

Baltic Biomaterials Centre of Excellence

The Baltic Biomaterials Centre of Excellence (BBCE) project's main objective is to establish a joint Centre for development of advanced biomaterials based on the long-term strategic cooperation between AO Research Institute Davos, Switzerland (ARI), Friedrich-Alexander University of Erlangen-Nuremberg, Germany (FAU), Riga Technical University Rudolfs Cimdins Riga Biomaterials Innovations and Development Centre (RTU RBIDC), Latvian Institute of Organic Synthesis (LIOS), Riga Stradins University (RSU) and Riga Stradins University Institute of Stomatology (RSU IS).

Development of BBCE

BBCE had a very successful year! We had 29 internal consortium meetings for planning the visits and events, and also for discussing the research directions, upcoming articles and overall cooperation. During this year BBCE members participated in 15 conferences, published 16 manuscripts with acknowledgement to BBCE and submitted 44 research grant applications. Consortium members were also active in disseminating project goals and results towards industry members, mainly through participating in exhibitions and meetings with enterprises. We could hear and see BBCE members on the TV and radio interviews, opening new possibilities for further cooperation with other organizations in Latvia. Highlights of the events during the year 2021 are:

1. Five short-term outgoing visits to FAU and ARI and eight short-term incoming visits to Riga.
2. Summer school organized by FAU, which provided a lot of new knowledge for Early Stage Researchers.
3. Six long-term visits to ARI and FAU.



BBCE team grows stronger

In 2021 BBCE leading staff had a great opportunity to communicate with the policy makers at the national level, through the Latvian Academy of Sciences (LAS) that has 415 elected members. One of the LAS operational objectives is to take an active part in the development and implementation of the Latvian science policy, as well as to promptly advise Saeima, President of the State, Government and the corresponding authorities on the scientific questions. BBCE researchers Dagnija Loca, Kristine Salma-Ancane, Liga Zvejniece and Reinis Vilskersts were nominated as the new members of LAS and presented summary of their scientific research to the LAS members. As a result, all of them have been elected as the new members of the Latvian Academy of Sciences: D.Loca and Liga Zvejniece as Full Members and K.Salma-Ancane and Reinis Vilskersts as Corresponding Members.

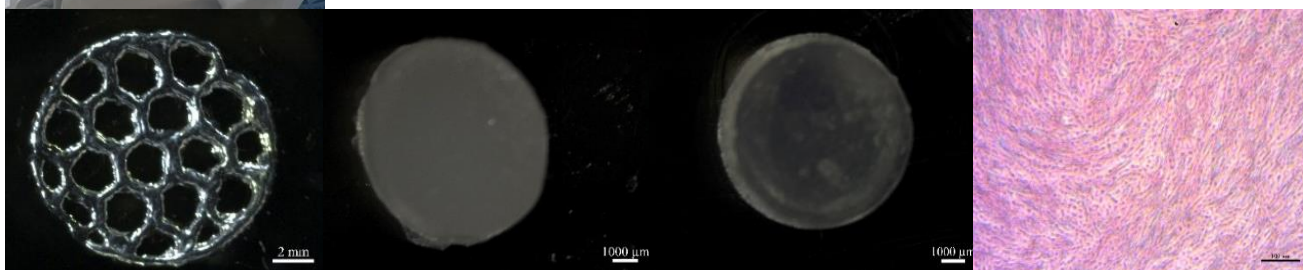


Like any amazing team, we now have our own mascot! Two colorful squirrels, that symbolize our energy and ability to work together. Furthermore, BBCE Early Stage Researchers surprised us not only with their outstanding publications, but also with some sweets. Now we have our own design for the BBCE cake!



Group 1 - Calcium phosphates and composites

PhD student Abhishek Indurkar has spent 6 months in 2021 and 2022 at FAU (Germany) facilities and received training on advanced 3D bioprinting and bioink formulations and on analysing the biocompatibility of synthesized inorganic/organic composites. During this tenure, amorphous calcium phosphate reinforced bioink was formulated, optimised for 3D bioprinting, mixed with pre-osteoblasts (MC-3T3E1) and finally the 3D tissue construct was fabricated. This long-term training program has ensured that a substantial experience in the field of biofabrication is brought back to Riga and it will open new directions, as well as reveal potential for future common publications, projects and perspectives for contemporary PhD Thesis.



