Design and characterization of pixelated needle probe for molecular neuroimaging on awake and freely moving rats

J. Heymes[1], L. Ammour[2], M. Bautista[3], G. Bertolone[1], A. Dorokhov[1], S. Fieux[4], F. Gensolen[3], M. Goffe[1], F. Guezzi-Messaoud[1], C. Hu-Guo[1], M. Kachel[1], F. Lefebvre[2], F. Pain[2], P. Pangaud[3], L. Pinot[2], P. Gisquet[5], P. Laniece[2], C. Morel[3], M.-A. Verdier[2], M. Winter[1], L. Zimmer[4], J. Baudot[1]

Contact: julian.heymes@iphc.cnrs.fr

[1]Université de Strasbourg, CNRS, IPHC UMR 7178, F-67000 Strasbourg, France
[2]IMNC UMR 8165, Université Paris-Sud, Université Paris Diderot, CNRS/IN2P3, Université Paris Saclay, 91405 Orsay, France
[3]Aix Marseille Université, CNRS/IN2P3, CPPM, Marseille, France
[4]LNRC, CNRS/INSERM, Univ. Lyon 1, Lyon, France
[5]NeuroPSI CNRS/INSB, Univ. Paris Sud, Orsay, France

I. MAPSSIC PROJECT

Motivation

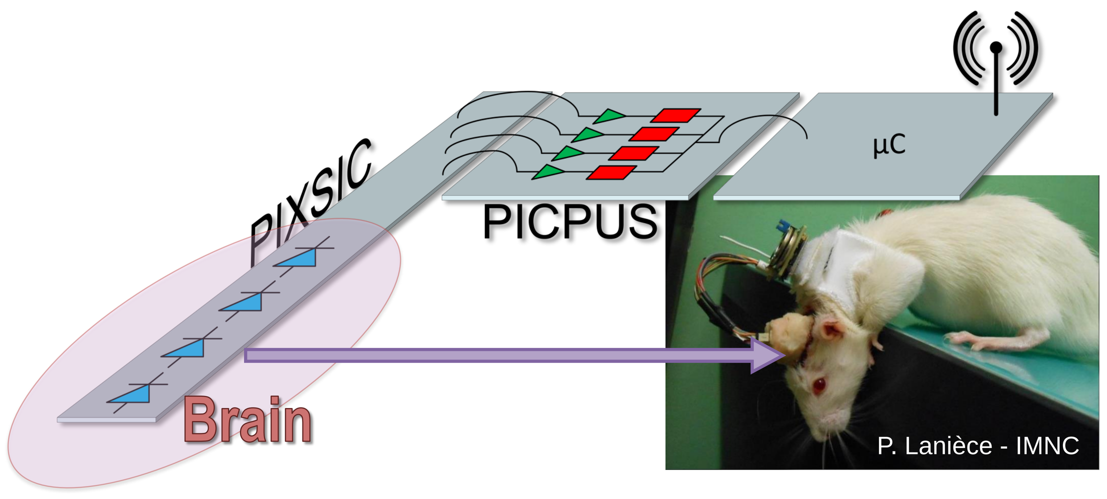
- Neuroimaging on awake [1] and freely moving animals
- Localization of β+ radiotracer clusters close to the pixelated sensor

➔ Implantation of a pixelated needle-shaped sensor in the brain

Requirements

- Sensor
  - ➤ **Small size ➔ Limitation of the impact on the brain tissue**
  - ➤ **Immunity to the 511 keV γ-rays background**
  - ➤ **Low power ➔ Limited heat dissipation**
- System
  - ➤ Compact with wireless data transmission
  - ➤ Autonomous

