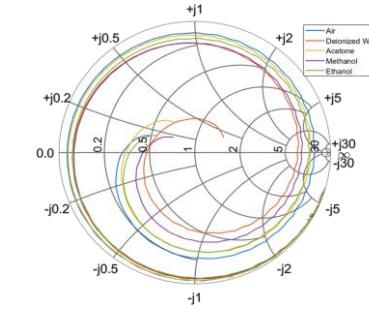
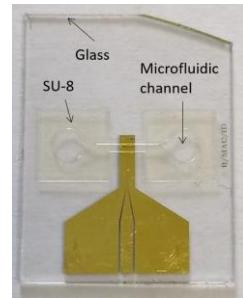
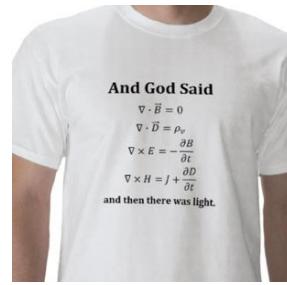




Capteurs électromagnétiques (RF) pour la caractérisation diélectrique de milieux biologiques : apport des Microtechnologies

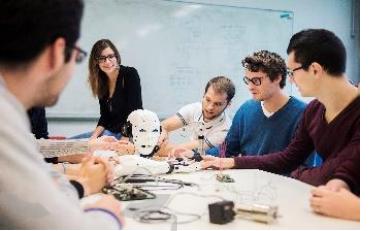


Olivier Français

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GDR SEEDS : Energie Electrique – Santé – Environnement

Juin 2022



Research Interests : Applied Physics and Biology

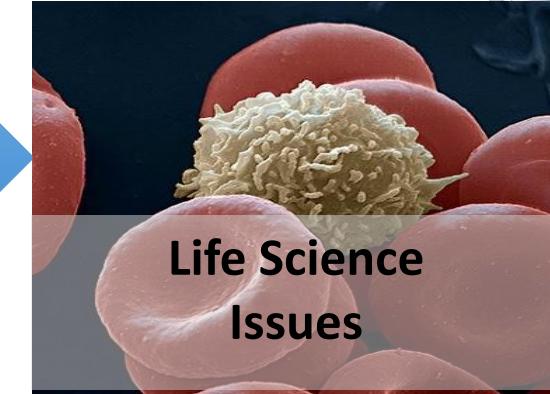


Maxwell's
Equation

$$\begin{aligned}\nabla \cdot D &= \rho \\ \nabla \cdot B &= 0 \\ \nabla \times E &= -\frac{\partial B}{\partial t} \\ \nabla \times H &= \frac{\partial D}{\partial t} + J\end{aligned}$$

Interaction

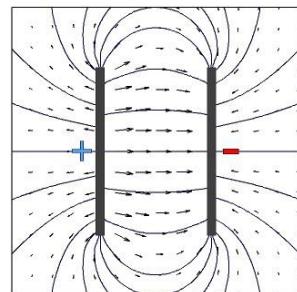
Case of
« Electric » Field



Life Science
Issues

« Electrical Engineering approach on biology»

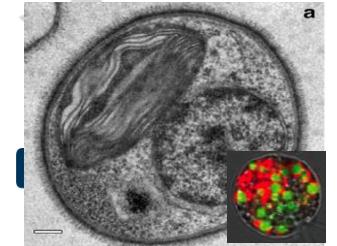
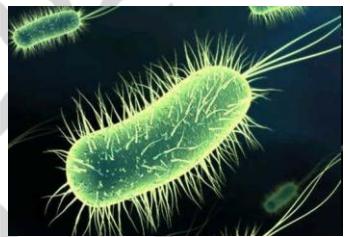
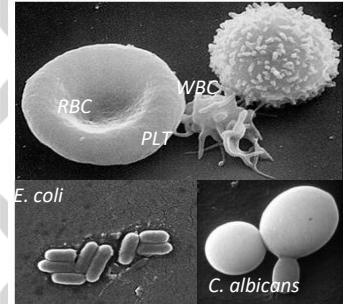
- Fundamentals aspects : understand the effects of Efield on living things
- Application aspects : imaging and acting on living organisms using Efield Sensors and Actuators



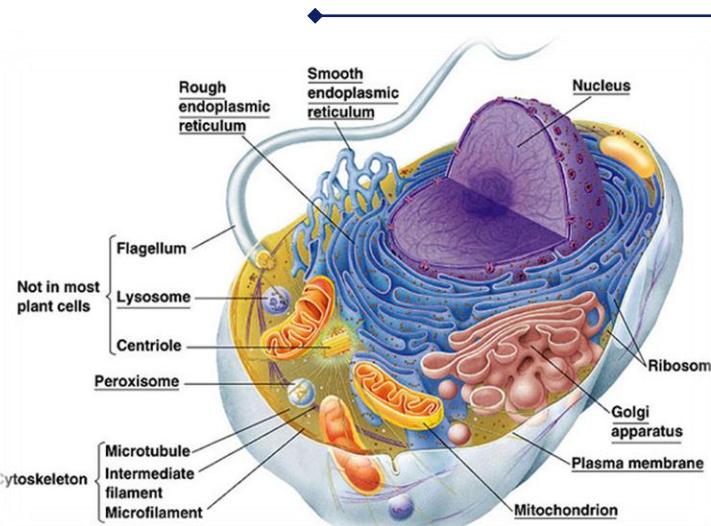
$$\vec{E} = \frac{U}{d} \vec{u}_x$$

Techniques

- | | | |
|---------------------------------------|-----------------------------------|------------------|
| - Impedancemetry (AC) | - Di-Electrophoresis (AC) | - Electroosmosis |
| - Electrochemistry; EIS (AC/DC) | - Electropermeabilisation (Pulse) | - Electrothermal |
| - Dielectric spectroscopy (AC) | - Electrophoresis (DC) | - ... |



Biological Cell for an Applied Physicists : Electrical modeling



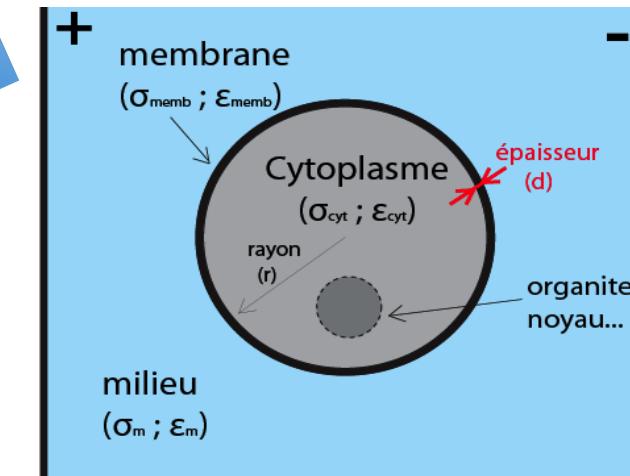
	Conductivity (S/m)	Permittivity (F/m)
Membrane	3e-7	6
Cytoplasm	0.4	40
Medium	1.5	80



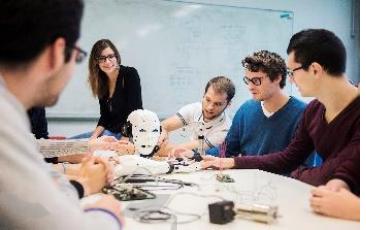
An assembly of several dielectric materials within liquid (**water**)
Equivalent to a « complex » **electrolyte**

Complex permittivity

$$\epsilon_{(i)}^* = \epsilon - j \frac{S}{W}$$

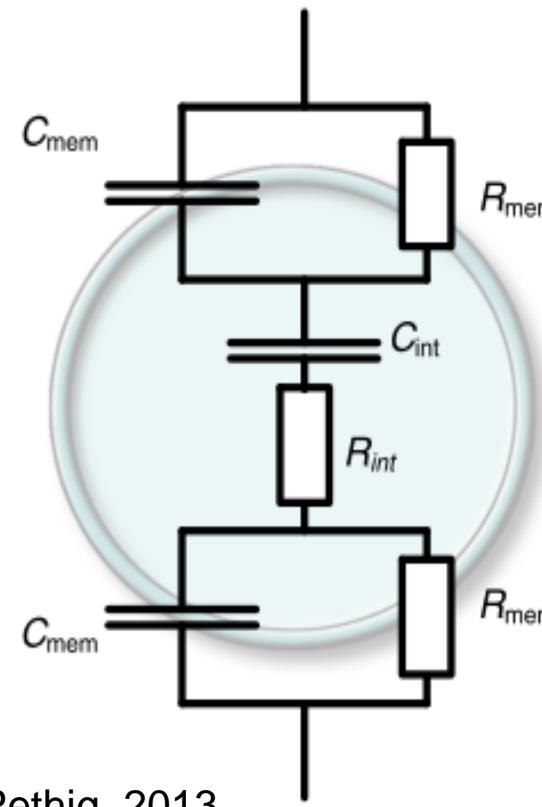


Ion	K^+	N_a^+	M_g^{2+}	C_a^{2+}	Cl^-	HCO_3^-
$C_{intracellulaire}$ (mM)	160	7-12	5	$10^{-4} - 10^{-5}$	4-7	8
$C_{extracellulaire}$ (mM)	4	144	1-2	2	120	26-28



Cellular behavior under Electric Field

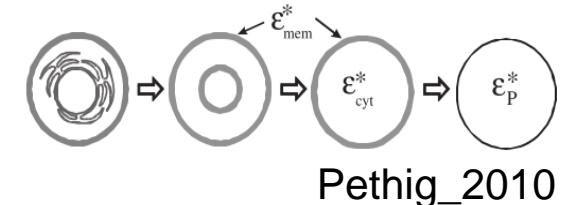
* Electric Schematics



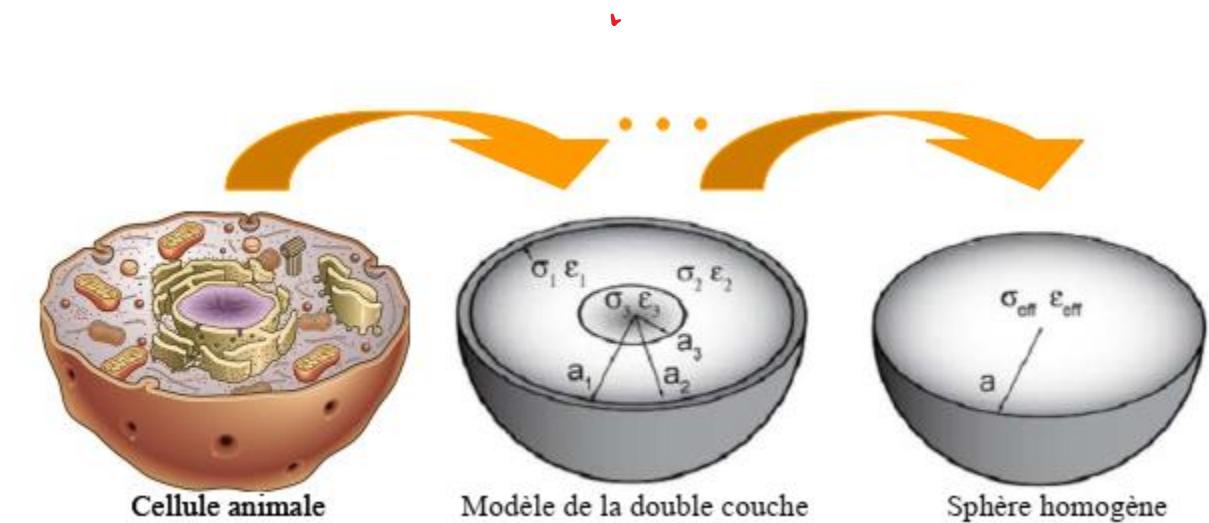
Pethig_2013

→ Bio-Impedance (Ionic conduction)
frequency range below 100 MHz

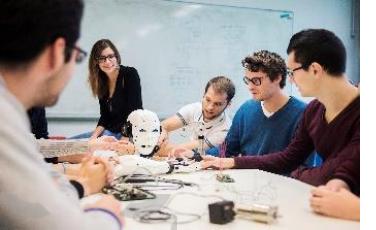
* Dielectric Material



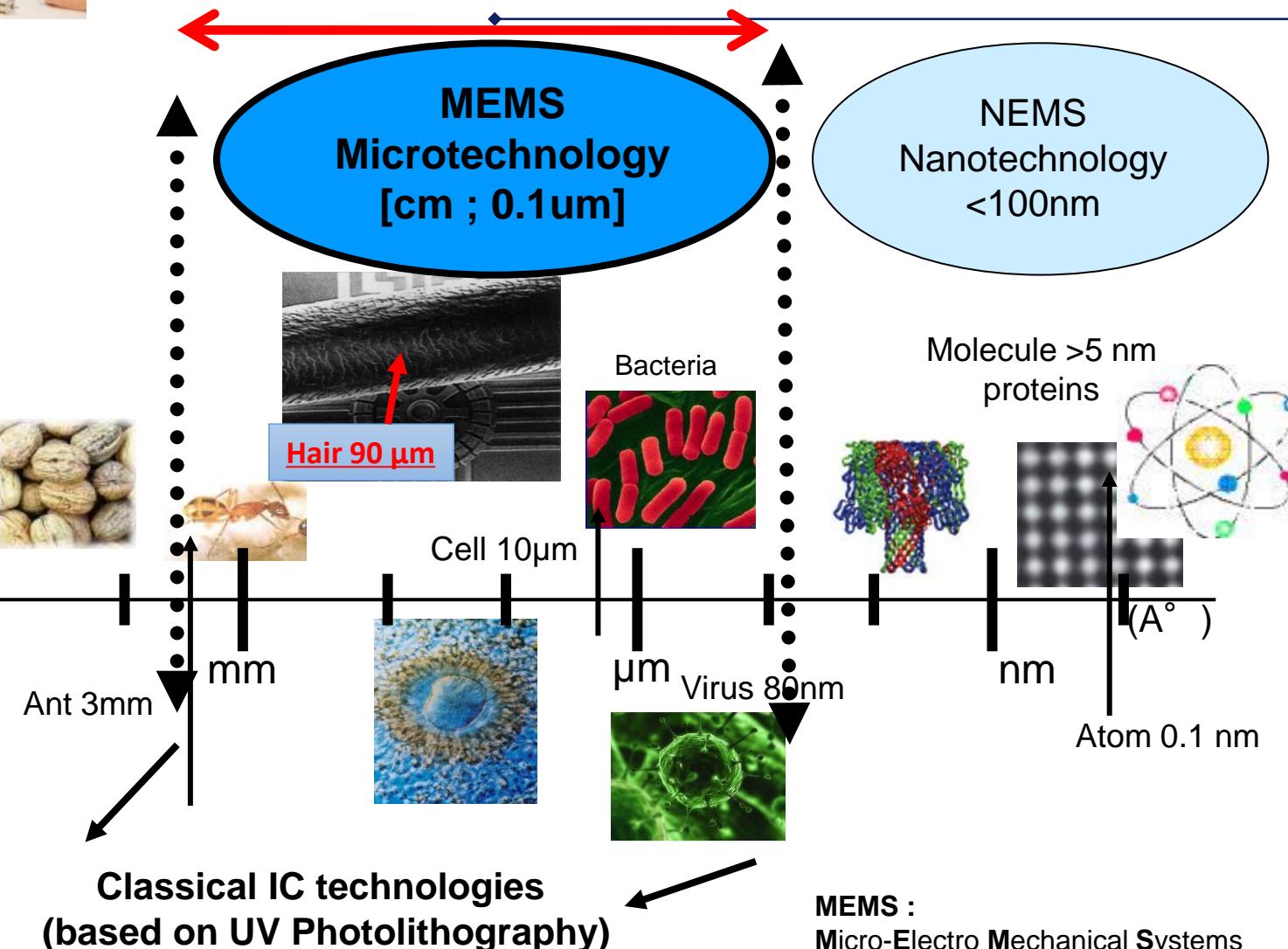
Pethig_2010



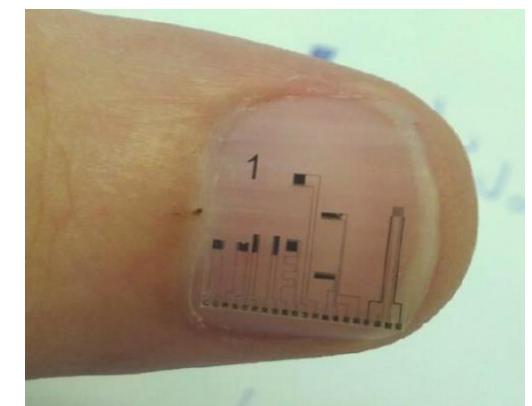
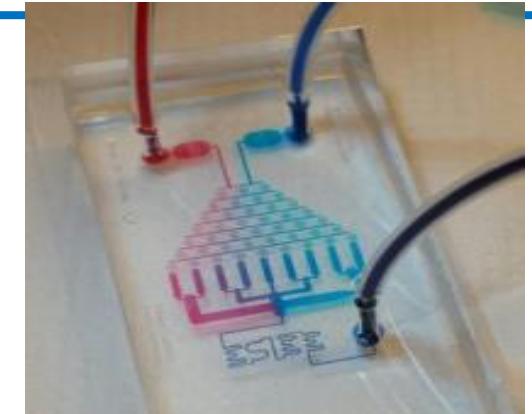
→ Dielectric properties (Polarisation effects)
frequency range above 100 MHz up to several GHz



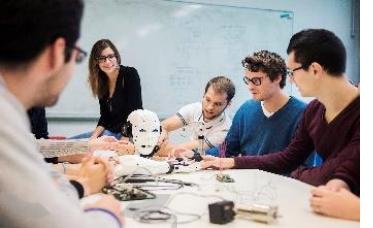
Micro-devices and biology : Order of magnitude Size and scale



Technology associated :
MEMS & Microfluidics

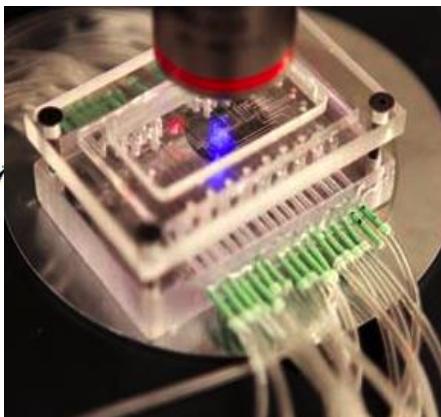
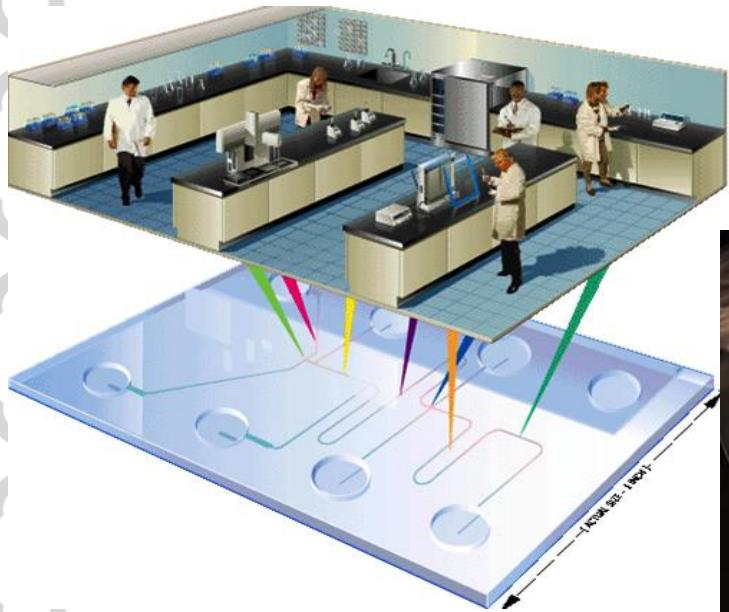


Process : Silicon, Glass and polymer
 \rightarrow μ Sensors, Lab On a Chip...



