A MEMS actuator and sensor for understanding cell-cell adhesion

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We have designed and fabricated a silicon-based Micro Electro-Mechanical System (MEMS) that can apply forces in shear and tension to a sheet of epithelial cells with a resolution of ~20 nN. This device has been designed to study the cell-cell adhesions in clusters of Madin-Darby Canine Kidney (MDCK) epithelial cells. However, it will find use in studying other monolayer forms of cells, e.g., endothelium. The importance of cell mechanics in tissue development, function, and even disease states has been studied for many years. Only recently have scientists begun to recognize the importance of cell-cell adhesion in mechanobiology. For example, it is still not well understood how cells send and sense mechanical signals to and from their neighboring cells. In addition, while there is an appreciation of the fact that disease states such as cancer metastasis include a down-regulation of proteins known to be involved in cell-cell adhesion (e.g. cadherins, beta-catenin, etc.), the exact mechanisms of this change are not well understood. Devices that can apply physiological, measurable, and repeatable forces to cells, combined with a mechanism to quantify the response of the cell to such forces will be important in understanding cell-cell adhesion. Our device consists of two 200 um X 1000 um silicon nitride (transparent glass-like material) cell attachment pads, that can each fit ~500 confluent MDCK cells. After the cells spread on each pad, the two pads can be brought together so that a single attachment line forms between the two sheets. We can then move the two pads with respect to each other in shear or tension and apply forces to the cell sheet in these two dimensions. The pads are electro-statically actuated, but the device is coated with a dielectric and the electrical signals are in high frequency Alternating Current (AC), which allows the device to be fully submerged in ionic media (e.g., cell culture media). With this device, we will characterize the force response of cell-cell adhesions and associated proteins, and also apply pharmacological treatments (e.g., blebbistatin, cytochalasin D, etc.) to understand the role of cytoskeletal tension in cell-cell adhesion. Importantly, the optically transparent silicon nitride sample substrates allow not only application of calibrated, repeatable forces but also live cell imaging with inverted fluorescence microscopy.