



**Joint  
KMM-VIN / ViCEM / ESB  
cross-disciplinary workshop on**

# **Biomedical and bioinspired materials and structures: a cross-disciplinary approach**

**combining the  
9th KMM-VIN Industrial Workshop  
Biennial ViCEM Meeting  
Austrian Chapter Meeting of ESB**

## **PROGRAMME & BOOK OF ABSTRACTS**

**September 22-23, 2022  
Vienna, Austria**

## About the Organizers

**KMM-VIN AISBL** ([www.kmm-vin.eu](http://www.kmm-vin.eu)) is an international non-profit association that creates conditions for conducting joint research on advanced materials. It offers mobility programme for young researchers, courses and trainings on materials for Transport, Energy and Biomedical sectors.

**TU Wien** ([www.tuwien.ac.at](http://www.tuwien.ac.at)) is one of Europe's leaders in science and technology-related research and education. As part of TU Wien, the Institute for Mechanics of Materials and Structures (**IMWS**) ([www.imws.tuwien.ac.at](http://www.imws.tuwien.ac.at)) is at the international forefront in the broad field of mechanics-driven engineering sciences, delivering fundamental knowledge and technology towards the relief of our challenged planet through sustainable building materials and technologies, circular economy, and health. We teach the next generation of civil, material, and biomedical engineers in a seamless education path from essential topics of continuum mechanics and strength of materials, via structural engineering, to timber construction, green building, and computational biomedicine.

**ViCEM** ([www.vicem.at](http://www.vicem.at)), the Vienna Center for Engineering in Medicine is a joint cooperation center of TU Wien and Medical University of Vienna. This center is entitled both to research and teaching at a top international level, and to a leading role in the national context - as a competent partner for the public sector and the industry. The cooperation partners look back on a decade-long tradition of joint research activities at the research group level. These activities have triggered joint teaching activities, such as the master study for biomedical engineering at TU Wien.

**ESB-AC**, the Austrian chapter of the European Society of Biomechanics ([www.esbiomech.org/affiliated-societies/esb-national-chapters/austrian-national-chapter/](http://www.esbiomech.org/affiliated-societies/esb-national-chapters/austrian-national-chapter/)), represents all ESB members who are affiliated with an organization in Austria. The vibrant Austrian biomechanics community spreads over almost all Austrian universities and research institutions.

## Objectives

This workshop is the ninth in the series of industrially oriented workshops organized by KMM-VIN in collaboration with leading research centres and industries. Presenting the most recent advances in material science and technology, the KMM-VIN workshops provide a unique opportunity for starting and/or intensifying the communication and cooperation between scientists and engineers, aiming at material-driven transformation of various industrial sectors.

In order to broaden the effect of the event, this time, KMM-VIN joined forces with ViCEM, the cooperation center linking engineering with the biomedical world; and with the Austrian Chapter of the European Society of Biomechanics, which encourages, on a general level, research, disseminate knowledge and promote progress in Biomechanics.

## Workshop Chairs

Christian HELLMICH (TU Wien, Austria)

Katarzyna KOWALCZYK-GAJEWSKA (IPPT PAN, Poland)

Andrés DÍAZ LANTADA (Universidad Politécnica de Madrid, Spain)

Dieter PAHR (Karl Landsteiner University of Health Sciences & TU Wien, Austria)

Siegfried TRATTNIG (Medical University of Vienna, Austria)

# AGENDA

## Thursday, September 22, 2022

09:00-10:00 **Registration**

10:00-10:10 **Workshop Opening**

10:10-10:40 **Keynote Lecture 1**

Chair: **Christian Hellmich**

**Prevention and treatment of aortic aneurysms using computational biomechanics combined with cell mechanobiology**

**S. Avril**

10:40-12:00 **Mathematical modeling, experimentation, and design of biomedical and bioinspired materials and structures**

Chair: **Francesco Moscato**

10:40-11:00

**Investigations on the rheology and deagglomeration of digital light processing based vat polymerisation of Si<sub>3</sub>N<sub>4</sub>-slurries containing different dispersing additives**

**A. L. Kutsch, C. Hofstetter, S. Nistler, S. Baudis, M. Schwentenwein, J. Stampfl**

11:00-11:20

**Permanent damage on implanted bone screws occurs significantly earlier than the apparent failure**

**J. D. Silva Henao, D. H. Pahr, A. G. Reisinger**

11:20-11:40

**The BeneFit socket, an adjustable temporary socket for a transradial prosthesis**

**B. L. Baumgartner, I. Vujaklija, E. Kaniusas, O. Aszmann, A. Sturma**

11:40-12:00

**Magnesium implants in rats: an analytical multiscale model**

**L. Pircher, T. Grünewald, H. Lichtenegger, C. Hellmich**

12:00-12:20 **Poster presentations**

Chair: **Dieter Pahr**

12:00-12:03

**Effect of DLC coating of growth-guidance system implants on changes in mechanical and kinematic properties of the spine**

**M. Žak, S. Szotek, K. Szkoda- Poliszuk, J. Filipiak, M. Wrzosek, K. Kottowski, P. Menartowicz, C. Pezowicz**

12:03-12:06

**Finite element analysis of titanium-based hip implant modified surfaces**

**A. Vulović, F. G. Warchomicka, F. Pixner, N. Filipović**

12:06-12:09

**From 2D ultrasound images to 3D patient-specific models of atherosclerotic carotid bifurcation**

**T. Djukic, S. Tomasevic, B. Arsic, M. Anic, B. Gakovic, N. Filipovic**

12:09-12:12	<p><b>Methods of evaluating mechanical parameters and the stability of the cervical interbody fusion cage</b>  <b>M. Żak, A. Nikodem, C. Pezowicz</b></p>
12:12-12:15	<p><b>The effect of the addition of bioglass, Zn and graphene on the resorption rate of PCL scaffolds after 18 months of incubation in PBS solution</b>  <b>A. Nikodem, A. Kurowska, I. Rajzer</b></p>
12:15-12:18	<p><b>The potential of mulberry and non-mulberry silk fibroin bioinks for meniscus regeneration by 3D-bioprinting</b>  <b>J. Fritz, V. Jeyakumar, A.-C. Moser, C. Bauer, S. Nehrer</b></p>
12:18-12:21	<p><b>Use of plasma electrolytic oxidation on electron beam structured surface of titanium alloy</b>  <b>H. Mora-Sanchez, F. Pixner, R. Buzolin, M. Mohedano, R. Arrabal, F. G. Warchomicka, E. Matykina</b></p>
12:21-13:30	<b>Lunch Break &amp; Poster Discussion</b>
13:30-14:00	<p><b>Keynote Lecture 2</b>  Chair: Katarzyna Kowalczyk-Gajewska</p>
13:30-14:00	<p><b>Mathematical modeling of innate immune response to viral infection</b>  <b>F. Grabowski, M. Kochanczyk, W. Prus, Z. Korwek, M. Czerkies, T. Lipniacki</b></p>
14:00-15:40	<p><b>Mathematical modeling, experimentation, and design of biomedical and bioinspired materials and structures</b>  Chair: Stéphane Avril</p>
14:00-14:20	<p><b>Conducting polymers in medical applications: cardiovascular stents, biosensors, neural electrodes</b>  <b>K. Cysewska, P. Jasiński</b></p>
14:20-14:40	<p><b>Lattice structures for high performance biomimetic implants</b>  <b>E. Kornfellner, S. Reininger, S. Geier, M. Schwentenwein, S. Scheiner, F. Moscato</b></p>
14:40-15:00	<p><b>Natural biomolecules for surface functionalization and coating of titanium alloys</b>  <b>S. Spriano, E. Vernè, S. Ferraris, M. Miola, F. Baino, M. Lallukka, F. Gamna</b></p>
15:00-15:20	<p><b>Development of individual rib implants using thorax simulations and 3D printing technology</b>  <b>A. Gradischar, C. Lebschy, W. Krach, M. Krall, M. Fediuk, A. Gieringer, D. Auinger, F. Smolle-Jüttner, N. Hammer, B. Beyer, U. Schäfer</b></p>
15:20-15:40	<p><b>Machine learning based prediction of layer-by-layer coating thickness</b>  <b>T. Sustersic, V. Gribova, M. Nikolic, P. Lavale, N. Filipovic, N. E. Vrana</b></p>

