International Conference on Engineering for Life Sciences

ENROL 2025

June 29 – July 3, 2025 | Vienna, Austria

Book of Abstracts

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Contents

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General Information

Local Organizing Committee

- Ioanna Giouroudi (Technische Universität Wien, Austria)
- Gerhard Schütz (Technische Universität Wien, Austria)
- Gerhard Kahl (Technische Universität Wien, Austria)
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- Eva Sevcsik (Technische Universität Wien, Austria).

Chair of ENROL Conference 2025	Ioanna Giouroudi
Chair International Scientific Committee	Wilfred G. van der Wiel
Chair Technical Program Committee	Gerhard Kahl
Co-Chair of ENROL Conference 2025	Gerhard Schütz
Co-Chair International Scientific Committee	Verónica Martins

Venue:

The conference will take place at TU Wien, Karlsplatz 13, 1040 Wien.

Introduction

It is with great pleasure that I welcome you to the **1st International ENROL - Engineering for Life Sciences 2025 Conference**, hosted in Vienna.

ENROL marks the beginning of a new platform for exchange across disciplines, where engineering, biology, and the life sciences come together. With its single-track format, this conference is designed to facilitate real conversations and meaningful collaboration.

The idea for ENROL grew from a shared belief: that by bringing together researchers, professionals, and early-career scientists from different backgrounds, we can better tackle the complex challenges of our time, whether relating to health, sustainability, or the development of innovative technologies for life sciences.

As Chair of this first edition, I am proud of the diverse and thought-provoking program we have assembled. This **Book of Abstracts** reflects the range of ideas and perspectives that make this community so exciting. I hope it will ignite new ideas and meaningful conversations.

A heartfelt thank you to the ENROL 2025 Committees, our invited speakers, session chairs, reviewers, the organizing and technical teams, volunteers, and all of you who contributed with your time, ideas, and enthusiasm. Your commitment made this event possible.

On behalf of the organizing team, I wish you a rewarding and enjoyable conference.

Warm regards,

Priv.-Doz. Dr. Ioanna Giouroudi
Head TU Wien Doctoral School
Senior Scientist

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 101034277

Sunday, June 29, 2025

16:00 - 19:00 **Registration and Welcome Reception**
Location: **Festsaal (AA0148)**

Monday, June 30, 2025

8:15 - 8:45 **Registration**
Location: **Festsaal (AA0148)**

9:00 - 9:15 **Opening Remarks**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**

9:15 - 10:30 **Machine Learning & Modeling in Life Sciences**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Gerhard Kahl**

9:15 - 10:00
Information Processing in Intelligent Matter
Wilfred Gerard van der Weil

10:00 - 10:15
Liquid Capacitance-Extended Neural Circuits: Synaptic Activation and Dual Liquid Dynamics for Interpretable Bio-Inspired Models
Monika Farsang, Radu Grosu

10:15 - 10:30
Deep Learning for Automating the Immunophenotyping Assessment in Childhood Acute Leukemia Diagnosis
Elpiniki Maria Lygizou, Michael Reiter, Margarita Maurer-Granofszky, Michael Dworzak, Radu Grosu

10:30 - 11:00 **Coffee Break**
Location: **Festsaal (AA0148)**

11:00 - 12:15 **Machine Learning & Modeling in Life Sciences**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Radu Grosu**

11:00 - 11:15
Training of a "smart" triangular swimmer with the help of genetic algorithms
Ruma Maity, Maximilian Hübl, Julian Lemmel, Benedikt Hartl, Gerhard Kahl

11:15 - 11:30
Non-equilibrium Phase Separation Dynamics Under Shear and Transport Properties in a Binary Mixture of Ultrasoft Particles
Tanmay Biswas, Gerhard Kahl, Gaurav P. Shrivastav

11:30 - 11:45
Free Energy Computation and Phase Behavior of Bent-Core Patchy Colloids for Potential Biomedical Applications
Jenis Thongam, Emanuela Bianchi, Eva Gonzalez Noya, Anuj Kumar Singh, Arunkumar Bupathy, Varsha Banerjee, Gerhard Kahl

11:45 - 12:00
Gas-liquid phase separation, bonding valence and charge heterogeneity
Daniele Notarmuzi, Emanuela Bianchi

12:00 - 12:15

Equilibrium phase behavior of heterogeneously charged nanoparticles

Vanessa Schweidler, Eva G. Noya, Daniele Notarmuzi, Gerhard Kahl, Emanuela Bianchi

12:15 - 12:30 **Biophysics & Tissue Engineering**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Gerhard J. Schütz**

12:15 - 12:30

Injectable scaffolded spheroids to promote nucleus pulposus regeneration in degenerated intervertebral discs

Rathina Vel Balasubramanian, Marcia Mürner, Sibylle Grad, Julia Fernández-Pérez, Aleksandr Ovsianikov

12:30 - 13:30 **Lunch**
Location: **Festsaal (AA0148)**

13:30 - 15:00 **Biophysics & Tissue Engineering**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Gerhard J. Schütz**

13:30 - 14:15

Emulsion templated scaffolds for cell culturing

Peter Krajnc

14:15 - 14:30

Bioprinting of immunogenic skin model for psoriasis

Andrea Ulloa-Fernández, Lisa Kleissl, Georg Stary, Marica Marcovic, Julia Fernández-Pérez, Aleksandr Ovsianikov

14:30 - 14:45

An innovative bioartificial graft system

Cornelia Blume, Krueger Jana, Renzelmann Hannis, Heene Sebastian, Loewner Sebastian, Stanislawski Nils, Holger Blume

14:45 - 15:00

Mechanical stimulation using custom-made bioreactors or shockwaves to trigger tissue formation and regeneration

Andreas Teuschl-Woller

15:00 - 15:30 **Coffee Break**
Location: **Festsaal (AA0148)**

15:30 - 15:45 **Biophysics & Tissue Engineering**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Franziska Chalupa-Gantner**

15:30 - 15:45

Towards the Evaluation of Toxic Compounds in In Vitro Blood-Brain Barrier Models for Safety and Sustainability Assessments within the CHIASMA Project

Duygu Turan Sorhun, Anna Kruselj, Katrin Panke, Andreas Brachner, Winfried Neuhaus

15:45 - 17:00 **Biophysics & Bioimaging**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Markus Valtiner**

15:45 - 16:00

Antigen binding kinetics and organization for effective T-cell activation

Anežka Májková, Joschka Hellmeier, René Platzer, Vanessa Mühlgrabner, Caroline Kopittke, Johannes Huppa, Gerhard Schütz, Eva Sevcsik

16:00 - 16:15

A Closer Look at the Dynamics of T Cell Receptor Microclusters

Neetu Rajendran, Gerhard J Schütz

16:15 - 16:30

Standardizing Immunothrombotic Blood Cell Aggregate Diagnostics with Quantitative Phase Imaging Flow Cytometry for Acute Care Diagnostics

Muhammad Mohsin Malik, Marco Schernthaner, Martin Knoop, Ellen Emken, Manuel Lengl, Simon Schumann, Stefan Holdenrieder, Zsuzsanna Wolf, Oliver Hayden

16:30 - 16:45

The physics of highly crosslinked cytoskeletal networks

Sebastian Fürthauer, Cédrik Barutel

17:45 - 17:00

Improving the Resolution of Single-Molecule Localization Microscopy by Leveraging Spatiotemporal Information

Fatemeh Valeh, Gerhard Schütz, Radu Grosu

18:30 - 22:30 **Keynote Event**

Location: **Wien Museum (Karlsplatz 8, 1040 Vienna)**

18:30 - 19:00

Reception

19:00 - 20:00

A journey from race cars to respiratory research

Josue Sznitman

20:00 - 22:30

Standing reception with drinks and flying buffet

Tuesday, July 1, 2025

9:00 - 10:30 **Biochemistry & Biomolecular Engineering**

Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**

Chair: **Christian Dank**

9:00 - 9:45

Universally Applicable Surface Functionalization Chemistries

George Tsekenis

9:45 - 10:00

BioSWITCH: Expanding Iontronic Drug Delivery Through Bioorthogonal Click-to-Release Strategies

Sebastian Hecko, Nikolaus Poremba, Sebastian Schnöll, Christian Bayer, Marle Vleugels, Donghak Byun, Moa Hörberg, Rassen Boukraa, Daniel Simon, Magnus Berggren, Linda Waldherr, Hannes Mikula, Johannes Bintinger

10:00 - 10:15

On the trail of Gliflozins' secret to cardioprotective effects

Julia Höhlschen, Émilie Gosset, Dominik Hofreither, Tamara Tomin, Ruth Birner-Grünberger

10:15 - 10:30

Bioorthogonal tools for accelerated click-triggered cleavage and dual-release

Nithyashree Babu, Hannes Mikula, Jonathan Carlson

10:30 - 11:00 **Coffee Break**

Location: **Festsaal (AA0148)**

11:00 - 12:30 **Biochemistry & Biomolecular Engineering**

Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**

Chair: **Ruth Birner-Gruenberger**

11:00 - 11:15

Synthesis of Quinolinone Compounds with Potential Kinase Inhibitory Activity for the Treatment of Respiratory Diseases

Cesar Eduardo Gutierrez Quevedo, Christian Dank

11:15 - 11:30

Exploring the HOG Pathway Mediated Stress Response in Aureobasidium pullulans

Zainab Abdul Qayyum, Robert L Mach, Astrid R Mach-Aigner, Christian Zimmermann

11:30 - 12:15

Beeswax particles with S-layer Functionality for Biomedical Applications

Andreas Breitwieser, Sonja Zayni, Uwe B. Sleytr, Darren Tan, Eva-Kathrin Ehmoser

12:15 - 12:30

Elucidating Stress Response Mechanisms in Trichoderma reesei: Insights into Unfolded Protein Response and Repression under Secretion Stress

Reshma Kailash Jadhav, Robert L. Mach, Sharief Barends, Igor Nikolaev, Astrid Mach-Aigner

12:30 - 13:30 **Lunch**

Location: **Festsaal (AA0148)**

13:30 - 15:00 **Poster Session**

Location: **Prechtlsaal (AAEG18)**

P1 **Microfluidic Engineering for the Development of Ozonized Oil Microemulsions Aimed at Canine Leishmania Treatment: Implementation of 3D Skin Models**

Inês MC Lopes, Vitória Tavares, Débora Cerqueira, Juliana Weber, Micheli Ferla, Liege Martins, Elisa Cimetta, Sara Micheli, Eleonora Zanrè, Vinicius RC Souza, Gabriela Santos-Gomes, Armanda Rodrigues, Verónica C Martins

P2 **Computational and Mathematical Modeling for Describing Biological Systems – Application in Pharmacology and Biomedicine**

Mihajlo Marković, Darija Obradović, Sofija Stanimirović, Andrey N. Stavrianidi, Saša Lazović, Oleg A. Shpigun

P3 **Laser surface functionalization of biomedical Ti-TiB2 composite in different gas atmospheres**

Richard Antala, Peter Šugár, Jaroslav Kováčik, Jana Šugárová, Filip Ferenčík

P4 **Classification of Leukocyte Subtypes Using Digital Holographic Microscopy**

Muhammad Mohsin Malik, Bartu Schimschek, Martin Knoop, Manuel Lengl, Simon Schuman, Stefan Röhrl, Oliver Hayden

P5 **Enhanced Liver-Targeted Gene Delivery through Rational Engineering of AAV8 Capsid Mutants**

Thi Thuy Tien Vu, Jinsung Yang

P6 **Advanced Polymers for Biomaterials and 3D Printing**
Chrissie Baltzaki, Danijela Bogdanovic, Barbara Dellago, Antonella Fantoni, Tina Gurmann, Carola Haslinger, Sarah Nistler, Raffael Reichsöllner, Lisa Sinawehl, Anna Schmidbauer, Patrick Steinbauer, Anna Zahoranova, Stefan Baudis

P7 **Exploring Binary Cluster Crystals via Molecular Dynamics Simulations**
Vanessa Schweidler, Gerhard Kahl

P8 **Hydrodynamics and Chemotaxis of Active Chiral Rotors**
Ruma Maity, Snigdha Thakur, P. Sekhar Burada

P9 **Phase Separation Dynamics in a Symmetric Binary Mixture of Ultrasoft Particles**
Tanmay Biswas, Gerhard Kahl, Gaurav P. Shrivastav

P10 **Investigating Displacement-Controlled Stimulation Profiles in the MagneTissue Bioreactor through Force-Controlled Testing**
Felix Groß, Ekaterina Oleinik, Lune Teplitchi, Andreas Herbert Teuschl-Woller, Philipp J. Thurner

P11 **Integration of Bioorthogonal Chemistry into Iontronically Controlled Drug Release Systems**
Nikolaus Poremba, Sebastian Hecko, Sebastian Schnöll, Christian Bayer, Marle Vleugels, Donghak Byun, Moa Hörberg, Rassen Boukraa, Daniel Simon, Magnus Berggren, Linda Waldherr, Hannes Mikula, Johannes Bintinger

P12 **A Strain-inducing Bioreactor to Mature Muscle and Peripheral Nerve Tissue In Vitro**
Carina Hromada, Dorota Szwarc-Hofbauer, Janine Tomasch, David Hercher, Andreas Teuschl-Woller

P13 **Phase Transitions in Bent-Core Patchy Colloids: A Free Energy Perspective**
Jenis Thongam, Emanuela Bianchi, Eva Gonzalez Noya, Anuj Kumar Singh, Arunkumar Bupathy, Varsha Banerjee, Gerhard Kahl

P14 **Flexible Inkjet-Printed Electrodes for Extracellular Neural Signal Recordings and Electrical Stimulation**
Amelie Ziller, Günther Zeck

P15 **Influence of Stent Strut Thickness on Local Hemodynamics and Vascular Cell Response**
Veronica Viola, Margit Gföhler, Thomas Czerny

P16 **Surface modifications of chitosan coatings with femtosecond laser pulses**
Peter Andras Viragh, Roland Fürbacher, Marianne Raith, Sabine Gruber, Andreas Otto

P17 **Thermodynamic consistent theory of crosslinkers on biological filaments**
Cedrik Marius Andre Barutel

P18 **Ceramic-fiber reinforced photopolymers: Enhanced interfacial strength by modification of surface properties**
Philipp Schlossgangl, Jürgen Stampfl, Ioanna Giouroudi, Marianne Raith, Aleksandr Ovsianikov

P19 **Immune responses to biomaterials**
Christina Winter, Ines Swoboda, Andreas Otto, Sabine Gruber

P20 **Morphological and Functional Analysis of Alpha versus Non-Alpha Retinal Ganglion Cells**
Viktoria Kiraly, Günther Zeck, Paul Werginz

P21 **Are energy storing and positional equine tendons made of the same fibrils?**
Magdalena Fuchs, Orestis G. Andriotis, Philipp J. Thurner

P22 **Characterization of Flow Behavior Around Sinusoidal Fibers with Blood-Mimicking Fluids**
Jing Jing Xu, Seyyed Hossein Monsefi, Michael Harasek, Margit Gföhler

P23 **Adaptable, Rapid, and Simple Sensing of Cellular Oxygen Consumption in Microfluidic Systems for Point-of-Care Diagnostics**
Nicole Eger, Max Schimpf, Martin Frauenlob, Torsten Mayr, Peter Ertl

15:00 - 15:30 **Coffee Break**
Location: **Festsaal (AA0148)**

15:30 - 16:00 **Biochemistry & Biomolecular Engineering**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Franziska Chalupa-Gantner**

15:30 - 15:45
Advancing Unambiguous Image Detection and Bioorthogonal Intervention of Cellular Senescence
Fatima Yaghi, Florian Gruber, Hannes Mikula, Martina Marchetti-Deschmann

15:45 - 16:00
Confirmation of Jarzynski's equality based on single molecular and macroscopic interaction force measurements
Iago Peters, Markus Valtiner

16:00 - 17:00 **Lab & Organ-on-a-Chip Technologies, Biomicrofluidics**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Hannes Mikula**

16:00 - 16:45
High-Throughput Roll-to-Roll Manufacturing of Foil-Based Microfluidic Chips for Scalable Diagnostics
Anja Haase, Martin Smolka, Laura Angermann-Krammer, Pakapreud Khumwan, Maria R. Belegratis

16:45 - 17:00
Temperature Control System for Multi-Cavity Acoustofluidic Platform
Zhijin Li, Qian Liu, Martin Brischwein, Shilpi Pandey, Oliver Hayden

Wednesday, July 2, 2025

9:00 - 10:30 **Lab & Organ-on-a-Chip Technologies, Biomicrofluidics**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Sonia Prado López**

9:00 - 9:45
Lab-on-PCB technology
Despina Moschou

9:45 - 10:00
Towards individualised treatment of urinary tract infections
Ellen Veronika Stadler, Alison Holmes, Timothy Miles Rawson, Danny O`Hare

10:00 - 10:15
Yeast enrichment using microfluidic deterministic lateral displacement (DLD)
Violina B. Barbosa, Laura Cerqueira, João M. Miranda, Nuno F. Azevedo

10:15 - 10:30
Guided vascularization in organs-on-chip using High-Definition laser patterning
Alice Salvadori, Masafumi Watanabe, Marica Markovic, Ryo Sudo, Aleksandr Ovsianikov

10:30 - 11:00 **Coffee Break**
Location: **Festsaal (AA0148)**

11:00 - 12:00 **Antimicrobial Technologies and Innovative Delivery Systems**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Eva Sevcsik**

11:00 - 11:15
A TCO-masked iRGD-Fluorophore Conjugate is Activated via a Bioorthogonal Tz-Triggered click-to-release Reaction, Performed Under in-situ Conditions on a Microfluidic Chip.
Soumya Dafadar, Martin Wilkovitsch, Hannes Mikula, Peter Ertl

11:15 - 12:00
Development of Topical Ozone-Based Antimicrobials: A Promising Strategy Against Antimicrobial Resistance
Veronica Cristina Martins Romao

12:00 - 12:30 **Biosensors, Biomaterials & Biodevices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Heinz D. Wanzenboeck**

12:00 - 12:15
A Paper-Based Point-of-Care Diagnostic for Urinary Tract Infections and Antimicrobial Resistance Profiling
Sarah Wali, Henning Sabersky-Müssigbrodt, Azur Causevic, Oliver Hayden

12:15 - 12:30
Investigation of the Cytocompatibility of different Diazosulfonate-based and Water-soluble Photoinitiators for two-photon Polymerization
Thomas Schmidt, Franziska Chalupa-Gantner, Marica Markovic, Stefan Baudis, Robert Liska, Aleksandr Ovsianikov

12:30 - 13:30 **Lunch**
Location: **Festsaal (AA0148)**

13:30 - 15:00 **Biosensors, Biomaterials & Biodevices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Eugenijus Kaniusas**

13:30 - 14:15
Magnetic Biodevices
Jürgen Kosel

14:15 - 14:30
Multi-analyte magnetic sensing – from cells to vesicles and proteins
Moritz Leuthner, Mathias Reisbeck, Michael Helou, Florian Ehrmeier, Sanja Tosheska, Rafael Vorländer, Oliver Hayden

14:30 - 14:45
Field Potential-impedance recording of doxorubicin induced cardiotoxicity in human cardioids
Neda Karami, Sebastian Knafl, Amra Mujadzic, Seyda Kigili, Fatemeh Azizian Farsani, Sasha Mendjan, Heinz D. Wanzenboeck, Sonia Prado-Lopez

14:45 - 15:00
Biosensors for the detection of allergens
Ines Swoboda

15:00 - 15:30 **Coffee Break**
Location: **Festsaal (AA0148)**

15:30 - 16:15 **Biosensors, Biomaterials & Biodevices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Stefan Baudis**

15:30 - 16:15

The CellFACE platform for label-free blood cell function and cytology diagnostics at the point-of-care using phase imaging flow cytometry
Oliver Hayden

16:15 - 17:00 **Biomechanics & Biomedical Devices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Philipp J. Thurner**

16:15 - 17:00

Potential Roles for Lymph Node Fluid and Mass Transport in Immunology
James Moore, Daniel Watson, Jennifer Frattolin

19:30 - 24:00 **Conference Dinner**
Location: **Zwölf Apostelkeller (Sonnenfelsgasse 3, 1010 Vienna)**

Thursday, July 3, 2025

9:00 - 10:30 **Biomechanics & Biomedical Devices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Philipp J. Thurner**

9:00 - 9:45

Rigidity Transition in Epithelial Tissues
Jan Rozman, Matej Krajnc, Primož Ziherl

9:45 - 10:00

Comparative analysis of static and cyclic mechanical stimulation for tendon tissue engineering
Ekaterina Oleinik, Büsra Külekci, Andreas H. Teuschl-Woller, Philipp J. Thurner

10:00 - 10:15

Development of a Digitalized Spacer for Longitudinal Monitoring of Infection in Two-Stage Total Joint Replacement
Christoph Dillitzer, Nguyen Bach Tran, Paul Morandell, Andreas Obermeier, Rainer Burgkart, Oliver Hayden

10:15 - 10:30

Micromechanical Assessment of Cardiac Spheroids
Dimosthenis Giannopoulos, Maja Schlittler, Marzia De Bortoli, Raffaele Coppini, Mina Petrovic, Elisabetta Cerbai, Gerhard J. Schütz, Philipp J. Thurner, Alessandra Rossini, Orestis G. Andriotis

10:30 - 11:00 **Coffee Break**
Location: **Festsaal (AA0148)**

11:00 - 12:00 **Biomechanics & Biomedical Devices**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Orestis G. Andriotis**

11:00 - 11:15

Uniaxial Tensile Loading of the Single Collagen Fibril: How to Test it and How to Model it?
You-Rong Chiang, Orestis G. Andriotis, Claire Morin, Christian Hellmich, Philipp J. Thurner

11:15 - 12:00
Learning tissue engineering principles from axolotl regeneration
Wouter Masselink

12:00 - 12:30 **Sustainable Engineering & Environmental Sustainability**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Ioanna Giouroudi**

12:00 - 12:15
Nano-engineered Materials for Wastewater Remediation
Ajay Kumar Mishra

12:15 - 12:30
CO2 conversion to CO by Fluidized Bed Biomass Gasification
Florian Müller, Franz Winter, Stefan Müller, Josef Fuchs

12:30 - 13:30 **Lunch**
Location: **Festsaal (AA0148)**

13:30 - 15:00 **Sustainable Engineering & Environmental Sustainability**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Sebastian Fürthauer**

13:30 - 14:15
New era of plasma engineering for the design of catalyst in biomass upgrades
Oi Lun Helena Li

14:15 - 15:00
An overview of Sol Gel Technology: Nanoscale methodology for industrial and environmental applications
Shivani Bhardwaj Mishra

15:00 - 15:30 **Coffee Break**
Location: **Festsaal (AA0148)**

15:30 - 16:15 **Sustainable Engineering & Environmental Sustainability**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**
Chair: **Sebastian Fürthauer**

15:30 - 16:15
Fungal secondary metabolites – from pharmaceuticals to toxins
Reinhard Fischer

16:15 - 17:00 **Closing Session**
Location: **Lecture Hall 17 – Friedrich Hartmann (AE0341)**

Keynote Speech

A journey from race cars to respiratory research

Dr. Josué Sznitman

Technion – Israel Institute of Technology, Israel

Dr. Josué Sznitman is the Dean of the Faculty of Biomedical Engineering at the Technion – Israel Institute of Technology, where he has been a Full Professor since 2023. Prior to joining the Technion in 2010, Josué earned a BSc in Mechanical Engineering from MIT (2002) and a Dr. Sc. from ETH Zurich (2008). Thereafter, he spent time as a Postdoctoral Researcher at the University of Pennsylvania and later moved to Princeton University as a Lecturer and Research Associate appointed by the Princeton Council of Science & Technology. With over 100 published journal articles and several patents to his record, Josué's research stronghold lies in the field of pulmonary bioengineering for translational endpoints in respiratory medicine, including drug delivery to the lungs. Among his accolades, Josué received the Young Investigator Award (2015) from the International Society of Aerosols in Medicine for a researcher under the age of 40 and the 2018 Emerging Scientist Award in Drug Delivery to the Lungs (The Aerosol Society, UK). Since 2019, he has served as an Associate Editor for the journal Clinical Biomechanics and was previously an Associate Editor for the Journal of Biomechanics. He sits on the Editorial Board of Biomicrofluidics and the European Journal of Pharmaceutical Sciences, and is a member of the World Council of Biomechanics.

Abstract

I will recount a personal journey that first brought me to study engineering driven by a kid's dream to pursue a career in automobile racing and enter the world of automobile aerodynamics – how air flows around the body of a car. Following a change of heart, the same curiosity for the physics of flows took me into an unexpected direction during my PhD to begin exploring breathing in our lungs, motivated by the delivery of inhalation aerosols for therapeutic treatments of the lungs. Since then, I have built my academic career around pulmonary research topics, with a special interest in pulmonary drug delivery and building lung models, using various 3D printing and microfluidics techniques. In this talk, I will exemplify some examples of biomedical engineering in the field of lung research and ongoing questions and research topics we have worked on over the past decade.

