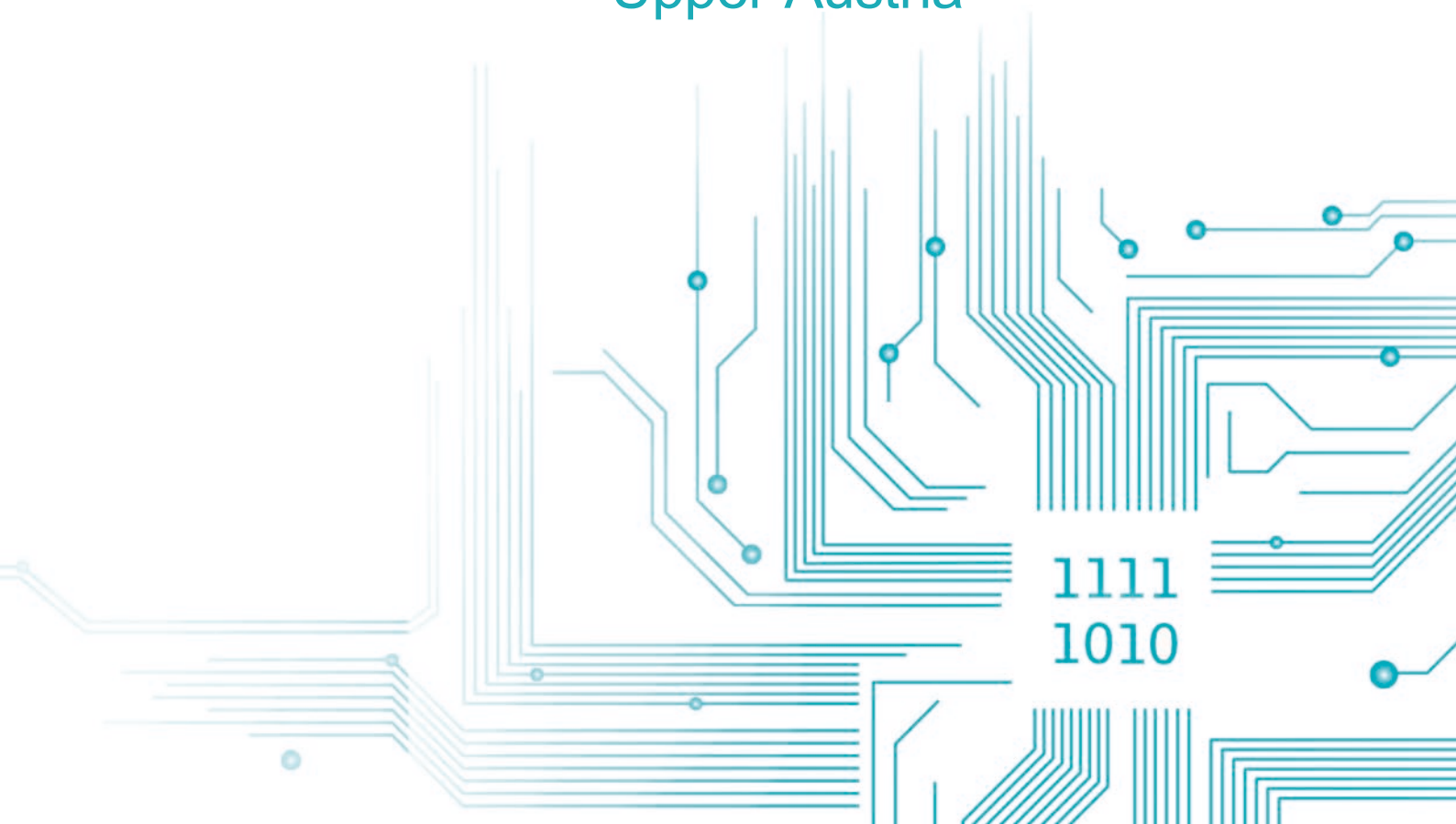




JKU

& Partners

Medical Technology
Upper Austria



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Establishing Interdisciplinary Approaches and Strengthening an Innovative Location



Health care in Austria is exemplary, both in terms of technology and quality. Continual investment in local research and development is crucial in order to pursue sustainable and pioneering advancements. The future market for medical technology has enormous innovative potential. In this regard, I am particularly pleased to see that the Johannes Kepler University (JKU) Linz is at the forefront, taking the initiative to encourage local partnership collaborations designed to pool resources as well as drive growth and foster new synergies.

The Whitebook contributions are impressive, displaying the broad spectrum of what individual JKU institutes have to offer ranging from the computational fields of excellence at the Faculty of Natural Sciences & Engineering in computer science, mathematics, mechatronics, information processing, nanosystems, biosystems, and polymer systems to the respective expertise at both the Faculty of Law and the Faculty of Social Sciences, Economics & Business. The JKU is an institution where active and successful interdisciplinary approaches are alive and well.

By creating a Faculty of Medicine in Linz, the JKU has ushered in a new era of interdisciplinary, cross-sector research. Clinical research on ageing and preventative medicine is unique in Austria and this field is becoming increasingly significant in terms of socio-political contexts. Crucial factors include taking advantage of a particularly outstanding outset position and actively including all corresponding participants in Upper Austria. This not only applies to companies and industries in the field of medical technologies, but also to universities of applied sciences and the Kepler University Hospital.

I strongly believe that close, strategic collaboration between business, medicine, and science & academia is pivotal in order to ensure Upper Austria's long-term success as an attractive and competitive location. Hence, the Johannes Kepler University's supportive contributions are invaluable.

A handwritten signature in black ink, appearing to read 'Harald Mahrer', written in a cursive style.

Mag. Dr. Harald Mahrer
*Austrian Federal Minister of Science,
Research and Economy*

Medical Valley Upper Austria – A Milestone in Medicine



Focusing specifically on people and health, the new “Health & an Ageing Society” campaign is now an integral part of the current strategic economic and research program “Innovatives OÖ 2020”. The program focuses on health care and how to make health care more effective as well as how to provide a higher quality of medical care. Research and development not only targets strengthening quality aspects, but also boosting efficiency, and increasing effectiveness. The idea is for Upper Austria to become a leading region in the field of “individualized medicine”.

This includes, for example, creating high-tech solutions in medical technology, improving modern diagnostic methods, studying preventative medicine and therapies, developing data analysis methods and sensor technology, as well as creating advanced software for medical applications. Modern technologies can improve everyone’s quality of life, particularly the elderly so they can lead independent, active, healthy lives for years to come.

As this sector is particularly important, it is crucial to seamlessly merge research and development-driven universities with the business expertise at local companies. Creating the Upper Austrian Medical Valley is a fundamental milestone. This platform bridges the divide between academic studies in medicine and medical technologies offered at local universities and universities of applied sciences and application-oriented environments found at research institutions and regional companies. Together - and with a high level of competence - we will build on existing strengths and focus on selected areas of research such as clinical ageing, preventative healthcare, and medical technology. We aim to become a driving force behind innovative strategic projects and the development of new technologies and methods. Close, interdisciplinary collaboration will result in rapidly putting findings in research & development in to practice.

A handwritten signature in blue ink, appearing to read 'Stelzer', written in a cursive style.

Mag. Thomas Stelzer
Governor of Upper Austria

Networking as a Success Factor



We hear the magic words “future of networking” often, even in the field of healthcare. The new Faculty of Medicine will work closely together in the future with the Kepler University Hospital, the University of Applied Sciences for Health Professions along with the medical technology cluster, the religious order hospitals, and local companies.

It will not cost much but it will help to create a “Medical Valley” that will put Linz above the medical universities in Vienna, Graz, and Innsbruck. In a few years, we will have a very unique feature and selling point. The most important thing is that we bring these diverse areas together and not drive them apart. This will benefit Upper Austria as location of business by supporting medically-related industries so outstanding companies can take advantage of these cooperative opportunities. This also means the “Medical Valley” of Upper Austria will become a driving force in the job market, particularly when it comes to high-skilled jobs. The “Medical Valley” represents a part of our future prospects. Experts say that our fields of research need to be broader in order to make better use of international market potential. Topics such as “healthy aging” and “eating right” are enormous international market opportunities that continue to pass us by. Like medical technology, we can only conduct qualitatively, high-quality research and make the findings a part of providing innovative services when accompanied by scientifically sound base-knowledge research in medicine and educational programs.

I would like to thank everyone involved in creating the “Whitebook” and I would like to wish all of the cooperation partners the greatest possible success.

A handwritten signature in blue ink that reads "Josef Pühringer".

Dr. Josef Pühringer
Governor of Upper Austria (Retired)

In Upper Austria, Progress in Medicine is a Step Forward



Medical breakthroughs go hand-in-hand with technological advancement. Many recent advancements - from human genome sequencing to developing new surgical tools - would never have been possible if were not for research conducted in new technologies. Over the past few years, Upper Austria's technological landscape has changed considerably. The newly established University of Applied Sciences for Health Professions, the new Faculty of Medicine at the JKU, and the decision to create a "Medical Valley in Upper Austria" coordinated by "Business Upper Austria" (a medical technology business agency) means many large, but also many small, steps will continue to drive innovation in medicine and medical technology.

A New Market with Unimaginable Potential

The medical technology industry is one of many future markets in Upper Austria. An increasing number of entrepreneurs are recognizing the potential of healthcare and medical technology. According to forecasts published by the Economic Chamber, by 2020 Austrian consumers will spend up to 67.8 billion Euros for privately financed healthcare products and services, sports and wellness programs, and health tourism – almost double the amount within a 15 year period. These figures underscore how important the medical and healthcare sector is for Upper Austria as a location of business.

Created in Upper Austria 15 years ago, the medical technology cluster is a networking and communication platform designed to support business and science in medical technology as well as expand and strengthen Upper Austria as a long-term location of medical technology. The cluster now includes over 235 partner companies. A strong feature is the interdisciplinary cooperation with other industrial areas ranging from polymer technologies to IT. This means we can ensure that progress in medical technology will continue to prosper in Upper Austria.

A handwritten signature in black ink that reads "Michael Strugi".

Mag. Dr. Michael Strugi, MBA

Vice-Governor of Upper Austria

*Economy, Labour, Research, Science, Energy, Tourism,
Regional Development, Shareholdings, European Affairs
and Sports State*

Utilizing and Supporting Potential



When it comes to healthcare, we face considerable challenges today and in the future. Whereas people should benefit from medical advancements, at the same time, healthcare also needs to remain affordable.

Ongoing development and innovation can help make healthcare more effective and efficient. This includes products used in diagnostics and therapy sessions, as well as optimizing treatment procedures. There is growing interest to find solutions aimed at helping seniors lead independent lives in their own homes for longer periods of time. By using new diagnostic methods, we can detect

disease and illnesses earlier, improve recovery time, find cures, and shorten long and grueling procedures. We also need to find new approaches in the area of prevention, for example, to motivate and encourage people to live a healthier lifestyle.

The “Medical Valley” in Upper Austria will be a network cluster that includes the JKU Faculty of Medicine along with the Kepler University Hospital, the religious order hospitals, the local business community, existing medical technology clusters, outside university research facilities, the universities of applied sciences, Upper Austrian Research, and the Upper Austrian government as well as all other corresponding stakeholders. The goal is to make the most of existing and available expertise while also supporting innovative potential.

There are many outstanding research findings and innovative ideas in our state but people can only benefit directly when these products, processes and services when they become available to them. In addition, new jobs can be created, resulting in strengthening our economic output.

The White Book is a profound scientific basis and I wholeheartedly thank the initiators as well as everyone who contributed to this project.

Mag. Christine Haberlander
State Minister
Education, Health, Women

In Upper Austria, Progress in Medicine is a Step Forward



The Johannes Kepler University is renowned and recognized for its visionary and innovative work. The breakthrough research conducted in various fields over the past decades and the unique educational programs we offer in Linz not only benefit the state of Upper Austria, but extend beyond Upper Austria's borders.

Medical technology is a prime and sustainable example of our endeavors and reflects the self-perception of the JKU and those at the university. We do not think of the JKU in terms of just 'faculties and subject areas'; we provide space to build contacts, network, communicate, and exchange information. Close to 70 departments and institutes at the Kepler University are currently conducting research in medicine and in the field of medical technology.

The Medical Valley is continuing to grow and prosper. Creating the JKU Faculty of Medicine - and including the Kepler University Hospital - was not only an enormous challenge but also a unique opportunity. We also work closely with our longtime, reliable partners: religious order hospitals, local companies, the medical technology cluster, external research institutions, universities of applied sciences, Upper Austrian Research, and the Upper Austrian government.

Medicine is a part of our everyday lives and medical research is indispensable and of utmost importance. It calls on the close co-operation of everyone involved to work toward a common goal and not only advance one's own health and the healthcare system, but also strive toward safeguarding Upper Austria as a location of business and the long-term sustainment of a countless number of local companies and employees.

Designed to bring diverse achievements in medical technology together, the Whitebook provides a clear and comprehensive account of applied sciences at the Johannes Kepler University and in Upper Austria: It allows us to accept new things, go beyond the limits, spark one's curiosity, and move the country toward an exciting future.

I would like to thank the editors and authors who presented these broad topics in all of their varied facets. I wish you exciting and stimulating reading.

A handwritten signature in blue ink, appearing to read 'Meinhard Lukas'.

Univ.-Prof. Mag. Dr. Meinhard Lukas
Rector
Johannes Kepler University Linz

Collaboration in Excellence



Established in 2014, the Faculty of Medicine is the newest academic addition at Johannes Kepler University. However, research in medicine and medical technology began long before the Faculty of Medicine's inception at the JKU. Particularly in the field of biophysics, researchers and scientists work closely together with local hospitals, and in recent years, numerous publications have appeared in high impact journals. The annual Winter School is also gaining

a strong foothold within the scientific community and strengthening its reputation. The university has been awarded a number of highly competitive bids and has acquired millions in research funding and scholarships. Many important contributions to medicine and research in medical technology stem from JKU-researchers in the fields of physics, chemistry, mechatronics, computer science, and mathematics.

The JKU's pursuit of excellence in research has resulted in creating the Linz Institute of Technology (LIT), with the first set of approved projects to include sensor systems for arthropathy, finding the causes for cancer resistance, and tracking technologies in psychological research.

The Whitebook provides a comprehensive overview of research collaboration efforts together with universities in Austria and abroad, as well as with hospitals and non-academic research facilities.

Driven to support ground-breaking science, the new Faculty of Medicine has been attracting a steady stream of new collaboration requests from the medical sector and the local business community. The next logical step at the JKU includes plans to create a research center for medical technology, which the JKU will actively support!

A handwritten signature in black ink, appearing to read 'Alexander Egyed'. The signature is fluid and cursive.

Univ.-Prof. DI Dr. Alexander Egyed
Vice-Rector of Research
Johannes Kepler University Linz

The Faculty of Medicine as a Driving Force for Medical Technology



By creating a Faculty of Medicine at the Johannes Kepler University (JKU) Linz, the JKU is generating forces in Upper Austria that will not only work toward consolidating the region's potential, but will serve toward strengthen the local economy. The Faculty of Medicine is a cornerstone for the Upper Austrian Medical Valley, taking on a nationwide pioneering role in the future. Research, hospitals, and companies are intertwined like cogwheels and gears in a clock, creating innovative symbiosis.

The Upper Austrian Medical Valley is just now in its beginnings but when it comes to progressive medical technology, the region of Upper Austria is anything but an unwritten page. As Vice-Rector for Medicine and Dean of the Faculty of Medicine at the state's largest institution for research and teaching, I am pleased that the JKU has taken the initiative to co-ordinate and publish a "Whitebook Medical Technology of Upper Austria". The Kepler University Hospital, successful companies in Upper Austria, the universities of applied sciences in Upper Austria, and naturally the JKU, have provided numerous and exciting contributions that give us a profound overview of current expertise in medical technology and competence in Upper Austria. The compendium impressively documents Upper Austria as a location at the forefront of advancement and cutting-edge ideas.

The Whitebook has been designed to quickly and easily identify leading fields of medical technology in Upper Austria. Externally interested parties and potential partners can refer to this special collection of information and directly contact all responsible parties. I strongly believe that this will not only provide fertile ground for many new and successful collaborations, but this publication will also contribute significantly to providing general information about Upper Austria's Medically Valley and the JKU in particular, creating momentous drive and an advantageous upswing.

Dr. Petra Apfalter
*Vice-Rector of Medicine**
Johannes Kepler University Linz

* until June 30, 2017

Better Research for Better Health ...



... is the manifesto of the European Commission's Scientific Panel for Health (SPH) towards a holistic approach to challenges and opportunities in the health and biomedical research domain – with public health and wellbeing as the ultimate goal. In a changing society, new health challenges demand a new research and innovation framework. In quest are novel research strategies that are (i) long-term, (ii) value-based, (iii) health- and people centered, (iv) science-led, and (v) multi-stakeholder. The Faculty of Medicine (MED) at JKU has been founded along such a new research and innovation strategy.

Building on top of “*the enjoyment of the highest attainable standard of health*” as being a fundamental human right of every human being without distinction (UDHR), and considering health not just as the absence of disease or infirmity, but as a “*state of complete physical, social, and mental wellbeing*” (WHO), paves the value base of MED.

As for long-term and health and people centered, this Whitebook connects MED to the EC prioritized key research areas in health, among them being Brain Research, Antimicrobial Drug Resistance, Cancer Research, Cardiovascular Diseases, Chronic Diseases, and most prominently Human Development and Aging. Likewise it relates to the H2020 Societal Challenge “*Health, Demographic Change and Wellbeing*”, the European Innovation Partnership on Active and Healthy Ageing, to Europe's Virtual Physiological Human initiative, and the recently founded International Consortium for Personalised Medicine.

In addition, this Whitebook is a manifesto for the science-led entanglement of MED and the research (and education) competencies of the Faculty of Engineering and Natural Sciences (TNF) at JKU – complementing the *in vitro* and *in vivo* medical research also with an *in silico* medicine perspective. Fundamental as well as translational TNF research in Biomedical Science (Biomarkers, Photo-Induced Microstructures, Photopharmacology, NMR), Mathematical and Computational Methods (AI, Machine Learning, Pervasive Computing, Neuroscience, Image-/ Signal Processing, BCI, Virtual Anatomy, Lab-on-a-Chip, Data Warehousing, Security), Neuroscience (RT functional MRI), Nanobiotechnology (3D Lithography, Microfluidic Prototyping) and Bioengineering (Drug Administration, Bioorganic Semiconductors) involves multiple stakeholders, ranging from governmental, institutional health care, clinical hospitals and medical centres, universities and applied science institutions, to medical technology industries – to name a few.

Many thanks to everyone for laying ground for a fruitful development of better health through better research with this Whitebook.

Univ.-Prof. Mag. Dr. Alois Ferscha
Dean of Faculty of Engineering and Natural Sciences (TNF)
Johannes Kepler University Linz

Table of Contents

06-14	Preface
18	Work and Health
20	New Options to Treat Cardiovascular Patient
22	Machine Learning-Based Individualized Prognosis
24	Functional Polymers for Controlled Drug Delivery and Tissue Engineering
26	Analytical Technologies – a Key Tool to Understand Disease-Related Processes
28	Mathematical/Stochastic Neuroscience
30	Surgical Instruments Featuring Embedded Intelligence
32	Biostatistics
34	Chances and Obstacles to Increase Patient Safety at Medical Institutions
36	Antimicrobial Materials and Surfaces
38	Imaging and Image Processing for Radiation Oncology
40	Microstructures Control Cell Attachment
42	Molecular Recognition Force Microscopy
44	Biomedical Signal Processing
46	Miniaturized Sensors and Actuators for Integration into Lab-on-a-Chip (or the surface of medical instruments)
48	3D Lithography for Nanobiotechnology
50	Molecular Photomedicine and Photopharmacology
52	Semantic Data Warehousing & Process-Oriented Medical Information Management
54	Additive Manufacturing of Medical and Assistive Devices
56	Security for Medical Data and Processes
58	Polymer Processing Technologies for Reinforced Bionic Products such as Exoskeletons, eLegs and eArms
60	Nuclear Magnetic Resonance (NMR)
62	SENEX ¹ - <u>S</u> ensor <u>N</u> etworks for <u>E</u> xploring Dementia
64	Membrane Channels and Transporters in Health and Disease
66	Wireless Communication Networks
68	Industrial Mathematics and Medical Imaging
70	Institute for the Rights of Basic Social Care and Health Care Law, Johannes Kepler University Linz
72	Sperm Fertility and Calcium Signaling
74	Medical Device Security
76	Artificial Retina
78	Formation and Governance of Innovation Clusters: Regional and Transregional Network Dynamics
80	Electromagnetic Tomography for Brain Imaging
82	TourGuide - Navigation System for Capturing and Analyzing Complex Clinical Data

JKU	84	Age-Induced Mutagenesis in the Male Germline
	86	Legal Issues of Research in Medicine Technology Affecting People and the Environment
	88	High-Tech ORs: Software Solution “KABOP”
	90	Networked Labs-on-Chips: From the Specification to the Physical Realization
	92	Design Automation for Labs-on-Chip
FH	94	Ultrasonic and Tomographic Signal Processing
	96	Solving Research Questions in Life Sciences Using Data Science Methods
	98	A Prosthetic Leg That Can Feel
	100	Medical Information, Simulation and Visualization Systems
	102	Medical Simulators and Simulation
AIT	104	Impact of Phytochemicals on Disease-Related Regulatory Signaling Hubs
	106	CoTrain - ICT-Based Coaching System to Physically Train the Elderly
	108	DayGuide - Helping Seniors Manage Everyday Situations
	110	Antimicrobial Resistance and Antibiotic Stewardship
	112	Research on Human Endoprostheses
HOSPITALS	114	Medical Imaging for Virtual Anatomy
	116	Biomechanical Devices Fracture Risk Estimation in Patients with Osteoporosis
	118	Impact of Different Flow Conditions on Endothelial Cell Activation and the von Willebrand Generation
	120	Real-Time Functional MRI
	122	Clinical Evaluation of Electromagnetic Navigation Bronchoscopy
	124	Targeted Lung Denervation
	126	Using Zirconia-oxid Ceramics in Cranio-Maxillofacial Surgery
	128	Shifting the Limits of Resuscitation Using “CIRD - Controlled Integrated Resuscitation Device”
	130	Extracorporeal Shock Wave Therapy (ESWT) for Tissue Regeneration
	132	Parkinson’s Disease - Motion and Gait Lab
	134	CUNECI - Clinical Use Cases for Non-Invasive Electrophysiological Cardiac Imaging
	136	Vascular Neurosurgery - “Virtual Aneurysm” and Intraoperative Imaging
COMPANIES	138	Brain Computer Interface
	140	EEG Signal as Biomarker
	142	From Non-Destructive to Non-Invasive and POC
	144	Rapid Prototyping of Nanostructured Functional Microfluidic Devices
	146	Research Unit Medical Informatics
	148	3D Reconstruction for Healthcare Applications
	150	Interoperability between Medical Information Systems

Work and Health



“Work can impact and affect one’s health. More research is needed in order to improve the quality of life and enhance one’s well-being.”

Bernad Batinic

Research Focus

- Meaning of Work – Job Characteristics and Well-Being / Health
- The Use and Impact of New Media and Technology
- Collecting Online Data and Wearable Tracking Technologies

Coordinators



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Vision

Although work is an important factor when it comes to a person's health and well-being, at the same time work can make people ill. Our research focuses on this conflicting area and aims at revealing some of the mystery surrounding work. Our findings can provide organizations and political institutions with information to create a productive and healthy work environment now and in the future.

Over the past few years, our empirical studies have shown that people engaged in a paid employment experience more so-called latent benefits (e.g., a collective purpose, social contact, time structure) than those who are unemployed or out of the labor force [1]. These aspects of work are beneficially important to maintain health and well-being [2] as well as experience meaningfulness [3]. However, certain working conditions, such as lower status jobs [4] or job insecurity [5], substantially diminish any benefits and have detrimental consequences for employees and organizations.

Our current studies focus on the changing nature of work (such as flexible working arrangements, virtual work, accelerated work, more opportunities for - and the necessity of - computer-mediated communication), [6] and its significance to support latent benefits and an individual's health and well-being. Some studies have shown that the "new" working conditions can be both beneficial to health as well as detrimental. We are exploring whether or not this ambivalent relationship can be explained through the differential effects of modern working conditions in relation to latent benefits (such as providing increased latent benefits while reducing access to others). Our research aims to shed light on contradictory findings in this field and develop solid recommendations to support work design and health prevention programs that meet the requirements of today's work environment and the various ways of working.

Approach

Our research is conducted mainly in field settings following a quantitative empirical approach. A large part of our research consists of longitudinal data collected by conducting follow-up surveys online [7]. In addition, we are beginning to focus on the potential of wearable tracking technologies designed to collect less reactive "objective" data from real-life settings. We believe that complementing survey data containing less reactive behavioral or physiological data can enhance scientific knowledge and help test the staying power of questionnaire-based findings.

Collecting scientific data for psychological research by implementing the use of wearable technologies is still in its infancy and requires multidisciplinary expertise. Incorporating these new forms of technology into our data collection procedures is a challenge that crosses disciplinary borders. Dealing with these new sources of information requires collaborating with researchers in other fields ranging from data collection technology to taking statistical, ethical, and legal aspects into consideration.

Our academic teaching program includes offering courses in work and organizational psychology, media psychology, and quantitative (online) research methods to students in all majors. These courses facilitate knowledge transfer by providing a strong balance of theory, empiricism, real-

world approaches, and also giving students an opportunity to apply computer-supported cooperative learning models.

Impact

Work and working conditions have changed considerably over the past two decades. On one hand, employees have more opportunities and resources but on the other, there are new challenges and increased demands. Current discussions fluctuate intensely between the pros and cons of these "new" working conditions and the potential impact on one's health. Scientific evidence, however, is not largely available and inconclusive, also lacking in empirically tested interpretations to outline both beneficial and detrimental effects. Our research contributes to the available pool of knowledge and aims to provide conclusive recommendations to create contemporary work design and health prevention programs.

Competencies

Research in work and well-being is currently being conducted by the Department of Work, Organizational and Media Psychology at the Institute of Education and Psychology.

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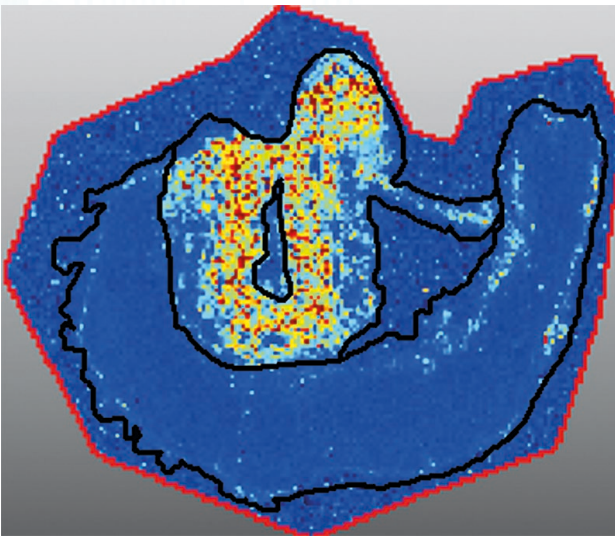
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Keywords

job characteristics, stressors, resources, benefits of work, well-being, health, online research, tracking technology

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New Options to Treat Cardiovascular Patients



“By combining and applying the entire spectrum of modern research technologies, we can generate a new spectrum of treatment options for cardiovascular patients.”

David Bernhard

Research Focus

- Prevention
- Early diagnosis
- Pathophysiology
- New drugs and treatments
- Optimizing clinical decisions

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Vision

Age is a major risk factor for cardiovascular diseases (CVDs), and more people worldwide die annually from CVDs than from any other cause (~ 18 million deaths each year) [1].

Western societies are increasingly confronted with an aging population and innovative applications to clinically treat CVD - such as new procedures, new tools, and new drugs - are not only in high demand, they are essentially missing.

Chemists, biomedical researchers, and clinicians are currently aiming to forge new paths in early CVD disease detection by characterizing diseases (progression), creating tools to support clinical decisions (risk prediction, time to operate), and by treating diseases (new drugs).

Approach

Clinical scientists are involved in joint projects that are currently addressing CVD specific issues by studying organic, analytical, synthetic chemistry, biomedical research in molecular biology, as well as cell and tissue biology in animals.

Early diagnosis: Thoracic aortic aneurysms (TAAs), which often occur in the absence of clear clinical symptoms, lead to a weakened aortic vessel wall prone to rupture. Aneurysms are usually detected by chance during the course of clinical imaging. As TAAs occur frequently in the population, there is a demand to create a test system that can detect TAAs during the course of a routine medical examination. We recently published study describing a rise in sphingomyelins (fatty acids) in the aortic wall seen in some forms of TAAs [2]. A currently ongoing project is testing whether or not these results could lead to creating a blood or urine test. Additional analyses are planned to define TAA type-specific processes and profiles of metabolites.

Disease Characterization, Risk Prediction, Staging: aside from knowing some of the basic risk factors, it is not known why TAAs form. New tools are needed in order to develop valid detection parameters that not only determine the disease stage, but also how fast it is progressing. Being able to determine the disease's progress would help physicians better determine when to apply invasive intervention. In this approach, clinical samples (surgical waste material) are subject to mass spectrometry imaging, intensive histological analyses, and OMIC-based studies. This information - together with clinical information from patients and their follow up treatments and diagnoses - will give us new insight into these diseases, supplying us with information that can be used for disease staging and when making medical decisions.

New drugs: the search for new drugs to treat CVDs aims to increase the patency of bypass grafts and develop a therapeutic option for post-myocardial infarction. Promising compounds have been identified for both applications and have already been successfully tested in animals and in

isolated human vein grafts. [3, 4] These drugs will now be analyzed further. Therapeutic procedures are also being developed and prepared for human testing.

Impact

The described project will provide new information on the origins of CVD and pathophysiology and may also give us new types of disease markers and treatment targets. Furthermore, the discovered compounds' mode of action could be used to develop new drugs or treatment procedures for cardiovascular patients. Based on the information we already have, our results may also be useful in preserving and protecting transplant organs. We ultimately hope to play a role in extending the life span of a healthy human being.

Competencies

Chemical, biomedical, and clinical expertise is represented by the following institutions:

- **Center for Medical Research** with knowledge in molecular biology, primary cell isolation and cell biology, histology, and animal testing.
- **Department of Cardiac, Vascular, and Thoracic Surgery** with expertise in advanced surgical procedures, clinical trials, and clinical data analyses.
- **Institute of Organic Chemistry, University of Innsbruck** with a high level of expertise in DESI as well as MALDI-mass spectrometry imaging, and associated data handling and analyses.

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Keywords

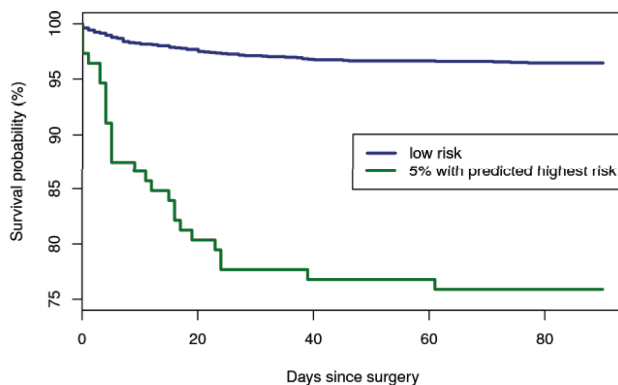
metabolomics, mass spectrometry imaging, intra-operative storage solution, cardio protection, decision to operate, bypass, aneurysm, myocardial infarction

Machine Learning-Based Individualized Prognosis



“Modern hospital management systems store detailed patient records, allowing us to identify statistical relationships that are highly beneficial in assessing individual risk. Without the assistance of the latest research in machine learning technologies, these statistical relationships would remain concealed.”

Ulrich Bodenhofer



Research Focus

- Machine Learning
- Individualized Medicine
- Cardiac Surgery
- Medical Data Analysis

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Vision

Informing patients about the potential risks of elective surgery is often a matter of referring to the overall complications or survival rates. Individual patient risk factors are taken into account only if they are well-documented in medical literature. Many modern hospitals keep detailed patient medical records, including general patient data, medical history, results from pre-operative examinations, surgery documentation, post-operative clinical data, and data regarding overall survival rates. This immense quantity of information has the potential to identify previously unknown statistical relationships between pre-operative data and the surgery results, including risk factors that can lead to complications or affect overall patient survival. We aim to use this information to devise highly accurate risk models for many types of surgeries, particularly high-risk procedures such as cardiac surgery. These models should then be used to provide each patient with personal information pertaining to individual risks.

Approach

We initially looked at all of the heart valve surgeries performed at Linz General Hospital (now known as the Kepler University Clinic) between 2008 and 2014. We exported the information from the hospital's information system and pre-processed it for later analysis using machine learning methods. The goal was to take the patient's clinical pre-operative information and predict his/her 30-day survival prognosis. High-quality machine learning tools, such as support vector machines and deep neural networks, were tested in order to select the best possible methods and see how well they could perform the task at hand. In the end, random forests turned out to not only be the easiest and most robust method, but also the most accurate.

The resulting predictor's discriminant function turned out to be a generally well-performing risk indicator that clearly outperformed the well-established EuroSCORE I & II risk scoring systems.

Random forests also allow us to identify the most relevant input features. When we looked at heart valve surgeries, several interesting and previously unknown facts were revealed. It turns out that kidney function parameters in particular are highly predictive when it comes to patient survival, even though the EuroSCORE scoring system does not even take them into account. It is unlikely that poor kidney function is the cause of patient death after a heart valve surgery and more likely that kidney function parameters are good proxies to determine a patient's general health. In any case, our findings require further study as this phenomenon could also pertain to our patient population.

Impact

While the results pertaining to heart valve surgeries are highly promising, the models are biased as they are based only on medical records from patients at the Kepler University Clinic. In order for hospitals to create customized risk models tailored to their particular needs and their patients, we are currently developing software that will easily allow a hospital to create a risk model based on their patient records. We expect the software to be available for use at hospitals that perform many high-risk surgeries. In the future, we will also study applied approaches to other types of surgeries. We expect this to be successfully applied to all surgeries that are considered routine (there is not much to be learned from individual cases) and show any relatively high risk (a sufficient ratio of post-operative deaths is necessary to identify consequential statistical relationships).

Competencies

Research is represented and conducted by the following departments:

- **Institute of Bioinformatics** contributes its expertise in machine learning and clinical data analysis.
- **Department of Anesthesia and Operative Care** provides data and medical expertise to evaluate and interpret results.

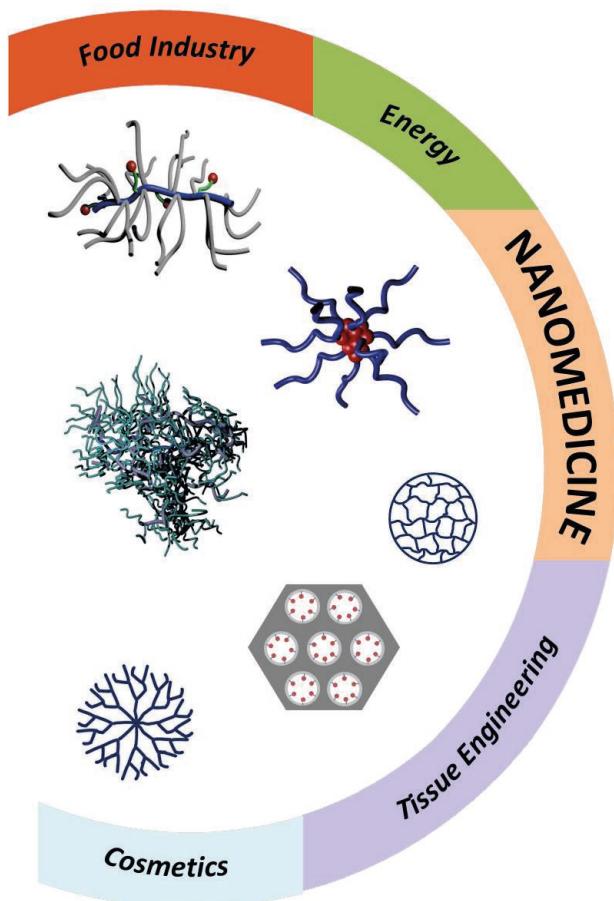
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Keywords

machine learning, individualized risk assessment, random forest, cardiac surgery, medical data analysis, survival analysis

Functional Polymers for Controlled Drug Delivery and Tissue Engineering



“These approaches could contribute to the development of future therapies on a more targeted and less harmful level, leading to more gentle treatments of patients.”

Oliver Brüggemann

“Precision synthesis of novel phosphorus-based polymers offer unique properties above and beyond conventional carbon based polymers to meet the demands of advanced biomedical applications”

Ian Teasdale

Research Focus

- Signal Processing and Analysis
- Pattern Recognition, Classification, Prediction
- ECG Morphology
- Heart Rate Variability

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Vision

Drug administration is commonly non-specific, the impact of which is usually dose-limiting. Thus, for the treatment of diseases such as cancer, the drugs are not only active at the tumor site, but also affect healthy tissue, leading to well-known and severe side effects. Polymers are known to act as carriers in the controlled delivery of anti-cancer drugs, for example, inside tumor tissue [1,2]. However, these kinds of polymer-drug conjugates are often not tailored for specific treatments, but used as general purpose systems. Furthermore, after achieving their purpose, these polymeric taxis may accumulate in the body when showing only low rates of degradation to fragments small enough for renal clearance. Alternative degradable polymers, usually based on polylactic acid and similar polyesters, may degrade but do not provide the required chemical functionality.

Our newly designed tailor-made phosphorus-based polymer carriers (polyphosphazenes) aim to improve future chemotherapies [3]. By offering phosphorus-based polymeric systems with a number of individualized properties, we are able to improve the drug's blood solubility, and directly address tumor cells with specific tags [4]. Additionally, the polymers may be equipped with a molecular degradation timer. Furthermore, polymers in form of hybrid materials (together with silica) are being developed for later treatment applications in which diagnosis and therapy are combined and performed with the same nanoparticles [5].

Similar phosphorus based polymers (but in a solid matrix form) are also being designed for use in cultivating tissues for later implantation. In this application, polymers act as tailored, bioactive degradable scaffolds facilitating the proliferation of healthy cells [6]. The use of phosphorus based polymers allows for controllable degradation rates to non-toxic degradation products. These polymers are currently being explored as scaffolds for tissue engineering.

Approach

Polymers for both drug delivery and tissue engineering applications are customized with respect to specific treatments and to specific service lifetimes by designing them on a molecular level, i.e. linking different chemical functions to these polymer chains, side by side, for each individual purpose. Meanwhile, polymer-silica hybrids have broad applicability within a wide range of applications due to their simple loading capabilities, including theranostic approaches [7], combining diagnosis and therapy in one material, such as nanoparticles with detectable tags and molecular gates activated by external triggers. Subsequently, these highly individualized systems are thoroughly chemically and physically characterized by equipment provided by the institute itself or by the department of chemistry. Additional tests are being performed in strong collaboration effort with outside medical research facilities.

