PERSPECTIVE ARTICLE

A Perspective on Using Machine Learning in 3D Bioprinting

Chunling Yu[1], Jingchao Jiang[2*]

[1]Faculty of Maritime and Transportation, Ningbo University, Ningbo 315211, China

[2]Department of Mechanical Engineering, University of Auckland, Auckland 1010, New Zealand

Abstract: Recently, three-dimensional (3D) printing technologies have been widely applied in industry and our daily lives. The term 3D bioprinting has been coined to describe 3D printing at the biomedical level. Machine learning is currently becoming increasingly active and has been used to improve 3D printing processes, such as process optimization, dimensional accuracy analysis, manufacturing defect detection, and material property prediction. However, few studies have been found to use machine learning in 3D bioprinting processes. In this paper, related machine learning methods used in 3D printing are briefly reviewed and a perspective on how machine learning can also benefit 3D bioprinting is discussed. We believe that machine learning can significantly affect the future development of 3D bioprinting and hope this paper can inspire some ideas on how machine learning can be used to improve 3D bioprinting.

Keywords: 3D printing, Bioprinting, Machine learning

***Corresponding Author:** Jingchao Jiang, Department of Mechanical Engineering, University of Auckland, Auckland 1010, New Zealand; jjia547@aucklanduni.ac.nz

Received: November 24, 2019; ***Accepted:*** December 23, 2019; ***Published Online:*** January 24, 2020

Citation: Yu C, Jiang J, 2020, A perspective on using machine learning in 3D bioprinting. *Int J Bioprint*, 6(1):253. DOI: 10.18063/ijb.v6i1.253

1 Introduction

Currently, three-dimensional (3D) printing technologies have been widely applied in many fields, including aerospace, medicine, industry, and esthetic[1-3]. The process of 3D printing starts from the bottom to the top of a product in a point-by-point and layer-by-layer manner[4-8]. It is an additive process that adds materials gradually until the whole part is fabricated. **Figure 1a** shows a typical extrusion-based 3D printing process to manufacture a component. 3D bioprinting is a process that uses 3D printing-like technologies to fabricate biomedical parts that consist of biomaterials, growth factors and cells, with the aim of maximally imitating natural tissue characteristics[9-11]. The fabrication process of 3D bioprinting is similar to 3D printing that uses a layer-by-layer method to deposit materials[12-14]. The raw materials used in 3D bioprinting are bio-inks, rather than polymer, metal or ceramic in traditional 3D printing processes[15]. 3D bioprinting can create tissue-like structures that can be utilized in tissue or medical engineering fields.

Currently, there are five major bioprinting techniques available, including stereolithography-based, inkjet, extrusion-based, and laser-assisted bioprinting. The details of these techniques have been described[16]. Among them, extrusion-based bioprinting is the most common technique. **Figure 1b** shows the typical three extrusion-based bioprinting processes. The difference among them is the type of force that can be either air pressure (pneumatic dispensing), direct

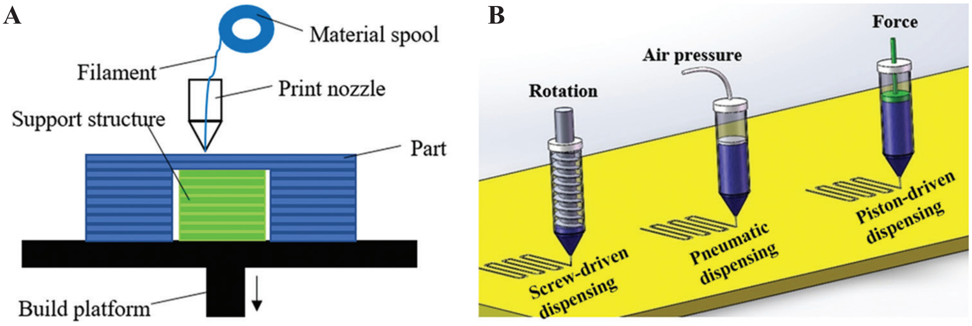

Figure 1. Typical three-dimensional printing process (a) and extrusion-based bioprinting methods (b).

force (piston-driven dispensing), or rotation (screw-driven dispensing).

