European Innovation Council

Funded by the European Union

HORIZON-EIC-2021-PATHFINDEROPEN-01

EIC Pathfinder Open 2021

VerSiLiB

Versatile Amplification Method for Single-Molecule Detection in Liquid Biopsy

Start date: 01/04/2022, Duration 48 months

Deliverable D3.1

Model sensor chips delivered to support photonics, assay and integration developments

Due date: 31/03/2023

Submission date: 28/03/2023

Responsible work package leader: Prateek Singh, WP3, FAD

Responsible task leader: Prateek Singh, FAD

Deliverable type: Demonstrator

Version: V1.1

Dissemination level: Public

This project has received funding from the European Union's European Innovation Council (EIC) under Horizon Europe program. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Innovation Council. Neither the European Union nor the granting authority can be held responsible for them.

Authors

Tuan Nguyen, FAD
Prateek Singh, FAD
Annukka Kokkonen, VTT
Sanna Aikio, VTT

Revision log

Version	Date [DD/MM/YYYY]	Change
V0.1	20/03/2023	1st draft
V0.2	21/03/2023	Edits from 1st Coordinator review
V0.3	21/03/2023	2nd Coordinator review, minor readability edits
V1.0	24/03/2023	Final
V1.1	06/11/2023	Figure 2 broken image reference corrected at page 6

Reviewed by

Role	Name	Date
Work package leader	Prateek Singh	20/03/2023
Coordinator	Sanna Aikio	21/03/2023

Keywords

Microfluidics, model sensor chips

Acronyms

Acronym	Definition
PDMS	Polydimethylsiloxane
PET	Polyethylene terephthalate
PSA	Pressure sensitive adhesive

Executive summary

In this deliverable, the first version of the microfluidic sensor chip for the VerSiLiB sensing system development is reported. Report discusses about the chip design and manufacturing. Chapter 1 describes the objectives, the manufacturing technologies, and the workflow in terms of collaborations between the consortium partners from the design and manufacturing to chip testing. Chapter 2 describes the main tasks including the chip design, computational simulation, and fabrication. Chapter 3 concludes the deliverable and Chapter 4 states the progress compared to the Description of Action.

In the chip design, ANSI/SLAS well plate format was utilized to ensure compatibility with future automation systems. This increases the chip's versatility and adaptability for use in various applications. Chip has standardized quarter well plate size, making it scalable up to a full plate, providing a unique level of scalability and versatility unmatched in the industry.

Contents

1. Introduction

The objective of the reported work was to create the first version of microfluidic sensor chips for the development of the VerSiLiB system. Chip was developed in collaboration by Finnadvance Oy (FAD), VTT Technical Research Centre of Finland (VTT), Austrian Institute of Technology (AIT), Institute of Physics of the Czech Academy of Sciences (FZU), and University of Catania (UNICT). Chips were designed based on the specifications from WP2 'Assay development', WP4 'Photonic signal enhancement' and WP5 'System integration'. Fluid dynamic simulations were used to validate the design.

Rapid prototyping methods were employed to iteratively prototype and produce the optimized designs. Laser cutting and soft-lithography techniques were used for chip fabrication. In this work, FAD is responsible for designing, manufacturing and assembling the microfluidic chips. In the manufacturing, FAD has collaborated with VTT that has provided the laser cutting of microfluidic structures. Materials have been selected and provided in collaboration by FAD and VTT. FZU, AIT, VTT and UNICT will utilise the sensor chips in the development of system hardware and test chemistry.

2. Results and Discussion

2.1. VerSiLiB microfluidic sensor chip design and material selection

A planning phase was undertaken to achieve the project objectives, with particular emphasis placed on the definition of design requirements, technical dimensions, and material selection for the microfluidic sensor chips. To ensure the highest level of precision and accuracy, various design constraints were taken into account, such as the chip's overall thickness, dimensions, inlet/outlet positioning, and reaction chamber placement. During this process, the ANSI/SLAS well plate format was utilized to ensure compatibility with future automation systems, thereby increasing the chip's versatility and adaptability for use in various applications.

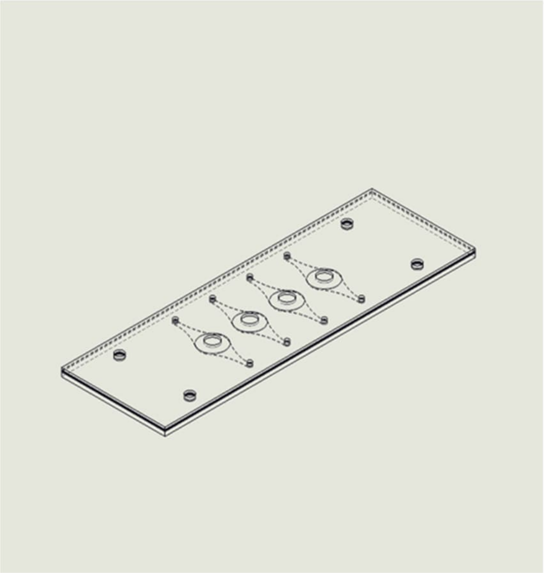

Figure 1. The 3D design of the sensor chip

In addition, strict criteria were set for the materials used in constructing the chip, such as the requirement that they have low autofluorescence and are optically transparent, to ensure optimal accuracy and easy signal interpretation. The chip's thickness was also a crucial factor in the design process to ensure compatibility with the reader hardware. The chip's size is comparable to that of a microscope slide, which makes it simple to fabricate and test. Each chip contains four microfluidic test units to run multiple or parallel tests. This combined with its standardized quarter well plate size, making it scalable up to a full plate, provides a unique level of scalability and versatility unmatched in the industry (Figure 2).

