Calibration and evaluation of a machine learning algorithm for β+ brain imaging using an intracerebral micro probe

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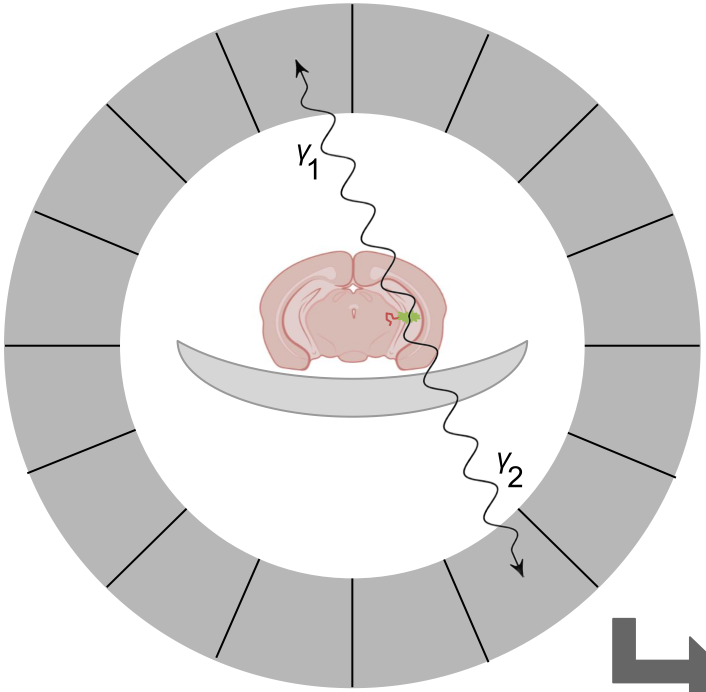
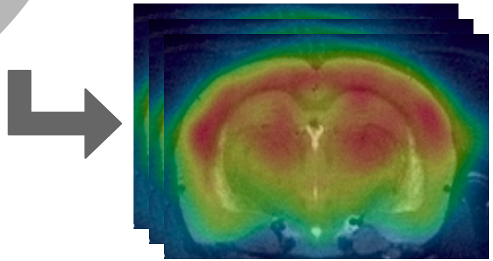
Context: Preclinical neuroimaging with micro-PET





micro-Positron Emission Tomography (micro-PET):

- Use injected β^+ radioisotopes
- Detects gamma rays from β^+/e- annihilation
- High sensitivity (pmol)
- **Requires anesthesia**

→ What is the effect of the **anesthesia**?

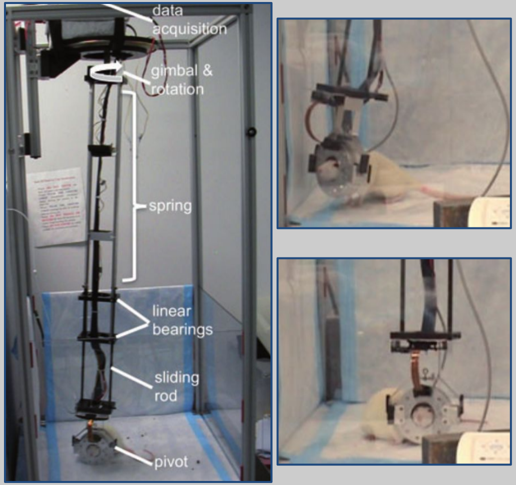
→ Perform **simultaneous behavior** studies and real time **neuroimaging**

Context: Neuroimaging in awake and freely moving small animals

Stakes:

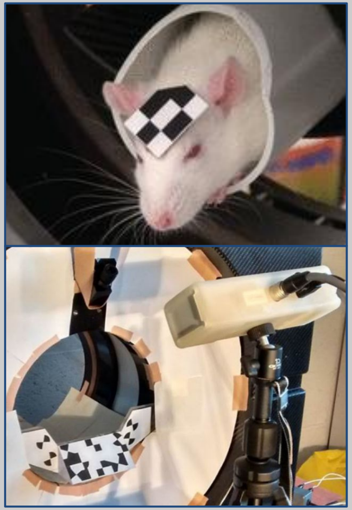
- Understand **anesthesia** effects on neuroimaging
- Perform **simultaneous behaviour** and **neuroimaging**