Lab - On – a - Chip

Combining MicroTechnology – Physics - Biology



Integrating in a « Credit Card » format
all steps of a sample analysis

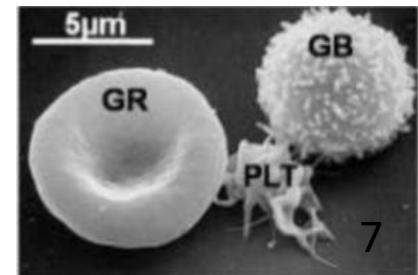
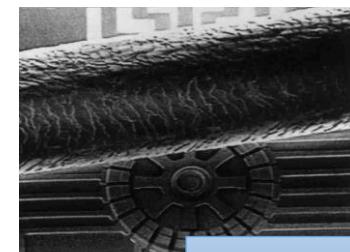
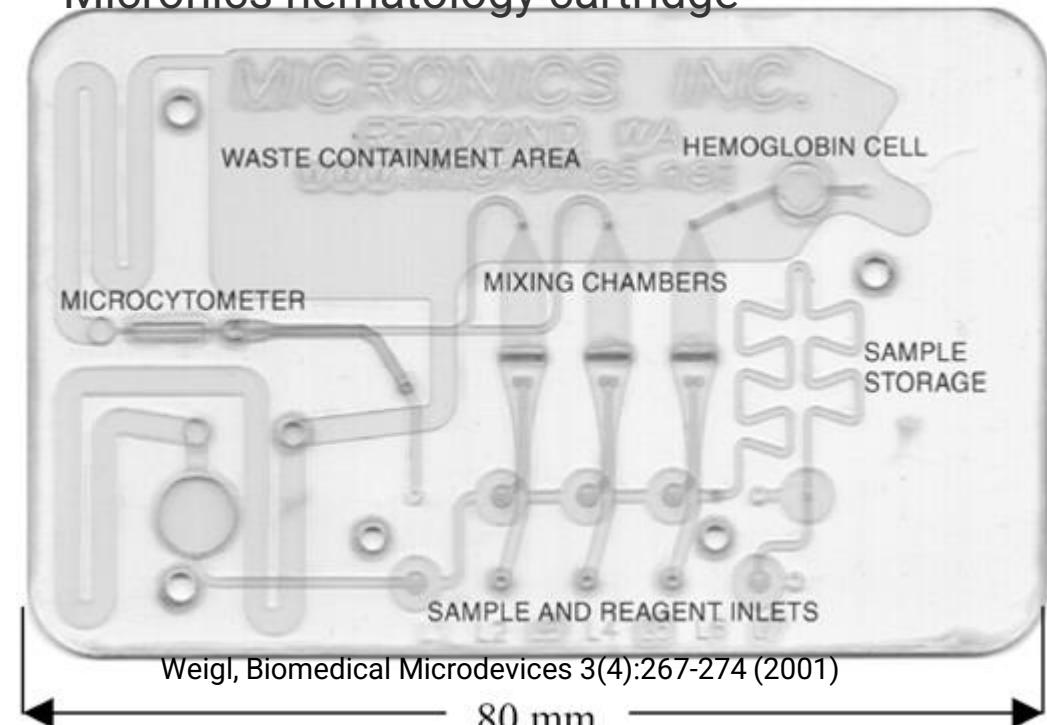
Sample → Separation → Detection → Analysis

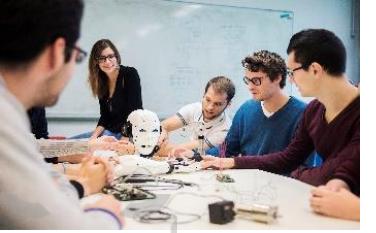


Blood
Food
Air...



Micronics hematology cartridge





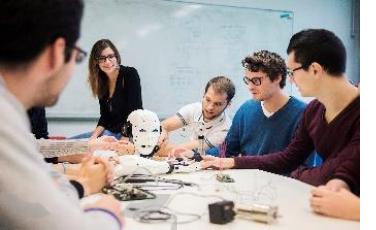
Interaction between Cells and Electric Field within microfluidic devices



Bio-Impedance
↓
SENSING

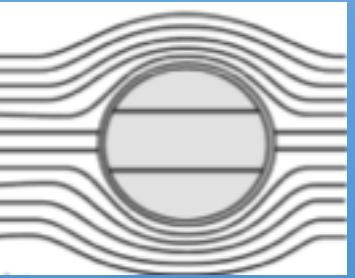
Dielectric Spectroscopy
↓
Medium analysis

Cell polarisation
↓
Cell sorting and trapping



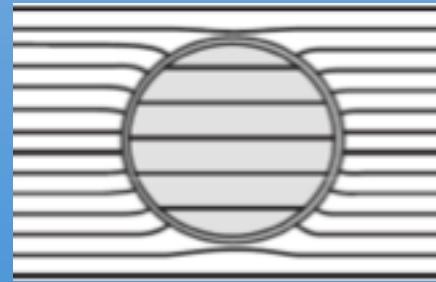
Global Cell behavior submitted to an AC electric field – Static field

$f < 1\text{kHz}$



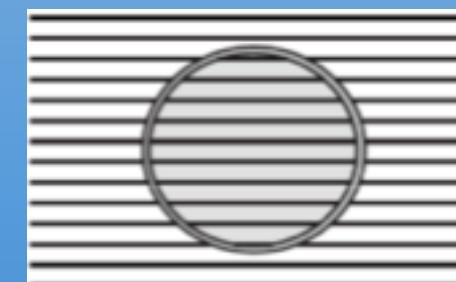
Insulator
Link to the size of the cell

$f \approx 100\text{ kHz}$

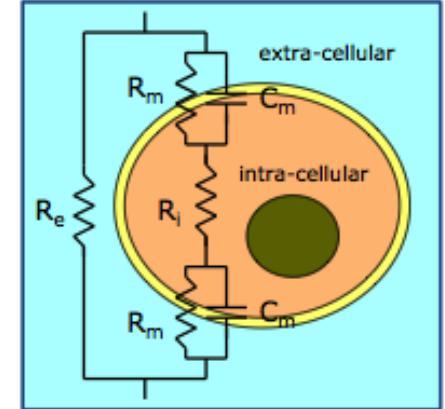


Membrane polarisation
Link to the membrane structure

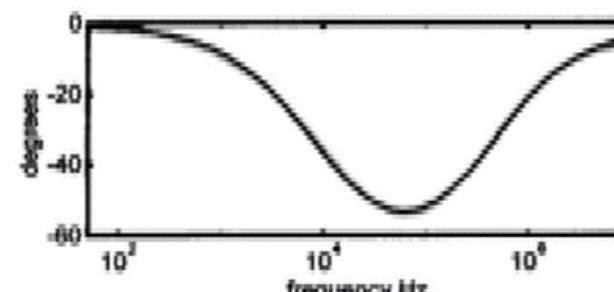
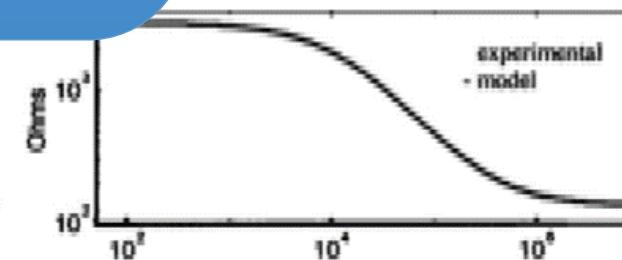
$f > 10\text{MHz}$



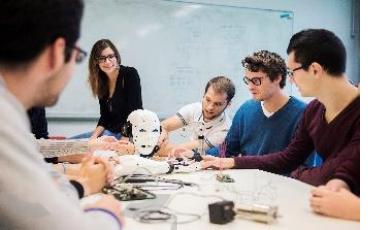
Access to the cytoplasm
→ Cytoplasm Conductivity



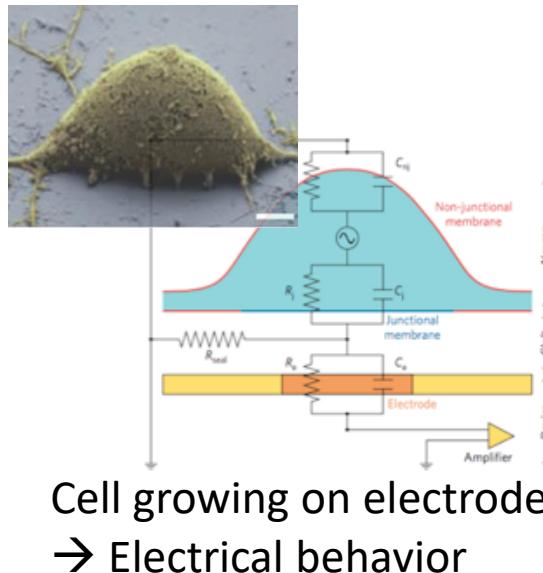
Frequency dependance behavior
→ Electrical Impedance Spectroscopy to monitor physiological state



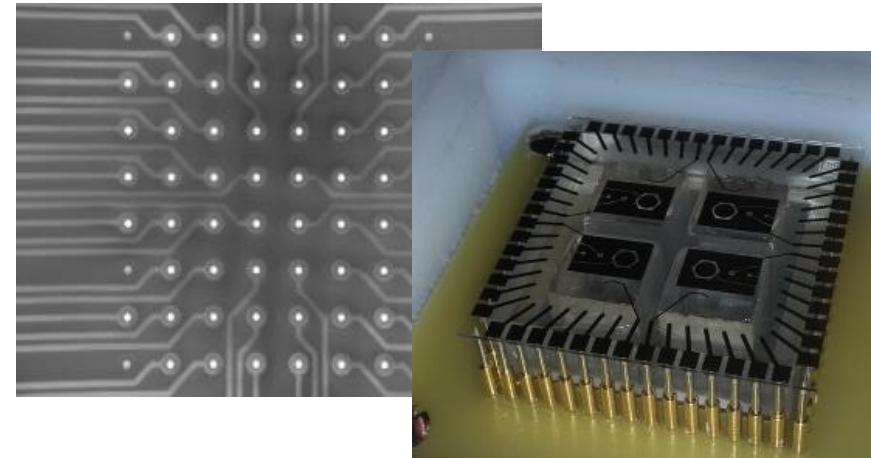
10



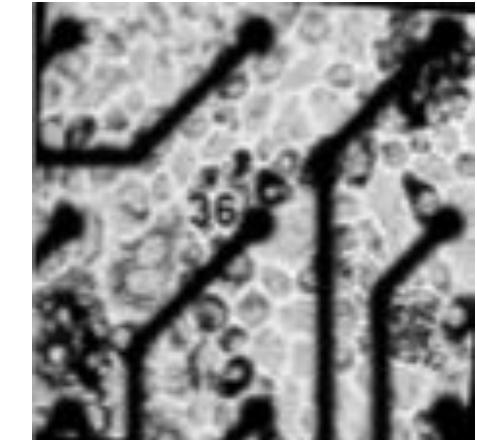
Monitoring of cell growth using bio-impedance



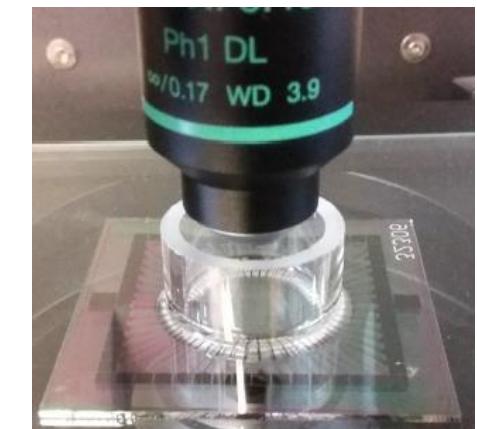
Petri Dish (cell culture box) with Micro Electrode Array



Biosensors and Bioelectronics, Elsevier, 2020, 161, pp.112180. (10.1016/j.bios.2020.112180)



Impedance monitoring with time



Non contact cell monitoring (label free) :
Optical and electrical without « probes »

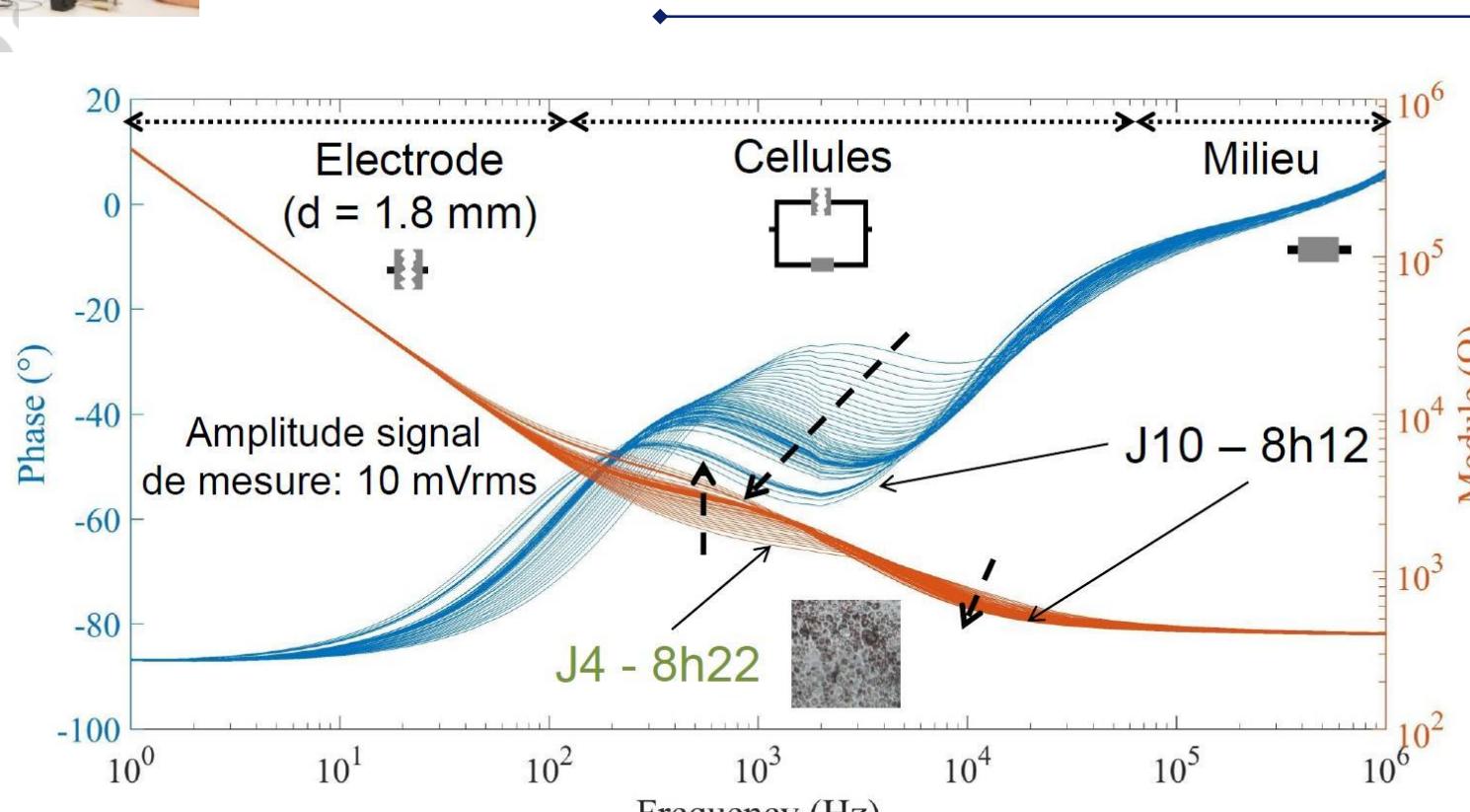


ESIEE
PARIS

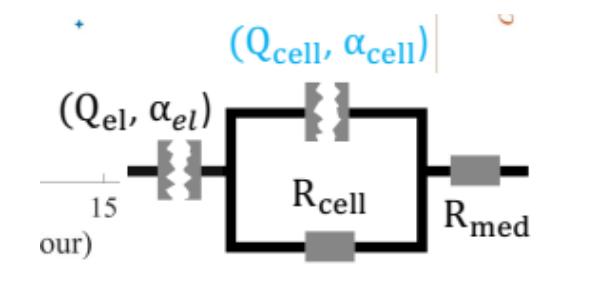
J. Boutzen Thesis



Monitoring of retinal cell development : long time (2 weeks)



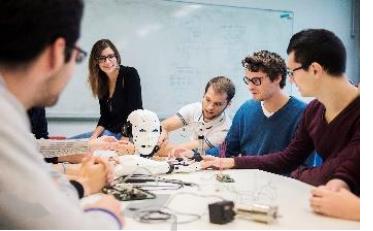
Biosensors and Bioelectronics, Elsevier, 2020, 167,
pp.112469. (10.1016/j.bios.2020.112469).



