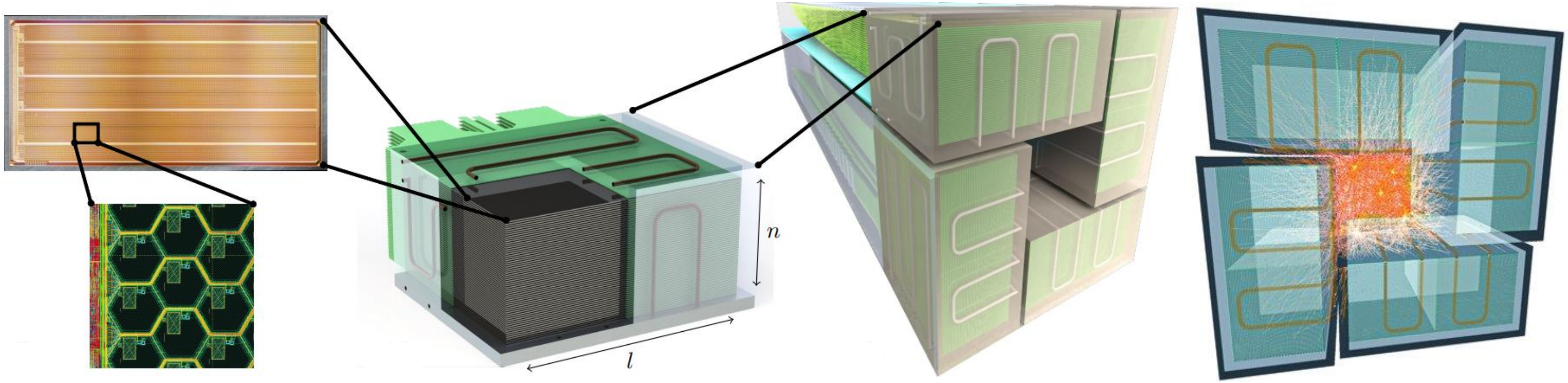
The 100μPET project: a small-animal PET scanner for ultra-high-resolution molecular imaging with monolithic silicon pixel sensors

L. Paolozzi

on behalf of the 100uPET collaboration



The Project & Collaborators

The **100µPET** project: molecular imaging with ultra-high resolution

- **SNSF SINERGIA** grant among **UNIGE** (scanner construction) **EPFL** (imaging) and **UNILU** (medical application studying atherosclerosis in ApoE+/- mice)
- **Deliverable:** Small-animal PET scanner with monolithic silicon pixel detectors

UNIVERSITÉ DE GENÈVE

Giuseppe Iacobucci
- project P.I.
- System design

Roberto Cardella
- Sensor design
- Laboratory test

Yannick Favre
- Board design
- RO system

Lorenzo Paolozzi
- Sensor design
- Analog electronics

Mateus Vicente
- System integration
- Laboratory test

Stéphane Débieux
- Board design
- RO system

Didier Ferrere
- System integration
- Laboratory test

Jihad Saidi
- Detector simulation
- Data analysis

Franck Cadoux
- Mechanical design

Sergio Gonzalez-Sevilla
- System integration
- Laboratory test

Luca Iodice
- Chip design
- Firmware

Thanushan Kugathasan
- Lead chip design
- Digital electronics

UNI LU

Martin Walter
- P. I.

Pablo Jané
- Nuclear Medicine
- PET imaging
- Translational imaging

Vincent Taelman
- Molecular biology
- Radiopharmacy

EPFL

Michäel Unser
- P. I.

Pol del Aguila Pla
- Statistical signal processing

Aleix Boquet-Pujadas
- Signal/image processing
- Physical modeling

Funded by:

Swiss National Science Foundation

European Research Council

Sinergia

ATTRACT

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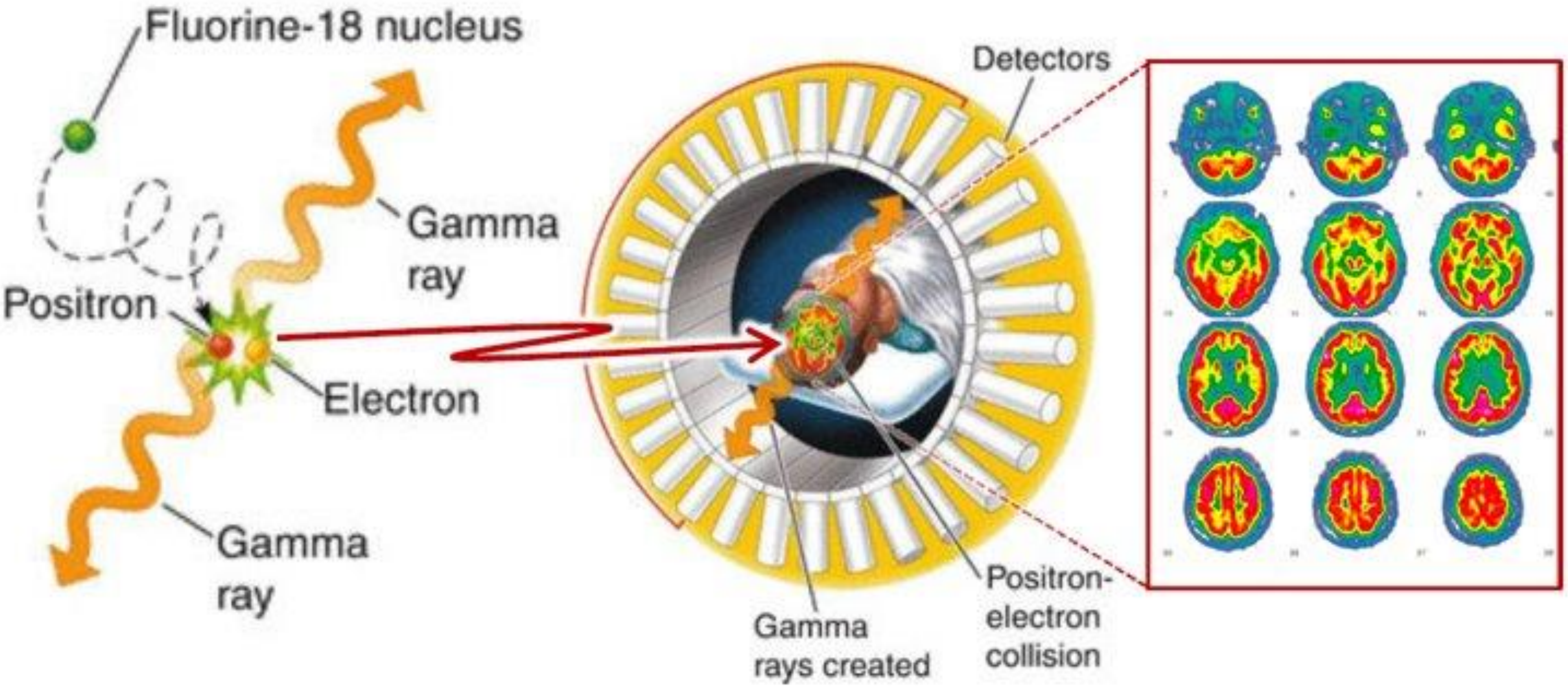
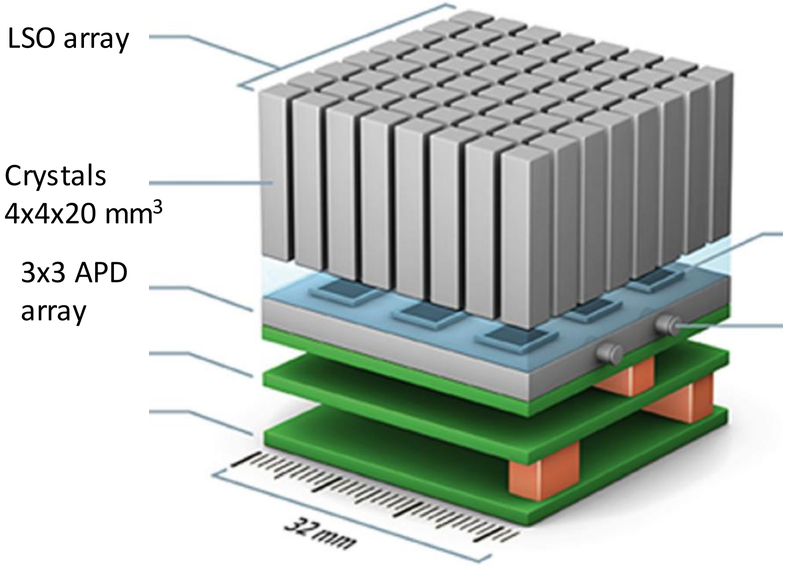
Positron Emission Tomography (PET)



Detector Granularity - DOI and LOR

Ultra-high resolution is obtained by increasing the granularity inside a detection volume thanks to small silicon pixel size (~150 microns)

