



Interests of Microwave Dielectric Spectroscopy for biological characterizations

O. Peytral-Rieu, Y. Kozhemyakin, B. Cerdan, A. Calvel, Y. Li, D. Dubuc, and K. Grenier

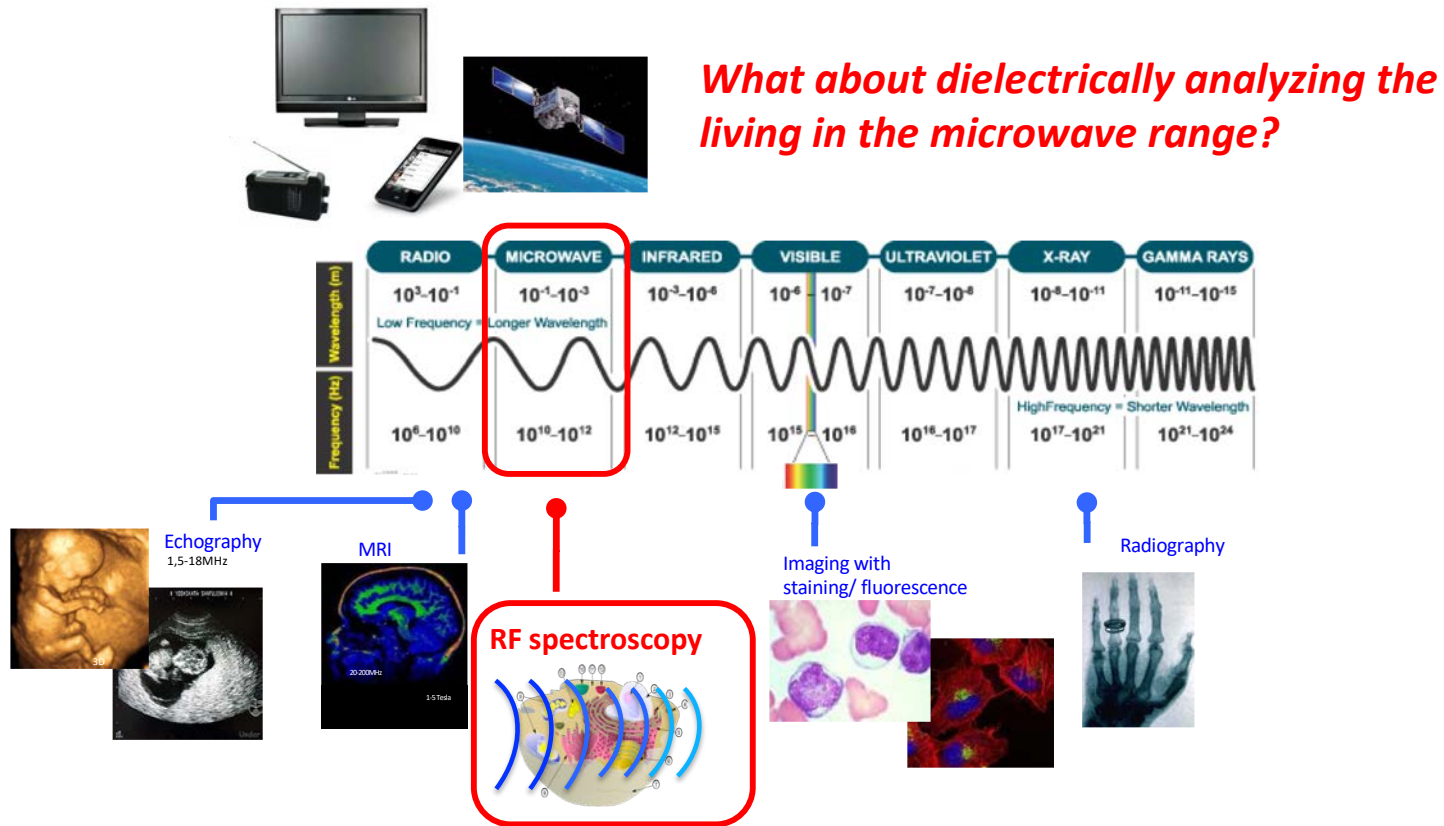
LAAS-CNRS, Université de Toulouse, CNRS, UPS, Toulouse, France

<https://www.laas.fr/public/en/mh2f>



Université
de Toulouse

Microwaving the living matter for sensing

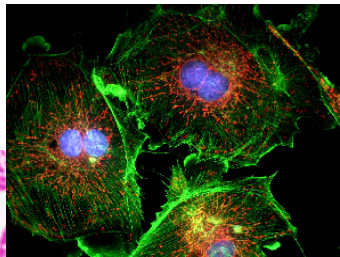


Main motivation

Cells and tissues analysis for biological and biomedical applications

Traditional techniques:

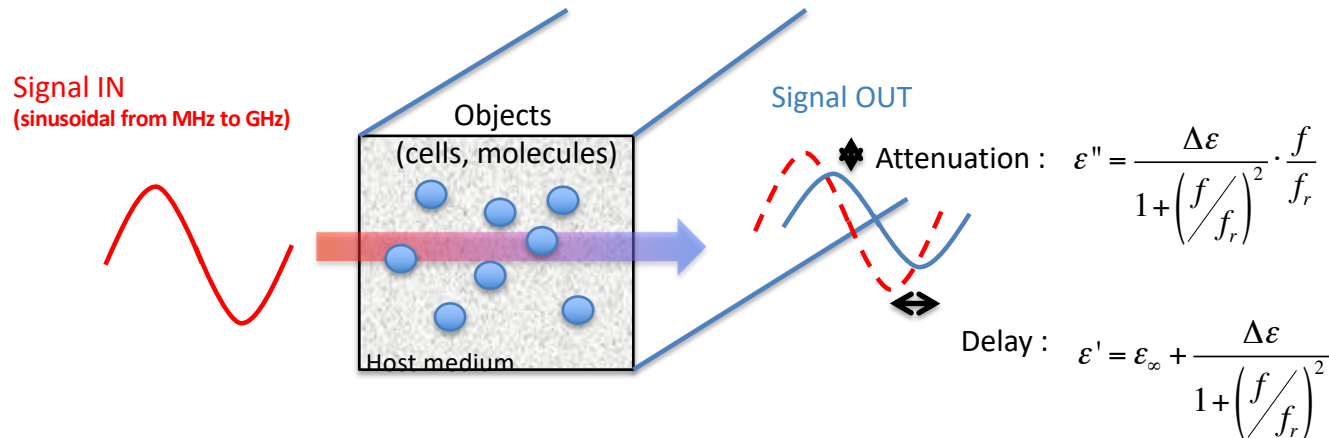
- Microscopy with stains or labels
- Laser detection
- Flow cytometry



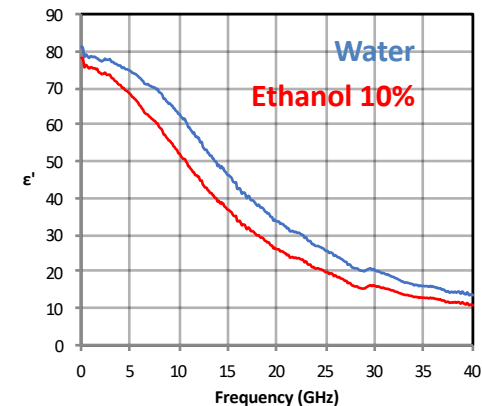
Invasive and toxic for cells
Destructive
Time consuming
Costly

