



HORIZON WIDERA Twinning

Grant agreement n°: 101079473

Call topic identifier: HORIZON-WIDERA-2021-ACCESS-03-01

Organ-on-a-Chip Focused Strategic Partnership (OrChESTRA)

Deliverable D4.3

Report on collaboration activities - 1

Work Package 4

Engagement and strategic networking activities

Document type	: R - Document, report
Version	: 1.0
Date of issue	: M24 (31.08.2024)
Dissemination level	: PU - Public
Lead beneficiary	: 2 - TU/e
Partners contribution	: Prepared by TU/e with input from all partners

This project has received funding from the European Union's Horizon Europe Programme HORIZON-WIDERA action under grant agreement No 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.

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Table of Contents

1	INTRODUCTION	3
2	COMMON ACTIVITIES AND RESEARCH COLLABORATION	3
2.1	Regular Project Meetings	3
2.2	Visits Between Partners	4
2.2.1	Visits of EU Partners to ODTÜ MEMS	4
2.2.2	Visits by ODTÜ MEMS Researchers to EU Partners	5
2.3	Other Fostering Events	7
2.4	Joint Proposal Submissions	9
2.5	Joint Scientific Publications	10
2.6	Joint Attendance at Conferences	12
3	NEW COLLABORATIONS.....	17
4	FUTURE PLANS AND CONCLUSION	19
5	APPENDICES	20
	Appendix I: The programme of the 2nd BioMEMS and Microfluidic Technologies Workshop	20
	Appendix II: The programme of the 3rd BioMEMS and Microfluidic Technologies Workshop	21
	Appendix III: The programme of the International Workshop on Emerging Organ-on-Chip Technologies	22

1 INTRODUCTION

Effective collaboration activities form the backbone of successful research partnerships. This report provides a detailed overview of the ongoing collaborative efforts undertaken by the consortium members of the OrChESTRA Project. These activities encompass a broad spectrum, from regular project meetings that ensure all members are aligned with current research directives to dynamic research visits that foster direct knowledge transfer and technical skill development. Such interactions are crucial for maintaining synchronized efforts across borders and disciplines and ensuring that all participants are working towards common research goals with a unified strategy.

The consortium's commitment to fostering strong collaborative ties is manifested through the active pursuit of joint project proposals and co-authored publications in prestigious journals, as well as participation in key conference proceedings such as μ TAS and EUROoCS. These scholarly activities are complemented by a proactive approach to identifying and seizing funding opportunities presented by Horizon Europe and other R&D programs, ensuring a continuous exchange of ideas and resources.

Furthermore, acknowledging the important link between academia and industry, ODTÜ MEMS has initiated efforts to establish new industrial collaborations. By mapping out potential industrial partners within proximity to METU and across the broader Organ-on-Chip (OoC) value chain, the project aims to forge connections that extend from module manufacturers to end users in pharmaceuticals and biotechnology. This effort involves personalised introductions to identified industrial players, participation in relevant conferences, and the organization of outreach events aimed at aligning academic research with industry needs.

Through these varied activities, the consortium seeks to improve scientific research and development and to create a sustainable model of innovation that bridges academic and commercial sectors. The collaborative efforts outlined here play a key role in supporting the consortium's mission to make progress in microfluidics, biosensors, and organ-on-chip technologies.

2 COMMON ACTIVITIES AND RESEARCH COLLABORATION

Common activities are crucial for fostering successful research partnerships within the OrChESTRA Project, as they bring together diverse expertise and resources to enhance innovation and increase funding opportunities. By integrating diverse skill sets and perspectives, consortium members effectively tackle complex challenges and generate novel insights. Collaborative efforts also expand networking and dissemination opportunities, strengthen capacity building, and amplify the impact of scientific discoveries. This synergy fosters a creative and supportive environment, enabling research partnerships to achieve greater success and contribute significantly to scientific and technological progress.

2.1 Regular Project Meetings

Throughout the first 24 months of the OrChESTRA Project, more than 25 consortium and 30 technical meetings have been conducted online, pivotal in driving the initiative forward. These meetings served as critical platforms for discussing the project's operation, reviewing ongoing activities, and planning future tasks. Essential topics such as potential collaborations, upcoming calls for research funding, and strategic research planning were routinely addressed, ensuring all consortium members were aligned and informed.

The gatherings were instrumental in fostering a cohesive environment where members could openly share updates, challenges, and insights, thereby enhancing the collaborative spirit of the project. Discussions often centered around optimizing project workflows, identifying opportunities for joint proposals, and enhancing the quality and impact of research outputs. These meetings also provided a platform for brainstorming and detailed planning of joint publications, which are crucial for disseminating research findings to a broader scientific community.

2.2 Visits Between Partners

Visits between consortium partners are a fundamental component of the OrChESTRA Project's strategy to deepen collaboration and foster a cohesive research community. These exchanges, both to and from ODTÜ MEMS, provide invaluable opportunities for direct, face-to-face interaction among researchers, which is critical for sharing intricate knowledge and technical skills. Visits to the cleanroom facilities of other consortium members are particularly beneficial, as they demonstrate various applications and methodologies effectively. Moreover, these visits serve as pivotal moments for brainstorming for future collaborative activities. The enriched understanding and personal connections developed through these visits not only enhance the productivity of current projects but also lay the groundwork for future collaborations. As such, these partner visits are instrumental in creating a dynamic and interconnected research network, driving forward the project's goals with enhanced synergy and efficiency.

2.2.1 Visits of EU Partners to ODTÜ MEMS

Over the course of the OrChESTRA project, consortium partners TU/e, UFR, and IMEC have made several visits to the ODTÜ MEMS Center at different times. Each visit included not only seminars presented by the visiting researchers but also workshops focused on exploring potential collaborative topics. These activities proved highly beneficial, enhancing the exchange of knowledge and fostering a collaborative spirit among the partners. The workshops and seminars held during these visits enabled participants to further explore shared research interests and innovative approaches together. This hands-on engagement has significantly enriched the project, strengthening existing partnerships and sparking ideas for new collaborative endeavours. The following workshops were organised during these visits:

- **“Potential collaboration opportunities workshop”** was organised together with **UFR** and **ODTÜ MEMS** on 13 September 2023.
Participants: Can Dinçer (UFR), Ender Yıldırım (ODTÜ MEMS), Ezgi Salmanlı (ODTÜ MEMS), Gamze Kozanoğlu (ODTÜ MEMS), Haluk Külâh (ODTÜ MEMS), Pınar Burat (ODTÜ MEMS), Selin Önen (ODTÜ MEMS), Tuğba Tezcan (Gazi University), Uğur Tamer (ODTÜ MEMS),
- **“Potential collaboration opportunities workshop”** was organised together with **TU/e** and **ODTÜ MEMS** on 21 September 2023.
Participants: Hans Wyss (TU/e), Uğur Tamer (ODTÜ MEMS), Altuğ Özçelikkale (METU), Barbaros Çetin (Bilkent University), Ender Yıldırım (ODTÜ MEMS), Gamze Kozanoğlu (ODTÜ MEMS), Haluk Külâh (ODTÜ MEMS), Petek Korkusuz (ODTÜ MEMS), Pınar Burat (ODTÜ MEMS)
- **“Potential collaboration opportunities workshop”** was organised together with **IMEC** and **ODTÜ MEMS** on 31 January 2024.
Participants: Wolfgang Eberle (IMEC), Atilla Hakan Özdemir (ODTÜ MEMS), Ender Yıldırım (ODTÜ MEMS), Gamze Kozanoğlu (ODTÜ MEMS), Gizem Özdemir (ODTÜ MEMS), Haluk Külâh (ODTÜ MEMS), Pınar Burat (ODTÜ MEMS).

