NSF CDS&E-MSS Proposal # 1317671

Title: Mathematical Models and Computational Methods for the Tumor Microenvironment
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The main objective of this work is to develop comprehensive mathematical models and computational methods at the microscale for the emergence of ductal carcinoma in situ (DCIS) and the transition to invasive ductal carcinoma (IDC) both *in vivo* and *in vitro* microfluidic devices. The investigator and his colleagues develop computational methods for the microenvironment models based on integrated second-order finite volume methods for each of the system components - fluid mechanics, chemical and ion transport in the bulk fluid, reactions on the cell membrane, transport through the cell membrane, and fluid/structure interaction of the elastic biological cells. The modeling innovation includes the incorporation of ion transport, reaction, and diffusion in a cells-based model with detailed membrane reaction kinetics and membrane transport. This is coupled with internal kinetics and growth processes of individual cells. Another innovation is the incorporation of Lagrangian mesh based models for the viscoelastic properties of matrigel and extracellular matrix.

Breast cancer is the second-leading cause of death in women in developed countries. In USA alone, 230,480 women were diagnosed with invasive breast cancer in 2011 and an estimated 57,650 women were tested positive with non invasive ductal carcinoma (DCIS). Although DCIS itself is not life-threatening, it has a high probability of progression to IDC if left untreated. In this project, the investigator and his colleagues study tumor microenvironments in DCIS and its progression to IDC. Successful completion of this project provides a fundamental change in modeling of tumor evolution where the identity of each cell is of importance. Although focus has been placed on modeling ductal carcinoma, one can extend these techniques to the study of *variety of* biological processes. A number of research fields are benefited from this work. These include cell biology, systems biology, biomedical engineering, computational fluid mechanics, and applied and computational mathematics. In addition to this technical impact, the project provides a unique educational opportunity to train graduate and undergraduate students as well as high school teachers in multidisciplinary environments.