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

Michael Conneely
Electronic Engineering & Physics

Excerpt from the Proceedings of the 2012 COMSOL Conference in Boston

Overview

- Motivation
- Experimental Setup
- Modelling Goals
- Model Overview
- Model Validation
- Results and Conclusion

Motivation

Concepts & **I**nnovation in **C**avitation **a**nd **S**onoptic **S**ciences

- Enhance understanding of microscopic & [sub] microsecond behaviour of microbubbles in Ultrasound fields.

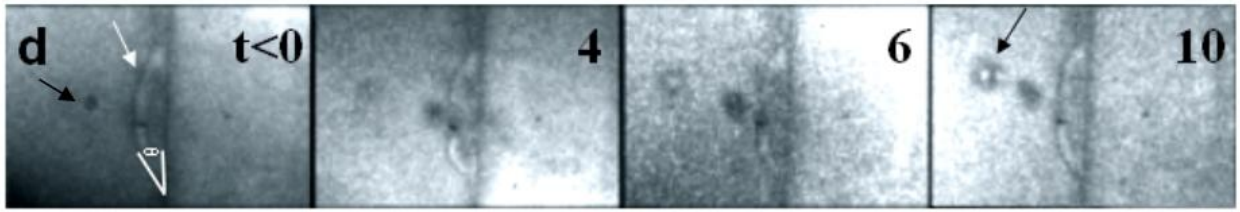
- Direct relevance across therapeutic and diagnostic clinical modalities; namely targeted drug delivery and molecular imaging.

