Fast Timing in Medical Imaging

Friday, 3 June 2022 - Sunday, 5 June 2022

Parador El Saler, Valencia, Spain

Book of Abstracts

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Motivations for the workshop on Fast Timing in Medical Imaging

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Why this workshop ?
Why in Valencia ?
Why now ?

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 64

Reflections on Time-of-Flight for PET imaging

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The benefits of measuring the time difference between the arrival of the two photons from positron annihilation was recognized from the very early days of PET imaging in the 1960s. However, at that time the scintillator light decay time and the timing of the electronics was insufficient to implement a measurement of time-of-flight (TOF) that could have a beneficial effect on the image quality. The first PET devices to realistically explore TOF were not developed until the 1980s by groups at LETI in France, Washington University, St Louis and Houston, Texas. The TOF resolution achieved by the LETI system was around 750 ps. However, during the 1980s, the emphasis in PET imaging was more focused on achieving better spatial resolution and sensitivity, neither of which was a strength of the early TOF scanners. Following the development of 3D PET imaging and the emergence of new, fast scintillators in the early 2000s, the interest in TOF was revived and is now one of the most important parameters to optimize in new PET scanner designs. To set the scene for the meeting, this presentation will briefly review the progress in TOF measurement and highlight some of the milestones in achieving the current timing resolution of around 200 ps in commercial PET scanners.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 23

Clinical experience on the merit of TOF in PET imaging

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This presentation will make an overview of the present clinical TOF PET imaging and its benefit brought about by lowering the TOF CTR slightly above 200 ps. These advantages will be even more apparent when pushing for ≤ 100 ps TOF PET CTR paving the ground for having a 10-ps TOF PET challenge.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 58

Reconstruction-free total-body PET: Realizing the full potential of the tracer kinetic method

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The radiotracer principle, as first introduced by George Hevesy in 1923 [1], and supported by sophisticated radiation imaging systems, highly specific radiotracers, and mathematical modeling, has been a powerful tool with broad uses in biomedical research. Applications span animal models, and in vivo human imaging in many disease states and the tracer method has been used to interrogate and elucidate physiology, metabolic pathways and molecular targets. The recent advent of long axial field of view and total-body PET scanners [2] now permits application of these approaches across the entire human body, and provides a unique new tool to contribute to the burgeoning field of systems medicine.

PET is unique among tomographic medical imaging modalities in that timing resolution at the level tens of picoseconds is sufficient to directly generate 3-D images of the radiotracer distribution. Advances in radiation detector science, technologies and electronics, as showcased by this workshop, now tantalizingly offer the prospect of practical reconstruction-free radiotracer imaging in the not-too-distant future.

This presentation examines the possible impact of combining total-body PET with radiation detectors capable of a timing resolution of 30 ps or less. What are the capabilities of such an instrument? What new opportunities would this present for biomedical research and ultimately for clinical applications? This envisioned scanner would represent the ultimate embodiment of Hevesy's vision, and the tracer principle, in living human beings.

1. Hevesy G, "The absorption and translocation of lead by plants." Biochem J 17; 439-445 (1923)

2. Badawi RD et al, "First Human Imaging Studies with the EXPLORER Total-Body PET Scanner." J Nucl Med 60; 299-303 (2019)

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 74

Clinical and Technical Impact of Fast TOF PET

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The paradigm shift in medicine from treatment of acute and/or advanced disease to very early diagnosis and even prevention in cancer, neurodegenerative as well as cardiac fields, puts more stringent requirements on PET imaging both in terms of sensitivity as well as specificity. Likewise, recent developments in Targeted Radionuclide Therapy (TRT) where theragnostic pairs are used to tailor a personalized treatment in terms of dose using PET initial imaging and subsequent alpha or beta emitting radionuclides have introduced a clear and urgent need for more widespread and accurate PET imaging. Standard clinical scanners are sub-optimal both in terms of cost and performance. Standard clinical PET scanners cover only a limited solid angle, and just a few percent fraction of the positron decays is registered. Novel long axial PET scanners with axial field of view offer a very attractive solution to many of the challenges detailed above, especially in terms of increased sensitivity and enabling fast dosimetry and biodistribution for pharmacokinetic studies, that will pave the way to personalized TRT. However, these scanners pose significant challenges both financially and logistically. In this talk we present a joint effort between JSI-Ljubljana, FBK-Trento, Univ-Barcelona, Oncovision and MGH-Harvard-Boston to address these challenges using fast coincidence timing resolution. On the front electronics, our challenge is to develop a low-noise, high-dynamic-range ASIC with a time resolution of 20 ps or better, and with on-chip time-to-digital converter (TDC). To achieve sub-100 ps CTR we intend to explore 2.5 D integration with the photo-sensor. Recent advances in Time-of-flight (TOF) PET technology afford a rare opportunity to improve signal-to-noise-ratio (SNR) without increasing the cost associated with axial coverage by resorting to very sparse angular coverage of the patient and long axial field coverage (>1m). This would yield affordable long axial PET scanners.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 52

Introduction to a High-Resolution Fast-Timing PET Project

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With the aging of the global population, neurodegenerative diseases such as Alzheimer's and Parkinson's are becoming more common. In addition, PET is a useful clinical tool for accurately visualizing the presence of biomarkers in the brain associated with various neurodegenerative diseases (e.g., amyloid-β plaques or microtubule-associated protein tau strands). However, the relatively high level of radiation exposure and long scan times, along with the high cost of hybrid PET/CT and PET/MRI scans, are the main disadvantages of current PET examination. To address these shortcomings, we are developing standalone PET scanners dedicated for the brain and other peripheral organs. The main goal of this project is to develop a high-resolution, high-sensitivity PET scanner with a moving gantry for flexible patient and organ positioning with time-of-flight measurements and depth-of-interaction encoding capabilities. A reliable deep learning-based PET denoising and quantification solution is also being integrated. This talk introduces the progress of this project.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 75

Concepts and systems to advance coincidence time resolution for time-of-flight positron emission tomography

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We are studying new detection concepts, methods, and system designs to advance time-of-flight (TOF) positron emission tomography (PET). In this talk we will describe three efforts in this direction. The first is a 'radio-frequency-penetrable' PET insert design that we are building for simultaneous brain TOF-PET/MRI of neurological disorders that employs novel design features to enable ~230 ps FWHM annihilation photon pair coincidence time resolution (CTR), which would be a notable achievement for MR-compatible TOF-PET. The second is a TOF-PET/CT system under construction for cancer imaging applications that achieves ~100 picoseconds (ps) FWHM CTR by employing a novel scintillation detector configuration and electronic readout. The third is completely new concept for a 511 keV photon detector that probes the modulation of a material's optical properties that results from an ionizing interaction instead of scintillation, which, if successful, could in theory achieve ~1 ps CTR. If successful, these technologies will lead to next generation systems that enhance TOF-PET's ability to visualize and quantify disease

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 13

Design and initial results of a total-body PET with TOF and DOI capabilities

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Interest towards high sensitivity multiparametric imaging modalities has increased during the last years. In this context, high precision Positron Emission Tomography (PET) scanners have shown great potential. Two paths to further enhance PET sensitivity have been outlined: (i) including photon Time-of-Flight (TOF) information during the image reconstruction process; or (ii) increasing the axial length of the scanner, i.e., total-body PET (TB-PET). Yet, the ideal scenario would be a TB-PET with precise TOF capabilities but, this imposes major technological challenges.
Following this goal, the I3M is developing a clinical TB-PET scanner of approximately 80 cm diameter and 70 cm axial coverage, based on 7 rings. The detector design is based on 8 slabs of 25.8×3.1×20 mm3 LYSO crystals coupled to an array of 8×8 SiPMs from Hamamatsu Photonics. The slab configuration is key to achieve good timing resolution while providing accurate 3D photon impact positioning, and our custom designed electronics includes a novel multiplex readout electronics that reduces from N2 to 2N the number of signals to digitize. In addition, the electronic chain is combined with PETsys ASIC for compactness and scaling up of the detector technology.
Simulations of the system have been carried out demonstrating a Noise Equivalent Count Rate (NECR) of 91 kcps at 9.1 kBq/mL (for a 20 cm axial coverage), which is comparable with state-of-the-art scanners.
Moreover, the first modules have been already ensembled. Experiments have been carried out by displacing a collimated 22Na source - using a slit of 0.45 mm thick- across the entire entrance and lateral faces of the module. In a first stage without including the multiplexing readout electronics, the x- and DOI- coordinates were estimated using a Neural Network and the timing was estimated applying an energy-weighted average method. Average results for one mini-module showed energy resolution of 10±1.8%, 221±9 ps CTR, 2.9±0.6 mm FWHM along monolithic direction and 3.9±0.9 mm FWHM DOI resolution. In a second stage, the multiplexing readout was included and energy resolution values of 13.4±0.9% and CTR of 305±5 ps were achieved. The flood map quality was also good. Note that these values were calculated analytically, without using the NN which is being implementing at this moment. Results will be shown at the conference.
These promising results brings us closer to the goal outlined at the beginning of this abstract: boosting sensitivity by building practical and transferrable TB-PET systems.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 54

Development of a fast Cherenkov detector dedicated to Prompt Gamma Time Imaging

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We are conceiving a new imaging modality called Prompt Gamma Time Imaging (PGTI) to achieve the real time measurement of the proton range during particle therapy treatments. The goal of PGTI is to reconstruct an image of the vertex distribution of Prompt Gamma rays (PG) emitted from the patient, through the exclusive measurement of particle Time-Of-Flight (TOF). The start trigger is given by a diamond-based beam monitor measuring the proton arrival time, while the stop trigger is provided by a gamma detector. The spatial resolution on the PG vertices strictly depends on the system Coincidence Time Resolution (CTR) between the start and the stop triggers. From MC simulation [Jacquet et al. PMB 2021], we expect a spatial resolution of 1 mm (at 2σ) under the hypothesis of a CTR of 100 ps rms (235 ps FWHM).

In order to achieve these performances within the first (few) second(s) of the treatment, we are developing a dedicated gamma ray detector with a high detection efficiency (~1%) and an excellent time resolution. The TOF Imaging ArRAy (TIARA) will be composed of ~ 30 $1\times1\times1$ cm3 monolithic PbF_2 crystals read out by SiPMs isotropically arranged around the patient.

Two identical block detectors read-out by a dedicated preamplifier and irradiated in coincidence by gamma rays of ~1.25 MeV from a ^{60}Co source achieved a CTR of 278 ps FWHM. The module was also tested with PGs produced at a proton therapy facility using non-dedicated electronics: we obtained a CTR of 317 ps FWHM corresponding to a measured proton range precision of 4 mm (at 2σ) with only 600 events. More recently, the use of a new dedicated preamplifier has allowed us to reach a CTR of 235 ps FWHM under the same experimental conditions.

We will present the PGTI technique and the experimental characterisation of our block detector.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 21

On a way to clinical positronium imaging with the high time resolution total-body J-PET system

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J-PET is a multi-photon PET system prototype [1] enabling multi-photon and positronium imaging. The quality of these images relies strongly on the system's time resolution. In this presentation, we will explain the newly developed method of positronium imaging and present the first multi-photon [2] and in-vitro positronium images [3]. We will discuss the clinical motivation for improving the system time resolution and present arguments demonstrating that the high sensitivity and high time-resolution multi-photon total-body PET systems [4] open realistic perspectives for the application of positronium as a biomarker for in-vivo assessment of the tissue pathology and the degree of hypoxia [5].

