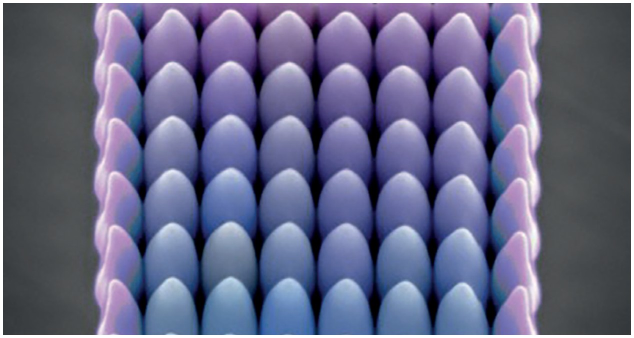
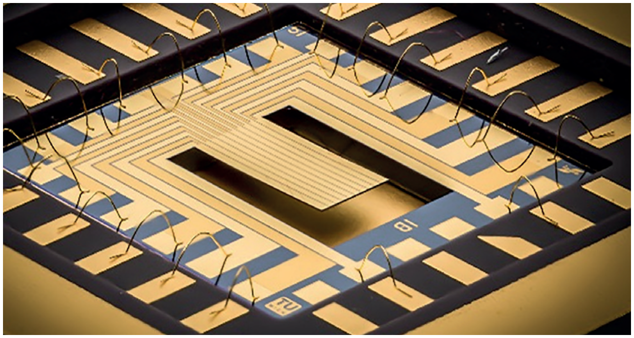
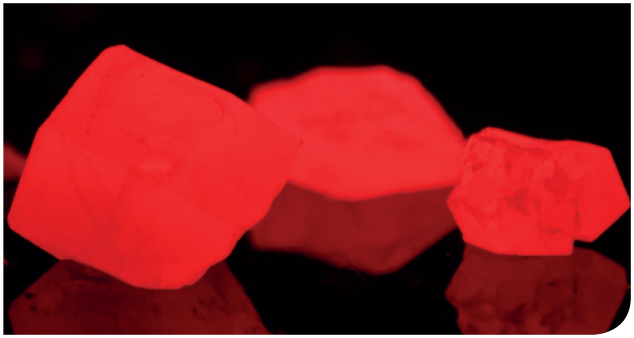
BIONANONET
MEMBERS' EXPERTISE

SENSOR TECHNOLOGIES & APPLICATIONS







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SENSOR TECHNOLOGY

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Content

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A

APPLICATIONS

PROCESS MONITORING

Chemical Imaging for High Throughput Processes

Spectroscopy allows to access chemical information on the molecular level, for example to determine chemical bonds, entities and complexes, but also secondary structures (e.g., in proteins). In addition, it is often vital to have spatial information to understand the constitution of a sample. Chemical Imaging provides both pieces of information at the same time and allows the researcher to locate and identify substances, as well as determine physical structures.

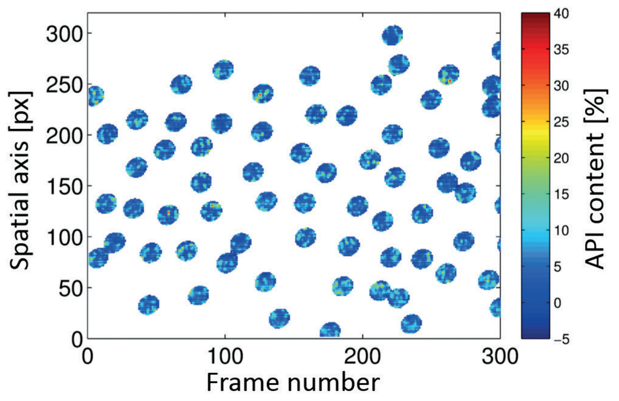
Depending on the acquisition technique, the focus can either be placed on highly resolved frequencies (whereas the most common applications function in the optical and near infrared range), highly resolved lateral spaces (down to a tenth of a millimetre), or speeds (by capturing images with several Hz). The resulting amounts of data are often quite large, and statistical (chemometric) methods are used to analyse the data.

Hence, method applications can include the detection and quantification of small amounts of substances or the high throughput screening of materials. Chemical imaging is already commonly used and applied for sorting and quality control of agricultural products and classification of waste materials. Applications in the pharmaceutical industry include accurate quantification of active pharmaceutical ingredients in complex matrices (e.g., printed on paper) and 100% quality control of tablets (see figure).

A plethora of information that is accessible by chemical imaging can be gained and visualized, such as the concentrations of chemical substances, hetero- or homogeneity of granular or combined materials, and surface texture and roughness of surfaces.

Technological Readiness Level:
5 (set-up in plant environment)

Reference publication: Scheibelhofer O, Koller DM, Kerschhaggl P, Khinast JG. Continuous powder flow monitoring via near-infrared hyperspectral imaging. IEEE International Instrumentation and Measurement Technology Conference (I2MTC) Proceedings. Graz; 2012. p. 748–53.



Automated monitoring of single tablets via chemical imaging provides real-time information about the distribution of the active pharmaceutical ingredient (API) during production.

CiP and Sterilisation-Resistant Optochemical Oxygen Sensors for Process Monitoring

Superior stability of optochemical oxygen sensors when exposed to harsh chemical cleaning agents and high temperatures

The dissolved oxygen concentration is one of the most important parameters for process control in many chemical and biotechnological processes. Rigorous monitoring of the oxygen concentration is required to control fermentation reactions such as the ones used in the food and beverage industry and other fields of industrial biotechnology. In addition, oxygen sensing is a key parameter that is part of many other process control tasks (e.g., in chemical or pharmaceutical engineering). In such applications, however, the sensors must withstand harsh chemical environments and elevated temperatures, yet remain functional for several months while ensuring signal stability and high accuracy. Chemical cleaning/sterilisation of the process installations (“Cleaning in Place”, “CiP”) is regularly applied in the food and beverage industry. This also implies a high demand for chemical and temperature stability of the sensors installed in such process plants.

Optical oxygen sensors have been developed that are particularly well-suited for such applications. After operational interruptions, such optical sensors immediately resume taking measurements without accuracy losses. In contrast, electrochemical oxygen sensors (i.e., “Clark electrodes”) often require several hours of polarization before the full accuracy of their measurements can be restored.

The developed oxygen sensor does not require removal from the process during CiP and remains fully operational for up to 6 months without calibration. The measurement range of the system precisely meets the requirements of the brewing industry. Its applicability is, however, by no means limited to breweries, but extends to all fields in the beverage, food and biotechnological industries due to their demand for sterilisable, CiP-resistant oxygen sensors.

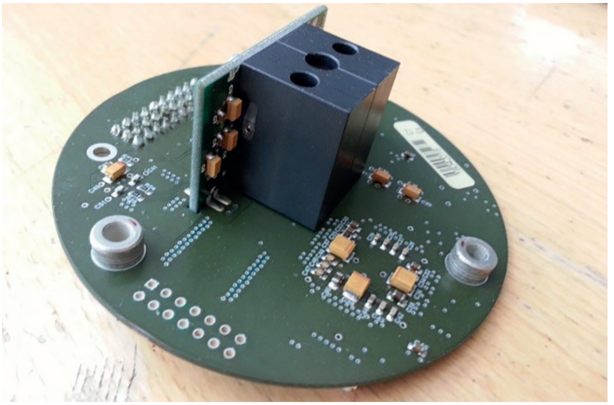
Specifications:

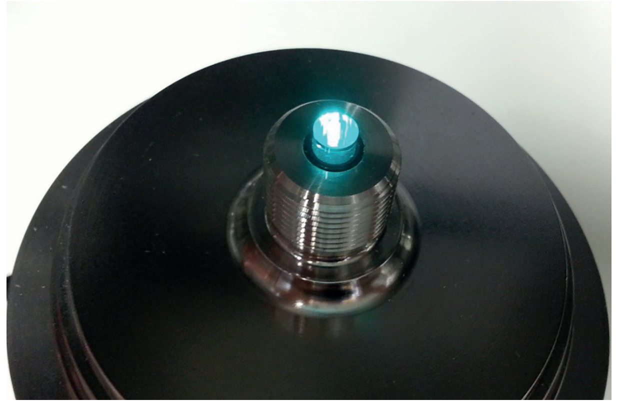
Measuring Range O_2:	0-2000 µg/L
Accuracy:	+/- 2% (or +/- 2 µg/L)
Resolution O_2:	< 1% (or <0.5 µg/L)
Detection Limit O_2:	0.5 µg/L
Max. Temperature (CiP):	110 °C (1 h max).
Response (Air→N_2):	t_{98} ~40s
Service Life:	up to 6 months without calibration
Food compatibility:	FDA-“GRAS”-Statement (=“Generally Recognized As Safe”)

Technological Readiness Level: 8 (actual system completed and qualified through tests and demonstrations)

Reference to part B:
Additive Printing Technologies for Sensor Fabrication (page 42).
Optical Simulation of Sensor Systems (page 63).

Process plant installation.





Optoelectronic module (left) and front view of the optical oxygen sensor readout device (right).

In-Line Quality Control for Tablet & Pellet Coatings by OCT

Optical coherence tomography (OCT) uses the technique of white light interferometry to detect interfaces with different refractive indices within materials, with µm scale accuracy. A typical point scan is performed rather rapidly (in the order of several kHz), enabling the acquisition of cross-sections nearly instantaneously, or even allowing three-dimensional reconstructions to be completed within minutes.

Until now, optical coherence tomography had primarily been applied in the field of ophthalmology, when creating cross sections of the retina of the eye in patients, in order to detect lesions or degradations of the retina or nerves. Now that greater computing power is available and calculations are performed using a GPU, OCT can now be regularly applied for industrial purposes, either in process or quality control.

Due to its ability to provide high-resolution, depth-resolved information without contact at a high acquisition rate, OCT has a great potential as an in-line quality control tool. Because it can be used to detect interfaces that have different refractive indices, it can be used to determine the thickness and uniformity of coatings and roughness of surfaces (see figure). Obviously, this is of use in quality control of tablets, but the technique can also be used in different applications such as lacquer and thin film quality control.

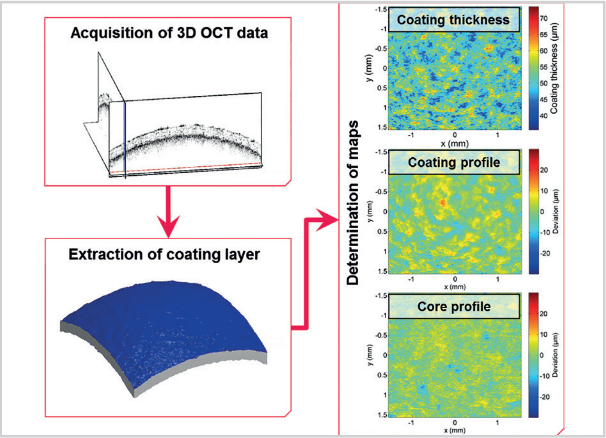
Additionally, OCT can be used to analyse stratified or non-homogeneous materials (e.g., foams and particles in suspensions), but also electronics. The ease of use and low costs of OCT as compared to other methods makes it an attractive alternative technology for use in in-line process monitoring.

Reference publication:
Markl D, Hannesschläger G, Buchsbaum A, Sacher S, Khinast JG, Leitner M. In-line quality control of moving objects by means of spectral-domain OCT. Opt Lasers Eng. Elsevier; 2014 Aug; 59:1–10.

Reference project: http://www.phyllon.at

Technology Readiness Level: 8 – 9 (system complete, qualified and proven in some operational environments)

Reference to part B:
OCT Imaging on the way to monitor biotechnology & production (page 61)



Analysing the coating thickness uniformity of a pharmaceutical tablet at a high level of resolution by measuring the coating and core profile with OCT.

Non-Invasive Oxygen Measurement in Sealed Containers - Smart Packaging

New packaging techniques such as modified atmosphere packaging (MAP) have been developed to preserve the quality of goods. Their main feature is that they prevent O_2 from being introduced into the packaging. O_2 contributes to oxidative processes and creates favourable conditions for the growth of aerobic, microbial spoilage organisms, which affects the quality, safety and freshness of many industrial products. The integrity of the packaging is, therefore, one of the most important requirements of the modern packaging industry, and the measurement of the O_2 concentration serves as an indicator of the integrity and quality both of sealed packaging and the packaged goods.

An optochemical sensor system for the contactless measurement of the oxygen concentration inside packaging has been developed, which is suitable for on-line, non-destructive quality control purposes.

Sensor spots are directly printed onto the packaging material (e.g., plastic trays or films) or other containers (e.g., bottles, windows, reactors). After sealing the packaging/container, the sensor spots can be optically detected from outside.

Typical fields of application include the food and beverage, pharmaceutical, or biotechnology industries and offer various opportunities:

- on-line non-destructive quality control of sealed packages in the processing line
- leakage inspection of sealed packages throughout the whole distribution chain
- as part of packaging technology and food research, for example, to investigate O_2 diffusion and permeation through packaging materials
- monitoring of processes in sealed reactors
- non-destructive determinations of the inert gas filling of insulating glass windows

Technological Readiness Level:
8 - 9 (system complete, qualified and proven in some operational environments)

Reference to part B:
Additive Printing Technologies for Sensor Fabrication (page 42)

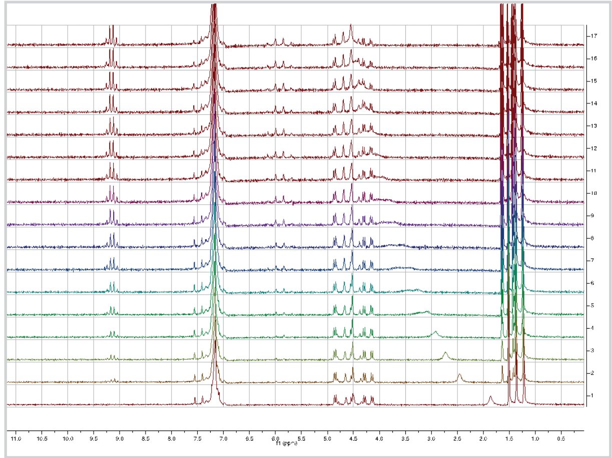
The opto-chemical O_2 sensor system based on printed sensor-spots (left), complete measurement system (middle) and packaging line for MAP of meat (right) (Images courtesy of Tec-Sense GmbH).

Process Monitoring by Process NMR

Online reaction monitoring is one of the major tasks that is part of process analytics for (bio-) organic reactions. NMR spectroscopy is well-suited for this task because it can be used as a quantitative technique, which also delivers a huge amount of structural information. A benchtop NMR offers a very attractive solution for process monitoring, since this NMR spectrometer can be brought to the samples, as opposed to being required to take the samples to the spectrometer.

Another advantage of the benchtop NMR is that regular solvents can be used instead of deuterated solvents.

For reaction monitoring, the sample passes through a flow-through cell at an optimised flow rate, allowing complete magnetization of the sample before it enters the detection area and complete relaxation before it leaves the detection area. This helps prevent the introduction of measurement artefacts. An aliquot of the reaction mixture is pumped directly from the reaction vessel through the bore of the magnet and back to the reaction vessel. In this manner, the reduction of substrate material and the increase of product can be monitored, as is shown in the exemplary figure.



Watching an enzyme-catalysed transesterification employing benchtop-NMR: Reaction monitoring for about 70 hours is depicted. The increase of reaction products e.g. at 9.2 ppm (acetaldehyde) or phenyl ethyl acetate around 5.8 ppm can be monitored. Additionally the shift of an acidic proton indicating a pH-change in the sample can be seen.

Technological Readiness Level:
4 (commercial benchtop NMR-spectrometer, method validated in lab)

Reference project:
K-Project: ”imPACts”
(www.k-pac.at)

Ultra-Low Oxygen Transmission Rate Measurement

Optochemical oxygen detection provides a powerful alternative to established methods that allow the measurement of oxygen transmission rates through flexible ultra-barriers such as the encapsulation materials used in organic electronics.

The development of flexible organic electronic devices such as OLEDs and organic photovoltaic cells has resulted in the achievement of a continuous series of successes for years now. Organic semiconductors have often been applied and structured by using simple and cheap processes such as inkjet printing, because they are mechanically flexible and offer a number of advantages over silicon-based semiconductors. A drawback of the technology, however, is its extraordinary sensitivity to oxygen and water vapour. These omnipresent atmospheric gases rapidly degrade the sensitive substances and, thus, destroy the devices. Consequently, organic electronics must be encapsulated, using absolutely air-tight materials.

Although some progress has been made towards the development of less sensitive organic semiconductor materials, meeting the requirements of proper encapsulation remains challenging. Remaining with the limits for oxygen transmission rates (“OTR”) as low as 10^{-5} cm^3 m^{-2} day^{-1} bar^{-1} and water vapour transmission rates (“WVTR”) of 10^{-5} g m^{-2} day^{-1} is required to ensure sufficient shelf-life and operation time, as well as permit the technical application of the organic electronic devices in the first place.

Even the best analytical instruments currently available on the market have limits of detection that miss these permeation rates by orders of magnitude and are unsuitable for the characterization of such ultra-barriers.

