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Finite Element Modeling of a Cell Lysing Chip

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Abstract:

Cell lysis is important for the release of intracellular materials (DNA, RNA, proteins, etc) through disruption of the cell integrity. Ultrasonic energy is commonly utilized to induce cell lysing by mechanical means in laboratory procedures. Integration of an ultrasonic lysing mechanism into microelectromechanical systems (MEMS) is expected to reduce the lysing time while improving the lysing efficiency. Finite element modeling (FEM) is a powerful tool to study the coupled interaction between fluid flow and ultrasonic actuation in a micro-environment.

The device contains pillars with varying dimensions. We hypothesize that increasing the aspect ratio of pillars will increase the efficiency of the transfer of ultrasonic energy into the fluid phase and enhance the lysing efficiency. The fluid structure interaction, coupled with the piezoelectric strain models in the MEMS module of COMSOL will be used to analyze and compare the fluid flow inside the lysing chip.

Keywords: Lysis, Ultrasound, Piezoelectric, FEM.

1. Introduction

The lab-on-a-chip (LOC) technology integrates macroscopic laboratory functions onto a microfabricated device. This leads to the creation of a large variety of microdevices with reduced cost, lower reagent and sample consumption, faster analysis and response times, and increased portability. One example application of LOC is the real-time polymerase chain reaction (PCR) that detects the genetic information of virus, bacteria or other cell types. We are working on an integrated system containing an ultrasonic cell lysing chip, an mRNA binding chip, a real-time PCR chip, and a micropump. Such a system allows us to conduct complete genetic analysis from a single drop of blood.

Cell lysis breaks apart a cell to release the genetic materials (DNA, RNA, proteins, etc…) that are inside the cellular membrane. It is an important aspect of biological screening technique. The mechanism of lysing is believed to be cavitation of the liquid which forces dissolved gases to form and collapse violently causing damage to the cells [1, 2]. Several different methods for cell lysis exist utilizing mechanical, chemical, enzymatic, thermal or ultrasonic energy. We chose to use the ultrasonic lysing for our system as it can be easily integrated onto our LOC platform and does not involve change in chemical conditions.

In the current design, a microfluidic chamber is created with a flexing membrane to provide ultrasonic energy to the cells. A piezoelectric (PZT) plate placed on the exterior of the membrane oscillates under high frequency and transmits ultrasonic energy to the chamber and breaks open the cells. To increase the effectiveness of the device during lysis, a micro-pillared structure is fabricated onto the actuating membrane. This is useful in three ways: to increase the amount of cavitation by increasing the surface area for bubble formation, to physically inflict damage onto cells as the membrane flexes, and to create turbulent flow in the microchamber. We hypothesized that a larger pillar aspect ratio could improve the lysing efficiency by introducing more turbulence to the fluid.

Finite element modeling provides a useful tool to test this hypothesis and guide our lysing chip design by comparing the fluid flow with different pillar dimensions as well as with varying membrane thicknesses. COMSOL Multiphysics can be used to model the piezoelectric effect of the PZT and how it affects the fluid flow in the microchamber. Our model consists of two parts: a piezoelectric actuator and a constant laminar flow inlet. All the constraints used in the biological testing and actuation of the device are kept in the simulation. The model will test the effect of pillar width to pillar height (aspect ratio), spacing between pillars, and frequency of actuation. These results will later be compared with experimental results from biological testing.

2. Methods

2.1 Microdevice Construction

The micro lysing chip consists of a silicon wafer, a PZT piezoelectric actuator and a fluid chamber. A main inlet port branches into four channels that lead into a central chamber measuring 7 mm x 7 mm. Square micropillars along the top side of the chamber form a grid across the entire membrane (Figure 1). We expect that changing the dimensions of the pillar array will have a direct effect on the lysing efficiency as cells pass through the chamber. Like the inlet ports, four outlet ports on the opposing side of the chamber, funnel into one major outlet, allowing the fluid to flow continuously through the system. For our modeling we will consider the cross-section between one inlet and one outlet. A PZT piezoelectric plate is placed on top of the chamber to fluctuate the pillared structure causing deformation in the silicon membrane. The amplitude of this fluctuation will be directly related to the efficiency of our lysing chip.

