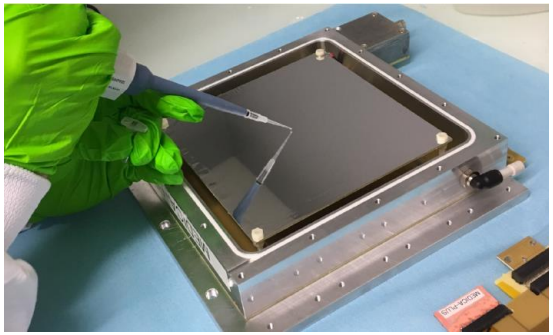
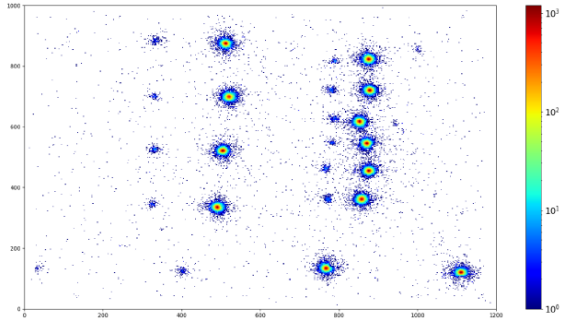
DE LA RECHERCHE À L'INDUSTRIE

OPTIMED-β (OPTIcal MicroMEgas Detector for β imaging):

un détecteur Micromegas à lecture optique pour l'imagerie β





1st December 2022

Esther Ferrer Ribas

CONTEXT: β IMAGING IN ONCOLOGICAL RESEARCH

Different types of cells in a tumor

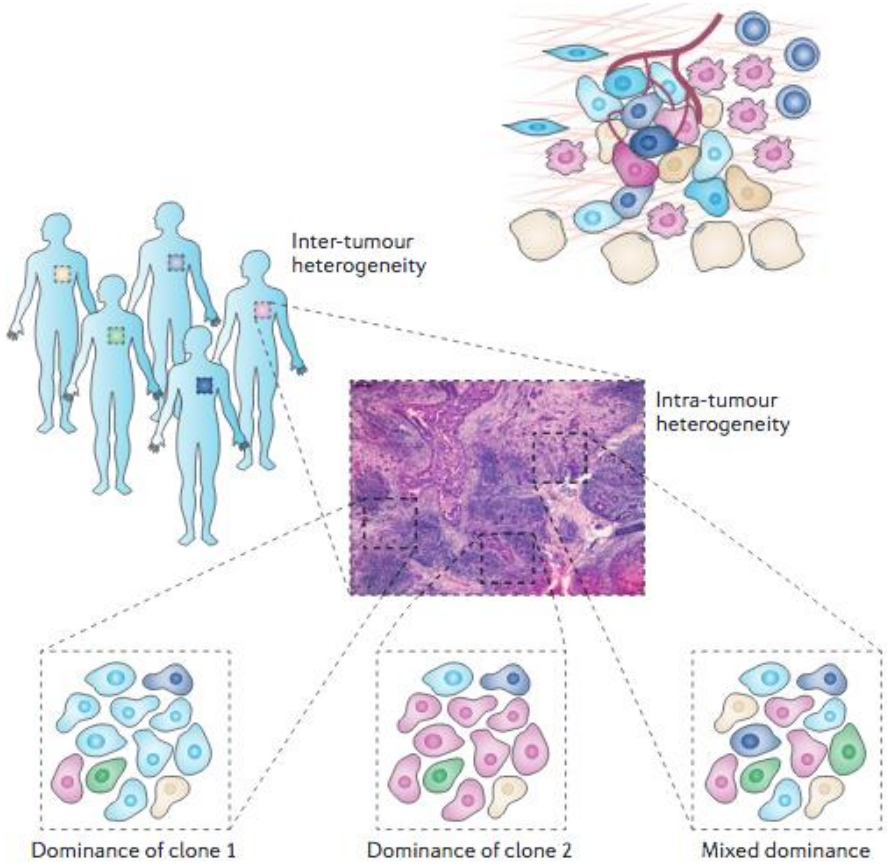
Large variability among tumoral cells

Biologists questions:

Impact of this hetereogeneity on the distribution of drugs at the cell level

➔ **Drug biodistribution at the single cell level**

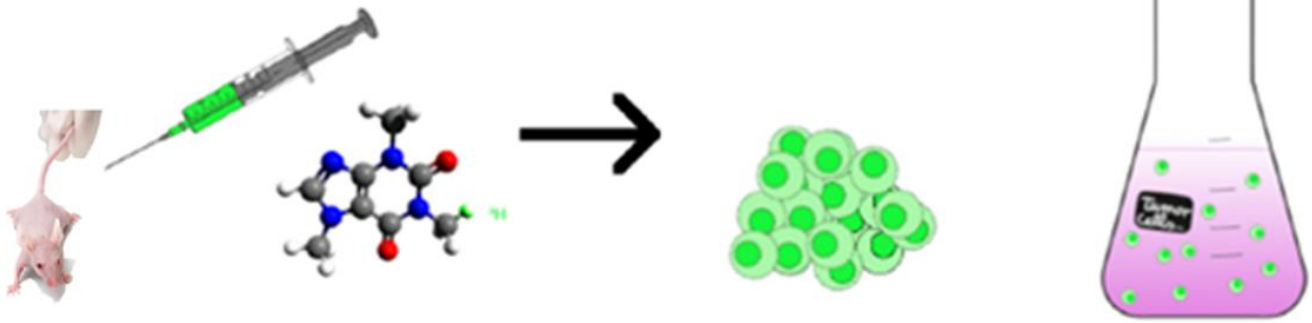
➔ **Use of isotopic marking with ^{3}H**



Marusyk, Nature Reviews Cancer 12(5) (2012) 323-34

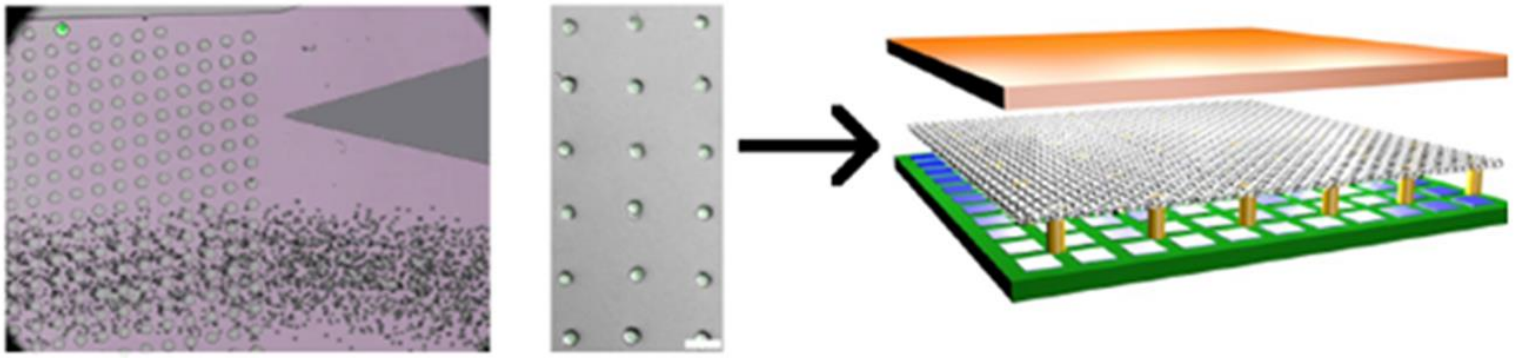
CONTEXT

CEA/INSTITUT JOLIOT



Tumoural cells collected from an animal – Tritium tracking

Cellular culture



Cell deposit by microfluidics techniques

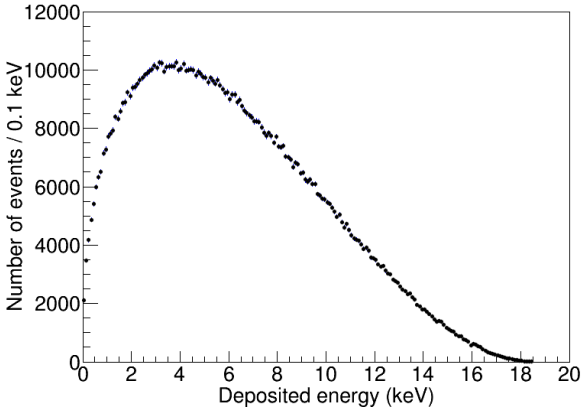
Tritium activity counting with gaseous detector