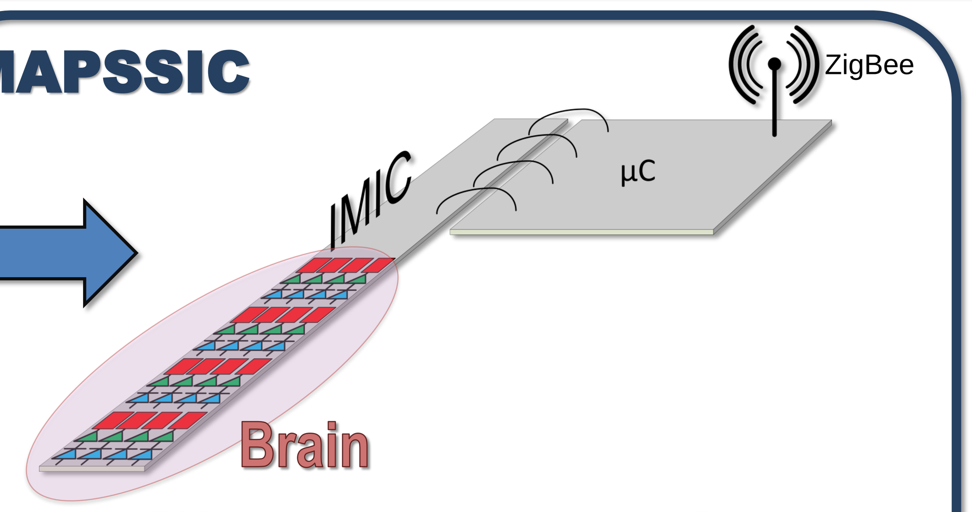
➔ Limitation of the discomfort that may alter normal behavior



Previous attempt: A passive pixelated in-brain sensor [2]

- Silicon probe with 10 passive pixels of 200 x 500 µm² each ➔ PIXSIC
- External readout circuit (PICPUS) and microcontroller
- Experiments validated the proof of concept [3,4] but…
- S/N ratio too low for low energy β-rays (~ 2 cm from the diode to the amplifier)
- Thinned probes to 200 µm still sensitive to γ-rays and brittle

MAPSSIC



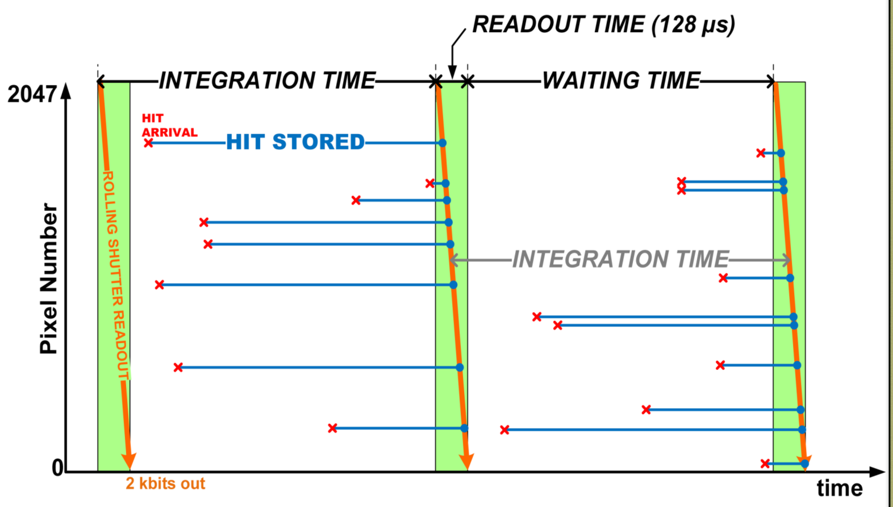
- Monolithic CMOS active pixel sensor ➔ **IMIC**
- Amplification next to the sensing node
  - ➔ S/N ratio improvement
- 18 µm thick sensitive volume ➔ γ-rays immunity
- Embedded data processing
- Dissipated power < 1 mW

II. IMIC SENSOR DESIGN

Size: 610 x 12000 µm² (pixelated needle-shaped sensor)
Sensitive area: 16 x 128 pixels ➔ **480 x 6400 µm²**
Technology: 0.18 µm CMOS process on 18 µm thick high resistivity (> 1 kΩ·cm) epitaxial layer