RatCAP



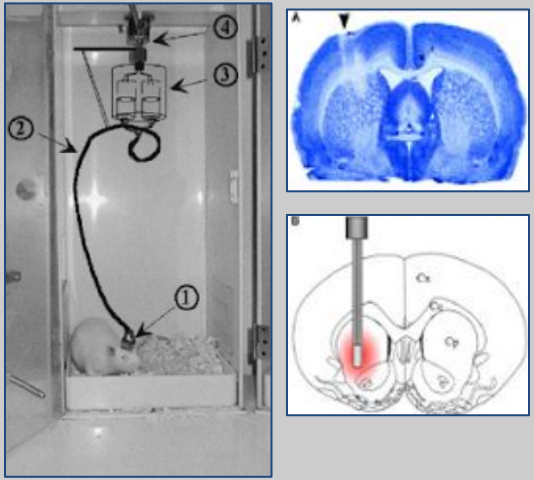
Schulz et al., Nature methods, 2011.

Motion tracking



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

Beta Microprobe



Pain et al., PNAS, 2002.

Context: Neuroimaging in awake and freely moving rats

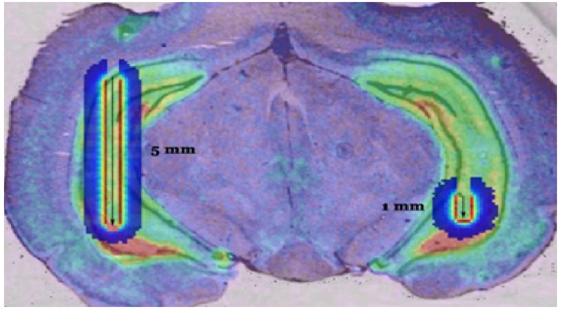
MAPSSIC Project

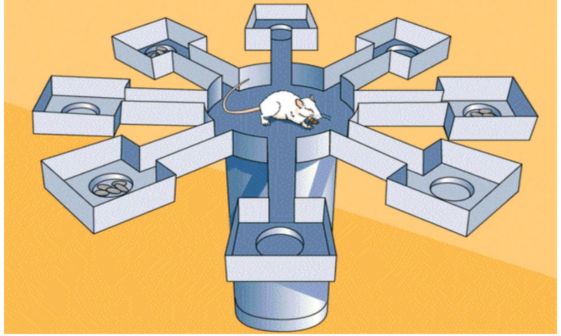
Goals

- To develop a pixelated β+ sensitive imaging device
- **Direct detection** of short range β+
- To give a real **autonomy** to the rat