- **“Workshop on Developing Potential Proposal”** was organised together with **TU/e** and **ODTÜ MEMS** on 11 July 2024.
Participants: Hans Wyss (TU/e), Ender Yıldırım (ODTÜ MEMS), Özlem Yeşil Çeliktas (ODTÜ MEMS)

2.2.2 Visits by ODTÜ MEMS Researchers to EU Partners

Throughout the OrChESTRA project, representatives from ODTÜ MEMS have made several visits to TU/e, UFR, and IMEC. These visits also included tours of their state-of-the-art cleanroom facilities. These cleanroom visits were particularly valuable, allowing ODTÜ MEMS representatives to observe cutting-edge practices and technologies first-hand, which fostered a deeper understanding of the advanced methodologies applied in different research environments. Such interactions have significantly enhanced the exchange of knowledge and strengthened the collaborative spirit among the consortium members. The seminars complemented these visits by providing a platform for ODTÜ MEMS to engage in-depth with mutual research interests and explore innovative approaches together. This active participation has greatly benefited the project, reinforcing existing relationships and inspiring ideas for future collaborative projects.

Cleanroom visits:

- Researchers from ODTÜ MEMS, Evren Erdil and Evrim Özçakır, visited UFR’s cleanroom facilities, from July 24 to 26, 2023.
- Researchers from ODTÜ MEMS, Evren Erdil, Ali Can Atik, and Macit Araz, visited TU/e’s cleanroom facilities from September 4 to 6, 2023
- Researchers from ODTÜ MEMS, Evren Erdil, Meltem Okan Aydın, and Zeynep Çağlayan Arslan, visited IMEC’s cleanroom facilities from June 3 to 5, 2024.

During the cleanroom visits, the focus extended beyond just lab-management and cleanroom technology; the sessions also included in-depth discussions on potential future collaborations and joint research activities. These conversations aimed to explore synergistic opportunities that could leverage the unique capabilities of each institution, enhancing their collective research outputs.

Visit and Seminar by Prof. Dr. Petek Korkusuz at Eindhoven University of Technology (TU/e):

As part of the ongoing collaboration efforts under the OrChESTRA project, Prof. Dr. Petek Korkusuz from ODTÜ MEMS visited TU/e on May 28, 2024. The primary purpose of this visit was to discuss potential collaboration opportunities with TU/e researchers, focusing on enhancing joint research initiatives and exploring new avenues for academic partnership.

During her visit, Prof. Korkusuz also delivered a seminar entitled "Niche Based Cellular Therapeutic Platforms". The seminar provided valuable insights into the latest advancements in cellular therapy, highlighting innovative therapeutic strategies that could be developed through collaborative research efforts. This event not only facilitated knowledge exchange but also served to strengthen the research ties between ODTÜ MEMS and TU/e, further aligning both institutions towards common scientific goals and objectives.

- “Potential collaboration opportunities workshop” was organised together with TU/e and ODTÜ MEMS on 28 May 2024.

Participants: Petek Korkusuz (ODTÜ MEMS), Hans Wyss (TU/e), Burcu Gumuscu (TU/e), Oscar Stassen (TU/e), Jaap den Toonder (TU/e).



ODTÜ MEMS' Visit to IMEC

On June 4-5, 2024, representatives from ODTÜ MEMS visited IMEC. The purposes of the visit were to:

- Establish new contacts between ODTÜ MEMS and IMEC scientists and management,
- Gain insights into the setup and operations of IMEC's facilities, particularly the fabrication environment and laboratories,
- Participate in topic sessions on fabrication operations, quality, safety, ICT, and training,
- Engage in discussions on organ-on-chip, life science technologies, microfluidics, and MEMS,
- Explore non-technical topics such as collaborations, venturing, innovation, and intellectual property.

During the visit, meetings were held with key figures at IMEC, including Wolfgang Eberle, a senior executive in public funding and R&D policies and programs for health technologies; Dries Braeken, R&D manager in life sciences; Chengxun Liu, program manager in life sciences; Alexandru Andrei, program manager in MEMS technologies; Bastien Duckert, project manager in life sciences; and Paru Deshpande, vice president of R&D for life sciences technologies.

These discussions showcased ongoing high-impact projects in the life sciences department and provided insights into IMEC's organizational structure. The visit also included a tour of IMEC's facilities and cleanrooms, where detailed information on their operations was shared.

At the conclusion of the meetings, discussions on potential short-term and long-term project and collaboration partnerships were fruitful, leading to the identification of joint project topics. It was agreed to organize follow-up meetings in the coming period to finalize the details of these joint project topics.



2.3 Other Fostering Events

In the scope of the OrChESTRA Project, several strategic events have been designed, which also facilitated collaboration among consortium partners. These initiatives are critical for enhancing synergy and driving collective research objectives within the field of BioMEMS and microfluidics. The key events include:

- BioMEMS and Microfluidic Technologies Workshops
- Career Development Programme

BioMEMS and Microfluidic Technologies Workshops

As part of a series that ODTÜ MEMS regularly organises, the second and third “International BioMEMS and Microfluidic Technologies Workshops” were successfully hosted by the ODTÜ MEMS Centre as part of the OrChESTRA Project. These events were organised in collaboration with OrChESTRA project partners, showcasing the strength of our cooperative network.

• 2nd BioMEMS and Microfluidic Technologies Workshop

The 2nd International BioMEMS and Microfluidic Technologies Workshop was successfully organised on March 28 and 29, 2023, in an engaging online format. Spanning two days, the workshop brought together renowned experts from across Europe, including project partners TU/e, IMEC, and UFR, offering a truly enlightening experience for all attendees. The event underscored the collaborative spirit of the OrChESTRA partners, providing a platform for sharing cutting-edge research and advancements in the field of BioMEMS and microfluidics. The programme of the workshop is given in Appendix I.