D◆GEM
DERMATOLOGY & GENETIC MEDICINE

Division of MOLECULAR MEDICINE

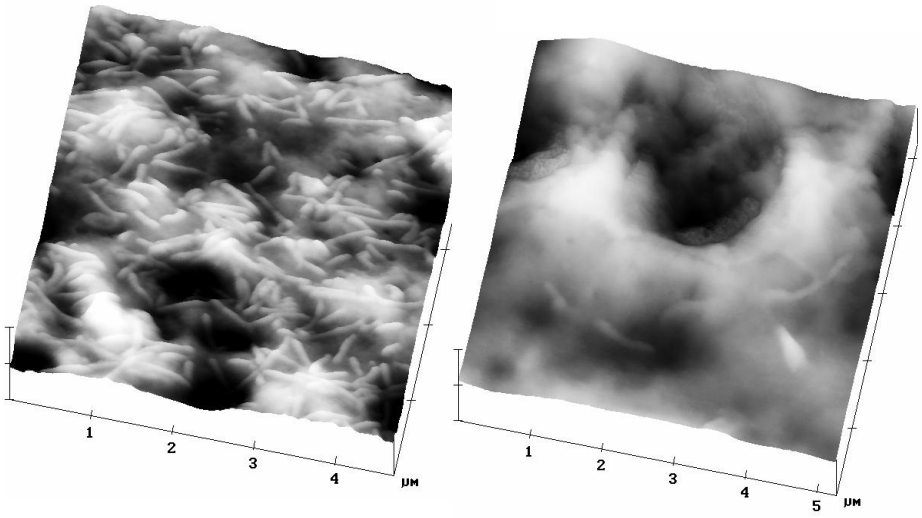
Motivation

High speed imaging of microbubble collapse next to cell monolayer

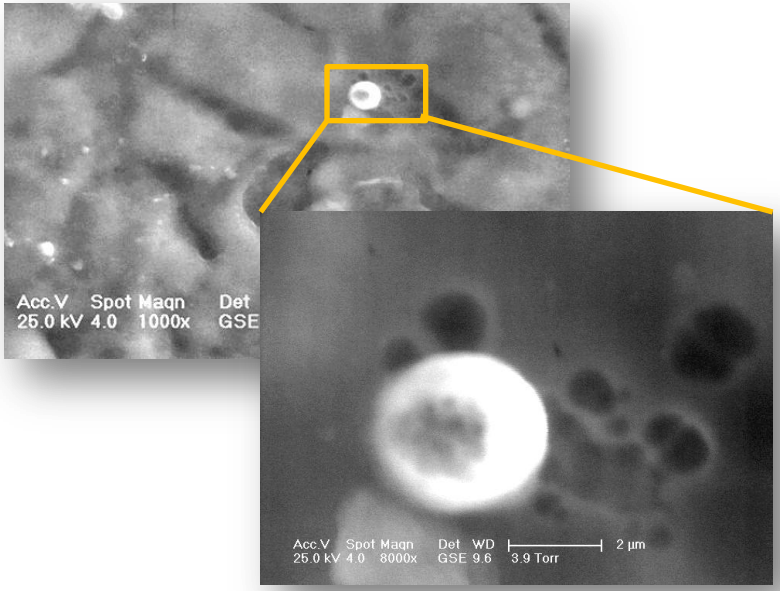


Nature Physics 1 (2) 107 (2005)

AFM image of cell membrane pre and post exposure

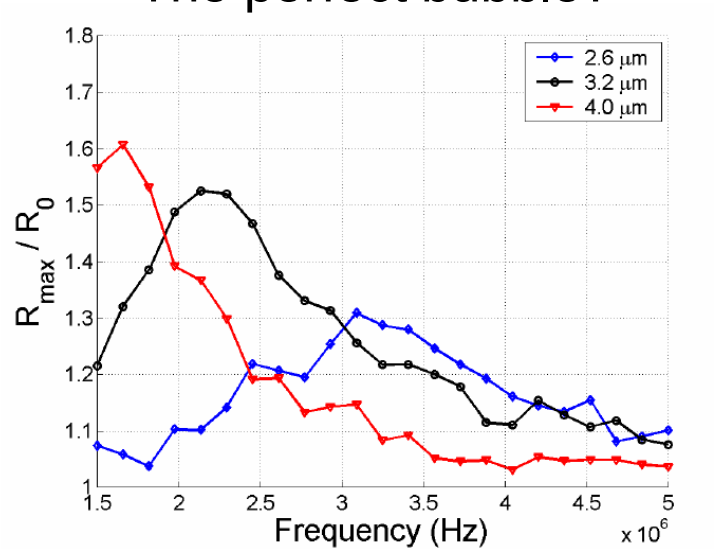


SEM image of cell monolayer

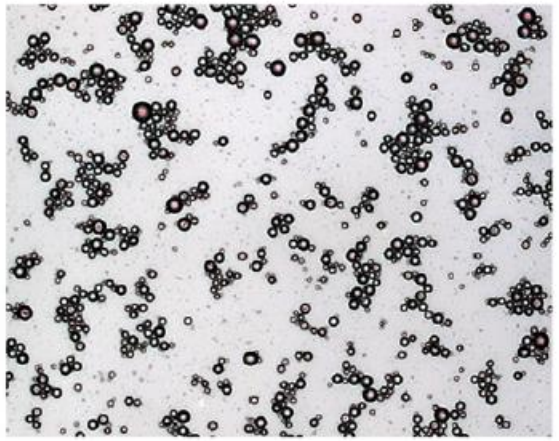


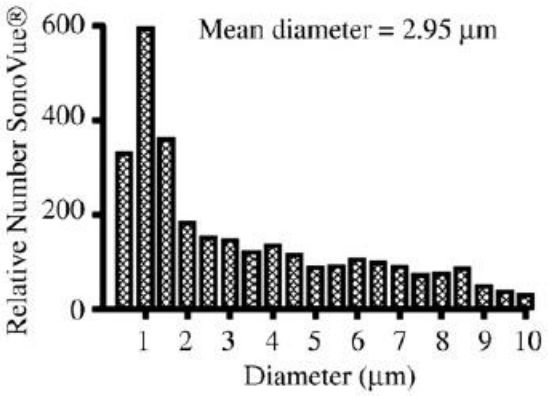
Motivation

- The perfect bubble?



