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Electrochemical Sensors for Animal Welfare

Ilaria Sorrentino, Claire Verplanck and Yohann R.J. Thomas

Monday, September 11 2023

BIOMEDICAL SENSORS & DIAGNOSTICS I



CEA : a public research organization



4 MAIN RESEARCH AREAS



Defense and national security



Nuclear and renewable energy



Fundamental research



Technology research

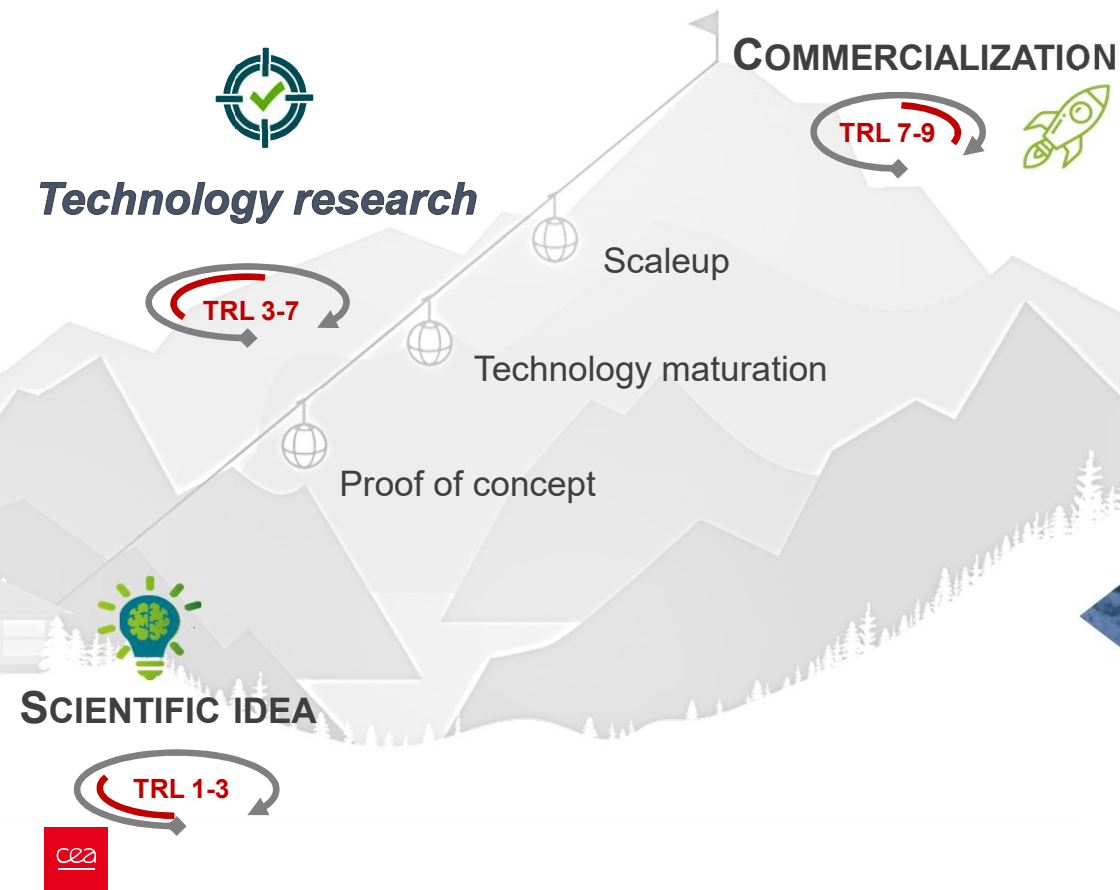


CEA-Leti
Grenoble

CEA-Leti is one of the 3 technological research institutes of CEA

Our mission: transfer technology to industry

Connect academic research directly to industrial R&D to catalyze innovation and shorten time-to-market for businesses.





“3rd Innovative Public Research Organization Worldwide” 2012 -2020

Derwent™
A Clarivate Analytics company



Since **1967**



2,000 people

Patents:



- > 3,000 in portfolio
- 40% under license agreement

Startups:



- 68 created for 20 years (75% in activity)
- 3500 jobs created

Cleanrooms:



- 500 state-of-the-art equipment in 200 & 300 m²
- 10 000 square meters cleanroom

Budget:



- 315 M€
- 85% from R&D contracts

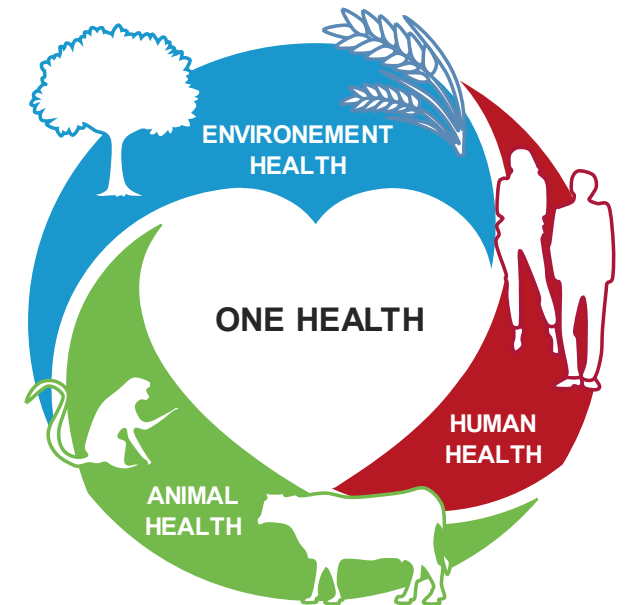
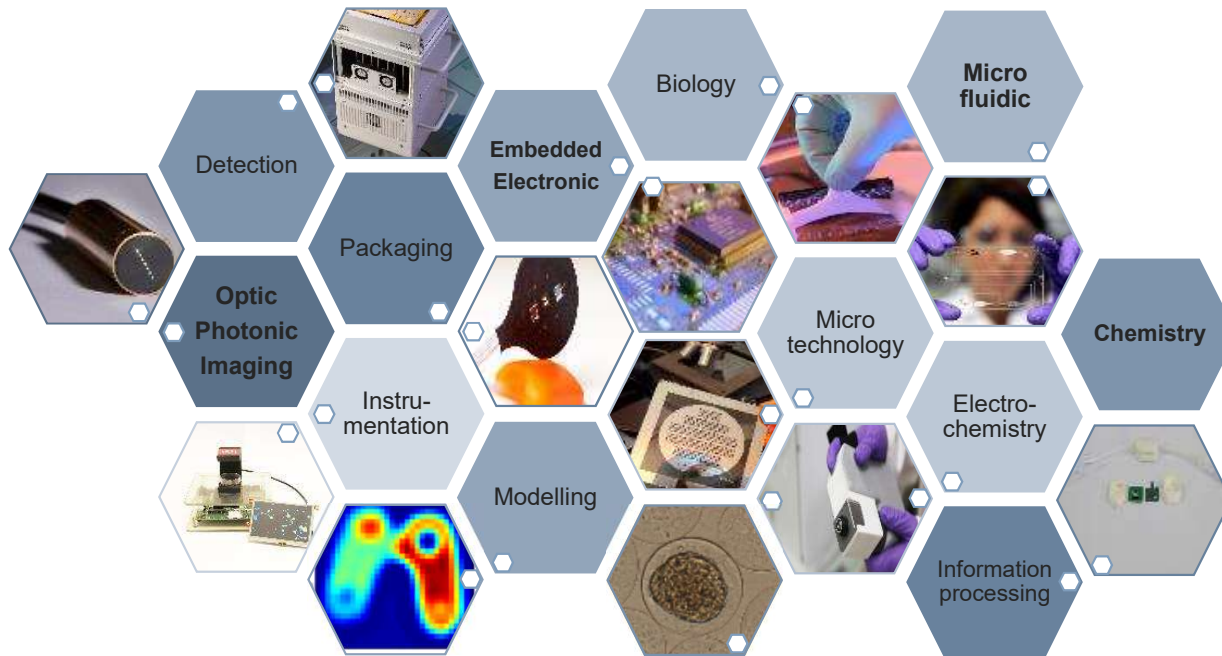


Leti health

Mission and Expertise

Address societal needs in the fields of biology, healthcare, environment and security

Create & develop innovative solutions for our industrial partners

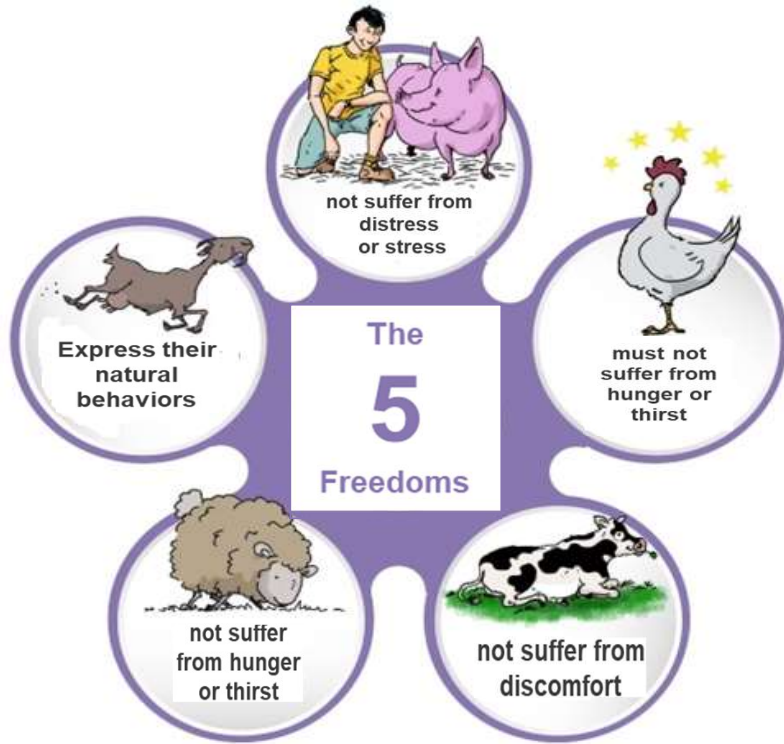


Multidisciplinary teams - One stop shop for completely integrated systems



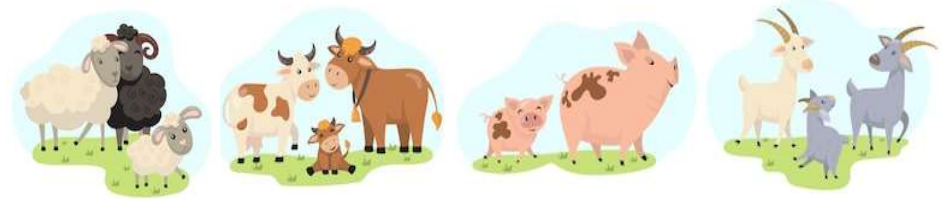


WAIT4: Welfare Artificial Intelligence and new Technologies for Tracking key indicator Traits in animal facing challenges of the agro-ecological Transition



To be proactive for **animal welfare** (AW), we need to understand their **point of view** and **needs**

Project goal: Increasing research-based capacities to quantify and characterize AW in the **agro-ecological (AE)** perspective and revising **farming practices** and **decision-making tools** by considering interactions between the animal and its environment



Source: Website of the Chamber of Agriculture for Animal Welfare (France)












<https://bien-etre-animal.chambres-agriculture.fr>

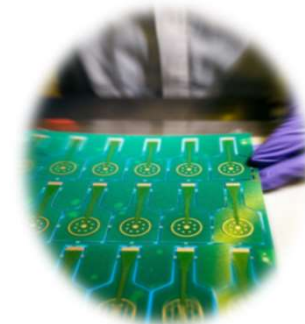
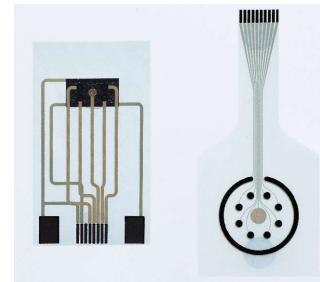


WAIT4: Welfare Artificial Intelligence and new Technologies for Tracking key indicator Traits in animal facing challenges of the agro-ecological Transition



