Research Activities 2022-2023

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

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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 workina the field of in micro/nanotechnologies and BioLIMMS was created in 1995 as a cooperation unit between CNRS (SPI Department and now INSIS) 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/Meguro-Ku), where exceptional technological facilities are provided.





Since the acquisition of a status of IRL 2820 in 2004 (UMI= Unité Mixte Internationale, was renamed to IRL= International Research Laboratory on Jan. 1st 2021), 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.

During the 2016-2022 term, LIMMS was involved as a partner of the iLite consortium (for innovation in Liver tissue engineering), a 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. The same year, 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 2022/2023 about 90 people were involved in LIMMS activities including Host Professors (17) and their teams, CNRS researchers (11), engineers (2), JSPS post-doctoral fellows (4), contract based post-doctoral fellows (12), PhD students (8), internships (19), collaborators (11) and administration staff (5).

> 2019-2024 JSPS C2C 2019-2025 CREST-JST 2021-2031 LIMMS Kiko 2022-2029 PEPR



Organization

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

structure is organized to LIMMS' handle challenging joint projects. These projects follow the scientific policy promoted by both Directors (CNRS and IIS), and approved by CNRS INSIS 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 of Tokyo), (The University and associated members (see lab 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 the JSPS (post-doctorates).

The University of Tokyo covers the group of salaries of host provides professors and all technological platforms (1200 m² of cleanrooms, biological and biophysic labs. experimental 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.





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, LIMMS researchers obtained worldclass results with the development of phononic crystals for heat focusing. LIMMS technologies at the cutting-edge are regarding thermoelectric micro-devices have and 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 with Smart MEMS devices.

The Quantum and Molecular Techologies 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 endeavour 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 and detection is prevention by developing investigated 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 **BioMEMS** between and Organ modelling.

SMMiL-E

Seeding Microsystems in Medicine in Lille – European Japanese technologies against Cancer

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 highlevel collaboration. The project will synergize 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 biorelated experiments, as an original interdisciplinary approach to the SIRIC ONCO-Lille program. The projects aim at bridging fundamental and clinical research around four workpackages: 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

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





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.

Core-to-Core Program





JSPS Core-to-Core program JETMeE



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. Beomioon 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 UTokyo-IIS 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/

The University of Tokyo Integrated Research Network - LIMMS KIKO

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 declinina population and which developed countries will face, by applying the results of international collaborative research in the Micro-nano interdisciplinary fields such as Nanobiology, uTAS, 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 based on 10 vears and is the LIMMS/CNRS-IIS IRL 2820, which has been managed by CNRS and IIS for 25 vears Japan-France as а collaborative research center, in order to transcend departmental boundaries and comprehensively bring in the intellectual creativities of the University of Tokyo.



LIMMS Key Figures and Collaborations

Since its creation, the LIMMS has welcomed in total 349 members including 46 CNRS researchers, 78 JSPS post-doctorates, 22 CNRS Postdoctorates, 15 IIS Post-doctorates, 31 PhD students. 9 CNRS research engineers, 14 collaborators, 2 industrial collaborators. 83 internships, 21 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 2022-2023, our members published 54 journal papers and 40 communications in international conferences.

In this period, LIMMS members have

managed 7 Kakenhi grants (financial support coming from MEXT, the Japanese ministry of education, culture, sports, science and technology) and 16 contracts [EU, 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

International Workshop on Micro-and Nano-Technologies for Energy, Bio-engineering and Bio-sensing with JETMeE Workshop -June 13th-14th, 2022

On June 13th and 14th 2022, an International Workshop on Micro-and Nano-Technologies for Energy, Bioengineering and Bio-sensing with JETMEE Workshop was held in LAAS-CNRS, Toulouse(France).

A group of Japanese host Professors from LIMMS and LAAS researchers presented their activities to open for collaboration. LIMMS alumni and potential candidates were also present.

LIMMS Steering Committee 2023 -January 17th, 2023

On January 17th 2023, LIMMS Steering Committee was held in IIS, Tokyo for the first time since the beginning of the pandemy. A special workshop was organized to present the activities of LIMMS. SMMiL-E/UTC 2023 School on BioMEMS -February 13th to 25th, 2023

SMMiL-E, the site of LIMMS/CNRS-IIS IRL 2820 in Lille, held an international school on bioMEMS, the third time, from February 13th to 25th, 2023. This educational event targeted introducing the main aspects of bioMEMS technology multidisciplinary bv а team with biological (3 lecturers). clinical (12 lecturers) and engineering (16 lecturers) backgrounds. The school contents were grouped as device development (e.g. design, fabrication, characterization and operation), fundamental techniques (e.g. biological, clinical and microfluidics) and examples of applied systems (e.g. organon-a-chip and single-cell characterization).

9 students from the Institute of Industrial Science, The University of Tokyo, 8 students from the University of Lille, 3 students from JUNIA (French graduate school of science and engineering) and 7 students from UTC (University of Technology of Compiègne) attended a 2-week-long program and were highly encouraged to join projects between SMMiL-E and IIS.

This year the school also partly took place in the BMBI CNRS laboratory of UTC.





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

MEMS-based Terahertz Bolometer





Single Molecule Transistors

Novel Cooling Device Using Semiconductor Heterostructure

Ga. As



Strong coupling between quantum dot and terahertz resonator



http://thz.iis.u-tokvo.ac.ip

Associate Pr. Yoshiho IKEUCHI

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





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Pr. Hideki KAWAKATSU

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



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- 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

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



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

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





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Pr. Yukiko MATSUNAGA

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





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

Associate Pr. Tsuyoshi MINAMI

- Organic TFT-based chemical sensors
- Supramolecular sensor arrays





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

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

Pr. Masahiro NOMURA

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



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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



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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

of Solar Ce

Pr. Takuji TAKAHASHI

- Multiple analyses of solar cell materials by photoassisted 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



Pr. Shoji TAKEUCHI

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





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

Cells patterning

Associate Pr. Agnès TIXIER-MITA

- Thin-Film-Transistor
 multi-sensing platform
- TFT-platform for electrophysiology of neurons and cardiomyocytes network
- TFT-platform for biosensing





http://toshi.iis.u-tokyo.ac.jp/toshila b/?Members/Agnes%20Tixier-Mita

Pr. Hiroshi TOSHIYOSHI

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





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Research Projects

The laboratory operates in three fields:

- Energy
- Quantum and Molecular Technologies
- Biology

Details about all research projects conducted from April 1st 2022 to the March 31st 2023 will be given in the following part of the booklet.

