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Highly Permeable, Transparent and Degradable Membranes for Tissue Scaffolding

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A new class of porous membrane has been fabricated that is unique in its combination of nanoscale thickness (< 100 nm) with macroscopic, yet robust, centimeter-scale lateral dimensions and tunable pore sizes in the range of 5 to 100 nm. The membrane material is porous nanocrystalline Si (pnc-Si), first reported in a 2007 Nature paper [1] and now being scaled-up to sheets that are suitable for cell culture and tissue engineering applications. Pnc-Si is ideally suited for cell culture and tissue engineering due to its unique combination of nanometer thinness and high permeability that enable rapid diffusion of low abundance species with minimal loss. Pnc-Si membranes support cell culture similarly to other surfaces, with comparable cell viability and low cytotoxicity [2]. Two cell types can be cultured within tens of nanometers from one another, allowing cell-cell communication, feeder-layer support of a second cell type and other microenvironment-dependent co-culture studies. Cells grown on pnc-Si membranes also experience a highly permeable apical and basal microenvironment, possibly creating a more biologically relevant substrate. For example, endothelial and epithelial cells spontaneously form lumen-like structures due to the increased basolateral permeability. Endothelial cells and astrocytes co-cultured on opposite sides of the membrane synergistically form tighter junctions than when grown alone, mimicking the blood-brain barrier. Additionally, pnc-Si membranes are extraordinarily transparent to light, permitting their use in image-based, high-content screening assays. Surface modification is used to control rates of dissolution to enable a two-dimensional degradable scaffold on the time-scale of monolayer confluence.

Pnc-Si and other ultrathin silicon-based films are typically fabricated through deposition onto a polished silicon wafer. The thin membranes are revealed by selectively etching through the wafer and stopping at a barrier layer. This approach yields small rigid silicon devices with minimal active area. While this approach is fruitful for producing silicon nitride TEM window grids, it is not easily amenable to cell culture and tissue engineering needs. We have developed an approach to free the silicon-based membranes from the silicon wafer on which they were deposited. A polymeric mesh with >90% porosity is bonded to the surface of the silicon membrane, which is deposited on top of a sacrificial layer. The sacrificial layer is chemically dissolved through the porous membrane allowing for lift-off of the film. This results in flexible ultrathin (~100 nm) membranes with many square centimeters of active area. This approach has been demonstrated with both nanoporous pnc-Si and lithographically patterned microporous silicon nitride membranes.

References
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FIG. 1. 50 nm thick microporous silicon nitride with a polymeric scaffold has been lifted off from its silicon wafer substrate. The membrane has been transferred to silicone microwells on a glass slide that span more than 1 square cm.

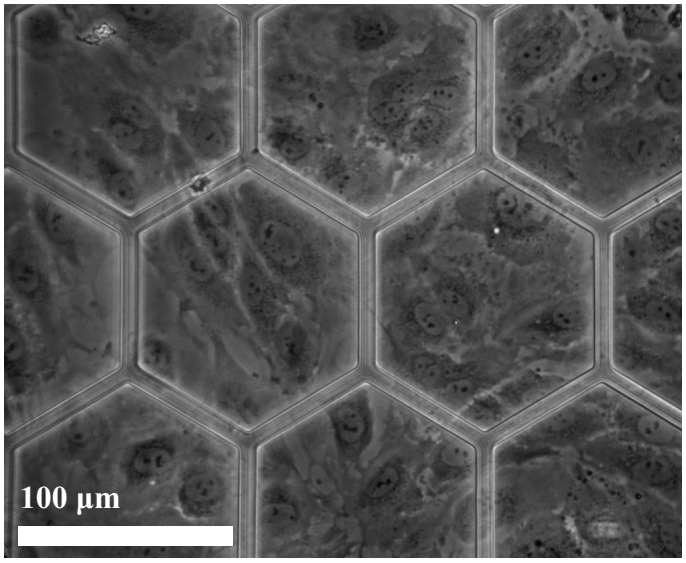

FIG. 2. A phase contrast image of human umbilical vein endothelial cells (HUVEC) cultured to confluence on the transparent and permeable nanoporous silicon support. The hexagonal structures are a reinforcing mesh of silicon nitride.

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