BIO NANONET

NEWSLETTER

02/2018

June 2018

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- Exchanging knowledge within the NANOGENTOOLS Project, Secondment of Bio-NanoNet to NIA (Nanotechnology Industries Association), March/April/May 2018, Brussels, Belgium & Nicosia, Cyprus
- Think Tank - Life Sciences in Digital Transformation, 5 April 2018, Graz, Austria
- Workshop: The Blockchain Technology for new Applications, 17 April 2018, Graz, Austria
- BioNanoMed 2018, 25 – 27 April, 2018, Graz, Austria
- EUFEPS Annual Meeting 2018, 24 – 26 May, 2018, Athens, Greece
- ETPN Annual Forum 2018, 28 –30 May, 2018, Berlin, Germany
- EU Brokerage Event on KET in Horizon 2020, 7 June, 2018, Mainz, Germany

Conference calendar

- BioNanoNet events
- BioNanoNet on-site-events

Finally

Editorial -
Contemporary issues from the network

Dear Ladies and Gentlemen,

ahead of summer we are pleased to update you with this newsletter on exciting activities of the last months as well as upcoming tasks on our agenda to support our members. The **nanomedical focus** which spanned over the past months highlighted in a special "nano-innovation" session co-organized by BioNanoNet and presenting several members as speakers and/or poster presenters during the international conference BioNanoMed. Furthermore, our members benefitted from our role as "enabler" and supporter of promising research results along the way to the market, e.g. in terms of participation in the healthtech-translational services (former nanomedTAB).

Apart from this the **networking activities** are focussed these weeks intensively on the development and initiation of project proposals, mainly for the 2019-call series within H2020-funding program, but not limited to those. The areas in which BioNanoNet members can provide top-level expertise for projects span over a broad range enabling them to participate in proposals answering to calls in NMBP, ICT, FOF, SPIRE, Biotec, BBI, MSCA-ITNs, BHC, FET, etc. Participation in brokerage events and stakeholder meetings are of course channels to spread the word about the excellent expertise of our members.

Once more we like to announce our **autumn meetings** (Graz, September 12th - 14th) which will take place at the premises of Medical University of Graz, JOANNEUM RESEARCH – HEALTH, University of Graz, as well as Technical University of Graz – thus, at different venues to directly access scientific expertise and to give you space to discuss future collaborations with the BioNanoNet community. Furthermore, international colleagues from ongoing EU-projects will be present at these meetings, opening the opportunity to find fitting collaborators for your activities.

We wish you a great summer and hope to see you at our meetings in September!

Sincerely,

BioNanoNet-Team

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BioNanoNet *project presentations*

ACEnano: pursuing analytical and characterisation excellence in nanomaterial risk assessment

Nanomaterials are man-made materials of a size thousands of times smaller than the width of a human hair. They have fascinated scientists and industry with their unique and unpredictable properties, which have given rise to an endless variety of new applications in every sector of technology and medicine. As a result, an ever-increasing number of nanomaterials are entering the market in everyday products spanning from healthcare and leisure to electronics, cosmetics and foodstuffs. However, the novelty in exploitable properties may be mirrored by new hazards and, in order to manage these, a well-founded and robust legislative framework that will ensure safe development of nano-enabled products is needed.

The development of such a framework has proven particularly challenging; at the heart of the challenge lies the difficulty in the reliable and reproducible characterisation of nanomaterials given their novelty, variety in properties and forms and dynamic nature, particularly in complex conditions, such as within different biological, environmental and technological compartments.

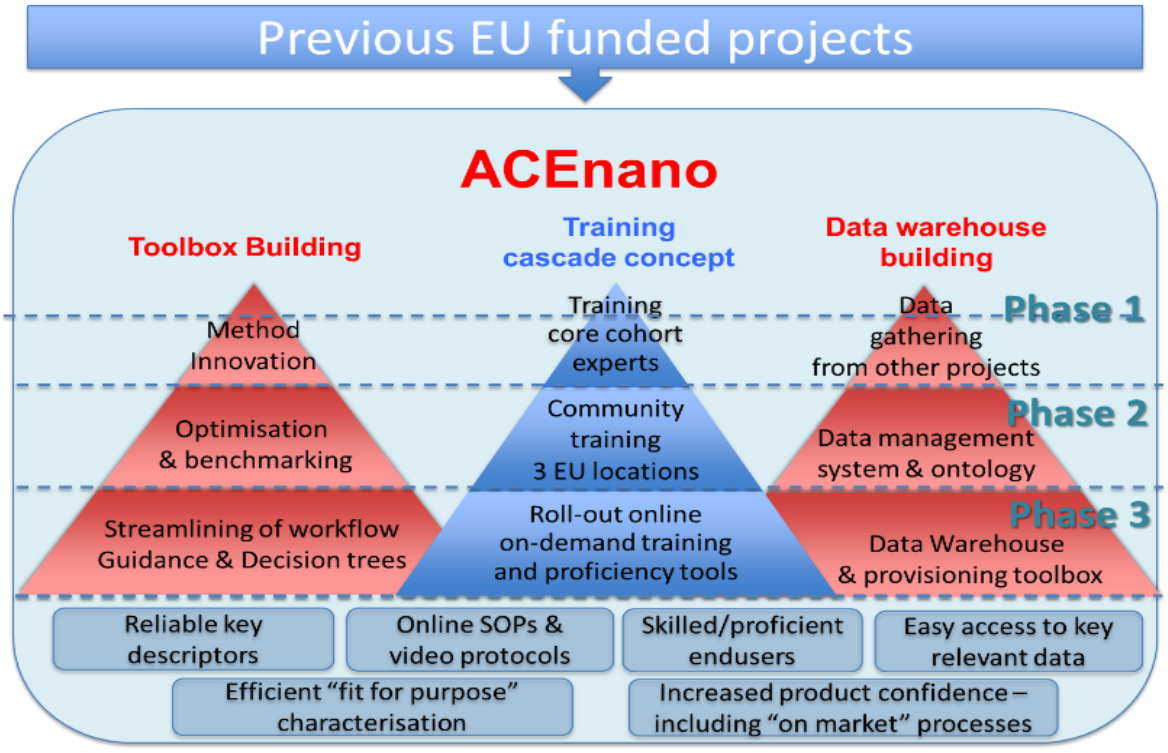
To resolve this, the ACEnano project, coordinated by the University of Birmingham (UK), is working towards introducing confidence, adaptability and clarity into nanomaterial risk assessment by developing a widely implementable and robust tiered approach to nanomaterials physicochemical characterisation that will simplify the choice of characterisation methods, and facilitate contextual (hazard or exposure) description and its transcription into a reliable nanomaterials grouping framework.

ACEnano is structured into three phases of instrument and method development: innovation to develop new methods, new means of instrument hyphenation, novel sample introduction, or miniaturised equipment; optimisation of workflows and sample introduction systems; and benchmarking of both existing methods and those developed and optimised within ACEnano. In all cases, full protocols and SOPs, and training materials (video protocols, online tutorials, libraries of representative results…) will be provided, alongside a decision tree to support

users (industry, regulators…) in the selection of the most appropriate combination of methods to address their specific analysis or characterisation need. The decision tree approach for method selection will be based on an online platform consisting of a set of pre-designed questions (based on case studies from previous projects, such as NanoFASE or NanoDefine, which specifically addressed the question of whether a material is "nano" or not).

The first year of the project (which runs from January 2017 to December 2020) focused on partner integration and on addressing the project's technical challenges. In particular, excellent progress is being made on methods that enable more precise characterisation of complex multi-component matrices. Also, in order to achieve a major project impact via improved technologies, a selection of methods to be benchmarked and initial training efforts were made. Work mainly related to information and knowledge gathering related to decision-tree building was also carried out.

ACEnano's impact will thus be achieved through new characterisation tools and services that are robust, reliable, more user-friendly and fit for purpose for risk assessment and regulation, enabling greatly increased confidence in datasets, and identification of quantitative nano-materials structure-activity relationships (SARs) as the basis for grouping and read-across.



ACEnano vision

The multi-disciplinary project consortium consists of 26 partners from UK, Austria, Switzerland, Germany, the Netherlands, Sweden, Belgium, Korea and China. Partner expertise spans chemistry and materials science, statistical, engineering, physical, mathematical, environmental and biological sciences. These are complemented by industry partners who specialize in instrumentation and integration at various technology readiness levels and various scales from SMEs to global leaders, knowledge management, risk assessment, innovation management and regulatory consultancy. This combination of partners, working together, is bringing the needed experimental, analytical, modelling and dissemination skills required for successful delivery of the project work plan.

ACEnano consortium

Role of BioNanoNet: *BioNanoNet contributes to the review of guidelines, supports interaction with standardization bodies and supports dissemination activities.*

For more details visit the project website: http://www.acenano-project.eu or contact project coordinator: Prof. Éva Valsami-Jones: e.valsamijones@bham.ac.uk

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 720952.

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BioNanoNet *Success Stories*

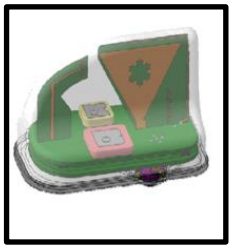
Hi-Response facilitates printed electronics by using ESJET – A success story

The EU funded H2020 project Hi-Response (http://hi-responseh2020.eu/) is geared towards developing a mid to high range productivity printing system (Electrostatic Jet Printing (ESJET) to surpass any inkjet system in the printed electronic market place today. This patented printing technology provides both higher resolution and a broader range of ink type compatibility than conventional inkjet technologies. ESJET is very novel and in contrast to current high resolution piezo based inkjet printers, it has no moving parts. As a promising digital printing technology it can be utilized for high resolution printing of functional materials, e.g., copper and silver inks. Examples for possible applications include (but are not limited to) printing of OLED pixels, encoder patterns, antennas, touch-screens, and chip repair.

Moreover, ESJET printing can be conducted on various substrates, e.g. plastic foils (PET, PEN, Polyimide), glass and paper. The dependence of the printing results on the substrate (type and thickness) as well as on parameters like printing speed, printing distance and voltage is also investigated.

Hi-Response: Pilot Line for End User Applications

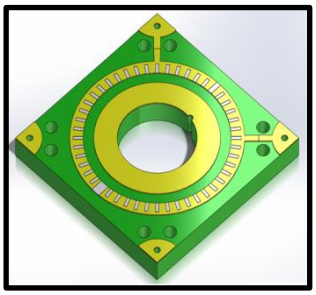
The Innovative Concepts in relation to the end-use applications



Automotive Antennae (A3)

High conductivity Cu/Ag Fractals printed onto polymer substrates.

Automotive contact sensors (Piher)



High conductivity Cu wiper encoders printed onto FR4 substrates sequentially with a dielectric material.

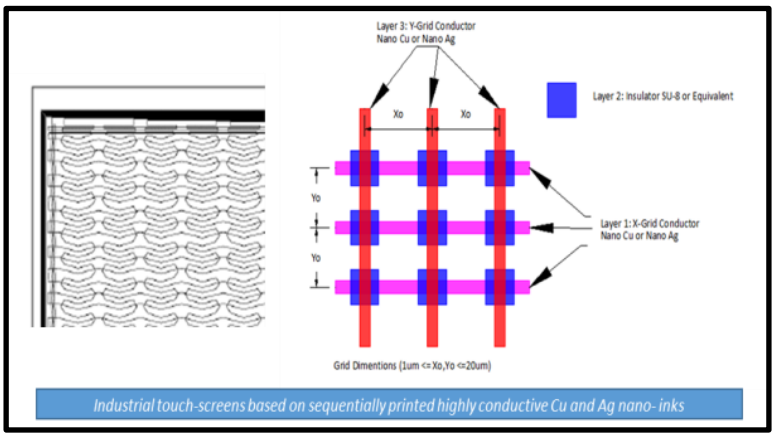
- Increased pulse from 12 to 48.
- Reduced wear.

Printing of deep copper filled trenches for through silicon via (TSV) for Silicon (Infineon)

- Copper filled trenches for TSV applications using printing of high solid content Nano-Cu filled inks.
- Good electrical conductivity.
- Low mechanical stress.
- Increased thermal stability.
- Replacement of current electroplating manufacture – Which is expensive, slow and environmentally unfriendly.

Metal mesh ITO replacement for touch screens (Zytronic)

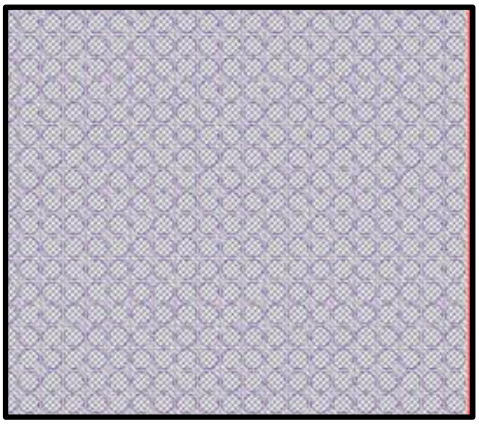
- Wire thickness of <5µm, one order of magnitude less than current printed meshes and better than world leading Chinese Academy (Nanchang O-Film) mesh based on complex structuring.
- High conductivity Cu or Ag (>50% bulk) allowing surface resistance <100Ω/Sq. at 1µm wire thickness.



- Transparency of >95% and elimination of other optical inconsistencies.
- Sequential multi-layer / multi-material printing for x-, y- and dielectric layers.
- Patterning of desired structure without additional post-processing steps.
- Reduction of current production times of up to 9 hours for large screen manufacture down to <30 minutes.

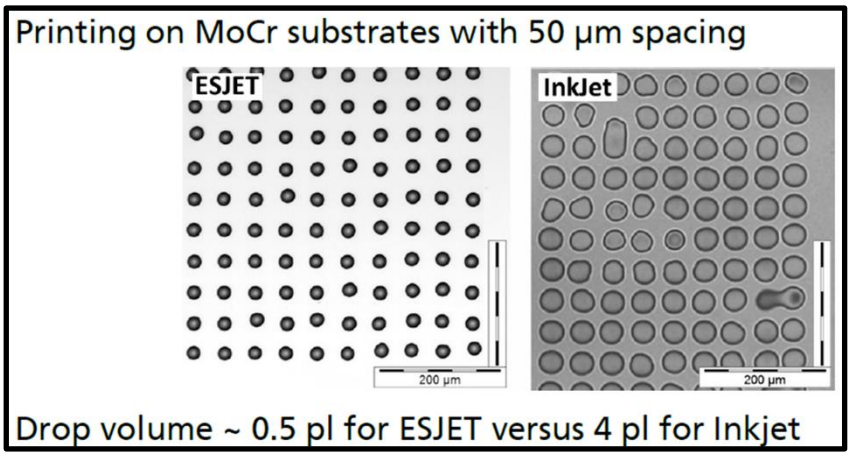
Metal mesh ITO replacement for OLED displays and lighting (IAP/IMEC/TNO)

- Wire thickness of <5µm, one order of magnitude less than current printed meshes and better than world leading Chinese Academy mesh.
- Sequential multi-layer / multi-material printing for x-, y- and dielectric layers.
- Patterning of desired structure without additional post-processing steps.
- High conductivity Cu/Ag allowing sheet resistance <5Ω/Sq
- Transparency of >95%.



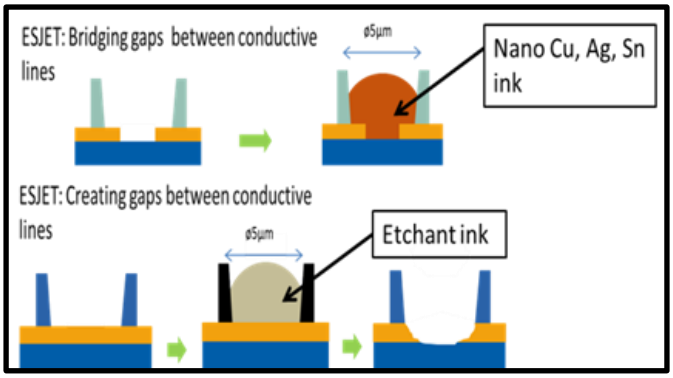
Printed active pixels for OLED displays and lighting (IAP/IMEC/TNO)

- Printing of active OLED materials for display and lighting applications at resolutions of <10µm allowing printing at 300dpi.
- Increased material yield due to direct printing process with material usage of > 90%, current vacuum based processing technologies suffer from low material yield depending on the tool system, which is often reported to be between 10-50% at maximum.
- Faster processing times.
- Easier scalability to larger substrate size as compared to vacuum processing.
- R2R production potentially achievable, easier and more cost effective than with vacuum techniques.
- Potential to manufacture without need for inert atmosphere.

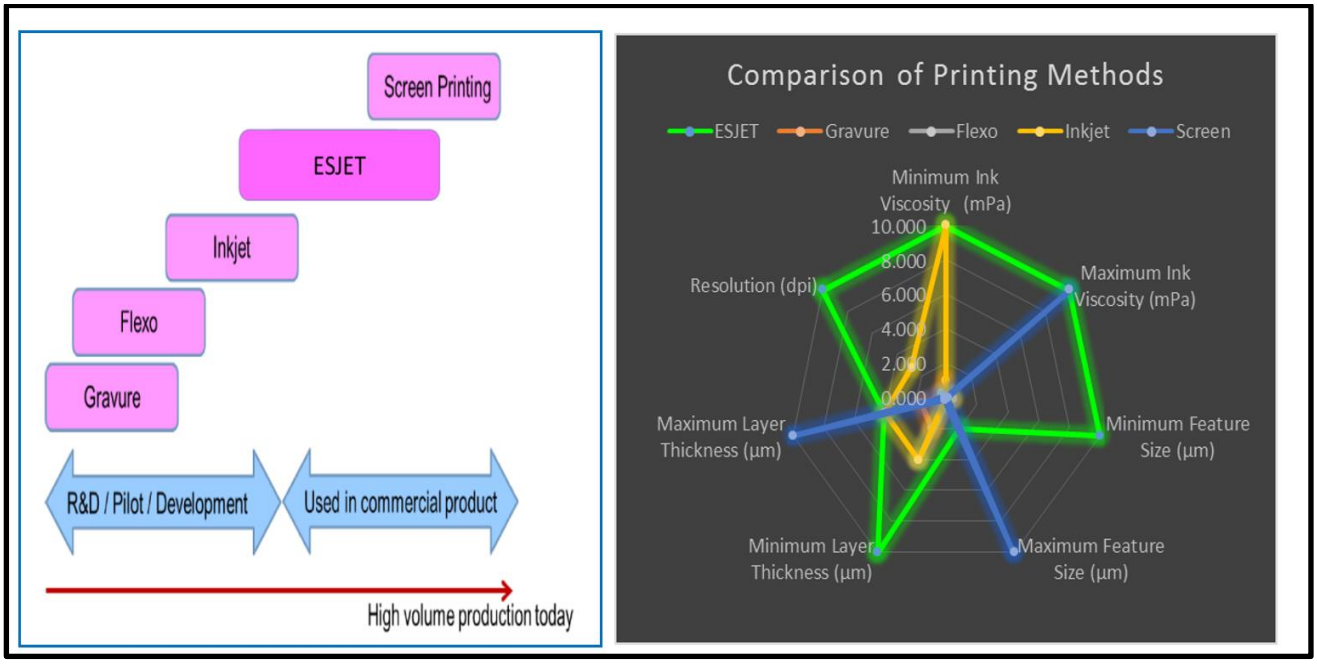


IC Chip Tuning (Infineon)

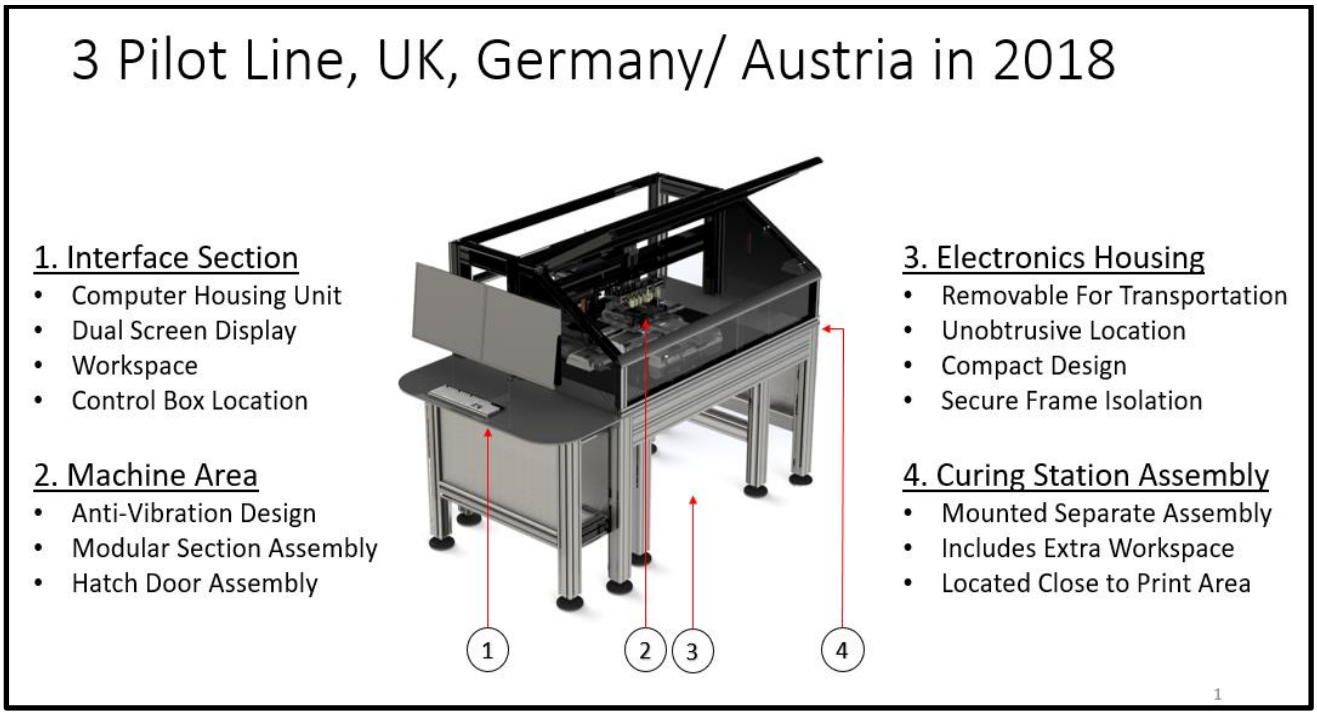
- Deposition of printing sub ø5µm deposits of highly filled (up to 60 Vol.-%), high viscosity metal Nano inks to bridge conductive lines in IC devices in a single pass which cannot be achieved by conventional inkjet printing.
- Deposition of printing sub ø5µm deposits of etchant material to un-bridge conductive lines in IC devices in a single pass which cannot be achieved by conventional inkjet printing. A new fuse concept.
- Reduced packaging size for IC devices.
- Process cost reductions.



