CIRP Annals - Manufacturing Technology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

CIRP Annals - Manufacturing Technology

journal homepage: http://ees.elsevier.com/cirp/default.asp

Hierarchical and spatial modeling and bio-additive manufacturing of multi-material constructs

Navid Khani [a,b], Ali Nadernezhad [a,b], Paulo Bartolo (1)[c], Bahattin Koc [a,b,*]

[a] Faculty of Engineering and Natural Sciences, Sabanci University, Orhanli-Tuzla, Istanbul 34956, Turkey
[b] 3D Bioprinting Laboratory, Sabanci University Nanotechnology Research and Application Center, Orhanli-Tuzla, Istanbul 34956, Turkey
[c] School of Mechanical, Aerospace and Civil Engineering, Manchester Institute of Biotechnology, University of Manchester, Manchester, UK

ARTICLE INFO

Keywords:
Biomanufacturing
3D bioprinting
Modelling of multi-functional structures

ABSTRACT

In this paper, a novel method of integrated modelling and bio-additive manufacturing of hybrid bioinspired structures is presented. An algorithm is developed to generate optimized and continuous path plan while changing material and internal composition spatially and hierarchically based on the assigned functionality. Biodegradable polymers and hydrogels are used as reinforcing and biological functional bioinks respectively. A new hybrid multi-head 3D bioprinter is developed to manufacture designed three-dimensional constructs depositing bioinks layer-by-layer. Simultaneous incorporation of multiple deposition heads and integrated path planning provide the benefits of using the deposition-on-demand of multi-material bio-inks. The modelled constructs are analyzed and bioprinted.

1. Introduction

Bottom-up assembly approaches in bioprinting of multifunctional structures provide the opportunity to control over the structural features within artificial tissue engineering constructs, while several essential manufacturing parameters and materials properties can be optimized synergistically. Bioinspired reconstruction of artificial tissues generally involves modeling and fabrication of spatially defined regional features to mimic targeted tissues [1]. The intrinsic complexities and the spatial arrangement of functional components of native tissues demand switching from traditional fabrication techniques [2] to more sophisticated hybrid bioprinting approaches where the bioinspired features could be mimicked to a whole extent. However, some concerns regarding both bioprinting strategies and hardware designs hinder the further development of hybrid processes. In the literature, there are a few studies on developing hybrid multi-material bioprinting [3–7]. The complexities of hardware and processes are mainly due to the multi-material and hierarchy nature of the mimicked tissues, which resulted in bioprinters with several active heads operating independently [4,5], or printheads based on switching mechanisms [8,9]. However, these designs are complicated and computationally expensive in terms of control systems and process planning, and limitations in materials selection. In addition to the hardware complexities, instantaneous material switching in hybrid multi-material bioprinting is mostly overshadowed by the efforts to extend the number of deposition systems in a single device. In hybrid multi-material bioprinting, the bioprinted structures must be spatially and biologically active to mimic the targeted tissue and mechanically strong to be implantable. The ideal design features in a bioprinting setup should be as simple as possible and at the same time, capable of processing of several materials with substantially not-similar properties like thermoplastics and hydrogels.

In this paper, we present a novel hybrid and hierarchical multi-material bioprinting technique by integrating path planning and optimization algorithms with multi-material hydrogel and biodegradable polymer dispensing system. The proposed algorithm is used to generate path plans for controlling the developed multi-head hybrid bioprinter directly from multi-functional design.

2. Bioprinter design and fabrication

To be able to bio-manufacture the hybrid multi-material constructs, a custom-made bioprinter is developed as shown in Fig. 1. The developed bioprinter is a three-axis robotic platform motorized by three AC servomotors, ball screws and linear guides to provide principal XYZ axes motion with the repeatability of $<\pm 10$ μm. Three dispensing heads, each assigned to deposition of specific types of inks were mounted on three stepper motors on the Z stage. All the steppers are connected to the high precision ball screw linear positioning guides with 1 mm lead size and maximum speed of 190 mm s^{-1} with actuation limit of 200 mm. Head I is dedicated to aspiration/extrusion-on-demand of hydrogel bioinks [10] with basic step angle of 0.9° and 1 mm lead size of linear guides, which provided the resolution of 2.5 μm.

