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Modeling of an Acoustic Microfluidic Trap

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MEMS400 Independent Study Report

Dept. of Mechanical Engineering & Materials Science

Washington University in St. Louis

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Introduction

Motile (moving) cells are cells that have structures that propel them through fluids in which they propagate. Two common structures that create propulsion in cells are cilia and flagella. Cilia are also found in static cells, e.g., in the human airway to eject unwanted material from the lungs (1). These structures work together to exert mechanical forces to propel foreign objects. Flagella, on the other hand, are a form of cilia that are typically longer and fewer in number per cell. Unlike cilia, flagella exert their mechanical force independently and do not necessarily coordinate to beat (2). Although the roles of these structures (clearing airways or propelling swimming cells in fluids) are well understood, there is much to be discovered and learned about the mechanisms underlying their motions. Unfortunately, the nature of these structures creates an unstable environment that is difficult to observe; thus, especially for motile microorganisms, it is mandatory to develop a method of trapping these cells to analyze how cilia/flagella function both from engineering and biological points of view.

There are multiple existing methods to trap motile cells including acoustic confinement, optical tweezers, magnetic trapping and hydrodynamic trapping (3). Acoustic methods are the focus of this report; therefore, discussion is limited to this topic. Acoustic microfluidics permit us to encage microparticles, cells and microorganisms by applying ultrasonic standing waves (4). Our objective is to apply a standing ultrasonic field to a fluid volume containing cells and to actively move cells to prescribed zero pressure nodes of the field. If the microfluidic layout is carefully designed, it is theoretically possible to trap microparticles (or motile microorganisms) in a well-defined, repeatable process for subsequent analysis of behavior (e.g., response to chemical, optical, and/or other stimuli).

Here, I discuss development of an acoustic trapping device for motile *Chlamydomonas reinhardtii* (CR) cells propagating through microchannels. As the system represents a complex interaction between actuator vibrations, vibration propagation in solids, and acoustics in microfluidic channels, it was important to develop an accurate computational model for predicting trapping performance of candidate microchannel geometries. Therefore, the Acoustics module of COMSOL Multiphysics simulation software was used to create a model that predicts device performance under realistic experimental conditions (i.e., actuation of a fluid-filled glass chip with etched microstructures for the trapping chamber and fluid inflow/outflow). After initial modeling, device fabrication was attempted; however, a number of challenges were encountered preventing completion of proposed experimental tasks.

Methodology

Modeling with COMSOL

COMSOL Multiphysics is used in many areas of engineering for predicting the behavior of real-world systems. Capabilities include finite element analysis (FEA), which is typically used for investigation of structural vibrations and acoustic wave propagation in static fluids (5). The COMSOL platform has a user-friendly interface that outlines sequential steps for model creation and analysis: 1) geometry creation, 2) selection of appropriate physics (governing equations and boundary conditions) for a specific study, 3) selection of (or entry of custom) material properties, and 4) meshing of the model domain. Although there are many existing parameters incorporated into COMSOL by default, definitions of some functions of variables (e.g., acoustic energy density) were input to the model as needed.

For analysis of acoustic microfluidic trapping of motile cells, we started by creating a geometry. The representative geometry shown in Fig. 1 consists of a square reservoir and inlet/outlet channels. In the experimental device, the inlet allows incoming flow of cell-containing fluid and the outlet is for sample ejection after an experiment is complete. Here, the channel length was 25 mm with a width of 0.2 mm. The reservoir is the region where the trapping of motile cells occurs. After defining the geometry, I selected the *acoustics module*. The two most important parameters for trapping motile cells are the pressure distribution (mode shape) throughout the fluid and the frequency at which the mode shape is occurring. For that reason, *pressure acoustics* and *eigenfrequency analysis* were chosen for study. After completing the simulation, these studies provide detailed information regarding the pressure distribution throughout the channel/reservoir geometry as a function of ultrasound frequency without modeling the solid structures. Since water approximates the cell medium, I chose water as the material for the domain.

