CMOS-BASED LUMINESCENCE DETECTION FOR LAB-ON-A-CHIP

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ABSTRACT

This work describes a stable and versatile sensing system based on the CMOS array and polarization signal isolation. As a proof-of-concept, an oxygen sensor was demonstrated based on this system. Taking advantage of the spectral and spatial characteristics of the CMOS image sensor, emissions from the oxygen-sensitive platinum octaethylporphine (PtOEP) luminophore and oxygen insensitive Rhodamine B dye were monitored simultaneously. Any fluctuations in light source intensity can be detected and compensated, which is especially important for optical battery-operated point-of-care (POC) instruments or applications where stable power is not available.

KEYWORDS: CMOS image sensor, optical detection, oxygen sensing, point-of-care

INTRODUCTION

Optical detection (e.g., luminescence, absorption) is the most commonly used approach in the mainstream biological analyses. These optical detection systems typically require sophisticated instrumentation, such as spectrophotometers, photomultiplier tubes, or microscopes. The need for portable and low-cost point-of-care (POC) instrumentation has led to intense focus on miniaturization of optical sensor components. Semiconductor and organic LEDs are gaining wide accepted as portable light sources in such systems. However, signal detection and isolation remain challenging and active areas of research.

Herein we describe a versatile optical sensing system based on a CMOS image sensor and explore the feasibility of using it as a detector in a POC oxygen sensor. The CMOS detector is inherently color discriminating and provides spatial resolution. Polarization is a wavelength-independent scheme for filtering excitation light [1]. Combination of these two components generates a filter-free multi-color detection system applicable to luminescence-based sensing.

We demonstrated an oxygen sensor based on such system as a proof-of-concept. Oxygen detection is important in clinical diagnosis, biological research and environmental monitoring. The developed oxygen sensor (Fig. 1*a*) is based on metalloporphyrin luminophore platinum octaethylporphine (PtOEP) luminophore, whose emission at 620 nm is quenched by oxygen. An oxygen insensitive Rhodamine B (RhB) dye proves a stable reference. The CMOS image sensor is inherently color discriminating, and permits selective detection of the red PtOEP emission. Yet any fluctuations in light source intensity can be detected and accounted for by monitoring RhB emission.

BACKGROUND

A CMOS image sensor is built in the same process as integrated circuits but with some sensor-specific modifications. It is commonly used in digital cameras and consists of an array of millions of photodetectors covered by a mosaic of microscale band-pass (Bayer) filters. Four photodetectors are in a group, of which two are covered by green filters and two are covered by a red and a blue filter, respectively (Fig. 1*c*). Raw data taken by a CMOS image sensor are grids of three primary colors: red, green and blue (RGB). Each pixel contains the intensities information of one color. In order to build up a complete image, the intensities of the missing colors are obtained by interpolation in the de-mosaicing process. Thus, each pixel in a complete image consists of three color channels [2]. The intensity of each color is described within a given range from a minimum and a maximum which are dependent on the resolution of the analogue to digital converter.

The PtOEP emission at 620 nm is quenched by oxygen. The standard approach to characterizing luminescence quenching based oxygen sensors is using Stern-Volmer analysis in which,

$$\frac{I_0}{I} = 1 + K_{SV}[O_2]$$

where I_0 and I are the emission intensities in the absence and presence of oxygen at concentration of $[O_2]$, respectively, and K_{SV} is Stern-Volmer constant. The CMOS image sensor was used to record the emission of oxygen sensitive PtOEP and oxygen insensitive RhB. The RhB emission signal (625 nm) is used to compensate the measurement error caused by the fluctuation of batteries [3].

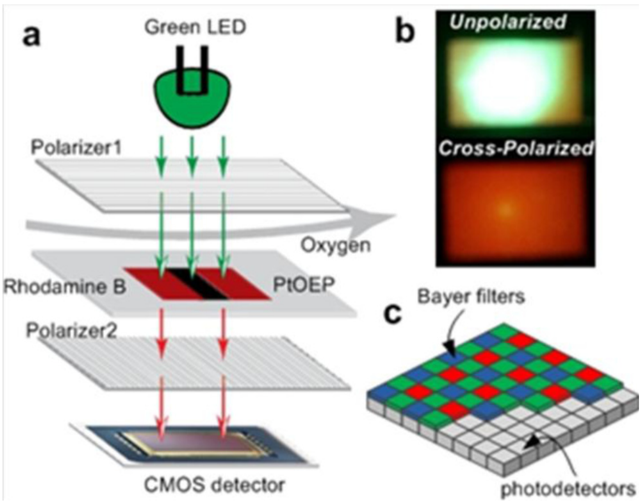

Fig. 1: *(a) Arrangement of the light source (LED), detector (CMOS), polarizers, oxygen-sensitive PtOEP film and oxygen-insensitive Rhodamine B reference. (b) Illustration of polarization filtering which permits isolation of optical signal (Rhodamine B emission at 625nm) from high background signal due to leaking excitation light (530nm). (c) Pixel structure of the CMOS detector.*

