Bern University of Applied Sciences

UNIVERSITÄT BERN

Master Biomedical Engineering

Annual Report 2019

Contents

Introduction

Following the 10th birthday of our master's program three years ago, we honored its founder, Prof. Lutz Nolte, who retired from his full professorship at the University of Bern in 2019. Starting at the M.E. Müller Institute for Biomechanics, his network and his vision of a hub for biomedical engineering at the University of Bern shaped the content and orientation of our program and contributed widely to the emergence of the ARTORG Center.

On a more practical note, the study coordination of the BME program moved from the Wankdorf site of the former Institute for Surgical Technology and Biomechanics (ISTB) to the new glass building of the Swiss Institute for Translational and Entrepreneurial Medicine (SITEM) located next to the university hospital. This location increases visibility, while the translational environment reinforces the integration of BME in the medical faculty.

The replacement of lecturers who retire or leave our universities remains always a challenge but gives also opportunities to new researchers to participate in our educational effort and to refresh the content and pedagogical scenarios of our courses. I am particularly grateful to Prof. Rouven Porz, head of medical ethics at the university hospital, who accepted to take over the ethics lecture for BME with an updated and attractive roadmap.

In the spring, the Biomedical Engineering Day 2019 reunited again our students with our research institutes, spin-offs and industry partners. The live surgery was performed by Prof. Klaus Siebenrock from the Clinic of Orthopedic Surgery and Traumatology. He performed a total hip replacement that was moderated in the auditorium by Dr. Johannes Bastian. For the first time, a comic science slam was organized that allowed researchers to engage their theater skills and bring some humor to this rigorous and demanding engineering field.

In the fall, the number of starting students reached 59, which represents a slight but motivating increase with respect to previous years. The continuous evaluation of all courses by the university indicates that we are on the right track and encourages further initiatives to improve not only the content but also quality of the courses. The potential initiation of new engineering programs at the university of Bern may help introduce novel pedagogical concepts to make engineering studies even more attractive.

In conclusion, I wish to praise the remarkable performance of our teachers, who represent the heart of our master's program. I would also like to reiterate my appreciation to the study coordination, Mrs Ulla Jakob, Alexandra Neuenschwander-Salazar and Julia Spyra for improving continuously the service to the students and lecturers of the program. I am truly proud to present our 2019 activity report and wish you an enjoyable reading.

Philippe Zysset
Program Director

Organization

Management

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Program Director, University of Bern

V. M. Koch
Deputy Program Director,
Bern University of Applied Sciences

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Study Coordinator, University of Bern

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Study Coordinator, Bern University of Applied Sciences

A. Neuenschwander Salazar
Study Coordinator, University of Bern

J. Spyra
Event Organization, University of Bern

Ph. Büchler
Master Thesis Coordinator, University of Bern

Retirement Symposium Prof. Lutz Nolte

On the 29th of January 2019, Prof. Dr. Lutz Nolte took his well-deserved retirement. It was marked with a symposium that celebrated his two decade contribution to the field of biomedical engineering and his outstanding activities as an ambassador for research and teaching at the University of Bern. Despite leaving one role behind, we knew that we were not parting ways entirely, as he continues to contribute and lead various initiatives at the University of Bern as emeritus faculty.

Many former students, partners, colleagues and peers joined friends and family to share stories and experiences that acknowledged and honoured the many ways in which Prof. Nolte established wholly new areas of biomedical engineering research and pursued the translation of his findings into the clinic for the benefit of patients.

Notable contributors honouring Prof. Nolte included:
Prof. em. Dieter Weichert (RWTH Aachen), Dr. Heiko Visarius, Prof. Leo Joskowitz (Hebrew University, Jerusalem), Prof. Stephen Ferguson (ETH Zürich), Prof. em. Gabor Szekely (ETH Zurich) und Dr. Walter Steinlin (former President KTI/Innosuisse). As a dedicated inventor and developer Prof. Nolte took on singular research challenges and added to the state of the art with his work; as a gifted leader of networks, he enabled others to take on entrepreneurial opportunities.

Only few can claim to master several careers in parallel, let alone succeed in them equally at the highest level. Prof Nolte with his outstanding contribution to biomedical engineering research, entrepreneurship, innovation and improvements to patient care is that kind of exceptional individual. We thank you for your contribution Prof. Nolte.

Stefan Weber, ARTORG Center

Lutz Nolte receives a caricature from Ben Gantenbein.

Form left to right: Walter Steinlin, Stephen Ferguson, Heiko Visarius, Lutz Nolte, Gabor Szekely, Leo Joskowicz, Dieter Weichert

Structure of Courses in the Master's Program

Since the start of the Master's Program Biomedical Engineering in March 2006, the constant effort to improve the quality of our curriculum has resulted in substantial changes of the course structure over the past years. The first curriculum consisted of a number of individual courses that were either mandatory or elective, but their coherence with regards to contents was in most cases not expressed by a defined structure. However, two major modules (formerly called "focus areas") already existed.
As of Fall Semester 2009, all courses were grouped in a strictly modular way in order to enhance both the clarity and the flexibility of the curricular structure. A main idea was to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called "Image-Guided Therapy".
Adaptations in the legal framework of the master's program are now offering more flexibility in the design of courses and modules, thus providing the basis for a second fundamental restructuration of the curriculum as of Fall Semester 2013. In particular, a module called "Complementary Skills" was introduced. In addition, the list of mandatory courses in both basic and major modules was revised.
More recently, in Fall Semester 2017, a module "preparation courses" was created. The courses in this module are intended to fill gaps regarding prerequisites for basic and advanced courses in the master's program Biomedical Engineering. In 2018, the basic module "Biomedical Engineering" was re-structured and augmented by new courses in "Medical Informatics" and "Introduction to Biomechanics".

The Curriculum

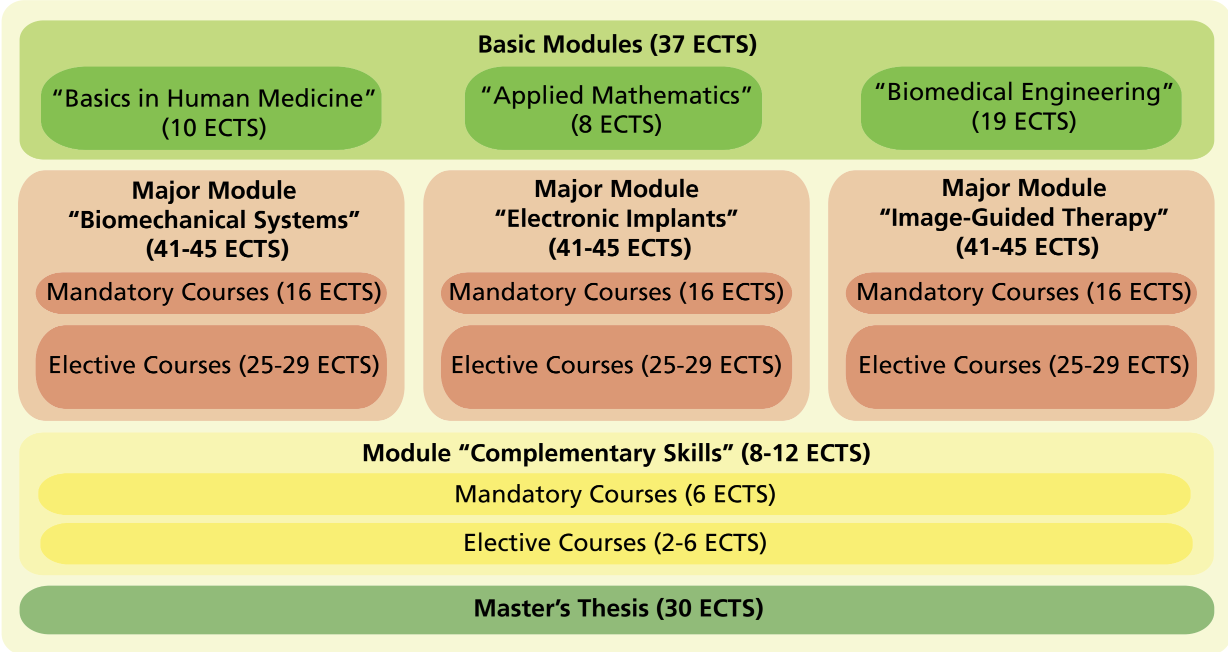
Duration of Studies and Part-Time Professional Occupation
The full-time study program takes 4 semesters, which corresponds to 120 ECTS credits, one ECTS credit being defined as 25–30 hours of student workload. It can be extended to a maximum of 6 semesters. When a student decides to complete the studies in parallel to a part-time professional occupation, further extension is possible on request. To support regular part-time work, mandatory courses take place (with rare exceptions) on only 3 days per week.

Preparation Courses
Owing to the interdisciplinary nature of the BME master's program, our students come from various fields of study. Especially students with a non-engineering background – for example in medicine – do not fulfill all prerequisites for the courses of the master's program. Therefore, introductory courses in MATLAB, C++ programming, Electrical Engineering and Engineering Mechanics as well as the tutorial-based course "Selected Chapters in Mathematics" were introduced and allow to create a tailor-made curriculum for these students. Students with a background in engineering, on the other hand, have the possibility to select these courses freely if they feel the need to refresh some of the knowledge provided.

Basic Modules
The basic modules provide the students with the necessary background to be able to fully understand the complex subject matter in the specialized courses. All students have to complete all courses in the Basic Modules Human Medicine, Applied Mathematics, and Biomedical Engineering. In the first semester, all mandatory courses belong to this group, whereas in the second and third semester, the courses from the basic modules make up for approximately 30 %.

Major Modules
The choice of one of three major modules Biomechanical Systems, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization.
Approximately one third of the major modules consist of mandatory courses. In the elective part of the major module, the student is allowed to select every course from the list of courses in the master's program, giving rise to a high degree of diversity and flexibility and allowing for numerous course combinations. However, this freedom makes it somewhat difficult for the student to make reasonable choices regarding professional prospects.
This is why the responsible lecturers developed a recommended study plan to guide the students through the course selection process and to avoid organizational problems such as overlapping courses. If a student follows the recommended path, he or she can be sure to establish a sound professional profile.

Module "Complementary Skills"
Apart from the rapid development of technology itself, today's biomedical engineers are increasingly challenged by complementary issues like ethical aspects, project planning, quality assurance and product safety, legal regulations and intellectual property rights, as well as marketing aspects. Language competence in English is of paramount importance both in an industrial and academic environment. This situation has been accounted for by the introduction of a new module called "Complementary Skills" where students are required to complete two mandatory courses (Innovation Management; Fundamentals of Quality Management and Regulatory Affairs) as well as 2–6 ECTS from the electives courses (Ethics in Biomedical Engineering; Scientific Writing in Biomedical Engineering; Clinical Epidemiology and Health Technology Assessment.)



Master's Thesis

The last semester is dedicated to a master's thesis project on an individually suited topic in an academic research group at the University of Bern or the Bern University of Applied Sciences or, for particular cases, in an industrial research and development environment. As a rule, all 90 ECTS credits from the course program have to be completed, thus ensuring that the student is able to fully concentrate on the challenges imposed by exciting research activities. The master's thesis includes the thesis paper, a thesis presentation and defense as well as a one-page abstract for publication in the Annual Report of the master's program.

List of Courses

- Advanced Topics in Machine Learning
- Applied Biomaterials
- Basics in Physiology for Biomedical Engineering
- Biological Principles of Human Medicine
- (Bio)Materials
- Biomechanics Labs
- Biomedical Acoustics and Audiology
- Biomedical Instrumentation
- Biomedical Laser Applications
- Biomedical Sensors
- Biomedical Signal Processing and Analysis
- BioMicrofluidics
- C++ Programming I
- C++ Programming II
- Cardiovascular Technology
- Clinical Applications of Image-Guided Therapy
- Clinical Epidemiology and Health Technology Assessment
- Computer-Assisted Surgery
- Computer Graphics
- Computer Vision
- Continuum Mechanics
- Design of Biomechanical Systems
- Dynamical Models: Analysis, Conception and Simulation
- Ethics in Biomedical Engineering
- Finite Element Analysis I
- Finite Element Analysis II
- Fluid Mechanics
- Functional Anatomy of the Locomotor Apparatus
- Fundamentals of Quality Management and Regulatory Affairs
- Image-Guided Therapy Lab
- Innovation Management
- Intelligent Implants and Surgical Instruments
- Introduction to Biomechanics
- Introduction to Digital Logic
- Introduction to Electrical Engineering
- Introduction to Engineering Mechanics
- Introduction to Medical Statistics
- Introduction to Programming
- Introduction to Signal and Image Processing
- Introductory Anatomy and Histology for Biomedical Engineers
- Lecture Series on Advanced Microscopy
- Low Power Microelectronics
- Machine Learning
- Medical Image Analysis
- Medical Image Analysis Lab
- Medical Informatics
- Medical Robotics
- Microsystems Engineering
- Molecular and Cellular Biology Practical
- Numerical Methods
- Ophthalmic Technologies
- Orthopaedic Surgery – Practical Course
- Osteology
- Principles of Medical Imaging
- Programming of Microcontrollers
- Regenerative Dentistry for Biomedical Engineering
- Rehabilitation Technology
- Scientific Writing in Biomedical Engineering
- Selected Chapters in Mathematics
- Short Introduction to MATLAB
- Technology and Diabetes Management
- Tissue Biomechanics
- Tissue Biomechanics Lab
- Tissue Engineering
- Tissue Engineering – Practical Course
- Wireless Communication for Medical Devices

Major Modules

Biomechanical Systems

Prof. Dr. Philippe Zysset

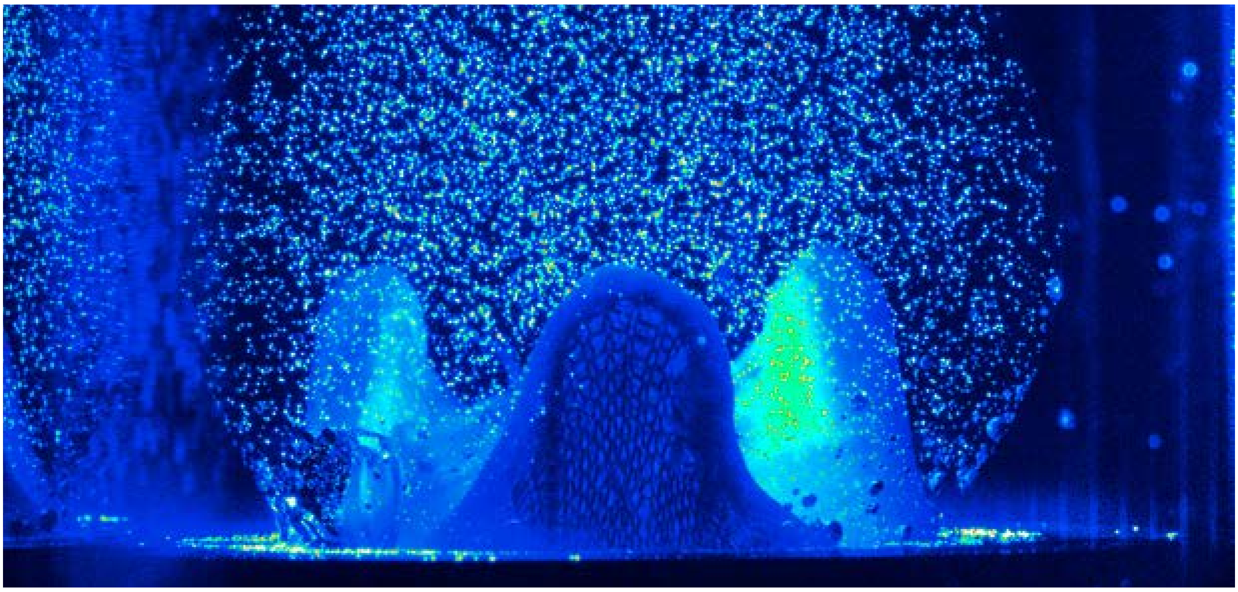
The respiratory, cardiovascular and musculoskeletal systems are the transport and structural bases for our physical activities and their health have a profound influence on our quality of life. Lung diseases, cardiovascular diseases, musculoskeletal injuries and pathologies are costly ailments facing our health care systems, both in terms of direct medical costs and compensation payments related to loss-of-work.

In this module, students will gain a comprehensive understanding of the multi-scale organisation of the respiratory, cardiovascular and musculoskeletal systems, combining knowledge from the cell, tissue, organ to the body level. They will learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechano-biology. Students will learn to draw connections between tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of pneumology, cardiology, cardiovascular surgery, orthopaedics, dentistry, rehabilitation and sports sciences.

The mandatory courses in this module provide the student with fundamental knowledge of fluid and solid mechanics, tissue engineering, tissue biomechanics and finite element analysis. This provides an overview of the functional adaptation of the respiratory, cardiovascular or musculoskeletal system to the demands of daily living, and the necessary conditions for its repair and regeneration. This major module requires a prior knowledge of mechanics, numerical methods and related engineering sciences, as many of the mandatory and elective courses build upon these foundations. Elective courses allow the students to extend their competence in a chosen direction, gaining knowledge in analytical methodologies, medical device design, minimally invasive surgery or rehabilitation.

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application and the lab benchtop to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of recent master thesis projects include mechanical characterization of collagen-elastin membranes for lung-alveoli-on-chip, human cornea after chemical crosslinking for treating keratoconus or implant press-fit for validation of computational models.

Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering, lab on chip or development of biomaterials. Most of the major companies in the fields of cardiovascular technology, orthopaedics, dentistry, rehabilitation engineering and pharmaceuticals are strongly represented within the Swiss Medtech industry and have an ongoing demand for graduates of this major module. At the interface between biomedical engineering and clinical applications, graduates may also pursue careers related to the evaluation and validation of contemporary health technology, a cornerstone for future policies on the adoption of these new methods in the highly competitive health care domain.



Laser-based measurement of the flow field through a heart valve prosthesis by seeding blood-mimicking fluid with fluorescent particles.

