FH AACHEN
UNIVERSITY OF APPLIED SCIENCES

Conference Abstracts

9th International Conference on Cell and Stem Cell Engineering

Organised by the

Center of Competence in Bioenginneering

Endorsed by the

International Federation of Medical and Biological Engineering (IFMBE)

Aachen,

11.09.2014 – 13.09.2014

Content

Welcome

9th International Conference on Cell- and Stem Cell Engineering

Chairperson:

Prof. Dr. rer. nat. habil. G. M. Artmann

Cellular- and Stem Cell Engineering have become key engineering disciplines in life sciences because of their important roles in biotechnology and medical technology as well as in biology and industry. Many biomedical engineers, physicists, chemists, biologists and physicians have moved closer to the biological cell as part of a new era in the engineering of sensors, devices and of cell based organ implants and tissues. The benefits of bringing together relevant disciplines to unite the experience of different professional backgrounds are enormous.

The purpose of the upcoming conference is to present and discuss new technology. We will also present and discuss recent scientific data on selected topics in cell and stem cell engineering. New trends of research reaching far into the 21st century will become visible.

The organizing committee extends its cordial invitation to you to participate in this conference. Eight preceding and highly successful International Conferences on Cell Engineering were held in Keele (UK), in San Diego (USA), in San Remo (Italy), in Nara (Japan), in Aachen (Germany), in Sydney (Australia), in Seoul (Korea), and in Dublin (Ireland). They have attracted great attention of the international community of scientists. The “9th International Conference on Cell and Stem Cell Engineering” will be held in Aachen (Germany) again. The event will be hosted by the University of Applied Sciences Aachen. The local scientific organization will be supported by the Center of Competence in Bioengineering, Aachen, because of the 10th Anniversary after it was founded. Thus, chairpersons of the upcoming Conference will be all members of this center.

Bioengineering has become one of the most important fields for innovation of our times. With its Center of Competence for Bioengineering, the Aachen University of Applied Science puts a special emphasis on both research and teaching in this vital field. It is the crossing of disciplinary borders between biology and engineering which enables innovation and which is facilitated by the institutional setup of our university.

Rector of FH Aachen:
Prof. Dr. rer. nat. Marcus Baumann

Our researchers do not only cross disciplinary borders, they also collaborate with other research institutions – producing results which gain recognition both nationally and internationally wide. I would like to welcome you to the Aachen University of Applied Sciences in Jülich and I wish all participants of this year's ICCE lively debates and a fruitful scientific exchange!

Dr. Shankar Krishnan has over thirty years of broad spectrum professional experience in biomedical engineering education, R&D, medical product development and clinical engineering. He is the founding director of the biomedical engineering department and an endowed chair professor at WIT in Boston. He received his Ph.D degree from the University of Rhode Island with research work done at Rhode Island Hospital.

IFMBE Secretary General
Prof. Dr. Shankar Krishnan

Previously, he was an assistant director at Massachusetts General Hospital and a teaching affiliate of Harvard Medical School in Boston. He has also held faculty appointments in Illinois, Miami and Singapore. At NTU in Singapore, he was the founding director of the BME Research Center and the founding head of the bioengineering division. He also worked in R&D at Coulter Electronics in Miami and in hospital design and operations management at Bechtel for healthcare megaprojects. He has been a consultant to few medical companies, software firms and hospitals. He has served in the National Medical Research Council in Singapore.

Local Organizing Committee

Prof. Dr. rer. nat. habil. G. M. Artmann
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Chair Center of Competence in Bioengineering

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International Scientific Committee

Prof. Dr. habil. G. M. Artmann, Germany

Prof. Dr. Dr. A. Temiz Artmann, Germany

Prof. Dr. D. Bader, UK

Prof. Dr. R. Brown, UK

Prof. Dr. R. S. Bustillos, Venezuela

Prof. Dr. J. J. Chiu, Taiwan

Prof. Dr. B. Dachwald, Germany

Prof. Dr. I. Digel, Germany

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Prof. Dr. Y. D. Shi, China

Prof. Dr. H. Suh, Korea

Prof. Dr. I. Tokin, Russia

Scientific Program

Registration and Help Desk

Thursday, 11.09.2014; 18:00-19:00; Lecture Auditorium D

Friday, 12.09.2014; 7:30-17:15; Lecture Auditorium D

Welcome & Opening

Friday, 12.09.2014; 9:00-9:45; Room D110

Gerhard Artmann - Speaker of the Center of Competence in Bioengineering, North Rhine Westfalia

Marcus Baumann - Rector of the University of Applied Sciences Aachen

Shankar Krishnan - IFMBE Secretary General, Boston, USA

Plenary Lecture

Friday, 12.09.2014; 9:45-10:30; Room D110

Jürgen Hescheler: 'Pluripotent stem cells for basic research and later clinical application'

Expert Seminars

Friday, 12.09.2014

13:30 - 14:15; *Georg Büldt* 'Molecules in Action – from Lipids to Membrane Proteins'

Saturday, 13.09.2014

8:30-9:30; *Jerry Pollack:* 'The Fourth Phase of Water'

12:45-13:30; *Giuseppe Zaccai:* 'Cell Biology with Neutrons'

Keynote Lectures

Friday, 12.09.2014

10:45 - 11:15; *Jean-Pierre de Vera:* 'Habitability of planets: How biological planetary analog field research, planetary simulation in the lab and space exposure platforms in low Earth orbit are supporting future exploration missions with the aim to search for life on other planets'

12:15 - 12:45; *Saul Yedgar* 'The role of red blood cell mechanical properties in blood circulation'

14:15 - 15:00; *Peter Lelkes: '*Modulation of Stem Cell Differentiation by Microenvironmental Cues'

15:15 - 15:45; *Wilhelm Roell: '*Magnetic Nanoparticle assisted cardiac cell engraftment in a murine infarct model'

16:45 - 17:15; *Stefan Jockenhövel*: 'Tissue Engineering & Textile Implants'

17:15-17:45; *Wolfgang Heiden:* 'Visualization issues of biological and chemical models'

Saturday, 13.09.2014

10:30-11:00; *Petra Kleinbongard*: 'Endogenous cardioprotection- from animal studies to clinical relevance'

14:45-15:15; *Björn Neu:* 'Polyelectrolyte nano- and micro-capsules as drug carriers'

Sessions

Friday, 12.09.2014

Session - Life in extreme environments

11:15 - 12:15; Chair: Bernd Dachwald, DE

Ilya Digel: 'Cold, dark and no oxygen - Living beneath an arctic glacier'

Bernd Dachwald, Marco Feldmann, Clemens Espe, Gero Francke, Julia Kowalski: 'A Maneuverable Subsurface Probe for Clean Access to Terrestrial and Extraterrestrial Subglacial Environments'

Klemens Weisleitner, Birgit Sattler, Lars Hunger, Christoph Kohstall, Albert Frisch: 'L.I.F.E. (Laser Induced Fluorescence Emission) as NOVEL Non-invasive tool for in-situ measurements: Calibration and application on samples from svalbard'

Clemens Espe, Marco Feldmann, Gero Francke: 'Biological Payloads for Clean Access of Subglacial Aquatic Environments'

Session - Progress and challenges in cardiac cell replacement therapy

15:45 - 16:45; Chair: Kurt Pfannkuche, DE

Wilhelm Roell

Carlos O. Heras-Bautista: 'Culture of stem-cell derived cardiomyocytes on mechanically-defined substrates'

Benjamin Krausgrill

Martin Groeger: 'Minimally invasive robotic surgery and examples of autonomy in the DLR MiroSurge system'

Saturday, 13.09.2014

Session - Ageing and cellular engineering

9:00 - 10:45; Chairs: Aysegül (Temiz) Artmann, DE and Siming Chen, USA

Wolfgang Wagner: 'DNA Methylation Changes in Ageing and Replicative Senescence'

Seda Baykal, Ahmet Sinan Yavuz, Halil Ateş, Uğur Sezerman, Hayri Guner Ozsan, Hakki Ogun Sercan, Zeynep Sercan: 'Prolonged exposure to tyrosine

kinase Inhibitors cause phenotypic plasticity in K652 cells, resulting in morphology transition, drug resistance and escape from cellular ageing'

Siming Chen, Qian Zheng, Ying Chen, John Lyga, Uma Santhanam, Aysegül Temiz Artmann, Matthias Gossmann, Peter Linder, Kurt Scudder: 'Critical Role of Paxillin in Cell Shape and Cellular Mechanical Tension during Human Skin Aging'

Robin Bayer, Peter Linder, Larissa Kaever, Ying Chen et al., Gerhard Michael Artmann, Aysegül Temiz Artmann: 'Quantifying the order of cell internal fibrous structures - The Cell Morphologie Index'

Session - Affairs of the heart

11:00 - 12:00; Chair: Petra Kleinbongard, DE

Oliver Drews: 'Targeting proteasomes in heart disease'

Nilgün Gedik: 'Background of myocardial protection: Signal transduction' *Sabine Gent*: 'Is your life span determined by the number of heart beats?'

Amir-Abbas Mahabadi: 'Non-invasive assessment of calcification of the coronary arteries using cardiac computed tomography: How does it work and what does it mean?'

