https://the10ps-challenge.org

10ps Time-of-Flight PET scanner: The Odyssey From Hope to Practice

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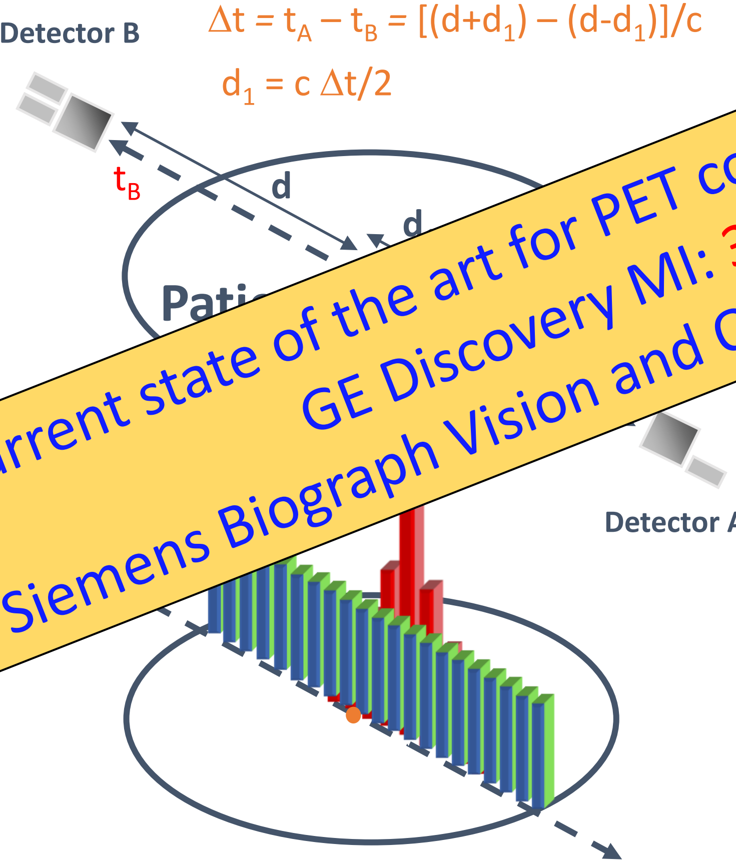
CERN, Geneva, Switzerland

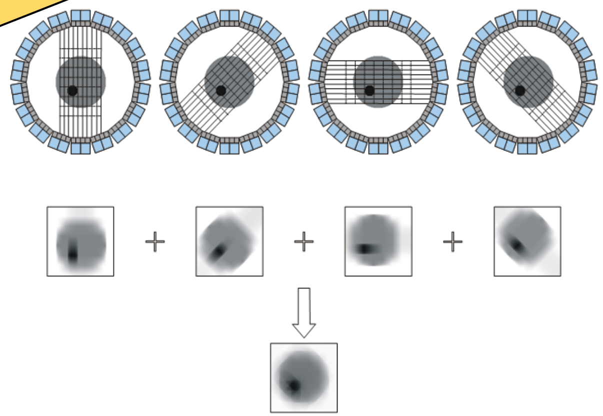
Increasing effective PET sensitivity

- PET is the imaging modality with the highest sensitivity, at the picomolar level
- Personalised medicine and new medical challenges require a significant sensitivity increase
  - Tracking small number of cells
    - Stem cells biodistribution and differentiation studies
    - Immune cells tracking for immonutheraty
  - Quantitative & dynamic pharmacodynamic studies
    - Increased sensitivity: extension of temporal dynamic range for measuring the entire course of tracer biodistribution
  - Dose reduction and opening PET scans to new categories of patients (pregnant women, children, fœtus)

Time of Flight PET



Current state of the art for PET commercial devices:
GE Discovery MI: 375 ps
Siemens Biograph Vision and Quadra: about 200 ps



Time of Flight PET

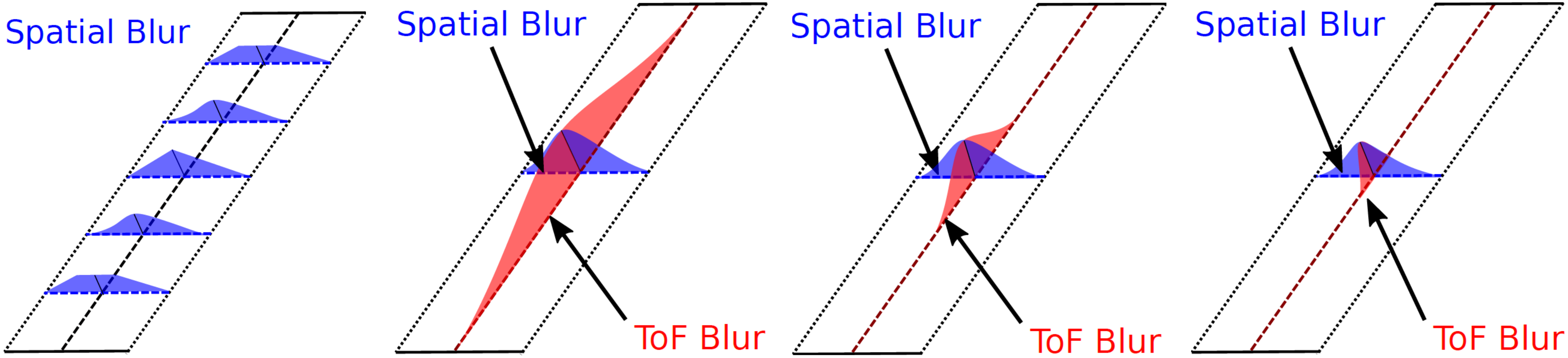
$$SNR_{TOF} = \sqrt{(2D/c\Delta t)} \cdot SNR_{conv}$$

The 10ps TOFPET challenge

https://the10ps-challenge.org

Ultimate Time of Flight objective

Would time-of-flight be also helpful to improve spatial resolution?



No ToF	**Current**	**Near future**	**Far future?**
Classical tomographic reconstruction	CTR ~200 ps ToF-weighted reconstruction	CTR ~ 30 ps $R_{ToF} \approx R_{det}$ No more reconstruction*!*	CTR ~ 10 ps $R_{ToF} < R_{det}$ ToF-enhanced reconstruction*!*

