The Effect of Processing and Rheological Variables on the Morphology of Dermal Electrospun Scaffold

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Abstract: The human skin is the largest organ which protects the body from disease and physical damage. When the skin has been seriously damaged through disease or burns, the body cannot act fast enough to produce necessary replacement cells. Artificial skin grafts were developed as a way to prevent such consequences. This work is related to the design of advanced dermal scaffolds (non-woven fibrous mats) to provide multifunctional properties. Defined target properties are attained by distributing specified base materials at multiple length scales ranging from several nanometers to millimeters. Tissue scaffolds were developed using the electrospinning process, which creates a non-woven fibrous construction of high permeability and proper mechanical integrity similar to the scale of the extra-cellular matrix of cells.

Keywords: Elecrospun processing, dermal scaffold, structural optimization, rheological parameters.

1. Introduction

The problem of slow replacement cells production on a seriously damaged human skin, through diseases or high level burns, results death of the burnt victim, due to infection and loss of plasma. To overcome the problem, artificial dermal scaffolds (non-woven fibrous mats) are being developed, providing functional material concepts with enhanced properties [1].

The primary requirements for a scaffold are temporary mechanical support and tissue regeneration through cells and proteins [1]. The complex network of structural and functional proteins in the fibrous matrix of the ECM (extra-cellular matrix cells) is a major challenge in the dermal scaffold design. Biocompatibility and biodegradability of the materials, chemo-mechanical properties and morphological characteristics at different length scales are the main demands for the cell-scaffold interface [2].

The process technique implemented nowadays for the production of the forth-mentioned fibrous mats is the electrospinning process. It is particularly appealing for fabricating large sheets of nanoscale fibrous scaffolds suitable for dermal implantation.

Recent studies have reported a multiscale 3D scaffold design via multimodal electrospinning (Soliman S. et all). The study concerns a modified electrospinning process (implementing two parallel syringes) used for the production of multimodal MIX scaffold (comprising nano and microfibers) that shows important improvements over the unimodal scaffolds in terms of mechanical and biological performance.

Another study has reported on the computer simulating approach of a cell growth inside the scaffolds. The cell activity during the tissue regeneration has been simulated by a lattice incorporated within a finite element model. Such developed mechano-biological model is reported to be a good prediction tool for the optimal design parameters for scaffolds. The investigations suggested experimental analysis as such that cells exposure is within optimal mechanical simulation and cell seeding optimal for vascular ingrowth's [3, 4].

An important issue investigated is the cells motility in a (e.g. damaged skin) during their growth (tissue regeneration). Multiscale models have reported on the cell and tissue dynamics. Single cell model simulates the deformations of the cell itself and the substrate. Mechanical principle incorporated in a single cell model is essential for a model simulation of cells interactions and tissues. With this model different traction patterns of the cells can be measured. Further numerical investigation is needed in order to represent a detailed cell-substrate dynamics [5].

When modeling biological systems, one should be able to produce different mathematical models at different scales and provide a link between each model to get a complete description of the system.

Molecular level is the fundamental scale for understanding or predicting the structure of a molecule. The stochastic changes of particle numbers in the volume elements representing intracellular space become possible to simulate through generalizations of Gillespie's algorithm that include molecular diffusion

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events in addition to chemical reactions. The cell-cell contact, stochastic diffusion trajectories molecular particles and cellular membrane may be simulated. Models of cell state transitions and their consequences are formulated in terms of finite state automata, the cellular automata treat the single 'cell' as agents that can carry their states with them as they move on the grid space. There are some simulation examples of multicellular systems such as the adaptive immune system, populations and migrating cells, organ level phenomena. The aim of this paper is to examine the range of elastic and permeability properties using electrospinning.

2. Initial work

Tissue scaffolds were developed using the electrospinning process, which creates a non-woven fibrous construction of high permeability and proper mechanical integrity similar to the scale of the extra-cellular matrix of cells. Dramatically increased specific surface, excellent mechanical strength, and highly open porous structures are the unique properties of the electrospun fibers non-woven fabrics. Figure 1 illustrates dermal scaffold used for tissue regeneration of damaged human skin.

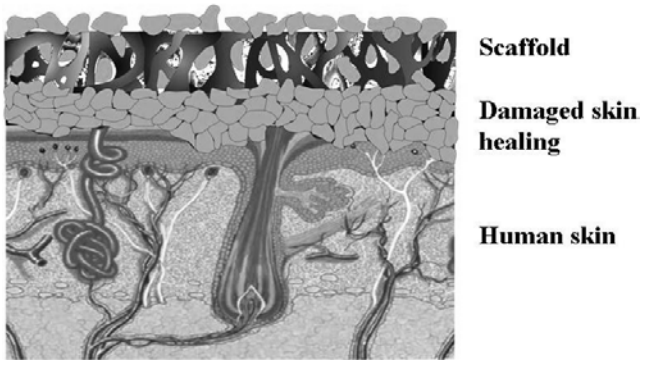

Figure 1 Dermal scaffold for the acceleration of the cell growth on damaged skin.

The principle behind the electrospinning process is in the usage of electricity to move fluids (e.g. polymer solutions). A charged jet is ejected beyond a critical value of the electrical field intensity, at which the repulsive electrical forces overcome the surface tension of the polymer solution (or melt) droplet at the tip of the nozzle. Traveling towards the grounded collector the jet either cools down (in case of the melt) or the solvent evaporates (in case of the solution) to obtain ultrafine fibers in the form of a non-woven nanofabric. The non-woven fibrous structure resembles an intricate forest of overlaid fibers [2].

A number of nanofiber assemblies have been developed using electrospinning by incorporating functional agents to achieve antibacterial and magnetic, properties. The morphology of the electrospun fibers depends on a number of factors, such as solution properties (e.g., concentration, viscosity, conductivity, surface tension, etc.), processing conditions (e.g., electrical potential, collection distance, etc.), and ambient conditions (e.g., temperature, humidity, etc.).

2.1. Optimal scaffold design

Tissue engineering scaffolds must serve three primary purposes: they must define a space that will shape the regenerating tissue, they must provide temporary function in a defect while tissue regenerates and they must facilitate ingrowth of tissue and possibly allow inclusion of seeded cells, proteins and/or genes to accelerate tissue regeneration.

To describe how the load-bearing tissue grows within the scaffold pores, the remodeling rules established in nanofibre surface are considered applicable [7].

Therefore, cost function is often formulated in terms of the first invariants of permeability tensors. The constraints come as desired effective elasticity constants that are met within a specified tolerance and a porosity constraint.

$$\begin{aligned} &\max_{\rho} \psi\left(K_{ii}^{scaffold}\right) \\ \textit{subject to} \quad &\left\| C_{ijkl}^{scaffold} - C_{ijkl}^{target} \right\| \le \alpha \\ &1 - \frac{V}{V_{micro}} \le \textit{porosity}\,. \end{aligned} \tag{1}$$

where $K_{ii}^{scaffold}$ denotes the first invariant term of the effective permeability tensor, $C_{ijkl}^{scaffold}$ is the effective elasticity tensor for the scaffold, C_{ijkl}^{target} is the target value of the effective elasticity tensor, V_{micro} denotes the volume of the unit cell architecture, V denotes the volume of the solid material, and α is a tolerance term that is gradually reduced during the course of iteration until convergence is achieved. Eq. 1 is a multiphysics optimization problem and is solved using the combination of a Method of Moving Asymptotes [8, 9] to update elasticity, and an evolutionary structural optimization scheme to update the density distribution