Oliver Drews: 'Targeting proteasomes in heart disease'

Session - Biomolecular structure and dynamics

13:30 - 14:30; Chair: Andreas Stadler, DE

Gergely Nagy, Renáta Ünnep, Ottó Zsiros, Győző Garab: 'Small-angle neutron scattering: a powerful tool for the investigation of photosynthetic organisms'

Chris Garvey: 'Dynamic and structural heterogeneity in red blood cells'

Ulrich Krauss: 'Light, Oxygen, Voltage (LOV) photoreceptors – promising new tools for the monitoring and control of biological processes'

Renu Batra-Safferling: 'Structural studies on LOV (Light-Oxygen-Voltage) photoreceptor proteins and their applications in synthetic biology'

Andreas Stadler: 'Structure and Dynamics of Intrinsically Disordered Proteins'

Session - Nano and microcapsules for biomedical application

15:15 - 16:15; Chair: Uta Reibetanz, DE

Uta Reibetanz: 'Layer-by-Layer Self-assembled Polyelectrolytes on Spherical Templates: A combined Drug Delivery System and Sensing Element for Biomedical Application'

Mandy Fichtner, Claus C., Arnhold J., Reibetanz Uta: 'LbL-Coated Microcarriers as Drug Delivery System for the Treatment of Chronic Inflammation: Monitoring the Influence on Vitality of Inflammatory Cells'

Martin Göse, Strehlow V., Huster D., Uta Reibetanz: 'Lipid Membrane Functionalization of LbL-Microcarriers: Mimicking a Cell for Drug Delivery'

Session – Biomechanics and modelling

16:45-17:45; Chair: Manfred Staat, DE

Bhattarai A., Frotscher R., Staat M.: 'Mechanics of the soft tissue reactions to different textile mesh implants'

Duong M.T., Seifarth V., Temiz Artmann A., Staat M: 'Investigation of smooth muscle cells of porcine tubular organs in a tubular fibrin-PVDF scaffold by mechanical stimulation and computational growth modeling'

Frotscher R., Koch J.P., Temiz Artmann A., Staat M.: 'Towards patient-specific computational modeling of hiPS-derived cardiomyocytes'

Posters

Nuraly Akimbekov, Ilya Digel, Z. A. Mansurov, A. A. Zhubanova: 'Biocompatibility of Carbonized Rice Husk in Respect of a Rat Heart Cells Line h9c2'

Nuraly Akimbekov: 'The Influence of the Carbonized Rice Husk on Wound Repair Process of Human Dermal Fibroblasts'

Rasha Bassam, Mirella Fiebes, Dariusz Porst, Aysegül Temiz Artmann, Gerhard M. Artmann,Ilya Digel: 'New Generation of Hemoglobin Structural Transition Studies: Reversed Phase High-Performance-Liquid-Chromatography'

Rasha Bassam, Christina Kordewiner, Dariusz Porst, Aysegül Temiz Artmann, Gerhard M. Artmann, Ilya Digel: 'Effects of Salts, Nitric Oxide Donors and ATP on Protein Unfolding and Aggregation'

Rasha Bassam: 'Micropipette Aspiration of Human Erythrocytes in Buffers Having Different Chemical Composition: Influence of Na+, K+, ATP and NO'

Ilya Digel, Alexandra Lösch, Stephan Neumann, Shahriar Dantism, Nuraly Akimbekov: 'Detachment of Viable Bacteria form Different Surfaces Using Ultrasound'

Ilya Digel, Stephan Neumann, Peter Linder: "BacHarvester" – a Novel Tool for Sonication-Aided Microbiological Sampling'

Hulia Qimaz Izadin Khayyat, Aylin Figiel-Lange, Gerhard Artmann, Andre Schieffer, Ilya Digel: 'Isolation and Identification of Viroid RNA from Solanum jasminoides'

Negar Firoozi: 'Design and synthesis of highly porous and biodegradable polyurethane scaffolds on star-shaped block copolymer caprolactone-isocyanate for skin tissue regeneration'

Özgen Özturk, Deniz Hür, Lokman Uzun, Betül Çelebi, Emine Kýlýç, Duygu Uçkan Çetinkaya, Bora Garipcan: 'Cartilage Mimicked Structures for Chondrogenic Stem Cell Differentiation'

Rustam Sadykov, Ilya Digel, Aysegül Temiz Artmann, Dariusz Porst, Peter Kayser, Gerhard Artmann, Azhar Zhubanova: Dysbacteriosis in Rats Induced by Small Concentrations of Lead II'

Conference Dinner

Conference Dinner Venue:

Friday 12, September at 7:30 -11:30 pm

Transport details will be announced at the conference site

Hotel Kasteel Bloomendal
Bloemendalstraat 150
6291 CM Vaals
Tel +31 (0)43 365 98 00

Plenary Lecture

Pluripotent Stem Cells for Basic Research and Later Clinical Application

Jürgen Hescheler

Institute for Neurophysiology, University of Cologne, 50931 Cologne, Germany

There is no doubt that work on stem cells will be the most promising approach for the medicine of the 21st century and probably revolutionize the therapy of many diseases including cardiac infarction and failure, diabetes, Parkinson's disease, spinal cord lesion etc.

It is our aim to provide a fundamental basis to the development of new medical treatments. Stem cell research is a broad field which requires nearly all techniques of modern life science such as genetics, cell biology, physiology, biochemistry, histology, etc. - but it also requires the input of experimental surgery and bioengineering technologies.

Induced pluripotent stem (iPS) cells represent the most promising approach for future stem cell-based tissue repair in regenerative medicine. iPS cells are functionally highly similar to embryonic stem (ES) cells, but have in addition the advantage of being ethically non-controversial, and are obtainable from readily accessible autologous sources. However, although proof of principle for the therapeutic use of iPS cells in neuronal and cardiac diseases has been shown both at the laboratory scale and in animal models, the methods used today for generation, cultivation, differentiation and selection still have to be translated for their later clinical usage.

This presentation will give an overview on our recent research work on human embryonic in comparison with iPS cells. Starting from our basic investigations on the physiological properties of cardiomyocytes developed from pluripotent stem cells we have established *in vitro* and *in vivo* transplantation models enabling us to systematically investigate and optimize the physiological integration and regeneration of the diseased tissue. Our main focus is the cardiac infarction model. Moreover, *in vitro* culture and expansion of stem cells is far from optimal and needs further research in order to overcome problems related to insufficient numbers of obtained stem cells and aging of the obtained stem cell population.

Expert Seminars

Molecules in Action – from Lipids to Membrane Proteins

Georg Büldt

Laboratory of Advanced Research on Membrane Proteins, Moscow Institute of Physics and Technology, Dolgoprudniy, Moscow Region 141700, Russia

Institute of Complex Systems (ICS), Molecular Biophysics (ICS-5), Research Center Jülich, 52425 Jülich, Germany

The chemical composition of lipids create various interactions responsible for the special geometry of bilayers which form the fundamental architecture of cell membranes. In membranes, lipids are the solvent molecules of membrane proteins giving rise to their hydrophobic and hydrophilic surfaces. What is the structure of a lipid molecule? Their crystal structure is not expected to give a satisfying answer since they crystallize in a special phase not common in biological membranes. By labelling all segments of lipids by deuterium we determined their structure in super-resolution neutron diffraction experiments for different phases.

The different phases of lipids were also used for a new crystallization method providing after 40 years of unsuccessful trials a high resolution structure of the photoexcitable retinal protein bacteriorhodopsin. By low and high resolution diffraction experiments we were able to determine structures of photocycle intermediates establishing the foundations for an understanding of light driven proton pumpin.

Another interesting retinal protein is sensory rhodopsin (SRII) from the haloarchaeon *Natronomonas pharaonis* responsible for the photophobic behavior of this organism. Again by trapping photocycle intermediates we were able to show the structural changes developing in SRII and the transfer of this signal to the next molecule in the signaling cascade the cognate transducer.

The Fourth Phase of Water: Beyond Solid, Liquid, and Vapor

Gerald H. Pollack

University of Washington, Seattle, USA

School children learn that water has three phases: solid, liquid and vapor. But we have recently uncovered a *fourth* phase. This phase occurs next to water-loving (hydrophilic) surfaces. It is surprisingly extensive, projecting out from the surface by up to millions of molecular layers. And, its properties differ substantially from those of bulk water.

Of particular significance is the observation that this fourth phase is charged; and, the water just beyond is oppositely charged, creating a battery that can produce current. We found that light charges this battery. Thus, water can receive and process electromagnetic energy drawn from the environment in much the same way as plants. Absorbed electromagnetic (light) energy can then be exploited for performing work, including electrical and mechanical work. Recent experiments confirm the reality of such energy conversion.

The energy-conversion framework implied above seems rich with implication. Not only does it provide an understanding of how water processes solar and other energies, but also it may provide a foundation for simpler understanding natural phenomena ranging from weather and green energy all the way to biological issues such as the origin of life, transport, and osmosis.

The lecture will present evidence for the presence of this novel phase of water, and will consider the potentially broad implications of this phase for physics, chemistry and biology, as well as some practical applications for health and technology.

Cell Biology with Neutrons

Giuseppe Zaccai

Institut Laue Langevin and CNRS, European Photon Neutron Campus, Grenoble, France

Since a first publication in *EMBO Reports*, revealing the dynamic basis of adaptation to extreme temperatures [1], *in vivo* molecular dynamics measured by neutron scattering emerged as a new method in cell biology. Atomic scale water and macromolecular dynamics has been characterized in bacteria [2], red blood cells, where it was correlated with body temperature [3], germinating seeds [4] and in neural tissue, in the context of medical imaging [5]. In a recent study [6], *in vivo* molecular dynamics in extreme halophile cells under stress conditions was measured by neutron scattering experiments coupled with microbiological characterization. Molecular dynamics alterations were detected with respect to unstressed cells, reflecting a softening of protein structures consistent with denaturation. The experiments indicated that the neutron scattering method provides a promising tool to study molecular dynamics modifications in the proteome of living cells induced by factors altering protein folds.