CREST project: surface phonon-polariton heat transfer (2019-2025)

5Y



Sebastian Volz (CNRS)

Host Lab

Nomura Lab

Keywords: Radiation, Cooling, Nanoscale

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.

Tasks

6 demonstrators include:

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



Perspectives

Developments of transient experiments and SPP resonators.

JST CREST



Method

- Fabrication: Conventional Clean-Room silicon wafer processes.
- Characterization: Time-Domain Thermo Reflectance (TDTR), TEM and 3w.

Modeling: Solving Maxwell, Boltzmann and Heat conduction Equations.



Consortium

LIMMS CNRS/IIS

NomuraLab, The University of Tokyo PPRIME, Université de Poitiers

Publications/References

S Volz et al., Phys. Rev. Appl. 18 (5), L051003, 2022
 Y Wu et al., App. Phys. Lett. 121 (11), 112203, 2022
 J Ordonez et al., Phys. Rev. App., Accepted.

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Thermal properties using 3ω method at extreme temperature (RT~1200 K)

Laurent Jalabert (IR, CNRS)

6Y

Host Lab

Nomura Lab

JST CREST (S. VOLZ)

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

Context and Objectives

Thermal properties of materials at temperatures above 800K, are usually measured on bulk by hot wire or laser flash methods that are very expensive.

The 3ω method [1] allows measuring bulk, membrane, thin films, superlattice... However, the maximum temperature is limited to 800 K with standard Vacuum Probe Station (VPS).

For many scientific researches, like corrosion, space, reliability of power devices etc..., operation at extreme temperatures (>800K) is needed while measuring electrical signals continuously. This is challenging.



Top view of the inside of the VPS during the measurement at 1200 K

Method

We developed a prototype of extreme temperature vacuum probe station reaching routinely 1200 K, with 6 probes [2].

We tested the $3\omega/2\omega$ thermal method on a reference sample (a-quartz from NMIJ) with calibrated diffusivity data up to 800 K.



Results

We developed a model to extract both the thermal diffusivity and conductivity from a set of 3ω experimental data [3].

The in-plane diffusivity (bottom graph) of quartz is consistent with the calibration (black) data provided by National Metrology Institute of Japan.

Perspectives

Test of reference samples having known diffusivity and/or conductivity up to 1200K are on going.

Selection of metal transducer with good stability up to 1200K is challenging.

Publications/References

- [1] Cahill, PRB, 35,8 (1987)
- [2] Jalabert et al., MRS (2022).
- [3] Ordonez et al., submitted to JAP (2023)

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Modeling of the heat transport driven by surface electromagnetic waves

Jose Ordonez-Miranda (CNRS) 4Y

Host Lab Nomura Lab

Keywords: Heat transport modeling, Surface phonon-polaritons, Maxwell equations of electromagnetism, Boltzmann transport equation, Super Planckian thermal emission.

Context and Objectives

The overheating of nanomaterials ever thinner limits their applicability in electronics and can be overcome by transporting heat not only inside their decreasing volumes, as is the case via electrons or phonons, but also along their interfaces via surface electromagnetic waves, such as surface phononpolaritons (SPhPs) in polar dielectrics and surface plasmon- polaritons (SPPs) in metals. The main goal of our research is to develop analytical and numerical models for predicting the polariton heat transport along nano-, micro-, and macrostructures.

Results

The plasmon thermal conductivity of a gold nanofilm takes its maximum of 15 $Wm^{\text{-}1}K^{\text{-}1}$ for a film thickness of 10 nm.

This high polariton thermal conductivity is about 25% of its electron counterpart.



Perspectives

Comparative modeling of the SPhP thermal conductivity of thin films and nanowires based on the Boltzmann transport equation and the fluctuation-dissipation theorem.

SPhP heat transport along anisotropic and complex structures.

Method

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

ANR ICIC

Solutions of the Boltzmann transport equation for temperature and heat flux.

Fourier's law of heat conduction and Stefan-Boltzmann's law of thermal radiation to describe experimental data.



Results

A maximum SPhP thermal conductance per unit width of 103 mWm $^{-1}$ K $^{-1}$ is found for a 1-cm-thick cavity surrounded by SiO₂ at 500 K.

This high polariton thermal conductance is pretty much equal to the radiative one predicted by Planck's law and can therefore generates a super-Planckian emission.

Publications/References

- [1] J Ordonez et al., Phys. Rev. App., 19, 044046 (2023).
- [2] S Volz et al., Phys. Rev. Appl. 18, L051003 (2022).
- [3] Y Wu et al., App. Phys. Lett. 121 (11), 112203 (2022).

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Far-field thermal radiation enhancement via surface phonon-polaritons

Maelie Coral (PhD student)

Host Lab Nomura Lab

JST CREST,

JSPS KAKEN-HI B

Keywords: Surface phonon-polaritons, Far-field thermal radiation

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 the in-plane heat flux emitted by macroscopic cavities. For a vacuum cavity in between two parallel flat plates of SiO₂, theory predicts a enhancement maximum of the radiative heat flux for a cavity width of 1 cm (2).



Perspectives

We aim at observing the cavity width and height influence on the emitted flux. Macroscopic cavity will also be studied to impact applications.

Method

Cavity flux will be studied by IR camera and FTIR spectroscopy comparing Si and SiO2 cavities at different temperatures. In this study, the size of the cavities are of the order of tens of microns. As Si 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 thermal emission.



Scheme of a vacuum cavity between two identical polar materials supporting the inplane propagation of SPhPs via cavity modes (blue lines) and Planck radiation (red arrows).

Publications/References

 S.-A. Biehs and al.: Rev. Mod. Phys. 93, 025009, 2021.
 S. Volz and al.: Phys. Rev. Applied 18, L051003, 2022.