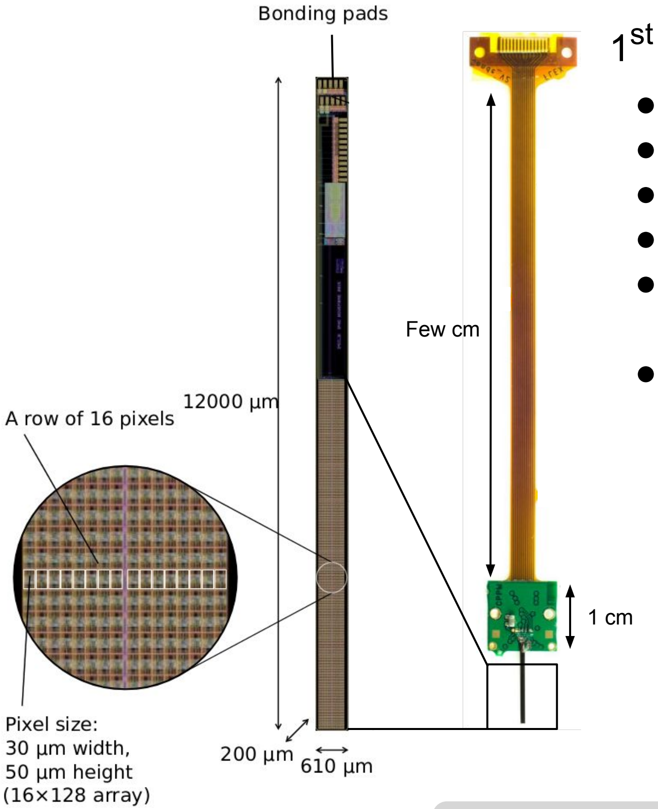
Constrains

- **Weight limit**: 10% of the animal ≈ 35g
- **Low electrical consumption**



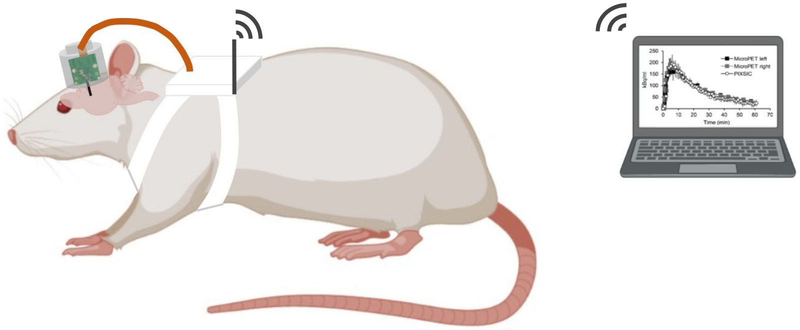


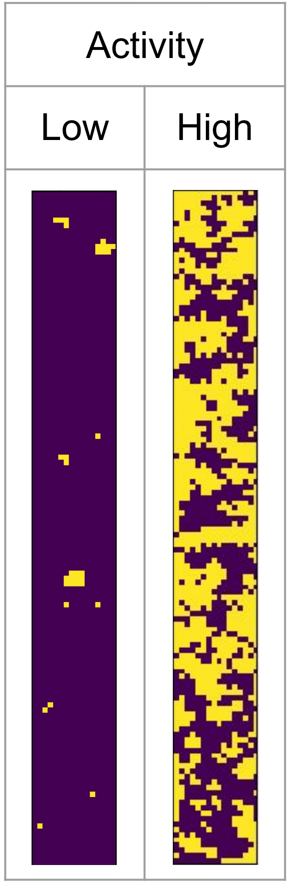
Context: Neuroimaging in awake and freely moving rats



1[st] digital sensor prototype (IMIC-1, 2018):

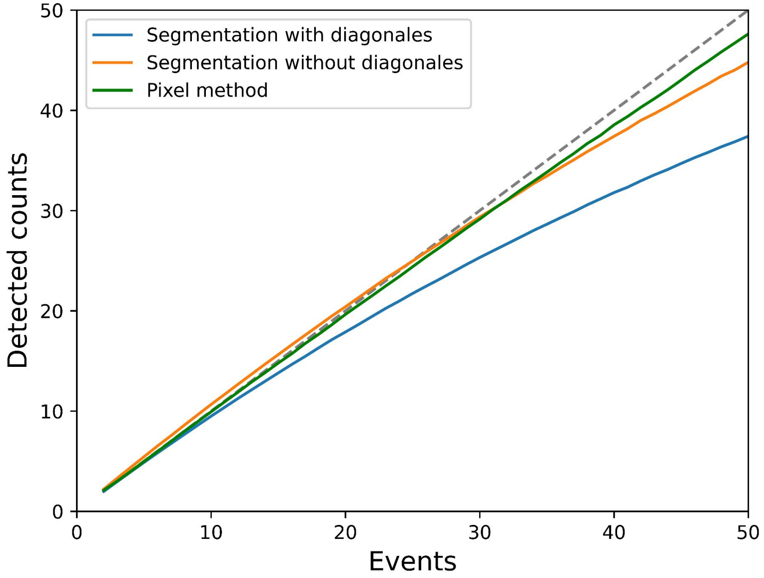
- Based on **MAPS technology**
- Sensitive thickness: 18 µm
- Pixel digitation: **1 bit**
- Probe made with 2 sensors glued back to back
- **Rolling-shutter** + microcontroller, 500 ms integration time
- **Expecting 100 counts/s** max at in vivo use





Consequence : **Pile up** occurs at high count rates

Pile up issue



Previously explored methods[1] :

1. Simple segmentation = contouring (with/without diagonals)
2. Cluster size method: Estimate counts number using the number of activated pixels over the mean number of activated pixels per clusters:

$$\text{Cluster number} = \frac{\#\ \text{activated pixels}}{\text{mean}\ \#\ \text{of pixels per cluster}}$$

→**Best method so far :** Cluster size method.

