

Simulation of a neuroimaging acquisition with MAPSSIC, a β^+ sensitive intracerebral microprobe for rats imaging

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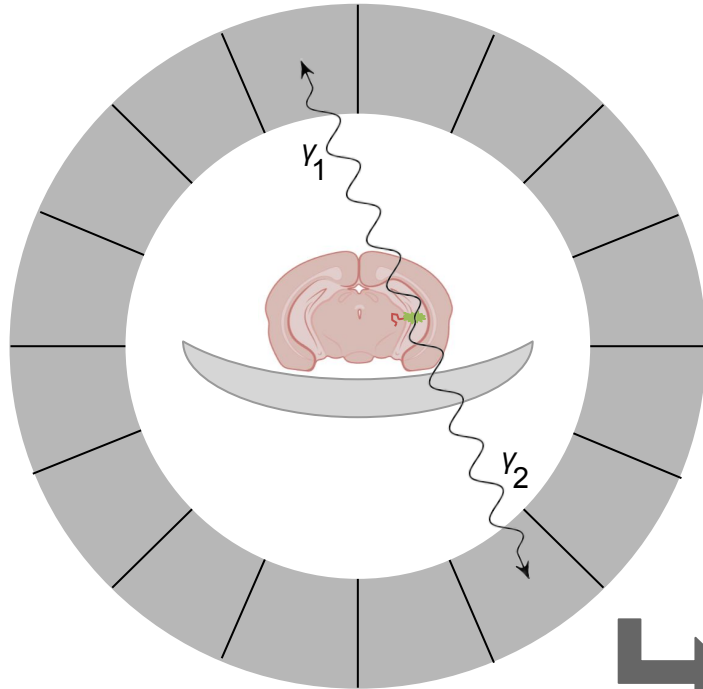
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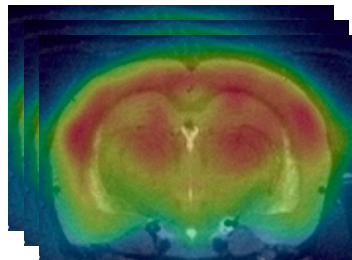
Context: Preclinical neuroimaging with micro-PET



micro-Positron Emission Tomography (micro-PET):

- Use injected β^+ radioisotopes
- Detects gamma rays from β^+ /e⁻ annihilation
- High sensitivity
- Allows for quantification
- **Requires anesthesia**

→Need for **awake imaging** data





Neuroimaging of awake and freely moving rats, why?¹

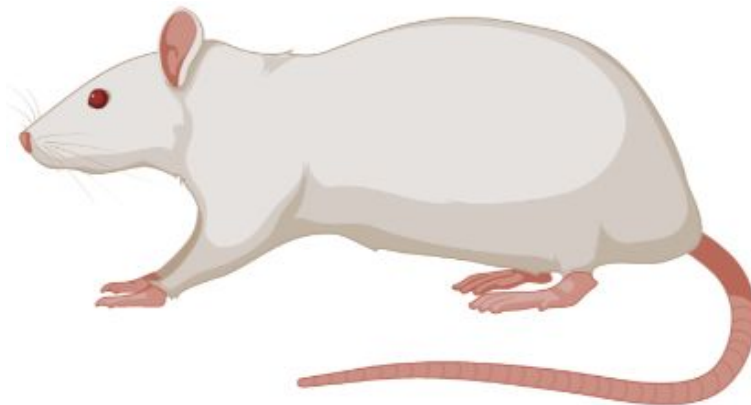
Majority of preclinical imaging performed under anesthesia

Effect of anesthesia

- Potential biases
- Many anesthetics²

Get closer to clinical practices

- No anesthesia in clinical imaging



Perform **simultaneous neuroimaging** and **behaviour** studies

- Correlation between behavior and brain images
- Molecular processes allow better understanding of behavior

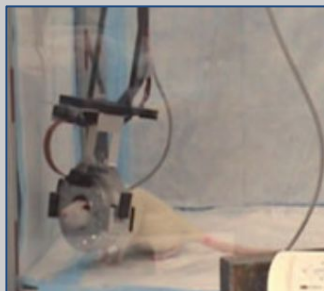
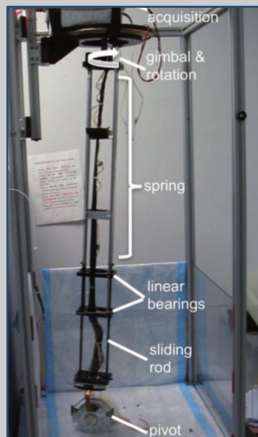
¹Y.R. Gao et al, *NeuroImage*, 2017

²J. Silverman, *Laboratory animal science*



Neuroimaging in awake and freely moving rats, 3 approaches

1 mini microPET



Schulz et al., Nature methods, 2011.

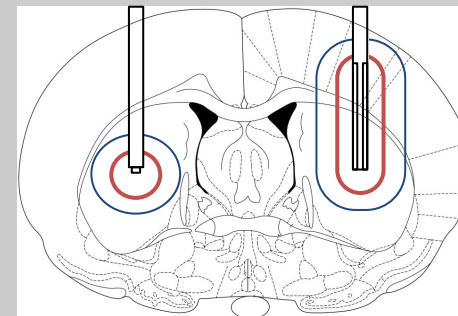
2 Regular microPET with Motion tracking



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



3 Implantable Microprobe



Mean range of ^{18}F
Mean range of ^{11}C



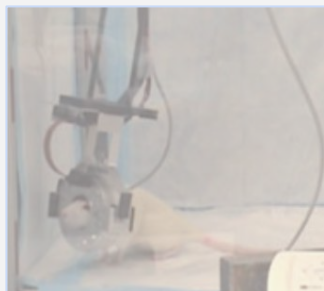
Pain et al., PNAS, 2002.

L. Balasse et al., Mol Imaging Biol, 2015



Neuroimaging in awake and freely moving rats, 3 approaches

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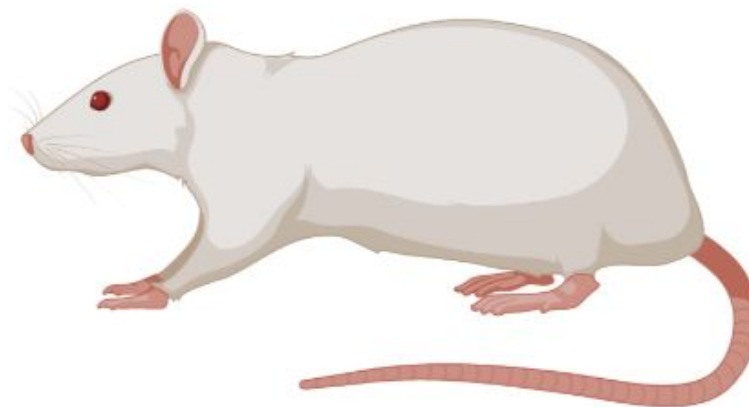