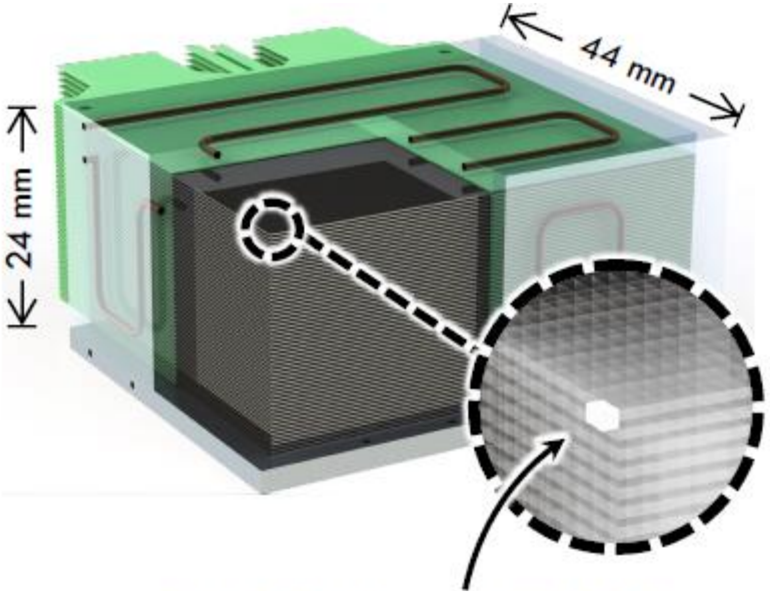
PET tower with LSO crystals



Courtesy of Siemens Healthcare

DOI: 20 mm
Sensor granularity: **320 mm^3**

100µPET stack

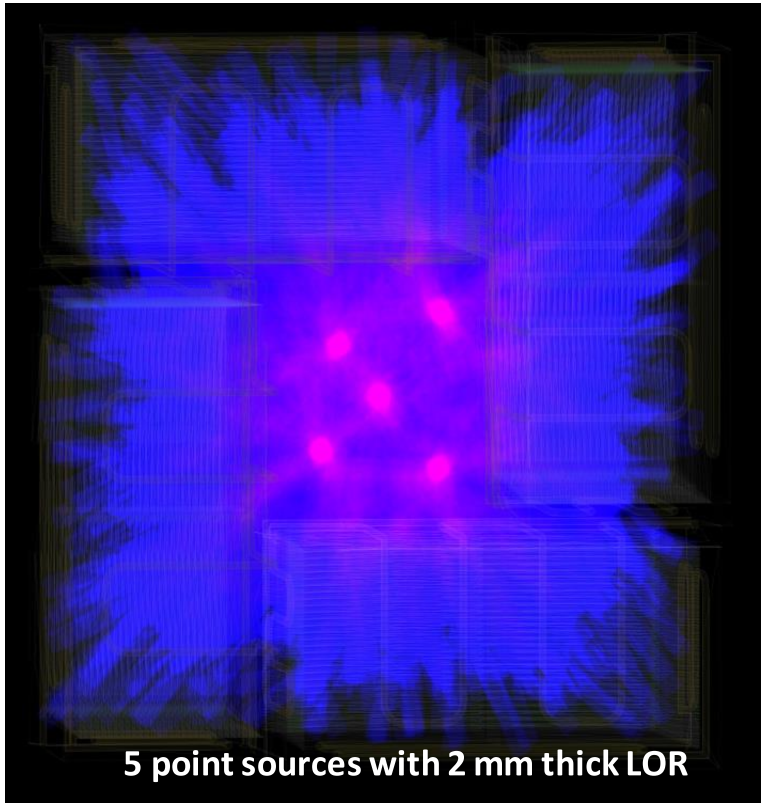


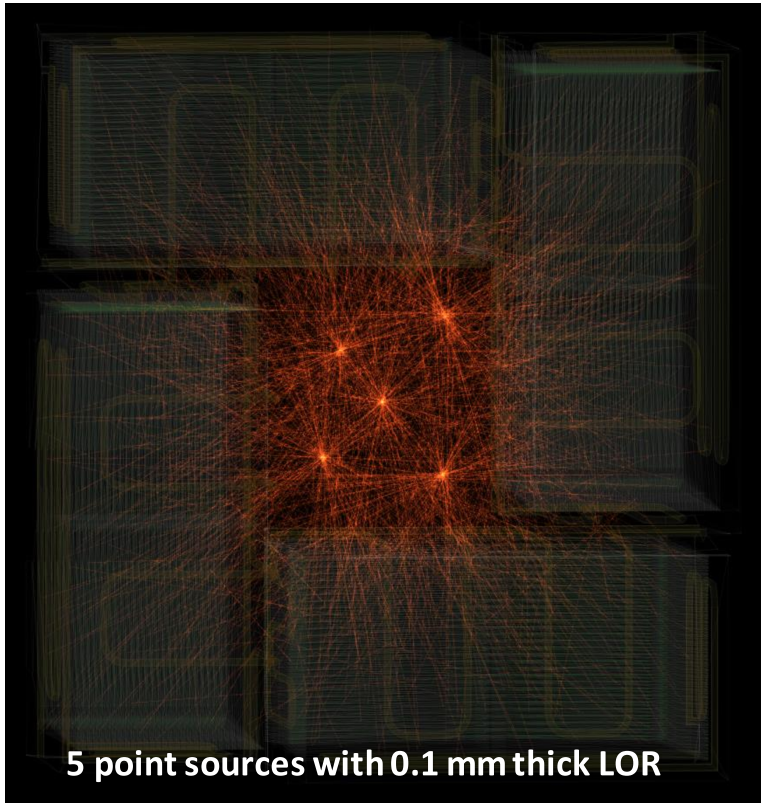
Pixel pitch: 150 µm | DOI: 400 µm
Sensor granularity: **0.009 mm^3**

Scanner granularity: ~35’000 times finer with silicon pixel sensors
LOR volume: ~700 times smaller **& DOI: 50 times** smaller

Detector Granularity - DOI and LOR

Ultra-high resolution is obtained by increasing the granularity inside a detection volume thanks to small silicon pixel size (~100 microns)