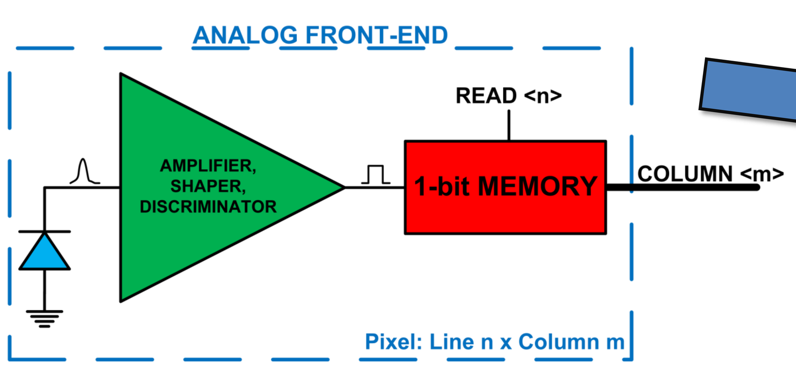
Strategy for low power dissipation

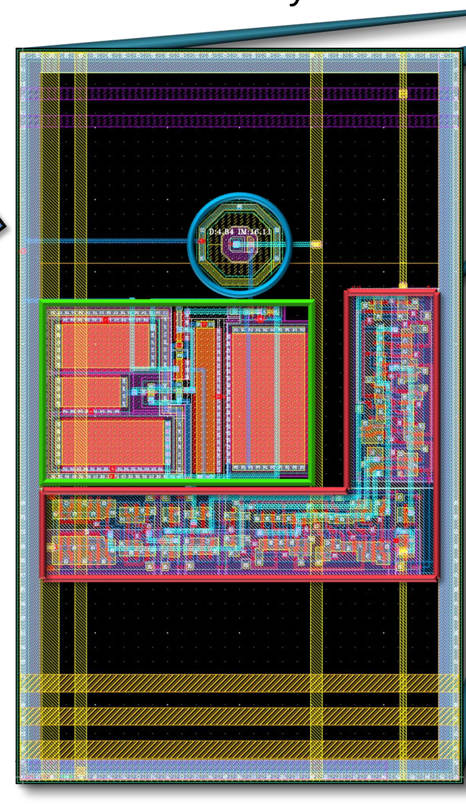
- Very low readout rate (~ Hz)
- Information of the hit stored in the pixel between two readouts



Pixel design

- Detection efficiency ➔ Small pixel pitch: 30 x 50 µm²
- Based on a front-end amplifier of ALPIDE (**AL**ice **PI**xel **DE**tector) [5]
  - Low power (55 nW/pixel)
  - Asynchronous operation
  - Memorization (on 1 bit) of the information of the hit until the readout ➔ Synchronization





Readout

- Column parallel **rolling shutter readout**
- **Complete matrix readout in 128 µs**
- Typical bandwidth: few kbits/s

Chip configuration: SPI protocol to steer on-chip DACs ➔ Polarization of the front-end