Major Modules

Electronic Implants

Prof. Dr. Volker M. Koch

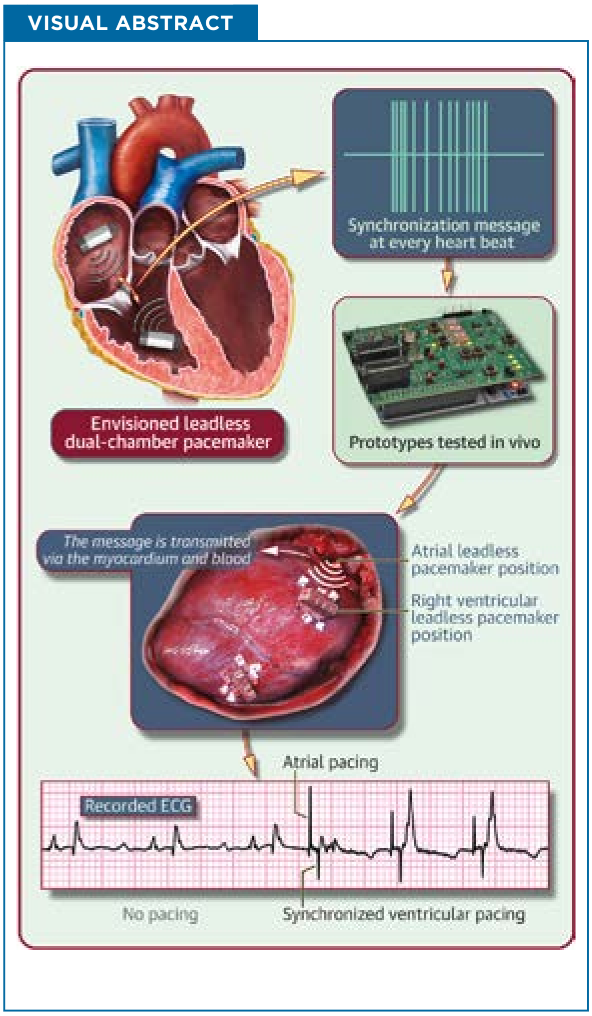
Electronic implants are devices like cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications become feasible and this exciting area is growing rapidly. For example, cochlear implants provide already approximately more than 320’000 people worldwide a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words. There are many more applications for electronic implants beyond treating heart problems, hearing loss or blindness. For example, there are electronic implants that treat Parkinson’s disease, obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

In this module, students will gain a comprehensive technical and application-oriented understanding that will allow them to select, use, design, and optimize electronic implants and similar biomedical systems. Since the work on such complex systems is usually done in interdisciplinary groups, another important goal is that graduates are able to work and communicate in teams consisting of, e.g., engineers, scientists, and medical doctors.

Specifically, students will learn about technology basics including intelligent implants and surgical instruments, biomedical signal processing and analysis, low-power microelectronics, wireless communications for medical devices, and microsystems engineering including MEMS technology. Application-oriented elective courses are also taught, e.g., cardiovascular technology, biomedical sensors, biomedical acoustics, biomedical laser applications, ophthalmic technologies, and diabetes management.

Students may already apply their knowledge as a part-time assistant in an institute and/or during their master’s projects. After finishing the degree program, a wide variety of career paths are available, ranging from research and development to project and product management. Many companies in Switzerland work in this field and “traditional” implants manufacturers have recently become interested in electronic implants, e.g., to measure forces in knee implants.

This major is open to all students of our master’s program. However, typically, students have an engineering-related background, for example, electrical engineering, microtechnology engineering, systems engineering, mechatronics engineering, mechanical engineering, or computer science.



Bereuter, L. et al. J Am Coll Cardiol Basic Trans Science. 2018;3(6):813–23.

Image-Guided Therapy

Prof. Dr. Stefan Weber

Image-Guided Therapy refers to the concept of guiding medical procedures and interventions through perceiving and viewing of medical image data, possibly extended by using stereotactic tracking systems. Medical imaging typically relates to a great variety of modalities ranging from 2D fluoroscopy and ultrasound to 3D computed tomography and magnet-resonance imaging, possibly extended to complex 4D time series and enhanced with functional information (PET, SPECT). Guidance is realized by determination of the spatial instrument-to-patient relationship and by suitable visualization of tracking and medical image data. Image guidance is very often accompanied by other surgical technologies such as surgical robotics, sensor enhanced instrument systems as well as information and communication technology.

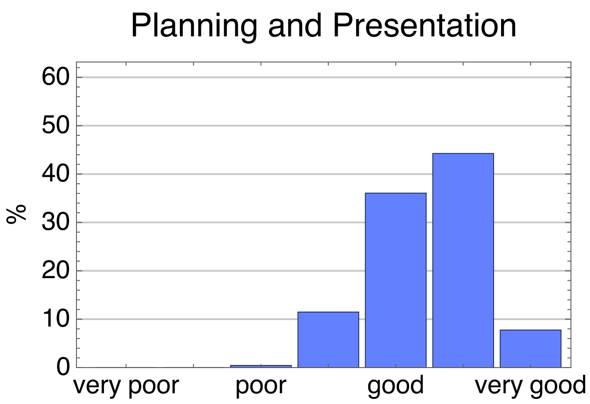
Students of the IGT module will study the clinical and technical fundamentals of image-guided therapy systems. They will develop an understanding of currently applied clinical standards as well as an overview of latest advancements in research. Successful students will be enabled to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches. This will be the basement for successful careers both in the industrial and academic sector.

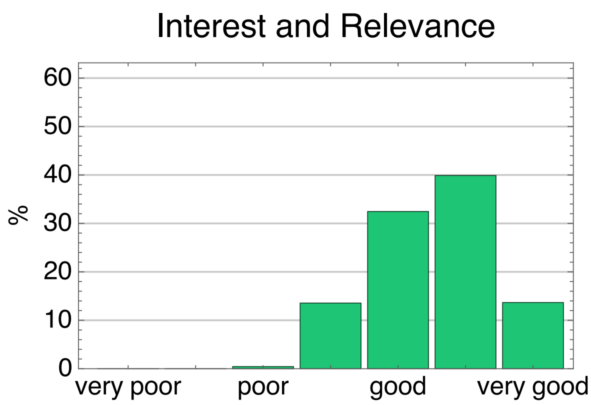
Mandatory courses of this module are concerned with the fundamentals of Signal and Image Processing and Medical Image Analysis. Furthermore, fundamental aspects of stereotactic image guidance, tracking, patient-to-image registration and basic clinical applications are taught in the course Computer-Assisted Surgery. Recent trends and fundamental aspects in surgical robot technology, minimally invasive procedures and its applications within IGT are introduced in the course Medical Robotics. Additional elective courses extend students competencies in related areas such as computer graphics, pattern recognition, machine learning, and regulatory affairs.

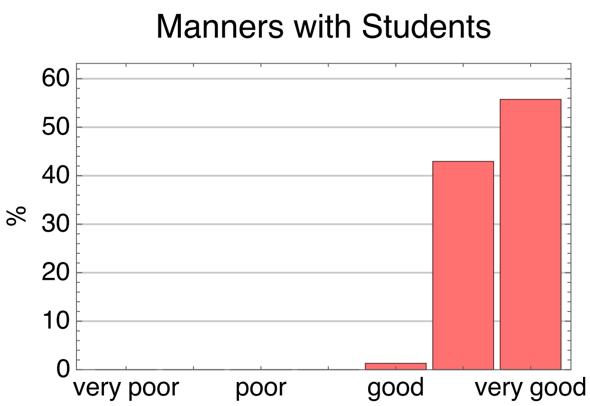
Assembly of surgical robot system for hearing aid implantation. (© ARTORG Center, University of Bern 2019)

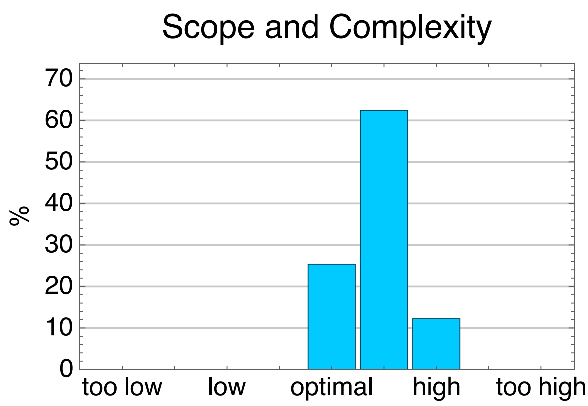
Evaluation of Courses in the Academic Year 2019 / 2020

Like in the previous years, a centralized evaluation was performed in the master's program in Fall Semester 2018 and Spring Semester 2019 according to the guidelines of the University of Bern. Both semesters were considered leading to 58 course evaluations involving more than 900 forms in total. The results regarding all forms (see below) reveal that the students are very satisfied with the course program and that the courses are interesting and demanding at the same time.









Faculty

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Jürgen Burger, Prof. Dr.
Ramona Buser, Dr.
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Paolo Favaro, Prof. Dr.
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Rainer Egli, Dr.
Jens Fichtner, Dr. med.
Michael Fix, Prof. Dr.
Martin Kompis, Prof. Dr.
Hubert Kössler
Kurt Lippuner, Prof. Dr.
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Thomas Pilgrim, Prof. Dr.
Rouven Porz, Prof. Dr.
Lorenz Räber, Prof. Dr.
Mauricio Reyes, Prof. Dr.
Waldo Valenzuela, Dr.
Christophe Von Garnier, Prof. Dr.

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Heiner Baur, Prof. Dr.
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Kenneth James Hunt, Prof. Dr.
Marcel Jacomet, Prof. Dr.
Jörn Justiz, Prof. Dr.
Theo Kluter, Prof Dr.
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André Lisibach, Prof. Dr.
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Lukas Rohr, Prof. Dr.
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David Eglin, Dr.
Lukas Eschbach, Dr.
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Daniel Haschtmann, PD Dr.
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Thomas Imwinkelried, Dr.
Björn Jensen, Dr.
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Reto Lerf, Dr.
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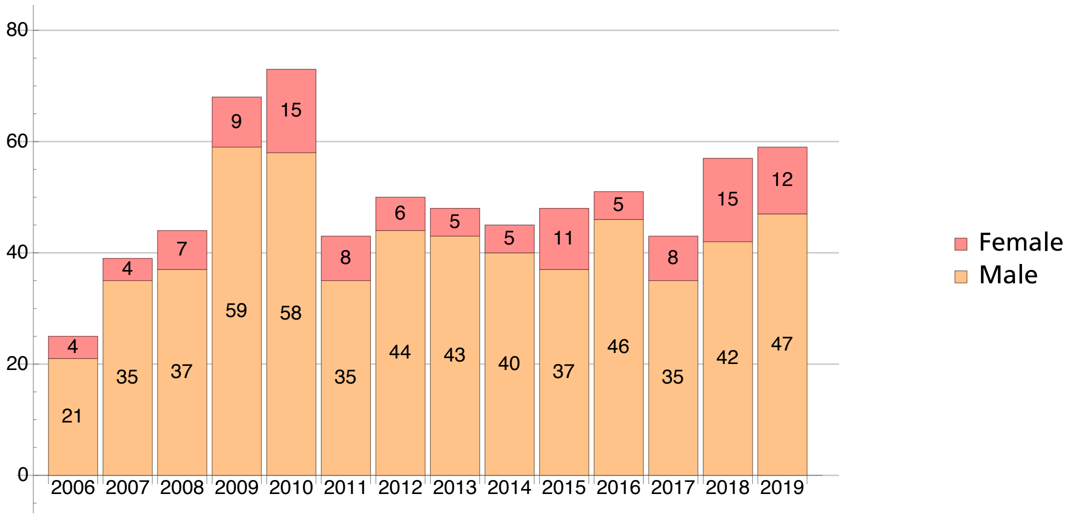
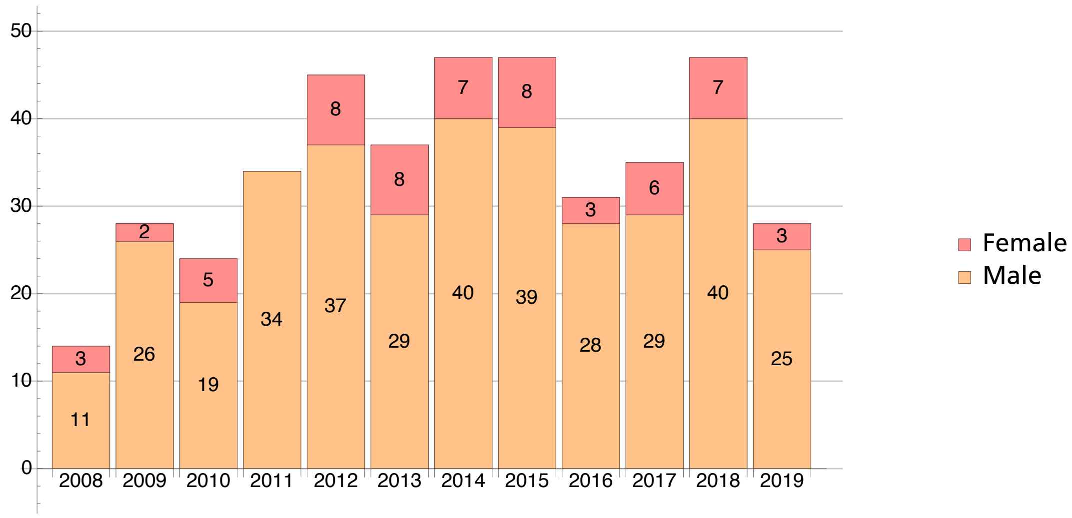
Alexander Mack, Dr.
Katharina Maniura, Dr.
Simon Milligan, Dr.
Walter Moser, Dr.
Richard Nyffeler, PD Dr. med.
Jean Pascal Pfister, Prof. Dr.
Benjamin Pippenger, Dr.
Felix Reinert, Dr.
Barbara Rothen-Rutishauser, Prof. Dr.
Jorge Sague, Dr.
Birgit Schäfer, PD Dr.
Matthias Schwenkglenks, Prof. Dr.
Johann Jakob Schwiedrzik, Dr.
Jivko Stoyanov, PD Dr.
Peter Varga, Dr.
Jürgen Vogt, Dr.
Peter Wahl, Dr. med.
André Weber, Dr.
Tobias Wyss, Dr.
Andreas Zumbühl, Prof. Dr.
Thomas Zweig, Dr. med.

Statistics

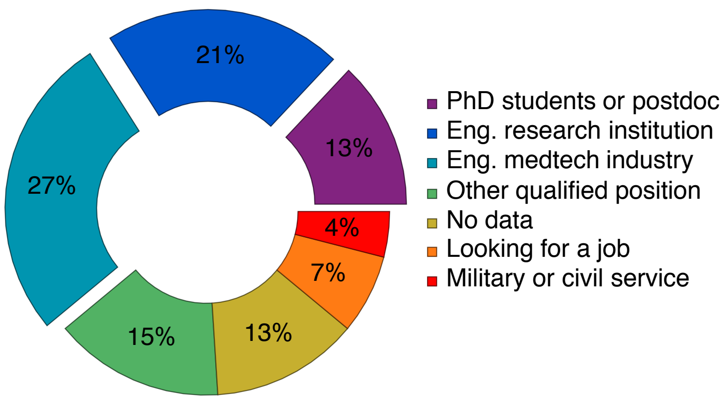
Number of New Students (above) and Graduates (below)



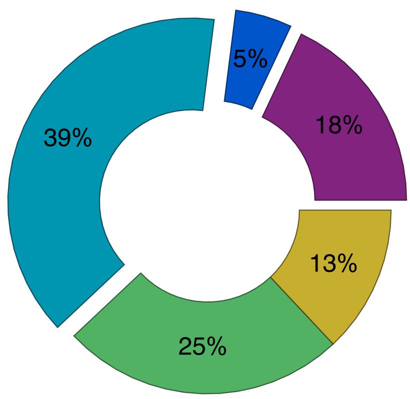


Profession after Graduation

Activity after 1 year



Activity after 5 years



Graduation Ceremony

The graduation ceremony of the academic year 2018/19 took place on 1st March 2019 at the mighty Berner Münster Cathedral, Bern. The program was organized by the Faculty of Medicine and included graduating students from all study programs within the Faculty. We all gathered together along with our beloved ones to get officially designated as Biomedical Engineers. Since we hadn't seen each other for a long time after the exams, the ceremony was a sort of reunion for us. It has been a memorable journey during the past two years and now we were together to celebrate the achievement of a significant milestone in our lives.

We were welcomed by the enchanting music by the Mediziner-Orchestra, Bern. Prof. Dr. Hans-Uwe Simon, Dean of the Medical Faculty delivered the welcome speech. The commencement speech by Dr. Fritz Schiesser, President ETH-Board enlightened a spirit of motivation and self-belief among the fresh graduates. He insisted the students to follow their passion and be confident to make right decisions without the fear of failure.

The presentation of the degrees started with the graduate doctors in medicine and dentistry followed by our turn. The degrees in biomedical engineering were awarded by Prof. Dr. Philippe Zysset. I had a roller coaster of emotions while walking up the stage to receive my degree and I am pretty sure that my friends had also experienced the same. The RMS award of excellence was awarded to our fellow mate Mr. Michael Rebsamen for attaining the best grade point average over the course of BME master program.

We were a group of students from different educational backgrounds when we first met but now after the successful completion of BME master program, we stand together as a group of highly skilled Biomedical Engineers. We are thankful to all our esteemed faculty members, guest lectures, members of the study coordination office and all other well-wishers who have contributed during this developmental transition.

Vikas Mathew, BME Alumnus 2019

Front row from left to right: Mathieu Jaquet, Michael Rebsamen, Joy Roth, Joy Roth, Lea Dal Fabbro, Martin Hofmann
Second row from left to right: Sakia Perret-Gentil-dit-Maillard, Dorian Thomet, Raphaël Wenger, Simon Wüthrich, Marco Dubach, Christian Burri, Martin Wigger, Yannick Soom
Third row from left to right: Vikas Mathew, Flavio Traversa, Christian Wüthrich, Samuel Knobel, Luca Sahli, Philippe Zysset, Marcel Vogt, Yves Jegge, Camilo Mendez Schneider (Photo: Adrian Moser)

RMS Award

The RMS Award is an award of excellence. Each year, the Robert Mathys Stiftung (RMS), an independent service laboratory and research institute, gives it to the best BME student for his/her outstanding achievements.
The award of 1000 CHF honors the student who receives the best grade point average over the course of the two-year BME master's program.
The study direction wishes to thank Dr. Beat Gasser and the executive board of the Robert Mathys Foundation for this contribution to the excellence and visibility of our biomedical engineering field.

RMS Award 2019
Michael Rebsamen receives the RMS Award 2019 from Philippe Zysset, Program Director Master Biomedical Engineering. (Photo: Adrian Moser)

Graduate Profile

Simon Scheurer, BME Alumnus 2019

Q: What was your academic and professional background prior to your BME studies?

A: I started my professional career with an apprenticeship as an electronics engineer. After my apprenticeship, I completed my bachelor's degree in electrical engineering at the Bern University of Applied Sciences.

Q: Why did you choose to pursue your master's studies at the University of Bern/Bern University of Applied Sciences?

A: From a technological point of view, the medical industry has always fascinated me. This field of industry works with the most modern and innovative technology to help people. To work in this field is extremely interesting and satisfying.