Impact

Precision synthesis of novel phosphorus-based polymers offer unique properties above and beyond conventional carbon based polymers to meet the demands of advanced biomedical applications. Meanwhile, polymer-silica hybrids offer broad applicability within a wide range of applications due to their simple loading capabilities in combination with triggered release mechanisms. These different approaches can lead to the development of future therapy treatments on a more targeted and less harmful level, leading to less harsh medical treatment.

Competencies

Research at the Institute of Polymer Chemistry focuses on the design, synthesis and characterization of functional polymers for medical and pharmaceutical applications. Polyphosphazenes and polymer-silica hybrids as exemplary materials are developed for the purpose of utilizing them as carriers for drugs and scaffolds for cultivating cells. Furthermore, the institute possesses expertise in the design of molecularly imprinted polymers, i.e. artificial antibodies and enzymes, for, e.g., controlled release applications.

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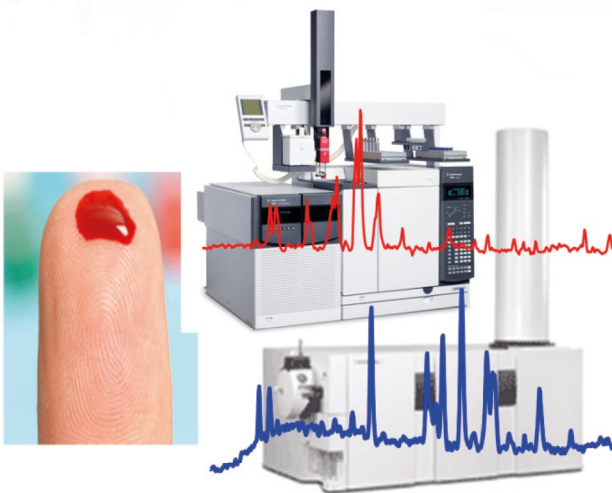
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Keywords

polymer chemistry, functional polymers, (bio) degradable polymers, polyphosphazenes, polymer-drug conjugates, drug delivery, controlled release, tissue engineering, nanomedicine, theranostic nanoparticles, biomimetic polymers, molecularly imprinted polymers, polymer-silica hybrids

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Analytical Technologies – a Key Tool to Understand Disease-Related Processes



“The availability of improved analytical methods for investigating complex samples from a clinical environment will imply a major step forward in the understanding of fundamental biological processes associated with ageing”

Wolfgang Buchberger

Research Focus

- Metabolomics
- Analytical technologies for clinical analysis
- Biomarkers

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Vision

The chemical analysis of biological samples (such as serum, blood, liquor, urine, tissue) is of significant importance for diagnosing diseases, understanding the biological mechanisms involved in the development of diseases, and for taking measures to prevent the progress of malfunctions in the organism [1].

Advanced analytical instrumentation including chromatography and mass spectrometry opens new ways to obtain information about disease-related changes of biochemical reactions and about changes in metabolic pathways. These kinds of advanced technologies often go well beyond the capabilities of routine clinical laboratories. Cooperating with analytical chemists working with the latest generation of analytical instruments and clinical specialists can allow for the development of new and significantly improved approaches to discover disease-related biomarkers, monitor levels of pharmaceuticals, and detect xenobiotics in biological samples.

Approach

The discovery of disease-related biomarkers and the quantitation of metabolites relevant for a patient's health status are based on analytical techniques such as gas chromatography, high-performance liquid chromatography, and capillary electrophoresis, all of them hyphenated with high resolution mass spectrometry or tandem mass spectrometry. These instruments are continually increasing in performance efficiency, allowing for new fields of application to be approached.

In an effort to provide metabolic information essential to a patient's health status in this context, we focus on the development of analytical methods and the optimization of relevant technologies. This type of research is conducted by students as part of the Bachelor's and/or Master's program at the Institute of Analytical Chemistry in cooperation with medical departments that provide patient samples.

Impact

The availability of advanced analytical methods based on the most recent technologies in analytical sciences and their use for metabolomics as well as monitoring disease-related biomarkers will allow for a better understanding of the development and progress of diseases and could help improve ways of finding more reliable diagnosis and improved medical care. The introduction of advanced analytical technologies will also lead to new screening tools for routine analysis in clinical laboratories.

Competencies

The Institute of Analytical Chemistry has been involved in researching new analytical technologies in organic analytical chemistry for many years. Our expertise lies in measuring disease-related metabolites and biomarkers in complex biological samples. The sophisticated analytical instrumentation required in this field is available. Strategies have been developed to optimize and fine-tune analytical methods for specific applications.

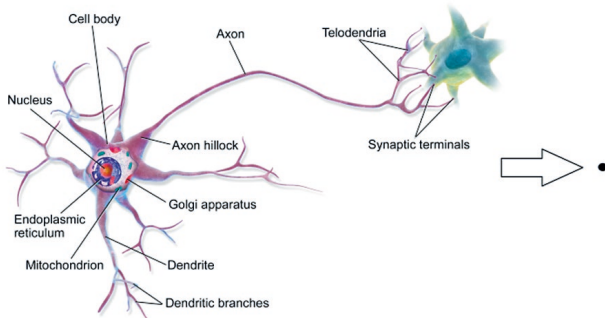
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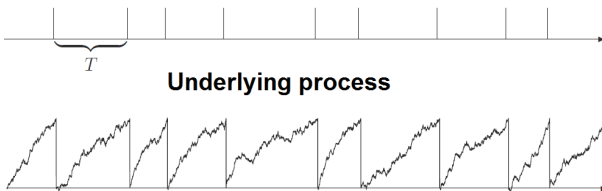
analytical chemistry, clinical chemistry, analytical instrumentation, metabolomics, biomarkers in aging

Mathematical/Stochastic Neuroscience



“Stochastic modelling, statistical and numerical methods, and advances in Mathematical Neuroscience give us a unique opportunity to better under-stand the brain.”

Evelyn Buckwar



Research Focus

- Stochastic Processes in Neuroscience
- Numerical Methods for Stochastic Models
- Statistical Inference for Stochastic Processes
- Monte-Carlo Methods and Simulation
- Neural Network Connectivity
- Mathematical Modeling of Physiological systems
- Mathematical Modeling of Visual Attention

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Vision

The field of Neuroscience requires the precise understanding of the principles of information processing in the nervous system, such as the networks of neurons. Neurons communicate through short, precisely shaped electrical impulses, so-called action potentials or spikes. Our goal is to strengthen the understanding of the principles underlying spike generating mechanisms, starting by investigating and understanding the membrane potential dynamics in a single neuron. Biophysical neuronal models take the dynamics of ion channels or synaptic activity into account, yielding multidimensional models. These models are based on the seminal work by Hodgkin and Huxley in 1952 [1]. Due to the complexity and the nonlinearity of most biophysical models, it is crucial to reduce the detailed neuron models to more simplified models in order to understand the spike generation mechanism. Several approaches have been studied, fitting, for example, the simplified model to simulated data generated by the detailed model. A different approach consists of developing a mathematical framework to simplify detailed models. The proposed stochastic models should then be able to reproduce the observed interspike interval statistics, predict model behaviour, and generate new hypotheses that can be first tested through simulations and then experimentally. Despite the large focus on the mathematical modelling of single neuronal dynamics, it is worth mentioning that the cerebral cortex in the human brain is estimated to contain 10-20 billions of neurons, each of them connected to thousands of other neurons. Neural networks are commonly studied either by simulation or by mathematical reduction, see e.g. [2], [3], requiring advanced mathematical techniques such as mean-field analysis, Langevin approximation or limit theorems.

Approach

Our group's ambitious goal is to provide mathematical, statistical and numerical results to strengthen the understanding of single neuron and neural network dynamics under the assumption of the single neurons modelled by "realistic" and biologically motivated stochastic models, such as multi-timescale adaptive threshold models that incorporate the effects of both adaptive current and adaptive threshold models, and can accurately predict spike times as well as be mathematically derived from the Hodgkin-Huxley model [4]. Studying the behaviour of these stochastic models brings about new numerical, statistical and mathematical challenges. For example, one of our goals is to provide statistical inference of the underlying model parameters, as well as develop suitable numerical algorithms to preserve the model's property. This can be particularly difficult in the presence of partially observed processes, requiring the study of new ad-hoc mathematical and statistical techniques to address it. Switching from a single neuron to neural network dynamics generates new mathematical challenges. We extend available results on neural networks by mathematically reducing systems of single neuron models either to one-dimensional stochastic processes (using e.g. mean field approximations)

representing average properties of the neural population, or to systems of firing rate (deterministic) models. These reduced models are then used to develop new statistical methods for neural network connectivity.

Impact

Attaining our research goals requires developing innovative methods that would provide deeper insight into understanding the brain by studying the adaptation at a single and a population level, and would also contribute greatly to the fields of numerics, statistics, stochastic analysis, neurosciences, as well as other fields ranging from engineering to psychology.

In addition, a better understanding of the neural network connectivity would also be of considerable interest in regards to human vision, particularly pertaining to functional connectivity in the retina.

Competencies

Research will be conducted by the Institute for Stochastics based on our expertise in statistical methods for stochastic processes, in computational neurosciences, in combining theory, practice and simulations, and in stochastic numerics. This rare combination represents a unique opportunity to make a significant contribution to the increasingly important field of Mathematical Neuroscience.

Furthermore, we plan to extend our collaboration efforts and pursue joint study and research with corresponding companies, industries and medical research groups located in Upper Austria.

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Keywords

stochastic modelling in neuroscience, neuronal response latency, single neuron dynamics, neuron network dynamics, neural coding, stochastic neural field equation, statistical inference, Monte Carlo methods.

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Surgical Instruments Featuring Embedded Intelligence



Pro²Future

Research Focus

- Laparoscopic surgical suboptimal outcomes
- Surgeon-friendly ICT for minimal invasive surgery
- Types of human attention and established theories of individual attention
- Aware surgeon assistance systems.
- Evidencing surgeon attention

“We are heading towards a next generation of minimal invasive technology based on embedded intelligence: ‘assistive surgical instruments that think!’ ”

Alois Ferscha

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Vision

Today's world of information overload means people are deluged with signals and messages on all levels of perception and modalities (visual, auditory, tactile, olfactory). Finding ways on how to divide one's attention efficiently and best address the overload of information is one of the most demanding challenges that ICT mediated communication faces. Indeed, some two decades of HCI and pervasive/ubiquitous computing research have clearly revealed that out of the many indicative design factors supporting modern ICT, human attention is the first source of perception - and also awareness - when it comes to information and other individuals. In support of advancements in the design and implementation of innovative, future ICT systems, it is important to understand just how spontaneous, local, and individual attention to new information items occurs, is propagated, and how it eventually merges.

Approach

Our focus lies in creating a foundational basis for attention-aware ICT, i.e. developing (i) formal models of human attention along with (ii) multisensory recognition architectures and reasoning algorithms to estimate and assess levels of human attention together with their (iii) embedding into modern ICT systems.

We are actively studying approaches in Minimal Invasive Surgery (MIS) together with our research partners at the Kepler University Clinic (KUK) as well as with fellow international researchers. Specifically, we are studying whether or not surgical suboptimal or even erroneous outcomes of MIS are a result of (i) the cognitive load and level of focused and sustained attention of the operating surgeon, (ii) the frequency and degree of disruptions to the surgical workflow, or (iii) the misalignment of visual and motor axes in today's laparoscopic equipment (eye-hand coordination). By analyzing our findings, we aim to excel on evident limitations of current endoscopic and laparoscopic workflow techniques, such as the loss of depth perception, the comparably poor field of view, and the significant cognitive load induced by unnatural, non-intuitive eye-instrument coordination.

On the formal models and methods side, we are attempting to identify types of surgeon attention, as well as cognitive and physiological mechanisms revealing their relation to perception, memory, decision-making, and learning. Starting with established theories of individual attention (Capacity Theory, Multiple Resource Theory, Feature Integration Theory) and the respective attention models (Broadbent, Kahneman, Wickens) to characterize aspects of a single individual's attention span, we extrude these models towards formalized models of collective attention. To this end, we are utilizing a synthesis-driven research method that combines (i) existing theory and its assessment, as well as (ii) insight from analyzing large data sets collected during operations.

Impact

Our work aims to develop a framework of theories, models and systems that explain, react to, and possibly predict how a surgeon's attention is divided in the operating theatre. More precisely, we want to derive a foundation of clear, well-defined concepts necessary to explore and test theories on attention in surgical situations, to serve as the theoretical underpinning for future generations of surgeon support systems. To this end, we draw on competing theories from psychology, cognitive neuroscience, human computer interaction, and social sciences to provide a foundation of computational models of attention.

Competencies

Our main research expertise, and that of our collaborators, is described as follows:

- **Institute of Pervasive Computing** contributes expertise on complex, data-intensive ICT systems, goal oriented, opportunistic sensing frameworks and context driven social coordination architectures.
- **KUK** collaborates on identifying surgeon body signals indicative of attention, on the identification of suitable feedback modalities and conduct of studies.
- **STORZ** as a major industry player offers avenues to realize and disseminate our research results.
- International partners at **Sussex** University and University of **Fribourg** support our efforts with machine learning, sensor modules, result analyses, and activity recognition.

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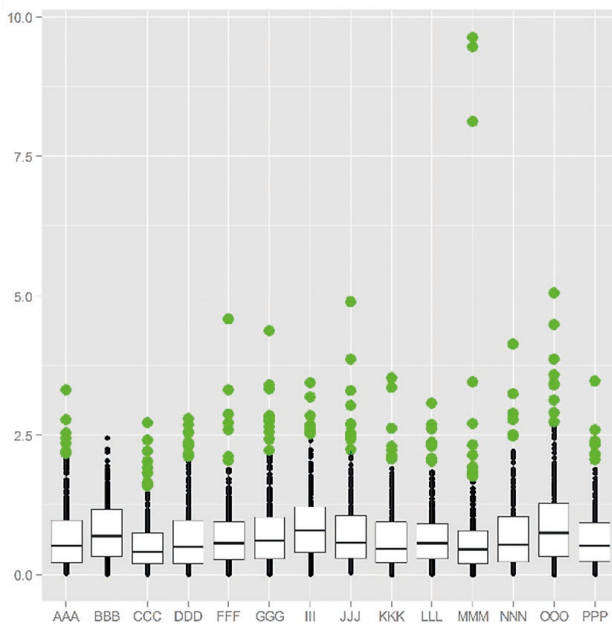
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Keywords

attention management, minimal invasive surgery, eye, body, infrastructure-based recognition methods

Biostatistics

(at the Department of Applied Statistics)



“With the burgeoning amount of data generated in many medical fields, both new and conventional techniques in statistics are essential in order to make sense of the data.”

Andreas Futschik

Research Focus

- Experimental Design
- Statistical Analysis
- Statistical Decision Support
- Reliability and Survival Analysis
- Analysis of Genomic Data
- Personalized Medicine

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Vision

Developing methods of personalized medicine, genomic predictive marker detection, eQTL, and more generally, the application and development of new methods in support of medical data analyses.

Examples of Recent and Ongoing Projects

The Department of Statistics contributes its expertise in statistical modelling and data analysis as a partner in several medical projects. Two examples include the following:

Example 1

Long-Term Mortality in Pediatric Hydrocephalus

This project in cooperation with the Department of Neurosurgery, Kepler University Hospital performs a retrospective analysis of patients with hydrocephalus who received their first shunting procedure at Children's Hospital in Linz between 1982 and 1992. The project aims to provide information about long-term survival and the causes of death in shunted pediatric patients. To identify factors affecting risk of death after the first operation, we compared Kaplan-Meier curves for subgroups of patients and fitted a Cox regression model. All analyses showed higher survival probabilities of children who had their first operation between 1988-1992 as compared to between 1982-1987. One of the main causes of death is shunt infection. A competing risk analysis from the time of first operation to death revealed that the risk of death unrelated to shunt is similar in both time periods, whereas the risk of death related to shunt is significantly lower during the later time period.

Example 2

Caregiver Burden in Dementia-Results from the Prospective Dementia Registry (PRODEM) of the Austrian Alzheimer Society. This project is being conducted together with the Department of Neurology 2, Kepler University Hospital, Faculty of Medicine JKU (Head: Prof. Ransmayr).

The underlying data have been collected within the Prospective Registry on Dementia in Austria (PRODEM) study, an ongoing longitudinal multi-center project initiated by the Austrian Alzheimer's Disease (AD) Society in 2008 and performed at 13 clinics. For this project, we provide the necessary statistical modelling and analysis in order to find factors affecting the burden of caregivers (often spouses, children or relatives), as well as the changes in the burden induced by progressing dementia. Influential factors found included dependency (need of the patient for care) and neuropsychiatric symptoms. The family relationship between patient and caregiver also seems to be relevant (partners versus sons/daughters.)

Impact

Medical (and other) data usually contain components, such as patients' different reaction to treatment, that cannot be foreseen with certainty. These components are commonly modelled as random. Statistics provides and develops methods to analyze this type of data permitting, for instance, an assessment and testing for treatment effects. The development of prognostic scores helps to predict a patient's future well-being.

Competencies

Other members at the Department of Applied Statistics are also experts in experimental design and/or the analysis of medical data routinely applying both frequentist and Bayesian methods for this purpose. Experience in analyzing large scale genomic data is also available at the department. Among other methods, multiple testing is used to separate signal from random noise. This helps, for instance, to identify predictive biomarkers that are of interest in personalized medicine.

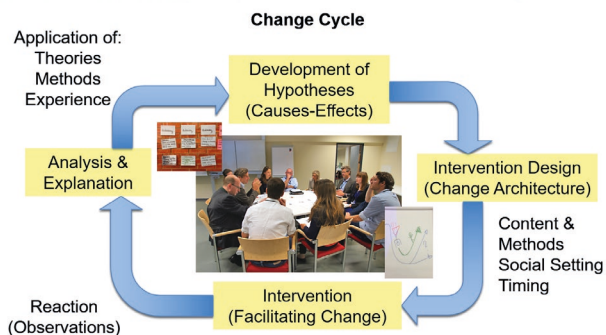
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Keywords

developing methods of personalized medicine, genomic predictive marker detection, eQTL, and more generally, the application and development of new methods in support of medical data analyses

Chances and Obstacles to Increase Patient Safety at Medical Institutions



“Technical advances and resources can only contribute to patient safety when grounded deeply in the organizational culture.”

Wolfgang H. Güttel

Research Focus

- Organizational Change
- Leadership
- Safety Culture
- Case Study Research

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Vision

Improving patient safety has become top priority in the healthcare sector as recent numbers indicate that in 2014 alone, over 18,000 patients died at German hospitals as a result of medical errors [1]. To prevent as many fatalities as possible in the future, an increasing number of healthcare organizations have been adopting standards and procedures from the aviation industry aimed at learning from errors and near misses [2]. CIRS (Critical Incident Reporting System) is an IT-based error reporting system and a prominent tool focused on learning from errors and near misses. Our studies analyze how organizational members at hospitals execute these kinds of systems. Our findings show that in addition to good intentions, efforts to implement a new safety culture only succeed frequently at the surface [3]. Changing the way organizational members perceive and deal with failure requires more than just adding new procedures. Because of fear of blame and an effort to protect hierarchical positions, failure remains an organizational taboo that is covered up rather than learned from [4]. Improving patient safety therefore requires hospitals to change cultural norms and attitudes toward failure.

Our research aims to discover the underlying mechanisms required to successfully introduce patient-safety systems such as integrating acceptance into doctors' and nurses' value systems.

Approach

We follow a case study research strategy [5] by collecting data from interviews, workshops, and by analyzing reports. Data analysis is primarily conducted by means of techniques in qualitative content analysis and by using the method of objective hermeneutics. We frequently discuss our preliminary findings with interviewees in order to enhance the quality of our analysis and to enable practical learning. Our research approach helps provide rich descriptions to refine theories [6] in the field of organizational change, leadership, and HRM.

Impact

Because Austrian hospitals are required to regularly report quality measurement and performance indicators to the government, established techniques and procedures in other contexts have been formally introduced, but are rarely internalized. By identifying the drivers and obstacles of change, we expect to explain the dynamics behind developing a safety culture in the healthcare sector. In the long run, understanding these contributions to develop measures in support of increased patient safety will facilitate learning from errors and near misses.

Competencies

Research on organizational change, leadership, & HRM is conducted by the team of the Institute of Human Resource and Change Management at the JKU Linz.

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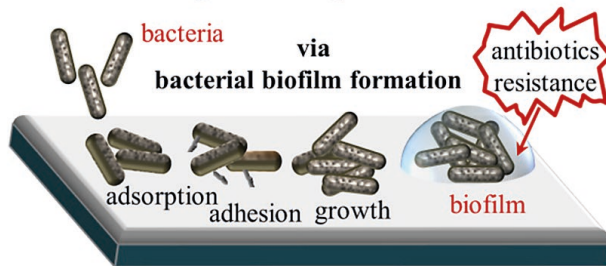
Keywords

patient safety, medical error, change

Antimicrobial Materials and Surfaces

PROBLEM

HAI - Hospital Acquired Infections

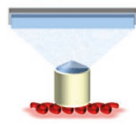


SOLUTION

Antimicrobial materials development

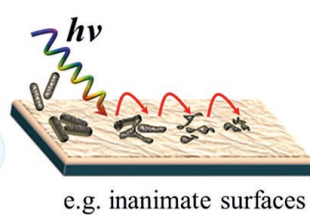
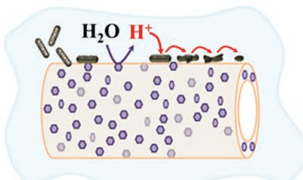
metals and metal oxides

powder synthesis thin films combinatorial libraries



Implementation

hybrid polymer-powder system functional coatings



“Survival of the Fittest was the phrase that Herbert Spencer used to describe Darwin’s evolutionary theory. We are using nature’s concept of combination (=mutation) and screening (=selection) to develop innovative materials to help people in need of health care.”

Achim Walter Hassel

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Research Focus

- Combinatorial materials development
- Inorganic powders and functional coatings
- Antimicrobial activity screening & mechanistic
- Applications and implementation

Vision

Healthcare-associated infections (HAI) have become a major problem for hospitalized patients, particularly those in intensive care units. Approximately 4 million patients in EU countries contract HAI annually, resulting in 110,000 avoidable deaths [1]. Due to the upsurge in the number of multi-drug resistant microorganisms, the types of antibiotics that can be administered to infected patients are severely limited. As a result, there is a need to develop new, low cytotoxicity materials that bear less surface contamination in order to reduce and prevent the transmission and growth of microorganisms, thereby limiting patient exposure. When considering inorganic and organic compounds for this application, there are certain advantages to the former, such as stability, robustness, and a long shelf life. These types of antimicrobial compounds (metal and metal oxides) can be incorporated in polymers as powders to create hybrid systems which can be used, for example, to manufacture urinary catheters. The result could reduce the number of urinary tract infections that currently arise when biofilms form on the catheters' surface and trigger antimicrobial properties in the hybrid material used to manufacture catheters. In addition, when it comes to specific applications (such as inanimate surfaces, surgical instruments), applying inorganic coatings is the technological choice for surface functionalization. Functional coatings (which, for example, are antimicrobial under visible light illumination or when it comes in contact with humidity in the environment) would be a smart and cost-effective solution to self-disinfecting surfaces.

Approach

A key approach is the development of antimicrobial materials. There is an enormously vast field of inorganic materials and some of these stand out in terms of interesting properties in that they are photocatalytic under light irradiation (e.g. TiO_2 under UV-light), or in close vicinity they acidify the environment (e.g. MoO_3) [2]. These special features are also responsible for the antimicrobial properties found in these compounds. Initial steps in the direction of optimization (such as optical bandgap tuning for light absorption in the visible range) have already been taken, however, in addition to optimizing functional properties, materials showing antimicrobial properties must also show low cytotoxicity and/or a long-lasting antimicrobial property. This means that screening suitable materials is a complex procedure that requires various approaches depending on the desired function. Material properties can be tuned by finding suitable multi-element chemical compounds through combinatorial methods. Combinatorial thin film material libraries (e.g. Mo-W-oxides) are used to create mixed, new complex oxides and screen antibacterial properties which might occur only in a very limited compositional range [2]. Powder synthesis via green chemistry is used to tune metal oxide particle size, shape and crystalline structure (e.g. ZnMoO_4) to optimize antibacterial properties [3]. Advanced antimicrobial testing is conducted in cooperation with expert partners (AMiSTec GmbH). Label-free electrochemical sensors for pathogens based on specific sensitive DNA detection using graphene based FETs is conducted in cooperation with the Austrian Institute of Technology GmbH (AIT). As part of the framework at the COMET Competence Center CEST, we have begun a highly interdisciplinary joint 3-year project with these two partners since January 2017.

Impact

An aging society means an increase in the number of patients admitted to hospitals, as well as extended periods of treatment. At the same time, there is a problem regarding even last-line antibiotics (such as carbapenems) due to an upsurge in the number of multi resistant germs. The result is a high increase in health care costs (currently 1.5 billion € per year in EU) as well as hundreds of thousands of unnecessary deaths. The development of self-disinfecting, antimicrobial materials would have an enormous impact in the health care sector in general as well as direct benefits to patient health and safety.

Competencies

Research in material development, antimicrobial screening, further implementation, and sensor development will be conducted at the following institutions:

- **Institute for Chemical Technology of Inorganic Materials** with research focused on developing a large variety of inorganic materials (powders, multi-component coatings, etc.), testing and antibacterial screening.
- **AMiSTec GmbH & Co. KG** with research focused on antimicrobial (bio)-materials development and testing against a variety of bacterial strains and viruses of materials that mimic the natural acidic surface of human skin.
- **AIT Austrian Institute of Technology GmbH** with research focused in the field Diagnostic Biosensors which merges surface engineering with micro and nanotechnologies, and the detection of environmental pathogens.

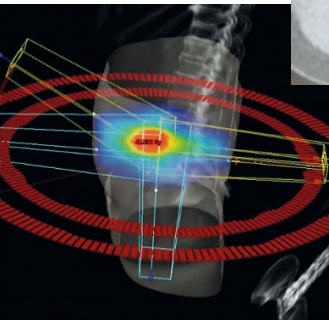
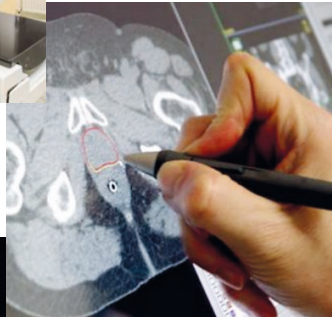
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Keywords

hospital acquired infections, antimicrobial materials, inorganic materials research and development, powders and coatings, antimicrobial testing and mechanistic, implementation

Imaging and Image Processing for Radiation Oncology



“Nowadays, radiation oncology delivers volumetric modulated tumor arc therapy with high spatial accuracy based on 3D treatment planning and image guidance. Improving daily pre-radiotherapy (RT) imaging quality will enhance precision and safety of the delivered RT, possibly leading to higher tumor cure rates and less late side effects.”

Hans Geinitz

Research Focus

- Imaging, Image and Signal Processing
- (Low) Coherent Microscopy
- Programmable Optics
- (Bio) Material Inspection
- Classification, Machine Learning
- Radiation Oncology
- High Precision Radiotherapy (RT)
- Volumetric Intensity Modulated Whole Body Arc Therapy
- Intraoperative Radiotherapy
- Patient Reported Outcomes

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Vision

Many scientific disciplines are intertwined, complementing and fostering each other. Radiotherapy and imaging have been traditionally dependent on one another. Over time, patients will increasingly benefit from advancements in medicine, engineering sciences, physics, and mathematics. Advances in image-guided radiotherapy in particular will enhance precision and safety, resulting in higher cure rates. Optical Coherence Tomography will be able to detect skin damage early and help determine individual medical treatment.

Approach

Advances in physics, engineering, and mathematics will result in interdisciplinary, scientific research collaborations in the fields of radiation oncology, therapy as medical disciplines, imaging techniques, image processing, and data analysis.

Modern linear accelerator systems at the Department of Radiation Oncology provide advanced treatment such as image-guided and intensity-modulated radiation therapy [1].

Imaging techniques such as computer tomography and magnetic resonance tomography are essential in order to diagnose and surveil radiotherapy. In addition, optical coherent microscopy and tomography show great potential in the early detection of skin damage caused by radiation treatments [2]. This could be taken into consideration when planning additional radiation treatments and help to determine individual medical treatment.

Techniques in data analysis envisaged to develop biomedical image processing software will support stronger visualization, registration, and tracking critical tissue regions of interest, as well as modeling expert knowledge through machine learning, and decisions in support of individual radiotherapy and patient care.

Impact

Improved image processing techniques will not only enhance treatment safety and accuracy during daily radiotherapy sessions, advanced imaging techniques will also allow us to identify and treat early skin damage. This combination will lead to advanced treatment procedures and help to improve the patient's experience.

In addition, companies in the field of health technologies and medical imaging could benefit from documented experiences and initiate interdisciplinary discussions as part of planned research projects and cooperation efforts.

Competencies

Research in imaging as well as image processing and data analysis is conducted by the following departments and institutions:

The Center for Surface- and Nanoanalytics (ZONA), JKU focuses on research in surface analytics. Experience in microscopic and spectroscopic imaging for material characterization could be acquired during the CDL MS-MACH project period.

Our collaboration in *coherent imaging techniques* [3], such as (full field) OCT and OCM, is provided by ZONA, also in scientific collaboration with the **Research Center for Non-Destructive Testing (RECENDT GmbH)** and the **Institute of Polymer Product Engineering (IPPE)** at the JKU.

Institute of Knowledge-based Mathematical Systems (FLL), JKU conducts research on intelligent data mining, data interpretation, decision support, and machine learning strategies. We provide *classification and learning methods*, also in scientific collaboration with research facilities at the **Software - Park Hagenberg**.

Research and longstanding experience in radiation oncology, radiation therapy, and medical imaging are provided by the

Department of Radiation Oncology, BHS. Equipped with 6 linear accelerators, one especially designed for intraoperative treatment, specialized in volumetric and intensity modulated arc therapy, stereotactic brain surgery as well as total body irradiation [4].

These collaboration efforts are driven by the challenges of radiotherapy. We offer all clinically relevant irradiation processes and patient related surveys and follow up monitoring:

- Reporting, patient grading, (or patient grading reports?) and physician reported outcomes, including quality of life.
- Use of electronic devices to collect patient reported symptoms.
- Evaluation of clinical radiation sensitivity and correlation with DNA repair disorders.

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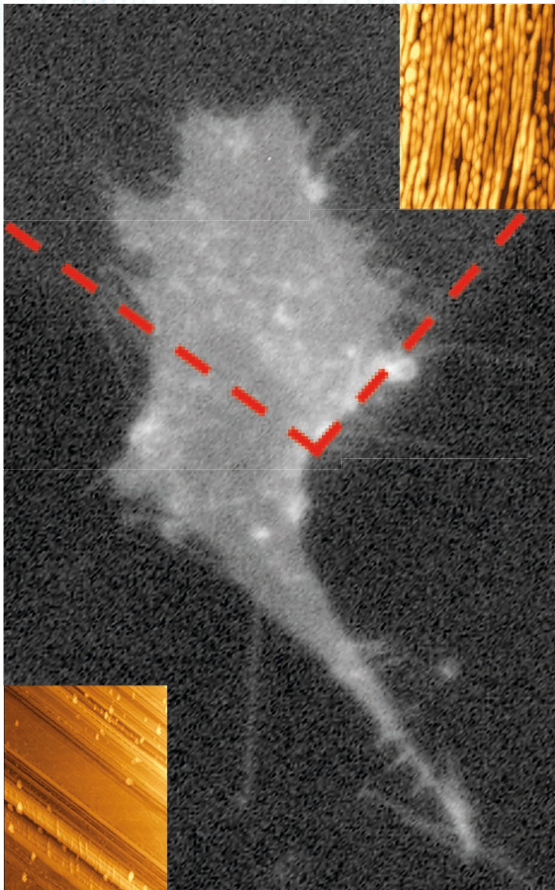
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Keywords

medical imaging, Radiation Oncology, Optical Coherence Microscopy/Tomography (OCM/OCT), Early Skin Damage Detection, Image-based Biomarkers, Image-guided Radiotherapy, Computer Tomography (CT), Cone Beam CT, visualization; tracking, machine learning

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Microstructures Control Cell Attachment



“Laser-techniques can be employed to generate defined microstructures on otherwise flat surfaces of biomaterials that are in contact with cells, tissue, and body fluids. These microstructures can strongly influence the adhesion, proliferation, and morphology of biological cells growing at these surfaces.”

Johannes Heitz

Research Focus

- Generation of Photo-Induced Microstructures
- Biomaterial Surfaces
- Control of Cell Attachment
- Cardio-Vascular Implants and Prostheses

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Vision

Microstructures at the surface of cardio-vascular implants and prostheses are key to interacting with cells, tissue, and body fluids: microstructures can improve or hinder the devices' ingrowth. Good ingrowth of the devices into the tissue is required for many applications and could be achieved by optimizing surface microstructure that supports cell-adhesion and the proliferation of adherent cells.

For other applications, the implant may have to be removed after a number of years for any number of reasons, including battery replacement. In this case, only partial device encapsulation in the surrounding tissue would be desirable. We aim to attain this goal by means of cell-repellent microstructures.

Laser-techniques can be employed to generate defined microstructures on otherwise flat surfaces of biomaterials in medicines. As these microstructures can strongly influence the adhesion, proliferation, and morphology of biological cells growing at the surface, we aim to use them for control of cell attachment at cardio-vascular implants and prostheses.

Approach

Microstructures with various geometries can be written onto a substrate by a Ti-sapphire femtosecond-laser focused into a photo-active substance at the surface. They can be employed as three-dimensional tissue scaffold onto which adherent cells can be seeded [1]. Another example is the formation of self-organized regular parallel ripples or microgrooves observed on light-exposed biomaterial surfaces. Cell seeding experiments demonstrated that photo-modified polymer foils strongly enhance cell adhesion and proliferation. Cells seeded onto microgrooves aligned their shapes and elongated in the direction of the grooves [2]. Laser-induced sharp cones and spikes can hinder the attachment of cells. In preliminary experiments, we have demonstrated that laser-induced spikes on titanium alloy surface can reduce the attachment of fibroblast in the first days of cultivation and result in differences in cell morphology.

Impact

The endothelialization of implantable cardio-vascular devices, i.e. the overgrowths of the implant surface by heart or blood vessel endothelium, is of immense importance for the prognosis and treatment of patients in cardiology. Depending on the type and place of implantation, the endothelialization may be either highly desirable or unwanted.

Competencies

Research on the generation of photo-induced microstructures on surfaces of cardio-vascular implants and prostheses will be represented and conducted by the following departments:

- **Institute of Applied Physics (JKU)** with research focused on laser matter interaction, nano photonics and optical sensing.
- **Department of Cardiology (Kepler University Hospital)** with therapy and research focused on the application of cardio-vascular implants as stents, defibrillators, and cardiac pacemakers, including innovative lead-less minimally invasive transcatheter pacemakers [3].
- **Institute of Biomedical Mechatronics (JKU)** with research focused on the interaction of cells (in particular the adhesion), biomimetics and biomechanics.

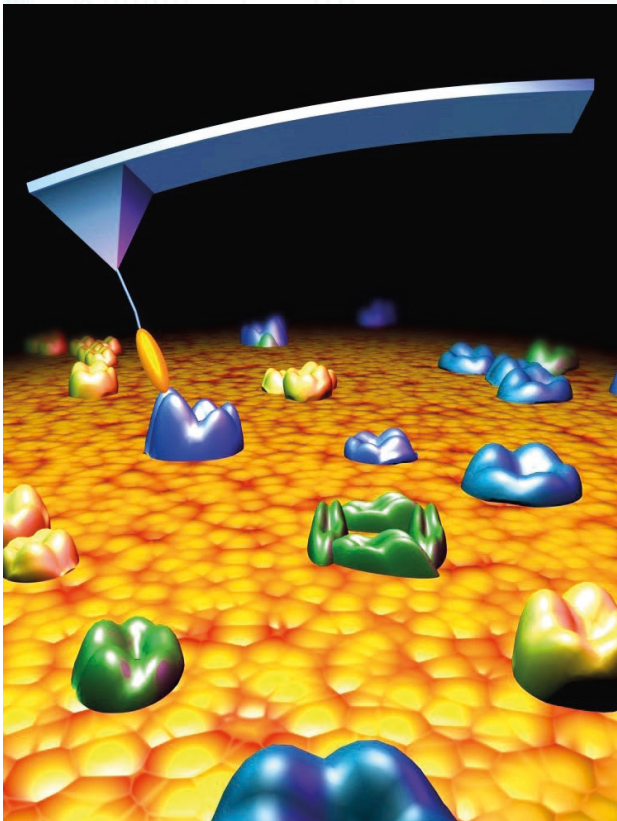
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Keywords

laser-induced structures, cell-adhesion, cell-proliferation, cell-morphology, cyto-compatible surfaces, cell repellent surfaces

Molecular Recognition Force Microscopy



“Graphics: Single molecule recognition force microscopy uses ligands or substrates tethered to tips of an atomic force microscope as a method for directly characterizing molecular interactions of functional receptors in cells and membranes on the single-molecule level while simultaneously probing the surface topology with nanometric resolution.”

Peter Hinterdorfer

Research Focus

- Single molecule biophysics
- Nanoscale topography & functional analysis
- Ligand/receptor recognition
- Cell morphology & receptor distribution
- Cellular & bacterial adhesion
- Protein structure & dynamics

Coordinator



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Vision

Molecular recognition plays a pivotal role in nature. Signaling cascades, enzymatic activity, genome replication and transcription, cohesion of cellular structures, interaction of antibodies and antigens, and metabolic pathways all critically rely on specific recognition. In fact, every process in which molecules interact with each other in a specific manner depends on this trait. Molecular recognition studies emphasize specific interactions between receptors and their cognitive ligands. Experiments at the single-molecule level are required in order to gain deeper insight into the molecular dynamics and interaction energy landscapes of receptor/ligand complex formation and dissociation. Studying the dynamics of single molecules under physiological conditions allows us to extract information not accessible by ensemble methods and static high resolution techniques. In addition, the precise identification and localization of receptor binding sites on cell surfaces remains a challenging task in molecular cell biology. We thus integrated an entire line-up of exquisite scanning probe microscopy methods into platforms designed for nano-metric and single-molecule research in biology and medicine.

Approach

The potential of the atomic force microscope (AFM) [1] to measure ultra-low forces at high lateral resolution has paved the way for studies in single molecule recognition force microscopy. AFM can be carried out in aqueous and physiological environments, opening up the possibility to study biological processes in vivo. The core methodology to study the molecular dynamics of receptor-ligand interactions, single molecule force spectroscopy (SMFS) [2], is based on scanning probe microscopy (SPM) technology. A force is exerted on a receptor-ligand complex and the dissociation process is followed over time. This requires a careful AFM tip sensor design, including tight attachment of ligands or whole viruses or cells to the tip surface. SMFS is a key tool to explore kinetic and structural details of receptor-ligand recognition. Recent applications in our lab include nano-mechanical force sensing approaches for methyl-cytosine sequencing in single-stranded DNA [3] and deciphering allosterically coupled binding sites in transmembrane transporters [4], as well as discovering viral [5] and bacterial adhesion mechanisms [6] to cellular components.