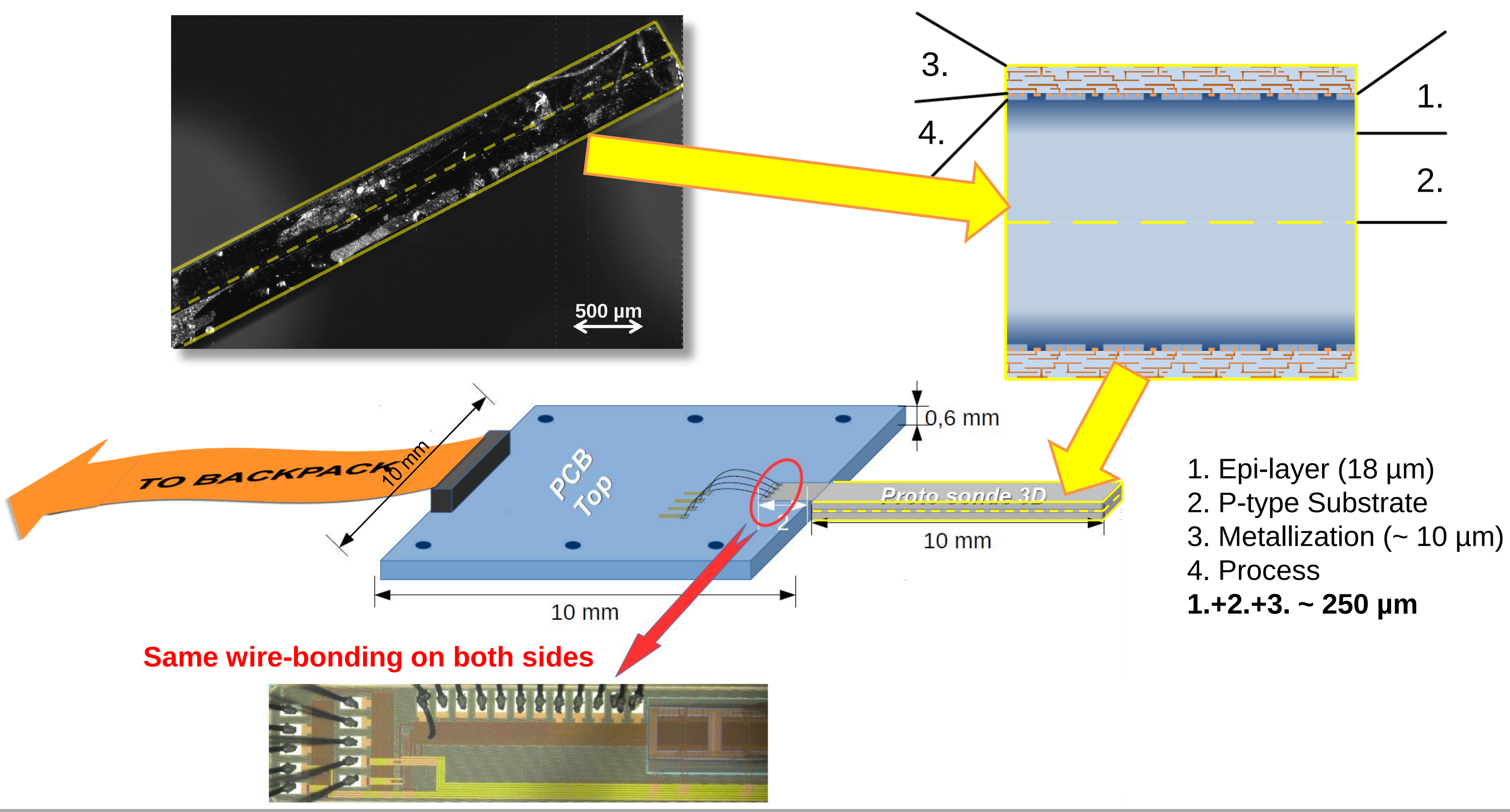
III. BACK-TO-BACK INTEGRATION

Concept

- Two sensors back to back
  - Robustness for manipulation and implantation
  - Large two-sided sensitive area
- Easy connection between the sensors and the backpack containing the microcontroller with wireless transmission and the battery

Realization

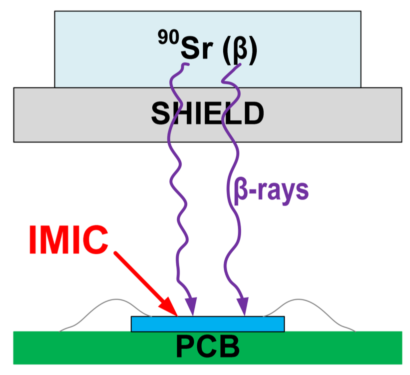
- Diced and thinned sensors glued back-to-back
  - Successful tests with individual sensors thinned to 150, 200, and 250 µm
  - **Total volume of the needle: 610 x 12000 x 500 µm³**



