USW Network
Meeting

University of Southampton

Ultrasound and Microsystems – sensing, streaming and resonator design.

Friday 8th July 2005
Nightingale Building 67/1003

School of Engineering Sciences and Centre for Ultrasonics and Underwater Acoustics,

EPSRC Engineering and Physical Sciences Research Council

http://www.ucl.ac.uk/medicine/hepatology-rf/research/usw-net/

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School of Engineering Sciences and Centre for Ultrasonics and Underwater Acoustics,

Programme

1045 - 1105 **Registration**

Session 1 Resonator Design

1110 - 1130 **Professor Tim Mason**
Standing waves: when, why and how they are used a gentle (non mathematical) introduction

1130 - 1200 **Dr. Jeremy Hawkes**
In search of the perfect standing wave

1200 - 1230 **Dr. Mike Lowe & Dr Frederic Cegla**
Resonant chambers using matched resonant components

1230 - 1300 **Dr. Tobias Lilliehorn**
Ultrasonic trapping of particles and cells in microfluidic systems.

Lunch

Session 2 Microsystems

1400 - 1430 **Mr. Andreas Nilsson**
Lipid microemboli reduction in autotransfusion blood using USW in microfluidic channels

1430 - 1500 **Dr. Adrian Stevenson**
Acoustic biosensor methodologies

1500 - 1530 **Dr. Martin Wiklund**
Ultrasonic manipulation in focusing resonators for ultrasensitive biochemical analysis and single cell handling

Afternoon Tea

Session 3 Streaming

1600 - 1630 **Dr. David Haydock**
Simulating the movement of particles in a sound field using lattice Boltzman

1630 – 1700 **Dr. Larisa Kuznetsova**
Acoustic streaming and its application in short pathlength ultrasound standing wave (USW) resonators and microfluidic devices.

1700 **Cheese and Wine**

EPSRC Engineering and Physical Sciences Research Council

Session 1 Resonator Design

Standing waves: when, why and how they are used a gentle (non mathematical) introduction

Tim Mason, School of Science and the Environment, Coventry University, UK

Session 1 Resonator Design

In search of the perfect standing wave

Jeremy J. Hawkes, School of Chemical Engineering and Analytical Science, University of Manchester

Two considerations for particle-positioning resonator construction will be explored they are, efficient standing wave production within the fluid and the control of induced fluid movements. Model and experimental results will illustrate; construction of multilayer resonators, control of modes, streaming of the fluid and indicate a relationship between particle size-dependant-entrainment and the ultrasound frequency. The aim of this work is to address the following problems: In a 3 MHz ultrasound standing wave 5 μm diameter biological cells move to stationary positions at the pressure nodes in aqueous media. Smaller particles may not become stationary or even not move to the nodal position and an alternative fluid or frequency introduces further variables that need inclusion in the chamber design process. In addition, the standing waves in a fluid form complex interactions with the external retaining vessel requiring analysis of multilayer structures and resonant modes in 3 dimensions. Clearly, standing waves in fluid filled resonators may never be perfect yet good design should consider a huge number of variables. A few commercial systems have succeeded in restricting the variables and using this acoustic cell positioning driving force, but this non-destructive force has potential for far wider applications in biology and elsewhere. Successful realization of new applications should follow from a clear set of design criteria.

Session 1 Resonator Design

Resonant chambers using matched resonant components

Mike Lowe & Frederic Cegla, Dept. Mechanical Engineering
Imperial College London, UK

A standing wave field can be created in air or fluid in a cylinder by "breathing mode" vibration of the cylinder, in which the walls of the cylinder oscillate in the radial direction. An attractive configuration for doing this is to use a piezoelectric cylinder which vibrates when an electric signal is applied. In order to achieve maximum amplitude of the standing wave field for a given electrical power input, a goal for such a setup is to tune the system so that the tube vibrates at a natural frequency which also corresponds to the natural frequency of the wave field in the air or fluid. The presentation will explain the physics of the waves in the cylinder and in the air or fluid, and how these can be tuned by choosing the materials and dimensions.

Session 1 Resonator Design

Localized ultrasonic trapping of particles and cells in microfluidic systems

Tobias Lilliehorn, Department of Engineering Sciences, Uppsala University, Sweden

This talk focus on the technological aspects of utilizing localized acoustic trapping of microbeads or cells in microfluidic systems. Applications can be found in the area of miniaturised total chemical analysis systems (μTAS). A device comprising an array of three individually addressable particle trapping sites in a flow-through channel has been evaluated. Each trapping site was designed as a local acoustic resonator consisting of a miniature multilayer piezoceramic ultrasonic transducer (<0.8 x 0.8 mm^2) and a glass reflector, enclosing a half wavelength bead conducting fluid layer. Particles in the fluid passing a transducer were drawn to pressure minima in the acoustic field, thereby being trapped and confined, vertically as well as laterally, at the transducer position. The bead trapping was found to be strongly affected by near field pressure variations due to diffraction effects associated with the finite sized transducer element. Since laterally confining radiation forces are proportional to gradients in the acoustic energy density, these near field pressure variations may be used to get strong trapping forces. It has been shown that the microbead clusters can be trapped at considerably high perfusion rates, up to 10 μl/min (corresponding to 2.4 mm/s). As an outlook, the technology is believed to be expandable to two dimensions, with the prospect of generating flexible bioanalytical arrays in microfluidic systems.