Development of porous inorganic/organic composite

Development of inorganic/organic composite with increased concentration of ACP

Cellular analysis

Group 2 - Drug/ion/cell delivery

In 2021 SFG2 had expanded its horizons in terms of new recruited group members from all over the world, comprehensive trainings at advanced partner ARI, Switzerland facilities, and acquisition of new equipment for material rheological property assessment. PhD student Artemijs Scegljovs had an unique opportunity to spend four months at ARI facilities and get the training on the evaluation of physicochemical and biological properties of chemically cross-linked ϵ -polylysine/hyaluronic acid hydrogel. During his training rheology strategy was applied to determine the gel viscoelastic properties. This working experience and acquired knowledge opened up new possibilities and revealed potential for future common publications and perspectives for contemporary PhD Thesis. Furthermore, at the end of 2021, master student Kristine Aunina visited ARI facilities during the short-term trainings on the development and characterization of drug delivery systems. In the course of trainings she learned how to use the rheological measurements to determine the effect of active substances on hydrogels. As the new rheometer from TA Instruments arrived to BBCE facilities, upon returning to Latvia, both Kristine and Artemijs have started to implement the acquired knowledge into the practice and train other BBCE members on material rheology assessment.





Group 3 - Materials *in vitro*

In 2021 the *in vitro* lab at RTU RBIDC facilities went through a major upgrade with the arrival and installation of important equipment that included the incubator, fluorescence microscope, and plate reader. The first “host” of the *in vitro* lab was NIH/3T3 fibroblast cell line. The SFG3 members have used the lab to learn various cell biology techniques such as cytotoxicity assays, live/dead staining, direct and indirect material *in vitro* tests. Acquired skills have been applied to study material-cell interactions within the scope of ongoing research projects. For example, cytotoxicity of biomaterials and drug delivery systems have been assessed. Moreover, several *in vitro* test systems have been established to assess biomaterial influence on cell metabolism. The results obtained in this lab have already been included in one research paper. SFG3 aims to further expand cell library, as well as learn and implement new assays and *in vitro* models.

From January to March 2022, Theresa Schiemer, a master student from the Medical University of Innsbruck (Austria), joined the SFG3 for her study internship. She was working on experiments to explore calcium phosphate based biomaterial influence on cell metabolism. Theresa learned about the preparation and characterization of calcium phosphate ceramic scaffolds and cell sample preparation for metabolite analysis. Inspired by her positive experience, she has decided to carry out her master thesis project at BBCE starting in May 2022.



Article

Enzymatically Crosslinked In Situ Synthesized Silk/Gelatin/Calcium Phosphate Hydrogels for Drug Delivery

Andra Grava ^{1,2}, Karina Egle ^{1,2} and Arita Dubnika ^{1,2}

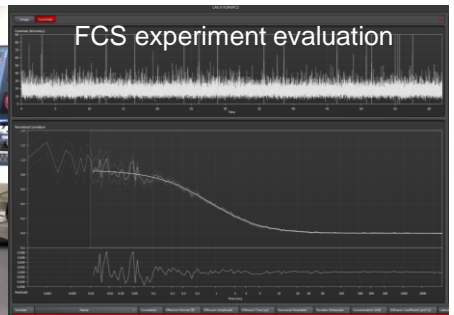
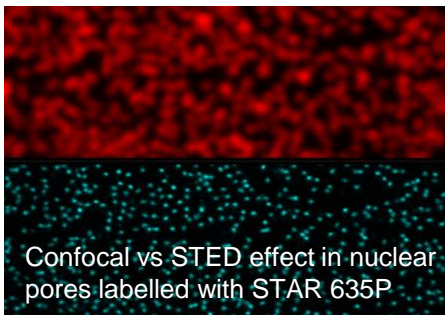
Group 4 - Kinetics and stability of drug delivery systems

RSU has established the 4th Group, which is in coordination with BBCE center since January 2021. The group’s objective is to study drug delivery systems, their kinetics and stability. Research group consists of several researchers from RSU. Group leader Dr. Agnese Brangule leads SFG4 and since January 2022 it includes two senior scientists (Postdocs) – Dr. Jhaleh Amirian and Dr. Supandeep Singh Hallan, the researcher – Assoc. Prof. Ingus Skadins and the student Ance Barzdina. The group is a multi-disciplinary team of students and researchers from different backgrounds and nationalities, all committed to advance novel drug delivery systems with micro/nanoscales technologies for minimally invasive therapeutics. Since the formation of the group, the researchers have focused on designing an effective drug delivery process that can be used for tissue engineering, regenerative medicine, and cancer therapy. Moreover, group members are focused on using naturally derived materials based on protein and carbohydrates to mimic the extracellular matrix present in cells and tissues. The group achievements so far are the submission of two book chapters, one review paper and one research paper, within a short period of time. In addition, the group members have applied for three RSU grants and all three grants have been awarded.



