5TH CLABIO
LATIN AMERICAN BIOIMPEDANCE
FLORIANÓPOLIS – BRAZIL - 2024

EIS-based health micro-instrumentation for measurement of drug transdermal delivery

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ABEE-SC

CREA-SC

mútua SC

scio spec scientific instruments

UNIVERSITY OF OSLO

UDESC
UNIVERSIDADE DO ESTADO DE SANTA CATARINA

30 years of EIS in operation

Research

1994-2007 2022-20224

- EIS for prosthesis osseointegration diagnostics in dentistry and audiology

2003-2009

- Artificial Intelligence for model definition in EIS

2007-2024

- EIS for transdermal delivery in aesthetics and in diabetology

1994

2004

2014

2024

Friends of operation

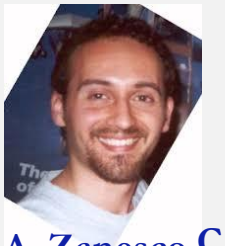
30 years of EIS friendship in operation


V. Bruno


M. Urquidi


M. Allocca


R. Schiano

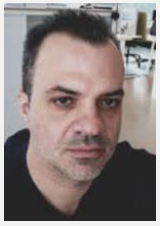

A. Zanesco


C. Romanucci


D. Acierno


I. Sannino


M. Frosolone


C. Manna


M. Taglialatela


O. Cuomo


M. Marvaso


P. Cimmino


U. Cesaro


G. Montenero


N. Moccaldi


F. Clemente

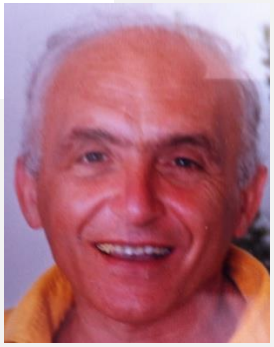

A. Smarra


G. Mastrati


F. Crauso

Family of EIS operation

More than 30 years of EIS family in operation



EIS for transdermal delivery

SCIENTIFIC REPORTS

nature

OPEN

Noninvasive measurement of transdermal drug delivery by impedance spectroscopy

Received: 18 November 2016

Accepted: 06 February 2017

Pasquale Arpaia[1,*], Umberto Cesaro[1,*] & Nicola Moccaldi[2,*]

"Best Demonstration Award"

IMEKO International Measurement Confederation — Technical Committee TC10 Technical Diagnostics

Context

Transdermal drug delivery advantages:

- no first-pass metabolism,
- less toxicity,
- less side effects
- greater patient compliance.

Strategies:

- Chemical Enhancers,
- Physical systems as:
    - Sonophoresis,
    - Iontophoresis,
    - Electroporation.

General problem

Different tissue conditions due to inter- and intra-individual characteristics (e.g. age, sex, ethnicity)

Lack for non invasive and in vivo assessment of the actual dose of drugs

Loss of the posology concept

State of the art

- Biopsy
- Suction blisters
- Tape stripping
- Confocal Raman Spectroscopy
- Colorimetric scale for corticosteroid

- No personalized dosages
- Possible waste of medication
- No real-time feedback to patient

Transdermal delivery in aestethics

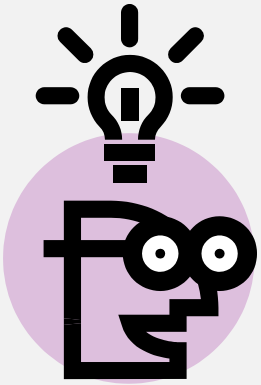
Aesthetics without posology

courtesy of: thedoctorstv.com.

Requirements

General aims

- Low cost
- Non invasive measurement method
- Immediate efficacy assessment for all non-invasive systems for intradermal convey.



Idea

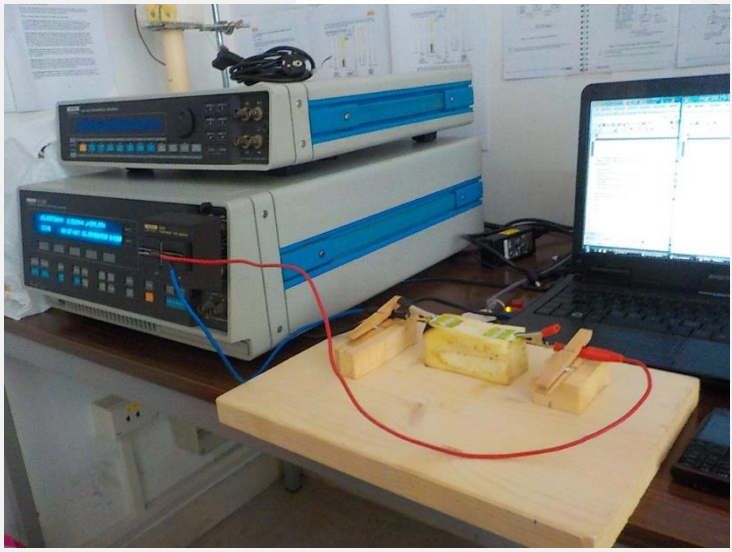
- A method based on impedance spectroscopy (f < 50 kHz) for measuring a substance delivered under the skin

Laboratory emulation

Screening measurement campaign

- A commercial drug used in aesthetics dermatology with a conductivity of 526 μS/cm
- Pre-gelled Ag/AgCl Electrodes
- Solartron 1260

Eggplants



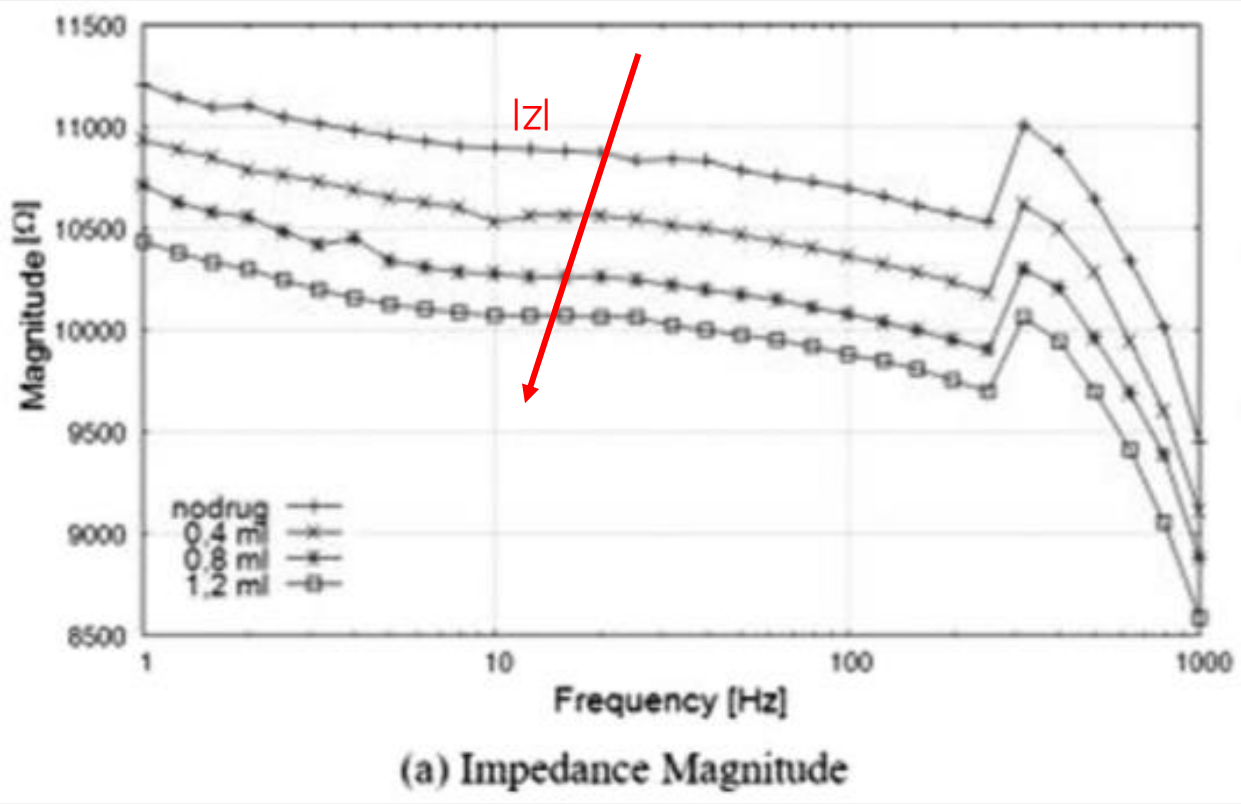
to investigate relationship among

1. (i) drug amount (ii) impedance
2. and (iii) uncertainty sources.

