Booklet outlines

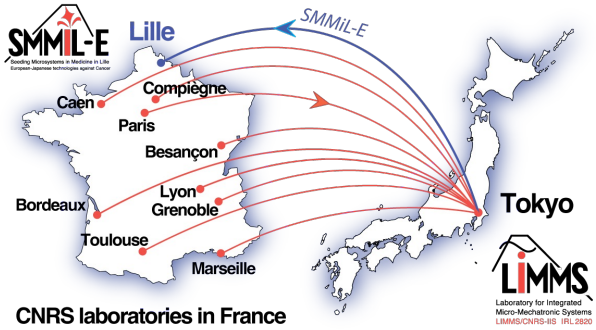
Welcome to the Laboratory for Integrated Micro-Mechatronic Systems (LIMMS/CNRS-IIS IRL 2820)

Creation and achievements

LIMMS (Laboratory for Integrated Micro Mechatronic Systems) is a joint laboratory between CNRS (INSIS Institute for Engineering and Systems Sciences) and the University of Tokyo (IIS - Institute of Industrial Science). LIMMS researchers are hosted in 17 research groups mainly located on Komaba Research Campus of the University of Tokyo. Since its creation in 1995 the laboratory has been working in the field of micro/nanotechnologies and BioMEMS.

LIMMS was created in 1995 as a cooperation unit between CNRS (SPI Department and now CNRS Ingénierie) and IIS, the University of Tokyo. It was located in the Roppongi Campus (Tokyo/Minato-Ku). Soon after it was established, the laboratory benefited largely from the strong support from the Japan Society for the Promotion of Science (JSPS).

In 2000, LIMMS was relocated, together with IIS, to the Komaba Research Campus (Tokyo/MeguroKu), where exceptional technological facilities are provided.



CNRS laboratories in France

SMMIL-E, Lille

1995
creation of LIMMS

3
research axis

Energy
Quantum & Molecular Tech.
Bio

2023 - 2024

42
papers

24
conferences

8
grants

2019-2024 JSPS C2C

2019-2025 CREST-JST

2022-2029 PEPR MoleculArchiv

…

Since 2004

500
papers

575
conferences

2023 - 2024

20
contracts

90
people

involved in LIMMS activities

Since 1995

380
people welcome

46 CNRS researchers

23 CNRS post-doc

78 JSPS post-doc

14 IIS post doc

10 CNRS Research Eng.

32 PhD students

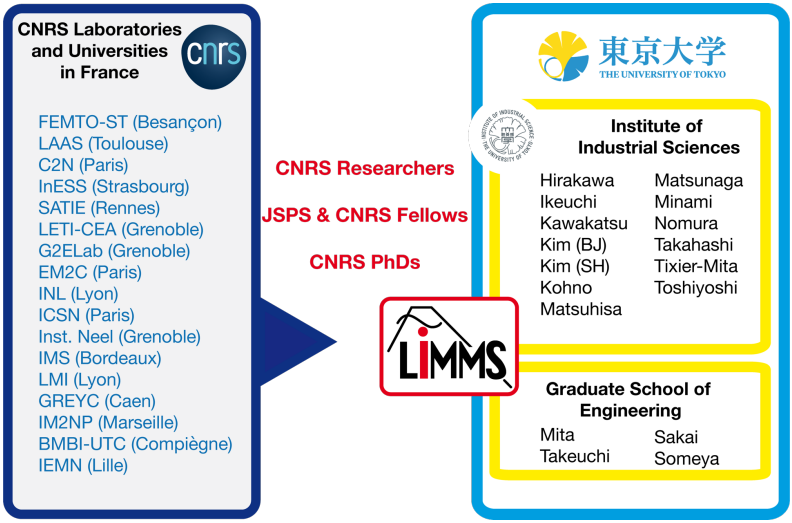
88 Internships

22 administrative staff

…

2023
ecoLIMMS started

16
New research teams created in France by former LIMMS members

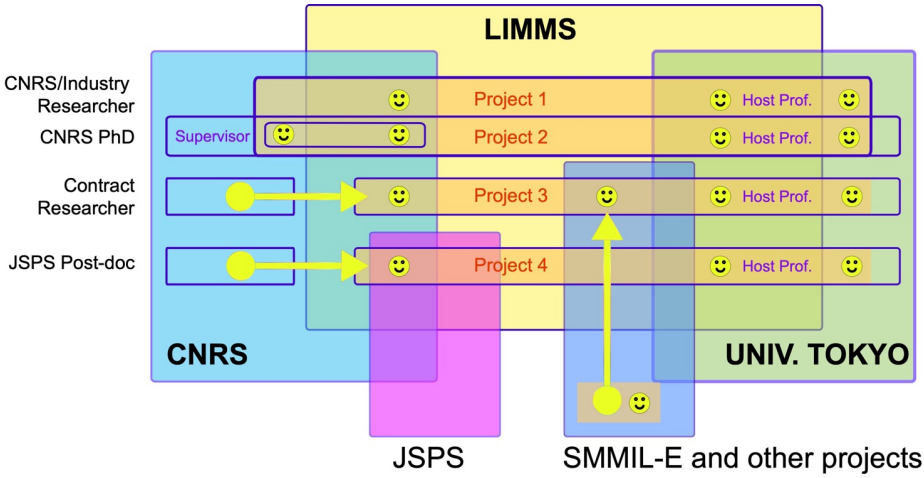


Since the acquisition of a status of IRL 2820 in 2004 (IRL= International Research Laboratory), LIMMS has been eligible to apply for French, Japanese and European research projects and grants-in-aid.

After successful review meetings, LIMMS was renewed for two terms (2010-2021). During this period, LIMMS extended its structure to European partners through EUJO-LIMMS, a project funded by the European Union (Dec. 2011 - May.2016) along with a first Core-to-Core program (April 2012 - March 2017) of the JSPS. In 2014, LIMMS took a new step in its development by inaugurating a mirror location in Lille (France) inside a hospital. The SMMiL-E project, Seeding Microsystems in Medicine in Lille, first research location of IIS out of Japan, gathers IIS, CNRS, Centre Oscar Lambret and Lille University.

In 2017, LIMMS was involved as a partner of the iLite consortium (for innovation in Liver tissue engineering, 2017-2022), an university research hospital project, granted by the French program-investment for the future (Program Investissement d'Avenir). In 2019, a second JSPS Core-to-Core program (JSPS) was assigned to LIMMS (April 2019-March 2024) to promote the interactions more specifically in Bio-oriented activities with SMMiL-E and the partners of iLite. In 2020, a CREST (JST) project targeting thermal management in silicon devices was attributed to LIMMS (October 2019-March 2025). In 2021, an Integrate Research Network 'LIMMS Kiko' (period 2021-2031) of the University of Tokyo centered on LIMMS activities was started to extend connections with 55 Japanese professors from 8 Institutes and Schools including fields such as engineering, medicine, information science and philosophy. Finally, in 2022, LIMMS was involved in the MoleculArxiv PEPR (French topical program) as one of its key laboratories.

In 2023/2024 about **90** people were involved in LIMMS activities including Host Professors (17) and their teams, CNRS researchers (11), engineers (2), JSPS post-doctoral fellows (1), contract based post-doctoral fellows (7), PhD students (5), internships (14), collaborators (27) and administration staff (6).



Organization

LIMMS combines the expertise of French and Japanese scientists in order to explore new scientific domains related to micro and nanotechnologies. Researchers who are recruited by LIMMS are hosted in the Japanese research groups affiliated to LIMMS. The scientific interaction is thus optimal.

LIMMS' structure is organized to handle challenging joint projects. These projects follow the scientific policy promoted by both Directors (CNRS and IIS), and approved by CNRS Ingénierie within its interdisciplinary policy with other CNRS Institutes, IIS and JSPS. Each scientific project gathers a LIMMS researcher, the Host Professor heading his/her host lab (The University of Tokyo), and associated lab members (see structure of LIMMS on the figure above).

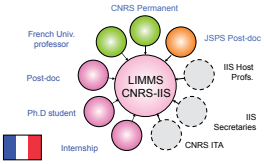
Research costs: salaries of researchers are supported by both CNRS and IIS (CNRS, IIS staff, post-doctorates, PhDs and trainees) or by JSPS, JST, ANR or EU (post-doctorates and PhDs).

The University of Tokyo covers salaries of the group of host professors and provides all technological platforms (1200 m² of cleanrooms, biological and biophysics experimental labs, AFM characterization lab, etc.), as well as its operational costs.

CNRS provides CNRS researchers salaries and the annual research budget, in the framework of a collaboration contract between CNRS and IIS, The University of Tokyo.

Laboratory for Integrated Micro-Mechatronic Systems
LIMMS/CNRS-IIS IRL 2820

LIMMS Recruiting Protocol



1. How to apply to LIMMS/CNRS-IIS (UMI 2820)

a. You have a CNRS researcher position

Step 1:	Step 2:	Step 3:	Step 4:	
(1) Visit to LIMMS for several days (2) Definition of research subject	Validation by LIMMS And by your laboratory	Applying for LIMMS position at INSIS (or institute you belong to)	Approval by National Committee Decision from INSIS	Arrival in Japan
Year N-1	Sep/Oct Year N-1	Autumn Year N-1	Autumn session Year N-1 or Spring session Year N	Sep/Oct Year N

b. You are (associate) professor in French University

Step 1:	Step 2:	Step 3:	Step 4:	
(1) Visit to LIMMS for several days (2) Definition of research subject	Validation by LIMMS And by your University	Applying for "Accueil en délégation" to move to CNRS temporary position	Transfer of the application with agreements to the Regional delegation of CNRS	Arrival in Japan
Year N-1	Sep/Oct Year N-1	Autumn Year N-1	January Year N	Sep N or Feb. N+1

c. You are Ph. D student (to apply for the JSPS Post-doc program)

Step 1:	Step 2	Step 3:		
Positions appear in LIMMS web sites and ABG	Application screening by LIMMS	Application screening by CNRS and JSPS	Expected arrival Sep. 1st – Nov. 30 for Spring Campaign	Arrival in Japan
Spring Campaign				

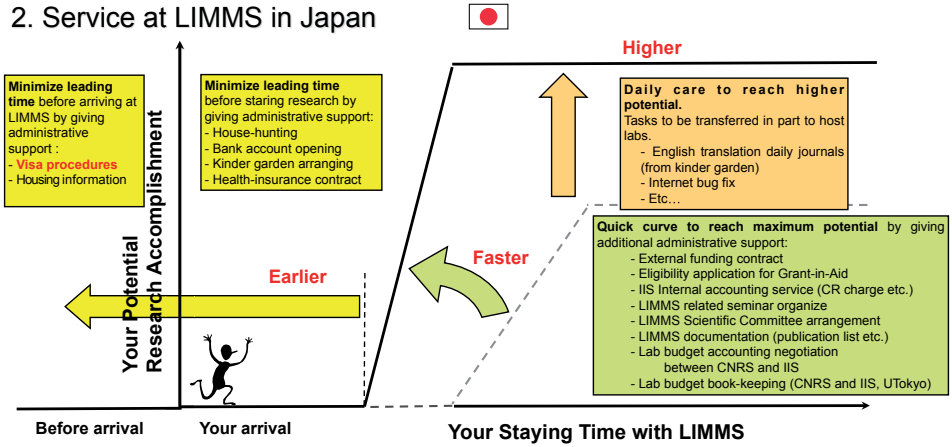
2 Campaigns / year

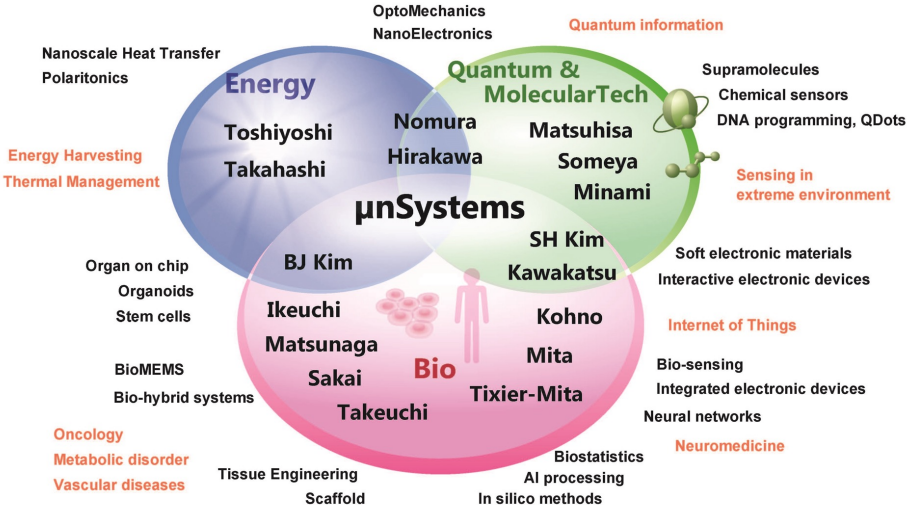
Step 1:	Step 2:	Step 3:	
Positions appear in LIMMS web sites and ABG	Application screening by LIMMS	Application screening by CNRS and JSPS	
Autumn Campaign		Expected arrival April 1 – Sep. 30 for Autumn Campaign	

d. You are student (to apply for Master internship , French doctoral program)

Step 1:	Step 2:	Step 3:	
Position available at LIMMS and Advertisement in web sites (CNRS, LIMMS …)	Application screening by LIMMS	Transfer of the application with approval to CNRS. Recruiting protocols	Arrival in Japan

2. Service at LIMMS in Japan





Scientific Policies

Since 2023, the LIMMS direction has highlighted three general fields of applications in micro and nanotechnologies by proposing three specific research axis:

- Energy
- Quantum and Molecular Technologies
- Bio

Those three fields are illustrating recent MEMS, BioMEMS and Nanotechnology developments. They reflect the orientations of LIMMS in new technologies related to societal demands.

In Energy axis, LIMMS researchers obtained worldclass results with the development of phononic crystals for heat focusing. LIMMS technologies are at the cutting-edge regarding thermoelectric micro-devices and have confirmed new concepts in thermionic cooling. Interface research programs are also settled to find solutions to power the Internet of Thing (IoT) based on energy harvesters integrated

The Quantum and Molecular Technologies axis is a highly interdisciplinary field that combines cutting research from physics, chemistry, and biology. This axis bridges the two other axes (energy and biology), while also exploring its own unique research questions. At the heart of this axis lies the exploration and integration of quantum technology and molecular technology. Quantum technology is concerned with the use of quantum mechanics to develop new technologies as for instance manipulating the transport of heat, electron or light, while molecular technology deals with the study and manipulation of molecules and their properties. Our research ranges from fundamental endeavor such single-electron transfer in electrochemistry to the storing of massive data in DNA, the sensing of biomolecules, or the integration of electronic into our everyday life with flexible electronics.

The new **Bio** axis gathers three themes. Disease treatment via prevention and detection is investigated by developing new devices for diagnosis and vaccine delivery. With a complementary approach, implantable tissues and devices are also key activities.

This branch is related to complex tissues opening to organ modelling where the cellular and even the molecular scale are investigated. Researchers seek to better understand the blood vessel formation, the neuronal communication behaviour and the interaction of the metabolic organs such as liver and pancreas. By studying different organs, LIMMS aims at understanding the role of tissues and especially cell interactions in diseased and healthy tissues.

BioMEMS such as platforms with multi-modal sensors and actuators are developed in LIMMS to help investigating organ behaviour and create biohybrid systems. Biocompatible materials and/or cells are also used to create Bio-robotic systems. A particularity of the Bio axis is the complementary contribution of an international team, SMMIL-E. Its activities are focused on research against cancer, at the interface between BioMEMS and Organ modelling.

SMMiL-E (Seeding Microsystems in Medicine in Lille)

The SMMiL-E project includes the setting-up of a new platform of the Institute of Industrial Science of the University of Tokyo (IIS) in the Lille university-hospital area, close to medical teams. First research location of IIS out of Japan, this implantation is backed by CNRS, Centre Oscar Lambret and Lille 1 University, as a IRL, International Joint Unit, mirror site of LIMMS/CNRS-IIS (IRL 2820). The new site was approved by the four partners and inaugurated on June 16th, 2014.

Goal : SMMiL-E aims at setting-up and implement a comprehensive research program on BioMEMS against Cancer in a sustainable international high-level collaboration. The project synergizes Bio-MEMS research from LIMMS/CNRS-IIS with research against Cancer performed in Lille under the labeled SIRIC ONCO - Lille program.

Research Activity in SMMiL-E

The scientific activities encompass BioMEMS research against Cancer, technology development and bio related experiments, as an original interdisciplinary approach to the SIRIC ONCO-Lille program. The projects aim at bridging fundamental and clinical research around four work packages:

WP1 Biomolecular mechanisms of the tumor resistance to treatment (DNA degradation under therapeutic irradiations, Microtubules stabilization in chemotherapy).

WP2 Cellular evaluation and diagnosis: Stem cells and circulating tumor cells detection and sorting, study of cell senescence and tumor dormancy.