* Corresponding author at: Faculty of Engineering and Natural Sciences, Sabanci University, Orhanli-Tuzla, Istanbul 34956, Turkey.
E-mail address: bahattinkoc@sabanciuniv.edu (B. Koc).

http://dx.doi.org/10.1016/j.cirp.2017.04.132
0007-8506/

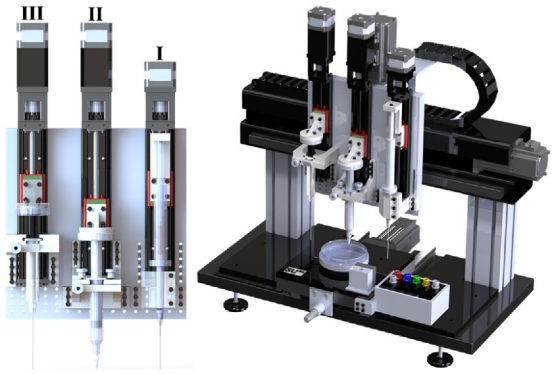

Fig. 1. Multi-head bioprinter with three reconfigurable heads.

Head II is used for deposition of thermoplastics with a controllable heating system and Head III is designed for continuous deposition of high viscous hydrogels or dispensing cell culture medium during bioprinting. Head II and III use stepper motors with the basic step angle of 1.8° and the gear ratio 36:1, yielding the maximum resolution of 134 nm. Hence, the developed bioprinter can manufacture not only 3D hybrid bio-structures with high resolution movements of motorized plungers but also to avoid applying excess shear stress on biological materials. Moreover, a head mounted temperature control unit on the dispensing heads provides keeping the process temperature of thermoplastics within a biologically safe window and gives a freedom of choosing different nozzles to fine-tune the flow of materials. Hydrogel ink's reservoir is separated from Head I with an independent heating/cooling unit. This separation results in availability of all inks throughout the bioprinting session, and every ink is accessible based on the hierarchy of the features in the printed model. The configuration of dispensing heads can be modified depending on the application by switching from piston driven plungers to pneumatic dispensing units.

3. Biomanufacturing procedure for multi-material structures

Fig. 2 shows the overall procedure for biomanufacturing of a multifunctional object which is composed of several regions of different materials/functionalities. In a typical process, the Computer-Aided Design (CAD) object is generated by applying the previously reported algorithms [11] on segmented MRI/CT images to produce Non-uniform Rational B-spline (NURBS) surfaces from mesh models (Fig. 2a). The illustrated object in Fig. 2a is composed of four different materials with irregular geometries which are shown in different colors. Reconstructed CAD object is further being processed by the developed algorithm to produce the ready-to-print modeled structure which is composed of spatially positioned hydrogel inks within a biodegradable thermoplastic cage (Fig. 2b). The details and pseudo code of the developed algorithm is provided in Section 4. Computer-controlled biomanufacturing of the modeled structure is accomplished by sequentially ordered deposition of inks and biodegradable thermoplastics with respect to the feature-based assignment of materials for each individual functionality (Fig. 2c).

Bio-additive manufacturing of a single layer of the multi-material object is shown in Fig. 2d. The hierarchy of the model is originated from the difference in functionalities and processing conditions of biodegradable thermoplastic cage and hydrogel inks. The hierarchical order in deposition of two constitutive material by using different heads provides the opportunity of tuning the overall mechanical stability and delivering the bio-functionality of spatial features. As shown in Fig. 2d, by changing the number of successively stacked sublayers n_t (i.e., $n_t = 3$) of thermoplastics, the strut diameter of hydrogel material can be matched at each layer. The hierarchical order of the deposition in each layer is as follows:

i: Deposition of zig-zag biodegradable thermoplastic sub-layers with total height equivalent to the diameter of Head I nozzle to preserve the dimensional accuracy in each layer. The number of sub-layers n_t can be adjusted to tune the mechanical properties.

ii: Aspiration of hydrogel bioinks from the inks reservoir (Fig. 2c) with respect to the hierarchical order of bio-functionalities followed by extrusion of each filament within each channel of the deposited zig-zag structure, with respect to the hierarchy of the model. The aspiration-deposition iterations will continue until filling all the channels of each single layer (including n_t sublayers) of deposited thermoplastic cage. The hierarchical order of bio-functionalities originates from the functionalities of each constitutive segments of the object, while the hierarchy of the model refers to the sequences of deposition of each constitutive element in the bioprinted structure.

