2nd International SIIRI Symposium 2024

January 24th - 25th, 2024

Courtyard Hannover Maschsee

Arthur-Menge-Ufer 3, 30169 Hannover

2nd International SIIRI Winter School

Interdisciplinary Implant Sciences

January 22 – 23, 2024

2nd International SIIRI Symposium

January 24 – 25, 2024

Impressum
CRC Safety-Integrated and Infection-Reactive Implants (SIIRI)
Lower Saxony Centre for Biomedical Engineering,
Implant Research and Development (NIFE)
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Dear Colleagues,

The 2^{nd} International Symposium of the Collaborative Research Center (CRC) SIIRI will be held at the Courtyard Hannover Maschsee from January 24^{th} to 25^{th}.

The interdisciplinary CRC SIIRI is funded by the German Research Foundation (DFG) and aims at the development of new strategies for the prevention, detection and treatment of implant-associated complications in order to ensure long-term implant safety in various medical disciplines.

At the International SIIRI Symposium, we will focus on novel developments in implant medicine, with particular emphasis on new concepts for implant safety, digital implant lifecycle management, implant developments in materials science and new strategies to detect, prevent and combat biological implant-associated complications. Further topics will be biointerfaces and micro environments as well as new strategies for implant functionalization and implant-associated sensor technology.

The symposium will bring together national and international experts from various areas of medicine, engineering, natural and social sciences to promote scientific exchange. You can expect an exciting interdisciplinary scientific program with inspiring lectures by international and SIIRI speakers, poster presentations and round table discussions.

We look forward to welcoming you to our 2nd International SIIRI Symposium in Hannover!


Meike Stiesch
Spokesperson of CRC SIIRI


Hans Jürgen Maier
Deputy Spokesperson of CRC SIIRI

SCIENTIFIC PROGRAM

January 24, 2024

WELCOME

08:00 **Coffee and Registration**

OPENING

08:30

Meike Stiesch
Spokesperson TRR 298 –SIIRI
(Safety-integrated and infection-reactive implants)

Michael Manns
President Hannover Medical School

Volker Epping
President Leibniz University Hannover

Falco Mohrs
Lower Saxony's Minister for Science and Culture

BIOMATERIAL-ASSOCIATED BIOFILM INFECTIONS (PART 1)

Chair: Meike Stiesch
Auditorium, Room 5

09:00	Implant-associated infections in orthopedic and trauma surgery – A combined experimental and clinical perspective **Volker Alt, Regensburg, Germany**
09:40	Peri-implant microbiome in health and disease **Egija Zaura, Amsterdam, Netherlands**
10:20	Bacterial adaptation to biofilm growth **Susanne Häußler, SIIRI, Hannover, Germany**

10:40	**Coffee break**

BIOMATERIAL-ASSOCIATED BIOFILM INFECTIONS (PART 2)

Chair: Henning Menzel

Auditorium, Room 5

11:10	Associations and causality of peri-implant and periodontal diseases with systemic diseases **James Deschner, Mainz, Germany**
11:50	Uncovering of molecular mechanisms involved in biofilm-associated peri-implant infections **Meike Stiesch, SIIRI, Hannover, Germany**
12:10	Controlled drug release from modified cells using physical and physiological triggers **Dagmar Wirth, SIIRI, Braunschweig, Germany**

12:30	**Lunch**

BIOINTERFACES

Chair: Dagmar Wirth
Auditorium, Room 5

13:30	Overcoming biological barriers in infectious diseases - Complex in vitro models and advanceddrug delivery approaches **Claus-Michael Lehr, Saarbrücken, Germany**
14:10	The synovium, biointerface between joint capsule and implant: Altered functions in revision arthroplasties **Andrea Hoffmann, SIIRI, Hannover, Germany**
14:30	On the thermodynamics of biofilm growth **Philipp Junker, SIIRI, Hannover, Germany**
14:50	**Coffee Break**

INTRACORPOREAL AND IMPLANT-ASSOCIATED SENSING

Chair: Henning Windhagen

Auditorium, Room 5

15:20 The challenges and opportunities of implantable sensors
Ben M. Maoz, Tel Aviv, Israel

16:00 Sensor principles and their applications in SIIRI
Merle Sehlmeyer, SIIRI, Hannover, Germany

16:20 Autonomous chemical sensor-actuator systems for the detection and control of implant-associated infections
Henning Menzel, SIIRI, Braunschweig, Germany

16:50 Optical sensing and detection of infections in implantology
Alexander Heisterkamp, SIIRI, Hannover, Germany

CONSIDERING SEX AND GENDER IN IMPLANT SCIENCE

Chair: Anette Melk

Auditorium, Room 5

17:00	Gendered innovations in health and biomedicine **Londa Schiebinger, Stanford, California, USA (hybrid)**
17:45	**Round Table Discussions on Hot Topics in Implant Research**
18:30	**Poster Session and Get Together**

SCIENTIFIC PROGRAM

January 25, 2024

WELCOME

NEW APPROACHES TO IMPLANT DEVELOPMENT IN MATERIALS SCIENCE

Chair: Hans Jürgen Maier
Auditorium, Room 5

09:00	Development of biodegradable surgical wires for veterinary medicine **Andrij Milenin, Krakow, Poland**
09:40	Integrating machine learning into metallurgy: road map to novel implants **Demircan Canadinç, Istanbul, Turkey**
10:20	Micro- and nanostructured surfaces and materials to control cell and bacterial surface interactions **Peter Kingshott, Melbourne, Australia**
10:40	Recent insights into a niobium-base alloy as an implant material **Julian Schleich, SIIRI, Hannover, Germany**
11:00	A 3D in vitro-model of implant-associated osteomyelitis: from biomimetic materials to multicellular systems **Cornelia Lee-Thedieck, Hannover, Germany**
11:20	**Coffee Break**

IMPLANT TECHNOLOGIES

Chair: Susanne Häußler
Room 6

09:40	The Effects of different grading approaches on peri-implant bone stress in additively manufactured dental implants **Osman Akbas, Hannover, Germany**
10:00	Phenotype of mesenchymal stromal cell and articular chondrocyte cocultures on highlyporous bilayer PLLA scaffolds produced by thermally induced phase separation and supplemented with hydroxyapatite **Camilla Carbone, Palermo, Italy**
10:20	Mitigating stress shielding in dental implants through topology optimization and fatigue modeling **Hüray Ilayda Kök, Hannover, Germany**
10:40	Native proteins in tissue engineered scaffolds **Sara Leal-Marin, Hannover, Germany**
11:00	Biomimetic bone implants: Developing a 3D-printable nanohydroxyapatite/ methacrylated gelatine-based nanocomposite hydrogel **Nadine Schadzek, Hannover, Germany**
11:20	**Coffee Break**

ACCEPTANCE OF MEDICAL TECHNOLOGY INNOVATIONS

Chair: Eva Baumann
Auditorium, Room 5

11:40	Taking the agency of medical technology users and social concerns seriously **Christopher Coenen, Karlsruhe, Germany**
12:20	Barriers and facilitators of information seeking about medical innovations in the public **Elena Link, SIIRI, Mainz, Germany (hybrid)**
12:40	The role of language regarding the acceptance of smart implants **Charlotte Schrimpff, SIIRI, Hannover, Germany**
13:00	Results Round Table Discussion
13:10	**Lunch**

IMPLANT SAFETY AND DIGITAL IMPLANT LIFECYCLE MANAGEMENT

Chair: Peter Wriggers
Auditorium, Room 5

14:00	Certification and management of endoprosthetics centers **Gabriela von Lewinski, Göttingen, Germany**
14:40	Implant safety in joint replacements **Jan-Philippe Kretzer, Heidelberg, Germany**
15:20	NeWTranslation - Implant Lifecycle Management software support for the development of medical devices up to the first-in-man study **Simon Pieske, Aachen, Germany**
15:40	Digital Implant Lifecycle Management – Implant monitoring from the idea to a digital twin **Marcel Wichmann, SIIRI, Hannover, Germany**

16:00	**Closing Remarks and End of Symposium**

SPEAKERS' SHORT BIOGRAPHIES

in alphabetical order

PROF. DR. DR. VOLKER ALT

University Hospital Regensburg, Germany

Professor Alt currently serves as the Director of the Clinic and Polyclinic for Trauma Surgery and holds the Chair of Trauma Surgery at the University Hospital Regensb urg. His academic journey includes attaining an extraordinary professorship at Justus-Liebig-Universität Gießen in November 2011.

In 2009, Professor Alt's extensive research and expertise were recognized through the habilitation process, earning him the Venia legendi in Orthopedic and Trauma Surgery at Justus-Liebig-Universität Gießen. His habilitation thesis focused on "Gentamicin-Hydroxylapatit and Gentamicin-Hydroxylapatit-RGD Coating for Cementless Endoprostheses." This experimental study in rabbits delved into antimicrobial efficacy, bone formation, and biocompatibility. Further enriching his academic profile, Professor Alt obtained a Ph.D. in Human Biology from Justus-Liebig-Universität Gießen in 2007. His dissertation delved into the health economic aspects of recombinant human Bone Morphogenetic Protein-2 in open tibia fractures.

A central theme of Professor Alt's research lies in the development of novel implants for trauma surgery and orthopedics. His investigations extend to innovative treatment methods for bone and implant-associated infections, as well as exploring biomaterial applications for healing fractures in osteoporosis. At the forefront of understanding the pathophysiology of bone and implant infections, Professor Alt pioneers new therapeutic strategies. He actively engages in scientific associations, holding memberships in esteemed organizations

PROF. DR. DEMIRCAN CANADINÇ

Koç University, Turkey

Following post-doctorate appointments at the University of Paderborn in Germany and the University of Illinois, He joined the Mechanical Engineering Department at Koç University in, where he is currently working as a full professor. Dr. Demircan Canadinç received his PhD in Mechanical Engineering from the University of Illinois at Urbana-Champaign in 2005.

Based on his scholarly activities in the broad field of mechanics of materials, Dr. Canadinç was awarded the prestigious Humboldt Research Award by the Alexander von Humboldt Foundation in Germany in October 2022.

His research focuses on the numerical and experimental characterization of metallic materials, and alloy design for structural, aerospace, and biomedical applications. Within the recent years, he has adapted the artificial intelligence techniques to metallurgical problems, focusing on the design of refractory high-entropy alloys and high-temperature shape memory alloys.

Professor Canadinç is internationally well known for his outstanding research in advanced metallic materials. He has made important contributions to the understanding of the micro-deformation mechanisms and the corresponding effects on the materials' performance. He combines machine learning, deformation modeling at different length scales with experimental methods. Prof. Canadinc has also owned and operated a Texas-based scientific consulting company serving industry since 2017.

DIPL.-POL. CHRISTOPHER COENEN
Institute for Technology Assessment and Systems Analysis, Karlsruhe, Germany

Christopher Coenen is a political scientist and works primarily in the highly interdisciplinary field of technology assessment. He is head of the research group "Life, Innovation, Health and Technology" at the Institute for Technology Assessment and Systems Analysis (ITAS) within the Karlsruhe Institute of Technology (KIT).

He has been a researcher at ITAS since 2003, working also for ITAS in the Office of Technology Assessment at the German Parliament (TAB). His previous topics at ITAS included information and communication technologies, biotechnologies, nanotechnology, transhumanism and human enhancement, neurotechnologies and prosthetics, amongst others.

In recent years, he coordinated the transnational NEURON-ERANET research project "The Future of the Human Body in the Light of Neurotechnological Progress (FUTUREBODY)", which was funded in Germany by the Federal Ministry of Education and Research (BMBF), led the work of ITAS in the BMBF-funded project "Intelligent Orthotics and Prosthetics" (INOPRO) and still does so in the EU Horizon Europe project "Inspiring and Anchoring Trust in Science, Research and Innovation" (IANUS).

He is also managing editor of the journal "NanoEthics: Studies of New and Emerging Technologies" and co-editor of the book series "Technikzukünfte, Wissenschaft und Gesellschaft". His research interests include intersections of human corporeality and technology as well as the democratisation of innovation processes.

PROF. DR. JAMES DESCHNER

Johannes Gutenberg University Mainz, Germany

James Deschner is a distinguished academic and researcher in the field of dentistry, with a notable career trajectory. He earned his doctoral degree in 1997 from the Freie Universität Berlin, focusing on cytokine release from human bone and periodontal ligament cells in response to Actinobacillus actinomycetemcomitans.

Following his doctorate, Prof. Deschner held various academic positions, including roles at the University of Cologne. His international exposure began in 2002 with a postdoctoral research fellowship at the University of Pittsburgh, USA. Subsequently, he served as a Visiting Assistant Professor at the Ohio State University from 2003 to 2006, displaying versatility in oral biology and orthodontics.

Returning to Germany in 2006, he joined the Department of Periodontology, Operative and Preventive Dentistry at the Rheinische Friedrich-Wilhelms-Universität Bonn. In 2007, he completed his habilitation on the regulatory effects of biomechanical forces on fibrochondrocytes in vitro, earning the Venia legendi for "Zahn-, Mund- und Kieferheilkunde."

From 2008 to 2015, he led the DFG-funded Clinical Research Group 208, exploring the causes and consequences of periodontal diseases. n 2018, he became a University Professor at Johannes Gutenberg University Mainz and currently serves as the Director of the Department of Periodontology and Operative Dentistry.

PROF. DR. SUSANNE HÄUßLER

Center for Experimental and Clinical Infection Research (Twincore), Hannover, Germany

Prof. Häußler studied human medicine at the Medical Faculty of the University of Lübeck and the Hannover Medical School (MHH), where she also obtained her doctorate in 1995. She then worked for a year in internal medicine at the Marienhospital in Vechta and began training as a specialist in medical microbiology at the MHH, which she successfully completed in 2002. Prof. Häußler habilitated in Medical Microbiology and Infection Epidemiology in 2004.

Her particular research interest is on novel approaches for diagnosing and treating acute and chronic infections caused by the problematic opportunistic pathogen Pseudomonas aeruginosa. In 2003 she became an independent research group leader at the former Gesellschaft für Biotechnologische Forschung (GBF), and from 2005 to 2009 she headed the junior research group "Chronic Pseudomonas Infections" at the Helmholtz Center for Infection Research (HZI) with close links to the MHH, before she accepted an appointment to the W2 professorship "Pathophysiology of Bacterial Biofilms" at the MHH at TWINCORE, Center for Experimental and Clinical Infection Research in Hannover.

Since 2012, she has been Head of the Department of Molecular Bacteriology at the HZI and W3 Professor at the MHH and since August 2019, she is running an additional Novo Nordisk Foundation-funded laboratory at the Rigshospitalet in Copenhagen with the aim of establishing modern molecular diagnostics to combat bacterial multi-resistance.

PROF. DR. ALEXANDER HEISTERKAMP
Leibniz University Hannover, Germany

“I am interested in developing optical tools for the study of life at the microscopic level, a field typically termed “Biophotonics.”

I received my doctorate in Physics for realizing a new type of laser surgery in the human eye at the Leibniz University in Hanover in 2002. In 2003/04 I worked as a postdoctoral researcher at Harvard University (DFG fellow) to transfer these techniques to the cellular level. Since then I am conducting research in the field of biophotonics, for some time at Friedrich Schiller University Jena at the Institute of Applied Optics and since 2014 at the University of Hannover.

With respect to transfer into industry and applications, I am part of the Scientific Board of Directors of the Laser Zentrum Hannover.

In brief, my research interests focus on biophotonics and laser medicine, ultrashort laser pulses and nonlinear optics, laser-based imaging in microscopy and sensing, and laser manipulation of cells and tissues using ultrashort pulses, nanoparticles or optogenetics.

PROF. DR. ANDREA HOFFMANN
Hannover Medical School, Germany

"I work with conjoined twins, and my work helps many people to move well and without pain again or even to dance. Less metaphorically speaking: In my research group, we use the body's own stem cells and immune cells as the biological basis to optimize biohybrid medical implants, fighting musculoskeletal disorders."

Prof. Hoffmann currently serves as university professor within the Clinic of Orthopaedic Surgeryat Hannover Medical School (MHH) and has strong expertise in research, teaching (teaching prize in 2022) and mentoring of young scientists. She obtained her doctoral degree in biochemistry at the university of Hannover. In 2007 Prof. Hoffmann completed her habilitation earning the Venia legendi for "Regenerative Medicine". After stages as postdoctoral and senior scientist at Helmholtz Centre for Infection Research (Braunschweig) and MHH she was appointed professor at MHH in 2009. Since 2015, she is member of the NIFE (Lower Saxony Centre for Biomedical Engineering, Implant Research and Development) and served as spokeswoman for the DFG Research Unit 2180 "Graded Implants for Tendon-Bone Junctions" from 2015 - 2023.

Prof. Hoffmann is actively involved in broadening her research towards new horizons through interdisciplinary cooperations with other biomedical fields. Her research topics include mesenchymal stem cells, macrophages, and molecular mechanisms in health and disease as well as the complex interaction of novel biomaterials (specifically "graded implants") with cells, tissues, and body fluids.