WP3 Cells interaction and therapeutic targets: in vitro tumor angiogenesis, cellular mobility and metastatic processes.

WP4 Biological adhesives and neotissues: cellular fibers and postsurgery recovery.

By means of an upstream research, this program targets more effective disease detection, a strengthened efficacy of therapy and posttreatment monitoring, for a better care to patient.

CREST (JST) project

2019 - 2025

A CREST project (JST program) was awarded to LIMMS in October 2019 supporting the Energy Harvesting and Management activities. This five years project (250 Millions Yen) involves a single team, and aims at developing scientific understanding and demonstrators of phonon polariton heat transfer in silicon micro and nanodevices.
This project involves three LIMMS researchers (from August 2020).

PEPR MoleculArxiv

2022 - 2029

The dazzling amount of data that humanity generates requires novel solutions for long-term storage. Storing data in the form of DNA, similar to living beings, is a promising option due to its enormous density: 100 g of DNA could in principle store all the data kept in datacenters around the world.

The PEPR MoleculArXiv aims to make of France a key player in DNA storage by involving more than 20 interdisciplinary laboratories from CNRS. LIMMS plays a key role as it is in charge of coordinating and integrating experimental and theoretical progress into a demonstrator that writes information in DNA at a rate of 1 bit per second -100x faster than commercial synthesis in 5 years.

The PEPR will also foster French and European communities and aim to propose a European FET-flagship. Applications will include cold data archiving, marking, calculation, and molecular engineering.

https://pepr-molecularxiv.fr/le-pepr/

LIMMS KIKO

2021 - 2031

The University of Tokyo Integrated Research Network

The LIMMS KIKO is engaged in a cross disciplinary research for the improvement of the Quality of Life including mental, physical and cultural aspects and addressing societal problems of aging and declining population which developed countries will face, by applying the results of international collaborative research in the Micro-nano interdisciplinary fields such as Nanobiology, μTAS, Silicon Neurons, IoT, and Energy Harvester, etc.

LIMMS KIKO, (LIMMS= "Laboratories for International Research on Multidisciplinary Micro Systems") was established April 1st 2021 for a period of 10 years and is based on the LIMMS/CNRS-IIS IRL 2820, which has been managed by CNRS and IIS for 25 years as a Japan-France collaborative research center, in order to transcend departmental boundaries and comprehensively bring in the intellectual creativities of the University of Tokyo.

https://kiko.limms-tokyo.org/en/

JSPS Core-to-Core program JETMeE

Core-to-Core Program
研究拠点形成事業

2019 - 2024

Since 2012, the Japan Society for the Promotion of Science (JSPS) has implemented the Core-to-Core Program, comprising two components: (A) Advanced Research Networks and (B) Asia-Africa Science Platforms.

In 2019, a second JSPS Core-to-Core program was assigned to LIMMS (April 2019- March 2024)to promote the interactions more specifically in Bio- oriented activities with SMMIL-E and the partners of iLite. JSPS granted "Core-to-Core (A) advanced research networks program" to the Institute of Industrial Science (PI: Prof. Beomjoon Kim, LIMMS director) with a 15 Million Japanese Yens / Year, for 5 years, as matching fund to SMMiL-E, iLite, and EPFL research funds.

This program aims at creating world-class research hubs and foster young researchers through networking to advance multilateral collaboration in cutting-edge fields of science. It funds matching activities to SMMiL-E and iLite by supporting UTokyoIIS to send Japanese researchers to CNRS and EPFL and to reinforce scientific collaborations. The Program name is JETMeE in frame of the Core-to-Core, meaning "Japan- Europe Research Hub for Translational Medical Engineering".

https://www.jetmee.jp/

EcoLIMMS

2023 ~

"We are part of the problem, so let's be part of the solution."

EcoLIMMS is a group of researchers who share a commitment for climate change questions, and ask ourselves how we can, as researchers, have a positive impact on the planet. EcoLIMMS was formed in April 2023.

The **two main missions** established are: (i) **act at the laboratory scale**, and (ii) **organize events** to communicate on scientific research and climate change (beyond the lab).

At the lab scale, a monthly **newsletter** is sent to the lab members to share information on a selected topic, and on specific events related to climate change and environment. The work group has also started working on the **greenhouse gas balance of LIMMS** which is an interesting tool to evaluate and then optimize our behaviours and practices.

Regarding the **events**, a crosstalk event was organized in February 2024 with a researcher from Human and Social Sciences and another one from Science and Technology. Other events will be organised over the coming year. This action is in line with the commitments of the CNRS and The University of Tokyo.

International Research Network EURA-LIMMS

IRN

The EURA-LIMMS network aims to create a Europe-Asia network for the development of innovative technologies in energy, bioengineering, and molecular sciences. The objective is to revive the success of the NAMIS network supported by the CNRS, by adapting the themes to the current research axes of LIMMS. The network will promote the education of students and the exchanges between member teams from: The University of Tokyo, Seoul National University, National Taiwan University, National University of Singapour, EPFL, Helmoltz, Imtek, University of Twente and CNRS.

Contact : N. Clément

International Project Team – Equipe Projet Internationale

EPI

International Project Teams that are joining researchers of LIMMS and of a CNRS laboratory in France on a given topic. The four following teams are presently running: BioMeg with IMS in Bordeaux on Biomorphic science, MinanoBio with LAAS in Toulouse on MIcro-&NANO-technology for BIO-engineering and bio-sensing, TEAMS with BMBI on Therapeutics and Engineering Against Metabolic Syndrome and SUNRYSE with IM2NP in Marseilles on Structured Nano-systems for energy conversion and management. The teams no only activiate student and researcher exchanges but also raise fund from CNRS and universities to promote research works.

LIMMS Key Figures and Collaborations

Since its creation, the LIMMS has welcomed in total 380 members including 46 CNRS researchers, 78 JSPS post-doctorates, 23 CNRS Postdoctorates, 14 IIS Post-doctorates, 32 PhD students, 10 CNRS research engineers, 34 collaborators, 2 industrial collaborators, 88 internships, 22 administration staff, etc...

Since 2004, LIMMS has published more than 500 journal papers (including publications in high impact journals such as Nature -/Chemistry, /Biotechnology, /Communications-, NanoLetters, Physical Review Letters...), and more than 575 communications to international conferences.

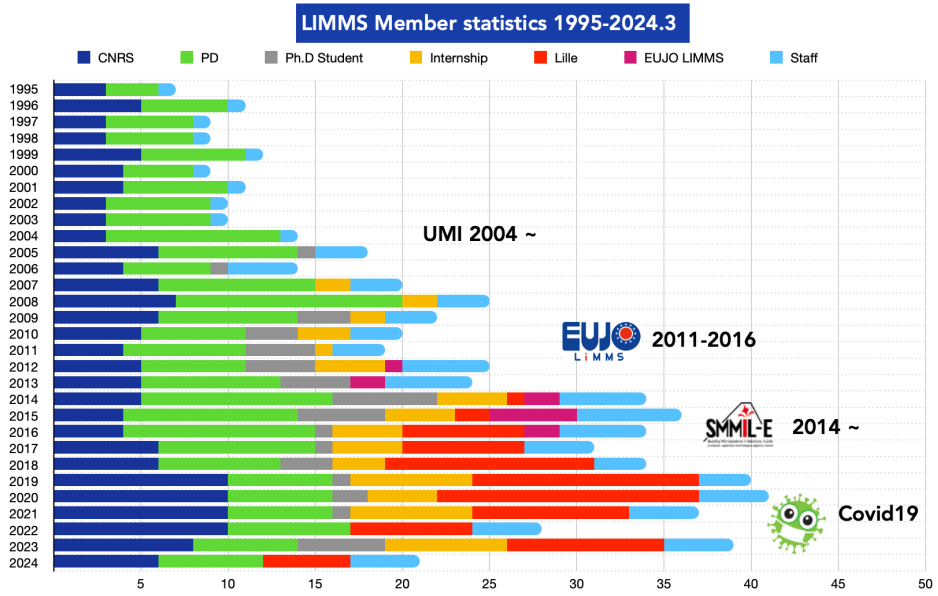
In 2023-2024, our members published 42 journal papers and 24 communications in international conferences.

In this period, LIMMS members have managed 8 grants (5 by JSPS, 1 by JST and 2 by others) and 20 contracts (EU, PEPR, ANR, Region...).

Former LIMMS members maintain collaborations with Japanese host professors and CNRS laboratories in France (SAKURA programs, PICS and JSPS Bridge).

More than 16 new research teams, often followed by technology exchanges and sharing from LIMMS, were created by former members back in France.

LIMMS has also been pivotal to launching **international research networks** such as the CIRMM/IIS « Center for International Research on Micro nano Mechatronics », the « Global Research Network » of IIS and the NAMIS « Nano Micro Systems » linking CNRS to IIS and to prestigious institutions such as EPFL, SNU, VTT, IMTEK.



Events

LIMMS International Workshop on Micro-and NanoTechnologies for Energy, Bio-engineering and Bio-sensing with JETMeE Workshop, Oct. 25-26, 2023.

On October 25th and 26th 2023, an International Workshop on Micro-and Nano-Technologies for Energy, Bioengineering and Bio-sensing with JETMeE Workshop was held in IEMN CNRS, Lille (France). A group of Japanese host Professors from LIMMS and IEMN researchers presented their activities to open for collaboration. LIMMS alumni and potential candidates were also present. (Co-organizers: LIMMS and IEMN Directions).

Workshop on CNRS - Industry Collaborations (IWCIC), Jun. 13-14, 2023.

On June 13th-14th, to mark the 15th anniversary of CNRS's collaboration with NTT on nano and molecular components, LIMMS organized a workshop [International Workshop on CNRS - Industry Collaborations (IWCIC)] featuring 9 industry presentations and a "rump session" for students and young researchers to ask questions. (Co-organizers: Nicolas Clément, Imran Mahboob, Akira Fujiwara).

JFK Workshop on Emerging Biomedical Science and Technology at the Nanoscale, Oct. 10-11, 2023

The JFK2023 (for Japan-France-Korea) workshop on emerging biomedical science and technology at the nanoscale was co-organized by LIMMS October 10th and 11th 2023, in two campuses of the University of Tokyo. Participants came from various institutions such as Paris-Saclay University, France, Pusan National University, Seoul National University, South Korea and The University of Tokyo, Japan. The second day of workshop was jointly held with the NANOHUB of The University of Tokyo. (Co-organizers: Gilgueng Hwang, Yoshio Mita, Pierre-Yves Joubert, Giancarlo Faini).

LIMMS Steering Committee 2024, Oct. 24, 2023.

On October 24th 2023, the LIMMS Steering Committee was held in CNRS headquarters, Paris. The IIS Director, Professor Toru Okabe and the LIMMS Direction with Professors Yoshio Mita and Soo Hyeon Kim met the direction of the CNRS Ingénierie institute, including Maria-Pilar Bernal, Deputy Director, Béatrice Dagens, Deputy Director for International Affairs, Olga Allard, admnistrator for International Affairs.

3rd Aix-Marseille University/IIS UTokyo, Oct. 31, 2023.

On October 31st, the 3rd Aix-Marseille University/IIS UTokyo Workshop on optical and electronic devices was co-organized with LIMMS in IIS. Speakers from the IM2NP laboratory and the Institut Fresnel of Aix-Marseilles University on one hand and from IIS in the other hand took part in the Workshop. (Co-organizers: Kazuhiko Hirakawa, Marc Bescond).

UTC joint workshop, Oct. 31~ Nov. 6, 2023.

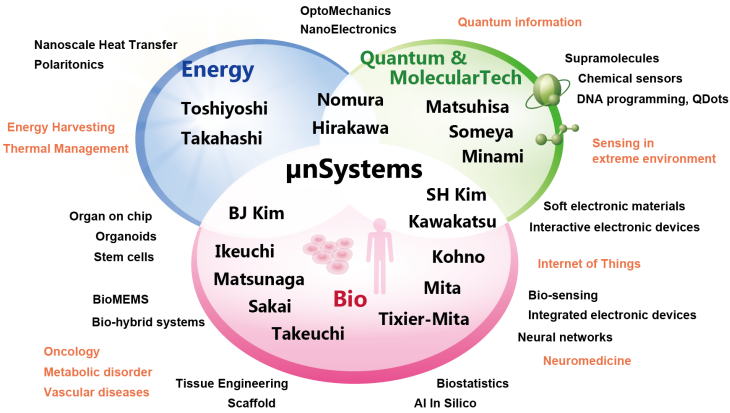
In the frame of the collaboration between The Université de Technologie de Compiègne (UTC), IIS, and CNRS, Professors Sakai and Minami co-organized a joint workshop and a UTC visit delegation held in Tokyo from October 31st to November 6th. The workshop was an opportunity to introduce French and Japanese advanced research programs, recent innovations. 68 participants registered. The UTC delegation, headed by the president of the UTC, Prof Rossi, took the opportunity to renew the IIS MOU, exchanged with Prof Okabe, IIS general director, and discussed future collaboration with Prof Fujii, the president of the University of Tokyo.

SMMiL-E/UTC 2024 School on BioMEMS, (4th Ed.) Feb. 6~16, 2024.

SMMiL-E, the site of LIMMS/CNRS-IIS IRL 2820 in Lille, hosted an international school on bioMEMS in collaboration with BMBI CNRS laboratory of UTC (University of Technology of Compiègne), from February 6th to 16th, 2024. This educational event, held for the fourth time, aimed to introduce the main aspects of bioMEMS technology through a multidisciplinary team (22 lecturers in Lille and 8 lecturers in Compiègne) with backgrounds in biology, clinics and engineering. The school's contents were grouped into three main categories: device development (e.g., design, fabrication, characterization and operation), fundamental techniques (e.g., biological, clinical and microfluidics) and examples of applied systems (e.g., organ-on-a-chip and single-cell analysis).

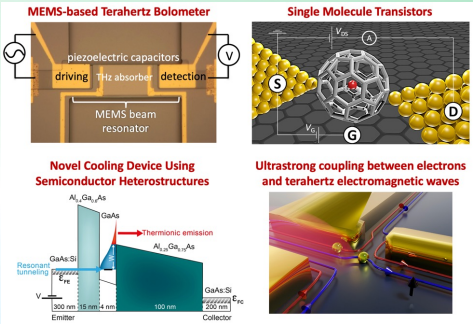
7 students from the Institute of Industrial Science, The University of Tokyo, 19 students from the University of Lille, 2 students from JUNIA and Polytech Lille (French graduate schools of science and engineering), and 10 students from UTC attended this program and were highly encouraged to join projects between SMMiL-E, UTC and IIS.

