

**ABSTRACT BOOK OF
4th BIOMEMS and MICROFLUIDIC
TECHNOLOGIES WORKSHOP**

**Jointly Organized with the
6th NOVEL FLUIDIC TECHNOLOGIES
WORKSHOP**

May 8-9, 2025

Abstract Book of
4th BioMEMS and Microfluidic Technologies Workshop
Jointly Organized with the
6th Novel Fluidic Technologies Workshop

© 2025

ISBN: 978-625-00-6998-1

Hybrid
Izmir Institute of Technology (IZTECH)
Izmir, Türkiye

Dates: May 8-9, 2025

This booklet is published as part of an event funded by the European Union's Horizon Europe research and innovation programme under grant agreement No 101079473

Dear Colleagues,

The 4th BioMEMS and Microfluidic Technologies Workshop is held jointly with the 6th Novel Fluidic Technologies Workshop in a hybrid format (online and in-person) at IZTECH on 8-9 May 2025.

The workshop will cover a range of topics, including but not limited to:

- Microfluidic-based biosensors and lab-on-a-chip systems
- Organ-on-a-chip technologies
- Point-of-care diagnostics
- Biomedical applications of MEMS
- Wearable and implantable BioMEMS
- Nanotechnology in microfluidics
- Single-cell analysis and manipulation
- 3D bioprinting and microfabrication techniques
- Emerging industrial applications in BioMEMS and microfluidics
- Other microfluidic applications

Thanks for joining us for this workshop gathering researchers, stakeholders from industry leaders, young researchers and both graduate and undergraduate students. We have organized excellent scientific talks flavored with interesting sessions, where we learn from the experience of ERC grantees and an industry panel with discussions regarding opportunities and challenges in commercialization. Notably, an honorary session dedicated to Prof. Banu Onaral, from whom we learned the most amazing life lessons.

With diverse expertise of invited speakers and interactive panels, this workshop aims to foster scientific collaboration and inspire young generations.

Organizing Committee

Hüseyin Cumhuri Tekin, İzmir Institute of Technology (co-chair)

Özlem Yeşil Çeliktaş, Ege University (co-chair)

Ender Yıldırım, Middle East Technical University (co-chair)

Haluk Külâh, Middle East Technical University

Gamze Kozanoğlu, ODTÜ MEMS Center

Gizem Özdemir, ODTÜ MEMS Center

Pınar Demirekler Burat, ODTÜ MEMS Center

Scientific Committee

Ali Koşar, Sabanci University

Arda Deniz Yalçınkaya, Bogazici University

Arif Engin Çetin, İzmir Biomedicine and Genome Center

Barbaros Çetin, İ.D. Bilkent University

Cihat Taşaltın, TUBITAK Marmara Research Center (MAM)

Devrim Pesen Okvur, İzmir Institute of Technology

Emine Yegan Erdem, İ.D. Bilkent University

Gizem Çalıbaşı Koçal, Dokuz Eylül University

Hasan Uluşan, Middle East Technical University

İlke Gürol, TUBITAK Marmara Research Center (MAM)

Sinan Güven, İzmir Biomedicine and Genome Center

Uğur Tamer, Gazi University



ODTÜ
MEMS
MERKEZİ



4th BioMEMS & Microfluidic Technologies Workshop jointly organized with the 6th Novel Fluidic Technologies Workshop

OrChESTRA

MAESTRO

AGENDA

8 May 2025, Thursday

09:00 - 09:45	Registrations
09:45 - 10:00	Opening Remarks
10:00 - 10:30	Plenary Session: Severine Le Gac, University of Twente (in-person)
10:30 - 11:00	Plenary Session: Fabiana Arduini, University of Rome Tor Vergata (online)
11:00 - 11:30	Plenary Session: Nicole Pamme, Stockholm University (online)
11:30 - 12:00	Invited Talk: Haluk Külâh, Middle East Technical University (in-person)
12:00 - 12:30	Invited Talk: Özlem Yeşil Çeliktaş, Ege University (in-person)
12:30 - 13:45	Lunch Break
13:45 - 14:45	Young Researcher Podium: Short presentations of selected abstracts
14:45 - 15:00	Coffee Break
15:00 - 16:00	Poster Presentations
16:00 - 17:00	ERC Grantee Session: Success Stories in Türkiye Panelists: Haluk Külâh (METU), Serhat Tozburun (IBD, DEU)

9 May 2025, Friday

09:30 - 10:00	Plenary Session: Niels Bent Larsen, DTU (online)
10:00 - 10:30	Plenary Session: Jonas Tegenfeldt, Lund University (in-person)
10:30 - 11:00	Plenary Session: Andreas Hierlemann, ETH Zurich (in-person)
11:00 - 11:30	Poster Presentations (with coffee break)
11:30 - 12:00	Plenary Session: Ender Yıldırım, Middle East Technical University (in-person)
12:00 - 12:30	Plenary Session: H. Cumhuri Tekin, Izmir Institute of Technology (in-person)
12:30 - 13:45	Lunch Break
13:45 - 14:45	Industry Session: Company Presentations & Panel – Opportunities and Challenges in Commercialization
14:45 - 15:00	Coffee Break
15:00 - 16:00	Honorary Session: A Tribute to Prof. Banu Onaral Speakers: Jamie Mak, Hasan Ayaz, Wan Shih
16:00 - 16:30	Plenary Session: Andries van der Meer, University of Twente (online)
16:30 - 17:00	Best Poster Award Ceremony & Closing Remarks



Funded by the
European Union

OrChESTRA has received funding from the European Union's Horizon Europe Programme under grant agreement N° 101079473. The dissemination of results herein reflects only the author's view and the European Commission is not responsible for any use that may be made of the information it contains.

USEFUL INFORMATION

Location, venue:

İzmir Institute of Technology (IZTECH) –
İzmir Yüksek Teknoloji Enstitüsü (İYTE)

Gülbahçe Kampüsü 35430 Urla İzmir Türkiye

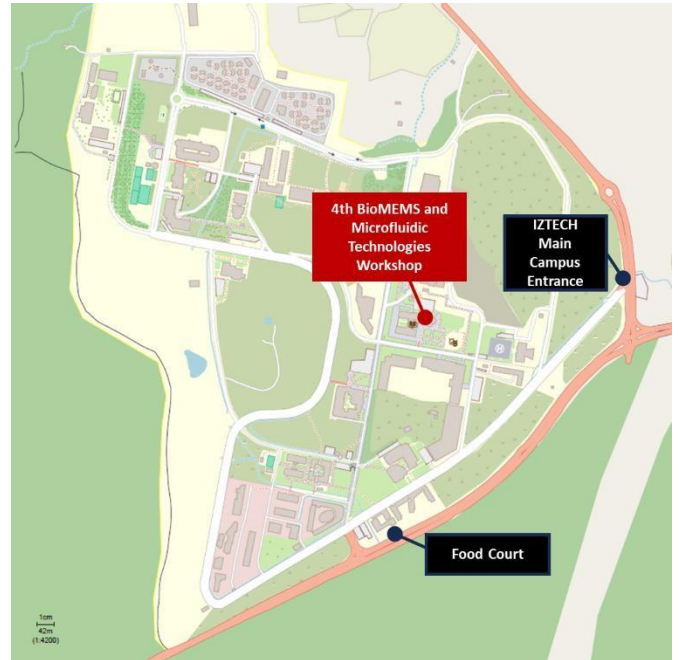
The event will take place at the Show Hall (Gösteri Merkezi) located inside the IZTECH Library (İYTE Kütüphanesi) building.

Google Maps link:

<https://maps.app.goo.gl/7hbfSxCygUC1ZNjr9>

For public transportation options and other travel information, please refer to the following link:

<https://iyte.edu.tr/iletisim/>



- For lunch, participants are expected to use the various dining options available on the IZTECH campus at their own convenience.

Acknowledgements

Organised within the framework of the OrChESTRA project coordinated by ODTÜ MEMS Center, the workshop benefits from the synergistic collaboration of leading European research organisations.

Izmir Institute of Technology (IZTECH) is generously hosting the workshop activities, providing the venue, logistical support, and on-site coordination.

The event is jointly organised with the 6th Novel Fluidic Technologies Workshop, with additional organisational support provided by Ege University.



Funded by the
European Union

OrChESTRA has received funding from the European Union's Horizon Europe Programme under grant agreement N° 101079473. The dissemination of results herein reflects only the author's view and the European Commission is not responsible for any use that may be made of the information it contains.

INVITED TALKS

Microphysiological Systems Featuring Microsensor Structures

Andreas Hierlemann

Department of Biosystems Science and Engineering, ETH Zürich, Switzerland

Recent technological advances in microfabrication techniques and the development of new biological model systems have enabled the realization of microphysiological systems capable of recapitulating aspects of human physiology in vitro with great fidelity. However, obtaining information from or performing manipulation of the samples of interest in real time still poses major challenges. Using microfluidic, microtechnological and microsensor structures and representative 3D in vitro models of human organs or tissue barriers allows for devising robust microphysiological systems that can accommodate high-resolution microscopy and complementary readouts.

We developed versatile microfluidic platforms for formation, cultivation, and analysis of organotypic spherical 3D microtissue (e.g., cardiac tissue, liver, pancreas) and barrier systems (e.g., lung, placenta, blood-brain barrier) that can be obtained from various cell types. Sensor modules allow for convenient functionalization and calibration of the sensors and do not interfere with the microfluidic functions.

Organs-on-Chips: From Platform Technology to Applications in Drug Development

Andries van der Meer

Department of Bioengineering Technologies, Faculty of Science and Technology, University of Twente, Netherlands.

Organs-on-chips are advanced tissue culture models that can mimic organ-level functionality in a controlled, dynamic microsystem. They differ from other cell culture models in that they use microenvironment engineering to capture increasingly complex physiological functions. In the past years it has been shown that organs-on-chips can provide accurate and relevant data for preclinical studies, thereby potentially reducing the time and cost of drug development and clinical trials. Moreover, with their unique combination of person-specific human cells and high-level tissue function, organs-on-chips challenge the strong reliance on animal models in life sciences.

In this talk, Prof. Van der Meer of the University of Twente will provide examples of how organs-on-chips can be used to study drugs, taken from his group's work on vessels-on-chips, heart-on-chip and retina-on-chip. He will discuss the importance of standards-driven open platform technologies in driving innovation of organs-on-chips. Finally, he will address the central challenge in the field: how far can we push the physiological realism of organ-on-chip models and how will we maximize their impact?

Ultrasonic Assisted Fabrication of SERS Substrates

Ender Yıldırım

Department of Mechanical Engineering, Faculty of Engineering, Middle East Technical
University

ODTÜ MEMS Center, Ankara, Türkiye

Ultrasonic-assisted methods offer a transformative approach for fabricating nanostructured metal layers on thermoplastics, providing a scalable and rapid route to SERS substrates. In this approach, a 30 kHz vibrating sonotrode is used to embed 14 nm gold nanopowders into polymethyl methacrylate (PMMA) substrates, forming conductive, nanostructured surfaces tailored for SERS applications. Unlike conventional thin-film deposition techniques, this method enables local sintering and consolidation of gold particles under simultaneous pressure and ultrasonic vibration, eliminating the need for costly and time-consuming processing. By sweeping a range of pressures (0.8–2.7 MPa) and vibration times (2–7 s), gold films with sub-50 nm surface roughness were achieved. Atomic force microscopy and four-point probe measurements confirmed the surface characteristics critical for SERS performance. As a showcase, these gold surfaces were then functionalized with anti-IgG antibodies and tested in a sandwich immunoassay format using DTNB-labeled nanoparticles. SERS spectra collected under a 785 nm laser demonstrated sensitive and specific detection of IgG in artificial saliva, achieving a detection limit of 1.67×10^{-5} $\mu\text{g/mL}$. This work demonstrates not just a fabrication method, but a shift in paradigm—where ultrasonic energy serves as an enabler for integration of biosensors on thermoplastic chips. The results underscore the potential of ultrasonic-assisted manufacturing as a fast, accessible, and effective strategy for developing disposable diagnostic platforms.

Acknowledgement: This study is funded by TÜBİTAK through 121M427

Viscoelastic Fluidics Components

Enrico Turato, Jason P. Beech and Jonas O. Tegenfeldt*

Division of Solid-State Physics and NanoLund, Dept of Physics, Lund University, PO Box
118, 22100 Lund, Sweden

* jonas.tegenfeldt@ftf.lth.se

We show advanced fluidic functionalities without any moving parts such as valves by leveraging our ability to control fluctuations at low Reynolds numbers, Re , in viscoelastic liquids through careful design of obstacle arrays in microfluidics [1]. Two key underlying mechanisms are used. First, there is an increase in flow resistance [2] at the onset of instabilities in viscoelastic aqueous solutions. Second, with broken symmetries in the structures in the microfluidic channels, we obtain fluidic diodes[3]. We combine these two mechanisms into fluidic networks exhibiting to gain novel functionalities.

We show proof of principle of several components. **The Filter** is a device composed of one inlet channel that branches into two outlet channels, both having the same flow resistance for a Newtonian liquid, e.g. water. In contrast, for a macromolecular solution that supports waves, the flow rates of the two outlets are different which leads to differences in two flow rates. By implementing an analogy to the well-known **Wheatstone Bridge** in electronics, through the observation of the flow in the diagonal channel, we demonstrate the detection of a small difference in flow resistance between three legs in the bridge with one design and one leg with a different design. A **Rectifier** is demonstrated in the same framework by selecting arrays of triangular posts arranged to form fluidic diodes, giving unidirectional flow in the diagonal channel, independent on the overall flow direction of the device. A more extensive network of diodes is demonstrated in the **Meander Generator** where the flow trajectory through the network is a function of flow rate and the characteristics of the liquid. We envision that our entirely passive non-linear fluidics devices will find use where there is a need for simple programmable autonomous flow control or sensing, e.g. in wearables, 3D bioprinting and process monitoring in the chemical industry.

References:

- [1] Ström, O.E., J.P. Beech, and J.O. Tegenfeldt, *Short and long-range cyclic patterns in flows of DNA solutions in microfluidic obstacle arrays*. Lab on a Chip, 2023. **23**(7): p. 1779-1793.
- [2] Browne, C.A. and S.S. Datta, *Elastic turbulence generates anomalous flow resistance in porous media*. Science advances, 2021. **7**(45): p. eabj2619.
- [3] Beech, J.P., O.E. Ström, E. Turato, and J.O. Tegenfeldt, *Using symmetry to control viscoelastic waves in pillar arrays*. RSC Advances, 2023. **13**(45): p. 31497-31506.

Electrochemical paper-based microfluidic devices

Fabiana Arduini

Department of Chemical Science and Technologies, University of Rome Tor Vergata

Via della Ricerca Scientifica, Rome, Italy

fabiana.arduini@uniroma2.it

As reported in my recent review entitled “Electrochemical paper-based devices: When the simple replacement of the support to print ecodedigned electrodes radically improves the features of the electrochemical devices” published in *Current Opinion in Electrochemistry SI: Emerging Opinions* (2022) [1]: “Paper-based electrochemical (bio)sensors have emerged as highly attractive analytical devices for their superior sustainable features, such as avoiding the use of polyester as support and the reduction of waste, being incinerated after use. However, paper-based electrochemical (bio)sensors have recently demonstrated further advantages, including the simple combination with vertical microfluidics and their use as a reservoir to deliver smart electrochemical (bio)sensors able to i) contain the reagents, ii) preconcentrate the target analyte, and iii) synthesize the nanomaterials inside the paper network. Furthermore, these devices have demonstrated their ability to overcome the limitations of the other printed electrochemical sensors in the measurement of entirely liquid samples by detecting the target analyte in the aerosol phase or solid sample, without the additional sampling system. These achievements highlight their valuable and varied advantages in the sensing sector”. In this lecture, I will report on the main points of the roadmap research activity carried out in the last 8 years related to the development of electrochemical paper-based microfluidic devices.

Acknowledgements Horizon Europe Phoenix-OoC Project GA N. 101130395.

Reference

- [1] F. Arduini. *Curr. Opin. Electrochem.* 2022, 101090

Centrifugal Filling and Fluidic Control in Dead-End Microchannels

H. Cumhur Tekin^{1,2}

¹ Department of Bioengineering, Izmir Institute of Technology, Izmir 35430, Türkiye

² ODTÜ MEMS Center, Ankara 06520, Türkiye

Conventional microfluidic systems rely on both inlets and outlets for fluid handling, often limiting sample efficiency, particularly for ultra-low volumes. In contrast, dead-end channels offer unique advantages, such as handling precisely sub-microliter samples and preserving no-flow conditions upon filling [1, 2]. However, current vacuum-based strategies to fill these channels suffer from slow operation times [3]. We introduce a centrifuge-compatible platform that enables rapid and controlled filling of nanoliter-scale fluids into dead-end microchannels using only centrifugation [4]. By leveraging the combined effects of centrifugal, capillary, and Coriolis forces, our method displaces trapped air within the channels and enables rapid filling, without requiring outlet structures or venting. The system allows programmable flow initiation through channel-specific hydraulic resistances, effectively acting as a passive fluidic diode mechanism controlled solely by rotational speed. We demonstrate the platform's utility in diagnostic applications by achieving plasma separation, hematocrit measurement, and white blood cell quantification from minimal whole blood volumes, while remaining within clinically acceptable error margins. Our approach eliminates the need for external reagents or complex valves, works with standard centrifuges via a simple adapter, and opens the door to streamlined, minimally invasive diagnostics on a chip.

Acknowledgement: The authors acknowledge financial support from The Scientific and Technological Research Council of Türkiye (22AG032) and from Izmir Institute of Technology (IZTECH) (2022-IYTE-2-0056).