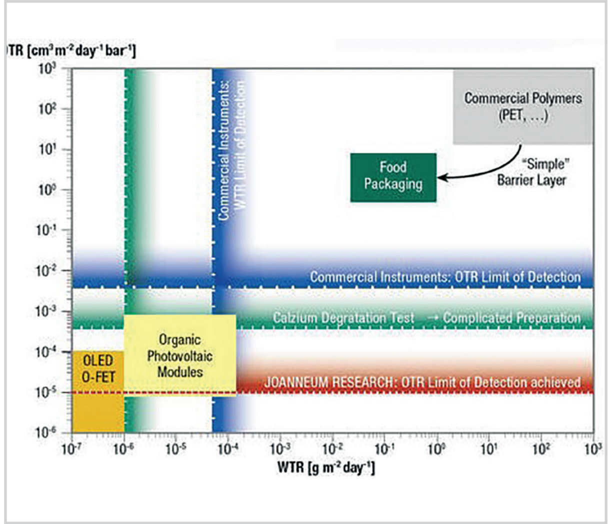
Using novel, highly sensitive, trace optochemical oxygen sensors in such instruments allows researchers to significantly improve the detection limits. Thus, demonstration devices have been constructed that achieve OTR limits of detection in the $10^{-5}cm^3$ m^{-2} day^{-1} bar^{-1} regime. They are, therefore, the most sensitive O_2 permeability testing pieces of equipment currently available and outperform the commercially available instruments by two orders of magnitude.

Technological Readiness Level: 6 (prototype demonstration in a relevant environment)

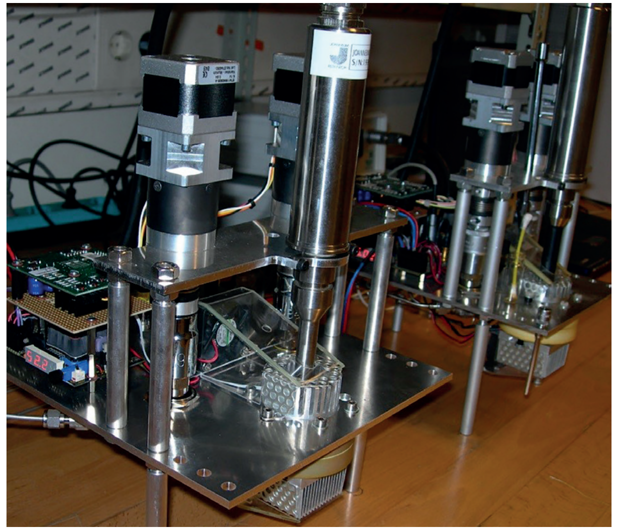
Reference link: www.tinyurl.com/ULOTRM

Reference publication:
M. Tscherner et al., “Opto-chemical method for ultra-low oxygen transmission rate measurement,” in Proc. IEEE Sensors, 2009, pp.1660-1665
www.dx.doi.org/10.1109/ICSENS.2009.5398515

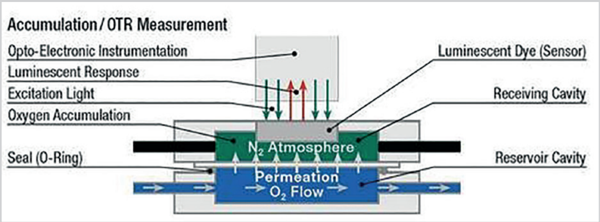
Reference project:
European Commission’s 6th framework programme FLEXONICS – Ultra-high barrier films for r2r encapsulation of flexible electronics (www.flexonics.org)



Comparison of barrier requirements and instrument performance.



Permeation-testing demonstration devices using opto-chemical sensors for oxygen sensing.



Schematic of the permeation measurement principle.

HEALTH MONITORING AND COMFORT SENSORS

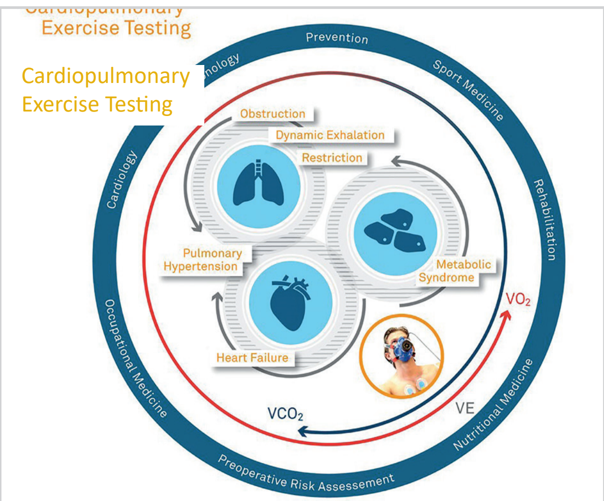
Breath Gas Monitoring by Optical Sensors

Ultra-fast nanostructured oxygen sensors increase diagnostic significance in ergospirometry

Ergospirometry involves the parallel evaluation of the function of a person´s heart, lungs and metabolic system while the person experiences physical stress. During the test, the exhaled breath is continuously monitored for its volume and oxygen and carbon dioxide concentrations using a face mask. These data are important markers with reference to pulmonary and cardiovascular diseases, training optimization in professional sports and general fitness applications.

With each breath, a large amount of data can be gathered and evaluated, remarkably exceeding the data-gathering capabilities offered by the standard lactate tests. The overall oxygen uptake is an important marker with reference to pulmonary and cardiovascular diseases, training optimization in professional sports and general fitness applications. During exercise, the breathing frequency can reach 1 Hz or higher, resulting in breathing exhalation periods of less than 500 ms. To precisely monitor the O2-profile and, therefore, provide an exact estimate of the overall oxygen uptake, a rapid oxygen sensor with response times of 50 ms or less is required.

Typical setup for ergospirometry (Courtesy of Cortex Biophysik GmbH).



Relevance of ergospimetry data for cardiopulmonary testing (Courtesy of Cortex Biophysik GmbH).

By means of electrospinning, nanostructured optical oxygen sensors can be created that have unmatched response characteristics, which contributes to the increased accuracy and enhanced diagnostic relevance of the ergospirometric tests. Furthermore, due to its small size and sturdiness, the sensor can be placed directly into the face mask, enabling the application of ergospirometry in mobile applications. Prototypes of complete integrated sensor systems in ergospirometric devices have been thoroughly tested for their performance.

Technological Readiness Level:
5 - 6 (prototypes tested under application conditions)

Reference to part B:
Electrospinning of Polymer Nanofiber Sensors (page 46)

Project reference:
m.era.Net - APOSEMA (Advanced Photonic Sensor Materials)

Implantable Fibre Optic Microsensors for *In-Vivo* Monitoring

A minimal invasive method enables the measurement and monitoring of pO_2 and pCO_2 in organ tissue

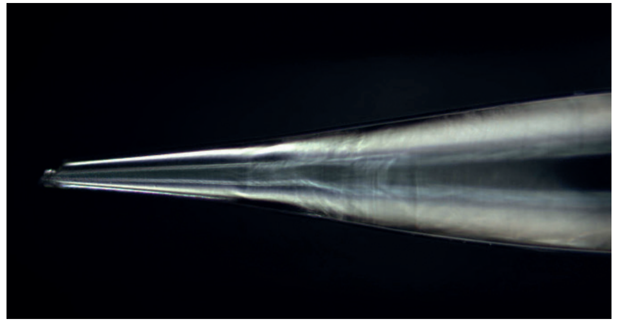
Implantable fibre optic microsensors, which perform detections based on luminescence decay time measurements, have been developed that are capable of monitoring dissolved pO_2 and pCO_2 levels in tissues. These implantable microsensors allow for the continuous monitoring of the O_2 and CO_2 supply to the brain, heart and liver during surgical interventions.

In animal experiments, the method was used to analyse oxygen levels and the formation of carbon dioxide during open heart surgeries, interventions that require the provision of an external oxygen supply. The effects of different methods of oxygen administration - such as minimal extracorporeal circulation (MECC) and conventional cardio-pulmonary bypass (CPB) - could be measured and compared, including differences in the organ-specific oxygen supplies and CO_2 accumulation.

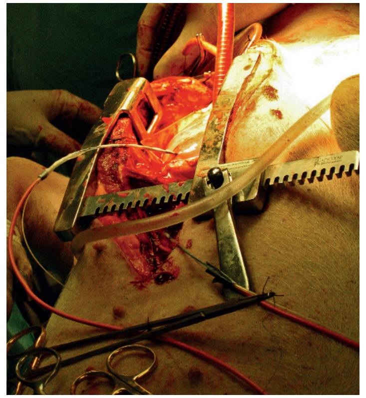
Based on a similar sensor set-up, fibre optic sensors can also be used ex-vivo and be combined with microdialysis technologies in order to probe different types of tissues. In such a setting, adipose tissue oxygen tension has been monitored in humans, which allowed the differences in adipose tissue function between obese and lean men to be investigated.

Technological Readiness Level: 5 (prototypes tested under application conditions)
Reference to part B: Optical Simulation of Sensors Systems (page 63)

Reference publication: G.H. Goossens, et al., Circulation. 2011;124: 67-76, doi:10.1161/CIRCULATIONAHA.111.027813.



Tip of optical fibre sensor.



Continuous in-vivo monitoring of pO_2 and pCO_2 during surgical intervention using implanted Fibre Optic Sensors.

Lung Monitoring by Electrical Impedance Tomography

A novel approach to individualized mechanical ventilation of critically ill patients is offered through Computed Tomography-enhanced bedside Electrical Impedance Tomography Imaging

The mechanical ventilation of an acutely injured lung can promote secondary lung damage, which is known as the ventilator-induced lung injury. By setting the ventilator to meet the patient’s individual needs, this damage can be avoided, but this remains a major challenge.

A novel dynamic bedside pulmonary imaging method is under development that would allow the optimal adjustment of the ventilator. Here, the dynamic method of Electrical Impedance Tomography (EIT) - operated using a chest belt with imbedded 32 electrodes - is combined with taking single images using Computed Tomography (CT) to create a novel, CT-enhanced, dynamic EIT.

The high spatial resolution of CT (pixel matrix 512 x 512) is algorithmically combined with the high temporal resolution of EIT (50Hz frame rate). To overcome the spatial limitations of EIT imaging, we used the anatomical information provided by CT-scans and integrated them into EIT image reconstruction algorithms and, subsequently, performed an analysis in the time and space domains. The aim was to distinguish - within each EIT pixel - between lung tissue that was either hyperinflated, normally aerated, cyclically recruiting and derecruiting, or non-aerated. This novel approach of “CT-enhanced EIT”.

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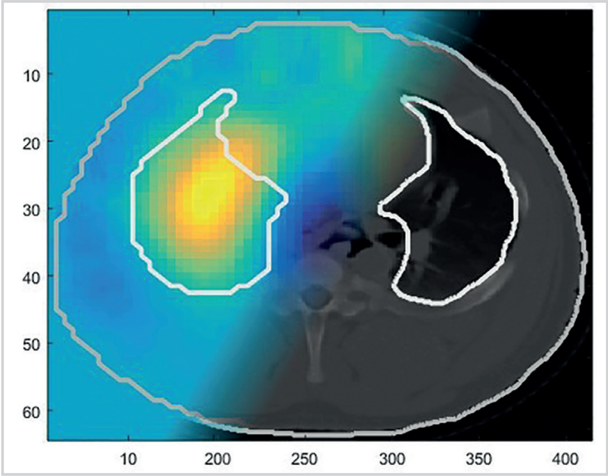
Technology Readiness Level:
5-6 (Prototypes under testing and adaptation)

Project reference:
This project is funded by the Vienna Science and Technology Fund (WWTF) through the project LS14-069 (Life Sciences 2014 / Innovative biological and biomedical applications of novel imaging technologies).



Reconstructed EIT (left upper part of image) based on contours from CT (right lower part of image).

CT-enhanced EIT in application (Courtesy of Swisstom AG).

Monitoring Pathogens in the Oral, Nose and Throat Cavities and Determining their Levels of Antibiotic Resistance in order to Provide Targeted Therapy for the General Practitioner and Dentist

Infectious disease diagnostics with rapid genomic and proteomic point-of-care tests

The treatment of infectious diseases by general practitioners and dentists is still based on symptomatic diagnosis and time-consuming, laboratory based microbiological analyses. Especially for respiratory tract infections (RTIs), in the absence of a clear diagnosis, doctors often prefer to be on the safe side by prescribing antibiotics, which in turn promotes antibiotic resistance. This phenomenon is estimated to cause 25,000 deaths each year in Europe and places a 1.5 billion euro burden on the health care system. On the other hand, oral diseases such as periodontitis and caries are typically diagnosed only when they are in a progressed stage. Therefore, there is a need for a rapid, highly specific chair-side test for oral and respiratory infections.

In response to the above medical needs, rapid molecular diagnostic tests in the form of qPCR and novel multiplex nucleic acid assays that can be used to genotype bacteria and assess their level of antibiotic resistance (in case of RTIs) are being developed and streamlined for point-of-care testing compatibility. In addition, protein biomarkers indicative of inflammation will be monitored by rapid protein microarrays. These central analytical methods are complemented by nucleic acid extraction, on-chip reagent storage, microfluidics and automatic processing. Those elements combined, provide a compact device with a self-contained disposable disk, and which is capable of yielding rapid diagnostic results from saliva and nasal or throat swabs within 60 minutes.

The new diagnostic device will be validated using clinical samples of patients with respiratory tract infections, caries and periodontitis. In view of the alarming increase in antibiotic resistance and the urgent need for rapid infectious disease monitoring, the novel device has a great potential to guide treatment of infectious disease directly at the point-of-need at the general practitioner, dentist and emergency room. As a further consequence antibiotic resistance can be contained, and rapid and targeted treatment can increase both healthcare efficiency and patient health. In addition the healthcare systems can be relieved as diagnosis will take a de-centralised form.

Technology Readiness Level:
3 (initial laboratory tests completed, proof-of-concept)

Reference project:
European H2020 project DIAGORAS: Chair/bedside diagnosis of oral and respiratory tract infections, and identification of antibiotic resistances for personalised monitoring and treatment (www.diagoras.eu)

Labdisk containing all required reagents for rapid monitoring of infectious disease. Saliva or swab samples are loaded onto the disk and the analysis is performed by an external device, providing dentists and general practitioners with a pathogen and host-response profile of the patient within 60 minutes (Copyright: Hahn-Schickard, Bernd Müller Photography).

Nanoprobe-Based Mix and Measurement Immunodiagnostics

Fast and sensitive homogeneous *in vitro* immunodiagnostics by mixing nanoprobes with the sample solution and measuring

Current *in-vitro* immunodiagnostics is usually based on ELISA techniques, which are widely applicable and sensitive, but which require substantial sample preparation and processing and, consequently, are limited in applicability when rapid results or continuous monitoring are required (e.g., in intensive care situations).

A novel technology-based solution has been developed to overcome these difficulties. The technology is based on the addition of specially designed, functionalized magnetic nanorods ('nanoprobes') directly into the sample solution (e.g., serum or saliva), which allows the analysis of target proteins by optically monitoring the dynamic response of these nanoprobes to the application of time-varying magnetic fields. This simple mix and measure approach allows rapid and sensitive monitoring of the patient's parameters without requiring any manual user interaction.

Compared to established in-vitro immunodiagnostic techniques, the technology offers the following advantages:

- only minimal sample preparation required (e.g. dilution)
- total analysis time is rapid (< 5 min) due to the simple mix & measure technique

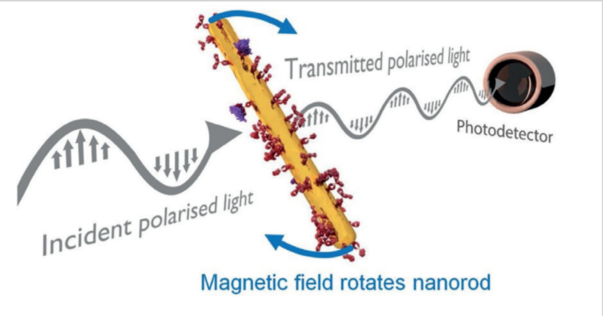
- small sample volumes are required (currently 20 µl, 1µl in development)
- the sensitivity is highly compatible with state-of-the-art techniques
- it is easy to integrate and only requires simple instrumentation

Possible applications of the technology are very broad and include, for example, the following:

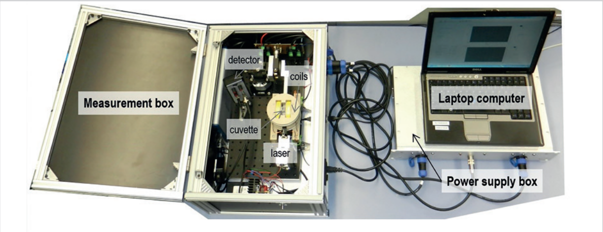
- offers general point-of-care diagnostics, such as:
    - Emergency care patient stratification and monitoring
    - Rapid diagnostics at medical and dental offices
    - Home-based diagnostics for the testing of biological samples (e.g., saliva, urine)
- offers field testing tools such as for veterinary testing by breeders and farmers
- protein size analysis
- binding affinity constant investigations

Technology Readiness Level:
4 (technology validated in lab)

Reference project:
European FP7 project NAMDIATREAM
(www.namdiatream.eu)



Detection principle: the presence of a bound analyte molecule is detected optically as a change in the nanoprobe rotational dynamics. (Illustration by Darragh Crotty, www.darraghcrotty.com)



Photograph of the prototype instrument, consisting of the components (i) measurement box, (ii) power supply box and (iii) laptop computer. The main functional components within the measurement box are also labelled (Image: AIT).