ESJET Compared to Other Direct Writing Paradigms



ESJET Pilot Lines Designed



In order to develop safe and legally compliant products, BioNanoNet focused on the development of a safety concept implementable in real-life innovation processes, which may help to plot a sensible path through the nano-risk landscape, without stifling innovation.

The approach provides a hazard-, exposure- and risk profile for a given nanomaterial, including:

- identification of potential exposure scenarios,
- use of qualitative and semi-quantitative tools to prioritize them,
- measurement of occupational exposure, both at lab and pilot scale, and
- introduction of the Safe-by-Design concept in the innovation and development phases of the pilot plant.

With the proposed concept, concrete and practical guidance to industry on how to deal with environmental health and safety (EHS) issues of manufactured nanomaterials and nano-enabled products along their lifecycle is provided, including, as appropriate, legislation/sector specific issues. The proposed approach aims to be universally applicable for various nano-related innovations and thus bringing them closer to the market.

Two BioNanoNet Members are part of the Hi-Response consortium:

As a leading European organisation with expertise in printing development, **JOANNEUM RESEARCH MATERIALS** (Institute for Surface Technologies and Photonics to applied research) leads the work related to the scale-up and development of the Hi-RESPONSE printing technology.

Infineon Technologies Austria AG provides top level semiconductor and system solutions. Within the project, Infineon is responsible for setting specification validation and exploitation of the technology specifically relating to the development of conductive through silicon vias for Si-wafers.

Hi-Response project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 646296.

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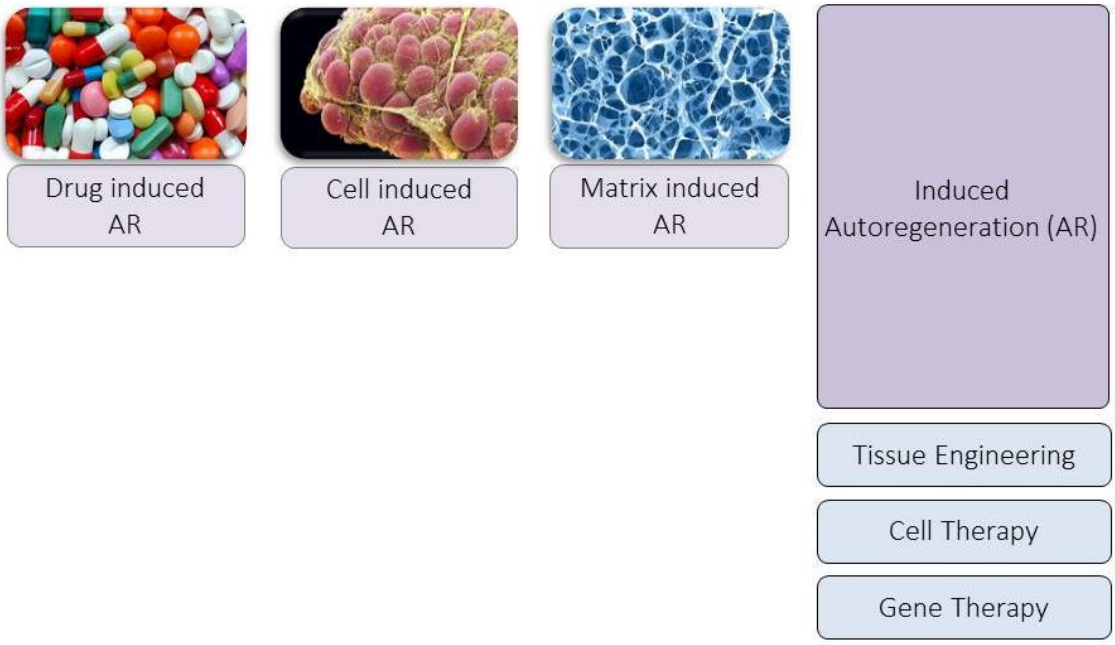
BioNanoNet *member presentations*

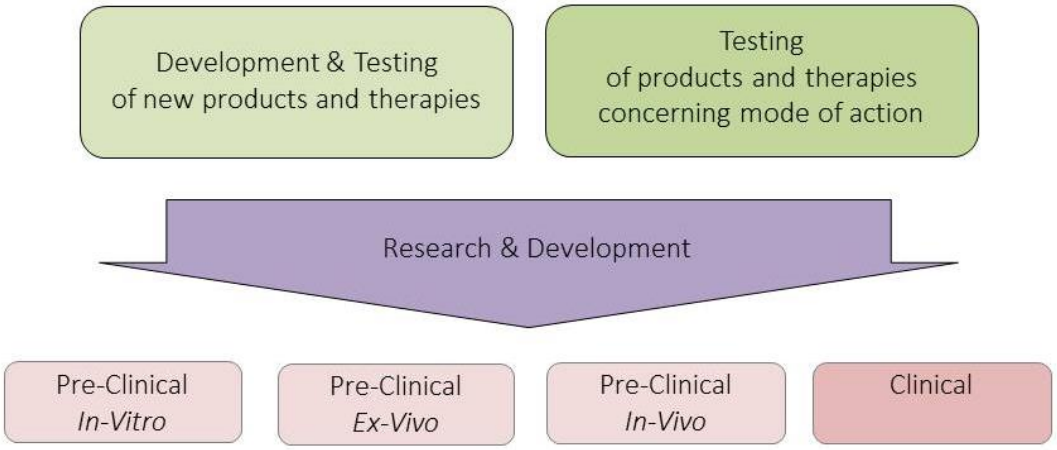
COREMED – Cooperative Center for Regenerative Medicine, JOANNEUM RESEARCH

Regenerative medicine is one of the fields within biomedicine with the strongest development dynamics and thus represents a hotspot in the field of medical research and development.

Regenerative medicine deals with the restoration of dysfunctional cells, tissues or organs by stimulating the body's own regenerative repair processes (induced auto-regeneration) or through biological replacement in the form of living cells or tissues specifically cultured in the laboratory (tissue engineering). The goal is always the same: to restore the original healthy and functional state of the affected tissue rather than merely replacing and repairing it temporarily. The motto of regenerative medicine is ‘healing instead of just repairing’.



COREMED – Cooperative Centre for Regenerative Medicine incorporates basic medical research, pre-clinical and clinical research and offers total interdisciplinary solutions in R&D services e.g. for the pharmaceutical and med-tech industry. The center works on the continuous improvement of medical care within the field of regenerative medicine in Austria and other countries.

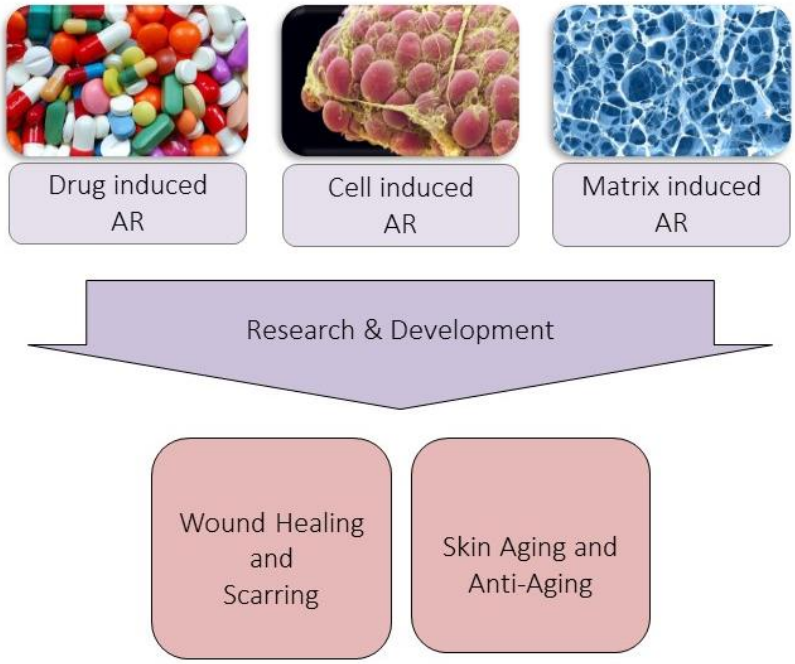


With respect to science and research, COREMED can rely on existing resources and cooperation due to its site at the MedCampus Graz. A strong local network of scientific and economic facilities and players in the field of life sciences exists at the site – first and foremost: Joanneum Research HEALTH Institute, Medical University of Graz, Karl-Franzens University

of Graz, Graz University of Technology and CBmed GmbH. Moreover, the center relies on close cooperation with national and international partners and companies.

Research Areas

COREMED is engaged in medical research as well as in related disciplines. The center has deliberately positioned itself as an interface between medicine and technology focusing mainly on the user's point of view and society's long-term benefit.



There are two main research areas within COREMED, which are working in strong collaboration with partners from science and research facilities:

- Wound Healing and Scarring
- Skin Aging and Anti-Aging

As well as the cross-sectional topic:

- Inflammation

Wound Healing and Scarring

Currently about 1-4% of the population of the western world suffers from chronic wounds. In Austria alone, about 200,000 to 300,000 people are affected.

Because of the fact that people are getting older in general and that the number of chronical illnesses is increasing continuously, it is anticipated that also the number of people suffering from chronical wounds will also rise significantly as well as the treatment costs.

At the moment, most treatment concepts for various diseases focus only on minimizing the disease symptoms as in those cases healing the disease is often not possible. This is the vital starting point for COREMED.

COREMED is aiming to understand healing processes better and to support these processes in specifically defined areas. This will lead to the development of new products and therapies. COREMED also aims to collaborate in order to verify/demonstrate the effectiveness of already existing products.

Skin Aging and Anti-Aging

The skin is functionally the most versatile organ of the human body. It serves as a borderline between the inside and the outside (wrapping organ), as protection from environmental influences, as well as for representation and communication. In addition, the skin fulfills important functions in the area of immunology and possesses various adjustment mechanisms.

Skin aging is a complex and multifactorial process continuously leading to a loss of structural integrity and physical function of the skin. Even though the skin is relatively resilient it is affected by aging as well as any other organ. The consequences are manifold. First, the skin barrier and the structural set-up weakens. Hormonal changes effect this process just as much as other factors. However, the structural changes of the skin are not only noticeable through visible changes, such as wrinkles, but also lead to a functional alteration followed by a higher risk of various skin diseases including skin tumors. This altered skin structure makes it more susceptible to traumatic damage and wound healing disorders.

COREMED has the goal to improve the understanding of the fundamental process of skin aging and, further, influence this process in specific ways. This additional knowhow should thus lead to the development of new products and therapies.

Scientific Excellence

COREMED is aiming to offer scientific excellence for applied research on the highest level. Therefore, the institute's strategy is to also invest into basic research as well as into applied research areas. This commitment in selected basic research projects shall secure existing excellence and thus enhance it. Exclusively top-level researchers carry out each project, and the results are being published accordingly.

Contact:

Univ.-Prof. Dr. Lars-Peter Kamolz, MSc
Cooperative Center for Regenerative Medicine, JOANNEUM RESEARCH
Tel: +43 316 876-6000
coremed@joanneum.at
www.joanneum.at/coremed

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Institute of Electrical and Biomedical Engineering, UMIT

The Institute of Electrical and Biomedical Engineering (IEBE) is part of the Department for Biomedical Informatics and Mechatronics within UMIT – Private University for Health Sciences, Medical Informatics and Technology in the city of Hall in Tyrol, Austria.

Team

All information about our team and our institute can be found on the website: www.umit.at/iebe

Objectives

Our key objectives comprise

- to investigate and understand complex biological systems from nano to macro scale,
- to exploit this knowledge for the development of effective technologies for medical diagnostics and therapy;

Research topics

Our primary research topics include

- biological modelling and simulation,
- bioelectric and biomagnetic mesurement and stimulation,
- biosignal and data analysis

Application fields

Our research aims at being applied in

- cardiology,
- nanomedicine,
- neuroscience;

Reference projects

K-Regio Project eVITA: electrical Vestibular Implant Tyrol Austria (Lead Partner: Medical University Innsbruck)

DFG Project CoS-MRXI: Compressed Sensing for Magnetorelaxometry Imaging of Magnetic Nanoparticles (Collaboration partner: University Münster, Germany)

FWF/DFG Project ONCE-TMS: Online Neuronal Connectivity Estimation and Neurofeedback with Transcranial Magnetic Stimulation (Collaboration partner: TU Ilmenau, Germany)

EMPIR Project MagNaStand: Towards an ISO standard for magnetic nanoparticles (coordinator: PTB Berlin)

Research portfolio

In the following, we are pleased to give an overview of ongoing research projects and research activities.

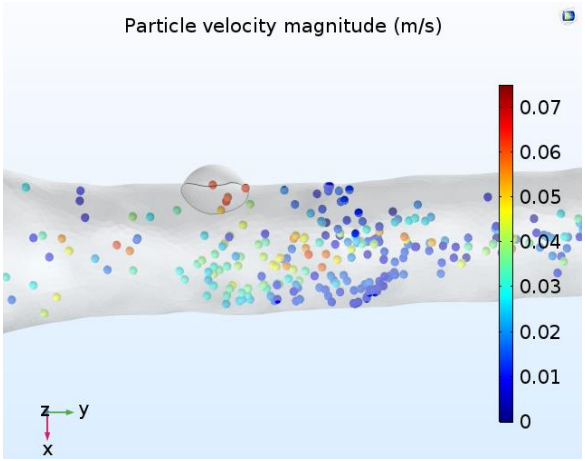
Magnetic Nanoparticles – computational modelling of their behaviour and distribution pattern inside the human body

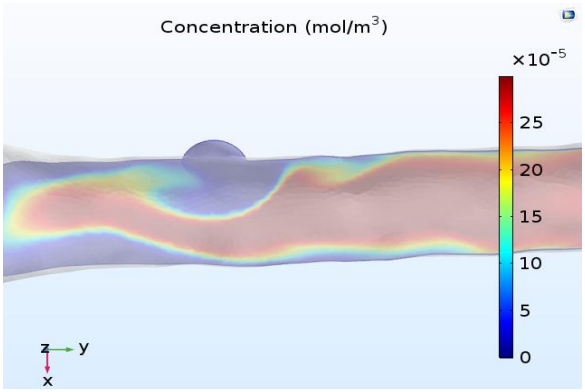
[Veronica Gonella, Friedrich Hanser, Daniel Baumgarten]

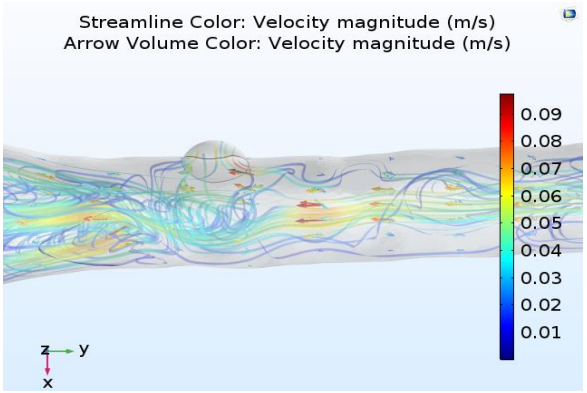
Magnetic nanoparticles (MNPs) offer a large variety of promising applications in medicine thanks to their exciting physical properties, e.g. magnetic hyperthermia or magnetic drug targeting for cancer therapies as well as medical imaging. For these applications, mathematical modelling is needed to investigate and understand the behaviour of the MNPs and their interaction with biological tissue after they are injected into the human body. For instance, the process of guiding MNPs to the target site, through an external magnetic field control, needs to be modelled mathematically to effectively plan patient-specific therapies.

This research project aims at modelling blood flow-mediated MNPs transport under the influence of an external magnetic field, as well as MNPs distribution pattern into tumour tissues. The numerical model will also take into account the interaction between magnetic nanocarriers and biological tissues. The framework of this project involves the Computational Fluid Dynamic (CFD) method: hemodynamics will be investigated in order to better understand

MNPs transport and distribution. A target tissue, representing a tumour geometry connected to the fluid domain, will be part of the model: it will be investigated how MNPs can reach the target site under pulsatile blood flow. In addition, the behaviour of MNPs inside the fluid domain will be investigated under two different points of view: the injection of a bolus of MNPs and the injection of a molar concentration representing common available MNPs solutions. Patient-specific geometries and experimental data will be included in the computational framework.





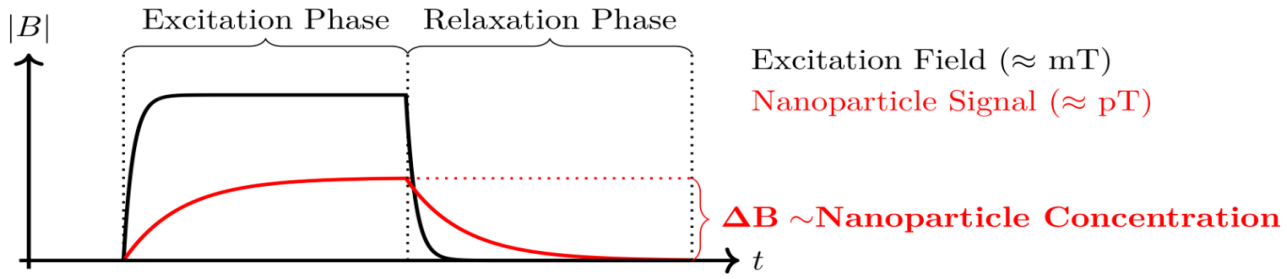


Magnetic Nanoparticles – Quantification using Magnetorelaxometry with Optically Pumped Magnetometers

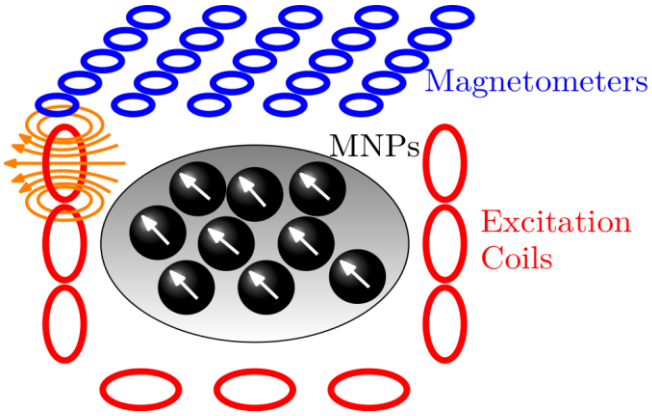
[Aaron Jaufenthaler, Peter Schier, Daniel Baumgarten]

For most biomedical applications of magnetic nanoparticles, it is crucial to quantify the amount and the distribution of MNPs, which can be obtained by means of magnetorelaxometry (MRX). Here, the magnetic moments of the MNPs are aligned by an external magnetic field, forming a net magnetic moment. After switching-off this field, the relaxation of this net

moment is commonly detected by a superconducting quantum interference device (SQUID). The amplitude of this relaxation curve is directly proportional to the MNP quantity, allowing for MNP quantification in MRX. Since the latest developments in OPM technology allow sensitivities comparable to those of SQUIDs, OPMs may be used in magnetorelaxometry, offering a reduced sensor-target distance and the omission of cryogenic cooling. Our objective is to investigate the use of OPM sensors for characterization and imaging of MNP distributions using OPM sensors.