15:40-16:10	<b>Coffee Break &amp; Poster Discussion</b>
16:10-16:40	<p><b>Keynote Lecture 3</b> Chair: <b>Andrés Díaz Lantada</b></p> <p><b>Additive manufacturing of advanced alloys for biodegradable and smart implants</b> <b>J. Molina-Aldareguia, L. Martín-Alonso, F. Sket, M. Li, M. Echeverry-Rendón, A. Kopp, J. LLorca</b></p>
16:40-18:20	<p><b>Manufacturing hierarchical biomaterials</b> Chair: <b>Michal Basista</b></p> <p>16:40-17:00 <b>Impact of 3d-printed microstructured surfaces on bacterial adhesion and growth</b> <b>S. Nilsson Zagiczek, C. Grasl, M. Weiss-Tessbach, M. Kussmann, D. Moser, F. Moscato, H. Schima</b></p> <p>17:00-17:20 <b>Electrophoretic deposition of bioinspired nacre-like chitosan/hydroxyapatite coating</b> <b>F. E. Baştan, A. R. Boccaccini</b></p> <p>17:20-17:40 <b>Individualized jawbone replacements by combining additive manufacturing with Freeze Foaming</b> <b>T. Moritz, M. Ahlhelm, E. Schwarzer-Fischer</b></p> <p>17:40-18:00 <b>Bioinspired individualized implants made of silicon nitride via Ceramic Additive Manufacturing by Vat Photopolymerization (CerAM VPP)</b> <b>E. Schwarzer-Fischer, E. Zschippang, U. Scheithauer</b></p> <p>18:00-18:20 <b>Tri-lineage differentiation potential of BMSCs grown on hiPSC-engineered extracellular matrix</b> <b>D. Hanetseder, V. Hruschka, H. Redl, D. Marolt Presen</b></p>
19:30-22:00	<p><b>Workshop Dinner</b> Location: <b>SalmBräu</b>, Rennweg 8, 1030 Vienna</p>

## Friday, September 23, 2022

09:00-09:30 **Keynote Lecture 4**

Chair: **Dieter Pahr**

**Dielectric elastomers - from experiments and modelling towards simulation based design of smart devices**

**A. Menzel**

09:30-11:10 **Microstructure-property relationship for hierarchical materials**

Chair: **Tomasz Lipniacki**

09:30-09:50

**Inverse bone remodeling allows for prediction of physiological peak joint loads using clinically feasible homogenized finite element models**

**S. Bachmann, D. H. Pahr, A. Synek**

09:50-10:10

**Accounting for space distribution of particles in two-phase particulate composites**

**K. Bieniek, M. Majewski, K. Kowalczyk-Gajewska**

10:10-10:30

**Computational fluid dynamics study of the influence of geometry and flow rate on mass transport in 3D scaffolds**

**T. Baumgartner, M. Bösenhofer, O. Guillaume, A. Ovsianikov, M. Harasek, M. Gföhler**

10:30-10:50

**Multiscale mechanics of a cementitious biomaterial: biodentine**

**P. Dohnalik, B. Pichler, G. Richard, C. Hellmich**

10:50-11:10

**Time-dependent mechanics of individual collagen fibrils and electrospun fibres**

**M. Nalbach, A. Sensini, N. Motoi, M. Rufin, O. G. Andriotis, A. Zucchelli, G. Schitter, L. Cristofolini, P. J. Thurner**

11:10-11:40 **Coffee Break & Poster Discussion**

11:40-13:20	<b>Medical perspectives and demands concerning biomedical and bio inspired materials and structures</b> Chair: <b>Christian Hellmich</b>
11:40-12:00	<b>Triaxial electrospun fibers for prolonged drug release</b> <u>S. Tabakoglu, D. Kołbuk, P. Sajkiewicz</u>
12:00-12:20	<b>Synthesis and characterization of drug loaded hybrid mesoporous silica particles for biomedical applications</b> <u>A. Witecka, G. Rydzek, C. Gerardin</u>
12:20-12:40	<b>Development and characterization of zein-based coatings incorporating fluoride- and copper-doped bioactive glass on titanium for biomedical applications</b> <u>Z. Hadzhieva, K. Cholewa-Kowalska, T. Moskalewicz, I. Dlouhy, A. R. Boccaccini</u>
12:40-13:00	<b>Alteration of vimentin cytoskeleton in senescent cells</b> <u>R. Khoshnevisan</u>
13:00-13:20	<b>Auricular cartilage scaffolds: an innovative tool to study cellular infiltration by glycosaminoglycans removal and altered stiffness</b> <u>I. Casado Losada, I. Hernández Lozano, X. Monforte, C. Schneider, B. Schädli, A. Teuschl, S. Nürnberger</u>
13:20-13:50	<b>Keynote Lecture 5</b> Chair: <b>Siegfried Trattinig</b>
	<b>Trends in the personalized design and manufacture of next generation implants</b> <u>F. Moscato</u>
13:50-14:00	<b>Workshop Closing</b>
14:00-15:00	<b>Lunch &amp; Poster Discussion</b>

# ABSTRACTS

## Keynote Lectures

### Prevention and treatment of aortic aneurysms using computational biomechanics combined with cell mechanobiology

**S. Avril**

Mines Saint-Étienne, France

Ascending thoracic aortic aneurysm (ATAA) is a life-threatening cardiovascular disease, leading to weakening of the aortic wall and permanent dilation. ATAA affects approximately 10 out of 100,000 persons per year in the general population, and this disease is associated to high risk of mortality and morbidity. The degeneration of the arterial wall at the basis of ATAA is a complex multifactorial process. Individual genetic, biological or hemodynamic factors are inadequate to explain the heterogeneity of ATAA development/progression mechanisms, thus stimulating the analysis of their complex interplay. We established a methodology to quantify non-invasively local stiffness properties of ATAA using electrocardiographic-gated computed tomography (ECG-gated CT) scans. We showed strong relationship between the extensional stiffness and the rupture stretch of the aortic tissue, supported by biomechanical explanations. Then we discovered the interrelationship between the obtained local stiffness with other established markers of aortic function such as intravascular flow structures. The observed interrelationship corroborate computational predictions of ATAA progression coupling hemodynamics with mechanobiology after hemodynamic insult. Recently, we eventually related these results to the existence of a specific smooth muscle cell phenotype found in ATAA, exhibiting stronger traction forces and thicker morphologies.

### Mathematical modeling of innate immune response to viral infection

**T. Lipniacki**

IPPT PAN, Poland

Recognition of viral RNA initiates a signaling cascade culminating in synthesis of interferons (IFNs). Secreted IFNs, by activation of transcription factors of STAT family in surrounding cells, prompt them to prepare for viral infection. Viruses, in turn, convey non-structural proteins to impede the innate immune response. Based on results obtained using single-cell techniques, we proposed an agent (single cell)-based, stochastic, computational model and used it to explain how an infected population of cells can stratify into distinct subpopulations. The winning cells, in response to viral RNA, produce  $IFN\beta$  (warning yet not infected cells), losing cells express viral proteins that inhibit innate immune signaling. The proposed model reproduces the experimentally observed complex spatial patterns of respiratory syncytial virus (RSV) spread and dichotomous cell responses.

### Additive manufacturing of advanced alloys for biodegradable and smart implants

**J. Molina-Aldareguia<sup>1,2</sup>, L. Martín-Alonso<sup>2</sup>, F. Sket<sup>2</sup>, M. Li<sup>2</sup>, M. Echeverry-Rendón<sup>2</sup>, A. Kopp<sup>3</sup>, J. LLorca<sup>1,2</sup>**

<sup>1</sup>Universidad Politécnica de Madrid, Spain; <sup>2</sup>IMDEA Materials, Spain; <sup>3</sup>Meotec GmbH & Co., Germany

Porous metallic scaffolds and devices manufactured by laser powder bed fusion (LPBF) are promising structures for tissue regeneration as they allow tissue ingrowth and permit body fluid transportation. The use of metals provides a substantial load-bearing capability, while the design envelop allowed by 3D printing technologies opens the possibility to design shape-morphing implants that can be implanted using less invasive procedures and that then undergo predesigned shape changes, leading to tissue expansion.

In this contribution, several design concepts will be shown using shape memory alloys and biodegradable metals that take advantage of 3D printing technologies. As an example, the potential use of porous Mg scaffolds manufactured by LPBF for bone regeneration will be addressed. Mg is a biodegradable metal and the mechanical properties are similar to those of bone, so it constitutes a perfect example of a metallic implant that can induce bone regeneration, while it is fully re-absorbed by the human body so the need for a second surgery for implant removal is prevented.

This application requires detailed knowledge of the degradation process and the load-bearing capability of the Mg scaffolds during degradation. This is particularly important in the case of scaffolds produced by additive manufacturing in which surface defects and porosity may lead to early failure of the implant. For

this, in situ synchrotron X-ray microtomography studies of the degradation process of 3D printed Mg scaffolds are particularly valuable, as will be shown in this presentation.

## Dielectric elastomers - from experiments and modelling towards simulation based design of smart devices

### **A. Menzel**

TU Dortmund University, Germany

Electroactive materials are most attractive for the development and design of smart systems and devices such as actuators and sensors. Typical examples are dielectric elastomers undergoing large strain deformations. Changes in shape can be induced by the action of an electric field, and vice versa. Electroactive polymers facilitate flexible and lightweight smart devices such as artificial muscles (stronger and faster than biological muscles relative to their weight), tunable lenses, acoustic devices and energy harvesting systems, to name but a few.