AFM also provides an exclusive opportunity to perform nanometer topographical resolution studies of functional biological specimens (proteins, DNA, membranes, cells, bacteria, virus) at physiological conditions and without any rigorous sample preparation protocols. By exploring the AFM-based topography and recognition (TREC) technique, we can now quickly and easily obtain recognition maps of receptors with the lateral accuracy of several nm across various sample surfaces, as it has been demonstrated on model receptor-ligand pairs [7], remodeled chromatin structures [8] and on bacterial surface layer templates [9]. Notably we have also pioneered TREC on cells [10] which permanently opens new application horizons in different cellular systems. Studies on macrophages revealed compact cluster organization of Fcγ receptors that would favor the rapid recognition of huge pathogens and thus their effective internalization [11]. Additional work on cancer cells

was focused on a human gonadotropin-releasing hormone receptor (GnRH-R; or type I GnRH-R) that expressed in tumor cells and gained a great deal of attention as a specific target molecule for cancer therapy. Given the clinical utility, the improved nano-organization GnRH-R is an important step in the development of more effective and possibly new therapeutic strategies [12]. Another application of TREC has been performed to elucidate the pro-tumor role of Hsp 70 on melanoma cells [13].

Impact

Over the past decades, the importance of characterizing living biological structures at the nano-scale in physiological environments has increased significantly. Moreover, with the invention of high-speed bio-AFM, watching dynamical structural changes in real time, such as the bi-pedal 'walking mechanism' of antibodies on bacterial and viral membranes [14], as well as filming the thermal motion of membrane protein moieties [15] has come into sight. The major expected long-term impact is to arrive at a detailed dynamic and functional picture in understanding the binding and transport mechanism of substrates and pharmaceuticals to aid drug design and develop new therapeutic strategies.

Competencies

BIO-SPM methods assisted with fluorescence microscopy on living cells, membranes, bacteria, viruses, proteins, DNA in physiological conditions.

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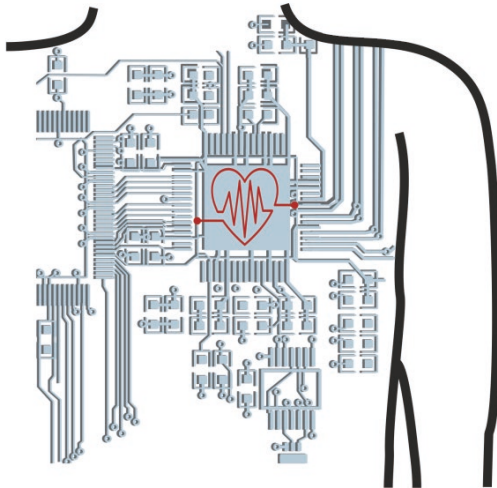
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Keywords

Scanning Probe Microscopy (SPM), Atomic Force Microscopy (AFM), Single Molecule Force Spectroscopy (SMFS), Single Cell Force Spectroscopy (SCFS), Topography & Recognition (TREC) Imaging, high-speed bio-AFM, molecular and cellular recognition & adhesion

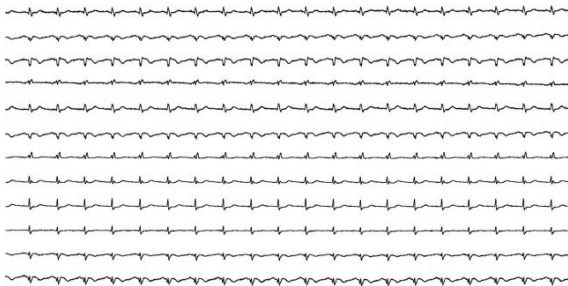
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Biomedical Signal Processing



“Advances in signal processing and machine learning give us an opportunity to uncover crucial, potentially life-saving information hidden in biosignals.”

Mario Huemer



Research Focus

- Signal Processing and Analysis
- Pattern Recognition, Classification, Prediction
- ECG Morphology
- Heart Rate Variability

Coordinators



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Vision

Demographic developments show Europe's aging population is growing steadily. The increase correlates to higher rates of age-related diseases and illnesses such as cardiovascular diseases and dementia. The JKU recently began conducting interdisciplinary research focused on developing more advanced, sensitive, and targeted analytical tools designed to explore cardiovascular diseases in intensive care patients and autonomic regulations in dementia patients.

Current research focuses on the well-established, conventional electrocardiogram (ECG). Obtaining physiological signals of remarkable diagnostic power is not difficult and provides a wide spectrum of information pertaining to the patient's condition. Over the past few years, however, clinical studies have revealed that even subtle ECG changes are important when it comes to detecting neurological disease [1] as well as in intensive-care medicine [2]. However, clinically important information of this kind is often transient or masked by noise and therefore difficult – if not even impossible – for a human observer to detect and interpret. In general, consistent ECG interpretation is a difficult task due to inter-patient and inter-observer variabilities. Our research aims to develop analytical tools tailored to an ageing population that provide reliable parameters and predictors for specific diseases, thereby supporting practicing clinicians in their everyday routines.

Approach

The basic technologies and corresponding research fields are biomedical, statistical and adaptive signal processing, machine learning, pattern classification and recognition as well as neurology and intensive-care medicine. Data is acquired using leading, cutting-edge technology at the Kepler University Hospital. The BedmasterEx™ system, for example, can continuously record a patient's biomedical signals and even track these signals along different departments, giving us an ideal baseline for subsequent data analysis [3].

We not only apply joint and interdisciplinary research, but also new teaching models. Bachelor and Master's degree theses are jointly supervised by engineering scientists and medical doctors. Students can use the laboratories and facilities at both the JKU as well as at the Kepler University Hospital and the highly attractive model appears to be well-received by JKU students. In addition, we are currently developing courses on biomedical signal processing to be taught jointly by engineering scientists and medical doctors.

Impact

When it comes to biomedical signals, there has been a significant increase over the past decades in regards to the importance of automated abnormality detection. This requires reliable algorithms to automatize information extraction and target visualization in order to be implemented in to new and existing medical devices. The expected long-term impact is improved, patient-centered medical care.

Competencies

Research in signal processing, neurology and intensive-care medicine is represented and conducted by the following departments:

- **Institute of Signal Processing** with research focused on algorithmic, architectural and hardware oriented aspects of signal processing systems in ICT as well as sensor and biomedical signal processing.
- **Department of Anesthesia and Operative Care** with research focused on the ECG's morphology for specific diseases, such as myocardial infarction, anemia, ischemia, hypoxia, etc.
- **Department of Neurology** with research focused on the evaluation of the autonomic nervous system for patients suffering from dementia.
- **Business Division for Biomedical Technology** with research focused on acquiring and processing biosignals as well as the development of tailor-made clinical solutions for distinct pathophysologies.

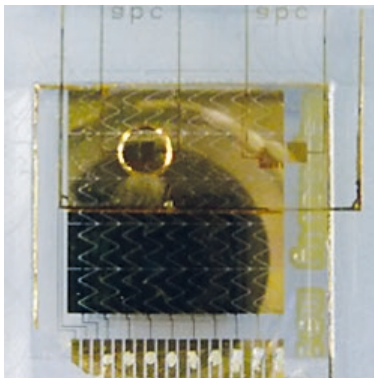
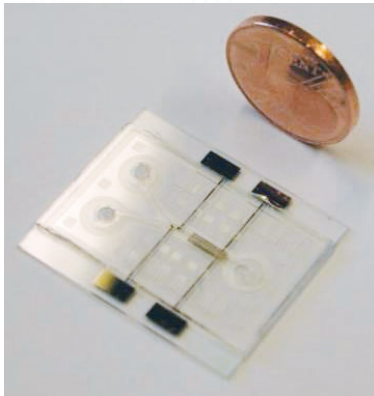
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Keywords

biosignal analysis, computer-aided diagnosis, ECG beat morphology, heart rate variability, pattern recognition, dementia, autonomic nervous system

Miniaturized Sensors and Actuators for Integration into Lab-on-a-Chip (or the surface of medical instruments)



“In the past, silicon-based microsystems have revolutionized mass market applications. Working with hybrid technologies that go beyond silicon-based micro-machining will pave the way for other applications in different markets and environments.”

Bernhard Jakoby

Research Focus

- Miniaturized sensors for physical fluid properties
- Embedded and hidden sensors in surface coatings
- Actuators for fluid actuation at small scales
- Versatile and low-cost fabrication technologies based on functional polymers
- Modeling and Simulation
- Readout Electronics and Algorithms

Coordinators



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Vision

In the fast-growing field of Lab-on-a-Chip (LOC) and micro-Total-Analysis-System (μ TAS) applications, the scientific community has already devised a large number of technological solutions for implementing CMOS-based ICs into polymer microfluidic systems. This represents the so-called active-electronic biosensor approach characterized by full integration of IC and microfluidic structures on the very same platform. For example, Charlot et al. [1] developed a low-cost technique for integrating silicon sensors or actuators into polymer-based microfluidic systems using only screen-printing and lamination processes. The converse approach is the so-called passive-electronic biosensor characterized by the utilization of a typically disposable microfluidic chip and separate off-chip readout and control electronics. While active-electronic biosensors typically feature excellent electrical performance and high levels of integration at the cost of additionally required post-processing effort as well as packaging and material compatibility issues, the performance of passive-electronic biosensors often suffers from the required longer interconnections between the sensing sites and the electronics. A strategy to tackle this drawback of passive-electronic biosensors was presented by Temiz et al. [2]; they introduced a three-dimensional, stacked CMOS architecture with a disposable bio-sensing layer on top which can be aligned and temporarily attached by vertical interconnections. Thus, this concept merges the advantages of active and passive electronic biosensors, featuring both increased functionality and reduced overall cost.

Recent trends in polymer-based transducers and their integration into microfluidic devices blur the line between active and passive biosensors. Polymer transducers can - in most instances - be merged with the microfluidic chip with little or moderate technological effort, which increases the degree of integration and functionality considerably, but retains the advantage of cost-effectiveness associated with polymer technology [3]. Additionally, the increasing performance of direct writing and additive manufacturing methods increases the attractiveness of polymer-based transducers and opens up new and exciting possibilities for the realization of specifically devised sensors and actuators without the need for time-consuming and cost-intensive process steps.

Approach

The fundamental technologies and relevant research fields comprise transducer design, hybrid fabrication technology, system integration on a microfluidic platform, as well as electronic circuit design and control algorithms. Special emphasis is being placed on the development and utilization of innovative functional materials, such as polymer composites that can be processed with low-cost and low-effort additive manufacturing techniques. Unlike the typical LOC integration strategies, cutting-edge approaches are also being pursued, such as embedding sensors into the organic coating of existing (medical) instruments, thus raising the degree of functionality and smartness. The associated research at our lab is conducted in cooperation with other departments at the JKU Faculty of Engineering and Natural Sciences, particularly with partners from the departments of mechatronics, physics, and chemistry.

Impact

The overall expected growth rate of the LOC market is expected to amount to ~18% from 2015 to 2021, eventually reaching a total value of approximately USD 15 billion [4]. The use of biochips, where multiple experiments can be performed on a single miniaturized platform, has steadily increased in the past decade, with applications not only in the medical area (e.g., personalized medicine, drug discovery, and high-throughput screening), but also in areas such as agriculture, environmental monitoring, engineering and science.

Competences

The core competences of the Institute for Microelectronics and Microsensors in the relevant field are:

- Design and fabrication of **miniaturized sensors for physical fluid properties**.
- Development of **small scale actuators for fluid manipulation**.
- **Microfluidic Chip** design.
- Low-cost **additive manufacturing** techniques based on polymers and composites.
- Layout and realization of **electronic circuits** as well as the programming of **control algorithms** associated with sensors and microsystems.

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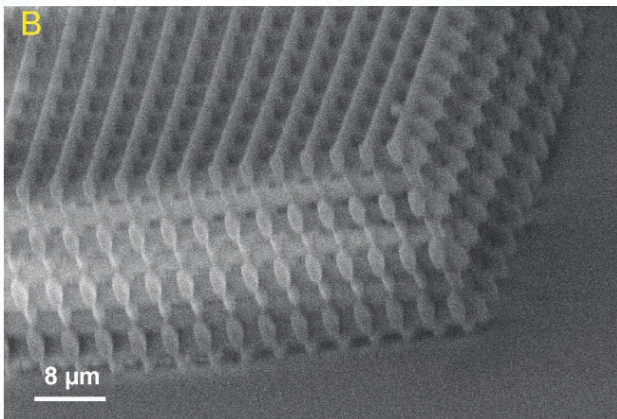
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Keywords

sensors, actuators, transducers, microfluidics, Lab-on-a-Chip, LOC, Micro Total Analysis Systems (μ TAS), embedded sensors, sensor actuator system, stimulus-active polymers, functional polymers

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3D Lithography for Nanobiotechnology



“Two-photon polymerization, optionally combined with stimulated emission depletion (STED) lithography, allows fabricating polymer structures with sub-100 nm precision. They provide new opportunities to a large field of biomedical applications and research, e.g. in the fields of biosensing and tissue engineering.”

Jaroslav Jacak

Research Focus

- 3D Micro- and Nanolithography
- Functional Polymers
- Cell Biology on Scaffolds

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Vision

Recent developments in biotechnologies indicate an ever-growing need to develop systems supporting personalized medicine. There is an overall constant growth in the in vitro diagnostic market as well as constant progress in tissue engineering and organ printing. The Institute of Applied Physics (IAP) at the JKU and Medical Engineering departments at the Upper Austrian University of Applied Sciences in Linz conduct interdisciplinary research focusing on the development of advanced and more sensitive, precision tools for use in the field of bioanalytics.

Our research on structuring biocompatible 3D scaffolds consists of working with functional polymers that carry proteins to either mimic tissue environment or support molecular biosensing, thus fostering the development of new polymers and setups resulting in improved 3D lithography performance. Techniques such as multiphoton and STED-lithography in particular have been introduced, permitting polymeric scaffolds structuring with features far below 100nm.

Our future objectives include the development of new types of polymers for a generation of platforms that support tissue repair as well as biosensors. An overall objective is to design three dimensional tools for point-of-care devices that provide reliable parameters and predictors for distinct diseases, thereby supporting practicing clinicians in their daily routines. Furthermore, tissue scaffolds might be used as an in vitro test system to mimic basic processes in tissues and help obtain deeper insight into molecular transport processes or tissue repair.

Approach

Our methods are based on two-photon lithography optionally combined with STED-lithography. Both technologies allow for the design of 3D structures in the micro to nanoscopic range using visible light. The library of accessible and biocompatible polymers available for 3D lithography has recently been extended by the most recent developments in our groups. New polymers carry functional groups and allow for selective binding of numerous proteins. For sample characterization, advanced imaging techniques such as electron microscopy, AFM and high-resolution fluorescence microscopy (STED, localization microscopy) are available. Information provided by these micro- and nanoscopic analytic tools will be fed back in order to improve the polymeric structures.

For several years now, undergraduate, graduate, PhD students, and post-doctorate researchers from both institutions have combined their expertise in support of collaborative projects. IAP experts in optics and laser physics meet routinely with experts in medical and bio-engineering at the University of Applied Sciences. This synergistic teamwork has resulted in several joint publications and we expect to strengthen joint collaboration efforts in the future.

Impact

Many devices, particularly in the medical field, are becoming smaller and more portable. Smaller devices can, for example, require less specimen material from patients in order to conduct medical analyses. Smaller devices also require less material during the manufacturing process. The growing market demands creating new, innovative materials to support the production of smaller biomedical devices and equipment.

The greater, long-term impact is expected to be significant improvement of patient-centered medical care as well as facilitating pioneering research in pharmaceutical and life sciences. In the coming years, new developments to enhance analytic devices used in the fields of molecular biology, clinical biochemistry, blood gas/pH, immunoassays and hematology will play a particularly important role within the industry.

Competencies

Basic research and application-driven development is carried out by the following partners:

- Institute of Applied Physics with research focused on STED-lithography and microscopy, as well as nanophotonics, laser-matter-interaction and optical sensing. The institute also cooperates with industry in application-oriented research.
- University of Applied Sciences – Medical Engineering with research focused on high resolution microscopy and 3D lithography. The department has many years of experience in bio-assay design, as well as fundamental and high-end techniques in cell biology.

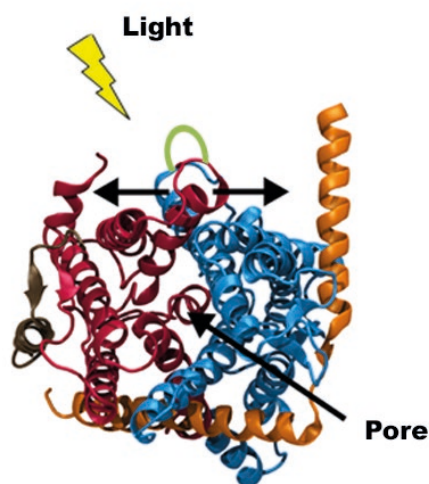
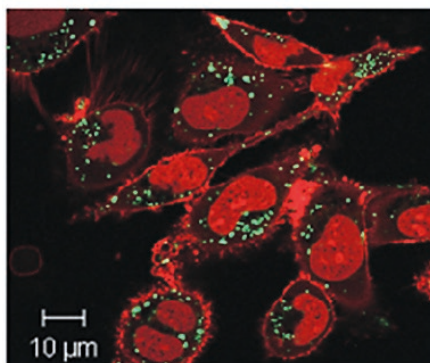
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Keywords

direct laser writing, three-dimensional optical lithography, STED-lithography, functional polymers, protein assays, tissue scaffolds

Molecular Photomedicine and Photopharmacology



“The interaction of living systems with light-responsive compounds has the potential to revolutionize molecular biology, genetics, neurosciences and drug design.

This fascinating approach will provide important tools for future precision medicine at the molecular level.”

Günther Knör

Research Focus

- Light-Controlled Reactions
- Photopharmacology, Phototherapy
- Synthetic Biology, Artificial Enzymes
- Metals in Medicine, Metal-based Drugs
- Small Molecule Activation and Re-lease
- Inorganic Biochemistry, Biomimet-ics
- Antiviral, Antimicrobial Agents
- Photoswitches as Optogenetic Tools
- Bioenergetic Model Systems
- Inflammation, ROS, Wound Healing

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Vision

The 21st century can be considered as the age of optical and photochemical technologies. Important aspects of light-dependent processes, luminescence and photonics have already been well established and extensively used in a variety of scientific fields, including many practical applications in biomedical research, diagnostics and medicine [1]. For example, the clinical use of lasers in medicine and the treatment of certain diseases by photodynamic therapy (PDT) have now been successfully performed for decades.

In photopharmacology, light of a specific wavelength can act as an external signal for the controlled release of physiologically active compounds [2]. Photoswitchable systems may help to trigger intracellular processes on demand. Light can also be systematically employed as a highly selective tool for spatial and temporal control over complex biological processes and biochemical reaction cascades at the molecular level, including the functions of enzymes and nucleic acids.

Pioneering research in photochemistry and life sciences is currently being revolutionized by the availability of optogenetic methods, and in the near future, molecular medicine and synthetic biology will benefit from the rational design of light-responsive chemical systems able to mimic the function of natural processes under remote control while even operating in life cells and living organisms [1].

Approach

Visible-light irradiation of sensitizer molecules can be used to generate reactive oxygen species (ROS) such as singlet oxygen or peroxides for phototherapeutic purposes [3-5]. We have developed and successfully applied an innovative concept which allows us to trigger the delayed release of ROS with excellent cytotoxic drug effects on human cancer cell lines, as well as possible implications for the controlled deactivation of bacteria, viruses and parasites [4]. The photochemical release of small signaling molecules, such as the gasotransmitter CO with highly biocompatible compounds, has also been demonstrated in our group [2]. A unique and innovative concept with excellent potential in synthetic biology and molecular medicine is the development of light-driven enzyme model compounds (artificial photoenzymes) which can be employed to fully replace the function of native biocatalysts while reversibly switched on and off upon light excitation as an external stimulus [1]. Many successful examples, including artificial endonucleases for DNA-double strand cleavage [1,6] and artificial oxidoreductases, have been designed thus far [1].

Impact

We can expect that the systematic application of light-mediated intracellular processes with temporal and spatial control at the molecular level will have a bright future in medicine and life sciences. Genetically encodable photoactuators emerging from the field of optogenetics are now available today. In the near future, bio-inspired chemistry and photocatalysis - together with approaches in synthetic biology - will contribute significantly to these exciting new developments. In the long term, potential clinical applications, such as highly selective drug delivery, reversible regulation of intracellular functions, and the development of personalized precision medicine, will be possible.

Competencies

Our research focuses on the spectroscopic and photochemical properties of inorganic, organometallic and organic compounds, including luminescent materials and synthetic systems of biological or medical relevance. Current studies explore the functional role of bioinorganic or bio-inspired systems in catalytic and light-dependent processes in particular. Applications and testing of innovative light-responsive compounds in the fields of life sciences, molecular medicine and photopharmacology (including experiments in cells or living organisms) are being conducted as part of collaboration efforts in Austria and abroad. The corresponding research projects are represented and conducted at JKU by the: Institute of Inorganic Chemistry and Center for Nanobionics and Photochemical Sciences (CNPS) Rational design, synthesis, structural and chemical characterization, as well as all photophysical and photochemical studies of biocompatible, luminescent and light-responsive systems.

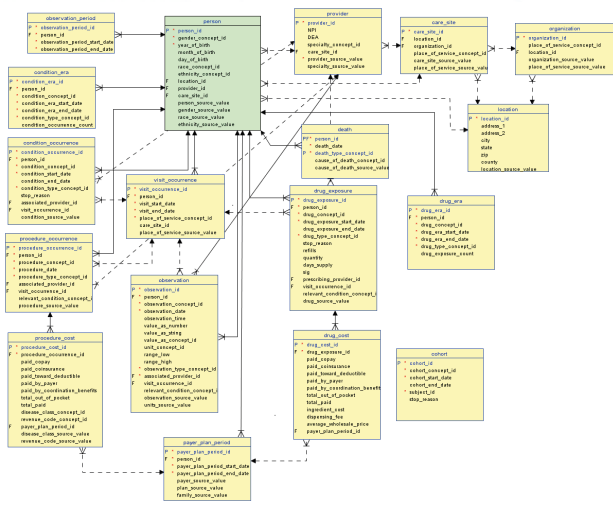
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Keywords

photochemistry, artificial enzymes, chemistry in life cells, optogenetics, nanomedicine, light therapy, anti-infective and anticancer drugs

Semantic Data Warehousing & Process-Oriented Medical Information Management



“Once semantic aspects of information become tangible, digital processing becomes supportive to organizations and their stake-holders.”
Stefan Koch, Michael Schrefl, Christian Stary

Research Focus

- Business Intelligence
- Semantic Systems
- Business Process Management
- Enterprise Systems and Business Value
- Information Management
- Organizational Learning

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Vision

Healthcare systems reveal increased complexity due to optimized resource planning, demographic development, and digitization efforts in data, information, and process management. These systems adapt to changes based on comprehensive analysis of intra- and inter-healthcare provider data on treatment and service processes. Interactive data analysis and data interpretation can be easily performed by domain experts (rather than IT experts) by complementing system interfaces and data by semantic descriptions based on medical ontologies that are in turn based on SNOMED CT, ICD-10, ACT, or HL-7. Findings from this type of data analysis direct the adaptation of processes and their execution.

As socio-technical design under economic constraints is an established area of interdisciplinary research at the JKU Departments of Business Information Systems, the vision researchers are pursuing is to gain meaning from (big) data analyses that triggers organizational development in terms of IT support and advanced patient and resource-centered process designs of information systems.

Current studies focus on specific healthcare data warehouses and information systems. A patient and resource-centered approach, however, requires a systemic or contextual approach. Knowledge needs to be acquired by integrating and analyzing intra- and inter-healthcare provider data. It frames re-engineering of work processes and information systems. The envisioned approach does not only allow various stakeholders (physicians, patient etc.) to trigger operational procedures, such as prevention measures, but rather to establish cross-organizational learning processes continuously adapting the healthcare system.

Approach

To implement the vision as outlined above, healthcare systems are considered to be Complex Adaptive Systems. These types of systems reflect the stakeholder's dynamic nature and thus, system behavior. Semantic data warehouses integrate intra- and inter-health provider data and employ domain ontologies (such as SNOMED CT or ICD-10), expressed in description logic such as OWL, to facilitate the formulation and execution of analytical queries in medical terms. This allows generating innovative knowledge about processes that in turn influence the development of healthcare information systems. Hence, the approach is a staged procedure finally leading to process-aware information systems supporting operational healthcare procedures, such as resource planning at hospitals. The ultimate goal is to recognize process-relevant events and information from intra- and inter-healthcare provider data warehouse analyses. It triggers stakeholder- and situation-specific procedures for patient treatment and healthcare information management.

Relevant research fields to implement the staged procedure include clinical knowledge management for domain-specific information, semantic data warehousing techniques, adaptive process and workflow management, information management and engineering, and organizational learning support. The latter is of crucial importance for continuous and sustainable adoption since, aside from operational support, healthcare systems need to be developed from a strategic perspective. The corresponding learning cycles

establish so-called double-loop learning processes. They are intertwined with operational process management by checking knowledge claims for embodying adaptations into running operation. These kinds of systems will also need to demonstrate their value to the respective organization and its stakeholders using appropriate methods, both before implementation and continuously afterwards to ensure uptake and continued use.

Impact

Big Data and Information Management developments require operational interfaces in healthcare for optimizing patient treatment and resource optimization. Inter-healthcare data warehousing provides for (1) comprehensive data analysis to assist in acquiring knowledge for improving clinical pathways and treatment processes and (2) to detect situations that trigger dynamic adjustments of patient-care or service provision processes.

Competencies

Research in data warehousing, semantic-based analytics, business process and workflow management, enterprise information systems, and organizational learning will be led by the following Departments of Business Information Systems:

- Communications Engineering with research focusing on process awareness, distributed system development and learning support.
- Data and Knowledge Engineering with research focused on Business Intelligence, in particular Big Data, Semantic Systems and Data Warehousing.
- Information Engineering with research focusing on Enterprise Resource Planning and Systems, Business Process Management, IT Governance and Business Value.

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Keywords

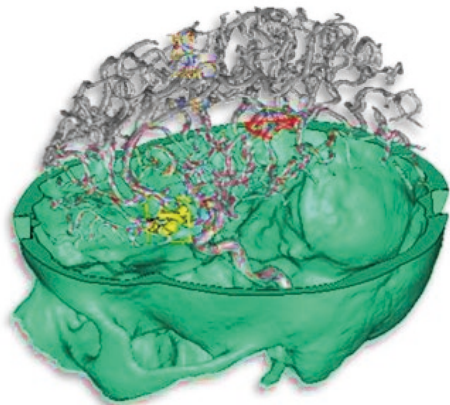
ontologies in medicine, data integration, analytics, process modeling, validation, single/double loop learning, operation support, knowledge processing

Additive Manufacturing of Medical and Assistive Devices



“New personalized polymer products adapted specifically to a single patient can be potentially life-saving and improve patient comfort.”

Zoltan Major



Research Focus

- Direct and Reverse Engineering
- Process Simulation and Advice
- Component Simulation and Testing under Biomechanical Loading Conditions
- Additive Manufacturing of Biomodels as well as Supporting and Assistive Devices

Coordinators



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Vision

Product development at the end of the last century focused on mass customization and product personalization [1]. Although product personalization is more common when it comes to “soft” products and can be implemented electronically, additive manufacturing (AM) makes it easier to produce “hard” personalized products as well. The steps used to generate 3D objects as also described by Rengier et al. (2010) are image acquisition, image post-processing and 3D printing [2]. As imaging quality improves, we can more accurately generate virtual 3D objects. These can then be manufactured within a resolution range and according to the material availability of the 3D printers.

In medicine, hard models mimicking a patient’s anatomy can be used for surgical planning and to train medical personnel. This can help reduce the planning and operating time as well as increase chances of survival, especially when it comes to emergency procedures. These models can also be used to help educate patients and their relatives to help them understand why a surgical procedure is necessary and how it will be performed. By providing a better level of understanding, we can reduce patient insecurity and put the patient at ease. Another application becoming more important pertains to 3D print implants and implant molds using the results of computer tomography (CT) or magnet resonance imaging (MRI) to accurately produce the patient’s needed implant geometry.

Approach

High quality image data are among the technologies required to produce “hard” devices imitating real people. When only an external body part is of interest, these can vary from a laser scan to medical image technologies such as a CT or MRI. A virtual 3D model is generated out of the 2D image stack and can be used correspondingly to create virtual models fitting a human body part. The virtual 3D models can be printed in 3D. At IPPE we focus on the following applications: Bio-Models and Supporting and Assistive Devices.

Bio-Models of the head and spinal cord have been successfully printed using a 3D printer. To facilitate brain aneurysm surgeries, models consisting of skull, brain and the artery system containing the aneurysm were derived using CT, MRI as well as angiography [3]. Parts of a spinal cord were also printed, combining hard and soft materials to mimic the elastic spinal disc properties between the dorsal vertebrae. Virtual models simulating mechanical spinal disc properties were also reverse engineered using the imaging data and we started the process of creating a simplified liver model. Mechanical testing of hip prostheses using state-of-the-art and innovative materials were conducted and analyzed.

As each individual is different, certain medical products have to be customized to individual patients, such as patients who have brain tumors and require immobilizing during radio therapy.

State-of-the-art procedures would require creating a mask directly on the patient’s face - a procedure that can take up to 45 minutes and could be quite distressing and uncomfortable for the patient. Using a 3D printer to make a customized mask of the patient’s facial features is a far less distressing. The masks are developed in cooperation with the Department of Radio-Oncology and Radiology of the

Barmherzige Schwestern Linz (Prof. H. Geinitz) and any precision influence on patient immobilization will be tested. Assistive devices can also be customized. Those who have reduced or no hand and arm mobility can use mouth sticks to help them perform everyday tasks. In collaboration with the Competence Network Information Technology to Support the Integration of People with Disabilities (KI-I), the Department of Women’s Studies and Gender Research, the University of Applied Sciences for Health Professions Upper Austria, the medical supply store Heindl Ltd., and EVO-tech Ltd., we have developed mouth stick prototypes using customized 3D printed mouth pieces as well as individual stick and tip systems for diverse applications.

Impact

By improving the image quality and 3D printing process now and in the future, we can provide patients and medical personnel with personalized products in a shorter amount of time. Regulations and requirements in the medical sector mean there is still room to continue development. We can provide support services pertaining to the material selection and the development of prototypes for medical and hygienic products.

Competencies

Research is conducted at the following departments:

- Institute of Polymer Product Engineering (JKU): product design, simulation, rapid prototyping and component testing
- Department of Radio-Oncology and Radiology Barmherzige Schwestern Linz: radio therapy
- Department for Neuroradiology: medical imaging
- Competence Network Information Technology to Support the Integration of People with Disabilities (KI-I): software development
- Department of Women’s Studies and Gender Research (JKU): participatory design

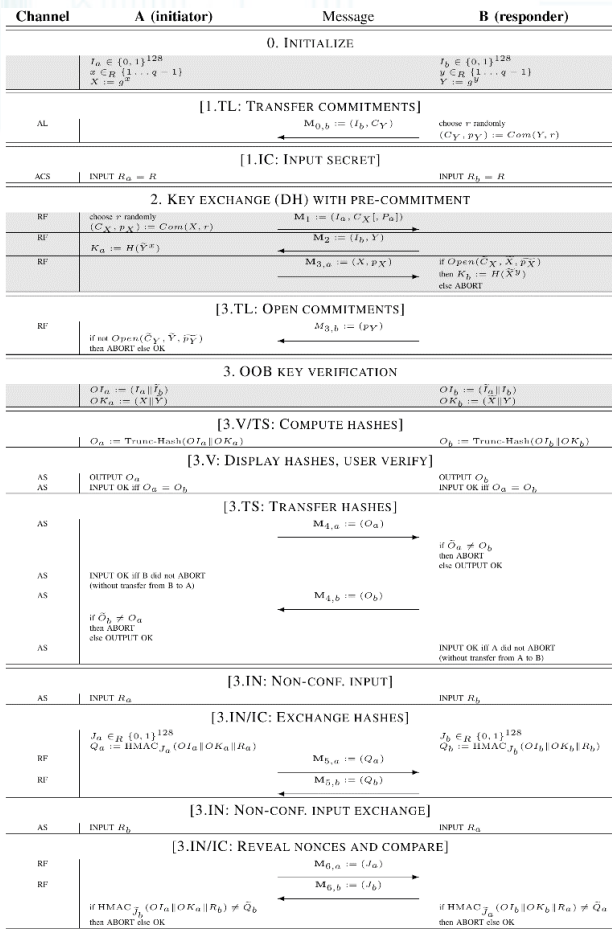
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Keywords

direct and reverse engineering, personalization, product development, medical image processing, additive manufacturing, component and process simulation, component testing

Security for Medical Data and Processes



“Securing electronic medical information, associated processing procedures, and involved devices are paramount considering more and more life-saving (and life threatening) decisions are determined automatically. Corresponding security and privacy safeguards need to be integrated into medical systems from the start, as retrofitting is often extremely costly or sometimes even impossible.”

René Mayrhofer

Research Focus

- Network and communication security
- System and code security
- Digital identity

Coordinator



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Vision

There is a vast volume of electronic patient medical records already being stored and digitally processed. This type of electronically stored data is only expected to grow. In addition, rapid advances in healthcare mean that many direct medical procedures to the human body - such as an embedded insulin pump regulated by wireless sensing and control devices for example - will be controlled automatically. In order to support new approaches in medicine, including personalized medication, access to this type of information and to these systems will need to be carefully monitored and controlled. Personalized medicine can only be effective on a daily basis if we can guarantee the necessary safety and security precautions. The issue is many-sided and complex, requiring consistent and attentive coordination among everyone involved, including patients, medical personnel, medical device manufacturers, legislators, and hospital administration.

Approach

Although computer and network security have been studied extensively and there are numerous solutions for conventional client/server environments, the proliferation of small networked devices has created significant new challenges in terms of security.

We are focusing on three areas:

- Digital identity regulates the authentication and use of access credentials, not just for digital access, but also for physical services. Biometric authentication can facilitate access to data, device control, and physical entrance without security tokens or passwords. In cooperation with the Josef Ressel Center for User-Friendly Secure Mobile Environments (u'smile) [1] and international partners, we are in the process of developing a mobile digital identity system for modern smartphones. An initial prototype will include encoding an Austrian driving license to become a purely digital document with optional features such as one's social security number, etc. The idea is that this will provide better privacy than current identification systems [2].
- Secure and reliable code is crucial for embedded systems, servers, mobile clients, and other computing devices to prevent malicious attacks or malfunction. In regard to medical devices, regular patching or software updates to fix problems discovered on a trial & error basis in the field are unacceptable. Instead, more rigorous design, development, and testing processes are required. In cooperation with other computer science institutes at JKU, we aim to improve formal methods and develop tools to support better code security.
- Latency is critical for all real-time systems, including medical devices directly interacting with a human body. We are currently studying the correlation between network communication systems, security measures, and latency in the specific use of power grids [3] and car-to-car communication by focusing

on the strict safety requirements in regards to the maximum amount of delay before cutting a line power or applying the emergency braking system. The findings and information acquired from these areas can be directly applied to medical devices.

Impact

Without adequate security measures, deploying smart, networked systems in the medical field poses an immediate and significant risk to human life. However, proper security and privacy safeguards for medical devices and processes can be integrated if they become part of the system design from the start.

Competencies

The Institute of Networks and Security (INS) provides broad theoretical and applied education in many areas of computer security. Our research fields as outlined above can potentially play a key role in the advancement of medical technology. In addition, the research group has many years of experience in secure user interaction, designed explicitly to take specific-use case requirements into account.

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Keywords

network security, communication security, code security, (embedded) systems security, mobile device security, secure data storage, digital identity, (biometric, token, or knowledge-based) user authentication, privacy

Polymer Processing Technologies for Reinforced Bionic Products such as Exoskeletons, eLegs and eArms



“In accordance with our maxim ‘Resource Efficient Smart Production and Products’, we combine increased production and resource efficiency with product development to meet both the principles of bionic-design and realize their full process and material potential.”

Jürgen Miethlinger

Research Focus

- New Polymer Processing Technologies
- Polymer Processing and Its Effects
- Process Analytics, Process Simulation
- Taylor made High Performance Compounds
- Processing of Thermoplastic Lightweight Constructions
- Smart Efficient Production

Coordinator



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Vision

The predominant objective is to realize a single-stage process that is as efficient as thermoplastics processing and, at the same time, results in creating products that could attain a performance level that comes weight-referred close to - or even outperforms - thermoset fiber reinforced composites and perhaps even metallic materials. The primary challenge is to wet and consolidate various solid reinforcement components in a single-stage economic process in order to end up with a sophisticated polymeric hybrid structure that has a unique value proposition. These thermoplastic lightweight constructions serve as the fundament for agile and smart exoskeleton, e-legs and e-arms. This is the kind of vision that will be a part of the future Linz Institute of Technology.

Approach

Polymer materials have been and always will be a source of new technologies and innovative products. Unlike any other material group, developments in morphological structure and the property profile strongly depend on the processing technologies. Our focus on exoskeletons, e-arms and e-legs include (i) multi component and hybrid structures, (ii) oriented and self-reinforced macromolecular materials, (iii) novel additive manufacturing technologies like extrusion deposition modelling and (iv), improved extrusion and compounding performance.

Impact

The scientific impact is a deeper understanding of fundamental principles such as the transport phenomena in screw processing related to improved mixing and plasticating performance, multi-component material flow for the production of light-weight structures (e.g. exoskeletons), new single-stage processing technologies that use less energy, new material processability, new machine concepts that demonstrate increased reliability and durability, new additive manufacturing methods for enhanced product performance, reversible multi-physic simulation methods, free surface numerical simulation, 3D simulation with automatic pre-processing of real-time simulation for model based control concepts, and finally, new concepts to increase the utility and value of polymeric systems.

Competencies

The Institute of Polymer Extrusion and Compounding conducts fundamental and applied basic research and conducts research on the application of new polymer materials and new polymer processing technologies together with an international interdisciplinary research team.

The Institute of Polymer Extrusion and Compounding has well-equipped laboratories at its disposal for: (i) Simulation, (ii) Polymer Processing, (iii) Material Characterization, as well as (iv) Polymer Welding and (v) Extrusion Deposition Modelling with, for example, single screw extruders containing additional sensors, co-rotating parallel twin-screw extruders featuring several gravimetric feeders, underwater and strand pelletizing and counter rotating conical twin screw extruders, a variety of on- and inline shear and extensional rheometers, different polymer welding methods, direct extrusion deposition modelling, sophisticated industry-like co-extrusion pilot lines as well as computational fluid dynamic tools.