Machine learning is an emerging technology that can optimize systems through smarter and effective use of products, materials, and services. In terms of 3D printing processes, machine learning can lead to a reduction of fabrication time, minimized cost, and increased quality. In literature, machine learning has already been applied to process optimization[17-21], dimensional accuracy analysis[22-25], manufacturing defect detection[26-28], and material property prediction[29-32]. However, machine learning has not been applied in 3D bioprinting yet. In this paper, the perspective on how machine learning can help to improve 3D bioprinting is discussed. Related machine learning used in 3D printing will be briefly reviewed for illustrating its effects on 3D bioprinting. We believe that machine learning can significantly affect the future development of 3D bioprinting and hope this paper can inspire some ideas on how machine learning can be used to improve 3D bioprinting.

2 Machine learning

Machine learning is one of today's most rapidly growing technical fields. It is a subset of artificial intelligence, mainly focusing on the designing of systems. Machine learning allows these designed systems to learn and make predictions based on the previous experience which is data in terms of machines. **Figure 2** shows a typical machine learning process. The data in the training set needs to be trained first by the algorithm. During the training process, the parameters in the algorithm will be improved and then generate a machine learning model. Using the updated machine learning parameters, it can then predict the results with new input data. The most commonly used machine learning methods include supervised learning[33], unsupervised learning[34], and reinforcement learning[35].

In supervised learning, the training data are a collection of x, y form pairs, and the objective is to get the predicted result y^ in response to a query x. x, y can be more than one element that will be expressed as a vector in machine learning. Currently, supervised learning has been used in spam classification of email, medical diagnosis systems for patients and face recognition over images.

In unsupervised learning, the input data are unlabeled data which are different from supervised learning. Algorithms will automatically learn and extract the features of the input data and then divide them into different clusters. The aim of unsupervised learning is to model the underlying distribution or structure of the input data for learning more about the data. Currently, unsupervised learning has been applied in market segmentation for targeting appropriate customers, clustering documents based on content, image division, and anomaly or fraud detection in banking companies.

In reinforcement learning, the information from the training data fed into algorithms is intermediate between unsupervised and supervised learning. Instead of indicating the correct output for a given input in supervised learning, the training data are assumed to provide only an indication as to whether an action is correct or not. Currently, reinforcement