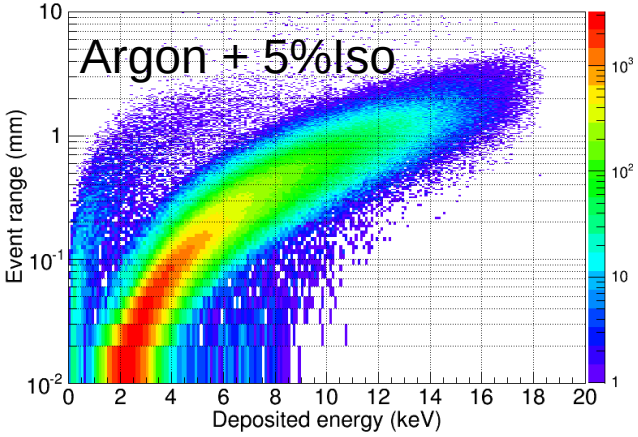
CEA/IRAMIS

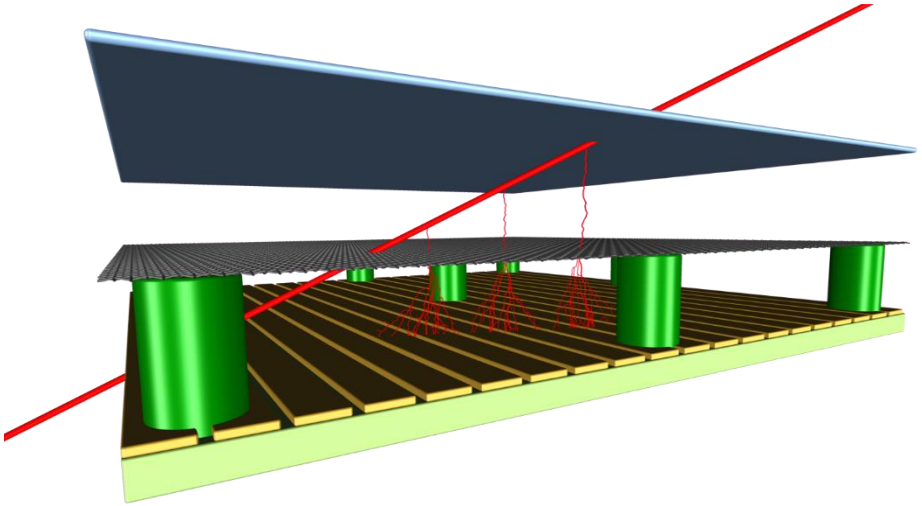
CEA/IRFU

CONTEXT: DETECTION OF ^{3}H WITH MICROMEGAS

Proposal of using a Micromegas detector





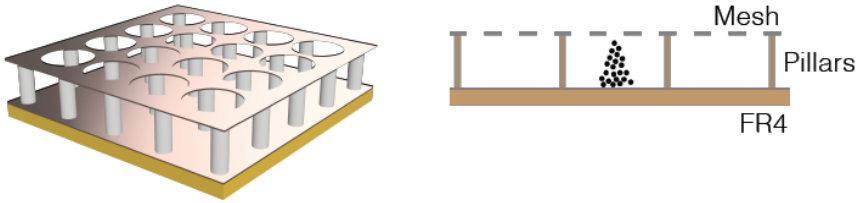


Low energy threshold
Good spatial resolution
Good background rejection capabilities

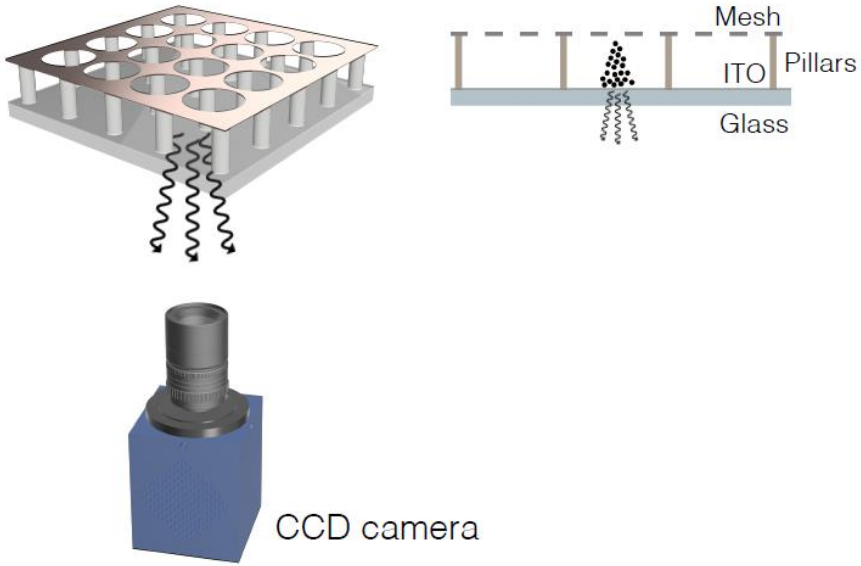
For this application: ^{3}H Samples inside the gas volume

CHARGE READOUT VS OPTICAL READOUT

Charge readout



Optical readout



F. Brunbauer

Optical readout of MicroPattern Gaseous detectors (MPGDs) relies on recording scintillation light emitted during electron avalanche multiplication

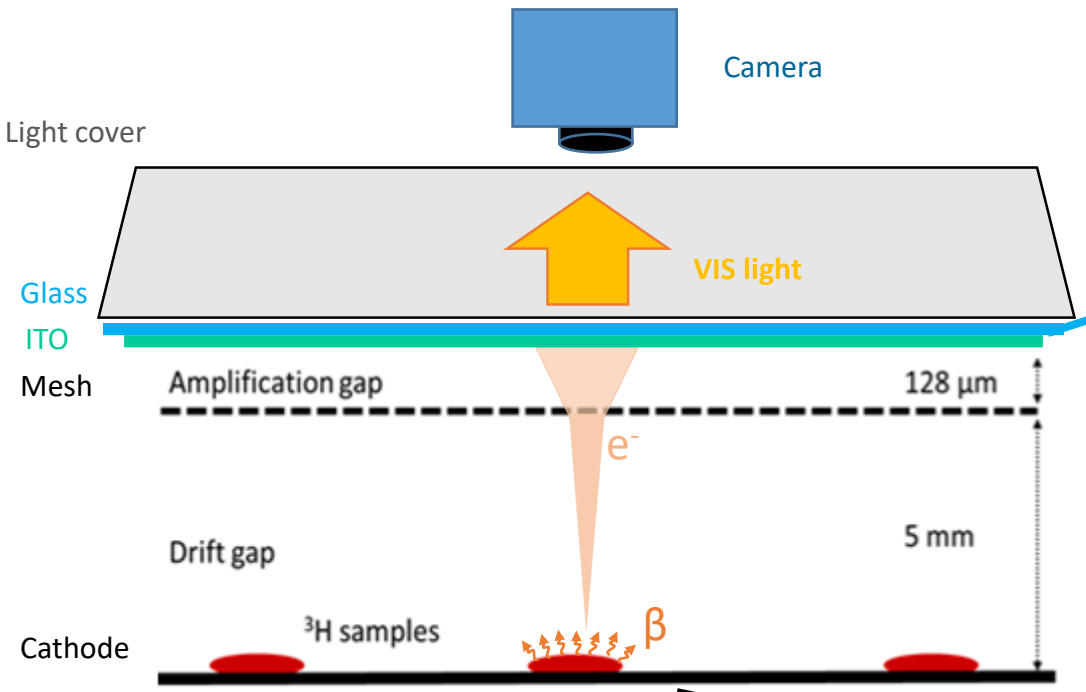
Advantages

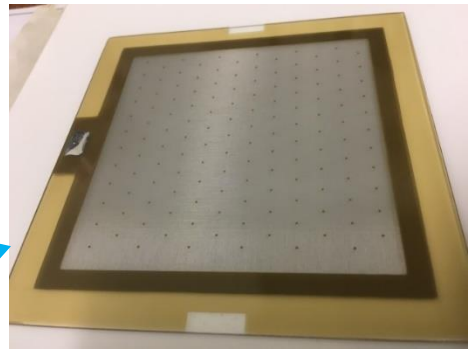
Intuitive pixelated readout with megapixel imaging sensors
High spatial resolution
Integrated imaging approach
Lenses and mirrors allow adjustable magnification and camera positioning

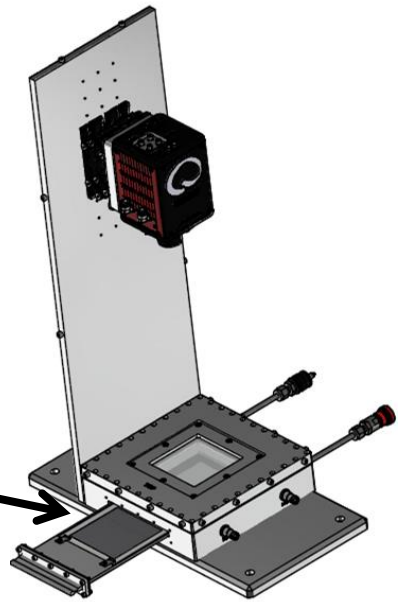
Disadvantages

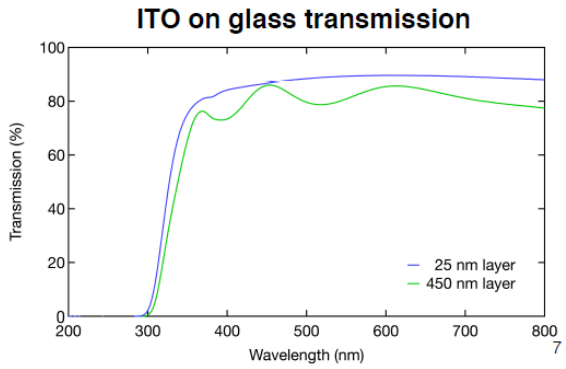
Limited frame rate
Need of CF_4 based gas mixtures

