MedPhab

Photonic Medical Devices

MedPhab - pilot line for **photonic medical devices.**

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Funded by:

PHOTONICS[21]

PHOTONICS PUBLIC PRIVATE PARTNERSHIP

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Content

Introducing MedPhab

Improved diagnostics, a higher level of support for chronic diseases as well as personalisation of treatments are enlarging the demand for medical devices. Photonics technologies have become a key enabler in the realization of modern medical devices with applications ranging from diagnostics to surgical tools and therapeutics. However, the diversity of photonics technologies and applications alongside the complexity of the ecosystem have led to challenges in the development and production of medical devices. Furthermore, strict regulations within the sector make the introduction of new solutions a lengthy and costly process.

Addressing these challenges, MedPhab is Europe's first Pilot Line dedicated to manufacturing, testing, validation, and upscaling of new photonic technologies for medical diagnostics. MedPhab pilot production line will accelerate the commercialisation of measurement, monitoring, and diagnostic devices and treatment instruments based on photonics technologies. Seamless operation between ISO13485 certified companies and RTOs makes MedPhab a single-entry point that can serve companies working at different technology readiness levels (TRLs). Furthermore, MedPhab operates within medical domain setting requirements, which considerable accelerates the regulatory approval process.

Hospital Use

In a hospital environment, the solutions assist doctors with diagnosis and by giving them real-time information of how the treatment is progressing, without the need to send patient samples to a laboratory.

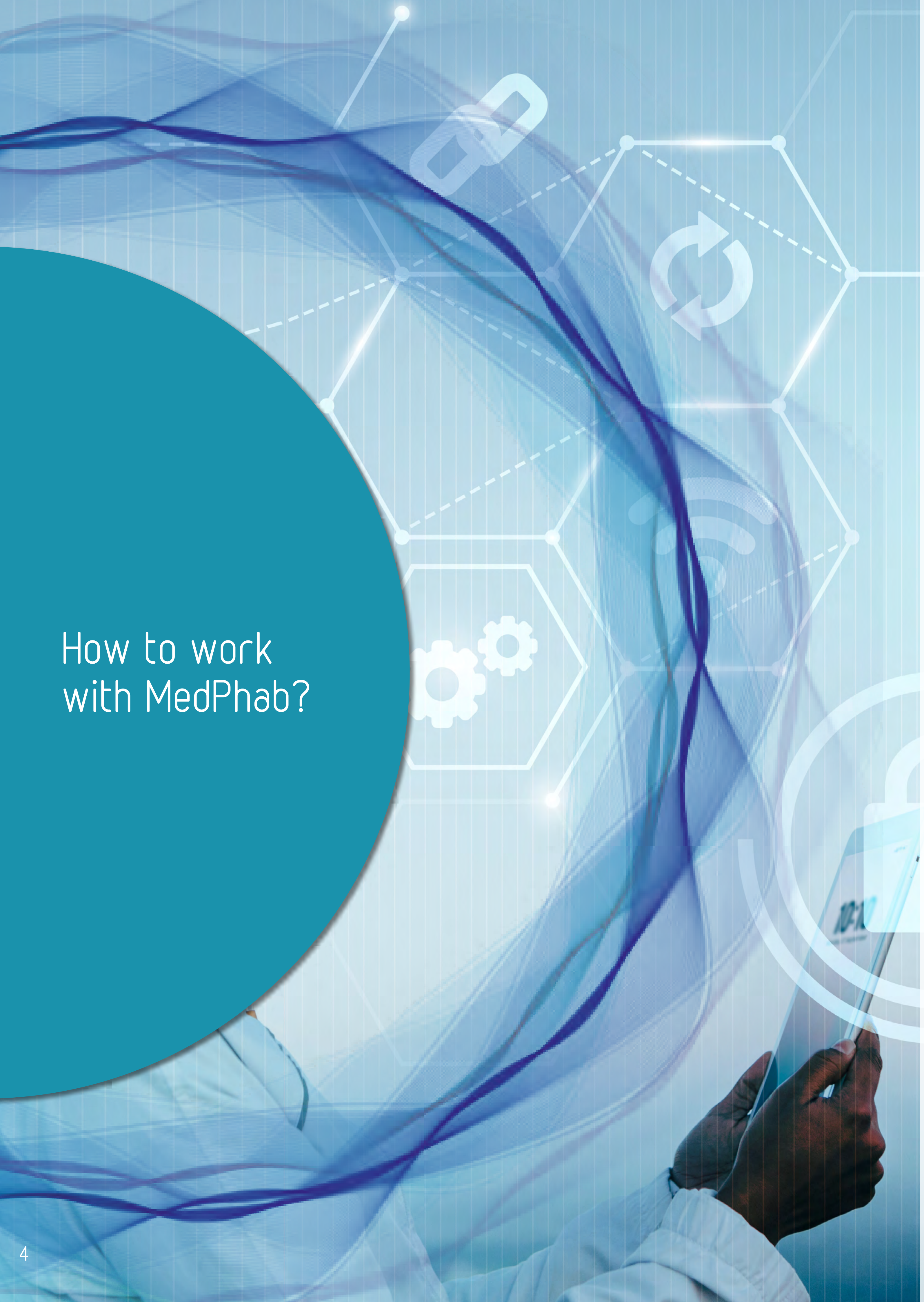
Home Care Services

Introducing MedPhab Home Care Services The equipment for home diagnostics can support non-invasive, continuous monitoring of patient's condition, supporting healthy living in a home environment. With remote diagnosis it is possible to increase value of care, provide telehealth services, early diagnosis of disease, and support recovery after treatment.

Equipment for Molecular Diagnostics

Molecular diagnostics supports establishing a clinical picture or diagnosing an infection based on a serum, saliva or urine sample.

How to work with MedPhab?



Apply for the Demo Cases Open Call. Please check www.medphab.eu for further information

Partners of MedPhab

VTT. Provides companies an easy access to new business development and pilot manufacturing resources with a key focus area in diagnostics.

Tyndall. Support the work of the relevant industrial end-use partners in the in-vivo diagnostic use-case and facilitate the transfer from pre-commercial fabrication to commercial production and ensure the post-project sustainability plan.

Joanneum Research. Leads the in-vitro diagnostics technology, providing development and manufacturing of microfluidic structures; manufacturing R2R UV NIL imprinting of structures on flexible foil substrates.

Imec. Implementation of manufacturing capability for IVD devices and for chip-level widely tuneable lasers for spectroscopic sensing in wearables, surgery tools, electronic pills and implants.

CSEM. Design and prototyping of Micro- and Nano optics, flexible hybrid circuits, microfluidic chips, biosurface functionalization; sensor integration and packaging.

Philips Innovation Services. Central integrator, providing access to an extensive infrastructure for microelectronics and photonics assembly technologies and providing manufacturing capabilities in an ISO13485 certified setting.

Jabil. With deep engineering, manufacturing and supply chain expertise, Jabil offer system integration and technology transfer to establish mature production solutions by providing the full suite of process and equipment development, installation and validation within a ISO 13485 certified environment.

Screentec Oy. Develop advanced, high-integration level manufacturing and packaging methods for photonic personalized health monitoring modules by creating disruptive process combinations.

III-V Lab. The epitaxy of III-V multilayers and quantum wells on InP wafers by MOVPE/GSMBE growth and the fabrication of transfer-print ready semiconductor optical amplifier gain-chips for the development of heterogeneously integrated III-V/Si widely tuneable lasers. III-V/Si photonic design.

Stryker. Is validating the pilot line services and development of a biophotonics tissue recognition (TR) medical device and technology platform for surgical guidance in-vivo.

Polar. Design, manufacturing and validation of non-invasive sensors for measuring biomedical signals using optical and galvanic measurement methods.

Radisens. Will develop cost-effective integrated photonics modules for a point-of-care blood monitoring platform.

Antelope. Uptake of the pilot line by industry engaged in in-vitro diagnostics.

GENSPEED Biotech. Design/simulation/verification of integrated micro-optical detection schemes and disposable microfluidics test-chip for fluorescence-based detection.

ViennaLab Diagnostics GmbH. (VL) contribute competence in developing and producing in-vitro diagnostic tests that comply with ISO standards as well as European (CE) and global IVD regulations.

The Netherlands Cancer Institute. (NKI), offers clinical feedback on user cases, defining clinical needs and requirements, testing possible prototypes when applicable and feasible.