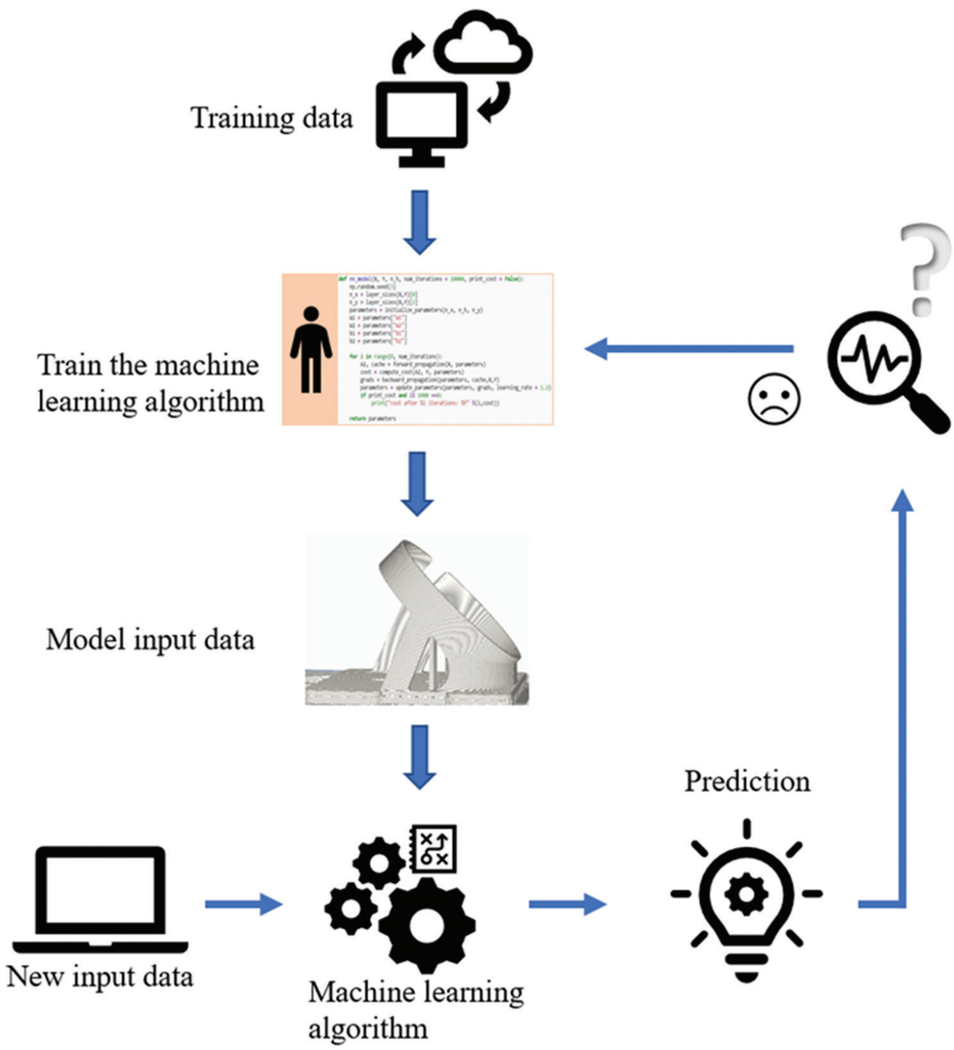

Figure 2. A typical machine learning process.

learning has been used in aircraft control, robot motion control, traffic light control, web system configuration, and games (e.g., AlphaGo).

In addition to these three learning paradigms, some new machine learning methods have also been developed, such as semi-supervised learning. More details can be found in a review paper on machine learning[36]. There are many algorithms available in each machine learning method; the main specific techniques in each method are listed in **Table 1**. Some of these specific techniques have been applied in 3D printing. In the next section, machine learning used in 3D printing processes will be briefly reviewed and the corresponding inspirations for 3D bioprinting will be proposed.

Table 1. Main specific techniques in each machine learning method

Machine learning methods	Main specific techniques
Supervised learning	Decision trees, logistic regression, decision forests, support vector machines, kernel machines, Bayesian classifiers
Unsupervised learning	k-means, generative adversarial networks, expectation-maximization algorithm, Hebbian Learning, self-organizing map, adaptive resonance theory
Reinforcement learning	Monte Carlo, Q-learning, Soft Actor-Critic, proximal policy optimization, Trust Region Policy Optimization, Deep Q-Network, deep deterministic policy gradient

3 Perspective on using machine learning in bioprinting

Machine learning has been integrated into 3D printing processes in many ways to improve applications, including process optimization, dimensional accuracy analysis, manufacturing defect detection, and material property prediction. However, machine learning has not been applied in 3D bioprinting yet. In this section, the perspective on how machine learning can help to improve 3D bioprinting will be illustrated.

3.1 Process optimization

In traditional 3D printing processes, Aoyagi *et al*.[17] proposed a method to construct a process map for 3D printing using a support vector machine. This method can predict a process condition that is effective for manufacturing a product with low pore density. Menon *et al*.[18] used hierarchical machine learning to simultaneously optimize material, process variables, and formulate 3D printing of silicone elastomer through freeform reversible embedding. He *et al*.[19] investigated using different machine learning techniques for modeling and predicting the proper printing speed in a vat photopolymerization process (Continuous Liquid Interface Production). In their study, siamese network model has the highest accuracy. In a previous study, the convolutional neural network (CNN) was applied to enable the angular re-orientation of a projector within a fringe projection system in real-time without re-calibrating the system[20]. In addition, a conceptual framework on combining mathematical modeling and machine learning to evaluate and optimize parameters in Powder Bed Fusion processes was proposed by Baturynska *et al*.[21]

