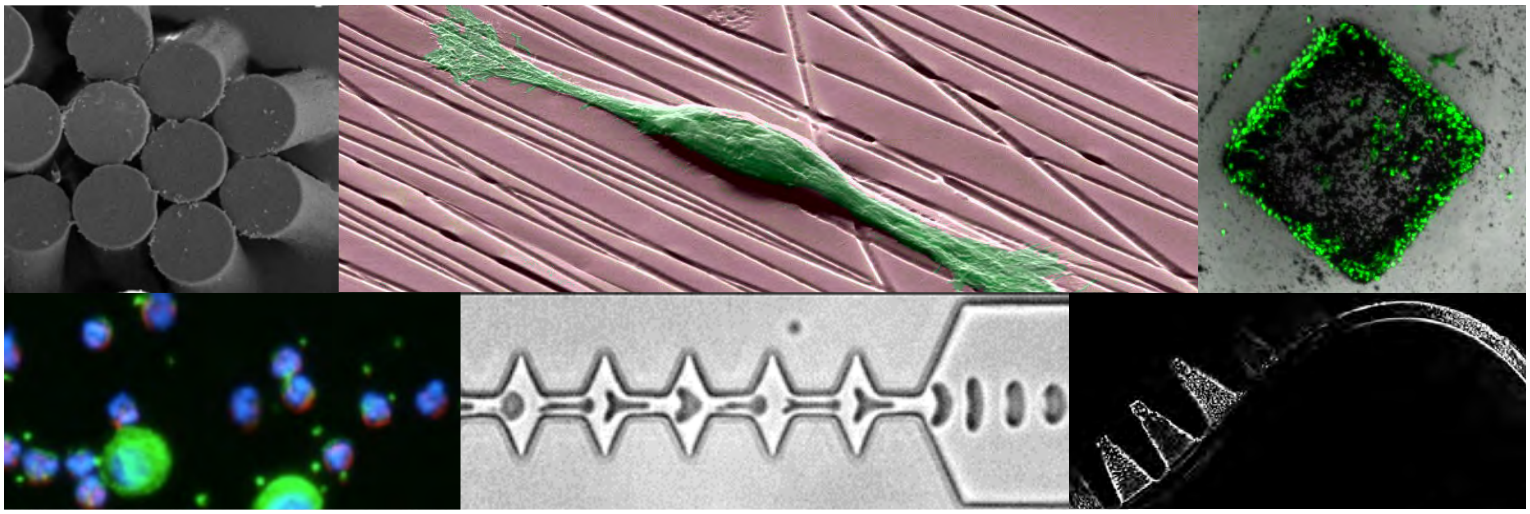


cnrs GDR Groupement de recherche

MNF Micro et nano fluidique

Journées Plénières

Lyon

3-4 Avril 2023

CPE LYON — ÉCOLE CENTRALELYON — département Génie Electrique et des Procédés, Université Claude Bernard Lyon 1 — inl Institut des Nanotechnologies de Lyon UMR 5270 — ENS DE LYON — iLM Institut Lumière Matière

AMC Advanced MicroFluidics — Cil Cluzeau Info Labo — eden Tech — FLUIGENT Smart Microfluidics — idylle — Kleria

KLOÉ — NETRI — microlight3D — TreeFrog therapeutics

About The Micro NanoFluidics GDR *3*

Schedule *4*

Monday, 3 of April **4**

Tuesday, 4 of April **5**

List of the speakers and abstracts *6*

Invited speakers **6**

Laureates of the "Young Researcher in Microfluidics 2023" prizes **6**

Selected speakers **7**

List of posters and abstracts *36*

Monday, 3 of April – Session A **40**

Tuesday, 4 of April – Session B **71**

Useful information *101*

How to get to the INL? **101**

Gala dinner **103**

Partner Institutions and Sponsors *104*

Sponsors **104**

Public institutions **109**

About The Micro NanoFluidics GDR

Micro and NanoFluidics is an emerging, dynamic field with strong development potential. The scientific community is young covering the fields of physics, process engineering, micro and nanotechnologies, (bio)chemistry and biology. This strong interdisciplinarity gives it its own identity and great strength, but in return involves an effort of exchange and communication.

The Micro and NanoFluidics GDR (https://www.gdrmicrofluidique.com) provides a framework for exchange and dialogue, to continue the effort initiated by the CNRS for several years.

The GDR is intended to be a dynamic structure, representative of the various disciplines concerned. It is organized into 6 scientific themes, led by the GDR steering committee:
• Nanofluidics and energy
• Microfluidics for diagnostics and clinics
• Organs-on-a-chip / cell-on-chip biology
• Flow chemistry
• Wave / flow interactions
• Flow, heat and mass transfer at microscale

Its strategic objective is to bring together a multidisciplinary community, active and visible at European and international level, by bringing together actors from public research, industrial actors and associations on the objectives of animation and foresight.

Organizing committee of the 2023 Plenary meeting
Anne-Laure Biance Researcher *Institut Lumière Matière-CNRS*
Jean-François Chateaux Associate Professor *Institut des Nanotechnologies de Lyon-UCBL*
Anne-Laure Deman Associate Professor *Institut des Nanotechnologies de Lyon-UCBL*
Magalie Faivre Researcher *Institut des Nanotechnologies de Lyon-CNRS*
Fabien Montel Researcher *Laboratoire de Physique ENS de Lyon-CNRS*
Caterina Tomba Researcher *Institut des Nanotechnologies de Lyon-CNRS*
Christophe Ybert Researcher *Institut Lumière Matière-CNRS*

Schedule

Monday, 03 of April

08h00-08h45	***Registration***		
08h45-09h00	***Welcome & Openings***		
09h00-09h30	IS	**Oriane BONHOMME** ILM, Villeurbanne	Soft nanofluidics: from electroosmosis in a liquid foam to the molecular scale description of interfaces
09h30-09h50	CT	**Noam DEMRI** LPCC, Paris	Remote magnetic alignment of spheroids in 3D matrix for muscle-on-chip
09h50-10h10	CT	**Blaise DELMOTTE** LH, Paris	Magnetic microrollers as a platform for active transport
10h10-10h35	SP	**Matthieu RAISON** **Aurélie MORYTKO** **Guillaume LAFFITTE** **Esther GRAUDENS**	Microlight 3D Fluigent Klearia Idylle
10h35-11h00	***Coffe break***		
11h00-11h30	IS	**Jean GAMBY** C2N, Palaiseau	Electrochimie en dispositifs micro nanofluidiques : Méthodes et Analyses
11h30-11h50	CT	**Théo ASPERT** IGBMC, Strasbourg	Tracking aging and environmental adaptation of single-cells with microfluidics, timelapse microscopy and deep-learning
11h50-12h10	CT	**Saranath SESHADRI** LIPhy, Grenoble	Membrane-free approaches to harvest osmotic Energy
12h10-12h30	CT	**Julie LACHAUX** LERI, Gif-sur-Yvette	Microfluidic biosensor for the continuous enzymatic detection of organophosphorus compounds
12h30-14h30	***Lunch break + Poster session A***		
14h30-15h00	IS	**Romain QUIDANT** *ETH*	Interfacing light and microfluidics: fluid actuation and bio-analytes detection
15h00-15h20	CT	**Anastasiia DUBROVA** CRIC, Paris	Tumor-on-chip model to decipher the effect of nanoparticle-mediated photothermia on tumor microenvironment of pancreatic ductal adenocarcinoma (PDAC)
15h20-15h40	CT	**Lilian MAGERMANS** LPMC, Paris	Kinetic Energy Harvesting System based on Selective Ion Sweeping under Flow Shear on Capacitive Electrode
15h40-16h05	SP	**Ferdinand ATIVON** **Jessica RONTARD** **Nour CHEBBI** **Catherine BALTHASAR** **Charlène CORON**	AMF Netri Edentech Cluzeau Kloé
16h05-16h35	***Coffe break + Poster session A***		
16h35-17h05	IS	**Marie-Line COSNIER** CEA, Grenoble	PEPS: An Innovative Microfluidic Device for Bedside Whole Blood Processing Before Plasma Proteomics Analyses
17h05-17h25	CT	**Gabriel RAMOS** IMFT, Toulouse	Nonlocal dynamics of biofilm clogging in a porous microfluidic device
17h25-17h45	CT	**Solène MOREAU** TECTST, Paris	Soft thermoplastic elastomer compartmentalized chip for neurofluidic: applications to neural organotypic culture
17h45-18h05	AW	**Lucie DESCAMPS** LI, Eindhoven	MagPure chip: a microfluidic device for the purification of Circulating tumor cells and the integration in liquid biopsy workflow
18h05-18h25	CT	**Menghua ZHAO** ILM, Villeurbanne	Anomalous ionic transport in tunable angstrom-size water films on silica
20h00-23h30	***Gala dinner at O'CAPOT***		

Tuesday, 04 of April

09h00-09h20	AW	**Baptiste ALRIC** LAAS, Toulouse	Confinement de bactérie à l'aide de puce nanofluidique
09h20-09h40	CT	**Philippe MARMOTTANT** LIPhy, Grenoble	Obstacle race of air invading biomimetic leaves
09h40-10h00	CT	**Léa CHAZOT-FRANGUIADAKIS** LPENSL, Lyon	Flow driven jamming of viral particles in nanopores
10h00-10h30	IS	**Delphine DELACOUR** IJM, Paris	Organoid engineering for new biomimetic tools to study the intestinal tissue
10h30-11h00	***Coffe break + Poster session B***		
11h00-11h30	IS	**Antonin EDDI** PMMH, Paris	Artificial ice packs: a model laboratory approach
11h30-11h50	CT	**Antoine BÉRUT** ILM, Villeurbanne	Designing microfluidic hourglasses to study flows of dense colloidal suspensions under gravity
12h00-12h20	CT	**Robin DEBUYSSCHÈRE** ULB, Bruxelles	Investigation of the shear-induced nucleation mechanisms in a micro-crystallizer
12h20-12h40	CT	**Pauline BREGIGEON** Ampère, Ecully	Microfluidic device for spheroid culture and anticancer drug testing with electrochemotherapy
12h40-14h30	***Lunch break + Poster session B***		
14h30-14h50	CT	**Valentin CHALUT** INL, Villeurbanne	Cell growth on moving curvatures, towards gut-on-a-chip
14h50-15h10	CT	**Brice CALVIGNAC** MNT, Angers	Development of the Galenic Lab-on-a-chip and Therapy-on-a-chip concepts for drug formulation / delivery
15h10-15h30	CT	**Corentin TREGOUET** ESPCI, Paris	Ion exchange membrane resistance from cm to micro scale: is the power per unit area a good indicator?
15h30-15h50	CT	**Fabien OLIVIER** NIMBE, Gif-sur-Yvette	Etude par microfluidique des procédés de recyclage de composants de circuits imprimés
15h50-16h00	***Closing remarks***		

CT Contributive Talk

AW Award Winner

SP Sponsor Presentation

IS Invited Speaker

All abstracts including full author list and references are available here. They can also be reached by clicking on the talk title on the online version of the program, they can be browsed by speekers at the following address https://gdr-mnf-2023.sciencesconf.org/browse/author or by flashing this QR-code:

Invited speakers

Nanofluidics
Oriane Bonhomme – ILM, Villeurbanne
Soft nanofluidics: from electroosmosis in a liquid foam to the molecular scale description of interfaces

Flow Chemistry
Jean Gamby – Université Paris-Saclay, Palaiseau
Electrochimie en dispositifs micro nanofluidiques : Méthodes et Analyses

Flow, heat and mass transfer at microscale
Romain Quidant – ETH Zürich
Interfacing light and microfluidics: fluid actuation and bio-analytes detection

Microfluidics for Diagnostics and Clinics
Marie-Line Cosnier – CEA Leti, Grenoble
PEPS: An Innovative Microfluidic Device for Bedside Whole Blood Processing Before Plasma Proteomics Analyses

Organs-On-Chip
Delphine Delacour – IJM, Paris
Organoid engineering for new biomimetic tools to study the intestinal tissue

Flow-waves Interactions
Antonin Eddi – PMMH, ESPCI, Paris
Artificial ice packs: a model laboratory approach

«Young Researcher in Microfluidics 2023» prizes

Lucie Descamps – Eindhoven University of Technology
MagPure chip: a microfluidic device for the purification of Circulating tumor cells and the integration in liquid biopsy workflow

Baptiste Alric – LAAS, Toulouse
Confinement de bactérie à l'aide de puce nanofluidique

Selected speakers

Noam DEMRI – LPCC, Paris
Remote magnetic alignment of spheroids in 3D matrix for muscle-on-chip

Blaise DELMOTTE– LH, Paris
Magnetic microrollers as a platform for active transport

Théo ASPERT – IGBMC, Strasbourg
Tracking aging and environmental adaptation of single-cells with microfluidics, timelapse microscopy and deep-learning

Saranath SESHADRI – LIPhy, Grenoble
Membrane-free approaches to harvest osmotic Energy

Julie LACHAUX – LERI, Gif-sur-Yvette
Microfluidic biosensor for the continuous enzymatic detection of organophosphorus compounds

Anastasiia DUBROVA – CRIC, Paris
Tumor-on-chip model to decipher the effect of nanoparticle-mediated photothermia on tumor microenvironment of pancreatic ductal adenocarcinoma (PDAC)

Lilian MAGERMANS – LPMC, Paris
Kinetic Energy Harvesting System based on Selective Ion Sweeping under Flow Shear on Capacitive Electrode

Gabriel RAMOS – IMFT, Toulouse
Nonlocal dynamics of biofilm clogging in a porous microfluidic device

Solène MOREAU – TECTST, Paris
Soft thermoplastic elastomer compartmentalized chip for neurofluidic: applications to neural organotypic culture

Menghua ZHAO – ILM, Villeurbanne
Anomalous ionic transport in tunable angstrom-size water films on silica

Philippe MARMOTTANT – LIPhy, Grenoble
Obstacle race of air invading biomimetic leaves

Léa CHAZOT-FRANGUIADAKIS – LPENSL, Lyon
Flow driven jamming of viral particles in nanopores

Antoine BÉRUT – ILM, Villeurbanne
Designing microfluidic hourglasses to study flows of dense colloidal suspensions under gravity

Robin DEBUYSSCHÈRE – ULB, Bruxelles
Investigation of the shear-induced nucleation mechanisms in a micro-crystallizer

Pauline BREGIGEON – Ampère, Ecully
Microfluidic device for spheroid culture and anticancer drug testing with electrochemotherapy

Valentin CHALUT – INL, Villeurbanne
Cell growth on moving curvatures, towards gut-on-a-chip

Brice CALVIGNAC – MNT, Angers
Development of the Galenic Lab-on-a-chip and Therapy-on-a-chip concepts for drug formulation / delivery

Corentin TREGOUET– ESPCI, Paris
Ion exchange membrane resistance from cm to micro scale: is the power per unit area a good indicator?

Fabien OLIVIER – NIMBE, Gif-sur-Yvette
Etude par microfluidique des procédés de recyclage de composants de circuits imprimés

Soft nanofluidics: from electroosmosis in a liquid foam to the molecular scale description of interfaces

O. Bonhomme[1]*
[1]Institut Lumière Matière, Univ. Lyon 1-CNRS, Villeurbanne, France
*oriane.bonhomme@univ-lyon1.fr

Transport at the nanoscale is encountered in many natural systems and applications, from physiology through protein nanopores in cell regulation, to liquid transport through porous materials, relevant to water treatment and filtration. At such scale, surface properties have strong influence on flows. For example, electroosmotic flows (flow induced by an external electric field) take their origin close to the surfaces and are expected to depend on interface properties at the molecular scale such as charge and composition. Since the 2010s, foam films (a lamella of liquid in air covered by surfactants) appear as tools of choice for nanofluidic characterization as they are intrinsically nanometric, have a large range of surface properties tunable through the soapy solution formulation and are deformable [1].

I will first present our recent studies of flows induced by an electric field in a 3D macroscopic dry liquid foam [2]. In such structure, gas bubbles are in contact through the nanometric-thickness foam films, which themselves combine as micrometric-size channels (Plateau borders): foam can thus be seen as poro-elastic media. I will notably show, thanks to experimental studies and modeling, that the expected electroosmotic flow is enhanced by the thermal-gradients-induced flows due to heterogeneous Joule effects in such deformable structure.

Next, I will present how we investigate the molecular structure of the soapy interfaces, of crucial interest for describing nanoscale flow , through surface Second Harmonic Generation experiments. This non-linear optical technique is inherently specific to interface and sensitive to its molecular composition and organization. I will notably present how we question the existence a surfactant-concentration gradient at a soapy interface in presence of an electroosmotic flow [3]. I will also present more general applications of this technique for probing interfacial properties of interest for flows.

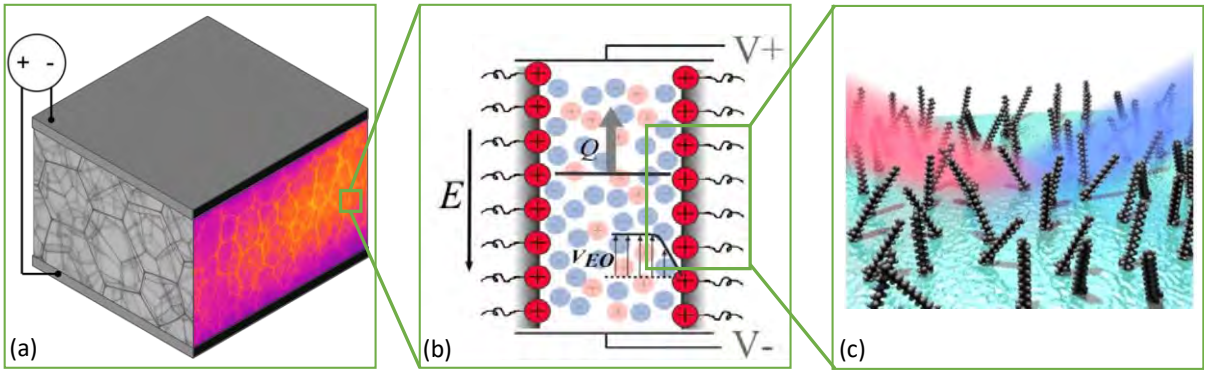


Figure 1: (a) Thermally-enhanced electroosmosis in a 3D liquid foam. (b) Electroosmosis in a nanometric foam film. (c) Surface Second Harmonic Generation experiments to probe surface composition of a soapy interface.

This work was made in collaboration with L. Peng, B. Blanc, E. Benichou, AL Biance

References

[1] O. Bonhomme, O. Liot, L. Bocquet, AL Biance, *Soft nanofluidic transport in soap film*, Phys Rev L, **110**, 054502 (2013)

[2] O. Bonhomme, L. Peng, AL Biance: *Thermally enhanced electroosmosis to control foam stability*. Phys Rev X, **10**, 21015 (2020)

[3] B. Blanc, O. Bonhomme, PF Brevet, E. Benichou, C. Ybert, AL Biance ; *Electroosmosis near surfactant laden liquid-air interfaces*. Soft Matter, **14**, 2604 (2018)

Remote magnetic alignment of spheroids in 3D matrix for muscle-on-chip

Noam Demri[1*], Simon Dumas[1], Manh-Louis Nguyen[1], Giacomo Gropplero[1], Ali Abou-Hassan[2], Stéphanie Descroix[1], Claire Wilhelm[1]

[1]Laboratoire Physico Chimie Curie, CNRS UMR168, Institut Curie, Sorbonne University, PSL University, Paris, France

[2]Nanosystèmes InterfaciauX, PHENIX, CNRS UMR234, Sorbonne University, Paris, France

*noam.demri@curie.fr

Organizing cells anisotropically is essential to recapitulate the skeletal muscle tissue's 3D microenvironment. Most cells alignment methods rely on contact guidance cues [1], but alignment in 3D [2], especially in a gel, remains challenging. Here we propose two innovative magnetic-based approaches for muscle tissue engineering [3]. The first approach generates magnetic spheroids as tissue building blocks, while the second one offers a new way to align magnetic cells or spheroids along a strong uniform magnetic field. Combined, the two-step process enables the on-chip creation of muscle fibers oriented in the magnetic field direction in collagen-based matrix. Cells were labeled with iron nanoparticles, and optimization led to 21pg of iron internalized per cell, with no impact on cell metabolic activity or capacity to differentiate. Microfabricated magnets could then attract the magnetically labelled cells and generate in 3 hours several thousand spheroids of controlled size (10-100 µm range). These spheroids could then be aligned on-chip in a 3D thermoresponsive collagen gel between two strong magnets. Once the gel polymerized, the chains of spheroids were trapped in this configuration. The chains were on average a few hundreds of microns long and could go up to 1 mm under optimal cell density and magnetic labeling. Such structures made with aligned spheroids remarkably maintained their anisotropy overtime. Besides, in a matter of days, the spheroid chains fused into fiber-like structures. These fibers could also be 20% stretched or co-cultivated in the 3D collagen gel with randomly dispersed fibroblasts, and several myofibers formed in the direction of the alignment. Overall, this work demonstrates that combining magnetically assisted 3D strategies with organ-on-chip technology is beneficial for the fabrication of muscle tissue engineered constructs. As many tissues in the human body are anisotropic, these technologies to produce and align magnetic spheroids could open new perspectives for 3D tissue engineering.

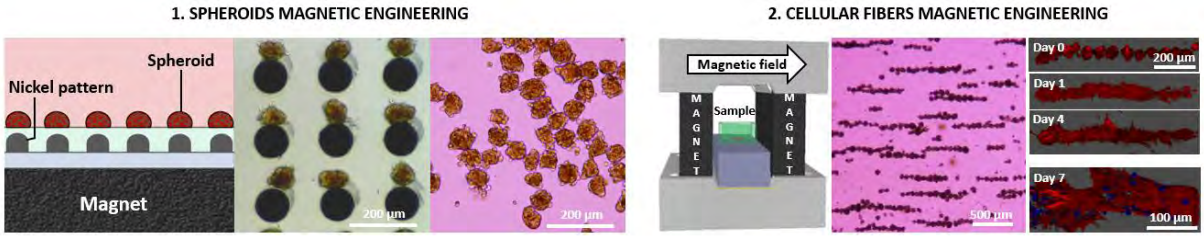


Figure 1: Spheroids' magnetic microfabrication and alignment to form a 3D cellular fiber

References

[1] A. Jain, M. Behera, V. Ravi, S. Mishra, N. R. Sundaresan, K. Chatterjee: *Recapitulating pathophysiology of skeletal muscle diseases in vitro using primary mouse myoblasts on a nanofibrous platform*. Nanomedicine: Nanotechnology, Biology and Medicine **32**, 102341 (2021)

[2] N. Takeda, K. Tamura, R. Mineguchi, Y. Ishikawa, Y. Haraguchi, T. Shimizu, Y. Hara. (2016): *In situ cross-linked electrospun fiber scaffold of collagen for fabricating cell-dense muscle tissue.* Journal of Artificial Organs **19(2)**, 141-148 (2016)

[3] N. Demri, S. Dumas, M. L. Nguyen, G. Gropplero, A. Abou- Hassan, S. Descroix, C. Wilhelm: *Remote Magnetic Microengineering and Alignment of Spheroids into 3D Cellular Fibers*. Advanced Functional Materials **32(50)**, 2204850 (2022)

Magnetic microrollers as a platform for active transport

Blaise Delmotte[1]*, Ernest van Der Wee[2], Aleksandar Donev[3], Michelle Driscoll[4]

[1]LadHyX, CNRS/Ecole Polytechnique, France
[2]Imaging Physics, Technische Universiteit Delft, Netherlands
[3]Courant Institute of Mathematical Sciences, New York University, USA
[4]Dept. Physics, Northwestern University, USA

*blaise.delmotte@cnrs.fr

Transport and mixing at the microscale are difficult due to the absence of inertia and strong wall friction in confined systems, and a wide range of solutions have been proposed to address this challenge. We propose a new strategy that leverages wall friction to achieve these tasks using microrollers.

Microrororollers are micron-sized particles that spin thanks to a rotating magnetic field, **B**, about an axis parallel to the interface (Fig. 1a). When these colloidal particles rotate adjacent to a nearby floor, strong advective flows are generated around them, even quite far away. When a group of these microrollers is driven, the strong hydrodynamic coupling between particles leads to formation of new structures with great potential for microfluidic and bio-medical applications.

Our experimental observations show that uniform suspensions of microrollers form active motile carpets with fast flows above them. By varying the direction of the magnetic field, these active layers can be used for the guided transport of passive cargos at large scales (Fig. 1b) [1].

When the suspension is not uniformly distributed, it undergoes a cascade of instabilities: an initially uniform front of microrollers evolves first into a shock-like structure, which then quickly becomes unstable, emitting fingers of a well-defined wavelength; then the fingertips pinch off to form compact motile structures translating at high speed (Fig. 1c) [1]. These colloidal creatures are self-sustained and form a stable state of the system. Combining experiments, large scale numerical simulations and continuum models, we will explain the predominant role of hydrodynamic collective effects in the development of these colloidal creatures.

We will further show how the nature of the surface underneath and the presence of obstacles affect their individual and collective dynamics [2,3].

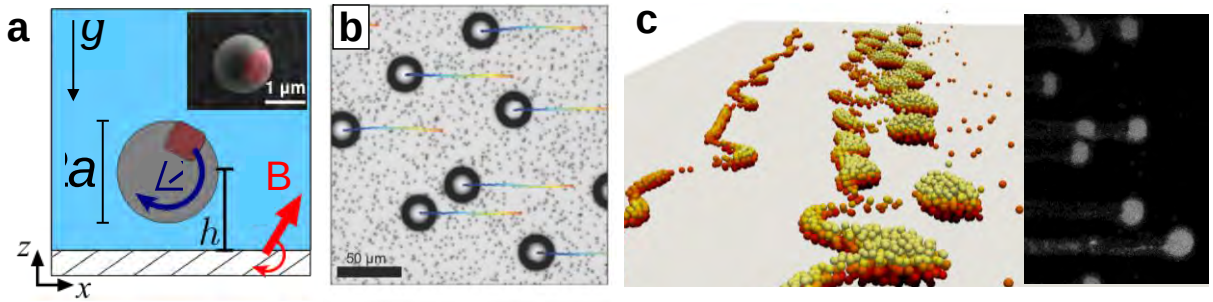


Figure 1: a) Sketch of a microroller rotating above a solid/liquid interface, b) Transport of large cargo particles (20 times bigger than rollers) by a uniform suspension. Colored lines indicate cargo particle tracks. c) Stable clusters emerging from a fingering instability. Particles are colored by speed. Inset : top view of an experiment

References

[1] M. Driscoll*, B. Delmotte*, M. Youssef, S. Saccana, A. Donev, P. Chaikin. Unstable fronts and motile structures formed by microrollers. Nature Physics, **13**, 375-379. (2017).

[2] B. Delmotte, Viscosity ratio across interfaces control the collective dynamics of microrollers, *submitted* (2023)

[3] E. van der Wee, B. Blackwell, F. Usabiaga, A. Sokolov, I. Katz, B. Delmotte, M. Driscoll. A simple catch: thermal fluctuations enable hydrodynamic trapping of microrollers by obstacles. arXiv preprint arXiv:2204.04995. (2022).

Electrochimie en dispositifs micro nanofluidiques : Méthodes et Analyses

Claire Poujouly[1], Marie-Charlotte Horny[1], Martina Freisa[1], Pedro Gonzalez-Losada[1], Djamila Kechkeche[1,2], Emilie Secret[2], Vincent Dupuis[2], Jean-Michel Siaugue[2], Jean Gamby[1]*

[1] Centre de Nanosciences et de Nanotechnologies (C2N), Université Paris-Saclay, CNRS, Palaiseau
[2] Physico-chimie des Électrolytes et Nanosystèmes Interfaciaux (PHENIX), Sorbonne Université, CNRS, Paris
*jean.gamby@c2n.upsaclay.fr

Dans cet exposé, je présenterai les intérêts de l'utilisation des méthodes électrochimiques appliquées au domaine de la micro nanofluidique, d'abord sur le plan théorique, puis en termes d'applications récentes pour l'analyse des micro-ARN (miARN). Sur le plan fondamental, nous aborderons les récentes avancées concernant l'expression théorique de l'impédance de diffusion-convection pour une électrode microbande placée dans un flux de Poiseuille dans des conditions microfluidiques [1]. L'utilisation de la spectroscopie d'impédance électrochimique (EIS) met en évidence un bon accord, dans l'intégralité du domaine de fréquences balayées, entre l'expression de l'impédance modélisée et l'expérimentale. Sur le plan applicatif, nous verrons comment la maîtrise des paramètres hydrodynamiques et électrochimiques permet d'augmenter l'efficacité du taux de collection lors de l'hybridation des séquences complémentaires sur microélectrodes [2],[3]. Enfin, je terminerai par la mise au point de la technologie HDE (Hyperthermie et Détection Electrochimique) basée sur la sur-concentration physique de brins d'acides nucléiques comme véritable alternative à l'amplification chimique de type PCR [4]. En bref, la technologie HDE est dans la philosophie du « laboratoire-sur-puce » idéal intégrant plusieurs opérations complémentaires. Ici, 3 opérations sont visées : la capture, le relargage et la détection des brins d'acides nucléiques (Figure 1).

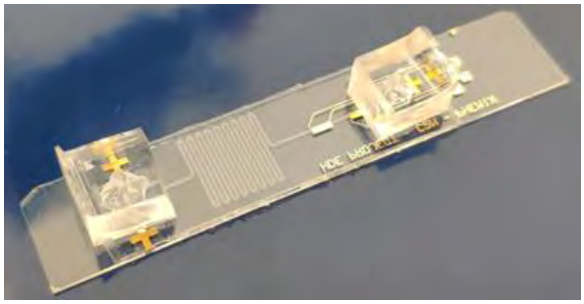


Figure 1: Laboratoire-sur-puce permettant de coupler les étapes de sur-concentration, de relargage et de détection d'acides nucléiques

References

[1] C. Poujouly, P. Gonzalez-Losada, R. Boukraa, M. Freisa, J. Le Gall, D. Bouville, C. Deslouis, J. Gamby, Diffusion–convection impedance for a micro-band electrode under microfluidic conditions, Electrochemistry Communications, 137 (2022) 107262.
[2] M.C. Horny, M. Lazerges, J.M. Siaugue, A. Pallandre, D. Rose, F. Bedioui, C. Deslouis, A.M. Haghiri-Gosnet, J. Gamby, Electrochemical DNA biosensors based on long-range electron transfer: investigating the efficiency of a fluidic channel microelectrode compared to an ultramicroelectrode in a two-electrode setup, Lab Chip, 7 (2016) 307.
[3] C. Poujouly, J. Le Gall, M. Freisa, D. Kechkeche, D. Bouville, J. Khemir, P. Gonzalez-Losada, J. Gamby, Microfluidic Chip for the Electrochemical Detection of MicroRNAs: Methylene Blue Increasing the Specificity of the Biosensor, Frontiers in chemistry, 10 (2022).
[4] M.-C. Horny, V. Dupuis, J.-M. Siaugue, J. Gamby, Release and Detection of microRNA by Combining Magnetic Hyperthermia and Electrochemistry Modules on a Microfluidic Chip, Sensors, 21 (2021) 185.

Tracking aging and environmental adaptation of single-cells with microfluidics, timelapse microscopy and deep-learning

T. Aspert[1,2,3*], **G. Charvin**[1,2,3]

[1]Institut de Génétique et de Biologie Moléculaire et Cellulaire
[2]Institut de Génétique Moléculaire Génomique et Microbiologie
[3]Université de Strasbourg
[*]theo.aspert@gmail.com

Microorganisms such as budding yeast are a powerful model to study cellular division, aging, or environmental adaptation. However, the intrinsic heterogeneous and dynamic nature of these phenomena requires their analyses at the single-cell level.
To address this technical challenge, we have developed two microfluidic-based platforms to follow single cells for several days in different contexts:

i) Replicative aging, where a mother cell divides and ages while its progeny is rejuvenated. Here, microfluidics is used to isolate and follow mother cells in a high throughput manner throughout their lifespan while automatically dissecting the daughter cells that would otherwise overwhelm the device due to their exponential growth [1].

ii) Adaptation to autonomous environmental degradation, where a growing culture progressively exhausts nutrients from its media. Cells have evolved to adapt to the different phases of this exhaustion, but studying the biological programs behind this adaption requires population-scale growth experiments to allow cell proliferation to have a collective impact on the environment, while tracking the same individuals for days. To this purpose, we developed an integrated microfluidic device based on continuous separation of the cells from the media (~5.10^5 cells/µL) and subsequent perfusion of the filtrated media into an observation chamber containing isolated single-cells [2].

Yet, these microfluidic tools coupled with video-microscopy offer such a quantity of data that it is not possible to analyze by conventional means, thus leaving their full potential unexploited. Therefore, we also developed a deep-learning approach to automate the detection of cell divisions, death, size, fluorescence, or temporal events, from week-long time-lapses [1]. It was proven to work equally well with data from different microfluidic devices, allowing widespread use of this tool among the community.

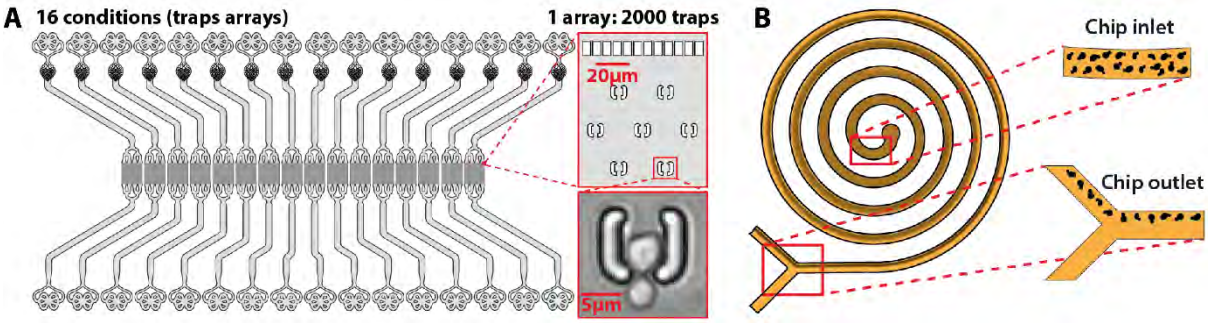


Figure 1: (A) Device to trap single yeast cells and track them throughout their replicative lifespan. (B) Device to separate yeast cells from the media in a continuous manner.

References

[1] T. Aspert, D. Hentsch, G. Charvin, DetecDiv, a generalist deep-learning platform for automated cell division tracking and survival analysis, Elife. 11 (2022) e79519.

[2] B. Jacquel, T. Aspert, D. Laporte, I. Sagot, G. Charvin, Monitoring single-cell dynamics of entry into quiescence during an unperturbed life cycle, Elife. 10 (2021) e73186.

Membrane-free approaches to harvest osmotic Energy

S. Seshadri[1], Heloise Ugo[1], Elisabeth Charlaix[1] and Cyril Picard[1]*

[1]Laboratoire Interdisciplinaire de Physique (LiPhy), Grenoble, France
*cyril.picard@univ-grenoble-alpes.fr

The mixing of two electrolyte solutions of different concentrations is characterized by a free enthalpy of mixing. Its conversion to useful mechanical work or electricity has the potential to be a source of renewable energy and is commonly called osmotic or blue energy in the case of mixing of river water with sea water. The remarkable development of membrane technology has opened new perspectives to harvest this osmotic energy. However, the establishment of several prototypes has resulted in the identification of some inherent limitations in membrane-based approaches, such as concentration polarization [1].

The first segment of this talk will introduce a top-down approach based on the design of a silicon nanofluidic exchanger[2]. This design gives the ability to minimize concentration polarization issues and to maintain the high conversion capabilities of individual nanopores. This section's main emphasis will be on the optimization of the coupled solute transport at multiscales and the subsequent design of a "Multi-Scale exchanger".

The second segment of this talk, concerns a bottom-up approach based on the usage of nanoporous hydrophobic materials[3]. Inspired from the pressure swing adsorption technologies, well known for gas separation, we propose a membrane-free method to recover osmotic energy based on osmosis between the inside and the outside of nanoporous particles. This method operates as a cycle with a characteristic time hundreds time quicker than the hydrogel method which makes it valuable to rich high power densities. The Zeolitic Imidazolate Framework 8 material (ZIF-8) is used to illustrate experimentally this approach.

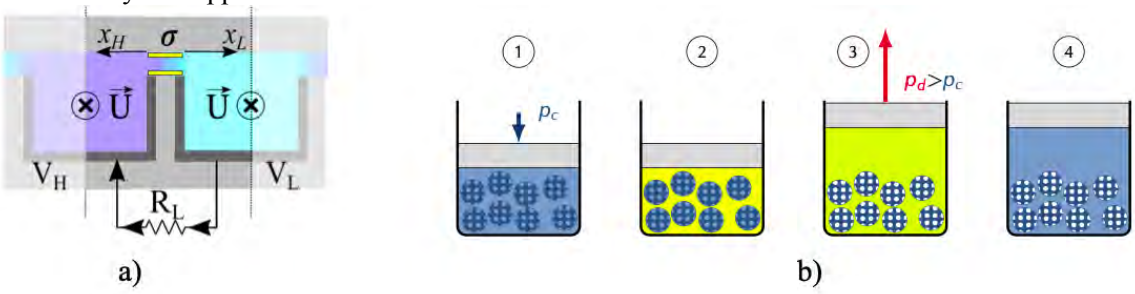


Figure 1: **(a)** Sectional schematic of an *Elemental nanofluidic Exchanger* **(b)** schematic of the principle of the volume swing osmosis method based on hydrophobic selective nanoporous material.

References

[1] L. Wang, Z. Wang, S. K. Patel, S. Lin, S. and M. Elimelech, M. *Nanopore-based power generation from salinity gradient: why it is not viable.* ACS nano, **15(3)**, pp.4093-4107 (2021).

[2] S. Seshadri, V. Larrey, F. Fournel, C. Picard and E.Charlaix, *Nanopore-Based Power Generation from Salinity Gradient*, in preparation, ACS nano.

[3] C. Picard, E. Charlaix, and W. Chèvremont. Procédé de conversion d'énergie osmotique en énergie hydraulique et de dessalement, WO2002/258912, (2022).

Microfluidic biosensor for the continuous enzymatic detection of organophosphorus compounds

J. Lachaux[1]*, C. Mairaville[1], M. Ben Frej[1], H. Volland[1], S. Simon[1] and K. Perez Toralla[1]

[1] Université Paris-Saclay, CEA, INRAE, Département Médicaments et Technologies pour la Santé (MTS), Gif-sur-Yvette, 91191, France
*julie.lachaux@cea.fr

The use of pesticide organophosphate (OP) has serious consequences for the contamination of soil and ground waters. Because of their high toxicity, there is a negative impact on aquatic wildlife and potentially also for human health. In particular, these compounds can inhibit acetylcholinesterase (AChE), blocking neurotransmission in the central nervous system. As compared to other OP detection techniques, measuring the activity of AChE and its inhibition in the presence of OP can provide a more rapid, sensitive and specific response. Although the development of AChE-based microfluidic devices has made significant progress in the last few years [1], only few systems can continuously analyze the presence of OP in circulating water (most providing only one result per time-point for each sample). We demonstrate here an integrated AChE-based biosensor allowing the continuous, on-site detection of liquid OP compounds, which could be used for water environmental monitoring.

In this work, we implemented an AChE inhibition colorimetric test based on the use of acetylthiocholine (substrate) and Ellman's reagent [2] to determine the half-maximal inhibitory concentration (IC50) of commercial OP pesticides (malaoxon) in aqueous solutions. A specific experimental bench (Fig 1.A) has been set-up in order to implement the enzymatic inhibition test in droplets-based microfluidic. Two off-chip incubation steps of 30 min each (Figure 1.A, steps 1 and 2) are performed in a continuous flow. Droplets generated by the injection of an oil flow at the T-junction (Figure 1.A, step 3) are analyzed continuously by microscopy through an observation chamber (Figure 3.A, step 4). Three inhibition experiments were performed at IC50 ($3{,}5.10^{-9}$ M for the malaoxon) with an analysis of the yellow signal intensity. Graph shows a significant variation in signal intensity in the presence of OP, showing inhibition of enzyme activity (Figure 3.B). The variation of yellow signal intensity can also be visually observed in microscope images (Figure 3.B). Under these conditions, we estimate that the microfluidic system has a very good sensitivity of $3{,}5.10^{-9}$ M for malaoxon. More experiments will be carried out to test a larger pesticides panel and concentration range. It is therefore a promising miniaturized device in term of liquid organophosphorus detection while permitting a continuous flow analysis.

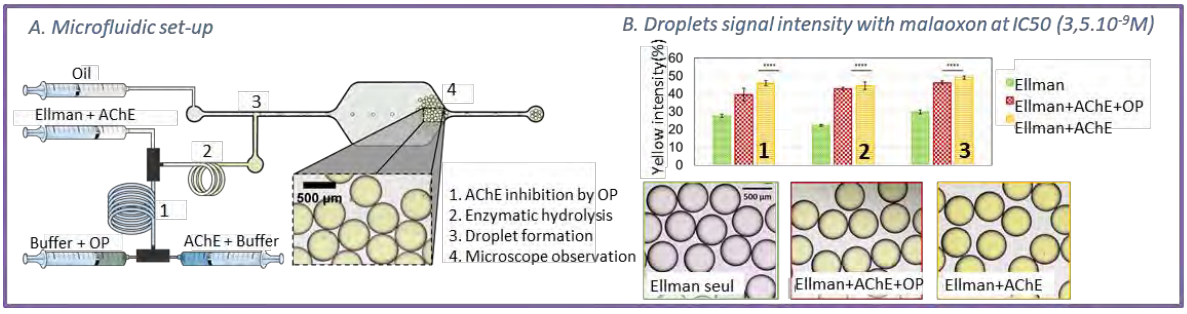


Figure 1: Experimental set-up of enzymatic inhibition in droplets-based microfluidic (A), and the results of yellow signal intensity for 3 experiments with malaoxon at IC50 (B).

References

[1] M. Bhattu, M. Verma, D. Kathuria: *Recent advancements in the detection of organophosphate pesticides: a review*. Anal. Methods **13**, 4390 (2021)

[2] G.L. Ellman, K.D. Courtney, V. Andres, R. M. Feather-Stone: *A new and rapid colorimetric determination of acetylcholinesterase activity.* Biochemical Pharmacology **7**, 88-90 (1961)

Interfacing light and microfluidics: fluid actuation and bio-analytes detection

R. Quidant*

[1]Nanophotonic Systems Laboratory, Department of Mechanical and Process Engineering, ETH Zurich, Zurich, Switzerland.
*rquidant@ethz.ch

In this presentation we discuss our recent work at the interface between photonics and microfluidics. First, we discuss how light interacting with absorbing nanoparticles can be used to engineer temperatures gradients at the microscale and enable controlling the dynamics of fluids in a microfluidic environment, both for actuation [1] and to overcome the diffusion limit in integrated biosensing [2]. The second part of the talk introduces several integrated bio-detection platforms involving optical interrogation. We discuss platforms exploiting colorimetric sensing with resonant metallic [3] and dielectric particles [4] for the detection of proteins. We also present our latest advances in multiplexed detection of exosomes using i-Scat microscopy [5].

