MAPSSIC

A novel CMOS intracerebral probe for brain imaging in freely moving rats

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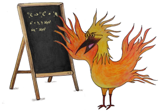
PHENIICS Fest

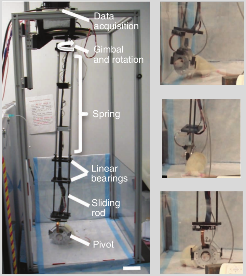
May 30–31 2017



What are anesthesia effects on neuroimaging studies ?

How to perform simultaneous behavior studies and real-time neuroimaging ?

RatCAP

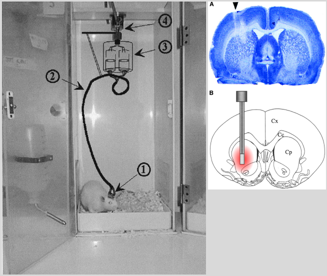


Schulz et al., Nature Methods, 2011.

Motion tracking

Spangler-Bickell et al., Phys. Med. Biol., 2016.

Beta Microprobe



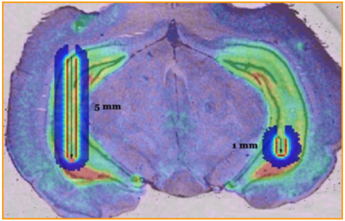
Pain et al., PNAS, 2002.

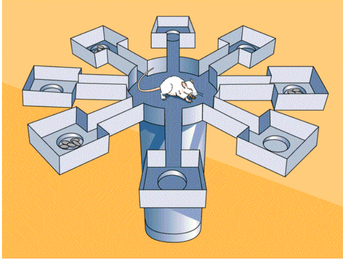
Project goals

To develop a pixelated $\beta+$ sensitive imaging device

To limit annihilation rays and visible light sensitivity

To give real autonomy to the rat

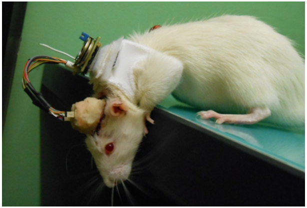




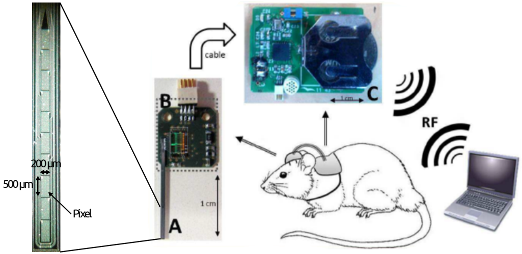
PIXSIC, the first pixelated β^+ microprobe

Reverse-biased high resistivity silicon diodes

- β^+ sensitivity
- Pixellated structure
- Wireless communication



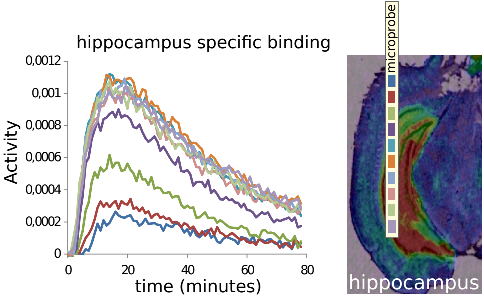
Fully freely moving animal with PIXSIC



A : Pixellated probe ; B : Readout electronic ; C : Battery and communication system

PIXSIC pharmacological validation

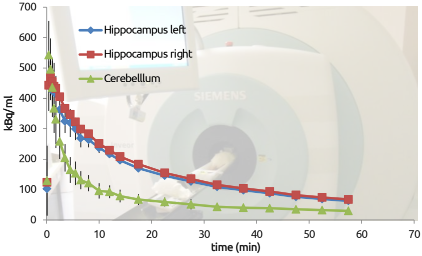
Several experiments validated PIXSIC biological and pharmacological suitability.

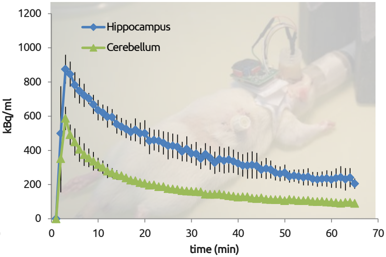


[18F]-MPPF injection - Hippocampus implantation.

