Getting under your skin— simulations of the human body

1 Purpose and aims

Investigation of the function or malfunction of the human body through experiments on human subjects is problematic both from an ethical and practical point of view. Numerical simulations are therefore very important as a complement to or a substitute for clinical studies. In this project, we focus on two categories of processes that are ubiquitous in our bodies:

Reaction-diffusion processes. These represent the dynamics of viral infections and the provoked immune responses as well as the chemical balance within organs and soft tissue.

Motion and deformation. The heart and the respiratory system are the most obvious (elastic) moving parts in the human body, but also general muscle function falls into this category.

The aim of the project is to develop robust numerical simulation methods for these two types of problems. The methods will be developed and tested in collaboration with medical experts to ensure that they are advanced enough to handle real problems.

2 The medical applications

One particular application is chosen to represent each category of problem.

2.1 Chronic liver infections

Assume that the liver of a patient becomes infected with a virus such as hepatitis C. This will trigger an immune response and lymphocytes will enter the liver through the blood vessels. In a favorable situation, the immune system will eliminate the virus. However, we are interested the case where the infection becomes chronic, i.e., a viable virus population remains. The virus and lymphocyte populations can be modeled by a system of reaction-diffusion equations. A chronic infection is represented by a non-trivial steady-state solution. In [5] it is shown that in a two-dimensional unit square liver, there cannot be any chronic infections. However, when a fissure is introduced in the liver geometry, it allows a fraction of the virus population to survive. Hence, the geometry is shown to be of crucial importance for the outcome. A real liver consists of several lobes as illustrated in Figure 1, and can also have other irregularities such as holes and fissures, particularly in patients with illnesses.

Figure 1: Left: An example of a real liver (sheep), clearly showing different lobes. Right: A mass-spring model of the diaphragm, constructed as two connected surfaces [8].

2.2 Ventilator induced diaphragmatic dysfunction

For patients in critical care, the life support may ironically enough cause further damage and later complications. Ventilator induced diaphragmatic dysfunction (VIDD) [7], simply explained, is caused by the fact that the ventilator that assists breathing forces air into the lungs, which in turn stretches the diaphragm muscles. In natural breathing, the diaphragm contracts to pull air into the lungs by creating a negative pressure difference. The unnatural state resulting from the ventilation causes the diaphragm muscles to atrophy rapidly. It is highly desirable to design counter measures to this problem, but it is not possible to perform experiments on critically ill patients. Some tests using rats have been performed, but this is also difficult due to the difference in scale. Hence computer modeling is a very attractive alternative.

3 RBF methods

Most of the computational difficulties in performing medically relevant numerical simulations of the human body lie in the mathematical modeling and in the meshing and re-meshing of the complicated and potentially moving geometries.

Radial basis function (RBF) approximation methods for numerical solution of differential equations are meshfree. However, scattered nodes still need to be distributed within the domain, but this is an easier task. RBF approximation has been used successfully for reaction-diffusion equations on three-dimensional surfaces in [3]. It is also a popular method for computing mesh deformations [1], which may have some bearing on the human body deformation problems.

Some of our recent results in RBF approximation can be particularly relevant in the context of this project. A persistent problem in RBF approximation has been the ill-conditioning of the linear systems that arise. However, in [2, 6] we have derived a way to circumvent this ill-conditioning both for interpolation and PDE approximation in up to three space dimensions. Another problem is the computational cost for global methods, which lead to dense systems of equations. What we could do when we had the stable method was to construct localized RBF approximation methods which then become computationally less expensive as well as more flexible with respect to the local properties of the solution. Preliminary results for an RBF-based partition of unity method are described in [4].

4 Project description

For both of the application areas, we will use RBF-based partition of unity methods. This means that the computational domain is covered by overlapping patches; for each of these patches, a local approximation function is defined; then the local solutions are added together using partition of unity weight functions to form the global solution.

Using RBFs for the local solutions means that no meshing is required and that whenever the solution is smooth, we can achieve spectral convergence. The partition of unity formulation allows for local adaptivity, since the local approximations can be varied independently of each other. It is also useful for separating parts of the computational domain that are close, but not connected, by assigning them to different patches.

The main challenge apart from those specifically connected with the problem is to design an efficient adaptive method. This will be necessary in order to keep the computational cost down in the presence of sharp gradients or local large deformations. Criteria for node refinement that are suitable for RBF methods are needed as well as

algorithms for node insertion and deletion that reuse previous computations.

5 Collaborations

- Dr. Antje Vollrath, Institut Computational Mathematics, Technische Universität Braunschweig, modelling of liver infections.
- MD, PhD Nicola Cacciani Dept. of Neurosciences (Basic and clinical muscle research laboratory), Uppsala University, VIDD.
- Dr. Alfa Heryudono, Department of Mathematics, University of Massachusetts Dartmouth, adaptive RBF approximation.
- Dr. Francisco Bernal, Departamento de Matemática, University of Lisbon, RBF approximation and non-linear problems.

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