

Biocompatible Surfaces with Locally Variable Rigidity

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Physical factors in the environment of a cell regulate cell function and behavior and are involved in the formation and maintenance of tissue. There is evidence that substrate rigidity plays a key role in determining cell response in culture. Previous studies have demonstrated the importance of rigidity in numerous cellular processes, including migration and adhesion^{1, 2} and mesenchymal stem cell differentiation.³ Atypical response to rigidity is also a characteristic of transformed (cancerous) cells.^{4, 5} Thus, it is critical to develop an understanding the role of force and rigidity in defining cell phenotype.

Until now, there has been no way to observe cell behavior on surfaces having a range of rigidities. Based on the observation by Tsougeni et al. that polydimethylsiloxane (PDMS) can be photocrosslinked in the DUV (and in the mid-UV with the addition of a photoactive compound),⁶ we have developed a technique to locally modulate the rigidity of PDMS films lithographically. PDMS is of particular interest because of its widespread use in cellular force transduction experiments.

We have used electron beam lithography to irradiate regions of PDMS at different doses and have characterized the rigidity as a function of dose. Cured PDMS films (~ 20 μm thick) were exposed to a 30 keV electron beam with exposure doses in the range ~ 10 – 200 $\mu\text{C}/\text{cm}^2$ (Fig. 1). (We also found that the PDMS base solution can be crosslinked by direct e-beam exposure.) The mechanical properties of the films were characterized using a Nanoindenter tool. Results of these measurements (Fig. 2) indicate that e-beam exposure over the range explored is more than sufficient to increase the Young's modulus of the PDMS up to several MPa or more.

The flexibility of electron beam patterning enables the modulation of PDMS rigidity over a wide range of dimensions. Thus, for example, we can explore cellular response to a well-defined boundary between regions of different rigidity.⁷ Continuously variable rigidity gradients can be used to determine if there is a preferred rigidity or range of rigidities for a given cell type, and how cells respond when different parts of the cell sense different rigidities. Force transduction measurements can be made as cells traverse areas of different rigidity, thus providing a key tool for exploring these critical factors in cell behavior. In addition, by creating patterns of different geometries and dimensions, we can determine the spatial resolution of cellular rigidity sensing and the molecular mechanisms involved in this process.

In addition to planar surfaces, we have been able to modulate the rigidity of three dimensional PDMS structures, such as pillar arrays used to monitor cellular force transduction. No changes to the pillar dimensions were seen as a result of the exposure (Fig. 3). Figure 4 shows an array of micron-scale PDMS pillars after their removal from water. The high surface tension of the liquid caused pillars in the unexposed region to collapse, whereas the e-beam-exposed pillars remained standing.

Variable rigidity surfaces can play an important role in finding answers to basic biological questions regarding cellular response to external physical factors. They may also be useful in the design of tissue scaffolds and “smart bandages” for wound healing. Beyond applications in biology and medicine, these types of surfaces may be useful in a wide variety of micro- and nanoscale sensors and actuators.

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Dose:
($\mu\text{C}/\text{cm}^2$)

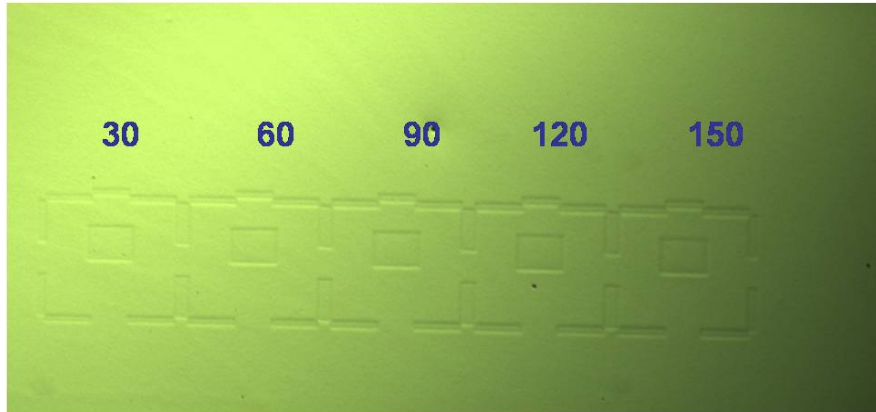


Figure 1. Optical micrograph of PDMS after e-beam exposure for a range of applied doses. AFM measurements indicate no discernable change in the film morphology in the exposed areas.

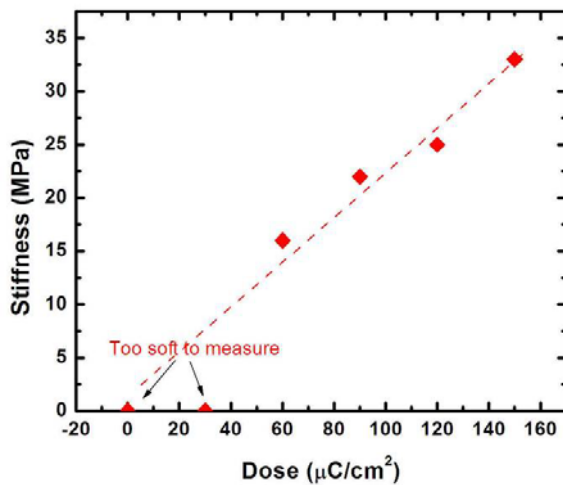


Figure 2. PDMS rigidity as a function of applied e-beam dose.

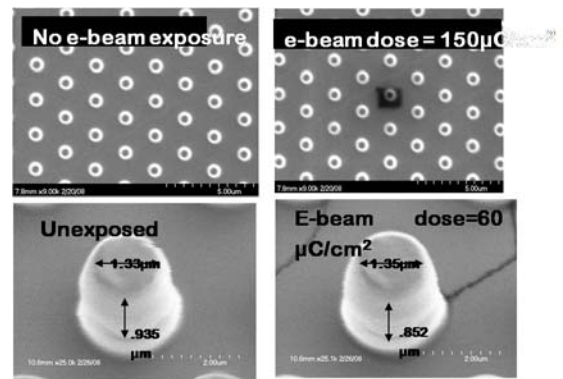


Figure 3. SEM of unexposed (left) and exposed (right) PDMS pillars. No dimensional changes were induced by the exposure.

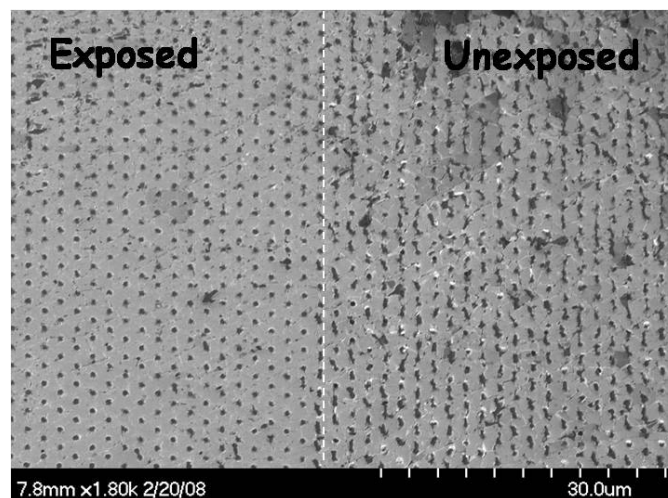


Figure 4. PDMS pillar array after removal from water. Pillars in the unexposed region collapsed due to the surface tension of the water; pillars in the exposed region remained standing.