Q: You continued to work during your studies. How was this experience?

A: During my studies, I worked 40 % at the Bern University of Applied Sciences. I worked in a project related to biomedical engineering. Therefore, I could transfer my recently acquired knowledge directly into practice. I highly appreciated this.

Q: What was your career plan after the completion of your degree? Where do you work now?

A: After graduation, my colleagues and I founded the company Oxomed AG. This foundation was among other things based on the results of my master's thesis.
Our company has specialized in the development and distribution of hardware and software for retirement and care homes.

Q: What is the benefit of the master's studies with regard to your current professional activity?

A: I acquired a lot of new knowledge about the medical industry, which allows me to develop technical devices according to the needs.
The master's studies also allowed me an insight into research, which was a completely new field for me. I was even able to publish a scientific paper based on my master's thesis. For my research, I received the Senior University Bern Award 2019 and the SSBE Student Award 2019.
In addition, the part-time job at the Bern University of Applied Sciences gave me an important insight into the biomedical field and the start-up world. This enabled me to found Oxomed AG together with my colleagues. This is and remains a unique experience.

Top down:
Graduation ceremony 2019 (Photo: Adrian Moser)
Senior University Award 2019, Dies Academicus Bern
SSBE Student Award 2019, Campus Biotech Geneva

Two BME Alumni are Key to the Swiss Medtech Award Win 2019

This year´s Swiss Medtech Award is closely linked to the University of Bern Master´s in Biomedical Engineering: The BME graduates Marco Matulic and Juan Ansó are key to the success of this year´s winner CAScination AG. One worked on the company side and one at the University, and they were instrumental in the development of the winning technology.

Common Beginnings – Joint Success

The finals Swiss Medtech Award 2019 took place in early June at the Kursaal in Bern. After a rigorous competition process over several months, three finalists were chosen. On the day, each team presented their nominated technology. For CAScination, Chief Technology Officer Marco Matulic "pitched" the Otoplan® and HEARO® robotic ENT microsurgery platform which is used to give deaf patients a cochlear implant hearing aid. In the audience Dr Juan Ansó, senior researcher at the ARTORG Center, kept his fingers crossed for his colleague because the CAScination technologies had partly originated in Juan's doctoral research at ARTORG. Over the last five years, the two colleagues had worked very closely on the development of a robotic cochlear implantation technology. And both are graduates of the BME Master's program at the University of Bern.

As the award ceremony approached in the Kursaal, Marco Matulic and Juan Ansó sat together with their team colleagues from CAScination and ARTORG. The projection of the three nominee names was running across the screen, only to stop at "The winner is: HEARO®", and everyone erupted in a huge cheer: The close collaboration between the two BME Master's alumni had awarded them the first prize.

Entrepreneur at Heart

"I always wanted to be part of a business and one day even lead it", says Chief Technology Officer Marco Matulic of CAScination. Marco started his career with an apprenticeship to become a qualified electrician but soon discovered that he wanted to deepen his engineering knowledge. After an undergraduate degree in Systems Engineering in St. Gallen und Buchs, he wanted to continue studies without losing time with the need to acquire additional entry credits to a Master´s program. "I came across the BME Master's at the University of Bern, which accepted my undergraduate degree for a seamless entry into a postgraduate qualification. That sold it for me."

Marco carried out his master's project in the Image-Guided Therapies (IGT) group led by Professor Stefan Weber at ARTORG, working on the cochlear robot project in the very early stages. Following his graduation in 2015, Marco decided to join CAScination AG, a spin-out of the University of Bern founded by Stefan Weber, as the technology lead on the surgical robotic project. In this role at CAScination, he still interacted closely with the IGT group at the University and the Inselspital, as much of the technical and clinical research on the cochlear robotic procedure was taking place there. "Now I am leading a business that allows me to develop my ideas into products and services in the medical technology sector.", he states. "The BME Master's was a key step for me to decide that I wanted to stay in industry and not become an academic researcher. I found out that I am an entrepreneur at heart."

BME Research in the Operating Room

Juan Ansó came to Bern in 2010 from several years in industry with an undergraduate degree in Telecommunications Engineering from the University of Zaragoza (Spain) to expand his knowledge in Biomedical Engineering. He chose the BME Master's program at the University of Bern for its embedding into the clinical environment. "Through this Master´s, students are taught to understand and solve unmet clinical needs. These can only be tackled by biomedical engineers that directly work with clinicians – seeing patients, interventions and surgery almost every week". Juan combined his BME studies with a part-time job working on the development of the cochlear robotic platform and followed his Master´s with a PhD to expand his research in neurology and ENT robotic surgery.

"Through the regular interaction with Marco Caversaccio, Director of the ENT, Head and Neck Surgery at Inselspital, I experienced how my research would be translated into the clinic." The prototype robotic surgery platform Juan helped to research and build was used successfully at Inselspital to give 6 patients a cochlear implant, leading to a high profile publication in Science Robotics in 2017. This milestone allowed Juan to workside-by-side with the CAScination R&D team to help integrate his research findings into the award-winning HEARO® platform as an inventor of a university patent on this technology. "I had both: my research at ARTORG and seeing the technology that I helped to investigate and the process at CAScination of how this was turned into a product. This meant a lot to me, and it confirmed that I wished to remain in academia." Juan will take the next step towards leading his own research group, investigating new technologies in neurology and neurosurgery for the treatment of Parkinson's Disease, through a recently awarded SNSF research fellowship at the University of California San Francisco.

Usha Sarma

Marco Matulic and Juan Ansó (Photo: Tanja Kurt)

Biomedical Engineering Day 2019

The industry, medical doctors, and engineers meet for the Biomedical Engineering Day at the Inselspital in Bern with great success.

On May 3, 2019, the Biomedical Engineering Day took place in the auditorium Ettore Rossi at the Inselspital in Bern. The Master in Biomedical Engineering program of the University of Bern organized this event for the eleventh time.

The event is an efficient platform in Switzerland for networking of Master and PhD students and alumni as well as Swiss and international medical technology companies. This year's companies introduced themselves through oral presentations and gave insight into their commercial activities and their company philosophies as well as showed their demands on junior employees. Students thus had the opportunity to get to know potential future employers and contact them directly. This was made possible between the sessions in personal conversations and at the exhibitors' booths.

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Bern University of Applied Sciences, a partner within the master's program, used the possibility of presenting current research projects to more approximately 350 participants. Interestingly, Master and PhD students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too.

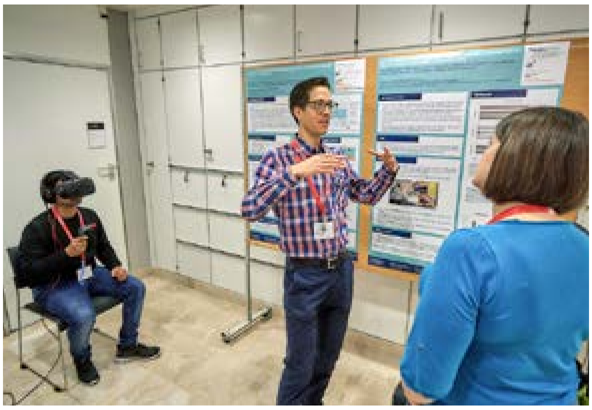
Besides company representatives, scientists, researchers, and young academics, medical doctors participated in this year's event as they had the chance for intensive communication with the biomedical engineers.

One highlight of the day was the successful live surgery by Klaus Siebenrock, Department of Orthopaedics Surgery and Traumatology, University Hospital Bern (Inselspital). Illustrative explanations in the auditorium were given by Johannes Bastian, from the same department.

Live surgery (Photo: Adrian Moser)

PhD students discuss latest results (Photo: Adrian Moser)

Research exhibition (Photo: Adrian Moser)



Experiment set-up gerontechnology (Photo: Adrian Moser)

Industrial exhibition (Photo: Adrian Moser)

Awards

At the end of the day, five awards for excellent academic achievements in the field of Biomedical Engineering at the University of Bern were presented:

1. Swiss Engineering Award for the best master's thesis (innovation): Jan Stapelfeldt (PeriVision – Visual field testing for everyone)
2. Swiss Engineering Award for the best master's thesis (basic science): Michael Rebsamen (Fast and Accurate Human Brain Morphometry Estimation with Deep Learning)
3. CCMT Award for the best PhD thesis: Stergios Christodoulidis (Lung Pattern Analysis using Artificial Intelligence for the Diagnosis Support of Interstitial Lung Diseases)
4. BME Club Award for the best poster: Mareike Apelt (Tissue Impedance Spectroscopy to Guide Resection of Brain Tumours)
5. BME Club Award for the best master's thesis abstract: Vikas Mathew (Erythrocyte-Based Nanotechnology for Personalized Drug Delivery Systems)

From left to right: Jan Stapelfeldt, Michael Rebsamen, Stergios Christodoulidis, Mareike Apelt, Vikas Mathew

We thank our sponsors and exhibitors

The Biomedical Engineering Club

The BME Club and Its Mission

The BME Club is an alumni club with the mission to provide and promote networking among its interdisciplinary members. We are a constantly growing group of biomedical engineers, scientists, past and present students and medical technology corporates eager to bring together the principles of engineering, biology, and clinical medicine. BME club accomplishes these goals by hosting events such as information sessions on the latest cutting-edge research in different fields of biomedical engineering, attendance of international conferences and organizing visits of various industrial plants and laboratories. A dedicated executive committee follows the principles of our constitution.
We are an enthusiastic and versatile group with diverse activities:

- visits to Swiss medical and engineering companies
- organization of the annual MEDICA trip
- information on career opportunities (including job offers)
- organization of the annual welcome event for new students of the BME Master program
- organization of an annual alumni gathering
- sponsorship of the poster and abstract awards at the annual BME day
- sponsorship of Conference Travel Grants
- automatic joint membership with Alumni UniBE
- offer joint membership with SSBE (Swiss Society for Biomedical Engineering)

In short, the BME club represents a unique platform for professional, lifelong communication and networking.
For further details look up our website at www.bmeclub.ch.

How to Join

Becoming a member is easy! Simply sign up at any BME Club event or visit us at www.bmeclub.ch. We are looking forward to welcome you!

The BME Club Board in 2019

Prabitha Urwyler
President
M.Sc. class 2006

Tamara Melle
Secretary, Treasurer, Master Student representative
M.Sc. class 2017

Tobias Imfeld
Webmaster
M.Sc. class 2009

Fredrick Joseph
PhD Student representative

BME Club alumni barbecue, August 2019.

BME Club city tour, September 2019

Trip to Medica 2019

Like a swiss clockwork, we are picked up at 11.45 pm in the evening by bus in Bern. Some people are having a nice little party with some music in the back of the bus, while others are sleeping already. After a short stop at the border to Germany we are heading towards our final destination, Düsseldorf.

At 7 o'clock in the morning the bus stops and we are standing in front of the youth hostel in Düsseldorf. After everyone stored their luggage it is time for some breakfast. Even if the coffee was not the best it was great to get energized a bit to be ready for our first day at Medica.

With public transport we reach the huge exhibition side where already a lot of people are heading towards the entries. How exciting to know that in every hall the latest technologies from today's Med Tech industry will be presented. First, we are looking for a map because we already know it will be hard to explore everything in one day. We are forming several groups and every single one is heading in another direction. Fun fact, you will meet the groups several times again by accident, but if you are looking for someone you will for sure not meet him or her until you are back in the hostel. Our group starts with the physiotherapy and rehabilitation halls. Here we can try out many things. At one booth a camera captures some of our body contours and pressure plates are analyzing where we are standing. Now we can show our skills as a goal keeper.

Plant your own vegetables or be the new goal keeper of your favourite soccer team. Try it out it is so much fun!

Walking all day can be exhausting, so some of us take the chance of getting a hydro-jet massage

"Would you like to get a massage for your neck?" – Trust me never say no to such an offer.

In every hall we can find something which is interesting for somebody of our group. If you should lose someone just go back the way from where you came and you will find your colleague at a booth talking to one of the industry representatives. With lunchtime hunger comes. You can go either to one of the restaurants or go outside and have a nice curry or some typical German dishes like "Bratwurst mit Sauerkraut".

After lunch we are ready for a massage, so why not trying out a hydro jet massage or massage belt for the neck?

For sure we are ready now for new conversations. Whenever we are having questions we are highly welcomed by the representatives from the industry and we can ask all our questions about the microprocessors, screws or robots which we see in front of us.

In the evening, we are ready for a nice BBQ at the youth hostel but trust me the day will not have an end yet. After the BBQ it is time to discover the nightlife of Düsseldorf.

After some beers we are heading back to the hostel with some fancy E-Scooters. See you tomorrow.

As typical for Swiss people, everyone is ready for check-out at 10 o'clock. Some of us are heading again to Medica, some are discovering Düsseldorf again, but this time during the day. At Medica some of us tried out cryotherapy where the body is exposed to super low temperatures around –110 C°. How refreshing ;)

In the city people are having a nice "Glühwein" at the Christmas market with all its wonderful lights and handcrafted gifts. The temperatures today are very low so we meet all together again at 8 pm in the restaurant "Hans im Glück". Here we can have burgers in all different styles. Vegetarians, vegans and people who love meat will find something delicious to eat.

At 10.30 pm we are all together back in our bus with our super friendly bus driver. The big difference; no music, no party, just a silent bus with tired students. ;) Back in Bern we can just say: "Bye and thank you all for this awesome trip!"

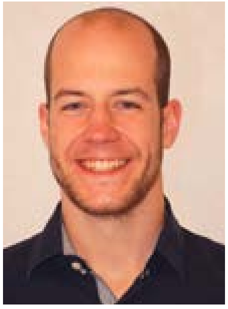
Tamara Melle, BME student

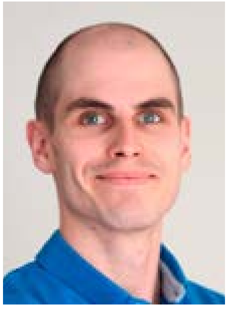
Who can say no to a delicious burger? – Enjoying the last evening together at the restaurant "Hans im Glück"

Going to bed early after the first day? No way! We discover the nightlife of Düsseldorf. Cheers!

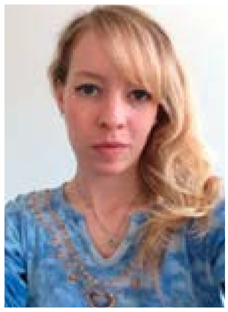




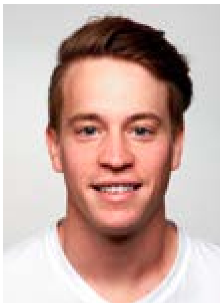
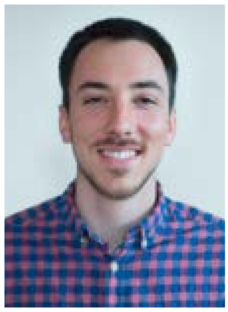



MASTER'S THESES 2019

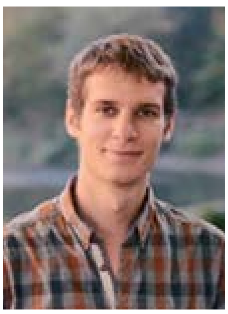




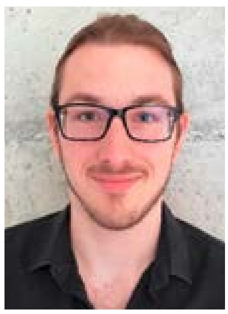







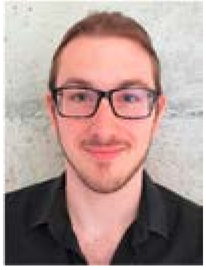






Experimental, Theoretical and Computational Analysis of Conical Implant Press-Fit in Bovine Trabecular Bone

Marcel Aeschlimann



Supervisors: MSc. Marzieh Ovesy, MSc. Benjamin Voumard
Institution: University of Bern, ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Philipp Zysset, MSc. Marzieh Ovesy

Introduction

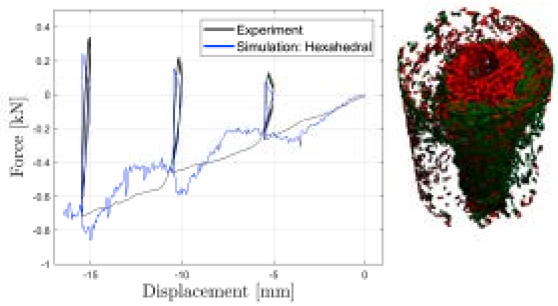
Nowadays, orthopaedic implants are widely used. A successful implant has the ability to sustain load without undergoing interface damage after surgery. This is determined by primary stability and micromotions at the bone-implant interface that are assessed either in vivo using roentgen stereophotogrammetry or in silico using the finite element (FE) method. The FE method reduces time and costs associated with the experiments and enhance reproducibility of the outcome. To increase the reliability of the FE method, validations with experiments are essential. Therefore, the goal of this thesis is the development of an *ex vivo* press-fit experiment resembling total hip arthroplasty (THA) and the validation of an explicit FE approach that models the bone-implant interface during insertion of a stiff implant.

Materials and Methods

Thirty trabecular bone samples from the bovine tibia plateau were extracted and machined into cylinders of size Ø15.5mm x 25.5mm. After embedding the samples in polymethyl methacrylate (PMMA), a centric hole (pilot hole) was drilled and micro-computed tomography (µCT) scans were made. The bone volume to total volume (BV/TV) ratio was determined using the µCT scans. The samples were divided into three groups with the same BV/TV distribution. Three cones, resembling a femoral stem, with different surface treatments (smooth, middle, and rough) were manufactured. The experiments were based on a displacement-driven quasi-static cone insertion into the pilot hole, while the force-displacement curve was acquired. Every 5 mm, the cone was retracted 0.5 mm to analyse the unloading stiffness of the samples at different cone insertion depths. A simple rheological model based on a spring-slider system was designed to understand the experimental force-displacement curves. The simulation was performed according to the experimental protocol, using an explicit homogenised finite element (ehFE) method with element deletion. The results were then compared with the experiments. Furthermore, a feasibility study on the lateral drift of the cone during insertion was conducted (n=1), using image registration and ehFE.

Results

A few samples had to be excluded due to an excessive shift in lateral direction. A typical force-displacement curve is shown in Figure 1a. The spring-slider model could reproduce qualitatively the experimental unloading/reloading cycles. The overall behaviour of the simulated force-displacement curves exhibited a good qualitative fit to the experimental ones. The findings showed that BV/TV was a dominating factor for the generated force. After normalising the resulting forces by its BV/TV, the influence of the cone surface treatment was clearly visible. Correlations between simulated and experimental forces were $R^2 > 0.90$ for all groups. Simulated unloading stiffness of the smooth group correlated nicely with the experimental data ($R^2 = 0.88$). Finally, the cone displacement direction and magnitude were qualitatively well predicted by the simulation (experiment: 1.25 mm, simulation: 1.44 mm) (Figure 1b).



a) b)

Figure 1: a) Experimental and simulated result of sample C1338 (BV/TV = 29.9%). b) Registered trabecular structure, before (red) and after (green) cone insertion.

