Empa
Materials Science and Technology

TECHNOLOGY BRIEFING

Precision Medicine Research at Empa

Friday, 25 June 2021, from 14:00 to 17:30
Online, via Zoom

Online registration: *www.empa-akademie.ch/technology*

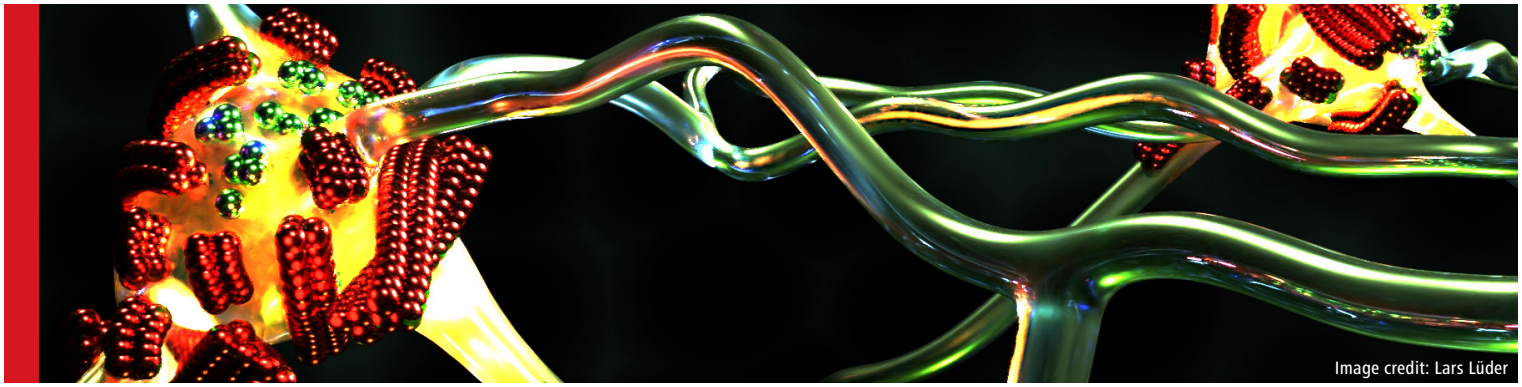
Image credit: Lars Lüder

Precision Medicine Research at Empa

Novel materials can be beneficial for a plethora of health and health care innovations in and on the human body. We develop and carry out cutting-edge research on new materials and systems to protect and support the human body and its function under different environmental conditions and in different health states. For this, we need to understand and steer materials-biology interactions on the level of biomolecules, bacteria, human cells and tissues from the nano- to the macroscale using state-of-the art and specifically designed analytical equipment. At Empa, we are capable of combining expertise of various imaging techniques, especially for the biomedical sector in collaboration with different Swiss hospitals.

Recent developments in imaging offer a new route to an improved diagnosis and a better analysis of a number of diseases. The global, longer-term vision of our research is to develop a holistic analysis workflow using such multi-level data integration for improved disease understanding in precision medicine. The major benefit of our multi-level data integration approach is a holistic understanding of diseases, which allows highly personalized treatments and follow-up procedures. The Technology Briefing "Personalized Health and Related Technologies (PHRT)" will help broaden the understanding of how we can improve collaboration with Swiss hospitals, through the support of the ETH Domain's Strategic Focus Area PHRT.

Program

14:00 **Welcome and Introduction**
Claudia Gonzalez, Empa Akademie

14:05 **PHRT Personalized Health and Related Technology – A Program of the ETH-Domain**
Francois Curtin, GeNeuro SA

14:45 **Precision Medicine Research at Empa**
Alex Dommann, Head of Department "Materials meet Life"

15:10 **Lab-on-Fiber: Fluorescence and Colorimetric Sensors for the Monitoring of Wounds and Other Diseases**
René Rossi, Head of Laboratory for Biomimetic Membranes and Textiles