→ Interest in non invasive and label-free bio-analysis

Microwave dielectric spectroscopy readouts



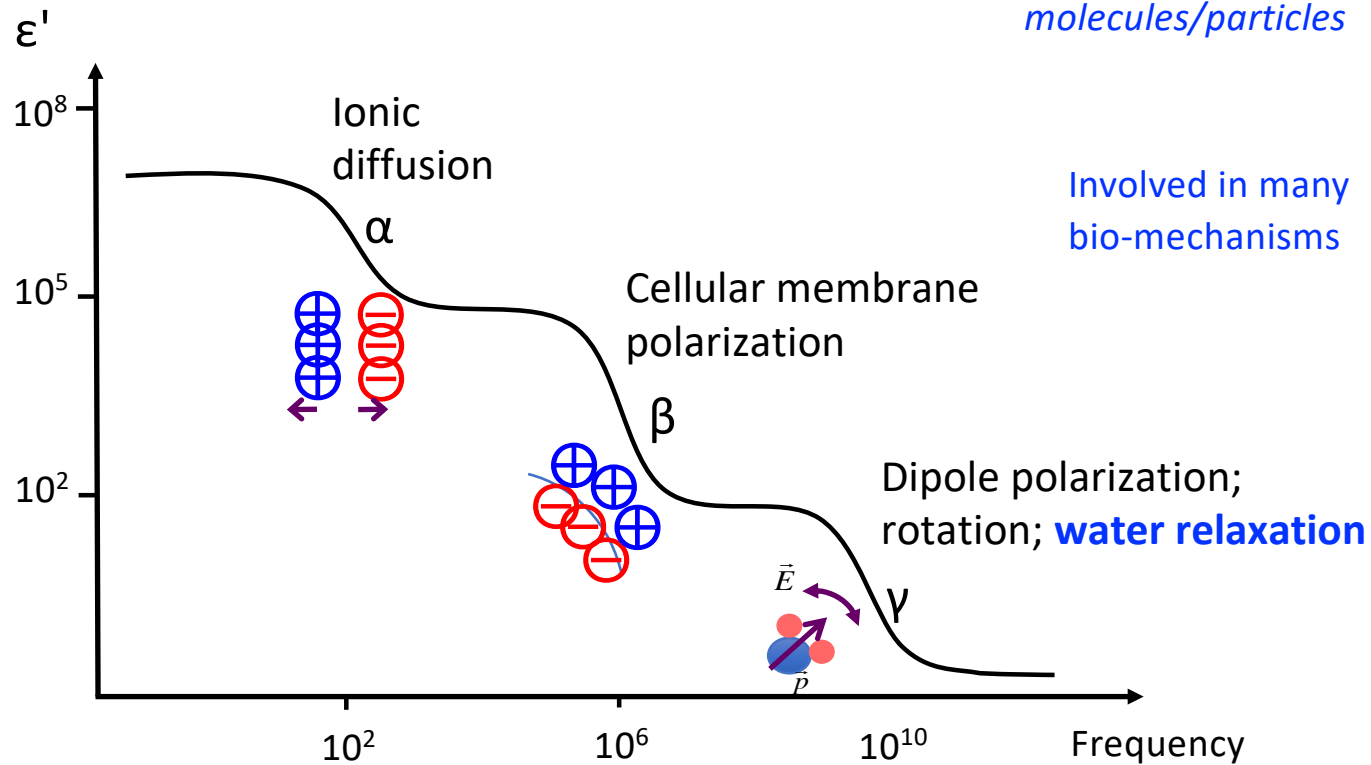
- Both ϵ' and ϵ'' are readouts of
 - scanning frequency,
 - dipolar moment,
 - size of the objects (volume fraction)
 - viscosity
- Modification of the molecular network structure
 - Change of the microwave dielectric response



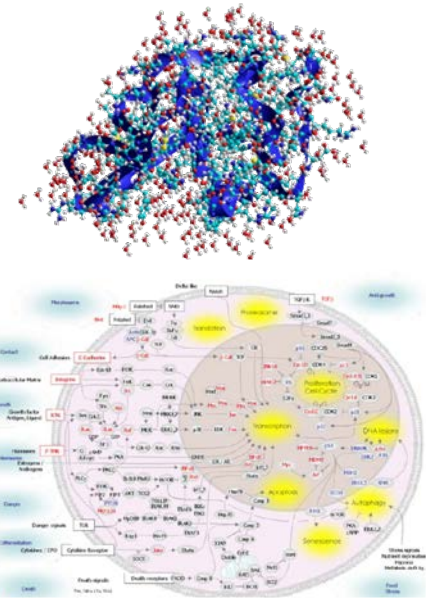
Electromagnetic wave interaction with the living

