High Surface Area Patterned Hydrogels for Drug Delivery or Tissue Engineering Applications

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Statement of Purpose: It has been shown that biocompatible hydrogels can be tailored to release pre-loaded drugs in a localized area of the body. To battle disease, drugs can be released in desired amounts by changing hydrogel pore size, crosslinking density, or the presence of nanofeatures. Upon the establishment of a hydrogel composition that swells and degrades at a predictable rate, a subcutaneous film could be developed to release drug as needed. Hydrogels can also be used as scaffolds to repair damaged tissues. By increasing the surface area of a hydrogel scaffold with a dense network of nanofibers, an environment not unlike the extracellular matrix can be simulated. In this research we aim to develop two different fabrication techniques: one to pattern poly(ethylene glycol) dimethacrylate (PEGDMA) based hydrogels with vertically aligned nanowire arrays and one to create a biocompatible network of PEGDMA based hydrogel nanofibers. It is hypothesized that with the resulting increase in surface area, these added nanofeatures will significantly affect gel swelling, degradation rate, and therefore the release of therapeutic agents while simultaneously mimicking the extracellular matrix of cells. A hydrogel patterned with vertical nanofeatures increases the surface area to volume ratio, thus allowing swelling to occur quickly. The increased area will also aid intelligent hydrogels in sensing and responding to stimuli. On the other hand, a hydrogel film with a surface topography composed of a network of biocompatible nanofibers offers applications in tissue engineering and scaffolding.

Methods: Alumina templates (13 mm diameter) with 200 nm pore sizes are obtained from Whatman® Inc. and utilized to fabricate nanofibers on the surface of a hydrogel. A vacuum filling process is used to draw polymer solution into the membrane's pores. Increasing the wettability of the alumina template with ethanol (EtOH) makes the sample more hydrophilic, thus allowing the hydrogel solution to easily fill the pores. The polymer solution used for these patterned hydrogels includes only three components: a cross linker, a photo initiator, and a solvent. The cross linker, poly(ethylene glycol) dimethacrylate (PEGDMA), is widely used due to its biocompatibility. After the alumina template is filled with solution, the membrane is place inside a mold where bulk solution can be pipetted into a well on top. This forms the base of the hydrogel. Curing under UV light at 30 mW/cm^2 takes only 10 minutes. The alumina can then be removed by either etching away with 1M Sodium hydroxide (NaOH) or mechanically breaking and removing the template.

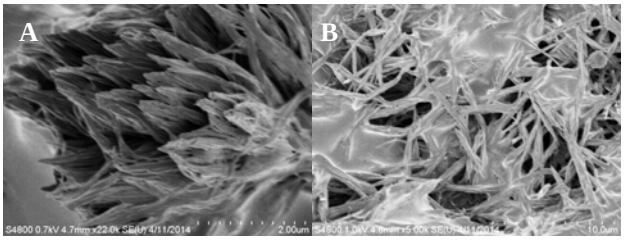

Figure 1, A: SEM images reveal clusters of vertically aligned hydrogel nanowires after dissolving away a porous alumina template. B: SEM images reveal a network of hydrogel nanofibers after dissolving away a porous alumina template. In the image there are areas that appear to be coated with a substance. This is most likely the gold (Au) that was sputtered on the sample before imaging.

Results: Scanning Electron Microscope (SEM) images obtained of the patterned hydrogels show two different nanowire orientations. Vertically aligned hydrogel nanowire arrays can effectively be used to increase surface area on a sample, proving them useful for drug delivery systems, while a slightly more horizontal network of hydrogel nanofibers appears to have strong resemblance to the extracellular matrix that surrounds cells *in vivo*. This brings forth possible applications in tissue engineering where the patterned hydrogels serve as scaffolds. For vertically aligned nanowire arrays it is expected that an increase in aspect ratio will significantly affect swelling. An escalation in surface area should induce a much quicker response time as the hydrogels swell in different environments (Figure 1A). A biocompatible network of hydrogel nanofibers can be used for tissue scaffolding applications. Also, it is known that cell differentiation can be influenced by surface topography, thus causing this fabrication technique to be of great interest to regenerative tissue engineers (Figure 1B).

Conclusions: The ability to pattern the surface of a hydrogel film is significant to the fields of drug delivery and tissue engineering. This project will move forward by beginning to incorporate patterning processes into the fabrication of cationic hydrogels, which swell in acidic conditions and can be used for drug delivery applications. Studies will also be conducted to determine how the hydrogel scaffolds that have been patterned to mimic the extracellular matrix will affect cell differentiation. It is predicted that different pattern shapes and densities will affect how cells grow and multiply.

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