Corresponding/Presenting Author: Josue Sznitman, sznitman@bm.technion.ac.il.

Oral Sessions

Monday, June 30, 2025

Information Processing in Intelligent Matter

Wilfred G. van der Wiel [1,2]
[1]*BRAINS Center for Brain-Inspired Nano Systems, University of Twente, PO Box 217, 7500 AE, Enschede, The Netherlands*
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Throughout history, humans have harnessed matter to perform tasks beyond their biological limits. Initially, tools relied solely on shape and structure for functionality. We progressed to responsive matter that reacts to external stimuli and are now challenged by adaptive matter, which could alter its response based on environmental conditions. A major scientific goal is creating matter that can learn, where behavior depends on both the present and its history. This matter would have long-term memory, enabling autonomous interaction with its environment and self-regulation of actions. We may call such matter 'intelligent'[1,2].

Here we introduce a number of experiments towards 'intelligent' disordered nanomaterial systems, where we make use of "material learning" to realize functionality. We have earlier shown that a 'designless' network of gold nanoparticles can be configured into Boolean logic gates using artificial evolution [3]. We later demonstrated that this principle is generic and can be transferred to other material systems. By exploiting the nonlinearity of a nanoscale network of dopants in silicon, referred to as a dopant network processing unit (DNPU), we can significantly facilitate handwritten digit classification [4]. An alternative material-learning approach is followed by first mapping our DNPU on a deep-neural-network model, which allows for applying standard machine-learning techniques in finding functionality [5]. We also can optimize DNPUs by using gradient descent in materia, using experimental gradient extraction [6]. Finally, we show that our devices are not only suitable for solving static problems but can also be applied in highly efficient real-time processing of temporal signals at room temperature [7].

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Liquid Capacitance-Extended Neural Circuits: Synaptic Activation and Dual Liquid Dynamics for Interpretable Bio-Inspired Models

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Previous work investigated saturated Electrical Equivalent Circuits (EECs) [1] using either electrical or chemical synapses in sparse or fully connected wiring architectures [2]. These studies demonstrated that sparse topologies enhance interpretability and that chemical synapses outperform electrical synapses in robustness. Particularly, [2] compared chemical synapse-based Liquid Time Constant (LTC) networks [3] against electrical synapse-based Continuous-Time Recurrent Neural Networks (CT-RNNs) [4], both rooted in neural ordinary differential equations (Neural ODEs) requiring computationally intensive hybrid ODE solvers for precise integration.

Recent advances introduced a *liquid capacitance* term into biologically inspired saturated LTC models, yielding Liquid Resistance Liquid Capacitance (LRC) networks [5]. This modification was motivated by findings showing nonlinear dependencies of the membrane capacitance on input and state variables [5–7]. Unlike LTCs, LRCs exhibit smoother dynamics due to their input- and state-dependent capacitance-resistance terms, enabling simpler explicit Euler solvers (one-step integration) instead of costly hybrid methods while keeping interpretable dynamics [5].

Building on these foundations, we extend the liquid capacitance concept to electrical synapse models - termed **Liquid Capacitance (LC)** networks - and systematically analyze mixed architectures. By default, chemical synapses have an activation per synapse, and electrical synapses have an activation per neuron. To have a systematic analysis, we also consider mixed models, both LCs and LRCs.

- **LC-Neural Activation (LC-NA):** Biologically plausible extension of CT-RNNs [4] using liquid capacitance, with per-neuron activation.
- **LC-Synaptic Activation (LC-SA):** Non-biological variant introduced here to ablate interpretability via per-synapse activation.
- **LRC-Neural Activation (LRC-NA):** Hybrid model assuming uniform synaptic dynamics per neuron (plausible in some biological contexts).
- **LRC-Synaptic Activation (LRC-SA):** Biologically plausible default LRC [5], featuring per-synapse activation.

Model	Best Epoch	Validation Loss	Weighted Val. Loss	NTA Summer	NTA Winter
LC-NA	52 ± 14	0.173 ± 0.011	0.015 ± 0.0004	0.477 ± 0.243	0.428 ± 0.254
LC-SA	46 ± 4	0.163 ± 0.004	0.015 ± 0.0004	0.462 ± 0.273	0.533 ± 0.246
LRC-NA	34 ± 7	**0.139 ± 0.008**	**0.011 ± 0.0004**	**0.652 ± 0.293**	0.693 ± 0.292
LRC-SA	**22 ± 3**	0.142 ± 0.004	**0.011 ± 0.001**	**0.645 ± 0.321**	**0.766 ± 0.243**

Table 1: Validation and weighted-validation losses across models of a Lane Keeping task adapted from [2]. The final columns report Neural Trajectory Alignment (NTA), calculated as the absolute correlation between road trajectories and neuron activity patterns [2], where values closer to 1 indicate stronger correlation. LRC-NA and LRC-SA exhibit 1.5× higher correlation values than LC-NA/LC-SA variants.

Our analysis reveals two key insights:

1. Synaptic activation in LRCs (LRC-SA) enhances interpretability compared to neural activation (LRC-NA).
2. The dual liquid capacitance-resistance dynamics in LRCs improve interpretability over single-term LC models (fixed resistance with liquid capacitance), regardless of activation type.

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Deep Learning for Automating the Immunophenotyping Assessment in Childhood Acute Leukemia Diagnosis

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Acute leukemias are a heterogeneous group of hematologic malignancies characterized by rapid progression, making early and accurate diagnosis critical for effective treatment. These diseases are primarily classified based on the lineage of the affected precursor cells, which begin to proliferate uncontrollably. Immunophenotyping using Multiparameter Flow Cytometry (FCM) is a key diagnostic tool [1], which provides high-dimensional, multi-parameter analysis of individual cells essential for distinguishing between the lineages and phenotypes of childhood acute leukemia. However, immunophenotyping evaluation remains a labor-intensive and expert-driven process, making it susceptible to subjectivity and variability across clinical settings. To address these challenges, we explore deep learning methodologies based on self-attention mechanisms to automate and enhance immunophenotyping assessment.

Our approach is based on transformer-derived architectures tailored to unordered, high-dimensional tabular data, making them particularly well-suited for modeling flow cytometric data where feature ordering holds no intrinsic significance. In particular, we refine the Set Transformer framework [2] to better capture complex feature dependencies while preserving permutation invariance, aligning naturally with the structure of flow cytometric data. Additionally, we integrate specialized activation functions that enhance representational capacity and optimization stability, resulting in improved classification performance compared to previous deep learning approaches [3].

The model is trained in a supervised manner, directly utilizing raw FCM data without requiring manual preprocessing, allowing it to fully leverage the richness of the high-dimensional input space. Experimental evaluations on a diverse dataset demonstrate that our approach effectively distinguishes between major lineages of pediatric acute leukemia, offering a promising step toward automating hematologic diagnostics. The results indicate that leveraging self-attention enhances both classification accuracy and generalization across heterogeneous patient samples.

This study underscores the potential of deep learning-driven immunophenotyping to complement traditional diagnostic workflows, paving the way for more efficient and reproducible leukemia assessments in clinical practice.

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Training of a “smart” triangular swimmer with the help of genetic algorithms

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Various microorganisms in nature use diverse non-reciprocal swimming gaits in search of nutrition or prey or to escape predators. A very common strategy comprises non-reciprocal deformation of the shape, ensuring propulsion in the medium. Inspired by natural swimmers, efforts have been made to design artificial swimmers to perform specific tasks, such as targeted drug delivery in the case of nanomedical applications. In this work, we train a two-dimensional, triangular swimmer [1] to move in a desired direction using different propulsion gaits (see Fig.1). This training is achieved with adaptive neural networks (which connect the degrees of freedom and the forces acting on the swimmer), involving thereby the NEAT algorithm [2] which optimizes the internal architecture of these networks. While in the previous work a simple one-dimensional, linear three-bead swimmer was trained to swim in a chemical landscape [3], here we focus on the considerably more challenging case of the triangular swimmer (see Fig. 1(a)-(c)): flapping, chiral and walking respectively are three emergent non-reciprocal propulsion modes. Since in two dimensions, a simple reward, for example, displacement, cannot induce motility in the swimmer, and in the absence of a well-defined reward scheme, the swimmer either stays stationary or rotates in a circular path with no net displacement, it is important to introduce a complex reward scheme which is a function of instantaneous displacement, average displacement, angular displacement, shape factor. We also demonstrate that in this setup, the swimmer can be trained to propagate in a desired direction and to develop swimming gaits that allows to find nutrient in a chemical landscape. Similar as in Ref. [1], we are able to extract valuable information about the swimmer’s strategies by analyzing the internal structure of the emerging networks. Notably, the former emergent networks are simple in nature though visibly different for different swimming gaits.

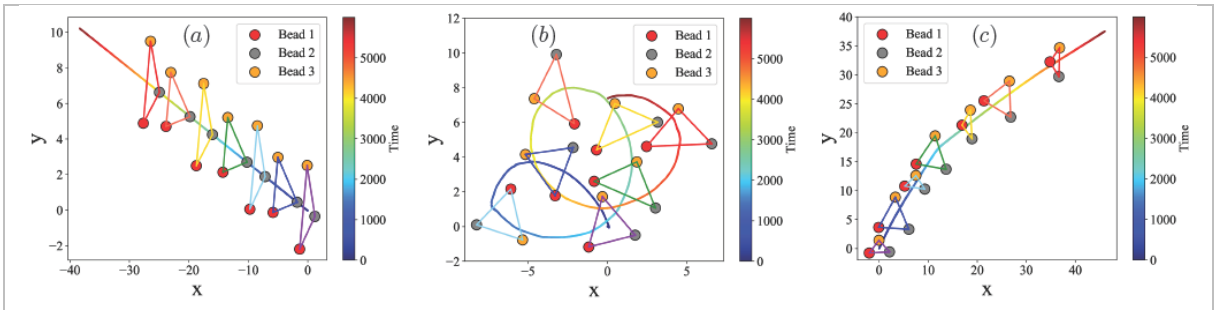

Fig. 1 Depicting trajectories of three different modes of propulsion of a triangular three beads swimmer (a) flapping, (b) chiral, (c) walking.

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Non-equilibrium Phase Separation Dynamics Under Shear and Transport Properties in a Binary Mixture of Ultrasoft Particles

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Phase separation plays a crucial role in determining the self-assembly of biological and soft matter systems. In the former case, liquid-liquid phase separation inside a cell leads to the formation of various macromolecular aggregates. The interaction among these aggregates is soft and the particles are generally modelled by ultrasoft particles [1-2]. We have studied the phase separation dynamics and the dynamical properties of a binary mixture of ultrasoft particles (species A and B with same concentration). Upon quenching from high temperature to below the critical temperature, the system undergoes a phase separation into an A-and a B-rich phase [1,3]. The domains of two components grow in a power-law manner (i.e. $l(t) \sim t^{\alpha}$ with exponent $\alpha = \frac{1}{3}$), consistent with the Lifshitz-Slyozov law [4]. In a subsequent step we have exposed the system – as it is cooled down to low temperatures - to shear. In presence of shear, the domains grow with exponents $\alpha = \frac{4}{3}$ and $\frac{1}{3}$ in the shear and the gradient direction, respectively. We also obtained self-diffusion coefficients from the Einstein relation and as well as from the Green-Kubo expression. The transport coefficient describing the collective transport, such as the viscosity is estimated [5]. In particular we have analysed the evolution of spatial inhomogeneities under shear and the transport phenomena.

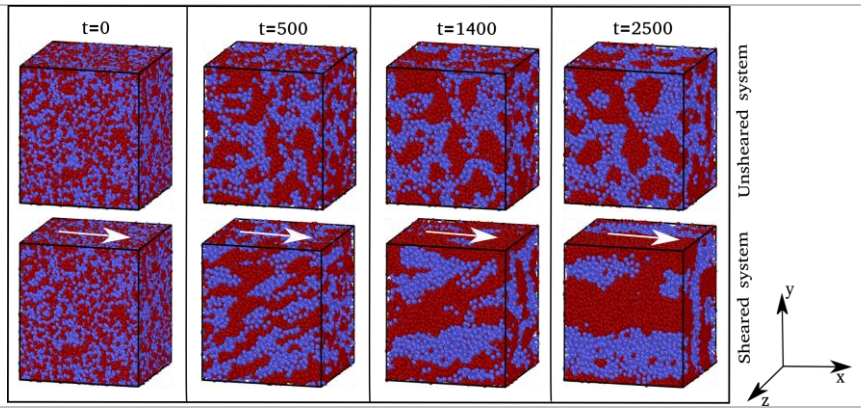

Fig. 1 Snapshots of the system at different time instants (as labelled) after having been quenched below the critical temperature. Upper panels: perspective views of snapshots of the system without shear. Lower panels: snapshots of system as exposed to external shear forces (in the direction of the white arrow).

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Free Energy Computation and Phase Behavior of Bent-Core Patchy Colloids for Potential Biomedical Applications

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We present a novel model of colloidal patchy ellipsoids [1] designed to study the self-assembly and phase behavior of bent-core liquid crystals [2], with potential applications in biomedical engineering, bio sensing, and nanotechnology. The system consists of a binary mixture of mirror-symmetric ellipsoids (left- and right-handed) interacting via a Gay-Berne potential and decorated with surface patches that guide a two-step assembly process. In the first stage, monomers form bent-core dimers with a specific bent angle, while the second stage leads to the emergence of mesoscopic liquid-crystal phases, including nematic, smectic, and twist-bend phases [3]. These phases exhibit unique optical and photonic properties, making them promising candidates for applications in biophotonics, biosensors, and lab-on-a-chip technologies.
Using molecular dynamics simulations, Monte Carlo methods, and advanced free energy calculations [4], we characterize the phase diagram of these systems, including transitions between isotropic, nematic, and smectic phases. Our approach employs thermodynamic integration [4] and the Einstein Molecule method [5] to compute free energies, providing insights into the stability and formation of these exotic phases. The model's flexibility allows for tuning parameters such as bent- core angle, interaction strength, and patch geometry [3], enabling the design of colloidal systems with tailored properties. This work has the potential to bridge the gap between soft matter physics and biomedical engineering, offering a computational framework to explore the phase behavior of patchy colloids and their role in advancing biotechnological innovations.

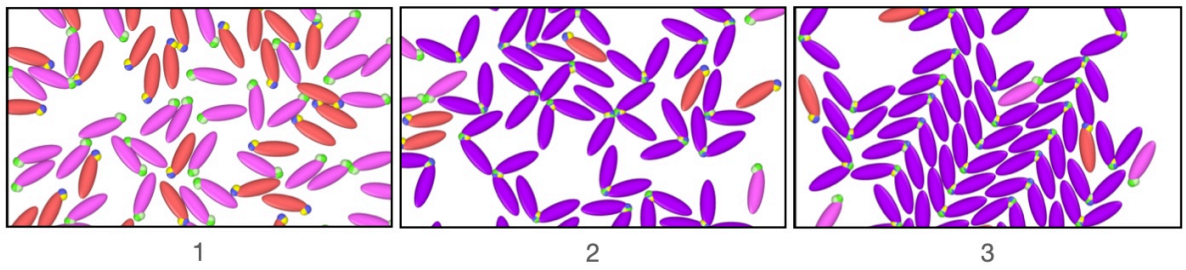

Fig. 1 Sketch of our two-step assembly process: from left- and right-handed ellipses (1), via the formation of bent-core particles (2), to the emergence of mesoscopic phases (3) under specific parameter combinations.

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Gas-liquid phase separation, bonding valence and charge heterogeneity

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Recently synthesized colloids as well as proteins and viral capsids have in common a reduced bonding valence and a complex interaction pattern dominated by like-charge attraction as well as opposite-charge repulsion [1,2]. The bonding valence is known to affect the condensation of the liquid phase [3] and the anisotropic nature of the interactions is often associated to a rich assembly behavior, leading to a wide range of ordered and disordered structures [4]. While the two aspects – bonding valence and particle charge heterogeneity – are often investigated separately, we want to understand what their combined effect is on the phase diagram. We numerically address this question in a systematic fashion by taking advantage of a relatively simple coarse-grained model grounded into a robust mean-field approach [5, 6]. We investigate how the charged patterns on the particle surface, the net particle charge and the screening conditions of the solvent where particles diffuse affect the critical point, the associated gas-liquid coexistence region and the gel phase. Our aim is to unveil the effect of the non-trivial interplay between attractive and repulsive directional interactions on the aggregation of the particles. Our results reveal how the geometry of the surface charge distribution and how the charge imbalance affect the location of the critical point in the phase diagram, the behavior of the binodal line and the properties of the gel. Results are fully understood by studying the properties of the particles individually and the structures they form when aggregating at or near criticality.

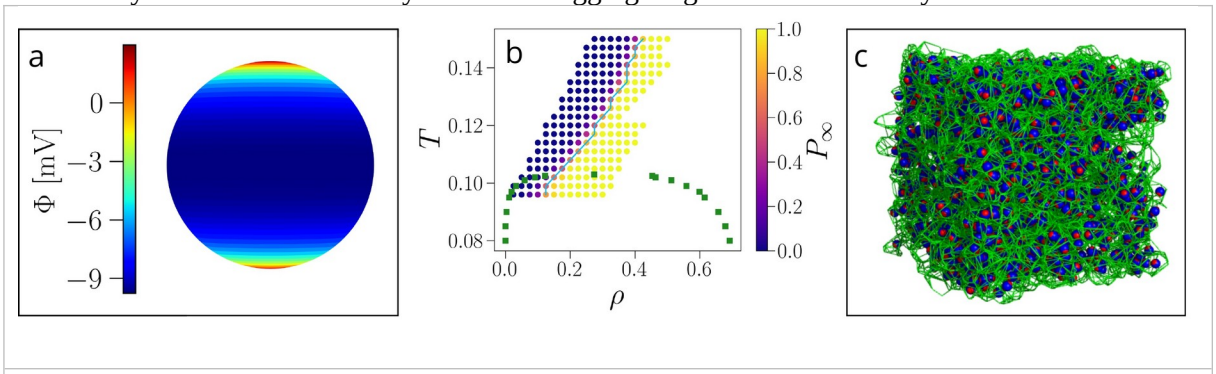

Fig. 1 (a) Mean Field electrostatic potential of a single particle. (b) Phase diagram of the corresponding coarse grain model. (c) Particles and Voronoi decompositon in the gel phase.

We acknowledge support from the Austrian Science Fund (FWF) under Project. No. Y-1163-N27.

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Equilibrium phase behavior of heterogeneously charged nanoparticles

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Colloidal particles with heterogeneously charged surfaces exhibit a complex interplay of electrostatic repulsion and attraction, resulting in direction-dependent interactions. Understanding the equilibrium phase behavior of such systems on a large scale is essential for advancing fundamental biological research and enabling the design of self-assembled nanostructures with tailored properties. Recent experimental studies have demonstrated that charge anisotropy can be engineered to guide self-organization in these systems [1].

To systematically investigate this phenomenon, we employ a coarse-grained model that, within well-defined limits [2], accurately reproduces the electrostatic potential derived from the linearized Poisson-Boltzmann framework [3]. This model is incorporated into Monte Carlo (MC) and Molecular Dynamics (MD) simulations, enabling a detailed exploration of how net charge and surface charge patterns influence phase behavior.

To analyze the stability and thermodynamics of these systems, we utilize Monte Carlo methods, thermodynamic integration, and the Einstein Molecule method to compute free energies [3,4]. Building on these established methods for phase diagram computation in molecular systems [5], we ensure precise predictions of fluid-solid and solid-solid phase equilibria.

By identifying stable equilibrium phases and phase transitions, our study provides critical insights into the self-organization mechanisms of charge-patchy nanoparticles. These findings contribute to the rational design of colloidal materials with tunable electrostatic interactions and complex self-assembled structures.

The computational results are obtained using the Vienna Scientific Cluster VSC (VSC). The authors acknowledge support from the Austrian Science Fund (FWF) under Project No. Y-1163-N27.

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Injectable scaffolded spheroids to promote nucleus pulposus regeneration in degenerated intervertebral discs

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Degeneration of the nucleus pulposus (NP) is the primary driver of degenerative disc disease (DDD), a condition that cannot be effectively treated or slowed using conventional open or minimally invasive surgical methods. To address this, we aimed to develop an injectable scaffolded spheroid [1] with optimal size, mechanical properties, and NP-specific phenotype to counteract NP degeneration.
We fabricated highly porous scaffolds (200 µm in diameter) using a custom-built two-photon polymerization (2PP) system based on a resonant scanner [2] with PCL-based resin (DEGRAD INX, BIO INX, Ghent, Belgium). These scaffolds were combined with human bone marrow-derived stromal cells to generate scaffolded spheroids (S-SPH), which were then induced to differentiate into an NP-like lineage using Growth and Differentiation Factor 5 (GDF-5) under hypoxic conditions. The biochemical and biomechanical properties of the engineered spheroids were thoroughly assessed, alongside the expression levels of NP-specific genes. Additionally, the injectability of the spheroids, with and without the scaffolds, was evaluated to determine their suitability for minimally invasive delivery.
The optimization of 2PP parameters enabled the fabrication of scaffolds with an elastic modulus of 160 ± 31 kPa. A seeding density of 2000 cells per spheroid was determined as optimal for scaffolded spheroid (S-SPH) formation, achieving a maximum Feret diameter of 213 ± 37 µm. During injectability assessments, S-SPH demonstrated superior metabolic activity (100 ± 26%) relative to non-scaffolded spheroids (SPH, 85 ± 12%), alongside reduced expression of stress-associated markers IL-6 and MMP13. GDF-5 effectively induced nucleus pulposus (NP)-like differentiation in S-SPHs, marked by elevated glycosaminoglycan synthesis, a ~135-fold increase in ACAN/COL2A1 expression, ~2-fold upregulation of KRT18, and suppression of the hypertrophic marker COL10A1 compared to TGFβ1-treated controls. Mechanically, GDF-5 stimulated S-SPH exhibited a significantly higher elastic modulus (91 ± 9 kPa) than SPHs (18 ± 14 kPa).
These results underscore the potential of S-SPH as robust, injectable microtissue units for NP regeneration, combining enhanced biomechanical properties, reduced stress response, and efficient differentiation capacity.

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Emulsion templated scaffolds for cell culturing

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Emulsion templating is a method for creating highly porous polymer monoliths with an interconnected hierarchically structured cellular internal morphology. When an emulsion with a high volume share of droplet phase (tipically over 74 %; termed high internal phase emulsion- HIPE) contains monomers in the continuous phase which are polymerised, after the removal of the droplet phase, a cellular interconnected porous monolith is produced, termed polyHIPE [1].
Typical polyHIPE morphology features up to several tens of micrometers sized primary pores, as a result of the droplet phase removal after the polymerisation of the continuous phase. Primary pores are usually interconnected with a series of secondary pores created during the polymerisation following phase transition and density alterations (Figure). The possibility of tuning the pore size and interconnectivity, as well as a wide range of possible chemistries, make polyHIPEs an attractive scaffold material for cell cultivation and proliferation. Recently, many examples of the application of polyHIPEs as tissue engineering scaffolds have been demonstrated [2]. The lecture will discuss the advantages and limitations of polyHIPEs as cell/tissue scaffolds as well as some recent upgrades using a combination of emulsion and hard sphere templating [3].

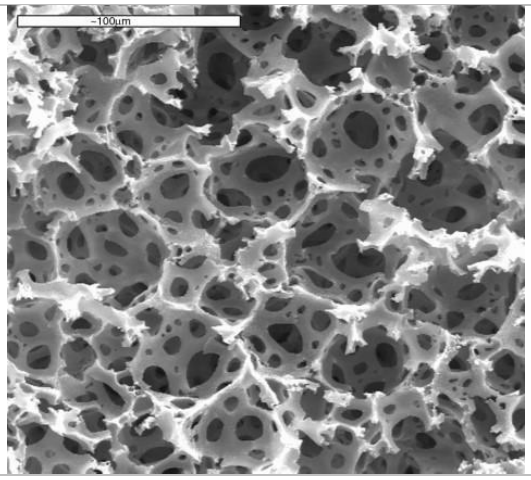

Fig. 1 Scanning electron micrograph of a polyHIPE monolith.

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Bioprinting of immunogenic skin model for psoriasis

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Psoriasis is a common chronic inflammatory skin disease driven by immune dysregulation. T cells and other immune cells activate pro-inflammatory cytokines, leading to keratinocyte hyperproliferation and psoriatic plaque formation [1]. Genetic predisposition, environmental factors, and microbiome imbalances contribute to disease progression. Current treatments manage active lesions but rarely achieve long-term remission due to the disease's relapsing nature. To investigate psoriasis pathomechanisms, preclinical mouse models—ranging from spontaneous mutations to transgenic and knockout models—have provided insights into cytokine and immune cell interactions [2]. However, there is growing interest in human-derived in vitro models as alternatives. Advances in tissue engineering and 3D printing have enhanced the complexity and precision of these models compared to traditional 2D models. Incorporating diverse immune cell subsets could further clarify disease mechanisms and aid in developing more effective treatments [3]. This work aims to use extrusion-based bioprinting techniques to create an immunogenic psoriasis model. The integration of Th17 immune cells, key drivers in psoriasis pathophysiology, enables the development of a more physiologically relevant system for studying disease progression.