Host Laboratories



Pr. Kazuhiko HIRAKAWA

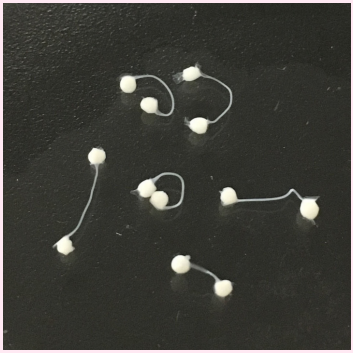
- MEMS/NEMS-based terahertz detectors
- Semiconductor heterostructure thermionic cooling devices
- Single molecule/quantum dot transistors
- Terahertz dynamics of quantum nanostructures for quantum information processing



http://thz.iis.u-tokyo.ac.jp

Associate Pr. Yoshiho IKEUCHI

- Neural tissue engineering and brain organoids
- Neuronal morphology and development
- Protein synthesis in neurons
- Human pluropotent stem cell-derived neurons

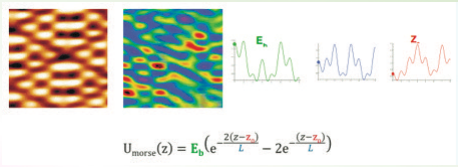


www.bmce.iis.u-tokyo.ac.jp

Host Laboratories

Pr. Hideki KAWAKATSU

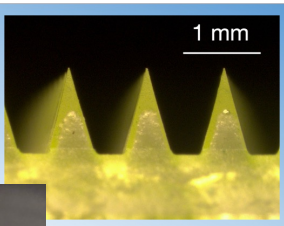
- Color AFM with chemical contrast
- Force and vibration measurement of reproductive cells
- Quantitative color AFM through Molecular functionalisation of AFM tips

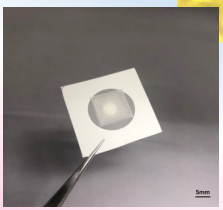


www.inventio.iis.u-tokyo.ac.jp

Pr. Beomjoon KIM

- MEMS, Bio-NEMS, Micro/nano patterning, soft lithography
- SAM patterning for cell culturing/bio sensors
- Heat transfer in nano structures, Micro/nano heaters for molecular Engineering
- Microneedle patch for new drug delivery system
- Energy harvesting, power MEMS



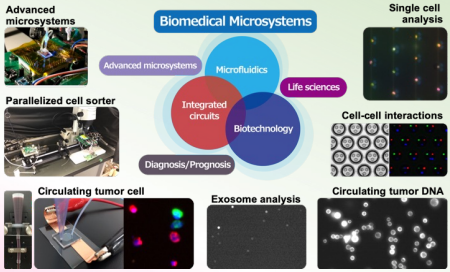


Health monitoring Microneedles patch

www.kimlab.iis.u-tokyo.ac.jp

Lecturer Soo Hyeon KIM

- Microfluidics-on-CMOS
- Single cell analysis
- Single molecule detection
- Cell-cell interactions
- Biomedical microsystems for liquid biopsy
- Parallelized flow cytometry

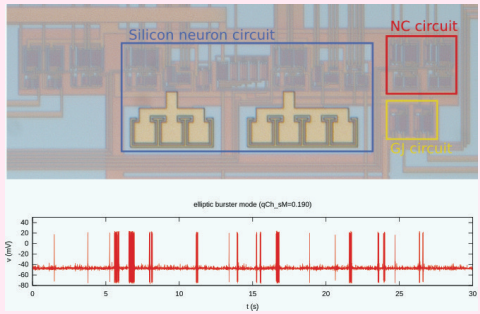


www.shkimlab.iis.u-tokyo.ac.jp

Host Laboratories

Pr. Takashi KOHNO

- Neuromimetic silicon neuronal network circuits and their application to neuromimetic artificial intelligence
- Architectural design of the neuromimetic computing



www.neumis.iis.u-tokyo.ac.jp

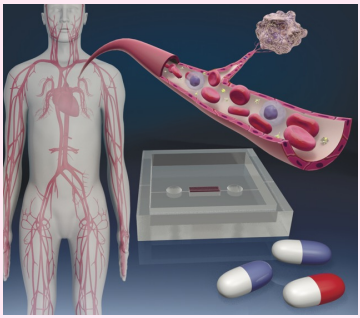
Associate Pr.
Naoji MATSUHISA

- Stretchable electronic materials and devices
- Wearable devices
- Human-computer interfaces
- Electronic skins for robots

https://www.naojimatsuhisa.com/

Pr. Yukiko MATSUNAGA

- Tissue engineering
- Biomaterials
- In-vitro microvessels model
- Vascular biology

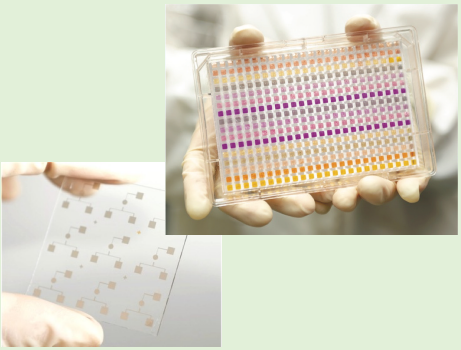


www.matlab.iis.u-tokyo.ac.jp

Host Laboratories

Associate Pr. Tsuyoshi MINAMI

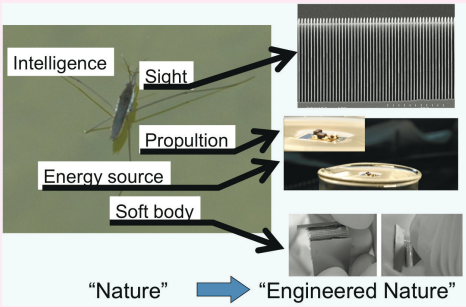
- Organic TFT-based chemical sensors
- Supramolecular sensor arrays



www.tminami.iis.u-tokyo.ac.jp

Pr. Yoshio MITA

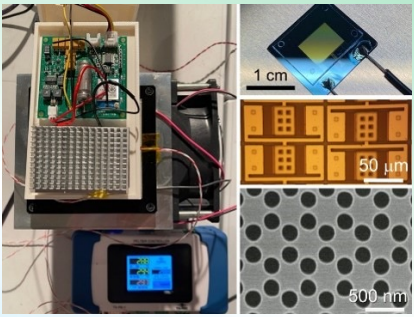
- Integrated MEMS-VLSI technology
- Nature Engineered Microdevices
- Nano deep 3D MEMS optoelectronic systems
- Autonomous microrobot
- Bio-inspired perception LSI systems



http://www.if.t.u-tokyo.ac.jp/

Pr. Masahiro NOMURA

- Physics of nanoscale phonon/heat transport
- Nano-Si thermoelectric energy harvesting
- Quantum transducer via spin-optomechanics

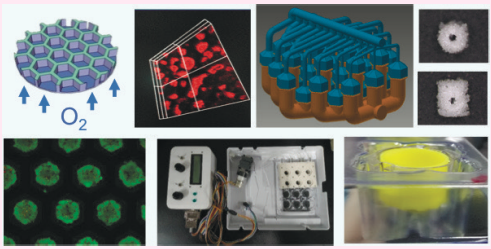


https://www.nlab.iis.u-tokyo.ac.jp/

Host Laboratories

Pr. Yasuyuki SAKAI

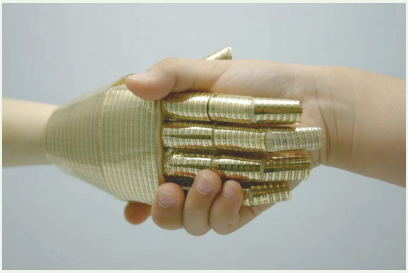
- Physiological micro cell culture system (MPS) based on microfluidics, micropatterning and hierarchical cellular organization
- 3D microfabrication and biofabrication for engineering of implantable tissues
- High-cell density propagation and differentiation of stem/progenitor cells



http://orgbiosys.t.u-tokyo.ac.jp/sakai/

Pr. Takao SOMEYA

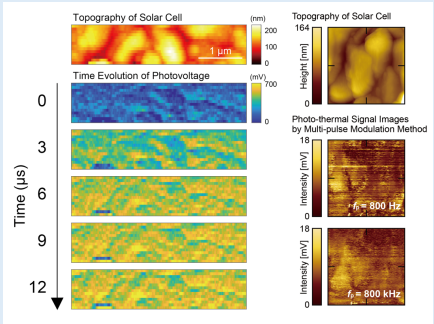
- Flexible electronics using organic transistors
- Large-area sensors and actuators
- Molecular/organic electronics
- Printing technologies for large-area electronics
- Printed MEMS switches for power transmission



www.ntech.t.u-tokyo.ac.jp

Pr. Takuji TAKAHASHI

- Multiple analyses of solar cell materials by photo-assisted nanoprobes
- Development of novel measuring methods to improve performance in SPMs
- Analysis of individual fine current paths in CNT-FETs by MFM

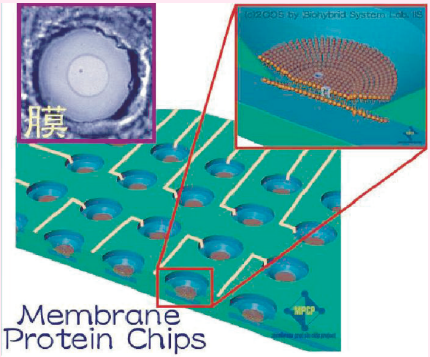


www.spm.iis.u-tokyo.ac.jp

Host Laboratories

Pr. Shoji TAKEUCHI

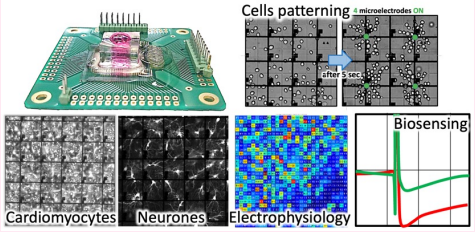
- Biohybrid MEMS
- Membrane protein chips
- MEMS for articial cells
- Neural interfaces
- Microchambers, droplets, capsules



www.hybrid.t.u-tokyo.ac.jp

Associate Pr. Agnès TIXIER-MITA

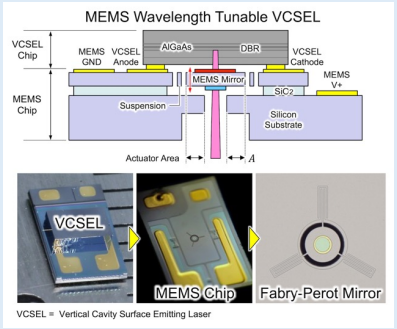
- Thin-Film-Transistor platform for multi-modal bio-sensing
- Real-time biomimetic platform for neuro-cardiac investigations
- Systems for simultaneous optical and electrical measurements on cardiomyocyte cell culture



http://toshi.iis.u-tokyo.ac.jp/toshilab/?Members/Agnes+Tixier-Mita

Pr. Hiroshi TOSHIYOSHI

- Optical MEMS
- RF-MEMS
- THz metamaterials
- CMOS-MEMS integration
- Energy harvesters



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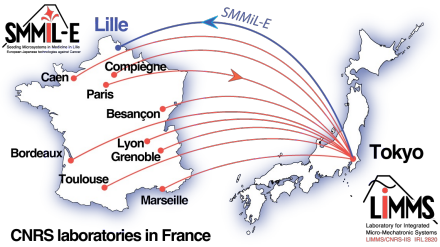
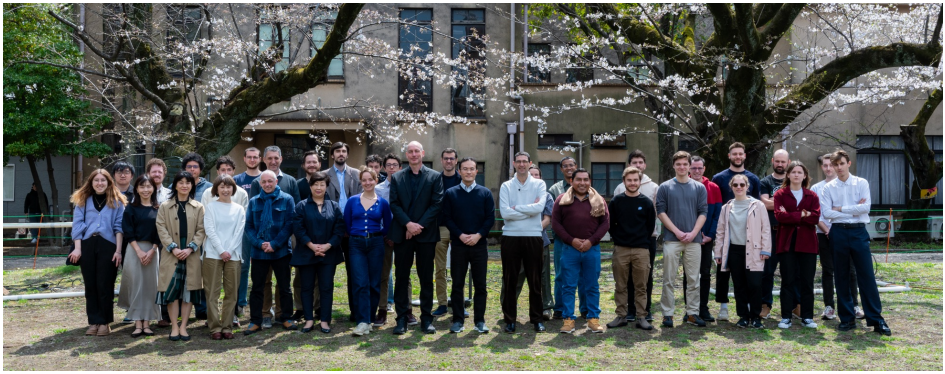


LIMMS, Tokyo



Research Projects

The laboratory operates in three fields:

- Energy
- Quantum and Molecular Technologies
- Biology

Details about all research projects conducted from April 1st 2023 to the March 31st 2024 will be given in the following part of the booklet.

Energy
Axis

CREST Project: Surface Phonon-Polariton Heat Transfer (2019-2025).

Sebastian Volz

Hosted in Nomura Lab

Keywords: Radiation, Cooling, Nanoscale

Fundings:
JST-CREST
Kakenhi B

Context and Objectives

Designing nanoscale heat spreaders in silicon devices.

Investigating a new heat transfer channel based on SPhP in the in-plane direction.

In ultrathin films at high-T, SPhPs are the predominant heat carriers.

We aim at experimentally demonstrating this prediction and then manipulate SPhP by guiding, tunneling, rectifying and focusing.

Methods

Fabrication:

Clean-Room silicon processes.

Characterization:

Time-Domain Thermo Reflectance;

3 omega; IR Camera and FTIR.

Modeling:

Analytical solution of Maxwell;

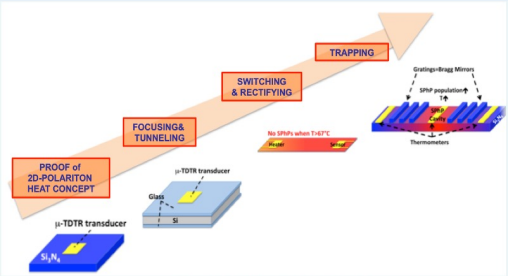
Boltzmann and Heat conduction Equations;

Fluctuational Electrodynamics (SCUFF-EM open source code)

Tasks

Demonstrators include:

- Proof of concept
- Focusing and tunneling
- Switching and rectifying
- Trapping



Project Workpackages

Perspectives

Design SPhP Diodes;

Exploiting 2D materials Polaritons;

Use SPhPs to control far-field thermal radiation.

References

[1] J. Ordonez-Miranda, et al., Physical Review B 108 (16), L161404, (2023).
[2] J. Ordonez-Miranda, Physical Review Applied 19 (4), 044046, (2023).

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Modeling of the Heat Transport Driven by Surface Electromagnetic Waves.

José Ordonez-Miranda

Hosted in Nomura Lab

Keywords: Surface phonon-polaritons, Heat transport modeling, 2D heat radiation.

Fundings:
JST-CREST (S.Volz)
Kakenhi B

Context and Objectives

With the continuous miniaturization of devices with enhanced operation rates, the overheating of the used nanomaterials has become very challenging, as it limits their applications and wastes energy that is mainly released into the environment. We are addressing this scientific challenge by studying the heat transport not only inside the nanomaterials' volume but also along their interfaces, via surface electromagnetic waves. These waves are powerful heat carriers that can enhance the heat transport by phonons, photons, and electrons [1,2]. Our research aims to develop analytical and numerical models for discovering new physical effects and predicting the polariton thermal energy.

Method

Maxwell's equations of electromagnetism for predicting the existence and propagation of surface polaritons.

Boltzmann transport equation for finding the temperature and heat flux profiles of nanostructures.

Generalization of Fourier's law of heat conduction and Stefan-Boltzmann's law of thermal radiation in 1D, 2D, and 3D structures.

Development of theoretical models for describing experimental data and measurement thermal properties.

Results

We have experimentally demonstrated a two-fold enhancement of the far-field thermal radiation between two non-absorbent Si microplates coated with energy-absorbent SiO_2 nanolayers (Fig. 1), which support the propagation of surface phonon-polaritons [1].

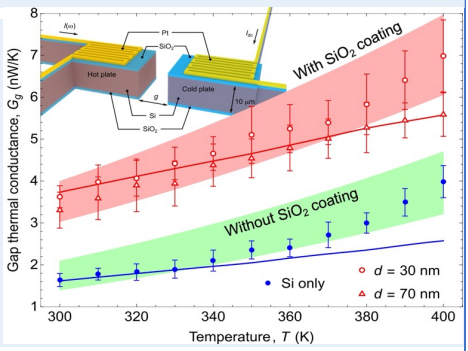

Fig.1 Measured thermal conductance between two Si plates with and without SiO_2 coating.

Perspectives

To compare the predictions of the Boltzmann transport equation (particle picture) with those of fluctuational electrodynamics (wave picture) for the polariton thermal conductivity of nanofilms, nanowires, and nanostructured materials.

References

[1] S. Tachikawa, J. Ordonez-Miranda et.al., Phys. Rev. Lett. 132, xyzabc (2024)

[2] J. Ordonez-Miranda, Y. A. Kosevich et al., Phys. Rev. B 108, L161404 (2023)

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Enhancement of Emissivity via Thermally Exited Guided Modes.

Maëlie Coral

Hosted in Nomura Lab

Keywords: Guided modes, Surfaces phonon-polaritons, thermal radiation

Funding:
JSPS Kaken-hi B

Context and Objectives

Surfaces phonon-polaritons (SPhPs) are electromagnetic surface waves generated by the coupling of infrared photons and optical phonons at the interface of polar materials. Even though these evanescent waves have been widely exploited to enhance the cross-plane heat transport in nanocavities (1), recent studies show that they can also enhance significantly their in-plane heat flux. In a vacuum cavity between two parallel plates of SiO_2, theory predicts that the maximum enhancement of the radiative heat flux appears for a cavity width of 1 cm (2). This enhancement results from the hybridation of longitudinal guided modes and SPhPs, as shown in Figure 1. The guided modes appear in materials with a moderate absorption such as silicon. Those modes can be thermally excited and therefore enhance the outgoing flux.

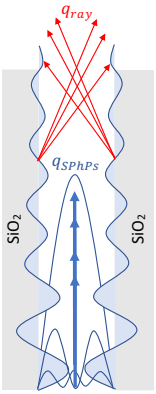

Figure 1 - Vacuum cavity between two polar materials supporting the in-plane propagation of SPhPs via guided modes (blue lines) and Planck radiation (red arrows).

Method

In this work, we aim at providing an experimental proof to this enhancement driven by SPhPs. First, the flux in silicon cavities with and without SiO_2 layer has been studied by directional emissivity measurement, FTIR with integration sphere and FTIR + IR microscope. As Si without SiO_2 does not support the SPhPs propagation, the comparison of both measurements is expected to provide a proof of concept of the SPhPs contribution to the heat emission. Secondly, TRSTM measurements will be performed to access the flux just above the cavity to reveal the the electromagnetic field structure.

Perspectives

The measurement with FTIR + integration sphere has shown promising results. In an effort to confirm and understand those results, several other measurements are expected to be done. Moreover, simulations using the code SCUFF-EMM will also be implemented.

