Chapter 4
Computer Aided Tissue Engineering from Modeling to Manufacturing

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ABSTRACT

Computer aided tissue engineering integrates advances of multidisciplinary fields of biology, biomedical engineering, and modern design and manufacturing. It enables the application of advanced computer aided technologies and biomechanical engineering principles to derive systematic solutions for complex tissue engineering problems. After an introduction to tissue engineering, this chapter presents the recent development on computer aided tissue engineering, including computer aided tissue modeling, computer aided tissue scaffold informatics and biomimetic design, and computer aided biomanufacturing.

INTRODUCTION

Tissue engineering, a field of science which is approximately a decade old, has been labeled as one of the more promising domains within the broader field of biotechnology. In a simple definition, it is an interdisciplinary field that applies the principles and methods of bioengineering, material science, and life sciences toward the assembly of biologic substitutes that will restore, maintain, and improve tissue functions following damage either by disease or traumatic processes. The general principles of tissue engineering involve combining living cells with a natural/synthetic scaffold to build a three-dimensional living construct that is functionally, structurally and mechanically equal to the tissue that is to be replaced. Tissue engineering is founded on three principal components (Scaffolds, Cells, Growth Factor and Mechanical Stress), which may be used independently or incorporated in combinatorial form (Figure 1).

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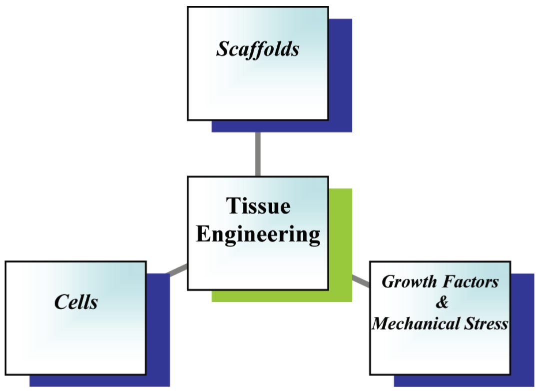
Figure 1. Principal components of the tissue engineering



Scaffold materials are three-dimensional tissue structures that guide the organization, growth and differentiation of cells. There are several requirements in the design of scaffolds for tissue engineering. Many of these requirements are complex and not yet fully understood. In addition to being biocompatible both in bulk and degraded form, these scaffolds should possess appropriate mechanical properties to provide the correct stress environment for the tissues. Also, the scaffolds should be porous and permeable to permit the ingress of cells and nutrients, and should exhibit the appropriate surface structure and chemistry for cell attachment.

Cells are a key to tissue regeneration and repair due to their proliferation and differentiation, cell-to-cell signaling, biomolecule production, and formation of extracellular matrix. The functionality of an engineered tissue may be structural (e.g., bone, cartilage, and skin) or metabolic (e.g., liver, pancreas), or both. Cells may be a part of an engineered tissue, or alternatively, these cells may be recruited in vivo with the help of biomaterials or biomolecules.

Growth factors are soluble peptides capable of binding cellular receptors and producing either a permissive or preventive cellular response toward differentiation and proliferation of tissue. All cells and tissues of the organism are continually subject to mechanical stresses. These forces have many various origins, from pressure forces linked to gravity to motion forces (i.e., blood circulation, loading on cartilage and bone during activity and etc.). Their range is a few Pascals in vascular wall shear stress and several mega Pascals in hip cartilage. It has now been accepted that these applied forces are likely to modify cellular behavior by affecting metabolism, paracrine or autocrine factor secretion and gene expression.

In early tissue engineering trials the aim of bioreactor culture was to provide nutrient perfusion to cells in the centre of a thick construct. There were two different bioreactors systems, in common usage; rotating wall or perfusion systems. In rotating wall bioreactors samples are suspended in culture medium in a cylindrical chamber and the cylinder rotated at a speed that allows the constructs to fall through the medium but not hit the sides. Perfusion bioreactors involve pumping of nutrient containing medium through the construct. Since these systems apply mechanical forces as well as allowing nutrient movement it is hard to separate the two effects. The stresses and strains applied to the cells are not measurable in these basic bioreactor systems, making it difficult to fine tune the system or understand the mechanism of increased tissue formation. While research in biorheology and biomechanics have in the last decades helped understanding the physical properties of cells and tissues, recent works have focussed on the physiological consequences of applied stresses and opened a new avenue for research that can be defined as mechanobiology, leading through its applications to a better understanding of a variety of diseases or pathological conditions and to novel therapeutical approaches using tissue engineering concept and the development of a new generation of biomaterials. In general mechanobiology is the study of how cells respond to mechanical forces and many cell types have been studied in vitro in order to tease out the signaling mechanisms by which a mechanical force results in a biochemical response. For instance, a layer

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