Meer van der, S.M et al. *IEEE Ultrasonics Symposium*, 2004





J. S. Cheung et al., *Neuroimage*. 2009 Jul 1;46(3):658-64.

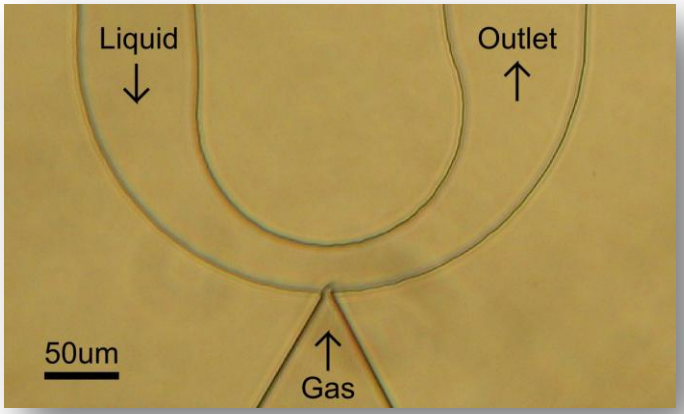
- Advanced preparation techniques required

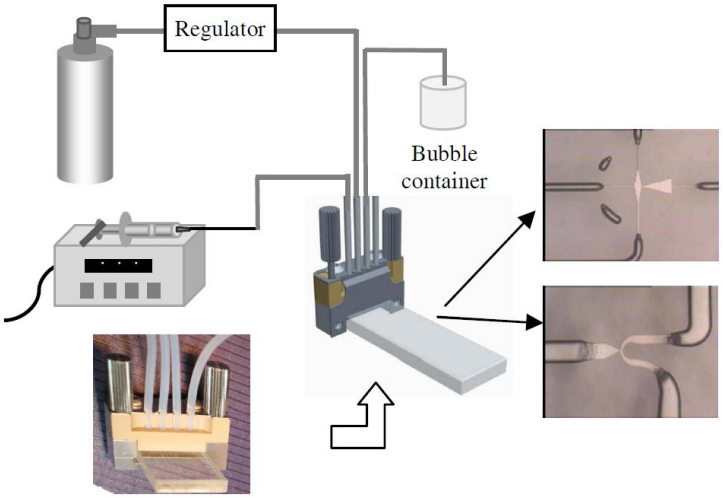
- Control over size, composition and stability with highly <u>monodisperse</u> populations

Experimental Setup

- Novel flow focused junction glass microfluidic channel geometry.

- Control over size, composition and stability with highly monodisperse populations.





- PEGylated lipid mixed with cholesterol liquid phase (shell material).

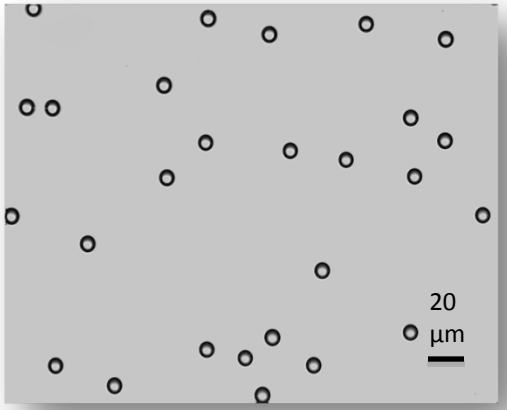
- High molecular weight gas phase, nitrogen or perfluorobutane.