Laboratory emulation

Although uncertainty (different eggplant pulpe, electrode configuration, etc.)

a clear relationship between amount of injected substance and impedance



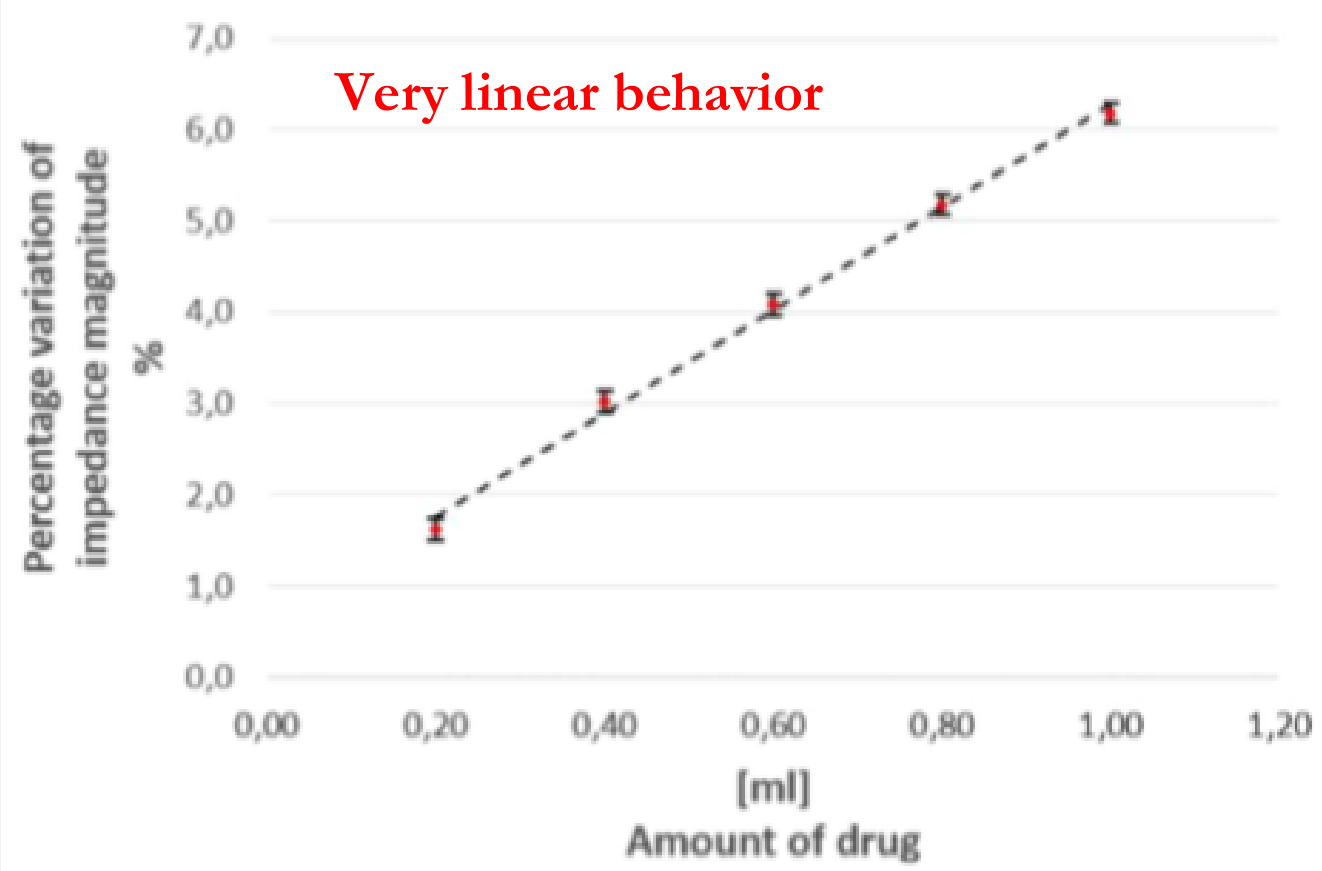
(a) Impedance Magnitude

A drug increase by 0.8 ml determines a decrease in impedance magnitude by 800 Ω.

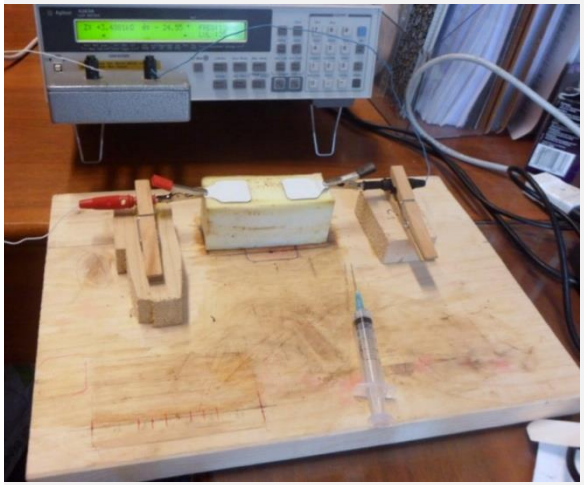
The trend of the phase is not correspondingly regular

Laboratory emulation

Drug Conductivity	Signal Frequency	Electrodes Area	Electrodes Gap	Signal Amplitude
666 μS/cm	1.00 kHz	3.64 cm^2	4.6 cm	20 mV
Sensitivity [ml^{-1}]	**Nonlinearity [%]**	**1 − σ Repeatability [%]**	**Accuracy [%]**	**Resolution [ml]**
3.8	0.47	0.07	0.68	0.005



