



PHOTONICS PUBLIC PRIVATE PARTNERSHIP



H2020-ICT-2019-2

Photonics Manufacturing Pilot Lines for Photonic Components and Devices

MedPhab

Photonics Solutions at Pilot Scale for Accelerated Medical Device Development

Starting date of the project: 01/01/2020

Duration: 48 months

= Deliverable D3.12 = **Dissemination material on in-vitro diagnostics** **(MODEL CASES)**

Due date of deliverable: 31/05/2021

Actual submission date: 27/05/2021

Responsible WPL: Sanna Aikio, WP3, VTT

Responsible TL: Jarkko Tuominen, VTT

Revision: V1.0

Dissemination level		
PU	Public	x
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 871345.

AUTHOR

Author	Institution	Contact (e-mail, phone)
Annukka Kokkonen	VTT	Annukka.kokkonen@vtt.fi
Anja Haase	JOR	anja.haase@joanneum.at
Aki Mäyrä	VTT	aki.mayra@vtt.fi
Noora Heinilehto	VTT	noora.heinilehto@vtt.fi
Sanna Aikio	VTT	sanna.aikio@vtt.fi
Jarkko Tuominen	VTT	Jarkko.tuominen@vtt.fi

DOCUMENT CONTROL

Document version	Date	Change
V0.1	21.5.2021	First full draft
v0.2	24.5.2021	Minor corrections and modifications
V1.0	25.5.2021	Minor corrections, final version

VALIDATION

Reviewers	Validation date
Work Package Leader	Sanna Aikio 24.5.2021
Project Manager	Mariana Pacheco Blanco 27.5.2021
Coordinator	Jussi Hiltunen 26.5.2021

DOCUMENT DATA

Keywords	Dissemination of pilot line capabilities, model-case, in-vitro sensor, molecular diagnostics
Point of Contact	Name: Jarkko Tuominen Partner: VTT Address: Kaitoväylä 1, 90590 Oulu, Finland Phone: +358405360104 E-mail: Jarkko.tuominen@vtt.fi
Delivery date	21.5.2021

DISTRIBUTION LIST

Date	Version	Recipients
27.5.2021	V1.0	Partners via owncloud, EC via Portal

DISCLAIMER

Any dissemination of results reflects only the authors' view and the European Commission Horizon 2020 is not responsible for any use that may be made of the information Deliverable D3.12 contains.

Executive Summary

The goal within MedPhab's two model-cases 'Disposable plasmonic fluidic sensor' and 'Wearable PIC temperature sensor' (WP3, Task 3.7) was to demonstrate and disseminate the pilot line capabilities through concrete example cases. Another target was to develop the pilot line ways of working.

In the model-case 'Disposable plasmonic fluidic sensor', the work consisted of design and implementation of a fully automated, high-volume manufacturing process for a disposable plasmonic-fluidic sensor chip by linking the capabilities at VTT Technical Research Centre of Finland (VTT) and Joanneum Research (JOR). Plasmonic sensors can be utilized in in-vitro molecular diagnostics applications.

Design for Manufacture (DFM) was essential in this work, and VTT and JOR considered several topics to enable the high-volume automated processes. Based on MedPhab's modular approach, a case-specific Production Kit was formed facilitating the collaboration. Design rules were identified and applied. Manufacturing steps, process interfaces, logistics chain and characterization steps between VTT and JOR were identified.

Key technologies were selected for the realisation of the manufacturing process. High volume roll-to-roll (R2R) manufacturing techniques were used for the sensor chip manufacturing. Polymeric sensor nanostructures were manufactured at large scale using roll-to-roll UV nanoimprinting lithography (UV-NIL). The large area roll-to-roll imprinting tool was manufactured by upstepping process. The nanostructures were metallized and sensor surfaces were singulated into microscope slide size pieces. The microfluidic structures were manufactured by roll-to-roll laser patterning and lamination process using double sided tape as a fluidic layer and clear polymer film as lid layer. Pick-and-place process was used to integrate the sensor surface with the microfluidics before the final singulation by rotary kiss cutting. The sensors were characterized by measuring the reflectance spectra from 20 sensors using a spectrophotometer and defining the depths of the intensity dips.

The results show that the sensor chip was fully roll-to-roll manufactured using automated equipment, and the standard deviation of the plasmonic resonance dip depths for 20 samples was 2%, which is less than the set target of coefficient of variation (CV) <5%.

As a conclusion, MedPhab's pilot line capabilities on high-volume sensor chip manufacturing for in-vitro molecular diagnostics applications were successfully demonstrated. Also, various kinds of dissemination material were prepared.

Table of Contents

1. Introduction	5
2. Disposable plasmonic-fluidic sensor	8
2.1. Design	8
2.1.1. Plasmonic surface	8
2.1.2. Design for manufacture	9
2.2. Manufacturing	9
2.2.1. Plasmonic surface imprinting	9
2.2.2. Plasmonic surface metallization	13
2.2.3. Tape fluidics roll-to-roll manufacturing by laser cutting	15
2.2.4. Hybrid integration and chip singulation	16
2.3. Characterization	17
2.3.1. Characterization method	17
2.3.2. Measurement results	18
2.3.3. Revised optical grating simulations	20
2.4. Conclusions reflected against the set goals	20
3. Dissemination material	20
4. Conclusions	25
5. Degree of Progress	25
6. Dissemination Level	25

1. Introduction

The aim of the task T3.7 ‘Model cases’ in the Work Package 3 ‘Manufacturing Acceleration’ was to demonstrate and disseminate the pilot line capabilities through concrete example cases and to develop pilot line ways of working. In the model-case ‘Disposable plasmonic fluidic sensor’, the goal was to develop and demonstrate a fully automated, high-volume manufacturing process for the sensor.

Plasmonic in-vitro sensors can be used to measure binding of biomolecules to the plasmonic surface that is formed by a metallized (typically gold) nanostructure. When plasmonic surface is illuminated, a surface plasmon is excited by a suitable wavelength, and this can be seen as a sharp intensity dip in the reflectance spectra (Figure 1). Binding of biomolecules changes the spectral position of this dip and phenomenon can be used to implement sensors for molecular diagnostics.

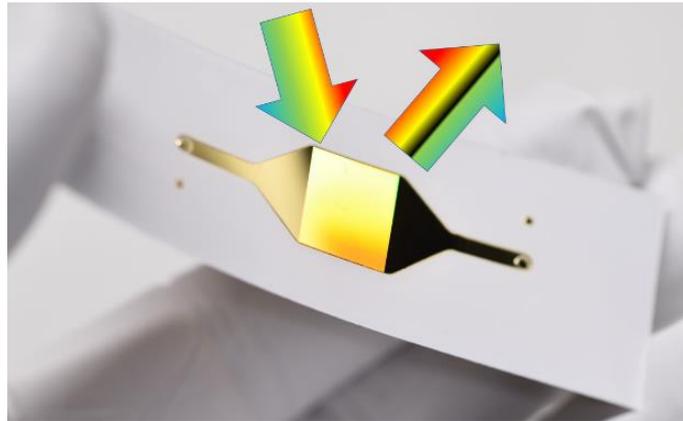


Figure 1. When light hits the plasmonic surface, intensity of the wavelength exciting the surface plasmon is reduced in the reflected light. This effect can be used to implement sensors for molecular diagnostics.

Schematic of the implemented sensor is shown in Figure 2. It has three layers that are laminated together to form a chip with photonic and fluidic functionalities. The bottom layer has a metallized nanostructured top surface for plasmonic function. The channel and cover layers form a fluidic structure for sample handling.

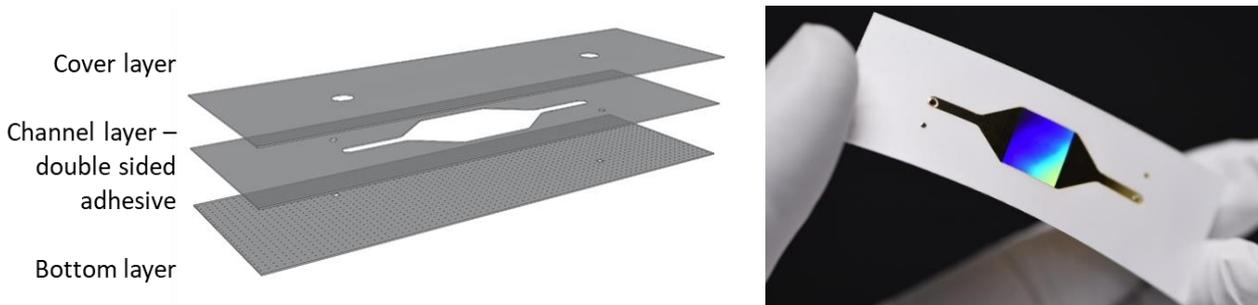


Figure 2. Left: Exploded view of the implemented sensor structure. The plasmonic bottom layer is combined with the fluidics part formed by the channel and cover layers. Right: Sensor chip manufactured by fully automated, high volume processes.

The aim of the work was to design and implement a fully automated, high-volume manufacturing process for the sensor chip by linking the capabilities at VTT Technical Research Centre of Finland (VTT) and Joanneum Research (JOR). The linking was based on the MedPhab’s modular approach shown in Figure 3 by first selecting the necessary modules and then identifying the processes, partners and production steps to form the Production Kit shown in Figure 4. This approach enables identification and visualization of process steps and sequences showing which processes can be carried out in parallel and what in succession, where are the process interfaces and what is the logistic chain. In the design and optimization of the nanophotonic structure (Section 2.1.1, page 8), the manufacturing aspects were taken into account. Design for Manufacture (DFM) had essential role in linking the processes of VTT and JOR (Section 2.1.2, page 9).

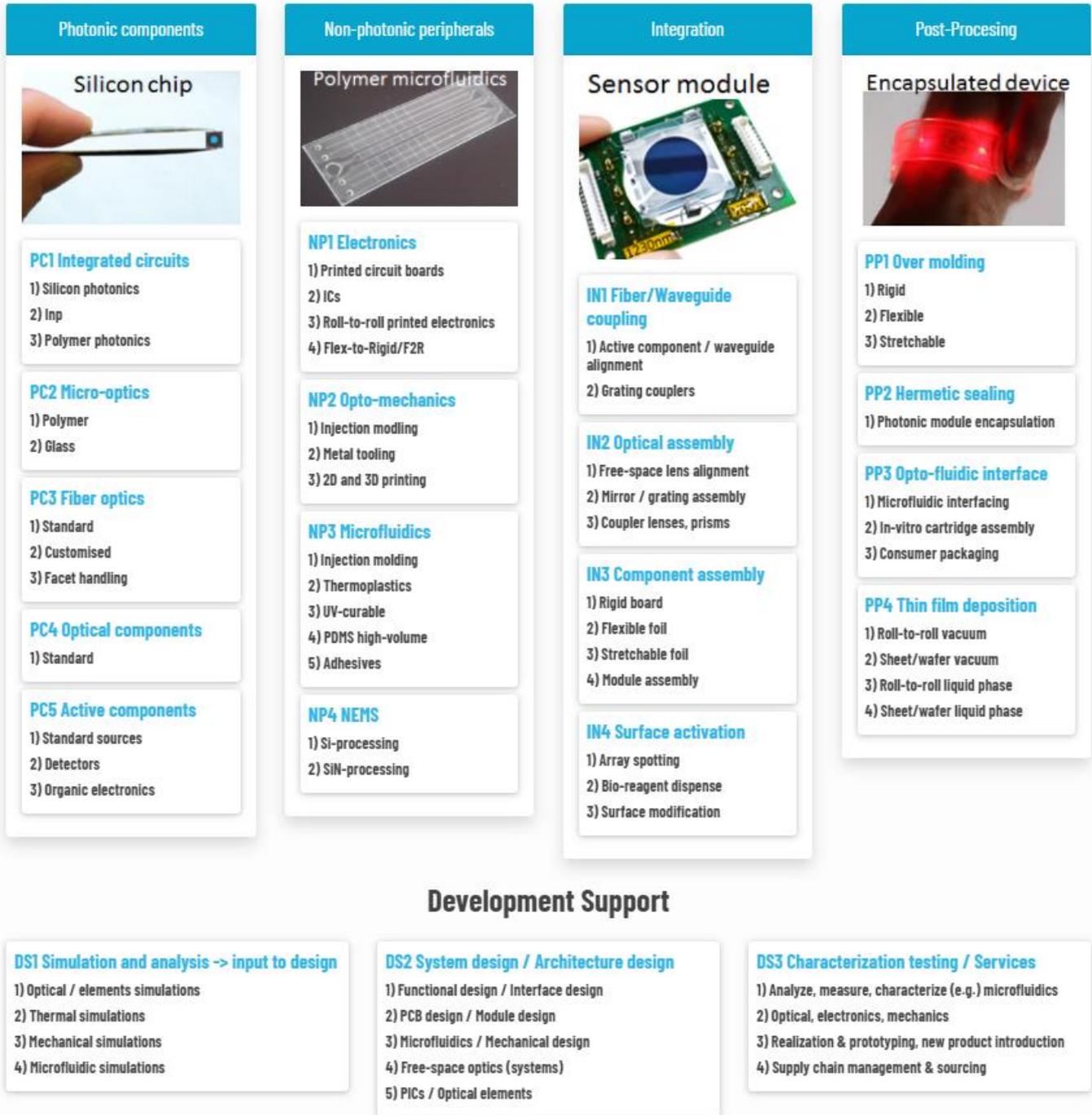


Figure 3. MedPhab’s modularity table shows the pilot line technology offering in *Photonic components*, *Non-photonic peripherals*, *Integration* and *Post-processing* verticals and in *Development support*. These are further divided into technology modules that contain the processes.