Water: abundant constituent of the living

Affinity with other molecules/particles

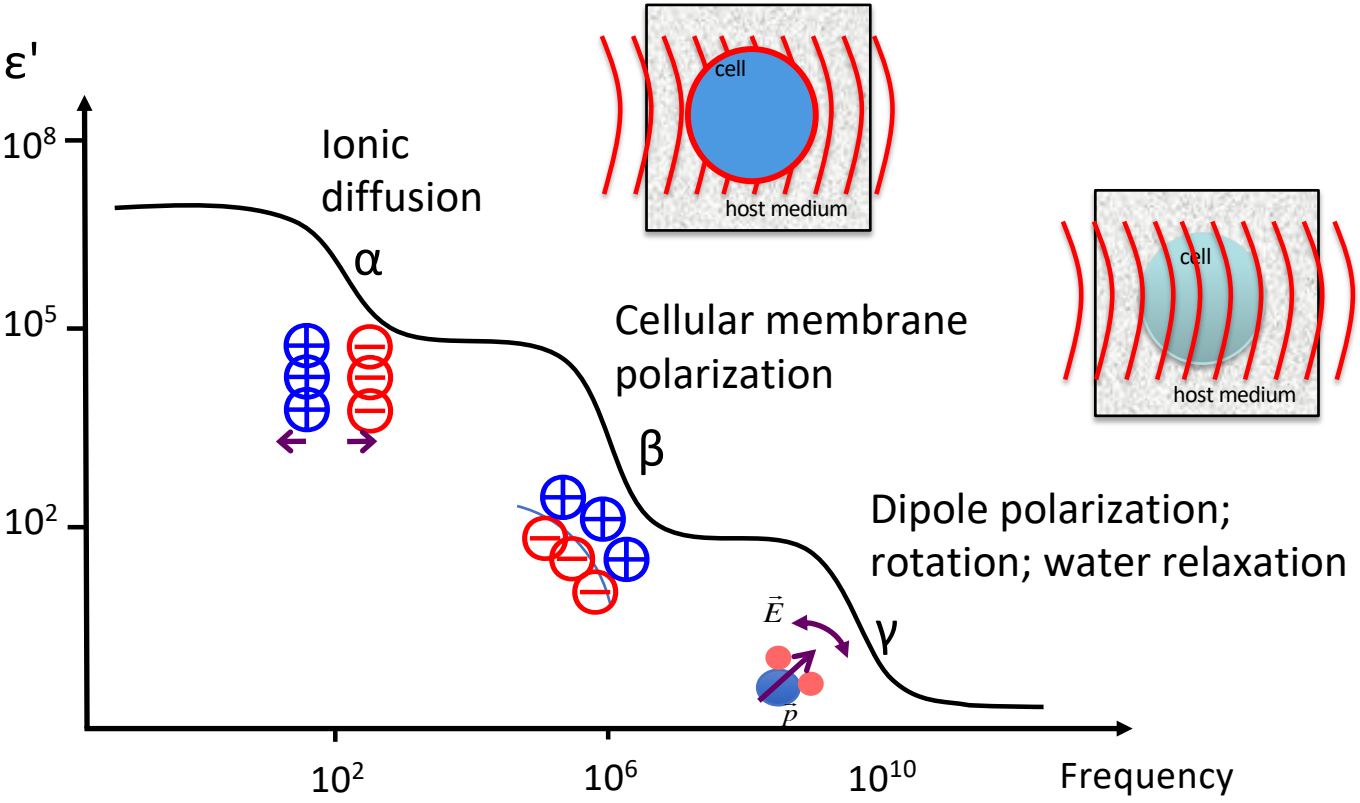


Involved in many bio-mechanisms



H. Schwan, 1985

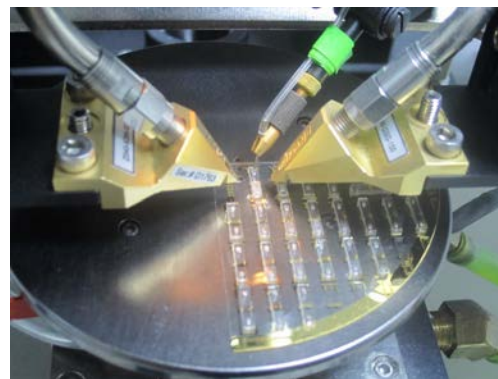
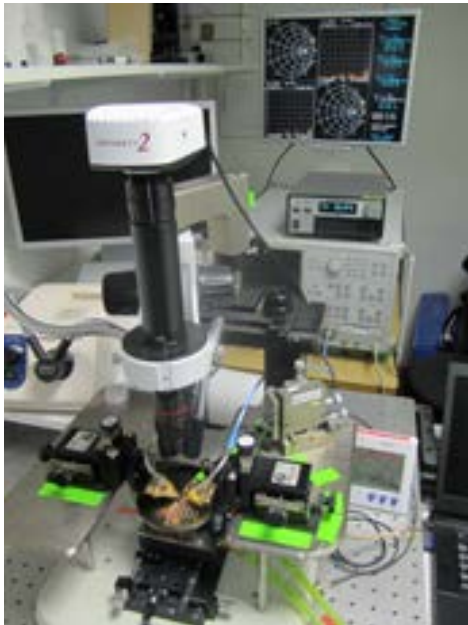
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Dielectric characterization of fluids

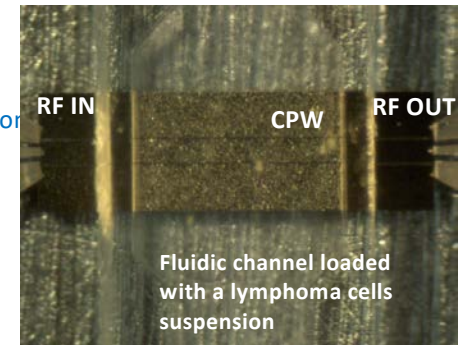
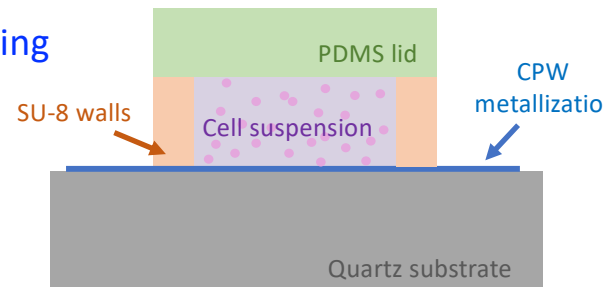
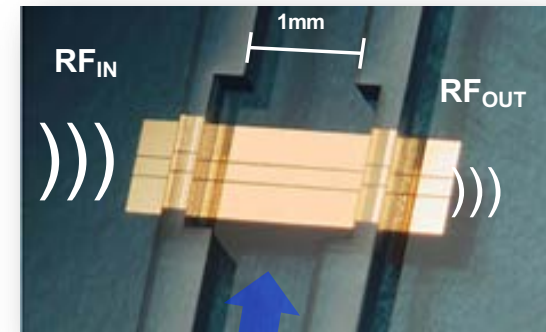
Coplanar waveguide sensor for biomolecules in aqueous solution and cells suspensions analysis



[S] parameters measurements

De-embedding

(ϵ', ϵ'') vs frequency

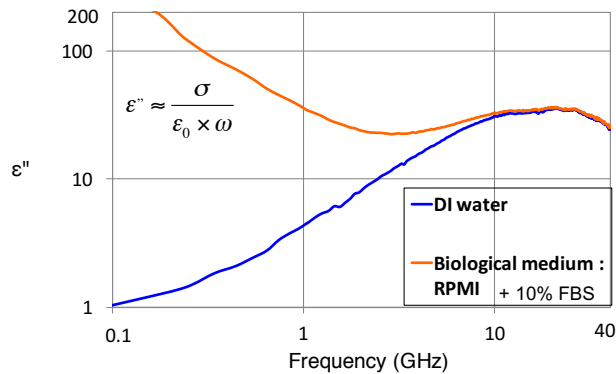


More details in Grenier et al., IEEE T-MTT 2009

Microwave dielectric spectroscopy for cell analysis



Cells analyzed directly
in their culture medium

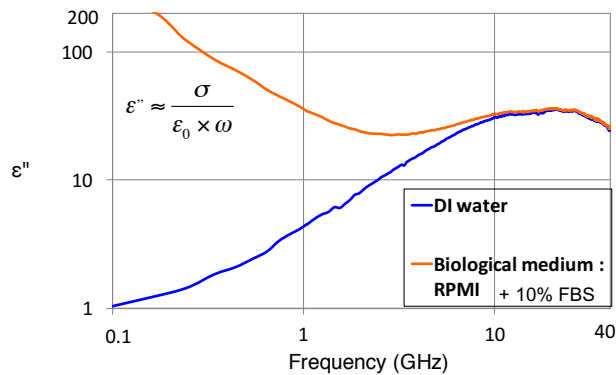


No screening with salt/ion content

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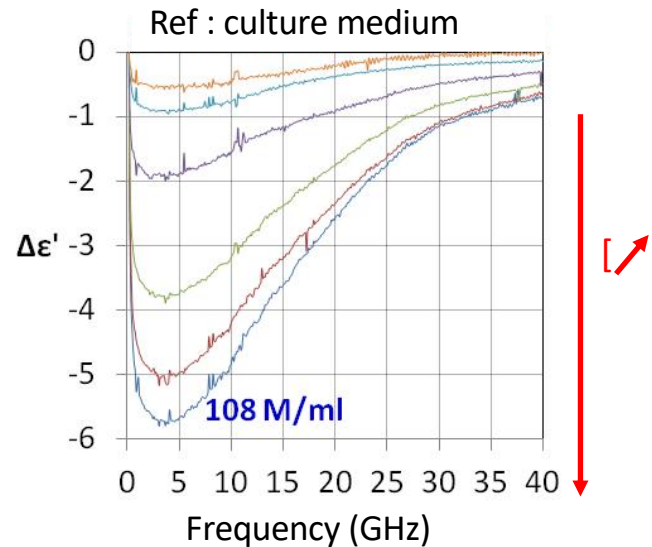


No screening with salt/ion content

$$\Delta\varepsilon = \varepsilon_{\text{fluid under test}} - \varepsilon_{\text{ref (host medium)}}$$