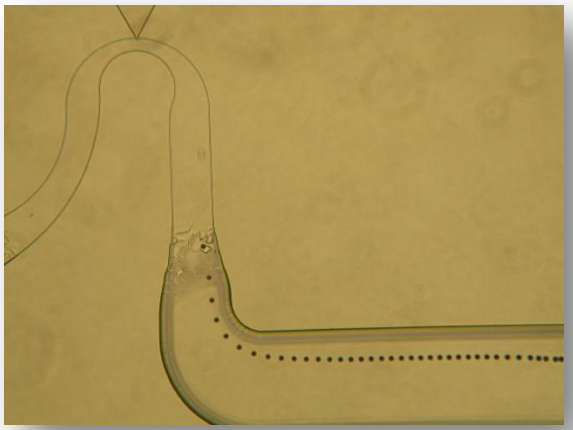
Experimental Results

- A highly monodisperse population of microbubbles was obtained.

- Bubbles stable for periods extending to 4 hours +

- Bubble diameters ranged from 2-10um depending on flow rates and pressures





Modelling Goals

UNIVERSITY OF DUNDEE

- Develop robust model validated against our experimental results.
- Investigate effects of chip design elements.
- Capture and probe mechanisms involved in bubble formation.
- Use parameterized studies to predict bubble sizes and generation rates.

Model Overview

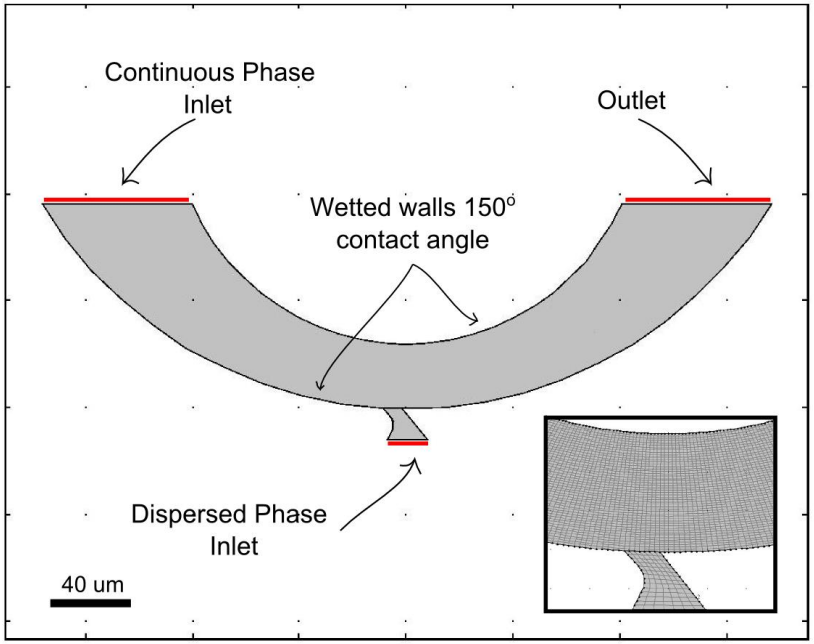
- COMSOL 4.1 – Laminar Two Phase Flow, Level Set
  - track multiphase flow interface

- Constrained geometry height → 2d model with shallow-channel approximation

- Reduced computational domain.