MedPhab

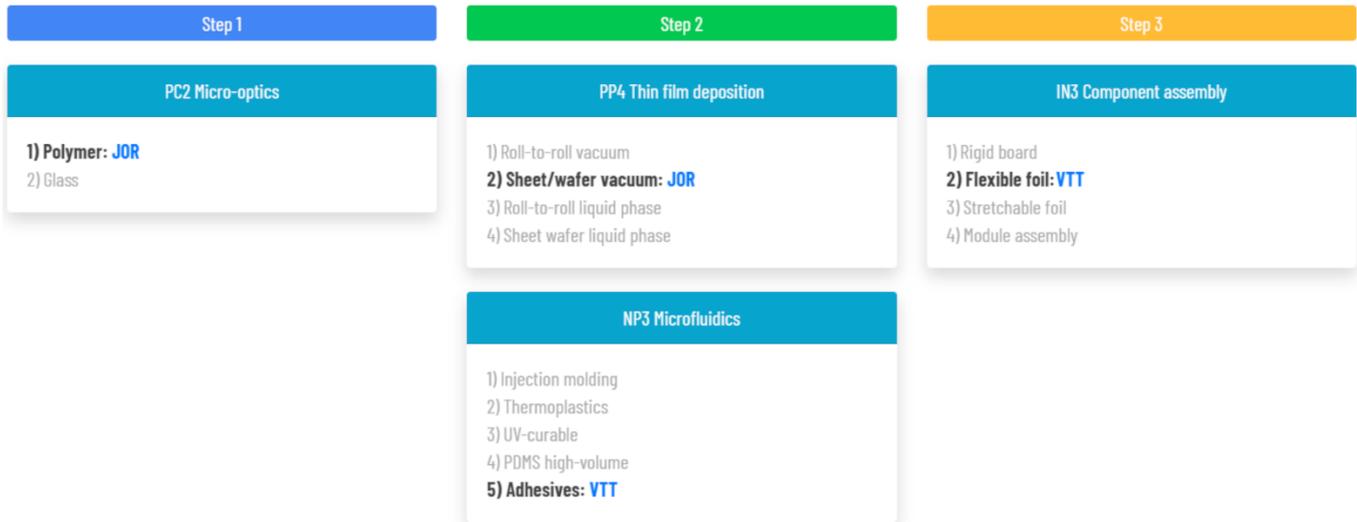


Figure 4. Production kit for the manufacturing of the optofluidic sensors. Production kit is a pre-defined collaboration between partners to accelerate the sensor realization and it is formed base on the pilot line Modularity table (Figure 3). Opto-fluidic sensor is manufactured in three steps by using the processes highlighted in the modules by the indicated partner.

High volume roll-to-roll (R2R) manufacturing techniques were used for sensor manufacturing. Polymeric sensor nanostructures were manufactured at large scale using roll-to-roll UV nanoimprinting lithography (UV-NIL) (Section 2.2.1, page 9). The large area roll-to-roll imprinting tool was manufactured by upstepping process. The nanostructures were metallized (Section 2.2.2, page 13) and sensor surfaces were singulated into microscope slide size pieces. The microfluidic structures were manufactured by roll-to-roll laser patterning and lamination process using double sided tape as a fluidic layer and clear polymer film as lid layer (Section 2.2.3, page 15). Pick-and-place process was used to integrate the sensor surface with the microfluidics before the final singulation by rotary kiss cutting (Section 2.2.4, page 16). The sensors were characterized by measuring the reflectance spectra from 20 sensors using a spectrophotometer and defining the depths of the intensity dips (Section 2.3, page 17). A roll of complete sensors and a singulated sensor are shown in Figure 5.



Figure 5. Left: Roll of complete sensors. Right: Sensor singulated from the roll by rotary kiss cut process.

Various kinds of dissemination material were prepared, and these are reported in Section 3, page 20.

2. Disposable plasmonic-fluidic sensor

2.1. Design

2.1.1. Plasmonic surface

Plasmonic surface was designed by VTT using commercial software (GSolver, Grating Solver Development Co.) and rigorous coupled wave method. Selected tool solves Maxwell’s equations at the grating region, and it is primarily used for optical grating design and optimization. Tool was verified against FDTD-simulations and for the simulated test case, these tools gave consistent results.

For structure optimization, the following parameters were varied: grating depth, period, and duty cycle. Incidence angle was kept constant and diffraction efficiency was studied as a function of wavelength. In addition, sensor response was simulated in air and in water to ensure feasible and measurable response with both superstrates.

The 1-dimensional binary grating structure for the plasmonic sensor surface, period 700 nm and height 30 nm, was chosen because it provides reasonable response and is easy to manufacture and measure. Manufacturing tolerances were studied especially for the grating depth, which is expected to vary due to the coating process and variations on the structure fill. Examples of the simulation results are shown in Figure 6 and Figure 7.

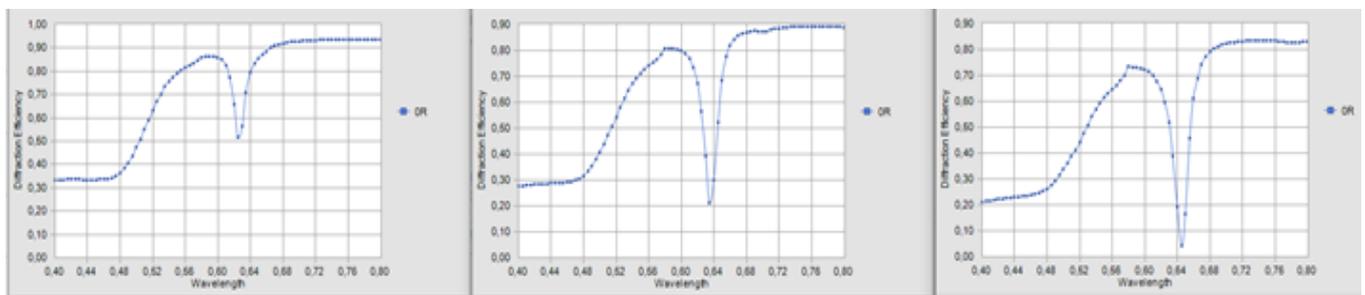


Figure 6. Simulated grating response for TM polarization in air for different grating depths. Depth is from left to right 20, 30 and 40 nm. It is expected that in the final sensors there is some deviation to nominal depth due to coating process.

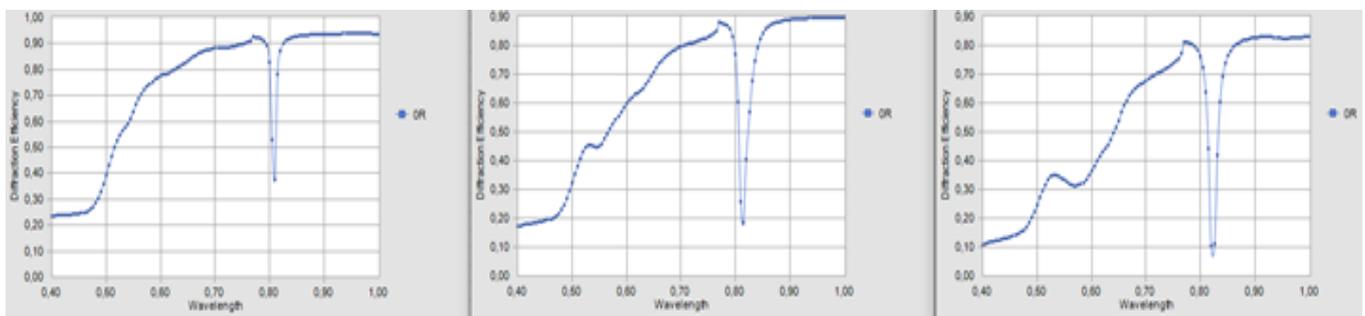


Figure 7. Simulated grating response for TM polarization in water for different grating depths. Depth is from left to right 20, 30 and 40 nm. The goal for the design was to have a measurable response in water superstrate.

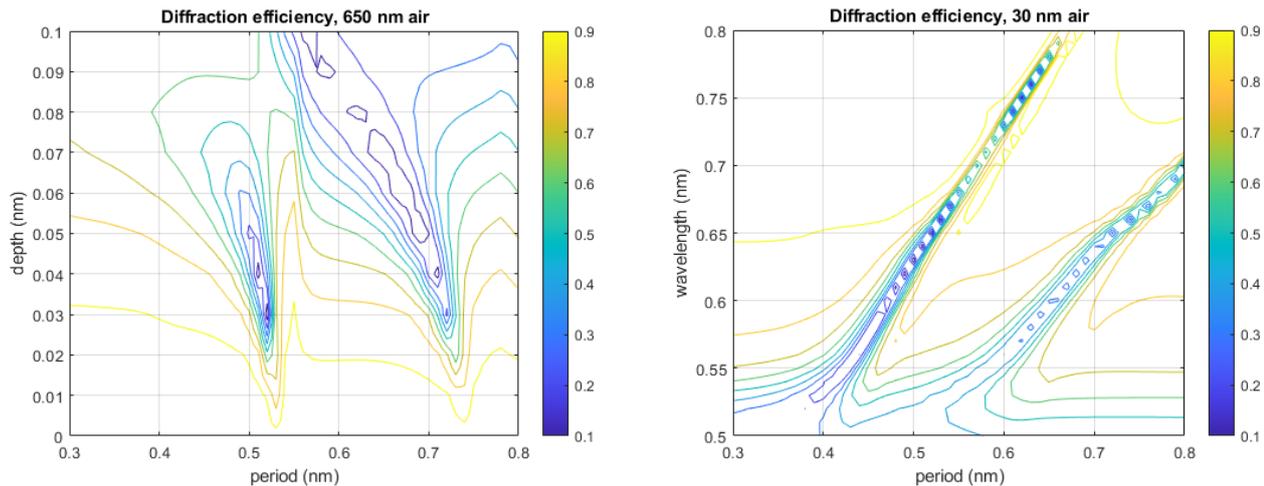


Figure 8. Examples of structure simulations for a fixed wavelength of 650 nm (left) and for a fixed grating depth of 30 nm (right).

2.1.2. Design for manufacture

Aim of the work was to design and implement a fully automated, high-volume manufacturing process for the sensor chip by linking the processes and capabilities at VTT and JOR. In this work, the Design for Manufacture (DFM) was essential. VTT and JOR considered the following topics to enable the high-volume automated processes.