Discussion

In this study, the force and stiffness generated through a conical press-fit mechanism were measured in experiments, analysed with a rheological model and simulated by ehFE. In particular, the influence of surface treatment could be reproduced in the simulation. Moreover, the lateral drift of the cone due to BV/TV variations, was well captured.

The developed ehFE methodology may become beneficial for assessing primary stability and micromotion of femoral stems in THA surgeries.

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Acknowledgements

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Detection of Focal Cortical Dysplasia in Epilepsy Patients from MRI using Atlas and Deep Learning Methods

Andreas Baur

Supervisors: Prof. Dr. Mauricio Reyes, Prof. Dr. med. Roland Wiest
Institutions: University of Bern, Institute for Surgical Technology and Biomechanics
University Hospital Bern (Inselspital), Institute for Diagnostic and Interventional Neuroradiology
Examiners: Prof. Dr. Mauricio Reyes, Prof. Dr. med. Roland Wiest

Introduction

Focal corticale dysplasias (FCD) are a cause of pharmacoresistant epilepsy. For epilepsy surgery, it must be defined whether it is a lesion or not. On MRI images these are characterised by blurriness. The lesions are sometimes difficult to recognise for radiologists and can also be overlooked. There are promising solutions that highlight the lesions on the MRI images. Deep Learning methods have not yet achieved equivalent results.

Materials and Methods

The MRI images were pre-processed with Freesurfer 6 and registered to the standard brain format of the Montreal Neurological Institute (MNI).
As a basis for comparison, an Atlas Based method was replicated. The method is a statistical evaluation of the grey-matter/ white-matter transitions [1]. The result is a binary image (Fig. 1, right). Thick transitions tend to be blurred, while thin lines show a sharp distinction between grey-matter and white-matter. To determine an abnormality in the brain, an atlas (mean image) of convolved binary images of healthy subjects is created. The difference between the convolved binary image of the patient and the atlas image results in the junction image (Fig. 1, middle). It highlights the blurred spots in the MRI.
The Deep Learning method was chosen unsupervised, which allows a general detection of abnormalities in the brain. A published code of an adversarial autoencoder was used as a template, which has been previously applied to medium and large-sized tumors [2]. The adversarial autoencoder was trained with healthy subjects so that it is not able to reconstruct abnormalities. The difference between the input image and the reconstruction at the output shows the location of the lesion.

Results

With the Atlas Based method it was possible to detect single FCDs. Fig. 1 shows an example. The blue arrow points to a lesion.
However, the method with the adversarial autoencoder reached its limits. Thus it is possible to detect large tumors. With small abnormalities, however, the adversarial autoencoder could not distinguish these from healthy textures.

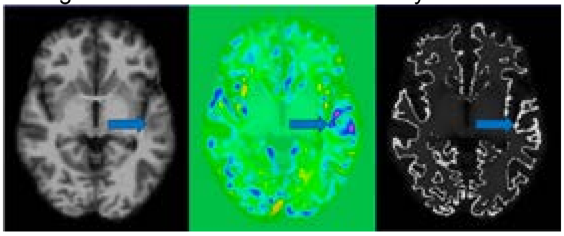

Fig. 1 Result of the atlas based method. (From left to right) Input image with an FCD lesion (blue arrow), junction image with highlighted lesion, binary image with marked gray matter white matter transition

Discussion

It was possible to detect lesions using the atlas based method. However, the method still needs to be tested to see how well it detects small FCD, especially on MRI where the radiologist has not previously detected anything (MRI negative).
The adversarial autoencoder is not a suitable architecture to detect small lesions.

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Acknowledgements

Thanks to the supervisors and their teams as well as to the computer vision lab, ETH Zurich for their support of the project .

Feasibility Study on Motivation Using a Magnetic Resonance Compatible Stepper in a VR Environment

Fabio Bernardoni

Supervisor: Prof. Dr. Laura Marchal-Crespo
Institution: University of Bern, ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Laura Marchal-Crespo, Dr. Karin Bütler

Introduction

During a rehabilitation program, patient's motivation could decline to a point where he/she may stop training if facing a very difficult task; on the opposite, the patient may perform well and consider the task boring if the task is too easy [1]. In this project, we evaluated the relationship between task's functional difficulty level and subjects' motivation. We are specifically interested in evaluating the effect of different control strategies that modulate movement errors on subjects' motivation. It has been suggested that error modelling controllers might effect subjects' motivation depending on the their specific skill level. Therefore, we took into account the subjects' skill in our evaluation. We designed a new locomotor task that consisted in steering a virtual recumbent bike in a VR environment, in which the objective was to follow a path. We then compared the effect of two error modulating controllers on subjects' motivation and performance.

Materials and Methods

The robotic device Magnetic Resonance Compatible Stepper (MARCOS) was employed to perform this experiment. Subjects interplayed with MARCOS and their resulting movement (comparable to periodic on the spot stepping) was represented in VR by an avatar on a modified recumbent bike (developed with Unity, Fig. 1). The aim of the game was to learn how to steer the bike to follow a desired path by changing the movement frequency of the dominant leg. A haptic assistance (HA) strategy was developed in order to reduce the tracking error during practice, specifically in subjects with lower skill level. The second strategy does not apply any haptic feedback or perturbation (No perturbation [NP]).

Fig. 1 The developed VR environment with the avatar on the virtual recumbent bike. By adapting the movement frequency of the of the dominant leg, subjects were able to steer the virtual bike to follow the path.

Eight healthy subjects (four female, age mean = 26.37, SD=3.7) from the lab participated in a feasibility study. The experimental protocol (within subject design) was divided into setup, prephase, and trials (with two trials of 3 minutes for each training condition). All participants were randomly assigned to one of the two groups with the training conditions in different sequential order. For each subject, the performance was calculated (tracking error), and motivation and embodiment levels were collected employing questionnaires.

Results

The haptic assistance (HA) training condition successfully reduced errors during the trials. Haptic assistance helped subjects with low skill level to decrease the mean absolute error by about 40%.
Participants were split within high and low skill level groups, based on their performance. Non-significant differences ($p>0.05$) were observed between the two strategies. We observed that high skilled subjects were more motivated when practicing without perturbation, while low skilled subjects were more motivated with haptic assistance (Fig. 2). However, differences did not reach significance.

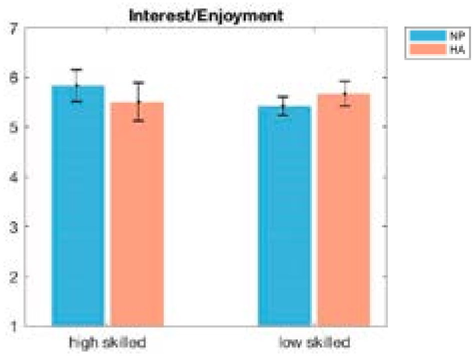

Fig. 2 Interest/Enjoyment subscale of IMI, error bars are SE.

Discussion

We found that haptic assistance increased motivation, specially in low skilled subjects. However, the small number of subjects induced insufficient statistical power (power = 0.13) to obtain significant differences. Probably, increasing the number of subjects would result in significant differences.

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Universal Depth Gauge in Trauma Surgeries

Jimmy Bron

Supervisors: Prof. Dr. Juergen Burger, Prof. Dr. Thomas Niederhauser
Institutions: University of Bern, Sitem Center for Translational Medicine and Biomedical Entrepreneurship
Bern University of Applied Sciences, Institute for Human Centered Engineering HuCE,
Examiners: Prof. Dr. Juergen Burger, Prof. Dr. André Weber

Introduction

Intramedullary nailing in trauma surgeries is one of the techniques used to stabilize and promote healing of several types of traumatic bone fractures. The operation involves the insertion of an implant into the intramedullary canal of long bones (e.g. femur or tibia). In a specific case; tibial nail is indicated for multiple types of fractures, such as metaphyseal and certain intraarticular fractures of the tibial head of the pilon tibial. Optimal stabilization of the proximal or distal fractured fragment(s) must be insured, this is possible using locking screws, of which the length is carefully chosen. Nowadays, most surgeons use a mechanical ruler to determine the correct screw length to prevent tissue damage as well as ensuring firm attachment of the nail to the bone.
The aim of this study was to develop a functional electronic prototype capable of detecting and displaying the linear displacement of a rotating drill bit without any contact. It must be disposable, have a minimum lifetime of 2 hours, and alert the surgeon when the second cortex of the bone is drilled.

Materials and Methods

The project was conducted in two main phases.
The first one consisted in characterizing an optical sensor by designing and programming a custom-made test setup. It had to be able to control several parameters, such as the direction, distance and axial displacement speed of a drill bit, its rotational speed, and record the data provided by the sensor.
The second part consisted in building a prototype by selecting the electronic components, desining the PCBs and the case, estimating the power consumption and programming it.

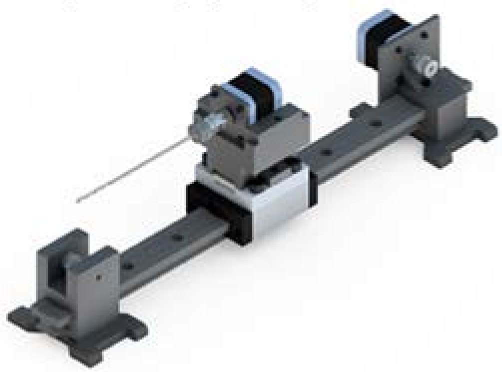

Fig. 1 Test setup used in order to characterize the optical sensor. The sensor was placed parallel to the surface of the drill bit.

Results

The optic sensor is able to measure a forward and backward displacement. It has a precision about 50µm, and when integrated within the prototype it achieve a relative error of about 1% for a 40mm distance.
The device, which indicates its current status by using a light tube placed on its upper surface, has an autonomy of more than 10 hours. This also includes storage time of one year in standby mode.
Finally, feasibility of cortical penetration detection using the optial sensor was confirmed by associating more than one physical variables, but should be further improved.

Fig. 2 3D rendering of the final prototype. It is clamped on a protection sleeve to ensure stability during the surgery.

Discussion

The optical sensor used was definitively able to provide reliable measurements for inclusion in the prototype. Therefore, although test setup demonstrated that the sensor was promizing in detecting a linear displacement of a drill bit in rotation, further characterization tests and signal processing are necessary to obtain a more efficient system.

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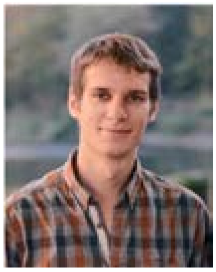
DePuy Synthes – Expert Tibial Nail, Surgical Technique (036.000.380 DSEM/TRM/0814/0173 – 04/16)

Acknowledgements

Juergen Burger, Thomas Niederhauser and Gasel El Zoghbi, who followed the evolution of the project and advised me, are gratefully acknowledged.

Feasibility of an Implantable, Flexible, Continuous ECG Monitor

Martin R. E. Clément



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Examiners: Prof. Dr. Marcel Jacomet, Dr. Thomas Niederhauser

Introduction

With the aging and increasing obesity rate among the population worlwide comes an increase in the prevalence of heart rhythm disorder. The need for performing diagnosis required for proper treatment and reduced costs is of top of the priority for health care providers.
The development of an ECG recorder able to detect paroxysmal heart disorders inserts itself in that context.

This master thesis covers the development of an implantable and flexible continuous cardiac monitor that aims to be the next generation of such devices.

Materials and Methods

The applied part of this project concerns the welding of the implant housing. Different types of welding have been investigated to seal the housing.

The welding quality has been determined using the following normed methods:

- Bubble emission test (integrity test) according to ASTM F2096
- Burst test according to ASTM F1140/F1140M
- Seal peel test according to ASTM F88/F88M

Fig. 1 Reveal LINQ from Medtronic: This event recorder is the leader of the implantable cardiac monitor market.

The conception part of the thesis covers the feature and design ideas from electrodes, battery, biocompatibility and implantation procedure for a new implant intended to replace the leading products on the market.

Results

The housing was successfully welded with lamination.

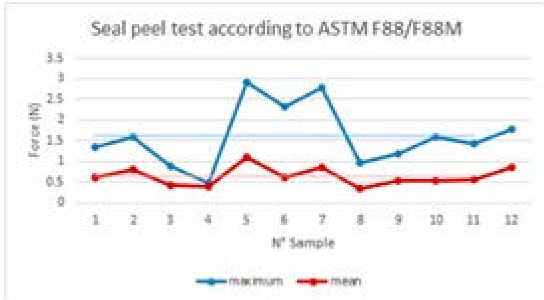

Fig. 2 Results of seal peel test of lamination

As shown in figure 2, the seal peal test indicates results of 0.64±0.23 N for the mean values of the seals and 1.60±0.74N for the maximum values. Moreover the seals were hermeticals.

Discussion

These results show that it is possible to weld a polymer, but the method needs further improvement. The seals lack regularity, but certain changes in the process could erase this problem.

Acknowledgements

The project was conducted between the Institute for Human Centered Engineering – microLab of the Bern Applied Engineering University and Artorg, Cardiology department in University of Bern.

3D Pose Estimation of Minimally Invasive Robotic Instruments

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Examiners: Prof. Dr. Raphael Sznitman, Prof. Dr. Stavroula Mougiakakou

Introduction

We proposed a 3D instrument pose estimation method from endoscopic images. Our final goal is to estimate the 3D world position of an instrument given an Image. This method aims to be implemented in a DaVinci robot developed by Intuitive Surgical. Thanks to the forward kinematic from the joint's encoder located in the robot's arms, surgical tools can be tracked. However, cascaded joints introduce errors resulting in an inaccurate tool position. Hence, acquiring enough data for learning the pose solely through regression is challenging and not feasible. Previous work in this area has focused mainly on a two-step procedure [1]. This work presents a method to perform tool tracking and pose estimation using stereo endoscopic images. We developed a CAD-based deep-learning algorithm that estimates the tool position with the segmentation mask of the object.

Methods

The pipeline (Fig. 1) has three main components, a pose estimator, a differentiable Renderer, and a loss function. Pose estimation is computed with a convolutional neural network based on a Resnet 50 architecture. The 3D Renderer [2] works with a CAD model of the surgical tool being tracked. We first train the pose estimator with images containing a surgical tool in different positions. For each image, the pose estimator computes the translation and rotation parameters of the object. Those parameters are given to the 3D Renderer that creates a binary mask of the surgical tool. Finally, the loss function compares the ground truth segmentation with the computed one to train the loop. The estimator does not only depend on the pose of the objects but also compares the different estimated binary masks.

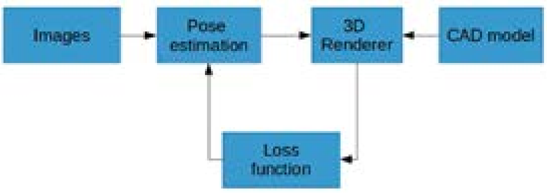

Fig. 1 System overview with the pose estimator, 3D Neural Renderer and the loss function

Results

After training with 10000 images, we show that translation parameters are successfully computed with the Renderer estimator. The current model cannot estimate the parameters of a 3-axis tool rotation correctly. Instead, our estimator is able predict the position of the object with a 1-axis rotation. Thanks to previous convergence tests, we know that finding 3-axis rotation parameters is possible through segmentation masks comparison.

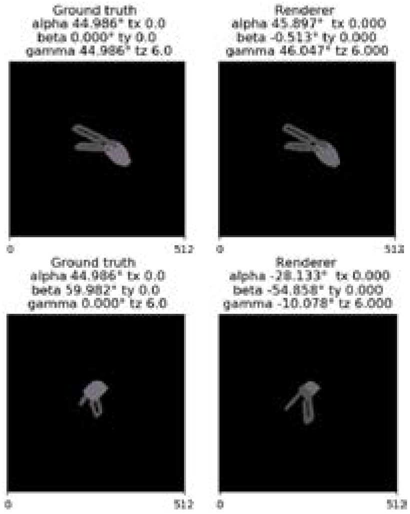

Fig. 2 Pose estimation result for a 3-axis rotation. The Renderer estimator does not always find the correct transformation parameters

Discussion

Seeing convergence with the 3D neural Renderer estimator is a good achievement. Although rotation results are not perfect, this method has room for improvement. Convergence is possible and has been demonstrated. Since pose estimation with regression only is difficult and not feasible, the Renderer estimator shows that pose estimation can be computed with segmentation masks.

References

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Acknowledgements

The continuous support, feebacks and insights of Prof. Dr. Raphael Sznitman and Thomas Kurmann are gratefully acknowledged.

Master's Thesis in Biomedical Engineering

Development of Microfluidic Platform for Organoid Vascularization

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Examiners: Prof. Dr. Olivier T. Guenat, Soheila Zeinali

Introduction

To study the biology of the diseases and develop therapeutic compounds for their treatment, scientists were using either in vitro two-dimensional (2D) cell culture platforms or animal models. While 2D cell culture models fail to reproduce the morphology and physiology found in vivo, the animal models are cost-expensive, time-intensive, ethically controversial, and have interspecies issues. To bridge the gap between these two models, organoids have been developed. An organoid is a three-dimensional (3D) aggregate of multiple cell types that originates from stem cells and reflects key structural and functional properties of specific organs. Present organoids models lack vascular inputs to transfer oxygen and nutrients. Addition of a vascular network would improve the supplying of nutrients and oxygen, and provide accesses for immune surveillance to maintain cellular viability and functions and thus to allows the development of organoids. Vascularized organoids could be obtained by integrating them in vasculature-on-chip platforms.

Materials and Methods

The microfluidic chip developed in this study is made of Polydiméthylsiloxane (PDMS) and has three different layers: bottom, middle, and top. The top layer of the platform has a cylindrical hole in the middle and is adjusted for growing organoid. In the middle layer, endothelial cells and fibroblasts embedded in fibrinogen are seeded for self-generation of vasculature network. The bottom layer has a microchannel which is connected to two reservoirs to supply nutrients for the cell constructs in the upper layers (Fig.1).

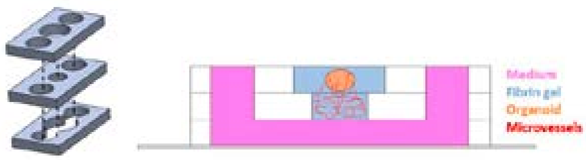

Fig. 1 Final design of the microfluidic chip to vascularize organoids.