OrChESTRA
Organ-on-a-Chip Focused Strategic Partnership

- HORIZON-WIDERA-2021-ACCESS-03 (September 2022)
- Aims to **promote new opportunities** via development of **productive and sustainable links** among the partners for **higher levels of excellence** in the field of organ-on-a-chip platforms, **with a major focus on enhancing the range of competences of the coordinator, ODTÜ MEMS.**
- Objectives
 - Raising the research profile of ODTÜ MEMS
 - Enhancing institutional capacity of ODTÜ MEMS
 - Excellence in the wider impact for the innovation ecosystem and beyond
 - Integration into European networks of excellence

Prof. Dr. Haluk Külah BioMEMS Research Group

• 3rd BioMEMS and Microfluidic Technologies Workshop

The 3rd BioMEMS and Microfluidic Technologies Workshop was held in a hybrid format at the ODTÜ MEMS Center on June 10 and 11, 2024. The workshop began with an open-doors event on June 10th, which provided an overview of the latest advancements and applications in the field, followed by a series of scientific sessions. On June 11th, a special session focused on medical device regulation (MDR) and in-vitro device regulation (IVDR), addressing current standards and future trends in regulatory practices. Additionally, the event provided students the opportunity to showcase their research through poster presentations. This platform allowed them to highlight their innovative work and engage with industry experts and academics, fostering a dynamic exchange of ideas and potential collaborations.



Over the course of two days, our hybrid international workshop attracted more than 100 researchers and experts, demonstrating its significance and impact within the academic and professional communities. The discussions and presentations not only fostered learning and collaboration but also set the stage for ongoing engagements and future initiatives. The event also received media coverage, further amplifying its reach and impact. Details on the coverage can be found at <https://www.aa.com.tr/tr/bilim-teknoloji/turk-arastirmacilarin-liderliginde-deney-hayvanlarinin-yerini-alacak-cip-gelistirilecek/3295239>. The fourth edition of this workshop is eagerly anticipated to be hosted next year, with plans to further expand its scope and impact.

The programme of the workshop is given in Appendix II.

Career Development Programme

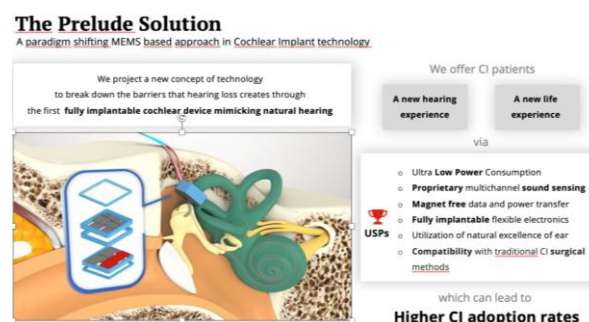
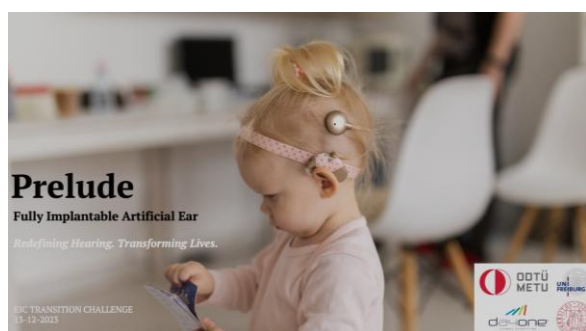
Another key activity fostering collaboration among OrChESTRA partners is the Career Development Programme. Launched on April 14, 2023, this initiative is specifically designed to empower Early-Stage Researchers (ESRs) with the necessary skills and competencies to excel in their research fields and prepare them for future career opportunities. Supported by a robust network of dedicated project partners, the programme serves as a platform for enhancing inter-partner cooperation and mentorship. This structured approach ensures that ESRs receive guided and substantial support, enhancing both their personal and professional development. Through such initiatives, the OrChESTRA project strengthens collaborative ties and builds a cohesive educational environment across the consortium.

2.4 Joint Proposal Submissions

Since the beginning of the OrChESTRA project, consortium partners have actively engaged in identifying and leveraging funding opportunities, particularly within Horizon Europe. These collaborative efforts have been structured around a series of strategic meetings and workshops, dedicated to discussing potential calls and aligning our joint research interests. These sessions have provided a platform for partners to synergize their expertise for proposals that address the complex challenges and innovative opportunities within the microfluidics and BioMEMS fields. The following proposal applications were submitted:

- **Prelude**

In 2023, a significant collaborative effort led to the submission of a project proposal titled "Prelude" under the EIC Transition Challenge, submitted by researchers from ODTÜ MEMS and UFR. This initiative represents a strategic attempt by the consortium partners to secure essential funding aimed at advancing their research capabilities. This proposal underscores the commitment of ODTÜ MEMS and UFR to fostering innovation and advancing the frontiers of scientific research within the OrChESTRA project framework.



- **ACCORDO**

ACCORDO proposal was submitted under the HORIZON-WIDERA-2023-ACCESS-07 call. This initiative, led by ODTÜ MEMS in collaboration with INESC MN (Portugal), aims to accelerate the collaboration and coordination between Organ-on-Chip ecosystems in Türkiye and Portugal. The proposal includes a consortium of 21 partners, representing a diverse and robust Organ-on-Chip cluster. Partners from the OrChESTRA project, TU/e, IMEC, and UFR, have been included as advisory board members, leveraging their expertise and insight to enhance the project's strategic direction.

- **MFMET II - Establishing Metrology Standards in Microfluidic Devices II**

As part of the collaborative initiatives within the ACCORDO project, ODTÜ MEMS was invited to join the 'MFMET II - Establishing Metrology Standards in Microfluidic Devices II' consortium, coordinated by IPQ (Portugal). This proposal, aimed at advancing metrology standards in the field of microfluidics, was submitted to the EURAMET call and successfully passed the first evaluation phase.

2.5 Joint Scientific Publications

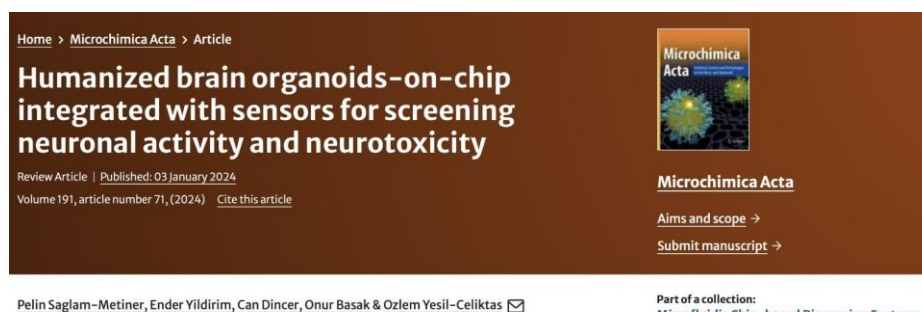
As part of the collaborative efforts under WP3 “Development of organ-on-a-chip platform (intestinal drug absorption)”, several joint scientific publications have been produced, demonstrating the fruitful outcomes of inter-institutional cooperation. These publications reflect the concerted efforts of consortium partners who have integrated their unique expertise and research capabilities to address pivotal challenges within the Organ-on-a-Chip field. The successful production of these scholarly articles underscores the project's commitment to advancing scientific knowledge and fostering a culture of collaboration. Each publication not only contributes to the body of global scientific literature but also showcases the innovative spirit and intellectual rigor of the OrChESTRA project team. This collective effort enhances the visibility of the research conducted, amplifies the impact of the findings, and solidifies the network of collaboration that OrChESTRA aims to build and extend.