PROF. DR. PHILIPP JUNKER
Leibniz University Hannover, Germany

Prof. Junker is the Managing Director of the Institute of Continuum Mechanics at Leibniz University Hannover. In 2011 he received his doctoral degree and worked as an assistant lecturer at the Chair of Mechanics of Materials at Ruhr-University Bochum until 2015. In 2016 he completed his habilitation earning the Venia Legendi for the field of “Mechanics”.

After holding several deputy professorships at the University of Wupppertal and the Ruhr-University of Bochum, he became senior engineer at the Chair of Continuum Mechanics at the Leibniz University Hannover. In 2021, after declining the call of the Technical University of Darmstadt for the professorship “Continuum Mechanics”, he accepted the call of Leibniz University Hannover to head the Institute of Continuum Mechanics. In 2023 he was awarded by one of the prestigious ERC Consolidator Grants for his research on the efficient modeling of materials with uncertain experimental data.
Central themes of Prof. Junker´s research are the theory of continuum mechanics, the mechanics of materials, including damage mechanics, stochastic material behavior and phase transformations, and topology and material optimization.

PROF. DR. PETER KINGSHOTT
Swinburne University of Technology, Melbourne, Australia

Prof. Dr. Kingshott is driven by many things but especially the fact that his research is highly multidisciplinary, and science brings together people from many different cultures all striving for the common goal of high impact research. He strives to perform research aimed at benefiting people with ailments needing real breakthroughs in short time frames. He also obtains great pleasure in seeing younger researchers gaining success in their research and his philosophy of mentorship allows them freedom to explore new ideas and think outside of the box.

Prof. Dr. Kingshott is an academic within the Faculty of Science, Engineering and Technology at Swinburne University of Technology, where he has worked since 2010. He has gained research experience at renowned institutes all over the world: CSIRO Molecular Science, Australia, the National ESCA and Surface Analysis Centre for Biomedical Problems (NESAC/BIO), Seattle, the Centre for Competence in Biomaterials at the RWTH Aachen in Germany, the Danish Polymer Centre, Riso National Laboratory, near Copenhagen and the Interdisciplinary Nanoscience Centre (iNANO) at Aarhus University in 2006 as Associate Professor.

His research interests focusing on biointerfaces and surface engineering have evolved during his research career. Recently his focus is on nanotechnology where he started developing new surface patterning techniques based on colloidal crystal layers and using functionalised polymer nanofibers by electrospinning for life science applications.

PROF. DR. JAN-PHILIPPE KRETZER
Heidelberg University Hospital, Germany

Prof. Kretzer is Director of the Section for Biomechanics and Implant Research at the Orthopaedic University Hospital in Heidelberg. Prof. Kretzer received his doctorate (Dr. sc. hum.) from the Medical Faculty of the University of Heidelberg.

His research focuses on tackling issues related to the musculoskeletal biomechanics of joints and artificial joint replacement. His main aim is to optimize implant-based treatment for affected patients. He currently focuses on understanding the failure of artificial joints, the optimization of material and design properties, as well as surgical treatment technology and patient-related factors and their influence on the durability of joint replacements.

Being a biomechanist Prof. Kretzer has made pioneering contributions to understanding the wear performance of implant components in knee, hip and shoulder endoprostheses for which he received several awards e.g. from the German Society for Orthopaedics and Orthopaedic Surgery.

PROF. DR. CORNELIA LEE-THEDIECK
Leibniz University Hannover, Germany

Prof. Dr. Cornelia Lee-Thedieck is currently heading the Institute of Cell Biology and Biophysics at Leibniz University Hannover. She studied biochemistry at the University of Tübingen. After completing her doctorate at the University Hospital in Tübingen, she moved to the Max Planck Institute for Intelligent Systems in 2007, where she initially worked as a postdoctoral researcher and later as a group leader. From 2012 to 2018, she was a junior research group leader at the Karlsruhe Institute of Technology (KIT) before taking up a professorship in cell biology at Leibniz University Hannover in October 2018.

She has successfully applied for multiple prestigious research grants. Among others, she received an ERC Starting grant for her project bloodANDbone in 2017, where she developed models of human bone marrow to study the regeneration of blood and bone by stem cells and the disruption of this regeneration in diseases such as leukemia or bone metastases. In 2023, she received an ERC Proof-of-concept grant where she and her team will validate a new, biomimetic, 3D printable material for bone regeneration.

PROF. DR. CLAUS-MICHAEL LEHR
Helmholtz Institute for Pharmaceutical Research Saarland, Saarbrücken, Germany

“The transport of active agents from the application site to the site of action plays an essential role in the successful development of new drugs. Personally, I am fascinated by the multidisciplinarity of the research approach, which reaches from molecular cell biology to macromolecular chemistry and nanotechnology.”

Claus-Michael Lehr is Professor at Saarland University as well as cofounder and head of the department “Drug Delivery and Biological Barriers” at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), which was established as a branch of the Helmholtz Centre for Infection Research (HZI) Braunschweig in 2009. Prof. Lehr has also been cofounder of Across Barriers GmbH and of PharmBioTec GmbH, a non-for-profit contract research organisation.

The research theme of Professor Lehr's team is (preferentially: non-invasive) drug delivery across biological barriers, in particular the epithelia of the gastrointestinal tract, the skin and the lungs. Recently, this has been expanded to microbial barriers, such as the bacterial cellular envelope, biofilms and host cell membranes. A substantial part of the lab’s activities is dedicated to innovative carriers systems, often based on nanotechnology, capable of safely and efficiently delivering drugs and vaccines across these barriers. In this context, the lab systematically investigates predictive cells and tissue models, preferentially human-based, to evaluate the safety and efficacy of novel therapeutic concepts and to facilitate their translation into the clinic.

JUN.-PROF. DR. ELENA LINK

Johannes Gutenberg-Universität Mainz, Germany

Since April 1, Junior Professor Dr. Elena Link has held the tenure-track junior professorship in the field of science communication at the Department of Communication, Johannes Gutenberg-Universität Mainz. Previously, she had been a research assistant at the Department of Journalism and Communication Research at HMTMH Hannover where she completed her dissertation on the role of trust in patients' health information behaviors in 2018 and then worked as a post-doctoral researcher at the Hanover Center for Health Communication.

Her research is dedicated to science and health communication. She is particularly interested in the influencing factors, types and effects of health information seeking and avoidance, the role of trust in health professionals, scientists, relatives, and media sources for patients' information behavior, as well as the potential and challenges of online communication. Her research focuses on the individual patient and their immediate support needs to take care of their health and participate adequately in their recovery. Prof. Link aims to better understand the specific information and emotional needs of patients and how physicians can support their fulfillment.

PROF. DR. BEN M. MAOZ
University of Tel Aviv, Israel

“The outcome of what we do translates into patients’ lives and improvement in their life quality. The fact that I know that we are pushing the barriers, working with amazing people and doing meaningful things gives me huge drive to do what we do. Furthermore, and not less important, is the fact that I truly love what I do, which is a hug added value.“

Prof. Ben M. Maoz, is a distinguished researcher with a rich academic background, and currently serving as an Associate Professor in Biomedical Engineering at Tel Aviv University. He completed his Ph.D. in Chemistry at Tel Aviv University in 2013, showcasing a strong foundation in the field of nanophotonics. Prior to his current position, he contributed significantly to research as a Post-Doc at Harvard University's School of Engineering and Applied Science from 2013 to 2018, in the field of Organs-on-a-Chip and tissue engineering.

Prof. Maoz's research extends into various domains, with a particular focus on advancing medical technology. Notably, he has been involved in pioneering projects, such as the development of Organs-on-Chips technology, aimed at understanding human physiology. His work involves the use of innovative sensors implanted in nerves to restore the sense of touch in limbs affected by amputation or injury, which recently he funded a startup company (Teng-able LTD.) which is based on this technology.

PROF. DR. HENNING MENZEL
Technical University Braunschweig, Germany

Prof. Menzel is a renowned academic and researcher in the field of Polymer Chemistry. He obtained his dotoral degree in Chemistry in 1990 at the Leibniz University Hannover. Afterwards he worked as assistant lecturer in the Institute for Macromolecular Chemistry and Leibniz University Hannover. As visiting scientist (Fulbright Fellow) he joined one year in the Department of Chemistry at University of Michigan. After his return to Germany he became Professor at the Institute for Technical Chemistry at the University of technology Braunschweig in 2001.

Prof. Menzel´s research focuses on application-oriented problems in synthetic macromolecular chemistry, with special interest in biomedical and biotechnological applications: Ultrathin polymer coatings are used to tailor the biointerfacial interactions with cells and bacteria. Polymeric drug delivery systems are used to implement biological signaling in biomedical devices or autonomous sensor-actuators systems to control infections

PROF. DR. ANDRIJ MILENIN
AGH University of Science and Technology in Kraków, Poland

“My motivation lies in the endeavor to develop bioresorbable metallic materials and methods of its manufacture that not only efficiently degrade in the body but also possess properties to combat cancer cells.”

Prof. Dr.-Ing. Andrij Milenin is currently a Professor at AGH University in Kraków. He can look back on many years of teaching and research experience. After receiving a degree in engineering in 1988, followed by a PhD in 1991 he received his Dr. hab. Inż. in 2001 from the National Metallurgical Academy of Ukraine. In 2003 he was nominated as professor in Ukraine and Poland ad has served as Professor at Czestochowa Technical University in 2002-2006. His career includes roles as a researcher at the National Metallurgical Academy of Ukraine. He also consulted the QForm Group (Oxford, UK).

Prof. Milenin’s research focuses on the computational mechanics procedures and metal forming processes, especially the development of software for simulation of metal working processes by Finite Element Modeling (FEM). During his career he has developed solutions for technological problems of hot metal forming using computational FEM. In the field of implantology he focuses on biodegradable surgical wires and multiscale FEM modeling of artificial heart chambers.

SIMON PIESKE, M.SC.

Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Germany

Simon Pieske completed his Master's degree (Automation Engineering) at the Chair of Automation and Control Engineering at the Laboratory for Machine Tools and Production Engineering (WZL) at RWTH Aachen University in 2018. He wrote his thesis on the "Development of a concept for the flexible sequence control of pipetting processes". He then moved seamlessly into his new role as a research assistant at the same institute and has since carried out various research projects in the field of life science and laboratory automation in particular..

PROF. DR. LONDA SCHIEBINGER
Stanford University, USA

“I’m driven by Truth, justice, and beauty achievable through.”

Londa Schiebinger is the John L. Hinds Professor of History of Science in the History Department at Stanford University and Founding Director of the Gendered Innovations in Science, Health & Medicine, Engineering, and Environment Project. Prof. Schiebinger is a leading international expert on gender in science and technology and has addressed the United Nations, the European Parliament, the Korean National Assembly, and numerous funding agencies on that topic. Schiebinger received her Ph.D. from Harvard University and is an elected member of the American Academy of Arts and Sciences.

Over the past thirty years, Prof. Schiebinger's work has been devoted to teasing apart three analytically distinct but interlocking pieces of the gender and science puzzle: the history of women's participation in science; gender in the structure of scientific institutions; and the gendering of human knowledge.

Londa Schiebinger has been the recipient of numerous prizes and awards, including the prestigious Alexander von Humboldt Research Prize and John Simon Guggenheim Fellowship.

She holds Honorary Doctorates from the Universitat de València, Spain, 2018; Lunds Universitet, Sweden, 2017; and Vrije Universiteit Brussel, Belgium, 2013.

JULIAN SCHLEICH, M.SC.
Leibniz University Hannover, Germany

Julian(-T.) Schleich studied mechanical engineering at the Leibniz University of Hanover and worked on the die forging of extruded hybrid semi-finished products made from aluminum and steel in his master's thesis. From 2018, he worked as a student assistant at the Institute of Materials Science during his studies and has been contributing his experience as a research assistant in the field of co-extrusion of implant materials since 2022.

CHARLOTTE SCHRIMPFF, M.A.

Hannover University of Music, Drama and Media, Germany

Charlotte Schrimpff finished her Master studies (Media and Music) at the Department of Journalism and Communication Research in Hanover in 2015. After various freelances (e.g. Hannoversche Allgemeine Zeitung newspaper, Leipziger Volkszeitung) and working as an online editor for the Music Festival Heidelberger Frühling and the Diocese of Feldkirch in Austria, she returned to Hanover to contribute her knowledge on health communication and strategic communication as a research assistant again at the Department of Journalism and Communication Research.

MERLE SEHLMEYER, M.SC.
Leibniz University Hannover, Germany

Merle Sehlmeyer received her B.Sc. in biomedical engineering in 2018 from the University of Applied Science Hamburg, Germany and her M.Sc. in mechatronics in 2020 from the Leibniz University Hannover, Germany. Since 2020, she is employed as a re-search engineer at the Institute of Electrical Engineering and Measurement Technology of the Leibniz University Hannover and is working on her Dr.-Ing. degree in electrical engineering. Her research focus is the impedance spectroscopy of cochlear implants.

PROF. DR. MEIKE STIESCH
Hannover Medical School, Germany

“I am fascinated by interdisciplinary research with colleagues from various disciplines to decipher the mechanisms of biofilm formation and develop innovative strategies to combat periimplant infections. As a clinician, I experience every day how important it is that our research benefits future implant and therefore patient safety. „

Prof. Meike Stiesch is the Director of the Department of Prosthetic Dentistry and Biomedical Materials Science at Hannover Medical School and currently also serves as co-director of the Management Board of NIFE (Lower Saxony Center for Implant Research and Development). Her major research focus is on biofilm-associated periimplant infections, the oral microbiome and dental materials science.
Prof. Meike Stiesch is member of acatech (National academy of science and engineering), the DFG Senate Committee for Guidelines in Clinical Science and was president of the German Society of Prosthodontics and Dental Materials from 2016 until 2021.

She was spokesperson of the research network BIOFABRICATION, funded by the Volkswagen Foundation, is a member of the Cluster of Excellence 2155 RESIST and since 2021 deputy spokesperson of the DFG Research Unit 5250 (Mechanism-based characterization and modelling of permanent and bioresorbable implants with tailored functionality based on innovative in vivo, in vitro and in silico methods). Since July 2021 she has been the spokesperson of the Collaborative Research Center SIIRI (Safety-integrated and infection-reactive implants), funded by the DFG.

PROF. DR. GABRIELA VON LEWINSKI
University Medical Center Göttingen, Germany

Prof. v. Lewinski has been Head Physician for Orthopaedics and Endoprosthetics at the Clinic for Trauma Surgery, Orthopaedics and Plastic Surgery at the Univerity Medical Center Göttingen since 01.01.2020. She previously worked as a senior consultant at the Orthopaedic Clinic at Hannover Medical School, where she also completed her training, in addition to study visits to Switzerland and the USA. She is a medical specialist in orthopaedics and trauma surgery, special orthopaedic surgery, orthopaedic rheumatology, and sports medicine.

Her clinical and scientific focus is on minimally invasive primary arthroplasty and revision arthroplasty.

DR. MARCEL WICHMANN
Leibniz University Hannover, Germany

Dr. Marcel Wichmann is a research assistant and division manager with seven years of experience and responsible for the area of Production Systems at the Institute of Production Engineering and Machine Tools (IFW) of the Leibniz University Hannover.

He obtained his Master of Science in Production and Logistics in 2016 and afterwards he worked as a research assistant at the IFW until today. In 2019, he became head of the department for process planning and simulation. Afterwards, Dr. Wichmann became head of the IFW division Production Systems since July 2021. He completed his PhD on the topic of self-optimizing process planning for tool grinding in 2022.

Dr. Wichmann is specialized in the planning of manufacturing processes in production systems. His team researches planning systems that enable autonomous and resource-efficient production by using digitalization approaches and process simulations. Mr. Wichmann has proven expertise in the field of automated process planning, especially regarding digital twins and technological process simulations. Handling cyber-physical production systems (CPPS) as well as standardized data formats and interfaces is part of his experience. This knowledge is important for the creation of digital twins and a successful processing of the subproject A01 of SIIRI.

PROF. DR. DAGMAR WIRTH

Helmholtz Center for Infection Research, Braunschweig, Germany

Prof. Wirth studied chemistry in Braunschweig. During her doctorate at the GBF - now the Helmholtz Centre for Infection Research (HZI) - she turned her attention to gene regulation in mammalian cells and studied chromosomal elements that influence the nuclear topology and gene regulation. As a postdoc, she investigated recombination in the context of virus-mediated gene transfer and developed recombinant viruses for gene therapy applications.

After working as a scientist in the Department of Clinical Immunology of the Medical University (MHH), she returned to the HZI in 2004 and shortly afterwards became Research Group Leader for Model Systems for Infection and Immunity (MSYS), which she still is today. She focuses on the investigation of immune defense mechanisms counteracting viral and bacterial infections with the aim to identify therapeutic intervention strategies. To this end, she implements advanced methods of Synthetic Biology and generates cellular and mouse-based model systems for the investigation of human-specific pathogens, with a focus on predictable and tightly controllable gene expression.

In 2014, she accepted an appointment to the Chair of 'Synthetic Biology of Cell Systems' at the MHH. Since 2020, she is deputy spokesperson of HZI's research focus CVIR (Chronic Viral Infections).

PROF. DR. EGIJA ZAURA

Vrije Universiteit Amsterdam & University of Amsterdam, The Netherlands

Professor Egija Zaura holds the position of University Research Chair Professor of Oral Microbial Ecology at Vrije Universiteit Amsterdam and serves as the head of the Division at the Academic Centre for Dentistry Amsterdam (ACTA), affiliated with VU Amsterdam and the University of Amsterdam in the Netherlands.

