Acoustic sensing of bioanalytes with functionalized microbubbles

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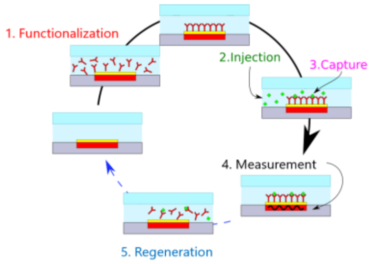
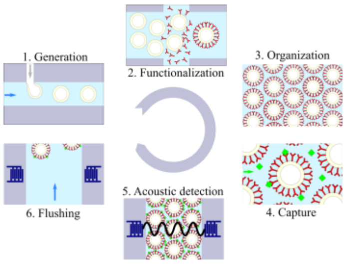
Abstract:

Biosensors are using specific biointerfaces for detecting analytes in biological fluids. For analytes capture, we propose to replace the single use planar biointerface of classic biosensors by the surface of a network of microbubbles. The ease of generation and evacuation of microbubbles in microfluidic chips give regenerable bio-interface for reusable biosensors. Moreover, the dense microbubble network yields increased detection efficiency and total surface capture [1]. In this project we will assess the capture by acoustic waves for sensitive and label-free detection.

Classic ***single use*** *biosensor with capture* ***on a plane***



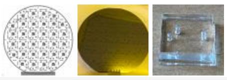
New paradigm



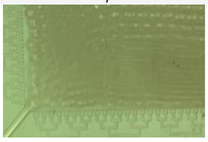
Bubbles based ***regenerable*** *biosensor with capture* ***in volume***

1. Microbubbles generation

- The microbubbles are generated with a T-Junction using **PDMS/Glass microfluidic chip** built by soft lithography
- The bubbles generated are **monodisperse**. Their diameter varies with pumps pressure and channel width and depth

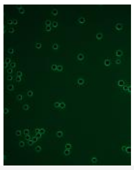


Design of the photomask, SU8 Mold and PDMS/Glass microfluidic chip

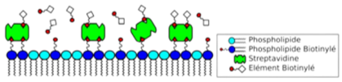


2. Microbubbles functionalization

- We functionalize the microbubbles **with biotin** at their surface in order to capture **streptavidin**
- The functionalization is **directly realized at bubbles generation**, by mixing surfactants and lipids in the continuous phase

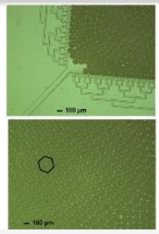


Fluorescent lipid at bubble surface

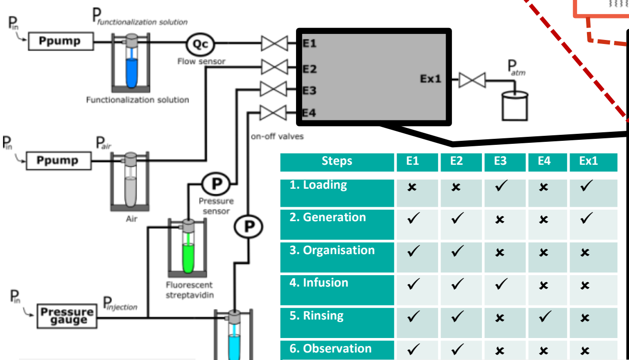


3. Organization

- We organize the bubbles in a dense array inside a square chamber by closing the exit valve (Ex1)
- The bubbles are static and are **organized in a hexagonal array**



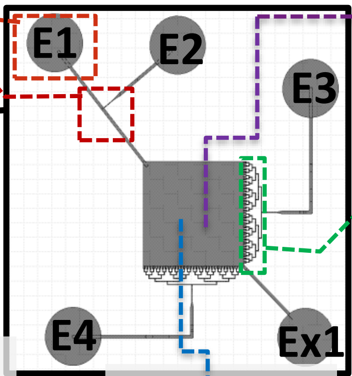
Static organization of microbubbles inside the chamber



