Polymer Pushes the Biocompatibility Envelope

Developing chemical sensors that can be placed in the bloodstream or under the skin to continuously monitor oxygen, pH, or glucose levels is a major challenge because the body responds to these foreign objects in ways that interfere with their ability to accurately measure blood chemistry *e.g.*, clots form on the surface of implanted sensors or blood vessels contract around them.

To improve sensor biocompatibility, chemists at the Univ. of Mich. led by chemistry professor Mark Meyerhoff are applying nitric-oxide (NO) releasing polymers as coatings. These functional materials are made of polyurethane, poly(vinyl chloride) and polydimethylsiloxane with pendant diazeniumdiolate functional groups that slowly release NO as water is absorbed into the polymer. NO, naturally secreted by the endothelial cells that line all blood vessels, prevents platelets from sticking to the vessels' walls. Although the polymers effect a dramatic decrease in platelet adhesion (compared to control films) during both *in vitro* and *in vivo* experiments, they are sensitive to moisture and heat. Further, since the coating must be very thin, the amount of NO that can be stored and released from the sensor surface is limited.

In turn, Meyerhoff has designed new polymeric films with catalytic sites made of a lipophilic copper(II) complex that is capable of converting endogenous *S*-nitrosothiols present in blood to NO. During the reaction, reducing agents (*e.g.*, thiolates or ascorbate) spark the initial conversion of Cu(II) to Cu(I) within the complex, followed by the reduction of *S*-nitrosothiols to NO by the Cu(I) complex at the polymer/solution interface. "The NO fluxes observed when the Cu(II) complex films are placed in solutions containing physiological levels of nitrosothiols are greater than that produced by normal endothelial cells (10^{-10} mol/cm^{2}min) that line all healthy blood vessels" notes Meyerhoff. "We expect that the spontaneous catalytic generation of NO from endogenous nitrosothiols will render these polymeric materials more thromboresistant when in contact with blood *in vivo*," he continues.

Since the sensors' lifespan depends on the availability of nitrosothiol in the blood, the researchers are assessing this molecule's blood concentration. Tests conducted thus far have shown that the coating remains effective after soaking in blood for three days.