This contribution shall focus on related modelling and simulation approaches to predict the response of electroactive polymers. Different fields of application are considered, starting with experimental investigations of the time dependent behaviour of a VHB 4910 based electroactive polymer. Of particular interest are aspects of form finding, control and visualisation of electromechanical coupling properties which, as a long term goal, may contribute to the improved design of electroactive polymer based devices and systems.

## Trends in the personalized design and manufacture of next generation implants

### **F. Moscato<sup>1,2,3</sup>**

<sup>1</sup>Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria; <sup>2</sup>Ludwig Boltzmann Institute for Cardiovascular Research, Austria; <sup>3</sup>Austrian Cluster for Tissue Regeneration, Austria

New tools lead to progress, but inevitably also to new challenges.

With the development of advanced Additive Manufacturing (AM) processes and materials, recent years have seen a steady increase in their application in medicine, especially in personalized medicine. The design and manufacturing freedom typical of AM, combined with increasing digitalization of these processes, enables the development of medical treatments that are highly tailored to the needs of the patient. Pre-operative planning tools and models, patient-specific surgical instruments and devices, and implantable prostheses customized for the individual patient have been introduced into medical treatment. In parallel, conventional tissue engineering has also benefited from AM with the establishment of multicellular tissue-like structures reproducing, at small scale, even simple biological functions.

The design of next-generation implants has evolved in recent years from implants fulfilling basic functions (e.g. biomechanics) to a more integrated design that perfectly matches patient and tissue anatomy, biomechanics and electrophysiology at the macroscopic and microscopic cellular level, while supporting tissue regeneration. With these advances, new challenges inevitably arise as new methodologies need to be developed to guide design within this wider range of possibilities now available.

This presentation will address trends, current advances and challenges in the design and manufacture of next generation implants.

## Oral Presentations

### Investigations on the rheology and deagglomeration of digital light processing based vat polymerisation of Si<sub>3</sub>N<sub>4</sub>-slurries containing different dispersing additives

A. L. Kutsch<sup>1,4</sup>, C. Hofstetter<sup>3,4</sup>, S. Nistler<sup>1,4</sup>, S. Baudis<sup>2,4</sup>, M. Schwentenwein<sup>3,4</sup>, J. Stampfl<sup>1,4</sup>

<sup>1</sup>TU Wien, Institute of Materials Science and Technology, Austria; <sup>2</sup>TU Wien, Institute of Applied Synthetic Chemistry, Austria;

<sup>3</sup>Lithoz GmbH, Austria; <sup>4</sup>Christian Doppler Laboratory for Advanced Polymers for Biomaterials and 3D Printing

Silicon nitride (Si<sub>3</sub>N<sub>4</sub>) is a non-oxide ceramic with excellent material properties such as high toughness and strength, high-temperature stability, and good wear and chemical resistance. Due to its good osseointegration and stimulated cell differentiation, as well as its osteoblastic activity and anti-infective behaviour, it can also be used as a medical implant. Its excellent biocompatibility and simultaneous mechanical strength are superior to calcium phosphates and make Si<sub>3</sub>N<sub>4</sub> very attractive as scaffolds for bone regeneration in biomedical engineering. [1]

Digital light processing-based vat polymerization (DLP) is an additive manufacturing technology and provides the possibility to produce complex-shaped, dense ceramic structures with high resolution. The ceramic component is mixed with a photosensitive formula to form a ceramic-filled resin (slurry) that is cured layer-by-layer with layer thicknesses between 10 and 100 µm. The structured body, the so-called green body, must then be further processed to remove the organic components by evaporation or decomposition during debinding and densification by fusing the ceramic particles during sintering.

In contrast to oxide ceramics, Si<sub>3</sub>N<sub>4</sub> as a non-oxide ceramic is more challenging to process as it absorbs and scatters light due to its dark colour and high refractive index. Therefore, properties such as curing and penetration depth, as well as critical energy of Si<sub>3</sub>N<sub>4</sub> slurries must be examined and tuned. Further requirements for good processability of a slurry are deagglomeration and stability, as well as suitable rheological properties. The agglomerates must not be larger than the layer thickness. Both, the agglomerates and the rheological properties can be influenced by dispersants. For this reason, we have investigated the effect of different polymeric dispersants in a 39 vol% Si<sub>3</sub>N<sub>4</sub> slurry.

[1] A. A. Altun, T. Prochaska, T. Konegger, und M. Schwentenwein, „Dense, Strong, and Precise Silicon Nitride-Based Ceramic Parts by Lithography-Based Ceramic Manufacturing“, 2020

### Permanent damage on implanted bone screws occurs significantly earlier than the apparent failure

J. D. Silva Henao<sup>1,2</sup>, D. H. Pahr<sup>1,2</sup>, A. G. Reisinger<sup>1,2</sup>

<sup>1</sup>Karl Landsteiner University of Health Sciences, Austria; <sup>2</sup>Technische Universität Wien, Austria

*Introduction:* Primary implant stability is critical for osseointegration and subsequent implant success. Small displacements on the screw/bone interface are necessary for implant success, however, larger displacements can propagate cracks and break anchorage points which causes the screw to fail. Limited information is available on the progressive degradation of stability of an implanted bone screw since most published research is based on monotonic, quasi-static loading [1]. This study aims to address this gap in knowledge.

*Methods:* A total of 100 implanted trabecular screws were tested using multi-axial loading test set-up. Screws were loaded in cycles with the applied force increasing 1N in each load cycle. In every load cycle, Peak forces, displacements, and stiffness degradation (calculated in the loading half of the cycle) were recorded.

*Results:* The stiffness degradation vs displacement results show a total displacement at the point of failure between 0.3 and 0.4 mm while an initial stiffness reduction close to 40%. It is also shown that at a displacement of ~0.1 mm, the initial stiffness of every sample had degraded by 20% (or more) meaning that half of the allowable degradation occurred in the first 25-30% of the total displacement.

*Discussion:* Other studies on screw overloading [1] suggests similar results to our concerning initial stiffness degradation at the end of the loading cycle. Our results also show that the initial stiffness degrades faster with relatively small deformations suggesting that the failure point of an implanted screw might occur before the common failure definition (pull-out force, for example). These results are of great significance since primary implant stability is better explained by the stiffness of the construct than by its failure point.

[1] B. Voumard et.al., “Peroperative estimation of bone quality and primary dental implant stability,” Journal of the mechanical behavior of biomedical materials, vol. 92, pp. 24–32

## The BeneFit socket, an adjustable temporary socket for a transradial prosthesis

**B. L. Baumgartner<sup>1</sup>, I. Vujaklija<sup>2</sup>, E. Kaniusas<sup>3</sup>, O. Aszmann<sup>1</sup>, A. Sturma<sup>1,4</sup>**

<sup>1</sup>Medical University of Vienna, Austria; <sup>2</sup>Aalto University, Helsinki, Finland; <sup>3</sup>Vienna University of Technology, Austria; <sup>4</sup>University of Applied Sciences FH Campus Wien, Austria

A prosthetic limb aims to support its user by restoring missing functionality. The acceptance of a prosthesis is highly influenced by the timely fitting as the timeframe between amputation and prosthetic limb restoration is crucial. A “Golden Period”, the first month after the amputation, has been identified as the optimal time when an upper-limb prosthesis should be fitted to an amputee in order to maximise their chances for a fast and successful return to their daily life.

Unfortunately, in most healthcare systems this time window is surpassed. Reasons for this inefficiency can be many, such as administrative hurdles or the many steps necessary in conventional socket fabrication, but the case is made ever more complex due to the fact that the design of each prosthetic socket has to be personally customized to fit an individual amputee. All the more the residual limb often changes its shape in the first weeks after the amputation. To better capitalize on the “Golden Period” and allow for early prosthetic training, we propose an adaptable and versatile temporary transradial socket design capable of multidimensional adjustments and easy user fitting for below elbow amputees.

A bone structure inspired design is 3D printed and assembled as to host all relevant myoelectric prosthetic hand components in a wearable prototype. This prototype, called the BeneFit socket, was evaluated in a monocentric, non-interventional explorative study with both experts and users.

The investigation shows that the proposed design is able to appropriately accommodate its diameter and length to user needs. Moreover, according to the conducted survey, it is perceived as satisfactory with respect to both user needs and expectations of the experts. While promising, further improvements towards even more versatile and robust design are needed before wider clinical application.

