Presented at the COMSOL Conference 2009 Milan

Modeling Interface Response in Cellular Adhesion

G. Megali, D. Pellicanò, M. Cacciola, F. Calarco, D. De Carlo, F. Laganà and F.C. Morabito
D.I.M.E.T. Department – Faculty of Engineering, Mediterranea University of Reggio Calabria
Reggio Calabria, Italy

COMSOL CONFERENCE 2009
OCTOBER 14-16 2009, MILAN, ITALY

ABSTRACT

Constitutive properties of living cells are able to withstand physiological environment as well as mechanical stimuli occurring within and outside the body. In this context, a quantitative study in single cell mechanics needs to be conducted. Particularly, we will examine fluid flow and Neo-Hookean deformation related to the rolling effect. A mechanical model to describe the cellular adhesion with detachment is here proposed. We develop a Finite Element analysis, simulating blood cells attached on vessel wall. Restricting the interest on the contact surface and elaborating again the computational results, we develop an equivalent spring model. The simulation notices deformation inhomogeneities (i.e. areas with different concentrations having different deformation values). This important observation should be connected with a specific form of the stored energy deformation. In this case, it loses the standard convexity to show a non-monotone deformation law. Consequently, we have more minimum and the variational problem seems more difficult.

INTRODUCTION TO THE PROBLEM

In order to physically model and determine the effect of the blood flow in presence of a human cell, a Finite Element Method (FEM)-based approach has been exploited. It requires the geometrical and physical definition of the blood vessel, the cell and flow parameters. For our purpose, we verify cell deformation under actual conditions. Thus, a brief description of the theoretical framework for the mechanical is given. Then, we describe the exploited approach through FEM analysis simulating the human cell and the blood flow, and so modeling an endothelial wall cross of a blood flow.

Our aim was to focus the contact part among cell and endothelial wall about the deformation field. Our opinion is that the simulation notice the deformation inhomogeneity namely different concentration areas with different deformation values. This important observation should be connected with a specific form of the stored energy deformation that, in this case, loses the standard convexity to show the multy-well form. Consequently, we have more minimum and the variational problem seems more difficulty.

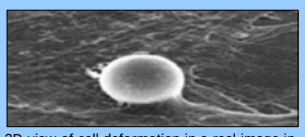
Solutions through minimizing sequence are applied and this relieve microstructure formation.

PROBLEM MODELING and FEM APPROACH

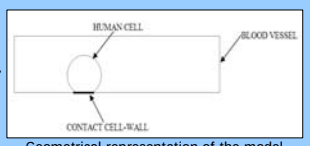
Using our FEM package, the blood flow and pressure drop across human cell have been studied and a mathematical model of the process has been constructed and analyzed. The constructed mathematical model consists of the equations of continuity (representing conservation of mass), motion (representing conservation of momentum) for the flow of blood through human cell.
The model consists of a fluid part, solved with the Navier-Stokes equations in the flow channel, and a structural mechanics part, which you solve in the human cell. Fluid flow is described by the Navier-Stokes equations for the velocity field, **u**=(u, v), and the pressure, p, in the spatial (deformed) moving coordinate system:

1. $\rho \frac{\partial \mathbf{u}}{\partial t} - \nabla \cdot [-p\mathbf{I} + \eta(\nabla \mathbf{u} + (\nabla \mathbf{u})^T)] + \rho((\mathbf{u} - \mathbf{u}_m)\cdot\nabla)\mathbf{u} = \mathbf{F}$
2. $-\nabla \cdot \mathbf{u} = 0$

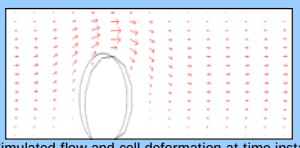
In these equations, **I** denotes the unit diagonal matrix and **F** is the volume force affecting the fluid. Assume that no gravitation or other volume forces affect the fluid, so that **F**=0. The Navier-Stokes equations are solved in the spatial (deformed) coordinate system. At the inlet, the model uses a fully developed laminar flow. Zero pressure is applied at the outlet. No-slip boundary conditions, that is **u** = 0, are used at all other boundaries. Note that this is a valid condition only as long as you are solving the stationary problem. In this transient version of the same model, with the cell starting out from an undeformed state, it is necessary to state that the fluid flow velocity be the same as the velocity of the deforming obstacle. The coordinate system velocity is $\mathbf{u}=(u_m, v_m)$. At the channel entrance on the left, the flow has fully developed laminar characteristics with a parabolic velocity profile (see figure on the left) but its amplitude changes with time. At first, flow increases rapidly, reaching its peak value at 0.215 (s); thereafter it gradually decreases to a steady-state value of 3.33 (cm/s). For boundary conditions, the cell is fixed to the bottom of the fluid channel, so that it cannot move in any direction. All other object boundaries experience a load from the fluid, given by $\mathbf{F}_T = -\mathbf{n}\cdot(-p\mathbf{I} + \eta(\nabla \mathbf{u} + (\nabla \mathbf{u})^T))$, where **n** is the normal vector to the boundary. This load represents a sum of pressure and viscous forces. With deformations of this magnitude, the changes in the fluid flow domain have a visible effect on the flow and on the cell, too (see figure on the right).