[1] P. Moskal et al., "Simulating NEMA characteristics of the modular total-body J-PET scanner - an economic total-body PET from plastic scintillators", Phys. Med. Biol. 66 (2021) 175015.

[2] P. Moskal et al., "Testing CPT symmetry in ortho-positronium decays with positronium annihilation tomography", Nature Communications 12 (2021) 5658.

[3] P. Moskal et al., "Positronium imaging with the novel multiphoton PET scanner", Science Advances 7 (2021) eabh4394.

[4] P. Moskal, E. Stepien, "Prospects and clinical perspectives of total-body PET imaging using plastic scintillators", PET Clin 15 (2020) 439-452.

[5] P. Moskal, E. Stepien, "Positronium as a biomarker of hypoxia", Bio-Algorithms and Med-Systems 17 (2021) 311–319.

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 30

Novel biomarker and drug delivery systems for theranostics – extracellular vesicles

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Extracellular vesicles (EVs) are nano- and micro-sized cell-derived entities, released from cells under physiological and pathological conditions [1]. EVs can be found in every biological fluid including blood, saliva, milk, or urine, serving as a liquid biopsy [2]. Their biological properties (cell-uptake, biocompatibility) [3], and chemical (composition, structure) or physical (size, density) [4] characteristics make EVs a good candidate for drug delivery systems (DDS). Recent advances in the field of EVs (e.g. scaling-up production, purification) and developments of new imaging methods (molecular imaging) revealed benefits of radiolabelled EVs in diagnostic and interventional medicine as a potential DDS in theranostics [5].

[1] Stępień E et al. Number of microparticles generated during acute myocardial infarction and stable angina correlates with platelet activation. *Arch Med Res.* **2012**;43:31-5.
[2] Stępień EŁ et al. Circulating ectosomes: Determination of angiogenic microRNAs in type 2 diabetes. *Theranostics.* **2018**;8:3874-3890.
[3] Stępień E et al. Microparticles, not only markers but also a therapeutic target in the early stage of diabetic retinopathy and vascular aging. *Expert Opin Ther Targets.* **2012**;16:677-88.
[4] Stępień EŁ et al. Fourier-Transform InfraRed (FT-IR) spectroscopy to show alterations in molecular composition of EV subpopulations from melanoma cell lines in different malignancy. *Biochem Biophys Rep.* **2021**;25:100888.
[5] Stępień EŁ, Rząca C, Moskal P. Novel biomarker and drug delivery systems for theranostics—Extracellular vesicles. *Bio-Algorithms Med-Systems* **2021**:17:301–309

Clinical motivation for pushing TOFPET CTR resolution ≤100ps / 72

The importance of fast-timing gradients in 3T MRI for diffusion and perfusion analysis in Prostate Cancer

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The characterization of cancerous tissue alterations in magnetic resonance imaging (MRI) requires the acquisition of demanding gradient pulse sequences that use a high slew rate. This allows for a high temporal resolution both in the sensitivity to the movement of water molecules diffusion in tissues and to the kinetics of blood flow through vessels and capillaries, the principles of diffusion weighted imaging (DWI) and dynamic contrast enhanced (DCE) examinations.
Prostate cancer is a neoplastic process usually detected by MRI using not only anatomical images, but also DWI and DCE through the quantification of parameters such as the apparent diffusion coefficient (ADC) and vascular permeability (K^trans). The combination of these imaging biomarkers quantification algorithms with novel artificial intelligence organ segmentation algorithms allow for the automation of the whole prostate gland analysis almost in real time.
These prostate MRI analysis pipelines will set the new paradigm for prostate cancer screening in clinical routine, assisted by AI, and benefiting from the fast - timing characteristics of diffusion and perfusion sequences in MRI.

Fast X-Ray imaging / 49

Toward a First Prototype Time-of-flight CT Scanner

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Recent developments have shown the potential of a time-of-flight measurement of individual photons using fast X-ray detectors to significantly reduce the adverse effects of scattered photons both in X-ray radiography and computed tomography (CT) without using anti-scatter grids. However, the improvements observed in simulations have yet to be confirmed experimentally using a system realistic for clinical use. Producing a first CT image with real-time discrimination of scattered photons requires an ultrafast single X-ray counting system and an ultrashort pulsed X-ray source. This contribution focuses on the design and preliminary characterization of a 16-channel scintillator-based scanner. The detector is composed of 16 4x4x2.5 mm3 LYSO scintillators coupled with 16 4x4 mm2 SiPMs from Broadcom (AFBR-S4N44C013). A Nino pre-amplifier and two time-to-digital converters designed in-house read the SiPMs' output to provide time and energy measurements using time-over-threshold. GATE simulations have shown that if a 200 ps time resolution is obtained, this system will be able to remove half of the scattered photon, resulting in a 20% increase in CNR. This system will be used to improve our understanding of time-of-flight scatter rejection and evaluate scintillators for fast X-ray measurements.

System considerations for TOFPET CTR resolution ≤100ps / 37

GATE simulation of a brain-dedicated PET system using metacrystals for optimized ToF capability

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PET technology has received several improvements in performance due to significant advances in instrumentation and software. Recent trends make use of the time-of-flight (ToF) information to increase the signal-to-noise ratio (SNR) in the reconstructed image and improve the location of the annihilation event. One of the most important components in ToF-PET instrumentation is the scintillation crystal. The development of scintillation crystals is illustrated by the advent of inorganic scintillators with better energy resolution, faster response and higher detection efficiency. Recently, the metascintillator approach has been proposed to overcome the timing resolution limits of the commonly used scintillators. The metascintillator is an engineered composition of small units that combines and optimizes several features in the same scintillator heterostructure. After incident radiation interacts with the metascintillator, a recoil electron is formed and gradually loses energy along its travel path. The scintillator heterostructure follows a probability distribution to share the energy of the radiation interaction with different materials and combine their properties. Therefore, scintillator heterostructure has to be designed considering the range of the recoil electron, which is typically 400 to 500 microns in BGO and LYSO crystals.

In this work, a metascintillator-based PET system was modeled using the GATE Monte Carlo simulations platform and compared against bulk LYSO and BGO PET systems. Several metascintillator thickness values were simulated to determine its equivalence to a bulk BGO crystal in terms of sensitivity, noise equivalent count rate (NECR) and scatter fraction, according to the NEMA guidelines. Only listmode data was used for comparison purposes to avoid the dependence of the image reconstruction algorithm. The main goal of this work is to determine the clinical added value by using metascintillator-based detectors in brain PET imaging.

System considerations for TOFPET CTR resolution ≤100ps / 22

Towards precise temporal resolution using highly multiplexed readout schemes for gamma-ray detectors

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Nowadays, the performance in Time-of-Flight (TOF) for Positron Emission Tomography (PET) detectors, which boosts the effective sensitivity of the system, is reaching the technological limit imposed by the scintillator crystal and photosensors used. Increasing the axial length of a PET scanner improves the solid angle coverage, thus allowing to boost the sensitivity. This are the so-called Total Body PET (TB-PET) scanners. Recently, the TB-PET systems for human use called Biograph Vision from Siemens and the uExplorer from United Imaging have been commercialized and first clinical studies have been shown. The Biograph Vision has remarkable TOF capabilities of 217 ps FWHM. Nevertheless, from the technical perspective, there is still room for further improving these systems with depth of interaction (DOI), and/or readout channel reduction as it is major concern to develop a long axial scanner. In this work, we will show the preliminary results addressing these two major concerns on a TB-PET system, both the reduction of readout channels as well as the DOI capabilities of the system by using a LYSO semi-monolithic scintillator crystal coupled to 3x3 mm^2 SiPM. The electronic chain comprises a reduction readout methodology and an ASIC for readout (TOF-PET2 from PETsys). This approach allowed us to achieve <300 ps TOF as well as sub-3mm spatial resolution and DOI.

System considerations for TOFPET CTR resolution ≤100ps / 61

Evaluation of a PET detector with ultra-high spatial and timing resolution suitable for preclinical systems

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In Positron Emission Tomography (PET), depending on the scintillator type and geometry, many events undergo Compton interactions before photoelectric absorption. If these interactions are not properly identified, an image blurring is observed. In this report, the main components of the scatter ring of a Compton-PET system for mice brain imaging with high timing and spatial resolution are described. We have carried out a performance study in terms of energy, spatial and timing resolutions.

Two detector blocks composed of 8×8 SiPM arrays of 3×3 mm2 elements and cell sizes of 50 µm have been employed. The scintillation material was LYSO:Ca crystal array of 12×12 with 0.95×0.95×3 mm3, the array is placed at the center of the SiPM array covering 4×4 photosensors. All surfaces of each pixel of the array were polished and all but the face coupled to the photosensor, covered with ESR. The crystal array was designed such that groups of 3×3 pixels match one photosensor active area (9-to-1 coupling). The frontend electronics used was the TOFPET2 ASIC.

All pixels were identified using CoG method, furthermore Voronoi diagrams were applied to identify each pixel. After applying a custom energy equalization procedure, the energy resolution decreases from 35% to 19% in arbitrary ADC units

The Detector Time Resolution (DTR) values for different energy windows (EW) applied to the energy spectra of both detectors were studied. The energy spectrum was divided into 4 different windows from low, medium to high Compton energies and the photopeak. For low EW, the measured DTR is around 275 ps. Better performance is observed at the photopeak energies, finding values of 130 ps DTR considering 9 pixels matching 1 SiPM, and an improved 112 ps at crystal pixel level.

In next steps, the size of the crystal array will increase covering the 8×8 SiPM array with 24×24 pixels. Moreover, we also will scale the system to 8 detectors forming a rectangular parallelepiped and fully characterize the system

System considerations for TOFPET CTR resolution ≤100ps / 19

Image quality of a pure Cherenkov TOF PET scanner: a simulation study

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In positron emission tomography, dense Cherenkov radiators provide an opportunity for high gamma detection efficiency and excellent CTR. However, because only a few tens of Cherenkov photons follow a gamma interaction in the radiator, the detection efficiency and the energy resolution of a pure Cherenkov detector are an issue. We study gamma detection efficiency and CTR of PbF_2 based detectors with different surface treatments and photo-detectors (SiPMs with realistic PDE and 70 ps FWHM SPTR) covering one, two, or all crystal faces. We investigate the potential performance of a full-size Cherenkov PET using the NEMA NU 2-2018 standard and compare image quality with a reference scanner - Siemens Biograph Vision PET scanner - with the geometry of Cherenkov scanners based on that of the reference scanner. Monte Carlo simulations were performed on a super-computing network using GATE, and CASToR was used for TOF-OSEM image reconstruction. Normalization, scatter, random, and attenuation correction factors were included in the reconstruction. Cherenkov scanner with 1-sided readout had similar TOF performance (~210 ps CTR-FWHM) and achieved very similar image quality as the reference scanner. By using 2-sided (SiPMs at the sides of the crystal) or 6-sided detector designs with better coincidence detection efficiency and ~120 ps CTR-FWHM, even better image quality was achieved. The main limitation of our simulation study is not including the noise in the simulation - especially the dark count events of the SiPMs. We demonstrate that even though pure Cherenkov scanners have basically no energy resolution, the scatter fraction is around 50%, compared to 33% with the reference scanner, and is not prohibitively large. Images comparable to the state-of-the-art clinical PET scanner can be achieved due to improved efficiency and CTR attainable with PbF_2. Low-cost Cherenkov detectors could become especially interesting for total-body scanners.

