



Physics problems in bio or bioinspired additive manufacturing

Jun Yin^{1,2} · Jin Qian³ · Yong Huang⁴

Received: 30 January 2023 / Accepted: 2 February 2023 / Published online: 28 February 2023
© Zhejiang University Press 2023

Additive manufacturing, also known as three-dimensional (3D) printing, has attracted increasing attention due to the innovations in materials science and manufacturing over recent decades [1]. Recently, innovations in biocompatible materials and biology have enabled the extension of 3D printing techniques into bioadditive manufacturing, which focuses on the fabrication of 3D engineered native-like tissues/organs [2]. Currently, bioadditive manufacturing technologies can be categorized into inkjet-based bioprinting, microextrusion-based bioprinting, digital light processing (DLP) bioprinting, electric field-assisted bioprinting, and fused deposition modeling (FDM), to name a few [3, 4] (Fig. 1). Artificial tissues and organs with delicate structures, such as the heart [5] and liver [6], have been successfully fabricated using various bioadditive manufacturing techniques. Bioadditive manufacturing has also been involved in drug screening due to its high deposition accuracy [7]. However, despite continuous improvements in printing techniques and the broader choice of materials for 3D bioprinting, it remains challenging for 3D bioprinted constructs to be deemed as substitutes for native tissues and organs at the present moment due to their limited printing reliability and functionality [8].

Amongst the various factors at play in bioadditive manufacturing, biomechanics and physics play essential roles during the printing process and can provide guidance for designing experiments and predicting printing outcomes [9]. However, lots of physics underlying printing techniques remains unexplored [10, 11].

Understanding the physics problems in bioadditive manufacturing is of great significance and requires a strong background in physics and mechanics. Numerous interesting phenomena during different bioadditive manufacturing processes remain to be elucidated: for instance, droplet formation due to hydrodynamic instability and droplet impact and coalescence while being collected on the substrate during inkjet 3D bioprinting [12], the stability of the formed structures containing uncured photocrosslinkable bioink during DLP 3D bioprinting [13], and the balance among the electric force, viscous force, and off-axis bending instability to ensure printing accuracy during electric-based 3D bioprinting [14], to name a few. Although numerous studies have been proposed, those phenomena are still not well understood. In addition, the deformation of mechanically unstable constructs due to insufficient crosslinking or lack of the capability to self-support has consistently restricted the broader applications of those types of bioadditive manufacturing.

In addition to shape fidelity, cell viability is another primary concern of 3D bioprinting. It is noted that the maintenance of cell viability is essential for the functionality of bioprinted cellular constructs [15]. Cellular activity reflects the environment that cells are experiencing during and after the printing process [16, 17]. Although it has been reported that the majority of cell deaths come from shear stress in nozzle-based bioprinting, while the majority of cell deaths come from radiative stress in light-involved bioprinting [18], there are still no universal criteria for cell damage during bioadditive manufacturing. In addition, although several physical/machine learning models [19, 20] have been proposed to analyze or predict cell damage during various printing techniques, a theoretical model revealing the entire bioprinting process is still missing. Therefore, the injury

✉ Jun Yin
junyin@zju.edu.cn

Jin Qian
jqian@zju.edu.cn

Yong Huang
yongh@ufl.edu

¹ The State Key Laboratory of Fluid Power and Mechatronic Systems, School of Mechanical Engineering, Zhejiang University, Hangzhou 310028, China

² Key Laboratory of 3D Printing Process and Equipment of Zhejiang Province, School of Mechanical Engineering, Zhejiang University, Hangzhou 310028, China

³ Key Laboratory of Soft Machines and Smart Devices of Zhejiang Province, Department of Engineering Mechanics, Zhejiang University, Hangzhou 310027, China

⁴ Department of Mechanical and Aerospace Engineering, University of Florida, Gainesville, FL 32611, USA