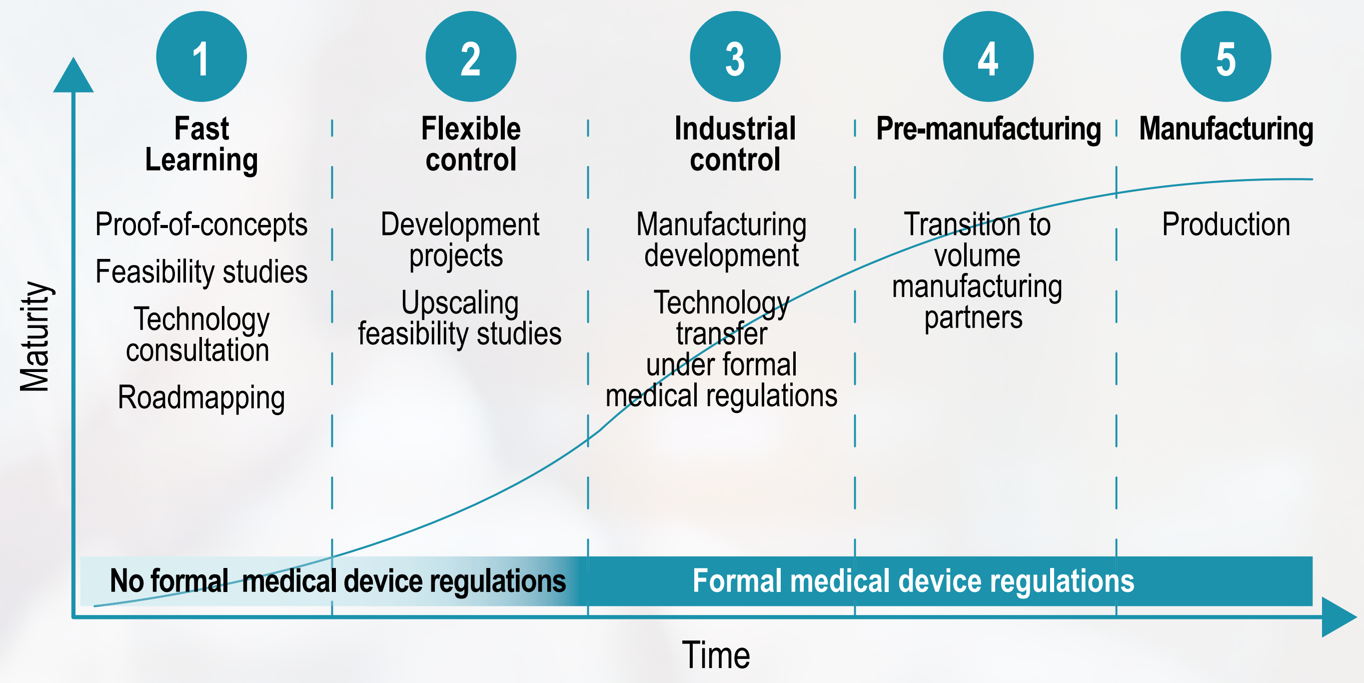
European Photonics Industry Consortium. (EPIC) is contributing to dissemination activities and the business development by promoting activities, planning, creating and hosting events and sharing market insights.

AMIRES. Is a consulting and management company for research, development and innovation projects, facilitating the access of European research to high-tech SMEs and improve exploitation of innovative ideas.

Development phases

Costs and duration of the projects will vary according to the stage of development and maturity of the technology, the requirements and expectation for the content and regulatory aspects. In MedPhab, a 1-5 maturity chart is designed to articulate the pilot line's position in a typical medical device development process flow. The MedPhab 1-5 maturity chart is an indication of a typical product development process flow as well as regulatory and cost aspects that need to be considered when maturing technology in the medical domain.

Plan jointly the route towards the product launch!



MedPhab is strongly positioned in the stages of product development which focus on advancing manufacturing and integration level. Basic research as well as high-volume manufacturing is not in the scope of MedPhab. In each maturity level varying regulatory guidelines will be applied.

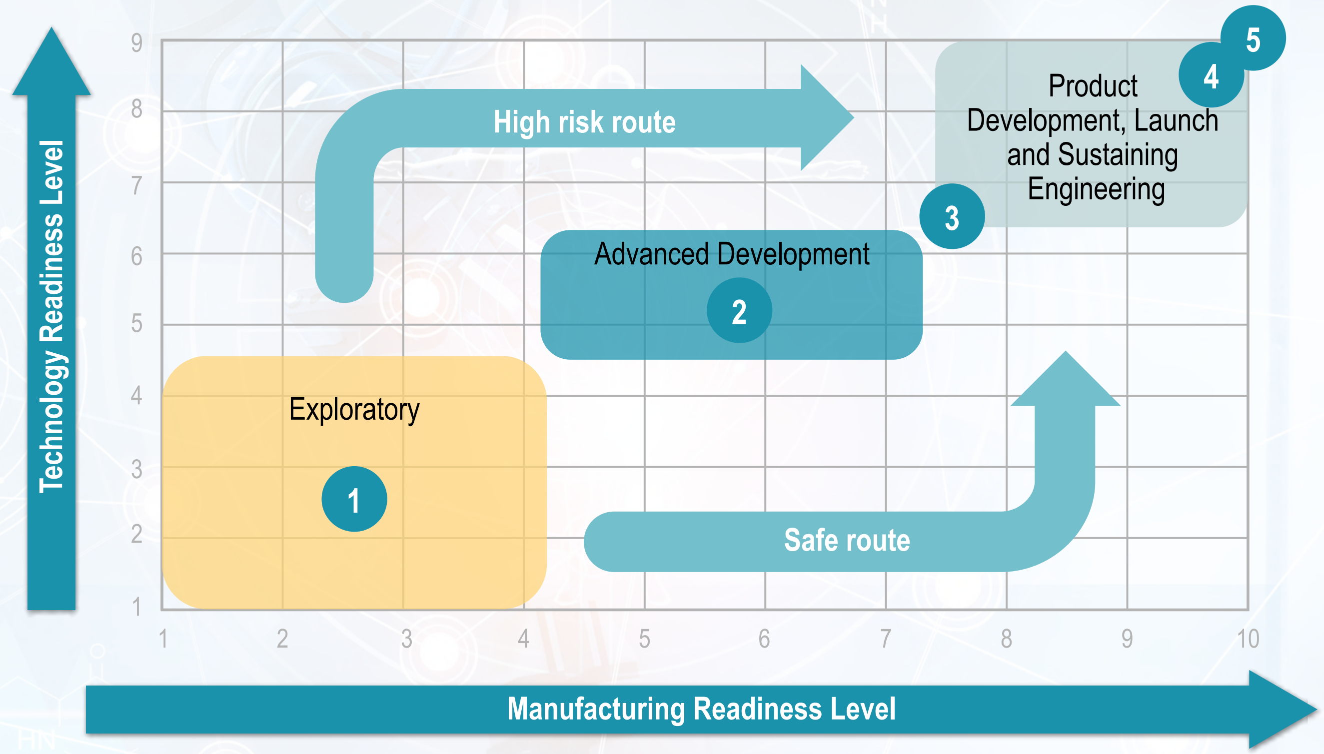
Maturity levels (TRL and MRL)

Technology Readiness Level (TRL) – is a measurement method for estimating the maturity of technologies. TRLs are based on a scale from 1 to 9 where TRL1 corresponds to “Basic principles observed” and TRL9 to “Actual system proven in operational environment”. MedPhab will bridge the gap between R&D (TRL4-5) and pre-commercial production. Additionally, MedPhab is taking care to carefully map the integration capabilities, thus also addressing the manufacturing readiness level.

Manufacturing Readiness Level (MRL) - is an indication of the maturity of a product or technology to be produced. The MRL scales from Basic manufacturing identified as (MRL 1) to Full rate production demonstrated with lean production practices in place (MRL 10).

With help of these definitions for TRL and MRL, at MedPhab we are able to describe the relation and interdependency of technology and manufacturing maturity as outlined in the chart below. The numbering from 1 to 5 in the chart refers to the maturity levels of projects enabled through MedPhab and helps to identify a project’s position in the development lifecycle.