EXPERIMENTAL

The PtOEP was encapsulated in ethyl cellulose (EC) and patterned on a glass slide [4]. The RhB dissolved in water, sealed in a glass capillary, and then placed next to the PtOEP film. The PtOEP and RhB were separated by a black tape (to reduce optical signal cross-talk). For oxygen measurements, a green LED (530 nm emission) was biased at 3.0 V for excitation of PtOEP and RhB. The gas testing chamber was filled with the mixture of oxygen and nitrogen at different ratios which was indicated by a commercial oxygen sensor (Nuvair, Pro O_2 remote analyzer). During oxygen measurement, the bias was varied by ±0.02V to simulate battery power source fluctuations. Measurements were performed by taking images of the emissions and analyzed using ImageJ (ver. 1.43u). The results were compensated based on the RhB emission.

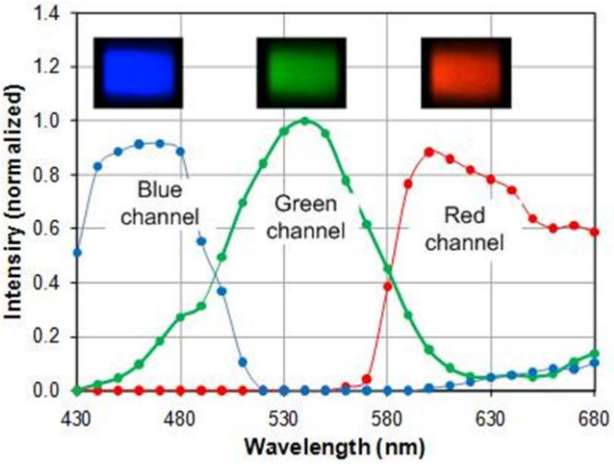

Fig. 2: *Responsivity of the CMOS sensors in each of its color channels.*

RESULTS AND DISUSSION

Responsivity of the RGB channels in the CMOS detector (OmniVision, OV9810) is illustrated in Fig. 2. Each channel of the CMOS detector exhibits a strong response to the corresponding wavelength range, as expected. The red channel, which has strong response to red light, was used to detect the PtOEP and RhB emission. Moreover, the response of red channel cuts off at around 580 nm, resulting in further filtering of the excitation light. This test confirms that the CMOS detector is inherently discriminating to the RGB colors and demonstrates the spectral response range of each color pixel type. These results are helpful in the development of sensors that take advantage of the CMOS detector's color discriminating capability.

The RhB emission does not change with the oxygen while the PtOEP emission is sensitive to oxygen. The intensity profiles of two images which were taken at high and low oxygen are illustrated in Fig. 3. The PtOEP emission decreases significantly from 190 to 20 a.u. when the oxygen concentration increases. On the other hand, the emission of RhB stays at the same level at different oxygen concentrations. The inset images clearly illustrate the quenching effect of oxygen on PtOEP. The black tape between the PtOEP and RhB blocks the bleeding light from PtOEP at low oxygen concentrations and thus enhances the stability of the RhB reference signal.

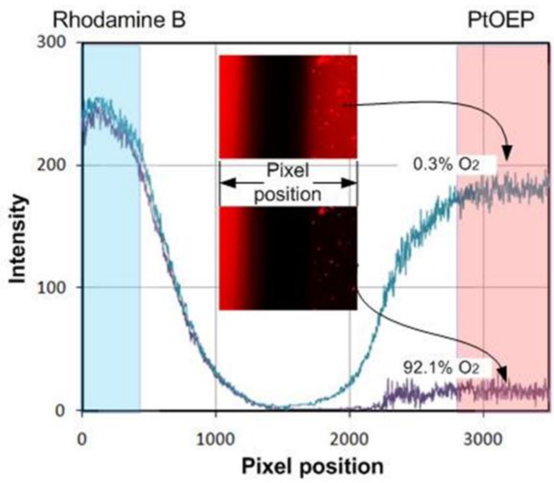

Fig. 3: *Emission of PtOEP is quenched by oxygen while emission of the reference Rhodamine B does not change. The two inset images illustrate light emission in red channel of the CMOS sensor.*

The integrated reference makes the oxygen sensor stable and accurate because any fluctuation of the power supply can be observed from the emission intensity of RhB and then calibrated. The oxygen sensor was firstly characterized when the LED was biased at 3.0 V using a Keithley 6487 voltage source. Then the bias was intentionally varied by ±0.02V which was ***less than 1%*** during oxygen measurement. Fig. 4*a* illustrates the resulting RhB and PtOEP emission intensities which deviate from the calibration curve (dot lines). After the RhB intensities were compensated to the calibration curve, the