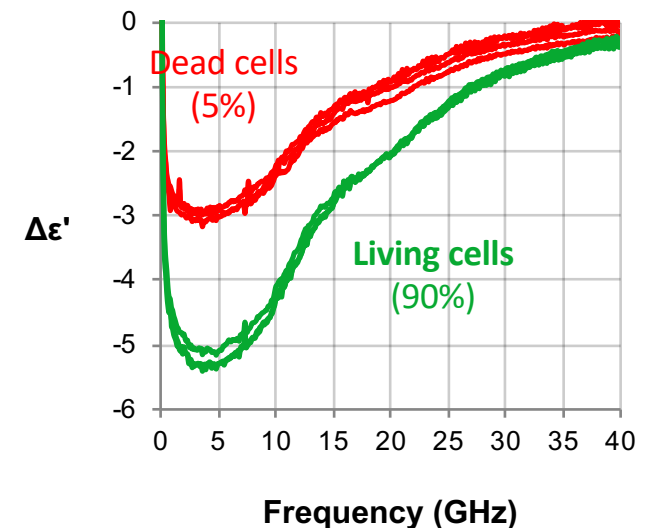


Quantification
of RL lymphoma cells



F. Artis et al., IEEE EuMW 2013
K. Grenier et al, IEEE Biowireless 2011

Dead/living discrimination
Use of saponin on DoHH2 cells



F. Artis et al., IEEE IMS 2014

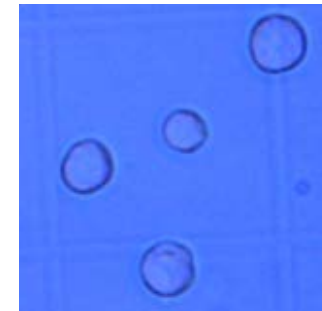
→ Reproducible measurements : RF measurement protocol is the key

Label free discrimination of cells

Case study : B lymphoma cell lines

Traditional equipments used for discrimination :

- B lymphoma cells from other lymphoma cells:
→ Recognition with antigenic labelings of CD19⁺ and CD20⁺
- Between B lymphoma cell lines :
→ heavy molecular cytogenetic characterization



Lymphoma cells in culture medium

Cell lines	Concentration (M/ml)	Viability (%)	Diameter (μm)
OCI-LY7	83.7 (11.1)	83.5 (10.5)	10.4
OCI-LY10	82.9 (10.1)	93 (2.9)	10.3
OCI-LY18	79.2 (21.4)	87 (9)	12.2

} Similar size
Larger diameter

Label free discrimination of cells

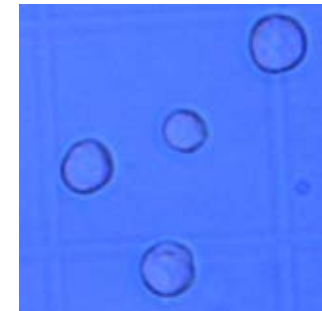
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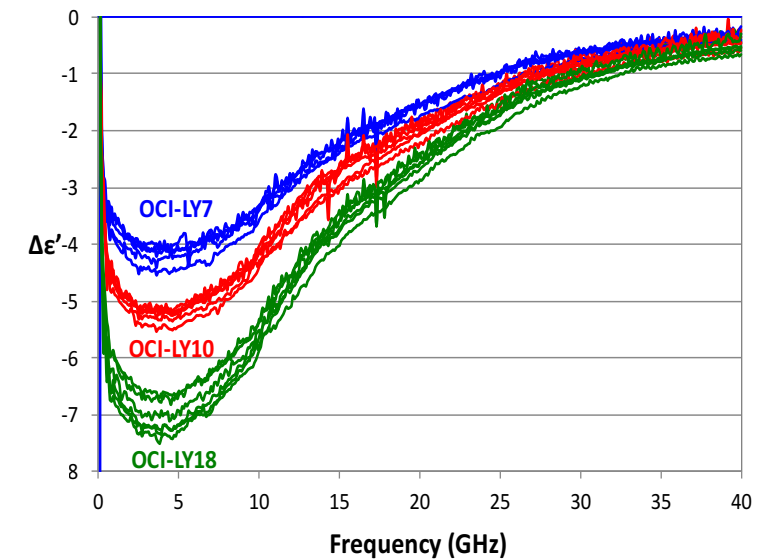
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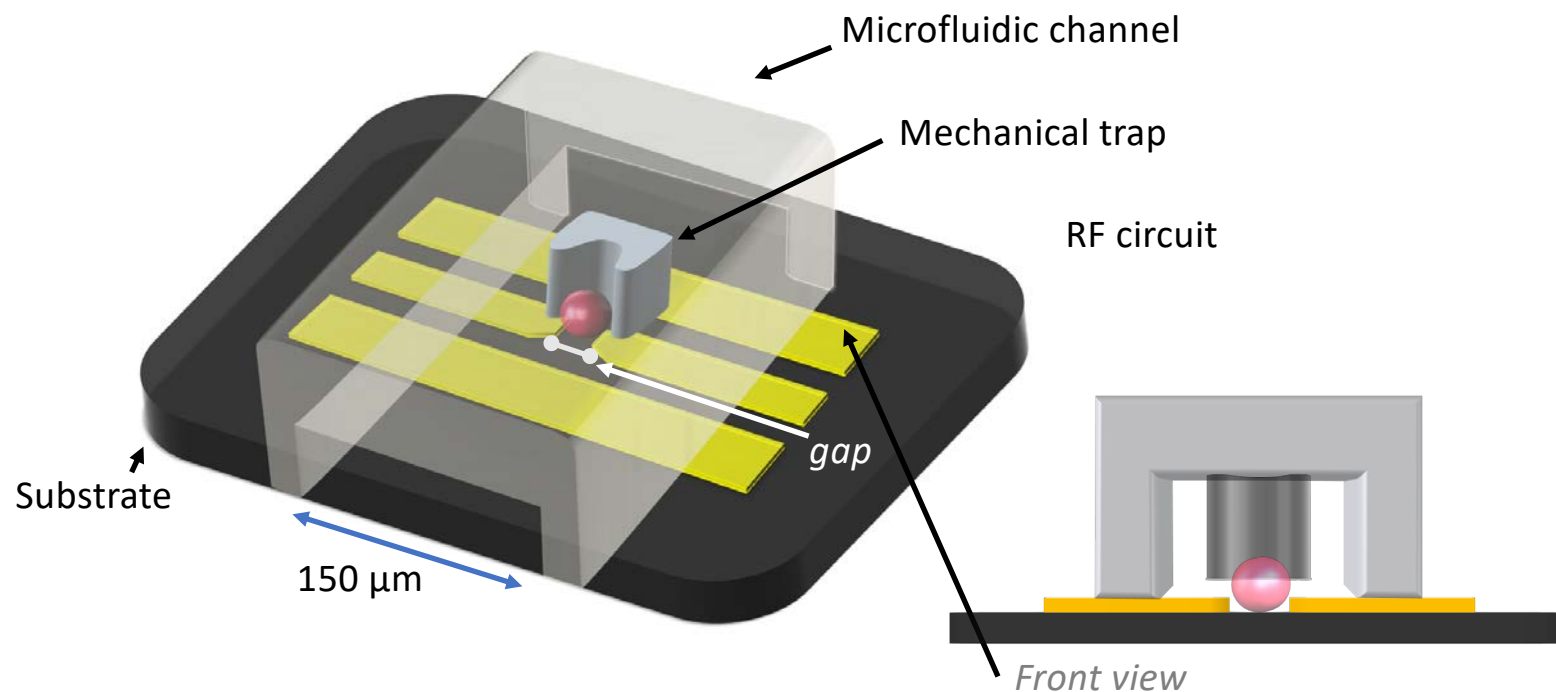
Lymphoma cells in culture medium