Keynote Lectures

How biological planetary analog field research, planetary simulation in the lab and space exposure platforms in low Earth orbit are supporting future exploration missions with the aim to search for life on other planets

Jean-Pierre de Vera

German Aerospace Center (DLR), Institute of Planetary Research, Rutherfordstr. 2, D-12489 Berlin, Germany

One of the main challenges in astrobiology and planetary research in the near future is to realize space missions to study the habitability of Mars and the icy moons of the Jovian and Saturnian system. Mars is an interesting object to search for fossilized life because of its past water driven wet history. River beds, sedimentary deposits indicating the presence of lakes as well as a supposed but highly debated presence of a former ocean on the north hemisphere are clearly showing that the atmosphere must have been much denser and the conditions much more habitable than nowadays. Even today still water activity is present in specific niches on the surface of Mars. This leads to the conclusion that the search for habitable environments on Mars and the presence of bio-traces of extinct or extant life is a reasonable enterprise to be conducted in the next space missions.

Besides the planet Mars other planetary objects in our solar system are promising candidates to find life as there are the icy moons. The Jovian moon Europa is one promising candidate, where water driven resurfacing activity of its icy crust must regularly happen because of the low amount of impact craters on the surface as well as the clear observations of cryo-volcanos which can only be explained by the presence of a liquid water ocean beneath the surface. Fissures and cracks with colored salty deposits coming from the inner side of the supposed global ocean are also clearly showing that this ocean can be a habitable environment and where it would be good to search for present life.

The Saturnian moon Enceladus seems also to be a promising candidate to search for life. On this moon high water plumes come out of an ocean covered by its ice crust.

Role of Red Blood Cell Mechanical Properties in Blood Circulation: Implications for Blood Flow Disorders and Blood Transfusion

Saul Yedgar and Gregory Barshtein

Hebrew University-Hadassah Medical School, Jerusalem, Israel

Red Blood Cells (RBC) have unique flow-affecting properties (FP) that play major roles in blood flow. These are RBC deformability (ability to change shape), potential adhesion to blood vessel walls endothelial cells (adherence) and self-aggregability (forming multi-cellular aggregates). Normally, RBC are sufficiently deformable, their adherence and aggregation is insignificant, thereby enabling adequate flow through the blood vessels, particularly in micro-vessels and capillaries. However, numerous pathological conditions (e.g., cardio-vascular/inflammatory diseases, diabetes, sickle cell, malaria, thalassemia) are associated with impairment of RBC FP, especially increased adherence and rigidity (reduced deformability), which contributes to blood flow disorders.

This study provides direct evidence, in humans, for the role of RBC hemodynamic properties in blood circulation, presenting RBC FP as a powerful tool for diagnosis and monitoring of clinical conditions and treatments. In particular, this study demonstrates that RBC FP define the hemodynamic quality of PRBC units, and the determination of PRBC FP in the blood bank is essential for assessing the transfusion impact on blood circulation in blood recipients. Selecting PRBC which is compatible with the recipient's RBC hemodynamic quality and clinical conditions, would enable the reduction of risk in transfusion, and the designing of patient-specific (personalized) transfusion. As the current blood bank routine does not address the functionality of blood units, testing the hemodynamic functionality of PRBC will introduce a new paradigm/practice into blood banking, which would revise and improve transfusion therapy.

Modulation of Stem Cell Differentiation by Microenvironmental Cues

Peter I. Lelkes

Professor and Chair, Dept. Bioengineering; Director Temple University Institute of Regenerative Medicine and Engineering (TIME), Temple University, Philadelphia PA 19122, USA

In this expert talk I will discuss work ongoing in our laboratory and elsewhere to optimize directed stem cell differentiation using engineering approaches. Specifically, in view of their translational applications, there is a vested interest in enhancing directed pulmonary and vascular differentiation of cultured pluripotent progenitor (ES and iPS) using a variety of "near-physiologic" microenvironmental cues, such as reduced ambient oxygen pressure and "tissue-specific" matrix stiffness.

In further developing an established chemical differential protocol, we recently reported that reduction in ambient oxygen levels significantly upregulated the differentiation of cultured ES and iPS cells towards definitive endoderm (DE), which constitutes the precursor cells for lung specific epithelia cells. This enhancement is mediated by activation of HIF-1α and reactive oxygen species. Furthermore, the duration of exposure to hypoxia during an embryonic-development mimicking, complex differentiation protocol critically affected the pathways of differentiation towards alveolar epithelial cells, such as AE , AEII, and club cells.

Similarly, modulating the stiffness of the substrate on which ES cells are grown, can also significantly affect their final fate. For example, using a "straightforward" chemical differentiation protocol, the yield of mESCs that differentiate into DE can be significantly enhanced (approximately 10-fold) by choosing a substrate stiffness (several kPA), which emulates that of the lung. Conversely, a stiffness in the range of MPa favors mesenchymal differentiation, specifically differentiation towards an endothelial phenotype.

Taken together, these studies demonstrate that in developing and optimizing scalable bioprocesses for efficient directed differentiation of pluripotent progenitor cells, the final cell fate can be effectively modulated by appropriate tissue-specific engineering of several microenvironmental conditions. We posit that these studies will open the prospect of effectively obtaining diverse cell types from one and the same donor population. In terms of potential clinical applications pure population of these diverse cells can then be used, alone or in combination, for cell-based pulmonary therapies *in vivo*, for reseeding the alveolar and vascular compartments of decellularized lungs *ex vivo* or for coating the blood and air contacting surfaces of bioartifical lungs *in vitro.*

Tissue engineering & textile implants

Stefan Jockenhoevel [1,2], Valentine Gesché [1], Robin Ross [1], Kathrin Kleinsteinberg [1],Lisanne Rongen [1], Lena Thiebes [2], Christian Cornelissen [2,3], Petra Mela [2]

[1] *Institute for Textile Engineering, RWTH Aachen, Germany*

[2] *Applied Medical Engineering, Helmholtz Institute Aachen, RWTH Aachen, Germany*

[3] *Department of Cardiology, Pneumology, Angiology and Intensive Care, University Hospital Aachen, Germany*

The biomechanical properties of the human body are mainly defined by fibre structures, like e.g. collagen bundles, elastic fibres, fibrin fibres, fibrous cartilage, and ligament etc. The aim of tissue engineering is to replace, repair, maintain and/or enhance tissue function. Herefore the classical tissue engineering requires an ideal combination of cellular component, scaffold materials and biomechanical and/or biochemical signals. The material plays a central role with regard to the 3D structure, the cell-to-cell-interaction and the biomechanical properties of the complete construct.

Textile Engineering offers a multi-scale toolbox for the development of scaffold structures on (1) the molecular level of polymer science and biochemical functionalisation, (2) the nano/micro-scale level of fibre production (e-spinning, melt-, wet-, dry-spinning) and on a (3) meso/macro-scale level for the production of 2D and 3D structures by weaving, knitting, braiding etc. Different textile technologies have been successfully evaluated as single technology or in combination with regard to cardiovascular and pulmonary implants like:

- Non-wovens as scaffold material for heart valve tissue engineering
- Warp-knitted structure for textile-reinforcement of biological vascular grafts2 and stents
- Braided structures for endobronchial stenting
- Combination of single-fibre-placement and e-spinning for biomimetic, textile-reinforced heart valve prosthesis

A variety of textile-based and textile-reinforced cardiovascular and endobronchial implants have been developed in our group. The presentation will give an overview about the different textile technologies and their impact for tissue engineering in general and cardiovascular tissue engineering specifically.

Visualisation Issues of Biological and Chemical Models

Wolfgang Heiden

Visualization of biological and chemical models has earned great merits both with (pseudo-)realistic representations as well as schematic diagrams of complex reactions and processes, particularly in drug design. However, during the past two decades little essential advances have been made in visualization for life science applications, as established display metaphors as well as rendering speed and quality had reached a level that met almost all requirements for standardized data processing.

With upcoming technologies and new generally accepted paradigms for data handling, visualization research may now address challenges that had seemed far beyond reach for a long time.

The lecture will present visualization-related aspects of some current problems in life science research and how emerging technologies maybecome helpful to solve these problems.

Polyelectrolyte nano- and micro-capsules as drug carriers

Björn Neu

Faculty of Life Sciences, Rhine-Waal University of Applied Sciences

Current carrier systems for the delivery of drugs, genes or peptides into cells and tissue are usually synthetic materials, such as polymers or synthetic liposomes, or viral vectors. However, these carrier systems have their limitations and risks. In recent years it has been demonstrated that colloidal particles and capsules coated with biocompatible poly-electrolytes might be a promising alternative. In this presentation an overview is given over some of our recent advances in the development of bio-compatible and -degradable polyelectrolyte capsules as potential carriers of drugs, genetic material or other agents.