She obtained her Dental degree in 1995 at Karolinska Institute, Sweden.

After graduation, she combined her work in the dental clinic in Riga with accomplishing a degree in General Dentistry at Riga Stradins University, Latvia, in 1997. In 2002, she achieved a PhD in Preventive Dentistry with honors (cum laude) at ACTA.

Since 2003, Prof. Zaura has been actively involved as a researcher and lecturer at the Department of Preventive Dentistry at ACTA. Her diverse research topics encompass biofilm models, clinical studies, advanced molecular technologies in oral microbial diagnostics, and complex sequencing data analyses. Her primary research focus revolves around oral microbial ecology in health and disease, with an emphasis on translating fundamental knowledge into clinical practice.

Notably, Professor Zaura serves as the project leader of the METAHEALTH project, funded by NWO, which commenced on January 1st, 2023, and as the director of Research Priority Area on Personal Microbiome Health at the University of Amsterdam.

POSTER ABSTRACTS

in alphabetical order

Page	Presenter	Title
72	Heine	The artificial mouth – Oral biofilms grown in the lab
74	Jemaa	Advancing Dental Prosthetics: A Parametric Remodelling of Connectors in Fixed Partial Dentures and its Application in Finite Element Analysis
76	Joshi	Identification of microbiome and metatranscriptome based biomarkers associated with peri-implantitis
78	Klempt	Implementation of a numerical diffusion-driven growth model into the Neighbored Element Method
80	Klodwig	Mechanical Adaptive Silicone Composites for UV-triggered Facilitated Cochlear-Implant Removal
82	Legutko	Junction strength of double modular hip endoprostheses depending on manufacturing-related deviations
84	Malekahmadi	Integration of bone-similar tissue into the (INTERbACT) model
86	Mukherjee	High-throughput characterization of interspecies interactions in oral implant-associated biofilms
88	Muñoz-González	Development and Characterization of PCL Electrospun Nanofiber Scaffolds with Graphene Nanofiller for Tissue Engineering
90	Nnane	Self-Immolative linkers in autoregulative drug delivery systems for antibiotics
92	Reiber	Real-time assessment of implant stability: a patient-specific modelling approach
94	Reulbach	Acoustic emissions resulting from friction of different species' bone tissue against implant material: Basic research for a new approach to implant loosening detection

Cochlear Implant: Ensuring Sensory Safety at the Electrode-Nerve Interface

Tatiana Blank[1,2], Christian Klose[1,2], Thomas Lenarz[1,3], Hans Jürgen Maier[1,2]

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Objectives: Enhancing cochlear implant reliability involves investigating electrode-nerve interfaces and exploring key material variables—impurities, grain orientation, and dislocation density. Electrochemical tests on monocrystalline and polycrystalline platinum are employed to assess their in vitro performance. In addition, special coatings are applied to gold electrodes to facilitate the accurate detection of degradation products of the therapeutic platinum electrodes. These degradation products serve as indicators of pathological processes. In this context, the cochlear electrodes act as sensor arrays that detect degradation products through impedance changes caused by the presence of platinum.

Materials and Methods: Cochlear implants are often made of platinum or platinum-iridium alloys. The corrosion properties of these alloys are examined using electrochemical techniques. A scanning electron microscope and a laser microscope are used to study the microstructure and surface. A long-term stimulation with increased parameters was performed over a period of four weeks to obtain assess the degradation mechanisms.

Results: Initial results indicate a close relationship between the microstructure of the material and the electrochemical properties since more and faster corrosion occurred when the number of grain boundaries increased. In addition, the surface roughness has an impact on the corrosion behavior. After four weeks of stimulation, signs of corrosion similar to those found in actual cochlear explants began to appear. Furthermore, contact angle measurements on an initial series of different gold coatings indicated promising results in terms of the wetting behavior of coated electrodes.

Conclusion / Outlook: The microstructure contributes significantly to the corrosion of the cochlear implant. Further research should clarify how the gold layers behave in terms of corrosion, and their capacity to catch platinum ions. Strategies to prevent further corrosion should be explored that can be applied once the limit of the gold coatings is reached. In addition, it should be investigated whether other types of coatings are more promising, for example to scavenge proteins instead of platinum, which are formed during the inflammatory processes.

Acknowledgment. Financial support of this study by Deutsche Forschungsgemeinschaft (project number 426335750) is gratefully acknowledged.

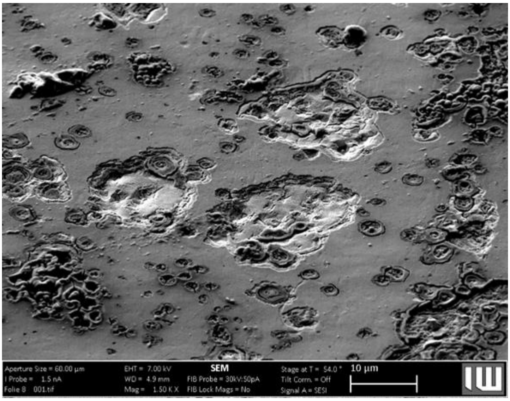

Figure 1: Pitting corrosion on platinum foils after stimulation with an alternating square wave signal

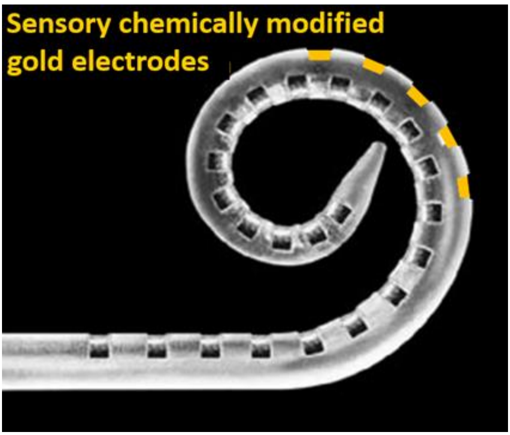

Figure 2: Schematic depiction of chemically modified gold electrodes used as sensors on the implant

Biological Lubrication of Electrospun Fiber Mats as a Versatile Platform for SLIPS-based Surface Coatings

Tom Bode[1], Jan Drexler[1], Marc Müller[1], Birgit Glasmacher[1]

[1]Institute for Multiphase Processes, Leibniz University Hannover, An der Universität 1, 30823 Garbsen

Objectives: Cell and protein adhesion around implants, biofouling and foreign body reactions after the implantation can lead to adverse events, for example in cochlear implants. Slippery Liquid Infused Porous Surfaces (SLIPS) poses unique properties due to their structure consisting of a hydrophobic substrate infused with a hydrophobic lubricant thus creating a superhydrophobic repellent surface that is able to limit cell and protein adhesion. We aim to develop an active, low friction surface coating using biological lubricants and highly porous electrospun substrates.

Materials and Methods: Using the predictive model of Preston et al. [1], combinations of polyurethane (PUR) substrates with different lubricants were investigated to determine their water retention properties. Electrospun poly[4,4′-methylenebis(phenyl isocyanate)-alt-1,4-butanediol/di(propylene glycol)/polycaprolactone] fiber mats were impregnated with clove oil (N), coconut oil (C), perfluorodecalin (P), silicone oil (S), and olive oil (O) through soaking and vacuum application. The contact angle (CA) with water was measured using the sessile drop method.

Results: The prediction model excluded certain combinations that could cause different failure modes. SLIPS systems. were created succesfully using the PU substrate and the mentioned lubricants. The addition of the remaining lubricants increased the water contact angle by 2.66° (P), 8.26° (K), and 10.6° (S) compared to untreated PUR-mats. Treatment with N and O, however, reduced the contact angle by 23.54° and 15.04° respectively.

Conclusion / Outlook: The PU used in the experiment showed minimal hydrophobicity, with a maximum CA of only 100.8° (K) despite the addition of lubricant. To achieve superhydrophobicity, a CA of 150° or higher is required. Further preliminary tests are necessary to evaluate the effectiveness of different substrates, such as Carbothane PU, PVDF, and PVDF-TrFe, as well as impregnation methods, including saturation by immersion and spin coating in combination with a pressure gradient, to increase the CA.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation)

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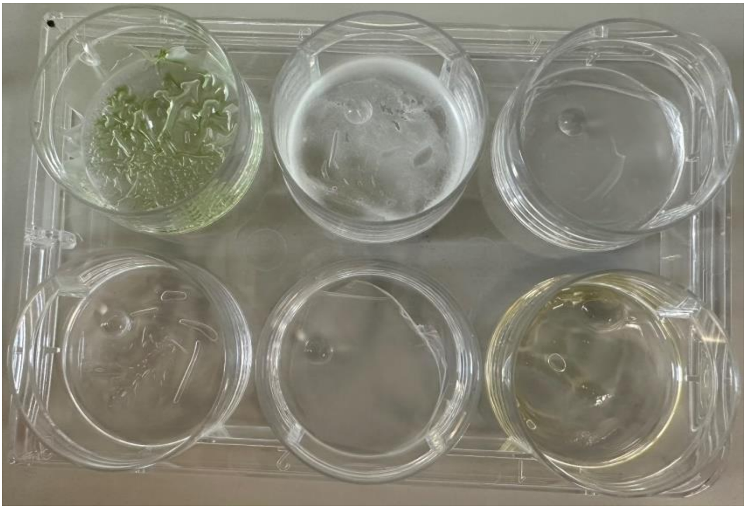

Figure 1: Water droplets on manufactured SLIPS systems. Counterclockwise from top right to left: perfluorodecalin, coconut oil, clove oil, olive oil, Novec 7500 (not analysed) and silicone oil

Adhesive bond to an experimental niobium-based material for dental implants and prosthodontics

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Objectives: SIIRI Subproject B04 is dedicated to develop dental implants made of an ultra-fine grained niobium alloy with integrated micropumps for a user-controlled release of anti-inflammatory substances. The micropump could be attached inside the implant using dental adhesive systems, materials that allow a stable bond to different substrates [Fig 1]. The aim of this study was to investigate bond strengths (SBS) between different adhesive-composite-combinations (ACC) and niobium alloy compared to the common implant materials titanium and zirconia.

Materials and Methods: 9 ACC consisting of the adhesive systems Futurabond U (FBU), Futurabond M+ (FBM), Futurabond M+ DCA (FBMD) and the composites BifixSE (BS), BifixQM (BQ), GrandioSO (G) (all VOCO GbmH) were tested on specimens from niobium alloy (N), Ti-6Al-4V (T) and zirconia (Z). Specimens surfaces were sandblasted with Al2O3 (110 µm). One adhesive system and one composite were applied using a plexiglass mold for a defined boning area and lightcured [Fig. 2]. SBS was measured. For aging simulation specimens prepared the same way underwent 5000 thermocycles prior to SBS measurement.

Results: SBS ranked between 19.88 □ 2.72 MPa (T_FBMD_BQ) and 14.30 □ 1.26 MPa (Z_FBM_BQ) prior to aging. There were no significant differences found neither between different ACC within the substrate groups nor between corresponding substrate-groups with identical ACC. After artificial aging SBS values between 19.39 □ 1.37 MPa and 12.61 □ 2.41 MPa were measured. Comparing corresponding substrate-ACC-groups prior to and after aging no significant differences were found. Between different ACC within the aged substrate groups no differences were discovered. [Fig. 3]

Conclusion / Outlook: The results show that a sufficient adhesive bonding between the niobium alloy and the tested ACC is achievable with bond strengths comparable to those on Ti-6Al-4V and zirconia. SBS is independent from artificial aging.
These findings support the aim of B04. The possibility of adhesive bond to niobium alloy opens up other conceivable applications within dentistry and beyond that. Facing rising allergies caused by titanium niobium alloy could be a promising material for partial dentures or crown bases as well as for orthopedic implants. These possible applications must be contemplated and explored in future studies.

Acknowledgment
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This study was supported with adhesive systems and composite materials by VOCO GmbH, Cuxhaven, Germany.

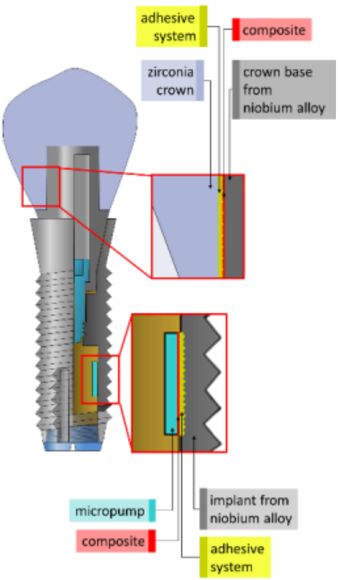

Figure 1: Implant with integrated micropump and zirconia crown on a niobium alloy base. Attachment of crown and micopump with dental adhesive systems and composites

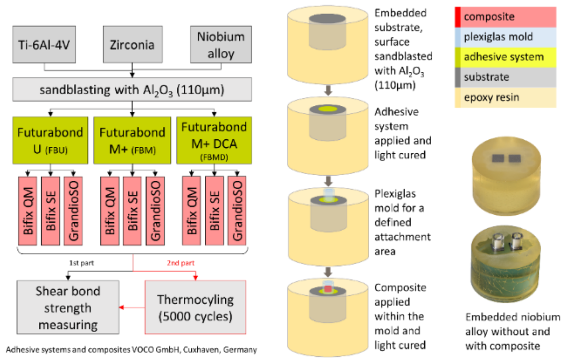

Figure 2: Study design and specimen preparation

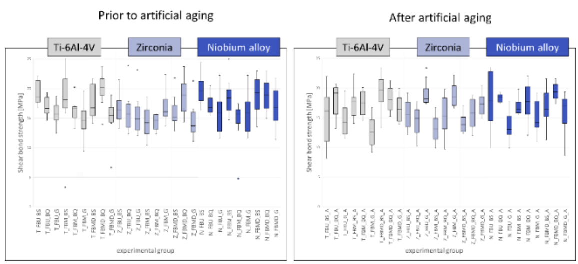

Figure 3: Boxplot diagrams of results

Immune cell integration in a 3D peri-implant oral mucosa-biofilm model (INTERbACT)

Shuli Chen[1,2,3], Carina Mikolai[1,2,3], Diana Strauch[2,3], Henning Hartwig[2,3], Jennifer Ulrich[2,3], Katharina Doll-Nikutta[1,2,3], Andreas Winkel[1,2,3], Muhammad Imran Rahim[1,2,3], Daniela Paasch[4], Nico Lachmann[4], Dagmar Wirth[1,5], Henning Menzel[1,6,] Meike Stiesch[1,2,3]

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Objectives: The aim of the study was to integrate macrophages into the existing 3D peri-implant oral mucosa-biofilm model (INTERbACT) and to validate macrophage presence after model build-up. Interaction between 3D model and multispecies biofilm as explored.

Materials and Methods: Macrophages differentiated from human leukemic THP-1 monocytes are common immune cells used in research models focusing on immune responses to metal implants. Using optimized culture conditions, macrophages were mixed with human gingival fibroblasts (HGF) and incorporated during the peri-implant mucosa model setup in different proportions. Oral keratinocytes (OKF6/TER-2) covered the collagen base containing the above cells and differentiated into multilayered structures only by contact with the culture medium from the bottom of the mucosa, a method also known as airlift. After 14 days of airlift culture, the maturated mucosa was harvested and the content and viability of macrophages was evaluated using microscopy and FACS analysis.

3D models with integration of different amounts of macrophages were co-cultured with a reproducible experimental 4-species bacterial biofilm on glass slides for 24 or 48 hours [3]. After co-culture, biofilms on the slides were stained LIVE/DEAD in order to document the effect of the 3D tissue on bacterial performances under co-culture conditions using CLSM. Sections of the 3D model were histologically analysed.

Results: It was possible to include different proportions of M0 macrophages in the models. The presence and viability of immune cells in the maturated 3D model could be documented. The comparison of CD14- versus CD33-positive cells proved the incorporation of M0. Different amounts of incorporated macrophages were detectable using FACS analyses. After co-culture, biofilms showed a gradually increase in dead bacteria as well as a loosened biofilm structure and even more isolated bacteria when cultured with mucosa including increasing amounts of macrophages. On the other side, different levels of disruption in the structure of the epithelium from the superficial to the basal layer as well as a partial detachment of epithelial cells could be observed. In cases when the epithelial cell layer appeared compromised, an increased number of macrophage clusters were located close to the destructed site.

Conclusion / Outlook: Macrophages could be integrated into the INTERbACT model of different levels of proportion. Cross-sections of the model demonstrated a highly organised cell structure in LIVE/DEAD staining. The presence of macrophages in the model could be verified by FACS analysis. After co-culture with 4-species bacterial biofilm, the structure of both the biofilm and the model epithelial layer was significantly altered.
Further study will focus on the analysis of the composition and structure of biofilms after co-culture. The immune response of macrophages during this process also needs to be further investigated. In the future, this model has potential to further improve in vitro testing of microbial infection of mucosa in peri-implant settings at an early stage close to clinical situation.

Acknowledgment

The project was funded by Deutsche Forschungsgemeinschaft (DFG, German Research Foundation)- SFB/TRR 298 – Project-ID 426335750.