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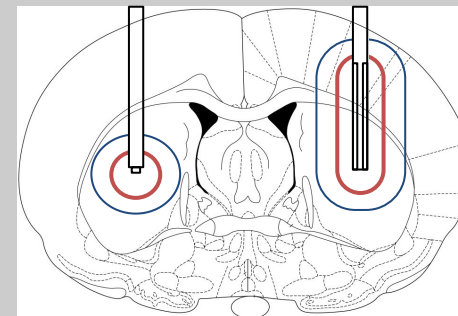
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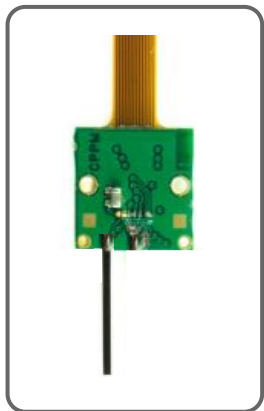


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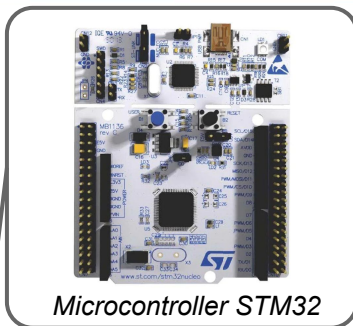
MAPSSIC project



1. Sensitive probe

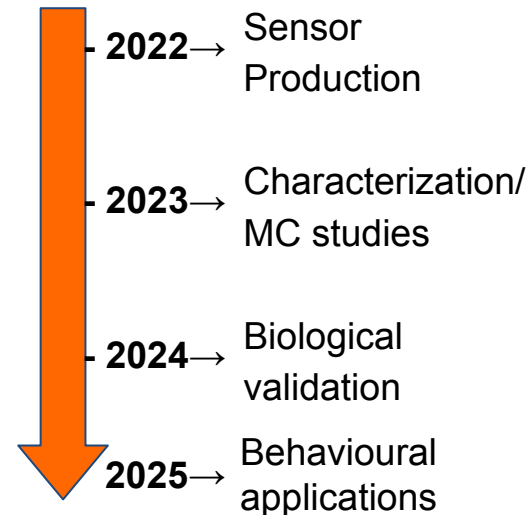
2. Backpack

- Microcontroller
- Power supply
- RF antenna



Features:

- Sensitive to **short range β^+**
- Record **kinetic** of **radiotracers**
- **Wireless** probe
- **Autonomy** to the rat



Constraints:

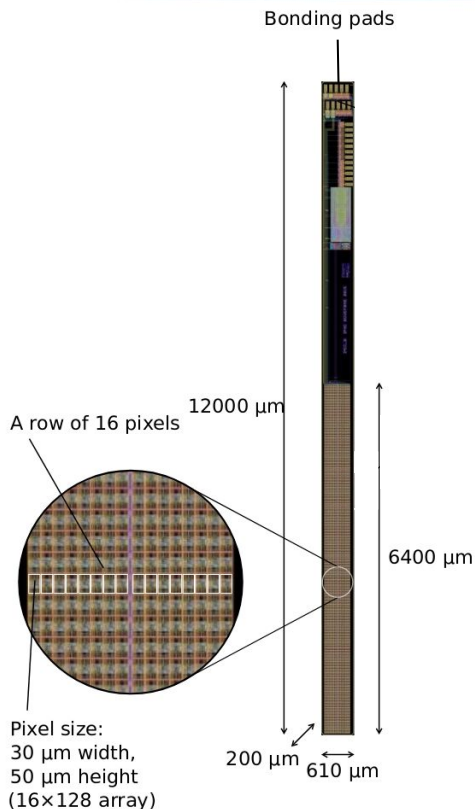
- **Gamma transparency**
- **Light: < 10% of rat weight**
- **Biocompatible**
- **Low power consumption**



Context: Neuroimaging in awake and freely moving rats

New digital sensor prototype (IMIC, 2022) based on a first prototype^{1,2} (2018):

- Based on **MAPS technology**
- Total / Sensitive thickness: 200 μm / 25 μm
- Pixel digitation: **1 bit**
- **Rolling shutter** readout