I next defined the mesh. Accuracy of results using any FEA method requires creation of a mesh that balances element size with computational expense. The maximum element size in the mesh was equal to 0.10 times the wavelength as determined by the ratio of speed of sound in water and the maximum allowable frequency of actuation. The maximum element size used in the meshing was approximately 0.3 mm. After establishing the maximum element size, COMSOL generated the meshed geometry shown in Fig. 2. After creating the mesh, I set the frequency range for the analysis to a range that is capable of encaging cells ($\sim 10\ \mu\text{m}$) and is also well-matched to available ultrasound transducers ($\sim 1\text{-}2\ \text{mm}$ thick PZT-8 piezoelectric elements). A frequency range from 500 kHz to 2 MHz was investigated. The COMSOL model was then complete and ready to run the simulation.

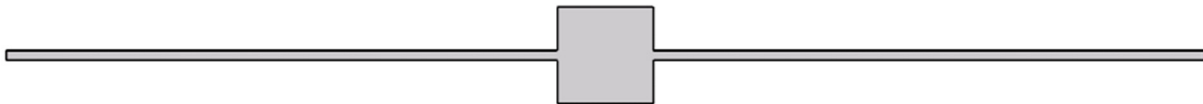


Figure 1 Channel- reservoir geometry built using COMSOL

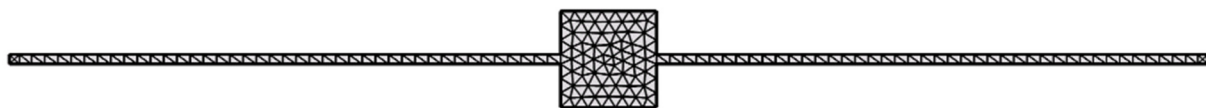


Figure 2 Meshed channel-reservoir geometry

Fabrication of Glass Based Acoustic Microfluidic Trapping Devices

After selecting a geometry of interest based on the results generated by COMSOL, I proceeded to fabricate a glass-based acoustic microfluidic trapping device. Soda lime glass mask blanks were used in fabrication of the trapping device. The channel-reservoir geometries were etched into the mask blanks following a standard process: 1) photolithography to transfer the channel pattern into a photo-sensitive polymer (6), 2) chrome etching using the polymer as a masking layer, and 3) glass etching in a hydrofluoric acid solution using the polymer/chrome layers as a mask. Inlet/outlet holes were then drilled into the completed channel layer before sealing the etched channels using thermal fusion bonding of a glass coverslip. Thermal fusion bonding achieves a permanent bond by applying a high temperature above the glass transition temperature of the two chip layers. For bonding our etched glass microfluidic chip and coverslip,

I placed both pieces between two ceramic plates of a heater set to 600°C. After a 10-hour heating process glass-glass chips should have been completely bonded; however, I had difficulty achieving a solid bond, and some of the assembled devices cracked during the heating (or possibly cooling) process. These challenges affected my ability to complete experimental analyses as described below.

Enhancing Baseline Computational Model

Because I was unable to fabricate suitable devices for testing, I shifted focus to developing a more realistic COMSOL model of candidate microfluidic chips for use in development of future trapping channels. The channel architecture described above was surrounded by a larger rectangle to represent the glass chip into which the microchannels are etched. A second smaller rectangle was added to represent a cross-section of the piezoelectric element used for actuation of the device.

