The 10ps TOFPET challenge

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When you have an impossible dream
Setup a challenge!

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in the frame of the ERC Advanced Grant Agreement N°338953–TICAL

European Research Council
Executive Agency

Why a challenge?

- There is a need
  - Modern medicine requires a 10-fold increase of the PET sensitivity
  - 10ps CTR would introduce the reconstructionless paradigm shift in PET imaging
- This is feasible: A detailed study in the frame of the ERC Advanced Grant TICAL has demonstrated that
  - There are no physical barrier at all stages of the detector chain
  - Enabling technologies are becoming available to break all the present limits
- A challenge is a very good way to federate a community around an ambitious goal

At the CCC brainstorming workshop of Oct 2015 in Cassis
C. Morel proposed to set a challenge

The 10ps challenge

1992: FAI raised a challenge for the first balloon circumnavigation

March 1999: Breitling Orbiter III circumnavigate the globe in 19 days 1 hour 49 minutes and won the Budweiser Cup

July 2016: Solar Impulse closed the loop of the Round-the-World without fuel attempt

This is a clear-cut case to shed light on TOF-PET with CTR < 10ps FWHM and raise a challenge on reconstructionless positron tomography

Courtesy of C. Morel, CPPM

The need: Why 10ps TOFPET?

- TOF for direct 3D information
  - Requires 10ps TOF resolution for 1.5mm resolution alon…
- Allows limited angle tomography withou…
- > 15-fold improvement in S/N ra… …andom rate
  - Equivalent potential in d…
    - Annual natural…
    - Retu…
  - …dies per injection
  - …radiotracer production infrastructures
- …ve to incorrect attenuation correction and normalization
  - Less stringent requirements on CT (cost, dose reduction)
  - Reduce problems of not direct attenuation measurement in PET/MR
- Open PET to new categories of patients (children, fœtus)

Current state of the art for commercial PET: 250-500ps
Current state of the art for PET demonstrators: 200-300ps
Current state of the art in the lab: 80-120ps (3-20mm crystals)

Feasibility: The conditions to be met

- Identify the critical parameters
  - Light production
  - Light transport
  - Photodetection
  - Readout electronics
- For each of the critical parameters
  - Make sure that no physics barrier will compromise the goal
  - Identify enabling technologies to reach the objective
    - Metascintillators, photonic crystals, 3D MD SiPM, etc…
  - Organize a vigorous, ambitious and coordinated effort to push the limits and transform the Myth into a Reality.

Requires a large scale collaborative effort

The detection chain

From the time of detection $t_{d,i}$ of n optical photons

$$T_d = \{ t_{d,1}, t_{d,2}, \ldots, t_{d,n} \}$$

which provides the Fisher information $I_{Td}(\Theta)$ of the γ ray interaction Θ

define the Cramer-Rao lower bound by minimizing the variance of the time estimator Ξ

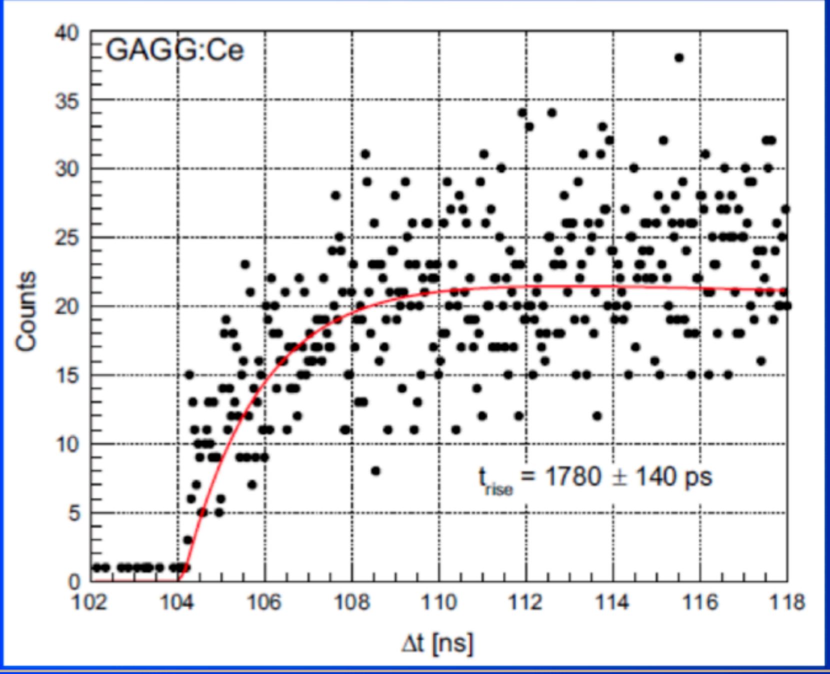
$$Var(\Xi) \geq 1 / I_{Td}(\Theta)$$

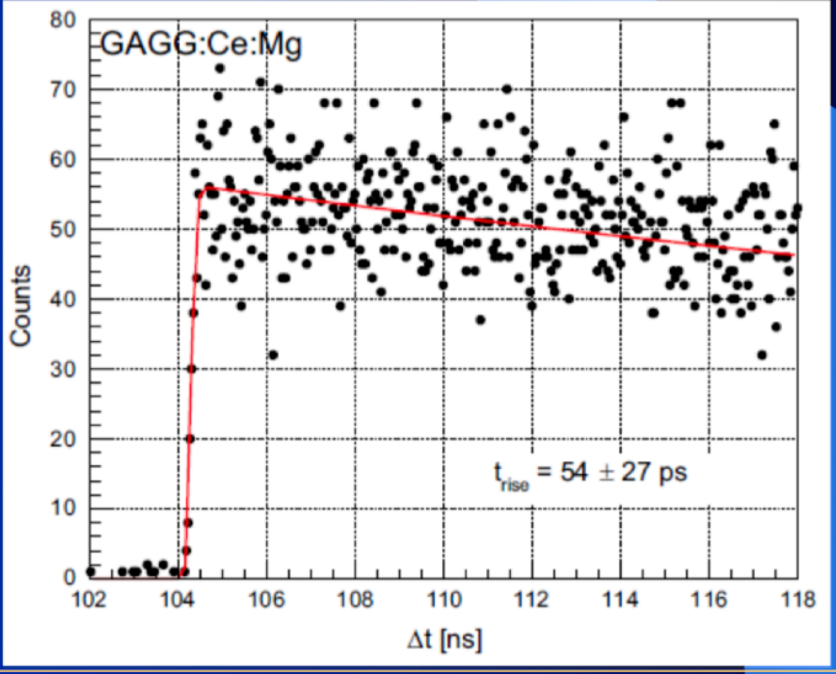
LIGHT PRODUCTION

Engineering known scintillators

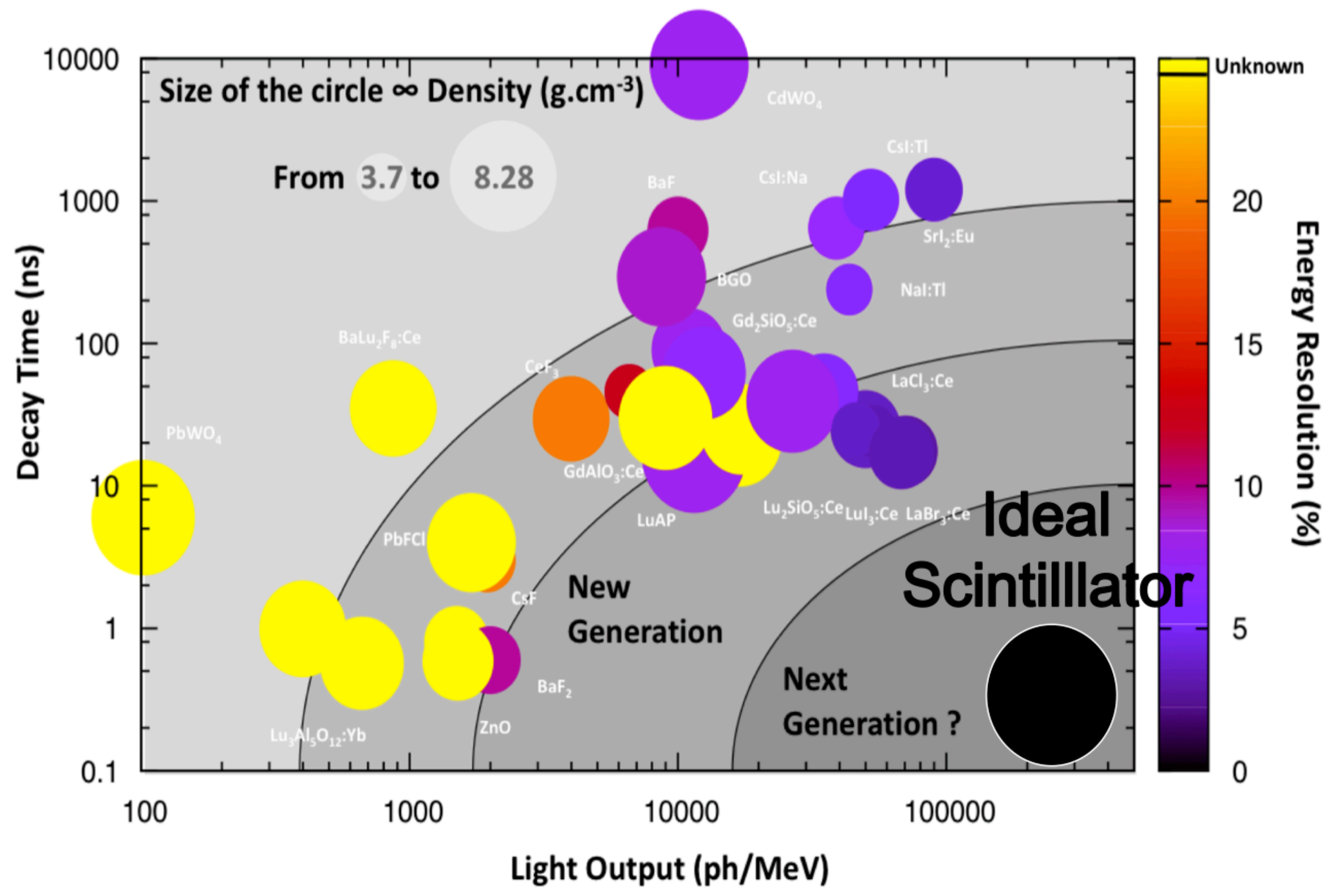
- Light yield: ≤ 100'000 ph/MeV
- Decay time: ≥ 10ns
- Rise time:
  - Typically 100ps (LYSO) to several ns
  - Can be reduced by co-doping to ~20ps (LYSO)

~ 30ph / 10ps @511keV



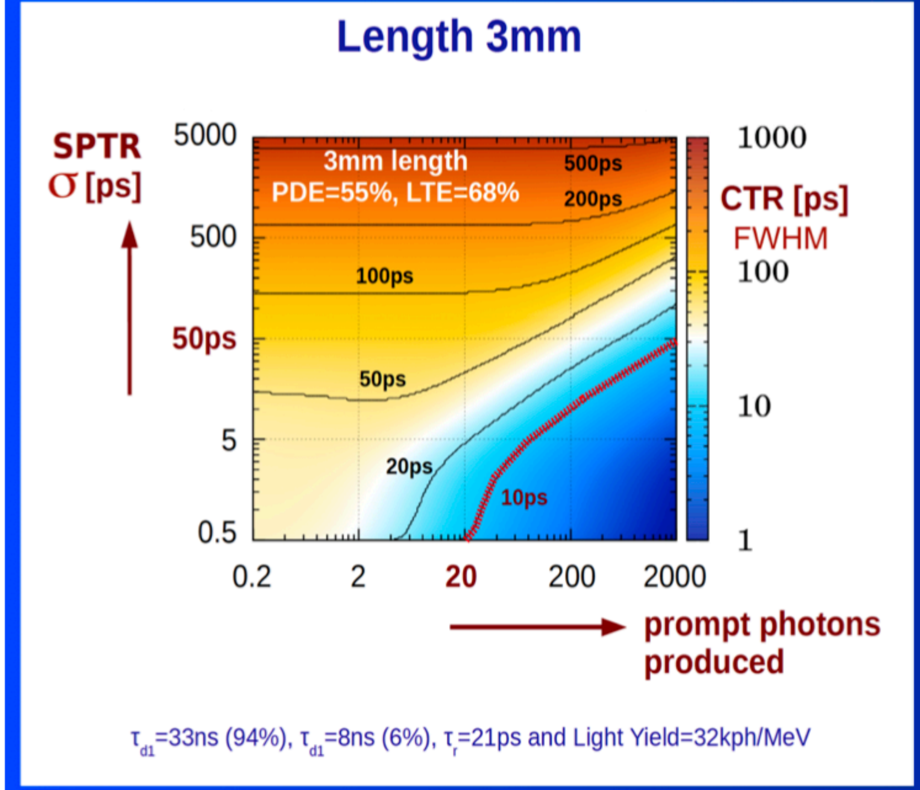


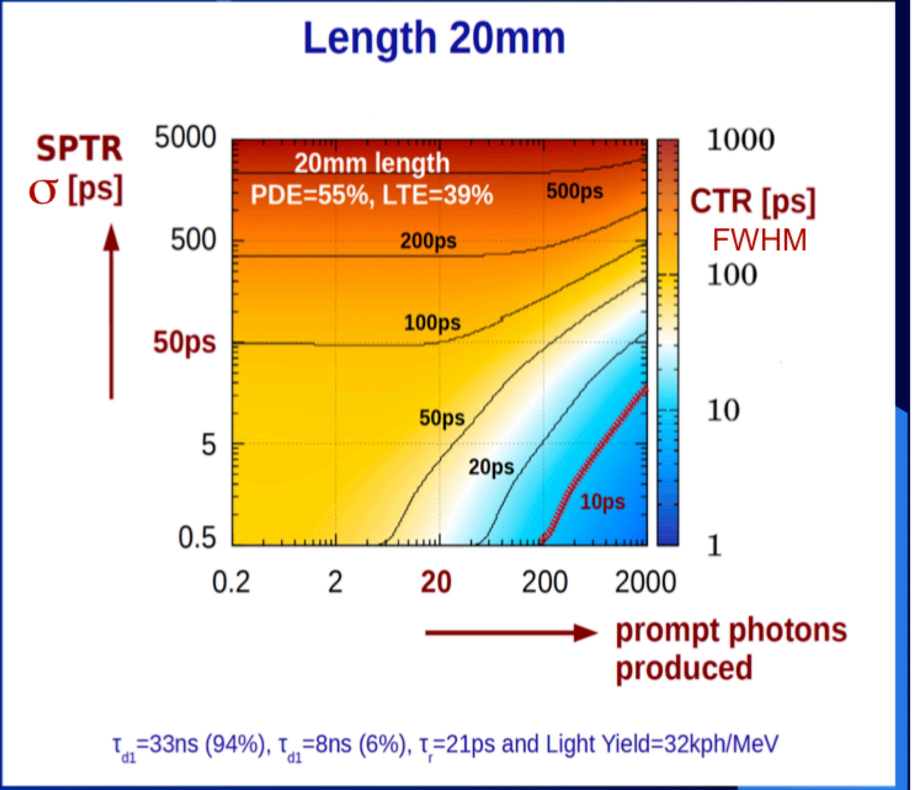
Classification of scintillators



Prompt photons to boost the timing resolution

Parameters for LSO: Ce, Ca and Hamamatsu S10931-050P MPPC



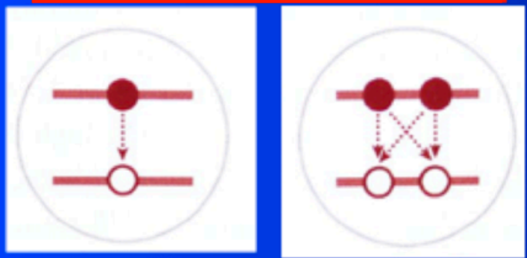


S. Gundacker, CERN-THESIS-2014-034 - 210 p.

Possible sources of prompt photons (< 1ns)