- **WP1:** Analysis of interactions between the animal and its environment, using artificial intelligence 
- **WP2:** Monitoring physiology for acute and mid-term adaptation to stress factors  
- **WP3:** Determining the impact of agro-ecological transition on animal welfare   
- **WP4:** Dissemination   

CEA Objective: Coupling hydrogel microneedles (MN) to electrochemical sensors in order to develop minimally invasive connected devices for real-time monitoring in animals Interstitial Fluid (ISF)

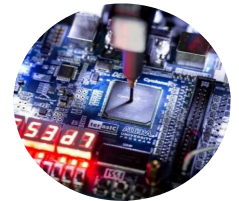
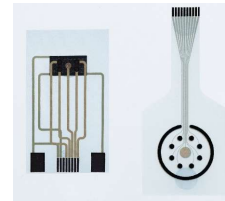


A.Aubert / CEA

WAIT4: Welfare Artificial Intelligence and new Technologies for Tracking key indicator Traits in animal facing challenges of the agro-ecological Transition



WP2- New sensors of animal physiology



Biomaterials

- Hydrogel formulation
- MN design
- Morphological and structural characterization

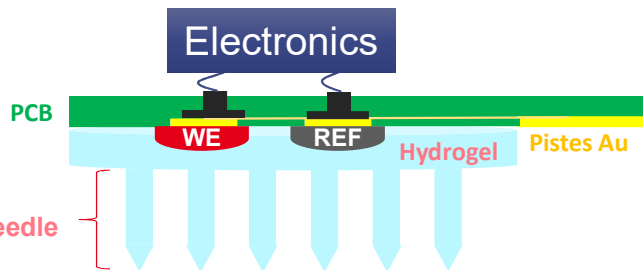
Electrochemistry

- Formulation ISE (Na^+ , pH) and REF
- Electrodes Design
- Calibration test on simple model solutions, complex and ISF sampling

Electronics

- Set up communication protocol
- collect data
- send data

Integration



- ✓ Sampling ISF (MN)
- ✓ Measuring in real time (Electrochemical sensors)
- ✓ Reporting data (Electronics)

WAIT4: Physiological variables of interest



Na⁺ and pH: concentration range (sensitivity & accuracy)

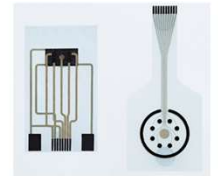
- **pH:** variation between 7.35 and 7.50 in blood (in cows)
Desired sensitivity range 0.03 to 0.05 pH point
 - ΔE over full range < 9 mV
 - Sensitivity range < 3 mV
- **Na⁺** – cow and sow in plasma: 130-145 mmol/L
Desired sensitivity range < 4-5 mmol/L
 - ΔE over full range < 3 mV
 - Sensitivity range < 1 mV



Very low values at the limit of possible detection



Electrochemical sensors



ADVANTAGES

Multiparametric measurements with one platform

Ions:
Na⁺, K⁺, Ca²⁺, Mg²⁺,
pH, NH₄⁺, NO₃⁻, Cl⁻
...

Metabolites:
glucose, lactate,
NO...

Conductivity

Complex fluids

Biological:
sweat, blood, plasma,
...

Aqueous:
Drinking water, rivers,
swimming pools, ...

Industrial

Adaptable to different substrates

Materials:
Silicon, polymers,
papers, fabrics, ...

Properties:
Flexible, stretchable,
wearable, ...

Fabrication processes adapted, collective

Other advantages

Continuous measurements

Miniaturization

Biocompatibility

Cytotoxicity

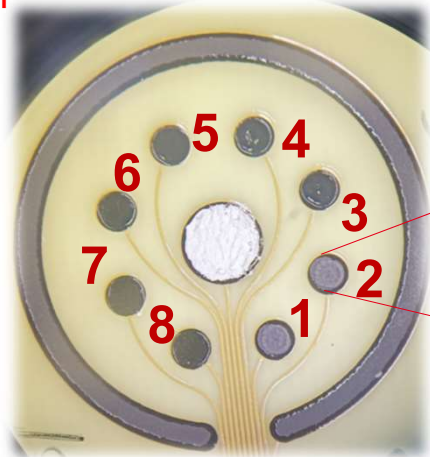
Platform adapted to the application



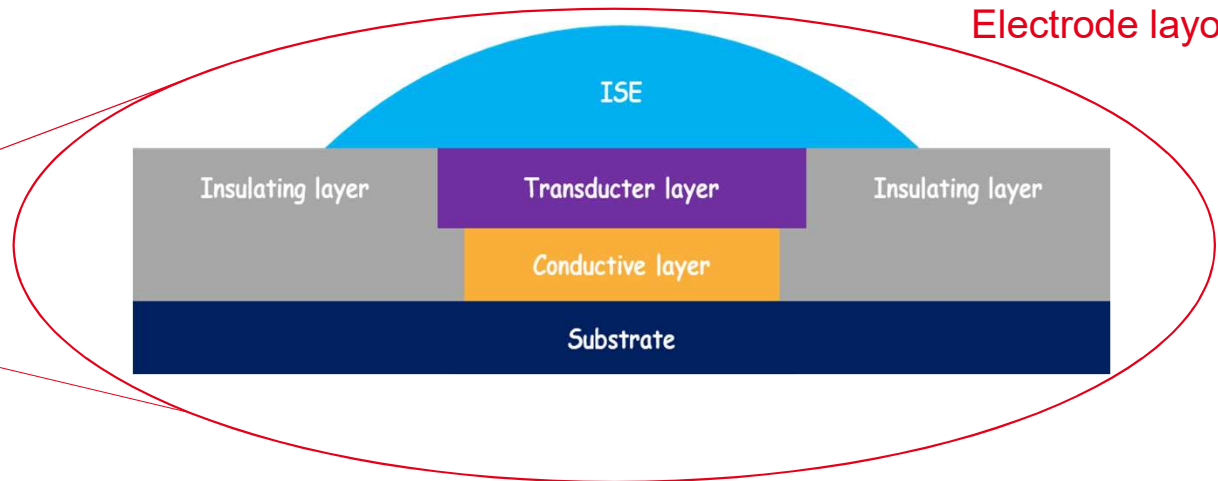
WAIT4: Electrochemical Sensors

Multi-parameter electrochemical platform for monitoring physiological variables of interest like sodium, potassium and pH in **animals Interstitial Fluid (ISF)**