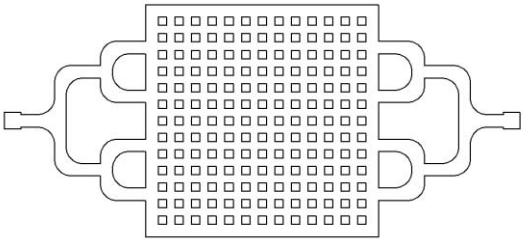

Figure 1: Planar View of Lysing Chip

2.2 FEM Considerations

To simplify the modeling process, a 2D cross section (Figure 2) was considered instead of a 3D structure. Finite element modeling of the lysing chip was conducted in two separate and coupled systems. First, the piezoelectric stack used to actuate the silicon membrane was modeled followed by the modeling of the fluid structure interaction between the fluid and silicon membrane. Next, the two systems were coupled together to obtain the effect of an actuating membrane on the fluid flow. The PZT stack was considered as a thin membrane attached to the exterior of the channel. Material properties of silicon and PZT used in this model are shown in Table 1. All variables were kept identical for each separate model created.

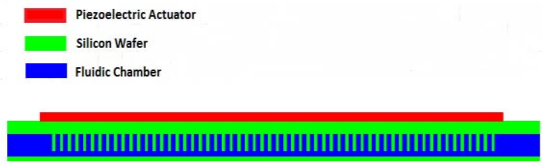

Figure 2: Cross Sectional View of Lysing Chip

	Silicon	PZT
Elastic Modulus	$1.9*10^9$ Pa	--------
Poisson Ratio	0.28	--------
Mass Density	7750 kg/m^3	2330 kg/m^3

Table 1: Material Properties

For the piezoelectrical system, the two ends of the silicon membrane were fixed in space with the rest of the boundaries free. This will allow the PZT to flex the membrane at these two points. The voltage was applied to the top of the PZT with the ground at the interior boundary between the silicon and the PZT. All other boundaries had a zero charge. The max actuation voltage was 1000 Volts with a frequency of 20 kHz. This can be represented as an AC voltage expressed by an equation

$$Vin=V_{max}*\sin(2\pi f*t) \qquad (1)$$

where V_{max} =1000V, and f=20kHz. This sinusoidal function will create a voltage applied in the range of [-1000V, +1000V] allowing the membrane to move up and down.

The fluid domain can be considered as an incompressible fluid traveling with constant velocity. Since fluid in a micro-environment generally has a low Reynold's number, the flow is laminar. The flow moves from left to right with an inlet velocity of 58 µm/s. This corresponds to fluid being in the chamber for approximately two minutes. The boundaries of the fluid domain are considered to be no-slip moving boundary. Because the deformation of the silicon membrane would affect the shape of the fluid domain, a moving mesh element was used to change the mesh as the system deforms. This system considers the movement of silicon as a physically induced mesh displacement and the fluid domain as a free mesh displacement. The solution was obtained between 0 and 1ms with a 10 µs step size. This is to ensure that the sine wave from the AC voltage supplied is solved with adequate representation of the true sine wave.

3. Results

A lysing chip without the pillared structure was used as the control chip in our analysis. Finite element modeling of the control chip formed the baseline in our analysis of the fluid flow. As shown in Figure 3, with no pillared structure there is hardly any turbulence in the fluid flow. The maximum deformation of the silicon membrane actuated by PZT is 59 µm. The von Mises stress in the membrane occurs at the fixed endpoints (Figure 4) of the chip and has a maximum value of 530 MPa. This falls far below the yield stress of silicon which is 7 GPa [3].

Comparison between a pillared surface and planar surface showed a significant difference in the fluid flow behavior in the microchamber. Square pillars with a length and height of 0.1mm were used to determine the effect of pillars with an aspect ratio of 1. In this model a small fluctuation in the velocity streamline was observed in the center of the chamber (Figure 5), suggesting a low degree of turbulence. The maximum deflection of the silicon membrane was 57 µm with the maximum stress at 495 MPa.