To prepare the model, the biocompatibility of 5% (w/v) methacrylate gelatin (GelMA) was determined by measuring the metabolic activity and live and dead staining for 13 days, and T cells isolated from peripheral blood mononuclear cells (PBMCs) were polarized to Th17. To determine if the polarized T cells can produce the psoriatic phenotype, skin equivalents were manually cast or bioprinted in GelMA 5% (w/v) using an extrusion-based bioprinter (BioX^{TM}, Cellink). Immortalized human keratinocytes, NHEK/SVTERT 3-5 were seeded on top, and the equivalents were cultured in an air-liquid interface (ALI) for 11 days to induce epidermal differentiation with IL-2 supplemented medium. As a control, the psoriatic condition was induced on GelMA skin equivalents by adding IL 17A, IL 6, and IL 1β from day 1 of ALI. The produced constructs were fixed and analyzed by histology to perform immunostaining of the tissue markers cytokeratin 10, loricrin, filaggrin, cytokeratin 16, and Ki67.

The viability of the fibroblasts and T cells co-culture was maintained for 13 days, with an increase in metabolic activity from 50% to 65% between day 1 and day 6. Polarization to Th17 cells resulted in 15-20% of IL 17-producing cells, with around 45% of CCR6^{+} T cells. The T cell fraction containing the IL-17-producing cells maintained viability in the GelMA constructs after 13 days of co-culture. In the skin equivalents containing immune cells or treated with cytokines, there was an increase in the psoriatic markers Ki67 and cytokeratin 16, along with a reduction in filaggrin and cytokeratin 10 expression, compared to the healthy condition. The results suggest a disrupted differentiation and hyperproliferation of the keratinocytes toward a psoriatic-like phenotype. The functionality of these model that incorporates disease-associated immune cells makes a more accurate replication of the inflammatory microenvironment, enables a more precise replication of the inflammatory microenvironment, and improves their relevance for studying immune-mediated skin conditions.

This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 101034277.

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An innovative bioartificial graft system

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Our aim is to develop an optimized manufacturing process for bioartificial vascular prostheses. Such tissue-engineered vascular grafts (TEVGs) should preferably be produced as a biohybrid based on a non-immunogenic scaffold structure. For this purpose, biodegradable scaffold structures from 3D printing made of a biodegradable polymer such as polycaprolactone are used, which are colonized with immune-neutral cells and can be exposed to further spontaneous colonization by monocytic cells circulating in the recipient's bloodstream. These autologous endothelial progenitor cells (in detail: endothelial colony-forming cells isolated from blood) are dynamically trained for thrombosis prophylaxis [Kraus et al, 2022] in a self-developed, suitable rotation-perfusion bioreactor [Stanislawski et al, 2020] with full monitoring capabilities. We were able to show that the cells release antithrombogenic markers such as thrombomodulin and others under an artery-like shear stress of up to 10 dynes * cm^{-2} [Renzelmann et al, 2024]. In comparison to previously available porcine decellularized carotid scaffolds, the non-immunogenic tubular 3D-printed vascular scaffolds are biomechanically stable, and thus prepared for use in the large animal model pig by fibrin coating.

Two complementary printing processes (Fused Deposition Modeling and Melt Electro Writing [Baroth et al, 2023]) were combined to produce the 3D-printed scaffolds. The micro-structured surface produced with MEW favors the ingrowth of cells, while the FDM strands ensure stability. Scaffolds were tested for their degradation behavior in the subcutaneous tissue of mice *in vivo*. The innovative scaffolds with endothelial cells out of an autologous cell source have the potential to counteract thrombosis and vascular occlusion after TEVG implantation in a potential TEVG recipient.

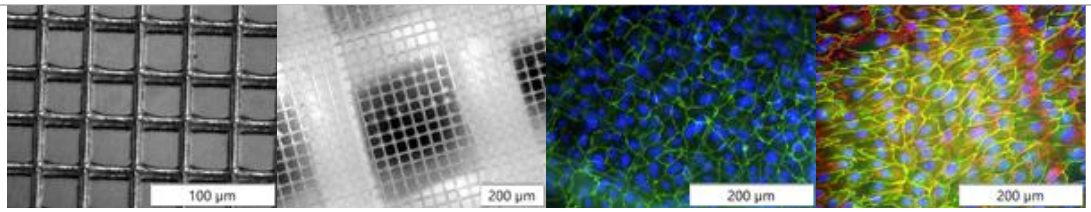

Fig. 1: Endothelial cells, cultivated on MEW/FDM fabricated PCL scaffolds. (A: FDM-produced PCL-ladder, B: with MEW-structured meshes), after seven days of static culture conditions (C) and after 3 days of dynamic cell culturing underflow (5 dyn cm-2) (D).
Blue: Cell nuclei, green: VE-cadherin, red: actin filaments

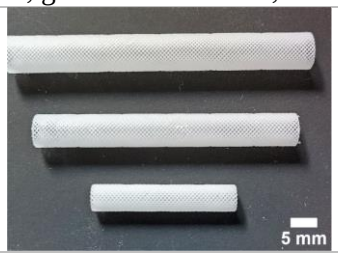

Fig. 2: Tubular PCL-scaffolds, manufactured by 3 D printing (MEW/FDM).

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Towards the Evaluation of Toxic Compounds in In Vitro Blood-Brain Barrier Models for Safety and Sustainability Assessments within the CHIASMA Project

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The increased development of novel chemicals and materials results in emergence of growing demand for fast and accurate methods to evaluate their potential risks to human health. In this context, the CHIASMA project focuses on advancing an enhanced Safety and Sustainability by Design (SSbD) framework to support the regulatory approval process for next-generation chemical and material hazard and risk assessments. This framework integrates in-project validated *in vitro* and *in silico* methods within a comprehensive platform that eliminates the need for animal testing. As part of this project, five toxic compounds, including genotoxic, reprotoxic, endocrine-disrupting, respiratory toxicant and cytotoxic agents, have been selected for evaluation across new approach methodologies (NAMs) developed within the consortium.

With this focus, we aimed to develop stable blood-brain barrier (BBB) models that meet key criteria such as repeatability, reproducibility, and ease of transferability. We established our model using a multicellular Transwell system to mimic dynamic cellular interactions in three-dimensional environment, with hCMEC/D3 brain endothelial cells on the apical side of the porous membrane and differentiated SH-SY5Y (neuroblastoma) cells on the basolateral side. For this purpose, SH-SY5Y cells were differentiated into neuronal cells using retinoic acid and brain-derived neurotrophic factor (BDNF), along with the serum reduction. The differentiated neuronal cells were then co-cultured with hCMEC/D3 brain endothelial cells, constructed the model for toxic chemical treatment apically. The harmful effects of the selected toxic compounds on BBB integrity were evaluated through transendothelial electrical resistance (TEER) measurements at 24, 48, and 72 hours and cell viability assessments at 72 hours of treatment. Furthermore, cell viability results were compared with two-dimensional cultures in 96-well plate cultures. During model optimization, the key experimental challenges such as the effects of bovine serum albumin (BSA) on toxic compound testing, solubility of the compounds and establishing appropriate vehicle control groups were also addressed. Using the Transwell model, an analytical approach was also planned to quantify the extent of toxic compound permeation through the membrane to the basolateral side and adherence to the plastic membrane. By refining the above-mentioned parameters for the model construction and chemical toxin treatment, we aim to enhance the reproducibility and relevance of our *in vitro* BBB model for chemical risk assessment.

As a key aspect of the CHIASMA project, transferability of the generated NAMs will be tested to ensure reproducibility across different laboratories. In this regard, standard operating procedures (SOPs) will be shared among project partners, allowing cross-validation of the models. Ultimately, data obtained from the *in vitro* models will support *in silico* methodologies, contributing to the generation of datasets and biomarkers for toxicological assessment and regulatory applications.

CHIASMA (*Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials) has received funding from the European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101137613.*

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Antigen binding kinetics and organization for effective T-cell activation

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The recognition of an antigenic peptide-MHC complex (pMHC) on the surface of an antigen-presenting cell (APC) by the T-cell receptor (TCR) is a remarkably fast and sensitive process. Despite its determining role in triggering a complex immune response, the exact mechanism of pMHC:TCR interaction is not yet completely understood. We propose that pMHC:TCR binding is a crucial parameter in T-cell activation. To investigate that, we engineered DNA origami-based biointerfaces and performed smFRET (single-molecule Förster resonance energy transfer) and smTracking (single-molecule tracking) experiments.

DNA origami approach allows the manipulation of the position and number of pMHC per given area with nanoscale precision. We used DNA origami platforms anchored to supported lipid bilayers (SLBs) to present single, well-isolated pMHCs to primary murine T-cells. We found out that such a pMHC is capable of efficient T-cell stimulation only if its TCR binding time is short (units of seconds). We proved this by smFRET experiments, where exact pMHC-TCR binding lifetimes were determined from the time AF647-labeled pMHC (anchored to SLBs) was in proximity (~5 nm) to AF555-labeled TCR of primary T-cells.

For the shortest binding pMHC, we performed smTracking experiments, where SLB-anchored pMHC is labeled with AF647 and primary T-cell TCR is label-free. Illuminating antigens for 250 ms with low laser power results in a discrete intensity signal if TCR is bound, in contrast to a blurry appearance of TCR-free antigen. From the duration of such immobilization event, we determined pMHC:TCR binding times, which were revealed to be higher than smFRET-determined lifetimes. Unlike smFRET experiments, smTracking lifetimes are limited by lateral resolution (250 nm), so a single immobilization event can contain multiple TCR binding to the same pMHC. Our smTracking data offer strong evidence of multiple TCR binding to a single antigen, supporting the "serial engagement model," where a single pMHC molecule with a short dissociation time may trigger several TCRs in quick succession, thereby improving the sensitivity and robustness of antigen recognition [1].

By combining DNA origami, smFRET, and smTracking approaches, we showed the correlation between efficient T-cell activation and antigen organization and binding, indicating binding kinetics to be a determining factor in T-cell stimulation. In my presentation, I will focus on the practical aspects of employing smFRET and smTracking experiments, comparing experimental implementation, analysis, and outcomes of each method.

This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 101034277.

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A Closer Look at the Dynamics of T Cell Receptor Microclusters

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T cell activation is initiated when the T cell receptor (TCR), recognizes antigens presented by antigen-presenting cells (APCs). TCRs form microclusters (MCs) within seconds of antigen recognition, which are believed to have an important role in early T cell signaling. During activation, these microclusters move centripetally toward the centre of the immunological synapse (IS) formed between the T cell and APC. Despite their critical role, the mechanisms governing the dynamics and integrity of TCR microclusters remain elusive.

This project utilizes Total internal reflection fluorescence microscopy (TIRFM) to investigate the spatiotemporal dynamics of TCR microclusters as they transit toward the IS centre. Mean Square Displacement (MSD) analysis of TCR microclusters provides a quantitative measure of their mobility. Our observations reveal that some microclusters merge and split on their way to the IS center, which indicates that TCR microclusters are far more dynamic than previously thought. To further probe the integrity of these structures, Fluorescence Recovery After Photobleaching (FRAP) is employed at the level of individual microclusters, uncovering whether TCR molecules remain within a microcluster or exchange with the surrounding membrane during migration. These investigations offer insights into TCR microcluster dynamics and their contribution to the spatial organization of signalling at the IS.

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Standardizing Immunothrombotic Blood Cell Aggregate Diagnostics with Quantitative Phase Imaging Flow Cytometry for Acute Care Diagnostics

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Cardiovascular diseases remain the leading cause of mortality worldwide, emphasizing the need for novel biomarkers to improve early diagnosis, risk stratification, and therapeutic monitoring. Immunothrombotic blood cell aggregates, particularly Platelet-Leukocyte Aggregates (PLAs), have emerged as promising biomarkers due to their role in thromboinflammation and immunothrombosis.[1][2][3] However, pre-analytical variables conditions significantly impact PLA stability, potentially leading to measurement variability and diagnostic inaccuracies. This study investigates the effects of pre-analytical factors on PLA formation and evaluates Digital Holographic Microscopy (DHM) as a label-free quantitative phase imaging method for cell function analysis.

Our DHM prototype allows high-throughput (~3,000 cells/s), phase-resolved detection of platelet-platelet and platelet-leukocyte aggregates in cardiovascular patients at the point-of-care. The evolving understanding of platelet signaling pathways reveals that traditional flow cytometry methods often introduce artificial aggregation due to complex sample preparation. To address this, our DHM-baseds ystem minimizes pre-analytical artifacts while providing high-resolution imaging of blood aggregates without the need for complex hydraulics and autofocusing.

The impact of sample storage time (0–4 hours), anticoagulant type (EDTA, citrate, heparin, CTAD), and transport conditions (standard vs. pneumatic tube system) on PLA formation and stability were assessed. Using fluorescence flow cytometry, we compared DHM measurements with established coagulation and platelet function diagnostics. Storage time significantly influenced PLA stability, with increased monocyte-platelet aggregates (MPAs) and decreased platelet reactivity. Artificial PLA formation was observed as early as 60 minutes post-collection, with MPAs comprising >90% of PLAs at 4 hours compared to ~20% at 1 hour. CTAD tubes provided the best protection among anticoagulants, effectively reducing spontaneous PLA formation and preventing artificial aggregation, particularly in samples transported via pneumatic tube systems.

This study underscores the need for standardized pre-analytical protocols in PLA-based cardiovascular diagnostics for reliable cell function diagnostics. Time-to-result, anticoagulant selection, and transport conditions significantly influence measurement reproducibility. CTAD emerged as the anticoagulant of choice for preserving sample integrity The standardized workflow allows true PLAs to be separated from artifacts, improving the accuracy of cell aggregate biomarkers for near-patient testing in acute care settings.

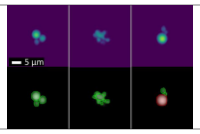

Fig. 1 Plt aggregates(green circle) & Leu-Plt aggregates (red circle) detected by DHM.

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The physics of highly cross linked cytoskeletal networks

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Living cells move, deform and divide. The engine of these behaviors is the cytoskeleton, a highly crosslinked network of polymer filaments and molecular scale motors that use chemical energy to do work. We develop a theory that predicts how the micro-scale properties of molecular motors and crosslinks tune the networks emergent material properties and generate predictable, and possibly controllable, behaviors. I will present how this theory is constructed, and show detailed comparison with a numerical implementation of the same system. I will then discuss its implications for cytoskeletal networks in vitro and in vivo.

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Improving the Resolution of Single-Molecule Localization Microscopy by Leveraging Spatiotemporal Information

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Single-molecule localization microscopy (SMLM) is a cutting-edge super-resolution technique that enhances microscopy image resolution by exploiting the temporal separation of fluorophore localizations across multiple frames. In SMLM, several images are captured from a region of interest, with only a subset of fluorophores activated in each frame. This selective activation of fluorophores ensures well-separated observations, which significantly improves spatial resolution. The final high-resolution image is then constructed by integrating the localization data across all frames.
However, the inherent stochastic blinking behaviour of fluorophores introduces significant challenges, as individual fluorophores can blink multiple times, appearing at slightly different positions due to measurement errors. These repeated observations are often misinterpreted as separate fluorophores, leading to overcounting artifacts that can compromise both the accuracy of molecule localization and the quality of quantitative analyses.
Various methods have been proposed to address these blinking artifacts, such as applying fixed spatial thresholds or clustering observations within spatial dimensions. However, these approaches often fail to account for the temporal dynamics of fluorophore blinking, which can provide critical insights, particularly in densely populated regions.
In this work, we present a robust algorithm designed to mitigate blinking artifacts and accurately localize true molecular positions, thereby enabling high-fidelity image reconstructions. Our approach effectively integrates both spatial and temporal information, with a particular focus on capturing long-term temporal dependencies inherent in fluorophore blinking behaviour. By leveraging the temporal dimension, our method provides more precise reconstructions and improves localization accuracy, especially in regions with overlapping or closely spaced molecules.
We have trained Long Short-Term Memory (LSTM) models on simulated SMLM data generated from short experimental datasets, demonstrating the effectiveness of our approach in these limited time frames. Moving forward, we aim to extend this methodology to real-world, long-duration experiments. To achieve this, we plan to utilize Large Language Models (LLMs), which are particularly well-suited for capturing long-range temporal dependencies, thus further improving the resolution and accuracy of SMLM image reconstructions in more complex experimental scenarios.

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Oral Sessions

Tuesday, July 01, 2025

BioSWITCH: Expanding Iontronic Drug Delivery Through Bioorthogonal Click-to-Release Strategies

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Systemic drug administration remains the standard approach for treating many diseases, including cancer. However, this mode of delivery often leads to significant off-target toxicity and systemic side effects, as the therapeutic agent is distributed throughout the body rather than concentrated at the site of disease. This is particularly problematic in oncology, where high systemic doses are often required to achieve therapeutic concentrations at the tumor site, increasing the risk of adverse effects in healthy tissues.

To address these challenges, localized drug delivery systems have gained attention. Among them, iontronic delivery technologies—such as organic electronic ion pumps (OEIPs)—offer precise, electronically controlled transport of charged molecules directly to a target site.[1,2] This allows for high spatial and temporal resolution without the need for systemic exposure. While iontronic devices are promising, they are inherently limited to delivering small, charged, and electrochemically stable molecules, restricting their utility for many clinically relevant drugs.[3]

To overcome these constraints, we propose a hybrid approach that pairs the precision of iontronic delivery with the versatility of click-to-release chemistries.[4] In this concept, the iontronic device delivers a small, reactive trigger molecule to a localized prodrug reservoir. Upon contact, a bioorthogonal reaction is initiated, resulting in controlled drug release. This strategy allows for the localized activation of therapeutic compounds—including both small-molecule drugs and larger, more complex biomolecules—that would otherwise be incompatible with iontronic transport. Such an approach holds strong potential in precision oncology, where local control of drug activation could enhance efficacy while minimizing systemic toxicity.

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On the trail of Gliflozins' secret to cardioprotective effects

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SGLT-2 inhibitors, a drug class that was developed and approved for the treatment of diabetic patients, have been found to additionally offer cardioprotective properties [1]. It still remains unclear what underlying mechanisms for this finding are since the drugs' target, sodium glucose co-transporter 2 (SGLT-2), is not expressed in heart tissue. To gain a more mechanistical understanding of the drugs, we decided to test their effect on AC16 human cardiomyocytes (derived from left ventricular heart tissue), primary Human Cardiac Myocytes (HCM) and human cardioids by means of a proteomic approach. In AC16 and HCM cells two concentrations were applied, one comparable to the physiological one used in patients, one higher one to catch concentration dependent effects. Empagliflozin was used for treatment in all three cell lines, Cana- and Dapagliflozin in AC16 and HCM cells. Next to quantitative proteomics also redox-proteomics and some metabolites of glutathione metabolism have been measured, the latter as marker for oxidative stress.

To our knowledge there has neither been a publication that provided comparative proteomic data on gliflozin treatments in cells, nor one comparing the mentioned cell types under this aspect.

We found that gliflozin treatments affect the cells' capacity of handling redox stress. On the proteomics level we were able to identify 16 proteins whose expressions were significantly changed in all HCM samples treated with higher drugs concentrations and cardioids. Among them GSR, PRDX2 and LAMTOR5. Redox proteomics data of HCM cells revealed 47 overlapping proteins and 56 peptides that overlapped between all treatments with higher drug concentrations. Of these 47 proteins, three were found to also overlap with the ones found to be significantly changed in cardioid samples, being PKM, PPP2CA and MDH2.

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Bioorthogonal tools for accelerated click-triggered cleavage and dual-release

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Bioorthogonal chemical reactions have emerged as powerful molecular tools for studying biomolecules in their native environment. Among these, the inverse electron demand Diels-Alder (IEDDA) reaction between tetrazines and *trans*-cyclooctenes (TCO) has garnered significant attention due to its exceptional reaction rates and molecular tunability.

We indulge in investigating the design, synthesis, and functionalization of bioorthogonal tools that achieve superior reaction rates that surpass the performance of existing bond-cleavage chemistries. Specifically, we introduce a novel strained cleavable *trans*-cyclooctene (sC_2TCO), engineered to exhibit enhanced click reaction kinetics with tetrazines while enabling controlled payload release. This molecule is inspired by the C_2-symmetric *trans*-cyclooctene previously developed in our group, known for its ability for complete bioorthogonal cleavage and traceless release from the allylic position. However, the incorporation of a cis-fused cyclopropane ring forces the new sC_2TCO into a half-chair conformation, a structural feature known to accelerate reaction kinetics. We have successfully developed a scalable synthesis route for sC_2TCO, enabling the isolation of its most potent isomer for further evaluations and applications. These advancements establish sC_2TCO as a powerful new tool for click-to-release chemistry, particularly suited for time-sensitive applications in chemical biology research based on biorthogonal ON/OFF control.

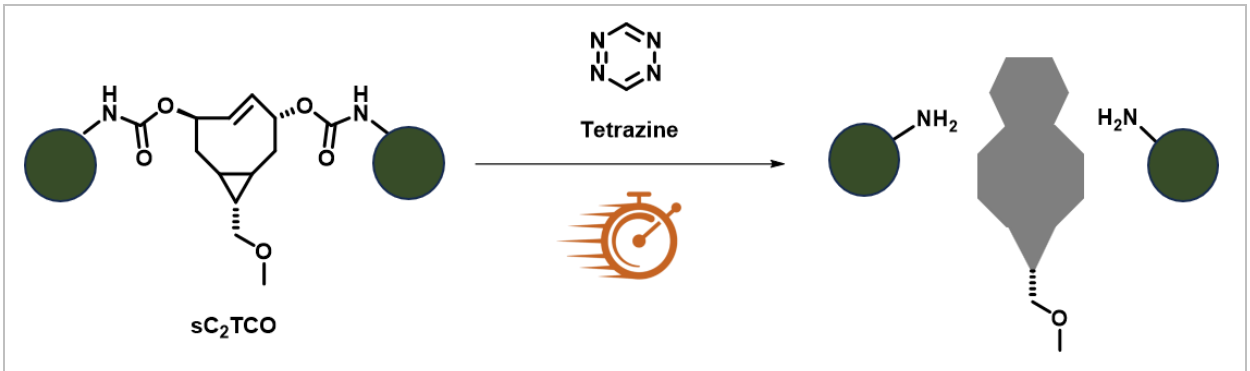

Fig. 1 sC_2TCO click with tetrazine and release of the payload

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Synthesis of Quinolinone Compounds with Potential Kinase Inhibitory Activity for the Treatment of Respiratory Diseases

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Quinolinones are a class of heterocyclic compounds that have been extensively studied due to their efficacy in modulating key biological pathways, including kinase inhibition and antifibrotic activity, which are relevant in conditions such as pulmonary fibrosis (PF) and other chronic respiratory disorders. [1,2]

Respiratory disorders affect millions of people worldwide, leading to substantial morbidity and mortality. [3] Nowadays, compounds such as Nintedanib and Pirfenidone have been approved for the treatment of PF, COVID-19, etc. However, their use is limited by side effects, contraindications, and variable patient response. [4,5] Therefore, compounds such as quinolinones which possess similar mechanisms of action could potentially being an alternative treatment option and may offer a dual benefit by potentially targeting both respiratory diseases, symptoms and progression of these.[5]

Our research aims to find molecules through rational drug design and innovative synthetic methodologies to contribute to the advancement of targeted therapies and foster further research and collaboration in this field.

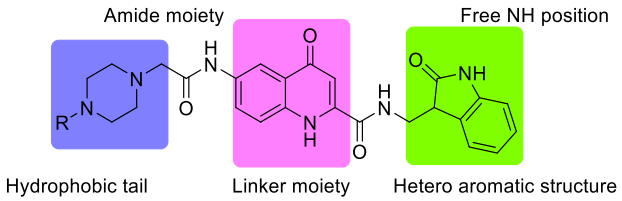

Fig. 1 Design of the Quinolone compounds.