Initially, I assigned inbuilt default COMSOL materials to the various model domains (piezo material (PZT-8) for the actuator, glass for the chip and default water for the fluid of interest). I then proceeded to account for losses during wave propagation by incorporating complex properties of our fluid and the rest of the elements of the device. This model enhancement should lead to a more accurate description of device operation. Specifically, I included a damping factor ϕ in the speed of sound in water modifying the default value from the real constant $c = 1497$ m/s to $c = 1497(1 + i\phi/2)$ m/s. The factor ϕ accounts for losses due to viscosity and thermal conduction in the bulk (sub VB and TB), and viscous and thermal boundary layers at the walls of the microchannels (and for suspended particles, at the particle surface) (sub VBL, TBL and VBLW). The total loss factor is thus $\phi = \phi_{VB} + \phi_{TB} + \phi_{VBL} + \phi_{TBL} + \phi_{VBLW}$, which for this case totaled 0.0032784. By including a more realistic representation of the fluid acoustic behavior, we removed a number of model idealizations and should be able to better predict real device performance.

Results and Discussion

In addition to the baseline case shown in Figs. 1 and 2, two reservoir geometries were investigated in this study. Both had nominal dimensions of 2 mm by 2 mm with 20 mm length by 100 μ m width inlet and outlet channels extending from the left and right bottom of the reservoir. The first of these reservoirs, a simple square, is shown in Fig. 3. The microchannels were surrounded by a larger rectangle of 50 mm length and 10 mm width, which represents the extents of the glass-glass chip into which the channel/reservoir geometry is etched. Inclusion of the glass is important for the model to accurately mimic the actual device. The model domain shown in Fig. 3 also includes a 1.5 mm by 10 mm rectangle extending from the right end of the glass chip to represent the vibration source, a PZT-8 piezoelectric element actuated in the longitudinal direction, i.e., voltage was applied across the 1.5 mm dimension, which is in the poled direction. As described above, simulations were run with water as the working fluid, and realistic damping in the fluid was accounted for by introducing a loss coefficient.

With the COMSOL model complete, I next ran a harmonic response analysis over the same 500 kHz to 2 MHz frequency range as used in the eigenfrequency study while driving the piezoelectric actuator with a constant 10 V_{pp} amplitude. Device performance was assessed by monitoring the absolute pressure amplitude averaged over the sample reservoir as a function of

frequency. Peaks in the harmonic response were used to identify potential trapping frequencies based on the shape of the pressure distributions at those frequencies. The response of the simple square reservoir is shown in Fig. 4. Because the constant voltage condition is somewhat arbitrary, the harmonic response is only used as a guide to compare possible operating frequencies; however, a number of interesting cases are observed. Since we are looking for relatively well-structured pressure minima (white lines) separated by regions of high pressure amplitude, the second case shown in Fig. 4 is most ideal from the selection of available fields.

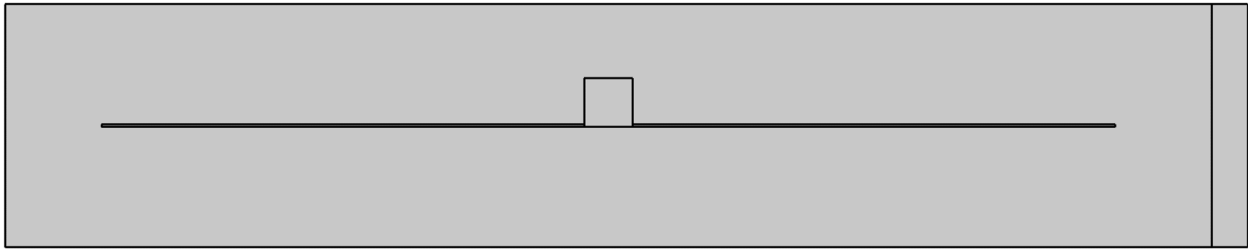


Figure 3 Acoustic microfluidic trapping device model comprising domains representing the fluid-filled reservoir geometry with inlet and outlet channels, a glass chip, and piezoelectric.