OPTIMED- β CONCEPT







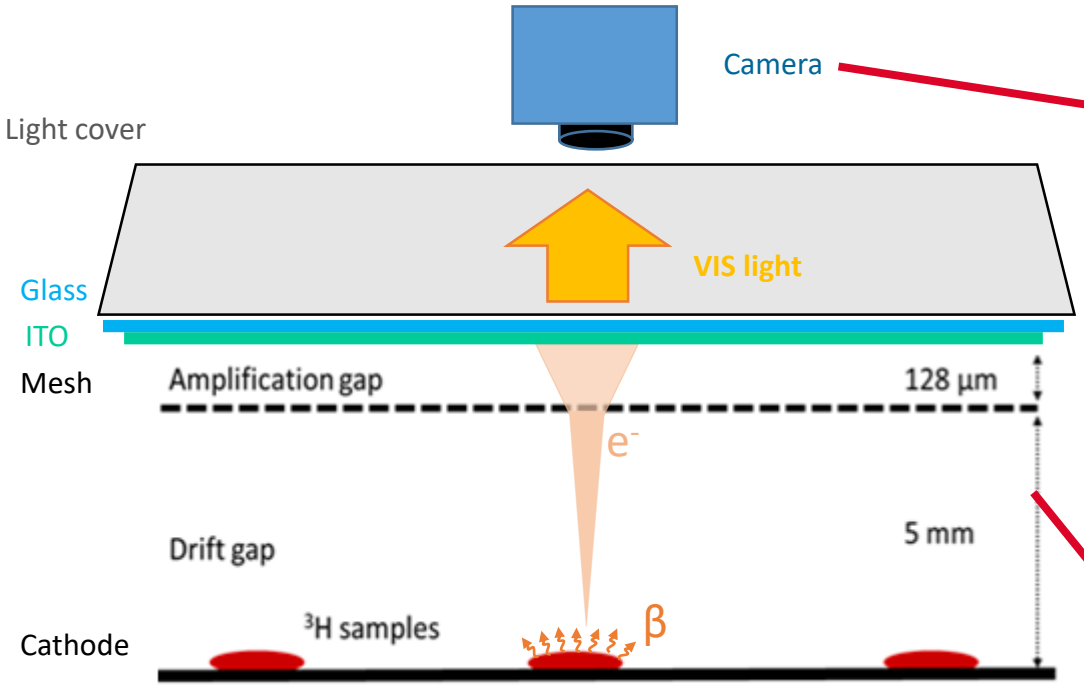


Integration of a Micromegas mesh on a transparent glass substrate coated with Indium Tin Oxide (ITO) layer

Scintillation visible light (630 nm) emitted through electron avalanche multiplication can be recorded

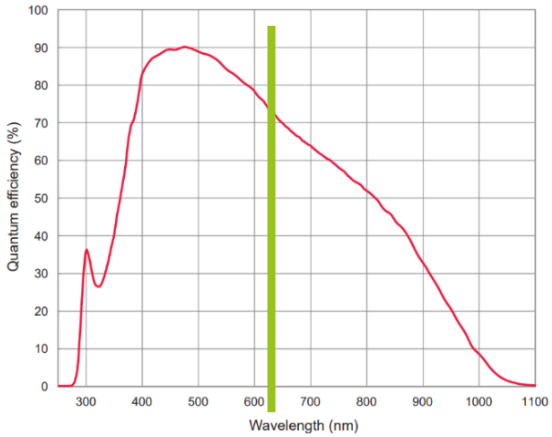
F. Brunbauer

OPTICAL READOUT SET-UP



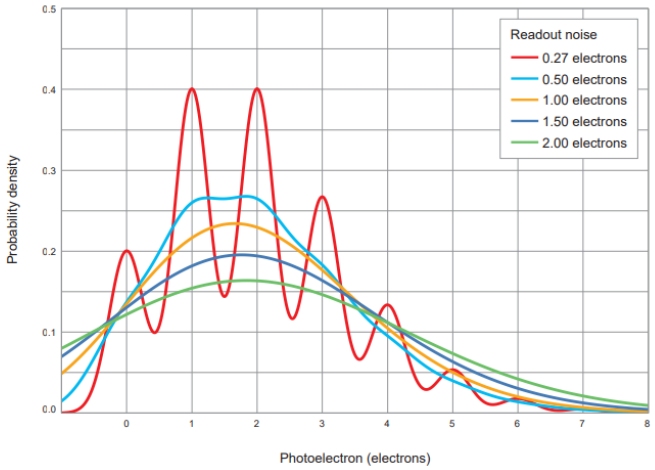
HAMAMATSU CMOS CAMERA

Quantum efficiency



ORCA-Quest

Photon number resolving



Rate

Mode	Rate
Standard	120 frames/s
Ultra quiet	10 frames/s

Readout noise

Standard scan	0.43 electrons rms
Ultra quiet scan	0.27 electrons rms

Pixels

Number
4096 x 2304

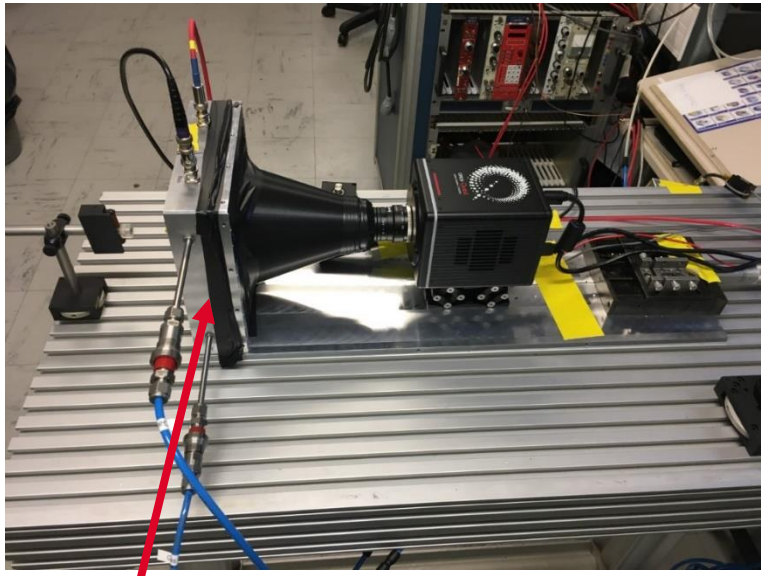
Size
4.6 µm x 4.6 µm

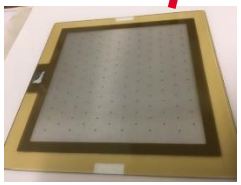
Dark current

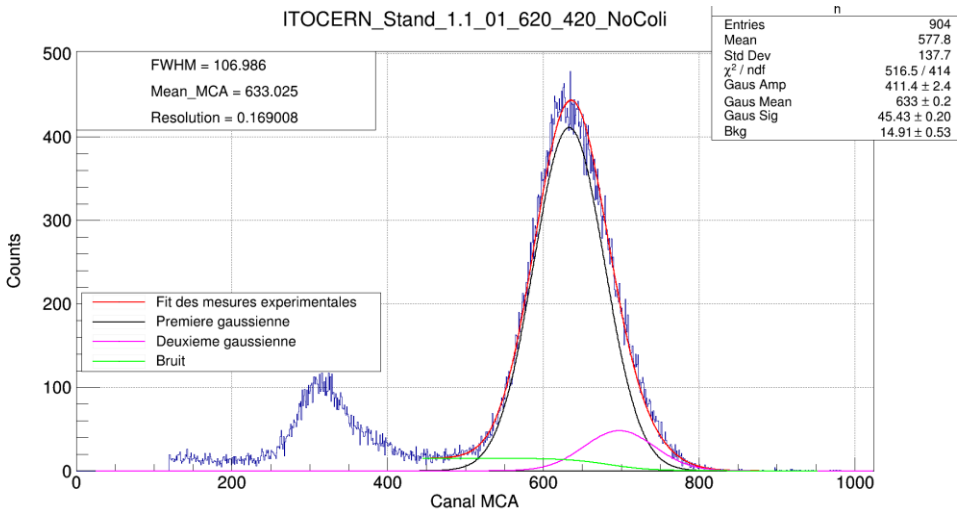
Cooling current	Sensor temperature	Dark
Air /pixels/s	- 20 °C	0.016 e^-
Watter /pixels/s	- 35 °C	0.006 e^-

CHARACTERISATION WITH X-RAYS (I)

- Micromegas on glass produced at IRFU and at CERN
- Charge readout test in Argon+5%Iso: gain above 10^4 and FWHM 14% (FWHM) energy resolution at 5.9 keV
- Tested in the lab with an ^{55}Fe