To obtain a spatial quantification and thus a quantitative image of the MNP distribution, the relaxation of the MNPs has to be measured with different excitation patterns. A classical magnetorelaxometry imaging setup is shown in the figure below. With the gathered data, an (ill posed) inverse problem can be formulated whose solution corresponds to the quantitative MNP distribution.



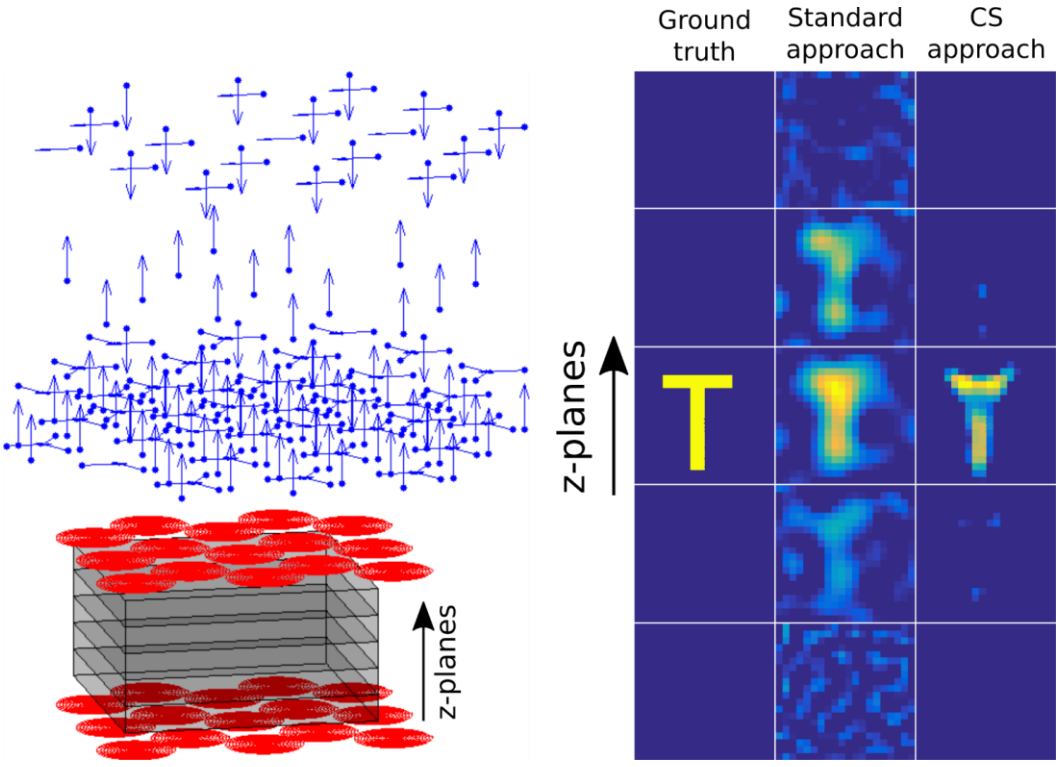
First results show promising results measuring the relaxation signal of immobilized MNPs using OPMs and distinguishing between various MNP concentrations. We are currently setting up a magnetic nanoparticle imaging lab. A magnetically shielded room and an OPM sensor system will soon be available for MNP characterization and imaging experiments as well as other biomagnetic investigations.

Magnetic Nanoparticles – Compressed sensing for magnetorelaxometry imaging of magnetic nanoparticles

[Peter Schier, Aaron Jaufenthaler, Daniel Baumgarten]

A quantitative knowledge about the distribution of MNPs is mandatory for the safety and efficacy of the novel cancer therapy approaches. To date, no clinically available modality is able to offer this information. As mentioned, magnetorelaxometry imaging (MRXI; see figures below, left) is able to detect particle distributions quantitatively using inhomogeneous excitation fields. However, long measurement times and large amounts of data are currently produced by this technology due to the consecutive activation of coils.

This project aims to combine compressed sensing (CS) methods with MRXI. The goal is to develop appropriate excitation sequences for existing setups as well as preferential designs for coil- and sensor positions and orientations. This will result in a fundamental advancement of the imaging technology, meaning a substantial improvement of spatial resolution and vastly reduced measurement times (see figure below, right). Theoretically, we expect a better understanding of CS-paradigms for applications in which only parts of the sensing matrix are fixed. Additionally, novel quantitative reconstruction algorithms for CS-paradigms are being developed. These findings can be adapted to other biomedical imaging modalities in the future.



Magnetic Nanoparticles – MagNaStand – Towards an ISO standard for magnetic nanoparticles

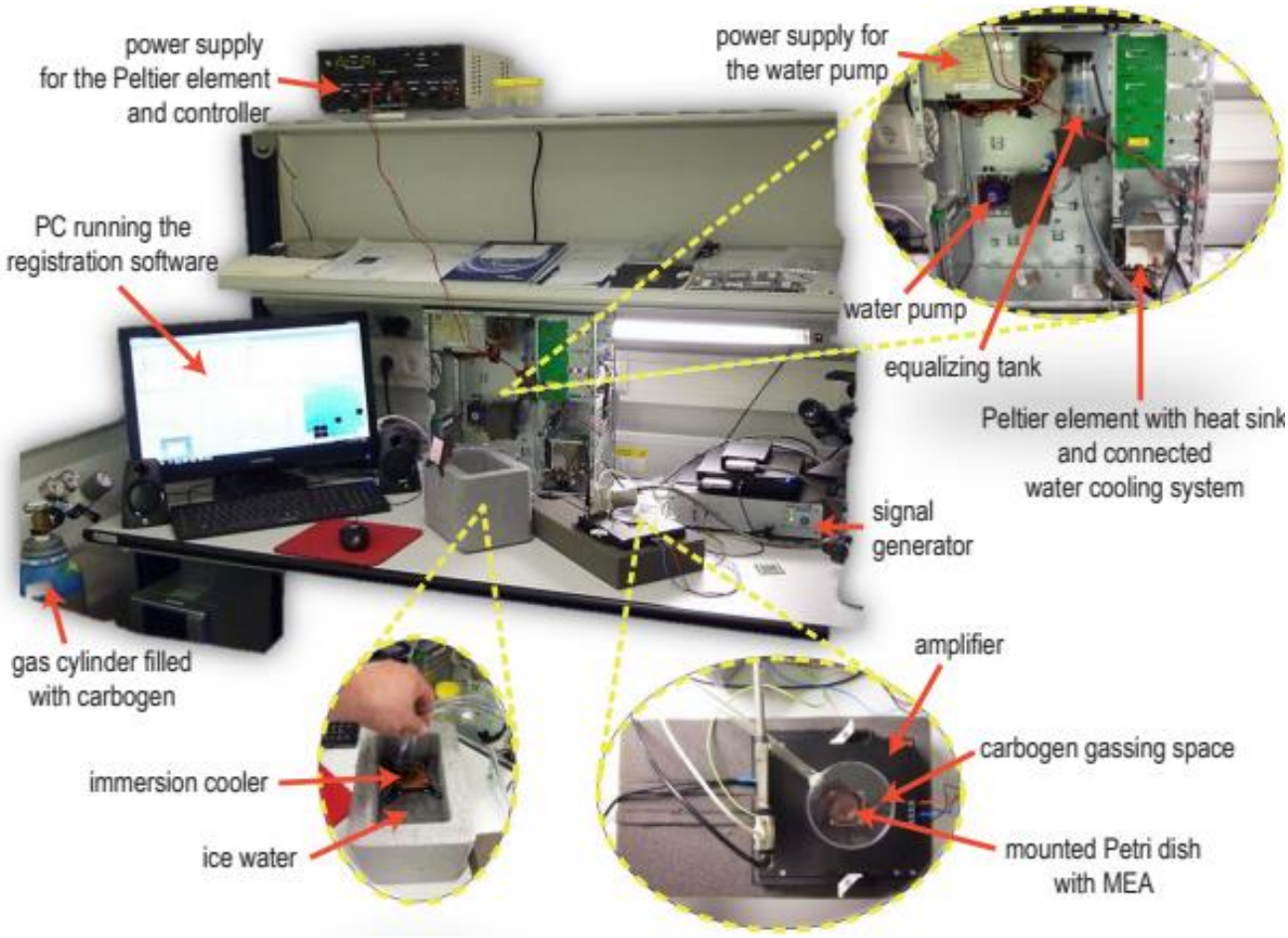
[Peter Schier, Daniel Baumgarten]

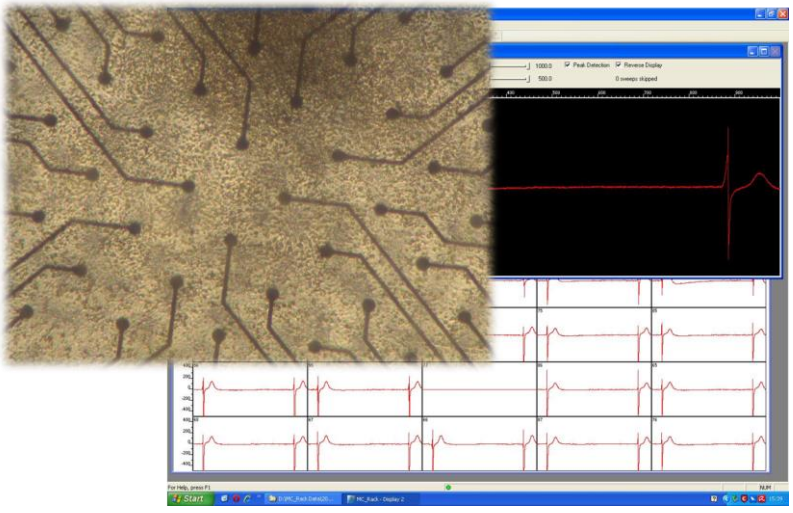
Magnetic nanoparticles (MNPs) find wide biomedical and technical applications, however, there are currently no existing standards for characterizing this material class. This project will expand and summarize the metrological knowledge on the measurement and characterization of MNPs and bring it into the current development of ISO 19807 “Liquid suspensions of magnetic nanoparticles” by ISO/TC229 WG4. This will involve a close collaboration with national and international standardization organizations, interaction with the involved European industry, and the uptake of results of about 90 previous EU research projects including “NanoMag” and “RADIOMAG”. In addition to the finalization of ISO 19807, a roadmap for further measurement standards for magnetic nanoparticles will be developed.

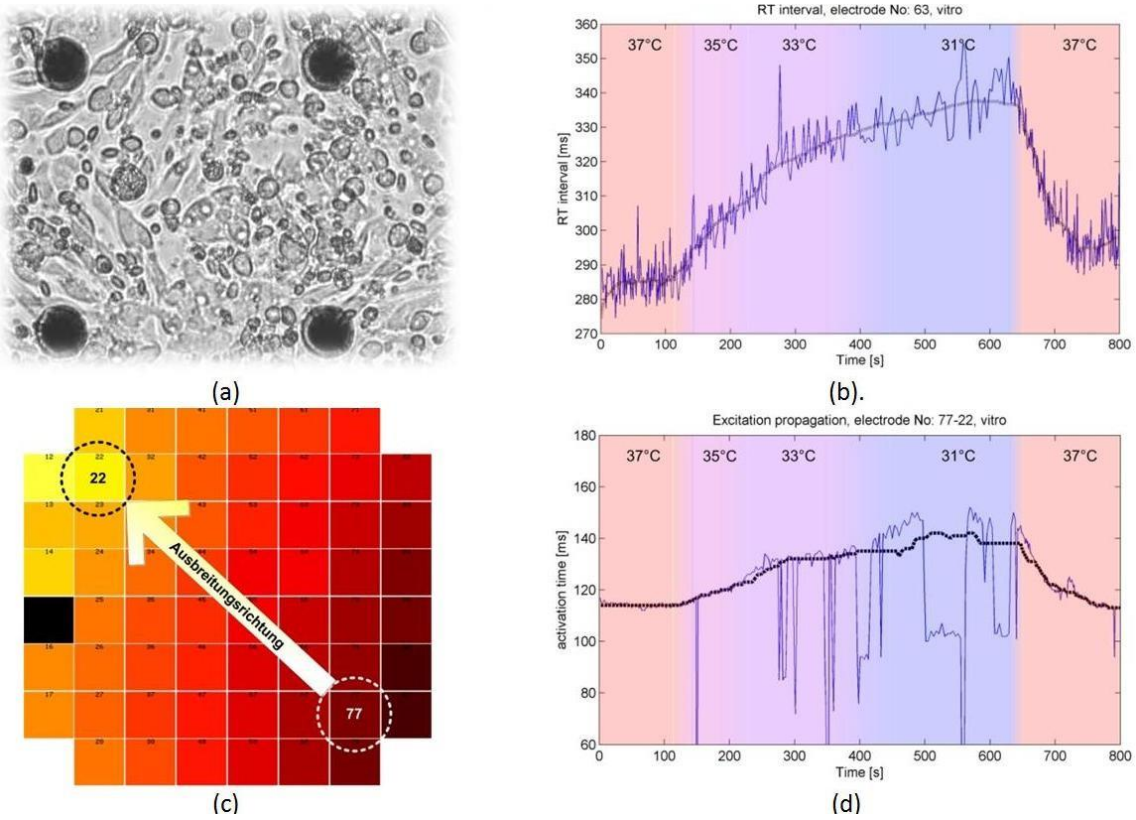
Cardiac cells – temperature-induced electrophysiological alterations

[Roland Kienast, Friedrich Hanser, Daniel Baumgarten]

It is well known that temperature has a profound impact on the electrophysiological mechanisms of the heart. Experimental in-vivo and in-vitro investigations utilizing micro-electrode-array (MEA) technology help obtaining a deeper understanding of temperature-induced electrophysiological alterations. The results of these experimental investigations allow for developing a computer model suitable to simulate temperature-induced electrophysiological alterations in the heart. The figures below show the experimental setup (for heating and cooling the cell culture including a Petri dish on a MEA, a Peltier heat sink, etc.), a close up of the cell culture and the MEA measurement system with recorded signals from the cell layer as well as plotted RR intervals as a function of temperature.


power supply
for the Peltier element
and controller
power supply for
the water pump
PC running the
registration software
water pump
equalizing tank
Peltier element with heat sink
and connected
water cooling system
signal
generator
gas cylinder filled
with carbogen
amplifier
carbogen gassing space
immersion cooler
ice water
mounted Petri dish
with MEA



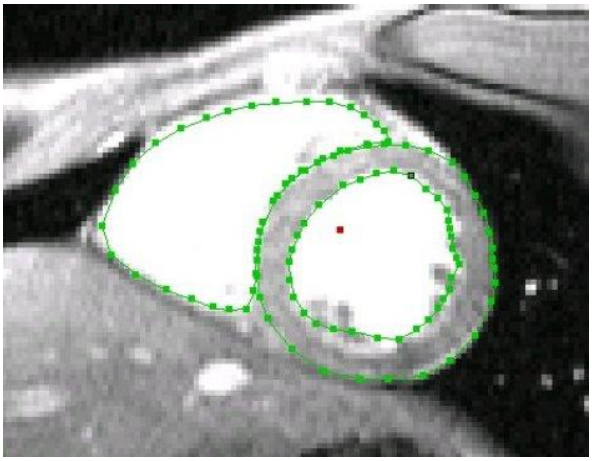


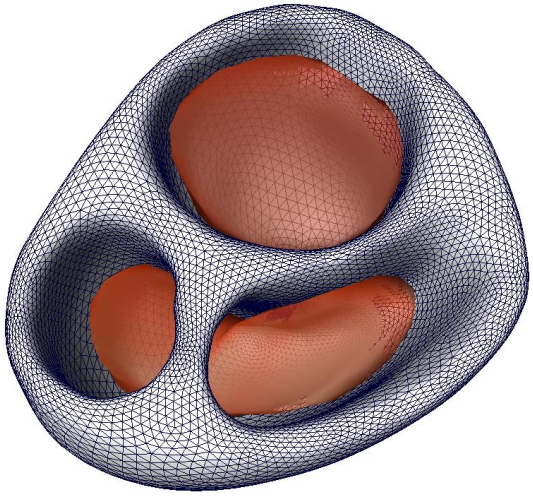
Cardiac tissue – optimizing antitachycardia pacing protocols

[Friedrich Hanser, Bernhard Pfeifer, Roland Kienast, Michael Netzer, Daniel Baumgarten]

Antitachycardial pacing (ATP) is a painless method for terminating ventricular tachycardias (Vts). If ATP does not succeed (in terminating the VT) a painful high energy shock has to be delivered. A method for maximizing the ATP success rate would, therefore, prove highly beneficial for the individual patient. ATP can be parametrized in several ways using burst, ramp or burst+ramp approaches and can be applied in the right ventricle or in both ventricles (biventricular). In the multicentric randomized ADVANCE-CRT trial the different ATP protocols were tested and it could be shown that biventricular ATP is safe, but there was no significant difference between right ventricular and biventricular ATP.

A computer simulation model has been developed capable of finding the optimal ATP protocol for an individual patient. A computer model of the individual patient's ventricle generated from a 3D/4D data set and a hybrid automaton was used for modelling and simulating different VT scenarios. For each VT scenario (cycle lengths ranging from288 [ms] to 408 [ms]) different ATP protocols derived from the ADVANCE-CRT trial were applied in order to evaluate their effectiveness in terminating the VT. This computer simulation study reconfirmed the results of the ADVANCE-CRT trial. Biventricular (BiV) ATP did not prove to be more effective than right ventricular ATP. The availability of a computer model for the individual patient combined with knowledge of the ischemic area and the underlying mechanism of the VTs will allow these models for optimizing ATP management. The number of painful high-energy shocks resulting, possibly, in adverse effects could, therefore, be maximizing the ATP success rate.





Biomedical modeling and simulation -- Computer simulation of cardiac cryoablation

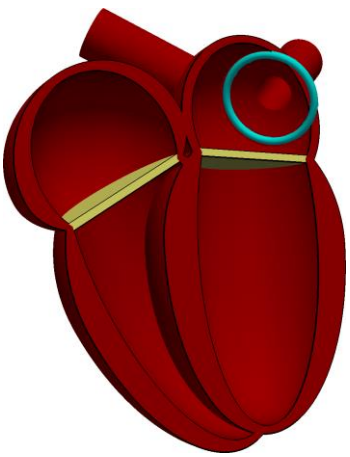
[Michael Handler, Gerald Fischer, Felix Wichum, Daniel Baumgarten]

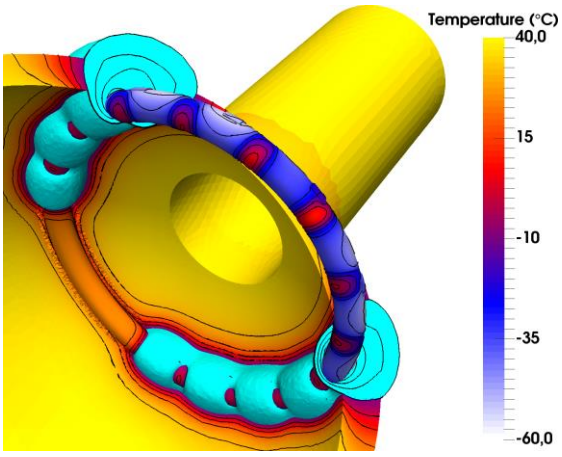
Cardiac cryoablation (CCA) is a minimally invasive procedure for the treatment of cardiac arrhythmias. During this procedure, the tissue responsible for the arrhythmia is either ablated directly or insulated from the remaining electrophysiological conduction system of the heart by ablating surrounding tissue. In contrast to radiofrequency ablation, in which the ablation is performed by heating, cryoablation creates lesions by freezing the targeted tissue. Many in-vivo and in-vitro investigations were performed to evaluate crucial factors for the success of CCA interventions (e.g., applicator geometries, freezing phase durations, application of mul-

tiple freeze-thaw cycles, contact pressure, …). In collaboration with AFreeze GmbH, our institute created a realistic computer framework for the simulation of various CCA scenarios that allows for a detailed analysis of temperature distributions (e.g., freezing rates, thawing rates, dimensions of lethal isotherms and ice volumes, …) within the myocardial tissue layer close to the applicator during the procedure. The framework is being continuously extended and applied for the analysis of established ablation procedures using available cryocatheter variants as well as for the evaluation of effects on myocardial temperature distributions caused by alterations of applicator geometries and ablation scenarios.