→ Possible discrimination of sub-populations of B lymphoma cell lines (with a common phenotype) due to internal molecular and constitutive variations of the cells

K. Grenier et al., IEEE IMS 2018

Broadband single cell detection

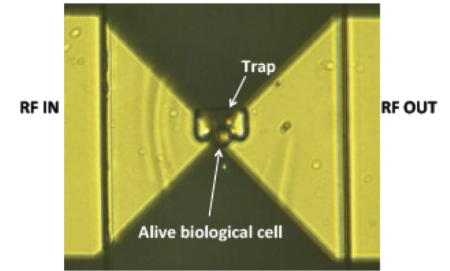


- **Substrate** : quartz
- **Coplanar waveguide**: gold layer of 0.3 μm thick, with a capacitive gap
- **Trap and fluidic channel**: polymer based technology

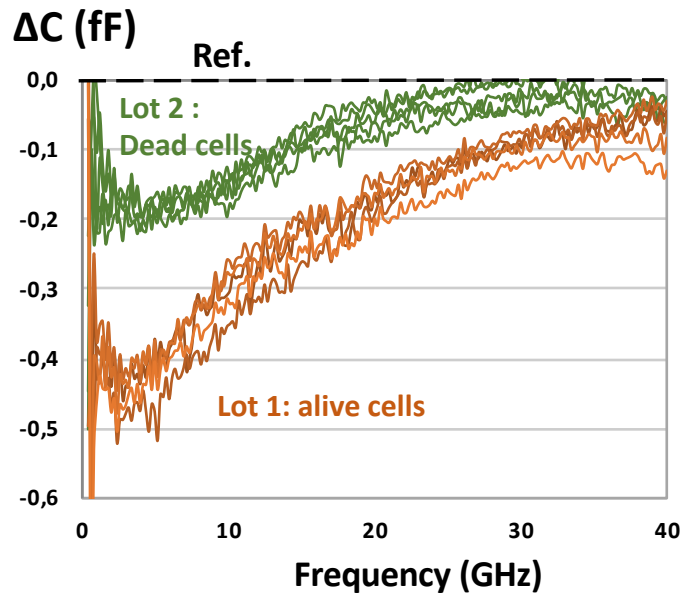
With single cells

Cell state

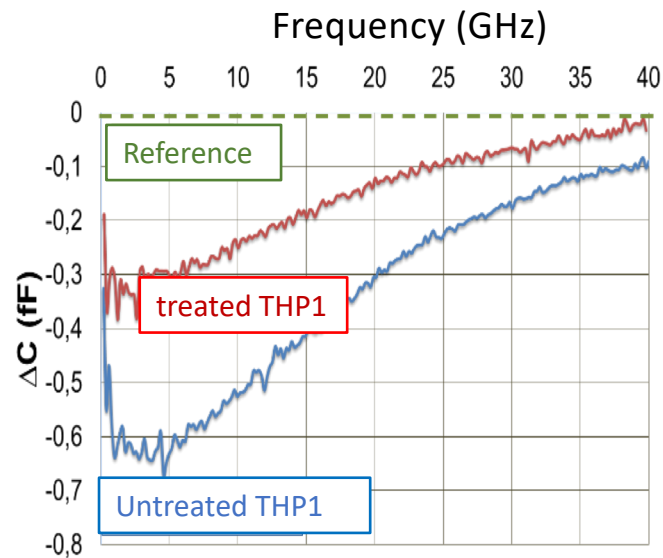
single THP1 cells in culture medium (RPMI+10%FVS)



Death induced by starvation

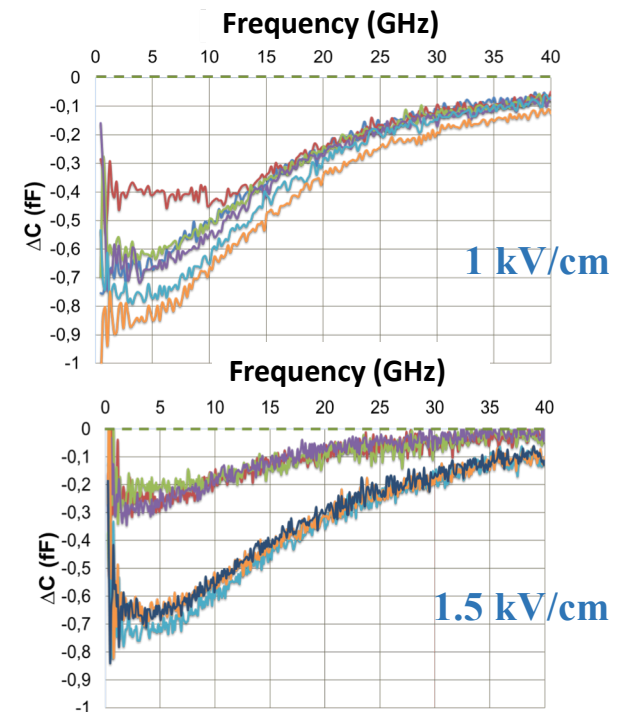


by a chemical agent (saponin)



F. Artis et al., IEEE IMBioC 2019

With electrical fields



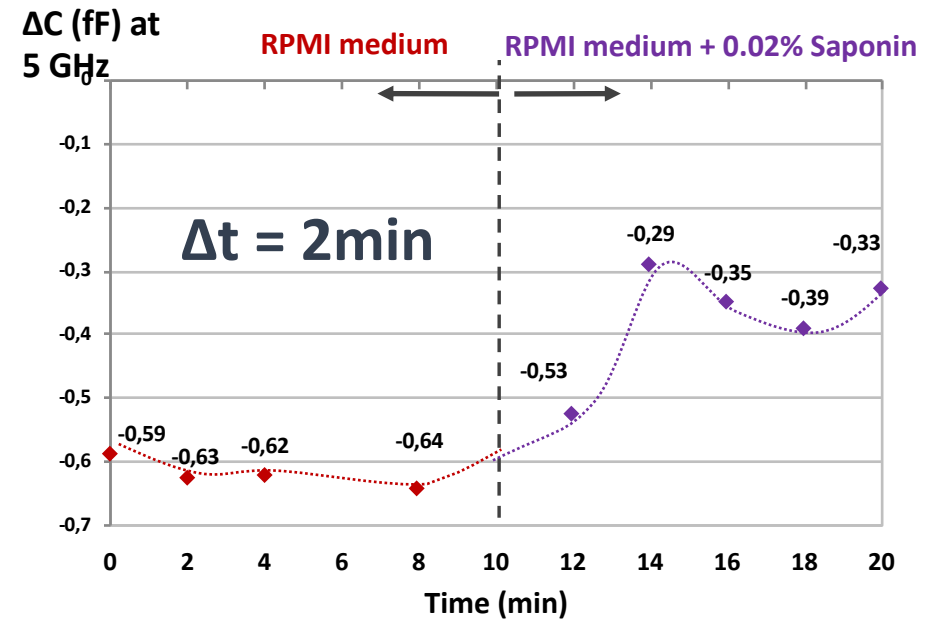
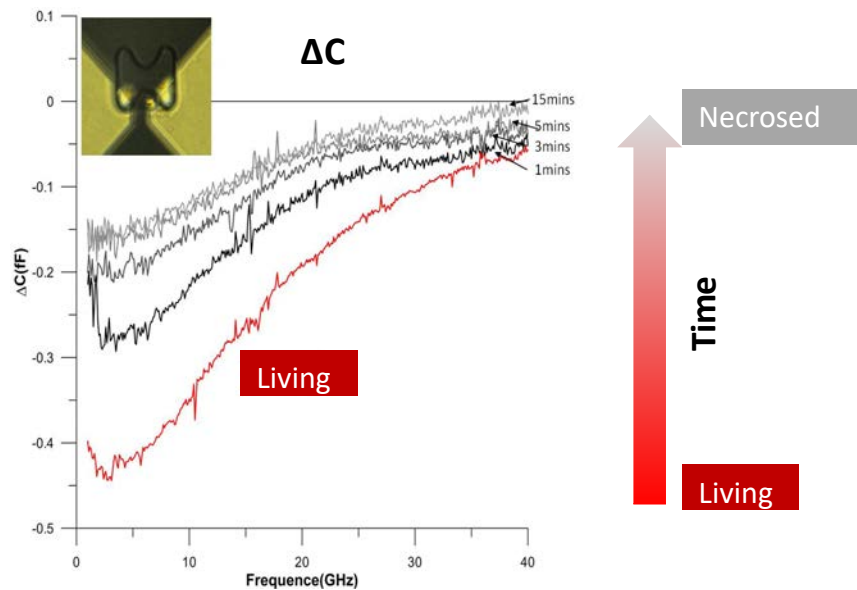
A. Tamra et al., URSI-GASS 2021