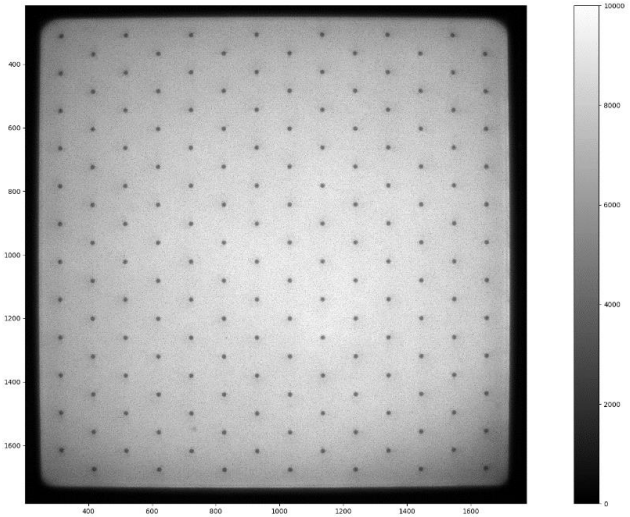




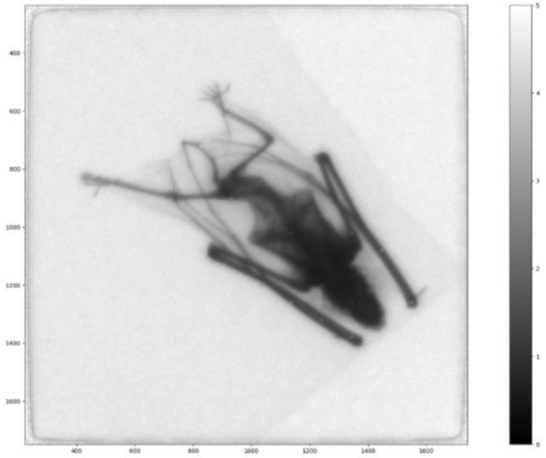
CHARACTERISATION WITH X-RAYS (II)

- Tested at CERN with X-ray generator

60 s background image

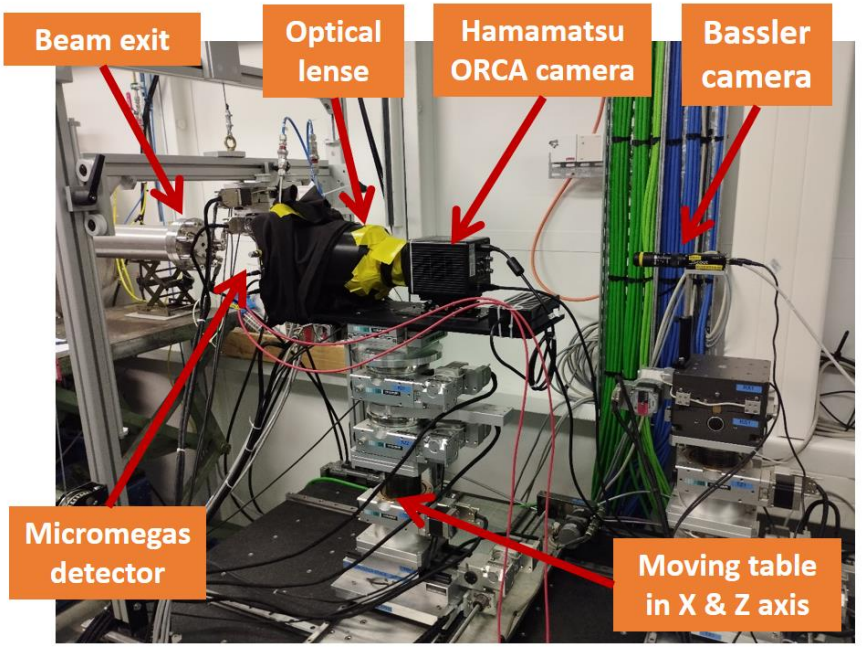


60 s simple background supression and beam profile correction

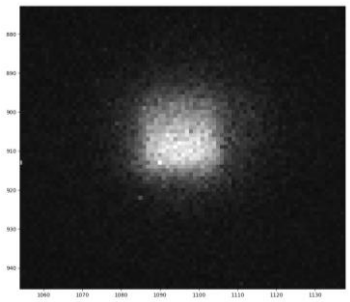


SOLEIL BEAM TEST 16-18 NOVEMBER 2022

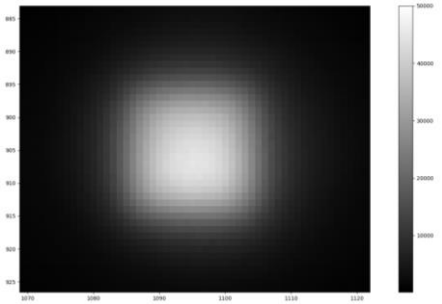
- Hard X-ray branch of METROLOGIE beamline
- Determination of Point Spread Function
- Spatial resolution
- Effect of gas diffusion on spatial resolution
- Detector homogeneity



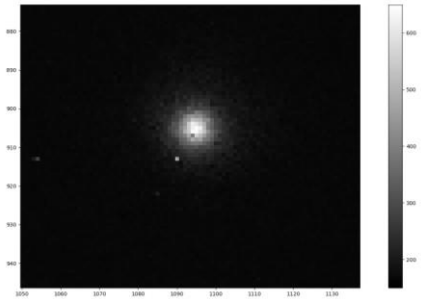
Test of OPTIMED-BETA detector at hard X branch of METROLOGIE beamline



1 x 1 mm beam, Primary Scintillation (Va=0 V, Vd=0 V)

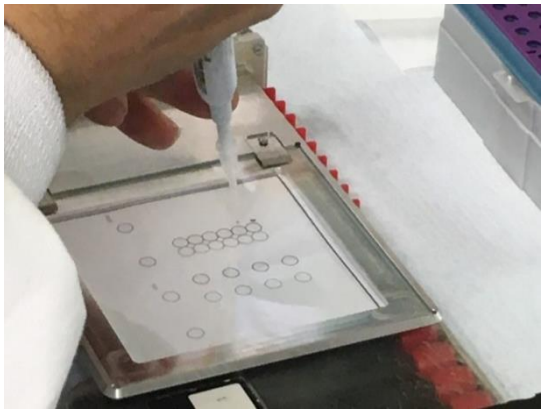


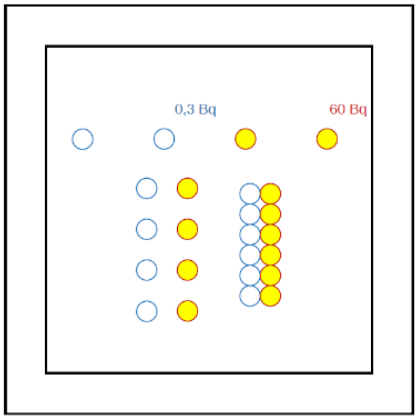
1 x 1 mm beam, Amplification (Va=400 V, Vd=210 V)

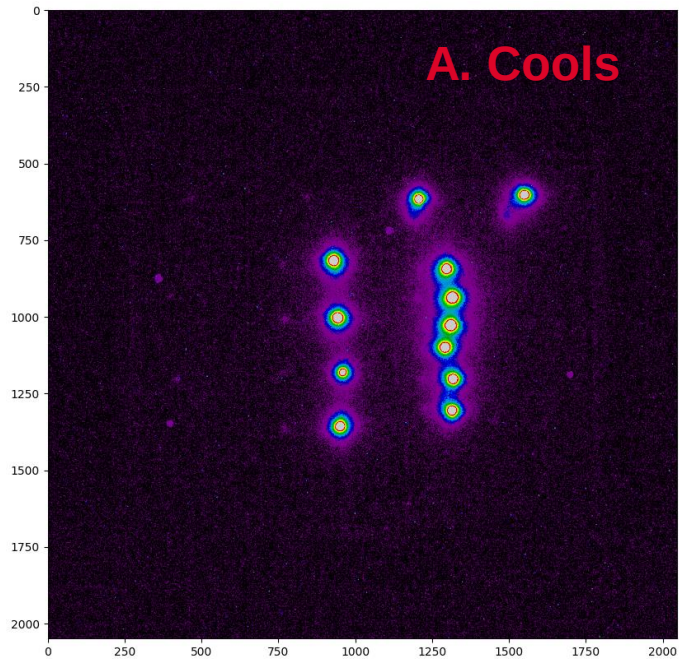


0.035 x 0.035 mm beam, Amplification (Va=400 V, Vd=210 V)