Multi-parameter electrochemical platform

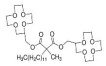


Electrode layout

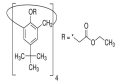


➤ Na⁺:

➤ Ion Selective Electrode (ISE) :3 ionophores



Ionophore Na VI



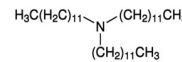
Ionophore Na X



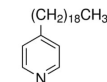
Ionophore Na IV

➤ pH :

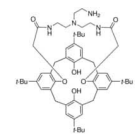
➤ Iridium Oxide: IrOx
 ➤ ISE: 3 ionophores pH



Hydrogen Ionophore I






Hydrogen Ionophore II



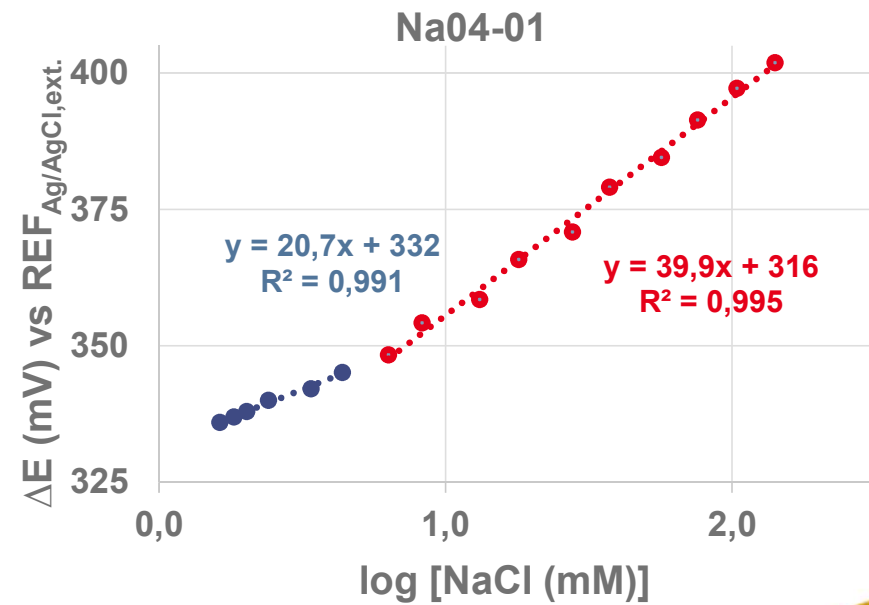
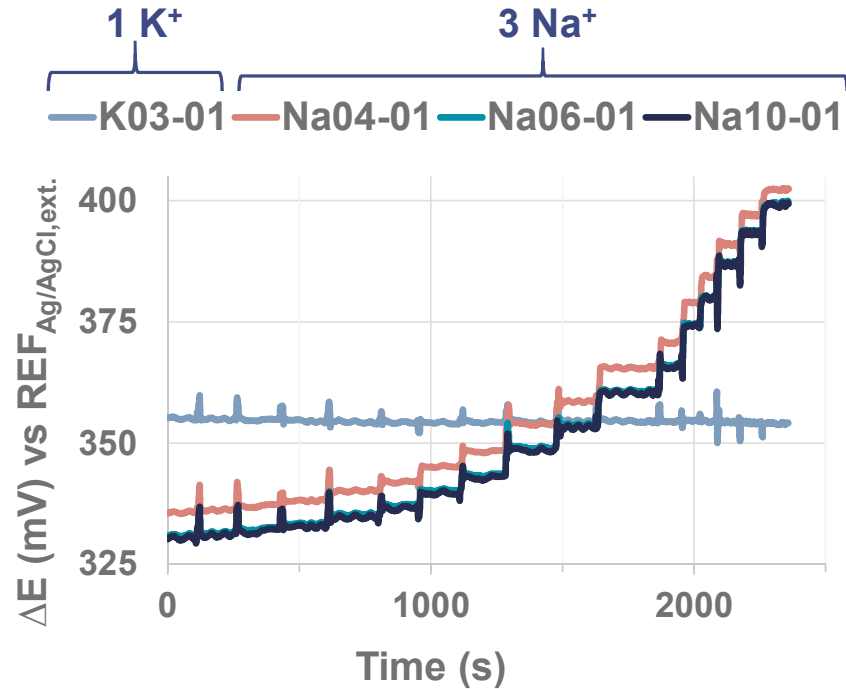
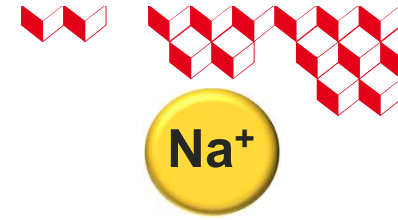
Hydrogen Ionophore V