References

[1] B. Ciraulo, J. Garcia-Guirado, I. de Miguel, J. Ortega Arroyo, R. Quidant, Nature Communications **12**, 2001 (2021)

[2] J Garcia-Guirado, RA Rica, J Ortega, J Medina, V Sanz, E Ruiz-Reina, R. Quidant, ACS photonics **5**, 3673-3679 (2018)

[3] O. Yavas, S. S. Aćimović, J. Garcia-Guirado, J. Berthelot, P. Dobosz, V. Sanz, and R. Quidant, *ACS Sens.* **3**, 1376–1384 (2018)

[4] J. Garcia-Guirado, M. Svedendahl, J. Puigdollers, R. Quidant, Nano letters **20**, 585-591 (2019)

[5] A. Stollmann et al, in preparation (2023)

Tumor-on-chip model to decipher the effect of nanoparticle-mediated photothermia on tumor microenvironment of pancreatic ductal adenocarcinoma (PDAC)

A. Dubrova[1*], C. Cavaniol[1], Y. Lalatonne[2], A. Van de Walle[1], C. Wilhelm[1], S. Descroix[1]

[1]Physico-Chimie Curie, UMR168 CNRS / Institut Curie, Paris, France
[2]Inserm, U1148, Hopital Avivennes-APHP, Bobigny, France
[*]anastasiia.dubrova@curie.fr

Pancreatic Ductal AdenoCarcinoma (PDAC) constitutes ~90% of pancreatic cancer cases and is characterized by poor prognosis partly due to therapy resistance [1]. Most of this resistance is attributed to the extensive fibrotic stroma with enhanced desmoplastic effect within the tumor microenvironment that impedes anticancer drug delivery [2]. Nanoparticle-mediated photothermal therapy (NP-PTT) presents a promising technique for adjuvant cancer treatment, through local heating of malignant cells, matrix denaturation, or T cell recruitment among others [3]. Herein, we implement for the first time the NP-PTT in PDAC tumor-on-chip (ToC) to better understand the effect of these NP-mediated therapies and improve their efficiency as combined therapies (with chemo- or immunotherapies).

Our microfluidic system consists of a central chamber for 3D tumor microenvironment modelling & 2 side chambers – for controlled injection of NPs and medium supply. Since collagen I is the most abundant protein in tumor microenvironment [3], we first studied diffusion, temperature increase, and degradation of the collagen matrix alone submitted to NP-PTT. Next, to mimic PDAC microenvironment, we cultured human PDAC cells (PANC-1) in collagen I matrix. NP-PTT treatment conditions combine: iron oxide magnetite NPs coated with PO-PEG-NH_2, 20min exposure to 808nm laser, 1-2W/cm^2 laser power density. The effect of NP-mediated PPT is assessed with confocal microscopy (live/dead assay) for cancer cells and second harmonic generation microscopy (SHG) for the matrix response.

We observed successful on-chip NPs diffusion in collagen I matrix with subsequent temperature increase (37-55°C) through PTT. Using SHG, we showed that collagen I matrix in the chip, in the exposure conditions starts to degrade above 51°C, as also reported previously [4]. Next, we successfully developed a PDAC tumor-on-chip model with formation of tumor spheroids (~100µm) from single pancreatic tumor cells (PANC-1) in collagen, exhibiting invasive phenotype after 7 days of culture (**Figure 1**). This indicates progressive tumor formation and its invasion of the collagen matrix, closely mimicking the *in vivo* conditions. PDAC-on-chip exposure to NP-PTT showed increasing tumor cell death with increasing temperature as a result of the treatment.

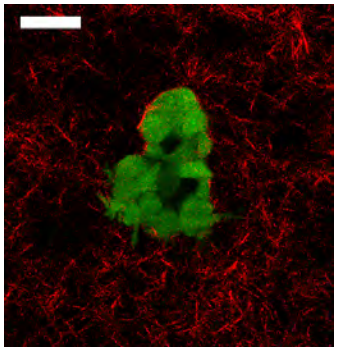


Figure 1: SHG image of PANC-1 cell culture (green) on chip in collagen I (red,6mg/mL), day 7.

With successfully implemented NP-PTT in PDAC-on-chip model, we showed that by tuning NP concentration and/or the heating protocol, ToC device can be finely controlled to promote matrix denaturation and cell death. Our next steps will consist in advancing our PDAC-on-chip model via co-culture of PANC-1 cells with stellate cells to induce the key desmoplastic reaction present *in vivo*. We will thus investigate the matrix remodeling and its effect on NP uptake, heating-induced cell death & matrix degradation to fully study the effect of PTT on PDAC microenvironment and its possible applications for synergized cancer therapies.

References

[1] Cai, J. et al.: *Advances in the epidemiology of pancreatic cancer: Trends, risk factors, screening, and prognosis.* Cancer Letters, **520**, 1-11. (2021)
[2] Yang, H. et al: *Photosensitizer nanoparticles boost photodynamic therapy for pancreatic cancer treatment.* Nano-Micro Letters, **13(1)**, 1-16 (2021)
[3] Maneshi, P. et al.: *Targeting Tumor-Stromal Interactions in Pancreatic Cancer: Impact of Collagens and Mechanical Traits.* Frontiers in Cell and Developmental Biology, **9**. (2021)
[4] Theodossiou, T. et al.: *Thermally induced irreversible conformational changes in collagen probed by optical second harmonic generation and laser-induced fluorescence.* Lasers in medical science, **17(1)**, 34-41. (2002)

Kinetic energy harvesting system based on selective ion sweeping under flow shear on capacitive electrode

L. Magermans[1]*, D. Lee[2], J. Kim[1], Z. Wang[1], S.W. Lee[2], T. Gacoin[1], J. Kim[1]

[1]Groupe de Chimie du Solide, Laboratoire de Physique de la Matière Condensée, CNRS, Ecole Polytechnique, IP-Paris, Palaiseau, France
[2]School of Electrical and Electronic Engineering, Nanyang Technological University, Singapore
*lilian.magermans@polytechnique.edu

When flowing electrolyte over a capacitive electrode, ions adsorbed on the electrode surface are swept away due to the interfacial shear stress. If this ion sweeping occurs at only one electrode of a circuit, it induces potential bias and can thus generate electric current [1]. This phenomenon enables us to harvest various types of kinetic energy on different scales (e.g. microbiological dynamics, human motions, ocean tide) and convert to useful electric energy sources. For this, a key is 1) to understand how the hydrodynamic parameters quantitatively regulate the ion sweeping effect and electrochemical responses, and 2) to design novel hydrodynamic-electrochemical hybrid device structure that is efficient for the energy transformation.

In this work, we create a selective ion sweeping device by incorporating ITO electrodes into a microfluidic channel with an architecture exposing only one of the two electrodes to strong interfacial shear stresses. We characterize electrochemical responses of this device as a function of the flow shear applied at the electrode surface. This requires flow shear measurements with high spatial and temporal resolution near the channel walls. We have developed such a technique using the shear-induced orientation behavior and the polarized photoluminescence property of LaPO4:Eu nanorods [2]. We can thus characterize the shear flow in our energy harvesting device by adding LaPO4:Eu nanorods to the electrolyte and collecting their polarized emission under flow. This allows us to study the fundamental relationship between shear flow and ion sweeping and aids in the optimization of the device.

References

[1] , I. D. Jung, M. Kim, C. Gao, Y. Liu, C. Park, H.-W Lee, S. W. Lee, *Selective Ion Sweeping on Prussian Blue Analogue Nanoparticles and Activated Carbon for Electrochemical Kinetic Energy Harvesting.* Nano Lett, **20 (3),** 1800–1807 (2020)

[2] J. Kim, S. Michelin, M. Hilbers, L. Martinelli, E. Chaudan, G. Amselem, E. Fradet, J.-P. Boilot, A.M. Brouwer, C.N. Baround, J. Peretti, T. Gacoin, *Monitoring the Orientation of Rare-Earth-Doped Nanorods for Flow Shear Tomography.* Nature Nanotech, **12 (9)**, 914–919 (2017).

PEPS: An Innovative Microfluidic Device for Bedside Whole Blood Processing Before Plasma Proteomics Analyses

Benoit Gilquin[1], Myriam Cubizolles[2], Remco Den Dulk[2], Frédéric Revol-Cavalier[2], Manuel Alessio[2], Charles-Elie Goujon[3], Camille Echampard[2], Gorka Arrizabalaga[3], Annie Adrait[4], Mathilde Louwagie[4], Patricia Laurent[2], Fabrice P. Navarro[2], Yohann Couté[4], Marie-Line Cosnier[2*] and Virginie Brun[4]

[1]Univ. Grenoble Alpes, CEA, LETI, Clinatec, F-38000 Grenoble, FRANCE
[2]Univ. Grenoble Alpes, CEA, LETI, Technologies for Healthcare and Biology Division, Microfluidic Systems and Bioengineering Lab, F-38000 Grenoble, FRANCE
[3]Univ. Grenoble Alpes, CEA, CEA Tech, Y.SPOT, F-38000 Grenoble, FRANCE and
[4]Univ. Grenoble Alpes, CEA, Inserm, IRIG, BGE, EDyP, F-38000 Grenoble, FRANCE
[*]marie-line.cosnier@cea.fr

Mass spectrometry (MS)-based proteomics analysis appeared promising to assess panels of protein biomarkers and provide protein profiles for health state monitoring. Nevertheless, the complexity and the time and human workforce necessary for sample preparation hamper translation of MS-based proteomics into the clinics. To address these challenges, microfluidic is a relevant choice. The plasma proteome is the source of more than 3000 proteins covering an extreme dynamic range (10^{10}) of concentrations [1]. Today, over 200 plasma proteins are biomarkers in clinical biology.

To accelerate, simplify and standardize the processing of biological samples before MS-based proteomics analysis, we have conceived a microfluidic device (PepS) to automate blood sample preparation in integrating a complete pre-analytical protocol into microfluidic platform [2].

The single-use microfluidic cartridge (Figure 1A) is made from Cyclo Olefin Copolymer (COC) and other materials (elastomeric valves, silicone pump membranes…) and contains channels, reaction chambers and dried or lyophilized reagents. The compact instrument (Figure 1B) is in-house developed. It provides fully automated fluid processing and thermal control and contains a pneumatic control unit, a heating element and a cartridge holder.

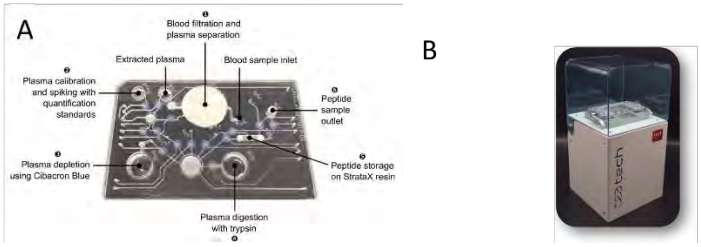


Figure 1: PepS microfluidic cartridge (A) and instrument (B)

The automated protocol takes less than 2 hours as compared to 6 hours for the same protocol performed manually (considering a classical 4-hours digestion step). Peptide digests obtained after PepS and manual processing were analysed using liquid chromatography-tandem MS (LC-MS/MS) for shotgun proteomic analysis and using liquid chromatography coupled to selected reaction monitoring (LC-SRM) for targeted proteomic analysis. Results obtained successfully assessed the performance of PepS device. The microfluidic PepS device offers the unique capability to process automatically and reproducibly plasma proteome from whole blood in 2 hours.

References

[1] T. Farrah, E.W. Deutsch, et al: *A High-Confidence Human Plasma Proteome Reference Set with Estimated Concentrations in PeptideAtlas*. Mol. Cell. Proteomics, **10**, M110 006353 (2011)

[2] B. Gilquin, M. Cubizolles, R. Den Dulk et al: *PepS: An Innovative Microfluidic Device for Bedside Whole Blood Processing before Plasma Proteomics Analyses*. Anal. Chem., **86**, 683-690 (2021)

Nonlocal dynamics of biofilm clogging in a porous microfluidic device

G. Ramos[1,2]*, M. Benbelkacem[1], T. Desclaux[1], O. Liot[1], P. Duru[1], Fatima El Garah[2], Y. Davit[1]

[1]Institut de Mécanique des Fluides de Toulouse UMR 5502, Toulouse, France
[2]Laboratoire de Génie Chimique, Université de Toulouse, CNRS, INPT, UPS, Toulouse, France
*gabriel.ramosperoni@imft.fr

Bacteria constitute about 15% of the global biomass on Earth [1]. The success of bacteria in colonizing a wide range of ecosystems is mainly due to biofilms, a sessile form of microbial life [2]. Biofilms are communities of interacting microbes that adhere to each other and to structures in their environment [3], making them more resistant to stress. Biofilms regulate critical processes in porous ecosystems [5], such as soils and groundwater systems, and are also key actors in bioengineering applications, such as biofilters [4]. These porous systems generally have a complex architecture, with structures that are connected, heterogeneous and exhibit strong couplings between flow and transport phenomena. Understanding the fundamental mechanisms of the colonization process in such systems may provide important insight into environmental processes and yield new approaches to bioengineering.

In this work, we study biofilm growth in porous media using microfluidics. The setup consists in a glass/PMDS honeycomb channel network, colonized by *Pseudomonas aeruginosa*, a known biofilm model bacteria [3]. Using microscopy techniques, image analysis and particle tracking velocimetry (PTV), we obtain both the distribution of biomass and the velocity field within the network. This allows us to study the coupling mechanisms between flow and biofilm growth. We further study how this evolves over a range of flow rates. Results show a spatial distribution of biofilm that is strongly correlated to the flow rate within each channel. For the low flow rates, the biofilm colonization at short times is rather homogeneous, while at long times the clogging of channels due to biofilm creates preferential flow paths. These paths are unstable with cycles of clogging/declogging due to a competition between growth and flow-induced detachment. Signal analysis of pressure and fluorescence signals show that these events have a characteristic frequency, and we propose a model taking into account the flow rate, the cross-section surface of the channel and the doubling time for the bacteria population.

References

[1] Y. Bar-On, R. Phillips, R. Milo: *The biomass distribution on earth*. PNAS **115**, 6506-6511 (2017)

[2] H. Flemming, S. Wuertz: *Bacteria and archaea on earth and their abundance in biofilms*. Nat. Rev.Microbiol. **17**, 247-260 (2019)

[3] V. Gordon, M. Davis-Fields, K. Kovach, C. Rodesney: *Biofilms and mechanics: a review of experimental techniques and findings*. J. Phys. D: Appl. Phys. **50**, 223002 (2017)

[4] C. A. Rolph, R. Villa, B. Jefferson, A. Brookes, A. Choya, G. Iceton, F. Hassard: *From full-scale biofilters to bioreactors: Engineering biological metaldehyde removal*. Science of the Total Environment **685**, 410-418 (2019)

[5] D. Scheidweiler, H. Peter, P. Pramateftaki, P. de Anna, T.J. Battin: *Unraveling the biophysical underpinnings to the success of multispecies biofilms in porous environments*. ISME J **13**, 1700-1710 (2019)

Soft thermoplastic elastomer compartmentalized chip for neurofluidic: applications to neural organotypic culture

S. Moreau[1*], R. Flores-Berdines[1], T. El Jalkh[2], C. Becker[1], S. Bernard[1], H. Salmon[1,3]

[1]T3S, UMR-S INSERM 1124, Université Paris Cité, Paris, France
[2]IMRB, INSERM U955, Université Paris-Est, Créteil, France
[3]MSC, UMR CNRS 7057, Université Paris Cité, Paris, France
*solene.moreau1@etu.u-paris.fr

Compartmentalized microfluidic chips have changed our way to study the nervous system and screen drugs. They now play an important role in the understanding of the cellular mechanisms involved in peripheral nervous system disorders and demyelination.. [1] Most of the microfluidic chips for cell culture are made of polydimethylsiloxane (PDMS), yet they present limitation in terms of fabrication, assembling and biological modeling. Easy to prototype and to translate, soft thermoplastic elastomers (sTPE) have emerged as an alternative material for on chip biology with a potential for cell biology to explore. sTPE are less expensive than PDMS and present an easy scale up for commercial or industrial purposes. [2]

Here, we develop the first sTPE compartmentalized device and compare it to a standard PDMS one, and grow embryonic Dorsal Root Ganglia (DRG) explants in standard well plates compatible with high content screening microscopy (HCS) (Fig.1A). We emboss a FDA approved copolymer of polystyrene and ethylene/butylene. This material has a Young modulus of 1.15 MPa, close to PDMS, is transparent, flexible and stable to treatments such as oxygen plasma and coating. We exploit its bulk properties for fast prototyping (less than 10 min/chip) and reversible adhesive bonding allowing easy and accurate manual assembly of two-level architectures. This sTPE is resistant to small particles adsorption and have a low reduced gas permeability, making it an ideal material for biological applications. We demonstrate its capacities on DRG cultures from mouse embryos in a well suited axisymmetrical design, with no impact on the axonal growth or the cell viability (Fig.1B). After more than 1 month of culture, we are able to open the chip without damaging the cells to realize direct analysis using atomic force or scanning electron microscopy (Fig.1C). After a simple washing and sterilization procedure, the chips can be re-used up to five time without impacting its bonding or the viability of the cells. The sTPE microfluidic chip paves the way to an alternative way of prototyping compartmentalized devices, widening their field of applications and making their manufacturing more accessible and sustainable.

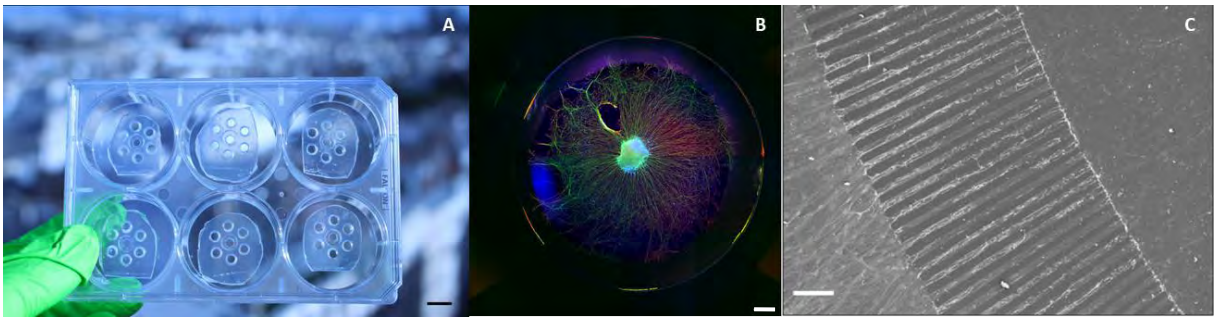


Figure 1: (A) sTPE compartmentalized chips in a standard well plate for HCS, scale=1cm (B) DRG explant at DIV3 inside a sTPE microfluidic chip, nuclei (blue), neurofilaments H (green), neurofilaments M and H (red), scale=500µm (C) SEM picture of aligned axons after opening of the microfluidic chip, scale=100µm

[1] S. Hyung, S.R. Lee, J. Kim, N.L. Jeon., *A 3D disease and regeneration model of peripheral nervous system–on–a–chip*, Science Advances, 7, n°5 (2021)
[2] H. Salmon, M. R. Rasouli, N. Distasio, M. Tabrizian, *Facile engineering and interfacing of styrenic block copolymers devices for low-cost, multipurpose microfluidic applications*, Engineering Report, **3**, n°7 (2020)

MagPure chip: a microfluidic device for the purification of Circulating tumor cells and the integration in liquid biopsy workflow

Lucie Descamps[1,2*], Jessica Garcia[3], David Barthelemy[3], Emmanuelle Laurenceau[4], Lea Payen[3], Damien Le Roy[2] and Anne-Laure Deman[1*]

[1] Institut des Nanotechnologies de Lyon, INL UMR5270, Université Claude Bernard Lyon 1, Villeurbanne, France.
[2] Institut Lumière Matière, ILM UMR5306, Université Claude Bernard Lyon 1, Villeurbanne, France.
[3] Laboratoire de Biochimie et Biologie Moléculaire, CICLY UR3738, Groupe Hospitalier Sud, Hospices Civils de Lyon, Pierre Bénite, France.
[4] Institut des Nanotechnologies de Lyon, INL UMR5270, Ecole Centrale de Lyon, Ecully, France.
[*]l.descamps@tue.nl

Circulating tumor cells (CTCs) have received significant attention over years for their potential clinical significance in assessing cancer diagnosis and prognosis earlier, as well as in tailoring anti-cancer therapies. Nevertheless, challenges raised by CTC rarity and heterogeneity within patient blood samples have hampered their wider use in clinical studies. To address these challenges, we report the development of an immunomagnetic-based microfluidic device, the MagPure chip [1], for the isolation and characterization of CTCs. In particular, the strategy relies on the depletion of background white blood cells (WBCs) and enrichment of CTCs (negative selection) via the integration into the MagPure chip of magnetic microstructures acting as WBC capture spots. The strength of this device relies on the fabrication and integration of permanent magnetic microstructures using the magnetic composite polymer approach [2], a straightforward and cost-effective fabrication process, which led to magnetic traps generating magnetic forces as high as several nanoNewtons, In the context of CTC sorting, the performances and biocompatibility of the MagPure chip were studied on model blood samples with spiked cancer cell lines. The MagPure chip achieved an average WBC depletion efficiency of 87% (corresponding to the average ratio of labeled WBCs) and an average CTC recovery rate of 81%. Furthermore, the MagPure chip showed compatibility with routine biological studies, including 2D and 3D cell culture, as well as phenotypic and genotypic analyses (Figure 1). Finally, aiming for a clinical context implementation, we successfully developed a two-step separation workflow for whole blood processing by combining a size-based pre-enrichment system (commercialized ClearCell FX1® system) with the MagPure chip as a subsequent purification step, thus benefitting from the advantages of both separation methods. The designed two-step workflow led to high throughput (7.5 mL blood processed in less than 4 h) and high purity, with a WBC depletion rate as high as 99.99% (947 WBCs/mL) and a CTC recovery rate of 70%. The highly purified sample thus obtained enabled downstream analysis such as long-term cell culture and phenotypic analysis, while preserving short processing time to ensure compatibility with clinical follow-up.

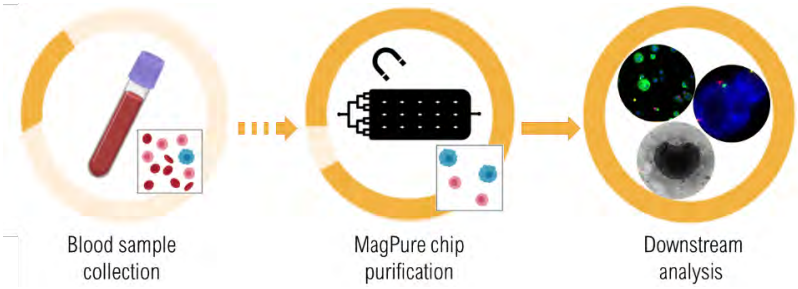


Figure 1: Liquid biopsy-based workflow for CTC isolation and analysis through MagPure chip purification

References

[1] L. Descamps, J. Garcia, D. Barthelemy, E. Laurenceau, L. Payen, et al, *MagPure chip: an immunomagnetic-based microfluidic device for high purification of circulating tumor cells from liquid biopsies*. Lab Chip **22**, 4151–4166 (2022).

[2] L. Descamps, M.-C. Audry, J. Howard, S. Mekkaoui, C. Albin, D. Barthelemy, et al., *Self-Assembled Permanent Micro-Magnets in a Polymer-Based Microfluidic Device for Magnetic Cell Sorting*. Cells **10**, 1734 (2021).

Anomalous ionic transport in tunable angstrom-size water films on silica

Menghua Zhao[1]*, Aymeric Allemand[1], Olivier Vincent[1], Remy Fulcrand[1], Laurent Joly[1], Christophe Ybert[1], Anne-Laure Biance[1]*

[1]Institution, Univ Lyon, Univ Claude Bernard Lyon 1, CNRS, Institut Lumière Matière, F-69622, VILLEURBANNE, France

*zhaomenghua88@gmail.com; anne-laure.biance@univ-lyon1.fr

Liquid and ionic transport through nanometric structures is central to many phenomena, ranging from cellular exchanges to water resource management or green osmosis energy conversion. While pushing down towards molecular scales progressively unveils novel transport behaviors, reaching ultimate confinement in controlled systems remains challenging and has often involved 2D Van der Waals materials[1-3]. Here, we propose an alternative route to molecular confinement, which circumvents demanding nanofabrication steps, partially releases material constraints, and offers a continuously tunable molecular confinement. This soft-matter-inspired approach is based on the spontaneous formation of a molecularly thin liquid film onto fully wettable substrates in contact with the vapor phase of the liquid[4, 5]. Using silicon dioxide substrates, water films ranging from angstrom to nanometric thicknesses are formed in this manner, and ionic transport within the film can then be measured. Performing conductance measurements as a function of confinement in these ultimate regimes reveals a one-molecule thick layer of fully hindered transport nearby the silica, above which continuum, bulk-like approaches account for experimental results. Overall, this work paves the way for future investigations of molecular scale nanofluidics and provides novel insights into ionic transport nearby high surface energy materials such as natural rocks and clay, building concretes, or nanoscale silica membranes used for separation and filtering.

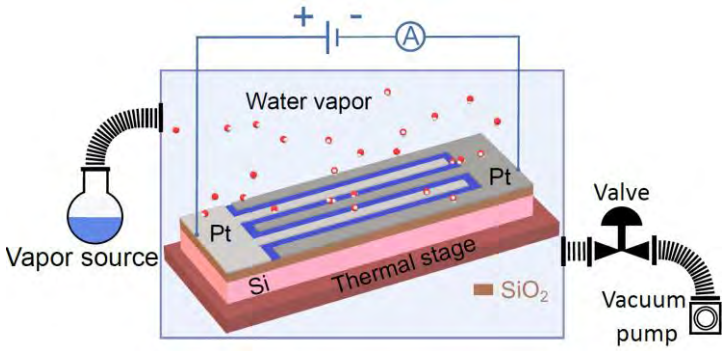


Figure 1: Experimental setup to probe the ion transport in a condensed nanometric water film.

References

[1] Bocquet L. Nanofluidics coming of age[J]. Nature materials, 2020, 19(3): 254-256.

[2] Kavokine N, Netz R R, Bocquet L. Fluids at the nanoscale: from continuum to subcontinuum transport[J]. Annual Review of Fluid Mechanics, 2021, 53: 377-410.

[3] You Y, Ismail A, Nam G H, et al. Angstrofluidics: walking to the limit[J]. Annual Review of Materials Research, 2022, 52: 189-218.

[4] Bonn D, Eggers J, Indekeu J, et al. Wetting and spreading[J]. Reviews of modern physics, 2009, 81(2): 739.

[5] Asay D B, Kim S H. Evolution of the adsorbed water layer structure on silicon oxide at room temperature[J]. The Journal of Physical Chemistry B, 2005, 109(35): 16760-16763.

Confinement de bactérie à l'aide de puce nanofluidique

ALRIC Baptiste[1]*, LEBLANC Laure[2], MAZENQ Laurent [1], DELARUE Morgan[1]

[1]LAAS-CNRS, Toulouse, France
[2]Institut Pasteur, Paris, France
* alric.baptiste@gmail.com

Dans le cadre des études de l'impact des contraintes mécaniques sur la croissance cellulaire, de nombreux outils microfluidiques ont été développés afin de pouvoir simuler l'environnement physico-chimique entourant les cellules dans leurs milieux naturels. Dans le cadre de ma thèse, principalement consacrée à l'étude de ces impacts pour la levure *S. cerevisiae*, j'ai utilisé un système décrit dans l'article [1] permettant aux cellules de se développer dans une chambre microfluidique tout en étant alimentées par des microcanaux. Grace à ce système nous avons pu montrer entre autres **une corrélation entre la pression mécanique développée par les cellules lors de leurs croissances avec une diminution du taux de croissance de celle-ci** [2]. Nos résultats suggèrent que l'origine de cette corrélation est biophysique, une augmentation de l'encombrement macromoléculaire à l'intérieur des cellules entrainant une diminution du taux de production protéiques. Nous avons alors posé comme hypothèse que **ce phénomène pourrait se retrouver dans d'autre type cellulaire tels que les bactéries** comme E. coli.

La réalisation de telles expériences sur un organisme sub-micrométrique est challenging. Ainsi, avant de faire ces expériences, nous avons dû adapter notre dispositif aux dimensions de nos nouveaux objets d'étude, en effet, les bactéries pouvant traverser les microcanaux d'alimentation de 1 micromètre de nos puces pour levure. Nous avons donc dû diminuer les dimensions de nos dispositifs afin de permettre de confiner efficacement les bactéries. Pour cela, avec l'aide des ingénieurs de la salle blanche du LAAS, nous avons utilisé la technique de photolithographie stepper afin de réaliser des nanocanaux d'alimentation permettant la bonne l'alimentation des cellules dans les chambres microfluidique tout en étant confinée. Cette technologie consiste à utiliser des lentilles afin de focuser les rayons UV et ainsi de diminuer la taille des zones exposées par les rayons (Fig1.a). Ce qui nous as permis de réaliser des moules avec **des nanocanaux d'une largeur de 400nm sur une hauteur de 400nm** (Fig1.b) qui permettent ensuite de réaliser des puces micro fluidiques en PDMS (Fig1.c)**.**

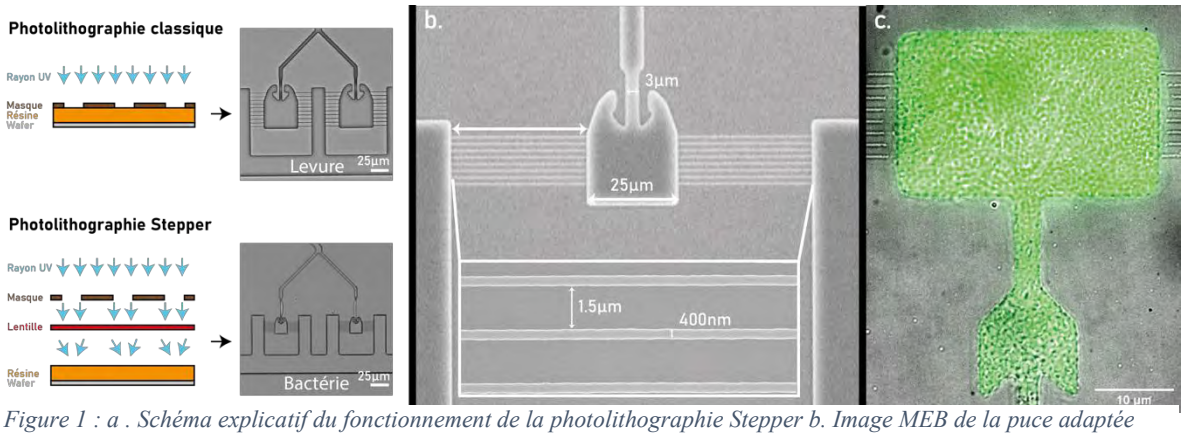


Figure 1 : a . Schéma explicatif du fonctionnement de la photolithographie Stepper b. Image MEB de la puce adaptée pour la croissance confinée des bactéries. c. Bactéries E.coli avec un marquage cytoplasmique fluorescent confinées dans la chambre microfluidique en PDMS.

References

[1] Delarue, M., Hartung, J., Schreck, C., Gniewek, P., Hu, L., Herminghaus, S., & Hallatschek, O. (2016). *Self-driven jamming in growing microbial populations*. **Nature physics,** *12*(8), 762-766.

[2] Alric, B., Formosa-Dague, C., Dague, E., Holt, L. J., & Delarue, M. (2022). *Macromolecular crowding limits growth under pressure*. **Nature Physics**, *18*(4), 411-416.

Obstacle race of air invading biomimetic leaves

Ludovic Keiser[1,2], Philippe Marmottant[1*], Benjamin Dollet[1]

[1]Laboratoire interdisciplinaire de Physique, CNRS and Univ. Grenoble Alpes
[2]Institut de Physique de Nice, CNRS and Univ. Cote d'Azur

In case of drought, the water in the xylem hydraulic circuits of trees falls down to very negative pressures. Cavitation bubbles can nucleate, initiating an air embolism that propagates, a process called air-seeding, leading to the failure of the water circulation. Observations on real leaves showed that the embolism advances by a succession of long stops and sudden jumps.

To understand the nature of jumps, we propose an experimental model using biomimetic leaves in silicone (PDMS), made of thin water-permeable membranes [1,2]. The veins of these artificial leaves are channels filled with water, and here we have introduced constrictions to mimic the pit in between real leaf channels (figure 1).

We observed that the jumps after each constriction are due to the sudden release of an elastic deformation of the channels, occurring when the meniscus is pinned and evaporation continues. The jumps of the meniscus can reach directly the next constriction (when it is nearby, as is the case in Fig 1b) or can reach the inside of next channel and are followed by a slow progression of evaporation (Fig 1a). For large number of constrictions, the pinning at the first constriction induces a long waiting time before the first jump, while the second waiting time is much smaller and the subsequent waiting times increase slowly until the complete drying of the channel. A simple model enables to capture this stop-and-go dynamics, and is successfully applied to quantitative data extracted from experiments realized with real leaves of the fern Adiantum.

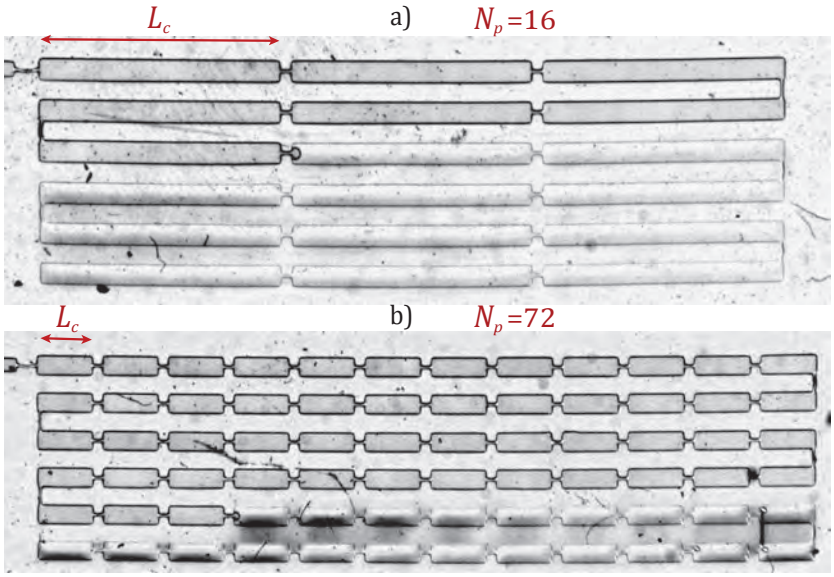


Figure 1: Long channel with a series of N_p constrictions. The air invasion starts on the top left entrance, the rest of the dead-end channel is prefilled with water. Evaporation occurs through a thin PDMS membrane covering the channels.

References

1 B. Dollet, J.-F. Louf, M. Alonzo, K. H. Jensen and P. Marmottant *Drying of channels by evaporation through a permeable medium mimicking embolism in plant leaves*, Journal of the Royal Society Interface, **16**, 20180690 (2019)

2 L. Keiser, P. Marmottant, B. Dollet, *Intermittent air invasion in pervaporating compliant microchannels* Journal of Fluid Mechanics, **948**, A52 (2022)

Flow driven jamming of viral particles in narrow channels

Léa Chazot-Franguiadakis[1]*, Fabien Montel[1]

[1]Laboratoire de Physique, UMR CNRS 5672, ENS de Lyon, Université de Lyon, Lyon, France
*lea.chazot-franguiadakis@ens-lyon.fr

The human cell is organized into compartments. The transport of biomolecules between them is an essential step in order to maintain cell function. Among the cell's communication pathways, the nuclear pore complex (NPC), which regulates transport between the cell nucleus and the cytoplasm [1], is certainly the most complex. This pore has exceptional adaptability and selectivity properties, due to the presence of a network of dynamic polymers inside its central channel. Many viruses (adeno-associated virus, hepatitis B virus, HIV, ...) must transport their genetic material across the nuclear membrane, via the NPC to replicate inside the cell nucleus.

Our project addresses the issue of virus transport through the NPC in a biomimetic environment, i.e. simplified and controlled, in order to facilitate the study. To this end, we mimic the nuclear pore by grafting nanoporous membranes with hydrophobic artificial polymers. We then use a highly sensitive optical system, developed within our team, which allows us to detect in real time and at the level of a single pore the transport of a single viral particle [2,3].

Using this device, we measure the translocation frequency of viruses (labeled with a fluorophore) through the pores as a function of a control parameter (pressure, concentration). We reveal a jamming phenomenon caused by the confinement of the viruses under flow. We study the determinants (physical, chemical) of this effect and propose a physical model of the phenomenon seen as a phase transition under flow. Extracted parameters are related to the interaction of the viruses with the pore. They can be used to study subtle structural and geometrical modifications of the viruses induced by topological defect modulators.

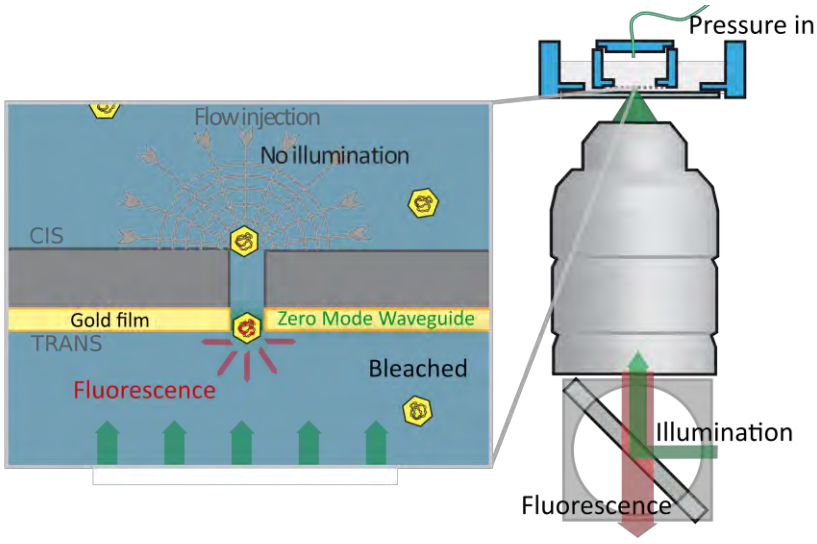


Figure 1: Experimental setup for translocation of (fluorescently labeled) viral particles through a synthetic nanoporous membrane.

References

[1] Wente S.R, et al. The nuclear pore complex and nuclear transport. Cold Spring Harb Perspect Biol.2, (2010).

[2] Auger T, et al, Zero-Mode Waveguide Detection of Flow-Driven DNA Translocation through Nanopores. Phys Rev Lett, Vol 113 (2), p028302-07, (2014).

[3] Chazot-Franguiadakis L., et al., Optical Quantification by Nanopores of Viruses, Extracellular Vesicles and Nanoparticles. Nano Letters, 22, 9, 3651–3658 (2022).

Organoid engineering for new biomimetic tools to study the intestinal tissue

W. Xi[1], J. Saleh[1], A. Yamada[2], C. Tomba[3], B. Mercier[1], S. Janel[4], T. Dang[1], M. Soleilhac[1], A. Djemat[1], H. Wu[1], B. Romagnolo[5], F. Lafont[4], R.M. Mège[1], Y. Chen[2], and D. Delacour [1]*

[1]Institut Jacques Monod (IJM), Paris
[2]Ecole Normale Supérieure (ENS), Paris
[3]INL Univ. Lyon, Villeurbanne
[4]Institut Pasteur, Lille
[5]Institut Cochin, Paris
*delphine.delacour@ijm.fr

The field of intestinal biology is thirstily searching for different long-term culture methods that complement the limitations of organoids. While being recognized as an important milestone for basic and translational biological studies, culture of primary intestinal epithelia besides organoids has been relied on empirical trails using hydrogels of various stiffness, whose mechanical impact on epithelial organization remains vague until now. Here, we report the development of Matrigel and polyacrylamide scaffolds with a range of elasticities and their influence on intestinal epithelium expansion, differentiation and organization. On flat stiff substrates (>5kPa), primary intestinal epithelia cells adapt a flat cell shape and detach in short-term. In contrast, on soft substrates (80 –1000 Pa), they sustain for a long-term, pack into high density, develop columnar shape with improved apical-basal polarity, a phenotype reminiscent of features in organoids. We then developed a novel soft gel molding process to produce 3D Matrigel scaffolds of close-to-nature stiffness, which support and maintain long-term culture of primary intestinal epitelial cells into crypt-villus architecture. Thus, the present work is up-to-date informative for the design of novel biomaterials for *ex vivo* intestinal models, offering new tools to study the intestinal tissue *in vitro*.

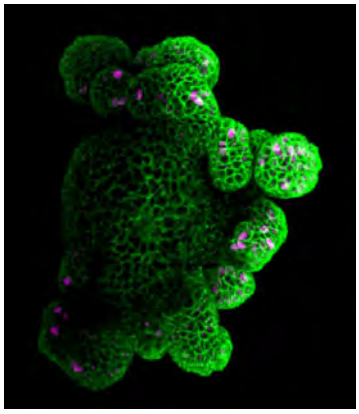


Figure 1: Intestinal organoids cultured in 3D Matrigel matrix

References

[1] Xi W, Saleh J, Yamada A, Mercier B, Dang T, Janel S, Soleilhac M, Wu H, Tomba C, Romagnolo B, Lafont F, Mège RM, Chen Y, **Delacour D**. *Modulation of designer biomimetic matrices for optimized intestinal epithelial cultures.* Biomaterials **282**,121380 (2022).

[2] Saleh J, Fardin MA, Frenoy O, Soleilhac M, Gaston C, Ciu H, Dang T, Gaudin N, Vincent A, Minc N*, **Delacour D***. *Length-limitation of astral microtubules orients cell divisions in intestinal crypts.* BioRXiv doi: https://doi.org/10.1101/2022.09.02.506333 (2022).

[3] Steinway SN, Saleh J, Kim DH*, **Delacour D***. *Microphysical models of the human intestine and gut microbiome in health and diseases.* Frontiers in Bioengineering and Biotechnology **8**,1-17 (2020).

Artificial ice packs: a model laboratory approach

Antonin Eddi[1]

[1] PMMH Laboratory, UMR 7636, CNRS, ESPCI, Sorbonne Université, Université Paris Cité
7 Quai Saint Bernard, 75005 Paris - FRANCE
antonin.eddi@espci.fr

The Arctic ocean is covered with an ice pack of about 1m in thickness, generated during winter by sea freezing. Polar ice packs play an important role in global climate dynamics through their high albedo limiting radiative heating and their cooling properties of atmospheric and oceanic circulations. Their melting mainly occurs in the marginal ice zones (MIZ) [1], where oceanic swells break the ice pack in smaller fragments (see fig. 1a), leading to their increased melting and enhanced reduction thus affecting the dynamics of the whole Arctic region [2]. In this presentation, I'll show how we designed a set of model experiments that are able to scale down some of the physical phenomena at play in the MIZ.

In a first part, I will discuss the Hydro-elastic waves that appear when the water surface is covered by a thin elastic sheet, their physics being dominated by the bending elasticity of the sheet. I will then show that HEW open promising possibilities for wave control [3]. In particular, I will present experimental configurations that allow for building an HEW based "optics", revisiting Snell's law and geometrical optics in an hydrodynamical experiment.

In a second part, I will present a model experiment where we study the fracture of a thin and brittle elastic sheet under surface wave mechanical loading (see fig. 1b). I will show that this system is able to mimick both the elastic response of ice packs as well as their fragmentation, shedding a new light on the criteria for ice pack rupture and fragment size distributions.

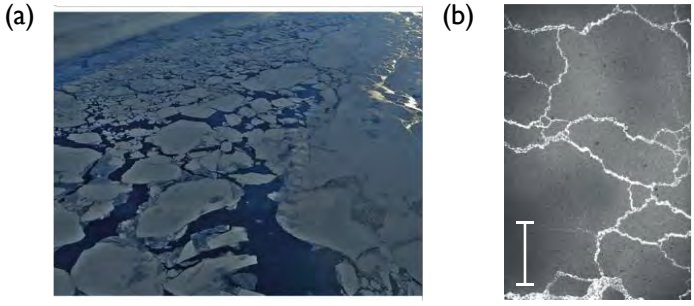


Figure 1: (a) Aerial view of the MIZ close to the occidental shore of Greenland. Credits: W. Malik. (b) Fragmented artificial elastic sheet under wave mechanical loading. The scale bar is 10 cm.

References

[1] T.D. Williams *et al.*, Wave–ice inter- actions in the marginal ice zone.part 1 : Theoretical foundations. Ocean Model, **71** :81–91 (2013).