β DETECTION: IMAGE INTEGRATION





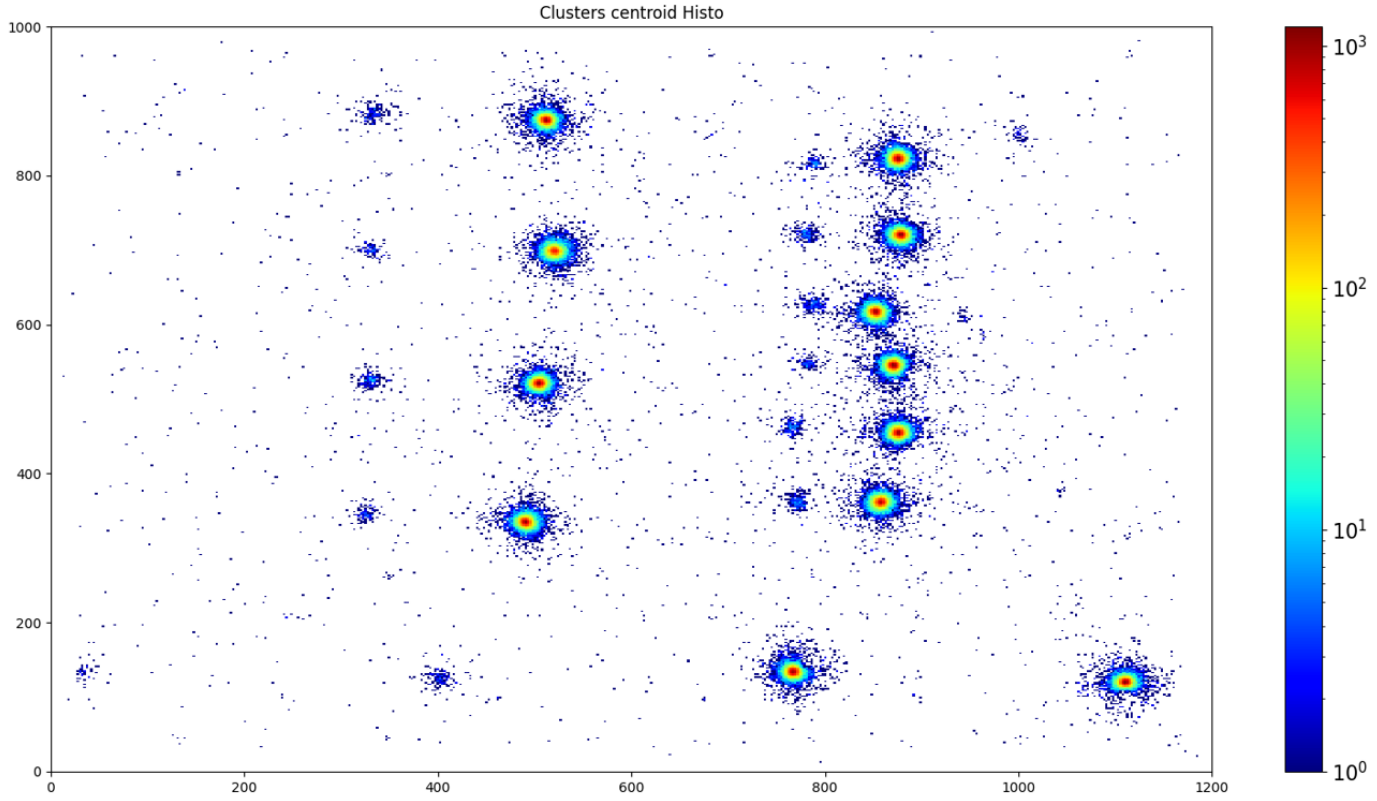


180 frames of 10 s (30 min) with simple background suppression Argon-20% CF_4

- Activity measurement limits and dynamic range → Activities: 0.3 Bq and 60 Bq tritiated glucose
- Space between drops : 2 cm – 1 cm – 5 mm
- 60 Bq drops positions are well assessed
- 0.3 Bq drops hardly visible

β DETECTION: CLUSTERING

A. Cools

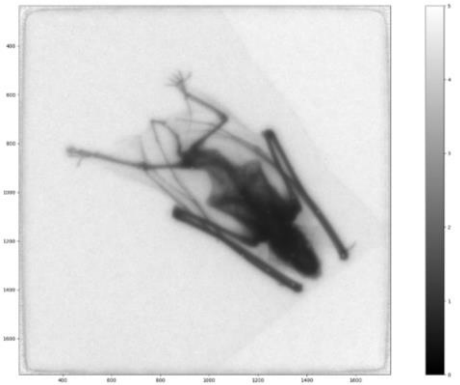


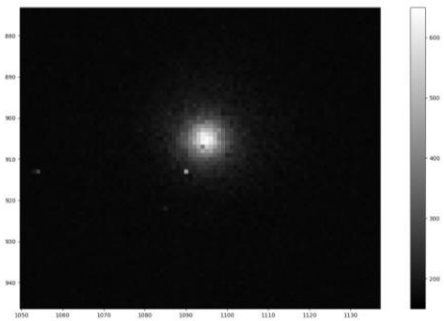
20000 frames of 100 ms (33 min), individual pixel background thresholding, Argon-20% CF_4

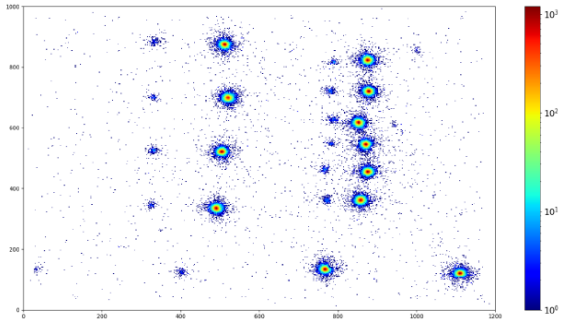
- Both 60 Bq and 0.3 Bq drops positions are visible
- Better signal-to-noise ratio and counting events capability

CONCLUSIONS

- Feasability of measuring sub-bequerel tritium activity has been proven with the optical Micromegas readout
- Image processing in progress: SOLEIL data, β activity estimation…
- New tritium samples will be studied: single cell samples
- Biologists interests: correlation between the amount of drug accumulated in different population of cells and the observed phenotype
- Optical readout Micromegas opens new possibilities: β-imaging, neutron radiography…







MEDICAPLUS/OPTIMED-B TEAM

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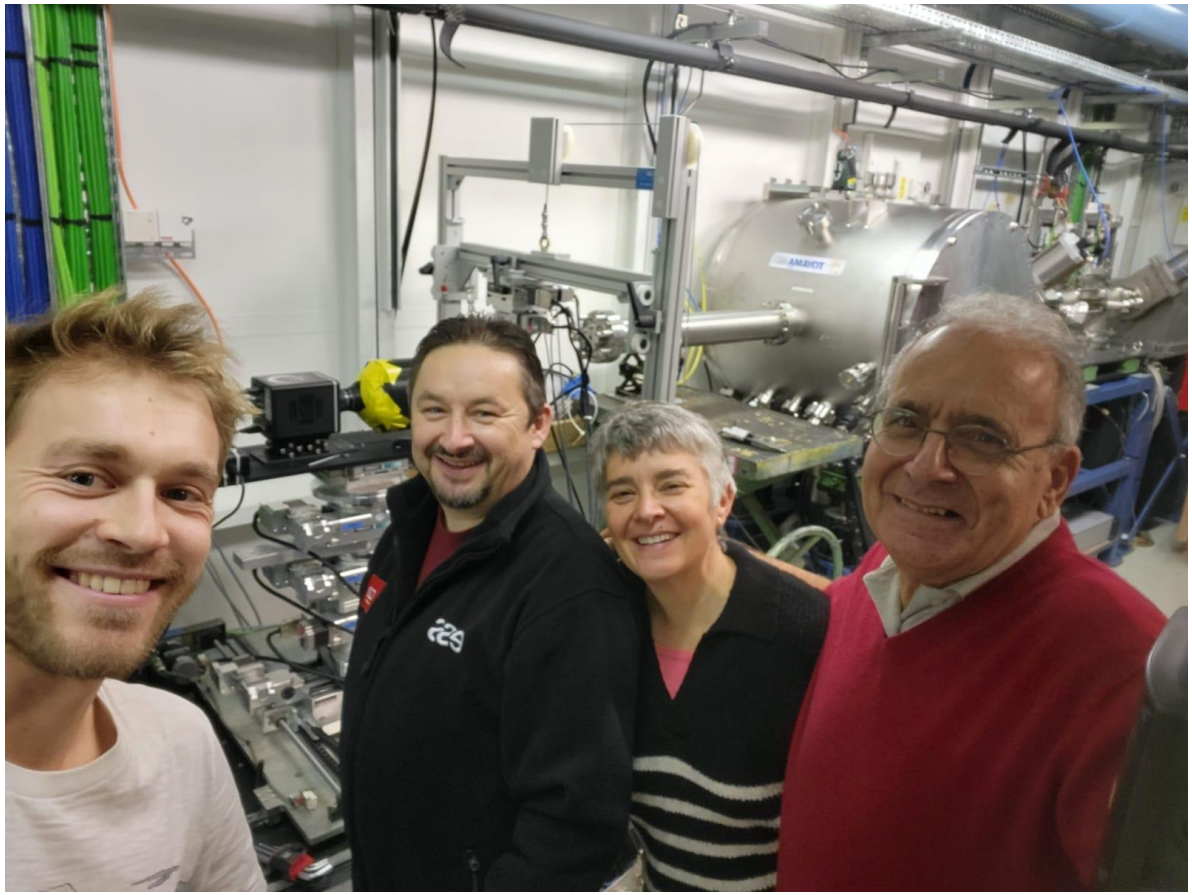
CEA/DRT/LIST (Neutron imaging)
Adrien Sari