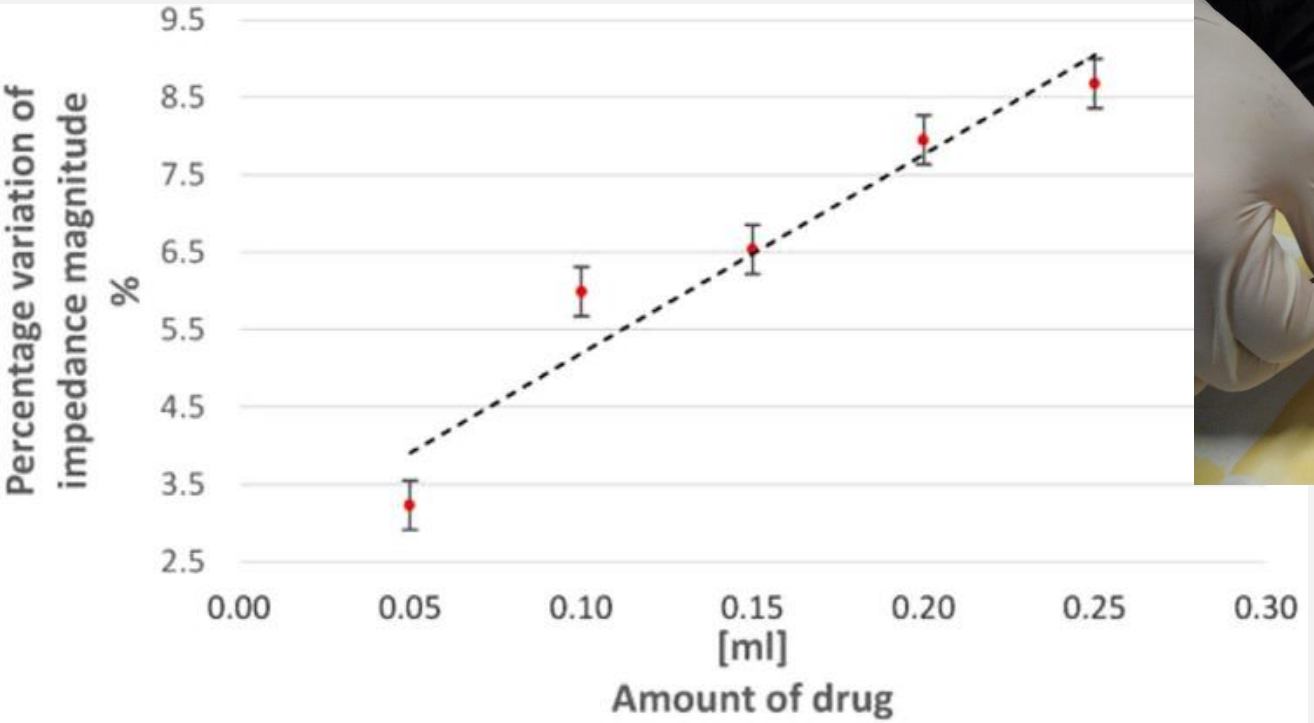
Eggplants



Ex-vivo tests

	Sensitivity [ml^{-1}]	Nonlinearity [%]	$1-\sigma$ Repeatability [%]	Accuracy [%]	Resolution [ml]
Laboratory exp.	30.6	3.64	0.11	4.38	0.35
Ex-vivo exp.	34.4	5.04	0.47	6.20	0.44

Still good linear behavior

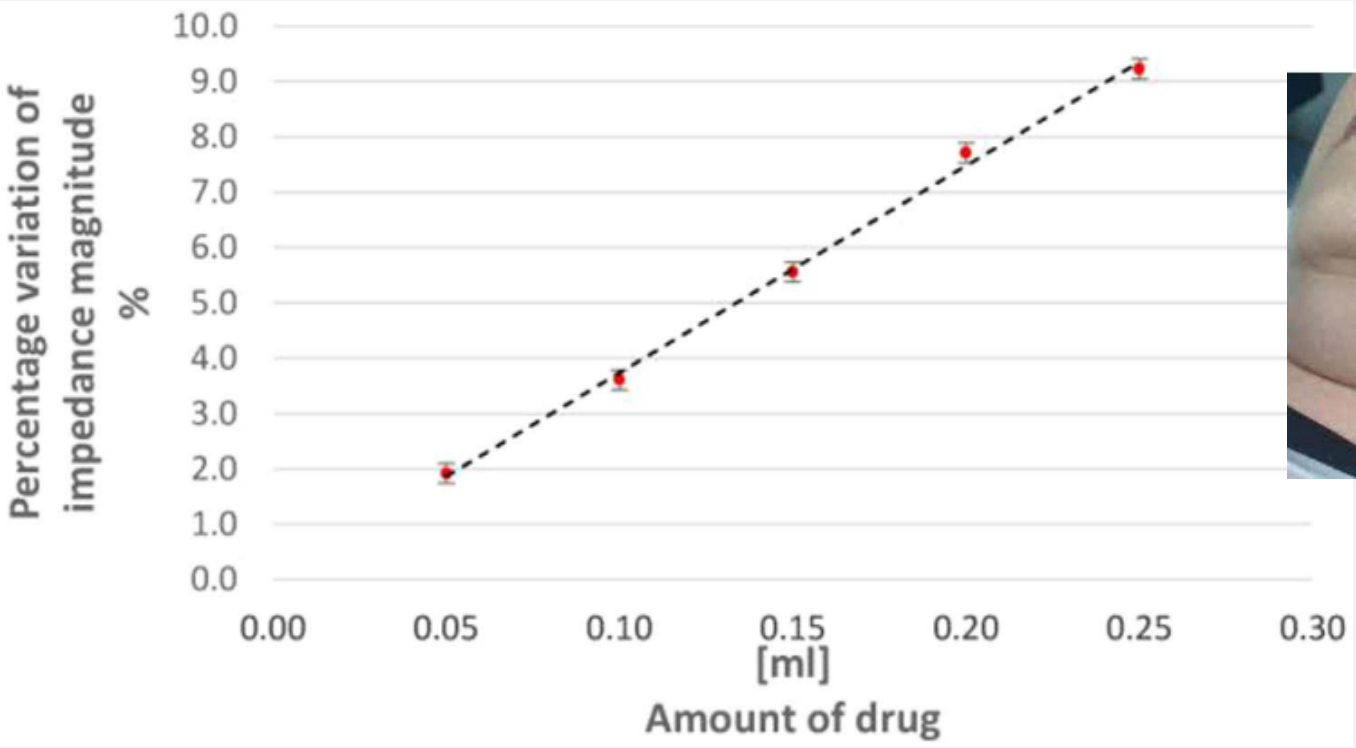


Pig ears

Clinical tests

	Sensitivity [ml^{-1}]	Nonlinearity [%]	$1-\sigma$ Repeatability [%]	Accuracy [%]	Resolution [ml]
Laboratory experiments	29.5	2.35	0.07	5.23	0.23
Ex-vivo experiments	24.5	4.25	0.16	7.40	0.37
In-vivo experiments	22.7	3.31	0.27	5.71	0.19

Satisfying linear behavior



Human subjects

EIS in diabetology

XXII World Congress of the International Measurement Confederation (IMEKO 2018) IOP Publishing
IOP Conf. Series: Journal of Physics: Conf. Series 1065 (2018) 132008 doi:10.1088/1742-6596/1065/13/132008

PAPER · OPEN ACCESS

Non-invasive real-time in-vivo monitoring of insulin absorption from subcutaneous tissues

Pasquale Arpaia[1], Ornella Cuomo[2], Nicola Moccaldi[1], Alessandra Smarra[1], and Maurizio Taglialatela[2]

[1] Department of Electrical Engineering and Information Technology,
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University of Naples Federico II, Naples, Italy.





Diabetes: a pancreas desease

courtesy of: 10insalute.com

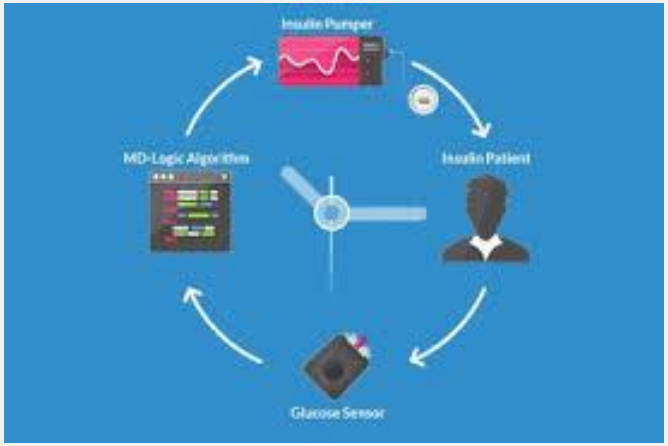
Artificial Pancreas

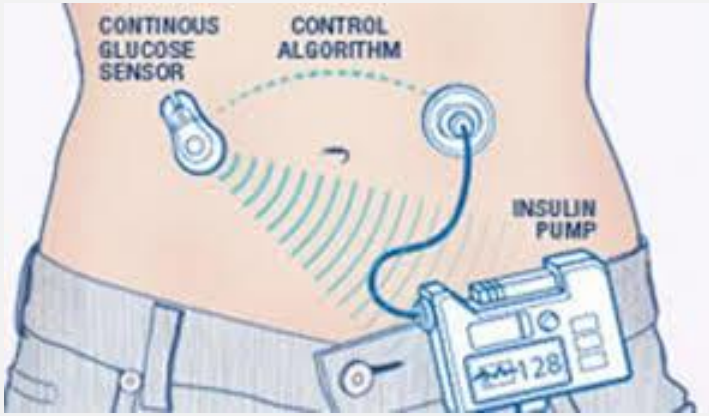
Artificial Pancreas (AP) consists of closed-loop control of blood glucose in diabetes)

AP operation

The loop is closed in case of basal insulin administration (i.e. long term, e.g. daily).

