Interaction of acoustic waves and shelled microbubbles/droplets for sensing application

M.Prudhomme, M. Addouche, F. Chollet

Femto-ST Institute, Besançon, France.
marc.prudhomme@femto-st.fr, mahmoud.addouche@femto-st.fr, franck.chollet@femto-st.fr

Abstract: *In the field of microfluidic, microbubbles and microdroplets are studied for many applications. For instance, microbubbles are used as Ultrasound Contrast Agent (UCA) to enhance the acoustic contrast of the human blood pool during an echography, and microdroplets are mainly used as reaction chambers, leading to the development of digital microfluidics. In this project, we propose to use the surface of microbubbles and droplets for acoustic sensing application. This presentation will be focused on simulations performed to study the interaction between the acoustic wave and the microbubbles-droplets, in order to detect the capture of analytes on their surface.*

Context

This project aims at using the surface of microbubbles/droplets in order to replace the single use planar biointerface of classic analysis devices. The ease of their generation and evacuation in a microfluidic chip allow to make a non-disposable biosensor, while increasing its efficiency and the total surface capture[1]. The capture of analytes at surface will be assessed by acoustic probing, as acoustic sensors offer the possibility to identify a wide range of physical properties while being a label-free and highly integrable detection method.

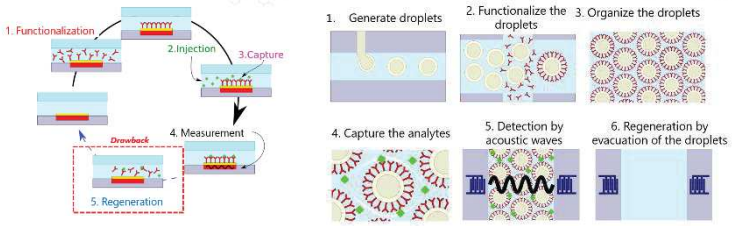

Figure 1: (Left) Operation of classic biological analysis devices. (Right) Operation of the bubbles/droplets-based biosensor

Acoustic behavior of microbubbles/droplets

The presentation will be focused on the interaction between the acoustic wave and the bubbles/droplets. The acoustic behavior of microbubbles is well documented[2]: the dynamic of a bubble is governed by the non-linear *Rayleigh-Plesset* equation. Besides, bubbles can have several vibration modes, the most well-known being the *Minnaert* mode.

$$\ddot{R}R + \frac{3}{2}\dot{R}^2 = \frac{1}{\rho}(P_L(r) - P_\infty(t)\,;\, f_{Minnaert} = \frac{1}{2\pi R_0}\sqrt{\frac{3kP_0}{\rho}}$$

For our sensor application, we decided to organize periodically the bubbles/droplets inside a microfluidic chamber in order to obtain the properties of a phononic crystal[3], especially the existence of band-gaps within which a guided wave can be transmitted thanks to the resonances of bubbles. Indeed, bubbles-based phononic crystals are known to give large hybridization band gaps[4] whose position and width are very responsive to the material constitution of the bubbles and which, moreover, survive the dispersion of the periodicity. Therefore, we expect to have a good sensitivity of the capture of analytes at bubbles/droplets surface.

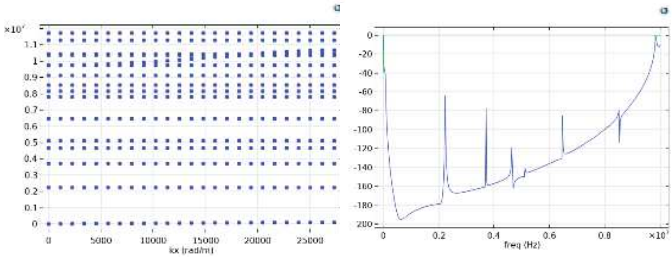

Figure 2: Acoustic probing of bubbles. (Left) Dispersion diagram with band-gaps. (Right) Transmission diagram associated

Capture of analytes at bubbles/droplets surface

Simulation of the capture of analytes at surface is based on studies related to Ultrasound Contrast Agents (UCA). The microbubbles involved share the same characteristic in size and composition of the shell, as UCAs can be functionalized for targeted imagery applications[5].