References

1. Near-field Radiative Heat Transfer in Many-Body Systems. S.-A. Biehs and al Rev. Mod. Phys. 93, 025009, 2021.
2. Resonant Polariton Thermal Transport Along a Vacuum Gap. S. Volz and al. Phys. Rev. Applied 18, L051003, 2022.

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Measurements of Quartz Thermal Diffusivity by the 3ω Method up to 875 K.

Laurent Jalabert

Host Lab Nomura Lab

Funding:
JST-CREST (S.Volz)

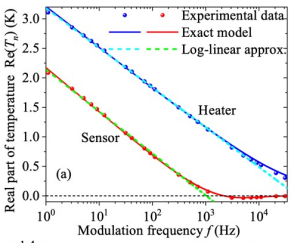
Keywords: Extreme temperature, thermal properties, 3-omega method, thermal diffusivity and conductivity, reference sample

Context and Objectives

Electrical measurements by contacting probe tips with a sample, can be performed up to a maximum temperature of 800K using conventional Vacuum Probe Station (VPS). But nowadays, wide band gap semiconductors and sensors developed for harsh environment, need higher temperature test to evaluate their reliability. There is a need to engineer an extreme temperature vacuum prober.

Method

By combining two different know-hows, we created a prototype of vacuum probe station operating routinely at 1200 K [2].
We tested the 3ω/2ω thermal method on a reference sample (α-quartz from National Metrology Institute of Japan) with calibrated diffusivity measured by laser flash method up to 800 K. The results are presented below.



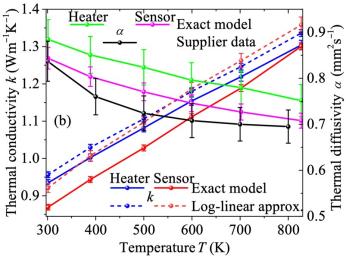


Fig1 (left). Top view of the inside of the VPS during the measurement at 1200 K. Fig 2. Fitting experimental data with the analytical model [3] from heater and sensor signals. Fig 3 (right). The extracted thermal properties of a calibrated quartz diffusivity provided by NMIJ [3].

Results

The prototype could operate safely up to 875 K. We calculated the analytical solution of the 3-omega method [3], and fit a set of 3ω data to extract both the thermal conductivity and diffusivity of a quartz bulk sample. We found a good agreement with the calibrated data provided by NMIJ using laser flash method.

Perspectives

We are now challenging suspended thin film measurements at high temperature to compare results obtained with optical TDTR, in order to confirm the surface phonon polariton detection at high temperature.

Publications/References

[1] Cahill, PRB, 35,8 (1987)

[2] Jalabert et al., MRS (2022).

[3] Ordonez, Jalabert et al., JAP (2023)

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Nanophononics for Future Quantum Technology.

Michele Diego

Hosted in Nomura Lab

Keywords: nanophononics, nano-resonators, optomechanics

Fundings:
- Japan Science and Technology Agency Moonshot R&D
- JSPS

Context and Objectives

Controlling the mechanical and optical properties of nano-objects is of paramount importance in modern technology. By structuring matter at the nanoscale, we can design and characterize exotic devices to achieve specific functionalities.

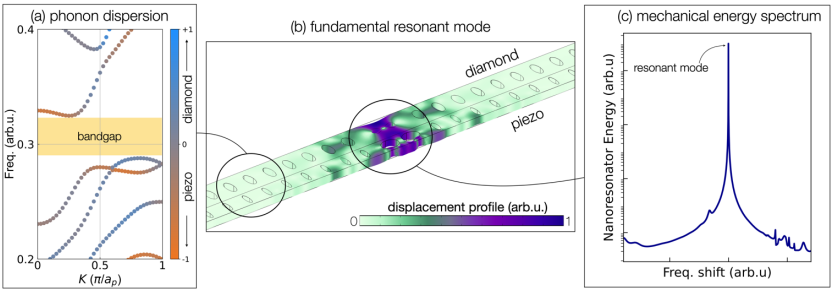
As a main example, by periodically nano-patterning unit cells in a material, we induce a modification in its photonic and phononic dispersion relations [1]. This opens the doors to a variety of applications, ranging from heat and acoustic transport [2] to optomechanical cavities and quantum interfaces [3].

Methods

Fabrication:
- Electron beam lithography
- Reactive-ion etching

Characterization:
- Brillouin light scattering spectroscopy
- Vector network analyzer
- Pump&probe optics

Design:
- Finite element methods
- Genetic algorithm optimization



Quantum telecommunication interface formed by a double hybrid nanoresonator of diamond embedding color defects and a piezoelectric material (AlN). By exciting mechanical modes in diamond, the system behaves as a spin qubit.

***a**. phonon dispersion of the hybrid unit cell and relative bandgap. **b**. fundamental resonant mode of the nanoresonator. **c.** simulated energy spectrum while tuning the excitation frequency.*

Perspectives

- Diamond optomechanical cavities for quantum networking

- Introduction of automated methods to improve the structural design (genetic algorithm, machine learning, artificial intelligence, etc.)

References

[1] A. Balandin, JNN. 2005

[2] M. Nomura et al., Mater. Today Phys. 2022

[3] B. Kim et al., Phys. Rev. Appl. 2023

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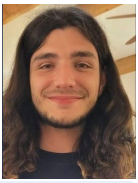
Heterostructure Cooler Fabrication and Characterization.

Louis Grandvaux

Hosted in Hirakawa Lab



Keywords: Nanoscale cooling Heterostructure

Context and Objectives

For more than fifty years, the number of transistors inside a chip has doubled every year following Moore's law. This results in a increase of power density inside chips leading to lattice heating at more than 400K.

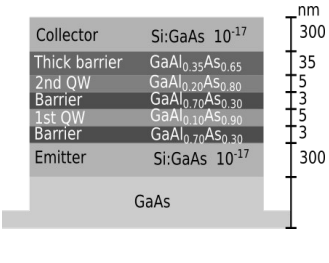
This problem can be solved using thermionic effect in a quantum well (QW) heterostructure where electrons absorb thermal energy when jumping from the emitter to the QW by phonon interaction [1].

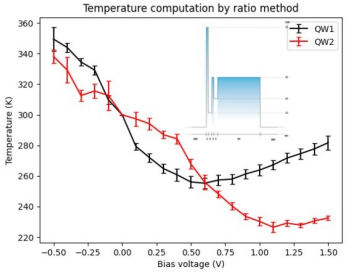
Cascade quantum cooler devices are investigated further.

Method

Cascade quantum well structure is made with layers of GaAs and $GaAl_xAs_{(1-x)}$ and is characterized by photoluminescence.

Barrier height is controlled by Al doping.





Double quantum well structure (left)

Temperature in each QW measured by photoluminescence (right)

Results

Several sample with different barrier heights were investigated. The best candidate can be seen on the side figure with a tall barrier between the emitter and 1st QW. The tall barrier acts as filter allowing only thermionic emission from QWs and preventing hot electrons from emitter to heat the QWs.

From sample with two tall barriers, a depopulation of electrons happens around 0,5V and temperature shows oscillation similar to what is observed in simulations [2].

Perspectives

Thermionic effect is a good candidate for nanoscale cooling device. However, more samples need to be made in order to better understand what happens in each QW and match simulation results.

References

[1] M. Bescond and K. Hirakawa, Phys. Rev.Appl. 14, 2020

[2] G. Etesse et al., "A novel structure of Cooling Nano-devices: The Quantum Cascade Cooler."

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Novel Cooling Nano-Device: The Quantum Cascade Cooler.

Guéric Etesse

Hosted in Hirakawa Lab

Fundings:
Internal project 2023
ANR GELATO

Keywords: Cooling, Quantum heterostructure, Quantum transport

Context and Objectives

With the miniaturization of microelectronic devices, self-heating effects are becoming a rising problematic for which low-scale heat management solutions are investigated.

The Quantum Cascade Cooler [1], a multiple quantum well structure whose cooling capabilities rely on combined resonant tunneling and thermionic emission filtering, shows promising results.

Method

Quantum transport simulations using NEGF formalism; Büttiker probes [2, 3]

Sample growth using molecular beam epitaxy and PL measurements for electron temperature determination.

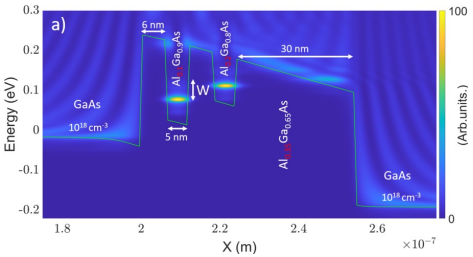

Fig. 1: Electronic density of states of the Quantum Cascade Cooler under a bias of 0.2 V.

Results

Theoretical and experimental evidence of anti-correlated oscillatory behavior of the electron temperature in the quantum wells.

Clear link established between the polar optical phonon energy $\hbar\omega_{LO}$ and the period of the oscillations.

Electron cooling of several tens of Kelvin achieved.

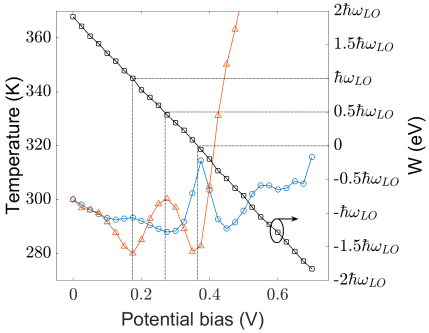

Fig. 2: Electron temperatures in the quantum wells as a function of bias. Energy difference W between the quantum wells ground state (black line).

Perspectives

Experimental evaluation of the lattice temperature.

Exploration of the cooling capabilities upon optimization.

References

[1] G. Etesse *et. al.* Phy. Rev. Appl. (accepted 2024)

[2] M. Bescond *et.al.* Phy. Rev. Appl. 17, 014001 (2022)

[3] A. Shastry *et.al.* Phy. Rev. B 94, 155433 (2016)

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Quantum and Molecular Tech.

Axis

PEPR MoleculArXiv (2022-2029):
Massive Data Storage on DNA and Artificial Polymers.

Anthony Genot, Sona Roy, Paul Bruand, Yannick Tauran, Elias Boudjella, Robin Deteix, Gwenael Bonfante, Axel Levy

Hosted in S.H Kim Lab

Keywords: DNA data storage, DNA synthesis, DNA sequencing, microfluidic platform

Context

Data storage is crucial in our society: exabytes of data are generated every year in France (communication, culture, finance, politics, industries, etc.) and the "digital universe" will grow to over 175 zettabytes (10^{21}) in 2025.

Current data warehouses use electronic, magnetic and optical media, which have limited durability and density. DNA, on the other hand, is extremely dense and stable, but it is currently costly and slow to synthetize.

Objectives and Methods

Write 1 unique bit per second (100x faster than currently)

Write 10GB of data in 24 hours with off-the-shelf parallelization

How?
Making synthesis fast and scalable (WP1&3)
Making storage efficient and secure (WP2)
Making DNA storage practical (WP4)

PEPR MoleculArXiv at a glance: an interdisciplinary project

ICS, IS2M	IPMC, ICR SACS, IGBMC	IRISA, I3S, LaTIM, LIP
POLYMER CHEMISTRY	SEQUENCING TECHNOLOGIES	BIOINFORMATICS
DNA&ENZYMES CHEMISTRY	MICROFLUIDIC & INTEGRATION	SIGNAL THEORY
Gulliver, UMR3523, UMR3528	LIMMS, LIP, LAAS, LMI	I3S, EURECOM, IRISA Lab-STICC

- 20M€ over **84 months**
- **LIMMS** is at the forefront of experimental implementation.
- **16 French laboratories**, including **6 flagship labs**

Perspectives

- Maturation of technology
- Collaboration with FR and JAP industrials
- Application to Japanese maching funds.

Publications/References

[1] Okumura et al., Nature, 2022

[2] Genot et al., Nature Chemistry, 2016

[3] Lobato et al., Nature Chemical Engineering, 2024

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Additive Manufacturing to Control DNA Hydrogels Spatial Organization.

Audrey Cochard, Vincent Salles, Yannick Tauran

Hosted in SH Kim Lab / BJ Kim Lab

Funding:
Internal project 2023

Keywords: DNA nanotechnology, DNA hydrogels, 3D printing.

Context and Objectives

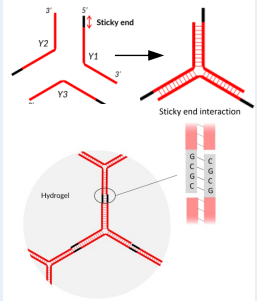
DNA hydrogels are interesting tunable and biocompatible materials.

Controlling the spatial organization of DNA hydrogels would be an interesting asset and would have applications in tissue engineering, artificial organs… However, it remains a challenge.

In this project, we combine the expertises of the SH Kim Lab in DNA hydrogels design and of BJ Kim Lab in 3D printing to develop a method to spatially control the organization of DNA hydrogels.

Method

To build DNA hydrogels, we use three complementary DNA strands able to form Y-motifs [1]. Through sticky-end interactions and Y-motifs binding DNA hydrogels are formed by phase separation (Fig. 1)



Molding methods were used in recent papers to form DNA gels with predefined shapes [2]. Here, additive manufacturing is used to have a more precise control (Fig. 2).

Figure 1: Formation of DNA hydrogels

Results

Predefined structures were obtained through additive manufacturing of DNA hydrogels.

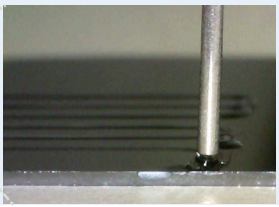


Figure 2: Experimental setup to print a DNA hydrogel with a predefined structure

Perspectives

We are currently working on improving the system to be able to create finer structures.

References

[1] Y. Sato et al., Sci. Adv. 2020

[2] J. Lee et al., Nature Nanotechnology, 2012

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Thermodynamic and Rheological Analysis of DNA Hydrogels.

Hajar Ajiyel

Hosted in SH Kim Lab

Keywords: DNA nanotechnology, design, calorimetry, rheology, soft matter

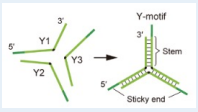
Fundings:
Internal project 2023
Internal project 2022
CNRS PhD grant

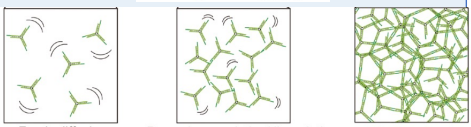
Context and Objectives

This project is a collaboration between labs in France (Grenoble and Lyon) and Tokyo. While state of the art research has primarily focused on the formation of DNA hydrogels [1], less attention has been paid to understanding their thermodynamic and rheological properties in relation to their sequence design. Our objective is to bridge this gap by investigating how the characteristics of DNA hydrogels relate to their design, conducting a comprehensive study across various scales. We anticipate that the insights gained from this study will have broad applications in fields such as therapeutics and biosensing.

Method

Design DNA sequences forming hydrogels, and study them with multiple techniques in calorimetry, and passive and active rheology

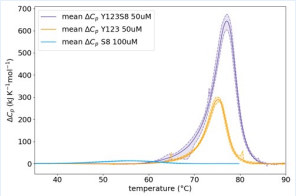




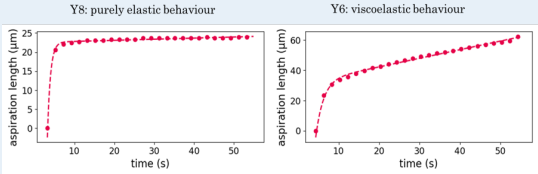
Formation of a DNA hydrogel from Y- shaped nanostars [2]

Results

An excess heat is generated when a DNA hydrogel is formed. Changing the length of the sticky end in the nanostars introduces different viscoelastic behaviors in the gel.



Specific heat of DNA hydrogel vs DNA nanostar



Micropipette aspiration experiment on different DNA hydrogel designs

Perspectives

Measure thermodynamic and rheological properties of DNA hydrogels with multiple techniques, to get a more comprehensive perspective of their behavior.

References

[1] Y. Sato et.al., Sci. Adv. 2020

[2] F. Li et.al., Progress in Polymer Science. 2019

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Ballistic Brownian Motion of Nanoconfined DNA.

Nicolas Clément

Hosted in S.H. Kim Lab

Fundings:
EU Attract Unicorn Dx
ANR SIBI

Keywords: Charge transfer, Electrodes,Genetics, Mathematical methods, Nanoconfinement

Context and Objectives

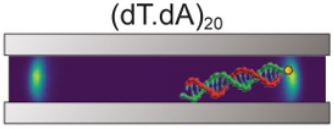
Theoretical treatments of polymer dynamics in liquid generally start with the basic assumption that motion at the smallest scale is heavily overdamped; therefore, inertia can be neglected. We report on the Brownian motion of tethered DNA under nanoconfinement, which was analyzed by molecular dynamics simulation and nanoelectrochemistry-based single-electron shuttle experiments.