Results

In development phase of the platform, the formation and shape of the suspended fibrin gel layer in the circular hole in the middle layer was examined. The shape of the gel layer was analyzed according to different parameters like the composition of the fibrinogen and thrombin and the diameter of the hole. Therefore, the optimum values of 750 µm, 10 mg/ml and 2 U/ml, and 20 minutes for the thickness of the gel layer, concentration of the fibrinogen and thrombin, and incubation time for gelation were obtained, respectively. After 7 days of culturing in the chip, a vascular network was self-formed within the gel layer whether with monoculture of endothelial cells or coculture of endothelial cells and fibroblasts. Coculture showed opened vessel sprouts towards the top of the chip (Fig. 2).

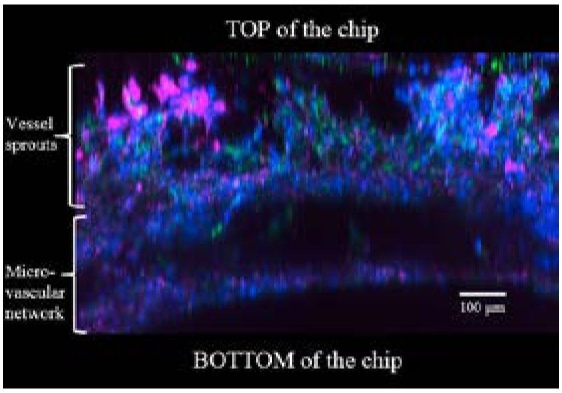

Fig. 2 Side view of 3D projection of coculture of HUVECs and HFL-1 after 7 days of culture. The vessel sprouts grow toward the top of the chip.

Discussion

So far, new developed microfluidic platform is able to reproduce microvessel network within the suspended fibrin gel layer. To study the vascular sprouting from the pre-existing network towards the other layer, a gradient of the angiogenic growth factor was generated in the chip for development of the vascular network towards the other layer and the potential organoid. By adding organoids, this platform will allow the creation of complex in vitro models able to mimic organ-level functions, such as immune responses, and will offer a new approach to model in vivo-like cellular microenvironments and to study cellular interactions through a microvascular network.

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Natural language processing for extracting information from food recipes

Matthias Andreas Fontanellaz

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Examiner: Prof. Dr. Raphael Sznitman, Prof. Dr. Stavroula Mougiakakou

Introduction

Despite a strong interest in food culture, global eating behavior is suboptimal and therefore contributing heavily to diet-related diseases and deaths. The need for nutrition consultation, especially meal assessment rises drastically for either personal reasons and/or to reduce health care costs.
Direct computer vision based-nutrient content estimation is a demanding task, due to deformation and occlusions of ingredients, as well as high intra-class and low inter-class variability between meal classes. In order to tackle these issues, we propose a system for recipe retrieval from images, using different kinds of attention mechanism in deep learning models for recipe instruction processing. These attention mechanisms enable our models to directly process raw instruction text, making them suitable as a first step in an automatic pipeline for the estimation of nutrition content by supporting hints related to ingredients and instructions.

Materials and Methods

We trained all our models on the multi-modal Recipe1M [1] database, which contains over 1 million recipes accompanied with over 13 million images and class meta-data for 1048 meal classes. The main objective of our multi modal embedding model is to align recipe representation and corresponding image representation (in terms of cosine similarity) in a joint embedding space. We adopted the idea of additive attention [2] and the concept behind self-attention [3] into our recipe processing model. In this setup recipe instructions are represented according to their similarity to ingredients, thus Ingredient Attention (IA).

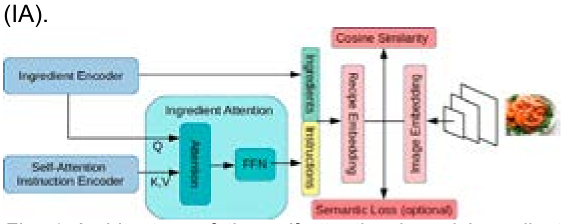

Fig. 1 Architecture of the self-attention based Ingredient Attention multi modal embedding model.

Through IA we are able to disclose the networks foci on recipe relevant instructions. We evaluated our models in terms of median rank (medR) and recall rates at top K percentage (R@K). Further we investigated qualitative results, such as recipe retrieval performance, joint embedding space analysis and network foci on recipe instructions.

Results

Our additive IA model outperforms our self-attention-based IA method and a baseline implementation regarding all evaluation scores. With focus on training and embedding time however, the light-weight architecture provided by the self-attention-based model exceeds its competitors.

Image to Recipe Retrieval				
	MedR	R@1	R@5	R@10
Baseline	3.0 ± 0.1	33.1	64.3	75.2
self-attention IA	2.9 ± 0.3	34.6	66.0	76.6
Additive IA	**2.0**	**40.0**	**70.7**	**80.6**

Tab. 1 Comparison between a baseline and our Ingredient Attention based models.

Discussion

Despite the strong performance of additive IA our main interest lies in the self-attention-based IA. The flexibility of this architecture makes this model well suited as a prestage for a holistic nutrient content estimation pipeline. Further this model with its unique attention mechanisms enables us to investigate the networks thinking about recipe preparation.

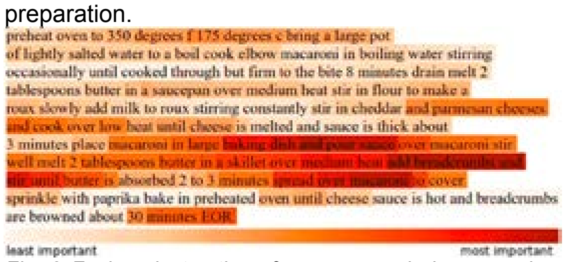

Fig. 2 Foci on instructions for a mac and cheese recipe, based on Ingredient Attention

References

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Acknowledgements

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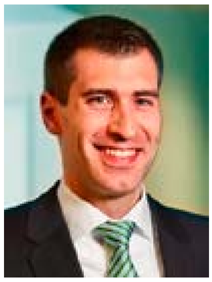
Optimisation of the Pressure Resistance of Polyamide Material for a Coronary Catheter System



Reto Furrer

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Introduction

Coronary artery disease (CAD) is prevalent in the worldwide elderly population. It is a significant cause of mortality and morbidity in developed countries [1]. Heavily resistant lesions remain a challenge in interventional cardiology. For a successful dilatation of the resistant lesion, a high force must be applied to the vessel wall. Hence, the rated burst pressure (RBP) of the balloon catheter must be high [2]. Designing a balloon catheter with a high RBP and a small crossing profile, able to reach the peripheral coronary arteries, is challenging. The aim of this study is to contribute towards high pressure resistance of percutaneous transluminal coronary angioplasty (PTCA) catheter systems. It is hypothesized that a single lumen polyamide shaft with a small crossing profile resists an internal pressure higher than 40 bar.

Materials and Methods

To optimize the pressure resistance of the polymer shaft of the catheter, computational models were developed to calculate stresses in single lumen tubes with mono- or multilayer walls. The polyamide material is assumend to have a plain or a necked state. A plethora of failure criteria for polymeric materials can be applied [3]. In this study three different criteria, the maximum distortion energy, the maximum shear stress, and the Altenbach-Bolchoun-Kolupaev criterion, were used to assess the failure of the material. For the use of more advanced material models, finite element method simulations were conducted. To validate both, the analytical models and the simulations with finite element method, an empirical study was conducted. Samples from four different suppliers and multiple wall thicknesses were included in the study. Descriptive statistics were used to report the results of the empirical study.

Results

The analytical triaxial stress analysis showed that the tangential stress is predominant over the whole wall thickness range. In the simulation with finite element method the maximum shear stress criterion was the most conservative. The plain material model showed lower stresses in the tube wall than the necked material model. The uniaxial tensile strength test in the empirical study showed, that the necked material state resists higher stresses than the plain material ($p < 0.05$). The study indicates that the material properties; yield stress, E-modulus, ultimate stress, and elongation at break are systematically higher for the necked- than for the plain material state. The between-group differences of the mechanical properties and the suppliers are significant ($p < 0.05$). The actual-nominal diameter ratio and the deformation rate of the tubes are different between the suppliers. The test with the hydraulic burst-leakage tester revealed only one sample (n = 53) that leaked or bursted at a inernal pressure of 67,9 bar.

Discussion

The computational models demonstrated efficiency and numerical stability. The analytical results showed close agreement with findings from relevant literature. Single lumen polyamide tubes with a small crossing profile were analysed. The analytical models and the finite element method simulations suggest that a pressure resistance can be higher than 40 bar. The results from computational models were confirmed by the empirical study. In the envelope of the analysed tube configurations, the pressure resistance can be achieved without an additional material treatment. However, the study was conducted on tubes and not on assembled catheters. Hence, a reasoning for direct design consequences for the catheter cannot be made. It is concluded that the proposed computational models are able to predict the behaviour of the polymer tube with a sufficient accuracy. Finally the tubes with a small crossing profiles, and a minimum wall thickness of 0,05 mm, are able to resist an internal pressure higher than 40 bar.

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Acknowledgements

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Optical Coherence Tomography for Real-Time Automatic Dosimetry Control in Selective Retina Therapy

Lorenz Grimm

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Examiners: Prof. Christoph Meier, Prof. Dr. Patrik Arnold

Introduction

Selective retina therapy (SRT) aims to treat retinal diseases related to the retinal pigment epithelium (RPE), by selectively targeting RPE cells with laser pulses in the microsecond range [1]. To ensure, that destruction of cells remains limited to the RPE, SRT requires a method to control the deposited energy. This is required due to the varying energy absorption of the RPE cells and the lack of visual feedback during treatment rendering reliable energy control challenging. Optical coherence tomography (OCT) has been proven to be able to predict the treatment success of SRT [2]. This prediction is based on intensity changes (washouts) in OCT M-scans, that arise from the formation of microbubbles around the melanosomes of the RPE. The aim of this master's thesis was the creation and implementation of an algorithm, which automatically detects these washouts to deliver a reliable real-time dosimetry control for OCT-based SRT.

Materials and Methods

24 porcine RPE explants, were treated at 100 spots each. However, only 10 could be used to develop and test the proposed detection algorithm, based on the quality of the associated microscopy images.

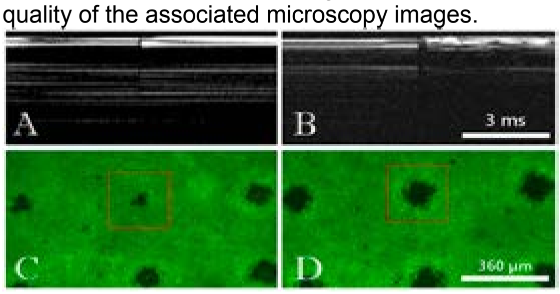

Fig. 1: OCT M-scan with a weak washout (A), indicating insufficient lesion size (C), OCT M-scan with a strong washout (B), indicating intended lesion size (D).

The RPE explants were treated with the HuCE-optoLab Spectralis Centaurus System while recording OCT M-scans (Fig.1, A&B). After the treatment, Live-Dead staining (EthD-1, Calcein AM) was used to analyze the treated RPE cell layers (Fig.1, C&D), which served as ground truth during the development. The proposed algorithm (Fig.2) sums up the intensity values of the M-scan, into a one-dimensional intensity array. The array is rescaled and convolved with a filter kernel to create a peak response to the washout. Afterward, a peak detection algorithm is employed to distinguish weak and strong washouts. These processing steps are done individually for every single recorded M-scan during a pulse ramp with increasing laser energy. The ramp is interrupted once a stopping criterion is met, which stops the treatment of the targeted spot.

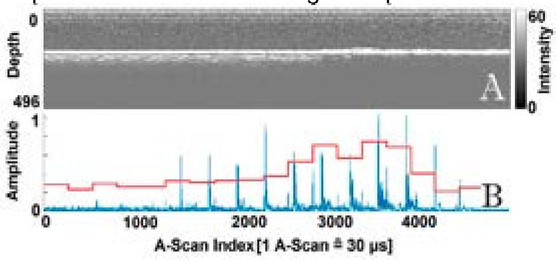

Fig. 2: Recording of 19 consecutive M-Scans (A) during a pulse ramp, some pulses resulted in a washout. Filtered data array (blue) with the dynamically calculated threshold (red)(B).

Results

The developed algorithm has been demonstrated to be capable to detect washouts with a speed of 2 ms per M-scan evaluation, reaching an accuracy of 86%. Using a multi-detection criterion (e.g. detection of 2+ washouts during a pulse-ramp), the probability for a successful treatment could be raised to over 99%.

Discussion

The multi-detection criterion might lead to over-treatment, which has to be weight against the chance to stop the treatment too soon. Since the required lesion size for a successful SRT treatment is still under investigation, the algorithm might have to be adjusted based on future research results. Future in-vivo studies on humans might show differences to porcine eyes, which have to be considered as well.

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Acknowledgements

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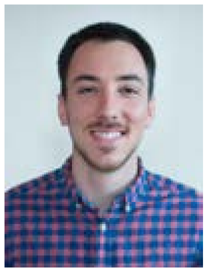
Stereo-Endoscope to CT Image Data Registration for Liver Surgery

Michel Hayoz



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Examiners: Prof. Dr. Raphael Sznitman, Prof. Dr. Stavroula Mougiakakou

Introduction

Developing Augmented Reality based guidance systems for laparoscopic liver surgery is an active research objective. These systems rely on the registration of a pre-operatively acquired liver model to the endoscopic video stream in real-time. This registration is very challenging due to the soft-tissue deformations, the feature-less liver surface, and the different modalities of pre and intra-operative imaging. This thesis aims at developing a Bayesian approach to non-rigidly register a pre-operative liver model to the intra-operative endoscopic video.

Materials and Methods

We propose a non-rigid registration method of the pre-operative to intra-operative model for image-guided laparoscopic liver surgery. Additionally, we propose a pipeline to reconstruct the intra-operative liver model from a stereoscopic video stream frame by frame. The registration uses an active test search strategy based on an information gain criterion to establish matching points between the pre and intra-operative models [1]. For a hypothesized match set, the rotation, translation, and deformation of the pre-operative model are expressed using Gaussian Process regression. A point-to-surface distance score with a trained noise model yields the likelihood of the hypothesized set. An additional iso-volume and a shape constraint are used to prune bad match sets.

We train the method on synthetic data, validate it on animal in vivo data with intra-operative ground truth, and compare it to the baseline Iterative Closest Point (ICP). Finally, we use the reconstructed liver surface from patient data, recorded during laparoscopic liver surgery, to qualitatively assess our registration.

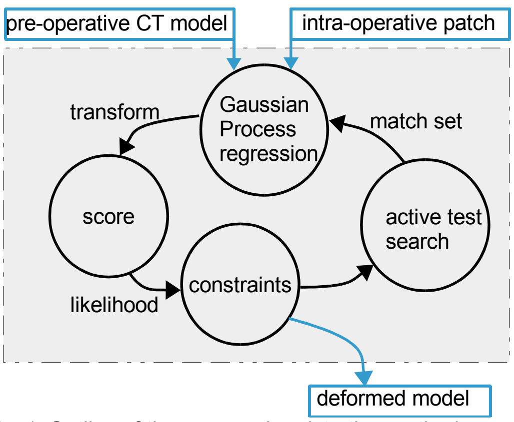

Fig. 1: Outline of the proposed registration method.

Results

Our proposed registration method achieves a median RMS error of 8.2 mm in the visible part of the liver and 20.5 mm on the whole liver surface for synthetic data. Moreover, the method achieves a median registration error of 15.5 mm on the whole liver surface for the animal in-vivo data. The visual assessment of the results for patient data suggests that the pre-operative model is well aligned with the intra-operative model. However, the registration yields several candidate deformations due to the small size of the intra-operative surface patch.

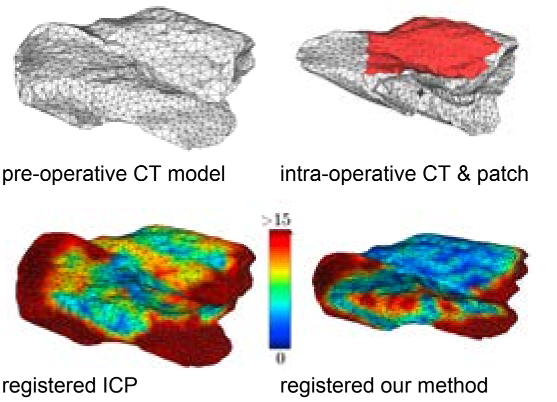

Fig. 2: Registration results for animal in-vivo example with color encoded registration error in mm.

Discussion

Experiments with synthetic data and animal in-vivo data show that our proposed registration outperforms the baseline registration (ICP), given a large enough intra-operative surface patch. However, the surface patches reconstructed from patient data are not large enough to recover the overall deformation. Fusing several frames to form a larger patch and reducing at the same time the reconstruction error, may improve the accuracy and robustness of the registration.

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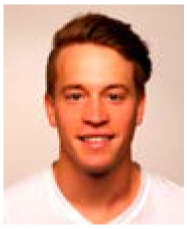
Acknowledgments

The continuous support of Prof. Dr. Raphael Sznitman, Dr. Mathias Gallardo and Iwan Paolucci is gratefully acknowledged.

Synthetic Aperture Optical Coherence Tomography

Hanspeter Hess



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Examiners: Prof. Ch. Meier, Prof. Dr. P. Arnold

Introduction

Optical coherence tomography (OCT) is a non-contact imaging modality, which is applied in various biomedical and industrial applications. OCT is interferometry applied with a low-coherent light source. The axial resolution of an OCT system depends only on the spectral bandwidth and the central wavelength of the laser source and is completely independent of the scanner optics. This is one of its key properties and allows measurements with the high axial resolution even with low numerical apertures optics. However, the lateral resolution of OCT data depends on the scanner optics. For measurements with better lateral resolutions, higher numerical aperture optics are used, which however decrease the axial range where the maximal lateral resolution can be achieved. This results in OCT acquisitions where structures distant to the focal plane are blurred in the lateral direction. If the scan beam is disturbed by optical aberrations, the diameter of the scan beam is enlarged, and therefore the lateral resolution of the OCT data is reduced furthermore.

Materials and Methods

The computational OCT technique named 'Interferometric synthetic aperture microscopy' (ISAM) is a post-processing technique which applies a three-dimensional resampling in the frequency domain of the data, to bring all depths into focus. The applied resampling grid stems from the Gauss-propagation of the scan beam. After application of the ISAM technique, the lateral resolution throughout the whole volume is minimized to the lateral resolution at the focal plane.