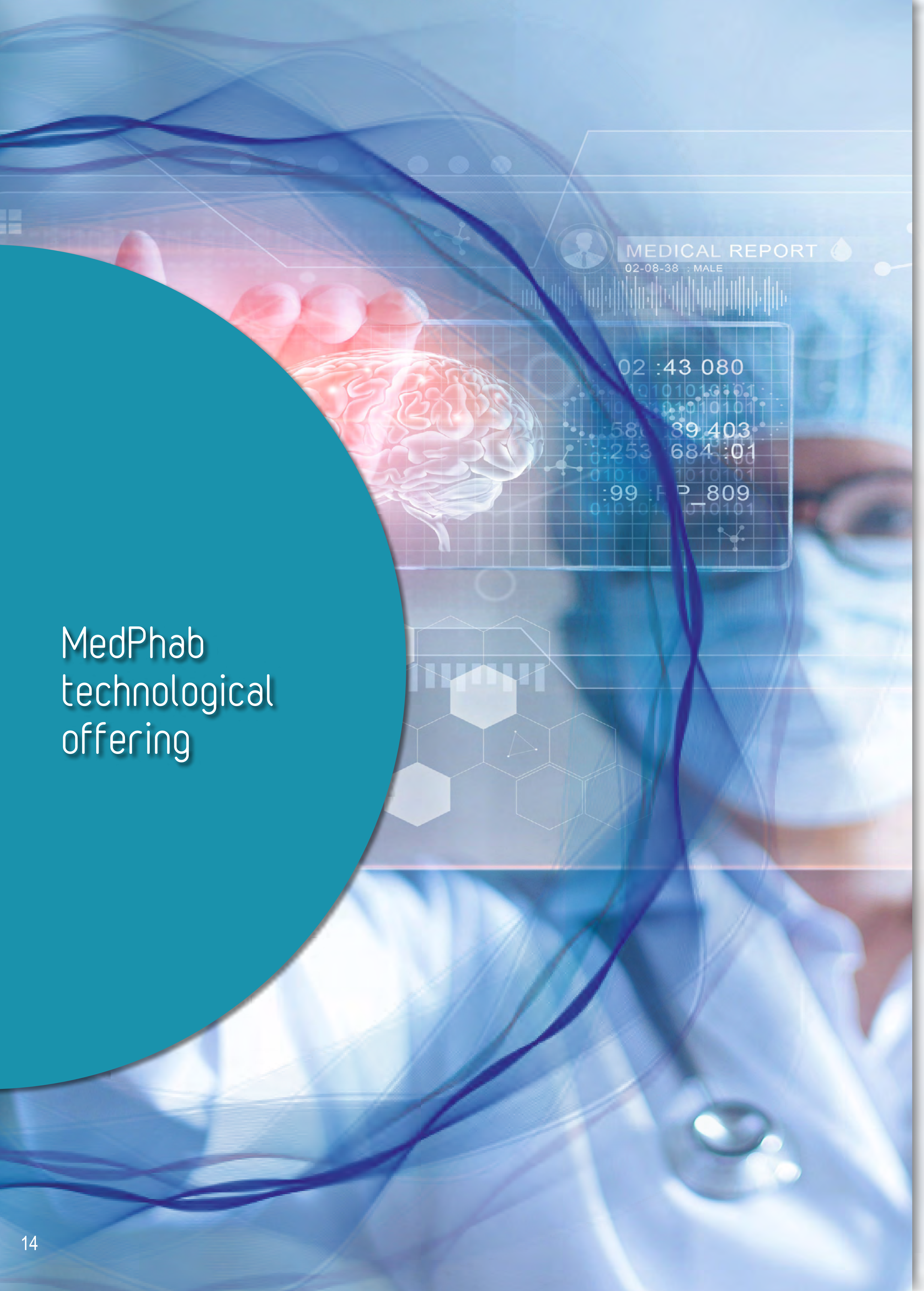
Innovation Maturity - Product vs. Process



ISO 13485

When putting in place a medical device, design, development project, or manufacturing line, three elements need to come together. ISO13485 is a standard that represents the requirements for a Quality Management System (QMS) for the design and manufacture of medical devices. SMEs lacking a sufficient QMS system need to outsource the manufacturing or invest in a QMS and manufacturing infrastructure. MedPhab puts in place and offers systems, procedures and protocols suitable for SME's to guide them through this very difficult part of their device development.

MedPhab operates in medical domain setting requirements to meet regulations and offers seamless operation between ISO13485 certified companies and RTOs. Production of a small to medium quantity of devices is done by MedPhab ISO13485 certified companies and RTOs, ensuring seamless transition from pilot line production to up-scaled production without the need for re-design.



MedPhab technological offering

MedPhab pilot line develops a technology map allowing a systematic matching between technology needs (customer) and the pilot line offering (modularized competences of MedPhab partners). Typical combinations of (sub-) technologies are combined in production kits to allow accelerated and more efficient development in previously tested and proven process flows between MedPhab partners.

Photonic components

Integrated circuits
- Silicon photonics
- InP
- Polymer photonics

Micro-optics
- Polymer
- Glass

Fiber optics
- Standard
- Customized
- Facet handling

Optical components
- Standard

Active components
- Standard sources
- Detectors
- Organic electronic

Non- Photonic peripherals

Electronics
- Printed circuit boards
- Ics
- Roll-to-roll printed electronics
- Flex-to-Rigid/F2R

Opto-mechanics
- Injection moulding
- Metal tooling
- 2D and 3D printing

Microfluidics
- Injection moulding
- Thermoplastics
- UV-curable
- LSR high volume
- Adhesives

MEMS
- Si-processing
- Sin-processing

Integration

Fiber/waveguide coupling
- Active component/ waveguide aligment
- Grating couplers

Opto assembly
- Free-space lens aligment
- Mirror/grating assebly
- Coupler lenses, prisms

Component assembly
- Rigid board
- Flexible foil
- Stretchable foil
- Module assembly

Surface acivation
- Array spotting
- Bio-reagent dispense
- Surface modification

Post-processing

Over moulding
- Rigid
- Flexible
- Stretchable

Hermetic sealing
- Photonic module encapsulation

Opto-fluidic interface
- Microfluidric interfacing
- In-vitro cartridge assembly
- Consumer packaging

Thin film deposition
- Roll-to-roll vacuum
- Sheet/wafer vacuum
- Roll-to-roll liquid phase
- Sheet/wafer liquid phase

Diagnostic devices consist of numerous photonic and non-photonic components that need to be integrated for the required overall functionality. For example, a typical spectroscopic unit requires combination of fiber optics, electronics and their hermetic sealing for an integrated system. In in-vitro diagnostics, low-cost fabrication of disposable microfluidic cartridges is key to commercially successful products.

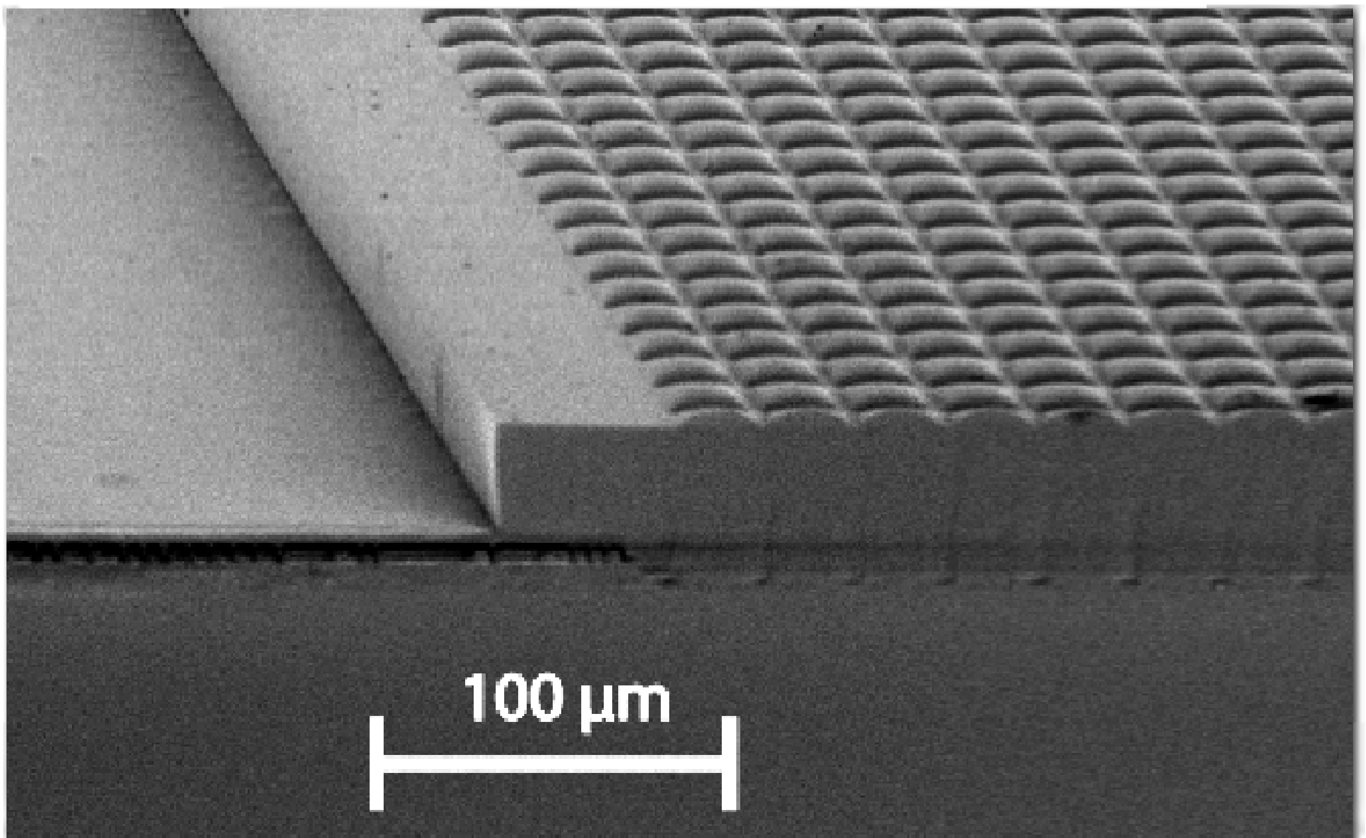
MedPhab uses an approach to simplify the development of these diverse systems by using modular technology blocks covering 1) Photonic components, 2) Non-photonic peripherals, 3) Integration and 4) Post-processing steps. This modular concept enables a structured approach to highly fragmented heterogeneous technologies. For fabrication cases, the fabrication chain is designed by choosing the relevant blocks. Depending on the customer's needs, either customized or standardized fabrication processes with ISO13485 certificate can be applied.