[2] J. Thomson *et al.*, Overview of the arctic sea state and boundary layer physics program, Journal of Geophysical Research - Oceans, 123, 8674–8687 (2018).

[3] L. Domino *et al.,*Dispersion-free control of hydroelastic waves down to sub-wavelength scale. Europhysics Letters **121** (1), 14001 (2018).

Designing microfluidic hourglasses to study flows of dense colloidal suspensions under gravity

A. Bérut[1]*, A. Piednoir[1], R. Fulcrand[1]

[1] Université de Lyon, Université Claude Bernard Lyon 1, CNRS,
Institut Lumière Matière, F-69622, VILLEURBANNE, France
*antoine.berut@univ-lyon1.fr

We study dense colloidal suspensions, made of particles that are heavy enough to sediment in their surrounding fluid and form a well-defined pile, but small enough to be sensitive to thermal agitation (typically between 1 and 5 µm). Those colloidal suspensions are similar in appearance to granular materials, but show peculiar flowing properties. For example, when a pile is inclined in a microfluidic drum, two distinct regimes are observed. Above a critical angle θ_c a fast avalanche occurs, similar to what is expected for classical athermal granular media. However, below this angle, the flow never stops, and the pile slowly creeps under thermal agitation until it becomes completely flat. [1]

Therefore, one could wonder how such a suspension behaves when it flows through an orifice, as in a silo discharge experiment: would the flow rate be constant, as for a macroscopic granular material in an hourglass, or would it depend on the height of the pile, as for a clepsydra filled with a fluid?

To try to answer to this simple question, we have used microfluidic fabrication techniques to build microscopic hourglasses that are filled with suspensions of silica micro-particles (Figure 1). We have encountered different problems with classical soft-lithography set-up in polydimethylsiloxane (PDMS), and have instead used rigid closed cells made in SU-8 photoresists. Finally, we measured the flow rate of the suspensions as a function of the ratio between the particles diameters and the necks widths. The results are compared with the classical Berverloo law that predicts the rates of macroscopic granular materials flowing through an orifice [2].

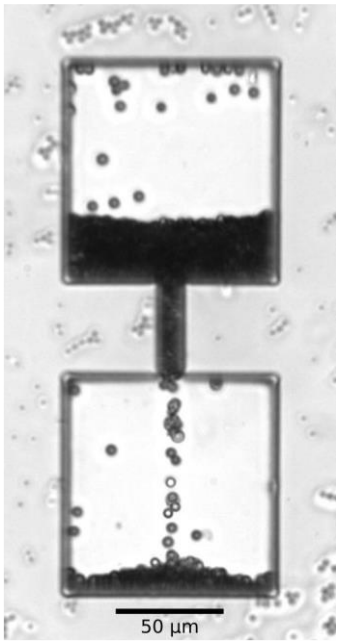


Figure 1: Microfluidic container, made with a deposit of SU-8 photoresist on a glass wafer (neck width = 11 µm), filled with a suspension of silica micro-particles (diameter = 3.97 µm) dispersed in bidistilled water.

References

[1] A. Bérut, O. Pouliquen and Y. Forterre, "*Brownian Granular Flows Down Heaps*" Phys. Rev. Lett. **123**, 248005 (2019).

[2] Beverloo W. A., Leniger H. A. and Van de Velde J., "*The flow of granular solids through orifices*" J. Chem. Eng. Sci. **15**, 260-296 (1961).

Investigation of the shear-induced nucleation mechanism in a micro-crystallizer

Debuysschère Robin[1]*, Bart Rimez[2], Alessio Zaccone[3], Benoit Scheid[1]

[1] Université Libre de Bruxelles, Brussels, Belgium
[2] Secoya-technologies, Ottignies - Louvain la neuve, Belgium
[3] Università degli Studi di Milano Statale, Milan, Italy
* robin.debuysschere@ulb.be

In industry, 90% [1] of the active pharmaceutical ingredients (API) are under a crystalline form. The crystallization kinetics is highly influenced both by the supersaturation conditions (temperature and concentration) and by the flow hydrodynamics [2], both thus influence the overall product quality and size. We developed a continuous seedless cooling micro-crystallizer [3]. Experiments pointed out that modification of the upstream flow conditions induces size changes of the obtained crystals [3-4], which we imputed to shear rate.

To the best of our knowledge, an in-depth knowledge of the shear-induced crystallization mechanisms is still missing. Thus, we performed a systematic analysis of the influence of the shear rate in the micro-crystallizer on the nucleation rate. We demonstrate experimentally that a nucleation rate maximum exists as a function of shear rate. We theoretically identified that shear, at first, induces the coalescence of intermediary structures which thus promote the nucleation. On the opposite, at higher shear rates, the flow induces mechanical deformation of the intermediary structures which counteracts the beneficial effect, leading to the experimentally observed non-monotonic behavior (figure 1).

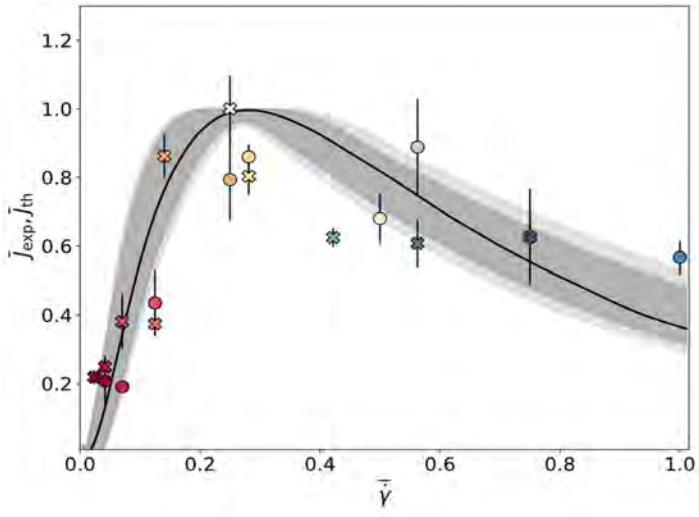


Figure 1: Influence of the shear rate on the nucleation rate of glycine

References

[1] AJ Alvarez, AS Myerson, *Continuous plug flow crystallization of pharmaceutical compounds.* Cryst. Growth & Des. **10**, 2219–2228 (2010).

[2] A Myerson, *Handbook of Industrial Crystallization.* Butterworth-Heinemann, **2nd ed edition** (2002).

[3] B Rimez, et al., *Continuous-Flow Tubular Crystallization To Discriminate between Two Competing Crystal Polymorphs. 1. Cooling Crystallization.* Cryst. Growth & Des. **18**, 6431–6439 (2018).

[4] Rimez, R Debuysschère, B Scheid, *On the effect of flow restrictions on the nucleation behavior of molecules in tubular flow nucleators*. J. Flow Chem. **10(1)**, 241-249 (2019).

Microfluidic device for spheroid culture and anticancer drug testing with electrochemotherapy

P. Bregigeon[1*], T. Le Berre[1], J. Marchalot[1], L. Franqueville[1], C. Vollaire[1], C. Rivière[2,3,4] and M. Frénéa-Robin[1]

[1]Univ Lyon, Ecole Centrale de Lyon, INSA Lyon, Université Claude Bernard Lyon 1, CNRS, Ampère, UMR5005, 69130 Ecully, France
[2]Institut Lumière Matière, Claude Bernard Lyon 1 Université, CNRS, F-69622, Villeurbanne, France
[3]Institut Universitaire de France (IUF), France
[4]Institut Convergence PLAsCAN, Centre de Cancérologie de Lyon, INSERM U1052-CNRS UMR5286, Université de Lyon, Université Claude Bernard Lyon 1, Centre Léon Bérard, Lyon, France
*pauline.bregigeon@ec-lyon.fr

In the search for new drug delivery strategies, relevant in vitro tumor models are needed, as part of the process of reducing preclinical trials. They also to offer the possibility to design patient-specific medicines [1]. 3D aggregates called spheroids have been identified as a good tumor model, able to reproduce cell-cell interaction. We have developed a microfluidic device (Fig.1b) allowing spheroid culture inside agarose hydrogel microwells (Fig.1a) [2], and their monitoring with both electrical bioimpedance and high-content microscopy. This hydrogel is chemically bonded to a glass slide acting as an electrode and integrated into a microfluidic chamber enabling medium exchange and drug injection (Fig.1b). A first application of the device has recently been published [3]. HT29 colorectal cancer cell spheroids were treated with electrochemotherapy (ECT), a physical method based on a pulsed electric field to enhance drug intake in cells. Preliminary results also showed it was possible to monitor spheroid growth by measuring the evolution of bioimpedance Z with coplanar interdigitated electrodes, but with more precision and reliability when the conductivity inside the chamber is reduced from 1.3 S/m (high σ, culture medium) to 0.03 S/m (low σ, Hepes buffer) (Fig.1c). A device with two chambers, one with medium only for control (Z_0) and one with spheroids (Z_S), was used for this experiment (Fig.1d), and the cell index $CI = \frac{|Z_0|-|Z_S|}{|Z_0|}$ was measured (Fig.1e). The impact of a surfactant to permeabilize cells (TritonX-100) on the growth curve could also be monitored in less than an hour. Taking advantage of the electrodes, we intend to monitor the effect of ECT on spheroids with bioimpedance in future work.

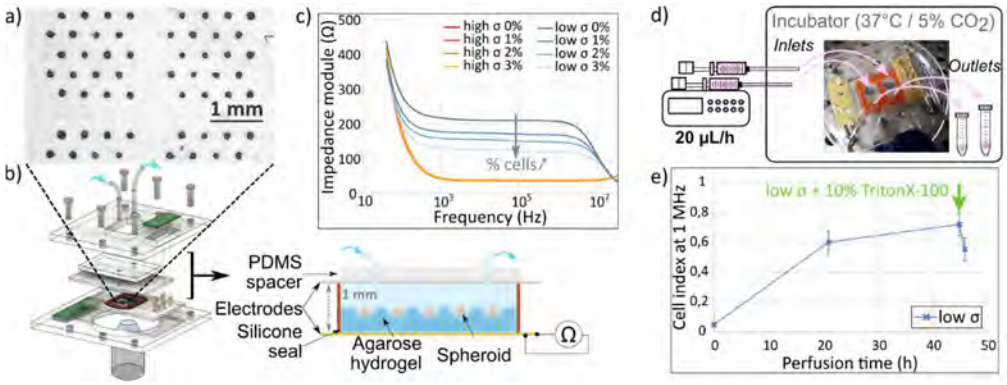


Figure 1: (a) Microscope image (2.5X) of spheroids after 3 days of culture. (b) Exploded view of the CAD of the microsystem and side view of the microfluidic chamber. (c) Impedance measure on cell suspensions in high and low conductivity mediums. (d) Picture of the microsystem during culture under perfusion (20 µL/h) with two chambers. (e) Spheroid growth monitoring with bioimpedance in Hepes buffer and impact of TritonX-100.

References

[1] K.A. Fitzgerald, et al: *Life in 3D is never flat: 3D models to optimise drug delivery.* Journal of Controlled Release **215**, 39–54 (2015).

[2] C. Rivière, A. Prunet, L. Fuoco, H. Delanoë-Ayari: Patent FR3079524A1 (2018).

[3] P. Bregigeon, et al: *Integrated platform for culture, observation, and parallelized electroporation of spheroids*. Lab on a Chip **13**, 2489–2501 (2022).

Cell growth on moving curvatures, towards gut-on-a-chip

Valentin Chalut[1]*, Damien Le Roy[2], Delphine Delacour[3], Anne-Laure Deman[1], Caterina Tomba[1]

[1]Univ Lyon, Université Claude Bernard Lyon 1, CNRS, INSA Lyon, Ecole Centrale de Lyon, CPE Lyon, INL, UMR5270, 69622 Villeurbanne, France
[2]Institut Lumière Matière, ILM-UMR 5306, CNRS, Université Claude Bernard Lyon 1, 69622 Villeurbanne, France
[3]Cell Adhesion and Mechanics Lab, Université de Paris, CNRS, Institut Jacques Monod, F-75006, Paris, France.
*valentin.chalut@univ-lyon1.fr

The intestine is an organ with many levels of curvature, deformed by a combination of muscular, mainly related to digestion, and external movements, produced for example by the passage of the food bolus. This complex architecture can be affected in case of severe pathologies that are not yet fully understood and still require effective treatments, such as the Hirschsprung's disease(1).

As the standard 2D *in vitro* and animal models may be inadequate for such organ modelling, a new promising *in vitro* approach has been recently investigated, the Organ-on-Chip. The Gut-on-Chip consists in partially reproducing the intestine to study the influence of a treatment on its various structural, mechanical and chemical parameters(2). However, the movement and deformation of the intestinal epithelium remain poorly studied, although they are predominant in the gut.

To develop this aspect, we grew several types of epithelial cells, such as intestinal organoids (Fig. 1a), on different substrates reproducing the intestinal barrier (Fig. 1b), and which can be deformed by a magnetic field (Fig. 1c) taking inspiration from the soft robots technology(3). Such wavy membranes can remotely achieve deformation amplitude of 1.4 to 1.7 mm at 140 mT (Fig. 1d & e) and a radius of curvature of about 1 to 2 mm. This technology also provides the advantage of supporting Matrigel intestinal villi replicas, which are 500 µm high and 200 µm wide in the real organ(4).

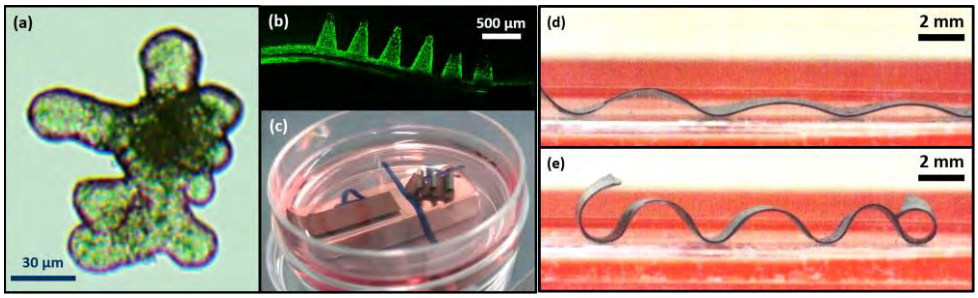


Figure 1: (a) Phase contrast image of a gut organoid cultured in 3D. (b) PDMS villi replicas on a deformed membrane covered with MDCK (Madin-Darby Canine Kidney) cells (nuclei in green, H2B-GFP). (c) Magnetic membranes covered with Caco-2 (Cancer Colon) cells in a 35 mm petri dish on a permanent magnet. (d) Magnetic membranes in water under a magnetic field of 5 mT and (e) 140 mT.

References

[1] S. J. Mckeown, L. Stamp, M. M. Hao and H. M. Young, *Hirschsprung disease: A developmental disorder of the enteric nervous system*, Wiley Interdisciplinary Reviews: Developmental Biology, **2, 1**, 113-129 (2013)

[2] D. Vera, M. García-Díaz, N. Torras, M. Álvarez, R. Villa and E. Martinez, *Engineering Tissue Barrier Models on Hydrogel Microfluidic Platforms*, ACS Applied Materials and Interfaces, **13, 12**, 13920-13933 (2021)

[3] R. Zhao, Y. Kim, S. A. Chester, P. Sharma and X. Zhao, *Mechanics of hard-magnetic soft materials*, Journal of the Mechanics and Physics of Solids, **124, 3**, 244-263 (2019)

[4] H. M. Poling, D. Wu, N. Brown, M. Baker, T. A. Hausfeld, N. Huynh, S. Chaffron, J. C. Dunn, S. P. Hogan, J. M. Wells, M. A. Helmrath and M. M. Mahe, *Mechanically induced development and maturation of human intestinal organoids in vivo,* Nature Biomedical Engineering, **2, 6,** 429-442 (2018)

Development of the Galenic Lab-on-a-chip and Therapy-on-a-chip concepts for drug formulation / delivery

Laurent LEMAIRE[1], Guillaume BROTONS[2], Marie BONNIN[1], Guillaume LEFEVBRE[1], Florence FRANCONI[1,3], Franck LETOURNEL[1], Jean-Christophe GIMEL[1], Sylvain Verron[4], Sylwester BARGIEL[5], Jean-Pierre BENOIT[1], Brice CALVIGNAC[1]

[1]Univ Angers, CHU Angers, Inserm, CNRS, MINT, SFR ICAT, F-49000 Angers, France
[2]Institut des Molécules et Matériaux du Mans, UMR 6283 CNRS, Le Mans Université, France
[3]Univ Angers, PRISM, SFR ICAT, F-49000 Angers, France
[4]LARIS, SFR MATHSTIC, F-49000 Angers, France
[5]FEMTO-ST Institute, Dpt. MN2S, Univ. Bourgogne Franche-Comté, CNRS, Besançon, France

Currently, medicine is faced with many therapeutic challenges that the development of new drug delivery systems is trying to overcome: *How to deliver the drug to the exact right place, in the desired dose and at the required time, while limiting undesirable side effects?*
In the last decades, drug delivery systems (DDS) have developed considerably (in the form of medical devices and micro/nanoparticulate drug carriers) and are now taking a prominent place in human medicine. Particulate DDS are obtained by encapsulating active ingredients that can be released in a controlled and targeted manner within the body. In this sense, nanomedicines are used for targeted therapeutic action and can cross certain barriers in the body such as the blood-brain barrier (BBB) or the intestinal barrier to treat cancers or infections for examples. Continuous production of DDS assisted by microfluidics has drawn a growing interest because of the high reproducibility, low batch-to-batch variation of formulations, narrow and controlled particle size distribution and scale-up facilities induced by this process. Besides, microfluidics offers opportunities **(1)** for high throughput screening parameters and scale-up of process and the implementation of process analytical technologies (PAT) as close to the nanomedicine candidates as possible, and also **(2)** to propose miniaturized medical devices as microneedle-based drug delivery systems.
In this context, the MINT laboratory developed and patented two technological concepts (Figure 1) combining microfluidics and microfabrication/3D printed technologies:

(a) ***GALECHIP*, as an instrumented microfluidic platform such as a Lab-on-a-chip dedicated to the formulation/production under controlled operating conditions of Lipidic Nanocapsules (LNC) as drug nanocarriers (20-100 nm with a polydispersity index < 0,15) and the implementation of PAT such as an X-ray *in operando* characterization technique (Small Angle X-ray Scattering,).**

(b) ***THERACHIP*, as a microfluidic medical device (MMD) with microneedles which is per-operatively implantable (after surgery), biocompatible and compliant with magnetic resonance imaging (MRI) techniques. This MMD is applied to locally deliver drugs to treat brain tumors as glioblastoma (GBM), and to bypass the BBB in the case of operable GBM.**

These proven concepts intended to propose personalized therapeutic strategies for the management of the patient's pathology such as (1) drug administration as close as possible to the target (organ, cells, bacteria, etc.) and (2) the production of nanomedicines as close as possible to the patient.

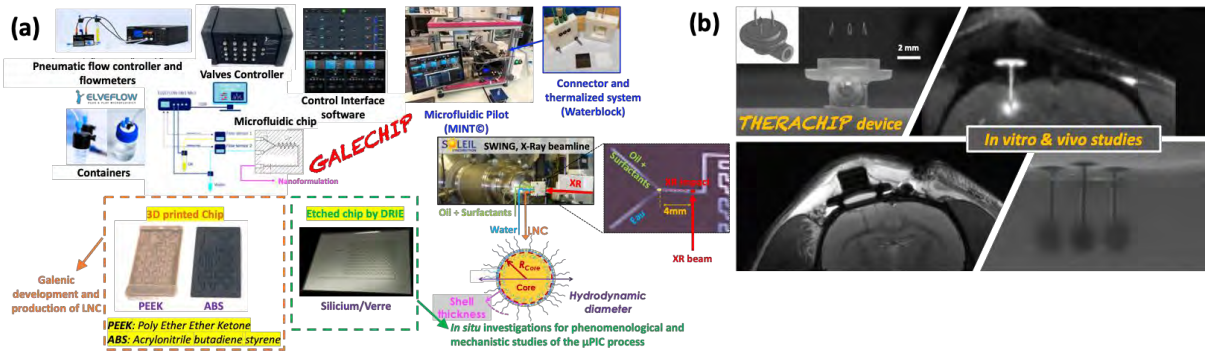


Figure 1: GALECHIP (a) and THERACHIP (b) microfluidic and technological concepts

Ion exchange membrane resistance from cm to µm scale: is the power per unit area a good indicator?

T. Derkenne[1], *C. Trégouët*[1], *A. Colin*[1]

[1]MIE, CBI, ESPCI Paris, Université PSL, CNRS 75005 Paris, France

Since the beginning of blue-energy harvesting researches, a lot of work and advances have been made about membrane design and nanofluidic diffusio-osmotic transport, but the efficiency gap of several orders of magnitude between micro-scale designs and industrial power plants remains unsolved.[1]

The output power is usually calculated based on the membrane conductance per unit area, and the measured Donnan potential. This measurement method of power per unit area based on membrane conductance is therefore a key point to be able to compare several devices and their efficiency.

Our experimental work shows that on the contrary to the common belief, the device conductance is not proportional to the membrane area. Indeed, at small scale, the conductance is limited by the resistance of the junction between the membrane and the reservoir.

We made measurements with masking windows on the membrane varying from 25 square microns to square centimeters. We measure the conductance as a function of the masking but also as a function of the salt concentration solution in presence or not of salt gradient concentration.

These measurements imply that the power densities recovered in the presence of salt gradients grow by orders of magnitude as the membrane surfaces decrease.

The consequence is that the power per unit area obtained at the micro scale cannot be extrapolated to larger membranes. It follows that the comparison is biased between large scale commercially available membranes, and nano-engineered microscale membranes. This raises the urgent need for new indicators different from power per unit area, or standard measurement protocols allowing meaningful quantitative comparison between the different membranes.

References

[1] J. Gao, X. Liu, Y. Jiang, L. Ding, L. Jiang, and W. Guo, 'Understanding the Giant Gap between Single-Pore- and Membrane-Based Nanofluidic Osmotic Power Generators', *Small*, vol. 15, no. 11, p. 1804279, Mar. 2019, doi: 10.1002/smll.201804279.

Etude par microfluidique des procédés de recyclage de composants de circuits imprimés

Fabien L. Olivier[1,2]*, Jean-Christophe P. Gabriel[1,2]

[1]SCARCE Laboratory, Energy Research Institute @ NTU (ERI@N), Nanyang Technology University, 637553, Singapore.
[2]Université Paris-Saclay, CEA, CNRS, NIMBE, LICSEN, F-91191, Gif-sur-Yvette, France.
*fabien.olivier@cea.fr

Afin de répondre à une demande toujours croissante en métaux, le recyclage des métaux présents dans les déchets électroniques et électriques (DEEE) se présente comme une solution complémentaire intéressante face aux ressources minières limitées. Aujourd'hui, la majorité des procédés de recyclage mis en œuvre consiste à bruler les circuits imprimés puis à en séparer une dizaine d'éléments métalliques. Toutefois, afin d'augmenter la quantité d'éléments chimiques recyclés (jusqu'à une soixantaine sur un circuit imprimé), de nouvelles étapes de procédé, notamment d'hydrométallurgie, sont à l'étude. Ainsi, une fois les métaux issus des composants électroniques dissous dans un milieu généralement acide, une solution de lixiviation complexe est obtenue, présentant une large gamme à la fois en composition ionique élémentaire et en concentration. Cependant, la séparation des ions métalliques contenus dans ces solutions peut s'avérer complexe du fait de la variabilité importante de composition chimique des déchets entrants.
Dans ce contexte, une plateforme microfluidique instrumentée et entièrement automatisée, a été construite dans le but de faciliter le développement et l'optimisation des procédés chimiques d'extraction et de séparation des métaux. Munie d'une mesure des concentrations en ions métalliques dans les phases en sortie d'extraction, par fluorescence X [1], ce système permet de réaliser très précisément des mesures de propriétés physico-chimiques de procédés d'extraction et de séparation des métaux telles que les mesures (i) d'activité chimique de solvants [2], qui sont nécessaires pour la compréhension et la simulation des phénomènes impliqués ; (ii) des vitesses de réaction d'extraction ou de séparation grâce à sa puce d'extraction modulaires dédiée [3]–[5] ; (iii) de la capacité d'adsorption d'une colonne de séparation d'ions [6]. Tous ces procédés chimiques sont clés pour donner accès aux métaux stratégiques nécessaires à notre industrie car ils permettent d'extraire et de séparer ces métaux après l'étape de dissolution du matériau initial les contenant.

References

[1] A. A. Maurice, J. Theisen, V. Rai, F. Olivier, A. El Maangar, J. Duhamet, T. Zemb, and J. C. P. Gabriel, "First online X- ray fluorescence characterization of liquid- liquid extraction in microfluidics," *Nano Sel.*, no. March, pp. 1–12, 2021, doi: 10.1002/nano.202100133.

[2] V. Kokoric, J. Theisen, A. Wilk, C. Penisson, G. Bernard, B. Mizaikoff, and J. C. P. Gabriel, "Determining the Partial Pressure of Volatile Components via Substrate-Integrated Hollow Waveguide Infrared Spectroscopy with Integrated Microfluidics," *Anal. Chem.*, vol. 90, no. 7, pp. 4445–4451, 2018, doi: 10.1021/acs.analchem.7b04425.

[3] A. El Maangar, J. Theisen, C. Penisson, T. Zemb, and J. C. P. Gabriel, "A microfluidic study of synergic liquid-liquid extraction of rare earth elements," *Phys. Chem. Chem. Phys.*, vol. 22, no. 10, pp. 5449–5462, 2020, doi: 10.1039/c9cp06569e.

[4] J. Theisen, C. Penisson, J. Rey, T. Zemb, J. Duhamet, and J. C. P. Gabriel, "Effects of porous media on extraction kinetics: Is the membrane really a limiting factor?," *J. Memb. Sci.*, vol. 586, no. April, pp. 318–325, 2019, doi: 10.1016/j.memsci.2019.05.056.

[5] F. Olivier, A. A. Maurice, D. Meyer, and J.-C. P. Gabriel, "Liquid-liquid extraction: thermodynamics-kinetics driven processes explored by microfluidics," *Comptes rendus - Chim.*, vol. 25, pp. 137–148, 2022, doi: 10.5802/crchim.172.

[6] F. L. Olivier, S. M. Chevrier, B. Keller, and J.-C. P. Gabriel, "On-line quantification of solid-phase metal extraction efficiencies using instrumented millifluidics platform," *Chem. Eng. J.*, vol. 454, no. P3, p. 140306, 2023, doi: 10.1016/j.cej.2022.140306.

List of posters

Session A (Monday, 03 of April)**:**

A1	Adaptive networks: erosion of microfluidic channels	J. Bouvard, LadHyX, Palaiseau
A2	Controlled evaporation of droplets on hierarchical superhydrophobic devices coupled with plasmonic nanoantenna for environmental applications	S. Ramos, LAAS, Toulouse
A3	Development of a microfluidic chip for the characterization of nano and micro suspensions characterization by digital in line holography	T. Kurdadze, CEA, Bagnols-sur-Ceze
A4	Beads, bubbles and drops in microchannels: stability of centred position and equilibrium velocity	J. Cappello, TIPs, Bruxelles
A5	Wetting 2D materials at the microscale	F. Vialla, ILM, Lyon
A6	Capture of CO2 using aqueous foam: a 2D case study in microchannels	C. Aprili, LiPhy, Grenoble
A7	A skin-on-a-chip microfluidic platform to investigate neurovascular interplays in rosacea	M. Bellenguez, LOF, Pessac
A8	Actuation of droplets using opto-electrowetting, models and application for single cell analysis	S. Mekkaoui, CEA, Grenoble
A9	Mechanical oocyte measurement as a predictive biomarker for assisted reproductive technologies	L. Barbier, CIRB, Paris
A10	Functionalization of air microbubbles in a microfluidic chip for a novel biosensor	M. Prudhomme, FEMTO-ST, Besançon
A11	Fast cancer cell deformation under flow and morphological recovery	E. Gasser, LIED, Paris
A12	Relaxation of a colloid clog formed under hydrodynamic flow	O. Liot, IMF, Toulouse
A13	Hydrogel-based microsystem to study coupling between diffusion and cellular volume in living tissues	G. Jardiné, ILM, Lyon
A14	Lab-on-a-chip for the isolation of circulating Adipose Stem Cells: Preprocessing blood using the hydrodynamic filtration module	M. H. Baz, LAAS, Toulouse
A15	Optimizing liquid-solid slip in nanofluidic systems	L. Joly, ILM, Lyon
A16	Role of surfactant chemistry on the dynamic of confined droplets.	L. Jannin, IPR, Rennes
A17	Lab-on-disc for in situ monitoring of surface water quality by algae biosensors and physicochemical sensors	J.F. Chateaux, INL, Lyon

A18	Probing spheroids rheology with a microfluidic aspiration pipette	P. Joseph, LAAS, Toulouse
A19	CO2 evaporation in microchannels: numerical simulations and microfabrication of cooling chips	M. Vacher, LEGI, Gières
A20	Towards microfluidic separation processes using Switchable Hydrophilicity Solvents	M. Zollo, LdF, Pessac
A21	Transport of fibers in structured media: toward a sorting device	C. Bielinski, LadHyX, Paris
A22	Lubrication and flow of microgels in square constrictions	C. Moore, LADHYX, Paris
A23	Acoustically activated shell-based microswimmers	A. Feasson, LiPhy, Grenoble
A24	Development of a microfluidic device for the analysis of nuclear samples	M. Boudias, UPS, Gif-sur-Yvette
A25	Coupled transport mechanisms to harvest energy from thermal waste	A. Allemand, ILM, Lyon
A26	Facile bacterial encapsulation for digital antimicrobial susceptibility testing of colistin	J. Riti, CEA, Saclay
A27	Tortuosity-governed droplet transport in a microfluidic porous network	E. Speirs, IPR, Rennes
A28	Microfluidic devices for studying swimming plant pathogens interactions with their host root.	C. Cohen, IPN, Nice
A29	Flow instabilities in microvascular network	G. Coupier, LiPhy, Grenoble

Session B (Tuesday, 04 of April)**:**

B1	Biomimetic leaf-on-a-chip to study embolism	F.X. Gauci, UCA, Nice
B2	Development of geoelectrical monitoring on microfluidic chips for reactive transport and multi-phase flow characterization in the shallow subsurface	F. Rembert, BRGM, Orléans
B3	Dynamic monitoring of cytokine-secreting immune cells at the single-cell level using droplet-based microfluidics	L. Descamps, LI, Eindhoven
B4	A microfluidics-assisted photopolymerization method for high-resolution multimaterial 3D printing	V. Fournie, LAAS, Toulouse
B5	Bio-sourced polymer for the elaboration of lab-on-a-chip	M. Zimmer, INL, Lyon
B6	Characterisation of artificial polymers translocating through nanopores	C. De Blois, LP, Lyon
B7	First steps towards a glomerular filtration barrier-on-chip	M. Miran, LRS, Paris
B8	On-chip immuno-extraction of extracellular vesicles to reveal hidden sub-populations	L. Alexandre, LPCC, Paris
B9	Encapsulation by AESO bio-based polymers through microfluidic tools	E. Lu, PASTEUR, Paris
B10	Evaluation of cancer cells mechanical phenotype associated with the resistance to treatment in myeloid leukemia	C. Martin Cardozo, INL, Lyon
B11	Reversible and selective trapping of micro-algae in microfluidic chips	M. Coux, PASTEUR, Paris
B12	Controlling fast and versatile thermo-osmotic flows with a pinch of salt	C. Herrero, LCC, Montpellier
B13	Helical Fungi under Physical Constraints	C. Villard, PCC, Paris
B14	Investigation of microbial communities in glacial meltwater utilizing deterministic lateral displacement (DLD) array	T. W. Wong, LiPhy, Grenoble
B15	Lab on Chip for the isolation of circulating adipose stem cells: Module for leucocyte separation by Cell Rolling	L. Charpin, LAAS, Toulouse
B16	Equilibrium and transport of micro-to-nanoconfined electrolytes	C. Cramail, LIP, Grenoble
B17	Lymphatic clearance studied in a lymphatic vessel-on-a-chip platform	J. Edwards, LAAS, Toulouse
B18	Study of oscillating flow inside a matrix regenerator: impact of internal scale on the operating frequency	B. Bataille, CEA, Grenoble
B19	Relaxation des profils d'hématocrite après une bifurcation en T	K. Useo, IMFT, Toulouse
B20	Topological optimization of heating resistors for controlling temperature in a microfluidic cavity	T. Mabit, IPR, Rennes
B21	Influence of surfactants in bubble transport under an electric field	C. Bae, ILM, Lyon

B22	A method for single-cell multiomic barcoding, enabled by physical bioseparation in high-throuhput droplet microfluidics	S. Dumas, PCC, Paris
B23	Precise and fast control of the dissolved oxygen level for tumor on chip	C. Bouquerel, MMBC, Paris
B24	Microfluidics to study the permeability of a yeast clog	T. Desclaux, IMFT, Toulouse
B25	Boosting the blue energy to the next level	N. Wu, ESPCI, Paris
B26	Design and optimization of a magneto-plasmonic sandwich biosensor for integration within microfluidic device	W. Ait Mammar, LRS, Paris
B27	Droplet microfluidic platform for drug screening on tumoroids	C. Parent, Institut Curie, Paris
B28	Thermal conductivity measurement of liquids using single resistive sensor within a Silicon-Pyrex microfluidic device	R. Moreno Jimenez, IFP, Rueil-Malmaison

All abstracts including full author list and references are available here. They can also be reached by clicking on the talk title on the online version of the program, they can be browsed by speakers at the following address https://gdr-mnf-2023.sciencesconf.org/browse/author or by flashing this QR-code:

Abstracts of the posters

Session A (Monday, 03 of April)

Adaptive networks: erosion of microfluidic channels

Julien Bouvard[1]*, Charlott Leu[2], Onurcan Bektas[2,3], Joachim Rädler[2], Karen Alim[3], Gabriel Amselem[1]

[1]LadHyX, CNRS, École polytechnique, Institut Polytechnique de Paris, 91120 Palaiseau, France
[2]LMU Munich, Soft Condensed Matter Group, München, Germany
[3]Physics Department and CPA, Technische Universität München, 85748 Garching, Germany
*bouvard.julien@gmail.com

Microfluidics has enabled major advances in biology, where it has allowed to study and explore microscopic flows as they happen in biological systems. To go one step further towards biomimetism, microfluidic devices need to become responsive to their environment – like living systems. One key question is how to design such microfluidic devices, *i.e.* dynamic systems able to adapt their morphology to an incoming flow [1].

In this study, we make a first step towards adaptive microfluidic networks, by working with microfluidic networks of hydrogels that erode in the presence of a flow of chemical. The hydrogel channels are made of PEG-NB (polyethylene glycol norbornene) and degrade under the action of the enzyme MMP-1. We follow the degradation of the hydrogel (in green) as the enzyme (in red) is injected through the channels, see Fig. 1.

By analyzing the erosion in single straight channels and networks of channels with different sizes (see Fig. 1), we determine the characteristics of the hydrogel degradation as well as the homogenization of the channel sizes in complex networks. Instabilities also arise because of the erosion (see Fig.1(d)).

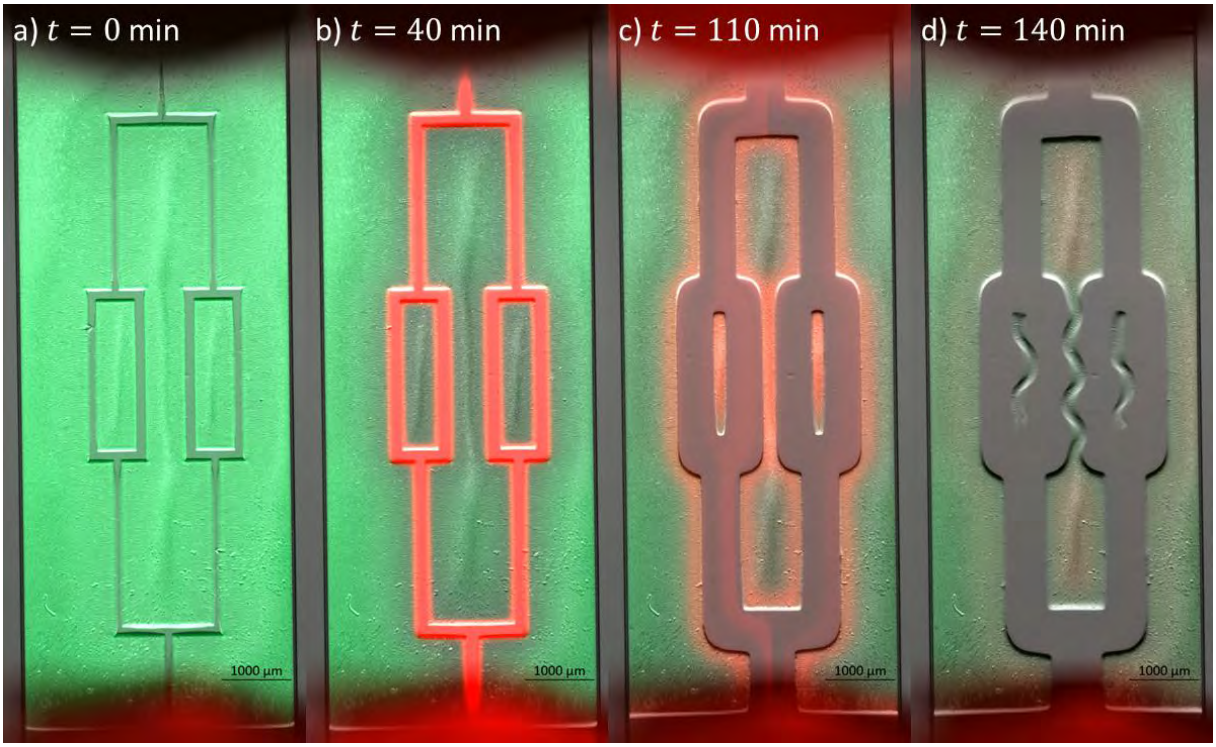


Figure 1: Erosion of a channel network in hydrogel (green), due to the injection of an enzyme (red). Black bars represent 1 mm. Pictures are taken at $t = 0$ min (a), $t = 40$ min (b), $t = 110$ min (c) and $t = 140$ min (d).

References

[1] Beebe, D., Moore, J., Bauer, J. *et al. Functional hydrogel structures for autonomous flow control inside microfluidic channels*. Nature **404**, 588–590 (2000). https://doi.org/10.1038/35007047

Controlled evaporation of droplets on hierarchical superhydrophobic devices coupled with plasmonic nanoantenna for environmental applications

S. Ramos[1*], V. Fabre[1], F. Carcenac[1], A. Laborde[1], C. Vieu[1], E. Trevisiol[2], P. Louarn[3]

[1] LAAS-CNRS, Université de Toulouse, CNRS, INSA, 31400, Toulouse, France
[2] TBI, Université de Toulouse, CNRS, INRAE, INSA, 31400, Toulouse, France
[3] IRAP, CNRS, Université de Toulouse, CNES, 31400, Toulouse, France
[*] sramos@laas.fr

Superhydrophobic (SH) surfaces are currently used in various industrial and research fields such as self-cleaning, waterproof textiles, antibiofouling surfaces, anti-icing or oil/water separation. The micro/nano scientific community has also identified the potentiality of these surfaces to concentrate molecular traces in solution for analytical purposes in the sub femto-molar range[1]. Despite exceptional results obtained when SH surfaces are coupled with surface enhanced Raman spectroscopy (SERS), the method has not been popularized for applicative uses.

Our ambition is to develop such devices for applications related to the detection of environmental pollutants such as endocrine disrupting chemicals (EDCs) or drugs. EDCs have the particularity to have consequences at low-dose level[2] (sub picomolar range). In this context developing a microfluidic system to analyze molecules well below the picomolar range is of high interest.

This contribution presents a fabrication process of specific hierarchical SH-SERS devices (fig. 1) which allows to precisely concentrate analytes in a small region of interest – called a pedestal[3]. The pedestal can be laser scanned at high resolution for Micro-Raman spectroscopy identification of analyte molecules thanks to the integration of plasmonic nano-antennas all over the pedestal area.

Use of such device for environmental analysis will be demonstrated based on dedicated experiments using droplets of propranolol, a well-known beta-blocker drug, dissolved in de-ionised water and tap water.

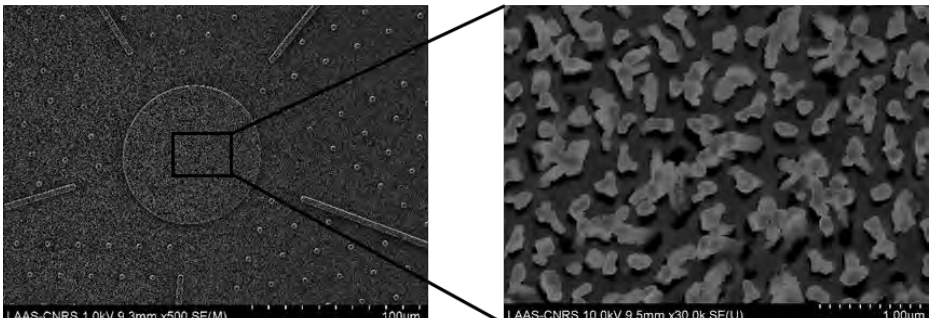


Figure 1 Electron micrographs of a typical SH-SERS device. The pedestal can be seen on center of the left side image and plasmonic silver nano-antennas can be seen in the enlarged view on the right side.

References

[1] F. De Angelis *et al.*, « Breaking the diffusion limit with super-hydrophobic delivery of molecules to plasmonic nanofocusing SERS structures », *Nature Photonics*, vol. 5, n° 11, p. 682‑687, nov. 2011, doi: 10.1038/nphoton.2011.222.

[2] L. N. Vandenberg *et al.*, « Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses », *Endocr Rev*, vol. 33, n° 3, p. 378‑455, juin 2012, doi: 10.1210/er.2011-1050.

[3] V. Fabre *et al.*, « Hierarchical Superhydrophobic Device to Concentrate and Precisely Localize Water-Soluble Analytes: A Route to Environmental Analysis », *Langmuir*, vol. 38, n° 46, p. 14249‑14260, nov. 2022, doi: 10.1021/acs.langmuir.2c01690.

Development of a microfluidic chip for the characterization of nano and micro suspensions characterization by digital in line holography

T. Kurdadze[1], F. Lamadie[1], I. Rodriguez-Ruiz[2]

[1]CEA, DES, ISEC, DMRC, Univ Montpellier, 30207 Bagnols-sur-Ceze, France
[2]Laboratoire de Génie Chimique – CNRS, UMR 5503, 4 Allée Emile Monso, Toulouse, France
*tamar.kurdadze@cea.fr

Nowadays, novel hydrometallurgical recycling processes are actively developed via microfluidic studies, helping to minimize both reagent consumption and waste, and therefore reducing research costs and environmental footprint. Additionally, microfluidic scale allows reaching the extraction equilibrium in much shorter time than traditional bulk devices [1]. Concretely, microfluidic systems with segmented flows are of particular interest, as each droplet can be considered as an independent reactor allowing the reproduction of several hundreds of experiments in a short period of time. To ensure in-situ monitoring, microscale analytical detection techniques must be adapted for in-line measurements to characterize the chemical composition of droplets. In this background, the aim of this work is to develop a microfluidic device for the characterization of nano- and micro-suspensions inside droplets using a simple and efficient 3D imaging technique, Digital Inline Holography (DIH). For this purpose, we have designed and fabricated a microfluidic chip adapted for the implementation of DIH measurements [2]. The microfluidic chip is based on a flow-focusing geometry adapted for the production of spherical aqueous droplets. The droplet generator ($75\mu m \times 75\mu m$ cross section) is coupled to a $1\,mm$ wide $\times$ $360\,\mu m$ deep detection channel. Channel dimensions allow for the formation of completely spherical droplets, while avoiding interference with the channel walls during measurements. In addition, to avoid multiple optical interferences caused by too small spaces between each droplet, a second concentric inlet for continuous phase injection has been added, to space the generated droplets by increasing the velocity of the liquids flowing in the detection channel. Schematics of the chip and the experimental DIH setup are shown in the Figure 1. The operating conditions of the chip and the hydrodynamic behavior of the droplets have been characterized as a function of flow rates Q_d/Q_c and viscosity ratios η_d/η_c of the dispersed and continous phase respectively. The first numerical simulations and experimental validations have been performed for droplets ranging in size from 100 to $250\,\mu m$ of different chemical composition, in order to assess DIH sensitivity within microfluidic environment.