In 3D bioprinting, similarly, machine learning can be used for improving the fabrication process, such as predicting process conditions and optimizing process parameters. Taking extrusion-based bioprinting as an example, it is now able to stably fabricate organoids using low-concentration gelatin-methacryloyl with the help of electrostatic attraction[37]. However, what are the best values of these parameters? This still can be further explored using machine learning. **Figure 3** shows an example case of using neural networks to improve the bioprinting process. The variables are the inputs influencing the objective results (e.g., cell damage, cost, and time). In the case here, voltage, gas, nozzle size, pressure, etc., can be fed into the neural network for training. Corresponding outputs (cell damage, cost, time, etc.) need to be provided to tune machine learning parameters. Once the algorithm is done, new input data can be used for performance evaluation.

3.2 Manufacturing defect detection

In the traditional 3D printing process, Scime and Beuth[26] used computer vision techniques and unsupervised machine learning to identify *in situ* melt pool signatures indicative of flaw formation in a laser powder bed fusion process. Caggiano *et al*.[27] developed a machine learning method to timely recognize metal material defects in Selective Laser Melting processes. Images obtained from the layer-by-layer manufacturing process are analyzed through a bi-stream deep CNN for identifying defects. Zhang *et al*.[28] described a CNN strategy for monitoring porosity in laser additive manufacturing (AM) processes. The melt-pool data were gained through a high-speed digital camera for in-process sensing. Then, the data were analyzed by their developed neural network.

In 3D bioprinting, similarly, machine learning can be used to detect defects such as wrong

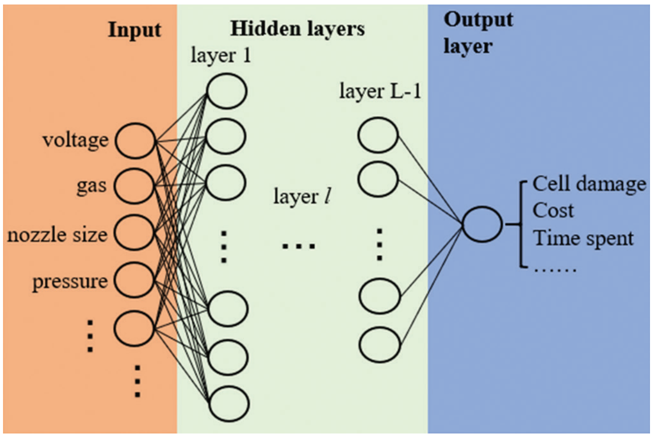

Figure 3. Example neural network for process optimization in three-dimensional bioprinting.

positioned cells, curved layers, and microstructure errors in a fabrication process which can monitor the whole bioprinting process. **Figure 4** shows an example of using CNN to detect flaws, errors, or defects in 3D bioprinting. The input data can be the images from high-quality cameras during the bioprinting process. Then, the data are analyzed by the CNN model to predict a defect or other objectives.

3.3 Dimensional accuracy analysis

In the traditional 3D printing process, Francis and Bian[22] developed a deep learning method that can accurately predict the distortion of parts in laser-based AM. Similarly, Khanzadeh *et al*.[23] proposed an unsupervised machine learning approach (self-organizing map) to quantify the geometric deviations of additively manufactured parts in fused filament fabrication processes. In addition, Zhu *et al*.[24] also developed a strategy coupled with machine learning to address the modeling of shape deviations in AM. Tootooni *et al*.[25] compared six machine learning techniques (sparse representation, k-nearest neighbors, neural network, naïve Bayes, support vector machine, and decision tree) with regard to the accuracy of predicting dimensional variation in fused deposition modeling (FDM) printed parts. Based on their study, the sparse representation approach has the best classification performance.