Online Analyses in Microfluidics and Microreactors with Integrated Optical Chemical Sensors

A lab-on-a-chip is a device that represents a newly developed technology used in the field of microfluidics, variants of which have found manifold applications during the last decade in areas such as medical diagnostics, environmental analyses, flow chemistry and biotechnology. However, the demand for online analytical tools that allow the manipulation of fluids in the micrometre range is steadily increasing. Optical chemical sensors (see page 42) are ideally suited for their integration into the miniaturized structures. They are cheap, can be processed easily and contactless signal transmission is used to send information to read-out devices located outside the reaction chamber.

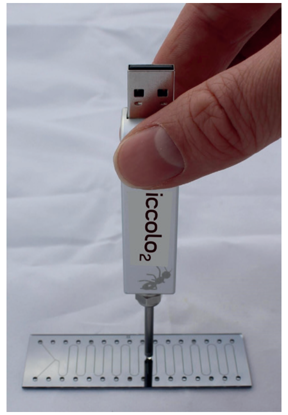
Oxygen, pH, carbon dioxide and glucose levels are key analytical parameters in biotechnology. Optical sensor layers or spots that can measure these parameters are integrated into microfluidic devices made of glass or polymers. The integration is compatible with mass production processes. The sensor layers can be miniaturized down to a size of 100 µm. The combination with laboratory measurement equipment from PyroScience GmbH enables high precision measurements to be made with miniaturized tools.

Inline analysis in microbioreactors using the integrated sensors has been demonstrated by enzymatically catalysing reactions. The microreactors with integrated sensor represent new tools that can be used for process optimisation and intensification as well as flow chemistry [1]. In addition, the sensors can be applied in microfluidic cell cultures or an organ-on-a-chip. [2]

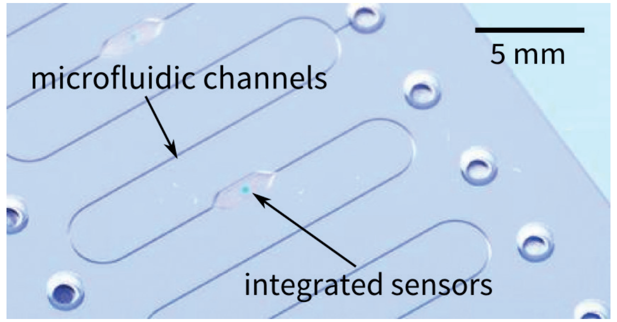
Technology Readiness Level: 9 (oxygen sensor), 7 (pH sensor), 4 (CO_2 and glucose sensor)

Reference projects:
EU-Project: BIOINTENSE - Mastering Bioprocess Integration and Intensification Across Scales (www.biointense.nu).
Marie-Curie ITN – EUROMBR - European network for innovative microbioreactor applications in bioprocess development (www.eurombr.nu).

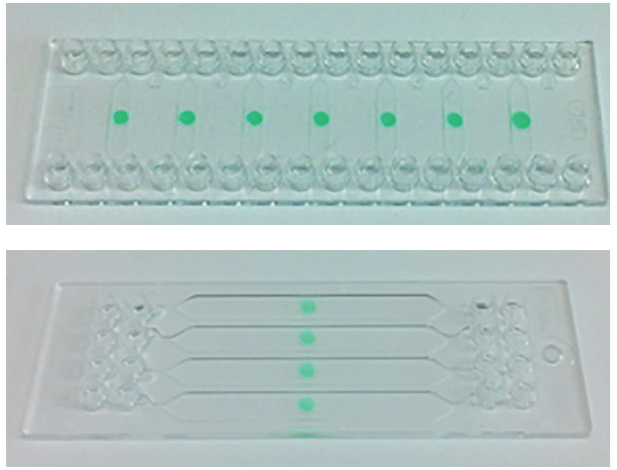
Reference publications:
[1] OPEN ACCES - Ehgartner, J. et al. Online analysis of oxygen inside silicon-glass microreactors with integrated optical sensors. Sensors and Actuators B: Chemical doi:10.1016/j.snb.2016.01.050.
[2] Rennert, K. et al. A microfluidically perfused three dimensional human liver model. Biomaterials 71, 119–131 (2015).



Microreactor made of silicon and glass consisting of one meander channel with integrated sensors (volume: 6 µl; channel width: 200 µm; channel depth: 400 µm) and a miniaturized read-out device.



Magnified view of the channel with integrated sensor spots (diameter 100 µm). Chip developed in collaboration with iX-factory.



Microfluidic chips with integrated sensors (green dots) for on-line control of cell cultures. Developed in collaboration with microfluidic chipshop.

Plasmonics for Ultrasensitive Biosensors

The label-free detection of low concentrations of an analyte is a continual challenge in the development of biosensing techniques. To address this challenge, surface plasmon resonance (SPR) sensing has been developed, which provides a commercially available solution that relies on the extraordinarily sensitive response of optical metal-bound surface waves (plasmons) to the presence of analyte molecules. However, in addition to the flat gold films as used in SPR, any gold structure can sustain the plasmonic modes. In particular, gold nanoparticles display nanometre-confined plasmon fields. The extent of these fields is small enough to be significantly disturbed by the presence of a single molecule, which allows the achievement of an ultimate level of sensitivity. Because the field disturbance leads to a spectral change in the light scattered by the nanoparticles, a simple optical read-out platform can be used.

In order to detect thrombin, the following components were developed.

- Shape-tailored gold nanoparticles, because the particle geometry dictates both the extent of the plasmon field and the spectral scattering response. Both were optimized by electron beam lithography as a rapid prototyping tool (> Part B, page 57), while remaining within the parameter range for nanoimprinting fabrication (> Part B, page 53) to meet future fabrication up-scaling requirements.
- A real-time spectroscopic analysis tool, which can detect spectral changes as small as 1/1000 nm.
- A small and compact measurement cell including microfluidic devices.

By providing an aptamer layer for specific analyte binding, thrombin was detected at a 3 nanomolar concentration with a signal-to-noise ratio greater than 100, outperforming reference measurements taken with a microbalance by more than a factor of 10 and demonstrating that this tool could be used in the picomolar range. In addition, optimised geometrical shapes of nanoparticles could allow the detection limit to be lowered even more.

<u>Technology Readiness Level</u>: 4 (validated in lab)

<u>Reference to part B</u>:
Nanoimprint Lithography: Micro- and Nanofabrication for Chemo- and Biosensing Applications (page 58).
Rapid Prototyping on the Micro- and Nanoscale via Focused Particle Beams (page 64).

<u>Reference project</u>:
Particle plasmon biosensors (2012-2015, Region of Styria HTI)

<u>Reference publications</u>:

V. Haefele, A. Trügler, U. Hohenester, A. Hohenau, A. Leitner, J.R. Krenn, Local refractive index sensitivity of gold nanodisks, Opt. Express 23, 10293 (2015).

V. Leitgeb (Haefele), A. Trügler, S. Köstler, M. K. Krug, U. Hohenester, A. Hohenau, A. Leitner, J.R. Krenn, Three dimensional sensitivity characterization of plasmonic nanorods as refractometric biosensors, Nanoscale 8, 2974 (2016).

PyzoFlex® for Ambient Monitoring: Large Area Sensing of Pressure and Temperature Changes

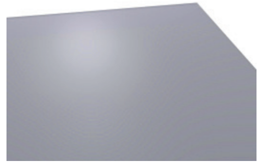
PyzoFlex® is a piece of printable sensor technology. A PyzoFlex® sensor is built with the ferroelectric material P(VDF:TrFE), supporting the exploitation of both the pyro- and the piezoelectric effects, which can be used to sense pressure changes and bending effects on large, flexible surfaces.

The sensor foil is constructed as a sandwich structure made up of four layers that can easily be printed onto any substrate (e.g., plastic foils, paper and textiles). The resulting PyzoFlex® sensors are sensitive to pressure and temperature changes, are bendable, energy efficient and can be created sheet to sheet using a screen-printing process. Because the PyzoFlex® sensor acts as a piezoelectric energy-converter, any deformation energy of the sensor foil is converted into electric energy. The charges that are generated by such a deformation can be measured as voltage produced between the electrodes of the ferroelectric sensor.

An important advantage of the PyzoFlex®-technology is its self-sufficient, energy-sensing principle. The sensor can operate in a passive (high impedance or current) mode, whereby any deformation/pressure change generates electric charges that indicate the bending radius/pressure being applied. The PyzoFlex® sensing concept, therefore, can also be used for energy harvesting purposes.

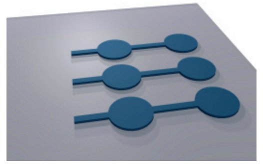
Standard fabrication process by screen-printing

Substrate



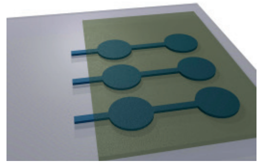
Plastic, paper, textile, glass, metal, transfer foils …

1st Electrode



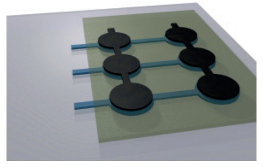
PEDOT: PSS (conductive, transparent polymer).

Active Material



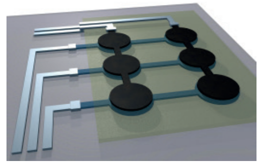
Copolymer: PVDF:TrFE-Ink (patented synthesis).

2nd Electrode



PEDOT:PSS (for semi-transparent sensors) Carbon.

Connections



Ag lines for connection to electronics.

Key facts about sensor fabrication:

- Low temperature fabrication on flexible/rigid substrates possible (≤ 100°C)
- Substrate sizes up to 420 x 420 mm with a thickness ≤ 20mm can be used
- Semi-transparent sensors are possible if solely PEDOT:PSS is used as electrode material
- Cost efficient sheet to sheet manufacturing is possible using industrial screen printing processes
- Application of specific sensor shapes is based on CAD designed screen masks (max. resolution = 12,000 dpi)
- Sizes as small as 100 µm are possible (depending on the material and screen)

Technology Readiness Level:
6 (technology demonstration)

Reference to part B:
Additive Printing Technologies for Sensor Fabrication (page 42)

Reference link: www. tinyurl.com/PYZOFLEX

Reference project: FLASHED (Flexible Large Area Sensors for Highly Enhanced Displays) www.flashed-project.eu

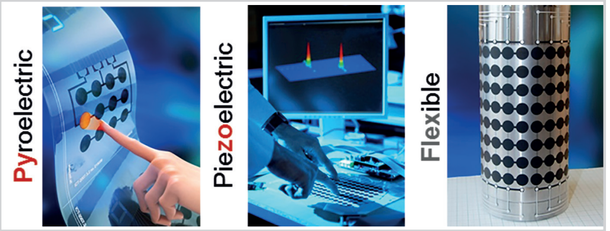
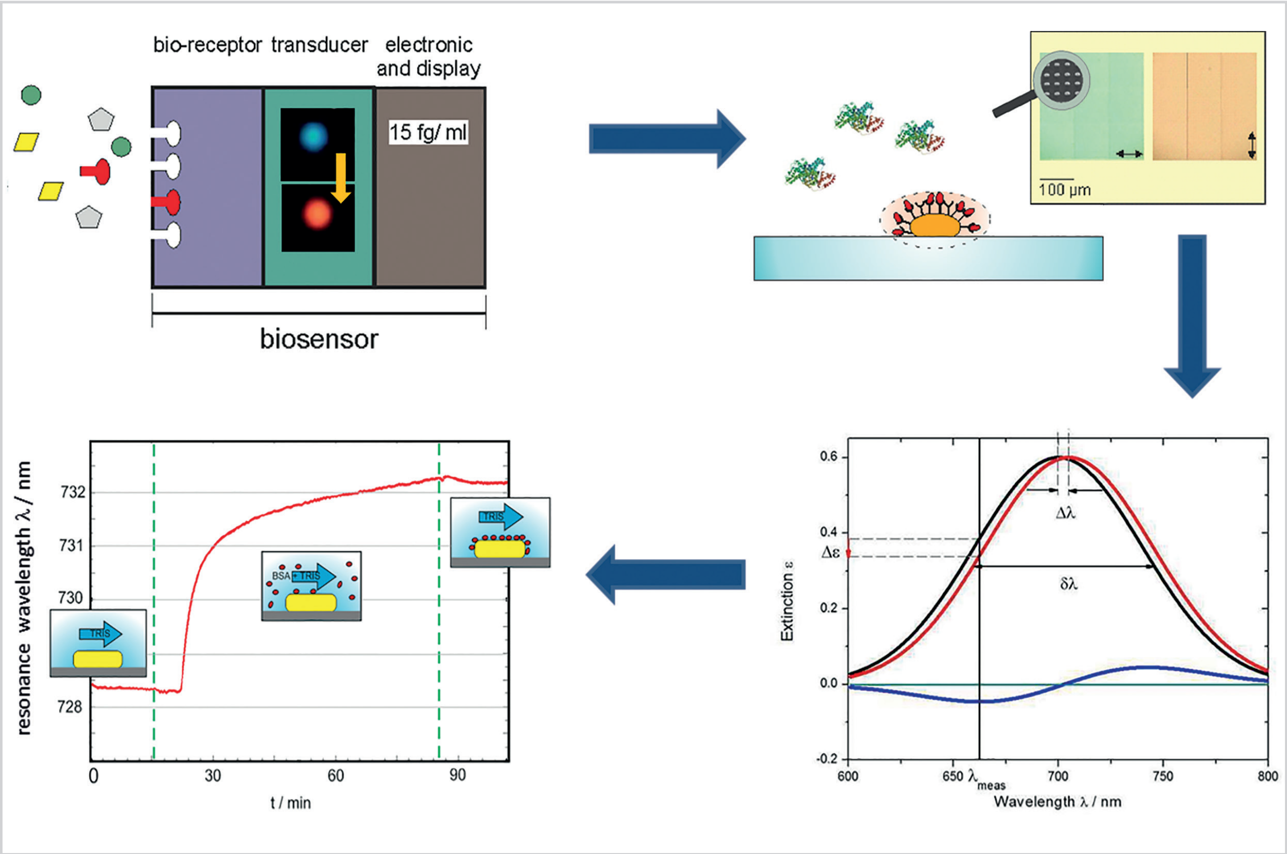


Illustration of the three key-properties of the PyzoFlex®-Technology.

Vision of an intelligent floor based on PyzoFlex for Ambient Assisted Living applications. (Courtesy of Weitzer Parkett GmbH & CO KG).



Plasmonic biosensing tool: schematic of the progression from an idea to use the analyte-induced spectral shift as a transducer mechanism to the tailored development of plasmonic nanoparticles as a sensor surface, allowing sensitivity to be gained by improving spectral resolution and taking measurements with the fully integrated sensor system; clockwise from top left (image: Verena Leitgeb, Nanooptics Group, University of Graz).

Sensor for Detection of Wound Infection

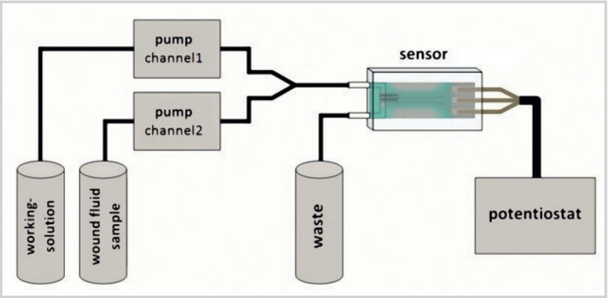
Infection of chronic wounds is a common problem that can result in prolonged hospital stays, inhibit healing and increase mortality in patients. The correct identification of infection is a complex issue because not all clinical symptoms such as redness, heat, swelling, pain and impairment of function can be consistently observed. Clinical examinations are unreliable for the diagnosis of wound infections. The quantitative results of ulcer biopsies have shown that bacterial counts of greater than 10^5 were observed in 28% of participants, who had not displayed any clinical signs of infection.

A new sensor-supported strategy for the rapid diagnosis of wound infection, based on the quantification of the activity of the neutrophil-derived enzyme myeloperoxidase (MPO), has been developed. MPO uses hydrogen peroxide (H_2O_2) to oxidize chloride ions and produce antimicrobial hypochlorous acid (HClO). Since the recruitment of neutrophils increases with as the bacterial infection spreads, the enzymatic MPO-activity can indicate the status of the infection at a very early stage. A screen-printed sensor in the 3-electrode configuration is used to amperometrically detect H_2O_2. MPO activity can be quantified on the basis of the reduction rate of H_2O_2 by MPO present in the wound fluid sample in a predefined test solution. Because the test solution is measured before introducing each sample, the system is virtually calibration free.