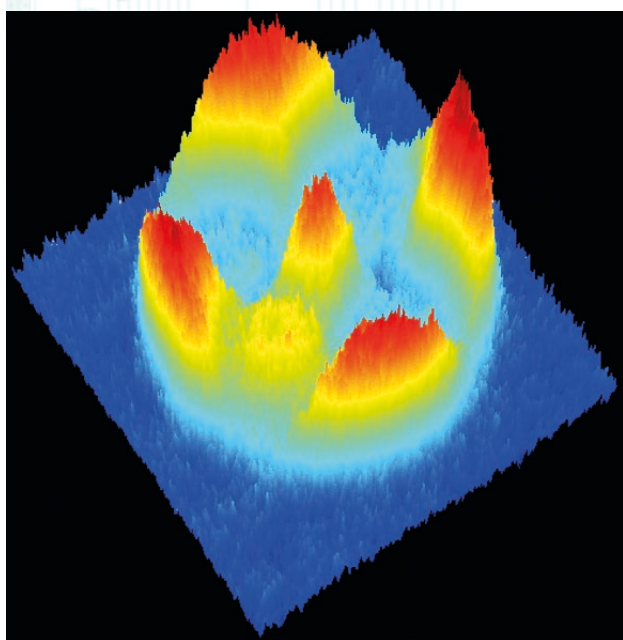
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Keywords

bionic, exoskeleton, eLegs, eArms, reinforced profiles, process engineering, process analytics, composites, compounds, computational fluid dynamics

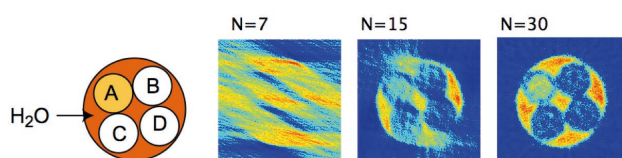
Nuclear Magnetic Resonance (NMR)



Spin noise imaging of a phantom
Norbert Müller, Alexej Jerschow (2006)
PNAS 103, 6790

“Magnetic resonance techniques are rapidly developing in new areas of bio-medical research and (molecular) imaging.”

Norbert Müller



Research Focus

- Development of spectroscopic techniques for NMR
- Nuclear spin noise imaging and spectroscopy
- Solid state NMR
- Molecular imaging by NMR

Coordinator



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Vision

Magnetic resonance is the least invasive three-dimensional imaging technique available today. Hardware development is currently most prominent in two orthogonal directions - higher fields and smaller systems. By focusing on alternative detection techniques, we want to respond to the challenges of these developments and extend the scope of the MRI and MRS method methodology.

Many of the latest hardware developments have pushed conventional approaches for resonance excitation and raw signal acquisition close to the physical limits. Non-linear effects in particular are becoming apparent and need to be either compensated or actively exploited as an additional source of information.

Metabolomic tissue analysis by NMR is an emerging field which has even already found its way into some advanced operating theatres.

Both NMR spectroscopy of biomedical samples for diagnostic or metabolomics purposes as well as imaging applications will benefit from technological progress enabled through fundamental research in magnetic resonance.

In addition, nano-scale NMR has the potential to match the methodology's sensitivity to currently established high throughput methods. Our vision includes employing the latest technological developments such as DNP (dynamic nuclear polarization), alternative detection principles, and advanced data processing to achieve enhanced performance in emerging application areas.

Competencies

Established at the JKU in 2011 together with the University of South Bohemia with funding by the European Union, the **RERI-uasb NMR Research Center** conducts research in developing nuclear magnetic resonance methods as well as creating sophisticated NMR techniques and applications designed to solve analytical problems. The research center's three NMR spectrometers are located at the **Institute of Organic Chemistry** at the JKU.

NMR researchers at the JKU are experienced in countless NMR-based techniques such as multiple quantum spectroscopy, (cross-correlated) relaxation measurements, diffusion and convection, paramagnetic relaxation, spin noise, non-linear effects, and most recently DNP (dynamic nuclear polarization). The application areas range from biomolecular structures to medical chemistry and theoretical modelling. Spin noise imaging was invented at the JKU. A multitude of international collaboration efforts as illustrated in the reference list allows us to successfully network within an active community.

Headed by Prof. Norbert Müller, former colleague of two Nobel laureates, the NMR research center provides expertise in most branches of NMR spectroscopy.

Researchers at the center have different scientific and academic backgrounds (chemistry, physics, biology) and outstanding track records in methodological research, fundamental and applied spectroscopy, as well as in finding solutions to issues in a wide range of application areas.

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Keywords

Nuclear Magnetic Resonance (NMR), magnetic resonance imaging, molecular imaging, spin noise, non-linear response

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SEW SYSTEMS

Kepler
Universitäts
Klinikum

JKU
JOHANNES KEPLER
UNIVERSITY LINZ

SENEX¹

Sensor Networks for Exploring Dementia



“Can we technically (by using unobtrusive body-worn sensor networks, for example) detect or even predict phases of confusion for people afflicted by incipient dementia?”

A clinical study on affected patients aims to explore this question and establishes a basis to develop new assistive systems to improve the life of those affected.”

Wolfgang Narzt

“Detecting a state of awareness using sensor technology will open a new window to diagnose, treat, and ensure patient safety for those who have awareness affecting diseases.”

Tim von Oertzen

Research Focus

- Attention Estimation
- Gesture Recognition
- Biosignal Analysis
- Sensor Networks
- Pattern Recognition, Classification, Prediction
- Dementia, Epilepsy

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Vision

People displaying incipient dementia can still independently manage everyday life. They often try to circumvent phases of confusion that go unnoticed by others and continue everyday tasks in public for as long as possible [1]. While we consider a lost moment at home in a sheltered environment as not too serious, being disorientated in public may have severe consequences.

Smart technical support systems could help those affected to recall their temporarily forgotten intentions on their own. These systems should be designed to react automatically, meaning without any user interaction, and provide context-sensitive assistance in the moment of confusion. Electronic reminders and to-do lists are ineffective when disoriented individual does not previously remember having created these lists or reminders.

Our focus is as follows: We want to explore whether or not it is technically feasible to automatically detect moments of confusion and quantify them. If so, which measuring method could be the best when it comes to inconspicuous use and when outside in public?

Approach

In regards to dementia, we know that episodes of confusion cannot be measured via brain waves and that other vital signs are also not conducive to support real-time recognition. We therefore focus on visually and kinetically identifiable symptoms, such as uncontrolled or abnormal body or organ movements (including repetitive head turns or rapid eye movements). We want to explore whether or not common symptoms of confusion can be mapped to behavioral patterns, classified, and we will investigate technical measuring methods supporting reliable detection (or even prediction). This includes wearable instruments (such as accelerometers or eye-tracking cameras) as well as infrastructural solutions (such as depth cameras to analyze movement patterns – keywords: attention estimation [2] / gesture, pattern or emotion recognition [3]). This project aims to design and implement various technical procedures that could recognize confusion, conduct a clinical study focusing on affected patients, and compare the measurements in terms of reliability, practical application, and economic viability. Although the challenge of developing appropriate recognition methods is difficult (because patients display distinctive and very individual symptoms), it is even harder to systematically capture moments of confusion (as these occur only randomly [4]). Thus, we are also including epileptics into the study as these patients often demonstrate an instantaneous disorientation phase following an epileptic seizure. This will allow us to methodically observe behavioral patterns during moments of mental absence.

Impact

Unobtrusive, body-worn sensors may directly impact affected patients, helping to automatically detect medical symptoms and bypass lost moments. Those experiencing a deterioration of physical activities and mental capacities do not want to lose social contact as remaining active and social can evidently help to decelerate the progress of dementia [5]. We also anticipate indirect implications in regards to the social system as the need for in-home care may be delayed due to longer patient independence. These technologies could also be applied to epileptic patients with

a focus on treatment management.

In general, the study findings will serve as a basis to continue exploring innovative, application-oriented research on medical assistive technology and develop suitable user-interfaces for context-based support systems that can react automatically in a moment of medical indication.

Competencies

Research in sensor networks, neurology and motion recognition will be represented and conducted by the following departments:

- **Department of Business Informatics – Software Engineering** with research focused on mobile systems (including sensor networks, distributed software development, and algorithmic and architectural aspects of attention estimation).
- **Department of Neurology 1** with research focused on epilepsy, transient loss of consciousness, dementia, stroke, multiple sclerosis, neuroimaging.
- **sew systems gmbh** with expertise focused on Medical and Bioinformatics, mobile and geo-information systems, and software development.

Funding

A research study as part of the FTI initiative „Mobility of the Future“(research focus „Mobility and Dementia“) 6th call, (August 2016 - July 2017), funded by the Austrian Ministry for Transport, Innovation and Technology bm:vit.

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Keywords

attention estimation, gesture recognition, biosignal analysis, sensor networks, computer-aided diagnosis, pattern recognition, dementia, epilepsy, clinical study

Membrane Channels and Transporters in Health and Disease



“The reconstitution of purified channels and carrier proteins into pure lipid bilayers offers an opportunity to investigate molecular transport mechanisms without interference by other cellular components.”

Peter Pohl

Research Focus

- Water transport by aquaporins and ion channels
- Solute and solvent transport by carriers (e.g. the sodium-glucose cotransporter)
- Function of the protein translocation channel
- Role of lateral proton migration along membranes in cellular bioenergetics

Coordinators



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Vision

The majority of all pharmaceuticals are targeted against membrane proteins. Many medications have been discovered by chance, meaning they had been in use long before their molecular mechanisms of action were identified. Both structural examinations of membrane proteins together with functional studies now give us the opportunity to design new drugs that could target individual transport steps and individual conformations of the transporter.

To this end, detailed insight into the transport mechanism is required and often obtained by closely studying the isolated membrane protein. The protein function can be made visible by adding fluorescent dyes or other markers. Assigning specific functions to protein domains or individual moieties is often accomplished by targeting functional impairment via genetic modification.

This type of interdisciplinary research is conducted by biologists, physicists, chemists, and medical researchers at two divisions of the JKU's Institute of Biophysics: (i) Molecular and Membrane Biophysics and (ii) Applied Experimental Biophysics.

Current studies of the Membrane Transport Group at the Division of Molecular and Membrane Biophysics focuses on water channels, so-called aquaporins [1], [2], ion channels [3], sodium coupled cotransporters [4], the protein translocation channel [2], [5], the characteristics of water in proteinaceous cavities [6], and the role of interfacial protons [7].

Approach

The Membrane Transport Group carries out protein overexpression in yeast and bacterial cells, followed by several purification steps and protein reconstitution into vesicular and planar lipid bilayers. Protein function is then explored by single molecule methods such as: current electrophysiological recordings, fluorescence correlation spectroscopy and fluorescence microscopy. Ensemble measurements such as scanning electrochemical microscopy, light scattering, luminescence resonance energy transfer, and particle electrophoresis are also applied. Studies of wild-type and mutant proteins go hand-in-hand to elucidate the function of protein domains and individual moieties.

We apply joint and interdisciplinary research as well as new teaching models. Ph.D. students are funded by the Austrian Science Fund (FWF) as part of the "NanoCell" graduate school. The "NanoCell" consortium includes professors from the JKU, IST Austria, and the Technical University of Vienna.

Impact

The significance of targeted drug design has increased tremendously over the past decades. Our contributions to the field include learning more about how target proteins function at the molecular level. The foreseeable, major long-term impact is to improve, patient-centered medical care.

Competencies

Research in the Membrane Transport Group is conducted by Prof. Peter Pohl from the Division of Molecular and Membrane Biophysics at the Institute of Biophysics. The following scientists are also strongly involved in this field:

- Dr. Christine Siligan: focuses on the production of wild-type and mutant recombinant membrane proteins.
- Dr. Denis Knyazev: specializes in electrophysiological investigations of reconstituted membrane proteins
- Assist. Prof. Dr. Andreas Horner concentrates on optical techniques to evaluate membrane protein function.

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Keywords

water homeostasis, aquaporins, sodium-coupled cotransporters, drug targeting, osmotic water flux, fluorescence correlation spectroscopy, electrophysiology, scanning electrochemical microscopy, wide-field and confocal fluorescence imaging

Wireless Communication Networks



“... the 5G network is expected to support over 50 billion connected devices by the end of the decade. One industry that will benefit substantially from this growth is healthcare, where we can expect a new generation of wearables for tracking heart health and fitness, diagnostics for proactive patient care, powerful data analytics and more. ...”

Bob Rogers,
Chief Data Scientist at Intel Corp.

Research Focus

- 5G communication transceiver RF-ICs
- Wireless sensor and body-centric networks
- Remote sensing and remote operation
- Functional electrical stimulation therapy

Coordinators



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Vision

The acronym 5G (fifth generation of wireless networks) refers to the next step in the evolution of communication technology beyond 3G (UMTS) and 4G (LTE). The anticipated, outstanding properties of 5G in the areas of large data rate (Gigabit-per-second range), low latency, large area multi-device coverage, low-power operation, and enhanced mobile broadband services will be highly applicable to future massive machine type communications such as medical technologies [1]. For example, advanced medical instruments will be operated wirelessly and remotely around the world by highly skilled and experienced healthcare professionals during tele-surgeries. The low-latency, high reliability, and broadband links will be provided by a flexible small cell, ultra-dense, and heterogeneous 5G mobile communication infrastructure.

Furthermore, wireless sensor and body centric networks will allow for an efficient collection of health relevant data to enable wireless patient monitoring or tele healthcare. Brain computer interfaces (BCI) can be used for therapeutic or assistive purposes at the patients' side but also to assist doctors during complex surgeries. 5G can also simply be used as data transfer link to support high quality VR video links for medical purposes.

On the technical side, designing corresponding devices is enormously challenging and often complex. As a result, research tends to focus on innovative technologies, combined radio frequency and baseband system architectures (software defined radios), and corresponding integrated circuit design methods (such as electronic design automation) to be used in creating 5G transceiver RF-IC structures.

In addition to 5G communication and data transfer, the institute also focuses on research in functional electrical stimulation (FES) to advance non-standard sensing and sensor techniques. The interface design to support communication and energy transfer to implanted sensors and actuators is the driving force behind this area of research.

Approach

We conduct interdisciplinary research on low-power 5G wireless transceivers and sensor networks, especially when these networks have medical features and need to be customized for low-power but large data-rate medical applications. Consequently, research conducted on modern RF-IC structures does not only require a strong background in system engineering, computer science, as well as mixed signal and digital signal processing techniques, but also in mechatronics. In order to successfully turn research ideas into production-ready projects and components, the institute has long-standing, successful industrial experience and strong professional relationships with leading partners in the semiconductor industry (Infineon AG subsidiary DICE Ltd. & Co KG, Intel Corporation subsidiary DMCE Ltd. & Co KG, and Austria Microsystems AG) [2,3].

Impact

The ongoing progress to develop mobile communications continues to influence our everyday lives. Soon, 5G wireless communications will open the field to a wide variety of new applications including medical treatment, video documentation, and healthcare sensing services.

From a technological perspective, creating underlying 5G wireless RF-IC transceivers will have a scientific impact on semiconductor technology, low-power RF and mm-wave circuit design methodology, energy harvesting methods, and advanced sensing techniques.

Competencies

The Institute for Integrated Circuits (IIC) provides expertise in the design and realization of integrated circuits, embedded systems, as well as cyber-physical systems. This includes modeling corresponding architectures in early stages of the design flow and their final application in integrated circuits. The institute focuses strongly on the design of low-power but high-speed analog and mixed-signal RF-IC circuits up to mm-wave frequencies for applications in 5G communication systems, wireless sensor networks (Internet of Things), and medical applications.

Competencies at the IIC are condensed at three departments:

- **The Department for Energy-Efficient Analog Circuits and Systems** focuses on the design of analog and mixed-signal circuits and systems for 5G communication with emphasis on low-power circuit techniques, radio-frequency integrated circuits, power-management, and energy harvesting
- **The Department for Medical Electronics** focuses on both base-knowledge as well as application-oriented aspects of medical technology
- **The Department for Integrated Circuit and System Design** covers the development of methods for electronic design automation of circuits and systems

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Keywords

integrated circuit design for low-power, low latency, large bandwidth radio frequency-ICs, 5G transceivers, sensor- and body-centric networks, Electronic Design Automation (EDA), power management and energy harvesting, remote sensing and operation, brain computer interface, functional electrical stimulus therapy

Industrial Mathematics and Medical Imaging



"Developing efficient algorithms for medical imaging improves diagnostic possibilities and helps both doctors and patients."

Ronny Ramlau

Research Focus

- Medical Imaging and Image Reconstruction
- Tomography (CT, MRI, SPECT, etc.) and Shape Reconstruction in Tomography
- Image Segmentation and Analysis
- Magnetic Resonance Advection Imaging

Coordinator



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Industrial Mathematics Institute

The chair for Industrial Mathematics was created at the Johannes Kepler University Linz in 1988. Under its founder and first department head, Prof. Heinz W. Engl, the institute became internationally renowned for its groundbreaking work on regularization methods, first for linear and then for nonlinear inverse and ill-posed problems which arise in medical imaging applications and in tomography. Under the current department head, Prof. Ronny Ramlau, the successful trend continues and a new branch of Adaptive Optics was added to the institute's areas of expertise. As a result, the IndMath institute can now look back on countless high-quality publications and cooperation efforts with industrial partners such as HILTI and Siemens. A strong research bond with the Johann Radon Institute of Computational and Applied Mathematics (RICAM) of the Austrian Academy of Sciences ensures IndMaths' firm foothold in both the academic and the industrial world in the future.

Medical Imaging and Tomography

As mentioned above, inverse and ill-posed problems arising in medical applications require special treatment. Image denoising, edge detection and resolution enhancement are classic examples of the types of problems that can be tackled using algorithms designed or improved by members of the IndMath institute. Examples of ill-posed problems with the greatest medical importance by far are the various tomography methods such as Computerized Tomography (CT), Magnetic Resonance Imaging (MRI) and Single Photon Emission Computerized Tomography (SPECT).

While many general algorithms applicable to all of the above problems were developed and analyzed thoroughly by members of the IndMath institute in the past, more recently the SPECT and the CT problem in particular have attracted considerable attention. Efficient and robust algorithms for reconstructing images from noisy measurement data are being designed and a strong focus is placed on high-quality and sparse reconstructions [1].

The IndMath institute also focuses on application problems such as extracting additional information from tomographic images. For example, in cooperation with the UKH Linz, the institute was provided with CT data and tasked with accurately and automatically detecting the border of the human lungs in order to facilitate the treatment of patients who have collapsed lungs. Our cooperation with the UKH will expand to automatically classify heel bone fractures via reconstructed CT images.

Whereas reconstructing a tomographic image from measured data and retrieving information from the image was usually a two consecutive step procedure, it has recently become popular to combine these two problems into one, leading to so-called Mumford-Shah type methods. Here, the aim is to compute an image of an object's interior as well its set of discontinuities (e.g., the boundaries of inner organs) [2,3]. As existing scanning devices are improved and new ones are developed, extending research in this direction will prove very valuable for both the IndMath institute and medical professionals.

Finally, a collaboration effort between the Industrial Mathematics Institute, the Doctoral Program "Computational Mathematics" in Linz and the Weill Cornell Medical College,

Manhattan, New York, in the development of Magnetic Resonance Advection Imaging (MRAI), a method for estimating the velocity of the pulse wave in the brain from MRI data, will explore new ground [4]. As this velocity is a reliable prognostic marker for cardiovascular morbidity and mortality - and hence also correlated to cognitive decline - many possible applications are conceivable and are indeed the goal of future research in this area.

In cooperation with the Medical University of Vienna, there are further plans to extend our expertise in Adaptive Optics towards Retina Imaging.

Impact

Based on a unique combination of profound theoretical knowledge and practical experience, the IndMath institute has become an ideal partner to improve existing solutions and create innovative solutions, methods, and algorithms to address problems in medical imaging, tomography and beyond.

Competencies

Research in medical imaging, inverse problems and tomography will be represented and conducted by the following departments:

- **Industrial Mathematics Institute** with research focused on medical imaging, tomography, shape reconstruction, image segmentation and development and analysis of algorithms.
- **Doctoral Program "Computational Mathematics"** with research focused on MRAI and efficient solution methods.
- **Johann Radon Institute for Computational and Applied Mathematics (RICAM), Austrian Academy of Sciences**, focused on medical imaging, Adaptive Optics, Tomography

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Keywords

medical imaging, image reconstruction, inverse problems, tomography, shape reconstruction, sparse recovery, image segmentation, Magnetic Resonance Advection Imaging (MRAI)

Institute for the Rights of Basic Social Care and Health Care Law, Johannes Kepler University Linz



“Medical law is an indispensable part of a clinical physician’s working environment.”

Reinhard Resch

Research Focus

- Our institute provides a foundational understanding of core issues in the field of medical law and conducts interdisciplinary research
- Our multifaceted courses in “Medical Law” are designed for legal and healthcare professionals to help expand on their current level of knowledge and expertise in law and medicine
- Courses in “Medical Law” have been incorporated into the curriculum at the JKU School of Medicine
- The “Recht am See” conference, for example, gives legal and healthcare professionals a structured atmosphere to address and discuss current and pressing medically-related issues in the legal system

Coordinator



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Vision

Medical law is an indispensable part of a clinical physician's working environment. We aim to provide both aspiring and professional physicians with a deeper understanding of specific issues in medical law and health sciences. In turn, an increasing number of legal professionals find themselves addressing cases and issues related to the medical field. Our courses facilitate a further understanding of these intersections between medicine and law for both faculties. Physicians acquire a more in-depth, meaningful understanding of legal issues in the scope of their professional activities and legal professionals learn to approach the medical influence in our judicial system with more awareness.

Approach

Our courses target medical students, providing them with a skilled understanding of the realities surrounding legal practices and the issues involving the medical system. The course "Medical Law" has been designed for students of medicine.

Students also conduct research designed to provide an in-depth, holistic look at legal issues. The institute has the educational capacity to teach courses focusing on legal issues pertaining to medical law.

We not only provide a post-graduate degree program for legal professionals and physicians, we also assist professionals addressing real-world issues in medical law.

Our institute also organizes conferences that give experts in law and medicine an opportunity to discuss the complex interactions of certain subject areas in law and medicine. Taking part in the "Recht am See" conference allows participants to professionally target and debate the legal context of medical law and raise awareness on a wide range of medical and legal subjects.

Impact

Because the fields of legal and medical sciences are closely linked, an increasing number of professionals in both law and healthcare have expressed a strong interest in approaching and understanding topics in law and medical science from the other side. Clinical physicians and legal professionals well-trained in their own respective fields have a unique opportunity to come together and explore these issues from different perspectives. Today, there are many complex concerns and repercussions in the field of medical law and new issues and challenges loom on the horizon. Our approach includes providing high quality education and conducting high-value research.

Organizing Institute

Institute for the Rights of Basic Social Care and Health Care Law, Johannes Kepler University, Linz.

www.jku.at/sdmr/content

Keywords

medical law, interdisciplinary discourse

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Sperm Fertility and Calcium Signaling



“Calcium signaling is a key process in cell communication, including sperm competition for fertilization”

Christoph Romanin

Research Focus

- Improving Sperm Fertility
- Sperm activity related to Ca²⁺
- Ca²⁺ currents and Ca²⁺ imaging of sperm
- Sperm capacitation
- Fertilization and development
- Single molecule DNA analysis
- DNA epigenetics

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The last steps in sperm maturation include changes in the sperm membrane occurring after ejaculation in the female reproductive tract. These changes are mainly in the membrane permeability with an increase in intracellular Ca^{2+} that endows the mammalian sperm with fertilizing capacity, known as capacitation [1], [2]. At the molecular level, capacitation involves a series of signal transduction events, including hyperpolarization of the sperm plasma membrane and changes of ion permeability. Specifically, large numbers of calcium ions enter the sperm via a channel called CatSper, one of the most complex ion channel known, and found only in sperm [3], [4]. Once the calcium ions enter the tail, they initiate an unknown and seemingly complex cascade of phosphorylation events that result in the hyperactivated sperm motility that is an essential prerequisite for successful fertilization [3], [5]. If any of the CatSper genes is faulty, mice or men are infertile. In vivo, capacitation of sperm occurs in the Fallopian tubes where the motility facilitates passage of the sperm to the outer shells of the oocyte. In intracytoplasmic sperm injection (ICSI), several of these steps are circumvented since the male gamete is directly injected into the cytoplasm of the egg.

Although, the different molecular events occurring during capacitation and fertilization have been studied independently, our understanding how they interconnect and the exact outcome is still limited, including the downstream changes in the epigenetic packaging and integrity of the genetic information. Especially, sperm from older men or infertile men (particularly ICSI patients) could be associated with deficient transduction of signaling cascades leading to a higher number of aberrant DNA changes or DNA fragmentation. In order to address these questions, we have combined the expertise from 3 different fields: Ca^{2+} signaling in single cells, DNA analysis at the single molecule level, and IVF methodologies and assessment of sperm quality.

Approach

Here we want to examine the correlation of molecular events occurring during sperm capacitation at the level of calcium signaling and DNA modifications in individual sperm. Specifically, we want to correlate sperm motility with calcium signaling and the downstream DNA modifications in individual sperm cells. Our understanding of Ca^{2+} signaling in sperm has been greatly improved as a result of patch clamp experiments in which glass electrodes provide researchers with electrical control over the membranes of individual sperm cells and access to the interiors of these cells [6]. Patch clamp can also be applied to single sperm selected by means of a Zech chamber [7] into fast and slow moving sperm. Then, the DNA of individually screened sperm will be assessed in terms of their DNAase hypersensitivity, epigenetic modifications, and accumulation of mutations at genes controlling tyrosine signaling cascades. The combination of our different competences and methodologies will allow us to analyze the key players in the steps necessary to prepare the sperm for fertilization.

Impact

Understanding what factors control fertility of sperm is important for future development of in vitro fertilization techniques. Moreover, an evaluation of how sperm quality, motility, and age correlate with downstream factors influencing the integrity of our DNA might be very valuable to improve the quality of assisted fertilization. In addition to joint and interdisciplinary research, new teaching models will be also approached in facilities at the Kepler University Med Campus.

Competencies

Research in sperm fertility will be represented and conducted by the following departments:

- **Ion Channel Group, Institute of Biophysics, JKU** with research focused on the Ca^{2+} signaling by techniques ranging from Ca^{2+} imaging to Ca^{2+} electrophysiology.
- **Single Molecule Genetics Group, Institute of Biophysics, JKU** with research focused on the analysis of single molecule DNA to experimentally measure changes in our genetic information.
- **Department of Gynecology, Obstetrics, and Gynecological Endocrinology, KUK** with research focused on the fertilization and sperm and egg quality for effective embryonic development.

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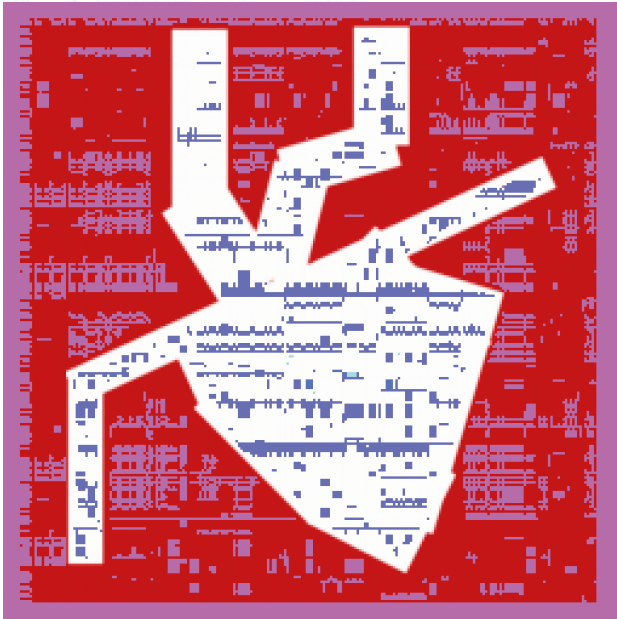
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Keywords

sperm fertility, Ca^{2+} signaling of sperm, sperm electrophysiology, sperm Ca^{2+} imaging, sperm Ca^{2+} -mediated downstream signaling, patch-clamp, fluorescence microscopy, sperm capacitation, DNA epigenetic modification, DNA fragmentation

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Medical Device Security



“Healthcare poses security challenges due to the sensitivity of health records, the increasing interoperability of medical devices, and simply the fact that human well-being and life are at stake.”

Johannes Sametinger et al.

Research Focus

- Medical device security
- Cardiac pacemaker security
- Threat resilience
- Hardware/software co-design for secure device architectures

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Vision

On several occasions, security experts have been able to successfully hack medical devices. For example, commands were sent wirelessly to insulin pumps (to raise or lower insulin levels) and disable these pumps from within a distance of up to 50 meters. Security attacks and defenses were shown for diabetes therapy systems. While we have not yet read about any resulting deaths or injuries, the hypothetical ramifications cannot be ruled out. The non-medical IT landscape can also pose a threat to medical operations. For example, when computers around the world came to a halt after an antivirus program identified a normal Windows file as a virus, hospitals had to postpone elective surgeries and stop treating non-critical patients in emergency rooms. Medical devices are unique, but cybersecurity threats to medical device security are similar to those that threaten other software-controlled devices that are connected to networks.

Information Technology (IT) security is essential for any business or organization, including healthcare. This sector poses additional challenges due to the sensitivity of health records, the increasing interoperability of medical devices, and simply the fact that human well-being and life are at stake. Implantable devices are especially critical as they may potentially put patients in life-threatening situations when not properly secured. Medical devices are becoming noticeably important for millions of patients worldwide. Their growing dependence on software and interoperability with other devices via wireless communication and via the Internet increasingly puts security at the forefront [3]. Medical security requires new methods of design and engineering so that devices continue to function correctly under malicious attacks.

Approach

The FDA has expressed concerns for the safety and security of medical devices and is attempting to quantify the level of such concerns. It is a measure referring “to an estimate of the severity of injury that a device could permit or inflict, either directly or indirectly, on a patient or operator as a result of device failures, design flaws, or simply by virtue of employing the device for its intended use”. The FDA’s severity of injury makes a distinction between death, minor and serious injury. In addition to device impact, we also suggest considering whether or not the devices store and process sensitive information and how much the device has been exposed to its environment. We propose a level of concern for medical devices based on whether or not they process or communicate sensitive information, whether or not they process or communicate safety-critical information, and how exposed they are to their environment [1].

There are several reasons that prohibit patching any medical device as we do with general purpose computers. First, regulations often hinder device manufacturers from rolling out new versions without new certification. Second, these devices typically do not provide an automatic update mechanism that per se would increase the device’s attack surface. Third, updates may require a system to reboot. This is typically okay for regular PCs, but definitely not for cardiac pacemakers, for example, that are currently in use. Our approach regarding medical devices is to reduce sensitivity, impact and exposure as well as to increase

authentication measures in specific circumstances in order to reduce security risks. We can achieve these kinds of measures via rigorous modelling and analysis [2, 4] as well as via hardware/software co-designs. Hardware security technology incorporated into processors cover memory and peripherals and provide security extensions for additional countermeasures against malicious attacks.

Impact

Medical devices are indispensable for millions of patients worldwide. They increasingly depend on software and hardware components, and interoperate with other devices wirelessly and through the Internet. Additionally, we see an increased use of mobile medical applications in connection with a plethora of medical sensors still to come. The sensitive nature of health records, the increasing interoperability of medical devices, and the fact that human well-being and life are at stake, puts medical device security at the forefront in healthcare technology [3].

Competencies

Research in medical device security is represented and conducted by the following departments:

- **JKU - Department of Business Informatics – Software Engineering** with research focused on software security, medical device security, security scoring, and risk assessment.
- **KUK - Cardiology** with research focused on cardiac pacemakers, e.g., laser-induced modification of a pacemaker’s surface texture as well as the cell population of the titanium coating.
- **UofA – Electrical and Computer Engineering/ Surgery** with research focused on design and analysis of complex systems, embedded systems design, hardware/software co-design, and healthcare simulation.

Additional medical partners include the Medical Center of the University of Arizona and the Elisabethinen Linz.

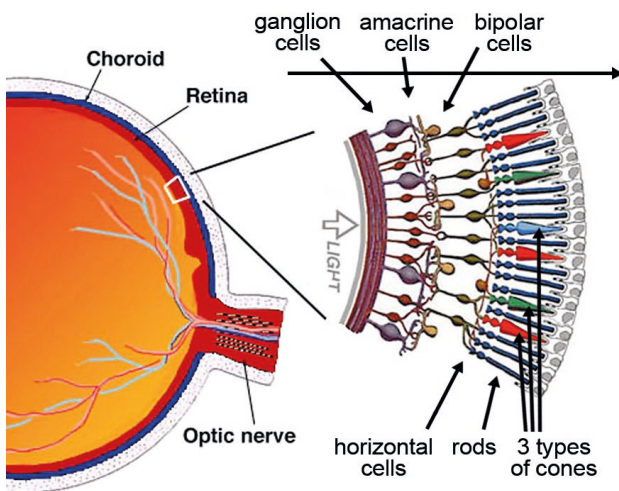
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Keywords

medical devices, cardiac pacemakers, security, security risk, sensitivity, impact, exposure, safety, vulnerability

Artificial Retina



“Human vision is based on molecular photo-receptors which are also found and used in organic photodetectors and organic photovoltaic solar cells. Why don't we use this knowledge at the JKU to fabricate an artificial retina?”

Niyazi Serdar Sariciftci

Research Focus

- Organic photoreceptor materials
- Fabrication of photodiodes
- Biocompatibility tests of these materials
- In vitro photo bioactivity tests (in collaboration with Prof. Yael Hanein in Israel)
- In vivo implantation tests (in clinical stadium)

Coordinators



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Vision

By creating an artificial retina, our collaboration aims to restore human eyesight for user-friendly technology. The artificial retina will be based on organic and bio-organic semiconductors and photodiodes.

The Linz Institute for Organic Solar Cells (LIOS) at the Johannes Kepler University (JKU) has many years of experience in the field of research on organic solar cells and organic photovoltaic elements. Its researchers are experts at the highest international level. The Center for Innovative Methods of Visual Rehabilitation at the Kepler University Hospital has a strong interdisciplinary group that specializes in problems pertaining to the human retina.

LIOS is also already internationally involved in making organic photovoltaic materials research available for the artificial retina. The materials used in organic photovoltaic cells and photodetectors are similar to the photoreceptors found in the retina. If successful, these materials can readily be developed into an artificial diode array which then can be surgically implanted in the patient at the Kepler University Hospital in Linz. This kind of implantation expertise can be developed by Kepler Universitätsklinikum ophthalmic clinic in accordance with newly developed organic photodiode arrays. As a result, the Kepler University Hospital will have enormous site advantage.

Impact

There have been recent, great worldwide efforts to develop medical technology that could restore human sight. These kinds of new technologies require new materials and new devices. The JKU has the material science of organic photoreceptors as well as an interdisciplinary center for ophthalmology, both of which have been very successful over the past few years. The end results of the artificial retina project will be to bring the various fields of expertise together – from materials science and surgical implantation to patient rehabilitation - at a globally recognized center specializing in artificial retina implants. The site advantage would be unparalleled, helping the JKU to establish a competitive advantage in medical technology.

Competencies

- **The Linz Institute for Organic Solar Cells (LIOS)** is ranked as one of the most cited groups (#14) worldwide among material scientists (ISI Thompson ranking 2010) and is a pioneering center for organic semiconductors and organic solar cells. Prof. Sariciftci is the inventor of bulk heterojunction solar cells, based on organic photodiodes.
- **The Department of Ophthalmology** at KUK has a strong interdisciplinary group specializing in problems pertaining to the human retina. The highly regarded department is internationally renowned and active in clinical and academic programs.

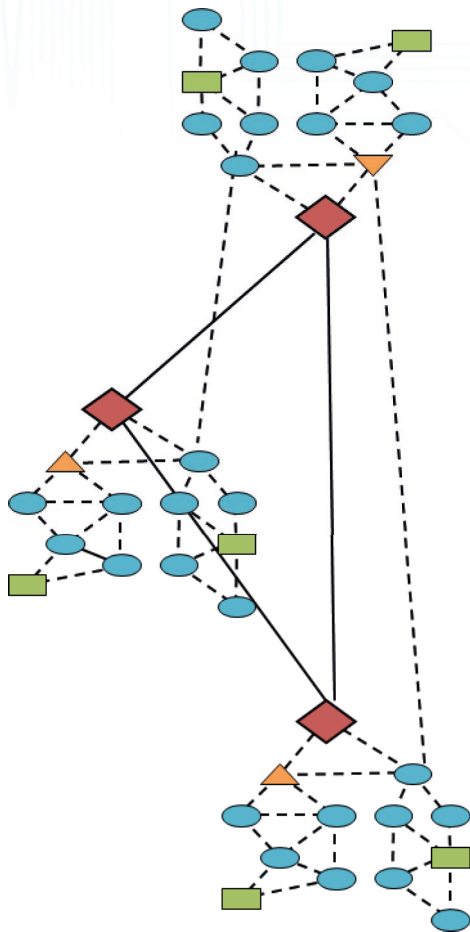
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Keywords

artificial retina, photoreceptors, human vision restoration, organic photodiodes, bioorganic semiconductors

Formation and Governance of Innovation Clusters: Regional and Transregional Network Dynamics



“Regional clusters thrive when organizations that are spatially co-located form networks, and when these kinds of inter-organizational networks also span across the cluster’s boundaries.”

Elke Schüßler

Research Focus

- Technical, social and cultural innovation in cities, clusters and regions
- New forms of value creation at the interface of different clusters (“cross-clustering”)
- Interorganizational networks in and across clusters
- Governance of clusters and cluster networks
- Innovation ecologies

Coordinators



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Vision

In an early study on innovation dynamics in the life sciences, a group of North American scholars concluded that interorganizational networks rather than individual firms are the locus of innovation [1]. The underlying argument is that in fields characterized by rapid development as well as sophisticated and dispersed knowledge, no single organization is equipped with the skills necessary for breakthrough innovations. These kinds of networks are commonly spatially concentrated in so-called regional clusters, defined as agglomerations of “interconnected companies, specialized suppliers, service providers, firms in related industries, and associated industries in a particular field that compete but also co-operate” [2]. These clusters contribute to an increasingly spiky economic landscape, marked by income and education differences between booming and struggling regions [3].

Several life science clusters have emerged in Europe, including the BioCon Valley in Mecklenburg-Vorpommern, the Medical Valley in the Nürnberg region, and the Medicon Valley in Southern Denmark and Sweden. Clusters, however, are not isolated islands. The Israeli biotech and medical technology industry has close links to Silicon Valley, forming a globally dispersed “super-cluster of innovation” [4]. Likewise, the ScanBalt Bioregion is a network of life science clusters located near the Baltic Sea, having established a formal cross-cluster governance body to foster the emergence of cross-cluster ties so as to increase global competitiveness.

Research at the Institute of Organization and Global Management Education aims to understand how clusters and cross-cluster relationships form, and how they can effectively be governed, meaning how it can be ensured that actors engage in collective and supportive action, that conflict is addressed, and that network resources are acquired and utilized efficiently and effectively [5].

With regard to the emerging Medical Valley in Upper Austria, the following aspects appear to be important for success: (a) identifying a strong anchor tenant (i.e. a central organization, well-connected to diverse actors); (b) establishing appropriate governance structures and mechanisms to facilitate the formation of networks among individual and organizational actors; (c) getting firms or entrepreneurs to take on a leadership role, supporting more formal institutions in setting goals, brokering ties, or forming a common culture or identity from the bottom up; (d) attending to clusters’ propensity for path dependency (i.e. self-reinforcing both beneficial network effects and potentially negative lock-ins); (e) stimulating positive public discourse that draws attention to the region and inspires innovative initiatives; (f) establishing links beyond the Medical Valley itself: to other clusters in Upper Austria, to other Austrian regions, and to life science clusters in Europe and across the globe [6, 7].