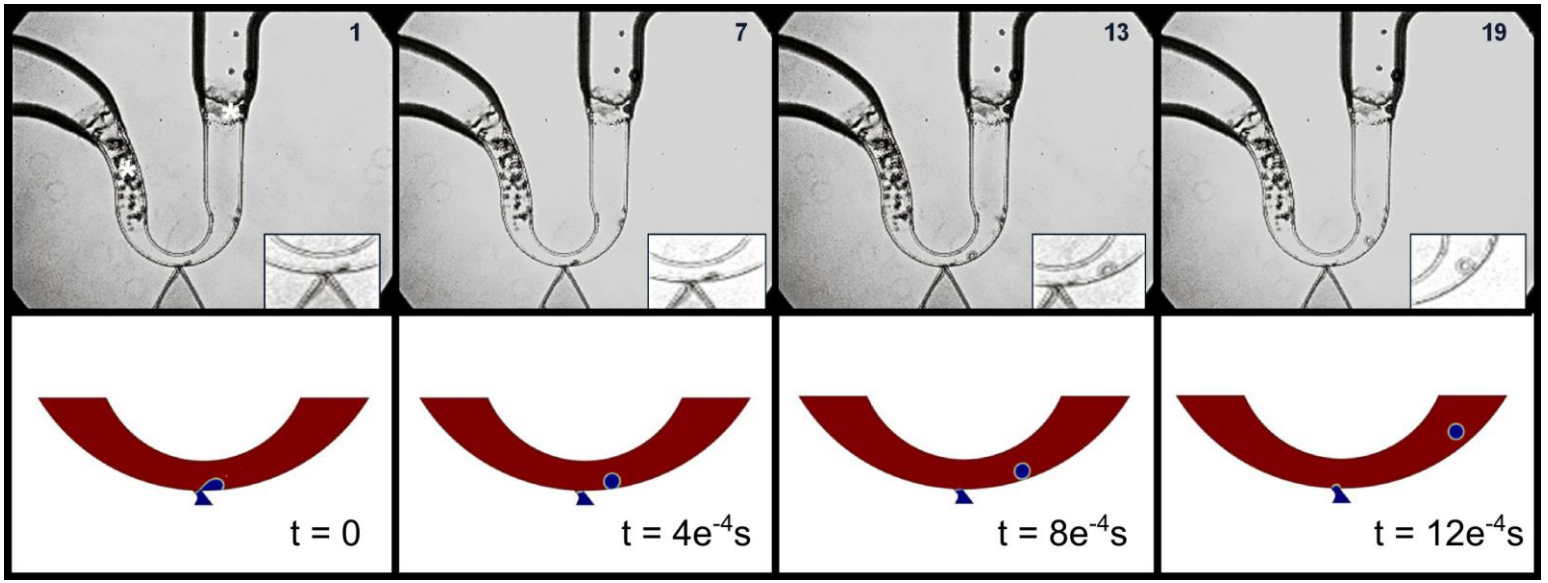
- Velocity boundary inlet conditions

- <1um quadrilateral mesh elements (20,365)