## Magnesium implants in mice: an analytical multiscale model

**L. Pircher<sup>1</sup>, T. Grünewald<sup>2</sup>, H. Lichtenegger<sup>3</sup>, C. Hellmich<sup>1</sup>**

<sup>1</sup>Vienna University of Technology, Austria; <sup>2</sup>Institut Fresnel, Marseille, France; <sup>3</sup>BOKU University, Austria

Magnesium implants appear as an interesting innovative solution in orthopedics, as they combine mechanical stability with the ability to dissolve over a several months period, giving way to newly grown mechanically stable bone tissue. We investigate pin shaped Mg-implants in femurs of rats, which we model mathematically, as a system of intersecting cylinders onto which a higher-order 3D-analytical beam theory is applied. The latter model is mapped onto a set of experimental data (3D-small angle x-ray diffraction tensor tomographies, computed tomography [1]), by establishing equivalence, in terms of volume-inertia properties, of the simple geometrical shapes associated with the analytical beam model, and the imaging data representing the actual anatomy. First result suggests correlation of principal stress directions and directions obtained from 3D small angle X-ray tensor tomography - underlining the role of mechanical forces driving the micro-morphology of bone tissue.

[1] M. Liebi, V. Lutz-Bueno, M. Guizar-Sicairos, B. M. Schönbauer, J. Eichler, E. Martinelli, J. F. Löffler, A. Weinberg, H. Lichtenegger, and T. A. Grünewald. “3D nanoscale analysis of bone healing around degrading Mg implants studied by X-ray scattering tensor tomography”. In: (2020). doi: 10.1101/2020.11.09.375253.

## Conducting polymers in medical applications: cardiovascular stents, biosensors, neural electrodes

**K. Cysewska, P. Jasiński**

Gdańsk University of Technology, Laboratory of Functional Materials, Poland

Recently, conducting polymers (CPs) have become promising coating materials in different medical applications. The principal property of conducting polymers is their metallic-like conductivity due to the conjugated double bond in their backbone. Besides interesting electronic properties, CPs reveal many other attractive characteristics including ion-transport, high biocompatibility, electrode effects allied to polymeric physical properties, or reversible switch between insulating and conducting forms. Another significant advantage of CPs is their processability. They can be synthesized on the conducting surfaces by electrodeposition. This process allows for the precise and controllable deposition of the coating, for example, onto a stent, leads to the formation of the coating with high adhesion to the metallic surface, allows incorporation of drug molecules into the coating in a one-step process, while the degradation and drug release rate could be tailored by deposition parameters. Because of the significant advantages of CPs, they began to be used commercially as an efficient anti-corrosive coating, smart active layers in bioelectronics, scaffolds for drug reservoirs, and more. Currently, the scientific work in our laboratory is

focused on the use of CP in three main applications: cardiovascular stent, biosensor, and neural electrode. The presentation will show a cross-section of the promising results and the possibilities of cooperation with the industry in these specific areas. The presentation will answer the following specific questions: is it possible to tailor the degradation rate of active metals by CP coatings? Is it possible to use CP as an efficient drug reservoir without any external electrical stimulation? Or whether measurement conditions have a significant influence on the properties of the electrical interface of the CP electrode for neural stimulation.

(The work was supported by National Science Centre (NCN), Poland: Sonata grant based on the decision 2021/43/D/ST7/01362. K. Cysewska acknowledges the Polish Ministry of Education and Science for stipend)

## Lattice structures for high performance biomimetic implants

**E. Kornfellner<sup>1</sup>, S. Reininger<sup>1</sup>, S. Geier<sup>2</sup>, M. Schwentenwein<sup>2</sup>, S. Scheiner<sup>3</sup>, F. Moscato<sup>1,4,5</sup>**

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Advances in materials science and in additive manufacturing allow more versatile structures to be produced as implants. Especially lattice structures, with their macro-porosity allowing better tissue integration, offer a wide range of possibilities. Aim of this study was to investigate the mechanical and geometrical properties of 3d printed lattices using non-metallic materials: high performance ceramic (ZrO<sub>2</sub>) and photopolymers.

Seven different lattice structures with each 80% porosity and a cross section dimensions of 4x4 mm were designed and 3d printed, in sets of each ten samples per mechanical tests. Optical profilometry and  $\mu$ -computer tomography ( $\mu$ CT) was used to investigate the printed lattices. Four mechanical tests were performed: compressive, tensile, shear and 4-point bending, to measure the elasticity and breaking strength. Finite element simulation (FEM) was then utilized to predict the elastic properties of lattice structures.

The measured samples showed uniaxial Young's moduli between 5% to 19% of the bulk materials Young's modulus and breaking strength of 100MPa to 550MPa, depending on their individual structure. Lattices with continuous struts in direction of loading exert higher mechanical stability than those with diagonal or transversal structures. Struts dimensions with deviations of up to 30% in diameter were found, which can be related to manufacturing and post processing. FEM simulations showed satisfactory fit to the measurement results when the actual and not the nominal dimensions were used for simulations.

Lattice geometries fabricated in ceramic can not only mimic trabecular bone, but are also able to withstand physiological loads while providing good tissue integration, therefore making it a viable choice for implants. When considering small structures such as lattices, geometry deviations from the original design during the fabrication process must be taken into account. When planning and designing lattices, from photopolymer prototypes only inaccurate extrapolations can be anticipated, but with FEM simulations the lattice properties can be precisely adjusted.

## Natural biomolecules for surface functionalization and coating of titanium alloys

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Several molecules of natural origin (derived from plants or animals) are of great interest for surface functionalization (grafting of a molecular layer) or coating (nano or micrometric continuous films) of titanium alloys. They can be polypeptides, proteins, vitamins, oils, organic compounds, or natural polymers. Functionalization or coating of titanium must be coupled to a proper surface chemistry and topography according to the type of biomolecule to be grafted and the specific application or purposes. The modified titanium surfaces acquire biomimetic or antibacterial functionalities and/or ability to guide the tissue growth. Positive outcome on inflammatory or anticancer properties can be also induced. New characterization protocols (biological, chemical, physical, mechanical tests and analyses) are needed for characterizing the modified surfaces and the post-processing steps (packaging, sterilization) must be adapted.

An overview of the strategies and the benefits from grafting or coating titanium with nisin, vitamin E, tocopherol phosphate, mentha essential oil, chitin derivative, polyphenols, and keratin will be presented.

## Development of individual rib implants using thorax simulations and 3D printing technology

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Surgical resection of chest wall tumours may lead to a loss of ribcage stability and requires reconstruction to allow for physical thorax functioning. When titanium implants are used especially for larger, lateral defects, they tend to break. Implant failures are mainly due to specific mechanical requirements for chest-wall reconstruction which must mimic the physiological properties and which are not yet met by available implants.

In this context, the implants must show some important characteristics: On the one hand, there are a variety of loads that they must be able to withstand permanently. On the other hand, they must have an appropriate stiffness to enable all daily movements and at the same time protect the vital inner organs. To meet these requirements, it is essential to understand the biomechanics of the thorax. For this purpose, a full thorax FEM model was developed.

This model was assembled stepwise. First a chest CT scan of a fresh, unembalmed cadaver in the supine position was made to reconstruct the bony and cartilaginous structures. Further CTs in different positions as well as stiffness measurements on several anatomical structures were used to define properties of the FE model and for step-by-step calibration and verification. Various activities such as ventilation, breathing, resuscitation, lying on the side or coughing were simulated on this verified FE model and the stresses and deformations were evaluated. The same simulations and evaluations were carried out with defects on ribs 5 to 9 and with corresponding implants according to the current state of the art. In this way, the critical activities that lead to damage of the implants could be identified. Based on these findings, an algorithm for determining the implant dimensions for different materials to achieve an appropriate stiffness of 3D-printed rib implants was developed.

## Machine learning based prediction of layer-by-layer coating thickness

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*Introduction:* Layer-by-layer film coatings are an effective technique for surface modification, particularly in the biomedical industry. Despite the large number of papers on LbL assembly, prediction of LbL coating thickness, as a functional property, is a challenging and time consuming task from the aspect of experiment. Machine learning (ML) approaches that are already being developed have the potential to speed up and improve novel coating development thus reducing time and material consumption.

*Materials and methods:* The data used represented a combination of the literature and experimental data generated in-house using a Quartz Crystal Microbalance with dissipation monitoring (QCM-D). The whole dataset for coating thickness [nm] prediction included the 22 input features (Polycation, Polyanion, Polycation unit MW, Polyanion unit MW, Polycation MW, Polyanion MW, Number of the bilayer, Ending polymer etc.). In total, there were 98 instances from the literature and 33 from the in-house experiments. Proposed methodology included several preprocessing steps (such as outlier removal and missing data imputation) and machine learning techniques for coating thickness prediction (Linear regression, Logistic regression, Support Vector Regressor, Random Forest Regressor, and Extra Tree Regressor). SMOGN was used to deal with skewed data.