Photonic Components

MedPhab offers a wide portfolio of photonics technologies: fiber optics, micro-optics, integrated circuits and active components.

Photonic integrated circuit technologies within MedPhab offering include silicon photonics as well as III-V materials with wafers of different sizes and thickness. Variation of processing techniques allows fast prototyping and verifying design, wafer level manufacturing, advanced packaging options and hybrid integration of III-V materials on silicon.

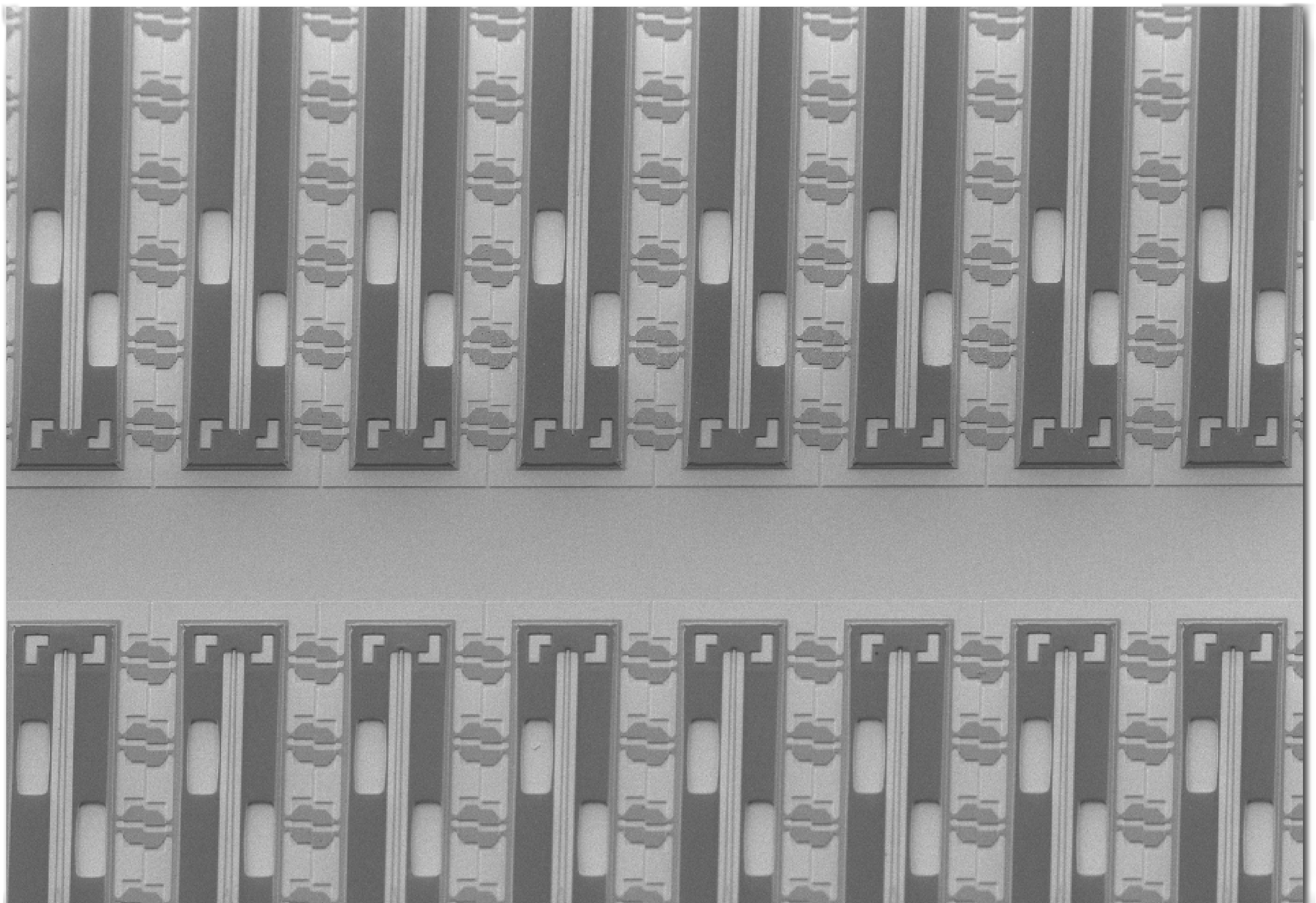
Micro-optics manufacturing technologies are heavily explored in MedPhab. Master tooling and upscaling using UV and R2R nano imprint lithography replication processes enable the manufacture of micro/nanostructures on polymer, glass and silicon-based material. Also available are commercial applications such as: replicated micro-lenses with micrometric inter-lens gap on bare die or on wafer chunk with gap-independent specification, as well as the transfer of grating/lens master structures into glass or silicon.



Replicated microlenses with micrometric inter-lens gap on bare Silicon die — Courtesy of CSEM

Fibre optic sensing probes can be used for clinical applications, such as tissue identification for diagnostics and surgical guidance. The optical fibres can be integrated into a standalone probe or integrated into surgical tools. The probes design can include a single optical fibre or multiple optical fibres in an optimum probe geometry for a given application. MedPhab offers design and build of fiber optic including fiber splicing, tapering, cleaving, polishing, laser processing and connectorizing.

All-printed electrocorticography arrays (MEA) can be fabricated by inkjet printing of ultra-pure platinum or gold ink formulations (bio-compatible) electrodes and screen printing of polyimide as a passivation layer.

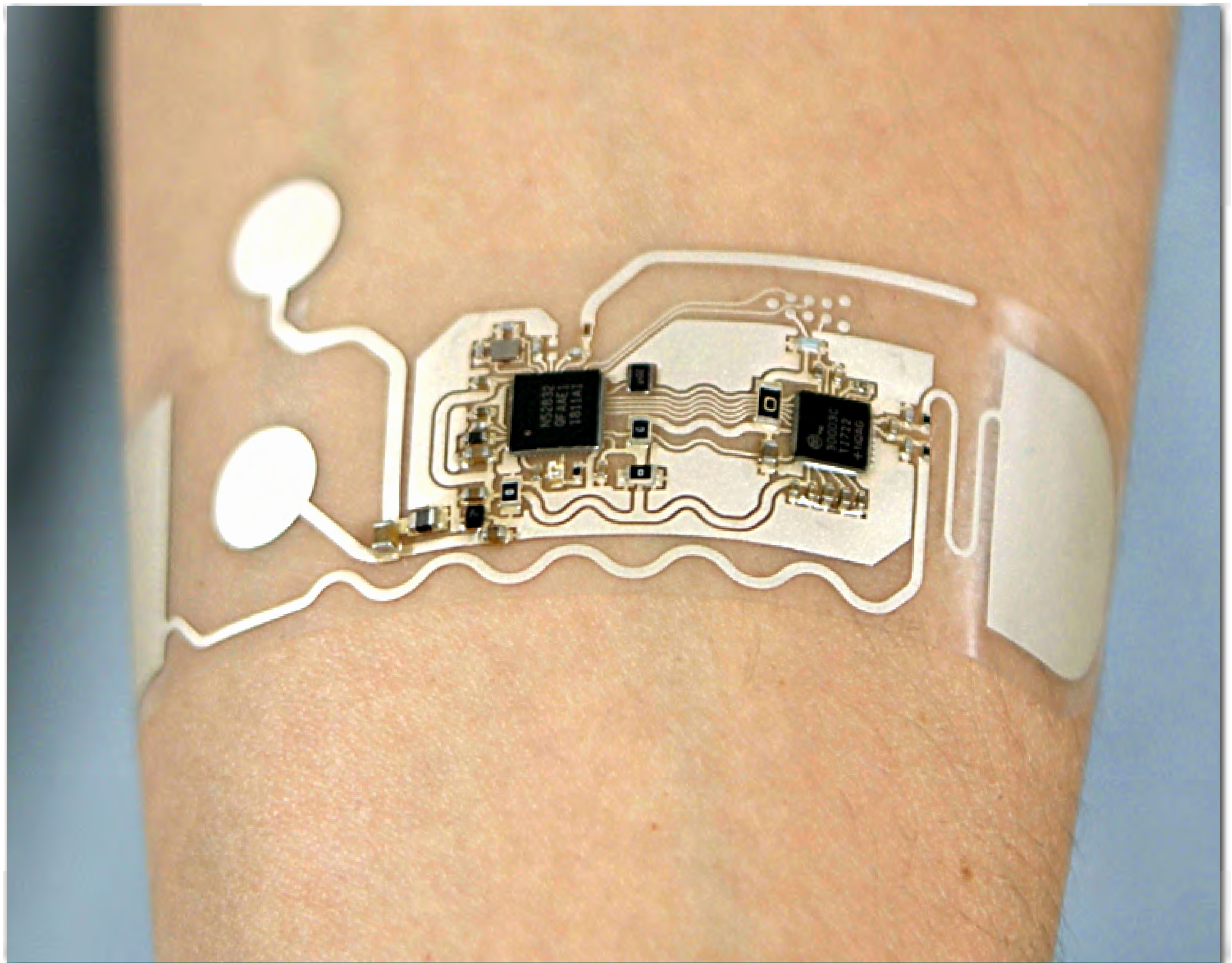


SEM image of a field of transfer-print-ready semiconductor optical amplifiers fabricated on an InP platform — Courtesy of III-V Lab

Non-photonics Peripherals

Roll-to-roll printing and digital printing of ultrapure gold allows production of multilayer circuitries and multilayer medical electrodes and other printed electronics components/parts. Flex-to-Rigid platform enables the integration of highly miniaturized electronics functionalities.