IV. SINGLE SENSOR VALIDATION

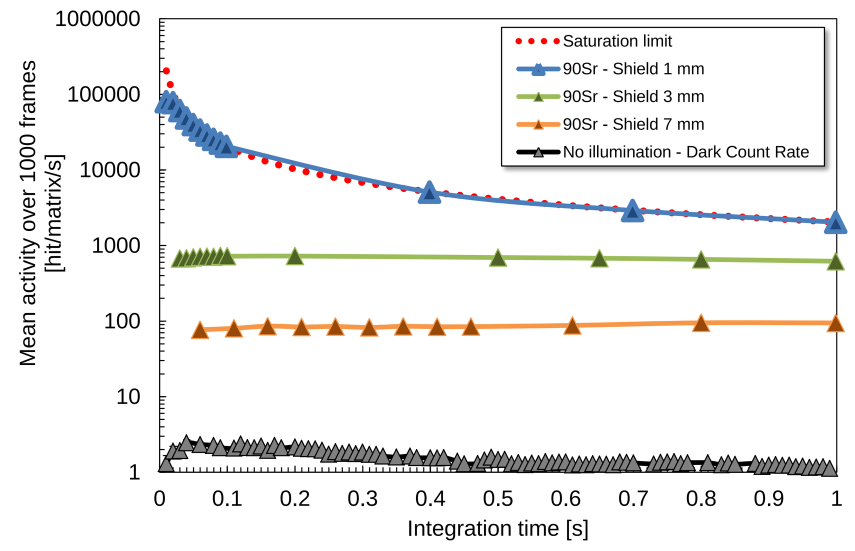
Laboratory tests

- **Power consumption of the whole sensor: 161 µW**
- Integrated DACs fully operating



Measurements with β- source (^{90}Sr)

- Integration time between 10 ms and 1 s
- Room temperature operation
- β source activity regulated with various shield thickness