Courtesy of R. Lecomte, Sherbrooke

High density
High Z

Sensitivity

Scintillating detector is the eye of PET scanner

It needs a 10/10 vision

Time resolution

High Light Yield
Fast kinetics

$$CTR \approx \sqrt{\frac{\tau_r \tau_d}{N_{ph}}}$$

Energy resolution

High Light Yield
High linearity

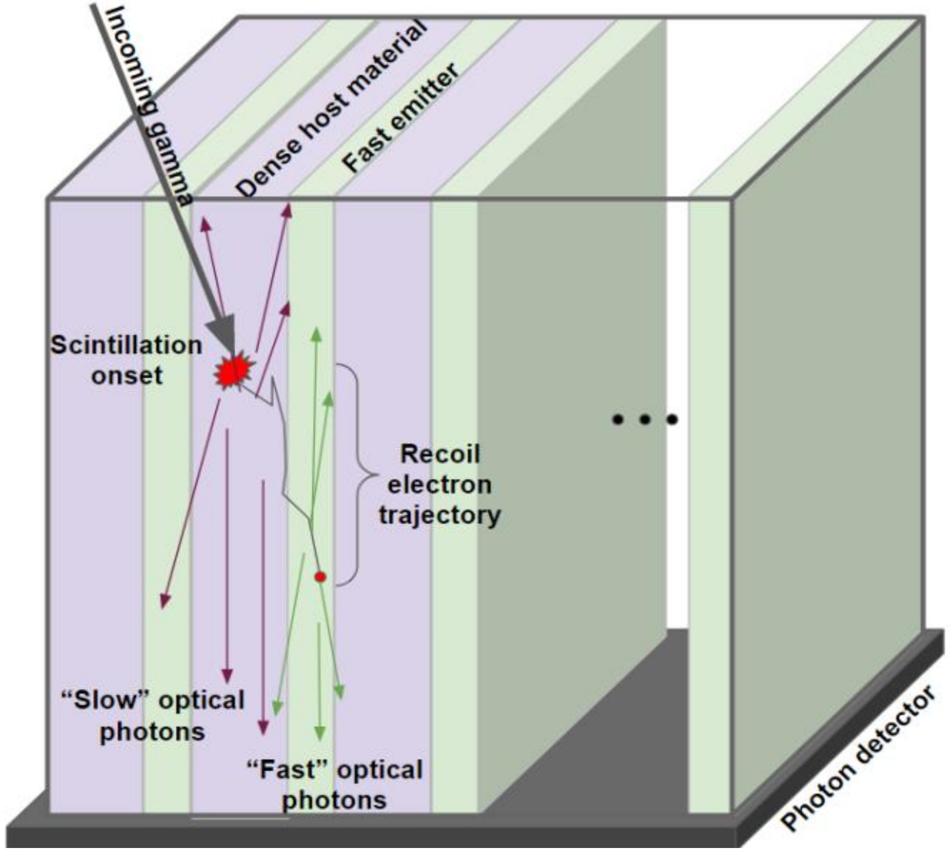
Spatial resolution

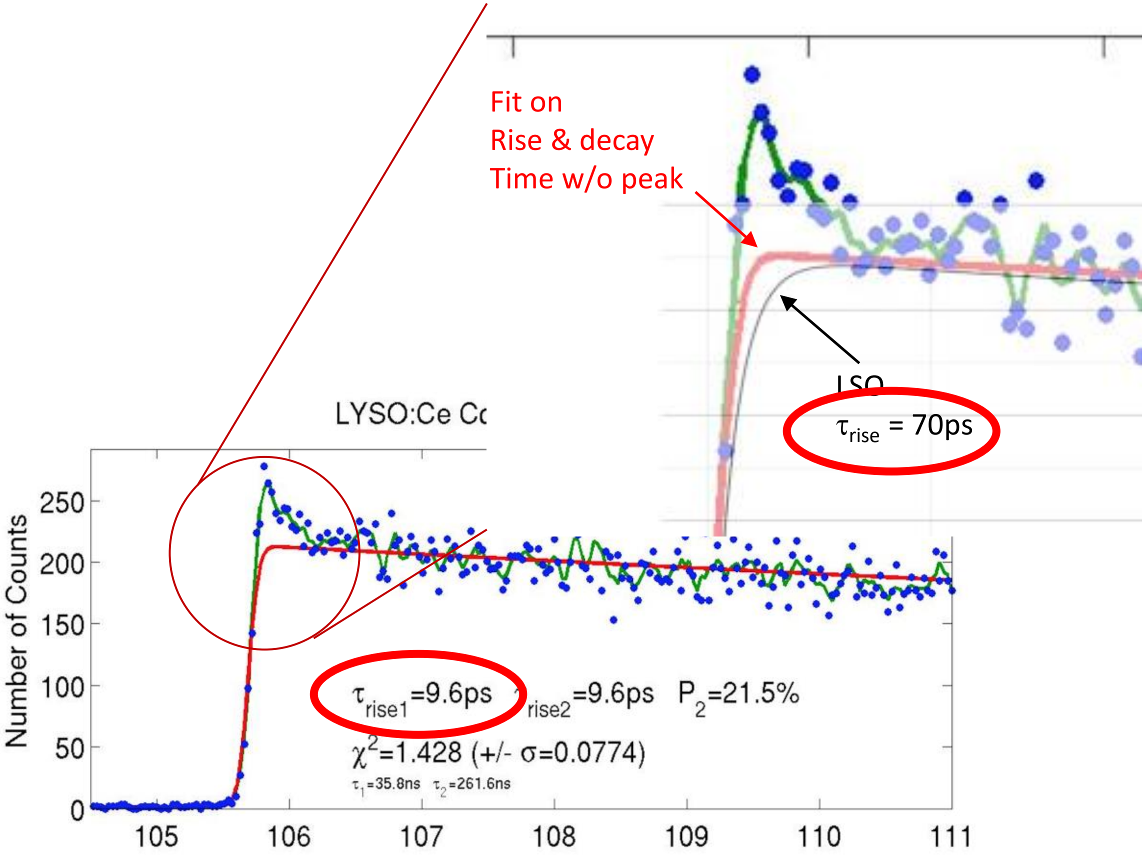
High density

Metascintillator principle

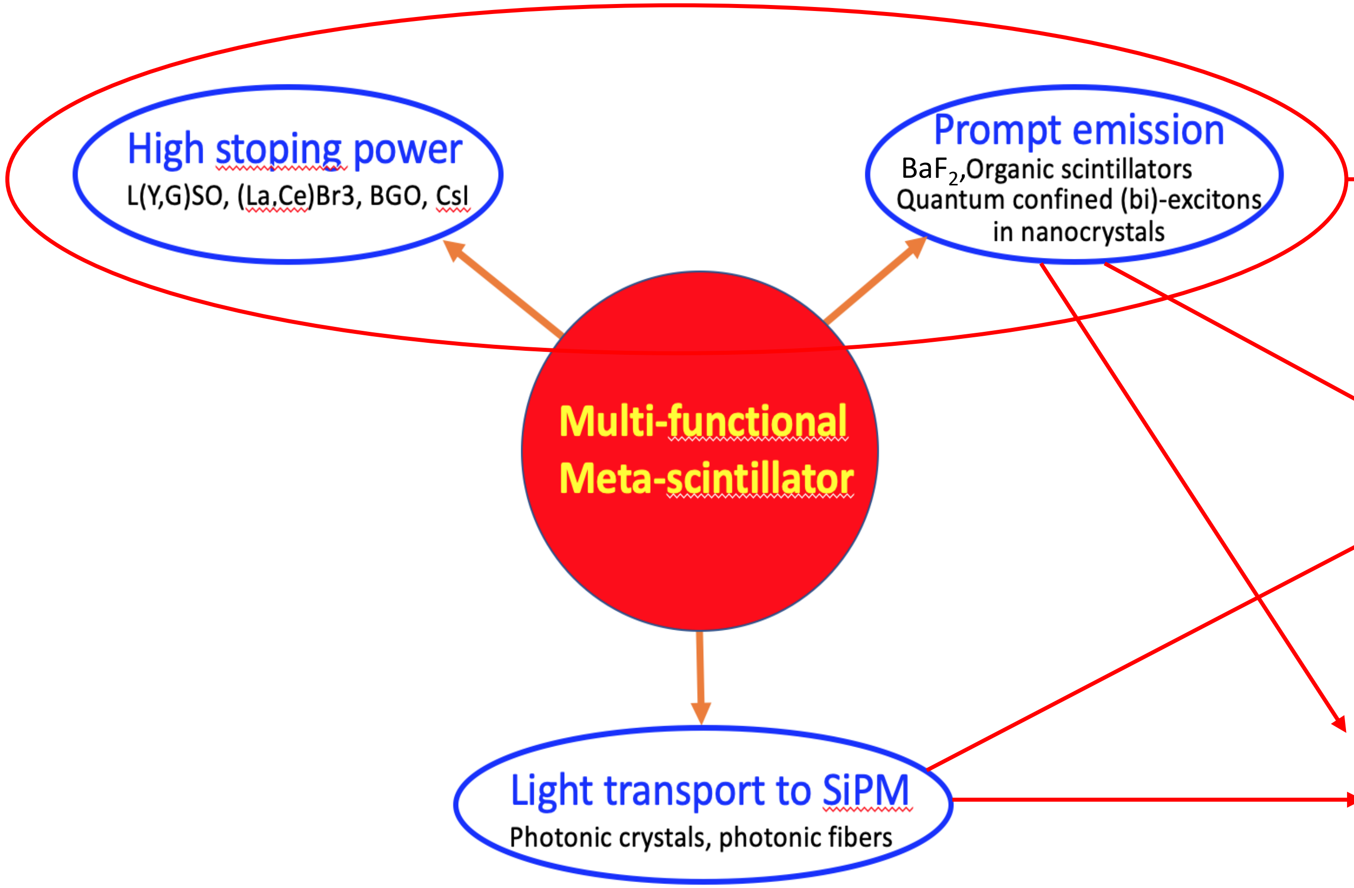
Metascintillators for ultra-fast gamma detectors: a review of current state and future perspectives

G. Konstantinou, P. Lecoq, J. M. Benlloch and A. J. Gonzalez, *IEEE TRPMS.2021.3069624*





From scintillator heterostructures to Metascintillators



1st generation: scintillator heterostructures

- 100ps CTR at system level, LYSO /BaF_2 ,LYSO/EJ232
- 200ps CTR at system level, BGO/BaF_2 ,BGO/EJ232

2d generation: Metascintillators

- 50-70ps CTR at system level, LYSO/BaF_2 ,LYSO/EJ232
- 100ps CTR at system level, BGO/BaF_2 ,BGO/EJ232

3d generation: Metascintillators

- 10-30ps CTR at system level
  - New nanoscintillators
  - New nanophotonic features

CPI Crystal Photonics, Inc.

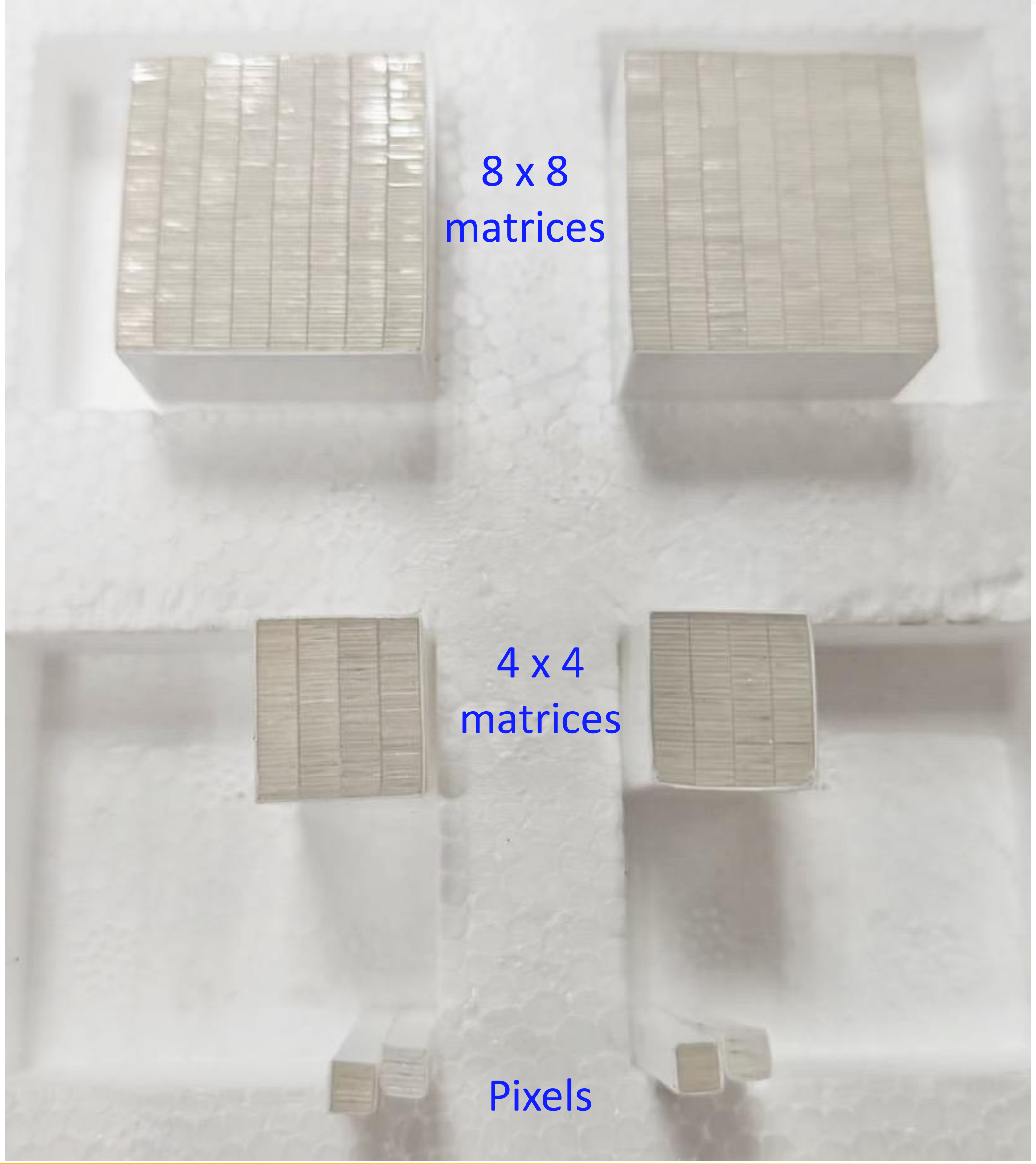
Exclusive partnership between
Multiwave Metacrystal and CPI to develop
Metascintillators of different types and geometry
with high cost/performance ratio