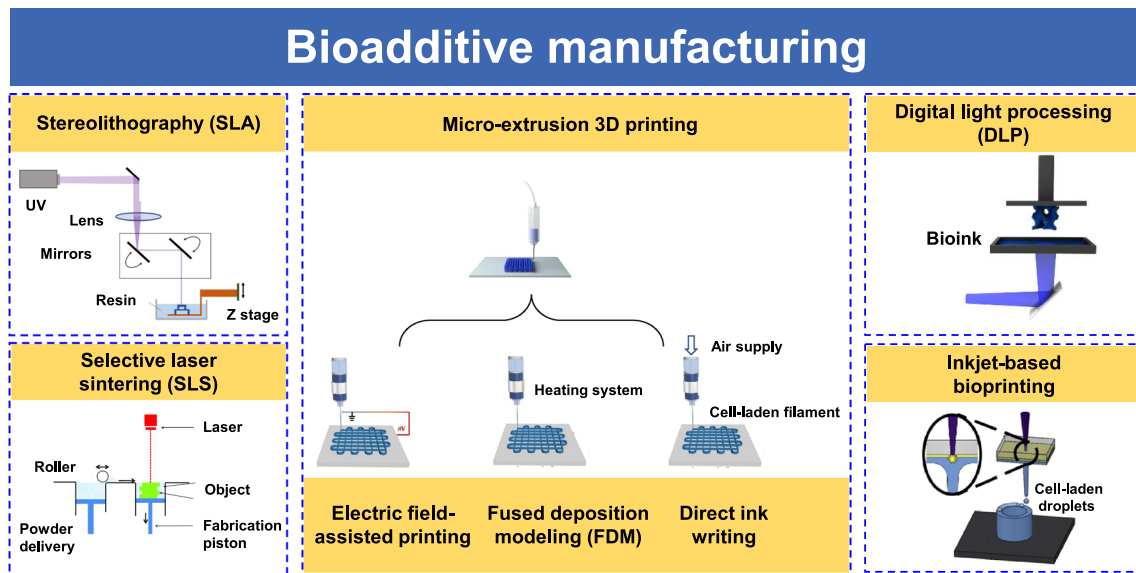


Fig. 1 Schematic diagram of bioadditive manufacturing techniques

of cells throughout the whole bioprinting process remains unknown.

Overall, for the reasons mentioned above, it is critical to understand the involving physics and mechanics underpinning various bioprinting techniques and help researchers in bioadditive manufacturing better understand the whole printing process and optimize the printing system design. Therefore, exploring the physics of bioadditive manufacturing will undoubtedly benefit future developments in bioadditive manufacturing and bridge the gap between biological structures and clinical translation [21].

To emphasize the importance of physics in bioadditive manufacturing, we have organized a themed issue on the topic of “Physics problems in bio or bioinspired additive manufacturing.” First, we prepared this editorial, mainly outlining the major physics problems in the design of bioinspired manufacturing and physical mechanisms during bioadditive manufacturing processes. In this special issue, we collected six research articles focusing on the forming mechanisms and design methods in different bio or bioinspired additive manufacturing processes. Yang et al. [22] investigated the impact of laser power and scanning speed during the laser powder bed fusion (LPBF) process on the development of surface quality, relative densification, and texture on Zn implants. By reasonably selecting the laser power and scanning speed, the thermal expansion and contraction caused by excessive energy storage and accumulation in the matrix can be avoided. Thus, this study provided a basis for selecting process parameters to optimize the comprehensive properties of LPBF-processed Zn parts for biodegradable applications. Valentin et al. [23] presented an innovative method to print

titanium-6-aluminum-4 vanadium (Ti64) ink via the direct ink writing method, followed by heat treatment processes to form a porous morphology with microsized pores. By optimizing the printing conditions and studying the cure depth, complex structures such as honeycombs have been printed benefiting from their self-supporting capability. By introducing peptide grafting and fibrin in alginate, Qiu et al. [24] developed alginate-based bioinks for high-resolution electrohydrodynamic (EHD) bioprinting. The printed filament, as thin as 30 μm , had the capability to guide cellular orientation and provide a suitable environment for cell survival (>90%) and spreading. Liu et al. [25] presented a composite hydrogel composed of chitosan/gelatin and egg white, serving as a novel bioink for extrusion-based printing. In addition, from the crosslinking mechanism perspective, tripolyphosphate (TPP) was found to maximally enhance the physical and biological properties of the scaffolds fabricated with the proposed composite hydrogel, showing great potential for future tissue engineering-related applications. Huo et al. [26] utilized a dual-temperature controlling system to improve the printing resolution of traditional one-temperature controlling FDM. Both the experimental results and the numerical analysis focused on the effects of two different temperature modes on the rheology of melted polymeric ink, which is of great importance to the FDM printing quality, and demonstrated that dual-temperature controlling FDM was superior to one-temperature controlling system on the printing resolution. Inspired by kirigami arts, Yue et al. [27] designed and fabricated two-dimensional (2D) sheets into 3D with different mechanical properties by optimizing the geometric parameters in 2D. Formed structures have shown excellent

shape memory capability and programmability, indicating their great potential to be used for smart load bearings in equipment, especially when space is limited.

