Modelling of a Single Cardiomyocyte Interaction with a Microcantilever Using COMSOL Multiphysics®

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Abstract: One of the most commonly used techniques for quantification of beating forces exerted by cardiomyocytes is culturing them on a bed of vertical microcantilevers or microposts. The position of the microcantilevers is observed through advanced imaging techniques and the displacements are observed over a period of time. The stiffness of the microcantilevers is known and thus the force can be calculated from the displacements observed. In this paper, an effort is made to develop a computational model of the interactions between the cardiomyocytes and the microcantilevers based on the Fluid-Structure Interaction interface in COMSOL Multiphysics®. The cardiomyocyte along with its culturing medium is considered as a homogenous fluid exerting forces on the microcantilevers as they start maturing and beating.

Keywords: Cardiomyocytes, Microcantilevers, Fluid structure Interaction.

1. Introduction

The mechanics behind contraction and expansion phenomenon of cardiomyocytes or heart cells is still to be understood fully. Information on the contractile force of heart cells will be very helpful in understanding the precise mechanism of heart failure as well as the molecular alterations involved in diseased heart cells. Several theoretical models have been developed for explaining the contraction and expansion phenomenon in cells , the interaction between cellular substrate and cytoplasm as well as the interaction between the cells and their culture medium. Three-dimensional finite element models have been used for the computation of relationships between the applied torque and deformation in cardiomyocytes. Mijailovichand his group [1]evaluated the effects of different degrees of bead embedding and cell height within a geometrically linear range of cell deformation. The cell was modeled as a three dimensional slab with constant height and lateral expansion with spherical beads embedded in it. Further it was considered as a elastic substrate of infinite or semi infinite thickness. For a torque applied across the x axis, displacements were calculated using a Finite Element software. Over the last decade, a number of Finite Element softwares have evolved like COMSOL Multiphysics and ANSYS. Mijailovichand and his group used the PAK Finite Element Software. Satcheret. al [2] modeled the F Actin network of a cell and was able to calculate the deformations using open lattice unit cells which were cubical in shape. They termed it "open cell foams" all of which were interconnected at their midpoints and consisted of struts representing the actin filaments. Deshpande et. al [3] proposed a mechanical model which accounted for the dynamic reorganization of the cytoskeleton. But this was no simple mechanical model and was influenced by three important biochemical processes based on actin and myosin reactions , their assembly into stress fibers and cross bridge cycling between actin and myosin filaments. Ingber and his group did pioneering research on tensegrity in cell mechanics. It seems that the role of the cytoskeleton in the overall mechanical response of the cell was not appreciated until Donald Ingber put a strong emphasis on it. He was the first one to link the cytoskeletal structure to the fascinating art of tensegrity architecture [4,5]. It has been a common practice to culture cellular mediums on a bed of vertical microcantilevers and then observe the deflections produced in the low stiffness microcantilevers as the cells start maturing on the bed of microcantilevers. If the stiffness of the microcantilevers is measured , then from the deflections observed through a high resolution CCD camera , the forces generated by the beating cells can be calculated. In this paper, an effort has been made to model the fluid structure interactions between the cellular substrate and a single microcantilevers. It is probably one of the first efforts to model such an interaction on COMSOL Multiphysics.

2. Background And Governing Equations.

Navier Stokes equation is used for describing the flow of incompressible fluids with velocity field u= (v,u) and pressure p, where u and v denote the two dimensional coordinates of the velocity field.

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

$$-\nabla \cdot \mathbf{u} = 0$$

In our case , we consider the cellular substrate as an incompressible fluid over a bed of vertical microcantilevers where one vertical microcantilever acts as the solid interacting with the incompressible fluid. The structural deformations in the single microcantilever is solved using an elastic formulation and a nonlinear geometry formulation so that large deformations are allowed.

$$\mathbf{F}_T = -\mathbf{n} \cdot (-p\mathbf{I} + \eta(\nabla\mathbf{u} + (\nabla\mathbf{u})^T)) \tag{2}$$

So, the cell is considered as a fluid over the vertical microcantilever bed and each of these microcantilevers are firmly fixed to this bed. Figure 1 shows a typical arrangement of the cellular substrate over a bed of vertical cantilevers.
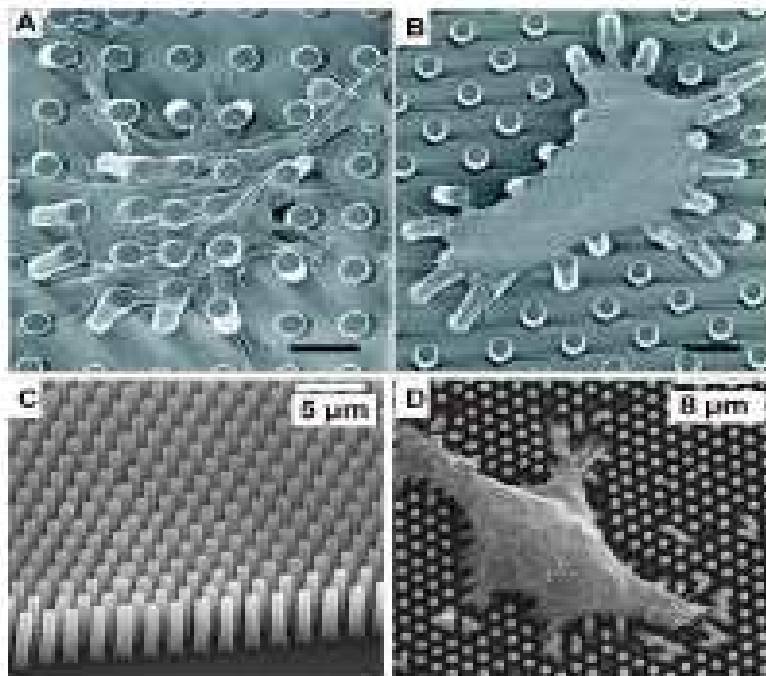

