Organ on Chip Platform with an Integrated Acoustic Biosensor and Polished Silicon Porous Membrane

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Sensor integration for real-time monitoring is crucial to ensure the relevance and usefulness of Organ-on-Chip (OoC) devices for biomedical applications [1]. There is a recent interest in going beyond polydimethylsiloxane (PDMS) as a standard material of OoC devices to avoid adsorption of pharmaceutical drugs and other molecules of interest, and to improve the scalability and the production throughput [2,3]. Therefore, we propose a PDMS-free OoC platform with an integrated acoustic sensor and polished silicon porous membrane. The main objective is to achieve versatility in the porous membrane design and demonstrate an efficient microfabrication process of the OoC platform.

OoC Platform Design

The structure of the OoC platform with an integrated acoustic sensor and porous silicon membrane is shown in figure 1. The OoC device consists of a GaAs piezoelectric substrate, a silicon-on-insulator (SOI), and a glass wafer, forming a microfluidic channel thanks to standard bulk micromachining microfabrication processes.

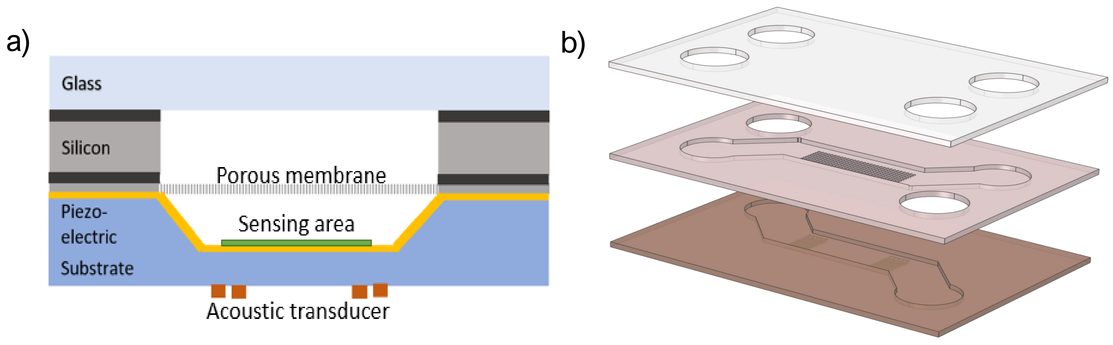
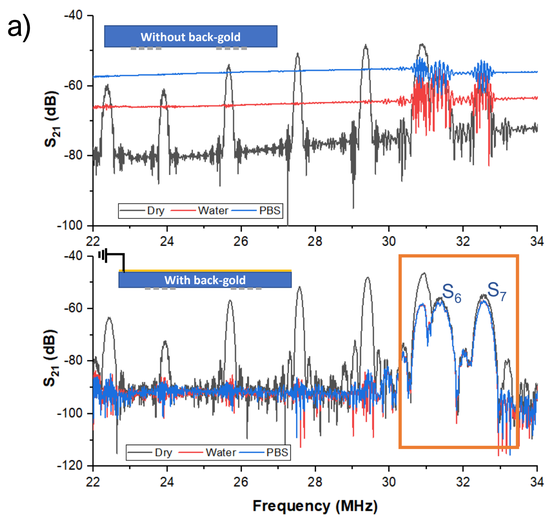


Figure 1. (a) Cross-section view of the OoC platform with acoustic biosensor and porous membrane, and (b) the stacking of multiple layers to form a multi-channel microfluidics system separated by porous membrane.

Biosensor Development and Miniaturization

Higher-Order Plate Acoustic Waves (PAW)-based Biosensor



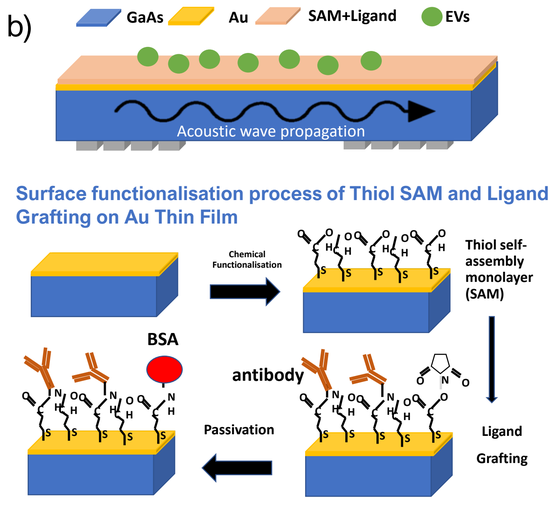


Figure 2. (a) PAW-based sensor signals with and without electrically grounded Au layer and (b) Surface functionalisation process of Au thin film to capture specific biomolecules.

