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Applications of Nanotechnology in Biomedical Micro/Nano Devices

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1. Introduction

Nanotechnology refers broadly to the use of materials and systems whose unifying subject is the control of matter at the atomic, molecular and supramolecular levels, and the fabrication of devices ranging from 1 to 100 nm. Nanobiotechnology is the branch of nanotechnology that has biological and biochemical applications or uses. In this presentation, fabrications of biomedical micro/nano devices such as the orderly nanostructured Poly (lactic-*co*-glycolic acid) (PLGA) scaffold, nano-patterned microvessel scaffold, high aspect ratio alumina-metal coaxial nanorod and nanotube, and high sensitive 3D nanobiosensor using the anodic aluminum oxide (AAO) templates are introduced.

2. Fabrication of Orderly Nanostructured PLGA Scaffolds

Two simple fabrication methods to fabricate orderly nanostructured PLGA scaffolds using anodic aluminum oxide (AAO) template were conducted. In the vacuum air-extraction approach, the PLGA solution was cast on an AAO template first. The vacuum air-extraction process was then applied to suck the semi-congealed PLGA into the nanopores of the AAO template to form a bamboo sprouts array of PLGA. The surface roughness of the nanostructured scaffolds, ranging from 20 nm to 76 nm, can be controlled by the sucking time of the vacuum air-extraction process. In the replica molding approach, the PLGA solution was cast on the orderly scraggy barrier-layer surface of an AAO membrane to fabricate a PLGA scaffold of concave nanostructure. Cell culture experiments using the bovine endothelial cells (BEC) demonstrated that the nanostructured PLGA membrane can increase the cell growing rate, especially for the bamboo sprouts array scaffolds with smaller surface roughness.

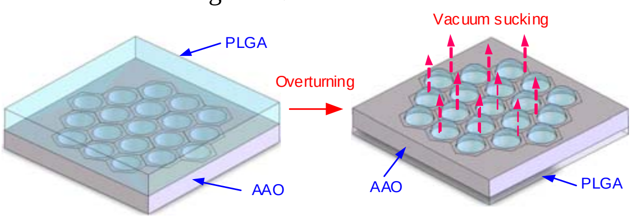

Fig. 1 Schematic illustration of the nanostructure imprinting scheme.

3. Fabrication of PLGA Microvessel Scaffolds with Nano-Patterned Inner Walls

Poly (lactic-*co*-glycolic acid) (PLGA) is one of the most commonly used biodegradable, biocompatible materials. Nanostructured PLGA has immense potential for application in tissue engineering. In this article we discuss a novel approach for the fabrication of PLGA microvessel scaffolds with nanostructured inner walls. In this novel nano-patterning approach, the thermal reflow technique is first adapted to fabricate a semi-cylindrical photoresist master mold. A thin film of titanium and a thin film of aluminum are sputtered in sequence on the semi-cylindrical microvessel network. Aluminum foil anodization is then executed to transform the aluminum thin film into a porous anodic aluminum oxide (AAO) film. During the casting process a PLGA solution is cast on the AAO film to build up semi-cylindrical PLGA microstructures with nanostructured inner walls after which inductive coupled plasma (ICP) is implemented to assist bonding of the two PLGA structures. The result is the building of a network of microchannels with nano-patterned inner walls. Bovine endothelial cells (BECs) are carefully cultured in the scaffold via semi-dynamic seeding for 7 days. Observations show that the BECs grew more separately in a nano-patterned microvessel scaffold than they did in a smooth surface scaffold.

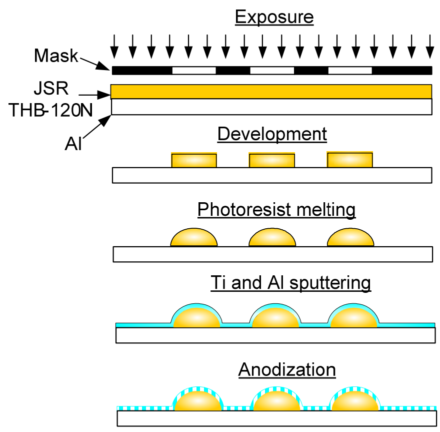

Fig. 2 Manufacturing procedures for the nano-patterned semi-cylindrical photoresist replica mold

4. Fabrication of High Aspect Ratio Alumina-Nickel Coaxial Nanorod Array by Electrodeposition

The fabrication of high aspect ratio (~500), larger area alumina-metal coaxial nanorod arrays using electrodeposition with an anodic aluminum oxide (AAO) template is presented. An annealing process was implemented after electrodeposition to enhance the mechanical properties of the deposited metal nanorods. Phosphoric acid was then used to gradually etch off the alumina that enclosed each individual metal nanorod starting from the borders between the hexagonal cells. The transmission electron microscopy (TEM) and selected area electron diffraction (SEAD) analyses were implemented to verify the alumina/nickel coaxial structure. The alumina shell wrapping each individual metal nanorod served as an insulator for the core metal. The high aspect ratio of the alumina-metal coaxial nanorods described herein make them practicable for use as nano probes or electrodes capable of penetrating individual cell membranes to sense the biological functions of the cells.