A **production kit** (Figure 4) was formed for the sensor manufacturing based on the pilot line Modularity table (Figure 3). The sensor chip was manufactured in three steps by using processes at VTT and JOR, and the process interfaces were identified, and the logistic chain was defined.

Design rules were identified and applied to the design process. Design rules considered web width limitations on separate machines; alignment marks compatible with all machines; layout dimensions taking in account each machine's properties; repetition length of the layouts; and the file exchange formats.

Tooling strategy was agreed. Plasmonic structure master was planned, modelled, and ordered by VTT. Dimensions, orientation, and alignment marks were agreed between VTT and JOR.

Alignment of the process requirements at JOR and VTT were agreed. Designs rules were applied, and samples were sent in sheet and roll format from JOR to VTT. VTT's and JOR's roller equipment were aligned to each other in terms of roller width (300 mm) and core diameter of the imprinted roller (6 inch). In fact, this alignment action was considered when JOR set up its equipment in year 2010.

Manufacturability of the components was verified. The manufacturing process chain was defined, and a demonstration processing run was carried out. Plasmonic fluidic sensors were fabricated and characterized.

2.2. Manufacturing

2.2.1. Plasmonic surface imprinting

JOR's task within this model-case was roll-to-roll UV-NIL (nanoimprint lithography) imprinting of the plasmonic part of the chip. For large-scale imprinting, an imprinting stamp with dimensions of 280 x 620 mm² is required. Generally, these imprinting stamps (so-called shims) preferably consist of Ni, because Ni shims are more stable and can be easily cleaned. On the other side, Ni shims are very expensive. A good alternative are polymer shims, which can be fabricated by simply placing multiple imprints on a large area PET substrate, and a subsequent surface metallization acts as a varnish for protection.

The imprinting shim is then mounted in the Roll-to-Roll pilot line and replicated into a custom-made optical resin by continuous UV-NIL. A process scheme can be seen in the following picture (Figure 9).

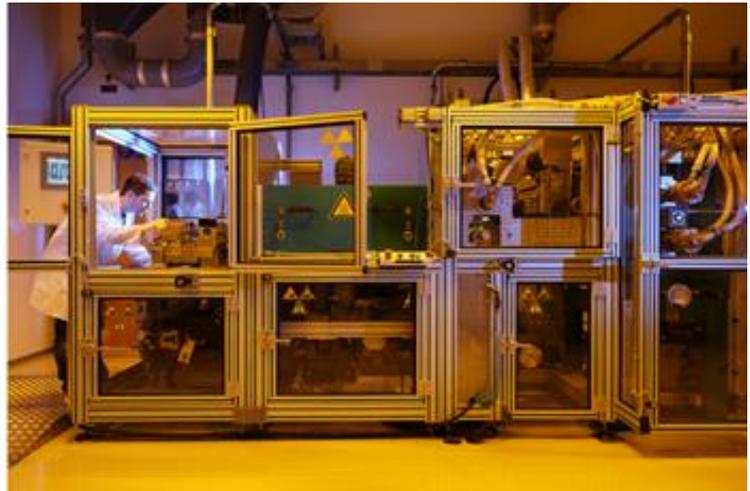
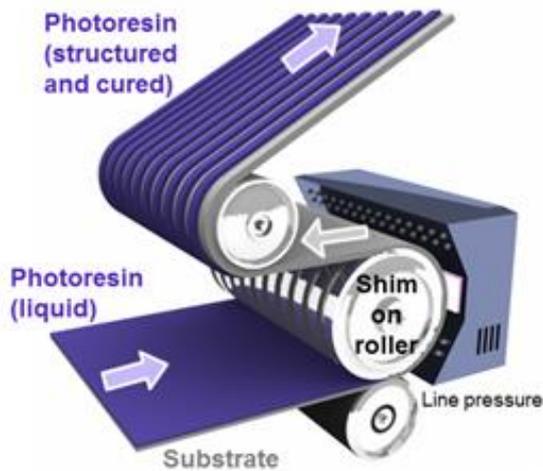


Figure 9. Process scheme (left) and a photograph of the JOR's Roll-to-Roll pilot line (right).

In the following, each process step is described in detail. JOR started with a randomly chosen plasmonic structure for process evaluation. The structure is a test grid with a line pitch of 500 nm and a structure depth of 250 nm, available as Ni master. Figure 10 shows a microscope and a SEM picture of this grid.

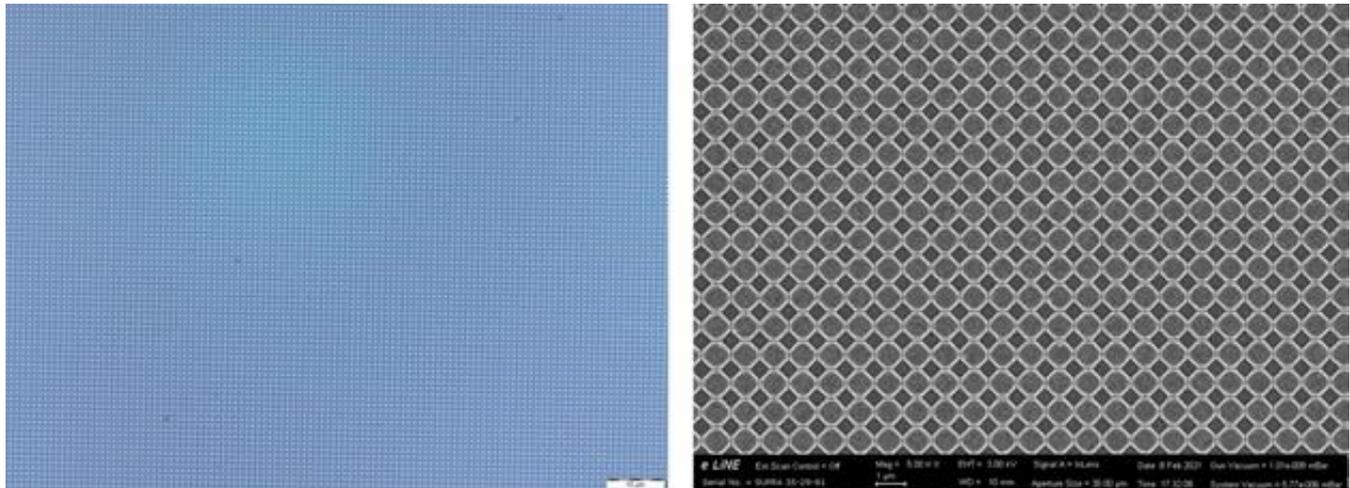


Figure 10. Microscope (left) and SEM image (right) of the investigated test grid.

These masters usually have small dimensions and do not cover the large shim area. Therefore, an upstepping process of the single structure has to be performed to result in a large area imprinting tool. JOR uses a customized foil stepper based on an EVG 770 UV-NIL step&repeat (S&R) machine for pattern upscaling and poly-shim fabrication. The master patterns are step-wise multiplied in a UV-curable imprint resin with good adhesion to the flexible (polymer foil) substrate. The involved resin materials are in-house developed compositions that are constantly optimized towards pattern and application specifications. Especially the shim resins have to fulfil a series of requirements, above all an excellent filling and demolding behaviour whilst showing a high shim substrate adhesion and stability in subsequent conversion processes (i.e. galvanization).

For conducting such an S&R process, the original master is replicated to fabricate a working quartz template by UV molding. Figure 11 shows the process file for the shim layout. Within the S&R machine, a small amount of UV resin (JR82) is dispensed on the PET substrate and the quartz template is lowered with controlled force onto the resin. UV-exposure and demolding is also controlled by the machine.

MedPhab

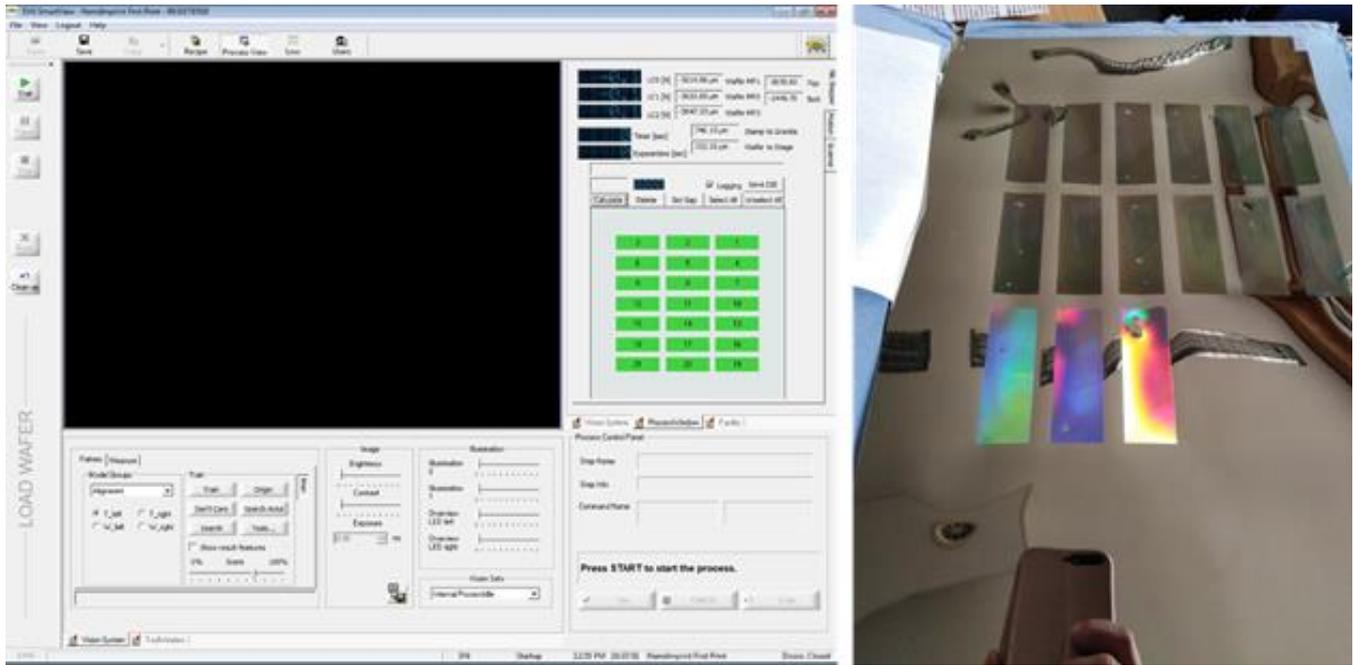


Figure 11. Process file (left) and resulting shim (right).

It turned out that the combination of template size (microscope slide dimensions) and the used plasmonic structure was not favourable for resin spreading. Nearly with every imprint, air bubbles were entrapped and could not be removed due to the hardness of the quartz template. One setting of parameters was more or less successful, but then each imprint took about 4-5 hours, which is not an acceptable time for prototyping. A photo of one row of imprints can be seen in Figure 11. After these five imprints, the template started to disintegrate, and the process was stopped.

As an alternative, a manual upstepping was chosen, which is not as accurate as the S&R tool in terms of positioning precision, but in this case, much faster and entrapped air could be easily removed by pressing with a fingertip. First, the Ni master is covered with a measured amount of UV resin (JR82). Second, the polymer substrate PET is placed on top of the master and third, the resin is distributed with a hand roller. During the rolling phase, air bubbles are pressed out. Prior to UV-curing, the area around the desired structure size is shielded with a metal frame. UV irradiation is at 320-400 nm (Waldmann UV 236) for 3 min 30 seconds. After the irradiation phase, the structure is rinsed with acetone and non-cured resin (i.e., non-irradiated parts) are removed. The next imprint is performed similarly and positioned manually on a grid. Additionally, an alignment cross is replicated at each line of structures. Figure 12 shows the manually fabricated polymer shim.



Figure 12. Manually fabricated polymer shim after fabrication (left) and mounted in the R2R pilot line (right).