Higher-order modes, such as S_6 and S_7, have negligible acoustic energy radiation when in contact with liquid. The shift in the Radio Frequency (RF) signals can thus be used to quantify biomolecules (e.g. extracellular vesicles) captured in the sensing layer.

Advantages of Higher-Order PAW :

- Separation of the interdigitated transducer from the sensing area → **IDTs outside the channel**
- Electrically grounding of the surface opposite to the IDTs with a thin metal film of Au
  → improves signal stability and decouples liquid conductivity's effect
  → Au commonly used for **biosensor surface functionalisation.**
- Possibility of having both **sensor and actuation components** in the same device

Miniaturization of GaAs Acoustic Sensor and Direct Integration in a Microfluidic Channel

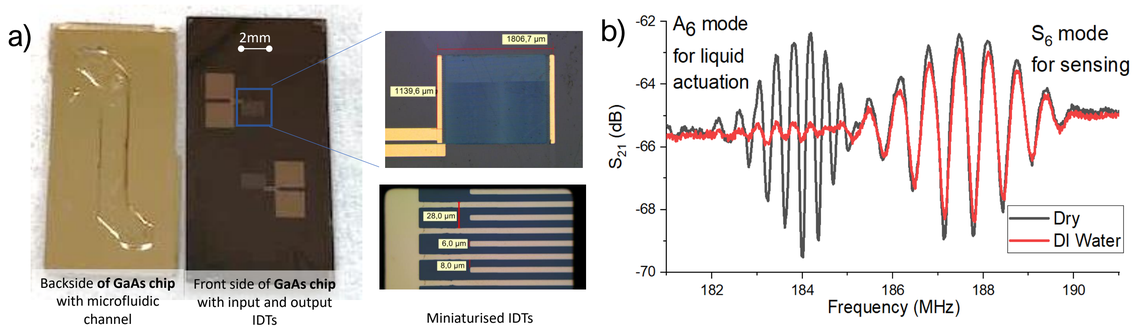


Figure 3. (a) Miniaturised sensor and (b) RF signals in dry and liquid environment.

- Scaling down the IDTs periodicity to 28 µm and the plate thickness reduced to 100 µm, by chemical wet-etching and to form a microfluidic channel
- Higher operating frequency **(189 MHz)**, lower periodicity → **higher theoretical sensitivity.** Theoretical limit of detection (LOD) is **10^5 EVs particles/mL,** comparable with surface acoustic waves biosensors reported in [4], with similar operating frequency and CD63 antibody surface functionalisation.

Polished Silicon-based Porous Membrane

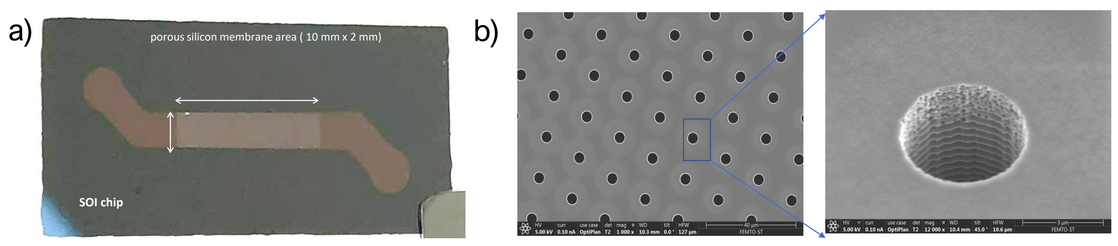


Figure 4. (a) The SOI chip with suspended 5 µm thin silicon membrane (b) the SEM images of the porous membrane area.

SOI wafer with a thin (µm down to nm) polished silicon top layer, with Deep Reactive Ion Etching (DRIE) process, a standard microfabrication process to obtain a free-standing silicon membrane → **versatility and flexibility in membrane thickness, porous size and porosity.**

With **a standard photolithography process on polished silicon surface**→ porous size as low as **800 nm**, and **up to 20% porosity** → comparable with non-PDMS polymer membrane[5], but with simpler and more robust fabrication process.