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Exploring the HOG Pathway Mediated Stress Response in Aureobasidium pullulansSSK1

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The High Osmolarity Glycerol (HOG) pathway is a critical signaling cascade mediating fungal adaptation to environmental stressors. In yeast, this pathway is primarily activated through two sensory branches namely SLN1 and SHO1, while filamentous fungi typically utilize one of the two branches. Although the HOG pathway is well-characterized in model organisms, its role in non-model fungi, remains underexplored. Our research focuses on *A. pullulans*, a dimorphic, black, yeast-like, known for its ability to thrive in a wide range of environments, including high osmolarity conditions In *A. pullulans*, the SLN1-SSK1 branch, predicted to function as a negative regulator, remains functionally uncharacterized. This study employs CRISPR-Cas9 to generate sln1Δ and ssk1Δ deletion strains to dissect their roles in stress adaptation and HOG pathway regulation. We hypothesize that sln1Δ mutants will exhibit constitutive HOG pathway activation, while ssk1Δ mutants will demonstrate attenuated pathway activation and increased stress sensitivity. We observed that an impaired SLN1 branch increases stress sensitivity and locks the fungus in a yeast-like morphology, highlighting the critical role of this branch in stress tolerance and morphological plasticity. We aim to uncover how this branch impairment affects downstream HOG pathway components, compatible solute production, melanin biosynthesis, and overall stress response in *A. pullulans* using quantitative real-time PCR (qRT-PCR) and transcriptomic analysis (RNA-seq). This research will provide the first comprehensive analysis of SLN1-SSK1 regulation within the HOG pathway in *A. pullulans*. These findings will contribute significantly to our understanding of fungal stress response mechanisms and have implications for biotechnological applications requiring enhanced stress resistance.

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Beeswax particles with S-layer Functionality for Biomedical Applications

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The application potential of drug carrier systems has been demonstrated in medical applications, owing to their ability to deliver drugs and modulate specific cellular behavior. State-of-the-art carriers comprise lipids, synthetic polymers, paramagnetic nanoparticles, quantum dots, and even carbon nanotubes. However, issues such as non-biodegradability and toxicity have been identified as significant drawbacks.

Beeswax has been recognized as a solid core/phase particle with remarkable properties in biomedical applications, including wound healing and serving as a universal binding matrix for drugs. In a previous study, we investigated the coating of beeswax particles derived from tree resin as a passive protective layer [1]. Nonetheless, these core-shell particles were unable to target specific topologies and failed as effective drug delivery systems.

Our research has integrated the neutral characteristics of beeswax with nanocoating based on the well-established S-layer protein species [2] to enhance targeting capabilities. Beeswax particles combined with S-layer functionalization present the foundation for unique and innovative bio-architectures. The S-layer toolbox, a paradigm in synthetic biology, enables incorporation of active moieties at the genetic level without hindering its capacity to form a 2D crystal layer on virtually any surface, including beeswax.

These novel beeswax/S-layer particles will be examined for cellular adhesion *via* specific receptor binding interactions and their potential translation into therapeutic regimens. Presented here are preliminary data concerning this interesting nano-bioarchitecture composed of true biomaterials. The beeswax core preserves active molecules within a well-preserving beeswax matrix, such as essential oils from herbs and other volatile substances, while the S-layer functions as an engineerable coating for targeted delivery.

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Elucidating Stress Response Mechanisms in *Trichoderma reesei*: Insights into Unfolded Protein Response and Repression under Secretion Stress

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The unfolded protein response (UPR) and repression under secretion stress (RESS) are critical regulatory mechanisms influencing protein secretion in *Trichoderma reesei*, a hyper-secreting cellulase strain. Under laboratory conditions, UPR was induced by dithiothreitol (DTT) [1] and decrease in transcript levels of genes encoding hydrolytic enzymes indicated the presence of RESS. RESS operational at the mRNA level, [1] occurs due to mRNA instability or is related to the initiation of transcription or due to both was investigated with a transcription inhibitor 5,6-Dichloro-1-β-D-ribofuranosylbenzimidazole (DRB) under UPR and Non-UPR conditions [3]. The results suggested that both of the mechanisms, both are affected. To confirm this, expression cassettes (with the change of Terminator; preventing mRNA degradation and Promoter; to assess the extent, RESS impacts the initiation of the transcription) will be introduced into the genome of a *pyr4*- deleted *T. reesei* strain using goxA from *Aspergillus niger* as a reporter gene. Cycloheximide, previously reported to mitigate RESS [1] [2], failed to reverse RESS in our study, suggesting a translation-independent regulatory mechanism. To assess these responses under industrially relevant conditions, transcriptome analysis was performed on samples collected at multiple time points. Analyses of the UPR target genes and cellulase enzyme, coupled with differential expression profiling, confirmed the absence of UPR activation, and consequently, RESS was not detected. Additionally, calcium-calmodulin signaling was investigated for its role in UPR modulation as depletion of calcium ions (Ca^{2+}) from the endoplasmic reticulum of yeast cells resulted in the unfolded protein response signaling pathway via Ire1p and Hac1p [4]; however, no significant effect was observed, indicating it is not a major contributor to UPR regulation in *T. reesei*. To further explore cellular adaptations to secretion stress, morphological changes will be examined using label-free Nanolive imaging. These findings refine our understanding of UPR and RESS dynamics in *T. reesei*, providing insights that may inform strategies for optimizing industrial enzyme production.

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Advancing Unambiguous Image Detection and Bioorthogonal Intervention of Cellular Senescence

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As the accumulation of senescent cells has extensively been proven to contribute to the onset of a wide range of age-related diseases, including cancer, the design of a biocompatible strategy capable of achieving high detection accuracy and specificity is highly desired [1]. However, the lack of a single biomarker able to uniquely identify cellular senescence poses a significant challenge for precise detection and selective intervention *in vivo*. Therefore, inspired by our recent achievements in bioorthogonal chemistry, along with our increased understanding of the biology of senescence, we aimed to develop a **synergistic molecular approach**, which advances the concept of bioorthogonal reactions performed inside senescent cells. This strategy is designed to simultaneously target a specific cell-surface marker and an elevated enzymatic activity, particularly of senescence-associated β-galactosidase (SA-β-gal)[2]. After successfully developing a non-clickable masked tetrazine (mk-Tz) with lysosomal targeting ability, its fast and complete activation by SA-β-gal was demonstrated in solution through UV-Vis absorption spectroscopy and HPLC-MS analysis. To extend these studies to a cellular context and investigate the enzymatic activation of the mk-Tz inside senescent cells, a lysosome-targeting fluorogenic *trans*-cyclooctene derivative (iTCO-caged resorufin) was synthesized. The enzyme-catalyzed activation of the bioorthogonal turn-on reaction was evaluated in solution under physiological conditions using fluorescence spectroscopy and HPLC-MS analysis. Its potential application was further confirmed *in vitro* upon passive uptake and sequential lysosomal accumulation of both compounds inside primary human senescent fibroblasts (sn-hFB) and normal proliferating human fibroblasts (hFB). These results serve as a promising proof of concept, paving the way for an advanced biocompatible strategy to achieve unprecedented precision in targeting senescence.

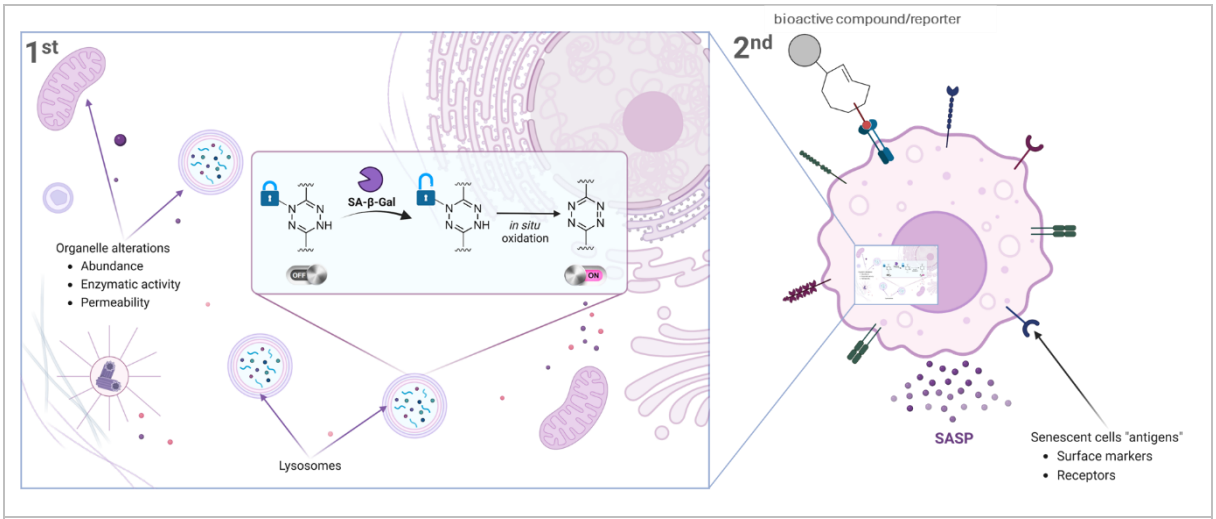

Fig. 1 Dual-targeting mechanism to direct the two compounds into senescent cells, enabling the detection of senescence with significantly enhanced specificity and selectivity.

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Confirmation of Jarzynski's equality based on single molecular and macroscopic interaction force measurements

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Knowledge about the free energy landscape of biomolecular reactions is necessary to understand how life works on the smallest scale. Unfortunately, obtaining experimental values of the free energy difference between two states like an unbound and a bound state of two molecules is rather difficult. [1] Jarzynski proposed an equality (eq. 1) that connects the free energy difference between two states with the irreversible work that leads from one state to the other. Precisely, an average of all possible realizations of a process that moves the system from an equilibrium state to another state in equilibrium. Here, we test this hypothesis with experimental values. Using a simple model system, the different nucleobase-pair interactions are measured using three different techniques that are able to measure the interactions force between two single molecules and up to 10^7 interactions in a single experiment run. Using the Atomic Force Microscope (AFM), Optical Tweezers and the Surface Force Apparatus allows us to additionally investigate the scaling of biological single molecule interactions. Together with molecular dynamics simulations a strong foundation is laid to confirm Jarzynski's equality and investigate the scaling of single-molecule interactions.

$$exp\left(\frac{-\Delta F}{kT}\right) = \left\langle exp\left(\frac{-W_n}{kT}\right)\right\rangle_n \tag{1}$$

Jarzynski's equality relates the free energy difference ΔF to the work W_n done on the system with k being the Boltzmann factor and T being the temperature.

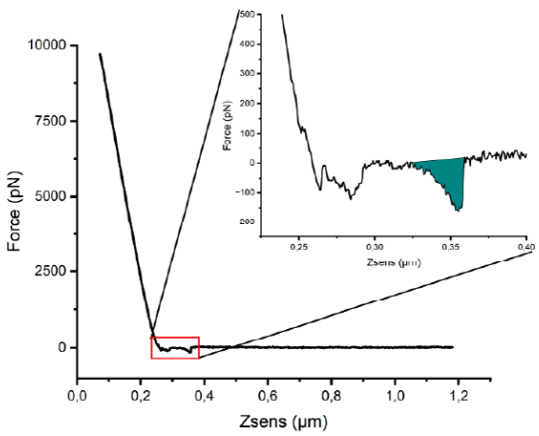

Fig. 1 example of a force-distance run of a single-molecule force experiment with the AFM. The insert displays the region of interest and the integral of the marked area gives the work required to break the bond.

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High-Throughput Roll-to-Roll Manufacturing of Foil-Based Microfluidic Chips for Scalable Diagnostics

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Lateral flow tests have played a crucial role in mitigating the spread of the SARS-CoV-2 virus throughout the COVID-19 pandemic, primarily due to their affordability, simplicity, and ease of use, which have enabled widespread accessibility. However, despite their relatively low cost for both consumers and manufacturers, traditional paper-based fluidics used in lateral flow tests face significant limitations in scalability and versatility for broader bioassay applications. To address these challenges, we explore the potential of roll-to-roll (R2R) UV nanoimprint lithography (UV NIL) for the high-throughput production of foil-based microfluidic chips.

UV NIL operates on imprinting principles that allow for high-volume, continuous structuring of microfluidic patterns within the R2R production system. In this study, we successfully adapted a commercial multiplexed micro-ELISA test for COVID-19 antibody detection (COVID-19 IgG xPOC, Genspeed Biotech, Austria) onto foil-based chips fabricated using PET substrates. Compared to conventional microfluidic fabrication techniques, UV NIL provides unparalleled advantages in terms of speed, seamless handling, scalability, and surface modification capabilities, which are essential for precise biofunctionalization.

The evaluation of 200 test chips produced through UV NIL against the standard COVID-19 xPOC chips demonstrated comparable chemiluminescence signal performance. These promising results highlight the feasibility of translating biochemical assays to R2R-manufactured foil-based chips and underscore the potential of this technology for in vitro diagnostics (IVD) applications. Furthermore, the implementation of microfluidic biosensors on polymer foils, combined with an R2R manufacturing platform, offers a viable solution for upscaling production to meet the demand for millions of chips required for mass screening in pandemic scenarios.

Our high-throughput R2R pilot line facilitates microfluidic channel patterning via R2R UV NIL, bio-functionalization through R2R microarray-spotting, and chip closure using UV-assisted R2R lamination. The high degree of process parallelization enables an efficient and cost-effective production workflow, significantly outperforming conventional injection molding techniques. Additionally, to overcome challenges related to limited on-chip volume, particularly in assays with increasing complexity, we propose an origami-like folding approach. This method allows for the creation of multi-layered microfluidic structures or deeper channels, thereby enhancing fluid handling capacity without increasing the overall chip footprint.

Multiple other applications where R2R patterning is used for the fabrication of foil based microfluidic devices, ranging from organ-on-chip platforms, exact metering systems, plasmonic substrates to amplification of DNA on chip are possible. These examples will be also shown.

Keywords: Roll-to-Roll processing, imprinting of microfluidic patterns, roll-to-roll microarray spotting, roll-to-roll lamination, Lab on chip, organ on chip, amplification, blood metering

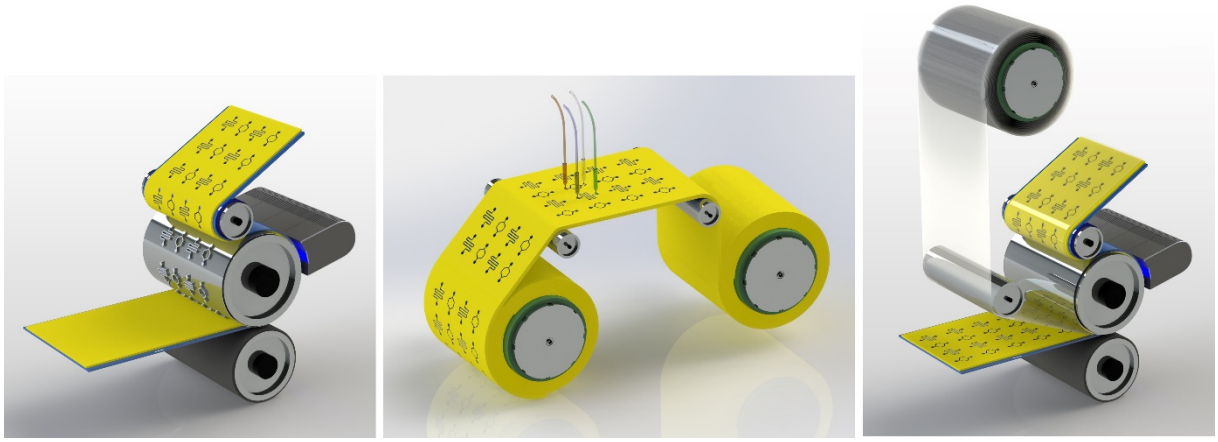

Fig 1: Schematic illustration of the R2R pilot line – R2R UV-NIL (left), R2R micro array spotting (centre), R2R lamination (right)

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Temperature Control System for Multi-Cavity Acoustofluidic Platform

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CellLEGO is an acoustofluidic trap for cell culture experiments, which tries to develop a "digital microscope slide" for label-free cell manipulation in any microscope system [1]. Acoustic trapping is an attractive method to control the 3D position of cells even with background flow due to higher trapping forces compared to optical traps. However, due to the acoustic forces, temperature control is crucial for long-term cell culture experiments. In the previous experiments, we verified the system's effectiveness in 3D cell culture using a K562 cell line as a model in a continuous perfusion experiment in continuous levitation while system temperature was kept at 37 °C by using a single-sensor temperature control system [2]. For future pre- and clinical applications, we aim for massive trap arrays. In a multi-cavity microfluidic chip, the temperature regulation is more complex [3].

In this study, we present the development of a temperature measurement and control system specifically designed for the multi-cavity CellLEGO prototype, as illustrated in Fig. 1. The system integrates an Arduino and multiple calibrated sensitive sensors for real-time global monitoring, ensuring fast and accurate temperature regulation. Additionally, the system supports continuous data recording, improving experimental reproducibility in microfluidic-based cell culture [4].

By offering precise thermal management, our system enhances the reliability of acoustofluidic cell culture, facilitating cell manipulations and lab-on-a-chip technologies.

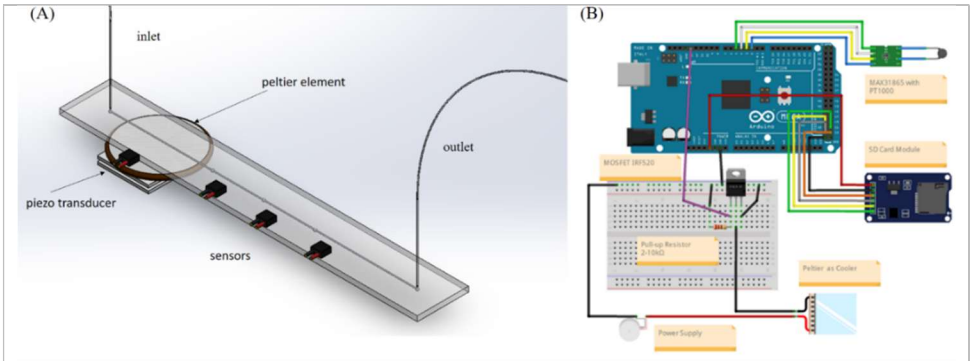

Fig. 1 (A) Microfluidic system (B) Circuit of temperature control system

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Oral Sessions

Wednesday, July 02, 2025

Lab-on-PCB technology

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Lab-on-Chip technology aspires to shrink biomedical laboratories in few cm microchips, in a technological revolution step analogous to the introduction of computer technology in the 20th century. In this presentation Dr Moschou will provide an overview of this technology and its impact on healthcare. She will then focus on manufacturing techniques for integrated Lab-on-Chip biomedical diagnostic chips and in particular the Lab-on-PCB technology that has been the forefront of her work for the past 12 years. The role of this technology in the COVID-19 outbreak will be presented, along with its potential in reshaping the future of testing and data-driven management of emerging pandemics and non-communicable disease management.

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Towards individualised treatment of urinary tract infections

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Objectives: Antimicrobial drugs are often prescribed using a one-size-fits-all approach, ignoring individual variations in pharmacokinetics (PK) and pharmacodynamics (PD). Estimated PD values alongside drug titration in patients is linked to better outcomes **[1]**. However, PD estimation and dose optimization for UTIs, a common cause of antimicrobial prescriptions, remains underexplored. This study investigates using the bacteria specific marker nitrite (NO_2^-) to monitor antimicrobial PD and introduces a novel point-of-care diagnostic tool to quantitatively measure nitrate (NO_3^-) and nitrite, overcoming false-negative results due to dietary nitrate variations.

Methodology: Susceptible and resistant *E. coli* strains were grown for 72 hours in artificial urine. 164mg/mL amoxicillin added after 15hrs. Samples were plated on Agar to count colony forming units (CFUs), and NO_2^- levels were measured using the Griess method. Urine samples from 25 non-UTI and 25 UTI patients were tested for bacterial growth and NO_2^-. NO_2^-/NO_3^- detection was performed by electrodepositing 0.05mM Cu_2SO_4 on a carbon rod electrode at -1VC, followed by Cu reduction step at -0.12V and NO_2^- and NO_3^- reduction (-0.35V and -0.55V) in 0.1M Na_2SO_4 + 0.1M HCl.

Results

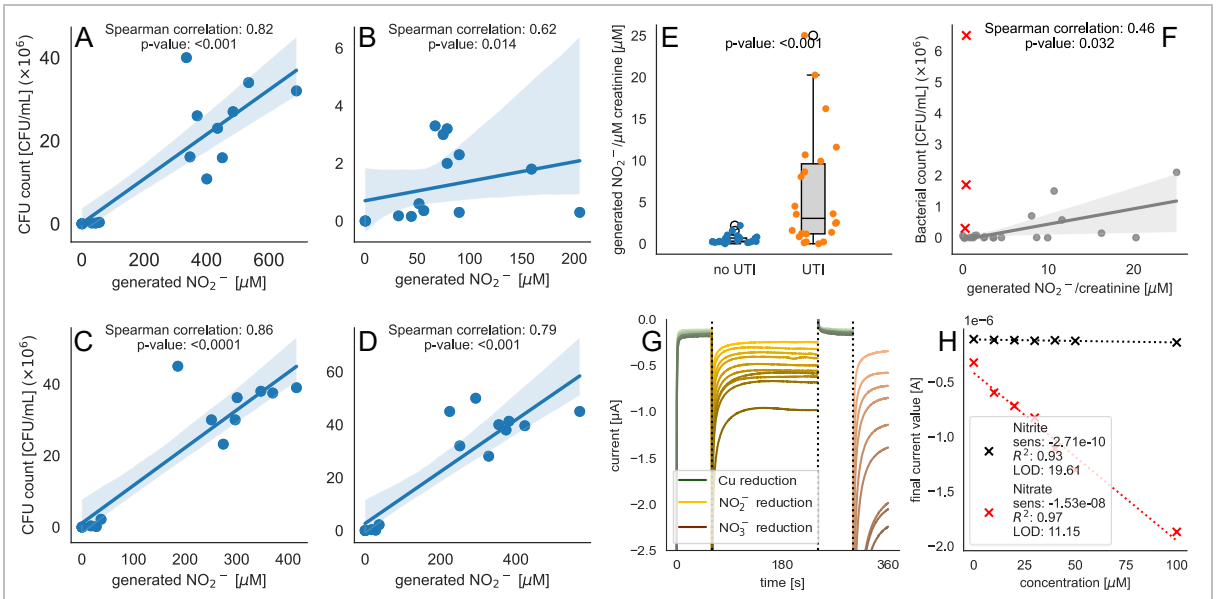

Fig. 1 CFU against generated NO_2^- in susceptible A), resistant strain C) and susceptible and resistant strain after addition of amoxicillin (B, D). E) generated NO_2^- in non-UTI vs UTI patients. F): NO_2^- vs CFU in UTI patients. G) Amperometry for NO_2^-/ NO_3^- detection and H) linear calibration

CFU and generated nitrite is correlated across all strains (A-D) and in patients with UTIs F). Amperometric measurement of NO_2^- and NO_3in the same sample on a Cupper modified carbon electrode yields linear calibrations for NO_2^- and NO_3 with limit of detection of 19.6 and 11.1µM respectively.

Significance of the work: Our findings suggest that monitoring a bacteria-specific biomarker in urine could track UTI progression and antimicrobial efficacy. With developed biosensors like the NO_2^-/NO_3 sensor, combined with other UTI biomarkers, this could enhance the way we treat UTIs.

Ellen Stadler's PhD is funded by the Presidents PhD Scholarship at Imperial College London.

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Yeast enrichment using microfluidic deterministic lateral displacement (DLD)

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Microbial contamination in industry presents a public health risk and causes product deterioration resulting in economic losses. Standard detection relies on culture-dependent or -independent methods coupled with microorganism enrichment, which typically requires several days. Alternatively, microfluidics allows target microorganisms enrichment from heterogenous mixtures in several hours. Here, we evaluate microfluidic deterministic lateral displacement (DLD), as a size-based separation method for microbial enrichment [1].
Microchannels were designed with AutoCAD® with different DLD array lengths (short [1987.54μm]; long [13697.84μm]) a 3.36μm critical diameter (Dc) [2] and fabricated in polydimethylsiloxane (PDMS) using soft-lithography. Then, enrichment in the microchannels was evaluated using fluorescent polystyrene particles (D=2μm; D=6μm) and model microorganisms (Escherichia coli and Saccharomyces cerevisiae) suspended in sodium dodecyl sulfate (SDS) supplemented with dextran (40,000g/mol) at 0.2 μL/min (Qinlet=0.001m/s; Re=0.11, laminar flow). Trajectories of individual particles and microorganisms were visualized through streak image photography, followed by quantification of displaced and non-displaced modes to evaluate separation efficiency. In long DLD array, qualitative data indicate that 2μm particles and E. coli were non-displaced, while 6μm particles and S. cerevisiae were displaced and as predicted by theoretical Dc (3.36μm). The quantitative data from spatial distribution revealed concentration of 6μm (>90%) particles and S. cerevisiae (84.1%) in long DLD array. Then enrichment was evaluated in both DLD array lengths. Also, as expected, the enrichment efficiency was better for the long DLD array when compared to the short. Overall, this work demonstrated the potential of DLD to enrich yeast over bacteria.