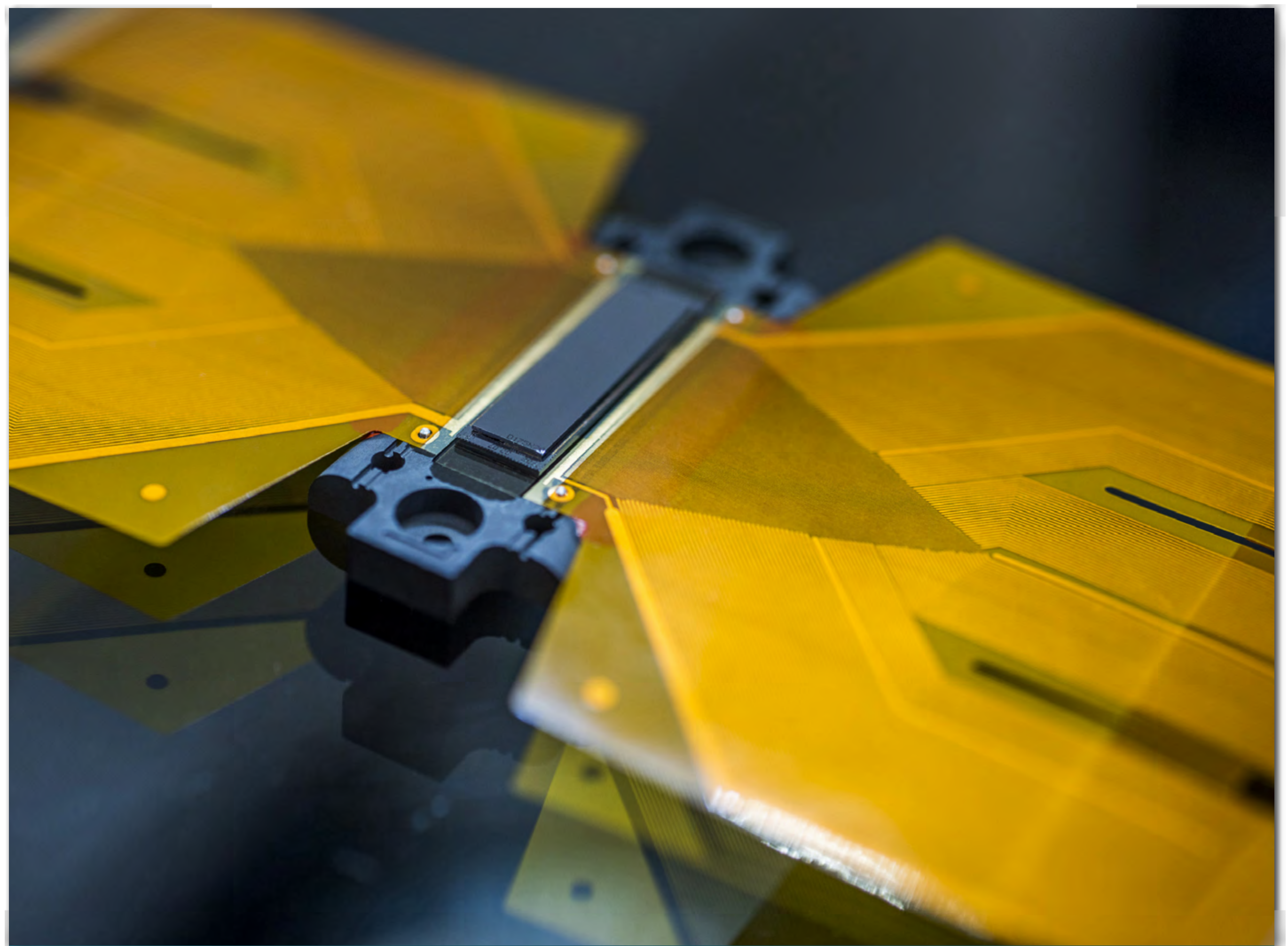
Opto-mechanical components production techniques include FDM and SLA 2D and 3D printing, 3D printing in steel as well as flex-to-rigid printing enabling processes from rapid prototyping of low resolution parts to production of high resolution and complex parts with integrated structures.



Printed and hybrid integrated electronics on a digital patch for patient monitoring Courtesy of VTT

Microfluidics manufacturing services include production of microfluidic structures based on polymer or liquid silicon rubber materials, thermoplastics and others. Production techniques include micro-milling, adhesive bonding, laser welding, injection molding, R2R UV Nano Imprint Lithography. Laser lamination and adhesive die bonding with various materials are also offered.

For MEMS development and production, MedPhab exploit 2D and 3D printing, Chemical Mechanical Planarization (CMP), Dry etching and Lithography, furnace processing (oxidation, annealing, curing, etc.). Additionally, plasma enhanced chemical vapor deposition (PECVD) and Sputtering are available for thin films and extreme fine thin layer deposition.

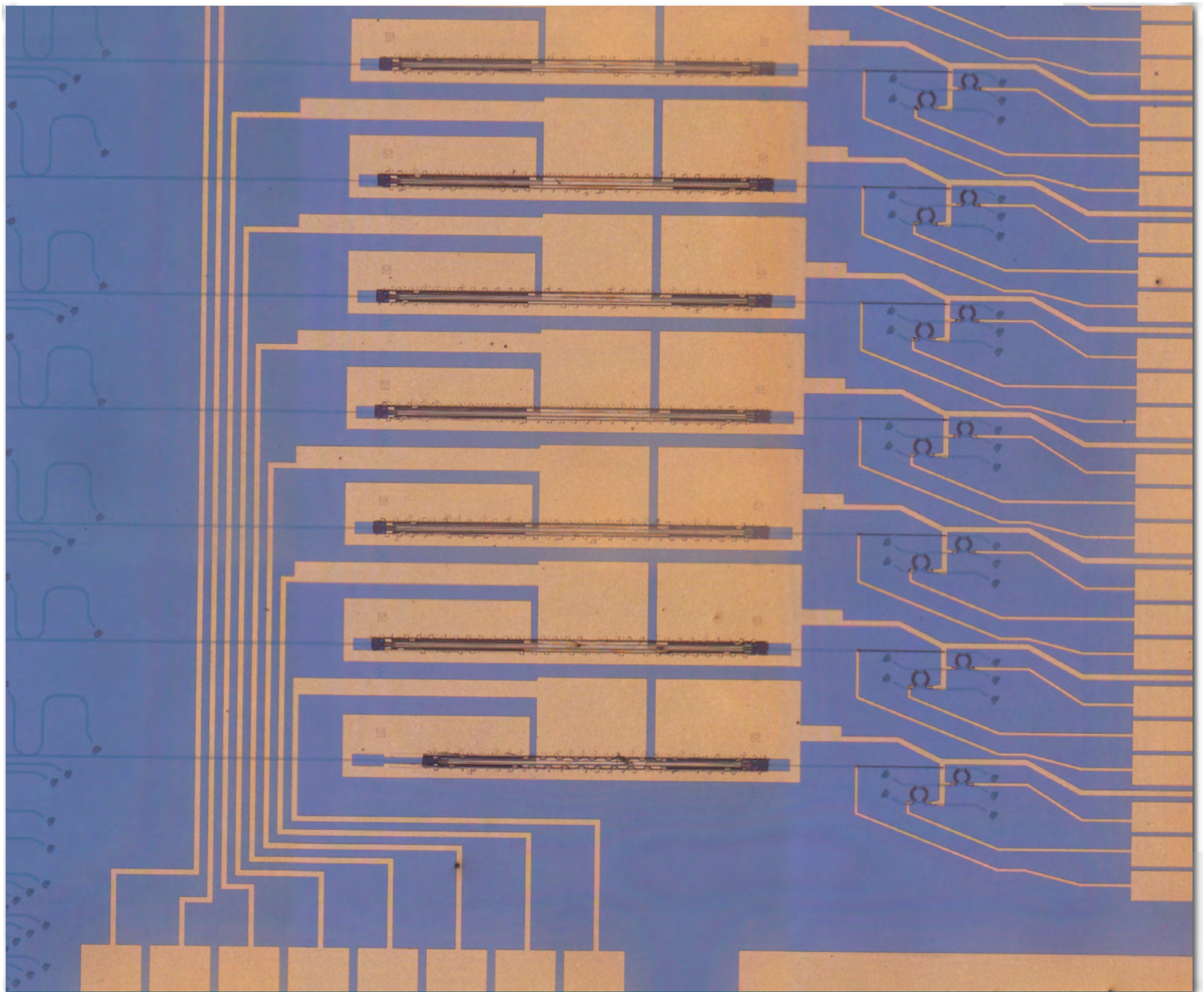


MEMS-based microfluidic device Courtesy of Philips

Integration

Fiber-waveguide coupling, optical and other component assembly alongside surface activation comprise MedPhab's multiple integration capabilities.