Articles in Renowned Journals

The following article have been published in Microchimica Acta (Web of Science, Q1). The review article discusses how scientists use bioengineering techniques to improve brain organoids, which are lab-grown structures that resemble parts of the brain. They explain how these improvements can be used for medical research. The article also provides a detailed look at devices that combine brain organoids with sensors, which could potentially lead to artificial intelligence and biocomputing. The article was also covered on digital media¹, highlighting OrChESTRA and the efforts on creating organ-on-chip platforms equipped with sensors to improve efficacy of drug screening studies.

¹<https://www.psychreg.org/advanced-sensor-integrated-brain-organoid-on-chip-platforms-enhance-neurotoxicity-screening-finds-new-study/>

- 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. *Mikrochimica Acta*, 191(1), 71. [doi:10.1007/s00604-023-06165-4](https://doi.org/10.1007/s00604-023-06165-4)



In addition, the following article is under review and awaiting publication in Communications Biology (Web of Science, Q1) from Nature Portfolio. This forthcoming article discusses the challenges of measuring glutamate levels in organ-on-a-chip platforms. We propose using electrochemical sensors for in situ glutamate detection to improve accuracy. For the particular use case of organ-on-chips for modeling neuroinflammation, we envisage that by not only integration of sensors, but also integration of actuators, such as drug delivery systems, the precision of organ-on-a-chip platforms could be enhanced.

- Pelin Saglam-Metiner, Sena Yanasik, Yusuf Caglar Odabasi, Jennifer Modamio, Moritz Negwer, Cigir Biray-Avci, Ali Erturk, Ayse Guler, Ozlem Yesil-Celiktas. "CU patient-on-a-chip: orchestration of mast cells and cerebral organoids in neuroinflammation", *Communications Biology*, *under review*.

Poster Presentations in European Organ-on-Chip Society (EUROoCS) Annual Meeting, Milano, Italy: The EUROoCS 2024 Conference was held in Milan from July 3-5, 2024. This event, organized by the European Organ-on-Chip Society, serves as a cornerstone for advancing the fields of organ-on-chip and microphysiological systems. It provides a vital platform for engaging with leading global experts and peers, uniting innovators to highlight the growing importance of this technology in biomedical research. At this conference, four posters prepared collaboratively by project partners were accepted and presented, showcasing the collective research achievements and ongoing efforts within the consortium:

- Salmanli, E., Atik, A. C., Arslan, Z. Ç., Okan, M., Wyss, H. M., Dinçer, C., Eberle, W., Tekin, H. C., Külah, H., & Yıldırım, E. (2024, July 3-5). **Effect of coating formulations on differentiation of Caco-2 cells on Gut-on-a-Chip platform:** The presentation focused on the effect of coating formulations on differentiation of Caco-2 cells on a gut-on-a-chip platform, developed as part of the OrChESTRA Project. This research specifically targets the development of a gut-on-a-chip system, analyzing outputs from cellular, genomics, and proteomics perspectives. The work was enriched by collaboration with authors from various research facilities, bringing together diverse perspectives and expertise. The positive feedback we received underscores the value of these interdisciplinary efforts.
- Çağlayan Arslan, Z., Atik, A. C., Okan, M., Wyss, H. M., Dinçer, C., Eberle, W., Tekin, H. C., Külah, H., & Yıldırım, E. (2024, July 3-5). **Development of MEMS Fabricated Parylene Membrane for Organ-on-Chip Applications:** The presentation detailed the development of MEMS-manufactured parylene membranes for use in the gut-on-chip platform being developed as a part of OrChESTRA project, highlighting their superior biocompatibility, transparency, and precise pore patterning. These

membranes, with a pore diameter of 10 μm and a porosity of 35%, play a crucial role in providing the necessary cellular environments, facilitating cell imaging, and enabling precise control of mechanical parameters. These innovations are instrumental in advancing tissue engineering, drug discovery, and the exploration of organ physiology and disease mechanisms.

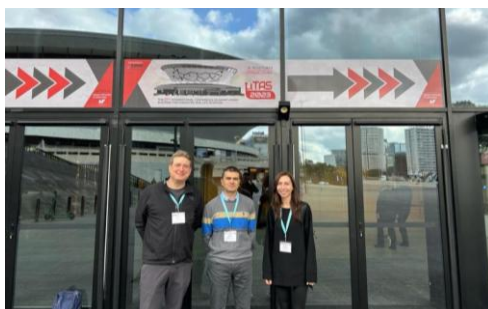
- **Atik, A. C., Arslan, Z. Ç., Okan, M., Wyss, H. M., Dinçer, C., Eberle, W., Tekin, H. C., Külâh, H., & Yıldırım, E. (2024, July 3-5). *Modelling of villi differentiation in a gut-on-a-chip platform integrated with interdigitated TEER sensor*:** This study presented the numerical modelling of transepithelial electrical resistance (TEER) sensor with interdigitated electrodes (IDEs) for real-time non-invasive monitoring of the integrity and villi-like differentiation of intestinal epithelial cell monolayer within a gut-on-a-chip organ platform. The focus of the study is to propose an electrode configuration to achieve a more uniform current density field, thereby ensuring consistent sensitivity across the entire cell monolayer to prevent the misestimation of the electrical impedance.
- **Okan, M., Çağlayan Arslan, Z., Atik, A. C., Salmanlı, E., Wyss, H. M., Dinçer, C., Eberle, W., Tekin, H. C., Külâh, H., & Yıldırım, E. (n.d.) Levodopa and dopamine imprinted polymeric nanoparticles as a recognition layer in gut-on-a-chip applications targeting Parkinson's Disease:** Dr. Okan's poster presentation, highlighted the ongoing research efforts in developing molecularly imprinted polymers (MIP) for detection of levodopa, a drug for treating Parkinson's disease, and dopamine in the gut that. Initial findings on the characteristics of the developed MIPs and their potential use as recognition layer in an electrochemical sensing scheme were presented.

2.6 Joint Attendance at Conferences

Joint attendance at conferences by project partners is a strategic component of our collaborative efforts within the OrChESTRA project. These gatherings provide a vital platform for consortium members to showcase their research findings, engage with the wider scientific community, and foster relationships that are crucial for the advancement of our collective objectives. By presenting unified fronts at these significant events, partners not only increase the visibility of the project but also enhance networking opportunities that can lead to further collaborations and innovations. This section details the various conferences attended by OrChESTRA partners, highlighting the impact and outcomes of their joint participation.