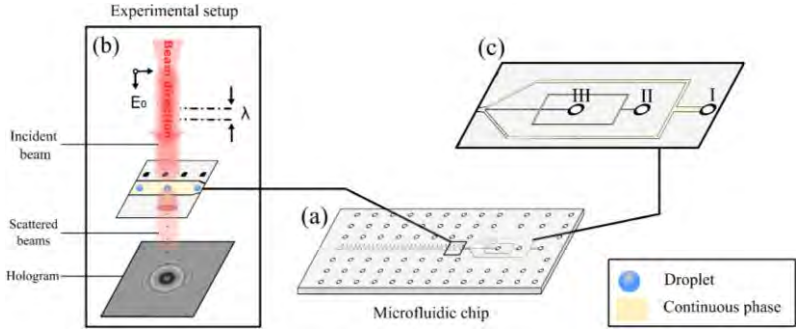


Figure 1.a) Overview of the microfluidic chip for DIH measurements. b) Zoom on the detection area of the chip. c) Zoom on the chip inlets I, II, II- Spacing, continuous and disperse phase inlets respectively.

References:

[1] H. Zhang et al., "*Toward a mechanistic understanding of microfluidic droplet-based extraction and separation of lanthanides*," Chem. Eng, 356, 673–679, (2019)

[2] G. Ding et al., "*A Novel Method Based on Optofluidic Lensless-Holography for Detecting the*

Beads, bubbles and drops in microchannels: stability of centred position and equilibrium velocity

Jean Cappello[1], Javier Rivero-Rodríguez[2], Youen Vitry[3], Adrien Dewandre[3], Benjamin Sobac[4] and Benoit Scheid[1]

[1] Transfers, Interfaces and Processes (TIPs), Université libre de Bruxelles, 1050 Brussels, Belgium
[2] Escuela de Ingenierías Industriales, Universidad de Málaga, Campus de Teatinos, 29071 Málaga, Spain
[3] Secoya Technologies, 1348 Louvain-la-Neuve, Belgium
[4] Laboratoire des Fluides Complexes et leurs Réservoirs (LFCR), UMR 5150 CNRS, Université de Pau et des Pays de l'Adour, Anglet, France

Understanding and predicting the dynamics of dispersed micro-objects in microfluidics is crucial in numerous natural, industrial and technological situations. In our study, we experimentally characterized the equilibrium velocity V and lateral position ε of various dispersed micro-objects such as beads, bubbles and drops, in a cylindrical microchannel over an unprecedent wide range of parameters. By systematically varying the dimensionless object size ($d \in [0.1; 1]$), the viscosity ratio ($\lambda \in [10^{-2}; \infty[$), the density ratio ($\varphi \in [10^{-3}; 2]$), the Reynolds number ($Re \in [10^{-2}; 10^{2}]$) and the capillary number ($Ca \in [10^{-3}; 0.3]$), we offer a general study exploring various dynamics from the non-deformable viscous regime to the deformable visco-inertio-capillary regime, thus enabling us to highlight the sole and combined roles of inertia and capillary effects on lateral migration. Experiments are compared and agree well with a steady three-dimensional Navier–Stokes model for incompressible two-phase fluids including both the effects of inertia and possible interfacial deformations. This model enables us to propose a useful correlation for the object velocity V as functions of d, ε and λ, obtained in the $Re = Ca = 0$ limit, but that appeared to be valid for a large range of values of Re and Ca delimited by the validity of the linear regime. We also present stability maps for the centered position showing that undeformed objects dominated by inertial effects are only stable if large enough, typically for $d > 0.7$, whereas deformable objects dominated by capillary effects can be stable for much smaller sizes, provided the viscosity ratio is outside the range $0.7 < \lambda < 10$, in which deformability also plays a destabilizing effect, as for inertia.

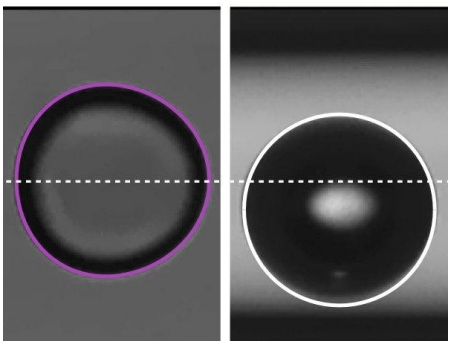


Figure 1: Equilibrium position and shape of bubbles transported by an inertial flow in a regime dominated by (a) capillarity and (b) inertia. Dotted lines show the channel centreline. Scale bar is 100 µm.

Wetting 2D materials at the microscale

M. Zhao[1], A.-L. Biance[1], and F. Vialla[1*]

[1]Institut Lumière Matière UMR 5306, Univ Lyon, Univ Claude Bernard Lyon 1, CNRS, Villeurbanne, FRANCE
[*]fabien.vialla@univ-lyon1.fr

Nanofluidics has benefited in the recent years from the implementation of original devices based on 2D materials (graphene, MoS_2, hBN…) in geometries such as nanotubes, nanopores drilled membranes or lithographed slits [1]. Those materials are presented as atomically flat, with no dandling bonds at their surface, and with tunable interface properties. Yet, complex nanofabrication and limited knowledge on their actual cleanliness and behavior at the nanoscale in devices still hinder their full potential. In particular, an on-going debate remains about their intrinsic properties and the influence of the supporting substrate when the number of layers is reduced, the so-called wetting transparency and translucency [2-4]. Surface inhomogeneities, including crystalline defects, layer wrinkles, and adsorbed contaminants, are also key elements to consider.

Here we focus on the study of the wetting properties of freshly exfoliated 2D materials, presenting flat and pristine surface, at the micron-scale level. We introduce an original experimental setup and demonstrate the deposition and study of few-micron-diameter droplets on samples placed in a chamber with saturated humidity environment to prevent evaporation. Micro-controllers and coupled microscopies allow for micron-scale localized deposition and contact angle measurement. We explore the influence on the wetting properties of the 2D materials nature, the number of layers, and the underlying substrate.

References

[1] Mouterde, T., Keerthi, A., Poggioli, A.R. et al. Molecular streaming and its voltage control in ångström-scale channels. **Nature 567, 87–90** (2019).

[2] Rafiee J., Mi X., Gullapalli H., Thomas A. V., Yavari F., Shi Y., Ajayan P. M., Koratkar N.A.Wetting transparency of graphene. **Nature Materials 11, 217–222** (2012).

[3] Shih, C. J.; Strano, M. S.; Blankschtein, D. **Nature Materials 12**, 866−869 (2013)

[4] Hong G., Han Y., Schutzius T.M., Wang Y., Pan Y., Hu M., Jie J., Sharma C.S., Müller U., and Poulikakos D. On the Mechanism of Hydrophilicity of Graphene. **Nano Letters 16, 7, 4447–4453** (2016)

Capture of CO_2 using aqueous foam: a 2D case study in microchannels

C. APRILI[1]*, B. DOLLET[1], G. COUPIER[1], E. LORENCEAU[1]

[1]LIPhy, Grenoble, France
*cecile.aprili@univ-grenoble-alpes.fr

In order to limit global warming, several IPCC scenarios are based on an intensive capture of CO_2 from the atmosphere to reduce the greenhouse effect induced by it. This objective is technically ambitious since it requires the development of processes to capture the diluted CO_2 from air (relative concentration of 0.04%), to separate it from other gases in the atmosphere and to concentrate it in order to limit the storage volumes. Solutions involving liquid gas interfaces exist [1] and adding microparticles that can fix or consume the CO_2 dissolved in the liquid phase increases the efficiency [2, 3]. In this context, aqueous foams have several advantages, namely: a very large liquid/gas exchange surface, they can be dynamically solicited to mix the gas thus preventing the apparition of limiting gradient of CO_2 concentration in the gas phase and the selectivity of CO_2 transfer compared to nitrogen can be enhanced depending on the nature of the continuous phase and on the surfactants used [4]. Yet, the kinetics of gas transfer through the soap film - quantified using k, the gas permeability, which encompasses the subtlety of micro-scale transfer, can reveal surprising features, such as a reversible adsorption of a gas onto the self-assembled monolayer [5]. To better understand CO_2 transfer within the different elements of an aqueous foam (bubbles, films, plateau borders and nodes), we follow the evolution of size of the bubbles of a foam confined in a 2D microfluidic geometry. An air bubble is introduced in a CO_2 foam (cf Fig 1). In this experiment, the area and perimeter of the air bubble grows greatly at the expense of the small CO_2 bubbles near it.

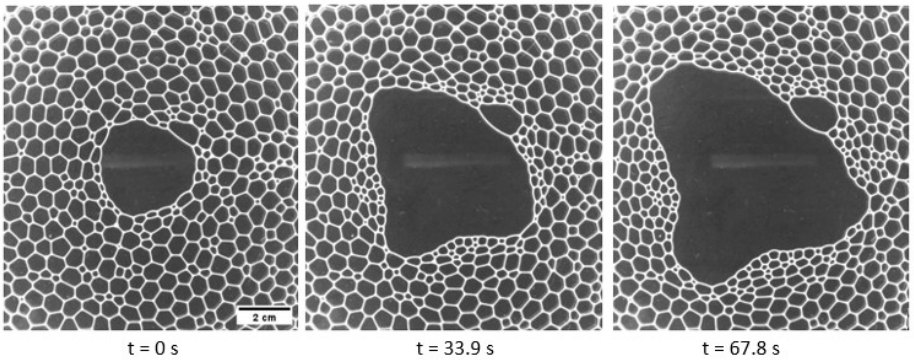


Figure 1: Evolution of an air bubble in a CO_2 foam. The CO_2 in the foam is transferred in the bubble and in the liquid phase to satisfy concentration equilibrium.

References

[1] C. Even, D. Hadroug, Y. Boumlaik, G. Simon: *Microalgae-based Bioenergy with Carbon Capture and Storage quantified as a Nagative Emissions Technology*. Energy nexus **7**, 100117 (2022)

[2] S. K. Watson, K. Han, W.W. Su, M.A. Deshusses, E. Kan: *Carbon dioxide capture using Escherichia coli expressing carbonic anhydrase in a foam bioreactor*. Environmental technology **37(24)**, 3186-3192 (2016)

[3] A. Jonaska, P.P. Lamers, A. Hamhuis, Y. Van Eimeren, R.H. Wijffels, M. Janssen: *Bioreactor for microalgae production*. Chemical Engineering Journal **313**, 1206-1214 (2017)

[4] G. Falciani, R. Franklin, A. Cagna, I. Sen, A. Hassanali, E. Chiavazzo: *A multi-scale perspective of gas transport through soap-film membranes*. Molecular Systems Design & Engineering **5**, 911-921 (2020)

[5] C. Hadji, B. Dollet, H. Bodiguel, W. Drenckhan, B. Coasne, E. Lorenceau: *Impact of Fluorocarbon Gaseous Environments on the Permeability of Foam Films to Air*. Langmuir **36(44)**, 13236-13243 (2020)

A skin-on-a-chip microfluidic platform to investigate neurovascular interplays in rosacea

M.Bellenguez*, J.Leng

LOF-Solvay-CNRS UMR 5258, Pessac, France
*margot.bellenguez-ext@solvay.com

By combining tissue engineering with microfluidic technology, microdevices known as organs-on-chip have been developed in the past few years to provide more relevant in vitro models that mimic the microenvironment of living organs.

Essential for skin disease modelling and pharmaceutical research, various skin-on-a-chip models have been constructed. However, most models focus on co-cultures of fibroblasts and keratinocytes with endothelial cells to form a vascularized skin equivalent [1, 2, 3]. Our aim is to study specifically the role of innervation in a skin disease, rosacea.

To this end, we designed a two-layer PDMS device with a lower chamber containing a 3D skin equivalent and sensory neurons communicating through a physical barrier presented in Figure 1. Separated from the lower chamber by a porous membrane, the upper chamber consists of two separate microfluidic channels that deliver nutrients to the cells by diffusion of the medium across the membrane. These separate channels allow each cell culture to be supplied with specific media at different flow rates. It is important that the device allows not only microscopic observations, but also the collection of culture media and cell material for analysis, as well as the use of drugs to induce or prevent rosacea.

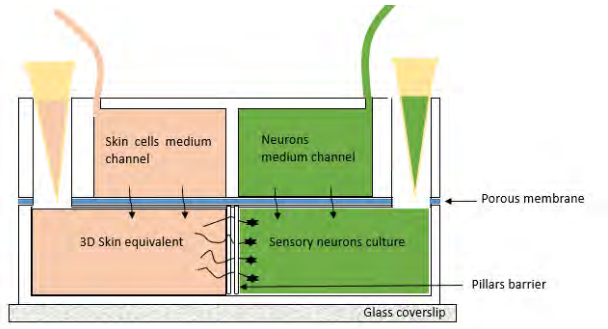


Figure 1: Schematic representation of the skin-on-chip device

References

[1] S. Lee, SP. Jin, YK. Kim, GY. Sung, JH. Chung, JH. Sung: *Construction of 3D multicellular microfluidic chip for an in vitro skin model.* Biomed Microdevices **19**, 22 (2017)

[2] A. Varone, JK. Nguyen, L. Leng, R. Barrile, J. Sliz , C. Lucchesi , N. Wen, A. Gravanis, GA. Hamilton, K. Karalis, CD Hinojosa: *A novel organ-chip system emulates three-dimensional architecture of the human epithelia and the mechanical forces acting on it.* Biomaterials **275** (2021)

[3] M. Wufuer, G. Lee, W. Hur, B. Jeon, BJ. Kim, TH. Choi, S. Lee: *Skin-on-a-chip model simulating inflammation, edema and drug-based treatment.* Sci Rep. (2016)

Actuation of droplets using opto-electrowetting, models and application for single cell analysis

Samir Mekkaoui[1]*, Pierre Blandin[1], Xavier Mermet[1], Benoît Racine[1], Etienne Quesnel[1], Cedric Ducros[2], Fabrice Emieux[2], Yves Fouillet[1]

[1]Univ. Grenobles Alpes, CEA, LETI, DTBS & DOPT, 38000 Grenoble, France
[2]Univ. Grenoble Alpes, CEA, LITEN, DTNM, 38000 Grenoble, France
*Corresponding author: samir.mekkaoui@cea.fr

Droplet based microfluidics is an increasingly studied field for chemical and biological assays. This approach permits to process a large number of samples simultaneously. The control of such dense array of droplets requires methods to easily actuate individual samples in an emulsion. A widespread application is to use individually addressable digital microfluidics systems such as electrowetting-on-dielectric devices (EWOD). Chiou et al. proposed an alternative with optoelectrowetting (OEW) [1, 2] devices, using light as "virtual" electrodes, the droplets following the movements of light patterns projected on the device's surface. This suppresses the technical limitations of printing a limited amount of metallic electrodes on a chip, by biasing a continuous photoconductive film with light patterns.

These systems exhibit different behavior depending on the materials and light sources used. A classical approach to describe OEW is a simplified electrical model for a better representation of the device's functional parameters. The chip is considered equivalent to an RC circuit (Figure 1a) with a cut off frequency value dominated by the photoresistance R_a. The variation of this resistivity due to light illumination shifts the cutoff frequency. This simple model is limited by the fact that it does not consider the photoconductive layer's optical absorption. Indeed, the creation of charge carriers is not uniform in the layer, and this depends on the emitting wavelength (Figure 1b). Here we present a discretized model, allowing an analysis of the device performances as a function of the wavelength. This model has permitted the development of OEW chips integrating a a-Si:H (hydrogenated amorphous silicon) photoconductive layer, as well as an Al_2O_3 dielectric layers. An experimental bench integrating the light source, the electrical source and fluidic pumps was set-up to characterize the devices parameters. For the light actuation, commercial videoprojector and Oled are experimented. Finally, we were able to use the aforementioned architecture to successfully actuate 25 nL PBS1X droplets emulsified in silicone oil (Sigma-aldrich) with triton X100 surfactant (Figure 1c). This paves the way for further developments of single cell assays in droplets and automated sorting of samples of interest.

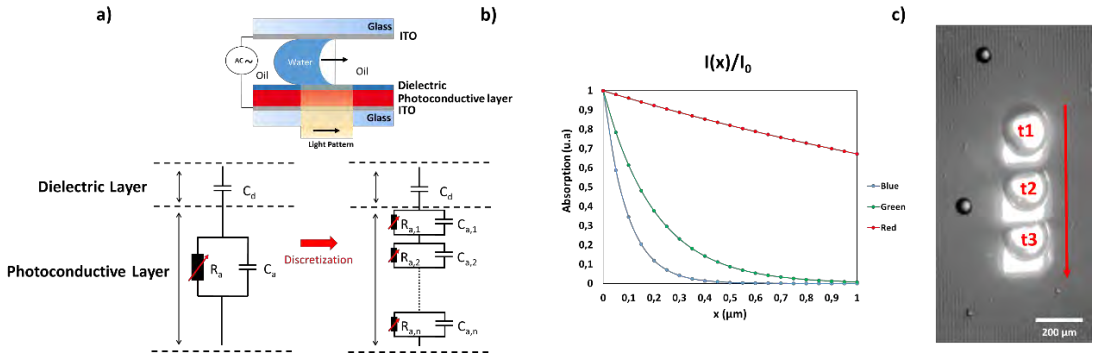


Figure 1: a) schematic representation of OEW device with classical electrical model (left) and discretized electrical model (right) b) Normalized absorption curves in a-Si:H according to the incident wavelength c) stacked image of a PBS1X droplet actuation using a light spot at 3 successive times (along the red arrow)

References

[1] P. Chiou et al.: *Light actuation of liquid by optoelectrowetting.* Sensors and actuators A:physical **Volume 104**, 222-228 (2003)

[2] S.Pei et al.: *Distributed circuit model for multi-color light-actuated opto-electrowetting microfluidic device*, Journal of lightwave technology, **vol.33**, 3486-3493 (2015)

Mechanical oocyte measurement as a predictive biomarker for assisted reproduction technologies

Barbier L.[1*], Bulteau R.[1,2], Panier T.[3], Campillo C.[2,4], Terret M-E.[1]

[1]Center for Interdisciplinary Research in Biology (CIRB), Collège de France, CNRS, INSERM, Université PSL, Paris, France
[2]LAMBE, Univ Evry, CNRS, CEA, Université Paris- Saclay, 91025, Evry- Courcouronnes, France
[3]Sorbonne Université, CNRS, Institut de Biologie Paris-Seine, Laboratoire Jean Perrin (LJP), France
[4]Institut Universitaire de France (IUF)
[*]lucie.barbier@college-de-france.fr

Female gamete morphogenesis is error-prone, producing a high basal rate of poor-quality oocytes, a feature that increases with maternal age, along with the risk of miscarriage and infertility. In this context identifying appropriate biomarkers to assess oocyte quality in assisted reproductive technologies is crucial to better manage patients suffering from infertility. Recent work has established a link between oocyte mechanical properties and post-fertilization developmental potential. However, state-of-the-art methods for assessing oocyte mechanical properties are low throughput, lack robustness and invasive, which precludes their use for medical application. In this context, I aim to develop a user-friendly microfluidic platform to assess non-invasively the mechanical properties of mammalian oocytes. I based my approach on micro-metric constrictions as cells mechanical properties can be linked to different transit score parameters. I designed a microfluidic set-up adapted for oocytes handling which are large cells only available in small quantities (~100 µm in size; ~15 oocytes/ *in vitro* fertilization cycle). To microfabricate the constriction in the microchannel, I combined conventional photolithography with direct micro-milling onto the cured resin. I first validated that my microfluidic approach allows for non-invasive mechanical measurement of oocytes on a well characterized mouse model of extra-soft oocytes. I am now applying rheological models to establish discriminant morphological and transit parameters allowing to identify high quality oocytes within a mixed population. In a future step of the project, I aim to developed the microfluidic device towards a turn-key platform and test its implementation in clinical routines for diagnostic purposes.

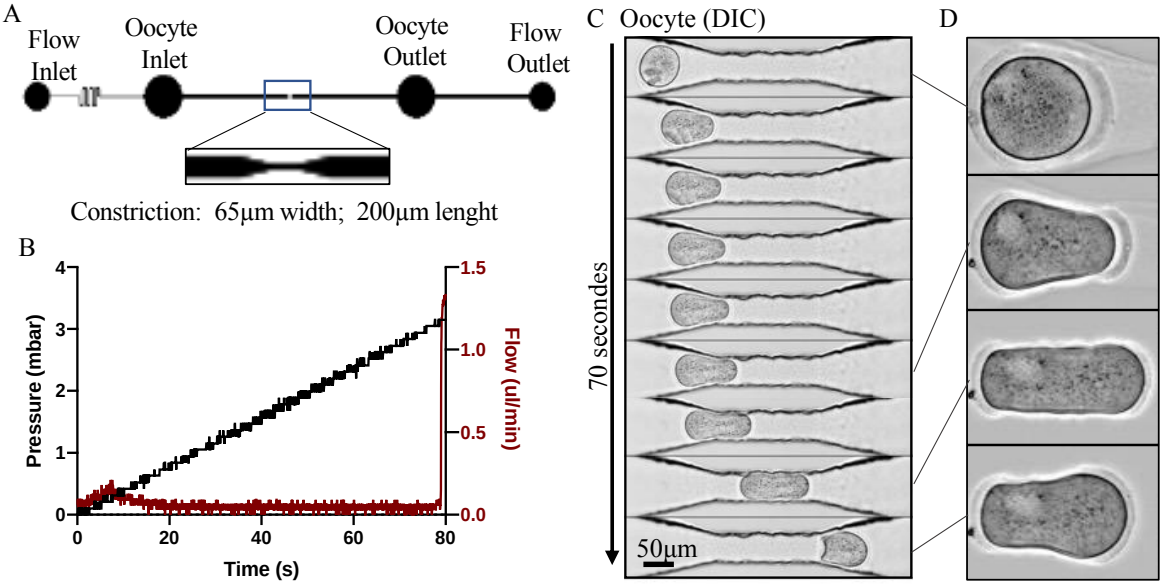


Figure 1: Microfluidic approach for the evaluation of oocyte mechanical properties.
(A) Schematic representation of the microfluidic device developed to measure the mechanical properties of oocytes. The zoom shows the constriction where the measurement is performed. (B) Stepwise pressure is applied until the oocyte is squeezed through the constriction. The flow measurement indicates when the oocyte blocks the constriction. (C) Representative image sequence of an oocyte passing through the constriction. (D) Example

Functionalization of air microbubbles in a microfluidic chip for a novel biosensor

M. Prudhomme[1*], C. Lakdhar[1] J.Fattaccioli[2], F.Chollet[1]

[1]Institut FEMTO-ST, Université Bourgogne Franche-Comté, Besancon, France
[2]IPGG, Ecole Normale Supérieure, Sorbonne Université, Paris, France
[*]marc.prudhomme@femto-st.fr

Microbubbles are widely studied in microfluidic as they provide promising results in biomedical applications, especially for imaging and drug delivery applications. Indeed, their particular acoustic behavior enables to improve the possibilities in ultrasound imagery with the visualization of the human blood pool [1], and they can be acoustically actuated to deliver the drugs they carry [2]. Furthermore, the surface of these microbubbles can be functionalized in order to perform targeted imaging or targeted delivery [3].

In this project, we want to develop a novel application of microbubbles, by using them for a new paradigm of biosensing. More precisely, we aim to use the surface of microbubbles generated in a microfluidic chip as a biointerface for the capture of biological elements before they can be acoustically detected. By using the surface of microbubbles, we largely improve the operation of classic microfluidic based biosensors: we avoid a single use planar biointerface, while having a better capture efficiency [4].

In this poster, we present the functionalization aspect of air microbubbles within the microfluidic chip and the possibility to capture elements at the surface. To demonstrate the capability of our biosensor, we simply functionalize the bubbles with biotin in order to capture streptavidin afterwards. Bubbles are directly functionalized at their generation thanks to special functionalization solutions made of a mix of surfactants and lipids. Bubbles are then statically organized in a chamber forming a hexagonal network. Then, we inject a solution of streptavidin through the bubbles network. Both functionalization and capture are assessed using fluorescent microscopy thanks to fluorescent labeled chemicals. This microfluidic structure will be combined with acoustic detection to allow label-free sensing and improve sensitivity.

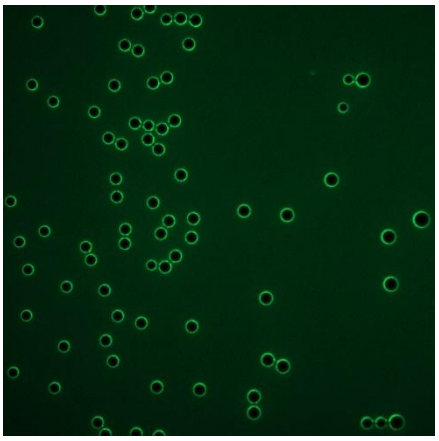


Figure 1: Functionalized microbubbles visualized with fluorescent microscopy

References

[1] David Cosgrove*: Ultrasound contrast agents: An overview*,.European Journal of Radiology,Volume 60, Issue 3, Pages 324-330, 2006

[2] Klazina Kooiman, Hendrik J. Vos, Michel Versluis, Nico de Jong: *Acoustic behavior of microbubbles and implications for drug delivery*. Advanced Drug Delivery Reviews, Volume 72, 2014, Pages 28-48

[3] Tom van Rooij, Verya Daeichin, Ilya Skachkov, Nico de Jong & Klazina Kooiman: *Targeted ultrasound contrast agents for ultrasound molecular imaging and therapy*. International Journal of Hyperthermia, 31:2, 2015, Pages 90-106.

[4] C.-L. Azzopardi, F. Chollet, J.-F. Manceau, W. Boireau: *Analyte capture in an array of functionalized droplets for a regenerable biosensor*. Biomicrofluidics, Volume 13, Issue 5, 2019, Pages 9

Fast cancer cell deformation under flow and morphological recovery

Emile Gasser [1,2*], Kyohei Terao[3], Emilie Su[2,4], Nassiba Abbade[1], Kotryna Vaidziulyte[5], Jean-Baptiste Manneville[4], Mathieu Piel[5], Jean-Yves Pierga[6], Catherine Villard[1]

[1] Laboratoire Interdisciplinaire des Énergies de Demain, CNRS et Université Paris Cité (UPC), UMR 8236, F-75013 Paris

2 Physico-Chimie Curie, Université PSL, CNRS & Institut Curie, UMR 168, F-75005 Paris

3 Faculty of Engineering and Design, Kagawa University, Japon

4 Laboratoire Matière et Systèmes Complexes, UPC & CNRS, UMR 7057, F-75013 Paris

5 Biologie Cellulaire et Cancer, Université PSL, CNRS & Institut Curie, UMR 144, F-75005 Paris

6 Département d'oncologie médicale, Université PSL et Institut Curie, F-75005 Paris

*emile.gasser@curie.fr

Metastases, which are responsible for about 90% of cancer-related deaths, are formed by a complex process involving an intermediate phase in the bloodstream. There, cells from the primary tumor acquire the status of circulating tumor cells (CTCs). As blood capillaries display diameters typically smaller than cancer cells as well as their nuclei, CTCs experience high shear stress and high deformations. We are investigating how these cells respond to the harsh bloodstream conditions, and how this relates to their metastatic potential.

The past [1] and present development of dedicated microfluidic devices allowed us to decipher short-term dynamics of deformation and recovery at the single cell level (see Fig.1). In the present work, we show that the arrest time of circulating breast cancer cells in constrictions depends firstly on their size, and then on their aggressiveness: for the same size, cells from a more aggressive cancer cross the constriction more quickly. At the sub-cellular scale, the arrest time is under the control of the nucleus positioning into the constriction. Interestingly, we observed that the nuclei of more aggressive cells recover almost instantly. This extent of this dominant elastic recovery regime might be linked to the presence of a Vimentin cage-like structure around the nucleus, missing in the less aggressive cancers, besides to a higher level of Lamins A/C. On the other hand, the recovery of the whole cell consists of a quasi-instantaneous elastic regime, followed by a longer-term viscoelastic regime on the order of ten seconds. The recovery time constant is larger for more metastatic cells.

By understanding the mechanisms governing the response of CTCs to deformation, we hope to identify new therapeutic targets to disrupt these mechanisms and prevent CTCs from surviving in the blood circulation

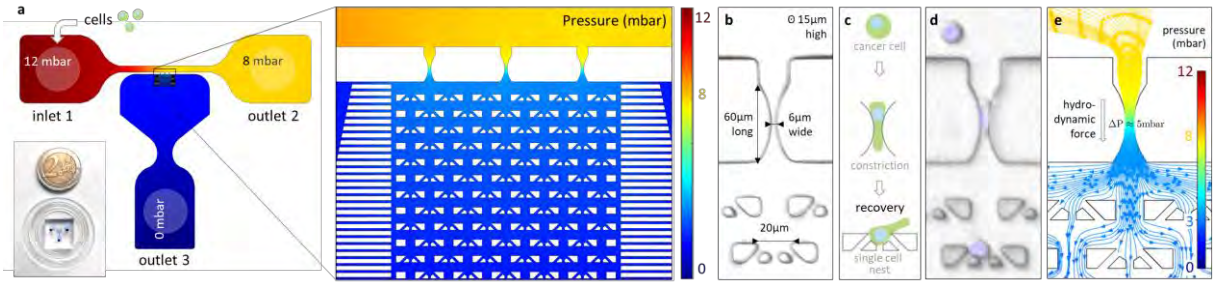


Figure 1: Design and operating principle of the Pachinko device

Reference

[1] H. A Cognart, J. L. Viovy, C. Villard: *Fluid shear stress coupled with narrow constrictions induce cell type-dependent morphological and molecular changes in SK-BR-3 and MDA-MB-231 cells*. Scientific reports **10**, 1-14 (2020)

Relaxation of a colloid clog formed under hydrodynamic flow

O. Liot[1]*, T. Desclaux[1,2], M.L. Mokrane[1], J.F. Morris[3], P. Joseph[2]

[1] Institut de Mécanique des Fluides de Toulouse, Université de Toulouse, CNRS, Toulouse, France
[2] LAAS-CNRS, Université de Toulouse, CNRS, Toulouse, France
[3] Levich Institute and Chemical Engineering, CUNY City College of New York, New York, USA
*olivier.liot@imft.fr

Liquid-solid separation is a central process in many fields of application, such as water treatment, ink-jet printing or bioprocessing. When a suspension flows through a membrane, many objects such as colloids can accumulate at the solid surface. Understanding the increase of hydrodynamic resistance induced by particle accumulation is key for improving filtration processes. For decades, filtration studies at membrane scale have focused on global hydraulic response or membrane material. Since the advent of microfluidics, the study of microfiltration has become a very active field of research, aiming at relating microscale phenomena to macroscale ones. Wyss et al. [1] were precursors in this domain, followed by many others as detailed in a recent review [2].

Our work is an experimental study of filtration of a colloidal suspension using microfluidic devices. A suspension of 0.2 or 1-µm-diameter colloids flows through parallel slit-shaped pores at fixed pressure drop and ionic strength leading to an accumulation of colloids at pore entrance (clog). We recently showed that the layer of colloids close to the device wall reveal large heterogeneities in both porosity and particle organization [3]. Porosity decreases and crystallinity increases moving away from the pore, where hydrodynamic forcing decreases, which lets the colloids rearrange more. The effect is stronger for lower ionic strength, i.e. higher electrostatic inter-particle repulsions.

Once the hydrodynamic forcing is stopped, a portion of the clog is reversibly resuspended whereas the other is irreversibly stuck to the membrane. We show that the fraction of resuspended colloids mainly depends on the hydrodynamic forcing under which the clog was formed. We also study the dynamics of resuspension of the particles, which reveals a transition from high collective diffusion coupled to low self-diffusion, induced by very high particle concentration in the clog, towards standard Brownian self-diffusion.

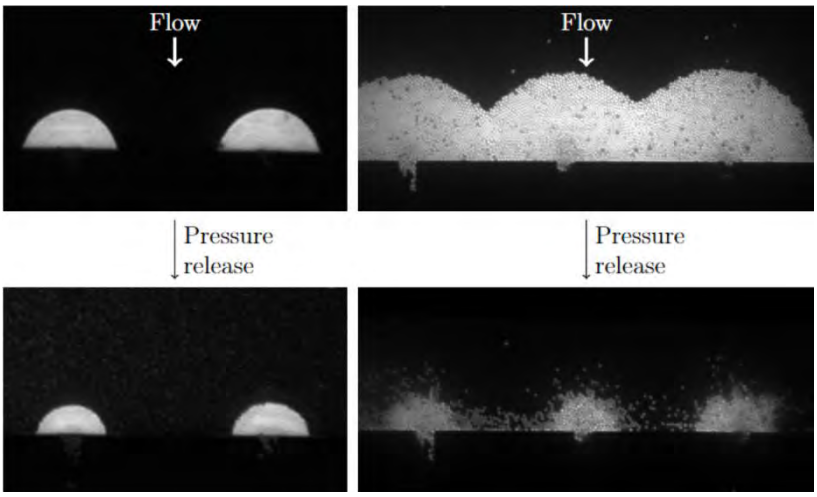


Figure 1: Examples of clogs before and after unclogging process. Left: diameter 200nm, right: diameter 1µm.

References

[1] H.M. Wyss, D.L. Blair, J.F. Morris, H.A. Stone, D.A. Weitz: *Mechanism for clogging of microchannels*. Physical Review E **74**, 061402 (2006)

[2] E. Dressaire, A. Sauret: *Clogging of microfluidic systems*. Soft Matter **13**, 37-48 (2017)

[3] M.L. Mokrane, T. Desclaux, J.F. Morris, P. Joseph, O. Liot: *Microstructure of the near-wall layer of filtration-induced colloidal assembly*. Soft Matter **16**, 9726-9737 (2020)

Hydrogel-based microsystem to study coupling between diffusion and cellular volume in living tissues

Gaëtan JARDINÉ[1]*, Charlotte RIVIÈRE[1], Sylvain MONNIER[1]

[1]Institut Lumière Matière UMR5306 Université Lyon 1-CNRS, Villeurbanne, France
*gaetan.jardine@univ-lyon1.fr

Tissues are spatially heterogeneous structures which give rise to their specific biological functions. This heterogeneity is essential in both physiological, e.g. embryogenesis, and pathological processes, e.g. the organization of multiple cell subpopulations within a tumor. The emergence of such spatial distribution can be due to gradients of biomolecules for example. Additionally, in pathological and physiological conditions, tissues can be confined and will therefore exert forces on their surroundings which will in turn reacts by generating stresses. We hypothesize that these stresses will mainly affect intercellular spaces and the extracellular matrix within it, impeding diffusion and leading to the establishment or enhancements of chemical gradients [1]. This phenomenon could therefore influence the emergence of a biological heterogeneity in growing tissues.

Our aim is to assess cell volume, diffusion in the intercellular space and stress in growing tissues. Getting these parameters requires live imaging of dense tissues, which is challenging due to light scattering and absorption. Indeed, clearing techniques for imaging deep tissues required fixed (dead) tissues which do not allow dynamic measurements. Additionally, cell volume is sensitive to these techniques. To approach physiological effects, we want to measure these parameters over long periods of time: up to several weeks. This requires both a renewal of the culture conditions and a perennial biocompatibility of the system.

Hence, to test our hypothesis, we developed a hydrogel-based microsystem to grow dense but thin confined tissues compatible with high content imaging. The thinness of the tissue allows us to free ourselves from the limitations of image depth. This growing tissue will take the shape of a ‘cylindroid’ / pancakes. The thin top layer of agarose used to limit cylindroid growth shall not restrict diffusion of nutrients or drugs used to disturb the system. We have therefore characterized the transport through this layer. The growth of several tens of "cylindroids" is possible in parallel within the same system. We can thus image all the nuclei of numerous cylindroids of a system for more than 10 days. With the help of custom image analysis tools, we can extract the individual volumes of the nuclei within these densely packed 3D systems and follow their dynamics.

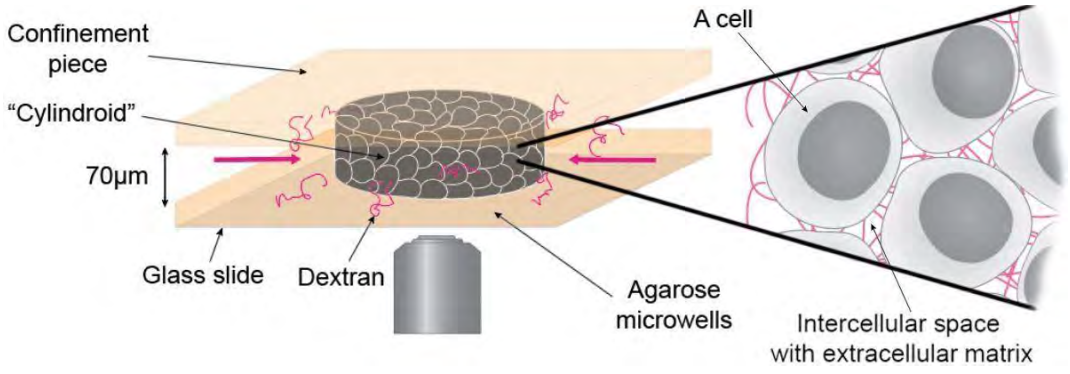


Figure 1: A microsystem to look into dense tissues. The microsystem is built in 2 main parts: bottom agarose microwells where cells lie and eventually form cylindroid; and the top one, which limits tissue thickness. Since the microsystem is hydrogel-based, drugs can be easily added like dextran to mimic growth-induced pressure.

References

[1] ME. Dolega, S. Monnier: *Extracellular matrix in multicellular aggregates acts as a pressure sensor controlling cell proliferation and motility*. Elife **10**, e63258 (2021)

Lab-on-a-chip for the isolation of circulating Adipose Stem Cells: Preprocessing blood using the hydrodynamic filtration module

M. H. Baz[1]*, L. Charpin[1], E. Trevisiol[2], C. Sengenes[3], A. M. Gué[1]

[1]LAAS, Toulouse, France
[2]TBI, Toulouse, France [3]Restore, Toulouse, France
*mhbaz@laas.fr

Adipose Stem Cells (ASC) have gained popularity in the field of regenerative medicine due to their multipotent stem cell characteristics, relative abundance and their association with the onset of type 2 diabetes (T2D) when released from subcutaneous adipose tissue in mice [1]. Strong evidence also suggests that they might circulate in peripheral blood similar to other blood-derived SC. However, it is difficult to prove this notion due to their extremely low concentrations, broad size variation and lack of particular membrane markers. Hence, it is essential to consider isolating ASCs from peripheral blood by combining complementary selection criteria i.e. size and surface markers.

Introduced in 2006 by Yamada and Seki, hydrodynamic filtration is a powerful, yet simple, technique capable of particle separation according to size. Knowing that ASC have a diameter of 10 to 40 µm, we developed a hydrodynamic filtration chip with a predefined cut-off radius Rc of 5 µm in order to sort whole blood into two sub-categories: small-diameter cells < 10 µm (which are typically red blood cells, platelets, and small lymphocytes) and larger cells >10 µm (leukocytes and other bigger cells where the ASCs may lie) in order to pretreat whole blood. Very promising results were obtained using this hydrodynamic filtration module with whole blood where we were able to eliminate 99 % of smaller cells from whole blood without compromising the integrity of leukocytes [2]. Additionally, we were able to filter large beads at "rare-event" concentrations (100 part/mL) from whole blood with negligible loss.

After size selection, the remaining cells, which are mostly leukocytes, are separated from the ASCs by another negative immune-selection module, which is currently under construction, to deplete the remaining leukocytes from the filtered blood and obtain the ASCs.

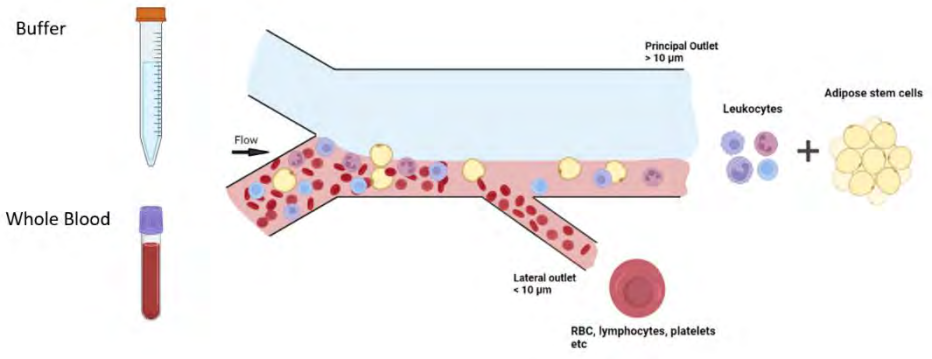


Figure 1: Schematic of the hydrodynamic filtration module

References

[1] A. Girousse, M. Mathieu: *Endogenous Mobilization of Mesenchymal Stromal Cells:A Pathway for Interorgan Communication*. Frontiers in developmental biology **Volume 8 :** 598520 (2020)

[2] M. H. Baz, L. Charpin *Lab-on-a-Chip for the isolation of circulating Adipose Stem Cells* hal-03823431 (2022)

Optimizing liquid-solid slip in nanofluidic systems

Laurent Joly[1]*

[1]Université Lyon 1 – Institut Lumière Matière, Vileurbanne, France
*laurent.joly@univ-lyon1.fr

Nanofluidic systems, e.g. natural nanoporous materials or engineered nanochannels made from new 2D materials, could provide alternative solutions to critical societal challenges such as water desalination or energy harvesting. At the nanoscale, surface effects become crucial; in particular, liquid-solid slip arising from low liquid-solid friction can boost the performance of nanofluidic systems. In that context, I will illustrate with some recent work how molecular dynamics simulations can help understand the molecular mechanisms of liquid-solid friction, and optimize liquid-solid slip. First, I will briefly discuss some recent progress regarding the molecular modeling of interfacial slip and friction [1]. Then, I will discuss a challenge related to nanofluidic systems for electricity production: optimal performance indeed requires charged and slipping surfaces, while these two properties are contradictory. Here we have shown that the charge-friction relationship strongly depends on how the surface charge is generated, and identified promising candidates for optimal charge-friction coupling [2]. Finally, I will show that water slip can be boosted when the liquid is "supercooled", and investigate the origin of this unexpected effect [3].

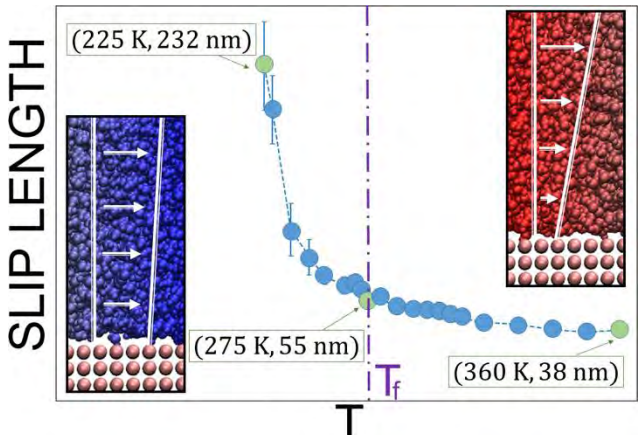


Figure 1: You want water to slip? Supercool it! (image C. Herrero)

References

[1] H. Oga, T. Omori, C. Herrero, S. Merabia, L. Joly, Y. Yamaguchi: "Theoretical framework for the atomistic modeling of frequency-dependent liquid-solid friction", Phys. Rev. Research 3, L032019 (2021)

[2] Y. Xie, L. Fu, T. Niehaus, L. Joly: "Liquid-solid slip on charged walls: the dramatic impact of charge distribution", Phys. Rev. Lett. 125, 014501 (2020)

[3] C. Herrero, G. Tocci, S. Merabia, L. Joly: "Fast Increase of Nanofluidic Slip in Supercooled Water: the Key Role of Dynamics", Nanoscale 12, 20396 (2020)

Role of surfactant chemistry on the dynamic of confined droplets.