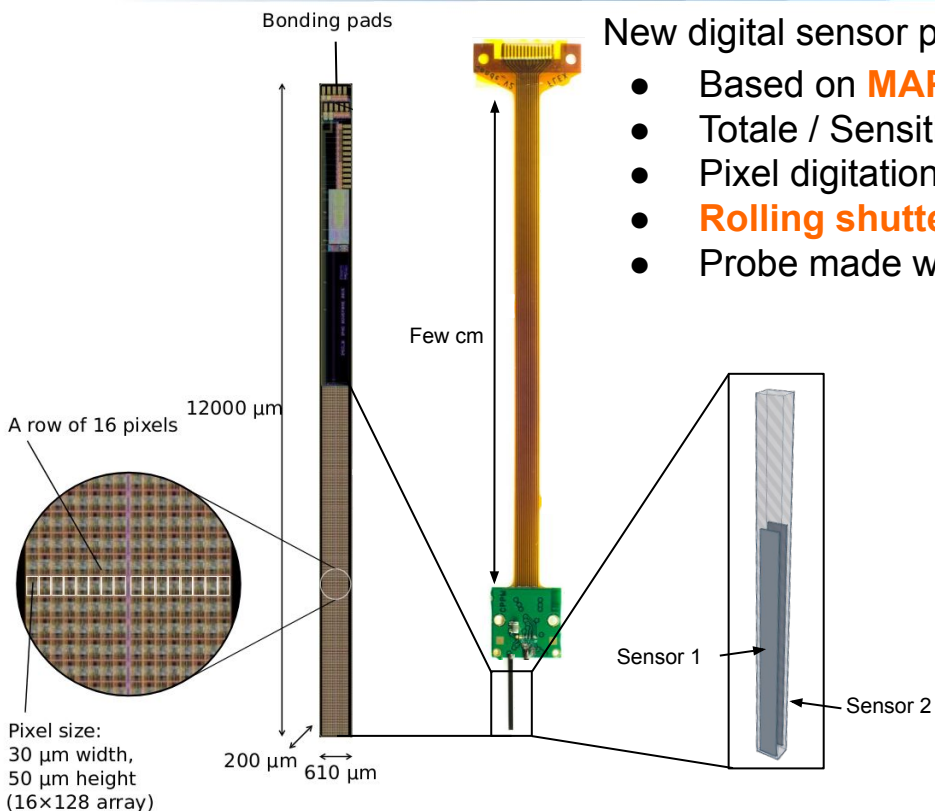


¹L. Amour, *IEEE Transactions on Radiation and Plasma Medical Sciences*, 2019

²J. Heymes, *IEEE Nuclear Science Symposium, Medical Imaging Conference*, 2016



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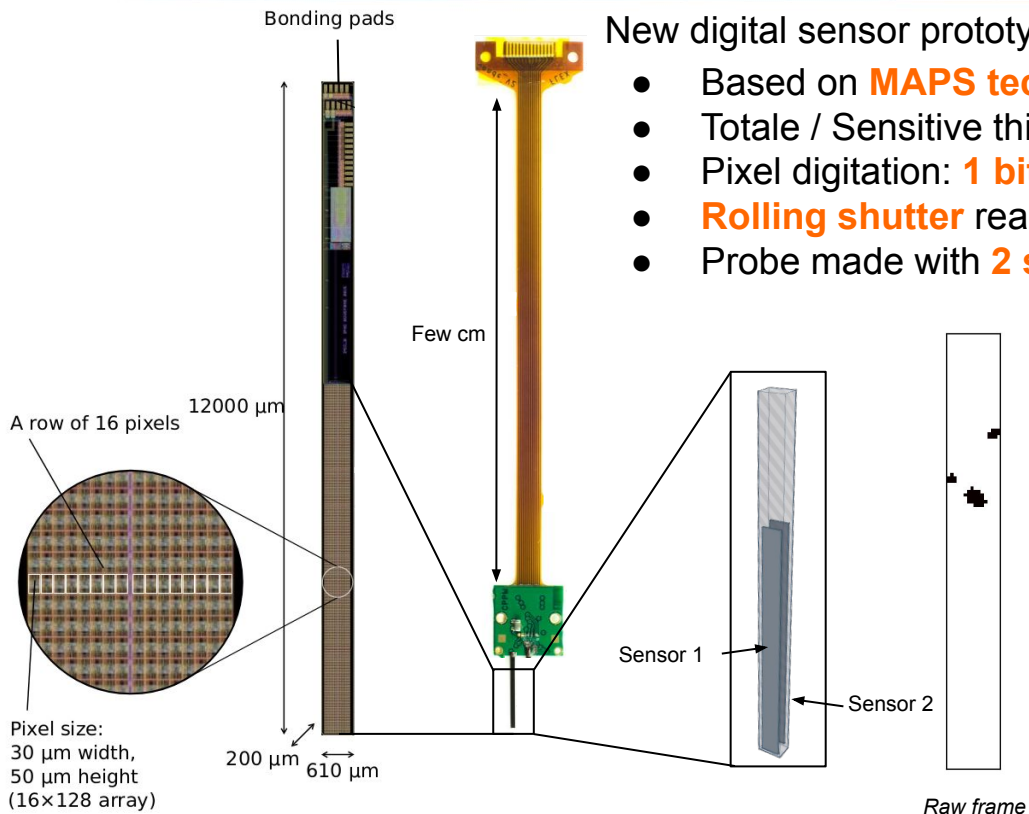
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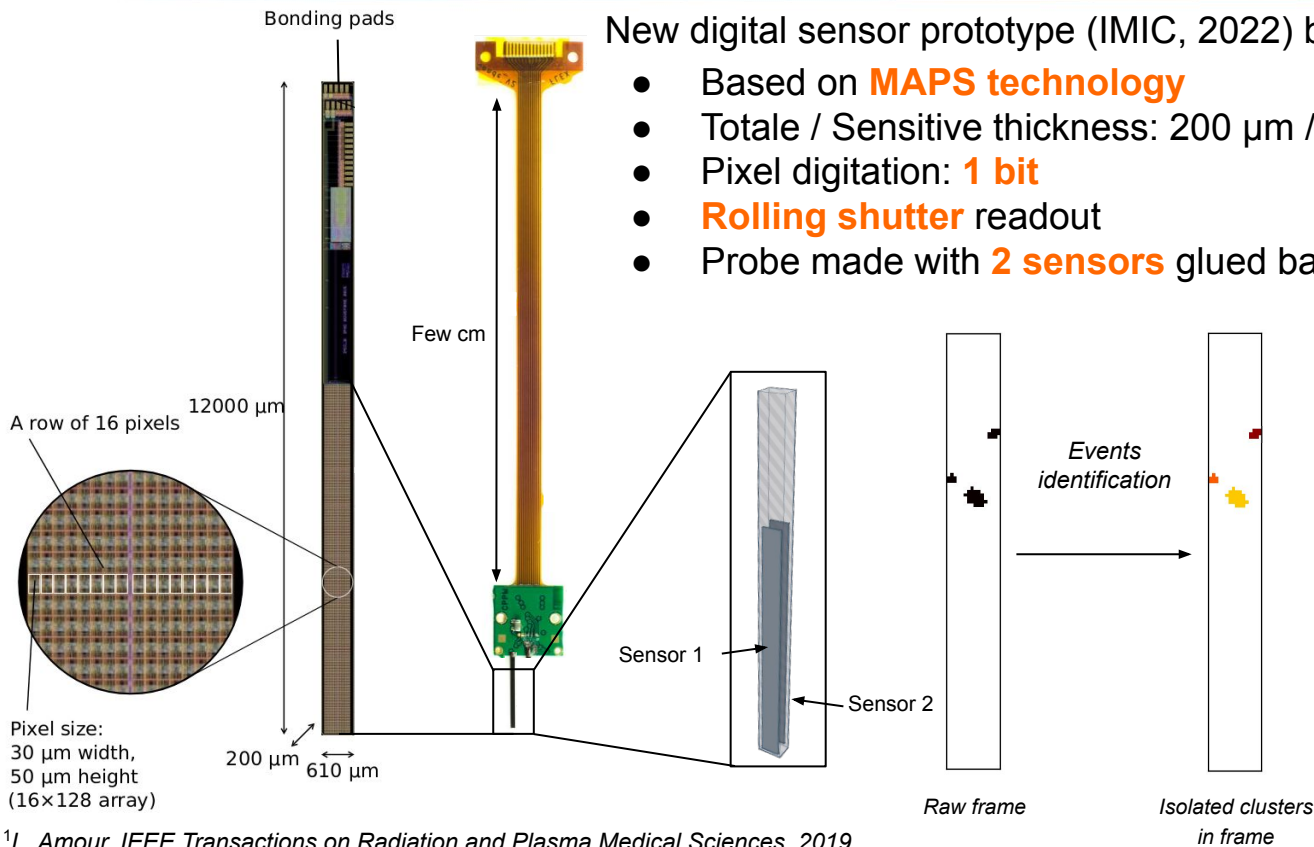
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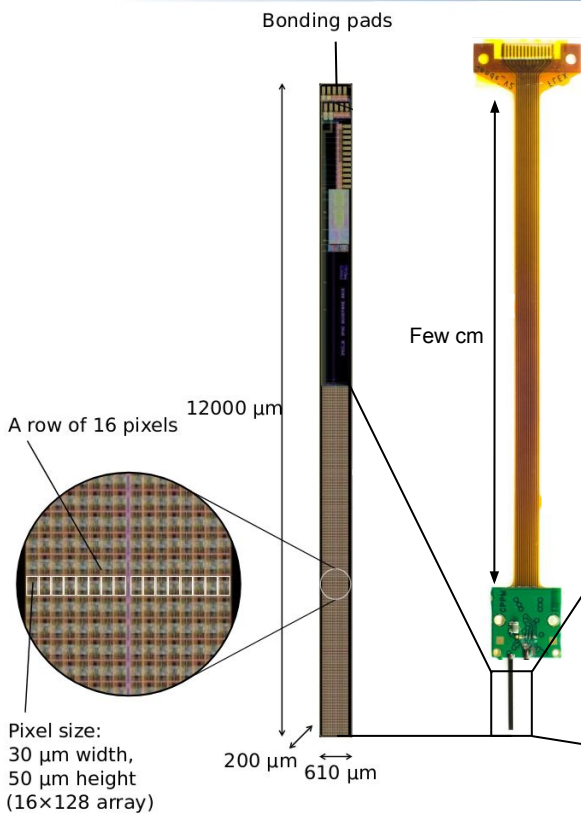