Computational adaptive optics (CAO) is a post processing technique similar to the ISAM technique. In the CAO technique, a phase is multiplied to the data in the frequency domain to reduce aberration effects. The aberration of the scan beam is not known, and therefore the appropriate correction phase must be found with an iterative optimization technique that seeks the maximal image sharpness. After applying CAO to the data, the lateral resolution in the whole volume is maximized.

These two computational OCT techniques do not require any ancillary equipment of an ordinary OCT system. However, whereas in conventional OCT the individual depth scans are post-processed separately and then stitched together to a volume, the resampling in CAO and ISAM is done in the lateral direction. To allow successful ISAM or CAO processing, additional stability requirements are claimed during the OCT data acquisition.

Results

The mentioned post-processing methods ar integrated in the existing OCT processing software. Data of a transparent sample with sub-resolution scatterers is acquired with a stabilized OCT system and post processed with ISAM and CAO.

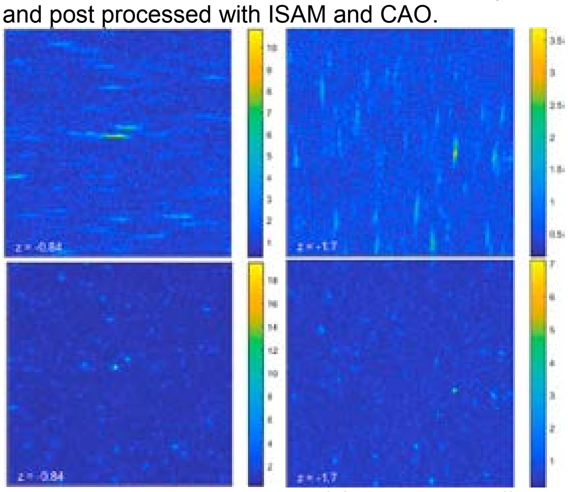

Fig.1: Lateral slice through the OCT volume at different depths. Top row shows the original data whereas in the bottom figures the processed data is presented.

Discussion

The data shown in figure 1 is acquired with a scan beam with strong astigmatic aberrations. Therefore, the scatterers in the original volume are extended to lines along the horizontal axis at depth z= -0.84 mm and distorted along the vertical axis at other depth where z= -1.7 mm. In the processed data the resolution of the acquisition is enhanced significantly. Neighboring scatterers which were fused to one line in the original data can be distinguished in the post-processed data. The results prove that the ISAM and CAO techniques can enhance image quality in the entire OCT volume.

References

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Acknowledgements

Particular thanks to my supervisors Prof. Christoph Meier and Prof. Dr. Patrik Arnold for their support and helpful advice.

An Electro-Magnetic Power Supply for Leadless Cardiac Pacemakers

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Introduction

Heart diseases are among top causes of death in the world. Bradycardia is one of those diseases and is commonly cured by implantation of artificial cardiac pacemakers. Contemporary pacemakers are powered by batteries. Due to this reason, after few years post implantation these devices have to be replaced. This following intervention is costly and poses additional unwanted risks. Devices that could harvest energy inside of our bodies pose a solution of this problem, possibly overcoming the shortcomings of current pacemakers. One potentially promising solution is a harvester that would utilize the mechanical principle of automated wristwatches, converting kinetic energy of heart movement into usable electrical power. So far, a prototype based on this principle was developed using a commercially available micro electrical generator. Unfortunately, the power output of this device was insufficiently low, causing search for better solutions of mechanical to electrical energy conversion.
The aim of this project was to study the possibility to use special class of soft magnetic materials in development of better electrical generator for mentioned device.

Materials and Methods

Based on current developed prototype, a possible design of electro-magnetic power supply was conceptualized. To develop a model that could describe the behavoiur of different soft magnetic materials, simulations were made using COMSOL software.

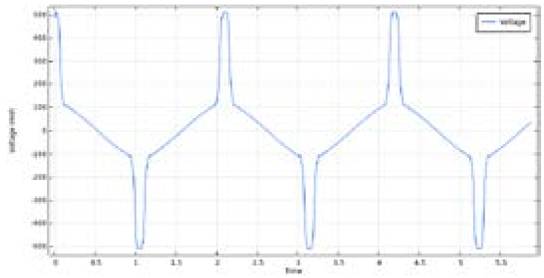

Fig. 1 Sample simulation of induced voltage with soft magnetic material core

In parallel to simulations, several magnetic materials were tested on a custome designed test bench. These materials were tested under variety of conditions that could have place in a final device.

Results

Different COMSOL models were developed that showed the possibility to simulate behavior of specific soft magnetic materials(fig. 1). Test bench results allowed to compare behavior of different materials as well as their potential to be used in designed generator(fig. 2).

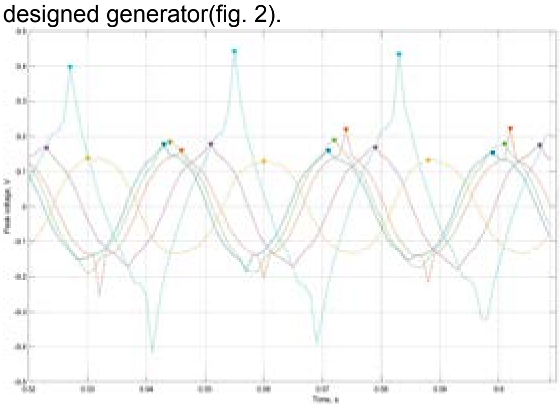

Fig. 2 Voltage measured with the use of several different soft magnetic materials as coil core as well as with empty coil

Discussion

These results correspond to the findings of similar studies performed under different conditions but focused as well on topic of medical device power supply. There is a clear possibility to develop a lead- and batteryless cardiac pacemaker that could be in future implemented and made available to general public.

References

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Robotic Electrode Lead Management for Cochlear Implants

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Introduction

Cochlear implantation is an otologic microsurgical procedure for patients with profound sensorineural hearing loss. To restore hearing, an electronic device, cochlear implant (CI), is implanted in the lateral skull base with an electrode array placed in the scala tympani of the cochlea. Although the surgical technique for implant fixation has been unchanged for the past 30 years, complications still occur including electric failure, slip-out of the cochlea and exposure. Most slip-outs can be avoided by anchoring the electrode in a press-fit canal, the split-bridge technique. In robotic cochlear implantation (RCI), a tunnel for the electrode is drilled based on an image-guided approach using a high-precision surgical robot. A technique analogue to the split-bridge method has not yet been employed. The aim of this thesis is to demonstrate the feasibility of planning and execution of a full electrode embedding and fixation below the temporal bone surface level into a robotically milled electrode lead channel (ELC) to minimize postoperative dangers to the electrode.

Materials and Methods

Progressive experiments were conducted to test the current robot and the navigation and tracking system. The capability to mill accurately in bone, the limitations of the kinematics and the stability of the robot were equally evaluated. Proposed changes to the current workflow for RCI [1] to implement robotic lead channel milling (RLCM) are tested for different path designs on a phantom skull model, see Fig. 1.

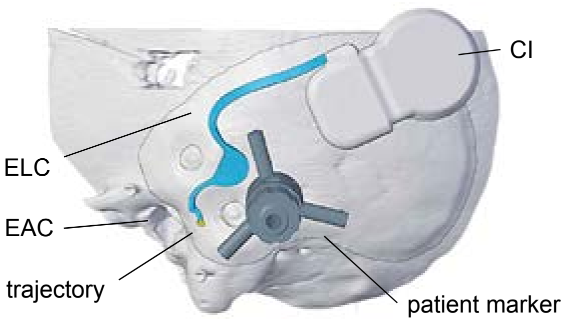

Fig. 1 Phantom skull model experiment plan.

In a last experiment, the gained knowledge of the previous experiments is applied and validated by simulating parts of an RCI surgery on a cadaveric head following the proposed workflow for RLCM.

Results

The maximal accuracy error for milling in fresh bovine bone specimen using the proposed milling parameters is 0.38mm in depth direction and 0.33mm in lateral direction. The proposed milling parameters lie at a cutting velocity of 2mm/s and a rotational speed of 45'000 RPM and ensure a good channel surface quality. A full embedding of the electrode into the ELC after RLCM was feasible for both the phantom skull models and the validation in the cadaveric head, Fig. 2.

Fig. 2 Embedded electrode lead in ELC after RLCM in cadaveric head

Discussion

We presented the first workflow to robotically mill an ELC to fully embed the electrode underneath the temporal bone surface level. Electrode fixation was achieved for a channel configuration similar to the split-bridge method with a press-fit of -0.1mm. It has to be considered, that the number of samples in all of the experiments was too low to have statistically significant results. More full surgeries including skin management, drilling, RLCM and electrode insertion on cadaveric heads need to be performed to have significant results on feasibility, safety and accuracy of RLCM.

References

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Design and Operation of an Automated 3D Ultrasound Tomography Lab System

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Introduction

Ultrasound (computed) tomography (UCT) is a form of ultrasound (US) imaging based on analyzing US after transmission through a tissue sample. One possible application of UCT is mammography[1]. Within the project PAMMOTH, a consortium of academic and industry partners is developing a novel breast imaging device with the goal to allow accurate breast cancer diagnosis by combining US with photoacoustic imaging[2]. The recorded transmission US data will be used to reconstruct a cross sectional speed of sound (SoS) map, which can be used to detect lesions within healthy tissue. To get high resolution images, diffraction and refraction of US signals must be compensated during reconstruction. For this purpose, a ray-based reconstruction algorithm was developed at the Institute of Applied Physics which is numerically less cumbersome than conventionally used full-wave inversion approaches. The aim of this thesis was to design and test a lab prototype system which allows to perform *in vivo* experiments to verify the developed reconstruction algorithms.

Materials and Methods

The novel designed system consists of an outer framework with an aperture for the sample. A separate setup underneath includes a watertank onto which linear array transducers are mounted and acoustically coupled with the water bath to measure a 2D scan plane. The tank setup can be translated vertically to position the scan plane. At each plane position, the tank rotates around the vertical axis and can furthermore be translated in tangential direction to the sample circumference. By the latter, the field of view of the limited transducer array size is enlarged to encompass a bigger sample size. After a cross section is scanned, the UCT setup can be moved vertically to acquire multiple slices of a sample. The slices can afterwards be combined for a 3D reconstruction.

Fig. 1 The system which was designed during this thesis allows to perform in vivo experiments with the experimental imaging modality

Results

Since now the whole UCT setup including the water tank rotates, the sample can stay still, pendant through an aperture. With the novel designed lab system it is thus possible to perform *in vivo* breast measurements to test the developed reconstruction algorithms. No acoustic obstacles are within the transmission path so artefacts are reduced. Multiple 2D and 3D phantoms made of tissue substitutes with similar acoustic properties than soft tissue were imaged to validate the novel system. It has been shown that 2D phantoms can be imaged by the system with high contrast (Fig. 2). The reconstructed SoS-values correspond within a permissible tolerance to reference measurements.

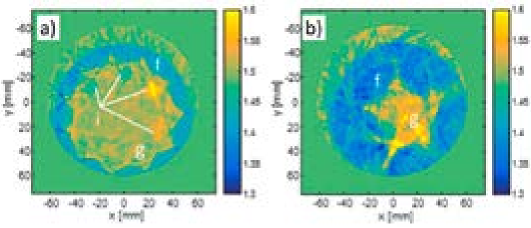

Fig. 2 SoS reconstructions of cross sections from a 2D breast phantom with four inclusison in a) and from a 3D phantom in b)

Discussion

The main structures (i.e. fat and glandular layer, indicated by *f* and *g* in Fig. 2) are well reconstructed in 2D phantoms. Also the SoS values of the inclusions (indicated as *i* in Fig. 2) follow the trend. However, distortions and low sharpness are observed due to strong acoustic scattering and damping. While this affects mainly the reconstruction of the inclusions within the 2D phantom (Fig. 2a), it can be seen throughout the main layers within the 3D phantom (Fig. 2b). It is assumed, that distortions and low resolution are both mainly related to missing US signals which are caused by refraction.

References

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[2] PAMMOTH consortium: PAMMOTH - publishable summary, 2018

Identification of Mechanical Properties of Human Corneas after UVA Crosslinking using Finite Element Analysis

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Introduction

Keratoconus is one of the most common corneal dystrophies. This disease causes a weakening of the central cornea, which leads to a progressive conical bulging forward of the cornea, and consequently to altered refractive properties and blurred vision. Chemical crosslinking (CXL) has been proposed as a novel treatment to restore the stiffness of the cornea and stop the progression of the disease. However, the mechanical changes induced by this treatment in different regions of the cornea remain poorly understood. The cornea is formed by a collagen network filled with water (~ 80%) that can be regarded as a biphasic material in which the matrix is characterized by a viscoelastic material. Initial analytical models suggested that corneal properties are non-homogeneous, with a gradient from center to the periphery. Therefore, this thesis aimed at identifying the parameters of a region-dependent poroviscoelastic model for healthy control corneas before and after CXL. The model was calibrated using a grid-based optimization on bioindentation tests data.

Materials and Methods

Nanoindentation creep tests carried out in 11 donor samples for control and CXL eyes were used for the parameter identification (Anton Paar TriTec). A 3D quarter-symmetric visco-poroelastic FE model was developed in the open-source FE software FEBio (https://febio.org) to reproduce the experimental creep test; The spherical indenter had a radius of 500µm, and a trapezoidal loading profile was used (30s loading, 180s hold period and 30s unloading). The maximal load was 50µN.

A grid-based optimization was carried out to identify the 4 material parameters of the model (*E*: Young's modulus; *k*: permeability; γ: viscoelastic coefficient; τ: relaxation time; ν =0.075). This results in about 10,000 simulations for each region (A, B, C) of the control and CXL samples. The loss function compared the average numerical and experimental displacement of the indenter. An iterative regularization was also used to limit the deviation of the material parameters identified for samples obtained from the same region.

Results

Control and CXL corneas showed a heterogeneous distribution of the material properties; Young's modulus decreases from center to periphery while hydrologic permeability showed an opposite behaviour. Collagen crosslinking also induces significant changes in the material parameters; the most noticeable effect was an important increase of Young's modulus in the central and peri-central regions. However, the Young's modulus in the periphery was not affected by CXL.

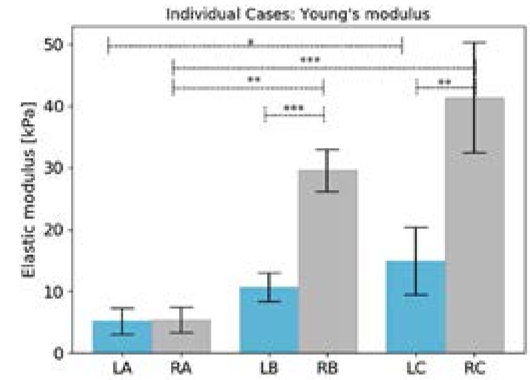

Fig. 1 Young's modulus identified for control (blue) and crosslinked (grey) corneas; peripheral (A), paracentral (B) and central (C) region. Error bars indicate plus/minus one standard deviation. (=p<0.05; **=p<0.01; ***=p≤ 0.001).*

Discussion

These results confirm that crosslinking has a non-uniform effect with a strong stiffening impact on the central region, but also affect the permeability of the tissue. These findings can be explained by the distribution of the collagen fibers in the cornea; collagen fibrils are 5-7% tighter packed, which might explain some regional differences in the biomechanical response like increased stiffness and decreased permeabilitypermeability. In addition, the increased number of fibers could also provide more binding site and increase the efficiency of central crosslinking. These results also agree with previous findings reporting a densification of the extracellular matrix following CXL, which explains the observed decrease in hydraulic conductivity. This study represents a first description of the regional variation of the visco-elastic properties of the healthy and CXL cornea.

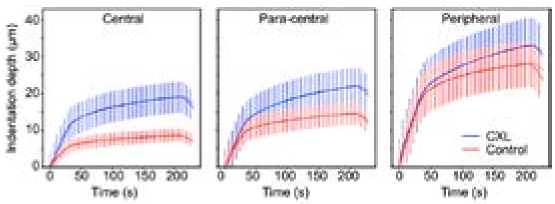

Fig. 2 Comparison bw the numerical time-displacement response from an average loading amplitude (solid line) with its experimental counterpart. Red: Crosslinked cornea, Blue: Control cornea.

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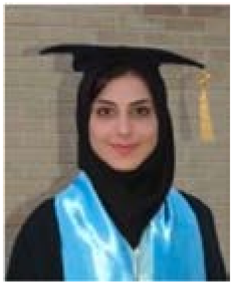
Cognitive Workload Detection Based on Physiological Signals and Machine Learning



Niloofar Momeni

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Introduction

High levels of cognitive workload can decrease human's performance and lead to failures with catastrophic outcomes in risky tasks. One of the cognitive workload detection applications is in rescue missions with drones [1]. When a disaster occurs, the rescuer has to handle many complex activities involving cognitive workload. As a result, detecting the excessive workload induced during flying a drone is important for preventing hazards. Today, reliable workload detection presents a major challenge, since the workload is not directly observable. However, the cognitive workload affects several physiological signals including respiration, electrocardiogram, photoplethysmogram, and skin temperature that can be measured noninvasively. This opens up new opportunities for continuous cognitive workload monitoring. The main goal of this thesis is to develop a reliable multi-modal workload detection machine learning algorithm using such physiological signals during rescue missions with drones.

Materials and Methods

The proposed approach has three main stages. First, a simulation environment is set up to induce workload in the subjects while playing a simulator as shown in Fig. 1. Subjects' physiological signals are acquired during the experiment. Secondly, the data preparation in which the dataset is generated, including signal pre-processing, feature extraction, outlier handling, and data normalization. Thirdly, state-of-the-art machine learning algorithms are investigated for cognitive workload characterization using the learning curve, data augmentation, and cross-validation analyses.

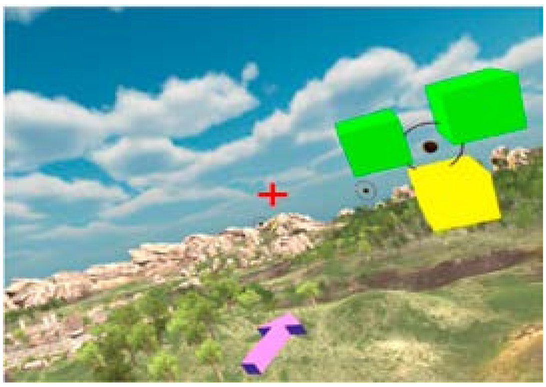

Fig. 1 Simulation environment to induce cognitive workload

The best classification algorithm is adopted, optimized, and the most informative features are selected. The generalization power of the model is evaluated on an unseen test set.

Results

The XGBoost algorithm is selected, because it demonstrates the highest performance in cross-validation accuracy among the others. The XGBoost algorithm achieves the accuracy of 82% on the unseen test set using only the original dataset. By utilizing the data augmentation technique, the accuracy is improved by 2%. The 26 most important features, out of the total 385, are selected by recursively training the model and removing the irrelevant and redundant features. The model's accuracy further improves to 86% by optimizing the model's hyperparameters.