Jannin Lucas[1]*, Baué Jacques-Teïva, Gans Adrien[2], Cantat Isabelle[1], Jullien Marie-Caroline[1]

[1]Institut de Physique de Rennes, Rennes, France
[2]LEMTA, Nancy, France
*lucas.jannin@univ-rennes1.fr

In this work, we focus on the dynamics of confined pancake-shaped droplets, in an aqueous solution containing surfactants. Theoretical models of droplet dynamics [1], as well as numerical simulations [2], predict an increasing velocity as the droplet radius increases. Some preliminary works show that the trend is reversed for experiments using different kind of surfactants, which has important consequences on droplet and emulsion dynamics. For this reason, we have performed a full set of experiments of droplet velocity measurements, using surfactants of the same family but with different carbon chain lengths (10 to 14 carbons). If the surfactant has less than 11 carbons, the droplet velocity increases with the radius (at a given external phase velocity) in agreement with theoretical and numerical models; on the other hand, if the surfactant has more than 11 carbons, the velocity decreases with the radius (still at a given external phase velocity). The reversed trend is thus confirmed and shows that the solubility of the surfactant, which depends on the carbon chain length, is a key parameter.

We propose a scaling law using a characteristic time of the surfactant based on the sorption kinetics and the diffusion from bulk towards the interface. Using two limits of this characteristic time (0 and infinity), we recover the two regimes.

To understand these dynamics, it is necessary to know the distribution of the surfactant at the interface of the drop. An indirect signature of the surfactant distribution along the interface can be extracted by a local measurement of the lubrication film thickness [3, 4]. An interferometric device (RICM) [5], inspired by the work from A. Huerre et al. [4], has been built at IPR. It allows performing measurements in dynamical situation, with droplets velocities up to 15 $mm.s^{-1}$. Surprisingly, we observe a thickening at the back of the drops for surfactant with short chain length (whose velocity is in recovered by the models), and a flat film for longer chain length surfactants (which velocity is not recovered by the models). We are currently working on a theoretical model that we hope to present at GDR.

References

[1] R. Dangla: *2D droplet microfluidics driven by confinement gradients.* PhD Thesis (2012).

[2] B. Shen et al.: *Dynamics of a small number of droplets in microfluidic Hele-Shaw cells.* Experiments in fluids. **55**(5), (2014).

[3] B. Reichert et al.: *Topography of the lubrication film under a pancake droplet travelling in a Hele-Shaw cell.* Journal of Fluid Mechanics, **850**, 708-732 (2018).

[4] A. Huerre et al.: *Droplets in Microchannels: Dynamical Properties of the Lubrication Film*. Phys. Rev. Lett. **115**, 064501 (2015).

[5] L. Limozin, K. Sengupta: *Quantitative Reflection Interference Contrast Microscopy (RICM) in Soft Matter and Cell Adhesion*. ChemPhysChem, **10**, 2752-2768 (2009).

Lab-on-disc for in situ monitoring of surface water quality by algae biosensors and physicochemical sensors

J. F. Chateaux[1*], S. Mekkaoui[1], L. Renaud1, C. Bene[2], L. Lozano-Hernandez[2], P. Temple-Boyer[2], V. Bardinal[2], E. Bedel Pereira[2], I. Seguy[2], J. Launay[2], Q. Eynaud[3], O. Margeat[3], J. Ackermann[3], C. Videlot-Ackerman[3], E. Gautreau[4], C. Durrieu[4], M. Valay[5]

[1]Institut des Nanotechnologies de Lyon (INL, UMR5270), Lyon
[2]Laboratoire d'analyse et d'architecture des systèmes (LAAS, UPR8001), Toulouse
[3]Centre Interdisciplinaire de Nanoscience de Marseille (CINaM, UMR7325), Marseille
[4]Laboratoire d'Ecologie des Hydrosystèmes Naturels Anthropisés (LEHNA, UMR5023), Vaulx-en-Velin, [5]SAS OrigaLys ElectroChem, Rillieux-la-Pape, France.

[*]jean-francois.chateaux@univ-lyon1.fr

Anthropogenic activities generate a large number of contaminants (heavy metals, polychlorinated biphenyls (PCBs), pesticides, drugs ...) that endanger both the sustainability of ecosystems and human health. The measurement of surface water contaminants is traditionally carried out in an analytical laboratory using conventional techniques allowing the detection of a large panel of molecules. The representatively and reliability of the final results depend on the handling from water source to the laboratory. Technologies for water quality monitoring are numerous but are not totally integrated, can be human and time consuming as well as expensive.

The requirement of a surveillance with better time and space sampling involves the development and the optimization of new low-cost tools accounting for all eco-toxic risks. In this way, monitoring the effects of chemical contamination using living organisms associated with physicochemical sensors represents a very promising approach. Compared to bio-sensors, living organisms do not exhibit high specificity to a given pollutant but on contrary can be used as early alert systems sensitive to a wide range of pollutants affecting organism's physiology.

The BELUGA project (ANR-18-CE04-0007) aims to develop a microfluidic platform to offer a sample-to-answer demonstrator in a Lab-On-a-Disc (LOD) format (fig 1). Temperature, pH, conductivity, nitrate sensors will be integrated as well as dissolved O_2 and chlorophyll-a fluorescence sensors for micro-algae photosynthetic machinery monitoring. The goal is to design a system that can be used on the field. For that, the LOD format has the advantage to avoid the need for pumps in order to move the water sample into the microfluidic structures. The electronics for sensors driving and data recording will be provided by a commercial portable electrochemistry apparatus (OrigaStat - OrigaLys) into which the LOD will be integrated.

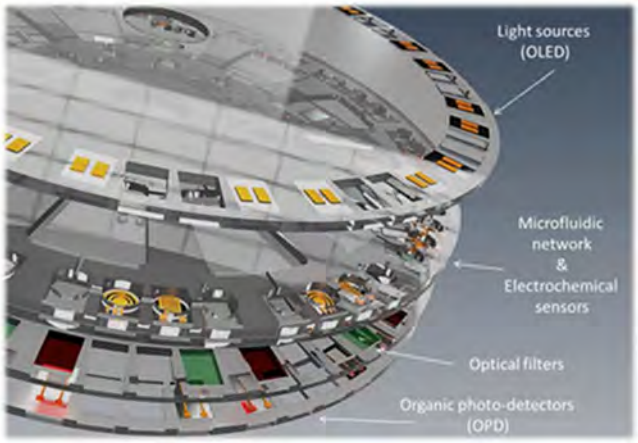


Figure 1 : LOD for surface water monitoring based on micro-algae assay and physicochemical sensors.

Probing spheroids rheology with a microfluidic aspiration pipette

Sylvain Landiech [1], Marianne Elias[1], Morgan Delarue[1], Fabien Mesnilgrente[1], Adrian Laborde[1], David Bourrier[1], Clément Roux[2], Léo Garcia[3], Pierre Joseph[1*]

[1]LAAS-CNRS, Université de Toulouse, UPS, Toulouse, France
[2]Laboratoire des IMRCP, CNRS UMR 5623, Univ Toulouse
[3]IUT Mesures Physiques, UT3 Paul Sabatier, Univ Toulouse
[*]pierre.joseph@laas.fr

Viscoelastic properties of tissue play an important role in many cases like embryonic morphogenesis, wound healing or cancer growth. Indeed, the mechanical properties can change radically during those processes and in the case of cancer, these changes can be the basis for the development of a metastasis.

Spheroids, spherical cell aggregates ranging in size from 100 to 500µm, are very good in vitro tissue models, because they recapitulate a large part of the complexity of a real tissue (extracellular matrix, cell-cell junctions, 3D architecture).

Micropipette aspiration is one of the most complete methods to probe the mechanics of such model tissues [1]. It consists in measuring the dynamics of spheroid's "tongue" in the pipette upon a constant pressure of aspiration. It is quantitative, but is limited to single objects, does not permit to change easily the surrounding medium, and is long and tedious to realize.

We are developing a more efficient on-chip microfluidic micropipette thanks to an original approach derived from [2]. This innovative technology permits the integration of any trap shape to block vesicles, cell or spheroids. In particular, we integrate cylindrical traps (constituting the pipette). Up to 5 spheroids can be aspirated in parallel. By analyzing the dynamics of the cell flow in the micropipette, we can measure the elasticity, the viscosity and the surface tension of the spheroid. For spheroids composed of mouse pancreatic cancer cells, the values we obtained are in line with the literature.

In conclusion, our approach enables on-chip micropipette measurements, with a better throughput than the standard aspiration setup. Microfluidics is versatile, and we are currently working at variants enabled by design changes: rheology of spheroids under growth pressure or chemical stress.

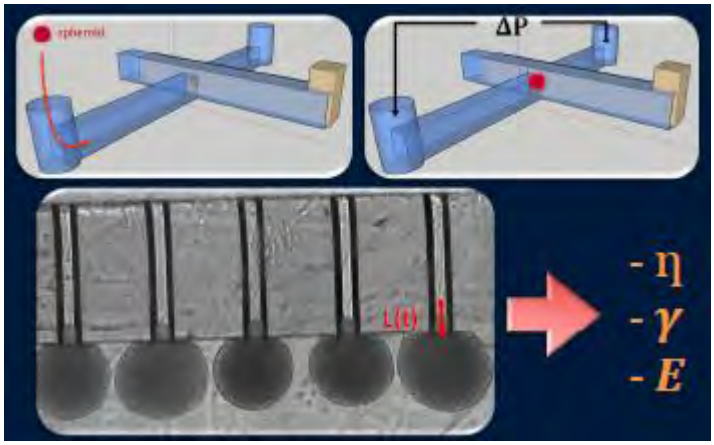


Figure 1: Schematic of the on-chip micropipette and photo of 5 spheroids during aspiration. This technique allows us to measure the viscosity η, surface tension γ and elasticity E

References

[1] Guevorkian K *et al.*: *Aspiration of Biological Viscoelastic Drops.* Phys Rev Lett **104**, 218101 (2010)

[2] Venzac B *et al.*, *Sliding walls: a new paradigm for fluidic actuation and protocol implementation in microfluidics.* Microsystems & Nanoengineering, **6**, 18 (2020)

CO2 evaporation in microchannels: numerical simulations and microfabrication of cooling chips

VACHER Maxime[1*], COLOMBET Damien[1], AYELA Frédéric[1], DELEBECQUE Pierre[2], JEZEQUEL Stéphane[2], KOSSAKOWSKI Roman[2]
*maxime.vacher@univ-grenoble-alpes.fr

[1]Laboratoire d'Ecoulements Géophysiques et Industriels, 1209 Rue de la Piscine 38610 Gières
[2]Laboratoire d'Annecy-le-Vieux de Physique des Particules, 9 chemin de Bellevue 74940 Annecy-le-Vieux

Due to its good thermo-physical properties, in particular a high latent heat, CO2 is considered a suitable fluid for boiling flow cooling of electronic devices. The next generation of trace detectors at the LHC (CERN) will be cooled to temperatures between +10°C and -40°C, by evaporating liquid CO2 circulating in titanium mini channels attached to 4cm² silicon PIXEL sensors [1]. For the next generation of PIXEL detectors to be installed on the Future Circular Collider (FCC), a new solution developed by the LEGI-LAPP team is to make the CO2 circulate in micro-channels integrated in the silicon, covering the entire surface of the detectors. For the current decade, their thermal performances will be evaluated to validate this choice. For this purpose, numerical simulation of two-phase flows should help to predict the efficiency of heat transfer within microchannels, over a wide range of operating conditions (saturation temperature, heat flux, hydraulic diameter and roughness of the channels, mass flow rates, etc.). So far, 2D numerical simulations have been performed on isolated bubbles with the Fluent software, using the VOF (Volume Of Fluid) method, and have allowed to understand how to better control the parasitic currents induced by the surface tension modelling, and also to elaborate a first evaporation model able to determine the bubble growth rate corresponding to a given liquid superheat. In parallel to this simulation work, first samples of silicon microchannels sealed with Pyrex were made in a clean room. The first pressure tested samples largely resist to the maximum operating pressure of the LAPP CO2 test bench, i.e. 45 bars. Before these tests, a long work consisted in testing the pressure resistance of the connectors used to connect the CO2 supply tubes to the samples. Brass tubes soldered with tin on copper washers were validated at pressures close to 80 bars, contrary to connectors glued directly to the silicon, which showed numerous leaks or detachments during the tests. Recently, first prototypes of multi microchannels have been realized on 400 microns thick wafers, and will be tested soon on the LAPP test bench. One of the realized chips can be seen on figure 1 below. The visualization of the flow with a high speed camera should provide useful information on the flow regimes, and the characteristics of the nucleation, which can be injected into our numerical models. The final goal of this thesis will be to compare the results of the numerical simulations with the experimental data.

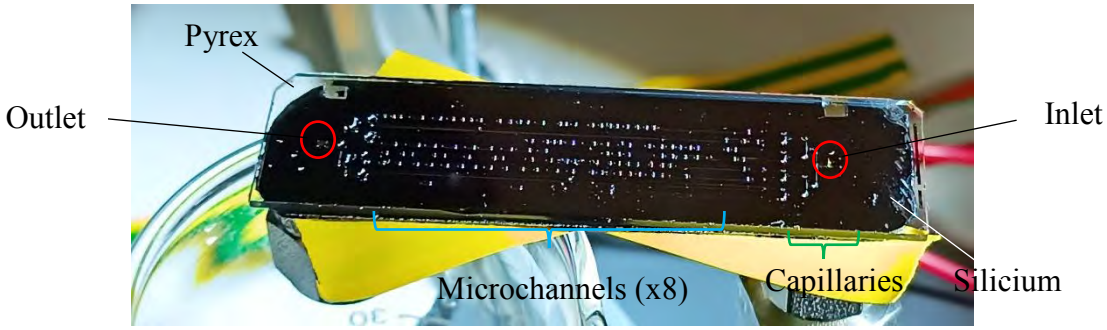


Figure 1. Two-phase flow in a cooling chip with 8 channels in parallel.

References

Towards microfluidic separation processes using Switchable Hydrophilicity Solvents

M. Zollo[1]*, J.-B. Salmon[1], Y. Medina Gonzalez[1]

[1]Laboratoire du Futur (CNRS, Solvay, Université de Bordeaux, UMR 5258), 178 avenue du Dr. Albert Schweitzer- 33600 Pessac, France.
*margaux.zollo-ext@solvay.com

Solvent engineering aims at controlling the solubility and transport properties of a solvent medium, in order to optimize the chemical or physical processes performed. Among the strategies of Solvent Engineering, reversible CO_2-switchable hydrophilicity solvents (CO_2-SHS) represent a promising route to reversibly switch the properties of a solvent.

The final goal of this work is to combine microfluidic technologies and CO_2-SHSs to perform liquid-liquid separation processes at microscale and in optimized experimental conditions. 2, 2-Dibutylaminoethanol (DBAE) was chosen as this solvent is able to switch from a tertiary amine (hydrophobic form), to the corresponding bicarbonate salt (hydrophilic form) at room conditions (see Figure 1(a)) [1].

In a first step, we developed microfluidic chips made of poly(dimethylsiloxane) (PDMS) using soft lithography (typical channel height 10-50µm), PDMS being the material of choice, not only for the versatility and simplicity of microfabrication, but also for its permeability to gasses. We observed that DBAE is able to extract uncross-linked PDMS oligomers from the PDMS matrix of the chip as other organic solvents [2]; this phenomenon interfered with our observations. To overcome this drawback, we developed protocols to wash-out these uncross-linked oligomers leading to PDMS chips fully compatible with DBAE. We then developed two-level PDMS chips (see Figure 1 (b-d)). This allowed us to impose either a CO_2 or an N_2 flow in a channel superimposed to a fluidic channel in which we established a co-flow between DBAE and water. Because of the permeability of PDMS to gasses, we were able to induce the phase change of the SHS and modulate its solubility into water. We are currently exploiting these microfluidic experiments to design a liquid-liquid separation process in a microchannel.

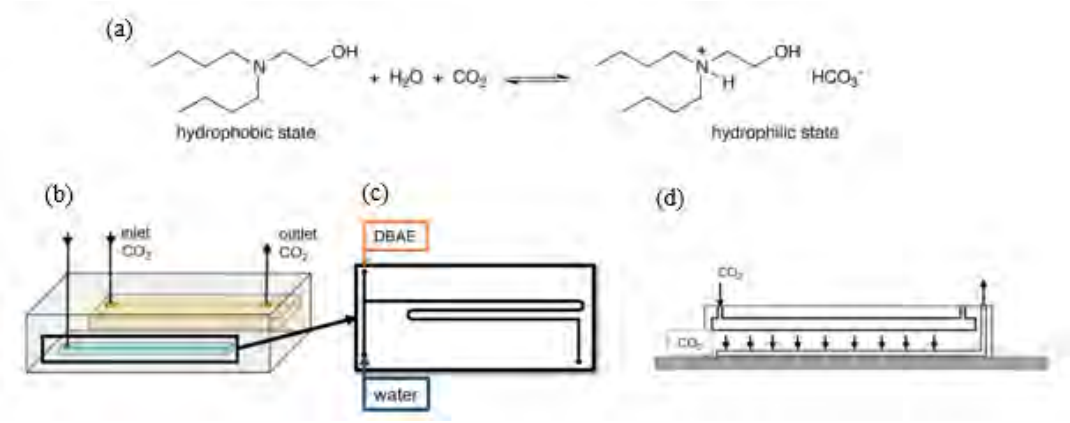


Figure 1: (a) Reaction scheme of the reversible switch of DBAE forming its corresponding bicarbonate salt. (b) Schematic representation of a 2-level PDMS chip assembly for the phase-change of DBAE, with its lateral cross section (d) and the co-flow path drawn for the lower channel (c).

References

[1] P. Jessop: *Switchable solvents as media for synthesis and separations*. Aldrichimica Acta, **48**, 18-21 (2015)

[2] J. N. Lee, C. Park, G. M. Whitesides: *Solvent Compatibility of Poly(dimethylsiloxane)-Based Microfluidic Devices*. Analytical Chemistry **75**, 6544-6554 (2003)

Transport of fibers in structured media: toward a sorting device

C. Bielinski[1]*, Z. Li[2], B. Delmotte[1], O. du Roure[2], A. Lindner[2]

[1]Laboratoire d'Hydrodynamique (LadHyX), CNRS, École Polytechnique, Institut Polytechnique de Paris
[2]Laboratoire de Physique et Mécanique des Milieux Hétérogènes (PMMH), ESPCI Paris, Université PSL/Sorbonne Université/Université de Paris
*bielinski@ladhyx.polytechnique.fr

Flowing suspensions of particles in structured media are encountered in many biological and industrial systems. The motion of the particles results from the complex interplay between the surrounding flow, internal elastic forces, as well as hydrodynamic and steric interactions with obstacles. In this work, we study numerically and experimentally the dynamics of flexible and rigid fibers interacting with triangular pillars in a microfluidic channel. Long and rigid fibers are found to be laterally shifted by the obstacles while short and flexible fibers tend to remain on their initial streamline with no visible deviation. In the rigid case, we identify four types of dynamics (see Fig. 1) depending on the initial position and angle of the fibers with respect to the pillar. We also show that the dimensions of the channel strongly affect the flow field around the pillars, and therefore the fiber motion. We finally suggest how these findings could be used to optimize a microfluidic device to sort fibers by length and/or deformability.

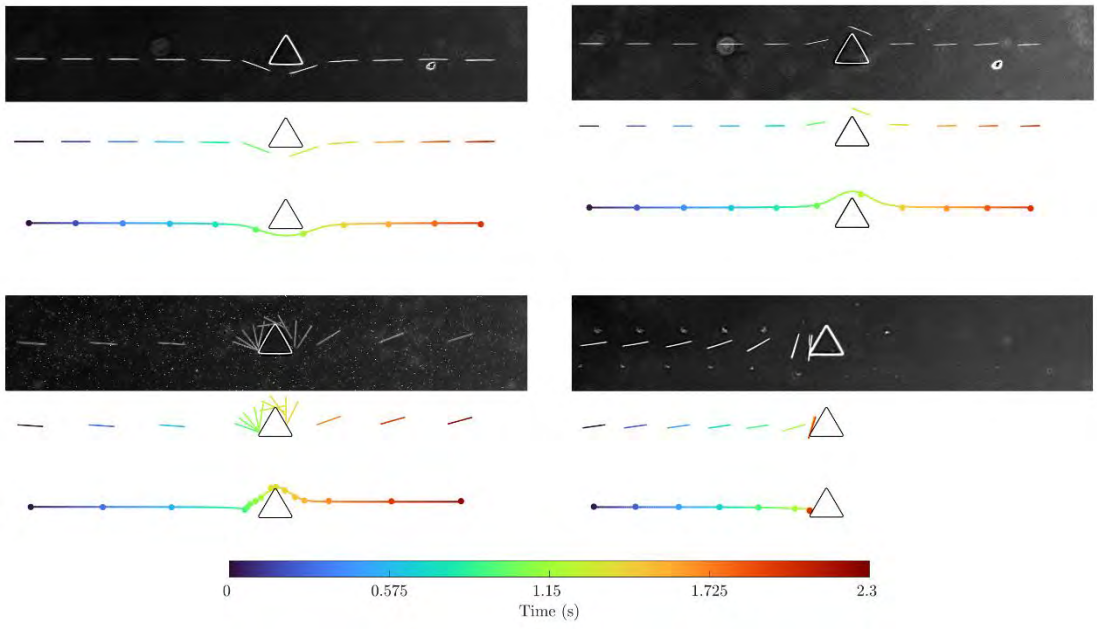


Figure 1: The four fiber dynamics observed experimentally and recovered by numerical simulations. The first two rows show chronophotographs from the experiments and simulations. The third row represents the experimental (dots) and numerical (solid line) trajectories.

Lubrication and flow of microgels in a square constriction

C. P. Moore[1,2]*, H. Belkadi[1,2], B. Safi[1], G. Amselem[1], C. N. Baroud[1,2]

[1]LADHYX, Ecole Polytechnique, Institut Polytechnique de Paris, Paris France
[2]Physical Microfluidics and Bioengineering Group, Institut Pasteur, Paris France
*cpmoore@ualberta.ca

Cells and microfluidic particles are often forced to pass through narrow constriction in both laboratory and natural environments. In passing through narrow constriction, these particles are forced to deform in order to fit, causing a change in the pressure drop across the particle, and a change in the particle velocity. This interaction is further complicated in microfluidic applications where approximately spherical particles are forced through rectangular channels, breaking axisymmetry.

To understand the pressure-velocity relationship of particles passing through constricting channels, we flow spherical polyethylene-glycol microgels through a square microfluidic comparator[1]. The added pressure necessary to transport the microgels is measured by the deflection of the ink line in the bypass channel, as illustrated in Fig. 1a. The speed of the microgels follows closely that of the surrounding fluid. Meanwhile, the added resistance of the microgels is found to be weakly dependent upon the size and thus constriction of the microgels, as well as their elasticity.

In order to understand the coupling of microgel velocity, pressure drop, and fluid velocity, analysis was separated into a gutter and a lubrication domain. To aid in this analysis, contact simulations were used to estimate the microgel deformation under confinement. Using a combination of simulation, shown in Fig. 1b, and experimental data, flow through the gutters links the microgel velocity and pressure drop with the overall fluid velocity. Meanwhile, flow in the lubrication domain is modeled as an elasto-hydrodynamic lubrication interaction, where solid deformation of the microgel is coupled with pressure in the thin fluid layer between the microgel and channel wall, as illustrated in Fig. 1c. Scaling analysis, in combination with experimental data, shows the lubricating friction to be a function of the microgel shear and the contact force deforming the microgels.

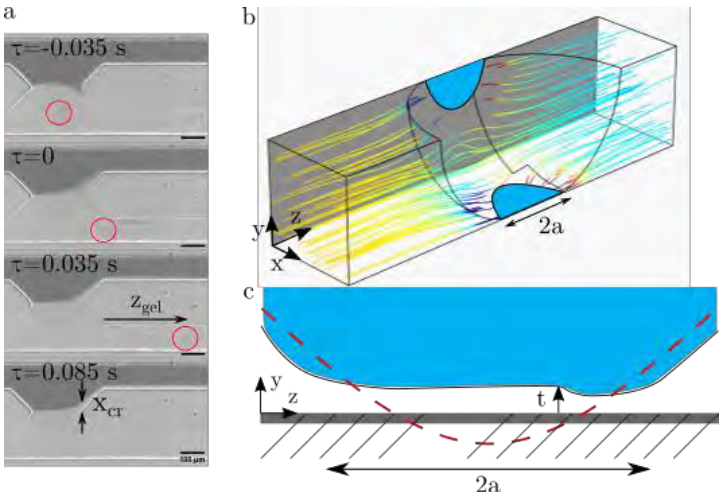


Figure 1: (a) The passage of a microgel, highlighted in red, through the microfluidic comparator over time, τ. Microgel position, z_{gel} and pressure induced flow deflection, x_{cr}, are highlighted. Scale bar 100 µm. (b) Simulated Couette-Poiseuille flow through the gutter domain. The lubrication domain is highlighted in blue, with a radius of a. (c) A diagram of the lubrication domain, of thickness t, due to elasto-hydrodynamic coupling of fluid pressure and microgel deformation.

References

[1] S.A. Vanapalli, A.G. Banpurkar, D. van den Ende, M.G.H. Duits, F. Mugele: *Hydrodynamic resistance of single confined moving drops in rectangular microchannels*. Lab on a Chip **9:7**, 982-990 (2009)

Acoustically activated shell-based micro swimmers

A. FEASSON[1]*, B. van ELBURG[2], M.VERSLUIS[2], T.SEGERS[2], E. BOSSY[1], C. QUILLIET[1], G. COUPIER[1]

[1]LIPhy, Grenoble, France
[2]University of Twente, Enschede, The Netherlands
*andrea.feasson@univ-grenoble-alpes.fr

Ultrasound contrast agents (UCAs) are coated microbubbles that are used in medicine in echographies to enhance the contrast of, for example, blood vessels. Due to their tie to medicine, a lot of research has been done to understand and model their interaction with ultrasounds [1]. Those UCAs have been proven recently to swim when submitted to a slow cycle of pressure (1 Hz), via buckling instability [2,3]. It is a new mode of propulsion based on a deformation mechanism that breaks the reversible symmetry in time, necessary to be able to move at the micrometric size. To increase the speed of the swimming, one of the parameters to play with is the frequency of the pressure wave. That is why we use a low-frequency ultrasound transducer, around a dozen of kHz, inside an aquarium to excite UCAs that flow inside a glass capillary. The imaging is done with an echographic probe thanks to their echogenicity. The presentation will be about what is observed under low-frequency ultrasound in terms of propulsion via buckling instability.

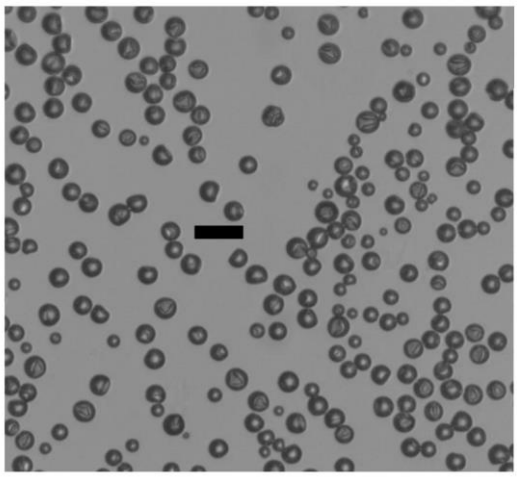


Figure 1: Zoology of shapes of UCAs after buckling. The scale bar represents 6 µm [2].

References

[1] M.Versluis, E.Stride, G.Lajoinie, B.Dollet, T.Segers.*Ultrasound contrast agent modeling: a review*. Ultrasound in medicine & biology, **46**(9), 2117-2144 (2020).

[2] G.Chabouh: *Ultrasound contrast agents: from spherical oscillations and buckling dynamics to swimming*. Thèse de doctorat. Université Grenoble Alpes (2022)

[3] A.Djellouli, P.Marmottant, H.Djeridi, C.Quilliet, G.Coupier. *Buckling instability causes inertial thrust for spherical swimmers at all scales.* Physical review letters, **119**(22), 224501 (2017).

Development of a microfluidic device for the analysis of nuclear samples

M. Boudias[1*], E. Dupuis[1], S. Mialle[1], A. Quémet[2], C. Bresson[1]

[1]Université Paris-Saclay, CEA, Service d'Études Analytiques et de Réactivité des Surfaces, Gif-sur-Yvette, France
[2]CEA, DES, ISEC, DMRC, Univ Montpellier, Marcoule, France
[*]marine.boudias@cea.fr

The miniaturization and integration of analytical tools in microfluidic devices, in the form of labs-on-chip or micro total analysis systems (μ-TAS), currently offer several advantages: the opportunity to analyze rare samples with limited quantities available, to better control parameters that influence reactions, and to develop portable systems for on-site analyses. In the nuclear field, an additional advantage consists in reducing the volume of samples to handle and the corresponding doses, the amount of reagents, as well as the amount of produced waste and the necessary costs for their specific management. Indeed, in order to characterize the elemental and isotopic composition of samples for the management of effluents from nuclear facilities, of those resulting from processing steps or of spent fuels, various purification steps by solid phase extraction are necessary, upstream of mass spectrometry measurements (ICP-MS, TIMS). While there are established protocols to perform radionuclides separation such as U and Pu from commercial resins (e.g. UTEVA™, TBP™, TRU™), those are time-consuming and require large volumes of resins and eluents. This work aims to develop a separative microsystem including a monolithic support in order to reduce the scale of nuclear samples purification protocols.

First, different materials (e.g. glass, thermoplastics) for the microsystem conception were evaluated in order to find the best compromise in relation to the targeted application. These were compared in terms of resistance to concentrated acids which are associated with the sample matrices and the radiochemical separation conditions; in terms of ease and repeatability of monolith anchoring process in the microsystem channels; and of cost and ease of shaping. To date, most monoliths described in literature are synthesized and anchored in silica capillaries or glass chips, materials that are easily functionalized unlike thermoplastic polymers such as cyclic olefin copolymer (COC) or polytetrafluoroethylene (PTFE), which are known to be chemically inert but easily shaped. Organic monoliths bearing phosphate monomers with a good affinity for actinides have been synthesized by photopolymerization in commercial microsystem channels or internally fabricated by micromilling. Particular attention was paid to limit diffusion effects during monoliths synthesis.

The different functionalized microsystems were characterized in terms of morphology and permeability before developing their coupling with an Inductively Coupled Plasma Mass Spectrometer (ICP-MS). Dedicated quantification methods have been developed to determine on-line their selectivity towards simulants (U, Th, and Eu as simulants for radionuclides U, Pu, and Am) in different media as well as their loading capacity. The development of these different steps in a conventional laboratory is essential to validate the downscaling of the separation protocol before applying it to the purification of radioactive samples, requiring a transposition in a glove box in a controlled area.

Coupled transport mechanisms to harvest energy from thermal waste

A. Allemand[1]*, A.-L. Biance[1], L. Joly[1], C. Ybert[1]

[1]University Claude Bernard Lyon 1, CNRS, Institut Lumière Matière (ILM), F-69622, Villeurbanne, France
*aymeric.allemand@univ-lyon1.fr

Nanofluidics describe ionic and fluidic transports at the nanoscale where interfacial interactions are dominating **Erreur ! Source du renvoi introuvable.**. It occurs in numerous natural processes, such as protein and ion transports through membrane nanopores in a cell, water imbibition in the soil or in designed membranes for desalination, filtration and water resource management [2]. In the last decades, a technical effort has been made to develop such membranes and to reach systems with a confinement reaching the angstrom scale [4]. However, it is crucial to understand these nanofluidic transports.

Numerous theoretical, numerical and experimental studies have been carried out. In the framework of hydrodynamics and electrostatics, electrokinetic effects, i.e. fluidic and ionic transports induced by actuations such as electric potential, solute concentration or pressure gradients are now well-known and have reached a good agreement with experimental studies [1]. Even though a description of thermal transports exists [5], coupled thermal transports are not fully understood and a theoretical description is missing. In this research, we study direct and coupled transports driven by pressure, solute concentration, voltage and temperature gradients. We use out-of-equilibrium thermodynamics to theoretically describe a nanochannel based on the linear theory of Onsager [6].To confirm our theoretical results, finite element simulations have been carried out thanks to *Comsol Multiphysics* software. This allows us to describe this multi-scale system ranging from a few tens of nanometers down to the angstrom scale to fully describe the so-called electrical double layer [7].

Preliminary work has been developed to study a first asymmetrical system: a conical channel. An induced differential heating is set thanks to Joule effect (see figure 1) and the competition between flows induced by an electric field and this induced thermal gradient is studied. This theoretical framework and preliminary work pave the route to study other fluxes competition in order to develop

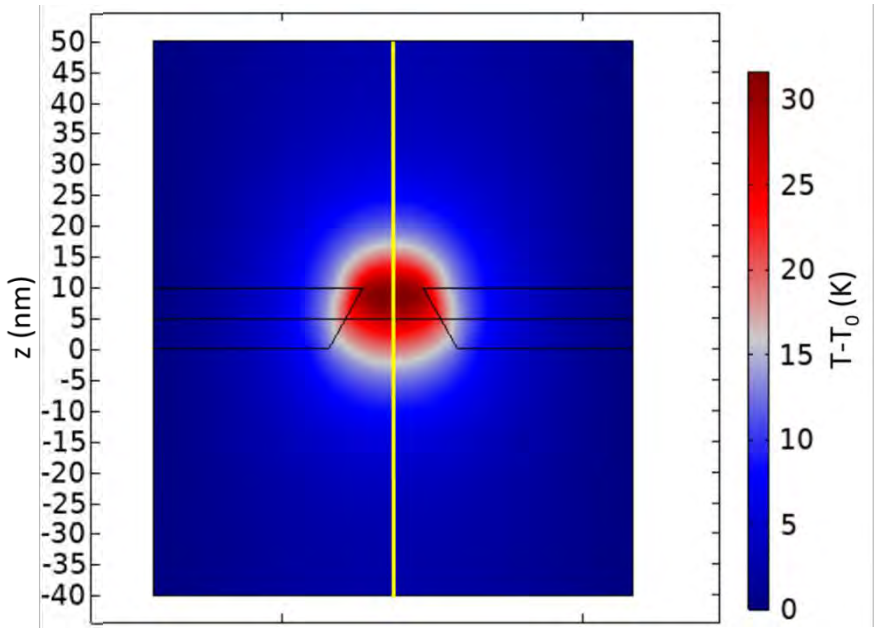


Figure 1 : Temperature map of a conical nanochannel for a HI solution at 1mol/L

new nanofluidic device to harvest energy from thermal waste.

References

[1] L. Bocquet, E. Charlaix: *Nanofluidics, from bulk to interfaces*. Chemical Society Reviews, 39(3), 1073–1095 (2010)

[2] L. Bocquet: *Nanofluidics coming of age*. Nature Materials, **19**, 254–256 (2020)

[3] N. Kavokine, R. R. Netz, L. Bocquet: *Fluids at the Nanoscale: From Continuum to Subcontinuum Transport*. Annual Review of Fluid Mechanics, **53**, 377–410 (2021)

[4] C. Duan, W. Wang, Q. Xie: *Review article: Fabrication of nanofluidic devices*. Biomicrofluidics **7**, 026501 (2013)

[5] A. Würger: *Thermal non-equilibrium transport in colloids*. Reports on Progress in Physics, **73**, 12 (2010)

[6] S.R. De Groot, P. Mazur: *Non-equilibrium thermodynamics*, Courier Corporation (2013)

[7] J Lyklema: *Fundamentals of Interface and Colloid Science: Solid/Liquid Interfaces*. Academic press, **Vol II** (1995)

Facile bacterial encapsulation for digital antimicrobial susceptibility testing of colistin

Justine Riti[1]*, Guillaume Sutra[2], Hervé Volland[1], Stéphanie Simon[1], Karla Perez-Toralla[1]

[1]CEA Saclay, Joliot Institute, Medicine and technology for health department
[2]CEA Saclay, Institute of applied sciences and simulation, System and structures modeling department
*justine.riti@cea.fr

Antibiotic resistance (ABR) is a big threat to global healthcare today and there is an increasing need for efficient tools for the rapid antibiotic susceptibility testing (AST). Particularly, bacteria that are resistant to both carbepenem and colistin have been identified [1]. These strains lead to therapeutic failure as these antibiotics are often referred to as last resort antibiotics [2]. Digital microfluidics offer several advantages over conventional, population-based methods in microbiology (resolution, quantification, automation, rapidity). However, with conventional methods, droplet characteristics (size, frequence) are highly dependent of flow rates of both phases. Gradient of confinement allows creating monodisperse emulsions with little influence of flow rates, simplifying device operation and use in L2 biosafety laboratories [3].

Here, we developed a simple microfluidic platform, using a gradient of confinement method to encapsulate and grow 5 clinical isolates (*E. coli* and *K. pneumoniae*) in 1.4 nL monodisperse droplets in multiple storage chambers simultaneously (~3000 droplets/chamber). Bacterial solutions were supplemented with colistin to reach 0, 1, 2 and 4 µg/mL framing the minimum inhibitory concentration breakpoint prior to on-chip encapsulation (Figure 1). We implemented a machine learning algorithm for the automated analysis of bright-field images of individual droplets to detect bacterial growth and evaluate the cytotoxicity of antibiotics.

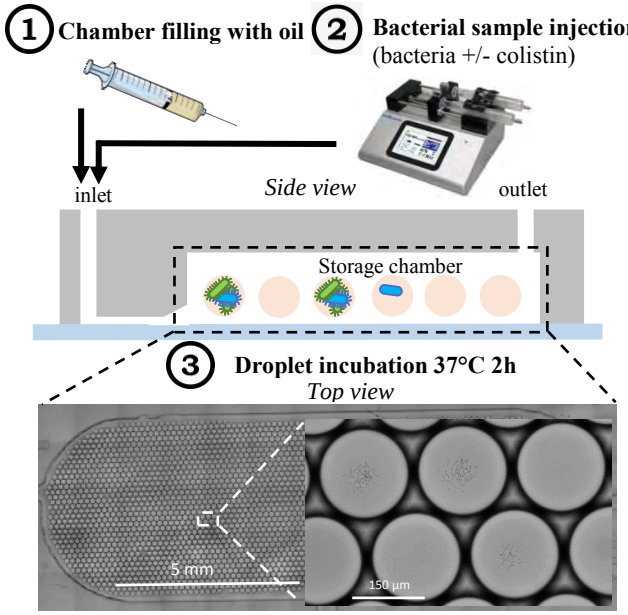


Figure 1: Workflow for antimicrobial susceptibility testing of colistin on chip

Thanks to this technique we detected bacterial growth after 2 hours, shortening the response time by 10-fold as compared to standard Broth Microdilution method (BMD). Among the 5 tested strains, 2 were susceptible, and 3 resistant, in agreement with the BMD reference method. We measured the occupation ratio (% droplets containing bacteria over the total droplet population), obtained when using different initial concentrations of bacteria, showing a complete agreement with the predicted values.

To conclude, we developed a microfluidic-based method for susceptibility testing to colistin in 2h, regardless of the resistance mechanism involved. Our results were in agreement with the reference method for AST and showed that this phenotypic digital test is accurate and rapid. Future work will be focused on testing a larger panel of susceptible and resistant strains and the use of infected biological fluids to validate the method further.

References

[1] Osei Sekyere J. : *Current State of Resistance to Antibiotics of Last-Resort in South Africa: A Review from a Public Health Perspective*. Front Public Health **4**, 209 (2016).

[2] Andrew P. Norgan, Jarred M. Freese, Patricia M. Tuin, Scott A. Cunningham, Patricio R. Jeraldo, Robin Patel: *Carbapenem- and Colistin-Resistant Enterobacter cloacae from Delta, Colorado, in 2015*, Antimicrobial Agents and Chemotherapy **60**, 5,3141-3144 (2016).

[3] Dangla, R.; Kayi, S. C.; Baroud, C. N: *Droplet microfluidics driven by gradients of confinement*. Proc. Natl. Acad. Sci. U. S. A., **110**, 853– 858 (2013).

Tortuosity-governed droplet transport in a microfluidic porous network

E. SPEIRS[1,2]*, N. PANNACCI[2], M.C. JULLIEN[1], M. MOREAUD[3]

[1]IPR - Institut de Physique de Rennes, 263 Avenue Général Leclerc, 35700 Rennes, France
[2]IFP Energies nouvelles, 1-4 avenue de Bois-Préau, 92500 Rueil-Malmaison, France
[3]IFP Energies nouvelles, Rond-point de l'échangeur de Solaize BP3, 69360 Solaize, France
*elliot.speirs@ifpen.fr

Multiphase flow in porous media is widely studied and impacts countless applications in many natural and industrial processes, such as geologic CO2 sequestration, water infiltration into soil, and particle filtration. However, many questions remain, particularly with regard to the effect of the confinement and the geometry of the porous medium on the transport of dispersions.

We address these issues experimentally using controlled porous media: micromodels. We designed polydimethylsiloxane (PDMS) micromodels consisting of regular networks of vertical cylindrical posts, at the centres of which we injected water droplets in a continuous oil phase. A priori, no preferential paths are expected, except in a stochastic manner. However, we show that the radial alignment of the posts, i.e., the geometric tortuosity of the network, varies angularly in a periodic manner and plays a key role in droplet transport by generating reproducible preferential paths. By systematically varying the geometrical configuration of the posts, injection capillary number, droplet size, and droplet concentration, we characterise the droplet transport and the conditions for droplet breakup. At low capillary numbers, radial droplet transport is homogeneous. By increasing the capillary number, droplets initially follow the least tortuous paths before transitioning to a stable flow regime whereby droplets flow primarily in the most tortuous paths. Through large-scale droplet tracking, we demonstrate the influence of the geometric tortuosity of the media on the resulting droplet flow patterns and the counter-intuitive responses that can arise. Through this analysis, we emphasise the role of local geometrical configuration and propose a new metric for droplet transport which is the tortuosity of the porous media.

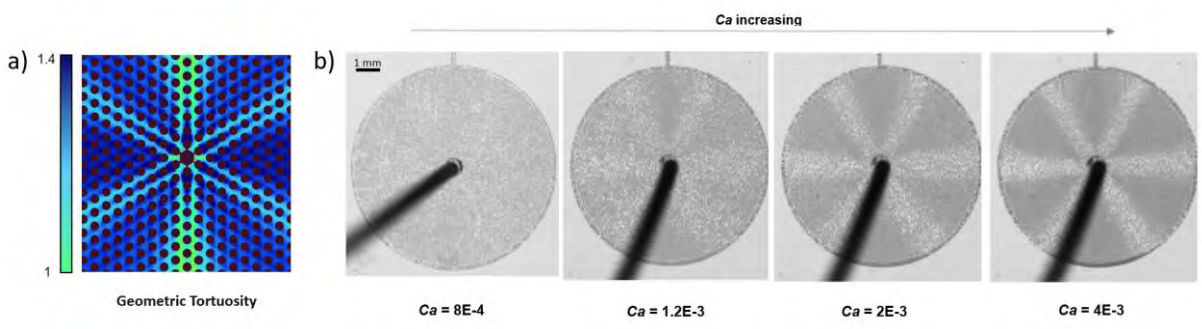


Figure 1. (a) Map of the geometric tortuosity of the porous network at all points from the central injection point. The porous network consists of a regular lattice of cylindrical posts of diameter 50 µm. (b) Radial droplet transport for different injection capillary numbers. The droplets consist of water and blue methylene (grey) and are transported in a continuous phase of mineral oil and SPAN 80 (1 wt% ≈ 60 x CMC).