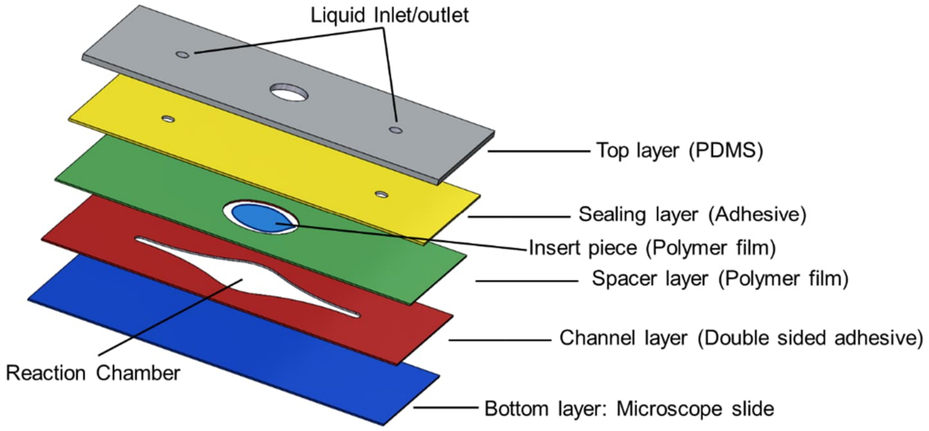

Figure 2. Layers of the microfluidic chip. The bottom layer and the insert piece can be easily modified by partners as needed for test chemistry and photonics development.

2.2. Computational simulation

After completing the design phase, FAD conducted a thorough computational study to verify the suitability of the microfluidic channel dimensions for fluidic flow and assay performance requirements. COMSOL software was used to analyze the fluids' behavior and identify potential design issues or limitations. The study took into consideration various factors such as the viscosity of the fluids, the pressure drops, the mixing efficiency of the channels, and the flow rate. The dimensions of the channels were carefully selected to enable the smooth and consistent flow of the fluids, preventing any blockages or disruptions in the assay process.

2.3. Fabrication and testing of the chips

The sensor chips comprise of multiple layers of materials (Figure 2) that were micro-fabricated to form the microfluidic structures. Fabrication was a joint effort between VTT and FAD, where we utilized advanced techniques like UV laser cutting, soft-lithography, and pressure-sensitive adhesive bonding to iteratively prototype and produce the chips.

First, FAD produced the top layer from PDMS using the soft-lithography method. The part was cast from a 3D-printed negative mold, giving a thin layer containing the chip’s inlet/outlet and opening areas according to the approved design. Next, the other 3 layers including the pressure sensitive adhesive (PSA) for the detection lid’s holder, the PET polymer film for the detection lid’s housing, and the microchannel layer were laser cut by VTT according to the CAD files provided by FAD. Finally, the detection lid inserts were designed and made by VTT by laser cut from PET polymer film followed by an evaporated gold coating process to provide a thin, see-through layer of gold on the PET film as required by the photonic sensing principle.

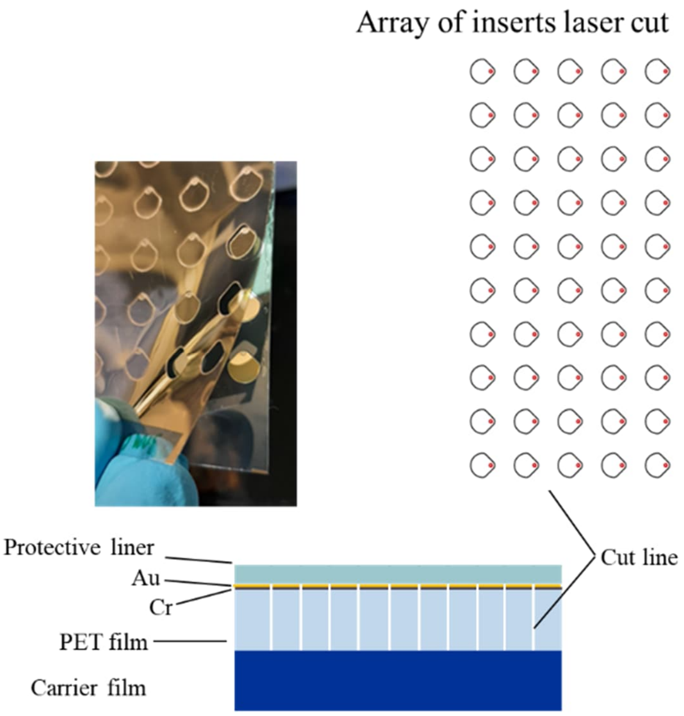

Figure 3. The detection lid inserts made by VTT. The pieces were cut through the PET film leaving the carrier intact to facilitate the piece handling. Upper left: Finalized insert pieces.

