Time-of-flight PET with SiPM sensors on monolithic scintillation crystals
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7 LaBr$_3$:Ce and SiPMs for time-of-flight PET: achieving 100 ps coincidence resolving time


Abstract

The use of time-of-flight (TOF) information in positron emission tomography (PET) enables significant improvement in image noise properties and, therefore, lesion detection. Silicon photomultipliers (SiPMs) are solid-state photosensors that have several advantages over photomultiplier tubes (PMTs). SiPMs are small, essentially transparent to 511 keV gamma rays and insensitive to magnetic fields. This enables novel detector designs aimed at e.g. compactness, high resolution, depth-of-interaction (DOI) correction and MRI compatibility. The goal of the present work is to study the timing performance of SiPMs in combination with LaBr$_3$:Ce(5%), a relatively new scintillator with promising characteristics for TOF-PET. Measurements were performed with two, bare, 3 mm $\times$ 3 mm $\times$ 5mm LaBr$_3$:Ce(5%) crystals, each coupled to a 3 mm $\times$ 3 mm SiPM. Using a $^{22}$Na point source placed at various positions in between the two detectors, a coincidence resolving time (CRT) of $\sim$100 ps FWHM for 511 keV annihilation photon pairs was achieved, corresponding to a TOF positioning resolution of $\sim$15 mm FWHM. At the same time, pulse height spectra with well-resolved full-energy peaks were obtained. To our knowledge this is the best CRT reported for SiPM-based scintillation detectors to date. It is concluded that SiPM-based scintillation detectors can provide timing resolutions at least as good as detectors based on PMTs.

7.1 Introduction

The use of time-of-flight (TOF) information in positron emission tomography (PET) has recently been demonstrated to enable significant improvement in image noise properties and, therefore, lesion detection, especially in heavier patients [7, 51, 98–100]. This warrants further research into TOF-capable PET scintillation detectors, in particular with the aim to obtain better timing resolution.
The relatively new inorganic scintillator LaBr$_3$:Ce has high potential for TOF-PET [101]. Commercial-grade LaBr$_3$:Ce(5%) has a fast decay time of $\sim$16 ns [102], a high light yield of $\sim$70,000 photons MeV$^{-1}$ [103], an excellent energy resolution of $\sim$2.6% FWHM at 662 keV [104], a mass density of 5.1 g cm$^{-3}$ [105] and an effective atomic number of 46.9 [25]. To optimally benefit from the advantages of LaBr$_3$:Ce in a PET detector, the scintillation light should be read out using a photosensor with fast response and high photodetection efficiency (PDE) at the LaBr$_3$:Ce emission wavelengths ($\sim$380 nm).

Excellent coincidence resolving times (CRTs) have already been demonstrated with LaBr$_3$:Ce crystals of various dimensions and Ce concentrations, coupled to fast photomultiplier tubes (PMTs) [106–108]. However, silicon photomultipliers (SiPMs) are turning into a promising alternative for PMTs, as of recently [42, 109–117]. Similar to PMTs, SiPMs have a gain in the order of $\sim$10$^6$. In addition, these solid-state devices are much more compact and essentially transparent to 511 keV gamma rays. This enables novel detector designs aimed at, for example, compactness, high resolution, depth-of-interaction (DOI) correction, etc [86, 118–124]. Moreover, in contrast with PMTs, SiPMs are compatible with magnetic fields, a feature that is very interesting in light of recent endeavours to combine PET and MRI into hybrid imaging devices [94, 125–127].

The goal of the present work is to study the timing performance of commercially available 3 mm $\times$ 3 mm SiPMs in combination with LaBr$_3$:Ce(5%) for TOF-PET. We use relatively small LaBr$_3$:Ce(5%) crystals to minimize time walk due to the variation of photon path lengths with the position-of-interaction. However, when using larger crystals, one may attempt to achieve similarly good timing resolution by applying a position-of-interaction correction to the timing information [61, 89, 128].

