Optical Sensors for Spatially-Resolved Measurement of Oxygen in Microfluidic Devices

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Oxygen concentration is a central parameter in cell studies. In a natural environment, such as in mammalian organs, cellular oxygen is maintained to normoxic (12% to <0.5% O_2) conditions[1]. Regulation to within this relatively narrow range is necessary in-vivo to prevent oxidative damage to the cell from excess oxygen (hyperoxia) and metabolic demise from insufficient oxygen (hypoxia)[2]. Recent research has indicated that in-vitro cell-culture experiments performed in air (~21% O_2) may introduce excessive stress on cells due to exposure to unnaturally high oxygen concentrations[1]. For example, fibroblasts cultured under different oxygen concentrations were found to adjust to high oxygen levels by reversible growth inhibition and differentiation.

Measurement and control of oxygen concentration in the cellular microenvironment thus is of special importance when in-vitro results are compared to cell behavior observed in-vivo. While microfluidic lab-on-a-chip (LOC) devices provide such control, the lack of suitable integrated oxygen sensors has limited their application. To facilitate the visualization and measurement of dissolved oxygen (DO_2) in LOCs we have recently demonstrated a process for the soft-lithographic patterning and integration of optical oxygen sensor films[3]. As illustrated in Fig. 1, this technique has been extended further for use with photo- and electron beam lithography (EBL) to yield high-resolution arrays of polymer-encapsulated sensor material[4]. In this paper we will introduce the fabrication process and discuss patterning results (see Fig. 2). We will further demonstrate the use of these sensor patterns for spatially-resolved measurement of DO_2 in multi-stream microfluidic devices[5], shown in Fig. 3, and discuss current efforts to extend their application to single-cell studies.

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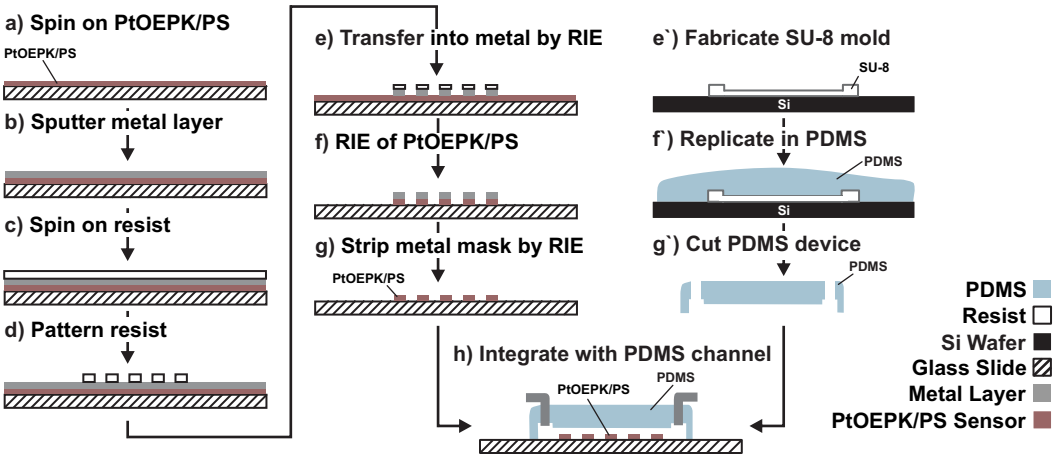

Fig. 1: Schematic of the sensor patterning and integration process. (a) PtOEPK/PS is spun onto glass. (b) A film of metal is sputter-deposited onto the sensor layer. (c,d) The metal layer is patterned using photolithography or EBL. (e,f) Patterns are transferred into PtOEPK/PS and (g) the metal mask is stripped using RIE. (e`-g`) PDMS microfluidic devices are fabricated using a SU-8 master and replica-molding. (h) Sensor patterns are integrated with the devices using plasma bonding.

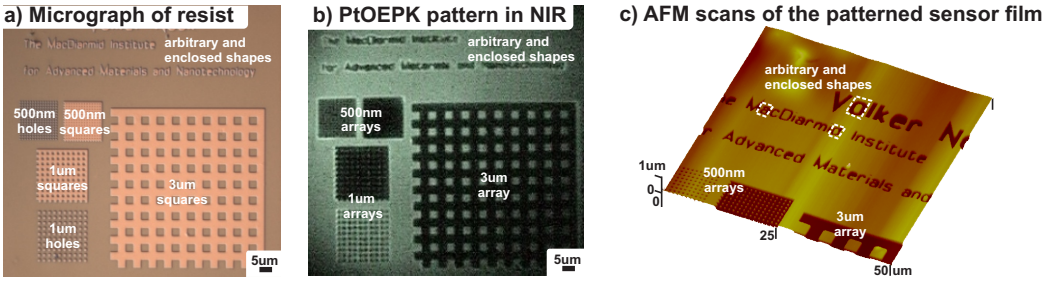

Fig. 2: (a) Optical micrograph of high-resolution sensor arrays in resist. (b) Fluorescence image of the same pattern after transfer into PtOEPK/PS. (c) AFM micrograph showing replication of arbitrary shapes and sub-micron features.

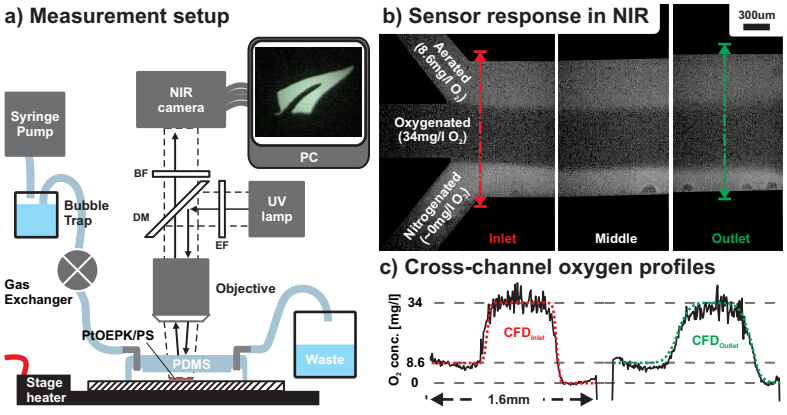

Fig. 3: Application of the oxygen sensor. (a) Schematic of the measurement setup. (b) Dissolved O_2 visualization in a microfluidic multi-stream flow device. (c) Cross-channel DO_2 concentration at the inlet and outlet.