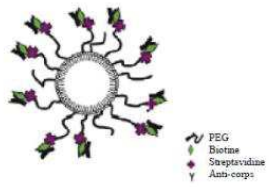

Figure 3: Functionalized microbubbles used as UCA

Publications shows that the acoustic response of the shelled microbubble is sensitive to the viscoelastic properties of the shell: elasticity of the shell increases the resonant frequency of the bubble, while the viscosity is responsible of the damping of the acoustic transmission[6]. The functionalization as well as the capture of analytes is therefore modelized with a shell model.

Mechanical models allow us to estimate the elasticity of a microbubble's shell based on an indentation test[7]. We decided to simulate an indentation test of a shelled-microbubble to verify the validity of the so-called *Reissner* model.

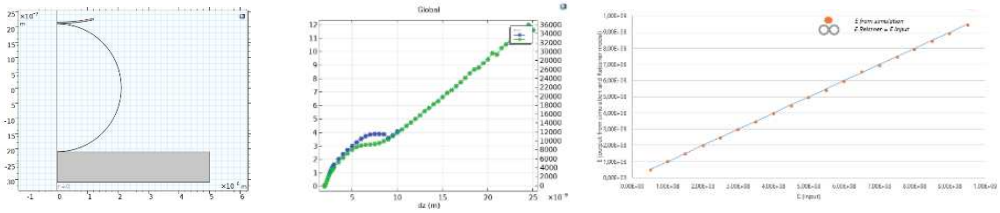

Figure 4: Indentation of a shelled microbubble. (Left) Geometry of the Comsol model. (Middle) F-ε curves result. (Right) Validity of the Reissner model

Then, we simulated the effect of the shell's elasticity on the Minnaert frequency of a bubble. The result obtained agrees with a previous paper on the subject[6]. Moreover, for our application, we use the couple biotin/streptavidin to simulate the capture of analytes. The values of elasticities of a UCA's biotin-shell with and without streptavidin can be found in literature[8]. We simulated the acoustic transmission through a 1D phononic crystal of biotin shelled-microbubbles and found a good sensibility of the *Minnaert* frequency to the capture of streptavidin. Integration of the viscosity in the model is yet to come.

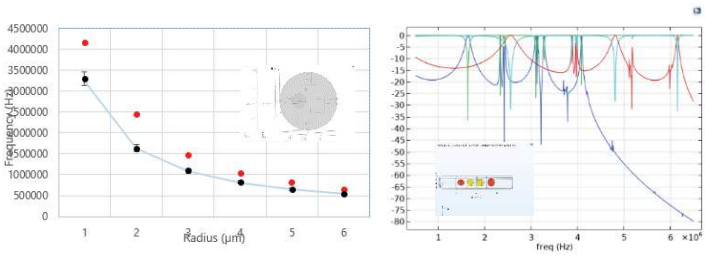

Figure 5: Effect of the shell's elasticity on Minnaert mode. (Left) Influence of the presence of a phospholipids shell on the frequency according to the radius. (Right) Influence of the capture of streptavidin on the acoustic transmission

Further ongoing simulations will be presented that need to be finalized until the presentation in July.

References

1. *C.-L. Azzopardi, F. Chollet, J.-F. Manceau, W. Boireau "Analyte capture in an array of functionalized droplets for a regenerable biosensor", Biomicrofluidics, doi:10.1063/1.5115494, Vol. 13 (2019).*
2. J. Chaline, *« Analogie macroscopique et acousto-mécanique d'une microbulle : application aux agents de contraste ultrasonore »*, Thesis, Université François-Rabelais de Tours (2015).
3. A. Khelif, A. Adibi, *« Phononic Crystals: Fundamentals and Applications »,* Springer (2015).
4. V. Leroy *et al.*, *« Band gaps in bubble phononic crystals »,* AIP Advances (2016).
5. L. Aired-Selmani, *« Caractérisations théoriques et expérimentales d'agents de contraste ultrasonore ciblés »,* Thesis, Université François-Rabelais de Tours (2013).
6. S. M. van der Meer *et al.*, *« Microbubble spectroscopy of ultrasound contrast agents »,* Acoustical Society of America (2007).
7. J.K. Morris, *« The Mechanical Properties of Phospholipid Coated Microbubbles »*, Thesis, University of Edimbourgh (2014).
8. R.H. Abou-Saleh *et al.*, *« Nanomechanics of Lipid Encapsulated Microbubbles with Functional Coatings »,* ACS Publications (2013).