Advantage **:** Allows a limited loss in sensitivity

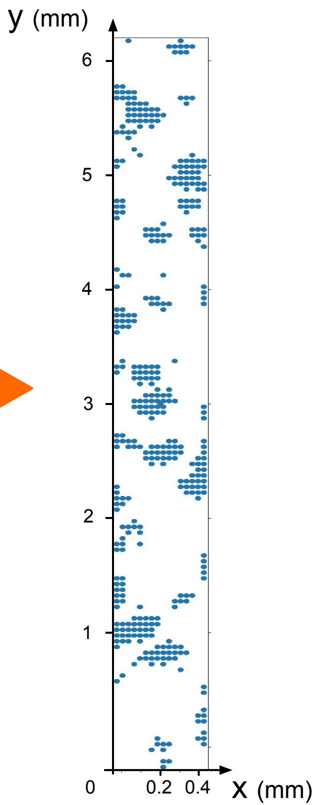
Drawback **:** **No event localization**

1. *Luis Ammour. Développement d'une sonde intracérébrale à pixels actifs pour l'imagerie bêta du cerveau du rat libre de ses mouvements. Université Paris Saclay (COmUE), 2018. Français.*

Clustering

Frame

Coordinates

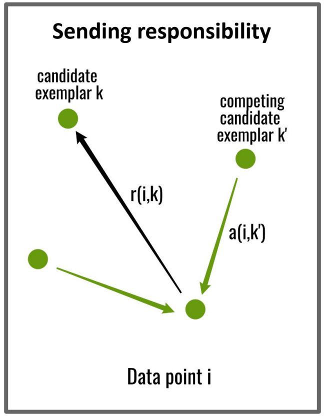


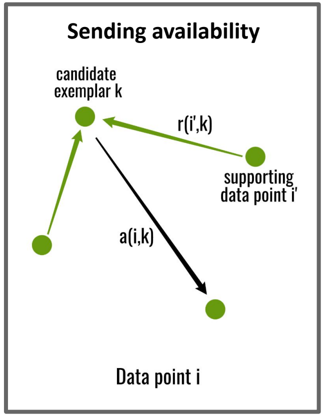
AFFINITY PROPAGATION algorithm[2] :

- Based on iterative message passing between Data points
- Implemented in Scikit-Learn

2. *Brendan J. Frey and Delbert Dueck, "Clustering by Passing Messages Between Data Points", Science Feb. 2007*

Affinity propagation algorithm



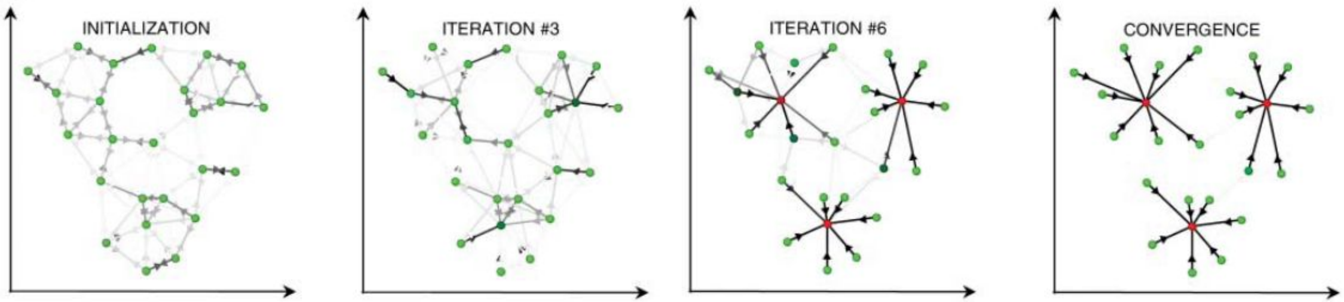


AFFINITY PROPAGATION algorithm[2] :

- Based on iterative message passing between Data points
- Implemented in Scikit-Learn
- 2 types of passing messages:
  - *responsibility r(i,k):*
  - *availability a(i,k):*
- Determine the **number** and the **position** of clusters
- **No cluster number needed as input**
- Each cluster is composed by an *exemplar* (which better represents the distribution) and targets (points associated to an exemplar)

2. *Brendan J. Frey and Delbert Dueck, "Clustering by Passing Messages Between Data Points", Science Feb. 2007*

Affinity propagation algorithm



Brendan J. Frey and Delbert Dueck, “Clustering by Passing Messages Between Data Points”, Science Feb. 2007

