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RESEARCH PAPER

Mathematical analysis of oxygen transfer through polydimethylsiloxane membrane between double layers of cell culture channel and gas chamber in microfluidic oxygenator

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Abstract For successful cell culture in microfluidic devices, precise control of the microenvironment, including gas transfer between the cells and the surrounding medium, is exceptionally important. The work is motivated by a polydimethylsiloxane (PDMS) microfluidic oxygenator chip for mammalian cell culture suggesting that the speed of the oxygen transfer may vary depending on the thickness of a PDMS membrane or the height of a fluid channel. In this paper, a model is presented to describe the oxygen transfer dynamics in the PDMS microfluidic oxygenator chip for mammalian cell culture. Theoretical studies were carried out to evaluate the oxygen profile within the multilayer device, consisting of a gas reservoir, a PDMS membrane, a fluid channel containing growth media, and a cell culture layer. The corresponding semi-analytical solution was derived to evaluate dissolved oxygen concentration within the heterogeneous materials, and was found to be in good agreement with the numerical solution. In addition, a separate analytical solution was obtained to investigate the oxygen pressure drop (OPD) along the cell layer due to oxygen uptake of cells, with experimental validation of the OPD model carried out using human umbilical vein endothelial cells cultured in a PDMS microfluidic oxygenator. Within the theoretical framework, the effects of several microfluidic oxygenator design parameters were studied, including cell type and critical device dimensions.

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1 Introduction

Oxygen transport in biological culture has been essential to many microfluidic applications, including cell-based assays (Brischwein et al. 2003; Tourovskaia et al. 2005; Kane et al. 2006a, b; Wang et al. 2007; Lam et al. 2009; Polinkovsky et al. 2009), bioreactors (Szita et al. 2005; De Bartolo et al. 2006; Sud et al. 2006), and tissue engineering (Radisic et al. 2006a). Tissue engineering often involves moderate/long-term mammalian cell growth within culture platforms or scaffolds to obtain multi-dimensional structures for in vivo implantation (Radisic et al. 2006b; Toh et al. 2007). However, the relatively low solubility of oxygen in aqueous solutions ($\sim$0.2 mM/atm) is often insufficient to satisfy the demand of dense cell cultures (10^7–10^9 cells/ml) via passive diffusion alone.

Miniaturization of the culture environment combined with an external oxygen supply is an effective approach to increase cell culture oxygenation rates, as diffusion time is proportional to the square of the path length. Researchers