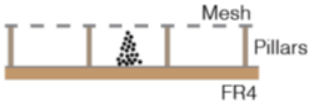


@ SOLEIL 16-18 November 2022

BACK-UP

FUNDING CONTEXT

Charge readout



Optical readout

MedicaPlus (2019-2020)

IRFU
IRAMIS
Institut Joliot

Optimed Beta (2021-2022)

IRFU
IRAMIS
Institut Joliot

OMNIS (2020-2023)

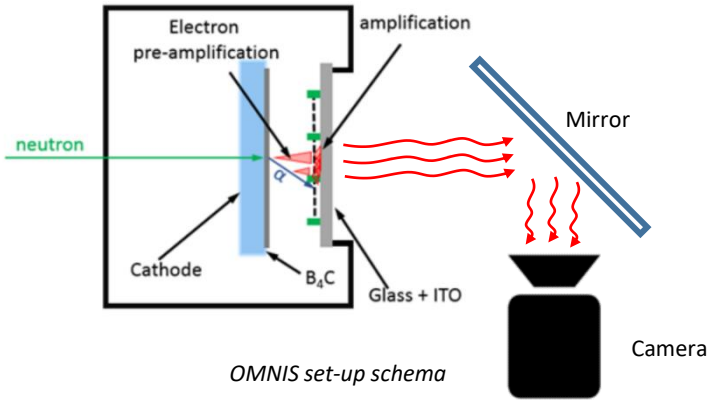
IRFU
LIST
IRESNE

NEUTRON DETECTION

- Acquisition modes :
  - **Event-by-event** : track reconstruction :

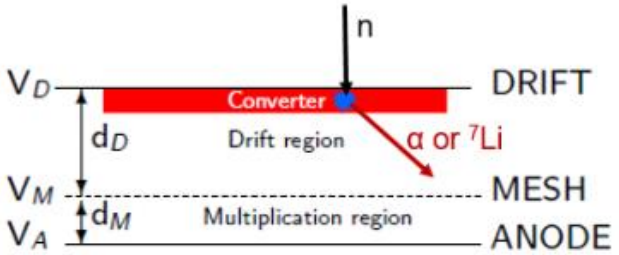
    potentially higher resolution (100 µm), better ɣ-to-n suppression
  - **Integrated** : real-time radiography :

    best camera operation mode, ɣ-to-n suppression less efficient



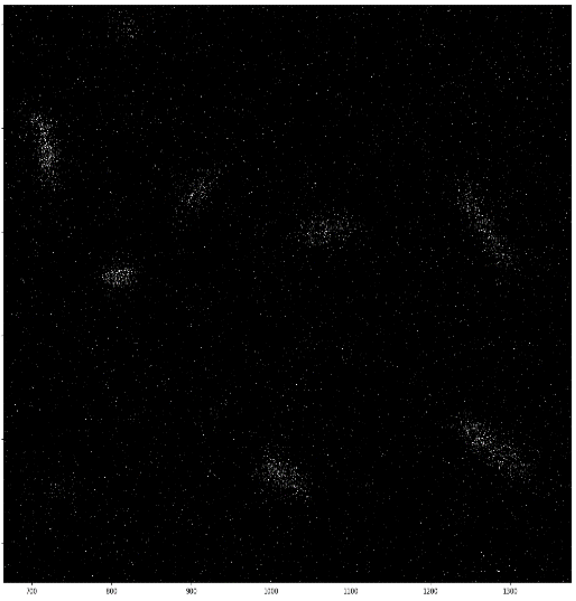
OMNIS set-up schema

- $^{10}B_4C$ neutron-to-charge converter
  - **Thermal neutrons** created by 2 µm thin $^{10}B_4C$ layer
  - Conversion efficiency : 5%
  - (α or Li) fragments causes strong ionisation compared to electrons
  - Drawback : fragments long range in the gas (10 mm)