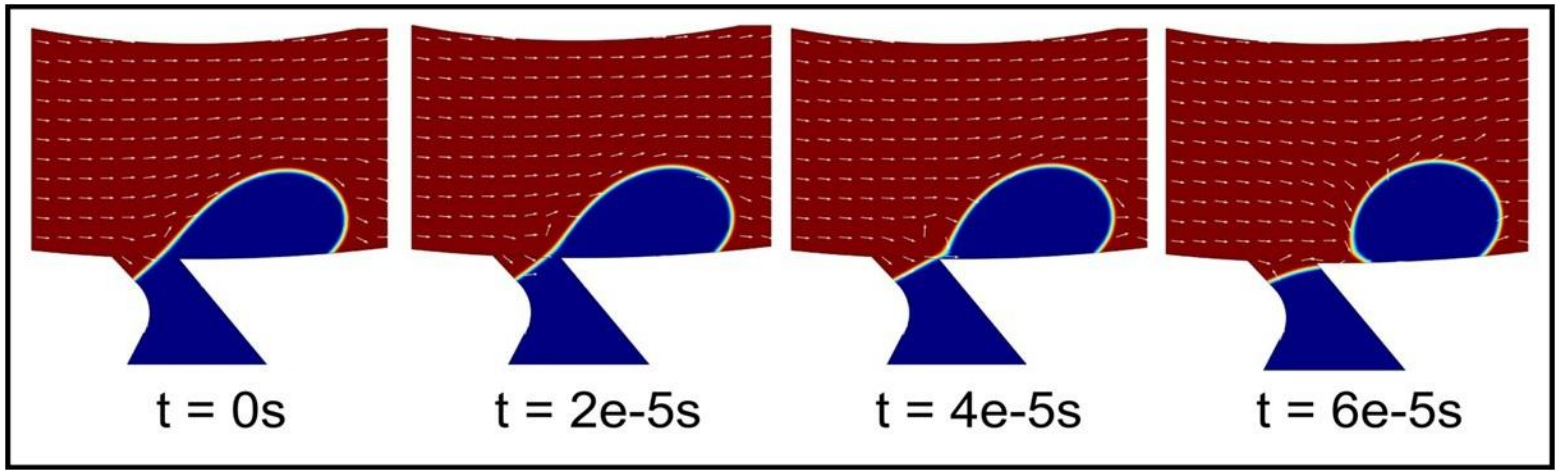
Model Results

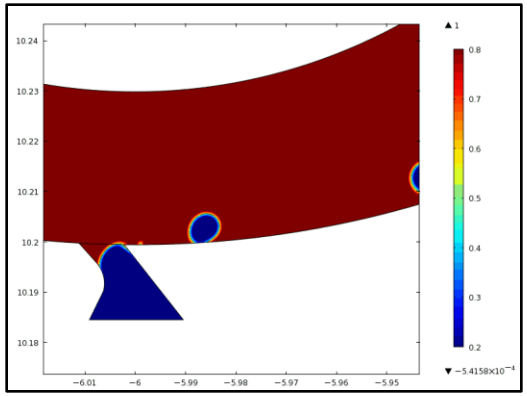
- Model firstly validated against experimental high speed imaging data.