Session 2 Microsystems

Lipid microemboli reduction in autotransfusinon blood using USW microfluidic channels.

Andreas Nilsson, Filip Petersson and Thomas Laurell, Department of Electrical Measurements, Lund Institute of Technology, Lund University, Lund, Sweden

During cardiac surgery, shed blood is returned to the patient introducing fat particles into the cardiovascular system. The fat particles, microemboli, will flow through the blood vessels and finally end up in the fine capillaries where they will form occlusions, especially harmful in the brain. Every open heart surgery results in about 3 million embolis which results in various degrees of brain damage. To avoid damage to the brain the lipid microemboli needs to be removed from the blood before given back to the patient. No current technique can remove the fat sufficiently; however, our separation technique using USW in mircofluidic channels enables a removal ratio up to 95% of the fat particles and a simultaneous red blood cell recovery up to 95%. The particles will be separated from each other in the acoustic standing wave because of their different physical properties. By using a microchannel, the laminar flow enables a split of fluid fractions removing the fatty solution from the enriched erythrocyte solution at the exit of the USW separation chip.

Session 2 Microsystems

Acoustic biosensor methodologies

Adrian Stevenson, Institute of Biotechnology, University of Cambridge, UK

Quartz crystal microbalances and surface acoustic wave devices are familiar components in TV and radio receivers and in recent years have been utilised for constructing sensors that operate in air and liquid environments. This presentation considers the issues surrounding their use as biological sensors or biosensors that respond selectively to a molecular soup consisting of proteins, antibodies and DNA, and how several adaptations have been needed to develop their real value in this contrary environment: Our group initially utilised Love waves to focus sound at the solid liquid interface for increased sensitivity in a liquid environment. However the difficulty of modifying the electrodes, led us to a novel wireless method for interrogating resonant elements based on the Magnetic Direct Generation principle, discovered in the early 1960s. The advantage of the instrument format was that inexpensive acoustic elements that were either conductive or had magnetic or electric dipoles could be interrogated with electromagnetic to acoustic transduction mechanisms, via a local spiral coil antenna. More recently, the simplicity of this format has been utilised by our group's biochemists and microbiologists, and found to support acoustic switches that are modulated by chemically responsive hydrogels and spectral measurements of biomolecules from 6 MHz to 1 GHz.

Session 2 Microsystems

Ultrasonic manipulation in focusing resonators for ultrasensitive biochemical analysis and single cell handling

M. Wiklund and H. M. Hertz, Biomedical and X-Ray Physics, Royal Inst. of Technol., AlbaNova, SE-106 91 Stockholm, Sweden

Ultrasonic standing-wave (USW) radiation forces can be used for particle manipulation, separation and enrichment. While most applications of USW microparticle manipulation technologies employ the plane-parallel resonator, we have investigated different focusing resonator geometries for improved performance and flexibility. The goal is to use the devices for ultrasensitive biochemical analysis and for single cell handling in lab-on-chip systems. In the first appclication, two different systems has been developed for particle-based biochemical analysis by separation and/or enrichment of functionalized latex beads. Both systems employ the hemispherical resonator geometry. In the first approach, a longitudinal flow-through capillary ultrasonic trap (CUT) is used for size-selective separation and retention of microparticles[1]. The CUT device may be used for enrichment and detection of particle pairs formed during the initial stage of particle immuno-agglutination[2]. In the second approach, a miniature focusing transducer assembly (FTA) is combined with a commersially available 96-well microplate for particle enrichment in bulk samples[3]. The FTA/microplate device is tailor-made for the imaging properties of a confocal microscope, resulting in two-dimensional particle rearrangement matching the confocal laser-scanning plane. The system is developed for a separation-free immuno-assay based on antibody-coated beads and fluorophore-labelled tracer antibodies. In the second application, a flow-through lab-on-chip system is developed with the aim to allow manipulation of single cells and single particles. Such manipulation is important for cell programming by surface imprinting of cells by, e.g., particles with individually tailored macromolecular landscapes on their surfaces[4]. We will present preliminary experimental results and videosequences. In the present talk, the advantages of focusing resonators are discussed, both from a theoretical and from an experimental point of view. The different systems are described together with their applications and current experimental status.

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[1] M. Wiklund, S. Nilsson and H. M. Hertz, J. Appl. Phys. **90**, 421 (2001).
[2] M. Wiklund, O. Nord, R. Gothäll, A. V. Chernyshev, P-A. Nygren and H. M. Hertz, Anal. Biochem. **338**, 90 (2005).
[3] M. Wiklund, J. Toivonen, M. Tirri, P. Hänninen and H. M. Hertz, J. Appl. Phys. **96**, 1242 (2004).
[4] More information available at http://www.cellprom.net.

