Novel Photoinitiated Nitric Oxide Releasing Compounds for More Biocompatible Coatings on Blood and Tissue Contacting Medical Devices

B. M. Burgess, G. E. Gierke, and M. C. Frost
Michigan Technological University, Houghton, MI USA

Biomedical devices that contact blood and tissue universally inspire a host response that often compromises the function of the device (i.e., intravascular sensors become coated with thrombi, artificial vascular grafts become coated with thrombi, artificial vascular grafts become occluded with thrombus formation and neointimal hyperplasia). Nitric oxide (NO) has been shown to be a potent inhibitor of platelet adhesion and activation and has been implicated in mediating the inflammatory response and promoting would healing. We are currently developing NO-releasing compounds based on S-nitrosothiols derived from substituted aromatic compounds that utilize light as an external on/off trigger capable of releasing precisely controlled surface fluxes of NO. The level of NO generated is dependent on the wavelength and intensity of light shown on the compounds. Data will be presented that show the synthesis and NO-release properties of three novel compounds, S-nitroso-2-methoxybenzene, S-nitroso-3-methoxybenzene and S-nitroso-2-chlorobenzene. Ultimately, these compounds will be tethered to the surface of polymer fillers that will then be blended into hydrophobic polymers and used as coatings on biomedical devices. A model system that will be used to demonstrate the utility of this approach will be a multi-element fiber optic sensors that will contain sensing elements capable of measuring blood gases and NO-releasing fibers that locally generate enough NO to inhibit clot formation on the sensor surface, thus allowing the sensor to function reliably in vivo.

Microfabrication of a Device to Evaluate the Swelling of Glucose Sensitive Hydrogels Under Isochoric Conditions

D. Barriet and R. A. Siegel
Department of Pharmaceutics, University of Minnesota, Minneapolis, USA

Diabetes has been the focus of intense research for more than half a century both in academia and in industry. The number of diabetes cases (especially type II) continues to increase due to the obesity pandemic in western societies and the cost of treatment of diabetes and its severe side effects will undoubtedly continue to drive development of wide ranging technological means to better understand and treat diabetes. Tight blood sugar regulation has been shown to delay or limit side effects and prolong lifespan in patients. Continuous glucose monitoring (CGM) is expected to provide information that can be used in better regulating patient behavior, or as part of a closed loop feedback control system for administering insulin at appropriate times. Our approach to CGM involves a hydrogel whose swelling depends on glucose concentration, coupled to an LC microresonator circuit, whose resonant frequency depends on hydrogel swelling due to impingment of the hydrogel on one plate of the microcapacitor. The whole sensor is microfabricated and implantable. Wireless determination of the resonant frequency permits continuous glucose sensing without chronic skin breach. We are in the process of designing hydrogels that swell/shrink with decreasing/increasing glucose concentration to test for hypoglycemia or hyperglycemia. In collaboration with Professor Babak Ziaie's group at Purdue, a first generation microdevice was fabricated. Since the full sensor requires a significant investment in time and money for its fabrication, the incorporation and testing of diverse hydrogel systems in the full device is unrealistic at the present stage of development. We are currently fabricating a testbed device to allow for the selection of lead hydrogels, which will evaluate quantitatively the relationship stimuli/pressure. Few examples exist in the literature to measure the swelling pressure of hydrogels under isochoric conditions (V =constant) experimentally. We will describe our progress toward the fabrication of a test device to evaluate the pressure developed by a hydrogel sample inside a cavity. We used a commercial pressure die with a very small piezoresistive element (500μm by 500μm), and packaged it such that the pressure sensitive membrane was in contact with a hydrogel sample a few tens of μm thin separated from the external environment by a commercial Anodisc? membrane (0.02 and 0.2 μm pore diameter). Details of design and preliminary results will be presented.