Department of Chemical and Biomedical Engineering

Dissertation Defense

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MICROPARTICLES FABRICATED BY SOFT LITHOGRAPHY FOR PROBING AND STIMULATING CELLS

Abstract

Microparticles are small particles typically ranging in size from 1-100 micrometers. They have a wide range of applications in biomedicine, including drug delivery, cell labeling and separation, tissue engineering, and biosensing. However, conventional bottom-up fabrication methods, such as self-assembly, emulsification, and precipitation, often have limited control over the size, shape, and internal structure of the particles. This limitation has prompted the development of top-down fabrication techniques, such as soft lithography, which offer greater control over particle properties. Soft lithography is a set of microfabrication techniques that use elastomeric stamps or molds to pattern and transfer materials onto substrates. It is a versatile and low-cost method that can produce complex and precise microstructures with high reproducibility. In recent years, soft lithography has been widely used in biomedical applications, including microfluidics, cell culture, and tissue engineering. This dissertation focuses on the development of microparticles using the soft lithography technique. Firstly, we apply this technique for specific labeling of phagosome-derived vesicles in macrophages with a membrane dye delivered through microfabricated microparticles made of a thermosensitive nonbiodegradable polymer called ploy(N-isopropylacrylamide) (PNIPAM). These microparticles contain a membrane dye and can be phagocytosed by RAW264.7 macrophages into their phagosomes, resulting in the formation of intracellular labelled vesicles derived from the phagosomes. This method has the potential to advance our understanding of phagocytosis in various diseases and injuries. Secondly, we develop a robust method for osmotically rupturing phagosomes in macrophages using microfabricated microparticles made of uncrosslinked linear PNIPAM. The method involves exposing the microparticles containing macrophages to a cold shock, which creates an osmotic pressure to rupture the phagosomes. To calculate the osmotic pressure in the phagosomes and the surface tension of the phagosomal membrane, we employ the Flory-Huggins theory and the Young-Laplace equation. The modeling results are consistent with the experimentally observed dependence of phagosomal rupture on the cold-shock temperature and suggest the existence of a cellular mechanism for resisting phagosomal rupture. Lastly, we apply this technique for the development of poly(3-hexylthiophene) (P3HT)-based microdevices for photoelectrical stimulation of cells. These microdevices have a disk-like shape and a sub-10 μm size, with a well-defined layered structure that converts light to electrical signals via the photovoltaic mechanism and have cell adhesive properties. Together, these studies demonstrate the potential of microparticles fabricated using the soft lithography technique for various biomedical applications and pave the way for further advancements in this field.