Sessions

Life in extreme environments

Chair: Bernd Dachwald, DE

A Maneuverable Subsurface Probe for Clean Access to Terrestrial and Extraterrestrial Subglacial Environments

Bernd Dachwald[1], Marco Feldmann[1], Clemens Espe[1], Gero Francke[1], Julia Kowalski[1], Jill Mikucki[2], Slawek Tulaczyk[3], Ilya Digel[4]

[1]*Aerospace Engineering, FH Aachen Univ. of Appl. Sci., Aachen, Germany*

[2]*Dept. of Microbiology, University of Tennessee, Knoxville, TN 37996, USA*

[3]*Dept. of Earth and Planetary Sci. University of California, CA 95064, USA*

[4]*Institute for Bioengineering FH Aachen Univ. of Appl. Sci., Jülich, Germany*

There is significant interest in sampling subglacial environments on Earth and in space for geobiological and astrobiological studies. Clean access to such environments, however, is very difficult to achieve and a subsurface ice exploration probe is an important building block for

such applications. Extensive water ice bodies exist on Mars and the icy moons of the outer Solar System. Europa is probably most interesting from the astrobiological perspective, but access to subsurface material might be easier on Enceladus, where – according to measurements of the Cassini spacecraft – ice grains with organic compounds escape via cryovolcanism from "warm" fractures in the ice, known as "Tiger Stripes". Because landing in close vicinity to such a fracture is very risky, it might be preferable to land at a safe distance and to use a maneuverable subsurface ice

probe to navigate to such a water-bearing fracture at a depth of ~100m below the surface. Once there, the subsurface ice probe can sample and analyze the materials in the fracture. Existing ice-drilling technologies make it cumbersome to maintain microbiologically clean access for sample acquisition and environmental stewardship of fragile subglacial ecosystems.

The IceMole is a maneuverable subsurface ice probe for clean in-situ analysis and sampling of glacial ice and subglacial materials. The design is based on the novel concept of combining melting and mechanical propulsion.

L.I.F.E. (Laser Induced Fluorescence Emission) as NOVEL Non-invasive tool for in-situ measurements: Calibration and application on samples from svalbard

Klemens Weisleitner [1], Birgit Sattler,[1] Lars Hunger [2], Christoph Kohstall [3],Albert Frisch [3]

[1] *University of Innsbruck, Institute of Ecology, Technikerstrasse 25, 6020 Innsbruck, Austria*

[2] *University of Innsbruck, Institute of Astro- and Particle Physics, Technikerstrasse 25, 6020 Innsbruck, Austria,*

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Rising temperatures change microbial communities in supraglacial ecosystems and hence on the availability of organic carbon. There hardly exist data dealing with carbon sink rate estimates in the cryosphere (e.g. Anesio et al., 2009, 2010). Among other concerns, using standard methods for sample aquisition implies three major problems: A) for high resolution data, a sufficient amount of samples is logistically challening and expensive B) a severe manipulation of the ecosystem leads to a falsification of *in situ* conditions (cutting, sawing and melting ice cores) C) ice alage might play a crucial role for carbon sinks. Due to insufficient data resolution , the supraglacial distribution could not be assessed yet on a large scale in a sophisticated manner.

We have developed a portable dual-wavelength spectrophotometer for high resolution and non-destructive *in-situ* measurements in terrestrial and ice ecosystems. Based on a laser-induced fluorescence emission technique (L.I.F.E.), the device targets for porphyrin structures in highly autotrophic surface communities. The instrument was tested during a Mars analog mission in the Kess Kess formation near Erfoud (Morocco) while mounted on a rover. Additional field tests took place in the high Arctic and the Antarctic. Here, we present data from our laboratory calibration for pigment standards of chlorophyll$_a$ and phycoerythrin and discuss sample measurements from a glacier in Svalbard. We found that 532nm lasers excite phycobiliproteins in cyanobacteria, red algae and cryptomonads which produce multiple fluorescence signatures between 550nm and 750nm - depending on species and metabolic state. Furthermore, a 405nm laser excites chlorophyll$_a$ with highest fluorescence counts at 680-690nm. For data validation, we compared our L.I.F.E. results with a traditional method, using a common double-beam spectrophotometer and standard laboratory protocols.

For the first time, phototrophic organisms in ice ecosystems can be investigated by the use of an *in-situ* and non-destructive method. Data aquisition with high spatial and temporal resolution of chlorophyll$_a$ and phycoerythrin contents is possible. Further, it can be attached to an autonomous rover. Hence, large areas can be investigated without difficulties in logistics. We propose that the L.I.F.E. instrument can be used for monitoring purposes of carbon fluxes in cryospheric environments.

Cold, Dark and no Oxygen: Living beneath an Antarctic Glacier

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First discovered by the British National Antarctic Expedition (1901–04), the Taylor Glacier in Antarctic buries a fascinating microbial ecological system, supported by chemical energy present in reduced iron and sulfur compounds. This location belongs probably to the most hostile environments on the earth, combining high salinity, darkness, low temperatures, high pressures, low availability of some biogenic elements and limited organic carbon supply and therefore representing a very interesting object from astrobiological point of view.

Any living system we know relies on energy and carbon sources. The system of interest is a sulfate-rich ancient marine brine overlain by about 400 m of ice, with the underlying iron-rich bedrock. Due to such a geochemical composition, some organisms living there (closely related to Thiomicrospira (Gammaproteobacteria) and other groups (Betaproteobacteria, Deltaproteobacteria), apparently facilitate a catalytic sulfur cycle where ferric ion Fe(III) serves as the terminal electron acceptor instead of oxygen. For both autotrophic and heterotrophic organisms using Fe(III), the electron flow is similar to the “classical” oxygen-based scheme, except of the peculiar final enzyme called ferric iron reductase.

Iron bacteria and their ecological partners preferably colonize the transition zone between an anaerobic environment (de-oxygenated medium) and an aerobic environment, actively cycling carbon, iron and sulfur. Reducing equivalents (electrons) can be shared between different species of microbes, establishing the basis for cooperation. The interspecies electron transfer probably occurs either via diffusion or via direct contact in cell aggregates or via electric currents through natural conductive minerals. Sophisticatedly coupled biogeochemical processes enable several groups of subglacial microbes to grow in relative isolation from the rest of the world.

Biological Payloads for Clean Access of Subglacial Aquatic Environments

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The access to subglacial aquatic environment provided by melting probes offers a chance to deploy instruments as payloads into these environments.

This talk gives an overview about current and future development of these payloads in the scope of the IceMole and Enceladus Explorer Project.

The data from those payloads or sensors are used to characterize the environment, determine the ice/brine boundary and to retrieve samples of the subglacial water.The challenge to obtain water samples in extreme environments like subglacial lakes is a clean access through the ice sheet and a sample free of contamination. The Clean Access and Sampling Subsystem (CASS) does provide this possibility to take clean samples of subsurface

materials. The CASS is capable to be integrated in melting probes or other ice penetrating systems. The subsystem is designed and manufactured for the existing maneuverable melting probe IceMole (IM). Both systems are developed at the FH Aachen University of Applied Sciences. The IM combines conventional melting with drilling by implementing an additional ice screw at the tip of the melting head. The second use of the ice screw is the integrated proboscis which is necessary for the clean sampling process. The subsystem has been designed to sample subglacial water probes of a depth of approx. 50 m from the so called Blood Falls at the McMurdo Dry Valleys, Antarctica. In this contribution we will describe the design and functionality of the IM CASS and line out the fundamental sampling strategy. To determine the ice/brine interface an integrated conductivity sensor is used which constantly monitors the conductivity of the produced meltwater.

We also present a fluorescence biosensor as payload module to map the distribution of fluorescing substances along the melting channels.

Progress and challenges in cardiac cell replacement therapy

Chair: Kurt Pfannkuche, DE

Culture of stem-cell derived cardiomyocytes on mechanically-defined substrates

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Native cardiac tissue possesses specific elastic modulus values that differ from those found on glass or polystyrene by several orders of magnitude. Cardiomyocytes are typically seeded into substrates that are far from being optimal in terms of elastic modulus. Such cells respond by adapting their internal machinery to the stiffness of the material used as substrate. Controlling such cell adaptations by culturing cells on matrices with stiffness that mimic the elastic modulus of native tissue is achieved by using polyacrylamide hydrogels. Substrate stiffness was adjusted to simulate not only healthy but also diseased heart.

Polyacrylamide hydrogels provides several advantages as cell culture substrate. It is chemically stable, optically clear, its porous structure provides a more physiological environment, and its stiffness can be easily regulated. However, it must be activated to provide ligand immobilization. Crosslinkers create a bridge between the polymer backbone and the ligand of interest. 2,5-Dioxopyrrolidin-1-yl 6-acrylamidohexanoate was synthetized, characterized and furthermore analyzed.

Our findings indicate that the stiffness of the extracellular environment affects the contractile properties of iPS cell derived cardiomyocytes. Overall, taking in account cell spreading, frequency response, well defined sarcomeres and striations, indicate that substrates of stiffness of 55 kPa are the most desirable for cultivation of heart cells in comparison to cells cultured on stiff polystyrene cell culture dishes.

Minimally invasive robotic surgery and examples of autonomy in the DLR MiroSurge system

Martin Groeger

German Aerospace Center (DLR), Oberpfaffenhofen, Robotics and Mechatronics Center (RMC)

Minimally invasive robotic surgery and examples of autonomy in the DLR MiroSurge system abstract: Different aspects of minimally invasive robotic surgery are presented in the example of the DLR MiroSurge system. MiroSurge is a versatile robotic system for the surgery of the future, developed by the Robotics and Mechatronics Center (RMC) at DLR Oberpfaffenhofen. Next to the setup of the robotic system and its components (robotic arms, instruments, endoscope, 3d display, surgeon console), the way how the surgeon uses the system to perform surgery and the feedback provided (vision and force / torque) are described. With techniques to process sensors such as imaging, support of the surgeon by autonomous functions is possible, e.g. by automated camera guidance and motion compensation of the beating heart.