- **μ TAS 2023 Conference, Katowice, Poland**

Researchers from ODTÜ MEMS, Dr. Ender Yıldırım and Ayşen Gümüştâş, along with Dr. Hans Wyss from TU/e, attended the 27th International Conference on Miniaturized Systems for Chemistry and Life Sciences (μ TAS 2023) conference in Katowice, Poland, from October 15-19, 2023. During the meeting, the partners had the chance to build a network with prominent researchers not only in the organ-on-chip field but also more broadly in the wider fields of microfluidics and miniaturized analytical systems.



- **EUROoCS Conference 2024, Milan, Italy**

At EurOOCS Conference 2024 (July 3-July 5, in Milan, Italy), organized by the European Organ-on-chip Society, several OrChESTRA researchers, Dr. Haluk Külâh, Dr. Ender Yıldırım, Dr. Wolfgang Eberle, Dr. Meltem Okan Aydın, Dr. Ezgi Salmanlı, Zeynep Çağlayan Arslan, and Ali Can Atik, attended and presented their works as four posters. The details of the poster presentations are stated above in Section 2.5. This congress provided a valuable platform to exchange knowledge, discuss advancements, and explore potential collaborations, significantly contributing to our shared goal of advancing organ-on-a-chip technologies. Dr. Yıldırım also presented the organ-on-a-chip initiative in Türkiye enabled by the OrChESTRA project, in the special “National OoC Initiatives” session along with the initiatives in Italy, Finland, France, United Kingdom, Portugal, and the Netherlands.



- **COST Action CA21135 IMMUNO-model, Microphysiological Systems Training School, 20-22 September 2023, Izmir, Türkiye**

This training program organized at Izmir Institute of Technology and funded by European Cooperation in Science and Technology (COST) aimed training the researchers about microphysiological systems. Participants were taught about these systems through lectures and hands-on activities and will also have the chance to design their own. OrChESTRA researchers Dr. H. Cumhur Tekin and Dr. Ender Yıldırım, delivered talks on “3D Cell Culture in Microfluidic Devices by Leveraging Magnetic Techniques” and “Fabrication of microfluidic devices as microphysiological systems”, respectively.



- **Workshop on Biosensors and Bioanalytical Microtechniques in Environmental, Food, and Clinical Analysis (BBMEC) 2024, Izmir, Türkiye**

This workshop provided an invaluable platform for discussing cutting-edge developments in biosensor technology. Both Dr. Can Dinçer (UFR) and Dr. Meltem Okan (ODTÜ MEMS) participated in this event, representing the OrChESTRA project. Dr. Okan's talk on "Development of an Integratable Electrochemical Dopamine Sensor for Assessing Levodopa Efficacy in Gut-on-a-Chip Models" emphasized the project's relevance and innovation. The event facilitated meaningful exchanges with other partners, reinforcing our collaborative efforts to push the boundaries of biosensing and organ-on-a-chip systems.

- **International Workshop on Emerging Organ-on-Chip Technologies, Eindhoven, the Netherlands**

As part of the OrChESTRA Project, an international workshop on Emerging Organ-on-Chip Technologies was held in Eindhoven, the Netherlands. This one-day workshop, conducted on June 27, 2024, was designed to provide a comprehensive overview of the current state and future prospects of microfluidics and microfabrication technologies, with a particular emphasis on their biological applications in Organ-on-Chip technologies. The program featured a line-up of talks by leading experts in microfluidics and Lab-on-a-Chip technologies, offering insights into their pioneering research and achievements. Additionally, the workshop included both in-person and online presentations by junior researchers, enriching the event with a wide range of perspectives and ongoing studies in the field.



Researchers from ODTÜ MEMS Centre also participated in this workshop and they contributed to the event by delivering the following presentations, also showcasing studies conducted under Work Package 3 "Development of organ-on-a-chip platform (intestinal drug absorption)" of the OrChESTRA Project:

"Modelling of Villi Differentiation in a Gut-on-a-Chip Platform Integrated with Interdigitated TEER Sensor"
by **Ali Can Atik, ODTÜ MEMS Center:** We present the numerical modelling of transepithelial electrical resistance (TEER) sensor with interdigitated electrodes (IDEs) for real-time monitoring of the integrity and villi-like differentiation of intestinal epithelial cell monolayer within a microfluidic organ platform. The electrode configuration and placements should ensure a uniform current density field, thereby a uniform sensitivity, across the entire cell layer as possible to prevent misestimation of impedance when cells aggregate or disintegrate in a high-sensitivity area. The finite element method (FEM) analysis has been performed to evaluate the electrical impedance along the cell barrier by utilizing COMSOL. Multiphysics® v5.6. In accordance with the reciprocity theorem, the normalized sensitivity is calculated, where the current

density distribution from the applied current in the excitation electrodes and from the identical current in the readout electrodes are superimposed over entire cell layer of the cross-sectional area. The IDE structure achieves improved sensitivity without altering the electrode-occupied area, thus allowing for microscopic visualization. Electrical simulations were conducted with varying villi heights (25-175 μm) while maintaining the input TEER at 750 Ωcm^2 . The modelled impedance spectra predicts that villi formation increases capacitance due to the larger surface area of the villus epithelium, as an indicator of villi differentiation.

“Magnetic Levitation for 3D Cell Culture in Miniaturized Platforms” by H. Cumhur Tekin, Izmir Institute of Technology and ODTÜ MEMS Center: Traditional two-dimensional (2D) cell cultures, which consist of monolayers of cells, are commonly used in in vitro studies but fall short in replicating essential cell-cell and cell-extracellular matrix (ECM) interactions. In contrast, three-dimensional (3D) cell cultures more accurately simulate the cellular microenvironment, fostering realistic cell-cell and cell-ECM interactions. Moreover, 3D cultures ensure the uniform distribution of nutrients, gases, and metabolites, which is crucial for proper cellular function. Magnetic forces have emerged as powerful tools for cellular organization, facilitating the formation of spheroids and cell sheets. In 3D cell culture, positive and negative magnetophoresis enable the aggregation of cells within a magnetic field generated by permanent magnets, resulting in the formation of cellular clusters. The principle of magnetic levitation, based on negative magnetophoresis, allows for precise cell manipulation by leveraging differences in cell densities. This enables cells to be levitated at points where the magnetic force balances the buoyancy force. This talk delved into the innovative use of magnetic levitation techniques in cell culture studies, highlighting their applications and benefits for advancing cellular research without the use of labels.