## 7.2 Materials and methods

### 7.2.1 Detectors

Measurements were performed with two, identical, SiPM-based scintillation detectors. In each detector a bare 3 mm $\times$ 3 mm $\times$ 5 mm LaBr$_3$:Ce(5%) crystal (Saint-Gobain BriLanCe 380) was enclosed in a reflective casing made from Spectralon, a PTFE-based material with reflectivity specified to be better than 98% at 380 nm, i.e. the wavelength of maximum emission of LaBr$_3$:Ce(5%). A 3 mm $\times$ 3 mm SiPM (Hamamatsu MPPC-S10362-33-050C) was coupled directly to each of the LaBr$_3$:Ce crystals using a transparent silicone encapsulation gel (Lightspan LS-3252). Each SiPM consists of an array of 3600 self-quenched Geiger Mode Avalanche Photodiodes at a pitch of 50 $\mu$m. Both SiPMs were operated at $\sim$2.0 V above their breakdown voltages, which were measured to be $\sim$69.7 V and $\sim$70.1 V,
7.2 Materials and methods

Figure 7.1: Schematic overview of the experimental setup. See the text for explanation.

respectively. All experiments were performed at room temperature and in a dry atmosphere to protect the hygroscopic LaBr$_3$:Ce crystals.

7.2.2 Measurement setup

Figure 7.1 shows a schematic representation of the measurement setup. The two detectors and a $^{22}$Na point source (Isotope Products Laboratories, active volume $\varnothing$ 0.5 mm $\times$ 1 mm) were mounted on an optical rail, such that the source could be placed at various positions $x$ in between the two detectors.

The SiPM charge pulses were converted to voltage pulses by means of 15 $\Omega$ shunt resistors and fed into voltage preamplifiers made in-house. Each preamplifier consisted of two cascaded amplification stages, as indicated in figure 7.1. The first amplification stage (gain $\sim$13) consisted of a Texas Instruments OPA847 opamp in a non-inverting configuration with a feedback resistor of 270 $\Omega$ and a 22 $\Omega$ resistor to ground. The second stage (gain $\sim$5) consisted of an ac-coupled monolithic microwave integrated circuit (MMIC) low noise amplifier (Avago Technologies MGA-61563). Care was taken to minimize the total length of the leads...
between the SiPM and the preamplifier (< 1 cm).

In the timing experiments, the signals of the first amplification stages were used to obtain a coincidence trigger, by feeding them into LeCroy 825 leading edge discriminators (LEDs) and connecting the discriminator outputs to a LeCroy 465 coincidence unit. The signals of the first amplification stages were also used to determine the two pulse heights of each coincident pulse pair. This was done by feeding these signals into a CAEN N568B multi-channel shaping amplifier (shaping time 100 ns) connected to a CAEN V785 multi-channel, peak-sensitive ADC.

The pulses from the secondary amplification stages of the two preamplifiers were digitized by two, synchronized, Acqiris DC282 fast sampling ADCs. Both ADCs were operated at the maximum sampling rate of 8 GS s\(^{-1}\) and at a 10-bit resolution. The synchronization clock jitter between the two ADCs is specified to be \(\leq 1\) ps. The trigger for the two synchronized ADCs was provided by the above-mentioned LeCroy 465 coincidence unit. The gain of the secondary amplification stages was chosen such that the ADC input range (set to 500 mV) corresponded to only \(12.5\%\) of the amplitude of a 511 keV pulse. As the optimum trigger threshold for timing lies within this portion of the pulse rising edge, this approach minimizes the contribution of ADC noise to the overall signal-to-noise ratio of the digitized (partial) pulse traces. The traces of each coincident pulse pair were stored in a PC, together with the corresponding pulse heights recorded by the CAEN V785 ADC. The stored data were subsequently used for offline, digital time pick-off as described in section 7.2.3.

Experiments were also performed by irradiating the detectors with a \(^{22}\)Na source and feeding the signals from the first amplification stages of the preamplifiers directly into the Acqiris ADCs, using an ADC input range larger than the maximum pulse amplitude and applying no coincidence condition. About 105 full pulse traces thus acquired were stored for offline analysis of the pulse shape and energy content.

