Recent Progress in AI-Driven 3D (Bio)Printing for Tissue Engineering

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1. Introduction

In recent years, regenerative medicine has experienced a major paradigm shift, driven by advances in additive manufacturing (AM) techniques as well as the accelerated progress of artificial intelligence (AI) technologies. Such breakthroughs have generated increased scientific interest toward integrating AI methods into all phases of the three-dimensional (3D) printing and bioprinting processes for tissue engineering. In this context, the current study provides an overview on the use of AI in different stages of tissue additive manufacturing in an effort to identify both the opportunities and challenges of this emerging field.

2. Applications of AI in the bioprinting processes

In tissue engineering, 3D bioprinting has grown into a very promising technology that allows the controlled deposition of bioinks to create intricate biological structures. This technology allows the fabrication of constructs with a microarchitecture that can resemble the complex microstructure of natural tissues through direct integration of cells into the manufacturing process. However, there are several drawbacks to the bioprinting process, including the difficulty of maintaining cell viability, the variability of bioink properties, the complexity of controlling process parameters, and the need to achieve high structural fidelity. Furthermore, employing conventional trial-and-error techniques makes it difficult to simultaneously optimize the many parameters involved in the process. These difficulties have led to a rise in interest in the application of AI-based techniques that can handle massive datasets, identify the complex relationships between parameters and outcomes, and efficiently optimize the manufacturing system [1-2]. The 3D printing process is generally structured in three main stages: pre-printing, printing, and post-printing. The pre-printing stage includes the design of the digital printing model and the selection of the bioink, including biomaterials, cell cultures and biomolecules. The printing stage consists of actual layer-by-layer deposition of the bioink according to the given digital model, using various bioprinting methods. During this phase, printing parameters must be carefully controlled to ensure structural stability and cellular viability. The final stage, post-printing, involves the stabilization of the biological scaffold, including material cross-linking, culturing in bioreactors, cell proliferation and differentiation, and assessment of the functionality of the final tissue scaffold [3-4]. Various AI and ML models have been used to streamline each stage of this workflow. The majority of research has focused on the pre-printing stage, specifically on the use of large databases to optimize the selection of printable formulations. Achieving a bioink that enables high cell viability without compromising the scaffold's strength and long-term stability represents a critical milestone in 3D bioprinting research. In terms of the printing process itself, AI-based methods have relied on the use of sensors and cameras to provide real-time feedback and build a system for automatic adjustment of the parameters used based on the input results. Lastly, in the post-printing stage, AI systems enable high-throughput rapid evaluation of a large set of outcomes, allowing for much faster and more efficient characterization the results, and even enabling real-time optimization of the maintenance parameters for the bioprinted structures.

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