Wireless Microrobotic Oxygen Sensing for Retinal Hypoxia Monitoring*

Olgaç Ergeneman[1,**], George Chatzipirpiridis[1], Salvador Pané[1], Georgios A. Sotiriou[2], Christos Bergeles[1], and Bradley J. Nelson[1]

[1] Institute of Robotics and Intelligent Systems, ETH Zurich, 8092, CH
{oergeneman,chgeorge,vidalp,cbergeles,bnelson}@ethz.ch
[2] Particle Technology Laboratory, ETH Zurich, 8092, CH
sotiriou@ptl.mavt.ethz.ch

Abstract. This paper presents a luminescence oxygen sensor for retinal-hypoxia monitoring. The sensor coats a wirelessly controlled magnetic microrobot that will operate in the human eye. The coating embodies Pt(II) octaethylporphine (PtOEP) dyes as the luminescence material and polystyrene as a supporting matrix. It is deposited on the microrobot as a thin film and this film is experimentally evaluated using a custom optical setup. Due to the intrinsic nature of luminescence lifetimes, oxygen concentration was determined using a frequency-domain lifetime measurement approach.

Keywords: wireless, microrobot, oxygen sensing, ophthalmology.

1 Introduction

Retinal hypoxia (i.e., inadequate oxygen supply at the retina) is related to age-related macular degeneration, retinal-vein occlusion, and glaucoma, diseases that are responsible for the most cases of legal blindness [1,2]. For better understanding and monitoring of the progress of these diseases, *in vivo* oxygen sensing is essential.

Microrobots are proposed for targeted drug delivery and wireless sensing in the human body [3], but their actuation and control remains a challenge. Recently, [4] introduced an electromagnetic control system capable of accurately controlling magnetic microdevices with five degrees-of-freedom. This system will be employed to magnetically guide microrobots operating in the human eye. The microrobots are inserted in the human eye through a small incision at the sclera and are wirelessly controlled to the locations of interest using position information from conventional ophthalmoscopic systems [5].

Implantable MEMS-based oxygen sensors for intraocular measurements have been proposed [6]. However, implantable sensors do not possess mobility, and are, thus, limited to oxygen measuring at a fixed position.

* This work was supported by the NCCR Co-Me and the Nr. 200020-126694 grant of the Swiss National Science Foundation.

** Corresponding author.

K.S. Nikita et al. (Eds.): MobiHealth 2011, LNICST 83, pp. 75–79, 2012.

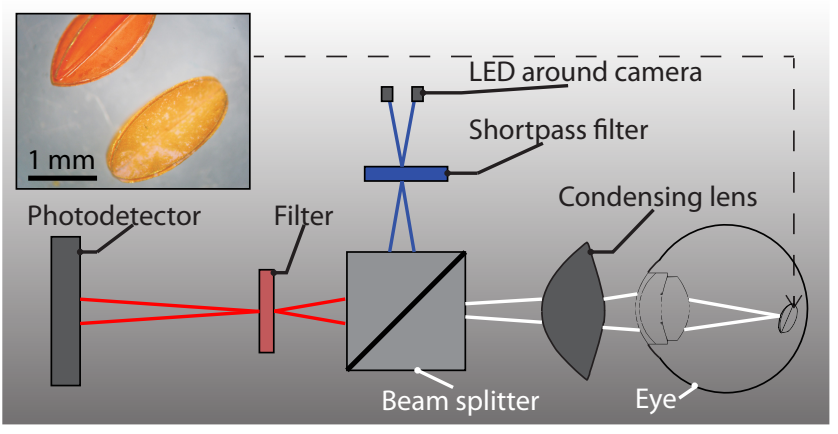


Fig. 1. Setup for oxygen detection. The oxygen-sensing microrobots can be used in the posterior eye segment. The inlet photo shows a microrobot coated with PS film with PtOEP dyes (top), and a microrobot coated with gold (bottom). A condensing lens is required for intraocular observation.

In this paper, a method to functionalize mobile microrobots for intraocular oxygen sensing is presented. The research builds on [7] and proposes luminescence-based oxygen sensing using thin-films. The sensors used in [7] are further miniaturized and the readout setup is improved to utilize smaller microrobot sensors. The coated microrobots are used in an experimental setup that acts as a human-eye phantom (Fig. 1). The experimental results show the feasibility of oxygen sensing using microrobots.