- Influence parameter :
    - ***Preference*** : Calculated number of clusters is **directly influenced** by the *preference* value

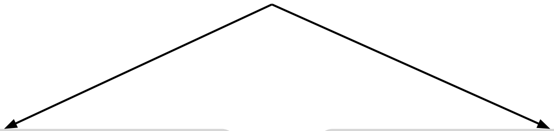
→Need for **calibration** of the algorithm : Search for the optimal *preference* value for AP clustering on frames containing from 1 to 100 clusters

Data generation

Affinity propagation algorithm - Data generation

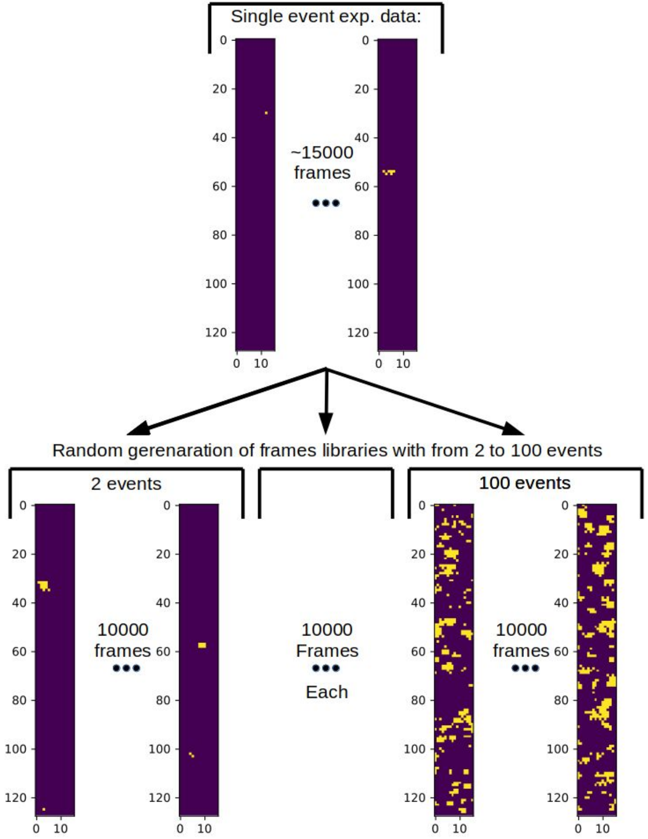
Data generation:

- From **experimental frames** (N ≈ 15 000)
  - Obtained with **18F source** →(liquid source in contact with the sensor)
  - Containing exactly 1 cluster
- **Random generation** of 1 to 100 clusters frames (N = 2 million)



Calibration frames (50 %)

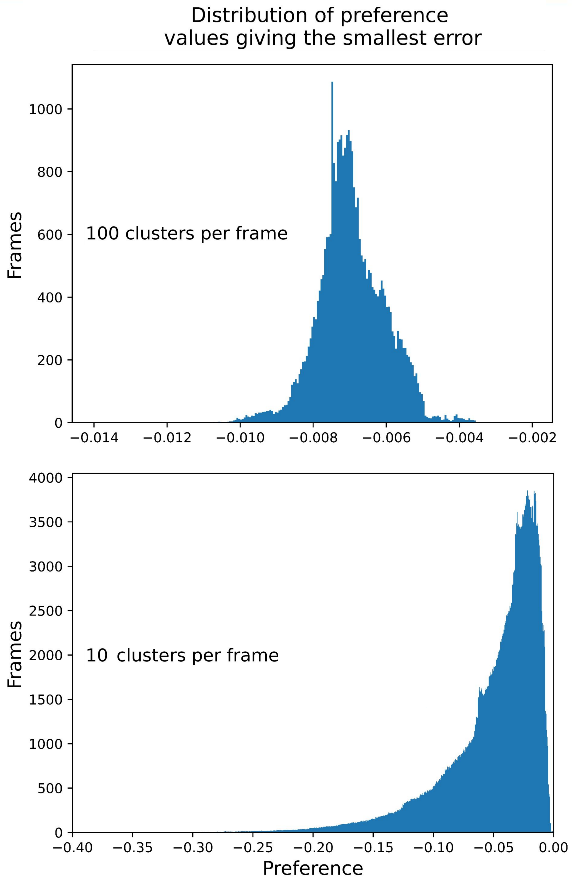
Validation frames (50 %)