Table 1 Results of the cognitive workload classification

Solution	Advance Algorithm	Augment-ation	Feature Selection	Optimiz-ation	**Test Accuracy**
Initial					**74%**
1st	✓				**82%**
2nd	✓	✓			**84%**
3rd	✓	✓	✓		**84%**
Final	✓	✓	✓	✓	**86%**

Conclusion

We have shown that the proposed machine learning framework outperforms the initial solution reported internally in this study from 74% to 86%. In addition to achieving a high detection performance comparable to the state-of-the-art studies, we decrease the complexity of our model by selecting the most informative features and model optimization for future implementation of the model on the resource-constrained embedded systems.

References

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Acknowledgements

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Ensemble Learning Strategies for Accurate and Robust Brain Tumor Segmentation using Deep Learning Technologies

Michael Müller

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Examiners: Prof. Dr. Mauricio Reyes, MSc Alain Jungo

Introduction

Glioblastoma multiforme is a rare but very aggressive brain tumor in adults. Although tremendous efforts for different therapies, the outlook for the patients with a median survival of 14-15 months is devastating. Magnetic resonance imaging (MRI) is the neuroradiological method of first choice for diagnosing brain tumors and evaluating tumor progression and response to treatment. This technique provides important information concerning the structure and physiology of the tumor. In brain cancer patients, effective diagnosis, treatment, and patient follow-up heavily rely on the ability of the neuroradiologist and neurosurgeon to understand the complex set of information provided by MRI. This has motivated the development of automated brain tumor segmentation approaches based on deep learning technologies. Recent findings have demonstrated the benefits of ensemble learning strategies to improve the robustness of these systems, however, no extensive analysis of them has been performed to this date.

Materials and Methods

The ensembles were built with the officially released and containerized algorithms of participants, who attended the brain tumor segmentation challenge (BraTS). The performance of those containers was evaluated. We introduced the forced majority vote (FMV) to account for the multi-label issue, which often occurs in existing ensemble strategies. Furthermore, investigations were carried out in a proof of concept for a U-Net based fusion approach. The different ensemble strategies were examined and compared on a BraTS 2015 test-set containing 200 cases. The comparison with the majority vote (MV) and the winner container DKFZ 18 [1] from BraTS 2018 gave insights about the robustness and performance of our approach. We evaluated the ensembles with the Dice similarity coefficient (DSC) of each tumor with region. Additionally, the results of the ensembles were inspected by raters in a clinical evaluation.

Results

The comparison of the DKFZ 18, MV, U-Net fusion and the FMV are shown in Fig. 1. The DKFZ 18 and the FMV show an equal performance, which is better than the MV and U-Net fusion for the whole tumor. On the tumor core, the DKFZ 18 and the U-Net fusion are identical, but lower than the MV and FMV. On the enhanced tumor region, the MV and FMV achieved the best performance followed by the U-Net fusion and the DKFZ 18. The FMV was able to perform equally or better than the classical MV in mean DSC and standard deviation (SD). Furthermore, the FMV surpassed the winner container DKFZ 18 from BraTS 2018 for the tumor core and enhanced core. The findings were supported by the raters in the clinical evaluation.

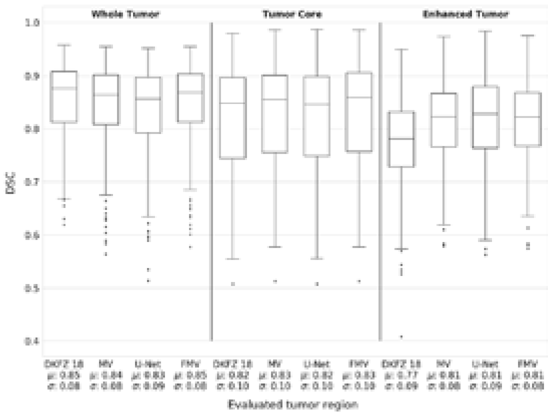

Fig. 1 Comparison of DKFZ 2018, MV, U-Net fusion and FMV.

Discussion

The FMV addresses and resolves the multi-label issue and was, therefore, able to improve the fusion accuracy. Furthermore, show, that the U-Net fusion approach is feasible as an ensemble strategy.

References

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ArXiv, 1809.10483, 2018

Acknowledgements

I would like to express my sincere gratitude to my supervisor Prof. Dr. Mauricio Reyes for his support and helpful advice.

Master's Thesis in Biomedical Engineering

Development of an Implantable Wireless Sensor System for Cow: Sensor Evaluation

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Examiners: Prof. Daniel Debrunner, Prof. Dr. Volker M. Koch

Introduction

Illnesses and the oestrus cycle are highly correlated to a cow's temperature, which is commonly measured to determine the health state. Unfortunately, when manually done, temperature measurements take time especially for a large herd.

This study is part of a three-part project aiming at the development of an implantable wireless sensor system for cow monitoring and focuses on sensor evaluation. The device is expected to measure the temperature with an accuracy of at least 0.1°C. As the final system will not be rechargeable, the sensors are required to have a low current consumption to ensure functioning over a period of 5 years.

Materials and Methods

A test bench was specially designed (figure 1). Three families of temperature sensors were selected: Si7051, TMP117, TSYS01. Three sensors of each sort were placed on the PCB. A STM32F412ZG Nucleoboard was programmed to watch over the temperature sensors. Temperature data was sent to a computer through a UART. Currents were measured with the Keysight B2901A connected by triaxial cables to achieve high precision. Currents were sampled at 1Hz while the sensors are sleeping. Once they awake, the rate was increased to 4.5kHz. Temperatures and currents were measured in an oven set at a temperature of 40°C.

Accelerometers were characterized on a custom-made PCB. Four types were selected: ADXL362, LIS2DWT12, MC3630 and MMA8491Q. Both dynamical and static behavior were tested. Another STM32F412ZG Nucleoboard was programmed to handle accelerometer measurements.

Figure 1: PCBs designed to characterize temperature sensors and accelerometers. On the right side, the accelerometer PCB. On the left side, the PCB for temperature sensor. Behind, the STM32F412ZG

Results

As shown by the temperature's distributions (Figure 2), the temperature measured by the three TSYS01 sensors are not identical. The two other families are equivalent, but the TMP117 shows a better stability.

The "1 cycle" consumption was computed by adding the sleep consumption to the measurement consumption. Overall, the Si7051 is the lowest power consuming sensor.

Stability measurement of accelerometers during a 48 hours test showed that the lowest drift of measurement was performed by the MMA8491Q. The lowest standard deviation during the 48 hours test was measured with the ADXL362.

Table 1: Mean currents and consumption for a cycle of 60 seconds, supply voltage of 3.3V, given within the picoammeter accuracy

	Sleep [nA]	Measuring [µA]	1 cycle [µAs]
Si7051	66.6 ± 0.5	156 ± 3	5.6 ± 0.1
TMP117	208.0 ± 0.7	125 ± 2	14.7 ± 0.1
TSYS01	6.9 ± 0.5	620 ± 2	57.6 ± 0.2

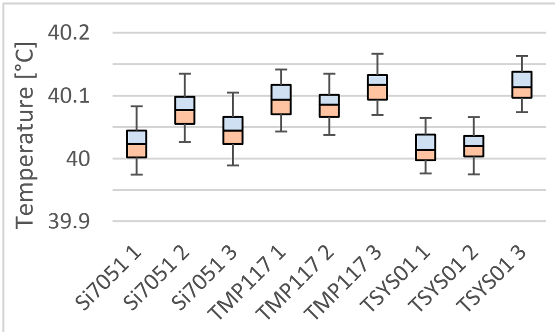

Figure 2: Temperature measured by each sensor for 40 minutes. Red boxes include 25% of data below median; Blue boxes 25% of data above median. Bracket includes 95% of all data.

Discussion

To select the sensors to be used in the implant, three scenarios were elaborated: Lowest consumption, lowest price and a compromise between cost and consumption. The first scenario lead to choosing the Si7051 and the MMA8491Q. In the second scenario, Si7051 and LIS2DWT12 will be chosen. TMP117 and MMA8491Q are selected in the third scenario. The choice of scenario must be made in accordance with the budget of power consumption and the selling price of the implant.

Master's Thesis in Biomedical Engineering

Increasing Full-Body Ownership in VR using Physiological Signals Projected on a Virtual Avatar

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Examiners: Prof. Dr. Tobias Nef, Samuel Knobel

Introduction
Today chronic pain is a major health care problem, and its treatment remains difficult. A promising new therapeutic approach is based on altering the self-consciousness. The so-called rubber hand illusion (RHI) experiment showed a decrease in pain perception, if a patient gets ownership over a virtual body. While the RHI is restricted to the upper limb, it is possible to extend the experiment to a full-body illusion. The focus of this thesis is in the development of an easy-to-use, mobile, virtual reality (VR) setup that can be applied as a long-term treatment for patients with chronic pain. To induce the full-body illusion, the heart rate of the patient should be displayed as a flashing silhouette on a virtual avatar sitting in front of the patient in the virtual environment. The technical feasibility, the usability, and the acceptance will be investigated.

Materials and Methods
The setup consists of two parts: a head-mounted display (HMD) to show the virtual environment and a device to measure the patient's heartbeat. The virtual environment (Fig. 1) shows an avatar in front of the observer in a room with big windows and basic furniture. For the HMD, a setup with a smartphone (Samsung Galaxy S8+) was chosen for its mobility advantage. The heart rate was measured with smartwatches using photoplethysmography (PPG) and sent to the smartphone via Bluetooth. Three different PPG devices were evaluated, and two of them were compared against a five-point ECG measurement regarding their accuracy. The processing of the PPG signal was done directly on the smartwatch using a first-order FIR Chebyshev II bandpass filter and an algorithm to detect the peaks of the pulse waves.
A study with healthy subjects (n = 11) was conducted to test the usability, acceptance, and accuracy of the setup. All participants were tested in two conditions: one with a heartbeat-synchronised flashing and one with asynchronized flashing. The usability, eventual symptoms of cybersickness, and the strength of the full-body illusion were investigated with questionnaires. The self-location (a measure for ownership) was additionally assessed with a walk test. To compare different smartwatches and the effect of the location of measurement, the participant wore three watches. A Polar M600 at the upper arm and another Polar M600 and a Huawei Watch 2 at the wrist.

Fig. 1 The virtual environment with the blinking avatar (left) sitting in front of a participant (right) wearing a HMD.

Results
The usability scores were close to the maximum (i.e. the device is easy to use and well accepted) and those for sickness were close to the minimum (i.e. symptoms negligible). None of the questions to investigate the self-identification nor the measured self-location showed any significant difference between the two conditions.
The verification of the heart rate measurement by the PPG device showed a root mean square error (RMSE) of 4.772% (±4.32%) when compared to the ECG, which got further improved to 2.081% (±1.515%) by optimizing the filtering and peak detection algorithms. While no difference was found between the two locations of measurement, the Polar M600 worn at the upper arm had a significantly lower RMSE than the Huawei Watch 2 worn at the wrist ($t(42) = -2.699$, $p = 0.01$).

Discussion
The high usability and low sickness scores confirm that the system is highly accepted by the users. The results for the ownership measurements are probably mainly insignificant because of the small sample size. From the high precision of the heart rate measurement compared to the ECG, it can be concluded that, especially after improving the filtering and peak detection, the PPG measurement method is well suited for our application.

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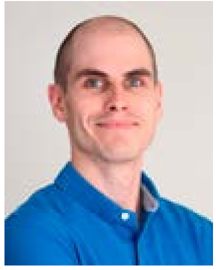
Deep Learning-based Approach for Variable Candidate Segmentation

Jan Riedo



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Examiners: Prof. Dr. Mauricio Reyes, Dr. Raphael Meier

Introduction

Highly specialized medical diagnostics and therapies require accurate semantic segmentations of certain body parts. In radiation therapy for brain tumor treatment, organs at risk (OAR) need to be marked to prevent them from irradiation during the procedure. The gold standard in therapy planning and treatment are time-consuming manual single-rater segmentations. To enhance the reliability and clinical acceptance of automated deep neural network segmentations, rater behavior need to be taken into account.

Therefore, we propose several networks which aim at generating variable candidate segmentations, imitating the inter-rater variability and going beyond. Further, we show that our segmentation samples can be used for additional steps in the medical imaging pipeline by the example of automated quality control.

Materials and Methods

We employ two datasets for training and testing our proposed approaches. For a proof of concept we use a syntheticly generated dataset with five artificial rater segmentations provided for each image. Clinical examination is conducted on contrast-enhanced T1-weighted MR images of an OAR dataset (3 raters) with focus on the brainstem.

Our proposed approach (see Fig. 1) to introduce variability in the segmentation output consists of a state-of-the-art U-Net [1] with an incorporated variational autoencoder [2]. This architecture provides an interface to a standard Gaussian distribution, from which a continuous sampling of candidate segmentations is possible.

The variable candidate segmentations are employed to train a regression network to estimate the quality of produced segmentations. The perceived quality is evaluated by a clinical expert.

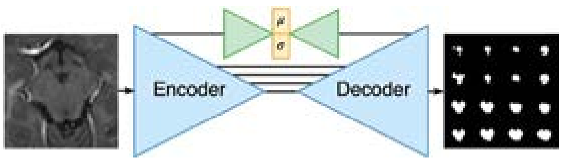

Fig. 1 Proposed VU-Net model consisting of a U-Net with incorporated variational autoencoder for variable candidate segmentations shown in tiled mode over the latent space.

The samples are assessed on a precision weighted variability metric and the maximum Dice similarity coefficient (DSC) between the candidates and the expert segmentations. The Pearson correlation coefficient is used to evaluate the quality estimates.

Results

The experiments on synthetic data confirmed the feasibility of employing a U-Net for variable candidate segmentation. Applied on OAR data (Fig. 2), the variability of segmentations was increased by a factor of ten compared to the experts (0.077 vs. 0.743), while keeping the max DSC at inter-rater level (0.944 vs. 0.945).

The regression network was able to lift the correlation coefficient from 0.790 when trained on deterministic data to 0.983 with variable segmentations. Clinical examination verified the proposed segmentations and DSC estimates.

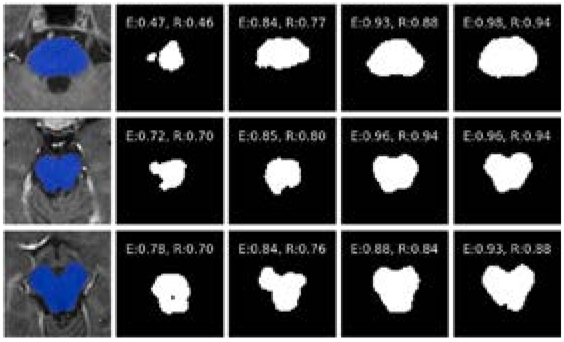

Fig. 2 Deterministic segmentations of the brainstem by the basic U-Net (first column) and sample segmentations obtained from the VU-Net. E: estimated max DSC obtained from the quality control pipeline. R: Real max DSC between sample and any of the raters.

Discussion

We demonstrated the feasibility of employing U-Net based architectures for variable but sensible segmentations, based on label and feature map variability. The networks are successful on synthetic data, as well as on OAR patches and whole slices. The incorporation of variability on whole slices was more challenging, with the results being inferior.

Technical and clinical validation of the proposed quality controlled sampling was successful and showed the need for a training set with segmentations of diverse quality. The success of quality controlled sampling is one step towards artificially generated valid rater segmentations.

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Capturing Spatial Relationships with Capsules for the Segmentation of Organs at Risk

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Introduction

Glioblastoma (GBM) is the most common and aggressive malignant primary brain tumor with rapid growth, low survival and no curable treatment. The limited treatment options consist, typically, of surgical resection, followed by radiotherapy treatment. Modern radiotherapy equipment, feasible to deliver varying irradiation doses to distinctive spatial locations, require laborious and error prone manual or semi-automatic segmentation of organs-at-risk (OAR), which should be spared from inappropriate irradiation to avoid therapy-associated impairments. Advancements in the field of deep learning motivated the application of convolutional neural networks (CNN) for segmentation tasks and demonstrated the feasibility to automate this task to a higher degree than current techniques. Relying on different underlying ideas than CNNs, the recently proposed capsule-based artificial neural network (CapsNet) [2] claims of being able to capture spatial relationships between structures and demonstrated promising performances in image classification tasks. An improved understanding of spatial relations could be beneficial for the OAR segmentation task, which is why, we aimed at developing and examining a multi-class capsule-based OAR segmentation network based on SegCaps [1].

Materials and Methods

We used a private dataset containing 30 GBM cases, each consisting of four MRI sequences (T1c, T1w, T2w, FLAIR) and annotations for 17 OAR segmented by three independent experts. We adapted the idea of SegCaps to the multi-class segmentation task and compared it to a U-Net baseline and to human experts by considering the inter-rater variability.

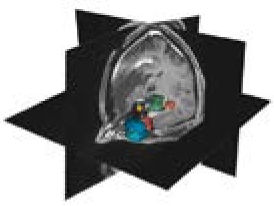

Fig. 1 Example of an OAR segmentation on T1c.

We evaluated the methods in terms of Dice similarity coefficient (DSC), volume similarity (VS), and Hausdorff distance (HD) and determined statistical differences between expert rater, U-Net, and SegCaps by the Kruskal-Wallis test followed by the Conover-Iman test for pair-wise testing.

Results

Comparisons of both neural network architectures yielded a significant better segmentation quality for the U-Net (DSC: 0.71±0.158; VS: 0.87±0.135; HD: 11.18±18.436mm) as for the SegCaps (DSC: 0.48±0.238; VS: 0.71±0.264; HD: 72.12±51.886mm) for all considered evaluation metrics (all metrics $p<0.001$). Compared to the experts (DSC 0.70±0.154; VS: 0.86±0.133; HD: 5.69±4.168mm), the U-Net showed different results depending on the reference (i.e. rater vs. rater, rater vs majority voting) to be compared with.

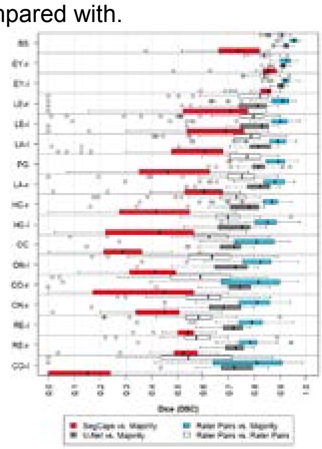

Fig. 2 Overview of Dice similarity results for all comparisons and OAR.