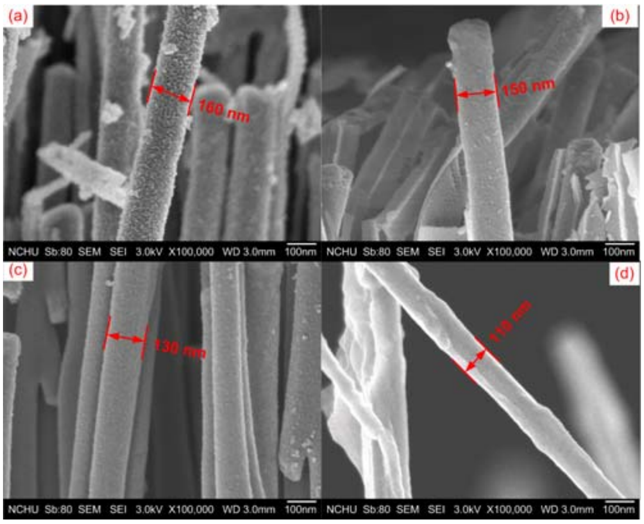

Fig. 3 SEM images of alumina-nickel coaxial nanorod arrays etched by a 30 wt% phosphoric acid solution for (a) 30 min; (b) 40 min; (c) 60 min; (d) 90 min

5. A Lab-on-a-Chip Capillary Network for Red Blood Cell Hydrodynamics

The main function of red blood cells (RBCs) is to circulate oxygen and carbon dioxide throughout the human body. Accurate modeling of the transportation mechanism of RBCs inside microvessels will lead to better clinical diagnosis and prophylaxis of blood disease. This study combined hydrodynamics and basic circuit theory to model the fluid mechanisms of the circulation of blood cells inside capillaries. The variations of physical properties inside the capillaries due to clogging by RBCs were analyzed. A lab-on-a-chip for RBC deformability diagnosis was fabricated using soft lithography. Real experiments were conducted to verify the theoretical analysis and illustrated the capability of the device which was able to observe pathological changes in RBC deformability. The proposed device could be a convenient tool in the field of blood rheology and clinical applications.

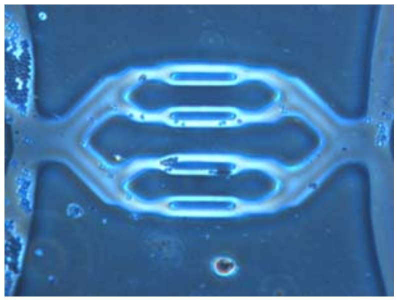

Fig. 4 OM image of the diagnostic chip after injection of RBC solution

6. High Sensitive Nano Biosensor

Group 2 allergen, Der p2, has been reported to activate innate toll like necoptous (TLRs) on respiratory epithelial cells and aggravate respiratory diseases. In this study, a high sensitive nanobiosensor based on a 3D sensing element that has uniformly deposited gold nanoparticles for the detection of dust mite antigen Der p2 is proposed. In this high sensitive nanobiosensor, the barrier layer of an anodic aluminum oxide (AAO) film was used as the template; a reducing agent and stabilizer-free method where the electrochemical deposition was utilized to synthesize uniformly distributed gold nanoparticles on the surface of the barrier layer; the size and the distribution density of the nanoparticles can be well controlled by the potential applied during electrochemical deposition; following, the monoclonal antibodies against dust mite antigen Der p2 were immobilized to the gold nanoparticles through the MUA, EDC/NHS self-assembled monolayer approach. The proposed nanobiosensor was able to examine the Der p2 down to the concentration of 1ng/mL through the electrochemical impedance spectroscopy analysis.

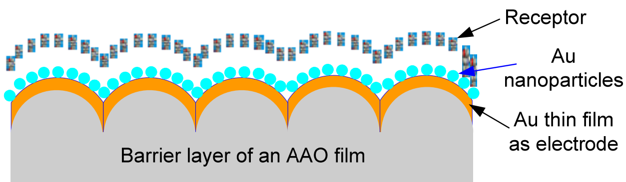

Fig. 5 Schematic drawing of the 3D nano biosensor

References

[1] G. J. Wang, Y. C. Lin, J. W. Lee, C. C. Hsueh, S. h. Hsu, H. S. Hung, Biomedical Microdevices, **11** (2009) 843.
[2] G. J. Wang, Y. C. Lin, and S. h. Hsu, Biomedical Microdevices, in press (2010).
[3] C. W. Hsu,Z. D. Chou, and G. J. Wang, ASME/IEEE J. of Microelectromechnaical System, in press (2010).
[4] Y. C. Chen, G. Y. Chen, Y. C. Lin, and G. J. Wang, Microfluidics and Nnaofluidics, in press. (2010)