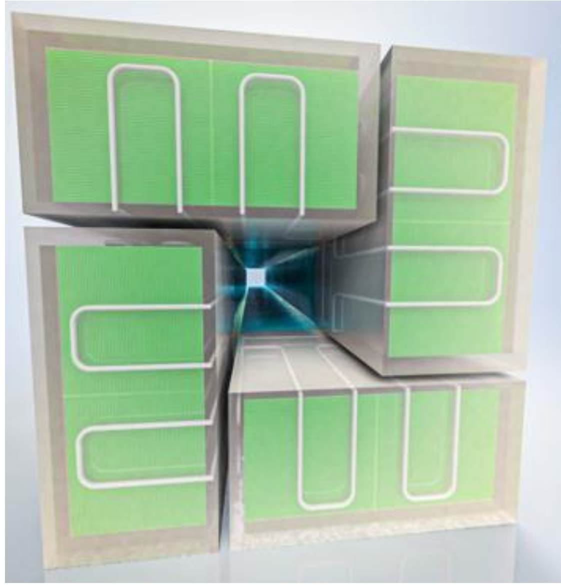

5 point sources with 2 mm thick LOR

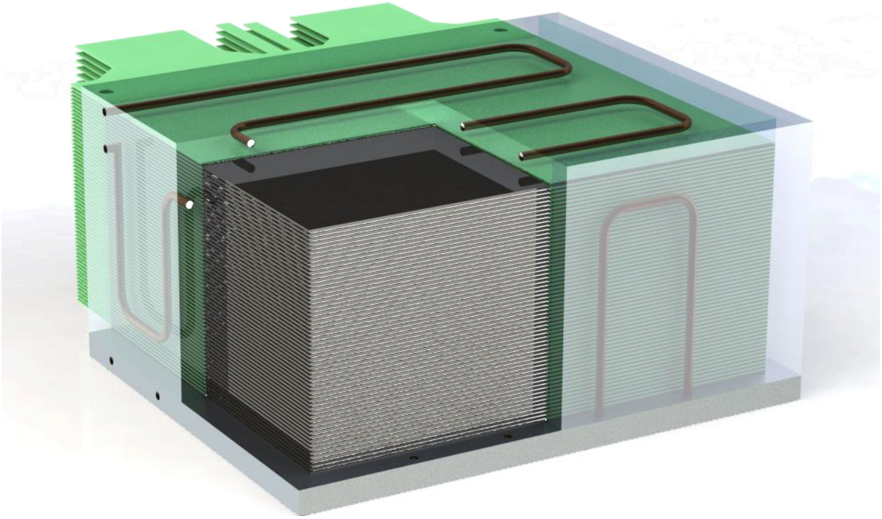

5 point sources with 0.1 mm thick LOR

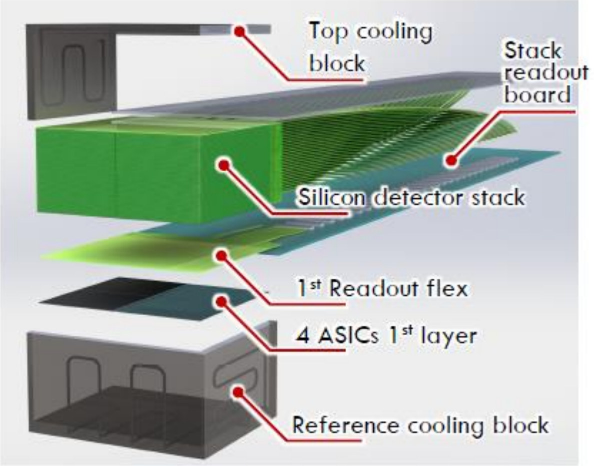
Only a factor of 20

100µPET Layout using MAPS

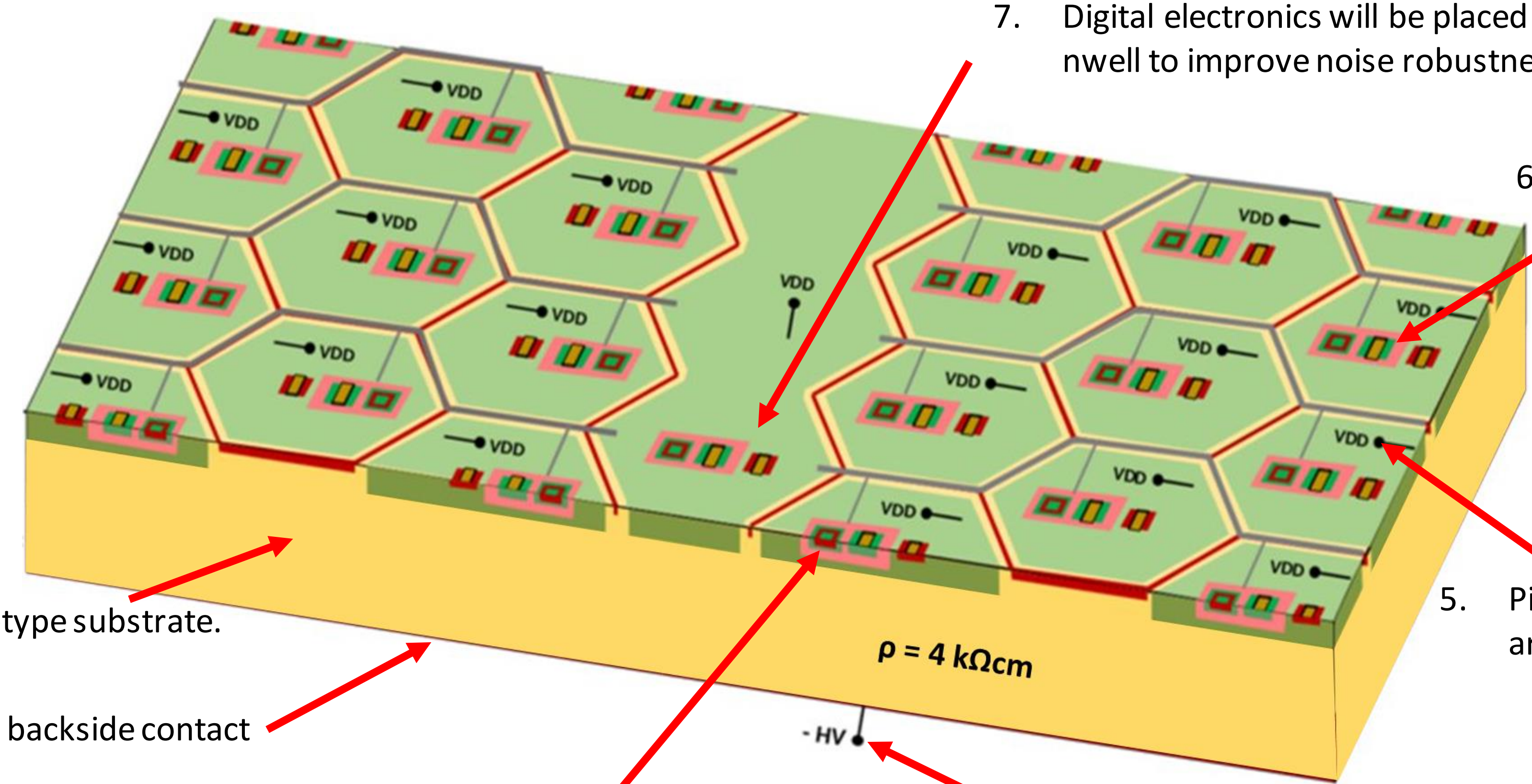
- The 100µPET Scanner consists of 4 towers with a total of 960 chips!
- A tower is composed of 60 Si-detection layers
- Multi-layer stack of CMOS imaging sensors based on silicon pixel detectors used in HEP
  - Monolithic 100µPET ASIC: 130 nm SiGe BiCMOS using high resistivity wafer (4 kΩcm)
  - Large size reticle sensor-ASIC: 30 x 22 mm^2
  - Optional 50 µm thick Bismuth layer to increase the photon conversion efficiency (w.r.t. only silicon)







The Sensor-Asic Design - MAPS



7. Digital electronics will be placed in a separate deep-nwell to improve noise robustness.

6. Analogue electronics in pixel.

5. Pixel and electronic deep n-wells are kept at positive low voltage.

1. High resistivity P-type substrate.

2. P+ backside contact

3. Electronics inside the guard-ring, isolated from substrate using deep n-well.

4. Negative High Voltage applied to the substrate.

The Sensor-Asic Design - MAPS

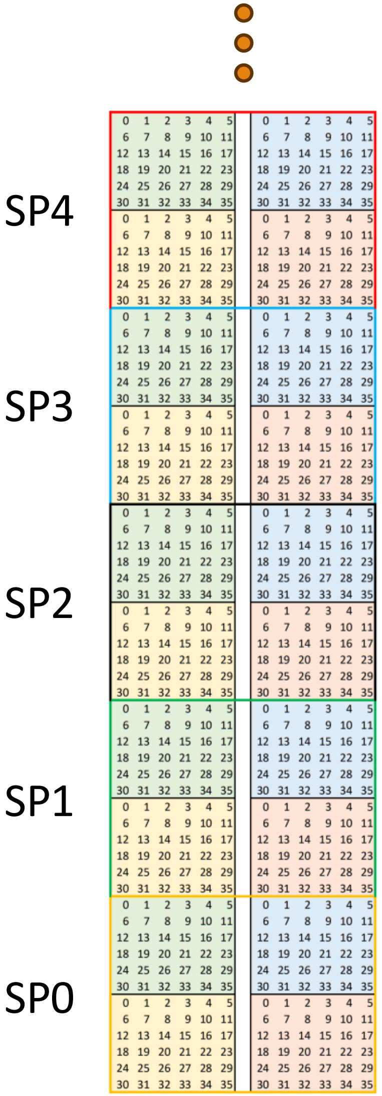
- **SiGe technology** for monolithic timing pixel development profited from ~8 years of R&D development now used for HEP experiments and for 100µPET
- **Asic design** In-house design and submission booked for October 24th

Main features	
Depletion depth	250 [µm]
Pixel (hexagonal) pitch	~ 160 [µm]
Nb of pixels	25344
Max cluster size	< 25 pixels (5x5)
Front end noise (ENC)	200 [electrons]
Operation Threshold	3000 [electrons]
Power consumption	70 [mW/cm^2]
Time resolution RMS (Qin > 5 ke-)	200 [ps]
TOA and TOT	Per each super-pixel line
Readout speed	50 [Mb/s]
Event size	143 [bits]
Max expected data rate	40 kHit/s @ 20 MBq
Chip readout daisy chained	1 readout line / 4 chips

Chip size: ~ 30.2 x 22.8 mm^2

16 Super columns of 11 Super pixels of 144 pixels

The Sensor-Asic Design - Architecture



- No readout in the matrix, only configuration circuits.

- Cluster mapping based on FAST-OR projections: 51 lines
  - 36 cluster lines – direct routing
  - 4 PAD lines – direct routing
  - 11 Super-Pixel lines – tree routing to compensate delays.

- TOA and TOT measurement **of the OR of the Super-Pixel lines** in each column. TOT used for time walk correction, no charge measurement.

- Univocal cluster definition for single cluster events or multiple clusters in non-adjacent super columns.

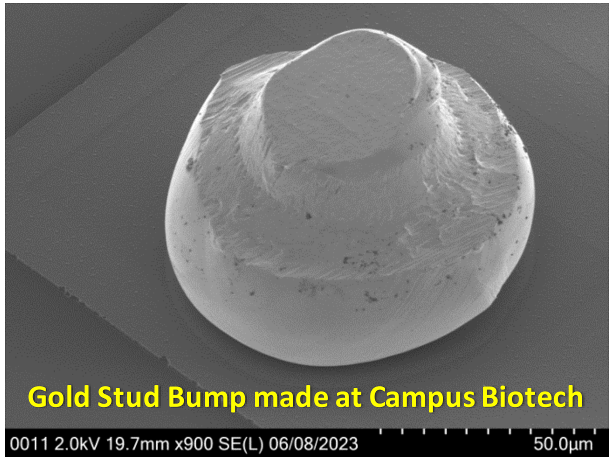
- All readout logic in periphery: simpler physical implementation.

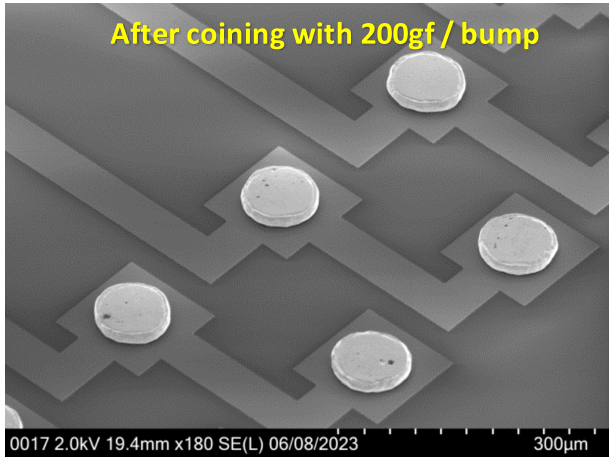
- Configuration logic in column (lower frequency).

