# Computationally Assisted Design and Experimental Validation of a Novel 'Flow-Focussed' Microfluidics Chip for Generating Monodisperse Microbubbles

Michael Conneely[1], Vikas Hegde[2], Hans Rolfsnes[1], Adrian Mason[2], Donald McLean[1], Charlie Main[1], Frances JD Smith[2], WH Irwin McLean[2], Paul A Campbell[1]

[1]Carnegie Physics Laboratory, University of Dundee, Dundee, Scotland, UK
[2]Division of Molecular Medicine, University of Dundee, Dundee, Scotland, UK

## Abstract

Gas-filled lipid microbubbles are emerging as a next generation 'theranostic' tool in the medical arena. Initially developed as a diagnostic aid to improve echogenicity in ultrasound imaging, their therapeutic potential has now been realized also through their unique ability to deliver molecular species such as drugs and genes by disrupting the cell membrane, again in response to ultrasound wave stimulus. The main aim for the present study was to computationally validate a novel glass microfluidic chip we designed. The chip encompasses a distinctive junction geometry where the liquid and gas phases meet and more importantly produce stable monodisperse microbubbles, which it is hoped will have a more easily controlled, and thus clinically reliable response to pulsed ultrasound. To model our chip design the Laminar Multi-Phase Flow, Level Set physics were used in COMSOL Multiphysics version 4.1 to generate a 2D model of the system as shown in Figure 1. Wetted wall boundary conditions were defined on the channel walls with a specified contact angle (150deg) estimated from a visual observation of our physical chip in operation. Due to the constrained height (4 um) of our channels in relation to their widths the "shallow channel approximation" feature was implemented to approximate a quasi 3-D flow more closely. It accomplishes this by introducing a volume force to the fluid flow equation to account for drag effects of the top and bottom boundaries. The COMSOL model was compared directly against our observational results to validate its accuracy, Figure 2 shows the bubble formation process as observed with a high speed camera (above) and as modeled in COMSOL (below). The diameter of the microbubbles formed ranged from 2-10 um, depending upon the liquid and gas flow parameters. At the high flow rates required (152 kPa gas pressure and 1.5-2 uL/min liquid flow rate) for reasonable throughput, specific nuances of the bubble formation process such as pinch-off and location within the flow arc of the microfluidic channels not easily observed in our experimental data could be readily discerned in our model (Figure 3). Through parameterized studies easily implemented in COMSOL, factors that will inform next generation designs for our chip and the optimum operational parameters for said chip can be rapidly investigated, significantly accelerating development.

# Figures used in the abstract

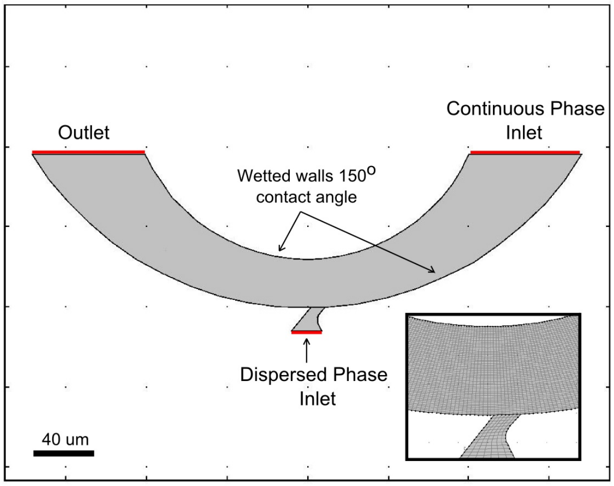


**Figure 1**: Model domain, boundary conditions and mesh grid (inset).

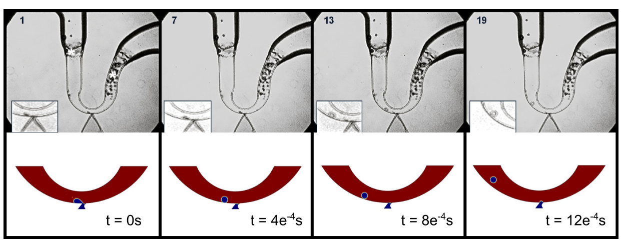


**Figure 2**: Comparison of experimental and numerical model results.

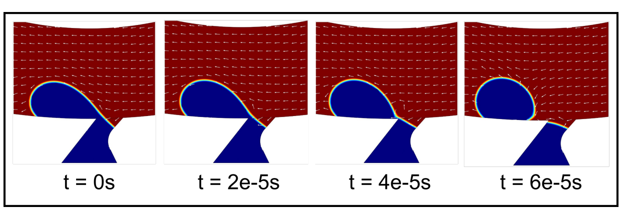


**Figure 3**: Bubble pinch off process.