The assembly steps of all the layers mentioned above are shown in Figure 4. In short, the different adhesive and polymer layers were self-bonded together by laminating one by one. Before sealing the chip onto the bottom glass substrate, the detection lid inserts were placed onto the openings in the ceiling areas of the microchannels having an adhesive surface.

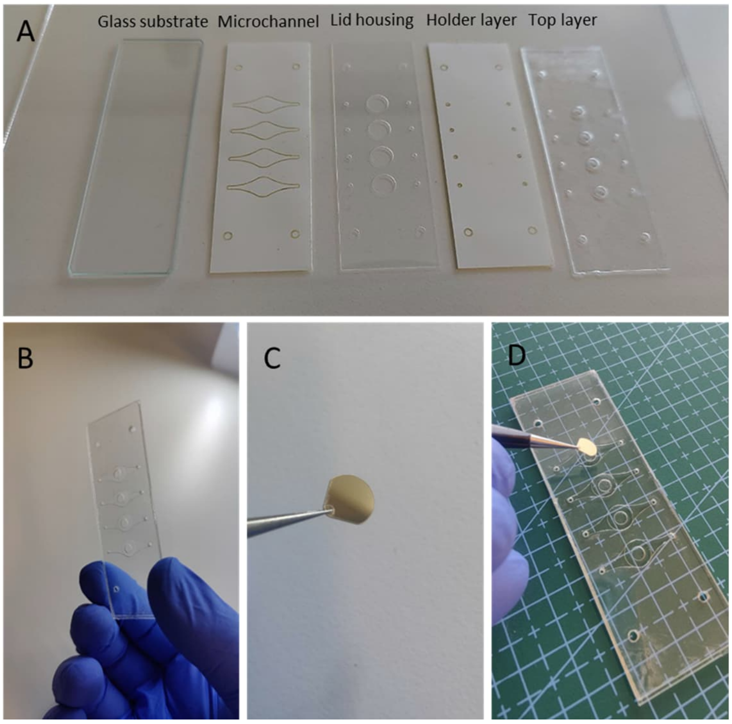

Figure 4. (A) different layers of the chip before assembly, (B) an assembled chip without the glass substrate, (C) the gold coated detection lid insert, (D) placing the insert to the opening ceiling areas of the microchannels

After the chips were fully assembled, VTT verified that the design works seamlessly with the first hardware prototype developed in WP2 'Assay development' (Figure 5).

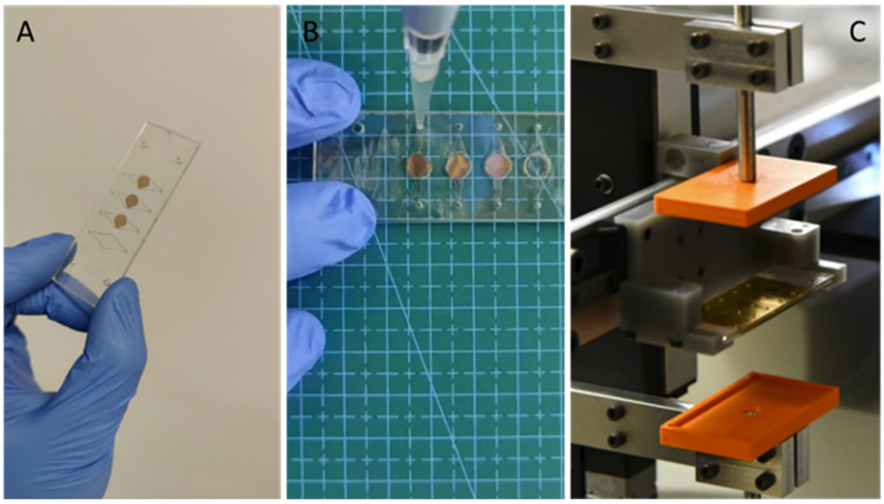

Figure 5. (A) the fully assembled sensor chip, (B) flow test is performed by injecting 70% ethanol or PBS into the chip and observing the flow, (C) the chip was tested with the first hardware prototype and showed a perfect fit

3. Conclusions

FAD has led the WP3 'Microfluidics' as well as the task T3.1 'Model sensor chip' to full fill the objectives of this deliverable. The sensor chip's design, fabrication and other technical requirements were discussed and manufactured in close collaboration with the other consortium partners. With VTT, FAD has carried out successfully the flow tests for the first-generation design of the sensor chip. FAD ships the developed and batch fabricated sensor chips to consortium partners as needed for the test chemistry and hardware development.

4. Progress compared to the Description of Action

This deliverable reports the work to design and manufacture microfluidic sensor devices aimed to VerSiLiB test chemistry and hardware development. The sensor requirements, design and implementation has been discussed. The work has been fulfilled 100% according to the Description of Action.