Ce^{3+} Activator: 5d-4f
Ca^{2+} & Mg^{2+} co-doping
$\tau_r \sim 20$ ps $\tau_d \sim 16$ ns

Excitons/Bi-exciton stable at 300 K



$$\frac{1}{\tau} = \frac{4e^2}{3\hbar c^3}\omega_{21}^3 \left|\vec{r}_{21}\right|^2$$

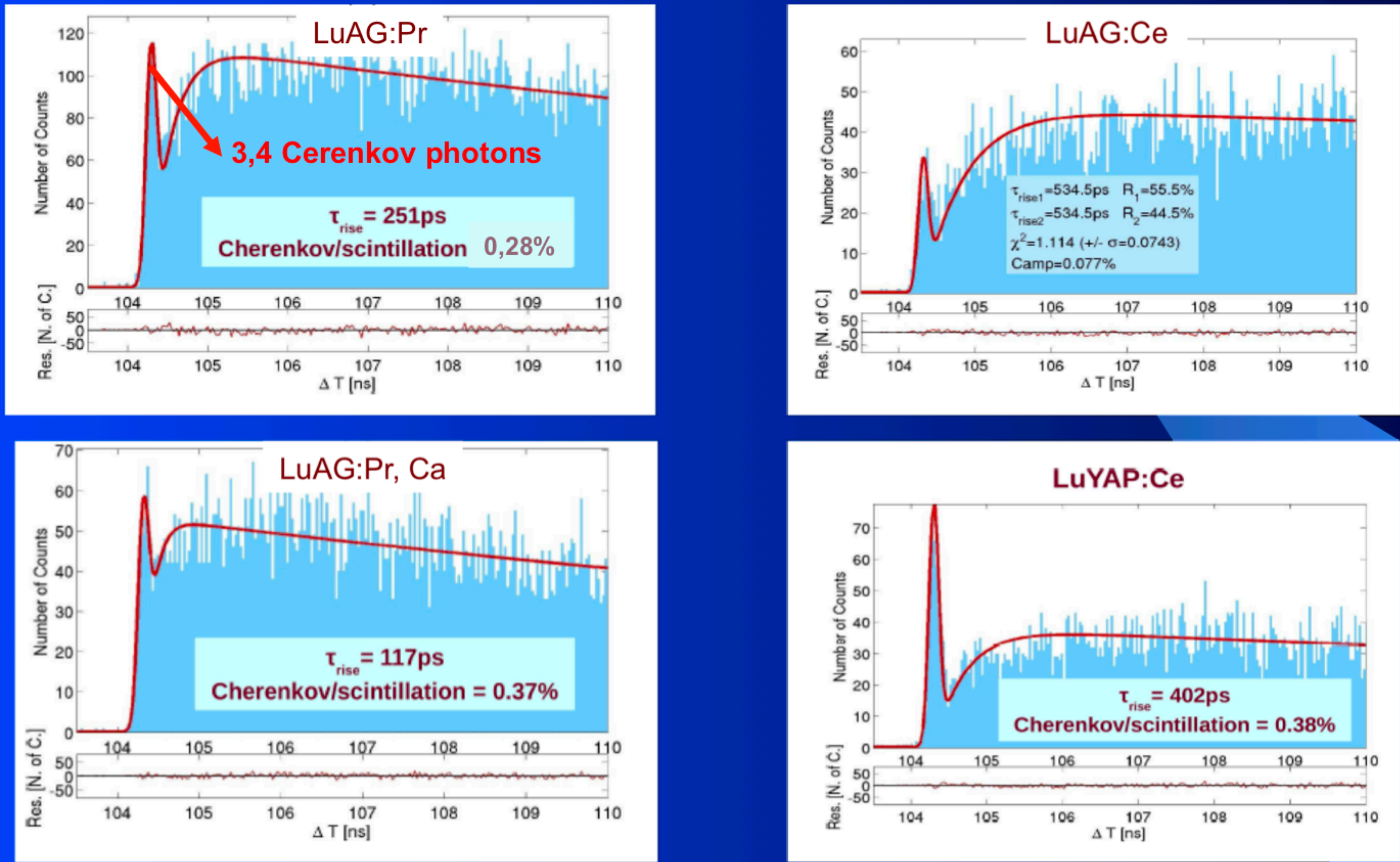
Hot Intraband Luminescence
0.1 - 10 ps

Cross Luminescence
<1ns
<300 nm – low LY

Cerenkov
$\tau \sim$ 5-10 ps

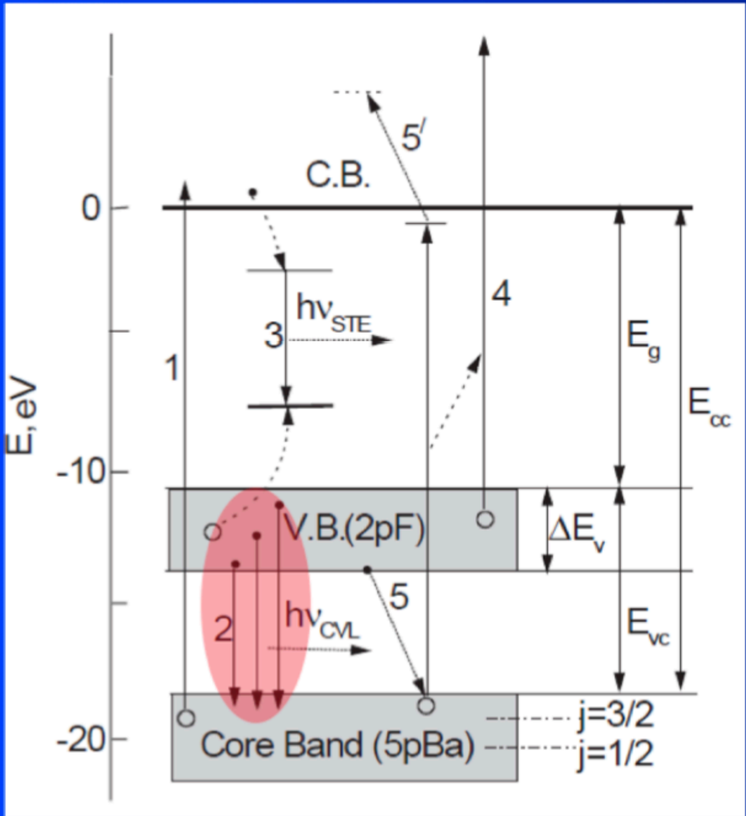
High donor band semiconductors
<1ns
quenched at room temperature

Cerenkov contribution

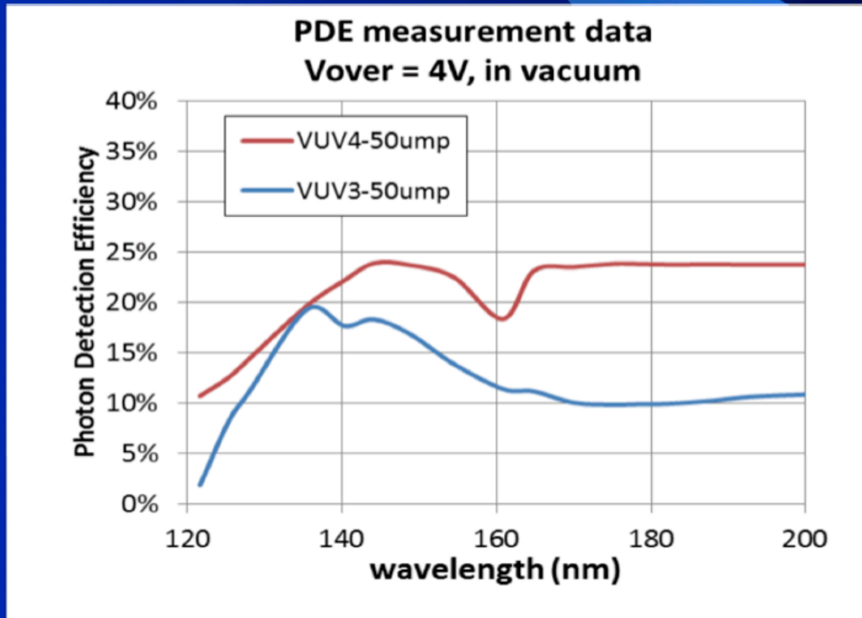


S. Gundacker, E. Auffray, K. Pauwels, and P. Lecoq, Phys. Med. Biol. , vol. 61, pp. 2802–2837, 2016.

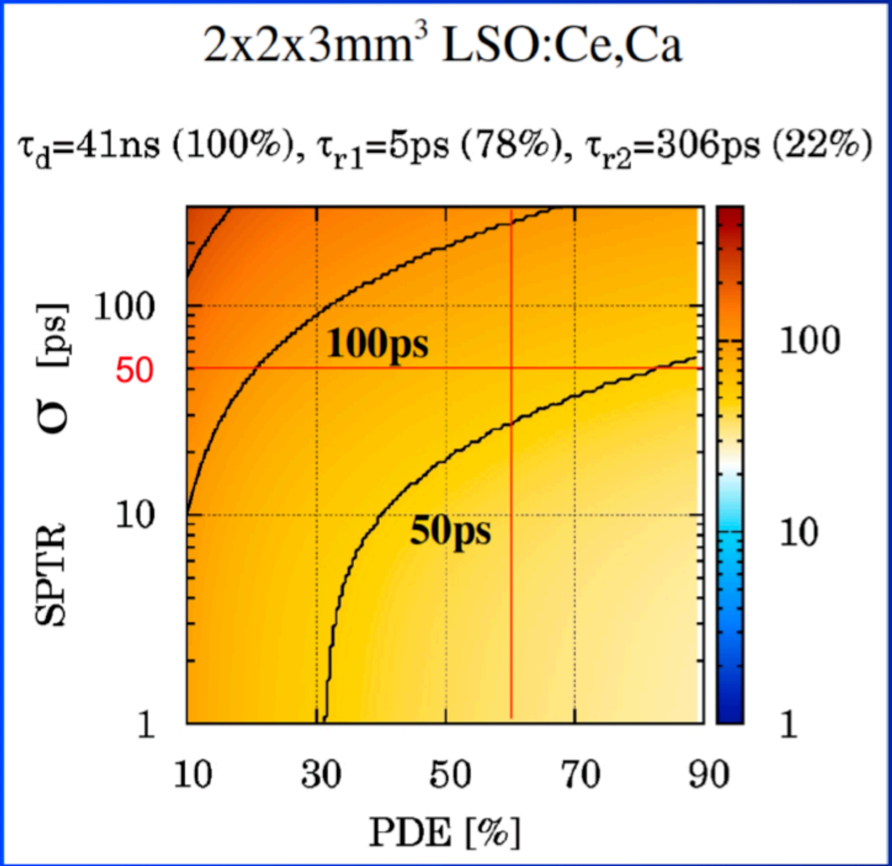
Cross luminescence with new UV sensitive SiPM?