In a current collaboration with AFreeze GmbH and Griffith University (Nathan, Queensland) the existing computer models are further extended to simulate electrical signals delivered and recorded by electrodes close to the ablation site for diagnosis and monitoring before, during and after a CCA intervention.

The figure below, left shows the CoolLoop® applicator (cyan ring) positioned at the opening of a pulmonary vein (PV) in a cross section of a self-designed parameterizable heart geometry. Arrhyhtmogenic tissue within the PV is a common cause for atrial fibrillation. The creation of a circular lesion around the opening of a PV leads to an electrical insulation of the arrhythmogenic tissue within the PV from the remaining myocardial tissue in the left atrium. The figure below, right shows a simulated temperature distribution considering the applicator position from the figure below, left with highlighted frozen volume (cyan) around the CoolLoop® applicator and isotherms in 10°C increments (black lines). The visualized transmural cut through the myocardial tissue shows that the ice front surpassed the epicardial boundary in the simulation.

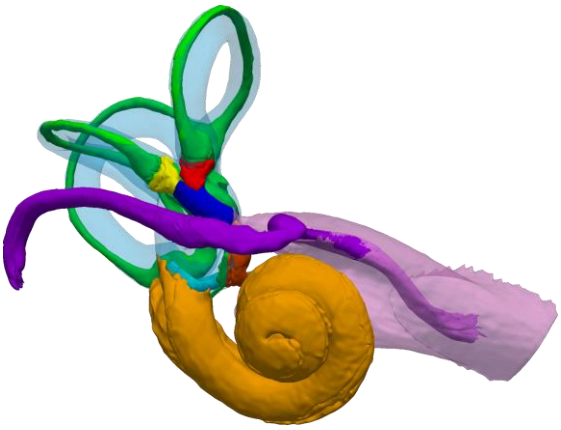


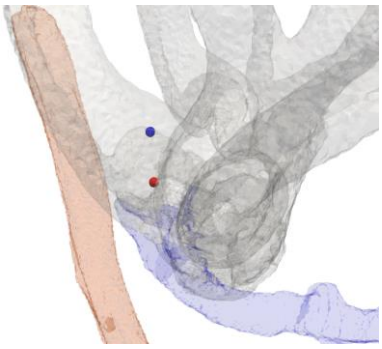


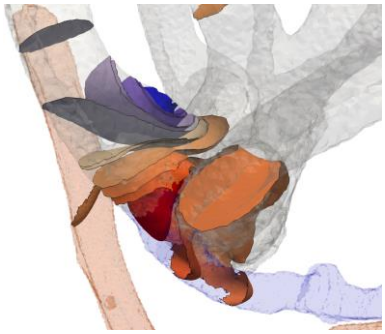
Simulation based optimization of vestibular implants

[Michael Handler, Simone D'Alessandro, Peter Schier, Daniel Baumgarten]

The vestibular organ is the main organ of balance where a system of interconnecting fluid-filled chambers containing hair cells convert head motion into nerve impulses. Patients with severely impaired vestibular function suffer from dramatic, disabling vertigo, followed by chronic unsteadiness and blurred vision when the head is in motion. Vestibular implants can (partially) restore the function of the vestibular system and contribute to a significant increase of quality of life for affected persons. For that reason, we are working on the development of realistic computer models specific for human anatomy to simulate the biological response to electrostimulation considering different electrode designs, electrode positions and stimulation strategies for vestibular implants. Based on the results of the computer simulation, the targeted stimulation of the vestibular organ can be optimized considering also the anatomical variations of different individuals. The figures below show an exemplary human anatomy of the inner ear and a bipolar electrode configuration with its corresponding isopotentials.



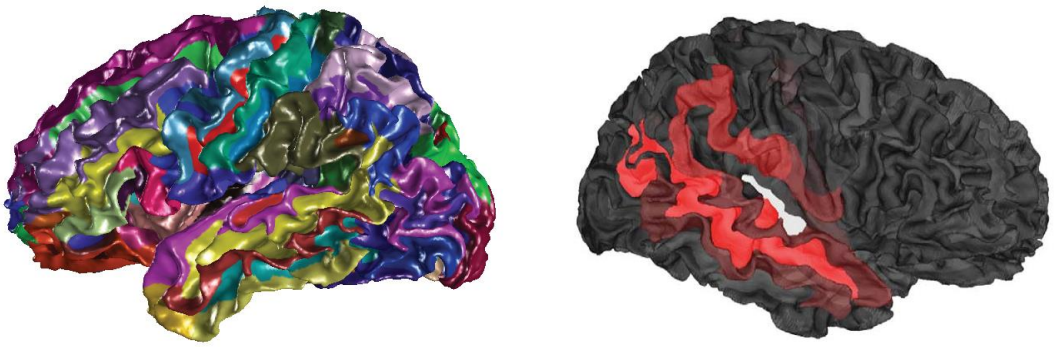




This work is performed amongst others in collaboration with Med-El and the Medical University Innsbruck and is cofunded by the Standortagentur Tirol and the European Regional Development Fund.

Brain tissue – online Neuronal Connectivity Estimation and Neurofeedback with Transcranial Magnetic Stimulation

[Peter Schier, Daniel Baumgarten]



Human capabilities are characterized by fast and parallel processing of information across local and long-range brain networks. Understanding the dynamic neural processing underlying our capabilities requires an electrophysiological technique capable of identifying the networks and their functions with a millisecond resolution. Today, electroencephalography (EEG) and magnetoencephalography (MEG) are the only non-invasive techniques that can estimate the neuronal activity with such resolution. On the contrary, techniques such as (functional) Magnetic Resonance Imaging (MRI/fMRI) measure comparatively slow, but with a much higher spatial resolution. Regarding the proposed project with the title “Online Neuronal Connectivity Estimation and Neurofeedback with Transcranial Magnetic Stimulation” we will establish new real-time methods to analyze and process MEG/EEG data for subsequent cortical stimulation scenarios. The overarching objective is to develop real-time computational tools for advancing our understanding of electrophysiological functions of neuronal networks and cortical stimulation in the human brain in health and disease. During the project methods for estimating functional connectivity in real-time MEG/EEG scenarios will be established. Furthermore, ways to integrate Transcranial Magnetic Stimulation (TMS) into a real-time scenario will be investigated. Such real-time scenarios can be found in neurofeedback and Brain

Computer Interface (BCI) research. Both fields address data processing pipelines, which present specific stimuli to the subject, measure the corresponding brain activity, process the measured data in real-time and readjust the upcoming stimulus. This way the subject is part of a close-loop data processing pipeline with a direct feedback. This is for example useful when learning to regain motor function during stroke rehabilitation treatment. The proposed work will advance knowledge regarding the network activity in human with a millisecond resolution and thus contribute to one of the promising research field of our time, the decoding of the human brain.

Contact:

Institute of Electrical and Biomedical Engineering
UMIT – Private University for Health Sciences, Medical Informatics and Technology
Prof. Daniel Baumgarten
daniel.baumgarten@umit.at
www.umit.at/iebe

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TEMAS AG

TEMAS AG is a 25-year-old company which has re-invented itself to keep up with the pace of the innovative world. As a private SME (service provider) in Switzerland, we are strongly engaged in technology transfer and innovation-oriented programmes and projects as well as open innovation consulting. Our target groups are SMEs and larger industries, as well as research teams, public authorities, promotion agencies, business associations and interest groups. The core competence of TEMAS is building bridges between science communities and industry, from early stages of technology development, by applying specific processes for knowledge transfer, invention, and innovation management.

Our Vision:

At the centre of TEMAS AG vision are humans and their challenges. TEMAS works together with the client to tackle their challenges and to assist them in being successful through participative and solution-oriented activities.

Our Strategy:

Our strategy is resource-oriented and not only based on TEMAS expertise. TEMAS has access to a large network of experts to identify the right provider for our customers. Our customers benefit from our continuous feedback on the work. TEMAS guides the customer until the finalization of a project.

Our team:

The TEMAS team provides support in different domains to become the “all-around carefree package”.

In a nutshell TEMAS stands for Technology, Expertise, Management, Academy and Services. Each area is supported by a team of experts to provide first class support to our customers in different areas of concern, all out of one source. TEMAS aims to be a company's one stop shop in the areas of:

Technology:

TEMAS supports their customers with the testing, planning and implementation of projects with technology background and high innovation structure.

1. Basic research

   Our goal is to find the appropriate resources for each technological question, which is carried out either under our customers leading role or through us. This entails for the following steps:

   - In the first step, the resource needs will be determined together with the customer for the resource procurement. For that, search fields will be used.
   - The second step includes either a resource offer from the TEMAS staffing pool or an external resource search.
   - The third step of the resource evaluation includes an assessment with recommendation from TEMAS.

- The fourth step entails the actual resource procurement and the support for your project. Through this step-by-step and transparent process, it will be ensured that the right resources will be found, together with the customer. These resources will either be provided by the TEMAS staffing pool or be found within the TEMAS wide-spanned network. The network comprises of personal contacts for basic and applied research, product and process development, analysis, regulatory affairs and more in various institutions (colleges, research institutions, industry, service provider, public agencies etc.).

2. Project support and project management, trust management of technical projects

   TEMAS provides support along the entire innovation processes from the best idea to the innovative product. TEMAS helps you with:

   - Know-how (self-developed or retrieved through an international network)
   - Project structure
   - Project management and project management support (including training and coaching of your project managers)
   - Project administration
   - Project control
   - Vacation and/or sick-leave coverage for team members or short-term project support in case of time delay or the danger of a time delay

3. Know-how management:

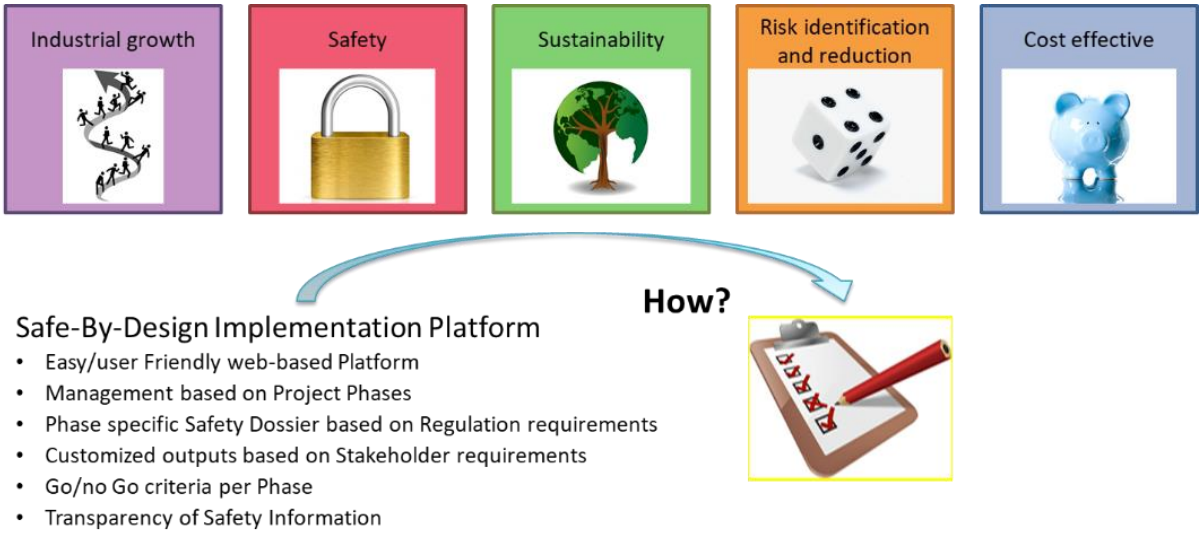
   This area includes particularly the analysis, definition and development of expertise with the goal to find solutions both effectively and efficiently. Possible expertise fields are Nanosafety (TEMAS has been a major contributor to the Swiss Precautionary Matrix), regulatory compliance in several sectors (medical devices, chemicals, cosmetics, food), market analysis, risk assessment, business plan development, etc. The expertise is used for different purposes:

   - Assist as a catalyst with the search of ideas and solutions
   - Structured, methodical and systematic generation of ideas

Expertise:

1. Safe by Design concept:

   The Safe-by-Design (SbD) concept was largely developed by TEMAS within the framework of the European research project NANoREG (http://www.nanoreg.eu/). It enjoys high acceptance among the wide base of stakeholders. The SbD concept serves to improve existing innovation processes dealing with uncertainties and risks (see below).



In order to ensure a simple industrial implementation, the SbD concept was designed as an expansion of the structured innovation processes used in today's industry, starting from stage – gate, but moving toward a more complex model, including open innovation and a flexible innovation management process adapted to SMEs as well.
The SbD concept was developed to assist with the development of sustainable and safe nanotechnological products and processes in a regulatory framework, taking into account their unique characteristics, but it can as easily be used for traditional chemicals in any industrial sector.

What added value does the TEMAS Safe-by-Design concept bring?

- Products that comply with regulatory requirements
- Recognizing and reducing of uncertainties and risk (Estimating remaining residual risks and uncertainties providing more clarity about the risks handling in the shortest and most reasonable time

- Developing external knowledge to close knowledge gaps
- Efficient supplementation of existing innovation processes

2. Safe by Design Implementation Platform and training

   Safe-by-Design helps you to more transparency, safer nanomaterials and products as well as lower cost. The Goal being to bring regulatory compliant nano-inspired products that have preferably low uncertainties and risks, into the market. We assist customers getting closer to this goal through our dedicated training sessions on Safe-by-Design.

3. Regulatory affairs compliance

   Compliance to regulation is mandatory to enter the European market. Safety and functionality can be measured with many different testing strategies, standards and accepted methods. There are many parameters to be considered, and they vary for different products and use scenarios. A guidance supporting the innovator to build a tailored testing strategy supporting at the same time regulatory demands can cut costs and optimize resources. TEMAS covers different sectors, from Medical Devices, Chemicals, Cosmetics, Food and Food contact materials, and Occupational Health.

Management:

1. Business strategy

   The art of successful business leadership lies within the skilful balance between spontaneity and flexibility to take advantage of opportunities in the moment with a dynamic business strategy. TEMAS AG works to find the balance and to successfully put it into practice. The balance is achieved through a management path of hard work and professional discipline. A lot along this path is just like playing the piano of a virtuoso: 90% practice and 10% talent. We support you to develop the 90%. For the last 10% we can give you impulse and feedback as well as offer you coaching.

   The business pyramid:

In general, businesses develop many of these elements, but lack in entrepreneurial structure. Which elements are missing and have to be developed in your business strategy will be determined in a collective discussion. Many businesses see this type of work as awful, a thing that can be just skipped over. But you wonder then why the employees, leaders and customers don't understand what the business stands for and where it wants to go. It does always need much more transparency to become more successful.

2. <u>Developing customer relationships and training for employees</u>

   TEMAS AG with a client business analysis offers you to identify for which of your departments there is contact between customer and employees, and trains employees for optimal interactions with customers. This occurs on the bases of your business concept and your business philosophy. However, an even more important aspect of the analysis is to find out which competencies your employees have when interacting with the customer.

3. <u>Help with mergers</u>

   In the most recent publish McKinsey study on average only 20% of employees and managers said that the transformation process was successful. Therefore, 80% were convinced that it did not work. TEMAS AG will help you rewrite the statistics and prove the opposite.

4. Team building and team development

   Every other team building fails and the desired outcome will not be achieved or just be burden to downbeat and broken employees. TEMAS AG helps you to find the right people for the team and counsel the team so that the highest possible can be achieved.

Academy:

The TEMAS Academy is a modern training institute of the future and offers amongst other things the following advantages: 1) Free eLearning for self-study on our open Learning Management System. Learn whenever and wherever you want; 2) Modular and competence-oriented education and training for various roles and functions; 3) Modern blended learning approach with needs analysis, knowledge learning, behavioural training, transfer tasks, learning community and coaching; 4) The strengths and the network of TEMAS AG. We consult your company and stay until the desired success; and 5) New findings from science combined with the practical experience of our employees and trainers.

Among others, the TEMAS Academy focuses on:

1. Leadership training

   TEMAS AG Leadership classes help to understand what leadership is and the effects of it. Only a complete understanding helps the individual to decide if leadership is something they want to do and only then can you develop a leadership style.
2. Coaching

   Coaching allows for a change in perspective which points out brand new opportunities. TEMAS AG offers coaching sessions to give you the understanding of change in perspective and in doing so help our customers to ask the right questions.
3. Professional presentations

   TEMAS AG runs courses to provide our customers with the “do’s” and “don’ts” of successful presentations. We help our customers with the 1) Preparation of a presentation; 2) History of the presentation; 3) Key elements and central message; 4) Body language and the Image composition; 4) Text composition; and 5) Interaction with the audience.

Services:

1. Technical event management

   TEMAS AG specializes in planning and implementing of events for our customers, where technology is at the center.

2. Scientific/technical staff placement

   The TEMAS AG partner scouting allows our customer to single-mindedly obtain the right partner for a specific purpose. It entails the steps development of a search profile (anonymous documentation), partner search, partner evaluation (testing the ability and willingness to cooperate, assessment and recommendation), as well as making contact.

   As a tailored service, the detailed execution and scope of the partner scouting depends on precise questioning and will be determined together with the customer. The customer will be continuously informed about the activities and has the possibility to intervene as necessary at any point in time.

3. Innovation consulting

   Please visit www.temas.ch to find out more on how TEMAS helps customers through innovation consulting

4. Digital 4.0 consulting

   Assist companies with their needs in their conversion to Digital 4.0, with a special focus on medical devices and health sector.

5. Federal representation (Switzerland) for technical organization and products (Marketing support)

   TEMAS can help you represent your products in Switzerland.

At TEMAS we observe and analyse your problems holistically

We plan and implement your goals.

Contact:

Blanca Suarez Merino DPhil
Hermetschloostrasse 77, CH-8048 Zürich
Phone +41 (0) 71 446 50 30
Blanca.SuarezM@temas.ch
http://www.temas.ch

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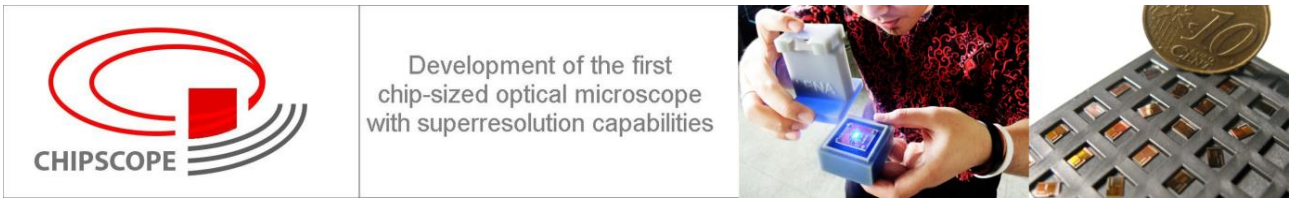
BioNanoNet *member contributions*

Contribution of AIT Austrian Institute of Technology GmbH

The EU-funded ChipScope Project Gets Leading Companies on Board



Two international players in the field of imaging and microscopy, Nikon and Carl Zeiss GmbH, have joined the Industrial Advisory Board of the European funded research project ChipScope. Both companies will accompany the project consortium during the next 3 years and contribute to transform the project results into new products.

In addition to Nikon and Carl Zeiss Microscopy GmbH, four SMEs are enclosed in the board and will be closely linked to the project: endoASIC Technologies from Spain, Adimec Advanced Image Systems from The Netherlands, TissueGnostics GmbH from Austria, GATTAquant DNA nanotechnologies from Germany as well as two divisions of the National Metrology Institute PTB in Germany.

Innovation Potential to Strengthen the European Industry

The ChipScope project aims to develop a completely new and extremely small optical microscope capable of observing the interior of living cells in real time. The new microscope will be affordable and ubiquitously available. It will allow researchers in developing nations as well as scientists out in the field to take reliable and affordable images of viruses, DNA, living cells and more.

The collaboration established with industry will contribute to keep the research done by the ChipScope scientists close to the market needs. It is the basis for a successful transfer of project results to European industry and for the development of new technical solutions and products.