→ Parameters extraction



Establishment of indicators for monitoring cell growth



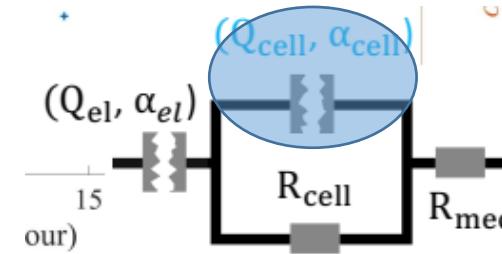
Monitoring retinal cell mortality under blue light exposure

Case of retinal pigment epithelium

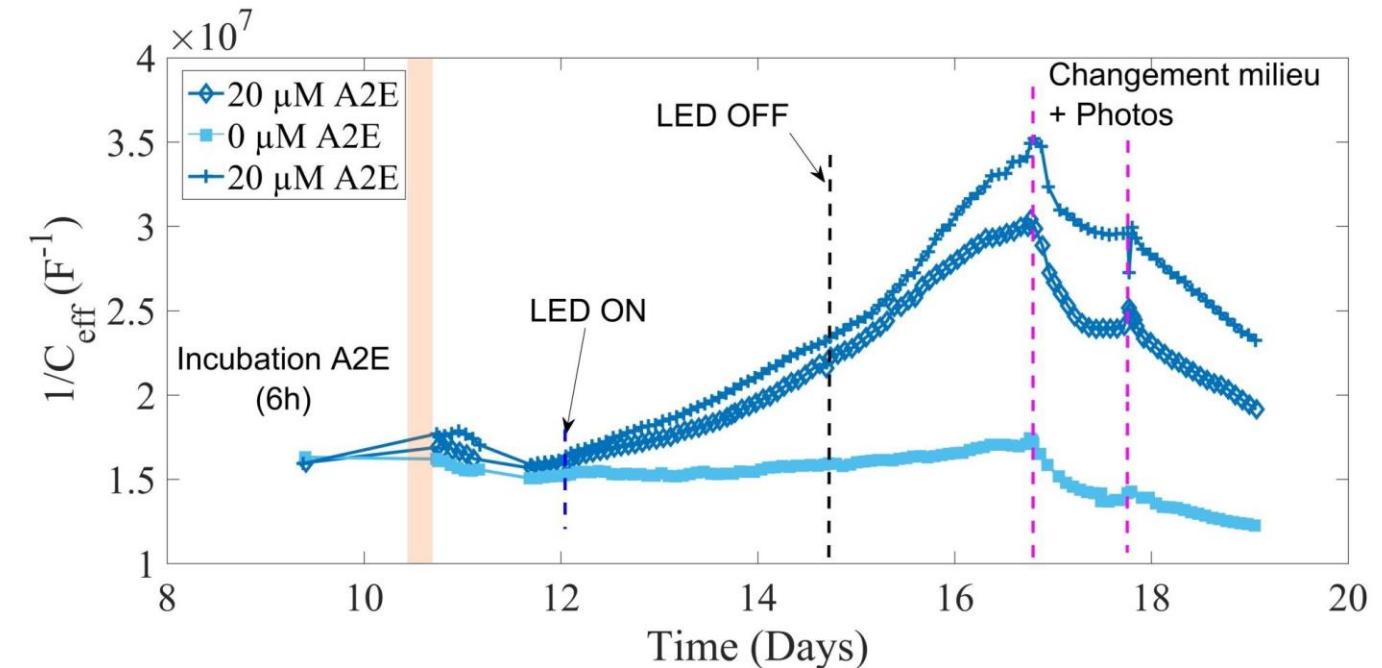


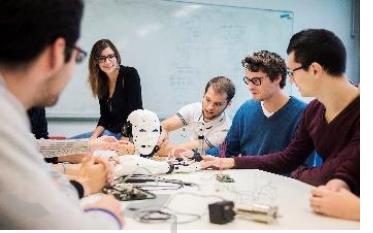
Impact of A2E (photosensitizer) inducing lesion on RPE under Blue light exposure

A2E : N-retinylidene-N-retinylethanolamine



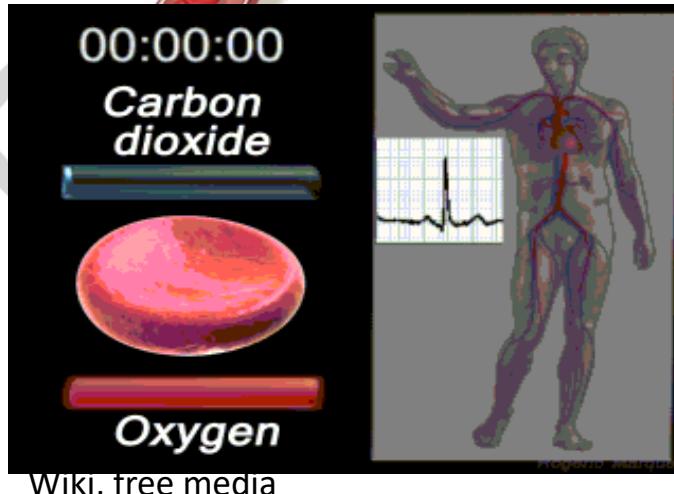
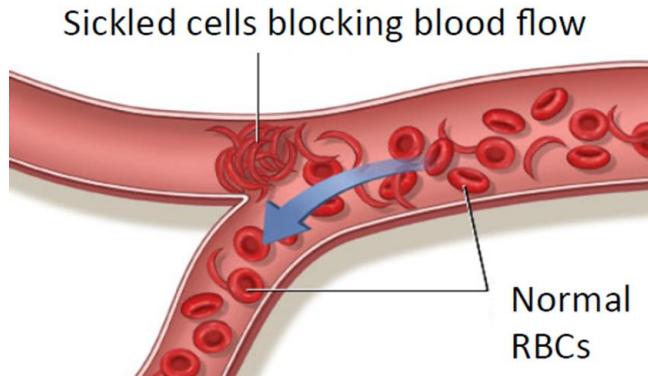
Membrane capacitance monitoring
→ Integrity of the cellular membrane



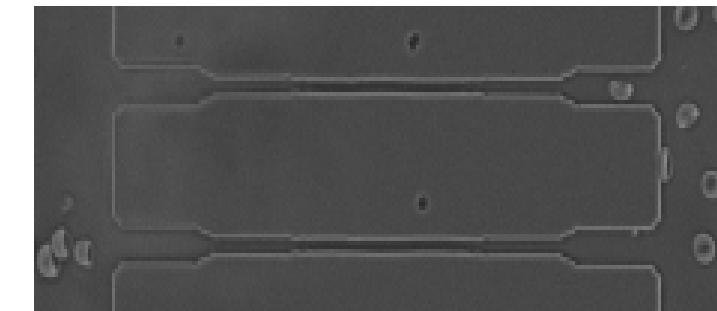
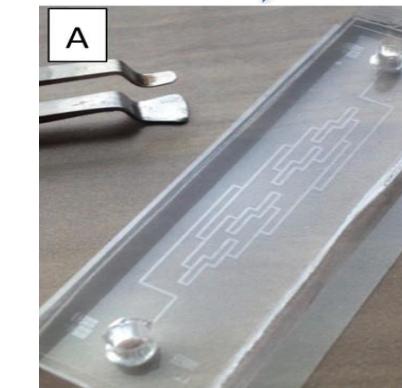


Micro-devices for sickle cell disease study

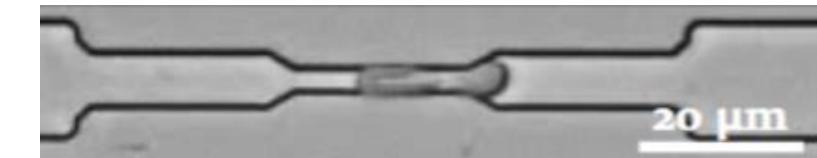
Sickled cell



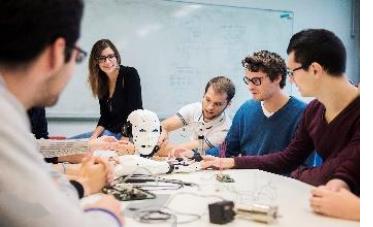
Blood flow mimetic micro-device



[Picot_2015_AMJH]

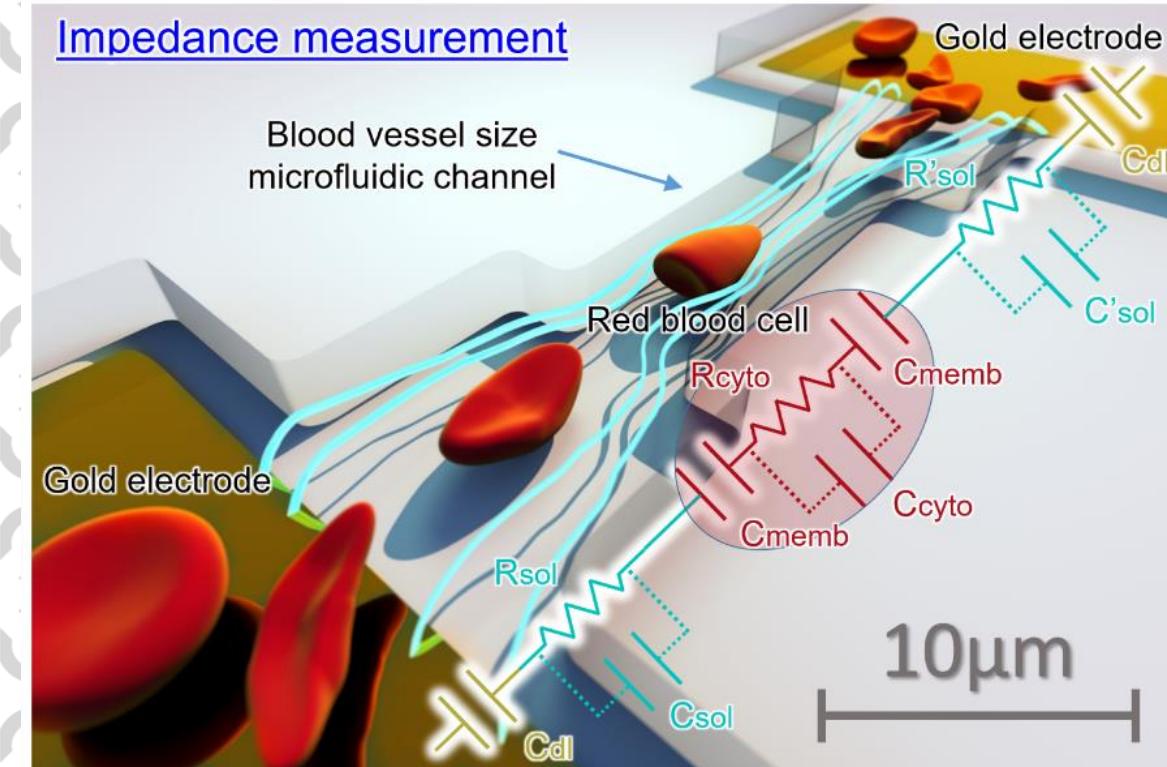


Use of electric measurement to analyse the RBC passage within the capillary



Design and fabrication process

Impedance measurement

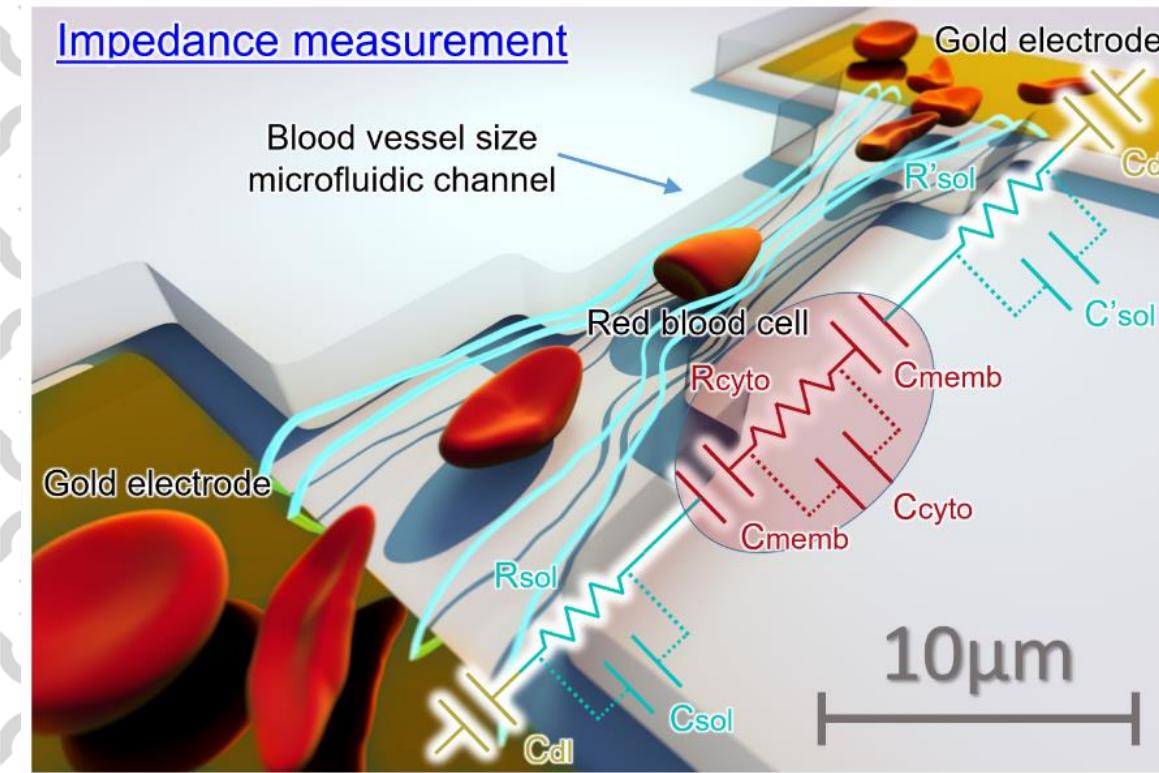


Scientific Reports, Nature Publishing Group, 2020,
(10.1038/s41598-020-66693-4)

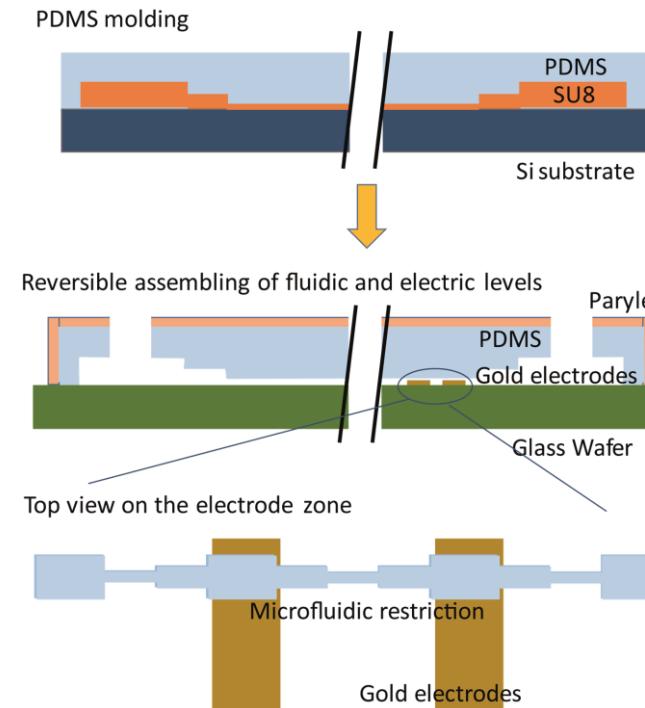


Design and fabrication process

Impedance measurement



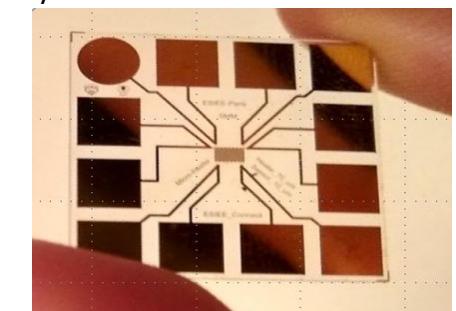
Scientific Reports, Nature Publishing Group, 2020,
(10.1038/s41598-020-66693-4)



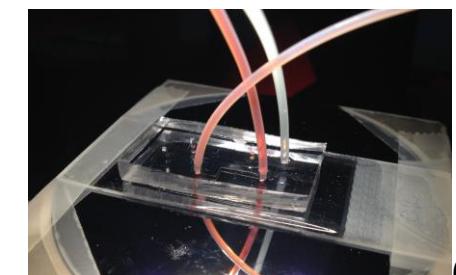
Microfluidic : Molding of polymer material (elastomer PDMS)

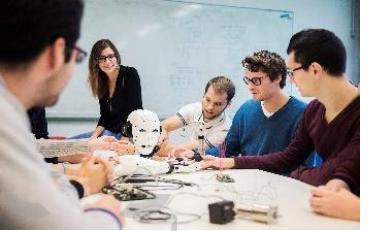


IC Chip: Photolithography of conductive thin layer



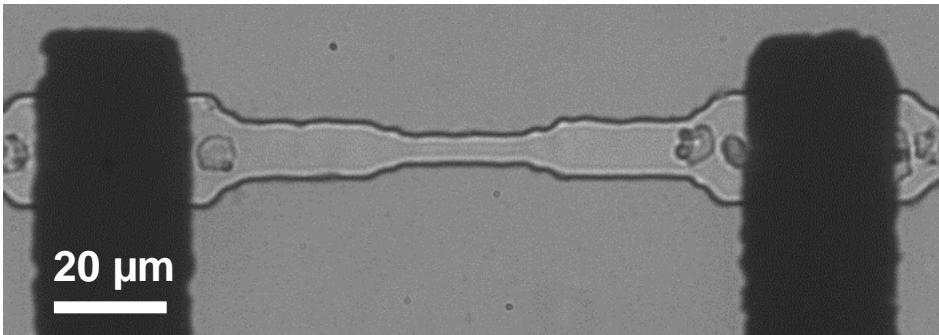
Assembly of Microfluidic channel and IC chip



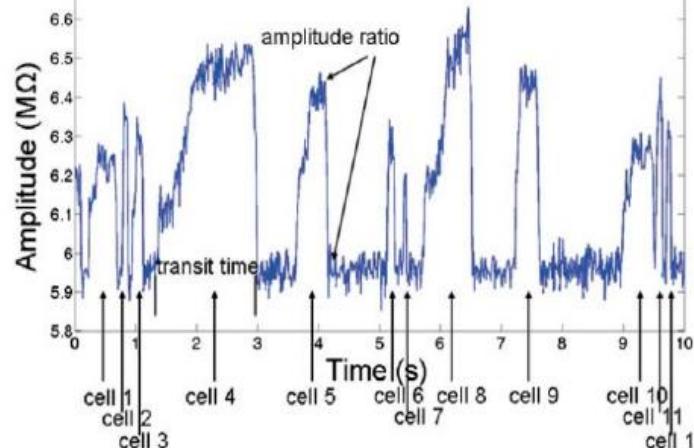


Micro-devices for sickle cell disease study

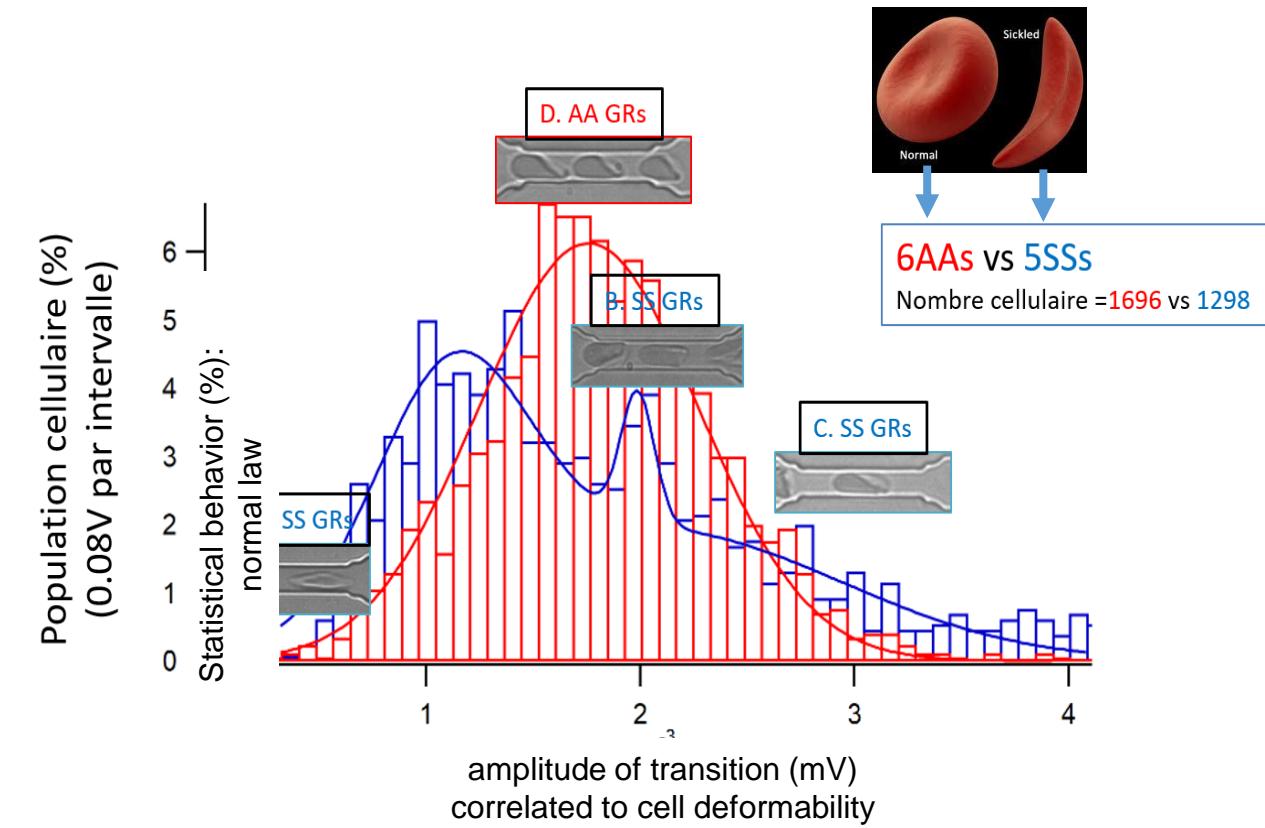
PDMS microfluidic chip combined with electrode for electrical recording