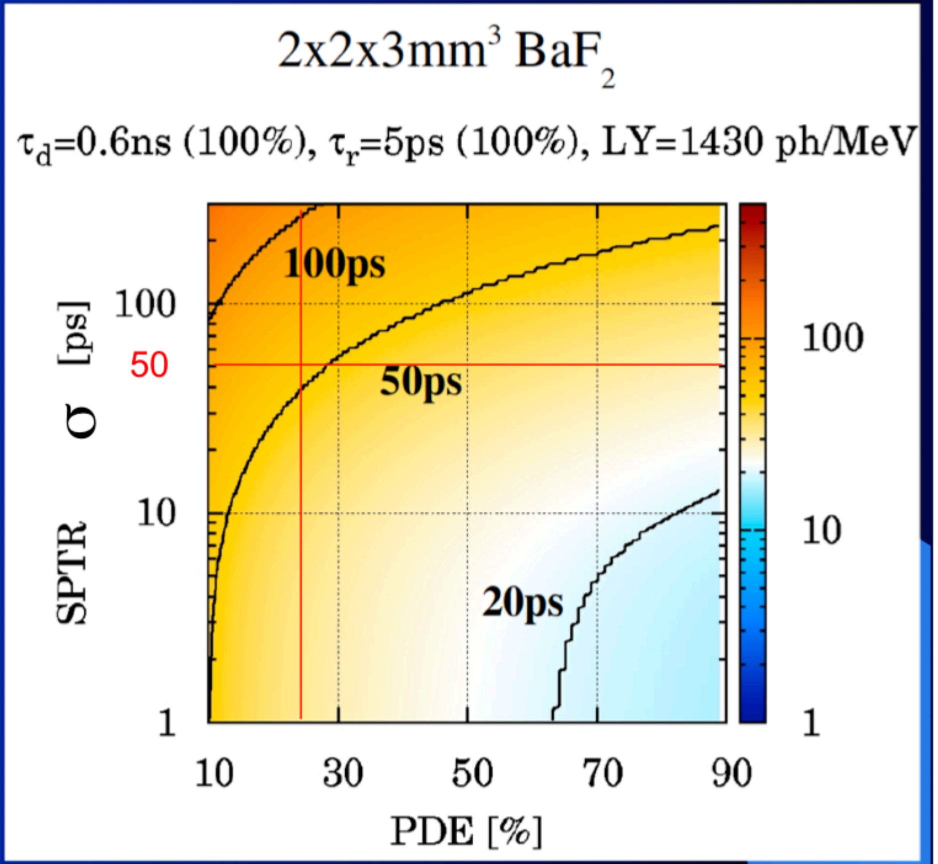


Crystal	$h\nu_{em}$ (eV)
BaF_2	5.6/6.4
CsF	3.1
CsCl	5.1
CsBr	6.0
RbF	5.25



LSO:Ce,Ca / BaF2

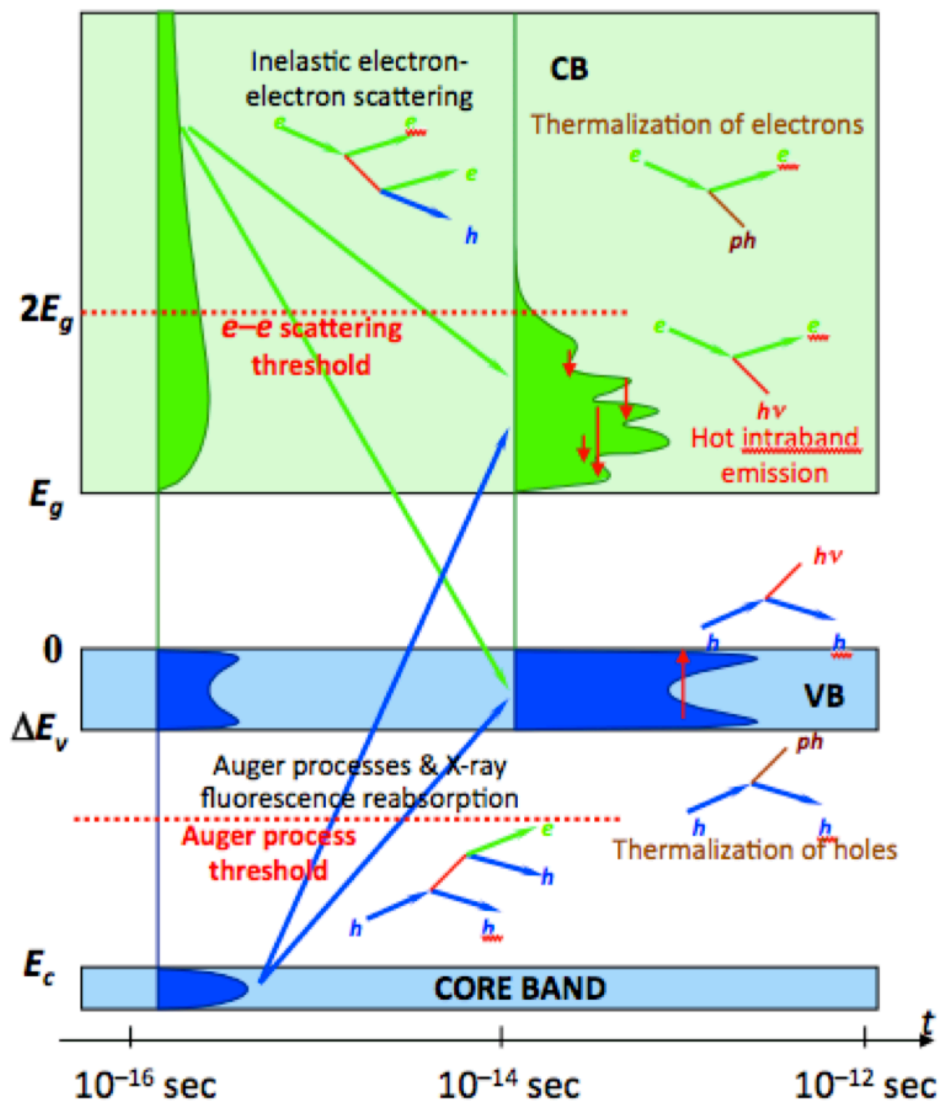


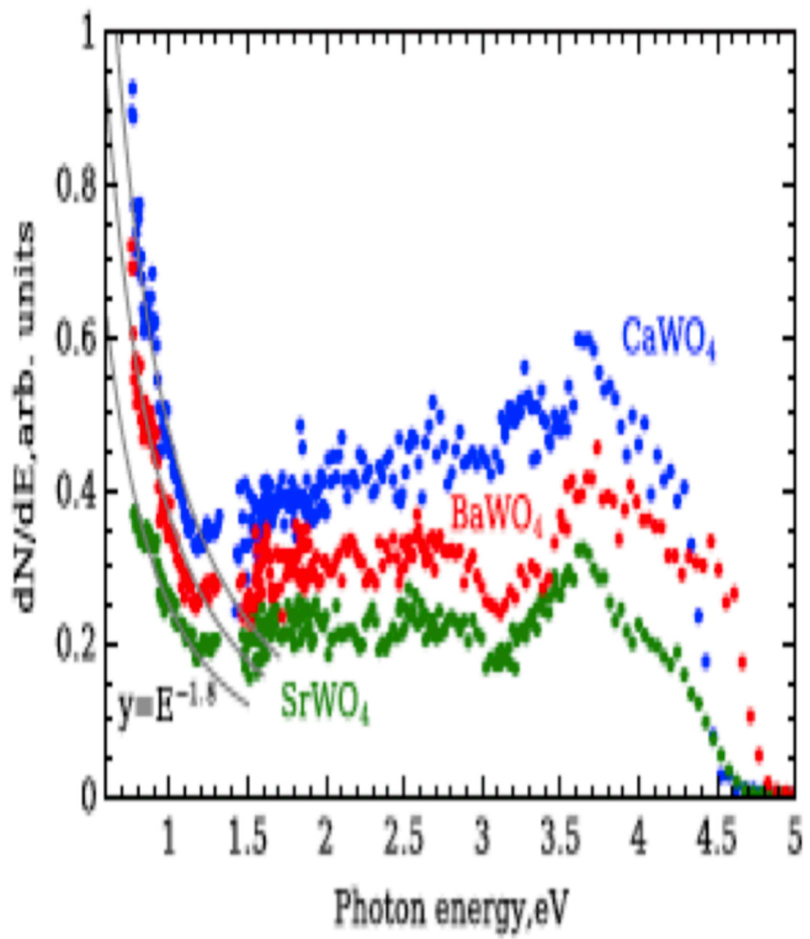


Glue coupling: LTE = 68%

Air coupling: LTE = 35%

Hot intraband luminescence

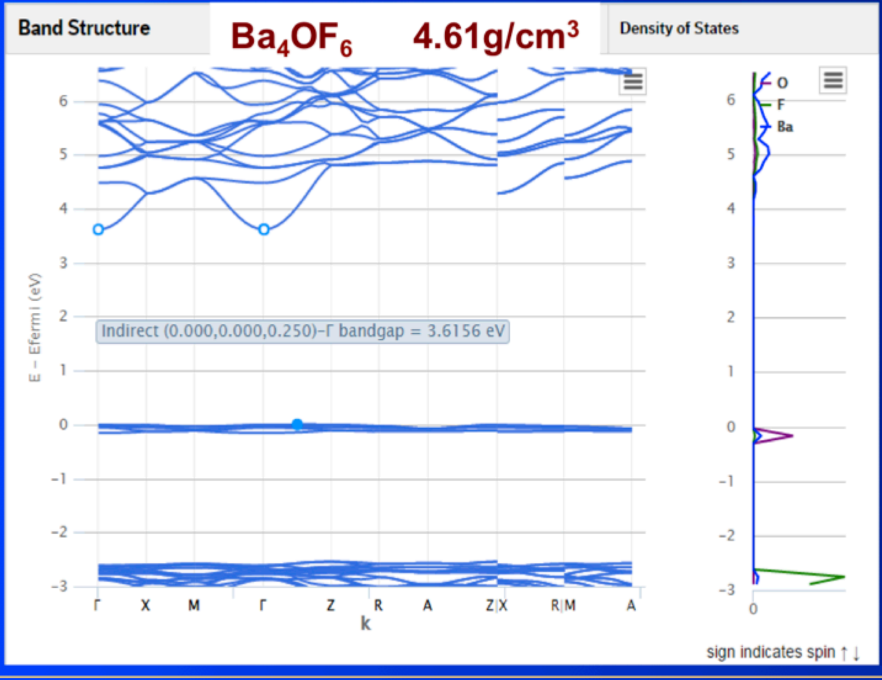


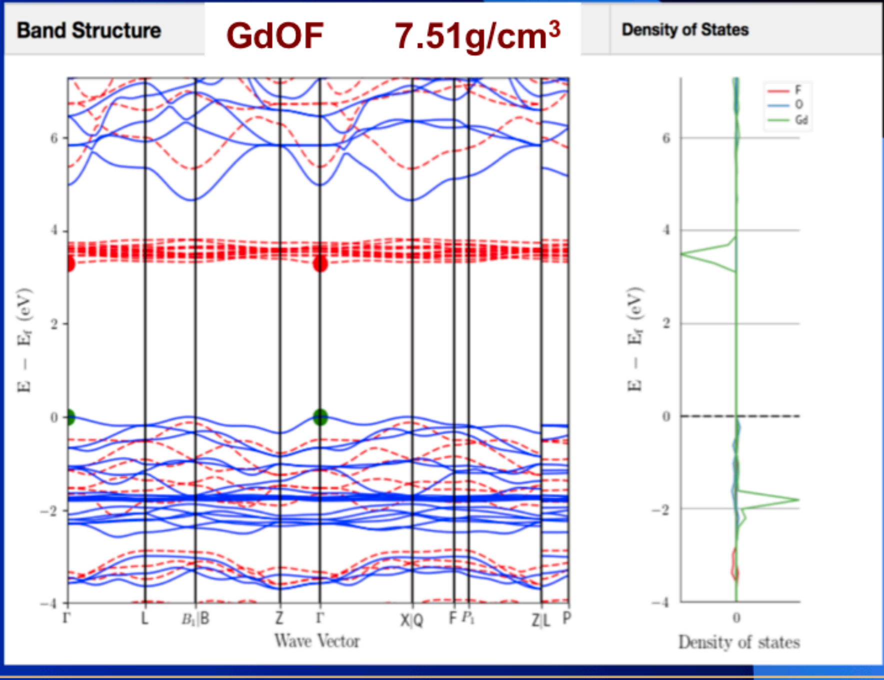


Omelkov et.al., J. Lum., 176 (2016) 309–317

Search for Candidates for Hot intraband luminescence

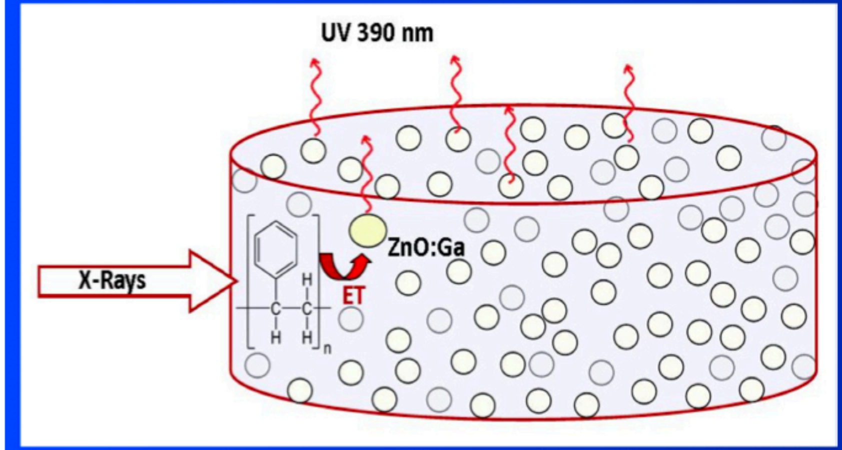
- Search for materials with splitting of the conduction/ valence band
- Search for materials with flat sub-bands for a perfect delocalization of the electrons/holes
  - Examples Oxy-halide compounds

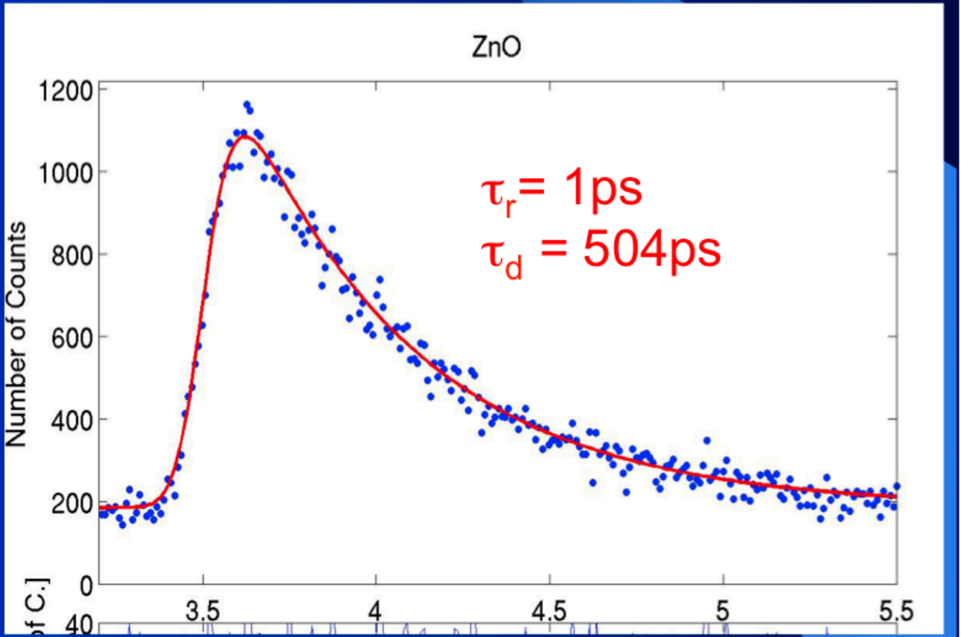




Quantum confinement ZnO:Ga PS composite scintillator

- Highly luminescent ZnO:Ga nano crystals 80-100nm
  - Prepared by a photochemical method
  - 4000 pe/511keV in powder (same as LSO)
  - Embedded in a polystyrene sheet 10%weigth