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Integration of optical sensors into microsystems for the detection of specific biofilm patterns

Nicolas Debener [1,2] , Nils Heine [1,3], Katharina Frings [1,4], Maria Leilani Torres-Mapa [1,4], Alexander Heisterkamp[1,4], Meike Stiesch [1,3], Katharina Doll-Nikutta [1,3], Thomas Scheper[1,2] ,_Janina Bahnemann[1,5]

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Objectives: Notwithstanding the tremendous technological advances in the field of biomedical engineering that we have all witnessed in recent years, implant failure due to implant-associated infections still remains a significant challenge in modern dental medicine [1]. The main cause of these infections are the formation of mature pathogenic biofilms which show a reduced susceptibility to both the host's immune response as well as to antibiotic treatment [2](Figure 1). In order to investigate the formation of such biofilms in greater detail, a 3D-printed and optically-accessible microfluidic flow chamber in which important parameters can be monitored in close proximity to the growing biofilm (while simultaneously requiring less growth medium, as well as fewer analytes for subsequent analyses) was integrated into an in vitro biofilm model [3]. The early detection of such biofilms will help to facilitate the development of new and more effective strategies for medical treatment against implant-associated infections.

Materials and Methods: The miniaturized flow chamber consists of a 3D-printed body into which pH-sensitive sensor spots can be integrated (Figure 2, 3). The pH value close to the forming biofilms can be measured via an optical fiber through the transparent 3D printing material. Within the cultivation system itself, the bacteria are co-cultivated in a bioreactor under anaerobic conditions and directed past bubble traps and through the flow chambers via peristaltic pumps. Biofilms featuring five bacterial species were cultivated for 24 hours at 37 °C. After separating the chambers from the cultivation system, the biofilm volume, as well as the live/dead distribution, was then measured and assessed using a live/dead fluorescence staining assay evaluated via confocal laser scanning microscopy.

Results: A 3D image of the grown biofilms is shown in Figure 3; Figure 4 additionally illustrate the live/dead distribution

Conclusion / Outlook: These results confirm that oral biofilms can be cultivated in the presented flow chamber. Due to the high customizability of additive manufactured systems, the microfluidic flow chamber can quickly be expanded to include additional sensors such as oxygen or fluorescence sensors. In addition, the system can easily be parallelized to achieve high throughput while still maintaining low medium consumption.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750

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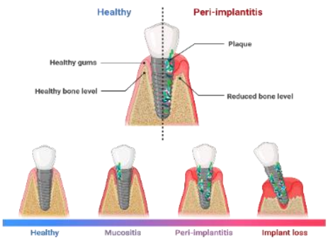

Figure 2: Sketch of the experimental procedure.

Figure 1: Schematic overview of peri-implant diseases.

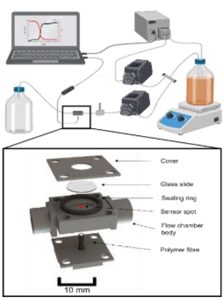

Figure 3: Sketch of the flow chamber model and explosion view of the microfluidic flow chamber.

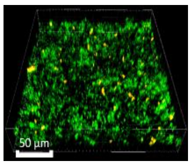

Figure 4: Visualization of a multispecies biofilm

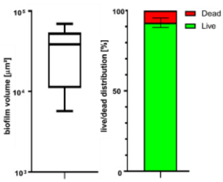

Figure 5: Biofilm volume and live/dead distribution.

Implant regeneration and lifecycle management

Max-Enno Eggers[1], Dr.-Ing. Marcel Wichmann[1], Prof. Dr.-Ing. Berend Denkena[1]

1 Institute of Production Engineering and Machine Tools

Objectives: The project utilizes digital implant lifecycle management (DILM) to enhance the patient-friendly regeneration of defective implants in joint replacement surgeries, focusing on total knee arthroplasty (TKA) for personalized revisions. The research includes investigating micro-structuring, semi-automated planning, and online quality control to optimize the process and reduce morbidity in joint replacement operations.

Materials and Methods: A concept called DILM (Device Information Lifecycle Management) is developed to standardize and structure information and data across the entire lifecycle of a specific implant, from conception to disposal. The implant lifecycle is categorized into Development, Manufacturing, Use-Phase, Check-Up, and Disposal, represented in XML-form. Sub-categorization enhances information retrieval for stakeholders and facilitates interdisciplinary communication. Patient data inclusion distinguishes between patient-specific and serial-manufactured implants. Initially applied to a Total Knee Arthroplasty (TKA) inlay, the concept aims to assess wear through radiographic stereometry analysis and minimum joint space width, with plans to enhance this method using radiopaque markers. Research on microstructuring in ultra-high molecular weight polyethylene (UH-MWPE) involves milling or drilling cavities filled with BaSO4 + HDPE markers, aiming for condition-oriented inlay revisions. Process efficiency is improved through modeling sub-processes and researching partial automation, with integrated monitoring data in DILM to enhance implant manufacturing, quality, and patient monitoring for stakeholders.

Results: The study aimed to implement the DILM (Digital Image-based Local Material) concept by enhancing the material removal simulation IFW CutS with a plug-in for importing and displaying various file formats, successfully tested with a dataset representing different DILM phases. The research also developed a process scheme for producing inlays with X-ray markers, involving subtractive milling, extrusion filling, and addressing increased burr formation through tests and a predictive model based on process parameters.

Conclusion / Outlook: The Digital Implant Lifecycle Management (DILM) concept was developed to standardize and structure implant-related data, particularly focusing on Total Knee Arthroplasty (TKA). The DILM, illustrated in Figure 1, has been implemented using the IFW CutS simulation software with partial automation of X-ray marker and microcavity production; ongoing research aims to integrate automated process monitoring through a digital twin. Future plans involve iterative improvements to the DILM software, incorporating additional data from TKA examples, and enhancing the production of customized implants through an additive-subtractive process chain for increased efficiency.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750.

Investigating the accuracy of model-based radiostereometric wear measurement in estimating insert thickness in total knee arthroplasty

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1 Laboratory for Biomechanics and Biomaterials (LBB), Department of Orthopaedic Surgery, Hanover Medical School –DIAKOVERE Annastift, Anna-von-Borries-Strasse 1-7, 30625 Hannover, Germany

2Institute of Production Engineering and Machine Tools, Leibniz Universität Hannover, Hannover, Germany

Objectives: The wear of ultra-high molecular weight polyethylene in total knee arthroplasty causes early implant revisions, with about 20% revised in Germany in 2021. Early detection of polyethylene wear is challenging unless catastrophic. This study aims to investigate the accuracy of model-based radiostereometric wear measurement in determining minimum insert thickness of a TKA and the effect of flexion angle on this measurement. Model-based radiostereometric wear measurement (RSACore v.4.10, Leiden, The Netherlands) was conducted using radiographs and 3D surface models generated using a structured light scanner (HP 3D Structured Light Scanner, HP HQ-TRE, Boeblingen, Germany). The results were compared to those acquired from a 3D coordinate measuring machine (Leitz PMM 866). Accuracy was defined using mean absolute error (Δmodel-based-ΔCMM), where CMM was considered the true value. Paired t-tests ($p < 0.05$) were used to compare data.

Materials and Methods: Eight insert retrievals with moderate to severe wear (Stryker Triathlon, Cruciate-Retaining, fixed-bearing), were made available by the DIAKOVERE Anna Stift. Four size-5 measuring 11 mm in thickness and four size- 4 (2 x 9 mm, 2 x 11 mm). For X-ray imaging, implant components corresponding to the respective insert size, and the inserts were fitted into a phantom knee model. For size-5 inserts, sizes 6 and 5 (femur, tibia) were used as a size-5 femur was unavailable. Anterior-Posterior radiographs were taken at flexion angles 0°, 30° and 60° (DigitalDiagnost, Philips Medical Systems, Amsterdam, The Netherlands) with parameters (1.7 mAs, 63 kV, source-to-detector distance 1.15 m), resulting in 24 images.

Results: A positive measurement error is evident across all flexion angles indicating a tendency of the model-based method to overestimate true thickness (Figure 1 & Table 1). This error increases significantly as

flexion increases from 0° and 60° (t-test, $p< 0.05$).
The highest accuracy was found at 0° flexion medially and at 30° flexion laterally (Table 1). Nevertheless, the accuracy between 0° and 30° had no statistically significant difference.

Conclusion / Outlook: 1. Overestimation of thickness possible result of phantom positioning – backside damage of inlay prevented proper fitting. 2. 0°-30° flexion sufficient for imaging insert thickness accurately.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750.

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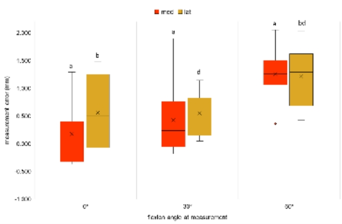

Figure 1 Measurement error between model-based and CMM-measured insert thickness for the 8 inserts at flexion angles 0°, 30° and 60°. Shared letters indicate statistical significance.

	Retrieval	Size 4				Size 5				mean error (SD)	MAE (SD)
		1	2	3	4	5	6	7	8		
Medial	CMM	6.606	6.275	6.076	8.163	6.074	6.506	6.432	6.377		
	MBRSA										
	0°	7.895	5.920	5.704	7.910	6.503	6.710	6.583	6.682	0.18(0.55)	**0.42 (0.36)[a]**
	30°	8.503	6.191	6.104	7.980	6.966	6.677	6.730	6.763	0.43(0.68)	**0.49 (0.63)[b]**
	60°	8.821	7.601	7.267	8.523	7.522	7.566	7.498	7.896	1.25(0.48)	**1.25 (0.48)[ab]**
Lateral	CMM	8.262	6.473	6.664	8.209	6.143	6.483	6.459	6.380		
	MBRSA										
	0°	7.998	6.474	6.572	8.186	7.456	7.537	7.469	7.860	0.56(0.72)	**0.67 (0.62)[c]**
	30°	8.928	6.591	6.711	8.451	7.287	7.138	7.081	7.259	0.55(0.38)	**0.55 (0.38)[d]**
	60°	8.821	7.780	7.724	8.633	7.857	7.809	7.737	8.414	1.21(0.54)	**1.21 (0.54)[cd]**

Table 1 Mean absolute error and standard deviations between model-based and CMM-measured insert thickness at flexion angles 0°, 30° & 60°. Shared letters show statistical significance.

Inverse determination of thermal conduction coefficient for bone cement layers on CoCrMo

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Objectives: In Germany, approximately 10% of joint surgeries are revision surgeries [1]. The conventional method of implant removal through chiseling often inflicts damage to the surrounding bone, leading to longer recovery times and reduced stability of the renewed implant [2]. This creates demand for gentler methods of implant removal. Induction heating is one such method. For a controlled heating of the implant without thermal damage to the surrounding tissue, precise knowledge of the heating and the influencing parameters is essential. Therefore, Finite Element Analysis is used to characterize the heating process and design inductors that allow for optimal heating. The thermal conduction coefficient (TCC) between implant and bone cement cannot be directly measured. Hence, an inverse determination through in-silico matching of empirically determined surface temperature curves by means of a variation of TCC is utilized.

Materials and Methods: PMMA-based bone cement mantles made from Palacos R on CoCrMo specimens were analyzed. The specimens were manufactured with the tools commonly used in surgery to mimic the results usually achieved by surgeons. One half of the samples produced were aged for 14 days in Ringer's solution to account for the effects body fluid usually has on implants [3]. The other half was aged for the same time in air. The specimens were then inductively heated and the change of maximum surface temperature of the mantle was recorded using IR-thermography. The process was modelled in ANSYS APDL, where the heating curves were matched through adjustment of TCC.

Results: The determined values for TCC agree with typical values for thermoplastic to metal contact, residing in the lower range [4]. Wet aged specimens are grouped significantly closer together than dry aged specimens, suggesting water improving the contact between bone cement and CoCrMo by bridging gaps created through surface roughness and trapped air.

Conclusion/Outlook: Inverse in-silico determination from surface temperature thermography proved to be a viable option for identifying TCC. Convection effects were negligible for the setup used. Water uptake lead to a homogenization of surface contact between bone cement and implant while also increasing the heat capacity of the bone cement leading to overall lowered maximum surface temperatures.

Acknowledgment: Financial support of this study by Deutsche Forschungsgemeinschaft (project number 426335750) is gratefully acknowledged.

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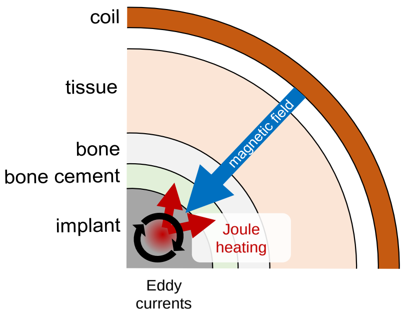

Fig. 1: Schematic diagram of bone cement softening by inductive implant heating

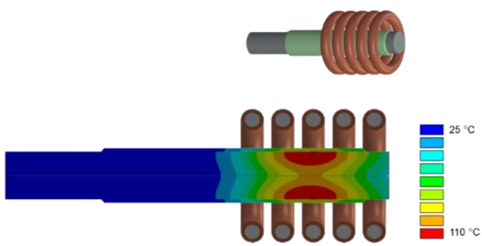

Fig. 2: Current state of in -silico model

Ultrathin surface-attached hydrogel coatings for intentional implant removal

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Objectives: In the further development of implant materials, it is of utmost interest to make the implants safer. Not only the prevention of infections but also easy removal should be considered. The aim is to develop implant coatings that facilitate the removal of an implant by a trigger. Hydrogels are suitable for this application since their structure and mechanical properties are very similar to human tissue. It is known in the literature that nanoparticles can glue synthetic hydrogels with other hydrogels or soft tissue,[1] and this gluing can be reversed at higher temperatures. The use of superparamagnetic core-shell nanoparticles, which allow extremely localized heating[2], should enable release of adhesion with an alternating magnetic field as external trigger. The superparamagnetic nanoparticles can generate heat through magnetic hyperthermia[2,3] to separate the bonded materials and facilitate explantation without damaging the surrounding tissue.An ultrathin hydrogel shall be covalently bonded to the implant surface for the coating. For this purpose, a copolymer was prepared that can bind to the implant surface (titanium) via a phosphonate group.[4] Furthermore, a photo-crosslinkable group like arylazide[5] and hydrophilic groups to form a hydrogel were incorporated. The coatings were characterized via in-situ ellipsometry measurements.

Materials and Methods: An Optrel Multiskop Ellipsometer was modified with cuvettes as light guides to perform in-situ measurements. Scanning electron micrographs were obtained using a Helios G4 CX Dual Beam.

Results: Layer thicknesses of between 40 and 140 nm in the dry state can be adjusted via the concentration of the spin-coating solution. The coatings swell in water to about twice their thickness. The immobilization of different nanoparticles can be confirmed by SEM.

Conclusion/Outlook: The production of ultrathin polymer coatings was demonstrated using ellipsometry. These coatings can swell in water and immobilize nanoparticles on their surface.

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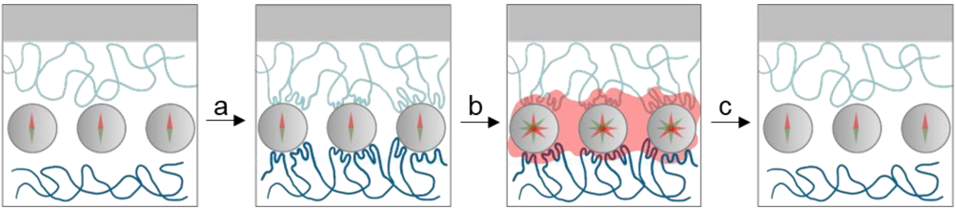

Figure 1: Schematic representation of the reversible nanoparticle adhesive. a) Adsorption of polymer strands onto the surface of the nanoparticles, b) AMF as trigger leads to heating of the nanoparticles, c) Polymer adsorption is released by high temperature.

Social support through shared experiences. An exploratory analysis of various manifestations, reasons, and outcomes of implant patients interacting with affected others

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Objectives: Social support, covering informational, tangible, emotional, esteem, and network support, can be crucial for coping with the challenges of illness (Cutrona & Suhr, 1992). The purpose of this study is to explore social support that implant patients (orthopedic, cochlear) receive from affected others. Different forms of social support and various types of relations with affected others (bilateral, group-related, person-centered) are considered. The research question is: *Which forms of social support are sought and gained comparing the different types of relation?*

Materials and Methods: Informational and emotional needs were central motives to connect with other patients – often compensating for unmet needs from interaction with other sources. Group-related relations were associated with motives such as entertainment and relief by expressing anger. Regular use of self-help groups fostered a sense of belonging, leading to the motive to keep up with group members' lives. Both group-related and bilateral relations were associated with the motive of providing support. Regarding gained forms of support, patients described functional and dysfunctional outcomes. Among functional outcomes, all interactions could provide informational and emotional support. Additionally, they could promote esteem support as patients gained empowerment through role models and comprehensive information. Person-centered relations, including identification with fictional characters, allowed patients to enhance disease-related self-acceptance. Network support was evident in bilateral and group-related relations, fostering friendships and a sense of purpose through providing support.