At each meal, when food is ingested, further insulin is administered specifically (Bolus).





The Bolus problem

Even most recent systems cannot react to such quick glucose swing.

Needs for new control inputs: e.g.,

1. **insulin sensitivity factor (ISF)**
2. **and insulin duration of action. (IDA)**

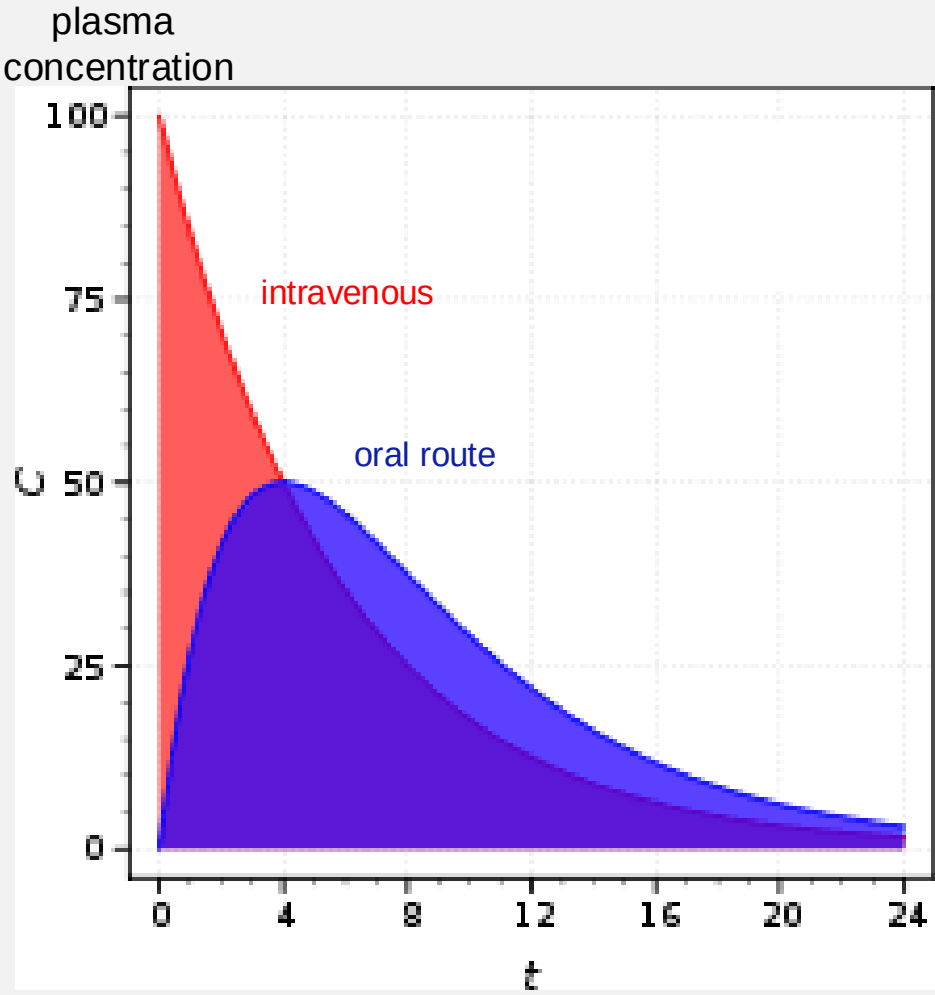
They are both fixed during Artificial Pancreas calibration.

Bioavailability

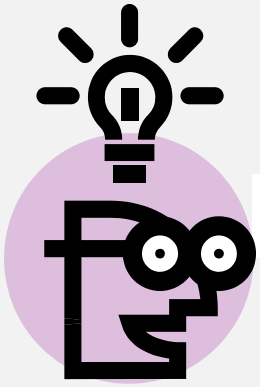
However, ISF and IDA can be subject to significant variations depending on the kinetics of the insulin absorption (bioavailability).

Fraction of an administered dose of unchanged drug reaching the systemic circulation.

The insulin bioavailability over time is assessed indirectly from the measurement of its time dependent disappearance from the administration volume

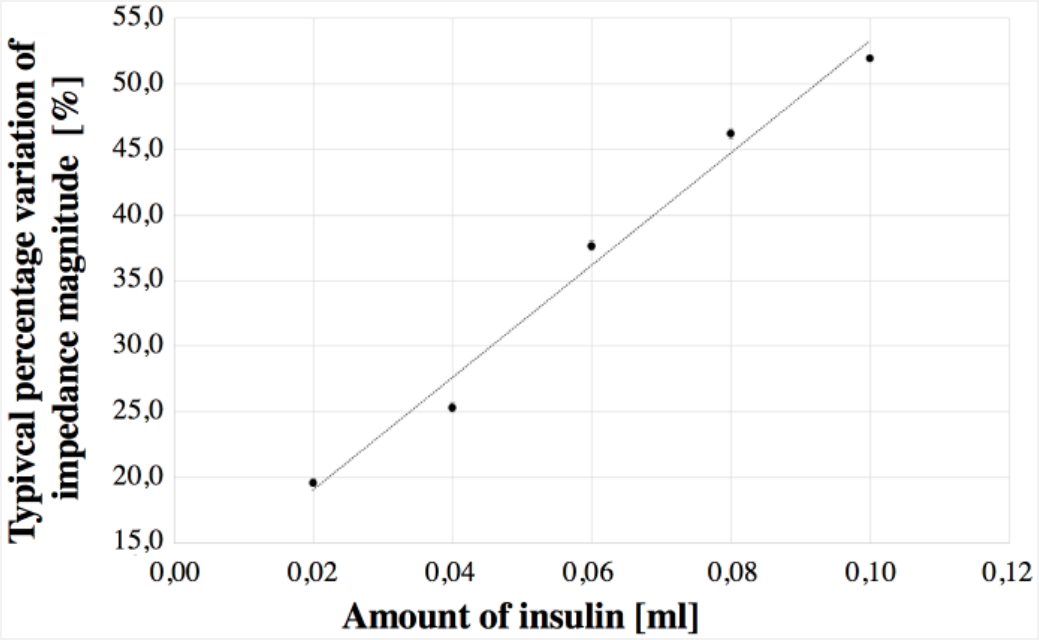


The idea - 1

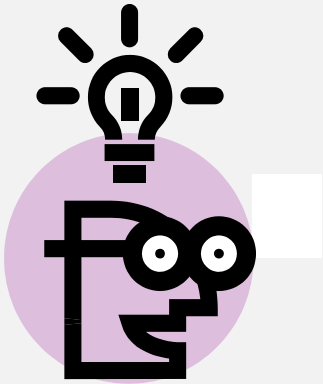


The insulin variation is assessed noninvasively by EIS.

The leakage of a given amount of insulin (ml) produces a corresponding variation in the measured equivalent impedance in the administration volume.