Monitoring of blockade events

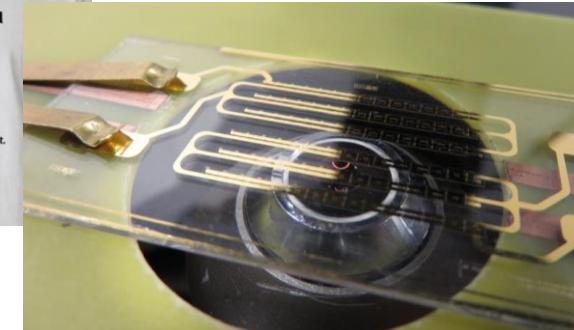
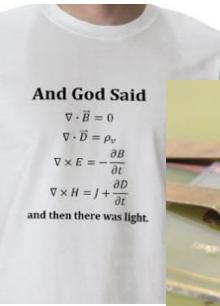
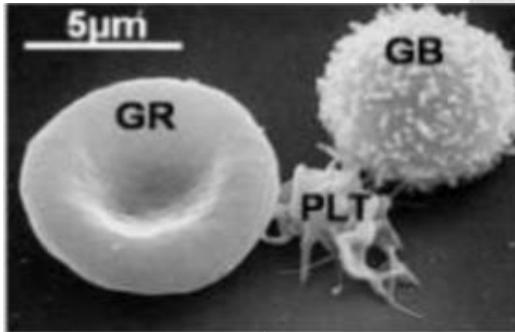


- Time of transition and - Amplitude of the transition





Interaction between Cells and Electric Field within microfluidic devices



Bio-Impedance
↓
SENSING

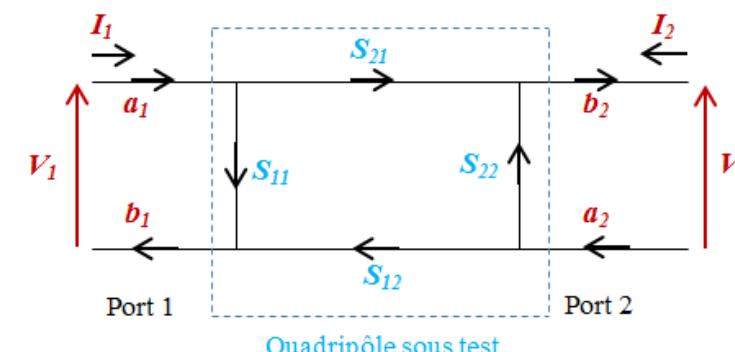
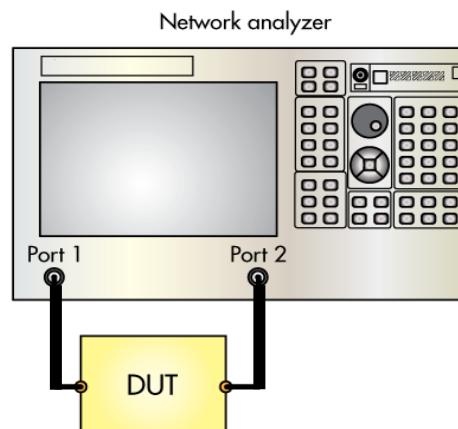
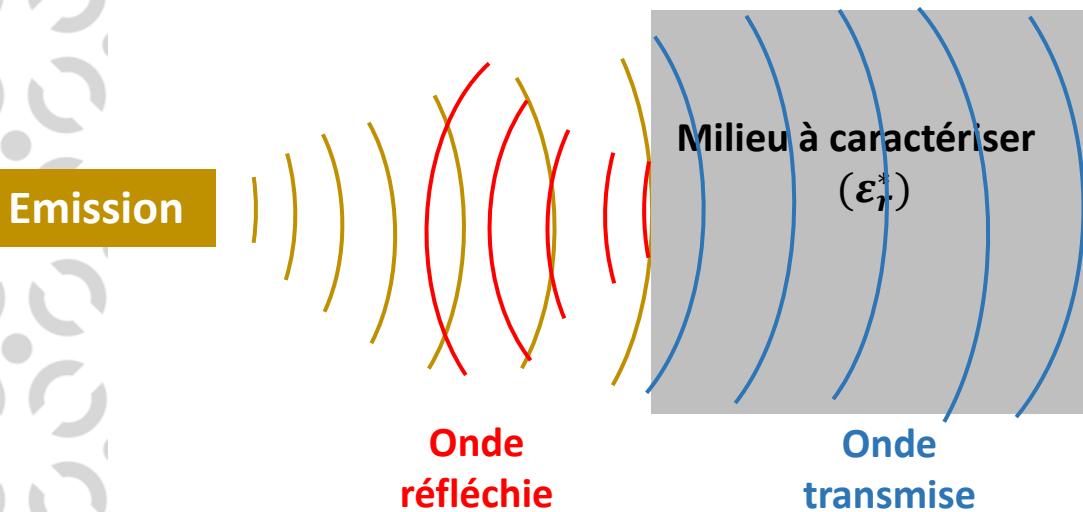
Dielectric Spectroscopy
↓
Medium analysis

Cell polarisation
↓
Cell sorting and trapping



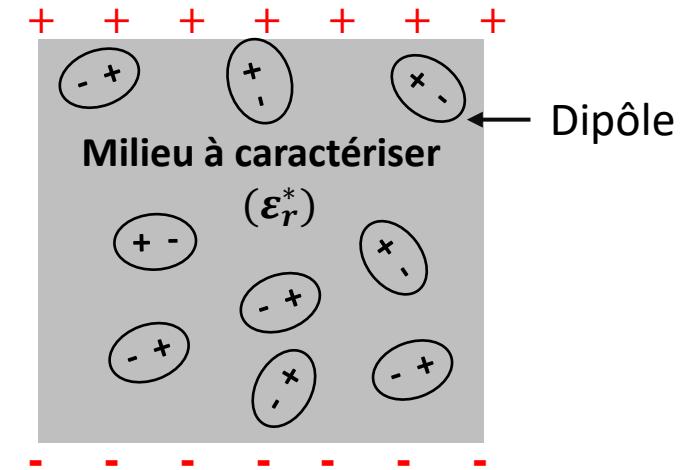
Interactions « onde électromagnétique » et « matière »

Principe de caractérisation



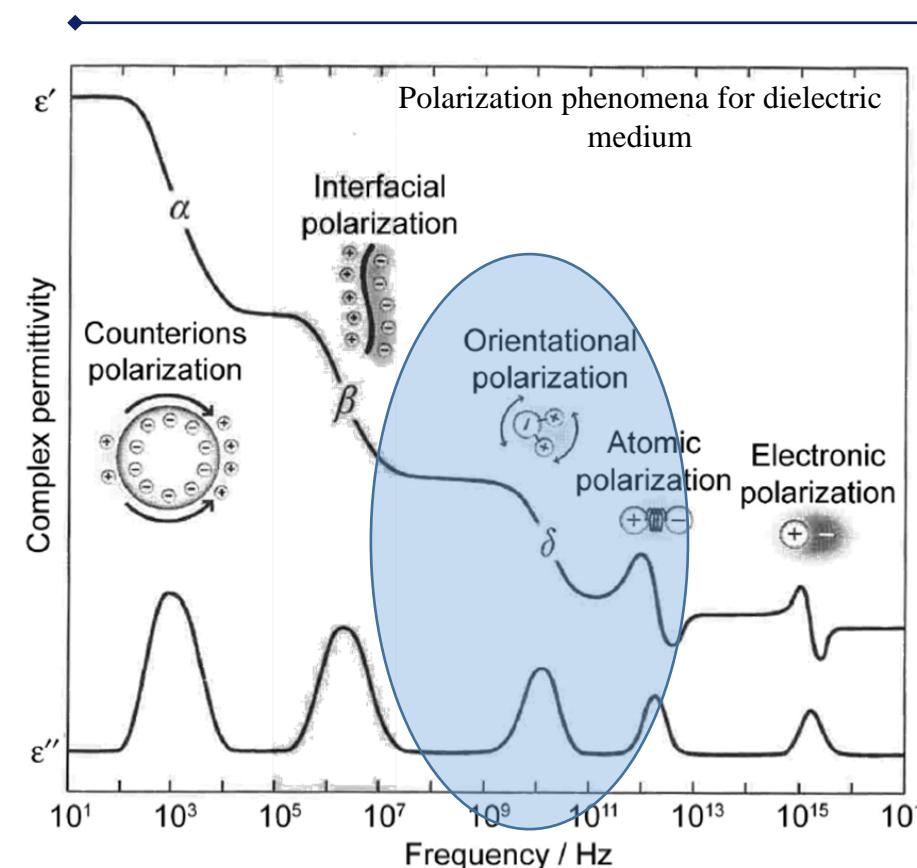
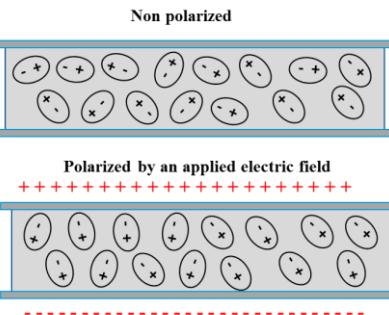
Phénomène de relaxation diélectrique

Polarisé par un champ électrique appliqué



$$\epsilon_r^* = \frac{\alpha_1 S_{11,més} - \alpha_2}{\alpha_3 - S_{11,més}}$$

$$\epsilon_r^* = \frac{\beta_1 S_{21,més} - \beta_2}{\beta_3 - S_{21,més}}$$



- Model associated :
-> Debye Relaxation

$$\epsilon_r^*(\omega) = \epsilon_\infty + \frac{\Delta\epsilon}{1 + j \cdot \omega \cdot \tau_r f}$$

- > Cole-Cole Relaxation

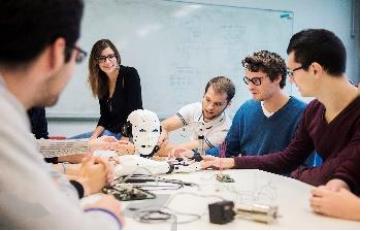
$$\epsilon_r^*(\omega) = \epsilon_\infty + \frac{\Delta\epsilon}{1 + (j \cdot \omega \cdot \tau_r f)^\alpha}$$

- **Complex relative permittivity:**

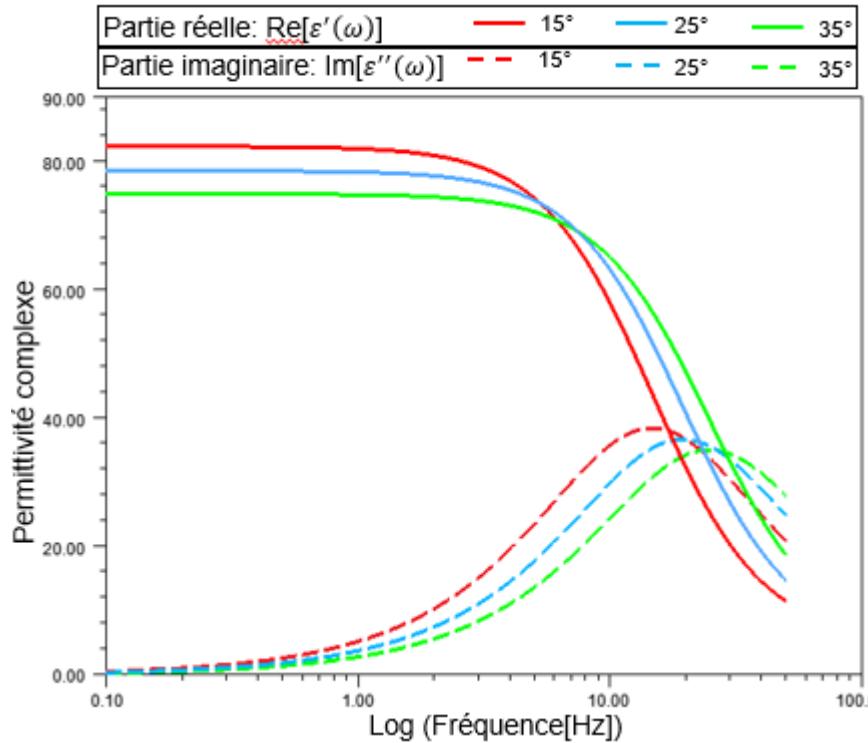
$$\epsilon_r^*(\omega) = \epsilon'(\omega) - j\epsilon''(\omega)$$

- **Relaxation time:**

$$\tau_r = \frac{1}{2\pi i \cdot f_r}$$

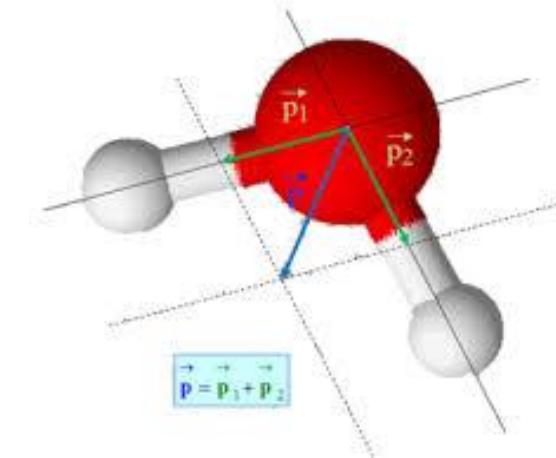


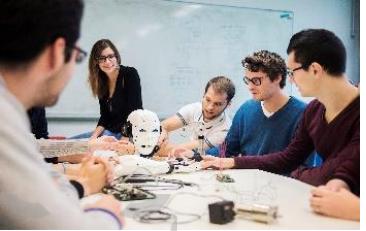
Electromagnetic properties of pure water



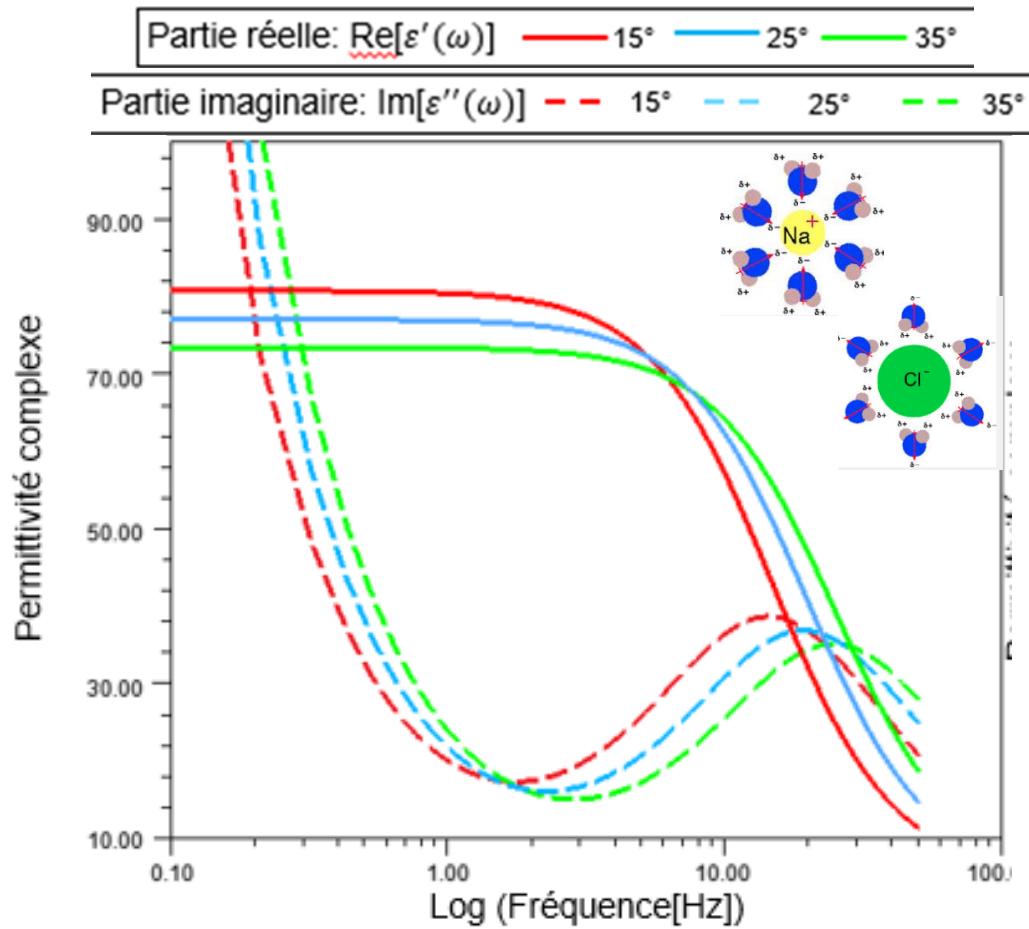
Debye Relaxation Model

$$\varepsilon_w(\omega, T) = \varepsilon_\infty(T) + \frac{\Delta\varepsilon_w(T)}{1 + j\omega\tau_w(T)}$$

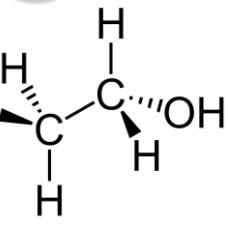
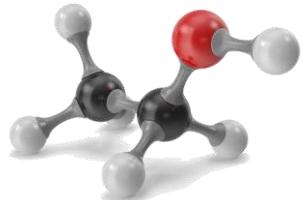
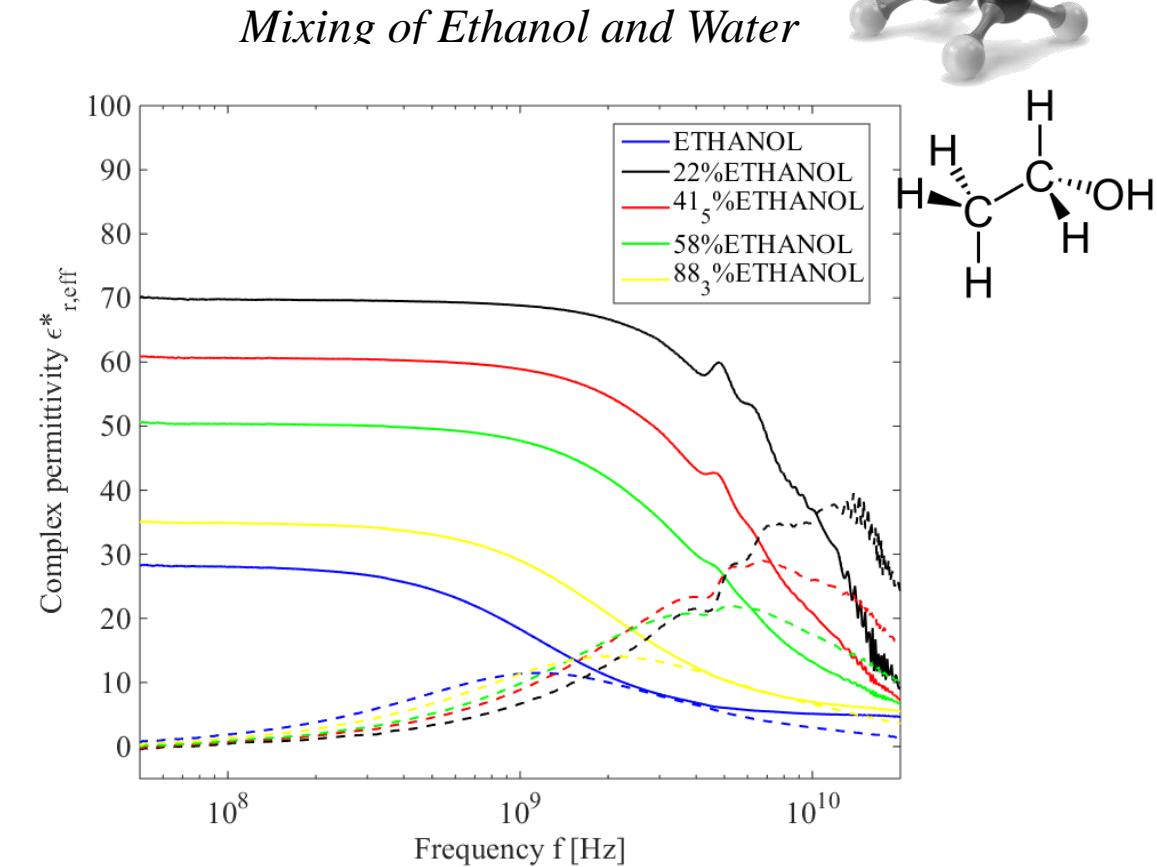




Electromagnetic properties of liquids...