In 3D bioprinting, similarly, machine learning can be used for analyzing the accuracy of fabricated bio-parts. For example, the tissue-engineered scaffolds are generally very complex because they supporting cell growth in an expected way to achieve corresponding functions. If the accuracy can be analyzed by machine learning in advance, the final fabricated bio-parts can then be guaranteed in good quality. The process is similar, as shown in **Figure 4**, while the input data are different.

3.4 Material property design or prediction

In traditional 3D printing, Gu *et al*.[29] proposed a machine learning-enabled method to design hierarchical composites for fabrication, trained with a database of enough structures from finite element analysis. Hamel *et al*.[30] presented a machine learning method to design active composite structures where target shape shifting responses can be achieved in a 4D printing process. Li *et al*.[31] proposed a predictive modeling method with machine learning that can predict the surface roughness of FDM printed parts with high accuracy. Currently, Jiang *et al*.[32] used backpropagation neural network to analyze and predict printable bridge length[38] in FDM processes.

Similarly, machine learning can also be used to design or analyze material properties in 3D bioprinting process. For example, tissue-engineered scaffolds are very important in 3D bioprinting, whose structures should be carefully designed for successful cell growth and function achievement. For example, if we want to bioprint an organ in the future, the scaffolds should have the specific structure for the successful growth of cells to form a functional organ. In the case here, what kind of complex scaffold structure is the most suitable? How the properties (e.g., density and strength) of the scaffolds will influence the printed organ function? If machine learning can be used to generate these qualified

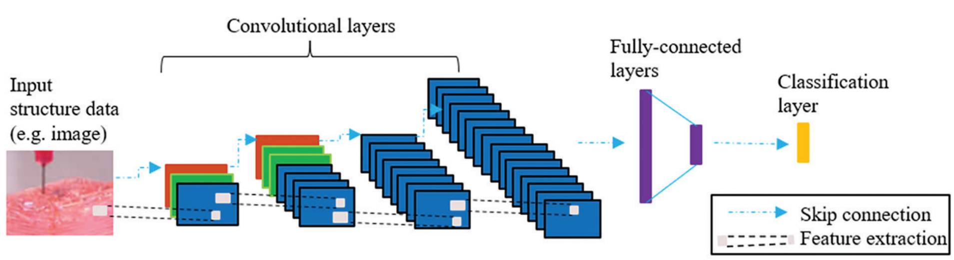

Figure 4. An example of using machine learning (convolutional neural network) in three-dimensional bioprinting.

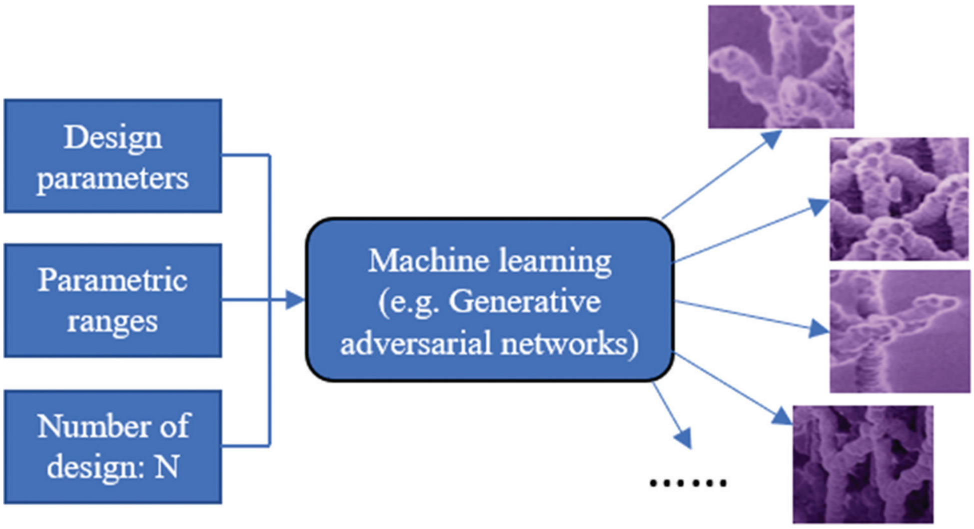

Figure 5. An example of using machine learning to design scaffolds for three-dimensional bioprinting.