*Results and discussion:* The results show that Extra Tree Regressor outperformed other algorithms when combined with optimal hyperparameters and missing data imputation. Relevant metrics achieved were  $R^2 = 0.980$ ,  $MSE = 46933.204$ ,  $RMSE = 216.64$  and  $MAE = 111.414$  on the test dataset. The 6 best predictors of coating thickness were identified, with top three being Polyanion, Number of the bilayer and Ending polymer, which can be used to predict coating thickness without the need for numerous parameter measurements.

*Conclusions:* Further research will focus on outputs associated with antibacterial, anti-inflammatory, and antiviral capabilities, allowing researchers to respond to real-world biomedical issues like as antibiotic resistance, implant rejection, and COVID-19 outbreaks.

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## Impact of 3d-printed microstructured surfaces on bacterial adhesion and growth

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**Objectives:** Implantation of a foreign body is often associated with restoration of natural body functions to prolong life expectancy and improve quality of life. However, the procedure involves considerable risk for bacterial infections. Device-related infections account for a large proportion of hospital-acquired infections, and the ability of bacteria to form a biofilm as a protective shield usually makes treatment impossible without removal of the implant. Recently, there have been several approaches to prevent bacterial attachment and biofilm formation. In particular, topographic surfaces have attracted considerable attention in studies seeking antibacterial properties without additional antimicrobial reagents.

**Methods:** Several surfaces with microcylinders in three different dimensions (1, 3 and 9  $\mu\text{m}$ ) were fabricated with a nanoprinter using two-photon lithography and evaluated for their antibacterial activity in terms of biofilm formers. The microstructured surfaces were cultured for 24 hours with different strains of *Pseudomonas aeruginosa* and *Staphylococcus aureus* to study bacterial attachment to the patterned surfaces. In addition, surface wettability was measured by contact angle measurement.

**Results:** The contact angles increased with the size of the cylinders, indicating that the hydrophobic properties of the surface were favored. Since previous studies have proven that bacterial attachment is usually affected by surface wettability, a difference in bacterial adhesion should be observed. However, the results demonstrated that *S. aureus* was not affected by the microstructures, while for *P. aeruginosa* the bacterial amount increased with the size of the cylinders, and compared to a flat surface, a reduction of bacteria was observed only for one strain on the smallest cylinders.

**Conclusions:** This study indicates that microstructures from 1 to 9  $\mu\text{m}$  have little to no antibacterial properties and that a change in wettability due to surface structures has no effect on bacterial adhesion.

## Electrophoretic deposition of bioinspired nacre-like chitosan/hydroxyapatite coating

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Recently, chitosan (CS) based composite coatings have been devoted considerable attention in the biomaterials field, but their mechanical properties need to be addressed. In this study, therefore, we aim to mimic the brick and mortar microstructure of nacre, retaining superior durability by its intricate and hierarchical stacking, and we design nacre-like CS-hydroxyapatite (HA) coatings by electrophoretic deposition (EPD). For this purpose, we synthesized the building blocks, HA particles, with plate-like morphology ahead of preparing a suspension for coating containing CS molecules with HA particles. We then successfully fabricated the hybrid layers by the EPD, harnessing the particles towards the counter electrode under an electric field, and optimized the microstructure of the coating by tuning the process parameters (voltage, electrode distance, etc.). The microstructure images taken by the scanning electron microscope (SEM) proved the layered hierarchical coatings. Consequently, we hypothesized that the electrical force turns HA particles' plate surface parallel to the substrate and moves them towards the substrate with chitosan molecules. This study highlights that EPD is a practicable procedure for producing advanced hierarchical composite coatings for biomedical applications and could be used to surge conventional hybrid coatings' mechanical properties.

## Individualized jawbone replacements by combining additive manufacturing with Freeze Foaming

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Vat Photopolymerization as Ceramic Additive Manufacturing method (CerAM VPP) and Freeze Foaming have been used for developing individualized jawbone replacement material.

CerAM VPP was used for fabricating individualized and biomechanically designed load-bearing support structures made of hydroxyapatite (HAp) and zirconia. For enabling an ingrowth of bone tissue and a vascularization of bone-mimicking components those hollow structures were filled with a so-called Freeze Foam made of hydroxyapatite. Freeze Foaming is a direct foaming technique which allows the production of an open-cell foam structure with adjustable porosity.

In a two-step approach, firstly the CerAM VPP supporting component was additively manufactured, debinded and pre-sintered. The pre-sintered parts were then filled with an aqueous hydroxyapatite paste and enclosed in a mold corresponding to a certain part of a jawbone. Those parts were transferred into the chamber of a freeze drier. By reducing the ambient pressure, the HAp paste gets inflated to a stable foam thereby filling the individualized support structure completely. The dried Freeze Foam consists of large cells resulting from the expansion of vapor and entrapped air in the paste whereas the struts show a microporosity resulting from ice crystal growth.

Both, the additively manufactured support structure and the Freeze Foam were then treated by a co-sintering step, which requires a very exact adjustment of the shrinking behavior of both structures. Thereby, the initially used bioactive HAp is transformed to biodegradable tricalcium phosphate (TCP).

Those novel individualized bone graft substitutes had been successfully tested *in-vitro* and *in-vivo* by ingrowth tests in the jaws of minipigs proven on their degradability and new bone formation.

The contribution documents a longer development period of these hybrid bone replacement structures and shows the research results from several already completed and still ongoing projects on this topic.

## Bioinspired individualized implants made of silicon nitride via Ceramic Additive Manufacturing by Vat Photopolymerization (CerAM VPP)

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Hardness, high mechanical strength, wear and corrosion resistance or even heat resistance, for instance, are the most important properties of silicon nitride, which make the material interesting for various applications. This includes cutting tools, crucibles for molten metals, bearings or prostheses in medical technology. Up to now, the demands on the geometry of silicon nitride-based components could largely be met by using conventional shaping methods such as pressing and green machining or injection moulding. However, requirements in terms of complexity and function are constantly increasing. By using additive manufacturing (AM) technologies for ceramic materials, the complexity of components can be significantly increased and additional functions such as bioinspired structures with a defined porosity as well as modified surfaces, for instance, can be integrated. High-resolution AM processes such as stereolithography enable the production of very accurate and complex ceramic components. Unfortunately, for silicon nitride the state of development in lithography-based AM processes is limited and commercial systems or service providers are rare. Therefore, the authors would like to give an insight into the development status of silicon nitride at the Fraunhofer IKTS for the so-called CerAM VPP technology (Lithoz LCM process) by showing results of the "Fingerkit" project, which deals with the development of novel finger implants with integrated bioinspired structures.

## Tri-lineage differentiation potential of BMSCs grown on hiPSC-engineered extracellular matrix

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Mesenchymal stem cells (MSCs) have the potential to repair and regenerate damaged tissues in response to injury, such as fracture or other tissue injury. Bone marrow and adipose tissue are the major sources of MSCs. Previous studies suggested that the regenerative activity of stem cells can be enhanced by exposure to tissue microenvironments. The aim of our project was to investigate whether extracellular matrix (ECM) engineered from human induced pluripotent stem cells-derived mesenchymal-like progenitors (hiPSCs-MPs) can enhance the regenerative potential of human bone marrow mesenchymal stromal cells (hBMSCs).

ECM was engineered from hiPSC-MPs. ECM structure and composition were characterized before and after decellularization using immunofluorescence and biochemical assays. hBMSCs were cultured on the engineered ECM, and differentiated into osteogenic, chondrogenic and adipogenic lineages. Growth and differentiation responses were compared to tissue culture plastic controls.

Decellularization of ECM resulted in efficient cell elimination, as observed in our previous studies. Cultivation hBMSCs on the ECM in osteogenic medium significantly increased hBMSC growth, collagen deposition and alkaline phosphatase activity. Furthermore, expression of osteogenic genes and matrix mineralization were significantly higher compared to plastic controls. Chondrogenic micromass culture on the ECM significantly increased cell growth and expression of chondrogenic markers, including glycosaminoglycans and collagen type II. Adipogenic differentiation of hBMSCs on the ECM resulted in significantly increased hBMSC growth, but significantly reduced lipid vacuole deposition compared to plastic controls. Together, our studies suggest that BMSCs differentiation into osteogenic and chondrogenic lineages can be enhanced, whereas adipogenic activity is decreased by the culture on engineered ECM. Contribution of specific matrix components and underlying mechanisms need to be further elucidated.

Our studies suggest that the three-lineage differentiation of aged BMSCs can be modulated by culture on hiPSC-engineered ECM. Further studies are aimed at scaling-up to three-dimensional ECM constructs for osteochondral tissue regeneration.