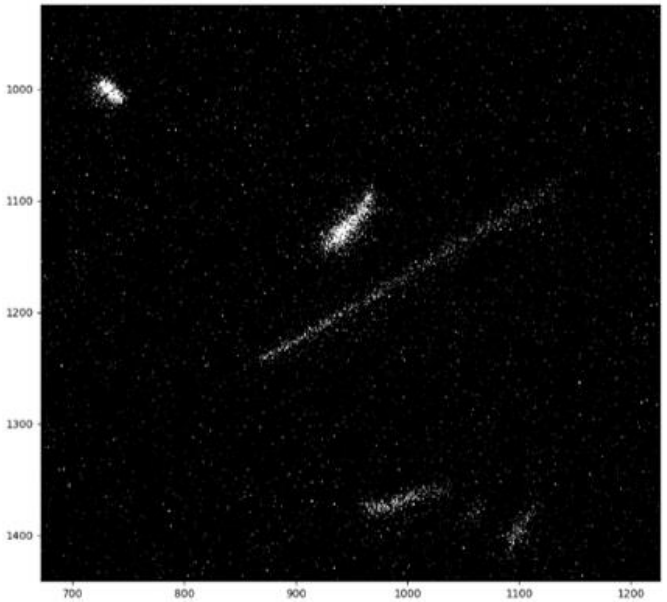


Boron converter principle

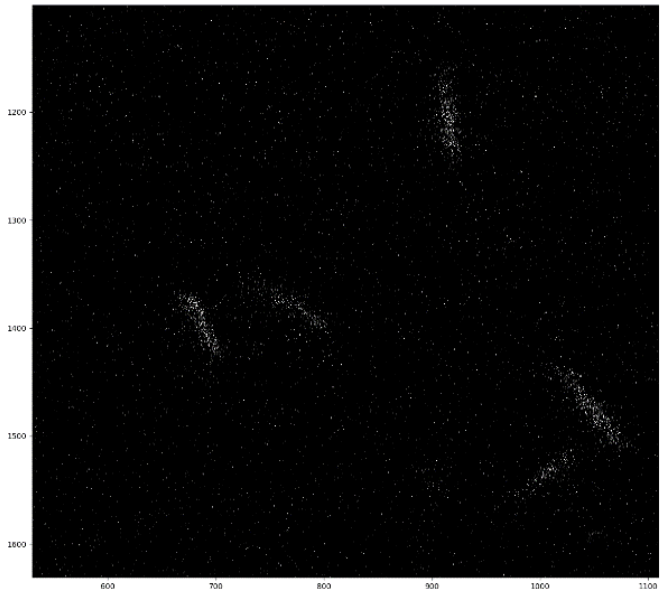
FIRST IMAGES WITH A NEUTRON SOURCE



50 *V/cm drift field*

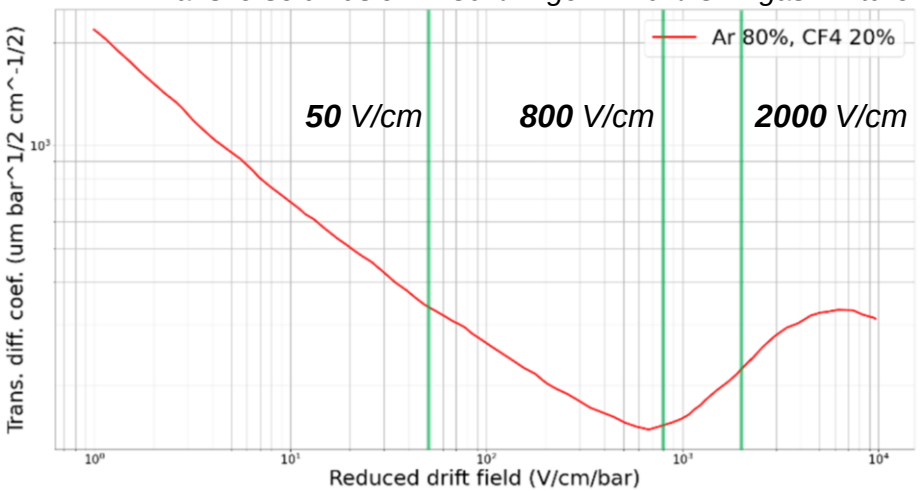


800 *V/cm drift field*

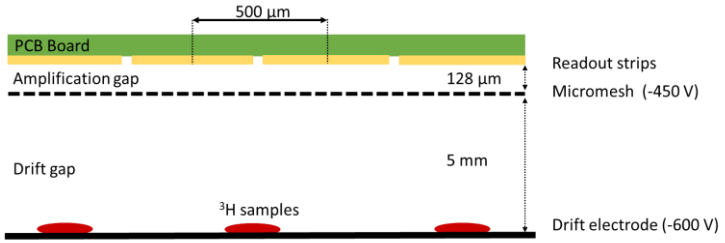


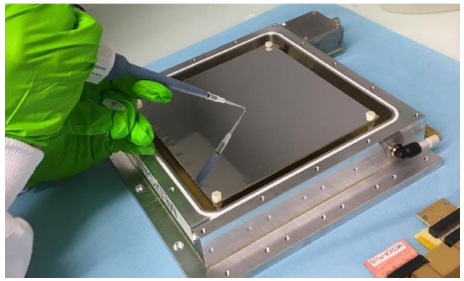
2000 *V/cm drift field*

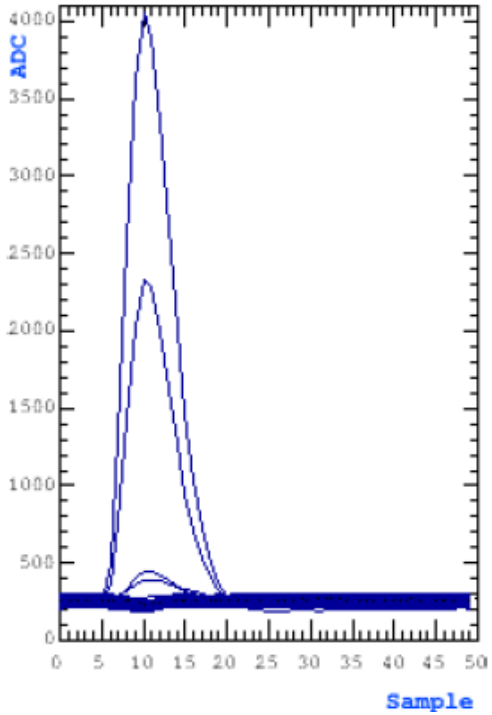
Transverse diffusion in 80% Argon + 20% CF4 gas mixture.



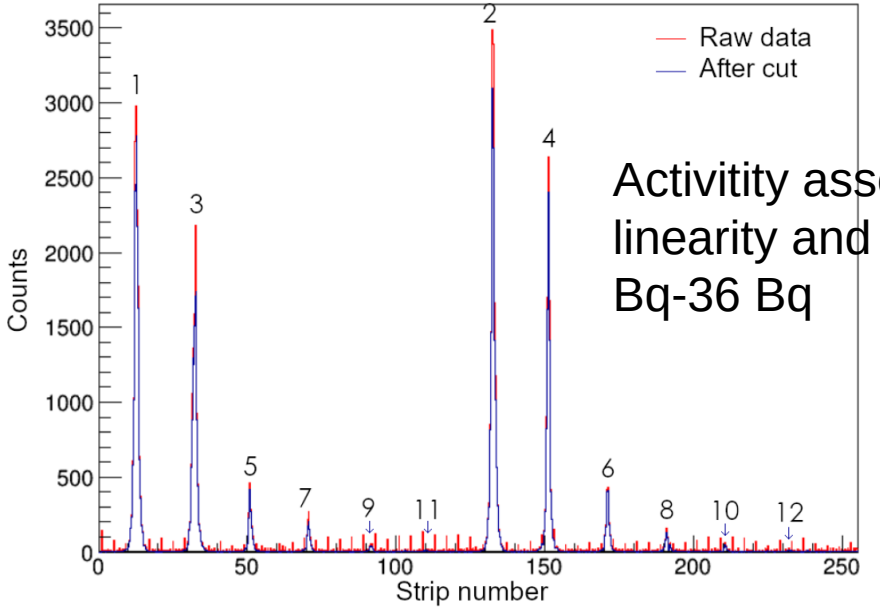
CHARGE READOUT RESULTS







Tritiated glucose samples : 370 Bq-0. 37 Bq

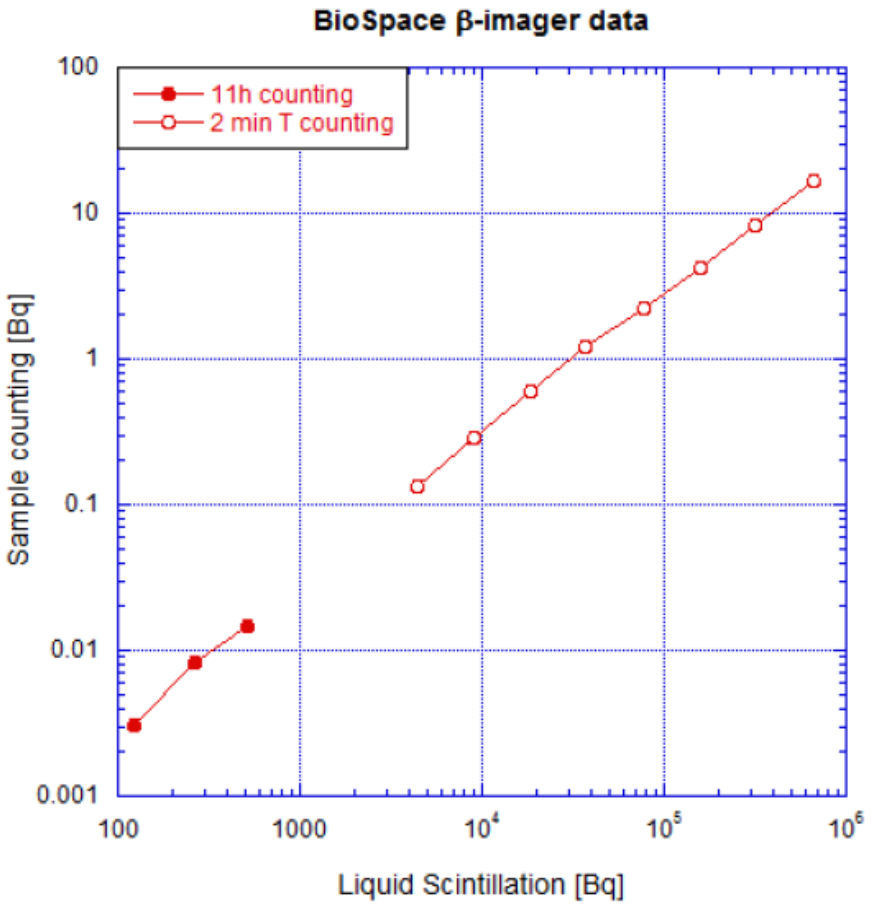


Activitity assessment, linearity and stability 0.1 Bq-36 Bq

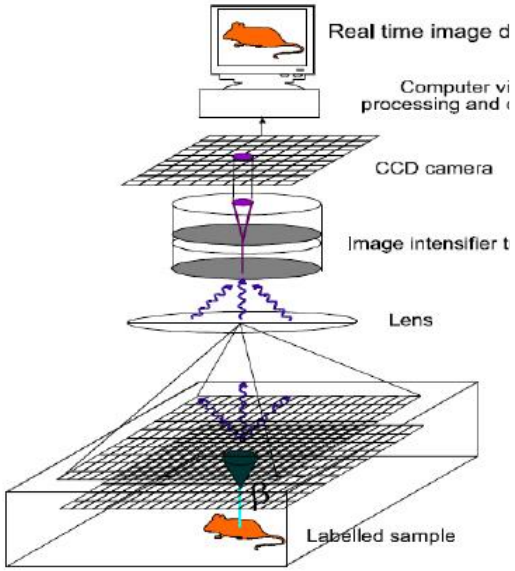
F. Jambon et al., Journal of Physics 1498 (2020) 012046
F. Jambon et al, ArXiv [2109.09411](2109.09411) [physics.ins-det] submitted to NIMA

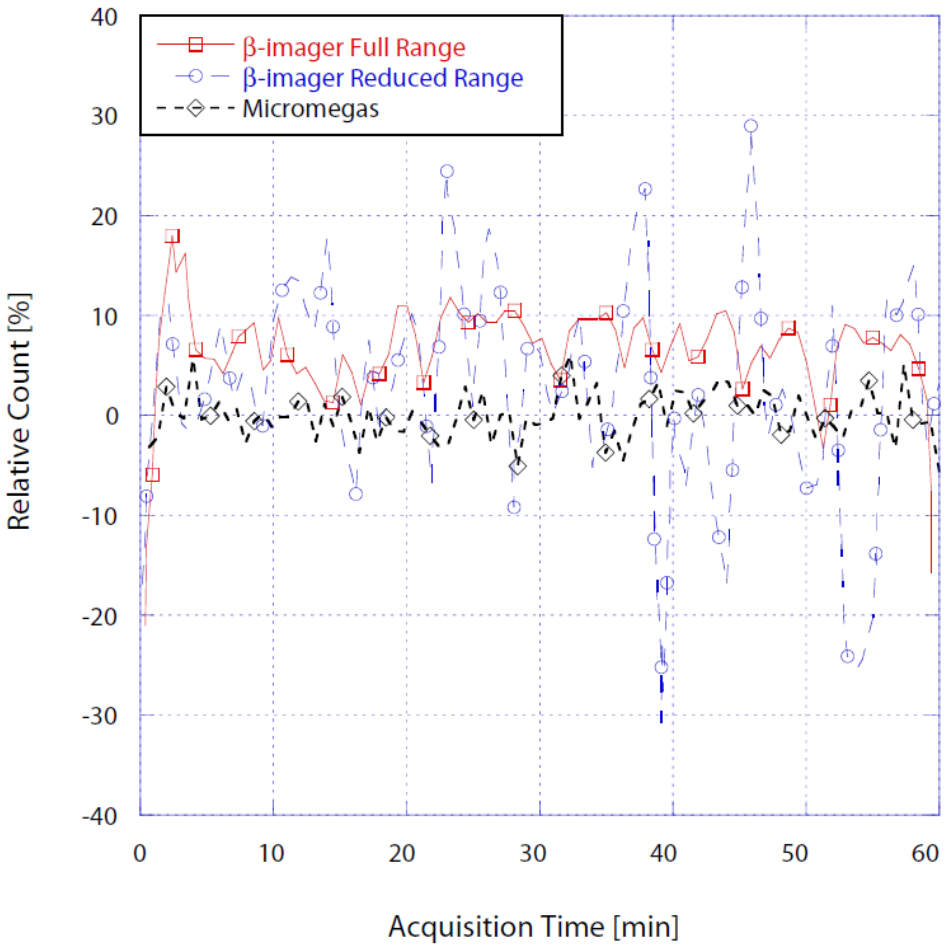
Biospace β-imager characteristics

- Linearity (not dynamic range !) over 4 orders of magnitude
- Spatial resolution (^3H) 50µm
- Sensitivity : 1mBq/mm^2
- Field of view : 24 x 32 cm^2
- Using Ar + TEA
- 180k€ + 16k€ maintenance
- A 150 kg "Black Box"