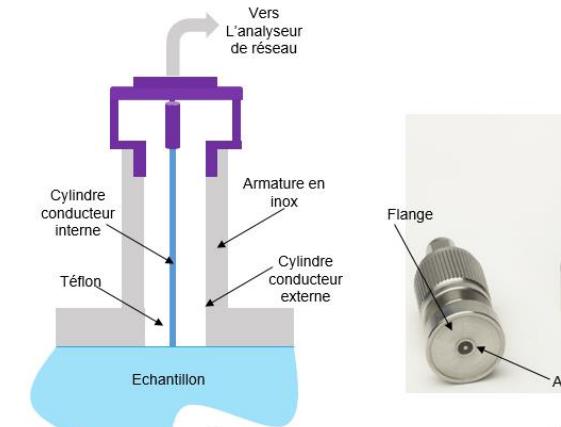
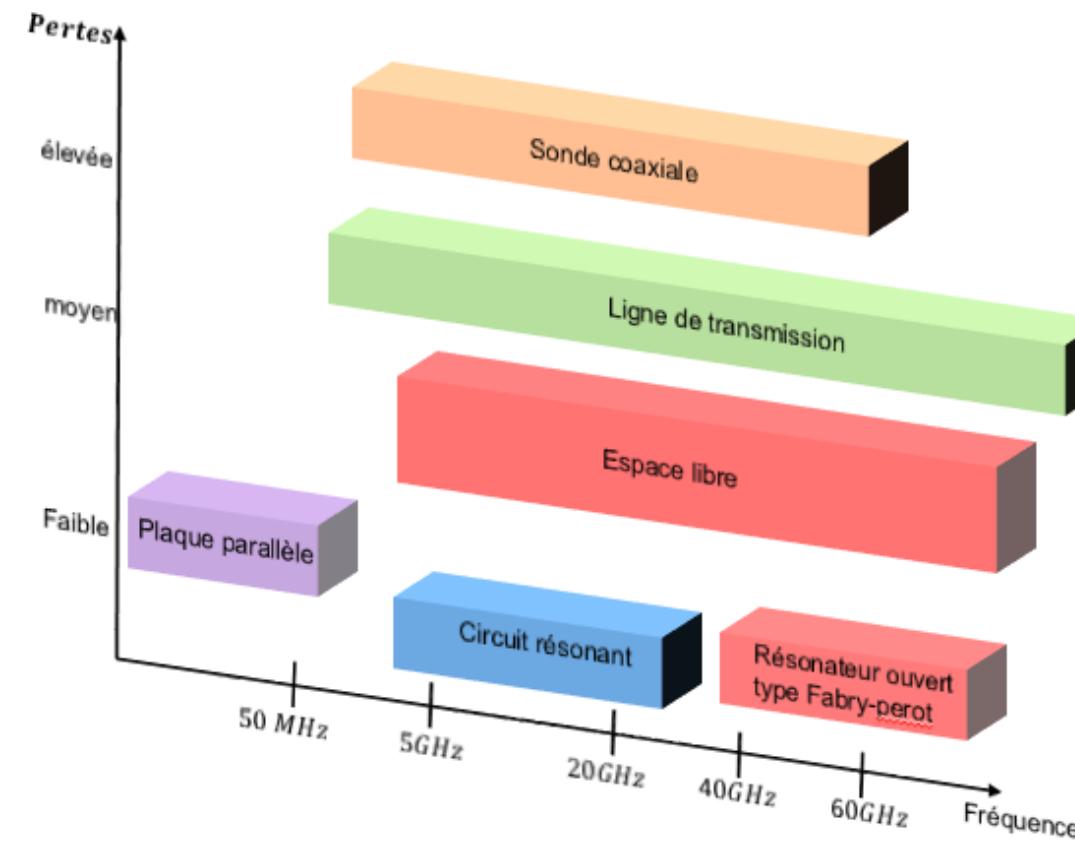
Saltwater : 0.1 mol/L of Sodium chloride





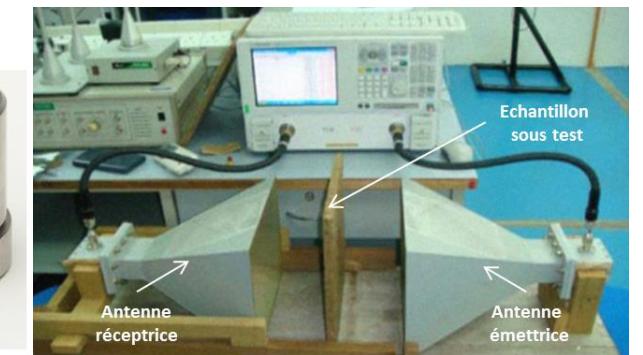
Spectroscopie diélectrique hyperfréquence

Réflexion ou transmission des ondes EM :
cas grand volume



Sonde à effet de bout

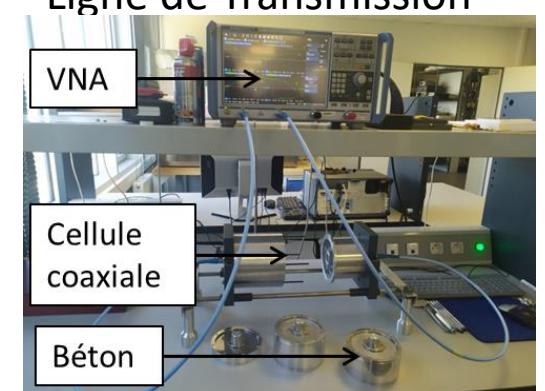
Transmission en espace libre]

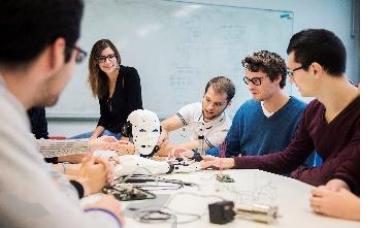


Ligne de Transmission



résonateur

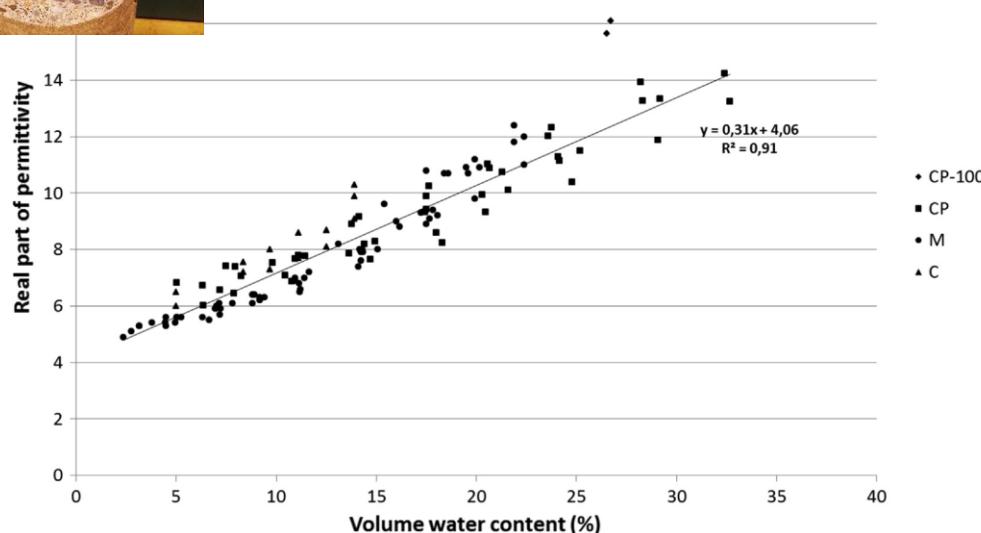




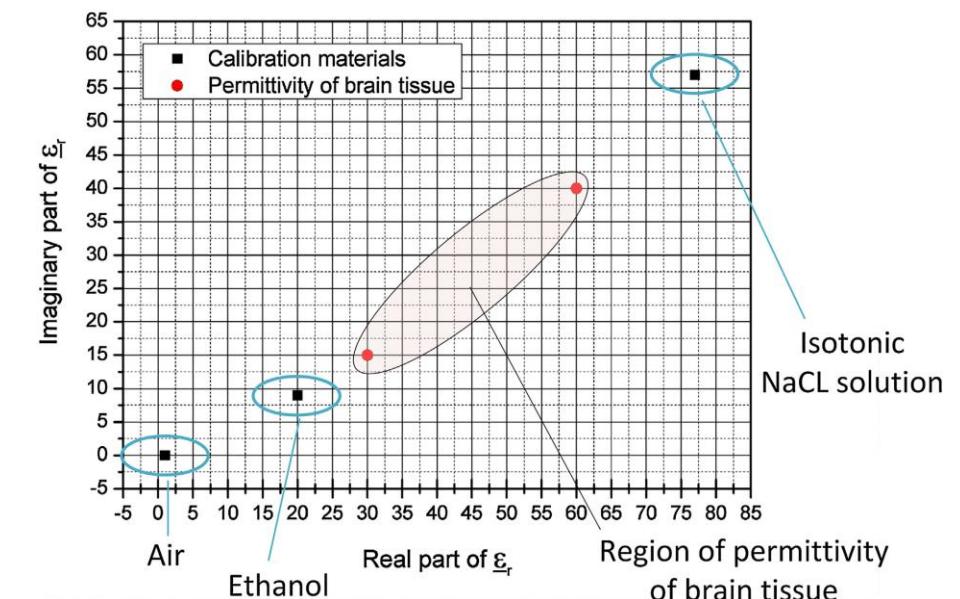
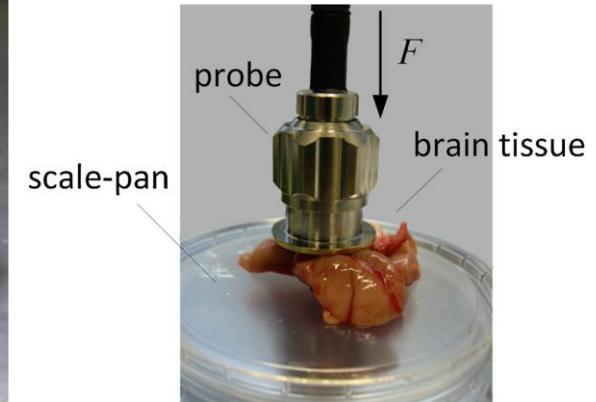
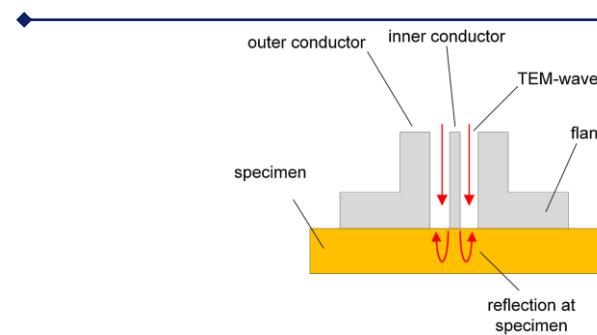
Sonde à effet de bout : « Open Ended Probe »



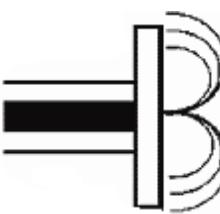
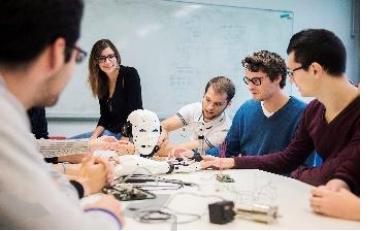
Acquisition of the S11 parameter on the surface of a concrete sample.



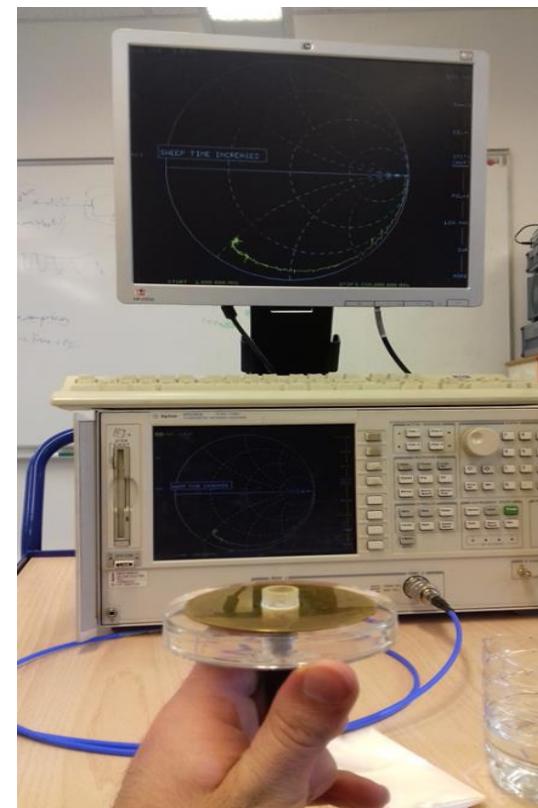
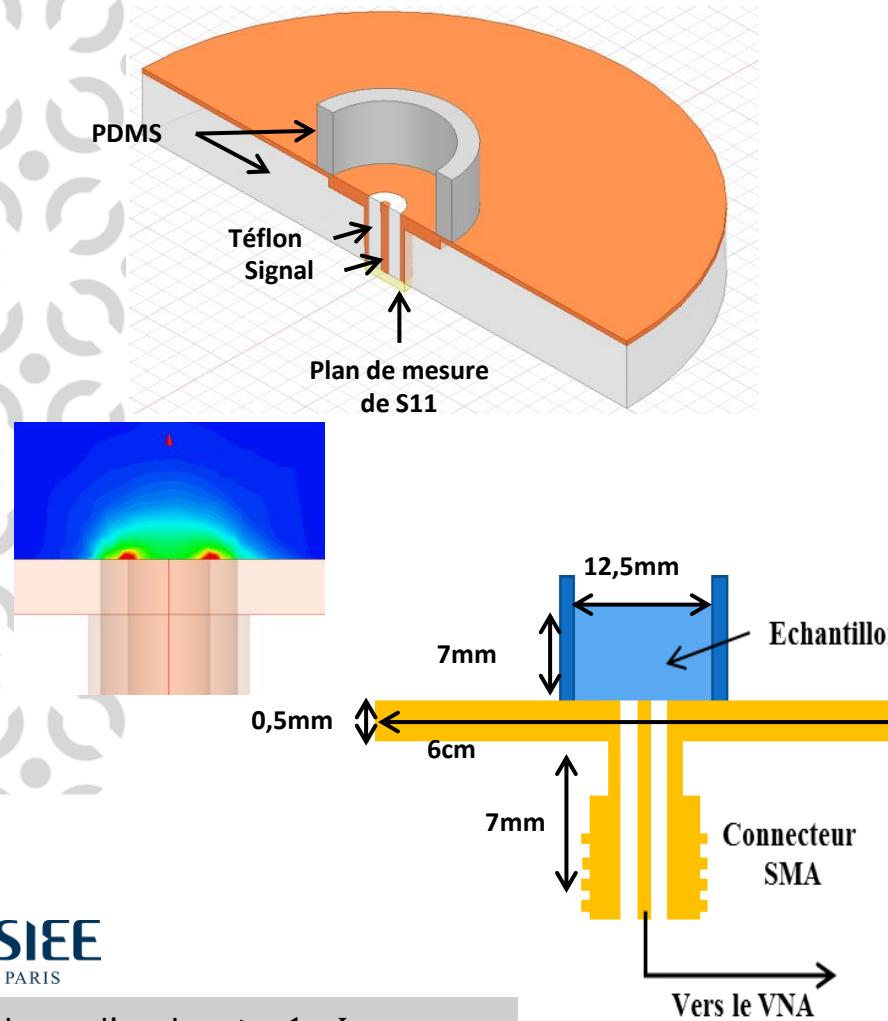
Guihad, Vincent, et al (2020) *Construction and Building Materials*, 230(), 116946– doi:10.1016/j.conbuildmat.2019.116946



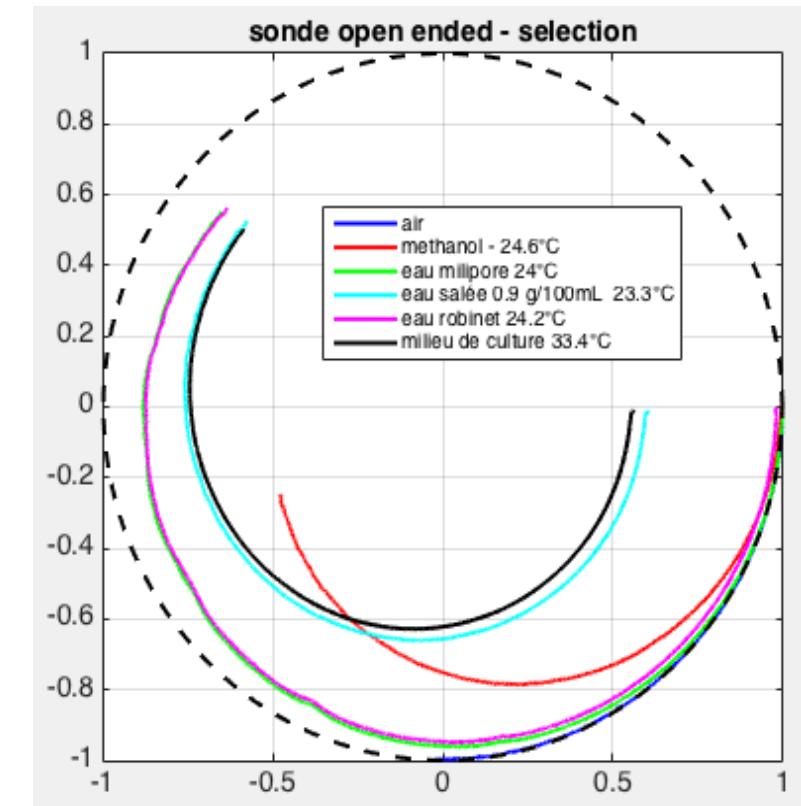
T. Reinecke, et al (2014), Sensors & Actuators, B

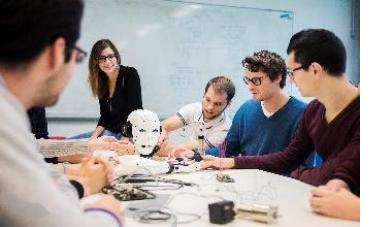


Case of open-ended probe (home-made)



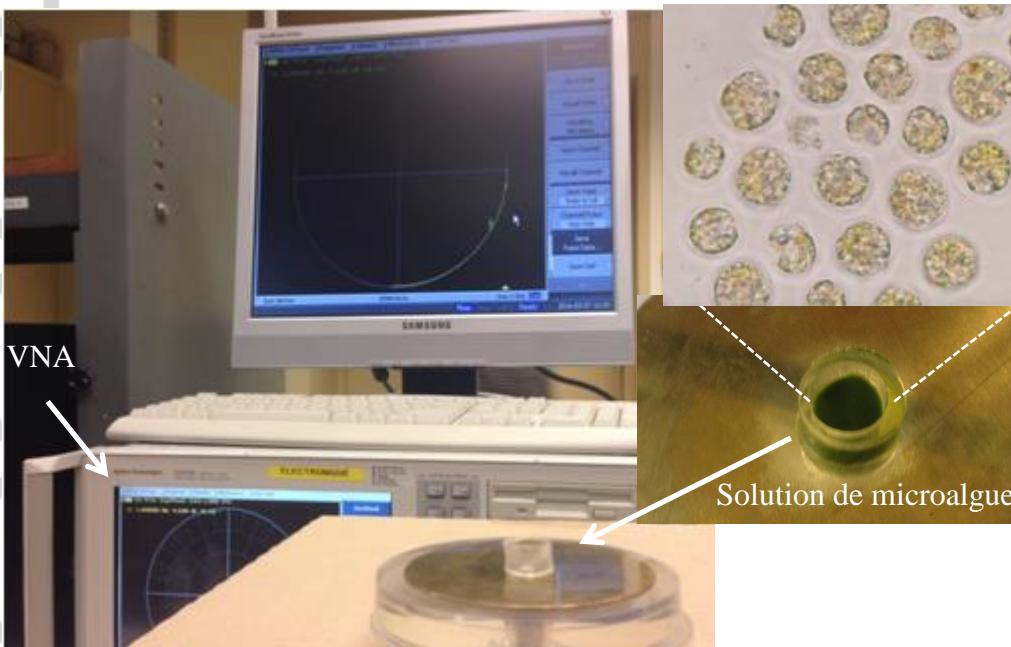
El Fellahi (2017). *IEEE sensors letters*, 1(4), 1-3.