References

- [1] Li L et al. (2010). Dead-end filling of SlipChip evaluated theoretically and experimentally as a function of the surface chemistry and the gap size between the plates for lubricated and dry SlipChips. *Langmuir*, 26(14), 12465–12471
- [2] Yeh et al. (2017). Self-powered integrated microfluidic point-of-care low-cost enabling (SIMPLE) chip. *Sci. Adv.*, 3, e1501645
- [3] Oksuz C, Tekin HC (2021). A vacuum-integrated centrifugal microfluidic chip for density-based separation of microparticles. 34th IEEE International Conference on Micro Electro Mechanical Systems (MEMS 2021).
- [4] Oksuz C, Bicmen C, Tekin HC (2025). Dynamic fluidic manipulation in microfluidic chips with dead-end channels through spinning: the Spinochip technology for hematocrit measurement, white blood cell counting and plasma separation. *Lab on a Chip*, 25, 1926-1937.

Microfluidic approaches for analysis in resource-limited settings

Nicole Pamme

Department of Chemistry, Stockholm University, Sweden

Traditional analysis workflows rely on samples being collected and taken to centralised laboratory facilities for processing by highly skilled operators. This approach limits our ability to collect data with high frequency and in many locations. Microfluidic systems offer the possibility to carry out measurement on-site, in-the-field and at the point-of-care, provided they are portable, require minimal external instrumentation and provided workflows are robust to be carried out by minimally trained operators. In our research group we aim to develop such integrated workflows for clinical diagnostics in particular for clinical diagnosis of infection in lower- and middle-income countries. Furthermore, we design paper-based microfluidic systems for on-site chemical analysis of water and soil, that can be operated by members of the general public.

Diagnosis of pathogenic microorganisms is commonly performed via nucleic acid amplification tests, which require relatively costly equipment and are run by specialized operators in centralised laboratories. This hinders their use for point-of-care diagnostics. We have been working on integrated workflows for pathogen analysis that can be operated in low-resource settings. We employ a microfluidic platform featuring a series of interconnected chambers that are filled with aqueous and oil-based solutions, so that liquids sit side by side. Surface-functionalised magnetic particles are added to a chamber containing the sample and bind to the analyte of interest. The surface tension between the immiscible water and oil phases allows pulling the particles through the liquid interfaces, thereby isolating the analyte from the sample matrix. Downstream, detection reactions such as bioluminescence assays for ATP or colorimetric loop-mediated isothermal amplification (LAMP) can be carried out. We have investigated this approach for detection of *E. coli*, sexually transmitted infections (*Neisseria gonorrhoeae* and *Chlamydia trachomatis*) [1], SARS-CoV-2 RNA [2] and the fungus *Sclerotium rolfsii* [3].

Our group also develops paper-based microfluidic devices for on-site measurement of water quality markers and soil nutrients. These are to be used by members of the general public who upload results via an app for data collection with high spatial and temporal resolution. Readout can be based on colour intensity as well as colour distance, sometimes in combination with on-site pre-concentration approaches to reach lower concentration ranges. Examples include analysis of dissolved inorganic carbon [4] and analysis of nutrients and pH in soil samples [5].

References

- [1] P Rodriguez-Mateos, B Ngamsom, D Ameyo, P Wakaba, C Shiluli, A Iles, J Gitaka, N Pamme, *Anal. Bioanal. Chem.*, **2023**, 415, 5129–5137.
- [2] B Ngamsom, A Iles, M Kamita, R Kimani, P Wakaba, P Rodriguez-Mateos, M Mungai, CE Dyer, C Walter, J Gitaka, N Pamme, *Talanta*, **2022**, 6, 100166.
- [3] P Changtor, P Rodriguez-Mateos, K Buddhachat, W Wattanachaiyingcharoen, A Iles, S Kerdphon, N Yimtragool, N Pamme, *Biosens. Bioelectr.*, **2024**, 2050, 116051. [4] P Giménez-Gómez, I Hättestrand, S Sjöberg, C Dupraz, S Richardson, N Pamme, *Sens. Actuat. B*, **2023**, 385, 133694. [5] P Giménez-Gómez, N Priem, S Richardson, N Pamme, *Sens. Actuat. A*, **2025**, 424, 136881.

3D Microperfused Microphysiological Systems

Niels Bent Larsen

Department of Health Technology, Technical University of Denmark, Lyngby, Denmark

nibl@dtu.dk

Inadequate oxygen supply is the major factor limiting the engineering of tissues thicker than a millimeter. Numerous concepts to overcome this limitation have been proposed. We and others have approached the reproduction of tissue vasculature function by engineering massively parallel microfluidic 3D networks in materials open to diffusion of oxygen and nutrients. In vitro models of liver tissue are highly valuable for drug development and disease modeling, yet present significant challenges to establish due to the mechanical fragility and high oxygen consumption rate of hepatocytes. Functional liver models additionally require a gradient in oxygen tension along each liver sinusoid, thought to be key in establishing metabolically essential liver zonation. In our engineered microfluidic network solution, the liver-like 3D tissue is cultured between the perfusion channels, thereby shielding the sensitive hepatocytes from shear stresses of the medium flow. The developed platform has been employed for the culture of primary human hepatocytes at in vivo-like cell densities for weeks as well as culture of human induced pluripotent stem cell-based liver-like cell tissues for months. Gradients in oxygen tensions naturally develop within the tissue models due to cellular oxygen consumption, as observed in vivo. However, in vivo-mimicking oxygen microenvironments and gradients cannot be verified without access to a ground truth of the culture-dependent oxygen distribution in vitro. We have met this generic challenge by the development of a method for mapping the oxygen concentration in 3D using advanced phosphorescence lifetime confocal microscopy of oxygen-sensitive microbeads embedded in the cultured tissue.

The triple Helix: Pharmaceuticals, Environment and Organ-on-chips

Ozlem Yesil-Celiktas

Department of Bioengineering, Faculty of Engineering, Ege University, Izmir, Türkiye

Translational Pulmonary Research Center (EgeSAM), Ege University, Izmir, Türkiye

ODTÜ MEMS Center, Ankara, Türkiye

ozlem.yesil.celiktas@ege.edu.tr

The sustainable development goals (SDG) set by United Nations has increased environmental, social, and corporate governance commitments significantly. Particularly, the industry faces obstacles to achieving more rapid progress in decarbonisation, climate change and greenhouse gas reduction efforts. Goal number 3 of the UN-SDGs “ensure healthy lives and promote well-being for all at all ages” as well as goal number 12 “ensure sustainable consumption and production patterns” provide a framework for fine chemicals and pharmaceutical industry to rethink processes and contribute to the sustainability goals. However, development of green processes alone does not sufficiently fulfill this requirement.

The preclinical research, translation to clinical settings and challenges associated with decarbonisation of clinical trials and the R&D phase more generally should be critically assessed and contribution of emerging technologies such as organ-on-chips should be considered especially given the proportion of development products that never make it to market. In the scope of this talk, efforts of pharmaceutical companies in fulfilling sustainability goals and the role of organ-on-chips in this endeavor will be evaluated by providing insights from our studies carried out at the Biomimetic Microsystems Research group. Specific emphasis will be on cerebral organoid-on-chip systems representing a promising advancement in brain-mimetic in vitro models to recapitulate disease pathology and test the efficacy and safety of potential drug candidates. Overall, development of green processes, microfluidic based platforms for high-throughput screening during early stages of drug development and utilization of organ-on-chips for assessment of efficacy and safety would accelerate the sustainability efforts, while leading to environmentally friendly approaches and contributing to decarbonisation of pharmaceutical industry.

Acknowledgement: This study is funded by TUBITAK through 123M406

Organ-on-Chip for disease modeling

S  verine Le Gac

Applied Microfluidics for BioEngineering Research, MESA+ institute for Nanotechnology &
TechMed Centre, University of Twente, the Netherlands

s.legac@utwente.nl

Organ-on-a-chip (OoC) technology has become a game-changer by providing advanced *in vitro* models of human tissues and organs, allowing thereby conducting a variety of experimentation and assays, ranging from drug testing, toxicity screening, tissue engineering, to disease modeling to, *e.g.*, elucidate mechanisms at play in disease onset and progression. Organ-on-a-chip devices are hybrid models combining cells and microfabricated structures in a microfluidic format, aiming altogether to mimic functional and/or structural features of an organ. OoCs exhibit several advantages compared to conventional *in vitro* and *in vivo* models: an *in vivo*-like and tunable microenvironment, dynamic culture, possibility to incorporate a variety of (bio)chemical and (bio)physical cues, with spatial and temporal control thereon, suitability to prepare patient-specific (disease) model, amenability to parallelized and automated studies, and compatibility with routine imaging and molecular assay. As such, OoC is currently acknowledged as a promising technology to reduce and replace experimentation on animals, which are poor mimics of human diseases and physiology.

In my presentation, I will briefly introduce OoC models, present current work from our group (i) to introduce mechanical actuation in OoC devices in the context of developing a joint-on-chip model, (ii) to model fibrotic diseases, and finally (iii) discuss recent developments around the use of 3D printing to produce microfluidic devices.

YOUNG RESEARCHER PODIUM PRESENTATIONS

Mass-Sensitive Detection of Hypoxanthine Using a MIP-Modified QTF Sensor: Toward Microfluidic Integration

Fahriye Arslan^{1*}, Safiye Betül Bulut¹, Gizem Kaleli Can¹

¹IDepartment of Biomedical Engineering, Izmir Democracy Univesity, Izmir 35140, Türkiye

*arslan989904@gmail.com

Hypoxanthine (Hx) is an important biomolecule that results from the catabolism of high-energy purine derivatives such as adenosine triphosphate (ATP) and accumulates under conditions of cellular oxygen deprivation [1]. Recognized as a distinct biochemical indicator of energy metabolism disruption during oxidative stress, ischemia, or hypoxia, Hx holds significant clinical, biomedical, and forensic value [2]. The quantitative determination of Hx levels is critically important for the early diagnosis of life-threatening conditions, particularly cardiac ischemia [3]. Furthermore, Hx serves as a diagnostic tool in forensic science for estimating the postmortem interval (PMI) [4], and plays a key role in monitoring metabolic alterations associated with systemic inflammatory responses such as sepsis [5] and assessing renal dysfunction in various pathological conditions [6]. In this study, a mass-sensitive biosensor based on a quartz tuning fork (QTF) was developed for the selective and sensitive detection of hypoxanthine (Hx) using a molecular imprinting technique. The surface of the biosensor was coated with a molecularly imprinted polymer (MIP) layer formed by employing chitosan, a biocompatible polymer, to create specific recognition sites for hypoxanthine molecules. The binding of Hx molecules to the QTF surface was quantitatively monitored through shifts in the resonance frequency of the sensor. The QTF-based sensor offers advantages in biosensor design due to its high frequency stability, ability to detect nanogram-level mass changes, and low production cost [7]. Preliminary results demonstrated that when the modified sensor was immersed in an Hx-containing buffer solution, a frequency shift of 112.63 ± 6.76 Hz was observed. In contrast, when the same experimental setup was used with phosphate-buffered saline (PBS) solution, a frequency shift of only 2.77 ± 2.77 Hz was recorded. These findings indicate that the developed sensor provides a specific and reliable response to hypoxanthine. The results will be further supported by selectivity, reproducibility, and stability tests. Although integration with a microfluidic chip has not yet been implemented, it is planned for future stages to enable rapid and multiplexed analyses with lower sample volumes. Such integration would facilitate the development of a portable, cost-effective system suitable for point-of-care (POC) diagnostic applications. This study presents an innovative approach that lays the groundwork for the accurate and selective determination of hypoxanthine levels and the future development of microfluidic-based biosensor systems.

Acknowledgements: The author gratefully acknowledges Fatih Uğur for his continuous moral support and encouragement throughout the course of his scientific endeavors.

References

[1] Locci, E., Chighine, A., Noto, A., Ferino, G., & d'Aloja, E. (2021). *Metabolomics improves the histopathological diagnosis of asphyxial deaths: an animal proof-of-concept model*. Scientific Reports, 11(1), 10102. <https://doi.org/10.1038/s41598-021-89570-0>

- [2] Sacco, M. A., Aquila, I., Sablone, S., Gratteri, S., Ricci, P., De Donno, A., ... & Cantatore, S. (2024). *Post mortem molecular biomarkers of asphyxia: A literature review*. International Journal of Molecular Sciences, 25(21), 11607. <https://doi.org/10.3390/ijms252111607>
- [3] Mahanty, A., & Xi, L. (2020). *Utility of cardiac biomarkers in sports medicine: Focusing on troponin, natriuretic peptides, and hypoxanthine*. Sports Medicine and Health Science, 2(2), 65–71. <https://doi.org/10.1016/j.smhs.2020.05.003>
- [4] Cardinale, A. N., Di Lorenzo, A., Bellino, M., Strisciullo, G., Mussi, V., & Sablone, S. (2025). *Thanatochemistry and the role of hypoxanthine in the post-mortem interval estimation: A systematic literature review*. International Journal of Legal Medicine. Advance online publication. <https://doi.org/10.1007/s00414-024-03378-x>
- [5] Tao, Y.-L., Wang, J.-R., Liu, M., Liu, Y.-N., Zhang, J.-Q., Zhou, Y.-J., Li, S.-W., & Zhu, S.-F. (2024). *Progress in the study of the correlation between sepsis and intestinal microecology*. Frontiers in Cellular and Infection Microbiology, 14, 1357178. <https://doi.org/10.3389/fcimb.2024.1357178>
- [6] Alsawaf, Y., Maksimovic, I., Zheng, J., Zhang, S., Vuckovic, I., Dzeja, P., Macura, S., & Irazabal, M. V. (2024). *A brief harvesting-freezing delay significantly alters the kidney metabolome and leads to false positive and negative results*. American Journal of Physiology-Renal Physiology, 327(5), F697–F711. <https://doi.org/10.1152/ajprenal.00131.2024>
- [7] Gürcan, D., Baysoy, E., & Kaleli-Can, G. (2024). *Anti-IgG doped melanin nanoparticles functionalized quartz tuning fork immunosensors for immunoglobulin G detection: In vitro and in silico study*. Sensors, 24(13), 4319. <https://doi.org/10.3390/s24134319>

Fabrication of Microfluidic Platform to Investigate the Adaptive Immune Response in Melanoma Tumor

Fatih Özefe^{1,2*}, Ramsés Martínez², Adama M. Sesay², Erdal Bedir¹, H. Cumhur Tekin^{1,3}

¹ Department of Bioengineering, Izmir Institute of Technology, İzmir, 35430, Türkiye

² Wyss Institute for Biologically Inspired Engineering at Harvard University, Boston, 02215, Massachusetts, USA

³ ODTÜ MEMS Center, Ankara, 06520, Türkiye

* fatihozefe@iyte.edu.tr

Organ-on-a-Chips (OoC) are microfluidic platforms that mimic three-dimensional (3D) tissue and organs architecture to eliminate the limitations of two-dimensional (2D) cell culture models.¹ Although many OoC platforms were developed to emulate the various human organs, such as lung, liver, brain, and skin, for various applications until today,² the immune system-related OoCs are currently restricted to the study of inflammatory responses.³ This work describes the modeling immune system integrated melanoma microenvironment to demonstrate T cell mediated anti-tumoral activity against melanoma tumor. Firstly, microfluidic platform was modeled using finite element simulations. It consisted of two specific chambers (separated by micro-channels) for melanoma microenvironment and lymph node, and one main channel for T cell circulation. After modeling, microfluidic device was produced using PDMS replica molding. Next, melanoma spheroids and dendritic cells (DCs) in the 3D collagen scaffold were seeded into chambers, while T cells were perfused through the main channel. Lastly, the anti-tumoral effect of T cells were investigated by analyzing the changes in structural and functional properties of melanoma spheroids. As microfluidic devices contain chambers and channels for tumor microenvironment and T cell circulation, we could sequentially investigate the migratory behaviour of T cells towards melanoma tumors, and anti-tumoral activity of T cells on melanoma spheroids. Hence, developed microfluidic devices could serve as the example of mimicking adaptive immunity in microfluidic technologies.

Acknowledgements

This study was supported by IZTECH-BAP (Project No: 2022İYTE-3-0017). The author acknowledges the Biotechnology and Bioengineering Application and Research Center in IZTECH (BIOMER), TUBITAK-2214A, and Wyss Institute for their financial and technical support.

References

- [1] Ajalik, R. E., Alenchery, R. G., Cognetti, J. S., Zhang, V. Z., McGrath, J. L., Miller, B. L., & Awad, H. A. (2022). Human organ-on-a-chip microphysiological systems to model musculoskeletal pathologies and accelerate therapeutic discovery. *Frontiers in bioengineering and biotechnology*, 10, 846230.
- [2] Kang, S. M. (2022). Recent advances in microfluidic-based microphysiological systems. *BioChip Journal*, 16(1), 13-26.
- [3] Pavesi, A., Tan, A. T., Koh, S., Chia, A., Colombo, M., Antonecchia, E., ... & Bertoletti, A. (2017). A 3D microfluidic model for preclinical evaluation of TCR-engineered T cells against solid tumors. *JCI insight*, 2(12), e89762.