System considerations for TOFPET CTR resolution ≤100ps / 65

Exploration of the physical limits for Cherenkov PET using tiny crystals and a large cube

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This study is performed within the scope of the SwissPix project, which aims at developing a new photo-sensor for Positron Emission Tomography with ~10 ps FHWM timing resolution, capable of exploiting the prompt nature of Cherenkov radiation. Using Monte Carlo simulations, we estimated the physical limits of timing resolution for two possible detector geometries: a radiator of 3x3x3 mm^3 with one photo-sensor attached opposite to the side the gamma enters, and a 25x25x25 mm^3 cube with photo-sensors fully covering all six sides. The 25x25x25 mm^3 cube required reconstruction of the gamma interaction position that it performed using arrival times and the Cherenkov photons detection positions, minimizing a cost function for the gamma interaction position. Monte Carlo information confirmed the reconstruction of the gamma interaction position inside the cube. We simulated a whole-body PET system with GATE (Geant4 Application for Tomographic Emission). As a result, the spatial resolution in three directions of the point source was obtained reconstruction-less.

System considerations for TOFPET CTR resolution ≤100ps / 12

Timing with (semi-)prompt photons: a review and perspective on the full detector chain

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Accurate time estimation utilizing (semi-)prompt photons can benefit Time-of-Flight Positron Emission Tomography. However, we are limited to fewer detected photons with current state-of-the-art ultra-fast detectors, ultimately resulting in the pursuit of every single photon.

In the lab, this quest starts with light production (Cherenkov photons, quantum confinement luminescence etc), continues with the efficient light transport to the photodetector (high refractive index materials, photonic crystals, novel readout designs) over the photodetector (SPTR, PDE, correlated noise) and finishes with signal processing (low noise, high bandwidth electronics, fast ASIC, power consumption) and digitization. Finally, the measured data can be reconstructed to images using the appropriate TOF system response matrix. However, even the best time resolution does not achieve the desired image quality if quantities such as sensitivity, energy resolution, or depth-of-interaction are overlooked.

This contribution provides an extensive review of recent developments in fast timing with (semi-)prompt photons, emphasizing the whole radiation detector chain. In addition, we discuss system integration aspects, limits and paths for future detector improvements toward and below 100 ps CTR with PET-sized geometries.

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Power efficient high-frequency readout of timing optimized SiPMs for Cherenkov radiation

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Recent SiPM developments and improved front-end electronics have opened new doors in TOF-PET with a focus on prompt photon detection. For instance, the relatively high Cherenkov yield of Bismuth-Germanate (BGO) upon 511keV gamma interaction has triggered a lot of interest, especially for its use in total-body PET scanners due to the crystal's relatively low production costs. However, the electronic readout and timing optimization of the SiPMs still poses many questions. Lab experiments have shown the prospect of Cherenkov detection, with coincidence time resolutions (CTRs) <200ps FWHM achieved with small pixels, but lack system integration due to an unacceptable high power consumption of the used amplifiers.

In this contribution, we will discuss different readout concepts of analog SiPMs for which we studied several high-bandwidth amplifiers with a power consumption ranging from 288mW to 17mW. We found that all tested amplifiers showed similar CTR performance of ~100ps FWHM coupling 3x3x3mm³ LYSO:Ce from Epic-crystals to an S14160-3050HS Hamamatsu SiPM. In addition, we identified the noise contribution to the timing as negligible for all designs.

In a further step, we selected the most practical circuit, having 70mW power consumption per channel, and tested with BGO the CTR performance of newly developed SiPMs from Fondazione Bruno Kessler, optimized for highest single photon time resolution (SPTR). We achieved a best CTR FWHM of 127ps for 2x2x3mm³ and 245ps for 3x3x20mm³ BGO crystals.

To give an insight in the timing properties of these SiPMs, we measured the SPTR with black coated PbF2 crystals of 2x2x3mm³ size. We confirmed an SPTR of 68ps FWHM published in literature for standard devices and show that the optimized samples can improve this value to 55ps. Pushing the SiPM bias to its limits, we even measured an SPTR as high as 40ps FWHM. In an extended discussion we will give a roadmap to best timing with prompt photons and an outlook on system integration.

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Nanophotonic particle detectors: how quantum optics can contribute to scintillators and Cherenkov detectors

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Nanophotonics - the control of the flow of light on the nanoscale - had immense impact on technology in recent years, with example spanning from solar cells and LEDs to the telecommunication industry.
We will discuss the prospects of nanophotonics for the development of future scintillators.

In particular, I will focus on two recent experiments:
1. At MIT, we observed a ten-fold enhancement by a nanophotonic surface-patterned scintillator.
2. At Technion, we observed a 30-50% enhancement of scintillation lifetime, directionality, and efficiency, by a nanophotonic multi-layered scintillator.

I will conclude with recent ideas that utilize new concepts from quantum optics for advancements in scintillator science.

Round Table discussion / 77

Introduction to the Round table

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Recent developments in the field of scintillator for fast radiation detectors

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Since many decades scintillating crystals have been used for radiation detectors such as high resolution electromagnetic calorimeters and positron emission tomographs. Significant progress has been made in the field of inorganic scintillators in the understanding of their scintillation properties, radiation hardness and production methods over the last 30 years. In addition many applications also have more and more need for an improved timing resolution. To this purpose many studies have been carried out in the framework of the Crystal Clear Collaboration on the investigation, improvement and exploitation of different processes for new fast light emission such as wideband semiconductor nanomaterials, hot intraband luminescence, cross luminescence and Cerenkov light, as well as on the production and the assembly of such material: crystal fibers, 3D printing, hybrid structure combining materials with different properties.
In this contribution, a review of recent research efforts and developments on fast timing scintilllators for future detectors will be presented.

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Timing limits and estimators in the presence of prompt photons in TOF-PET detectors

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Ultrafast emission processes are required to further improve the coincidence time resolution (CTR) of time-of-flight PET detectors. Extensive research efforts are underway in trying to generate and detect so-called prompt photons having much faster emission dynamics than conventional scintillation. In this contribution, we provide an analysis on key aspects to better model and understand the effects of prompt photons on CTR in the presence of slower scintillation processes. As some current and promising future detectors can produce both scintillation and prompt photons, we compare standard timing estimators to a statistical lower bound dedicated for these double-population detectors. We carry out this comparison for various prompt photon emission dynamics and various amounts of time overlap between the prompt and scintillation signals. Event-by-event fluctuations on the prompt photon production and detection yield are also included in the analysis of estimators and lower bounds. We show that this feature enables a better CTR match with experimental values obtained for BGO whose timing spectrum is strongly altered by a fluctuating Cherenkov yield. Finally, we discuss the effects of the anisotropic emission of Cherenkov photons. This review of key aspects of prompt-generating detectors can help define the requirements towards ultrafast timing.

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Scintillator response time probed at femtosecond photoexcitation

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Time-of-flight positron emission tomography (TOFPET) is currently one of the key directions in medical imaging enabling substantially higher spatial resolution and lower radiation dose for patients. This trend requires new scintillators with faster response and currently results in the substitution of BGO by LYSO:Ce as the scintillator of choice in TOFPETs. The scintillator material represents the major part of the total TOFPET production costs, thus the tradeoff between the less expensive technologies for growing LYSO:Ce single crystals and the response time of these crystals to annihilation gamma-quanta become an important issue for future TOFPETs.

We report on a method for express testing the response time of scintillators, particularly LYSO:Ce, which is based on measuring the transient optical absorption induced by a resonant photoexcitation of activator ions Ce3+ [1]. We show that the electrons optically excited to Ce3+ higher energy levels laying in the conduction band of the host matrix have two relaxation routs to the lowest excited level 5d1 serving as a radiative level: the intracenter relaxation, which is found to have a characteristic time of ~500 fs, and the relaxation via the extended states in the conduction band with subsequent trapping at shallow traps. As at the excitation by ionizing radiation, the latter process governs the rise time in the population of the lowest excited state 5d1, which is of the order of a few picoseconds at resonant Ce3+ excitation and can be reliably measured using femtosecond laser pulses without any problems of optical coupling and readout electronics.

We demonstrate that the technique based on the transient optical absorption measurements in subpicosecond domain is a powerful tool for both searching for novel fast scintillators and express routine testing of scintillator crystals selected for TOFPET devices.

[1] M. Korzhik, G. Tamulaitis, A.N. Vasil'ev, Physics of Fast Processes in Scintillators, Springer, 2020.

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Optically stimulated luminescence in state-of-the-art LYSO:Ce scintillators

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In this contribution we extend the current understanding of the different energy-transfer mechanisms present in state-of-the-art Lu(2−x)YxSi2O5:Ce scintillators. We present results of a photon emission mechanism known as optical stimulated luminescence (OSL), able to efficiently trap a fraction of the energy deposited in the material. OSL competes with the non-radiative energy transfer to luminescent centers responsible for the scintillation pulse and it is estimated to have a yield below 1000 ph/MeV. We use spectrally and temporally resolved OSL readout to characterize such process and show that OSL makes use of the same Ce3+ luminescent centers that were engineered for the scintillation. While OSL degrades the intrinsic scintillating performance by reducing the amount of photons emitted following the passage of ionizing radiation, it is able to encode highly resolved spatial information of the particles's interaction point. A proof of concept readout yielding sub-1mm^3 spatial resolution is demonstrated using a cubic LYSO crystal to image dose profiles and the attenuation length of 511 keV gamma photons.

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Characterization of a semi-monolithic detector with DOI and TOF capabilities for preclinical PET

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A semi-monolithic scintillator crystal consists of a monolithic block segmented in only one direction in different pieces called slabs. This approach is intended to combine the benefits of both pixelated and monolithic crystals, which are usually employed in PET detectors, preserving the good timing resolution of pixelated crystals, and the high sensitivity and good spatial resolution of monolithic crystals.
In this work, a semi-monolithic block consisting of 24 LYSO slabs of 25.4×12×1 mm3 coupled to a matrix of 8×8 SiPMs of 3×3 mm2 active area each with 50 µm cell size and 3.2 mm pitch has been characterized. The 64 individual signals are read out by the TOFPET2 ASIC. Different treatments have been applied to different surfaces of the detector block in order to assess their impact on the detector performance. In "All ESR" configuration, all the faces of the slabs are polished and ESR is employed as separator between the slabs and also on the lateral and top faces. In "ESR+B+RR", all the faces of the slabs are polished, ESR is employed as separator between the slabs and also on the two monolithic outer faces, retroreflector (RR) is applied on the top face and black (B) painting on the two pixelated outer faces. "ESR+B+RR unpolished" configuration is identical to "ESR+B+RR", but the two pixelated outer faces have been mechanically unpolished.
The energy, spatial and MAE resolutions are, respectively, 13.1%, 1.7 mm and 0.8 mm for the "All ESR", 13.8%, 1.6 mm and 0.7 mm for the "ESR+B+RR" and 15.5%, 1.5 mm and 0.7 mm for the "ESR+B+RR unpolished". The DOI resolution has been evaluated for the "ESR+B+RR unpolished" detector showing 2.0 mm FWHM and 1.0 mm MAE. The coincidence time resolution (CTR) for two identical blocks of the "All ESR" configuration is 336 ps when the first timestamp is used and it improves to 276 ps when energy-weighted averaging of the timestamps belonging to the same event is applied.