Figure 6 shows the modeling result of a pillared surface with an aspect ratio of 1.5 (150 µm X 100µm). As expected, more turbulence was shown in the fluid as illustrated by the streamline plot. It is also interesting to note that the maximum deflection of this membrane (30 µm) and the maximum stress (209 MPa) were both lower compared to the structure with a lower aspect ratio.

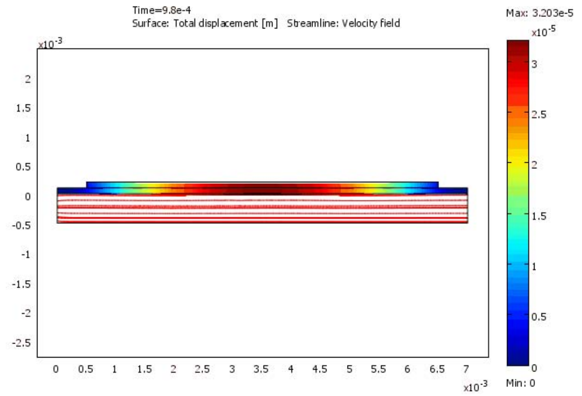

Figure 3: Analysis of the Control Chip

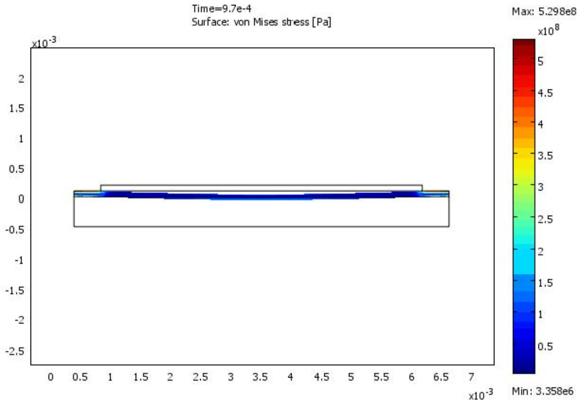

Figure 4: von Mises Stress in the Membrane

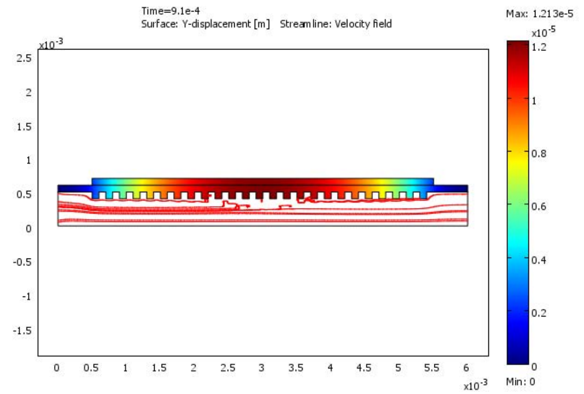

Figure 5: Lysing Chip with Aspect Ratio of 1

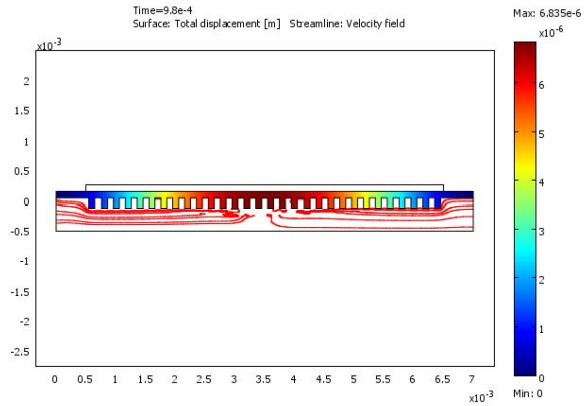

Figure 6: Lysing Chip with Aspect Ratio of 1.5

4. Conclusions

In this study, we used COMSOL Multiphysics to analyze the fluid flow in a micro-lysing chip chamber ultrasonically driven by a piezoelectric transducer. A pillared silicon membrane was designed and modeled with varying aspect ratios and spacing. The modeling results show that increasing the aspect ratio and decreasing the spacing of the pillars generated greater turbulence in the fluid flow, which is expected to higher disruption force to the cells in the lysing chip.

5. References

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