Biosensor development - Experimental section

1. Sensing Na^+ 
2. Sensing pH 
3. Multiparameter platform – Interference such as K^+ 

1. Sensing Na⁺

Method of standard additions in complex buffer pH = 7,4



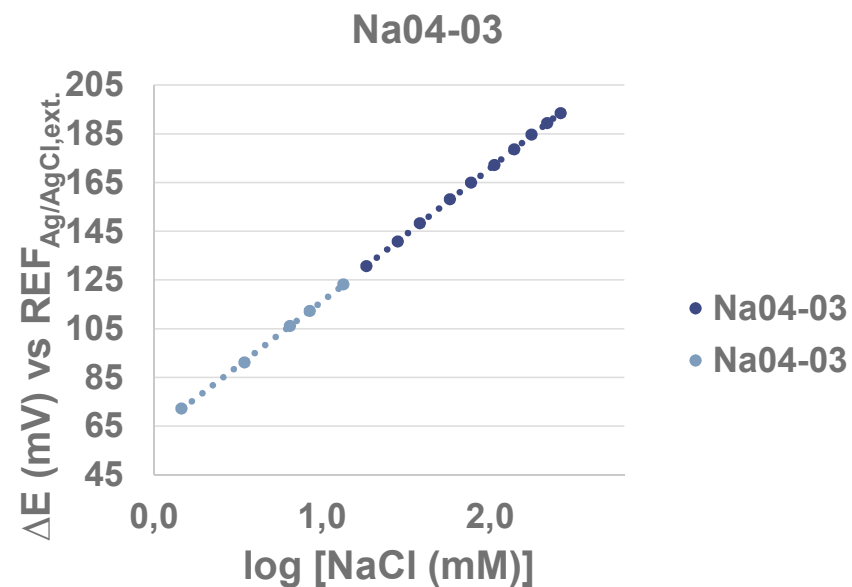
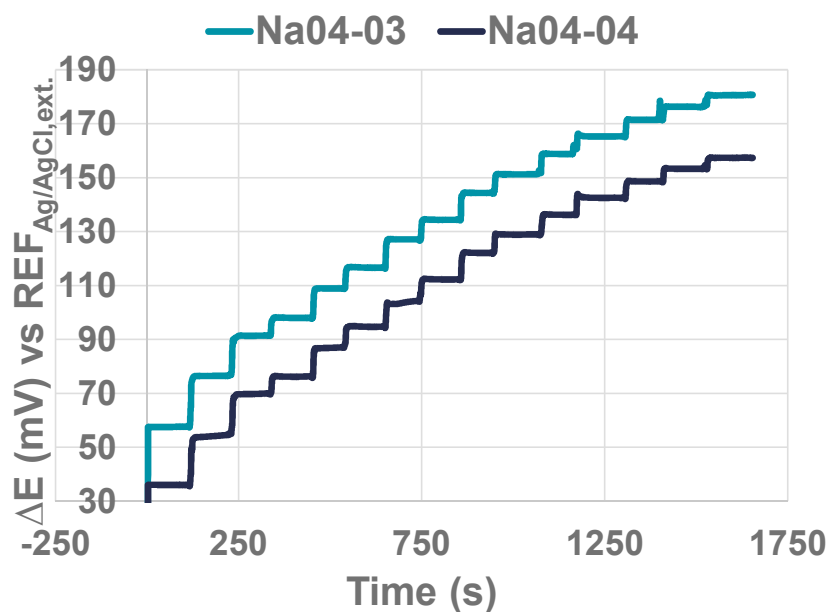
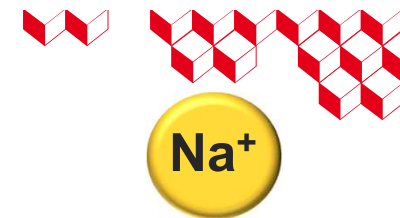
ISE	Na04-01
S (mV/dec)	39,9
R ²	0,995
E ₀ (mV)	315,6

Linearity between 6mM et 150mM



1. Sensing Na⁺ - New formulations

Method of standard additions in complex buffer pH = 7,4



ISE	Na04-03	Na04-04
S (mV/dec)	55,0	54,4
R ²	0,999	0,999
E ₀ (mV)	46,8	27,1

linearity over the whole range (1.5mM-260mM)

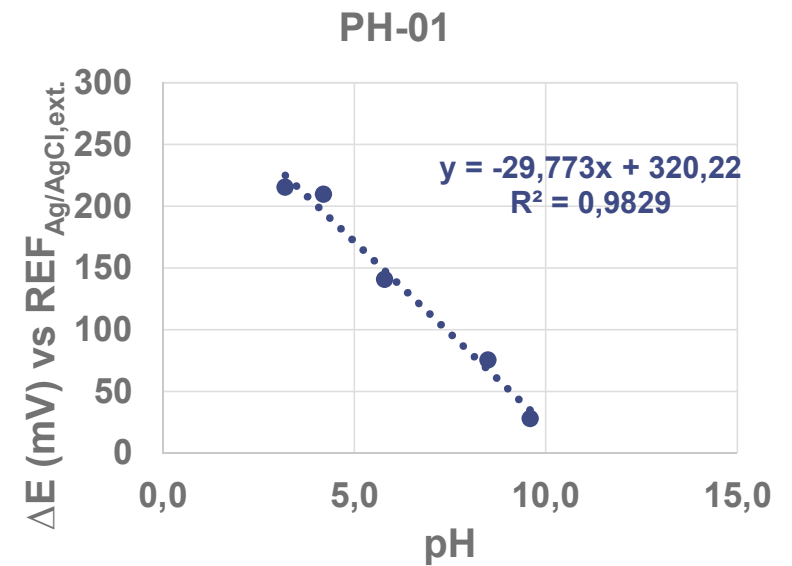
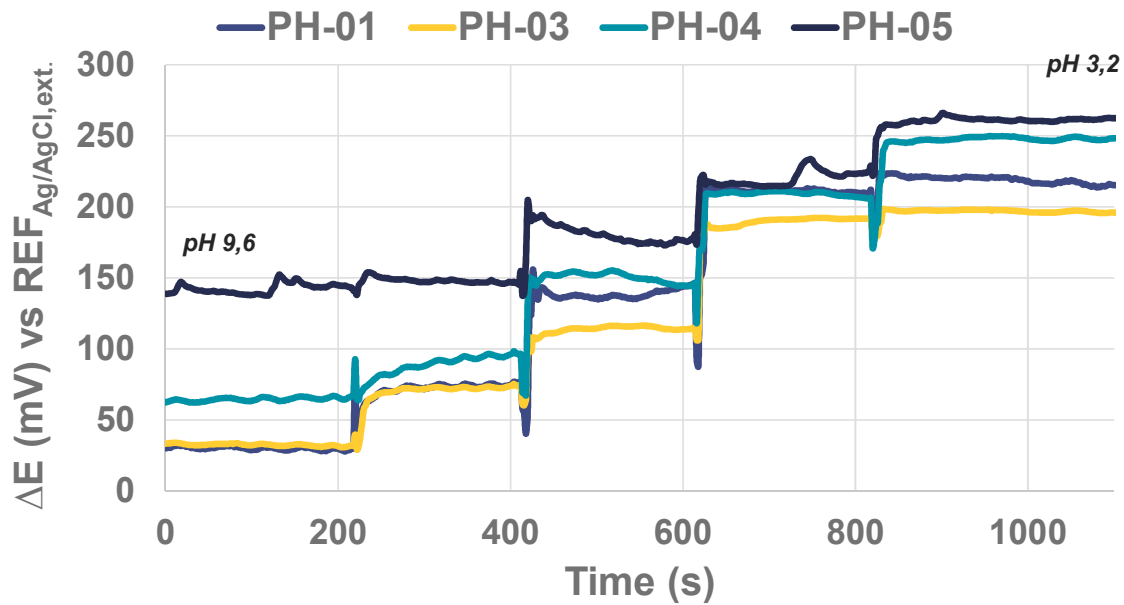
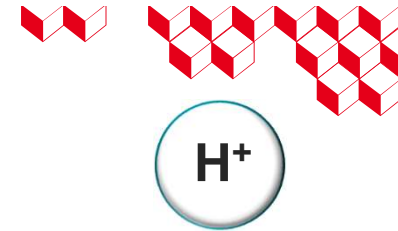
The new ISE Na⁺ formulations show improved sensitivity and a lower LOD