Computational Design and Additive Manufacturing of a Microfluidic System for the Controlled Iron Oxide Nanoparticle Synthesis

Göktürk Cinel¹, Eyüp Bilgi¹, Ceyda Öksel Karakuş^{1*}

¹Department of Bioengineering, İzmir Institute of Technology, İzmir, Türkiye

*ceydaoksel@iyte.edu.tr

ABSTRACT

Iron oxide nanoparticles (IO NPs) exhibit unique magneto-optical properties, making them highly suitable for various applications such as magnetic resonance imaging (MRI) contrast enhancement, magnetic cell separation and magnetic hyperthermia. Beyond their magnetic nature, the surfaces of IO NPs can be functionalized for diverse biomedical purposes including tracking (e.g., contrast agents, fluorescent probes), targeting (small molecules, antibodies, cell receptors), delivering (active ingredients, drug payload and active compounds) and stabilizing (surfactants, ligand exchange and zeta potential [1]. Among various synthesis methods, co-precipitation is favored for its simplicity, scalability, and cost-efficiency. However, the high tendency of IO NPs to aggregate demands strict control over reaction parameters to minimize polydispersity and ensure reproducibility [2].

In this study, we present a microfluidic system that integrates geometry-driven computational design and additive manufacturing to enable the controlled synthesis of IO NPs via co-precipitation. The platform provides precise control over heating, mixing, and timing, facilitating the reproducible and uniform production of nanoparticles. It comprises three key components: a Tesla valve-based mixing channel, a reaction chamber, and two magnetic field generating components. The Tesla valve enhances mixing by inducing passive turbulence. Reactants enter the reaction chamber through a primary inlet, while a secondary inlet introduces nitrogen gas to create an inert atmosphere and initiate the siphoning process. A siphon mechanism removes by-products once a critical volume is reached. An N52 magnet beneath the chamber generates a downward magnetic field to retain IO NPs on the chamber surface, while a second N52 magnet above the chamber produces an upward magnetic field to lift the particles, enabling their collection through an oil phase.

This modular system provides a reproducible, scalable, and efficient method for synthesizing stable IO NPs and can be adapted for larger-scale or multifunctional nanoparticle production.

References

- [1] Ghazi, R., Ibrahim, T. K., Nasir, J. A., Gai, S., Ali, G., Boukhris, I., & Rehman, Z. (2025). Iron oxide based magnetic nanoparticles for hyperthermia, MRI and drug delivery applications: A review. *RSC Advances*, 15(28), 11587–11616. <https://doi.org/10.1039/d5ra00728c>
- [2] Eigenfeld, M., Reindl, M., Sun, X., & Schwaminger, S. P. (2024). Exploring multi-parameter effects on iron oxide nanoparticle synthesis by SAXS analysis. *Crystals*, 14(11), 961. <https://doi.org/10.3390/cryst14110961>

Lensless Digital In-Line Holographic Microscopy for the Detection of Microplastics

Hilal Döğner¹, H. Cumhur Tekin^{1,2}

¹Department of Bioengineering, Izmir Institute of Technology, Izmir 35430, Türkiye.

²ODTÜ MEMS Center, Ankara, Türkiye

Microplastics, defined as plastic particles smaller than 5 mm, pose growing risks to aquatic ecosystems and human health due to their persistence and bioaccumulation potential¹. These particles are widely detected in oceans, rivers, and even drinking water, underscoring the need for fast, low-cost, and field-ready detection methods. Traditional techniques like FTIR spectroscopy and staining are accurate but rely on complex equipment and chemical processing, making them less suitable for real-time, in-situ analysis².

This study proposes the use of lensless digital in-line holographic microscopy (DIHM) integrated with a microfluidic chip for label-free detection of microplastics in water. The microfluidic system ensures controlled flow and stable particle alignment, improving imaging consistency and analysis speed. DIHM reconstructs digital holograms into high-resolution phase and intensity maps³, allowing non-destructive characterization of particles. Optical features such as size, shape, and refractive index are used to differentiate microplastics from natural particulates. With advancements in portable imaging and microfluidics⁴, this method shows promise for real-time environmental monitoring, especially in remote or resource-limited areas.

Acknowledgement

We would like to thank the Scientific and Technological Research Council of Türkiye (TÜBİTAK) for their financial support (Project No: 124E059).

References

- [1] Li, J., Liu, H., & Chen, J. (2023). Microplastic pollution: A review of analytical methods, occurrence and characteristics in environmental matrices. *Science of The Total Environment*, 857, 159422.
- [2] Singh, D. K., & Kazmi, A. A. (2022). Emerging technologies for microplastic detection in environmental matrices: A review. *Environmental Pollution*, 307, 119600.
- [3] Kwon, W., Lee, S., Kim, M. K. (2021). Digital holographic microscopy for label-free environmental particle analysis: A review. *Sensors*, 21(7), 2453.
- [4] Chen, Z., Wang, Y., & Xu, W. (2022). Recent advances in lensless imaging technologies for biomedical and environmental applications. *Trends in Analytical Chemistry*, 157, 116759.

Analysis on microfluidic chip integrated surface acoustic wave resonator for biomedical applications

İsmail Bütün^{1,2*}, Rabia Mercimek², Ali Koşar³

¹ Faculty of Engineering and Natural Science, Sabancı University, 34956 Istanbul, Türkiye.

² Sabancı University Nanotechnology Research and Application Center (SUNUM), 34956, Istanbul, Türkiye.

³ Sabancı University, Center of Excellence for Functional Surfaces, and Interfaces for Nano Diagnostics (EFSUN), Faculty of Engineering and Natural Sciences, Tuzla, Istanbul, 34956, Türkiye.

⁴ Turkish Academy of Sciences (TÜBA), Çankaya, 06700, Ankara, Türkiye

* Corresponding Author: Ali Koşar; Email: kosara@sabanciuniv.edu

This study presents the design, simulation, and fabrication of a microfluidic chip-integrated surface acoustic wave (SAW) biosensor for biomedical detection. SAW-based sensors enable highly sensitive, label-free, and miniaturized analysis at low cost. Finite element modelling (FEM) was used to investigate acoustic wave propagation, resonance shifts, and mass loading effects. The sensor was then fabricated, integrated into a microfluidic system, and experimentally validated across a wide range of biomolecular concentrations. Frequency response analysis revealed a clear shift in resonance frequency with increasing analyte concentration, while return loss (S11/SWR) measurements have a positive correlation with mass loading. Additionally, impedance analysis demonstrated a linear relationship between the real part of impedance shift and the logarithmic concentration of the biomolecule. Phase shift analysis also indicated strong sensitivity, with a linear decay versus concentration. These results confirm the robust, concentration-dependent response of the SAW device and highlight its potential for quantitative biosensing in integrated microfluidic systems.

Acknowledgements

This project was supported by the Scientific and Technological Research Council of Türkiye (TÜBİTAK), NANOSİS 1004 platform, project number: 20AG012.

References

- [1] S. P. Mohanty and E. Kougianos, "Biosensors: a tutorial review," IEEE Potentials, vol. 25, no. 2, pp. 35-40, 2006, doi: 10.1109/MP.2006.1649009.
- [2] M. Selvaraj, S. B S, and M. Aly Saad Aly, "Terahertz-based biosensors for biomedical applications: A review," Methods, vol. 234, pp. 54-66, 2025/02/01/ 2025, doi: <https://doi.org/10.1016/j.ymeth.2024.12.001>.

- [3] E. Liu, Z. Cai, Y. Ye, M. Zhou, H. Liao, and Y. Yi, "An Overview of Flexible Sensors: Development, Application, and Challenges," *Sensors*, vol. 23, no. 2, p. 817, 2023. [Online]. Available: <https://www.mdpi.com/1424-8220/23/2/817>.
- [4] P. Scrimin and L. J. Prins, "Sensing through signal amplification," *Chemical Society Reviews*, 10.1039/C1CS15024C vol. 40, no. 9, pp. 4488-4505, 2011, doi: 10.1039/C1CS15024C.
- [5] A. Chieng, Z. Wan, and S. Wang, "Recent Advances in Real-Time Label-Free Detection of Small Molecules," *Biosensors*, vol. 14, no. 2, p. 80, 2024. [Online]. Available: <https://www.mdpi.com/2079-6374/14/2/80>.
- [6] L. Rayleigh, "On Waves Propagated along the Plane Surface of an Elastic Solid," *Proceedings of the London Mathematical Society*, vol. s1-17, no. 1, pp. 4-11, 1885/11/01 1885, doi: <https://doi.org/10.1112/plms/s1-17.1.4>.
- [7] M. Aleixandre and M. C. Horrillo, "Recent Advances in SAW Sensors for Detection of Cancer Biomarkers," *Biosensors*, vol. 15, no. 2, p. 88, 2025. [Online]. Available: <https://www.mdpi.com/2079-6374/15/2/88>.
- [8] D. J. Collins, T. Alan, and A. Neild, "The particle valve: On-demand particle trapping, filtering, and release from a microfabricated polydimethylsiloxane membrane using surface acoustic waves," *Applied Physics Letters*, vol. 105, no. 3, 2014, doi: 10.1063/1.4891424.
- [9] S.-C. S. Lin, X. Mao, and T. J. Huang, "Surface acoustic wave (SAW) acoustophoresis: now and beyond," *Lab on a Chip*, 10.1039/C2LC90076A vol. 12, no. 16, pp. 2766-2770, 2012, doi: 10.1039/C2LC90076A.

Label-Free Magnetic Force-Guided Cell Patterning for Tissue-Specific Applications

Melike Cagan Algan¹, Muge Anil Inevi¹, Seren Kecili¹, Ece İnal², Huseyin Cumhur Tekin¹,
Gulistan Mese², Engin Ozcivici¹

¹Department of Bioengineering, Izmir Institute of Technology, Izmir, Türkiye

² Department of Molecular Biology and Genetics, Izmir Institute of Technology, Izmir,
Türkiye

melikecagan@iyte.edu.tr

Cell patterning is crucial in tissue engineering, enabling precise spatial cellular arrangement to mimic biological structures¹. Conventional cell patterning approaches such as surface modification and bioprinting often involve time-consuming procedures that may compromise cellular viability². This study presents an innovative, single-step magnetic patterning technique that facilitates label-free, linear arrangement of cells through negative magnetophoresis³. Utilizing a custom-designed magnetic setup and culture chamber, we successfully patterned 7F2 cells on surfaces within 3 hours without substrate modifications. Our method generated ~1 mm thick linear cell patterns using a safe concentration (5 mM) of the paramagnetic agent Gadobutrol. These cellular patterns-maintained stability for up to 48 hours. Additionally, we showed successful implementation for patterning both osteogenic and adipogenic differentiated cells. To validate lineage commitment of magnetically patterned cells, we conducted gene expression analyses. The lineage-specific functionality was verified through qPCR quantification of key differentiation markers, which showed significantly elevated expression of OCN in osteogenic patterned cultures and notable upregulation of PPAR γ , Resistin, and ENC-I in adipogenic patterned cultures relative to appropriate controls. This technique offers a cost-effective, contact-free solution, with considerable potential for applications in tissue engineering research.

References

1. Guillotin, B., & Guillemot, F. (2011).
2. Wright, D., et al. (2007).
3. Anil-Inevi, M., et al. (2021).

Localized Surface Plasmon Resonance-Based Microfluidic Biosensor for the Early Detection of the Border Disease Virus (BDV)

Nazlı Hilal Altun^{1*}, Abdullah Alakbarov¹, Selin Erhan¹, Volga Bulmuş¹

¹İzmir Institute of Technology, Department of Bioengineering

*nazlialtun@iyte.edu.tr

+ these authors contributed equally to this work

Border Disease Virus (BDV) is a pestivirus that affects sheep and goats, causing reproductive failure, congenital defects, and significant economic losses in the livestock industry. The disease leads to reduced productivity, increased veterinary costs, and trade restrictions, highlighting its economic and social impact (Righi et al., 2021). Early and accurate detection of BDV is crucial to prevent outbreaks and mitigate losses. Conventional diagnostic methods, such as PCR and ELISA, are time-consuming and require specialized laboratory facilities, underscoring the need for a rapid and portable point-of-care (POC) diagnostic solution.

Localized surface plasmon resonance (LSPR) biosensors based on gold nanorods (GNRs) offer high sensitivity and label-free detection capabilities, making them ideal for POC applications (Huang et al., 2009). In this research, a microfluidic LSPR biosensor was developed for BDV detection. Glass surfaces were functionalized with GNRs and a self-assembled monolayer, modified with a BDV-specific primer sequence targeting a complementary 19-base single-stranded DNA sequence. The biosensor was integrated with polymethyl methacrylate (PMMA) microfluidic channels to enable controlled sample management. Different concentrations of the BDV-DNA target sequence, ranging from 0.01 pM to 100 nM, were introduced into the microfluidic system, and the LSPR response was measured using a visible-near infrared (Vis-NIR) spectrometer.

The results demonstrated a concentration-dependent LSPR shift, confirming the biosensor's capability to detect BDV-DNA with high sensitivity. The integration of microfluidic technology with LSPR-based detection provides a promising platform for rapid, on-site BDV diagnosis, reducing reliance on centralized laboratories and enabling timely disease management in livestock populations. This biosensor represents a significant advancement toward accessible and efficient BDV detection, with potential applications in veterinary disease surveillance and outbreak prevention.

References

- Huang, C., Bonroy, K., Reekmans, G., Laureyn, W., Verhaegen, K., De Vlaminck, I., Lagae, L., & Borghs, G. (2009). Localized surface plasmon resonance biosensor integrated with microfluidic chip. *Biomedical Microdevices*, 11(4), 893–901. <https://doi.org/10.1007/s10544-009-9306-8>
- Righi, C., Petrini, S., Pierini, I., Giammarioli, M., & De Mia, G. M. (2021). Global Distribution and Genetic Heterogeneity of Border Disease Virus. *Viruses*, 13(6), 950. <https://doi.org/10.3390/v13060950>

Investigation of the biological effects of nano-plastic inhalation exposure using *in silico* and epithelial barrier-on-a-chip models

Omur Sert¹, Reyhan Coban¹, Eyup Bilgi², Suleyman Selim Cinaroglu¹, Ceyda Oksel-Karakus², Ozlem Yesil-Celiktas^{1,3}

¹Department of Bioengineering, Faculty of Engineering, Ege University, Izmir, Türkiye

²Izmir Institute of Technology, Department of Bioengineering, Izmir, Türkiye

³ODTÜ MEMS, Ankara, Türkiye

Plastic pollution poses serious threats to human health beyond exhibiting ecological consequences. Polypropylene (PP) wastes decompose under the influence of environmental factors such as temperature, UV radiation, mechanical abrasion, turning into nano-plastics (NPs), and spread throughout the ecosystem, causing biological effects on organisms [1]. NPs entering the body through inhalation first interact with the lung epithelial barrier (EB), while some are eliminated by the innate defence system (IDS) [2], some escape the radar of the IDS [3], which in turn triggers inflammation and apoptosis that lead to the disruption of the epithelial barrier integrity [4]. Leakages caused by EB dysfunction cause NPs to get into the blood circulation, where they bind to proteins and change the structural functions [5]. Molecular dynamic simulations can be used to understand the behaviour of NPs in high spatial-temporal detail compared to *in vitro* methods. Molecular pathways inducing each other have starting points that are difficult to detect in complex *in vivo* systems. Thus, *in vitro* engineered microfluidic systems are more advantageous to study these processes. Here, we designed and fabricated an epithelial barrier-on-a-chip platform and exposed PPs at biomimetically inhaled concentrations to the platform, while optimizing the flow rate, shear stress and shape. Morphological and cytotoxicity analyses are carried out to investigate the NP exposure alterations on the EB. In parallel molecular dynamic simulations are used to examine the NP-protein interactions.

Acknowledgement: This study is funded by TUBITAK through 123M406

References

- [1] Goksel et al., 2024, Allergy, 79, 2953-2965
- [2] Adami et al., 2022, RMD Open, 8, e002055
- [3] Boraschi et al., 2017, Semin. Immunol., –
- [4] Ramsperger et al., 2023, NanoImpact, 29, 100441
- [5] Wang et al., 2023, TrAC Trends Anal. Chem., 166, 117206

Microfluidic-based approaches for enhanced cerebral organoid maturation

Pelin Saglam-Metiner^{1,2,3*}, Utku Devamoglu⁴, Severine Le Gac⁴, Onur Basak², Ozlem Yesil-Celiktas^{1,3,5}

¹Department of Bioengineering, Faculty of Engineering, University of Ege, Izmir, Türkiye

²Department of Translational Neuroscience, Division of Neuroscience, UMC Brain Center, University Medical Center Utrecht, University of Utrecht, Utrecht, The Netherlands

³Ege University Translational Pulmonary Research Center (EgeSAM), Izmir, Türkiye

⁴Applied Microfluidics for BioEngineering Research, Faculty of Electrical Engineering, Mathematics and Computer Science, University of Twente, Enschede, The Netherlands

⁵ODTÜ MEMS Center, Ankara, Türkiye

*pelin.metiner@gmail.com

The bioengineered cerebral organoids, as a multicellular neural tissue architecture, recapitulate *in vivo* brain framework in a physiological and functional manner, and have become imperative for modelling various neurological diseases. However, traditional dynamic systems such as spinner and orbital shaker employed for cerebral organoid maturation are limited in their ability to replicate the *in vivo* biomechanical forces and natural microenvironment, owing to the absence of resident immune cells, stromal cells, and endothelial cells. Additionally, these systems face issues related to variability, limited reproducibility, and reduced long-term survivability [1]. To overcome these challenges and emulate the spatiotemporal dynamics of regulating mechanosensitive pathways in cerebral organoids, we utilized our custom-designed microfluidic systems, with the first perfusable system providing controlled dynamic flow conditions that replicate laminar blood flow within the brain [2,3]. The second tubing free system mimics bidirectional fluid flow, emulating the behavior of cerebrospinal fluid. The microfluidic platform-engineered organoids exhibited 95% harvestability with uniform sizes and enriched cellular diversity, including CD31+/β-catenin+ endothelial-like cells, CD11b+/IBA+, microglia, MAP2+/NEUN+ neurons, GFAP+/S100b+ astrocytes and MBP+/Olig2+ oligodendrocytes. Structural morphogenesis, including cortical plate, ventricular zone, subventricular zone, and preplate, along with presynaptic-postsynaptic interactions, was demonstrated. The organoids exhibited diverse neuronal identities, including GABAergic, glutamatergic, progenitor, mature, forebrain, and hindbrain neurons. Prolonged survivability was evident with Ki67+/TUNEL- proliferative non apoptotic cells at day 120. These findings have been leveraged to advanced maturation of cerebral organoids derived from various iPSC lines across multiple laboratories, with their reproducibility having been firmly validated.