Contact: paul.lecoq@metacrystal.ch

3 x 3 x 20mm

LYSO/BaF2

BGO/BaF2

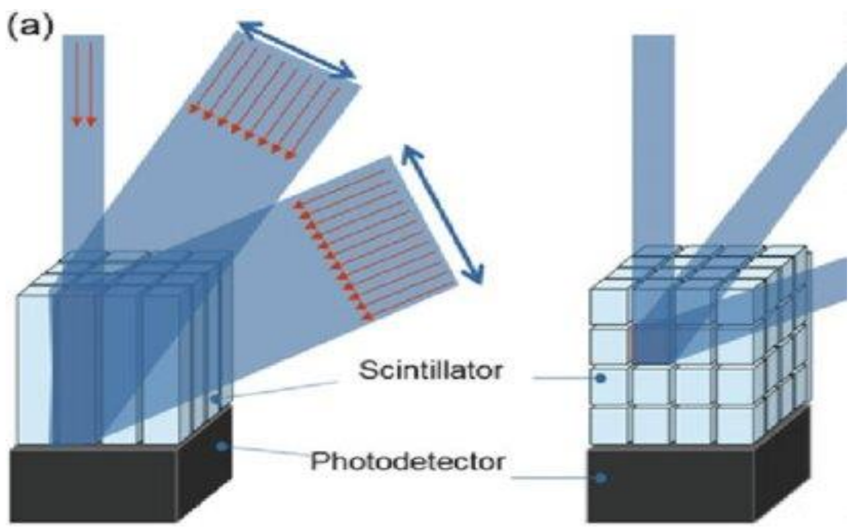


1st generation in the lab

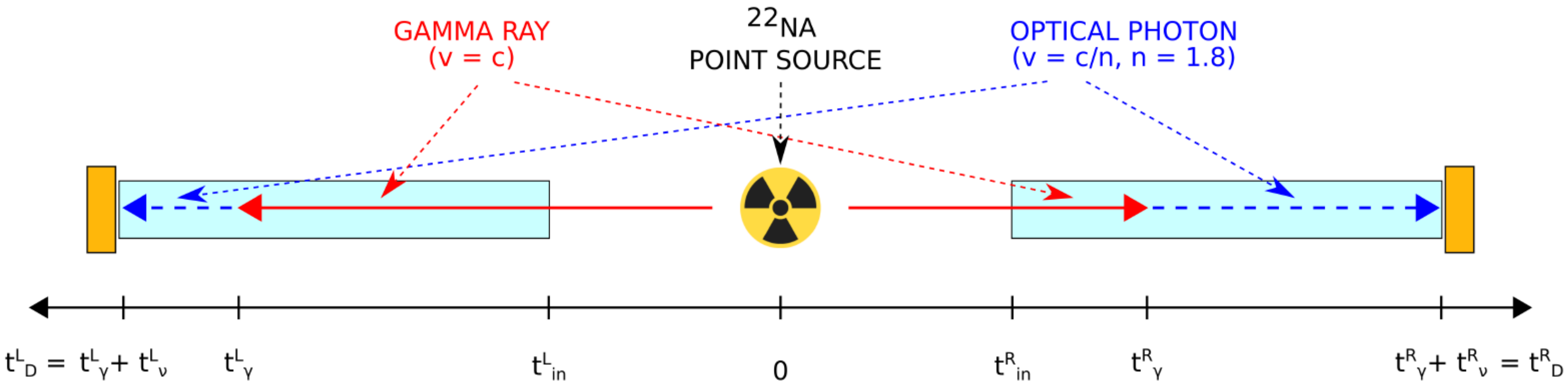
- We have selected 2 BGO-based configurations on the basis of a reasonable compromise between performance and cost
  - BGO/BaF_2 300/300 microns metascintillator pixels, $3x3x20mm^3$ achieved 22% energy resolution and 242 ps CTR, with a fast dataset (13%) at 108 ps.
  - BGO/EJ232 300/100 microns metascintillator pixels achieved 18.5% energy resolution and 204 ps CTR with a fast dataset (10%) at 75 ps
- Several LYSO/BaF2 and LYSO/EJ232 $3x3x15mm^3$ and $3x3x20mm^3$ metapixels are also tested
  - CTR resolutions in the range 120-140ps (depending on the configurations) consistently measured with a fast subset (10%) at 90ps
  - On-going work for improving the light transport/collection of the fast scintillator.

Depth-of-interaction (DOI)

- DOI is **generally useful** to improve spatial resolution and correct parallax error.
- More than that, DOI is an important bias for CTR as the depth-of-gamma interaction becomes prevalent for ultra fast materials.
- Ultrafast metascintillators need DOI characterization on an event-to-event basis.



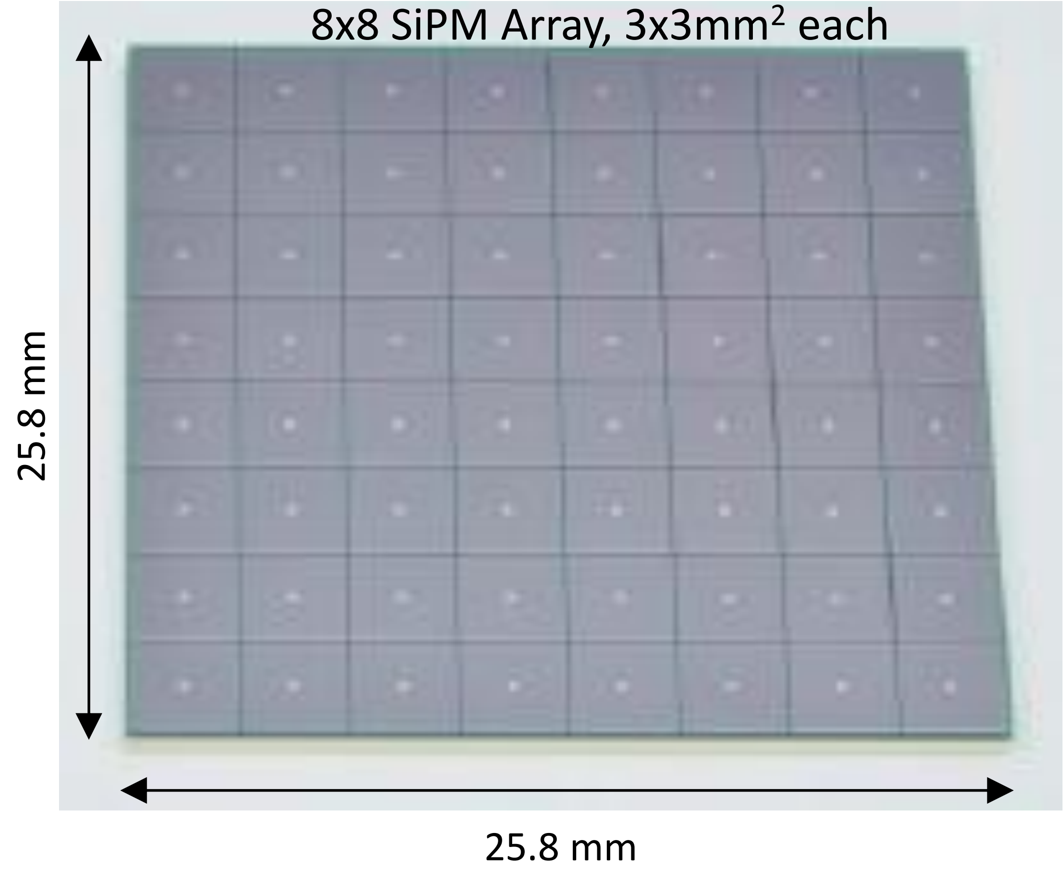
Parallax error effect in standard (left) and elemental (right) detector (Yamaya, T. 2016)

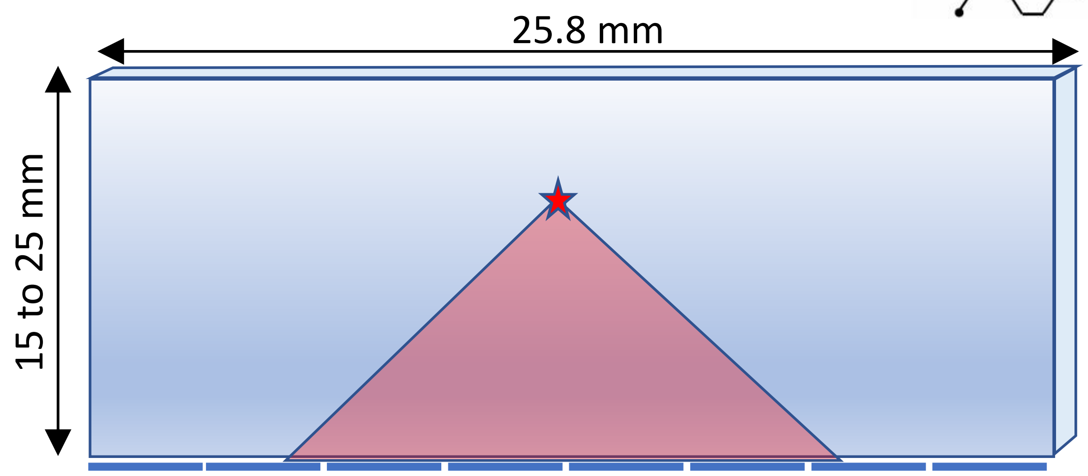


M. Pizzichemi et al., 2019 *Phys. Med. Biol.* **64** 155008

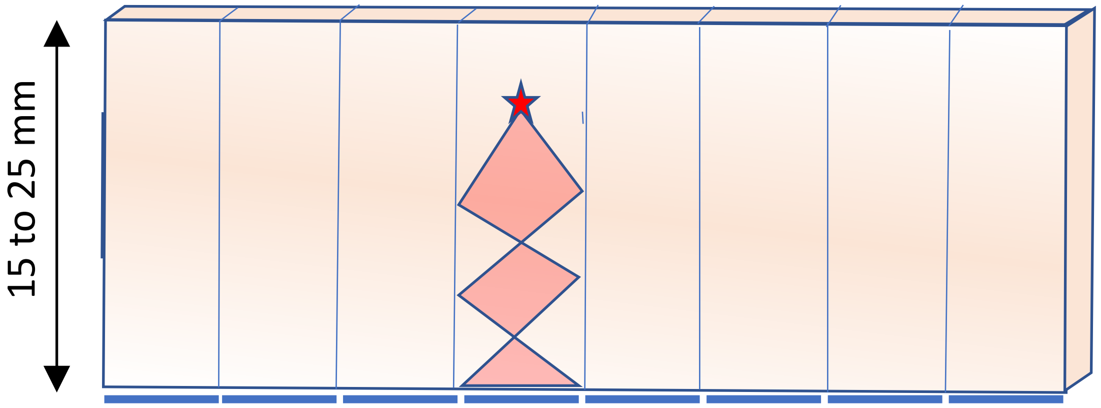
Semi-monolithic Metascintillators: SMMS

We propose the new detector paradigm, combining
- TOF (metascintillator) and
- DOI (semi-monolithic)



