ME MTech (Res) Thesis Colloquium

Mechanics of Collective Cell Migration on Substrates of Different Stiffness

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ABSTRACT

Collective cell migration is characteristic in many physiological processes such as wound closure, morphogenesis, and cancer tumour metastasis. Experiments on cell monolayers demonstrated the formation of finger-like patterns that are guided by leader cells at their tips which help advance the edge during migrations. Recent studies also showed that the substrate stiffness was a critical factor in altering cell migrations on different substrates which were quantified based on areal expansion of the monolayer and peripheral speed of the cells in the edge. These differences correlated with the presence of differential acto-myosin cable tension in the monolayer edge, the creation of differential numbers of leader cells in the monolayer, focal adhesion areas and cell expansion on the various substrates. These studies provided valuable insights on collective cell migrations but did not discuss the mechanistic reasons underlying these differences. In silico studies have showed the importance of intercellular forces, cell expansions, proliferations, and contour forces in the monolayer in modelling the monolayer expansion over time.

The goals of my study are to better understand the influence of various factors in the monolayer cell migrations on substrate of different stiffness. We developed a particle - particle interaction model to simulate the circular expansion of cell monolayers that were based on published experiments. The model allows us to vary the acto-myosin contractility on the edges, border forces and cell expansions qualitatively as shown in the experiments on different substrate stiffness. We parametric varied these terms to quantify their individual roles in the collective behaviours of cells on two dimensional substrates of 9.4 kPa and 33 kPa which is similar to that of tissues. Our results show that the peripheral velocities and areal expansion of simulation were in the range of experimentally reported values as also the percentage of leader cells that have not been shown earlier. We also show that the percentage of leaders depend on the difference in the magnitude of border migration force and the bulk actomyosin contractility force. We used these parameters to explore the cellular migrations on substrate with stiffness of 21 kPa which demonstrated a higher percentage of leader cells as compared to migrations on 9.4 and 33 kPa substrates. The actomyosin contractility force and the border forces were similar to those in the case of the stiffer gel that had a lower number of leader cells. We show that the individual cell expansions greatly reduced the overall monolayer expansion in the model and also created consistently higher percentage of leader cells which were similar to that reported in the experiments. Together, these results demonstrate that the leader cell formation in monolayer expansions not only depend on actomyosin contractility force and border force, which act on the contour, but also depend on the expansion of individual cells in the monolayer.

ABOUT THE SPEAKER

Suvakash Dey is a M.Tech (Research) student in the Biomechanics laboratory in the Dept. of Mechanical Engineering, IISc. His research interests include biomechanics, solid mechanics.

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