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Optical-based integrated oxygen sensor for long-term O_2 monitoring for use in organ-on chip platforms

Amir Sanati Nezhad[1,2,3], **Seyed Ali Mousavi Shaegh**[1,2,3], **Yu Shrike Zhang**[1,2,3], **Mehmet Dokmeci**[1,2,3] and **Ali Khademhosseini**[1,2,3]
[1]University of Calgary, Canada
[2]Harvard-MIT, USA
[3]Harvard Medical School, USA

Detection of oxygen concentration is essential to regulate cellular functions in both normal physiology and disease conditions for application in bioassays, tissue engineering and particularly for organ-on-chip platforms that needs long-term and sensitive monitoring. In addition, recent advances in integrated microfluidic systems necessitate the development of flexible and low-cost oxygen sensors that can be rapidly integrated to the system. Amperometric electrochemical and luminescent-based oxygen sensors are known as the two predominant sensing technologies for real-time and sensitive detection of dissolved oxygen in bioreactors. However, amperometric method suffers from difficulty in miniaturization, signal variation at various flow rate and consumption of dissolved oxygen during the sensing process. Luminescent oxygen sensor is expected to be an ideal method for real-time and long-term detection of dissolved oxygen. Here, we developed an optical-based oxygen sensor for long-term and real-time monitoring of dissolved oxygen concentration in a bioreactor. The sensor relies on reduction in luminescent intensity of a sensing dye due to oxygen quenching of the emitting excited electronic state. We chose ruthenium tris(2,2'-dipyridyl) dichloride hexahydrate (RTDP) as the optical sensing element due to its low photobleaching, long lifetime, and linear Stern-Volmer plots. Shadow masking technique was used to pattern the Rt dye layer on a hydrophilic cover slide. A thin layer of PDMS (5 μm) was then coated onto the patterned dye layer to protect the dye from direct contact with the culture media and to inhibit contamination. The channel of top PDMS fluidic layer was aligned with the patterned dye layer and plasma bonded to the cover glass. To excite the dye, a high power light (200 mW) along with a 455 nm bandpass excitation filter were assembled over the microfluidic chip. A 610 nm highpass filter was assembled at the bottom layer to filter the light emitted to the integrated photodiode. The photodiode-based detection method enabled detection of overall fluorescence signal emitted from the oxygen-sensitive dye in form of an electrical current. An electric circuit was integrated to convert the current to a sensible electrical voltage which was read out using the LabView software. The response of the photodiode to the change in fluorescent intensity under different concentrations of oxygen gas and dissolved oxygen in both DI water and culture media was detected. The sensor was found to be more sensitive to the dissolved oxygen in DI water than in media. The electrical circuit, the thickness of the PDMS layer, the amount of dye patterned and the optical detection platform was optimized to make it sensitive enough for organ-on-chip applications. The sensitivity of the sensor was estimated to be 0.67 millivolt per % oxygen. We used the sensor to detect the dissolved oxygen concentration in a HepG2 cell cultured bioreactor for two days.

Biography

Amir Sanati-Nezhad received his MSc degree in Mechanical Engineering from Amir Kabir University of Technology, Iran and PhD degree from the Optical Bio-Microsystems Laboratory, Mechanical and Industrial Engineering, Concordia University, Canada. He did two years of postdoctoral research in the Department of Biomedical Engineering at the McGill University and Harvard– MIT Health Sciences and Technology for development of microdevices for single cell analysis and tissue engineering. His current research interests include BioMEMS, bioinspired microfluidics, lab-on-a-chip, tissue engineering and single cell analysis. He is currently an assistant professor in the department of Mechanical and Manufacturing with a joint affiliation to Center for Bioengineering Research and Education and Biomedical Engineering program at University of Calgary. He has a research focus on development of organ on chip platform using integrated microfluidics and tissue engineering approaches for disease modeling and drug discovery.

amir.sanatinezhad@ucalgary.ca