Ageing and cellular engineering

Chairs: Aysegül (Temiz) Artmann, DE and Siming Chen, USA

DNA Methylation Changes in Aging and Replicative Senescence

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Aging of the organism and replicative senescence during in vitro culture seem to resemble related processes. Both are associated with highly reproducible DNA methylation (DNAm) changes at specific sites in the genome – yet, there are significant differences in DNAm patterns of long-term culture and aging. So far, there is little evidence how DNAm is regulated at specific sites in the genome and whether these modifications are cause or consequence of the aging process. I will demonstrate that specific epigenetic modifications are reliable biomarkers: senescence-associated DNAm changes can be used to track the number of population doublings for quality control of cell preparations (Koch et al., Aging Cell. 2012 and Genome Res. 2013) whereas analysis of

age-related CpG sites facilitate predictions of donor age (Weidner et al., Genome Biol. 2014). These epigenetic age-predictions are affected by disease and life-style parameters and may therefore rather reflect biological age than chronological age. Notably, senescence-associated as well as age-associated DNAm changes are reversed in induced pluripotent stem cells (iPSCs; Frobel et al., Stem Cell Reports, accepted) and this may play a central role for their escape from both – replicative senescence and aging.

Prolonged exposure to tyrosine kinase Inhibitors cause phenotypic plasticity in K652 cells, resulting in morphology transition, drug resistance and escape from cellular ageing

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Currently there are several approaches for engineering cell fate. The generation of IPSCs as well as direct conversion between two mature cell states are the two major processes used in the field of induced cellular potency. Research so far supports that transcription factors are predominantly responsible for the phenotypic plasticity observed in direct cellular conversion. Transcription factors are end targets of signaling pathways.

We hypothesized that alteration of signal transduction pathways by therapeutic drugs such as tyrosine kinase inhibitors (TKIs) have the potential of inducing phenotypic conversion in a subset of cells; which in turn may have important consequences ranging from drug resistance or inducing senescence to generating dormant cancer cells. TKIs are used as first line therapy in chronic myeloid leukemia (CML). We used the CML cell line K562 to generate a TKI resistant sub-clone. Resistance to 1st, 2nd and 3rd generation TKIs was confirmed by annexin-V staining, caspase activation and MTT assays. ABL kinase domain mutations, BCR-ABL amplification and deficient cellular uptake were ruled out. Prolonged growth in the presence of TKİs resulted in the selection of cells with fibroblastoid morphology and the ability to grow as a monolayer.

Cellular characterization showed enrichment in pluripotent and mesenchymal surface markers in addition to resistance to stress-induced replicative

senescence and cellular aging. Our findings have important clinical implications as well as supporting research that aim to induce cellular potency and targeted cell fate decisions by more efficient and less laborious/consuming methodologies.

Critical Role of Paxillin in Cell Shape and Cellular Mechanical Tension during Human Skin Aging

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Skin aging is a complex process involving a series of cellular and extracellular matrix events. Recent studies indicate that loss of mechanic tension by intrinsic factors or photodamage can lead to the disruption of normal cellular and tissue behaviors and function. The outcome of these changes in turn causes winkle formation in skin. Paxillin is a key focal adhesion adaptor protein that mediates cell-matrix signaling and regulates cytoskeleton assembly, which provides the essential mechanic tension for cell attachment, spreading, and migration. Loss of Paxillin activity has been related to impaired cellular functions in various animal and cell experimental models, however, a direct link between Paxillin and human skin aging is yet to be established.

To better understand the function of Paxillin during skin aging, we performed a combination of molecular, cellular, and *in vivo* studies. The role of Paxillin in cellular functions was studied via targeted gene disruption, and the effect of age on Paxillin expression levels in human dermal fibroblasts was investigated. We also developed a computer program to measure the cell shape, as well as a method to measure the cell tension. By employing these newly developed methodologies, we examined both cell shape and tension in young vs. old dermal fibroblasts *in vitro*. The reciprocal relationship between cell shape and tension vs. age was discerned. We further developed a blend of a novel plant extract with a synthetic compound that can partially restore cell shape and tension in older fibroblasts. Results of these experiments will be presented.

Quantifying the order of cell internal fibrous structures - The Cell Morphologie Index-

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Numerous cellular functions depend to a great extend from the cell internal order of protein fibers as for instance alignment, destruction, disordering or restoration, respectively. The order of such protein structures so far could only be evaluated by an individual researchers subjective classification. The Cell Morphology Index (CMI) calculates a numeric value between `zero` and `one`. `Zero indicates that there is no cell internal order of fibrous structures at all as for example induced by cytoskeletal destructive agents or environmental factors, respectively. In contrary, `One´ would stand for full parallel fiber arrangements in the cell as it appears in certain cell types after cyclic uniaxial loading. CMI analysis requires image analysis of fluorescence stained cells. Multicolor staining of different fibers and subsequent CMI analysis is possible. The CMI-method is based on the intensity distribution of stained fibers and a 2-dimensional Fourier Transformation of a region inside the cell-body. The cell's nucleus and other corpuscular structures do not affect CMI data. With the help of this new method, the effect of photo induced skin aging (photoaging) could be quantified and evaluated. In this study, we focused on the distribution of F-actin fibers in normal human dermal fibroblasts (NHDFa). To mimic environmental affects, cells were exposed to UV light. Treatment effects on the f-actin fibers were observed after 24 h. Our data represent the CMI for f-actin fibers of single cells. In order to include different human skin cell types into our research we performed also preliminary studies with human keratinocytes. Data will be presented and discussed during the presentation.

Biomolecular structure and dynamics

Chair: Andreas Stadler, DE

Small-angle neutron scattering: a powerful tool for the investigation of photosynthetic organisms

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During the past years we have investigated various photosynthetic organisms and membranes with small-angle neutron scattering (SANS). We determined characteristic repeat distances and revealed light induced structural reorganizations during photosynthesis in isolated plant thylakoid membranes, living unicellular organisms [1-3] and intact leaves [4] with a time resolution of seconds and minutes [5]. We also provided experimental evidence for changes in thylakoid membrane stacking in green algae during state transitions of the photosynthetic machinery [6].

Recently we also investigated the effects of Hofmeister salts and variations in the pH on plant thylakoid membranes as well as micronutrient-induced ultrastructural changes in the chloroplasts of tobacco leaves.

These studies, in addition to providing statistically averaged quantitative data on the macroorganization of thylakoid membranes and on ultrastructural changes involved in different regulatory mechanisms, also demonstrate the power of neutron scattering, a non-invasive technique, in investigations of complex biological systems.

Dynamic and structural heterogeneity in red blood cells

Chris Garvey

Australian Nuclear Science and Technology (ANSTO), BRAGG Institute, Australia

The highly penetrative and non-ionizing nature of neutrons can provide an ideal probe of structure and dynamics in cellar systems. The low information content of neutron scattering data can provide an important barrier to extracting meaningful information from experiments. While many cellular systems can be quite complex the red blood cell provides a simple system in which useful quantitative information can be extracted. Here we discuss the analysis of scattering from red blood cell and define a simple scattering problem where it is the intra-cellular solution of hemoglobin which provides the

only resolvable component to the neutron scattering. In particular we discuss ultra-high resolution small angle neutron scattering (USANS) collected from suspensions of red blood cells (RBCs) at rest (not flowing) in D20 saline

solutions on the S18 instrument (Institute Laue Langevin, Grenoble, France). We discuss the approximation that the contrast in USANS from suspensions of RBCs is due to the difference in haemoglobin concentration inside and outside the cells. This conclusion allows us to use USANS as a simple probe of cell volume in collections of metabolically active cells.

Light, Oxygen, Voltage (LOV) photoreceptors – promising new tools for the monitoring and control of biological processes.

Ulrich Krauss

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Light, Oxygen, Voltage (LOV) domains, as the sensory module of various blue-light photoreceptors, regulate various physiological responses in both eukaryotes and prokaryotes. Their light sensitivity is intricately linked to the photochemistry of the non-covalently bound flavin mononucleotide (FMN) chromophore, that forms a covalent adduct with a conserved cysteine residue in the LOV domain upon illumination with blue light. Considerable variation is found in the lifetime of the adduct state, that can vary from seconds to several hours. From a bioengineering perspective, LOV domains represent promising new tools for the non-invasive monitoring (fluorescence reporters) and the spatiotemporal control (optogenetics) of cellular and biotechnological processes. For the efficient engineering and the design of those tools an in-depth (structural) understanding of the underlying photochemical and intramolecular signal-relay processes is indispensable. In this contribution, general principles of LOV photoreceptor function, photo-activation, signalling-state stability and signal-relay are discussed with regard to the natural photoreceptor system and are placed in the context of the rapidly growing field of LOV-based optogenetics.

Structural studies on LOV (Light-Oxygen-Voltage) photoreceptor proteins and their applications in synthetic biology

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Blue light photoreceptors containing light-oxygen-voltage (LOV) domains are widely distributed in plants, algae, fungi, bacteria, and regulate a myriad of different physiological responses. Their photocycle involves the blue-light triggered adduct formation between the C(4a) atom of a non-covalently bound

flavin chromophore and the sulfur atom of a conserved cysteine in the LOV sensor domain. Although LOV domain itself is structurally well-conserved, LOV proteins show considerable variation in the structure of N- and C-terminal elements which flank the LOV core domain, as well as in the lifetime of the adduct state. In this presentation, we will present the photochemical, structural and functional characterization of full-length 'short' LOV proteins. Unique properties of these proteins have proven them suitable for several biotechnological applications such as fluorescence reporters *in vivo* in both aerobic and anaerobic biological systems. Recent advances in their applications such as *in vivo* photoswitches to regulate cellular function will be discussed.