Acknowledgments: This study was financially supported by The Scientific and Technological Research Council of Türkiye (TUBITAK) under grant number 119M578. PSM gratefully acknowledges the TUBITAK 2211/A National PhD Scholarship Program and TUBITAK 2214/A International Doctoral Research Fellowship Program.

References

[1] Saglam-Metiner, P., Yildirim, E., Dincer, C., Basak, O., & Yesil-Celiktas, O. (2024). Humanized brain organoids-on-chip integrated with sensors for screening neuronal activity and neurotoxicity. *Microchimica Acta*, 191(1), 71.

- [2] Saglam-Metiner, P., Devamoglu, U., Filiz, Y., Akbari, S., Beceren, G., Goker, B., ... & Yesil-Celiktas, O. (2023). Spatio-temporal dynamics enhance cellular diversity, neuronal function and further maturation of human cerebral organoids. *Communications Biology*, 6(1), 173.
- [3] Saglam-Metiner, P., Yanasik, S., Odabasi, Y. C., Modamio, J., Negwer, M., Biray-Avci, C., ... & Yesil-Celiktas, O. (2024). ICU patient-on-a-chip emulating orchestration of mast cells and cerebral organoids in neuroinflammation. *Communications Biology*, 7(1), 1-19.

Automated Cell Sorting via Image Analysis in a Magnetic Levitation System

Sadik Koc¹, Furkan Bora Cehiz¹, Busra Erimez¹, Huseyin Cumhuri Tekin^{1,2*}

¹Department of Bioengineering, Izmir Institute of Technology, Izmir 35430, Türkiye

²ODTÜ MEMS Center, Ankara 06520, Türkiye *cumhurtekin@iyte.edu.tr

Magnetic levitation-based cell analysis systems provide a label-free and rapid assessment of cell density by measuring the levitation height of cells under the effect of a magnetic field applied in a paramagnetic environment (Durmus et al., 2015). On the other hand, image-based technologies are widely used in real-time cell analysis today (Gordonov et al., 2016). The integration of these two approaches allows cells to be distinguished without the need for labeling (Delikoyun et al., 2021). Within the scope of this study, an image-based cell separation platform was developed, where magnetic levitation and microfluidic systems are used in an integrated manner. In the designed system, a single-inlet and dualoutlet microfluidic chip was used, and cells suspended in a paramagnetic environment are injected into the chip with a certain flow rate and remain suspended at different levitation heights depending on their density under the effect of the applied magnetic field. The levitation behaviors of the cells are analyzed through live video obtained with a camera integrated into the microscope; this analysis is performed with a specially developed Python software, and the levitation height, density value, elongation rate and environmental morphologies of the cells are determined. Cells with defined properties can be automatically separated during flow by directing them to appropriate outlets under the control of microfluidic valves. This developed system offers a label-free, cost-effective and automated cell separation method, and can be used in various biomedical applications such as live-dead cell separation, drug response analyses and cancer research.

Acknowledgements This study was supported by the Scientific and Technological Research Council of Türkiye (TUBITAK) under Grant Number 22AG032 and 124E059. The authors thank TUBITAK for their support. S.K. would like to express gratitude to TUBITAK for financial support through the 2211-A Domestic General PhD Fellowship Program.

References

- [1] Durmus, N. G., Tekin, H. C., Guven, S., Sridhar, K., Arslan-Yildiz, A., Calibasi, G., ... & Demirci, U. (2015). Magnetic levitation of single cells. *Proceedings of the National Academy of Sciences*, 112(28), E3661–E3668. <https://doi.org/10.1073/pnas.1504031112>
- [2] Gordonov, S., Hwang, M., Wells, A., Lauffenburger, D. A., & Haney, S. A. (2016). Time series modeling of live-cell shape dynamics for image-based phenotypic profiling. *Integrative Biology*, 8(1), 73–90. <https://doi.org/10.1039/C5IB00258H>
- [3] Delikoyun, H., Tümer, B. M., Yalçın, H. C., & Aydın, M. (2021). HologLev: A hybrid magnetic levitation platform integrated with lensless holographic microscopy for density-based cell analysis. *ACS Sensors*, 6(6), 2191–2201. <https://doi.org/10.1021/acssensors.1c00433>

Sustainable Synthesis and Evaluation of Rice Husk-Derived Mesoporous Silica Nanoparticles for Drug Delivery Under Dynamic Physiological Conditions

Sahar Porrang^{1*}, Gulin Baran¹, Nur Mustafaoglu^{1,2}

¹ Molecular Biology, Genetics and Bioengineering Program, Faculty of Engineering and Natural Sciences, Sabanci University, Istanbul, Turkiye

² Sabanci University Nanotechnology Research and Application Center (SUNUM), Sabanci University, Istanbul, Turkiye

*Sahar.porrang@sabanciuniv.edu + these authors contributed equally to this work

Mesoporous silica nanoparticles (MSNs) synthesized from agricultural biowaste, specifically rice husk (RH), represent a sustainable and cost-effective strategy for drug delivery applications (Porrang et al., 2021a, 2021b). In this study, a green chemistry approach was developed to produce MSNs for healthrelated uses, and their drug-loading performance was evaluated under physiologically relevant conditions using microfluidic platforms. Silica was first extracted from RH via acid treatment followed by calcination, and characterized using FTIR, XRD, TGA, and BET/BJH analyses. Rice husk-derived MSNs (RMSNs) were then synthesized via a sol-gel method employing CTAB as a surfactant (Porrang et al., 2022). The resulting RMSNs exhibited improved surface area, mesoporosity, and a narrow pore size distribution compared to raw rice husk material. To assess their drug delivery potential, RMSNs were loaded with doxorubicin (Dox), and in vitro release studies revealed pH-responsive behavior, with accelerated drug release under acidic conditions that mimic the tumor microenvironment. The RMSNs demonstrated pronounced sensitivity to pH changes, supporting their potential for controlled drug release in cancer therapy. Biocompatibility was confirmed through viability assays using human dermal fibroblasts (HDF) and human umbilical vein endothelial cells (HUVECs), indicating the non-toxic nature of RMSNs. Cellular uptake studies using fluorescence microscopy and flow cytometry showed efficient, dose-dependent internalization of RMSNs, with significant uptake observed even at low concentrations. A three-dimensional microfluidic platform simulating dynamic physiological conditions was used to further investigate nanoparticle-cell interactions. Under continuous flow, RMSNs exhibited enhanced cellular uptake compared to static conditions. The flow not only promoted uniform nanoparticle distribution but also facilitated deeper internalization, likely by mimicking blood circulation and influencing the polarization of transport proteins (Garcia-Castillo et al., 2017). These results highlight the promise of rice husk-derived MSNs as environmentally friendly, tunable nanocarriers for drug delivery. Importantly, this study underscores the value of evaluating nanomaterials under dynamic, physiologically relevant conditions to better inform the design of targeted cancer therapies and scalable drug delivery systems.

Acknowledgements The authors express their sincere gratitude to the Marie Skłodowska-Curie Actions (MSCA) postdoctoral grant (Project No. 101110722, awarded to Sahar Porrang) for financial support.

References

- [1] Garcia-Castillo, M. D., Chinnapen, D. J.-F., & Lencer, W. I. (2017). Membrane transport across polarized epithelia. *Cold Spring Harbor perspectives in biology*, 9(9), a027912.
- [2] Porrang, S., Davaran, S., Rahemi, N., Allahyari, S., & Mostafavi, E. (2022). How advancing are mesoporous silica nanoparticles? A comprehensive review of the literature. *International journal of nanomedicine*, 1803-1827.
- [3] Porrang, S., Rahemi, N., Davaran, S., Mahdavi, M., & Hassanzadeh, B. (2021a). Preparation and in-vitro evaluation of mesoporous biogenic silica nanoparticles obtained from rice and wheat husk as a biocompatible carrier for anti-cancer drug delivery. *European Journal of Pharmaceutical Sciences*, 163, 105866.
- [4] Porrang, S., Rahemi, N., Davaran, S., Mahdavi, M., & Hassanzadeh, B. (2021b). Synthesis of temperature/pH dual-responsive mesoporous silica nanoparticles by surface modification and radical polymerization for anti-cancer drug delivery. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 623, 126719.

Characterization of Protein Corona on Nanostructures Using Magnetic Levitation

Sezin Cakal¹, Eyup Bilgi¹, Meltem Guzelgulgen¹, Muge Anil-Develi¹, Engin Ozcivici¹,
Ceyda Oksel Karakus^{1*}

¹Department of Bioengineering, Izmir Institute of Technology, Izmir, Türkiye.

*ceydaoksel@iyte.edu.tr

Magnetic Levitation (MagLev)-based systems have been primarily applied in biomedical literature for cell separation and three-dimensional (3D) cell culture studies in tissue engineering [1]. This study explores an innovative application of MagLev technology for characterizing protein corona (PC) formation around Carbon Nanotubes (CNTs), which are widely used nanoparticles in biological applications [2]. We designed and optimized a standard MagLev platform incorporating two N52-grade neodymium (NdFeB) rectangular magnets (40 mm length, 40 mm width, and 20 mm height) in an anti-Helmholtz configuration with varying separation distances for CNT levitation. Initially, CNTs underwent carboxylation through strong acid treatment and were subsequently incubated in serum-containing medium under various conditions to facilitate PC formation around carboxylated CNTs. Following morphological assessment using scanning electron microscopy (SEM), the PC characterization was performed using our custom designed MagLev platform and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) simultaneously. Our findings demonstrated that MagLev can serve as an orchestral platform for detecting PC structures based on density differences, offering a sensitive method to distinguish subtle variations in the composition and structure of the PC with no need of protein separation from CNT surfaces.

Acknowledgements: The authors thank Uğur Kartal for providing carbon nanotubes used in the research.

References

- [1] Example Karakuzu, B., Anil İnevi, M., Tarim, E. A., Sarigil, O., Guzelgulgen, M., Kecili, S., Cesmeli, S., Koc, S., Baslar, M. S., Oksel Karakus, C., Ozcivici, E., & Tekin, H. C. (2024). Magnetic levitation-based miniaturized technologies for advanced diagnostics. *Emergent Materials*. <https://doi.org/10.1007/s42247-024-00762-6>
- [2] Murjani, B. O., Kadu, P. S., Bansod, M., Vaidya, S. S., & Yadav, M. D. (2022). Carbon nanotubes in biomedical applications: Current status, promises, and challenges. *Carbon Letters*, 32(5), 1207–1226. <https://doi.org/10.1007/s42823-022-00364-4>

POSTER PRESENTATIONS

Directed Tissue Morphogenesis on Microfluidic Chip Systems

Ali Eren Evranos^{1,2}, Hülya Erboğa^{1,2}, Esra Nur Yiğit^{3,4}, Sinan Güven^{1,2,5*}

¹İzmir Biomedicine and Genome Center, 35340, İzmir, Türkiye

²İzmir International Biomedicine and Genome Institute, Dokuz Eylül University, 35340, İzmir, Türkiye

³Regenerative and Restorative Medicine Research Center (REMER), Research Institute for Health Sciences and Technologies (SABITA), Istanbul Medipol University, 34810 Istanbul, Türkiye

⁴Department of Physiology, International School of Medicine, Istanbul Medipol University, 34810 Istanbul, Türkiye

⁵Department of Medical Biology and Genetics, Faculty of Medicine, Dokuz Eylül University, 35340, İzmir, Türkiye

*sinan.guven@ibg.edu.tr

Tissue morphogenesis involves changes in cell properties to shape tissues. Traditional 2D cultures replicate biochemical conditions but lack topographical cues [1]. 3D culture systems improve the study of cell morphology, proliferation, and differentiation. Microfluidic chips further enhance this by mimicking in-vivo conditions and integrating stem cell-derived organoids for tissue and disease modeling [2]. The lacrimal gland supports corneal and conjunctival epithelial tissues, ensuring their function and viability. This study aims to design a microfluidic chip system that recapitulates the morphology of the lacrimal gland and assists in the morphogenesis of stem cell-derived lacrimal gland organoids. The developed system and approach have the potential to be used in a broader platform capable of investigating different tissue morphologies. In this study, the microfluidic chip systems were designed using SolidWorks software and the molds were fabricated with 3D printer. These molds were then utilized to produce polydimethylsiloxane (PDMS) chips. To provide an extracellular matrix-like (ECM) structure, collagen gel was incorporated into the chip and laser patterning was employed to create a lacrimal gland-like design. The Zeiss PALM MicroBeam Laser was used for microchannel generation. The laser's properties were adjusted according to the collagen gel (1-ns pulses, 100-Hz frequency, 355 nm). The fabricated microfluidic chip system facilitates the cell alignment while mimicking the morphology of the lacrimal gland. This study's findings suggest that microfluidic chip systems designed to align with tissue morphology can yield structures that more closely resemble the target tissue. **Keywords: organoid, lacrimal gland, microfluidic, morphology, microenvironment**

Acknowledgements: This work was funded by the Scientific and Technological Research Council of Türkiye (TÜBİTAK, project no. 121C313) and the BİDEB 2210A National Graduate Scholarship Program. The authors thank Seren Keçili and Cumhuri Tekin for assisting in 3D printing of microfluidic molds.

References

- [1] Nikolaev, M., Mitrofanova, O., Broguiere, N., Geraldo, S., Dutta, D., Tabata, Y., Elci, B., Brandenburg, N., Kolotuev, I., Gjorevski, N., Clevers, H., & Lutolf, M. P. (2020). Homeostatic mini-intestines through scaffold-guided organoid morphogenesis. *Nature*, 585(7826), 574–578. <https://doi.org/10.1038/s41586-020-2724-8>
- [2] Elci, B. S., Nikolaev, M., Rezakhani, S., & Lutolf, M. P. (2024). Bioengineered Tubular Biliary Organoids. *Advanced* <https://doi.org/10.1002/adhm.202302912>

Investigation of monocyte amoeboid movement using alginate-PLL hydrogel in lab-on-a-chip

Aslınur Ulucay^{1*}, Devrim Pesen Okvur^{1,2}

¹Department of Molecular Biology and Genetics, Faculty of Science, Izmir Institute of Technology, Izmir, Türkiye

²Initio Cell BV, Leiden, Netherlands

*aslinurulucay@gmail.com

Monocytes are highly mobile cells with amoeboid migration properties, enabling them to navigate through extracellular matrix (ECM) pores and play critical roles in immune responses and inflammation, relevant to both health and disease states. Most existing models utilize hydrogels such as collagen and Matrigel, which are animal-derived, expensive, and susceptible to degradation by enzymes secreted by monocytes. Alginate, a non-biodegradable material, can be modified with positively charged poly-L-lysine (PLL), offering distinct advantages for studying cell motility. This project aims to explore the effects of alginate- PLL complexes on cell migration in three-dimensional (3D) environments using lab-on-chip (LOC) systems, providing a biologically compatible model.

The ICS-Chip device, fabricated from PDMS, features three continuous reservoirs separated by single capillary burst valves and a user-friendly open-top design. This innovative platform facilitates the straightforward placement of hydrogel in the central channel while enabling observation of cell movement dynamics in response to chemoattractants in the side channels. The migration of cells can be tracked, offering valuable insights into cellular behavior under environmental stimuli.

In this study, green fluorescently labeled U937 human monocytes were encapsulated in alginate-PLL hydrogel, and their migration towards serum-free and serum-containing channels was observed. Cells were imaged using confocal microscopy, and data were analyzed with Fiji and R-Studio. Results showed that monocytes exhibited significant migration towards serum-containing media compared to serum-free media. Future studies will expand the application of the ICS-Chip to investigate amoeboid cell migration in various cell types. This platform holds potential for cancer research, immunotherapy, and modeling immune responses, presenting an innovative and sustainable alternative in LOC technology.

Acknowledgements

This project was funded by TÜBİTAK under the 2209-B Industry-Oriented Undergraduate Research Projects Support Program. The authors would like to thank TÜBİTAK for their financial support. Also, would like to thank INITIO Cell Biotechnology company for ICS CHIP support and design. Cell culture and invasion assays were performed at controlled in vitro Microenvironment (CivM) laboratory from Izmir Institute of Technology.