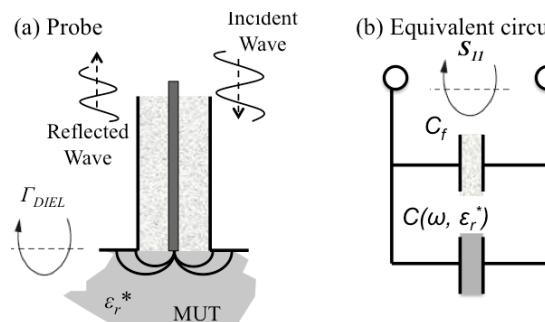


CARACTÉRISATION DE CELLULES BIOLOGIQUES PAR LA MESURE DE PERMITTIVITÉ

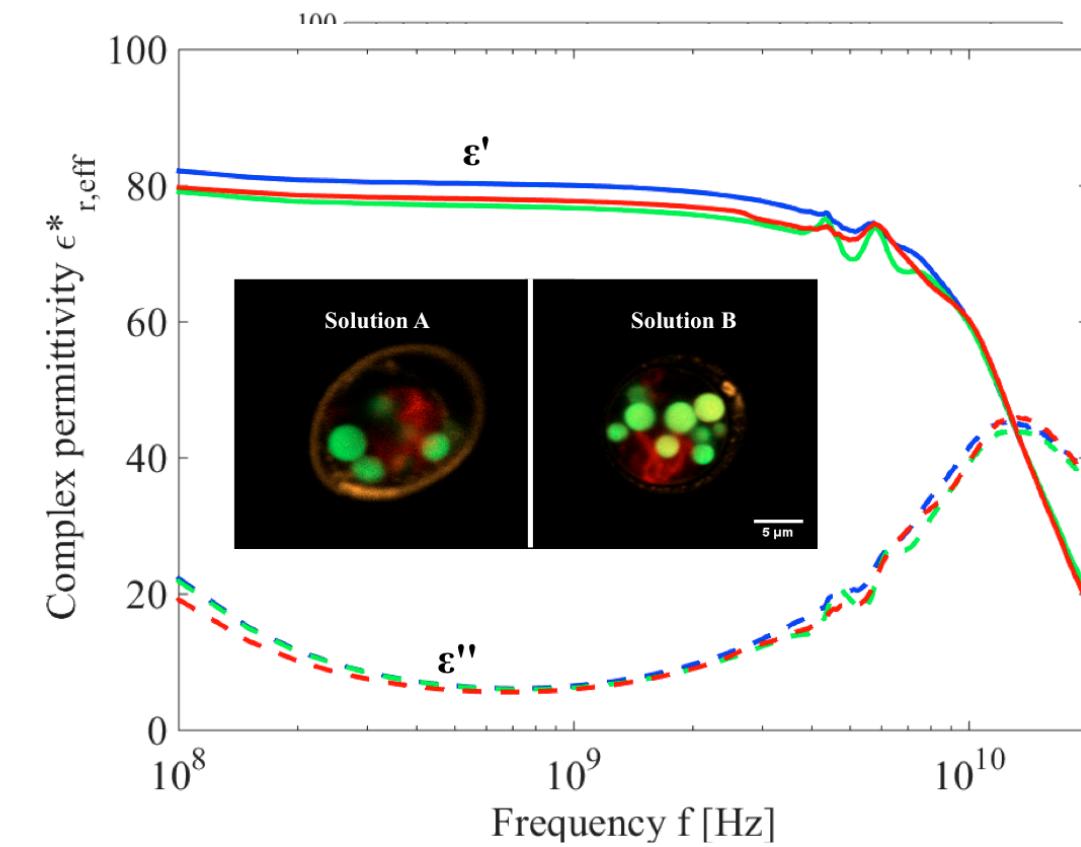
Mesure intracellulaire d'accumulation de lipide dans les microalgues (10MHz – 3 GHz)

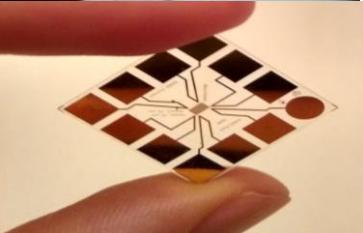


El Fellahi, (2016). *Procedia Engineering*, 168, 1287-1290.
El Fellahi (2017). *IEEE sensors letters*, 1(4), 1-3.



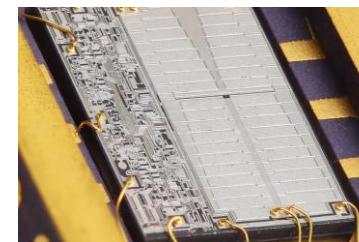
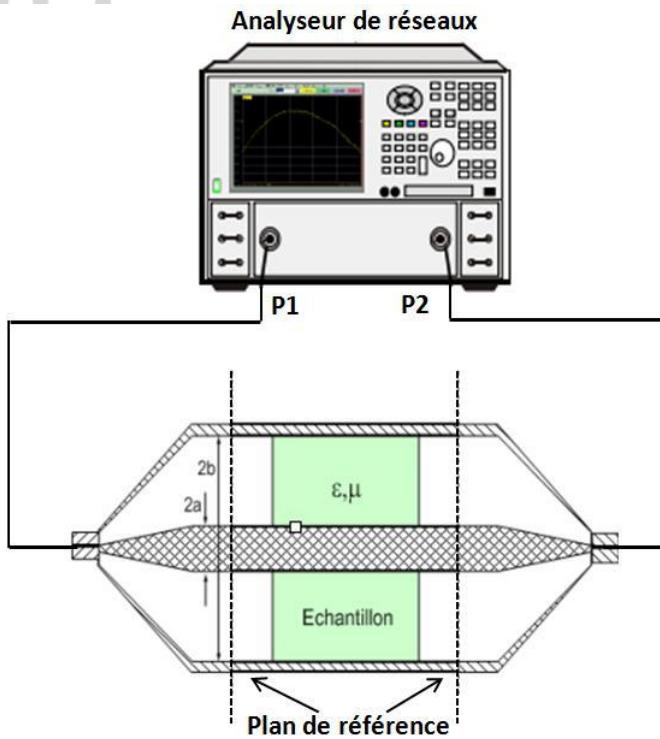
- Banc de mesure**
- ✓ Solution de 1 ml
 - ✓ Nombre de cellules: 70 Millions
 - ✓ Fraction volumique : 1,5 %



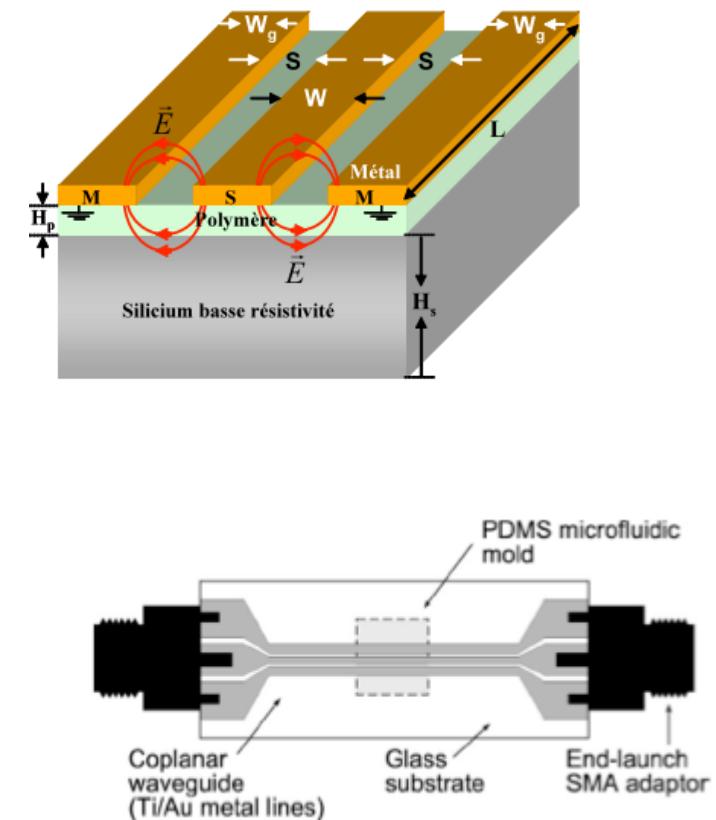
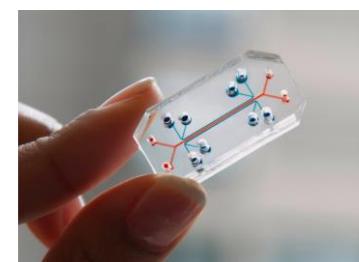


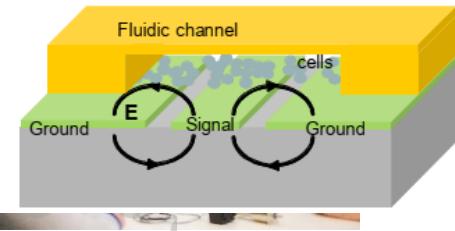
Spectroscopie diélectrique hyperfréquence Miniaturisation - ligne de transmission

Caractérisation de matériaux fluides de faible volume : $\leq 2 \text{ nL}$

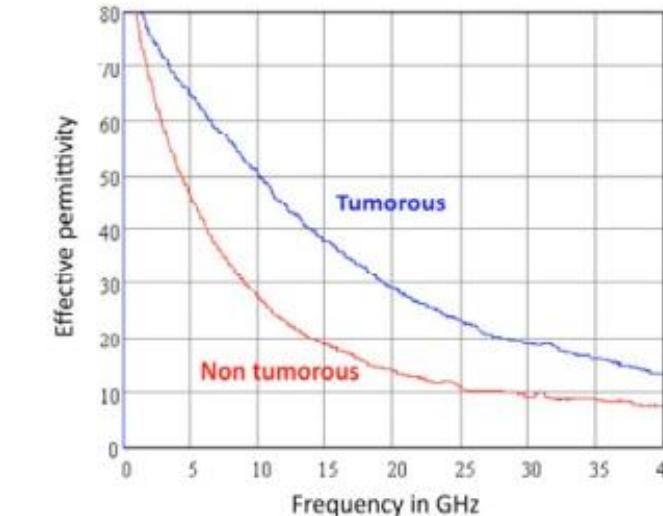
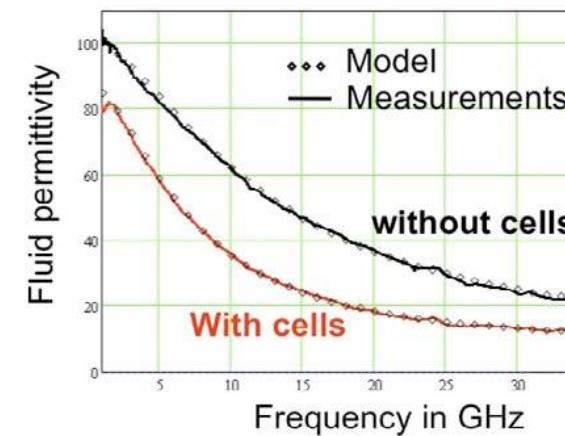
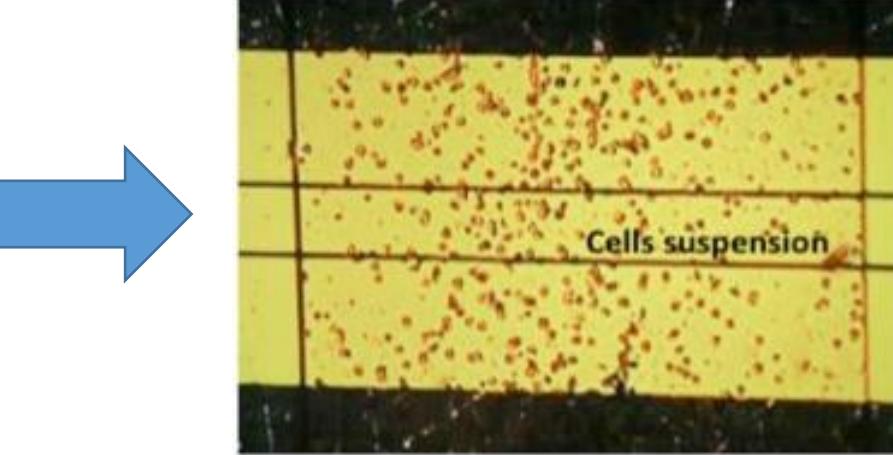
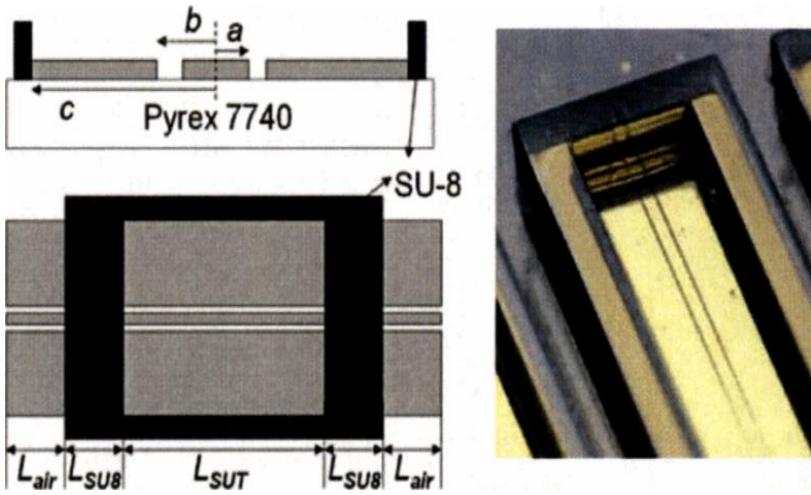


Technologie planar + gestion des fluides à l'échelle de la biologie

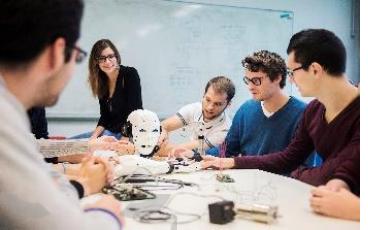




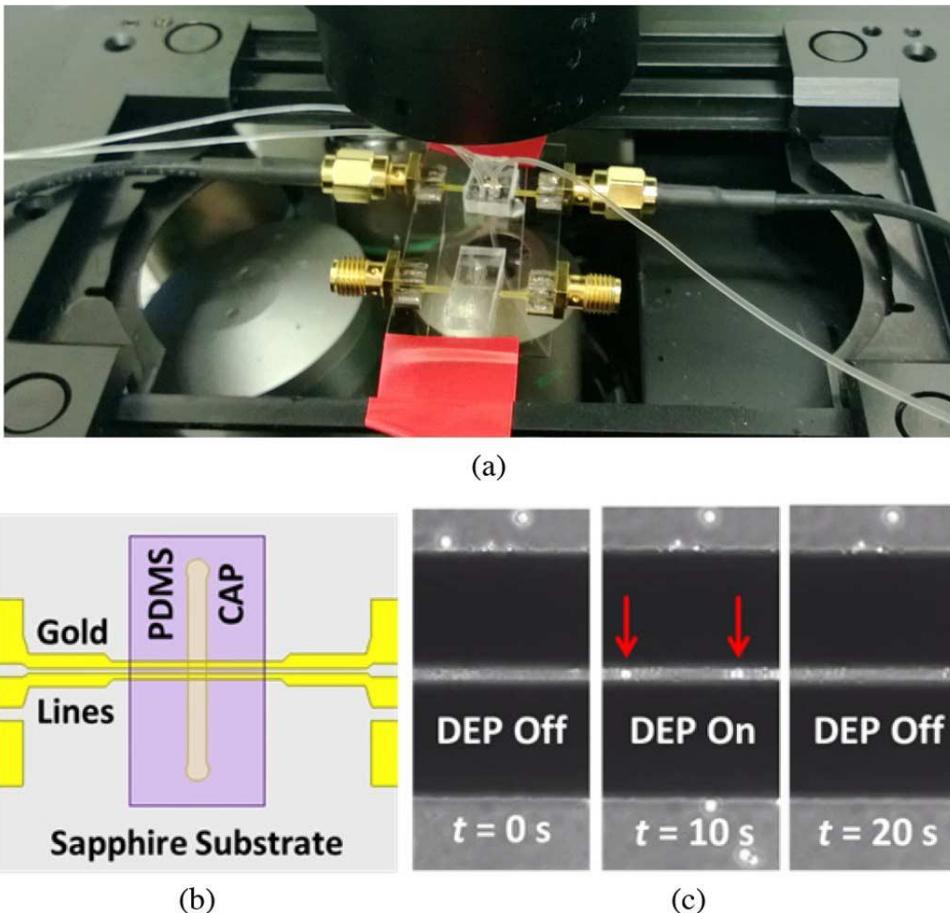
Ligne coplanaire à microréservoir



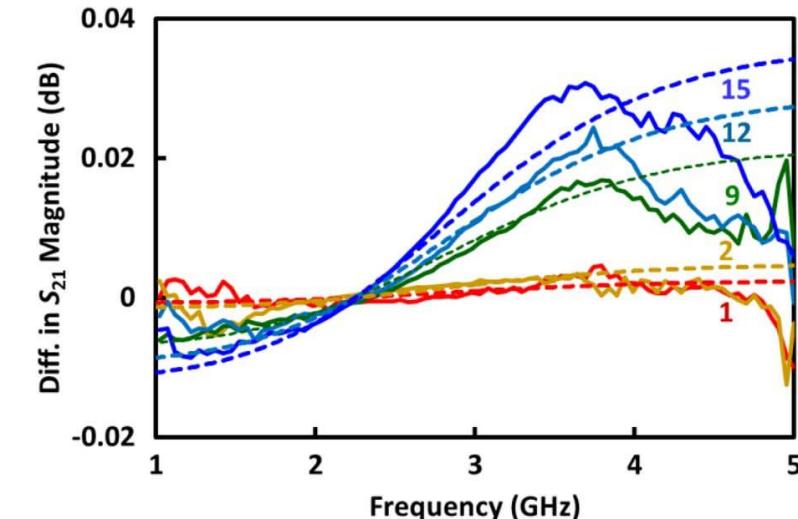
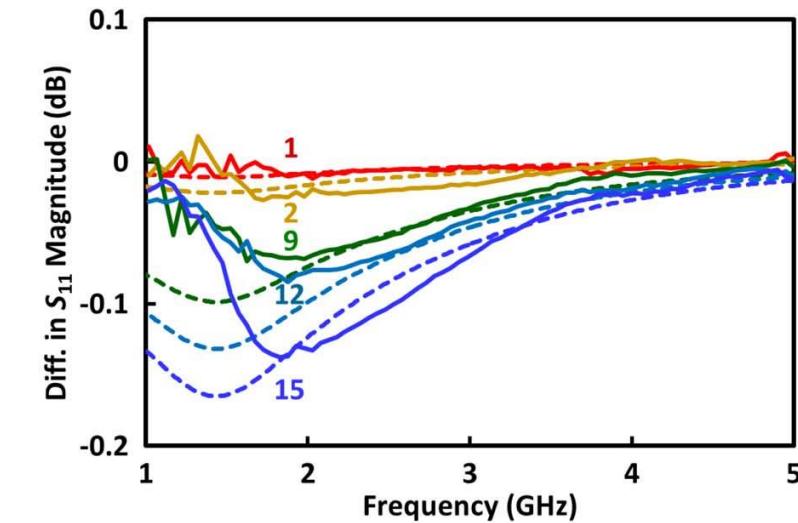
Signature électrique de cellules vivantes
HUVEC (non tumorales) et SK-HEP-1 (tumorales)