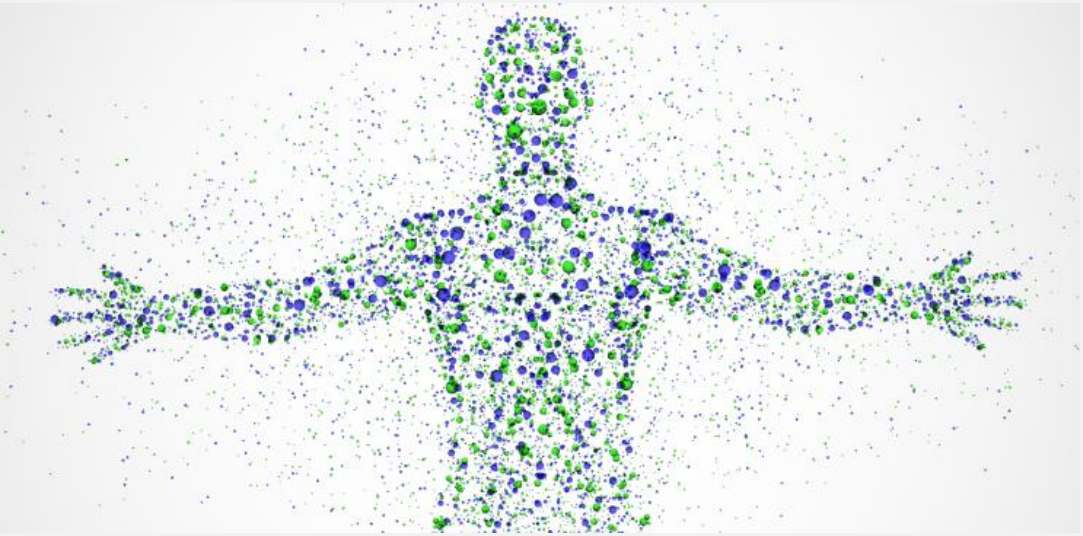


The idea - 2



Personalized medicine

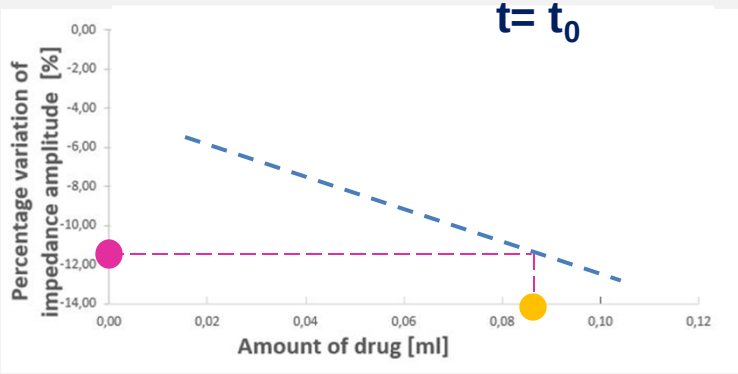
At each administration, a linear model for the individual subject in each his/her condition is identified (personalized medicine).

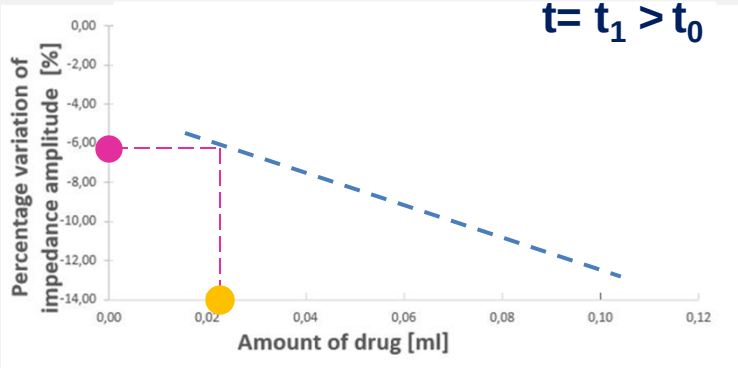


Significant increase in inter- and intra-individual reproducibility of bioavailability measurements

The idea - 3

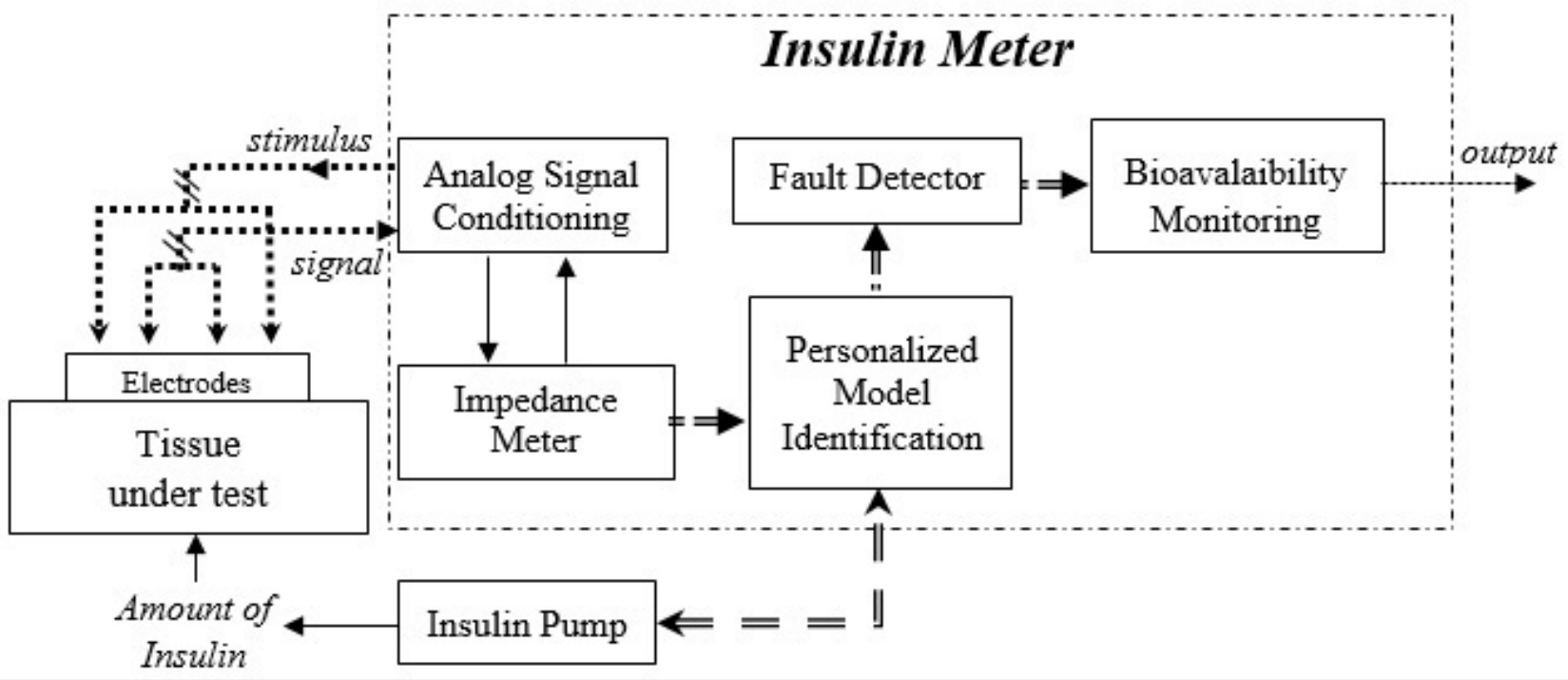
Inverse model of insulin **appearance** is used in the absorption (**disappearance**) phase