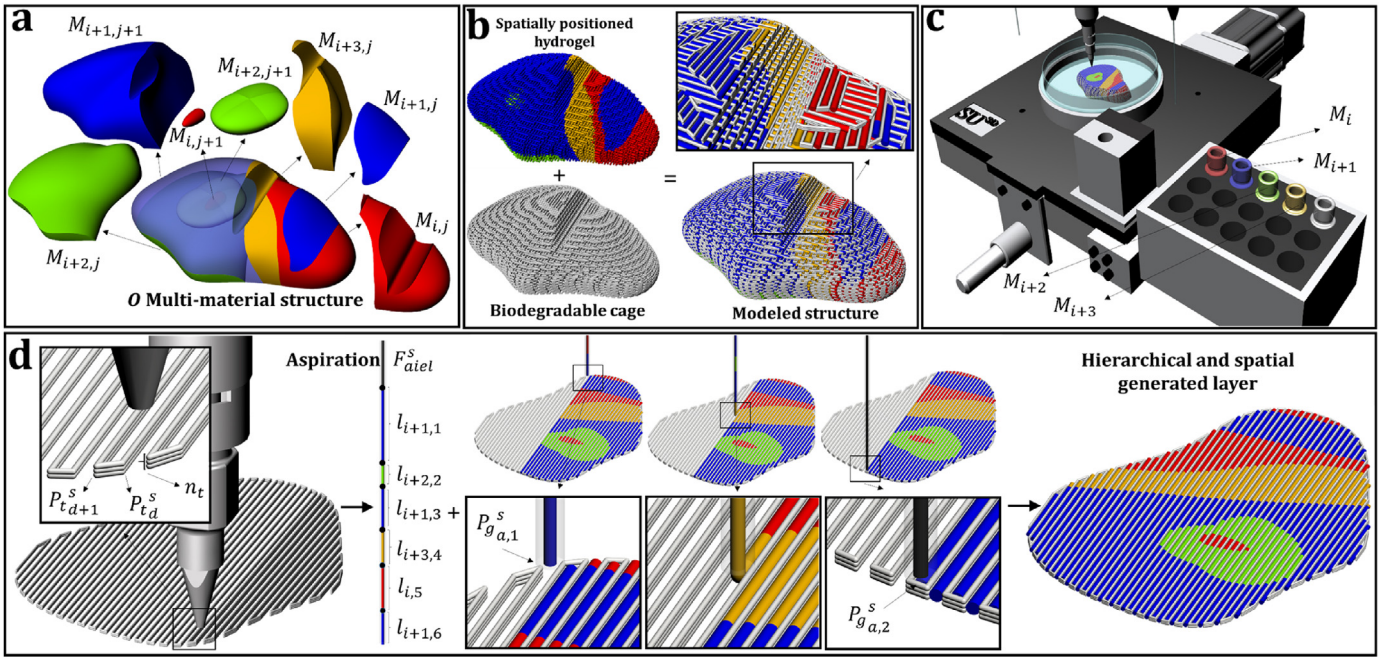

Fig. 2. Bio-additive manufacturing procedure, (a) multi-material object, (b) modeled structure, (c) bioprinting, (d) fabrication procedure in one layer.

Please cite this article in press as: Khani N, et al. Hierarchical and spatial modeling and bio-additive manufacturing of multi-material constructs. CIRP Annals - Manufacturing Technology (2017), http://dx.doi.org/10.1016/j.cirp.2017.04.132