One-Step Emulsion Polymerization in a Microfluidic Reactor

Synthesis of Fluorescence Hybrid Nanoparticles

Teoman Utku Yeğenoğlu^{1,2}, Efe Berk Altın², Atalay Bozdoğan³, Güneş Kibar^{1*}

¹Micro Nano Particles (MNP) Research Group, Materials Science and Engineering
Department, Adana Alparslan Türkeş Science and Technology University, Adana 01250,
Türkiye

²Hacettepe University Biology Department, Ankara, 06800, Türkiye

³Akdeniz University Mechanical Engineering Department, Antalya, Türkiye

*gkibar@atu.edu.tr

Fluorescent hybrid particles play a crucial role in nanomedicine and biological applications, including imaging, diagnostics, drug delivery, biosensing, multimodal imaging, and theragnostic. Polyhedral oligomeric silsesquioxane (POSS) is particularly promising for these applications due to its distinctive hybrid structure, consisting of an inorganic silica-cage core surrounded by functional organic substituents such as vinyl end monomers. This unique architecture facilitates the formation of micro- and nanoparticles via free-radical emulsion polymerization (Kibar, 2020). While traditional batch synthesis methods rely on well-defined emulsification parameters, including emulsifier concentration and ultrasonic treatment, achieving stable emulsions with ultra-small droplets through microfluidic systems remains an area requiring further investigation (Kılınçlı et al., 2024). Recent studies have demonstrated the feasibility of producing POSS hybrid nanoparticles using self-assembly emulsification within a microfluidic reactor, providing an alternative to conventional ultrasonic emulsification. In this study, we introduce a method for generating self-assembled emulsions in a microfluidic reactor, enabling the continuous and one-step synthesis of fluorescent POSS nanoparticles via UV polymerization. This streamlined approach offers a scalable and highly controlled method for producing fluorescent hybrid nanoparticles with tailored properties. The synthesized nanoparticles will be characterized using scanning electron microscopy (SEM), fluorescence microscopy, and Fourier-transform infrared spectroscopy (FTIR). These fluorescent POSS nanoparticles hold significant potential for fluorescence imaging applications, particularly in bio-detection for array-based systems.

Acknowledgements: TUBITAK 2218 award (project number: 122C228), Special thx to Dr. Altuğ Özçelikkale for microfluidic-mold

References

- [1] Kibar, G. (2020). Spherical shape poly (M-POSS) micro/nano hybrid latex particles: One-step synthesis and characterization. *Journal of Applied Polymer Science*, 137(41), 49241.
- [2] Kılınçlı, B., Çınar, A. D., Çetin, B., & Kibar, G. (2024). Microfluidic vs. batch synthesis of fluorescent poly (GMA-co-EGDMA) micro/nanoparticles for biomedical applications. *Emergent Materials*, 1-10

Development of a novel hydrogel based extracellular matrix for use in organ-on-chip platforms

Aysel Saskara¹, Yagmur Arslan¹, Ozlem Yesil-Celiktas^{1,2,3}

¹Department of Bioengineering, Faculty of Engineering, Ege University, Izmir, Türkiye

²Translational Pulmonary Research Center (EgeSAM), Ege University, Izmir, Türkiye

³Department of Pulmonary Medicine, Faculty of Medicine, Ege University, Izmir, Türkiye

⁴ODTÜ MEMS Center, Ankara, Türkiye

ayselsaskara01@gmail.com

The development of effective therapeutic strategies remains a fundamental challenge in medical research. Three-dimensional (3D) preclinical models that mimic the tissue microenvironment are used to develop new therapeutic strategies. However, most of these models lack the essential extracellular matrix (ECM) proteins that influence disease progression. Therefore, developing bioengineered biomaterials that better recapitulate the native ECM is crucial for preclinical research. In this study, we developed an ECM-based hydrogel by decellularizing bovine lung tissue and integrating it with GelMA to investigate its potential for modeling disease progression, cell behavior, and ECM remodeling. The optimized decellularization protocol successfully removed nearly 98% of DNA while preserving the structural integrity of key ECM components, including collagen, elastin, and sGAG, demonstrating the protocol's efficiency. The decellularized ECM was then enzymatically digested to form a pre-gel, which was combined with GelMA at varying concentrations. To replicate tissue interactions, cells were embedded within the hydrogel, fibroblasts were seeded around the affected area, and epithelial cells were layered on top, forming a structured tissue environment within a dynamic microfluidic platform under controlled conditions. Rheological analysis revealed that the disease model exhibited greater stiffness compared to the healthy model, reflecting the altered mechanical properties of the affected tissue. This increase in stiffness was associated with elevated collagen and elastin levels, suggesting a role in ECM remodeling. Overall, our hybrid hydrogel provides a physiologically relevant platform for studying biochemical and mechanical alterations in the tissue microenvironment, offering valuable insights into disease progression and potential preclinical applications.

Acknowledgement: This study is funded by Health Institutes of Türkiye (TUSEB) through grant number 36064

Lung Cancer Metastasis-on-a-Chip: A Preclinical Model for Studying EMT and Tumor Progression

Basar Dogan^{1*}, Pelin Saglam-Metiner^{2,3}, Tuncay Goksel^{3,4}, Ozlem Yesil-Celiktas^{2,3,5}

¹ Department of Biotechnology, Graduate School of Natural and Applied Sciences, Ege University, Izmir, Türkiye

²Department of Bioengineering, Faculty of Engineering, Ege University, Izmir, Türkiye

³Translational Pulmonary Research Center (EgeSAM), Ege University, Izmir, Türkiye

⁴Department of Pulmonary Medicine, Faculty of Medicine, Ege University, Izmir, Türkiye

⁵ODTÜ MEMS Center, Ankara, Türkiye

*basardogn@gmail.com

Lung and breast cancers are among the most common malignancies worldwide, with approximately two million new cases annually. The late onset of symptoms in lung cancer leads to high mortality rates. Additionally, after breast and prostate cancer, lung cancer is the most frequently associated with bone metastasis, observed in 30-40% of cases. This condition causes severe skeletal complications that significantly reduce patients' quality of life. Therefore, there is an increasing need for preclinical models that can effectively mimic lung cancer metastasis to bone. Organ-on-chip platforms provide an innovative approach by modeling physiological functions in micro-scale systems, making them valuable tools for studying tumor metastasis. One of the key steps in the metastatic process, epithelial-mesenchymal transition (EMT), can be investigated using these platforms. Understanding the factors influencing EMT may contribute to the development of novel therapeutic strategies targeting metastasis.

In this context, the lung cancer metastasis-on-a-chip (LCMoC) platform has been developed, which consists of two PMMA sheets enclosing two PDMS layers, where two tissue chambers represent the lung and bone compartments, and a single microchannel serve as the vascular lumen. The lung compartment includes a co-culture of A549 lung cancer cells, Beas-2B bronchial epithelial cells, and CCD34Lu fibroblasts, while the bone compartment contains hFOB osteoblasts. To better mimic the extracellular matrix (ECM) and support cellular interactions, GelMA hydrogel was used in the tissue chambers. Under dynamic flow conditions, experiments conducted over 14 days demonstrated that lung cancer cells migrated through the vascular space and reached the bone compartment. These findings suggest that the LCMoC platform provides a powerful preclinical model for studying lung cancer metastasis and EMT processes, offering valuable insights into tumor progression and potential therapeutic strategies.

Acknowledgement: This study is funded by Health Institutes of Türkiye (TUSEB) through grant number 39471.

3D in vitro Blood Brain Barrier (BBB) -on-a-Chip Model

Begum Gokce^{1*}, Ramazan Temizkan², Devrim Pesen-Okvur^{2,3}, Yasin Kaymaz¹

¹ Department of Bioengineering / Graduate School of Natural and Applied Sciences, Ege University, Türkiye

² Department of Molecular Biology and Genetics, Faculty of Science, Izmir Institute of Technology, Izmir, Türkiye

³ INITIO Cell BV Leiden, Netherlands

The objective of this study is to develop a microphysiological system (MPS) for the blood-brain barrier (BBB) that mimics permeability properties observed in vivo. The novelty of this MPS lies in utilizing brain tissue from deceased mice as a rich source of brain cells and extracellular matrix. The tissue was combined with fibrin gel and placed into the central channel of a microfluidic chip with three channels separated by capillary burst valves. bEnd.3 endothelial cells were integrated into the tissue-gel mixture to form vascular networks and added to the side channels to create monolayers. The development of vascular networks and monolayers was confirmed through confocal microscopy imaging of endothelial cells expressing green fluorescent protein. Structural integrity was verified by fluorescent phalloidin staining. Permeability was assessed using 70 kDa red fluorescent dextran. The adaptation of this MPS system will improve BBB investigation in both preclinical and clinical studies.

Micro-rotator to induce microgravity on human cell lines to make spheroids

Cihan Erkan¹, Devrim Pesen Okvur^{1,2}

¹Department of Molecular Biology and Genetics, Faculty of Science, Izmir Institute of Technology, 35430 Izmir, Türkiye

²Initio Cell BV, Leiden, Netherlands
cihan.erkn41@gmail.com

Animals used in product testing and scientific research have ethical concerns and these models do not fully replicate the human response and physiology. 2D techniques used to replace animals such as cell cultures grown in petri dishes are an efficient and cheaper way of in vitro testing, but they cannot fully replicate the dynamic biological environment due to lack of cell-cell and cell-matrix interactions (1). 3D spheroids and organoids are a solution to problems represented by both animals and 2D techniques by usage of human cell lines to produce tissue like 3D constructs, but these techniques require meticulousness and extra materials such as microwell plates, collagen or Matrigel to form aggregates.

Microgravity is one of the techniques used to make 3D cell constructs. It depends on the shear stress free environment so cells can develop into spheroids (2). In our system, microgravity is induced to cells by a DIY micro rotator made with custom 3D printed parts and Arduino microcontrollers. Cells are placed in the PDMS vessel with media normally used for 2D cell cultures and rotated to induce microgravity. Usage does not require additional materials such as collagen or Matrigel and compact size makes it so that it can be placed in standard cell incubators.

HepG2 liver carcinoma cells served as the first cell lines to make spheroids because of their natural tendency to aggregate. The system was rotated for 14 days, adjusting the speed of rotation according to size of cell aggregates observed under light microscope. To assess the cell viability and 3D structure Calcein and DAPI were used. Future applications aim to make variety of different spheroids using other human cell lines and testing these spheroids to be used in scientific research.

References

- [1] Unsworth, B. R., & Lelkes, P. I. (1998). Growing tissues in microgravity. *Nature Medicine*, 4(8), 901–907. <https://doi.org/10.1038/nm0898-901>
- [2] Kapałczyńska, M., Kolenda, T., Przybyła, W., Zajączkowska, M., Teresiak, A., Filas, V., Ibbs, M., Bliźniak, R., Łuczewski, Ł., & Lamperska, K. (2018). 2D and 3D cell cultures - a comparison of different types of cancer cell cultures. *Archives of medical science: AMS*, 14(4), 910–919. <https://doi.org/10.5114/aoms.2016.63743>

Advancing Brain Organoid Research with AI: Image Analysis and Deep Learning for Enhanced Neurobiological Insights

Dogu Can Seyidoglu¹, Pelin Saglam-Metiner^{2,3}, Ozlem Yesil-Celiktas^{2,3,4}

¹ Department of Biotechnology, Graduate School of Natural and Applied Sciences, Ege University, Izmir, Türkiye

²Department of Bioengineering, Faculty of Engineering, Ege University, Izmir, Türkiye

³Translational Pulmonary Research Center (EgeSAM), Ege University, Izmir, Türkiye

⁴ODTÜ MEMS Center, Ankara, Türkiye

seyidogludc@gmail.com

Brain organoids derived from human induced pluripotent stem cells (iPSCs) serve as powerful *in vitro* models for studying neurodevelopment, disease mechanisms, and therapeutic interventions [1]. However, the complexity of their morphology and dynamic cellular interactions presents significant challenges for quantitative analysis. Recent advancements in artificial intelligence (AI), particularly deep learning-based image processing [2], offer novel solutions for extracting meaningful patterns from high-resolution microscopy data.

This study explores the integration of AI-driven image analysis techniques to enhance the characterization of brain organoids. By leveraging convolutional neural networks (CNNs) and advanced segmentation algorithms [3], we aim to improve the accuracy and reproducibility of organoid morphological assessment. Such approaches enable precise detection of structural variations, neurodevelopmental trajectories, and potential pathological changes, paving the way for more robust and scalable organoid-based studies [4].

The implementation of deep learning in organoid research holds promise for accelerating discoveries in neuroscience, from fundamental brain development studies to applications in neurodegenerative disease modeling and drug screening. This work highlights the transformative role of AI in biological image analysis, bridging the gap between computational power and experimental neuroscience.

References

- [1] Lancaster, M. A., & Knoblich, J. A. (2014). Generation of cerebral organoids from human pluripotent stem cells. *Nature Protocols*, 9(10), 2329–2340.
- [2] LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature*, 521(7553), 436–444.
- [3] Litjens, G. J. A., Kooi, T., Bejnordi, B. E., Setio, A. A. A., Ciompi, F., Ghafoorian, M., van de Laak, J. A. W. M., van Ginneken, B., & Sánchez, C. I. (2017). A survey on deep learning in medical image analysis. *Medical Image Analysis*, 42, 60–88.
- [4] Paşca, A. M., Sloan, S. A., Clarke, L. E., Tian, M., Makinson, C. D., Huber, N., Gage, F. H., & Kriegstein, A. R. (2015). Functional cortical circuits from human pluripotent stem cells in vitro. *Nature Neuroscience*, 18(3), 407–415.

Bioengineered Microfluidics for Corneal Organoids

Gaye Su YIGIT

Izmir Biomedicine and Genome Center (IBG), Izmir, Türkiye

gayesuyigit@gmail.com

The cornea constitutes a specialized anatomical structure characterized by its specialized structure and unique composition, which play vital roles in visual function and eye health. In this study, we have developed a microfluidic system designed to optimize the dynamic microenvironment of corneal organoids. This approach aims to enhance our understanding of organoid development and its implications for further research.

Corneal organoids were developed using iPSC lines registered in the Human Pluripotent Stem Cell Registry (hPSCreg) and approved by ethical committees. A microfluidic system with an air-liquid interface was designed using SolidWorks software, considering the anatomical and physiological characteristics of the corneal microenvironment. PDMS was prepared and cured at 65°C for 2 hours. pH and O₂ sensors were integrated into the air-liquid interface microfluidic system.

To generate cornea organoids from hiPSC, differentiation media were applied for 2 days, after which retinal differentiation media was utilized for 30 days. On day 32, the culture was confidently transitioned to suspension culture and from day 47 onward, the distinct morphologies of the corneal organoids began to take shape. Fibrin gel effectively immobilized the cornea organoid into the microfluidic system. Optical sensors were integrated into the microfluidic system, enabling the measurement of pH and O₂ levels.

The presented results have provided more detailed information regarding the pH and O₂ levels of the organoids studied within the microfluidic system. The differences observed in the pH and O₂ levels during the development process of corneal organoids have the potential to lead the way for future molecular biology studies.

Tree Fractal Inspired Obstacle Type Micromixer

Giray Yüksel^{1,2}, Mehmet Oğulcan Güngör^{2,3}, Ender Yıldırım^{2,4}

¹ İhsan Doğramacı Bilkent University, Department of Mechanical Engineering, Ankara,
Türkiye

² ODTÜ MEMS Center, Ankara, Türkiye

³ Middle East Technical University, Department of Micro and Nanotechnology, Ankara,
Türkiye

⁴ Middle East Technical University, Department of Mechanical Engineering, Ankara, Türkiye

*Correspondence: yender@metu.edu.tr

Microfluidics is the study that investigates and utilizes fluid flow in micro scale. Mixing is one of the challenges in microfluidics because of the laminar nature of fluid flow in microchannels. In this study, we present a novel micromixer design that utilizes the concept of tree fractals by integrating it into obstacle type micromixers. Designs of the micromixer have been specifically engineered to be manufactured by thermoforming using micromilled molds. Designs of the micromixer have been characterized by the number of tree fractal designed obstacles' branching and the number of obstacles. Mixing efficiencies of these designs for different Reynolds numbers are calculated numerically by the Laminar Flow and Transport of Diluted Species Modules of COMSOL Multiphysics. Results of the numerical analysis showed that the mixing efficiency increases as both the number of branching and the obstacles increase. It is shown that the mixing efficiency increases by 2.04% to 9.76% as the branching number increases for different designs with different numbers of obstacles. As future work, these micromixers will be fabricated with thermoforming following the fabrication of their molds by milling and their mixing efficiencies will be verified experimentally.

Acknowledgement: This study is funded by the ODTÜ MEMS Center under project no. BIO-IP25-006.

Density-Based Identification of Osteogenic Differentiation Using Magnetic Levitation

Husniye Buyukcakil^{1,*}, Oyku Sarigil¹, Melike Cagan Algan¹, Muge Anil Inevi¹, Engin Ozcivici¹

¹Department of Biotechnology and Bioengineering, Izmir Institute of Technology, Izmir, Türkiye

*husniyebuyukcakil@iyte.edu.tr

Magnetic levitation(MagLev) is a technique to suspend objects against gravity through magnetic interactions, meanwhile separating them by density via the competition between gravitational and diamagnetic forces[1]. Cell manipulation using magnetic forces offers advantages including excellent cell viability and minimal environmental disturbance due to its label-free nature[2,3]. In this study, we utilized a magnetic levitation device consisting of two same pole permanent magnets to produce a magnetic force, opposite mirrors placed with 45° for real time imaging, a capillary channel for cell loading and a structural holder. The working distance was first calibrated with polymeric beads of known density using 25mM Gadavist solution, yielding a linear equation that enabled the determination of cell density from levitation height. 7F2 mouse osteoblast cells were differentiated in osteogenic medium over 14 and 21 days with appropriate inducing agents. Successful mineral accumulation was confirmed through alizarin red staining. Following differentiation, cells were trypsinized and levitated at a concentration of 105cells/ml in medium containing 25mM Gd3+. Differentiated 7F2 cells demonstrated higher levitation positions, with an average levitation height of 802.1µm compared to undifferentiated 7F2 cells which levitated at an average height of 774.6µm. Based on known density of the calibration beads, the density of differentiated 7F2 cells was determined to be greater than 1.07 gmL⁻¹. Cell viability was assessed using calcein/propidium iodide(PI) staining determining the effect of dead cells on single cell measurements. Our results demonstrate that magnetic levitation provides a promising label-free method for identifying osteogenically differentiated cells through density-based separation.