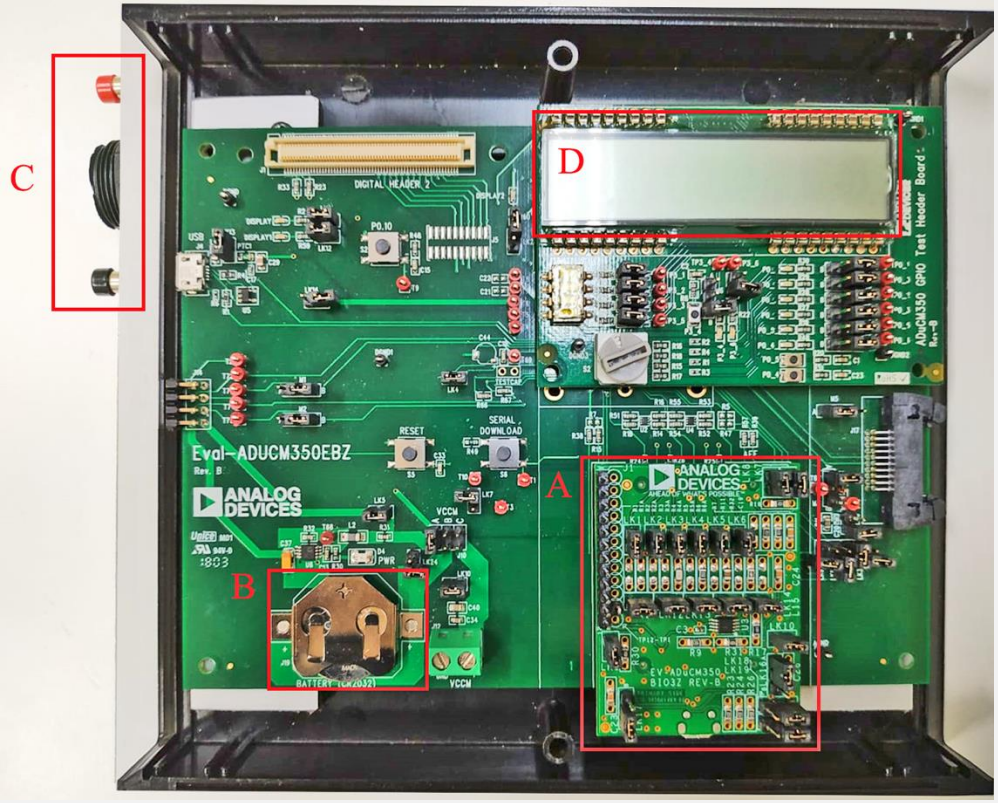


- Measured Impedance
- Estimated amount of drug still not absorbed

EIS Insulin Meter



Prototype



A. Doughterboard BIO3Z for 4-wire bioimpedance measurement

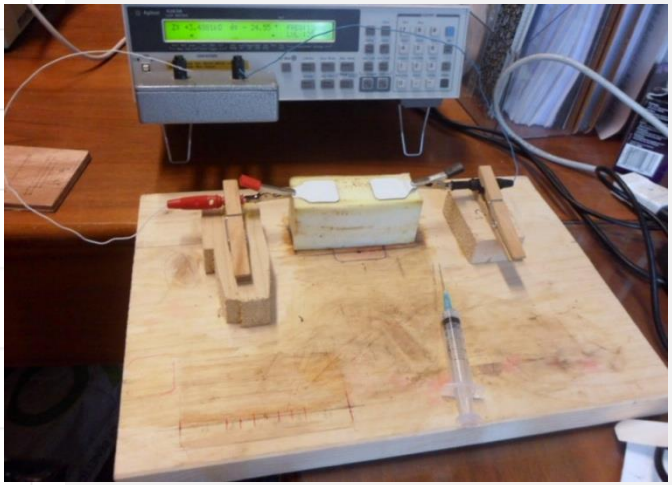
B. Battery

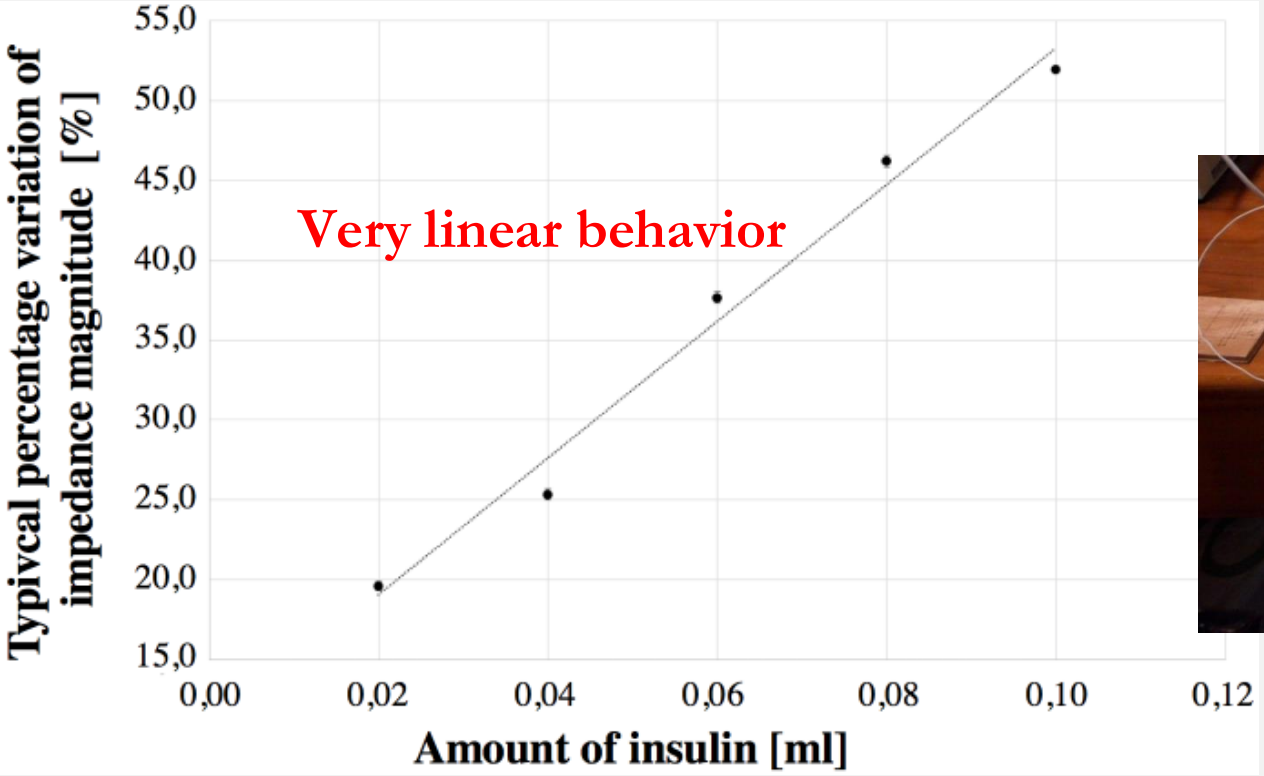
C. ON and Reset buttons

D. Display

In-vitro results

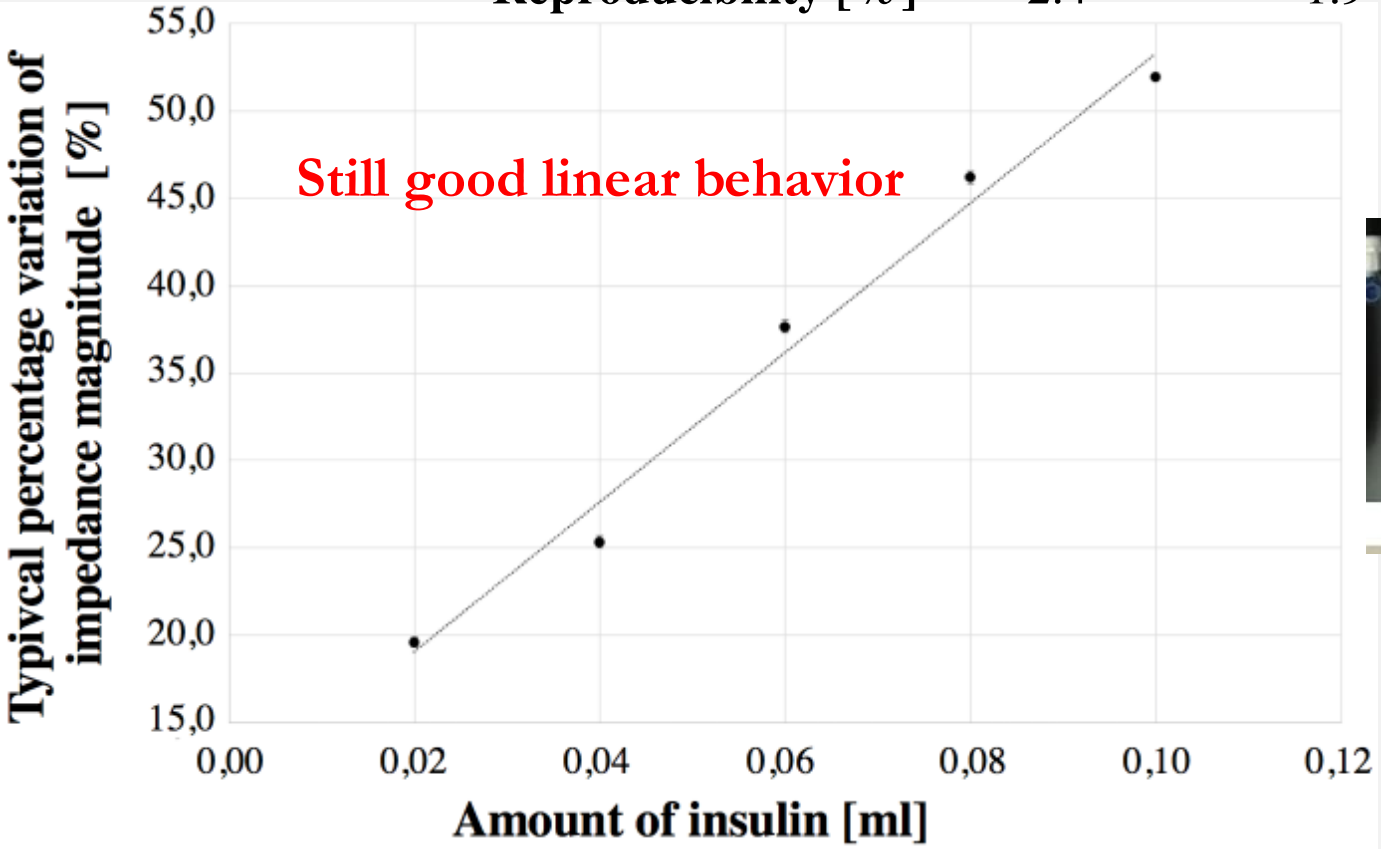
Eggplants





Ex-vivo results

	Pig	Dried Eggplant
Sensitivity [ml^{-1}]	157,2	497.3
Non-Linearity [%]	2.1	4.0
1-σ repeatability [%]	1.6	1.3
Reproducibility [%]	2.4	1.9