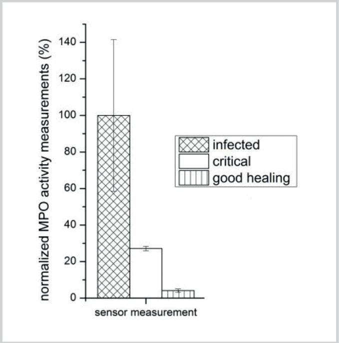
During a clinical trial, real wound fluid samples were characterized as "infected", "critical", and "good healing", depending on the presence of potentially pathogenic microorganisms. The sensor readings showed an excellent correlation with the microbiological characterization characterization and the doctor's diagnosis. The sensor system clearly allowed the differentiation of "infected", "critical", and "good healing" wounds, which had not been the case when chlorination - and peroxidation activities were optically detected.

Technology Readiness Level: 4 - 5 (prototypes tested with real samples)

Reference publication:
www.dx.doi.org/10.1016/j.snb.2014.11.125



Setup of the measuring system.



Result from clinical sensor evaluation.

Sensor for Monitoring Potassium at Home

The electrolyte balance of patients with chronic heart failure and chronic renal failure can be affected by diuretic medications and the metabolic disorders caused by the diseases. Therefore, frequent monitoring of serum potassium levels is required in these patients, which usually requires a doctor’s visit or a visit to a hospital’s outpatient clinic.

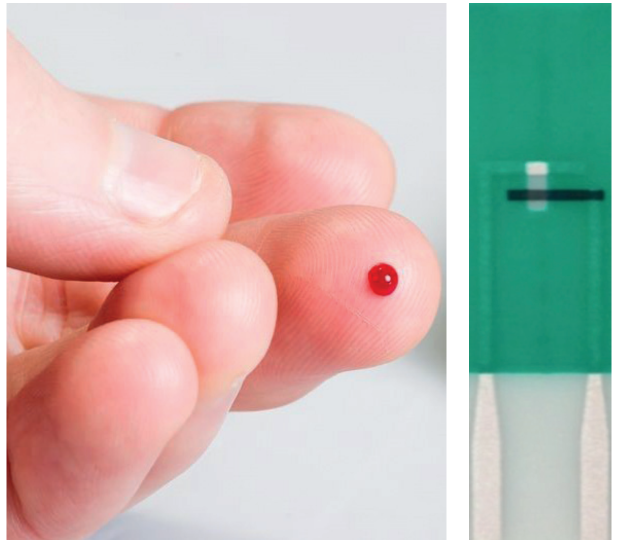
Alterations in the electrolyte balance and even cardiac decompensations can occur due to the large intervals that take place between these medical checks. Consequently, emergency admissions to the hospital and treatments over a longer period are necessary to restore the patients to a status of good health.

A potassium sensor in a test strip design has been developed that can be used in the same way as glucose test strips are used by diabetes patients. This enables the patients to monitor their potassium levels and adjust their medication themselves.

The sensor consists of two screen-printed electrodes applied on a polymer substrate. To create an ion selective electrode (ISE), a carbon ink electrode is covered by a screen-printed, potassium-selective membrane. A screen-printed silver/silver-chloride electrode with an additional screen-printed chloride reservoir serves as the reference electrode.

Because haemolysis can lead to false results indicating high potassium levels, additional electrodes have been integrated to measure the degree of haemolysis as a fail-safe feature.

Technology Readiness Level:
4 -5 (prototypes tested with real samples)



Drop of blood from finger-pricking and potassium sensor test strip.

Silicon Nitride Based Photonic Sensing Devices for Medical Diagnostics

CMOS-compatible, integrated-optical, waveguide devices for the label-free detection of biomolecules and miniaturization of optical coherence tomography systems

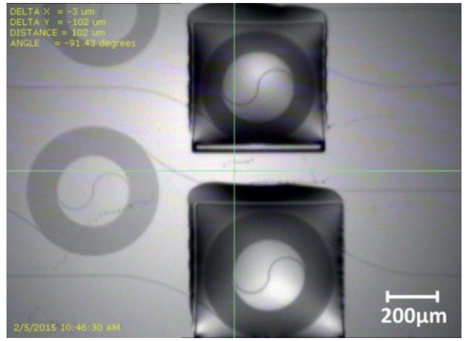
Photonic integrated circuits offer an excellent potential to develop cost-effective, compact sensing devices for various medical diagnostic applications. In collaboration with the technology partner ams AG, a silicon nitride (Si_3N_4) waveguide-based sensor technology platform has been developed that is both compatible with mass fabrication methods and allows the use of integrated optoelectronics.

The silicon nitride waveguide technology platform was used for the development of Mach-Zehnder interferometer-based (MZI-based) biosensor arrays that allow the simultaneous, label-free detection of different target biomolecules. This technique allows researchers to measure the biomolecular interaction between the receptor and target biomolecules in real-time, which permits the determination of the associated kinetic parameters. Various surface biofunctionalization protocols have been developed that allow specific target molecules such as DNA, proteins and peptides to be optimally sensed. These protocols have also been adopted for the local biofunctionalization of sensor arrays by means of inkjet printing. The detection of biomolecules has been successfully demonstrated in serum and saliva samples.

Another application of the silicon nitride waveguide technology platform is related to optical coherence tomography (OCT). In this context, the integration of optical functionality into a single chip promises to significantly reduce the cost of OCT systems and, thus, allow their widespread use in point-of-care diagnostic settings.

Technology Readiness Level: 4 (component and breadboard evaluation in laboratory environment)

Reference projects: COHESION (FFG – Production of the Future, www.cohesion.researchproject.at), OCTchip (H2020 – ICT-27-2015, www.octchip.researchproject.at), PASSION (FFG – Production of the Future, www.passion.researchproject.at), PLATON SiNsor (FFG – Austrian NANO Initiative)



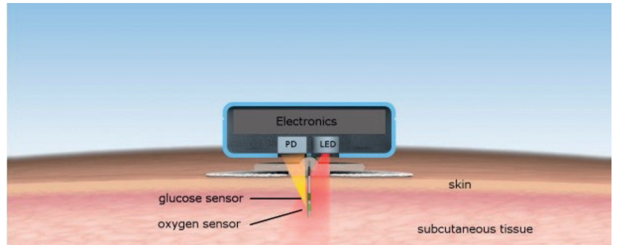
Si_3N_4-based, spiral-shaped optical waveguides of an MZI array. The reference spiral waveguides on the left are covered with an SU-8 cladding. The spiral waveguides responsible for taking measurements are located within the square-shaped window in the SU-8 cladding and are covered with a liquid that has been locally deposited by means of inkjet printing. (Image: AIT).

Single-Port Glucose Sensor

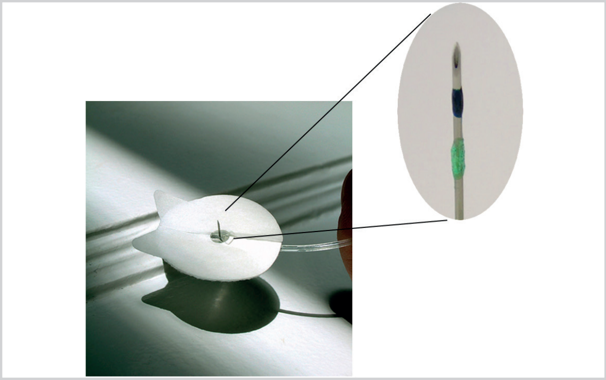
The SPIDIMAN (Single-Port Insulin Infusion for Improved Diabetes Management) system is an innovative artificial pancreas approach that can support the improved glycaemic management of type 1 diabetic patients by combining continuous glucose monitoring (CGM) and continuous subcutaneous insulin infusion (CSII) in a single system. The novel single-port approach allows the measurement of blood glucose concentrations directly at the site of insulin infusion. The glucose sensor is applied as a thin coating on the needle of the insulin infusion set and, thus, combines CGM and CSII. The novel glucose sensor technology is a phosphorescence-based glucose sensor that can be read transcutaneously by an optical read-out unit, which is placed on the skin surface above the sensor. SPIDIMAN will pave the way for the application of a new single-port device with improved acceptance, which will advance diabetes management strategies, especially for young and adolescent patients.

<u>Technology Readiness Level</u>:
5 - 6 (prototypes tested under application conditions)

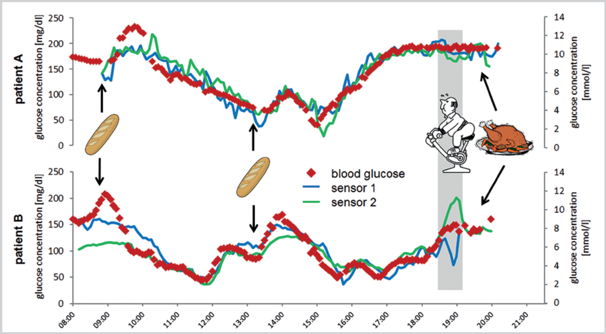
<u>Reference link</u>:
www.spidiman.eu (This project has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 305343.)



Scheme of transcutaneous readout.



Insulin infusion set with sensor detail.



Glucose profiles from clinical trial (two sensors per patient).

Smart Textile Integrated Sensor Systems

Indicator swabs and washcloth formonitoring pH in wounds and personal care

Chronic wounds are both painful and problematic for elderly and diabetic patients. Recent research has shown that the pH of the fluid in wounds is correlated with the stage in the healing process. A pH above 8 indicates that treatment is necessary, since efficient healing can only take place when the pH is in the range of 5 to 7.

Likewise, skin-friendly (so-called 'pH skin-neutral') personal care products have a slightly acidic pH. Soaps and cheaper cleaning products, however, are often alkaline (pH above 8), which can lead to skin irritation in both infants and dermatitis patients.

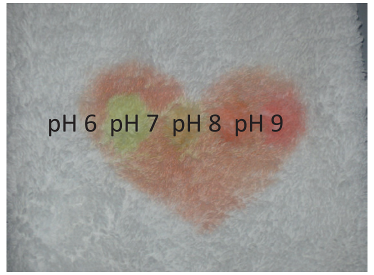
pH-sensitive, indicator cotton swabs have been developed in order to obtain information on the wound status quickly and simply. The swabs simultaneously allow wound cleaning and pH measurement. The indicator dye is covalently immobilized on the swabs and displays a clearly visible colour change from green (ideal pH) to red (treatment necessary). This colour change can be interpreted with the naked eye as well as by using an optical measurement device. Furthermore, an indicator washcloth has been developed that changes colour from green to red if an irritating (alkaline) washing agent is used by the consumer. The washcloth is useful for use with infants that have highly-sensitive skin, dermatitis patients and elderly people. It can be used repeatedly and can be washed in conventional washing machines. The pH-sensitive sensor swabs are compatible with gamma-sterilisation methods and have already passed cytotoxicity tests as well as tests for endotoxin levels. Furthermore, the textiles with immobilized indicator dyes have been certified as having met the OekoTex® standard.

The pH indicator cotton swabs are new tools that allow the simple and rapid analysis of a wound status and facilitate appropriate treatment. The sensor washcloth is a product that allows parents to feel more secure when providing daily care for their infants, since they can identify irritating personal hygiene products immediately.

<u>Technology Readiness Level</u>: 6 – 7 (prototypes tested under application conditions)

<u>Reference project</u>: Research Studio Austria (RSA) - SmartColorTextiles

Cotton sensor swabs for simultaneous wound cleaning and pH monitoring.



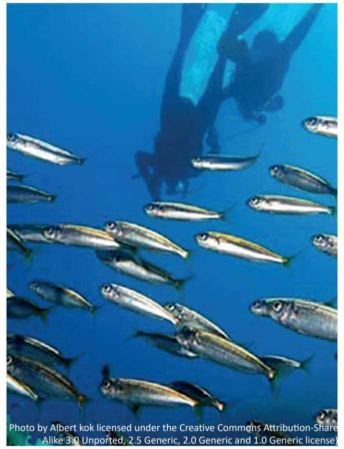
pH indicator washcloth surface, displaying the visible colour change.

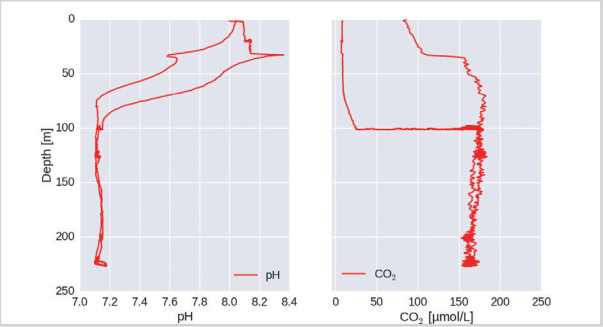
ENVIRONMENTAL MONITORING

An Optical Sensor System for the Measurement of pH, O_2 and CO_2 in Seawater and Fresh Water

Oxygen, pH and CO_2 levels are among the most important parameters for measurements made in a marine environment. A modular, compact and cost-effective measurement system for all three parameters has been developed. The system is composed of a waterproof and pressure-resistant read-out device with exchangeable sensor caps for measuring oxygen, pH and CO_2. The read-out device features an internal logger and a battery that enables continuous measurements to be taken for one year at a logging interval of 5 minutes. Different sensing materials can be mounted on the device using simple screw-caps. Thereby, the system can be serviced extremely quickly and used for the measurement of different analytes.

The sensing materials are based on stable dyes embedded in polymers. The materials have been optimized to enable reliable, referenced read-outs and low-interference measurements to be taken. The temperature dependences of all three types of materials have been well characterized and are compensated via the temperature probe of the measurement device. Notably, all sensors are also compatible with the laboratory measurement devices available from PyroScience GmbH, which can be used to take ex situ measurements. Although the dynamic ranges of the pH- and CO_2-sensing materials have been optimized for taking measurements in seawater, a set of alternative materials that are fully compatible with the read-out device is available. Oxygen sensors are available for taking physiological range and trace concentration measurements. The device was field-tested using the different sensor materials in the Baltic Sea during October, 2015. The materials performed very well and the profiling measurement can be seen in the figure.





The device and an example of profiling measurements taken down to a depth of 230 m in the Baltic Sea with a pH and CO_2 sensor.

Technology Readiness Level:
9 (oxygen sensor), 7 (pH sensor), 6 (CO_2 sensor)

Monitoring Fish Farms using Optical Sensors

Sensors for on-line monitoring of an aqueous environment in aquaculture

Today, nearly 45% of the fish consumed by humans, estimated at 48 million tons in all, is raised on fish farms. Currently, 1.3 million tons of fish farmed products are produced for the European market every year, which represents an approximate value of 3 billion euros. Due to the highly competitive market, the aquaculture business has been challenged to increase its productivity.

Therefore, sensing systems that allow the accurate on-line measurement of parameters such as levels of dissolved O_2, CO_2, NH_3 and pH are required. Accurate monitoring and controlling of these water quality indicators contributes to the sustainability of the health of the fish and, consequently, ensures the productivity of the fish farms and the quality of this food for humans.

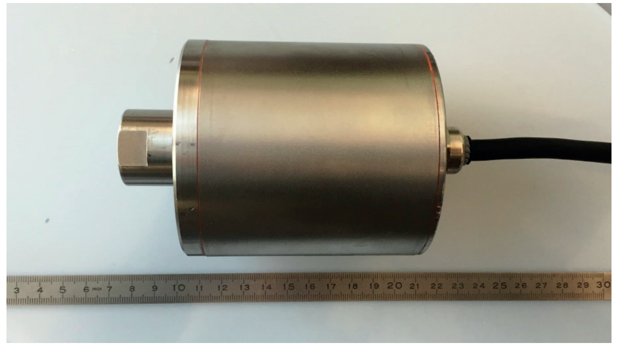
Optical sensor systems, based on the measurement of luminescence decay times, have been developed that can be used to monitor dissolved O_2 and CO_2 levels in aquaculture environments. These kinds of sensors find applications in both fresh- and seawater settings, are robust and can easily be miniaturized. A major advantage is the use of a disposable, sensitive transducer element that does not contain any liquid components, which ensures rapid sensor response times and makes the sensors nearly maintenance-free.

Accurately controlling the dissolved O_2 and CO_2 levels is necessary to provide optimal growth conditions for the fish, which can greatly improve the productivity and competitiveness of the aquaculture industry. Additional relevant parameters can be monitored in order to further optimize the environmental conditions in fish farms.

Technology Readiness Level: 5 - 6 (prototypes tested under application conditions)

Reference project: EC 7th framework program: OptoCO2Fish (www.optoco2fish.eu)

Fish farming.



Optical CO_2 Sensor System for aquaculture.

Thin Metal-Oxides for Selective Gas Sensing Implemented on CMOS-Chips

Gas sensors are of high importance for many applications, ranging from indoor air quality monitoring and personal safety systems to outdoor environmental monitoring. Many variants of gas sensors, based on metal oxides, have been developed in the last decade for established devices. Their success can be explained by their high sensitivity to a broad range of flammable and toxic gas species and their simple detection principle relying on changes of electrical conductance, due to the interaction with the gas. However, the performance of today`s commercial gas sensors, dedicated to industrial applications, is insufficient with respect to emerging applications in electronics such as smart phones, because of their high power consumption and the cross-sensitivities of most sensors.

Solving these issues and developing smart sensor systems for smart life applications needs:

- The use of nanocomponents as sensing elements to optimize gas sensor performance, while reducing their size.
- The heterogeneous integration of the nanocomponents with CMOS devices to ensure low power operation and low-cost fabrication.