References

- [1] Ge, S., et al., (2020) Magnetic levitation in chemistry, materials science, and biochemistry. Angewandte Chemie International Edition, 59(41), 17810-17855.
- [2] Karakuzu, B., et al., (2024) Magnetic levitation-based miniaturized technologies for advanced diagnostics. Emergent Materials, 7(6), 2323-2348.
- [3] Sarigil, O., et al., Scaffold-free biofabrication of adipocyte structures with magnetic levitation. Biotechnology and bioengineering, 118(3), 1127-1140.

Scalable Production of Heterogeneous 3D Cellular Models Using Ring Magnet-Based Magnetic Levitation

İlayda Ozkan¹, Muge Anil Inevi¹, Ozden Yalcin-Ozuysal², Gulistan Mese², Engin Ozcivici¹

¹Department of Bioengineering, Izmir Institute of Technology, Izmir, Türkiye

²Department of Molecular Biology and Genetics, Izmir Institute of Technology, Izmir, Türkiye

ilaydaoalkan@iyte.edu.tr

Magnetic levitation has emerged as an important bioprinting method for fabricating 3D heterogeneous *in vitro* models to advance cell biology and tissue engineering studies. This technique can be implemented either by incorporating magnetic labeling molecules with the cells or by label-free paramagnetization of the cell culture medium. Label-free magnetic levitation is applied based on the principle of negative magnetophoresis [1,2] and offers a practical and rapid approach for producing a 3D culture model while preserving cell viability by eliminating the need for labeling or scaffold materials. The magnetic levitation system accommodates diverse cell types, either individually or in combination, depending on the specific research objectives. Various magnet configurations have been implemented for magnetic levitation studies. Among these, a ring-shaped arrangement with a single magnet [3] provides significant advantages by enabling manipulation of the cellular environment and facilitating the formation of scalable structures for homogeneous or heterogeneous cell loadings. In this study cancer cells, epithelial cells, and fibroblasts were cultured both individually and in co-culture within the single ring magnet-based levitation system, resulting in the formation of scaffold-free spheroids of varying sizes. Our findings demonstrate that scaffold-free spheroids, recognized for their superior tissue mimicry compared to other *in vitro* models, can be generated in a scalable and enlargeable manner using the ring magnetic levitation system. These *in vitro* models provide a valuable foundation for specialized studies in tissue engineering and disease biology research.

References

- [1] Yaman, S., et al., (2018). *Frontiers in bioengineering and biotechnology*, 6, 192
- [2] Sarigil, O, et al., (2019) *Analyst*, 144.9 (2019): 2942-2953.
- [3] Anil-Inevi, M et al., (2021) *Biotechnology and Bioengineering*, 118, (12) 4771-4785

Preparation of Hydrogel Coatings Containing Drug-Loaded Liposomes Using a T-shaped Microfluidic Junction Device Technique

Ismail BAL^{1,2}, Güleengül DUMAN³, Muhammad S. Arshad⁴, Zeeshan Ahmad⁵, Israfıl KUCUK¹

¹ Institute of Nanotechnology, Gebze Technical University, Kocaeli, 41400, Türkiye

² Vocational School of Health Services, Istanbul Okan University, Istanbul, 34959, Türkiye

³ Department of Pharmaceutical Technology, Faculty of Pharmacy, Yeditepe University, 34755, Istanbul, Türkiye

⁴ Department of Pharmacy, Bahauddin Zakariya University, Multan, 60800, Pakistan

⁵ Leicester School of Pharmacy, De Montfort University, Leicester, LE1 9BH, UK

*ismail.bal@okan.edu.tr / i.bal2019@gtu.edu.tr * gduman@yeditepe.edu.tr

*i.kucuk@gtu.edu.tr

Liposomes are microscopic vesicles typically ranging in size from 10 nm to 1 µm, with an aqueous core surrounded by one or more concentric lipid bilayers. Due to their unique characteristics, they are capable of encapsulating both hydrophilic and hydrophobic therapeutic agents [1]. Due to their excellent biocompatibility, membrane-like structure, and capacity to encapsulate hydrophilic and hydrophobic drugs, liposomes can be used in ocular systems. Pharmaceutical compounds often exhibit very low stability within the body. Liposome-based encapsulation acts as a barrier against enzymatic degradation, leading to improved drug stability in physiological environments. Yet, the natural instability of these compounds may reduce their potential as therapeutic agents. A promising strategy to mitigate this problem is embedding liposome-encapsulated drugs within polymeric hydrogel matrices, which further stabilizes the drug [2]. This study reports a moxifloxacin (MXF)-encapsulated liposome-enriched alginate nanocomposite hydrogel coating obtained using microfluidic method. Moxifloxacin (MXF) was encapsulated in soy lecithin (SL) to form liposomal nanoparticles using a probe sonicator and then incorporated into an alginate hydrogel system. SL and MXF were dissolved in pure water and produced by changing the parameters (2 min–10 min, 2 min intervals) and amplitude (20%, 40%, and 60%) values. The prepared liposomal nanoparticles were freeze-dried for 24 hours using a lyophilizer and incorporated into the alginate hydrogel system. Structural and physical characterizations were performed on the synthesized MXF-encapsulated liposome-enriched alginate nanocomposite hydrogel coating. The in vivo drug release performance of the hydrogels and the effect of crosslinker concentration on drug release were investigated. MXF-encapsulated liposome-enriched alginate nanocomposite hydrogel structures produced via microfluidic techniques have demonstrated strong potential for use in biomedical and ocular applications.

References

- [1] M. Feghhi, B. Sharif Makhmalzadeh, F. Farrahi, M. Akmalı, and N. Hasanvand, “Anti-microbial Effect and in Vivo Ocular Delivery of Ciprofloxacin-loaded Liposome through Rabbit’s Eye,” *Curr Eye Res*, vol. 45, no. 10, pp. 1245–1251, Oct. 2020, doi: 10.1080/02713683.2020.1728777.
- [2] L. K. Widjaja, M. Bora, P. N. P. H. Chan, V. Lipik, T. T. L. Wong, and S. S. Venkatraman, “Hyaluronic acid-based nanocomposite hydrogels for ocular drug delivery applications,” *J Biomed Mater Res A*, vol. 102, no. 9, pp. 3056–3065, Sep. 2014, doi: 10.1002/jbm.a.34976.

Assessment of the co-effects of NRF2 activator and inhibitor with a novel organ-on-chip model

Manolya Yıldız^{1*}, Devrim PesenOkvur^{1,2}

¹ Department of Molecular Biology and Genetics, Izmir Institute of Technology, Izmir, Türkiye

² Initio Cell BV, Leiden, Netherlands ³ Affiliation 3

* manolyayildiz@iyte.edu.tr

NRF2 (Nuclear-factor-erythroid2-related-factor-2) is a transcription factor essential for the antioxidant system and involved in various diseases, including cancer. In cancer, NRF2 has a dual role as both a tumor suppressor and a proto-oncogene, complicating therapeutic strategies. Our long term goal is to determine the combined effects of NRF2 activators and inhibitors by developing an organ-on-chip (OOC) that allows for 3D co-culture and local application of inhibitor. An OOC system of multiple channels with access to a common continuous interface was designed. OOCs were fabricated using soft lithography and molds fabricated with 3D printing. Local diffusion was examined theoretically by VCell simulations and experimentally using Alexa488 and fluorescence microscopy. MDA-MB-231, MCF7, SKBR3 and MCF10A cells were used to represent different breast cancer types and normal mammary epithelial cells, respectively. Cell viability was determined using Calcein AM/PI as well as Alamar Blue staining followed by fluorescence microscopy.

Local diffusion results from VCell simulations and fluorescence microscopy were in agreement indicating that local inhibitor application is possible in the OOC. Cell seeding densities of 2x10⁶, 1x10⁶, and 5x10⁵ cells/ml were tested. Highest cell viability as determined by Alamar Blue fluorescence intensity measurements was observed for all cell lines at 5x10⁵ cells/ml. Cell viability results were confirmed using Calcein AM/PI staining imaged using fluorescence microscopy and quantified via image analysis. A patent application for the OOC has been filed.

An OOC system that allows local maxima of soluble molecules was optimized for 3D co-culture of cancer and normal cells. Future studies will determine the co-effects of NRF2 inhibitor and activator in the presence and absence of drug.

Acknowledgements: This research project is supported by COST Action CA20121: Bench to bedside transition for pharmacological regulation of NRF2 in noncommunicable diseases and TUBITAK project number 122E069.

ISO 22916-Compliant Organ-on-Chip Block for Fluidic Circuit Integration Using Thermoforming and 3D Printing

Mehmet Oğulcan Güngör^{1,2}, Zeynep Çağlayan Arslan^{1,3}, Meltem Okan Aydın¹, Vildan Şanko¹, Haluk Külâh^{1,3}, Ender Yıldırım^{1,4}

¹ ODTÜ MEMS Center, Ankara, Türkiye

² Middle East Technical University, Department of Micro and Nanotechnology, Ankara, Türkiye

³ Middle East Technical University, Department of Electrical and Electronics Engineering, Ankara, Türkiye

⁴ Middle East Technical University, Department of Mechanical Engineering, Ankara, Türkiye

*Correspondence: yender@metu.edu.tr, ogungor@mems.metu.edu.tr

Standardization is critical for the integration and scalability of microfluidic systems, especially in organ-on-chip (OoC) technologies where component compatibility is essential for system-level development. In this work, we present an ISO 22916:2022-compliant organ-on-chip block designed for seamless integration into modular fluidic platforms. The chip adheres to the 4-port microfluidic building block (MFBB) layout defined in the standard, with a footprint of 30 × 15 mm, ensuring interoperability through standardized port spacing, clamping zones, and exclusion areas.

The device consists of a multi-layered assembly, including two thermoformed Flexdym layers forming the microfluidic channels, separated by a microporous parylene membrane for cell culture and diffusion. These are sandwiched between CNC-milled PMMA layers — a top optical window and a bottom layer with inlets/outlets precisely drilled in a single setup to ensure port alignment. The assembly is enclosed within a rigid SLA 3D-printed housing, which provides mechanical integrity and sealing without adhesives or bonding.

The block is designed for integration into a fluidic circuit board (FCB) matching the dimensions of a standard microtiter plate and including interfaces for electronic valves. This rapid fabrication workflow supports scalable and reusable organ-on-chip applications in modular platforms.

Acknowledgement: This study in the scope of OrChESTRA project has received funding from the European Union's Horizon Europe Programme under grant agreement No 101079473.

A biomimetic human breathing alveolus-on-a-chip model for NP delivery

Melih Engur

Imperial College London, London, United Kingdom

melih.engur20@imperial.ac.uk

Lipid nanoparticles (LNPs) are an emerging platform for pulmonary drug delivery, offering biocompatibility, structural versatility, and the ability to encapsulate a wide range of therapeutic agents. This study presents a microfluidic approach to synthesising LNPs optimised for aerosolised alveolar delivery. Using a flow-focusing microfluidic chip, lipids dissolved in isopropanol are rapidly mixed with an aqueous FITC-Dextran phase under laminar flow. Solvent exchange drives lipid self-assembly through nucleation and growth into uniform nanoparticles. By varying the flow rate ratio (FRR), particle size and monodispersity can be precisely tuned.

The resulting LNPs exhibit size and distribution characteristics suitable for deposition in the distal lung. Encapsulation of FITC-Dextran allows fluorescence-based tracking and delivery studies. To assess physiological performance, synthesised LNPs are applied to a dynamic alveolar-on-a-chip model, which mimics the cyclic stretch and air–liquid interface of the human alveolus. This biomimetic system enables evaluation of LNP aerosol deposition, epithelial uptake, and potential for trans-barrier drug delivery.

Overall, this work establishes a reproducible and scalable LNP formulation strategy for inhalable drug delivery, supported by a physiologically relevant in vitro model for translational screening in pulmonary nanomedicine.

Size-Dependent Levitation of Primary Tissues Across Different Maglev Platforms

Meltem Guzelgungen¹, Zehra Elif Gunyuz², Sezin Cakal¹, Eyup Bilgi¹, Muge Anil-Inevi¹,
Ceyda Oksel-Karakus¹, Huseyin Cumhuri Tekin¹, Devrim Pesen-Okvur², Merve Gursoy³,
Ozden Yalcin-Ozuyisal², Gulistan Mese², Engin Ozcivici^{1*}

¹ İzmir Yüksek Teknoloji Enstitüsü, Biyomühendislik Bölümü, İzmir, Türkiye

² İzmir Yüksek Teknoloji Enstitüsü, Moleküler Biyoloji ve Genetik Bölümü, İzmir, Türkiye

³ İzmir Katip Çelebi Üniversitesi, Tıp Fakültesi, Radyoloji Anabilim Dalı, İzmir, Türkiye

*enginozcivici@iyte.edu.tr

Breast cancer remains the most prevalent cancer among women and a leading cause of cancer-related mortality. While conventional markers like Her2, PR, and ER help identify tumor features, additional biomarkers are necessary due to significant patient variability (1). Magnetic levitation (MagLev) has emerged as an innovative diagnostic technique capable of determining cell density and distinguishing between healthy and dead cells at the single-cell level (2). This research extends to use MagLev technology, which has previously demonstrated effectiveness at the single cell level, to develop a diagnostic tool that uses height as a determining criterion in 3D breast primary tissues. In our study, biopsy samples were obtained from breast tumors with suspected BI-RADS 5 radiological evaluation, with tissue vitality assessed using the PrestoBlue test. We evaluated the levitation responses of the whole biopsy samples (~9.45 mm³), homogeneous sized disks (~1.26 mm³) and homogeneous sub-discs taken from the horizontal plane of the previous disks (~0.05 mm³) across increasing Gd concentrations, with optimal results achieved at 150 mM concentration. Using these optimized parameters, we examined the levitation behaviors of live and dead tissues as well as 24 hours later follow-ups for the identical samples. Our study represents the first example of magnetic levitation application at the tissue level, presenting a cost-effective and easily implementable approach for sensitive oncological assessments in breast cancer patients.

Acknowledgements: The authors gratefully acknowledge the support of IYTE-BAPK (Grant Nos. 2022IYTE-2-0047 and 2022IYTE-2-0030) and TÜBİTAK (Grant No. 22AG032) for funding this project.

References

- [1] Loibl, S., Poortmans, P., Morrow, M., Denkert, C., & Curigliano, G. (2021). Breast cancer. The Lancet, 397(10286), 1750–1769. [https://doi.org/10.1016/S0140-6736\(20\)32381-3](https://doi.org/10.1016/S0140-6736(20)32381-3)
- [2] Anil-Inevi, M., Yaman, S., Yalcin, H. C., & Elçin, A. E. (2020). Assessment of cell cycle and viability of magnetic levitation assembled cellular structures. In 2020 Medical Technologies Congress (TIPTEKNO) (pp. 1–4). IEEE. <https://doi.org/10.1109/TIPTEKNO50054.2020.9299283>

A Microfluidic- Based Chip Platform for *ex vivo* Spermatogenesis of Human iPSCs- Derived Spermatogonial Stem Cells

Merve Gizer¹, Selin Önen¹, İmran Özge Çolak², Meltem Okan¹, Mehmet Oğulcan Güngör¹, Zeynep Çağlayan Arslan^{1,3}, Özgür Doğuş Erol², Fatima Aerts Kaya², Ender Yıldırım^{1,4}, Haluk Külâh^{1,3}, Petek Korkusuz^{1,5}

¹ODTÜ MEMS Center, Ankara, Türkiye

²Department of Stem Cell Sciences, Graduate School of Health Sciences, Hacettepe University, Ankara, Türkiye

³Department of Electrical and Electronics Engineering, Middle East Technical University, Ankara, Türkiye

⁴Department of Mechanical Engineering, Middle East Technical University, Ankara, Türkiye

⁵Department of Histology and Embryology, Faculty of Medicine, Hacettepe University, Ankara, Türkiye

Abstract

Germ cell aplasia results in the absence of sperm in 10-15% of male patients' ejaculate. Human-induced pluripotent stem cells (hiPSCs) show potential as an autologous germ cell source for obtaining haploid germ cells [1]; however, their success rate has been limited to 10-14% in a small number of studies [2]. Furthermore, it is not possible to translate obtaining male germs with a low yield rate to assisted reproduction technologies in a clinic. Thus, there is a need for a platform that will support and enhance human spermatogonial stem cells (hSSCs) and spermatogenesis, while modeling the hSSCs' microenvironment in an *ex vivo* setup [1, 3, 4]. Based on the needs of systems, our group is working on platforms that can mimic the pattern of the physical microenvironment of hSSCs with MEMS approaches. So, our developing platforms could promote the maintenance and increase of the testicular cell populations by providing the pattern of the testis' seminiferous tubule. Our group aims to establish a biomimetic microenvironment for *ex vivo* spermatogenesis of hiPSC-derived hSSCs using platforms developed through 3D printing and MEMS technologies, and to validate the system's functionality and reliability. The successful implementation of this platform could offer a potential solution for individuals facing infertility or limited access to sperm donation in various countries, enabling them to have biological children.

Acknowledgement: These studies were funded by The Scientific and Technological Research Council of Türkiye (#223S711) and The Council of Higher Education (#21836).

References

- [1] Gizer M, Önen S, Erol ÖD, Aerts-Kaya F, Reçber T, Nemutlu E, Korkusuz P. Endocannabinoid system upregulates the enrichment and differentiation of human iPSC- derived spermatogonial stem cells via CB2R agonism. Biol Res. 2025 Mar 12;58(1):13.
- [2] Gizer M, Önen S, Korkusuz P. The Evolutionary Route of in vitro Human Spermatogenesis: What is the Next Destination? Stem Cell Rev Rep. 2024 Aug;20(6):1406-1419.