“Capillary pressure barriers for spatial confinement in organ-on-a-chip devices and their fabrication” by Ender Yıldırım, Middle East Technical University and ODTÜ MEMS Center: Organ-on-a-chip systems have been investigated for more than a decade and are becoming more pronounced especially as potential alternatives to animal testing in drug development. Fundamentally the devices are composed of microfluidic channels to provide perfusion of the culture medium and compartment in which the cells can be cultured. The compartment can either be separated from the perfusion channel via a membrane so that the cells can be directly cultured on the membrane, or via pillars so that the cells suspended in a matrix are confined in the chamber on one side of the pillar. In the second arrangement, the pillars act as capillary pressure barriers preventing overflow of the cell-laden matrix through the perfusion channel. In this work, numerical and experimental investigation of different capillary pressure barriers and their fabrication are presented.

“Synthetic Receptors: Harnessing Molecularly Imprinted Polymers for Advanced Sensing Platforms” by Meltem Okan Aydın, ODTÜ MEMS Center: Molecularly imprinted polymers (MIPs) represent a class of synthetic receptors tailored with high specificity and selectivity towards target molecules. These polymers are fabricated through a template-assisted polymerization process, where the template molecule's shape and functional groups dictate the polymer's structure and recognition capabilities. The inherent stability and cost-effectiveness of MIPs make them attractive candidates for various sensing platforms. The employment of MIPs is explored across cutting-edge sensor technologies, including surface plasmon resonance (SPR), quartz crystal microbalance (QCM), microcantilever mass sensors, and organ-on-a-chip platforms. In SPR, MIPs are utilized as recognition elements integrated into the sensor's surface, enabling real-time detection of target analytes based on changes in refractive index. Similarly, in QCM systems, MIP-coated electrodes enhance the sensitivity and specificity of mass detection through frequency shifts caused by analyte binding. Microcantilever mass sensors leverage MIPs to detect minute mass changes, offering high sensitivity suitable

for biomolecular detection. Furthermore, the integration of MIPs into organ-on-a-chip platforms facilitates precise molecular recognition within complex biological environments, mimicking physiological conditions for drug testing and disease modelling. Here, the versatile and promising applications of MIPs in advancing sensor technologies are highlighted, underscoring their pivotal role in enhancing detection capabilities across diverse analytical and biomedical fields.

“A Fully Implantable Artificial Ear” by Haluk Külah, Middle East Technical University and ODTÜ MEMS

Center: Today, congenital or acquired hearing loss affects around 5% of the world population and presents a significant impact on people’s social, emotional, and economic wellbeing. Sensorineural impairment is caused by irreversible damage to cochlear hair cells, rendering them non-functional/missing. It can be restored using cochlear implants (Cis), which are used to bypass the damaged hair cells and directly stimulate the auditory nerve by means of a cochlear electrode to repair hearing in people with severe-to-profound sensorineural hearing loss. However, conventional CIs have major drawbacks. In this presentation, a new generation CI system eliminating these drawbacks with ultra-low-power, fully implantable approach will be presented. The presented system is the first fully implantable CI mimicking the natural hearing mechanism. As the most unique feature, the proposed CI benefits eardrum or ossicular vibrations through frequency-selective piezoelectric cantilevers to generate the signals for neural stimulation, mimicking the natural hearing mechanism, and extracting energy from this vibration. This approach eliminates most of the power-hungry electronics, such as microphones and active bandpass filters, while keeping the healthy portions of the middle ear functional. This feature creates a paradigm shift in the operation principle of the conventional CIs.

“The promise of engineered multicellular systems-on-chip” by Ozlem Yesil Celiktas, Ege University, Izmir, ODTÜ MEMS Center:

Engineered multicellular systems-on-chip represent a transformative advancement in bioengineering, merging the principles of microfabrication and cellular biology to create intricate, functional biological models on microchips. These systems emulate the complex interactions and behaviours of living tissues and organs, providing a high-fidelity platform for biological research, drug discovery, and personalized medicine. By incorporating multiple cell types and mimicking the three-dimensional architecture and microenvironment of native tissues, on-chip platforms offer unprecedented insights into cellular dynamics and tissue physiology. In this talk, a number of use cases developed in our Biomimetic Microsystems Research group will be presented, highlighting the possibilities to accelerate preclinical testing by improving the predictive accuracy of disease models and reducing the reliance on animal testing. Despite the challenges in standardization, scalability, and integration with existing biomedical workflows, the advancements in materials science, microfluidics, and stem cell technology continue to drive the rapid progress of this field. As the research arena evolves, engineered multicellular systems-on-chip are poised to become an indispensable tool in both fundamental research and clinical applications, heralding a new era of precision medicine and innovative therapeutic strategies (Acknowledgement: Financial support provided by TUBITAK under grant number 123M406).

These presentations highlighted the significant contributions and ongoing research projects of ODTÜ MEMS in the field of Organ-on-Chip technologies, further enriching the discourse and collaborative potential of the workshop.

The programme of the workshop is given in Appendix III.

3 NEW COLLABORATIONS

In an effort to expand its role within the region, ODTÜ MEMS has actively pursued new collaborative opportunities as a key component of its strategic development. By engaging extensively with the regional and international ecosystem, ODTÜ MEMS has conducted over 75 one-to-one meetings with regional business, public, and research organizations, along with three additional meetings with international entities. These interactions have been instrumental in establishing and fostering new partnerships, essential for broadening the project's research and development reach. This proactive approach enhances ODTÜ MEMS's network and significantly contributes to the project's overarching goal of advancing Organ-on-Chip technologies through collaborative innovation.

To provide a detailed breakdown of these meetings:

- **Business Organizations:** 44 meetings were conducted with various business entities, aiming to foster industry collaborations and commercial applications of research.
- **Public Organizations:** 13 meetings with public sector agencies helped align the research objectives with public health goals and regulatory frameworks.
- **Research Institutions:** 16 meetings with other research organizations facilitated the sharing of scientific knowledge and the exploration of joint research initiatives.
- **International Organizations:** 4 meetings with international organizations were aimed at enhancing global research collaborations and tapping into wider networks and resources.

These efforts underscore the dynamic and multi-faceted approach of ODTÜ MEMS towards building a robust and innovative research ecosystem, positioning it as a hub in the region.

Other significant collaborations:

Collaboration with AZAR Innovations (<https://azar-innovations.com>): As part of the new collaborations developed under the OrChESTRA project, ODTÜ MEMS Centre has successfully partnered with AZAR Innovations to conduct educational workshops on Organ on a Chip technologies. These masterclasses, led jointly by experts from AZAR Innovations and ODTÜ MEMS, provided an in-depth exploration of the latest advancements and applications in the field. The sessions were highly successful, marked by active participation and positive feedback from attendees who benefited from the hands-on learning experience and the expertise shared by the facilitators.

The success of these events has led to a strategic decision between ODTÜ MEMS and AZAR Innovations to continue collaborating on similar activities in the future. Both parties are committed to fostering a long-term partnership that will include regular educational and training events at the ODTÜ MEMS Centre. This ongoing collaboration aims to enhance the educational offerings in microfluidic and organ-on-chip technologies and to establish ODTÜ MEMS as a leading hub for research and innovation in this evolving field.



