Instructive physical microcues in Nervous system-on-Chips

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Novel technical solutions for neurodegenerative disease models are urgently needed in the pharmaceutical industry. Organ-on-Chip technologies exploiting stem cell technologies now demonstrate a high enough technology readiness level to be deemed fit for this purpose[1]. Here, we designed a Nervous system-on-Chip (NoC) with instructive physical microcues to be utilized in the culture of neuronal cell networks as a highly simplified construct for the complex interactions taking place in the extracellular microenvironment of real nervous system tissues. This approach falls into the research domain studying 3D brain models[2]. Previously, we applied a silicon microsieve originally developed by Schurink et al.[3] as a mold and transferred these pyramidal features into the optical adhesive, NOA 81, by soft lithography and opened the cavities in NOA 81 by laser ablation[4]. To yield well-defined 3D micropores as a cellular microenvironment, optimization of the microfabrication method was achieved by spin-coating NOA 81 onto the mold rather than drop-casting[5]. In this work, here, ablation took place either from the top or from the rear of the NOA81 foil and also multiple shots were evaluated to create unique mechanical features inside of individual pores of the microsieve structure[6]. The resulting 3D micropore shapes could physically instruct a neuroprogenitor cell captured in the pore since the material's properties and the specific geometry of the 3D environment are important factors in cell differentiation[7]. Our numerical model revealed that the cytosol can interact with such specific geometric microenvironments as indicated in the tensegrity models depicted in Figure 1 for two cases[6]. Furthermore, we prepared ablation tests for such 3D micropores (Optec Micro Master KrF-Laser set-up) and by example we characteried the achieved 3D micropores for one hole using scanning electron microscopy. Figure 2 (iv.1) and (iv.2) display the results for a top shot versus a rear shot configuration, respectively.

Next, we will investigate the assembly of such instructive microsieves with our microtunnel devices to also induce flow across the captured cells as illustrated in Figure 2 (i-iii) to yield novel instructive NoC microenvironments.

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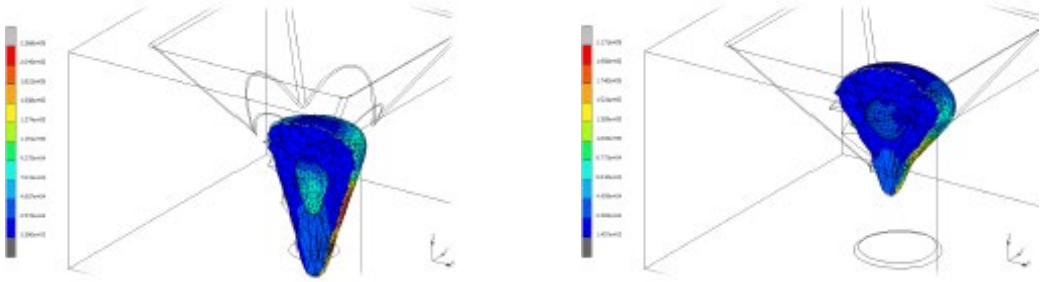

Figure 1. Cross section comparison of the cell model under a gravity load in a micropore, ablated from the front (left) and from the rear (right), respectively. The colors represent the Von-Mises stresses[6].

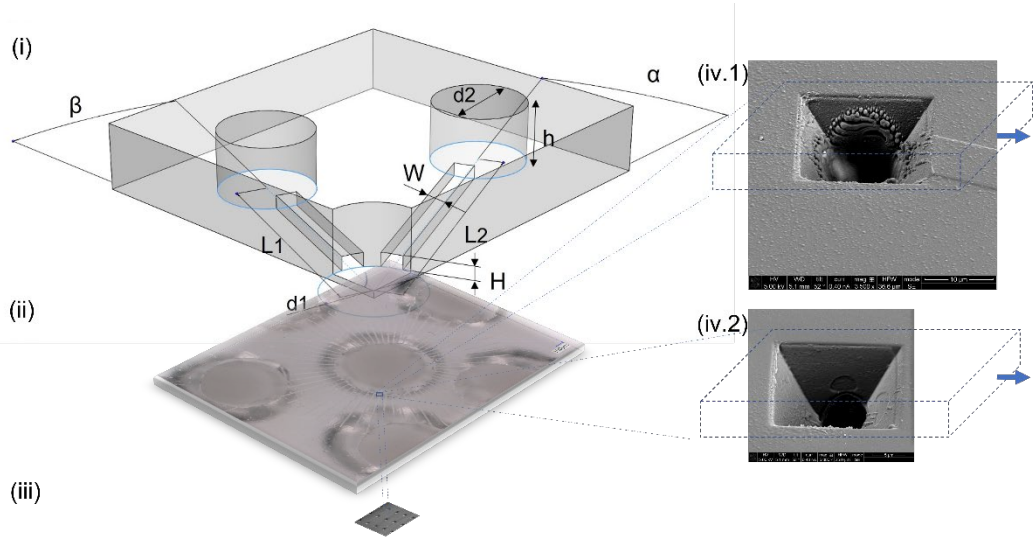

Figure 2. Conceptual assembly of a Nervous system-on-Chip with instructive physical microcues consisting of a microtunnel device and a microsieve. (i) schematic representation of design parameters of a microtunnel device, (ii) perspective view of an optical micrograph of a realized microtunnel device, and (iii) NOA 81 microsieve (here also shown as a perspective illustration of one of such realized microsieves). Scanning Electron Micrographs of the ablation tests of two configurations: (iv.1) front shot and (iv.2) rear shot.