Prior to roll-to-roll imprinting the polymer shim is coated with a thin metal layer (3 nm Cr, 20 nm Al) for structure protection and for enhanced demolding properties. Then the shim is mounted in the pilot line and replication is done into UV resin JR48 with a web speed of 1 m/min and a UV power of 50 %. Figure 13 shows the imprinted structures on PET Melinex ST505.

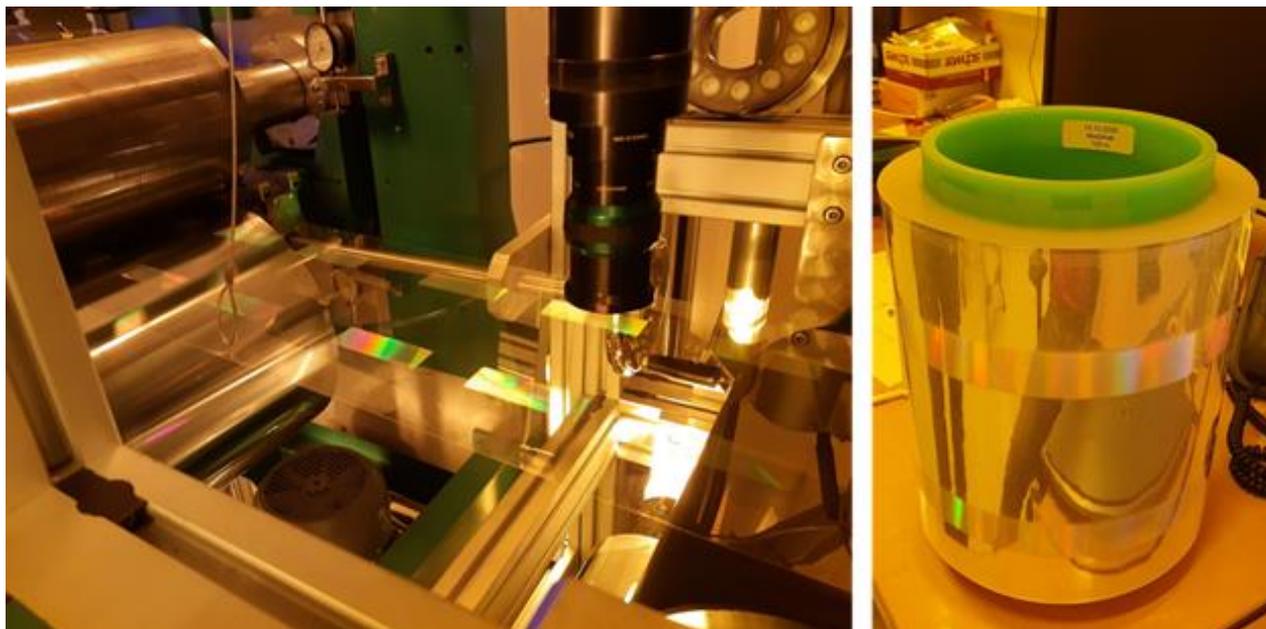


Figure 13. Roll-to-roll imprinted structures on PET foil (Melinex ST505) using the fabricated polymer shim.

After these successful upstepping and imprinting experiments, VTT provided a small-scale Ni master¹, which included the structures according to the final grating design parameters: period 700 nm; height 30 nm; area of 10 mm x 12 mm; grating lines along 12 mm axis. Figure 14 shows a SEM image of the line structure.

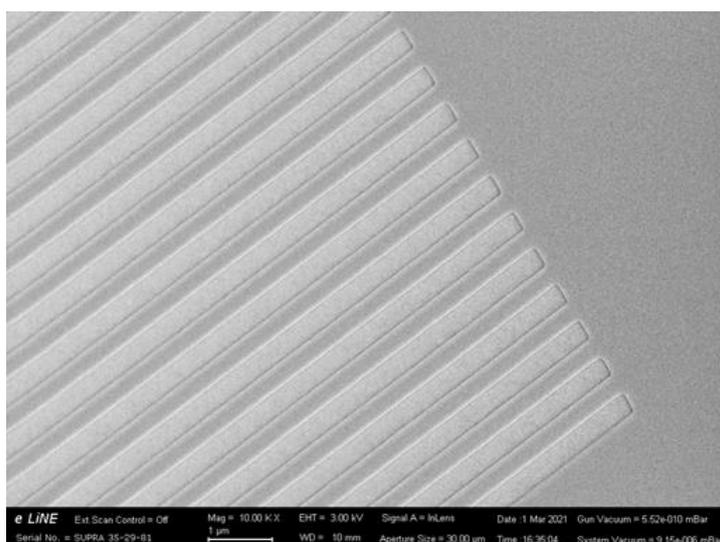


Figure 14. SEM image of the small-scale Ni master with line structures, according to the final plasmonic design provided by VTT.

The Ni master was directly replicated for shim fabrication in the above-described manual way, using JR 82 as the UV resin and PET Melinex ST505 as a substrate material. A grid was drawn to position the structures as precise as possible. Figure 15 shows the positioning plan as well as the first imprints on the shim.

¹ University of Eastern Finland is acknowledged for preparing master tool by e-beam lithography.

MedPhab

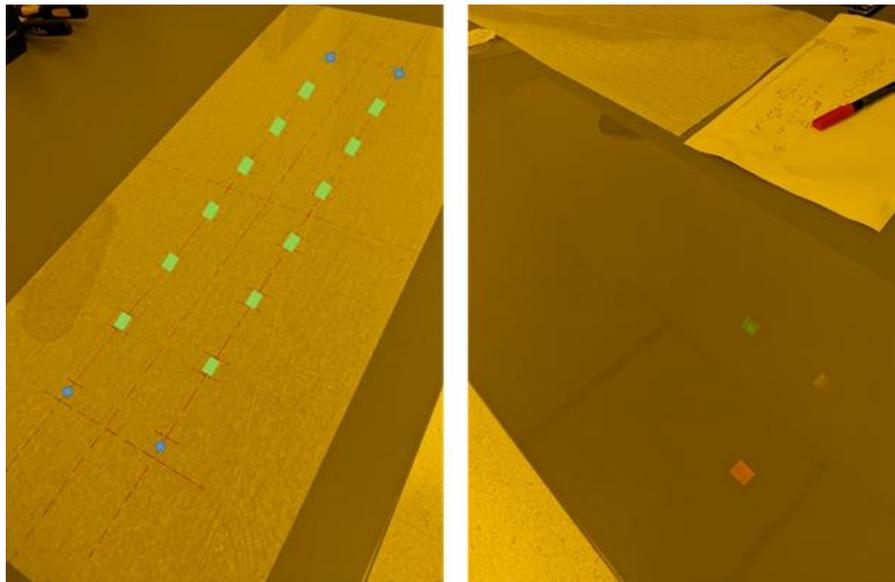


Figure 15. Positioning plan for shim fabrication (left) and first imprints on the shim (right).

The manually fabricated shim was coated with a thin metal (Cr/Al) varnish for surface protection and for better demolding. Next, the shim was mounted on the R2R machine and the structures were replicated into JR48 on PET substrate by roll-to-roll (R2R) UV-NIL with a web speed of 1 m/min and a UV power of 50 %. Due to the small master area, it was very hard to see any structures during replication. The arrows in Figure 16 indicate the imprinted structures during the roll-to-roll imprinting process.

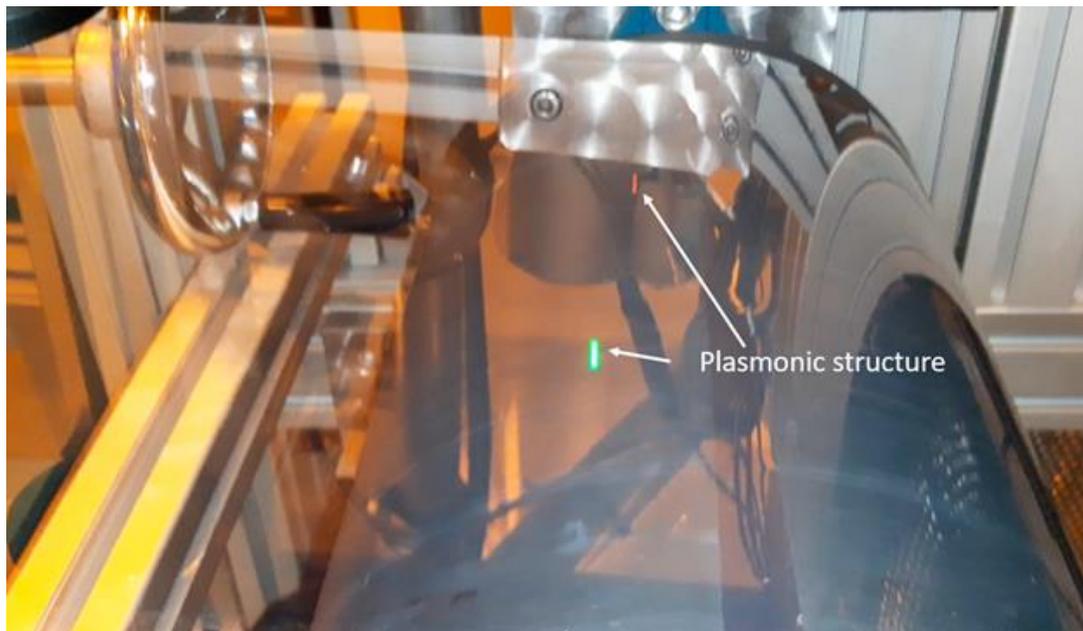


Figure 16. Imprinted structure on PET foil (Melinex ST505) using the fabricated shim. Due to the small master area, it is very hard to see any structures. The arrows indicate the imprinted structures during the roll-process.

2.2.2. Plasmonic surface metallization

In this model-case work, various metallization possibilities were tested. For aluminium (Al) metallization on R2R basis, JOR has a cooperation partner (Hueck Folien GmbH) who can coat flexible films in an industrial R2R coating machine. On the other hand, gold (Au) evaporation is not available at Hueck Folien. JOR has a laboratory evaporation chamber for small-scale samples up to 6" diameter. Within this machine, several metallization sources are available. For Au evaporation, electron beam (e-beam) deposition is the most favourable and was chosen for the small-scale samples. Both metal layers (Au and Al) are deposited on a chromium (Cr) seed layer for improved adhesion.

Aluminium metallization of the imprinted plasmonic structures

For these experiments, the imprinted rolls of the first described structures were sent to Hueck Folien GmbH and coated with Cr/Al. Hueck Folien is an expert in converting flexible substrates, and possesses a variety of roll-to-roll coating lines. For metallization, they have a pilot vacuum coating line with various metallization techniques such as sputter coating, thermal evaporation and e-beam evaporation. For the imprinted plasmonic roll, e-beam evaporation was chosen, and a 1-2 nm thick layer of Cr was applied and without leaving the vacuum, a 100 nm thick layer of Al was deposited on top.