Therefore, current research is focusing on gas sensor devices, based on ultrathin SnO_2 films and different types of metal oxide nanowires, such as CuO, ZnO, WO_3, SnO_2 nanowires (NWs). The sensor materials are additionally functionalized with (bi)metallic nanoparticles, in order to optimize sensor response and minimize cross-sensitivities. All nanocomponents are implemented on CMOS fabricated micro-hotplate (µhp) devices by specific post processing technologies. Such CMOS integrated nanosensor arrays are highly promising candidates for realizing smart multi gas sensing devices for the consumer market.

Technology Readiness Level:
5 (for NW based sensors) – 7 (for SnO2 thin film sensors)

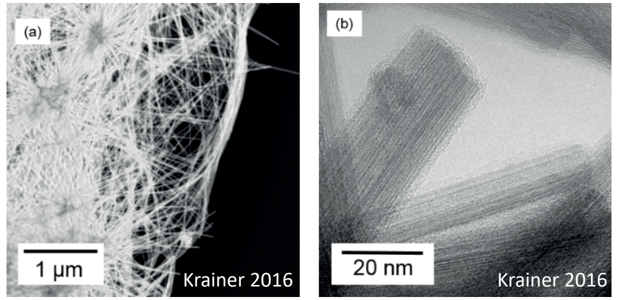
Reference publications:

Krainer, J., Deluca, M., Lackner, E., Wimmer-Teubenbacher, R., Sosada, F., Gspan, C., Koeck, A. (2016). CMOS Integrated Tungsten Oxide Nanowire Networks for ppb-level H2S Sensing. Procedia Engineering, 168, 272–275. https://doi.org/10.1016/j.proeng.2016.11.189

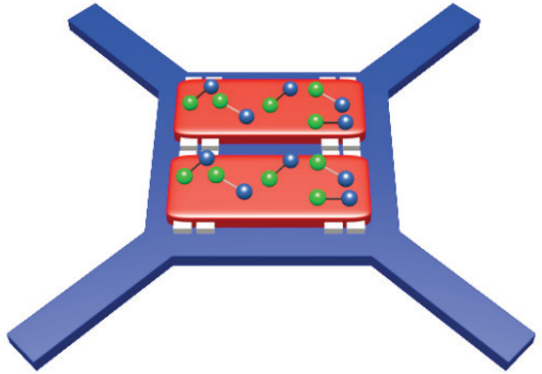
Lackner, E., Krainer, J., Wimmer-Teubenbacher, R., Sosada, F., Gspan, C., Rohracher, K., Koeck, A. (2016). CMOS Integrated Nanocrystalline SnO2 Gas Sensors for CO Detection. Procedia Engineering, 168, 1–2. https://doi.org/10.1016/j.proeng.2016.11.200

Reference project:
This work has been performed within the projects “MSP - Multi Sensor Platform for Smart Building Management” (FP7 -ICT-2013-10 Collaborative Project, No. 611887) and “RealNano - Industrial Realization of Innovative CMOS based Nanosensors” (Financial support by the Austrian Federal Government (in particular from Bundesministerium für Verkehr, Innovation und Technologie) represented by Österreichische Forschungsförderungsgesellschaft mbH within the framework of the „4. Ausschreibung Produktion der Zukunft nat. Projekte“ Programme (project number: 843598 project name: RealNano) is gratefully acknowledged).

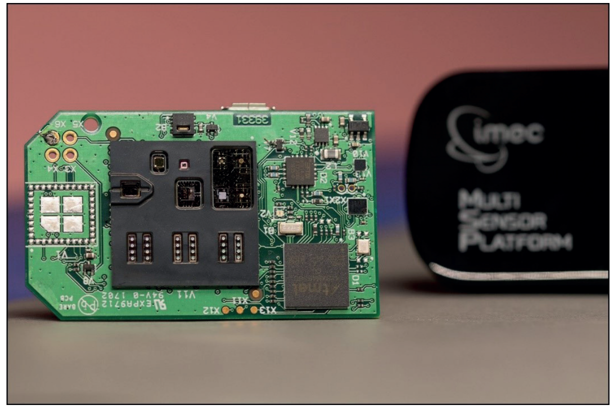
Reference link: http://www.multisensorplatform.eu



(a) TEM images of the dense tungsten oxide nanowire network; (b) Single tungsten oxide nanowires with fibrous texture (right).



Schematic of a double metal-oxide sensor on a CMOS micro hotplate chip reacting with gaseous molecules. ©mcl



The MSP demonstrator system implemented in a wearable wristband application comprises a total of 57 sensors, therefrom 48 sensors are based on thin metal-oxides fabricated on CMOS micro hotplates. ©mcl

B

TECHNOLOGIES

A Single-Chip Solution for Mid-Infrared Range Spectroscopy

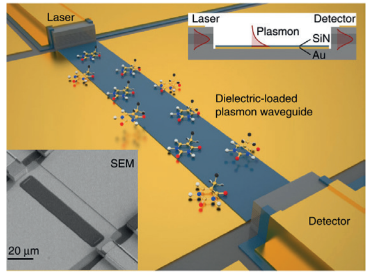
The integration of optical setups enables extremely compact and cost effective sensing solutions to be developed. The mid-infrared range of the light spectrum is particularly interesting, because the fundamental vibration-rotational resonances of molecules are found exactly within this spectral range. During recent years, quantum cascade lasers (QCLs) appeared on the commercial market and have enabled the realisation of compact, but not yet chip-integrated, optical systems. A functional heterostructure is formed from several hundred crystalline semiconductor layers, which determines the laser gain medium and such designable properties as emission wavelength and gain bandwidth.

Moving one step further, QCL heterostructures can be designed such that they possess photodetection capabilities. At laser bias, the device acts as a coherent light source and, at zero bias, as a detector for the same wavelength. These bi-functional devices allow single-chip sensors to be implemented in a straightforward way based on established mid-infrared quantum cascade technology. Once the bi-functional heterostructure has been grown, different parts of the chip can be used to build lasers and others to build photodetectors. The devices are connected with surface plasmon-polariton (SPP) waveguides that interact strongly with chemicals on the chip surface. An array of such laser-waveguide-detector units serves as a single-chip spectrometer, which can cover a part of the mid-infrared spectrum to address multiple absorption lines. The prototype sensor chip was tested with a mixture of isopropanol and water, and a limit-of-detection of 50ppm was achieved. Because the particular spectral region is defined by quantum design, the concept presented can be adapted to a wide range of applications.

<u>Reference publications</u>:

(1) B. Schwarz et al. "Monolithically integrated mid-infrared lab-on-a-chip using plasmonics and quantum cascade structures," Nature Communications 5, 4085 (2014). doi: <u>10.1038/ncomms5085</u>

(2) D. Ristanic et al. "Monolithically integrated mid-infrared sensor using narrow mode operation and temperature feedback," Applied Physics Letters 106, 041101. (2015). doi: <u>10.1063/1.4906802</u>



Sketch of the sensor chip comprising a laser, plasmon waveguide and detector with the inset showing an SEM image of the fabricated device.

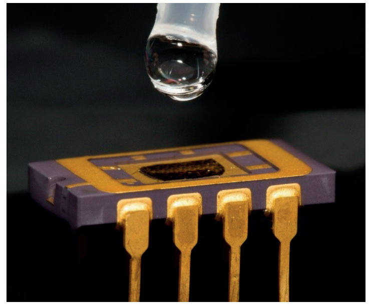


Illustration of the sensor chip; only one droplet is needed to detect the chemical concentration.

Additive Printing Technologies for Sensor Fabrication

Printing technologies provide powerful additive manufacturing tools for the fabrication of novel sensors.

In recent years, a new class of manufacturing techniques that are collectively known as additive manufacturing techniques have become available, which can offer significant cost, time and quality benefits to a variety of industries. Unlike subtractive methods, whereby masking and etching processes are used to remove material from the bulk material, structures or features are built up layer by layer by deposited material in an additive manufacturing process. Its advantages include the direct, CAD-driven, “Art-to-Part” processing method, avoiding the use of expensive hard-tooling, masks and vertical/horizontal integration methods. Thus, the overall number of manufacturing steps is reduced.

Screen printing is a well-known, versatile and cost efficient method that is used to fabricate electrodes and other printed sensor structures. Furthermore, screen printing has been applied to deposit active sensor materials such as functional recognition layers for optical chemosensors or ferroelectric polymers.

In addition to the traditional technical screen printing techniques, digital techniques such as inkjet printing or innovative Aerosoljet printing techniques are being more frequently used for the fabrication of sensors. The latter methods allow easy and rapid pattern changes to be made and provide the operator with good lateral control over both printed structures and deposited volume.

Furthermore, damage or contamination of substrates can be avoided using these contactless technologies.

Examples include the fabrication of enzyme-functionalised, biosensor electrode structures through inkjet printing, using different materials such as platinum, gold, carbon and silver, together with the development of certain specialized inks that are based on metal nanoparticles or metal organic precursor compounds.

The innovative Aerosoljet printing technique allows many materials to be processed that are cannot be processed using inkjet printing, but which offers the advantages of a digital technique. In addition, AerosolJet allows printing to take place on uneven substrates, over steps in the substrate, or in microchannels.

Reference to part A:

CiP and Sterilisation-Resistant Optochemical Oxygen Sensors for Process Monitoring (page 10).
Non-Invasive Oxygen Measurement in Sealed Containers - Smart Packaging (page 13).
PyzoFlex® for Environmental Monitoring: Large Area Sensing of Pressure and Temperature Changes (page 28).

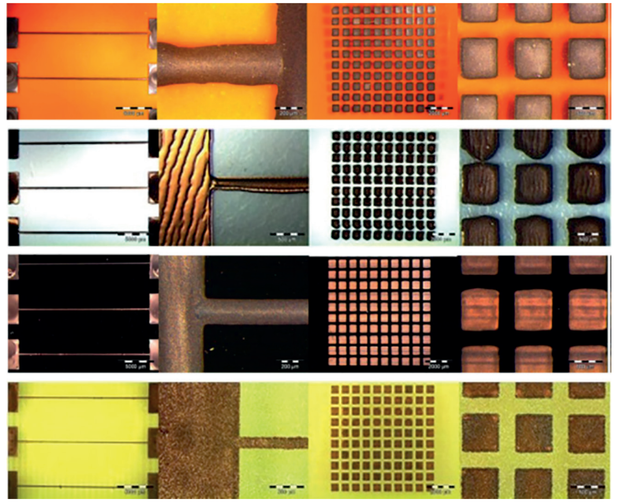
Reference projects:

INSPIRED
www.nano-inspired.eu

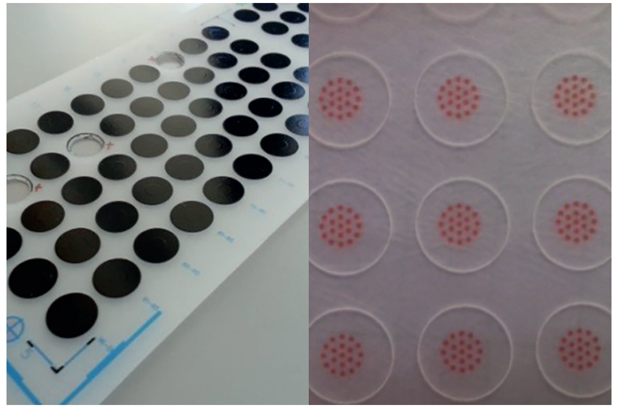
HI-Response - Innovative High Resolution Electro-Static printing of Multifunctional Materials (www.hiresponseh2020.eu)

JetBioSens – (HTI - Human Technology Initiative, Region of Styria)

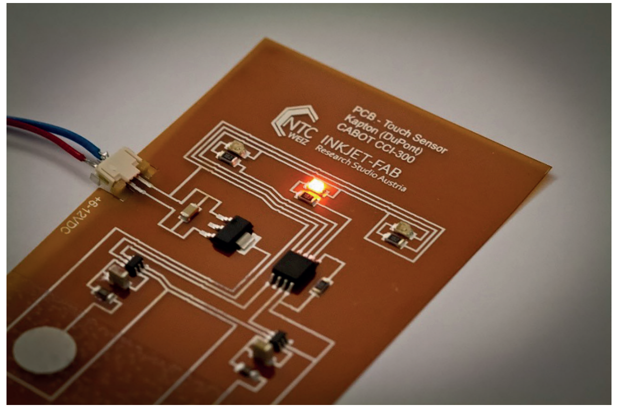
AFMI – AerosolJet for Medical Implants (Austrian Research Promotion Agency - FFG)



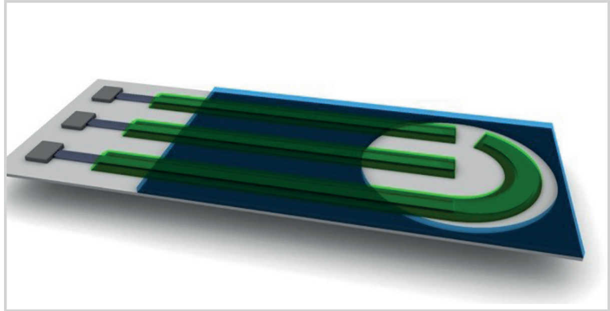
Inkjet printed nano-copper structures on various technological substrates (Source: NanoTecCenter Weiz Forschungsgesellschaft mbH).

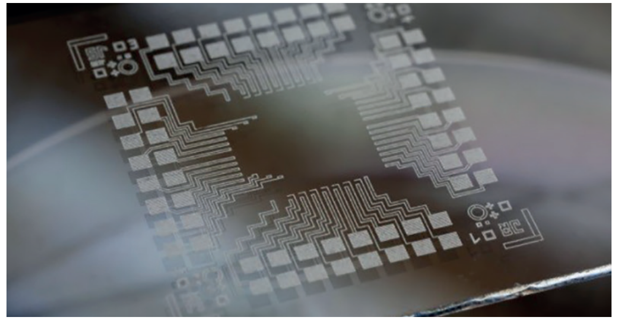


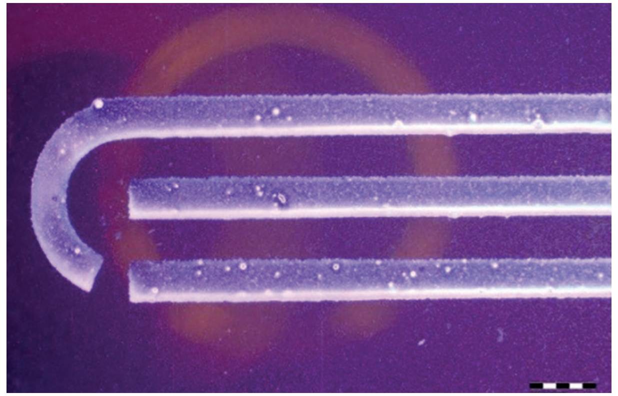
A batch of sterilisable optochemical oxygen sensor elements manufactured by means of screen printing.

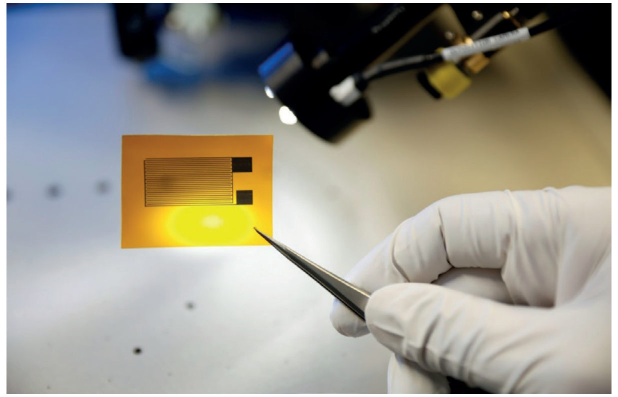


Hybrid capacitive touch sensor label based on inkjet printed nano-silver circuitry with SMD-components (Source: NanoTecCenter Weiz Forschungsgesellschaft mbH).









Inkjet printed electrochemical glucose biosensor based on platinum electrodes manufactured by jetting of a platinum nanoparticle ink.

Sensor structures manufactured by Aerosoljet printing of silver inks.

Assay Development

Highly sensitive immunological assays are developed and validated by following international guidelines, resulting in robust assays that work daily. Furthermore, immunological assays for Point of Care systems have been developed or adapted by drawing on the extensive expertise in the development and fabrication of innovative sensor and detection systems and the design of sophisticated Point of Care systems.