Microfluidic devices for studying swimming plant pathogens interactions with their host root.

Céline Cohen[1], François-Xavier Gauci[1], Agnès Attard[2], Xavier Noblin[1], Eric Galiana[2], Philippe Thomen[1]

[1]Institut de Physique de Nice (INPHYNI), Université Côte d'Azur, CNRS UMR 7010, 06108 Nice.
[2]Institut Sophia Agriobiotech (ISA), UMR INRA 1355, Université Côte d'Azur, CNRS 7254, 06903 Sophia Antipolis.
*celine.cohen@unice.fr

Zoospores are flagellated spores, asexual and motile cells, produced by different organisms including oomycetes. Oomycetes of the genus *Phytophthora* are plant pathogens (e.g. potato blight). The zoospores of oomycetes are biflagellates and are able to swim in aqueous environments by using chemotaxis. Zoospores of some phytopathogenic *Phytophthora* species spontaneously aggregate within minutes in suspension.

We have developed different microfluidic devices to address the dynamics of aggregation of zoospore in response to a K^+ gradient [1] and the swimming hydrodynamics of this new type of micro-swimmers [2].

We now focus on the plant- pathogen interactions, in the first events of infection: attraction of the pathogen toward the host, adhesion, aggregation. To do this we use a new microfluidic device in which a root is introduced and grows in a channel where zoospores are swimming. We are developing a second type of device without root in which we impose a stationary gradient of a chemical species in order to characterize its attractive properties on the zoospores. In this talk, I will present our results, our recent achievements and perspectives.

Figure 1. Arabidopsis plant growing in a microfluidic chip.

References

[1] E. Galiana, C. Cohen, P. Thomen, C. Etienne, X. Noblin, *Guidance of zoospores by potassium gradient sensing mediates aggregation.*., Interface **16(157)** 20190367, 2019.

[2] Q.D. Tran, E. Galiana, P. Thomen,, C. Cohen, F. Orange, F. Peruani, X. Noblin, *Coordination of two opposite flagella allows high-speed swimming and active turning of individual zoospores*., Elife, **11**, e71227, 2022.

Flow instabilities in microvascular network

Gwennou Coupier[1]*, Thomas Podgorski[2], Nathan Karst[3], John Geddes[4]
[1]LIPhy, UGA & CNRS, Grenoble, France
[2]LRP, UGA & CNRS, Grenoble, France
[3]Babson College, Wellesley MA, USA
[4]Olin College, Needham MA, USA
*gwennou.coupier@univ-grenoble-alpes.fr

In the microcirculation, blood flows through a complex network of capillaries where the coupling between the local rheology and phase separation at bifurcations of the network is known for long to lead to strong *spatial heterogeneities* of the red blood cell distribution. This have been reported for the first time by Poiseuille, about 2 centuries ago [1].

More recently, theoretical predictions have revealed the possibility of *temporal heterogeneities* due to the existence of multiple solutions for the stationary equations and/or of oscillatory states for the distribution of particle concentrations and flow velocities in the different branches [2,3].

We confirmed recently that these multiple solutions are visible in simple experimental network. As shown in Fig 1, flow of red blood cells in geometrically symmetric network may exhibit asymmetric flow patterns. In this presentation, we will detail this symmetry breaking mechanism and discuss the different solutions for the flow and cell concentration distributions, with an emphasis on the agreement between experimental results and theoretical predictions.

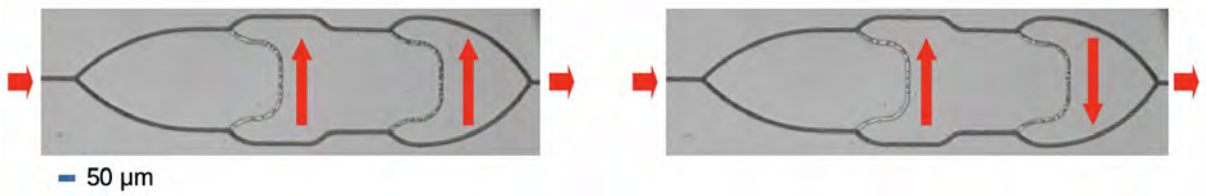


Figure 1: Different asymmetric flow patterns develop spontaneously in a symmetric network caption

References

[1] J.-M. Poiseuille, *Annales des Sciences Naturelles*, volume 5, Ed. Crochard, (1836)

[2] N. J. Karst et al., "*Oscillations and multiple equilibria in microvascular blood flow* " Bull. Math. Biol. **77**, 1377 (2015)

[3] N. J. Karst et al., "*Model Microvascular Networks Can Have Many Equilibria* ", Bull. Math. Biol. **79**, 1-20 (2017)

Abstracts of the posters

Session B (Tuesday, 04 of April)

Biomimetic leaf-on-a-chip to study embolism

F.X. Gauci[1]*, L. Keiser[1], C. Cohen[1], A. Vigna-Brummer[1], B. Dollet[2], P. Marmottant[2], X. Noblin[1]

[1] Université Côte d'Azur, CNRS UMR 7010, Institut de Physique de Nice (INPHYNI)
[2] Université Grenoble Alpes, CNRS UMR 5588, Laboratoire Interdisciplinaire de Physique (LIPHY)
*francois-xavier.gauci@univ-cotedazur.fr

Global warming will lead to increasingly severe droughts and threatens most of the forests across the globe [1]. One of the main dangers of droughts for trees comes from the generation of air embolism, which impairs the sap conduction and potentially leads to their death. In leaves, embolism has been shown spreading intermittently and exhibiting catastrophic events [2]. By using PDMS-based biomimetic leaves to reproduce evapo-transpiration, it has been shown for a linear geometry that the presence of narrow constrictions in the leaf veins enables to generate intermittent embolism propagation. This intermittency appears to originate from an elasto-capillary coupling between the air / water interfaces and the compliant structure of the biomimetic leaf venation [3]. We currently work on extending this study on more complex channels systems, closer to veins networks in real leaves. It includes ramifications with different orders of channels and multiple connections between them. I will present the work done on this subject and the various perspectives opened by the validation of this leaf-on-a-chip.

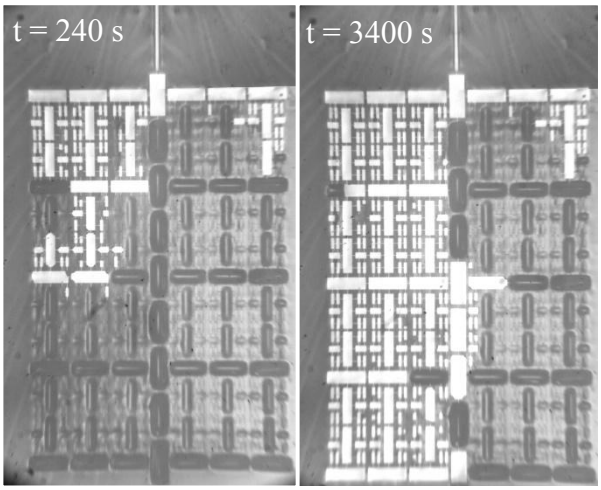


Figure 1: Embolism (bright part) spreading in an artificial venation network initially filled with water (dark part)

References

[1] Brodribb, T. J., Powers, J., Cochard, H., & Choat, B. *Hanging by a thread? Forests and drought.* Science, **368** (6488), 261-266 (2020).

[2] Brodribb, T. J., Bienaimé, D., & Marmottant, P. *Revealing catastrophic failure of leaf networks under stress.* Proceedings of the National Academy of Sciences, **113**(17), 4865-4869 (2016).

[3] Keiser, L., Marmottant, P., & Dollet, B. *Intermittent air invasion in pervaporating compliant microchannels.* Journal of Fluid Mechanics, **948**, A52 (2022)

Development of geoelectrical monitoring on microfluidic chips for reactive transport and multi-phase flow characterization in the shallow subsurface

F. Rembert[12]*, S. Roman[1], A. Stolz[2], C. Soulaine[1]

[1]Univ. Orléans, CNRS, BRGM, ISTO, UMR7327, FR-45071, Orléans, France
[2] Univ. Orléans, CNRS, GREMI, UMR7344, FR-45067, Orléans, France
*flore.rembert@univ-orleans.fr

Ensuring sustainable water resources and soil pollution management strategies requires a better understanding of the underlying microscopic mechanisms in the porous rock matrix, as well as the development of detection methods. Among the various geophysical tools, geoelectric methods have already demonstrated their ability to monitor the hydrological and biogeochemical processes of the shallow subsurface in a non-intrusive and cost-effective manner [1, 2]. However, the interpretation of geoelectrical signals is often approximate as it is based on superimposed microscopic source mechanisms (e.g. ion concentration gradients, surface charge, fluid-mineral interfaces, pore-clogging). This work proposes to miniaturize the geoelectrical acquisition for microfluidic experiments coupled with high-resolution imaging, offering, for the first time, precise control and direct visualization of the microscale processes. We address the dissolution of a calcite mineral, a geochemical reaction implying reactive transport and multi-phase flow [3]. The geoelectrical monitoring shows clear correlations associated with the gas phase production, the area of the reactive surface, and the surface roughness [4]. This study has proven the feasibility of geoelectrical monitoring at the microscale, thus paving the way for further investigations of subsurface processes.

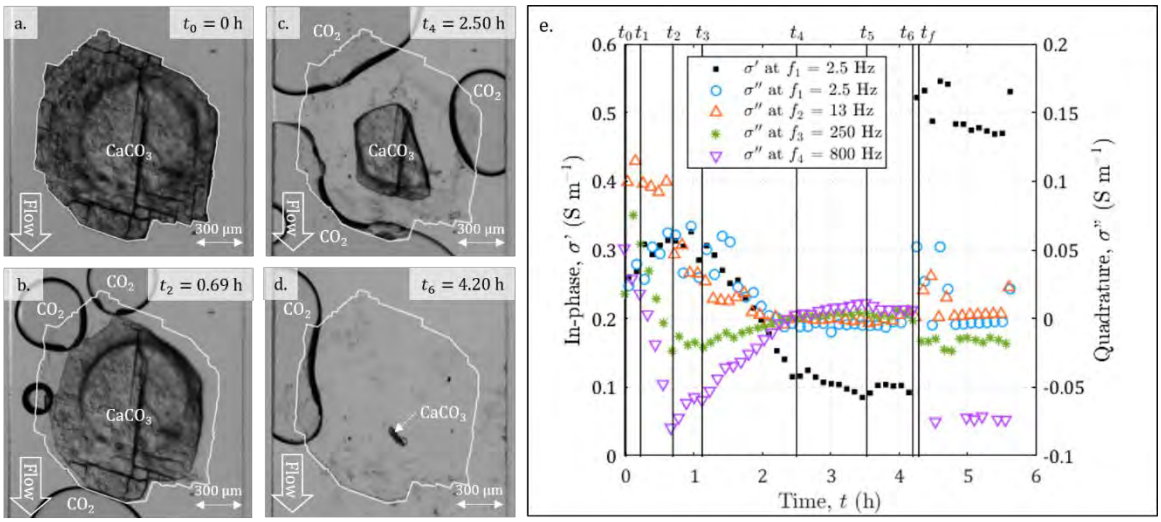


Figure 1: (a–d) images from the image series acquisition with ×5 magnification for four times of interest. The channel walls are visible as vertical lines on the left and right sides of each image. The flow of acid solution is vertical from top to bottom for each image. (e) Time evolution of the electrical signal components during the dissolution of calcite at various frequencies. The vertical black lines correspond to times of interest.

References

[1] F. Rembert, D. Jougnot, L. Luquot, R. Guérin: *Interpreting self-potential signal during reactive transport: application to calcite dissolution and precipitation.* Water **14**, 1632 (2022)

[2] F. Rembert, M. Léger, D. Jougnot, L. Luquot: *Geoelectrical and hydro-chemical monitoring of karst formation at the laboratory scale*, EGUsphere (accepted)

[3] C. Soulaine, S. Roman, A. Kovscek, H.A. Tchelepi: *Pore-scale modelling of multiphase reactive flow: application to mineral dissolution with production of CO2*. Journal of Fluid Mechanics **855**, 616–645 (2018)

[4] F. Rembert, A. Stolz, C. Soulaine, S. Roman: *A microfluidic chip equipped for geoelectrical monitoring of the critical zone processes.* Lab on a Chip (submitted)

Dynamic monitoring of cytokine-secreting immune cells at the single-cell level using droplet-based microfluidics

Lucie Descamps[1,2*], **Bart Tiemeijer**[1,2], **Nikita Subedi**[1,2], **Jurjen Tel**[1,2]

[1] Laboratory of Immunoengineering, Dept. Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands.
[2] Institute for Complex Molecular Systems (ICMS), Eindhoven University of Technology, Eindhoven, Netherlands.
*l.descamps@tue.nl

Our immune system comprises a complex network of distinct cell subsets that orchestrate protection against potential threats. Cytotoxic T cells (CTLs) exhibit stronger effector functions to recognize and kill infected and mutant cells than other reported immune cells. However, it has been shown that CTL responses and disease control rely on the quality of these cells rather than on their quantity [1]. CTLs of interest can be selected based on the secreted cytokines, which play crucial roles across the biological spectrum, from cell survival to migration and killing. In order to identify cytokine-secreting CTLs playing a key role in anti-viral and anti-tumor activities, we developed a droplet-based microfluidic platform, combined with an immunoassay detection technology, to achieve real-time and quantitative cytokine profiling in individual immune cells. Single CTLs are encapsulated in 70-pL droplets together with assay reagents, including functionalized magnetic nanoparticles, fluorescent probes, and stimuli (Figure 1-A). The generated droplets, acting as bioreactors, are further loaded into a custom-made observation chamber (glass slide format) for timelapse imaging in a magnetic field (Figure 1-B). Under the application of a magnetic field, the magnetic nanoparticles align to form a beadline in the center of the droplets [2]. The magnetic nanoparticles were functionalized with capture antibodies targeting IFN-α, IFN-γ, and IL-2 cytokines to perform concurrent detection in plasmacytoid dendritic cells (pDCs) and CTLs. Upon cell activation, cytokines are captured on the antibody-coated beadline and further detected through the binding of the freely floating detection antibody to the captured cytokines (Figure 1-C). The relocation of this fluorescently labeled detection antibody, depicted by a fluorescent beadline, was monitored in real-time to study the secretion kinetics in individual cells (Figure 1-C) and analyzed using a custom-made Matlab script. A critical step of this detection is the activation of immune cells. CTLs were stimulated by soluble stimuli or specific antibodies to study heterogeneity in cytokine secretions among individual cells, or by pDCs via cell pairing for cellular communication study.

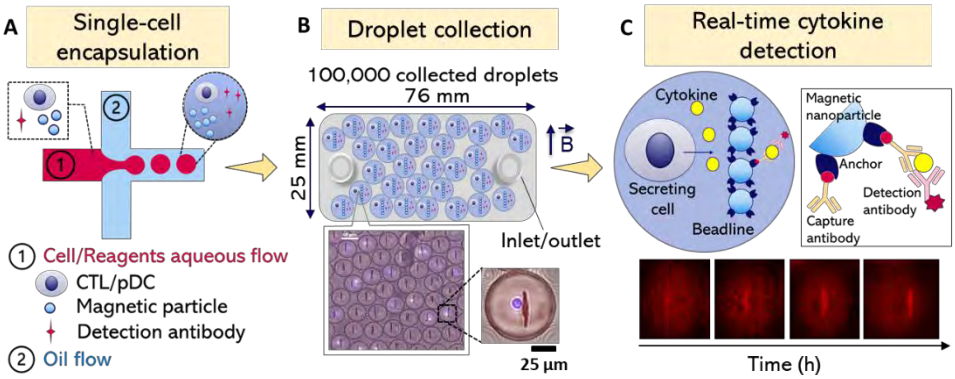


Figure 1: Droplet microfluidic platform for the dynamic detection of secreted cytokines in single cells. **A.** Encapsulation of single cells along with assay reagents. **B.** Collection of droplets in a chamber. Inset of a compact array of single-cell containing droplets. **C.** Illustration of the beadline for the dynamic detection of secretions (e.g. IFN-γ secretion). IFN-γ secretion is depicted by a bright red line in fluorescent images.

References

[1] F. Wimmers, E. H. J. G. Aarntzen, T. Duiveman-deBoer, et al. *Long-lasting multifunctional CD8+T cell responses in end-stage melanoma patients can be induced by dendritic cell vaccination*. Oncoimmunology **5**, e1067745 (2015).

A microfluidics-assisted photopolymerization method for high-resolution multimaterial 3D printing

V. Fournié[a,c*], B. Venzac[a], E. Trevisiol[b], J. Foncy[a], J. Roul[a], S. Assie-Souleille[a], M. Escudero[d], P. Joseph[a], A. Reitz[c], L. Malaquin[a]

[a] Laboratoire d'analyse et d'architecture des systèmes-CNRS, Toulouse, France
[b] Toulouse Biotechnology Institute-INSA-CNRS, Toulouse, France
[c] Fluigent SA , Kremlin-bicètre, France
[d] RESTORE Research Center, Toulouse, France
[*]vfournie@laas.fr

3D printing and bioprinting are recognized as key technologies for the construction of complex micro-devices, micro-environments, and culture models [1]. Nevertheless, combining multimaterial and high-resolution printing is still a major challenge, and the available technologies do not provide simultaneously the resolution and multiplexing capabilities required to create heterogeneous 3D environments [2]. In this work, we introduce the 3D-FlowPrint concept, which involves an opto-microfluidic printhead immersed in a liquid and moved above a surface. This technology combines the convenience of microfluidics in terms of the handling and delivery of small volumes of materials with the resolution provided by laser lithography. Delivered materials are hydrodynamically confined under the printhead owing to controlled aspiration of the injected material, ensuring a continuous supply of material and avoiding cross-contamination issues. Combining microfluidics with photo-polymerization provides unique advantages as it separates the polymerization process from the material delivery, permitting high-resolution polymerization (down to 10 µm) and multimaterial handling (switching time below 60 s). We worked with poly(ethylene glycol) diacrylate hydrogels as proof-of-concept materials and investigated the influence of exposure parameters, printhead velocity, and hydrodynamic parameters on the fabrication of 2D and 3D heterogeneous structures. 3D-FlowPrint allows the creation of sub-millimetric to millimetric scale objects with multimaterial designs. A validation was performed to show the potential of the approach in biology for the creation of engineered microenvironments for cell culture.

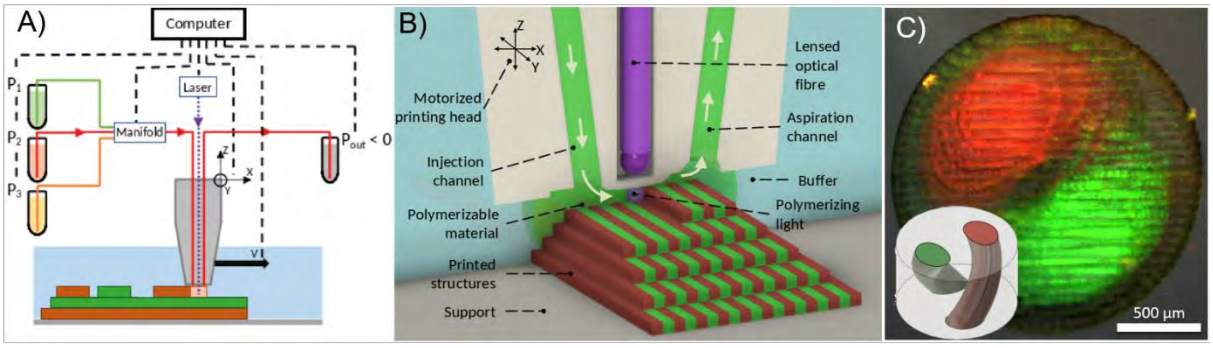


Figure 1: 3D illustration of the 3D-FlowPrint concept. (A) Planar schematics showing the setup of the instrument, including a library of materials connected to a manifold, a positive pressure controller, a printhead integrating an optical fiber and a negative pressure controller. The printhead operates in immersion with controlled XYZ motion. (B) Schematic of the opto-fluidic processes with a XZ cross section of the head. (C) Double helicoidal structure made from three PEGDA solutions (with 300-nm mCherry particles, 200-nm GFP particles, and no nanoparticles), h = 500 µm. Image in the lower left corner shows a CAD image and the lower right corner shows an SEM image of the printed structure.

References

[1] A. C. Daly, M. E. Prendergast, A. J. Hughes, et J. A. Burdick: *Bioprinting for the Biologist* , Cell **184**, 18-32 (2021)

[2] H. Ravanbakhsh, V. Karamzadeh, G. Bao, L. Mongeau, D. Juncker, et Y. S. Zhang: *Emerging Technologies in Multi-Material Bioprinting*, Advanced Materials **33**, 2104730 (2021)

Bio-sourced polymer for the elaboration of lab-on-a-chip

M. Zimmer[1]*, A.-L. Deman-Him[1], S. Trombotto[2], E. Laurenceau[1]

[1] Univ Lyon, Ecole Centrale de Lyon, Université Claude Bernard Lyon 1, CNRS, INSA Lyon, CPE Lyon, INL, UMR5270, 69130 Ecully (France)
[2] Université De Lyon, UCBL, CNRS, IMP UMR5223, 69622 Villeurbanne (France)
*morgane.zimmer@ec-lyon.fr

Lab-on-a-chip (LoC) seek to miniaturize conventional methods used in laboratories, which enables experiments at the scale of a single cell and in a controlled environment. These properties open up promising prospects for biomedical applications. However, in the biomedical field, the LoC must be single-use to avoid cross-contamination. Considering that the main polymers used to fabricate LoC, PDMS or thermoplastics, are derived from the petrochemical industry, their impact on the environment is an issue. [1] Thus, we aim to develop a sustainable manufacturing chain for fluidic microsystems by introducing a bio-sourced material to replace the usual polymers.

Among the possible candidates, chitosan is a very abundant polysaccharide resulting from the valorization of waste from the seafood industry. Moreover, it presents many interesting physico-chemical and biological properties: it is film-forming, non-toxic, biodegradable, biocompatible and antimicrobial. [2]

In this study, we developed a fabrication protocol (Fig 1-a) to produce chitosan films with a few millimeters thickness, transparent and rigid. Micro-channels of 105 to 1000 µm width were successfully engraved (Fig 1-b). Besides the filmification, a step of neutralization is necessary to reduce the water uptake of chitosan films (Fig 1-d). After bounding to a glass slide, a colored aqueous solution was injected into the micro-structured films and no leaking of the microfluidic system was observed (Fig 1-c). This study paves the way for the fabrication of eco-responsible LoC offering more complex functions.

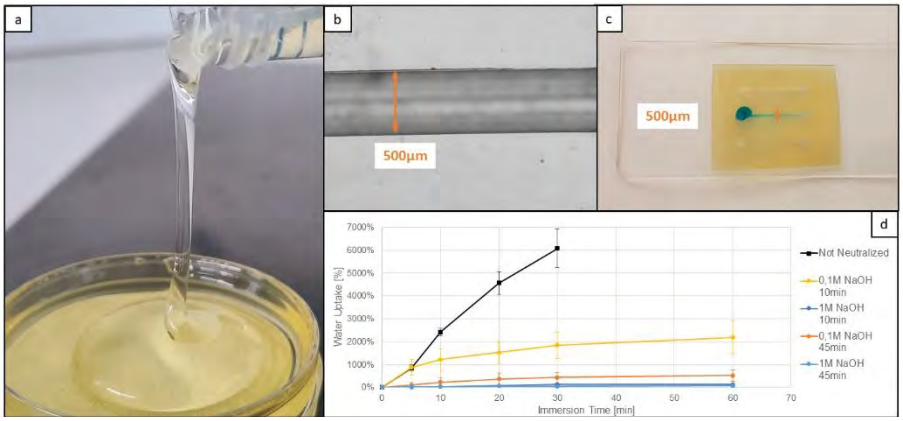


Figure 1: Pictures of chitosan film preparation: (a) Pouring of chitosan solution into a petri dish with a cellulose filter, (b) Engraved channel of 500µm width on optical microscope, (c) Bounded chitosan film on glass slide with engraved microchannels of 250, 500 and 1000µm, (d) Water uptake in function of immersion time in purified water of chitosan films with different neutralizations.

References

[1] A. E. Ongaro et al.: *Engineering as sustainable future for point-of-care diagnostics and single-use microfluidic devices.* Lab on a Chip **22**, 3122-3137 (2022)

[2] J. Fernandez: *Bioinspired chitinous material solutions for environmental sustainability and medicine.* Advanced Functional Materials **23**, 4454-4466 (2013)

Characterisation of artificial polymers translocating through nanopores

Charlotte de Blois[1,2]*, Arnaud Favier[2], Fabien Montel[1]

[1]Laboratoire de Physique, Université Claude Bernard, ENS de Lyon, Université de Lyon, France
[2]INSA-Lyon, Laboratoire Ingénierie des Matériaux Polymères, Villeurbanne, France
*charlotte.de-blois-de-la-calande@ens-lyon.fr

The translocation of (bio)polymers through pores smaller than their size occurs in various biological and technological process, such the extra-nuclear transport of messenger RNA, or the filtering of polymer solutions. The flow-driven injection of fluorescent labelled (bio)polymers can be visualized at the level of single molecule using a near-field optical technique (Zero Mode Wave Guide for nanopore) at the entrance or at the exit of a nanopore. It has been shown experimentally that the passage of DNA molecule is controlled by an energy barrier [1]. As proposed in the de Gennes–Brochard suction model [2], this energy barrier depends only on the pore size, the temperature and the viscosity of the surrounding fluid, but not on the structure of the (bio)polymer itself. However, the size and shape of the translocating object should affect the optical measured signal (duration, intensity, shape). With this idea, we synthetize block copolymer labelled with fluorophore, and using image processing analysis, we characterize the translocation signal of a polymer and corroborate it with its structure.

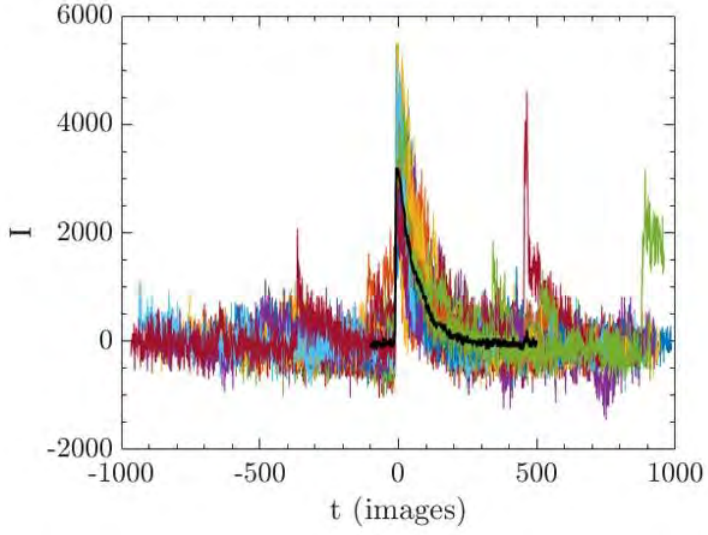


Figure 1: Optical detection of the translocation of polymers through nanopores. The black line corresponds to the average of all signals.

References

[1] T. Auger, J. Mathé, V. Viasnoff, G. Charron, J.-M. Di Meglio, L. Auvray, F. Montel, *Zero-Mode Waveguide Detection of Flow-Driven DNA Translocation through Nanopores*. Phys. Rev. Lett. **113**, 028302 (2014).

[2] L. Béguin, B. Grassl, F. Brochard-Wyart, M. Rakib, H. Duval, *Suction of hydrosoluble polymers into nanopores*. Soft Matter. **7**, 96–103 (2011).

First steps towards a glomerular filtration barrier-on-chip

Manon Miran[1,2,3]*, A. Miche[1], S. Boujday[1], K. Ngo[1], F. Soncin[4] and G. Perry[2,3]

[1]LRS, Sorbonne Université, CNRS, Campus Pierre et Marie Curie, F-75005
[2]CoRaKiD, Sorbonne Université, INSERM, Hopital Tenon, F-75020
[3]GeePs, Sorbonne Université, CNRS, Université Paris Saclay, CentraleSupelec, Campus Pierre et Marie Curie, F-75005
[4]SMMIL-E, Université de Tokyo, Université de Lille, CNRS, Oncolille, F-59000
*manon.miran@sorbonne-universite.fr

Chronic kidney diseases are a major public health issue due to their debilitating effects on the patients and the high cost of the treatments in advanced stages of the disease. They affect more than 10% of the world's population and this number increases each year. Therefore, it is crucial to study those diseases to have a better understanding of their mechanisms in order to improve the daily life of the patients.

The objective of this interdisciplinary project is the development of an innovative microfluidic glomerular filtration barrier-on-chip that reproduces the capillary wall of the glomerulus involved in blood filtration. Several steps are needed in order to achieve this objective:

i) Development of the basement membrane based on a type IV collagen hydrogel and its integration into the microfluidic device.

ii) Differentiation of human induced pluripotent stem cells into glomerular endothelial cells and podocytes on each side of the previously formed membrane (Figure 1).

iii) Integration of sensors allowing the real-time impedance measurement of the membrane that reflects its physiopathological modifications.

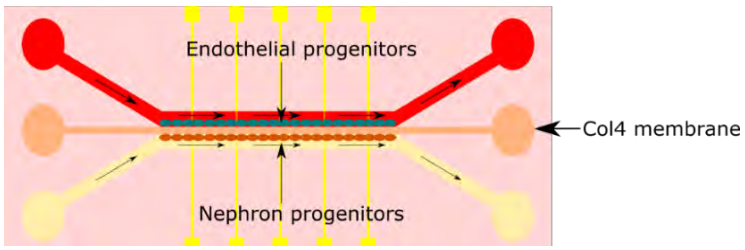


Figure 1: Scheme of the glomerular filtration barrier-on-chip

The work presented here is the first steps of the basement membrane development, which involves surface functionalization in order to immobilize proteins and type IV collagen. The characterization of theses surfaces has been carried out with quantitative QCM measurements and qualitative IR spectroscopy.

On-chip immuno-extraction of extracellular vesicles to reveal hidden sub-populations

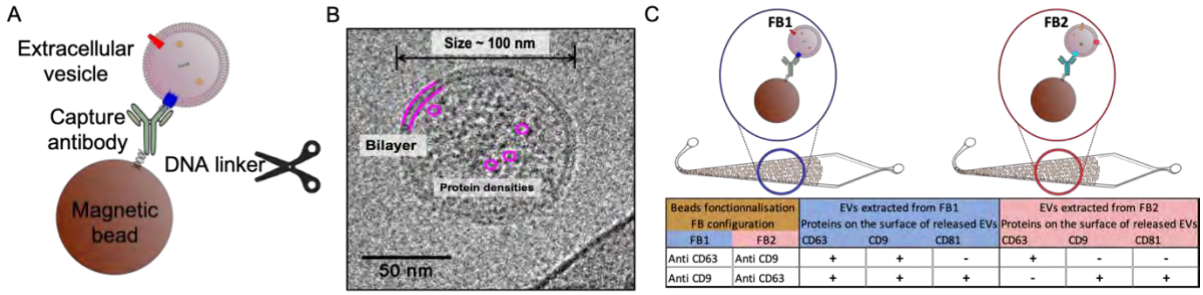
Monica Araya-Farias[1,2♦], Lucile Alexandre[1,2♦*], Dario Brambilla[3], Giacomo Gropplero[1,2], Laura Trapiella-Alfonso[1,2], Marina Cretich[3], William Cesar[4], Marine Verhursel[4], Marcella Chiari[3], Stéphanie Descroix[1,2]

[1] Laboratoire Physico-Chimie Curie, CNRS, Institut Curie, PSL Research University, Paris, France,
[2] Institut Pierre-Gilles de Gennes for Microfluidic (IPGG), Paris, France,
[3] CNR, Instituto di Scienze e Tecnologie Chimiche "Giulio Natta" (SCITEC), Milan, Italy,
[4] Fluigent, Paris, France
[*]lucile.alexandre@curie.fr [♦]Co-first authors

Extracellular vesicles (EVs) are naturally produced nanometric lipid bilayer micelles, carrying proteins and nucleic acids, involved in cell-to-cell communication [1]. They reflect the biological signature of their parent cells, which make them promising biomarkers. As EVs are highly heterogenous in their physical and biological characteristics, a strategy focuses on the extraction of specific subpopulations to study targeted profile linked to a disease.

Here we present a new microfluidic tool for immuno-extraction of EVs from human plasma samples and release of pre-concentrated subpopulations of EVs after wash of contaminants. Magnetic beads (MB) are homogeneously dispersed inside a microfluidic configuration, named fluidized bed (FB), perfused by the sample to analyze. The surface of the MB is functionalized by a specific antibody targeting a protein on the membrane of the EVs, by using a novel DNA-directed immobilization (DDI) strategy [2], as shown on Figure 1A.

A first proof of concept of the microfluidic system was performed on engineered vesicles to show the capture and release of EVs. Extraction of EVs from human plasma samples was then performed, reaching a yield of 40% higher than experiments performed in tubes, targeting of subpopulation of EVs with a diameter between 100 and 200 nm. The shape and physical integrity of EVs was confirmed by Transmission Electron Microscopy (TEM) and Cryo-Electron Microscopy (Cryo-TEM), Figure 1B. Relying on those first results, we designed a new system allowing the extraction of different subpopulations of EVs in flow. The analysis of co-expression of tetraspanins (CD63, CD9 and CD81) on extracted sample reveals that the extraction sequence impacts the protein profile of EVs, giving access to hidden subpopulations.



Beads fonctionnalisation FB configuration		EVs extracted from FB1 Proteins on the surface of released EVs			EVs extracted from FB2 Proteins on the surface of released EVs		
FB1	FB2	CD63	CD9	CD81	CD63	CD9	CD81
Anti CD63	Anti CD9	+	+	-	+	-	-
Anti CD9	Anti CD63	+	+	+	-	+	+

Figure 1: A. Representation of functionalized MB with capture antibody targeting a protein of the membrane of EVs and the breakable DNA linker B. Image by Cryo-TEM of the released EVs after capture in human plasma sample C. Capture on FB with analyse by multiplexed flow cytometry assay (MACSPlex)

[1] M. Colombo, G. Raposo, and C. Théry, *Biogenesis, Secretion, and Intercellular Interactions of Exosomes and Other Extracellular Vesicles* Annu. Rev. Cell Dev. Biol., **vol. 30**, no. 1, pp. 255–289 (2014) doi: 10.1146/annurev-cellbio-101512-122326.

[2] D. Brambilla, L. Sola, A. Ferretti, E. Chiodi, N. Zarovni, D. Fortunato, M. Criscuoli, V. Dolo, I. Giusti, V. Murdica, K. Kluszczyńska, L. Czernek, M. Düchler, R. Vago, M. Chiari, *EV Separation: Release of Intact Extracellular Vesicles Immunocaptured on Magnetic Particles* Anal. Chem., **vol. 93**, no. 13, pp. 5476–5483 (2021) doi: 10.1021/acs.analchem.0c05194

Encapsulation by AESO bio-based polymers through microfluidic tools

E. Lu[1, 2]*, B. Bresson[3], J. Fattaccioli[1, 2]

[1]PASTEUR, Département de Chimie, Ecole Normale Supérieure, PSL Université, Sorbonne Université, CNRS, 75005 Paris, France
[2]Institut Pierre-Gilles de Gennes pour la Microfluidique, 75005 Paris, France
[3]Laboratoire Sciences et Ingénierie de la Matière Molle, ESPCI Paris, 10 rue Vauquelin, Cedex 75231 Paris, France
*estelle.lu@ens.psl.eu

With the increasing environmental concerns, the polymers field is aiming towards a greener behavior, regardless of the domain of application [1]. In particular, the growth of bio-based polymers is gradually replacing petro-sourced ones. This rapid development has been helped by the infinite resources of the former's source.

However, this substitution should at least maintain the properties of the replaced materials, without adding great complexity to the synthesis. Namely, soybean oil has been the target as a viable source for green polymers. As a matter of fact, recent works have been focusing on the synthesis of a polymer based on acrylated epoxidized soy bean oil (AESO) [2].

Here, we show the use of AESO as a bio-based polymer for microencapsulation, using microfluidics systems.

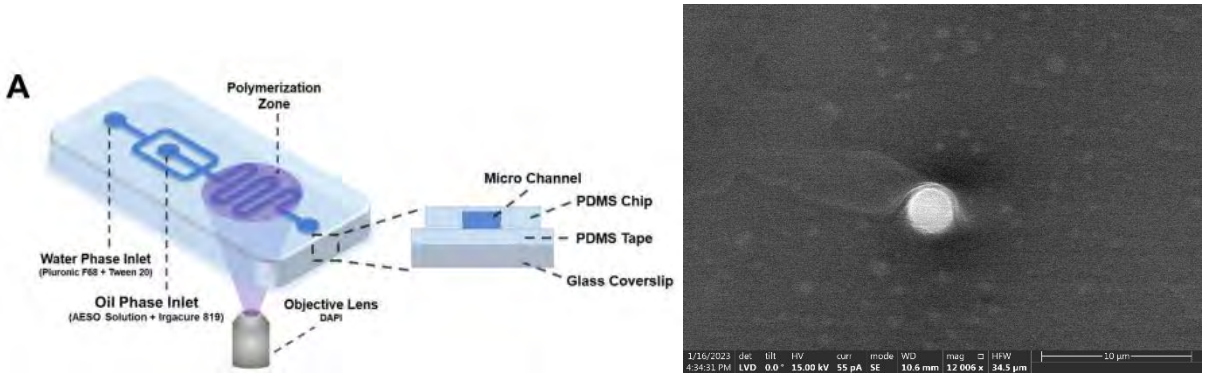


Figure 1: (a) Microchip for AESO particles (b) SEM image of an AESO microparticle

References

[1] C. Vazquez-Martel, L. Becker, W.V. Liebig, P.Elsner, E. Blasco: *Vegetable Oils as Sustainable Inks for Additive Manufacturing : A Comparative Study.* ACS Sustainable Chemistry & Engineering **9**, 16840-16848 (2021)

[2] C.Hu: *Versatile biobased particles of acrylate vegetable oil : Synthesis and applications.* (2022)

Evaluation of cancer cells mechanical phenotype associated with the resistance to treatment in acute myeloid leukemia

Martin Cardozo C.[1,2]*, Lefort S.[2], Faivre M.[1]

[1]Institute des Nanotechnologies de Lyon, Lyon, France
[2]Centre de Recherche en Cancérologie de Lyon, Lyon, France
*camila.martin-cardozo@univ-lyon1.fr

Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the abnormal proliferation of leukemia cells - or blasts - that build up in the bone marrow and blood and interfere with normal blood cell production due to their inability to differentiate into mature cells. Recent findings have highlighted an increase of the mechanosensitive pathways (BMP and YAP) in AML relapsed patients and cell lines. Moreover, recent publications reported that cancer cells undergoing confined migration, present a better survival rate after exposition to treatment (chemo- and radiotherapy) [1]. All these elements demonstrate a strong interconnection between the cell's mechanical properties, their migratory properties, and their ability to survive chemotherapy.

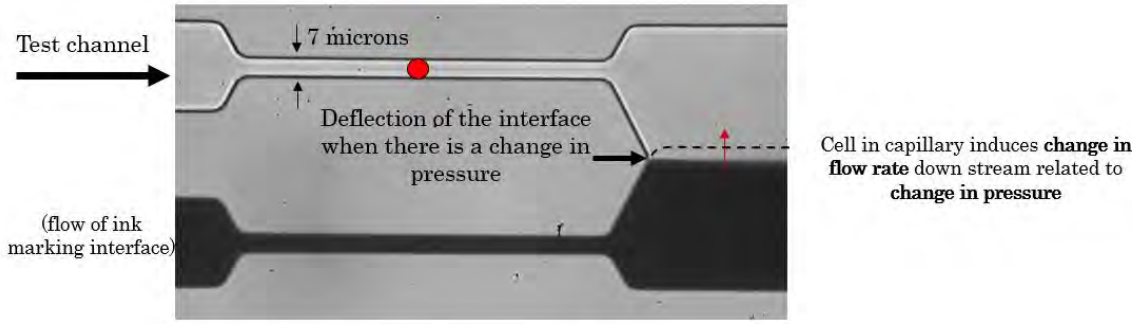


Figure 1: microfluidic device displaying the test channel (up) where the cell flows and a bottom channel with a contrasting agent that creates an interface. Figure originally from Abkarian et al. (2006) [3].

The main goal is to understand if the modulation of the mechanosensitive pathways and the adhesion mechanisms are associated with a modulation of the intrinsic deformability of resistant AML cell lines and therefore, if the cell mechanical properties can be used to predict the response to treatment. We propose to use a passive microfluidic approach (Figure 1), quantifying the way cells obstruct a geometric constriction in which they flow [2] and thus obtaining measurements of the mechanical signature of each cell line (both sensitive and resistant to several types of chemotherapy) from various readouts such as the cell transit speed and the pressure drop measurement associated.

References

[1] Shen et al., *Physical confinement during cancer cell migration triggers therapeutic resistance and cancer stem cell-like behavior*. Cancer Letters, **Volume 506**, pages 142-151 (2021).

[2] M. Abkarian, M. Faivre, H.A. Stone, *High speed microfluidic differential manometer for cellular-scale hydrodynamics*. PNAS, **Volume 103**, pages 538-542 (2006) .

Reversible and selective trapping of micro-algae in microfluidic chips

Martin Coux[1,2], Eliora Israelievitch[3], Benjamin Bailleul[3], Alix Boulouis[3], Stephan Eberhard[3], Thomas Le Saux[1], Ludovic Jullien[1], Jacques Fattaccioli[1,2]

[1]PASTEUR, Département de Chimie, Ecole Normale Supérieure, PSL Université, Sorbonne Université, CNRS, Paris, France, [2]Institut Pierre-Gilles de Gennes pour la Microfluidique, Paris, France, [3]Laboratoire de Biologie du Chloroplaste et Perception de la lumière chez les microalgues, Institut de Biologie Physico-Chimique, Sorbonne Université, CNRS, Paris, France

We are developing microfluidic tools to improve the understanding of phosphorus metabolism in the model microalgae *Chlamydomonas*, in order to use it to close the phosphorus cycle. This biogeochemical cycle is currently broken, in particular due to current agricultural practices [1]. These practices lead to the transfer of terrestrial mineral phosphorus resources (whose stock is limited and is estimated to last about 100 years at the current rate of extraction) to aquatic environments. The culture of micro-algae has been identified as a major lever for closing the phosphate cycle. These organisms are capable of storing large quantities of phosphates in the form of polyphosphates, which can represent up to 1% of their dry mass [2]. Unlike the phosphate recycling products that are currently used on a large scale, polyphosphates are a directly bioavailable source of phosphorus [3]. The accumulation and mobilisation of polyphosphate reserves in microalgae is poorly understood to date, which limits their large-scale use for the time being. Moreover, studies on the metabolism of microalgae are carried out at the scale of entire populations.

In our team, we developed microfluidic circuits to trap microscopic objects at the single object scale. These circuits allow, for example, to study the growth and development of hundreds of plant protoplasts at the single cell scale, under different illumination conditions [4]. While our colleagues in IBPC use these tools to study *Chlamydomonas* at the single cell scale, we are now working on the development of second-generation tools, which will make object trapping reversible and deterministic. This will allow us to select the individuals with the most interesting phenotypes within a population of microalgae. We will thus be able, for example, to study the hereditary (or not) character of superior phosphorus storage performance within a population. If this is the case, we will be able to develop promising microalgal strains for the recovery and recycling of phosphate fertilisers.

