# Simulation Of Oxygen Transport And Cellular Uptake In A Microphysiological System

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## Abstract

Microphysiological systems (MPS) combine microfluidics, MEMS, and biotechnology techniques to mimic human organ function in vitro. Such devices are being developed to provide better levels of tissue and organ functionality compared with conventional cell culture systems, and have great potential to advance the study of tissue development, organ physiology, disease etiology, and drug discovery and development.[1]

Modeling the multiphysics behavior of such biomedical devices is critical to their development and optimization. In this talk we report a COMSOL Multiphysics® model supporting the development of a liver MPS to study drug-drug interactions.[2] This liver MPS was designed to mimic a single liver sinusoid and consists of a culture media channel positioned over a cell culture chamber, separated by a thin porous membrane (Figure 1).[2] Liver cells (hepatocytes) uptake oxygen delivered both by flowing culture media and by diffusion from the ambient through the PDMS. Our model of the device uses COMSOL's laminar fluid flow and dilute species transport capabilities. Cell oxygen consumption was modeled by Michaelis-Menten kinetics.

Simulations showed that sufficient oxygen diffuses through the PDMS from the ambient to keep the oxygen concentration at the walls of the media channel and cell culture chamber nearly saturated (Figure 2). For a flow rate of 20 µL/h, small concentration gradients with physiologically relevant oxygen levels are observed when cells in the cell chamber consume oxygen and oxygen diffuses from the ambient through the PDMS (Figure 3a). When oxygen is not allowed to diffuse through the PDMS, cells become hypoxic after 300 seconds (Figure 3b), and higher flow rates would be needed to deliver sufficient oxygen to the cells. The oxygen concentration jumps observed in Figure 3 between media channel and cell chamber are due to diffusion across the porous membrane.

A dilute solution containing a small molecule entering the media channel at 20 µL/h diffuses across the porous membrane into the cell chamber and reaches a uniform concentration within the liver MPS within 300 s (simulation assumes impermeable walls and no cell consumption) (Figure 3c). Lastly, for cases where cells may be cultured along the media channel side of the membrane, shear stress predictions for a flow rate of 20 µL/h are shown in Figure 4.

Simulating the behavior and performance of microphysiological systems is an essential companion to experimental testing and development, reducing cost and saving time, and allowing new ideas to be rapidly tested.

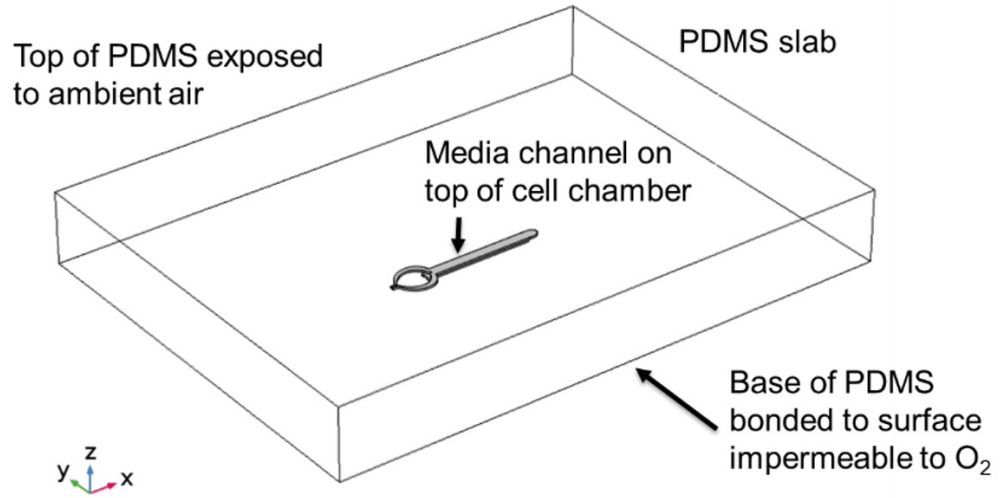
## Reference

1. S.N. Bhatia and D.E. Ingber, Microfluidic organs-on-chips, Nature Biotechnology, 32, 760-772

(2014)
2. F. T. Lee-Montiel, A. Laemmle, L. Dumont, C. S. Lee, N. Huebsch, V. Charwat, H. Okochi, M. J. Hancock, B. Siemons, S. Bogess, I. Goswami, E. W. Miller, H. Willenbring, and K. E. Healy, An integrated human hiPSC-based liver and heart microphysiological system predicts unsafe drug-drug interactions. https://doi.org/10.1101/2020.05.24.112771