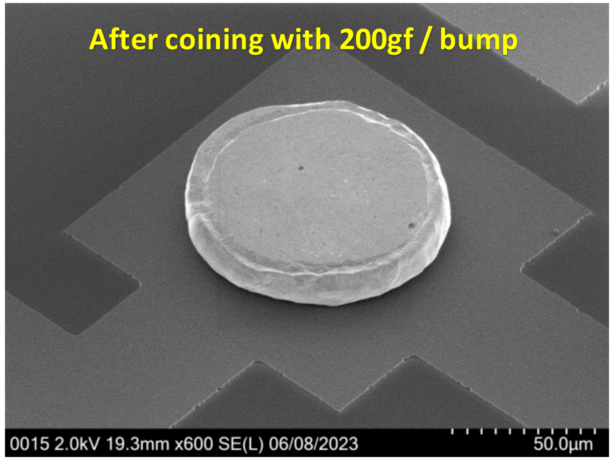
100µPET – Interconnections

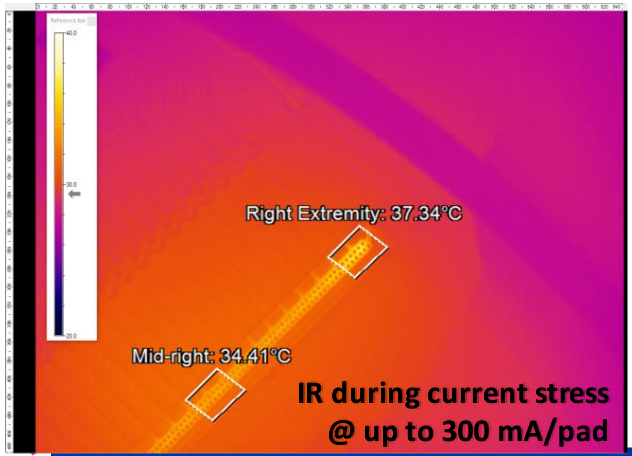
- **Several interconnection methods tested with the optimal method Gold stud bumps with NCP**

Most optimal electrical contact and passed all the qualification tests including current stress test up to 300 mA


Gold Stud Bump made at Campus Biotech


After coining with 200gf / bump


After coining with 200gf / bump



IR during current stress
@ up to 300 mA/pad

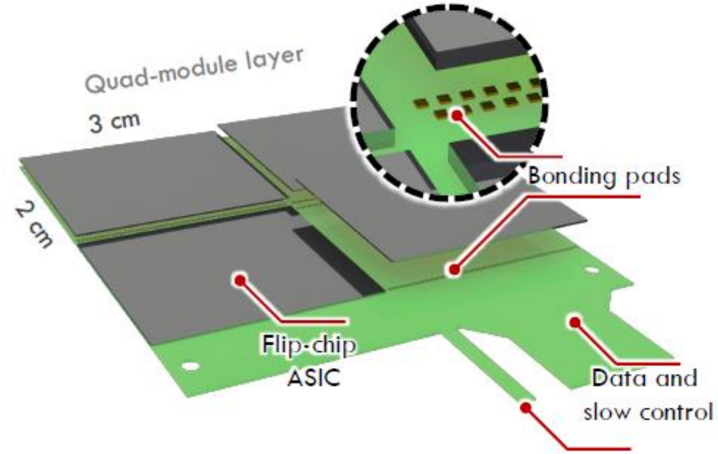
←

During current stress tests IR image checked

IR Inspection area (Interconnection pads underneath)

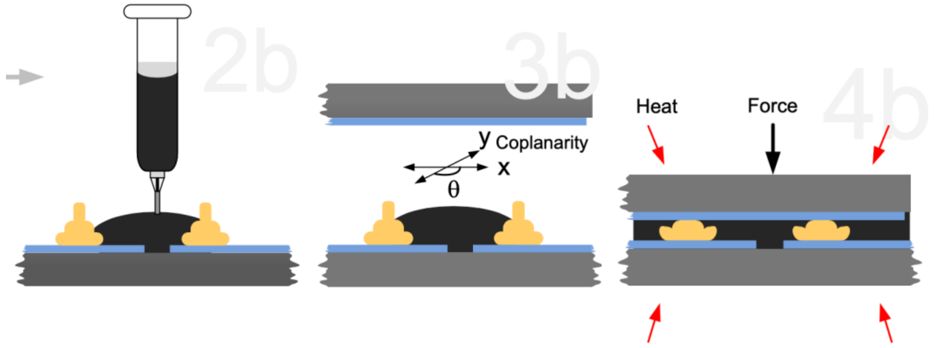
100µPET Module Construction

Baseline concept: Single module layer → Si to FCP interconnection



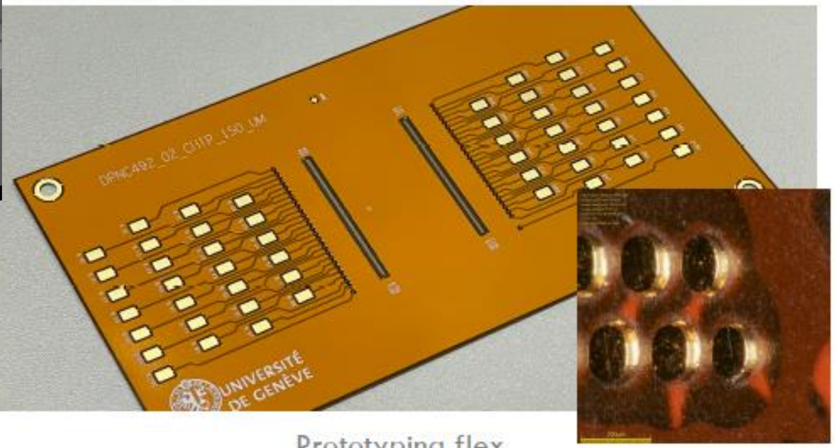
Flip-chip bonding thanks to:

- SET ACCURA100 machine
- Fused silica detector pattern matching flex PCB structure
- Flex PCB design on purpose to match the qualification bonding test



Pad wafer with 6 full chain dies

+



Prototyping flex

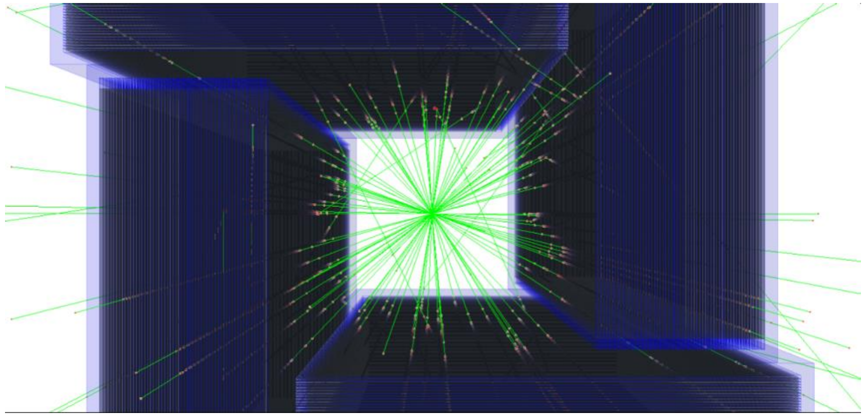
100µPET – Performance Simulation

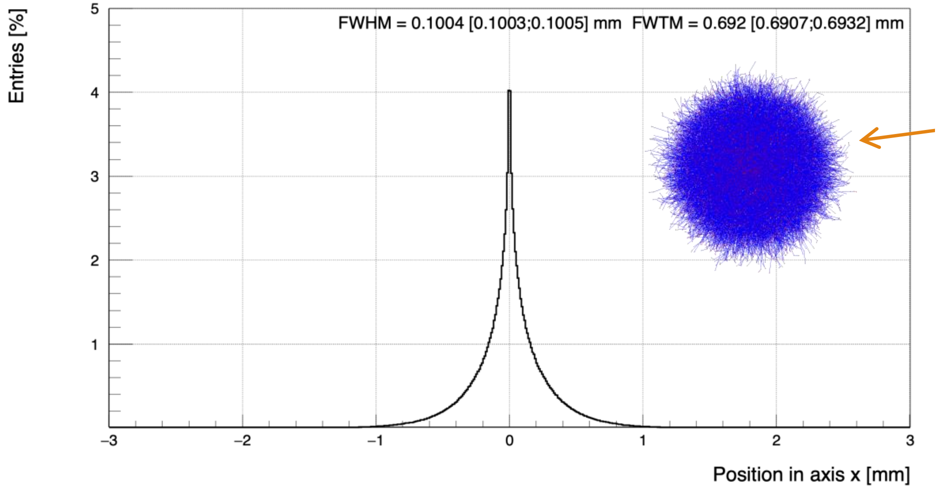
Monte Carlo simulation with Geant4 and Allpix2 allows:

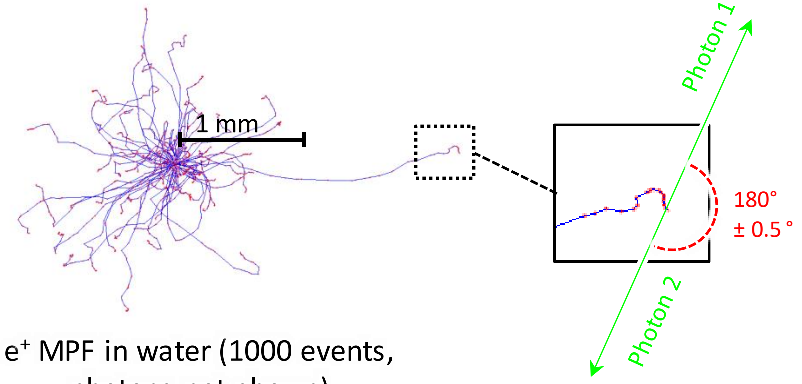
- Positron emission & photon conversion
- Detector performance with pixel ASIC
- Detector effects on sensitivity and resolution

Full scanner geometry (w/ or w/o Bi layers) + **water volume**

- Positron mean free path and annihilation from [^{18}F]FDG with acollinearity effect
- Photon interactions (scattering and photoelectric effect)
- Sensor/ASIC response + pixel clustering







e$^+$ MPF in water (1000 events, photons not shown)

