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

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Imaging brain on freely moving animal

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

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 $\beta^+$ microprobe

Reverse-biased high resistivity silicon diodes

- $\beta^+$ 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!
PIXSIC: It works!

- First autonomous $\beta^+$ probe
- Validated in pharmacological studies
- Biocompatibility validated

... but it shows major limits:

- Mechanical robustness.
- Electronic noise.
- $\gamma$ rays sensitivity.

CMOS MAPS technology

- Highly pixelated sensors.
- Direct amplification on the pixel.
- Data processing on the sensor.
- Low thickness of the sensitive volume.
MAPSSIC : A novel CMOS intracerebral probe

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
beaker filled with an homogeneous radioactive solution

MAPSSIC PIXSIC

\[
\begin{array}{c|cc}
\text{Isotope} & \text{MAPSSIC} & \text{PIXSIC} \\
\hline
^{18}\text{F} & 6.9 & 8.1 \\
^{11}\text{C} & 14.1 & 14.1 \\
^{15}\text{O} & 36.5 & \text{n/a} \\
\end{array}
\]

PIXSIC pixel vs MAPSSIC

10 rows sensitivity

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

Positron sensitivity is compatible with biological experiments

\(\gamma\) and \(e^-\) sensitivities are very low in typical biological volume sizes
Rat brain phantom

Simple brain model using 6 regions: cerebellum, 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

<table>
<thead>
<tr>
<th>Region</th>
<th>$\beta^+$</th>
<th>$e^-$</th>
<th>$\gamma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebelum</td>
<td>0.00</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>L. CPu</td>
<td>86.27</td>
<td>2.80</td>
<td>0.19</td>
</tr>
<tr>
<td>R. CPu</td>
<td>0.00</td>
<td>0.25</td>
<td>0.00</td>
</tr>
<tr>
<td>Brain (other)</td>
<td>7.90</td>
<td>1.42</td>
<td>0.23</td>
</tr>
<tr>
<td>L. HG</td>
<td>0.00</td>
<td>0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>R. HG</td>
<td>0.00</td>
<td>0.39</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Relative sensitivity (%)
Energy deposits

Mean deposited energy spectra in a single pixel

<table>
<thead>
<tr>
<th>Isotope</th>
<th>$\beta^+ E_{mean}$ (keV)</th>
<th>$\beta^+ E_{peak}$ (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}F$</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>$^{11}C$</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>$^{15}O$</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>

Noise level in biological medium should be low enough to allow detection.
Sensitive layer thickness is a trade-off between sensitivity and S/N ratio
Pixels size variation only influences deposited energy
First prototypes

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
Experimental testing setup

Acquisition of sensor images over time (451 ms/frame)
An incident particles leads to a cluster of activated pixels
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 ($3.58 \times 10^2$ 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: $9.0 \times 10^{-4}$ events/s
## Conclusion and outlook

**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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