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







Semi-conducting nanoparticles fabrication assisted by millifluidic

Gwenaël Bonfante (CNRS Post-doc) 1Y

Host Lab

SH Kim Lab

ANR WaterPV (S. Chambon)

Keywords : nanoparticles, nanoprecipitation, millifluidics, organic photovoltaic, 3D printing

Context and Objectives

Sustainable energy \rightarrow solar cell

Organic solar cell = complementary to current solar farm

Water based nanoparticles suspension

Active layer allowing collection of solar energy and transport of charge (intermixed morphology figure 1 (a))



Nanoprecipitation assisted by milli-fluidic

Fig1 – (a) schematic of solar cell (active layer in the middle) – (b) influence of Re on particle size [1]

Results

Same tendencies for each chip : decreasing of the size compared to batch method

ightarrow 80nm vs 120nm for standard conditions and 60 nm when using surfactant

Continuous fabrication of nanoparticles achieved BUT target size 30nm not yet reached



Fig2 – schematic of (a) batch method – (b) millifluidic chips and (c) mean size of particles as a function of the water pressure in the millifluidic system

Perspectives

Observation of mixing time by fluorescence microscopy

Publications/References

[1] Liu et al., Nano Lett. 17, 2017

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AlGaAs/GaAs heterostructures for evaporative electron cooling

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Host Lab Hirakawa Lab

Keywords: Electron and lattice cooling, quantum heterostructure, AlGaAs/GaAs

Context and Objectives

Innovative on-chip coolers are a soughtafter solution to the rising problematic of self-heating in condensed matter devices. Aluminum gallium arsenide / gallium arsenide (AlGaAs / GaAs) double-barrier heterostructures optimized for evaporative electron cooling have shown promising results in that domain.

Results

Double-barriers: increase of the Al concentration in the collector barrier creates a tilted structure that reduces undesirable tunneling effects.

cascade Quantum cooler (QCC) Δ heterostructure builds upon the results of the double-barrier structure. Matlab simulation results promise cooling powers up to 30 times higher than those obtained with double-barrier heterostructures. PL results show cooling of the order of 50K in the quantum wells at room temperature operation.

Perspectives

Developing a MEMs-based sensor to measure the lattice temperature.



Fig.3: Schematic representation of a double-clamped MEMs resonnator comprising the AlGaAs / GaAs heterostructure.

Method

Design and optimization: NEGF simulations and finite elements (COMSOL) modelling.

JSPS

Fabrication: molecular beam epitaxy for growing AlGaAs/GaAs heterostructures.

Characterization: I-V measurements for transport at room and cryogenic temperatures, and photoluminescence (PL) for electron temperature determination.







Fig.2: Characterisation of the 3-well QCC structure. a) PL spectra as a function of applied bias, from which we extract b) electron temperatures in each of the QWs.

Publications/References

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- [2] M. Bescond and K. Hirakawa, Phys. Rev. Appl. (2020).
- [3] M. Bescond et al., Phys. Rev. Appl. (2022).



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Colloidal quantum dots solar cells

Laurine Desbats (Internship student) 6M

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Keywords: Colloidal quantum dots, Solar cells, Field-effect transistors, Hole mobility, Halide ligands

Context and Objectives

Lead sulfide (PbS) colloidal quantum dots are promising materials for solar cell applications because of their capacity to harvest photons in the infrared [1].

Quantum dots are capped with halide ligands. Depending on the halide used, solar cell performances vary. We investigate halide ligand impact on hole transport in the PbS quantum dots layer.



Results (right figure)

Cl⁻ capped quantum dots show conductor like behaviour.

Perspectives

We wish to clarify the halide influence on the quantum dot structure and the conductor behaviour of Cl⁻ capped quantum dots.

Method

PbS quantum dots field-effect transistors are fabricated in order to examine the hole mobility of the quantum dots layer without the influence of other layers present in solar cells.

Three halides are studied: iodide (I⁻), bromide (Br⁻) and chloride (Cl⁻).

Results (left figures)

Cl⁻capped quantum dots \rightarrow High hole mobility but low solar cell efficiency.

I-capped quantum dots \rightarrow High solar cell efficiency but low hole mobility.

This means: Halide ligands impact quantum dots hole mobility. But solar cell efficiency is not influenced by hole mobility.



Publications/References

[1] Wang et al., ACS Energy Letters, 2017, 2,

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Nano-gap transistors for organic semiconductor nanoparticle characterization

Hugo Laval (PhD student) 6M

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Keywords: Organic field-effect transistors (OFET), Nanoparticles, Nano-gap transistors, Organic photovoltaics (OPV), Organic semiconductors (OSC)

Context and Objectives

In the field of OPV, high toxicity solvents are used for the deposition of the photoactive layer. Replacing these solvents with water is necessary to improve the sustainability of this technology. To do so, dispersion of OSC nanoparticles (NPs) in water seems to be a good strategy [1]. It is essential to obtain a good NP morphology to allow the hole and electron to flow. Therefore, using nano-gap transistors, we need to correlate the NP morphology with hole and electron mobility.



Method

In order to study the charge carrier transport at the NP scale, we use e-beam lithography to fabricate OFETs with sub-micrometer channel lenght. Nanoparticles are inserted in the OFET channel using dielectrophoresis force .

Results

The hole mobility (μ_h) extraced from the space-chargelimited current method was found to be dependent on the channel lenght. To reduce this dependency, we applied different surface treatments on the gate dielectric. The OTS treatment gave the best μ h with the least channel length dependency. Despite its inverted morphology, the μ_h of P3HT:eh-IDTBR NPs is similar to the μ_h of P3HT:o-IDTBR.

Perspectives

More systems with various morphologies will be studied to pursue the correlation with the mobility.

Results for P3HT:o-IDTBR



Publications/References

[1] A. Holmes et al., ACS Nano., 15, 3927(2021).