Method

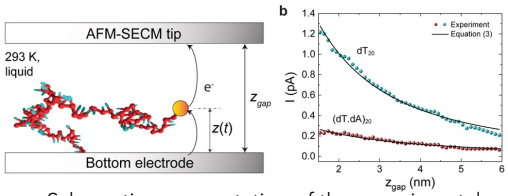
We introduce a new code (QBIOL) combining molecular dynamics of DNA (OxDNA) and quantum processes with stochastic electron transfer to a redox marker. These simulations are used to reproduce electrochemical experiments performed with an AFM-SECM microscope with precise nanogap.

Results

Our results show a transition into the ballistic Brownian motion regime for short DNA in sub-5 nm gaps, with quality coefficients as high as 2 for double-stranded DNA, an effect mainly attributed to a drastic increase in stiffness. The possibility for DNA to enter the underdamped regime could have profound implications on our understanding of the energetics of biomolecular engines such as the replication machinery, which operates in nanocavities that are a few nanometers wide [1,2].



Schematic representation of the system under study. A tethered ds-DNA nanoconfined between two electrodes. The heat map represents the position of the redox marker.



a Schematic representation of the experimental setup. **b** Experimental result of current as a function of the gap for ssDNA and dsDNA.

Perspectives

Qbiol is being transferred via a prematuration program of CNRS for softwares. We plan to further investigate this ballistic Brownian motion regime via shot noise measurements.

References

[1] I. Madrid, Z. Zheng, C. Gerbelot, A. Fujiwara, S. Li, S. Grall, K. Nishiguchi, S.-H. Kim, A. Chovin, C. Demaille, N. Clement, *ACS Nano* 17, 17031 (2023)

[2] Z. Zheng, S. Grall, S.-H. Kim, A. Chovin, N. Clement*, and C. Demaille*, *J.Am.Chem.Soc.* 146, 6094 (2024)

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Towards Multiplexed Electrochemical Single-cell Aptasensor Array.

Shuo Li

Host Lab S. H. Kim Lab

Fundings :

JSPS, NTT, EU ATTRACT 2

Collaborators:, N. Clément, S. Grall, S. H. Kim, H. Y. Dai (IIS, Utokyo), C. Lagadec (Inserm), Y. Coffinier, F. Cléri (IEMN), L. Jalabert, K. Nishiguchi, A. Fujiwara (NTT corporation), C. Demaille (CNRS, LEM)

Keywords: Nanobioelectrochemistry, cancer cell, Micro/Nano fabrication

Context and Objectives

Electrochemical (EC) aptasensor is very attractive for detecting and monitoring interactions with biological objects because of the high sensitivity, easy operation, low-cost, and benefit from ultimate scaling.

By using redox-labelled EC aptasensor, it enables to envision measurements and theory at the single-virus scale as well as statistical analysis on larger objects such as circulating tumor cells (CTCs). Here, a novel single-cell EC aptasensor array was introduced and opens new opportunities for ultra-sensitivity and selectivity of early cancer diagnosis and therapy.

Methods and Results

-A μm-scale gold surface (Au/Si) array was fabricated to graft ferrocene modified aptamers (SYL3C-Fc) to check the signal.

-Fabricating and achieving single-cell EC aptasensor array device. (All of the fabrication processes is developed in Utokyo, Nanostructure is obtained by using high resolution e-beam lithography.)

-The single-cell EC aptasensor was first time performed. A final sensor configuration is a nanoarray with multiplexed electrodes, towards multiple signal analysis at single-cell level

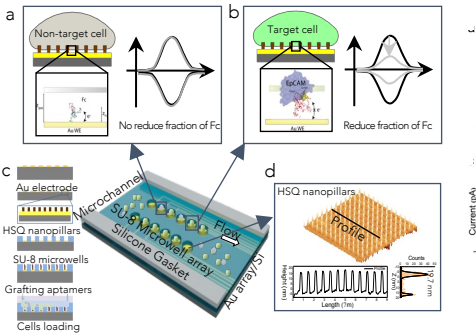

Figure 1. Principle of the single-cell EC aptasensor array.

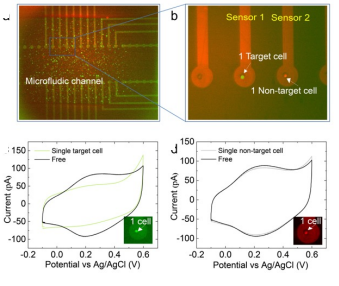

Figure 2. CV results to show the selectivity of the device.

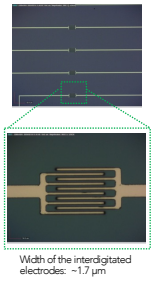

Figure 3. Photo of the multiplexed electrodes.

Perspectives

-This novel single-cell EC aptasensor offering unprecedented statistical analysis of CTC in clinical settings.

-The next gerneration device would be realizing multi-electrodes for multi-target detetion and 10 nm scale nanodots array biosensors for single molecule-single cell analysis.

Publications/Reference

[1] S. Li et al. Biosens. Bioelectron. 216, 114643, (2022).
[2] S. Li et al. ACS Sens. 8(8), 2921 (2023).
[3] K. Chennit et al. Nano. Res. 1-7. https://doi.org/10.1007/s12274-022-5137-1, (2023).

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Nanoelectrochemical Biosensors Simulation.

Simon Grall

Host Lab S.H Kim Lab

Collaborators: :, N. Clément, S. H. Kim, S. Li (IIS, Utokyo), L. Jalabert (LIMMS), K. Nishiguchi, A. Fujiwara (NTT corporation), C. Demaille (CNRS, LEM), T. Fukuba (JAMSTEC).

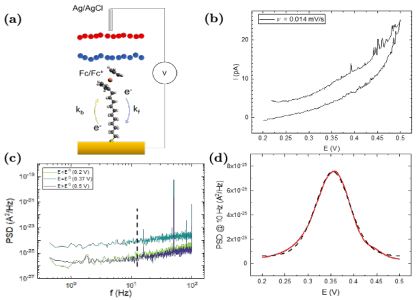
Fundings :
ANR SIBI, NTT,
EU ATRRACT

Keywords: Nanoelectrochemistry, shot noise, high-frequency, environmental sensing, energy harvesting

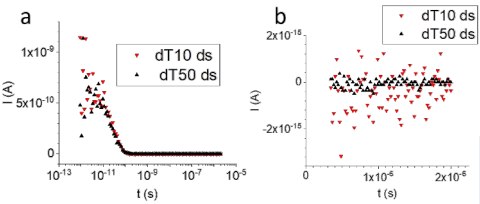
Context and Objectives

The concept of electrochemical shot-noise [1] opens up potential avenues for enhancing electrochemical sensors, offering promising prospects for nanoscale biosensor measurements. Leveraging the current understanding of GHz electrochemistry [2-3] and the recent advancements demonstrating low reorganization energy in confined polymers [4], we are optimistic about the possibility of creating devices like single molecule sensors and molecular rectennas operating at optical frequencies.

Electrochemical shot noise



(a) FcC11SH SAM on gold. (b) CV of a FcC11SH SAM on gold. (c) Noise spectra measured at 0.014 mV/s (d) Noise versus potential at 10 Hz.

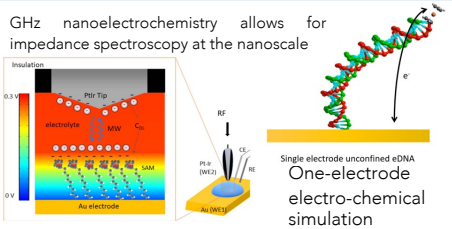


These two double-stranded (T sequences) have different lengths. They carry the same electrochemical marker. Though they show similar currents during a chronoamperometric measurement (a), they exhibit different noise signature (b).

Methods

To better fathom the limit of single-entity measurement foreseen thanks to noise and GHz measurements, we are developing a simulation framework to simulate stochastic fluctuation of charges for one-electrode electrochemical systems in the on-going project QBIOL.

GHz nanoelectrochemistry allows for impedance spectroscopy at the nanoscale



One-electrode electro-chemical simulation

Results

QBIOL already helped to solve the riddle of apparent slow DNA diffusion with a two electrodes framework [5], and is now on track to account for stochastic fluctuation in the time-dependant one-electrode case. This work allows to simulate electrochemical measurement techniques (square wave, CV, chronoamperometry) of single molecules and help understand their stochastic behavior in the frequency domain (noise).

Perspectives

It already provides useful insights for experimentalists developping DNA biosensors. More work is needed to simulate a wider variety of molecules and fully develop analytical models for the simulated noises. In the future, it will provides a digital experiment platform able to simulates devices from nano-biosensors to molecular rectennas.

Publications/Reference

[1] S. Grall et al, Phys. Rev. Lett., 2023
[2] J. Trasobares et al, Nat Commun, 2016
[3] S. Grall et al, Small, 2021.
[4] I. Madrid et al, ACS Nano, 2023
[5] Z. Zheng et al, JACS 2024

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Versatile Electrospun Nanomesh for Robust Skin Electrodes.

Dorina T. Papanastasiou

Hosted in Someya Lab

Keywords: e-skin, smart textiles, soft-rigid interconnection, mechanical properties

Funding: JSPS Postdoctoral Fellowship for Research in Japan (Standard)

Context and Objectives

Skin is the largest organ of human body with electrical properties of great interest for a large variety of applications[1]. Recording these properties can provide information for the thermoregulation or other stimuli to further diagnose the skin condition, as well as psychophysiological state[2]. Despite the extended biomedical research, there are unclear aspects requiring long-term monitoring that cannot be achieved using conventional electrodes.

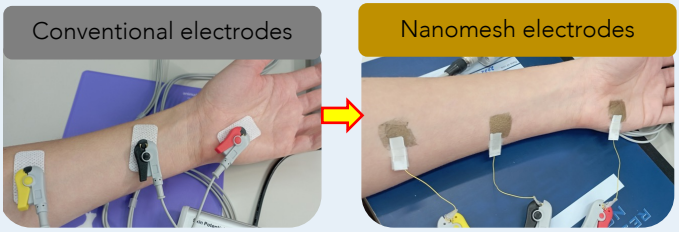
Skin electronics advances are remarkable, however there are remaining issues that hinder the integration of novel electrodes in commercial skin devices. One of the most important is the interconnection between soft, ultra-thin electrodes and data acquisition hard wiring. [3]

Method

Previous works of Someya Lab have demonstrated state-of-art, ultra-thin, skin-conformable, and bio-compatible electrodes, using scalable deposition techniques, i.e., organic electrospun nanofibers [4].

The present project has been focusing on remaining interface issues between soft and rigid parts, and the integration of nanomesh electrodes in textile-based substrates. Developing robust interconnections can contribute to the next-generation wearable devices with personalized healthcare features [5].

Results



References

[1] Kim et al., Adv. Funct. Mater. (2021), 31, 2009602

[2] Tronstad et al., Physiol. Meas. (2022), 43, 02TR01

[3] Jang et al., Nat Commun, (2022), 13, 6604

[4] Miyamoto et al., Adv. Healthcare Mater. (2022), 11, 2102425

[5] Papanastasiou et al., article under preparation

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A Camera System for Real-Time Monitoring Continuous Fluorescence Changes.

Yui Sasaki & L. Jalabert

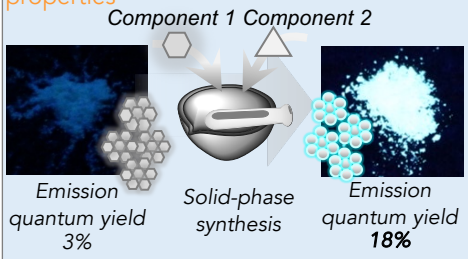
Hosted in Minami Lab & Nomura Lab

Keywords: Fluorescent materials, Real-time monitoring, Imaging analysis

Funding: Internal project 2023

Context and Objectives

Research background: Design of solid-state fluorescent materials with unique properties



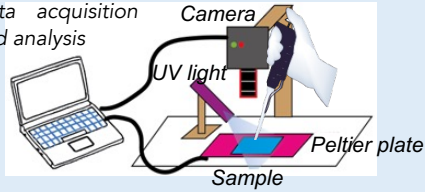
The obtained products show different fluorescent color depending on chemical structures and solvents.

Method

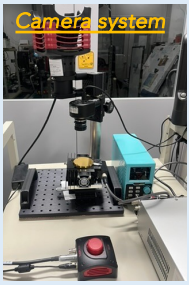
Time-dependent optical changes

This study

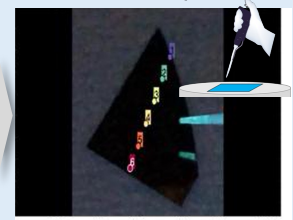
A camera system for the investigation of time- and temperature-dependent fluorescence properties



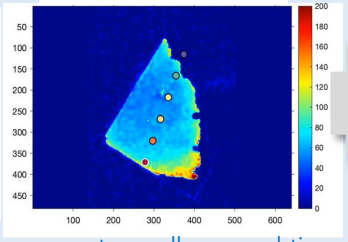
Results



Selection of points



Obtained pixel intensity

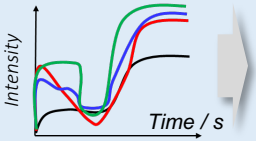


Data analysis

The developed camera system allows real-time monitoring of continuous fluorescence changes.

Perspectives

Real-time monitoring results



Collaboration with S.Chevalier group (U-Bordeaux) for analysis of kinetics

Discovery and investigation of new phenomena of functional materials

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Bio

Axis

Spiking Neural Network for Unsupervised Spike Sorting in Real-Time on FPGA.

Jérémy Cheslet

Hosted in Ikeuchi Lab

Keywords: Spike sorting, SNN, STDP, FPGA, real-time, HD-MEA

Fundings:
ANR BRAIN-Net
UBGRS 2.0
(ANR-20-SFRI-0001)

Context and Objectives

Neural prosthetics are potential treatments for neurodegenerative diseases, but it requires deep understanding of neural populations [1].

Spike sorting is an operation that extract important features from neural-recordings while considerably reducing the amount of data to save.

However, low-power, accurate, real-time spike sorting is still a challenge [1].

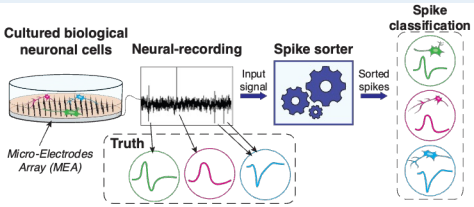


Fig.1 – Principle of spike sorting: find which neurons are spiking in the neuronal culture.

Method

Inspired from [2], we implemented a 3-layer SNN on FPGA. [3] shows a preliminary version for low-cost spikes/bursts detection.

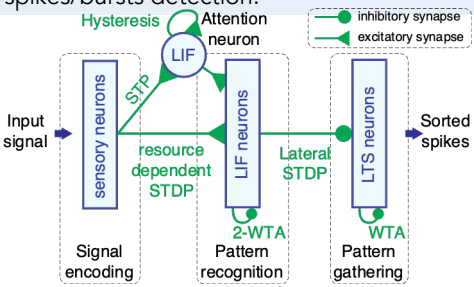
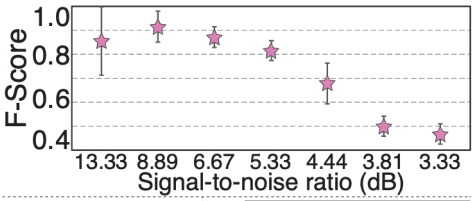


Fig.2 - Structure of the SNN

Results

The SNN sorts with an accuracy on par with offline methods after a few minutes of unsupervised training.

It processes in real-time at low-power due to its low hardware consumption.



AMD Kria KR260 board

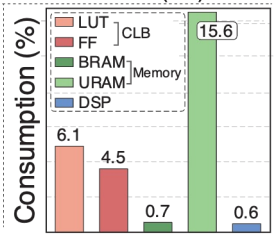


Fig.3 – Results on AMD K26 SOM

Perspectives

Use HD-MEA data to further improve the spike sorting accuracy.

Perform bio-hybrid experiments.

References

[1] Zhang et al, J. Neural Eng., 2023
[2] Bernert et al, Int J Neural Syst., 2018
[3] Cheslet et al, IEEE BioCAS, 2023

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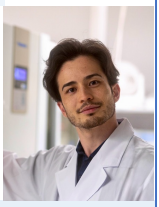
Understanding Human Brain Mechanisms Through Organoid Circuit Modeling.

Tomoya Duenki

Hosted in Ikeuchi Lab

Keywords: Neuroengineering, neural organoids, human pluripotent stem cell derived neuron, optogenetics

Fundings:
Spring GX Fellowship
ANRI Fellowship



Context and Objectives

Limited access to a living human brain tissue has made it very difficult to study it. Recent advances in stem cell biology has led to the discovery of neural organoids, which are artificially grown miniature organ-like tissues resembling the brain. This model recapitulates key features of the brain and has opened up new possibilities to study development, function and dysfunction of human brain cells in a dish.