Spatial distribution evaluation validated !

Several experiments validated PIXSIC biological and pharmacological suitability.

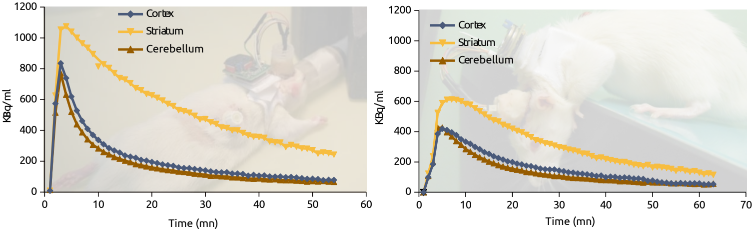




[18F]-MPPF 2 mCi injection - Hippocampus and cerebellum implantations.

Uptake measurement validated !

Several experiments validated PIXSIC biological and pharmacological suitability.



[11C]-raclopride 2 mCi injection - Striatum and cerebellum implantations.

PIXSIC shows anesthesia bias on neuroimaging results !

CMOS MAPS : towards an ideal probe

PIXSIC : It works !

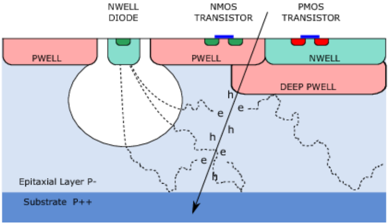
- First autonomous β^+ probe
- Validated in pharmacological studies
- Biocompatibility validated

... but it shows major limits :

- Mechanical robustness.
- Electronic noise.
- γ rays sensitivity.

CMOS MAPS technology

- Highly pixelated sensors.
- Direct amplification on the pixel.
- Data processing on the sensor.
- Low thickness of the sensitive volume.

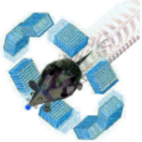


Charged particles detection in MAPS

MAPSSIC project aims to :

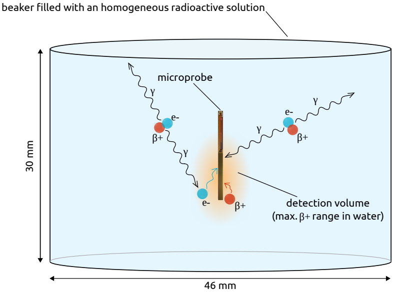
- Develop a CMOS MAPS sensor
- Develop front-end electronics
- Create an autonomous system on the animal head and back
- Validate the biological compatibility (temperature, size ...)
- Ensure mechanical and electrical robustness

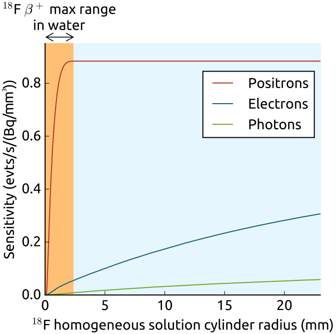
Use of Monte-Carlo simulations

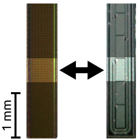


GATE
Simulations of Preclinical and Clinical Scans in Emission Tomography, Transmission Tomography and Radiation Therapy

Sensitivity







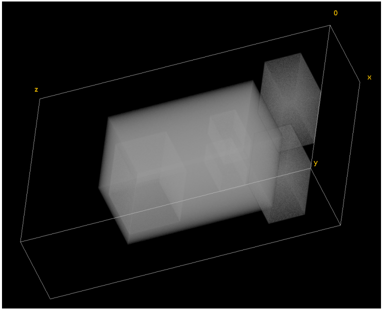
	MAPSSIC	PIXSIC
^{18}F	6.9	8.1
^{11}C	14.1	14.1
^{15}O	36.5	n/a

PIXSIC pixel vs MAPSSIC 10 rows sensitivity

($\times 10^{-2}$ evts/s/(Bq/mm^3))