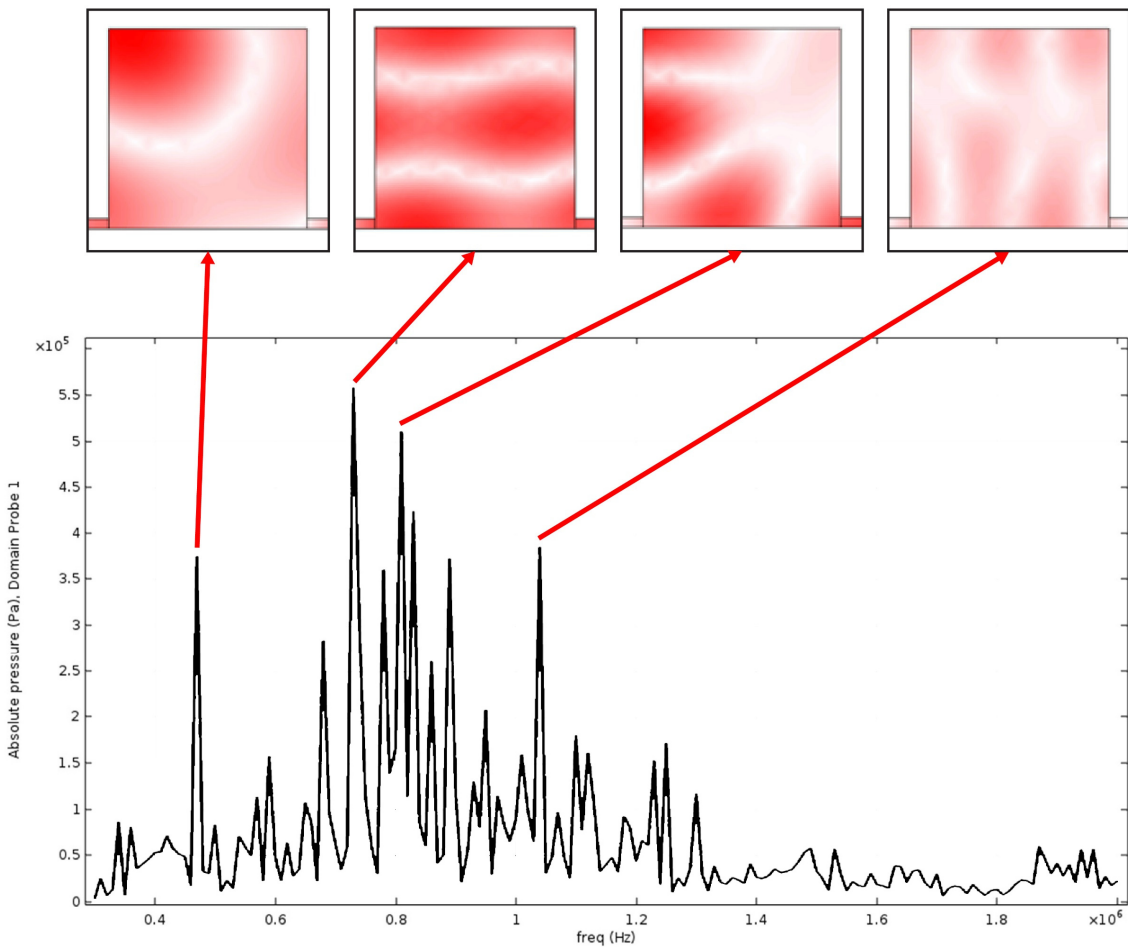


Figure 4 Harmonic response of simple square reservoir.

Fig. 5 shows the harmonic response of an alternative design that incorporates geometric features to support sample filling without the potential for trapping of air bubbles (which are detrimental to acoustic actuation of such devices). The response and representative pressure fields for this design are not as ideal for trapping of cells in distinct locations; however, both fields located at the pressure maxima would likely work for isolation of particles and cells in two bands near the central region of the reservoir. The last of the fields might also work as the two arcing bands within the chamber are discrete from other pressure minima.

