Mathematical models for simulating large cell colonies in parallel computer environments: application to burn injuries

Supervisor at DUT: Dr. Ir. Fred Vermolen
Supervisor at VORtech: Dr. Ir. Jok Tang

Biological- and mathematical background

Biomedical processes are often poorly understood in terms of the underlying biology and in many cases physicians need to decide which treatment is appropriate for the patient they are dealing with. To this extent, it is important to judge, and more importantly, to predict the patient's medical condition. Since *in vivo* (clinical) experiments are hard to carry out on patients and animals and since extrapolating the limited amount of experimental data is prone to errors, computational methods have gained increased interest among physicians over the last couple of decades. Next to the predictive power that computational methods can have, computational methods are also used to gain further fundamental insight into the underlying biological mechanisms for certain diseases, such as cancer, skin and organ injuries. For some decades, computational methods have existed in the form of solutions of complex systems of partial differential equations where finite-element methods are often used to solve problems on an organ scale. Next to the partial differential equations based models, new mathematical models have been developed that treat cells individually, where direct experimental input is used in the simulations. This class of models is based on systems of ordinary differential equations. Since cells have their individual properties (even cells of the same phenotype), it is not known in advance when they proliferate (divide), die (apoptosis), mutate or differentiate (specialise). These aspects introduce the concept of uncertainty into the model. A further source of uncertainty concerns the migratory pathways of the cells. A further important issue is the pulling forces of cells onto their environment as well as their secretion of chemokines over the region that they occupy. Combining all these aspects into a model gives a model consisting of large systems of ordinary and partial stochastic differential equations with several stochastic processes that need to be addressed using a combination of Euler-Maruyama methods and finite-element discretisations. Several versions of the model have been developed for modelling cell colonies in the context of cancer initiation, wound closure, wound contraction and even for the case of angiogenesis, which is the formation of blood vessels in several parts of the (human) body as an important biomedical process in wound healing, organ development and cancer metastasis.

Project description

In this project, we will mainly focus on the contraction of burns as well as on the formation of hypertrophic scar tissue, which lead to disability of the patient as well as to aesthetic problems. One of the main challenges is the creation of a parallel computational environment under CUDA so that the GPU of computers can be used to solve large colonies of cells. Such an environment will enable to deal with very large numbers of cells within reasonable computation times, which will further allow to treat the development of a contracture as well as a hypertrophic scar on the skin tissue. A further challenge is to implement a finite-element framework for the simulation of the mechanical balance around the burn. This mechanical process can possibly be modelled using morpho-elastic constitutive laws. A final challenge is the coupling of the cell-based model to the mechanical finite-element method.

Scientific challenge

It is not yet known how this system of coupled ordinary stochastic equations for cell migration, combined with the stochastic processes for death, mutation, proliferation and differentiation can be dealt with in the most efficient way. Once this interface has been created, then this will open the road to simulating alternative applications such as allergic reactions of skin to cosmetic products, or contractures and hypertrophic scars related with burn injuries, to mention a few scientific challenges to come. It is also noted that such models are very interesting for visualisation and suitable for educational purposes for health care students as well for patients and for the general audience. The project will be carried out at the VORtech in Delft. This is a company that focuses

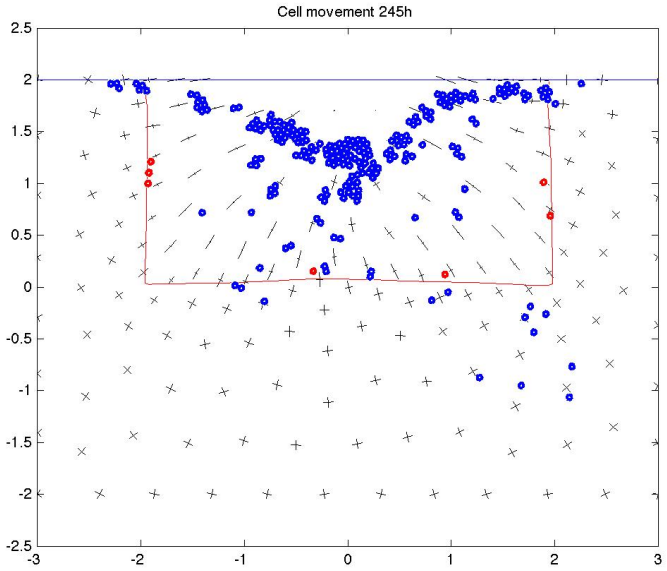

Figure 1: A snapshot of a simulation of contraction of a burn using a particle model. The red circles display immune cells that trigger the migration of (myo)fibroblasts (skin cells represented by the blue circles). The crosses reflect the dynamic orientation of the skin. The red curve represents the boundary of the damaged region.

on mathematical modelling and scientific software engineers. In the project, VORtech's scientific software engineers will assist to work on efficient algorithms and code to be run on the GPU. For an example of the visualisation of the angiogenesis model, we refer to Figure 1.

Planning

First some literature will be read about the model, as well as about the basics of the integration of ordinary differential equations for the migratory pathways of the cells. Further the project requires some basic knowledge about the stochastic processes that are important in this application. This will be done in the first month. In the period between the second and fifth month, the software will be developed for the implementation of large cell colonies. We will do so by starting with cell migration, where several parts, such long-distance communication and physical contact will be dealt with (in the second month). The third month will involve the introduction of stochastic processes in migration through Wiener and Levi processes, as well as Poisson processes for cell division, mutation, differentiation and death. The fourth–seventh month will deal with the concentration fields, where, in this project, Finite-element solutions to the diffusion equation will be used for the computation of concentration fields of chemokines and the coupling between the finite-element scheme and the cell-based method. The eight month can be used for the extension of the model to various applications, such as angiogenesis. The nineth month is meant for the finalisation of the MSc thesis and numerical simulations.