2 Luminescence Oxygen Sensor

Optical luminescence oxygen sensors work based on quenching of luminescence due to oxygen. A number of devices using this principle have been demonstrated, and the basic principles of different methods can be found in [8]. Luminescence-based oxygen sensors are attractive because they provide wireless readout, fast response, high accuracy, and they do not consume oxygen. They can be disposable and do not require reference electrodes or stirring. Additionally, they do not interfere with magnetic fields.

During sensing, the luminescent sensor is excited with a known input signal, and the intensity and lifetime of emission decrease due to quenching. Hence, the output signal can be correlated with oxygen concentration. The output signal intensity is difficult to control in an intraocular application. For example, it depends on the sensor's intraocular location, the input signal's incidence angle, etc. In this work, a lifetime measurement approach was chosen. The lifetime is an intrinsic property of the sensor material and is more robust to environmental conditions.

Lifetime is measured in the frequency domain. The sample is excited with a periodic signal that consequently causes a modulated luminescence emission at the identical frequency. Because of the lifetime of emission, the emission signal has a phase shift (i.e., time delay) with respect to the excitation signal. Measuring this phase shift provides the lifetime.

3 Experiments

3.1 Preparation of the Film Sensor

Figure 1 shows two assembled CoNi microrobots. For biocompatibility and surface functionalization they are first coated with a thin layer of gold by electroless deposition. To prepare the luminescence film, 3 mg of PtOEP (Frontier Scientific, UT, USA) and 197 mg of polystyrene (PS) were dissolved in 2 ml of chloroform by stirring. The microrobots are dip-coated and stored 2 hours, allowing evaporation of chloroform. Gold-coated silicon chips (10 mm^2) were also spin-coated with the prepared solution for characterization.

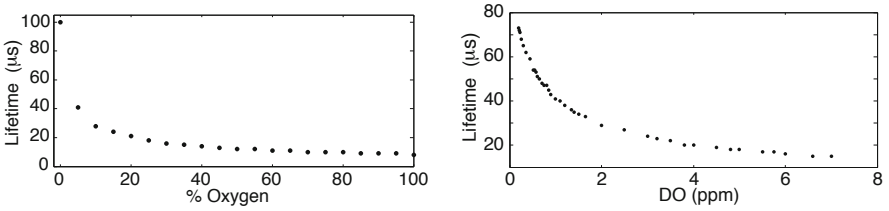
3.2 Characterization Setup

A Cary Eclipse fluorescence spectrophotometer (Varian Inc.) was used to characterize the luminescence of the sensors. Excitation scan, emission scan, kinetics, and lifetime measurements were performed. A custom flow cell was built and used in all experiments. Oxygen and nitrogen were mixed at different ratios using two gas flow controllers (Bronkhorst High-Tech B.V.) and applied to the cell. A total gas flow of 500 ml/min was maintained in all gas measurements.

Dissolved oxygen (DO) measurements were also performed using the same chamber with circulating water instead of gas. The oxygen concentration in water was changed by bubbling nitrogen or oxygen in a container. A commercial DO sensor (Oxi 340i, WTW Gmbh) was used to monitor the DO concentration in a second chamber in order to avoid possible interference by gas bubbles. The water was circulated using a pump, and the fluid flow rate was kept constant.

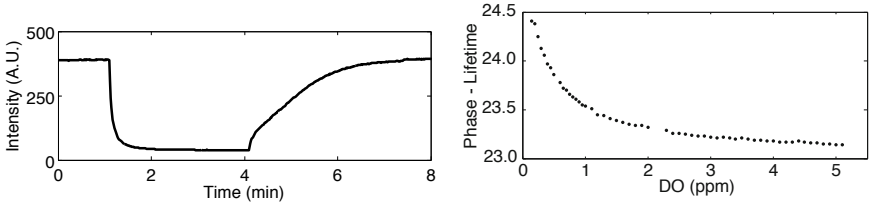
3.3 Intraocular Sensing Setup

A custom setup was built for wireless oxygen concentration measurements considering the anatomy of the eye and the control system described in [4]. A UV LED and a shortpass filter were used as the excitation source, and a Si photodetector (PD) (PD-100A, Thorlabs Gmbh) with a longpass filter were used for the read out. Using a beamsplitter (Edmund Optics) two separate optical paths were generated, one for the detecting system and the other one for the excitation system and tracking camera. Figure 1 shows an illustration of the measurement setup. A lock-in amplifier (HF2LI, Zurich Instruments) was used for the detection of phase change as a function of oxygen concentration. Its internal signal generator modulated the excitation circuit of the LED and acted as the reference signal for the detection of the PD signal. By this method, effective noise cancellation was obtained.



