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Modeling and additive manufacturing of biomimetic heterogeneous Scaffold

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Abstract

In this paper, a feature-based bio-CAD modeling of three-dimensional tissue scaffolds by considering spatial distribution of biologically active materials is presented for biomanufacturing and tissue engineering applications. Proposed model is based on uniform distribution of bio-active particles in different regions of scaffold, which is constrained by geometrical and biological features. The proposed method was integrated with a recently developed method of multi-material additive manufacturing of hydrogel structures, for bio-additive manufacturing of the heterogeneous scaffolds. 3D bioprinted heterogeneous scaffolds were provided as an example for physical implementation of developed algorithm to validate the model.

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1. Introduction

Tissue engineering is a complex process where a porous scaffold with or without cells is used to heal or regenerate the targeted tissue. The sequence of events is guided by a series of growth factors, cytokines, cell-cell and cell-matrix interactions. To imitate nature's healing environment, these scaffolds must incorporate vital growth factors or proteins that are able to act on cell migration, differentiation, proliferation and organization in a functional tissue. These growth factors are polypeptides that transmit signals to modulate cellular activities. Thus, proliferation and other behaviors of cells on advanced bio-specific materials can be controlled by incorporating a controlled release of bioactive particles, such as natural growth factors, hormones, enzymes or synthetic cell cycle regulators [1]. These bioactive particles will deliver the appropriate, necessary cues in a controlled spatial and temporal fashion to improve healing or tissue regeneration. However, a major challenge lies in developing efficient delivery mechanisms to mimic the in vivo release profiles of growth factors produced during natural tissue morphogenesis or repair [2].

In the literature, several heterogeneous object modeling techniques have been proposed for solid modeling of consumer products: the r_m-object approach is used for representing heterogeneous objects by Kumar and Dutta [3]. This method represents the material variation as functions of spatial position relative to a reference entity and material variations were assumed to be given a priori. Samanta and Koc [4] have proposed feature based heterogeneous object modeling using B-spline surfaces and B-spline volumes to represent 2D and 3D-dependent material distributions using the same set of control points for both the geometries and the material compositions. Weiss et al [5] have presented a Bayesian methodology for computer-aided experimental design of heterogeneous fibrin-based scaffolds having spatial distribution of growth factors designed to induce and direct the growth of new tissue as the scaffold degrades.

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However, these heterogeneous object modeling techniques assume a continuous variation of materials throughout the designed object, whereas in tissue scaffolds bioactive particles are discrete entities and need to be spatially distributed in a controlled manner within the porous scaffold. Af

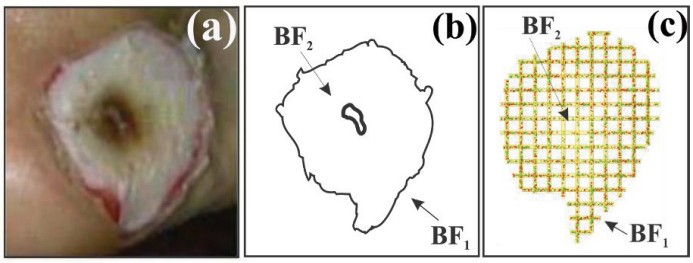

Fig. 1. Overall procedure of modeling and design of biomimetic tissue scaffold

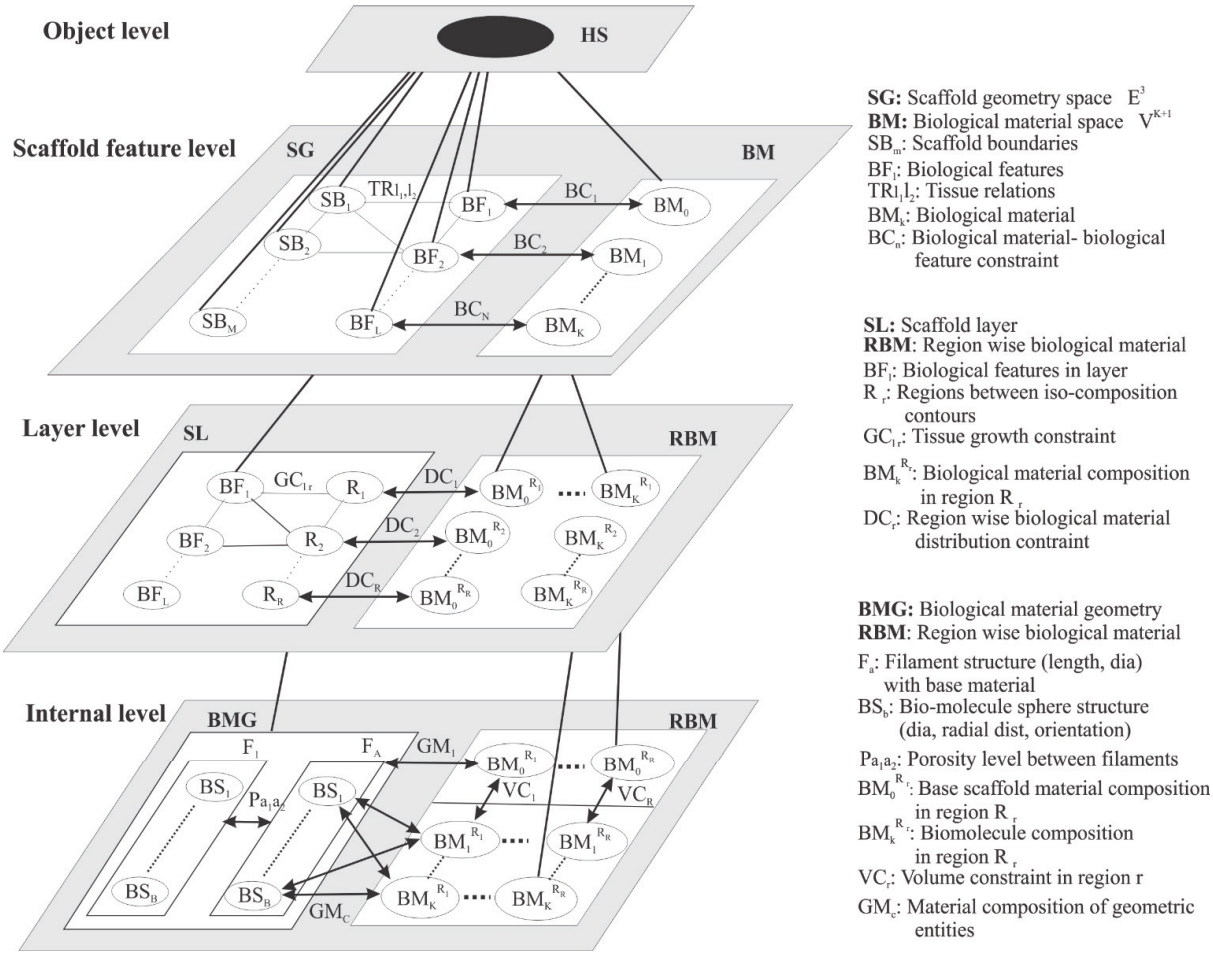

Fig. 2. Feature based heterogeneous scaffold model hierarchy

Hence, the existing heterogeneous object modeling techniques cannot be directly used in modeling of tissue scaffolds with controlled distribution of bioactive particles.

During the past decade, extensive studies on multi-material additive manufacturing by using multi-nozzle deposition systems were resulted in numerous reports on fabrication of heterogeneous scaffolds addressed to be used in biomedical