## Inverse bone remodeling allows for prediction of physiological peak joint loads using clinically feasible homogenized finite element models

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Obtaining physiological loading conditions of joints in-vivo can be challenging. An invasive method to measure such loads are instrumented prostheses, but also, the bone microstructure, which can be measured non-invasively, contains information on the physiological loads. The loads are “imprinted” by bone (re)modeling and can be predicted using inverse bone remodeling (IBR). In brief, IBR uses finite-element (FE) models and scales applied unit loads such that the tissue is loaded homogeneously. It was shown to predict peak joint loads in agreement with measurements of instrumented prostheses at the proximal femur. Yet, IBR requires high-resolution CT scans, which are often unavailable in a clinical scenario. To overcome the requirement for fully depicting the microstructure and reducing the computational costs, we recently adapted IBR to utilize homogenized-FE models instead of micro-FE. The objective of this study was to test the viability of IBR with clinically feasible homogenized-FE models to predict in-vivo hip joint loading.

The peak joint loads were predicted for 19 proximal femora using homogenized-FE models. Trabecular and cortical bone was modeled separately using a density-dependent material. Four unit loads of 1kN each were applied at the femoral head, coplanar to the frontal plane, at -20°, 20°, 60°, and 100°.

The predicted peak angle was 20° in 18 of 19 samples, and the average peak magnitude was 3.23kN±0.5kN. The predicted angles and magnitudes were similar to those previously presented in literature using micro-FE-based IBR (20°, 3.37kN±0.6kN) or instrumented prostheses (18.2°±2.0°, 2.7kN±0.4kN). The average solving time was reduced from 497 CPU-hours (micro-FE) to just 50 CPU-seconds (homogenized-FE).

These preliminary results show, that IBR can be used with homogenized models to predict physiological peak joint loads. However, the FE models were created from micro-CT data. Thus, it still has to be investigated if real clinical CT data can be used similarly.

## Accounting for space distribution of particles in two-phase particulate composites

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In the following study, predictive capabilities of the mean-field cluster model [1,2] in accounting for the space distribution of inclusions in two-phase particulate composites are demonstrated. In particular, the case of multiple families of inclusions is addressed. The analysis is performed for the linear and nonlinear regime (elastic-plastic or elastic-viscoplastic). For the inelastic regime, the incremental linearization of elasto-plastic law or the additive tangent interaction law for elastic-viscoplastic case are used to adopt the scheme for non-linear material behaviour. The formulated micromechanical scheme is implemented and verified with respect to the results of numerical homogenization using the finite element method. Representative volume elements (RVE) containing multiple inclusions, arranged in regular or random patterns, and subjected to periodic boundary conditions are considered. Predictive capabilities of the

method are verified as concerns estimation of the overall response, as well as the mean stress and mean strain within each inclusion in the RVE. The possibility of using the tool in the material morphology optimization is assessed.

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## Computational fluid dynamics study of the influence of geometry and flow rate on mass transport in 3D scaffolds

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Tissue engineering and regenerative medicine are promising biomedical approaches to regenerate severe bone defects, caused by trauma, diseases or prolonged physical activities. Scaffold structures support seeded cells and should provide an optimal environment for cell growth. Computational fluid dynamics (CFD) simulations are a key component to investigate the influence of the scaffold structure on flow characteristics and mass transfer. Wall shear stresses (WSS) are of specific interest. The aim of this work is to optimize sinusoidal scaffold structures to improve and optimize cell proliferation and cell nutrition conditions. The scaffolds are computationally created and meshed using SALOME®, while the CFD simulations are carried out using the open-source CFD toolbox OpenFOAM®. A diffusive-advective mass transport equation is solved on a laminar flow field using the solver *scalarTransportFoam* for the evaluation of the nutrient distribution of the scaffolds. The fluid flow is described by the three-dimensional Navier-Stokes equations. CFD results are validated via  $\mu$ -particle image velocimetry ( $\mu$ PIV) measurements using scaffolds that are printed into a microchannel using the Two-Photon polymerization technique. The numerical results indicate that both increased frequency and amplitude of the sinusoidal channel regions lead to a velocity decrease inside the sinus regions and vortex formation at high frequencies.  $\mu$ -PIV measurements confirm that the CFD simulations predict vortex formation and WSS as a function of flow rate with reasonable accuracy, which also allows to predict influence on mass transport. These results confirm the potential of CFD for design and evaluation of optimized scaffold structures. Geometric variations can be easily pre-evaluated and optimized before printing the scaffolds for experimental evaluation. This integrated computational and experimental design loop is important because minor changes in the flow field, especially near the walls, can directly affect the cell bioactivity.

## Multiscale mechanics of a cementitious biomaterial: biodentine

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Biodentine is made of calcium silicate, calcium carbonate, zirconium dioxide, and water. It is used for dental replacement. It significantly outperforms the stiffness and hardness of construction cement pastes, which are chemically similar. We here report a comprehensive investigation on the multiscale mechanics of Biodentine, combining grid nanoindentation, ultrasonic testing, statistics-informed micromechanical modeling. The key to the superior properties of Biodentine is a highly dense, calcite-reinforced hydrate phase, with surprisingly uniform load levels, underlining the high level of optimization of the material.

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## Time-dependent mechanics of individual collagen fibrils and electrospun fibres

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Collagen is the most abundant protein in human body. At the nanoscale, collagen forms collagen fibrils (CF) with diameters between 50-500 nm. CFs show time-dependent material behavior, which suggests they are also viscoelastic. Current available tools and methods are not able to measure viscoelastic material properties in a reproducible manner. Here, we present methods to perform force-controlled creep as well dynamic nano-mechanical analysis (DMA) in tension. The method is applied to individual CFs and electrospun PLLA nanofibers (PLLAs). Electrospinning is an emerging technique for fabrication of nanofibrous biomaterials similar to CFs of musculoskeletal tissues [1, 2].

We conducted creep experiments on CFs from and mouse tail tendon collagen fibrils and nano DMA experiments on obth CFs and electrospun PLLAs. Both experiments are facilitated through a recently developed instrument then NanoTens, for testing of nano- and microscale fibers with quick coupling and uncoupling [3].

In creep experiments we show that the transient behaviour at medium strains can be empirically described using a linear Burgers model in Kelvin-Voigt configuration. Here elastic elements exhibit moduli in the range of 0.2-10 GPa and viscous elements exhibit viscosities in the range of 10<sup>2</sup>-10<sup>4</sup> MPa.s for the dashpot within the Kelvin-Voigt body and 10<sup>3</sup>-10<sup>6</sup> MPa.s for the dashpot in series.

In nano DMA experiments We observe similar elastic behavior in monotonic tensile tests and elastic response in nanoDMA for CFs and PLLAs. However, the loss modulus and tangent of PLLAs is significantly higher compared to CFs. This warrants room for further optimization of PLLA material properties.

In conclusion, the the NanoTens opens the door for assessing the time-dependent properties of individual CFs and thus to establish a unified constitutive CF model.

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## Triaxial electrospun fibers for prolonged drug release

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Electrospun nanofibers are a challenging system for effective and targeted drug delivery in tissue engineering applications. The triaxial technique is a fairly new method under investigation. The fibers obtained by this method consist of three layers: a core and two layers surrounding the core. Triaxial electrospinning is a competitive method to solve the critical limitations in other techniques, i.e. uniaxial, and coaxial, such as lack of sustained and controlled drug release, poor solubility of drugs, problems with loading multiple drugs, and biodegradation, not adequate biocompatibility.

The first objective of the research is to optimize the manufacturing process using triaxial electrospinning to get homogenous-free beads fibers and beneficial effects on drug release.

For the development of the fibers, a combination of biodegradable synthetic and natural polymers were used: polycaprolactone (PCL) (core layer), poly(lactic-co-glycolide) (PLGA) (shell layer), and gelatin (intermediate layer). Natural polymer improves biocompatibility, while the combination of PCL and PLGA is expected to maintain preferred structural properties e.g. hydrophilicity and morphology. As a model of the drug, Rhodamin B (Rh B) was loaded for the optimization process.

Preliminary investigations including optimization of manufacturing triaxial fibers are discussed. Microscopic images demonstrated homogenous free-beads fibers were developed as a result of many trials. Furthermore, it was observed fibers are covered with an outer layer according to the expectancy. Under the shell layer, there is a middle surrounding the core layer indicating that the proposed process with parameters selected in this way allows producing of core-shell fiber structure. Preliminary *in-vitro* studies were performed with Rh B to investigate release profiles from triaxial fibers compared to coaxial fibers. The results showed triaxial fibers decreased initial burst release significantly over the coaxial fibers.

The research reported here shows triaxial fibers as promising biomaterials that can be used as novel drug delivery systems in biomedical applications.

## Synthesis and characterization of drug loaded hybrid mesoporous silica particles for biomedical applications

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Mesoporous silica materials are promising candidates for drug delivery systems, due to their high specific surface area, large pore volume, ordered network and narrow pore size distribution.

Traditionally, non-ionic or ionic surfactant micelles were used as a structure directing agent of silica. However, a polyion complex (PIC) assembly, which is based on interactions between a pH stimuli-responsive double-hydrophilic block copolymer (DHBC) with a weak polyamine, benefits from functional hybrid silica mesoporous shell and a tuneable stimuli responsive copolymeric core [1]. This gives them specific functionalities, such as the ability of drug encapsulation and release in a specific pH[2].