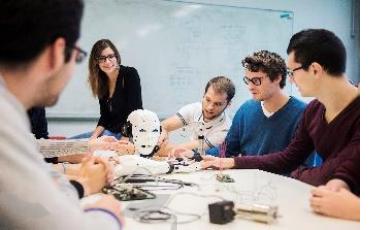


Ligne coplanaire à piégeage par diélectrophorèse



1, 2, 9, 12, and 15 live Jurkat cells trapped

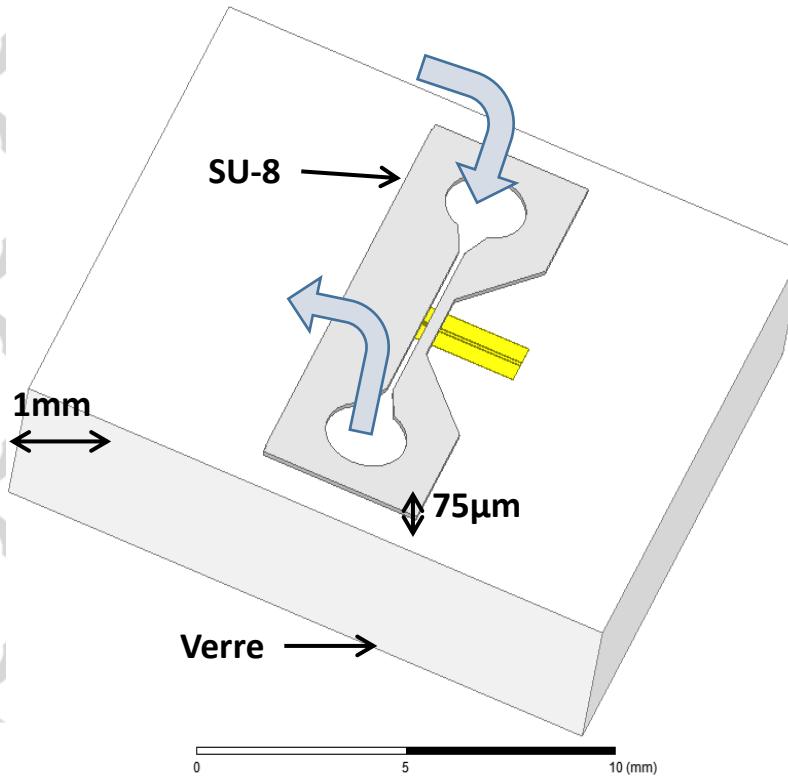




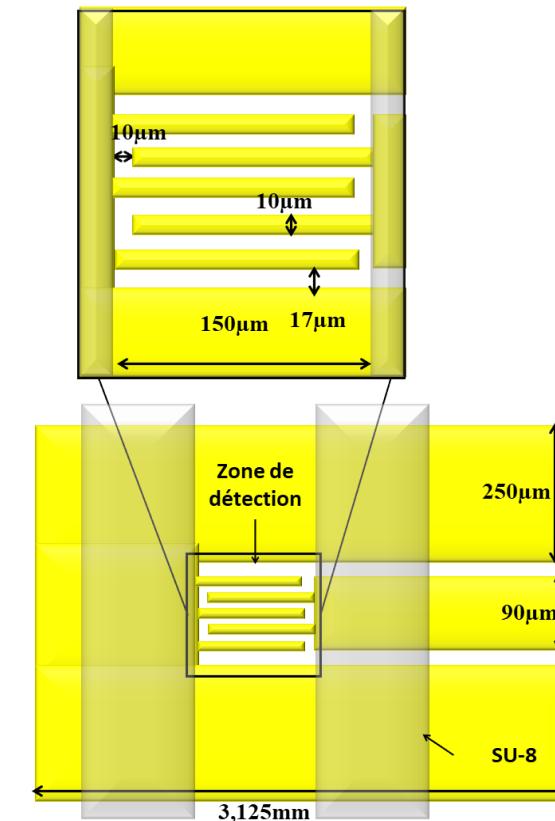
Structure miniaturisée à effet bout : cas du peigne interdigité

Analyse d'une population réduite de cellules

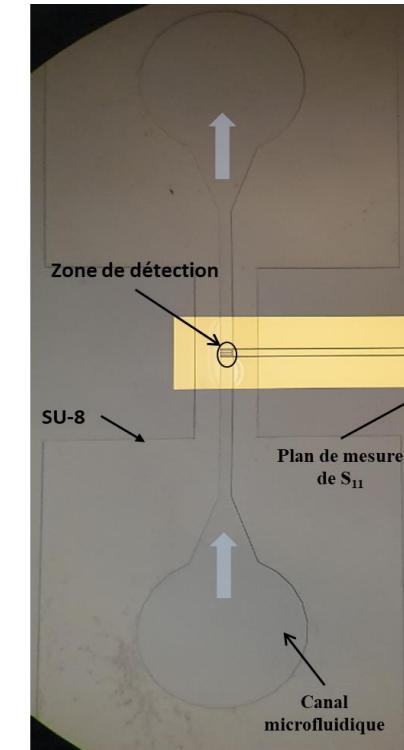
IDR – CPW sous pointes en vue 3D



IDR – CPW sous



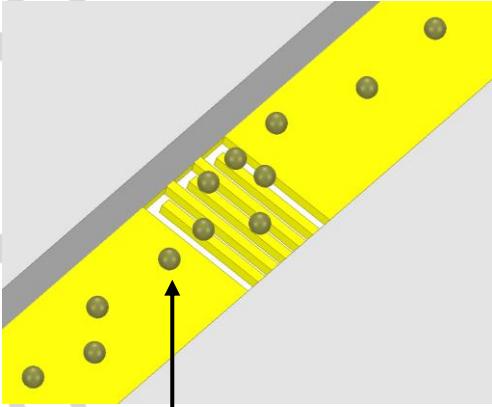
Volume d'analyse $\leq 1\text{nL}$



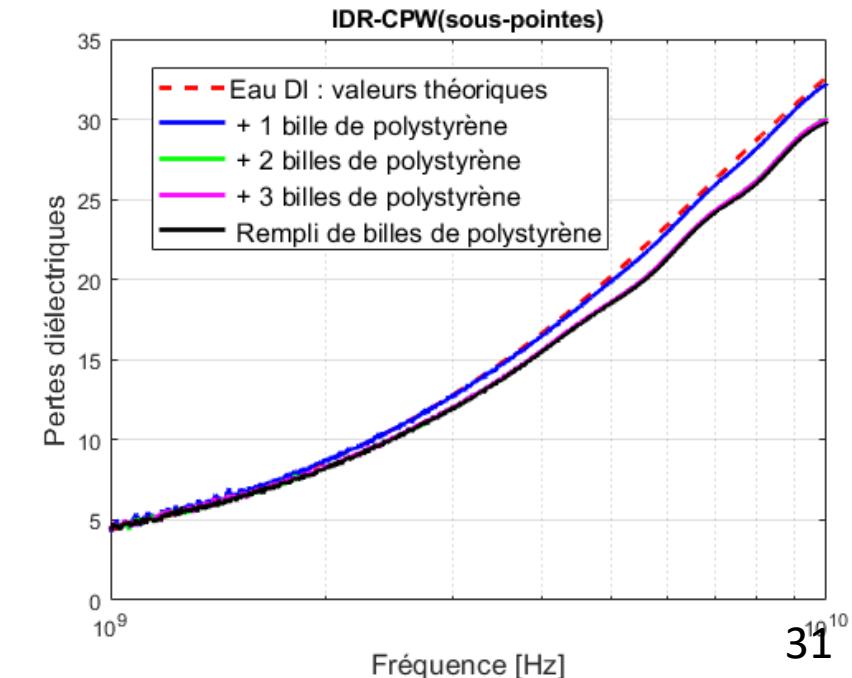
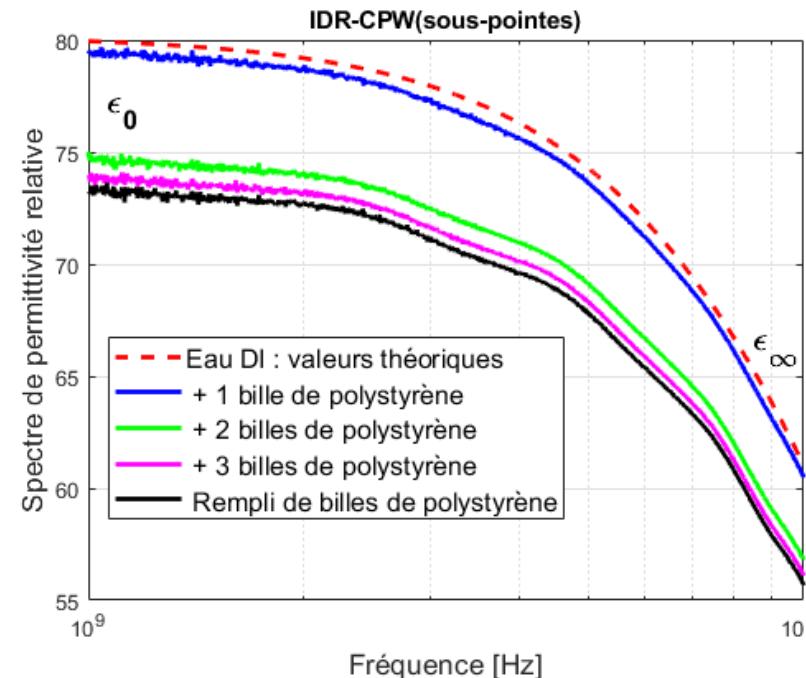
Banc de mesure sous-pointes

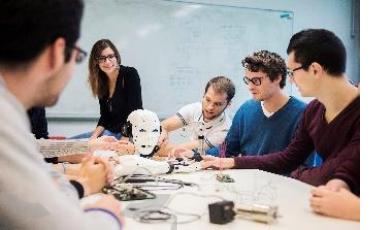


Open ended integrated probe



Case of Polystyrene
beads
 $(d = 20 \mu\text{m}, \epsilon_r^* = 2,6)$

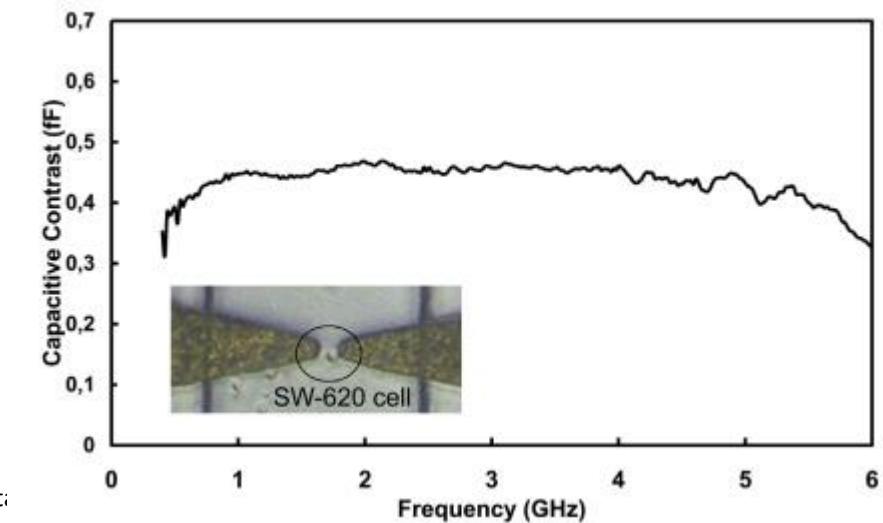
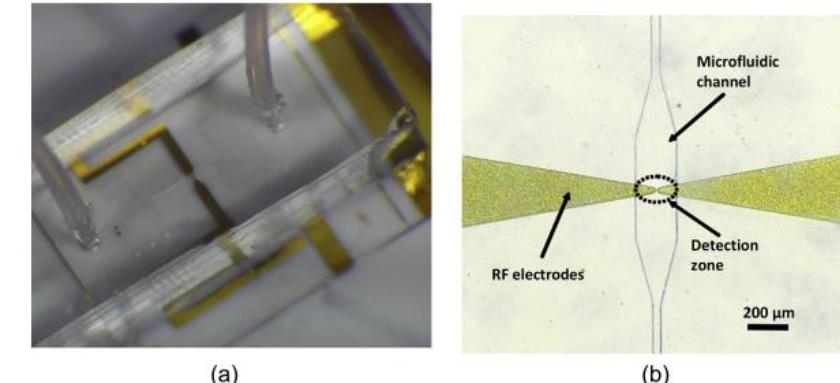
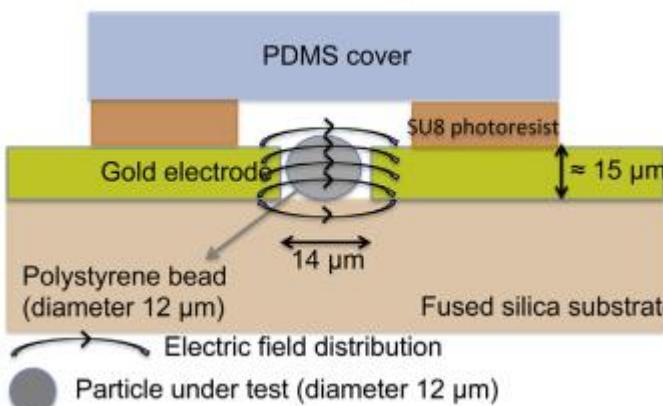
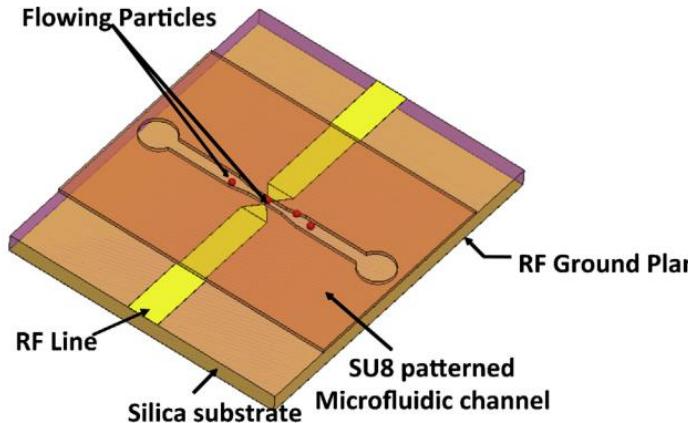




Spectroscopie diélectrique hyperfréquence

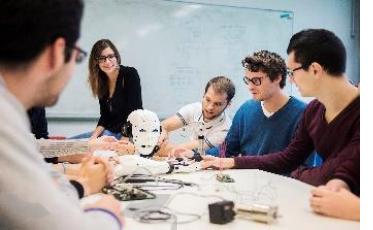
Biocapteurs appliqués à la caractérisation d'une cellule

ligne micro-ruban



Landoulsi et al, IEEE Radio and Wireless Week (RW 2015), Biosensor Conference, Jan 2015, San Diego, United States

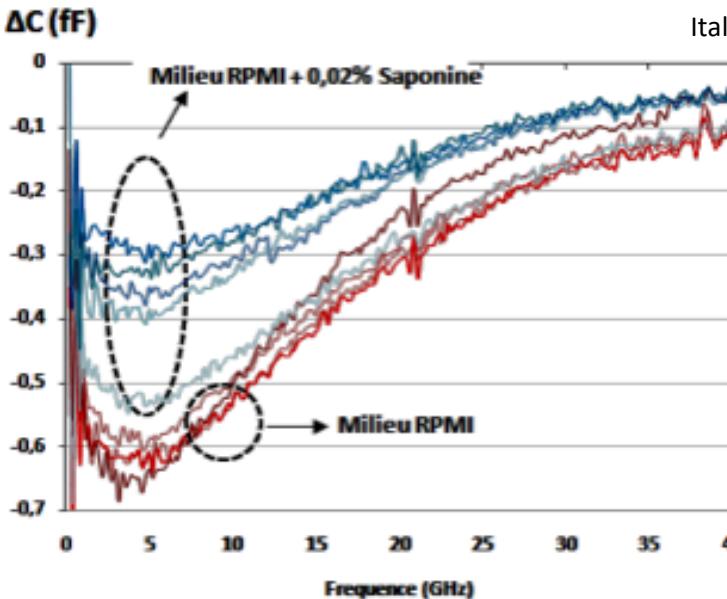
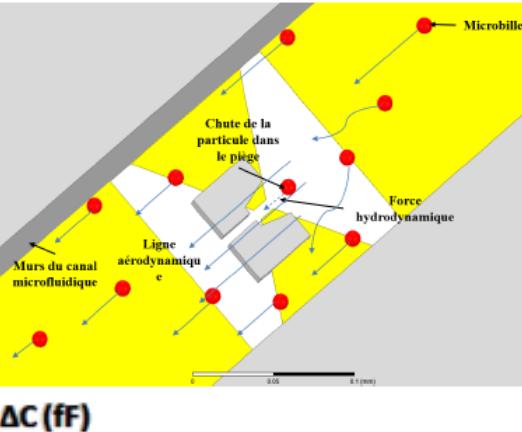
Zhang L.Y., et al, Sensors and Actuators A, 2014, Vol. 216, pp. 405–416.