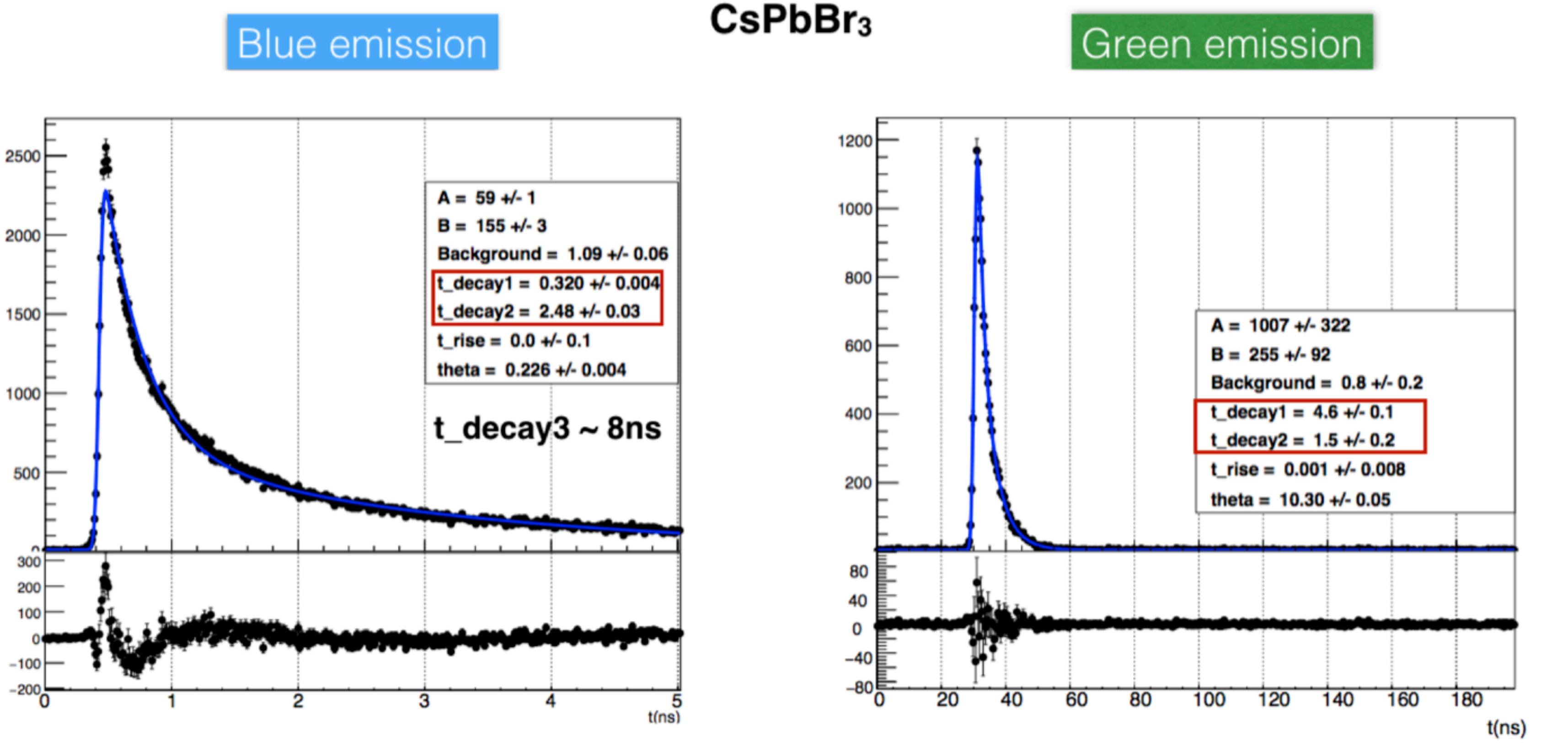


R. Martinez Turtos et al., Phys. Status Solidi RRL 10, No. 11, 843–847 (2016)

Quantum confinement
Lead halide perovskite nanocrystals

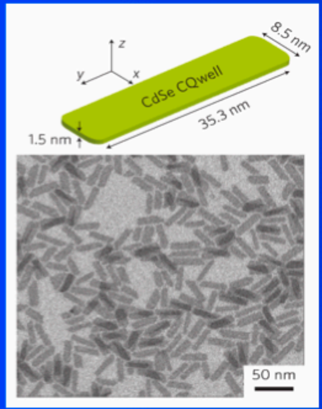
Perovskite nanocrystals exhibit high "defect tolerance", meaning that, unlike conventional semiconductors, they can be bright emitters without electronic passivation of their surfaces.