Structure and Dynamics of Intrinsically Disordered Proteins

A. Stadler

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Intrinsically disordered proteins lack a well-defined folded structure and contain a high degree of structural freedom and conformational flexibility, which is expected to enhance binding to their physiological targets. In solution myelin basic protein (MBP) belongs to that class of proteins. Structure and dynamics of MBP were investigated using small angle scattering of X-rays and neutrons, and neutron spin-echo spectroscopy (NSE). The NSE technique allowed the measurement of very slow diffusive motions of the protein up to 150 nanoseconds. The measured dynamics were interpreted using a coarse-grained structural ensemble and concepts derived from polymer theory.

Nano and microcapsules for biomedical application

Chair: Uta Reibetanz

Layer-by-Layer Self-assembled Polyelectrolytes on Spherical Templates: A combined Drug Delivery System and Sensing Element for Biomedical Application

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The application of Layer-by-Layer constructed microcarriers offers new and promising transport options in drug delivery. The alternating assembly of oppositely charged biopolymers (multilayer) onto a spherical template facilitates the integration of active agents into different layer positions as well as into the porous template material or the hollow capsule after core dissolution.

In order to apply those carriers as a transport system it is necessary to get a detailed understanding about possible single or multiple functionalization as well as about carrier processing within the cell. The emphasis here is on the design of a tailored system to provide the secure transport of therapeutics without side-effects and the specific release of therapeutics within aimed cell compartments.

This presentation will give an insight into potential designs of LbL-microcarriers including biopolymer basis multilayer coating and the assembly of both active agents and additional functional components without interference. Here, functional components may serve in different ways: Sensor molecules and particles, such as for intracellular carrier localization based on pH-differences or for the detection of time-dependences of drug release within cells, will be integrated into inner layers or core. Additionally, surface modifications are used to facilitate enhanced carrier interaction with cells such as for adsorption and uptake, e.g. by the assembly of antibodies or cell-penetrating peptides.

LbL-Coated Microcarriers as Drug Delivery System for the Treatment of Chronic Inflammation: Monitoring the Influence on Vitality of Inflammatory Cells

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Chronic inflammation is characterized by a massive invasion of polymorphonuclear leukocytes (PMNs) into the affected tissue followed by insufficient clearance, secondary necrosis and lysis of PMNs. This leads to subsequent release of highly degradative enzymes which are responsible for further pro-inflammatory signaling. Since current medical treatment of chronic inflammation induces several side effects, layer-by-layer (LbL) coated microcarriers provide a local and low-dose application as well as a time-controlled release of the assembled therapeutic agent. This new concept facilitates the transport of anti-inflammatory substances (AIS) into inflamed tissue via biopolymer multilayer to effectively inhibit destructive enzymes at their place of origin.

Nevertheless, drug delivery systems themselves are expected not to induce immune response or seriously affect cell vitality. Thus, un-functionalized as well as AIS-functionalized LbL-microcarriers have been investigated regarding an apoptotic or necrotic influence on inflammatory cells. In this study, the cationic dye JC10 was used to detect changes in mitochondrial inner-membrane electrochemical potential as indicator for early apoptosis. Investigations concerning time- and concentration-dependent incubation of microcarriers with two inflammatory cell model systems show only a minor influence on cell vitality in case of un-functionalized microcarriers, whereas AIS-assembled microcarriers exhibit even a positive effect regarding cell vitality.

Those results show the high potential of LbL microcarriers as drug delivery system.

Lipid Membrane Functionalization of LbL-Microcarriers: Mimicking a Cell for Drug Delivery

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In current applications many systemically applied therapeutics cause side effects due to non-targeted transport and highly dosed amounts of active agents. Therefore, new drug delivery systems are required to overcome those problems. One promising approach is based on the (1) Layer-by-Layer (LbL) technique using biocompatible polymers combined with (2) the liposome spreading (LS) technique and (3) the integration of specific binding sites for further modification applied onto spherical microparticles.

In this study we used those techniques to build up a modular, multiple surface-functionalized microcarrier:

(1) According to the LbL technique, using the stepwise assembly of oppositely charged bio-polyelectrolytes (protamine sulphate, dextran sodium sulfate) a multilayer was formed with the opportunity to integrate active agents.

(2) The LS of small unilamellar vesicles was applied assembling a lipid membrane on top of the polyelectrolyte multilayer to mimic a cell like surface and enhance biocompatibility.

(3) Specific biotinylated lipids have been integrated into this lipid surface to provide a binding site for functional or targeting molecules.

Nevertheless, a complete, homogenous lipid membrane is essential for therapeutic application since unspecific serum protein interaction and uptake by non-targeted cells have to be avoided. It could be shown that specific coating conditions (e.g. concentration of liposomes, microcarriers and functional lipids) are necessary to obtain an appropriate functionalized lipid membrane. Finally, such microcarriers exhibit a sufficient amount of specific streptavidin binding as a precondition for optimal binding of replaceable functional biotinylated molecules.

Biomechanics and Modelling

Chair: Manfred Staat, DE

Towards patient-specific computational modeling of hiPS-derived cardiomyocytes

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Quantitatively accurate computational modeling of any cell with respect to drug action, mutations or individualization often fails due to numerous influences on the model parameters, like cell type, mixture of cell types, maturity, cell production batch, the in vitro environment, temperature or donor. Moreover, individualization with respect to a specific patient and modification with respect to diseases of the widely used Hodgkin-Huxley models requires an immense amount of experiments that cannot be performed in time-critical

patient-specific treatment. It is already known that a possible remedy is the combination with Markovian processes that allow the modeling of an ion channel genotype and determine the ion channel expression rather than modeling the ion channel phenomenologically. Changing the model with respect to known changes in protein function that result from a disease, a drug or a different cell type and species (e.g. human), experimental results for easily available hiPS- derived cardiomyocytes can directly be used to study those effects on the target cell type. In this paper, we describe how to combine electrophysiological data, mechanical experiments and the modeling of ion channel expression to simulate drug action, diseases and mutations on patient-specific human cardiomyocytes.

Mechanics of the soft tissue reactions to different textile mesh implants

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It is estimated that 20 million prosthetic meshes are implanted each year worldwide. An ideal prosthetic mesh with perfect mechanical and biological properties has not been found yet. A simple selection of one sole synthetic mesh construction for any level and type of pelvic floor dysfunctions without adopting the design to specific requirements will increase the risks for mesh related complications. Adverse events are closely related to chronic foreign body reaction with enhanced formation of scar tissue around the surgical meshes, and manifest as pain, mesh migration, mesh shrinkage, and eventually recurrence. The extent of fibrotic reaction is increased with higher amount of foreign body material, larger surface, or in with inadequate elasticity of the textile with collapse of pores under strain. Objective and standardized studies of different meshes are essential to evaluate the many influencing factors for the failure and success of the reconstruction. Measurements of elasticity and tensile strength have to consider the specific anisotropic behavior as result of the textile structure. An appropriate mesh then should show an integration with limited scar reaction and preserved pores that are filled with local fat tissue (so called effective pores). On this basis, this paper facilitates the mechanical behavior of different types of supportive synthetic meshes that are used for the treatment of the urinary incontinence. The measurements help to predict the functional and biological outcomes after tissue reinforcement with meshes, and permits further optimization of the mesh devices for the specific indications to improve the success of the surgical treatment.

Investigation of smooth muscle cells of porcine tubular organs in a tubular fibrin-PVDF scaffold by mechanical stimulation and computational growth modeling

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Living cells are capable of growing, adapting, remodeling or degrading and restoring in order to deform and respond to stimuli. For tubular organs, for example ureter and bladder, their shapes and microstruscture change during growth and these changes are strongly depended on external stimuli such as training. In this paper, we present the mechanical simulation of smooth muscle cells in a tubular fibrin-PVDF scaffold and the modelling of the growth of tissue by stimuli. Intraluminal mechanotransduction was performed with a balloon catheter that was guided through the lumen of the tubular structure. Urea and creatinine diffusion was investigated in an Using chamber. The bursting pressure was examined to compare the stability of the incubated tissue constructs. The results showed the changes on tissues with training by increasing the mechanical properties and the smooth muscle cells were more oriented with uniformly higher density. However, urea and creatinine permeability did not differ significantly between stimulated and unstimulated tissue constructs. Besides, the computational growth models also exhibited the accurate tendencies of growth of the cells under different external stimuli. Such models may lead to the design of better structural setups for the reconstruction of tubular organs characterized as composite materials such as intestines and arteries.

Posters

The Influence of The Carbonized Rice Husk on Wound Repair Process Of Human Dermal Fibroblasts

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Some previous in vitro studies have demonstrated that carbonized materials can induce cytotoxicity in different cells, whereas several other research groups argued that such materials are not cytotoxic. Furthermore, the influence of carbonized materials on some other important cellular physiological events such as cell adhesion and migration remains mostly unexplored.

In this study, human dermal fibroblasts (NHDF) from primary cultures were used as in vitro models to examine their interactions with carbonized materials in terms of cell viability, adhesion and wound healing ability. The fibroblasts were selected as an abundant cell type most probably contacting with carbonized materials in open wounds and playing a vital role in the wound repair process. The carbonized material based on rice husk (CRH) has been obtained in Combustion Problems Institute in Almaty, Kazakhstan.

Our experiments showed no CRH cytotoxicity on NHDF at moderate doses, though a gradual dose-dependent decline in cell viability has been observed. Also, according to the results, the migration ability of fibroblasts was not impaired by the CRH treatment. These findings may contribute to the development of novel CRH-based medical preparations facilitating wound-healing.