(a) (b)

Fig. 2. (a) The lifetime of emission of a coated microrobot in response to different ratios of oxygen to nitrogen. The total flow rate was 500 ml/min, (b) The lifetime of emission of the coated microrobot at different dissolved oxygen concentrations in water. The oxygen concentration was obtained by the commercial oxygen sensor.



(a) (b)

Fig. 3. (a) Response time of the film sensor. The high intensity state is 100 % nitrogen and the low intensity state is 100 % oxygen flow. (b) The response of the microrobotic sensor under different oxygen concentrations using the custom ophthalmic setup with the lock-in detection.

4 Results

4.1 Sensor Film Characterization

The excitation and emission characteristics were first obtained for the sensor film containing PtOEP. The peak emission wavelength was found to be 645 nm. Excitation wavelengths between 300 nm to 400 nm produced high emission intensity. Next, using the flow cell described, the oxygen sensitivity of the sensor was measured in gas and in water. Figure 2(a) shows the lifetime of emission of a coated microrobot with respect to different oxygen-to-nitrogen ratios under a constant flow. In Fig. 2(b), lifetime of emission of the same microrobot is shown in water with a flow rate of 3.15 l/min at different dissolved oxygen concentrations observed by the commercial oxygen sensor. An unquenched emission lifetime of 100 μs was observed. Finally, the response time of the sensor was obtained going from 100 % nitrogen gas to 100 % oxygen gas and back to 100 % nitrogen gas. The decay time of the sensor was determined to be approximately 30 seconds and the rise time approximately three minutes, as seen in Fig. 3(a).

4.2 Measurements Using Lock-in Amplifier

The film coated microrobot sensor was used in the custom-built setup. To mimic the optical properties of the eye an eye model was used. Using the commercial sensor the oxygen concentration was observed and the phase change was acquired from the lock-in amplifier. Figure 3(b) shows the response of the sensor under different dissolved oxygen concentrations. A curve similar to that obtained from the spectrophotometer was obtained, indicating that DO concentration can be successfully measured with the custom setup and the microrobot.

5 Conclusions and Future Work

Microrobotic oxygen sensors were developed using PS film with PtOEP dye. A custom setup for excitation and readout was implemented, and oxygen sensing was demonstrated. The sensors can be precisely controlled in the ocular cavity by applying magnetic fields as described in [4]. Future work will focus on using the readout system together with the control and tracking systems to create oxygen maps.

References

1. Congdon, N., O'Colmain, B., Klaver, C.C., Klein, R., Munoz, B., Friedman, D.S., Kempen, J., Taylor, H.R., Mitchell, P.: Causes and prevalence of visual impairment among adults in the United States. Archives of Ophthalmology 122(4), 477–485 (2004)
2. Galloway, N.R., Amoaku, W.M.K., Galloway, P.H., Browning, A.C.: Common eye diseases and their management, 3rd edn. Springer, Heidelberg (2005)
3. Nelson, B.J., Kaliakatsos, I.K., Abbott, J.J.: Microrobots for minimally invasive medicine. Annual Review of Biomedical Engineering 12, 55–85 (2010)
4. Kummer, M.P., Abbott, J.J., Kratochvil, B.E., Borer, R., Sengul, A., Nelson, B.J.: OctoMag: An electromagnetic system for 5-DOF wireless micromanipulation. IEEE Trans. Robotics 26(6), 1006–1017 (2010)
5. Bergeles, C., Kratochvil, B.E., Nelson, B.J.: Model-based localization of intraocular microrobots for wireless electromagnetic control. In: IEEE Int. Conf. Robotics and Automation, pp. 2617–2622 (2011)
6. Chen, P.J., Rodger, D., Saati, S., Humayun, M., Tai, Y.C.: Implantable parylene-based wireless intraocular pressure sensor. In: IEEE Int. Conf. Micro Electro Mechanical Systems, pp. 58–61 (2008)
7. Ergeneman, O., Dogangil, G., Kummer, M.P., Abbott, J.J., Nazeeruddin, M.K., Nelson, B.J.: A magnetically controlled wireless optical oxygen sensor for intraocular measurements. IEEE Sensors 8(1-2), 29–37 (2008)
8. Lakowicz, J.R.: Principles of fluorescence spectroscopy, 2nd edn. Kluwer Academic/Plenum Publishers (1999)