In this study, silica particles were prepared by (i) micellization of cationic surfactant cetylpyridinium chloride (CPC), (ii) PIC assembly of neutral-ionizable poly(ethylene oxide)-block-poly(acrylic acid) copolymer (PEO-b-PAA)/CPC and silica condensation. CPC is an oral antiseptic and it was used both as an active component of PIC assembly, due to electrostatic complexation with CPC/-PAA at pH > 4.5 and antibacterial drug which can be released from pores below pH 4.5.

FTIR and ICP confirm presence of CPC or CPC/DHBC components in obtained silica powders. DHBC has a positive impact on decreasing size of particles, improving their homogeneity and imputes mesoporosity depending on synthesis conditions: DHBC concentration, complexation between the carboxylate (AA) and amine (N) groups, ratio between the Si species/EO units. In the CPC-based system, particles are in the size range of 46-535 nm with majority ~150 nm, while in the DHBC/CPC system particles are below 50 nm. BET surface area increases from 129.4 m<sup>2</sup>/g for CPC-based silica to up to 1045 m<sup>2</sup>/g for CPC/DHBC-based silica. TEM confirms mesoporous structure for CPC/DHBC particles. Kinetics of the CPC uptake was evaluated by UV-Vis at pH of 1, 3 and 7.4 and confirms a pH stimuli-responsive release at pH 1 and 3.

[1] <https://doi.org/10.1002/anie.200802431>

[2] <https://doi.org/10.1021/acs.langmuir.5b03221>

## Development and characterization of zein-based coatings incorporating fluoride- and copper-doped bioactive glass on titanium for biomedical applications

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The long-term application of metallic implants is limited due to their poor osseointegration capability and proneness to bacterial infections. In order to tackle these issues, the surface of the metallic implant can be coated with bioactive and antibacterial organic-inorganic composite coatings, e.g., by using electrophoretic deposition (EPD) [1,2]. Thus, the present work aims to develop coatings based the natural polymer zein and SiO<sub>2</sub>-CaO-P<sub>2</sub>O<sub>5</sub> bioactive glass particles (BG) doped with fluoride (BG-F) and copper (BG-F-Cu) on titanium by EPD. Morphological observations demonstrated that the glass particles were homogeneously embedded in the polymeric coating matrix, while pull-off and tape tests indicated that the addition of BG particles improved the coating adhesion to the substrate. Nanoindentation measurements and scratch tests showed that zein/BG coatings possessed higher hardness and improved scratch resistance in comparison to zein/BG-F and zein/BG-F-Cu coatings. The ion substitution in the BG structure did not affect the bioactivity of the coatings as apatite formations could be detected on all composite coatings after 3 days of immersion in simulated body fluid (SBF), according to FTIR, XRD, SEM and EDX analyses. All composite coatings showed decreased wettability, higher susceptibility to collagenase degradation and lower swelling capability than pure zein coatings. Both direct and indirect cytocompatibility assays revealed significantly improved viability of osteoblast-like MG-63 cells on all composite coatings after 1 and 3 days of incubation. Moreover, the presence of ion-doped bioactive glass endowed antibacterial activity of the coatings against Gram-positive *S. aureus* and Gram-negative *E. coli* as confirmed by Alamar blue assay and SEM observations. The obtained results prove that the prepared coatings can be promising candidates to facilitate bone tissue integration and to prevent infections around orthopaedic and dental implants.

[1] Maciag et al., Materials, 14, 2021, 312.

[2] Meyer et al., Coatings, 8, 2018, 27.

## Alteration of vimentin cytoskeleton in senescent cells

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Cellular senescence occurs in response to various triggers, including DNA damage, telomere dysfunction, oncogene activation, and organelle stress. It has been linked to tumor suppression, tissue repair, embryogenesis, and organismal aging. It is known that senescent human fibroblasts show an increase in an intermediate cytoskeletal protein, vimentin, yet the senescence-associated alteration of the function of vimentin in senescent cells is largely unexplored.

Here, we present unpublished results showing that vimentin accumulates in senescent cells and forms a highly compacted, juxtannuclear, and monopolar structure. Vimentin accumulates in close proximity to the nucleus, and our findings indicate an association between the accumulation of vimentin and the deformation of the nucleus in senescence. We demonstrate that nuclei of senescent cells showing deposition of vimentin have further increased number of DNA damage foci and display chromatin structure

changes. Finally, accumulation of vimentin in senescent cells is also associated with changes in microtubular but not actin cytoskeleton and re-positioning of cytoplasmic organelles. Experiments in vimentin knock-out (KO) fibroblasts provide further evidence on the relationship between nucleus structure and vimentin, as senescent cells deprived of vimentin show reduced DNA damage and lack of nuclear distortions and structure of chromatin resembling that in young cells. Overall, our findings indicate that induction of senescence causes immense changes in the vimentin cytoskeleton in a process that has consequences on the re-arrangement and damage response of cellular structures such as the nucleus and cytoskeleton and cytoplasmic organelles.

## Auricular cartilage scaffolds: an innovative tool to study cellular infiltration by glycosaminoglycans removal and altered stiffness

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**Background:** Decellularized materials are an ideal candidate for articular cartilage regeneration due to the similarity of its structure and composition with the native tissue. However, the modulation of the materials properties, such as topography or porosity remain as a challenge. Our group previously developed a biomaterial based on auricular cartilage by removal of the elastic fibers and glycosaminoglycans (GAGs) with tunable mechanical stiffness. Hence, we aim to investigate cellular ingrowth into the matrix according to different stiffnesses.

**Methodology:** Auricular cartilage discs were harvested from bovine ears and enzymatically treated with pepsin and elastase. A pepsin concentration series was used to gradually remove the GAGs from the matrix. First, GAG content was quantified by histology and Dimethylmethylene Blue assay. Second, a stepwise compressive test using a Zwick uniaxial testing machine was performed to characterize the mechanical properties (i.e: viscosity and elasticity), which were computed using a mathematical model. Last, cell infiltration was monitored by confocal microscopy and immunohistochemistry using fluorescently labelled adipose derived stromal cells and human articular chondrocytes.

**Results:** GAG concentration and mechanical properties varied according to the concentration of pepsin used. Residual GAG content differed significantly between the highest and lowest concentration (1 mg/mL: 0.058 0.014 mg/ $\mu$ g vs. 0.2 mg/mL: 0.15 0.042 mg/ $\mu$ g;  $p = 0.0022$ ). Similarly, native scaffolds and those treated with 0.2 mg/mL pepsin showed a viscoelastic behavior and higher stiffness, while concentrations above 0.4 mg/mL led to a more viscoplastic and fluid-like behavior. Cellular migration into the scaffolds followed the inverse trend, higher concentrations of pepsin (i.e.: fewer GAGs and stiffness) increased cellular infiltration. Nevertheless, cells were still able to migrate into the matrix with the lowest pepsin concentration. Interestingly, without pepsin cells could not penetrate the open channels.

**Conclusion:** By diminishing the GAG content, the stiffness of auricular cartilage scaffolds is reduced, translating into differences in cellular infiltration.

## Poster Presentations

### Effect of DLC coating of growth-guidance system implants on changes in mechanical and kinematic properties of the spine

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Early onset scoliosis (EOS) is a three-dimensional curvature of the spine and trunk that occurs in children nine years of age or younger. The EOS tend to develop progressively, requiring early surgical intervention with spine stabilization. Currently stepwise treatment method involving the displacement of the stabilizer by operating methods is being used. It is necessary to develop a solution that would allow scoliosis to be corrected as soon as possible while reducing the number of operations and the risk of complications.

The research aimed to develop a modification of the internal spine stabilizer for the treating scoliosis in children by increasing its abrasion resistance and thus reducing the risk of tissue degradation and disorders in the kinematics of the spine column. The study used the scoliosis stabilisation system offered by Novaspine, which has kinetic pairs in its design to allow relative displacement of stabiliser components without external intervention.

In order to increase the abrasion resistance of the mating surfaces and increase the mobility of the stabilizer-spine system, a DLC (Diamond Like Carbon) coating was applied to the implant components. Then, tests were carried out to assess the mechanical and kinematic properties of the spine-stabilizer (SI) system for selected modifications. At this study stage, a more than 8% decrease in SI stiffness was demonstrated for DLC-coated implants compared to implants without DLC. Then, in vivo study was carried out on domestic pigs, assessing the effect of the applied modification on the reduction of the mass of titanium alloy particles infiltrating into the tissues surrounding the implant and determining the effect of modified stabilizing systems on changes in the vertebra bone structure. As a consequence, the increased mobility of the stabilizer follower node led to excessive movement between the transpedicular screw and the bone tissue, leading to their loosening and inflammation.

