Three dimensional traction forces exerted by migrating amoeboid cells


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Summary: We have developed a new method to measure the three dimensional traction stresses exerted by cells migrating over flat substrates. Our measurements suggest two different mechanisms for the generation of the stresses: a contractile tangential force to the substrate (reduced in Myosin II null cells) and a cortical 3D force perpendicular to the substrate (reduced in Cortexillin null cells).

Cell migration is involved in many physiological human processes including embryonic development, wound healing, and the metastatic spreading of cancer. We have developed a method that enables us to determine the cellular traction forces exerted perpendicular to the substrate in addition to the in-plane forces. Therefore we also can analyze the errors associated to existing two-dimensional traction cytometry methods. We obtain information about the substrate deformation by imaging a small volume of the elastic substrate with embedded fluorescent marker beads. Correlation with a reference image enables us to obtain the 3D deformation of the substrate. The corresponding traction forces are obtained by solving the elastostatic equation for a linearly elastic medium using the calculated deformation of the substrate.

Fig. 1. a) Tangential traction forces to the substrate exerted by a Wild type cell at an instant of time. b) Normal traction forces to the substrate exerted by a Wild type cell at an instant of time. The arrows represent the forces direction and the colormap their magnitude. The substrate deformation is increased by a factor of 20 in order to make it better visible.

Our studies of Dictyostelium cells moving over flat substrates are designed to characterize the role of various cytoskeletal components in the organization of the three-dimensional stresses by using Wild type cells and mutants with contractility or adhesion defects. We are looking at Myosin II null and Cortexillin I null mutants in order to study the role that these cytoskeletal components play in the overall distribution of the traction forces. We find that the three cell lines studied push downward on the substrate near the center of the cell and pull up at the periphery. The magnitude of the perpendicular forces is comparable to the magnitude of the tangential forces to the substrate, therefore this perpendicular component is expected to play a significant role in the cell behavior and cannot be neglected. Our initial findings show that the effects of mutations on the tangential forces do not necessarily predict their effect on the perpendicular forces, i.e. myosin II-null cells show a significant reduction of the magnitude and polar distribution of the tangential traction forces while the perpendicular distribution of forces and its magnitude remains unaffected. Our traction force measurements for these three cell lines suggest that the generation of the perpendicular and tangential stresses to the substrate is possibly controlled by two different mechanisms.