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PEPR MoleculArXiv (2022-2029): massive data storage on DNA and artificial polymers



<u>Anthony Genot</u> (CNRS), Gwenaël Bonfante (CNRS Post-doc), Robin Deteix (IR, CNRS), Sona Roy (CNRS Post-doc), Yannick Tauran (University of Lyon)

Hosted in S.H Kim Lab **7Y**

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

Context

Data storage is crucial in our society: exabytes (10¹⁸) of data are generated every year in France (communication, culture, finance, politics, industries, etc) and the "digital universe" will grow to over 175 zettabytes (10²¹) in 2025. Current warehouses use magnetic and optical media which show limitations in 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
- 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



Perspectives

- Application to matching fund with Pr. Kim SH (JST/Adcorp)
- Maturation of technology and creation of startups
- Collaboration with FR and JAP industrials

Publications/References

- [1] Okumura et al., Nature, 2022
- [2] Genot et al., Nature Chemistry, 2016

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Thermodynamic and rheological characterization of DNA hydrogels

Hajar Ajiyel (PhD student) 8M

Hosted in SH Kim Lab

Keywords: DNA nanotechnology, Calorimetry, Rheology, Soft matter, Hydrogels

Context and Objectives

The sequence of nucleic acids can be designed to program self-assembly into a multitude of forms, such as DNA hydrogels. Their study has focused on their formation and not so much on the thermodynamic and rheological properties with relation to the sequence design.

Therefore, we aim to link the various characteristics of the DNA hydrogel to its design, and make a global study at different scales. Applications of DNA hydrogels are anticipated in many fields; in therapeutics, biosensing, etc [1].

600

Method

Design DNA sequences that will assemble into a hydrogel with prescribed properties



Self-assembled DNA hydrogels [2]



Phase-separated DNA hydrogel

Results



Autocorrelation function of DNA hydrogel at different temperatures

Perspectives

- Measure thermodynamic and rheological properties of DNA hydrogels with multiple techniques
- Design and test new DNA hydrogels

References

- [1] Y. Sato et.al., Sci. Adv. 2020
- [2] F. Li et.al., Progress in Polymer Science. 2019

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Quantum bioelectrochemical sensors and devices



S. H. Kim Lab

Host Lab

EU ATRRACT 2. ANR SIBI, NTT BRL, JSPS Kakenhi B



Internal Collaborators:, S. Li, S, Grall, L. Jalabert, F. Tastuhiro, I. Madrid, Y. Gosselin, T. Fujii, S. H. Kim

Keywords: Quantum bioelectrochemistry, Nanosensors, Brownian motion under confinement, Single-cell array, Single-electron counting, Single-molecule array



Single-cell electrochemical aptasensor array

Shuo Li (CNRS, IIS Post-doc)

Host Lab S. H. Kim Lab

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

2Y

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.



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

Methods and Results

A mm-scale gold surface (Au/Si) is used to graft ferrocene modified aptamers (SYL3C-Fc) and analyze their weak interactions with target cancer cells by measurements and simulation (All-atom and coarsegrained molecular dynamics).

Projects: JSPS, NTT, EU ATRRACT 2

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 side electrodes, towards single-cell/single molecule analysis.



Figure 2. Statistical analysis of the single-cell EC aptasensor.

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

S. Li et al. Biosens. Bioelectron. 216, 114643, (2022).
 K. Chennit et al. Nano. Res. 1-7. https://doi.org/10.1007/s12274-022-5137-1, (2022).
 S. Li et al. BirRixv, doi: https://doi.org/10.1101/2023.03.16.532912 (2023).

Figure 3. Mt/AFM-SECM images of a single antiboday nanoarray.

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Nanoelectrochemical devices and sensors

Simon Grall (CNRS Post-doc) 2Y

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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).

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

Context and Objectives

Electrochemical shot-noise [1] brings perspectives of improvements in electrochemical applications. From existing know-how in GHZ ejectrochemistry [2-3] and recent development showing low reorganization energy for confined polymer [4], we believe there is an opportunity for developing molecular rectennas at optical frequencies.

Methods and Results

Better sensitivity can be achieved with shotnoise measurements, potentially resolving fast kinetics without the need for GHz/THz equipment. Confined electroactive polymer are keys to obtain good diode performance and electronic coupling at the same time [4].

ANR SIBL NTT.

FU ATRRACT



measurement concept (c) Liquid gated nanotransistor (d) Measurements of LaNO3 rare earth ions.

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Ambient pressure-driven sensors for low-power deep sea sensors

Massami Bergaud (Internship student)

ANR SIBL

Host Lab Kim Lab

Collaborators: T. Fukuba (JAMSTEC), N. Clément, S. Grall, S. H. Kim, S. Li (IIS, Utokyo), L. Jalabert (LIMMS) Keywords: Nanoelectrochemistry, shot noise, high-frequency, environmental sensing, energy harvesting

Context and Objectives

Deep sea sensing plays a major role in understanding the climate and exploring the marine resources. Currently existing autonomous underwater vehicles (AUV) are often large, costly and energy consuming, with a poor payload/cost ratio. We propose another approach to conventional AUV with a novel pump-free system leveraging on ambient pressure gradient in the deep sea.



Fig. 1 Schematic diagram of the sensor device with ambient pressure-driven pumping technology







Fig. 4. Relationship between the flow rate and pressure for (a) the microfabricated pressure reducer device and (b) the microtube.

Methods

3M

A 3D-printed housing was designed and tested successfully under 100 bars (\approx 1000 m deep equivalent pressure). A pressure reducer is designed to decrease the pressure outside the housing (100 bar) to the inside pressure (1 bar), using this difference to run the microfluidic carrying the sea water to the nanotransistors used here as ion sensors.



Fig. 2 (a) Nanotransistor measurements PCB (b) Deep sea ion measurement concept (c) Liquid gated nanotransistor (d) Measurements of LaNO3 rare earth ions. Right panel shows the actual 3D-printed high pressure housing.

Results

Two approaches were implemented to reduce pressure: a custom made silicon chip with a microchannel groove (50 μ m x 10 μ m x 13 μ m), and a commercial microtube (25 μ m 0.5m). The pressure is reduced successfully in both cases, with a non-linear flow/pressure relationship in the case of the homemade chip most likely due to the PDMS part of the chip. The electrical measurements on the nanotransistors along with the microfluidic control stage were successfully integrated in an onboard electronic circuit

Publications/Reference

 M. Bergaud et al, Proceedings of International Symposium on Underwater Technology (UT23), 03/2023

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Versatile electrodes for long-term monitoring of electrodermal activity

Dorina T. Papanastasiou (JSPS Post-doc) 2Y

Hosted in Someya Lab

JSPS



Keywords: skin electronics, wearable sensors, nanomesh electrodes

Context and Objectives

Skin is the largest organ of human body with electrical properties that has been of great interest for a large variety of applications[1].