2. Sensing pH

Method of standard additions in complex buffer

Range pH:9-8-5-4-3 (+Aj Lactic acid)



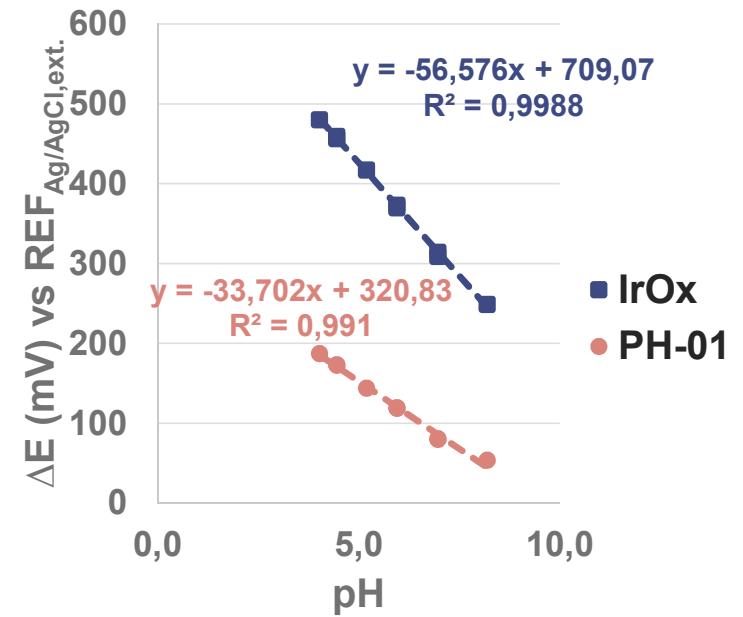
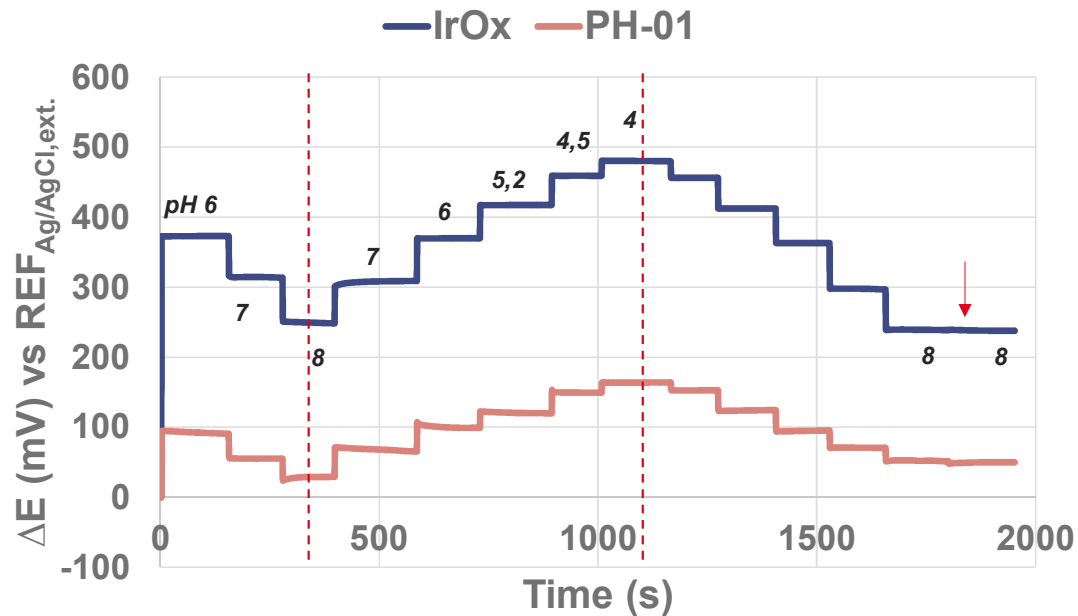
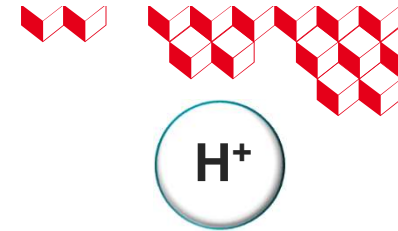
ISE	PH-01
S (mV/dec)	-29,8
R ²	0,983
E ₀ (mV)	320,2

Not yet as sensitive as expected, needs to be optimised



2. Sensing pH

Method of standard additions in complex buffer Range pH:4->8 (+Aj Lactic acid)