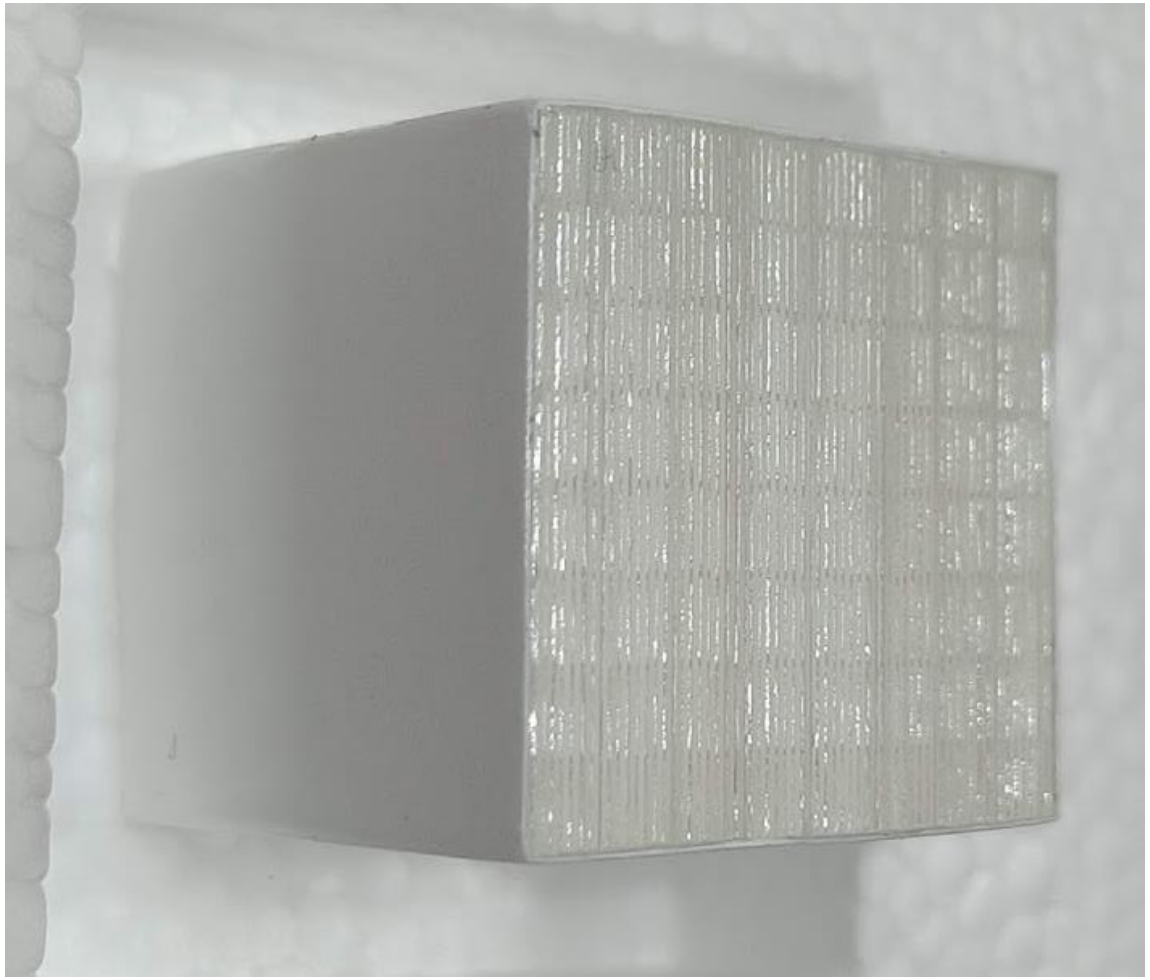


Long and thin dense scintillator plates



Thin ultrafast scintillator pixels

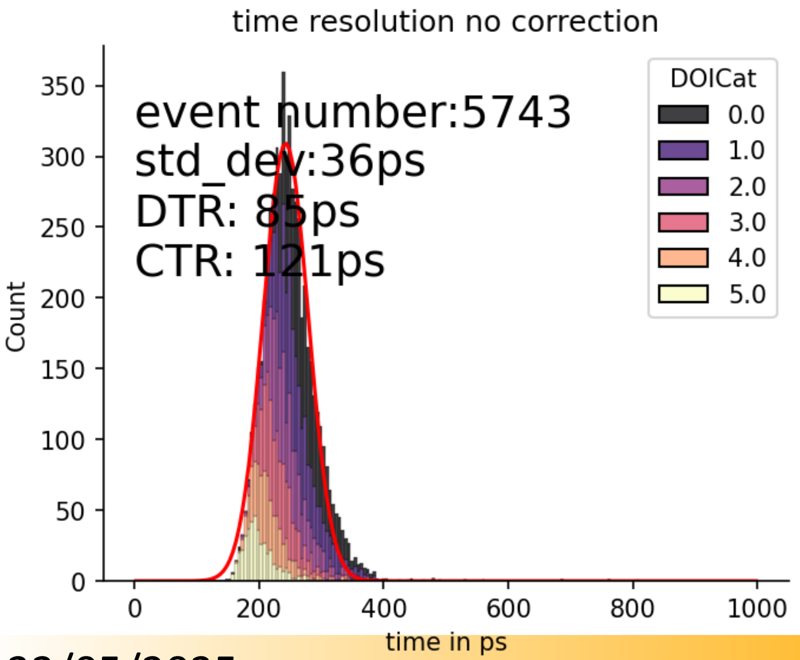
SMMS in real life testing

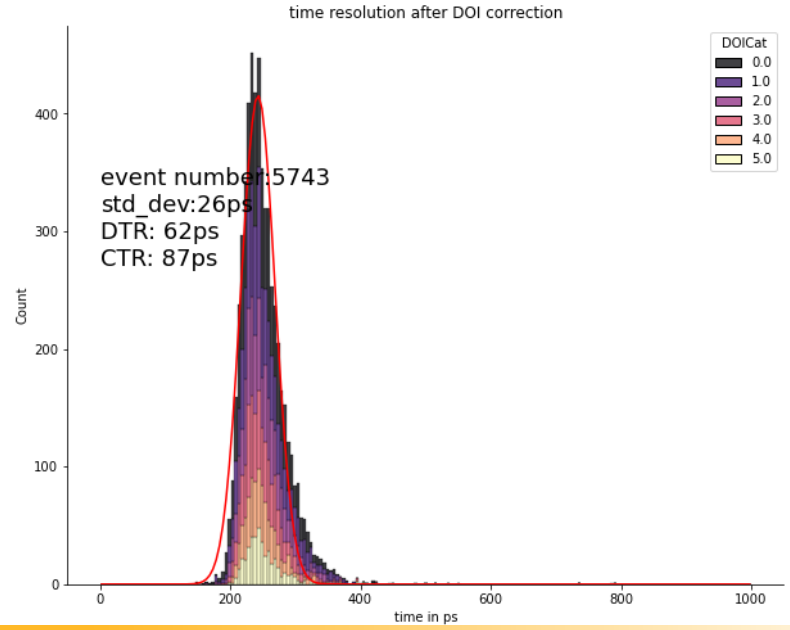


- 25.5x25.5x24 mm^3 LYSO:Ce+EJ232 SMMS
- ESR separating in the semi-monolithic sense
- Dimensions designed to couple with a Hamamatsu S13 8x8 MPPC matrix

SMMS simulation: CTR

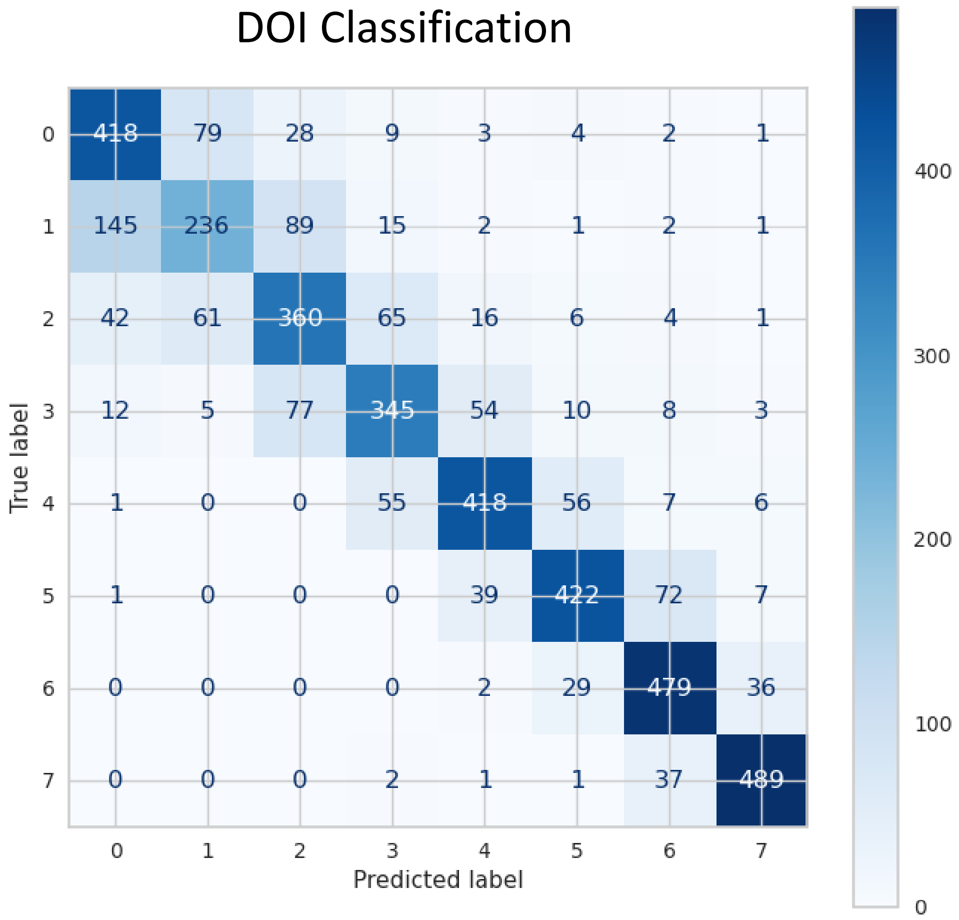
- Coincidence time resolution results:
  - Without correction → CTR: 121 ps
  - Including 4 mm DOI bias correction (timewalk): → CTR:87 ps
  - For 40% of singles (with highest energy sharing): → CTR: 56 ps





SMMS simulation: DOI

- DOI confusion map for CNN
- Discrimination quality threshold equivalent to FWHM of Gaussian (75% precision)
- Variability in DOI prediction quality for different DOI levels
- Overall precision for 3 mm at 78%