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A Comprehensive Study on the Timing Limits Using High Light Yield Crystals and High-frequency Front-end Circuit for TOF PET Detectors

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Purpose– The coincidence time resolution (CTR) values can be improved by increasing photostatistics, which in the PET detector occurs with a high light yield (LY) of scintillation crystals. The two main contributors to the LY are the intrinsic LY of the scintillation crystal and the light transfer efficiency, which depend on crystal material, dimensions, and wrapping conditions. We report on a systematic study on achievable CTR performance with high LY scintillation crystals coupled to state-of-the-art high-frequency electronics followed by a DRS4-based 1GSPS digitizer.

Methods– Various high LY scintillation crystals, including LGSO, LYSO:Ce:Ca, LYSO:Ce:Mg, were investigated to measure relative LY and achievable CTR values under differing physical conditions such as crystal pixel size and reflector material. For a fast timing channel, high-frequency readout electronics were constructed employing passive compensation for the SiPM detector capacitance. The compensation was implemented using a 3 GHz balun transformer connected between both ends of the SiPM so that a balanced-to-unbalanced converted signal propagates into the RF amplifier.

Results– With the optimized leading-edge threshold, the measurements yielded CTR values of 177 ps for LGSO crystal wrapped with ESR film, 142 ps with Teflon, and 377 ps with the black tape. The Teflon tape yielded not only the best LY but also in terms of the CTR among different reflector materials. With the crystal wrapped with black tape, the LYs significantly deteriorated, which also caused the worst CTR value. The double-doped crystals showed sub-150 ps CTR, which is similar to or slightly better than the LGSO crystals and corresponds to the increased LY.

Conclusion– In this study, the photostatistical effect on the potential temporal resolution was comprehensively demonstrated. Also, it was also shown that high-frequency electronics still can be fully exploited with a relatively low sampling ratio showing encouraging results.

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Defect process in BGO: A precursor to band-edge engineering and design of stable scintillators

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Scintillating materials suffer degradation while in operation due to defects induced in the process. Lattice defects could severely impact detector efficiency via non-radiative transfer of electron excitation. Like most materials for this kind of applications, there is a strong performance-structure relationship. An understanding of the defect formation process is therefore important in the design of resilient scintillators. Bismuth germanate Bi4 Ge3 O12 (BGO) has been extensively studied as a luminescent material that emits light in the visible region upon exposure to ionizing radiation. Investigating the likelihood of band gap engineering (BGE) in bismuth germanate considering trap depths of intrinsic defects is essential for improving existing materials and in the design of new ones. In this work, using density functional theory, we studied the formation energies of vacancies/interstitials, cation antisites in pristine BGO. To provide insights into factors affecting the stability of doped systems and unravel the origin of the activity of doped BGO, we investigate the structural properties, energetics of pristine and REE (Nd, Pr, Ce and Tm) doped BGO using first principles methods. We reproduced the band gap of the pristine BGO to within experimental reported value using the hybrid PBE0 functional. Analysis of defect energetics reveals a strong dependence of properties on defect types. Further investigations lead to the discovery of energy levels induced by the defects providing a route for the possibility of manipulating the electronic properties for target application. It provides an understanding of ways that could be adopted to suppress hot electron thermalization that could lead to intra-band luminescence of charge carriers. Our analysis of the role of doping on BGO confirms route for the modification of the stability of the system in presence of defects. Analysis of the optical properties reveals variations in different regions of photon energy spectra.

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A proof-of-concept of cross-luminescent metascintillators

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— In order to achieve superior timing for time-of-flight positron emission tomography, combined with high detection efficiency and cost-effectiveness, we probe the applicability of BaF2 in metascintillators driven by timing of cross-luminescence photon production. Building on simulation study of energy sharing and analytic multi-exponential scintillation pulse and sensitivity characteristics, we build a 300 μm BGO:300 μm BaF2 pixel of 3x3x15 mm3 and test it in the laboratory. In order to harness the deep ultraviolet cross-luminescent light component which provides the timing, we use the FBK VUV SiPM and cold glycerin for coupling. Metascintillator energy sharing is addressed through a simple double integration approach, algorithmically developed in Python. We reach an energy resolution of 22%, comparable to an 18% resolution of simple BGO pixels for the same system, through the optimized use of both integrals of the metascintillator pulse. We demonstrate our ability to measure the energy sharing extent of each individual pulse in a pipelined manner and match the measured distribution with the features of the simulated one. With the knowledge of energy sharing, a timewalk correction is applied which brings significant improvements in both coincidence time resolution (CTR) and fitting quality of the Δt histogram. We reach a 242 ps CTR for the entire photopeak, while for a subset of 13% of the most shared events isolated, the CTR value reached is at 108 ps, better than the 3x3x5 mm3 LYSO:Ce:Ca reference crystal, thus limited by the measurement setup. While we are considering different ways to further improve these results, this proof-of-concept system and measurements demonstrate the applicability of cross-luminescence for metascintillator development through the application of UV friendly optical devices and simple and easily implementable digital algorithms.

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A Study of Mass Production of Metacrystal Pixels and Arrays

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There is a desire to continue reducing the time resolution of scintillator based detectors without sacrificing the space resolution to further improve the image resolution of current ToF PET scanners. Unfortunately, we have reached a limit of finding one ideal single crystal candidate that can achieve both aims. Current commercial LSO and LYSO crystal detector can offer time resolution near 200 ps at the system level with light yield close to 50K/MeV. Among all known fast decay scintillating crystals, BaF2 stands out with a decay constant of 0.6 ns for its short emission component near 200 nm. However, BaF2 has a lower than LYSO Z (53),density (4.88) and light yield (1,400/MeV) for the fast emission. Deep UV emission can also create serious problem of low photon detection efficiency even for the current state-of-the-art UV-sensitive SiPMs.

The idea of meta-crystal pixels and arrays can offer a solution to overcome this impasse. Meta-crystal pixels consist of interlayers of two kinds of thin crystal plates with different scintillating properties to complement each other, typically one with fast decay and one with high light yield. Given the current knowledge, the combination of BaF2 and LYSO seems to offer the best solution. The goal for the LYSO/BaF2 meta-pixel is to reach 100ps at the system level,a factor of 2 better than that of bulk LYSO.

These meta-crystal pixels will be made with BaF2 and LYSO thin crystal plates of 0.3 mm thick or less. With such large quantity of crystal plates needed even for one single scanner, it is imperative to develop a cost effective manufacturing process to control the cost.

CPI has been involved with other collaborators to optimize the meta-crystal pixel and array design. At the same time, we also start to make the effort to establish a cost-effective mass production process. We will report our preliminary result at this workshop.

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Exploiting Cherenkov radiation and cross-luminescence emission with BGO/BaF2 metacrystals

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In the field of time-of-flight positron emission tomography (PET-TOF), the time resolution of the scintillation based detector is an essential feature. Recent studies have shown that some materials have fast emissions in the vacuum ultraviolet (VUV) region.
To acquire the fast-rising signals of these emissions, we are using optimized Coincidence Time Resolution (CTR) test boards with two output signals (timing and energy). Since the VUV silicon photomultipliers (SiPMs) do not have a protective layer on top of the metal, two different coupling materials are used and
compared. The experiment is focused on Barium Fluoride (BaF2) crystals exploiting their cross-luminescence characteristic using VUV (SiPMs) from Fondazione Bruno Kessler (FBK). Moreover, a yttrium doped variant of these crystals (BaF2-Y) has been considered for comparison. The results show a DTR of 123.6 ps and 93ps for the pure and doped variants, respectively. As reference detectors, we use a near-ultraviolet (NUV) from FBK coupled with a 3×3×5 mm3 LYSO:Ce,Ca and a 3×3×15 mm3 BGO pixels, with time resolutions (DTR) of 65.1 ps (Gaussian) and 300 ps (Laplacian), respectively.

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GATE optical simulations of DOI enabled metascintillator based on semi-monolithic design

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The novel concept of metascintllator, topologies consisting of heterogeneous scinitllating and light-guiding materials has been proved to achieve an equivalent CTR of 200ps for BGO-based set and 140ps for LYSO-based set even with an non-optimized configuration. In this work, we evaluate a novel architecture: The principle is to slice a slow scintillator (BGO or LYSO) monolithic in thin slabs, then interlaeve them with thin segmented fast scintillators (plastic EJ232 or EJ232Q), and finally couple them to an array of SiPMs, in what we term semi-monolithic meta-scintillator (SMMS). As the fast scintillator retains an 1-to-1 coupling with independent SiPMs, fast photons are contained within the limited space and statistical variation is similar to that of single pixel. At the same time, photons of the high-Z material are distributed over the SiPM array, providing Depth-of-interaction encoding according to the semi-monolithic paradigm. We combine layers of slow scintillator of dimension 0.3 x 25.5 x 15.0 mm3 or 0.2 x 25.5 x 15.0 mm3 and layers of fast scintillator of dimensions 0.1 x 3.1 x 15.0 mm. We used the Monte Carlo Ray-Tracing Gate simulator to study and investigate the performance of this new type of semi-monolithic. Based on the simulation results, it is shown that the time resolution of semi-monolithic metapixel is equivalent to the single metapixel with the same scintillator mix. In particular, LYSO based designs lead to an overall DTR of 80 ps after implementation of timewalk correction, while BGO based designs lead to equivalent DTR of 160 ps. On top of that, the detected visibly variable photon distributions along the SiPM array, which allow a determination of the depth-of-interaction with < 3mm precision leading to a detector cell of 3x3x3 mm3, combining such element size with ToF capabilities in a cost-effective design.Further developments include the implementation of machine learning for further improving both DoI and ToF performance of the SMMS.

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Toward a new generation of detectors for TOF-PET with heterostructured scintillators

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Lutetium-based scintillators (LSO, LYSO, LGSO) are commonly used for TOF-PET, representing the better compromise between stopping power, light yield, energy and time resolution. However, the limit in the improvement of time performances of these materials has been reached, and new technologies to break the current boundaries are being investigated. Heterostructured scintillators are gaining ground as a possible solution to the conflict between high sensitivity and fast timing (coincidence time resolution below 100ps) of TOF-PET detectors. They rely on the combination of two materials with complementary properties (e.g. high stopping power and ultra-fast scintillation kinetics) and the mechanism of energy sharing by the recoil photoelectron. For the energy sharing to be effective, the geometry of heterostructures must be chosen carefully, taking into account conflicting factors (i.e. overall sensitivity, percentage of shared events, amount of energy deposited in the fast material). We performed such an optimization study for heterostructures made up of alternating layers with Monte Carlo simulations (Geant4 toolkit), using as heavy material BGO and as fast material EJ232 plastic scintillator. Afterward, the timing performances of two different configurations were assessed experimentally and compared to those of bulk BGO and layered BGO (stack of BGO plates having the same thickness as those used in real heterostructures). Collimated depth-of-interaction (DOI) measurements were also performed, allowing us to conclude that the main limiting factor of heterostructures is represented by light transport and DOI contribution. Carrying on previous development of our group, preliminary tests on the inclusion of these heterostructured pixels in a full matrix, which allow for a DOI correction based on a light sharing method, are already ongoing. In this way, it will be possible to push even further the timing capability of this new emerging generation of TOF-PET detectors.