Electrodermal activity (EDA) is directly related to the Autonomic Nervous System that controls sweat gland activity, during thermoregulation and in response to other emotional stimuli[2].

Recording the skin electrical properties, such as skin conductance, capacitance and potential, can provide information about EDA, to study and diagnose the skin condition and psychophysiological state[3].

Despite the extended biomedical research, there are remaining unclear aspects about EDA, i.e., understanding the reproducibility of EDA patterns and improving the prediction through inverse modeling.

Such challenges require the accurate long-term, multi-site, and multi-person monitoring, with the suitable electrodes. Although the recent advances on skin electronics (e-skin) are significant, there are several issues that hinder the longterm use in ambulatory conditions[4].

References

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[3] Tronstad et al., Physiol. Meas. 2022, 43, 02TR01

[4] Jang et al., Nat Commun, 2022, 13, 6604

[5] Matsukawa et al., Adv. Healthcare Mater. 2020, 9, 2001322

[6] Miyamoto et al., Adv. Healthcare Mater. 2022, 11, 2102425

Method & Results

Prof. Someya Group Laboratory is world pioneer in organic e-skin devices, having achieved ultra-thin, biocompatible, skin conformable, breathable electrodes[5,6]. Based on scalable deposition techniques i.e., polymer nanofibers electrospinning, such electrodes are now investigated to replace the conventional electrodes in EDA measurements. Solving contact and interfacial issues between soft and rigid parts, improving the mechanical limits, designing and optimizing a versatile skin platform are the first steps of this study.



Perspectives

The successful integration of electrodes in patch-like and textile-based substrates is indispensable for the development of next-generation wearable devices with personalized healthcare features.

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Real-time bio-hybrid system using SNN for neurological disorder studies

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Host Lab Ikeuchi Lab

Keywords: Bio-hybrid, SNN, Hodgkin-Huxley, FPGA, bio-mimetism

Context and Objectives

Characterization and modeling of biological neural networks is important field to understand the mechanisms governing the functioning of the brain and the different pathologies that can affect it. We intend to provide a tool to investigate neurological disorders through bio-realistic models working real-time.

Method

Highly biologically coherent neuron models are implemented on FPGA (programmable logic circuits) to emulate neuronal networks in real-time. Tuning the different parameters of the model or of the network allows to emulate or reproduce behaviors of the biology.

Results

We show that we can reproduce :

- Spontaneous activity of neurons
- Simple inteconnection of neurons



Perspectives

We wish to improve the biological coherence of the model to include spatial dimension, thus providing higher accuracy of the model. Additionally, we wish to perform bio-hybrid experiments including the system.

Results

We show that :

- More complex network can be modeled
- Behaviors of the living such as network bursts can be reproduced

Publications/References

[1] DOI: 10.1109/EMBC48229.2022.9871176

[2] DOI: 10.1109/EAEEIE54893.2022.9820523

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Understanding human brain mechanisms through organoid circuit modeling

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Host Lab Ikeuchi Lab

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

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 so-called 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

fabricate 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 [1]. These 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 the 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 is placed on an electrode array to record neural activity. Optogenetic stimulation of the left organoid induces a burst. The initiated burst propagates to the connected right organoid, which starts to burst with a small time delay.

Perspectives

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

Publications/References

[1] Osaki et al., bioRxiv, 2021

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- Require long time - Need precise control

Mita Lab / B. J. Kim Lab

Biological applications

Gilqueng Hwang (CNRS)

soft micro-swimmer

Context and Objectives

- Risk of contamination

Bio/chemical sample preparations

- Remote bioanalysis
- Drug delivery

Host Lab

Result: Soft Milliswimmer [3]

Liquid sample handling by soft robotic milliswimmer





Bending/unbending soft milliswimmer



Approach of this work

Development of soft robotic multiphase microswimmer for (air/liquid) sample handling by such mobile micro devices.

Miniaturized Soft Microswimmer [4] 3D printed miniaturized soft microswimmer and fabrication



Multi-swimmer Selectivity

Control



Perspectives

Further miniaturization 3D bv nanoprinting integration of micro pumping functionality multiplexing the same handling biological sample handling/preparations.

Publications/References

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- [3] G. Hwang et al., Des. Test, Integ & Packaging of
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3Y

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





Motion

Microstructuring of resorbable scaffolds for vascularized in-vitro 3D tissues

2Y



Vincent Salles (CNRS)

B.J. Kim Lab Host 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. architecture an 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 processes are based on a combination of a 3D printer and an electric field applied between a nozzle and a printing stage.[1] For this project, a peculiar machine was designed and supplied. This project is carried out in collaboration with 3 laboratories, as shown below.



Direct-write electrospinning

Perspectives

The project continues with co-culture trials to test the formation of vascularized tissues, in vitro. The scientific approach is based on an experimental plan with progressive complexity in terms of architectural design.

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 were used to optimize the preparation of the scaffold and the cell culture conditions. These preliminary results were obtained by using PCĹ (Polycaprolactone) as resorbable polymer.[2] Other biocompatible polymers are also considered in the present work to facilitate the construction of the scaffold.



Publications/References

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- [2] R. Gauthier et al., Biomimetics 2023, 8, 108

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Snake robot design using biomimetic artificial neurons on FPGA



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Host Lab Kohno Lab

Keywords: biomimetic neural network, closed-loop biohybrid experiment, CPG, FPGA, silicon neuron

Context and Objectives

Interaction between biological living neurons and artificial neurons in a closed-loop could help us gain insight on neuronal culture. This closed-loop experiment aims to create such interactions with the medium of a robot equipped with sensors. The robot is driven by a biomimetic artificial neural network, the latter being triggered by living neuron.

Method

Central Pattern Generators (CPGs) are biological neural circuits oscillators responsible for the motion of some vertebrate species [1]. Using, biomimetic neurons and synapses models, it is possible to recreate biologically plausible CPGs on neuromorphic hardware. Then, we interconnect the artificial network to biological living primary rat neurons.