Biocompatibility of Carbonized Rice Husk InRespect Of A Rat Heart Cells Line H9c2

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Growing interest to novel nanostructured carbonized preparations obtained from vegetative raw materials by high-temperature carbonization and their promising performance in medicine and biotechnology urge closer investigation their health-related effects. In particular, studies at the cellular

level could deliver valuable information on their biocompatibility. The objective of this in vitro study was to explore the cytocompatibility-related properties of purified carbonized rice husk (CRH) with respect to cardiomyocytes. Microscopic observations evidenced that CRH caused slight modification in cell shape and in cell count only after >five days of exposure in culture. The effect of CRH bound to cells was tested by reseeding of the previously exposed H9c2 cells. The cells from a CRH-treated sample showed an unaffected ability to proliferate at small concentrations of CRH. The concentrations higher than 0.1 mg/ml slightly prohibited cellular proliferation. However, later the cells subjected to such concentrations continued to grow and recovered in shape and number. This work also demonstrated that the interaction of CRH with cardiac muscle cells in culture neither involves binding to the cell membrane nor induces a short-term toxicity toward H9c2 cells.

New Generation of Hemoglobin Structural Transition Studies: Reversed Phase High-Performance-Liquid-Chromatography

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High performance liquid chromatography (HPLC) is an advanced chromatographic method widely used for detection of human hemoglobin (hHb) variants. Former investigations by G. M. Artmann's group using micropipette aspiration technique, circular dichroism and dynamic light scattering showed the existence of Hb structural transition point at around 37 ^{o}C. According to our current understanding of the mechanisms of this transition, it is related to a non-linear change of the surface hydrophobicity of Hb with temperature. In this study, the method of reversed-phase HPLC was used to detect changes in overall hydrophobicity of Hb-samples by analysis of their retention times.

The influence of different mobile phase compositions on hemoglobin structure was previously tested by recording the absorbance spectra with the Jasco V-550 spectrophotometer and Jasco HPLC using a C4 column. The retention time data were collected for seven temperature steps between 25 °C to 40 °C in eleven repeated independent measurements. Although more measurements need to be done to provide a robust statistical proof, the results showed a mostly linear decrease of retention times with increasing

temperature except a small fluctuation at 37 °C. Thus, our pilot RP-HPLC measurements seemed to support the current Hb-transition model.

Effects of Salts, Nitric Oxide Donors and ATP on Protein Unfolding and Aggregation

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Protein activity regulation by small molecules provides a rapid, flexible and fine-tunable tool of metabolic control and is known to be a key event in cellular signaling pathways. However, biophysical mechanisms of interactions between proteins and low-molecular messengers are poorly understood and studied so far. The effects of small solutes on protein behavior can be studied for instance by examining changes of protein secondary structure, of protein hydrodynamic radius or as well of protein thermal aggregation.

This study aimed at investigating aspects of the impact of the nitric oxide donor spermine NONOate, of adenosine-5'-triphosphate (ATP) and of sodium/potassium on the dynamics of thermal unfolding and aggregation of human hemoglobin (Hb). The effect of those molecules on thermal behavior of Hb was examined by two techniques; 1) The dynamic light scattering technique (DLS) provided data on the protein´s aggregation behavior, and 2) the circular dichroism spectrometry (CD) addressed predominantly molecular unfolding events. Measurements were carried out in the temperature range between 25 °C and 70 °C.

Major obtained results were: 1) Irrespectively of the Na^+/K^+-environment, Hb's unfolding temperature was persistently decreased by spermine NONOate and increased by ATP and 2) mutual effects of ATP and NO were strongly influenced by particular buffer ionic compositions. Moreover, the presence of potassium facilitated a partial unfolding of Hb alpha-helical structures even at room temperature. The obtained data might shed more light on molecular mechanisms involved in the regulation of protein activity by small solutes.

Micropipette Aspiration of Human Erythrocytes in Buffers Having Different Chemical Composition: Influence of Na^+, K^+, ATP and NO

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The remarkable RBC deformability in microvasculature governs the cell's ability to fulfil the various mechanical challenges of circulation and can be altered by a variety of chemical and physical stresses. Understanding of biochemical aspects of the RBCs microrheology is highly interesting from both basic science and clinical point of view. Hemoglobin, being the main constituent of an RBC is mostly responsible for RBC functions and characteristics. Many alterations in the RBC properties are initiated in the Hb molecule, for example, due to binding of low-molecular weight messengers. The molecules like ATP, 2,3-DPG, potassium and sodium ions, nitric oxide NO, CO_2 and probably many others are able directly or potentially modify and control the Hb (and hence RBCs) properties.

Micropipette aspiration is a valuable technique applied to study mechanical behavior of cells and can provide quantitative information about the elasticity and viscosity of the RBCs. We employed the micropipette system and determined various volume compartments of single RBCs in order to investigate the effects of spermine NONOate (NO donor), ATP as well as buffers based on sodium and potassium ions on the elasticity and stability of RBCs at 25 °C.We have found that the RBCs in the K buffer surprisingly could not be trapped by a (1.3±0.2) µm micropipette as they were always passing through. RBCs showed the highest elasticity and resilience in presence of ATP, whereas an NO-donor made RBCs relatively less soft and less resilient.

Detachment of Viable Bacteria form Different Surfaces Using Ultrasound

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Ultrasonic microbiological sampling potentially brings several advantages over conventional swabbing and scrubbing recovery methods but not yet thoroughly studied. Ultrasonic waves cause and distribute cavitation implosions in a liquid medium. Microbubbles formed close to a attached bacteria will undergo symmetric or asymmetric cavitation, causing significant shear forces. The released energies reach and diffuse deep into crevices,

blind holes, and other areas that are inaccessible by other sampling methods. Thus, the recovery of single bacteria and biofilms can be consistent and uniform regardless the complexity and geometry of the part being cleaned.

Because of the mechanisms and intensities involved, the main concern for the ultrasound-aided sampling is the preservation of microbial viability for further analysis. Here, both applied ultrasonic frequency and intensity play an important role. As the frequency increases, the cavitation bubbles and their resulting implosions become more numerous but less energetic. At the same time, the thickness of the barrier layer (the zone near a surface where cavitation cannot occur due to physical constraints in the liquid) is reduced. In other words, higher frequency ultrasonic waves (~40 kHz) produce smaller cavitation bubbles which can form closer to the surface. These considerations are critical for the efficient detachment of microbes from a surface. By adjusting the intensity and the frequency of the applied acoustic field, we were able to quantitatively recover viable cells of *Bacillus subtilis*, *Escherichia coli* and *Micrococcus luteus* from various surfaces.

Search of Extra-terrestrial Life: General Thermodynamic Approach

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Finding appropriate criteria for recognizing, detection and comprehension of extraterrestrial life is one of the “eternal” mind-boggling problems in astrophysics. It is tightly connected with the actual absence of the definition and understanding what life on the earth really is. An intuitive feeling, “an insight” usually allows us to classify something as being alive or dead but there is apparently no universal ultimate rule that would guide us on an alien planet.

Here we assume that the Second Law of Thermodynamics that means that any irreversible process is accompanied with the production of dissipation heat is of universal nature. Living systems possess peculiar enthalpy and entropy dynamics, opposing the classical decay behavior and governing self-organization. E.S. Bauer (1890-1938) argued that all known life functions (growth, reproduction, metabolism, excitability, death) are barely manifestations of more deep and universal life properties that reflect thermodynamic uniqueness of living organisms. What underlies all vital processes is that living systems are open, organized, thermodynamic systems, always possessing excess of energy and for which the principle of minimum energy dissipation in a steady state is true. The Bauer’s (1) principle of the living matter's stable non-equilibrium (“Only living systems never reach

equilibrium, for they constantly work against stability"); (2) principle of minimum energy dissipation and (3) the law of replenishment of "structural energy" together open interesting opportunities in recognition of totally strange life forms.

These ideas can be implemented, for example, by the analysis of emergence and disappearance of energy/matter gradients and corresponding fluxes existing in a given system. The practical measurements can rely on the fact that for all known living organisms the emergence and disappearance of any kinds of gradients causes discrepancy between the data of the direct and indirect calorimetry, i.e. positive or negative bound dissipation function must appear.

"BacHarvester" – a Novel Tool for Sonication-Aided Microbiological Sampling

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Various types of surfaces used today in biotechnological and food industry, healthcare facilities and other epidemiologically relevant fields are subject to continuous contamination by microorganisms. Regular sampling and adequate cleaning of such surfaces mainly composed of metal, plastic and glass represent the main preventive approach to control the hygiene of medical and food products.

The method of recovering microorganisms from different solid surfaces is critical for reliability and objectivity of sampling and microbiological risk assessment. Today, sampling by cotton or rayon swabs is undeservedly considered the "gold standard". In reality, the swabbing methods suffer from numerous drawbacks. Therefore, efficient, reliable quick and cheap sampling methods still have to be defined and standardized for better control of microbiological hazardous events, especially for porous and irregular materials.

Here we introduce a concept and a prototype of a novel device called "BacHarvester" for a high-throughput microbiological sampling using ultrasound waves. The pilot experiments have demonstrated the excelling performance of the "BacHarvester" as compared to the swab-based standard protocol.

Isolation and Identification of Viroid RNA from *Solanum jasminoides*

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Viroids are infectious pathogenic RNA-genomic agents that have been detected in many economically important plants and are notoriously responsible for significant economic losses. Although many basic features of viroids as sub-cellular pathogens are already understood, there is still no satisfying treatment for viroid diseases. Recently, outbreaks of viroid diseases were detected in ornamental plants belonging to the family *Solanaceae*.