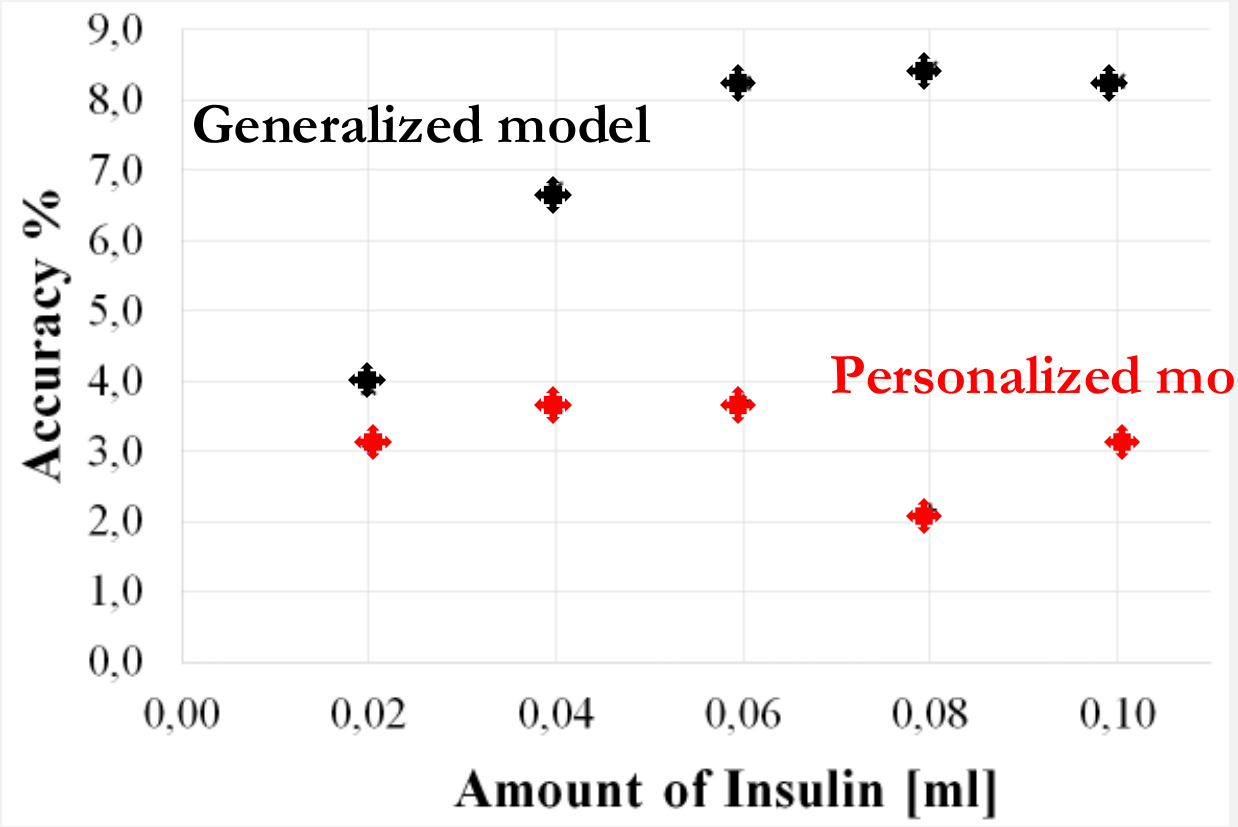


Pig muscle

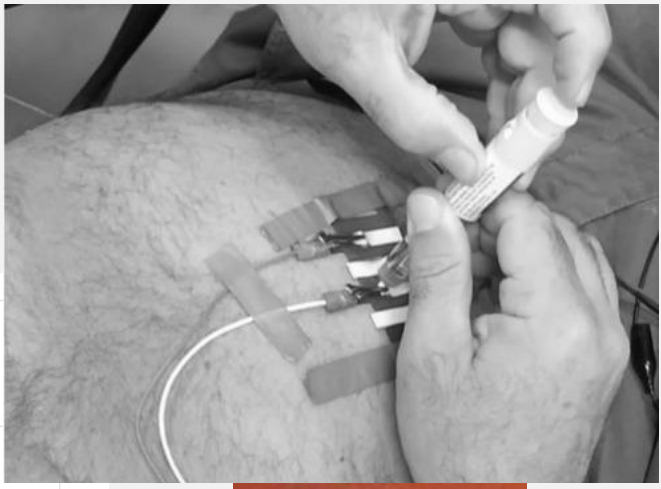
Ex-vivo results

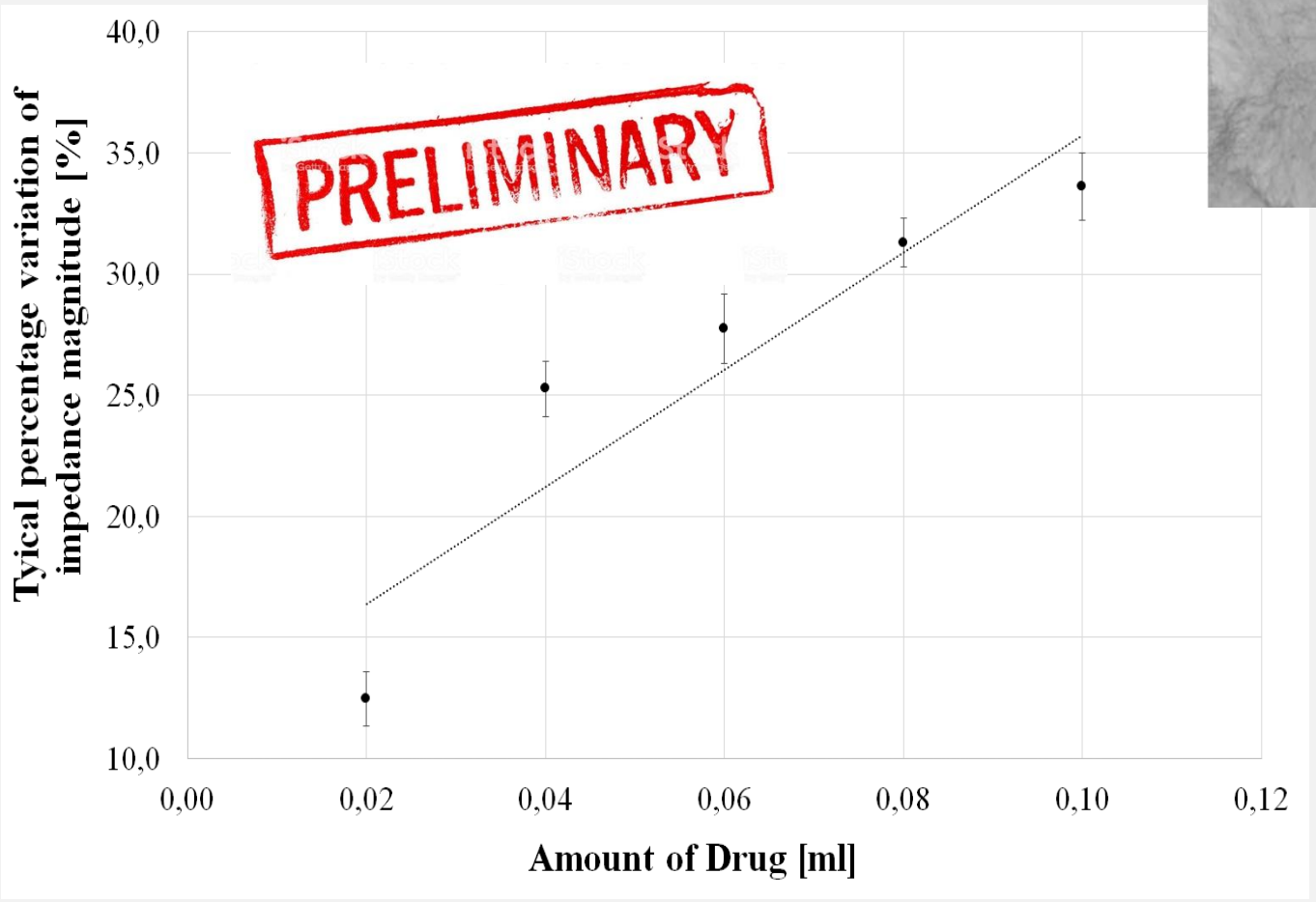
Pig muscle

Personalization accuracy

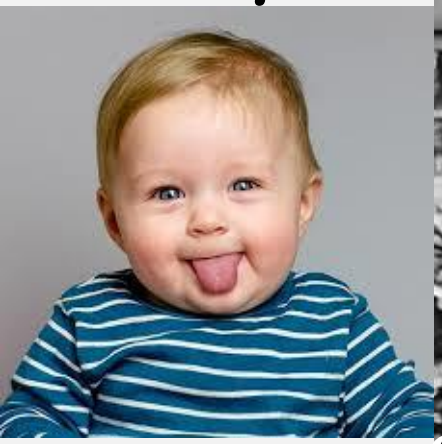


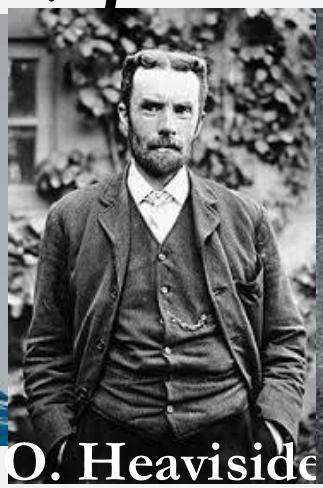
In-vivo results





EIS past, present and …





O. Heaviside