References

- Murphy SV, Atala A (2014) 3D bioprinting of tissues and organs. *Nat Biotechnol* 32(8):773–785. <https://doi.org/10.1038/nbt.2958>
- Stanton M, Samitier J, Sanchez S (2015) Bioprinting of 3D hydrogels. *Lap Chip* 15(15):3111–3115. <https://doi.org/10.1039/c5lc90069g>
- Cheng L, He H, Rajput RS et al (2021) 3D printing of micro-and nanoscale bone substitutes: a review on technical and translational perspectives. *Int J Nanomed* 16:4289–4319. <https://doi.org/10.2147/IJN.S311001>
- Derakhshanfar S, Mbeleck R, Xu K et al (2018) 3D bioprinting for biomedical devices and tissue engineering: a review of recent trends and advances. *Bioact Mater* 3(2):144–156. <https://doi.org/10.1016/j.bioactmat.2017.11.008>
- Lee A, Hudson A, Shiwarski D et al (2019) 3D bioprinting of collagen to rebuild components of the human heart. *Science* 365(6452):482–487. <https://doi.org/10.1126/science.aav9051>
- Ma X, Qu X, Zhu W et al (2016) Deterministically patterned biomimetic human iPSC-derived hepatic model via rapid 3D bioprinting. *Proc Natl Acad Sci USA* 113(8):2206–2211. <https://doi.org/10.1073/pnas.1524510113>
- Mazzocchi A, Soker S, Skardal A (2019) 3D bioprinting for high-throughput screening: drug screening, disease modeling, and precision medicine applications. *Appl Phys Rev* 6(1):011302. <https://doi.org/10.1063/1.5056188>
- Murphy SV, De Coppi P, Atala A (2020) Opportunities and challenges of translational 3D bioprinting. *Nat Biomed Eng* 4(4):370–380. <https://doi.org/10.1038/s41551-019-0471-7>
- Ning L, Gil CJ, Hwang B et al (2020) Biomechanical factors in three-dimensional tissue bioprinting. *Appl Phys Rev* 7(4):041319. <https://doi.org/10.1063/5.0023206>
- Yang Q, Lv X, Gao B et al (2021) Mechanics of hydrogel-based bioprinting: from 3D to 4D. *Adv Appl Mech* 54:285–318. <https://doi.org/10.1016/bs.aams.2021.03.001>
- Shafiee A, Ghadiri E, Ramesh H et al (2019) Physics of bioprinting. *Appl Phys Rev* 6(2):021315. <https://doi.org/10.1063/1.5087206>
- Yarin AL (2006) Drop impact dynamics: splashing, spreading, receding, bouncing. *Ann Rev Fluid Mech* 38(1):159–192. <https://doi.org/10.1146/annurev.fluid.38.050304.092144>
- Li Y, Mao Q, Yin J et al (2021) Theoretical prediction and experimental validation of the digital light processing (DLP) working curve for photocurable materials. *Addit Manuf* 37:101716. <https://doi.org/10.1016/j.addma.2020.101716>
- Chortos A, Mao J, Mueller J et al (2021) Printing reconfigurable bundles of dielectric elastomer fibers. *Adv Funct Mater* 31(22):2010643. <https://doi.org/10.1002/adfm.202010643>
- Hölzl K, Lin S, Tytgat L et al (2016) Bioink properties before, during and after 3D bioprinting. *Biofabrication* 8(3):032002. <https://doi.org/10.1088/1758-5090/8/3/032002>
- Vining KH, Mooney D (2017) Mechanical forces direct stem cell behaviour in development and regeneration. *Nat Rev Mol Cell Biol* 18(12):728–742. <https://doi.org/10.1038/nrm.2017.108>
- Kechagia JZ, Ivaska J, Roca-Cusachs P (2019) Integrins as biomechanical sensors of the microenvironment. *Nat Rev Mol Cell Biol* 20(8):457–473. <https://doi.org/10.1038/s41580-019-0134-2>
- Xu HQ, Liu JC, Zhang ZY et al (2022) A review on cell damage, viability, and functionality during 3D bioprinting. *Military Med Res* 9:70. <https://doi.org/10.1186/s40779-022-00429-5>
- Xu H, Liu Q, Casillas J et al (2020) Prediction of cell viability in dynamic optical projection stereolithography-based bioprinting using machine learning. *J Intell Manuf* 33:95–105. <https://doi.org/10.1007/s10845-020-01708-5>
- Yu C, Jiang J (2020) A perspective on using machine learning in 3D bioprinting. *Int J Bioprint* 6(1):253. <https://doi.org/10.18063/ijb.v6i1.253>
- Gu Y, Forget A, Shastri VP (2022) Biobridge: an outlook on translational bioinks for 3D bioprinting. *Adv Sci* 9(3):2103469. <https://doi.org/10.1002/advs.202103469>
- Yang M, Yang L, Peng S et al (2022) Laser additive manufacturing of zinc: formation quality, texture, and cell behavior. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-022-00216-0>
- Valentin N, Hua W, Kasar AK et al (2022) Direct ink writing to fabricate porous acetabular cups from titanium alloy. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-022-00222-2>
- Qiu Z, Zhu H, Wang Y et al (2022) Functionalized alginate-based bioinks for microscale electrohydrodynamic bioprinting of living tissue constructs with improved cellular spreading and alignment. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-022-00225-z>
- Liu S, Zhang H, Ahlfeld T et al (2022) Evaluation of different crosslinking methods in altering the properties of extrusion-printed chitosan-based multi-material hydrogel composites. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-022-00194-3>
- Huo XD, Zhang B, Han QL et al (2023) Numerical simulation and printability analysis of fused deposition modeling with dual-temperature control. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-023-00239-1>
- Yue CB, Zhao W, Li FF et al (2023) Shape recovery properties and load-carrying capacity of a 4D printed thick-walled kirigami-inspired honeycomb structure. *Bio-Des Manuf* (Early Access). <https://doi.org/10.1007/s42242-022-00230-2>



