How Adhesion Regulates Cell Migration Plasticity: A Computational Study

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Short Abstract — Cell migration is important for development, wound healing and cancer invasion. It is a complex process that involves multi-scale interactions between cells and the extracellular matrix (ECM). Empirical evidence of cell migration showed that the cell substrate interaction through focal adhesion is a key mechanism to regulate cell migration plasticity. How the cell integrates the biomechanical properties of microenvironment with cytoskeleton remodeling to initiate polarity, adhesion and regulate migration modes is still not clear. Increasing experimental evidence suggests that migration behaviors differ and transit over physical parameters, including substrate rigidity, topography, and cell property. We built a 3-D cell model with cell motility signaling pathway and explicit cell membrane, cytoskeleton, nucleus. We simulated cell migration in 1-D and 2-D substrates with varied distribution and intensity. The model provides a flexible platform for investigating cell migration plasticity with complex microenvironments through biomechanical cell-substrate interactions.

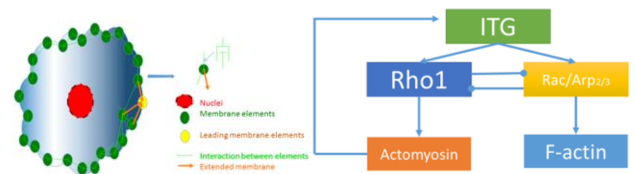
***Keywords* — 3D cell migration, amoeboid, mesenchymal, cancer invasion, signal pathway.**

I. Introduction

CELL migration is a fundamental process that regulates numerous physiological functions of biological system [1]. Migrating cells exhibit distinct motility modes and can switch between mesenchymal and various amoeboid motilities [2]. The formation of integrin-mediated adhesion breaks the cell symmetry, followed by signal transduction and generations of interruptions of lamellipodial extension [3]. Contraction is the main part of the motility process during which the cells explore micro-environment, together with activated cell motility signal pathway, regulate actin and actomyosin spatial intensity and membrane deformation including lamellipodia, filopodia, stable and unstable blebs [2]. To characterize how the adhesion site dimensionality and adhesion intensity regulates cell migration plasticity, we developed a computational model of 3D cell migration in micro-patterned substrate, which reproduces the experimental measurements and provides new insights into the cell migration plasticity.

II. Results

We model cell migration using a subcellular element model [4], which represent a cell as interacting membrane elements together with a deformable cell nucleus through cytoskeletal dynamics. The intracellular reaction-diffusion dynamics of F-actin and actomyosin determine the protrusion *vs*. contractile forces on each membrane element. The cell deforms and moves as a result of force calculation of every membrane element.



The key features of the model are 1) the substrate and integrin distribution regulate focal adhesion formation and adhesion strength, 2) the cell morphological adaption and integrin transportation are solved using 3-D moving boundary diffusion-reaction method, 3) the duration for the cell and substrate binding depends on the number of focal adhesion [5].

From *In vitro* experiments of single cell migration in 3D collagen, we quantify the cell protrusion number and velocity. With our 3-D cell migration model, we simulate the detailed morphological evolution and molecule diffusion-reaction and investigate the cell migration plasticity as a function of binding set width and adhesion intensity. In particular, we focus on studying the resulting cell deformation and migration directionality, cell diffusion coefficient. The results resemble those observed in 3D cell traction experiments as well as 3D cell migration assays.

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