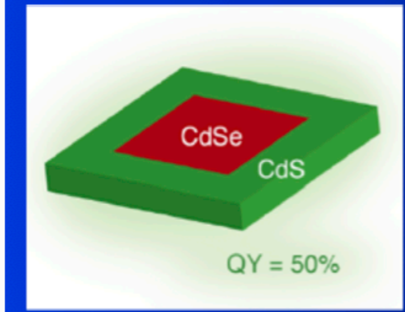
$CsPbBr_3$



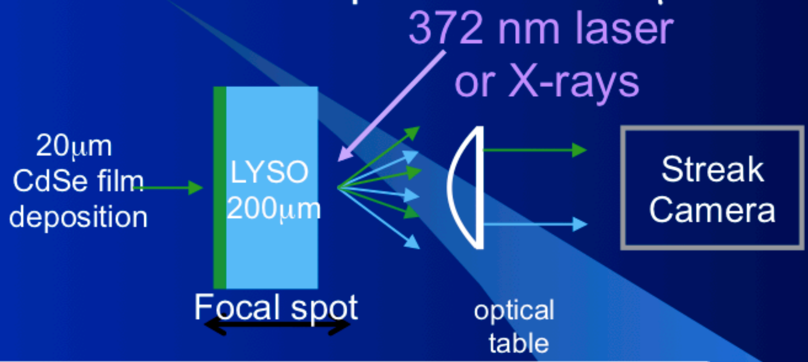
Quantum confinement CdSe nanoplatelets

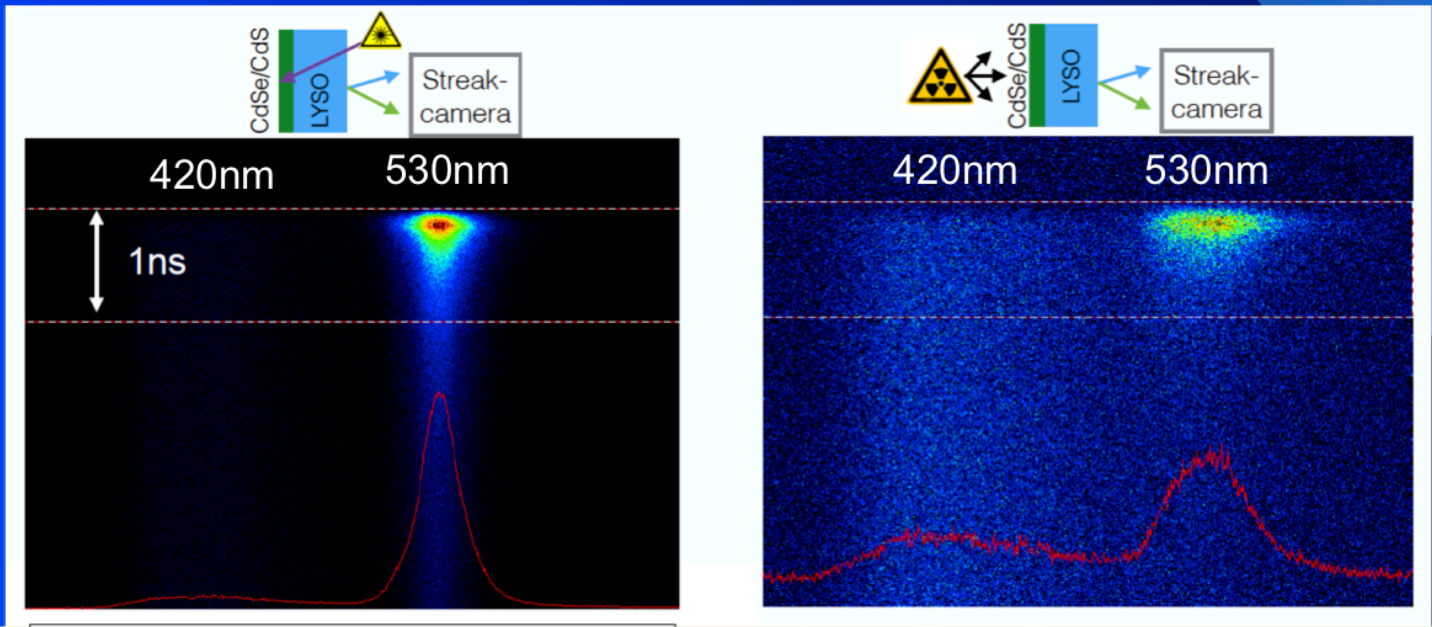
J.Grim, ITT, Italy



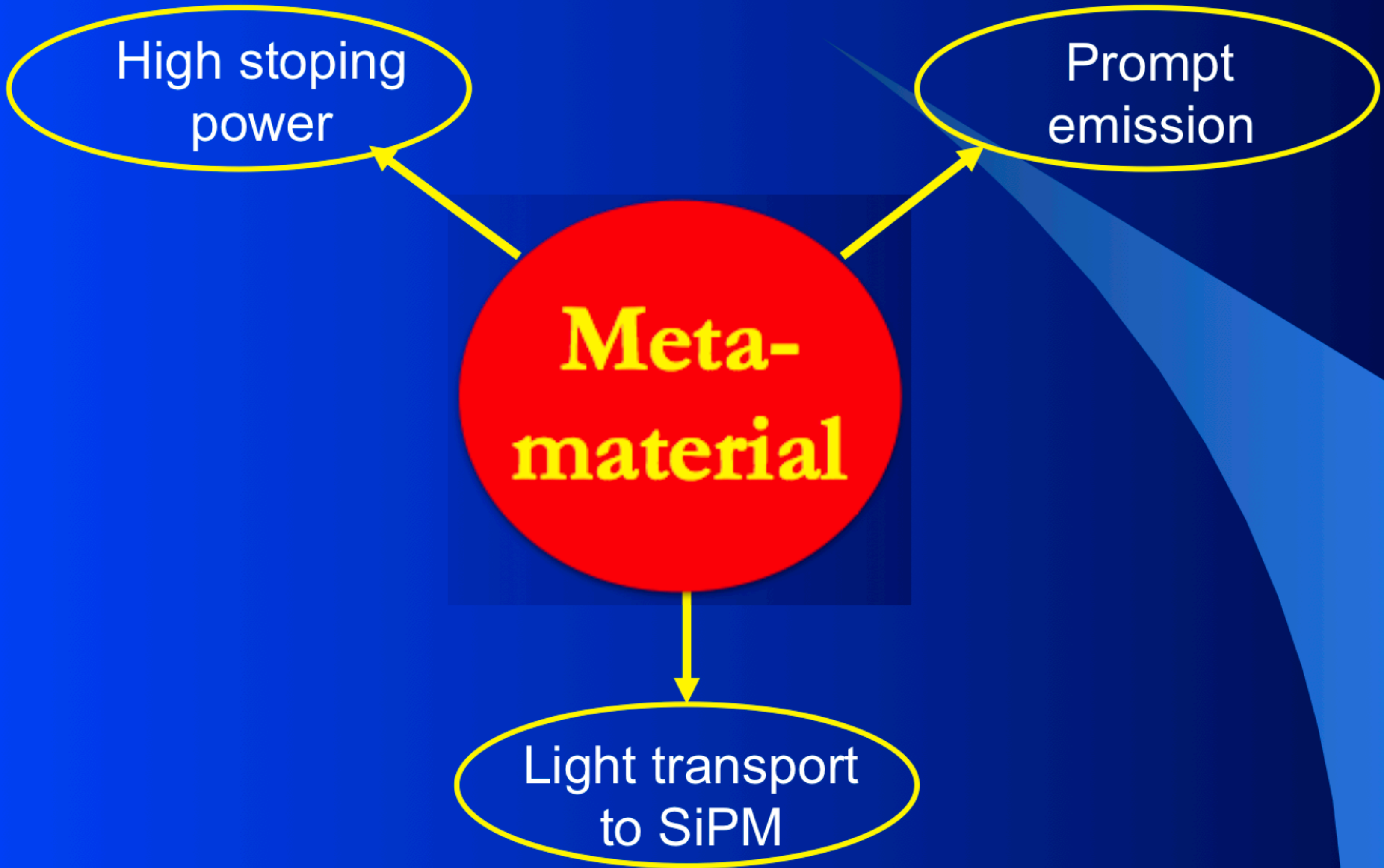


LYSO plate 200μm thick
+ **CdSe/CdS** nanoplate film 20μm thick

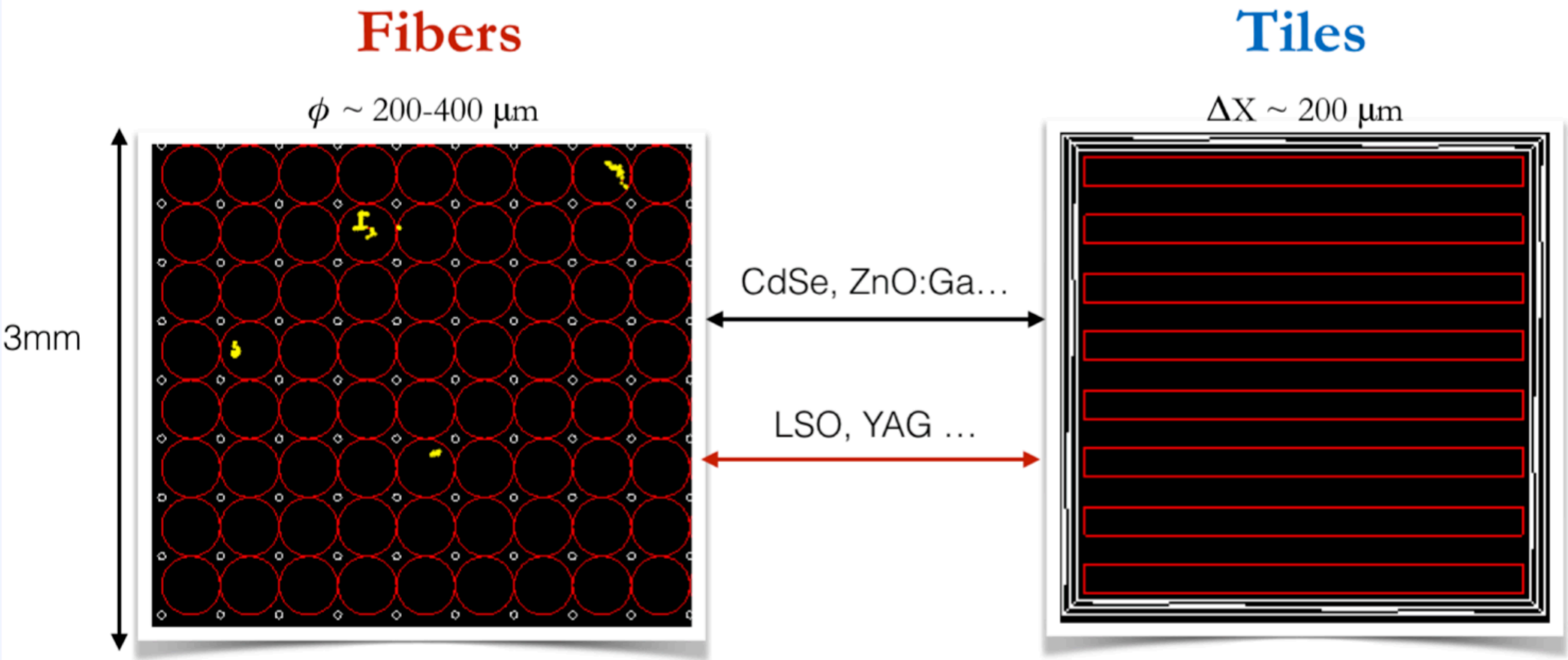




Metamaterials

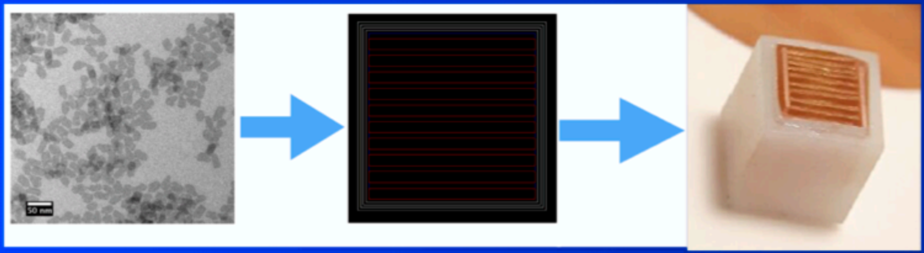


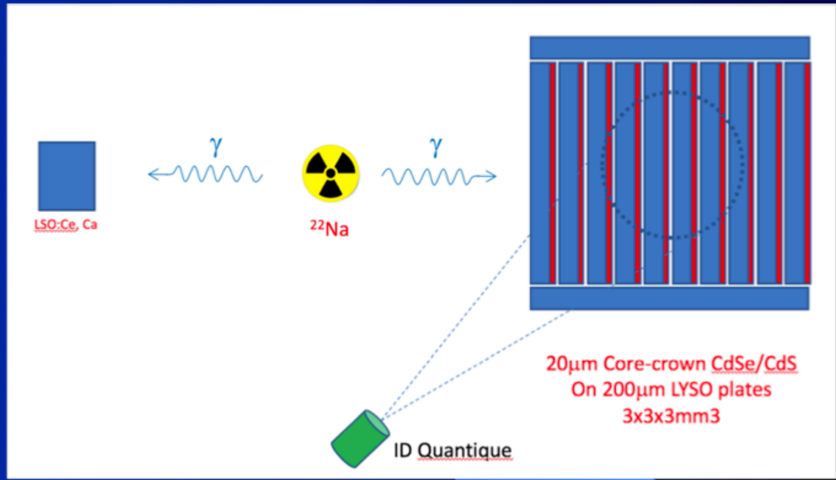
Metapixels under study

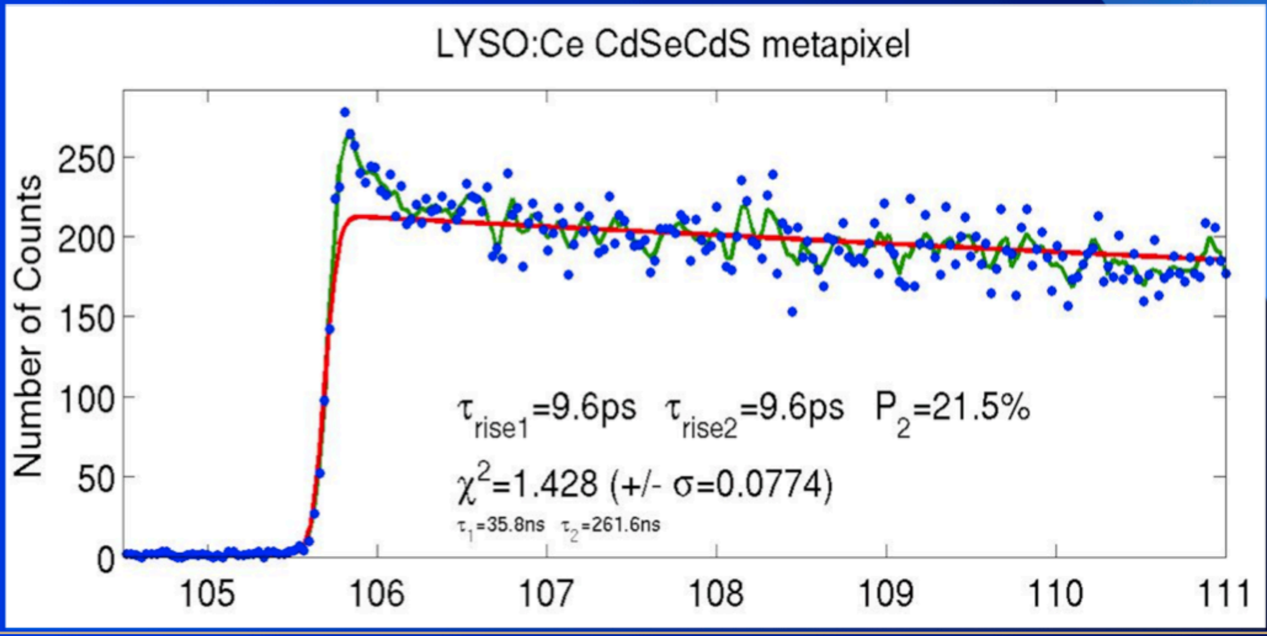


- Evaluation of the photodetection efficiency in a sampling geometry with 2 active materials
- Evaluation of the energy leakage from the dense to the fast material
- CTR estimation from a full MC simulation of prompt and scintillation photons

Metapixel with plates



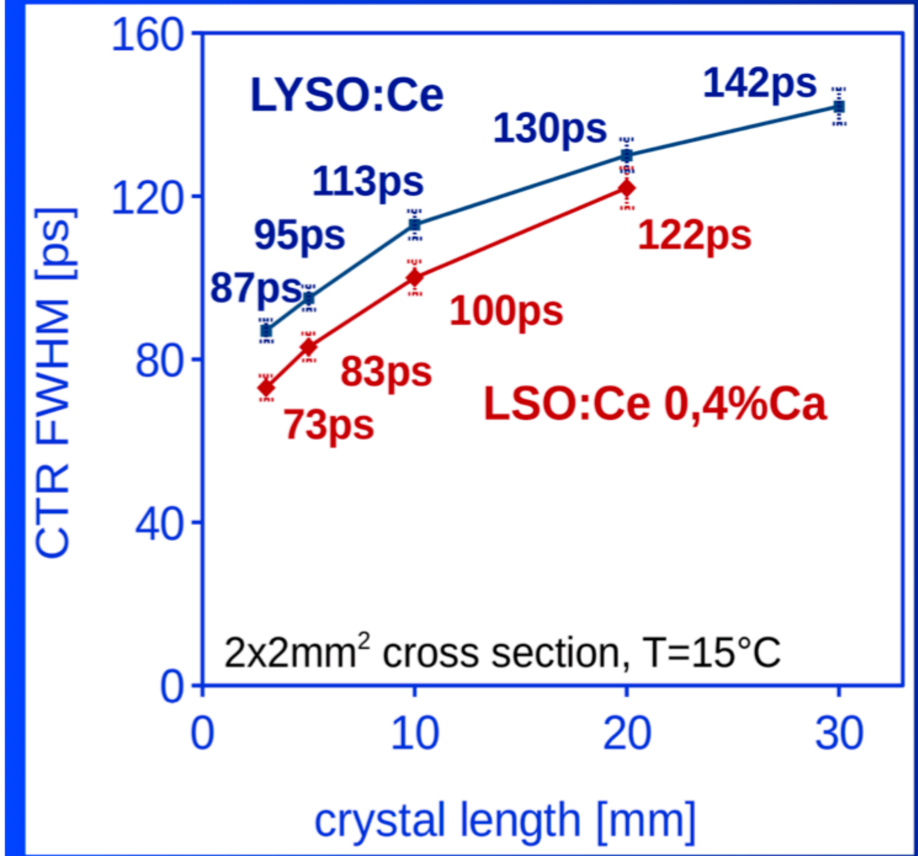


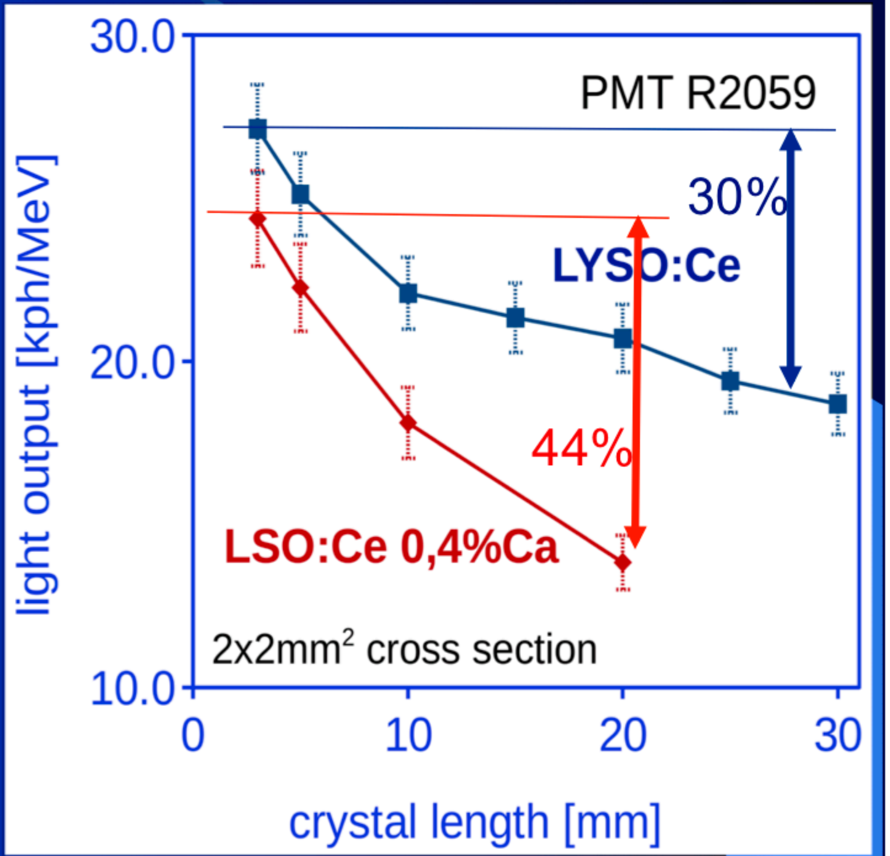


LIGHT TRANSPORT

Influence of crystal length on timing resolution

Measured with FBK NUV-HD (25µm SPAD size, 4x4mm^2 device size)
2x2mm^2 crystal cross section, T=15°C

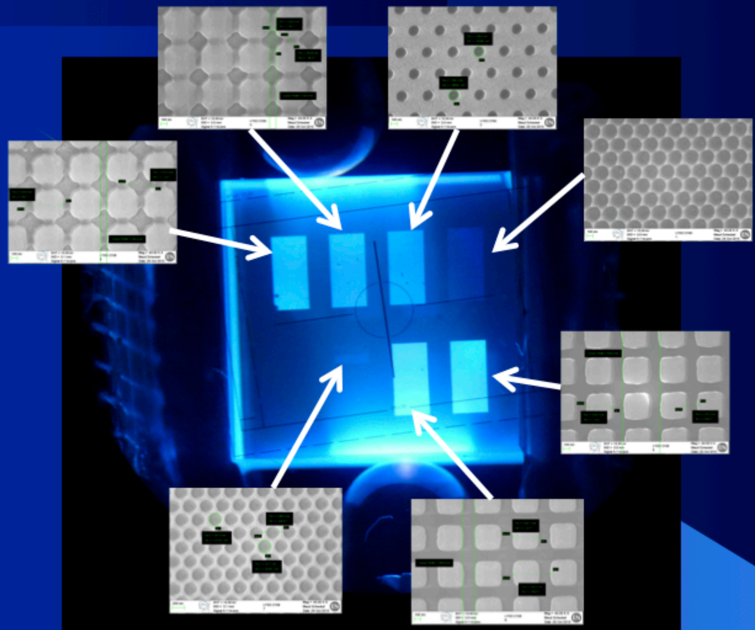


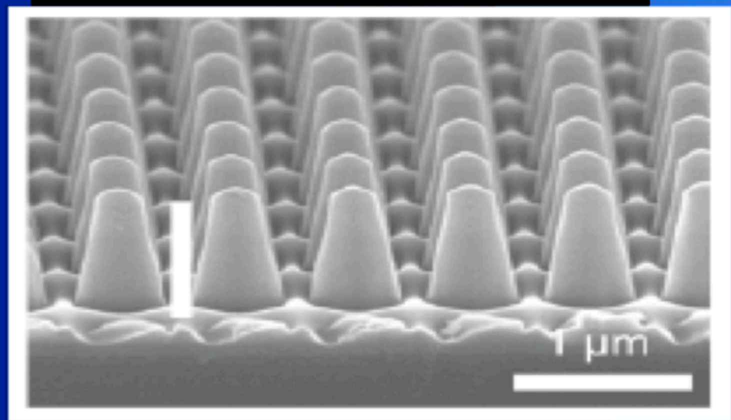


S. Gundacker et al, 2016 JINST 11 P08008

Photonic crystals to improve scintillator performance

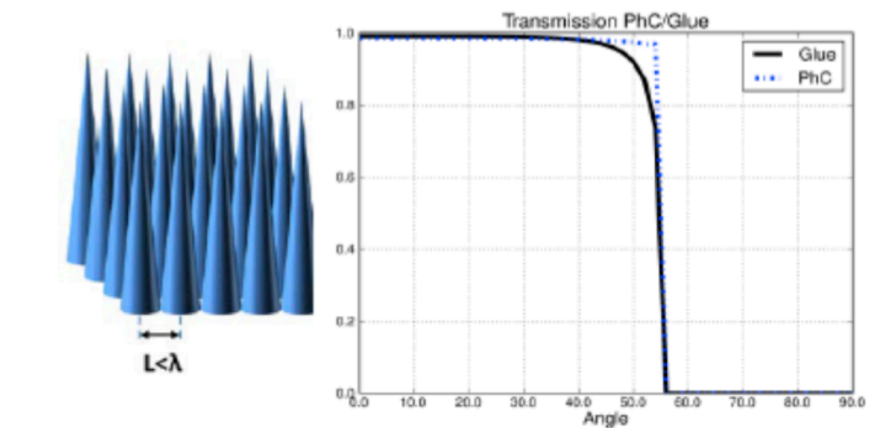
- Photonic crystals improve scintillator energy resolution:
  - By increasing the light output
- Photonic crystals improve scintillator timing resolution by two means:
  - By increasing the light output and therefore decreasing the photostatistics jitter
  - By redistributing the light in the fastest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

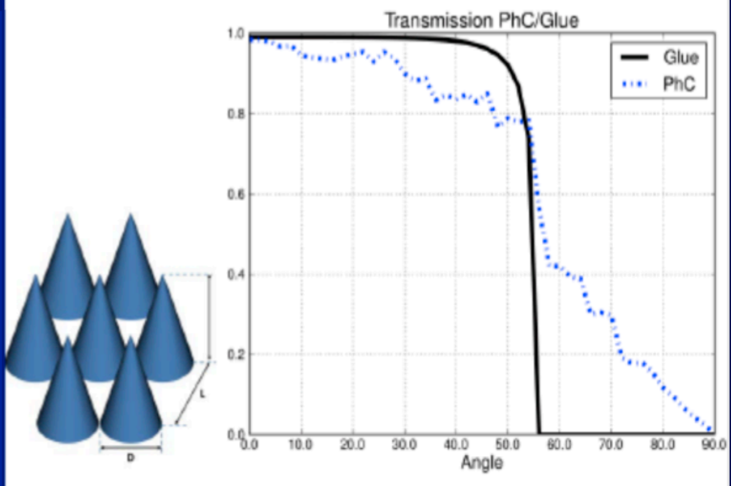




Hybrid PhC patterns: CERN-MIT-RMD collaboration

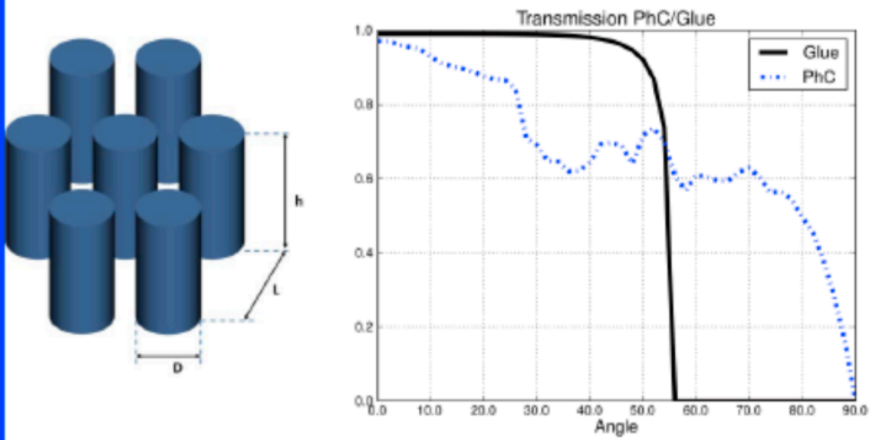
Sub-wavelength anti reflection cones:

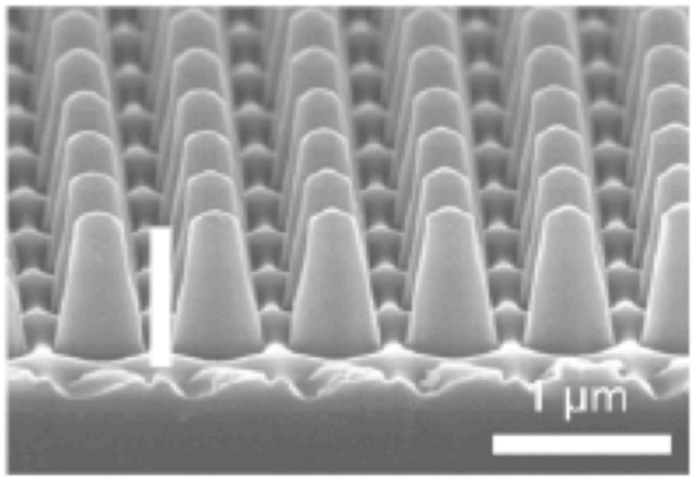




+ =

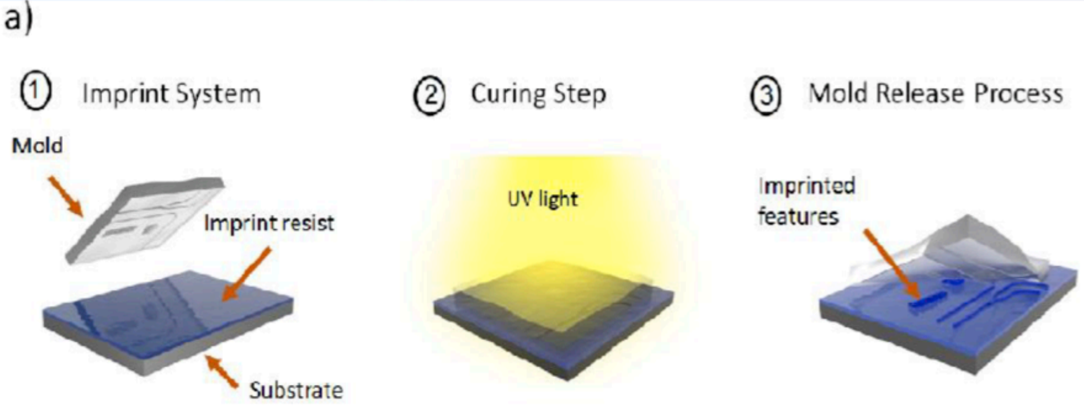
PhC diffraction Grating:

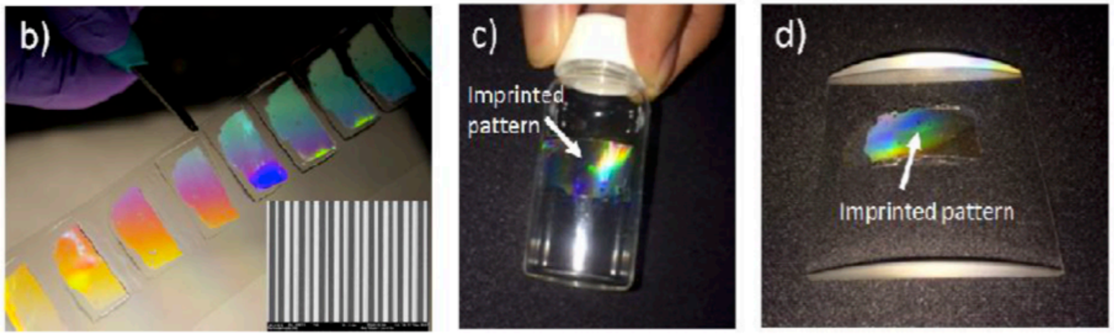




RMD nanoimprinting process

CERN, RMD, MIT, Abeam Technologies



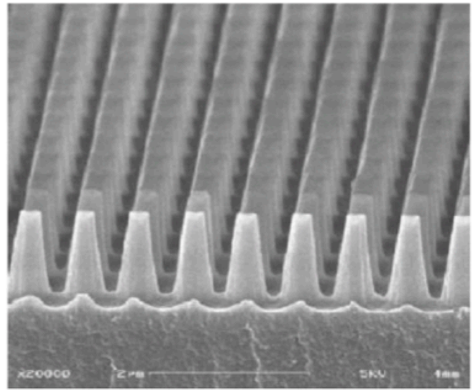


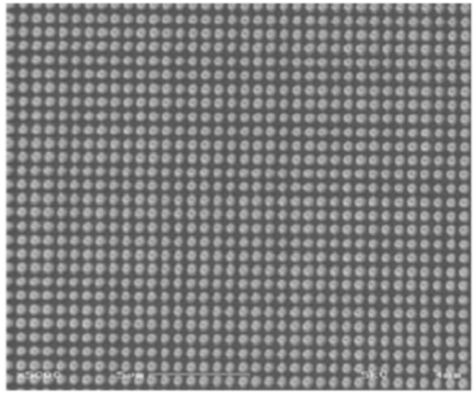
Optical grating (700 nm pitch)

Grating on a curved glass vial surface

Grating on cylindrical lens

Conical PhC Master in Polymer

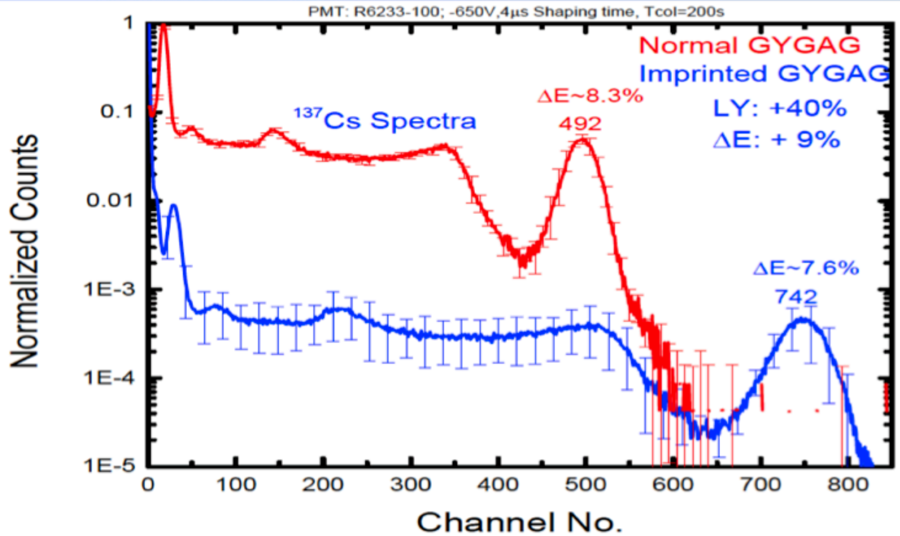




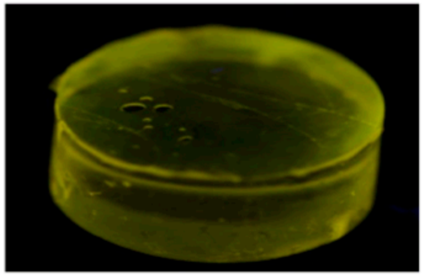
Uniform, large-area coverage

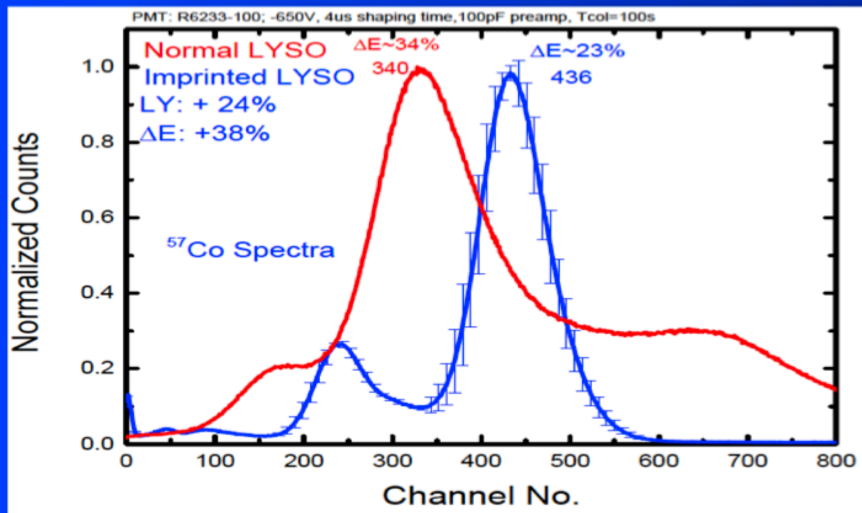
LY and energy resolution gain

CERN, RMD, MIT, Abeam Technologies

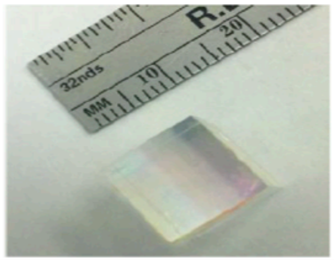


Custom Polymer	RI	Gain in LY	Gain in Energy Resolution
CP5	1.88	40%	9%
CP2	1.82	33%	3.6%





- Imprinting in CP4 polymer (RI=1.78).
- 38% improvement in energy resolution.
- Nanoimprinted LYSO exhibits large gains in energy resolution.
- Large gains in light output.

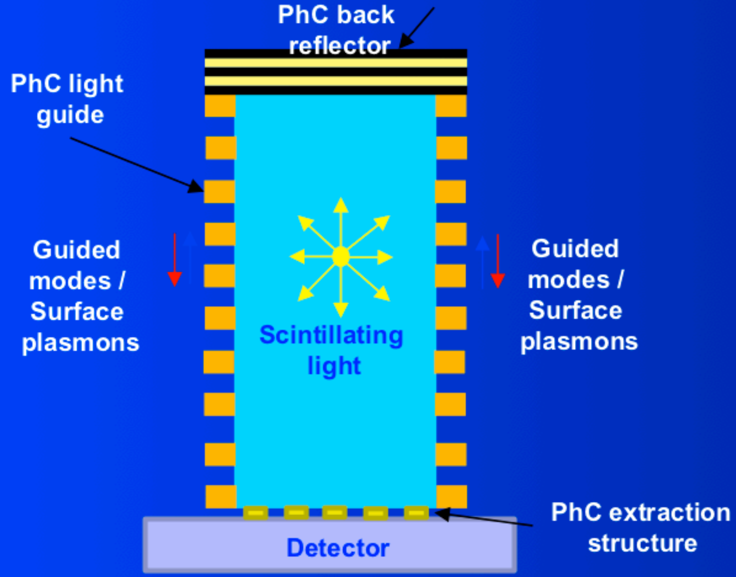


1 × 1 × 1 cm LYSO scintillator, with the imprinted nanostructured surface displaying optical interference effects.

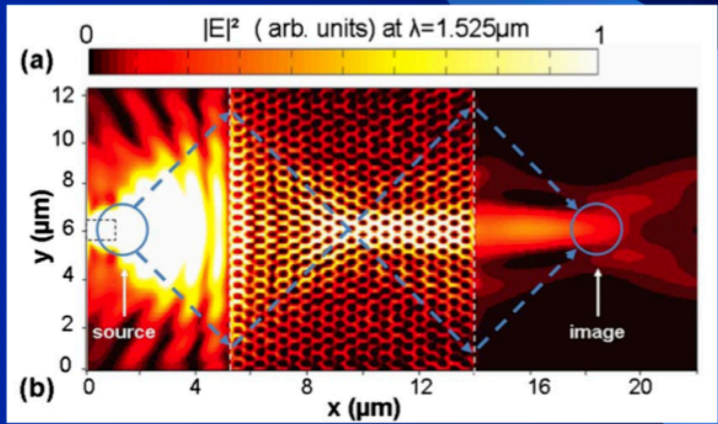
Future PhC Applications

More advanced PhC applications for scintillation based detectors:

- PhC light guides for the crystal wrapping



- Light collimation

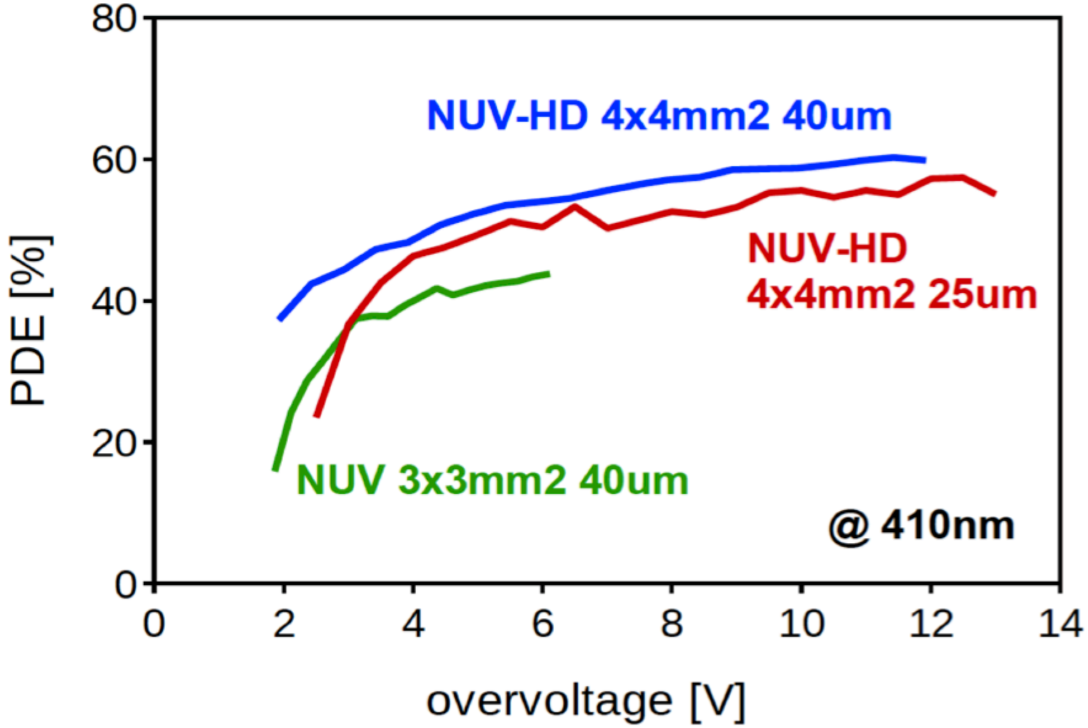


[Fabre08]