Results

- Snake-like motion induced to a snake-like robot using biomimetic CPGs

- Living neurons change the direction of the robot

- Sensors controls the simulation of the neuronal living culture which directly impact the spiking activity



Perspectives

We wish to add various sensors, improve the culture analysis process and generate meaningful stimulation in order to recover from obstacles and to teach a parcour to the biological neural network.

Publications/References

[1] Levi et al., Journal of Robotics, Networking and Artificial Life, Vol. 4, No. 4, 2018, 299-302

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Control of vascular transport with pressure

Aurélien Bancaud (CNRS) 3Y

Host Lab Matsunaga Lab

Keywords: microvessel, collagen, pore model

Context and Objectives

The endothelial layers of the microvasculature regulate the transport of solutes to the surrounding tissues. It remains unclear how this barrier function is affected by blood flowinduced intraluminal pressure. Using a 3D microvessel model, we compare the transport of macromolecules through endothelial tissues at mechanical rest or with intraluminal pressure, and correlate these data with electron microscopy. We suggest that paracellular transport is controlled by the deformation of the gaps between cells.

Method

monitor fluorescent panel in Fig. 1) or convective regime (right which microscopy.



Fig. 1: Fluorescence confocal micrographs of the same MV recorded 30 s after the injection of dextran using the static and pressure assays.

Perspectives

Next, we aim to investigate whether and how microvessels can adapt to hydrostatic pressure as generated by the heart in human bodies. We will also compare the structure of microvessels with more realistic biological settings (e.g. pericytes).

Results

Microvessels are made inside a collagen The vessel is deformed by pressure by 25% matrix.[1] A 3D-printed piece is mounted and the flux of macromolecules increases by on the microvessel chip so as to allow us to 135%. We explain the onset of the crossmacromolecule barrier flux induced by intraluminal pressure redistribution kinetics in a diffusive (left with the deformable monopore model. speculates that the diffusive panel in Fig. 1) with fluorescence confocal permeability increases under pressure as a consequence of the remodeling of the endothelial tissue and the thinning of paracellular junctions. [2].



Fig. 2: Representation of the deformable monopore model to account for the data from the static and pressure assays.

Publications/References

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- [2] Cacheux/Bancaud, 2023 biorxiv.org/content/10.1101/2023.01.24.5 25266v1.full.pdf

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Poromechanic response of in vitro tissue models

Jean Cacheux (JSPS, IIS Post-doc) 2.5Y

Host Lab Matsunaga Lab

Keywords: Microphysiological systems, Collagen gel, Elasticity, Permeability

Context and Objectives

Diseases and aging disrupt homeostasis by altering vascularization and remodeling tissue, and in turn dysregulate cellular functions. While the Starling principle describes exchanges between blood and tissues based on the balance of hydrostatic and osmotic flows, it neglects the coupling between mechanics and hydrodynamics, a questionable assumption in strained elastic tissues due to interstitial flow.

We reasoned that this imperfect description was explained by the lack of methods to simultaneously measure the permeability and elasticity of soft tissue models, such as collagen gel.

Method

Hence, we developed a contact-free technology [1] to determine the elasticity and permeability of collagen gels under tensile and compressive stress by comparing the change in pressure in an air cavity sealed at the outlet of a collagen slab over time with an analytical kinetic model.

Results

We observe an enhanced strain-stiffening of native collagen gels under compression and a drop in the permeability, both effects being essentially lost after chemical cross-linking. Further, we prove that the amplitude of sinusoidal fluid injection controls the permeability of native collagen gel only, as a consequence of its asymmetric response. [2]



We finally suggest that blood-associated pulsations could contribute to exchanges within tissues. To test this assumption, we next plan to characterize ex vivo and in vivo tissues.

Publications/References

- [1] CNRS patent. Dispositif et procédé de mesure de perméabilité. PCT No: EP2023053024.
- [2] Cacheux et al. arXiv.2212.00915 (2022).

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Investigation of the metabolic syndrome's progression using organ on chip technologies

5Y

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Keywords: Human induced pluripotent stem cells, Microfluidics, Organ-on-achip, Liver, Pancreas, Adipocytes, Metabolic syndrome

Context and objectives

Metabolic Syndrome (MSy) has а 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 MSv 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-onchip technology to address these key challenges, to move a step closer towards understanding, diagnostics and therapies of metabolic syndrome.

Method

We propose to

- To build a research strategy in which human cells will be used to generate a relevant MSy model
- To establish a specific metabolic syndrome disease model with which we will track the heterogeneity and the kinetics of the disorders
- To identify biomarkers and therapeutic solutions using multi omic technology

Results

- Liver¹ (Fig 1A), pancreas² (Fig 1B) and liver-pancreas cocultures using hiPSC derived model were established.

- Hepatic and pancreatic responses to high glucose and fatty acids were characterized.



Perspectives

- Develop multi cellular liver model
- Investigate liver pancreas crosstalk with fatty acids and diabetogenic environment
- Integration of adipocyte organ on chip

Publications

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[2] Essouiba et al., <u>10.1016/j.jbiotec.2021.02.009</u>

Supports

Chaire UTC JSPS: 22H03934 and JPJSCCA2019000

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Designing a real-time biomimetic plateform on FPGA reproducing neurocardiac function

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Host Lab Toshiyoshi Lab

Keywords: FPGA, biomimetic, nervous system-heart connection, cardiomyocytes

Context and Objectives

Heart disease constitutes the first mortality cause in the world. For improving our knowledge about the implicated mechanism, we proposed to design a platform which reproduce the link between heart pace and neurons to study interactions between these systems. To achieve real-time performance, we target a FPGA.

Results

We successfully stimulated contractile cardiomyocytes which follow the rythm generated by our FPGA.



Method

We implemented the real-time design for Sinusal Node Cardiomyocytes (SANC) which generates the heartbeat. For that we used the Maltsev-Lakatta model. We solved the first-order differential equation system on our FPGA with Euler method. After that, we used the membrane potential obtained to stimulate nonpacemaking cardiomyocytes.



Perspectives

We aim to add а layer that reproduces the Autonomic Nervous System which will allow us to accelerate or decelerate heart pace. This implementation will follow the same biomimetic logic thus, it can use indistincly as input stimulation biomimetic neurons or biological neurons.