Approach

Our research is conducted in the form of externally funded research projects and utilizes qualitative as well as quantitative data to assess the following factors:

- *Input-oriented*, such as the kinds of activities and measures initiated to support networking and cluster-building
- *Intermediary*, such as the development of relationships

and networks in the region and beyond

- *Output-oriented*, such as value creation, firm foundation or rise in employment opportunities

Impact

By feeding back the results of our analyses to cluster actors and policy makers, cluster development processes can be designed and, possibly, redirected. We also make our students aware of the importance of managing interorganizational relationships, in clusters and beyond.

Competencies

The Institute of Organization and Global Management Education has a broad knowledge of intra-organizational and inter-organizational dynamics and is familiar with a variety of social science research methods. Our expertise on clusters is currently applied in the context of two research projects:

- *Organized Creativity*, an international Research Unit funded by the German Science Foundation to understand how creative processes are organized on different levels in the music and pharma industries.
- *Innovationsstadt Linz*, a three-year project supported by the city of Linz aimed at mapping innovative initiatives and achievements in the Greater Linz area, identifying and explaining the conditions that enable and constrain innovation in the region, and developing policy implications.

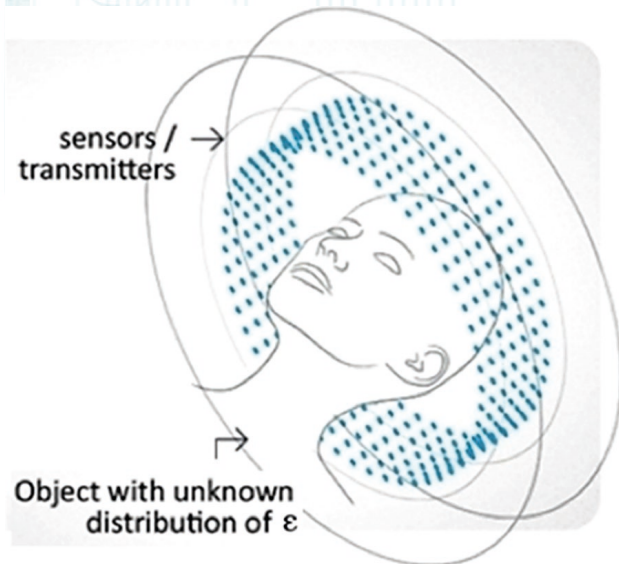
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Keywords

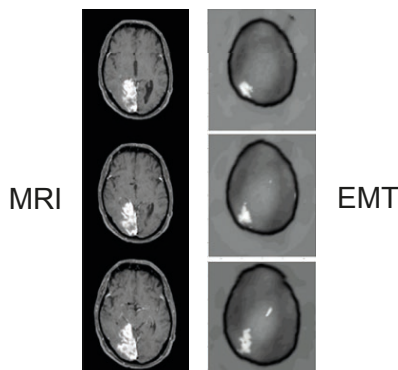
clusters, cities, cross-clustering, organizations, networks, governance, innovation, creativity, life sciences

Electromagnetic Tomography for Brain Imaging



“The “tricorder” from the Star Trek series has inspired generations, able to sense unseen health conditions not visible to humans. Nowadays, electromagnetic waves support functional imaging, making fiction reality by allowing us to look into the brain and obtain a fast diagnosis of acute stroke.”

Andreas Stelzer



Research Focus

- Microwave and mm-wave electro-magnetic sensing in the frequency range from 300 MHz to 0.3 THz
- Electromagnetic tomography systems and their integration
- Electromagnetic tomography for medical diagnosis and monitoring
- Electromagnetic image reconstruction algorithms and implementation
- Clinical studies on electromagnetic tomography for acute stroke monitoring

Coordinators



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Vision

In the event of an acute stroke, reducing the time between the stroke and receiving treatment is the only way to prevent brain cells from dying off due to ischemia. Innovative and flexible diagnostic methods applied directly in an ambulance or at the patient's home in a timely manner could prove to be life-saving, especially to administer medication. Electromagnetic Tomography (EMT) is an innovative technique featuring appealing properties that can complement classical imaging methods for diagnosis. Medical imaging, such as ultrasound, conventional X-rays, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), are widely used and have become indispensable part of the diagnostic process. The image quality, especially from the latter, is beyond question. These applications, however, can be costly, bulky to use, and require safety measures, such protection against X-rays or strong magnetic fields. They are hardly a choice when it comes to creating a mobile or personal medical device. Electromagnetic tomography, unlike X-rays, is based on non-ionizing electromagnetic waves in the Gigahertz (GHz) frequency range, which use lower power levels than that of a mobile phone and are therefore considered inherently safe. In contrast to existing methods that mainly visualize differences in the material and proton density, electromagnetic imaging analyzes electrical properties, mainly permittivity. This makes it suitable to, for example, characterize tissue properties or determine blood content, blood oxygenation and ischemia because these parameters map to permittivity, resulting in a detectable contrast. Current applications for EMT are to detect malignant tissue [1] or a stroke [2].

Another benefit of EMT includes the possibility of creating a small, portable measurement device. Electromagnetic waves can be generated using Monolithic Microwave Integrated Circuits (MMICs). Mechanical movement for scans can be substituted by using a stationary application of hundreds of low-cost chips. This will create a type of innovative mobile diagnostic device that can be used to examine a patient being transported to the hospital. The hospital personnel will have the EMT results even before the ambulance arrives, thereby reducing the time between diagnoses and administering medication.

Approach

Basic measurement principles, and thus a proof of concept, can be demonstrated by using commercially available microwave measurement equipment, such as a vector network analyzer. Vector network analyzers are more compact than the equipment required for MRI or CT scans, but they are still far too bulky to be used as a compact, portable medical device. Additional drawbacks include the limited number of measurement ports, which require additional hardware to support the time consuming switching between the large number of antennas used in a massive MIMO configuration.

We are currently exploring how to create a new, innovative system designed specifically to meet the needs of a compact imaging system. The device must contain hundreds of perfectly synchronized RF-sensors and conduct measurements in parallel to decrease measuring times, which is important to, for example, measure synchronized to heart beats. A major challenge in applying

brain imaging is the fact that the electromagnetic wave is attenuated by approximately 100 dB when going through a human head. Thus, we need to operate the device close to physical noise levels but still maintain high precision.

Reconstructing the image is a rather complex process. First, EM waves are scattered in all directions, meaning there is no straight single line being illuminated. Second, due to the limited, finite number of antennas, the total number of MIMO measurements is several magnitudes of orders lower than the number of desired reconstructed voxels. As a result, reconstructing EM data leads to a nonlinear and heavily under-determined problem. Consequently, we are considering different iterative solutions with given constraints. Having a reliable and fast converging signal processing strategy is important, especially for medical diagnostic applications. The number of voxels is a tradeoff between signal-frequency and number of antennas in which the frequency is limited by a decreasing penetration depth for decreasing wavelengths. Also, the number of antennas is limited by size, which is inversely proportional to the frequency.

Impact

Microwave imaging used for medical applications is advantageous as it is non-invasive, meaning there is less physical risk to patients and it can be applied with fewer restrictions, e.g. allowing long-term monitoring of a patient's healing process. Being able to create portable measurement instruments will lead to a new generation of diagnostic devices which could drastically reduce the treatment time between having a stroke, diagnosis, and administering medication. Electromagnetic tomography has the potential to become indispensable, life-saving technology.

Competencies

- **Department of RF-Systems:** RF Sensor system concept, hardware design, raw data signal processing and integration
- **EMTensor GmbH:** Imaging algorithm and medical device development
- **Clinic of Neurology 2, Med Campus III:** Clinical trials and medical supervision

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Keywords

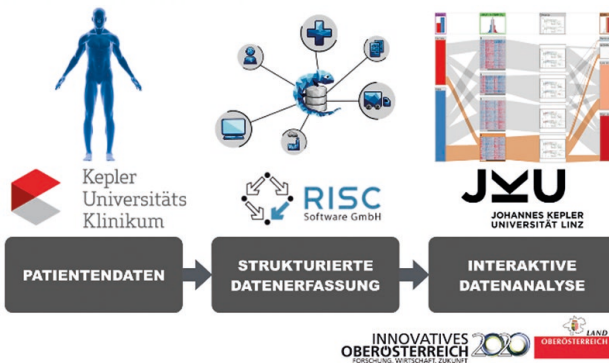
electromagnetic tomography, brain imaging, stroke detection, microwave imaging, RF-System, Massive MIMO Sensor

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TourGuide

Navigation System for Capturing and Analyzing Complex Clinical Data



“Big Data is like teenage sex: everyone talks about it, nobody really knows how to do it, everyone thinks everyone else is doing it, so everyone claims they are doing it.”

Dan Ariely

Research Focus

- Interactive data visualization
- Data handling and processing
- Guidance for medical researchers
- Uncover hidden patterns in complex data

Coordinators



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Vision

Medical researchers face a rapidly growing amount of data, both on an overall level as well as on an individual patient level. Navigating this maze of increasingly complex and heterogeneous data is a challenge, resulting in a situation that often leaves medical researchers overwhelmed [1]. In an effort to address the problem, data acquisition, handling, and analysis is delegated to computer science specialists who, in turn, lack the biomedical expertise necessary to adequately deal with the research questions [2, 3].

The TourGuide project aims to create a system that helps lead the biomedical researcher to find relevant information focal points and successfully navigate through the vast amounts of data. We combine interactive data visualization techniques with a generic medical research platform. The integrative research platform spans the process of knowledge discovery ranging from data modeling, acquisition, and handling, all the way to interactive visual data analysis.

Approach

TourGuide gives biomedical experts an opportunity to visually explore clinical datasets and identify patterns and correlations.

As part of the project, we visually analyze data provided to us by the Kepler University Hospital's tumor database. This data contains clinical information about patients who have malignant diseases and are being treated at the Kepler University Hospital. The clinical dataset includes information such as diagnosis, treatment, laboratory results, and demographics. The dataset is comprised of information provided by 5,300 patients. 2,700 of those patients are aged 65+.

Data will be transferred to the CALUMMA framework, an ontology-based data infrastructure which supports data acquisition, integration, validation, and analytics.

The Institute of Computer Graphics at the Johannes Kepler University contributes innovative visual analysis techniques that are developed as part of the Caleydo project (<http://caleydo.org>, [4, 5]), which is a long running collaboration between the Graz University of Technology, Harvard University, and the University of Utah. Based on interactive visualizations and suggestions provided by the Caleydo framework, researchers can then decide which findings warrant closer examination.

Impact

TourGuide will be a navigational system used to actively guide medical researchers through analysis procedures. The human analyst at the center of the knowledge discovery process will be able to sift through vast amounts of data to search, identify and validate patterns. In turn, this will lead to improving our medical knowledge as to the cause of diseases, what impact therapies and treatments have, and patient survival, particularly in regards to older patients who tend to be under-represented in current clinical trials.

Competencies

Research in the TourGuide project is conducted by the following partners:

- **Institute of Computer Graphics**, JKU Linz provides expertise in the interactive data visualization of large and complex data.
- **Research Unit Medical Informatics, RISC Software GmbH** has research and practical experience in data acquisition, handling, validation and analytics. RISC has developed the CALUMMA framework which is actively used in a number of research projects [6].
- **Department of Internal Medicine 3, Kepler University Hospital** is an established cancer center with experience in biomedical research.

Acknowledgements

The TourGuide project (FFG Project Number 851460) is supported by the State of Upper Austria as part of the Innovative OÖ2020 Call.

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Keywords

Interactive data visualization, data processing, data integration, oncology, breast cancer, geriatric oncology

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Age-Induced Mutagenesis in the Male Germline



“The highly sensitive measurement of changes in our genetic information gives us an unprecedented insight into the processes driving mutagenesis”
Irene Tiemann-Boege

Research Focus

- Ultrasensitive sequencing technology
- Genetic changes in the male germline
- Mutagenesis
- Genetic factors of sterility
- Fertilization and development

Coordinators



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Austrian Red Cross (Blood Center)

Vision

New point mutations are transmitted mainly by the father (~80%). Moreover, children from older fathers carry more mutations than offspring from younger ones, and it was estimated that the paternal genome gains two new mutations every year in the life of a man [1-3]. Most of these mutations might be harmless, but some of these paternally transmitted mutations are highly recurrent with a mutation rate ~1000x higher than genome average and cause congenital disorders. These mutations have been associated with skeletal dysplasias, they occur exclusively in the male germline and older men have a higher probability of having an affected child than younger ones, known as the paternal age-effect (PAE) [4,5]. The mechanisms propagating these mutations are not well understood, but all of these mutations affect a cellular signaling cascade (RAS/MAPK) that confers the male stem cells in the testis (spermatogonial stem cells) a proliferative advantage, such that more mutant sperm is produced in older men [5-7]. These mutations have been called “selfish” or “driver” mutations since the mutation itself, by a change in the gene product, causes its self-propagation [5]. In cancer genetics, these driver mutations have also been identified in somatic tissue [8]. Given the replicative nature of the male germline throughout the lifetime of men, it is possible that driver mutations could be an important mutagenic mechanism affecting a range of different disease-causing genes that expand with the paternal age.

Approach

So far, our understanding of mutagenic processes in our germline is still very limited given the technical difficulty of measuring rare mutations. The Single Molecule Genetics group at the Johannes Kepler University has developed a highly sensitive in-house approach to measure rare mutations. Our methods count rare known mutations at a very high sensitivity by amplifying millions of single DNA molecules in an emulsion on microscopic beads. An additional ultrasensitive sequencing technology is being developed to complement the existing methods and discover unknown rare mutations. The two methods provide a very powerful combination to assess the mutation expansion patterns in the male germline. In collaboration with the Kinderwunschzentrum of the Kepler Universitätsklinikum, semen samples of different aged-donors are analyzed.

Impact

Given that parenthood is delayed in our society (also with the help of in vitro fertilization), the question of the risk of transmitting more mutations is of high relevance in these times. Although, it is well known that the maternal age plays an important role in chromosomal aberrations, with the results of this research, the age of the male might also become also a concern when taking the decision for conception.

From the technological standpoint, the analysis of rare mutations by ultrasensitive measurements have been relevant in a range of diverse fields such as cancer research to understand tumor development, evolutionary biology to study mutagenesis, and epidemiology to assess the expansion of new mutations with paternal age, just to mention a few. Ultrasensitive technologies are of high interest, and are becoming standard in precision medicine.

Competencies

Research in mutagenesis, fertility, and sequencing is represented and conducted by the following departments:

- **Single Molecule Genetics** with research focused on the analysis of mutagenic events in our germline and the development of highly specialized expertise and techniques to experimentally measure changes in our genetic information.
- **Department of Gynecology, IVF clinic** with research focused on the fertilization and sperm and egg quality for effective embryonic development.
- **Sequencing Facility, Kepler Universitätsklinikum** with research focused on next generation sequencing applications.

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Keywords

aging in the male germline, paternal age effect, mutagenesis, sperm quality, driver mutations, ultrasensitive sequencing methods

Legal Issues of Research in Medicine Technology Affecting People and the Environment



“The development of technologies in medicine and in the medical field must be based on a solid legal framework in order to guarantee the best possible outcome for everyone involved. According to the precautionary principle, rest risks must be excluded as much as possible.”

Erika M. Wagner

Research Focus

- Liability for and rest risk of medical technologies and developments
- Product liability for medicine, medical devices and chemicals
- Legal issues of biotechnology and genetic engineering
- Legal issues of organ transplantations
- Poisonous substances found in the home and environmental pollutants as challenge for technology

Coordinators



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Vision

The development of technologies in medicine and in the medical field must be based on a solid legal framework in order to guarantee the best possible outcome for everyone involved (doctors, patients, entrepreneurs and scientists). While creating new technologies can save lives and improve the quality of life, new technologies (organ transplantations [1], biotechnological procedures, etc.) can also pose a risk to both people and the environment and the risk is often unforeseen.

When it comes to advancements in medical technologies and risk, finding solid answers to address liability issues and potential risk is absolutely necessary as there are many grey areas when it comes to product liability, especially medicine, medical devices, and chemicals. Advancements in organ transplant procedures can open the door to countless legal issues pertaining to the personal rights of both organ donors and organ recipients. There are still disputes as to where the ethical limits of new biotechnological processes can be drawn and if applying legal bans are justified [2].

Law must keep pace with advancements in medicine and technology! Medical technology also does not focus enough on preventative healthcare in an effort to reduce exposure to toxic chemicals and poisonous substances presently found in many homes as well as toxic environmental pollutants (such as pesticides, antibiotics and cytostatics) that are currently affecting many people's health [3].

Creating effective health policies in lieu of advancements in environmental technologies will be one of the century's greatest challenges.

Approach

New technologies come with new legal challenges and considering the precautionary principle is unavoidable, especially when the cause-effect relations have not been resolved.

There are implications in material law: Juridical norms (norms of material-juridical nature as well as laws concerning burden of proof) then go back to the results pertaining to risk assessment on the dangers. In lieu of unpredictable and potentially occurring damages, new tools are necessary in order to address and close any gaps in the causal chain. Applying causality suppositions in particular and addressing the divisions pertaining to burden of proof (which takes uncertainty into account) must be demanded. In the end, we have to ask who is to be held accountable: the public because bearing the brunt of risk and danger makes technological advancement possible, or the manufacturers of the technology, or the individual user of the technology in question. Faculty members at the Institute for Environmental Law have successfully published numerous books and articles on these topics as part of the institute's commitment to conducting strong base-knowledge research. In addition, the Institute of Environmental Law contributes to the education of medical students and law students by offering several courses designed to address these questions and tackle complex issues. We are also working together with environmental experts as part of an interdisciplinary working group in the field of environmental medicine. An interdisciplinary base

is necessary in order to zero in on the legal implications when it comes to developments in medicine and medical technology: An interdisciplinary working group featuring experts and engineers should commit itself to addressing these challenges.

Impact

This approach can facilitate advancements in medicine and medical technology as well as guarantee a high degree of legal safeguards. The subsequent effect could greatly improve the social welfare of everyone involved, especially patients and medical technology companies.

Competencies

Research on legal issues regarding medical technology affecting people and the environment is conducted by Univ. Prof. Dr. *Erika M. Wagner's team* at the Institute for Environmental Law and at the Institute for Civil Law.

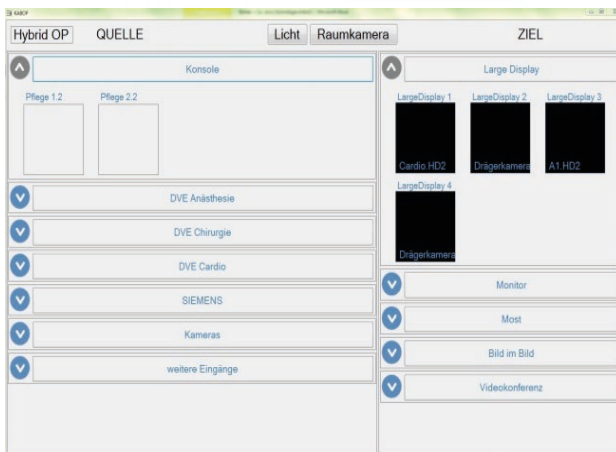
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Keywords

liability law, product law, drug law, law on chemicals, law on medical devices, law on organ transplantations, environmental medicine law

High-Tech ORs: Software Solution “KABOP”



“KABOP - One advanced software program to support high-tech OR's.”

Franz Markus Simader

Research Focus

- High-Tech-OR
- Video Routing
- Medical IT networks
- UI-Design

Coordinators



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Vision

There are numerous restrictions when converting normal operating rooms to high-tech ORs. The shortage of software solutions means there are many different systems and the following problems arise:

- Usability mismatch
- Missing technical interoperability (hardware)
- Different user understanding → Look & Feel
- High acquisition and maintenance cost
- High dependence on the manufacturer

These problems mean we cannot use custom hardware and our employees cannot maintain this hardware. When specific hardware fails, the result is higher repair costs by external employees. In addition, the longer the system is unavailable, the longer the OR cannot be used, resulting in higher costs for the hospital.

Approach

The first step in response to the situation was to find hardware to support high technology standards but also reuse existing hardware and existing components in order to guarantee strong support. We discussed the required functions with department members and OR managers and noted requests from all sides.

We aimed to design one application-oriented software program for differently equipped ORs that could adjust to individual changes quickly and rapidly.

The software should include the following functions:

- Video routing with different input sources
- Light control based on defined scenes
- Ceiling camera control
- Video conferencing (outgoing & incoming signals)
- Sources and destinations grouped in panels
- Video digitization with the MOST system

Software Overview

The software structure is self-explanatory. The left side contains output signals (sources) grouped in panels. The right side contains input targets which are also grouped in panels. The design is user-friendly as it edges the current input selection and only shows one extended panel on each side. The midsection contains two buttons. The left button controls the lighting by using predefined settings. These settings are also available as hardware switches and the LED brightness can be individually adjusted as required in each OR. The right button controls the ceiling camera. By displaying a preview stream, the camera can be more accurately controlled. There are standard PTZ features (UP, DOWN, LEFT, RIGHT, ZOOM).

Technical Information

The software works together with our current video digitalization hardware and is directly displayed on a touch screen monitor. The software was designed for touch screens and human interface devices (HID) in order to support easy, user-friendly use. LED light control uses a bus system based on the KNX [4] standards. The IPS/S2.1 interface between the ethernet and bus makes it possible to directly send standardized packages to the bus.

The ceiling camera is made by SONY and uses a VISCA [5] communications protocol to interact with the connected devices. A library based on this standard allows the camera

to pan, tilt and zoom (PTZ). The library was extended by an IP-PTZ interface to support SONY's newest IP cameras. Any IP-PTZ camera can be adapted by an independent producer with minimal adaptation of the manufacturer's specific Common Gateway Interface (CGI).

An Axis Video Encoder is used to preview the selected input source. The AXIS Media Control SDK [1] is functional enough to provide image previewing and receive H.264 video streams with a maximum resolution of 720P over IP. The Blackmagicdesign Smart Videohub [2] offers a high scalability solution for multi Serial Digital Interface (SDI) format video routing. It allows us to work with the following SDI formats: SD, HD and Ultra HD. The SDI standard is used primarily to transmit uncompressed and unencrypted video data via a coaxial cable. The IP interface provides quick communication and signal routing (1:1; 1:n):

- Easy routing in any input device camera
- Video signals in any supported format
- Monitor mirroring

To any outputs (monitor, video conference output, video digitalization, ...). The network structure isolates the ORs from each other, complying to DIN EN 80001 medical IT network standards.

User Evaluation

The software has been well-received by OR staff and personnel. The main benefits include unified user interface (UI), good UI screen readability, and an intuitive understanding of operability.

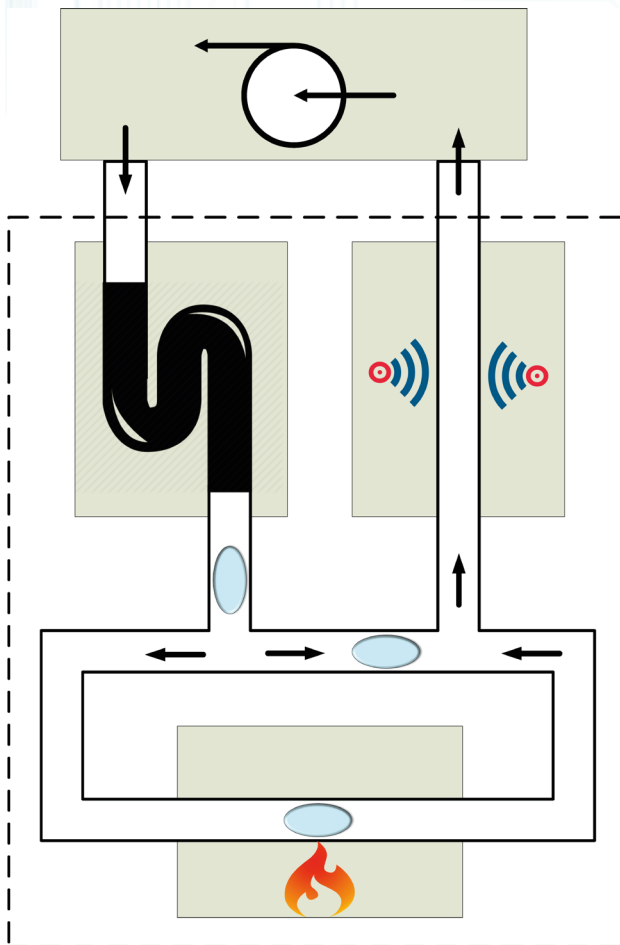
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Keywords

High-Tech-OR, KABOP [3], video routing via smart-video-hub, KNX Bus Control, LED light, Dome Camera PTZ

Networked Labs-on-Chips: From the Specification to the Physical Realization



“Networked Labs-on-Chip foster a paradigm shift in the Lab-on-Chip domain.”

Elena de Leo¹

Research Focus

- Networked Labs-on-Chip (NLoCs): An LoC technology introducing biocompatibility
- Design of NLoCs: Application-specific architectures, proper droplet sequences, etc.
- Development and utilization of methods for Electronic Design Automation
- Simulative and experimental validation

Coordinators



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¹ Elena de Leo first introduced the idea Network Labs-on-Chip [5].

Vision

Labs-on-Chip (LoC) allow for the miniaturization, integration, and automation of medical and biochemical procedures. To this end, LoCs combine different laboratory functions on a single chip thus yielding a faster analysis as well as larger throughput while at the same time, requiring significantly lower reagent consumption. LoCs are successfully used for in-vitro diagnostics, for example, DNA sequencing, cell analysis, protein crystallization, and drug discovery.

Droplet-based microfluidic systems [1] are a promising platform to create LoCs. Droplet-based microfluidics contain tiny volumes of fluids that can be controlled and manipulated by means of two different approaches. The surface-based approach allows us to arbitrarily move droplets on a planar (open) surface by electrowetting-on-dielectric [2] or by surface acoustic waves [3]. This approach offers higher flexibility because the droplet's path is freely programmable. However, surface-based approaches suffer from the evaporation of liquids, the fast degradation of the surface coatings, its lacking biocompatibility and the complex and costly fabrication process [4]. Channel-based approaches (see [1]) allow the droplets to flow in closed microchannels, triggered by some external force (such as pressure pump) at the chip boundary. The closed channels incubate and store liquid assays over a long period of time thereby warding off evaporation and unwanted reactions [4]. However, the channel-based approach lacks flexibility since current LoC solutions are designed for a specific application. To overcome this issue, networking and communication capabilities were added to LoCs [5] – yielding so-called networked LoC (NLoC). In NLoCs, the droplets are passively routed in the channel by exploiting hydrodynamic forces. Thus, NLoCs are a promising solution to create flexible and biocompatible LoCs that can be manufactured at a low cost (such as for use in 3D printers).

Currently, the design and physical realization of NLoCs are in its infancy stage. Thus far, only a small number of very prototypical and highly restricted NLoC devices have been manufactured [6], [7]. Their design relies almost entirely on manual labor. Our objective is to take this promising technology from the basic research level to an application-oriented domain by developing applicable physical attributes and automated design solutions in order to eventually get biocompatible NLoC technology market-ready.

Approach

To accomplish the proposed vision we have brought in expertise from interdisciplinary fields. We will apply methods of electronic design automation in the field of computer sciences in order to obtain application-specific architectures and determine the desired droplet sequences. To incite the droplet to proceed to the desired destination within the network, we will adopt addressing schemes from the fields of communications engineering. Our laboratory experiments will require basic knowledge about the physics of the fluids.

In addition, the technology will only be accepted by stakeholders by providing tool support for all steps ranging from the initial medical or biochemical specification to the final physical realization. Hence, the results of the interdisciplinary efforts will eventually be combined and integrated into an automated design flow.

Impact

One target application for biocompatible NLoCs is point-of-care diagnostics, designed to bring medical tests and results immediately and conveniently to the patient. This is especially important in healthcare environments where structures are weak and access to quality and timely medical care is challenging. Other important applications include the automation of standard laboratory routines. Any application that can be executed automatically without any human intervention would benefit scientists during their daily routines.

In summary, NLoCs may be applied as fully automatic, high precision diagnostic tools in various areas. This work provides substantial contributions to the physical realization of corresponding devices and, for the first time, allows users to easily and automatically design their experiments on them.

Competencies

The research in this area is conducted by the following institutes:

- Institute for Integrated Circuits with research focused on design automation, optimization, and verification of circuit and systems in general and LoCs in particular.
- Institute for Communications Engineering and RF-Systems with research focused on molecular communications, wireless sensor networks and radar systems.

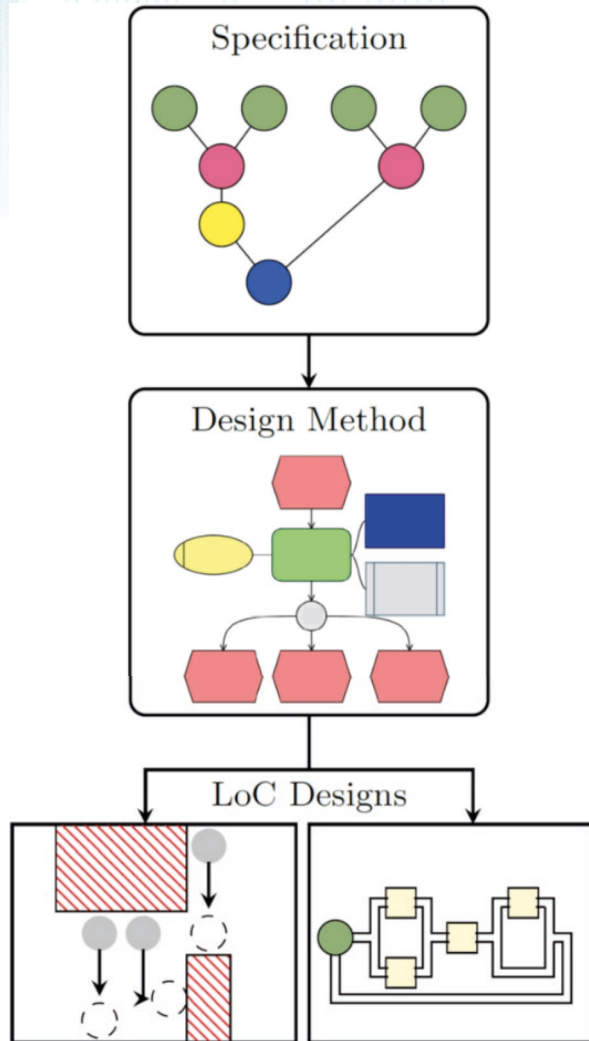
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Keywords

biocompatibility, droplet-based microfluidics, labs-on-chip, networked Labs-on-Chip, hydrodynamic switching

Design Automation for Labs-on-Chip



“A post-doctoral researcher can take up to one year to designing a biochip containing 918 valves. Thus, it is essential to create customized computer-aided tools.” [1]

Research Focus

- Design of Labs-on-Chips
- “Push-button” methods for the synthesis and optimization of LoCs
- Development of proper models, design procedures, and data-structures
- Development of technology-independent solutions for various LoC types
- Application and evaluation in practically relevant environments

Coordinator



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Vision

In recent years, microfluidic technology has paved the way for so-called Labs-on-Chips (LoCs) – a convenient and cost-effective way to conduct biochemical, biological, or medical experiments. Instead of conducting tests manually in a fully equipped lab and using up lab equipment and human resources, LoCs allow us to conduct biochemical and medical experiments on a small chip. Conducting automatic laboratory procedures requires much smaller sample/reagent volumes as well as significantly higher throughput.

At the same time, designing the corresponding chips has become a considerably complex task. State-of-the-art LoCs are comprised of thousands - even tens of thousands – of entities and a million features in order to conduct certain experiments with increasing tendency. Time to market constraints and fault tolerance considerations are increasingly significant and will further complicate the design. Despite the complexities, most of the LoCs are designed manually. Engineers draw the designs for corresponding devices by hand. Manual design will become difficult to sustain as LoCs become more complex and this promising technology could be hindered from reaching its full potential.

Our research focuses on overcoming this barrier by means of sophisticated methods and supporting Electronic Design Automation (EDA). To be more precise, we envision the development of generically applicable design solutions that can cover all major tasks related to LoC design as well as support a wide range of different LoC technologies. For the first time, LoC end-users and stakeholders will have a “push-button” solution that could alleviate most of today’s design concerns.

Approach

- LoC devices need to be designed so they can successfully attain the desired experiment results in an acceptable timeframe. To this end, the stakeholder will provide the designer with initial input such as a sequencing graph specifying the experiment and the involved liquids as well as the respective steps (in terms of operations) and their dependencies of execution,
- Create LoC technology to achieve the desired experiment results, and
- Address any other additional limitations, such as the grid size, on which the experiment will be conducted or the maximum duration time of the experiment.

This kind of input is conducive to attaining the experiment’s overall result using the desired technology within the given limitations. Automatic solutions can be developed covering each step from the architectural synthesis to the actual physical design, including defining proper models as well as developing corresponding procedures and data-structures. We aim to support a broad variety of different LoC technologies and, whenever possible, apply technology independent solutions. To this end, we intend to make use of efficient heuristic solutions as well as powerful solutions based on formal reasoning.

Impact

The research findings will significantly change our understanding of future LoC design. The resulting methods will be integrated into an automated LoC design flow (“push-button”), taking previously created manual designs into account and considering designs drawn manually in a distributed, non-integrated way. Dedicated (technologically motivated) constraints and restrictions will be guaranteed while again, the current state-of-the-art often produces impractical designs. Finally, solutions resulting from our work can be easily adapted to additional designs, particularly new and upcoming LoC technologies.

Competencies

The research in this area is conducted by the Institute for Integrated Circuits with research focused on the development of EDA methods for the design of circuits and systems. In the past, the group has successfully applied EDA methods to various disciplines (hardware design as well as electrical engineering, quantum physics, optical physics, medicine, etc.). In support of LoC design, the institute has built a strong network of stakeholders and applicants and frequently organizes networking and information exchange events.

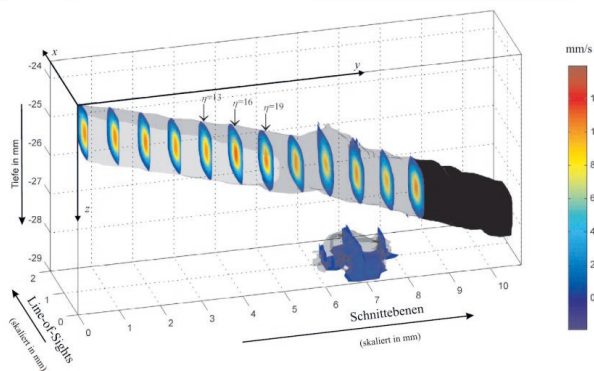
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Keywords

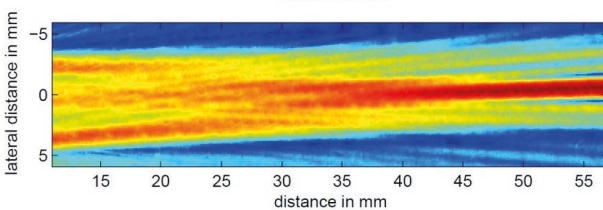
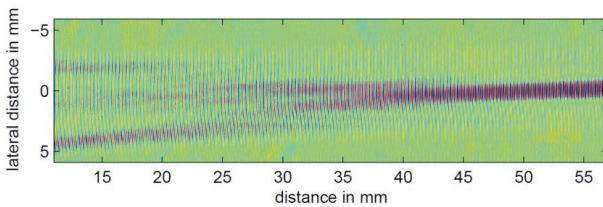
Labs-on-Chip, microfluidics, design automation, synthesis, optimization, models, procedures, data-structures

Ultrasonic and Tomographic Signal Processing



“Innovative algorithms to render and combine high quality tomographic images from various imaging procedures will provide us with crucial information to further enhance patient care.

Bernhard Zagar



Research Focus

- Ultrasonic Imaging
- Magnetic Tomography
- Digital Signal and Image Processing

Coordinator



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Vision

Applying advanced state-of-the-art signal processing algorithms in combination with improved excitation strategies from ultrasound transducers enable us to extract the theoretical limit on information conveyed by the US returns. This not only includes structural information, but also contains information about the mechanical properties of imaged tissue reminiscent of the classical palpation.

Approach

In the future, improving existing medical imaging procedures such as magnetic resonance imaging (MRI), positron emission tomography (PET), X-ray computed tomography (CT-scan), single-photon emission computed tomography (SPECT), and medical sonography (US) by applying even more powerful signal processing algorithms will allow us to not only determine one's health more accurately, but will also allow us to guide surgical instruments during surgery with more precision [3]. Accurately delivered and stereoscopically steered high powered ultrasound [4, 5] could advance further as a tool to treat malignancies. Magnetic tomography, based on highly integrated GMR or TMR (giant magneto resistance or tunneling magneto resistance) line-scan arrays [1], might pave the way to image signaling pathways.

Students who have studied engineering and show an interest in conducting challenging research in biomedical engineering at the Johannes Kepler University Clinic could prove beneficial to both sides. Both undergraduate and graduate theses are jointly supervised by academic engineers and medical professionals. Students can conduct research at JKU laboratories and also use the JKU clinical facilities. This highly attractive model has been well received by JKU students. In addition, we have already begun to offer courses in statistical signal processing to graduate students studying bioinformatics and have had impressive results.

Impact

Although ultrasonic imaging [8] is becoming more advanced, there is still room for improvement, especially in the target area of imaging structures as well as tissue properties. Recently there have been considerable improvements, such as in the field of ultrasonic shear wave elastography, a procedure that detects malignant tissue based on its deviating elastic properties due to mechanical shear waves induced by properly chosen excitation signals to the US transducers.

The field of in vivo ultrasound microscopy is also far from being a theoretical limitation [6, 7]. Superficial malignancies such as prostate or breast cancer might benefit from advanced highly spatial resolution imaging, leading to treatment using minimally invasive surgery.

We can already provide imaging of a beating heart's magnetic field wave, for example. Given recent developments in magnetic camera resolution and sensitivity [1, 2], pursuing other imaging possibilities may be worth following up on.

Competencies

Advanced capabilities in ultrasonic imaging procedures as well as optical and magnetic tomography imaging are provided by the

- **Institute for Measurement Technology** with research focused on sensor development (magnetic line-scan camera, ultrasound microscope, schlieren optics for ultrasonic beam characterization, etc.) and advanced signal processing of two and three-dimensional sensor signals.