MedPhab offers coupler lenses, prisms and Grating couplers. By means of active alignment, optical components such as fibers, lenses, beamsplitters, etc can be aligned in 6 degrees of freedom, down to sub-micrometer precision. Pick and place technology offers a superb placement accuracy while fulfilling other requirements.



Transfer printed active components on photonic integrated circuit — Courtesy of IMEC

Various component assembly techniques are available depending on the application. Glue Dispensing, STM or R2R line assembly and pick and place technology enable assembly on Flexible and Stretchable foil or rigid boards. Other techniques include wire bonding between an integrated circuit (IC) and its packaging; anisotropic conductive film (ACF) for the electrical and mechanical connections; thermocompression bonding and soldering with a metal filler.

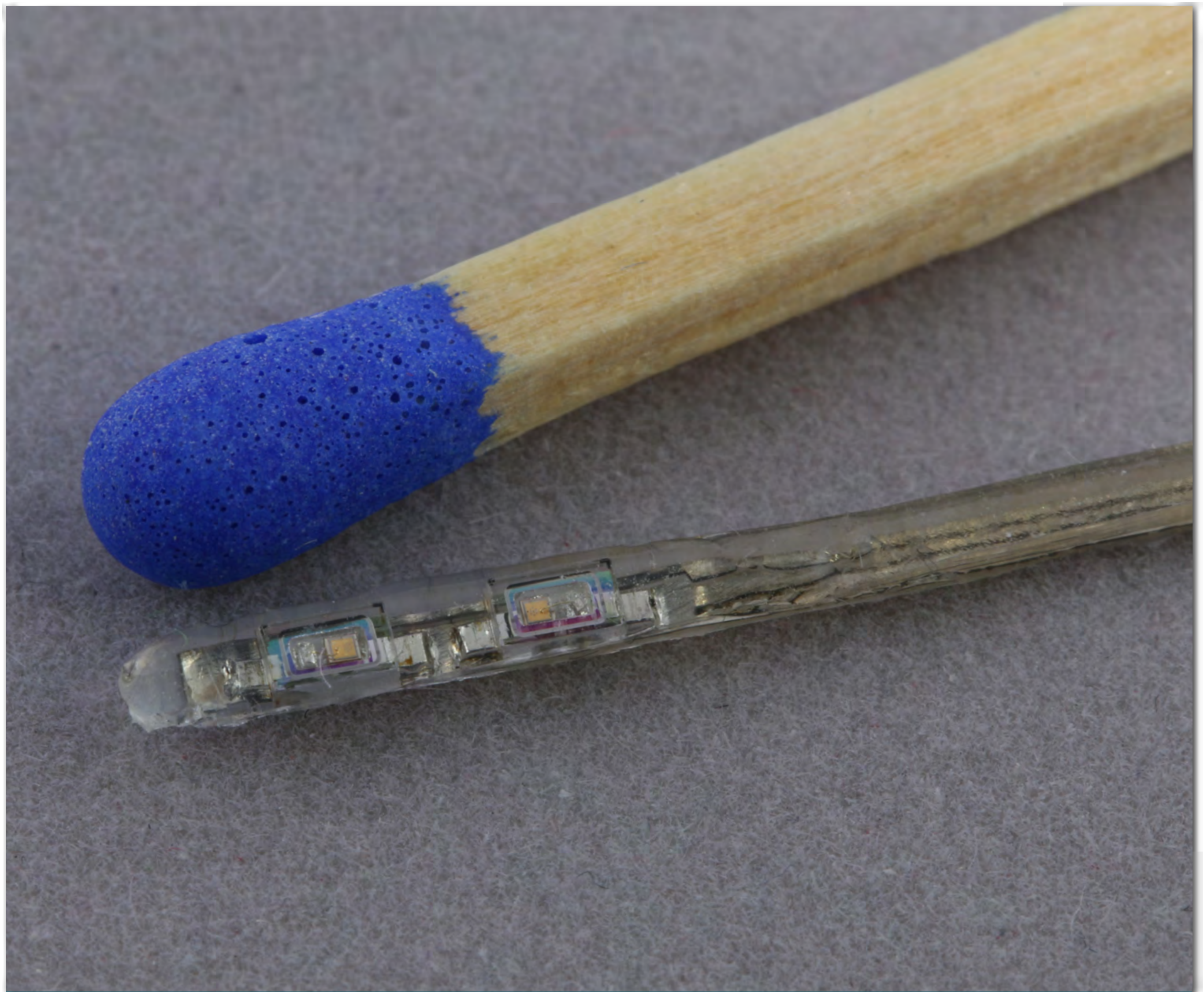
Surface activation technologies include bio-reagent dispense, array spotting at the micro-, nano- or pico-liter scale, vapour phase deposition of surface chemistry as well as surface activation of foil substrates or thin-film deposition.

Industrial SMT assembly line — Courtesy of Philips

Post-processing

Postprocessing MedPhab capabilities include overmolding, hermetic sealing, opto-fluidic interface and thin film deposition.

Rigid or stretchable overmolding can be done, using processes such as adhesive roll lamination, injection overmoulding or with LSR (liquid silicon rubber). Cold and heat lamination capability of flexible foils in sheet and R2R processes are also available.

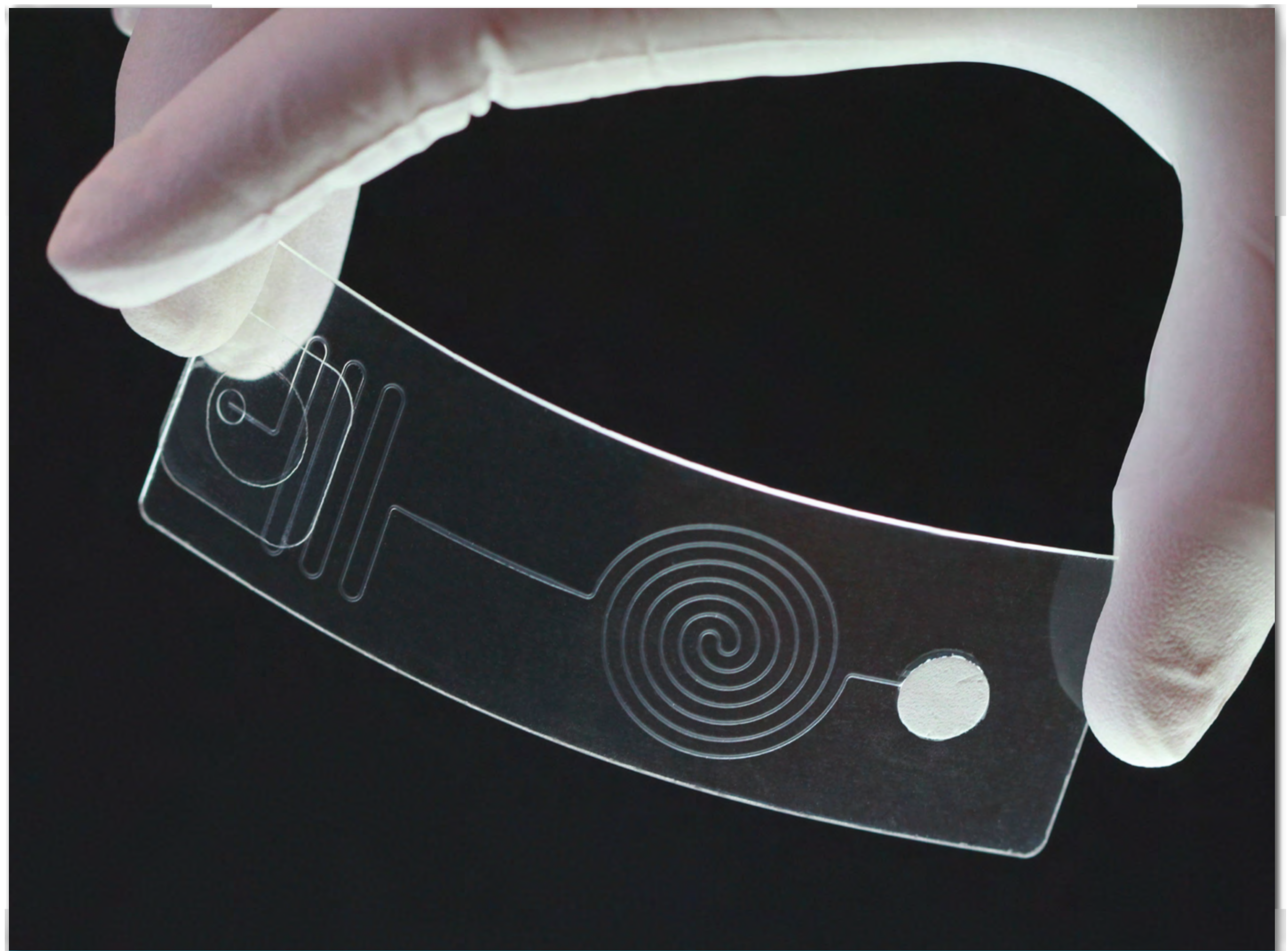


Hermetically sealed VCSEL package for a cochlear implant to stimulate hearing — Courtesy of CSEM

Highly-reliable hermetic, ceramic micro-packages can be performed with bio-compatible / bio-stable materials. Butterfly packaging or golden can be used, also allowing very low CTO and high thermal conductivities. Alternatively, soldering or other custom packaging solutions can be developed.