Assay Development

- Optimizing assay components to deliver a robust assay for reliable daily results
- Elisa development services
- Luminex development services (1-plex to 8-plex)
- Biochemical assay development services
- Immunological and enzymatic assays

Assay Validation

- Validation following the NIH Chemical Genomics Center Development and ICH Guidelines
- Plate uniformity, accuracy, precision, dilution linearity, stability
- Delivering an assay, for which you can trust the results

Transfer/Development of Assays to LFD or Point of Care Systems

- Adaptation of your assay to a Point of Care system or the delivery of a new system according to your needs, integrating the most advanced sensor and detection technologies

Assay Automation

- Integration of a robotic workstation that combines liquid handling, microplate handling and scheduling with multimode reader access, allowing total automation of your assay

Technologies

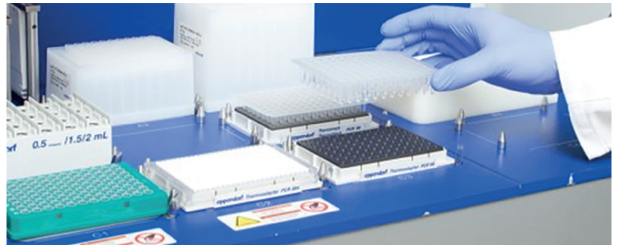
- UV, FI, TRF, HTRF, Delfia, Lance, Flash & Glow Chemo/Bioluminescence, Alphascreen/Alphalisa

Equipment

- Enspire multimode reader with injector, BioTek 405 Microplate Washer with magnet, Caliper Zephyr pipetting workstation, Caliper Twister II microplate handler (completely integrated system for total automation of Elisa assays), Luminex XMAP system

Sample Matrices

- Saliva, serum, plasma, urine



Pipetting workstation for assay automatization (Image: AIT).

Electrospinning of Polymer Nanofiber Sensors

Polymer nanofibers for ultra-fast optical gas sensors

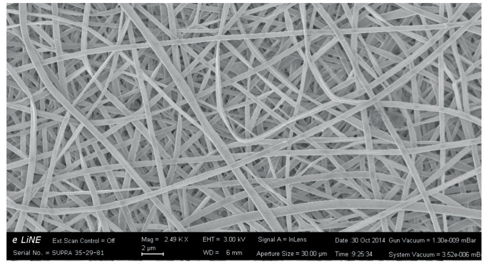
By means of electrospinning, many polymers can be processed into nanofibers that have diameters normally within the range of 50-1000 nm. During the spinning process, a layer of nanofibers is deposited on a substrate, resulting in the production of a non-woven, textile-like fleece with a high surface-to-volume ratio and outstanding analyte accessibility. Such nanofiber materials are well-suited for a broad range of applications, for example, in optical and electrochemical sensing or as three-dimensional scaffolds for cell culturing. When doped with luminescent senor dyes or indicators, these nanofiber layers are also well-suited for sensing applications where response time is a critical issue.

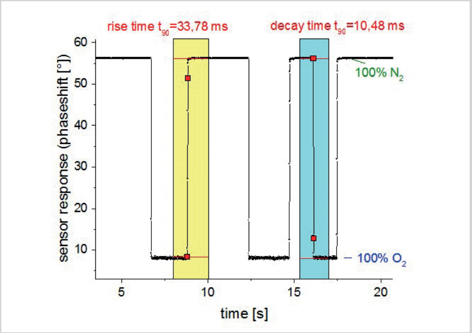
In general, optochemical sensors consist of luminescent dyes embedded in a compact, polymeric layer matrix. The response dynamics of such sensors are limited by the diffusion kinetics of oxygen in the polymer matrix; the thicker the layers, the slower the response. By electrospinning the oxygen-sensitive nanofibers, the response time t_{90} can be decreased from several seconds down to approximately 20 ms without losing signal quality. Prototypes of complete sensor systems with optical and electronic equipment are available that have a sampling rate of 10 ms, representing one of the fastest oxygen sensor systems currently available.
One application of such fast oxygen sensing systems is the detection of the O_2-concentration in exhaled breath. Due to the rapid breathing rate that occurs under physical stress, fast oxygen sensors with response times that are well below 50 ms are useful in spirometric devices.

Reference to part A: Breath Gas Monitoring by Optical Sensors (page 17)

Reference project: m.era.Net - APOSEMA (Advanced Photonic Sensor Materials)

Reference publication: C. Wolf, M. Tscherner, S. Köstler; Sensors and Actuators B: Chem., Vol.209, 1064–1069 (2015).


Electron microscopic image of electrospun polymer nanofibers (reproduced with permission of Elsevier).



Response characteristics of an optical oxygen sensor based on polymer nanofibers.

Fast, Compact and Low-Cost NIR Spectroscopy

Near-infrared (NIR) spectroscopy allows for the non-destructive quantification and classification of material and their properties. This measurement technology has therefore been widely implemented in scientific and industrial application scenarios for many decades, with a strong focus on inline measurements. The most important applications of NIR-spectroscopy include process analytical chemistry, quality control and material identification in many different fields including pharmaceutical, biological and chemical industry as well as agriculture, food industry and medicine. With the very recent advent of compact MEMS-based NIR microspectrometers (see Fig. 1), this measurement technology has turned itself into being among the best and economically feasible choices for numerous measurement applications. Obvious advantages compared to conventional NIR spectrometers include their very compact size (cm-scale), high ruggedness due to the lack of moving parts and their low price (< € 3000.- and expected to further decrease significantly). These properties combined with the ability for wireless communication, makes this technology also suitable for compact handheld devices (Fig. 2). Additionally, the possibility for contactless measurements in reflection geometry allows for easy and safe measurements of both sensitive and toxic materials or products. In most cases manual sample handling can be significantly reduced or even be omitted.

Reference link: https://tinyurl.com/LowCost-NIR

Reference project: COMET K-Project “imPACts” (www.k-pac.at)

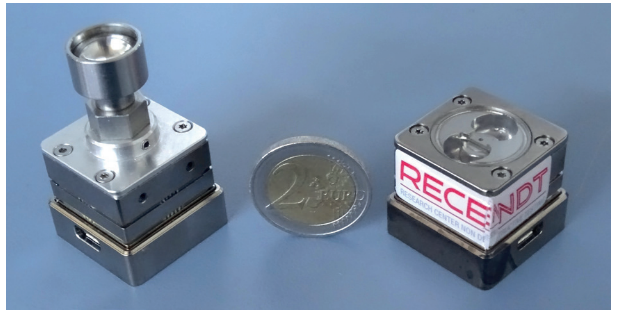


Figure 1: Photograph of two exemplary microspectrometers with a 2€ coin for size comparison. The left one features free-space coupling using collimation optics and the right one reflection optics.


Figure 2: Microspectrometer with Bluetooth communication module in combination with a smartphone for hand-held food quality control.

imPACts

Health Oriented Research in the Health Perception Lab

Competences in applying scientific methods allow to examine factors that affecting the perinatal programming of infants by:

- Testing methods for the analysis of sensory perception parameters
- Examining anthropometric and biomedical markers associated with metabolic programming in children
- Examining possible inter-relationships between the various anthropometric, sensory and biomedical parameters involved in the metabolic programming of children.

The data are recorded with the use of innovative technical aids, such as an advanced 3D Facial Analysis Coding System designed to determine taste preferences in babies and infants.

The use of both bio-impedance analysis and densitometry (PEA POD®) for infants makes it possible to determine the body composition of children and adults with precision, which then allows specialists to draw conclusions about their nutritional state.

Sensory cabins in the Health Perception Lab.

Measuring body composition via PEA POD®.

In addition the HPL develops product concepts that are set up in response to specific needs and to examine the special dietetic requirements of the target group. Product concept's practical feasibility, packaging design, sensory aspects and the accompanying information can be evaluated too, followed by the deployment of new technical processes, such as the above mentioned Facial Analysis Coding System and eye-tracking.

Face reading and other visual observation methods in the perception room.

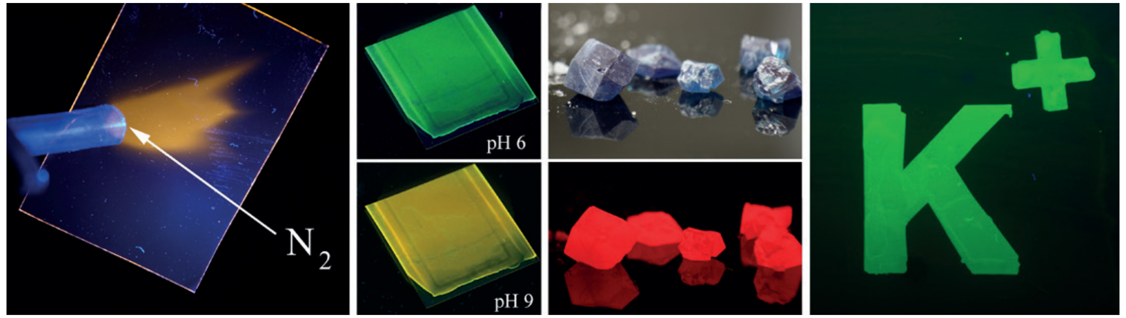
Also sensory-oriented trainings within game-based learning concepts allow to sensitize specific target groups (e.g. children) to use all their senses when eating and thus to be aware of how and what they eat.

High Performance Materials for Optical Sensors

The levels of oxygen, carbon dioxide, pH, and ions are among the most important parameters in various scientific and technological fields. Conventional analytical tools such as electrodes do not allow researchers to exploit the full spectrum of potential applications. Optical sensors offer unique advantages, because electromagnetic interference is absent, they are minimally invasive, come in a variety of formats, can be miniaturized and be produced at a low cost. The development of conventional and new applications has been hampered by the lack of availability of advanced materials for optical sensors.

Luminescent dyes and high performance materials have been newly developed that enable the sensing and imaging of numerous parameters (figure) such as gaseous species (oxygen, carbon dioxide, and ammonia), pH, physiologically relevant ions, glucose and temperature. They have been variously modified to allow these functions to be carried out across a variable dynamic range and, therefore, allow researchers to attain the optimal resolution for a desired application. For instance, sensors to measure physiological, trace and ultra-trace oxygen concentrations have been produced for application in gas and liquid phases and even in organic solvents.

They possess features of high chemical and photochemical stability, excellent luminescence brightness, a self-referenced read-out and low levels of interference from ambient light and background fluorescence. Advanced near-infrared probes allow the monitoring of metabolic parameters in highly scattering and absorptive media such as tissues. A broad range of nanoparticles have also been developed for taking extra and intracellular images of analytes using various methods (e.g., confocal microscopy, 2-photon microscopy). Most of the materials used are compatible with phase fluorometers commercially available from PyroScience GmbH and can be used in a wide variety of formats such as planar sensor spots, fiber-optic sensors and microsensors.



Gas sensors **pH sensors** **Temperature probes** **Ion sensors**

Examples of the optical sensors developed.

High Q-Factor Piezoelectric MEMS Resonators in High Viscosity Liquids: Challenges and Benefits

MEMS (micro electromechanical systems) sensors have found numerous application scenarios in modern technical systems and serve due to their miniaturised design to increase as almost invisible assistants our daily quality of living. These sensors are increasingly implemented in consumer products like smartphones, gaming consoles or for image stabilisation purposes in video cameras, but are already well established for the monitoring of technical processes by providing data on e.g. temperature, pressure and flow conditions of gaseous or liquid media. The highly sought after application field of continuous monitoring of liquid properties like density and viscosity on the other hand has not yet been permeated by MEMS bases solutions and still relies on sampling and expensive macroscopic measurement equipment.

MEMS resonators with high quality factors offer excellent measurement sensitivity when operated in resonance, since variations in resonance frequency and quality factor due to changes of the surrounding medium properties can be detected very accurately. Resonators immersed in liquids will exhibit increased mechanical damping with increased liquid viscosity and density, which in return leads to drastically reduced quality factors compared to operation in air. Therein lies the fundamental challenge: How to provide high quality factors in high viscosity liquids while still using the impact of damping on the resonator as a measurement signal. This challenge can be solved by utilising a new class of resonance modes called the roof-tile shaped modes as depicted in figure 2. These modes offer a quality factors of 10 even in highly viscous calibration standards S200 or D500 and a quality factor of 366 in water, which is the highest value of a mechanical micro resonator observed in water so far.

Piezoelectric excitation offers significant benefits over more commonly used approaches like electrostatic, thermal or electromagnetic actuation, especially when targeting operation in liquid media. Electrostatic actuation will not work in conductive liquid media, which typically limits this approach to non-liquid applications. Thermal excitation can result in local heating of the liquid, which will result in locally changed properties and a distorted measurement signal. Electromagnetic actuation always relies on integrated permanent magnets, which makes the assembly of such a system more complex and expensive. Piezoelectric thin films can be integrated directly into the MEMS fabrication process and with a proper passivation operation even in conductive liquids without reversely affecting the medium properties is feasible. Aluminium nitride is chosen as the piezoelectric material, since it offers compatibility with CMOS processes as well as bio compatibility and the potential to be operated in harsh environments.

The developed MEMS resonators depicted in figure 1 offer high quality factors in high viscous liquid media and therefore a promising platform for future inexpensive liquid monitoring solutions. The liquid under test can be characterised at varying controlled temperatures (see figure 3). This approach provides additional information on liquid properties and further opens up potential new application scenarios e.g. in the field of bio chemical analysis.

Reference publications:

Pfusterschmied et al. “Temperature dependent performance of piezoelectric MEMS resonators for viscosity and density determination of liquids,” J. Micromech. Microeng. 25 (2015) 105014. doi: 10.1088/0960-1317/25/10/105014 (Highlight of the year 2015, www.iopscience.iop.org/0960-1317/page/Highlights-of-2015)

Kucera et al. “Characterization of multi roof tile-shaped out-of-plane vibrational modes in aluminum-nitride-actuated self-sensing micro-resonators in liquid media,” Appl. Phys. Lett. 107 (2015) 053506. doi: 10.1063/1.4928429

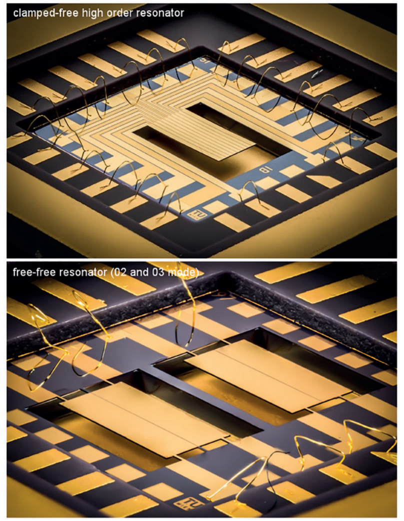


Figure 1: Typical MEMS resonator designs with shaped electrodes for mode selective operation at high order modes (i.e. clamped-free as an example) and additional tailored boundary conditions for a low loss support (i.e. quasi free-free as an example).

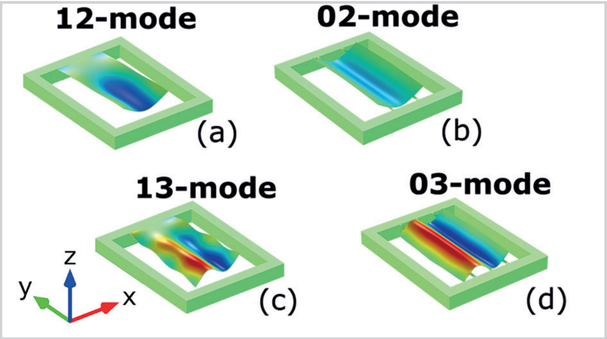


Figure 2: Finite element analysis of the first and second order roof-tile shaped modes in different boundary configurations: clamped-free (a,c) and quasi free-free (b,d).

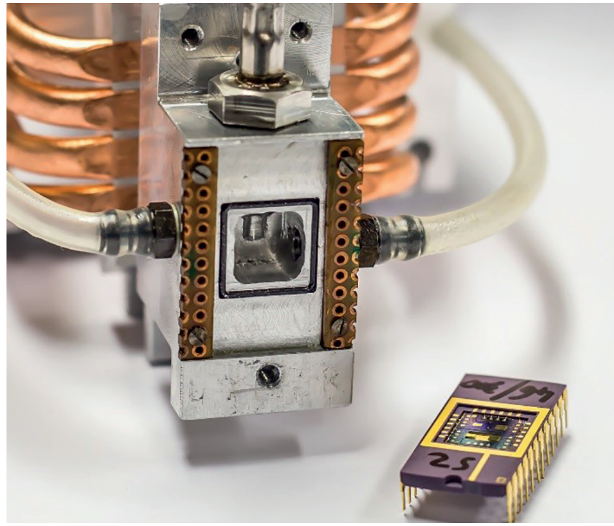


Figure 3: Setup for measurements at controlled temperatures (from Pfusterschmied et al. J. Micromech. Microeng. 25 (2015) 105014).

Inkjet Printing

Inkjet printing is a method whereby droplets are dispersed on-demand from a liquid reservoir in response to various actuation principles, including thermal and piezo-electric principles.

The current challenge is to print on curved substrates as well as on substrates that consist of different materials such as glass, plastics, textiles and metals. Surface recognition and treatment to ensure adhesion are crucial to obtain high quality prints.

A special example of this technology is 3D ink jet printing, which is based on a 3D CAD file, and layers of UV-curable liquid polymer are sprayed onto a substrate. These layers form the required 3D model or part. Certain complex geometrical shapes require the addition of support materials, which can later be removed by washing the 3D object in water.

The technology can be used to create smooth, detailed prototypes from different types of photopolymers. The advantages of this technology are the high degree of flexibility in terms of the structures produced and materials used as well as the efficient use of building material.

The inks and their formulations are constantly being developed in order to include a broader range of materials and more functionalities.

The development of the ink printing process of metal-based, nanoparticle-enriched conductive inks is a big issue. These inks can be applied to print circuit boards, RFID antennas and electric grids on screens and bus bars on photovoltaic cells.