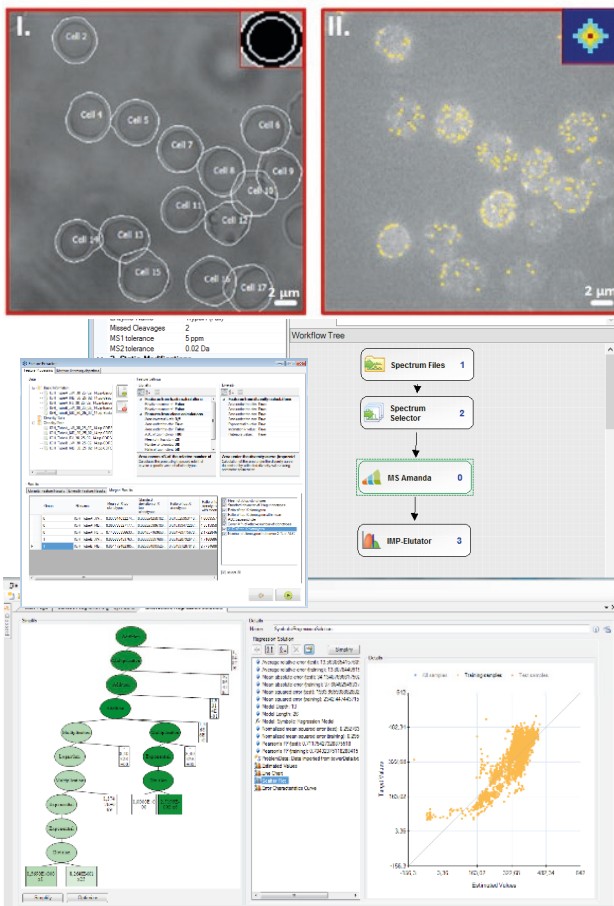
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Keywords

ultrasonic imaging, US color-flow mapping, ultrasound sources, image processing, signal processing, tomography, magnetic tomography

Solving Research Questions in Life Sciences Using Data Science Methods



“The problem nowadays is not how to obtain data – the problem, rather, is that the amount of collected data is growing exponentially. We need methods that can analyze huge amounts of data efficiently to find answers to critical questions in life sciences.”

Stephan M. Winkler

Research Focus

- Machine Learning
- Computational Proteomics
- Immune Repertoire Profiling
- Image Processing
- Evolutionary Computation
- Symbolic Regression and Classification
- Design of Virtual Sensors

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Vision

The importance of analyzing big scale medical and biological data has increased significantly over the past years. Whereas in the past the problem was acquiring large amounts of data, we can now collect large amounts of data - particularly in the field of life sciences which included medicine, biology, and chemistry – and the amount of data collected is growing exponentially. Researchers at the University of Applied Sciences in Upper Austria (Faculty for Informatics, Communication, and Media) are developing algorithms to analyze the data in detail. Research groups in Bioinformatics (BIN) and Heuristic & Evolutionary Algorithms (HEAL) are particularly active in conducting research in data science methods to help find answers to critical questions in medicine and biology.

Approach

We use HeuristicLab (HL, <https://dev.heuristiclab.com/>) for machine learning tasks in biomedical research, a software framework for heuristic algorithms developed by HEAL researchers. HL offers a rich and user-friendly interface, enabling users to apply numerous modern algorithms for learning classifiers, regression models, and prediction models [1]. For example, we collaborated closely with medical doctors at the Kepler University Hospital's Central Laboratory and analyzed data from thousands of patients to develop virtual tumor markers (models that can be used to estimate tumor marker values) as well as prediction models to diagnose cancer. The analysis also helps us to identify corresponding features that have an impact on the disease and patient treatment. [2]

Our research also focuses on analyzing microscopy images by using a combination of image processing, feature extraction techniques, and machine learning. In collaboration with the Red Cross Transfusion Center Linz, Trauma Care Consult, and Olympus Austria, we have identified classifiers that can determine the state of blood samples and tissues. [3]

Often, the cause for various illnesses is the absence or presence of specific proteins. As determining the proteins in a biological sample is of highest importance, mass spectrometry data analysis is applied. In close collaboration with the Institute for Molecular Pathology in Vienna, we have developed MS Amanda, a peptide identification algorithm for mass spectrometry data that outperforms common search strategies

. [4]

The human adaptive immune system strongly impacts human health and analyzing and understanding the repertoire not only benefits research, it can help to optimize medical treatment for patients. In close collaboration with researchers at the Medical University of Vienna and at the University of Salzburg, we have designed algorithms to sequence data based on analyzing human antigen receptor repertoires [5].

Impact

Over the past few years, the analysis methods designed and implemented at FH Upper Austria in Hagenberg have helped to address several critical research issues in life sciences such as:

- Developing virtual tumor markers as well as prediction

models to detect cancer, including identifying relevant impact factors.

- Identifying classifiers that automatically detect the Rhesus D antigen state of blood cells.
- Implementing and publishing MS Amanda, a peptide identification algorithm that is now a part of the Thermo's Proteome Discoverer and used at dozens of proteomics research facilities worldwide.

We have implemented and published IMEX, a software suite for the detailed characterization and visualization of the state of human B and T cell receptor repertoires. This is also now available worldwide at several immunology departments.

Competencies

Research in analyzing life sciences data is represented at FH Upper Austria by the following research groups:

- **Bioinformatics** with research focused on the analysis of biological data
- **Heuristic and Evolutionary Algorithms Laboratory** with research focused on heuristic algorithms, evolutionary computation, and machine learning

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Keywords

patient data, blood parameters, virtual sensors, mass spectrometry, next-generation sequencing, immune repertoire profiling, image processing, cell identification, machine learning, classification, time series modeling

A Prosthetic Leg That Can Feel



“Many amputees suffer from phantom pain caused by the brain trying to retrieve sensory information from a limb that is no longer there. Approximately 25,000 Austrians have been affected by foot or leg amputation and the numbers are rising: according a forecast by the WHO, the number of amputations in the western world is expected to double by 2050. The WHO estimates that 0.5 to 0.8 percent of the population has lost one or more limbs; that is 40 to 64 million amputees worldwide. In developing countries, amputations occur as a result of natural disasters, war, or accidents. In the western world, over half of all performed amputations are a result of diabetes and the number is expected to rise over the next decades.”

Hubert Egger

Research Focus

- Bionic Prosthetics
- Phantom Pain
- Fall Prevention
- Improvement of Gait Pattern

Coordinators



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Vision

We aim to develop a feedback system that will allow amputees to feel foot-rollover from heel to toes. A prosthetic leg containing touch sensors could allow the leg to 'feel', resulting in less phantom pain as well as reducing the risk of falling. In addition, the patient could better feel and be aware of the type of the ground he/she is walking on. A stronger awareness of obstacles can result in an improved gait pattern. The primary objective is to make the patient forget that the limb is artificial.

Approach

During Targeted Sensory Reinnervation (TSR), severed sensory nerve endings are surgically rerouted into skin areas of the amputation stump so they can establish connections with receptors (biological stimulus sensors) [1]. In the study, six stimulators (artificial stimulus creators) placed on the skin surface proceeded to excite the receptors in the skin area that had been treated with reinnervation in accordance with the pattern of the current pressure distribution [2]. The pressure distribution is recorded by six force sensors on the sole of the prosthetic foot. Different signal processing algorithms can be activated to optimize the link between sensors and actuators and thus, the feeling properties. The electric signals generated in the nerve endings (action potentials) are then relayed to the brain in a similar way that information is sent from a natural foot [3]. They represent actual information of the foot that no longer needs to be compensated by autonomously generated signals.

Impact

Re-establishing the transfer of information is conducive to more naturally integrating the prosthesis and making it a part of the patient's body concept. A case study at the University of Applied Sciences in Upper Austria conducted in cooperation with the University Clinic for Plastic, Reconstructive and Aesthetic Surgery in Innsbruck has resulted in the complete loss of previous long-lasting pain.

Competencies

Research in signal processing, neurology and intensive-care medicine is represented and conducted by the following departments:

- **Rehabilitation Institute of Chicago (RIC);** 345 E Superior St, Chicago, IL 60611, USA
- **Department of Plastic, Reconstructive and Aesthetic Surgery** with research focused on targeted muscle und sensory reinnervation

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Keywords

bionic leg, feeling leg prosthesis, sensitive leg prosthesis, Targeted Sensory Reinnervation, Targeted Muscle Reinnervation, phantom pain treatment, lower leg amputee

Medical Information, Simulation and Visualization Systems



e-Health
Integrierte Versorgung

“The IT-support of integrated healthcare (“e-Health”) allows the definition, analysis and optimization of suitable interfaces, more ad-equate healthcare processes, as well as affordable business models for high-quality care- and case-management for the health system.”

Herwig Mayr

Research Focus

- Interoperability of Medical and Health
- Information Systems
- Standards for Health Information Exchange
- eHealth Applications
- Simulation and Visualization of Medical Processes
- Augmented and Virtual Reality
- Emergency Detection and Simulation

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Vision

Ageing will affect the population in every country in the European Union. Whereas the working population (ages 15-64) will decrease, the ageing population will increase consistently over the years, resulting in Europe having to confront demographic and cultural challenges. The World Health Organization (WHO) suggests life-long health prevention as a way to overcome the challenges caused by the rapid demographic change. Healthcare institutions will have to cope with various issues, such as: (i) providing efficiency and economic sustainability, and (ii) providing easy access to care and patient safety. Home and community health services will provide opportunities for preventive healthcare.

The cornerstone of integrated healthcare and eHealth applications lies in the efficient communication efforts between healthcare providers. In order to maintain a high quality of healthcare across institutional borders, it is important to know a patient's medical history, the kinds of medical examinations and therapies he/she has been subjected to, medical results as well as patient response. Our interdisciplinary research aims to compare and integrate medical history information as well as explore non-functional processes found in various healthcare environments.

Approach

Our research addresses some of the demanding factors when integrating electronic health information systems and processes such as different domain languages and understanding, special processes and workflows in and across various organizations, varying documentation that has different objectives, varying structures in documentation, different designations and little-to-no use of coding systems.

The challenge lies in successfully combining technologies and information models in order to develop tools and methods enabling technical, semantic and process interoperability in the exchange of health information. In addition, these processes need to be visualized in order to identify problems and potential optimization opportunities.

The fundamental technologies and corresponding research fields are: Integrating the Healthcare Enterprise, Continua Health Alliance as well as suggested standards such as HL7 V2, CDA, FHIR, DICOM etc., MOF, BPMN, and state-of-the-art modeling technologies. Active participation in standardization organizations as well as national and international working groups allow us to integrate research results directly by developing new standards and refining existing standards.

In addition to joint and interdisciplinary research, ongoing research includes the direct involvement of medical institutions, the medical informatics industries, standardization organizations, and students. Student involvement includes participating in various student projects, completing an undergraduate or graduate thesis, awards, and working in research projects. International exchange with other universities, industries, and institutions takes place in the form of actively participating and organizing workshops, conferences and so-called "developer days".

Impact

The importance of interoperable health information systems has increased significantly over the past few decades. It requires reliable methods and algorithms for model transformation and process visualization to enable semantic and process interoperability as well as newly developed standards in medical informatics. These methodologies can be used not only in a medical environment, but are also applicable to other industry settings.

Competencies

Research in eHealth and interoperable healthcare information systems will be represented and conducted by the following departments:

- **Department of Software Engineering**, with research focused on information systems, augmented and virtual reality, data engineering, algorithms for big data analytics and engineering, model driven development, mobile systems and software architecture.
- **Department of Medical and Bioinformatics**, with research focused on interoperability of medical information systems, augmented and virtual reality, knowledge engineering, medical boards, health processes and interoperability of health institutions.
- **Research Group for e-Health**, with research focused on standards for health information exchange, interoperability of medical information systems, semantics and processes, eHealth Applications, simulation and visualization of medical processes, augmented and virtual reality, emergency detection and simulation.

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Keywords

health information exchange, interoperability, process mining, model engineering

Medical Simulators and Simulation



Hybrid Surgical Simulator – Cement Augmentation.

“Surgical procedures using real instruments can be practiced by using hybrid surgical simulators under realistic and safe conditions.”

Andreas Schrempf



Artificial vertebra, fluoroscopy and CT-image.

Research Focus

- Hybrid Surgical Simulators
- Artificial Bone and Soft Tissue
- Simulated Imaging
- Biomechanical and Medical Validation

Coordinators



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Vision

Surgical field training today applies a traditional “learning-by-doing” approach or is conducted in simulated environments [1]. Surgical simulators are a cost-effective learning resource that allows surgical residents to practice surgical procedures unsupervised and without being exposed to radiation. Residents can practice as often as they want as there are no specimen costs. Hybrid simulators combine a patient phantom with a computer model to provide realistic haptic feedback and residents use real surgical instruments. Our vision is to make medical simulators - hybrid surgical simulators in particular - an authentic, accepted and well-founded learning resource in medical education.

Approach

Hybrid simulators to practice needle insertions close to the spinal cord are currently a major field of application and include simulators for cement augmentation techniques, pedicle screw insertion, joint puncture, spinal and epidural anesthesia [2,3]. The corresponding research fields include artificial bones and soft tissue, smart surgical instruments, simulated medical imaging as well as simulator validation.

A high-fidelity phantom patient provides realistic situ and haptic feedback and simulates man-made bones, artificial soft tissue as well as critical anatomical structures such as blood vessels and nerves. Developed artificial bones are characterized by a cortical shell and an open-celled trabecular structure [4, 5], suitable for implant placement, the application of bone cement and also provide a realistic contrast in fluoroscopy and CT imaging. Soft tissue featuring integrated sensor layers provides information for surgical tool placement. Biomechanical validation in relation to a human specimen is conducted in all artificial anatomical structures.

A key advantage of using hybrid simulators includes the use of real surgical instruments that feature custom sensors that can provide productive feedback, control the simulator, and record objective data for assessment purposes [6]. Smart surgical instruments should be scaled down in size, energy efficient, have wireless charging capabilities, and be able to transmit recorded data.

When practicing image-guided surgical procedures, the need for imaging modalities would limit the simulator’s applicability and availability. Thus, simulated imaging techniques are being developed for fluoroscopy and ultrasound imaging to provide images independent of any device and without being exposed to radiation. Developed algorithms deploy 3D-models of anatomical structures together with tool position and placement obtained from 3D tracking devices (optical or electromagnetic) for real-time imaging.

Simulator development and medical validation providing measurement for face, content and construct validity in particular is conducted together with clinical partners.

Impact

Medical education between medical experts and medical students is labor intensive and expensive in terms of time and money. Demographic changes mean that the need for

medical care is expected to rise. These changes - and complying with the European Working Time Directive – mean less opportunities for conventional, mentor-based education as physicians will be focusing more on patient care. Medical simulators are innovative, educational methods of learning. They are independent of existing clinical infrastructures, not subject to a certain number of trials, and require less mentoring. The expected, long-term impact is constructive advancement in medical education and, in turn, improved reliability and safety for both patients and physicians.

Competencies

Research in surgical simulators, biomechanical evaluation, medical validation, orthopedic surgery, anesthesia and intensive care will be represented and conducted by the following departments:

- **Research Group for Surgical Simulators** with research focused on development of hybrid surgical simulators, artificial bones and soft tissue, smart surgical instruments, simulated medical imaging, biomechanical validation
- **Department of Anesthesia and Operative Care** with research focused on simulation in anesthesia, critical care and emergency medicine.
- **Department of Orthopedic Surgery** with research focused on orthopedic surgery, arthroplasty, rheumatoid arthritis and bone tumors.

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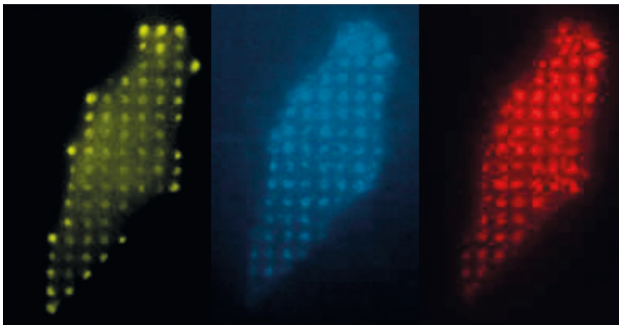
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Keywords

medical simulation, hybrid surgical simulator, artificial bones, simulated medical imaging, spine surgery, anesthesia

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Impact of Phytochemicals on Disease-Related Regulatory Signaling Hubs



"We can treat diseases more efficiently and faster - and with fewer side effects - by applying new strategies and approaches to customize medicine."

Julian Weghuber

Research Focus

- High-content phytochemical screening to develop pharma/nutraceuticals
- Live-cell micro-biochips for signal transduction analysis
- Gen and protein-expression analysis
- Bioavailability studies

Coordinators



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Vision

Cardiovascular diseases, various cancers, diabetes, and chronic respiratory problems are among the most common, non-infectious diseases worldwide that contribute significantly to the global mortality rate. Most of these diseases are also linked to poor nutrition [1]. Whilst the macroscopic effects of nutrition are well described, there is still little basic information about the nutritional influence on underlying key regulatory signaling processes. Characterizing food's modulatory bioactive components in order to optimize nutrition and prevent the aforementioned diseases would be of great importance.

In essence, good nutrition does not often prevent severe diseases. New strategies and approaches in customized medicine are currently focusing on health strategies that could improve the way we treat epidemic diseases such as cancer or diabetes [2]. These strategies should include customized drug therapies in order to not only treat patients faster and more efficiently, but also with fewer side effects.

Approaches

Insulin mimetic phytochemicals: Insulin stimulates the transport of glucose in target tissues by triggering the translocation of glucose transporter 4 (GLUT4) to the plasma membrane. Resistance to insulin, the major abnormality in type 2 diabetes, results in decreased GLUT4 translocation efficiency. Special studies are currently focusing on finding compounds that can enhance the translocation process in the absence of insulin. A high-content screening approach based on total internal reflection fluorescence (TIRF) microscopy is used to quantify the effect of potential insulin mimetic phytochemicals on the GLUT4 translocation [3, 4]. **Inhibition of intestinal glucose uptake:** In addition to directly manipulating blood glucose levels via insulin mimetic substances and enhancing GLUT4 activity, there are other options based on strategies to lower nutrient absorption. Inhibited or delayed intestinal glucose absorption in particular can contribute to better managing diseases such as diabetes and obesity. In order to estimate the impact of selected phytochemicals on the intestinal glucose transport, we use a well-characterized colon cell model (Caco-2).

Tyrosine-kinase receptor inhibitors: Identifying various receptor tyrosine-kinases as oncogenes has led to the development of several anticancer therapies targeting these membrane receptors. Drug resistance and low efficacy, however, continue to be a severe challenge and have created a demand for new systems in which new substances can be efficiently identified and characterized. We are currently developing a medium-to-high approach throughput based on micro-patterned surfaces (micro-patterning assay) and FRET read-out for the quantitative analysis of novel anti-cancer agents [5-7]. In the near future, this micro-patterning-assisted cell screening assay could be used for selected applications in customized medicine.

Storage of fatty acids in lipid droplets: Lipid droplets are important cellular organelles designed to regulate the intracellular fat storage and metabolism. Excessive and/or deregulated incorporation of fatty acids into lipid droplets are related to diseases such as obesity, cancer and atherosclerosis. Established cell culture models as well as primary adipocytes are used to identify pharmacological substances which inhibit excessive fat storage. There is a

special focus on phytochemical constituents.

Impact

Illnesses such as diabetes, cancer and obesity have become a global, public health crisis and can threaten a country's economy. New strategies are needed that would allow us to reliably analyze important related molecular parameters in a fast, easy, more efficient way. Our research addresses these issues as we work toward creating a basis for future innovative developments.

Competencies

Research on phytochemicals, disease-related signal transduction processes and personalized medicine will be represented and conducted by the following departments:

- **Institute for Food Technology and Nutrition (Wels)** with research focused on development of relevant cell culture models, screening applications and molecular biology.
- **Institute for Medicine and Bioinformatics (Hagenberg)** with research focused on data analysis, biostatistics, machine learning, bioinformatics and development of user interfaces.
- **Institute for Medical Engineering and Applied Social Sciences (Linz)** with research on spatial receptor organization and surface design and characterization.

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Keywords

phytochemicals, micropatterning, signal transduction, cancer, diabetes, fluorescence microscopy, personalized medicine

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CoTrain - ICT-Based Coaching System to Physically Train the Elderly



“Physical and strength training is essential to improve the quality of life and mobility of the elderly.”

Gerhard Ransmayr

Research Focus

- Elderly people
- Frailty
- Cognitive impairment
- Physical training
- ICT-based coaching system
- Mobility
- Health
- Quality of life

Coordinators



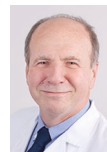
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Vision

By applying ICT based physical training programs and a communication platform (CoTrain), we can help to improve an elderly individual's physical health, which in turn can also improve mental health. The goal is to draft a list of outcome parameters and provide expert consultation to devise a special training program designed to improve the individual's gait, balance, and physical strength. The program could serve to counteract social isolation, improve mental health, and reduce caregiver burden.

Goals

According to a recent US study, 10.7 % of those in the general population over the age of 65 suffer from frailty and 41.6 % suffer from pre-frailty. There is a link between general cognitive function and physical frailty. Physical frailty can lead to a less active everyday life, loss of independence, secondary health problems, a higher risk of falling, and other issues including depression, anxiety, and social isolation. Frailty can also result in utilizing more healthcare services.

Dementia patients who also suffer from frailty can find themselves in a "vicious cycle" that can lead to a rapid physical decline. On one hand, cognitive deficits can restrict one's mobility and opportunities to be physically active and on the other hand, inactivity fosters further cognitive decline. Dementia patients should acquire, re-acquire or maintain a degree of self-confidence to be able to, for example, leave the house, communicate effectively with others, and exercise, thus remaining socially integrated and able to live well in the community.

CO-TRAIN is an ICT-based tool designed to provide instructions and follow-up information in regards to physical activity, serve as a communication platform for mild dementia patients who also show signs of frailty, and provide informal and formal support to caregivers (i.e. spouses, relatives and friends).

CO-TRAIN is an evidence-based training tool that can be customized to help improve professional care services.

Tertiary end-users will also benefit from broad use of the CO-TRAIN system. Designed to decrease healthcare costs and effort, remote coaching will reduce the number of personal visits to a physiotherapy unit, thus decreasing the therapists' workload. Many older adults can exercise more intensely and avoid the stress of traveling to and from the clinic.

Competencies

The research project is funded by the EU and the Austrian Research Promotion Agency (Project number 7965211) and is represented and conducted by the following departments/partners:

- **Austrian Institute of Technology-Project Lead;** Medico-technical projects and solutions www.ait.ac.at.
- **Department of Neurology 2;** Expertise in neurocognitive impairment including rehabilitation www.kepleruniklinikum.at
- **M.A.S. Alzheimer Hilfe OÖ;** Professional expertise in dementia care www.alzheimer-hilfe.at
- **CareCenter Software GmbH;** Software expert www.carecenter.at
- **Movieie.** Experts in social development www.movieie.nl
- **Terzstiftung** A general service provider for the elderly. www.terzstiftung.ch
- **De Wever** Geriatric services www.deweever.nl
- **Synappz** Mobile Health Expert www.synappz.nl
- **Creagy. Switzerland.** Expert information technology. www.creagy.com

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Keywords

frailty, elderly, cognitive impairment, medical training, information communication technology, quality of life

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DayGuide - Helping Seniors Manage Everyday Situations



“Elderly individuals experiencing cognitive deficits can take advantage of ICT-based solutions to improve and maintain an independent lifestyle.”

Gerhard Ransmayr

Research Focus

- Mild Cognitive Impairment
- Dementia
- ICT-based support for everyday living
- Self-dependence
- Safety
- Quality of Life
- Caregiver Support

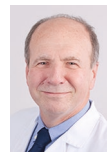
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Vision

Demographic studies show that the number of elderly individuals in Europe is on the rise. The higher number of elderly individuals in the population corresponds to the rise in the number of age-related diseases, such as dementia. The project utilizes newly designed, smart information communication technology to find solutions that not only help older individuals live an independent lifestyle for as long as possible, it would also help to reduce caregiver burden. The technology is aimed at individuals who have mild to moderate cognitive impairment and will ultimately improve their independence, personal safety, and quality of life.

Approach

DayGuide is developing a new, ICT-based system to support an active and independent lifestyle for seniors. Cognitive impaired individuals can encounter challenging situations that making living an independent lifestyle difficult.

Even a type of **reminding system** would not only help seniors lead an independent lifestyle for a longer period of time, but also allow them to have more confidence in their own abilities, raise self-esteem, and prevent depression. Taking the long duration of these early MCI phases and dementia into account, we could prevent early institutionalization which would, in turn, result in substantial cost savings.

Day Guide is a new, location-specified support service with reminder and assistance features

Information is available in several areas throughout the home by means of messages displayed on either a smartphone (worn by the person), on a tablet or other PC screens, and/or – if needed by the individual - expressed via voice output. The system can be individually configured in accordance with the person's individual needs. Message examples would include reminders (such as a message at the front door: "Please lock the door and take the key with you."), information (such as scheduled dates, appointments, and events), and assistance (such as cooking, dressing, shopping). A person's messages can also be changed accordingly by the individual or by another designated person (such as a family member or a close friend). To make the messages informative, the smartphone's logic engine decides on applicability based on pre-set messages, the time of the day, scheduled dates, events and appointments, outside weather conditions, and any information one wishes to add.

The **DayGuide** services become more superior when they are integrated as part of a required service platform. A secure, closed web-based social **platform** serves to supplement the DayGuide services and provide older individuals with media access as part of a "**family**" network.

Competencies

The research projectis funded by the EU and the Austrian Research Promotion Agency (Project number 5852188) and is represented and conducted by the following departments/partners:

- **Austrian Institute of Technology-Project Lead;** Medico-technical projects and solutions www.ait.ac.at.
- **Department of Neurology 2;** Expertise in neurocognitive impairment including rehabilitation www.kepleruniklinikum.at
- **M.A.S. Alzheimer Hilfe OÖ;** Professional expertise in dementia care www.alzheimer-hilfe.at
- **Movisie.** Experts in social development www.movisie.nl
- **Terzstiftung** A general service provider for the elderly. www.terzstiftung.ch
- **Kadex.** Dutch experts in wireless automatization. www.kadex-domotica.com
- **Cubigo.** Living adopted technology. Belgium www.cubigo.com
- **Creagy. Switzerland.** Expert information technology. www.creagy.com
- **De Wever** Geriatric services www.deweever.nl

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Keywords

dementia, mild cognitive impairment, Ambient Assisted Living, ICT based reminding system, communication platform, self-dependence, quality of life

Antimicrobial Resistance and Antibiotic Stewardship



“Conventional Microbiology and correct Antimicrobial Susceptibility Testing are the backbone and the flagship disciplines behind every new diagnostic tool and strategy to combat emerging infectious diseases.”

Petra Apfalter

Research Focus

- Antimicrobial Resistance (AMR)
- Microbiological Diagnostics - POCT
- Antimicrobial Susceptibility Testing
- Antibiotic Stewardship
- Surveillance of AMR

Coordinator



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Vision

One of the major challenges for healthcare systems around the world today is the growing recurrence of antibiotic resistance (AMR) [1-5]. Our mission statement: *“To be – and in the future remain - a leading Austrian institution in association with Clinical Microbiology and a special focus on Antimicrobial Susceptibility testing to detect new resistance mechanisms”*.

Impact

Since 2003, the Institute of Hygiene, Microbiology and Tropical Medicine (IHMT) has dealt with many aspects of AMR and infection and has collaborated with an accredited laboratory partner, analyse BioLab Ltd., since 2007. IHMT has been nominated by the BMGF as a National Reference Center for AMR and Nosocomial Infections (NRZ) and is a unique institution in Austria: one-stop diagnostics in microbiology, consulting, specific prophylaxis, therapy, and follow-up care.

Competencies

The NRZ is a networking platform engaged in a number of European projects designed to coordinate the ECDCs network programs for Austria such as EARS-Net, ESAC, EUCAST and EuSCAPE. The NRZ has state-of-the-art diagnostic tools and well-defined strain collections of microorganisms at its disposal. The NRZs Gram negative multi-drug resistant strain collection in particular is a sought-after source for researchers and industry alike in order to develop new diagnostic tests based on molecular techniques as well as point-of-care testing POCT [5].

Approach

The NRZ can provide the following services as well as competencies to interested researchers in Life Sciences, to those in fields of technology, as well as to companies:

- Strain collections
- Clinical specimens
- Pilot testing for newly designed diagnostic tools in various methodologies to detect microorganisms and AST in S2 and S3 lab environment
- Pilot testing for new antimicrobial agents
- Networking at a national and European level in accordance to various topics: experts for special bugs / AMR; EUCAST; national and international scientific societies (ÖGHMP, ÖGIT, ÖGACH, ESCMID, EUCAST, etc.)

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Keywords

Antimicrobial Resistance (AMR), resistance mechanisms, antimicrobial susceptibility testing, POCT, epidemiology, AURES, surveillance, antimicrobial consumption, EUCAST, EARS-Net, ESAC-Net, Carba-Net, antibiotic stewardship

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1010

Research on Human Endoprostheses



“The Orthopedic Clinic has long-term expertise in the development and research of Human Orthopedic Implants. We are very active in hip, knee, shoulder and ankle endoprosthetics and we cooperate with Zimmer Biomet, a leading global company in this field of healthcare as well as other medical device companies.”

Nikolaus Böhler

Research Focus

- Hip arthroplasty
- Knee arthroplasty
- Shoulder Arthroplasty
- Ankle Arthroplasty

Coordinators



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Dr. Hassan Achakri
Director Global Clinical Strategy
Zimmer Biomet Company

Vision

The world's population is ageing due to longer life spans during the second half of the 20th century. These so-called "Baby Boomers" are now 65 years of age or older and the result is an increased demand for endoprostheses. In addition, we are seeing higher body weight in our patients and a higher numbers of patients practicing sports, leading to the demand in artificial joints.

Over the next 15 years, the number of implants (both primary and revision) is expected to increase. We will also see revision surgery and infection becoming important research and development topics in the near future.

Approach

The Orthopedic Clinic at the JKU is a potentially strong partner for the development of medical devices.

We have a long history of expertise in orthopedic surgery and implant research as well as a high volume of operations featuring excellent results controlled by Endocertcriteria. Together with our radiology department, we have been using standardized x-ray techniques for years to analyze bone-implant interfaces. This radio- graphic method allows us to analyze early changes in implant fixation and document progression.

New European medical device regulations require long-term, clinical follow-up studies and in the future, we aim to collect performance and safety information pertaining to orthopedic implants.

In addition, new technologies designed to ease revision surgery and minimize the risk of infection need to be created. New technology research requires conducting base-knowledge research at the new labs as well as conducting clinical studies in our department that focus on the potential integration of radiostereographic controls. This will help us obtain accelerated results and interpret data regarding bone-implant interface analyses.

Impact

Although the standards for endoprosthetics are high, there are still ongoing issues related to long-term bony integration and early and late implant infection.

In order to tackle these issues, we need to cooperate with experienced partners in order to obtain new materials, discover new operative techniques, and provide continuous quality control.

Competencies

- **The Orthopedic Clinic** is certified for the highest quality of standards (Endocert) and has many years of professional experience with implant research.
- **The Radiological institute** has developed techniques t to carefully study bone-implant interfaces and produce detailed, analytical studies.
- **Zimmer-Biomet** is one of the world's largest manufacturers of human endoprostheses

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Keywords

research on hip and knee arthroplasties, shoulder arthroplasty, ankle arthroplasty

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Medical Imaging for Virtual Anatomy



“Advances in the 3D post-processing of medical imaging data sets obtained from CT and MR scans provides us with an innovative approach to visualize human anatomy for educational purposes. In this regard, we are heading towards the next generation of tools to teach medicine.”

Franz A. Fellner

Research Focus

- Medical imaging
- Computed tomography
- Magnetic resonance imaging
- 3D visualization
- Education

Coordinators



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Vision

Our vision is to improve conventional classroom instruction in anatomy by developing and utilizing virtual and augmented reality-based tools. This kind of technology would take classroom instruction to new heights, allowing students to learn human anatomy through the 3D visualizations of living persons. A conventional dissection course, for example, would mean that the virtual sectioning of anatomic structures is nondestructive and the procedure can be repeated as often as required. In addition, certain complex topographies deep inside of the human body - and various structures such as blood-filled vessels - can be better analyzed and understood.

Approach

Imaging methods in medicine, such as computed tomography and magnetic resonance imaging, not only enable evidence of lesions and illnesses; due to their high resolution of soft tissue and precise localization, with corresponding processing they also prove highly suitable for visualizing the anatomy of the human body.

Interpretation of sectional images and especially the development of the anatomy of the human body from such sections requires many years of expertise. For nonexperts, a three-dimensional visualization approach is required. Sectional image examination in radiology already has various postprocessing methods. One method that is particularly useful for this purpose is Volume Rendering, which was developed in the 1980s. Future Lab of Ars Electronica Center in Linz (AEC) advanced the capability of this method to stereoscopy; this is displayed at AEC in an installation called Deep Space, a high-resolution 8K projection space with a projection area of 16 x 9 meters. Here anatomy lectures can be held for medical experts and their associates as well as for the public at large in the sense of an open university [1].

Meanwhile Siemens Healthcare's Medical Imaging Technologies in Princeton, NJ, USA has developed a prototype of a Volume Rendering method with photorealistic quality; this Cinematic Rendering [2-5] enables 3D imaging that is closer to reality than previous methods can deliver. In July 2015 a Cinematic Rendering prototype with stereoscopic capability was installed in Deep Space at AEC. Using licensed CT und MR data, the anatomy of various regions of the body can be projected realistically in 3D. Since then, public lectures have been held on anatomy, and to date over 12,000 visitors have participated. The range of visitors extends from the general public to medical specialists from universities and non-academic fields. Since September 2016 the required lecture "Introduction to Anatomy" (25 LVA) has been held for students of the University of Applied Sciences for Health Professions of Upper Austria as well as for advanced training for intern doctors of the Kepler University Clinic (ESTRAGON project). For the budding area of Virtual Anatomy, the combination of conventional instruction with 2D presentation followed by specialization via interactive 3D visualization using Cinematic Rendering has yielded positive effects on the learning success of the students, based on these initial experiences.

Building on this prototypical experience, it makes sense to develop the broad concepts and tools for virtual anatomy lectures and anatomy discussion forums to market maturity.

Impact

The interactive 3D visualization of the human body via Cinematic Rendering on the basis of routine CT and MR examinations in the environment of Deep Space is a new, particularly innovative approach for education in the field of virtual anatomy. In addition to students of medicine and other health care professionals, this could benefit intern doctors in their foundation program as well as doctors completing training for various specializations, especially surgeons. Moreover, it could be of interest for special lectures in the schools sector concerning the education in the subject biology.

Competencies

Research medical imaging (computed tomography and magnetic resonance imaging), postprocessing and 3D visualization by the following departments:

- **Central Radiology Institute** with research focused on medical imaging data sets, live cinematic rendering processing and virtual anatomy education.
- **Software Engineering Department** with research focused on software architectures, software development processes, software quality management, augmented and virtual reality applications

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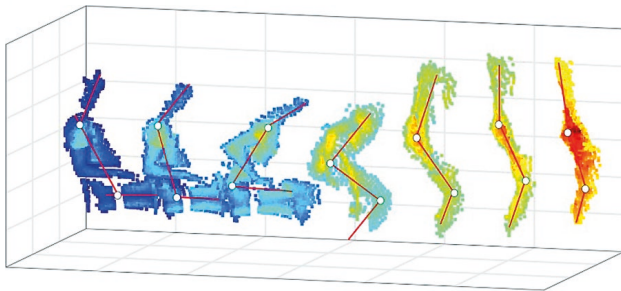
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Keywords

visualization, 3D rendering, cinematic rendering, volume rendering, computed tomography, magnetic resonance imaging, education, anatomy, virtual anatomy

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Biomechanical Devices Fracture Risk Estimation in Patients with Osteoporosis



“Advances in pattern recognition for patients with osteoporosis assists clinicians in choosing a therapy procedure to prevent falls”

Michael Gabriel

Research Focus

- Signal Processing and Analysis
- Pattern Recognition, Classification,
- Prediction
- Osteoporosis and Risk of Falls
- Assessment of Outcome, Monitoring of Therapy

Coordinators



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Vision

In Austria, approximately 763,000 patients suffer from osteoporosis, with the most frequent form (80%) being postmenopausal osteoporosis. In Austria, 140,000 patients are treated with osteoporosis-targeting drugs but half of these patients discontinue medication within one year due to various reasons. The most common form of osteoporosis in men is secondary osteoporosis caused by glucocorticoids or alcohol and hypogonadism (between 50% and 70% of cases in men). Senile osteoporosis manifests approximately 7-10 years later in men than in women. The costs due to osteoporotic fractures amount to several billion euros annually, mostly related to osteoporotic fractures. [1,2]. We aim to create a standardized gait analysis in an effort to predict and help prevent falls.

Approach

Osteoporotic patients can experience severe fractures, including minor falls from a standing height or lower. It is essential to monitor the patient's balance and physical strength in order to assess and reduce to the risk of falling. At the moment, we clinically test functional mobility by observing patients complete certain tasks (getting up from a chair, "timed-up-and-go", ...), and counting the number of repetitions within a specified time period. The procedure can be time-consuming for both the patient and therapist and has drawbacks such as long waiting periods between tests, a lack of physiological data, and possible bias due to the patient's cooperation and participation (or lack of).

By implementing modern technological solutions and innovative signal processing algorithms, we can supplement the results of clinical mobility tests by providing a set of objective parameters that describe the risk of falling. 3D-imaging technologies (stereo vision, time-of-flight, light field cameras) have emerged only recently and are conquering the consumer market. Affordable products, such as the Microsoft Kinect, can capture posture and gait in high temporal and spatial resolution without requiring intimidating technical equipment. In combination with a selected set of sensors (wireless and wearable solutions to measure acceleration, location, muscular activity, respiration, pulse, ...), 3D imaging techniques will be used unobtrusively during the functional mobility tests to fully capture an osteoporotic patients' level of activity. Signal processing and pattern recognition methods will be used to interpret the available data [3,4]. An interdisciplinary research team will jointly define a set of parameters to objectively describe the patient's physical mobility and development.

Impact

The ability to predict the risk of falling in osteoporotic patients can lead to taking certain measures to provide these patients with special protectors or recommend that they take part in certain fall prophylaxis training programs. We also plan to use technical approaches monitor the success of these training programs.

Competencies

Research in gait recognition, signal processing, and recruiting osteoporotic patient for studies will be represented and conducted by the following departments:

- **Sensors and Communication, Linz Center of Mechatronics GmbH**, with research and development focused on image processing, wireless sensing & communication, pattern recognition and condition monitoring.
- **Institute of Nuclear Medicine and Endocrinology**, Kepler University Clinic, Linz, Clinical care of osteoporotic patients as a central care facility in Upper Austria.

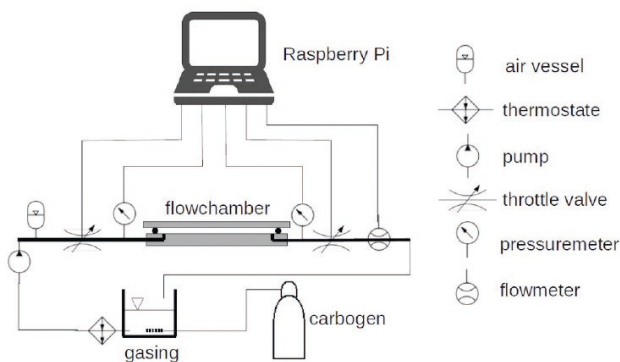
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Keywords

osteoporosis, gait recognition, signal processing, pattern recognition, remote sensing, wearables

Impact of Different Flow Conditions on Endothelial Cell Activation and the von Willebrand Generation



“Recent research conducted in sheer-stress induced endothelial cell activation has revealed new pathomechanisms for various cardiovascular diseases”

Jörg Kellermair

Research Focus

- Impact of physical stimulation on endothelial cell activation and molecule secretion
- Flow-dependent gene regulation
- Flow-induced disorders of primary and secondary haemostasis

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Vision

Endothelium plays a key role in various cardiovascular diseases, such as arterial and venous thrombosis and thrombus resolution [1]. These cardiovascular diseases are as main cause of morbidity and mortality in the West, however, the precise pathomechanisms are still not completely understood. Endothelium is a part of both primary and secondary hemostasis and helps maintain the balance between pro and anti-coagulation factors in the vessel system.