Next step:
Apply nanophotonics to scintillator science

- Increase the radiative recombination rate of excitons through quantum confinement in nanocrystals

- Enhance light-emission through engineering of optical density of states
  - *Hyperbolic metamaterials*
  - *Purcell effect (Plasmonic materials)*

- Combine both ☞ Nanophotonic scintillators

Scintillator engineering to boost the light emission yield and rate

- Crystal engineering limited so far to controling or compensating crystallographic defects to limit afterglow and improve radiation resistance
- Can we engineer the oscillator strength?
- Decay time is driven by the electric dipole moment between the excited and fundamental states

$$\Gamma_\nu = \frac{1}{\tau_\nu} \propto \frac{n}{\lambda^3}\left(\frac{n^2+2}{3}\right)^2 \sum_f \left|\langle f \,|\quad|\, i \rangle\right|^2$$

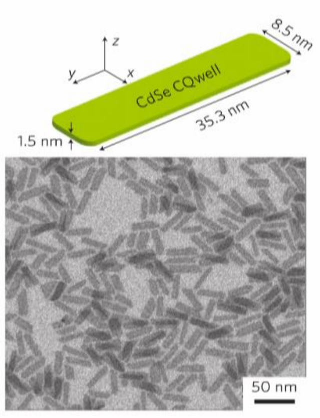
Local polarization field
Related to ion coordination
and local symetry level

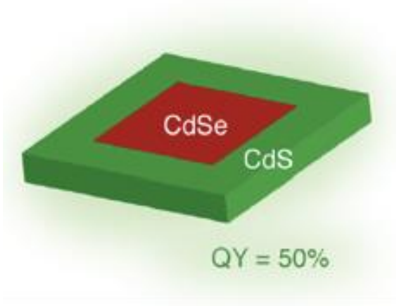
Electric dipole moment operator

- Exciton confinement in quantum wells leads to efficient and sub-ns luminescence
- Properly designed quantum dot-based heterostructures can produce coherent phasing of dipoles over many unit cells and achieve Giant Oscillator Strength (GOS) in specific directions