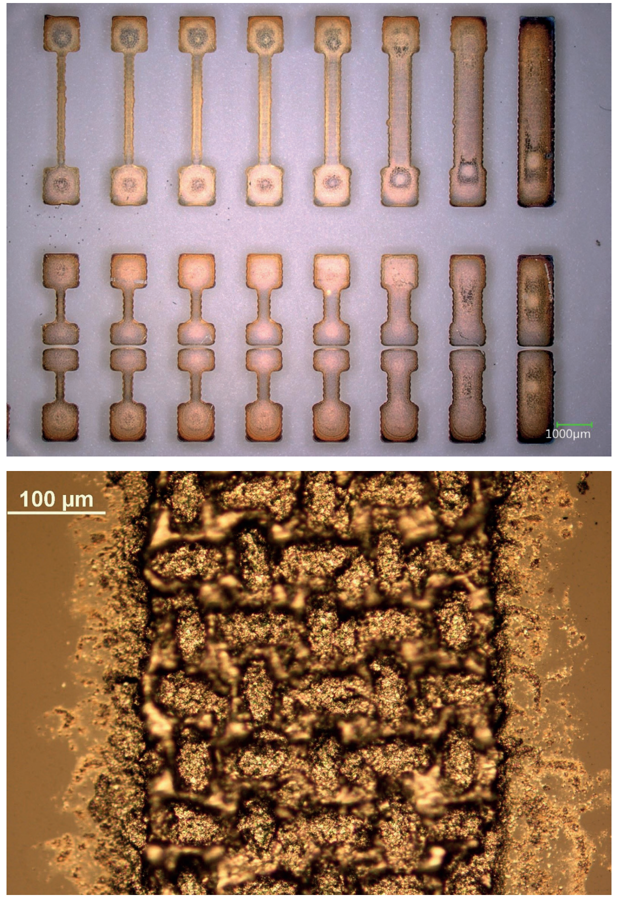


Photo (a) and microscopic image (b) of inkjet-printed metallic inks that form conductive lines for printable electronics.

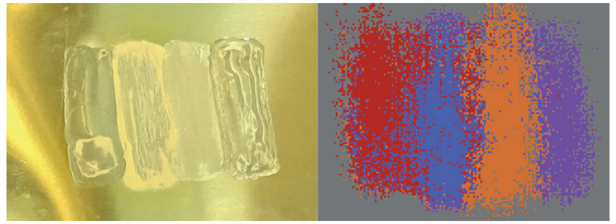
Another field of development is that of new, non-soluble, UV-curable inks that can be used for labelling food packaging and printing 3D parts that have the potential for skin contact.

A topic that is based on the development of new hardware is that of printing on curved surfaces, which requires the application of mechanical engineering, automation and 3D-printing skills.

Reference projects:
NextFactory (www.nextfactory-project.eu)
DiMaP (www.dimap-project.eu)
iTextil
ePaper (www.tinyurl.com/e-Paper-wall)
ANIIPF (www.tinyurl.com/ANIIPF)
MEM4WIN (www.mem4win.org)
AddManu (www.addmanu.at)

Low-Cost MIR Hyperspectral Chemical Imaging Solution

Non-destructive spatially resolved chemical identification of macroscopically sized samples is of great benefit in many fields. A key technology to gain this kind of information is mid-infrared (MIR) hyperspectral imaging. Commercially available MIR hyperspectral imaging systems are usually expensive, not portable, not capable of real-time acquisition and bound to fixed sample sizes, making them unsuitable for many potential application areas. Due to recent advantages in MIR spectroscopy technology, accompanied by significant cost reductions in hardware, it is now possible to offer customer specific low-cost (less than € 500 hardware costs) imaging solutions, capable of imaging macroscopic samples at large distances of tens of cm. The involved hardware offers high ruggedness and very compact size making it particularly suitable for handheld devices and industrial applications. Despite its low price this technology in combination with multivariate image analysis can achieve high accuracies with short acquisition times (video frame rate), making it especially useful for e.g. real-time quality control or inline sorting of materials. The main fields of application are currently found in industrial process analytics and process control in different industries including food, pharmaceutical, biomedical and chemical industry as well as in forensics, cultural properties science or atmospheric gas sensing applications.



Photograph of four different types of glue (left) and the processed spatially resolved hyperspectral chemical image (right); each of the four colours corresponds to one type of glue that was identified from the hyperspectral image data by a classification algorithm based on the measured chemical properties.

Reference link: https://tinyurl.com/LowCost-HSI

Reference publication: J. Kilgus, R. Zimmerleiter, K. Duswald, F. Hinterleitner, G. Langer and M. Brandstetter, "Applications of a novel low-cost hyperspectral imaging setup operating in the mid-infrared region", EUROSENSORS 2018, MDPI Proceedings, Vol.2, Issue 13, September 2018

Reference project: COMET K-Project "imPACts" (www.k-pac.at)

Materials and Development of Components

While developing sensors, the development of both the core sensing technology and the mechanical components and housings are important. Such developments involve the selection of materials and production processes that include the production of prototypes and tests of the final products. The entire profile of properties, covering its functionality, reliability and work life must be considered and optimised with regard to the specific application.

Currently, the design of the polymeric components and the processes related to their production are performed using advanced numerical methods such as simulations.

In general, the following expertise areas can be applied during sensor development:

- Material selection
- Material development and characterisation
- Optimised design with regard to materials
- Analyses of service strength and calculation of durability
- Quality and functionality assessments of surfaces
- Mechanical testing of components
- Selection and design of production processes
- Modelling and simulation

Micro & Nano Technology

Fabrication, Characterization, Simulation and chemical surface modification

Functional thin films and coatings have been developed using the opportunities offered by micro- and nanotechnology to devise and implement innovative concepts and systems for biomedical diagnostics, lab-on-a-chip components and sensors. Apart from these specific research applications, customized services have also been offered to other industrial sectors for the simulation, fabrication and characterisation of micro- and nanotechnological structures and devices. Our expertise lies in our ability to combine semiconductor technologies and thin-film processes with innovative concepts from the micro-, nano- and bio-science fields.

Fabrication

- Material inkjet printing: functional materials (e.g., metals, bio-inks) on various substrates (film, bulk)
- Magnetron sputtering: more than 30 different materials available
- Evaporation: more than 10 different materials available
- Micromilling (e.g., for microfluidic application)
- Optical, electron-beam and AFM lithography

Characterization

- Atomic (AFM), Chemical (CFM), Magnetic (MFM) Force Microscopy
- Scanning Electron Microscope (SEM)
- Contact angle measurement tool
- 4-point probe station: electrical measurement up to 20 GHz, magnetoresistance characterization
- Electrochemical potentiostat (e.g., electrochemical impedance spectroscopy)
- setup for the characterization of integrated optical waveguide devices
- UV-VIS-NIR-MIR spectrometer, monochromator

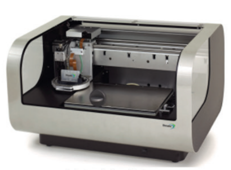
Simulation

- Magnetic Systems
- Photonic waveguides
- Optical systems
- Microfluidic

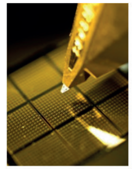
Chemical surface modification and functionalization

- Development of protocols
- Formulation of inkjet printable (bio)functional inks
- Hydrogel technology

References to part A: Monitoring Pathogens in the Oral, Nose and Throat Cavities and Determining their Levels of Antibiotic Resistance in order to Provide Targeted Therapy for the General Practitioner and Dentist (page 22); Nanoprobe-Based Mix and Measurement Immunodiagnostics (page 23); Silicon Nitride Based Photonic Sensing Devices for Medical Diagnostics (page 33)



Material printer



Probe station

Simulation cluster (Images: AIT)

Micro-Stereo-Lithography (μ-SLA)

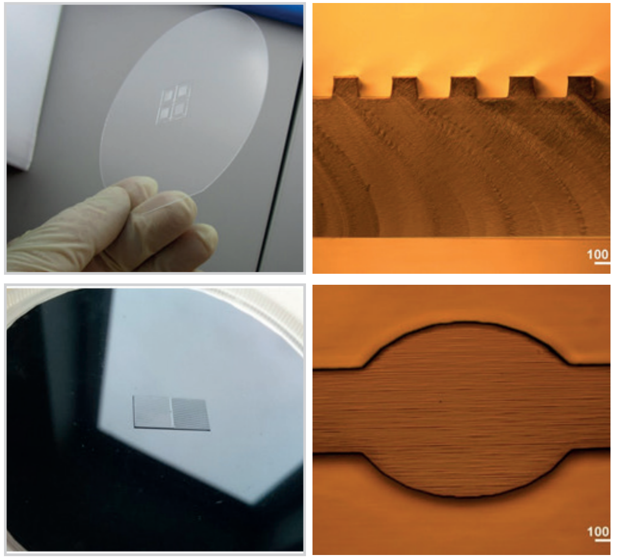
The technique of micro-stereolithography allows small features in photosensitive materials to be directly structured, without the use of photomasks or subtractive processes.

First, a computer-generated, 3D model is divided into layers using software tools. During the printing process, a laser spot scans each layer and cures the photosensitive materials at the given areas. In this way, the printer creates a replica of the CAD model, layer by layer. The stereolithographic process is a rapid process that enables the creation of macroscopic objects a high level of resolution.

This method can be used to create prototypes of different devices:

- Lab-on-a-chip devices
- Microfluidic devices and the fabrication of biomimetic structures

Reference projects:
ePaper (www.tinyurl.com/e-Paper-wall)
ANIIPF (www.tinyurl.com/ANIIPF)



Picture and microscopic picture of patterned surface and of a microfluidic channel .

Nanoimprint Lithography

Nanoimprint lithography (NIL) is a process whereby nanostructures are copied from a mould (master) form using curable materials. During the NIL process, the polymer is mechanically deformed, and NIL can be used to create high-resolution, complex, multi-layered nanostructures without using sophisticated optics.

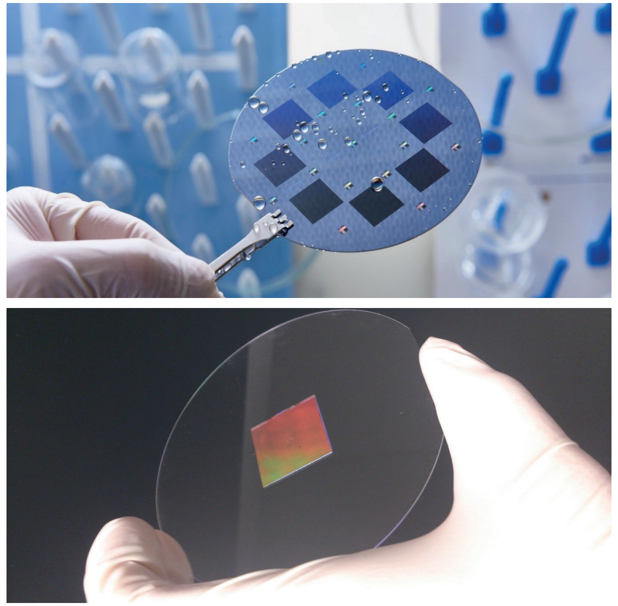
By creating a stamp substrate of silicon, quartz or nickel from the master mould, the process costs can be reduced dramatically and thousands (or even more) imprints can be created using a single master mould. Furthermore, precise nano-scale structuring over large areas is made possible, either at the wafer scale, step and repeat stage or during the continuous rolling process.

Therefore, NIL is a high-throughput and high-resolution method that can be used to create patterned features, from 10 nm up to several tenths of a µm, which allows the application of complex, multilayer designs to a very broad range of substrates using functional materials.

The range of materials available allows more freedom to design new functional materials and sensors, which results in a highly versatile range of applications:

- In biotechnology, where surfaces are nano-patterned for cell growth experiments
- Micro-needles used for intradermal and transdermal drug delivery
- Sensors, with metal patterns structured for Surface Enhanced Raman Spectroscopy (SERS)
- Microfluidic and Lab-on-a-chip (LOC) devices with high and well-defined aspect ratios
- Optics, where the formation of metamaterials with a designable refractive index and the structuring of LED devices are very prominent applications.

Reference projects:
NILgraphene (www.tinyurl.com/NILgraphene)
Platon SiN
NILbiochip (www.tinyurl.com/NILbiochip)
NILquantumdot I (www.tinyurl.com/NILquantumdot)
NILquantumdot II (www. tinyurl.com/NILquantumdot-II)
SolarTrap (www. tinyurl.com/SOLARTRAP)



Nanoimprinted, UV-curable polymer on a silicon and glass substrate with strong refractive colour effects.

Nanoimprint Lithography: Micro- and Nanofabrication for Chemo- and Biosensing Applications

Fabrication of microfluidic and optical micro/nanostructures using Nanoimprint lithography (NIL) in Roll-to-Roll (R2R) processes

Driven by global trends that are increasingly favouring personalized medicine and Point–of-Care testing, a steadily increasing demand exists for miniaturized analytical systems. At the same time, the use of cell-based assays in applications such as high throughput screening and toxicity testing is gaining more importance, due to efforts to reduce the costs of drug development and the number of animal experiments.

Therefore, novel assay formats are continuously being developed, and many innovative microfluidic and lab-on-a-chip systems have progressed from prototypes into real applications. The adoption of such bioanalytical systems by industry and their eventual commercial success will be greatly dependent on the implementation of new, cost-efficient production technologies. Low production costs and high throughput in the fabrication of precise micro- and nanostructured devices are among the most important criteria for such production technologies.

Nanoimprint Lithography (NIL)-based methods directly address this demand. The desired micro- or nanopatterns are replicated by imprinting a feature on a stamp onto a thermoplastic or UV-curable polymer substrate. Such imprinting methods can also be carried out using the continuous Roll-to-Roll (R2R) process with polymer foils and a roller-based stamp. Different types of structures, geometric shapes and length scales can be easily integrated onto foil substrates in a single processing step by use of R2R imprinting:

- Micro-/Nanofluidics
- Nanooptics (Plasmonic and Photonic Crystal structures)
- Microoptic structures
- Micro-/Nanostructured surfaces for cell culture

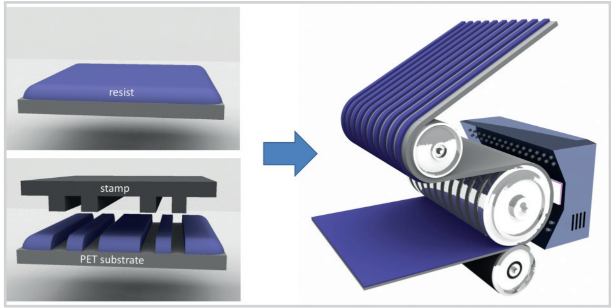
As in production processes used in graphical printing or papermaking, R2R processes allow for the rapid production of a large number of micro- or nanostructured pieces and, thus, result in low unit costs.

Reference to part A+B: Plasmonics for Ultrasensitive Biosensors (page 27); Optical Simulation of Sensors Systems (page 63)

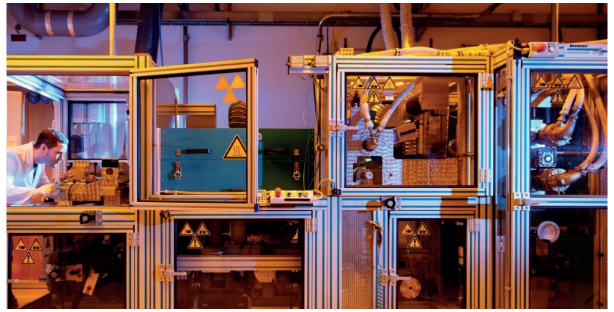
Reference projects:

R2R Biofluidics - Large scale micro-and nanofabrication technologies for bioanalytical devices based on R2R imprinting (www.r2r-biofluidics.eu). This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement n° 646260.

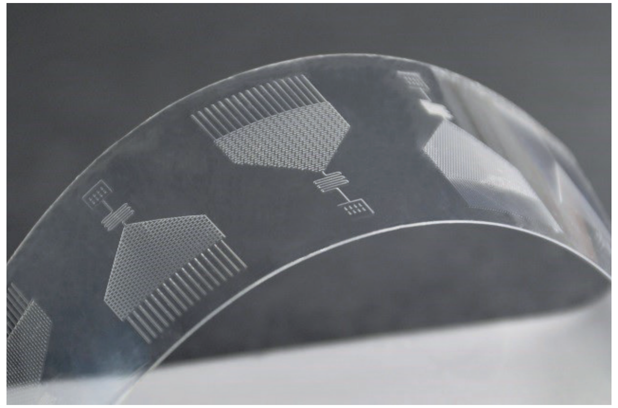
Research Studio Austria (RSA): Modular microfluidic Systems on Foil - MoMiFlu@Foil (www.tinyurl.com/MOMIFLUFOIL).



Schematic illustration of Nanoimprint Lithography (NIL) in batches and Roll-to-Roll (R2R) production.



Roll-to-roll (R2R) Nanoimprint Lithography Pilot Line.



Microfluidic structures imprinted on polymer foil.

Microstructured polymer foil assembled on 96-well micro-titer plate.

OCT Imaging on the way to monitor biotechnology & production

Optical Coherence Tomography (OCT) represents a modern imaging technology, able to image sub-surface structures. Initially, it was developed for ophthalmology, where its use is widely accepted. In the mean-time, its impressive potential has also been demonstrated in other areas of medicine and biology, as well as in the field of industrial inspection and process control.