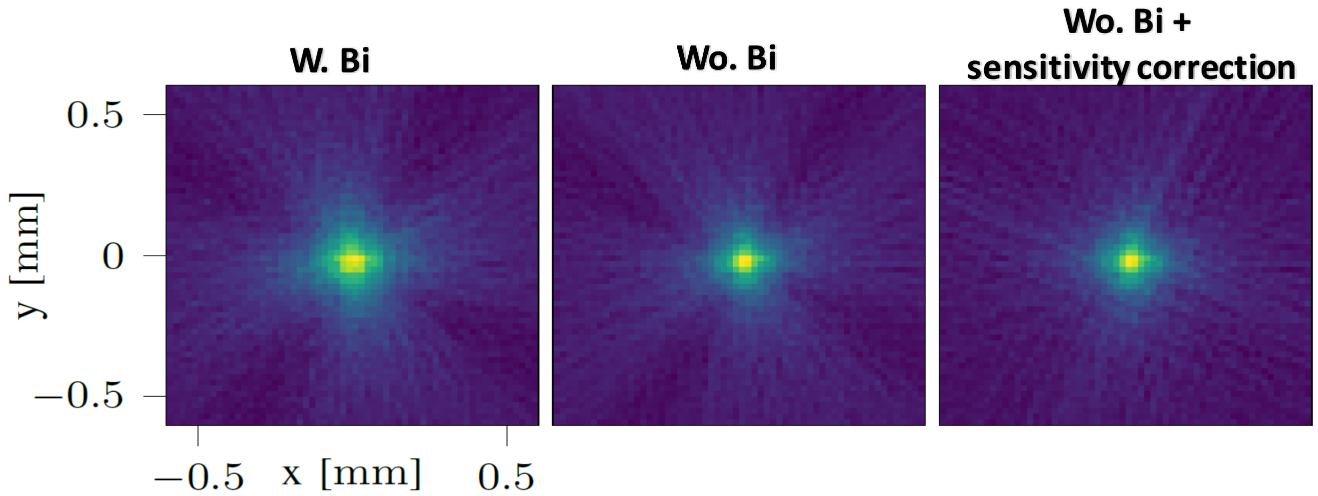
Performance with Single Point Source

- **Sensitivity:** amount of unambiguous LoR measured as a function of the total number of positrons
  - **3.3%** and **4.8%** detection efficiency, without and with Bi respectively
- **Spatial resolution:** Point Spread Function with FBP (Filtered Back Projection)
  - **0.22 mm** at minimum and **0.25 mm with Bi**
  - Due to acolinearity of the 2 photons → not a big change between 100 vs 150 µm pitch
  - **Negligible parallax distortion**

Point Spread Function from FBP

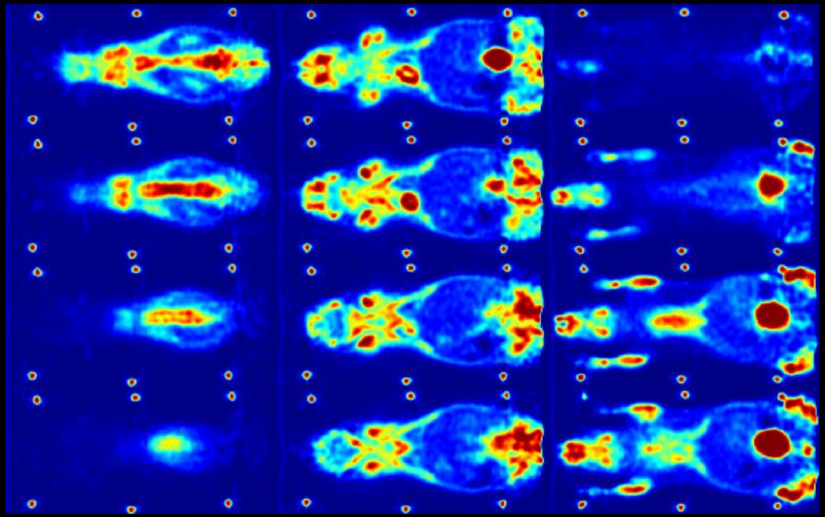
off-axis (mm)		0	5	10	15
FWHM (100 µm pixel)	No Bi	0.22	0.23	0.24	0.24
	Bi	0.25	0.26	0.27	0.28
FWHM (150 µm pixel)	No Bi	0.24	0.25	0.26	0.25
	Bi	0.27	0.28	0.28	0.28

NB: *The mean-free path of the positron (100 µm FWHM and 1000 µm FWTM) is included in the simulation as well as the acollineraity*
→ Only unambiguous event were used

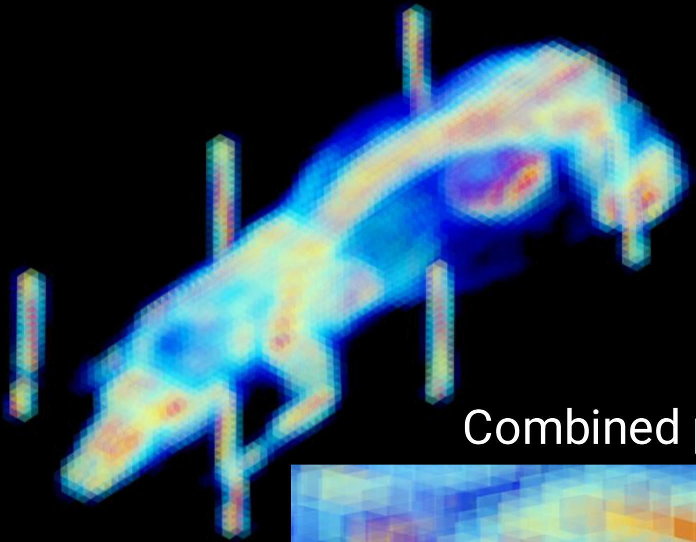


100µPET Artery Plaque

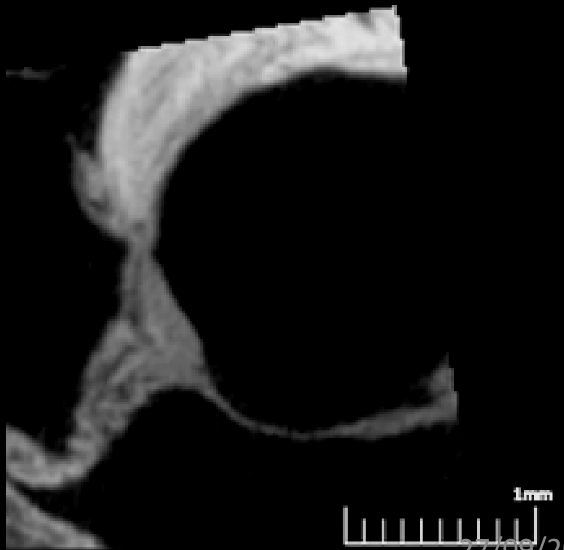
Digimouse: a 3D whole body mouse atlas from CT and cryosection data. doi: 10.1088/0031-9155/52/3/003



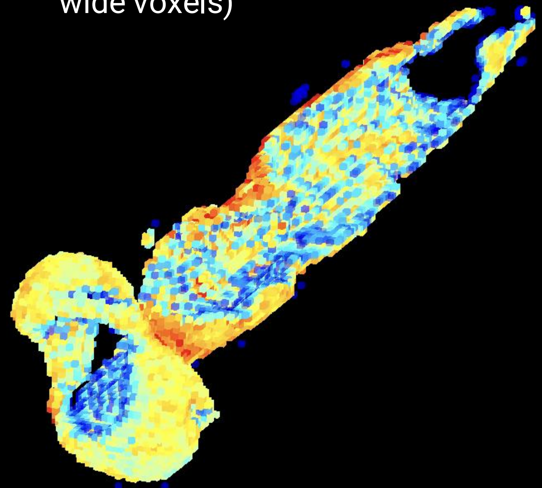
3D voxels from Digimouse PET scan (1 mm wide voxels)



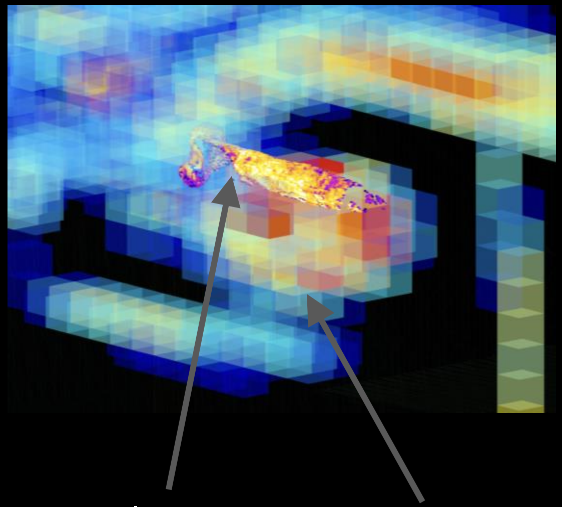
A volumetric method for quantifying atherosclerosis in mice by using microCT doi: 10.1371/journal.pone.0018800



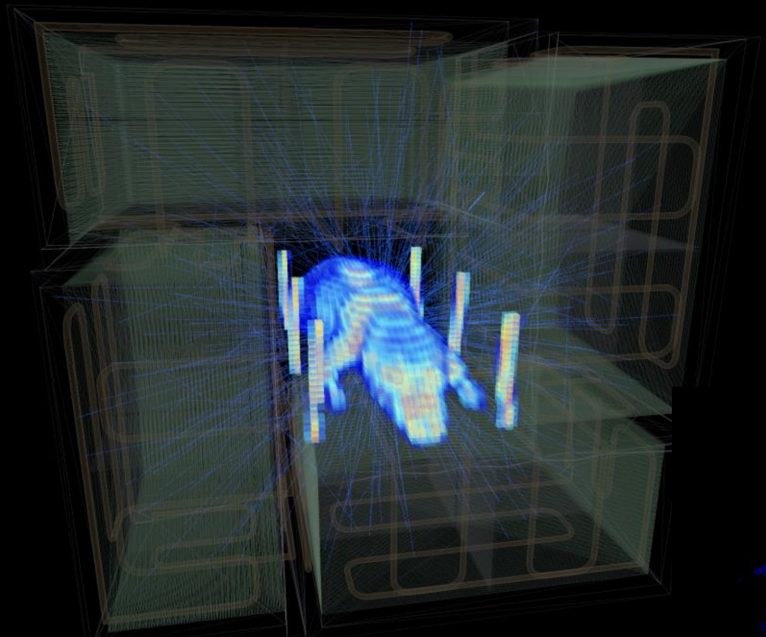
3D voxels from plaque (50 µm wide voxels)