Guest Editor of the Special Issue:

Prof. Jun Yin received the Ph.D. degree in mechanical engineering from Clemson University, USA in 2011, M.S. degree in solid mechanics from Chinese Academy of Sciences, China in 2007, and B.S. degree in Mechanics from Peking University, China in 2004. From 2011 to 2013, he was a post-doctoral scholar with the School of Medicine, University of California, USA. Since 2014, he has been a Professor with the School of Mechanical Engineering, Zhejiang

University. His main research interests are focused on 3D bioprinting, design and modeling of biofabrication processes, synthesis and application of biomaterials, and biomechanics. He is an associate editor of *Bio-Design* and *Manufacturing*, and he has published more than 70 journal papers, including *Matter*, *Advanced Materials*, *Additive Manufacturing*, *Biofabrication*. His research contribution covers the areas of soft robotics, tissue engineering, and regenerative medicine.

**Guest Editor of the Special Issue:**

Prof. Jin Qian received his B.E. degree from Peking University in 2000, and his M.S. degree from Institute of Mechanics, Chinese Academy of Sciences in 2003. He entered Brown University in March 2006, obtained his Sc.M. degree in Applied Mathematics in May 2009, and defended his Ph.D. dissertation (Solid Mechanics) in August 2009. He spent two years at Georgia Institute of Technology as a Postdoc Fellow. He is now a Professor of Zhejiang University, and serves as

the Deputy Dean of the School of Aeronautics and Astronautics. His research interests include the mechanics and 3D printing of soft materials, mechanics of bio-inspired materials and structures, cell mechanics, etc.

**Guest Editor of the Special Issue:**

Prof. Yong Huang is a professor of Mechanical and Aerospace Engineering, Biomedical Engineering, and Materials Science and Engineering at the University of Florida, Gainesville, Florida. His research interests are two-fold: (1) processing of biological and engineering materials for health-care/energy applications, and (2) understanding of dynamic material behavior during manufacturing and process-induced damage or defect structures. He received his

Ph.D. degree in Mechanical Engineering from the Georgia Institute of Technology in 2002 and is a Fellow of American Society of Mechanical Engineers (ASME).