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TFT bio-sensing platform for real-time, high resolution analysis of cell culture by impedance sensing



Host Lab

Context and Objectives

on

cartography of impedance.

Tixier-Mita Lab

In-vitro biological cell analyses is fundamental

to study cell culture and to develop disease

models. In that aim, we are developing large

scale, high resolution bio-sensing platforms

technology. Here impedance spectroscopy

technique is used to monitor cell culture by 2D

Thin-Film-Transistor

Keywords: Microelectrode array, Thin-Film-Transistors, Cell culture monitoring, Impedance Spectroscopy

(TFT)

Method

The devices consist in a matrix of microelectrodes controlled by an array of transistors. Impedance Z of a single point is measured in between 2 microelectrodes. To drive the matrix and obtain a 2D cartography, a multiplexer circuit has been fabricated.

Results

based

We show:

- The multiplexer which has been fabricated;
- First results of 2D impedance cartography on a 3x2 matrix, with air, DIW and PBS conditions.





Perspectives

Improvement of the multiplexer and the measurements will be performed for more stable measurements. This system will be applied to cardiomyocyte cell culture in the future.

Publications/References

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CYTOMEMS : instrumentation for biophysical cytometry with statistical learning

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Host Lab

SMMiL-E (Lille)

anr®

Keywords: MEMS cytometry, biophysical cell characterization, IA

Context and Objectives

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



Method

Cell characterization is carried out by a BioMEMS device incorporating а microchannel for the passage of cells and beqqipped 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 classification statistical analyzing а comprehensive set biophysical of (electrical and mechanical) parameters.



Figure 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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Distinguishing cancer cell lines based on their biophysical properties

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Host Lab SMMiL-E (Lille)

Keywords: Single-cell analysis, biophysical characterization

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?

Results

Integrating SNT with microfluidics allows single cell characterization. Only tips enter a microfluidic channel (via a side opening) to capture a cell. Displacement sensor allow compression assays during continuous sensing. Al algorithms distinguish 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

Method

- Microfluidic device for cell handling
- Silicon NanoTweezers 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

Two different breast cancer cell lines were captured and analyzed. The cell line with high metastatic potential (SUM159PT) shows softer mechanical properties than the cell line with low metastatic potential (MCF7).

Publications/References

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Vascular barrier models in cancer

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SMMiL-E (Lille) Host Lab

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

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

Results

Alice Leroy (Ph.D student) studies the effects of anti-cancer drugs on the vascular barrier and immune activation in our blood vessels on chips models

> Dana Simiuc (post-doc fellow) develops vessel-on-chip devices using a proprietary hydrogel

Géraldine Tellier (IR CNRS, CDD) participates in liver endothelial cell integration into biochips

> Marie Guilbert (IR CNRS, CDD) has setup microfluidic components & lines which are used to perfuse the vessel-on-chip devices

Ibtihal Hezili (M2 student) has setup and characterized a microfluidic chain to perfuse vessel-on-chip devices

Perspectives

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

Publications/References

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Developing the interdisciplinary space for SMMiL-E projects

Jean-Claude Gerbedoen (IR CNRS) Géraldine Tellier (IR CNRS)

4Y/3Y

SMMIL-E (Lille) Host Lab

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

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, FI, 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, profilo-meter, 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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High-throughput single cell pairing for cellcell interaction study

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Keywords: Cell-cell interaction, cell pairing, immunological synapse

Context and Objectives

- Immunological synapse (IS) is essential for investigating efficient immunologic treatments for cancer studies
- Here we aim to develop a practical method for single-cell pairing of individual immune cells and leukemic cells for this purpose.

Results

- T-cells and leukemia cells are captured.
- IS are monitored for four hours.
- Cell pairing is established for monitoring Ca²⁺ signature of Tcells.



- Characterization of patients sample.
- Calcium signature study.

Method

A multilayer microfluidic platform with specific geometries targeting highthroughput 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 high-throughput single-cell pairing for immunological synapse study.



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High-throughput identification of circulating tumor cells using biophysical signature

Quentin Rezard (IEMN Post-doc)

Host Lab SMMiL-E (Lille)

Keywords: Single-cell analysis, biophysical characterization

Context and Objectives

- High heterogeneity and scarce concentration of CTCs in blood make them difficult to detect
- We aim to develop a reliable and high throughput method to distinguish CTCs according to their biophysical signature with enough practicality to be use in a medical context.

Results

- Breast cancer cell lines SUM159 PT were successfully detected both electrically and mechanically.
- The accuracy of real-time measurements was tested by comparing the detected cell motion with optical results.
- A correlation between signal amplitude and optical size was established



Perspectives

• Distinguishing different cell lines using their biophysical signature in a highthroughput way.

Method

Electrical det. area

Mechanical det. are

Sensiná tir

3Y

Our device is divided in two layers. The MEMS layer hold 3 functional parts. A microfluidic channel handles cells to be characterized in a continuous flow at an electrical characterization area (consists of 3D electrodes placed on the channel walls) and a mechanical characterization area (consists of a converging wall and a tip linked to a displacement sensor).

In short, we perform high-throughput, simultaneous electrical and mechanical measurements of single cells.

Publications/References

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Observing cell motion

Sensing

Applying

signa

Passing



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Subcellular imaging during single cell mechanical characterization

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Keywords: Single cell analysis, subcellular imaging, mechanical characterization