Schematic of the microfluidic set up

Steps	E1	E2	E3	E4	Ex1
1. Loading	×	×	✓	×	✓
2. Generation	✓	✓	×	×	✓
3. Organisation	✓	✓	×	×	×
4. Infusion	✓	✓	✓	×	×
5. Rinsing	✓	✓	×	✓	×
6. Observation	✓	✓	×	×	×

Operation of the different on (✓) – off (×) valves for each steps of the sensor



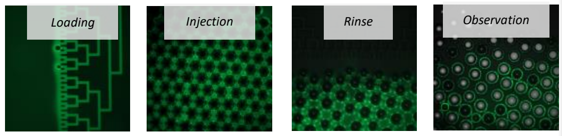
Microfluidic chip architecture

4. Injection and capture of analytes at bubbles surface

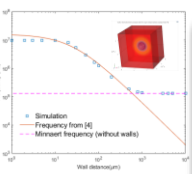
- We validate the injection of fluorescent streptavidin through the bubble network by controlling precisely the pressures
- We observe **the capture** at bubbles surface within the microfluidic chip using a fluorescent microscope

SCAN ME

Video test with a blue dye solution injection



5.1 Acoustic detection – Numerical studies *(Comsol Multiphysics)*



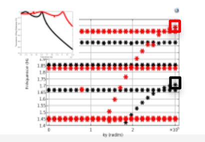
Influence of walls proximity [4]

Acoustic of a free bubble in an infinite media [2,3]

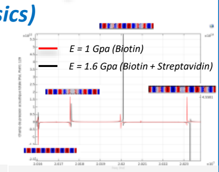
Rayleigh-Plesset equation:

$$\ddot{R}R + \frac{3}{2}\dot{R}^2 = \frac{1}{\rho_l}(P_L(r) - P_\infty(r))$$

Minnaert frequency: $f_M = \frac{1}{2\pi R_0}\sqrt{\frac{3\gamma P_0}{\rho_l}}$

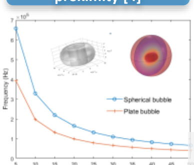


Dispersion of bubble phononic crystal, exhibits capture dependent bandgap

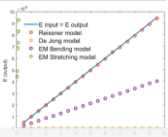


Exciting coupled cavity/bubbles modes increases sensitivity to capture

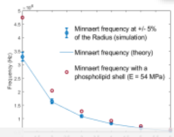
Comparing strategies for bioanalytes capture detection



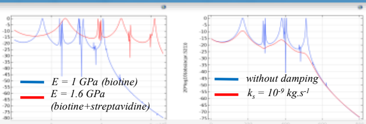
Influence of bubble geometry



Comparison of mechanical models for shell's elasticity [5]



Influence of shell elasticity on Minnaert Frequency

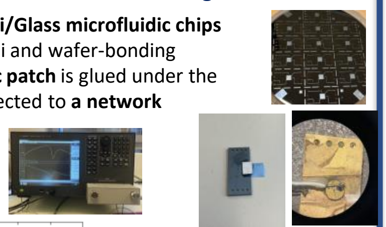


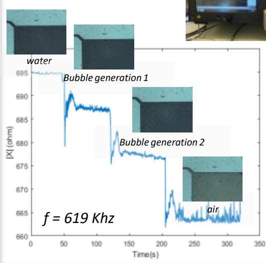
Elasticity of a lipidic shell increases the resonance frequency by nearly 50% while its viscosity induces a tree-fold increase of the damping [6]

Modelisation of the functionalization and capture at bubble surface using a viscoelastic shell

5.2 Acoustic detection – Integration

- We fabricate **Si/Glass microfluidic chips** using DRIE of Si and wafer-bonding
- A **piezoelectric patch** is glued under the chip and connected to **a network analyzer**





- We show large sensitivity to the nature of the fluid inside the cavity (air / water ratio)
- Further tests are ongoing to detect the capture on bubbles surface

References

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