[3] Önen S, Atik AC, Gizer M, Köse S, Yaman Ö, Külâh H, Korkusuz P. A pumpless monolayer microfluidic device based on mesenchymal stem cell-conditioned medium promotes neonatal mouse in vitro spermatogenesis. *Stem Cell Res Ther.* 2023 May 11;14(1):127.

[4] Önen S, Köse S, Yersal N, Korkusuz P. Mesenchymal stem cells promote spermatogonial stem/progenitor cell pool and spermatogenesis in neonatal mice in vitro. *Sci Rep.* 2022 Jul 7;12(1):11494.

Human Jejunal Enteroids as an Advanced 3D Model for Intestinal ADME Research

Merve Ceylan

Uppsala University, Uppsala, Sweden

merve.ceylan@farmaci.uu.se

In the process of drug development, it is well recognized that the intestine plays a significant role in determining the systemic exposure and pharmacological response of orally-administered drugs. However, the physicochemical and absorption characteristics of the drug candidates are a challenge to predict the exact characterization of oral absorption. Currently used in vitro systems employed to predict the intestinal first-pass effect and oral bioavailability are suboptimal for various reasons. Adult stem-cell derived enteroids capture the different intestinal cell types, but ADME characterization in enteroids has thus far been limited. We therefore aimed to characterize adult stem-cell derived enteroids by global proteomics approach and perform functional drug studies. Proteomic analysis indicated that apical-out, differentiated enteroids exhibit ADME protein profiles better comparable to native tissue than the current golden standard, Caco-2 cells. Protein profiles correlated with detected drug and metabolite levels in enteroids. Global proteomics analysis and drug studies show that enteroids provide a more in vivo-like alternative for establishing in-vitro-in-vivo correlations and they possess an important potential for bridging the gap between the laboratory and the clinic for drug research.

Magnetic Levitation for Toxicity Screening: Distinguishing Cell Responses to DMSO and Paclitaxel

Muge Anil Inevi¹, Oyku Sarigil¹, H. Cumhuri Tekin¹, Gulistan Mese², Engin Ozcivici^{1*}

¹Department of Bioengineering, Izmir Institute of Technology, Izmir, Türkiye

²Department of Molecular Biology and Genetics, Izmir Institute of Technology Izmir, Türkiye

*enginozcivici@iyte.edu.tr

Negative magnetophoresis is a label-free technique that utilizes differences in magnetic susceptibility between cells and their surrounding medium, offering an effective approach for cell detecting and sorting across various biotechnology and bioengineering applications. The technique has been successfully implemented for detecting rare cells and infections by leveraging its ability to separate cells based on their density profiles [1]. Our study aimed to analyze different cellular toxicity mechanisms using a magnetic levitation technology. We employed two mechanistically distinct agents: dimethyl sulfoxide (DMSO), which at high concentrations disrupts plasma membrane integrity via lipid bilayer destabilization [2], and paclitaxel, a microtubule-stabilizing chemotherapeutic that induces apoptosis without immediate membrane compromise [3]. Our findings revealed that DMSO-treated cells exhibited a ~20% decrease in levitation height compared to untreated controls, whereas paclitaxel-exposed cells maintained levitation profiles similar to controls with no significant shift. These results suggest that DMSO's membrane-disruptive effects likely enable paramagnetic agent (gadolinium, Gd³⁺) infiltration to cells, thereby reducing the magnetic susceptibility difference between the intracellular environment and the surrounding media. Conversely, paclitaxel's apoptotic mechanism—characterized by preserved membrane integrity until late-stage cell death—appears to maintain susceptibility contrasts, resulting in stable levitation profiles. This label-free approach offers a promising, cost-effective methodology that can differentiate between membrane-compromising and apoptosis-inducing compounds that can differentiate between membrane-compromising and apoptosis-inducing compounds.

References

- [1] Yaman, S., Anil-Inevi, M., Ozcivici, E., & Tekin, H. C. (2018). Magnetic force-based microfluidic techniques for cellular and tissue bioengineering. *Frontiers in bioengineering and biotechnology*, 6, 192.
- [2] Notman, R., Noro, M., O'Malley, B., & Anwar, J. (2006). Molecular basis for dimethylsulfoxide (DMSO) action on lipid membranes. *Journal of the American Chemical Society*, 128(43), 13982-13983.
- [3] Wang, T. H., Wang, H. S., & Soong, Y. K. (2000). Paclitaxel-induced cell death: where the cell cycle and apoptosis come together. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, 88(11), 2619-2628.

A Novel 3D Culture of Mature Adipocytes Using Magnetic Levitation for Adipose Tissue Modelling

Oyku Sarigil^{1,*}, Muge Anil-Inevi¹, Gulistan Mese², Huseyin C. Tekin¹, Engin Ozcivici¹

¹Izmir Institute of Technology, Department of Bioengineering, Izmir, Türkiye

²Izmir Institute of Technology, Department of Molecular Biology and Genetics, Izmir, Türkiye

*oykusarigil@gmail.com

Adipose tissue engineering has gained significant attention for its potential to develop tissue constructs that replicate native adipose tissue characteristics, enabling studies of physiology and pathophysiology, as well as clinical applications for repairing defects resulting from severe burns or tumor removal [1]. While previous research has primarily focused on creating adipose tissue constructs by utilizing stem cells or preadipocytes to form spheroids, followed by their subsequent differentiation into adipocytes, a significant challenge remains in directly culturing mature adipocytes that fully replicate native tissue properties. This challenge stems from limited cellular interactions and the buoyant characteristics of mature adipocytes, which complicate handling and culture protocols [2,3]. To address these limitations, we present a novel technique combining magnetic levitation (MagLev)-based self-assembly with liquid overlay culture for the 3D culture of mature adipocytes. We evaluated a horizontally deployed MagLev setup for the biofabrication of the adipose tissue model by performing the culture of adipocytes at varying cell concentrations (1000, 2500, 5000 cells/capillary) in a paramagnetic medium (Gadavist, Gd). Under magnetic force influence, adipocytes formed distinctive string-like structures within the MagLev system. The 3D levitated cell structures at the lowest seeding density exhibited an area of $0.086 \pm 0.039 \text{ mm}^2$, which increased by 115% and 247% at cell densities of 2500 and 5000 cells, respectively. Following transfer onto agar gel, the cellular structures developed into more compact and uniform aggregates with an area of $0.026 \pm 0.067 \text{ mm}^2$ after 5 days of culture at the highest cell concentration. Our findings demonstrate that magnetic levitation-based self-assembly effectively cultures mature adipocytes, offering a promising approach for developing advanced adipose tissue models for both research and clinical applications

Acknowledgements: The authors acknowledge the financial support of the Izmir Institute of Technology (research grant 2024IYTE-1-0049-EO), the Scientific and Technological Research Council of Türkiye (grant 2211-A-OS and 22AG032-HCT, EO, OS), and the Council of Higher Education (100/2000 doctoral scholarship-OS).

References

- [1] Choi, J. H., Gimble, J. M., Lee, K., Marra, K. G., Rubin, J. P., Yoo, J. J., ... & Kaplan, D. L. (2010). tissue engineering for soft tissue regeneration. *Tissue Engineering Part B: Reviews*, 16(4), 413-426.
- [2] Liu, J., DeYoung, S. M., Zhang, M., Zhang, M., Cheng, A., & Saltiel, A. R. (2005). Changes in integrin expression during adipocyte differentiation. *Cell metabolism*, 2(3), 165-177.
- [3] Sarigil, O., Anil-Inevi, M., Yilmaz, E., Mese, G., Tekin, H. C., & Ozcivici, E. (2019). Label-free density-based detection of adipocytes of bone marrow origin using magnetic levitation. *Analyst*, 144(9), 2942-2953.

On the effects of 3D Printed Mold Material, Curing Temperature, and Duration on Polydimethylsiloxane (PDMS) Curing Characteristics for Lab-on-a-Chip Applications

Rabia Mercimek ^a, Ünal Akar ^a, Gökmen Tamer Şanlı ^a, Süleyman Çelik^b, Omid Moradia^c,
Morteza Ghorbani^{b,c} * and Ali Koşar ^{b,c} *.

a. Faculty of Engineering and Natural Sciences, Sabanci University, 34956 Tuzla, Istanbul, Türkiye.

b. Sabanci University Nanotechnology Research and Application Center, 34956 Tuzla, Istanbul, Türkiye

c. Center of Excellence for Functional Surfaces and Interfaces for Nano-Diagnostics (EFSUN), Sabanci University, Orhanli, 34956, Tuzla, Istanbul, Türkiye

*corresponding authors: kosara@sabanciuniv.edu, morteza.ghorbani@sabanciuniv.edu

Lab-on-a-chip (LoC) systems have become essential tools in biomedical diagnostics, environmental sensing, and drug delivery, offering advantages like rapid analysis, low reagent use, and portability [1]. Among materials used for microfluidic device fabrication, polydimethylsiloxane (PDMS) stands out due to its optical clarity, elasticity, biocompatibility, and ease of molding [2,3]. Traditionally, SU-8 molds produced via photolithography have been employed to cast PDMS. However, their reliance on cleanroom environments and high fabrication costs has driven the search for more accessible alternatives [6]. In this context, 3D printing has emerged as a promising technique, offering design flexibility, cost efficiency, and faster prototyping [7]. Recent studies have demonstrated the use of 3D printing in fabricating both molds and full microfluidic systems, including organ-on-a-chip devices and cell encapsulation platforms [8–10]. PDMS curing behavior is influenced by three key parameters: temperature, curing agent ratio, and curing time [11–13]. Higher temperatures accelerate cross-linking but may lead to side reactions; increased curing agent concentration enhances stiffness but can reduce elasticity; and longer curing times improve network formation but risk thermal degradation [14,15]. While the chemical aspects of curing have been widely studied, the influence of mold material properties—especially thermal conductivity on PDMS curing kinetics and quality remains largely unexplored, particularly at the microscale. Differences in thermal behavior of mold materials like PLA, PET, resin, and aluminum may lead to variable heat transfer rates, affecting PDMS crosslinking and thus its mechanical and optical characteristics [19].

Acknowledgements: This study was funded by the Turkish Academy of Sciences (TUBA) under the grant: Member Grant and TUBITAK (The Scientific and Technological Research Council of Türkiye) 1004 NANOSIS Programme, Grant Number 20A6012.

References

[1]: F. C. P. Sales, R. M. Ariati, V. T. Noronha, J. E. Ribeiro, *Procedia Structural Integrity* 2022, 37, 383. <https://doi.org/10.1016/j.prostr.2022.01.099>

- [2]: H. Cong, T. Pan, *Advanced Functional Materials* 2008, 18, 1912. <https://doi.org/10.1002/adfm.200701437>
- [3]: I. Namli, S. Seyedmiraç Sarraf, A. Sheibani Aghdam, G. Celebi Torabfam, O. Kutlu, S. Cetinel, M. Ghorbani, A. Koşar, *ACS Applied Materials & Interfaces* 2022, 14, 40688. <https://doi.org/10.1021/acsami.2c12356>
- [4]: C. Ma, Y. Peng, H. Li, W. Chen, *Trends in Pharmacological Sciences* 2021, 42, 119. <https://doi.org/10.1016/j.tips.2020.11.009> Get rights and content
- [5]: G. M. Whitesides, *Nature* 2006, 442, 368. <https://doi.org/10.1038/nature05058>
- [6]: M. de Almeida Monteiro Melo Ferraz, J. B. Nagashima, B. Venzac, S. Le Gac, N. Songsasen, *Scientific Reports* 2020, 10. <https://doi.org/10.1038/s41598-020-57816-y>
- [7]: Carvalho, V., Gonçalves, I., Lage, T., Rodrigues, R. O., Minas, G., Teixeira, S. F. C. F., Moita, A. S., Hori, T., Kaji, H., & Lima, R. A. (2021). In *Sensors* (Vol. 21, Issue 9). <https://doi.org/10.3390/s21093304>
- [8]: Khalid, M. A. U., Kim, Y. S., Ali, M., Lee, B. G., Cho, Y. J., & Choi, K. H. (2020). *Biochemical Engineering Journal*, 155. <https://doi.org/10.1016/j.bej.2019.107469>
- [9]: S. Musafargani, S. Mishra, M. Gulyás, P. Mahalakshmi, G. Archunan, P. Padmanabhan, B. Gulyás, *Journal of Neuroscience Methods* 2020, 331, 108525. <https://doi.org/10.1016/j.jneumeth.2019.108525>
- [10]: K. Alessandri, M. Feyeux, B. Gurchenkov, C. Delgado, A. Trushko, K.-H. Krause, D. Vignjević, P. Nassoy, A. Roux, *Lab on a Chip* 2016, 16, 1593. <https://doi.org/10.1039/C6LC00133E>
- [11]: Y. Konku-Asase, A. Yaya, K. Kan-Dapaah, *Advances in Materials Science and Engineering* 2020, 2020, 1. <https://doi.org/10.1155/2020/6562373>
- [12]: F. Prabowo, A. L. Wing-Keung, H. H. Shen, *Advanced Materials Research* 2015, 1112, 410. <https://doi.org/10.4028/www.scientific.net/AMR.1112.410>
- [13]: Prabowo, F., Wing-Keung, A. L., & Shen, H. H. (2015). *Advanced Materials Research*, 1112. <https://doi.org/10.4028/www.scientific.net/amr.1112.410>
- [14]: Kulkarni, S. D., Manjunatha, B., Chandrasekhar, U., Siddesh, G. K., Lenin, H., & Arul, S. J. (2023). *Advances in Polymer Technology*, 2023. <https://doi.org/10.1155/2023/9964610>
- [15]: Seghir, R., & Arscott, S. (2015). *Sensors and Actuators, A: Physical*, 230. <https://doi.org/10.1016/j.sna.2015.04.011>
- [16]: Ozogul, B., Akar, U., Mercimek, R., Talabazar, F.R., Sarraf, S.S., Aghdam, A.S., Hamedani, A.A., Villanueva, L.G., Grishenkov, D., Amani, E., Elverdi, T., Ghorbani, M. and Koşar, A. (2024), *Adv. NanoBiomed Res.* 2400112. <https://doi.org/10.1002/anbr.202400112>
- [17]: J. He, J.R. Sootsman, S.N. Girard, J.C. Zheng, J. Wen, Y. Zhu, M.G. Kanatzidis, V.P. Dravid, *J. Am. Chem. Soc.*, 132 (25) (2010), 10.1021/ja1010948
- [18]: X. Hou, Y. Chen, L. Lv, W. Dai, Zhao, Z. Wang, L. Fu, C.-T. Lin, N. Jiang, J. Yu *ACS Appl. Nano Mater.*, 2 (1) (2019), 10.1021/acsanm.8b01939
- [19]: D.D.L. Chung, *J. Mater. Eng. Perform.*, 10 (1) (2001), pp. 56-59, 10.1361/105994901770345358

Lab-on-a-chip device (LOC) for determining drug dose response

Ramazan Temizkan^{1*}, Devrim Pesen Okvur^{1,2}

¹Department of Molecular Biology and Genetics, Faculty of Science, Izmir Institute of

Technology, 35430 Izmir, Türkiye 2Initio Cell BV, Leiden, Netherlands

*ramazantemizkanacademic@gmail.com

Effective drug dosing is critical in cancer treatment, balancing therapeutic efficacy with minimal side effects. Traditional 2D cell cultures, widely used for drug testing through serial dilutions, face challenges such as pipetting errors and a lack of physiological relevance. Animal models on the other hand do not faithfully mimic human physiology and present ethical concerns. Lab-on-a-chip (LOC) devices address these limitations by enabling controlled generation of drug concentration gradients and using human samples, but existing models often rely on complex designs (difficulties in manufacturing), require fluid flow (external equipment), and are limited in throughput. The DRCHIP device, fabricated using 3D printing, provides an innovative, flow-free solution for generating drug concentration gradients within a single chip. This user-friendly LOC platform supports simultaneous exposure to varied drug doses, enabling high throughput drug testing. Alexa488 dye served as a model compound to assess drug diffusion profiles through fluorescence microscopy and VCell simulations, both confirming expected diffusion patterns. The performance of DRCHIP was evaluated using MDA-MB-231 breast cancer cells, MCF-10A mammary epithelial cells, HepG2 liver cancer cells, mouse liver tissue and mouse heart tissue exposed to a gradient of paclitaxel. Cell viability assays, including Calcein-AM and Alamar Blue, demonstrated a dose-dependent response, with cell viability decreasing in regions exposed to higher paclitaxel concentrations. The results indicated an IC₅₀ of approximately 65 mg/kg for paclitaxel, suggesting that the DRCHIP can bridge the gap between traditional in vitro and in vivo assays, offering a more predictive model for drug screening. Future applications aim to expand the utility of DRCHIP to test diverse drug types, combinations, and biological samples, paving the way for more personalized and effective preclinical drug evaluation. By addressing the limitations of existing systems, the DRCHIP device represents a promising advancement in drug discovery, providing a scalable and physiologically relevant method to study dose-response relationships and improve the translation of in vitro findings to in vivo contexts.

Comparative Investigation of PDMS Surface Modification by Nitrogen and Argon Plasma in Atmospheric Conditions

Safiye Betül Bulut^{1*}, Fahriye Arslan¹, Gizem Kaleli Can¹

¹Department of Biomedical Engineering, İzmir Democracy University, İzmir 35140, Türkiye

*betulbulut001@gmail.com

Polydimethylsiloxane (PDMS) is widely used in microfluidic systems due to its elastomeric structure, biocompatibility, ease of fabrication, and excellent optical transparency [1]. However, its inherently hydrophobic surface limits fluid flow and surface interactions within microchannels, adversely affecting the overall device performance and reliability. To overcome this major limitation, plasma-based surface modification techniques have been extensively employed to impart hydrophilic properties to PDMS surfaces and enhance their wettability [2].