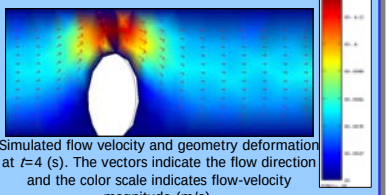
3D-view of cell deformation in a real image in presence of blood flow



Geometrical representation of the model



Simulated flow and cell deformation at time instant t_0=0 (s) and t_1=0.215 (s).



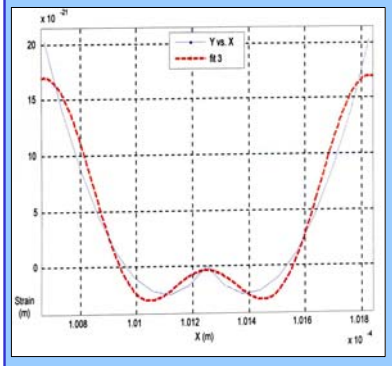
Simulated flow velocity and geometry deformation at *t*=4 (s). The vectors indicate the flow direction and the color scale indicates flow-velocity magnitude (m/s).

The amount of deformation as well as the size and location of the swirls depend on the magnitude of the inflow velocity. Figure further illustrates this point; it compares the average inflow velocity to the horizontal mesh velocity and the horizontal mesh displacement just beside the top of the structure at a generic physical point. Most of time, the deformation follows the inflow velocity quite never the inflow velocity starts to decrease. Toward the end of the simulation, when inflow and structure deformation approach their steady-state values, the mesh velocity also decreases to zero. The edges of the cell are characterized by conditions wall mobile dispersant (structural displacement) with the exception of the base cell which is fixed and not involved in the dynamic physical process, according to

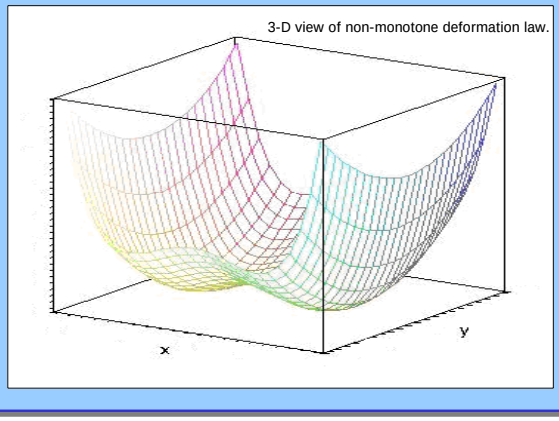
$$\mathbf{n}(\eta_1(\nabla \mathbf{u}_1 + (\nabla \mathbf{u}_1)^T) - \rho_1\mathbf{I} - \eta_2(\nabla \mathbf{u}_2 + (\nabla \mathbf{u}_2)^T) - \rho_2\mathbf{I}) = 0$$

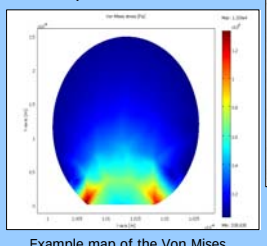
FINAL RESULTS

Simulated results were highly reliable, so our FEA package was very successfully simulating fluid–structure interaction in the human blood vessel. Our interest was to point out the concentration or inhomogeneity of the deformation on the contact area cell-wall. This particular result open the way to simulate the adhesion-detachment problem through more sophisticated model (i.e. functional analysis tools) such that microstructural characterization can be emphasized.

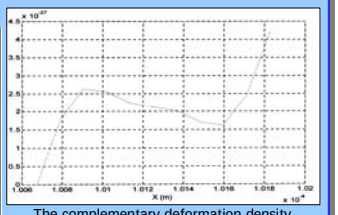


The non-monotone deformation law for a red blood cell.





Example map of the Von Mises stress in a red blood cell.



The complementary deformation density as integral of the deformation function

Acknowledgements
Many thanks to doctor and scientists of Transplant Regional Center of Stam Cells and Cellular Therapy, "A. Neri", Reggio Calabria, Italy, for the availability and for medical support useful to write this paper.
Many thanks also to researcher Buonsanti Michele, professor of mechanical engineering materials at the University "Mediterranea" of Reggio Calabria, Faculty of Engineering - MECMAT Department , for his support about mechanical aspects in human cells analysis.