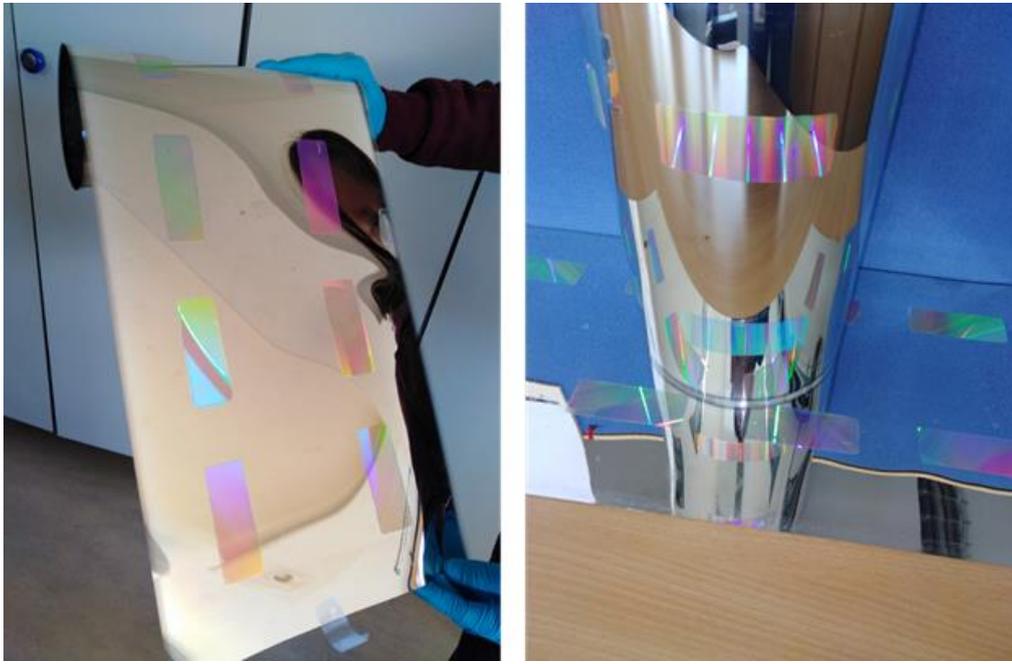


Figure 17. Aluminium metallized imprinted plasmonic structures.

The metallized roll was sent to VTT for further processing. Figure 18 shows a SEM image of the metallized R2R imprint.

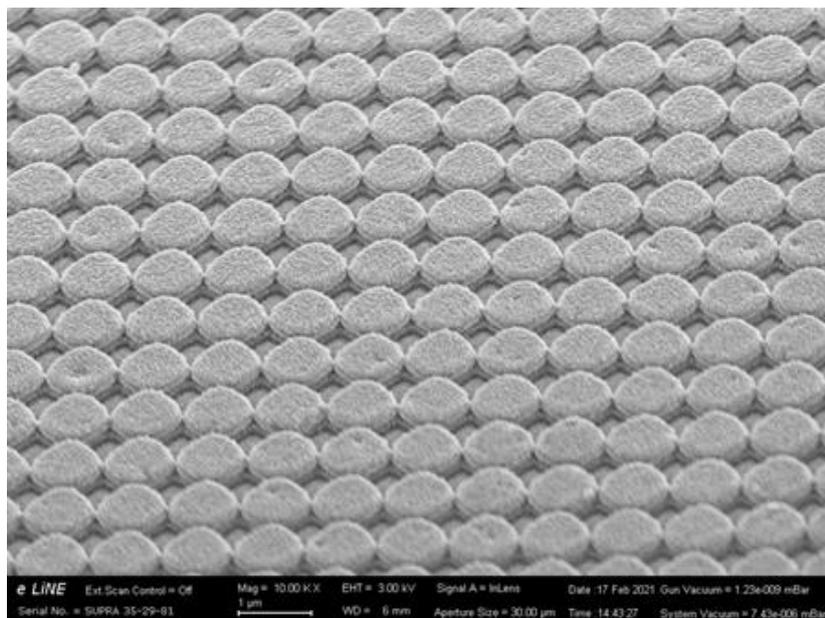


Figure 18. SEM image of metallized R2R imprint.

Gold coating of plasmonic structures

For the optimized plasmonic structure, a gold coating was essential to fully exploit the plasmonic effect. Since JOR only has the possibility to deposit gold on small-scale samples, the imprinted roll was cut into microscope slide-sized samples with a plasmonic structure located in the middle of each layer sample. Using the JOR's laboratory metallization equipment, a 3 nm thick layer of Cr and an 80 nm thick layer of Au was deposited by e-beam evaporation, using the parameters displayed in Table 1.

Table 1. Material deposition parameters.

Material	Power [%]	Deposition Rate [Å/s]	Thickness [nm]
Cr	3,5	0,5	3
Au	12	0,2	80

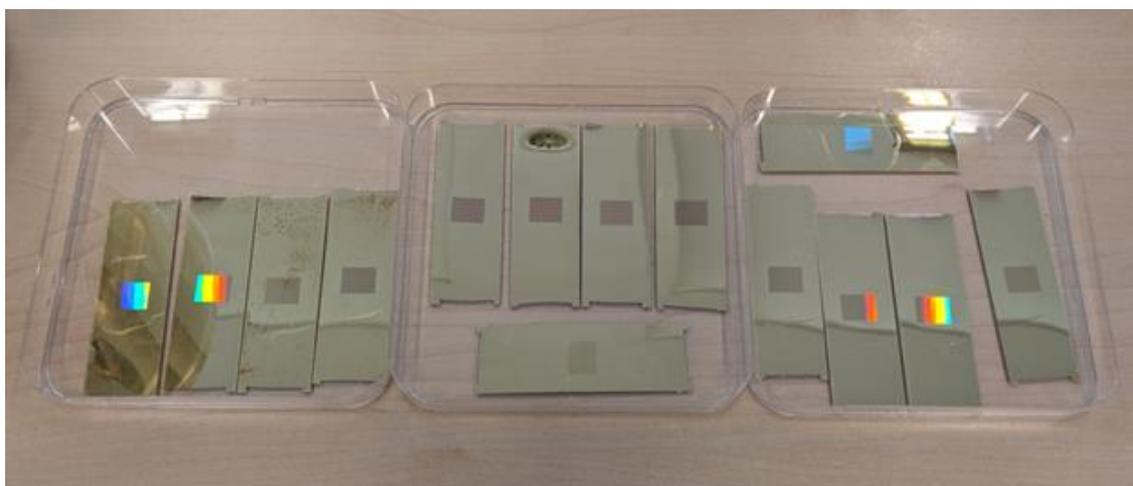


Figure 19. Gold coated imprinted plasmonic structures.

2.2.3. Tape fluidics roll-to-roll manufacturing by laser cutting

Tape microfluidics was roll-to-roll manufactured using the conversion line (DELTA) at VTT, which includes an integrated CO₂ laser-cutting unit. Figure 20 A shows the overall view of the DELTA line.

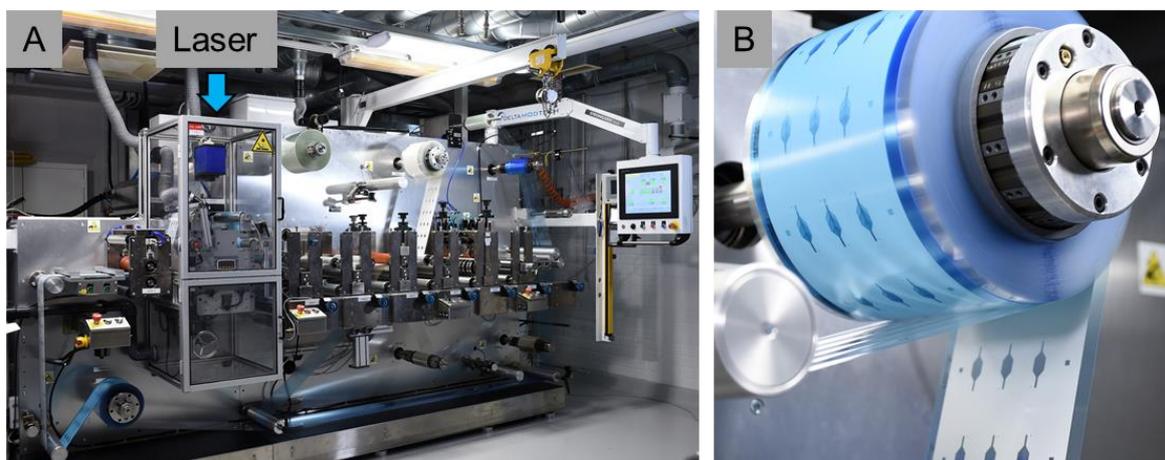


Figure 20. A) DELTA conversion line at VTT with integrated CO₂ laser unit. B) Lamination of a protective liner to a roll of tape-based microfluidics at DELTA line.

The manufacturing process consists of two consecutive production runs that are shown in Figure 21. In the first production run, the first step is laser cutting of microfluidic channels into the double-sided tape while leaving the bottom liner intact. In the next step, removal of the bottom liner and the cutting waste is done simultaneously. The following step is the lamination of the fluidics cover layer with its own protective liner.

In the second process run, the first step is the laser cutting of vias into the cover layer for the fluidic connection and air venting. The next step is the simultaneous lower liner and cutting waste removal. Then, a protective liner is laminated to preserve the cover layer’s optical quality.

If the fluidics bottom layer material is available in roll format, it can be laminated directly after the protective liner lamination step. If the bottom layer (see Figure 2) is supplied as separate pieces, e.g. as microscope-slide-sized pieces as in this model-case, an intermediate protecting liner is laminated, and the sensor bottom layers are assembled in a separate pick-and-place process at VTT’s hybrid integration line. Figure 20 B presents a roll of fluidics containing bottom, fluidic and cover layers and liners at both sides.

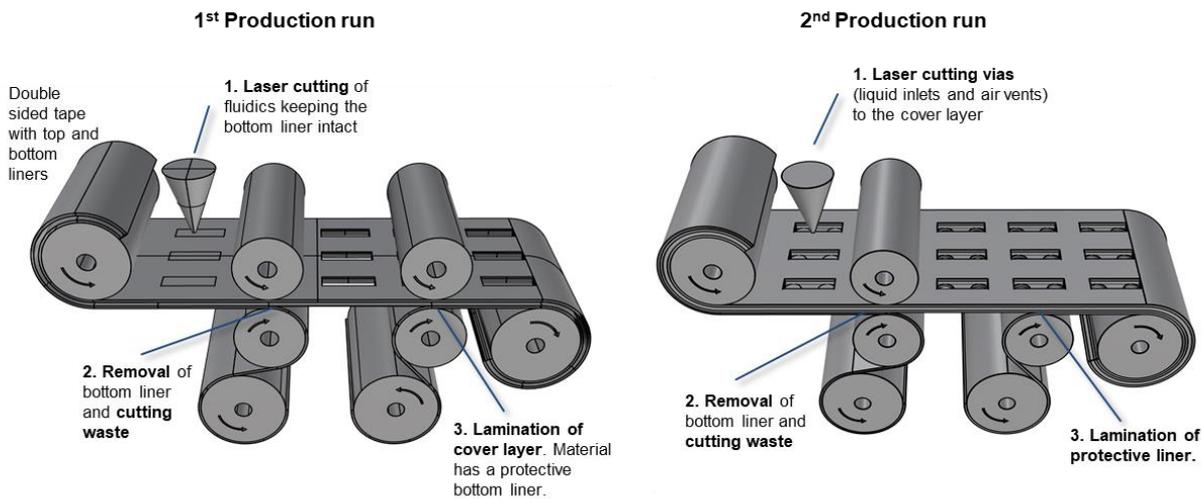


Figure 21. Key manufacturing steps of laser cut R2R tape microfluidics done in two consecutive production runs.

2.2.4. Hybrid integration and chip singulation

After the R2R manufacturing of tape fluidics, the fluidic roll is transferred to VTT’s EVO hybrid integration line for the bottom foil assembly. Figure 22 A presents the EVO hybrid integration line at VTT.