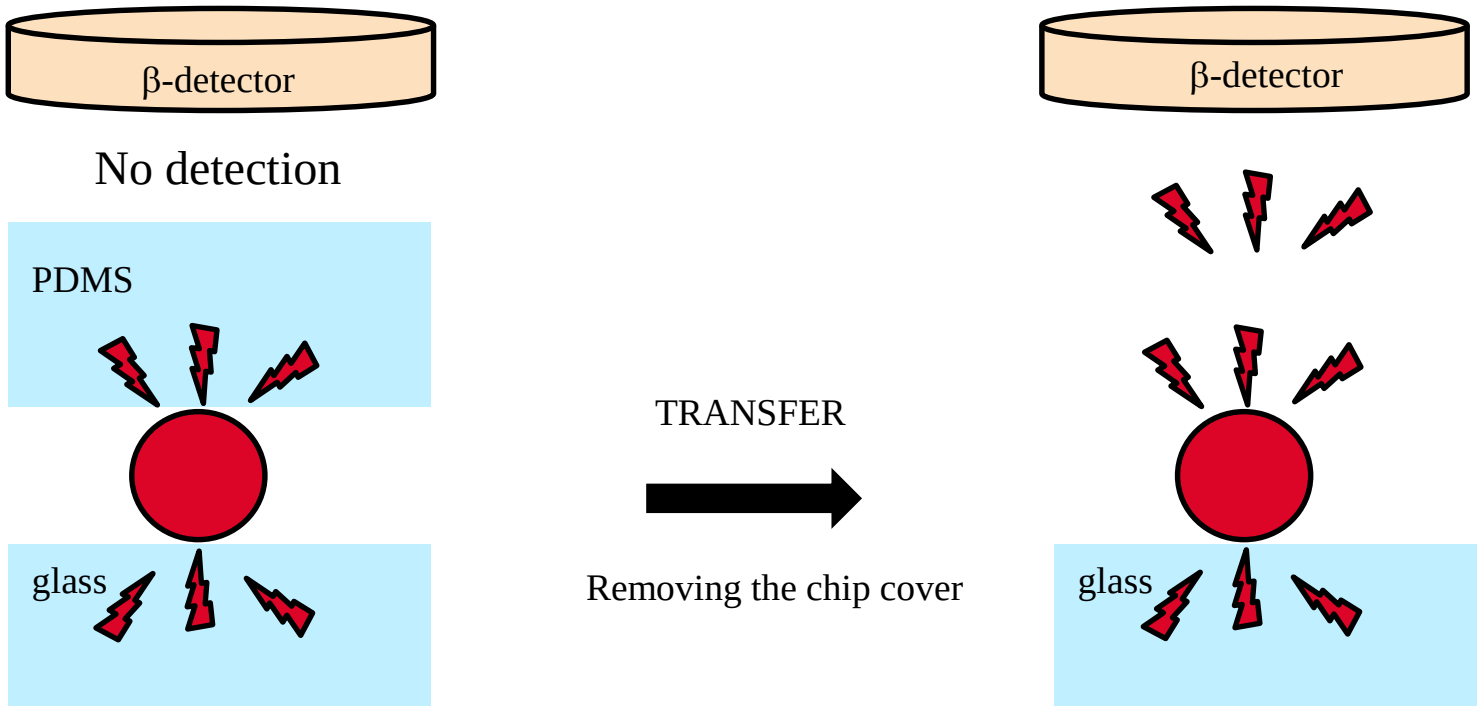


COMPARISON WITH A COMMERCIAL BETA-IMAGER



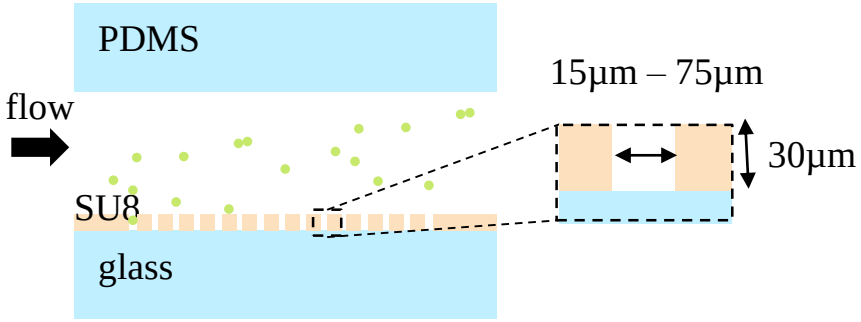


MICROFLUIDICS : USING HYDRODYNAMICS TO TRAP CELLS



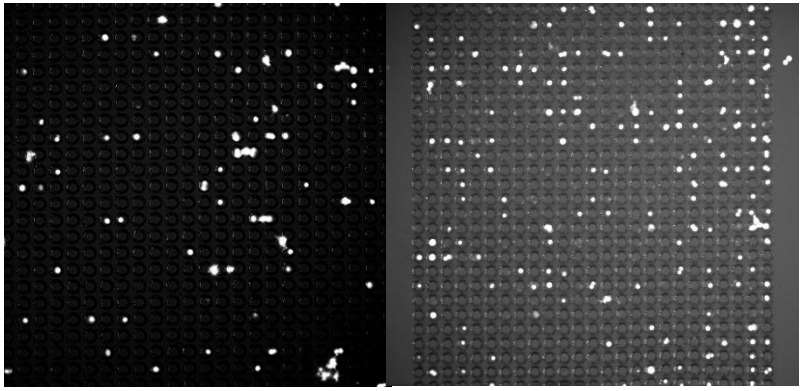
TRAPPING CELLS WITH MICRO-WELLS

Cells loading

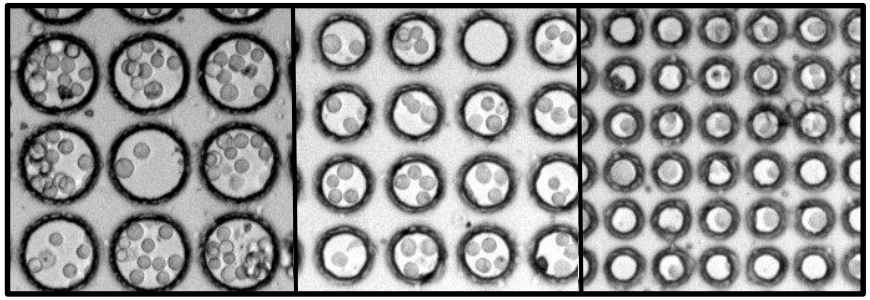


Wells microfabricated on glass slide

Top view

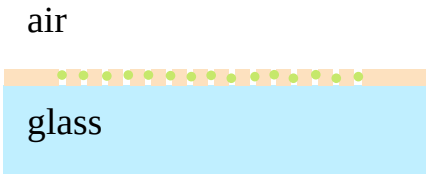


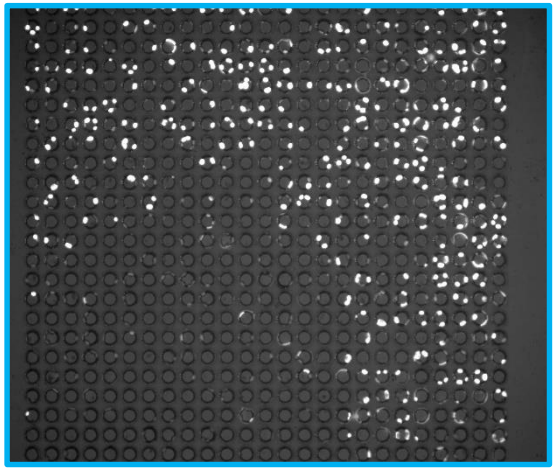
75µm *50µm* *30µm*



trapped cells ↗ with larger wells

Cells trapped





Next step
tritiated cells for beta imaging