Affinity propagation algorithm - Calibration

Data processing from AP calibration runs:

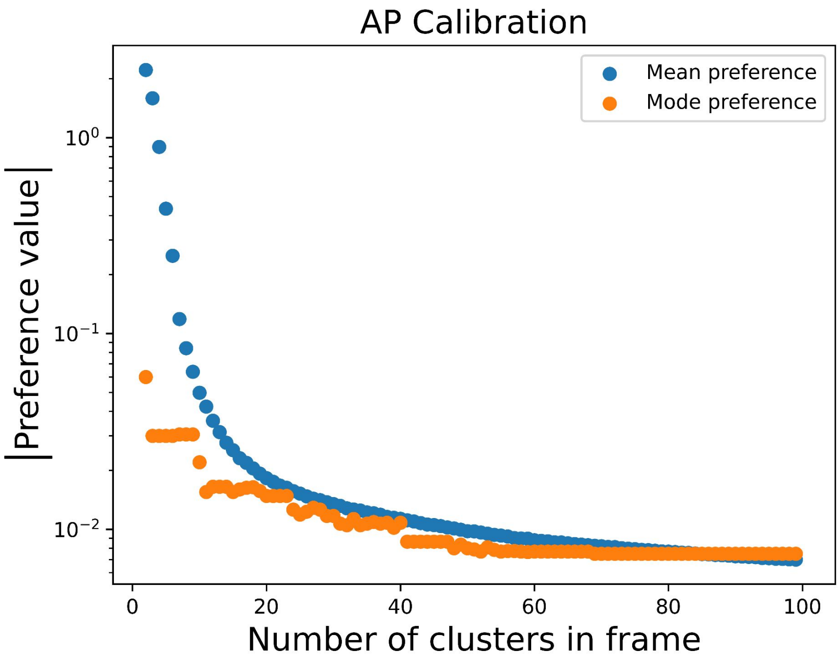
- Determination of the optimal *preference*:
  - AP runs on calibration frames **scanning** the previously determined ***preference* range**
  - **Mean** and **Mode** of the distribution *preference* values leading to the **smallest error** between calculated and actual cluster number for a given frame
  - Gaussian draw of a new *preference* value if the previous does not converge to an answer (400 times maximum)



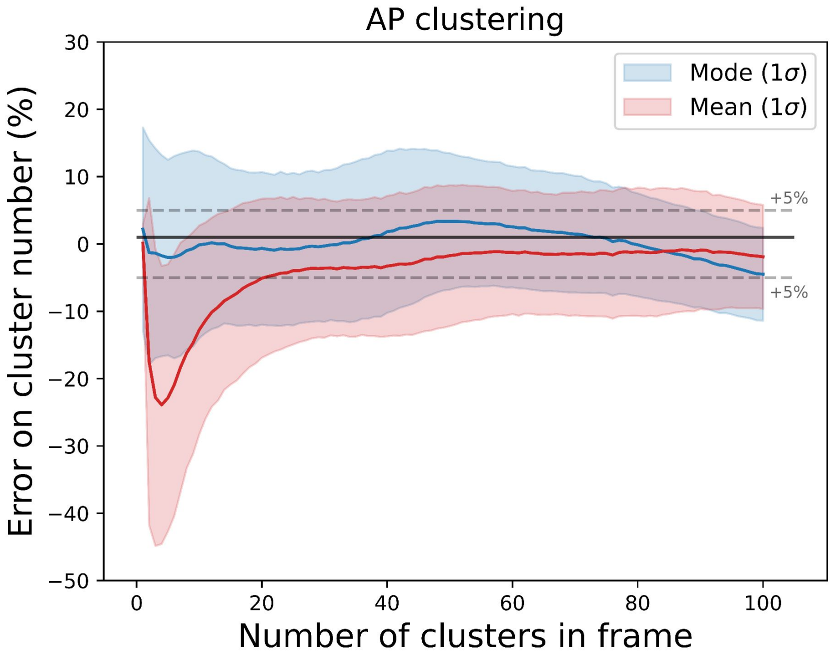
Affinity propagation algorithm - Validation

Run of AP algorithm on the validation data set with both mean and mode *preference* values :

- Actual operating conditions
- **No *a priori*** on the cluster number per frame. →**Rough estimation** of the cluster number based on the number of activated pixels
- Run of AP algorithm with the selected *preference* values according to the estimated cluster number (taking into account the estimation bias).