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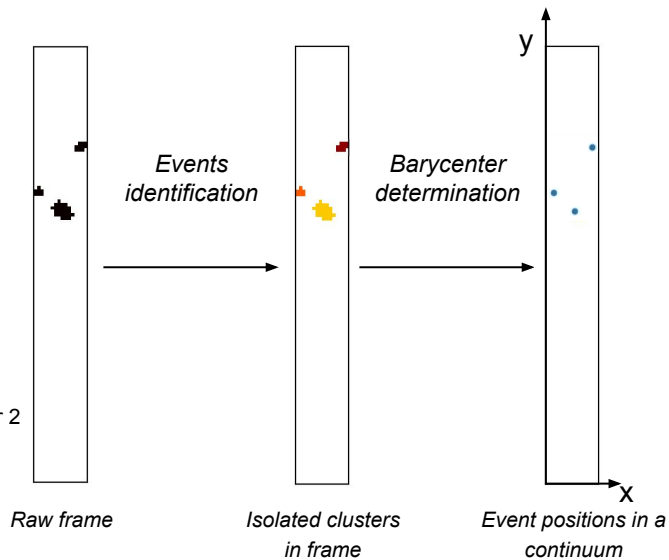


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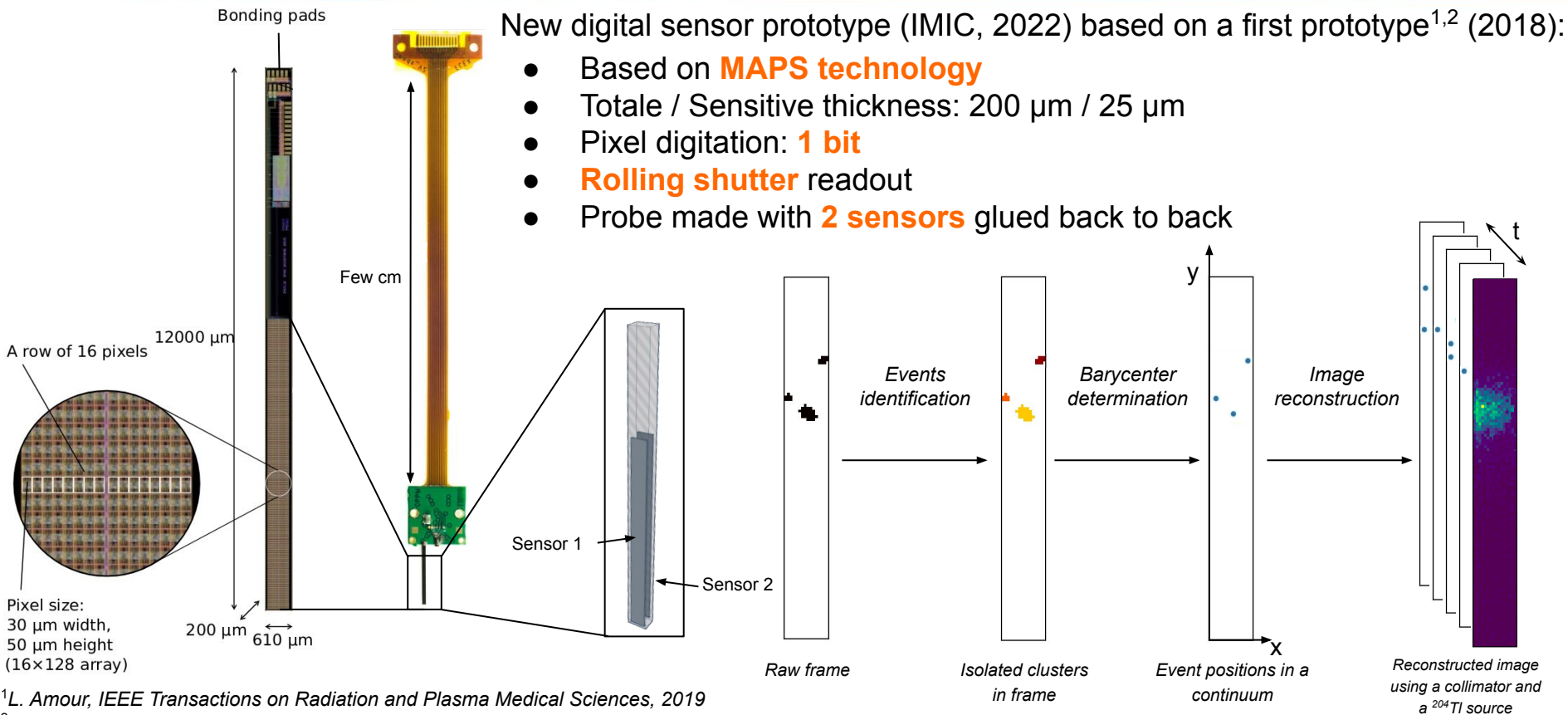


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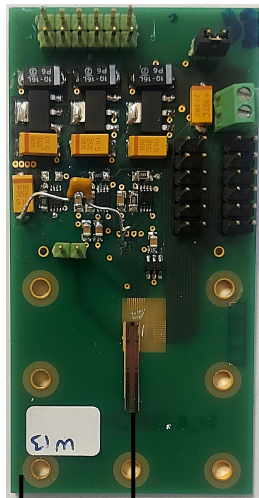


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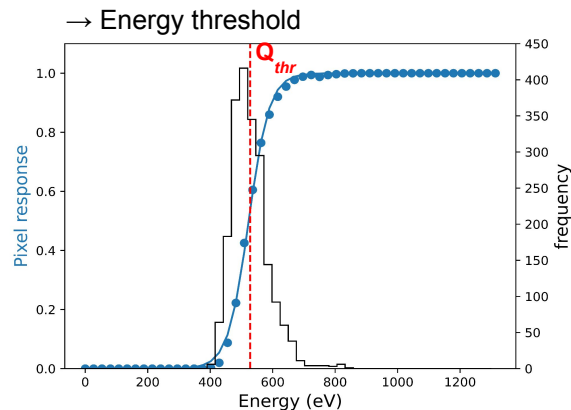