Collaboration with Microfluidic ChipShop

(<https://www.microfluidic-chipshop.com>): ODTÜ MEMS had the opportunity to connect with Microfluidic ChipShop at the microfluidics masterclass. They provided us with microfluidic chips for the hands-on training of masterclass participants and offered online support and advice. Currently, we are collaborating with Microfluidic ChipShop to seek advice on microfluidic designs and to access their pre-made solutions for lab-on-chip applications. We are also exploring the possibility of partnering with Microfluidic ChipShop as an industrial partner in a consortium to apply for research funding.



Collaboration with Portuguese Institute for Quality Services, IPQ: A significant development in ODTÜ MEMS's collaborative network is the new partnership with IPQ, which was fostered through the ACCORDO project. This collaboration originated from the ACCORDO project and was further strengthened when IPQ invited ODTÜ MEMS to join a prestigious consortium including 19 partners from Portugal, France, Denmark, Germany, the Netherlands, UK, Japan, Czech Republic, and Türkiye acting in microfluidics and metrology for a project proposal under the EURAMET call (European Partnership on Metrology, Metrology Partnership - Normative Call 2024). The partnership has facilitated mutual engagement in discussions and planning of joint research activities that focus on establishing metrology standards in microfluidic devices. This collaborative effort not only strengthens the scientific and technological exchange between the two institutions but also expands ODTÜ MEMS's influence in international research networks.

Collaboration with INESC MN, Portugal: The collaboration with INESC MN was facilitated through the joint efforts of both INESC MN and ODTÜ MEMS in shaping the ACCORDO project, which aimed place-based development of organ-on-a-chip ecosystems in Lisbon, Portugal and Ankara, Türkiye. These efforts also enabled national organ-on-a-chip initiatives in Portugal and Türkiye coordinated by Dr. Vania Silverio from INESC MN and Dr. Ender Yıldırım from ODTÜ MEMS, respectively. Currently, the teams at Portugal and Türkiye are pursuing opportunities to grow the ecosystem by receiving the support of the industrial partners and public authorities. We also look forward to national and international collaboration opportunities to grow the network and enhance the impact of the initiatives.

Collaboration with Biomimetic Microsystems Laboratory at Ege University, Ankara, Türkiye: Within the scope of the ACCORDO project, a partnership has been established with the principal investigator of Ege University Biomimetic Microsystems Lab, Dr. Özlem Yeşil Çeliktaş. Thanks to this partnership, 2 joint articles have been prepared, one of which is under review. In addition, a joint project application has been submitted to The Scientific and Technological Research Council of Türkiye (TÜBİTAK) for the development of a sensor-integrated artificial lung. In order to sustain the partnership, the Dr. Çeliktaş been assigned to the ODTÜ MEMS. The collaborative efforts are ongoing to develop new joint project proposals.

Collaboration with MedTech Europe: In the scope of the 3rd BioMEMS and Microfluidic Technologies Workshop, ODTÜ MEMS have organised a special session of the Panel on Implementation of MDR and IVDR, considering the demand from national medical device and analytical device manufacturers, and the researchers. For this purpose, we reached out MedTech Europe. Jana Russo (Moravcova), Manager Medical Devices, kindly accepted our invitation and delivered a presentation at the 3rd BioMEMS and Microfluidic Technologies Workshop online. She also contributed to panel discussions by providing insight, particularly on fostering innovation in the field of medical devices.

4 FUTURE PLANS AND CONCLUSION

ODTÜ MEMS is dedicated to advancing its mission through a robust set of strategic initiatives designed to foster educational growth, enhance research capabilities, and deepen local and international collaborative ties. One of the key components of ODTÜ MEMS's strategy is the organization of a Summer School, aimed at bringing together students and experts from partner institutions to engage in a dynamic educational exchange. This event will not only feature lectures and practical sessions led by renowned speakers from our network but will also open doors for students from these institutions to participate, thereby enriching the learning environment with diverse perspectives and expertise.

In addition to educational activities, ODTÜ MEMS plans to enhance professional development through staff exchange programs. These exchanges will facilitate hands-on experience and foster collaboration on joint projects, further strengthening our research ties across borders. Following the completion of the first Career Development Programme, we have initiated the second phase to further support the professional growth of ODTÜ MEMS's researchers. This ongoing effort is designed to equip researchers at ODTÜ MEMS with advanced skills and knowledge, enabling them to lead and innovate in their respective fields.

Moreover, as part of Work Package 3, a joint paper on the 'integration of MEMS and microphysiological systems' is being prepared, demonstrating the project's contribution to cutting-edge research. Additionally, due to time constraints, a proposal could not be prepared for the last EIC Pathfinder Open in 2024. Preparation is now underway to engage with the next call, anticipated in 2025.

OrChESTRA partners will maintain an active presence in the scientific community by organizing and participating in various workshops, conferences, and events. These gatherings are essential for showcasing research progress, exchanging cutting-edge ideas, and exploring new avenues for collaboration. Through these multifaceted activities, ODTÜ MEMS aims to sustain its momentum in scientific excellence and innovation, ensuring a lasting impact on the global research landscape.

5 APPENDICES

Appendix I: The Programme of the 2nd BioMEMS and Microfluidic Technologies Workshop



ODTÜ MEMS Center
Workshop on BioMEMS and Microfluidic
Technologies
28-29 March 2023



	TR time	CET	28 March 2023, Tuesday
Session 1	09:30-10:00	08:30-09:00	Haluk Kùlah, Middle East Technical University
	10:00-10:30	09:00-09:30	Roland Zengerle, University of Freiburg <i>Microfluidic platforms and commercialization strategies at IMTEK and Hahn-Schickard</i>
	10:30-11:00	09:30-10:00	Hans Wyss, Eindhoven University of Technology <i>Using microfluidics as a toolbox for studying the behavior of soft materials</i>
	11:00-11:30	10:00-10:30	Paul Vulto, MIMETAS B.V. <i>Organ-on-a-Chip technology for comprehensive disease modelling and drug development</i>
	11:30-13:00	10:30-12:00	Lunch Break
Session 2	13:00-13:30	12:00-12:30	Vania Silverio, INESC MN <i>Accelerating Innovation of Microfluidic Technology – the Role of Standardization</i>
	13:30-14:00	12:30-13:00	Özlem Yeşil Çeliktaş, Ege University <i>Have organ-on-chips contributed to breaking Eroom's law?</i>
	14:00-14:30	13:00-13:30	Wolfgang Eberle, IMEC <i>Scalable microfabrication for high-content organ-on-a-chip applications</i>
	29 March 2023, Wednesday		
Session 3	09:30-10:00	08:30-09:00	Jaap den Toonder, Eindhoven University of Technology <i>Microfluidics technology for Organ-on-a-Chip</i>
	10:00-10:30	09:00-09:30	Ali Koşar, Sabancı University <i>Micro Scale Hydrodynamic Cavitation and its Biomedical Applications</i>
	10:30-11:00	09:30-10:00	Can Dinçer, University of Freiburg <i>CRISPR-powered multiplexed biosensors for point-of-care management of infectious diseases</i>
	11:00-11:30	10:00-10:30	Ender Yıldırım, Middle East Technical University <i>Ultrasonic assisted methods for scalable manufacturing of lab-on-a-chip</i>
	11:30-14:30	10:30-13:30	Lunch Break
Session 4	14:30-15:00	13:30-14:00	Devrim Pesen Okvur, Izmir Institute of Technology <i>Organ-on-Chip Disease Models</i>
	15:00-15:30	14:00-14:30	Hüseyin Cumhuri Tekin, Izmir Institute of Technology <i>Magnetic-based 3D cell cultures in miniaturized systems</i>
	15:30-16:00	14:30-15:00	Petek Korkusuz, Hacettepe University <i>In vitro Spermatogenesis Platforms</i>
	16:00-16:30	15:00-15:30	Petra Ditttrich, ETH Zurich <i>Single-cell analysis in microfluidic chamber</i>
	16:30-17:00	15:30-16:00	Discussions and Closing Remarks