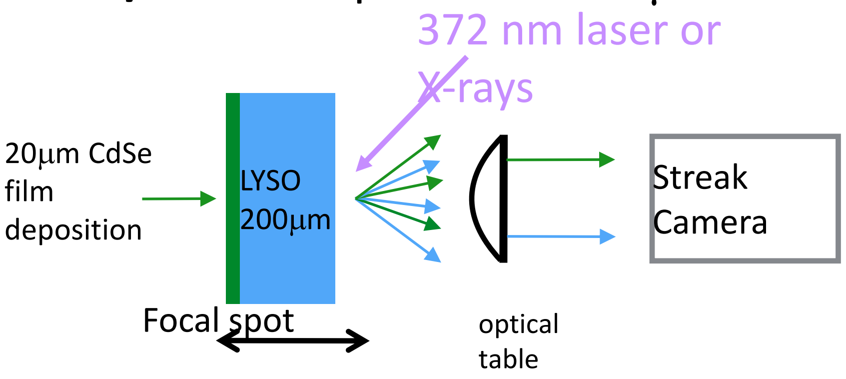
CdSe nanoplatelets on LYSO plates

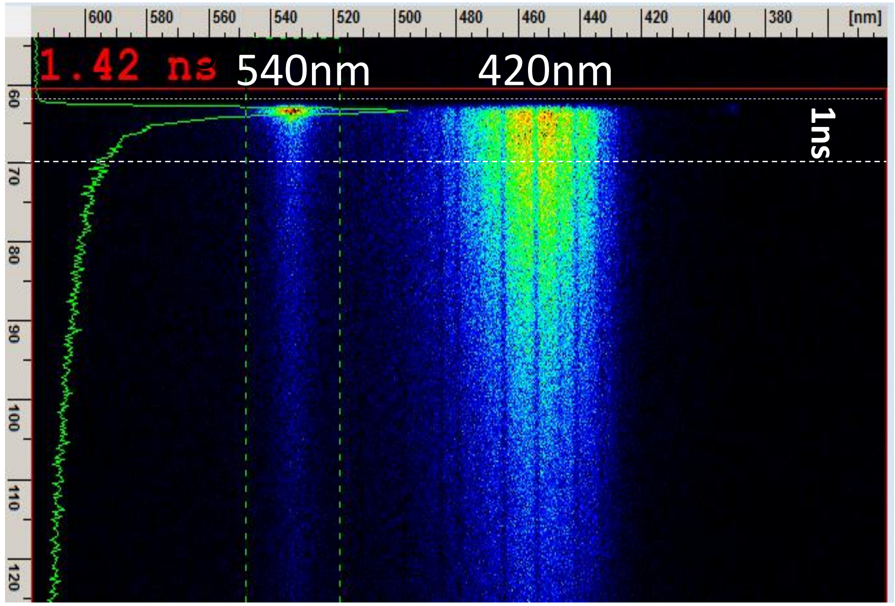
J.Grim, I. Moreels
ITT, Italy

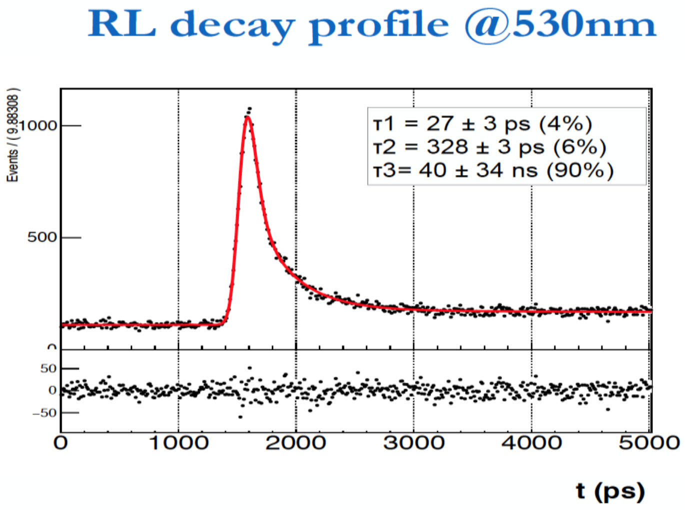




LYSO plate 200μm thick
+ CdSe/CdS nanoplate film 20μm thick

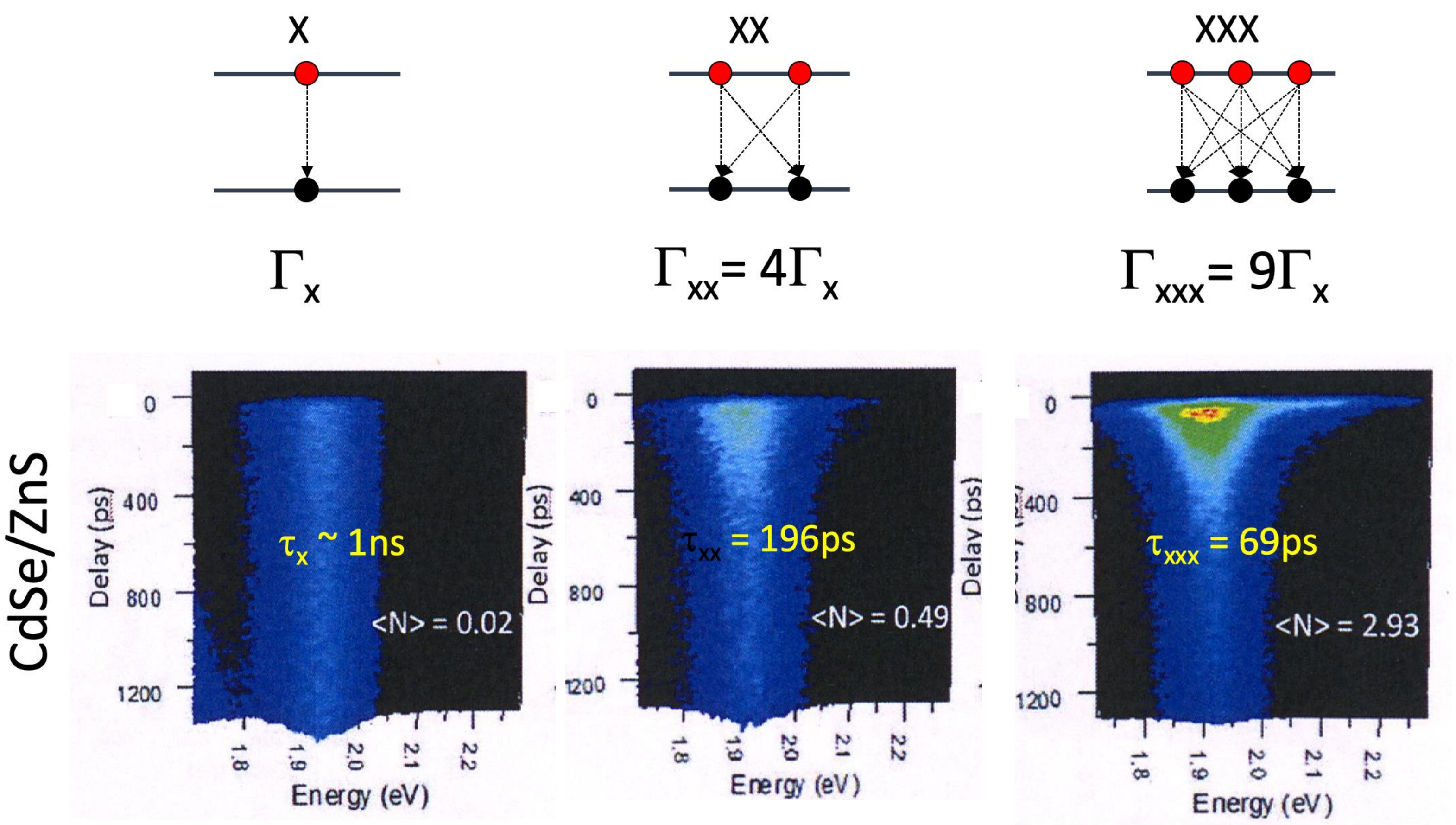






R. Martinez Turtos et al., JINST_068P_06

Multi-exciton quantum confinement



Padilha et.al., Nano Lett. 2013, 925-932

ZnO:Ga QDs

Metal halide Perovkites

CdSe/CdS Nanoplatelets

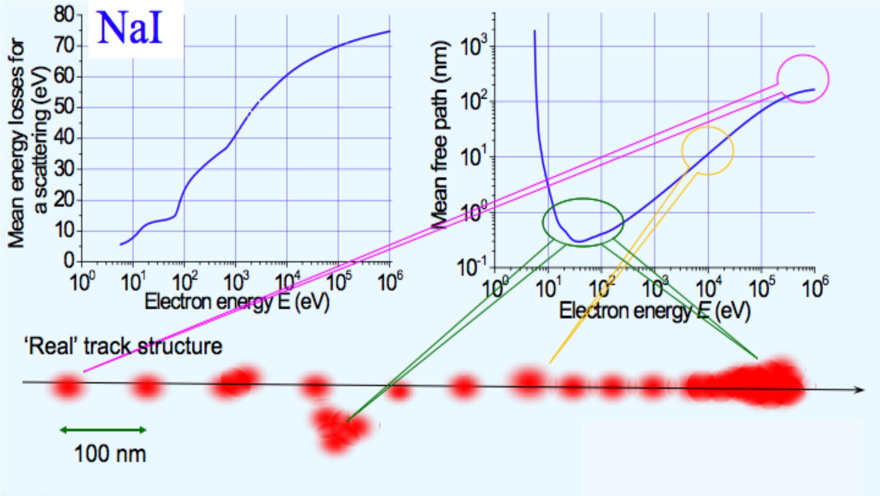
InGaN/GaN Quantum wells

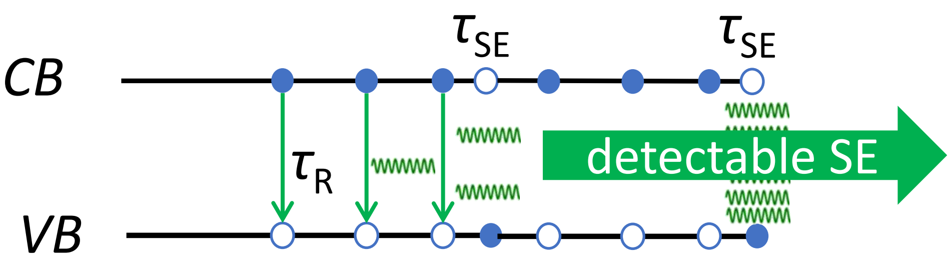
Towards a self-triggered lasing γ-ray detector

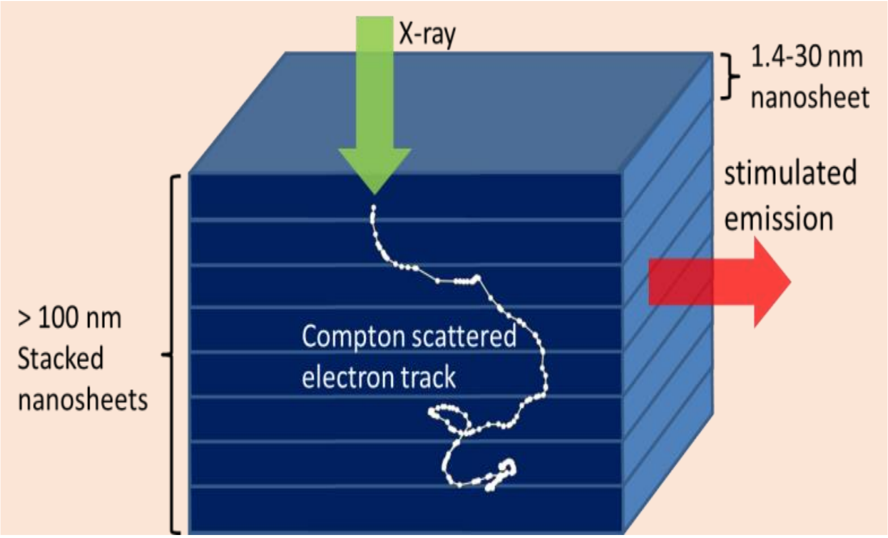
- Ionization density per dE/dx event can reach

  $> 10^{20}$ eV/ $cm^3 \approx 10 J/cm^3$

- Ultrafast X-ray or γ-ray self-triggered stimulated emission is within reach





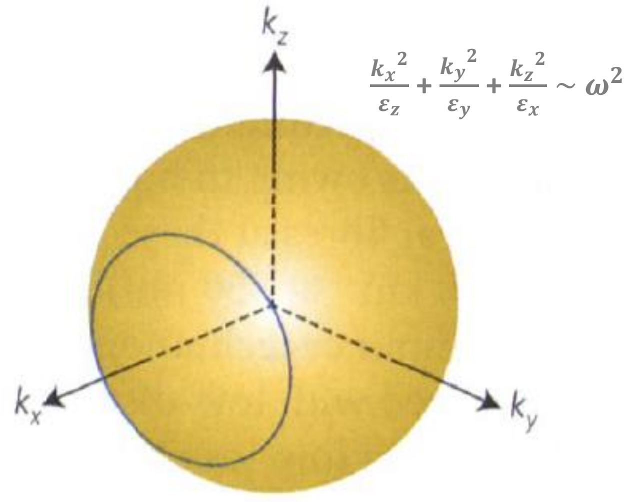


Courtesy J.Grim, I.Moreels, ITT, Italy

Increasing the Photonic Density of States with Hyperbolic Metamaterials

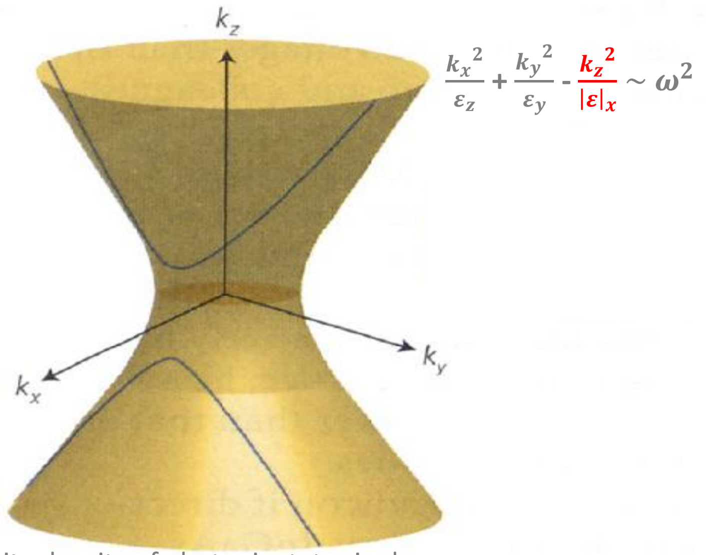
Isofrequency contour from dispersion formula: $k = \frac{2\pi}{\lambda} \sim \omega \frac{n}{c} \sim \omega\sqrt{\epsilon}$

for isotropic dielectric material

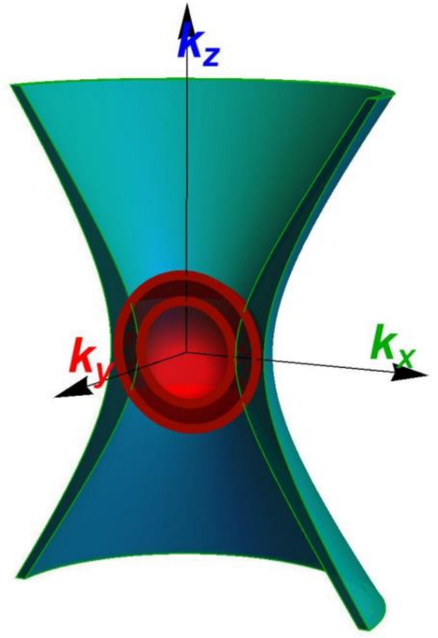


Finite density of photonic states in dω

for anisotropic hyperbolic material



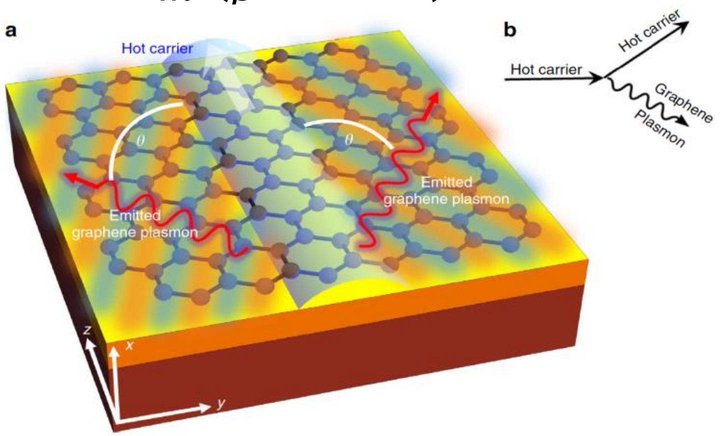
Infinite density of photonic states in dω



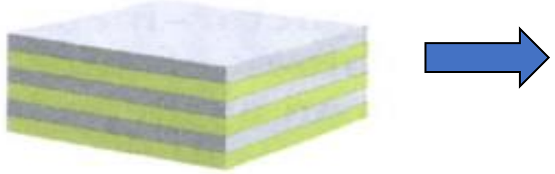
An intuitive counting procedure in k-space consists of calculating the volume between the isofrequency contours at ω(k) and ω(k) + Δω.

Lowering Čerenkov threshold ?

- The Čerenkov effect offers the fastest energy conversion scheme from charge particles to photons
- Čerenkov threshold (101 keV in LSO) can be strongly lowered (↘100's eV) in specifically designed nanostructured metamaterials
- Produce transition radiation constructive interference through resonant plasmonic states in photonic crystals
- Related more formally to the Smith Purcell effect
  - A kind of Cerenkov or transition radiation emission → free electron lasers
  - $\lambda = \frac{a}{m}\left(\frac{1}{\beta} - cos\theta\right)$!! No velocity threshold !!