Physical validation



IMIC sensor

Testing PCB



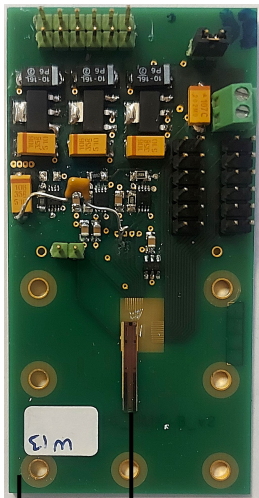
Understand the sensor's characteristics

Set nominal parameters

- Charge injections
- Sealed sources
 - beta: ^{204}Tl , ^{22}Na
 - X ray: ^{55}Fe

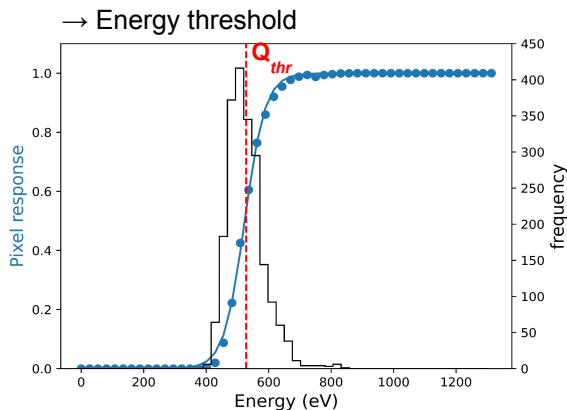


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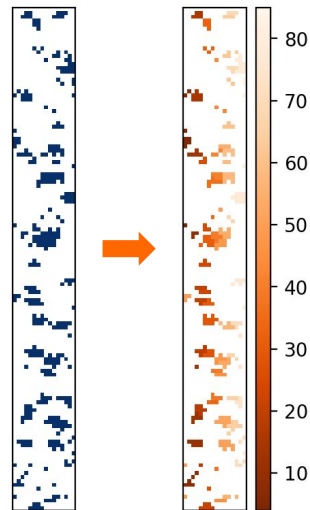


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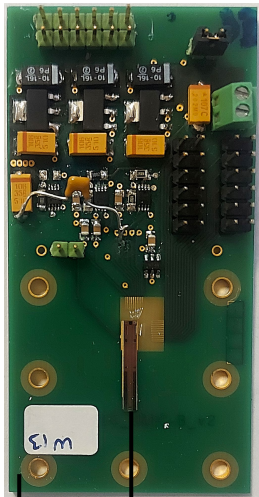
Clustering analysis



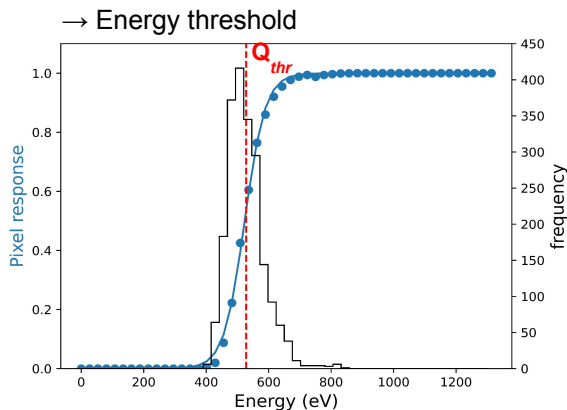
Machine learning algorithm:
95% efficiency in event
detection at 100 events/s



Physical validation



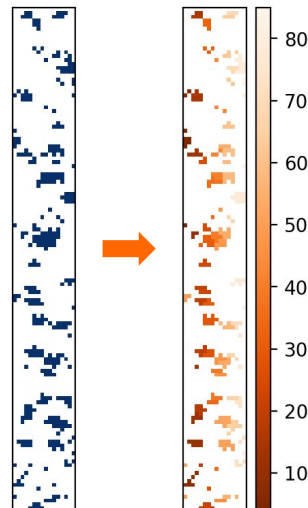
IMIC sensor
Testing PCB



Understand the sensor's characteristics
Set nominal parameters

- Charge injections
- Sealed sources
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Clustering analysis



Machine learning algorithm:
95% efficiency in event
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Methods development

- Set up **stereotactic surgery** protocols

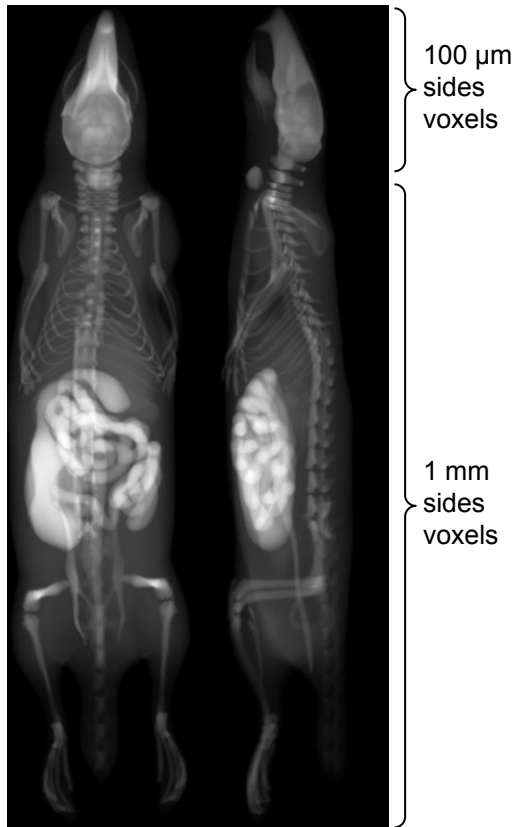
→ Implantation tests using
3D printed phantoms



3D rat skull

- Confirm the relevance of the probe
 - Validate its use *in vivo*

→ **GATE Simulation**

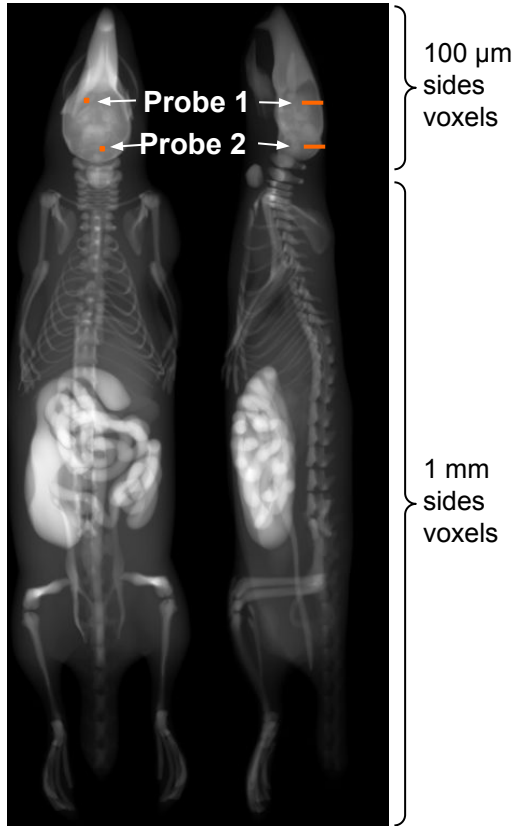


ROBY phantom¹

Voxelized rat phantom:

- Generated with the **ROBY program**¹
 - Skull area: cubic voxels of 100 μ m sides
 - Body area: cubic voxels of 1 mm sides
- Used for both **attenuation** and **activity** ranges
- Addition of **Harderian glands** from MRI images

¹W. P. Segars, *Molecular Imaging and Biology*, 2004.



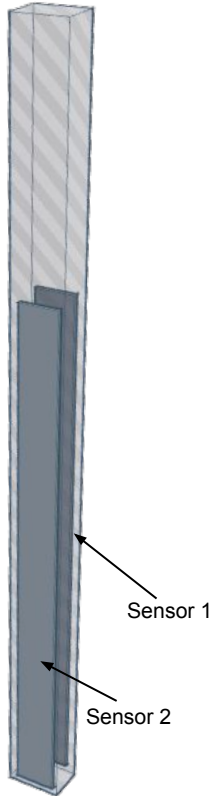
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Probes geometry:

- **2 Silicon boxes** of 9500 μm x 450 μm x 650 μm
- Physical volume inserted within the voxelized phantom using the **Merge Volume Actor**
- In the **cerebellum** and **striatum** region
- **Sensitive areas** of 6400 μm x 25 μm x 480 μm (2 per probe) filtered post simulations

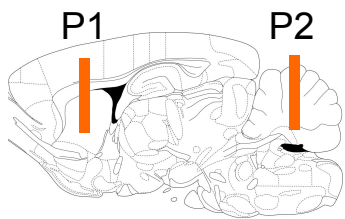


¹W. P. Segars, *Molecular Imaging and Biology*, 2004.



Radiotracer: [¹¹C]Raclopride

- ¹¹Carbon radiolabeled **dopamine D2 receptor antagonist**^{1,2}
- Preclinical/clinical research **schizophrenia, addictions**
- **Uptake in Harderian glands** (potential source of noise)
- Mean **range** of ¹¹C positrons \approx **1.1 mm** ($>$ ¹⁸F \approx 0.6 mm)



Striatum: **Specific signal**

Cerebellum: **Reference tissue**
→ Free radioligand concentration:
nonspecific **binding in the brain**

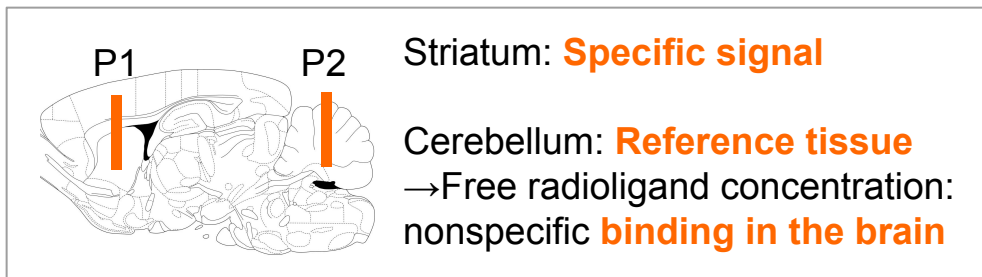
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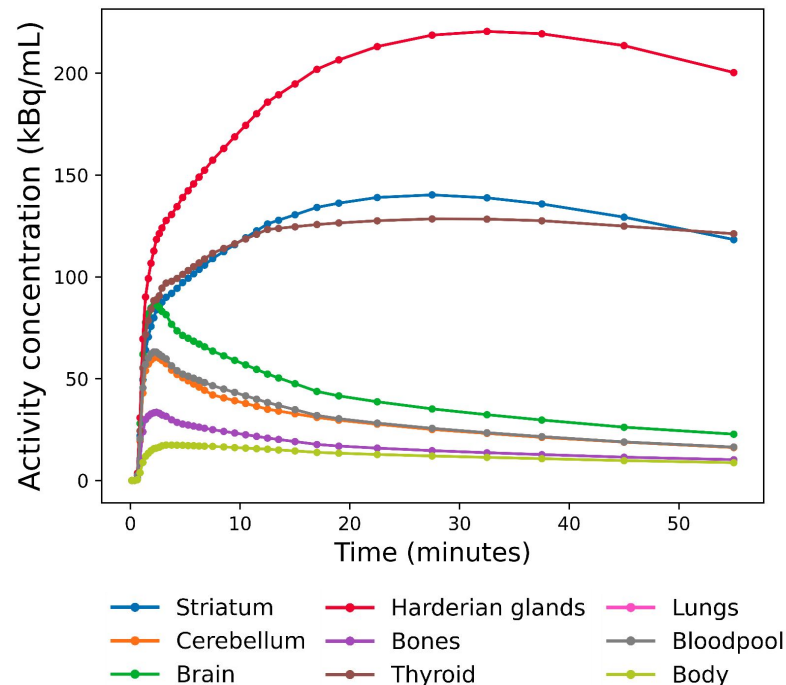


- [¹¹C]Raclopride time activity curves of **anesthetized rat** (from database³) → 11 MBq injection

¹H. Hall et al, *Prog Neuropsychopharmacol Biol Psychiatry*. 1988

²N. Ginovart et al, *Mol Imaging Biol*, 2005

Time-activity curves (OSSl-PET data)