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Fast timing with nanocrystalline lead halide perovskite thin films on scintillating wafers

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In recent years the need for ultrafast detection of ionizing radiation is being pushed particularly by high energy physics and medical imaging. It requires detection systems involving scintillating materials able to produce quasiprompt photons. To achieve that, there are several concepts currently being pursued, one of them being exploitation of quantum confinement effect in nanoparticles. Eventually one can create heterostructures combining nanocrystalline material with standard dense scintillators having the high stopping power for ionizing radiation.
Lead halide perovskite nanocrystals of the formula CsPbBr3 have recently attracted attention as potential time taggers in such scintillating heterostructures thanks to their ultrafast decay kinetics. We investigate the potential of this material experimentally. We fabricated CsPbBr3 thin films on scintillating GGAG:Ce (Gd2.985Ce0.015Ga2.7Al2.3O12) wafer as a model structure for the future sampling detector geometry. We focus on the radioluminescence (RL) response of such composite material. We compare the results of two spin-coating methods, namely the static and the dynamic process, for the thin film preparation. We demonstrate enhanced RL intensity of both CsPbBr3 and GGAG:Ce scintillating constituents of a composite material. This synergic effect arises in both the RL spectra and decays. Our study confirms that the thin nanocomposite layer is able to perform as efficient time tagger in the sandwich detector for ultrafast timing applications.

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Extreme γ-ray radiation hardness and high scintillation yield in perovskite nanocrystals

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Radiation detection is of outmost importance in fundamental scientific research and applications including medical diagnostics, homeland security, environmental monitoring, and non-destructive inspection in industrial manufacturing. Lead halide perovskites (LHP) are rapidly emerging as high-Z materials for next generation of solution processable scintillators and photoconductors for ionizing radiation detection. To unlock their full potential as reliable and cost-effective alternatives to conventional scintillators, LHP urge to conjugate high scintillation yields with emission stability over prolonged exposure to high doses of ionizing radiation. To date, however, no definitive solution has been devised to suppress parasitic processes affecting the scintillation efficiency and resulting in undesiderable after-glows in LHP. Similarly, nothing is known of their radiation hardness for doses above a few kGy. Here, I demonstrate, for the first time, that CsPbBr3 nanocrystals (NCs) exhibit exceptional radiation hardness for 60Co gamma radiation doses as high as 1 MGy. Side-by-side spectroscopic and radiometric experiments further highlight that, despite their defect tolerance, scintillators based on standard CsPbBr3 NCs suffer from electron trapping in highly dense surface traps. This limitation is effectively overcome through a post synthesis surface fluorination treatment resulting in over 500% enhancement of the scintillation efficiency which becomes comparable to commercial scintillator crystals, while still retaining exceptional levels of radiation harness. These results have profound implications for the widespread of LHPs in radiation detection schemes for high-energy physics, nuclear monitoring, nuclear batteries and space-grade solar cells where high radiation hardness is critical for successful and long-running operation, as well as for ultra-stable scintillators in medicine, environmental/industrial monitoring and border control.

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Nanocrystals for fast timing applications embedded in a polystyrene matrix

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Nanocrystals like ZnO:Ga or $CsPbBr_3$ were identified as potential scintillators for fast timing applications, including medical imaging techniques such as TOF-PET (time-of-flight positron emission tomography) or TOF-CT (time-of-flight computed tomography). Both feature sub-nanosecond scintillation decays which is a crucial property for this type of application.
However, such materials with desired properties are available either as a colloidal solution, or in powder form, and thus unsuitable as bulk scintillating detectors with sufficient ruggedness. Therefore, the small-sized materials need to be incorporated into a suitable matrix, improving their durability, applicability, absorption of radiation or light extraction efficiency.
We will present our recent progress with ZnO:Ga and $CsPbBr_3$ nanocrystals embedded in a polymer matrix. The main focus will be kept on nanocomposites using $CsPbBr_3$ nanocrystals because we recently characterized their timing capability with a unique novel setup coupled to analog Silicon Photomultipliers and low energy X-ray excitation. This allowed for the characterization of low-stopping power scintillator, such as low-filling (up to 10 %) of nanocrystals in a polystyrene matrix. Even though the nanocomposite samples of $CsPbBr_3$ in polystyrene were not fully optimized, a more than twofold better time resolution with respect to conventional LYSO:Ce was achieved for the low-energy X-rays. Our study represents a promising starting point for the optimization of such nanocomposites towards their use in TOF-PET or TOF-CT.

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Perpendicular photonic devices for scintillation detectors

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In the quest for optimized time-of-flight scintillation detectors, an important physical barrier is the statistical variation of photon production, propagation, extraction and detection. While nothing can be done for the isotropic production of scintillation light, we simulate a way to alter propagation and extraction of optical photons from the scintillator, using photonic crystal (PhC) slabs organized in a perpendicular orientation to the photodetector surface. We try different designs using several approaches such as Rigorous Coupled Wave Analysis, Plane Wave Expansion, Guided Mode Expansion and Finite-difference time-domain methods, implemented in proprietary and open-source software. We compare the results of different optical simulations that demonstrate the ability of designed PhC slabs to bend light towards its extraction surface, reducing the propagation modes of light within the scintillator. This reduces the corresponding statistical variation, the main obstacle in achieving superior timing results. These designs are developed using the characteristics of commonly available materials such as Silica (SiO2), Gallium arsenide (GaAs) and niobium pentoxide (Nb2O5) and in dimensions within the machining capabilities of available deposition and printing methods. To investigate the performance of optimized PhC slab design, a domain of hexahedron with dimension of 2.4x2.4x2.1⊠m has been simulated via FDTD. The lateral energy flux ratio to source radiation has been improved by around 30% for target wavelength of 375nm. Simulated PhC slabs are ideal for soft scintillators, such as organic ones, but can also be applied to standard crystals, and can be used either as separators in pixels or the metascintillator paradigm. Further investigation on the optimized design of PhC slabs is taking place through development of automatic optimization routines, with optimization potential depending on the wavelength and favored incidence angle of the chosen scintillating light.

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Scintillation mechanisms in II-VI semiconductor nanostructures

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II-VI semiconductor nanocrystals (NCs) are known to show very good optical fluorescence quantum yields. As direct band gap semiconductors they also exhibit a fast excitonic emission in the order of a few tens of ns. In addition, because of their reduced size, multiple excitation generation are favoured, resulting in a significantly faster emission which can be attractive for the scintillation field. Nevertheless, the stopping power for x-ray and gamma-ray requires to handle materials in bulky form or to implement strategies with hybrid materials. As an illustration, for CdSe nanoplatelets deposited on Lu2SiO5Ce3+ single crystal, the energy sharing has demonstrated a coincidence time resolution improvement, a crucial parameter for time of flight positron emission tomography. Nevertheless, the use of semiconducting NCs at very high concentrations is facing the self-absorption issue due to a small stokes shift, leading to a decrease of the light extraction efficiency. One strategy to overcome the self-absorption issue is to use core/shell NCs, allowing to increase the stopping power of the media while keeping constant the concentration of emitting centers and thus the self-absorption. The shell acts in this case as an "antenna" or collector for the ionizing radiation, and does not contribute to the self-absorption. On the other hand, large shells reduce the confinement effect and may induce bulk crystal defects.

Therefore, exploring nanocrystals-based materials in a large variety in morphologies and sizes is of high interest to describe the underlying physics of the energy deposition and relaxation process under ionizing radiation in nanoscintillators. In this contribution, we present the cases of CdSe/CdS based spherical quantum wells, CdSe-based nanoplatelets as core/crown and core/shell, and discuss the comparison of optical response under intense optical excitation and x-ray excitation as compared to simulations of energy relaxation.

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Toward Ultrafast Scintillators with Fluorescent Colloidal Nanocrystals

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Colloidal nanocrystals combine the flexibility of solution-processed materials with the enhanced stability of inorganic semiconductors. They are typically composed of heavy-metal chalcogenides and have a high fluorescence quantum efficiency, which makes them suitable for the detection of high-energy photons and subsequent conversion into visible radiation.

In this presentation, I will discuss the opportunities and challenges when using colloidal nanocrystals for scintillation with a targeted resolution of 10 picoseconds. By controlling the shape, and embedding the emitting core in a second, protective semiconductor shell, we can tune the emission rate and efficiency, and reach nanosecond fluorescence decay times. In addition, the nanocrystal core/shell architecture allows for minimizing nonradiative Auger recombination, so that we can also exploit nonlinear emission processes, which yield a sub-nanosecond fluorescence decay time. However, to obtain a high overall light outcoupling, we also need to focus our attention on the elimination of reabsorption losses of the emitted light. This is, for instance, mediated again by the proper design of the nanocrystal heterostructure.

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GaN-InGaN multiple quantum well (MQW): superfast semiconductor scintillator for time tagging in composite pixels for TOF-PET

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To improve timing coincidence resolution to the time scale of few tens of picoseconds in future generations of TOF-PET, among others, scintillator material producing more light in subnanosecond time scale is needed. Semiconductors with Wannier exciton emission in quantum confinement regime are an option as their radiative lifetimes can be shortened down to subnanosecond time scale thanks to the microscopic superrradiance effect. These luminescence phenomena are studied for more than 40 years. In bulk semiconductors, given the nature of this kind of excitonic emission, there is very small Stokes shift which results in huge reabsorption in cases when optical path of generated luminescence is of about just few mm. This problem can be solved by thin QWs with redshifted emission energy with respect to the surrounding material. Among direct band semiconductors the nitrides, such as AlGaN, GaN or InGaN, offer the advantage of high binding energy of exciton which is necessary to prevent ionization losses (exciton disintegration) around room temperature. InGaN/GaN QWs can significantly enhance fast excitonic emission. Their emission wavelength can be tuned by In content and wells dimension within 400-450nm. Radiative lifetimes are of the order of 1 ns with negligible ionization losses around room temperature. The main technological challenge is to achieve sufficient total thickness of MQW to share reasonable amount of the absorbed energy of incoming 511keV photons and to suppress the visible defect emission which is slow and competes with fast excitonic one.
We will discuss potential of GaN-InGaN multiple quantum well scintillators (MQW) for TOF-PET detector where this material would constitute a „fast part" of a composite pixel.

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Small and Fast : Nanophotonics for Fast Timing

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This presentation will present the opportunities offered by nanophotonics to improve the performance of detectors including results obtained from the ATTRACT-Photoquant project [1] that aimed at demonstrating that recent nanophotonics innovations such as metalenses and more generally metamaterials could allow a breakthrough in single-photon time resolution. Silicon photomultipliers are bidimensional arrays of single photo-avalanche diodes (SPADs). Many applications would benefit from a single photon time resolution much lower than what is the current state of the art, ideally 10 ps, or even less. Moreover, a photo-detection efficiency as close as possible to 100% is also required. Simulations and measured results show that, using both a light concentrator and including light trapping features to the device stack, the photo-electron generation can be confined in a region as small as 820×780×500 nm3, which could greatly improve the single-photon time resolution and the sensitivity of the device. A concentrator based on a metatamerial gradient index (MM GRIN) lens was created as a 2D square lattice of holes with different diameters [2]. The focusing effect is generated by the refractive index gradient, with bigger holes in the outer region of the concentrator. Moreover, we have shown thanks to numerical simulations that modified SPAD with a thickness reduction of the Si layer down to 500 nm (usually several µm Silicon thickness) and a grating at the bottom or above of the stack resulted in a photon absorption efficiency of nearly 100% in the Si layer.

1 - https://phase1.attract-eu.com/showroom/project/nano-photonics-applied-to-ultrafast-single-photon-quantum-sensors-photoquant/
2 - Mikheeva, E., et al. (2020). CMOS-compatible all-dielectric metalens for improving pixel photodetector arrays. APL Photonics, 5(11), 116105.