MedPhab offers design, automation and production of electronics on stretchable / conformal substrates using printed electronics processes.

Roll-to-roll (R2R) liquid phase deposition allows production of nano-scale thin films, micro-optical or functional nanostructures as well as microfluidic chips.



Assembled in-vitro cartridge for inflammation detection — Courtesy of VTT

MedPhab offers a service to help companies developing Photonics-based medical devices move forward to the Pilot Production Phase. MedPhab connects these users with investors interested in photonics and provides coaching material, which increases the chance of raising capital.

Investment offering

Model cases

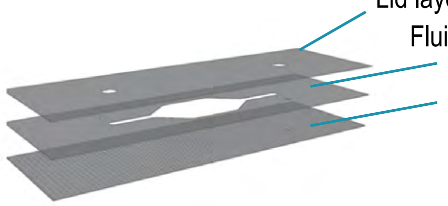
Disposable plasmonic-fluidic sensors for molecular diagnostics

Diagnostic devices consist of numerous photonic and non-photonic components that need to be combined for the required functionality. Modular blocks with preliminary division enable 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.

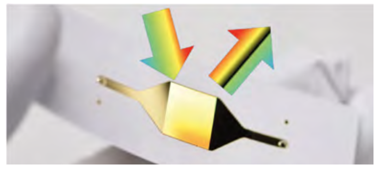
Plasmonic in-vitro sensors can be used to measure binding of biomolecules to the plasmonic surface that is formed by a metallized nanostructure. When plasmonic surface is illuminated, a surface plasmon is excited by a suitable wavelength, and this can be seen as a sharp intensity dip in the reflectance 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.

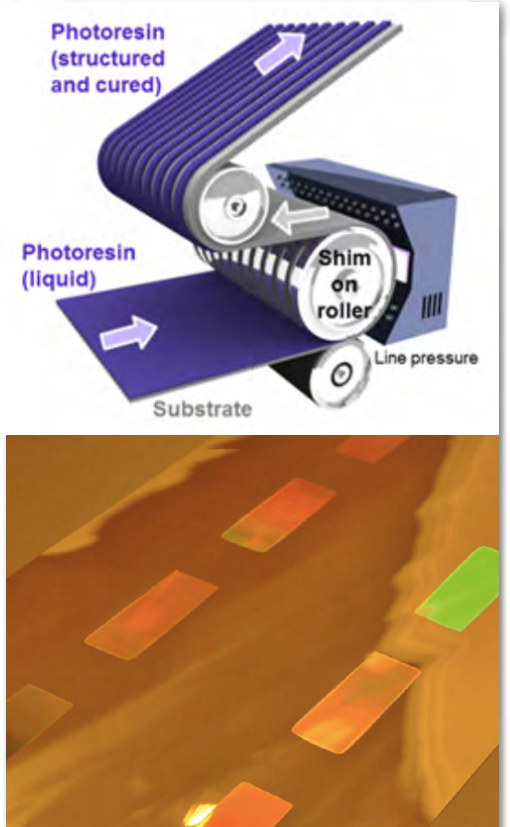
Sensor chips with plasmonic surface and integrated microfluidics — Courtesy of VTT

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.



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

Roll of laser patterned microfluidics
Courtesy of VTT

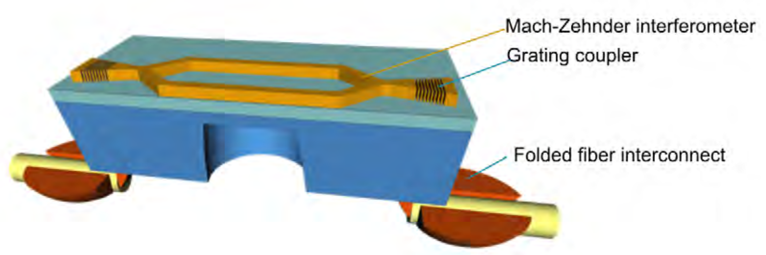
Model cases

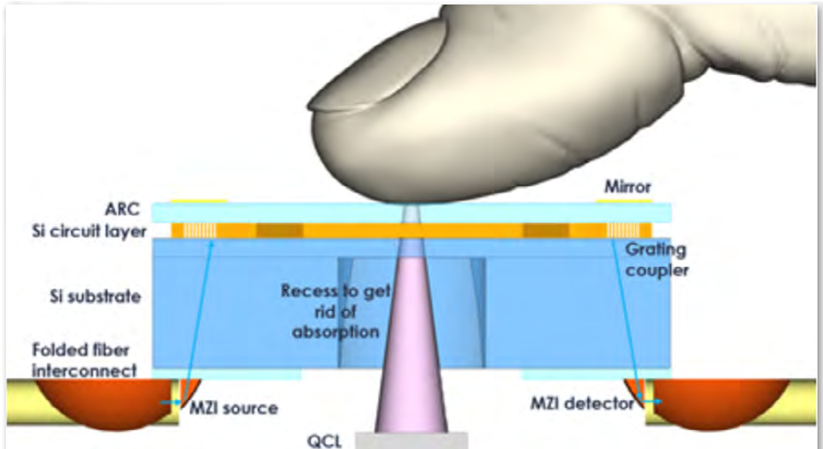
Wearable temperature sensor for blood components measurement

The vision of the model case is to miniaturize a non-invasive measurement method to analyze patient's blood components with a wearable device. The blood components measurement technology works with an invisible infrared light beam that interacts with your skin and counts specific molecules, by analyzing of the absorption spectra (heat induced refractive index change). We demonstrate an integrated device using a photonic integrated chip (PIC) assembled with optical fibers. The targeted device features an innovative Mach-Zehnder Interferometer (MZI) designed to be highly sensitive to temperature, incorporating low loss silicon waveguides, grating couplers for optical input and output, backside processing and ultraviolet (UV)-replication technology for compact folded fiber interconnects.

As a result, prototypes of very compact MZI-PIC's (1x3 mm2) were realized. Capability to detect temperature for wearable applications was studied. A size reduction of 99% and an increase of mechanical stability was obtained compared to non-integrated implementation.

Integrated MZI-PIC assembled with optical fibers



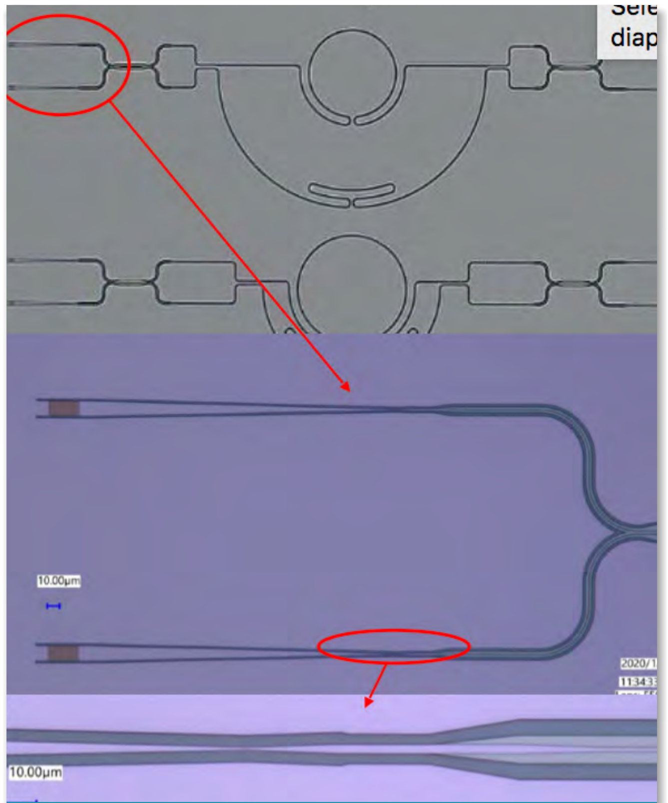


Mach-Zehnder interferometer based wearable temperature sensor for blood composition measurement Courtesy of CSEM