scaffolds with different functions, the timescale for developing biomedical or tissue engineering coupled with bioprinting can be largely reduced in the future. Most importantly, machine learning may be able to generate some unexpected novel structures that can better support cell growth and functionalization than ever before. **Figure 5** shows an example of using machine learning (e.g., generative design method) to generate a lot of qualified scaffolds for being chosen or tested in 3D bioprinting. Once the design variables and their corresponding range values are provided, the number of expected generated scaffolds can then be set. With many options generated by machine learning, the scaffolds can then be tested for different objectives.

Another example is that machine learning can be used to design better combinations of materials at different concentrations for bioprinting. Currently, researchers have blended different gels such as collagen or hyaluronic acid to enhance mechanical and degradation properties. However, experiments on testing combinations of materials at different concentrations are a time-consuming and expensive process. Thus, if machine learning can be used to predict the temporal or structural impact of cell proliferation and extracellular matrix deposition on the tissue construct, machine learning will be an effective tool to develop or design novel biomaterials or bioprinting techniques.

4 Conclusions

Machine learning has been widely applied in 3D printing for optimizing its performance and applications. However, few studies have been reported on using machine learning in 3D bioprinting processes. The reason for this may be due to the lack of data of bioprinting as machine learning needs enough data to do predictions and optimizations. While in traditional 3D printing, it has much more data than 3D bioprinting. Another reason is that 3D bioprinting is still new compared with 3D printing, and the bioprinting technique itself still has many challenges to be solved. However, we believe that bioprinting will benefit a lot from machine learning in the future. In this paper, a perspective on how machine learning can be used in bioprinting is proposed and illustrated. Specifically, machine learning can be used to optimize the process of bioprinting, improve or analyze dimensional accuracy, defect detection, and material property design.

Acknowledgments

This research is sponsored by K.C.Wong Magna Fund in Ningbo University.

References

1. Ng WL, Yeong WY, 2019, The Future of Skin Toxicology Testing 3D Bioprinting Meets Microfluidics. *Int J Bioprinting*,

5:237. DOI: 10.18063/ijb.v5i2.1.237.