Positron sensitivity is compatible with biological experiments

γ and e^- sensitivities are very low in typical biological volume sizes



Simple brain model using 6 regions : cerebelum, striatum (left and right), other brain tissues and harderian glands (left and right)

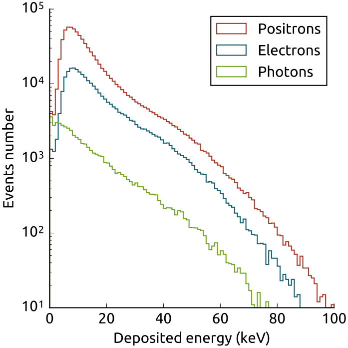
Probe is inserted into left putamen region (LCPu), activity is distributed as in typical 11C-raclopride experiments

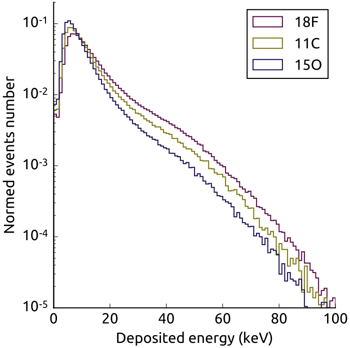
	β^+	e$^-$	γ
Cerebelum	0.00	0.04	0.01
L. CPu	86.27	2.80	0.19
R. CPu	0.00	0.25	0.00
Brain (other)	7.90	1.42	0.23
L. HG	0.00	0.29	0.10
R. HG	0.00	0.39	0.10

Relative sensitivity (%)

The probe is sensitive to local radioactivity

Energy deposits



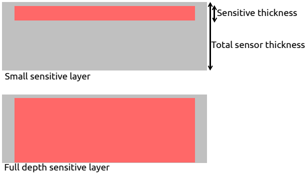


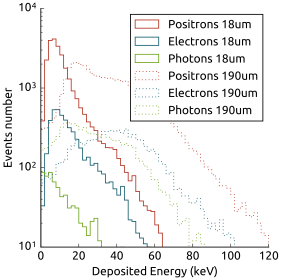
Mean deposited energy spectra in a single pixel

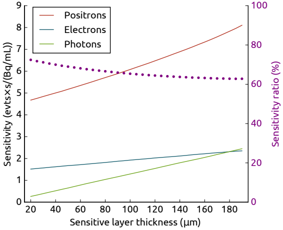
	$\beta^+ E_{mean}$	$\beta^+ E_{peak}$
^{18}F	15 keV	6 keV
^{11}C	13 keV	6 keV
^{15}O	10 keV	7 keV

Noise level in biological medium should be low enough to allow detection

Sensitive layer thickness

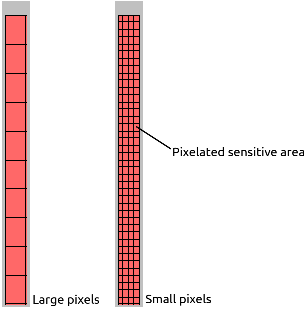


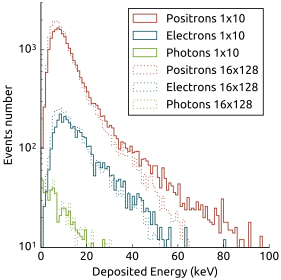




Sensitive layer thickness is a trade-off between sensitivity and S/N ratio

Pixels size





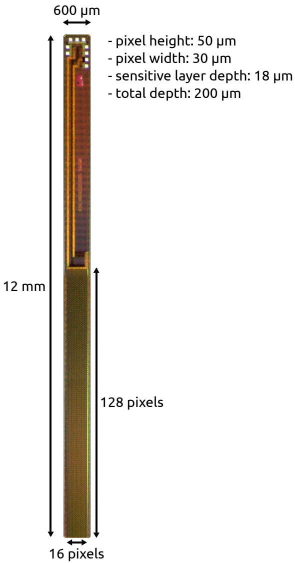
Pixels size variation only influences deposited energy

