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Replication of high aspect ratio pillar array structures in biocompatible polymers for tissue engineering applications

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ABSTRACT

We developed a simple two-step replication method to transfer arrays of high aspect ratio nanopillars into films of poly(L-D,L-lactic acid) (PLLA). Such structures are promising model surfaces for tissue engineering applications. From arrays of 1 μm high and 200 nm wide pillars produced with e-beam lithography and reactive ion etching negative replicas were first formed by polydimethylsiloxane (PDMS) casting. The final replicates were produced by solvent casting from 1% to 4% solutions of PLLA in chlorinated solvents on the PDMS templates. The silicon masters provide excellent stability and reusability, whereas the flexibility and low surface energy of the PDMS are necessary for the separation of the casts made with PLLA, a brittle material which is difficult to handle. AFM and SEM characterizations confirmed a high fidelity reproduction of the structures with aspect ratios of 1:5. *In vitro* tests using mouse neural stem cells seeded on nanopillars showed that the cells sense the nano-sized topography and respond accordingly by orienting themselves.

1. Introduction

High aspect ratio structures are promising model systems to study the influence of well defined features on cell growth. In particular, structures in the size range of 100 nm–10 μm appear important for the control of migration, adhesion and cytoskeletal organization of a range of cell types [1–3]. Understanding size effects on such length scales is fundamental for cell biology and tissue engineering. Recent studies include the measurement of forces implied by cells to randomly distributed silicon nanowires grown perpendicular to a substrate surface [4].

The technology to produce well defined structures, e.g., in silicon substrates, of dimensions interesting for studying interactions with cells is well established, but the production of high aspect ratio features of reproducible quality is still a challenge. Furthermore, to make such structures attractive for cell growth studies they need to be replicated in high numbers into biologically relevant materials.

Polydimethylsiloxane (PDMS), casting is a suitable method to produce replicates from surface topographies. Due to the elasticity and the low surface energy the detachment from structured surfaces is relatively simple and works with a resolution down to the nanometer scale [5,6]. However, due to the material properties, PDMS casts are of little interest to be used in cell growth studies, but they are well suited as intermediate replicates to obtain desired structures in other polymeric materials. For example, casting of liquid polymers into a PDMS mold followed by UV-induced curing was used to replicate high aspect ratio microstructures produced with deep X-ray lithography [7]. Furthermore, PLLA was pressed into a PDMS mold above its glass transition temperature of 180 °C to yield microstructured surfaces for cell growth experiments [8].

Here we present a two step casting replication process with the intention to provide model surfaces for cell-growth studies made from biodegradable polymers. While the first replication step is a conventional PDMS casting to produce an intermediate replicate from the microfabricated master structure, the second replication step is done by polymer casting from a solution pipetted onto the PDMS replica. This step takes advantage on the one hand of the solubility of various polymers including PLLA and PLGAs in chlorinated organic solvents such as dichloromethane, and on the other hand of the ability of PDMS molds to absorb significant amounts of such solvents. The penetration of the solvent of the polymer into the PDMS facilitates the formation of a compact film of polymer along the PDMS surface, finally leading to very high reproduction fidelity of the sub-μm sized features.

Modification of surfaces through the production of nanoscale surface features is attractive for many *in vitro* and *in vivo* biomaterial

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