Discussion

The SegCaps results for the OAR segmentation showed little segmentation quality compared to the U-Net, despite of promising results reported for the binary SegCaps [1]. This shows that multi-class in combination with high class imbalance remains a problem. Compared to the experts, the U-Net achieved results on par with the experts in terms of Dice and volume similarity. However, distant errors of the U-Net for some OAR render human verification of the segmentations unavoidable.

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Auditory Performance of CI Recipients with Temporal Fine Structure Preserving Coding Strategies

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Introduction

Cochlear Implant (CI) patients can hear by means of electrical impulses stimulating the hearing nerve. Most CI users can recognize sounds, understand speech in quiet, and even localize sounds to a certain degree. Nevertheless, speech comprehension in noisy environments and localization abilities are limited and music perception is often poor. This thesis aims to investigate the latest advances in CI coding strategies, and compare the abilities of bilateral CI users to NH controls. A coding strategy delivering more temporal information (FS4) is compared to its precursor (HDCIS). Although there are studies comparing speech perception and subjective satisfaction using the two strategies, specific information about spatial hearing is sparse. The work presented focuses therefore on the perception of temporal information and frequency limen. The aim of the tests is to find out, whether bilateral CI users can exploit and binaurally integrate fine-structure information.

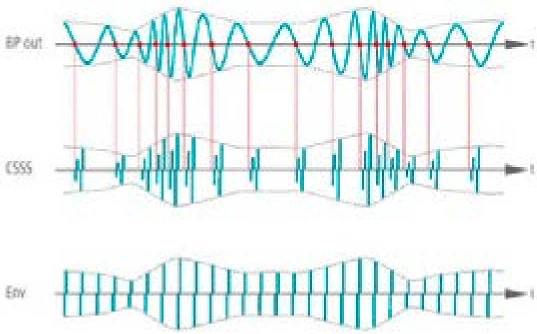

Figure 1: Bandpassed audio signal with envelope and fine structure (top) and resulting stimulation pulses for FS4 (middle) and HDCIS (bottom) coding strategy, source: Med-El

Materials and Methods

Bilateral CI users and normal hearing controls were tested in a prospective study. To assess the capability to exploit the acoustic fine structure, three different tests were conducted. The sensitivity to interaural time differences (ITDs) was measured, just noticeable differences (JNDs) for frequencies were determined, and sensitivity to binaural beats was tested. The appropriate stimuli for each test were generated in MATLAB and presented via cable to the speech processor or via headphones. For each condition, a series of trials controlled by an updated maximum-likelihood method was tested [1]. The results were analyzed using linear mixed effects models.

Results

JNDs for frequency were significantly lower, i.e. better, with the new coding strategy for 135Hz pure tones. For 250Hz pure tones however, no significant difference was observed.
The ITD thresholds for noise signals were not affected by the coding strategy but for 250Hz pure tones the new FS4 coding strategy yielded better results.

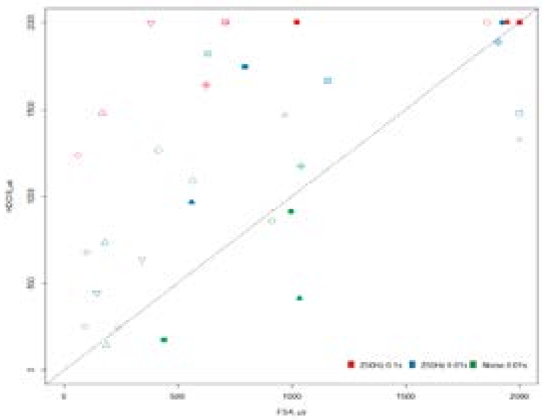

Figure 2: Comparison of ITD thresholds obtained with the FS4 and HDCIS coding strategy

Four out of twelve bilateral CI users were able to perceive and reliably identify binaural beats at 135Hz or 250Hz when using the FS4 coding strategy but not with the HDCIS coding strategy.

Discussion

The FS4 coding strategy demonstrated beneficial for frequencies of 250Hz and below. CI users however, show poorer and more variable results than NH subjects, with a considerably lower frequency limit for the exploitation of fine structure.
CI users being able to perceive binaural beats demonstrate the advances in CI coding strategies. However, the method to test sensitivity to binaural beats needs to be refined.

References

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Acknowledgements

I am grateful for the support of Martin Kompis, Wilhelm Wimmer and Tim Fischer.

Development of a Flexible Solar-Powered Cardiac Pacemaker

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Introduction

Contemporary cardiac pacemakers use primary batteries as power source. Due to the their limited capacity, the pacemaker has to be replaced after the battery is drained. To overcome these limitations, research projects showed that it is possible to generate power inside the body using different energy harvesting methods. One promising method is to use subcutaneous implantated solar cells and sunlight to power a pacemaker. After the implantation of such a device, wound healing takes place, which has an impact on subdermal solar energy harvesting. The goal of this thesis was to build a device capable of assessing this effect.

Materials and Methods

A prototype was built which can pace the heart (simulated by a shunt resistor). It uses an array of small solar cells (combined active area 2.56cm^2) to charge its flexible battery. The gained energy of the solar cells is measured. Additionally, to analyse the wound healing, it measures the changes in the spectral light transmission of the skin tissue above the device (18 channels, 410nm-940nm). Furthermore, the temperature and the open circuit voltage (V_{OC}) of a single solar cell are logged. All measurements are stored on a non-volatile data storage which can be accessed with a wireless bluetooth low energy module.

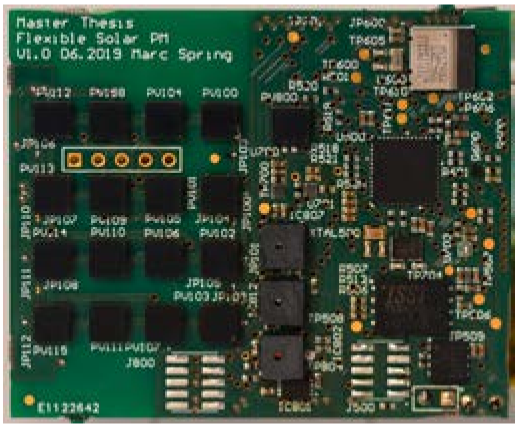

Fig. 1 Prototype of the solar powered cardiac pacemaker with an additional measurement part.

Results

An incandescent light source irradiated the solar cells, that were covered with 4mm bloodless porcine skin, in a distance of 23cm. An average output power of the solar cells of 7.38mW (2.88mW/cm^2) was measured. This was verified in an animal trial with a mean output power of 5.86mW (2.29mW/cm^2). Different irradiances from outdoor (direct sun) to office light and down to no-light condition can be clearly distinguished by analysing the output power. Although it is possible to measure the spectral distribution of the light for all these light conditions, the spectrometer calibration needs to be optimized.

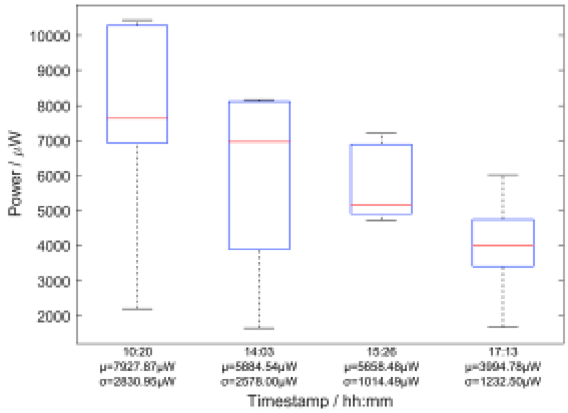

Fig. 2 Generated power of in-vivo validation measurements. Incandescent light source in a distance of 23cm.

Discussion

The results of the generated power correspond to findings of similar studies [1] performed on subdermal energy harvesting. After the implantation it is assumed that some blood gets accumulated in the device pocket, which results in a higher attenuation of the light transmission. This hypothesis is confirmed by the reference measurement that shows a decreasing behaviour over the animal trial. With this device new *in-vivo* insights can be gained on the wound healing and its influence on subdermal solar energy harvesting. Furthermore, it delivers data that has not been measured yet to this extend.

References

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On the Synthesis of Triphenylene Derived Conductive Metal-Organic Frameworks for Sensing Applications

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Institution: Federal Institute for material science and technology (Empa)
Examiners: Prof. Dr. Alex Dommann, Dr. Mathias Wipf

Introduction

Metal organic frameworks (MOF) are crystalline coordination polymers formed by organic linker molecules coordinated to metal centers. MOF materials offer a number of properties, as e.g. high surface areas, permanent nanoporosity, tunable pore geometries, which make them promising candidates for sensing applications of small biomolecules, metabolites or ions. Recently, a new class of electrical conductive MOF materials has been discovered, allowing the integration of MOF materials into electrical sensing devices as e.g. chemiresistors, chemicapacitors or in field effect transistor geometries.

Materials and Methods

Within the present work, the influence of (pH-) modulators, reaction temperature and solvent on the synthesis of the electrical conductive framework Cu_3HHTP_2, displayed in Figure 1, built of 2,3,6,7,10,11-Triphenylenehexaol (HHTP) coordinated to copper(II)ions was systematically investigated. The synthesis of Cu_3HHTP_2 was carried out in seven different solvents, that were select according to their free energy of solvation for the copper(II)ions, additionally different reaction modulators that were supposed to either promote or suppress the formation of the framework were tested. The obtained products were investigated regarding their structure, morphology and the reaction yield.

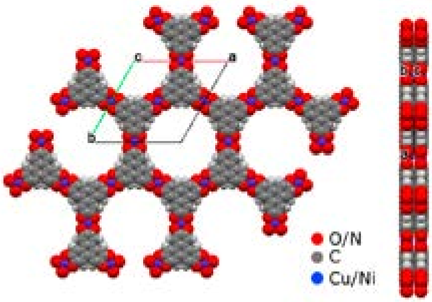

Fig. 1: Structure of the conductive framework Cu_3HHTP_2

Results

A general trend was observed that a higher free energy of solvation of the copper(II)ions hinders or completely suppresses the MOF formation. Furthermore, it was observed that the solvent exhibits an influence on the resulting morphology and structure of the framework, whereas the reaction temperature mainly exhibits an influence on the reaction yield. It could be shown that modulators tend to increase the yield of the reaction. Moreover, it was found that the modulators pyridine and triethylamine lead to phase-pure Cu_3HHTP_2 products.

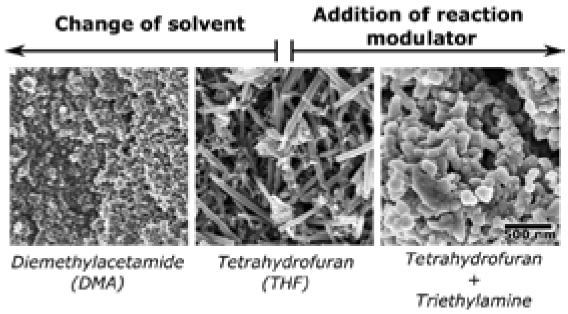

Fig. 2: SEM micrographs of Cu_3HHTP_2 synthesized (from left to right) in dimethylacetamide, tetrahydrofuran and in tetrahydrofuran with the addition of triethylamine.

Discussion

It can be concluded that the strength of solvation of both metal ions and organic linkers has a strong effect on the formation of Cu_3HHTP_2. Furthermore, it can be concluded that the application of reaction modulators and the selection of the solvent can be utilized to maximize the yield of the reaction. Fig. 2 reveals that both modulators and solvents can be employed to tune the morphology of the obtained product, from needle-like shapes to spherical crystallite agglomerates. Moreover, changes in the stacking order of the frameworks were observed by powder x-ray diffraction between the phases obtained in the different solvents and modulators.

References

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Lung-Alveoli-on-Chip:
Mechanical Characterization of a New Biological Membrane

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Introduction

Lung-on-chips (LOCs) are advanced in-vitro models, aiming at reproducing the complex microenvironment of the alveolar basement membrane. Since the lung extracellular matrix (ECM) is known to influence cellular behavior, it is essential for membranes to closely mimic composition and mechanical properties of the air-blood barrier. However, the currently used membrane is made of polydimethylsiloxane (PDMS), which poorly mimics the in-vivo chemical and physical properties. Hence, biological membranes were developed to replace this synthetic material. The aim of this study was to characterize their stiffness, to evaluate their possible integration into an in-vivo-like LOC generation. The ultimate goal was to reduce their Young's modulus, to approach the material properties found in-vivo.

Materials and Methods

The 8 µm thin biological membranes were made of collagen and elastin (CE membranes), and were supported by hexagonal gold meshes, mimicking the physiological structure of the lung alveoli. Mechanical characterization was performed via bulge test, a non-destructive method based on the measurement of the maximal deflection reached by thin films when subjected to uniform pressure (Fig. 1). A fit was then applied to the experimental data, to extrapolate the Young's modulus using a relation between deflection and pressure. Membranes made of various PDMS types were analysed as reference, to prove the reliability of the implemented bulge technique.

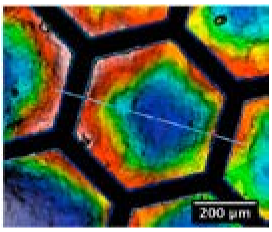

Fig. 1 Bulged shape of CE membranes, supported by hexagonal gold meshes and subjected to a pressure of -1 kPa. The picture was acquired using a 3D optical profiler.

Results

Membranes made of PDMS (Dow Corning, Sylgard 184) were found to be stiffer (E = 334 ± 129 kPa) than CE membranes with a 1:1 collagen to elastin ratio (E = 173 ± 37 kPa). A simple method to tune the stiffness of biological membranes was presented by adapting their composition. The Young's modulus was effectively reduced by gradually decreasing the collagen content in the material, reaching a value of 75 ± 43 kPa (Fig. 2).

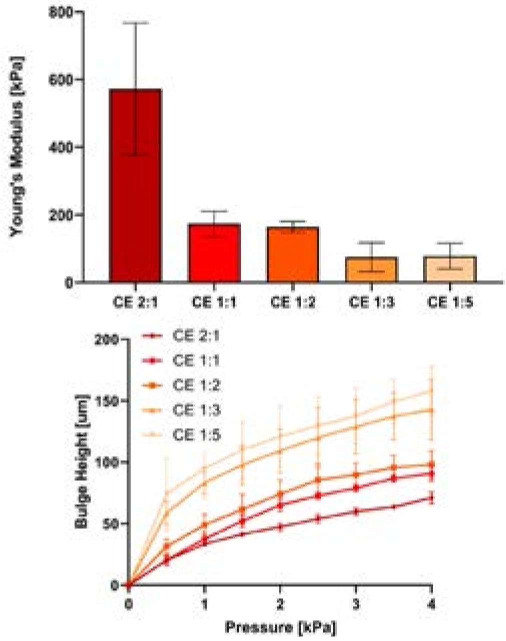

Fig. 2 Young's modulus and deflection obtained for CE membranes by varying their collagen and elastin content.

Discussion

To our knowledge, bulge test was performed for the first time at the micrometer scale, hence not allowing a direct comparison of the results with previous findings. However, as expected, the increase of elastin to collagen ratio allowed to obtain a more stretchable and softer material. Since the tuned stiffness was still far beyond that of lung ECM (E ≈ 2 kPa), the material still needs to be optimized to better mimic the cellular microenvironment of the lung alveoli. To conclude, bulge test was shown to be a promising method for mechanical characterization. It will allow further investigation of future biological membranes.

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Acknowledgements

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Investigation of an Implatable Cardiac Monitor

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Introduction

With the world's population growing and aging, more and more people are suffering from cardiovascular diseases such as cerebrovascular stroke, heart rhythm disorder, i.e. cardiac arrhythmia or heart attack Because of the risks these diseases involve, it is important to establish an efficient diagnosis. The most reliable method to diagnose arrhythmias is to place electrodes on the surface of the skin and measure an electrocardiogram (ECG). However, arrythmias may occur and terminate spontaneously and are rare. In such cases, ECG monitoring should be continuous and long-term, i.e. over several days, months or even years.
Since several years, there are implantable loop recorders available that allow patients to maintain their daily lifestyle. However, these implants are metallic and rigid, which can cause problems. The rigidity of the device and its thickness can make it noticeable even when implanted, which can bother some patients.
The goal of this thesis was to create a flexible implant that can follow the shape of the body and not use metals for the case.

Materials and Methods

The flexible printed circuit board (FPCB) used is already part of the housing and is made of flexible and biocompatible polymer. To protect the electronic components and make the implant hermetic, various welding technologies are tested: lamination, wire welding, ultrasonic welding and laser welding. This type of process consists of applying one polymer sheet to the other and welding them together (a). Thin film coating process such as plasma enhanced chemical vapour deposition (PECVD) is also tested (b). A third method used consists in using silicone as an encapsulation material (c).

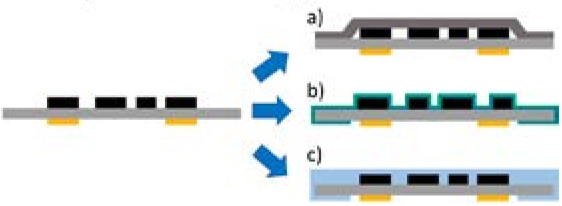

Fig. 1 Initial PCB and the different packaging methods: a) polymer welding, b) thin film coating and c) silicone encapsulation

With the silicone encapsulation process, an implant as shown in the Fig. 2 should be obtained. To validate the process, several standard tests as Seal Strength of Flexible Barrier Materials (ASTM F88/F88M), Rating Adhesion by Tape Test (ASTM D3359), Detecting Gross Leaks in Packaging by Internal Pressurization (ASTM F2096) and Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration (ASTM F1929) are performed to determine the adhesion strength and hemeticity of the product.

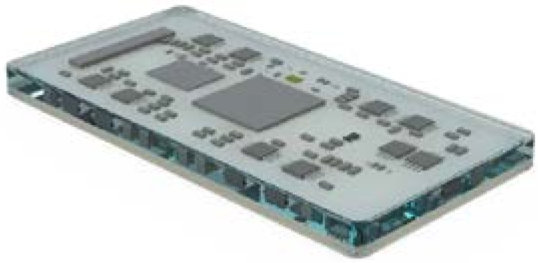

Fig. 2 Prototype of an implant made by surface technologies

Results

Of all welding technologies, only lamination provides welded and hermetically sealed samples, but to achieve this, temperatures of nearly 300°C must be applied. The PECVD allows the FPCB to be hermetically coated while maintaining its profile, whereas the silicone encapsulation produces a hermetic and smooth implant. The three results obtained are flexible.

Discussion

The high temperature required for lamination makes this process unusable with electronic components. The use of thin film is not recommended because the profile of the electronic components represents a risk of anchoring the implant. In the end, the most promising process is silicone encapsulation.

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