In this study, the effects of argon and nitrogen plasmas on PDMS surfaces were systematically investigated using a glow discharge plasma system operating under atmospheric pressure conditions. Surface wettability changes were evaluated through static contact angle measurements before and after plasma treatment. Initially, the PDMS surface exhibited a contact angle of $93^\circ \pm 2^\circ$. After 90 seconds of nitrogen plasma treatment, the contact angle decreased significantly to $29^\circ \pm 1^\circ$, while argon plasma treatment under identical conditions reduced it further to $24^\circ \pm 1^\circ$. Furthermore, reducing the electrode-to-surface distance during argon plasma exposure resulted in an additional decrease of the contact angle to $20^\circ \pm 1^\circ$, indicating enhanced surface activation. However, extending the plasma exposure duration to 10 minutes or employing sequential plasma pulses did not lead to further improvements in hydrophilicity. Electrode positioning was also identified as a critical operational parameter influencing plasma efficiency and uniformity.

Argon plasma, due to its chemically inert nature, does not chemically modify the surface [3]. Instead, physical effects such as ion-induced sputtering and surface roughening dominate the modification mechanism, leading to temporary increases in hydrophilicity. As no chemical functional groups are introduced, the structural integrity and chemical stability of the PDMS surface are preserved, making argon plasma treatment particularly suitable for applications requiring high biocompatibility and minimal surface damage [4,5].

In contrast, nitrogen plasma induces both physical and chemical modifications. Active nitrogen species can react with surface methyl groups, introducing amino ($-\text{NH}_2$) and nitrile ($-\text{C}\equiv\text{N}$) functional groups, thereby achieving more permanent hydrophilic properties and enabling further chemical functionalization [6]. Nevertheless, prolonged nitrogen plasma exposure may result in surface degradation, including the formation of cracks or mechanical weakening, emphasizing the need for careful optimization of treatment parameters [7].

In conclusion, while argon plasma provides a low-damage, purely physical activation of PDMS surfaces, nitrogen plasma offers chemical functionalization and long-lasting hydrophilicity. Therefore, selecting the appropriate plasma gas is crucial for tailoring PDMS surface properties to meet specific application requirements in microfluidics, biosensors, and biomedical devices.

References

- [1] Lai, R. H., Chen, Y. A., Chou, C. Y., Huang, H. Y., Mongkonkan, W., Chiu, C. A., ... & Chou, H. H. (2025). Toughening self-healable and recyclable PDMS supramolecular elastomers through an end-capping agent and a metallic crosslinker. *Journal of Materials Chemistry A*.
- [2] Stanton, M. M., Ducker, R. E., MacDonald, J. C., Lambert, C. R., & McGimpsey, W. G. (2012). Super-hydrophobic, highly adhesive, polydimethylsiloxane (PDMS) surfaces. *Journal of colloid and interface science*, 367(1), 502-508.
- [3] Juárez-Moreno, J. A., Brito-Argáez, L. G., Ávila-Ortega, A., Oliva, A. I., Avilés, F., & Cauich-Rodríguez, J. V. (2017). Effect of the type of plasma on the polydimethylsiloxane/collagen composites adhesive properties. *International Journal of Adhesion and Adhesives*, 77, 85-95.
- [4] Morent, R., De Geyter, N., Leys, C., Gengembre, L., & Payen, E. (2007). Study of the ageing behaviour of polymer films treated with a dielectric barrier discharge in air, helium and argon at medium pressure. *Surface and Coatings Technology*, 201(18), 7847-7854.
- [5] Nitschke, M., & Meichsner, J. (1997). Low-pressure plasma polymer modification from the FTIR point of view. *Journal of applied polymer science*, 65(2), 381-390.
- [6] Gomathi, N., Mishra, I., Varma, S., & Neogi, S. (2015). Surface modification of poly (dimethylsiloxane) through oxygen and nitrogen plasma treatment to improve its characteristics towards biomedical applications. *Surface Topography: Metrology and Properties*, 3(3), 035005.
- [7] Wang, M., Tian, Y., Tong, X., Lou, T., Xu, Z., Huang, X., ... & Xu, L. (2025). PDMS membranes with bioinspired mineral coatings for the enhancement of microbial adhesion and nitrogen removal performance in MABR system. *Applied Surface Science*, 685, 161998.

MEMS-based microfluidic cell therapy platforms for fertility preservation in prepubertal boys

Selin Önen¹, Merve Gizer¹, Ali Can Atik^{1,2}, Zeynep Çağlayan Arslan^{1,2}, Meltem Okan¹, Ege Tongün³, İmran Özge Çolak⁴, Ender Yıldırım^{1,5}, Haluk Külâh^{1,2}, Petek Korkusuz^{1,6}

¹ODTÜ MEMS Center, Ankara, Türkiye

²Electrical and Electronics Engineering Department, Middle East Technical University, Ankara, Türkiye

³Department of Bioengineering, Graduate School of Science and Engineering, Hacettepe University, Ankara, Türkiye

⁴Department of Stem Cell Sciences, Graduate School of Health Sciences, Hacettepe University, Ankara, Türkiye

⁵Department of Mechanical Engineering, Middle East Technical University, Ankara, Türkiye

⁶Department of Histology and Embryology, Faculty of Medicine, Hacettepe University, Ankara, Türkiye

Advances in pediatric oncology have significantly increased survival rates; however, gonadotoxic therapies such as chemotherapy and radiotherapy cause permanent infertility in male childhood cancer survivors¹. For prepubertal patients in whom spermatogenesis and the production of mature/functional sperm have not yet commenced, spermatogonial stem cell (SSC)-based fertility preservation represents a promising therapeutic avenue².

We focus on developing novel microfluidic culture systems that recapitulate the native testicular microenvironment^{3,4} and support SSC survival, proliferation, and differentiation. Specifically, we investigate the combined use of biomimetic microfluidic platforms and mesenchymal stem cell (MSC)-derived secretome to enhance in vitro spermatogenesis (IVS)^{5,6}. By integrating organ-on-chip technologies with cell-based therapies, we aim to create translational platforms for future clinical use.

The ultimate goal is to bridge experimental models with clinical translation to ensure fertility restoration options for boys at risk of infertility due to early-life cancer treatment. The high-tech platforms developed using the data obtained from this model have the potential to be introduced into clinical practice as a patentable therapeutic product (medical devices) aimed at preserving fertility in male childhood cancer patients. Beyond cancer-related infertility, the resulting device is expected to pave the way for advanced technological solutions addressing other causes of infertility and contribute to the development of personalized cellular therapy approaches. The Scientific and Technological Research Council of Türkiye funded the studies (#22AG008, #218S421). **Keywords:** Male Infertility, Microfluidic Systems, Spermatogonial Stem Cells, in vitro Spermatogenesis, Mesenchymal Stem Cells

References

- [1] Wasilewski-Masker, K., *et al.* Male infertility in long-term survivors of pediatric cancer: a report from the childhood cancer survivor study. *J Cancer Surviv* **8**, 437-447 (2014).
- [2] Gizer, M., Önen, S. & Korkusuz, P. The Evolutionary Route of in vitro Human Spermatogenesis: What is the Next Destination? *Stem Cell Rev Rep* **20**, 1406-1419 (2024).

- [3] Gong, D., *et al.* Are Sertoli cells a kind of mesenchymal stem cells? *Am J Transl Res* **9**, 1067-1074 (2017).
- [4] Köse, S., Yersal, N., Önen, S. & Korkusuz, P. Comparison of Hematopoietic and Spermatogonial Stem Cell Niches from the Regenerative Medicine Aspect. *Adv Exp Med Biol* **1107**, 15-40 (2018).
- [5] Önen, S., *et al.* A pumpless monolayer microfluidic device based on mesenchymal stem cell-conditioned medium promotes neonatal mouse in vitro spermatogenesis. *Stem Cell Res Ther* **14**, 127 (2023).
- [6] Önen, S., Gizer, M., Çolak, İ. & Korkusuz, P. Bioengineering Approaches for Male Infertility: From Microenvironmental Regeneration to in vitro Fertilization. *Adv Exp Med Biol* **1479**, 59-72 (2025).

Magnetic Levitation-Assisted Fluorescent Detection of Proteins Using Superparamagnetic Iron Oxide Nanoparticles

Seren Kecili¹, Hatice Ahsen Özcan¹, Zeliha Soran Erdem², H. Cumhuri Tekin^{1,3*}

¹Department of Bioengineering, Izmir Institute of Technology, Izmir, Türkiye

²Department of Engineering Sciences, Abdullah Gul University, Kayseri, Türkiye

³ODTÜ MEMS Center, Ankara, Türkiye

*cumhurtekin@iyte.edu.tr

Magnetic levitation (MagLev) is a label-free technique that levitates diamagnetic objects, such as cells and proteins, within a paramagnetic solution offering diverse applications across various fields [1]. MagLev enabled ~70% efficient sorting of rare cancer cells from white blood cells in a gadolinium-based solution. [2]. Using the same solution, mouse Immunoglobulin G (IgG) was detected in serum via MagLev-based sandwich immunoassay with a >10 ng/mL detection limit. [3]. Due to their high magnetic susceptibility and protein affinity, Superparamagnetic Iron Oxide Nanoparticles (SPIONs) may enable faster and more effective protein detection with MagLev than other paramagnetic solutions [4]. In this study, selective IgG detection was achieved using SPIONs in MagLev without assay surfaces. The platform consists of two magnets having dimension of 5 mm (W)×2 mm (T)×50 mm (L), mirrors, a 1 mm×1 mm microcapillary channel, and 3D-printed supports. A detection solution containing fluorescent-tagged anti-mouse IgG and SPIONs was prepared, followed by the addition of mouse IgG and loading into the microcapillary. Fluorescent images were captured over time to analyze intensity changes. In controls, fluorescence decreased over time, while it remained relatively low in samples with 10 µg/mL IgG. These results demonstrate that our MagLev-based method allows surface-free, selective IgG detection, offering strong potential for diagnostics.

Keywords: magnetic levitation, SPION, protein detection, Immunoglobulin G, homogenous assay

Acknowledgements: The authors acknowledge the financial support from The Scientific and Technological Research Council of Türkiye (grant number 22AG032).

References

- [1] Durmus, N. G., Tekin, H. C., Guven, S., Sridhar, K., Arslan Yildiz, A., Calibasi, G., & Demirci, U. (2015). Magnetic levitation of single cells. *Proceedings of the National Academy of Sciences*, 112(28), E3661-E3668.
- [2] Kecili, S., Yilmaz, E., Ozcelik, O. S., Anil-Inevi, M., Gunyuz, Z. E., Yalcin-Ozuysal, O., ... & Tekin, H. C. (2023). µDACS platform: a hybrid microfluidic platform using magnetic levitation technique and integrating magnetic, gravitational, and drag forces for density-based rare cancer cell sorting. *Biosensors and Bioelectronics: X*, 15, 100392.
- [3] Yaman, S., & Tekin, H. C. (2020). Magnetic susceptibility-based protein detection using magnetic levitation. *Analytical Chemistry*, 92(18), 12556-12563.
- [4] Ashkarran, A. A., Suslick, K. S., & Mahmoudi, M. (2020). Magnetically levitated plasma proteins. *Analytical Chemistry*, 92(2), 1663-1668.

Development of a Corneal Permeability Model for the Evaluation of Antibody-Based Therapeutics

Smyrna Ergönül^{1,2}, Ali Eren Evranos^{1,2}, Sinan Güven^{1,2,3*}, Sibel Kalyoncu^{1,2*}

¹ İzmir Biomedicine and Genome Center, 35340, İzmir, Türkiye

² İzmir International Biomedicine and Genome Institute, Dokuz Eylül University, 35340,
İzmir, Türkiye

³ Department of Medical Biology and Genetics, Faculty of Medicine, Dokuz Eylül University,
35340, İzmir, Türkiye

*sinan.guven@ibg.edu.tr *sibel.kalyoncu@ibg.edu.tr

Topical treatment of corneal diseases requires effective drug delivery strategies that ensure sufficient tissue permeability and bioavailability [1][2]. This study aims to develop an ex vivo microfluidic chip system serving as corneal tissue permeation model. Antibody-based therapeutics are evaluated, and their corneal tissue penetration kinetics are investigated towards topical eye drops using this model. The microfluidic chip is designed to mimic corneal transport dynamics, providing a controlled environment for real-time monitoring of penetration of therapeutics. Using this simulated corneal barrier system, transfer of anti-VEGF antibody is studied as model, and corneal penetration efficiency is analyzed through ELISA. By exploring different formulation strategies, including excipient selection and stabilization techniques, this study seeks to improve the efficiency of ophthalmic antibody-based therapeutics and drug delivery. The findings are expected to contribute to the development of novel drug delivery approaches for corneal diseases, offering a promising alternative to conventional treatments.

Acknowledgements: This work was funded by the Scientific and Technological Research Council of Türkiye (TÜBİTAK) BİDEB 2210A National Graduate Scholarship Program. Authors thank Gaye Su Yiğit assisting in microfluidic model.

References

- [1] Prausnitz, M. R., & Noonan, J. S. (1998). Permeability of cornea, sclera, and conjunctiva: A literature analysis for drug delivery to the eye. *Journal of Pharmaceutical Sciences*, 87(12), 1479–1488. <https://doi.org/10.1021/js9802594>
- [2] Toffoletto, N., Chauhan, A., Alvarez-Lorenzo, C., Saramago, B., & Serro, A. P. (2021b). Asymmetry in Drug Permeability through the Cornea. *Pharmaceutics*, 13(5), 694. <https://doi.org/10.3390/pharmaceutics13050694>

**BRIDGING DISCIPLINES, INSPIRING
GENERATIONS:
A TRIBUTE
TO
BANA ONARAL**

Prof. Dr. Banu Onaral, also known in Turkish as "Banu Hoca" (1949–2024) was a distinguished Turkish-American biomedical engineer, educator, and visionary academic leader whose work significantly advanced the fields of biomedical signal processing and translational research. She earned her B.Sc. and M.Sc. degrees in Electrical Engineering from Boğaziçi University and completed her Ph.D. in Biomedical Engineering at the University of Pennsylvania. Then, Dr. Onaral held the H.H. Sun Professorship in Biomedical Engineering and Electrical Engineering at Drexel University, where she joined the faculty in 1981 and later founded the School of Biomedical Engineering, Science, and Health Systems in 1997, serving as its inaugural director and dean.



A trailblazer in innovation-driven research, she led numerous programs funded by the National Science Foundation (NSF), National Institutes of Health (NIH), Defense Advanced Research Projects Agency (DARPA) and the Department of Homeland Security (DHS), and was instrumental in establishing Drexel's Translational Research in Biomedical Technologies program, securing the Coulter Translational Research Partnership to support medical technology commercialization. She served as President of the IEEE Engineering in Medicine and Biology Society, was elected Fellow Institute of Electrical and Electronics Engineers (IEEE), the American Association for the Advancement of Science (AAAS), and was a Founding Fellow of the American Institute for Medical and Biological Engineering (AIMBE), and contributed to national advisory boards, including the NSF Engineering Advisory Committee. Dr. Onaral, who is a true lover of Türkiye and Atatürk, came from a lineage of innovation and entrepreneurship, her grandfather, Nuri Demirağ, was a prominent industrialist and aviation pioneer in Turkish history. She was renowned not only for her internationally pioneering education and exemplary scientific contributions in the field of biomedical engineering, but also for the inspiration and valuable support she offered to a wide range of international initiatives, particularly to young academics and entrepreneurs.

This commemorative session assembles colleagues to chart the sweep of Prof. Onaral's scholarship, leadership, and humanitarian vision. The panel will discuss her technical advances and the philosophies that powered her mentorship; and showcase of translational success stories to demonstrate her lasting societal imprint. By celebrating a visionary who connected and empowered so many, we aspire not only to honor her legacy, but also to spark the next generation of bold, human-centered innovation she so passionately championed.

A Legacy that Lives On: Commemorating Professor Banu Onaral

Professor Banu Onaral's extraordinary life serves as a powerful testament to the transformative power of vision, dedication, and a deep commitment to serving humanity. Her embodiment of the ethos "Science serves humanity, transcends boundaries and thrives in world cultures" continues to inspire us. The seeds of collaboration and innovation she so diligently planted through the Global Innovation Partnership and her mentorship will continue to blossom, yielding fruit for generations to come. Her legacy is not just a memory; it is a living force that continues to shape our thinking, guide our actions, and inspire our aspirations. It lives on through the countless individuals she mentored, the collaborations she fostered, and the unwavering commitment to scientific excellence she instilled in all who had the privilege of knowing her. As we reflect on her remarkable contributions, let us recommit ourselves to the principles she so passionately championed. Let us embrace collaboration, let us break down boundaries, and let us always remember that the ultimate purpose of our scientific endeavors is to serve

humanity. Professor Banu Onaral's legacy will undoubtedly continue to shine brightly through everyone she touched, guiding us towards a future where science truly knows no borders and serves the betterment of all.

From Jamie Mak

BEST POSTER AWARDS

This year, two graduate students won the best poster awards

Basar Dogan from Department of Bioengineering, Ege University, received the best poster award with the study titled as “**Lung Cancer Metastasis-on-a-Chip: A Preclinical Model for Studying EMT and Tumor Progression**”

Göktürk Cinel from Department of Bioengineering, Izmir Institute of Technology, received the best poster award with the study titled as “**Computational Design and Additive Manufacturing of a Microfluidic System for the Controlled Iron Oxide Nanoparticle Synthesis**”