PHOTODETECTION

Progress in FBK-NUV SiPMs

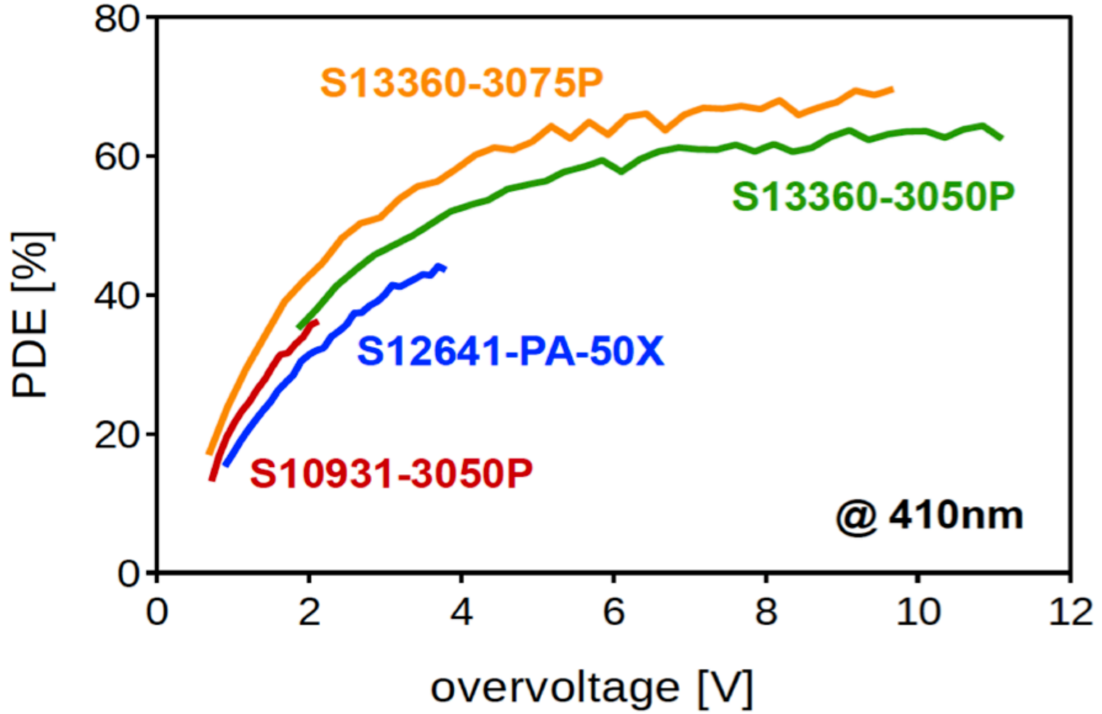
*SiPM + **2x2x3mm³ LSO:Ce:0.4%Ca**, Teflon wrapped + Meltmount (n=1.68)*	***CTR (ps)***	*PDE (%) @ 410nm*
FBK NUV 3x3mm² (40µm)	**85 ± 4**	42 ± 3
FBK NUV-HD 4x4mm² (25µm)	**73 ± 2**	55 ± 3
FBK NUV-HD 4x4mm² (40µm)	**70 ± 3**	60 ± 3



The SiPMs had no protective entrance window, which allowed to couple the crystal directly with Meltmount.

Progress in HPK SiPMs

*SiPM + **2x2x3mm³ LSO:Ce:0.4%Ca**, Teflon wrapped + Meltmount (n=1.68)*	***CTR (ps)***	*PDE (%) @ 410nm*
HPK S10931 3x3mm² (50µm)	**108 ± 5**	35 ± 3
HPK S12641 3x3mm² (50µm)	**99 ± 1**	43 ± 3
HPK S13360 3x3mm² (50µm)	**85 ± 3**	62 ± 3
HPK S13360 3x3mm² (75µm)	**80 ± 4**	67 ± 3

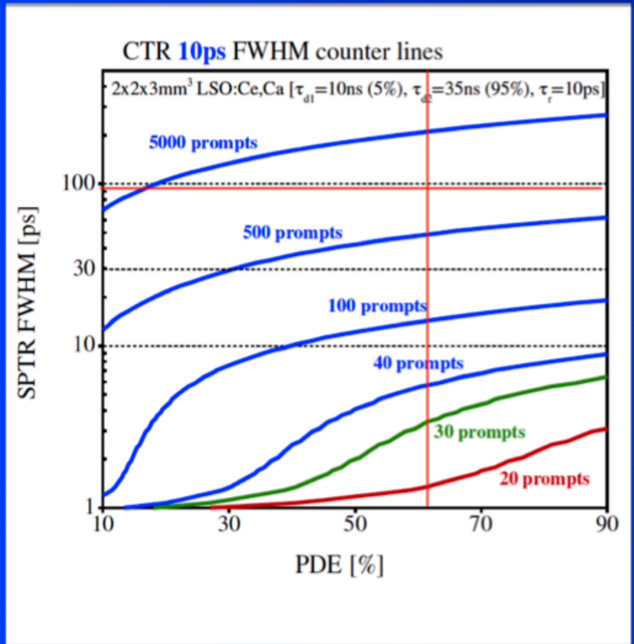


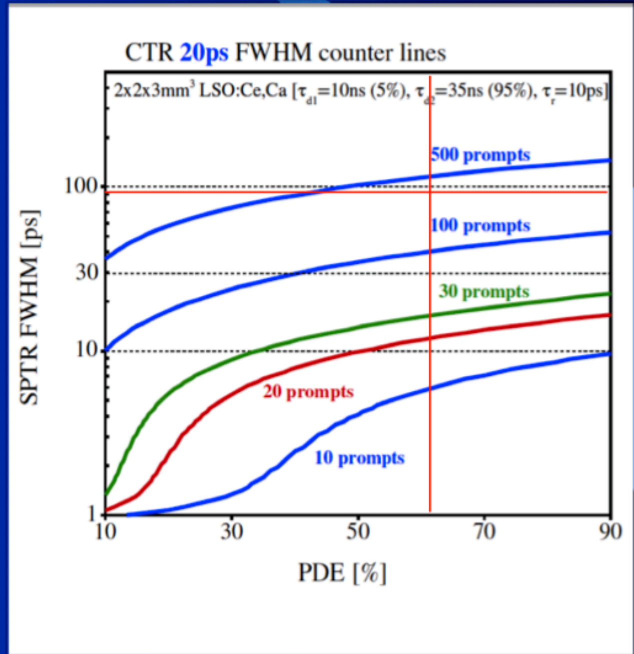
PDE improvement because of higher overvoltages possible.

CTR improvement almost entirely driven by improvement in PDE.

CTR as a function of SiPM PDE & SPTR

- Cramer Rao calculations including photon transfer time spread (PTS) and light transfer efficiency (LTE) of a $2x2x3mm^3$ LYSO:Ce ,Ca crystal

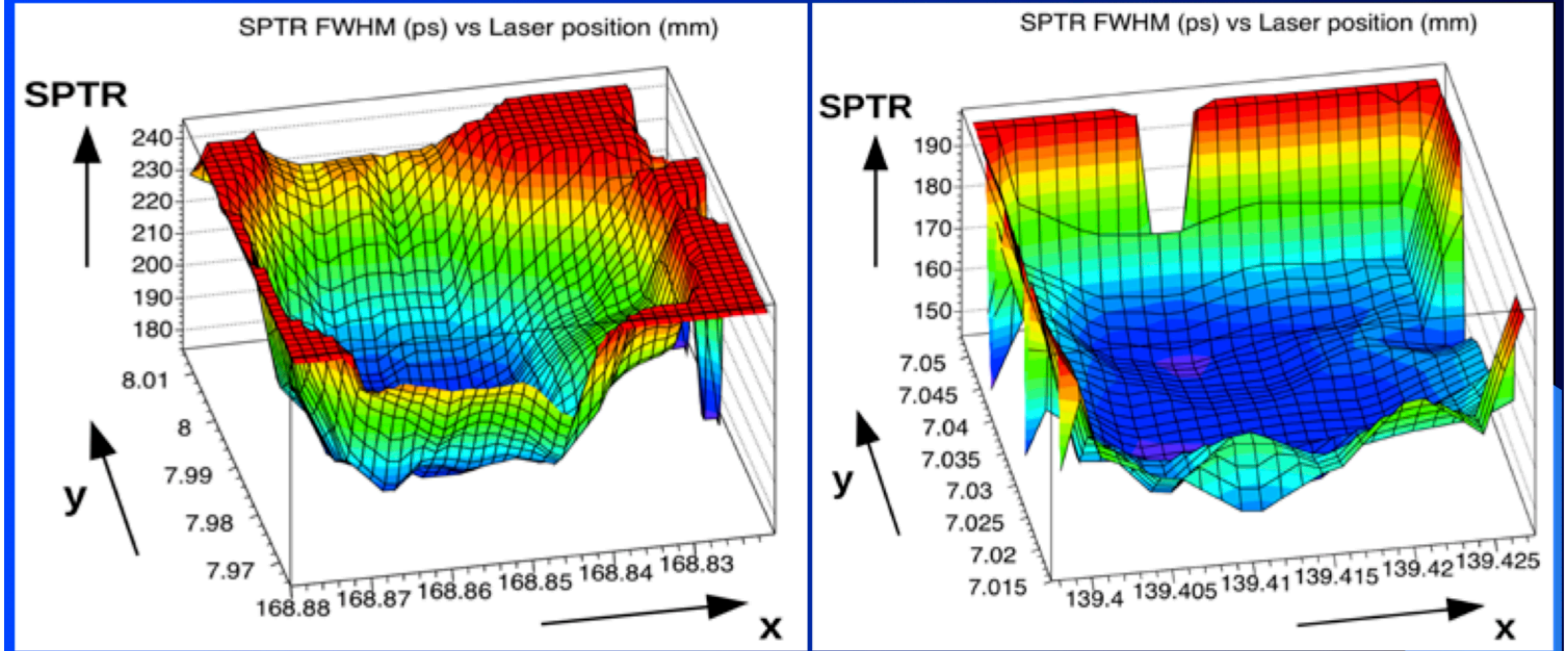




S. Gundacker, CERN

SPAD uniformity scan

Hamamatsu | FBK

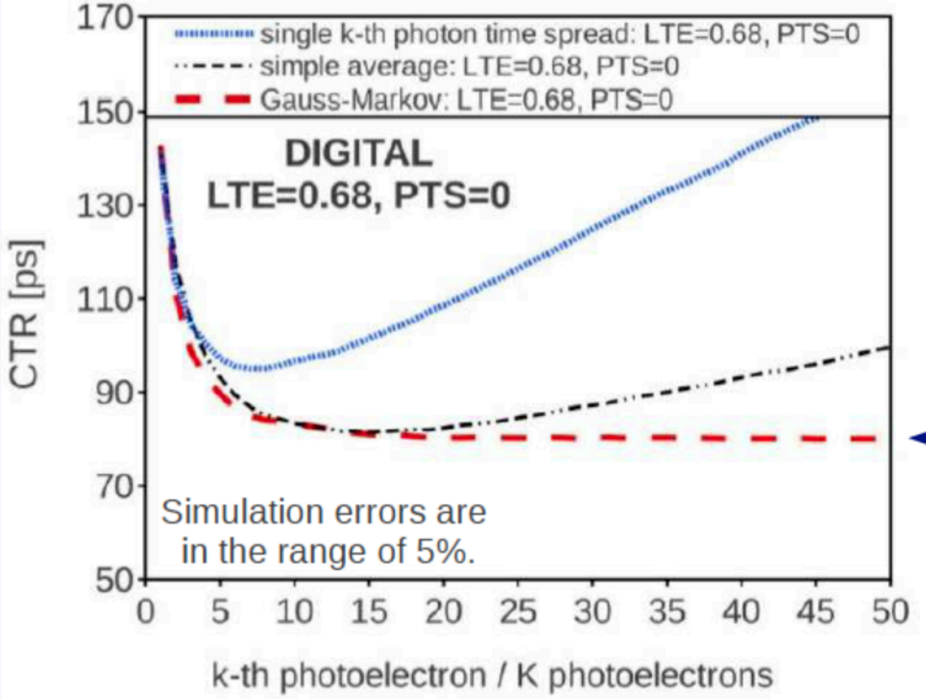


SPTR 22ps FWHM already measured on a single 30μm SPAD: FBK-NUV

M. Nemallapudi, S. Gundacker, P. Lecoq et al., submitted to JINST, May 2016

Maximum likelihood estimator

Statistical limit. PTS=0



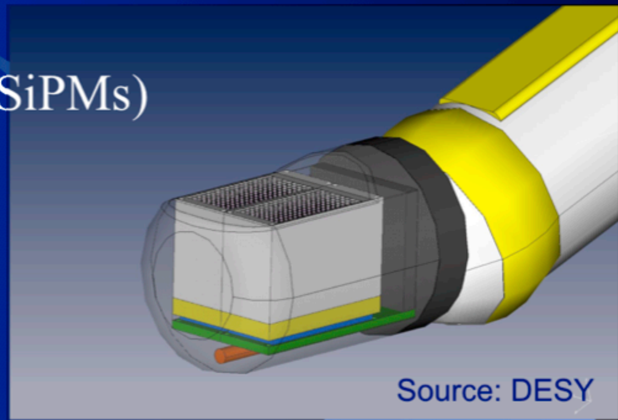
Maximum likelihood estimation saturates at best timing which is equal to the Cramer Rao lower bound of 81ps FWHM.

