Annals of DAAAM for 2010 & Proceedings of the 21st International DAAAM Symposium, Volume 21, No. 1, ISSN 1726-9679
ISBN 978-3-901509-73-5, Editor B. Katalinic, Published by DAAAM International, Vienna, Austria, EU, 2010
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DAAAM Symposium

CONSIDERATIONS ABOUT A 3D MATRIX BASED MODEL FOR A POROUS SCAFFOLD AND A CELL SUSPENSION

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Abstract: *One of the main objectives of tissue engineering is to produce porous structures made of biocompatible materials, allowing the proliferation, motility and cell differentiation to desired cell line. Scaffold of porous structure have a very important role in tissue engineering, representing the support for cells attachment, in order to create new functional and implantable tissues for the human body. This branch of tissue engineering represents an alternative to traditional transplants. The paper presents a mathematical model based on a three-dimensional matrix for a system containing a degradable porous scaffold and a cell suspension located in its neighborhood. This mathematical model represents a starting point for computational analysis of cell seeding process (the cells distribution on the scaffold, the influence of cells shape and cells type) and of cell division process.*
Key words: *porous scaffolds,cells,tissue engineering, modeling*

1. INTRODUCTION

Tissue engineering represents a complex area of regenerative medicine, which mainly studies in vitro development of living tissues and organs, representing a promising alternative to traditional transplants (Mironov et Al. 2006).

The biomedical research community insisted on developing a complete range of strategies which could be used for the treatment of sick or destroyed organs and tissues. These strategies are based on 3 fundamental terms:replacement, repair and regeneration of tissues or organs (Meyer et Al., 2009).

The process of creating living tissues in vitro implies the use of some three-dimensional support structures, named scaffolds which allow the attachment of specific types of cells on their surface as well as their division. The cells represent the key for the regeneration and repair of tissues through their proliferation, motility and differentiation, by producing biomolecules and forming the extracellular matrix.

In order to form new tissues, tissue engineering uses the principles of cellular biology, biochemistry and polymeric science (Griffth et Al., 2002).

Forming the tissue that will be implanted is greatly influenced by the composition, architecture and biocompatibility of the scaffold.

The mechanical properties of the scaffold's material must imitate the mechanical properties of the tissue that we want to repair or replace. The degradability of the scaffold is also an interesting problem in this field of research, since the scaffolds must be preferably absorbed by the surrounding newly created tissue, without removing it surgically (Hollister, 2005).

The porosity of the material from which the scaffold is made of, as well as the distribution and size of the pores, greatly influences the attachment of specific types of cells to the biomaterial and the interaction between the biomaterial and the host (Hollister, 2005).

Cell seeding on a porous structure biomaterial plays an important role in the generation of new tissues (Neagu et Al., 2005). That is the reason why the authors of this paper pursued the development of a mathematic model (based on a three-dimensional matrix) describing a porous structure scaffold with a controlled architecture and a suspension of cells of a certain concentration, located in its neighborhood. Based on this model, later on, cell seeding processes may be simulated, also studying the interaction manner between the cells as well as the cellular division processes (Doaga et Al., 2008).

2. POROUS SCAFFOLD MODELING

For the modeling of the porous structure biomaterial, a hexagonal network of some spherical pores (with *Rpor* radius) interconnected through circular orifices (with *rcon* radius), was created. By the means of these orifices, the cells will be able to penetrate the pores of the biomaterial, realizing in this way the cell seeding phenomenon with the goal to form new tissues.

The porous structure biomaterial is considered to be immersed in the culture medium, leading to the conclusion that the pores of the biomaterial contain medium particles.

In order to identify the positions occupied by the pores in the network, the *R* radius spheres which are concentric to the pores are taken into consideration. The following steps are performed:

- The *R* radius of these spheres is calculated:

$$R=sqrt(Rpor2-rcon2) \quad (1)$$

where *R* - radius of spheres that are concentric to the pores, *Rpor* - radius of pores and rcon is the radius of the circular orifices that connect the pores.

- The number of *R* radius spheres located on *Ox*, *Oy*, *Oz* axis is calculated using the following formulas:

$$Nx=round\ (i/2*R) \quad (2)$$

$$Ny=round(j/sqrt(3)\ *\ R)) \quad (3)$$

$$Nz=round(k/(2*sqrt(2/3)*R) \quad (4)$$

where *Nx*, *Ny*, *Nz* - number of spheres on the *Ox,Oy and Oz* axis, *i,j,k* – elements index on *Ox*, *Oy*, *Oz* axis.

