Advanced Modeling of a Lung-on-a-Chip Microdevice

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Abstract

Organ-on-a-chip microdevices combine microfluidics, MEMS, and biotechnology techniques to mimic the multicellular architectures, tissue-tissue interfaces, physicochemical microenvironments, and vascular perfusion of the body.[1] 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 devices is critical to their development and optimization. Last year we developed a COMSOL Multiphysics® software model [2] of the lung-on-a-chip device of Huh et al.[3] that mimics the essential features of the blood-air barrier in human and animal lungs. The microdevice consists of a flexible membrane separating chambers for air and blood. Auxiliary vacuum channels enable stretching of the membrane to simulate breathing. Our model employs the COMSOL software capabilities for modeling fluid-structure interaction, laminar fluid flow, dilute species transport, and particle tracing.

The lung-on-a-chip model shown in Figure 1 is based on Huh et al.'s device. Vacuum channels flank the midsection, which consists of an upper channel for air or cell culture medium and a lower channel for blood or cell culture medium. A thin 10 μm membrane separates the upper and lower channels. We model the PDMS membrane as a linear elastic material since the strains are less than 15%. Features presented in 2015 included predictions of overall function of the device (Figure 2) and particle tracing to model bacteria or particulate flow (Figure 3).

The new features we report this year include the effective elastic modulus (Figure 4) of the porous membrane based on the approximate formulas of Meijers [4] and numerical results of Slot & O'Donnell [5]. In addition, we model the effective molecular diffusivity and effective thermal diffusivity of the porous membrane, and their effects on heat and mass transfer within the air and liquid channels and in particular across the liquid/air menisci in the holes in the porous membrane. In addition, we present results on cell uptake of nutrients and shear stress on cells on the membrane.

Developing models for organ-on-a-chip devices is an essential companion to experimental testing and development, reducing lab time and expense, and allowing new ideas to be rapidly triaged and tested. COMSOL Multiphysics provides an ideal platform for developing

and exploring such organ-on-a-chip microdevice models, as evidenced by the lung-on-a-chip model reported herein.

Reference

1. S. N. Bhatia and D.E. Ingber, Microfluidic organs-on-chips. Nature Biotechnology, 32, 760-772 (2014)

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4. P. Meijers, Doubly-periodic stress distributions in perforated plated, Ph.D. Thesis, Delft University of Technology (1967).

5. T. Slot and W. O'Donnell, Effective elastic constants for thick perforated plates with square and triangular penetration patterns. Journal of Engineering for Industry, 93, 935-942 (1971).

Figures used in the abstract

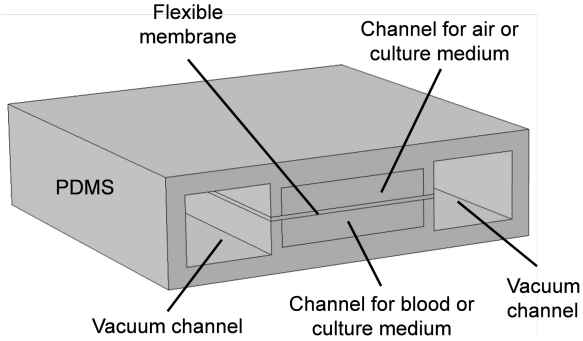

Figure 1: Setup for the lung-on-a-chip microdevice model.

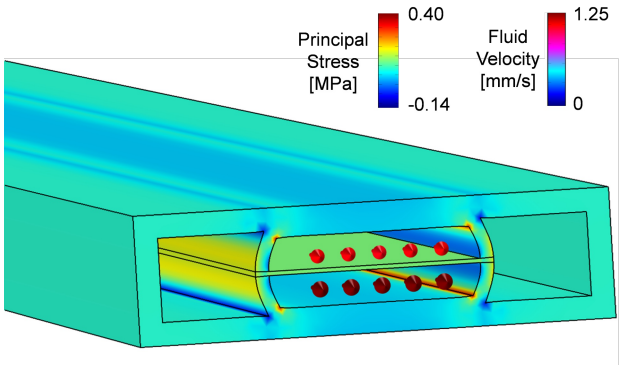

Figure 2: Principal stresses and flow in the lung-on-a-chip microdevice at t=7 s due to an applied 0.2 Hz sinusoidal vacuum pressure. Color denotes maximum principal stress. Arrows denote velocity of culture medium (lower channel, perfusion flow rate 20 µL/h) and air (upper channel).

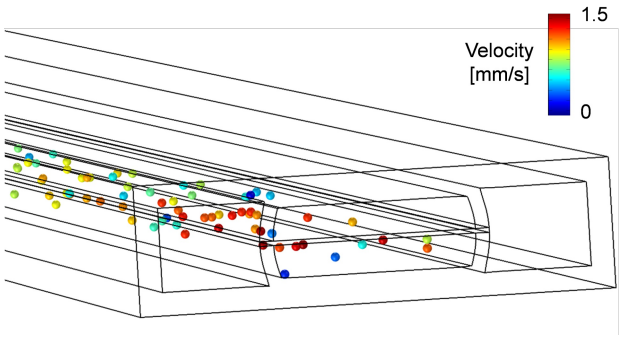

Figure 3: Particles moving with the flow in the lower channel at t=7.8 s during the oscillatory contraction and expansion of the channels due to the applied vacuum pressure. Color denotes particle velocity. Particle tracing allows the trajectories and fate of cells or particles to be tracked within the lung-on-a-chip microdevice.

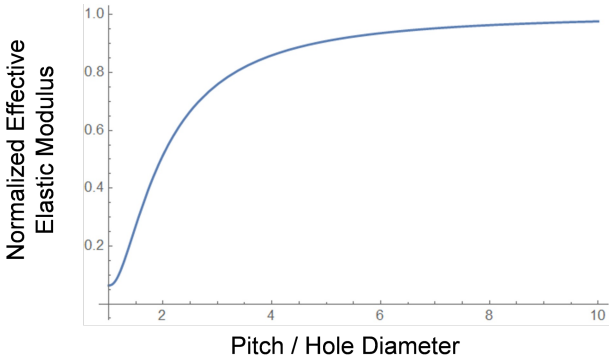

Figure 4: Effective elastic modulus of the membrane with holes normalized by the membrane material's elastic modulus, plotted vs. the ratio of pitch (hole spacing) to hole diameter. As the pitch increases, the effective elastic modulus approaches the material's elastic modulus.