15:35 **Assessing Bone Proteotype and Extracellular Matrix Properties for Improved Fracture Strength Prediction**
Johann Jakob Schwiedrzik,
Group Leader Architectured Materials

16:00 **Coffee break**

16:30 **A Mineralomics Approach to Personalized Medicine**
Elena Tsolaki, Postdoctoral Researcher at Empa

16:55 **Multi-Modal, Multi-Scale X-Ray Analytical Imaging Methods to Enhance Precision Medicine**
Robert Zboray, Group Leader X-ray Imaging

17:20 **Wrap-up, Closing**
Alex Dommann, Head of Department "Materials meet Life"

Lab-on-Fiber: Fluorescence and Colorimetric Sensors for the Monitoring of Wounds and Other Diseases

R.M. Rossi, Luciano Boesel
Laboratory for Biomimetic Membranes and Textiles
Empa, Swiss Federal Laboratories for Materials Science and Technology, St. Gallen, Switzerland

Fiber-based wearable devices show a high potential for unattended long-term monitoring of body parameters and early recognition of health problems. They can also be used as real-time feedback loop for the verification of treatments efficacy. However, in order to be used for medical purposes, these wearables have to be as reliable and precise as the gold standards used in hospitals. A very promising application of such fiber-based sensors is the monitoring of wounds, as the management of chronic and acute wounds remains very challenging. Available methods based on visual signs and symptoms provide limited accuracy and strongly rely on the practitioner's experience; moreover wound care technologies lack sufficient evidence of their impact to objectively support their utilization.

With the use of microfluidics or wet spinning technologies, multicomponent fibers incorporating fluorescent moieties or bioactive materials can be developed. Such sensing fibers can be used to measure different chemical quantities for non-invasive fluid monitoring (e.g. wound exudate or sweat): pH, glucose, lactate, different proteins or even volatile organic compounds. In this presentation, we will report our recent developments on fiber-based sensors, to realize a non-invasive multisensing platform for monitoring metabolites.

Assessing Bone Proteotype and Extracellular Matrix Properties for Improved Fracture Strength Prediction

PI: Dr. Jakob Schwiedrzik, *Empa*
Co-PIs: Prof. Philippe Zysset, *University of Berne;* **Prof. Klaus-Arno Siebenrock,** *Inselspital*

As modern societies age, the increasing number of fractures poses a challenge for health care systems worldwide. Hip fractures are especially deleterious, as they lead to a loss of mobility and show an increased mortality. Whole bone strength depends on bone mineral density measured by clinical densitometry, but also on the tissue quality resulting from a continuous remodeling of the bone extracellular matrix. It is therefore important to study structure-property relationships in bone at several length scales and combine this with complementary proteomics information in order to identify changes in tissue quality with age and in the presence of diseases such as osteoporosis or osteoarthritis.

Together with our partners at the University of Bern and the Inselspital, we established a novel methodology on bovine bone samples. We investigated the effect of local microstructure, especially mineralized collagen fibril (MCF) orientation, on the microscale mechanical properties of isolated bone lamellae. The combination of polarized Raman spectroscopy and micropillar compression made it possible to detect changes in mechanical properties with the bone MCF orientation, which allows us to reliably determine structure-property relationships of bone at the lamellar level (Kochetkova et al., Acta Biomat 2020). We furthermore combine microscale mechanical and compositional analysis with higher scale morphological characterization for bone quality estimation of three mini pig genotypes frequently used in dental research. For this we combine microscale mechanical testing: nanoindentation and pillar compression, with compositional analysis using Raman spectroscopy and structural characterization using micro Computed Tomography (micro-CT) scans. By performing a set of site-matched multiscale measurements, we are able to correlate the output parameters within and between the different genotypes.

