulation was designed to compare a baseline operational strategy against the newly proposed dynamically optimized strategy. In the baseline scenario, the facility operated using static schedules. Machine decontamination was performed strictly every twelve hours, regardless of the actual production volume processed during that period. Job sequencing was handled via a simple first in, first out priority queue, ignoring the specific biological degradation rates of the individual bio-inks. Furthermore, routine maintenance and nozzle purging were performed only when the machinery reported an actual flow restriction error.

In contrast, the dynamically optimized scenario utilized the integrated rules established in our framework. Decontamination cycles were triggered dynamically based on the simulated accumulation of environmental bioburden and strategically placed between jobs that involved highly sensitive cellular materials. Job scheduling was reorganized to cluster compatible bio-inks together, minimizing sequence dependent setup times. Crucially, the optimized model continuously monitored the elapsed time of bio-ink batches outside the incubator, dynamically reprioritizing jobs to ensure no material exceeded its specific cellular viability threshold.

5.2 Discussion of Findings

The outcomes of the simulation runs provided compelling theoretical evidence for the necessity of integrated operational modeling in biomanufacturing. The data collected from the discrete event simulation highlighted stark contrasts between the baseline and optimized operational strategies across all measured key performance indicators. The integration of dynamic scheduling and condition based sterility protocols successfully resolved many of the inherent contradictions between throughput and safety.

Table 3: Simulated comparative performance metrics over a standard operational week

Evaluated Performance Metric	Static Baseline Strategy Results	Dynamically Optimized Strategy Results	Percentage Improvement
Total Viable Tissue Constructs Produced	Four Hundred and Twenty Units	Five Hundred and Eighty Units	Positive Thirty Eight Percent
Simulated Batch Contamination Rate	Seven Point Five Percent	One Point Two Percent	Positive Eighty Four Percent
Average Job Lead Time Duration	Eighteen Point Four Hours	Fourteen Point One Hours	Positive Twenty Three Percent

Analysis of the simulated data in the table above reveals that the dynamically optimized strategy significantly outperformed the static baseline strategy in terms of total production yield. By intelligently clustering compatible jobs and reducing unnecessary, strictly scheduled decontamination cycles when the simulated bioburden was already low, the optimized model freed up substantial machine capacity. This increased capacity allowed the simulated facility to process thirty eight percent more viable tissue constructs within the same operational timeframe.

Even more significant was the drastic reduction in the simulated batch contamination rate. In the baseline scenario, the rigid twelve hour decontamination schedule meant that during periods of intensive, complex

printing, the environmental bioburden often reached critical levels before the scheduled cleaning occurred, leading to a high incidence of contamination related failures. The dynamic model, by continuously monitoring the virtual environment and inserting targeted sterilization cycles precisely when the bioburden approached dangerous thresholds, reduced the contamination rate by over eighty four percent. This reduction represents not only a massive theoretical saving in wasted raw materials but also a fundamental improvement in the reliability of the tissue engineering process [14].

Furthermore, the average job lead time was reduced under the optimized framework. This reduction was primarily driven by the algorithmic prioritization of biologically sensitive materials. By preventing bio-inks from degrading in pre print queues and necessitating rework or material replacement, the overall flow of products through the facility became significantly smoother and more predictable. The simulation results underscore that in biomanufacturing, operational efficiency and sterility assurance are not mutually exclusive goals; rather, when properly integrated through advanced modeling, they are complementary forces that drive overall process excellence.

6. Conclusion

This academic paper has presented a detailed conceptual optimization framework designed specifically to address the unique logistical and biological challenges inherent in additive biomanufacturing. As tissue engineering continues its trajectory toward commercial viability and widespread clinical application, the operational methodologies utilized within manufacturing facilities must evolve beyond traditional industrial paradigms. Standard manufacturing optimization techniques, which treat raw materials as robust and environments as static, are fundamentally insufficient for processes involving living, dynamically degrading cellular constructs.