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Monolithic integration of metalens array in multipixel photon counter for enhanced photodetection efficiency

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Silicon photomultiplier (SiPM) consisting of single photon avalanche diode (SPAD) array has been widely used in many types of applications, those requires photon counting capability. Dynamic range of SiPM, which is one of the representative characteristics, is generally limited by the number of SPADs composing the SiPM. Its dynamic range can be expanded by using small size SPAD, e.g., 10, 15, 25 um, and increasing the number of the SPADs, however, small size SPADs cannot keep high geometric fill factor (FF) basically due to existence of the trench, resulting in low photodetection efficiency (PDE). Although using microlens array on top of the SiPM surface has been proposed to avoid the degradation of the effective FF, microlens is not suitable for scintillation-based applications in terms of transparency, packaging, and coupling. Here, we propose the use of metalens array instead of the microlens array to overcome the problems abovementioned and investigate its applicability using multipixel photon counter (MPPC). Metalens array geometrically corresponding to SPAD array was directly fabricated and monolithically integrated in the MPPC. The metalens array correctly guides incoming photons to the center of the SPAD, where the relative photodetection efficiency is the highest. Thus, the metalens-integrated MPPC showed the enhanced FF, in other words, the enhanced PDE. Furthermore, we show, as a metric of scintillation-based applications, an improved coincidence time resolution using the metalens-integrated MPPC. Finally, we discuss our future strategies of the use of metalens.

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Progress in CMOS SPADs and digital SiPMs for fast timing applications

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Fast timing performance is of paramount importance in a number of time-resolved medical applications, including TOF-PET, FLIM and Raman. The EPFL AQUA lab has explored several strategies to increase the performance of miniature all-solid-state silicon detectors in the form of single-photon avalanche diodes (SPADs), also known as Geiger-mode APDs. SPADs feature an exquisite timing performance (tens of ps), together with single-photon sensitivity. Arrays of SPADs have encountered commercial success in the form of analog SiPMs, and lately in digital form for LIDAR, with an expanding applications portfolio.
Our investigations have focused on one side on the device design itself, together with the corresponding optimised front-end electronics. This has allowed us to break the 10 ps (FWHM) single-photon timing resolution barrier at device level, while maintaining high photon detection probability in the visible, coupled to low noise and dead times as small as 3 ns (and 1.5 ns in a different technology node).
Another track has investigated the 3D-stacking of a photodetection layer, coupled to a control and processing layer implemented in deep-submicron CMOS technology. This approach is aimed at increasing the granularity of timestamps, together with timing improvements by statistical methods. Furthermore, the spatial granularity can in principle be traded off, e.g. through the clustering in mini-SiPMs, with respect to additional functionalities in the bottom tier. This can lead to architectures which differ from conventional ones, possibly even with the inclusion of on-chip artificial intelligence functionalities.
Finally, we have also explored another class of time-resolved detectors, namely superconducting nanowires, coupled to large bandwidth and low power front-end electronics based on a SiGe platform. The latter could potentially find applications in the read-out chains of analog SiPMs, as a building block for short-term timing improvements using existing detectors.

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FBK SiPM roadmap for ultimate timing performance

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Optimization of the timing resolution in the scintillation light readout has been one of the most important challenges in the SiPM field since the beginning of their development. Several sensor parameters contribute to the timing performance achieved in the application. The latest iteration of the NUV-HD SiPM technology developed at FBK feature PDE in excess of 60% at 410 nm, DCR around 60 kHz/mm² and SPTR of 90 ps FWHM for a 4x4 mm2 device with 40 μm cells, when coupled to a discrete, high-frequency readout. Thanks to these parameters, it was possible to measure an excellent Coincidence Resolving Time (CRT) of 58 ps FWHM in the readout of a 2x2x3 mm³ LSO:Ce:Ca coupled to a 4x4 mm² SiPM with 40 μm cells. On the other hand, photon-starved applications, such as BGO readout with the timing resolution enhanced by the detection of Cherenkov photons, further underline the importance of improving the SPTR of the SiPMs. This parameter is heavily affected by both the output capacitance of the sensor and by the characteristics of the front-end electronics reading it. Considering that incremental improvements between subsequent generations of SiPMs are reaching saturation, a deeper redesign of the device structure is needed. In this context, FBK is working on the development of the next-generation of SiPMs, with a strong focus on 3D integration, such as SiPMs featuring fine-pitch Through Silicon Vias and Backside-illuminated (BSI) devices. A fine segmentation of the sensitive area in separated mini-SiPMs, each one connected to a dedicated readout channel through a low-impedance interconnection, will reduce output capacitance and optimize signal integrity. BSI-SiPMs will potentially bring additional advantages, such as reaching a PDE close to 100%, reduced output capacitance, enhanced radiation hardness, single-cell connection to the readout electronics and a uniform light entrance window, suitable for the most advanced optical stacks.

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VUV-SiPMs applied to BaF2 cross-luminescence detection for high-rate ultrafast timing applications

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Inorganic scintillators are widely used for fast timing applications in time-of-flight (TOF) positron emission tomography (PET), time tagging of soft and hard X-ray photons at advanced light sources and photon counting computed tomography (CT). As the best coincidence time resolution (CTR) achievable is proportional to the square root of the scintillation decay time it is worth studying fast cross-luminescence, for example in BaF2 which has an intrinsic yield of about 1400 photons/MeV. However, emission bands in BaF2 are located in the deep-UV at 195nm and 220nm, which sets severe constraints on the photodetector selection.

Recent developments in dark matter and neutrinoless double beta decay searches have led to silicon photomultipliers (SiPMs) with photon detection efficiencies of ~20% at wavelengths of 200nm. We tested state-of-the-art devices from Fondazione Bruno Kessler and measured a best CTR of 51±5 ps FWHM when coupling 2x2x3mm^3 BaF2 crystals excited by 511keV electron–positron annihilation gammas. Using these vacuum ultraviolet SiPMs we recorded the scintillation kinetics of samples from Epic-crystal under 511keV excitation, confirming a fast decay time of 855ps with 12.2% relative light yield and 805ns with 84.0% abundance, together with a rise time of <4 ps, beyond the resolution of our setup. We further show that different dopants effectively can suppress this slow decay component, enabling GHz rate capabilities.

In addition, we revealed an ultra-fast component with sub-100 ps decay time and 3.7% light yield contribution, which is extremely interesting for advanced timing applications. Especially in the rising new field of time-of-flight CT, these almost prompt photons could imply a real breakthrough in thoroughly needed detector developments.

We will conclude this talk with exploratory Monte-Carlo simulations to fully investigate the timing benefits of cross-luminescence in TOF-CT, with the intention to give an action plan on future research focus.

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

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Recent developments in semiconductor pixel detectors allow for a new generation of positron-emission tomography (PET) scanners that, in combination with advanced image reconstruction algorithms, will allow for a few hundred microns spatial resolutions. Such novel scanners will pioneer ultra-high-resolution molecular imaging, a field that is expected to have an enormous impact in several medical domains, neurology among others. The University of Geneva, the Hôpitaux Universitaires de Genève, and the École Polytechnique Fédérale de Lausanne have launched the 100μPET project that aims to produce a small-animal PET scanner with ultra-high resolution. This prototype, which will use a stack of 60 monolithic silicon pixel sensors as a detection medium, will provide volumetric spatial resolution one order of magnitude better than today's best operating PET scanners. The R&D on the optimisation of the monolithic pixel ASIC, the readout system and the mechanics, as well as the simulation of the scanner performance, will be presented.

In its present planning, the 100μPET project will use monolithic silicon sensors in SiGe BiCMOS technology which have already demonstrated 36 ps time resolution and full efficiency [JINST 17 (2022) P02019] with a PN-junction sensor. Future versions could envisage to use monolithic pixel sensors with internal avalanche gain (the PicoAD sensor, patent EP18207008.6/US-2021-0280734-A1, developed within the ERC Advanced project MONOLITH) which are expected to deliver time resolutions better than 10 ps. In this context, very fast electronics is being developed, among which a novel concept TDC with simple circuitry (patent EP3591477A1) that provided 1.4 ps in its first prototype realization.

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Hamamatsu technology for TOF PET

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The timing performance of the TOFHIR2 ASIC

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We present an overview of the TOFHIR2 ASIC design and experimental results on the timing performance. TOFHIR2 will be used in the front-end readout of the barrel section of the new MIP Timing Detector (BTL) developed for the HL-LHC upgrade of the CMS experiment. The BTL sensors are based on LYSO:Ce scintillation crystals coupled to SiPMs.

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Timing limits of the TOFPET2 ASIC

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Novel front-end designs have shown to push the timing performance of scintillators and silicon-photomultipliers (SiPMs) used in PET applications, such that their physical limits regarding timing performance can be established. Using an electronic high-frequency (HF) readout concept, we determine the contribution of a commercial application-specific integrated circuit (TOFPET2 ASIC by PETsys Electronics S.A., version 2c) on the time-of-flight (TOF) resolution after establishing the SiPM and scintillator performance as a benchmark. We furthermore adapt the SiPM readout prior to the ASIC front end, filtering and amplifying the signals to boost the timing performance. Small LYSO:Ce crystals (EPIC-crystals, 2x2x3mm3) and Broadcom AFBR-S4N33CO613 achieved a coincidence time resolution (CTR) of 82 ps (FWHM) if connected to an HF readout circuit, while measurements with the same SiPM-crystal configuration and the TOFPET2 ASIC result in a CTR of 142 ps (FWHM). This performance was boosted to 128 ps (FWHM) by an adapted version of the HF readout in combination with the TOFPET2 ASIC. The same method used with a 3x3x20mm3 LYSO:Ce crystal, led to a CTR improvement from 202 ps (FWHM) to 187 ps (FWHM). The intrinsic performance of the TOFPET2 ASIC was determined to 58 ps (FWHM). Evaluating all measurements, we could show that the TOFPET2 ASIC should be capable of achieving 100-ps CTR. The reason for this discrepancy is suspected to lay in the front-end design, but is currently still under investigation. Our attempts to boost the CTR revealed additional side peaks close to the main peak in coincidence time difference spectra. The appearance of these peaks is shown to be linked to the signal height routed into the ASIC front end.

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Pushing time resolution for ToF-PET molecular imaging employing the FastIC ASIC

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Time-of-flight Positron Emission Tomography (TOF-PET) scanning is a molecular imaging procedure for early diagnosis and even prevention in cancer disease. Standard PET scanners are mainly built by modules consisting of scintillation crystals optically coupled to photo-detectors with fast readout electronics. Pushing the limits of the readout system will improve tomographic image reconstruction quality by reducing background correlations and thus improving signal-to-noise-ratio (SNR).

The 8-channel FastIC ASIC developed in CMOS 65 nm technology is capable of processing fast signals with a precise time stamp and a linear energy measurement of the detected events. Power consumption per channel is ≈ 12 mW. Readout channels can be processed individually or they can be summed in groups of 4 channels in view of exploiting sensor segmentation. Time information is extracted from the resulting reconstructed pulse and thus lowering the electronic jitter contribution.

This work provides an extensive analysis of the potential capabilities of the FastIC ASIC coupled to different scintillators and photo-detectors from different manufacturers. For 2 × 2 × 3 mm3 LSO:Ce:0.2%Ca crystals coupled to SiPMs from HPK (S13360-3050PE) or FBK (NUV-HD-LF, 3.2 × 3.12 mm2, pixel 40 µm), coincidence time resolution (CTR) values of 94 ± 2 and 76 ± 2 ps FWHM were obtained respectively upon 511-keV gamma excitation. When increasing the crystal length toward 20 mm and coupling to SiPMs from FBK, the CTR slightly deteriorates toward 126 ± 3 ps, in line with the best achieved CTR results (using the NINO ASIC) for PET-sized geometries and about twofold superior to the Siemens Biograph Vision. Beside measurements with standard scintillators, the applicability of the chip for prompt low light emitters (eg. using Cherenkov radiators such as BGO, TlCl and PbF2) was investigated. Further, we will discuss measurements on the summation feature of the ASIC.