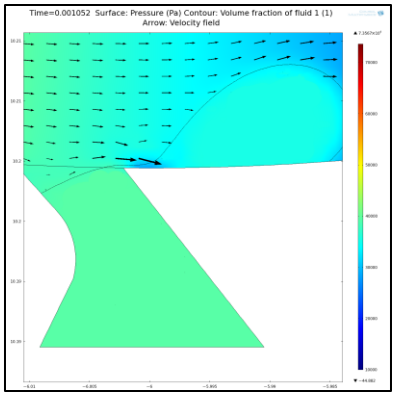


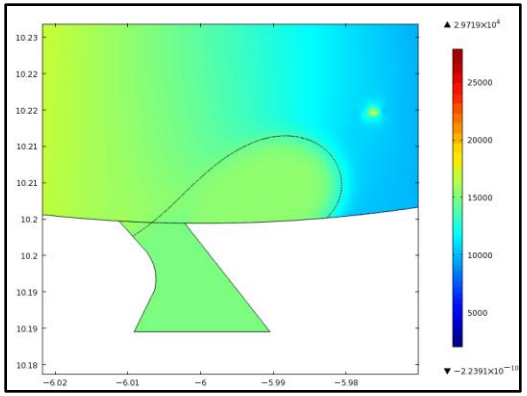
Model Results

- A closer look





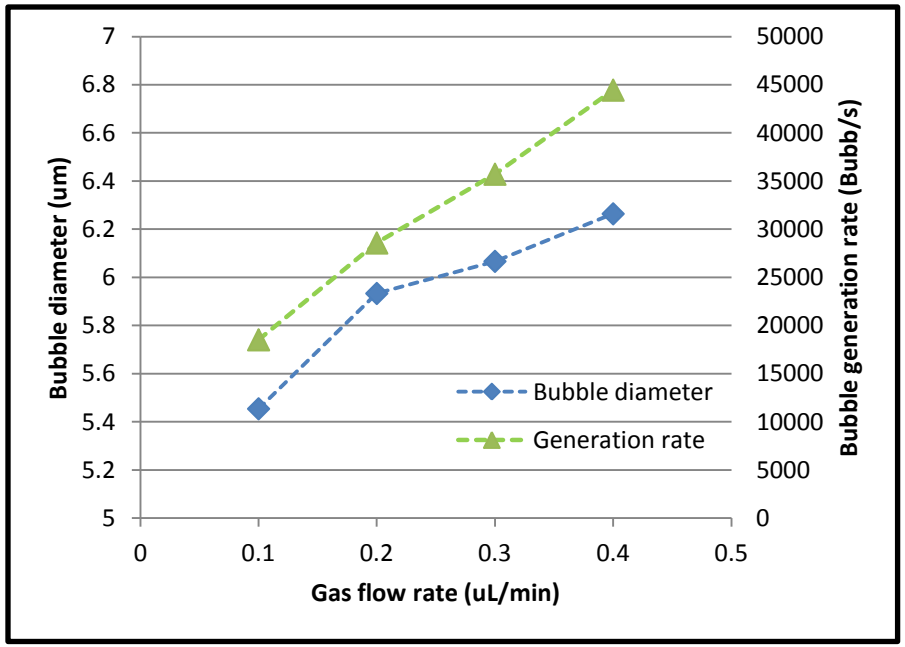




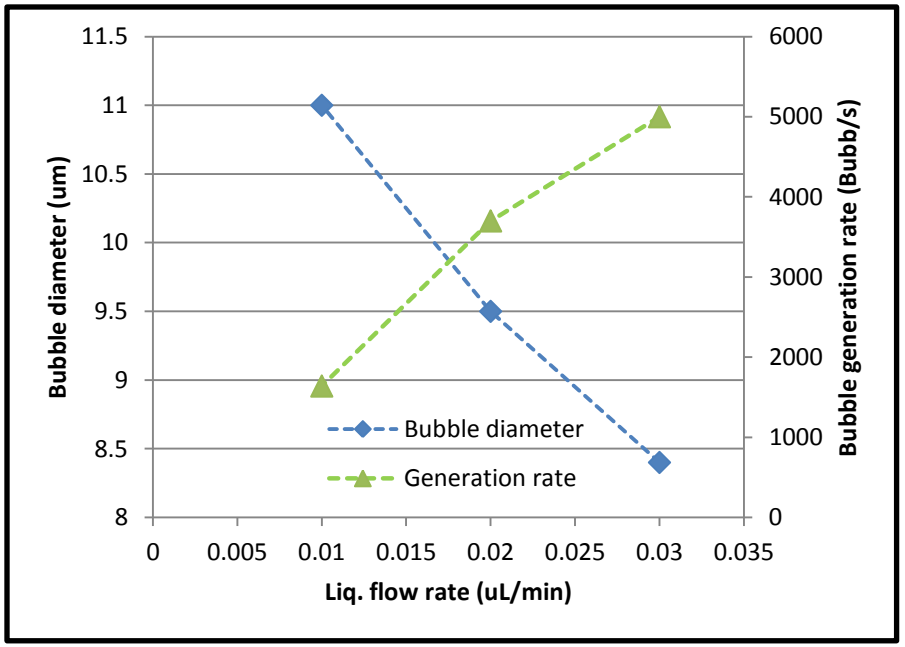
Model Results

• Parameterized studies to find effect of flow rates on bubble diameter and generation rate.

Fixed liquid flow rate



Fixed gas flow rate



Conclusions

• These results point towards point to the promise of using the COMSOL Multiphysics model to optimize our chip design and performance.

• Further work will involve elucidating the effects of other model variables, such as;

- Liquid viscosity and surface tension values
- Geometric changes, inlet angles and widths

• Rapid investigations accelerating development.

Acknowledgements

- H. Rolfsnes
- D. McLean
- C. Main
- P. Campbell
- V. Hegde
- A. Mason
- F. JD Smith
- WH I. McLean