### 7.2.3 Digital time pickoff

A selection of digitized pulse traces for timing analysis was performed using the pulse height information recorded by the CAEN V785 ADCs. Only events with energies between \(\sim 490\) keV and \(\sim 532\) keV were accepted, corresponding to the full-width-at-tenth-maximum (FWTM) of the full-energy peak. Time stamps were subsequently derived by interpolating each trace with a cubic spline and determining the intersection of the interpolated data with a fixed threshold relative to the baseline, set at approximately nine times the pulse height of a single photon pulse. The baseline was determined for each trace individually as the average signal in the region between \(\sim 1.2\) ns and \(\sim 0.2\) ns before the onset of the pulse.
7.3 Results

7.3.1 Pulse shape

Figure 7.2 shows some typical examples of 511 keV pulse traces from the two detectors. These were obtained by feeding the outputs of the first amplification stages of the preamplifiers directly into the Acqiris DC282 ADCs. The average 10-90% rise time of the pulses in the full-energy peak equals $\sim 9$ ns. As the pulse shape equals the convolution of the scintillation light pulse and the SiPM response, the rise time is primarily determined by the low pass (i.e. integrating) characteristics of the SiPM and the scintillation decay time. The influence of the high-bandwidth preamplifiers and other electronics on the pulse rise time is expected to be negligible in our measurements.

7.3.2 Timing spectra

Figure 7.3 shows the timing spectra obtained with the $^{22}$Na point source located at positions $x_1 = \pm 0.25$ mm (green diamonds), $x_2 = 0$ mm (black squares) and $x_3 = \pm 0.25$ mm (blue circles). These spectra were obtained using the digital time pickoff method described in section 7.2.3, using 3624, 7326 and 3346 coincident events per spectrum, respectively. The FWHM coincidence resolving times (CRTs), determined from Gaussian fits to the data.
Figure 7.3: Timing spectra recorded with two 3 mm × 3 mm × 5 mm LaBr$_3$:Ce crystals read out by 3 mm × 3 mm SiPMs, using a $^{22}$Na point source located at $x_1 = 20$ mm ± 0.25 mm (green diamonds), $x_2 = 0$ mm ± 0.25 mm (black squares), and $x_3 = 20$ mm ± 0.25 mm (blue circles). The red curves indicate Gaussian fits to the data. The average coincidence resolving time (CRT) equals 101 ps ± 2 ps FWHM, corresponding to 15.1 mm ± 0.3 mm FWHM.

(7.3.3) Pulse height spectra

Figure 7.4 shows the $^{22}$Na pulse height spectra measured with both detectors. These were derived by integration of the digitized pulses from the first amplification stages of the preamplifiers. A baseline correction was applied to each pulse before integration. The 511 keV full-energy peaks can be seen to be superimposed on the Compton ridges of the 1275 keV peaks. The latter peaks are relatively small due to the small crystal size.

The observed widths of the 511 keV peaks are ~3.7% FWHM and ~3.2% FWHM for detector 1 and detector 2, respectively. These small widths are partly due to SiPM saturation, as discussed in more detail in section 7.4.3. Nevertheless, all full-energy peaks are well resolved and can be clearly distinguished from the...
7.4 Discussion

7.4.1 Timing performance

The above results were achieved using detectors based on 3 mm × 3 mm × 5 mm LaBr$_3$:Ce(5\%) crystals and 3 mm × 3 mm SiPMs. To obtain sufficient system sensitivity, a clinical TOF-PET scanner might, for example, be based on several stacked layers of such detector elements. Alternatively, the detector design might be based on longer crystals. The use of monolithic crystals read out by position-sensitive SiPM arrays may also be considered. While many different detector designs could thus be envisaged, the timing performance is generally expected to deteriorate in larger crystals due to the variation of photon path lengths with the position-of-interaction. Fortunately, it may be possible to at least partly correct for this effect if the position-of-interaction in the crystal is known [61, 89, 128]. The results presented here may thus be seen as representing the CRT in principle achievable with LaBr$_3$:Ce(5\%) and 3 mm × 3 mm SiPMs commercially available at the time of writing.

The present work can be compared to results obtained with SiPMs by other authors. Several studies have been performed using LSO:Ce and similar materials.