First prototype : IMIC-B

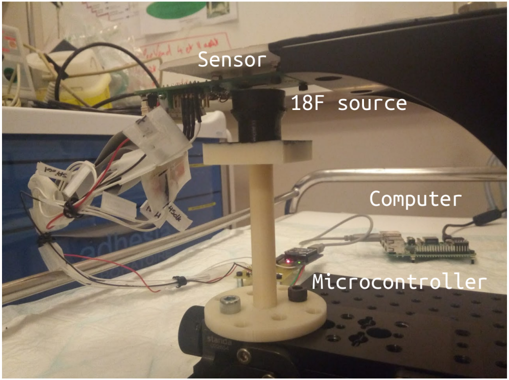
- 18 μm sensitive layer
- digital sensor
- 1 bit memory per frame
- Low power consumption (16 μW)

Second prototype : IMIC-LF

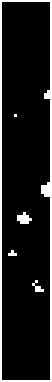
- HVCMOS
- 25 μm sensitive layer at 10 V
- Digital or analogic sensor



IMIC-B sensor photography



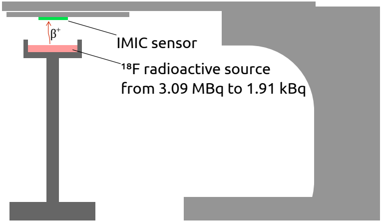
Experimental setup

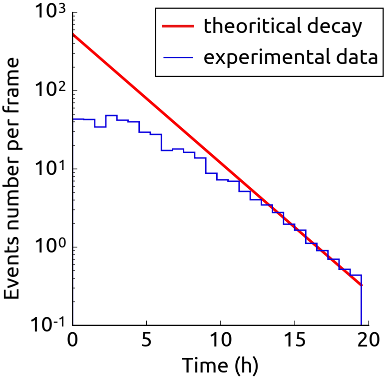


Example image

Acquisition of sensor images over time (451 ms/frame)
An incident particles leads to a cluster of activated pixels

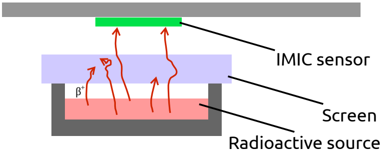
Count rate

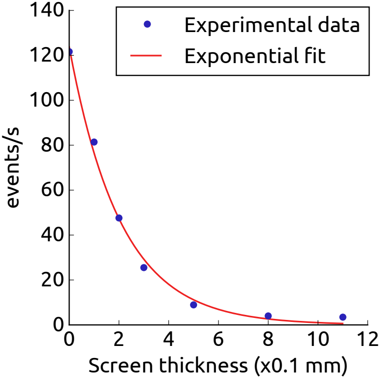




We observe events pile-up at high count rates but a good linearity at low count rates

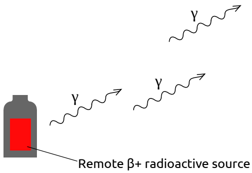
There is a good accordance between MC simulation and experimental sensitivity measurement in the linear region (3.58×10^2 evts/s/MBq)

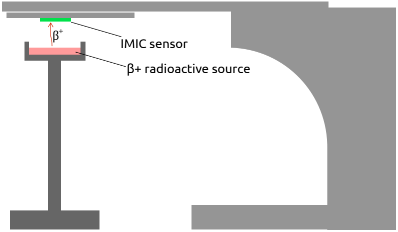




Typical positron attenuation profile (fitted by one exponential decay $I(l) = I_0 \times e^{-al}$ with linear coefficient $a = 4.8\ mm^{-1}$)

Remote annihilation gammas source :





No significant difference with or without remote $\beta+$ source.

Background noise (no source, no visible light) :

Low background noise : 9.0×10^{-4} events/s

Conclusion :

- CMOS MAPS are well suited for positron detection
- Our first sensor prototype is ready to be included in a probe setup

Outlook :

- Full probe design
- Control and acquisition electronics, backpack and connectivity
- Biocompatibility challenges (heat dissipation)
- Performances assessment in more realistic Monte-Carlo simulations and experimental conditions

Thank you for your attention

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