2. Jiang J, Weng F, Gao S, *et al*., 2019, A Support Interface Method for Easy Part Removal in Direct Metal Deposition. *Manuf Lett*, 20:30–3. DOI: 10.1016/j.mfglet.2019.04.002.
3. Liu J, Gaynor AT, Chen S, *et al.*, 2018, Current and Future Trends in Topology Optimization for Additive Manufacturing. *Struct Multidiscipl Optim,* 57:2457–83. DOI: 10.1007/s00158-018-1994-3.
4. Jiang J, Xu X, Stringer J, 2018, Support Structures for Additive Manufacturing: A Review. *J Manuf Mater Process*, 2:64. DOI: 10.3390/jmmp2040064.
5. Jiang J, Xu X, Stringer J, 2019, Optimisation of Multi-part Production in Additive Manufacturing for Reducing Support Waste. *Virtual Phys Prototyp*, 14:219–28. DOI: 10.1080/17452759.2019.1585555.
6. Weng F, Gao S, Jiang J, *et al.*, 2019, A Novel Strategy to Fabricate Thin 316L Stainless Steel Rods by Continuous Direct Metal Deposition in Z Direction. *Addit Manuf*, 27:474–81. DOI: 10.1016/j.addma.2019.03.024.
7. Jiang J, Xu X, Stringer J, 2018, A New Support Strategy for Reducing Waste in Additive Manufacturing. In: The 48th International Conference on Computers and Industrial Engineering (CIE 48). Curran Associates, Inc., Auckland. pp. 1–7.
8. Jiang J, Stringer J, Xu X, *et al*., 2018, A Benchmarking Part for Evaluating and Comparing Support Structures of Additive Manufacturing. In: 3rd International Conference on Progress in Additive Manufacturing (Pro-AM 2018). Singapore. pp. 196–202.
9. Lv S, Nie J, Gao Q, *et al*., 2019, Micro/Nanofabrication of Brittle Hydrogels Using 3D Printed Soft Ultrafine Fiber Molds for Damage-free Demolding. *Biofabrication*. DOI: 10.1088/1758-5090/ab57d8.
10. Nie J, Gao Q, Wang Y, *et al.*, 2018, Vessel-on-a-chip with Hydrogel-Based Microfluidics. *Small*, 14:1802368. DOI: 10.1002/smll.201802368.
11. An J, Chua CK, Mironov V, 2016, A Perspective on 4D Bioprinting. *Int J Bioprinting*, 2:3–5. DOI: 10.18063/IJB.2016.01.003.
12. Jiang J, Xu X, Stringer J, 2019, Optimization of Process Planning for Reducing Material Waste in Extrusion Based Additive Manufacturing. *Robot Comput Integr Manuf*, 59:317–25. DOI: 10.1016/j.rcim.2019.05.007.
13. Jiang J, Stringer J, Xu X, *et al.*, 2018, Investigation of Printable Threshold Overhang Angle in Extrusion-based Additive Manufacturing for Reducing Support Waste. *Int J Comput Integr Manuf*, 31:961–9. DOI: 10.1080/0951192X.2018.1466398.
14. Jiang J, Lou J, Hu G, 2019, Effect of Support on Printed Properties in Fused Deposition Modelling Processes. *Virtual Phys Prototyp*, 14:308–15. DOI: 10.1080/17452759.2019.1568835.
15. Ng WL, Chua CK, Shen YF, 2019, Print Me An Organ! Why We Are Not There Yet. *Prog Polym Sci*, 97:101145. DOI: 10.1016/j.progpolymsci.2019.101145.
16. 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*, 3:144–56. DOI: 10.1016/j.bioactmat.2017.11.008.
17. Aoyagi K, Wang H, Sudo H, *et al*., 2019, Simple Method to Construct Process Maps for Additive Manufacturing Using a Support Vector Machine. *Addit Manuf*, 27:353–62. DOI: 10.1016/j.addma.2019.03.013.
18. Menon A, Póczos B, Feinberg AW, *et al*., 2019, Optimization of Silicone 3D Printing with Hierarchical Machine Learning. *3D Print Addit Manuf*, 6:181–9. DOI: 10.1089/3dp.2018.0088.
19. He H, Yang Y, Pan Y, 2019, Machine Learning for Continuous Liquid Interface Production: Printing Speed Modelling. *J Manuf Syst*, 50:236–46. DOI: 10.1016/j.jmsy.2019.01.004.
20. Stavroulakis P, Chen S, Delorme C, *et al.*, 2019, Rapid Tracking of Extrinsic Projector Parameters in Fringe Projection Using Machine Learning. *Opt Lasers Eng*, 114:7–14. DOI: 10.1016/j.optlaseng.2018.08.018.
21. Baturynska I, Semeniuta O, Martinsen K, 2018, Optimization of Process Parameters for Powder Bed Fusion Additive Manufacturing by Combination of Machine Learning and Finite Element Method: A Conceptual Framework. In: Procedia CIRP. Elsevier B.V., Heidelberg. pp. 227–32. DOI: 10.1016/j.procir.2017.12.204.
22. Francis J, Bian L, 2019, Deep Learning for Distortion Prediction in Laser-Based Additive Manufacturing Using Big Data. *Manuf Lett*, 20:10–4. DOI: 10.1016/j.mfglet.2019.02.001.
23. Khanzadeh M, Rao P, Jafari-Marandi R, *et al.*, 2018, Quantifying Geometric Accuracy with Unsupervised Machine Learning: Using Self-Organizing Map on Fused Filament Fabrication Additive Manufacturing Parts. *J Manuf Sci Eng*, 140:301011. DOI: 10.1115/1.4038598.
24. Zhu Z, Anwer N, Huang Q, *et al*., 2018, Machine Learning in Tolerancing for Additive Manufacturing. *CIRP Ann*, 67:157–60. DOI: 10.1016/j.cirp.2018.04.119.
25. Tootooni MS, Dsouza A, Donovan R, *et al.*, 2017, Classifying the Dimensional Variation in Additive Manufactured Parts from Laser-Scanned Three-Dimensional Point Cloud Data