A. Tamra et al., IEEE TBME 2022

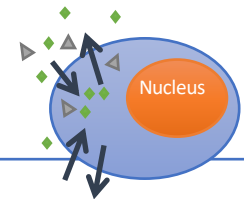
Real time monitoring of a cell permeabilization

RL lymphoma cell submitted to 2% methanol

THP1 cell submitted to 0.02% of saponin



→ Monitoring of biological process kinetic



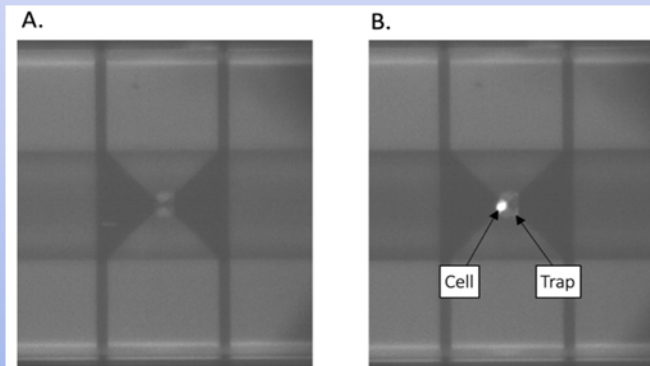
Toward ElectroChemoTherapy monitoring with microwaves

On going work of Anne Calvel

In situ electroporation at the single cell level

Before EP

20 mins after EP :
propidium iodide entrance

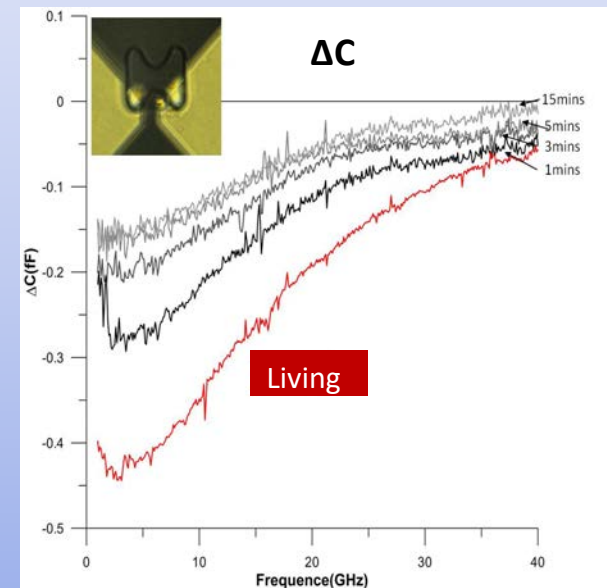


EP : 8 pulses of 5 ms duration at 1 Hz
on PC3-GFP cells

A. Calvel et al. WCT 2022

+

Real time monitoring with microwave spectroscopy



W. Chen et al. URSI GASS 2021

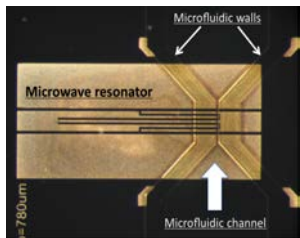
With a dedicated test setup

Extension of microwave analysis to microtissues

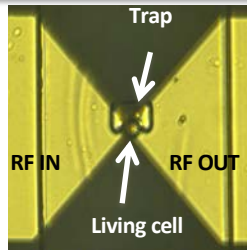
Different sensors and test setups solutions

IN VITRO

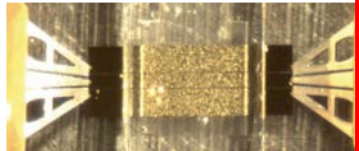
Ions; particles; molecules



Single cell

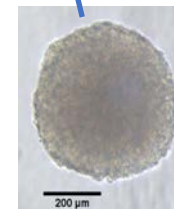
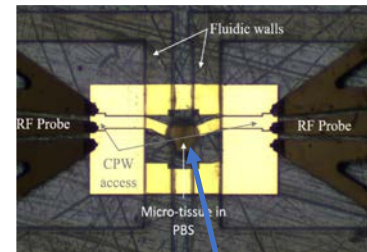