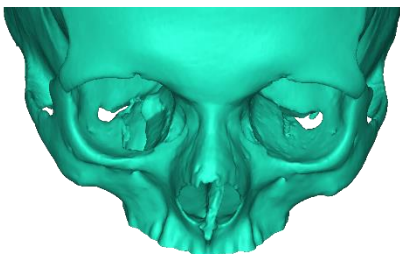
Group 5 - Preclinical biomaterial evaluation

New confocal fluorescence microscope with super-resolution capability was installed at LIOS-FFL in January 2022. Experts from Leica Microsystems visited FFL to give on-site training, and the pilot experiments were launched quickly after. Leica Stellaris 8 platform is upgraded to meet the latest state-of-the-art imaging technology. Various modalities altogether expand the imaging possibilities - it allows the design of complex, time-dependent experiments with multicoloured samples and high quality output images. Previous microscope generations were mostly equipped with a set number of excitation laser lines. The new Leica microscope overcomes this issue by using the supercontinuum white light laser tunable over a range of 440-790 nm, with steps of 1 nm. Essentially, a "laser rainbow" is available, in which one can choose the optimal wavelength(s) to work with. Nanoscopy is possible too! Additional STED lasers (STimulated Emission Depletion) can be used to show the fine details, as small as 50 nm in both 2D and 3D modes. It is quite useful if one wants to distinguish individual protein complexes or even observe single molecules. Furthermore, the dynamics of molecules in live cells can be described using the FCS technology (Fluorescence Correlation Spectroscopy). We look forward to many interesting experiments!

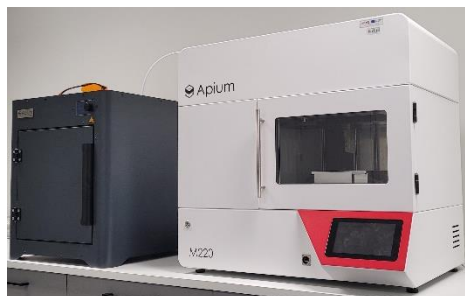


Group 6 - Clinical evaluation of materials and personalized implant development

In the last quarter of 2021 the RSU IS had procured two 3-D printing units: Asiga PRO 4K80 UV and Apium M220. The Asiga PRO 4K80 UV is intended for printing larger scale parts and models, such as full skulls, jawbones and guides, for surgical planning. The most prospective user is expected to be the new addition to the team – postdoc Ieva Bagante, who plans to evaluate the use of printed skull models for acute cases regarding orbital floor fractures. As for the Apium M220 unit, it is specifically aimed for printing individualized non-load bearing PEEK (polyether ether ketone) implants which are primarily intended for aesthetic improvements. It is also supplemented with an Apium F300 filament dryer unit to improve printed part quality and durability. This printer is expected to be adaptable for creating functional implants eventually. The current plan is to create and use personalized cranial plates, jaw, cheek, and orbital implants, however, there is not a finalized team for this task yet.



Anatomical model of an orbital floor fracture. Made to be printable and usable for surgical planning



Apium M220 3-D printer and Apium F300 filament dryer on RSU SI premises



Asiga PRO 4K80 UV 3-D printer unit on RSU SI premises

BBCE erudition competition «BIO-GO-Higher»



From 15th to 19th of August 2021, the students of the previous years' winning team "**Mitochondria are the powerhouse of the cell**", from Riga Technical University Engineering School, visited AO Research Institute in Davos, Switzerland. The students themselves say: "Overall, the trip was great and impressive, we learned a lot about animal and human bones, we saw really breathtaking views, and we felt as a part of the research community".



AO Research Institute in Davos, Switzerland
One of the world's leading research centers for biomaterials and bone fixation



New year- new tasks

The 2021/2022 competition started on September 27, 2021 and will end on April 14, 2022. One of the tasks was to create a model for the planned BBCE headquarters in RTU student campus in Ķīpsala. Have a look, maybe the amazing designs are something our architects could take into the count!
After 3 rounds, team from Sigulda State Gymnasium has taken the lead.



This year's main prize - a trip to BBCE partners at the University of Friedrich-Alexander Erlangen-Nuremberg and the Biomaterials Center in Erlangen, Germany.

If you want to know more about BBCE and the events that are organized - follow us on Twitter, Facebook and Instagram!



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What are we looking for:

- Cooperation with other institutions
- Cooperation with industry
- New project applications
- Staff mobility and training

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