I-Optimal Design and Topology Control of 3D Scaffolds Produced by Fused Deposition Modeling

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Statement of Purpose: Optimal scaffold design for tissue engineering is critical for cell attachment and survival. Therefore, solid freeform fabrication (SFF) techniques are becoming the method of choice for developing scaffolds with controlled internal architectures. Organic solvents are commonly used in producing polymeric scaffolds. Although solvent toxicity may not be considered critical for *in vitro* trials, such approaches will be subject to scrutiny once the technology is advanced to clinical trials. Research on rapid prototyping of 3D scaffolds by melt processing has been highly restricted, mainly due to the pronounced variations in the deposited strand diameter (extrudate swell) upon any variations in processing conditions and polymer viscoelasticity. In this study, we have performed a designed experiment to control the extrudate swell and maximize the mechanical properties of the scaffold, so as to facilitate the scaffold fabrication by a fused deposition modeling (FDM) process.

Methods: Polycaprolactone (PCL) and poly(L-lactic acid) (PLLA) were used in this study. To meet the need for more osteoconductive materials for bone tissue engineering, hydroxyapatite (HA) particles with two grain sizes (<200 nm; Sigma; and ~5 μm; Plasma Biotal) at a concentration of 20% w/w were incorporated into the cryogenically-ground polymers using a vortex mixer. For scaffold fabrication, the polymer powders and polymer-HA blends were processed using a 3D-bioplotter (EnvisionTEC). The number of key factors for the experiment was $N_F = 4$ as given in Table 1 (X1 to X4). To find the effect of needle diameter (D_{die}), dispensing temperature and pressure (T & P), and dispensing speed (u) on swell, three values (N_L=3) for each parameter were considered: low (L), medium (M), and high (H). A full factorial design would execute an experimental run at all possible combinations of the four factors, but this requires $N_L^{N_F} = 3^4 = 81$ runs. A 24-run split-plot I-Optimal design was used in this study; split-plot because this type of experiment reduces the number of times that temperature and needle diameter needed to be changed, and I-Optimal because precise prediction was desired. The scaffolds were tested under unconfined ramp compression (BOSE ElectroForce 3200) to measure the mechanical properties, targeting the modulus for trabecular bone. The constructs were also analyzed by microscopy to estimate the swell (D/D_{die}), where D is the diameter of the deposited strand.

Results: Figure 1 depicts a typical swell for PCL/HA as a function of temperature and dispensing speed. The effects of the needle diameter and pressure are presented by assigning three patterns to the data points. The pronounced swell indicates that a design-driven strand diameter and pore size cannot be achieved by FDM, and thereby emphasizes the need for a model to predict the extrudate swell. Response surface analysis enabled us to find compromise processing window for scaffold fabrication with a low swell and high modulus.

Table 1. The parameters used for the I-Optimal design.

Factors (X_1 to X_4)		L	M	H
Needle Diameter, D (X_1)		200 μm	400 μm	600 μm
Temperature T (X_2)	PCL & PCL/HA	100 °C	115 °C	130 °C
	PLLA & PLLA/HA	190 °C	205 °C	220 °C
Pressure, P (X_3)		2.5 bar	3.5 bar	4.5 bar
Dispensing speed, u (X_4)		1 mm/s	2 mm/s	3 mm/s

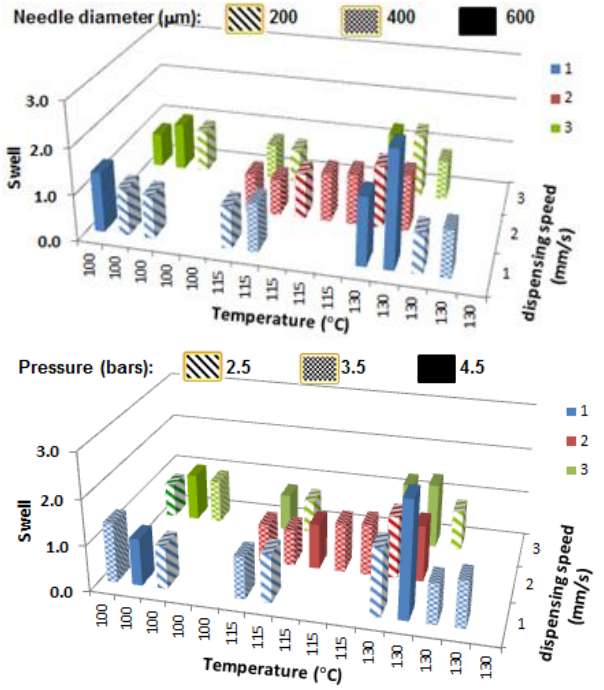

Figure 1. Extrudate swell for PCL-HA strands as a function of temperature and dispensing speed. Values of the needle diameter and pressure are shown by patterns.

Conclusions: A split-plot I-Optimal design was used in this study to maximize the modulus of the scaffolds, while keeping the extrudate swell at a low level. The ultimate goal of this study is to develop a model for extrudate swell and to enable a greater control over scaffold architecture, and therefore on the mass transport and mechanical properties of the produced constructs. To our knowledge, this work is the first to eliminate trial and error runs to achieve the desired internal architectures for melt-processed scaffolds. Since the effect of scaffold architecture on bone tissue regeneration is not fully understood and varies significantly between studies, this work will also contribute to understanding the effect of rigorously controlled architectures on bone formation.

References: 1) Hutmacher DW, Biomater 2000; 21:2529-43. 2) Dalton PD, *et al*. Biomacromol 2006; 7:686–690.