Cells in suspension

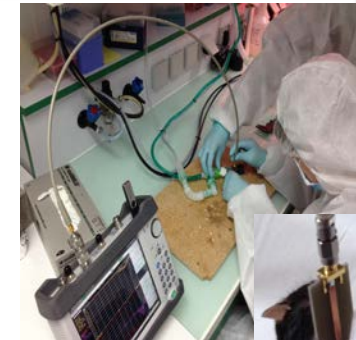


EX VIVO / IN VIVO

Micro-tissues



Tissues, organs

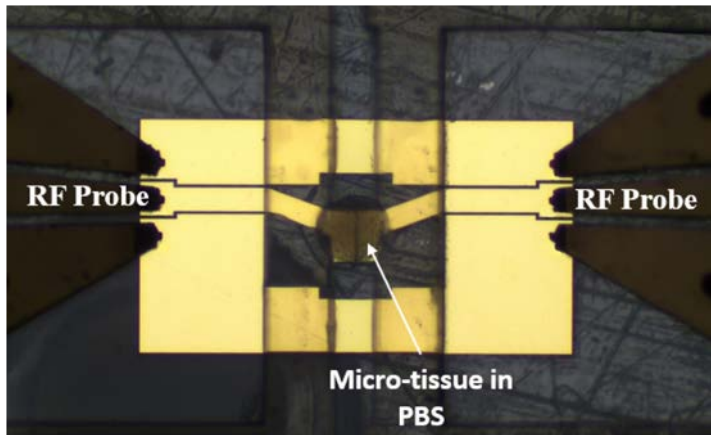


Animals, humans

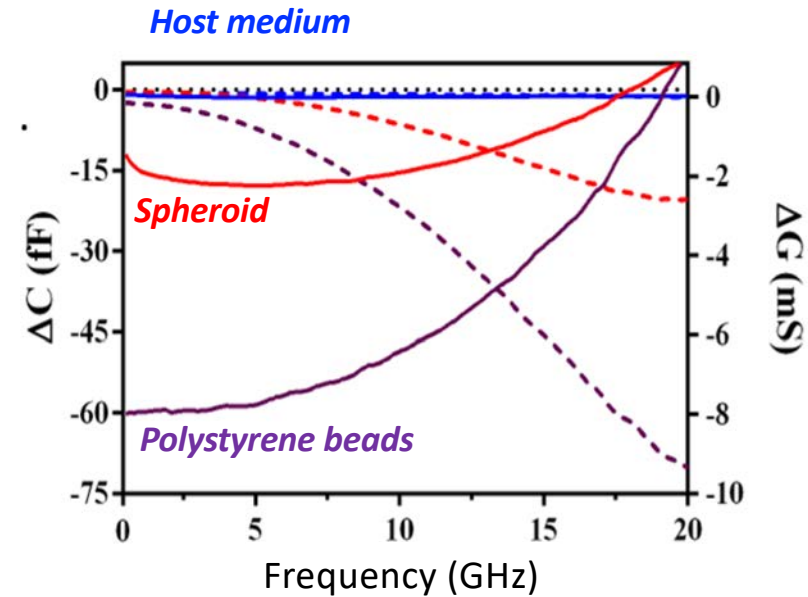


➔ 3D biological model close to the in vivo configuration, avoiding animal experiments

Microwave characterization of microtissues



O. Peytral-Rieu et al, IEEE IMS 2021



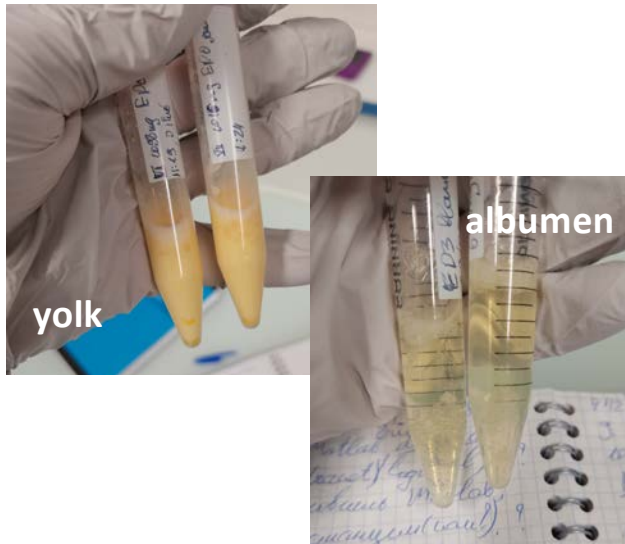
Extended to real time monitoring in *O. Peytral-Rieu et al, IEEE T-MTT 2023*

Applied to the study of drug impacts through the work of Yuwei Li

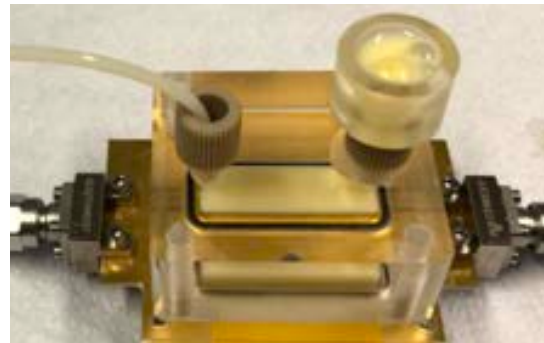
Extension of the sensing technique to agriculture studies



Study of egg constituents for quality assessment

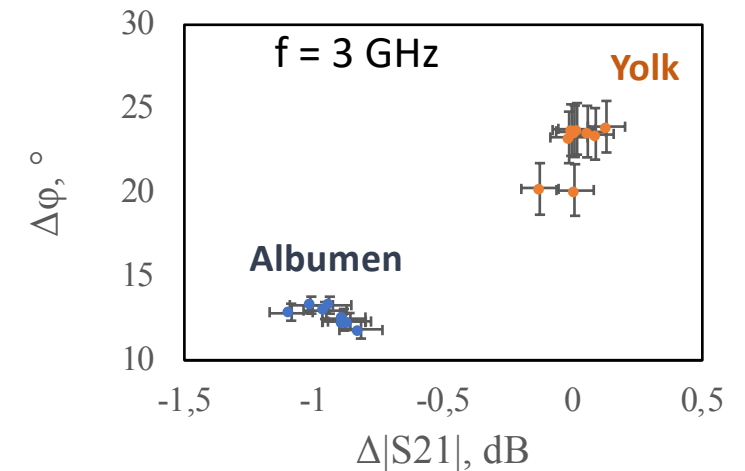


Millifluidic sensor with appropriate RF measurement and cleaning protocols



Fluids particularly sticky, viscous

For 9 eggs samples

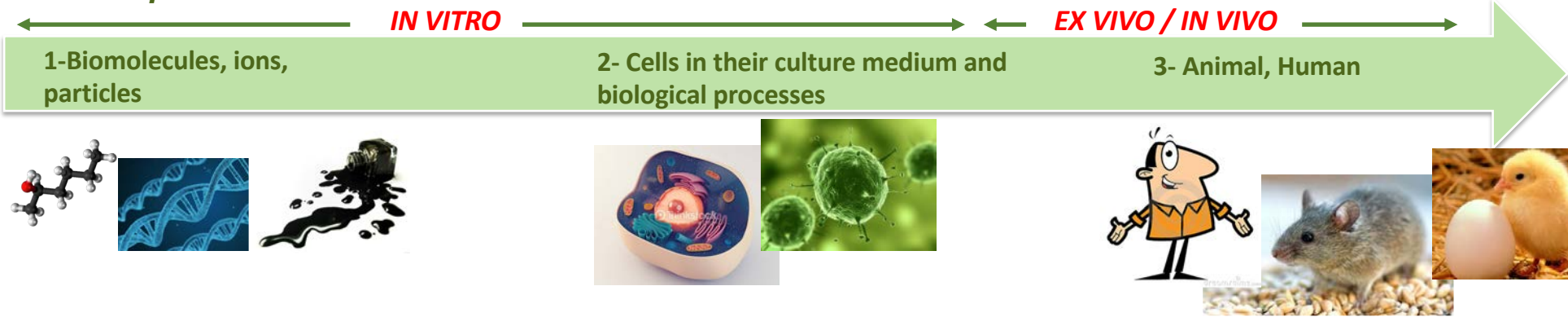


Y. Kozhemyakin et al., EuMW2022

➔ Evaluation of the possible discrimination of early in ovo sexing under investigation