References

[1] Slocombe, S. P. *et al.* Fixing the Broken Phosphorus Cycle: Wastewater Remediation by Microalgal Polyphosphates. *Frontiers in Plant Science* (2020)**;**

[2] Sanz-Luque, E. *et al*. Polyphosphate: A Multifunctional Metabolite in Cyanobacteria and Algae. *Frontiers in Plant Science* (2020)**;**

[3] Siebers, N. *et al.* Towards phosphorus recycling for agriculture by algae: Soil incubation and rhizotron studies using 33P-labeled microalgal biomass. *Algal Res.* (2019)**;**

[4] Sakai, K. *et al.* Design of a comprehensive microfluidic and microscopic toolbox for the ultra-wide spatio-temporal study of plant protoplasts development and physiology. *Plant Methods* (2019);

Controlling fast and versatile thermo-osmotic flows with a pinch of salt

Cecilia Herrero[1]*

[1]Université de Montpellier – Laboratoire Charles Coulomb, Montpellier, France
*cecilia.herrero-guillen@umontpellier.fr

Thermo-osmotic flows (flows generated in micro and nanofluidic systems by thermal gradients) could provide an alternative approach to harvest waste heat, by transforming waste heat into mechanical power. However, such use would require massive thermo-osmotic flows, which are up to now only predicted for special and expensive materials. Thus, there is an urgent need to design affordable nanofluidic systems displaying large thermo-osmotic coefficients, which has raised a renovated interest over the last recent years [1]. In this work [2], we propose a general model for thermo-osmosis of aqueous electrolytes in charged nanofluidic channels, considering hydrodynamic thermo-osmotic response. We apply this model to a wide range of systems by studying the effects of wetting, salt type and concentration, and surface charge. We show that intense thermo-osmotic flows can be generated using slipping charged surfaces and that, at high salt concentrations, the response was mostly dominated by the water contribution, it being orders of magnitude greater that the values expected from the classical electrostatic theory. We also predict for intermediate wettings a transition from a thermophobic to a thermophilic behavior depending on the surface charge and salt concentration. Such change of sign has already been observed in thermophoresis experiments and could explain thermo-osmosis experiments where the flow direction cannot be predicted by the classical theory. Finally, we have recently explored such theoretical predictions through molecular dynamics simulations, confirming deviations from the classical theory due to the importance of the solute contribution [3].

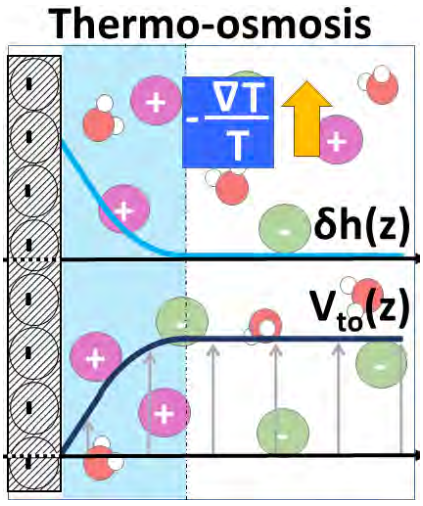


Figure 1: Thermo-osmosis, the generation of osmotic flows due to an applied thermal gradient, opens a venue towards waste heat harvesting

References

[1] R. Ganti, Y. Liu, D. Frenkel: "Molecular simulation of thermo-osmotic slip". *Physical review letters*, 119(3), p.038002 (2017)

[2] C. Herrero, M. De San Féliciano, S. Merabia, L. Joly: "Fast and versatile thermo-osmotic flows with a pinch of salt". *Nanoscale*, *14*(3), 626-631 (2022)

[3] M. Ouadfel, M. De San Féliciano, C. Herrero, S. Merabia, L. Joly. "Molecular contributions to thermo-osmotic phenomena for an electrolyte at a charged surface." arXiv:2211.16355 (2022).

Helical Fungi under Physical Constraints

Elodie Couttenier[1], Thong Hieu Dang[2], Eva Cabet[2], Sophie Bachellier-Bassi[3], Christophe d'Enfert[3], Igor M. Kulic[4], Catherine Villard[2]*

[1]Physico-Chimie Curie, Université PSL, CNRS & Institut Curie, UMR 168, F-75005 Paris
[2]Laboratoire Interdisciplinaire des Énergies de Demain, CNRS et Université Paris Cité (UPC), UMR 8236, F-75013 Paris
[3]Institut Pasteur & UPC, INRAE, USC2019, Unité Biologie et Pathogénicité Fongiques, F-75015 Paris
[4]Institut Charles Sadron, CNRS-UPR22, F-67034 Strasbourg
*catherine.villard@u-paris.fr

Helical filaments are represented in living organisms from the molecular to the multi-cellular scale. Described by Darwin in plants as early as the 19th century, they still raise fundamental questions about their roles and associated mechanisms. We here focus on the oscillatory shapes adopted by the filaments (hyphae) of the fungus *Candida albicans* in different physical confinement situations. Microfluidic channels successively presenting portions of different heights, more precisely just below (1.5 µm) and above (6.5 µm) the hyphal diameter (2 µm), allow the observation of a reversible geometrical transition between wavy shapes and helices. Unexpectedly, curvatures in wavy shapes are not built from a regular forward oscillatory movement of the tip alone, but by successive sliding events of a significant portion of the hypha at the rear of the apex. Moreover, these events follow relatively straight hyphal trajectories, suggesting a phenomenon of periodic release of elastic stress. Overall, our observations are in line with the squeelix ("squeezed helix") concept developed by Kulic et al., based on an interplay between bending and twisting energies of filaments [1]. We have also evaluated the possible advantages of these oscillatory growth patterns in the colonization of complex spaces by implementing micro-mazes in microfluidic devices. The hyphae navigate through networks of obstacles by making successive coordinated choices among the 3 possibilities offered at the corner of each individual obstacle. Strikingly, hyphae preferentially change their curvature at each step, drawing regular oscillations along a constant growth direction. This phenomenon of directional memory, which highlights an elementary sense of proprioception in these filamentous organisms, might result from the same mechanisms than the ones governing the spontaneous oscillations in confined environments.

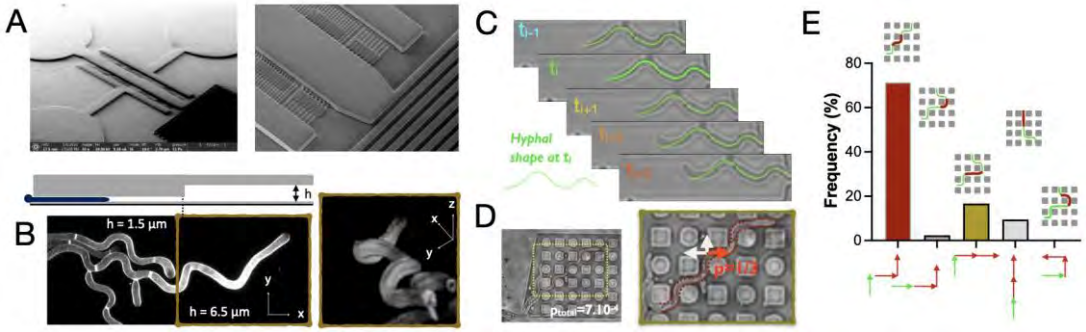


Figure 1: A – Overall design of the microfluidic mold (2 different magnifications). B - Scheme of a channel cross-section and corresponding hyphal shapes (top view and confocal 3D image). C – Hyphal elongation in a 1.5 µm high, 10 µm wide microchannel. Superimposition of the hyphal shape at t_i (green) and phase contrast images at different time points. D-E – Hypha (highlighted by a red dotted line) in a micromaze made of 8µm size obstacles (edge to edge distance: 4 µm). The arrows represent the possible growth directions. Individual (at each corner) and overall (corresponding to the highlighted portion of the hypha) probabilities are indicated. The graph shows the frequency of occurrence of the various observed configurations (11 hyphae, 42 counts)

References

[1] Nam, G. M. Nam, N. K. Lee, H. Mohrbach, A. Johner, & I. M. Kulić. *Helices at interfaces*. Europhysics Letters, **100**(2), 28001 (2012).

Investigation of microbial communities in glacial meltwater utilizing deterministic lateral displacement (DLD) array

Tin Wang, Wong[1 2] *, Gwennou Coupier[1], Aurelien Dommergue[2]

[1]LIPhy, CNRS, Université Grenoble Alpes, Grenoble, France
[2]Institut des Géosciences de l'Environnement, CNRS, IRD, Grenoble INP, Université Grenoble Alpes, Grenoble, France
[*]tin-wang.wong@univ-grenoble-alpes.fr

The glacial archives contains past airs, isotopes, ancient microorganism, etc. Therefore, it has been investigated profoundly for dating the paleoclimate data on earth. The genome of microbial communities in glacial meltwater were investigated since forty years ago, in which both culture dependent and independent methods were developed. A large portion of microbes are unculturable, thus, the culture-independent sequencing is inevitable for understanding the microbes in glacial meltwater. Besides, DLD array was emerging for separating microfluidic particles since 2004, notably, a submicron resolution of separation can be achieved. By utilizing the DLD array, dusts, cells, fungi, and bacteria are supposed to be separated and collected respectively. Each sample group with a specific size range with be, then, sequenced separately. This work aims to develop a microfluidic DLD device in order to categorize the microbes within glacial meltwater. It dedicates to explore the microbial genomes in glacial meltwater, and its correlation to the size of sample microbe.

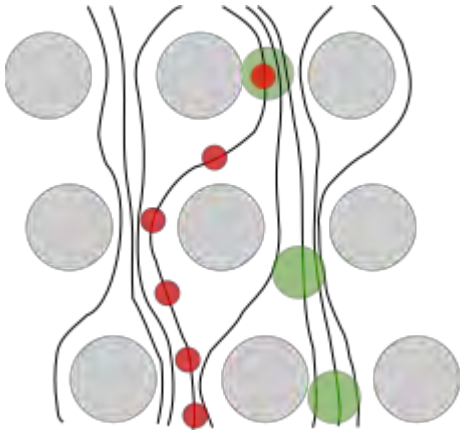


Figure 1: The principle of DLD array. Due to the special flow pattern in between the pillars, the small particle (red) will follow the flow line which is closest to the pillar and undergo a zig-zag pathway, whereas the larger particle (green) goes the another bumped pathway, and deviate from the small particle.

References

[1] Huang LR, Cox EC, Austin RH, Sturm JC: Continuous particle separation through deterministic lateral displacement. Science 304:987–990 (2004)
[2] Zhong Z-P, Tian F, Roux S, et al: Glacier Ice Archives nearly 15,000-year-old microbes and phages. Microbiome 9(1) (2021)

Lab on Chip for the isolation of circulating adipose stem cells: Leucocyte separation module by Cell Rolling

L Charpin[1]*, M H Baz[1], E Trevisiol[2], C Sengenes[3], A M Gué[1]

[1]LAAS, Toulouse, France
[2]TBI, Toulouse, France
[3]Restore, Toulouse, France
*lcharpin@laas.fr

Adipose Stem Cells (ASC) have become popular in regenerative medicine since they display multipotent stem cell properties and are relatively abundant compared to other types of SC. Recently, studies showed that the release of ASC by subcutaneous adipose tissue and their circulation correlates with type 2 diabetes development [1]. This suggests that ASC could be considered as a predictive biomarker of T2D. However, validating this hypothesis is difficult since ASCs are rare blood circulating events. Moreover, ASCs exhibit wide size distribution, do not express specific unique membrane markers compared to hematopoietic cells, which renders their isolation from whole blood a hard task. Hence, it is essential to consider isolating ASCs from peripheral blood by combining complementary selection criteria i.e. size and surface markers.

In this work, we present the second module of the ASCFinder project that aim to separate ASC from remaining leucocytes in peripheral blood by cell rolling. The challenge will be to deplete remaining hematopoietic cells according to their surface antigens, leading to a sample that ideally contains only ASC. The principle is based on cell rolling, and is already used to sort out circulating tumor cells (CTC) by using protein such as P-selectin or E-selectin in S. Choi works [2] Until now, work has been focused on developing a surface bio-functionalized by specific antibody toward hematopoietic cells. Two different ways to do so were studied, grafting antibodies on a SAM modified gold surface or grafting antibodies on a dendrimer modified glass surface.

Small cells such as red blood cells and platelets are considered removed thanks to the first module of the project, studied by Mohammad-Hussein BAZ [3].

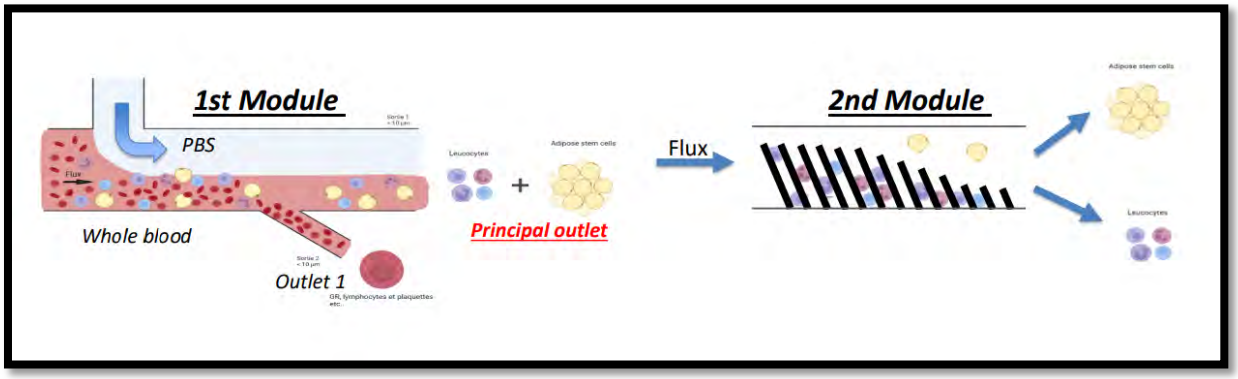


Figure 1 : Schematic summary of ASCFinder Lab-on-Chip's project.

References

[1] A. Girousse, M. Mathieu: *Endogenous Mobilization of Mesenchymal Stromal Cells:A Pathway for Interorgan Communication.* Frontiers in developmental biology **Volume 8** : 598520 (2020)
[2] S. Choi, J. M. Karp, et R. Karnik, *Cell sorting by deterministic cell Rolling*, Lab Chip, **Volume 12**, doi: 10.1039/C2LC21225K (2012)
[3] M. H. Baz, L. Charpin *Lab-on-a-Chip for the isolation of circulating Adipose Stem Cells* hal03823431 (2022)

Equilibrium and transport of micro-to-nanoconfined electrolytes

Caroline Cramail*, Dandara Velasco Anez, Benjamin Cross, Romain Lhermerout, Élisabeth Charlaix

Laboratoire Interdisciplinaire de Physique, Grenoble, France
*caroline.cramail@univ-grenoble-alpes.fr

Micro-to-nanoconfined electrolytes are widespread in industrial applications such as energy storage, filtration, or lubrication. New technologies, aiming at harvesting the osmotic energy available at the mouth of rivers –a non-destructive, clean, and non-intermittent renewable energy of great potential for the global energy transition–, also require understanding the flow of electrolytes confined at the nanoscale to become viable [1].
One of the parameters controlling the flow of confined electrolytes is the surface charge of the confining surfaces. However, previous studies have shown that the equilibrium surface charge and the surface charges at play in diverse transport phenomena (conductivity, electro-or diffusio-osmosis) are different: the surface charge is thus an ill-defined concept [2].
For ten years, our team in Grenoble has developed a unique dynamic Surface Force Apparatus (dSFA), which allows to simultaneously measure the equilibrium and transport properties of confined liquids over 4 decades in distance [3]. Our instrument is therefore perfectly suited for investigating the aforementioned surface charges. Besides, first measurements performed in the team revealed that the rheology of confined electrolytes is characterized by an overdissipation with respect to non-charged liquids. This overdissipation may be caused by a counterflow of ions, induced by a radial electric field, to restore the electroneutrality at the nanopore.
To interpret the dSFA measurements, especially to compare the static and dynamic surface charges and to understand the parameters controlling the overdissipation, a model needs to be built. We are currently working on a quantitative model applied to diluted electrolytes confined in a sphere-plane geometry within the linear response theory. The model aims at describing the force exerted by the electrolyte on the surfaces as a function of the relative positions and velocities of the surfaces. The description is divided into three distinct regimes, corresponding to different degrees of overlapping of the two electrical double-layers. My talk will focus on this model under construction.

References

[1] A. Siria, M.-L. Bocquet. L. Bocquet: *New avenues for the large-scale harvesting of blue energy*. Nat Rev Chem. **1**, 0091 (2017)

[2] R. Hartkamp, A.-L. Biance, Anne-Laure, L. Fu, J.-F. , O. Bonhomme, L. Joly: *Measuring surface charge: why experimental characterization and molecular modeling should be coupled.*

Curr Opin Colloid Interface Sci. **37**, 101-114 (2018)

[3] L. Garcia, C. Barraud, C. Picard, J. Giraud, E. Charlaix, B. Cross: *A micro-nano-rheometer for the mechanics of soft matter at interfaces*. Rev Sci Instrum. **87**, 113906 (2016)

Lymphatic clearance studied in a lymphatic vessel-on-a-chip platform

J. Edwards[1]*, A. Bancaud[1], B. Garmy-Susini[2], F. Morfoisse[2]

[1]LAAS-CNRS, Toulouse, France
[2]I2MC-INSERM, Toulouse, France
*jedwards@laas.fr

The human body contains two circulatory systems: the blood system and the lymphatic system. The former provides continuous perfusion of tissues through a central pump - the heart - while the latter drains and reinjects interstitial fluids from the tissues into the bloodstream, without any pump. The lymphatic system thus plays a key role in the control of tissue homeostasis, but also in the regulation of the immune system response and in the spread of cancer cells in metastasis processes [1]. But unlike the blood system, the limitation of in-vivo experiments and the difficulty of reproducing the morphology of the lymphatic system have hampered the quantitative description of its biomechanical function. Using a technology developed by the MASTUNAGA laboratory (Tokyo, Japan) to create micro blood vessels on a chip embedded in a collagen matrix [2], we report the fabrication of a lymphatic vessel on a chip. This model allows us to control the pressure and monitor the clearance flow, and hence to characterize the response of the lymphatic tissue, including the ability of the barrier to exchange fluids, molecules and even immune cells.

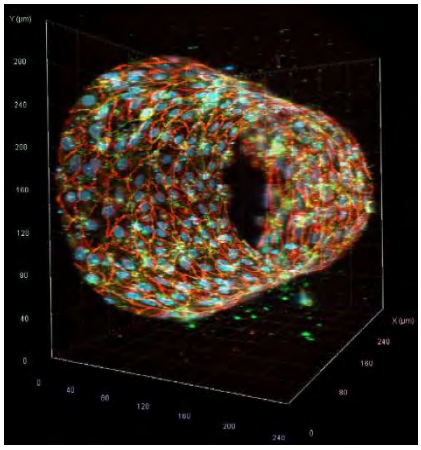


Figure 1: Confocal microscopy image of the lymphatic vessel on chip (F. Morfoisse, I2MC)

References

[1] M. Swartz: *The Physiology of the Lymphatic System*. Advanced Drug Delivery Reviews **50**, 3- 20 (2001)

[2] L. Eujin, H. Takahashi *et al*: *A 3D in Vitro Pericyte-Supported Microvessel Model: Visualisation and Quantitative Characterisation of Multistep Angiogenesis*. Journal of Materials Chemistry B **6,** 1085-94 (2018)

Study of oscillating flow inside a matrix regenerator: impact of internal scale on the operating frequency

B. Bataille*, M. Medrano Muñoz[1], D. Colombet[2], F. Ayela[2], N. Luchier[1]

[1]CEA Grenoble – DSBT, Grenoble, France
[2]LEGI, Grenoble, France
*benjamin.bataille@univ-grenoble-alpes.fr

Pulse tube cryocoolers (PTC) are a technology well adapted to space applications. Through their size is already contained, there is an interest to reduce it further. A key PTC component is the regenerator. It is usually an accumulation of metallic screen meshes, hard to miniaturize and to optimize.

According to some numerical works[2], regenerators formed by a matrix of profiled elements can exceed the performances of the meshes-based regenerators[1]. They are produced by micro machining silicon wafers enabling a precise reproducible control of their characteristics (size, porosity…). For a laminar stationary gas flow, a staggered diamond-shaped pillars matrix shows better hydrodynamic performances than meshes for porosities under 0.7[2].

The aim of this work is to study the hydrodynamic performances of staggered diamond-shaped pillars matrix micro regenerators subjected to a helium gas oscillating flow. Our micro regenerators are made with DRIE process on silicon wafers (Figure 1). Porosities between 0.4 and 0.7 and rhombus angles between 20° and 90° are studied. The matrix is encapsulated by a glass wafer. The samples are studied over a 20-150 Hz frequency range oscillating flow and the results are compared to the theoretical and experimental study of a parallel plates channel used as a reference. They show a similar behavior than parallel plate channels for frequencies under 80 Hz. Beyond, inertial effects appear with a phase lag between the pressure drop and the mean velocity.

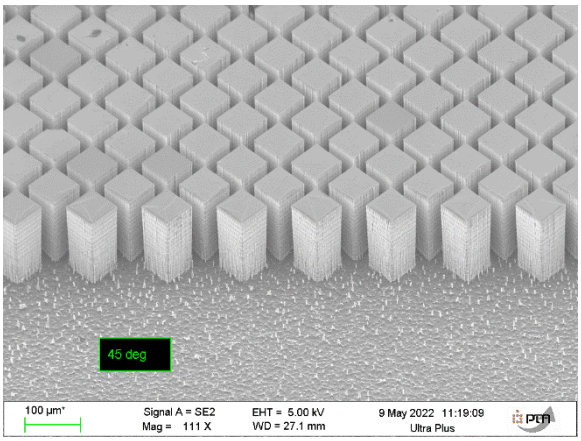


Figure 1: Diamond-shaped pillars matrix regenerator. Picture taken with a scanning electron microscope with a 45° tilt

Acknowledgement

The authors would like to thank CNES and particularly Lorenzo Marelli for supporting this work, and the technical staffs of PTA (CEA) and Nanofab (Néel Institute) for the assistance in micro fabrication of samples.

References

[1] I. Rühlich, H. Quack: *Investigations on regenerative heat exchangers*. Cryocoolers 10, 265-74 (2002).
[2] A. Sochinskii: *Premier pas vers la miniaturisation des cryoréfrigérateurs spatiaux.* (2018).

Hematocrit profile relaxation after a T-shaped bifurcation

K. Useo*, S. Lorthois, P. Duru, F.Risso

Institut de Mécanique des Fluides de Toulouse, CNRS et Université de Toulouse, France
*klervia.useo@toulouse-inp.fr

Blood circulation in capillary networks allows the diffusion of oxygen to living tissues and the discharge of wastes, including carbon dioxyde. In particular, O_2 and CO_2 are carried by the hemoglobin contained in red blood cells (RBCs). Therefore, a capillary-scale heterogeneity of the distribution of blood cells, both red and white, can impact the exchange of these solutes between blood and tissues; and play an important role in the genesis of pathologies such as Alzheimer's disease [1].

In vivo and *in vitro* studies have allowed a better description of the micro-channel flow phenomenology, and in particular the segregation of cells at bifurcations which leads to heterogeneities in their distribution. This phenomenon, called phase separation, depends on the partitioning of flows in the downstream daughter branches and impacts the distribution of RBCs at the network scale ; but it's not sufficient to explain all the heterogeneities observed experimentally [2] .

After each network bifurcation, the radial concentration profile indeed results from the flow partitioning as well as the upstream concentration profiles. Such a dependence leads to downstream asymmetrical concentration profiles that subsequently relax to a symmetric one along the channel. A better understanding of the physics of this phenomenon means a better understanding of the relationships between the architecture of micro-vascular networks and the dynamics of blood flows, at all scales.

Our aim is to model the relaxation of the hematocrit profiles for narrow channels of 10 and 20µm, over a wide concentration range (5-25%). We investigate the flow of an isodense suspension of RBCs at a T-bifurcation in a pressure-controlled glass/PDMS microfluidic device. At the bifurcation, some of the RBCs are deflected towards the opposite wall (c*f.* upper right panel, Figure 1) and then migrate laterally towards the center of the canal (c*f.* lower left panel, Figure 1), under the effects of lift forces and shear-induced migration.

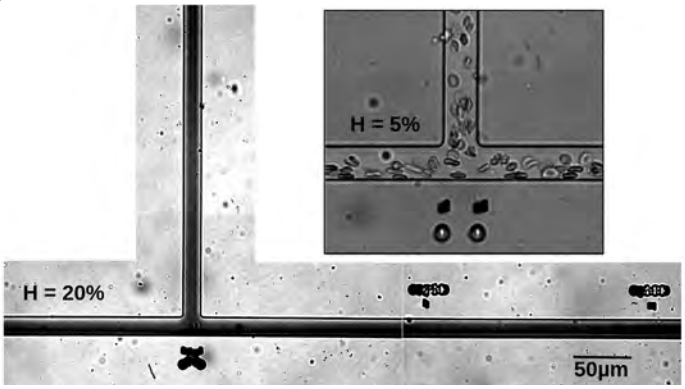


Figure 1: Average image of RBC flow after a T-shape bifurcation at H=20% (lower left panel) and H=5% (upper right panel).

References

1 J.C. Cruz, O. Bracko, C.J. Kersbergen, V. Muse, M. Haft-Javaherian, M. Berg, L. Park, L.K. Vinarcsik, I. Ivasyk, D.A. Rivera, Y. Kang, M. Cortes-Canteli, M. Peyrounette, V. Doyeux, A. Smith, J. Zhou, G. Otte, J.D. Beverly, E. Davenport, Y. Davit, C.P. Lin, S. Strickland, C. Iadecola, S. Lorthois, N. Nishimura, C.B. Schaffer: *Neutrophil adhesion in brain capillaries reduces cortical blood flow and impairs memory function in Alzheimer's disease mouse models*. Nature Neuroscience **22**, 413- 420 (2019)

2 A. Merlo, M. Berg, P. Duru, F. Risso, Y. Davit, S.Lorthois: *A few upstream bifurcations drive the spatial distribution or red blood cells in model microfluidic networks*. Soft Matter **18**, 1463-1478 (2022)

Topological optimization of heating resistors for controlling temperature in a microfluidic cavity

T. Mabit[1]*, M-C. Jullien[1], H. Ben Ahmed[2]

[1]IPR UMR 6251, Univ. Rennes1, CNRS, av. Général Leclerc, Rennes 35000, France
[2]SATIE, ENS Rennes, CNRS, av. Robert Schuman, Bruz 35170, France
*thomas.mabit@univ-rennes1.fr

The integration of temperature control in a microsystem is in itself a challenge. Among the different heating techniques, the Joule effect allows a simple integration in microsystems [1]. Previous works have shown that it is possible to generate linear or constant profiles by coupling an optimization algorithm determining the geometry of the heating resistors and a finite element solver to predict the temperature field generated by the geometry [2]. This optimization was based on the local width of the heating wires and only allowed to generate 1D temperature profiles (the temperature remaining homogeneous in the second dimension). In order to be able to generate more complex profiles, we have developed a new numerical tool which is based on Bézier curves (rather than the local width of the wires) coupled with an in-house temperature resolution code, allowing to get rid of expensive solvers. We show in this poster that complex profiles have been generated and validated by the experiment. The numerical tool developed is free and open-source (https://microheat.ppaduc.fr).

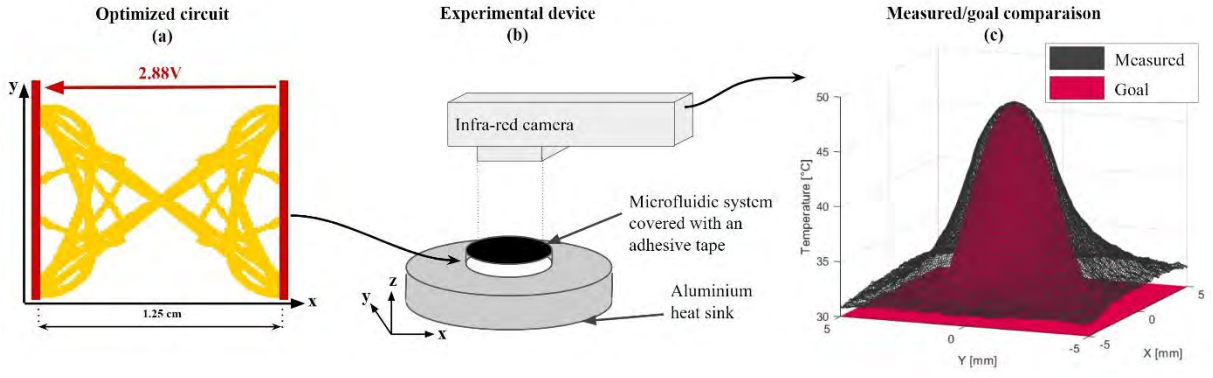


Figure 1: Example of optimized circuit for generating a 3D-cosine temperature profile at the fluidic layer (a). To allow visualization of the temperature (c), the infra-red measure (b) is performed at the substrate interface, i.e. without the PDMS layer. The surface is then covered with an adhesive tape as a black body.

References

[1] Miralles, V., Huerre, A., Malloggi, F., & Jullien, M.-C. (2013). A review of heating and temperature control in microfluidic systems: Techniques and applications. Diagnostics, 3(1), 33–67.

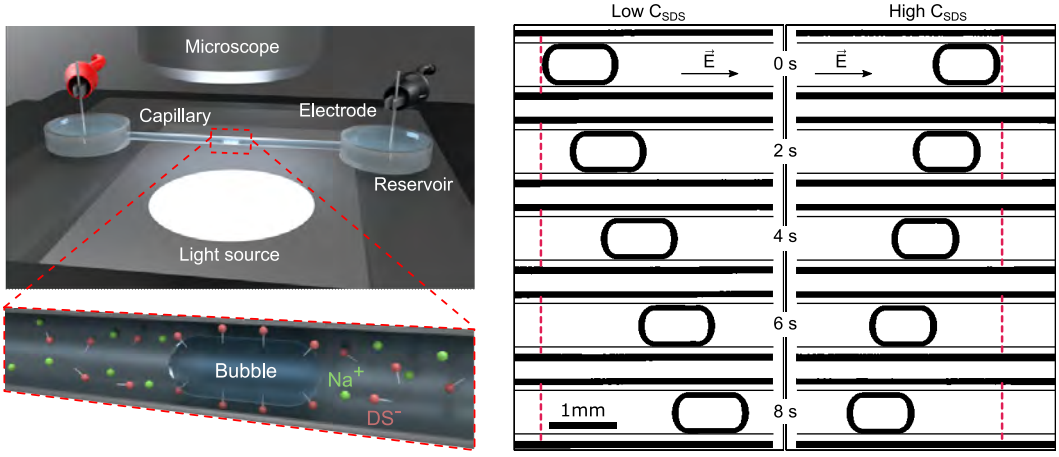
[2] Selva, B., Mary, P., & Jullien, M.-C. (2009). Integration of a uniform and rapid heating source into microfluidic systems. Microfluidics and Nanofluidics, 8, 755–765.

Influence of surfactants in bubble transport under an electric field

C. Bae, M. Zhao, O. Bonhomme, C. Ybert, C. Cottin-Bizonne, and A.-L. Biance*
Univ Lyon, Univ Claude Bernard Lyon 1, CNRS,
Institut Lumière Matière, F-69622, VILLEURBANNE, France

The motion of elongated bubbles in narrow tubes is a very old problem, investigated by Taylor who gave his name to the so-called Taylor bubbles [1]. Generally, the motion is generated by a pressure gradient, originating from buoyancy or applied forces. In these very classical cases, it has been shown that most of the dissipation takes its origin in the liquid film squeezed between the bubble and the wall. Its thickness is set by a balance between viscous and capillary forces, as shown by Bretherton [2, 3]. We consider here another type of bubble actuation, electrically driven motion. Generally, an electric field can induce bubble migration known as bubble electrophoresis due to the adsorption of ions around the bubble. In this study, we add an anionic surfactant, sodium dodecyl sulfate (SDS) to modify the adsorption and the corresponding zeta potential of the bubble. The response here differs significantly from pressure driven flows. We first found that the bubble velocity is linear at low voltage and becomes non-linear above a critical threshold. We also show, more unexpectedly, that varying the surfactant concentration results not only in the magnitude of the bubble motion but also in its direction. We will present here these experimental results together with an interpretation of these peculiar behaviours. These new findings will give some insights into the realization of soft reconfigurable nanofluidic channels [4].

Keywords: Bubble, Electrophoresis, Nanofluidics



[1] R. Davies and G. I. Taylor, The mechanics of large bubbles rising through extended liquids and through liquids in tubes, Proceedings of the Royal Society of London. Series A. Mathematical and Physical Sciences **200**, 375 (1950).
[2] F. P. Bretherton, The motion of long bubbles in tubes, Journal of Fluid Mechanics **10**, 166 (1961).
[3] I. Cantat, Liquid meniscus friction on a wet plate: Bubbles, lamellae, and foams, Physics of Fluids **25**, 031303 (2013).
[4] Y. Ma, M. Sun, X. Duan, A. van den Berg, J. C. Eijkel, and Y. Xie, Dimension-reconfigurable bubble film nanochannel for wetting based sensing, Nature communications **11**, 1 (2020).

* anne-laure.biance@univ-lyon1.fr

A method for single-cell multiomic barcoding, enabled by physical bioseparation in high-throuhput droplet microfluidics

Simon Dumas[1,2]*, **Eve Moutaux**[3], **Grégoire Lemahieu**[1,2], **Céline Vallot**[3,4], **Stéphanie Descroix**[1,2]

[1]PhysicoChimie Curie (UMR168), Institut Curie, Paris
[2]Institut Pierre-Gilles de Gennes, Paris
[3]Single-cell platform, Institut Curie, Paris
[4]DIG-Cancer (UMR3244), Institut Curie, Paris
*simon.dumas@curie.fr

Droplet microfluidics has revolutionized the field of single-cell sequencing, enabling high-throughput cell compartmentalization and barcoding. In recent years, single-cell sequencing has been moving toward multiomic, where several cellular modalities are addressed at the same time. They can include transcriptomics, genomics, epigenomics or proteomics [1]. Multiomic methods are however challenging to implement in droplets as the droplet chemistry must be compatible with the simultaneous analysis of several omics. For this reason, physical separation of the different analytes after cell lysis in droplets would be highly beneficial to allow their separate processing using optimized respective protocols. However, such technology is lacking, which represents a major limitation of current single-cell methods.

We developed a new method for multiomic single-cell barcoding based on the separation of analytes in droplets. First, we designed a robust microfluidic system exploiting the deformation of hydrogel barcoding beads at a constriction to extract them from nanoliter droplets at high throughput [2]. Second, we developed a multimodal bead approach, allowing the barcoding of one omic in droplet, while another one is captured and extracted on the bead for separate processing [3]. Finally, we employ this method for joint profiling of histone modification (Cut&Tag) and transcriptome (scRNA-seq) in single-nuclei. This versatile approach is fully compatible with state-of-the-art technology, and can be easily adapted to various cellular modalities to address relevant biological questions, such as to study epigenetic plasticity in cancer.

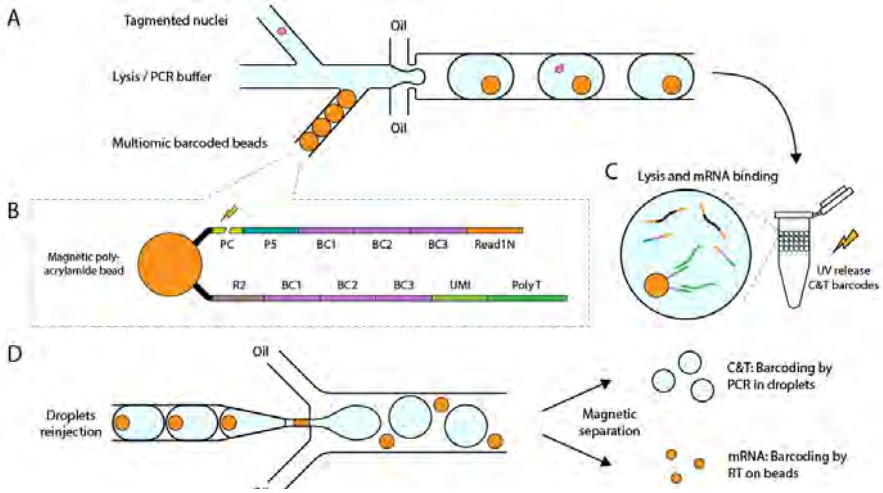


Figure 1: **A:** Encapsulation of tagmented nuclei (Cut&Tag) and multiomic barcoding beads. **B:** Structure of the multiomic barcoding beads. **C:** Barcoding primers for Cut&Tag are UV-released in droplets while the ones for mRNA remain on beads. **D:** Extraction of the barcoding beads to separate mRNA from tagmented DNA.

References

[1] J. M. Perkel, Single-cell analysis enters the multiomics age, *Nature*, 595, 2021.

[2] **S. Dumas**, G. Lemahieu, S. Descroix. Method of extracting a bead from a droplet. *European patent EP22306279*. Filed August 29, 2022.

[3] **S. Dumas**, E. Moutaux, L. Perié, S. Descroix, C. Vallot. Multimodal probe and method of manufacturing the same. *European patent EP22306280*. Filed August 29, 2022.

Precise and fast control of the dissolved oxygen level for tumor on chip

Charlotte Bouquerel [1], William César[2], Lara Barthod[1], Sarah Arrak[1], Aude Battisella[4], Giacomo Gropplero[1], Fatima Mechta-Grigoriou[3], Gérard Zalcman[3], Maria-Carla Parrini[3], Marine Verhulsel[2] and Stéphanie Descroix[1]

[1] Macromolécules et Microsystèmes en Biologie et Médecine, UMR 168, Institut Curie, Institut Pierre Gilles de Gennes, 6 rue Jean Calvin 75005, Paris, France. [2] Fluigent, 67 avenue de Fontainebleau, 94270, Le Kremlin-Bicêtre, France. [3] Stress et Cancer, Inserm, U830, Institut Curie, Equipe labelisée par la Ligue Nationale Contre le Cancer, PSL Research University, 26 rue d'Ulm, 75005, Paris, France
[4] Biochemistry Molecular Biology and Cells Platform, UMR 168, Institut Curie, PSL Research University, 26 rue d'Ulm 75005, Paris, France

In vivo tumor cells experience low oxygen levels (15mmHg for lung cancer), called "hypoxia", as compared to "physioxia" seen in healthy tissue (40-145mmHg for lung) [1]. This hypoxic environment is mainly due to the fast proliferation rate of tumor cells along with the creation of abnormal vasculature. Tumor-on-chip are promising models to recapitulate *in vitro* the 3D architecture and the physiology of human solid tumor, such as cell-cell and cell-matrix interactions as well as biochemical gradients of drugs and nutrients [2]. Up to date, there are no commercial systems capable to reproduce gradients of oxygen and pH inside microfluidic systems, mimicking not only global hypoxia, but also the fluctuations of local oxygen concentration due to angiogenesis and vessel leakages. We recently developed a new system, called OXALIS (Oxygen ALImentation System), to control the dissolved oxygen level in microfluidic chips. Various chip materials were tested (Figure 1A) and unprecedented performance were obtained in terms of response time (200sec), accuracy (2mmHg) and liquid flow control accuracy (0.1µL/min) [3]. This level of responsiveness provides the opportunity to apply fast oxygen cycles (Figure 1B) and thus to address new biological questions that have been unanswered because of technological limitations. Hypoxia promotes malignant progression and reduces drug efficiency. We demonstrated the capacity of the system to recapitulate hypoxia-induced gene expression (Figure 1C). Previous work highlighted that hypoxia may induce enlargement of mitochondria, due to abnormal fusion, which results in drug resistance [4]. Mitochondria may revert to their initial state in normal oxygen conditions, although the mechanisms are not yet fully understood. Despite its potential, mitochondrial phenotype, particularly at the cell population level, has not been studied extensively [5]. Combining computational imaging with OXALIS precise control of oxygen, we focus on mitochondrial morphology as a biomarker of cancer phenotype and drug response. We conduct a continuous monitoring of mitochondrial shape while oxygen cycles are applied in two populations of lung cancer cells, either resistant or sensitive to paclitaxel. This unprecedented monitoring of mitochondria morphodynamics in a tumor-on-chip pave the way to the identification of new mechanisms involved in hypoxic cell survival.

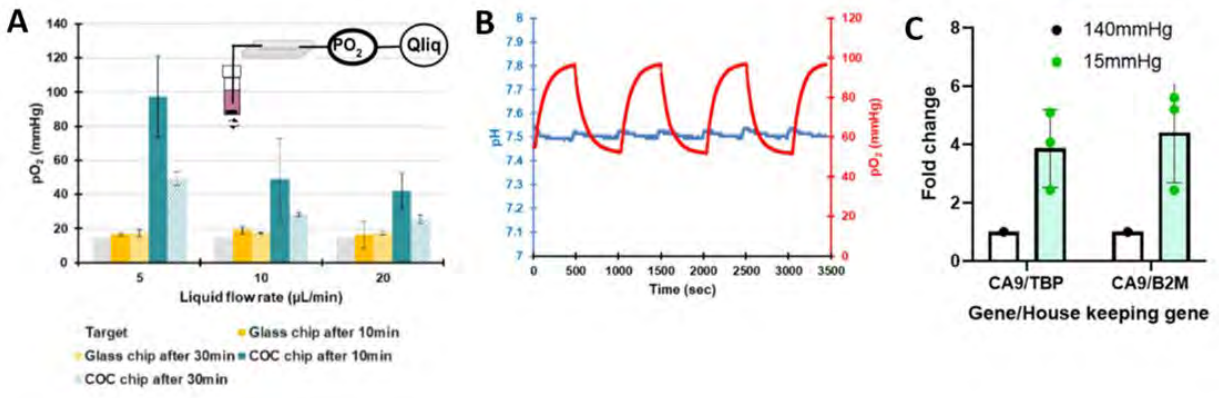


Figure 1 : OXALIS performances (A) Oxygen cycles are applied while pH is maintained constant (B) Glass chip should be preferred to control oxygen with high precision (C) The CA9 fold change is about 4 after 1h perfusión with OXALIS (N=3 chips seeded on independent days)

References

[1] Mckeown et al., Defining normoxia, physoxia and hypoxia in tumours, Br J Radiol 87, 1035, 2014
[2] Nguyen et al., Dissecting Effects of Anti-cancer Drugs and Cancer Associated Fibroblasts by On-Chip Reconstitution of Immunocompetent Tumor Microenvironments, Cell Reports 25, 3884–3893, 2018
[3] Bouquerel et al., Precise and fast control of the dissolved oxygen levels in tumor-on-chip, Lab On Chip, 22, 4443-4445, 2022
[4] Mazure et al., Hypoxic mitochondria: accomplices in resistance, Bulletin du Cancer, 98, 5, 2011
[5] Giedt et al., Computational imaging reveals mitochondrial morphology as a biomarker of cancer phenotype and drug response, Scientific Reports, 6:32985, 2018

Microfluidics to study the permeability of a yeast clog

T. Desclaux[1,2]*, L. Santana[1], I. Verdeille[1], P. Joseph[2], P. Duru[1], M. Delarue[2], O. Liot[1]

[1]Insitut de Mécanique des Fluides de Toulouse, Toulouse, France
[2]Laboratoire d'Analyse et d'Architecture des Systèmes - CNRS, Toulouse, France
*terence.desclaux@imft.fr

Capturing solid particles in a porous medium is essential for many processes but has a major drawback: the pores can clog, leading to the fouling of filtration systems. Clogging is now relatively well understood for inert and rigid particles, but the study of bioclogging - clogging by biological objects - opens many research questions, as living cells are endowed with special properties: they are deformable, have specific adhesion mechanisms and can proliferate. As a result, these cells can both change their shape or volume, leading to local cellular rearrangements, thus changing the microstructure of the clogs. Many studies on bioclogging have been carried out at the membrane scale, and report that the permeability of a clog formed by living particles is complex to predict. Indeed, there is a lack of micro-scale measurements to relate the permeability, measured at the macroscale, to the displacement and to the deformation of the cells inside the clog, and to the clog microstructure.

