

# A Review on 3D-printed Bioreactors

Bioreactors are essential tools that not only guide and support the event of in vitro live tissues but also act as culture vessels to review the biological response of the tissues to physiologically relevant conditions. Within the context of this review, bioreactors ask devices for cellular and biochemical assays. The planning and configuration of a bioreactor should complement the wants of biological systems. For instance, bioreactors for the study of vascularization and cardiac regeneration are including the pulsatile flow to reinforce cell differentiation and maturation. Similarly, bioreactors for lung tissue models are often linked to airflow setup to imitate native lung functions. Additionally, various operational parameters associated with the pliability, design, and other characteristics of bioreactors greatly influence the biological performance of bioreactors. Within the past few years, modeling and applications of bioreactors have evolved in various fields of research. Thanks to their enormous versatility, bioreactors are employed in many industries, including biological, biomedical, pharmaceutical, food, wastewater treatment, chemical, and fermentation. This review focuses on biological applications intimately.

## Three-dimensional (3D)-printed bioreactor

Conventional bioreactors grant operators the convenience of controlling the environment and experimental manipulation of two-dimensional tissue models. However, their incompatibility with in vivo systems and their inability to reflect true cell traits and tissue morphology has necessitated 3D systems which exhibit better spatial distribution and structurally complex tissue architecture. Nevertheless, it's challenging to supply 3D bioreactors with complex geometry using conventional manufacturing methods.

Additive manufacturing (AM), also referred to as 3D-printing technology, has shown enormous potential within the fabrication of complex, low-cost, and custom-designed structures constructed by depositing a layer on top of earlier printed layers. Over the past three decades, several 3D-printing strategies are established with attention on the fabrication of bioreactors of varied shapes and sizes. Through 3D-printing, specialized bioreactors are often engineered with high performance in terms of experimental throughput, liquid controllability, and stability. 3D-printing not only grants freedom to optimize new bioreactor designs but also enhances cellular functionality and suitability of bioreactor for specific applications like in vitro culturing and testing.

In view of this text, any 3D-printed culture apparatus, including chip, culture chamber, or filters that directly contact the cells, are considered as 3D-printed bioreactors. Moreover, various customized components and accessories of bioreactors like culture tube holders, test parts, chamber inserts, and sensors fabricated with various 3D-printing modalities are discussed. Several bioreactor models were designed to encourage the flow of medium for even distribution of nutrients throughout the culture vessel. The fluid flow in bioreactors might be manipulated at the micro-level by coupling bioreactors with microfluidic networks. The compartmentalized microfluidic devices with interconnected micro channels created cellular environments confined during a culture vessel that directed fluid flow through the cell culture. Additionally, these devices were shown to emulate physiological relevance

## SunaTimur\*

Department of Faculty of Science,  
Biochemistry Department, Ege University,  
Bornova-Izmir, Turkey

\*Author for correspondence:  
suna.timur@ege.edu.tr

by creating in vitro microenvironments on an equivalent scale of cells. However, devices with challenging functionalities and dimensional specifications, like channel height and ratio, are difficult to realize by conventional microfluidic techniques. Recent advancements have led to the event of 3D-microfluidics with intricate detailing, greater accuracy, and better resolution using 3D-printing techniques.

#### 3D-printed bioreactor for biological applications

3D-printing may be a rapidly evolving technology that gives a chance to fabricate complex 3D structures for biological applications. It's a crucial tool for translational research that focuses on the in vitro biology and disease models in bioreactors. The increasing accessibility to 3D-printing has spurred substantial efforts toward many creative developments of 3D-printed bioreactors for the cultivation of mammalian also as microbial cells. Various bioreactors are fabricated with 3D-printing to review the response of those cells to the littlest details of their local environments like substrate geometric arrangement, chemistry, and mechanics.

Much of our understanding of fundamental

cellular mechanisms is garnered from the aberrant interactions of cells on 2D substrates. As we move toward more-compliant microenvironment, it's vital to demystify exactly what factors are operative in 3D systems instead of simply considering a dimensionality factor at play. The increased capabilities of 3D-printers have resulted in well-architecture constructs with fine features and application-specific geometries. The key challenge here lies in achieving the geometry that gives the right degree of bio mimicry, mechanical and chemical cues needed for sufficient cell-cell signaling, cell development, and organic phenomenon. Indeed, surface parameters like porosity, roughness, and curvature are tunable consistent with experimental needs, and their effect on the collective cell behavior including adhesion, growth, alignment, proliferation, and differentiation has been demonstrated also. Ideally, the role of 3D-printing is to supply cells an appropriate environment supporting their transition into functional tissue in vitro. With 3D-printing, we are ready to fabricate bioreactors of various sizes and shapes and introduce cells into the bioreactors post-printing for in vitro testing. Overall, this text aims to hide 3D-printed bioreactors for the in vitro study of both mammalian and bacterial cell culture.