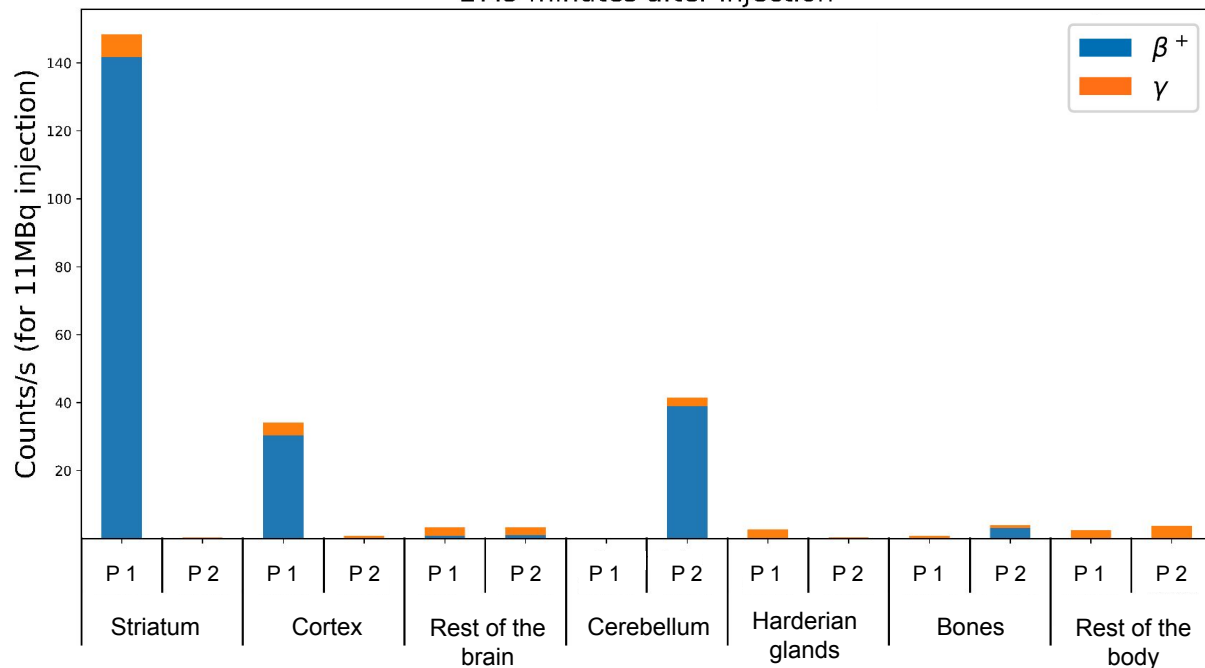


³M. -P. Garcia et al., *IEEE Transactions on Medical Imaging*, 2016



Results - Organ/particle contributions

27.5 minutes after injection



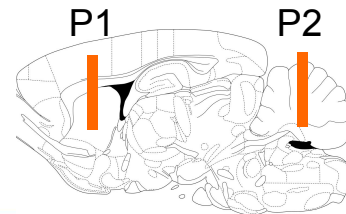
Source position of detected particles:

→ **Local information**: > 99% of detected particles from **skull area**

→ High **positron sensitivity** (direct detection)
≈ 90% of events in probe 1

→ Low **gamma sensitivity**

→ Harderian glands signal in probe 1 ≈ **1%**

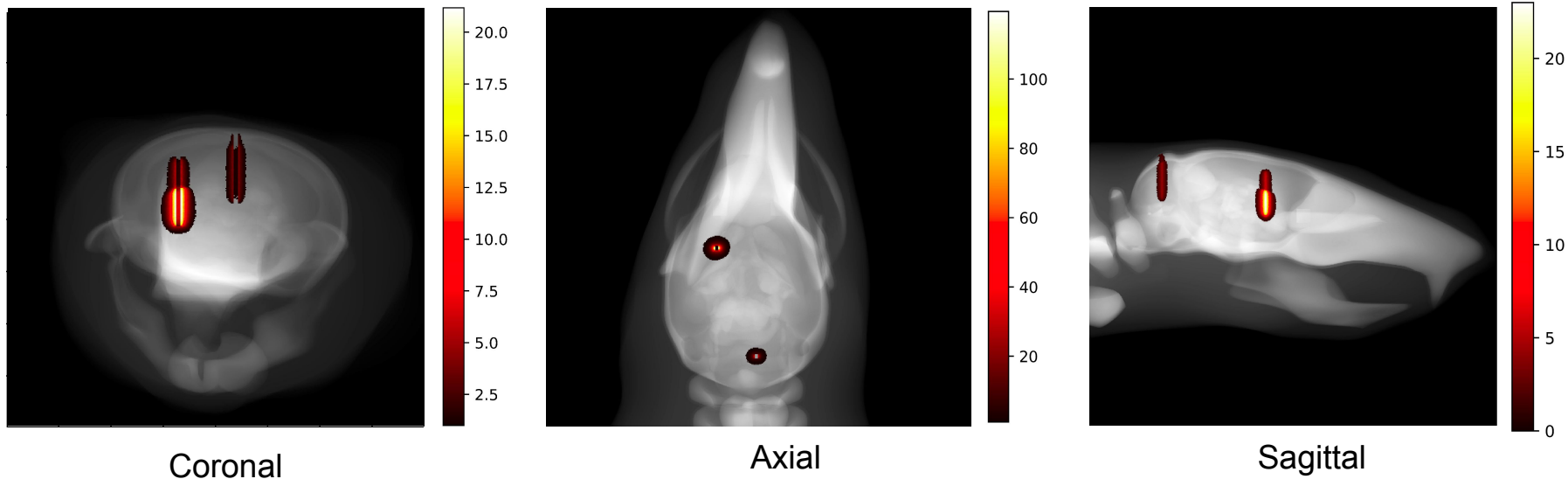




Results - Organ/particle contributions

Source position of detected particles:

→ **Local information**: majority of detected particles emitted in organs of interest

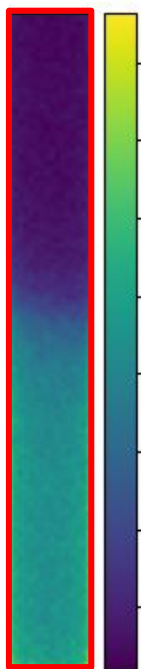


Integration over 1 minute, 27 minutes after injection

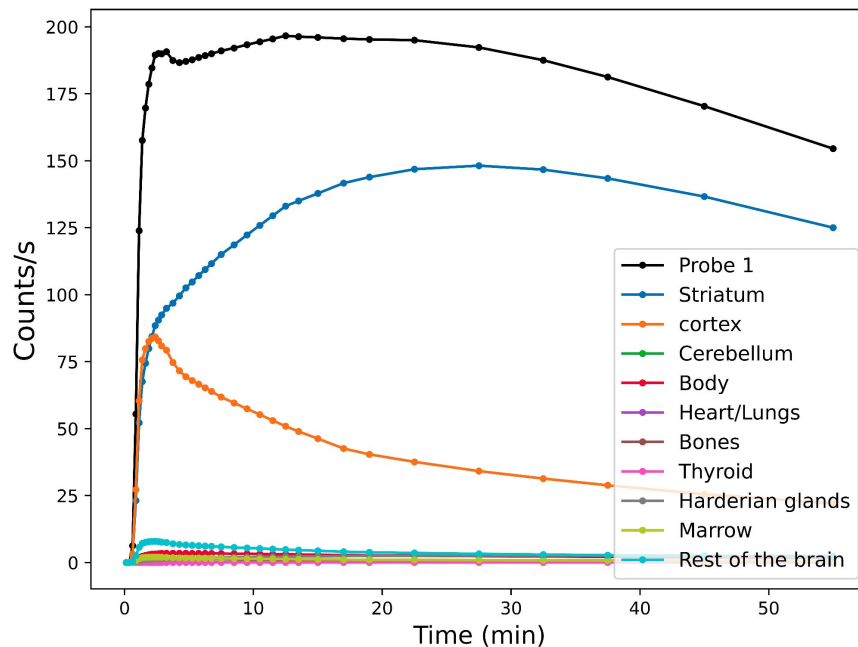


Probe 1

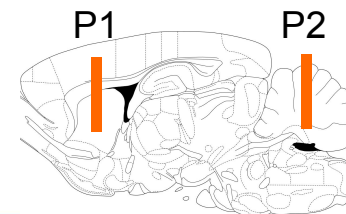
Probe 1 organs contributions



Probe 1 integrated image over 1 minute



Striata signal in ROI vs overall striata signal in frame	Other organs contributions in ROI
100 %	23 %