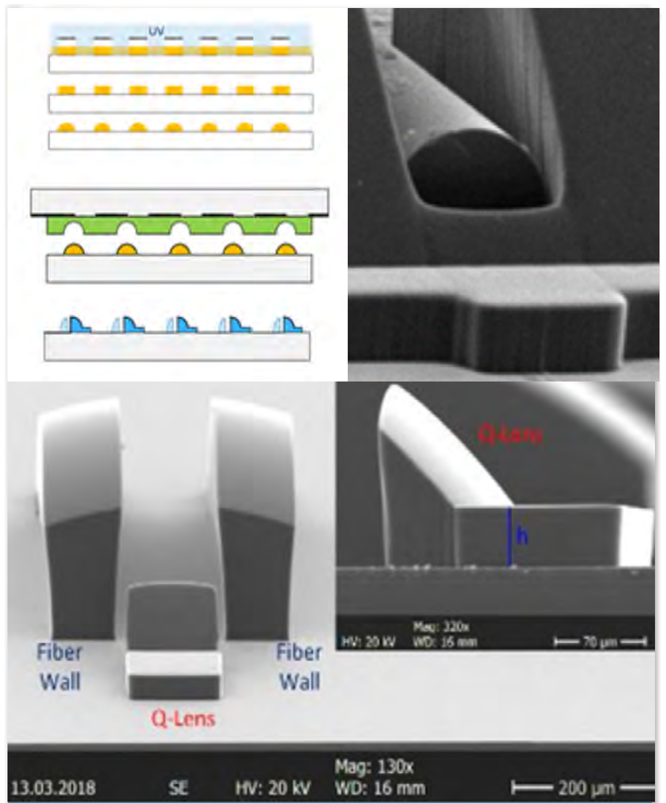
Key manufacturing technologies were selected, developed, and further advanced. Electron beam (e-beam) lithography enabled fast prototyping on silicon-on-insulator (SOI) structures. UV replication was used to realize polymeric folded micro-optical interconnects for self-aligned fiber assembly at wafer-scale.

Fiber-to-fiber losses were determined and were found to be around 12…18 dB. Electro-optical measurements were used to prove the prototype feasibility for wearable applications.

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



Microscope image of the waveguides fabricated using e-beam lithography Courtesy of IMEC



UV replication process to manufacture folded micro-optical interconnects Courtesy of CSEM

Use cases

Use Case for Hospitals

Biopsy needle with integrated sensor for tissue recognition

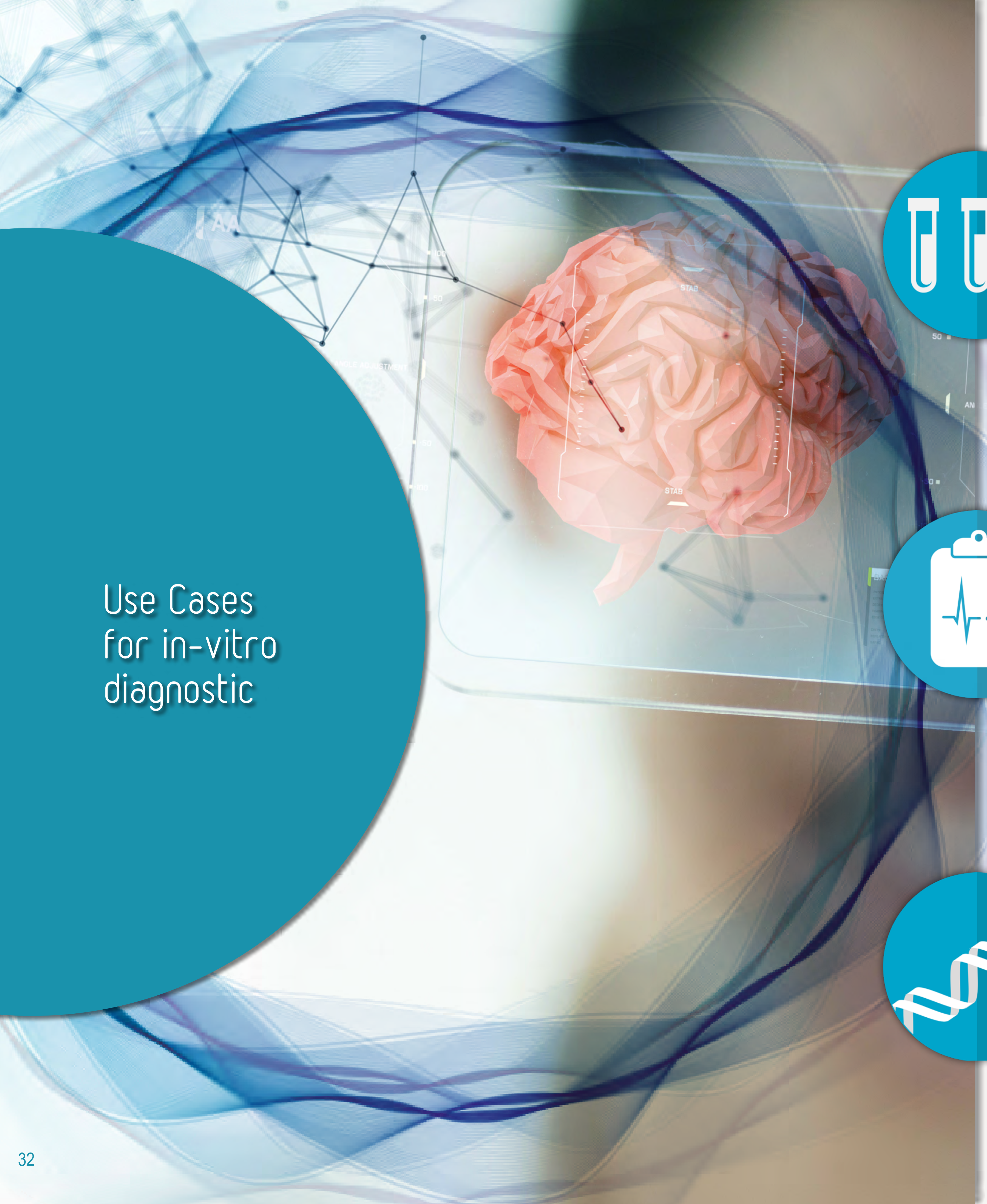
Optical techniques such as absorption spectroscopy can be used to recognise different tissue states. This recognition capability has the potential to compliment other medical imaging/detection modalities and deliver enhanced guidance during minimally invasive surgical procedures. Photonic miniaturisation, packaging and manufacture is key to enabling the translation of these technologies to the hospital. Stryker, Tyndall National Institute, Philips and NKI have come together to work on integrating photonics-based sensors with surgical instruments. The group will focus on biopsy of metastatic tumour in the liver and will demonstrate how application of these techniques could improve biopsy procedures and benefit both patient and clinician.

Use Case for Personalized Diagnostics

Wearable device with integrated photonic components

Medical wearable devices allow continuous, real-time information about physiological parameters via non-invasive measurements. Visible light LED and IR-laser systems can be used to monitor physiological parameters and changes related to cardiovascular symptoms and chemical composition of tissues, also enabling cardiovascular, respiratory and many other diseases to be addressed.

Mechanical (substrate materials, connection flex to cable, flex to flex etc.), electronical (circuit design, thermal behaviours, conductive traces, adhesion etc.), and optical (integrated LEDs, tuneable laser sources, photodiodes, micro-optics and lens window etc.) components will be integrated into an opto-mechanical sensor module. The photonic LED/laser modules and their hybrid integration on a carrier platform will be further assembled on a flexible wearable band.



Use Cases for in-vitro diagnostic

Point of care IVD reader

A miniaturized point-of-care reader will be created by the joint effort of Radisens Diagnostics, CSEM, VTT and Jabil. This optical-based reader will contain LED illumination sources (400-800nm), detectors, an infra-red thermometer, micro-optical elements, an incubation system, driver and control electronics, a servo-motor and a user-friendly cartridge handling system. These reader front-end modules will be integrated with the system electronics and a touchscreen user interface. The point-of-care IVD reader, combined with a microfluidics cartridge consumable, will be used to initially measure ferritin (iron stores) in a relevant environment and in future, other immunoturbidimetric or clinical chemistry tests.

Photonics based IVD consumable

Die-level biofunctionalization processes represent one of the challenges for scaling photonics-based IVD solutions. This issue will be addressed through development of a wafer-level process. Within this project, a wafer level scale process will be developed and tested using a blood based inflammation marker detector.

Genetic Analysis

IVDR compliant in vitro diagnostic system comprised of a multicolour fluorescence reader and disposable low-cost cartridge will be developed for the detection of genetic disorders, e.g. lactose intolerance. The development will include an IVD module for a multi-colour fluorescence readout and foil-based IVD chips with polarization filters, light guiding structures and biofunctionalization.

MedPhab

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