New Imaging Techniques for Medical Applications

As age-related illnesses such as cancer, cardiovascular, lung and neurodegenerative diseases become more and more relevant, new approaches and improved methods for medical diagnosis and therapy are required. New diagnostic methods help to determine early, precise and individual treatment decisions by enabling accurate and reliable identification of disease-specific parameters.

The optical microscope with super-resolution capabilities developed by ChipScope will provide valuable contributions to this by extreme miniaturisation, simplicity and cost-effectiveness.

A Highly Interdisciplinary Project Team

The ChipScope project is running from January 2017 to December 2020. The project team includes SMEs, universities and research organisations under the leadership of the University of Barcelona. Other partners are the Technical University of Braunschweig in Germany, the University of Rome Tor Vergata, the company Ymaging in Barcelona, the AIT Austrian Institute of Technology, the Medical University of Vienna, the FSRM Swiss Foundation for Research in Microtechnology and the Ludwig-Maximilians University (LMU) in Munich.

Contact:

Dr. Rudolf Heer, Austrian Coordinator
AIT Austrian Institute of Technology GmbH
Tel: +43(0) 50550-4303
rudolf.heer@ait.ac.at
www.chipscope.eu

The ChipScope project receives 3.75 M€ funding from the European Union's Research Programme Horizon 2020.

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Contribution of EMPA - Swiss Federal Laboratories for Materials Science and Technology Switzerland

Empa
Materials Science and Technology

contactpointnano.ch

Nationale Anlaufstelle
Point de contact national
Punto di contatto nazionale
National contact point

contactpointnano.ch

National contact point for the safe handling of nanomaterials, regulation and knowledge transfer

Mission of the contact point

The independent, national contact point combines all scientific and regulatory expertise available in Switzerland on the safe handling of synthetic nanomaterials – from production and application to disposal – and conveys high-quality information to companies (established companies, SMEs and start-ups) in an efficient way. The aim is to accelerate the transfer from invention to innovation, so that Swiss companies remain competitive in the international environment. The contact point is based on a broad network of proven experts and ensures a qualified and independent transfer of knowledge. It anticipates topics for regular workshops, training and events for information and experience exchanges in the area of nano-innovation, nano-safety, changes to Swiss and international regulation requirements, etc.

Services offered

The purpose of the contact point is to provide prompt and personalised contacts with experts who**:**

- can convey information on nanomaterials, their safe handling and regulatory provisions
- offer expert opinions, services, testing and analyses
- collaborate on research and development cooperations
- carry out training and workshops on relevant and current topics

At the contact point, companies will find competent partners who are able to help directly or point them in the right direction for available knowledge resources and other relevant agencies to contact.

Services not offered by the contact point

The contact point does not carry out R&D projects, provide expert opinions, complete analyses or testing, certify nanomaterials or processes nor offer innovation mentoring.

Target groups and benefits of the contact point

The specific benefit of the contact point:

a. **for target groups:**
   The contact point serves companies as a mediation agency on matters relating to the production, use and disposal of synthetic nanomaterials. The contact point coordinates expert knowledge for the respective needs of those that enquire.

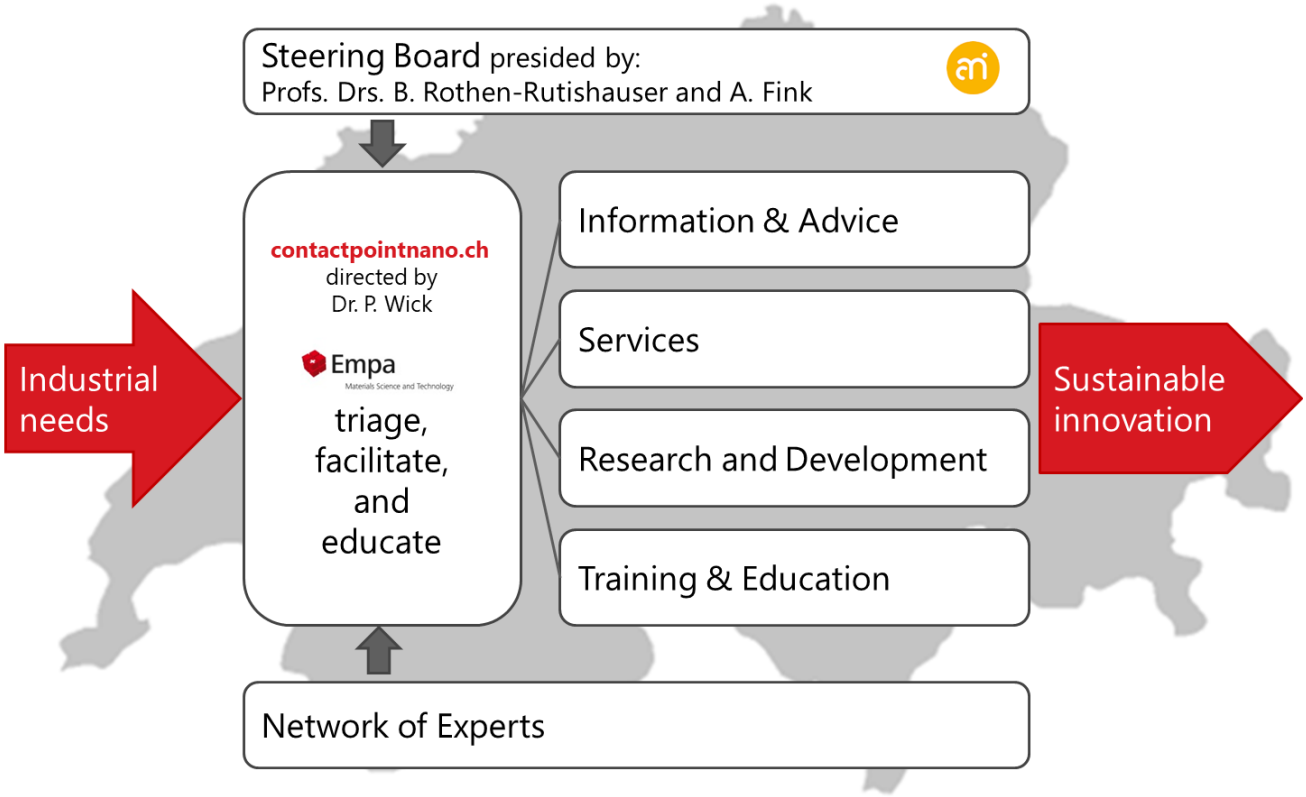
b. **for initiators:**
   This is a way for involved research, higher education institutions and authorities to fulfil their role as an interface to the economy. It is regarded as their obligation to ensure the transfer of knowledge between research and industry and to make every effort to exploit research findings and new insights in order to progress towards marketable products. For their part, they rely on feedback from industry and commerce to gain new inspiration for research and regulation, expand their network and develop interdisciplinary exchanges.

c. **for financial partners:**
   The contact point performs a key function that is currently not being carried out by any other central authority in Switzerland. In this way, it ensures the transfer of relevant information for the safe handling of synthetic nanomaterials in production, use and disposal. It supports the transfer of knowledge and expertise from research to the economy, promotes innovation and enables Switzerland as an economic location to capitalise cutting-edge technologies and consequently boost its competitiveness.

d. overall benefit

At societal level, the contact point contributes to advancing innovative applications of nanomaterials, taking into account the protection of human health and the environment.

Organisational structures



Operational level: the contact point

It receives, analyses, prioritises and coordinates enquiries from companies. The systematic monitoring of information ensures an ongoing improvement in the quality of services. It organises needs-focused and targeted workshops, for example as part of the EMPA Academy or as a satellite of existing events such as the SwissNanoconvention and KTI events, and so is at the same time also a platform for the sharing of experience among companies. The aim is to ensure consistently high quality of information.

Proactively and in close collaboration with BAG, the Federal Office for the Environment (FOEN) and the State Secretariat for Economic Affairs (SECO), the contact point anticipates

relevant changes to regulatory requirements at federal level (for example, potential new declaration and notification requirement for nanomaterials pursuant to the revision of chemical law at the end of 2017) and international level (EU/USA/Asia), as well as offering corresponding training and the necessary training material. In this, too, where possible, it draws on existing quality material (for example, scientific publications, documentation available either in print or online from BAG, BAFU, SECO and other institutions that focus on clarification, safety, regulations and application of nanomaterials in Switzerland and abroad).

Strategic level: Steering Board

The contact point is supported by a Steering Board of experts in the field of nano research, production, use and disposal. It carries strategic responsibility, ensures quality at operational level and promotes sustainable innovation. It focuses on publicising the contact point and its role, supporting the set-up and work of the contact point and helping it secure financial resources.

The Steering Board manages and advises the contact point, reviews its services and organisation and coordinates the ongoing demand-driven expansion of the services offered. It is presided over by Prof. Barbara Rothen-Rutishauser and Prof. Alke Fink from the Adolphe Merkle Institute at the University of Fribourg; the members are currently still being recruited through a process prioritising the inclusion of all language regions in Switzerland.

Quality guarantee: Expert network

The contact point has access to a varied virtual network of experts from different institutions in nanotechnology and nano consultancy.

contactpointnano.ch

The contactpointnano.ch team


Dr. Peter Wick, Head


Dr. Sergio Bellucci, Deputy


Ana Milosevic, Project Manager


Christine D'Anna-Huber,
Communications Advisor

Contact:

contactpointnano.ch
contactpointnano@empa.ch
Lerchenfeldstrasse 5, St. Gallen
+41(0)58 765 75 31

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Contribution of FELMI-ZFE Graz, Austria

Opening: Christian Doppler Laboratory for the Direct Fabrication of 3D Nano-Probes

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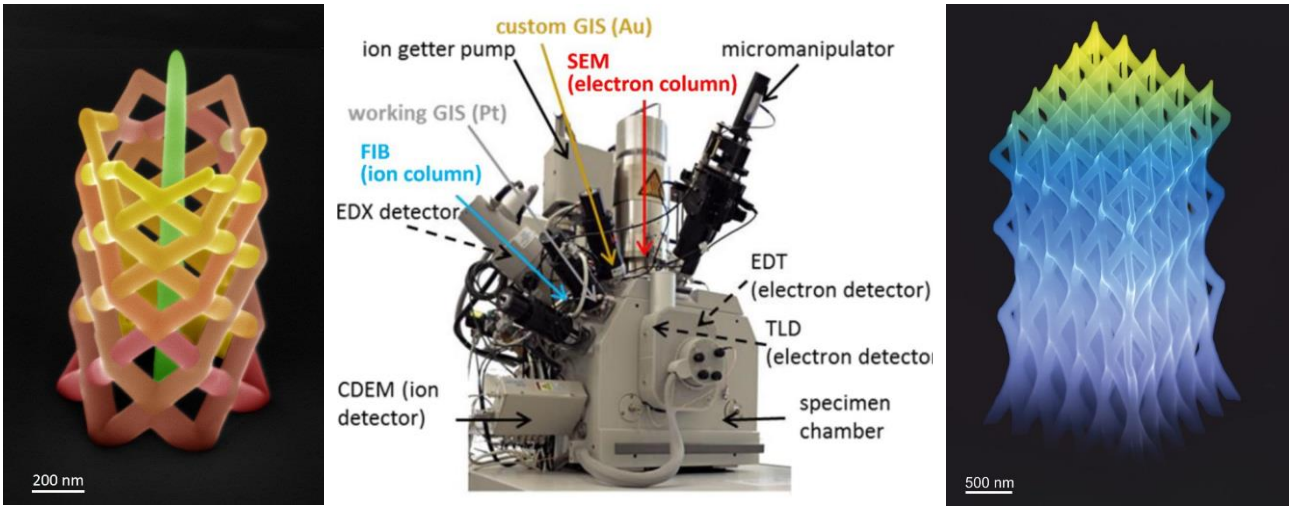
In April 2018 three Christian Doppler Laboratories were officially opened under the auspices of rector Harald Kainz in the assembly hall of Graz University of Technology. We are especially happy to host the Christian Doppler Laboratory for the Direct Fabrication of 3D Nano-Probes under the leadership of Harald Plank in the course of the upcoming years.

During the last decades, **Focused Electron Beam Induced Deposition (FEBID)** has attracted increasing attention in fundamental and applied research. This technology enables **flexible additive manufacturing thanks to the mask-less, direct-write character for 3D fabrication on the nanoscale**, which meet challenges when classical, resist based lithography methods run into their intrinsic limitations. In the course of the past ten years, Harald Plank has been focusing intensively on this topic. In 2015 he defended his Habilitation thesis where he summarised the scientific contribution to this field made at our Institute since 2008; deep insights into fundamental resolution limitations, proximity based broadening effects, high-fidelity shapes, and efficiency aspects have been gained which led to a strong performance improvement in this field.



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On the pursuit of industrial applications, he teamed up with **GETec Microscopy GmbH** to explore next-generation nano-probe concepts for Atomic Force Microscopes (AFM), which will push their performance beyond current limitations. The full potential of the anticipated 3D nano-probes will be exploited by GETec's state-of-the-art *in situ* AFM product line, which is designed for the seamless integration in Scanning Electron Microscopes (SEM) and / or Focused Ion Beam (FIB) systems. By combining these individual technologies, entirely new, yet unknown capabilities become possible.

Christian Doppler Laboratory for the Direct Fabrication of 3D Nano-Probes

Head of the CD-Laboratory
Ass.Prof. Priv.-Doz. Dipl.-Ing. Dr.techn.
Harald PLANK
Institute of Electron Microscopy and Nanoanalysis | Graz University of Technology
Steyrergasse 17 | 8010 Graz | Austria
harald.plank@felmi-zfe.at
www.felmi-zfe.at


Credit: Lunghammer TU Graz

Industrial Partner
GETec Microscopy GmbH

Aspern IQ Seestadt Aspern

Seestadtstraße 27 | 1220 Vienna | Austria

www.getec-afm.com/

Thematic Cluster
Advanced Materials Science

Period
1.3.2018 – 28.2.2025

Further reading:

High-Fidelity 3D-Nanoprinting via Focused Electron Beams: Growth Fundamentals
R. Winkler, B.B. Lewis, J.D. Fowlkes, P.D. Rack, H. Plank
DOI: 10.1021/acsanm.8b00158

Direct-Write 3D Nanoprinting of Plasmonic Structures
R. Winkler, F.-P. Schmidt, U. Haselmann, J.D. Fowlkes, B. B. Lewis, G. Kothleitner, P.D. Rack, H. Plank
DOI: 10.1021/acsami.6b13062

Simulation-Guided 3D Nanomanufacturing *via* Focused Electron Beam Induced Deposition
J.D. Fowlkes, R. Winkler, B.B. Lewis, M.G. Stanford, H. Plank, P.D. Rack
DOI: 10.1021/acsnano.6b02108

Tunable 3D Nanoresonators for Gas-Sensing Applications
G. Arnold, R. Winkler, M. Stermitz, A. Orthacker, J.-H. Noh, J.D. Fowlkes, G. Kothleitner, M. Huth, P.D. Rack, H. Plank
DOI: 10.1002/adfm.201707387

https://www.felmi-zfe.at/research/research-areas/functional-nanofabrication/

Did you already know?

FELMI-ZFE is one of the leading microscopy facilities in the physical and biological sciences; interdisciplinary research, teaching and industry services are the key to our success. We house some of the world's best microscopes. Our broad field of activity – ranging from fundamental to applied research – sets us apart. With a continuing tradition of excellence, we are trying to bridge the gap between academic research (FELMI – an Institute of Graz University of Technology) and practical problem solving as well as industrial needs (ZFE – Graz Centre for Electron Microscopy); for more than 65 years, we work in close cooperation with universities and enterprises throughout Europe.

Contact:

Austrian Center for Electron Microscopy and Nanoanalysis
Steyrergasse 17, 8010 Graz, Austria
Tel.: +43 (0) 316 8730 8320
www.felmi-zfe.at
office@felmi-zfe.at

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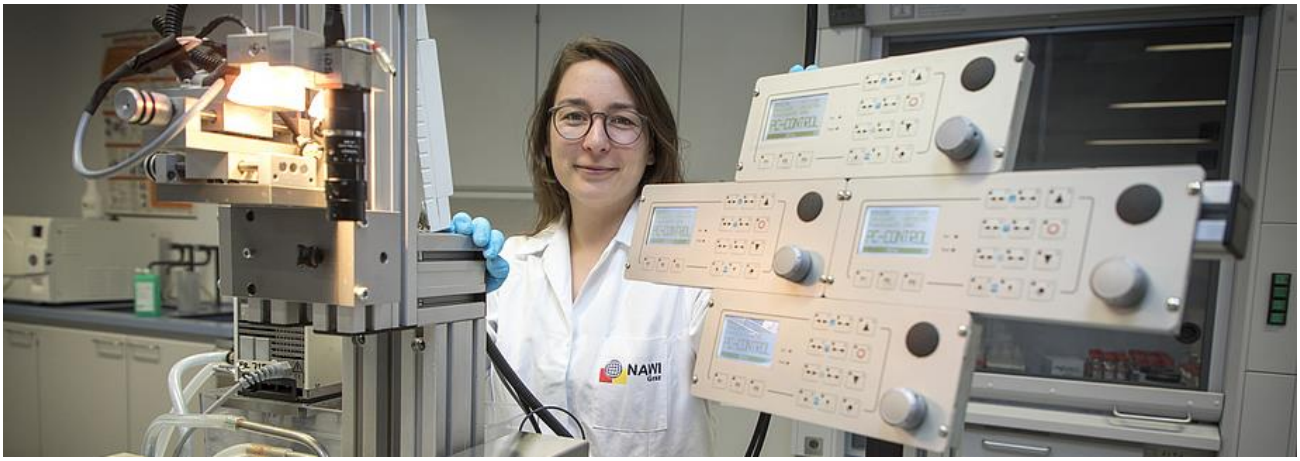
Contribution of Graz University of Technology

The mathematics of the human body

Biomechanical engineer Justyna Niestrawska investigates the mechanical behaviour of the aorta at TU Graz and represents it using mathematical formulas. And wins the German Aorta Prize while doing so.



Biomechanical engineer Justyna Niestrawska in her laboratory, where she examines healthy and diseased aortic walls. *© Lunghammer - TU Graz*

What has mechanical engineering got in common with the human body? Can you explain biological processes like the operations of a machine? The biomechanical engineer Justyna Niestrawska can answer these questions – straight out of her daily work. Her special field is continuum mechanics, in which the operations of the human body are described, modelled and simulated using mathematical equations.

German with Polish roots, she originally studied mechanical engineering at RWTH Aachen and specialised in plastics technology. She began to be interested in medical engineering during her master's programme when she conducted research on heart valves. During a research stay at the University of Auckland, New Zealand, she came across the field of continuum mechanics. On one of the last snowy days of winter in the warm kitchen of the Institute of Biomechanics surrounded by plants, she explains: 'I first came into contact with this research in New Zealand. It is known that heart muscle contracts less in certain diseases than in the healthy state. And the researchers in New Zealand were working on analysing the mechanics behind this using experiments, mathematically modelling them, and subsequently simulating the movements of the heart on computers.'

Thanks to Gerhard Holzapfel, Justyna Niestrawska moved to TU Graz to take up her place in his working group. He is head of the Institute of Biomechanics, has written several standard works on the topic of continuum mechanics, developed well-known material models, and has headed the TU Graz lead project Mechanics, Modeling and Simulation of Aortic Dissection since the beginning of 2018.

Since 2014 she has been conducting research at TU Graz on the stress limits of the aorta abdominalis – the main artery supplying the organs in the abdominal area. A very serious disease of the aorta is aortic aneurysm, which occurs predominantly in persons aged 65 or older, and in the worst cases ends in an aortic rupture. Operations are high risk and a decision to operate must be taken on the basis of as much information as possible. 'Currently operations are carried out with an aneurysm size of five centimetres in women and five and a half centimetres in men. But the size of an aneurysm is not the only factor which defines the risk of rupture,' explains Niestrawska. In her doctoral thesis she has worked on being able to predict the course of the disease, which can be represented and observed using high-definition imaging techniques. 'Some aneurysms under five centimetres have torn, and some have grown to ten centimetres without rupturing.' Together with a team of researchers from TU Graz and the Medical University of Graz the young researcher wants to demonstrate the stress limits of the aorta walls using mechanical stress tests.

