Stimuli-Responsive Triblock Polymers for Multipulse Drug Delivery

M. Gaumet, J. Xi, D. Barriet, and R. A. Siegel
University of Minnesota, Minneapolis, USA

Temperature and pH-sensitive ABC triblock polymers were prepared to form hydrogel membranes capable of changing their structure in response to environmental stimuli, allowing drug release, from a micro implantable device, in short and repetitive pulses. We have previously investigated the capacity of hydrogels to sustain open loop oscillatory behavior, with application in rhythmic hormone release. This novel oscillator is mediated by feedback instability between swelling/shrinking of the hydrogel and an enzyme reaction, whose product modifies pH in the hydrogel. The objective of this work was to prepare and characterize triblock polymer-based hydrogels, to overcome limitations of conventional hydrogels. Our strategy involves reversible arrangement of A and C thermosensitive domains within a strong network, whereas B block is also pH-sensitive. The triblock was mainly based on the use of NIPAAm (N, isopropylacrylamide) and AA (acrylic acid) monomers. Polymers were synthesized by reversible addition fragmentation chain transfer (RAFT) polymerization. Polymers molecular weight (Mn) and polydispersity index (PDI) were determined by matrix-assisted laser desorption ionization/mass spectrometry (MALDI). Monomers conversion was assessed by NMR and copolymers composition by NMR and pH-titration. Temperature and pH responsiveness was studied by turbidity and light scattering experiments. ABC triblock presented Mn close to 40,000 Da and was nearly monodisperse (PDI < 1.1). The monomers conversion was 92%, 97% and 39% for A, B and C blocks, respectively. The opposing effects of hydrophobicity and ionization on the aggregation behavior of the diblock have been highlighted through the turbidity and light scattering data. AB diblock cloud points were 32, 34, 35.5 and 37.5°C for 3, 5, 10 and 20% of AA, respectively. Micelles or aggegates were observed depending on pH and temperature. ABC triblock polymers with controlled architecture and Mn distribution were synthesized and fully characterized. The results suggest that these block polymers are promising materials for stimuli-responsive hydrogel membranes applied to medical devices.

Creating Low-Impedance Coatings for Neural Recording Electrodes Using Electroplating Inhibitors

J. E. Ferguson
Department of Biomedical Engineering, University of Minnesota

C. Boldt
Department of Neuroscience, University of Minnesota

A. D. Redish
Department of Neuroscience, University of Minnesota

Microelectrodes are routinely used for recording from ensembles of neurons for clinical and neuroscience research applications. The quality of the neural recording is highly dependant on the electrical properties of the microelectrode. Lowering the impedance of the electrode-electrolyte interface can improve the signal-to-noise ratio and the ability of the microelectrode to record from more distant neurons. Therefore, tetrodes, which are made by twisting four 12.7 μm nichrome wires together, are usually gold plated to lower impedances to 200–500 kΩ (measured at 1 kHz) before implantation. A further reduction in impedance could drastically improve recording quality but is not possible with standard gold electroplating methods without causing crossed connections (shorts) between the wires. Keefer et al. (2008, Nature Nanotechnology) reported that they could reduce electrode impedance and improve neural recordings by adding multi-walled carbon nanotubes to the gold plating solution, producing a "rice-like" texture on electrode coatings. We replicated this coating and were able to lower tetrode impedances to 120–150 kΩ without crossed connections. Furthermore, we found that by decreasing the electroplating current density and the concentration of multi-walled carbon nanotubes in the gold plating solution, we could create a 40–90 kΩ coating on each tetrode wire without any crossed connections. A scanning electron microscope (SEM) image revealed this 40–90 kΩ coating to be thick and globular with nano-scale texture, distinct from the "rice-like" coating of Keefer et al. The nano-scale texture coating had a large effective surface area likely responsible for the great reduction in impedance. In comparison, an SEM image of a standard gold-plated tetrode showed a thin coating with primarily lateral growth. The carbon nanotubes act as electroplating inhibitors by adsorbing onto the electrode surface and changing the dynamics of the gold electrocrystallization. We confirmed this by replacing the carbon nanotubes with polyethylene glycol (PEG), a known electroplating inhibitor, recreating the nano-scale texture and 40–90 kΩ tetrode impedances. By varying the concentration of electroplating inhibitors and the electroplating current, the dynamics of gold electrocrystallization can be controlled. This gives the ability to design an electrode coating with a specific shape, thickness, and texture that can be tailored to a specific application. Creating a low-impedance coating with a nano-scale texture using electroplating inhibitors can improve the recording quality of microelectrodes and can allow for the use of smaller microelectrodes that were previously limited by their high impedance. Corresponding author; email: redish@umn.edu