## Figures used in the abstract

**a**




**b**

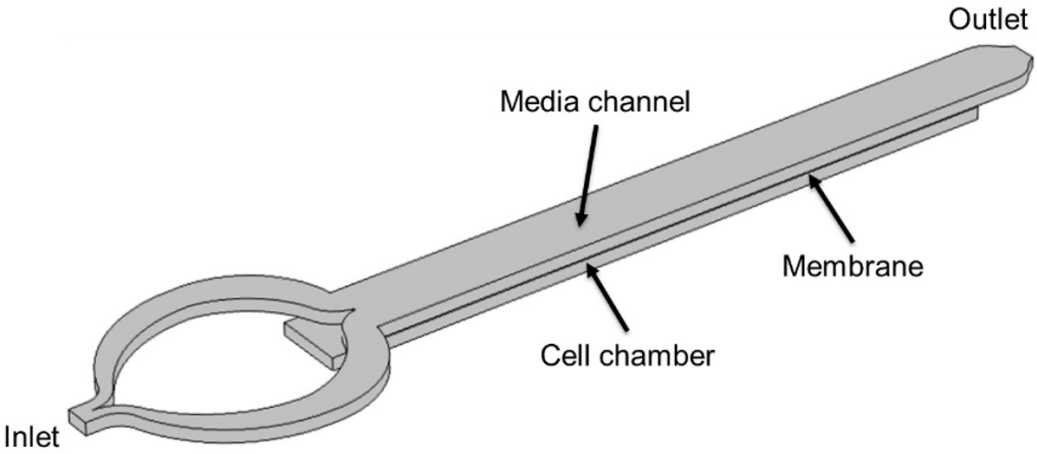



**Figure 1** : Microphysiological system (MPS) model geometry. (a) Overall device. (b) Closeup of microfluidic channels and chambers.

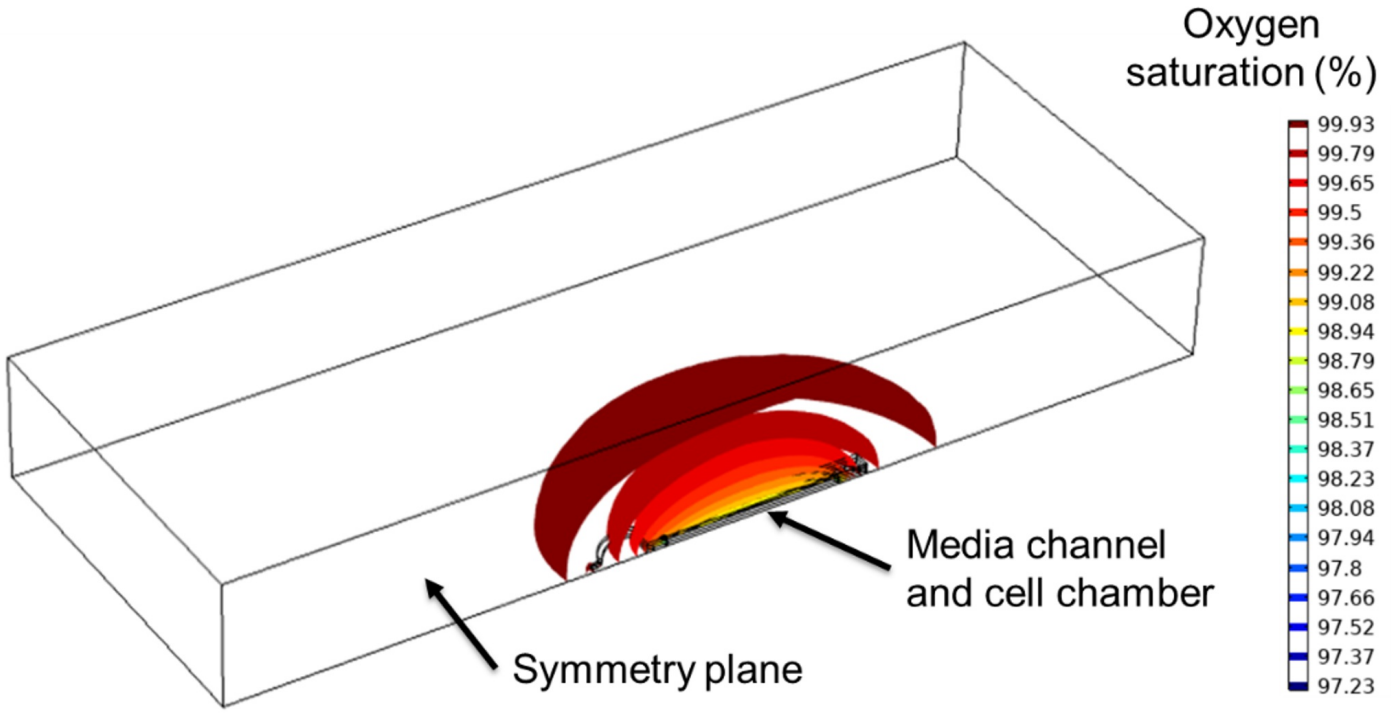



**Figure 2** : Oxygen concentration in the PDMS, including the media channel and cell chamber walls, are nearly saturated at 24 h.