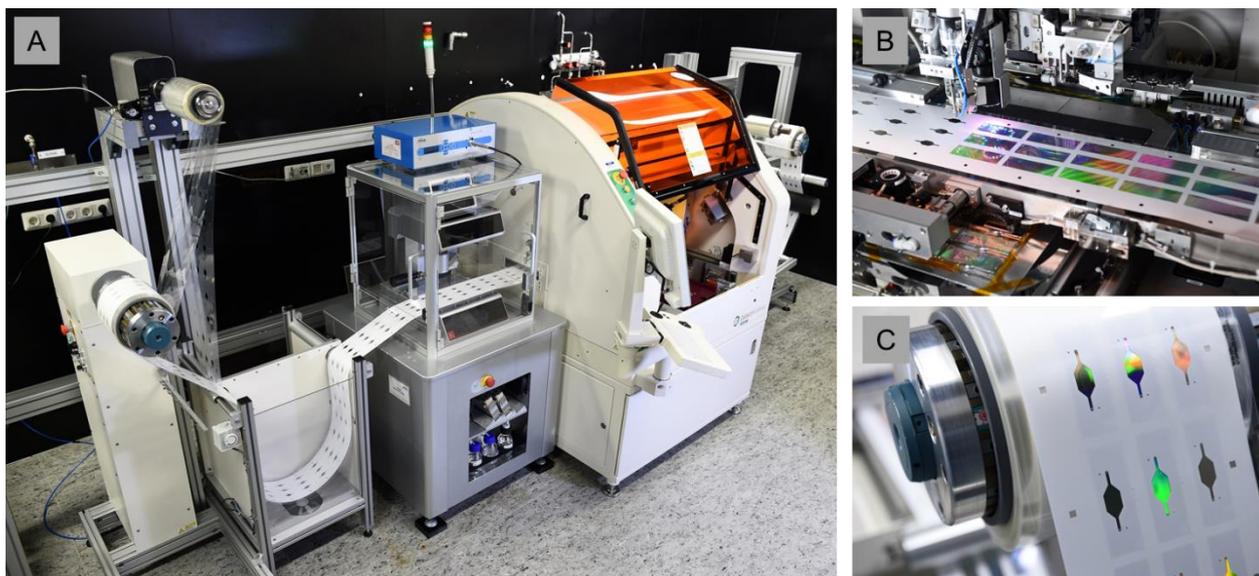


Figure 22. A) EVO hybrid integration line at VTT. B) Assembly of the plasmonic sensor surfaces and C) roll of plasmonic fluidic devices.

Plasmonic sensor surfaces fabricated by JOR were used as sensor bottom layers of the plasmonic fluidic device. The surfaces were laser cut at VTT's UV laser and then assembled in a pick-and-place process to the fluidic roll in the third production run, presented in Figure 23 (left). Liner is removed from the tape surface, plasmonic sensor surfaces are assembled and new liner added to cover the bare tape surface. Figure 23 (right) presents the fourth and the last production run, the sample singulation by rotary kiss cutting at DELTA conversion line. Figure 24 shows the singulation process and a final sample. After the production runs, the singulated sensors contain a protective liner on the top side of the sample, to keep the cover layer optically clear and to seal the fluidics until use.

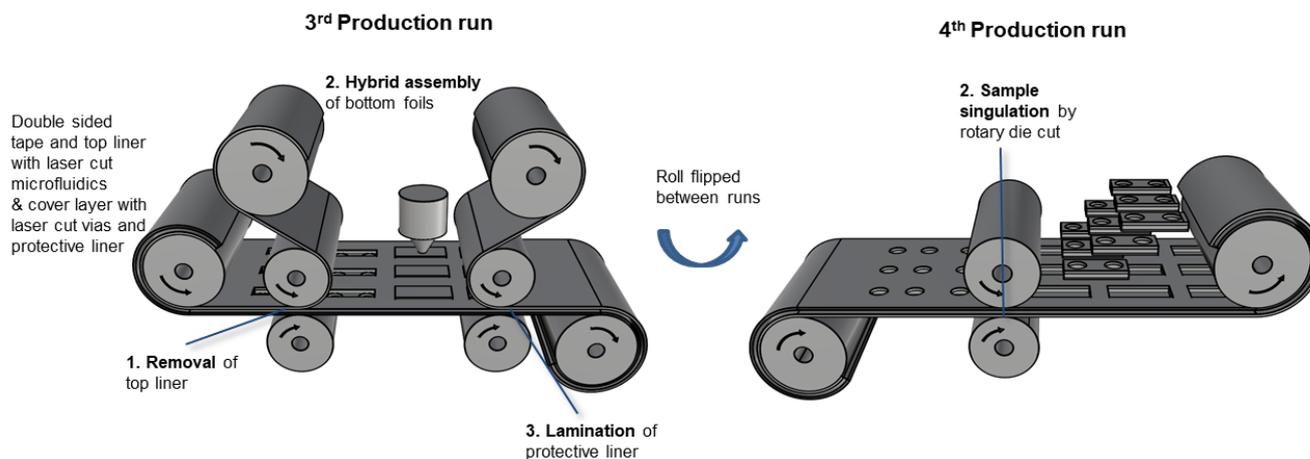


Figure 23. Manufacturing steps of hybrid assembly of the sensor bottom layers (left) and the sample singulation (right).

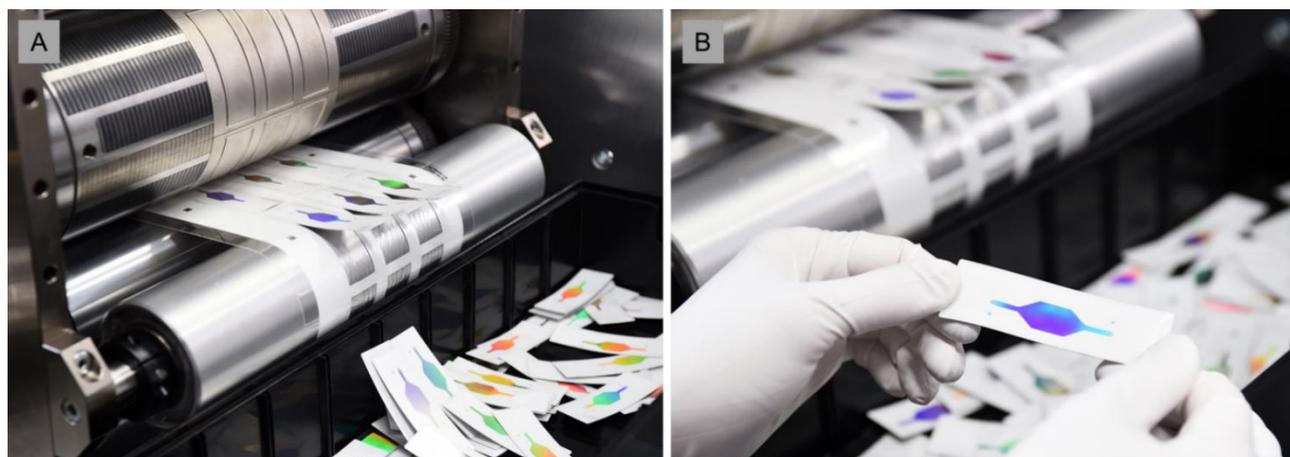


Figure 24. A) Sample singulation at VTT's DELTA conversion line and B) a singulated sensor chip.

2.3. Characterization

2.3.1. Characterization method

The characterization measurements were carried out with UV-Vis-NIR spectrophotometer (Cary 5000, Agilent Technologies) and related measurement accessory (Cary Universal Measurement Accessory (UMA)), both presented in Figure 25. The UMA enables the reflection measurements, which was used in the characterization. Wavelength range of 400-1000 nm was examined, and a detailed analysis was carried out in the 800-900 nm range. In preliminary measurements, the smallest aperture slit seemed to remain too wide, so it was reduced further to 1 mm. Sample angle of 10 degrees and P (90 degrees) polarization was used in the measurements. In total, 20 samples were measured.

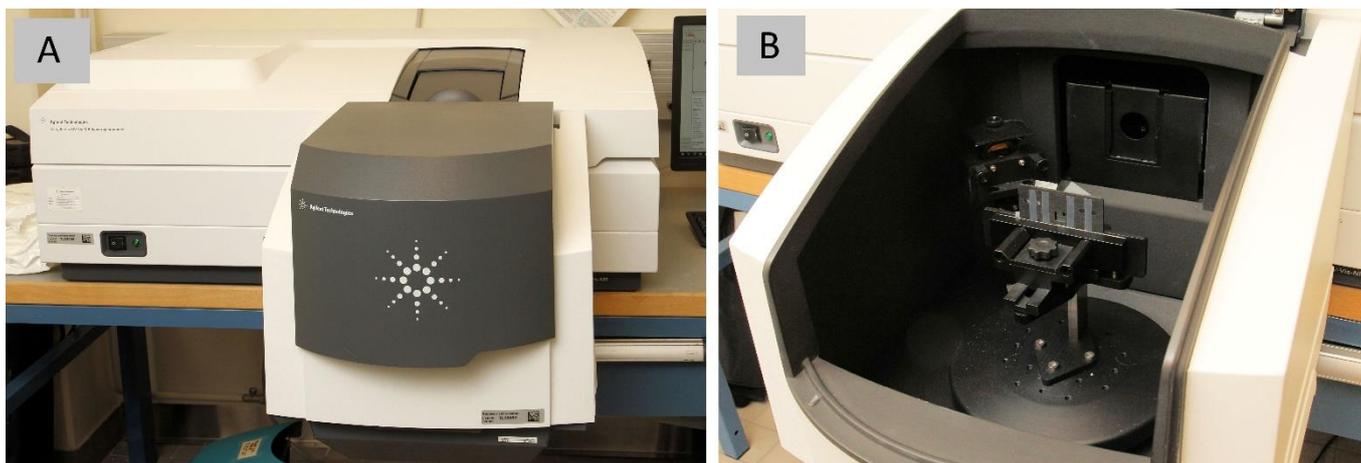


Figure 25. A) UV-Vis-NIR spectrophotometer (Cary 5000). B) Universal Measurement Accessory.

2.3.2. Measurement results

Figure 26 shows smoothed spectra measured from 20 sensor chips. Smoothing was made with Matlab to the wavelength ranges of 800-834 nm and 852-900 nm, leaving the range with a plasmon coupling induced intensity dip untouched. Figure 27 shows smoothed spectrum from one measured sample in the wavelength range of 400-1000 nm. Smoothing was made with Matlab to the wavelength ranges of 400-597 nm, 694-835 and 850-900 nm, leaving the wavelengths with plasmon coupling induced intensity dips untouched. The smoothing was used to reduce the noise caused by the spectrophotometer.

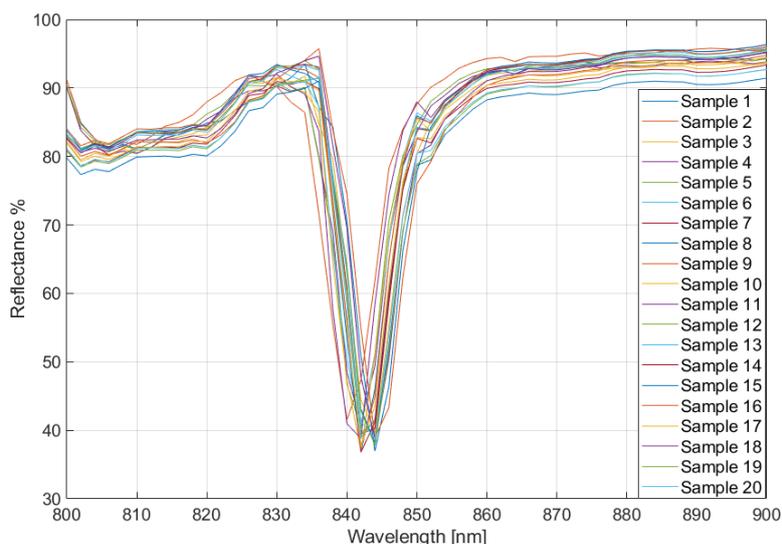


Figure 26. Smoothed spectrophotometer results from 20 samples in the wavelength range of 800-900 nm.

MedPhab

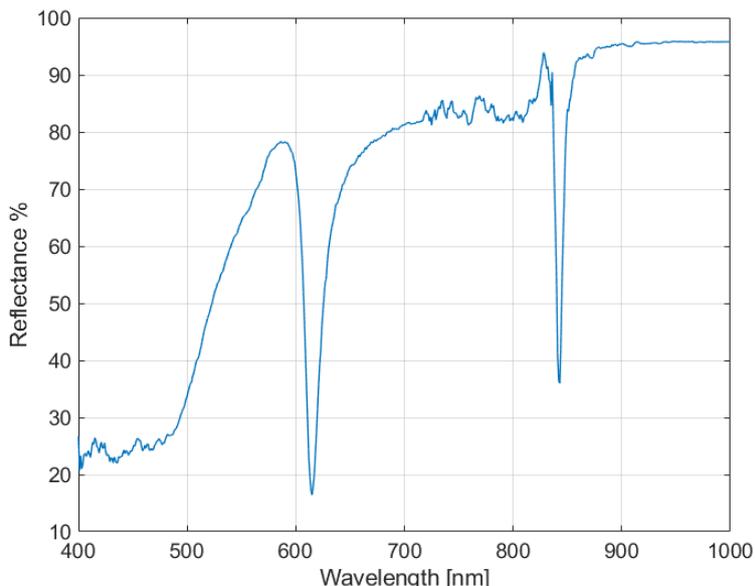


Figure 27. Smoothed spectrum from one measured sample in the wavelength range of 400-1000 nm.