The main study on femoral neck biopsies of patients who went total hip replacement surgery combines the multiscale analysis methods developed in the previous studies. The mesoscale morphology of the biopsies is assessed using micro-CT. Tissue quality is evaluated by identifying structure-property relationships on the microscale based on site-matched polarized Raman spectroscopy and micromechanical compression experiments. This knowledge is complemented by proteomics measurements to gain information on the bone extracellular matrix protein composition within the tissue. It is finally assessed by machine learning approaches if knowledge of proteotype and microscale structure-property relationships may help to estimate femoral strength of individual patients at higher accuracy and reliability.

A Mineralomics Approach to Personalized Medicine

Dr. Elena Tsolaki, *Empa*

Pathological mineralization of soft tissues is a well-known yet poorly understood clinical phenomenon associated with a range of diseases from cancer to cardiovascular and neurological pathologies. The minerals observed have been reported in older studies to be usually formed by calcium phosphates, while more recent research work has highlighted an enormous diversity in their crystallinity and microscopic structure. However, despite the high abundance of such minerals, in-depth nano analytical characterization of their properties has not been carried out in most cases, and their clinical significance has not been elucidated.

In this work, we seek to establish a cascade that allows the holistic analysis of minerals present in clinical specimens by applying advanced material characterization methods to address a specific clinical problem. We have demonstrated the significance of such an approach in two fields; breast cancer and aortic valve stenosis. In breast cancer, we seek to understand the types of mineral deposits present in different types of breast tissue biopsies and evaluate the prospect of correlating specific mineral properties with tumour malignancy. On the other hand, for aortic valve stenosis, the detailed characterization of native and bioprosthetic aortic valves will aid our understanding of the disease mechanisms and how calcification of native valves compares to that of bioprosthetic ones causing their failure.

In our view, data collected on the mineral deposits in soft tissue has the prospect to yield a disease- and patient-specific fingerprint, which is complementary to traditional clinical analyses already implemented. Such a mineralomics approach can impact clinical practice on an individual patient's basis, improve diagnosis, and provide new insights into diseases aetiology and mechanisms, allowing researchers to develop new preventive and curative measures for different patient subpopulations.

Multi-Modal, Multi-Scale X-Ray Analytical Imaging Methods to Enhance Precision Medicine

Robert Zboray, Alex Dommann and **Antonia Neels**
Centre for X-ray Analytics, Department Materials Meet Life,
Swiss Federal Institute for Material Science and Technology, Empa

Multi-modal, energy- and phase-sensitive X-ray microscopy combined with X-ray diffraction techniques can offer capabilities way beyond conventional, state-of-the-art clinical imaging methods (CT, MRI). Integrating these methods into the clinical workflow will open up unprecedented new opportunities for the analysis of soft tissue samples and biopsies. One very promising technique is high-resolution, virtual and unstained histopathology and tissue analysis. It can outperform standard clinical slice histology by being 3D, non-invasive and free of chemicals reflecting the uncompromised native tissue structures without the bias typical of histology slices (site, chemistry, cutting). Combined with X-ray diffraction analytical techniques, it will deliver spatial and molecular resolution that may give access to novel information of prognostic and predictive value. The virtual histopathology scanning also enables a non-compromised further use of the sample for further molecular analyses. These downstream analyses may involve (multi)omics approaches unravelling molecular fingerprints. The large size of the feature-rich datasets requires a multi-level data integration framework based on modern data science methods. The global, longer-term vision of our research is to develop a holistic tissue analysis workflow using such multi-level data integration for improved disease understanding in precision medicine.

In this talk, we will highlight two examples, where multi-modal and multilevel X-ray methods are applied for PHRT: one is non-invasive, unstained 3D digital histopathology and tissue mapping for thyroid tumors as a showcase for our holistic approach. The outcome of this project will be genuinely new 3D non-invasive tumor tissue analysis tools for the clinical use with a significant impact on personalized, targeted therapy and follow-up of thyroid carcinoma patients. The other one involves multi-level radiomics analysis of intravascular clots in acute stroke patients to establish a computer aided tool to support a personalized treatment decision making by high-fidelity outcome prediction for thromboectomy.