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Low Power Implementations of High Performance Electronic Readout to Advance TOF-PET Detector Module Performance

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State-of-the-art (SoA) electronic readout for silicon photomultiplier (SiPM)-based scintillation detectors that demonstrate experimental limits in achievable coincidence time resolution (CTR) leverage low noise, high frequency signal processing to facilitate a single photon time response that is near the limit of the SiPM's architecture. This readout strategy can optimally exploit fast luminescence and prompt photon populations, and promising measurements show detector concepts employing this readout can greatly advance PET detector CTR, relative to SoA in clinical systems (~200 ps FWHM). However, the technique employs power hungry components which make the electronics chain impractical for channel-dense TOF-PET detectors. We are developing readout circuits which are performant at low power and have small footprints, making them feasible for integration into TOF-PET detector prototypes. An implementation integrated with 3x3 mm2 Broadcom SiPMs exhibits sub-100 ps single photon time resolution (SPTR) at 10 mW/channel, with a minor performance degradation to 120±2 ps FWHM at 5 mW/channel. CTR measurements with 3x3x20 mm3 LYSO and fast LGSO scintillators demonstrated 127±3 ps and 113±2 ps FWHM at nominal power dissipation and 133±2 ps and 121±3 ps CTR at 5 mW/channel. 3x3x20 mm3 BGO crystals show 271±5 ps FWHM CTR at nominal power dissipation and 289±8 ps at 5 mW/channel. The compact and low power readout topologies that achieve this performance thereby offer a platform for TOF-PET to greatly advance system CTR, exploring novel detector concepts to push system CTR ≤100 ps, and also opportunities to provide high performance TOF-PET at greatly reduced material cost. We will present our readout developments for single pixel measurements and scintillation detectors comprising arrays of SiPMs with electronic multiplexing. We will also outline how this readout strategy can be employed in a novel photon counting detector concept that can facilitate ≤100 ps PET.

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Minimizing power consumption for Time-of-Flight PET SiPM readout

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Good energy and timing resolutions are key parameters for new generations of PET detectors. In particular, the implementation of detectors with minimum electronics, potentially only passive components, is desired. This will improve the cost but more importantly the power consumption of the final scanner, which will further reduce requirements for cooling and
space.
In this work, we benchmark four circuit configurations with low power consumption. The tests were carried out using 3x3x5 mm3 LYSO:Ce:Ca crystals and FBK NUV SiPM. The two best scenarios provide a combination of 7% energy resolution and 96.7 ps CTR for 300 mW power consumption per detector, with two
channels; and 115.1 ps and 12% energy resolution for a circuit without active components and a virtual zero power consumption, with one channel. We will further develop these solutions into system-level arrays with deployment potential.

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A Comparative Study on Various Capacitance Compensation Technique for SiPM based TOF-PET detector

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Purpose-SiPM is a highly used photosensor in PET systems, however, its detector capacitance needs to be compensated for fast timing. Two capacitance compensation technique has been proposed, active compensation using an op-amp, and passive compensation using a balun transformer. In this study, we evaluated the performance of two compensation technique by measuring the CTR with the same reference detector.

Methods-We used R9800 PMT coupled with 4 × 4 × 10 mm3 LYSO as a reference detector. The single timing resolution of the reference detector was 233.3 ps. For the active compensation, we used 4 × 4 mm2 SiPM coupled with 3 × 3 × 20 mm3 LGSO wrapped with ESR. and for the passive, we used 3 × 3 mm2 SiPM coupled with the same crystal. We also compared the CTR using the raw signal and the high pass filtered signal from the SiPM anode. The time constant of the high pass filter used was 0.5 ns (10 pF & 50Ω).

Results-The CTR of the raw and the filtered signal of SiPM anode were 541.6 ps and 400 ps respectively. The CTR of the active compensation technique was 397.1 ps, 26.7 % improvement from that of the raw signal, and that of the passive compensation technique was 272.4 ps, 49.8 % improvement from that of the raw signal. The calculated CTR of the active compensated pair was 454.6 ps and that of passive compensated pair was 192.1 ps. Optimal CTR obtained with the high pass filter had an equivalent performance with that obtained with the active compensation technique.

Conclusion-In this study, we built the first experimental basis that the passive capacitance compensation technique on SiPM based PET detector can improve the timing resolution better than the active capacitance compensation technique. Although, the set-up is not optimized for measuring CTR, the comparisons were made under the same conditions as possible. For the future work, we are planning to evaluate two different compensation technique with optimal timing measurement set-up to achieve sub 100 ps CTR.

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Comparison of time-walk compensation methods for Leading Edge Discriminators

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Purpose
Timing resolution of leading edge discriminators is affected by the time-walk caused by the uncertainty of interaction energy, thus several methods for time-walk compensation have been proposed. Most of the correction methods use the integral of the signal as a parameter for energy, while some studies tried amplitude or slew rate as a parameter for energy. In this study, we tested time-walk corrections using different parameters of energy to obtain optimal coincidence timing resolution.

Methods
We obtained the coincidence data using Hamamatsu R9800 PMT coupled with LYSO (4×4×10 mm3) with SiPM coupled with LGSO (3×3×20 mm3). Whole signals were digitized using digitizers (DT5742B; CAEN, Italy). To compensate for time walks, time differences were expressed as functions of parameters (integral, amplitude, and slew rate of signals). Linear fitting, quadratic fitting, and logarithmic fitting were tested. For linear fitting and quadratic fitting, the difference of parameters was used, while the logarithmic value of the ratio between parameters was used for logarithmic fitting. We performed principal component analysis on data, then divided them into 10 groups with the same numbers, selected median points for each group, then used them for curve fitting.

Results
With a 30 keV energy window, the detector pair showed 272 ps CTR. With time-walk correction using logarithmic fitting between energy and time, FWHM was reduced from 433 ps to 356 ps for the dataset obtained with a 500 keV energy window. Slew rate, amplitude, and energy showed similar performance in time-walk compensation.
No significant differences between linear, quadratic, and logarithmic functions were observed.

Conclusion
The log relationship between energy and timing was well known, but the amplitude and slew rate with appropriate curve fittings also showed similar time-walk compensation capability.

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Time based event positioning in monolithic detectors

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MOLECUBES detectors use monolithic scintillation crystals. This detector architecture demands high-speed readout because all pixels of the photodetector must be processed when an event occurs. An often used approach is integration of the current pulses generated by every pixel, but such circuitry quickly becomes bulky, power consuming and expensive. Alternative approaches are often integrated in an ASIC. Here we investigate if the task of event positioning can be accomplished by making use of time only. We propose the use of timing information, in the form of time-over-threshold (ToT), rather than energy information, in the form of integration, for the positioning of the interaction position in the crystal. There are multiple advantages to this approach. Firstly, the electronics are less complex and an off-the-shelf comparator for every pixel of the array would suffice. Secondly, timing information is inherently present in this approach. From the readout we will obtain as many timestamps as there are comparators and several studies showed the advantage in terms of timing performance when multiple are available. We evaluated the positioning accuracy and uniformity of a ToT detector with optical GATE simulations. For event positioning mean nearest neighbour (mNN) was used. We investigated the ability to position the events with ToT information (mNNToT) and the impact of the threshold. The results were compared to an integrating detector (mNNint), which has already proven to allow sub-mm resolution. We showed minimal degradation in spatial resolution (SR) and bias compared to mNNint. The highest threshold results in the worst SR performance but degradation remained below 0.1 mm. Bias is largely constant over different thresholds and close to identical to mNNint. Also, we showed that ToT performs well in terms of uniformity. This study indicates that a monolithic detector with timing information on all pixels is capable of providing high SR event positioning.

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Conceptual design of high-speed and low-noise receiver electronic systems

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Challenges in modern physics experiments and medical imaging call for continuous boosting of various specifications of detector instrumentation. While spatial and timing resolution, power consumption and data-rate reduction are among parameters, which require constant improvements, new signal analysis and feature extraction methods have to be developed in parallel to aid the performance enhancement.

To support the improvement of both parameters and methods, we are currently working on various electronics concepts spanning from development of readout electronic systems for analog silicon photomultipliers (SiPM) to various integrated circuit like new ADC designs, time-to-digital-converters and intelligent data analysis units. While former allows for further exploitation of conventional SiPMs, the latter, if integrated in an avalanche-photodiode based image sensor, can dramatically improve overall timing resolution and other key detector parameters.

In addition to improvements in the time-domain, we also work on optimization of power consumption, signal-to-noise ratio, develop new parameter extraction methods from digitized pixel data, and investigate electronics scaling options. In this presentation, we would like to discuss our recent developments in the field of detector design, with the focus on receiver electronics for SiPMs and APD based image sensors.

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Advances in electronics for a Compton camera

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Compton cameras can determine the origin distribution of emitted photons by exploiting Compton scattering kinematics and electronic collimation. The detectors operate in time coincidence and thus, good timing resolution is essential to reduce the amount of random coincidences by applying narrow coincidence windows. Backscattering constitutes an important source of image degradation, in particular for energies below 1 MeV. A timing resolution in the range of 100-200 ps would allow the interactions in the detectors to be correctly ordered, improving image quality. In the context of hadron therapy, in which Compton cameras are investigated as a promising tool for treatment monitoring, good timing resolution is crucial to reduce the background of undesired particles produced through the interaction of the proton beams with the patient.

The IRIS group of IFIC (Valencia) is developing a Compton camera for medical imaging and hadron therapy treatment monitoring. The system is composed of three planes of monolithic LaBr3 crystals coupled to SiPM arrays. Accurate timing resolution is challenging due to the large variety of signal amplitudes detected per channel for two different reasons: the different energies deposited in the crystal in each event through the Compton interactions and the spread of the light in the monolithic crystal.

The first MACACO prototype was developed employing the ASIC VATA64HDR16 from Ideas. With the aim of improving timing resolution, an alternative system, MACACOp, has been developed employing TOFPET2 ASIC from PETsys. This system, made of two detector planes, has been tested and characterized in the laboratory with different radioactive sources and at CNA (Sevilla) with 4.4 MeV photons. In addition to a significantly improved timing resolution, the system has wider dynamic range, achieving promising results for hadron therapy treatment monitoring. The ASIC HRFlexToT developed at the University of Barcelona is also being evaluated.

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Determining the equivalent Gaussian TOF-resolution of PET systems with multiple and non-Gaussian TOF-kernels

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The effective sensitivity of a PET system can be increased by improving its time-of-flight (TOF) resolution. For that purpose, new detectors are being developed, including detectors that use not only scintillation but also Cerenkov photons, and detectors consisting of two different scintillators. Such systems have events with different coincidence time resolution (CTR), i.e. different TOF-kernels, and the shape of these TOF-kernels can be non-Gaussian. In some systems, it may be possible to assign to each event an estimate of its CTR. This CTR can then be used during image reconstruction. If this is not possible, all events must be considered as samples from an overall TOF-kernel, which may have a non-Gaussian shape with a narrow peak (events with good CTR) and wide tails (poor CTR events). These developments raise two questions: (1) how can we compare systems that have TOF-kernels of different shapes and (2) how much information is added by labelling each event with its CTR.