Affinity propagation algorithm - Validation



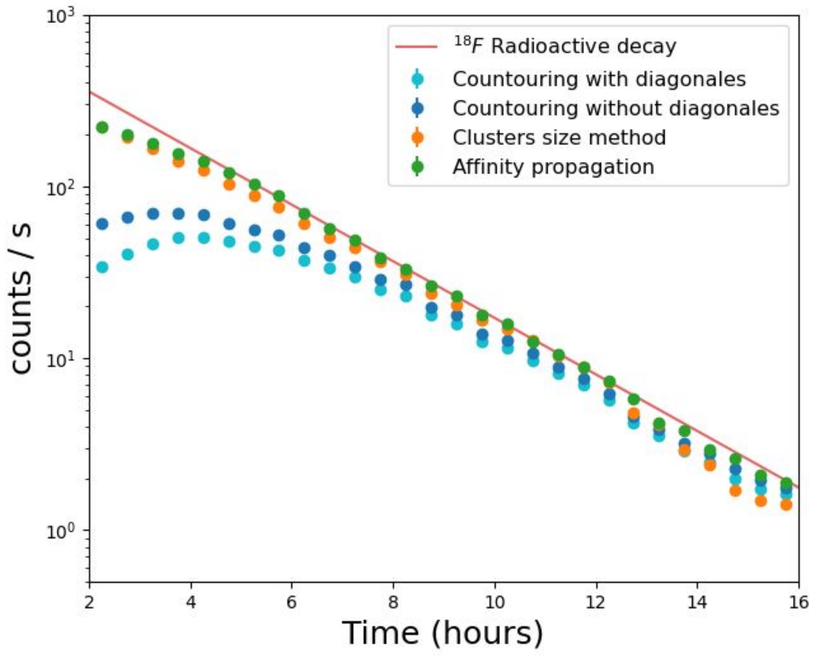
Results on validation frames:

- **≳ 50 clusters/frame**, the mode *preference* performed better than the mean *preference*
- **≲ 50 clusters/frame**, mean *preference* shows a drop in accuracy
- Using the mode *preference* gives an error not greater than 5% no matter the number of clusters per frame

Mix of AP algorithm with mean and mode *preference* values according to the estimation

Affinity propagation algorithm - Validation

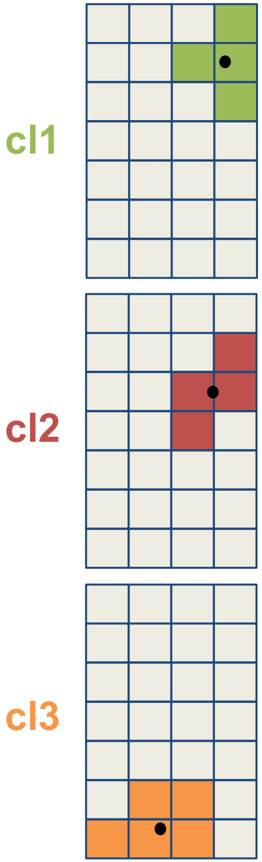
AP algorithm **performed on experimental Data** from ^{18}F radioactive decay measurement:



- **Achieved linearity** for the expected count rates for in vivo measurements
- Calculation time varies from **few milliseconds** to 0.5 seconds per frame