Figure 7.4: Pulse height spectra of the two detectors, measured using a $^{22}$Na source. The observed widths of the 511 keV peaks are $\sim$3.7\% FWHM and $\sim$3.2\% FWHM for detector 1 and detector 2, respectively.
Some of the best results reported are those from Göttlich et al [129], which reached a CRT of 460 ps FWHM using two 3 mm × 3 mm × 15 mm lutetium fine silicate (LFS) crystals coupled to the same Hamamatsu SiPMs as the ones used here, those from Burr and Wang [130], which obtained a CRT of 268 ps FWHM using two 3 mm × 3 mm × 10 mm LYSO:Ce crystals and prototypes of the same SiPMs as used in the present study and those from Kim et al [131], which achieved a CRT of 240 ps FWHM using 3 mm × 3 mm × 10 mm LYSO:Ce crystals coupled to the same SiPMs as those used here.

Few studies have so far been performed with LaBr₃:Ce [132], presumably because of the difficulties encountered in using this hygroscopic material. To our knowledge the CRT obtained with LaBr₃:Ce(5%) in the present work is significantly better than those reported for LSO:Ce, LYSO:Ce and LFS to date.

It is acknowledged that the performance of a PET scintillator is not only determined by its timing resolution. Compared to LSO:Ce and similar materials, a disadvantage of LaBr₃:Ce is its lower stopping power, giving rise to increased intra- and inter-crystal scattering and requiring thicker detectors to obtain equal detection efficiency. In principle, thicker detectors may give rise to increased parallax errors. However, these can be mitigated by using stacked layers of small detector elements as mentioned above or by implementing some form of depth-of-interaction (DOI) correction, see e.g. [42] and references therein.

An important advantage of LaBr₃:Ce is its much higher light yield, which is a crucial factor for obtaining high spatial resolution. Moreover, both its superior timing (randoms suppression, TOF) and its excellent energy resolution (scatter rejection) are of great advantage to improve image quality, especially in heavier patients [133].

Given the above advantages and disadvantages, at present it is difficult to predict the overall performance of LaBr₃:Ce in comparison to other PET scintillators, especially since the only LaBr₃:Ce-based prototype scanner realized to date [133] has not yet been optimized with respect to all of the above factors. In contrast, LSO:Ce and similar materials are used in many commercial systems, most of which have undergone multiple iterations of optimization. Thus, further research into the use of LaBr₃:Ce in TOF-PET is warranted.

### 7.4.2 SiPMs versus PMTs

The average 10-90% rise time of ~9 ns obtained in this study is relatively large compared to the values typically found with fast PMTs. For example, Kuhn et al [106] measured a 10-90% rise time of ~3 ns for a 4 mm × 4 mm × 30 mm LaBr₃:Ce(5%) crystal on a Hamamatsu R4998 PMT. In principle, a longer rise time is undesirable as the timing resolution ŐÅt associated with electronic and
7.4 Discussion

Sampling noise is equal to the ratio of the noise and the signal slope [96]:

\[ \sigma_t \sim \frac{\sigma_v}{dv/dt} \]

(7.1)

where \( \sigma_v \) is the RMS noise voltage and \( dv/dt \) denotes the slope of the pulse leading edge at the point where it crosses the trigger level.

However, the absolute slope \( dv/dt \) is proportional to the photosensor photodetection efficiency. It is not trivial to specify the PDE of the SiPMs used here, since it is a function of bias voltage, temperature, degree of saturation, etc and varies between individual devices of the same type. However, according to the manufacturer\'s data sheet [134], it may be as high as \( \sim 45\% \) at 380 nm, the wavelength of maximum emission of LaBr\(_3\):Ce(5\%). While it is to be noted that this figure includes contributions from cross-talk and after-pulsing [117, 135], it is considerably higher than the quantum efficiency (QE) of, for example, the above-mentioned R4998 PMT, which is estimated to be \( \sim 16\% \) at 380 nm from the manufacturer\'s datasheet [136]. A second advantage of a higher PDE is that a larger number of primary charge carriers per pulse reduce the influence of statistical fluctuations on the timing resolution.