An important goal in the development of an efficient anti-viroid treatment is an elaboration of reliable, fast and safe protocol for measurement of viroid-RNA concentration in the plants. Our pilot experiments were aimed to establishing and improvement of protocols for detection and analysis of the viroid RNA. The first step was optimization of homogenization of the *Solanum jasminoides* cells for subsequent RNA extraction. Afterwards, the RNA extraction with four different commercially available kits was performed. Using reverse transcription, the complementary cDNA of RNA was synthesized in order to allow a consistent detection of viroids using real-time PCR.

Our experiments have shown that the applied plant tissue homogenization methods have provided satisfactory results. The comparison of the RNA-extraction kits has shown that only the MasterPure kit (Biozym Co.) has provided satisfactory RNA-yield. Yet,the currently used PCR protocol requires further optimization in order to reach the desired level of specificity and sensitivity.

Cartilage Mimicked Structures for Chondrogenic Stem Cell Differentiation

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In this study, micro-environment of cartilage tissue was mimicked by adjusting the surface topography, stiffness and chemistry of polydimethylsiloxane (PDMS) which is a biocompatible synthetic elastomeric polymer. PDMS substrates were synthesized with different stiffness between 2.13-0.150 MPa and 0.56-0.06 MPa which were in the range of healthy human articular cartilage's stiffness (0.45-0.80 MPa) and measured by nanoindendation. A template mimicking the collagen type II bundle alignment, geometry and size of healthy human cartilage tissue were prepared (A= 100, 150, 200 µm; B= 30, 40, 50 µm; C= 30, 40, 50 µm) by photolithography. PDMS substrates with desired patterns were prepared by soft lithography. In order to mimic the chemistry of the cartilage tissue micro-environment, PDMS substrates were modified with amino acid conjugated self-assembled molecules and also with type II collagen. Stiffness of PDMS substrates were analyzed with nanoindentation measurements and chemical modifications of substrates were confirmed by using X-ray Photoelectron Spectroscopy and contact angle measurements. According to the characterization results, prepared substrates with cartilage like stiffness, chemistry and topography are possible cell substrates for cartilage tissue engineering and preliminary studies were done using bone marrow derived mesenchymal stem cells.

Dysbacteriosis in Rats Induced by Small Concentrations of Lead (II)

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Soluble lead Pb(II) is one of the oldest known and most widely studied occupational and environmental toxins. Decades of use of lead-based paints and leaded gasoline have resulted in widespread contamination of the environment with lead, which enters humans and animals predominantly orally. There is no apparent threshold for lead toxicity, suggesting that several different pathological mechanisms are involved. The fact that intestinal epithelium and intestinal microflora are usually subjected to the highest Pb(II) concentrations in the body implies the importance of detailed study of lead impact in this particular context. The influence of sub-chronic lead exposure on intestinal microbial community and its relationships with gut epithelium are mainly underestimated and poorly studied.

The aim of the present study was to investigate the influence of lead at different doses on the structure of intestinal microbial community in rat and its relationships to intestinal epithelium *in vitro*. Several conclusions can be drawn from the obtained data. First, the oral expose of human beings and animals to low Pb concentrations deserves more rapt attention. Lead doses that are much lower than those causing visible harmful effects on cell culture or on the level of the whole body, induce significant changes in intestinal microflora. The presence of Pb somehow creates selective advantages for pathological lactose-negative coli-forms and thus contributes into dysbacteriosis development. Second, the adhesion of bacteria to intestinal epithelium can be revealed as a possible clue to lead-induced dysbacteriosis. Third, the results could be possibly extrapolated to human beings, opening the opportunity to understand some mysterious cases of persisting dysbacteriosis as a result of latent Pb-intoxication. This, in turn, suggests a probiotic treatment as a promising therapy for lead-exposed patients on one hand and possible success of Pb-scavenging therapy for some patients with dysbacteriosis on the other hand.

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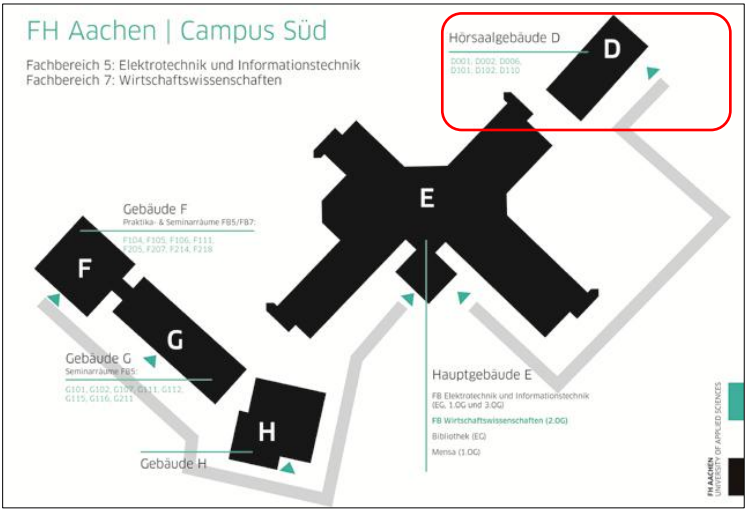
Location Plan: Campus FH Aachen, Eupener Straße 70



Registration:

Lecture auditorium D (Hörsaalgebäude D)

Thursday, 11.09.2014: 18:00 – 19:00

Friday, 12.09.2014: 7:30 – 17:15

Sessions:

Lecture auditorium D (Hörsaalgebäude D)

Poster exhibition:

Lecture auditorium D (see information on site)

Hanging of posters: Friday, 12.09.2014, 07:30 - 09:00 am

Cafeteria for lunch:

Main building E (Hauptgebäude E)

Arriving from the motorway (see overview on the next page)

If you arrived from the Netherlands, Düsseldorf or Cologne: at the Autobahn interchange "Aachen" take the A 44 in direction to Belgium until the exit "Lichtenbusch" where you turn right onto the "Monschauer Straße".

If you arrived from Belgium on the A 44 take the exit "Lichtenbusch" and turn left onto the Monschauer Straße.

Follow the Monschauer Straße until the crossing "Adenauerallee / Robert-Schumann Straße / Siegelallee. Turn left onto the "Siegelallee" and on the next crossing right onto the "Salierallee", which you follow until the crossing "Weißhausstraße / Eupener Straße". Turn right into the Eupener Straße and you will find the entrance to the Fachhochschul-area after 200m on the left (house nr. 70).

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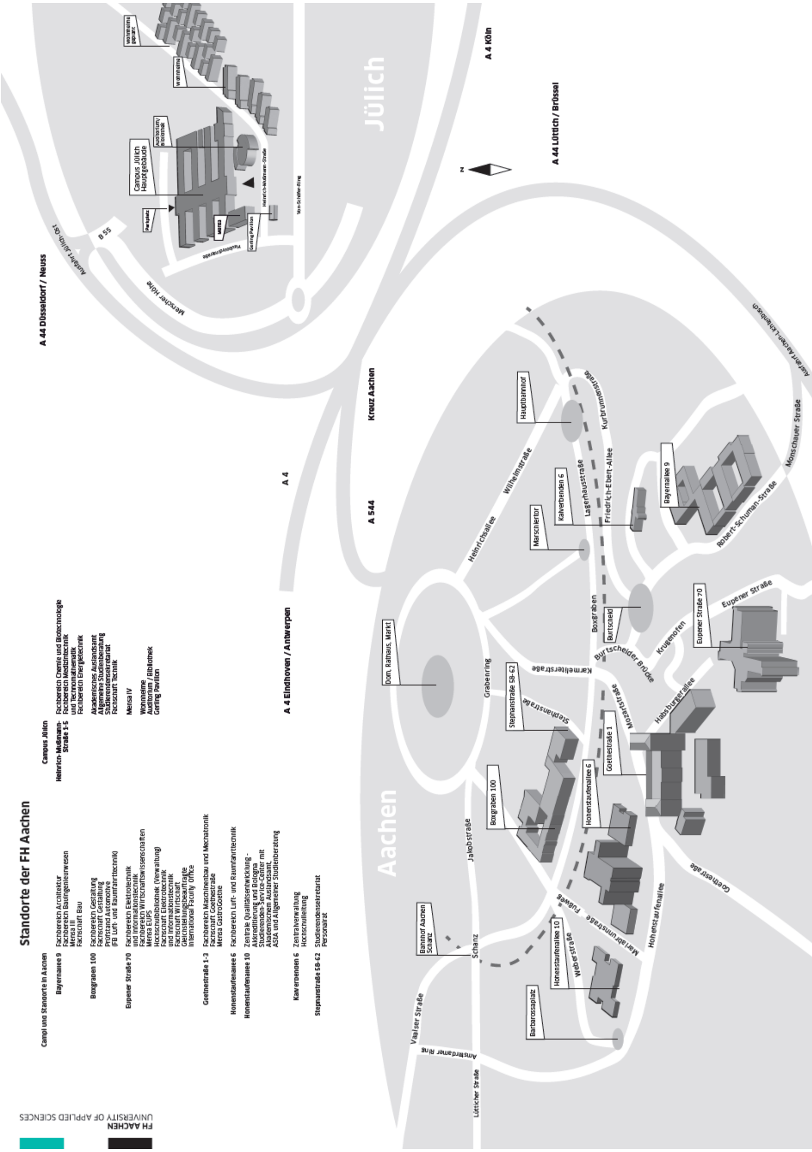
Ronheider Weg**,** Lines: 7, 14, 27, 37, 53, 77

Overview FH Aachen



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