Recent research indicates the impact physical stimulation has on endothelial gene expression and molecule secretion profile. Sheer-stress induced endothelial cell activation has already been shown to be involved in a wide range of cardiovascular diseases.

The von Willebrand Factor (vWF) is an important endothelial cell derived molecule that is essential for primary hemostasis [2]. The effect of different blood flow conditions on endothelial cells in the vWF generation has remained mostly unstudied. Our collaborative research project aims to highlight this topic.

Approach

Endothelial cells will be exposed to various physical stimuli mimicking different (patho) physiological conditions using a newly designed flow chamber. The flow chamber contains a micro-pump and will be able to simulate systolic and diastolic pressures at adjustable pulse frequencies.

This model can be utilized to study different pathways of stimuli-dependent endothelial cell activation and its effect on plasma protein composition. For data acquisition different laboratory techniques including Western Blot, (real-time) polymerase chain reaction (PCR), enzyme-linked immunosorbent assays (ELISAs), and (immuno) histochemical stains will be used.

The first specific topic that will be addressed focuses on vWF generation and secretion. Clinical observations point to a potential flow-dependent modulation.

Impact

The acquired data could contribute to understanding the precise disease mechanisms necessary to treat strategy development.

Competencies

The project will be conducted in cooperation with the following institutions

- Institute of Biomedical Mechatronics
- Department of Cardiology, Kepler University Hospital Linz

References

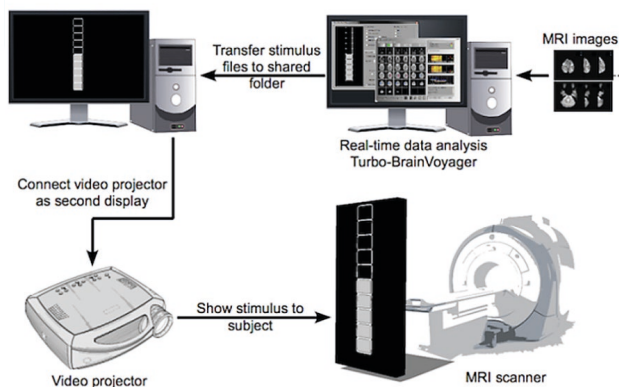
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Keywords

flow chamber, murine endothelial cells, endothelial function, physical stimulation, sheer stress, gene expression, von Willebrand Factor

Real-Time Functional MRI

Neurofeedback Setup



“fMRT neurofeedback will provides us with new approaches during therapeutic progression”
Raimund Kleiser

Research Focus

- Neurofeedback
- Real-time functional MRI
- New therapeutic approaches
- Reorganization
- Rehabilitation
- Plasticity

Coordinators



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Vision

Functional MRI has strongly influenced neuroscientific research in recent years. In addition, there are important clinical applications when conducting pre-surgical examinations of tumor patients. Current clinical projects of the Imaging Center at the Neuromed Campus focus on the use of this method to improve differential diagnoses but also to understand the processes accompanying the therapy. Recent developments have now made another milestone in regards to this method. Turbo Brain Voyager (Brain Innovation [1]) is a software tool that gives us an online analysis of functional data within a certain timeframe. Brain activation results can be directly returned to the patient [2]. Real-time fMRI is a new dimension of neurofeedback.

Approach

Neurofeedback has already been used in various applications to train self-regulation. Whereas, for example, an EEG can only be used to see global changes in brain activity, the real-time fMRI allows specific areas to be addressed [3]. By knowing which brain areas are involved in several pathologies, we can develop new therapeutic approaches by targeting these brain regions.

Areas of application that would join already existing projects at the Neuromed Campus focus on rehabilitation and reorganization processes of the brain after tumor resection, stroke, or even after amputation of external limbs. Training of specific brain areas could support these processes. Another main emphasis includes the potential treatment of several psychiatric disorders. Here, too, individual brain regions can influence the psychiatric disorders. By specifically regulating these areas, initial studies in standard therapy resistant depression patients show a significant improvement [4]. This could also apply to patients with addictive disorders whose cause may be diverse.

Impact

This methodological approach opens up a broad range of interdisciplinary research. The number of patients affected by a stroke, tumor, or depression - just to name a few - could benefit enormously from this new neurofeedback method.

Competencies

Research in real-time fMRI will be represented and conducted by the following departments:

- **Institute of Neuroradiology** develops and integrates the technical setup, carries out the measurements and elaborate analyzes.
- **Department of Neurosurgery** uses pre-surgical information on eloquent functional areas and provides information on the clinical development during post-surgery phase.
- **Stroke Unit - Department of Neurology** After a stroke, patients undergo challenging rehabilitation tailored to the individual.
- **Department for Psychiatry** Treatment of various psychiatric disorders that could benefit from self-regulation.
- **Department of Radiation Oncology, Ordensklinikum BHS, Prof. Dr. Hans Geinitz** is part of the therapeutic axis in tumor treatment and contributes significantly to the evaluation of the course.
- **Medical Engineering - FH University of Applied Science, Prof. Dr. Hubert Egger** with research in areas of "intelligent" prosthesis.

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Keywords

neurofeedback, real-time fMRI, new therapeutic approaches, reorganization, rehabilitation, plasticity

Clinical Evaluation of Electromagnetic Navigation Bronchoscopy



“Technology that lets us view previously inaccessible areas of the lung is changing the landscape of diagnosing lung cancer and helping to save patient lives.”

Bernd Lamprecht

Research Focus

- Diagnostic yield
- Safety of ENB

Coordinators



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Vision

According to the World Health Organization, lung cancer is the leading cause of cancer death worldwide, accounting for 1.59 million deaths in 2012. [1] In its early stages, lung cancer presents few, if any, symptoms. As a result, the vast majority of lung cancer patients are diagnosed in the late stages and the long-term survival rates drastically decline. When diagnosed early, an estimated 85 percent of lung cancer cases can be treated at a more curable stage. [2]

Early detection and immediate medical treatment can dramatically increase the conventional long-term survival rate from 15 percent at five years [3] to 88 percent at 10 years. [2] The rapid and precise diagnosis of a suspicious lesion is crucial in determining optimal treatment for lung disease.

Diagnosing peripheral lung lesions are particularly challenging. It is crucial to develop technologies that can detect lung cancer so that the treatment of malignant lung disease can begin, thus improving the patient's survival rate. Electromagnetic navigation bronchoscopy (ENB) is an image-guided approach using 3D-reconstructed computed tomography (CT)-scan and sensor location technology to guide a steerable endoscopic probe to peripheral lung lesions that may be beyond of reach of conventional bronchoscopes.

Approach

The early detection, diagnosis and intervention of lung cancer are crucial to a patient's survival. Technology that gives medical professionals the ability to view previously inaccessible areas of the lung is a major advancement that is not only changing the landscape of lung cancer diagnosis, but also helping to save patient lives.

Committed to reducing lung cancer morbidity worldwide, the Department of Pulmonology at the Kepler University Hospital joined the NAVIGATE clinical trial in 2015. NAVIGATE is an international study of 2,500 patient assessing the safety and efficacy of the so-called "superDimension™ navigation system" (a system to navigate endoscopic tools to targets in the lungs, such as lymph nodes and solitary pulmonary nodules). It consists of several reusable (non-sterile) hardware components used for ENB.

The superDimension system uses LungGPS™ technology, the first of its kind to enable electromagnetic navigation bronchoscopy (ENB) procedures. ENB procedures provide a minimally invasive approach to access difficult-to-reach areas of the lung, which can aid in the diagnosis of lung disease and lead to earlier, personally tailored medical treatment — potentially saving lives. ENB procedures not only help patients avoid surgery for benign disease, but also other invasive procedures such as transthoracic needle aspiration.

To date, nearly 100,000 ENB procedures have been performed globally and commercially at more than 600 hospitals and as part of prior clinical trials.

Impact

Up to 75 centers around the world – among them the Department of Pulmonology which enrolled the first ENB patient in Europe – will enroll patients in the NAVIGATE single-arm, multi-center observational study designed to evaluate the diagnostic performance of ENB procedures.

The NAVIGATE study aims to determine the success rate of physicians using the technology to obtain biopsy samples from the surrounding lymph nodes. In addition, the study will assess the effectiveness of physicians' placement of fiducial markers or dyes to guide subsequent procedures to ablate or remove lung tumors.

Competencies

Research in electromagnetic navigation bronchoscopy will be represented and conducted by the following departments/institutions:

- **Medtronic plc (medtronic.com)**, headquartered in Dublin, Ireland, is among the world's largest medical technology, services and solutions companies — alleviating pain, restoring health and extending life for millions of people around the world. Medtronic employs over 85,000 people worldwide, serving physicians, hospitals and patients in approximately 160 countries.
- **Department of Pulmonology** with research focused on early detection and diagnosis of lung cancer, part of the Austrian Lung Cancer Study Group (ALCG).

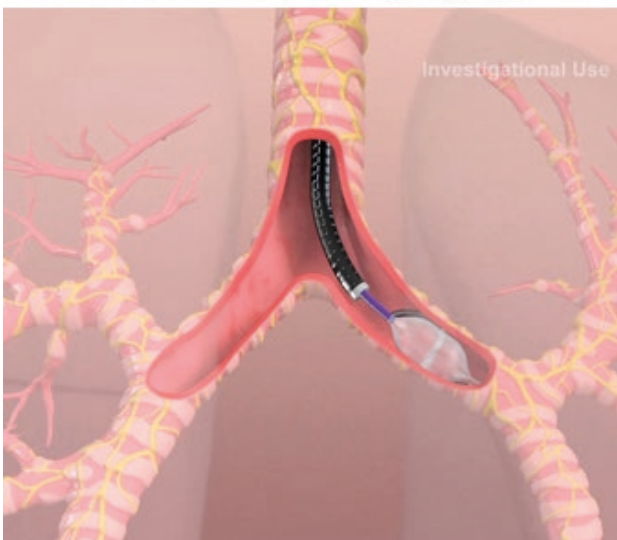
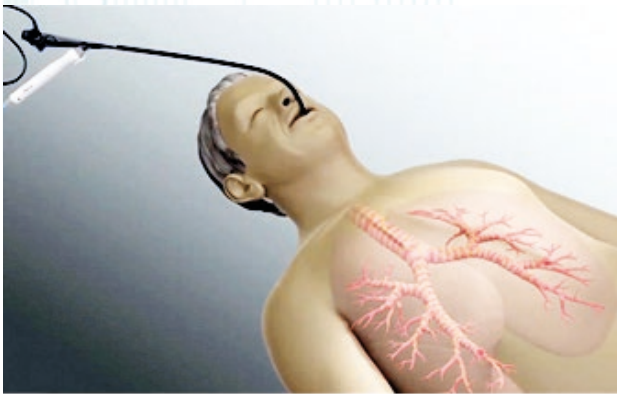
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Keywords

electromagnetic navigation bronchoscopy, diagnostic yield, safety

Targeted Lung Denervation



“Targeted Lung Denervation has the potential to provide lasting improvement for COPD patients by dilatation of obstructed airways.”

Bernd Lamprecht

Research Focus

- Safety and efficacy of TLD
- Radiofrequency (RF) energy
- Interruption of nerves outside of the airways

Coordinators



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Vision

Chronic Obstructive Pulmonary Disease (COPD) is characterized by a persistent limitation of airflow that is progressive and interferes with one's normal breathing. COPD is a less recognized yet leading cause of morbidity and mortality worldwide. An estimated number of nearly 190 million suffer from COPD [1].

Most patients are treated pharmacologically and use inhalers once or twice a day to relax and temporarily open airways. Other forms of treatment include pulmonary rehabilitation, oxygen administration, and surgical intervention.

Holaira Inc. is developing a minimally invasive device designed to treat COPD. This simple, one-time bronchoscopic treatment is called Targeted Lung Denervation (TLD) and has the potential to provide COPD patients with lasting, whole lung improvement by opening obstructed airways and making it easier to breathe.

Approach

The Department of Pulmonology is partnering in the airflow trial and attempting to establish targeted lung denervation as a viable option for COPD.

The study's purpose is to evaluate the safety of Targeted Lung Denervation (TLD) in patients suffering from moderate to severe COPD. It is hypothesized that TLD will have a similar safety profile and improved physiological and functional outcomes to a sham-control.

This one-time bronchoscopic procedure utilizes a special catheter, the dNerva™ Dual Cooled Radiofrequency Catheter, to provide an ablative therapy that opens obstructed airways.

Impact

Patients suffering from COPD may experience shortness of breath, wheezing, chest tightness, airway inflammation, and a productive cough.

Targeted Lung Denervation (TLD) is a non-surgical procedure that interrupts nerve signals and may reduce COPD symptoms, helping patients to breathe easier. A standard bronchoscope is passed through the patient's mouth and into the lungs and a special catheter, the dNerva™ Dual Cooled Radiofrequency Catheter, is passed through the bronchoscope to provide the treatment.

When activated, the electrode delivers a type of electrical energy called radiofrequency (RF) energy, which penetrates to interrupt the nerves located just outside of the airways. Upon completion, the catheter and the bronchoscope are removed and the nerves distal to the treatment site have been interrupted decreasing nerve signals throughout the lung on both sides.

Following TLD, it is expected to see a relaxation of the airway, a decrease in mucus production and a decrease in airway wall inflammation. With these improvements, the air can then more readily pass into and out of the lungs, breathing becomes much less labored and lung function may improve.

Competencies

Research in targeted lung denervation for lasting bronchodilation will be represented and conducted by the following departments/institutions:

- **Holaira Inc.** is committed to conducting rigorous clinical studies that help advance medical care for patients with obstructive lung diseases.
- **Department for Pulmonology** with research focused on COPD and interventional bronchoscopy.

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Keywords

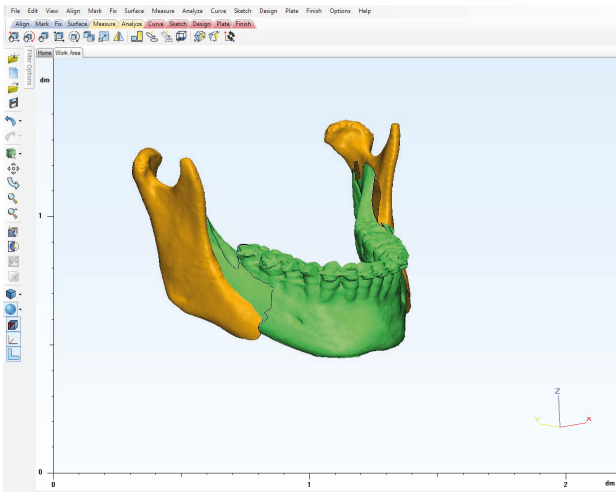
chronic obstructive pulmonary disease, lung function, targeted lung denervation, intervention, safety

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LITHOZ

Kepler
Universitäts
Klinikum

Using Zirconia-oxid Ceramics in Cranio-Maxillofacial Surgery



Writing is easy. All you have to do is cross out the wrong words.

Mark Twain

Research Focus

- Orthognathic surgery
- Visualization of the operation site
- 3-D planning of the operation result
- 3-D planning of the osteosynthesis material
- Printing of the osteosynthesis material in Zirconia-oxid-Ceramics

Coordinators



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Vision

Previously impossible until now, new production processes allow for the use highly bio-compatible materials during surgery. Lithoz®, a highly innovative company, can print zirconia oxide ceramics that are 15 µg thick. Studies have shown that zirconia oxide ceramics are advantageous due to their high level of bio-compatibility. [1-3] Due to the excellent properties of zirconia oxide ceramics, they have been used for decades in dentistry for crowns and dental implants. [4-6] Because of its brittle properties, zirconia-oxide cannot be adapted to the operation site. New technologies in the 3-D visualization, such as Mimics®/Materialise® used by our department for medical application, allow us to plan the operating result. Based on DICOM data, Mimics®/Materialise® visualizes the operation and the results are used to create osteosynthesis plates. The digital data produced by Mimics®/Materialise® is then sent to Lithoz® so that the osteosynthesis plates can be printed.

Approach

Orthognathic surgery is a well-established field in cranio-maxillofacial surgery. Until now, boney fragments were fixed using titanium plates. However, the micro-movements between the screws and the plates created titanium particles causing inflammation in the surrounding soft tissue. [7, 8] This resulted in the removal of osteosynthesis plates after a healing period of about 8 months. The highly bio-compatible zirconia-ceramics may justify maintaining the osteosynthesis materials and avoid a second surgery. In addition, the pre-formed, customized osteosynthesis plate could optimize operation results.

Visualization and 3-D planning should be available to a surgeon to allow him/her to prepare for complex operations in detail. This project gives students an opportunity to become familiar with the new technology early on. In addition to joint and interdisciplinary research, we also apply new teaching models. Bachelor and Master's degree theses are jointly supervised by engineering scientists and medical doctors. Students can work at the JKU laboratories and as well as at the Kepler University Hospital facilities. This model appears to be highly attractive and well accepted by JKU students.

Impact

Over the past few decades, orthognathic surgery has developed as an important area in the field of cranio-maxillofacial surgery. Steady efforts are being made to improve operation planning and accuracy and the new technologies in zirconia processing may help to avoid additional surgeries. Visualizing the operation in situ will be a new procedure for students to learn as well as a fundamental tool that will have a deep impact in the future.

Competencies

Research in visualization and 3-D planning will be represented and conducted by the following department:

- **Department of Cranio- Maxillofacial Surgery** with research focused on visualization and 3-D planning of tissue regeneration in the head and neck region.
- **Lithoz Ltd.**, based in Vienna, specializes in the development and production of ceramic materials and additive manufacturing systems (3-D printing) for the simple and cost-effective production of high-performance ceramic prototypes, small scale series, and complex parts.

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Keywords

zirconia-oxid ceramics: Le Fort I osteotomy, osteotomy technique, virtual surgical planning, 3-D printed surgical templates

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Shifting the Limits of Resuscitation Using “CIRD - Controlled Integrated Resuscitation Device”



CIRD 1.0 – First human use

“We can increase resuscitation time limits significantly by using CARL and CIRD”

Jens Meier

Research Focus

- Resuscitation
- Extracorporeal Life Support
- Intensive Care Medicine
- Ischemia/Reperfusion Injury

Coordinators



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Vision

Sudden cardiac arrest is one of the most frequent causes of death. The gold-standard medical therapy is “CPR – Cardiopulmonary Resuscitation”. In Europe, CPR is performed 400,000 to 500,000 times a year but the clinical outcome is dramatically poor: Only 3% of the patients survive out-of-hospital resuscitation and only 18% survive in-hospital resuscitation, most of them showing signs of severe irreversible brain damage. Over the past few decades, we have not seen any compelling improvement in the clinical outcome and there is no conclusively significant scientific advancement regarding resuscitation. Today, the time limit for successful resuscitation is 5 to 10 minutes after cardiac arrest. The new CIRID 2.0 is an innovative medical device system that can significantly shift the time limits of resuscitation, resulting in a higher patient survival rate and with little or no brain damage [1].

Approach

The overall concept underpinning the project is a completely new resuscitation therapy called “CARL – Controlled Automated Reperfusion of the whole body” [2]. In order to perform resuscitation, the user requires the “CIRID 2.0 – Controlled Integrated Resuscitation Device” developed by ResuSciTec [3]. Combined with a replenishment of substrates and cell energy to support the subsequent repair processes, CARL can minimize reperfusion injury [4]. There are two main features of this particular therapeutic strategy: (a) adapting the chemical composition of the reperfusion solution using drugs, and (b) controlling the physical conditions of reperfusion, such as flow, pressure, temperature etc. The core of this particular therapeutic approach is to measure a set of biomarkers in real-time and take immediate therapeutic measures by administering drugs. The following biomarkers are monitored and regulated: Arterial pO₂, saO₂, pCO₂, Ca²⁺, Na⁺, K⁺, pH, HcT, BE and venous svO₂, Hb. The rapid controlled and automated adaption of chemical and physical parameters during the treatment is a completely new approach in the field of cardiopulmonary resuscitation.

Impact

As most resuscitation efforts take place outside of a hospital environment, it was clear from the start that CIRID must be a mobile device that can be taken to a patient's location. Following an initial clinical study on CIRID 2.0's technical development, work began in 2013 to develop a miniaturized, mobile device. This revolutionary CIRID 2.0 device will be an innovative product in the field of resuscitation medicine designed to support individualized patient treatment. A significantly higher number of people will be able to survive cardiac arrest and the quality of survival will be better than it is today. Other benefits include a significant net cost savings to the health care system. This device is game-changing in a field of medicine that has seen little clinical improvement over the past few decades but is a continual social challenge as cardiac arrest is one of the leading causes of death. Based on the new personalized therapeutic concept CARL, the CIRID system is the first device in the world that lets the user successfully resuscitate patients either in or outside of a hospital environment and far beyond today's standard, recommended 10-minute timeframe after cardiac arrest.

Additional impacts include: (1) Prolonging the timeframe after cardiac arrest significantly in regards to the time in which resuscitation can be successful. (2) Avoiding and minimizing reperfusion injury during resuscitation. (3) Complete control of all corresponding diagnostic data and control parameters necessary to perform individual resuscitation. (4) Small, lightweight, modular device that can also be used outside of a hospital environment. CIRID 2.0 can be transported quickly and easily to resuscitate patients in need. (5) Safe, user-friendly system. Developed in a hospital environment, CIRID 2.0 adheres to the highest standards of usability.

Competencies

Research in resuscitation, ECLS, and ischemia/reperfusion injury will be represented and conducted by the following departments:

- **Research Group for CIRID and CARL at the Clinic of Cardiac Surgery, University of Freiburg** with research focused on developing CARL and CIRID and experience in developing advanced state-of-the-art resuscitation strategies using ECLS in an effort to prevent whole body ischemia/reperfusion injury.
- **Department of Anesthesia and Critical Care Medicine** with research focused on ECMO and ECLS, and technical resuscitation solutions.

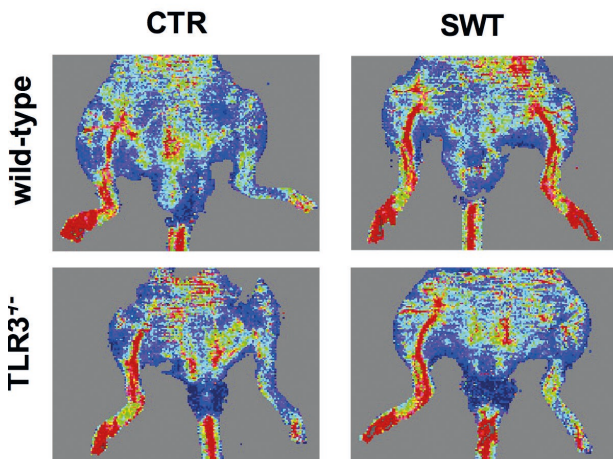
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Keywords

resuscitation, ECMO, ECLS, intensive care medicine, cardiac surgery, anesthesiology, ischemia reperfusion injury

Extracorporeal Shock Wave Therapy (ESWT) for Tissue Regeneration



“Low energy extracorporeal shock wave therapy is an emerging therapeutic option to treat all kinds of injuries. Since our group has discovered the mechanisms of mechanotransduction, we have been able to broaden applications to other areas, including cancer therapy.”

Patrick Paulus

Research Focus

- Analysis of the mechanisms of ESWT in different pathologies
- Target and indication research for ESWT
- Establish ESWT as treatment in wound healing
- Basic research on ESWT

Coordinator



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Vision

Over the past decades, the number of large surgeries due to severe illnesses such as cardiovascular disease has steadily increased. In this regard, we saw an increased number of severe complications pertaining to wound healing. Today, we see multi morbidities in patients, making major surgeries prone to complications such as impaired wound healing and thus leading to infections and sepsis. New therapies are needed to counteract these problems. Over the past several years, we have explored the potential of low energy extracorporeal shock wave therapy (ESWT) and its capability to improve wound healing and tissue regeneration.

Current studies focus on analyzing the exact mechanisms as to how ESWT mechanical stimulus translates into a biological action, the so-called mechanotransduction. During the course extensive research projects, we were able to demonstrate that ESWT not only improves tissue regeneration following myocardial infarction [1], but also that ESWT may even protect from neuronal degeneration as cause of spinal ischemia due to large operations on the aorta [2]. Our research group was recently able to discover the important ways that ESWT actions could pave the way to new indications[3].

ESWT has been showed to be highly effective when treating chronic wounds and the recorded side effects have been minimal. Our research aims to show that ESWT a highly effective treatment to regenerate tissue and improve wound healing. Older multi-morbid patients suffering from peripheral occlusive arterial disease or cardiac diseases combined with i.e. diabetes (that highly affects wound healing) will profit from this therapeutic concept in particular.

Approach

Biomedical base research in ESWT (fundamental technologies and corresponding research fields) is studied in perioperative and intensive-care patients as well as patients who have a history of cardiovascular disease and exhibit chronic wounds. Base-knowledge research will be conducted at the Laboratory for Experimental Anesthesiology and clinical studies will be conducted at the Department of Anesthesiology and Operative Care at the Kepler University Hospital. ESWT devices are being developed and enhanced together with industrial partners. In the future, research may be applied to other areas and fields - such as cancer and internal medicine - opening the door to greater cooperation opportunities at the medical campus.

In addition to joint and interdisciplinary research, we are also applying new teaching models. Bachelor and Master's degree theses are jointly supervised primarily by medical physicians. Students may work at the JKU laboratories or use the facilities at the Kepler University Hospital. This model appears to be highly attractive and well accepted by JKU students.

Impact

Over the past few decades, the demand for effective regenerative therapies has steadily increased due to a rise in co-morbidities, the numbers of wound healing impairments, ischemic diseases, and failure of tissue regeneration. In order to meet the demand, extensive research is required in this field and new medical devices, such as ESWT devices, need to be developed. The expected, long-term impact is to be able to provide improved, patient-centered medical care.

Competences

Research in anesthesiology and intensive-care medicine will be represented and conducted by:

Department of Anesthesia and Operative Care

with research focused on the application of ESWT for particular diseases, such as myocardial infarction, ischemic, resp. hypoxic tissues, chronic wounds. Future studies will also focus on new applications for ESWT .

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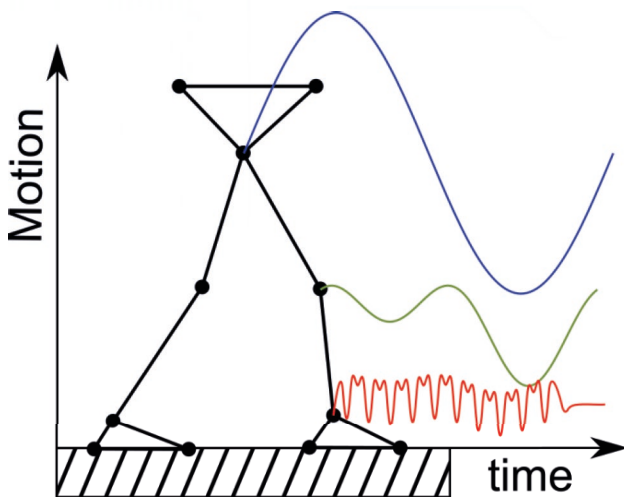
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Keywords

extracorporeal shock wave therapy, angiogenesis, mechanotransduction, tissue regeneration, chronic wounds, acute wounds, toll like receptor-3

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Parkinson's Disease - Motion and Gait Lab



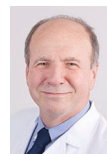
"Mobility and gait, essentials of quality of life - ambient quantitative assessment determines diagnosis and treatment"

Gerhard Ransmayr

Research Focus

- Movement and Gait
- Parkinson's disease
- Mobile Lab
- Signal Processing and Analysis
- Pattern Recognition, Classification, Prediction

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Vision

Following Alzheimer's disease, Parkinson's disease (PD), the second most age related neurodegenerative disease affecting the motor system as well as cognitive and behavioral functions [1,2]. Taking demographic development into account, the aging society's longevity and the age related prevalence of PD, the number of patients suffering PD will steadily increase. The annual occurrence over the age of 65 is 160 per 100.000 [3].

PD patients display motor system related symptoms such as bradykinesia, tremors, rigidity, and impairment of postural reflexes, gait and balance.

The state and progression of PD is measured by the Unified Parkinson's Disease Rating Scale (UPDRS) which consists of a four-part questionnaire. Part III covers the motor system evaluation by obtaining parameters such as determining rigidity, hand movements, toe tapping, gait and freezing of gait [4]. Most of these parameters are subjectively measured on an ordinal scale by the physician or caregiver. Similar parameters are used for the Tinetti test which provides a score to determine the risk of falling [5]. As the parameters can be subject to different interpretations, physicians and caregivers can lack the ability to objectively quantify the evaluation results. This can lead to inconsistent longitudinal measurements when assessing the progression of PD or if evaluating whether or not a particular therapy is effective.

The assessment process would be significantly improved and could better measure the pace and direction of PD if there were a reliable metric of the motor system parameters. A more precise UPDRS and Tinetti test would allow us to advance the development of **new PD treatments and therapies faster, better, and more cost effectively as well as lower the risk of falling.**

Approach

Implementing an interdisciplinary strategy based on sensor technology, optimized signal processing, pattern recognition as well as biomechanical and neurological knowledge will yield alternative and optimized methods, algorithms, and hardware designed to better assess the movement and gait parameters and thus alleviate the patients' motor system both at the hospital and at home.

The project focuses mainly on creating a mobile motion lab for either intra or extramural approaches and to conduct R&D for small wearable sensors that could record movement data 24/7.

Impact

Over the last few decades, obtaining an objective, independent assessment has become more important than ever before as evidence-based medicine is what helps physicians create customized therapies and treatments that can improve a PD patient's quality of everyday life.

Evidence-based assessments, however, require high end, interdisciplinary techniques in order to create reliable, standardized examination methods.

Competencies

Expertise in biomedical technology, data acquisition and signal processing focusing mainly on neurology and medical examinations is represented and conducted by the following departments:

- **Department of Neurology 2, Med Campus III** focuses on PD research and the development of new examination and therapy strategies.
- **Business Division for Biomedical Technology** conducts targeted research to acquire and process motion and gait parameters as well as develop a mobile lab.
- **Institute of Signal Processing** with research focused on algorithmic, architectural and hardware-oriented aspects of signal processing systems in ICT as well as sensor and biomedical, biomechanical signal processing.

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Keywords

motion and gait analysis, computer-aided diagnosis, pattern recognition, Parkinson's Disease, risk of falling, Tinetti Test

CUNECI - Clinical Use Cases for Non-Invasive Electrophysiological Cardiac Imaging



“The systematic search for Clinical Use-Cases for Noninvasive Electrophysiological Cardiac Imaging provides clinical professionals with modern diagnostic methods and therapeutic tools to benefit their patients. At the same time, the reasons why many promising developments never bridge the gap between engineering, research, and their clinical use can be studied and we can develop countermeasures, methods and processes to successfully bridge that gap.”

Christoph Hintermüller

Research Focus

- Clinical Use-Cases
- Diagnosis and Treatment
- Electrophysiological Imaging
- Cardiac Single Beat Imaging
- Cardiac Source Models

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Vision

Research in the field of biomedical and clinical engineering generates strong findings, results and prototypes for new and improved medical as well as clinical tools and processes. Utilizing these in a clinical context for diagnosis and treatment would be desirable but rarely happens. Questions posed by engineering, developers, and researchers remain unanswered when it comes to patient benefit, creating new methods and tools, the additional effort needed to apply and integrate new approaches and changes in the clinical process, and integrate these changes to become a routine part of clinical operations.

The “Clinical Use-Cases for Non-Invasive Electrophysiological Cardiac Imaging (CUNECI)” project aims to conduct research to explore non-invasive methods of imaging cardiac electrophysiology (NICE) as a clinical tool. The research will lay the groundwork for these clinical tools, methods and processes and help us to achieve our objectives. Over the next eight to ten years, these clinical tools will be used to create and coordinate new research projects focusing on the search for clinical use-cases that utilize NICE methods as well as the seamless integration in to existing clinical processes.

Approach

Two approaches will be applied. The first approach will be to develop a real-time NICE system. It will initially provide time-based, (AT) [1][2][3][4] NICE algorithms (which have been used in the past to study Wolff-Parkinson-White syndrome), atrial flutter, and atrial fibrillation [4]. All NICE methods carried out over the past decades require the same basic procedure as shown in the figure, which is independent of the targeted cardiac parameter and the affected part of the heart, the atria, ventricles, epicard or endocard.

The CUNECI project supports vital work that will not only help create an expert system allowing us to collect comprehensive information pertaining to electrophysiological cases and evaluate their clinical relevance in regards to NICE, but also take clinical efforts and achieved patient benefit into account. We will be able to monitor ongoing biological, medical and clinical research and collect the results as well as develop related technological advancements. The CUNECI project will play a key role in creating an expert system to support new research projects as well as monitor and adapt the research focus in other ongoing projects.

Impact

The CUNECI project will facilitate the transfer of research in NICE methods to help them become real-world applications at the clinic and be used as a valuable tool for cardiac diagnostics as well as the electrophysiology-guided and supported treatment of cardiac diseases. At the same time, CUNECI and its seeded projects will provide a better understanding of the requirements to successfully implement biomedical research as part of a clinical framework, helping to define necessary procedures and clinical tools.

Competencies

The study of non-invasive imaging used in cardiac electrophysiology and implementing biomedical research findings into a clinical context will be represented and conducted by the following departments:

- **Institute of Biomedical Mechatronics** with research focused on algorithmic, architectural and hardware oriented aspects of non-invasive imaging of cardiac electrophysiology as well as basic aspects of clinical implementation, such as necessary tools, and clinical recommendations.
- **Clinic for Cardiology and Internal Intensive Care** with research focused on the ECG's morphology for specific diseases, such as myocardial infarction, anemia, ischemia, hypoxia, etc.

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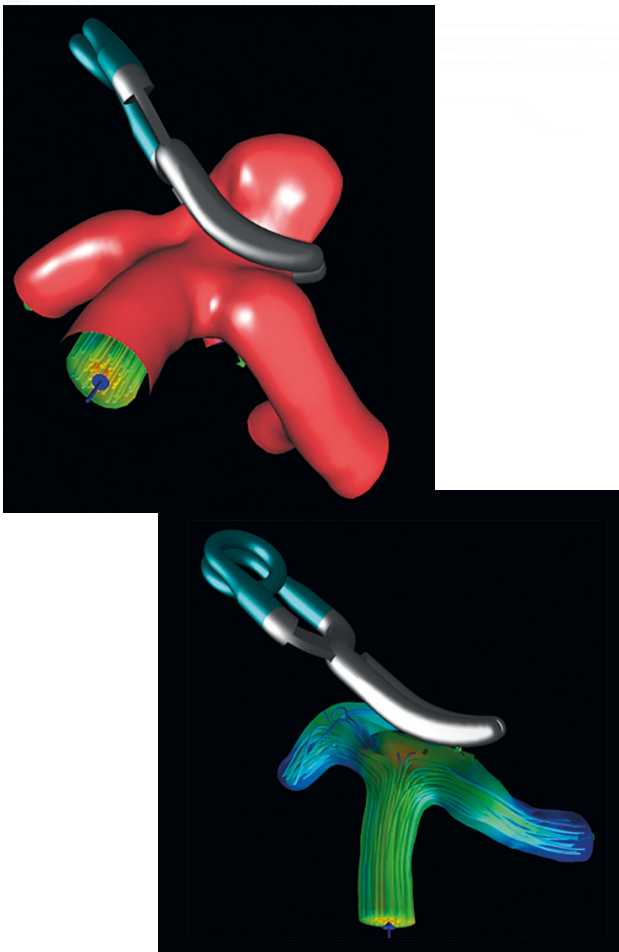
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Keywords

non-invasive imaging, cardiac electrophysiology, clinical use-cases, clinical tools and processes, source models, case models

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1010

Vascular Neurosurgery - “Virtual Aneurysm” and Intraoperative Imaging



“Precise surgical exposure is everything...”

Andreas Gruber

Coordinators



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Research Focus

- “Virtual aneurysm”
- Simulation-based training
- Vascular neurosurgery
- Biomodelling
- Indocyanin green (ICG)-Angiography
- Intraoperative imaging

Vision

Subarachnoid hemorrhage due to a ruptured cerebral aneurysm is an often fatal form of a stroke. Therapeutic interventions include surgical clipping and endovascular treatment options. Our project aims to improve surgical education and intraoperative imaging techniques that may contribute to patient safety as well as the successful outcome of a micro-neurosurgical cerebral aneurysm clipping.

Many simulation-based surgical training methods have been developed in recent years, particularly in the field of neurosurgery. Neurosurgery is a highly complex surgical discipline requiring realistic educational opportunities in a safe environment to enhance the quality and efficacy of surgical education. In addition to resident education, we could further increase patient safety by providing improved preoperative planning and using effective models as part of a daily routine to refine surgical skills.

A virtual surgical simulator could play a key role in medical education and practicing standard procedures during resident training. A virtual surgical stimulator would also benefit experienced neurosurgeons, giving them an opportunity to refine their own technical skills as well as provide a safe environment to review and discuss highly complex surgical cases, options, and potential procedures.

Approach

In cooperation with the Department of Neuroradiology and RISC Software Ltd. (Hagenberg), we are developing a virtual aneurysm clipping prototype simulator featuring real-time haptic force feedback. In order to create a realistic virtual environment, it is vital for software engineers and neurosurgeons to work closely together. Bimanual virtual surgery is performed using two haptic input devices. The aneurysm clipping is simulated by using original clipping forceps connected to these devices. Spatial depth perception is also required for the operation. The surgical performance is evaluated using blood flow simulation.

During microsurgical operations, the smallest vessels need to be preserved to avoid perioperative cerebral infarction. Research on intraoperative imaging using endoscopic Indocyanin Green (ICG) Angiography might enhance intraoperative possibilities that could preserve those important vessels.

Impact

Virtual simulation-based training can improve the quality and efficacy of surgical education. Our long-term objectives are to conduct research in surgical education and imaging so we can increase patient safety and improve surgical outcome.