I. Kaminer et al., Nature Comm., 13 June 2016



D. Lu et al., Nat. Photon. 11, 2017

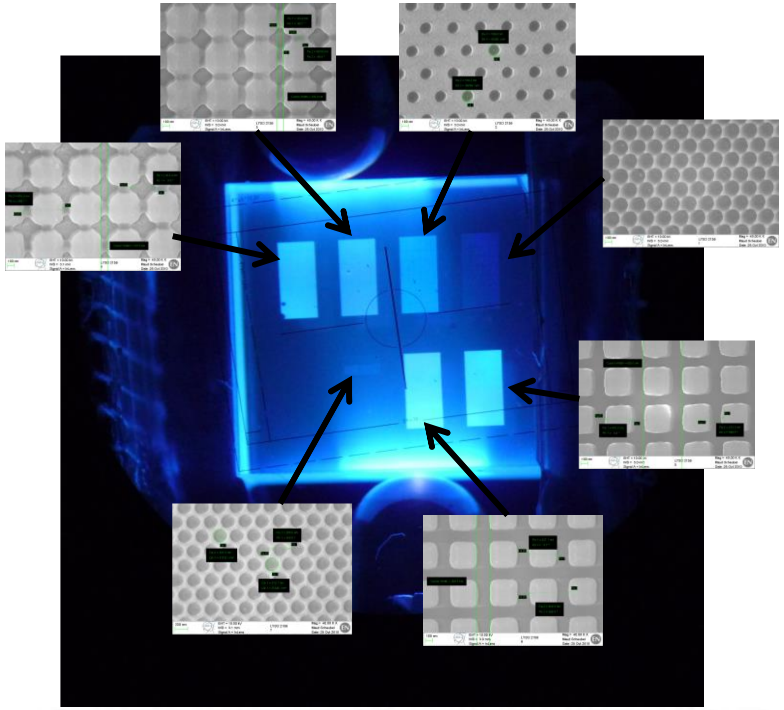
Stack of Gold + SiO_2

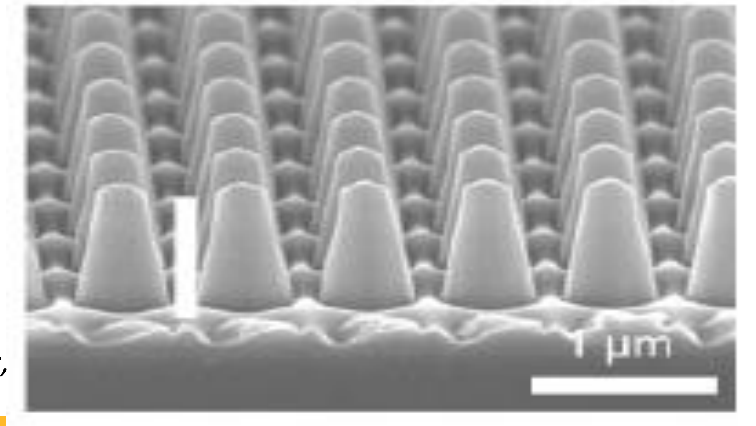
Cerenkov threshold ↘ 250eV

Cerenkov yield ↗ > 100

Photonic crystals to improve scintillator light extraction

- Photonic crystals improve scintillator energy resolution:
  - By increasing the light output
- Photonic crystals improve scintillator timing resolution by two means:
  - By increasing the light output and therefore decreasing the photostatistics jitter
  - By redistributing the light in the fastest propagation modes in the crystal
- Nanoimprint and colloidal technologies offer attractive solutions for cost effective mass production



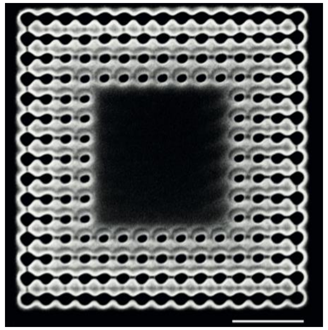


A. Knapitch, P. Lecoq, ***Review on photonic crystal coatings for scintillators,*** *International Journal of Modern Physics A, Vol. 29 (2014) 1430070*
M. Salomoni et al., ***Enhancing Light Extraction of Inorganic Scintillators using Photonic Crystals,*** *Crystals 2018, 8, 78; doi:10.3390/cryst8020078*

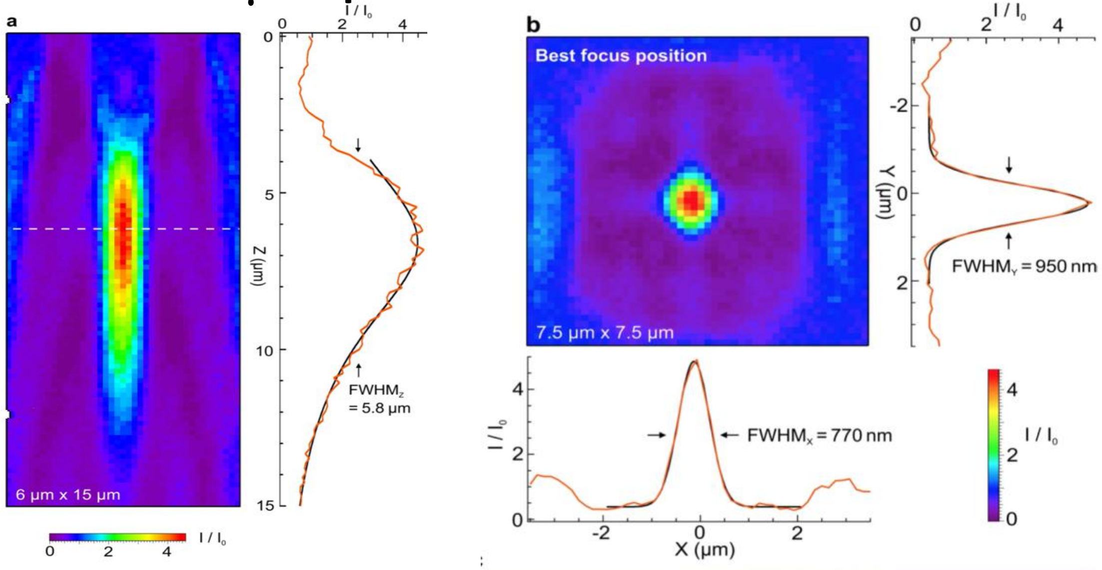
GRIN light concentrator

CERN Photoquant project

Designed and fabricated 4x4μm Nb_2O_5 metalens with refractive index gradient introduced by holes of varying diameter

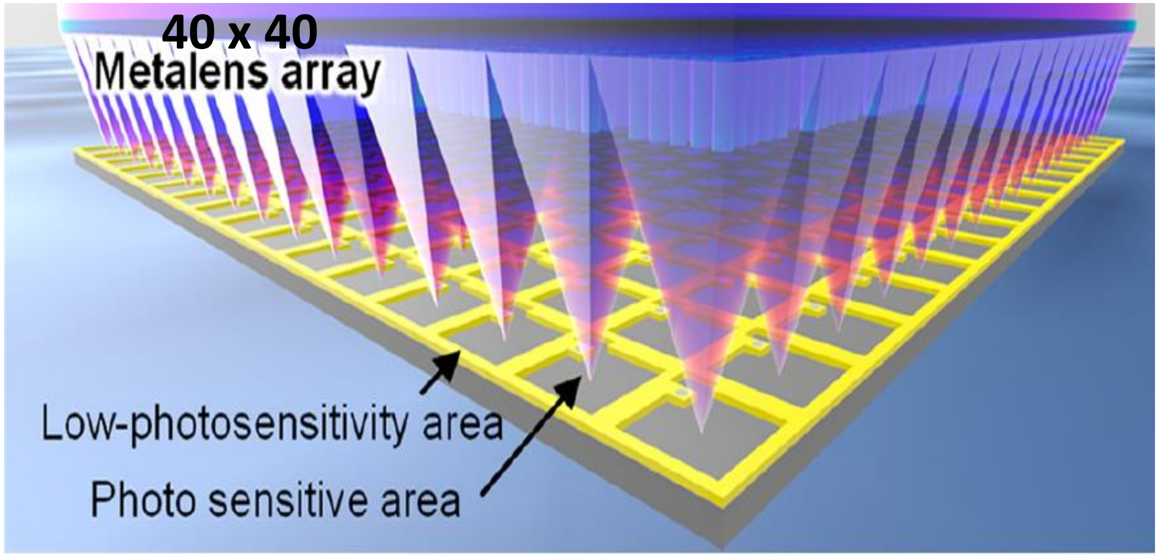


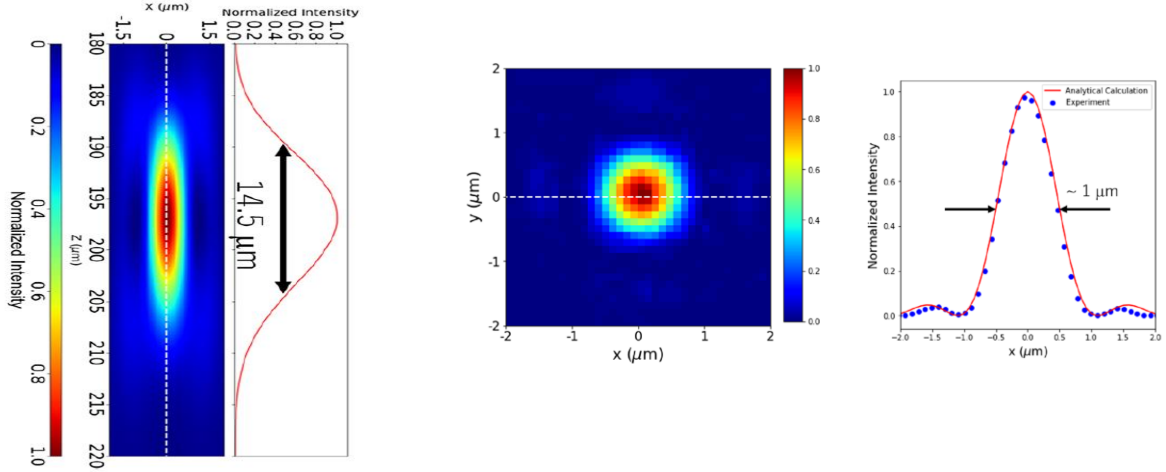
93% of incident light concentrated
In < 1μm spot diameter or <5% of total area



*E. Mikheeva et al., **CMOS-compatible all-dielectric metalens for improving pixel photodetector arrays,** APL Photonics 5, 116105 (2020, doi: 10.1063/5.0022162*