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Guided vascularization in organs-on-chip using High-Definition laser patterning

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Microvasculature plays a crucial role in nutrient and waste exchange across all organ systems. In organ-on-chip models, microvascularization is typically achieved by leveraging the self-assembly properties of cells within cell-remodelable 3D matrices, closely mimicking the *in vivo* process of vasculogenesis. However, creating functional microvascular networks that can be produced with precise spatial and temporal control and high repeatability remains a significant challenge [1]. This prevents consistency and reproducibility across different biological samples, therefore delaying the validation of organ-on-chip models for drug testing and toxicological assessments. Here, we demonstrate how High-Definition (HD) laser patterning enables the realization of microvascular templates directly on-chip which are then endothelialized by cells, under static and dynamic culture conditions. This approach is further used to replicate the microvasculature of a liver-on-chip model.

A three-channel microfluidic chip is filled with a collagen and matrigel mixture, and cylindrical templates are generated through femtosecond laser ablation. Endothelial cells are seeded into the side channels, allowing them to proliferate and migrate accordingly. After seven days of static or dynamic culture, the vascular structures are stained for key endothelial markers and perfused with 70 kDa FITC-Dextran to assess the permeability of the endothelial barrier. To evaluate the system's response to pro-inflammatory stimuli, the vascular structures are overnight treated with TNF-α. After encapsulating liver-specific cells within the bulk hydrogel, laser patterning is used to recreate the hepatic lobule-like microvasculature. Major liver functions, including albumin and urea production, as well as drug-induced hepatotoxicity (APAP treatment) are then evaluated to assess the functionality of the proposed liver-on-chip model.

HD laser patterning enables the creation of void patterns that closely match the size of the initial CAD model. Following seeding, cells proliferate and migrate into the laser-patterned channels, achieving successful endothelialization after seven days of culture, as confirmed by the expression of CD31 and ZO-1, along with lower permeability values compared to acellular channels. The system also demonstrates a strong response to overnight TNF-α stimulation, which significantly increases the endothelial permeability. When cultured under flow, the vascular structures show a significant enlargement of the vascular lumen and the formation of perfusable sprouts which connect adjacent main vascular channels. In the hepatic lobule-on-chip model, patterned microvascular structures enhance albumin and urea production, while APAP treatment significantly reduces cell viability, effectively mimicking acute liver failure caused by drug exposure.

In summary, we have established a method to create microvascular templates on-chip that enables controlled spatio-temporal endothelialization under both static and dynamic culture conditions. This approach improves reproducibility among samples, allowing for systematic investigation of the effects of various biological and physical cues on vascular formation and maturation. Additionally, it offers the ability to faithfully replicate organ-specific microvasculature in both size and spatial arrangement, providing a valuable platform for drug testing and toxicological assessments.

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A TCO-masked iRGD-Fluorophore Conjugate is Activated via a Bioorthogonal Tz-Triggered click-to-release Reaction, Performed Under *in-situ* Conditions on a Microfluidic Chip.

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We have developed a masked iRGD (CRGDKPDGC) peptide-drug/fluorophore conjugate by synthetically attaching a trans-cyclooctene (TCO) molecule to it which can be bioorthogonally activated within the tumor microenvironment through a Tetrazine (Tz) triggered click-to-release reaction. Research indicates that iRGD binds to receptors such as integrin and neuroprolin-1 (NRP-1), which are significantly overexpressed in various tumors [1]. The unique mechanism of action involves iRGD first binding to integrin, followed by proteolytic cleavage by native proteases at the C-terminus of the lysine. The resulting cleaved product, which carries the drug or molecule of interest, is then internalized by nearby NRP-1[2].

While integrin and NRP-1 are associated with tumors and are quantitatively abundant, they are not exclusive to tumor tissues. This can lead to off-target activation of state-of-the-art iRGD-drug conjugates, resulting in side effects. To mitigate this, we blocked the protease binding site of iRGD by attaching a TCO molecule to it, effectively hindering its internalization ability. Subsequently, we cleaved the TCO using Tz, providing an additional layer of spatiotemporal control over the release of cytotoxins in proximity to diseased cells, thereby sparing healthy cells.

Using Trypsin as a model protease, we demonstrated through LC-MS analysis that when a TCO molecule is attached to the iRGD, trypsin cannot cleave iRGD. In contrast, free iRGD is readily cleaved by trypsin, highlighting the masking efficiency of TCO against proteases. Fluorescence microscopy revealed efficient cellular uptake of non-masked iRGD-TMR (TMR=Tetramethyl Rhodamine) in A549 cells after three hours of incubation. Conversely, under identical conditions, treatment with the TCO-caged iRGD-TMR conjugate resulted in significantly reduced signal intensity, indicating much lower internalization compared to iRGD-TMR alone. Notably, upon in-situ reaction of TCO-iRGD-TMR with an advanced tetrazine for bioorthogonal click-to-release, efficient cellular uptake was restored, confirming the successful bioorthogonal activation of the iRGD peptide.

In the future, we plan to develop Tz-conjugated injectable hydrogels that can be deployed around tumor tissues. If the TCO-iRGD-Drug is administered sequentially, it should selectively release the iRGD-Drug conjugate in the vicinity of the tumor upon reacting with the Tz in the hydrogel. Additionally, we will utilize a two-chamber microfluidic platform—one chamber for the hydrogel and the other for the cells—to replicate the relevant *in vivo* conditions as previously mentioned.

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Development of Topical Ozone-Based Antimicrobials: A Promising Strategy Against Antimicrobial Resistance

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The escalating crisis of antimicrobial resistance (AMR) poses a significant threat to global health, rendering conventional antibiotics increasingly ineffective. The urgent need for alternative antimicrobial strategies leads to the exploration of novel antimicrobial agents beyond conventional antibiotics. Ozone (O_3), a reactive oxygen species (ROS) generator, has demonstrated broad-spectrum antimicrobial activity against bacteria, fungi, and viruses, offering a promising approach to tackle AMR (Fig.1). This talk highlights the mechanisms underlying ozone's antimicrobial effects and surveys its efficacy against clinically relevant drug-resistant pathogens. It is described that ozone induces rapid and potent microbial inactivation through multiple mechanisms, including lipid peroxidation, protein oxidation, and DNA damage. Importantly, ozone demonstrated significant efficacy against multidrug-resistant strains, highlighting its potential as a valuable adjunct or alternative to conventional antibiotics.

Ozone is a potent oxidizing agent, that reacts with the unsaturated fatty acid chains present in vegetable oils through a process known as ozonolysis, resulting in the formation of bioactive compounds, such as ozonides (1,2,4-trioxolanes) and other oxygenated products (aldehydes, ketones and peroxides). Such compounds have demonstrated to have antimicrobial activity by affecting bacterial cell membrane integrity, intracellular oxidative stress, and DNA integrity [1, 2].

2M Pharma in collaboration with academic partners has been developing and exploring the antimicrobial potential of a class of ozonized olive oil-based products of topical application for veterinary use. Clinical studies in pets and cattle with common infection-based pathologies in veterinary context has been conducted. Additionally, an in-vitro study is being conducted to assess the efficacy of ozonized oil against *Leishmania* infection in canine skin explants.

Future studies should focus on optimizing ozone delivery methods and evaluating its clinical efficacy in diverse infectious disease settings.

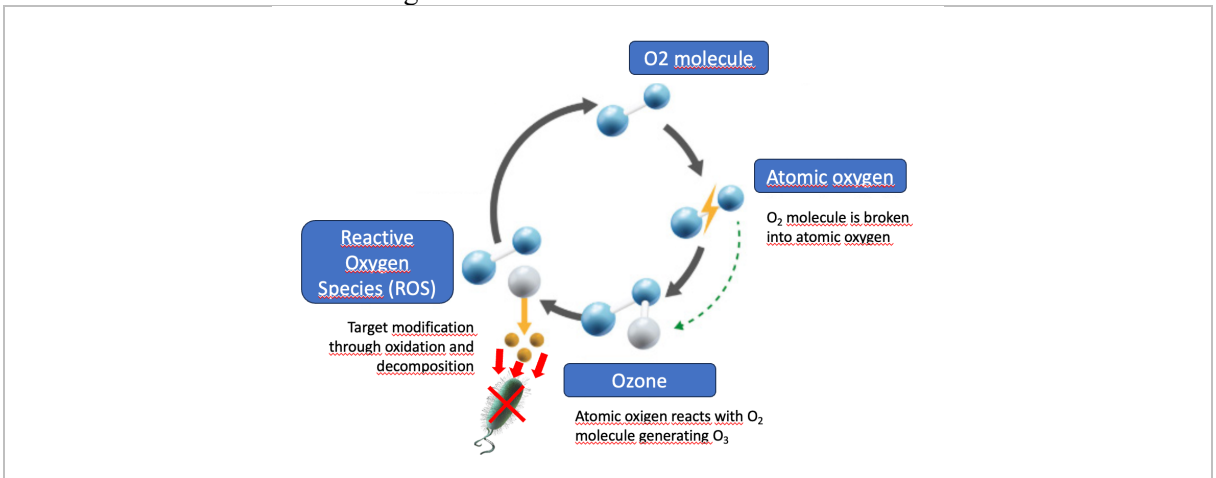

Fig. 1 Representation of oxygen – ozone cycle and antimicrobial actuation.

Acknowledgement: IPANEMA project, DOI: 10.3030/872662

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A Paper-Based Point-of-Care Diagnostic for Urinary Tract Infections and Antimicrobial Resistance Profiling

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Urinary tract infections (UTIs) impact over 400 million people annually, yet current diagnostic approaches rely on time-intensive urine cultures or empirical treatments, often leading to delayed or inaccurate antibiotic therapy. This study presents a novel paper-based point-of-care (PoC) diagnostic device that enables rapid detection of UTI-causing bacteria, species identification, and antimicrobial resistance profiling. The device aligns with the WHO's ASSURED criteria, ensuring affordability, sensitivity, specificity, user-friendliness, rapid results, and suitability for resource-limited settings.

Clinical evaluations demonstrated the device's high sensitivity and specificity, achieving up to 100% accuracy in differentiating sterile from infected urine samples. The system identified *Escherichia coli* and *Enterococcus faecalis* infections within 12 hours and successfully detected eight major UTI pathogens across concentrations ranging from 10^8 to 10^1 colony-forming units per milliliter. Additionally, the antimicrobial susceptibility testing module accurately determined bacterial resistance to Fosfomycin within 8.25 hours.

The device integrates multi-layered paper substrates with embedded chromogenic indicators and antibiotic gradients, allowing for standardized but individualized test results. Image-based analysis via smartphone or scanner provides immediate readouts, enabling faster clinical decision-making. This approach has the potential to transform UTI diagnostics by reducing diagnostic turnaround times, enhancing targeted antibiotic therapy, and addressing the challenge of antimicrobial resistance.

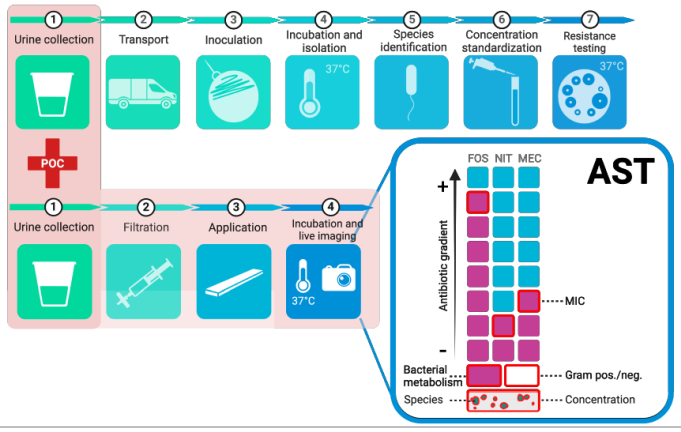

Fig. 1 Comparison of traditional AST testing and new diagnostic approach for UTIs. The new diagnostic method streamlines UTI testing by reducing traditional steps such as transport, incubation, and species identification, enabling faster analysis and clinical decision-making. By using a PoC-testing device, sample filtration and application to the test strip take only minutes, with incubation and real-time imaging significantly reducing overall diagnostic time.

This research was supported by the Bavarian Ministry of Economic Affairs, Regional Development and Energy (m4 Funding, FLÜGGE Funding) and the Federal Ministry for Economic Affairs and Climate Action of Germany (Go-bio initial).

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Investigation of the Cytocompatibility of different Diazosulfonate-based and Water-soluble Photoinitiators for two-photon Polymerization

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Two-photon polymerization is a specialized 3D printing technique, that is often used in biofabrication because of its excellent resolution down to the submicron range as well as the possibility for direct cell encapsulation.[1,2] One necessary component in the printing formulation is the photoinitiator, which often acts as the limiting factor when it comes to working with cells. Especially the well established P2CK photoinitiator exhibits significant cytotoxicity at concentrations above 0.5 mM.[1] To overcome this issue, the water-soluble diazosulfonate photoinitiator DAS, based on amsonic acid, was developed in 2018. The cytocompatibility was determined up to a concentration of 4.0 mM, however the phototoxicity increases significantly above a concentration of 2.0 mM.[1] Combined with the low two-photon cross section of only 40 GM, there is still room for improvement in the field of diazosulfonate-based photoinitiators for biofabrication.[1] The core molecule defines the absorption and the cross-section, while the diazosulfonate groups introduce water-solubility and two-photon activity. Three different new molecules were synthesized and investigated during this work. All photoinitiators (PI1, PI2, PI3) exhibited two-photon activity during the 3D printing tests and showed a sufficient water-solubility up to a concentration of 5.0 mM. Furthermore, during cell viability tests PI1 showed no decrease in cell viability up to 4.0 mM concentration and together with PI2 the stability at ambient light and room temperature was determined, where the ^{1}H-NMR spectrum of both photoinitiators did not show any changes after two weeks, which highly increases the ease-of-use.

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Magnetic Biodevices

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The ongoing developments in wearables, digitalization and green technologies require devices that can provide new features and functionalities while considering the availability of resources and sustainability. In these regards, magnetic biodevices are attractive, as they offer unique capabilities like remote interaction, and they can be environmentally benign. Therefore, various magnetic biodevices have been developed to obtain an optimized performance for specific applications.

This presentation provides insights into developments on magnetic biodevices like flexible magnetic skins and sensors, which feature high performance, biocompatibility and conformability. They can be employed in biomedical instruments, marine monitoring, or machine-user interfaces. Flexible and wearable magnetic systems can extend our senses and provide contactless control. Examples are flexible magnetic tunnel junction sensors, which are employed for 3-axes orientation monitoring on biomedical instruments. On the other end of the spectrum are printed graphene Hall effect sensors with less sensitivity but high temperature and corrosion resistance. Iron-based magnetic nanowires feature both a large remanent magnetization and biocompatibility. They can be fabrication by electrochemical deposition providing a high control over the structural and magnetic properties with diameters ranging from around 10 nm to a couple of 100 nm and lengths ranging from around 100 nm to several 10 µm. The magnetic properties of nanowires are intriguing, due to the effect of a pronounced shape anisotropy, as a consequence of the high aspect ratio. They typically display a single domain particle behavior; therefore, they can be considered as nanosized permanent magnets with a magnetization direction either parallel or antiparallel to the nanowire axis at remanence. By using them as fillers in polymer composite materials, flexible, biocompatible and conformable magnetic sensor skins can be created, which can be conveniently interrogated without batteries, wires or chips. Through the concentration of the filler particles, the magnetic and mechanical properties of the composite materials can be widely modulated and tailored for the specific needs of an application. Examples will be shown in which the magnetic composites are employed for the localization of subcutaneous medical devices or as tactile skins for flow measurements or braille reading. As ultra-flexible magnetic skins, they can be worn like tattoos or camouflaged with the color of the skin tone and enable gesture-controlled wireless operations. This is demonstrated by controlling a wheelchair with facial gestures. Such nanowires can also be used as bio-transducers for cell treatments. They are internalized by cells very efficiently, and depending on material and dose, they are well tolerated. After internalization and upon the application of a low-frequency magnetic field, cancer cells can be killed by a magneto-mechanical effect. Thereby, the nanowires are exerting a force on the cells, inducing their death by apoptosis. The killing efficacy can be enhanced by combining the magneto-mechanical treatment with a chemotherapeutical treatment or a photothermal laser treatment. To this end, a drug can be attached to the nanowires and released upon internalization by the cells, and the optical energy from a near-infrared laser can be photothermally converted into heat by the nanowires.

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Multi-analyte magnetic sensing – from cells to vesicles and proteins

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Liquid biopsies contain diverse biomarkers, including cells, proteins, and extracellular vesicles, but integrating these into a unified analysis platform for Point-of-Care testing (POCT) remains challenging. Traditional methods like enzyme-linked immunosorbent assays and optical flow cytometry have been centralized laboratories' gold standard for biomolecular detection and functional cell analysis. While highly sensitive and capable of multiplexing, these techniques are often hindered by bulky instrumentation, complex sample preparation, and the need for trained personnel, making them impractical for decentralized or resource-limited settings.

Magnetic biosensors offer a promising alternative, enabling miniaturization, microfluidic integration, and simplified workflows. We present a novel magnetic flow cytometry (MFC) platform designed to simultaneously detect multiple biomarker classes, from micron-sized cells to small molecules, within a POC framework. This system utilizes giant magnetoresistance (GMR) sensors integrated into a microfluidic cartridge, employing magnetophoretic enrichment and focusing for precise manipulation of magnetized cells and superparamagnetic beads. The direct measurement in complex biological fluids such as whole blood minimizes sample preparation and eliminates the need for expensive optical components. [1,2]

This approach allows biomarker quantification across a broad dynamic range, even in high-hematocrit samples, making it suitable for diverse clinical applications. For instance, it enables immune status assessments for HIV patients by quantifying of immune cells directly in whole blood. Additionally, extracellular vesicles and proteins can be selectively captured and quantified, facilitating disease and treatment monitoring. The platform's amplification-free and matrix-insensitive detection method further enhances its versatility, ensuring reliable performance across various sample types and conditions.

By integrating multiple biomarker classes into a single readout system, our magnetic flow cytometry platform significantly advances POC diagnostics. Its miniaturized, cost-effective, and user-friendly operation makes it highly adaptable for use in both clinical and resource-limited environments, paving the way for more accessible and efficient molecular and cellular diagnostics.

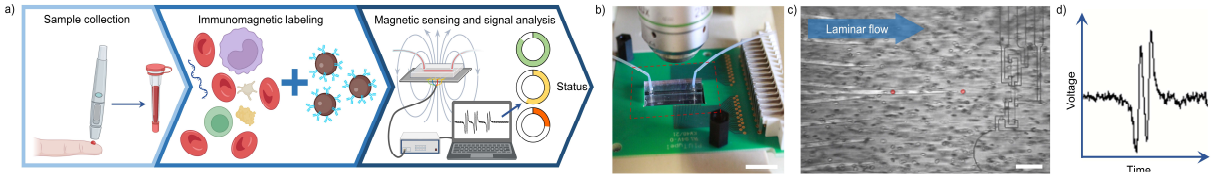

Fig. 1 Wash-free POCT workflow with MFC. **a)** Minimal volumes of blood are collected and immunomagnetically labeled for subsequent measurement with MFC. **b)** The assembly of the MFC with a fluidic and a permanent magnet placed below (red dashed rectangle). Scale bar 1 cm. **c)** Image of blood flowing in a channel over the GMR sensor. Two labeled cells are recolored in red. Scale bar 100 µm. **d)** A typical signal from a single labeled cell passing the GMR sensor.

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Field Potential-impedance recording of doxorubicin induced cardiotoxicity in human cardioids

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Among the most prescribed drugs in cancer therapy is doxorubicin. Due to significant increase in survival rate of cancer patients, the rise in the incidence of side effects of doxorubicin treatment is increasing as well. One of the most concerning of these side effects is doxorubicin induced cardiotoxicity (DIC).When treated with doxorubicin 25% of the patients present (DIC) at different levels. In this study we combined iPSC-derived human atrial cardioids in combination with microelectrode arrays fabricated in house to evaluate the DIC on chip. Our MEA system permits to do simultaneously field potential and impedance signals recording of atrial cardioids treated with different concentrations of doxorubicin (0.3, 1 and 3 micromolar, and 0.1% DMSO). Impedance spectroscopy gives data about the viability of cardioids on chip. Besides, Calcein/PI staining was performed, and IC50 was calculated. We conclude that the proposed MEA system permits to obtain field potential and impedance spectroscopy signals from our models. This data opens the possibility of studying doxorubicin induced cardiotoxicity and other cancer therapies on the proposed setup.

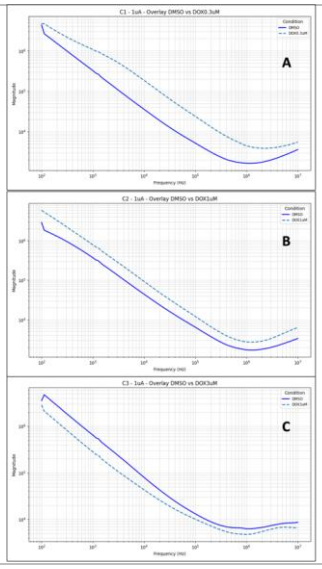

Fig. 1 line graph of EIS measurement at 1 micro ampere. A) cells treated with 0.1% DMSO as vehicle and cells treated with 0.3 micromolar of DOX.B) cardioids treated with 1 micromolar of DOX. C) cardioids treated with 3 micromolar of DOX.

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The CellFACE platform for label-free blood cell function and cytology diagnostics at the point-of-care using phase imaging flow cytometry

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For clinicians working in acute care [1] or with time constraints for pathology results, our sample preparation and label-free point-of-care test (POCT) provide early blood cell and cytological biomarkers within <10 minutes based on proprietary AI-powered real-time phase imaging flow cytometry [2]. We discuss the POC platform technology for next-generation hematology analyzers with cell aggregate biomarkers. CellFACE provides additional upside potentials for POC cytology of brush biopsy and aspiration samples, potentially supporting the decentralized interaction between clinician and pathologist. Last, we highlight recent advancements in the consumable design of microfluidics to improve the phase contrast for imaging without the need to improve the microscope.

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Potential Roles for Lymph Node Fluid and Mass Transport in Immunology

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Lymphatic vessels serve to return interstitial fluid centrally to the blood system, a process that relies on their biomechanical properties and active pumping. Prior to its return to blood, lymph must be "filtered" for antigens as an important component of the immune system. Lymph Nodes serve as information collection/distribution hubs for innate and adaptive immunity, actively delivering antigen information to the appropriate cell types. The size of a human lymph node (order of cm) is such that diffusive and flow-mediated processes are required to distribute information effectively. Specialized blood vessels also run throughout lymph nodes, providing transmural transport of millions of lymphocytes. Small (<70kDa) antigens arriving in solution via afferent lymph are transported via conduits formed of collagen fibers, while larger antigens are distributed through the parenchyma. Antigen presenting cells follow chemokine gradients to find their way to the appropriate nodal compartments. Both antigens and chemokines can be transported by diffusion or advection. Using a combination of multiscale experimental and mathematical approaches, we have investigated the transport of solutes and cells from interstitial spaces into and through lymph nodes. Our results indicate that transport in conduits is nearly entirely diffusive, with collagen fibers providing anisotropic diffusivity. This delivers small amounts of solutes efficiently to targeted locations. Lymph flow is important for formation of chemokine gradients in the parenchyma, which behaves more as a porous medium. These vastly different transport regimes can be targeted for optimal immune response to vaccines, and are likely involved in progression of cancer metastases.

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Oral Sessions

Thursday, July 03, 2025

Rigidity Transition in Epithelial Tissues

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The mechanics of epithelial tissues, which is governed by forces generated in various cell regions, is often investigated using the two-dimensional area- and perimeter-elasticity model that accounts for the apically positioned actomyosin structures but neglects basolateral mechanics [1]. One of the predictions of this model is the loss of tissue shear rigidity at the so-called rigidity transition [2]. We employ a more detailed three-dimensional vertex model to numerically study how lateral surface tensions affect the structure and rigidity of single-cell-thick epithelia [3]. We find that in this model, cells are apicobasally asymmetric, with one side appearing more ordered than the other depending on target cell apical perimeter. In contrast to the 2D model, which predicts a rigidity transition at large target perimeters, tissues in the 3D model remain solidlike across all parameter space. These results suggest that the reduced-dimensionality theories of tissues may not be adequate, and that some of their results may require revision.

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Comparative analysis of static and cyclic mechanical stimulation for tendon tissue engineering

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Mechanical stimulation is a critical regulator of tendon homeostasis and regeneration, and therefore, it is one of the key variables in tendon tissue engineering. While static loading (SL) and cyclic loading (CL) are both commonly employed in vitro to model physiological strain/stress, their comparative impact on tenocyte function and tissue maturation still remains poorly characterized. This study aimed to evaluate the effects of both SL and CL on cell behavior and extracellular matrix (ECM) remodeling in a 3D tendon-like construct using a custom-made bioreactor system (MagneTissue).