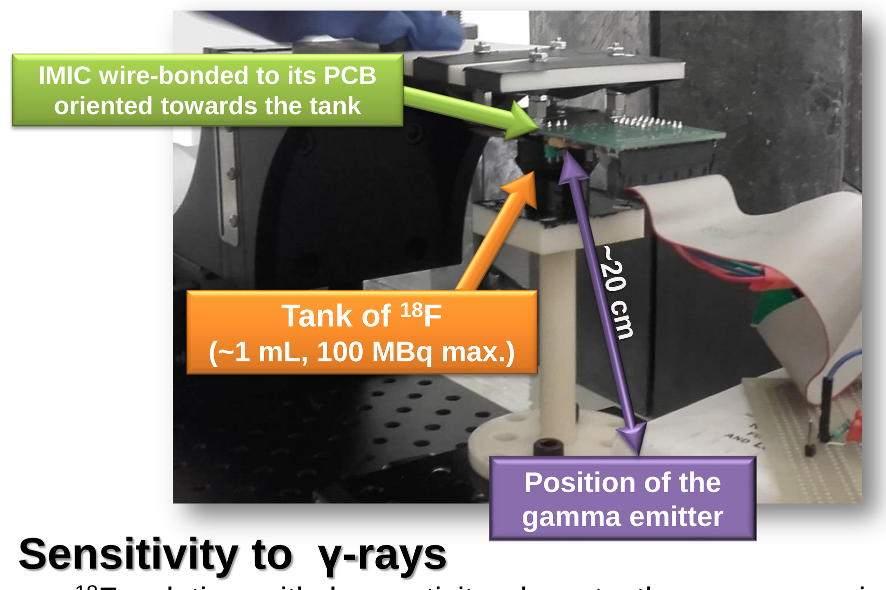


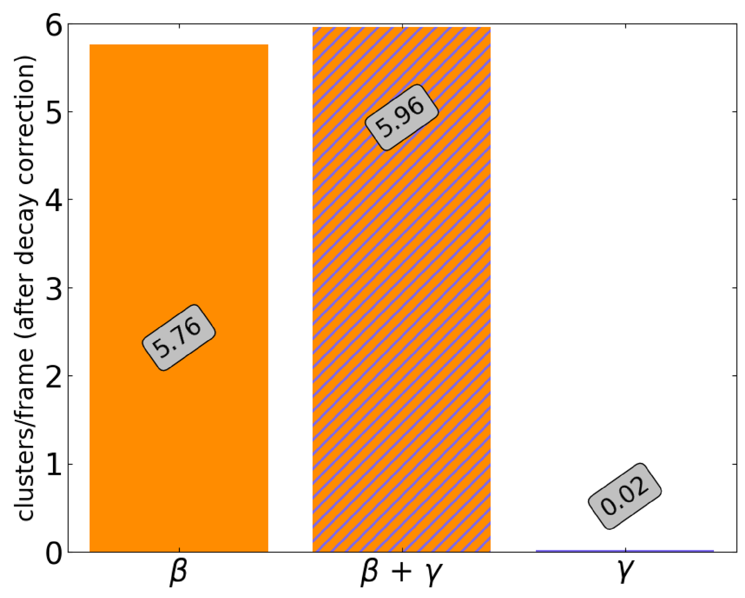
Detection performances

- For long integration time (~1 s)
  - ➤ Dark Count Rate ~ 1.15 hits/matrix/s
- For short integration time (< 20 ms)
  - ➤ Max. activity ~ 80 000 hits/matrix/s
  - ➤ Dark Count Rate ~ 2-3 hits/matrix/s
- **For expected activities (<< 100 hits/matrix/s)**
- ➤ **No hit losses with longer integration times (~1 s)**

Measurements with β+ emitter (^{18}F)

- ^{18}F: β+ and γ emitter in aqueous solution (100 MBq max. allowed in the laboratory)
- Produced at the Cyrcé cyclotron (IPHC)

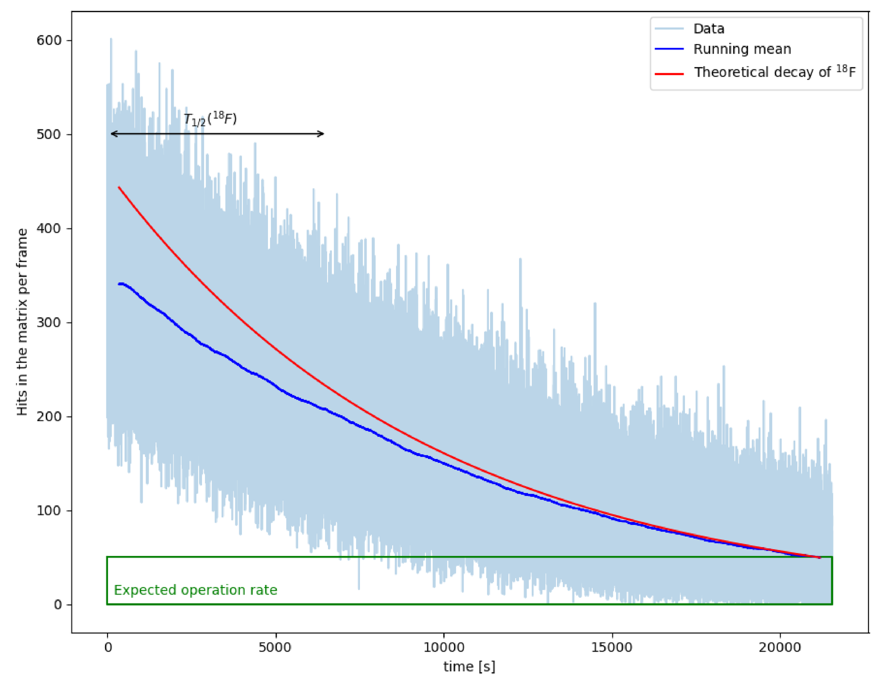




Sensitivity to γ-rays

- ^{18}F solution with low activity close to the sensor: majority of positrons measured
- ^{18}F solution with high activity (~100 MBq) ~ 20 cm away from the sensor (head-bladder distance) : γ-rays only
- The γ-ray contribution increases the mean #clusters/frame from positrons by 3.5 % only
- The beta+gamma measurement with the two sources at a time is 300x higher than for gamma only

➔ IMIC is immune to 511 keV γ-rays



^{18}F decay

- 6 hours = 3 periods
  - ➤ Starting activity ~ 24 MBq
  - ➤ Ending activity ~ 2.5 MBq
- Integration time: 500 µs
- Pile-up for high activity (counting limited to 1 bit)
- **Exponential decay measured at the expected operation activity**

V. CONCLUSIONS & PERSPECTIVES

- **Requirements reached:** functional CMOS monolithic active pixel sensor
  - Low power: 161 µW
  - Compatible to the awaited activities of the radiotracers
  - Immune to the 511 keV γ-rays
- **Outlooks**
  - Tests of the double-sided probe
  - System integration (backpack)
  - Coating with biocompatible polymer (Parylene)
  - In-situ experiments
  - Tests and characterization of IMIC-LF: DMAPS version of IMIC (CPPM)

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