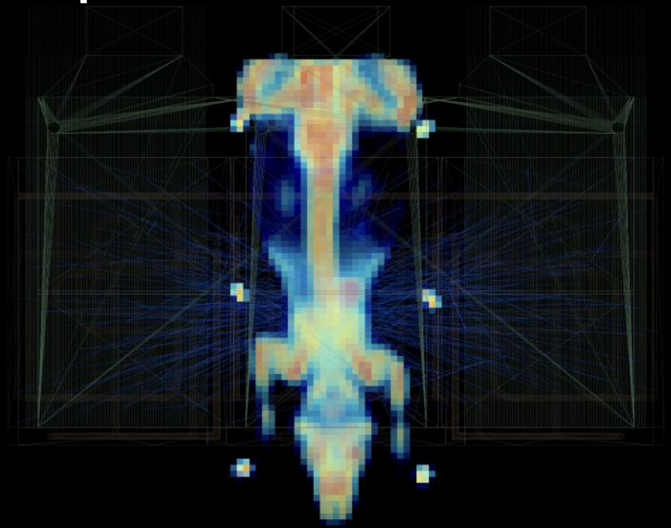
Combined parts



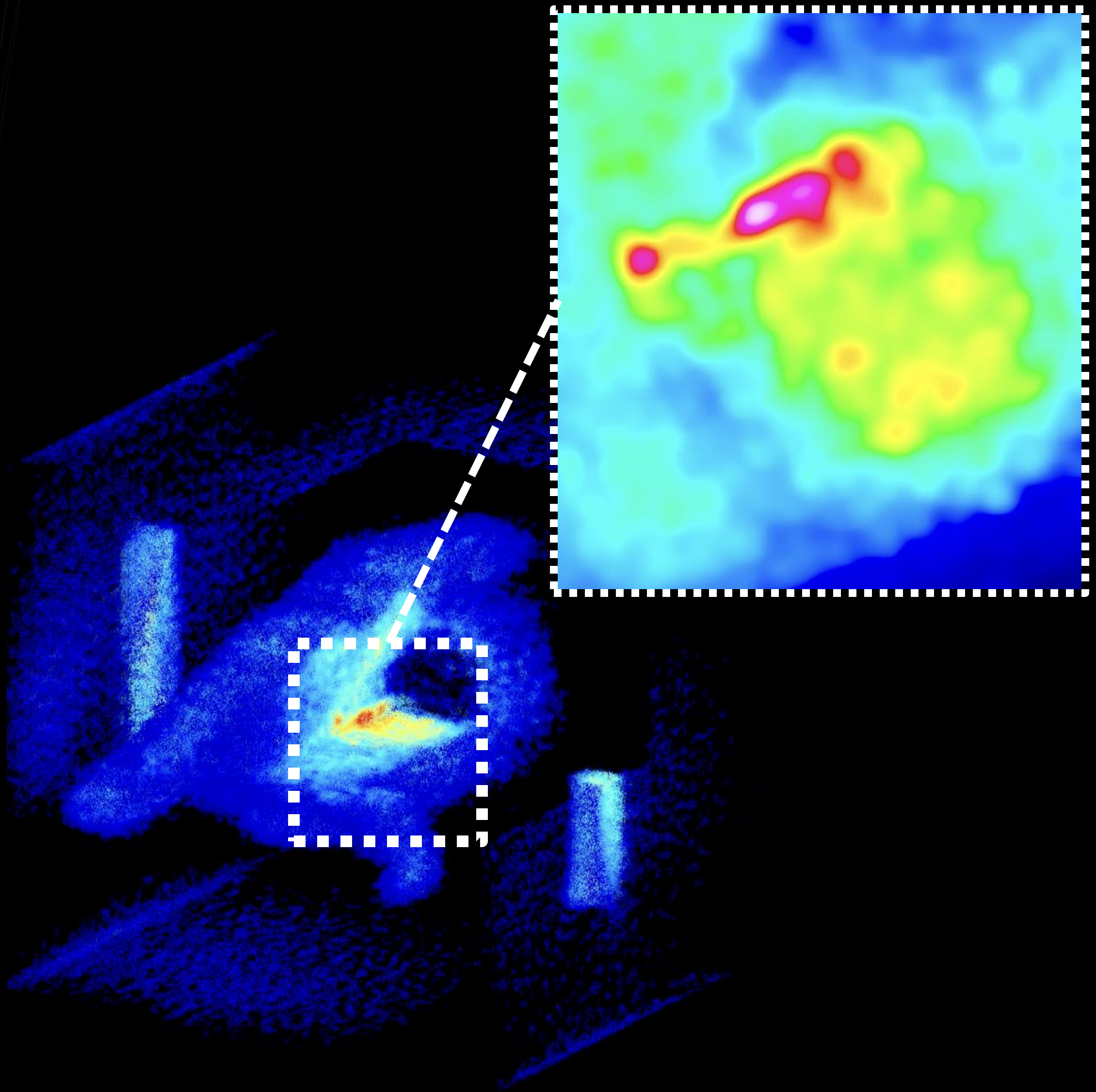
100µPET Artery Plaque



Monte Carlo simulation of Mouse + Plaque within scanner detectors

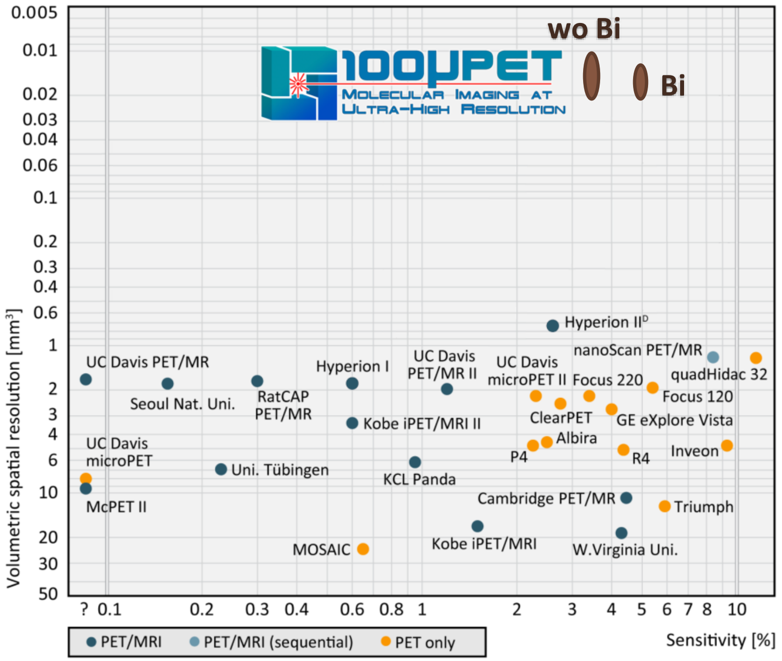


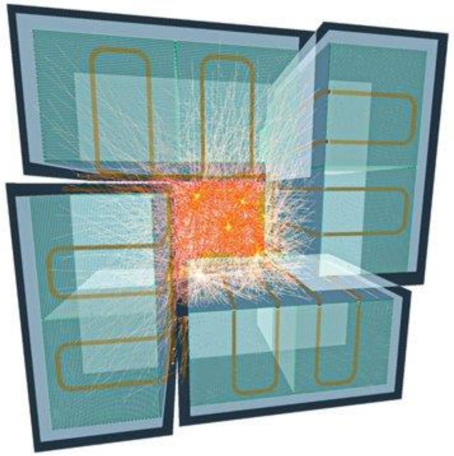
Reconstructed volume (110 µm voxels)



Summary

- **Potential ultra-high-resolution** molecular imaging **using MAPS**
  - ASIC designed within the UniGE DPNC group
  - Development of module construction technique based on flip-chip bonding for compactness
  - Monte Carlo simulation and imaging reconstruction are showing very promising performance
- **ASIC architecture optimized for PET**
  - Allows simple design and calibration
  - Can sustain high source activity
  - Submission in October 2023
- **4.8%** and **3.3% scanner sensitivity** (w/ or w/o Bismuth layer)
  - ***0.22-0.28 mm PSF → 0.010 - 0.022 mm3* volumetric spatial resolution**
- **Delivery of a proof-of-concept** scanner for small animals **in 2025**
  - Silicon-sensor technology advances and its cost will go down while larger scanners can be envisaged in the future





EXTRA SLIDES

Next steps: Introducing picosecond time resolution

100µPET – Performance Simulation

Monte Carlo simulation with Geant4 and Allpix2 allows:

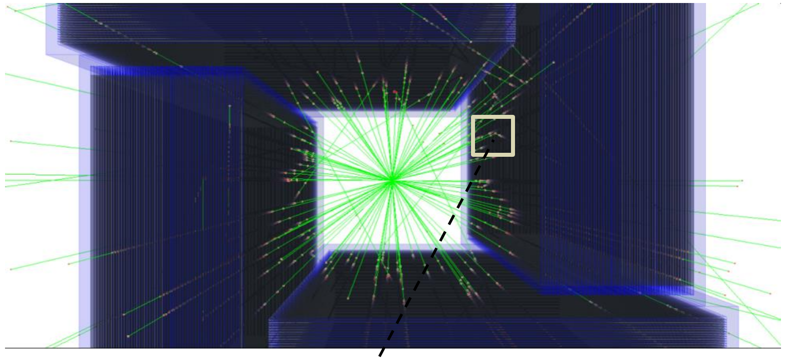
- Positron emission & photon conversion
- Detector performance with pixel asic
- Detector effects on sensitivity and resolution

Single positron annihilation per event:

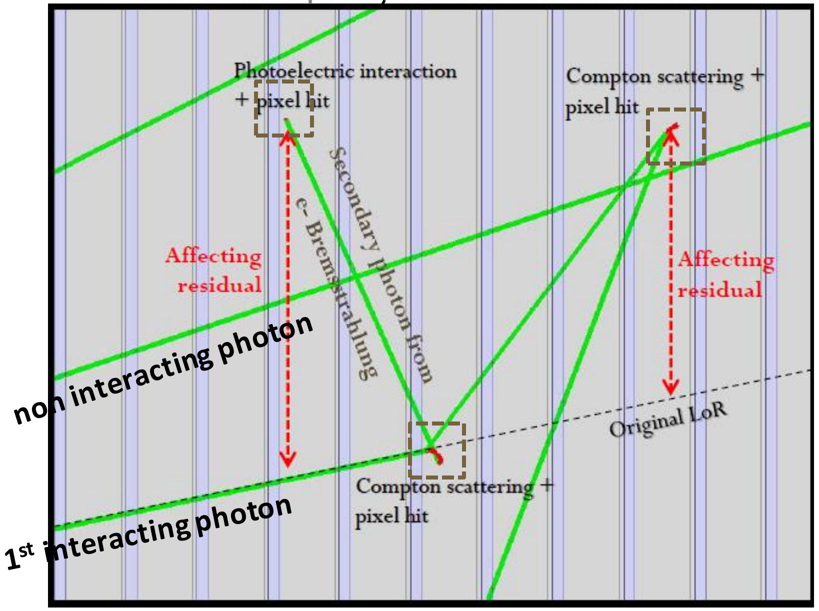
- Event filtering for **unambiguous** line-of-response acceptance
- Only events with two scanner towers having each a single cluster charge
- No energy window for discriminating signals form Compton or Photoelectric interactions

Resolution of the positron source:

- Single point: Point Spread Function
- Derenzo phantom: assess image reconstruction



Event with 3 possible clusters within a tower

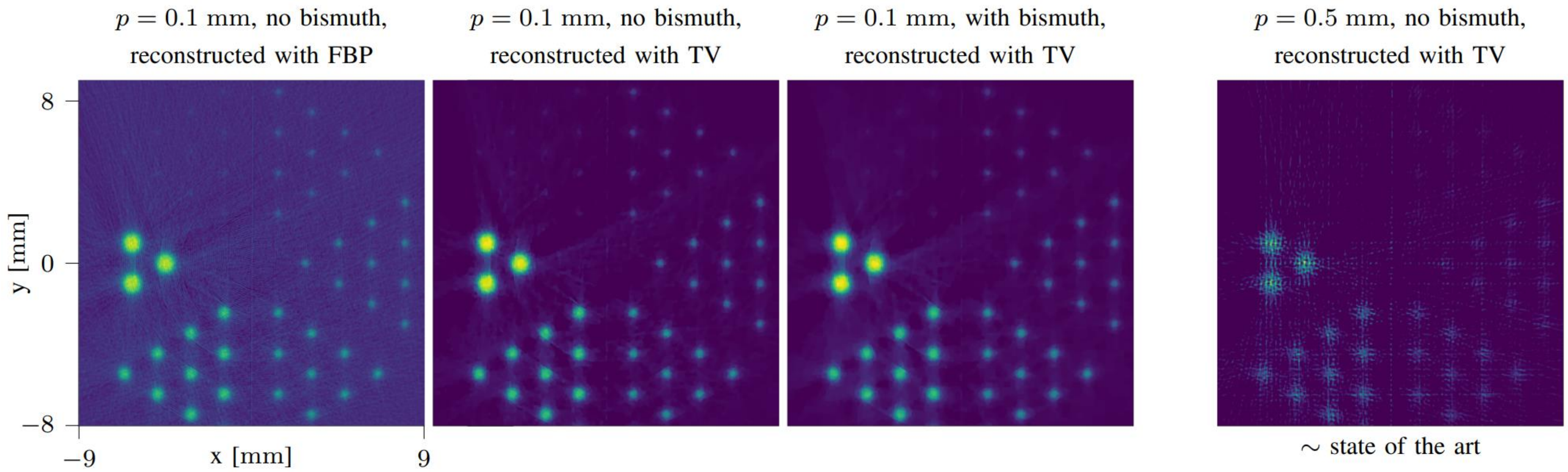


Performance with Single Point Source

Derenzo phantom to test reconstruction to a given feature size:

- 1.0, 0.6, 0.4, 0.3, 0.2, 0.1 mm rods
- Reconstruction using the 100muPET scanner

FBP: Filtered back projection
TV: Total Value



The MONOLITH Project

Our recipe for picosecond timing with silicon:

MONOLITHIC

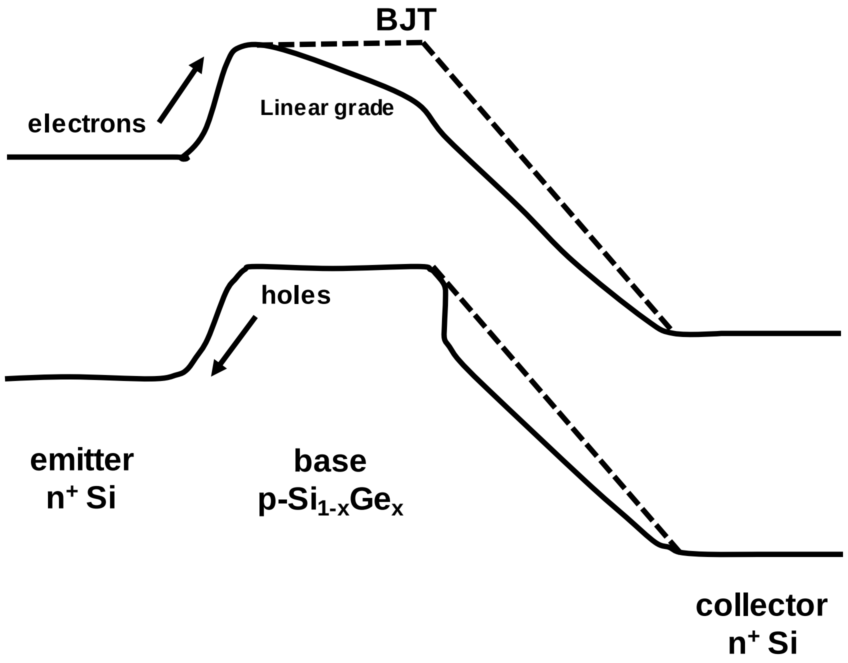
SiGe BiCMOS

PicoAD:
Picosecond
Avalanche
Detector

In collaboration with IHP microelectronics

SiGe BiCMOS electronics

In SiGe Heterojunction Bipolar Transistors (HBT) the **grading** of the bandgap in the Base changes the **charge-transport mechanism** in the Base from **diffusion** to **drift**:



Grading of germanium in the base:

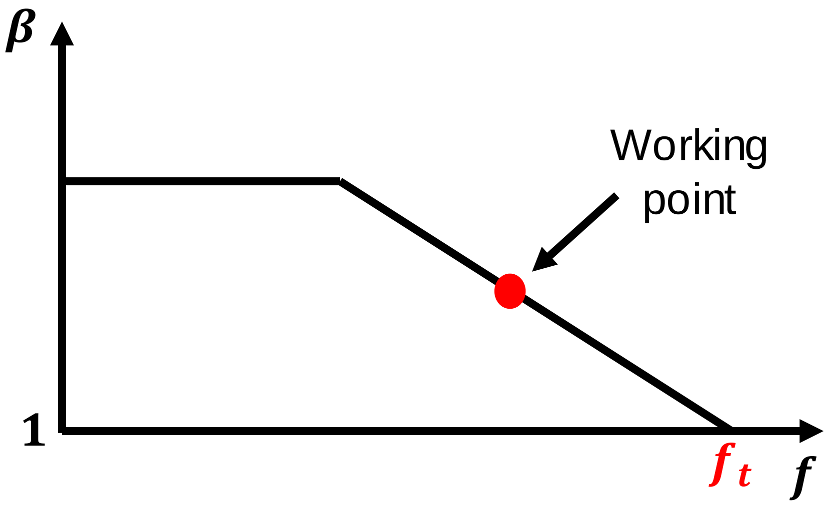
field-assisted charge transport in the Base,
equivalent to introducing an electric field in the Base

$\Longrightarrow$ short e^- transit time in Base $\Longrightarrow$ very high β

$\Longrightarrow$ smaller size $\Longrightarrow$ reduction of R_b and very high f_t