Session 3 Streaming

Simulating the movement of particles in a sound field using lattice Boltzmann

David Haydock, Oxford University and Unilever R &D, Colworth, UK

Particles move in a sound field due to the radiation force produced by momentum transfer from the wave to the object. The radiation force includes the time-averaged pressure, the effects of streaming and a contribution due to the movement of the object itself in the sound field. Analytical solutions generally assume that the fluid is inviscid so that only the time-averaged pressure and particle motion need to be considered. This significantly reduces the complexity of the analysis, and is reasonable if the acoustic boundary layer is small compared to the particle size. This is true for a large particle and a low viscosity fluid. However, if this is not the case, viscous effects such as acoustic streaming need to be considered and the motion can be much more difficult to predict. Here simulations are often the best approach.

In this presentation we discuss the application of the lattice Boltzmann modelling methodology to simulating the radiation force on an object. The lattice Boltzmann approach simulates the full Navier-Stokes equations, so includes viscous effects such as acoustic streaming. We begin by introducing the radiation force on an object including viscous effects. We show that we can quantitatively simulate the radiation force on an object and how this force is changed by viscous effects such as streaming. Finally we show that we can simulate geometries that are too complex for the analytical theories and that we can get unexpected particle motion.

Session 3 Streaming

Acoustic streaming and its application in short pathlength ultrasound standing wave (USW) resonators and microfluidic devices

Larisa Kuznetsova, School of Biosciences, Cardiff University, UK

Different types of acoustic streaming, which is a fluid motion originating from spatial non-uniformity of the sound field or from energy dissipation at the liquid/solid interfaces of a container, have been characterised in short pathlength (one half to one quarter wavelength λ) USW resonators. Particle image velocimetry (PIV) has been applied to acoustic streaming studies. Rayleigh-type streaming, which is a vortex flow outside the boundary layer (scale ≅ λ), has been studied in a 1.5 MHz λ/2 chamber with one central potential well. The streaming velocities as well as their dependence on distance and squared acoustic pressure amplitude were consistent with the Rayleigh model. Several smaller Rayleigh-type vortices were detected in λ/2 and λ/4 chambers with multiple potential wells. Wall-independent streaming in planes parallel to the transducer's radiating surface caused by lateral pressure non-uniformities has also been detected.

Acoustically induced streaming has been employed to non-invasively effect rapid convective movement in microfluidic devices and to enhance the rate of surface reactions or particle capture. The capture of 200 nm biotinylated particles on immunocoated reflector's surface of λ/4 USW resonator has been increased five times by streaming drag at 1.75 MHz in a 10 min assay comparing to the no ultrasound situation.

Poster Session

Temperature evaluation of soft and hard pzt transducers for ultrasonic trapping in a microfluidic platform

L. Johansson, M. Nilsson, T. Lilliehorn, M. Almqvist*, J. Nilsson*, T. Laurell*, S. Johansson, Uppsala University, *Lund University*

This paper reports a comparison of soft and hard piezoceramic transducer materials used for ultrasonic particle trapping in a microfluidal bioanalytical platform. The investigation is made with the objective to obtain high acoustic forces with a minimum of temperature increase. Temperature is a critical parameter for bioassays and most often need to be kept below a certain level to allow handling of cells and proteins. The main conclusions in this paper are that it is possible to get efficient trapping with a temperature increase of only a few degrees and that a soft piezoceramic material has advantages in an application such as this.

Several groups have reported using acoustic forces in fluidic systems for separation or trapping of particles and cells in macro-scale resonators. In our group, a technology has been developed that enables a micro-scale system with shorter path lengths yielding higher frequencies and thus stronger trapping force. The platform of an array of individually controlled trapping sites offers high versatility regarding bioassays.

The piezoelectric materials (EDO EC-69 and EC-76) have different piezoelectric constants and the acoustic pressure is therefore measured, with a miniature hydrophone (0.2 mm2 diameter) and at a distance of 35 wavelengths from the transducer, and the drive voltage adjusted to give the same output. Running the transducer at these voltages, fluid temperature is evaluated by measuring fluorescence intensity of temperature sensitive Rhodamine B dissolved in the fluid.

The surprising result at resonance is that the soft material (EC-76) gives a lower temperature increase (2°C) than the hard material (EC-69) (7°C). At anti-resonance however, the hard material (3 °C increase) is more favourable than the soft material (with 5°C increase). Loss mechanisms in these transducer materials are complex and the paper presents some of the issues that have to be considered in these ultrasonic trapping devices.

http://www.ucl.ac.uk/medicine/hepatology-rf/research/usw-net/

Acknowledgements

In addition to the speakers and poster presentations I would like to thank: the EPSRC for sponsoring this meeting and the USW Network and the University of Southampton for today's facilities.

Martyn Hill