Hamamatsu

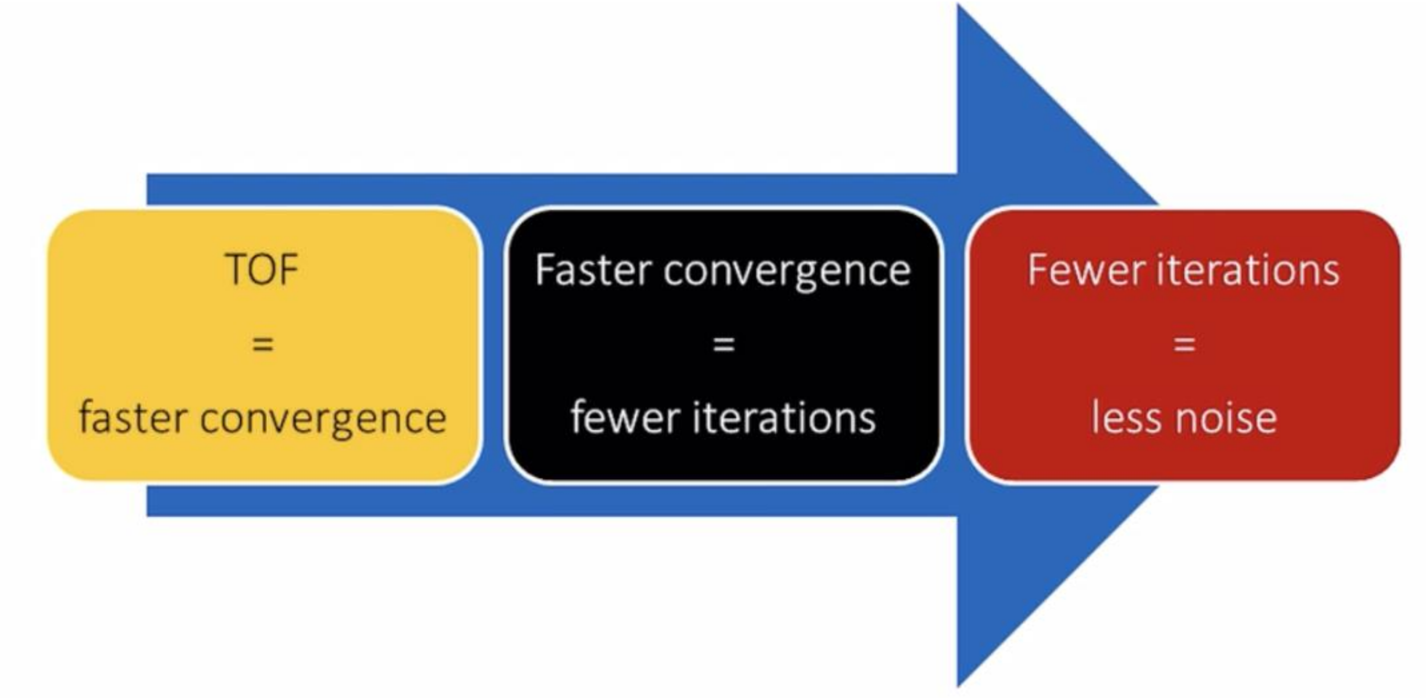


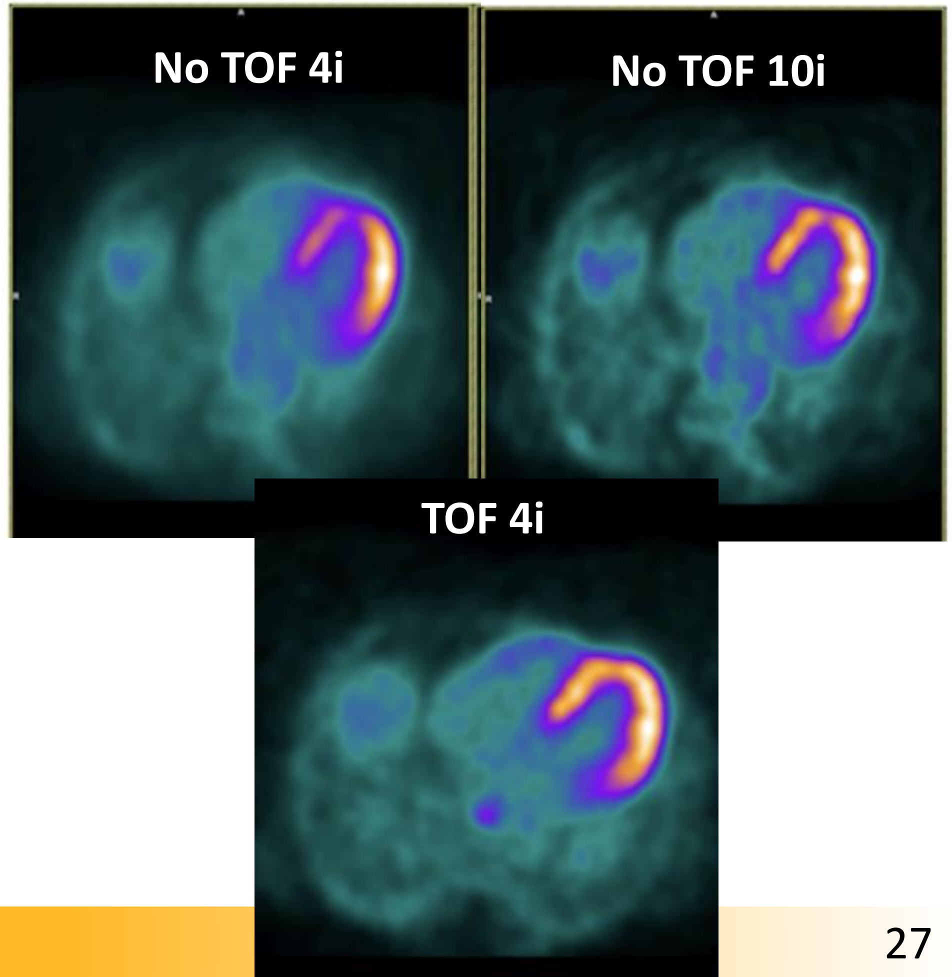


S. Uenoyama, R. Ota, ***40 x 40 Metalens Array for Improved Silicon Photomultiplier Performance,*** ACS Photonics, DOI:10.1021/acsphotonics.1c00257, May 2021

Conclusions: Medical

- Time of Flight is more than just post-acquisition enhancement
- It is a fundamental improvement in the PET acquisition process
- It allows detection of lesions to be seen that would otherwise be missed





Conclusions: Technical

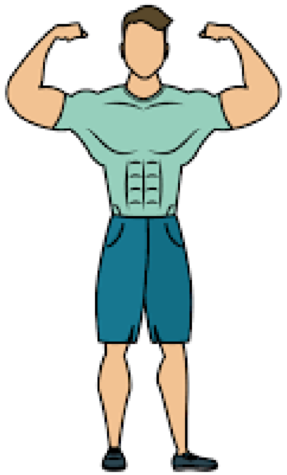
Metascintillators are a door open to the future of ionisation radiation detectors (not only for PET applications)

- By making use of light-management strategies, Nanophotonics privides a playground to make the unimaginable come closer
- This opens the way to transformation optics (a kind of extrapolation of Maxwell's equations invariance under Lorenz transformation), allowing to envision a distortion of real space that results in a desired functionality:
  - Ultrafast emission
  - Enhanced fluorescence yield through plasmonic resonances
  - Redirect light into preferred directions
- Generation of a much richer information for each event, which can be exploited by modern AI techniques

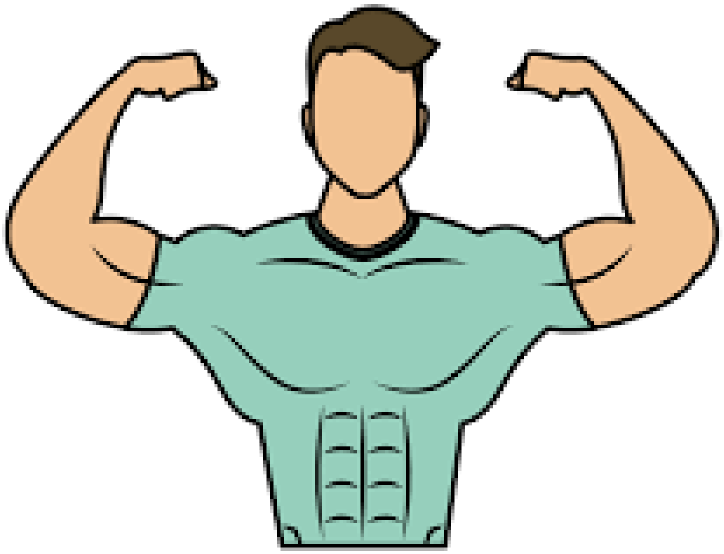
Toward intelligent γ- and X-ray detectors

Time of flight: the last frontier in PET

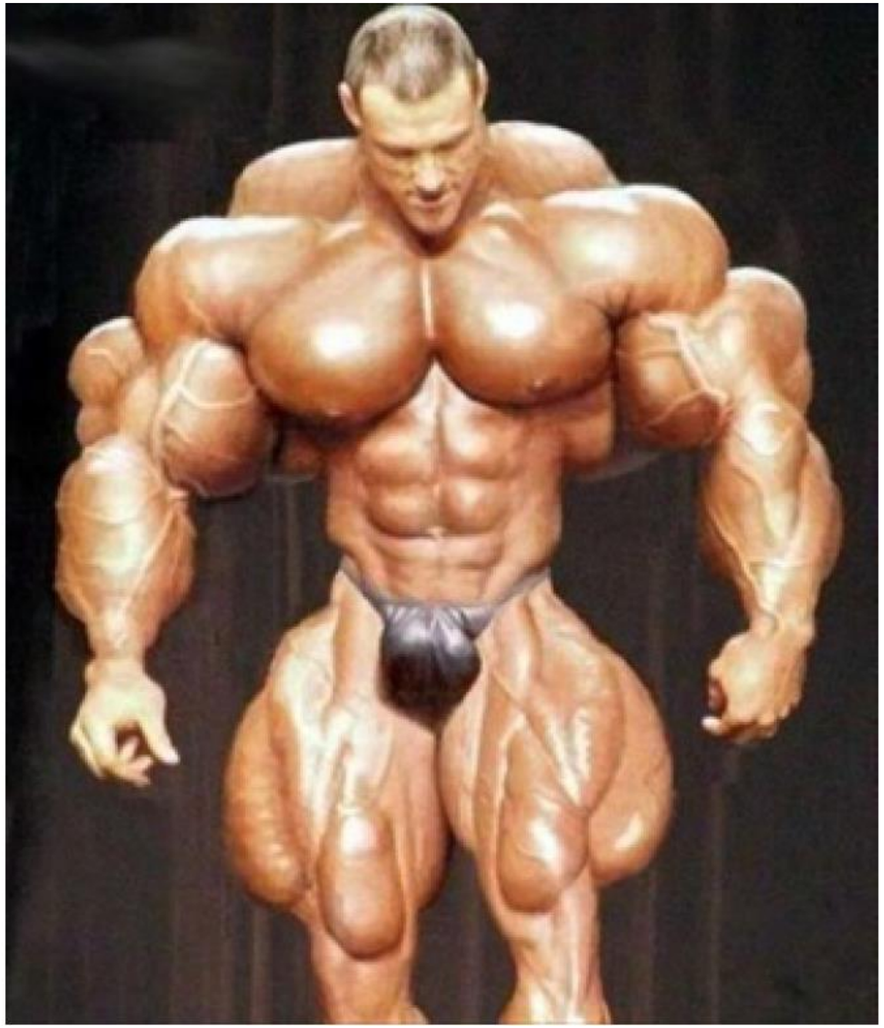
PET



200ps TOFPET



10ps TOFPET



CERN i3M Instituto de Instrumentación para Imagen Molecular

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https://the10ps-challenge.org

European Research Council Executive Agency

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