Rat tendon-derived progenitor cells (TDPCs) were embedded in fibrin-based ring scaffolds (10 mg/mL fibrinogen, 0.625 KIU thrombin) at a density of 4×10^6 cells/mL. Constructs were subjected to uniaxial tensile strain (10%) for 6 hours daily (7 days in total) using the MagneTissue bioreactor [1]. CL was applied at 0.5 Hz, with a baseline strain of 3% maintained during the resting period. Cell viability, proliferation (Ki67), and alignment (beta-Actin) were assessed using immunofluorescent analysis. To get a broad overview of how the type of mechanical stimulation affects the cells and their response to the loading, we used Oxford Nanopore Technologies (ONT) sequencing. Gene expression of the key extracellular matrix (ECM) remodeling (col1, col3, MMP-13), tendon-specific (Tnc, Tnmd, Scx, Sparc) and inflammation-related (Il6, Ccl2, Cxcl3) markers was analyzed by RT-qPCR.

We have shown that both loading protocols maintained overall cell viability and induced cell alignment along the strain axis. However, CL led to significantly greater cell elongation compared to SL. The proliferation rate was higher in the CL group, accompanied by a reduced number of fragmented nuclei, suggesting better cell survival. TUNEL staining confirmed a higher rate of cell survival upon CL stimulation, showing 13% cell death in this group compared to 20% in SL and 25% in gravity control groups. Transcriptomic analysis revealed an upregulation of inflammatory mediators (IL-6, Ccl2, Cxcl family members) under SL, indicating an inflammatory response [2]. In contrast, CL upregulated genes associated with matrix synthesis and tendon maturation, including Col1, Col3, Tnmd, and Sparc [3].

To conclude, we can say that cyclic mechanical loading provides more favorable conditions for 3D tendon cell culture than static loading by maintaining tenogenic phenotype, promoting cell survival, proliferation, and alignment while avoiding inflammatory response, suggesting that the use of CL should be prioritized when developing *in vitro* tendon models.

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Development of a Digitalized Spacer for Longitudinal Monitoring of Infection in Two-Stage Total Joint Replacement

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Introduction

In Germany, up to 30% of patients undergoing joint implantation experience infections. Spacers serve as temporary, polymer-based implants until the joint is considered healed, allowing for the reimplantation of a permanent prosthesis. Unfortunately, current decision-making processes are solely symptom-based and prone to errors [1;2].

Materials & Methods

Our approach involves upgrading established and approved knee spacers with encapsulated sensor systems (Fig. 1). This innovation enables real-time in vivo data collection, including temperature, infection status of the synovial membrane, and bacterial load (Fig.2). The data is transmitted wirelessly via WLAN to an evaluation system. This will allow treating physicians to track infection progression longitudinally, adapt antibiotic treatment, and determine the optimal time for final prosthesis implantation.

Results

Spectral analysis has successfully detected concentration changes in *Staphylococcus aureus* cultures, allowing for early bacterial load monitoring (with a AI resolution limit of 10^3 cfu/ml; Fig.3) [3;4]. Initial tests with digitalized spacer prototypes have demonstrated the ability to capture live video footage and various physiological measurements from porcine and human knee models (ex vivo), transmitting the data wirelessly (Fig. 4).

Discussion

By integrating optoelectronics, image analysis, and orthopedics, a continuous and non-invasive in vivo diagnostic approach becomes feasible. This will support surgical decision-making and antimicrobial therapy adjustments. Additionally, user-friendly interfaces will facilitate a Digital Health solution, addressing the unmet needs of clinical workflows while ensuring high patient acceptance.

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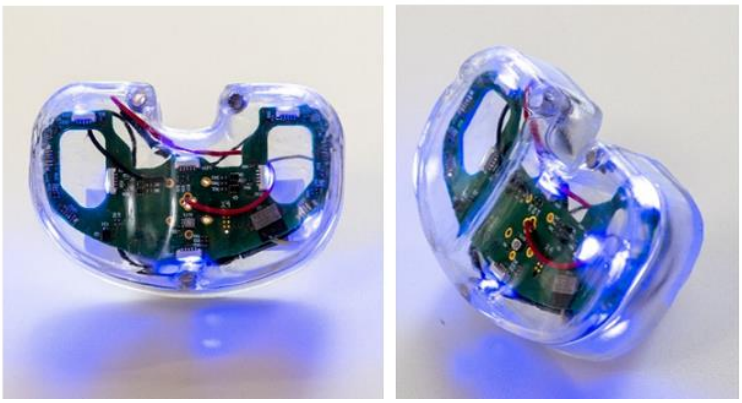

Figure 1: image of the digitized Smartspacer prototype

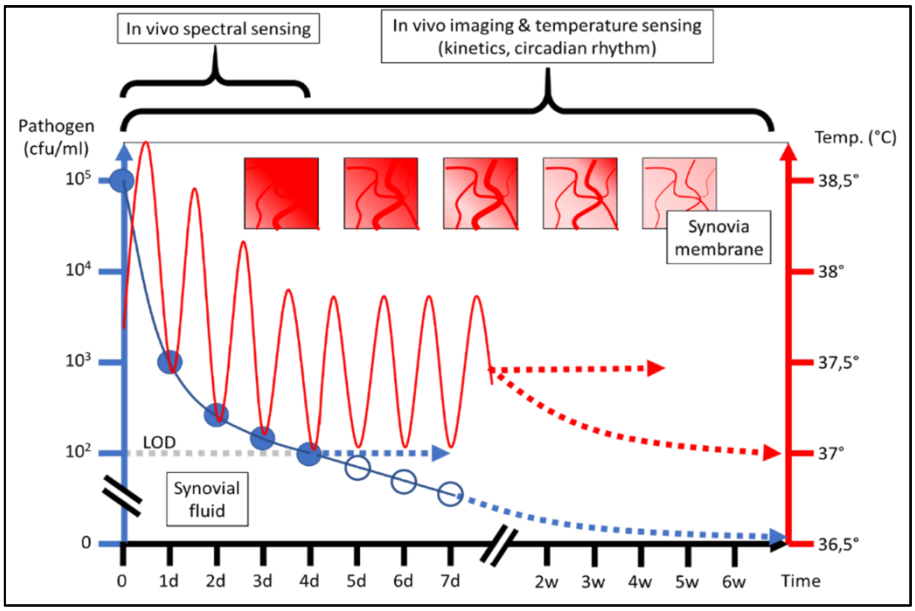

Figure 2: Presentation of the multi-parametric data acquisition

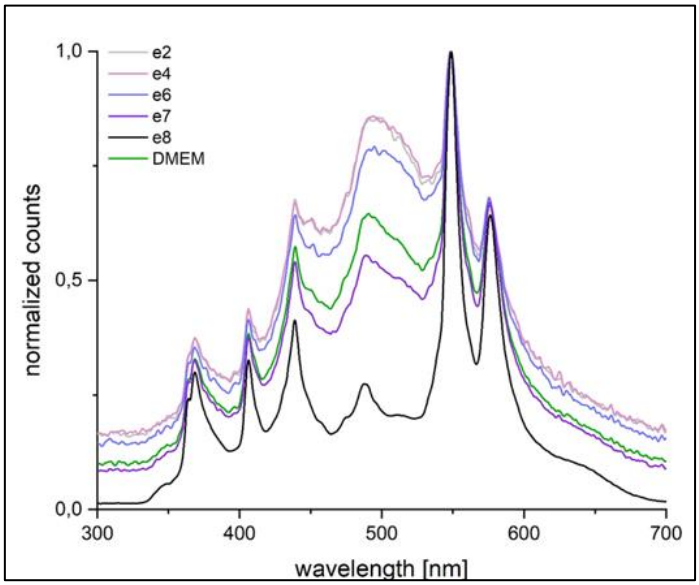

Figure 3: graphical representation of the discrimination of different SA concentrations

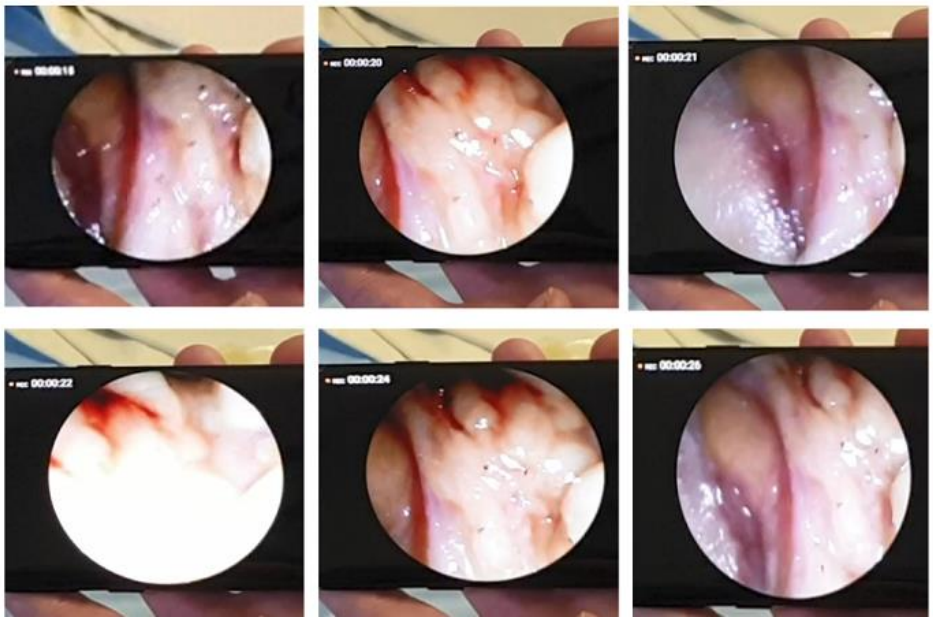

Figure 4:Single image recordings (second 16.26) of the video recording from the inside of a human ex-vivo knee, transmitted via wireless/app-supported connection to the smartphone

MICROMECHANICAL ASSESSMENT OF CARDIAC SPHEROIDS

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Cardiac fibrosis in hypertrophic cardiomyopathy (HCM) is characterized by extracellular matrix (ECM) post-translational modifications. These are driven by cardiac fibroblasts (CFs), mechanosensitive cells that respond to ECM stiffness, potentially accelerating disease progression [1]. A key regulator of fibrosis is TGF-β, which activates CFs and promotes ECM remodeling. Recent advances in 3D cell culture have enabled the study of microtissue biomechanics in cell spheroids (CSs), yet conventional models, i.e. Hertz theory, fail to capture their large deformations. Here, we utilized the extended Tatara model [2], incorporating Mooney-Rivlin hyperelasticity and nonlinear boundary effects, to investigate the mechanics of four CS groups (CU: control untreated; CT: control+TGF-β; HCMU: diseased untreated; HCMT: diseased+TGF-β) derived from human cardiac fibroblasts. To evaluate the effectiveness of the model, results were compared to ones derived from Hertz, Ding and simple Tatara models. The extended Tatara model demonstrates superior accuracy, enabling a more comprehensive mechanical analysis of CSs under parallel-plate compression of up to 50% strain (Fig1a), compared to the other models used. In addition, video footage captured during compression enabled estimation of Poisson's ratio through image segmentation and shape analysis. This allowed further refinement of the calculated compression modulus (Fig1b). Our findings reveal that HCM CSs are nearly three times stiffer than control CSs. TGF-β treatment increased stiffness two-fold in both groups (Fig1c). This study provides a robust framework for assessing micromechanics in patient-derived models of fibrosis, which may serve as an endpoint readout for testing drugs in a patient-specific setting.

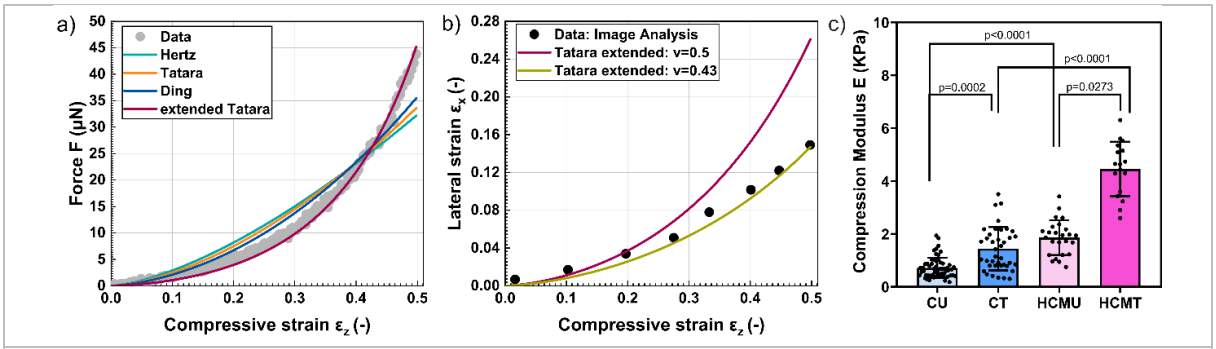

Fig. 1 α) Force-strain data of a CS and the corresponding best-fitted curves obtained by fitting four contact mechanics models, b) Lateral strain as a function of compressive strain assuming incompressibility and compressibility, c) Compression modulus of four groups of CSs.

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Uniaxial Tensile Loading of the Single Collagen Fibril: How to Test it and How to Model it?

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Collagen is the primary constituent in mammalians providing structural integrity in the musculoskeletal systems. The biomechanical properties of collagenous tissues are associated with their physiological state and thus are extensively investigated through experimental and computational mechanics. Uniaxial tensile testing is a commonly used experimental technique for assessment of mechanical properties and has been utilized at multiple length scales along the hierarchy of biological tissues. For instance, even the nanomechanical behavior of the basic unit of fibrous collagenous tissues, i.e. the individual collagen fibril, has been characterized using cantilever-based testing devices such as atomic force microscopy. The experimental results reveal nonlinear rate-dependent mechanical behavior of single collagen fibrils under uniaxial tension [1]. In this context, we employ the visco-hypoelastic model in the sense of the general hyperelastic constitutive equation, where the material elastic response is governed by the stored-energy function $\hat{\psi}$ [2,3]. The model is thus defined in the stress-rate-strain-rate space as:

$$\boldsymbol{\tau}^{\Delta} = \mathbb{C}:\mathbf{d} \; + \; \mathbf{d}_{\boldsymbol{p}}(\boldsymbol{\tau}, \mathbf{d}), \qquad \text{with } \mathbb{C} = 4\mathbf{b}\partial_{\mathbf{bb}}\hat{\psi}(\mathbf{b})\mathbf{b}, \tag{1}$$

where $\boldsymbol{\tau}^{\Delta}$ is the objective rate of Kirchhoff stress; $\mathbf{d}$ is strain rate; $\mathbb{C}$ is the fourth-order stiffness tensor defined by the Helmholtz potential $\hat{\psi}$ as a function of right Cauchy-Green deformation tensor $\mathbf{b}$; $\mathbf{d}_{\boldsymbol{p}}(\boldsymbol{\tau}, \mathbf{d})$ is the dissipative response as function of Kirchhoff stress and strain rate.

The elastic part of equation 1, modeled with a rate form of a Mooney-Rivlin solid describes adequately the nonlinear elastic response of single collagen fibrils stretched at strain rates varying over two orders of magnitude. Thereupon, we identify the inelastic behavior $\mathbf{d}_{\boldsymbol{p}}$ in the sense of visco-hypoelasticity by decoupling the elastic response from the experimental data of [1] and ascribe the dissipative behavior as the consequence of collagen molecule uncoiling and intermolecular sliding upon fibril stretching. In this study, we exemplify the standard methodology of mechanical testing and modeling for single collagen fibrils in terms of uniaxial tensile loading. Mechanical characterization at the fibrillar level provides critical information to the development of a multiscale model to analyze the mechanical behavior within the hierarchical structure of biological tissues.

Acknowlegement:
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Nano-engineered Materials for Wastewater Remediations

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Nano-engineered materials have been used extensively for a variety of applications. Environmental pollution raised bigger concerns on the discharge of textile waste. Nanotechnology is fast growing on research and bringing sustainable solution in the minimization of the waste. The minimization of the risk of risk and health hazards with the development of industry, environmental pollution and energy shortages have raised awareness of a potential global crisis. Nano-engineered materials can be better solution in finding solution of environmental sustainability more specific to the textile waste remediation due to the large surface areas, diverse morphologies, abundant surface states, and easy device modeling. It is a challenge of great importance to identify and design nano-engineered materials that are efficient, stable, and abundant for the remediation of textile waste. The current talk will be focused on the recent advancement and applications of nano-engineered materials for wastewater remediation.

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New era of plasma engineering for the design of catalysts in biomass upgrades and biodiesel production

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Plasma, consisting of electrons, ions, molecules, radicals, photons, and other excited species, has complex atomic and molecular processes and versatile physical and chemical reactions with solid materials. Frontier research based on plasma process and engineering has been expanded to electrochemical energy storage systems and renewable energy conversions. This presentation discusses the contribution of plasma engineering to the synthesis and surface modification of functionalized catalysts for biomass upgrades and biodiesel production. Unlike conventional syntheses, plasma engineering allows direct carbonization to synthesize carbon nanomaterials in organic solvent (e.g., benzene, pyridine, phenylamine) at ambient temperature and pressure. Specifically, the generation of NC can be achieved via rapid C-N and/or C-C integration during plasma discharge and the related chemical reactions. One-step hybrid metal/ carbon materials synthesis can be realized when metal precursors are introduced into the organic solution. In addition, when applied in-situ ultrasonic homogenizer during plasma engineering, ultra-fine and dispersed metal nanoparticles or even single-atom doped metal in carbon substrate was successfully synthesized. The design, synthesis, and DFT modeling on the multi-functional catalysts will be discussed, followed by the current progress on the performance of these catalyst on the upgrades of cellulose to fermentable sugars, as well as wasted oil to biodiesel will be covered. Finally, the future research directions, challenges, and opportunities of plasma engineering in biodiesel production, in particular, in the field of maritime and aviation application will be explored.

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An overview of Sol Gel Technology: Nanoscale methodology for industrial and environmental applications

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Sol gel technology is a wet chemical technique converting liquid colloidal suspension (Sol) to solid (Gels (wet / xero /aero)) for developing ceramics, thin films, glassy materials, nanomaterials for reinforcement in nanoscale. A simple and easy to handle technique provides a wide platform for different types of nanomaterials that is being used for many industrial and environmental applications. With different precursor materials and reaction conditions, sol gel methodology give rise new materials with tailor made material properties as shown in Fig 1. These reaction conditions deliver high surface area with tunable porosity and mixing of precursors in liquid phase provide the homogeneity. Some precurosrs being biocompatible are good sources for biomedical applications such as sensors and implants. The variety of applications include drug delivery systems, sensors and photonic devices, efficient catalysts for engineering applications, thin films and coating for optics, antireflective and protective layers. This talk will unfold the fundamental of sol gel technology leading to its potential for developing nanomaterials and nanocomposites for environmental and industrial applications.

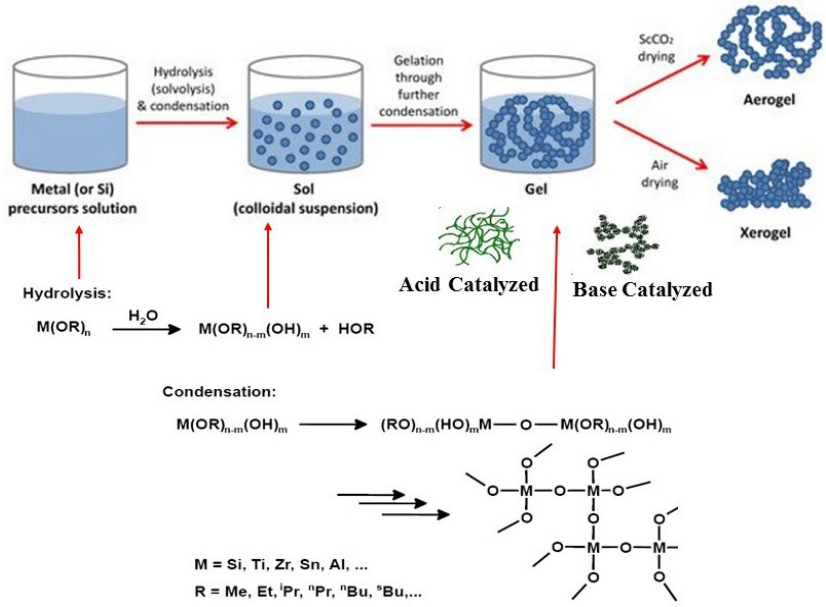

Fig 1. Schematic presentation of Sol-Gel Technology

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Fungal secondary metabolites - from pharmaceuticals to toxins

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Filamentous fungi are rich sources for pharmaceuticals but are also economically important producers of toxins. The first antibacterial substance, isolated from such a fungus, was penicillin, and other examples for active fungal metabolites are statins used for cholesterol control **(Fig. 1)**. About 70 % of all drugs today on the marked are derived from natural compounds (bacterial, fungal or plant origin), and the emergence of multi-resistant bacteria illustrates the urgent need for new pharmaceuticals. Genome analyses of thousands of fungi revealed a much greater potential to produce secondary metabolites than so far anticipated. The reason is that most secondary metabolites are not produced under laboratory conditions. The challenge for researchers today is to "wake-up" such "sleeping" genes to explore the full potential of fungi as producers of pharmacological-active compounds and thereby discover new drugs (Scherlach & Hertweck, 2021).

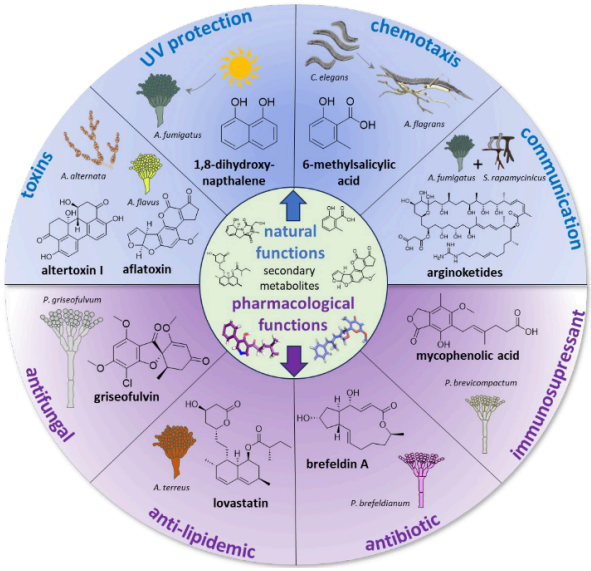

Fig. 1: Diversity of fungal secondary metabolites. Bottom, pharmacological functions assigned to fungal compounds, such as the mitosis-inhibiting antifungal compound griseofulvin, produced by *P. griseofulvum*; the HMG-CoA reductase inhibitor and hence cholesterol- lowering compound lovastatin, which led to the development of the statin blockbuster drugs; the protein-secretion inhibitor antibiotic compound brefeldin A, produced by *P. brefeldianum*; the purine-biosynthesis inhibitor mycophenolic acid produced by *P. brevicompactum*, which is used as an immunosuppressant drug. Top, recently discovered natural functions of fungal SMs, such as communication devices in the inter-kingdom species communication, as is the case for bacterial arginoketides recognized by *Aspergillus* fungi; volatile compounds such as the *A. flagrans*-produced 6-MSA which serves as a chemoattractant luring the nematodes into the fungal mycelial traps; 1,8-DHN, the monomer of the fungal black pigment melanin, which confers protection against UV damage; fungal toxins such as aflatoxin and altertoxin I, produced by *A. flavus* and *A. alternata*, respectively. Taken from (Stroe *et al.*, 2024).

A well-known mycotoxin is aflatoxin, produced by *Aspergillus flavus* and other fungi. The fungus *Alternaria alternata* is an important post-harvest food and feed contaminant and produces alternariol as typical mycotoxin. It also produces the cancerogenous altertoxins, whose biosynthesis route we discovered recently with a combination of genome-sequencing, gene-knock-outs and chemical and structural analysis of intermediates (Gao *et al.*, 2022; Gao *et al.,* 2025, *submitted*). The knowledge of the genes and enzymes involved in mycotoxin biosynthesis will enable us developing new strategies for preventing mycotoxin contaminations during food or feed storage and processing.

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Poster Session

Tuesday, July 01, 2025

Microfluidic Engineering for the Development of Ozonized Oil Microemulsions Aimed at Canine *Leishmania* Treatment: Implementation of 3D Skin Models

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The skin is the primary interface between the host and *Leishmania* parasites, where initial interactions can lead to severe cutaneous lesions [1]. *In vitro* 3D skin models allow for studying these interactions and exploring new therapies like ozone therapy, recognized for its antimicrobial and regenerative properties [2, 3]. However, ensuring the stability and bioavailability of ozone-derived compounds in ozonated vegetable oils remains a challenge, requiring innovative engineering approaches.