Tomitani [1] computed, for a uniform cylinder, how the variance in the centre of the reconstructed image depends on the CTR, assuming a Gaussian TOF-kernel. We extended his approach to non-Gaussian TOF-kernels, and found that the same result can be obtained by computing the SNR for a hot spot detection task. This enables us to assign an SNR to each TOF-kernel. For CTR-labelled events, the system SNR is obtained by averaging the squared SNRs of the TOF-kernels. If the events cannot be labelled, the system SNR is computed from the averaged TOF-kernel. Thus, one can compute an effective Gaussian TOF-resolution: a conventional system with this Gaussian TOF-kernel has the same effective sensitivity as the system with multiple and/or non-Gaussian TOF-kernels. The results were verified with 2D TOF-PET simulations, reconstructed with MLEM.

[1] T. Tomitani. "Image reconstruction and noise evaluation in photon time-of-flight assisted positron emission tomography". IEEE Trans Nucl Science NS-28.6 (1981).

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The influence of the number of Cerenkov photons on the timing resolution of a BGO PET detector.

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The PET-detector time resolution (DTR) using BGO can be improved by using not only scintillation, but also Cerenkov photons. Geant4/GATE Monte Carlo simulations were performed for 511 keV photon interactions in a BGO crystal of 3 x 3 x 20 mm3. In 13720 interaction events, the electrons, scintillation and Cerenkov photons were followed until the photons entered the SiPM, where immediate detection was assumed (SPTR = 0). We fitted the probability distribution model proposed in [1] to the resulting photon detection times, to obtain a model for scintillation and for Cerenkov detection times. On average, 924 photons were detected. A 511 keV interaction in BGO produces around 17 Cerenkov photons, on average only 3.24 were detected.
To determine the DTR provided by these optical photons, a maximum likelihood (ML) estimator was implemented, which estimates the interaction time from the sorted list of photon detection times.
To study the influence of the number of Cerenkov photons on the DTR, simplified simulations were done, using the model of [1] with the fitted parameters as ground truth. The number of detected scintillation photons was assumed Poisson distributed with expectation 924, the number of detected Cerenkov photons was also assumed Poisson, but different expectation values were simulated. For each Cerenkov expectation value, 10000 interaction events were simulated by randomly sampling the model of [1]. From each set of 10000 interactions, the DTR was quantified as the standard deviation (std) of the observed ML-estimated interaction times.
For an expected number of [0, 1, 2, 3.24, 4, 6] detected Cerenkov photons, the observed DTR-std was equal to [327, 267, 177, 109, 83, 48] ps. These results show that even a slight increase in the number of detected Cerenkov photons produces a noticeable improvement of the DTR.

[1] S. Seifert, H. van Dam, D. Schaart, "The lower bound on the timing resolution of scintillation detectors", Phys. Med. Biol. 2012; 57: 1797 - 1814.

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Improving Spatial Resolution with Ultrafast TOF in PET

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The benefits of time-of-flight (TOF) in positron emission tomography (PET) have long been recognized and later clearly demonstrated in terms of sensitivity and image contrast-to-noise ratio. However, the impact on spatial resolution is generally considered negligible, if not detrimental due to the trade-offs that must be made to optimize the detector coincidence time resolution (CTR). As progress is being made to ultimately achieve 10 ps CTR, the TOF resolution will eventually enable reconstruction-free positron imaging. Nevertheless, we have demonstrated that when the TOF resolution along the tubes of response (TOR) becomes similar or better than the intrinsic spatial resolution of the PET scanner, it may be advantageous to reconstruct the images with an iterative algorithm to enhance resolution. This is because the better localization along the TOR can compensate for the orthogonal blur induced by the scanner intrinsic spatial resolution by using measurements from the different TOR orientations. Simulation results show that ultrafast TOF can mitigate the lower bound in spatial resolution induced by the detector size and the discrete nature of the PET reconstruction scheme. Furthermore, our simulation results show that the ultrafast TOF reconstructed response resulting from the annihilation photon acollinearity tends towards a much sharper 1/r distribution than the expected 0.0022D Gaussian, which reduces the impact of one of the physical limits of spatial resolution in conventional PET. A potential application of reconstructed ultrafast TOF imaging would be the design of clinical scanners achieving image spatial resolution beyond the predicted classical theoretical limit. Another challenge that must be addressed with ultrafast TOF is the noisy data resulting from the required finer TOF discretization. New reconstruction schemes enforcing the parametrization of emission properties might be considered to tackle the bias induced by low counts acquisitions.

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Cross-sectional image generation and post processing in reconstruction-free direct positron emission imaging (dPEI)

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Coincidence detection of the two 511 keV annihilation photons from positron-emitting radiotracers provides an unrivaled mechanism for sensitive, specific, and quantitative molecular imaging in living objects. In positron emission tomography (PET), a large number of coincident 511 keV photons must be collected with sufficient angular sampling to provide the data needed for tomographic reconstruction algorithms to produce cross-sectional images. Once the timing resolution of gamma-ray detectors becomes adequate to directly localize the source, a cross-sectional image can be directly obtained by measuring the difference in arrival time of the two 511 keV photons of each annihilation event without any reconstruction step. We refer to this imaging technique as direct positron emission imaging (dPEI), as it does not require tomographic reconstruction. We recently demonstrated the first direct cross-sectional imaging of positron-emitting radiotracers without any image reconstruction. The prototype dPEI scanner employed two ultrafast lead-glass integrated microchannel plate PMTs and convolutional neural networks processing, resulting in an average coincidence timing resolution of 32 ps, corresponding to a spatial resolution of 4.8 mm. Different test objects representing pre-clinical and clinical size objects were scanned using the dPEI scanner with different configurations and activity levels. This presentation focuses on 1) details of direct image generation and post-processing methods and 2) development of simulation models to design future dPEI scanners and estimate their performance, and 3) technology roadmap for improving dPEI.

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The potential of AI-Deep learning for improving spatial and TOF resolution, acquisition time and scanner cost in PET

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Most developments in AI for medical imaging target the (semi-)automated analysis of images, these techniques have however also large potential for improving and accelerating the acquisition and for making the scanner lower cost. In monolithic detectors with SiPM array readout positioning can be improved by using a dedicated network for improving the estimation of the transverse position (about 10%) and estimating the DOI inside the detector. Also positioning accuracy at the edges is significantly improved compared to conventional positioning methods. Using these techniques in 16 mm thick standard LYSO results in an intrinsic resolution below 1.3 mm and shall at the system level approximate the 2 mm limit (due to positron accolinearity). Deep learning is also useful from improving TOF estimation in these detectors and especially for sampled waveforms from the SIPMs large improvements (roughly 25%) can be observed in TOF estimation. On the same detector this results in a coincidence time resolution of 140ps (simulation). CNN based methods are also very effective in lowering the dose. These CNN networks are typically trained on low (25 %) and high (100%) dose count images and can upgrade the low count images to equivalent quality as the high dose ones. This enables to reduce the scan time and/or lower the dose administered to patients. The same AI-dose reduction factor can also be used in the future for lowering the number of detectors or reducing the scintillator volume in expensive systems like Total body PET. Here a 50 % cost reduction (25 % of counts) is foreseen without image quality loss.

Deep learning is being implemented at different positions in the image acquisition chain. Interesting is that all these improvements can be easily combined with each other and have the potential to deliver High resolution clinical TOF-PET imaging at lower dose and with a quite reasonable system cost using a smaller amount of standard PET components (LYSO, analog SiPMs).

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Pushing the limits of high resolution detectors based on monolithic scintillators for fast timing in PET with an AI-boosted 4D positioning algorithm

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In the framework of the UTOFPET project, a new TOF-PET detector prototype has been developed to provide uncompromised beyond-state-of-the-art performance. The proposed technology is based on a monolithic LYSO scintillator coupled to a matrix of 16 x 16 SiPMs which is well known to be capable of a high intrinsic spatial resolution but is typically not considered the best solution for providing excellent timing performance.

To solve this issue and make monolithic crystals suitable for time-of-flight PET we have processed, in real-time, the 256 signal outputs with a novel algorithm for estimating simultaneously and synergically the 4D event position coordinates (x, y, depth and time). The algorithm is based on a neural network (NN) and and it is trained with both experimental and Monte Carlo generated data. The NN has a computational complexity and a memory footprint low enough to allow a per-detector, real-time hardware implementation in modern, low-cost FPGAs.

In our implementation, the SiPM outputs are read by 16 HRFlexToT ASICs and are digitised by an array of TDCs implemented on FPGA. A SoC-FPGA on the back of the detector runs the NN that processes the outputs of the TDCs to generate the event position, time and energy at input rates that exceed 1 MHz. Event data are stored on a local memory and then transmitted to a host PC via Ethernet connection.

The results obtained with a 51.8 x 51.8 x 12 mm3 crystal indicate performance beyond the state of the art with an event positioning precision of 0.8 mm, a DOI of 1.4 mm, a CTR of 150 ps and an energy resolution of 11%.

This work reports a description of the UTOFPET detector with details on the algorithm and the method used for the training of the neural network together with the experimental results obtained.

Although the UTPFPET detector seems to have reached its limits, the proposed AI-enhanced methodologies may contribute to breaking the 100 ps limit in CTR when new fast materials become available.

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Convolutional networks for gamma time estimation from raw detector waveforms in monolithic PET detectors

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Monolithic scintillation crystals can be used for PET detectors, offering good spatial resolution and depth-of-interaction decoding capabilities. Gamma time estimation however often suffers from the spread of scintillation light, leading to an increased influence of dark counts and other statistical fluctuations in analog SiPMs. Digitizing the SiPM waveforms enables us to perform an accurate baseline correction, minimizing the effects of dark counts. The usual methodology of averaging the first few timestamps obtained from leading edge discrimination however still discards a lot of potentially useful information contained in the SiPM waveforms. We propose the use of a 3D convolutional neural network to predict the gamma arrival time in the scintillation crystal, using a 3 ns time window of the array of detector waveforms as input. Specifically, we investigate a 50x50x16 mm^3 LYSO crystal coupled to an 8x8 readout array of SiPMs. The required data is obtained from Monte Carlo simulations in GATE, where we further simulate the SiPM signals as a sum of bi-exponential functions centered around the optical photon detection times. Our simulation includes the effects of limited photon detection efficiency, dark counts, optical crosstalk, photon transit time jitter and electronic noise. The neural network can achieve a coincidence time resolution of 141 ps FWHM, a 26% improvement over the conventional methodology of averaging the first few timestamps obtained by leading edge discrimination (177 ps FWHM). In addition, the time resolution for the CNN remains uniform over the crystal, whereas the traditional methodology shows a large deterioration for gamma interactions close to the SiPM surface.

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Fast prototyping of medical imaging detectors using AI methods

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Computationally expensive physics simulations involving Monte Carlo runs form the backbone of designing improved medical imaging detectors. We show initial results, from an EU-sponsored grant, leveraging uncertainty quantification (UQ) techniques to drastically reduce simulation time with negligible loss in fidelity. We outline the use of embedding such UQ techniques within a machine learning surrogate-based optimiser to achieve optimised detector configurations quickly.
As part of our software democratisation efforts, we showcase our Quaisr platform which can be used by non-specialist users to deploy and run such AI-driven simulation workflows in the cloud. We discuss other features unique to Quaisr which help engineers, data scientists, operators, and experimentalists to integrate simulations, machine learning, and real-world data; these features accelerate decision-making under uncertainty, rapid prototyping, collaboration, and standardisation.

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Conclusions