Using Machine Learning Approaches. *J Manuf Sci Eng*, 139:091005. DOI: 10.1115/1.4036641.

26. Scime L, Beuth J, 2019, Using Machine Learning to Identify *in situ* Melt Pool Signatures Indicative of Flaw Formation in a Laser Powder Bed Fusion Additive Manufacturing Process. *Addit Manuf*, 25:151–65. DOI: 10.1016/j.addma.2018.11.010.
27. Caggiano A, Zhang J, Alfieri V, *et al.*, 2019, Machine Learning-based Image Processing for On-Line Defect Recognition in Additive Manufacturing. *CIRP Ann*, 68:451–4. DOI: 10.1016/j.cirp.2019.03.021.
28. Zhang B, Liu S, Shin YC, 2019, In-Process Monitoring of Porosity During Laser Additive Manufacturing Process. *Addit Manuf*, 28:497–505. DOI: 10.1016/j.addma.2019.05.030.
29. Gu GX, Chen CT, Richmond DJ, *et al*, 2018, Bioinspired Hierarchical Composite Design Using Machine Learning: Simulation, Additive Manufacturing, and Experiment. *Mater Horizons*, 5:939–45. DOI: 10.1039/c8mh00653a.
30. Hamel CM, Roach DJ, Long KN, *et al.,* 2019, Machine-Learning Based Design of Active Composite Structures for 4D Printing. *Smart Mater Struct*, 28:065005. DOI: 10.1088/1361-665X/ab1439.
31. Li Z, Zhang Z, Shi J, *et al*., 2019, Prediction of Surface Roughness in Extrusion-Based Additive Manufacturing with Machine Learning. *Robot Comput Integr Manuf*, 57:488–95. DOI: 10.1016/j.rcim.2019.01.004.
32. Jiang J, Hu G, Li X, *et al.*, 2019, Analysis and Prediction of Printable Bridge Length in Fused Deposition Modelling Based on Back Propagation Neural Network. *Virtual Phys Prototyp*, 14:253–66. DOI: 10.1080/17452759.2019.1576010.
33. Caruana R, Niculescu-Mizil A, 2006, An Empirical Comparison of Supervised Learning Algorithms. In: ACM International Conference Proceeding Series. ACM, Pittsburgh. pp. 161–8. DOI: 10.1145/1143844.1143865.
34. Francis L, 2014, Unsupervised Learning. In: Predictive Modeling Applications in Actuarial Science. Predictive Modeling Techniques. Vol. 1. Cambridge University Press, Philadelphia, PA.
35. Arulkumaran K, Deisenroth MP, Brundage M, *et al*., 2017, Deep Reinforcement Learning: A Brief Survey. *IEEE Signal Process Mag*, 34:26–38. DOI: 10.1109/msp.2017.2743240.
36. Jordan MI, Mitchell TM, 2015, Machine Learning: Trends, Perspectives, and Prospects. *Science*, 349:255–60.
37. Xie M, Gao Q, Zhao H, *et al*., 2019, Electro-Assisted Bioprinting of Low-Concentration GelMA Microdroplets. *Small*, 15:1804216. DOI: 10.1002/smll.201804216.
38. Jiang J, Stringer J, Xu X, 2019, Support Optimization for Flat Features via Path Planning in Additive Manufacturing. *3D Print Addit Manuf*, 6:171–9. DOI: 10.1089/3dp.2017.0124.