Ultrasonic Force-fields for the Micro-manipulation of Cells

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INTRODUCTION TO ACOUSTIC FORCES

Particles within an ultrasonic standing wave experience acoustic radiation forces. These forces move the particles to acoustic nodes within the acoustic field, as demonstrated schematically in Figure 1. The particles are typically held within a layer of water, across which an acoustic standing wave is generated. The acoustic source is a piezo-electric transducer, and a glass layer is typically used to reflect the acoustic wave and help form the standing wave. Figure 2 illustrates how this has been used to separate particles from the water.

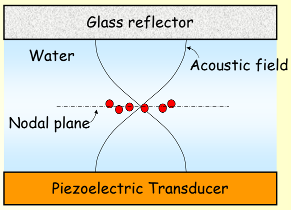


Figure 1: Schematic showing how particles move to the nodal plane of an acoustic standing wave.

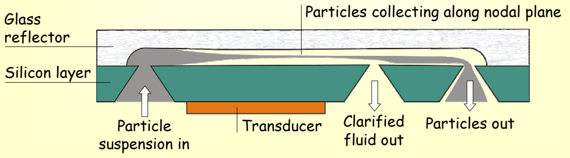


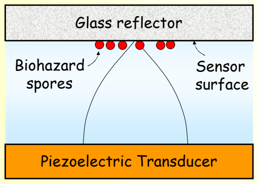
Figure 2: Acoustic particle separation in a micro-engineered device.

APPLICATIONS

This phenomenon is being used to control the movement of particles and cells for various bio-sensing and life science applications. For example:

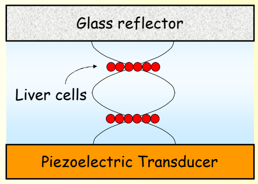
Biohazard detection

Figure 3: Pushing spores up to a surface where they can be detected and the environment monitored.



Tissue engineering

Figure 4: Agglomerating liver cells and controlling their growth for artificial organ development.



We are developing ultrasonic devices to develop these applications. Such devices can be realised using micro-engineering fabrication techniques and can ultimately be incorporated into **Micro-total-analysis-systems** (μTAS) for rapid processing and sensing of small fluid samples. This is one of the most rapidly advancing and exciting fields in sensing and analysis.

OUR RESEARCH – PREDICTING THE MOVEMENT OF PARTICLES

The challenge is to design reliable ultrasonic devices which can successfully control particle movement. The movement of particles depends upon the 3-dimensional acoustic and fluid characteristics of the device. We use numerical models to predict the exact nature of the acoustic field and fluid flow within these devices, then the resulting particle trajectories can be predicted. The influence of device geometry and materials used has been assessed and experimentally validated, and reveals how sensitive the performance of ultrasonic devices are to geometric changes.

NUMERICAL SIMULATIONS

Where particles are to be forced towards the reflector surface, acoustic simulations programmed in MATLAB show that the reflector thickness has a significant influence on the node position (figure 5). To get particles on the surface, the node needs to be positioned within the reflector which was only possible using reflector thicknesses of ≥1mm. These findings are supported by experimental data collected at Cardiff University (figure 6) which shows that the proportion of particles captured on the surface is low for thicknesses <1mm. Predicted capture was calculated by simulation particle trajectories as they pass through the acoustic field.

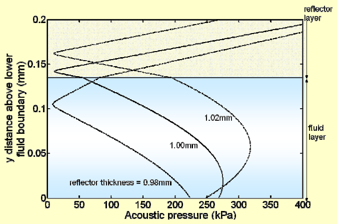


Figure 5: Pressure field in biohazard detection system for a range of reflector thicknesses.

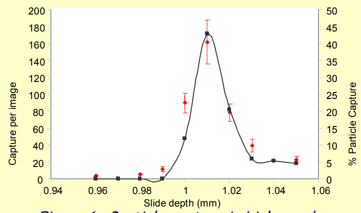


Figure 6: Particle capture in biohazard detection system for a range of reflector thicknesses (■ - modelled, ♦ - measured).

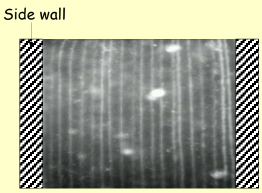


Figure 7: Striations across the width of water layer (looking down through glass reflector).

As well forming a standing wave between the transducer and reflector, a standing wave may also form across the width of the water layer. This makes particles agglomerate into striations (figure 7). To understand the causes of these lateral standing waves, a finite element analysis of one of our device was carried out. This predicted that the side-walls induce a complex 2-d acoustic field resulting in striations with similar spacing to that observed (figure 9). Further analysis has shown that the side wall geometry has a strong influence upon the occurrence of these striations.

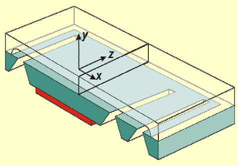


Figure 8: Cross-section of particle separator illustrating the yz plane simulated.

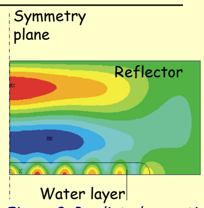


Figure 9: Predicted acoustic pressure showing variations across width of water layer.

CONCLUSIONS

Numerical simulations have improved our understanding of the use of acoustic radiation forces. This has helped us improve the design of these ultrasonic systems; for example, adjusting geometry to reliably position the acoustic node.

Although not described here, similar fluid simulation have been used to improve the **'microfluidic'** design of the separator device and uniformity of the fluid flow.

FUTURE WORK

Future work will look at realising the biohazard detection and tissue growth applications. This involves more extensive analysis of the acoustic field using the techniques described above. Part of this work aims to maximise the acoustic energy and therefore force acting on a particle, thus making the techniques more viable. Fabrication of these devices is an issue, too, and new micro-milling facilities at the university are now being used to make such devices.

This technique lends itself to many other applications. For example, Southampton University has EPSRC funding to develop a technique to evaluate **DNA sequences using fluorescent markers**. This relies on an acoustic field to control the position and orientation of the DNA strands attached to microbeads.

ACKNOWLEDGEMENTS

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