Appendix II: The Programme of the 3rd BioMEMS and Microfluidic Technologies Workshop



ODTÜ MEMS Center Open Doors Day &
Workshop on BioMEMS and Microfluidic Technologies (Hybrid)
10-11 June 2024



	TR-time	CET	10 June 2024, Monday
Open Doors	9:00-13:00	8:00-12:00	ODTÜ MEMS Open Doors Event Introduction of ODTÜ MEMS – Presentation Site visit
	13:00-13:30	12:00-12:30	Coffee break
Session 1	13:30-14:00	12:30-13:00	Opening Remarks
	14:00-14:30	13:00-13:30	Zeynep Altıntaş, <i>Kiel University</i> Hydrogel Microneedle Array for Multiplexed Assessment and Intelligent Therapy of Chronic Wounds
	14:30-15:00	13:30-14:00	Jerome Charmet, <i>Haute Ecole Arc (HES-SO), University of Bern</i> Going with the flow - fluid processing for biosensing
	15:00-15:30	14:00-14:30	Coffee Break
Session 2	15:30-16:00	14:30-15:00	Arda Deniz Yalçınkaya, <i>Boğaziçi University</i> Microfluidics Integrated Flexible Metamaterial Sensors
	16:00-16:30	15:00-15:30	Martinus Gijls, <i>EPFL</i> Studying the roundworm <i>Caenorhabditis elegans</i> using microfluidic chips
	16:30-17:00	15:30-16:00	Vania Silverio, <i>INESC MN</i> Development of a standardized 96-well platform for investigating cell cultures in static and dynamic flow environments
11 June 2024, Tuesday			
Special Session	10:00-12:00	9:00-11:00	Panel: Implementation of MDR and IVDR Jana Russo, <i>MedTech Europe, Manager Medical Devices</i> Fikret Küçükdeveci, <i>Kardiner Medical Systems Inc.</i> İlke Eren Karaca, <i>Health Industry Employers' Association of Turkey</i> Osman Dursun, <i>Medloft Consultancy Doo</i>
	12:00-13:00	11:00-12:00	Student Poster Presentations
	13:00-14:00	12:00-13:00	Lunch Break
Session 3	14:00-14:30	13:00-13:30	Elsa Batista, <i>Portuguese Institute for Quality, IPQ</i> Metrological traceability and accuracy of organ-on-chip related measurement quantities
	14:30-15:00	13:30-14:00	Levent Beker, <i>Koç University</i> Wireless skin-interfaced devices for preventive medicine
	15:00-15:30	14:00-14:30	Mahmut Kamil Aslan, <i>ETH Zurich, ODTÜ MEMS Center</i> Microfluidic Platforms for Single-Cell Manipulation and Analysis
	15:30-16:00	14:30-15:00	Hatice Ceylan Koydemir, <i>Texas A&M University</i> Engineering portable imaging and sensing technologies to advance human health
	16:00-16:30	15:00-15:30	Best Poster Award Ceremony & Closing Remarks

Appendix III: The Programme of the International Workshop on Emerging Organ-on-Chip Technologies

OrChESTRA



OrChESTRA



Timetable June 27 - Morning

9:00		Arrival and coffee	
9:20		Welcome & Opening remarks	
9:30	IS	Jaap M.J. den Toonder Microsystems, TU/e	"Microfluidic technology enables lumen-based Organ-on-a-Chip"
10:00	Short talks 1	Guillem Monso	"Brain-on-chip for AI Computing"
		Oksana Savchak	"Exploring digital microfluidics platforms for biomedical research"
		Ali Can Atik	"Modelling of Villi Differentiation in a Gut-on-a-Chip Platform Integrated with Interdigitated TEER Sensor"
10:30	IS	H. Cumhur Tekin Izmir Institute of Technology	"Magnetic Levitation for 3D Cell Culture in Miniaturized Platforms"
11:00		Coffee	
11:30	IS	Ender Yildirim METU MEMS, Ankara, Turkey	"Capillary pressure barriers for spatial confinement in organ-on-a-chip devices and their fabrication"
12:00	Short talks 2	Ana Carina Baeta Manjua	"Designing an electromagnetic microchip for cardiovascular studies"
		Gülden Akçay	"Brain-on-Chip: A New Approach for Studying Brain Microenvironment"
12:20		Lunch	

Timetable June 27 - Afternoon

13:30	IS	Burcu Gumuscu Biomedical Engineering, TU/e	"Exploring the Potential of Microfluidics for Automating Cell Experiments"
14:00	Short talks 3	Seren Kedili	"Magnetic levitation-based formation and dynamic rotation of 3D clusters of microspheres and HUVEC cells in a microfluidic chip"
		Mohammad JouyBar	"Tubular microchannels influence endothelial orientation: modeling cancer metastasis on a chip"
		Meltem Okan Aydin	"Synthetic Receptors: Harnessing Molecularly Imprinted Polymers for Advanced Sensing Platforms"
14:30	IS	Andries van der Meer Twente University, Enschede	"Organs-on-Chips: From Platform Technology to Applications in Drug Development"
15:00		Coffee	
15:30	IS	Haluk Kûlah METU MEMS, Ankara, Turkey	"A Fully Implantable Artificial Ear"
16:00	Short talks 4	Jia-Jun Yeh	"In-line biocompatible micropumping chip module for a standardized and modular organ-on-chip platform"
		Pan Zuo	"3D-Oxygen Gradient Chip for Cancer Cell Migration Research"
16:20	IS	Ozlem Yesil Celiktas Ege University, Izmir, Turkey	"The promise of engineered multicellular systems-on-chip"
16:50		Drinks and networking	
18:00		Dinner in town	