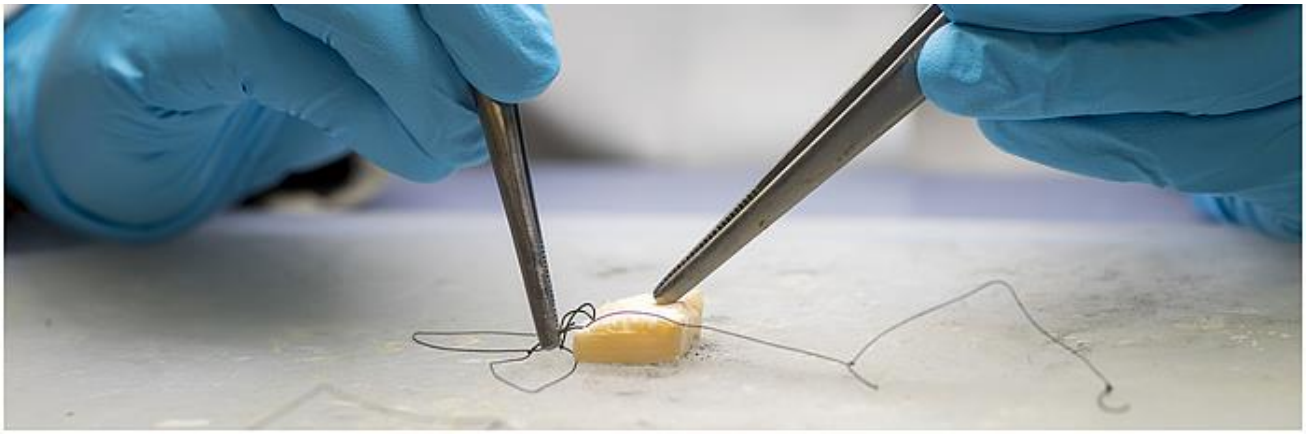
The 'garden hose' inside our body

In its healthy state, the aorta consists of three easily distinguishable layers which, together with their different structures, ensure that the aorta is flexible and stable and that it can withstand the pressure of pulsating blood without being damaged.

The innermost layer is called the tunica intima, consists of endothelial cells and is mechanically negligibly thin in a young person. The tunica media – the middle layer – gives stability to the vessel wall with its straight fibres. 'You can basically compare the structure of the aorta with a garden hose. As in a garden hose small fibres form a tissue which keeps it flexible and stable at the same time,' explains Niestrawska. The outermost layer – the tunica adventitia – forms a kind of protection against excess pressure and its corrugated fibrous structure allows the artery wall to expand without damage in the case of a sudden severe stress.

Mechanical tests show the stress-bearing capacity of the artery wall

To obtain reference data, the team initially studied healthy blood vessels. Using a biaxial stretching device developed at the Institute, small pieces of tissue are subject to stress in two directions at different forces. 'First of all we tested the complete wall, and then we separated the individual layers from each other and clamped them in the tension device,' explains Niestrawska.



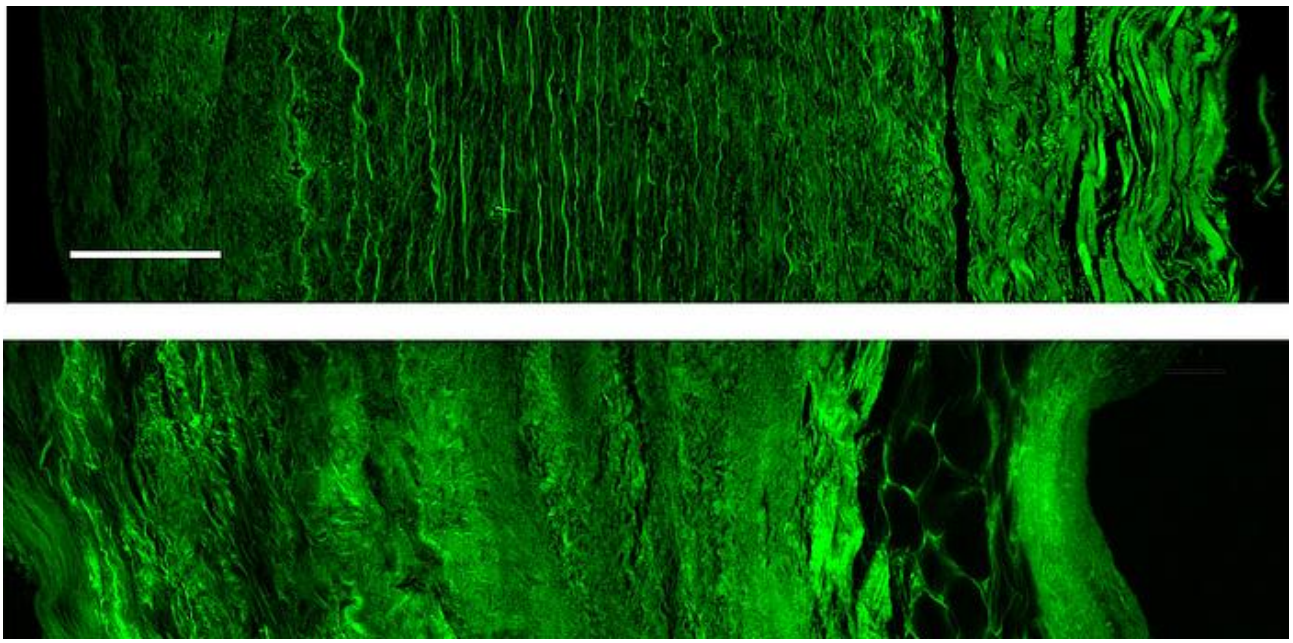
A sample is prepared for mechanical tests in the biaxial tractor using fishing hooks and yarn.© TUG

'Finally we wanted to perform the same tests but with samples from diseased aortas.' But this wasn't possible because the first big changes in the diseased aortas became apparent in the first step: 'Where we were able to separate the layers from each other easily in the healthy samples, the diseased samples had completely grown together and couldn't be manually separated or even optically distinguished,' explained the scientist.

For their research results on the aorta abdominalis, which is explained in the paper 'Microstructure and mechanics of healthy aneurysmatic abdominal aortas: experimental analysis and modelling' and published in the Journal of the Royal Society Interface, Justyna Niestrawska and the research team of TU Graz and Klinische Abteilung für Gefäßchirurgie, Universitätsklinik für Chirurgie and Diagnostik und Forschungsinstitut für Pathologie of the Medical University of Graz were awarded the Aorta Prize of the German Society of Vascular Surgery and Vascular Medicine.

The next significant differences became apparent under stress in the stretching device. 'In the healthy media, the structuring collagen fibres are embedded in an elastic layer so that the aorta can expand without any problems. But in the course of disease, this layer is the first to be degraded, and the fibres lose their orientation. We saw more behaviours in the mechanical tests. With some samples, there was no resistance at the beginning but after some time the fibres very suddenly became completely stiff. In the case of other samples, the fibres

were completely stiff right at the beginning. Under these conditions, of course, the risk of rupture to the artery wall strongly increases because the material cannot expand any more under increased pressure,' explains Niestrawska.



The 1st picture shows a healthy aortic wall with the 3 layers of intima, media and adventitia clearly visible from left to right. The 2nd picture shows a diseased aorta whose layers grew together and are difficult to distinguish
© TUG

Additionally, small fat cells could be detected in the tissue in the diseased samples. 'Our hypothesis is that these lipids are deposited from the outside of the wall to the inside, thus making it more fragile.'

Imaging techniques could show the course of the disease

Building on her basic research, Niestrawska would like to check her hypotheses in tests on living organisms in a next step. She has also got some ideas for a real application: 'In our work we could find indications for a course of disease which could be recognised and observed by certain high-resolution imaging techniques.' In any case she would like to continue research in her field and is already planning to submit a new project application after her doctoral thesis.

Contact:

Justyna Anna NIESTRAWSKA, Ph.D. M.Sc.RWTH
Institute of Biomechanics
Stremayrgasse 16/II | 8010 Graz
Phone: +43 316 873 35510
niestrawska@tugraz.at

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Contribution of Graz University of Technology

Improved “energy harvest” in solar cells

Oliver Hofmann, solid-state physicist at TU Graz, is working on the simulation and prediction of material properties. All this to optimise solar cells. He gets help from a supercomputer in the USA.

Oliver Hofmann is part of an international consortium researching the improvement of solar cells.
© Baustädter – TU Graz

A billion is a lot. We all know that. But can we imagine it? “If you start counting today – one number per second, eight hours per day, 40 hours per week, you’ll need 145 years before you’ve counted to a billion,” explains Oliver Hofmann from the Institute of Solid State Physics. The theoretical physicist is occupied with the design of materials and is investigating how the arrangement of molecules on the surface of a material influences its properties. His objective is to optimise material properties and, in the long run, to contribute to building more efficient solar cells. “In my work I very quickly approach the billion mark regarding possibilities of how molecules can be arranged. And each possibility confers different properties on the material,” he explains. “All this is calculated using complicated methods of quantum mechanics for which a computer doesn’t just need seconds but rather several days.” For this reason the researcher works with supercomputers, and these are located either at the Vienna Scientific Cluster in Vienna or in the federal state of Illinois in the USA.

Funding from the US Department of Energy

Computing time on supercomputers is expensive. One hour costs roughly one cent. The air-conditioning, in particular, is cost intensive because the computer cluster filling the room produces huge amounts of heat and has to be cooled down to provide flawless operation. “Basically, we get the very expensive air-conditioning paid for,” laughs Oliver Hofmann. Together with colleagues from Carnegie Mellon University, Duke University, Argonne National Laboratory (all in USA), the University of Potsdam and TU München (both in Germany) and Aalto University (Finland), he’s been working for several years on improving materials for solar cells in the “Materials and Interfaces for Organic and Hybrid Photovoltaics” project.

For the third time running the consortium has received a grant from the US Department of Energy for its computer-intensive research. The Department of Energy wants to advance sustainable and innovative research into green energy in the framework of its “Innovative and Novel Computational Impact on Theory and Experiment (INCITE)” programme. Altogether in 2018, 5.78 billion hours of computing time were made available worldwide on two of the fastest supercomputers of the USA at 55 research establishments. One of these supercomputers is at the Argonne National Laboratory, the other is at the Oak Ridge National Laboratory. Both laboratories specialise in physics calculations and new energy. A total of 160 million hours of computing time will be made available to the project consortium and Oliver Hofmann on the IBM Blue Gene/Q at Argonne National Laboratory in 2018. The research work and interpretation of results is carried out at the different locations of the research partners – the actual computing time takes place using countless input files either at the centre in Vienna or in the USA.

More efficient solar cells as overarching objective

Oliver Hofmann’s aim in the project is to optimise loading transfer at the surface of solar cells. Basically, a solar cell works just like the human body when it takes a medicine. When a tablet is swallowed, a substance is released in the stomach which can then be further processed. In the case of a solar cell, light strikes the material on the surface and free charge carriers are created which have to be dissolved out of the material in order to be able to continue working with it. How fast and efficient this is depends on the interface between the absorbing material and the receiving electrode. And the properties of the material depend in turn on the arrangement of the molecules on the surface.

This is where Oliver Hofmann comes in. He works on a software package which simulates countless possibilities and can find the optimal structure. Experimenters thus have a reliable tool which can calculate the optimum molecular arrangement in an initial step, can say precisely what environmental conditions (temperature, pressure, etc.) are necessary in a second step, and can even simulate the precise path of the desired structure in a third step. After all, not just one step but rather a much longer sequence is necessary to get the desired structure. The physicist's aim is not to get the software to spit out the theoretically best structure, but rather to find the most efficient structure which is practical and viable. "For example, it would be possible that the optimum structure is stable at a temperature of 5,000°C. Of course, this cannot be implemented in reality, and we have to specify several parameters for the programme," he explains.

Future hope

That the research group is on the right track with their work is shown among other things by the fact that the funding from the USA has been allocated to the project now for the third time. The Austrian Science Fund (FWF) is also funding the research project. Furthermore, a START application will be submitted in the summer to be able to continue intensive work. Oliver Hofmann: "I'm not saying we'll get it instantly. But we're well on track and I think that we'll soon find a solution to our problem.

Oliver Hofmann and his working group at TU Graz´s Institute of Solid State Physics. *© TUG*

Contact:

Dipl.-Ing. Dr.techn. Oliver HOFMANN
Institute of Solid State Physics
Petersgasse 16/II | 8010 Graz
Phone: +43 316 873 8964
o.hofmann@tugraz.at

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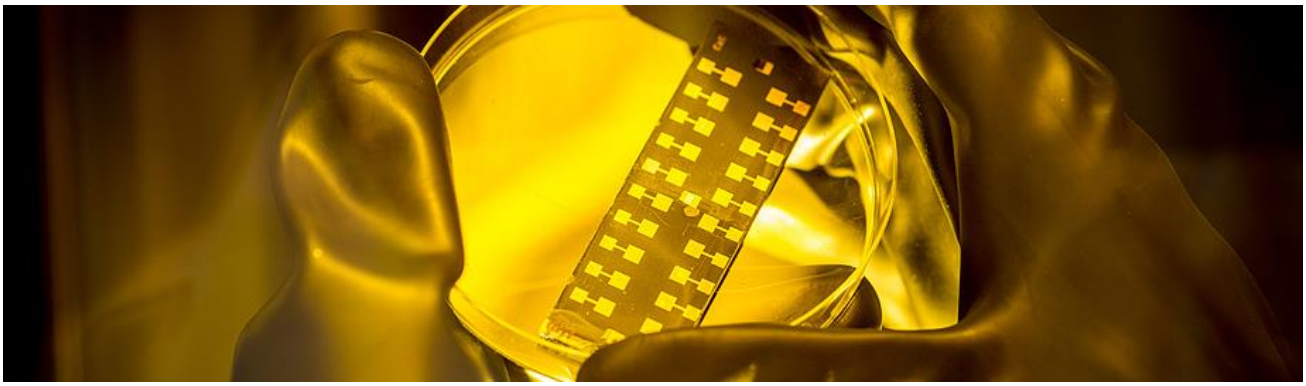
Contribution of Graz University of Technology

An International PhD via Thinface

In the last four years, 14 young scientists worked in the field of advanced materials across Europe in the training network Thinface and are now completing their cross-border doctoral degrees.



The fundamental idea of the Thinface training network was to promote research into sustainable, more efficient and economical energy solutions. *© TUG*

The fundamental idea of the Thinface training network was to promote research into sustainable, more efficient and economical energy solutions.

Joint research and international collaboration are the main cornerstones on which the work which is intensively promoted by TU Graz is built. Recently a Europewide project was brought to a successful conclusion with the centrestage involvement of TU Graz's Institute of Solid State Physics. Thinface is a European training network which was initiated by the European research network PCAM (Physics and Chemistry of Advanced Materials).

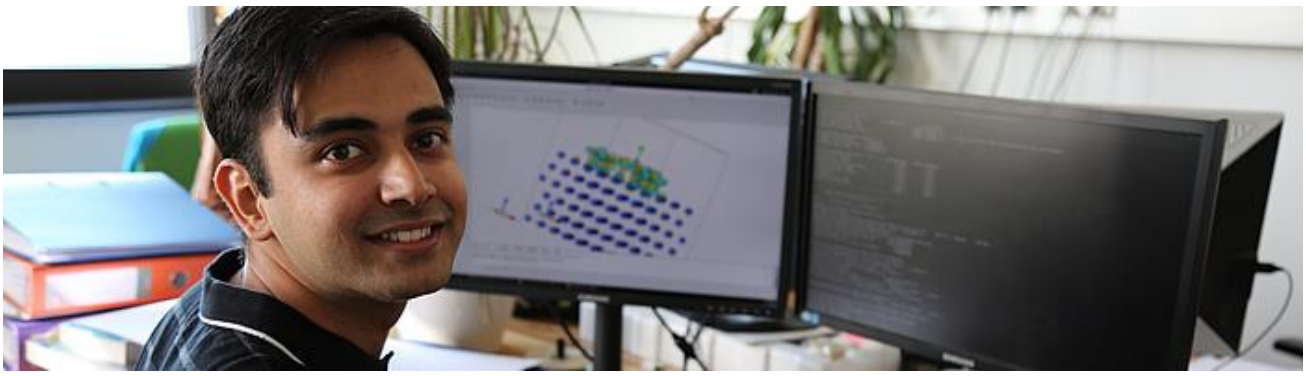
Thinface enabled 14 young scientists from all over the world to work together on a topic in a multidisciplinary way and to each further their own PhD thesis at a European university. The programme was funded by the EU funding scheme Marie Sklodowska¬Curie Actions. Two of these aspiring scientists have since taken up their jobs at TU Graz.

Sustainable energy solutions

The fundamental idea of the Thinface training network was to promote research into sustainable, more efficient and economical energy solutions. The research activities focused on novel ideas and techniques in the field of new energy systems and hybrid photovoltaics. Research was conducted in five areas of work – starting from the basics and moving towards

production and stability. But the students were not limited to their own research areas. A key element of the training programme was international mobility and specialized training of the scientists. To this end the students spent much time at one of the partner universities or partner companies. In other European countries to carry out research outside their own particular research areas. “I have a background in materials modelling and simulation – but during my six months at the University of Southern Denmark in Sønderborg I turned my attention towards device fabrication,” explains Shashank Harivyasi.

Shashank Harivyasi did his master's thesis in Graz and continued his PhD with the training network Thinface.



Shashank Harivyasi did his master's thesis in Graz and continued his PhD with the training network Thinface. *© TUG*

He is one of two international students who had been given a doctoral place at TU Graz through the programme. He did his masters’s studies at Amity Institute of Nanotechnology in Uttar Pradesh, India, and he concluded them by conducting research for his master’s thesis at TU Graz. He then continued the research by successfully applying for one of the Thinface¬associated PhD positions at Graz. “For my master’s thesis I particularly sought researchers in this field and came across Egbert Zojer,” explains the researcher. “This is a very unusual way to go about it. Usually students at the master’s level make their choice based on the name of their future host university, and only at the postdoc level seek out researchers which suit their field. I was impressed by Shashank doing that differently,” explained Egbert Zojer, supervisor of Shashank Harivyasi’s master’s and doctoral theses and researcher at TU Graz’s Institute of Solid State Physics.

In addition to TU Graz, the Thinface-network also includes the University of Southern Denmark (three students), TU Dresden (one student), Université Pierre et Marie Curie (one student), Università Degli Studi di Milano¬Bicocca (two students), Universidad Autónoma de Madrid (two students), Abengoa Research (one student) and CIC nanoGune (two students).

There was also support from Synchrotron SOLEIL and the five companies Novaled, Plasmore, Pirelli, Graphenea S.A. and Mecwins.

Egbert Zojer is part of the PCAM network and helped to initiate the Thinface project.

International exchange

Shashank Harivyasi also acted as a representative of the PhD students, championed their interests in the steering group of the network and helped organising the final summer school. “The network worked amazingly,” says the delighted physicist. “We had many opportunities to meet each other, to get to know new research communities and make contacts with other research institutes.” If students take an exam at another European institute, in addition to their PhD they can receive an international research certificate for their pan-European experience from the University of Milano-Bicocca.

Egbert Zojer is part of the PCAM network and helped to initiate the Thinface project. *© TUG*

Academic output

On top of the possibility for students to evolve personally, the academic output of the 14 doctoral students is not to be ignored. So far this includes 38 publications, two patents and two poster awards. “In the next few years this will probably amount to some 50 publications altogether. We’re currently waiting for several papers as well as jointly published books,” explains Shashank Harivyasi.

Contact:

Ao.Univ.-Prof. Dipl.-Ing. Dr.techn. Egbert ZOJER
Institute of Solid State Physics
Petersgasse 16/III | 8010 Graz
Phone: +43 316 873 8475
egbert.zojer@tugraz.at

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Contribution of JOANNEUM RESEARCH - DIGITAL

Dependable secure time-aware sensor networks

The acquisition, time-aware analytics and managing of complex processes by means of highly advanced and dependable wireless sensing systems are major challenges in the digital transformation of industry. K-Project DeSSnet aims to enable the future usage of sensor networks as dependable and as cost-efficient as possible. DeSSnet (http://www.dessnet.at) will thus concentrate on selected future-oriented Key Enabling Technologies for wireless sensors and communication to achieve security, dependability, interoperability and energy efficiency, as well as time-aware analytics in applications and services.

As part of a complementary consortium of globally active industrial and leading international scientific partners, DeSSnet covers the whole value chain of wireless sensor networks. DeSSnet establishes and sustains the vision of the involved regions Styria and Carinthia as the core technology cluster of electronic components and systems in Austria with a global leading position. The consortium partners represent **the whole sensor value chain**, ranging from chip and sensor developers and producers to application and solution providers, integrating also SMEs. In this way, DeSSnet differentiates itself from numerous projects, which are concentrating on rather one research challenge or tackling the IoT in a very broad sense.

The overall Research Programme will develop **Key Enabling Technologies** (KETs) in four subprojects and will probe them in an **Innovation Lab**.