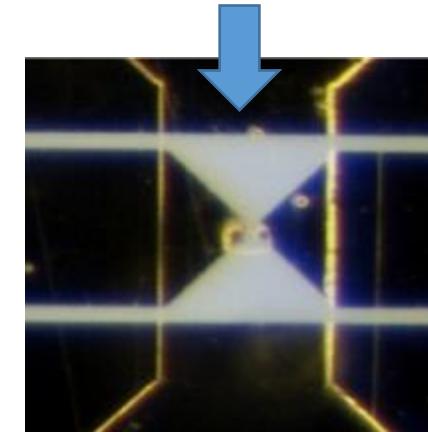
Spectroscopie diélectrique hyperfréquence

Biocapteurs appliqués à la caractérisation d'une cellule unique

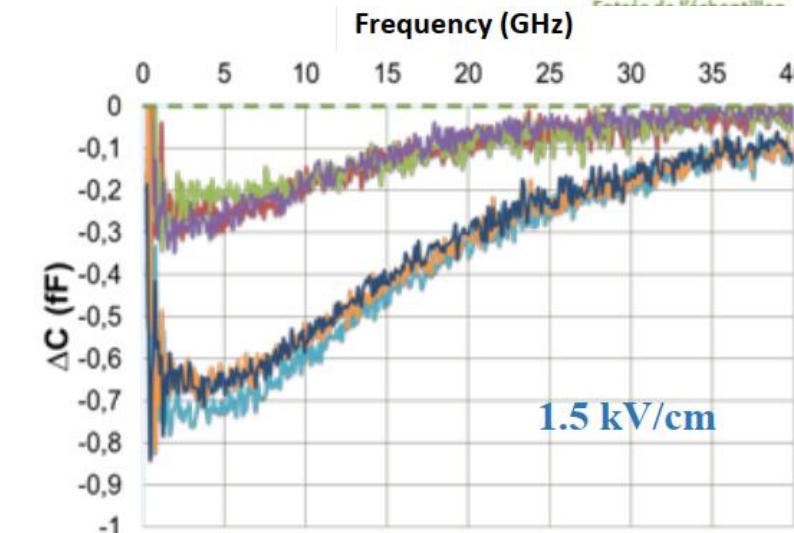
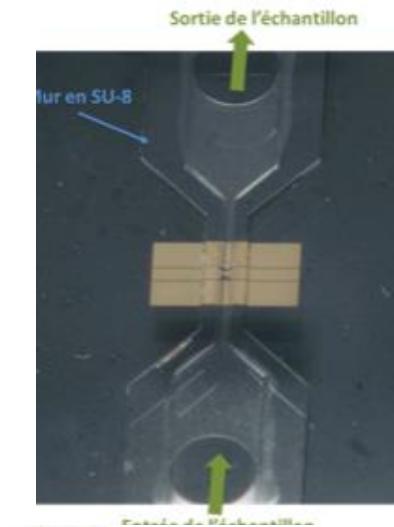
Cas utilisation d'un piégeage « mécanique »



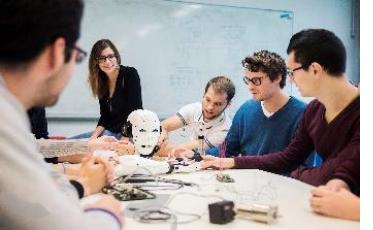
Impact d'un traitement chimique



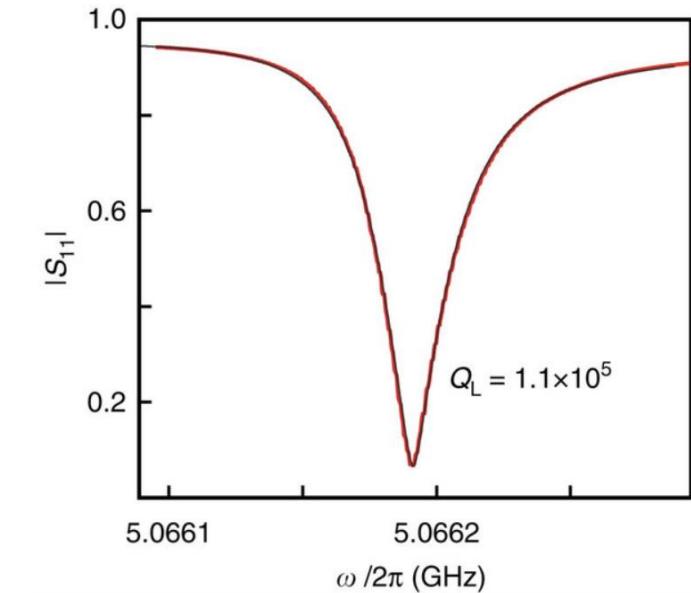
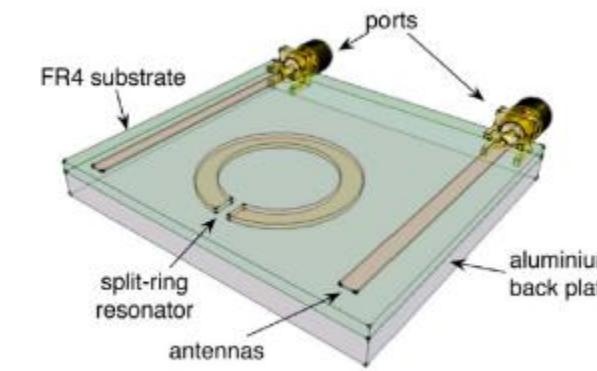
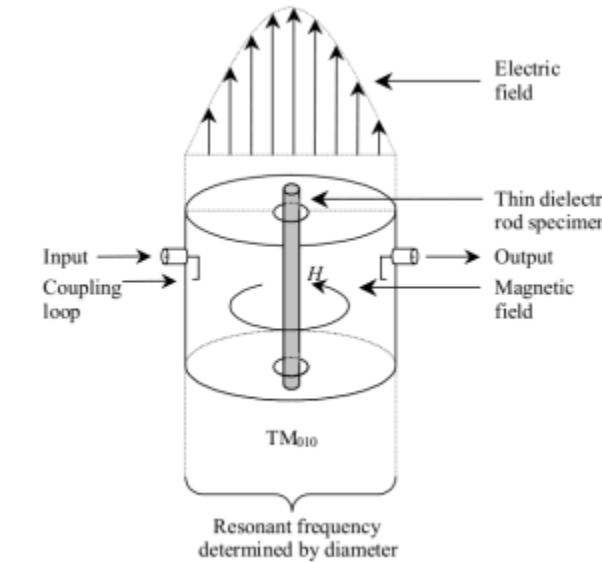
K. Grenier, 2021 XXXIVth (URSI GASS), Aug 2021, Rome, Italy. pp.1-3,



Impact d'un pulse d'électroporation

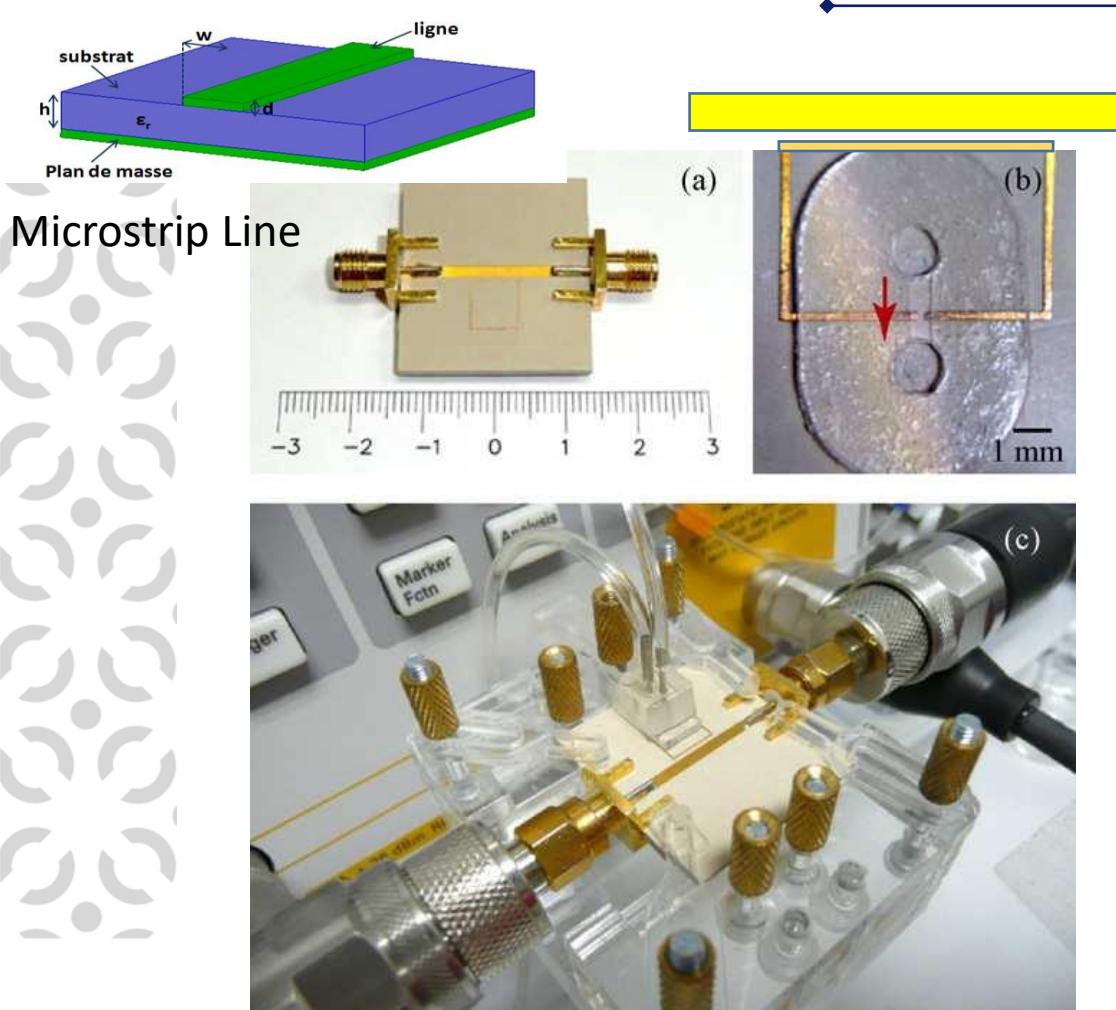


From broadband toward resonant sensor

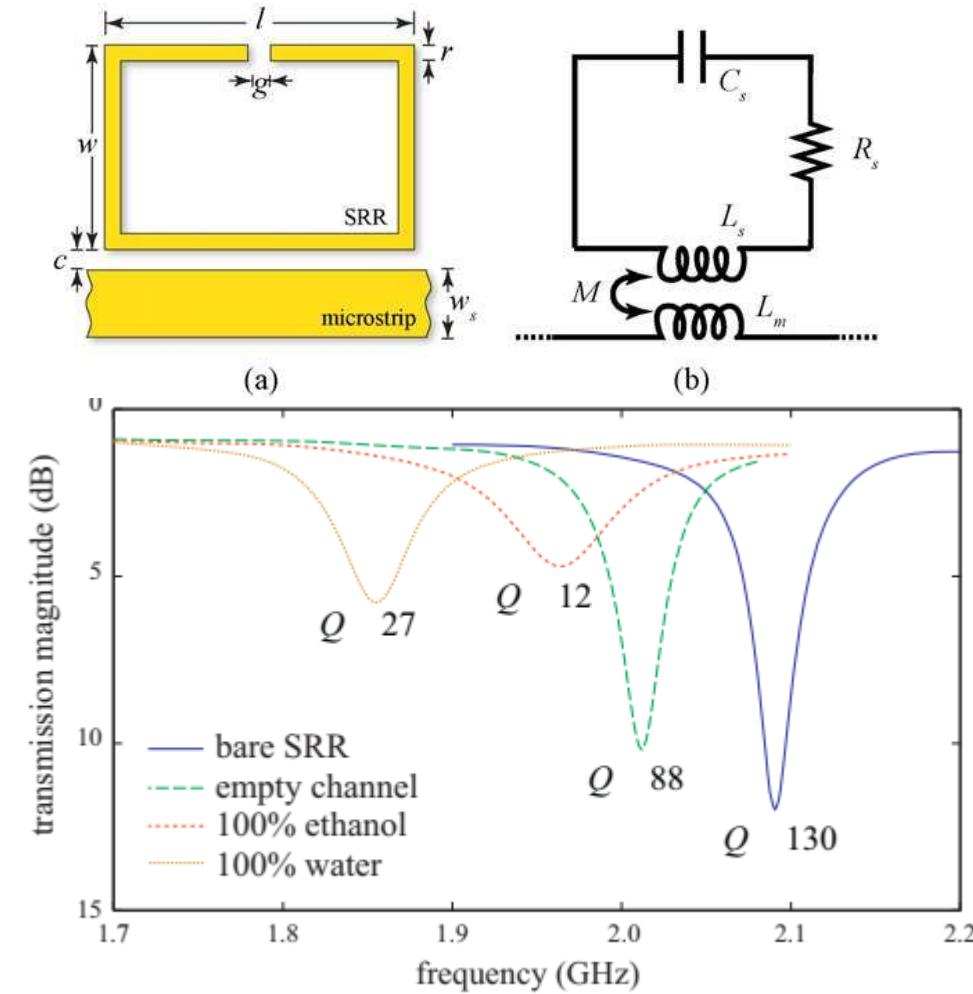


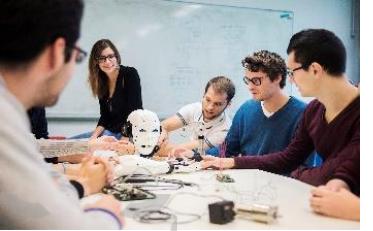


Single split-ring resonator (SRR) combined with microfluidic channel



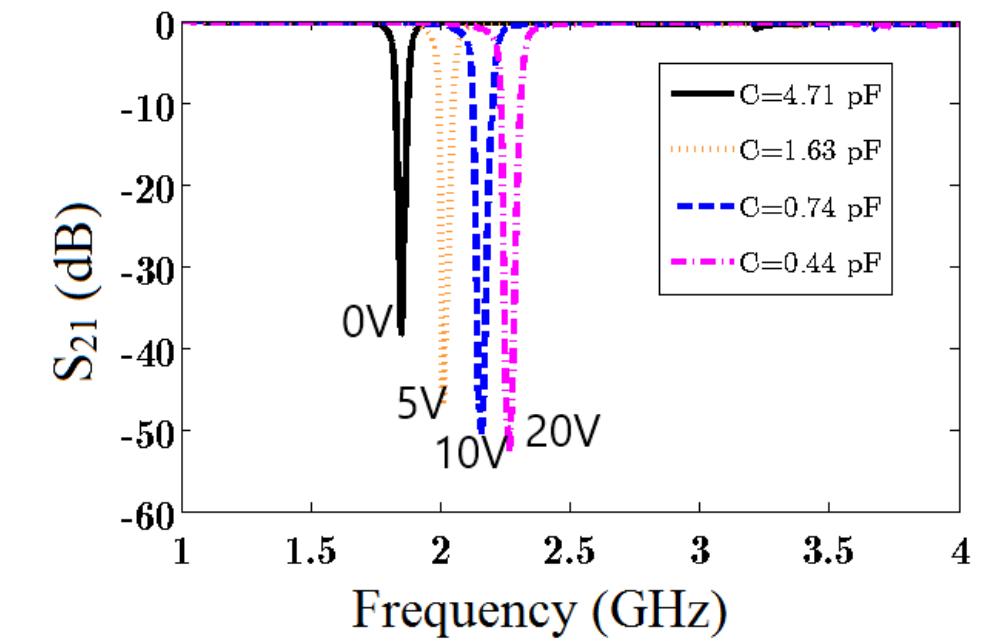
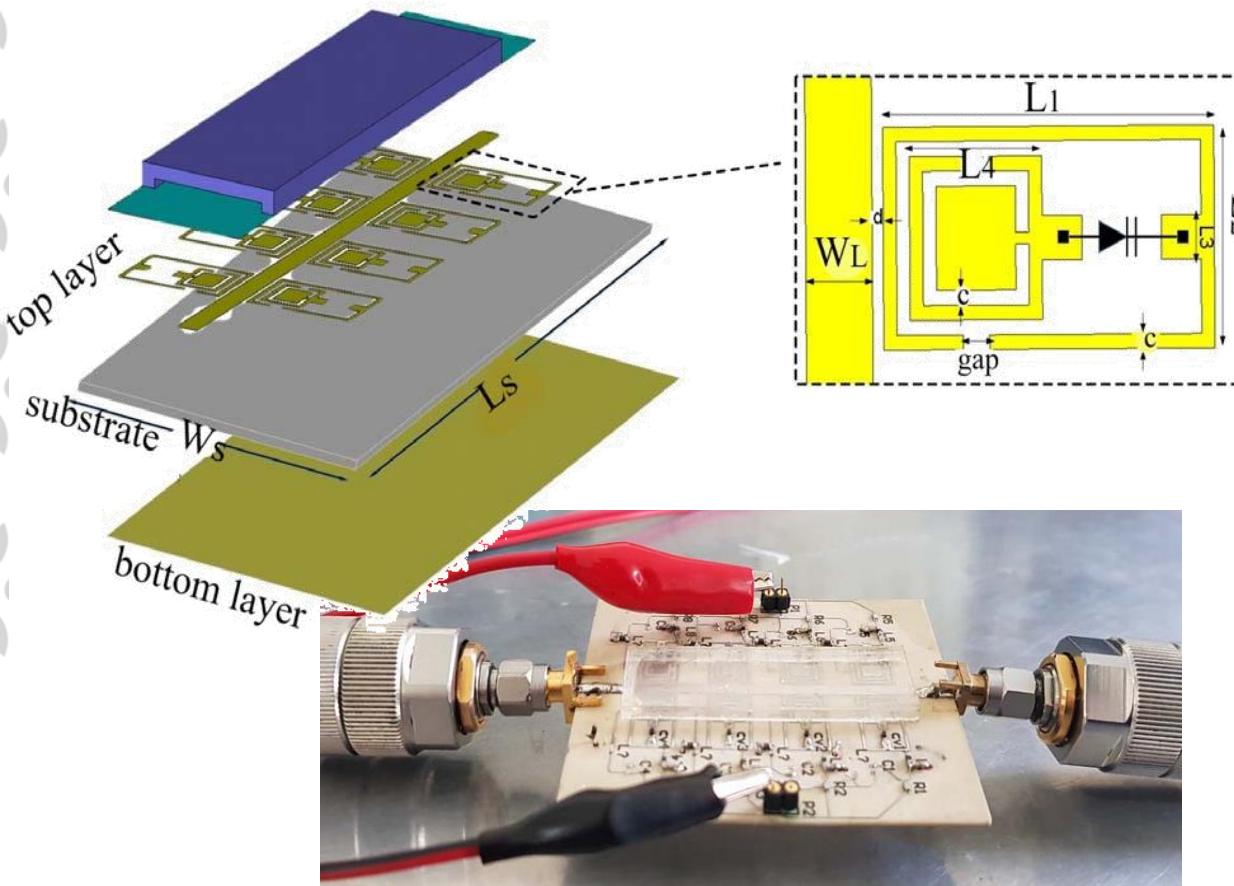
Withawat Withayachumnankul,
Sensors and Actuators A: Physical , 2013



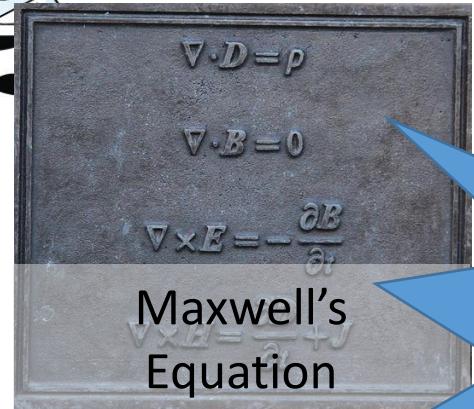


Tunable split-ring resonator (SRR)

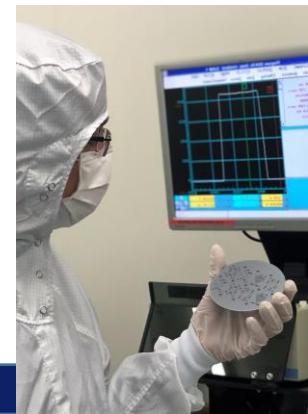
Diode Varactor loaded on a « SRR » : shift of the resonant frequency



Conclusion



Interface





Thank you for your attention



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Université
Gustave Eiffel

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