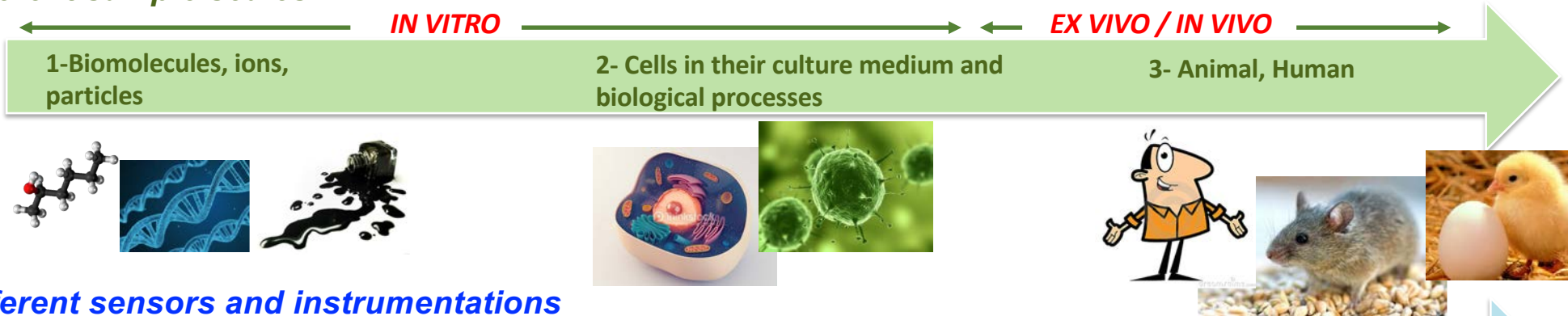
Multi scales // multi sensors // multi purposes

Different sample scales

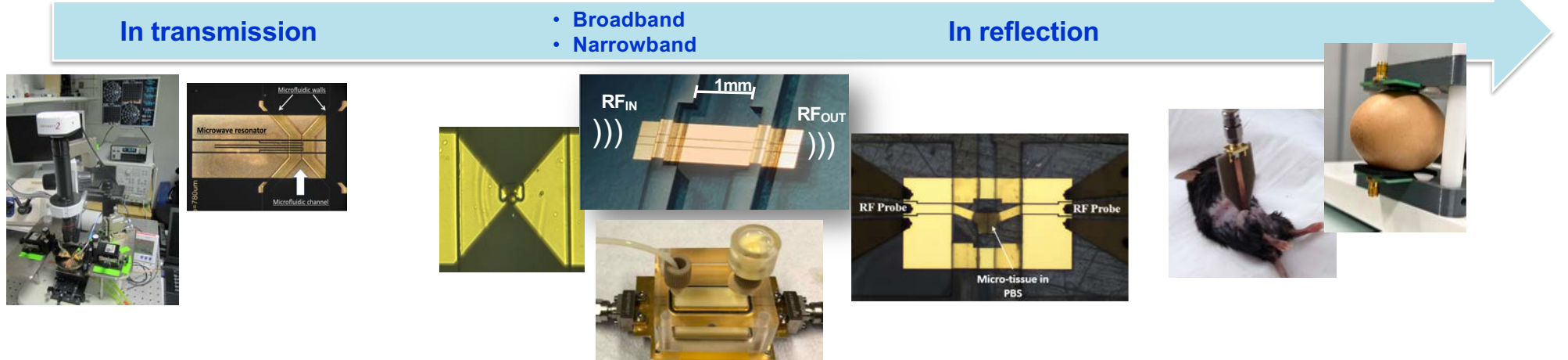


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Different sample scales

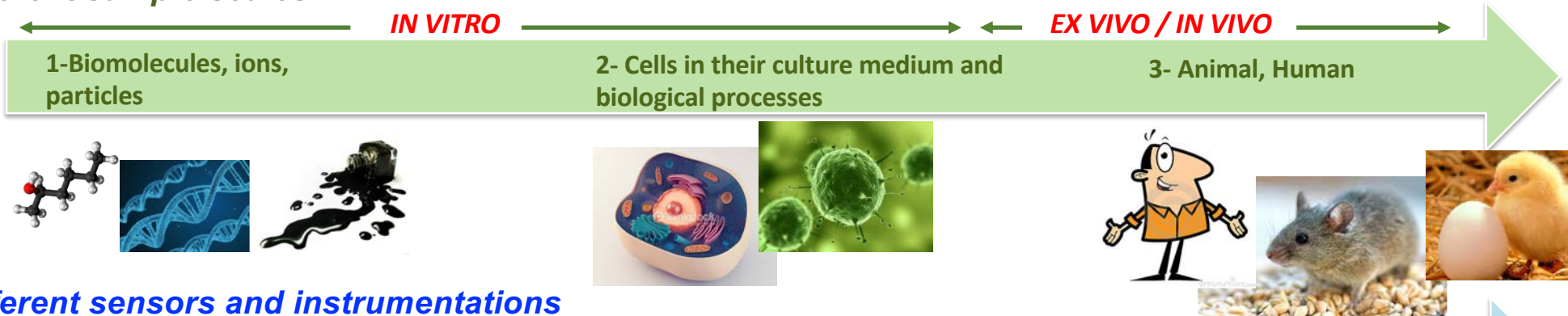


Different sensors and instrumentations

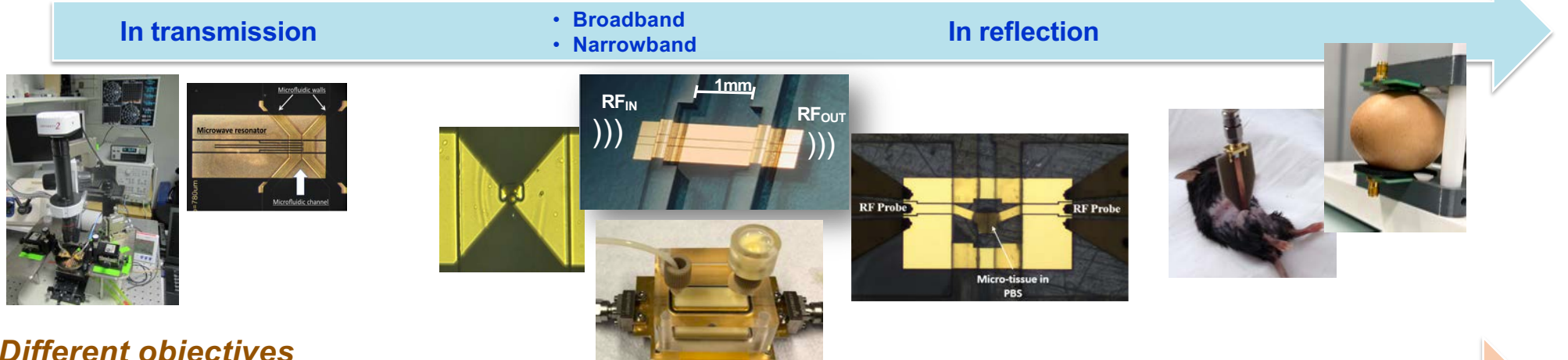


Multi scales // multi sensors // multi purposes

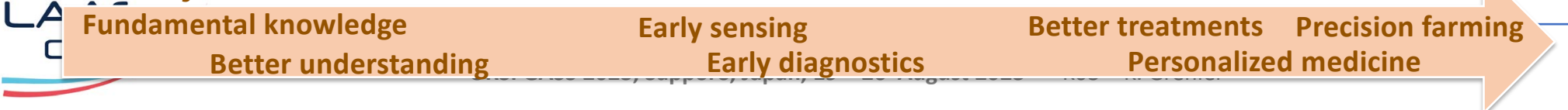
Different sample scales



Different sensors and instrumentations



Different objectives



Acknowledgments

In collaboration with

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IPBS, Toulouse



B. Susini-Garmy
I2MC, Toulouse



B. Ducommun,
V. Lobjois
ITAV, Toulouse



And fundings from



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Thank you for your attention

Any questions ?

Here is my contact

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