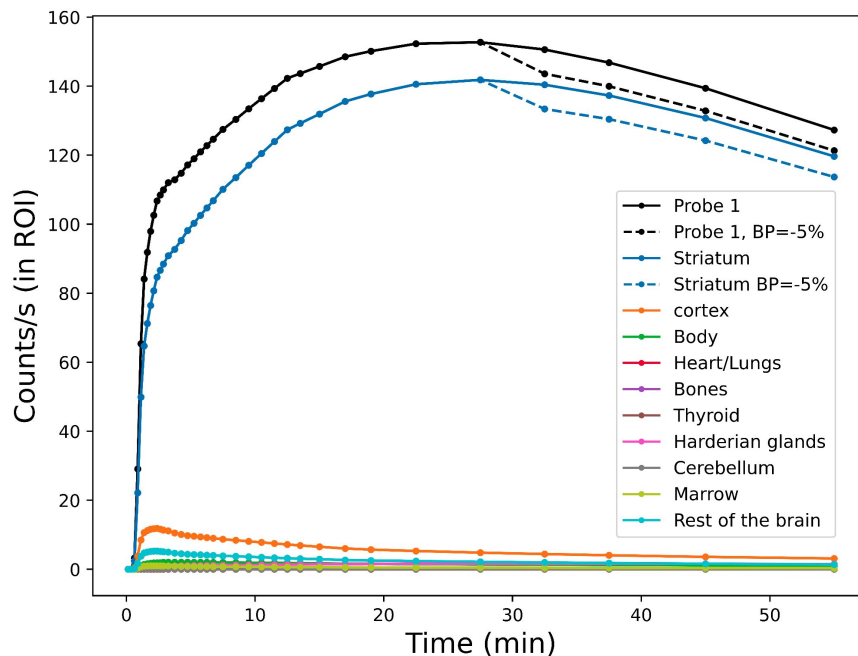


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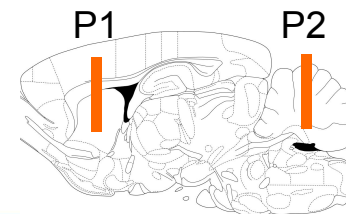
Probe 1 integrated image over 1 minute

Probe 1 organs contributions in ROI



Striata signal in ROI vs overall striata signal in frame	Other organs contributions in ROI
> 96 %	< 7 %

- Ability to highlight a loss in BP_{ND} (qualitatively)
- Work in progress for quantitative results





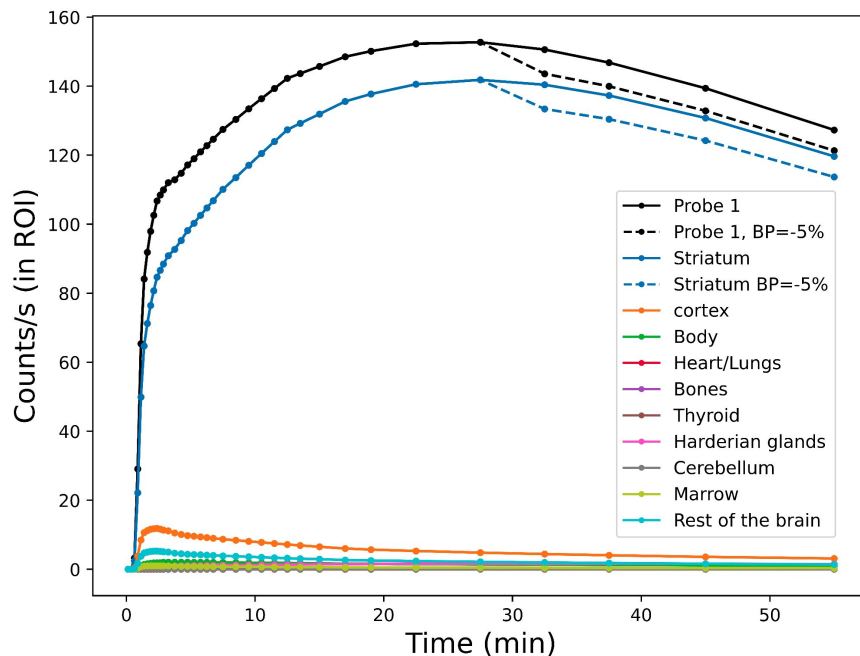
Results - Kinetic study

Probe 1



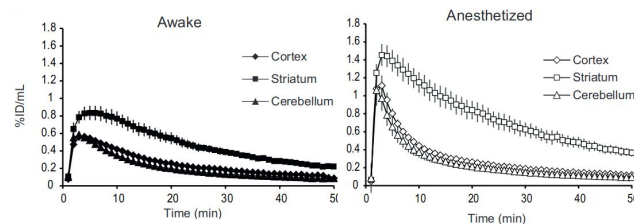
Probe 1 integrated image over 1 minute

Probe 1 organs contributions in ROI



Striata signal in ROI vs overall striata signal in frame	Other organs contributions in ROI
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- Ability to highlight a loss in BP_{ND} (qualitatively)
- Work in progress for quantitative results
- Next step: input data from **awake animals**



Balasse et al., Molecular Imaging, 2015



Conclusion

Simulation of an *in vivo* acquisition successful

- Proves that the probe provides a **local information**
 - **90 %** of the signal provided by **direct detection of β^+**
 - **High transparency** to gamma rays
- Image segmentation → **isolate signal** from specific structures
- kinetic studies

Perspectives

- Use **input** radioactivities from **awake animals**
- Carry on the sensor's **validation**
- **Biological validation** of the probe

THANKS FOR YOUR ATTENTION

MAPSSIC collaboration



Samir El ketara
Philippe Lanièce
Marc-Antoine Verdier



Franck Agnese
Jérôme Baudot
Maciek Kachel



Mathieu Dupont
Fabrice Gensolen
Jérôme Laurence
Christian Morel
Patrick Pangaud



Luis Ammour



Sandrine Bouvard
Luc Zimmer

With financial support from MITI (Mission pour les initiatives transverses et interdisciplinaires du CNRS)