Bromocresol Green pH Sensor in the Presence of Nitric Oxide

Matthew Nielsen, Megan C. Frost.
Department of Biomedical Engineering, Michigan Technological University, Houghton MI 49931, USA.

Statement of Purpose: An intravascular pH sensor can provide continuous monitoring and trend tracking of a patient's blood pH. Knowing the patient's arterial pH may improve care in patients that are at risk for base-excess and base-deficient disorders. A major problem for any intravascular sensor is thrombosis and subsequently, embolism. Platelets from the blood activate, adhere, and build a clot on the implanted sensor. Systemic anticoagulation can reduce thrombosis, but increases the patient's risk of bleeding complications. Nitric oxide (NO) has been shown to reduce platelet activation, adhesion, and reduce thrombosis on intravascular sensor surfaces when delivered locally (Frost, MC. Microchem J. 2003;74:277-288).

For NO to be a good candidate to reduce thrombosis on a sensor's surface, NO should not interfere with the transduction of the desired signal. A bromocresol green sol-gel pH sensor will be used to measure pH in the presence of NO. The bromocresol green sensor is based upon absorbance and a change in absorbance in the presence of NO would indicate NO reacting adversely with the sensor. While the bromocresol green sensor is in a planar format in a UV/Vis spectrometer, absorbance based sensors can be miniaturized on optical fibers to dimensions appropriate for intravascular sensing (Mahutte, CK. Clin Biochem. 1998;31:119-130). A bromocresol green pH sensor is chosen based upon a paper by Makote et al. (Makote, R. 1999;394:195-200) that characterizes the sensor as having a response time of less than 60 seconds, insignificant leaching, and is sensitive to the desired pH range of 6-8.

Methods: Bromocresol green sol-gel sensors were prepared (Maokote, R. 1999;394:195-200) by combining tetraethyl orthosilicate, methyltrimethoxysilane, ethanol, and HCl. After stirring the sol for 24 hours, the sol and bromocresol green were mixed together for 30 minutes. Films of the sol were deposited on clean microscope slides using a spin coater. Films were allowed to cure at 66°F (19°C) and 37% relative humidity for 24 hours. Spectra of the films were gathered using a Lambda 35 UV/Vis Spectrometer (PerkinElmer, Waltham, MA). The films were bathed in pH 7.4 phosphate buffered saline and NO was bubbled through the solution for 1 minute at a time before collecting a spectrum. After bubbling NO through the solution, spectra were collected every 5 minutes for the next 40 minutes. The phosphate buffered saline was changed back and forth between a pH of 6.8 and 7.8.

Results: Spectra of the bromocresol green sol-gel sensor were collected across wavelengths 375-700nm and the peak between 500 and 700nm can be seen in Figure 1. The blue lines consist of two spectra before NO exposure, five spectra during NO exposure, and eight spectra following NO exposure at a pH of 7.4. The green and red lines consist of three spectra at pH 6.8 or 7.8, respectively. The mean absorbance at wavelength 620.4nm at pH 6.8 is 0.078478 and pH 7.8 is 0.099706. The standard deviation at wavelength 620.4nm for pH 6.8 is 0.00054476 and pH 7.8 is 0.00047374. The composite mean at pH 7.4 is 0.093221 and composite standard deviation is 0.00031643. The standard deviation at pH 7.4 during NO exposure is 0.00043463 and after exposure is 0.00019422.

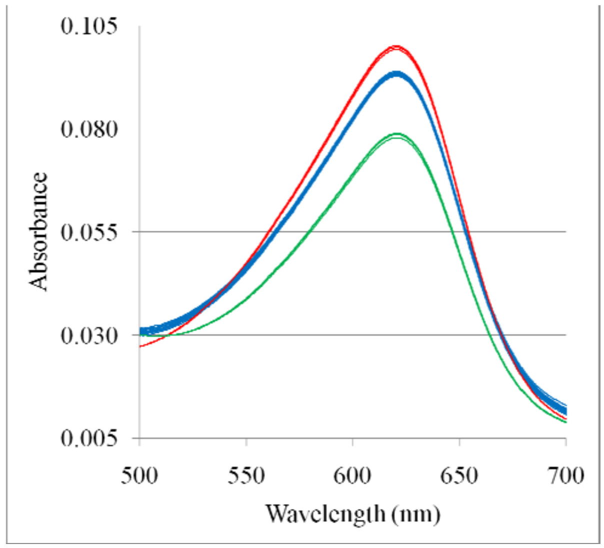

Figure 1. Absorbance spectra of the bromocresol green sol-gel sensor in phosphate buffered saline at different pH. The blue lines are pH 7.4, green are pH 6.8, and red are pH 7.8. The blue lines are a combination of before, during, and after exposure to nitric oxide.

Conclusions: Figure 1 and the standard deviations at the peak absorbance at wavelength 620.4nm suggest NO does not interfere with the operation of the bromocresol green sol-gel sensor. The standard deviations at pH 7.4 in composite, during NO exposure, and after NO exposure, have a smaller standard deviation than the spectra taken at pH 6.8 and 7.8. A bromocresol green sol-gel sensor on an optical fiber coupled with NO release should be able to measure blood pH intravascularly while reducing thrombosis and embolism. Local delivery of NO eliminates the bleeding complications associated with systemic anticoagulation. The pH sensor coupled with NO compatible oxygen and carbon dioxide sensors could be a valuable tool to better track base-excess and base-deficient disorders.

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