The dysfunctional outcomes were primarily emotional. In all types, patients felt anxiety and uncertainty when they learned of others' negative experiences. Bilateral and person-centered relations were associated with frustration when patients perceived others as doing

better. Group-related connections led to anger when the communication was perceived as unfriendly or too grieving.

Results: Layer thicknesses of between 40 and 140 nm in the dry state can be adjusted via the concentration of the spin-coating solution. The coatings swell in water to about twice their thickness. The immobilization of different nanoparticles can be confirmed by SEM.

Conclusion/Outlook: The production of ultrathin polymer coatings was demonstrated using ellipsometry. These coatings can swell in water and immobilize nanoparticles on their surface.

Our findings highlight the important role of social support from affected others. The results can be used to derive guidelines for promoting supportive communication in various types of relations.

Acknowledgment: This work was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID [426335750].

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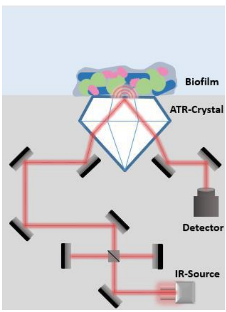

Fig.1. Schematic of the FTIR-ATR setup.

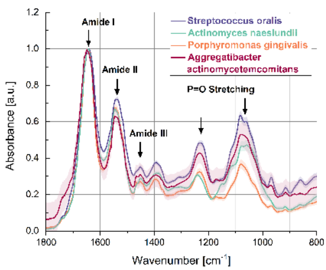

Fig.2. FTIR Spectra of four different oral

bacterial species

Characterisation and differentiation of oral bacteria using ATR-FTIR spectroscopy

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Objectives: Oral diseases like periimplantitis and other infections in the oral cavity are a major cause of implant loss, due to a large community of bacterial species. The aim of this study is to use spectroscopic methods combined with multivariate analysis and deep learning to allow for rapid identification of bacterial species. This study could offer an innovative approach to infection-associated biofilm detection.

Materials and Methods: Vibrational spectroscopy can be used for rapid and label-free chemical analysis of biological samples. In Fourier-transform-infrared spectroscopy (FTIR), the sample is illuminated by mid-IR radiation in the wavelength range between 2 µm and 25 µm (in wavenumbers: 4000 - 400 cm-1). The sample absorbs the IR light at frequencies resonant to the vibrational frequency of its molecules. The resulting absorption or transmission spectra show peaks at different wavenumbers that can be assigned to certain vibrational modes. Hence, a specific pattern of peaks corresponding to a molecule can be measured allowing for chemical identification [1]. The biological samples used were four different, individually cultured, oral bacterial species which were measured with a FTIR spectrometer in attenuated-total-internal reflection (ATR) mode. The resulting spectra were divided into a training and test set. A supervised learning algorithm called k-nearest neighbor (k-NN) was trained with the data to distinguish between the different species.

Results: The spectra of biological samples such as bacterial biofilms are very complex as shown in Fig. 1. Strong peaks at 1650 cm-1, 1550 cm-1 and 1460 cm-1 can be detected from all bacterial biofilms which can be assigned to proteins, Amide I, II and III, respectively [2]. Despite the

presence of these strong peaks, small chemical differences of the protein expressed by different species can be identified in their respective spectra. Each species shows a unique and individual spectral pattern. We were able to distinguish the different oral bacterial species by using a k-NN model with an accuracy of 99.81%.

Conclusion / Outlook

The k-NN model showed excellent classification results for individually cultured samples in planktonic form. The next step will be to identify biofilm samples using the existing model and analyze mixed bacterial samples using deep learning approaches.

Acknowledgment (e.g. funding agency)

Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750

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Antibacterial activity of ciprofloxacin against oral microbiota associated with peri-implant diseases

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Objectives: Cellular and chemical sensor actuator systems represent promising strategies to detect and combat peri-implant diseases. Ciprofloxacin could be implemented as an antibacterial agent in such systems.1 However, its antibacterial potential against the oral microbiota responsible for peri-implant diseases is not clear. Therefore, the objective of the current project is to assess the antibacterial activity of ciprofloxacin against Streptococcus oralis, Actinomyces naeslundii, Veillonella dispar, and Porphyromonas gingivalis.

Materials and Methods: The antibacterial activity of ciprofloxacin was determined by measuring the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) against four important oral species, including commensals S. oralis, A. naeslundii and the pathogenic species of V. dispar, and P. gingivalis as a single or as multi-species.2,3 The MIC assay was performed in 96 well plates containing ciprofloxacin concentrations ranging from 0.5 to 32 µg/mL. The MBC was estimated using concentrations obtained from MIC for each species. In addition, the live dead fluorescence staining was performed to validate the viability of planktonic bacteria at the attained MIC.

Results: The MIC of ciprofloxacin was 1 µg/mL against the planktonic cultures of S. oralis, V. dispar, and P. gingivalis but 8 µg/mL against A. naeslundii. The MBC of ciprofloxacin was 4 µg/mL against S. oralis, V. dispar, and P. gingivalis but 16 µg/mL against A. naeslundii. Within a multi-species environment, the MIC of ciprofloxacin decreased to 0.5 µg/mL thus highlighting its favorable antibacterial effects as well as the differences in testing outcomes when applying conditions which are more clinical relevant. Live dead staining within all tested planktonic cultures showed a substantial proportion of dead cells at MIC when compared to controls without antibiotic treatment.

Conclusion: Ciprofloxacin showed favorable antibacterial effects against oral microbiota causing peri-implant diseases cultured as a single species or in multi-species compositions. Hence, ciprofloxacin may be considered a promising drug for implementation in the proposed autonomous chemical or cell-based sensor actuator system.

Outlook: - Investigation of the antibacterial activity of ciprofloxacin within an oral biofilm environment

- Assessment of the antibacterial effect of ciprofloxacin within autonomous chemical sensor actuator systems in preclinical settings

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Core-Shell-Nanoparticles with Superparamagnetic Properties for Novel Applications as Biomaterials

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Objectives: Due to the increasing average age of the population, the number of implants is also increasing and with it the number of explantations. Therefore, facilitated implant removal is of great interest. A nanocomoposite consisting of superparamagentic core-shell nanoparticles (CSNPs) and synthetic polymer is supposed to be used as implant coating, aiming for a stimulus-inducible modification of the composites rheological properties. Modified CSNP should be thermoreversible and covalently bonded to the polymer strands and thus serve as crosslinking points. Application of an alternating magnetic field heats the nanocomposite up and the thermoreversible bond between particles and polymer is broken. This in turn is said to lead to a softening of the material, which should make an implant removal easier.

Materials and Methods: In a first step, the magnetite core was synthesised by co-precipitation of iron(II) and iron(III) salts and stabilized with citrate ligands. After this, a periodic mesoporous organosilica shell was built around the magnetite nanoparticle (MNP) core, using 1,4-bis-(triethoxysilyl)-benzol as silica precursor. In this step the number of cores is varied. Afterwards, the obtained core-shell nanoparticles were modified with a maleimide silane, using the post-grafting method.

Results: The particles are of spherical shape and show a size distribution of 168 nm ± 42 nm (15 mg MNPs used), 84 nm ± 17 nm (30 mg MNPs used) and 77 nm ± 7 nm (60 mg MNPs used). TEM images show that the PMO shell surrounds the magnetite core. FTIR spectra proves a successful modification with the maleimide silane, due to additional bands which occur after the modification. Also, a rise of the zeta potential from -29 mV to -17 mV after the modification indicates a successful attachement of the maleimide group.

Conclusion: Superparamagnetic core-shell nanoparticles were synthesized, consisiting of a citrate capped magnetite core and a PMO shell. Using more MNP cores makes the surrounding PMO shell smaller, so that the size of the particles can be controlled. Afterwards the particles were successful modified with a maleimide silane.**Outlook:** - Investigation of the antibacterial activity of ciprofloxacin within an oral biofilm environment

Acknowledgment: The work was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - SFB/TRR-298-SIIRI-Project 426335750.

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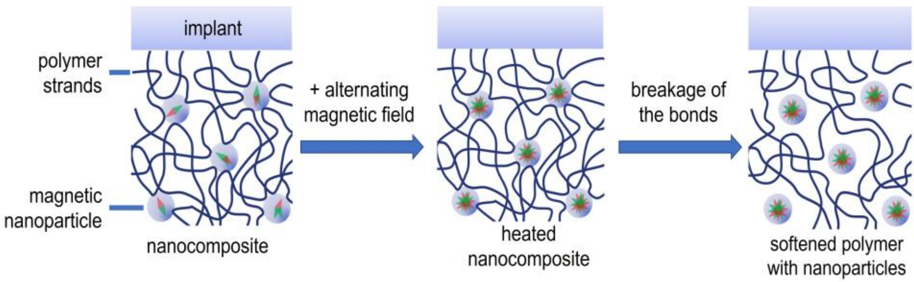

Figure 1: Schematic illustration of the concept for facilitated implant removal. By local heating, the crosslinks between the CSNPs and the polymer can be broken when the bonds are thermo-labile, as a consequence the nanocomposite softens.

The artificial mouth – Oral biofilms grown in the lab

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*contributed equally

Objectives: The human mouth contains a diverse microbiome. Solid surfaces inside the oral cavity, like teeth or implants, are almost constantly populated by multispecies bacterial biofilms [1]. Initially commensal and harmless to oral health, the species distribution inside these biofilms can shift to a pathogenic state and cause severe infections [2]. To develop, test, and verify systems for early detection and treatment of this biofilm dysbiosis, complex in-vitro models are required. The objective of this study is to establish and validate a reproducible in-vitro model for oral biofilm dysbiosis using five clinically relevant bacterial species and a saliva flow-simulating flow chamber system.

Materials and Methods: Streptococcus oralis, Actinomyces naeslundii, Veillonella dispar, Fusobacterium nucleatum, and Porphyromonas gingivalis were added to a flow chamber system to form multispecies biofilms on titanium samples placed in flow chambers. After 24 h, the bacterial suspension was replaced with sterile medium to allow further development only of the initially formed biofilm under flow for 20 more days. Flow velocity was set to 100 µL/min and the system was kept at 37 °C and anaerobic conditions. The pH value of the medium leaving the flow chambers was constantly monitored. At different time points, samples were taken out for analysis via fluorescent staining and microscopy as well as detection of an enzyme of P. gingivalis (gingipain) via an assay.

Results: Over time, a biofilm established until it became stable after 10 days. pH increased over the first 5 days, following the initial drop after exponential growth. Gingipain concentrations increased over the first 15 days.

Conclusion / Outlook: To validate diagnostic tools and therapeutics for associated infections, reproducible in-vitro models of complex biologic systems like multi-species bacterial communities are required. In this study, we presented an approach to obtain such a model for oral biofilm dysbiosis, based on the natural shift over time. qRT-PCR will be used to analyze species distribution.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750.

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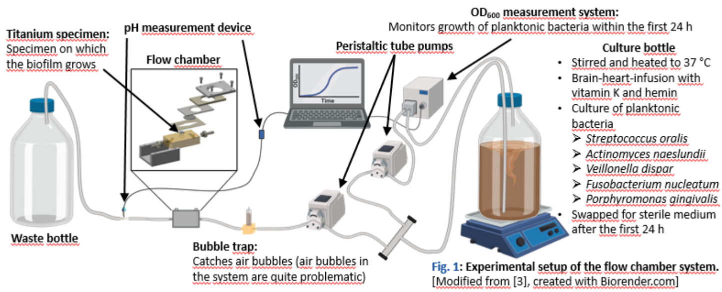

Fig. 1: Experimental setup of the flow chamber system. [Modified from [3], created with Biorender.com]

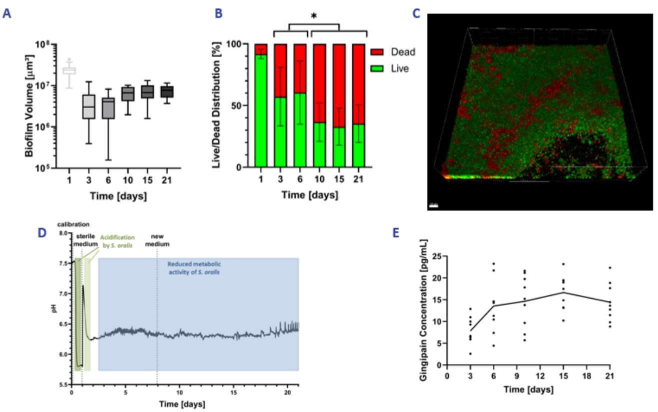

Fig. 2: A Biofilm volume on titanium specimen over time. **B** Live/dead distribution on titanium specimen over time. Statistically significant differences with $p \leq 0.05$ indicated by (*). **C** Exemplary image of live/dead stained biofilm on titanium specimen. **D** pH values of medium leaving flow chambers over time. **E** Gingipain concentration in medium leaving flow chambers over time.

Advancing Dental Prosthetics: A Parametric Remodelling of Connectors in Fixed Partial Dentures and its Application in Finite Element Analysis

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Objectives: Multi-unit fixed partial dentures are an effective prosthetic treatment option in dentistry for replacing multiple missing teeth. However, despite following the manufacturer's recommendations, failures often occur in the connector area [1]. Although extensive research has already been performed on multi-unit fixed partial dentures and their connectors, the question remains as to how the influence of the design of these connectors on patient-specific geometries can be investigated with reasonable effort. The aim of this study was to develop a robust algorithm that enables a parameterized adjustment of the connector region from different various directions (Figure 1(a)) for a four-unit monolithic fixed partial denture using parametric modelling.

Materials and Methods: The algorithm consists of adjusting the mesh vertices, which lie in the connector region (Figure 1(b)), based on the equations (1) and (2). Figure 1(c) illustrates an example of reducing the connector cross-sectional area from the occlusal side by computing a new x-coordinate for each point Pi-occlusal.

$$x_{new}(i)=x(i)-k\,(d_{yz}(i)\times B(d_{xy}(i)))*x(i) \qquad (1)$$

$$B(t)=((w-t)^3\cdot w)+(3t(w-t)^2\cdot 0.9\,w)+(3t^2(w-t)\cdot 0.1\,w) \qquad (2)$$

Using the proposed algorithm, a range of adjustment scenarios were generated for a four-unit monolithic fixed partial denture to evaluate the influence of different adjustment situations of the cross-sectional connector area on the stress distribution in FPD. The algorithm detects the positions of the connectors, adjusts the geometry according to user-defined parameters, and exports them to the FEA tools [2].

Results: The FE analysis showed that reducing the connector's cross-sectional area from the gingival side primarily affects tensile stress, while a reduction from the occlusal side has a significant effect on compressive stress

Conclusion / Outlook: The proposed parameterized adjustment of the connectors was successfully implemented. Automating the full FDP design including support in a parametrized way, seems in principle

reachable with today's tools, but still represents a formidable challenge.

Acknowledgment: This research was supported by the Deutsche Forschungsgemeinschaft (DFG), project number 462306304

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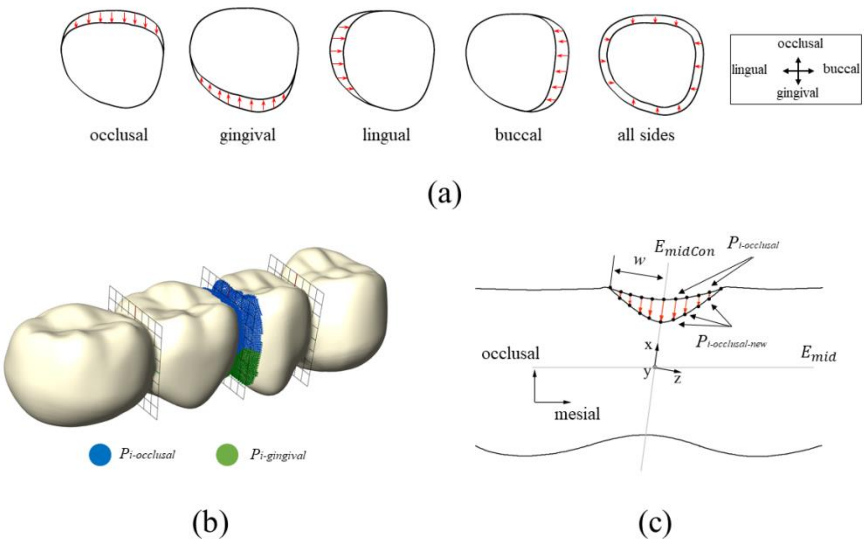

Figure 1: (a) Different types of connector shape adjustment. (b) Selected points $P_{i\text{-}occlusal}$ (blue) and $P_{i\text{-}gingival}$ (green) for occlusal/gingival adjustment. (c) Overview of the steps to adjust the occlusal points of the middle connector

Identification of microbiome and metatranscriptome based biomarkers associated with peri-implantitis

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Therapies for peri-implant diseases are mainly focused on the clinical phenotype. However, recognizing the pivotal role of peri-implant microbial and functional dysbiosis in tissue inflammation and damage is equally imperative.
In this cross-sectional study, we analyzed 48 peri-implant submucosal biofilm profiles from 79 implants placed in 32 patients to reveal disease signatures. Full length 16S rRNA gene amplicon sequencing (16Sseq) was employed for high resolution bacterial taxonomic identification, and metatranscriptomics (RNAseq) was applied to analyze the transcriptional activity within biofilms.
We observed significant differences in the microbiome profiles between healthy implants and those with peri-implantitis (PERMANOVA; $P<0.001$), and these distinctions were consistent across various taxonomic levels. Notably, these variations persisted when analyzing functional RNAseq data. 16Sseq revealed a substantial shift in the community composition from health, where mostly aerobic Gram-positive taxa were dominant, to peri-implantitis where mostly anaerobic Gram-negative bacteria were present. Also, strong correlation existed between the composition and the activity of biofilms in health and peri-implantitis ($r > 0.75$ for Bacilli, Bacteroidia and Actinobacteria).
RNAseq revealed the expression of distinct metabolic pathways in healthy and peri-implantitis samples. Anabolic pathways were enriched in health and included the synthesis of heme, cysteine, methionine and lysine. Butyrate producing pathways like the degradation of lysine, glutamate and aspartate increased in peri-implantitis. Bacteroidia and Fusobacteriia were attributed to be the major producers of butyrate.
For diagnosis prediction, canonical analysis of principal co-ordinates (CAP) and random forest (RF) models using microbiome and

metatranscriptome data showed a high predictive ability, with the highest area under the receiver's operating characteristics curve (AUC) of 0.82 for the combined analysis of species and functional enzymes. Furthermore, through a recursive feature elimination (RFE) method, two Streptococcus species and Rothia dentocariosa were identified as top biomarkers for health while Dialister invisus along with phosphoenolpyruvate carboxykinase, tripeptide aminopeptidase and urocanate hydratase were identified as top biomarker candidates for a diagnosis of peri-implantitis.
With this study, we demonstrate that our framework shows a high predictive ability and could be a viable option to identify further diagnostic biomarkers and therapeutic targets for peri-implant disease.