- The total number of centers of the *R* radius spheres in the hexagonal network is calculated, actually representing the total number of pores in the network

- The layers on *Oz* axis are run over, one by one, then for each layer, all the afferent lines are run over one at a time (odd, respectively even), and for each line all the afferent nodes are run over as the *x*, *y*, *z* coordinates of the pores' centers (respectively the centers of the spheres concentric to the pores) are calculated.

After creating the geometry of the controlled porosity biomaterial, knowing the radius and centers of the pores, we associate to the biomaterial a three-dimensional matrix which we initialize with biomaterial particles, identifiable in the matrix through an index. On the positions afferent to the pores, the value *0* which is associated with the medium particles will be subsequently placed, given the fact that the scaffold bathes in the medium culture (Neagu et Al., 2006).

The three-dimensional matrix associated to the porous scaffold with controlled architecture is saved in a text file, allowing the visualization of the obtained model in a graphical form.

3. CELL SUSPENSION MODELING

In order to model the cell suspension of a certain concentration, a three-dimensional matrix which is initialized with the value *0* (representing medium particles) is associated. It is considered that the cell suspension contains two different types of cells, each type of cell having an associated index (Neagu et Al., 2006).The indexes afferent to the cells are placed in different nodes of the matrix, randomly chosen, so that the concentration of the cells in suspension does not surpass *0, 1%.*

4. BIOLOGICAL SYSTEM MODELING

In order to achieve some simulations of cell seeding process on a porous scaffold, we considered the following biological system: a suspension of cells, located in the neighborhood of a porous scaffold bathed in culture medium.

The model associated with this biological system is represented by a three-dimensional matrix that is obtained by linking along the Oz axis the two three-dimensional matrixes, associated with the porous scaffold, respectively with the cell suspension located in the neighborhood of the scaffold (Semple et Al., 2005). The three-dimensional matrix associated with this biological system is stored in a text file, allowing the visualization of the obtained model in a graphical form.

5. GRAPHIC VISUALISATION

A dedicate software tool (Visual Molecular Dynamics) is used to perform a graphical representation of the mathematical model implementing the controlled structure scaffold and the cell suspension in order to validate the chosen modeling strategy.(Figure 1)(Robu et Al., 2010)

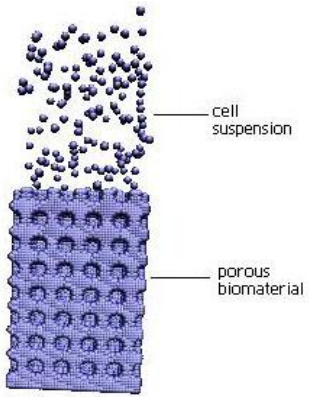

Fig. 1. Graphical representation of a porous scaffold and a cell suspension located in its neighbourhood

In Figure 2 we can see the graphic representation of several models of scaffolds with controlled porosity. The radius of pores and the radius of circular orifices that connect the pores are adjusted so that the pore size and the distance between their centers vary.

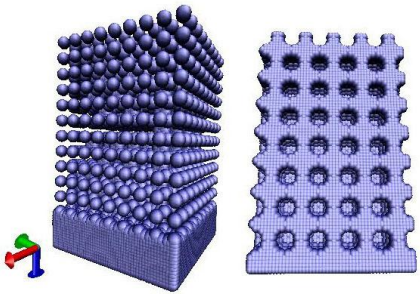

Fig. 2. Models of porous scaffolds

6. CONCLUSIONS

Tissue engineering is a relatively new domain, in full rise at present, and has as a main purpose to create in vitro new tissues capable to replace tissues destroyed or affected by different types of disease inside the human body.

The authors have developed a model based on a three-dimensional matrix for a porous structure biomaterial with a controlled architecture and a cell suspension located in its neighborhood, in order to simulate on a computer the cell seeding and cell division processes.

The importance of computer modeling and simulating in regenerative medicine and tissue engineering is very high, since the computer simulations are relatively quick and inexpensive means to test the work hypothesis and design of the parameters of the new experiments.

Obviously, in the absence of the modeling-simulating methods and instruments, the assigned time and resources for these experiments would be far greater and the analysis variants would be far fewer.

As future development directions, the following aspects are interesting:

- the study of cell seeding process based on the model created, including the time parameter
- development of new algorithms that analyze the influence of cell type and cell shape in the cell seeding process
- building models for the usual forms of scaffold in tissue engineering, such as tablets with a 1 cm diameter and 0.5 cm thick. The biological system studied will be formed from this scaffold bathed in cell suspension. We will study how this cell seeding process evolves on the scaffold, as a function of porosity and interactions between cell-cell and cell-biomaterial
- there can be implemented division and cell death phenomena, to follow the time evolution of tissue structures after cell seeding (during their cultivation on scaffolds).

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