A full analysis of the timing resolution would require additional factors to be taken into account, such as photosensor dark current, transit time jitter, etc, but this is left for future publication. In this note we merely wish to illustrate that the different characteristics of SiPMs and PMTs make it interesting to compare the timing resolution achieved in this work with those published for PMTs in combination with the same scintillation material.

For example, a CRT of 240 ps FWHM has been measured with two, 4 mm \( \times 4 \text{ mm} \times 30 \text{ mm} \) LaBr\(_3\):Ce(5\%) crystals coupled to R4998 PMTs [106], while Kyba et al [107] reported a CRT of 160 ps FWHM for two \( \sigma \text{ 13 mm} \times 13 \text{ mm} \) LaBr\(_3\):Ce(5\%) crystals coupled to the same PMTs, thereby demonstrating the dependence of CRT on crystal dimensions. A simulation by Kuhn et al [106] predicts a CRT of \( \sim 100 \text{ ps} \) FWHM for very small crystals. The dependence of CRT on the time pick-off method was tested by Wiener et al [137] by comparing analogue to digital methods. Although it was originally reported that the CRT with digital waveform sampling was superior, further work has since demonstrated that these measurements are sensitive to the assumptions made about the shape of the signal rising edge, and that the timing resolutions obtained with digital and analogue methods are comparable (private communication). Given these results, the present work indicates that SiPM-based scintillation detectors can provide timing resolutions at least as good as those obtained with PMTs.

It is noted that scintillators exist that may provide even better timing resolution than commercial-grade LaBr\(_3\):Ce(5\%). For example, increasing the Ce concentration in LaBr\(_3\):Ce to \( \sim 30\% \) appears to improve timing resolution signif-
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Significantly [106, 138]. Other materials, such as CeBr\textsubscript{3} and LuI\textsubscript{3}:Ce, are also investigated as candidates for TOF-PET [108, 139, 140]. Hence, it would be interesting to study the timing performance of SiPMs in combination with LaBr\textsubscript{3}:Ce(30\%) and other promising new materials.

7.4.3 SiPM saturation

In principle, it might also be possible to further improve the timing resolution by using SiPMs containing fewer but larger microcells, thus improving their fill factor and, therefore, their PDE. However, if the number of microcells would be made too small, this might lead to excessive saturation. Such saturation causes the pulse height spectra of SiPM-based scintillation detectors to increasingly be compressed along the energy axis with increasing gamma energy [141, 142]. As can be seen from the relative positions of the 511 keV and 1275 keV peaks in figure 7.4, a significant degree of saturation already occurs in the present experiments. While the excellent energy resolution of LaBr\textsubscript{3}:Ce already gives rise to a relatively small width of the 511 keV full-energy peaks, this implies that the peak widths observed in figure 7.4 are additionally reduced by SiPM saturation. From a practical point of view, however, it is important that well-resolved 511 keV full-energy peaks are still obtained. In a clinical PET system, this is crucial for accurate rejection of photons that have undergone Compton scattering in the patient. It is noted that, in addition to SiPM saturation, the pulse height spectra may in principle also be influenced by electronic non-proportionality as described by Seifert et al [143, 144]. However, this effect is expected to be small in our measurements.

7.5 Conclusions

The experiments presented here show that SiPM-based scintillation detectors for TOF-PET can provide timing resolutions at least as good as detectors based on conventional PMTs. At the same time, pulse height spectra with well-resolved full-energy peaks can be obtained, which is necessary for accurate rejection of Compton-scattered photons. The use of LaBr\textsubscript{3}:Ce(5\%) allowed us to achieve a CRT of ~100 ps FWHM for 511 keV annihilation photon pairs, corresponding to a TOF positioning resolution of ~15 mm FWHM. To our knowledge this is the best experimental figure reported for SiPM-based scintillation detectors to date. It is not unlikely that further optimization of scintillation materials and SiPM technology will lead to even better results in the near future. Given the advantages of SiPMs over PMTs, such as their small size, transparency to 511 keV gamma rays, magnetic field compatibility, etc, we conclude that detectors based on LaBr\textsubscript{3}:Ce and SiPMs have high potential for use in TOF-PET devices.
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