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

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

Mechanical characterization during intracellular



Subcellular element imaging at different compression levels



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- M Danoy, S Poulain, B Scheidecker, SH Kim, T Kido, A Miyajima, Y Sakai, E Leclerc, A transcriptomic study on the influence of the stimulation by a microfluidic environment for the induction of zonation-like patterns in carboxypeptidase M-positive human pluripotent stem cells-derived liver progenitor cells, 9th World congress of biomechanics, WCB, Taipei, August 2022; Taiwan
- 7. S. Volz, Surface Phonon-Polaritons as Efficient Cooling Vectors, Eurothem NMHTVII, Palermo, May 2022.
- 8. S. Volz, Surface Phonon-Polariton as Efficient Heat Carriers, Heraeus Seminar, Bad Honnef, invited, 2022.
- S. Volz, Controlling Thermal Radiation /in/ Micro and Nanosytems, MIPE2022, Nagoya, Japan, Plenary, 2022.
- 10. S. Volz, Temporal Coherence in Heat Conduction, ICTP, May 30, Trieste, Italy, invited, 2022.
- 11. S. Volz, How coherence is driving phonon heat conduction, **META2022**, July, TorreMolinos, invited, 2022.
- 12. S. Volz, Surface Phonon-Polaritons Conduction and Radiation, ICPPP, Slovenia, Plenary, 2022.
- 13. S. Volz, Wavelet Analysis Unfolds Thermal Phonon Coherence, MRS Spring 2022, Hawaii, invited, 2022.
- 14. S. Volz, How Coherence of Thermal Phonons Impacts Heat Transport, **APS Spring 2022**, Chicago, invited, 2022.
- L. Jalabert, J. Ordonez-Miranda, S. Tachikawa, Y. Wu, R. Anufriev, M. Nomura and S. Volz, Prototype of high-temperature vacuum prober from 300 K to 1200 K for continuous 3-omega thermal measurements, MRS Spring Meeting, SF15.14.07 (oral), May 23rd, Hawaii (2022).
- 16.Y. Guo, M. Nomura, S. Tachikawa, S. Volz, J. Ordonez-Miranda "Quantum of Thermal Conductance of Nanofilms due to Surface Phonon-Polaritons", MRS Spring Meeting & Exibits, (2022).
- Y. Wu, J. Ordonez-Miranda, L. Jalabert, S. Tachikawa, R. Anufriev, S. Volz, M. Nomura, Macroscale Ballistic Heat Conduction by Surface Phonon-Polaritons, MRS Spring Meeting & Exibits, (2022).
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- 22. R. Anufriev, A. Ramiere, J. Maire, J. Ordonez-Miranda, S. Volz, M. Nomura, Ballistic heat conduction at nanoscale: demonstrations and applications, **Telluride workshop: Thermal Transport at the Nanoscale**, (2022).
- X. Huang, S. Gluchko, R. Anufriev, S. Volz, M. Nomura, Surface nanocones control the heat transport in silicon membrane, The 2nd International Conference on Materials Science & Engineering (Virtual), (2022).
- 24.X. Huang, Y. Guo, Y. Wu, S. Masubuchi, K. Watanabe, T. Taniguchi, Z. Zhang, S. Volz, T. Machida, M. Nomura, Study of phonon hydrodynamics in submicroscale graphite ribbon structures, 第6回フォノンエンジ ニアリング研究会, (2022).

- 25. H. Xin, Y. Guo, Y. Wu, S. Masubuchi, K. Watanabe, T. Taniguchi, Z. Zhang, S. Volz, T. Machida, M. Nomura, Transition from ballistic to hydrodynamic phonon transport regime in submicroscale purified graphite ribbons, 第83回応用物理学会秋季学術講演会, (2022).
- 26. J. Ordonez-Miranda, S. Volz, M. Nomura, Resonant Polariton Thermal Transport along a Vacuum Gap, 第83 回応用物理学会秋季学術講演会, (2022).
- 27.Y. Wu, J. Ordonez-Miranda, L. Jalabert, R. Anufriev, S Volz, M. Nomura, Length-dependent Surface Phonon-Polaritons thermal conduction up to 500K, 第83回応用物理学会秋季学術講演会, (2022).
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- R. Anufriev, Y. Wu, S. Gluchko, S. Volz, and M. Nomura, Ballistic phonon and thermal transport at nanoscale, Seminar "Plasmons and Vibrational Dynamics in Nanomaterials", (invited, online), (2022).
- 31.R. Anufriev, A. Ramiere, J. Maire, S. Gluchko, J. Ordonez-Miranda, S. Volz, and M. Nomura, Ballistic heat conduction at nanoscale: demonstrations and applications, **Colloquium at Los Alamos National Laboratory**, (2022).
- J. Ordonez-Miranda, S. Volz, M. Nomura, Heat propagation driven by surface electromagnetic waves, NAMIS Marathon Workshop 2022, (2022).
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- 34.J. Cacheux, A. Bancaud, J. Ordonez-Miranda, L. Jalabert, Y. Matsunaga "Collagen matrix remodeling by fibroblasts monitored by interstitial flow metrology" Microphysio (2022), Cargèse (France)
- 35.S. Grall, Y. Gosselin, I. Muguet, L. Jalabert, S. H. Kim, G. Larrieu, and N. Clement, Na+ Sensing and Electrochemical Noise Measured with Nano FinFET, in SSDM 2022 (Makuhari, Chiba, Japan, 2022), pp. 247–248.
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- H. Laval, G. Wantz, S. Chambon, "Environmentally Friendly Organic Photovoltaics", (Poster), Les Houches School of Physics, Les Houches (France), 3-8 April 2022
- Gwenaël Bonfante, Anthony Genot, Soo Hyeon Kim, Sylvain Chambon, "Synthesis of organic semiconductor nanoparticles with 3D-printed millifluidic", (Flash talk + Poster), Cheminas 46, Tokushima (Japan), 14 – 16 November 2022
- 39. Sylvain Chambon, "De 1% à 19%, histoire des principales avancées du photovoltaïque organique et futures direction", (Invited talk), 12^{ème} Journée Nationale du Photovoltaïque (JNPV), 29 November 2 December 2022, Dourdan, France
- 40.F. Soncin, Blood vessel-on-chip model of the vascular barrier, 1st International conference on Blood-Tissue Interfaces, 03-04 Octobre 2022, Montpellier, France.

Patents

J. Cacheux, A. Bancaud, Y. Matsunaga, L. Jalabert, "Dispositif et procédé de mesure de perméabilité" brevet n°2201116 du 08/02/2022.

Book Chapter

L Morisseau, T Messelmani, A Essaouiba, Y Sakai, C Legallais, E Leclerc, R Jellali, Microfluidic and organ on chip based technologies for diabetes therapy and research, Nanotechnology for diabetes management, Royal Society of Chemistry, 2023, Edited by, Amar Abderrahmani, Sabine Szunerits, Rabah Boukerroub, Abdelfattah El Ouaamari, Paperback ISBN: 9781839164705

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