Competencies

Research in vascular neurosurgery medicine will be represented and conducted by the following departments:

- **Department of Neurosurgery** with research focused primarily on
 - 1) intraoperative imaging using endoscopic Indocyanin Green (ICG)-Angiography
 - 2) surgical education by the development of a virtual aneurysm clipping simulator and 3D printing models
 - 3) multicenter studies focusing on cerebral vasospasm after subarachnoid hemorrhage
 - 4) functional and neuropsychological outcome after aneurysm surgery
- **RISC Software Ltd.** - cooperation in the project virtual aneurysm
- **Department of Neuroradiology** - cooperation in the project virtual aneurysm

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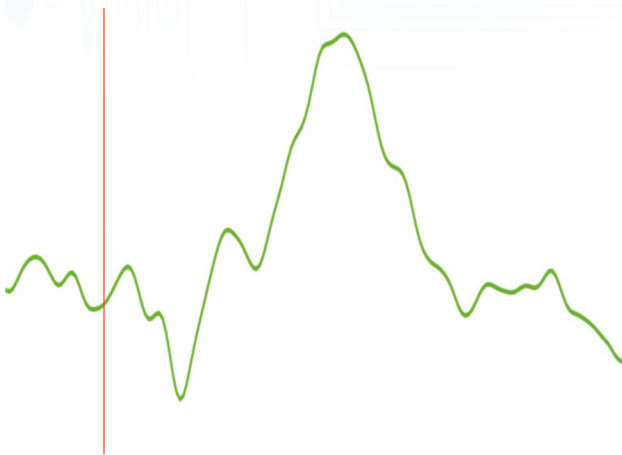
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Keywords

virtual aneurysm, real-time haptic force feed-back, cerebral aneurysm surgery, clipping, virtual aneurysm clipping, neurosurgery, surgical education, ICG Angiography, intraoperative imaging

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Brain Computer Interface



“Just how unconscious and unresponsive are comatose patients? Registering responses from comatose patients.”

Tim J von Oertzen

Research Focus

- Signal Processing and Analysis
- Evoked potentials, event related potentials
- Pattern Recognition, Classification, Prediction
- Disorders of consciousness
- Clinical correlation

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Vision

Diagnosing UWS or MCS patients is difficult, resulting often in misclassifications. A 2009 study on diagnostic accuracy compared clinical consensus versus a neurobehavioral assessment [1]. Out of 44 patients diagnosed with UWS based on a medical team's clinical consensus, 18 (41 %) were found to be in MCS following a standardized assessment using the Coma Recovery Scale-Revised (CRS-R). The result is consistent with previous studies that showed 37 % to 43 % of patients diagnosed with VS demonstrated signs of awareness [2,3]. Classification scales are based on behavioral observations or assessment of auditory, visual, verbal and motor functions as well as communication and arousal level. New technologies that could provide additional data about the brain's activity would be an ideal tool to overcome the restrictions imposed by behavioral rating scales. Patients may be able to modulate their brain responses despite being unable to produce the behavioral changes required for the rating scale. Monti et al. [4] demonstrated that functional magnetic resonance imaging (fMRI) could detect voluntary changes in the blood oxygenation-level-dependent responses that are related to imaginary motor movements or spatial imagery tasks, diagnosed in 5 out of 54 patients who have a disorder of consciousness (DOC). Four of them had previously been classified to be in MCS. Thus, in a minority of cases, patients who meet the behavioral criteria for a UWS have residual cognitive function and even conscious awareness. The approach could be twofold: the first step would be to assess the level of consciousness and the second step would be to use the BCI to open up a new channel of communication.

EEG based BCIs can also detect brain activity resulting from mental imagery or attempting a motoric movement. There are also other BCI paradigms that can determine whether or not someone can voluntarily respond to a predefined task, thus showing there is a level of awareness. EEG based BCIs have other advantages relative to fMRI-based assessments; for example, EEG systems are much more cost effective and portable, and can be easily used at the patient's bedside.

When working with DOC patients, we use tactile and auditory EP approaches as well as motor imagination (MI) to control the BCI. These can all be used without vision and each have unique advantages: MI can provide faster communication than a non-visual EP BCI, whereas EP BCIs requires very little training. Therefore, this hybrid BCI protocol can implement a wide range of EEG-based BCI approaches to treat DOC patients.

Approach

The fundamental technologies and corresponding research fields are Brain-Computer Interfaces, machine learning, computer science, biomedical signal processing, pattern classification and recognition as well as neurology and intensive-care medicine. Data is acquired by using active EEG electrode technology with a high resolution 24 bit bio-signal amplifier. The g.USBamp allows us to record 16 EEG channels with a sampling rate of 38400 Hz. The onset of auditory and tactile stimulation is recorded by the amplifier as well, resulting in high precision of trigger information. Data are analyzed both online and offline and can be imported to common biosignal analysis tools.

Impact

The methods we are working on will result in creating a relatively easy tool to assess brain response within the DOC patient's EEG signal. We can interpret classification results and accordingly adjust medication and/or change therapies and other medical treatments that have been prescribed by medical experts. The expected long-term impact is to improve diagnostic accuracy in patients who are unable to move. The second expected long-term impact will be to improve and enhance communication methods to not only improve the patient's quality of life, but also the quality of life for the patient's loved ones.

Competencies

Research in signal processing, neurology and neurorehabilitation will be represented and conducted by:

- **Coma Science group, Université de Liège** with research focused on the diagnosis and rehabilitation of patients suffering DOC, using neuroimaging techniques.
- **Laboratoire de recherche en neuroimagerie of Centre hospitalier universitaire vaudois (CHUV)** with research focused on prediction measures for coma rehabilitation and clinical trial validation.
- **g.tec medical engineering** with research focused on BCI software using machine-learning algorithms and BCI hardware, working on state of the art wireless biosignal data acquisition.
- **Department for Neurology 1** with research focused on patients who display disorders of consciousness, including unresponsive wakefulness and a minimally conscious state.

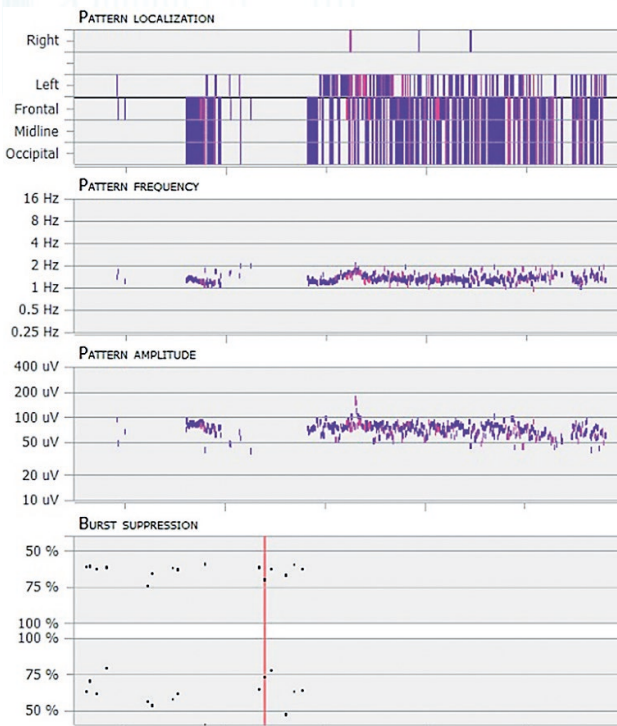
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Keywords

biosignal analysis, computer-aided diagnosis, Brain-Computer Interfaces (BCI), EEG, Evoked Potentials (EP), Unresponsive Wakefulness Syndrome (UWS), Minimally Conscious State (MCS), Disorders of Consciousness (DOC)

EEG Signal as Biomarker



“Detecting deteriorating brain function early as a biomarker in stroke medicine – an opportunity to revolutionize stroke care.”

Tim J von Oertzen

Research Focus

- Signal processing and analysis
- EEG recording, trend analysis
- Pattern Recognition, classification, prediction
- Cerebrovascular Disease
- Clinical correlation

Coordinators



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Vision

In recent years, there has been a growing interest to conduct application-oriented research in the field of continual EEG monitoring, particularly monitoring critically ill patients who have been diagnosed with brain diseases. In 2007, the American Clinical Neurophysiology Society (ACNS) created the critical care EEG monitoring research consortium to provide a forum for collaborative research and to support quality improvements and standardized clinical practices for critical care EEG monitoring. Published in August 2012, the guidelines for critical care EEG standardized terminology is an important milestone in this emerging field [1]. State-of-the-art, continual EEG is recommended when monitoring a non-convulsive epileptic status, non-convulsive seizures, and other seizure-like occurrences [2].

There are discussions that cEEG may be helpful in the early protection of brain ischemia. Up to 40 % of patients who have suffered from an ischemic stroke also suffer from epileptic seizures. Furthermore, there is evidence that EEG monitoring might detect early stages of acute ischemia at a point when neural damage could still be reversible [3]. Research shows that reduced cerebral blood flow results in slowing in EEG. Potentially, EEG might qualify as an outcome predictor or monitoring a therapeutic effect [4] namely δ (1-4 Hz, 20-200 μ V. Some authors support EEG to differentiate the type of ischemia between cortical infarct causing EEG abnormality and lacunar infarct, not being detected by EEG [5].

Approach

Using EEG analyses on critically ill patients to monitor seizure activity is a well-established practice. The goal is to focus on brain ischemia and further develop signal analysis and processing. In this regard, data pertaining to stroke patients - particularly those who have had a severe medial cerebral artery stroke or an intracranial bleed - will be monitored sooner for up to 7 days in order to acquire data sets for this particular patient group. EEG data and the patient's clinical course will be analyzed. The main goal is to develop an EEG algorithm that would give the clinician a better visual impression in regard to any EEG changes. Ideally, we could create a type of 'alarm' to alert the clinician if there are any significant pathological changes. More advanced phases would see the algorithm tested on patients in order to detect any changes in blood flow and edema early, particularly at a reversible stage

Impact

Stroke incidents have increased and a severe stroke is still the third most common cause of death. Being able to reliably detect deterioration early among patients in this group can lead to early, successful medical intervention. A hemispherectomy, for example, could improve patient survival rates and lessen the disability outcome. Early detection might open new therapeutic doors that could see the use of non-invasive procedures to save endangered brain tissue.

Competencies

Research in EEG signal processing, neurology, particularly epilepsy and stroke care, will be represented and conducted by the following departments:

- **Dr. Grossegger & Drbal GmbH** with research focused on EEG and SLEEP diagnosis.
- **Austrian Institute of Technology**, Business Unit Digital Health Information Systems with research on algorithms for computational analyses of clinical EEG, focused on epilepsy, neurocritical care, neuro rehabilitation, and neonatal intensive care
- **Department for Neurology 1** with research focused on EEG diagnostics, epilepsy and stroke medicine.

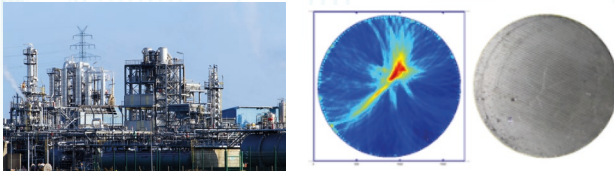
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Keywords

bio-signal analysis, computer-aided diagnosis, EEG, trend analysis

From Non-Destructive to Non-Invasive and POC



“Our task as a research company is to provide benefits to everyone who can profit from our research. Be it the heavy steel industry, chemical industry, medical personnel or, last but not least, patients in need.”

Peter Burgholzer, CEO
RECENTDT GmbH

Research Focus

- Photo-Acoustic Imaging
- Photo-Acoustic Microscopy
- Spectroscopic diagnostics at the Point-of-Care
- Early diagnostics of Breast Cancer

Coordinators



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Vision

RECENDT is active in two major fields of medical research: Photo-Acoustic Imaging (PAI) and Spectroscopic Diagnostics. Both of these fields provide benefits to support a daily clinical routine and aid patients in the future. Spectroscopic diagnostics aims to provide new, rapid diagnostic tests that generate results directly at the point-of-care. These user-friendly devices can allow patients to conduct daily diagnostic tests at home based on few drops of saliva, urine, tear fluid or even blood. New and easy analyses can be derived from one's breath, making a completely new range of non-invasive diagnostics available.

Photoacoustics, on the other hand, aims to make the following reality:

First, create a new method of early breast cancer detection by combining the most advantageous aspects of ultrasound diagnostics and X-ray mammography but avoiding ionizing radiation.

Second, we aim to develop a precision surgical tool used for open brain operations that provides a continuous high-resolution 3D-image of all cerebral structures. The tool will be designed to deliver optimum information but eliminate the cumulating dose of ionizing radiation.

Approach

Photo-Acoustic Imaging and Microscopy [1] rely on converting ultra-short pulses of laser light to acoustic waves. The conversion depends on the absorption properties of tissue irradiated by the laser. By measuring the emitted acoustic waves, we can reconstruct a 3D-image showing all spatial, localized variations of the absorption properties. The reason for variations can be numerous, such as cancer cells will show deviations and blood-vessels will relay different signals than muscular tissue.

Spectroscopy relies on the influence of matter when electromagnetic waves pass through it or at least interact on the surface. When passing through red or white wine (or when reflected from a stain on the white tablecloth) visible light changes color. The same happens to infrared light, or any light from ultraviolet to terahertz waves contained in the wide variety of wavelengths. Many of these wavelengths can be used to retrieve very specific information on the material being evaluated. Infrared spectroscopy is a standard analytical technique used to determine the chemical parameters mainly in fluids but also in gases. Ongoing technological advancement provides new opportunities to apply new methods of spectroscopy: higher sensitivity reduces the amount of fluid needed to obtain reliable analytics; smaller spectrometers could help to create handheld devices; new approaches in data processing can uncover concealed information and turn blurred, raw spectra into valuable data available in real-time [2].

RECENDT has been conducting research in these fields of technology for many years. We are also focusing on research in OCT (Optical Coherence Tomography), and a 3D-imaging technique to, for example, investigate superficial structures in the skin [3].

By working in these fields of expertise, we aim to try and increasingly combine technologies and focus on the benefits (e.g., OCT + Spectroscopy, PAI + OCT, Spectroscopy + PAI) [4].

By implementing the collective expertise of surgeons and physicians and cooperating with innovative medical technology companies, we aim to not only take our research results and products to the market, but also make it a part of daily clinical routines at hospitals worldwide.

Impact

Our techniques can be applied as a part of a regular hospital routine to provide easier diagnostic and imaging, reduce exposure to ionizing radiation, and shorten time and efforts when it comes to diagnostic analyses. This, in turn, saves money and benefits the patient by providing quick, accurate treatment options.

New methods in spectroscopic diagnostics will play a key role in bringing new devices to the market; devices that can provide easy, non-invasive and highly accurate diagnostic testing patients can do themselves in the privacy of their own home. By adding online-monitoring concepts, big data, and e-health, we can change our approach to preventative health care in ways once thought unimaginable ...

Competencies

RECENDT is a research company closely associated with the Johannes Kepler University Linz (JKU).

The topics as presented above are ongoing research in our groups for PHOTOACOUSTICS (Dr. Thomas Berer), INFRARED and RAMAN SPECTROSCOPY (Dr. Markus Brandstetter) and OCT (Dr. Andreas Buchsbaum).

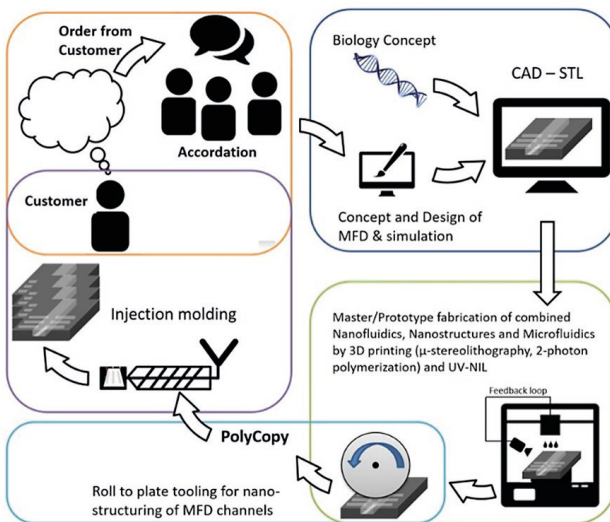
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Keywords

biomedical imaging, in-vivo imaging, photo-acoustic imaging, early diagnostics of breast cancer, point-of-care diagnostics, spectroscopy, NIR, IR, Raman, OCT/ Optical Coherence Tomography, malignant changes in the skin, tumor markers

Rapid Prototyping of Nanostructured Functional Microfluidic Devices



“The development of a true “Killer Application” for micro-fluidic devices requires standardized, flexible and fast processes ranging from biotechnology concepts to functional prototyping and mass fabrication.”

Dr. Thomas Lederer & Dr. Daniel Fechtig

Research Focus

- Biochemistry, Microfluidic Prototyping
- 3D printing
- Nanotechnology, surface functionalization
- Injection molding process simulation

Coordinators



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Vision

Biotechnological microsystems almost always require microfluidic concepts since biological targets are both in vitro and in vivo and almost always submersed in fluids [1]. The benefits of miniaturization in biotechnology and biomedical applications range from small volume requirements and reduced costs to parallelization of measurements and faster assays, drug delivery and diagnostics, highly effective point-of-care and point-of-analysis, detection of subtle phenomena, and high-throughput. Methods used in nanotechnology and conventional microfabrication are either not suitable for mass production and the production of micro and macro features and prototyping is too expensive and time-consuming for proof-of-principle studies. They require numerous processing steps as well as a plethora of high-level knowledge and expert skills [2]. In addition to these technical challenges, there is a great divide between innovative microfluidic concepts and ideas toward a final transition to commercial markets and applications. Basic concepts conceived by universities and research institutions bring forth many of the above-mentioned expertise, process knowledge, and ideas for developing innovative microfluidic concepts. There have been extraordinary advances in the development of individual lab-on-a-chip components, but few microfluidic technologies have made the leap to fully functioning integrated devices [3]. However, both the “idea” side and the “market” side have one common feature: both of these must demonstrate real social and economic value. The joint research chain starting with a biotechnological concept to a production ready prototype will enable short development cycles.

Approach

Common research is pillared by institutions and experts in biotechnology (PLUS: biochemistry, microfluidic prototyping), manufacturing technology (PRO: 3D printing, nanotechnology, surface functionalization), mass production technology (JKU: injection molding and simulation) and mainly focuses on matching ideas as well as bringing applications and markets closer together. This is envisaged by offering three distinct research services: (1) a product roadmap “manufacturing concept from idea to market”, (2) feasibility studies employing rapid prototyping methods, and (3) specific training in application and production. The main objectives include creating a fast, easy, flexible, and cost-effective manufacturing process and ready-to-use complex microfluidic concept prototypes to our key customers (researchers, device producers, biotechnology industry, the medical industry). We intend to make use of a unique combination of additive manufacturing, lithography, plastics replication techniques, and conventional mass fabrication techniques. We will provide a highly flexible prototyping/mastering system compatible with conventional mass production techniques while also integrating opto-electrical and nanofeatures into the devices. The services and products we can offer are of potential interest to small and large biotechnology companies that need mass production concepts as well as to universities that require fast microfluidic prototypes to assess biological and medical research.

Impact

By taking the projected microfluidic market size into account (annual 5.7 billion Euros in 2018), creating fast development cycles starting from the idea to application are essential. The process chain will bring new, innovative biotechnological and medical devices to the market. The targeted, long-term impact is improved, individualized health care.

Competencies

Research in signal microfluidic design, additive fabrication of micro inserts and micro-injection molding will be represented and conducted by the following groups:

- **PLUS** with research focused on assay design and readout parameters, sensory elements for biotechnology and diagnostics and the integration of nanostructured materials
- **JKU** with research focused on micro injection molding, with 3D printed mold inserts and process simulation.
- **Profactor** with research focused on the production of microstructures using stereolithography, 3D printing, nanoimprint lithography, and soft and hard replication techniques in order to produce master and injection mold inserts for micro injection molding

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Keywords

biochemistry, microfluidic prototyping, 3D printing, nanotechnology, surface functionalization, micro injection molding and process simulation

Research Unit Medical Informatics



“A unique combination of skills in mathematics, computer science and practical experience is helping us to develop solutions to address complex and challenging medical problems.”

Dr. Michael Giretzlehner

Research Focus

- Biomechanical modelling and simulation
- Medical image processing
- Medical education and training systems
- Expert-driven data analysis
- Medical product development

Coordinators



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Vision

Medical care has become increasingly important in our aging society and information technology is one of many key enabling technologies. Medical Informatics focuses on the systematic processing of data, information and knowledge in medicine and health care. Methodologies and tools in computer sciences, mathematics, physics, business and medicine are used to create specialized solutions for patients, doctors, and the health care system. Now and in the future, we feel a strong responsibility to support medical advancement by applying information technology, especially to improve diagnostic methods and optimize health care processes. Our vision is to improve medicine qualitatively and quantitatively in regards to procedures in medical processes as part of the health care system, research, and patient care. By closely observing future trends in the medical field, our focus and vision at the Research Unit Medical Informatics will be significantly influenced. Both basic research (RISC Institute) and applications (RISC Software Ltd.) endure to this day and we continue to cooperate closely with director Prof. Dr. Peter Paule in numerous ways.

Approach

As an institution of multidisciplinary research and development, the Research Unit Medical Informatics at RISC Software Ltd. (RISC-MI) has been successfully addressing and solving issues in the medical field for over a decade. RISC-MI develops software products and software systems that are used at many national and international medical institutions. This includes the continual advancement of existing projects such as See-Kid/CEVD [1], BurnCase 3D [2], MedVis 3D [3] and CALUMMA [4] as well as continually introducing new, innovative projects with both new and existing partners in the medical and technical field. RISC-MI is a non-university affiliated research department with years of experience in acquiring and managing research grants. RISC-MI is funded by the Upper Austrian strategic economic and research program "Innovatives OÖ 2020".

Impact

Owned by the Johannes Kepler University Linz (80%) and Upper Austrian Research Ltd. (20%), RISC Software Ltd. was founded in 1992 by Univ. Prof. Dr. phil. Dr. h.c.mult. Bruno Buchberger as part of the RISC Institute. RISC is a long-established, national and international IT service company focused on incorporating mathematics and computer sciences to create real-world software solutions for businesses as well as interdisciplinary medical and industrial teams. To this day, Dr. Buchberger continues to serve as a mentor and lend his expertise to RISC. Based on long-standing activities conducted together with physicians and hospitals, the Research Unit in Medical Informatics has established a strong market position and boasts an excellent reputation as a partner in the development of unique software solutions. Our target group primarily includes local hospitals in Upper Austria but also extends worldwide. We focus mostly on specialized medical areas (such as burns, aneurysms) to advance and develop strategic technologies that support competition and growth within the complex field of medicine. RISC-MI is also provides various types of simulation systems designed to educate and train surgeons. Collaboration efforts with

local companies enable us to transfer knowledge and technology throughout Upper Austria. Our research has been published in numerous international scientific and academic journals and presented at scientific conferences.

Competencies

Biomechanical Modelling and Simulation

- Simulating interaction between biological structures
- Anatomically correct adaptation of 3D patient models
- Simulation of blood flow, with deformation of vessel walls
- User interaction with haptic input devices

Medical Image Processing

- Reconstruction and patient-specific virtual replicas for visualization, simulation and calculation
- Objective assessment and documentation of body surface area based on photos [2]
- Feature extraction from medical images

Medical Education and Training Systems

- Neurosurgical operation simulator and for surgical planning
- Training ophthalmologists and orthoptists to better understand the basic function of eye movement
- Training opportunity to assess affected body surfaces

Expert-Driven Data Analysis [4]

- Structured generic ontology-based medical data collection
- Easy data integration from various existing systems
- Medical validation and plausibility check of data
- Enabling the (medical) domain expert to use complex IT methods (visualization, data mining, machine learning...) without any specific IT expertise
- Medical studies and documentation

Medical Product Development (requirements of ISO 13485)

References

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Keywords

biomechanical modelling, biomechanical simulation, medical image processing, medical education, medical training, expert-driven data analysis, medical product, medical software

3D Reconstruction for Healthcare Applications



“Advances in 3D signal processing and machine learning pave the way for personalized medicine.”

Andreas Pichler

Research Focus

- 3D reconstruction
- Photorealistic texture mapping
- Visual computing

Coordinators



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Vision

Due to demographic shifts and globalization, expenses for health care is on an unsustainable trajectory. The search for economic sustainability is present in different ways - from health care reforms in many markets to investments for better access in the developing world (e.g. Africa) respectively in emerging markets (e.g. China). Strongly influenced and driven by digital disruption, new sustainable approaches will be developed improving applications in this field. On the transition to a mobile decentralized health care, patients will turn from passive recipients of care to empowered consumers, with more information and control over their health decisions [1], [2].

Recent investigations in domain-independent 3D reconstruction towards anonymous and patient-specific 3D human body models resulted in a remarkable response from medical sector. PROFACTOR's activities [3] are characterized by using low-cost consumer market devices from a hardware perspective and sophisticated algorithms for 2D and 3D data processing. Focusing on ease of use, best possible reproduction of details and extensibility for new sensor technology led to domain-specific requests and subsequent research activities. Publishing an open programming development kit ("ReconstructMe SDK") encapsulating 3D reconstruction enabled independent and application-related research and developments. Potential use cases and applications with early adopters are already active in the field of orthotics and prosthetics, plastic surgery and custom wheelchairs. Moreover, the usage of technology as monitoring tool either for weight watching after bariatric surgery or when suffering from obesity is highly relevant. Finally, there are a multitude of application ideas involving the technology as 3D documentation concept [4], [5].

This research aims for leveraging the involvement of low cost 2D and 3D technology for smart and sustainable health care approaches supporting practicing clinicians in their daily business as well as empowering patients by providing better access to decentralized devices and applications bringing more information and control over their health decisions.

Approach

Relevant techniques and methods are used from established computer science disciplines such as image processing, computer graphics and machine vision. In particular, visual computing skills are used to apply existing scientific approaches to real world applications. Due to the embedding of this research within PROFACTOR's key research topics 'industrial assistive systems' there is also a strong knowledge on appropriate concepts and methods for adequate human computer interfaces. This is important to simplify the interaction for human users and to boost user-acceptance.

While current work is focusing on rigid reconstruction on local computing power, the research roadmap foresees the need for non-rigid reconstruction techniques to extend the scope of applications to moveable objects and also to leverage the process of digitization (e.g. natural movements while digitizing). In addition, emerging cloud-based infrastructures will serve as ubiquitous platform and computation power. This simplifies the usage and eliminates complex local configurations and boosts the access of services by lowering requirements for local computation power.

Impact

Modernization and innovations within the health care sector are strongly influenced by well-known megatrends such as 'digitization', 'personalization', 'globalization' and a 'sharing economy'. 3D reconstruction with low cost sensor devices, intuitive usability and accessibility via existing computing and communication infrastructures is one important fragment towards more sustainable approaches boosting decentralized, preventative and cost-effective health care.

Competencies

Research disciplines in image processing, machine vision, computer graphics and applied research skills related to visual computing will be represented and conducted by the following departments:

- **Machine Vision** team with a background in image processing, machine vision, computer graphics and machine learning using relevant methods in particular for production-relevant inspection challenges.
- **Visual Computing** with research focusing on visual perception technologies and software engineering disciplines, having the expertise to turn partial scientific approaches into applicable prototypes and components for products.
- **Assistive robotics** experts transferring expertise from collaborative robotics in respect to human-machine interaction concepts.

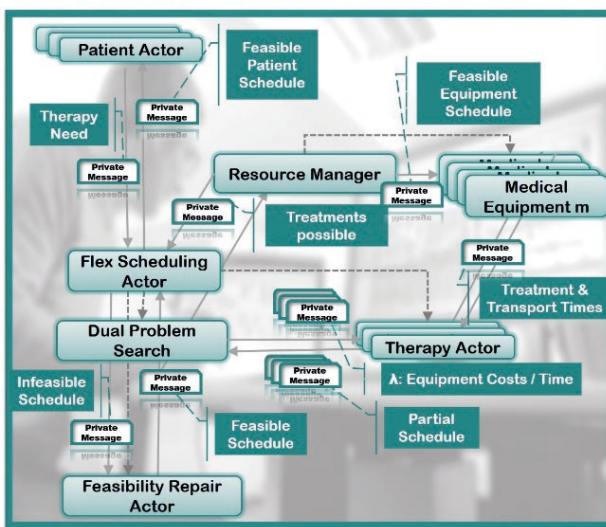
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Keywords

3D reconstruction, texture mapping, visual computing, ReconstructMe, low-cost body scanning, object recognition, object tracking, orthotics, prosthetics, 3D documentation, injury documentation, multi modal mapping, mobile health care, telehealth

Interoperability between Medical Information Systems



“While current Information Systems are networked, interaction between systems is limited. The next leap in medical information systems research will be made through making data and processes of multiple systems interoperable in a systemic manner.”

Georg Weichhart

Research Focus

- Information Systems
- Enterprise Interoperability
- Distributed Artificial Intelligence
- Complex Adaptive Systems

Coordinators



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Vision

Medical Information Systems today are rapidly evolving following the emergence of new knowledge within individual medical specialties. While it is important to be able to provide functionality in-line with the state-of-the-art, we increasingly aspire to be able to connect information stemming from multiple sources in an automated manner supporting the diagnosis. Available information should be made useful for other systems. Today data, services and processes are hardly interoperable between different medical specialties. A patient-focused approach to interoperability enables

- Semantic data exchange between heterogeneous systems [1]
- Process and Schedule Interoperability for treatments spanning multiple medical departments and specialties [2]
- Continuous learning and improving of loosely coupled information systems [3]
- Distributed and decentralized information storage and processing increased data privacy and security [4]

Approach

Enterprise Interoperability research promises to support heterogeneous information models on the data-level, service-level, process level, and business level [5]. New research is currently evolving to support the complex adaptive enterprise as a distributed information processing system [6], [1]. Interoperability – in contrast to application integration approaches – allows for a loose coupling while supporting learning and evolution of sub-systems [3]. This important aspect to not hardwire different systems allows individual parts to be updated and exchanged without impacting other parts of the overall system. This goes far beyond existing concepts such as DevOps which ensure compatibility without the direct support of exchanging information.

Subject Oriented Process Management is an approach related to Multi Agent Systems allowing to model workflows from the different participants' perspective. Multi-Actor Systems are a technological approach that supports distributed processing and modelling of a system as a complex adaptive system. The actors provide the means for abstraction and design. Using Algorithms from Distributed Artificial Intelligence, the distributed information and actors may be used to generate and optimize schedules and plans. These technologies and methods support Manufacturing Enterprises in the need for self-managed information flows enabling cognitive robotics.

Impact

The assumption of continuous developments and changes in the overall system's organizational and technological infrastructure requires a new information system middleware. A framework that includes knowledge management methods is available, but bringing it down to the specific field of application is very specific. The impact is to be able to dynamically connect information services and connect data ranges by enabling consistency checks through a better understanding of past treatments and be able to schedule patients and medical treatments in an optimized, yet still patient centered manner.

Competencies

Research in the above discussed Information Systems approach is represented and conducted by the **Distributed Information Systems** team at Profactor. The team is working on approaches involving Distributed Artificial Intelligence, Multi-Actor Systems, Enterprise Systems Interoperability, Subject-oriented Business Processes.

References

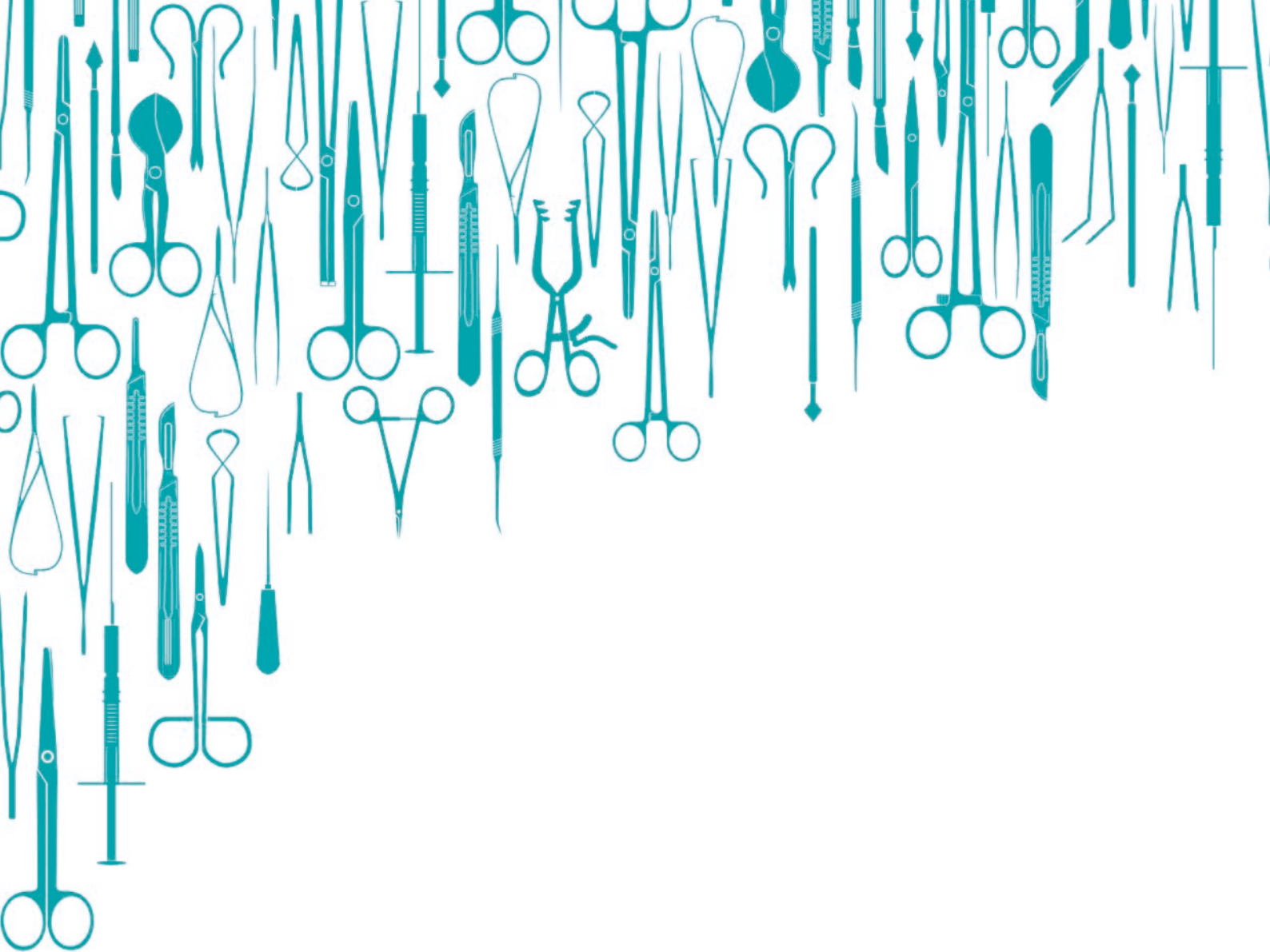
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Authors

- Achakri**, Hassan - 112
Affenzeller, Michael - 96
Apfalter, Petra - 110
Batinic, Bernad - 18
Baur, Eva-Maria - 98
Bauer, Robert M. - 78
Bauer, Harald - 148
Bauer, Thomas - 98
Baumgartner, Werner - 40, 118
Berer, Thomas - 142
Berger, Veronika M. - 54
Bergmair, Bernhard - 116
Bernhard, David - 20
Bodenhofer, Ulrich - 22
Böhler, Nikolaus - 112
Bolz, Matthias - 76
Brandstetter, Markus - 142
Brüggemann, Oliver - 24
Buchberger, Wolfgang - 26
Buckwar, Evelyn - 28
Burgholzer, Peter - 142
Dirnberger, Johannes - 136
Doppler, Christian - 20
Ecker, Julius - 86
Ebner, Thomas - 72, 84
Egger, Hubert - 98
Fechtig, Daniel - 144
Fellner, Franz A. - 112, 114
Fenz, Wolfgang - 136
Ferscha, Alois - 30
Franz, Barbara - 100
Fuchs, David - 82
Futschik, Andreas - 32
Gabriel, Michael - 116
Garn, Heinrich - 106, 108
Geinitz, Hans - 38
Girardi, Dominic - 82, 146
Giretzlehner, Michael - 146
Gmeiner, Matthias - 136
Grossegger, Dieter - 140
Gruber, Andreas - 120, 136
Güttel, Wolfgang - 34
Guger, Christoph - 138
Guggenbichler, Josef-Peter - 36
Hagelauer, Richard - 66
Haselmayr, Werner - 90
Haslinger-Eisterer, Bettina - 22
Haring, Hans-Peter - 120
Hassel, Achim Walter - 36
Heindl, Christoph - 148
Heise, Bettina - 38
Heitz, Johannes - 40
Hilber, Wolfgang - 46
Hinterdorfer, Peter - 42
Hintermüller, Christoph - 134
Hochholdinger, Bernhard - 44, 88, 132
Horner, Andreas - 64
Huemer, Mario - 44, 132
Hunger, Stefan - 126
Jacak, Jaroslav - 48
Jakoby, Bernhard - 46
Kellermair, Jörg - 118
Kisling, Rüdiger - 106
Klampfl, Christian - 26
Klar, Thomas - 48
Kleiser, Raimund - 120
Klinger, Markus - 116
Kluge, Tilmann - 140
Knör, Günther - 50
Knoll, Wolfgang - 36
Knyazev, Denis - 64
Koch, Stefan - 52
Kovacs, Carrie - 18
Kropfmüller, Roland - 122, 124
Lamprecht, Bernd - 122, 124
Lanzerstorfer, Peter - 104
Lepperdinger, Günter - 144
Major, Zoltan - 54
Malek, Michael - 126
Mardare, Cezarina Cela - 36
Mayr, Herwig - 100
Mayrhofer, René - 56
Meier, Jens - 22, 44, 102, 128
Miethlinger, Jürgen - 58
Müller, Norbert - 60
Müller, Thomas - 20
Narzt, Wolfgang - 62
Oppelt, Peter - 84
Ortner, Rupert - 138
Paulus, Patrick - 130
Pichler, Andreas - 148
Pohl, Peter - 64
Pomberger, Gustav - 74, 114
Pretl, Harald - 66
Pröll, Johannes - 84
Ramlau, Ronny - 68
Ransmayr, Gerhard - 106, 108, 132
Reiter, Martin - 54
Resch, Reinhard - 70
Romanin, Christoph - 72
Rozenblit, Jerzy W. - 74
Sametinger, Johannes - 74
Sariciftci, Niyazi Serdar - 76
Schrefl, Michael - 52
Schrempf, Andreas - 102
Schüßler, Elke - 78
Schwentenwein, Martin - 126
Semenov, Serguei - 80
Shamiyeh, Andreas - 30
Siligan, Christine - 64
Simader, Franz Markus - 88
Stiglbauer, Barbara - 18
Soler, Yolanda Salinas - 24
Stary, Christian - 52
Steinbichler, Georg - 144
Steinwender, Clemens - 40, 74, 118, 134
Stelzer, Andreas - 80
Streit, Marc - 82
Struhal, Walter - 44, 106, 108
Tamborrino, Massimiliano - 28
Teasdale, Ian - 24
Thumfart, Stefan - 146
Tiemann-Boege, Irene - 72, 84
Trenkler, Johannes - 120, 136
Trieb, Klemens - 102
Trummer, Georg - 128
v. Oertzen, Tim J. - 62, 138, 140
Vosko, Milan R. - 80
Wagner, Erika M. - 86
Wagner, Helga - 32
Wagner, Roland - 88
Weghuber, Julian - 104
Weichhart, Georg - 150
Weichselbaum, Otto - 62
Weiß, Rainer - 86
Wille, Robert - 66, 90, 92
Winkler, Stephan - 96, 104
Yazdi, Kurosch - 120
Zagar, Bernhard - 94
Zierer, Andreas - 20
Zwettler, Gerald - 100



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