This study aims to establish and evaluate the viability of canine skin explants *in vitro* as a platform for testing the efficacy of ozonized oil against *Leishmania* infection. Additionally, we explore different approaches for developing ozonized oil microemulsions. In this initial phase, a pre-existing microfluidic device was used to evaluate formulation stability.

Skin explants from five dogs (n=5) were maintained in culture and assessed at T0, T3, T5, T7, and T10. Metabolic Activity was analyzed using the resazurin assay, while histological integrity was assessed through hematoxylin-eosin staining.

In parallel, a microfluidic-based device was used to produce microemulsions of ozonized olive oil at 400 IP and 800 IP in an aqueous solution of surfactant (Tween 80 at 2.5%) and study formulation stability.

Preliminary results demonstrated that the culture system maintained viable skin explants for at least five days, supporting its feasibility for *Leishmania* infection studies. Microfluidic systems showed promise in developing ozonized oil microemulsions, with further optimisation needed. Future applications may extend beyond cutaneous treatments, potentially exploring ocular and other therapeutic uses.

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Computational and Mathematical Modeling for Describing Biological Systems – Application in Pharmacology and Biomedicine

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With the rapid surge of drug innovation and treatment option advancements, there is the urgent need for more effective and safer drug testing [1]. This research highlights the use of computational and mathematical modeling in advancing the effectiveness of drug testing with implementation of various biomimetic descriptor correlations with the designated compounds. These parameters provide an inside into how different compounds act in different environments of the human body and thus help us understand their effectiveness [2].

The first phase of our research focused on high performance liquid chromatographic testing of drugs which have effect on the central nervous system in a chromatographic C18 column with the flow rate of 1 ml/min, under the conditions of 0.1% of formic acid/20mM ammonium formate with the use of acetonitrile as a mobile phase. As a result, observed retention time values were used to calculate retention factors used to model different linear, logarithmic linear and quadratic equations as a function of acetonitrile percentage (later denoted as φ) and find the best fit based on the minimum values of AIC coefficients.

$$log\ k = A_0 + B_0\varphi$$
$$log\ k = A_1 + B_1 log\varphi$$
$$log\ k = A_2 + B_2\varphi + C_2\varphi^2$$

Coefficients defining those equations were used in correlation analysis between compounds and pharmacokinetic descriptors giving correlation factors as an output.

In the second phase of our research, we used those correlation factors with GA-MLR models to predict the retention factors of compounds enabling us to compute new biomolecular descriptors without executing a chromatographic experiment hence providing time efficiency and effectiveness of drug testing ($r^2_{\text{pred}} > 0.70$).

The obtained results can be successfully used in the prediction of biomimetic information of newly synthesized drugs with effects on the central nervous system with the possibility for further application in drug effect research on other parts of the human body.

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Laser surface functionalization of biomedical Ti-TiB_2 composite in different gas atmospheres

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The chemical nature of the surface layer plays a crucial role in the success of osseointegration, while structural connection with living tissue is greatly associated with roughness, topography, porosity, wettability, and surface energy. To reach optimal osteoblast differentiation and protein adhesion, surfaces with moderate Ra parameter values of 1-2 μm in a moderate range of hydrophilicity seem to be sufficient [1,2]. In fact, the mechanical properties of pure titanium are not similar to those of human bones; thus, the use of titanium-based composite materials (TiMMCs) with a low Young's modulus should be considered [3]. In terms of dental implant applications, a novel Ti-TiB_2 composite with 5 vol.% of TiB_2 was prepared with spark plasma sintering (SPS) and machined by a nanosecond laser beam in various gas atmospheres, namely air, argon and pure oxygen with different flow rates.

The influence of laser micromachining on the relationship between surface morphology, wettability, and chemical composition has been experimentally investigated via profile roughness evaluation, static contact angle (CA) measurement by sessile drop technique after 24 h and 30 days, SEM, and EDX analysis. The potentially sufficient surface structures with increased hydrophilicity were successfully prepared via laser modification technique in air on Ti-TiB_2 composite.

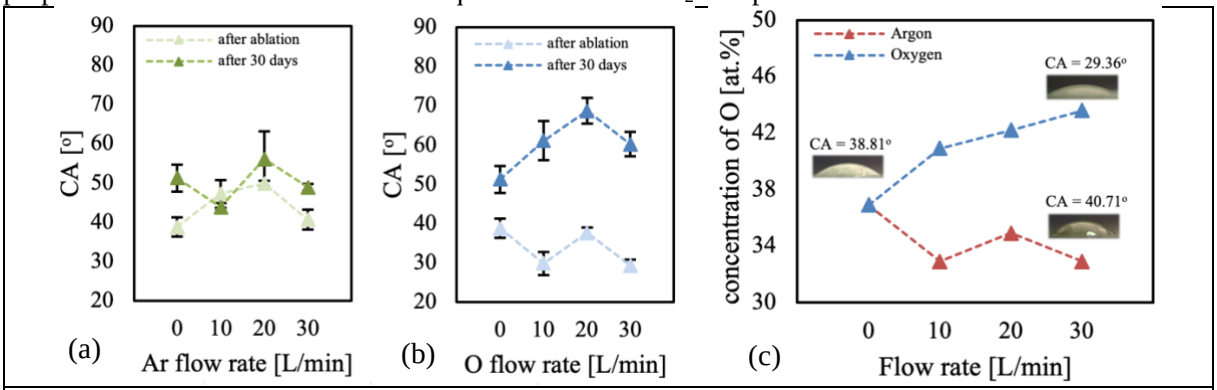

Fig. 1 The effect of (a) Ar flow rate, (b) O flow rate on contact angle and (c) concentration of O

From the results, it can be stated that the presence of an Ar atmosphere seems to have a diminishing effect on chemical composition and topographical changes compared to the presence of pure oxygen or ambient atmosphere. Conversely, the presence of oxygen flow rate seems to induce prominent cracking initiation. Surface wettability correlated with the presence of O atoms and transferred energy alternation.

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Classification of Leukocyte Subtypes Using Digital Holographic Microscopy

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Hematology analysis is the most requested in vitro diagnostic test. With the advancement of high-throughput microscopy methods, new workflows for automated analysis are developed, enhancing the opportunities for flow cytometry read-outs, such as scatter or impedance. This work introduces a label- and reagent-free diagnostic approach that combines off-axis differential digital holographic microscopy (DHM) and microfluidic flow techniques to derive biophysical cell information based on quantitative phase contrast. Our previous study (Fresacher et al., 2023) [1], which utilized Mask R-CNN for the segmentation and classification of phase-contrast images, demonstrated high precision in identifying three primary classes: erythrocytes, leukocytes, and platelets. Our current study uses advanced image processing pipelines to train state-of-the-art segmentation and classification models (YOLOv11 and Mask R-CNN). This approach enables the precise identification of erythrocytes, platelets, and leukocyte subtypes (basophils, eosinophils, lymphocytes, monocytes, and neutrophils). The framework achieved an overall 99.2% precision, 99.1% recall, and 99.3% mean average precision at threshold 50% (mAP_{50}) for the best weight across all classes in the test dataset, underlining its potential to replace conventional labor-intensive methods in routine clinical diagnostics. Next to single-blood cell analysis, the quantitative phase imaging allows us to extend a complete blood count and analyze complex cell aggregates label-free, such as leukocyte–platelet and platelet-platelet aggregates. This cell function information cannot be covered by a conventional hematology analyzer and allows integration of novel biomarkers for acute care diagnostics.

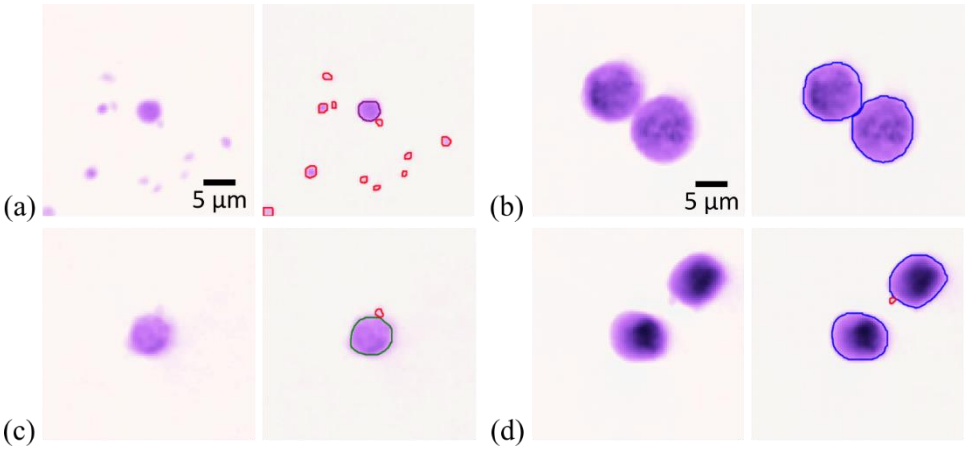

Fig. 1 Blood samples showing exemplary leukocytes and aggregates thereof recorded with quantitative phase imaging flow cytometry. (a) Basophil-platelet aggregate with multiple single platelets, (b) eosinophil, (c) lymphocyte-platelet aggregate, and (d) neutrophils, one of which is aggregated with a platelet.

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Enhanced Liver-Targeted Gene Delivery through Rational Engineering of AAV8 Capsid Mutants

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Adeno-associated virus (AAV) vectors have emerged as an essential resource for gene therapy. However, limitations such as suboptimal receptor binding and low infectivity stress the need for improved capsid designs. In this study, we engineered AAV8 capsid mutants to enhance liver-targeted gene delivery by introducing amino acid substitutions. These mutations are predicted to increase lamR receptor binding affinity, boost infectivity, and ultimately improve liver-specific transduction.

Infectivity assays were performed to evaluate the impact of these modifications, focusing on cell binding and transduction efficiency. Additionally, atomic force microscopy measures the binding properties between lamR and each AAV2/8 capsid mutant. The results showed several mutants significantly outperform the wild-type AAV8 in receptor binding and transduction efficiency. These findings demonstrate the potential of rational capsid engineering to overcome current barriers in AAV-based gene therapy.

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Advanced Polymers for Biomaterials and 3D Printing

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The CD Labs' research is focused on important research questions in oral and maxillofacial surgery: Materials for 3D printed implants and bone adhesives, especially for complex fractures.

The field of 3D printed implants has seen significant progress. Suitable implants are notable for their ability to be customized based on a patient's CT scans and for their use as support for tissue growth. They help bone tissue to regenerate while also breaking down over time. The material must meet these requirements: it must not be toxic, be able to be printed using 3D technology, and be able to be customized and integrated. The implants must be strong, porous, and provide nutrients.
We study individual components of complex formulations containing degradability enhancers [1], toughness enhancers [2-4], photoinitiators [5], fillers, bio-interactive components like hydrogels [6] etc. and final products, either biocomposites or bioceramics [7] from the viewpoints of biomedicine and material science.

Bone adhesives, on the other hand, are used when screws and/or plates are no option for fixing broken bones, like in cases of comminuted fractures. Like 3D printed implants, the ideal bone adhesive should be strong and porous, and it should break down over time, however, also needs to contain so-calles primer molecules, which establish adhesion to bone substance and also enable, e.g., light-triggered curing. [8]

Christian Doppler Research Association, Austrian Federal Ministry of Labour and Economy Affairs, National foundation for Research, Technology & Development.

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Exploring Binary Cluster Crystals via Molecular Dynamics Simulations

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Cluster crystals consist of particles governed by purely repulsive, bounded interactions, forming stable clusters whose centers arrange into a periodic lattice. The generalized exponential model of order 4 (GEM-4) potential, $\Phi(r)=\epsilon \exp[(r/\sigma)^4]$, permits significant particle overlap, enabling cluster formation. While one component cluster crystals are well studied [1,2], binary systems remain largely unexplored. We investigate the structural and dynamic properties of binary cluster crystals in an equimolar, symmetric system, where unlike particles experience an increased repulsion via a parameter ζ. Density functional theory predicts two dominant phases: a body-centered cubic (bcc) lattice and an interlaced tetragonal structure [3]. Using molecular dynamics (MD) and hybrid Monte Carlo-molecular dynamics (MCMD) simulations [4], we analyze the time evolution of the systems, structural transitions and particle dynamics. Beyond equilibrium, we examine the response of binary cluster crystals to shear. Studies reveal shear-driven transformations [5]: shear banding at low shear rates, string formation in the gradient-vorticity plane, and a shear-molten state at high shear. Extending these studies to binary systems will provide new insights into mechanical properties and transport behavior. This study advances the understanding of binary cluster crystals under equilibrium and shear. Future work will quantify shear-induced transport properties and explore mechanical tuning of crystalline phases.

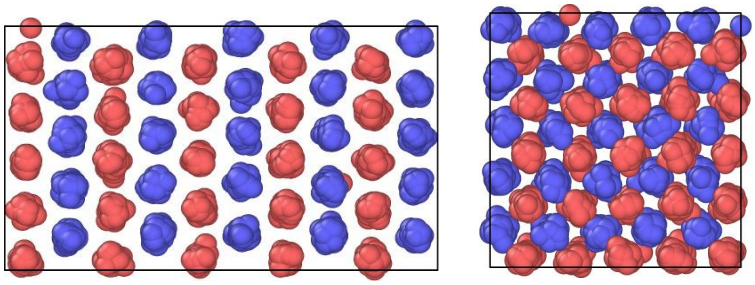

Fig. 1: *Binary cluster crystals: Interlaced tetragonal structure (left) and interlaced bcc structure (right).*

The computational results are obtained using the Vienna Scientific Cluster VSC (VSC).

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Hydrodynamics and Chemotaxis of Active Chiral Rotors

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A spinning active chiral rotor generates chiral flows in the medium due to its rotlet. The former system is related to the chiral squirmer system [1] by removing the self-propulsion part from it. In this work, we observe the dynamics of a pair of chiral rotors in the presence of a chemical field. Notably, a single rotor is not capable of motion but can only be propelled by the hydrodynamic perturbation coming from its neighbour. The hydrodynamic interaction among the rotors drives them either in straight line paths or circular orbits, see fig. 1 (a), (b). The nature of the trajectories depends on the type of rotors, such as clockwise and anticlockwise chirality, and the relative orientation of the rotation axis with respect to the rotlet direction. Moreover, the presence of a chemical field may drive the rotors either toward the chemical target (chemotaxis) or away from the target (anti-chemotaxis) [2].

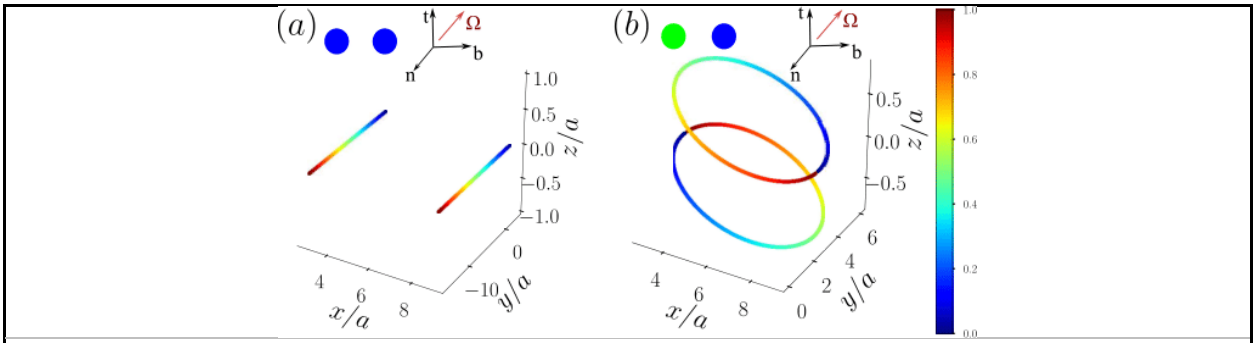

Fig. 1 (a) Two rotors with identical rotlet move in straight-line paths, (b) Two rotors with opposite chirality move in circular paths. The colorbar depicts the normalized time.

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Phase Separation Dynamics in a Symmetric Binary Mixture of Ultrasoft Particles

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Biological and soft-matter systems are significantly impacted by phase separation. Within cellular environments, this process, specifically liquid-liquid phase separation, drives the creation of diverse macromolecular clusters. These clusters exhibit weak interactions, allowing substantial overlap with minimal energy expenditure. In computational simulations, these structures are often parameterized as so-called ultasoft particles, interacting through a generalized exponential potential (GEM-n) where n is set to 4 [1,2]. We perform molecular dynamics simulations to investigate the phase separation behavior of a binary mixture, featuring size symmetric ultrasoft particles. When this mixture is rapidly cooled below its critical temperature, we observe a spontaneous separation of the two components [1,3]. This process results in the formation of distinct domains for each component. By analyzing two point equal-time correlation function of order parameter we find a power-law growth of these domains, characterized by an exponent of 1/3, consistent with the Lifshitz-Slyozov law for conserved systems [3,4]. Additionally, the static structure factor reveals a power-law decay with an exponent of 4, consistent with Porod's law [3].

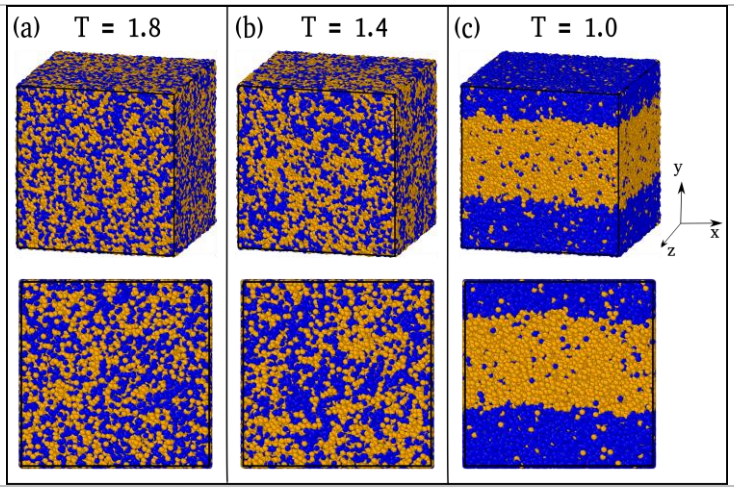

Fig. 1 Snapshots of the system at different temperature (as labelled). Upper panels: perspective views of snapshots of the system in 3D. Lower panels: cross sections of the respective upper panels at $z = \frac{L}{2}$.

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Investigating Displacement-Controlled Stimulation Profiles in the MagneTissue Bioreactor through Force-Controlled Testing

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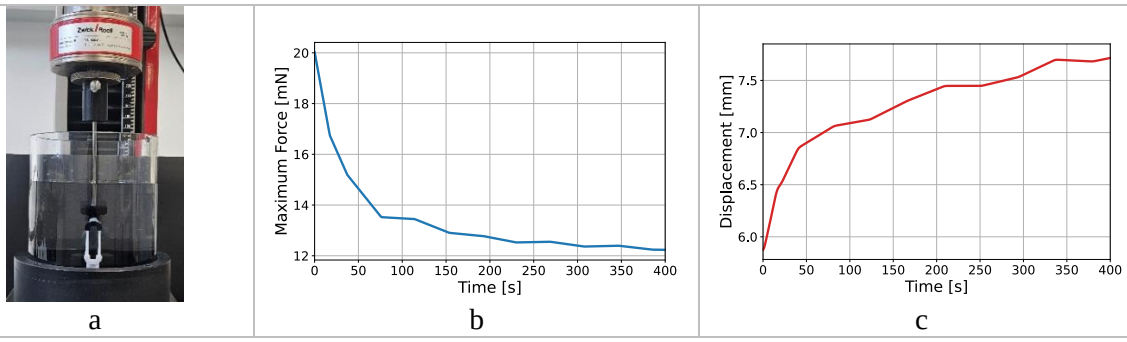
An approach to guide cell growth and tissue development in *in vitro* tissue engineering is the use of mechanical stimulation on cell scaffolds. Bioreactors that can apply constant or cyclic strain on tissues are currently being used in different applications. The custom-made MagneTissue bioreactor is one example of a bioreactor that enables mechanical stimulation to 3D tissue constructs in two different modes: static and dynamic loading [1]. As for most bioreactors, strain is induced in a displacement-controlled fashion, ignoring the actual forces and stresses acting on the scaffold. Emerging evidence suggests that cells respond primarily to stress rather than strain. In this study, the limitations of displacement-controlled bioreactors are investigated by determining the mechanical response of scaffolds. A possibility to improve their control of the acting stresses is proposed.

In previous studies, the MagneTissue bioreactor has been used to stimulate fibrin rings, acting as cell scaffolds for *in vitro* skeletal muscle tissue modeling. To measure forces that are acting on the scaffold during this stimulation, a displacement profile from the bioreactor was replicated on a universal testing machine in a PBS bath (figure 1a), measuring the mechanical response of fibrin ring-shaped constructs without cells. The stimulation profile cyclically applies a strain of 20% with a frequency of 0.5 Hz. Stress relaxation was observed as shown in Figure 1b, confirming the viscoelastic nature of fibrin rings and that stresses observed by the cells change over time.



a b c

Fig.1 (a) Experimental setup for mechanical characterization of fibrin ring-shaped scaffolds in a PBS bath. (b) Force relaxation curve after replication of bioreactor displacement profile. Maximum force values for each cycle of an exemplary experiment were interpolated. (c) Displacement during force-controlled testing. Maximum displacement values for each cycle of an exemplary experiment were interpolated. Displacement of 6 mm corresponds to 20% strain.

In the next step, force-controlled tests were conducted on the same setup, where each cycle of stimulation was limited by a maximum force. The force limit was chosen as the maximum force during the first cycle of the displacement-controlled experiment. The resulting displacement profiles (figure 1c) can be interpreted as an ideal loading protocol to ensure consistent stress for a specific sample. For displacement-controlled and force-controlled experiments, results vary. Further investigation aims to optimize the displacement profiles of the MagnetTissue bioreactor for better control of mechanical stimulation and tissue growth.

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Integration of Bioorthogonal Chemistry into Iontronically Controlled Drug Release Systems

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Iontronics focuses on the use of charged species to facilitate electrical, chemical, and biological signaling. Within this field, the organic electronic ion pump (OEIP) has evolved into a state-of-the-art device over the past decade.[1,2]

This innovation offers drug delivery with high spatiotemporal resolution and electronic precision while maintaining a constant target volume, thereby highlighting its potential, especially for localized treatments.

However, OEIPs are limited to delivering only charged molecules and impose a molecular weight restriction of 500 g/mol, thereby excluding the majority of top pharmaceuticals from their potential applications.

To overcome these limitations and expand the capabilities of OEIPs, we propose combining iontronics with biorthogonal release chemistry models.[3,4] In our approach, a charged, small molecular weight moiety can be iontronically delivered towards a caged molecule (fluorophore, drug), thus triggering a release reaction of the payload. As such, we aim to overcome the current weight and charge limitations of OEIPs and still enable a rapid, efficient, and controlled payload release.

As a molecular proof of concept investigation on kinetics, the stability of various synthesized compounds, as well as their feasibility within iontronic devices, will be presented.

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A Strain-inducing Bioreactor to Mature Muscle and Peripheral Nerve Tissue In Vitro

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The development of physiologically relevant 3D tissue models remains a major challenge in tissue engineering. To address this, a strain-based bioreactor system—MagneTissue—was developed at the University of Applied Sciences Technikum Wien. This system applies controlled tensile strain to fibrin-based scaffolds seeded with cells, enabling the maturation of aligned skeletal muscle and peripheral nerve tissue constructs in vitro.

The bioreactor uses magnetic force transmission via stepper motor-controlled scaffold holders to apply static, cyclic, or ramped strain protocols. C2C12 myoblasts and Schwann cells were cultured on fibrin hydrogels, allowing for the development of muscle- and nerve-like tissues. Morphological and molecular analyses showed that static strain induced myotube alignment and upregulation of myogenic markers such as MyoD, Myogenin, and TnnT1. Cyclic strain further enhanced these effects by activating hypertrophic signaling pathways, including mTOR and Erk1/2.

In nerve regeneration models, strained Schwann cell constructs mimicked bands of Büngner and expressed neurotrophic markers like BDNF, NGF, and p75NTR. Co-culture with dorsal root ganglia demonstrated guided axonal outgrowth, confirming functional relevance.

The MagneTissue system enables precise mechanical stimulation, supporting the development of biomimetic tissue constructs and advancing mechanobiological research. It is currently employed in several projects including the FWF-funded doctoral program MatureTissue (DFH-28) and the FFG-funded ArtNerve spin-off fellowship.