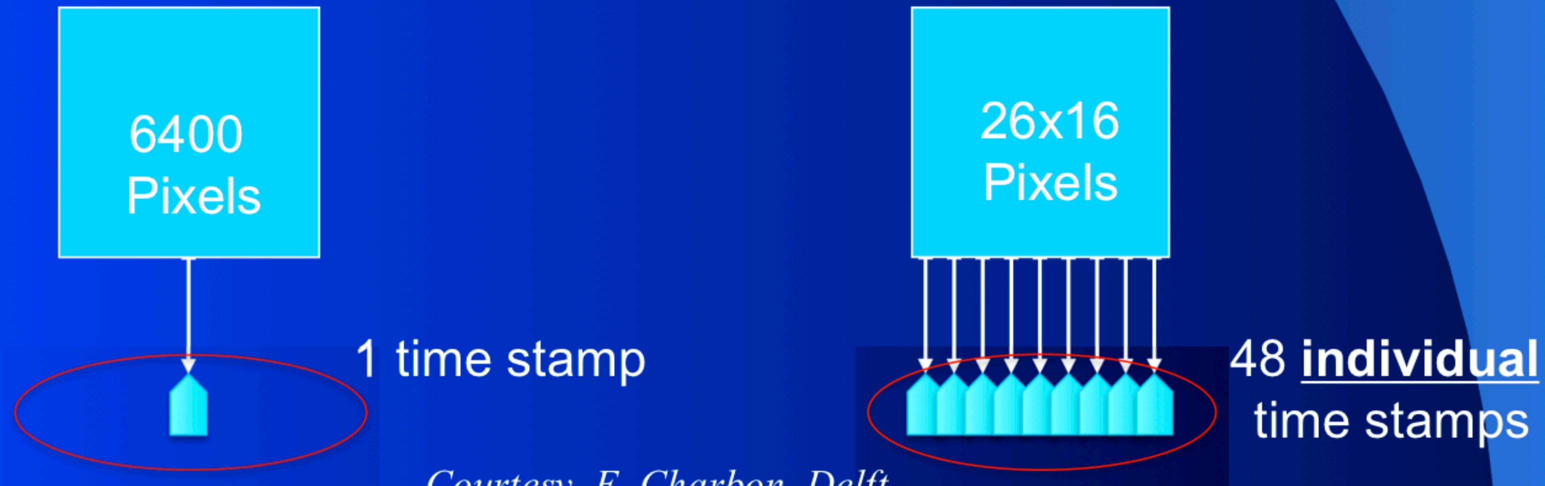
Gundacket et al., NIMA Volume 787, p. 6-11, July 2015

Multidigital SiPM

EU funded EndoTOFPET-US project

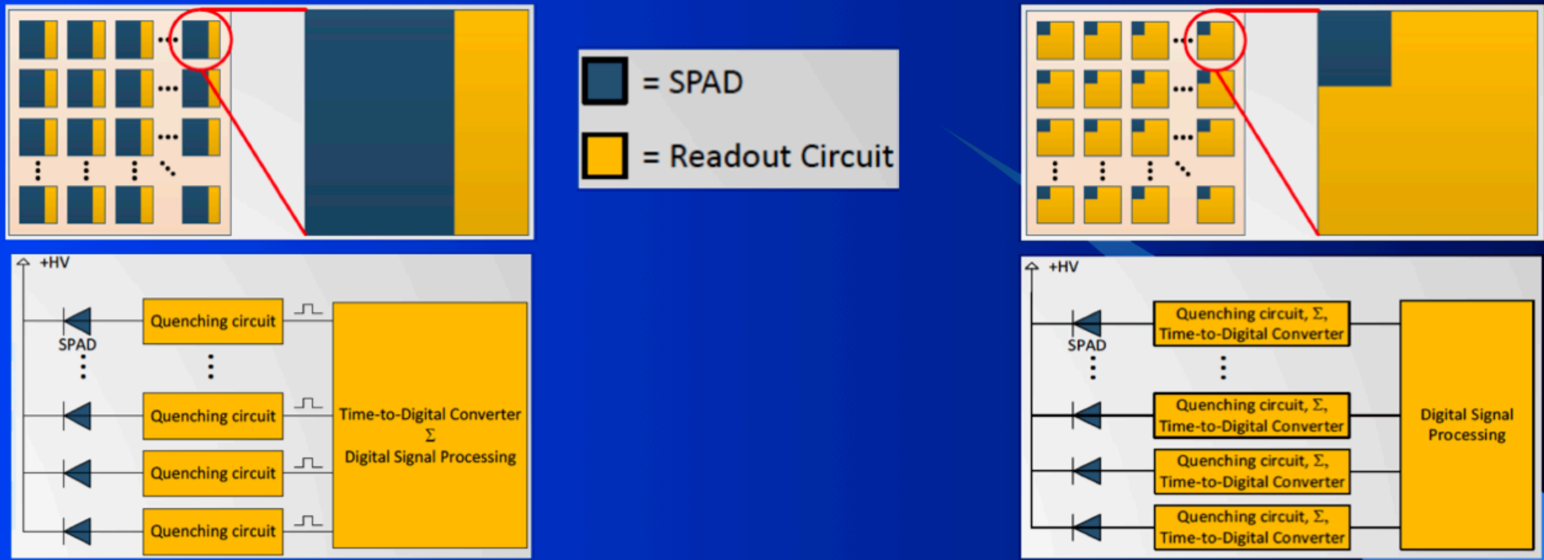
- Conceive and design endoscopic sensor
- Features
  - 9x18 Multi-channel silicon photomultipliers (SiPMs)
  - *In-situ* statistical analysis of gamma events
  - High-speed interface with system
  - Multi-channel timestamping
  - Real-time noise reduction

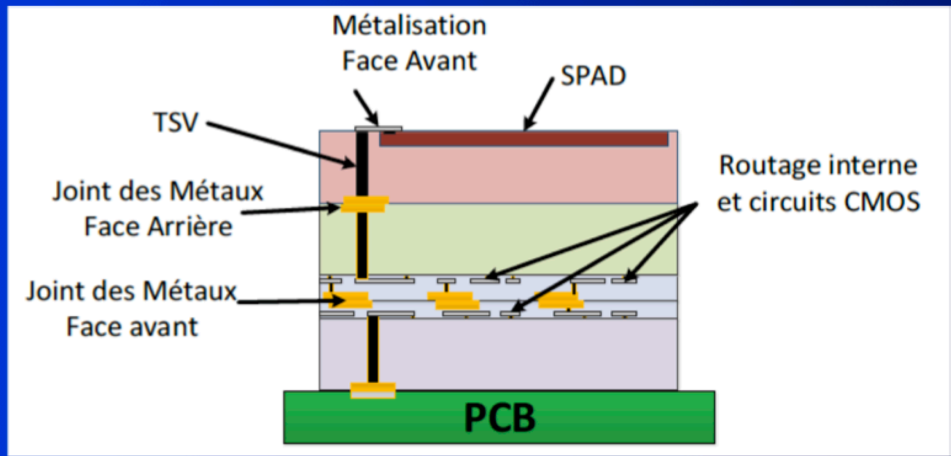




Courtesy E. Charbon, Delft

dSiPM: vertical integration

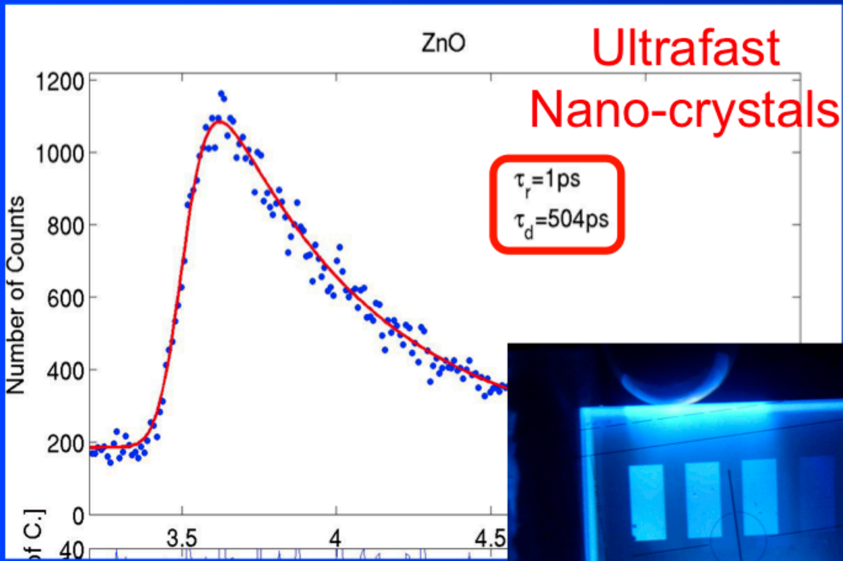


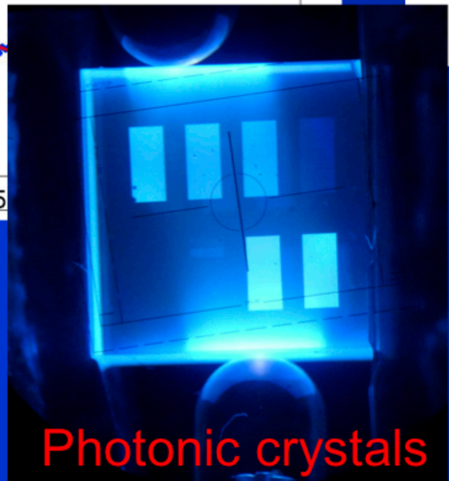


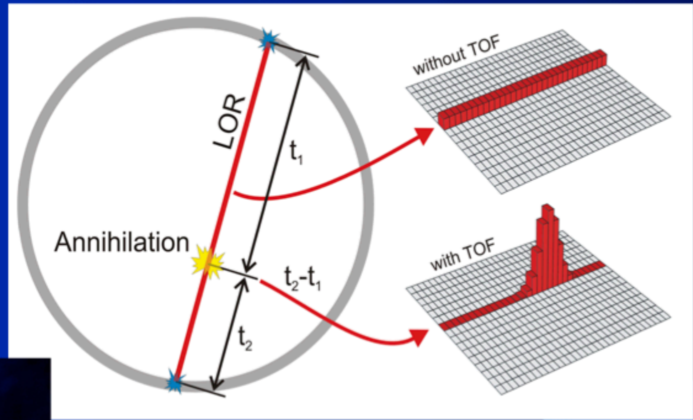
Courtesy M.A. Tétrault, J.F. Pratte, Sherbrooke

Fast sintillation timing: the way to reconstructionless TOFPET

P Lecoq et al. Nucl. Instrum. Meth. A 718 (2013) 569

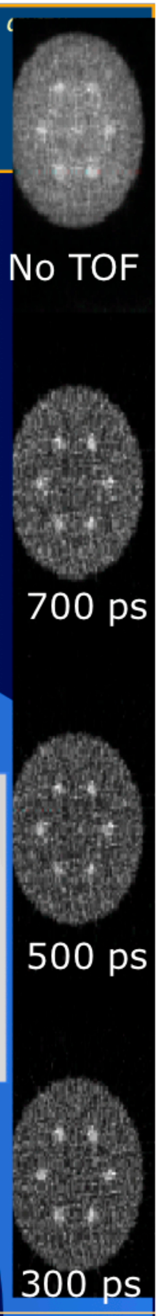






Digital 3D SiPM

- High fill factor - PDE
- Electronic flexibility
- Heterogeneous technologies
- The only way to eliminate the SPAD to TDC timing skew in the Single Photon Timing Resolution



4D Time Imaging CALorimeter

erc TICAL

Fast Advanced Scintillator Timing

cost TD1401 EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY FAST

The international context

- EXPLORER project for a full-body PET scanner
- Funded 15.5M$ by NIH

UCDAVIS UNIVERSITY OF CALIFORNIA · BERKELEY LAB · Penn UNIVERSITY of PENNSYLVANIA

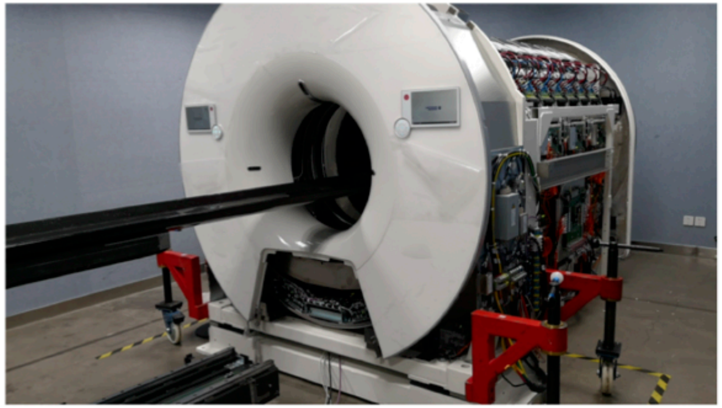
- Two machines to be built in collaboration with United Imaging (China) and installed for clinical research at
  - UC Davis
  - Upenn
- Will give them a clear competitive advantage for
  - Clinical research
  - Drug development

First EXPLORER is completed!

System:
Ring diameter: 78.6 cm
Transaxial FOV: 68.6 cm
Axial FOV: 194.8 cm

# of crystals: 564,480
crystal blocks: 13,440
of SiPMs: 53,760

April 2018



First EXPLORER is completed!

Federating power

- Was considered as a foolish dream 2 years ago
- More and more communications at major conferences mentioning the 10ps target
  - SCINT (Chamonix), NSS/MIC (Atlanta, Sydney), MEDAMI (Sardinia), …
- More and more dedicated workshops, particularly on fast SiPM
  - ULITIMA (Chicago), Pico-Second (Torino), NUVPET (Neuchâtel), Schwetzingen (DE), …
- More and more EU projects and proposals
  - FAST, at least 3 FET and 3 ERC proposals in the pipeline, .

Actions

- Define the conditions to run this challenge:
  - Milestones
  - Evaluation procedure
  - Liaison with public&private sectors:
    - funding agencies (physics, medicine), EU,
    - Companies, EFPIA, MITA
- Define who will be officially heading this challenge
  - EANM, ESR, EIBIR, EFPIA, Crystal Clear, CERN, …
- Look for sponsors
  - Imaging companies
  - Pharma companies
  - Other companies (crystals, SiPM, …)
  - Patient associations, charities, etc…

Conclusion

inspired by Maurizio Conti, Siemens (MEDAMI 2017, Sardinia)

- …looking forward to a 10ps TOF PET!

Or

- eagerly anticipating a 10ps TOF PET!
- eagerly/impatiently awaiting a 10ps TOF PET!
- anticipating with pleasure a 10ps TOF PET!
- hoping for a 10ps TOF PET!
- drooling/slobbering in anticipation of a 10ps TOF PET!
- envisioning with pleasure/delight/joy a 10ps TOF PET!
- confidently awaiting a 10ps TOF PET!

Organisation du défi 10ps

1. Qui doit porter le défi?
   a. un seul acteur ou plusieurs?
   b. organisation légale publique (institut, agence de financement, société savante (EANM, ESR)
   c. fondation publique, association de patients, ...
   d. Organisation privée (industrie ou groupement industriel (EFPIA, MITA), fondation privée, ...)
2. Comment financer le défi ?
   1. Fonds privés: industries, groupement industriel (EFPIA), fondation privée, mécénat,…
   2. Fonds publics: agences de financement, associations, …
3. Qui pourrait participer:
   1. Individuel
   2. une équipe, un consortium, national/international (au sens des projets européens)
4. Faut-il limiter le défi dans le temps à l'image des prix de la Fondation XPrize ?
5. Quel devrait être le montant du(des) prix ?
6. Quelle organisation faut-il mettre en place pour le défi 10 ps, pour sa validation et/ou sa certification ?