ISE	PH-01	IrOx
S (mV/dec)	-33,7	-56,6
R ²	0,991	0,999
E ₀ (mV)	320,2	709,4

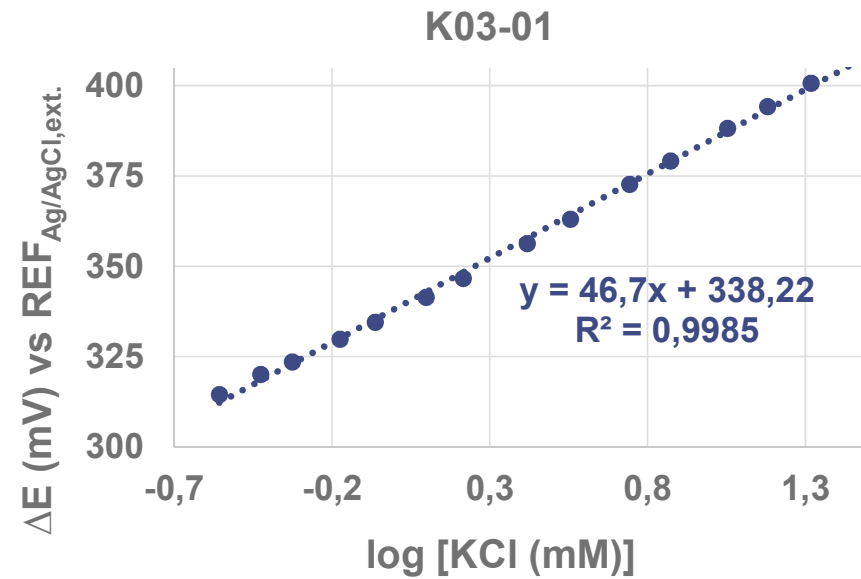
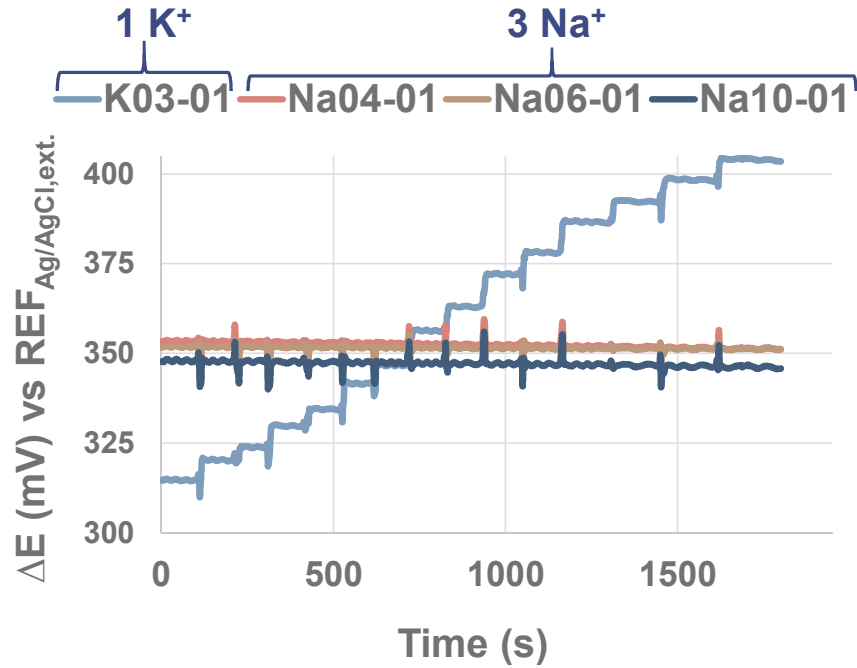
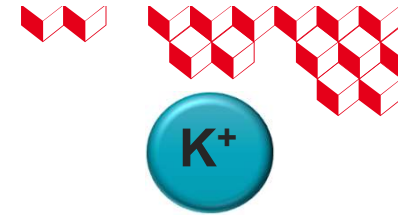
Comparing pH sensors IrOx and ISE (PH-01)

IrOx shows higher sensitivity and stability than ISE under the same conditions.



3. Interference - Sensing K⁺

Method of standard additions in complex buffer pH = 7,4

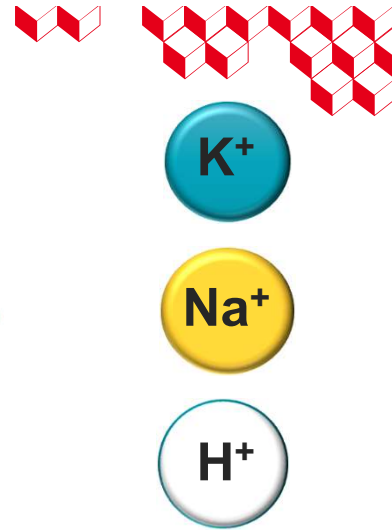
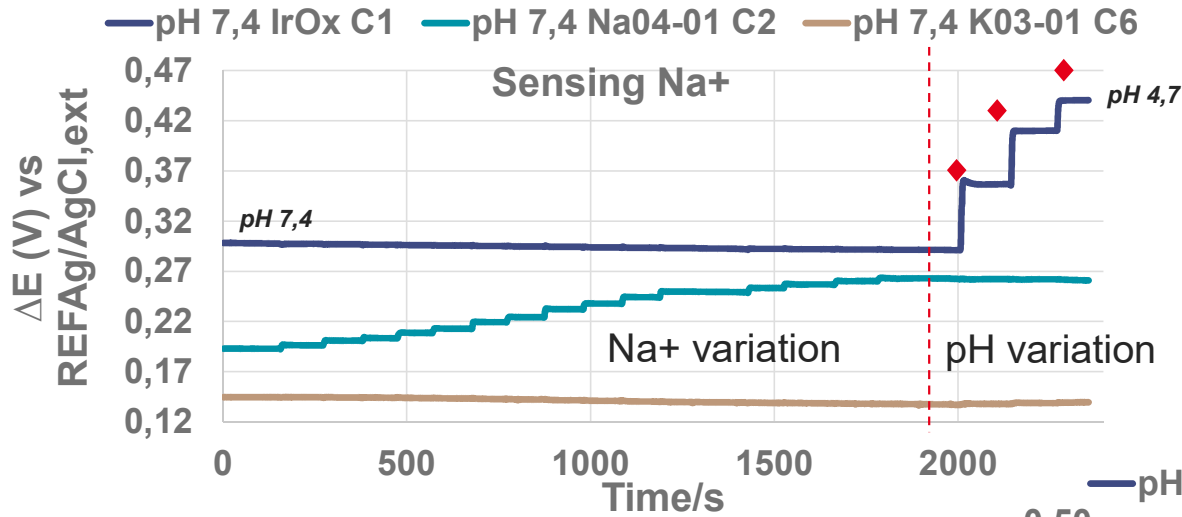