Results compatible with *in vivo* measurements

Affinity propagation algorithm - Spatial performances

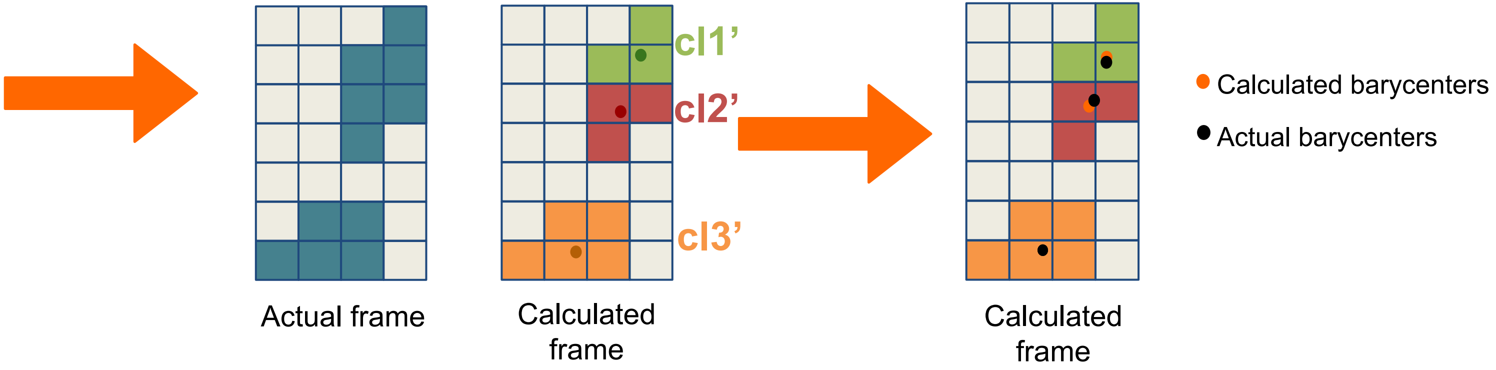


- Determination of the barycenter for each real cluster
- Determination of the barycenter for each calculated cluster
- Error on **weighted average barycenters**

$$cl1_{err} = (cl1 - (3 \times cl2' + 1 \times cl1' + 0 \times cl3'))/4$$

$$cl2_{err} = (cl2 - (1 \times cl2' + 3 \times cl1' + 0 \times cl3'))/4$$

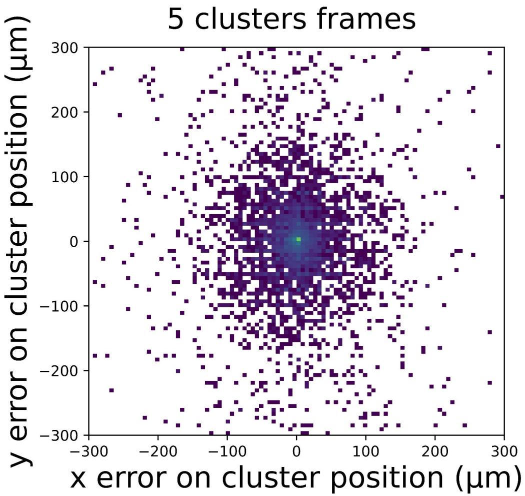
$$cl3_{err} = (cl3 - (0 \times cl2' + 0 \times cl1' + 5 \times cl3'))/5$$



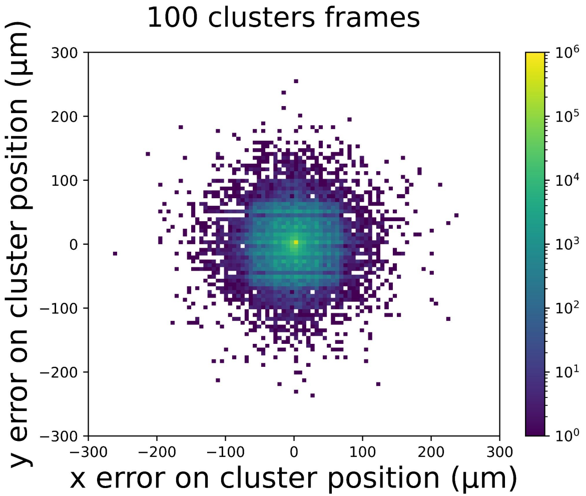
Affinity propagation algorithm - Spatial performances

Spatial study : Error on cluster barycenter

- **Errors** on x and y axis: mean σ of **16.5 µm** and **26.2 µm**
  → 95% error equal or smaller than pixels size (2σ)
- Error (≈ µm) **<** explored structures (ie: rat striatum ≈ mm)



σ_x = 23.9 µm σ_y = 88.9 µm



σ_x = 15.5 µm σ_y = 17.5 µm

Conclusion

The use of **Affinity propagation** algorithm:

- Offers a **fast and reliable** clustering of counts in frames
- Improves the counting of events
- Allows for an **accurate spatial localization** of events

Perspectives

Perspectives:

- Calibrate the algorithm with Data from the **new sensor prototype**
- Impact of other parameters $\longrightarrow$ improve **computing time**
- Apply AP for ***in vivo* measurements** (e.g. for non homogeneous frames)

New Sensor prototype and electronics developed and being tested

Acknowledgments

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cermep imagerie du vivant

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