Utilization of Smart Materials and Predictive Modeling to Integrate Intracellular Dynamics with Cell Biomechanics and Collective Tissue Behavior

A grand challenge in biomechanics and mechanobiology is that of understanding the complex interactions that occur between intracellular structures and how those interactions produce function at the cell and tissue levels. The goal here is to employ programmable materials from the field of biomaterials science, particle-tracking algorithms from the fields of biomechanics and biophysics, and molecular probes from the fields of cell and molecular biology to track and model the interaction of multiple intracellular components and the resultant large-scale cellular behaviors. Through three objectives, the project will yield a method for quantitatively characterizing interactions between intracellular components and linking those patterns with large-scale behaviors such as cell polarization. First, the biomechanical sequence of cell polarization at the intracellular

level will be elucidated via automated, synchronized tracking of multiple components in single cells in highly constrained environments. Second, cell polarization will be induced in individual cells using "smart substrates" and patterns in intracellular components will be linked to this large-scale cell behavior. Third, cell polarization will be studied and modeled, from the intracellular to multicellular levels, in a model of contact inhibition release/localized epithelial-mesenchymal transition with high cell densities.

Coordinated cell movements are critical to biological processes such as embryonic development, cancer progression, and wound healing. Although cell movement is generated

by structures inside cells, it is not known how interactions of those structures produce cell movement and resulting organization within groups of cells. This project will answer that question. A new computational approach will quantify the simultaneously interactions of several different important structures inside cells. New "smart" material will be used to trigger changes to cell movement, and the computational approach will determine how interactions of structures inside cells also change. Both low cell densities, where cells interact rarely, and high cell densities, where cells are always touching as happens in living organisms, will be studied. A model for collective movement of large groups of cells that can make predictions about tissues formation and disease will be developed. Research, education, and diversity at both collaborating institutions will be further integrated through a yearly summer research program that will recruit exceptional Hampton University students as undergraduate researchers. Society will benefit from the technical and professional development of the individuals involved, important advances in the fields of biomechanics, biophysics, and biology, and breakthroughs that can be anticipated in healthcare fields.

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