To compare the results, the reflectance value at the wavelength of 900 nm was normalized to one, which is shown in Figure 28. In Table 2, the dip depths as percentage from the normalized data point are listed. The average dip depth is 56 % from the normalized maximum and the standard deviation is 2 %.

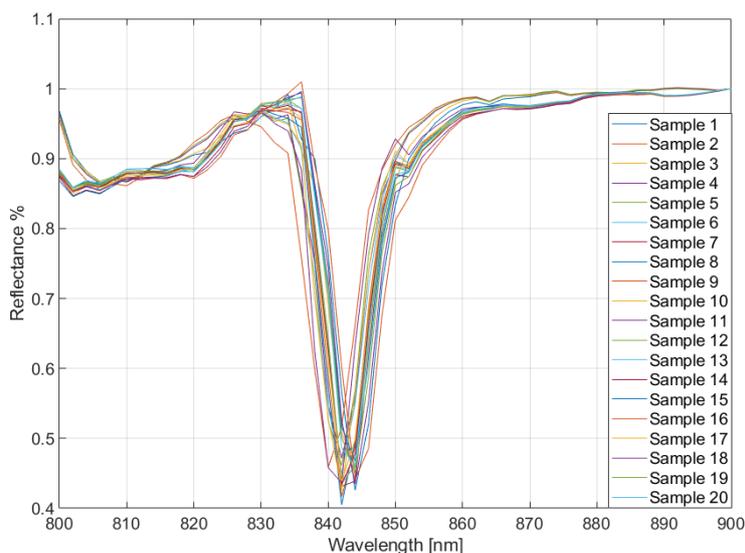


Figure 28. Normalized spectrum of the measured samples, smoothed.

Table 2. Dip depths from the normalized data

Sample no.	1	2	3	4	5	6	7	8	9	10
Dip depth [%]	57.4	54.1	53.9	52.8	53.9	55.0	56.9	59.5	58.3	57.4
Sample no.	11	12	13	14	15	16	17	18	19	20
Dip depth [%]	56.4	56.0	56.5	56.6	53.2	55.8	56.1	56.5	54.9	53.9
Average dip depth [%]	55.8									
Standard deviation	2 %									

2.3.3. Revised optical grating simulations

To cross-check the quality of the optical grating design and the simulation results (presented in Section 2.1.1.), the optical grating simulations were revised according to the measured structure dimensions of the manufactured samples. First, a three-level grating profile consisting of trapezoids stacked on top of each other was fitted to the measured AFM profile by open source software (Gwyddion). In addition to seven trapezoid parameters, also the grating period was defined. These values were used to define the exact manufactured grating profile in Gsolver, and simulations similar to the ones presented in section 2.1.1 were carried out. Revised simulation results were in good agreement with the measured values, as shown in Figure 29.

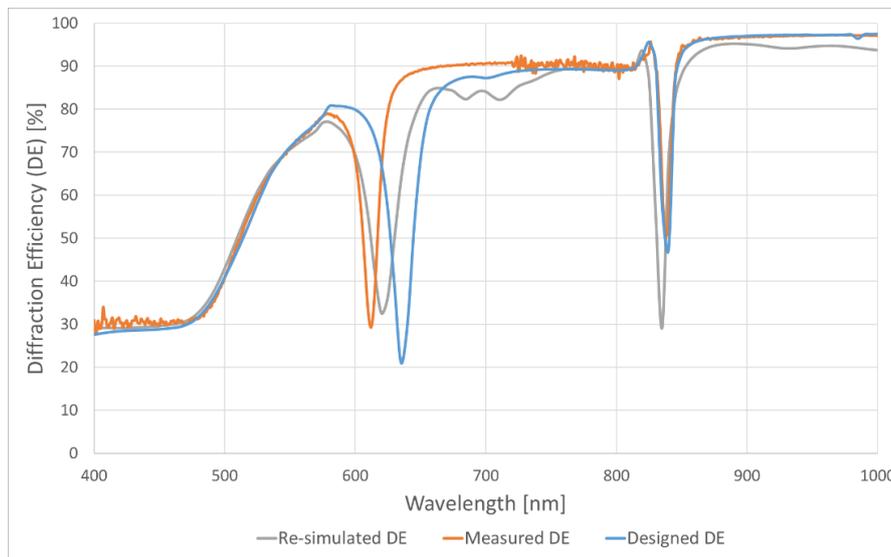


Figure 29. Diffraction efficiencies of the designed (blue), measured (orange) and re-simulated (grey) gratings.

2.4. Conclusions reflected against the set goals

Target set in the MedPhab's Description of the Actions for this model case was the following:

“Disposable plasmonic-fluidic sensor: R2R imprinting and metal deposition by JOR. R2R microfluidics and R2R integration of fluidics by VTT. Specifications: CV <5% and automated production.”

The results on manufacturing process descriptions show that the sensor surface was fully roll-to-roll imprinted using automated equipment. Metal deposition was carried out using roll-to-roll equipment at Hueck Folien for aluminium, whereas gold deposition tasks were carried out in sheet-level process at JOR due to cost reasons. Microfluidics structure manufacturing and integration of fluidics parts to the sensor's surfaces were both realized using fully automated roll-to-roll equipment.

The characterization results show that the standard deviation of the intensity dip depths in the reflectance spectra for 20 samples was 2%, which is less than the set target of CV <5%.

As a conclusion, the goals set for the model-case related to the sensor performance repeatability and automated production were fulfilled.

3. Dissemination material

To disseminate the pilot line capabilities, dissemination material from the model-case is prepared. In addition to this deliverable report, material includes flyer/brochure (Figure 30), one-slider for the pilot line Technical dissemination slide deck (Figure 31), model-case spread for the Handbook (Figure 32) and MedPhab web pages that provides access to the handbook, flyer, model-case reports and the model case dissemination video (Figure 33, Figure 34 and Figure 35).

Disposable plasmonic-fluidic sensors

Diagnostic devices consist of numerous photonic and non-photonic components that need to be combined for the required functionality. Modular blocks with preliminary division enables a structured approach to **highly fragmented heterogeneous technologies** used in component manufacture and device integration. For each case, the fabrication chain is designed by choosing the relevant blocks. Model-Cases are chosen to create libraries for four segments: photonics component manufacture, non-photonic peripheral manufacture, device integration and post-processing. MedPhab enables small and medium scale manufacturing of **nanostructured substrates** together with surface metallization processes and has established processes for their integration with microfluidic structures. This will help to address the need for signal enhancing substrates required for highly sensitive molecular diagnostics.

Medphab Partners

[linkedin.com/company/medphab](https://www.linkedin.com/company/medphab) |
 twitter.com/medphab |
 info@medphab.eu

www.medphab.eu

MedPhab has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 871345. www.photonics21.org

Disposable plasmonic-fluidic sensors

Pilot production of integrated microfluidic structures for highly sensitive molecular diagnostics

Model Case for Molecular Diagnostics

www.medphab.eu

Realisation of a fully automated, high-volume manufacturing process for plasmonic-fluidic sensors by linking capabilities at VTT and Joanneum Research

Design of photonic structure, VTT

- Plasmonic surface grating was designed using rigorous coupled wave method.
- Optimal structure was chosen regarding the performance and manufacturability.
- Small scale stamp master* according to design was realized.

Sensor chip structure

Operational principle

When light hits the plasmonic surface, intensity of the wavelength exciting the surface plasmon is reduced in the reflected light.

Sensor surface by roll-to-roll UV nanoimprinting lithography, Joanneum Research

- Large scale manufacturing of nanophotonic plasmonic sensor part.
- Large area imprinting tool for R2R UV-NIL by upstepping process.
- R2R replication of plasmonic sensor surface.
- R2R / Sheet-level metallization of sensor surfaces.

*University of Eastern Finland is acknowledged for preparing master tool by e-beam lithography.

Roll-to-roll manufactured tape microfluidics, VTT

- Laminated structure formed by fluidic layer (double sided tape) and lid layer with vias.
- Structures patterned by laser cutting.

Hybrid integration and singulation, VTT

- Plasmonic sensor surfaces hybrid assembled to the microfluidic roll by pick-and-place process.
- Complete sensors singulated from the roll by cutting tool.

Characterization, VTT

- Reflection spectra was characterized from 20 sensors using a spectrophotometer.
- Simulated and measured diffraction efficiencies were in good agreement.
- Coefficient of variation (CV) was 2%.

Reflectance spectrum

Full report and videos on manufacturing, see www.medphab.eu/offering

Figure 30. A dissemination flyer/brochure “Disposable plasmonic-fluidic sensors” was compiled, with a technical title “Realisation of a fully automated, high-volume manufacturing process for plasmonic-fluidic sensors by linking capabilities at VTT and Joanneum Research”. Upper picture: Brochure front page and back page. Lower picture: Brochure inside pages.

Model Case / Disposable plasmonic-fluidic sensors



Realisation of a fully automated, high-volume manufacturing process for plasmonic-fluidic sensors by linking capabilities at VTT and Joanneum Research

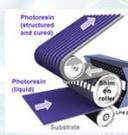
Manufacturing process chain

- Design of photonic structure, VTT
- Sensor surface by roll-to-roll (R2R) UV nanoimprinting lithography, Joanneum Research
- Roll-to-roll manufactured tape microfluidics, VTT
- Hybrid integration and singulation, VTT
- Characterization, VTT

Applications

- In-vitro molecular diagnostics

Roll-to-roll UV NIL process scheme and shim




Roll-to-roll manufactured tape microfluidics

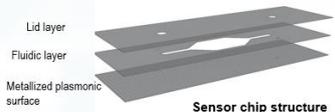


Hybrid integration and singulation



Full report and videos on manufacturing, see www.medphab.eu/offering

Sensor chip structure



Operational principle



Characterization

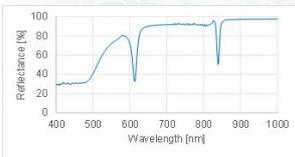


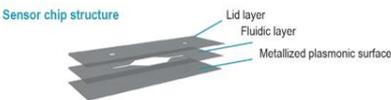
Figure 31. Dissemination material for the MedPhab’s Technical dissemination slide deck was compiled.

Model case: Disposable plasmonic-fluidic sensors for molecular diagnostics

Plasmonic *in-vitro* sensors can be used to measure binding of biomolecules to the plasmonic surface that is formed by a metallized nanostructure. When plasmonic surface is illuminated, a surface plasmon is excited by a suitable wavelength, and this can be seen as a sharp intensity dip in the reflectance spectra. Binding of biomolecules changes the spectral position of this dip and phenomenon can be used to implement sensors for molecular diagnostics.

MedPhab has developed a fully automated, high-volume manufacturing process for disposable plasmonic sensor chips by linking the capabilities at VTT and Joanneum Research. The sensor chip is formed by a plasmonic sensor surface that is combined with fluidic and lid layers forming microfluidics for sample application.

Sensor chip structure



Operational principle



When light hits the plasmonic surface, intensity of the wavelength exciting the surface plasmon is reduced in the reflected light.

Polymeric sensor nanostructures were manufactured at large scale using roll-to-roll UV nanoimprinting lithography (UV-NIL). The large area roll-to-roll imprinting tool was manufactured by upstepping process.