## Finite element analysis of titanium-based hip implant modified surfaces

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As we age, we are faced with a variety of health challenges. Some of those challenges require surgeries to improve the quality of life. One of the most common surgeries is hip replacement surgery which provides mobility improvement and pain relief. During this procedure, a damaged part of the hip joint is replaced with an artificial one. Titanium and its alloys, especially Ti-6Al-4V, are most commonly used for hip implants due to their mechanical properties, excellent biocompatibility, and corrosion resistance. Cementless hip implants are considered to be more durable than cemented hip implants and they are recommended for the younger population. In order to ensure the proper function of the cementless hip implant, the connection between the femoral bone and the inserted implant has to be as strong as possible. If the connection is not strong, the implant starts to loosen and revision surgery is necessary. According to the experimental studies, implants with a rough surface reduce micro-movements between femoral bone and implant, which helps to form a stronger connection with a femoral bone. The goal of the present study was to employ the Finite Element Method, in order to analyze how ten different surface topographies of Ti-6Al-4V hip implant affect the shear stress values and distribution. The criteria that shear stress values at the implant-bone interface should be minimized to promote bone ingrowth was used to decide on the optimal surface topography of the presented models.

## From 2D ultrasound images to 3D patient-specific models of atherosclerotic carotid bifurcation

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Carotid artery atherosclerotic disease is an important risk factor for ischemic cerebrovascular events (stroke and transient ischemic attack). In order to prevent such events and life-threatening consequences, different imaging techniques are used for timely diagnosis and estimation of the carotid artery stenosis (CAS) condition. The use of ultrasound (US) images for assessment of atherosclerosis in the carotid artery is widely adopted due to ease of use, low costs and wide availability. The US examination can identify the severity of CAS in order to pre-estimate the risk of cardiovascular disease and ensure appropriate medical treatment. On the other hand, there are technical limitations in detection and characterization of the complex 3D carotid bifurcations and plaque components, which make diagnose inconsistent, even for an expert clinician. In order to contribute to a more reliable CAS examination, this study proposes the 3D reconstruction of patient-specific carotid bifurcation from US images, combining deep learning and meshing techniques. Deep learning is used for the segmentation of the carotid lumen and wall (including atherosclerotic plaque), while meshing is applied to create the 3D finite element (FE) model that is adapted to the specific patient, using data obtained from the segmented areas. The presented approach and methodology which combines the U-Net Convolutional Neural Networks (CNNs) and 3D reconstruction of carotid artery enables efficient segmentation, extraction of the morphological parameters and creation of 3D meshed volume models, ready for the further computational examinations. Improved 3D visualization and characterization of the carotid artery and plaque components, as well as possibility for further

numerical simulations (atherosclerosis progression, stenting, blood flow, etc.) represent the step forward in risk assessment of the atherosclerosis disease.

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## Methods of evaluating mechanical parameters and the stability of the cervical interbody fusion cage

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In the case of interbody fusion cages, it is required to achieve optimal conditions between the geometry and the mechanical parameters to achieve a stable connection at the border with the bone tissue. In our work, we present the research results of the cervical interbody fusion cage based on assessing mechanical properties and the conditions related to osseointegration resulting from the adopted geometry. The cage was designed as a titanium alloy Ti6Al4V implant strengthened with mesh lattice structures to obtain larger osseointegration between the implant and bone tissue. Based on the indentation test, the stiffness and the maximum force values of the modification of the geometrical dimensions of the mesh lattice structures were determined. Also, was performed adhesion test for Balb/3T3 fibroblasts and NHOst osteoblasts. The research showed that an essential geometric parameter influencing the mesh strength is the height of the connection point between the arms of the mesh cells. There was no significant influence of the mesh geometry on the number and survival of Balb/3T3 and NHOst cells. Fibroblast cells more readily formed colonies in the area where cells of the mesh meet, unlike osteoblasts, which were more numerous at their tips. The mechanical parameters and quality of the construction cervical interbody fusion cage were determined in: a uniaxial compression test to the failure of the implant (with ASTM F2077 standard), CT scan and microscopic analysis. With a non-destructive load in the force range up to 500N, the implant stiffness was from 14 to 17kN/mm. On the other hand, the value of the ultimate forces does not exceed 40kN and the stiffness 22kN/mm. The CT scan showed that the structure of the implant is continuous and that there are no closed pores in the implants printed. The average porosity calculated from CT scans of control volume was  $0.15 \pm 0.3\%$ .

## The effect of the addition of bioglass, Zn and graphene on the resorption rate of PCL scaffolds after 18 months of incubation in PBS solution

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One of the main directions of research is still the assessment of the rate of bioresorption and the release of the active phase that stimulates the processes of hydroxyapatite growth, resulting in faster tissue reconstruction. One of such solutions is the introduction of HAp additives or bioglass into polymers, making them a more bioactive material.

The aim of the research is to assess the rate of bioresorption of scaffolds prepared with the FDM 3D printing method made of PCL doped with bioglass, Zn and graphene. The research material consists of 20 samples divided into 4 groups: I – pure PCL with a molecular weight of 80kDa, II - PCL doped with bioglass (A2); III - PCL doped with zinc-modified bioglass (A2Zn5), IV - PCL with graphene flake (GNP). Currently, the tests cover an 18-month period of degradation in PBS solution at 37C. Each month, both the incubation fluid for which we determine the pH and conductivity values, as well as changes in the structure of the scaffold, are tested. The mass is measured for each sample, the surface of the material is also assessed using the Olympus Discovery v20 microscope, and the recording with a microCT (SkyScan 1172, Bruker). Using DataViewer®, Bruker software, it is possible to analyze changes in the geometry, which enables the analysis of changes in the structure of the samples. In our research, after 18 months of degradation we observe a decrease in weight of 2%. Although the changes are not yet visible in the microscopic image, thanks to the use of microtomography, they can already be observed. When analyzing the results of degradation, the corners of the tested scaffold underwent changes the most, and it is also possible to observe slower changes in its conformation due to twisting of the samples immersed in the PBS fluid.

## The potential of mulberry and non-mulberry silk fibroin bioinks for meniscus regeneration by 3D-bioprinting

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*Introduction:* The meniscus is a vital structure for biomechanical and anatomical purposes and is frequently injured. Among the diverse biomaterials used for 3D-bioprinting in meniscus regeneration research, silk fibroin (SF) derived from mulberry *Bombyx mori* (BM) silkworm and from non-mulberry types like *Antheraea mylitta* (AM), with the inherent RGD motif, are being explored. Thus, we investigated the potential of mulberry and non-mulberry SF blends to obtain a printable hydrogel for meniscus regeneration.

*Materials and methods:* BM and AM SF were mixed with ruthenium photoinitiator for rheology and ATR-FTIR measurements and without any crosslinker to determine their gelation kinetics. The absorbance at 540 nm was monitored for 3 h at 37°C. For printing, SF blends were mixed with/without crosslinker. After gelation in syringes at 37°C, the gels were extruded into the shape of a meniscus on an Allevi bioprinter. To evaluate cell viability, human chondrocytes and infrapatellar fat pad-derived mesenchymal stem cells (IFP-MSCs) were seeded into SF blends with decellularized extracellular matrix (dECM) powder before gelation. After incubation of the chondrocyte gels in growth medium and the IFP-MSC gels in differentiation medium, the gels were stained with LIVE/DEAD® Viability/Cytotoxicity Kit and the gene expression of chondrogenic markers was analyzed in cast and printed gels.

*Results:* The elastomeric properties of the crosslinked SF blend resembled a solid and the addition of more AM SF than BM SF has proven to be advantageous for a shorter gelation time. Printing 10% (w/v) SF blend with crosslinking during printing led to the most stable condition for printing a meniscus. The addition of dECM to the hydrogels increased the number of live cells in comparison to the SF blend and the BM SF alone. The chondrocytes expressed all tested chondrogenic markers except COL2A1 and the IFP-MSCs all markers except COL2A1 and MMP13.

## Use of plasma electrolytic oxidation on electron beam structured surface of titanium alloy

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The development of surface modification strategies to enhance the osteoconductivity of metallic implants is a field of major interest. The use of multiscale topography and surface functionalization are two effective strategies to promote the generation of new bone on the implant surface. This work aims to combine electron beam surface structuring and plasma electrolytic oxidation in titanium alloys to develop surface with antibacterial properties, corrosion resistance and biomechanical interlocking. Ca and P containing coatings were produced via 45 s PEO treatments over multi-scale EB surface topographies. In general, the PEO process, morphology, composition, and growth rate of the coatings were almost identical independently of the topography treated. PEO coatings provided to the structuring an additional micrometre porosity and sub-micrometre scale surface roughness. All the PEO-coated substrates presented essentially the same corrosion resistance. Electrochemical tests revealed localised crevice corrosion susceptibility of all the bare EB topographies which was successfully prevented after the PEO treatment.

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