Acknowledgment: The present study is funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750

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Implementation of a numerical diffusion-driven growth model into the Neighbored Element Method

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Objectives

To further the understanding of oral biofilms and consequently prevent diseases related to those biofilms, in silico models can help to mitigate challenges that other modeling approaches such as in vivo or in vitro face. A commonly used approach is continuum-based modelling using the Finite Element Method, with which the collective behavior of biofilm can be investigated. For a sufficiently small number of unknown field variables, a Finite Element approach is very suitable and gives good results. Unfortunately, these types of models are restricted due to computational demands. Restrictions may be that only mono-species biofilms can be simulated, or that only two-dimensional simulations can be performed [1]. To overcome those restrictions and enable the computation of three-dimensional, complex multi-species biofilm containing interactions between those species, the Finite Element Method is combined with the Finite Difference Method to form the Neighbored Element Method as described by Blaszczyk et al [2].

Materials and Methods

The simulation is performed using the Finite Element software "ANSYS". First, the neighbor point search is performed, where the special relations between points is investigated. This only has to be done once per discretization, i.e., once for each finite element mesh. The displacements are solved using the Finite Element solver integrated into the software. Afterwards, the Finite Difference Method is used to calculate the gradients and Laplacians of the field variables, which are subsequently used to evaluate the evolution equation of those field variables. Field variables are variables, which indicate e.g. biofilm density and nutrient location. The Finite Difference Method is programmed in the APDL environment and invoked by ANSYS using command snippets. The Finite Element and Finite Difference simulations are then iterated back and forth for the duration of the simulation.

Results
The Neighbored Element Method was successfully implemented in context of a three-dimensional, mono-species biofilm model. The details of the model are discussed in [3]. Comparison with the purely FEM model shows a good agreement between both models.

Conclusion / Outlook
As stated in the objectives, future steps will include the incorporation of multiple biofilm species and their interactions with each other in a three-dimensional setting. Additionally, future research has to include the verification with in vivo experiments.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750

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Mechanical Adaptive Silicone Composites for UV-triggered Facilitated Cochlear-Implant Removal

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Objectives: Due to the increasing average age of the population, the number of implants is also increasing and with it the number of explantations. Therefore, facilitated implant removal is of great interest. Within this concept, the silicone of the cochlea implant is strengthened by nanoporous filler nanoparticles. When implant removal becomes a treatment option, the light-degradable mesoporous Organosilica nanoparticles (ld-MON) are irradiated with UV to induce the degradation of the particles. Thus, the strengthening effects disappear. To achieve the light-degradable properties, the material is constructed with a linker molecule containing a 2-nitrobenzyl group which is cleaved upon irradiation with UV light. The concept is shown in figure 1.

Materials and Methods: First the functionalized bissilane was synthesized in a two-step synthesis. Using the bissilane the ld-PMO was synthesized in a modified Stöber-Synthesis. Following the ld-PMOs were incorporated into silicone. The specimen were irradiated by UV lamp to measure mechanical properties before and after irradiation.

Results Particles with the size of ≈140 nm were obtained. Thermogravimetric measurements and Infrared spectra indicated a successful integration of the moiety. After irradiation at 327 nm TEM pictures show several disintegrated particles. UV-vis spectra are showing the shift of the maxima from 327 nm indicating the successful bond cleavage. Further, it was possible to integrate the particles homogenously into silicone. By irradiating, the composite turned brown until 0.4 mm into the silicone. Also, we observed a decrease in the storage modulus.

Conclusion / Outlook: It was shown, that PMO with a 2-nitrobenzyl group can be synthesized within in the nanoscale. Further the light-induced degradation could be shown. The integration into the silicone was possible. The irradiation in the composite works, which also leads to a change in the rheologic properties.

Acknowledgment: The work was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - SFB/TRR-298-SIIRI-Project 426335750.
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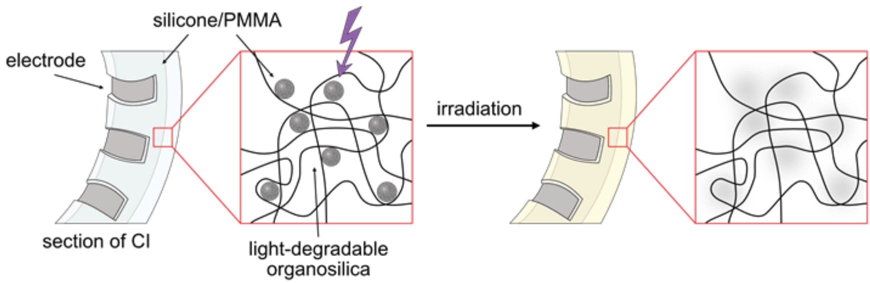

Figure 1: Schematic illustration of the concept, using ld-PMO nanoparticles integrated into a polymer matrix as an example. The PMO filler particles stiffen the nanocomposite. By UV irradiation the PMO nanoparticles are disintegrated and the material softens.

Junction strength of double modular hip endoprostheses depending on manufacturing-related deviations

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Objectives: Implantation of double modular hip endoprostheses enables the femoral angle to be adjusted individually to improve the biomechanics of the patient [1]. In the case of damages of the taper, the stem can remain in the femur, requiring only the replacement of the neck adapter. However, these advantages are countered by an increased risk of revision due to fretting at the additional connection due to angular deviations in the pairing [1, 2]. Therefore, initial investigations focused on understanding the impact of manufacturing-related angle deviations on the junction strength of Ti-6Al-4V ELI/Ti-6Al-4V ELI and CoCr28Mo6/Ti-6Al4V ELI pairings.

Materials and Methods: Manufactured outer tapers with different surface topographies and angular deviation were investigated regarding their influence on junction strength. The outer taper angle was varied by θn = 5.724 ° - 0.1 ° for the distal contact. The surface topography of the outer taper was measured with an optical measuring device Confovis DuoVario. After static force assembly of Fassembly = 4 kN, the separation forces and contact surfaces were analysed based on push-out tests.

Results: The contact area and the separation forces are material-specific. The contact area of the Ti-6Al-4V ELI/Ti-6Al-4V ELI pairing is larger than the contact area of the CoCr28Mo6/Ti-6Al-4V ELI pairing. This is due to the lower hardness of Ti-6Al-4V ELI. A decrease in surface roughness Sz leads to an increased contact area, attributed to twice as many peaks that can be plastically deformed. Separation forces are slightly influenced by the measured contact area. One contributing factor is that the contact area is not the main factor for

the friction between the pairing. Because of the different friction coefficients of CoCr28Mo6 and Ti-6-Al-4V ELI it was also recognised that the separation forces of the CoCr28Mo6/Ti-6Al-4V ELI pairing are higher.

Conclusion / Outlook: Based on the results, it is known that the separation force is only slightly affected by the topography and geometrical accuracy of the taper angle. However, its influence with regard to the dynamic load is not yet known and will therefore be investigated subsequently. Furthermore, the interface design will be adapted in order to increase the robustness of the interface to prevent damage.

Acknowledgment: The authors would like to thank the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) for their financial support within the SFB/TRR-298-SIIRI-Project-ID 426335750 “Safety integrated and infection reactive implants” in subproject A04.

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Figures

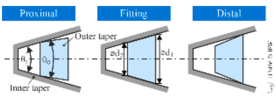

Fig. 1. Schematic illustration of different taper angle deviations according to [4]

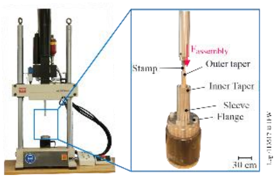

Fig. 2. Experimental setup of the push-out test

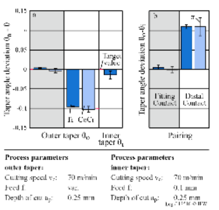

Fig. 3a. Angular deviations on the target value of the outer and inner taper, 3b. Angular deviation of the pairing

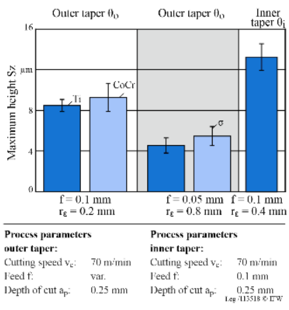

Fig. 4. Maximum height Sz of the outer and inner taper in dependence of the process parameters by turning

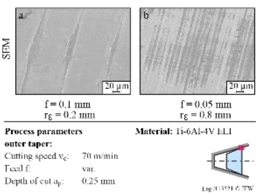

Fig. 5. SEM images of rough (a) and smooth (b) pushed-out Ti-6-Al-4V outer tapers

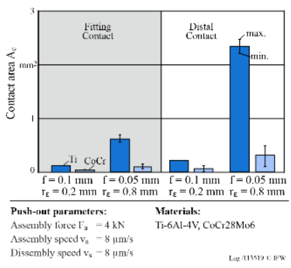

Fig. 6. Contact area in dependence of process parameters by turning and contact case

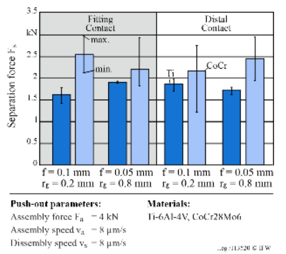

Fig. 7. Separation forces in dependence of process parameters and contact case

Integration of bone-similar tissue into the (INTERbACT) model

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Motivation: The oral host-microbe relationship plays an important role in the maintenance of oral health as well as in the development of peri-implant diseases (1). The development of new therapeutic strategies to prevent peri-implant diseases is a critical step that requires a comprehensive knowledge of the interaction between host and biofilm. However, the detailed mechanisms of these host-microbe interactions are currently not fully understood (2). Clinical relevant in vitro 3D-models are one opportunity to investigate this in more detail. Previously, an in vitro 3D-model comprising human gingival fibroblasts and human keratinocytes as well as implant material was established and used to investigate host-material-biofilm interactions (3, 4). However, this model lacks osteoblasts as an important part of peri-implant host tissue with relevant function in homeostasis and disease (5). Aim of this study is to expand the existing 3D-implant-tissue-bacterial biofilm model (INTERbACT) by adding an artificial bone component.

Milestones to Incorporate Osteoblasts in the INTERbACT model

- Loading of scaffold material with primary human osteoblasts
- Adapting scaffolds for application in the model set up (e.g. drilling)
- Merging of mucosa model and scaffold-based hard tissue
- Adapting culture conditions to the more complex set up

Achievements

- Sufficient scaffold material (60% HA, 40% β-TCP, ReproBone, Fa. Ceramisys) was identified and modified for integration in the INTERbACT model.
- Extended implants assembled in the punched mucosa model can be stabilized in a way to create extra implant areas below the

mucosa to be placed in the osteoblast-loaded scaffold for future merging of both components.

- Proliferation analysis of NHOst in adapted media considering different mixtures of aMEM (standard for NHOst) and airlift medium (standard medium in the INTERbACT model) were conducted. Activity of cells appeared reduced but not compromised.

Outlook

- Merging of peri-implant mucosa with scaffold pre-loaded with osteoblasts and successful cultivation in an airlift environment for several days
- Applying different analyses to the expanded INTERbACT model to evaluate sustainability and practicability (including Live/Dead, collagen immunofluorescent and Alizarin Red S staining as well as qRT-PCR and histological examinations)

Acknowledgment: The project was funded by Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - SFB/TRR-298-SIIRI - Project-ID 426335750.

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High-throughput characterization of interspecies interactions in oral implant-associated biofilms

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Background: During polymicrobial biofilm formation on implant surfaces, the involved species of oral microorganisms interact on different levels. In this regard, exploitation of metabolites released by other species can be an important survival strategy that contributes to biofilm fitness and leads to disease development and progression. Identification and characterization of these hallmark interactions are therefore imperative to detect early pathology and prevent implant-associated diseases.

Objectives: Characterization of synergistic metabolic interactions in implant-associated biofilms and tracing of chemical compounds that are actively involved in these inter-species metabolite flows are the primary goals of this study. The knowledge gained should contribute to the decoding of these interaction networks in complex clinical biofilms.

Materials and Methods: Interspecies metabolic interactions were characterized using diverse agar diffusion assays. Clinical oral biofilm samples, more than one hundred reference strains of diverse species, various metabolites and their corresponding combinations were studied. Liquid biofilm cultures were used to verify selected interactions.

Results: Porphyromonas gingivalis showed satellite growth exclusively around colonies of other species from classes such as Actinobacteria, Bacteroidia, Negativicutes and Gammaproteobacteria, thereby indicating metabolite exploitation under experimental conditions. Chemical complementation experiments identified menaquinones and their related precursors as major drivers of these interactions.

Conclusion: We were able to characterize exploitation interactions involving the key oral pathogen Porphyromonas gingivalis. Targeting these interactions may support the development of innovative preventive and therapeutic strategies for implant-associated infections.

Development and Characterization of PCL Electrospun Nanofiber Scaffolds with Graphene Nanofiller for Tissue Engineering

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Objectives: Graphene-based nanocomposites have emerged as a prominent material in tissue engineering due to their electrical conductivity, mechanical strength, and large specific surface area [1-2]. This research explores the development and characterizing of PCL nanofiber scaffolds embedded with graphene nanoparticles (Gnp) at 0.5%, 1.0%, 1.5%, and 2.0% (w/v) to improve the morphological, mechanical, and biocompatibility properties.

Materials and Methods: Electrospinning was performed with 20kV at a flow rate of 1ml/h. The scaffolds were characterized with Scanning Electron Microscopy (SEM) for morphological analysis, Fourier Transform Infrared Spectroscopy with Attenuated Total Reflectance (FTIR-ATR) for chemical composition, and tensile-deformation tests to evaluate mechanical properties. The biocompatibility was tested by cell adhesion of bone marrow mesenchymal stem cells (bmMSCs) and metabolic activity measurements.

Results: Findings highlighted a substantial decrease in fiber diameter, ranging between 40% to 59%, with the addition of Gnp, particularly the 2.0% Gnp-PCL scaffolds showing the smallest diameter at 321.67 nm. A clear interaction between Gnp and PCL was established, enhancing the mechanical attributes such as Young's modulus and tensile strength, particularly in the Gnp 0.5 % sample. Scaffolds with 1.5% and 2.0% graphene showed improved cell viability, particularly on days 7 and 10, consistent with the SEM observations of cell adhesion.

Conclusion / Outlook: In conclusion, the study of PCL nanofiber scaffolds embedded with graphene nanoparticles has demonstrated

Moreover, experiments concerning the impact of those phages on complex biofilms are planned.

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Self-Immolative linkers in autoregulative drug delivery systems for antibiotics

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Objectives: To address the problem of unwanted loss of dental implants caused by the invasion of implant surfaces by pathogenic bacteria. This work aims to synthesize a chemical-sensor-actuator (CSA) system. This system should detect the presence of bacteria on implants surrounding at an early stage of Mucositis, thereby releasing anti-bacterial drug and hence, preventing bacteria-associated infections.

Materials and Methods: In 7 steps a penicilline-g-amidase specific linker-Drug system was made and coupled through Diels-Alder reaction to chitosan modified with 3-maleimidopropanoic acid. These synthetic products were analyzed by GPC, NMR and IR measurements. Furthermore, Invitro and invivo testing are made using the 3-INTERBACT model.

Results: The successful synthesis of the cleavable linker-drug system was confirmed by NMR analysis. The cleavable, drug-release potential of this system in the presence of Penicillin-G-Amidase and the viability of Bacterial is currently under investigation. Also, chitosan of different degrees of modification (6.5%, 9.5% and 11.5%) was achieved and confirmed by NMR and IR spectroscopy.