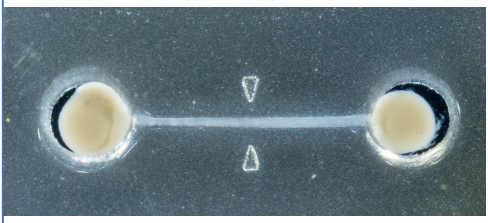


Fig. 1: Image of connected neural organoid in a microfluidic device.

Method

I create custom-made microfluidic devices that can guide axonal outgrowth of neurons between organoids. By doing so, I can control neural circuit formation, connect two neural organoids with a thick axon bundle. The connected organoids are plated on electrode arrays which allows me to monitor the electrical activity of the living neurons in the organoid. With optogenetic stimulations, I can control neural activity of cells and study response of neurons and signal propagation within and between organoids.

Results

We show that :
- Organoids in microfluidic devices can connect to each other via axon bundles.
- Connection between organoids show signal exchange and propagation.

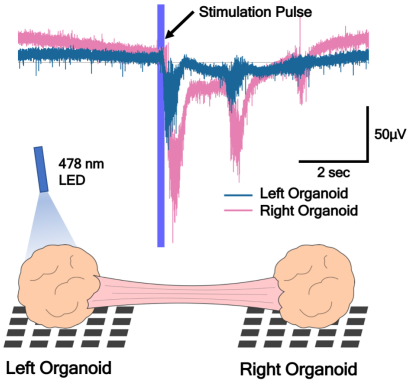


Fig. 2: Connected organoid on an electrode array. Optogenetic stimulation of the left organoid induces a burst. The initiated burst propagates to the connected right organoid, which also starts to burst with a time delay.

Perspectives

We connect different tissues and create circuits present in our body in order to build new platforms that can be used to study mechanisms of our nervous system.

References

[1] Osaki, Duenki, Chow et al., Nat. Commun., 2024

[2] Ikegami, Duenki et al., Front. Bioeng. Biotechnol., 2024

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Deciphering Neuron/ Breast Cancer Cell Interactions to Understand Metastasis.

Robert Alain Toillon

Hosted in Ikeuchi Lab

Funding:
Internal project 2023

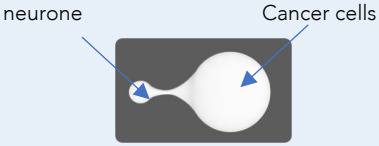
Keywords: Microdevice, neuron, breast cancer

Context and Objectives

Despite progress in the management of breast cancer, the development of metastases has a poorer prognosis [1]. It is therefore necessary to develop systems for studying the behavior of cancer cells during the development of metastases, and in particular the interactions between cancer cells and their environment [2]. In collaboration with Professor Ikeuchi's laboratory (Japan), the CANTHER laboratory (France) is seeking to set up a system for studying breast cancer cells and neurons in order to study the relationship between the 2 cell types.

Method

We used custom-designed compartmentalized chamber systems to study chemotaxis between triple-negative breast cancer cells and neurons. In this system, we were also able to study axonal growth and changes in membrane potential in neuronal cells as a result of their excitability.



A compartmentalzed chamber

Results

Under these conditions, we were able to observe that neurotrophin receptor overexpressing- cancer cells have an increased capacity to interact with neurons and are able to migrate along axons (Figure 1). In addition, we were able to demonstrate activation of intracellular signaling in cancer cells by FRET experiments using RhoA biosensors [3,4].

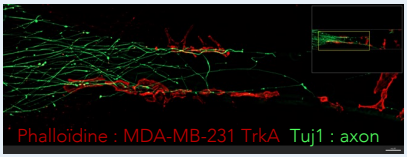
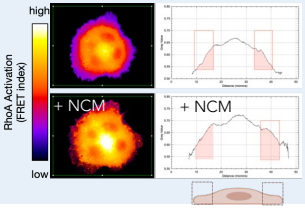


Figure 1: Migration of triple-negative breast cancer cells (MDA-MB-231) along the axon.

Figure 2: Activation of RhoA measured by Fret biosensor in MDA-MB-231 cells in presence of neuron conditioned media (NCM)



Perspectives

After highlighting the phenotypes induced by cancer cells in neurons and vice versa, we are going to study the importance of these in the mechanisms of metastasis in order to find either inhibitors that would act against metastatic development or predictive markers of metastasis, enabling better monitoring of patients at risk.

References

[1] Deluche *et al.*, Eur J Cancer, 2020.

[2] Cicero *et al.*, Exp. Hemat. & oncol, 2023.

[3] Pertz *et al.*, Nature, 2006.

[4] Trouvilliez et al, JECCR, 2022.

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Microstructuring of Resorbable Scaffolds for Vascularized *in-vitro* 3D Tissues.

Vincent Salles

Hosted in BJ Kim Lab

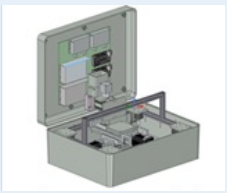
Keywords: Direct-write electrospinning, resorbable and functional scaffolds, tissue engineering

Context and Objectives

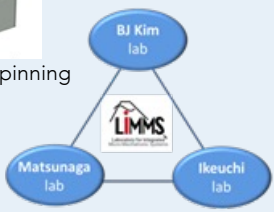
The proposed approach consists in creating in vitro, using resorbable materials, an architecture of interconnected vessels and micro-vessels connected to a microfluidic system to continuously feed the vascular system via which it will be possible to feed the cells positioned around. On a long term, complex architectures could be implanted and sutured to the patient's vascular system.

Method

The fabrication process of the scaffold is based on a combination of a 3D printer and an electric field applied between a nozzle and a printing stage. For this project, a peculiar machine was designed and supplied. This project is carried out in collaboration with 3 host-labs, as shown below.



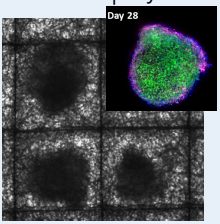
Direct-write electrospinning



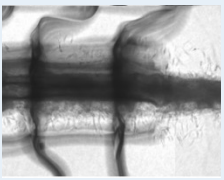
Involved collaborators

Results

A series of novel resorbable architectures were developed to prepare permeable sacrificial scaffolds. On the fabrication point of view, several useful patterns have already been produced (in 2D and 3D). These structures were tested separately with endothelial cells and neuronal cells to investigate the ability to produce new blood vessels and neural tissue, respectively. Different tests are used to optimize the preparation of the scaffold and the cell culture conditions. These preliminary results were obtained by using PCL (Polycaprolactone) as resorbable polymer.



Organoids in a grid of resorbable polymer



Vessel of endothelial cells through the grid

Perspectives

Gradually increase the complexity of cellular organisation.

References

[1] L. Bourdon *et al.*,J. Funct. Biomater. 2023, 14, 263

[2] C. Xu *et al.*, Biomed. Microdevices 2023, 25, 32

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A Biohybrid Neurocardiac Platform for Electroceutical Approach.

Pierre-Marie Faure

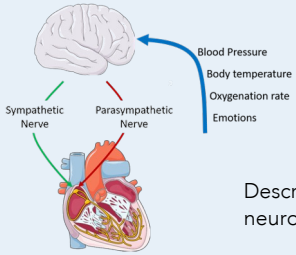
Hosted in Tixier-Mita Lab

Keywords: Cardiomyocyte, Real-time, Biohybrid, FPGA

Fundings:
Fondation Sasakawa
Région Nouvelle-Aquitaine

Context and Objectives

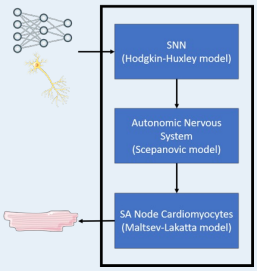
To investigate the neurocardiac axis involved in cardiovascular diseases, we are developing an electronic platform that reproduce the interaction between the brain and the heart in real-time.



Description of neurocardiac axis

Method

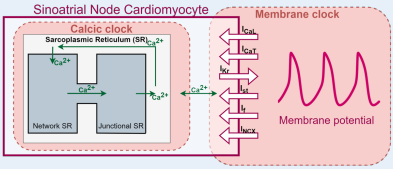
We target our implementation on FPGA to achieve real-time necessary for biohybrid applications. The chosen models are biological accurate to obtain a realistic description of involved phenomenon.



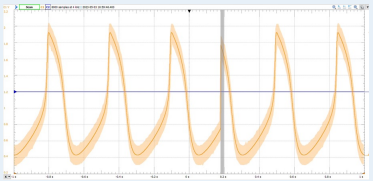
Layers of the platform, the input can be artificial neuronal network or biological neurons while output is a cardiomyocyte culture.

Results

We achieved to develop the sinoatrial (SA) node part on FPGA and using it to stimulate cardiomyocytes and trigger their beatings. In addition, the autonomic nervous system layer is able to interact with SA Node.



Implemented model of Maltsev-Lakatta on FPGA



Output signal generated in real-time

Perspectives

The different parts of our platform are developed. The next step is their combination to achieve the platform. After that, we aim to use it in experiments to connect biological cardiomyocyte with neurons culture.

References

[1] Maltsev & Lakatta, American Journal of Physiology-Heart and Circulatory Physiology, 2009

[2] Šćepanović, Massachusetts Institute of Technology, 2011

[3] Faure P-M., Tixier-Mita A., Lévi T., 29th AROB'2024, Beppu, Japan, Jan. 24-26 2024.

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Automatization of 2D Bio-Impedance and Cardiomyocyte Activity Investigation.

Alexis Mallet, Juliette Flamant, Romane Kessedjian & Thomas Menier

Hosted in: Tixier-Mita Lab

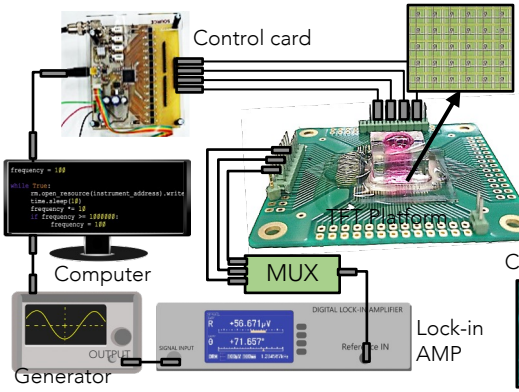
Keywords: Cardiomyocyte, bio-impedance, Nifedipine, PLL coating

Context and Objectives

Cardiovascular diseases are the first cause of death in the world. In order to investigate further heart diseases and find new treatments, it is essential to study the mechanism behind. Given the constraints on in vivo experiments and the ethical considerations involved, there is a compelling rationale for exploring in vitro approaches. The primary objective of the research presented here is to develop a platform to measure the multiple electrical and biochemical parameters involved in in-vitro heart cell culture. Here, automatization of 2D bio-impedance measurement to monitor cell culture and cell activity control are presented.

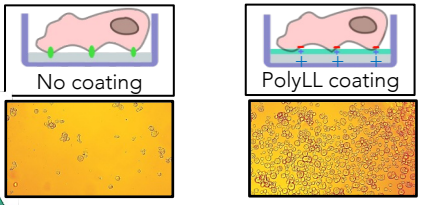
Methods & Results

The platform consists in an active matrix of microelectrodes controlled individually by switch transistors, and based on Thin-Film-Transistor technology. Thanks to the transparency and multitude of microelectrodes, simultaneous optical and electrical measurements can be performed. The microelectrodes are controlled by a control card. Bio-impedance measurements is automatized by a Python program. PLL coating is used to improvement cardiomyocyte cell attachment. Then, experiments of control of cell activity using Nifedipine chemical is performed. Ca^{2+} is the link between electrical signals in heart and contraction of cardiomyocytes. Nifedipine is a Ca^{2+} channel blocker which can modify cell contraction.

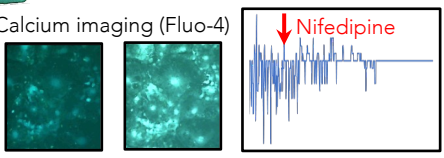


Automatisation of 2D bioimpedance measurements

Improvement of cell attachment with coating



Cell activity control with Nifedipine



No Nifedipine | With Nifedipine | amplitude of cell contraction with time.

Perspectives

Bio-impedance measurement will permit to monitor cell culture, and possibly to measure in real-time the contraction of cells. It will be confirmed by simultaneous optical observation and electrophysiology.

References

[1] Menier T. et al, "Open-source Live-Tracking Software for Cardiomyocyte Cells Analyses", Sensor Symposium'2023, Nov. 6-9 2023.

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Compact Microscope for Long Term Experiments.

Alex Dufour, Théo Foschia

Hosted in Tixier-Mita Lab

Keywords: Raspberry, arduino, real-time observation, dielectrophoresis

Context and Objectives

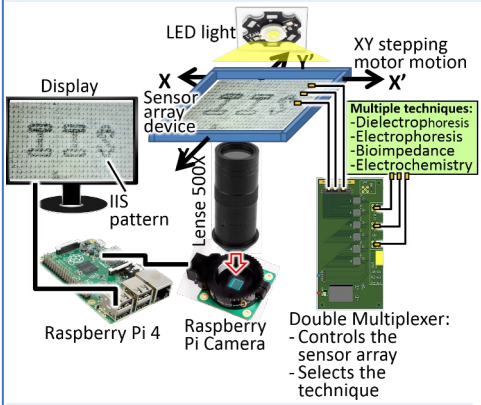
Incubators reproduce the optimal conditions for in-vitro cell culture and limits contamination. However, for practical reasons, cell culture analyses are usually performed outside the incubator, which modifies the cell environment. This is especially true for long term measurements. Here we propose to develop a compact microscope platform which will permit at the same time optical and electrical measurements (impedance, electrophysiology, dielectrophoresis).

Method

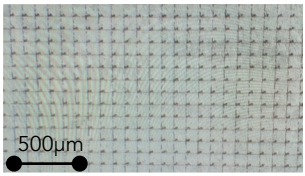
The compact microscope platform is inspired from [1]. It is composed of a 100X to 600X lens attached to a Raspberry Pi Camera, an XY stage moved by stepping motors and an LED light. They are all controled by a Rapberry Pi, in which a custom Python program has been implemented. It will be combined with a multiplexer system able to select various electrical measurement methods.

Results

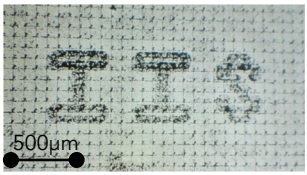
A first prototype of the microscope has been realized. It was applied to dielectrophoresis with microbeads. Further development is next necessary for long term compatibility with the high humidity of the incubator.



10µm microbeads placed on a Thin-Film-Transistor paltform



Dielectro-phoresis by applying an AC signal: 2V, 10kHz



Perspectives

This project is a key element of a wider project which purpose is to create an in-vitro model of the brain-heart system. Interactions at the cell and tissue level will be investigated especially when heart disease are mimicked. For that purpose a multimodal sensing platform will be realized, combining optical and multimodal electrical sensing.

References

[1] IBM MicroscoPy: https://github.com/IBM/Microscopy

[2] Eiler A-C., IEEE TED, Vol 68(4), April 2021.

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Microvessel-On-Chip for the Study of Intratissue Solute Transport.

Daniel Alcaide

Hosted in Matsunaga Lab

Keywords: Microfluidics, Vasculature-on-chip, Microvessel (MV), Permeability, Hydrogel, Brain, Glymphatic system

Fundings:
WINGS – QSTEP
University of Tokyo

Context and Objectives

The mechanisms through which neural waste and other toxic molecules are removed from the brain is not fully understood due to the lack of lymphatic vasculature in the brain. The current model, named glymphatic model, proposes arterial pulsation fluid motors that create the cerebrospinal fluid flow removing the waste from the tissue.

We aim to replicate the basic elements of the glymphatic model *in vitro* to study how the arterial pulsations can create such flows in a brain-like soft material.

Method

We fabricated a microfluidic device that hosts two in vitro MVs, one artery and one vein, suspended in a hydrogel. These MVs can be connected to a pressure controlling device to generate customizable arterial pulsations.

We observed how different settings of periodic pressure push and move fluorescent molecules in between the artery and vein

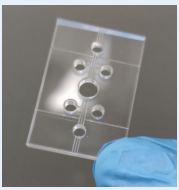

Figure 1 – Picture of the microfluidic device

Results

We observed the displacement of fluorescent dextran molecules due to MV pulsation. Different frequency and pulsation amplitude were tested. However, MV deformation and permeability seem to have a stronger relation to the type of fluid movement observed in the device. Brain-like, low permeability MV, induce a deformation-driven recirculation, likely relevant to the glymphatic model scope.

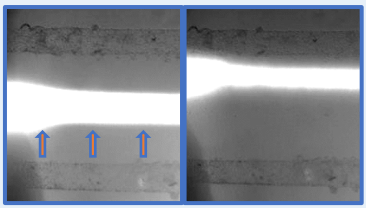

Figure 2 – Fluorescence picture of middle area of the device the two MV and FITC-Dextran displaced by pulsations of the bottom MV.