For info : m.j.conneely@dundee.ac.uk

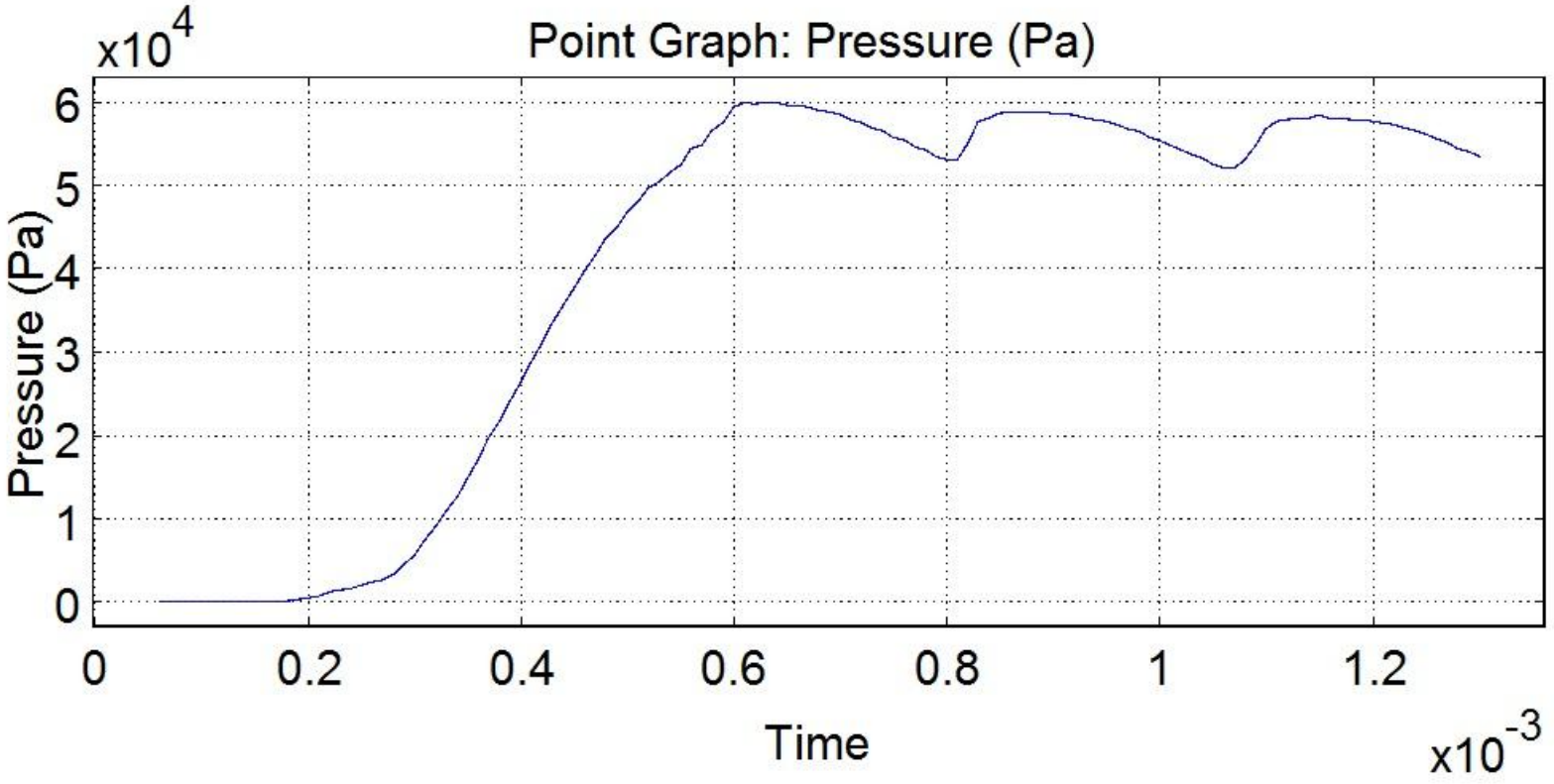
RESEARCH COUNCILS UK

EPSRC
Engineering and Physical Sciences Research Council

MRC Medical Research Council

P fluctuations at bubble pinch

- Pressure fluctuations induced by bubble pinch off.



Pressure vs Velocity Inlets

- Pressure fluctuations induced by bubble pinch off.
- Reduced geometry places inlet in close proximity to fluctuations.
- Model more stable with fixed V Inlet vs fixed P inlet.