Figure 1 (A,B,C,D) : An array of vertical microcantilevers on which cellular substrate is grown. A,B : Deformations produced in different microcantilevers can be seen due to the cellular substrate. [6]

3. Results And Discussion

For this case, the medium was modeled as an incompressible fluid with a density 1000 kg/m3 and viscosity 0.78×10–3 kg m–1 s–1 . The flow is governed by the continuity and Navier–Stokes equation. The flow is considered in both the directions with different velocities for the contraction and expansion phenomenon. The interactions between a culturing medium of cardiomyocytes with a single vertical microcantilever was modeled. The vertical microcantilever considered has dimensions of 500 um in length, 100 um in width, and 0.9 um in thickness with a nominal spring constant of 0.02 N/m. For these simulations, the Fluid-Structure Interaction interface in COMSOL Multiphysics® has been used. The fluid structure interactional model is modelled in Figure 2 shown below.
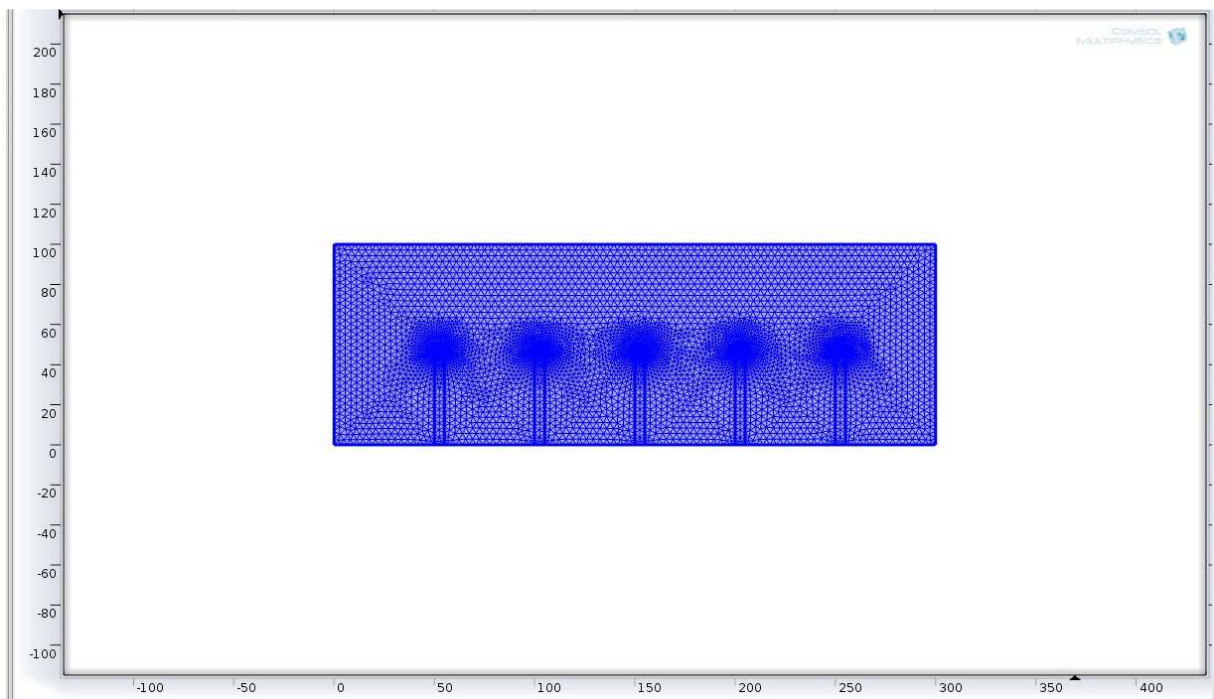

Figure 2 : Fluid Structure Interaction Model of five Vertical microcantilevers with cellular fluid, showing mesh at the top of the cantilevers at t=0s.

4. Conclusion

Such kind of models give a fair idea on how to model a cell if certain properties of the cell are known from previous experiments. This is a new computational modeling approach for quantifying the contactile forces in cardiomyocytes based on 3D Fluid–Structure Interactions (FSI) using COMSOL Multiphysics®.

A comparison of the experimental results with the proposed model showed that the new proposed model represented the real system well, and the differences between FSI results and the FEM results were small.

References

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