Perspectives

This device allows virtually for the visualization of interstitial fluid recirculation of virtually any organ. We look forward to expand its application further than brain parenchymal transport.

References

[1] - Iliff J. *et al.* Science Translational Medicine, 2012.

[2] - Soden P. *et al.* Advanced Biology, 2022.

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Physical Properties of an Artificial Microvessel System.

Baptiste Alric

Hosted in Matsunaga Lab

Keywords: Microfabrication, Organoid, 3D-cells culture, Physical properties quantification

Fundings:
IIS
JSPS fellowship

Context and Objectives

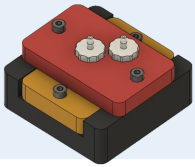
Our project aims to improve our understanding of the physical properties of artificial microvessels and their surrounding microenvironment.

Our goal is to develop more accurate organ-on-a-chip models. To realize that we are working closely with partners in both Japan and France to establish various cellular models and to develop unique methods to qualify these physical properties.

And we are showing that those physical properties are particularly important in the microvessels physiology.

Method

In our research, we use homemade microfluidic chips to fabricate our microvessels Fig1[1]. To achieve this, we use acupuncture needles to create channels within hydrogels - a type of protein-based gel consisting of 90% water - in which we can cultivate our endothelial cells in a channel shape. After establishing our system, we use various methods to extract the physical properties of these vessels[2,3].



Results

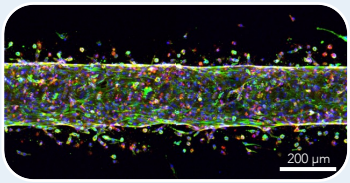


Fig.1 Artificial microvessel of HUVECs imaged by confocal microscope, the cell membrane is green, the cytoplasm is red, and the nucleus is blue.

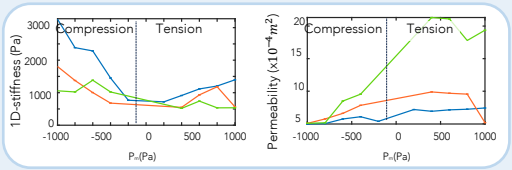


Fig.2 Physical properties extracted from different acellular hydrogels using a pressure measurement assay combined with a mathematical model [2]. These graphs show a clear asymmetry in the response of the hydrogels between compressive stress (negative pressure) and tensile stress (positive pressure).

Perspectives

These models not only facilitate a deeper understanding of various biological phenomena, but also aid in the development of drug screening processes to identify effective treatments for specific diseases.

References

[1] Pauty et al, 2018., EBioMed. 2018

[2] Cacheux et al ., Sci. Adv. 2023

[3] Cacheux et al ., ISci. 2023

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SOI-CMOS Large-Scale Integrated Circuit for Particle Detection.

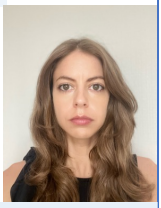
LIMMS
Laboratory for Integrated Micro-Mechatronic Systems
LIMMS/CNRS-IIS IRL 2820

Anne-Claire Eiler

Hosted in Mita Lab

Keywords: CMOS, silicon on insulator (SOI), large-scale integrated (LSI), coulter counter

Fundings:
JST CREST
JSPS Core-to-Core
MEXT X-nics
ARIM

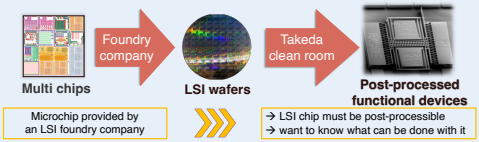


Context and Objectives

Large-scale integrated microchip for coulter measurement, using the SOI technology for faster switching and better performance:

- array of 320 electrodes
- electrode size: 44.0 µm x 36.4 µm
- sensing array: ~1.02 mm x 0.81 mm
- pitch: 51 µm

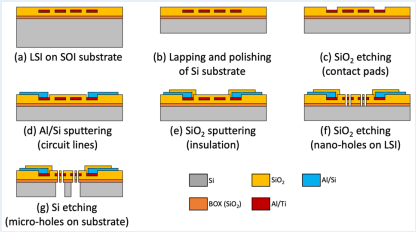
~386 electrodes/mm^2



Microchip from design, fabrication, and post-processing for desired applications

Method

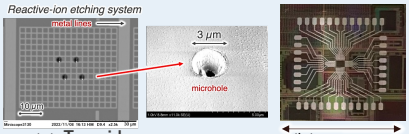
Post-processing on matrices of electrodes controlled by transistors integrated by LSI in open cleanroom facility.



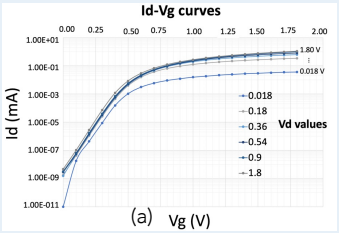
Post-processing workflow for fabrication of a coulter counter: lapping, polishing, top side etching, deposition, back side etching

Results

Post-process and characterization:



Post-process on the LSI microchip:
a) top side etching of 3 um holes;
b) fully processed microchip



Electrical characterization of the integrated transistors:
a) drain current vs gate voltage with logarithmic scale;
b) electrical parameters of the transistors

Perspectives

Fabrication of a fully functional LSI microchip to be used as a counter coulter. Another fabrication could involve the development of an electrode array for electrophysiological measurements.

References

[1] Y. Mita et al., Japanese Journal of Applied Physics 56, 06GA03, 2017

[2] Y. Chen et al., Sensors and Actuators B: Chemical 213, 375-381, 2015

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Investigation of the Metabolic Syndrome Development Using Organ On Chip Technologies

Eric Leclerc

Host Lab Sakai, Nishikawa lab

Keywords: induced pluripotent stem cells, Organ-on-a-chip, Metabolic syndrome

Fundings:
JSPS 22H03934;
JPJSCCA20190006;
ANR 23-CE18-003503;
Chaire UTC/DOT

Context and Objectives

Metabolic Syndrome (MSy) has a prevalence ranging to 24.6–34.7% of the population in Japan in early 2000s and up to 36% in European countries. MSy is a complex disorder involving several tissues and organs and their interactions resulting in diabetes (individuals with MSy are 5 times more likely to develop type 2 diabetes) obesity, non-alcoholic fatty liver disorder (NAFLD has a prevalence between 50% to 90% in obese patients and in 30% to 74% in MSy patients), cardiac failure (up to 49%), blindness . In this project, we will develop **on organ-on-chip technology** to address these key challenges, to move a step closer towards understanding, diagnostics and therapies of metabolic syndrome.

Methods

We propose to

To build an innovant bio artificial organ research strategy in which human cell model will be used to generate a relevant systemic MSy model (Fig 1)

To establish a specific metabolic syndrome disease model with which we will track the heterogeneity and the kinetics of the disorders thanks to the bioartificial organ human physiopathology

To identify biomarkers and therapeutic solutions regarding the disease specificity using multi omic technology, advanced sensors and clinical data

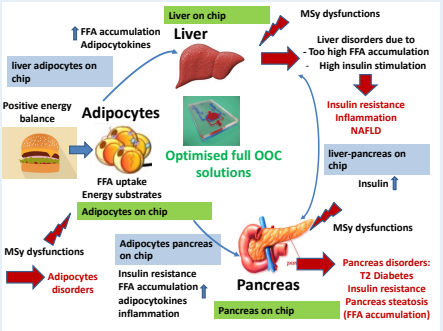

Fig 1: Metabolic syndrome concept using organ on chip

Results

We progressed on the liver and pancreas modules.

Human-induced Pluripotent Stem Cells (hiPSCs)-derived Liver Sinusoidal Endothelial Cells (LSECs), Hepatic stellate cells (HSCs), Hepatocytes-Like Cells (HLCs) were cultured and matured in a microfluidic environment. Liver maturation on chip was observed and subpopulation identification was performed (Fig 2).

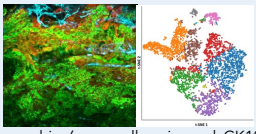

Fig 2: Liver on chip (green albumin, red CK19, blue PECAM1) and single sequencing clustering (Scheidecker et al., 2024)

Then, we proposed a protocol to differentiate hiPSCs into pancreatic-like-cells (created in 3D micro honeycombs). The protocol led to the development of spheroids producing C-peptide and containing cells positive to insulin and glucagon. Sequencing revealed complex heterogenous bi-hormonal profiles (Fig 3)

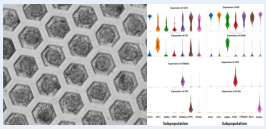

Fig 3: Beta like cells in honeycombs and bihormonal patterns (Morisseau et la., 2023)

Perspectives

The perspectives are the development of the adipocytes modules and the first test of liver pathology using the liver pancreas axis

References

Scheidecker et al., Biofabrication 2024, in press

Morisseau et al., Molecular omics, 2023

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Cryopreservation of IPSCs-Derived Liver Cells for Toxicological Studies.

Carla Meschini

Hosted in Sakai-Nishikawa Lab

Keywords: Cryopreservation, IPSCs, Organoids, Liver tissue

Fundings:
DOT Chaire
UTC (1/2)
Région des Hauts de France (1/2)

Context and Objectives

Among all *in vitro* models for toxicological studies, Induced Pluripotent Stem Cells (IPSCs) - derived cells constitute an alternative to primary cell lines regarding biomass availability [1]. However, the culture of this cell type is time-consuming and represent a significant financial cost.

The aim of this collaboration between the Sakai-Nishikawa laboratory and the Biomécanique et Bioingénierie laboratory (France, UTC) is to establish cryopreservation protocols for hepatic organoids, to provide readily usable biomass facilitating a broad range of applications such as high throughput drug screening or toxicological studies.

Method

IPSCs cells are differentiated into hepatocytes **using** carboxypeptidase M positive cells (CPM+ cells) sorting. **S**elected cells are seeded into PDMS honeycombs to **form** organoids [**2**].

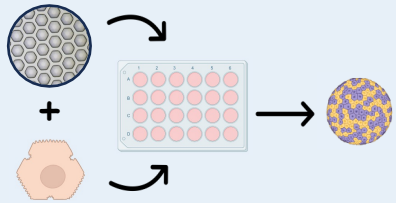
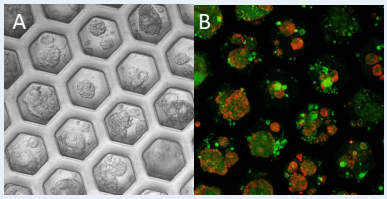


Fig 1 : Organoids formation using PDMS honeycombs technology (Created with BioRender.com)

Results



Microscopy photos of CPM+ cells in brightfield (A) and fluorescence showing albumin (red) and cytokeratin-7 (green) (B).

- 3D organoids 4 weeks cultures
- Hepatocytes/cholangiocytes markers
- Liver like hetereogeneous subpopulations
- Functional characterisations: Albumin, Bile, CYP450 assays Fatty acids metabolism

Perspectives

- Reproduce the protocol in France
- Controlled-rate slow freezing assay
- Comparison fresh vs freezing
- Functional and disease models

References

[1] M. Hussein et.al., Cells. 2023

[2] T. Utami et.al., Biotechnology and Bioengineering 2023

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Investigation of Non-Alcoholic Fatty Liver Disease by Organ-On-A-Chip.

Hanyuan Wang

Hosted in Sakai & Nishikawa Lab

Keywords: palmitic acid, hepatocyte like cells, organ-on-a-chip, fatty liver disease

Fundings:
JSPS grant-in-aid for scientific research (B) 22H03934; JPJSCCA20190006.

Context and Objectives

Non-alcoholic Fatty Liver Disease (NAFLD), a complex disorder with a high worldwide prevalence, is one of main cause of critical liver diseases. The lack of therapeutic solution of NAFLD leads to an unmet need to develop an efficient *in vitro* disease model to investigate its onset, propagation and the effects of drugs.

In our study, we tested the effect of palmitic acid, a dietary fatty acid, on hepatocyte like cells (HLCs) coupled with organ-on-a-chip technology. We plan to make an advanced NAFLD model with higher similarity to *in vivo* situations and better longevity, then apply it for pathological research and drug testing.

Method

HLCs were differentiated from human induced pluropotent stem cells[1]. After seeding in a microfluidic biochips [2] (Fig 1) HLCs took 7 days to mature under perfusion (Fig. 1). After maturation, the cells were exposed to 0.1 mM and 0.5 mM of palmitic acid (PA) for another 7 days to induce NAFLD.

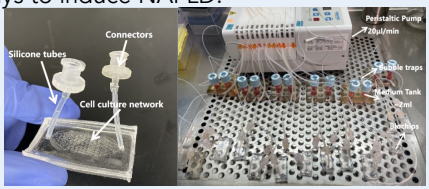

Fig 1:Photo of biochip and perfusion set up

Results

PA exposures modified cell morphology and 0,5 mM PA increased more collagen synthesis as shown in Fig. 2

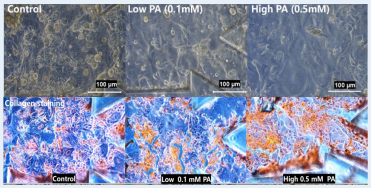

Fig.2 endpoint morphology & collagen staining

0.5 mM PA reduced lipidic genes expression and down regulated related pathways as shown in Fig 3.

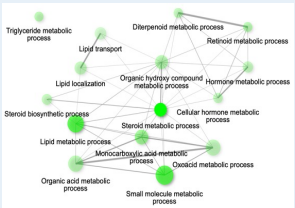

Fig.3 down regulated processes in 0.5 mM PA

Perspectives

1) longer maturation and longer exposure;

2) tri-culture model with stellate cells and endothelial cells;

3) mixed fatty acids to indice NAFLD.

References

[1] **Danoy**, **M**. et al. Biochemical Engineering Journal. 2022

[2] Baudoin, R. et al. Biotechnology Progress. 2007

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Investigation of the Liver Endothelium Inflammation During Steatosis.

Hanyuan Wang, F. Soncin, Y. Sakai, E. Leclerc

Hosted in Sakai & Nishikawa Lab/ SMMiLE

Keywords: Liver model, organ-on-a-chip, fatty liver disease

Fundings:
Internal Project 2023
JSPS 22H03934;
JPJSCCA20190006.

Context and Objectives

It is estimated that around 24% and 30% of European and Asian adults develop NAFLD, 10-30% of them will evolve to the most severe form of NAFLD, i.e. non-alcoholic steatohepatitis (NASH), among which 10-15% will develop liver outcomes (fibrosis). Industries face bottleneck to develop new therapies because of the lack of human relevant models.

In this study, we wish to extend our hepatocyte like cells (HLCs) monoculture to a more complex coculture including liver sinusoidal endothelial cells (LSECs) and hepatic stellate cells (HSCs). LSECs, HSCs and the liver endothelium are involved in the propagation of the inflammation during the progression of the NAFLD.

Method

LSECs[1], HSCs[2] and Hepatocytes-like cells[3] were differentiated from human induced pluripotent stem cells (Fig. 1). After making stocks, the cells were used in organ on chip cocultures (Sakai lab). In parallel, the cocultures will be tested using vessel like biochip (SMMiLE technology). To simulate the NAFLD, free fatty acids exposure were performed.

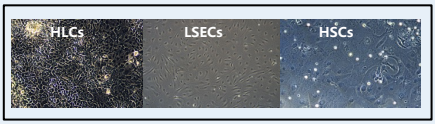

Fig 1: Typical morphologies of HLCs, LSECs and HSCs

Results

Tri cultures was succeed and FA exposures lead to intense fiber like structures as shown in Fig. 2.

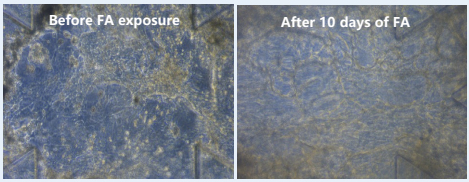

Fig.2: Morphologies before and during FA exposures

The immunostainings revealed the formation of a large endothelial-like network in FA treated conditions

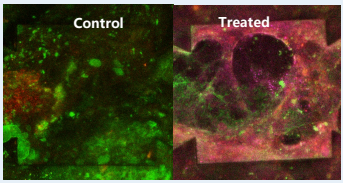

Fig.3 Staining in green of albumin (Hepatocytes) and red PECAM1 (LSECs)

Perspectives

1) Tri culture larger characterization;

2) Drugs testing;

3) Vessel coculture and ANR application

References

[1] Danoy, D. et al., Differentiation. 2021

[2] Ya, G. et al., Biotech. Bioeng. 2023

[3] Danoy, D. et al., Hepa. Res. 2023

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Full-Metal 3D Micro Fractal Pipette for Magnetically Driven Liquid Sample Handling.