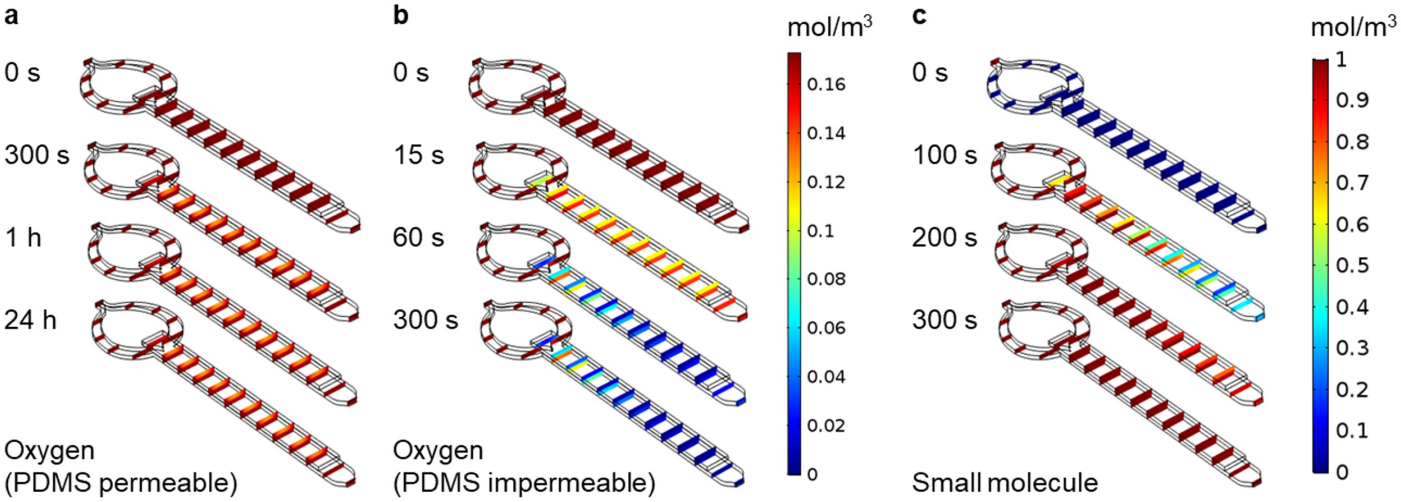



**Figure 3** : Oxygen and small molecule concentrations in the cell chamber (positioned on top in plots for clarity) and media channel, for a flow rate of 20 µL/h.

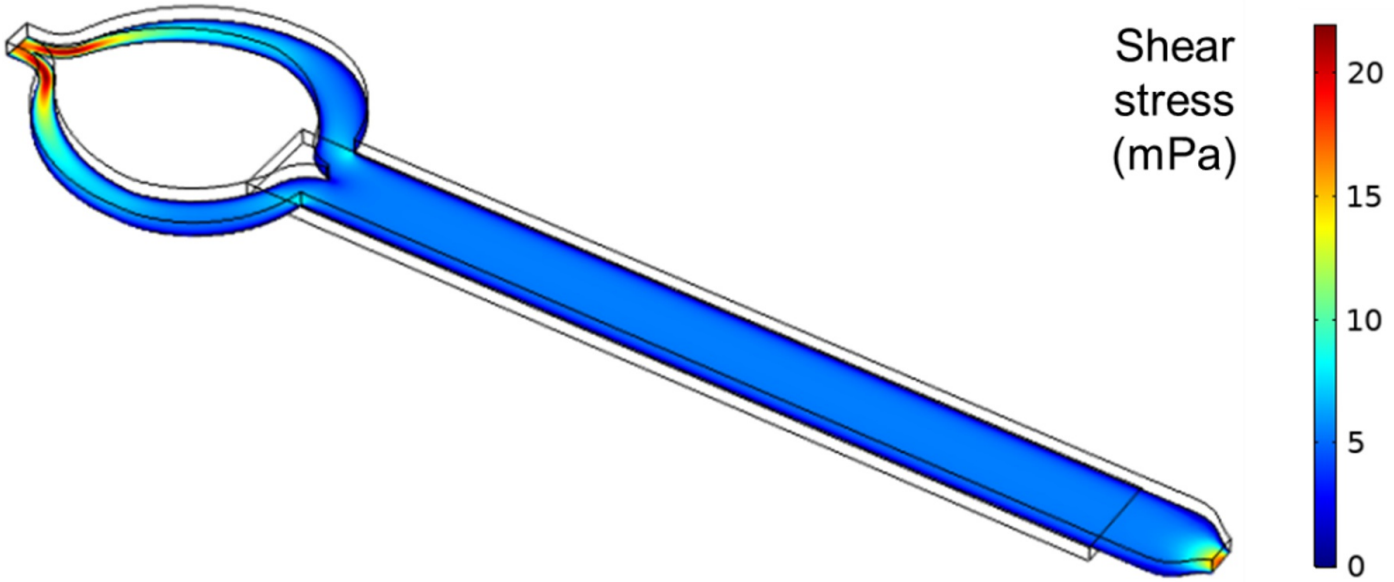



**Figure 4** : Shear stress on membrane (media channel side) at 20 µL/h.