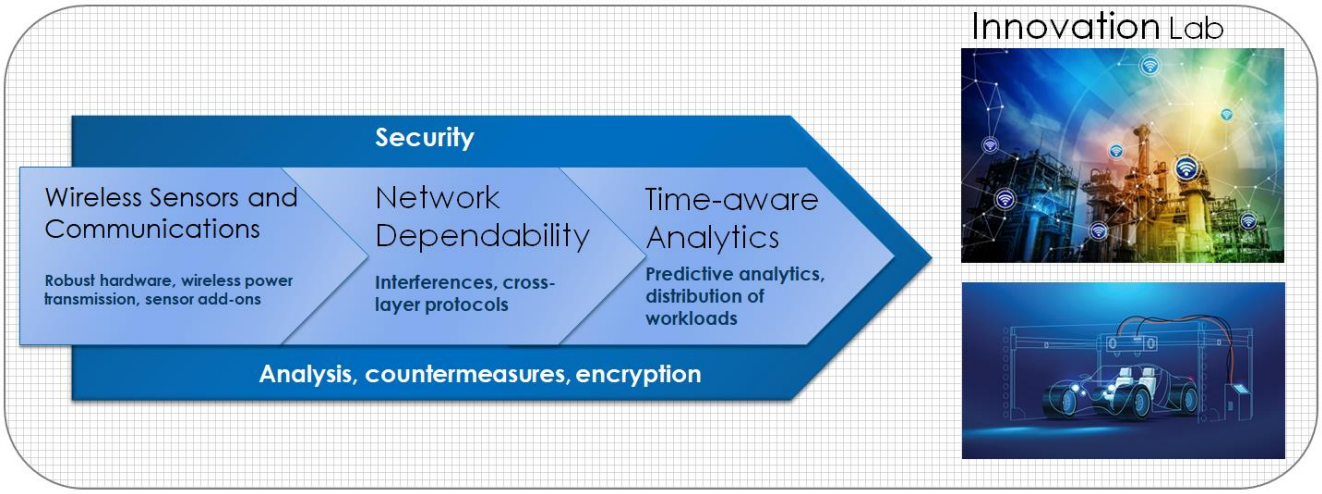

Figure 1: Project Structure

Research in DeSSnet will focus on the next generation of dependable IoT/CPS devices to enable new sensing services in harsh environments. Research topics range from development on the chip-level over the network-level to the individual application level:

- **KETs for Wireless Sensors and Communication**: The ultimate objective of this hardware related subproject is the research on and the development of key enabling wireless sensor and communication technologies for the next generation of dependable Internet of Things (IoT)/cyber physical system (CPS) devices to enable new sensing services. In this project, three key enabling wireless sensor and communication technologies will be investigated to pave the way for future applications of IoT/CPS devices by solving issues concerning current state-of-the-art IoT/CPS systems, i.e., their interoperability, resilience and energy efficient and cost-effective deployment in harsh application environments.

- **KETs for Security:** The connection of sensors and actuators via wireless communication links offers tremendous opportunities to increase productivity in many fields of applications (production, automobiles). However, the IoT also leads to unprecedented opportunities for attackers to reveal confidential information and to manipulate data even in such a way that physical processes are changed. The goal of DeSSnet concerning security is to address this challenge and to find secure and efficient technologies in order to secure heterogeneous sensor networks. In particular, we aim to work on three key enabling technologies that we consider the most critical ones for enabling security in heterogeneous sensor networks: (1) security analysis technologies, (2) software security technologies and (3) technologies for secure and efficient execution of cryptography.

- **KETs for Network Dependability:** The DeSSnet sensing services rely on a wireless network of sensor nodes (comprising sensor, processing unit, wireless interface, etc.) or (RFID-) readers.

Dependable wireless communication with self-sufficient sensor nodes, especially in harsh industrial and automotive environments where sometimes also deterministic Quality of Service (QoS) requirements have to be met, is still a challenging field of research. Therefore a top-down approach that models the requirements from the application viewpoint will be taken. To be optimized, this will be mapped into networking parameters and will be used to develop a set of cross-layer protocols.

- **KETs for Time-aware Analytics:** The next generation of sensor networks' analytics methods for many industries will improve all steps within their business processes to be fast, versatile and competitive. To make the right decisions on time, it is vital to move the data processing away from centralized nodes into the edge of networks, aiming at reducing the latency and minimizing essential information exchange between sensors and the analytics components. The main objective is to lower the integration barrier of time-aware data-analytics in the next generation of industrial application by researching on predictive analytics and cognitive methods using time-aware concepts. This will make the establishment of data driven applications much easier and cheaper.

Finally, during Innovation we build and verify the technological advances with company driven applications and use-cases.

BioNanoNet members in the consortium are **JOANNEUM RESEARCH Forschungsgesellschaft mbH, Technische Universität Graz with: Institute of Applied Information Processing (IAIK) and Communication, Institute of Microwave and Photonic Engineering (IHF) and Infineon Technologies Austria AG.**

The K-Project DeSSnet is funded within the context of COMET – Competence Centers for Excellent Technologies by the Austrian Ministry for Transport, Innovation and Technology (BMVIT), the Federal Ministry for Digital and Economic Affairs (BMDW), and the federal states of Styria and Carinthia. The programme is conducted by the Austrian Research Promotion Agency (FFG).

Contact:

Herwig Zeiner (Coordinator)
JOANNEUM RESEARCH - DIGITAL – Institute for Information and Communication Technologies
herwig.zeiner@joanneum.at
www.dessnet.at

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Contribution of Materials Cluster Leoben

Spotlight: Materials Research for Microelectronics in Leoben

The event „Materials Research for Microelectronics" (in original „Materialforschung für die Mikroelektronik in Leoben") organized in cooperation with the microelectronic cluster "Silicon Alps" took place on 17.05.2018 at the "Impulse Center Materials" in Leoben. It was hosted by the University of Leoben ("Montanuniversität Leoben"), the Erich Schmid Institute of the Austrian Academy of Science, the Polymer Competence Center Leoben (PCCL) and the Materials Center Leoben (MCL).

About 70 guests from academia and industry followed presentations and posters and participated in discussions. It was demonstrated how the material research in all material classes following the value chain for electronic-based systems leads to innovation in components and systems. The focus here was on flexible substrates, new sensory and optical properties and, in general, the design for increasing reliability. The close cooperation between the individual research facilities in Leoben enables the formation of multidisciplinary research teams for the design and synthesis of new materials, innovative manufacturing processes and the design and test of systems. This all together is enabled by the integrated computer-aided simulation and analytics of materials, processes and devices.

Keynotes

- **Opening speech by the Chancellor of Montanuniversität Leoben (MUL) Prof. Dr. Wilfried Eichlseder**: After a short introduction on the MUL and the offered studies, the speech highlighted that more than 600 researches are working in the field of Materials Science in Leoben. Their in-depth insights run from the raw materials over processing to the final product and back to raw materials in all classes. In the last part of the opening, Magn. Eichlseder emphasized the special importance of the field „Materials for Microelectronics", where currently about 100 researchers are performing applied and basic research in all material classes from the

atom-molecule level to the device level, using world class analytic, test and simulation infrastructure.

- **Dr. Günther Maier, Head of Department Microelectronics at MCL***:* In the first part a detailed overview of the involved organizational units in Leoben and an insight on the cooperation portfolio were presented. Based on success stories of bundled competences of participating institutions, the second part showed how materials research has enabled innovation in electronic based systems. This is often made possible by a strong interaction between simulation and analytical techniques. This strong interlink between simulation and analytics is considered a key factor for the full digitalization of materials, processes and products including subsystems and devices.

- **Dr. Megan Cordill, Erich Schmid Institute (ESI) of Austrian Academy of Science**: After a detailed overview of the ESI and an explanation of the link between ESI and Department of Materials Physics from MUL, the presentation focused on the analysis and tests of conductive layers on polymeric, flexible materials. Examples for mechanical and thermic fatigue tests coupled with electrical and structural characterization across all scales were shown. Special emphasis was laid on the explanation of how interfaces contribute to the reliability of flexible electronics. One special highlight was the presentation of „FLEXOTEST“ device, which allows for a fast and accurate testing of lifetime.

- **Dr. Marco Deluca, Materials Center Leoben**: The presentation has dealt with the matters of how the use of nano-materials innovates the application of highly functional gas sensors systems. Starting with the basic principles of electrochemical sensors Dr. Deluca illustrated and explained why different types of nano-materials should be used in chemical sensors. The heterogeneous material integration on sensor platforms produced by CMOS processes allowed for the design and test of an integrated multi-sensor system. Classifiers and algorithms are developed to enhance its sensitivity and selectivity. Finally, Dr. Deluca showed how rigorous 3D integration of sensors on a sensor platform chip enabled an international consortium for the fabrication of a world-wide unique sensor system with 57 sensors on one chip.

- **Prof. Dr. Christian Mitterer, Montanuniversität Leoben**: Prof. Mitterer introduced the capabilities and research portfolio on the Department Physical Metallurgy and Materials Testing with a special emphasis on vacuum deposition, simulation and characterization techniques. In the second part he focused on special barrier coatings to prevent Cu diffusion into silicon substrates. He pointed out that the key influencing parameters for diffusion like micro-structure and stress can be tailored by the design of processes. This was followed by a success story of the combined material and process design for flexible electronics. By means of this methodology it was possible to develop and produce coatings which are securely bendable with a radius of 3mm. These coatings allow for a completely new field of applications in IC, RFID and displays.

- **Prof. Dr. Wolfgang Kern, Polymer Competence Center Leoben and Montanuniversität Leoben**: Prof. Kern introduced the PCCL and the Institute of Chemistry of Polymers (MUL). He highlighted the broad applications of polymers in electronics and in electronics industry. Starting with an example of the use of nano-composites as reliable dielectric with high thermal conductivity he discussed the use of composites as conductive printable layers. Printed electrical layers on paper pave the way towards disposable electronic devices. The use of simulation and testing was highlighted on an example on printed circuit boards, where it was demonstrated that multi-scale simulations enable design tools for large and complex systems.

***Poster highlights*:** The 20 posters presented covered various aspects from computer aided materials design on atomic scale to applications near reliability testing. The common aim of all posters was to explain and show how material science enables innovations. The examples included sensors, printable electronics, fabrication by deposition, ceramic electronic, optical films, and reliability analysis of components and systems. One section was especially dedicated to the available numerical and analytical methods.

There was plenty of time for good discussions and networking, both extensively performed in a wonderful location with panoramic view to the mountains and the city of Leoben.

Impressions of the event:

Wolfgang Kern, Günther Maier, Magn. Wilfried Eichlseder, Megan Cordill, Christian Mitterer, Marco Deluca

Contact:

Materials Center Leoben Forschung GmbH
8700 Leoben, Roseggerstrasse 12
Tel: +43 3842/45 9 22-0
E-mail: mclburo@mcl.at
Internet: https://www.mcl.at/

Organiser of the Eurosensors 2018
https://www.eurosensors2018.eu

Silicon Alps Cluster GmbH
Europastraße 12
9524 Villach, Austria
office@silicon-alps.at

https://www.silicon-alps.at/

https://www.silicon-alps.at/spotlight-materials-research-for-microelectronics

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Contribution of TU Wien - Institute of Applied Synthetic Chemistry

Orange peel to wear

From a renewable and readily available waste product to produce a high-quality product such as polyester, is the goal of a new synthesis process, which is currently being developed at the Vienna University of Technology.

Polyester is a versatile starting material in industry, for example in the production of membranes or garment. At present, however, it is predominantly prepared from crude oil, which does not stand up to sustainable production. Assistant Prof. Florian Rudroff and his team, Dr. Nikolin Oberleitner and Dr. Anna Ressmann, from the Institute of Applied Synthetic Chemistry (FG Prof. Mihovilovic) of the Vienna University of Technology, have collaborated with the research group Prof. Gärtner / Prof. Schröder, showed how the sustainable production of a basic polyester material could work (Figure 1).

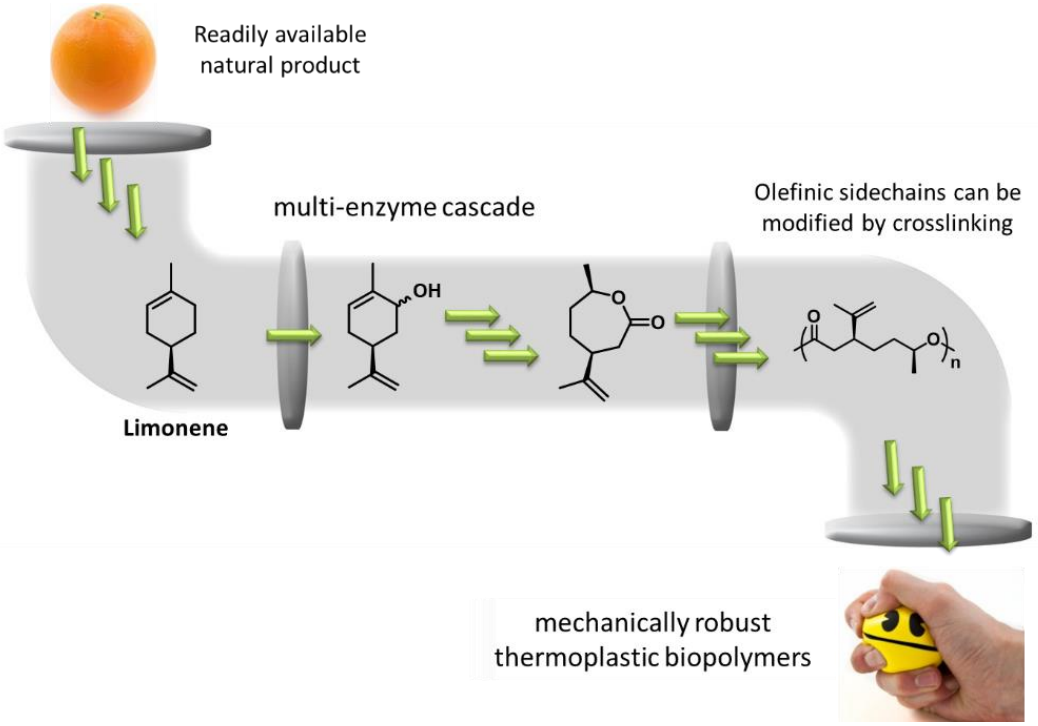

Figure 1 Sustainable synthesis of biopolymers by valorisation of orange peel.

Take: orange peel

Oranges not only taste delicious, they also have a typical smell. The aroma of limonene is responsible for this smell. It is a volatile substance in the skin of the fruit, with the average orange peel containing about 4-7% limonene. In order to extract limonene for further use, it must be released from the shell.

"We looked at a wide variety of extraction methods to find the most effective for us," explains Assistant Prof. Rudroff. "Limonene is also available on the market as a starting material, but we wanted to obtain an equally high-quality raw material directly from the waste product orange peel."

In order to gradually convert limonene to the desired product, special enzymes are needed that act as biocatalysts. In order to use the enzymes, they are produced in two genetically engineered bacterial species, namely *Pseudomonas putida* and *Escherichia coli*. As a targeted extraction and directly subsequent reaction method turned out to shake the cut orange peel in an aqueous buffer solution with the bacteria at room temperature for 12 to 24 hours. The bacteria convert stepwise, in a so-called concurrent cascade reaction, limonene into the basic building block for polyester. Depending on which enzymes are used, one can introduce different properties in the subsequent polymers. Besides the sustainable possibility of synthesizing a polyester, it was also important to show that this is possible at all.

Limonene can be chemically very difficult to modify, which makes it hardly interesting as a raw material for the industry. "Our next step is that we only need one more bacterium for the complete implementation. Thus, this synthesis method would be interesting for any industrial application" Rudroff confidently said. Further investigations focus on the polymerization and subsequent application of this new and sustainable building block.

Publication

Nikolin Oberleitner, Anna K. Ressmann & **Florian Rudroff*** *et al*.: **From waste to value – direct utilization of limonene from orange peel in a biocatalytic cascade reaction towards chiral carvolactone.** *Green Chem.* **2017**, *19*, 367-371 **DOI:** 10.1039/C6GC01138A.

Contact:

TU Wien - Institute of Applied Synthetic Chemistry
Getreidemarkt 9, 163-OC, BI02H18
1060 Vienna, Austria

Assistant Prof. Dr. Florian Rudroff
www.ias.tuwien.ac.at
florian.rudroff@tuwien.ac.at

Univ.-Prof. Dipl.-Ing. Dr. Marko D. Mihovilovic
Full Professor for Bioorganic Synthetic Chemistry
Head of Institute
http://www.ias.tuwien.ac.at/MDM/
marko.mihovilovic@tuwien.ac.at

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BioNanoNet *retrospect*

Blockchain on stage: future of life science

March 15th 2018, Graz, Austria

Blockchain, one of the new trendy technologies (or better to say a compendium of old technologies) is about to change many of the actual existing applications and to open the doors to new ones. It is still in its fledging stages but it is already being used in many companies.

Within the framework of the project NanoCommons, where BioNanoNet is working and researching new possibilities for the sustainability of this project, Blockchain stood out as one of the highlighted chances for making the project more attractive for the community of users. In order to keep up-to-date and to follow BioNanoNet's philosophy of exploring new branches of research, new applications and future technologies, as well as community building, BioNanoNet has attended to several events related to Blockchain.

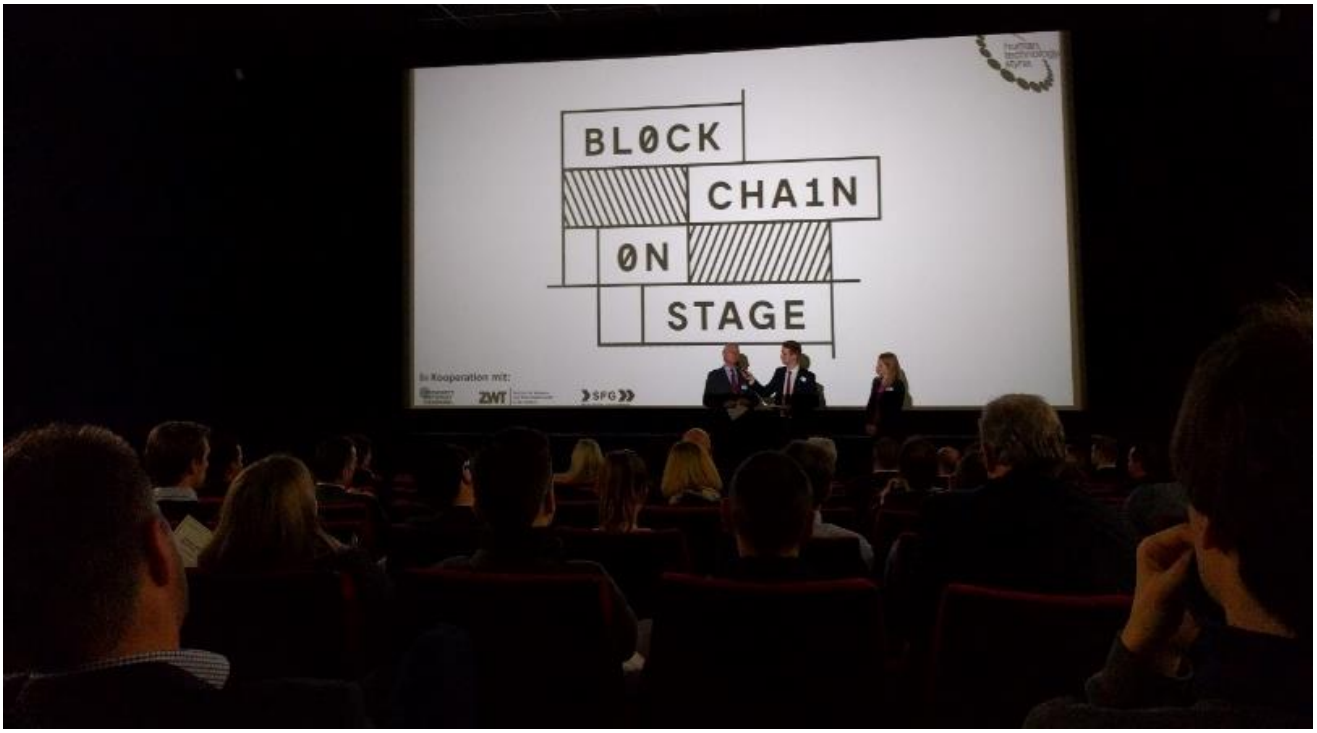
The first of them was organized by Human.Technology Styria. 130 attendees of different market branches updated their know-how thanks to the Blockchain experts who presented their experiences with Blockchain opening our minds to new areas of application and new possibilities and projects.