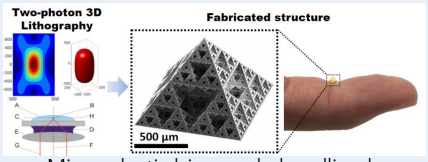
Gilgueng Hwang

Hosted in Mita Lab / B. J. Kim Lab

Keywords: Bio/chemical sample handling, bioanalysis, drug delivery, Microswimmer

Fundings:
Internal project 2023
Kakenhi C

Context and Objectives



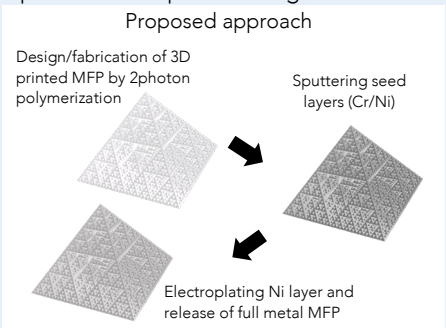
Microrobotic biosample handling by 3D printed polymer micro fractal pipette [1,2]

Current limitations:
- Polymer structure: mechanically fragile
- Tethered actuation: µ-robotic biosample handling currently limited to laboratory

Goal: Fabricate full metal micro fractal pipette (MFP)

Method

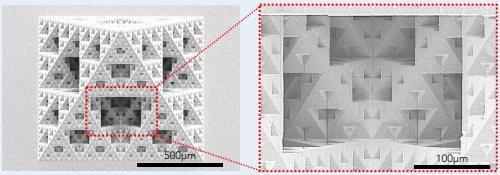
Development of full-metal MFPs for liquid/solid sample handling



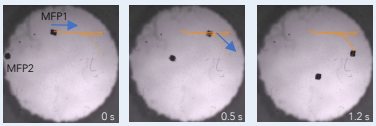
Fabrication of full metal MFP

Results

We fabricated full metal MFPs by electroplating of nickel layer on the 3D printed MFPs. They can be applied for magnetic propulsion to swim in fluidic environment.



SEM images of full metal MFP



Magnetic propulsion and trajectory control of full metal MFP

Perspectives

The proposed method could open a new possibility to fabricate metallic 3D micro/nano structures. They are promising towards the fabrication of magnetically propelling microswimmers. More metallization processes will also be tried to compare with the current process and further improve the process.

References

[1] D. Decanini, et. al., AIP Rev. Sci. Instrum. 91, 086104, 2020

[2] D. Decanini et al., JNTE 2022

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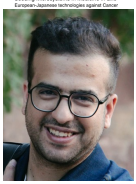
Subcellular Imaging During Single Cell Mechanical Characterization.

Bahram Ahmadian

Hosted in SMMiL-E

Keywords: Single-cell analysis, biophysical characterization, subcellular imaging

Fundings:
ANR
Region HdF / I-Site



Context and Objectives

- The state of a cell being linked to its mechanical properties
- Intracellular components having distinct effects on mechanical properties
- Can intracellular component properties be linked to biological properties?

Method

- Microfluidic device for cell handling
- Silicon Nano Tweezers for mechanical measurements
- Confocal microscopy for subcellular imaging

Results

- 3D confocal imaging of subcellular components during compression
- Measuring mechanical properties of cancer cells simultaneously with 2D imaging during compression

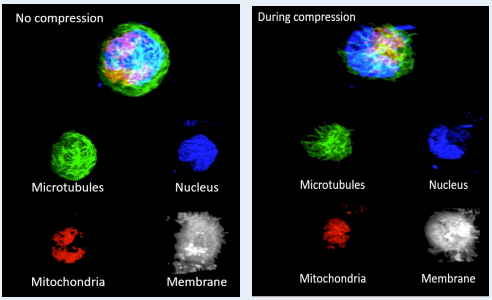


Fig.1: Subcellular element imaging at different compression levels.

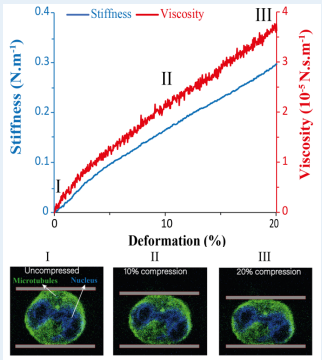


Fig.2: Mechanical characterization during intracellular visualization.

Perspectives

Obtaining mechanical properties of different cancer cell lines to distinguish them

Linking mechanical properties of cells with their subcellular components

Modelling cells to predict their metastatic potential from mechanical properties

References

[1] D. Pekin, G. Perret, et al, IEEE International Conf. on MEMS, 62-65, 2020.

[2] M. C. Tarhan, N. Lafitte, et al, Scientific Reports 6, 28001, 2016.

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CYTOMEMS: Instrumentation for Biophysical Cytometry with Statistical Learning.

Dominique Collard

Hosted in SMMiL-E (Lille)

Keywords: MEMS cytometry, biophysical cell characterization, AI

Funding:
ANR project

Context and Objectives

The objective of CYTOMEMS is to demonstrate the first smart MEMS equipment performing high content biophysical characterization of cells in flow for their classification by statistical learning.

Method

Cell characterization is carried out by a BioMEMS device incorporating a microchannel for the passage of cells and equipped with fixed and mobile electrodes enabling both electrical and mechanical measurements of these cells in flux. The position of the mechanical sensor is tuned in real time to characterize the cell under controlled deformations knowing the cell size from upstream electrical measurement.

After a phase of training on different cell lines, cell identification is performed by statistical classification analyzing a comprehensive set of biophysical (electrical and mechanical) parameters.

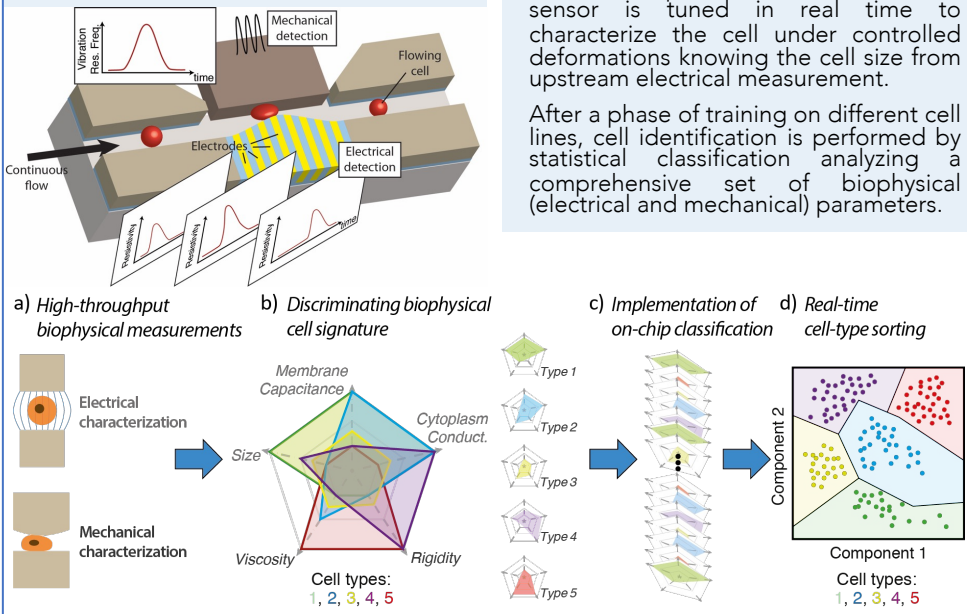

fig.1 : Graphical view of the main objectives of CYTOMEMS recapitulating the main hypothesis.

Perspectives

CYTOMEMS is a 3 years ANR projects 2022-2024 with the following 4 partners :

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Developing the Interdisciplinary Space for SMMiL-E Projects.

Jean-Claude Gerbedoen & Fabrice Soncin

Hosted in SMMIL-E (Lille)

Keywords: Microfabrication, cell culturing, molecular biology, cellular biology

Funding:
Internal project 2023

Context and Objectives

SMMiL-E projects being at the intersection of biology, engineering and clinics require dedicated facilities within the hospital campus.

Imaging

-Field emission scanning electron microscopy (with a cryo option)

-Airyscan confocal microscopy

-Inverted microscopy for BF, Fl, PC and DIC imaging

-Upright microscopy for brightfield imaging

L2 cell culture room

Bio-room

Molecular Biology

-Classic & real-time PCR systems

-DNA/RNA & protein quantification and analyses equipment

-Abs/Lum/Fluo/Alphascreen plate reader

-Nucleic acids & protein gel imaging systems

Microfabrication

-Lithography (direct writing, mask aligner)

-Deposition (sputtering, evaporator, parylene coater)

-Etching (Reactive Ion Etching, wet etching)

-Characterization (probe station, profilometer, SEM)

-Rapid prototyping (stereolithography SLA, nanoscribe with two-photon polymerization, computed numerical control)

View of microfabrication equipment in the cleanroom

Cell Biology

-Cell culture hoods

-Tri-gas incubators

-Culture under perfusion system

-Dedicated inverted microscopes with BF, PC, and Fl imaging

-Bioprinter

-Cell electroporation system

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Integrating Impedance Cytometry with MEMS: 3D Silicon Electrode Fabrication.

Faruk Azam Shaik

Hosted in SMMiL-E (Lille)

Keywords: Microfabrication, electrodes, MEMS, impedance.

Funding: ANR

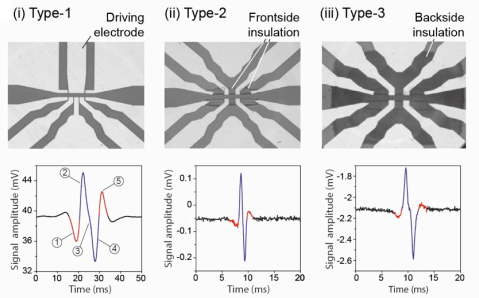
Context and Objectives

We aim to develop 3D silicon electrodes to perform impedance cytometry on single cells without compromising practical integration with sensors measuring complementary properties, e.g., mechanical properties.

Results

A trajectory-free measurement is obtained by replacing the silicon backside under the sensing area with an insulating material.

Widening electrode gaps and proper insulation improves signal quality and reduces parasitic effects



Method

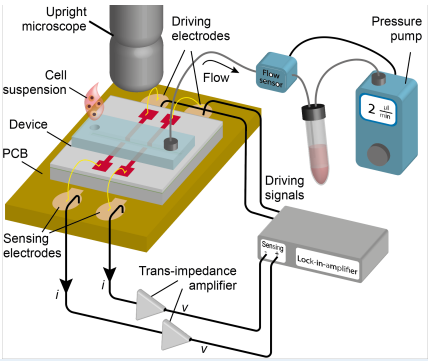
We tested the performance and feasibility of three different designs.

The first device type, i.e., type-1, was an all-silicon device.

The second device type, i.e., type-2, included an insulating material on the sides of the electrodes.

The third device type, i.e., type-3, had an additional insulating layer at the backside below the measurement area

A PDMS slab was placed on the fabricated silicon device to complete the channel.



Perspectives

The proposed process aims at creating silicon-based electrodes for impedance spectroscopy applications while providing opportunities to integrate them with MEMS actuators and sensors

References

[1] Q. Rezard, F. Shaik et al., MicroTAS, 805-806, 2020.

[2] Q. Rezard, F. Shaik et al., IEEE Int. Conf. on MEMS, 494-497, 2021.

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Cells pairing tunable BIOMEMS device for Immunology signaling protocol.

Dana Simiuc, Faruk Azam Shaik

Hosted in SMMiL-E (Lille)

Funding:
SATT Nord

Keywords: single cell interaction, cell pairing, immunological synapse

Context and Objectives

Immunological synapse (IS) is essential for investigating efficient immunologic treatments for cancer studies.

We aim to fabricate a MEMS device for single cell pairing of individual immune cells and leukemic cells for this purpose.

Method

A multilayer microfluidic platform with specific geometries targeting high-throughput deterministic pairing for two different cell sizes in a unidirectional flow format.

Introducing an auxiliary flow alters the effective channel height allowing efficient small-cell trapping.

In short, we perform controlled high throughput single-cell pairing for immunological synapse study.

Results

T cells and leukaemia cells are trap in controlled manner, with high throughput.

IS dynamics is monitored for hours.

Cell pairing is established for monitoring Ca^{2+} signature of T-cells.

Perspectives

Fabrication of integrated device for single cell pairing.

Characterization of patients sample.

Calcium signature study.

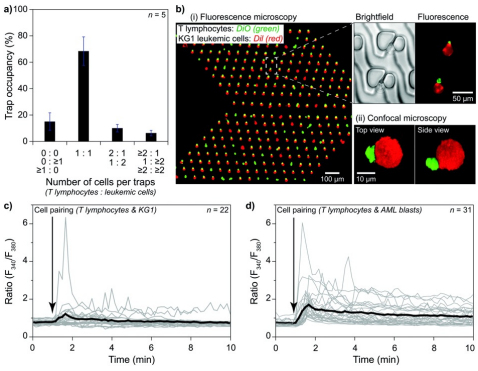

Figure 1: Cell pairing and monitoring their activities [1].

References

[1] Shaik F. A., et al, Lab Chip, 2022, 22, 908.

[2] Shaik F. A., et al, MicroTAS, 2022, 765-766.

[3] Shaik F. A., et al, MicroTAS, 2019, 634-635.

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Vascular Barrier Models in Cancer

Fabrice Soncin

Hosted in SMMIL-E (Lille)

Keywords: blood vessels, cancer, inflammation, immunity, microfluidics

Fundings:
ANR, Ligue contre le Cancer, Fondation ARC, IRCL

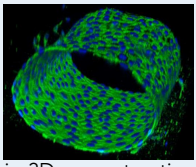
Context and Objectives

We design blood vessel on-chip devices to study the molecular mechanisms which regulate the vascular barrier, endothelial cell activation, and how they participate in vessel integrity, angiogenesis, and extravasation of blood-borne immune cells.

We also study the effects of anti-cancer therapies used in patients on the functions of this vascular barrier

Methods

Blood vessels-on-chip are made in PDMS-glass devices designed and fabricated at SMMIL-E facilities. They are seeded with primary human endothelial and perivascular cells from various organs. Biological validations are made using confocal microscopy, RT-qPCR and functional assays.

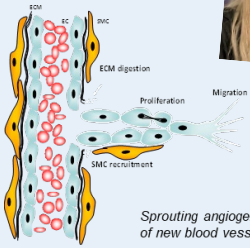


Blood vessel-on-chip 3D reconstruction

Results

Alice Leroy (Univ. Lille Ph.D student, Y2) studies the effects of anti-cancer drugs and radiotherapy on the vascular barrier and immune activation in our blood vessels on-chip models.

Ibtihal Hezili (Univ. Lille Ph.D. student, Y1) sets up a perfused blood vessel on-chip angiogenesis model to study the effects of anti-cancer drugs and therapies on this process.



Sprouting angiogenesis process of new blood vessel formation

Perspectives

Assess the role of biological signals & environment components on blood vessel functions, screen for active drugs on blood vessel permeability, activation, and angiogenesis.

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Distinguishing Cancer Cells Based on Their Biophysical Properties.

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Hosted in SMMiL-E (Lille)

Keywords: Single-cell analysis, biophysical characterization

Fundings:
ANR
Region HdF / I-Site

Context and Objectives

Biological processes related to cells are influenced by changes in cell shape and structural integrity.

Biophysical properties can potentially reflect the state of cells' health.

Can we use biophysical parameters as metastatic biomarkers?

Method

Microfluidic device for cell handling

Silicon Nano Tweezers for biophysical measurements

AI for distinguishing cells

(i) SNT tips for capturing single cells,
(ii) Actuators for manipulation & detection,
(iii) Capacitors as displacement sensors.

Results

Integrating SNT with microfluidics allows single cell characterization. Only tips enter a microfluidic channel to capture a cell (Fig. 1). A displacement sensor allows compression assays during continuous sensing. AI algorithms distinguish cell lines.

Three different breast cancer cell lines were analyzed. The cell line with high metastatic potential (SUM159PT) shows softer mechanical properties than the cell line with low metastatic potential (MCF7), which was softer than non-malignant cell line (MCF10A).

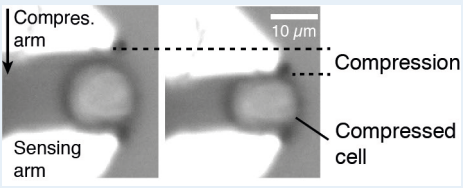

Fig.1: Compression assay with SNTs.

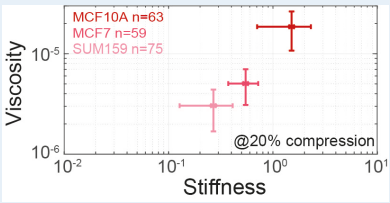

Fig.2: Comparison of three different cell lines.

Perspectives

Obtaining biophysical signature of CTCs distinguish according to metastatic potential

Towards diagnostic products, drug testing platforms, disease monitoring and treatment prediction instruments

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Book Chapters 2023-2024

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Notes