E. Warburg

Epelboin

Frumkin

Armstrong

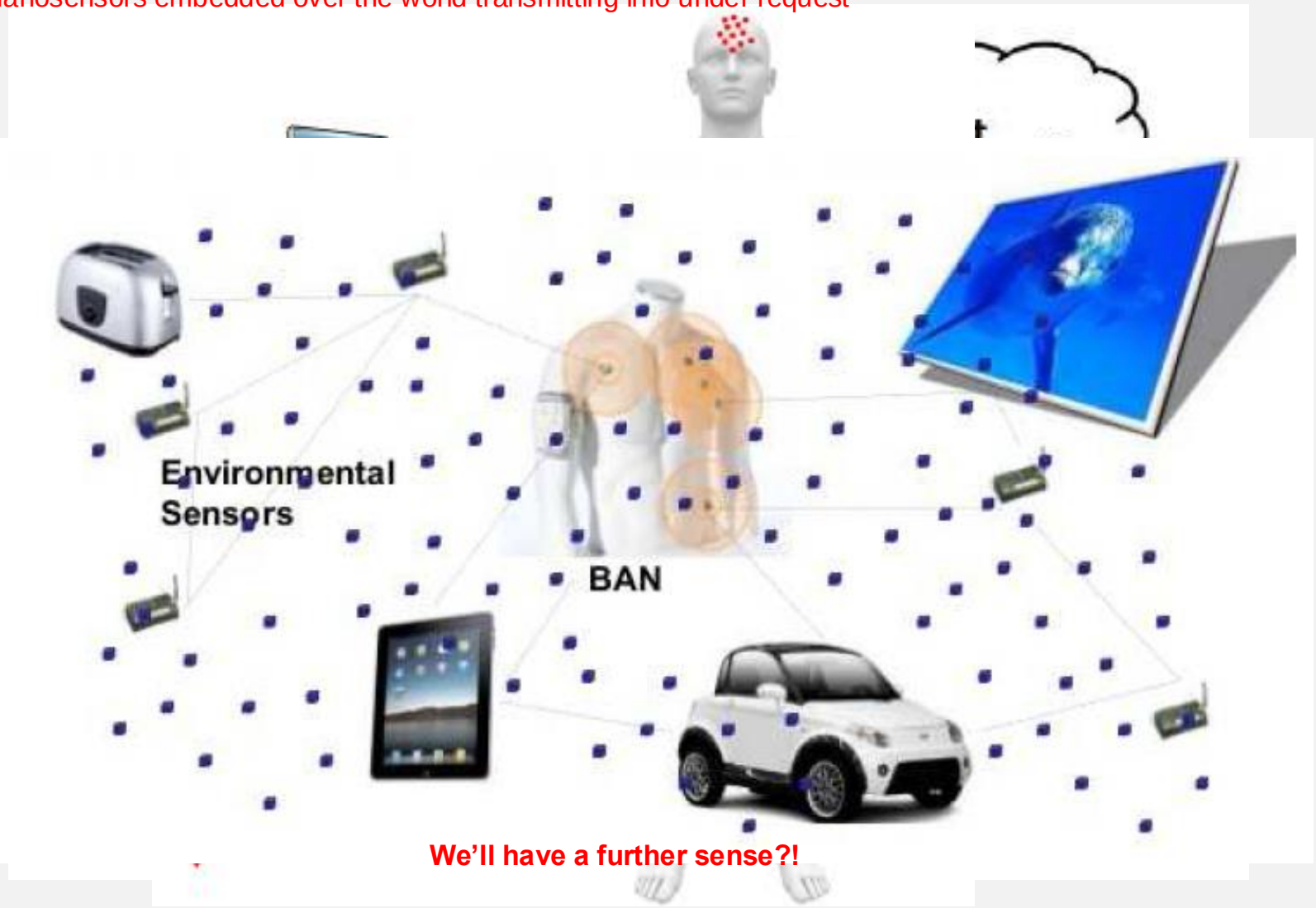
McDonald/Lasia

Kanoun/Arpaia

IWIS 2025

Internet of NanoThings (IoNT)

Nanosensors embedded over the world transmitting info under request



We'll have a further sense?!

THANK YOU

FOR YOUR ATTENTION!

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