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PROCEEDINGS

A Multiscale Dynamic Model of Cell–Substrate Interfaces

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ABSTRACT

Cell–extracellular matrix (ECM) interactions play a pivotal role in many functions of cells, for example, sensing, signaling, migration, and gene expression. The spatial-temporal dynamic evolution of cell–substrate adhesions involves complicated mechano-bio-chemical coupling mechanisms of integrin, adaptor and signaling proteins, and the interplay between the cytoskeleton and ECM as well. In this paper, we establish a multiscale dynamic model of cell–substrate interfaces considering intermolecular force transmission pathways, i.e., intra- and extra-cellular bond dynamics, and mechanochemical coupling regulations. To illustrate its applications, this model is used to reproduce several adhesion-related experimental phenomena of cells, including substrate rigidity sensing, actin-assisted focal adhesion formation and growth, and biphasic interface stress–actin speed relation. The results suggest that the cluster growth patterns are medicated by the intermolecular force transmission pathway and the actin flow speed, and that the integrin–ligand bond strengthening tends to inhibit the motion of clusters. We reveal that the monotonic-to-biphasic transition of force transmission and adhesion assembly is regulated by the bond rupture mechanosensitivity of integrin adhesion complexes. The adhesion cluster growth in response to substrate elasticity indicates the regulatory effect of integrin internalization. It is also demonstrated that this multiscale dynamic model can well describe the spatial-temporal evolutions of collective cell–substrate adhesions with the effects of actin flow and substrate deformation, and can also capture the morphological features of adhesion clusters and related interface force transmissions. This work provides a theoretical methodology for studying mechano-biochemical mechanisms of cell–substrate interactions and for understanding the subcellular and cellular dynamics of cells in, for example, tumors.

KEYWORDS

Cell–substrate interface; multiscale dynamic model; mechanobiochemical coupling; adhesion; cytoskeleton; integrin

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