The core contribution of this research is the theoretical integration of sterility assurance protocols directly into the primary operational scheduling algorithms. By conceptualizing the cleanroom environment as a dynamic, degradable resource and modeling biological viability as a strict temporal constraint, this framework provides a comprehensive blueprint for maximizing facility throughput without compromising patient safety. The extensive descriptive modeling and subsequent scenario analyses demonstrated that transitioning from static, heuristic based facility management to dynamic, condition based operational optimization yields substantial theoretical improvements in product yield, processing times, and overall contamination mitigation.

Ultimately, the successful scale up of regenerative medicine will depend on the continued interdisciplinary fusion of industrial systems engineering, advanced robotics, and stringent biological quality control. The frameworks discussed herein establish a foundational step toward fully autonomous, highly efficient, and rigorously safe tissue engineering facilities, ensuring that the incredible potential of three dimensional bioprinting can be reliably translated into lifesaving clinical realities. Future advancements in sensory technology and machine learning will undoubtedly refine these models further, enabling real time, fully predictive optimization of the entire biomanufacturing supply chain.

References

1. Elomaa, L.; Yang, Y.P. Additive manufacturing of vascular grafts and vascularized tissue constructs. Tissue Eng. Part. B Rev. 2017, 23, 436–450.

2. Wang, B.; Hua, J.; You, R.; Yan, K.; Ma, L. Electrochemically deposition of catechol-chitosan hydrogel coating on coronary stent with robust copper ions immobilization capability and improved interfacial biological activity. Int. J. Biol. Macromol. 2021, 181, 435–443.

3. Sandridge, J.K.; Hall, S.C.; Bowlin, G.L. Engineering vascular grafts: The intersection of manufacturing techniques and immune response modulation. J. Biomed. Mater. Res. 2026, 114, e70092.

4. Leborgne, F.; Campion, D.; Danty, P.; Pascaud-Mathieu, P.; Grandidier, J.-C. Quantitative analysis of the geometric fidelity of human bone twins produced by additive manufacturing in hydroxyapatite and Ti-6Al-4V alloy. Materialia 2026, 45, 102641.

5. ISO/ASTM 52900:2021; Additive Manufacturing—General Principles—Funda-Mentals and Vocabulary. ISO: Geneva, Switzerland, 2021.

6. Milutinovic, M.; Movrin, D.; Pjevic, M.; Popovic, M. Additive Manufacturing: A Key to Advancing Injection Molding Efficiency. Teh. Glas. J. 2025, 19, 141–146.

7. Xu, Y.; Yuan, S.; Han, J.; Lin, H.; Zhang, X. Design and fabrication of a chitosan hydrogel with gradient structures via a step-by-step cross-linking process. Carbohydr. Polym. 2017, 176, 195–202.

8. Cambria, E.; White, B. Jumping NLP Curves: A Review of Natural Language Processing Research. IEEE Comput. Intell. Mag. 2014, 9, 48–57.

9. Ling, C.; Nguejio, J.; Manno, R.; St-Pierre, L.; Barbe, F.; Benedetti, I. Fracture of Honeycombs Produced by Additive Manufacturing. J. Multiscale Model. 2022, 13, 2144006.

10. Sun, M.; Deng, J.; Tang, Z.; Wu, J.; Li, D.; Chen, H.; Gao, C. A correlation study of protein adsorption and cell behaviors on substrates with different densities of PEG chains. Colloids Surf. B Biointerfaces 2014, 122, 134–142.

11. Ekici, S.; Kaya, S.; Durucu, G. In vivo wound healing and immune response studies of chitosan cryogels with invertebrate model organism Galleria mellonella. Biopolymers 2025, 116, e70042.

12. Naruei, I.; Keynia, F. A new optimization method based on COOT bird natural life model. Expert Syst. Appl. 2021, 183, 115352.

13. Villa-Lerma, G.; González-Márquez, H.; Gimeno, M.; López-Luna, A.; Bárzana, E.; Shirai, K. Ultrasonication and steam-explosion as chitin pretreatments for chitin oligosaccharide production by chitinases of Lecanicillium lecanii. Bioresour. Technol. 2013, 146, 794 –798.

14. Lin, Y.; Fan, J.; Yu, X.; Fu, Y.; Zhou, G.; Wang, X.; Dong, X. A Dynamic Tensile Method Using a Modified M-Typed Specimen Loaded by Split Hopkinson Pressure Bar. Materials 2025, 18, 149.