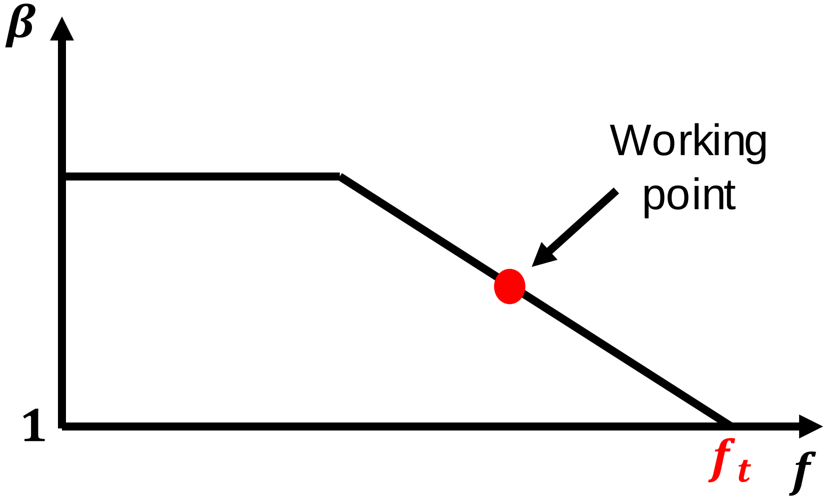
Hundreds of GHz

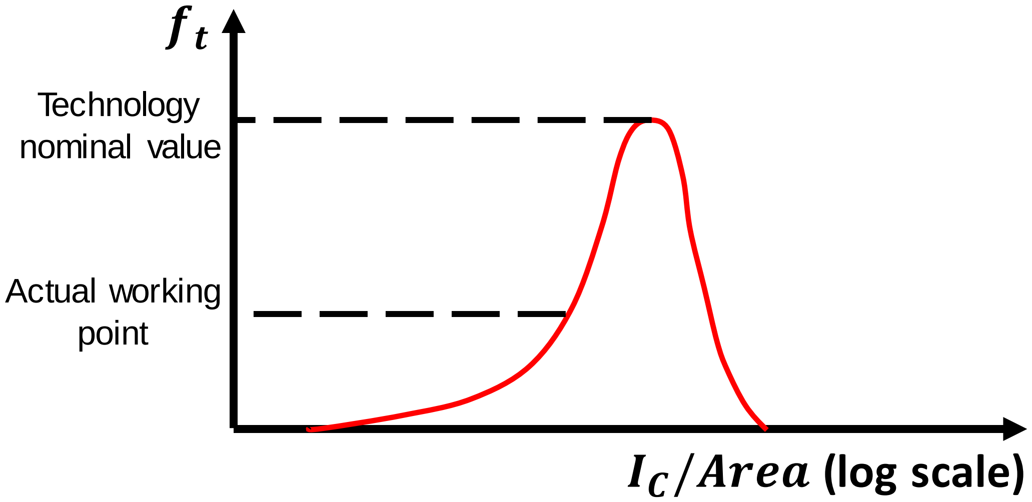
SiGe BiCMOS electronics



	$f_t = 10\ GHz$	$f_t = 100\ GHz$
β_{max} at 200 MHz	50	500
β_{max} at 1 GHz	10	100
β_{max} at 5 GHz	2	20

SiGe BiCMOS electronics





	$f_t = 10\ GHz$	$f_t = 100\ GHz$
β_{max} at $200\ MHz$	50	500
β_{max} at $1\ GHz$	10	100
β_{max} at $5\ GHz$	2	20

Trade-off: **ENC/σ_t** ⇔ **Power Consumption**

PicoAD Sensor Concept

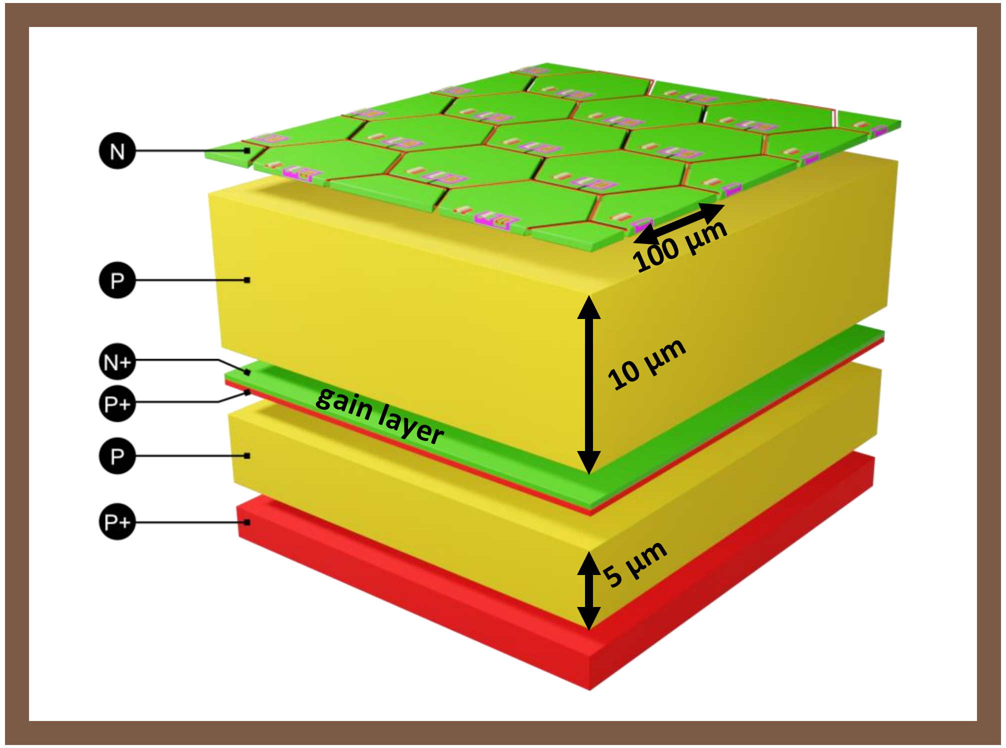
© G. Iacobucci, L. Paolozzi and P. Valerio. Multi-junction pico-avalanche detector;
European Patent EP3654376A1, US Patent US2021280734A1, Nov 2018

Multi-Junction Picosecond-Avalanche Detector©

with continuous and deep gain layer:

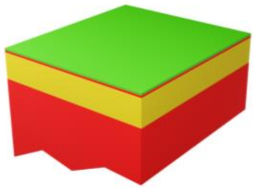
- De-correlation from implant size/geometry
  → **high pixel granularity and full fill factor**
  (high spatial resolution)
- Only small fraction of charge gets amplified
  → **reduced charge-collection noise**
  (enhance timing resolution)

$$\sigma_T \cong \frac{t_{rise}}{Signal/_{Noise}} \cong \frac{ENC}{I_{Ind}}$$

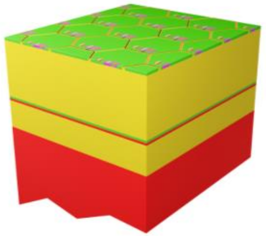


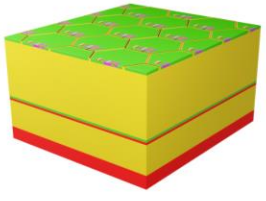

Step 1


Step 2

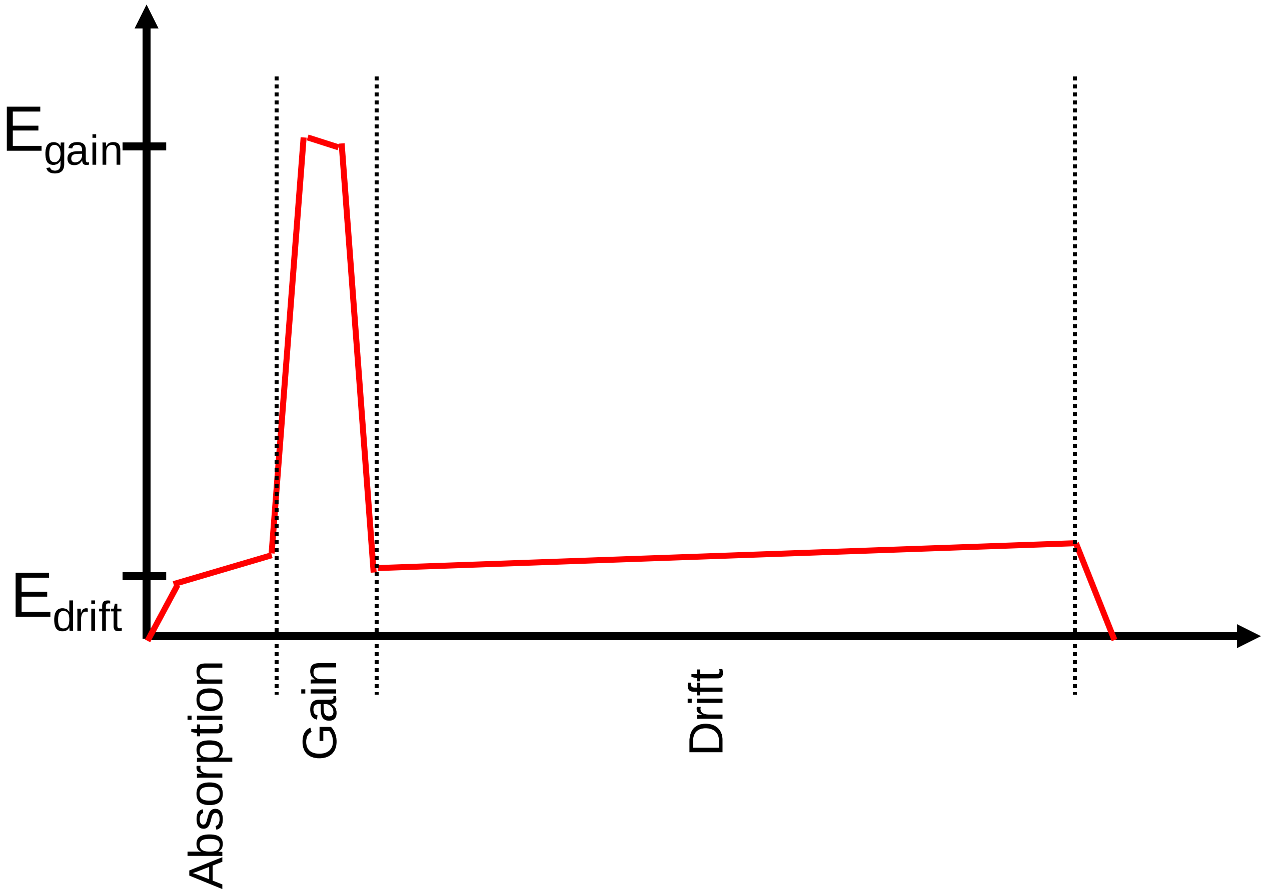

Step 3


Step 4


Step 5


Step 6

PicoAD Sensor Concept



- The introduction of fully-depleted multi-pn junctions allows to **engineer the electric field**.
- New device with unique timing and reliability performance.
- Gain with 100% fill-factor.
- Geant4 + Cadence simulations estimate ~**2ps time resolution** contribution from the sensor.
- Requires low-noise, ultra-fast electronics to be fully exploited.

First prototype test with MIPs

Best performance: (17.3±0.4) ps
for HV=125 V and Power = **2.7 W/cm^2**

Timing resolution of 30 ps even
at power consumption of 0.4 W/cm^2