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Phase Transitions in Bent-Core Patchy Colloids: A Free Energy Perspective

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We present a novel model of colloidal patchy ellipsoids [1] designed to study the self-assembly and phase behavior of bent-core liquid crystals [2], with potential applications in biomedical engineering, bio sensing, and nanotechnology. The system consists of a binary mixture of mirror-symmetric ellipsoids (left- and right-handed) interacting via a Gay-Berne potential and decorated with surface patches that guide a two-step assembly process. In the first stage, monomers form bent-core dimers with a specific bent angle, while the second stage leads to the emergence of mesoscopic liquid-crystal phases, including nematic, smectic, and twist-bend phases [3]. These phases exhibit unique optical and photonic properties, making them promising candidates for applications in biophotonics, biosensors, and lab-on-a-chip technologies.
To elucidate the intricate phase behavior of this system, we conduct extensive free energy calculations [4], employing thermodynamic integration methods [4] and the Einstein Molecule approach [5] to determine phase boundaries between isotropic, nematic, and smectic phases. Our findings provide key insights into the stability and transition mechanisms of these emergent mesophases. Furthermore, this study establishes a framework for investigating a broader class of colloidal patchy ellipsoids, including chiral variants, by tuning parameters such as the bent-core angle, flexibility, and interaction strength hierarchy. These results open avenues for designing novel self-assembling colloidal materials with tailored structural and functional properties.

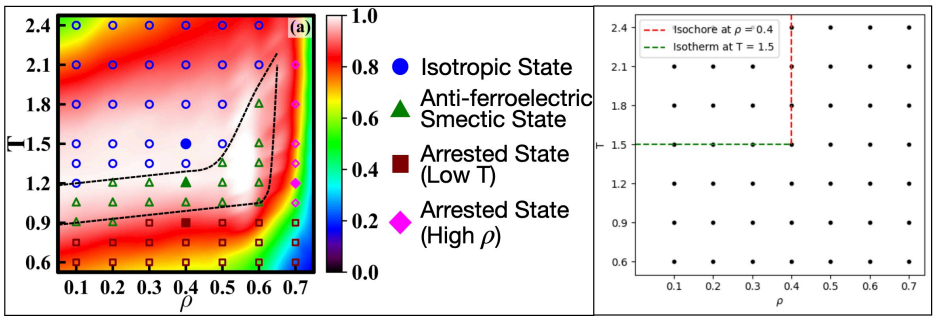

Fig. 1 (Left) State Diagram of bent-core patchy colloids [3]. The color bar indicates the amount of bent-core particles formed. (Right) An illustration of the free energy computation route taken to compute the free energy of the isotropic state at (ρ, T) = (0.4, 1.5).

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Influence of Stent Strut Thickness on Local Hemodynamics and Vascular Cell Response

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Coronary artery disease is one of the leading causes of mortality worldwide [1] and it is commonly treated by performing percutaneous coronary intervention with stent implantation [2]. However, stents inevitably alter local hemodynamics, potentially leading to in-stent restenosis caused by neointimal hyperplasia [3]. It is well established that regions of low wall shear stress promote this pathological response [4]. Wall shear stress is strongly affected by stent design, and parameters such as strut thickness play a key role in optimizing stent performances [5].

In this study, a coronary stent with a rhomboidal unit cell will be investigated (Fig.1-a), with strut thickness as a variable parameter. Three different thicknesses will be analyzed by designing microfluidic channels that mimic the vessel lumen, incorporating stent portions protruding at 50% of their total thickness (Fig.1-b). Computational fluid dynamics simulations will be performed to assess the effect of these variations on local wall shear stress, and the numerical results are planned to be validated through micro-particle image velocimetry. Finally, dynamic cell culture experiments are intended to be conducted within the microfluidic chips to correlate wall shear stress distributions with vascular smooth muscle cell migration and proliferation.

These findings are expected to contribute to a better understanding of the relationship between stent geometry, hemodynamics, and vascular cell behavior, providing insights into optimizing stent design to reduce restenosis risk.

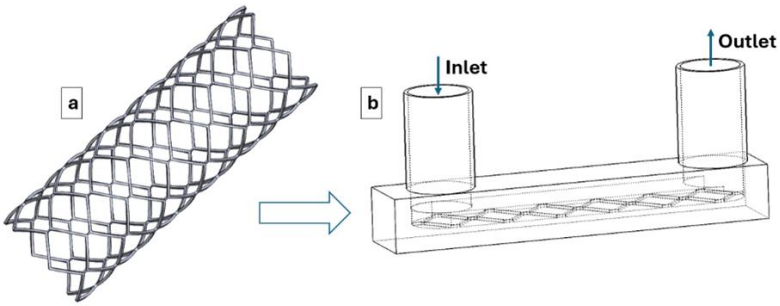

Fig. 1 a) CAD of the coronary stent, b) Microfluidic chip

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Surface modifications of chitosan coatings with femtosecond laser pulses

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Surface properties play a critical role in the performance of biomaterials, as they determine the interactions on the material-tissue interface [1]. Upon implantation there is a competition on the surface between bacterial colonization and cellular adhesion. The outcome of this „race for the surface" plays a crucial role in the long-term success of the materials integration in the body [2].
Among the surface characteristics chemical composition and topographical features are particularly influential and these can be controlled and precisely engineered with the use of surface coatings and subsequent laser structuring.

In this study, we create coatings using chitosan, a promising biopolymer with excellent biocompatibility and antibacterial properties. The coated surfaces are then modified with femtosecond laser pulses that allows for creating hierarchical surface structures without significantly altering the chemical composition. This approach enables the precise modulation of the interfacial properties that govern biological interactions. Femtosecond laser processing was shown to increase hydrophilicity on chitosan thin films [3]. This initially attracts both bone cells and bacteria. However, by creating micro and nanoscale surface features high mechanical stress can be induced on the bacteria that leads to the physical disruption of its membrane eventually hindering biofilm formation. [4]

Previous research [3] has shown that cellular orientation can also be modulated with varying surface structures and in this study, we aim to extend and bond these findings by characterizing new hierarchical patterns and their effect on various biological responses.

Using femtosecond laser pulses, with varying wavelengths, pulse durations and pulse energies we aim to create functional micro and nanostructures on chitosan coated samples. These surfaces are then systematically characterized by contact angle measurements, scanning electron microscopy, and profilometry to assess changes in wettability and morphology. Additionally biological assays will be conducted to evaluate cellular response and the antibacterial potential of the laser treated surfaces.

With this approach we aim to establish a more systematic understanding on how laser induced surface modifications influence bone as well as bacterial cell behaviour on biopolymer surfaces. An iterative method will be conducted in which the results from the biological assays will guide with the optimization of laser parameters, with the goal of developing functional biomaterial surfaces for improved orthopedic and dental implants where accelerated and controlled tissue integration and reduced infection risk are both essential.

This research was funded in whole by the Austrian Science Fund (FWF) 10.55776/DFH64

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Thermodynamic consistent theory of crosslinkers on biological filaments

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The cytoskeleton is the intracellular structure, that enables cellular motion and essential cell-mechanical processes like the cell division and chromosome segrega- tion. It consists of filaments (actin, microtubules, intermediate filaments) that are crosslinked by proteins, many of which are molecular scale motors that consume ATP to do work between cytoskeletal filaments. In roughly a hundred years of research, biologists and biochemists have uncovered and characterized many of the constituent proteins of the cytoskeleton. However, we are still lacking a deeper understanding how collective behavior of these parts working together emerges and specifically how the cytoskeleton self-organizes into useful cellular machines like the spindle or the cell cortex. We know that filaments and crosslinkers organize into a dynamic network, that keeps itself out of thermodynamic equilibrium by consuming chemical energy from the cellular environment. This make the study of the cytoskeleton and its compo- nents an essential step for understanding the physics and statistical mechanics of living, and out of equilibrium materials more broadly. I aim to develop the theoretical basis for understanding the forces that crosslink- ing proteins exert collectively between two filaments that they couple. More pre- cisely, I will study the non-equilibrium statistical mechanics of a gas of Motor (active) and non motor (passive) proteins on 1D manifolds (filaments). This will allow me to take a macroscopic point of view, which will complement more traditional agent based approaches. Using a macroscopic approach will allow me to be general - since I can write a complete thermodynamic consistent theory from conservation laws and symmetry principles alone - and thus simplify the exploration of different collective behaviors of the crosslinking proteins regardless of microscopic details, that are of- ten poorly characterized in experiment. Specifically, **I will use this theory to ask: What are the forces acting between filaments from the cytoskeleton and how do they depend on collective protein behaviors and properties?**

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Ceramic-fiber reinforced photopolymers: Enhanced interfacial strength by modification of surface properties

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Photopolymers are widely used in additive manufacturing, dentistry, and biomedical applications [1]. However, due to their predominantly covalent bonds and densely crosslinked network, they are inherently brittle and exhibit lower strength compared to other engineering materials [2]. To overcome these limitations, photopolymers are reinforced with ceramic fibers. The boundary between matrix and fiber, called interface, is a critical region in fiber-reinforced composites, as it governs the load transfer between the two components [3]. Therefore, we investigated the influence of different fiber surface treatments on the interfacial adhesion. The study demonstrates a significant improvement in interfacial shear strength (Figure 1, a), along with improved wettability of the fiber by both water and the photopolymer itself, as determined through contact angle measurements (Figure 1, b). These results underline the importance of the fiber/matrix interface and contribute to the development of high-strength, ceramic fiber reinforced composites.

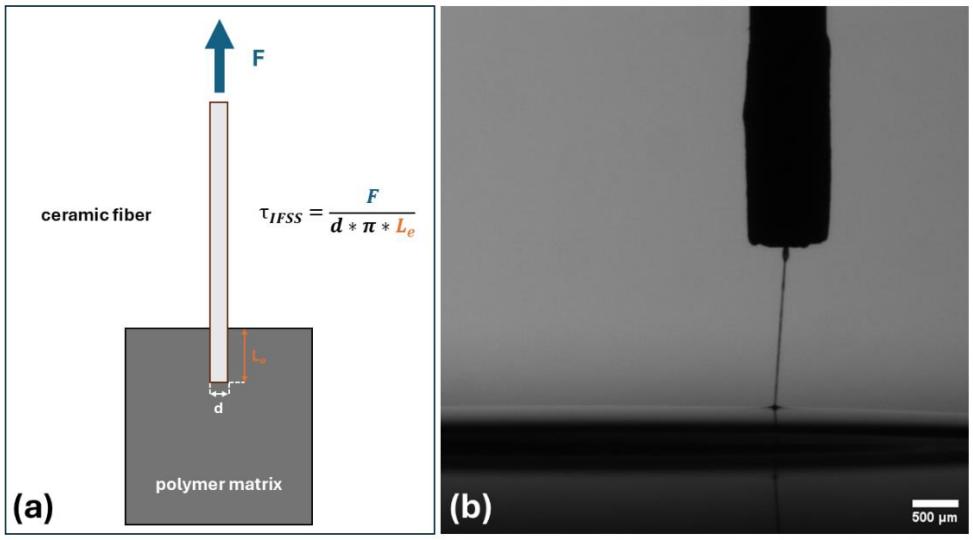

Figure 1: a) Single-fibelr pullout, adapted from [4]. b) water contact angle measurement of a single fiber.

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Morphological and Functional Analysis of Alpha versus Non-Alpha Retinal Ganglion Cells

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Retinal Ganglion Cells (RGCs) are the sole output neurons of the retina, transmitting visual information to the brain. While over 40 RGC subtypes have been identified in the mouse retina through electrophysiological, immunological, and transcriptomic approaches [1], research has predominantly focused on large soma-sized alpha-RGCs, leaving the majority of non-alpha RGCs poorly characterized. Prior work has established that intrinsic cellular properties critically shape postsynaptic signal propagation in alpha-RGCs, influencing spike thresholds, firing rates, and action potential kinetics [2,3]. However, whether non-alpha RGCs share similar morphological and functional principles remains unclear. Identifying potential morphological and electrophysiological distinctions between alpha and non-alpha cells is critical for optimizing electrode design and stimulation protocols for retina implants.

By utilizing advanced confocal imaging techniques and electrophysiological recordings, we provide insights into how alpha and non-alpha RGC subtypes might contribute differently to visual processing. Whole-cell patch-clamp electrophysiology was conducted on a genetically modified mouse line expressing EYFP in PV+ cells via the Cre-loxP system. Membrane voltage was recorded using PatchMaster Next software (HEKA). Current injections 3 ms and 500 ms in length were applied to assess transient and sustained spiking properties, as well as spike thresholds. Following immunostaining, a Leica Stellaris 5 microscope was used to image biotin-filled neurons.

Notably, alpha RGCs display significantly lower input resistance (α: 92.72 ± 43.17 MΩ vs. non-α: 237.58 ±140.84 MΩ) and higher maximum firing rates (α: 296.24 ±54.11 Hz vs. non-α: 208.43 ±49.03 Hz). Concerning the threshold results, alpha and non-alpha RGCs show significant differences in multiple properties, particularly in voltage threshold (α: -55.22 ± 2.66 mV vs non-α: -52.23 ± 3.74 mV) and action potential amplitude (α: 93.59 ± 7.62 mV vs non-α: 88.48 ± 8.12 mV). Immunostaining analysis of non-alpha RGCs revealed the following morphological characteristics: alpha RGCs exhibited significantly larger dendritic field diameters (305.29 ± 62.68 µm) compared to non-alpha RGCs (184.08 ± 26.58 µm).

These results demonstrate that alpha and non-alpha RGCs represent electrophysiologically distinct subpopulations with specialized morphological profiles. Alpha RGCs exhibit enhanced excitability, while non-alpha RGCs show slower signaling dynamics. Also, alpha cells possess broader dendritic field diameters, potentially reflecting morphological specializations among RGCs. These findings reveal fundamental differences in intrinsic physiological and morphological properties between alpha and non-alpha RGCs, with critical implications for retinal implants: precise targeting of RGC subtypes may enhance stimulation efficacy, improving vision restoration for blind individuals by mimicking natural retinal processing.

This work was supported by the Austrian Science Fund (FWF; 10.55776/P35488).

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Are energy storing and positional equine tendons made of the same fibrils?

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In horses, energy-storing superficial digital flexor tendons (SDFT) and positional common digital extensor tendon (CDET) differ in elastic modulus, water- and glycosaminoglycan content, as well as enzymatic and Advanced Glycation End product (AGE) crosslinking [1]. In contrast, individual tendon fascicle's elastic moduli were not found to differ between these tendon types [2]. The mechanical properties of individual collagen fibrils are steered by enzymatic and AGE crosslinks, AGE adducts, and hydration [3]. To investigate potential differences between collagen fibrils from the two tendon types, we conducted tensile tests and Atomic Force Microscopy (AFM) imaging on collagen fibrils from SDFT and CDET a 3- and an 18-year-old horse (samples provided by H. Screen, QMUL, UK)), and quantified fluorescent AGEs in bulk tendon tissue. Collagen fibrils were exposed by careful mechanical extraction and tensile tests were conducted in phosphate buffered saline (PBS) at a strain rate of $5\%s^{-1}$, using the NanoTens device [4]. AFM imaging (NanoWizard Ultraspeed A, JPK, Germany) was conducted in air and PBS to quantify fibril cross-sectional area and swelling. The first maximum of tangent tensile modulus (TM1) is reported in the following. For AGE quantification, the autofluorescence (λ_{ex} = 380/20nm, λ_{emiss} = 480/30 nm), of tissue hydrolysates was measured and normalized to tissue collagen content, determined via hydroxyproline content. TM1 and swelling were compared with ANOVA and Tukey's test, AGEs with a Kruskal-Wallis test and Dunn-Sidaks post hoc test. Significant differences in swelling were found between CDET 3yo (YC) and SDFT 3yo (YS), and between YS and CDET 18yo (OC). For TM1, no significant differences were found. For AGEs, significant differences were found between YC and YS, OC and SDFT 18yo (OS), and between YC and OS. In the young horse, fibril swelling with hydration was lower in SDFT, along with higher AGEs, supporting the image of AGE crosslinks restricting fibril swelling. The fact that this correspondence does not hold across age groups, and the lack of significant differences in TM1 between CDET and SDFT despite the expected stiffening effect of AGEs [3] motivates further studies using more specific and spatially resolved methods for the identification of AGEs and enzymatic crosslinking. The significant variation in measured tensile moduli demonstrates the importance of high-throughput methods for testing of collagen fibrils.

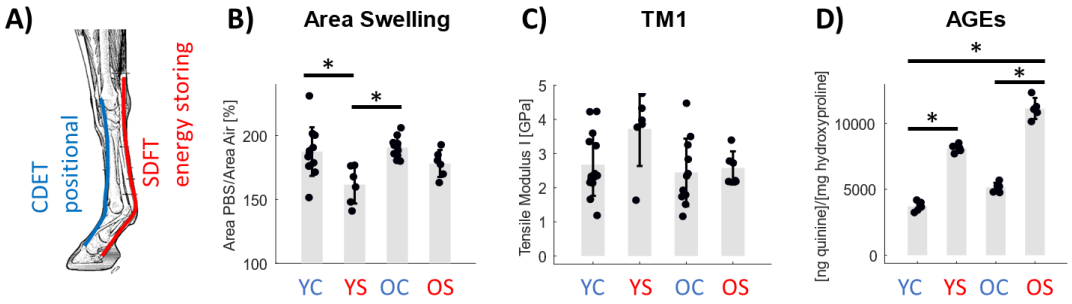

Fig. 1 A) adapted from [2], B) Swelling ratio C) TM1-first maximum of tangent modulus D) fluorescent AGEs = Non-Enzymatic crosslinking ; (YC = CDET 18 years (n = 14), YS = SDFT 3 years (n=6), OC = CDET 18 year (n = 10), OS = SDFT 18 years (n = 6))

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Characterization of Flow Behavior Around Sinusoidal Fibers with Blood-Mimicking Fluids

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Respiratory diseases are among the leading causes of death globally [1]. Current life-support treatments such as extracorporeal membrane oxygenation (ECMO) are limited by high morbidity, and complications related to blood handling. Gas exchange in ECMO occurs in bundles of circular hollow fibers, of which a new sinusoidal geometry is introduced in this study for improved efficiency. By varying wave number and amplitude, and using particle image velocimetry (µ-PIV) supported by computational fluid dynamics (CFD), fluid behavior around these fibers was characterized. Experiments on microfluidic chips with embedded sinusoidal fibers—3D-printed in transparent resin—enabled µ-PIV laser measurements. Two fluids were used: water and a 40 wt% water-glycerin solution (3.7 cP viscosity, mimicking blood at 37 °C [2]). Qualitative and quantitative analysis of velocity magnitude contours obtained by µ-PIV and CFD demonstrate excellent agreement in both shape and intensity distribution. This holds true for both working fluids. Increasing amplitude enlarged regions of low velocity (Fig.1A, depicted in blue), which are critical as potential sites for blood stagnation and coagulation. Determination of the residence time distribution (RTD) curves confirms greater fluid dispersion in channels where fibers with higher amplitude are embedded, indicating more complex flow paths and the formation of recirculation zones close to the large surface undulations (Fig.1B).

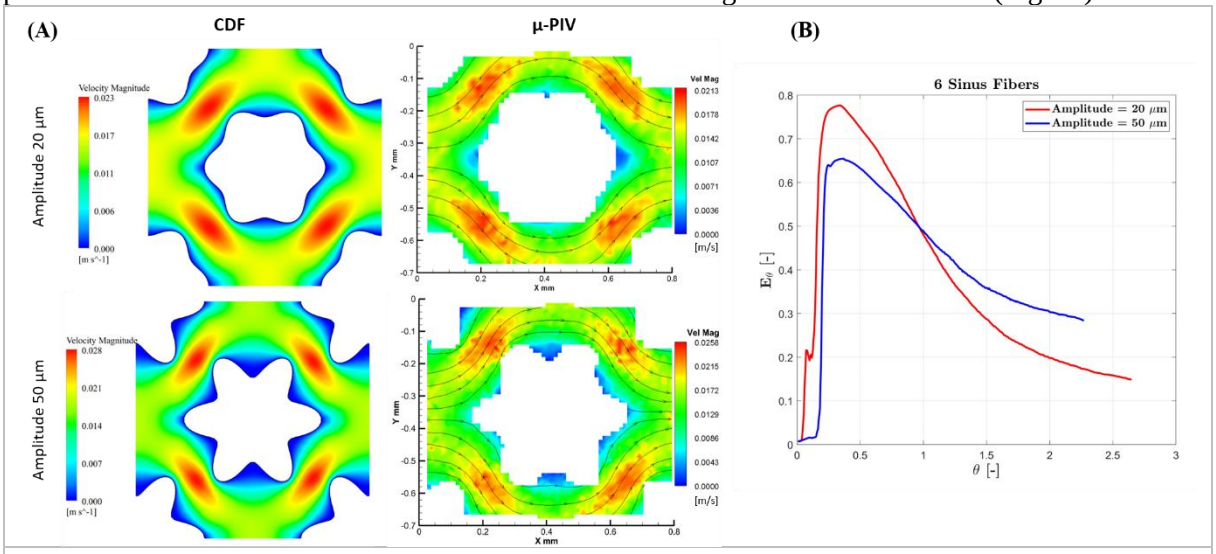

Fig. 1 (A) Velocity magnitude contours derived from CFD and µ-PIV of water flowing at 1.5 mL/min around fibers with 400 µm average diameter, 6 sinusoidal waves and amplitudes of 20 and 50 µm (top and bottom row, respectively). **(B)** Comparison of RTD curves (E_θ and θ are residence time distribution function and time, respectively, normalized by the mean residence time) of 6 sinus waves fibers with 20 µm (red) and 50 µm (blue) amplitude.

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Adaptable, Rapid, and Simple Sensing of Cellular Oxygen Consumption in Microfluidic Systems for Point-of-Care Diagnostics

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Rapid and accurate detection of bacterial infections and their resistance to antibiotics is becoming increasingly urgent as antimicrobial resistance continues to rise due to widespread misuse of antibiotics [1]. Current diagnostic methods are often slow, labor-intensive, and poorly suited for decentralized settings [2]. While recent technologies have improved testing speed, many lack phenotypic resolution or real-time analysis capabilities [3]. To address these limitations, we are establishing a microfluidic platform for a functional phenotypic antimicrobial susceptibility test. Unlike genetic methods that detect resistance genes or mutations, this approach directly measures bacterial response to antibiotics by continuously monitoring cellular oxygen consumption in small-volume samples, enabling point-of-care diagnosis. The device combines 3D-printed microfluidics with integrated fiber-optic oxygen sensors, allowing real-time tracking of bacterial metabolic activity under antibiotic exposure (Fig. 1). The system detects aerobic bacteria in aqueous samples (e.g., urine) and differentiates between resistant and sensitive strains within a few hours. Antibiotics are either pre-loaded onto the sensor or mixed with the sample before introduction into the microfluidic channel. Proof-of-concept experiments demonstrated that for each tenfold decrease in bacterial concentration, the detection time increased by approximately one hour in a 10 µL sample volume, starting from 10 min at 10^8 CFU/mL. Moreover, resistant and sensitive strains can be reliably distinguished within this time frame. The dynamic, label-free sensing mechanism provides highly sensitive readouts and does not require sample pre-processing. This technology may further enable applications beyond infectious diseases, such as in oncology, where metabolic profiling of patient-derived cells could support personalized therapy selection.

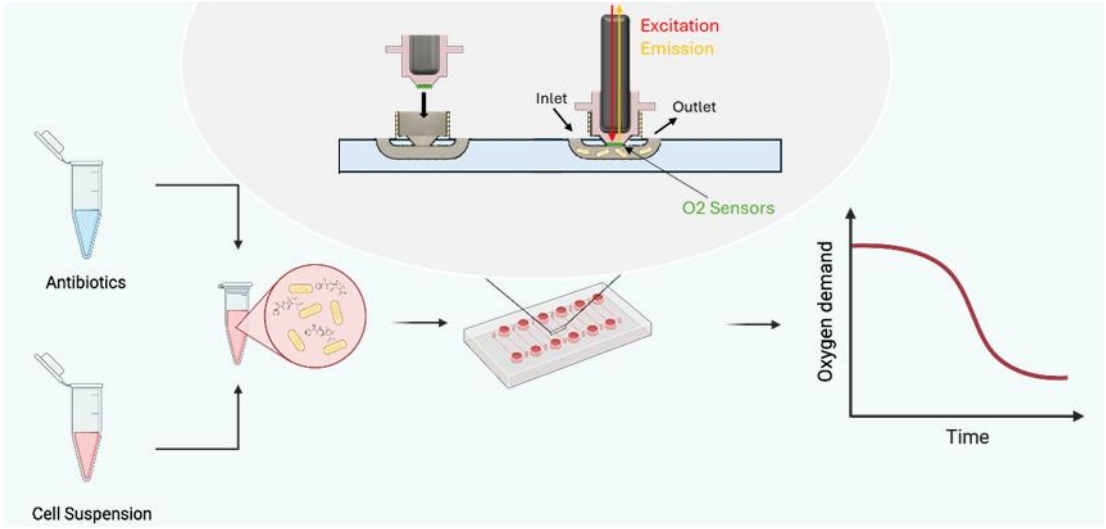

Fig. 1 | Schematic workflow of the microfluidic platform for phenotypic antibiotic resistance detection in aerobic bacteria via fiber-optic oxygen sensing.

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