Blockchain requires the willingness to share data between all participants in order to assure the integrity of the data contained in the chain.

These are some of areas where an implementation/use of Blockchain seems to have a big impact in the near future (2018 – 2022):

- Energy business
- Industry & Internet of Things
- Health system
- Payment systems, digital currencies & Fintech
- Smart City

More information about the event can be found here.



Human Technology Styria - Blockchain Event

This project has received funding from the European Union's Horizon 2020 programme under grant agreement No 731032.

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Exchanging knowledge within the NANOGEN-TOOLS Project

Secondment of BioNanoNet to NIA (Nanotechnology Industries Association)

March/April 2018, Brussels, Belgium

NANOGENTOOLS is a H2020 MSCA-RISE project to exchange knowledge in nanosafety. The 4-year European project, devoted to the development and implementation of a new generation of nanosafety assessment tools, was launched in January 2016, and addresses the challenge of identifying and controlling the hazards associated with Nanomaterials (NMs) by joining industry and academia to create a collaborative excellence-based knowledge exchange network in the MSCA-RISE framework. The project is delivered through cross-sectoral/disciplinary secondments linking EU academic institutes/networks with industry including SMEs and policy makers across 8 countries. The secondments play a key role in facilitating knowledge exchange between experts with different backgrounds and knowledge.

Secondment of BioNanoNet to NIA

In March/April 2018, BioNanoNet seconded Nikolaus Ladenhauf, MA to NIA, a Belgian non-profit organisation located in Brussels. NIA supports the development of nanotech innovations that improve the lives of consumers, preserve our environment and advance our world both across Europe and around the world. NIA and its Members are committed to the safe, sustainable and beneficial use of nanotechnology and nanomaterials across all industries. Also, they work towards a better understanding of nanotechnology's important role in society and economic development and building a positive global environment for nanotech innovation.

Through the close collaboration between BioNanoNet and NIA and knowledge exchange between this two organisations, a workshop event was organised to identify key requirements

for the successful economic development of key enabling technologies (KETs) in Europe, and to disseminate the NANOGENTOOLS project aims.

In addition to the events, the secondment gave NIA and BNN the opportunity to work in close collaboration to analyse how the organisation of the clusters are build up to allow sustainable collaboration in the future.

Secondment of BioNanoNet to NovaMechanics Ltd

May 2018, Nicosia, Cyprus

In May 2018, BioNanoNet seconded Mag. pharm. Susanne Resch to NovaMechanics Ltd located in Cyprus. NovaMechanics Ltd is an in silico material design company committed to the computer aided design of new materials, small-molecules and nanoparticles. Nova-Mechanics Ltd is focused in the development and implementation of in silico methods to guide decisions in the design and selection of promising new compounds. NovaMechanics contribution to the NANOGENTOOLS project is the application of cheminformatics methods such as quantitative structure-activity relationship (QSAR) modelling to establish statistically significant relationships between measured biological activity profiles of NMs and their physical, chemical, and other properties, either measured experimentally or computed from the structure of NMs. This secondment was the second secondment between the two partners and provided a great chance to further share and exchange knowledge, expertise and experiences. Based on the work performed by BioNanoNet in H2020-Pilot projects INSPIRED, Hi-Response, R2R Biofluidics and Smart-4-Fabry, the know-how of implementing safe-by-design in innovation processes paired with their modelling expertise could lead to better tools in the nanosafety area.

Further information on the NANOGENTOOLS project and updates on developments can be obtained from http://www3.ubu.es/nanogentools.

NANOGENTOOLS project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 691095.

R2R Biofluidics project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 646260.

Hi-Response project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 646296.

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Think Tank - Life Sciences in Digital Transformation

April 5th 2018, Graz, Austria

With the kind support of **Human.technology Styria GmbH, Know-Center GmbH** and **Bio-NanoNet** hosted the **first Life Science Event about "Life Sciences in Digital Transformation"** on 5th April 2018 at Know-Center, located at the Campus Inffeldgasse of Graz University of Technology.

The event was officially opened by Univ.-Prof. Dr. Stefanie Lindstaedt (CEO Know-Center GmbH), Mag. Susanne Resch (BioNanoNet) and Dr. Ing. Johann Harer (CEO of Human. technology Styria GmbH).

Dr. Roman Kern (Head of Knowledge Discovery, Know-Center GmbH) held a talk titled "Artificial Intelligence in Healthcare" with an introduction to the field of Artificial Intelligence (Machine Learning, Deep Learning, etc.) He explained the wide range of Artificial Intelligence applications for the health sector and pointed out that "the market around AI in health care would explode in the next 5 years". However, he also pointed out that expectations are very high and that Artifical Intelligence is currently being promoted as a "panacea" for the healthcare sector. In particular, this is the case because many celebrated successes had been more "low hanging fruits", and the real challenges are actually still ahead of us. However, let's not forget that AI will not establish itself in every area, according to Kern. Nonetheless, Artificial Intelligence offers a great deal of potential, "but it is hard work; and needs in particular one thing: Competence ".

Dr. Bernd Schandl (CTO, mySugr) presented the success story behind mySugr (an app-based diabetes all-round care for the daily hurdles and problems in everyday therapy) in his talk on "Development of patient-oriented medical software". mySugr started with the basic idea that "apps are just right for people with diabetes", and now there are even tattoos with the company logo on satisfied customers. Patient-centered development is the message of

many companies; Schandl explained in a clear and catchy way how mySugr integrates "User Centered Design" into all its corporate processes. For example, there are interviews with end users several times a week. "Know your users" - and success proves them right.

The next talk took the listeners into the field of sensor technology. **DI Robert Holzer** (Project Management and Business Development, RECENDT - Research Center for Non-Destructive Testing GmbH) highlighted some not so well known current sensor technologies in his talk with the title "Sensors - the digital new eyes of physicians - current sensor concepts, eg: for interoperative imaging or point-of-care diagnostics ". OCT (Optical Coherence Tomography), for example, provides cross-sectional images of optically semi-transparent objects without contact and in a non-destructive way, with short measurement times and high precision. As technology combinations often open up completely new possibilities, OCT has been very successfully combined with photoacoustics (imaging, opto-acoustic method for the display of e.g. biological / medical samples) or with Raman spectroscopy (spectroscopic investigation of the inelastic scattering of light on molecules or solids). The combination of new technologies opens up completely new possibilities, but "without digital evaluation and preparation of the raw measurement data, all these measurement methods remain virtually toothless".

After the break, **Mag. Caroline Schober-Trummler** (Vice Rector for Research & International Affairs, Medical University of Graz) presented a picture of digitalization in the health sector and its effects on patients and doctors and us as a society in her talk "Digitalisation in Medicine: Beautiful, New Medical World?". For the technical aspects of "digital medicine" - be it digital medical records, tablet visits, wearables, telemedicine, robotics, personalized medicine or a modern, digital research portfolio - are just one side of the coin. What kinds of challenges all these new technologies bring to patient (eg increasing health awareness and self-responsibility versus coercion for self-optimization), physicians (education, prediction of disease probabilities, prenatal diagnostics, liability issues with diagnostic (assistance) systems) and us as a society (Cost pressures, data protection, desolidarization, dealing with and health care of the elderly) is an equally interesting and socio-politically relevant issue.

To conclude the series of talks, **Dr. Martin Ellmerer** (Head of Development Office Graz, B. Braun Melsungen AG) gave a talk about "Digitalization in Intensive Care Medicine - Biosensors as Forerunners for Automated Therapy Systems" with insights into applications of biosensors, for example in insulin therapy or the fluid balance. The generation of medical data

is extremely complex due to security and quality standards, privacy regulations for the protection of patients, etc. Data are usually collected for regulatory purposes only but remain largely unused therapeutically. The ever-increasing volume of data is increasingly overburdening the nursing staff, opening up new, faster therapeutic decision-making channels and, in turn, requiring faster diagnostic procedures and, as a result, decision support systems and sensors. Conventional blood glucose management, for example, is still based to a large extent on manual processes and individual decisions and thus offers a high potential for automation and savings potential with regard to the nursing workload. Added to this is the lack of standardization in manual processes: The approach here is to also use infusion data for therapy control. The B.Braun glucose management therapy system is already CE approved and is currently undergoing clinical trials.

The program was rounded off by a World Café about the topics of the talk ("Artificial Intelligence in the Health Sector", "Digitalization in Medicine: Beautiful, New Medical Technology?", "Sensor Technology for Physicians, Where does the Journey go?" Patient in focus") and followed by networking at the buffet.

The following BioNanoNet members, which contributed to this successful event, can be acknowledged: KNOW Center, Medical University of Graz, RECENDT, HTS.

In connection with the event, the product "med360" of Know-Center's Life Science division was also advertised.

med360 is an information corridor that daily serves up-to-date new publications about the areas of interest of scientifically active physicians.

For further questions please contact Melanie Mayr, Product Management med360.

IMPRESSIONS FROM THE EVENT *(Copyright of the pictures: Know Center GmbH)*


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Digitalisierung in der Medizin:
Schöne, neue Medizinwelt?
Caroline Schober-Trummler
Vizerektorin für Forschung & Internationales
Think Tank - Life Sciences im digitalen Wandel
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Workshop: The Blockchain Technology for new applications

April 17th 2018, Graz, Austria

Once acquired the basic know-how of Blockchain at the Event organized by Human.technology Styria, BioNanoNet went deeper into this with some questions related to the technology, in order to go further within the NanoCommons project.

The very specific setup of this workshop enabled intensive exchange about detailed questions. Furthermore, it was a good opportunity to establish contacts in terms of community building in line with the role of BioNanoNet in NanoCommons project.

16 participants attended to this workshop organized by the Green Tech Cluster. After a short introduction to different new possibilities/applications using the blockchain technology in a variety of industries, the experts identified possible new applications and explained/presented how the development of those applications, risk assessment, data protection and necessary operational and technical processes should be managed in order to succeed.

In addition, two concrete companies were under study, analysing if the use of Blockchain technology could bring opportunities in those concrete companies.

More information about the workshop can be found here.

Green Tech Cluster - Blockchain Workshop

NanoCommons project has received funding from the European Union's Horizon 2020 programme under grant agreement No 731032.

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BioNanoMed 2018

9th International Congress
Nanotechnology in Medicine & Biology

April 25th – 27th 2018, Graz, Austria

From 25th to 27th April 2018, the 9th International Congress of Nanotechnology in Medicine & Biology took place at the University of Graz, Austria. The event provided a forum for researchers, engineers, students and practitioners from Natural Sciences, Medical Sciences and Engineering as well as from educational and non-governmental institutions to discuss current, emerging and future trends of the converging fields of nanotechnology, biotechnology and medicine. More than 50 exciting lectures and invited talks given by leading international scientists as well as poster presentations offered delegates an excellent opportunity to discuss pioneering developments and to initiate cooperation projects.

The programme covered the following panel sessions:

- **Novel Nanomaterials for Medicine**
- **Nanotechnology in Therapy**
- **Nanotechnology in Medical Diagnostics**
- **Pharmaceutical Nanotechnology In Research and Development**

The thematic session about **Nano-enabled Innovation for Medicine** was organized by Bio-NanoNet and supported by Human.technology Styria.

Jesus M. de la Fuente (CIBER, Spain) presenting his key note lecture, chaired by XX (Technical University Vienna) at BioNanoMed-conference 2018.

A very special pre-meeting was jointly organized by Human.Technology Styria GmbH and BioNanoNet to get very exclusive contact with the key note lecturer of the conference, Prof. Jesus M. d. Fuente. Several members of the network used this opportunity to discuss about scientific work and future collaboration.

Excellent networking opportunity during the pre-conference event "meet the key-note", jointly organized by Human.Technology Styria GmbH and BioNanoNet.

Furthermore, BioNanoNet participated the conference in cooperation with JOANNEUM RESEARCH - HEALTH and contributed poster presentations on BIORIMA-project as well as Smart-4-Fabry project, addressing the following topics:

- "OFM to investigate blood-brain barrier transport in a safe-by-design nanocarrier development in the H2020 project Smart-4-Fabry", *T. Altendorfer-Kroath, C. Schimpel, N. Ventosa, A. Falk, F. Sinner, T. Birngruber*

- "Open flow microperfusion investigates skin exposure of nanobiomaterials in the H2020 project BIORIMA – BIOmaterial RIsk Management", *J. Adamczak, S. Resch, F. Sinner, T. Birngruber, A. Falk*

BIORIMA project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 760928.

Smart-4-Fabry project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 720942.

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EUFEPS Annual Meeting 2018

"Crossing Barriers for Future Medicines"

24-26/05/2018
Titania Hotel
Athens, Greece

EUFEPS Annual Meeting 2018
Crossing Barriers for Future Medicines

May 24th – 26th 2018, Athens, Greece

From 24th to 26th May 2018, the Annual Meeting of the European Federation for Pharmaceutical Sciences (EUFEPS) took place at the Titania Hotel in the heart of Athens, Greece. The event provided scientific sessions on the following topics:

- Physiology of the GI tract relevant for drug absorption
- Nanomedicines and nanosimilars: How to assess how similar?
- Performance of dosage forms in the GI tract and impact on drug absorption
- Nanomedicines: Challenges on the road
- Drug absorption, dissolution and in-silico modeling-towards prediction paradise?
- Manufacturing of future medicines
- Systems pharmacology
- Biotech and biosimilars
- Regulatory science: Partnerships looking into the future
- New drugs in oncology
- Information on drug absorption in regulatory processes- nice to know vs. need to know
- EUFEPS Network on Pharmacogenetics Research and Implementation
- Nanomedicines: the European Platform

Highly interesting key note lectures, oral presentations and poster presentations by international researchers and scientists, engineers, students and practitioners in the field of Pharmaceutical Sciences showcased current, emerging and future trends in medicine.

BioNanoNet participated the conference in cooperation with JOANNEUM RESEARCH - HEALTH and contributed poster presentations on H2020 projects BIORIMA as well as Smart-4-Fabry. For her contribution on safe-by-design, which is done by BioNanoNet in the Smart-

4-Fabry project, Mag. pharm. Susanne Resch was awarded the **award "Women in Pharmaceutical Sciences"** by EUFEPS and its committee.

Group picture taken at Opening Ceremony in front of the University of Athens. *© EUFEPS*

Prof. Dr. Erem BİLENSOY, President of EUFEPS European Federation for Pharmaceutical Sciences, awarded Mag. pharm. Susanne Resch the WIPS prize. *© EUFEPS*

BIORIMA project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 760928.

Smart-4-Fabry project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 720942.

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ETPN Annual Forum 2018

13th ETPN Annual Event of the European Technology Platform on Nanomedicine

May 28th – 30th 2018, Berlin, Germany

ACEnano
Analytical and Characterisation Excellence

SMART4FABRY

ETPN2018 Event provides a unique place to discover, to network, to showcase, to design new projects, to brainstorm about the industrial expansion of Nanomedicine, all in a relaxed and friendly atmosphere. Most importantly, the ETPN has started a great evolution to interface Nanotechnologies with other emerging medical technologies, notably through the coordination of NOBEL, in preparation of ESTHER. Therefore, ETPN2018 was a great opportunity to be part of that convergence for smarter HealtTech in Europe!

The programme covered the following topics:

- Clinical nanomedicine & implications in clinical practice
- Strategic vision for the future of Healthcare in Europe
- Disruptive medical technologies: who will pay the bill?
- Translation of best HealthTech innovations to the market
- Funding opportunities / Brokerage
- Current European Projects in Nanomedicine
- Pitch me up sessions! Selected talks
- Electronic poster exhibition

BioNanoNet as chair of the ETPN-Working Group “Safety and Characterization” organized a working group meeting and contributed to the Annual Forum, also promoting the EC-projects ACEnano (characterization) and Smart-4-Fabry (nanomedicine).

Furthermore, BioNanoNet participated in the Healthtech-TAB-session, supporting Christian Hill (Medical University Graz) with his high-potential technology to move forward towards getting his exciting technology translated into a product.

Another important interaction in terms of supporting BioNanoNet members to be visible in European nanomedicine ecosystem is to be involved in the EC-project NOBEL. Coordinating the NanoMedicine-Austria technology platform is recognized by the ETPN as coordinator of NOBEL project by inviting us giving us the role as associated partner of this project. The kick-off meeting of all involved national platforms (at the moment from 6 European countries) took place during ETPN-annual forum.

ACEnano project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 720952.

Smart-4-Fabry project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement No 720942.

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EU Brokerage Event on KET in Horizon 2020

June 7th 2018, Mainz, Germany

BioNanoNet, was present at annual EU Brokerage, the event dedicated to the Key Enabling Technologies (KET) targeting the upcoming calls in the following thematic fields:

- Nanotechnologies and Advanced Materials (NMBP)
- Biotechnologies (Biotec)
- Advanced manufacturing and processing
- Energy efficiency in Buildings (EeB)
- Factories of the Future (FoF)
- Sustainable process industries (SPIRE)
- Open Innovation Test Beds (OITB)

The objectives of the brokerage event were to present the 2019 topics of the European Union's NMBP Work Programme 2018 – 2020 of the Framework Programme for Research and Innovation "Horizon 2020" and to prepare future cooperations between participants.

BioNanoNet performed 15 pre-scheduled meetings (and some more during the breaks) with interesting participants. The main aim was to prepare future cooperations for our members with brokerage-participants. The expertise of BioNanoNet's members were well represented and BioNanoNet manage to get in touch with interesting research groups, to be able to put in contact our members with and involve them into promising consortia.

If you are interested to become a member and thus also be supported by BioNanoNet team in finding consortia for future projects, please do not hesitate to contact us.

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Conference Calendar

BioNanoNet events

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BioNanoNet Focus on Nanomedicine and Nanosafety

“Bio-Nano-Interactions: Medical Breakthrough & Safety Aspects“

When? 12 September, 2018, 14:30 – 19:00

Where? Graz, Medical University of Graz, Austria

14:30 – 15:00 Registration

15:00 – 17:00 Scientific session with key note lectures

17:00 – 18:00 Lab Facilities Visit (optional)

17:00 – 19:00 Networking & Buffet

For registration please visit the event website.

BioNanoNet Strategic Development & Networking

“Multidisciplinary cooperation in research: nanotoxicology, sensortechnology, health-safety-medicine“

When? 13 September, 2018, 9:30 – 18:00

Where? Graz, University of Graz, Austria

Download Agenda

BioNanoNet Focus on Sensortechnology

“Nano-enabled sensing systems”

When? 14 September, 2018, 9:30 – 12:30

Where? Graz, University of Technology, Austria

Download Agenda

BioNanoNet on site events

Nanotech France 2018

When? 27 – 29 June, 2018

Where? Paris, France

For more information please visit the event website.

CLINAM 2018

When? 2 – 5 September, 2018

Where? Basel, Switzerland

For more information please visit the event website.

NanoTox 2018 - 9th International Conference on Nanotoxicology

When? 18 – 21 September, 2018

Where? Neuss, Germany

For more information please visit the event website.

OpenTox Euro 2018

When? 8 – 11 October, 2018

Where? Athens, Greece

For more information please visit the event website.

2nd EU-Asia Dialogue on Nanosafety

When? 29 October, 2018

Where? Vienna, Austria

For more information please visit the event website.

Industrial Technologies Conference 2018

When? 30 - 31 October, 2018

Where? Athens, Greece

For more information please visit the event website.

NanoSafe

When? 5 – 9 November, 2018

Where? Grenoble, France

For more information please visit the event website.

Workshop on SAFETY ASPECTS IN PILOT LINES an EPPN-NSC i2L joint session at NanoSafe conference

When? 7 November, 2018

Where? Grenoble, France

For more information please visit the event website.

For all events visit our BioNanonet website!

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Finally

We hope you enjoyed our BioNanoNet newsletter!

Please do not hesitate to contact us if you would like to give us any suggestions or feedback!

Our next BioNanoNet newsletter will be published in September 2018.
BioNanoNet partners are welcome to send their contributions until 14th of September 2018!

Contact:
BioNanoNet Forschungsgesellschaft mbH

Simone Jagersbacher
simone.jagersbacher@bionanonet.at or info@bionanonet.at
phone: +43 699 155 266 02
www.bionanonet.at

Your BioNanoNet team

from the left …

Christa Schimpel (scientist), Beatriz Alfaro Serrano (scientist), Susanne Resch (scientist), Andreas Falk (CEO), Gabriele Katz (CEO), Christine Halbedel (office), Angelika Halbedl-Herrich (office), Simone Jagersbacher (public relations & marketing) and Nikolaus Ladenhauf (project manager)

Impressum:
Owner and publisher:
BioNanoNet Forschungsgesellschaft mbH - FN 285326 y, Steyrergasse 17, 8010 Graz, Austria
UID: ATU 63046279

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