We have therefore developed a microfluidic device consisting of two identical channels. Each channel is quasi-2D, shallow and very wide, and blocked by a constriction. In one of the two channels, a suspension of yeast (*Saccharomyces cerevisiae*) is pushed. The constriction holds the yeast and allows the culture liquid to pass through. In the second channel, culture liquid with added dye but without cells is pushed. The pair of channels merges into a single channel. The position of the interface between the coloured and uncoloured fluids (see figure) allows to determine the ratio of the flow rates between the two channels, and thus the hydrodynamic resistance/permeability of the clog. Different clogs are then constructed under different hydrodynamic forcing, keeping the pressure constant at the inlets of the device. Each clog is then subjected to compression and decompression cycles, modulating the intensity of the hydrodynamic forcing, before finally being deconstructed and reconstructed abruptly, reversing the direction of flow cyclically and rapidly.

The hydrodynamic forcing is found to impact the permeability of the clogs, as the hydraulic resistance increases with the operating pressure. Besides, for a given clog and a given operating pressure, the permeability increases significantly after a single abrupt deconstruction/reconstruction event. The results obtained are then confronted with direct measurements of the microstructure, obtained by fluorescence microscopy, while the movements within the clog are quantified, using dedicated algorithms to distinguish collective movements and local rearrangements. This confrontation shows that several processes are at play in a yeast clog: modification of the microstructure by rearrangements (as in granular media), and poromechanical coupling between the fluid and the solid structure.

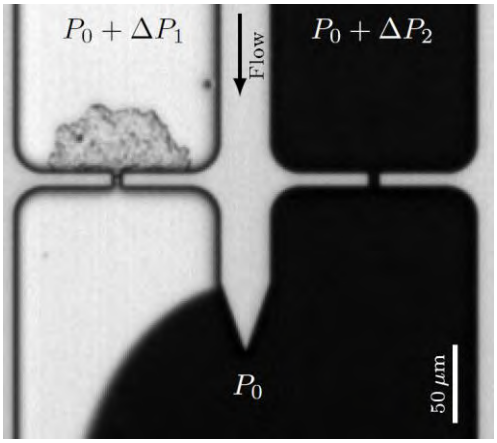


Figure 1: Micrograph of the microsystem. A clog is visible in the left-hand microchannel while coloured culture medium is flowed in the right-hand microchannel. Magnification: 5 times.

Boosting the blue energy to the next level

N.Wu[1]*, Y.Brahmi[1], A.Colin[1]

[1]MIE-CBI, ESPCI Paris, Paris, France
*nan.wu@espci.fr

As a novel form of renewable energy, "Blue energy" harvest the Gibbs free energy generated from the mixing of fresh and salt water for electricity generation. The power density generated by major approaches for blue energy harvesting (including pressure retarded osmosis, reverse electrodialysis and capmixing) remains insufficient to reach the threshold for industrialization and commercialization.

While general paths for the increase of power density rely on the amelioration of ion-selective membrane performances and the diminution of cell resistance, in this work, we point out a novel path by using booster system to reinforce the power output. The booster system, which generates a constant electrical voltage in phase of the switching period of the cell system, is added to the capacitive salinity-gradient cell-resistor circuit for power density enhancement. The net power density output in the resistor is calculated as the difference between gross power density dissipated in the resistor and the power density generated by the booster system. Experimental results indicate that the capacitive salinity-gradient cell coupled with a booster system could reach a maximum power density of 5.26 $W.m^{-2}$ (where the salinity difference of 0.17 $mol.L^{-1}$ and 5.13 $mol.L^{-1}$), which corresponds to a 59.8% increase compared with its power density of 3.29 $W.m^{-2}$ without the booster system. Influential factors including salinity difference, switching period, resistance of load resistors and boosting voltages are systematically studied to further reveal the boosting principle. The use of booster system opens up a brand-new path for power density improvement and will certainly accelerate the maturity process of blue energy harvesting technologies.

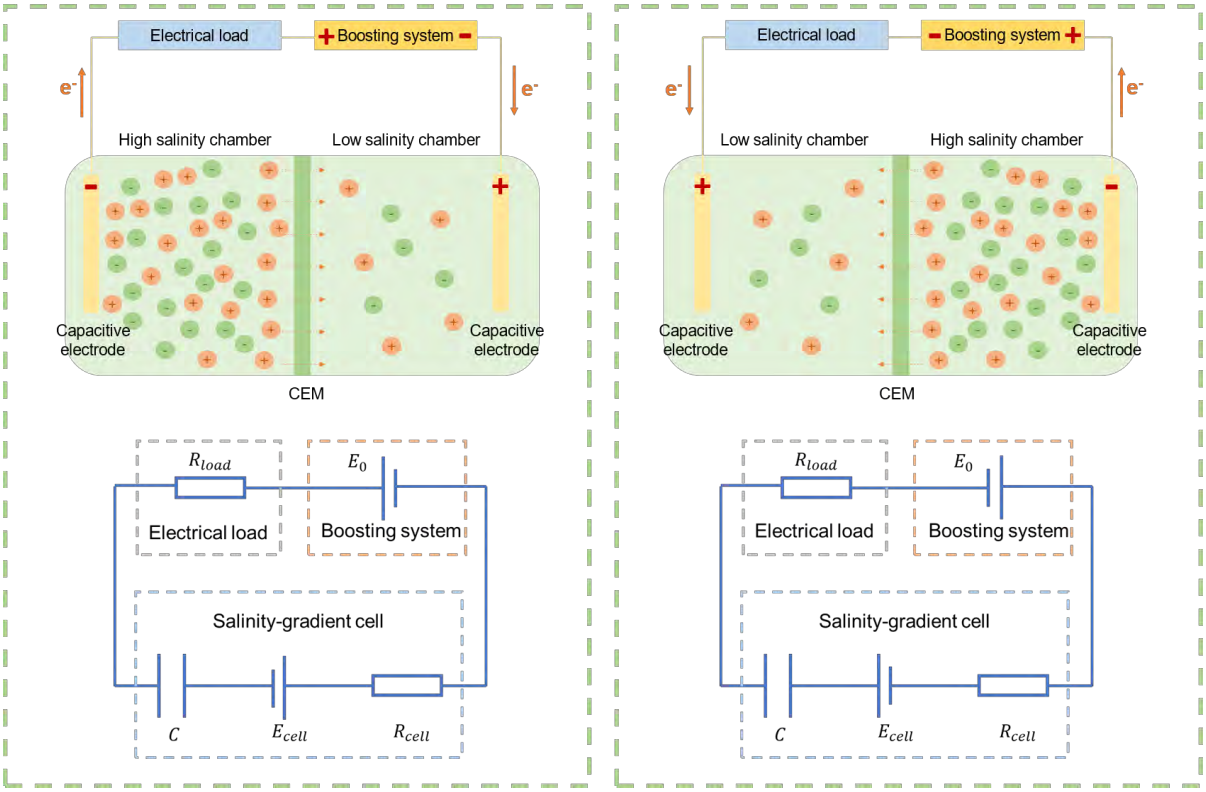


Figure 1: Illustration of the capacitive salinity-gradient cell coupled with a booster system.

Design and optimization of a magneto-plasmonic sandwich biosensor for integration within microfluidic devices

M. Soroush[1,2], W. Ait Mammar[1,3], A. Wilson[1], H. Ghourchain[2], M.Salmain[3], S. Boujday[1*]

[1] Sorbonne Université, CNRS, Laboratoire de Réactivité de Surface (LRS), F-75005 Paris, France
[2] Laboratory of Bioanalysis, Institute of Biochemistry & Biophysics, University of Tehran, Iran
[3] Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire (IPCM), F-75005 Paris, France
walid.ait_mammar@sorbonne-universite.fr

Monitoring biomarkers in clinical samples allows to predict the onset, development, and severity of diseases. Biosensors are among the most promising devices for detection of diseases-related biomarkers thanks to their capability to realize rapid, sensitive, label-free, cost-effective, and real time detection [1]. The high surface to volume ratio of the microfluidic device can enhance mass transport, resulting in shorter assay time and increased detection sensitivity.

In this project we have developed a magneto-plasmonic biosensor for the immunodetection of antigens in minute sample volume [2]. Both spherical gold nanoparticles (AuNP) and magnetic beads (MB) were conjugated to goat anti-rIgG antibody (Ab) capable of recognizing a model target, rabbit IgG (rIgG) (Fig.1 (a)). The AuNP bioconjugate was used as optical detection probe while the MB one was used as capture probe. Addition of target analyte followed by detection probe resulted in the formation of a sandwich immunocomplex (Fig.1 (b)) which was separated from the unbound AuNP-Ab conjugate by application of an external magnetic field. The readout was done either in direct or in indirect way by measuring the UV-Visible spectrum of each fraction in a specially designed microcell (Fig.1 (a)). Dose-response curves were established from the optical signal of the immunocomplex and unbound AuNP-Ab conjugate fractions (Fig.1 (c)).

To go further towards the development of a stand-alone device, we designed a microfluidic cell that integrates the magnetic separation and readout steps in a single device (Fig.1 (a)). Transposing the assay to a microfluidic chip enabled a dramatic decrease in the assay sensitivity with a LoD in the ng/mL range (Fig.1 (d)). In the future this immunosensor could be readily translated to more biological meaningful biomarkers related to health and/or food security.

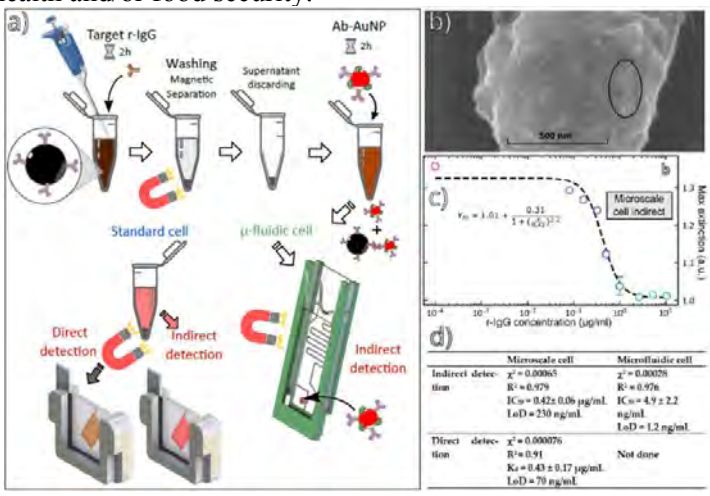


Figure 1 a) Schematic presentation of the general principal of magneto-plasmonic immunoassay, b) SEM image (15 kV, 10.3 mm, 80000×) of the magneto-plasmonic immunocomplex in the presence of 1 µg/mL of r-IgG and a black circle showing the presence of AuNPs, c) dose-response curve plotted from the maximum extinction at 530 nm vs. rabbit IgG concentration, d) Fitting parameters and analytical performances of the magneto-plasmonic immunosensor in the direct and indirect formats

References

[1] Wang, Yijia, et al. "Investigation of phase SPR biosensor for efficient targeted drug screening with high sensitivity and stability." Sensors and Actuators B: Chemical 209 (2015): 313-322

[2] Soroush, M., Ait Mammar, W., et al. "Design and Optimization of A Magneto-Plasmonic Sandwich Biosensor for Integration within Microfluidic Devices." Biosensors 12.10 (2022): 799.

Droplet microfluidic platform for drug screening on tumoroids

C. Parent[1]*, K. Raj[1], Y. Zhou[1], V. Aubert[1], O. Delattre[2], C. Wilhelm[1], J-L. Viovy[1]

[1]Institut Curie UMR 168, Paris, France
[2]Institut Curie, Paris, France
*caroline.parent3@curie.fr

Personalized medicine offers new perspectives for cancer treatment. Testing chemotherapies directly on the patient cells before treatment emerges as a significant improvement for both cancer treatment efficacy and time saving in the "race against cancer development". To do so, tumor spheroids or "tumoroids" are emerging as relevant models. They are easy and fast to produce and can in particular inform on the efficacy of different candidate drugs, directly on the patient's cancer cells. A main current limitation of this approach is the number of cells needed for multiplex assays, which is incompatible with micro-biopsies. This problem can be overcome by mouse "avatars" in which patient's cells are implanted and develop tumors ("PDX" for patient derived xenografts), but this takes several months [1]. Droplet microfluidic allows miniaturizing the assays and appears as an original and efficient tool for drug screening on tumoroids. Herein, we are proposing a microfluidic platform to culture tumoroids in droplets and test drugs on them. The system is based on an on-demand droplet merging strategy that allows sequential addition of compounds [2]. We then addressed the possibility to use this droplet microfluidic platform to determine efficiency of a compound through viability test on tumoroids issued from cells lines and primary PDX cells [3]. We were able to culture viable tumoroids for more than 3 days and to determine dose-response relationships to different drugs using the resazurin metabolic assay. It evidences that droplet microfluidics can be used to perform efficient drug screening on tumoroids and reveal a different response to chemotherapeutic drugs for such 3D environment, as compared to classical 2D culture.

References

[1] E. Stewart et al.: *Orthotopic patient-derived xenografts of paediatric solid tumours*. Nature **549.7670**, 96-100 (2017)

[2] J. Aubetert, A. Bendali: *Method of manipulating droplets in a channel*. Eur Pat Appl. N°18305818.9 (2018)

[3] V. Boeva, et al. : *Heterogeneity of neuroblastoma cell identity defined by transcriptional circuitries*. Nature genetics **49.9**, 1408-1413 (2017)

Thermal conductivity measurement of liquids using single resistive sensor within a Silicon-Pyrex microfluidic device

Rosa Moreno Jimenez[1,2*], Claire Marliere[1], Benoit Creton[1], Olivier Nguyen[2], Lionel Teule-Gay[2], Samuel Marre[2]

[1]IFP Energies nouvelles, 1 et 4 avenue de Bois-Préau, 92852 Rueil-Malmaison, France.

[2]CNRS, Univ. Bordeaux, ICMCB, UMR 5026, F-33600 Pessac, France

*e-mail: rosa.moreno@ifpen.fr

Thermal conductivity of liquids is an essential thermodynamic data required in the engineering design of thermal processes. For instance, transport properties involving mass and heat transfers are widely considered in industrial applications such as separators, reactors, or heat exchangers. More specifically, the knowledge of thermal properties leads to better designs and shorter development times for emission-control systems during the conversion process of biofuels containing oxygenated compounds.

Conventional methods to measure thermal conductivity are often time consuming and/or requires significant amount of products. Because of its low reagent consumption, fast screening, low operating times, improvement of heat and mass transfers, etc., microfluidics has been proven to be a viable solution that enables automated manipulation to conduct high throughput experimentation.

“High pressure and high temperature (HP-HT) microfluidics"[1] have gained great interest on the determination of the thermo-physical properties of fluids systems [2], [3], which are important because these address relevant industry needs. Microfluidic devices made of Silicon/Pyrex materials, provide thermal and mechanical resistance to temperatures up to 100 °C and pressures up to 100 bars. Besides, the high heat transfer coefficient of silicon allows accessing good control of the device temperature and Pyrex is used as a thermal/electrical insulator that provides an easy optical access for in-situ characterizations.

Because of the complexity of the sensor hardware or the data processing, existing techniques for measuring the thermal conductivity of small liquid samples or microfluidics, are frequently unsuitable for high throughput testing, restricted to room temperature conditions and to a small number of chemical families. This study presents a new microfluidic device made of Silicon/Pyrex materials that includes an in-situ resistive sensor capable of measuring thermal conductivity across a wider range of chemical families and temperature conditions [4]. We will also discuss the outcomes of the microfluidic device validation using model liquids at both room and high temperatures.

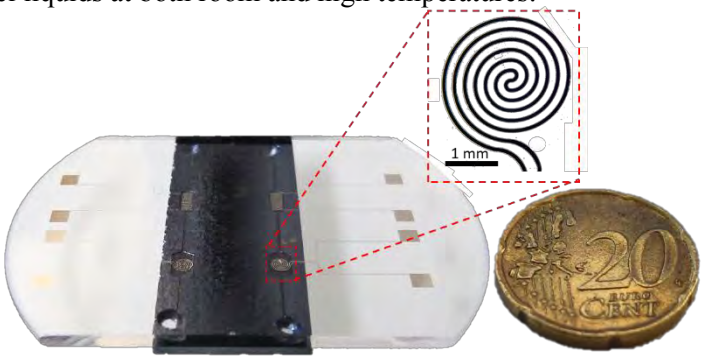


Figure 1: Schematic of the microfluidic device with a zoom in red frames of the sensor’s geometry: a metallic Spiral resistive element acting both as temperature sensor and heating source.

References

[1] Marre, S et al. Design and Packaging of Microreactors for High Pressure and High Temperature Applications. Ind. Eng. Chem. Res. 2010, 49 (22), 11310–11320

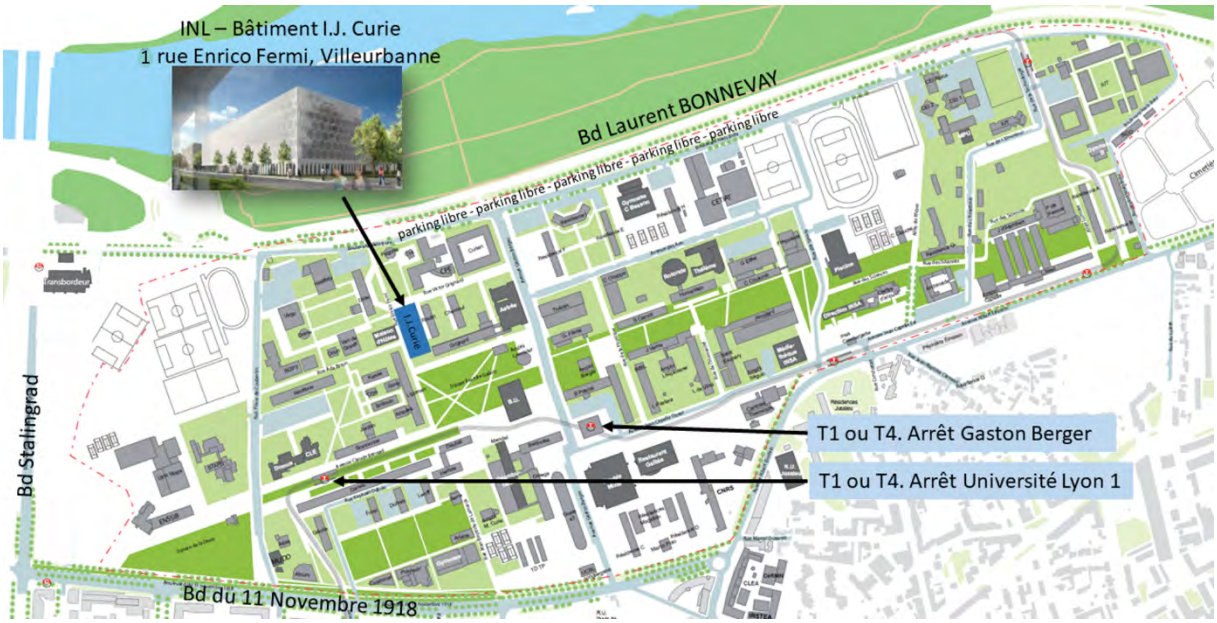
[2] B. Pinho et al. Microfluidic Investigation of Multicomponent Systems at high pressure and high temperature, Lab Chip, 2014, 14, 3843-3849

[3] T. Gavoille, et al. Microfluidics approaches for accessing thermophysical properties of fluids systems, Reaction Chemistry and Engineering, 2019, 4, 1721-.1739

[4] R. Moreno Jimenez, et al. A microfluidic device for accessing thermal conductivity of fluids systems over a wide range of temperature conditions. Submitted

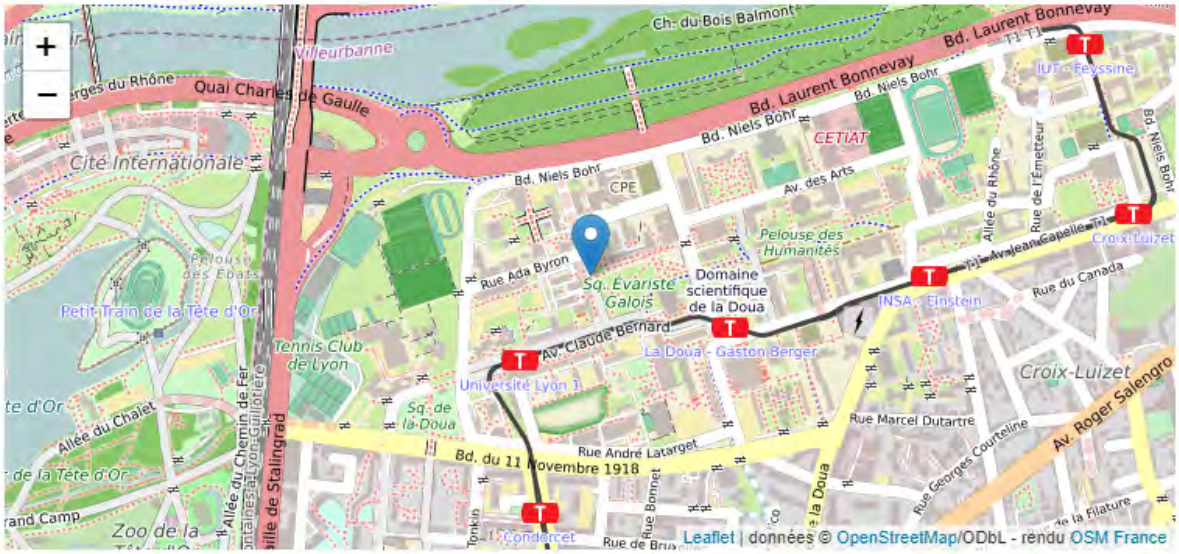
Useful information

The 2023 Plenary meeting presentations will take place in the **Irène Joliot-Curie building**, located at 1-3 rue Enrico Fermi on the Doua campus of Villeurbanne (see campus map below).



How to get to the Irène Joliot-Curie building?

• **By public transport:** The Lyon public transport network is operated by TCL. The Irène Joliot-Curie building is served directly by 2 tramway lines (T1 and T4) - at the same distance from « Université Lyon 1 » stop and « Gaston Berger » stop. Note that Lyon Part Dieu train station is also served by the T1 and T4 tramways (accessible at the normal price - 1.70 € the trip), and Perrache train station served by the T1 tramway.



Rejoindre le campus LyonTech – la Doua en tramway depuis les gares Part-Dieu ou Perrache
Itinéraires et horaires sur www.tcl.fr

T1 au départ de Lyon Part-Dieu (sortie gare côté Ouest)

15:09 Départ : Aujourd'hui
Gare Part-Dieu V.Merle (Lyon)
19 BOULEVARD MARIUS VIVIER MERLE (Lyon)
Prendre le **tramway T1**
Direction : **IUT Feyssine (Villeurbanne)**
Descendre à l'arrêt **Université Lyon 1**
11 min (6 arrêts)
15:20 **Université Lyon 1 (Villeurbanne)**
8 AVENUE CLAUDE BERNARD (Villeurbanne)

T4 au départ de Lyon Part-Dieu (sortie gare côté Est)

15:15 Départ : Aujourd'hui
Gare Part-Dieu Villette (Lyon)
Face au 53 RUE DE LA VILLETTE (Lyon)
Prendre le **tramway T4**
Direction : **La Doua - Gaston Berger (Villeurbanne)**
Descendre à l'arrêt **Université Lyon 1**
10 min (6 arrêts)
15:25 **Université Lyon 1 (Villeurbanne)**
8 AVENUE CLAUDE BERNARD (Villeurbanne)

T1 au départ de Lyon Perrache

15:13 Départ : Aujourd'hui
Gare SNCF Lyon Perrache (Lyon)
14 Cours de Verdun Rambaud (Lyon)
3 mn à pied
15:17 **Perrache (Lyon)**
25 COURS DE VERDUN PERRACHE (Lyon)
Prendre le **tramway T1**
Direction : **IUT Feyssine (Villeurbanne)**
Descendre à l'arrêt **Université Lyon 1**
27 min (15 arrêts)
15:44 **Université Lyon 1 (Villeurbanne)**
8 AVENUE CLAUDE BERNARD (Villeurbanne)

The Lyon Part Dieu train station can be reached from the Saint Exupéry Airport through the tramway line Rhône Express (round trip ~25€).

Rejoindre Lyon depuis l'aéroport Lyon Saint-Exupéry

La ligne de tramway RhôneExpress assure la liaison entre l'aéroport et la gare de Lyon Part-Dieu.
Aller-retour pour environ 25€.
Billetterie sur place ou sur www.rhonexpress.fr

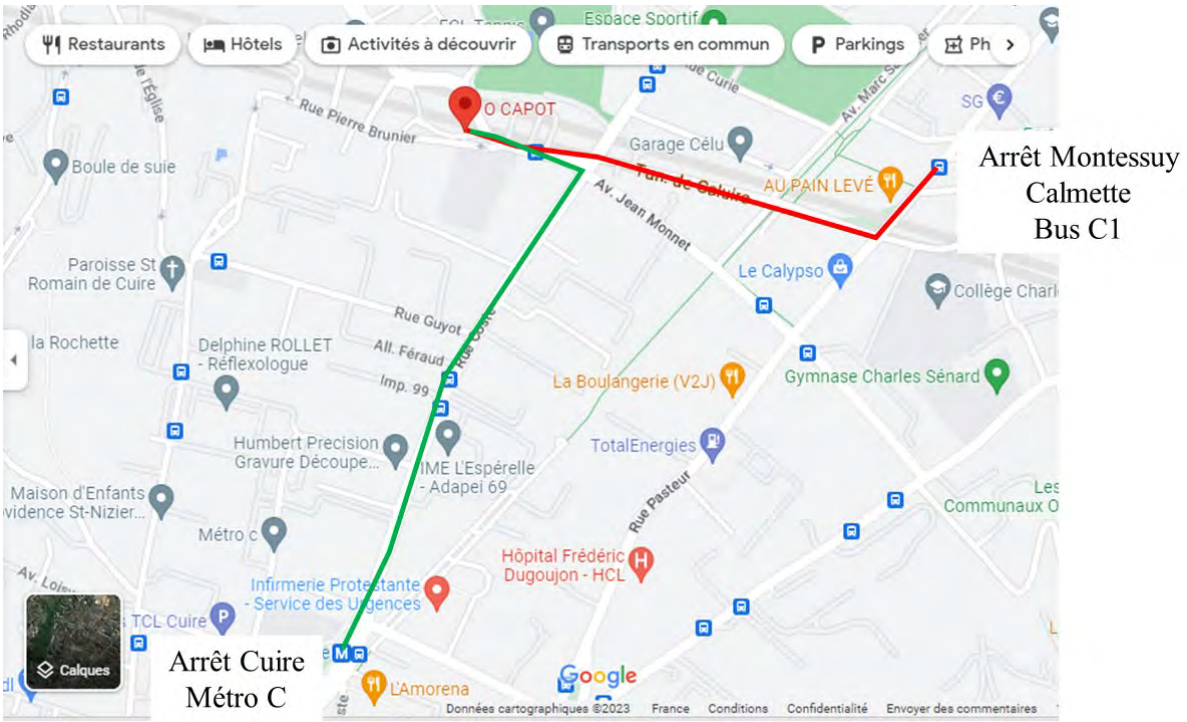
• **By car:** The Irène Joliot-Curie building is accessible by car. If you plan to park in the campus, please note that parking spaces are scarce and very quickly taken over. Possible parking spaces can be found at the periphery of the campus, on the side of Boulevard Laurent Bonnevay (see map).

Gala dinner

You are invited to a gala dinner on Monday 03 April at the **O'CAPOT restaurant** located at 51 Montée des Forts 69300 Caluire-et-Cuire.

We ask you to come between 8:00 pm and 8:30 pm.

To get to the restaurant from the Doua Campus, you can take the bus C1 at Cité Internationale (14 min by walk from Irène Joliot-Curie building), until "Montessuy Calmette" stop and walk 8 min to the restaurant (see red intinerary on the map). If you come from Hotel de ville de Lyon (city center), we advise you to take the Metro line C until the terminus « Cuire » station; then it is a 12 min walk to the restaurant (see green itinerary on the map).



Please make sure to bring **your badge**, your choice of menu is indicated on it.

Partner Institutions and Sponsors

Sponsors:

TreeFrog Therapeutics

TreeFrog Therapeutics is a French biotech company headquartered in Bordeaux, which aims to unlock access to cell therapies for millions of patients. Bringing together over 110 biophysicists, cell biologists, and bioproduction engineers, TreeFrog Therapeutics raised $82M over the past 3 years to advance a pipeline of stem cell-based therapies in immuno-oncology and regenerative medicine based on the proprietary C-Stem™ platform. TreeFrog's biomimetic technology allows for the large-scale expansion of pluripotent stem cells in standard bioreactors, and their differentiation into ready-to-transplant 3D microtissues. In 2022, the company opened technological hubs in Boston, USA, and Kobe, Japan, with the aim of driving the adoption of the C-Stem™ technology and establishing strategic alliances with leading academic, biotech and industry players in the field of cell therapy.
For more information: www.treefrog.fr

Fluigent

Fluigent is the global leader in providing fluid handling solutions for scientific & industrial research and a wide range of applications (diagnostic, vaccine, point of care, food) where fluid control is critical. Since its foundation, Fluigent has committed to set up the standards and to make progress in Microfluidics. More than 6 000 Microfluidics systems with the certification ISO 9001 have been employed by our customers in 50 countries around the world. For 15 years, Fluigent has strived to stay in the forefront of science. Our most innovative solutions facilitate and improve the work of worldwide R&D researchers. In 2020, Fluigent's microfluidic solutions saved 25,470 hours globally for R&D researchers.
For more information: www.fluigent.com

Kloé

Expertise in photolithography: mask aligners, maskless equipement & 3D printer
Benefitting from more than 22 years of experience, Kloe is a French **direct laser writer** and **mask aligner manufacturer** which offers the global range of photolithography equipment:

- The Dilase range, **maskless equipment** by direct laser writing and high resolution 3D printer, offers unique innovations: true vector writing mode, large depth of focus, dynamically controlled stages…
- The UV-KUB range, **exposure-masking system and new generation of mask aligners**, equipped with high quality collimated and monochromatic UV-LED light source.

All of this equipment can be used in laboratories, which eliminates the constraints and operating costs of a cleanroom.
Deployed in more than 45 countries around the world, soft lithography machines by Kloe are perfectly adapted to answer needs and constraints of researchers in many fields like microfluidics, microelectronics, photonics, MEMS, semiconductor manufacturing…
For more information: 2-4 rue des Arbousiers, 34270 St-Mathieu-de-Treviers, France - +33 467 821 910 - www.kloe-france.com - contact@kloe-france.com - https://www.linkedin.com/company/kloe-france/

Microlight3D

Microlight3D est un fabricant de machines de micro-impression 2D et 3D haute résolution. La société permet aux scientifiques et aux industriels qui recherchent de nouveaux outils de conception de produire des micro-pièces très complexes, dans n'importe quelle forme géométrique, avec une finition parfaite. En combinant des techniques de micro-impression 2D et 3D, Microlight3D offre à ses clients une plus grande flexibilité pour la création de pièces complexes. Les équipements de Microlight3D sont conçus pour des applications en micro-optique, en micro-fluidique, en micro-robotique, dans les méta-matériaux, la biologie cellulaire et la microélectronique. Créée en 2016, après 15 années de R&D à l'Université de Grenoble-Alpes (UGA) sur sa technologie de polymérisation à deux photons, Microlight3D est installée à Grenoble.
Pour plus d'informations: www.microlight3d.com et sales@microlight3d.com

Netri

NETRI is a technology enabling company that provides human cell based smart assays for high throughput preclinical data acquisition for the neurological Pharma & Cosmetics industries. NETRI provides organs-on-chip solutions & interoperable *in-vitro* models designed to deeply accelerate drug discovery and preclinical trials by mimicking in vivo neural connectivity. With more than 45 employees, including 12 PhDs as part of a multidisciplinary team (engineering, biology and digital), NETRI is located in Lyon (France) with 300 m² of clean rooms and P2 laboratories.
For more information: www.netri.com et contact@netri.com

Idylle

Idylle is the tech transfer platform that produces innovative tools for life sciences researchers.
We believe that the best R&D tools invented in the best laboratories can change and accelerate research. We want to build the flow that will bring these just-published technologies to the research communities. We have therefore created a product development platform which, in a few months, transforms a know-how into an innovative product. We manufacture and deliver these products for research use to scientific communities around the world.
This unique development and production framework creates immediate value both for innovative researchers who can use the most recently published tools, and for their inventors who disseminate them throughout the world.
Idylle was founded in 2019 by the CNRS and Quattrocento, the startup studio for the life science tools. The platform is driven by a solid industrial methodology based on continuous feedback from the product users. It is backed up by the intelligence of a proprietary machine learning software to help manage a pipeline of +100 projects. With a head office and 125m² of laboratories in Paris, its teams of tech transfer and product development experts are spread between Montpellier, Bordeaux, Grenoble and Annecy.
For more information: www.idylle-labs.com

Eden Tech

Eden Tech révolutionne l'ensemble du processus de la microfluidique, y compris le prototypage et la fabrication. En 2017, Eden Tech a été créée pour exploiter le potentiel de la microfluidique avec de nouvelles solutions permettant une production microfluidique massive pour une application industrielle. Par le biais d'Eden Materials, actuellement dans le marché, nous présentons notre produit principal Flexdym, un polymère de prototypage biocompatible, remplaçant le PDMS pour la fabrication de laboratoires sur puces (lab-on-a-chip), doté de propriétés de liaison et d'assemblage avancées. Bientôt, Eden Tech lancera une application en ligne, qui est un simulateur de conception microfluidique gratuit pour la validation rapide de l'écoulement des fluides, ainsi que l'impression 3D et l'usinage de haute précision pour la fabrication de moules à l'échelle nanométrique de haute qualité, y compris ceux à profil arrondi.
Aujourd'hui, Eden Tech grandit au-delà de uniquement Eden Materials, et apporte une nouvelle technologie révolutionnaire : Biomimétique & Microfluidique combinés, pour une nouvelle ère d'industrie durable, devenant la première compagnie à développer de nouveaux grands projets de Microfluidiques massifs. En nous inspirant des modèles de la nature et en utilisant nos solutions de microfabrication, nous concevons de nouvelles applications pour un traitement de fluide à grand volume dans un design compact. Notre projet ASCANDRA est le premier système de filtration d'eau ultra-compact, reposant sur des CD microfluidiques entassés et visant à filtrer les microplastiques de l'eau, avec un débit de 0.4 à 1.5m3/s. AKVO est notre solution de traitement de l'eau ciblant les micropolluants, bactéries et virus, dédiée aux traitements tertiaires pour la production d'eau, la réutilisation de l'eau et l'assainissement avant rejet. AKVO a remporté le prix i-Lab by BPI en 2020. La solution Green Hydrogen (MacGhyver) permet une grande production hautement efficace d'hydrogène à partir des eaux usées et de l'eau de mer. La microfluidique biomimétique peut aussi soutenir les systèmes dont elle a été inspirée, comme nous le faisons dans le développement de notre gamme MedTech, notamment le projet du poumon artificiel.
Contact :
Adresse : 4 Rue de Rambervillers, 75012 Paris
Numéro : 01 88 32 74 05
Mail: Mme Nour Chebbi, Cheffe Marketing & Communication
nour.chebbi@eden-microfluidics.com

Advanced Microfluidics SA

Advanced Microfluidics, spin-off from EPFL in Lausanne, provides innovative microfluidic technologies for instrumentation dedicated to industries and academics, with an important focus on robustness, quality, performance and cost. They create microfluidic solutions like valves or pumps with very low internal volumes and designed for easy and smart integration for biotech, Medtech and life science applications. They aim to make your sequential dispensing protocol simple, precise and with minimal contamination.
For more information : www.amf.ch

Klearia

Klearia is a Deep Tech company specialized in microfluidics, analytical chemistry and instrumentation.
With over 10 years of experience in numerous field such as food industry, cosmetics and healthcare, we help you develop disruptive technologies for your industrial or academic projects.
Our turnkey offer goes from early-stage development (design thinking, feasibility study, instrumentation…) to the scale-out/scale-up of a product.
Through our foundry LabinGlass®, we also propose custom glass chips manufacturing.

Marcela LAPARRA
International Business & Sales Manager
marcela.laparra@klearia.com

Guillaume Laffite, PhD
Project manager-Microfluidics
guillaume.laffite@klearia.com

Cluzeau

Depuis plus de 40 ans, l'activité de CIL CLUZEAU INFO LABO se développe autour de la fabrication et du négoce de consommables et accessoires pour les nanotechnologies, la Chromatographie Liquide Haute Performance, la Chromatographie Gazeuse et le Transfert de Fluides.

Nous proposons une large gamme de produits comprenant des raccords, des tubes, des vannes, des dégazeurs, des colonnes et phases HPLC & GC, des seringues, des filtres, des dispositifs d'étanchéité de solvant, des pompes, des diviseurs de débit, des flacons, des bouchons et des joints.
Distributeur officiel des sociétés Idex (Upchurch, Rheodyne, Systec, IST) et Vici/Valco/Jour, Cluzeau Info Labo est votre partenaire unique de haute qualité pour l'ensemble de la voie fluidique.
Conseil, disponibilité et service rapide au client sont notre philosophie.
Pour plus d'informations: www.cluzeau.com | cil@cluzeau.com | tel : 05 57 46 00 44

Public Institutions:

ENS – Ecole Nationale Supérieure de Lyon

L'École normale supérieure de Lyon est une grande école scientifique et littéraire française, l'une des quatre écoles normales supérieures. Elle forme à l'enseignement et à la recherche dans le domaine des sciences fondamentales et expérimentales ainsi que dans celui des lettres et sciences humaines.

Département GEP - UCBL

Le **Département - Composante Génie Electrique et des Procédés** de l'Université Claude Bernard Lyon 1 est une structure qui regroupe des acteurs (chercheurs, enseignants-chercheurs, personnels techniques et administratifs) et des moyens (financiers et matériels) impliqués dans le développement de la recherche et de la formation en **Génie Electrique et des Procédés** à l'Université.
Il organise des formations au niveau licence (Bac+3) et master (Bac+5) dans le domaine de **l'Electronique-Energie Electrique- Automatique**, ouvertes sur le monde socio-économique :

- **La licence EEEA** avec notamment un parcours de **Double licence EEEA-Physique**
- **Le master EEEA** avec quatre parcours, dont certains proposés en alternance : Automatique des systèmes intelligents, Electronique Instrumentation Informatique Embarquées, Electronique Systèmes Embarqués, Energie électrique

La formation à/et par la recherche est menée au sein des trois laboratoires de recherche associés à la composante dans les domaines de l'énergie, les micro-nanotechnologies et le traitement de l'image :

- le laboratoire AMPERE
- le Centre de Recherche en Acquisition et Traitement de l'Image pour la Santé (**CREATIS**)
- l'Institut des Nanotechnologies de Lyon (**INL**)

CNRS

Le Centre national de la recherche scientifique est une institution de recherche parmi les plus importantes au monde. Pour relever les grands défis présents et à venir, ses scientifiques explorent le vivant, la matière, l'Univers et le fonctionnement des sociétés humaines. Internationalement reconnu pour l'excellence de ses travaux scientifiques, le CNRS est une référence aussi bien dans l'univers de la recherche et développement que pour le grand public.

ECL – Ecole Centrale de Lyon

Fondée en 1857, l'École Centrale de Lyon est l'une des premières écoles d'ingénieurs en France ; elle accueille plus de 3000 étudiants de 50 nationalités sur ses campus d'Écully et de Saint-Étienne (ENISE, école interne), dans ses formations d'ingénieur généraliste et d'ingénieur de spécialité, en master et en doctorat. Les formations dispensées combinent sciences fondamentales et ingénierie, sciences économiques, humaines et sociales, au travers d'activité théoriques et pratiques, de projets de groupe et de mises en situation professionnelle. Elles mêlent expertise disciplinaire et capacité à interagir avec des disciplines multiples, dans le cadre d'une approche système particulièrement pertinente pour répondre aux grands enjeux scientifiques et aux transitions sociétales. Les programmes d'enseignement s'appuient sur l'excellence des travaux conduits dans 6 laboratoires de recherche (Unités Mixtes de Recherche avec le CNRS) situés sur les deux campus, 2 laboratoires internationaux avec les Universités de Sherbrooke et de Tohoku, 6 réseaux ou projets de recherche internationaux ainsi que 10 laboratoires conjoints avec des partenaires industriels. Membre du Groupe des Écoles Centrale, Centrale Lyon entretient des liens privilégiés avec trois écoles internationales affiliées, au Maroc, en Chine et en Inde. Les travaux de recherche en sciences de l'ingénieur, sciences de l'information et sciences exactes sont menés en partenariat fort avec des acteurs industriels, de grands organismes publics et des partenaires mondiaux pour apporter des réponses pertinentes aux défis sociétaux actuels : technologies plus sobres, transition énergétique, préservation de l'environnement et décarbonation. Le spectre disciplinaire des laboratoires de recherche reconnus internationalement est large : matériaux et leurs interfaces, acoustique, mécanique des fluides et des structures, génie civil, nanotechnologies, bio-ingénierie, électronique, électrotechnique, automatique, mathématiques, informatique, robotique, perception, usages, innovation et management. Des plateformes technologiques uniques en Europe permettent à la fois la compréhension de phénomènes physiques fondamentaux et la réalisation d'expériences répondant aux enjeux industriels dans les domaines de l'énergie, des transports, de l'environnement, de la santé, des nanotechnologies, de la bio-ingénierie, des procédés et de la construction.

INL – Institut des Nanotechnologies de Lyon

L'Institut des Nanotechnologies de Lyon (INL) est une Unité Mixte de Recherche (UMR 5270) dont les tutelles sont le CNRS, l'ECL, l'INSA, l'Université Lyon 1 et CPE Lyon. L'INL a pour vocation de développer des recherches technologiques multidisciplinaires dans le domaine des micro et nanotechnologies et de leurs applications. Les recherches menées s'étendent des matériaux aux systèmes, laboratoire s'appuie sur la plate-forme technologique lyonnaise NanoLyon. Les domaines d'application couvrent de grands secteurs économiques : l'industrie des semiconducteurs, les technologies de l'information, les technologies du vivant et de la santé, l'énergie et l'environnement.
Le laboratoire est multi-sites avec des localisations sur les campus d'Ecully et de Lyon-Tech La Doua. Il regroupe environ 200 personnes dont 121 personnels permanents. L'INL est un acteur majeur du Pôle de Recherche et d'Enseignement.

CPE

Située sur le campus universitaire LyonTech – La Doua, CPE Lyon forme des ingénieurs en chimie-génie des procédés et sciences du numérique depuis près de 30 ans.
Créée en 1994 de la fusion de deux écoles centenaires, CPE Lyon puise son histoire et son statut original dans le berceau industriel lyonnais.
Implantée sur un site unique au cœur d'un pôle de formation et de recherche majeur en France, de statut associatif privé mais adossée à des partenaires institutionnels publics, CPE Lyon rassemble une communauté de 8500 diplômés en activité.

ILM – Institut Lumière Matière

L'institut Lumière Matière (iLM) est une unité de recherche CNRS-Université Lyon 1 localisée sur le campus Lyon Tech La Doua. Avec environ 300 collaborateurs dont une centaine de doctorants et post-doctorants, l'iLM est un acteur majeur de la recherche en physique et chimie sur la région Auvergne Rhône Alpes, reconnu internationalement pour l'excellence de sa recherche.
Le continuum entre la recherche fondamentale, la réponse aux grands défis sociétaux et l'innovation est au cœur de la démarche de cette unité. L'ensemble du personnel s'engage pour promouvoir l'excellence et une recherche éthique et responsable.
Ses scientifiques explorent six grands champs thématiques :

- Matériaux, énergie, photonique
- Matière molle
- Nanosciences
- Optique et dynamique ultrarapide
- Théorie et modélisation
- Vivant, santé, environnement.

Sa plateforme technologique ILMTech, passerelle pour l'innovation, propose des instruments de pointe et une expertise au service des acteurs académiques et du monde socio-économique.