Conclusion / Outlook: 7-step synthesis of linker drug system and Chitosan of different degrees of modification were successfully achieved. Also, the Coupling of the modified chitosan and the linker-drug system is ongoing. Furthermore, the formation of coatings on the surface of the Ti-implant will be done and their biological activity will be tested using the INTERBACT model.

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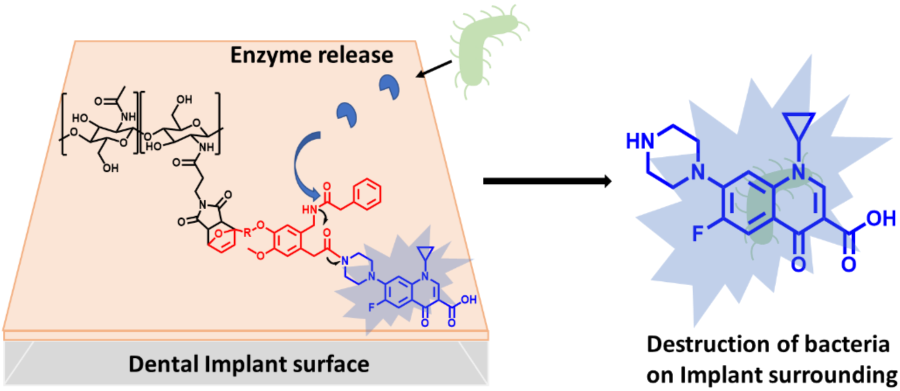

Figure 1: Schematic showing the implant surface coated with enzymatically cleavable samples and the drug release mechanism to overcome implant-associated infection.

Real-time assessment of implant stability: a patient-specific modelling approach

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Objectives: High-fidelity computational simulations enable the prediction of hip implant stability and possible failures, considering the patient's individual conditions. Short-term stability is assessed by modelling the migration of the implant and the osseointegration, the bony ingrowth of the bone into the implant. To evaluate long-term stability, simulations of the bone remodelling process around the implant are performed. However, the current high computational effort of these computational models and the time-consuming geometry generation are preventing their clinical application.

Therefore, this project aims to reduce the computational complexity by applying surrogate modelling techniques. The resulting surrogate models can efficiently predict changes in bone mass density after implantation, considering patient-specific conditions, which facilitates their integration into daily clinical practice.

Materials and Methods: In clinical practice, X-Ray images are routinely used to monitor the patient's condition before and after implantation. These images can be used to identify patient-specific parameters of the individual femur geometry. Consequently, these parameters are used to morph a generic femur model using radial basis functions (RBFs), creating a patient-specific Finite Element Method (FEM) model. To account for varying implant positions, isotopological FEM meshes are generated using the Laplace equation. Subsequently, a surrogate model is set up by combining Proper Orthogonal Decomposition (POD) and RBFs interpolation, enabling the prediction of changes in bone mass density after implantation for individual patient parameters [1,2].

Results: The application of the presented POD-RBF surrogate model reduces the computation time for a new set of parameters from hours to milliseconds. For an exemplary validation set a relative mean absolute error of 1.5% compared to the high-fidelity model is obtained.

Conclusion / Outlook: The proposed POD-RBF surrogate model paves the way for utilisation in clinical practice for the rapid evaluation of implant stability. The model ensures a patient-specific approach and maintains a predefined level of accuracy.

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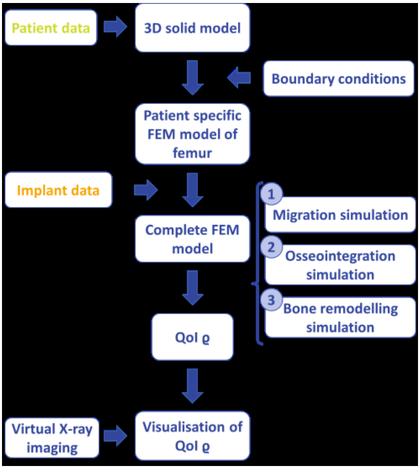

Figure 1: High-fidelity simulation framework

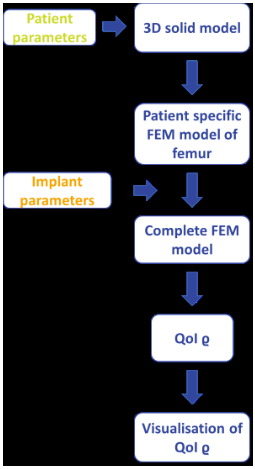

Figure 2: Surrogate model framework

Acoustic emissions resulting from friction of different species' bone tissue against implant material: Basic research for a new approach to implant loosening detection

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Objectives: During the loosening process of hip arthroplasties tolerable relative movements of 30-100 µm between prosthesis stem and bone will be exceeded and induce a loosening cascade [1]. This loosening is often recognized only late by pain. The introduction of acoustic emission (AE) analysis seems to be a promising approach to detect these early relative movements [2]. In in-vitro investigations, isolated relative movements between bone and implant will be induced to characterize AE-signals caused due to implant loosening. The inclusion of influencing parameters such as implant material, surface roughness and pressure at bone-implant interface lead to a wide variety of test combinations. Substituting human with animal bone for in-vitro testing would allow simplified sample preparation and a remarkable cost reduction. The aim of this study was to investigate whether AE-signals differ between different species' bone tissues.Therefore, this project aims to reduce the computational complexity by applying surrogate modelling techniques. The resulting surrogate models can efficiently predict changes in bone mass density after implantation, considering patient-specific conditions, which facilitates their integration into daily clinical practice.

Materials and Methods: According DIN-ISO-5832-3, Ti6Al4V (Ra 4.11±0.33 µm) was used as the implant alloy. Bone samples were taken from human, bovine and porcine cortical bone. To characterize AE-signals a test rig was developed to simulate standardized relative motions between bone and implant (Fig.1). AE-signals of 125 relative movements per species were captured using a piezoelectric AE-sensor (Vallen-VS45-H, frequency range: 20-450 kHz) placed directly on the implant sample. Data was processed with the AMSY-6 system and the

software AE Suite Vers. R2020.1124.2 (Vallen Systeme GmbH). The algorithms for AE hit detection and characterization were coded in Python version 3.9. AE characterizations were analyzed using an ANOVA with additional Bonferroni post hoc t-tests.

Results: The most important time and frequency features of AE-signals from human bone tissue differ significantly from those of both animal species (Fig.2). Signals of human origin are significantly longer ($p=0.001$-0.002) and exhibit a higher rise time ($p=0.012$-0.019). Additionally, the main frequency components of human AE-signals are in a significantly lower frequency range with a centroid frequency of 113.7 kHz ($p=0.003$). The features of animal AE-signals do not differ between species ($p=0.242$-0.999).

Conclusion / Outlook: Due to the clear differences in the characteristics of AE-signals, it is not advisable to replace human cortical bone with animal cortical bone in AE-related in-vitro studies.

Acknowledgment: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750.

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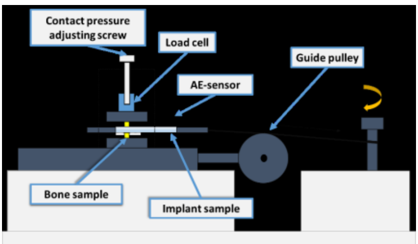

Figure 1: Experimental test rig for standardized AE characterization of friction between cortical bone and THA implant alloys

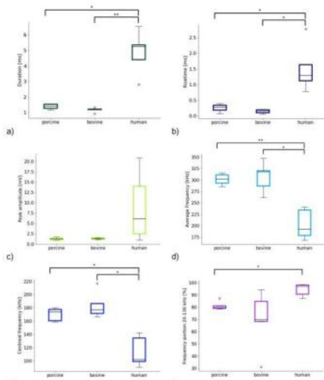

*Figure 2: AE signal features resulting from relative movements between porcine, bovine, and human cortical bone and $TiAl_6V_4$. Significant differences ($p<0.050$) are marked with * and highly significant differences ($p<0.001$) with **.*

Automatic adaptation of an occlusal surface of an implant-supported crown with Laplacian Mesh Editing

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Objectives: Nowadays, the restoration of missing teeth with dental implants is a common treatment method in dentistry. Achieving an optimal occlusion when designing the occlusal surface of an implant-supported crown is important for the patient. Although there are various occlusal concepts and guidelines for achieving optimal occlusion, the process automation of adapting an occlusal surface is challenging. The contact points must be established in certain areas of the occlusal surface without impairing the aesthetics of the teeth and the masticatory function. A computer-aided, automated modelling approach can help with the design and can reduce the need for manual labour. This study aimed to develop a modelling approach that enables the automatic adaptation of an occlusal surface to specific occlusal concepts while preserving the natural appearance.

Materials and Methods: In this study, the occlusal surface of a scanned, implant-supported crown that replaced the first right mandibular molar was adapted. Nominal contact points were first determined based on occlusal concepts from the literature. The position of the nominal contact points on the crown was then improved using an optimisation process. The shape of the occlusal surface was then adapted with regard to the desired contact points using Laplacian mesh editing. The results of the modification were validated with a finite element contact analysis. The second right premolar and the first right molar of the maxilla were used as antagonists in the contact analysis.

Results: The contact analysis results show that locations with high maximum principal stress correspond with the locations of the desired contact points. This indicates that contact between the crown and the antagonists occurs at the desired locations.

Conclusion: The presented method enables the automated adaptation of an implantsupported crown. It is planned to use the method as a basis for further optimisations. One main goal is to optimise the contacts in a way that reduces lateral reaction forces and avoids excessive strass concentrations on the occlusal surface.

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Autonomously-controlled synthetic cells for detection and treatment of peri-implant bacterial infections

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Objectives: Peri-implant bacterial infections often result in irreversible loss of peri-implant supportive structures, leading to implant failure. Although the host immune system detects the presence of bacteria early, frequently it fails to resolve the infection. Regardless, immune cells secrete cytokines in response to pathogen recognition adjacent to the site of the infection, e.g., implant surfaces. We designed a cell-based automated system that detects secreted type-I interferon, a cytokine produced in a wide range of inflammations, as a biomarker of infection. We rewired the activated cellular signalling pathways to specifically induce reporter genes and secrete factors that counteract infections.

Materials and Methods: An infection-responsive intracellular synthetic network was developed by integrating the synthetic transactivator tTA into the endogenous Mx2 locus, which is activated in the presence of type-I interferon (IFN-β). This module was rewired to Ptet promoter-controlled antibacterial genes of interest and reporter genes. A positive feedback module was implemented to achieve sustained activation of the system by IFN-β, which is controllable by doxycycline.

Results: To mimic physiological scenarios, co-cultures of the infection-responsive sensor-actor cells and macrophages were exposed to bacteria. Both gram-positive and gram-negative bacteria induced the synthetic cascade, enabling the sensitive visualisation of infections in a dose-dependent manner. Implementation of a positive feedback module induced a response that was maintained even if the trigger had faded out, while doxycycline treatment reset the sustained expression to the basal level. We demonstrated that this infection-induced synthetic cascade can be utilised to secrete functional proteins (antibacterial proteins or peptides), as well as

Rothia, and Haemophilus dominated in both smokers and non-smokers. However, smoking exerted a discernible influence on microbial composition. The number of species-level bacterial taxa was significantly higher in smokers, registering a mean of 140 ± 41 compared to 127 ± 33 in non-smokers. This difference extended to the overall composition as measured by weighted UniFrac distances. Furthermore, several taxa exhibited significant differences in abundance between adolescent smokers and matched non-smokers, indicating an early onset in smoking-related changes in the oral microbiome.

Conclusion / Outlook: Autonomously controlled sensor-actor systems are characterised by high sensitivity and have the potential to combat dental peri-implantitis in the early stages. Although this system has been developed to fight peri-implantitis, its application can be extended to any other type of implant and in general against bacterial infections. Additionally, this concept may help develop cell-based diagnostic and therapeutic alternatives relating to other inflammatory diseases.

Acknowledgement: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI – Project-ID 426335750

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Alteration of the oral microbiome by cigarette smoking in adolescents

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Objectives: The human oral microbiome contains more than 700 bacterial species[1]. While some of these taxa are crucial for maintaining oral homeostasis and health[2], others are associated with various oral diseases. Smoking, a risk factor for oral pathogenesis[3], is associated with shifts in the composition of the oral microbiome and can contribute to the development and progression of periodontitis[4]. While most smokers start smoking before the age of 18, data on the effects of smoking on the oral microbiome in adolescents is very limited. The current study investigates the effects of smoking on the composition of the oral microbiome in a local cohort of secondary-school pupils.

Materials and Methods: The adolescent cohort of this study comprised 196 secondary-school pupils aged 14 to 21, who were sampled between June and December 2020. We collected a swab of the buccal mucosa as well as information on smoking behavior from every participant. 98 adolescent smokers fulfilled the inclusion criteria. Their oral microbiome composition was compared to that of 98 non-smokers matched for age, gender, BMI and medication intake. The oral microbiome composition was analysed using high-throughput sequencing of the full-length 16S rRNA gene. Analyses of bacterial diversity, abundance comparisons of individual bacterial taxa in smokers and non-smokers, and other statistical analyses were performed with R.

Results: Smoking pupils were distributed over five categories of smoking frequencies from "less than once/month" to "every day". Thirteen of 98 smokers smoked daily. None of the pupils met the definition for heavy smokers (more than 20 cigarettes per day). The microbiome dataset contained 733 bacterial species or OTUs. The genera *Streptococcus*, chemo-attractants (i.e., CCL2) that boost immune infiltration to the site of infection.

Conclusion / Outlook: This study reveals a significant impact of smoking on the oral microbial composition of adolescents.

Acknowledgement: The study is funded by the Ministry of Science and Culture of Lower Saxony, Germany, reference number 14-76103-184.

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Co-extrusion of a Niobium Powder

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Current State/ Objectives: 20-25 % of dental implants fail due to periimplantitis [1, 2]. Traditional systemic therapies fall short in achieving effective concentrations of active substances at the inflammation site. This prompts the need for innovative approaches to enhance implant performance. This project aims to develop implants with a micropump system for controlled drug release through an open-porous layer. Key material requirements include high cyclic strength, low Young's modulus to prevent stress shielding, and superior biocompatibility for optimal osseointegration. These requirements can be met with a niobium-zirconium (Nb-1Zr) alloy that is based on powder material to reduce diffusion paths necessary for hardening of the alloy.

Materials and Methods: To prevent uncontrolled oxidation, the powder-based Nb-1Zr alloy is encapsulated in a C45 capsule for co-extrusion. The process involves filling the capsule, compacting the powder, sealing of the capsule by welding, and preheating before co-extrusion. During co-extrusion, different extrusion parameters (temperatures, extrusion ratio) are employed. Characterization of the co-extrudates employs radiography, light microscopy, and SEM for macro and microstructural analysis, while mechanical properties are assessed through hardness measurements and compression tests.

Results: The results demonstrate a significant impact of furnace temperature and extrusion ratio on the co-extrusion process. At 1300 °C, a continuous niobium core is achieved, reducing porosity from 1.7 % to 0.9 %. Varying the extrusion ratio at this temperature further reduces porosity from 0.9 % to 0.2 %, enhancing hardness and compression yield point. The study underscores the interdependence of niobium core properties on powder hardness and flowability.

Conclusion: Tailoring capsule material, furnace temperature, and extrusion ratio yields a homogeneous core with minimal porosity. The combination of lower temperature and higher extrusion ratio enhances hardness and compression yield point. Future research should focus on optimizing powder preparation, controlled oxidation of zirconium phases, and improving process chain reproducibility for in vitro testing.

Outlook

Successful implementation of suitable powder preparation methods and controlled oxidation strategies holds promise for enhancing the mechanical properties of niobium profiles. Continued efforts to increase the reproducibility of the process chain will contribute to the production of reliable samples for comprehensive in vitro testing, marking a significant step toward the development of advanced dental implants with improved longevity and therapeutic capabilities.

Acknowledgement: The study was supported by Deutsche Forschungsgemeinschaft (project number 426335750).

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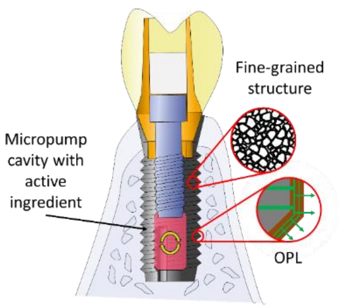
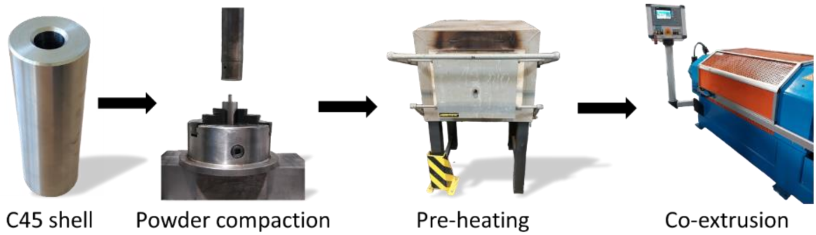
Figures





Diversity patterns of bacteriophages infecting Veillonella species across clades and niches

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Objectives: Veillonella species are relevant human commensals and accessory pathogens, which support the biofilm growth in the oral cavity. So major objectives were to uncover the prevalence and diversity of bacteriophages infecting Veillonella species which colonize the human oral cavity and understand the impact of those phages on the oral microbiome.

