Micromechanical Substrates for Reconfigurable Cell Culture

E. Hui, S.N. Bhatia
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We have previously demonstrated the use of microfabricated cell culture substrates (Figure 1) to implement reconfigurable cell culture [1]. Specifically, we studied interactions between liver hepatocytes and supportive stromal cells. We found that preservation of liver-specific function depended on signaling from the stroma. Specifically, signaling both through direct contact and through diffusible secreted factors was important. However, while the secreted factors needed to be maintained for the entire duration of culture (2 weeks), direct contact was required only for an 18-hour period early in culture. In addition, the secreted factors were found to have a limited effective range of less than 400 µm.

Through FEM diffusion modeling, we showed that a half-life on the order of hours would result in such short-range signaling.

Currently, we are exploring the use of this platform in a variety of applications including identification of the signaling factors in hepatocyte co-culture, stabilizing liver endothelial cells in culture, toxicity models for drug testing, preconditioning of hepatocytes prior to encapsulation in a 3D gel, and patterning cells directly on the combs to study contact signaling mechanisms.

**Figure 1:** Micromechanical substrate is composed of two parts that may be locked together with the fingers in contact or separated by a narrow gap of 80 µm. Switching between these states modulates interactions between cells adhered to the top surface of the fingers.

**Figure 2:** Fluorescent microscopy of dyed cells on the comb substrates, illustrating the various manipulations possible. Cell populations can be brought into and out of contact with each other. A single population can also be swapped out and replaced.

**References**