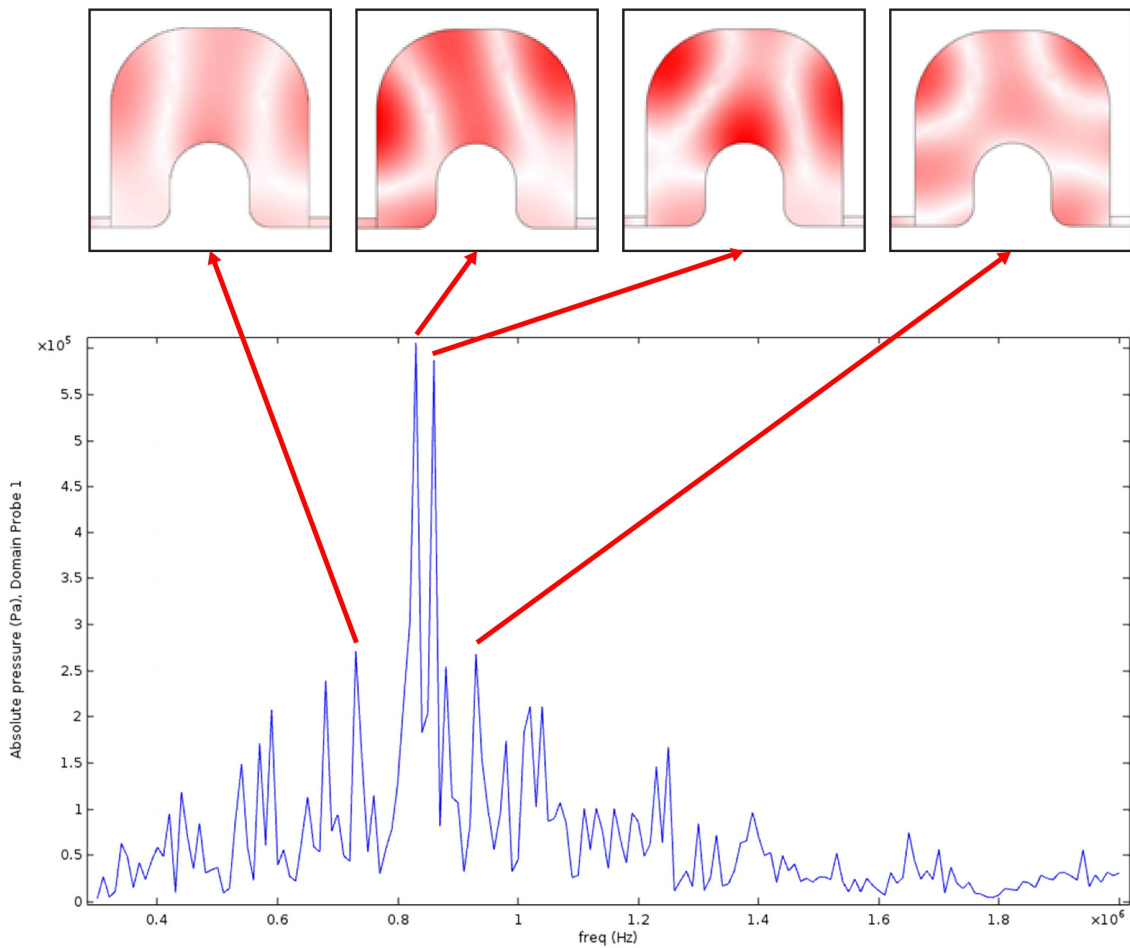


Figure 5 Harmonic response of alternative reservoir design.

I completed an analysis of the absolute pressure distribution as a function of frequency for two acoustic microfluidic trapping designs driven by realistic piezoelectric actuation. This work has improved my understanding of how best to design fluid structures to encage motile cells. An ability to explore not only the harmonic response but also specific pressure distributions of trapping chambers, provides information about the intensity of the pressure to which cells will be exposed at a given frequency. This is of high importance in assessing how harshly cells will be treated when in an environment where they can be trapped.

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