Simulation of Multiple Cell Population Dynamics Using a 3-D Cellular Automata Model for Tissue Growth

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ABSTRACT

In this paper, the authors describe a computational model for the growth of multicellular tissues using a discrete approach based on cellular automata to simulate the tissue growth rates and population dynamics of multiple populations of proliferating and migrating cells. Each population of cells has its own division, motion, collision, and aggregation characteristics. These random dynamic processes can be modeled by appropriately choosing the governing rules of the state transitions of each computational site. This extended model contains a number of system parameters that allow their effects on the volume coverage, the overall tissue growth rate, and some other aspects of cell behavior like the average speed of locomotion to be explored. These discrete systems provide an alternative approach to continuous models for the purpose of describing the temporal dynamics of complex systems.

Keywords: 3-D Modeling, Cellular Automata, Complex Systems, Computational Models, Tissue Growth

INTRODUCTION

A primary goal of tissue engineering is to create three-dimensional tissues with the proper structure and function. Natural tissues are multicellular and have a specific three-dimensional architecture (Palsson & Bhatia, 2004). This structure is supported by an extracellular matrix (ECM). The ECM often has the form of a three-dimensional network of cross-linked protein strands (see Figure 1). In addition to determining the mechanical properties of a tissue, the ECM plays many important roles in tissue development. Biochemical and biophysical signals from the ECM modulate fundamental cellular activities, including adhesion, migration, proliferation, differentiation, and programmed cell death (Soll & Wessels, 1998). Scaffold properties, cell activities like adhesion or migration, and external stimuli that modulate cellular functions are among the many factors that affect the growth rate of

Figure 1. A scanning electron micrograph showing the three-dimensional structure of an extracellular matrix
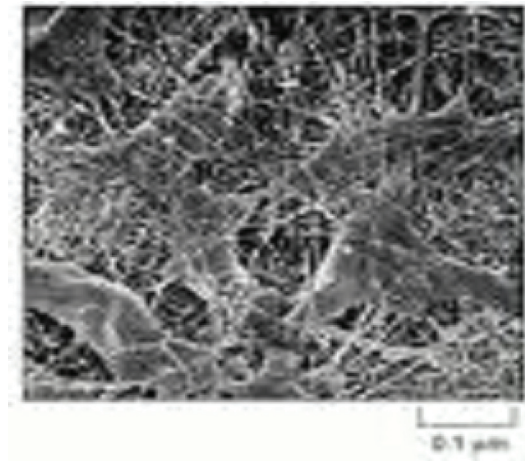
tissues (Langer & Vacanti, 1993). Hence, the development of bio-artificial tissue substitutes involves extensive and time-consuming experimentation. The availability of computational models with predictive abilities will greatly speed up progress in this area.

This research describes a three-dimensional cellular automaton model to simulate the growth of three-dimensional tissues consisting of more than one cell type. The corresponding discrete model is an extension of a previously developed base model that accounted for only a single type of cells in the simulation of cell population dynamics. The model incorporates all the elementary features of cell division and locomotion including the complicated dynamic phenomena occurring when cells collide or aggregate. Each computational element is represented by a site within a cubic lattice. While the assumption of cubic living cells does not reflect the true morphology of migrating or confluent mammalian cells, it allows us to use data structures that minimize memory and computational time requirements. Here, each computational site interacts with its neighbors that are to its north, east, west, south, and immediately above it or below it as shown in Figure 2. This is the *von Neumann* neighborhood in three dimensions (Tchuente, 1987).

In this article, we describe a three-dimensional computational model for tissue growth using multiple cell types. Based on the obtained simulation results, we analyze the effects of key system parameters on the tissue growth rate and volume coverage, in the context of a uniform seeding topology employing two types of cell populations. In particular, we explore the following three questions:

- What are the effects of cell distribution, seeding density, and heterogeneity on the tissue growth rate?
- What is the effect of cell motility on the tissue growth rate?
- Under what circumstances, a given type of uniform distribution may be the better choice for cell seeding?

We begin by defining cellular automata and listing their advantages in the next section. This is followed by a review of related work and a concise description of the development of the model. We then present the corresponding sequential algorithm. Before concluding this study, we give an overview of the important parameters and inputs of the model and discuss our performance and simulation results.

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