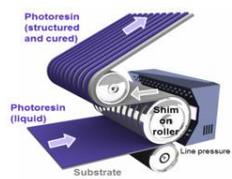
The microfluidic structures were manufactured by roll-to-roll laser patterning and lamination process using double sided tape as a fluidic layer and clear polymer film as lid layer. Pick-and-place process was used to integrate the sensor surface with the microfluidics before the final singulation by rotary kiss cutting.

Reflection spectra were measured from 20 sensors using a spectrophotometer. The depths of the intensity dips were characterized and the coefficient of variation (CV) was found to be 2%.

Further information of the manufacturing and characterization see www.medphab.eu/offering.



Sensor chips with plasmonic surface and integrated microfluidics
Courtesy of VTT



Roll-to-roll UV NIL process scheme & Shim
Courtesy of Joanneum Research



Roll of laser patterned microfluidics
Singulation
Courtesy of VTT

Figure 32. Draft version of the dissemination material for the MedPhab handbook was compiled. Material will be included to the next version of the Handbook.

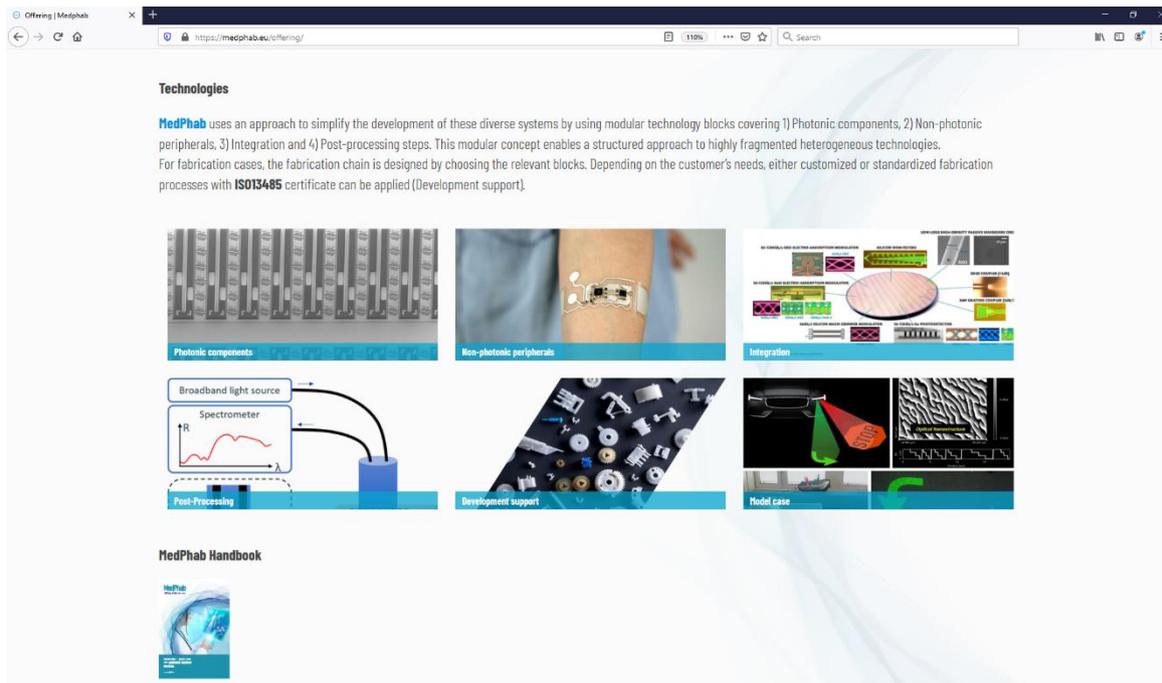


Figure 33. A screen capture image from the “Offering” page on the MedPhab’s webpages (<https://medphab.eu/offering/>), showing the reserved info slot for the model-cases, and the icon for downloading the MedPhab Handbook.

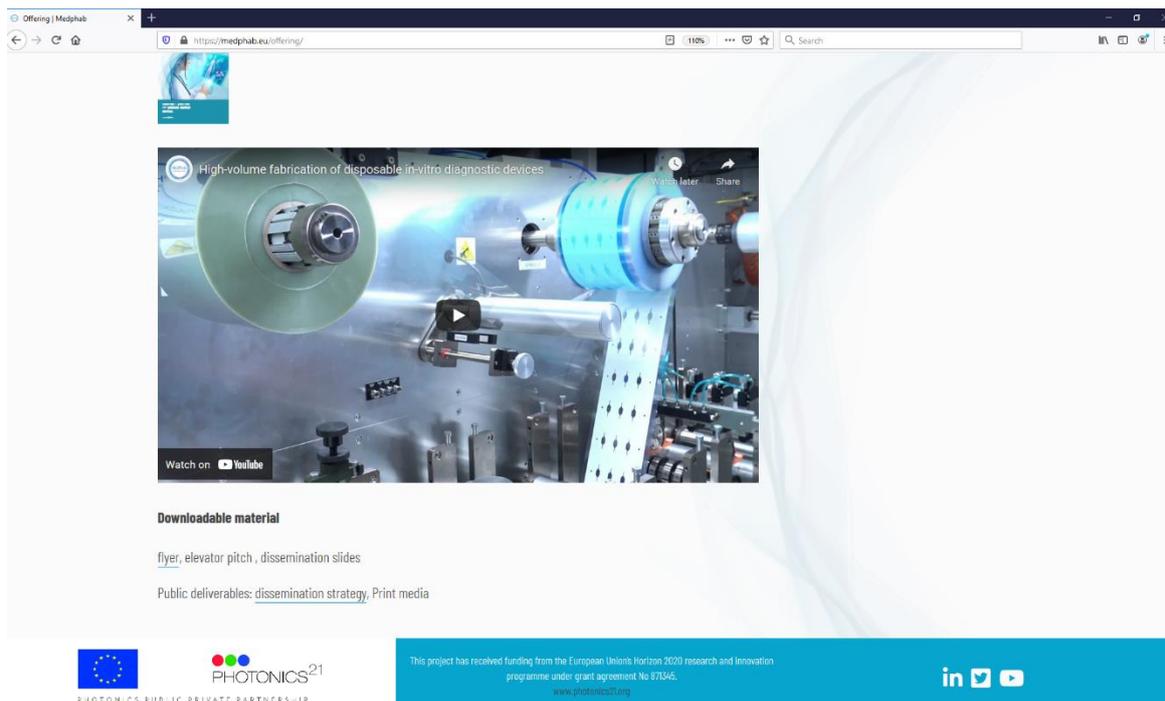


Figure 34. A screen capture image from the “Offering” page on the MedPhab’s webpages (<https://medphab.eu/offering/>), showing the link to the Model case dissemination video material on MedPhab’s YouTube channel. Also links to other downloadable materials, such as flyers and dissemination slides, are shown.

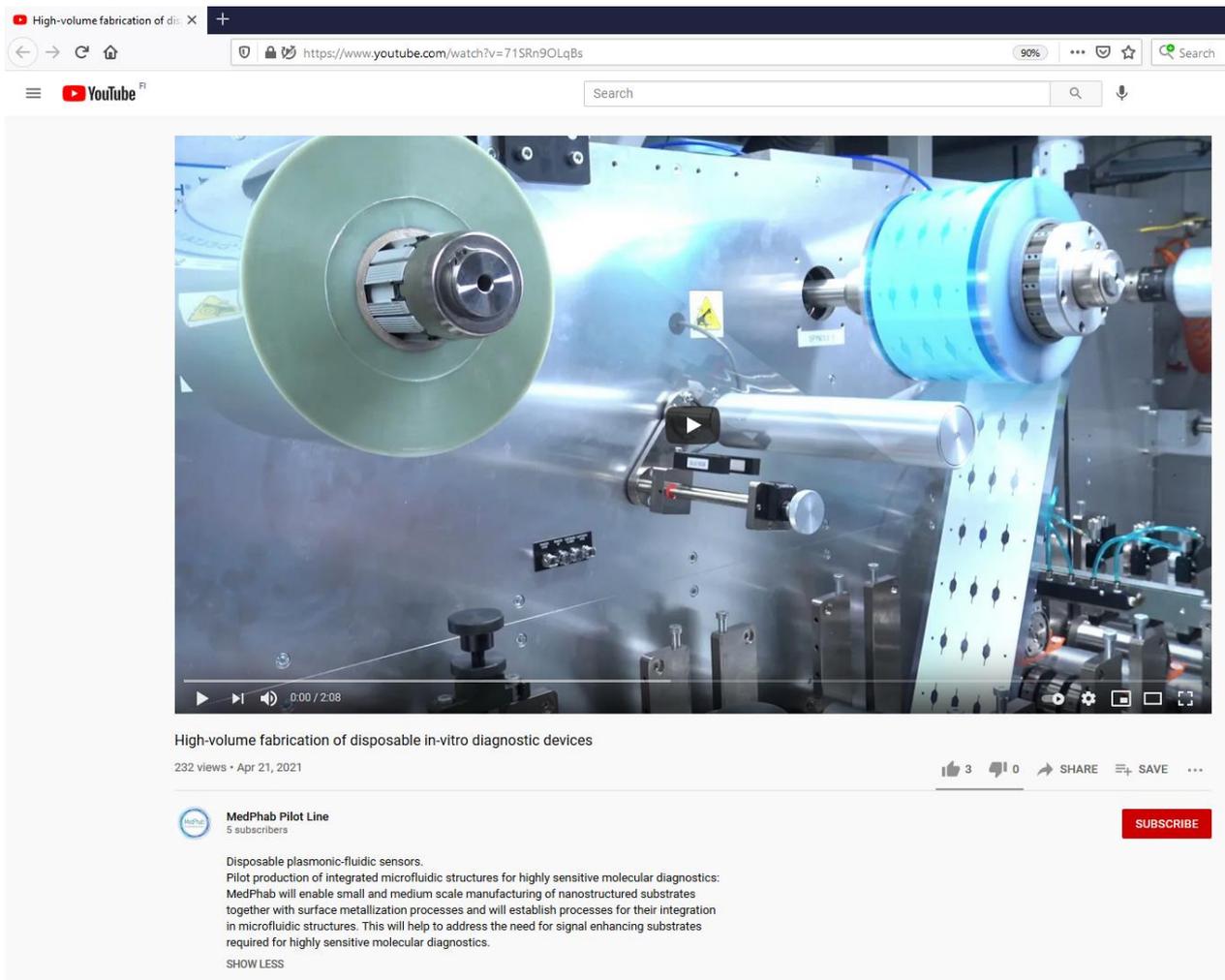


Figure 35. A screen capture image from the MedPhab's YouTube channel, showing the model case dissemination video (<https://youtu.be/71SRn9OLqBs>)

4. Conclusions

In this model-case 'Disposable plasmonic fluidic sensor', the work consisted of design and implementation of a fully automated, high-volume manufacturing process for a plasmonic-fluidic sensor chip by linking the capabilities at VTT and JOR.

Design for Manufacture (DFM) was essential in this work, and VTT and JOR considered several topics to enable the high-volume automated processes. Based on MedPhab's modular approach, a plasmonic sensor specific Production Kit was formed. Design rules were identified and applied. Manufacturing steps, process interfaces, logistics chain and characterization steps between VTT and JOR were identified.

Key technologies were selected for the realisation of the manufacturing process. High volume roll-to-roll manufacturing techniques were used for the sensor chip manufacturing.

The results show that the sensor chip was fully roll-to-roll manufactured using automated equipment, and the standard deviation of the plasmonic resonance dip depths for 20 samples was 2%, which is less than the set target of CV <5%.

As a conclusion, MedPhab's pilot line capabilities on high-volume sensor chip manufacturing for in-vitro molecular diagnostics applications was demonstrated successfully. Also, various kinds of dissemination material were prepared.

5. Degree of Progress

The progress of the task with respect to the DoA is on target. The core activity was to develop dissemination material based on the model-case "Disposable plasmonic-fluidic sensor". This deliverable is 100% fulfilled.

6. Dissemination Level

This deliverable is Public.