254d Controlling the Motion of Cells along a Compliant Substrate by Tailoring Its Mechanical and Topological Properties

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In order to perform various biological assays and tissue engineering studies, it is vital to control the dynamic behavior of in vitro cells. In particular, there is a critical need for "smart" surfaces that can effectively modulate the motion of the cells and thereby allow them to be readily sorted, isolated or encapsulated [1]. To design such smart surfaces, one needs efficient computational models that capture not only the fluid-membrane interactions within the cell, but also the cell-substrate interactions. Herein, we adapt our newly developed hybrid approach [2,3], which couples mesoscale models for hydrodynamics and micromechanics, to examine the dynamic interactions among an encapsulated fluid, the bounding elastic shell (membrane) and a compliant surface. What is unique to our simulations is that we consider how the surfaces' compliance and topography affect the cells' movement. By focusing on compliant surfaces, we find that simple modifications of these substrates permit significant control over the motion of cells. In particular, we isolate systems that affect not only the cell's velocity, but also its specific "gait" or way of moving along the surface. In addition, we uncover surface patterns that can drive the cells to stop at specified locations along the interfaces. Thus, the findings yield guidelines for controlling the in vitro trafficking of cells on elastic surfaces.

Our model of a cell, or vesicle, encompasses an elastic membrane and an encapsulated Newtonian fluid; such a coarse-grained view was adopted in other computational studies of the cells' motion along substrates [4]. We immersed this vesicle in an external host fluid that is confined between two parallel walls. One of these is flat and non-compliant; it moves with a fixed velocity and its sole function is to apply a uniform shear flow. The other one is stationary and serves as our substrate. We used the lattice Boltzmann method to simulate the dynamics of both the encapsulated and the host fluid. The membrane and the substrate were modeled by the lattice spring model, which simulates the dynamics of a continuum elastic material. We implemented solid-fluid interactions that give stick boundary conditions for the fluid and allow for a dynamic interaction between the elastic solids and the adjacent fluid. We focus on a single vesicle, which interacts with the substrate through a Morse potential.

Starting with the simplest case of a planar substrate that has uniform elastic properties, we examine how the vesicle's movement is affected by the magnitude of the interaction strength, and by the ratio between the membrane stiffness and the substrate stiffness. We will show that even for a simple uniform substrate, its compliant nature greatly affects the vesicle's motion along the surface. We then exploit the fact that the vesicle moves differently on a hard or soft surface by creating mechanically patterned surfaces [5], which encompass periodic variations in the stiffness of the substrate, to control the motion of the cells. We will discuss how these substrates can be utilized to control the motion of a vesicle. In particular, we will show that for a range of parameters, the patterned substrate acts to arrest the motion of the vesicle. Finally, we will consider the case where the substrate contains a regular array of compliant "posts", which extend from a flat surface. In the case of "active" cells, such substrates were used to probe the cells' inherent mechanical properties [6]. In the case of fluid driven cells, we find that these topologically patterned compliant substrates affect not only the rolling velocity, but also the manner in which the cells traverse the surface, leading to a "crawling", "walking" or "jumping" motion.

In summary, we will show that the mechanical or topographical patterning of substrates can be harnessed to regulate the motion of vesicles that are driven to move along the surface by an imposed flow. Both the mechanically and topographically patterned surfaces considered here can be readily produced from compliant polymeric substrates using soft lithography and microfabrication techniques [5]. The ability to actively regulate the motion of cells can allow researches to perform various well-controlled biological assays and tissue engineering studies [1].

[1] MRS Bulletin, March 2005, Vol 30, No. 3 [2] G. A. Buxton, R. Verberg, D. Jasnow, and A. C. Balazs, “A Newtonian fluid meets an elastic solid: Coupling lattice Boltzmann and lattice spring models”, Phys. Rev. E (2005), in press. [3] A. Alexeev, R. Verberg, and A. C. Balazs, “Controlling the gait of vesicles by tailoring the properties of compliant substrates”, in preparation. [4] S. Jadhav, C. D. Eggleton, and K. Konstantopoulos, “A 3-D computational model predicts that cell deformation affects selectin-mediated leukocyte rolling”, Biophys. J. 88 (2005) 96-104 (and references therein) [5] D. S. Gray, J. Tien, and C. S. Chen, “Repositioning of cells by mechanotaxis on surfaces with micropatterned Young's modulus”, J. Biomed. Mat. Res. 66A (2003) 605-614. [6] C. A. Lemmon, N. J. Sniadecki, S. A. Ruiz, J. L. Tan, L. H. Romer, and C. S. Chen, “Shear Force at the Cell-Matrix Interface: Enhanced Analysis for Microfabricated Post Array Detectors”, Mech. Chem. Biosys. 2 (2005) 1-16.