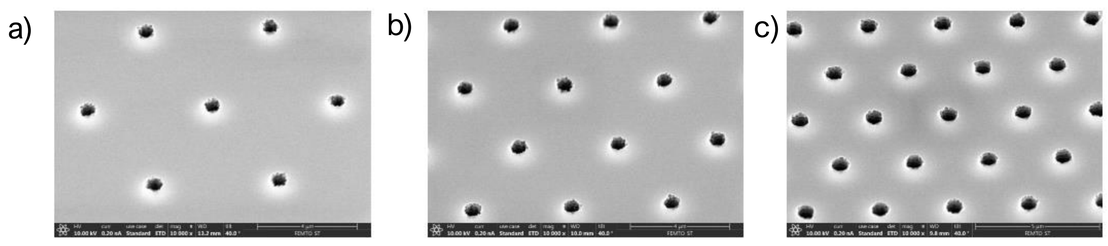


Figure 5. 800 nm porous sizes with different hole densities and total porosities. Holes centre to centre distance (a) 5 µm (b) 4 µm and (c) 3 µm.

Endothelial Cell Seeding with Collagen Coating

Preliminary result shows the feasibility of human endothelial cell seeding on collagen-coated porous silicon membrane.

- 1 mg/mL collagen type I coating: overnight at 4°C, 4 days drying at 4°C
- Human umbilical vascular endothelial cells (HUVEC) seeding at 21 K cells/cm^2

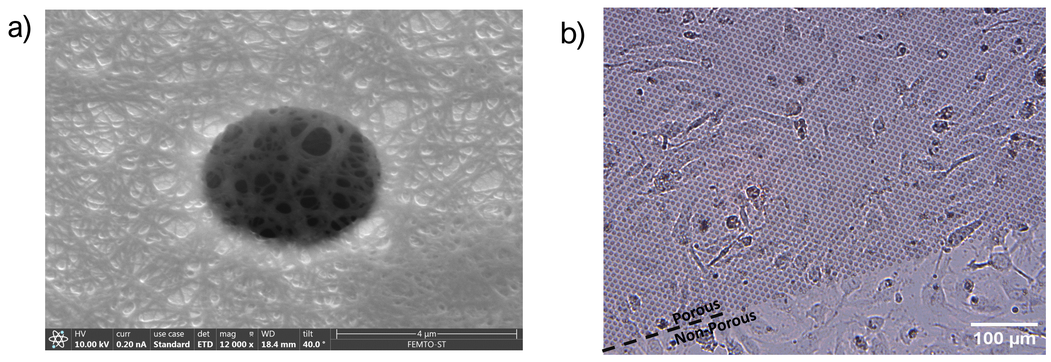


Figure 6. (a) SEM image of collagen coating on the silicon porous membrane and (b) HUVEC growth after 7 days

Wafer-level Microfabrication and Bonding of the OoC Platform

Integration and fabrication process of the proposed OoC platform can be done by standard wafer-level microfabrication and bonding process→ manufacturability, scalability and higher production throughput.

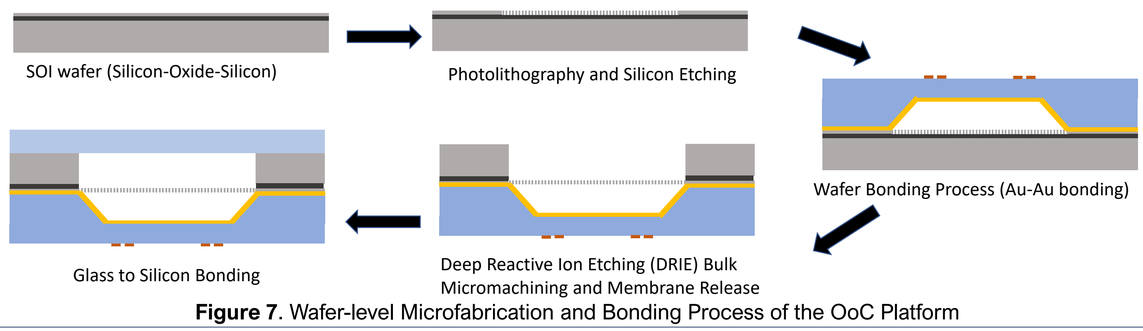


Figure 7. Wafer-level Microfabrication and Bonding Process of the OoC Platform

Conclusion and Future Work

- OoC platform is designed and fabricated with an integrated PAW-based acoustic biosensor and polished silicon porous membrane.
- The structure of the sensor and the SOI-wafer-based silicon porous membrane simplify the fabrication and integration process with a standard microfabrication process.
- Preliminary results shows feasibility of endothelial cell seeding on the porous membrane with collagen coating.
- **Future work** : application of the OoC platform for a specific study, especially related to drug-organ interaction study.

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[3] S.Schneider, et al., *Lab on a Chip* **21** 10 (2021)
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