Materials and Methods: Publicly available genome sequences for Veillonella strains and human oral metagenomes were retrieved. Genome mining was performed with PHASTER and VirSorter. Data from IMG/VR was integrated. Phage-specific PCRs were established (n = 50). Samples were taken from the oral surfaces of 35 individuals. Phage isolations were performed by overlay assays using samples with high phage loads.

Results: Genome mining with comparative genomics, screening of clinical isolates and samples, as well as profiling of metagenomes allowed characterization of fifteen major phage clusters, mostly represented by previously uncharacterized phages. Phage diversity patterns varied significantly for different phage types, host clades, and environmental niches. Veillonella phages were prevalent at multiple oral sites. Human tongue hosted the most abundant populations of these phages. Phage plaques have not been detected so far.

Conclusion: The results support the exploration of the eco-evolutionary forces shaping phage-host interactions in the human microbiome. Furthermore, putative lytic phages may provide new therapeutic options. In the future, the conditions for phage isolations will expended by additional host strains and culture conditions. Moreover, experiments concerning the impact of those phages on complex biofilms are planned.

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Lay experts' mental models of smart implant technology: A qualitative exploration of the role of initial information, labels, and information needs

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Objectives: Smart technology, exemplified by smart implants (SI) for orthopedic, dental, and auditory applications, is advancing medical research. Public perceptions of smart medical technology vary, with openness prevailing (Antes et al., 2021). However, concerns and anxieties are also discussed (Esmaeilzadeh et al., 2021; Yang et al., 2019). Participatory science communication can address and overcome barriers to understanding and acceptance of medical progress by involving target groups as "lay experts" early in technology development (Raupp, 2017). Analyzing the mental models (MM) of a target group is a way to uncover their initial understanding of a new technology (Joubert et al., 2020). This study thus aims to explore the MM that lay experts develop based on initial information on SI (RQ1) and identify associated information needs (RQ2).

Materials and Methods: In 2022, 45 qualitative interviews were conducted with patients who had received an orthopedic, dental, or cochlear implant within the past ten years. Before answering questions (Table 2), participants were introduced to SI technology and its conceptual label ("smart implants") through a vignette (Figure 1). Transcribed verbatim, the interviews underwent qualitative content analysis (Mayring, 2015) with both inductive and deductive coding. Relevant units were further scrutinized with automated content analysis methods such as topic modeling and sentiment analysis.

Results: Addressing RQ1, the corpus revealed five topics concerned with SI and their association with (artificial) intelligence ((A)I) (Table 3). Sentiment analysis indicated ambivalent yet slightly positive language in describing the topics (Figure 2). Regarding RQ2, diverse information preferences were noted, encompassing themes, information sources, and transmission methods.

Conclusion/ Outlook: Our study suggests that participants' MM not only incorporated information from the vignette, but often went beyond it.

To enhance their comprehension and create a cohesive understanding, respondents relied on inferences from their existing knowledge (Gentner & Gentner, 1983). The conceptual label played a significant role, guiding assumptions about the implants' functionalities and (A)I. Given the high demand for additional information and the potential influence of MM on behavioral intentions (Jones et al., 2011), further research is needed to better understand the processing and integration of information on unfamiliar topics into people's MM.

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Figures

Table 1. *Sample characteristics.*

implant type		≤ 60 years of age	> 60 years of age	M (SD)
orthepedic (knee, hip)	Female	n = 7	n = 5	64.29 (10.11)
	Male	n = 0	n = 5	
dental	Female	n = 5	n = 6	51.62 (15.32)
	Male	n = 5	n = 0	
CI	Female	n = 4	n = 4	53.15 (15.63)
	Male	n = 3	n = 2	

Table 2. *Lists of main domains covered in the interviews.*

Reactions to and attitudes towards smart implants, e.g.: • 'What do you think spontaneously when you hear 'smart implants'? Why?' • 'In your opinion, what are the advantages and disadvantages of smart implants?' • 'To what extent would you trust an intelligent implant? Why (not)?'
Information needs, e.g.: • 'What would you like to know about smart implants?' • 'How would you like to be informed about smart implants?' • 'To what extent do you feel able to understand how smart implants work?'

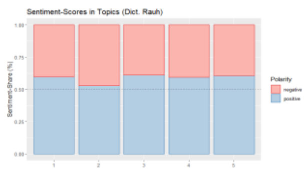

Figure 2. *Sentiment Scores per Topic, based on Rauh (2018).*

Development of an Impedance Spectroscopic Method to Monitor the Position of Cochlear Implants

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Objectives: Cochlear implants are hearing prostheses for deaf patients with an intact auditory nerve [1]. The stimulation efficiency of cochlear implants strongly depends on the possible maximum current stimulating the spiral ganglion cells which can be affected by the position of the cochlear implant inside the cochlea and its distance to the spiral ganglion cells [2]. But, also other effects, such as cell occupation on the stimulation electrodes and the composition of the perilymph, can influence the stimulation efficiency of a cochlear implant [3]. This work shows impedance spectroscopic measurements of a cochlear implant to monitor the influence of different effects on the impedance between two stimulation electrodes which can be used as a basis for the development of a position monitoring method while insertion and later to monitor the functionality of cochlear implants in long term use without radiation exposure.

Materials and Methods: In this work, we measured the impedance between two stimulation electrodes of a cochlear implant SlimJ from Advanced Bionics with an impedance analyzer E4990A from Keysight. Therefore, we constructed a measurement setup to change a) the position of the cochlear implant inside an enlarged cochlea model in the form of a spiral milled in bovine bone, b) the distance of the stimulation electrodes to a piece of bovine bone and c) the composition of the surrounding saline according to its sodium chloride concentration which simulates the perilymph. The three effects were investigated in separate experiments.

Results: The measurements show, that the three different effects can be measured separately with our impedance spectroscopic method. The smaller the distance between the stimulation electrodes and a piece of bone, the higher is the impedance between the two stimulation electrodes (see Figure 1). The higher the concentration of sodium chloride in the surrounding medium, the lower is the

impedance between the two stimulation electrodes (see Figure 2). The influence of the curvature could be measured as insertion depth but there was no clear pattern for the impedance change dependent on the insertion depth in the measurements yet (see Figure 3).

Conclusion/ Outlook: This work shows that different influences on the stimulation efficiency can be measured separately with the developed impedance spectroscopic method. In the next steps, the effects will be measured in combination and new electronics will be developed to measure capacities in the range of femto Farads for measuring the curvature of a cochlear implant inside the cochlea.

Acknowledgement: This work has been funded by the Deutsche Forschungsgemeinschaft (German Research Foundation) SFB/TRR 298 SIIRI Project ID 426335750 as well as under Germany's Excellence Strategy EXC 2177 1 Project ID 390895286. We thank Advanced bionics for the donation of three cochlear implant electrodes.

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Figures

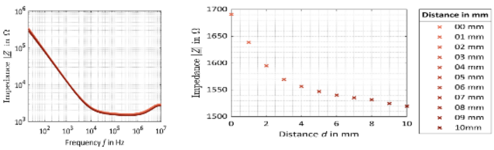

Figure 1: Impedance measurements between two stimulation electrodes in 0.9 % saline in dependence of the frequency *f* (left). Magnitude of impedance |*Z*| in dependence of sodium chloride concentration at 10 kHz (right).

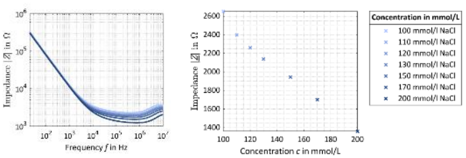

Figure 2: Impedance measurements between two stimulation electrodes in saline with different sodium chloride concentrations between 100 mmol/L and 200 mmol/L over frequency *f* (left). Magnitude of impedance |*Z*| in dependence of sodium chloride concentration at 10 kHz (right).

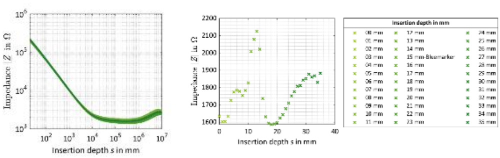

Figure 3: Impedance measurements between two stimulation electrodes in 0.9 % saline with different insertion depth *s* between 0 mm and 35 mm in a spiral milled in bovine bone over frequency *f* (left). Magnitude of impedance |*Z*| in dependence of the insertion depth at 10 kHz (right).

Cross-protection from antibiotics in polymicrobial biofilms

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Objectives: β-lactam antibiotics have been widely used to combat human pathogens but can fail to clear infection. Tolerance to β-lactams in biofilms can reduce treatment options, favor disease development and increase the risk of secondary complications. How complex biofilms can tolerate high concentrations of β-lactams is not fully understood.

Materials and Methods: We studied the tolerance of oral biofilms, a valuable model for complex biofilms in general, to amoxicillin, the most commonly used β-lactam in dental practice. We assessed the prevalence of β-lactamases and β-lactamase producers in human microbiome, with focus on the oral milieu, by integrating information from literature, 152,000 microbial genomes, and cultivation experiments. Evaluation of bacterial strains representing 20 genera and 6 classes using cross-protection assays showed that multiple enzymes representing molecular classes A, B, C, and D originating mostly from taxonomically allochthonous producers, can cross-protect other bacteria to different extent. Two most prominent mechanisms are derepression of the chromosomic cephalosporinase gene and carriage of multi-copy plasmidic β-lactamase genes. Even a single base mutation in gene controlling expression of β-lactamase genes can completely change the biofilm response to amoxicillin. The presence of a potent β-lactamase producer in biofilms inoculated from complex microbiota can confer high protection from β-lactams to other community members in vitro. Only a well-timed phage treatment of biofilms specifically removed β-lactamase producers and re-sensitized the biofilms to amoxicillin.

Results: Increased polymicrobial tolerance to β-lactams can develop in human-associated biofilms due to presence of potent β-lactamase producer strains. Specific removal of β-lactamase producers through bacteriophage therapy can broaden treatment options.

Conclusion/ Outlook: Dental plaque represents a reservoir for colonizing invader species producing β-lactamase and cross-protecting strains in physical proximity from β-lactam antibiotics. The dissemination of oral opportunistic pathogens via bloodstream or inhalation poses a health risk for immunocompromised, elderly patients with pre-existing conditions. A phage based therapy is a promising treatment option, which needs to be further investigated and developed.

Acknowledgement: Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB/TRR-298-SIIRI

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Figures

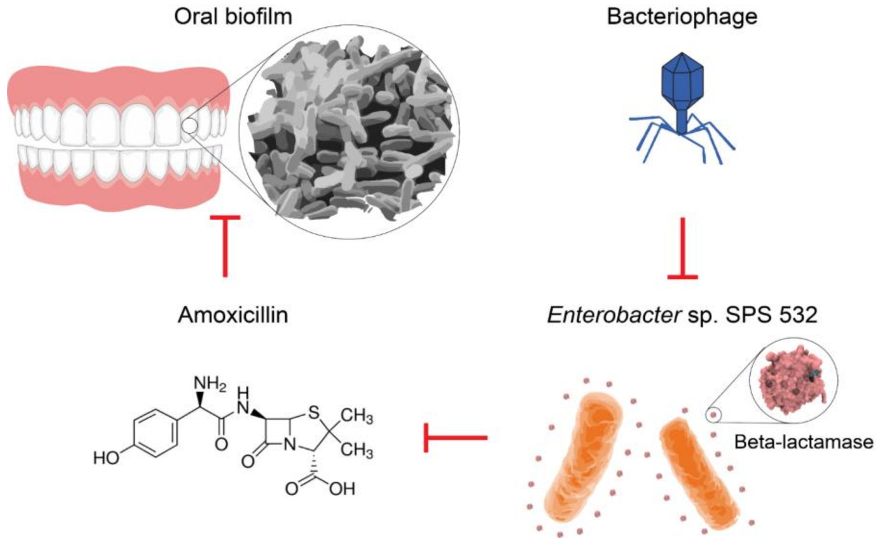

Figure 1 | Working hypothesis

A Comparative Analysis of an Oral Multispecies Biofilm Model under Various Oxygen Conditions

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Objectives: Biofilm-associated infections remain a significant challenge in peri-implant mucosal healthcare, leading to inflammation (peri-implant mucositis) and bone loss (peri-implantitis) [1]. A multispecies oral biofilm model has been already developed in our research group [2], consisting of the species Streptococcus oralis, Actinomyces naeslundii, Veillonella dispar and Porphyromonas gingivalis. However, the specific effects of various oxygen conditions on multispecies oral biofilm models are poorly understood, and the long-term behavior of existing biofilm models remains largely unexplored [3]. This study aims to investigate the consequence of normoxic (21 % O_2) and anoxic (0 % O_2) conditions in an in vitro four-species biofilm for a period of 21 days.

Materials and Methods: S. oralis, A. naeslundii, V. dispar, and P. gingivalis were cultured individually on FAA + sheep blood plates under anoxic conditions. After a separated preculture in BHI + Vitamin K1 for 24 hours, the species were combined and incubated in 24-well plates with titanium or glass platelets under varying oxygen conditions. A partial medium change was performed every 48 to 72 hours. Biofilms were stained at different time points (1 to 21 days) for LIVE/DEAD and FISH analysis using CLSM. Biofilm DNA was collected for PMA RT-qPCR, and RNA was analyzed regarding transcriptomics to quantify biofilm composition and activity.

Results and Discussion: Within the initial 48 hours, normoxic biofilm demonstrated a dominance of A. naeslundii, most likely attributable to the protein oxidation defense mechanism employed by A. naeslundii against peroxide generated under normoxic conditions. Over a 21-day period, both biofilms experienced increased dominance of V. dispar and co-localized P. gingivalis, particularly pronounced in anoxic conditions. Initial biofilm volume augmentation stopped after 7 days, accompanied by a notable reduction in bacterial cell membrane

integrity from day 1 to day 14, possibly linked to the sedimentation of deceased bacterial entities.

Conclusion/ Outlook: Based on the initial results, there is a significant difference between biofilms cultivated under normoxic and anoxic conditions, especially in the first two days. In the future, biofilm can be cultivated under hypoxic conditions to compare the outcomes with those from the normoxic and anoxic environments, as the clinically relevant oxygen condition at the infection sites corresponds to hypoxia. Additionally, biofilm composition can be quantified using RT-qPCR and PMA RT-qPCR techniques, and the pH value and the oxygen concentration levels within the biofilm matrix can be measured.

Acknowledgement: R2N Micro-Replace Systems, funded by Niedersächsisches Ministerium für Wissenschaft und Kultur

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Evaluating electrophysiological and behavioral measures of neural health in cochlear implant users based on a parametric computational model of an electrically stimulated cochlea

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Objectives: A computational model of the human cochlea with a cochlear implant (CI) previously developed at the German hearing center, Hannover Medical School (MHH), was updated and used to evaluate the effectiveness of two distinct methods for predicting neural health.

Materials and Methods: The first method measured the threshold and most comfortable levels for monopolar and focused quadrupolar (QP) stimulation. The second method assessed the interphase gap (IPG) slope or offset effects in electrically-evoked compound action potential (eCAP) experiments. Our experiments simulated the degeneration of auditory nerve fibers (ANFs) in different cochlea regions under three different neural health conditions (healthy, shrunk, and total degeneration). This model consisted of a 3D finite element method (FEM) model to predict the voltage spread in the implanted cochlea, and a neuron model to simulate peripheral neural responses, consisting of phenomenological ANF and physiological cable models.

Results: The experiment results demonstrated that the difference in threshold level between different neural health conditions with the QP configuration could indicate different neural health conditions. However, the results from the IPG-slope and IPG-offset effects in the eCAP experiments were not consistently related to the neural health conditions.

Conclusion / Outlook: Our results suggested that while the threshold level with the QP configuration may be a possible method for predicting neural health, further research is necessary to identify more accurate methods for assessing neural health in CI recipients.

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Figures

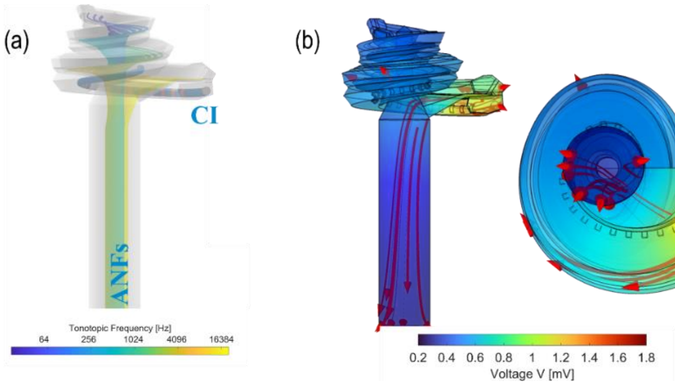

Figure 1: (a) An overview of the FEM and fiber models. The 3D model contains a CI electrode array in the scala tympani. (b) FEM simulation results when the most basal electrode is stimulated. The colors indicate Volt units and the red ribbons are current density streamlines.

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