ISE	K03-01
S (mV/dec)	46,7
R ²	0,998
E ₀ (mV)	338,2

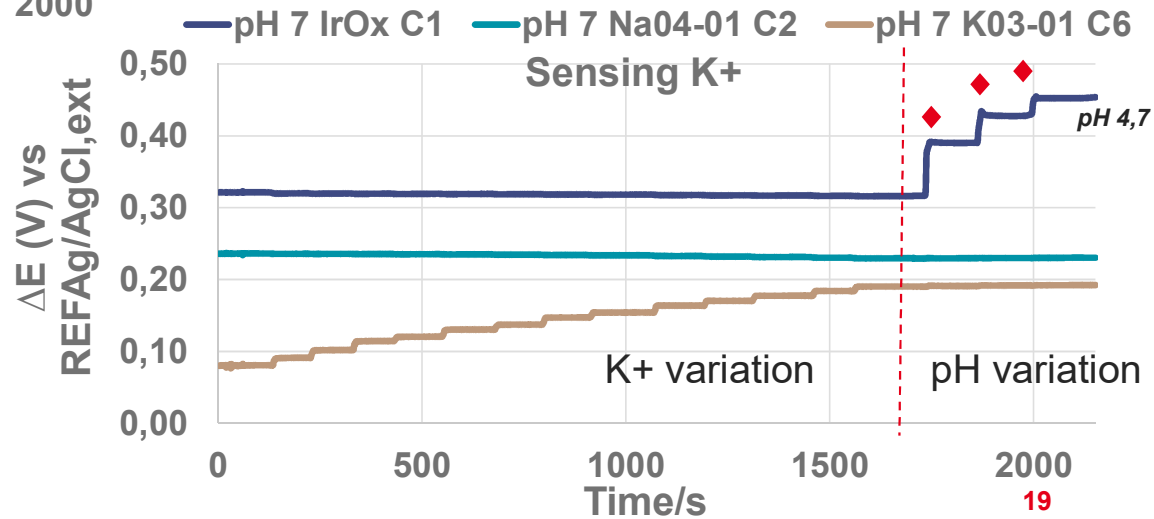
Linearity between 0,2mM et 28mM



2. Interference - Multiparameter platform



In multisensor experiments, **no interference was observed** between the detection of pH/K⁺/Na⁺



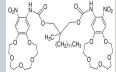

Conclusions



In this study, we demonstrate that applying **our design** and **our fabrication strategy** of this platform enables the detection of **multiple parameters** involved in the **animal stress**



Multi-parameter electrochemical platform validation

Capteur	pH	K ⁺	Na ⁺
Formulation	IrOx	 <i>Ionophore K III</i>	 <i>Ionophore Na IV</i>



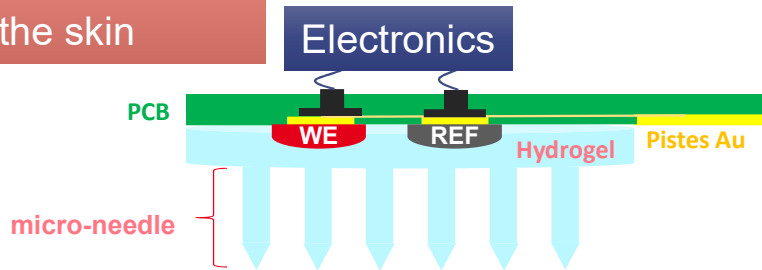
These are the first promising results of **potentiometric electrochemical detection** of Na⁺, pH and K⁺ in **artificial ISFs**

Future perspectives / challenges

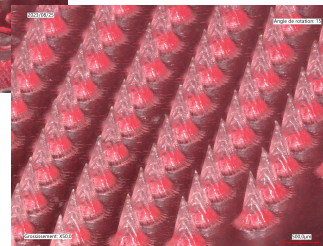
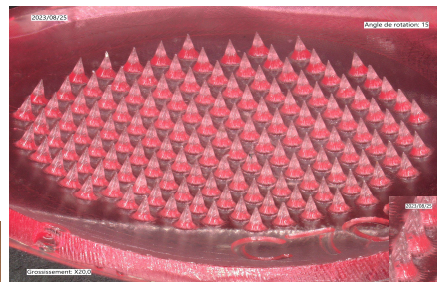
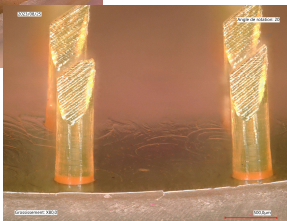
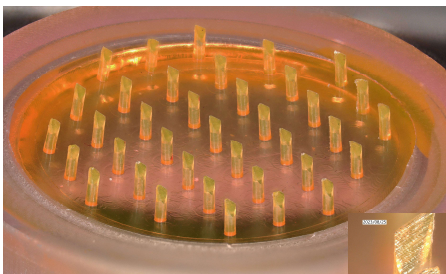
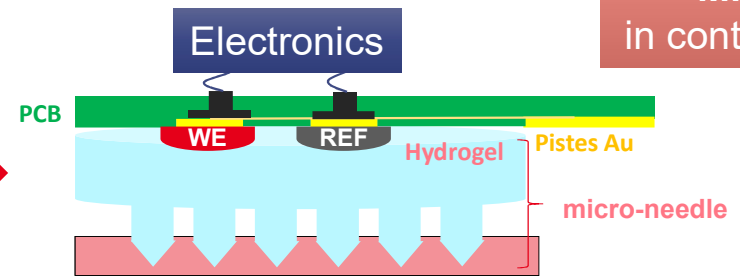
The next step will be the **integration** of **electrochemical platform** with the **micro-needle patches** to perform measurements of physiological parameters **minimally invasive** for the animals



Insertion of the dry MN patch in/onto the skin



Swelling of the MN patch in contact with ISF





Research Group
LMCD



Merci



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WAIT4 institutional consortium



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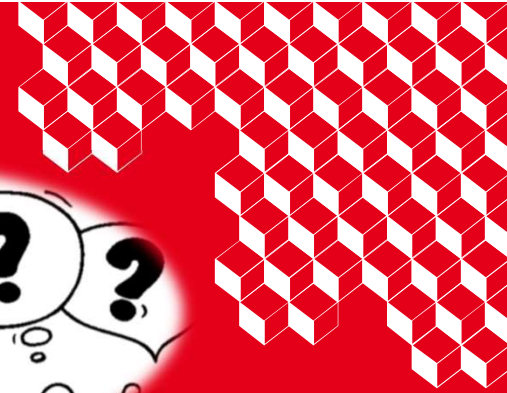
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Q&A



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