OCT imaging is based on an interferometric detection scheme (see Figure 1), allowing to obtain information from the sample inside. Imaging is done by scanning the light across the sample. Depending on material and used wavelength, varying penetration depth and resolution can be reached. Typical depths are up to some mm and depth resolution is up to 1 µm. Mostly, light in the near infrared range is used, enabling larger penetration depth than white light and completely non-destructive testing.

Those features allow for a wide range of use-cases, like endoscopic applications or process control in pharmaceutical, food and packaging industry. Coatings on such specimens can be properly characterized with respect to coating thickness, as well as detect hidden defects. Furthermore, scattering materials like coloured polymer materials and composites can be investigated.

Its capability to characterize multi-layer foils and to extract thicknesses of individual layers makes it a perfect inline capable sensor in the production processes of such factories. In particular, it is used in extrusion process monitoring, inspection of polymer bonding or welding seams (see Figures below). Currently, a lot of research is done to miniaturize the OCT devices, allowing for better integration in customized solutions.

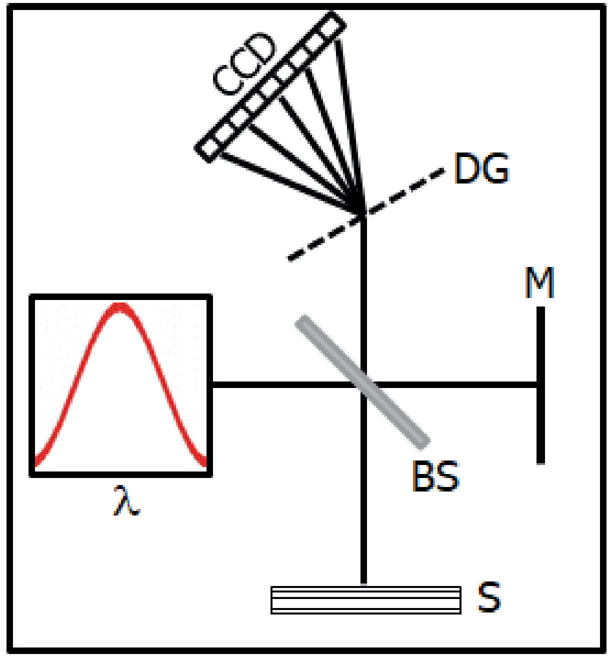


Figure 1: Scheme of a spectral domain OCT. OCT is based on an interferometric detection scheme. For this, light from a broadband coherent source is focused on the sample. On its way to the sample its split into two paths: i) a path to the sample and ii) a path to a fixed mirror. The reflected light of both paths give rise to an interference pattern, which, in spectral domain OCT, is detected in a spectrally sensitive manor. The depth scan can be calculated from the Fourier-transform of the so acquired spectra.

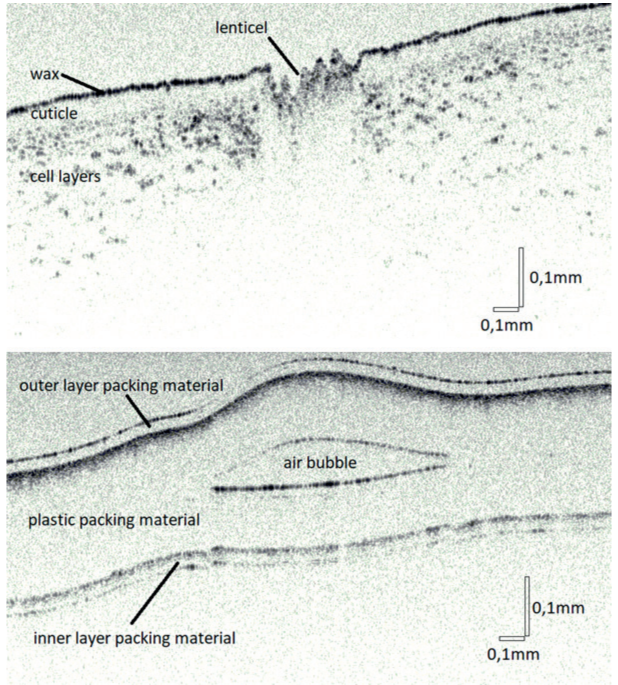


Figure 2: Example use cases of OCT imaging. Upper Image: cross section of surface area of an apple. Lower Image: cross section of welded plastic packaging film. An unwanted air bubble can be clearly identified.

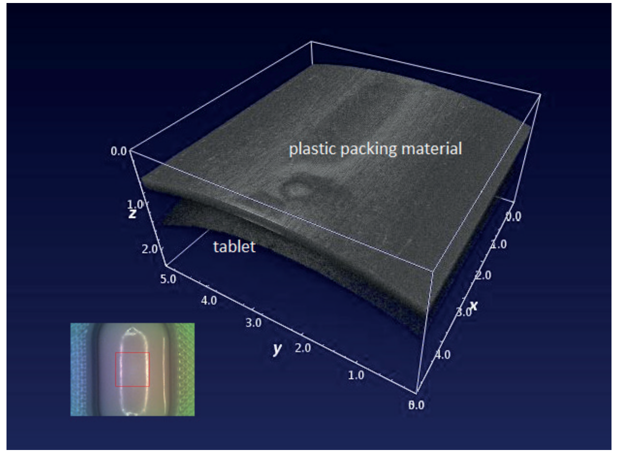


Figure 3: 3D OCT scan of a packaged tablet. The inset in the lower left corner shows a visual image of the table in the package. The red square indicates the scanned area (5 mm x 5 mm). It can be seen that observing the tablet through the packaging material is possible.

Reference publication:
Alexandra Nemeth et al., Optical Coherence Tomography – Applications in Non- Destructive Testing and Evaluation, Ch.9, Intech 2013, p. 163-179
www.intechopen.com

Reference link: https://tinyurl.com/OCT-Technology

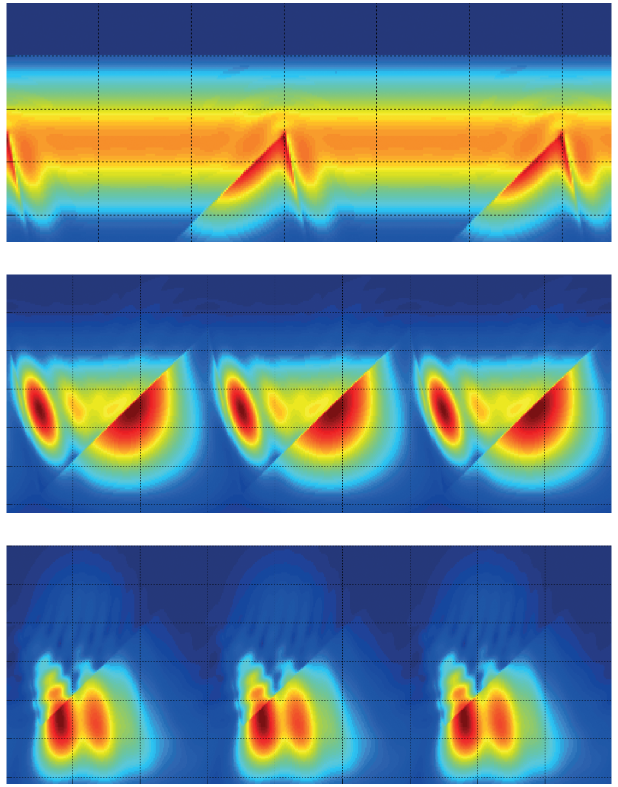
Reference to part A: In-Line Quality Control for Tablet & Pellet Coatings by OCT (page 12)

Optical Simulation of Sensor Systems

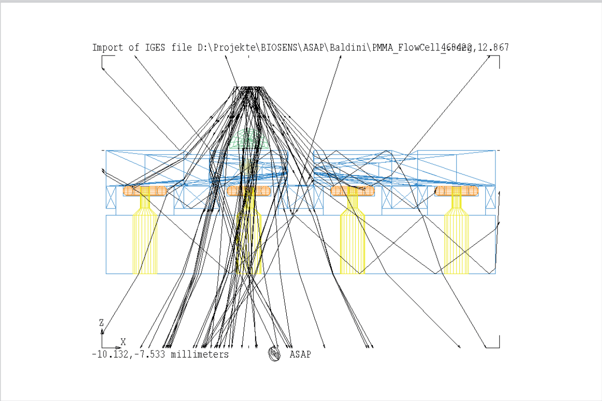
Light management of optical sensors

The performance of optical sensors in terms of effective light management, signal-to-noise-ratio, easy integration and miniaturization of the system plays an important role. All these aspects can be considered by running optical simulations. Even systems that are highly complex with regard to the required properties can be optimized. Since the simulation is carried out by using appropriate computer models, the time required and costs of development can be significantly reduced. The propagation of light and effects of optical elements can be calculated highly accurately using tools like ray-tracing. To consider wave optical phenomena such as diffraction effects, additional tools such as the finite different times domain method (FDTD) are indispensable.

These simulation tools allow researchers to gain all the information needed from the simulation model with regard to the influence of the individual optical elements on the complete optical sensor system. A complete description of the optical behaviour of complex optical sensor systems, made up of diffraction gratings or other diffractive optical elements and micro-lenses or other refractive or reflective elements, can only be handled by using a special tool: a multiscale-simulation approach that has been developed in-house. This approach combines ray-tracing and FDTD-simulation methods and can be used to design, simulate and optimize light management in complex optical sensor systems.
By applying our comprehensive simulation portfolio, we are able to design and optimize the light management of optical systems for many different applications and, specifically, for optical sensor systems.



Time study of the interaction of a plane wave with an asymmetric diffraction grating for light coupling.



Ray-tracing simulation of a biochip based on fluorescence detection.

Reference to part A+B:

CiP and Sterilisation-Resistant Optochemical Oxygen Sensors for Process Monitoring (page 10).
Nanoimprint Llithography: Micro- and Nanofabrication for Chemo- and Biosensing Applications (page 58).
Implantable Fibre Optic Microsensors for In-Vivo Monitoring (page 19).

Reference project:

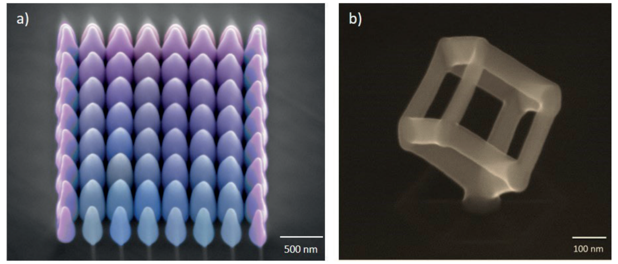
Research Studio Austria (RSA): Green Photonics
(www. tinyurl.com/GreenPhotonics)

Rapid Prototyping on the Micro- and Nanoscale via Focused Particle Beams

The growing demand for highly miniaturized electrical, optical and mechanical sensor components results in a corresponding demand for rapid prototyping capabilities. Focused electron and ion beam methods, which have unique capabilities, are arguably the most promising approach to meet these challenging demands. In electron beam lithography, targeted areas of initially prepared resist films are exposed to a nanometre-sized electron beam, which locally alters the material with even highly complex shapes. After the exposed areas have been removed using a wet chemical process, a mask is generated that can be used for subsequent steps of the process such as material deposition or etching.

Finally, the mask is lifted off, exposing the shaped structures, which can be used directly or in additional steps of the lithography process. In order to produce the desired structures on very challenging (e.g., non-flat or highly exposed) surfaces, electrons and ions also allow a direct-write fabrication without any pre- or post-treatments. To achieve this, functional precursor gases are injected in a vacuum chamber. The nanometre-sized particle beams then dissociate the precursor molecules into functional parts (e.g., a metal), which remain localized on the surface. The highly accurate nature of the beam control allows not only for the fabrication of complex structures at a spatial resolution of less than 10 nm, but also is one of the few techniques that allows for the direct-write fabrication of free-standing 3D architectural structures. Therefore, the combination of these approaches, lithography and direct-write fabrication, enables the creation of prototypes rapidly with a size of a few millimetres down to the nanoscale.

Reference to part A: Plasmonics for ultrasensitive nanosensors (page 27)



(Left) Pt-C nano-pillar array fabricated using a focused electron beam induced deposition process, which also allows the direct fabrication of free-standing 3D structures such as the Au nano-cube (right) (images: Harald Plank, FELMI-ZFE, Graz University of Technology).

Small- and Wide-Angle X-ray Scattering for Solids

Small- and wide-angle x-ray scattering gives direct access to the nanoscale environment. Wide-angle scattering, especially in the form of diffractometry, is commonly used to determine distances between atomic planes and the orientation of crystal unit cells. The smaller the angles acquired, the larger the structures investigated; small-angle scattering can be used over scales up to hundreds of nanometres.

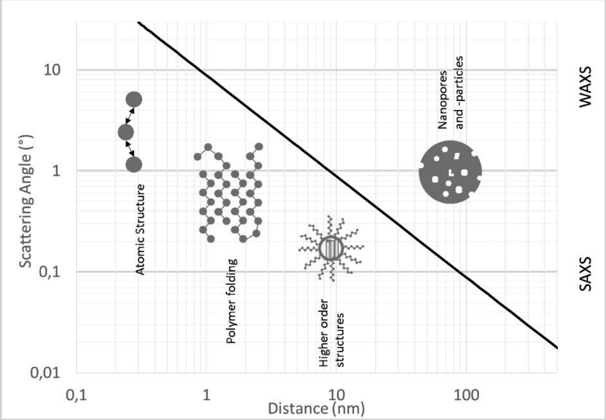
Hence, this method is especially useful for analyses of biological systems, many elements of which occur in these size ranges. Micelles and proteins can be accessed, and their sizes and shapes can be estimated. While the costly use of the synchrotron is often necessary to perform a detailed analysis, the less expensive laboratory equipment used to access the small-angle range can offer a good alternative.

A further application is in the estimation of the porosity of materials by assessing their scattering profiles, thus, complementing gas adsorption measurements. In contrast, however, the sealed pores inside the material can also be accessing using the former method).

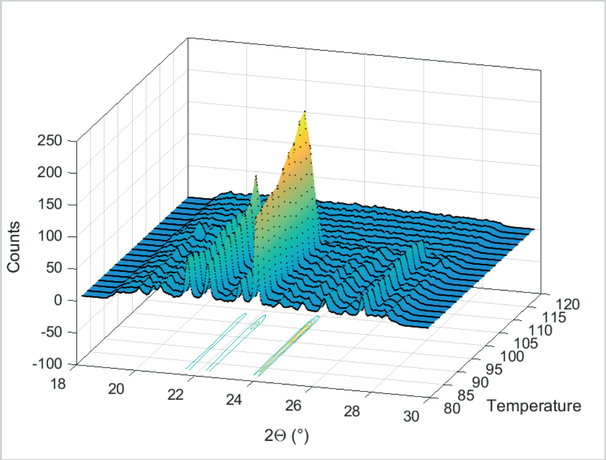
Once SWAXS and DSC (differential scanning calorimetry) have been combined in a single housing as planned, the thermodynamic and physical aspects of the melting, solidification and crystallization processes will be able to be simultaneously monitored. This will allow a deeper insight to be gained with regard to the behaviour of materials on the nanoscale and, therefore, support the development of increased quality and safety parameters for the latter.

The combination of SWAXS and DSC has been proven useful in pharmaceutical applications, whereby both the physical structures of samples and the polymorphic characteristics of the materials can be examined.

<u>Reference publication</u>: Wahl V, Saurugger EM, Khinast JG, Laggner P; Application Note XRD 601 (2015); SWAXS in Protein Drug Development; Link: http://my.bruker.com/acton/ct/2655/p-00d5/Bct/-/-/ct23_0/1



Size ranges and structures accessible using small- and wide-angle x-ray scattering.



Deformation and melting of a crystal during heating, monitored with x-ray scattering.

Notes

Notes

IMPRESSUM

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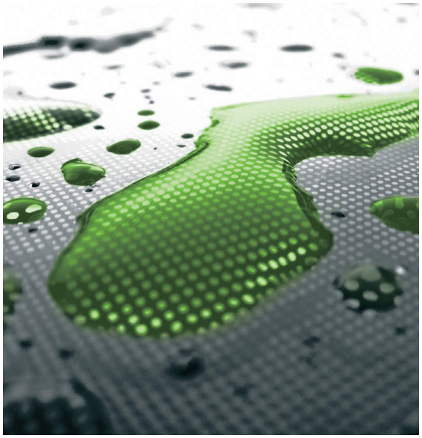

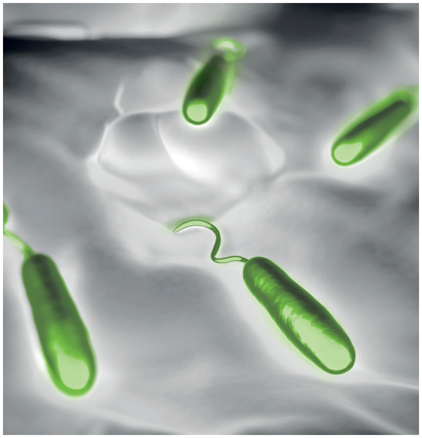

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