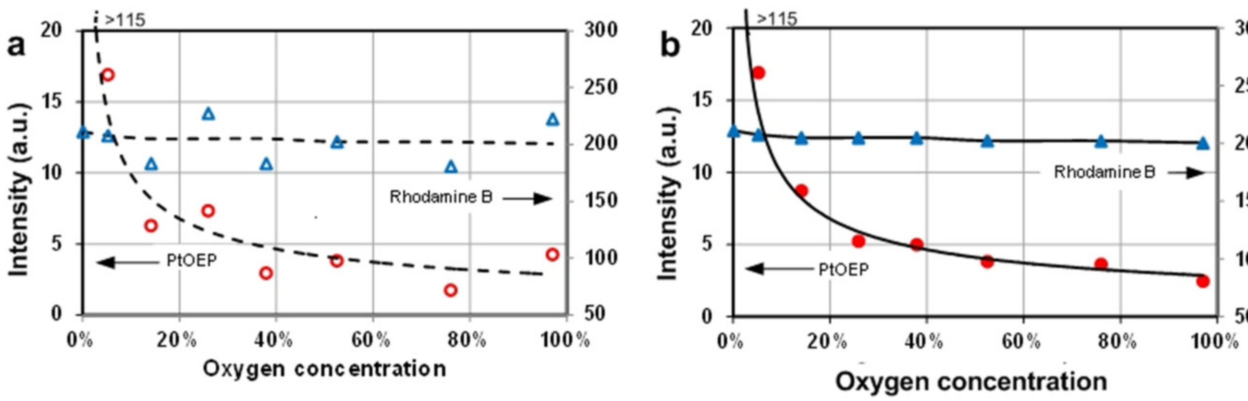

Fig. 4: *PtOEP and Rhodamine B emission at different oxygen concentrations when LED bias fluctuates. (a) Uncompensated; and (b) compensated.*

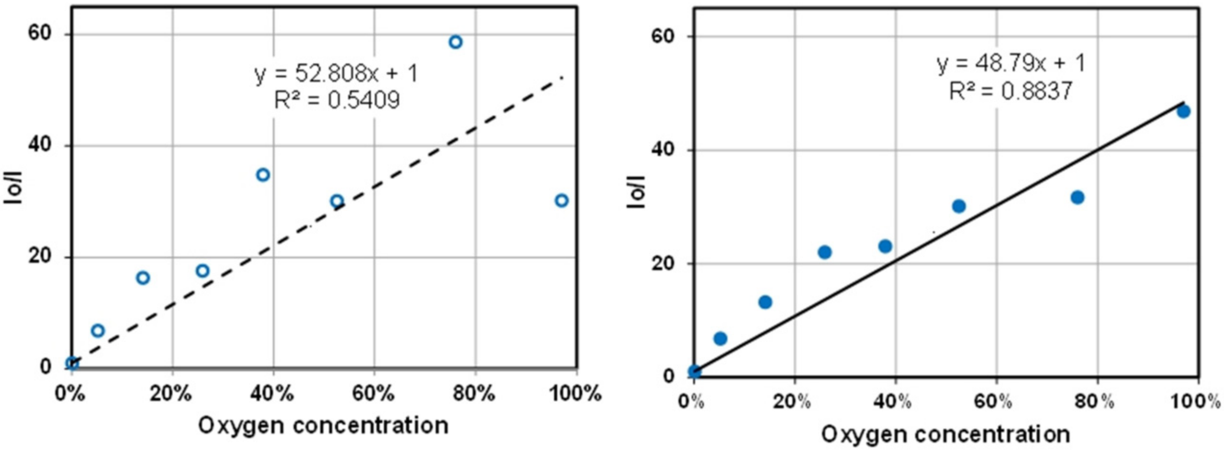

Fig. 5: *Stern-Volmer plot of the oxygen sensor when LED bias fluctuates by 1%. (a) Uncompensated; and (b) compensated.*

PtOEP intensities were calibrated using the same ratio (Fig. 4*b*).

The sensor with an integrated reference maintains good linearity in response even if the power supply is not stable. Fig. 5*b* illustrates the Stern-Volmer plot based on the calibrated PtOEP intensities. The coefficient of determination (R^2) of 0.88 demonstrates the good linearity of the sensor. Without the RhB reference, the R^2 decreases to 0.54 under less than 1% of power supply output fluctuation. Moreover, the sensitivity of the oxygen sensor is 48.79 which is comparable to the ~50 values reported using an external spectrophotometer [5] and is much higher than that of a portable integrated sensor (~1.4) [6].

CONCLUSIONS

In conclusion, a prototype luminescence detection system using CMOS sensor was successfully demonstrated. Taking the advantage of the spatial imaging capability of the CMOS detector, an oxygen sensor with integrated reference was developed. This oxygen sensor has high sensitivity and is immune to light source intensity fluctuation; it is ideally suited for use by first responders such as fire fighters. Overall, the developed detection system may be integrated with lab-on-a-chip for a variety of POC applications.

ACKNOWLEDGEMENTS

This work was partially supported by the NSF awards ECCS-0725812 and ECCS-0930305.

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