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The lower timing resolution bound for scintillators with non-negligible optical photon transport time in time-of-flight PET

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Abstract

In this work, a method is presented that can calculate the lower bound of the timing resolution for large scintillation crystals with non-negligible photon transport. Hereby, the timing resolution bound can directly be calculated from Monte Carlo generated arrival times of the scintillation photons. This method extends timing resolution bound calculations based on analytical equations, as crystal geometries can be evaluated that do not have closed form solutions of arrival time distributions. The timing resolution bounds are calculated for an exemplary $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry, with scintillation centers exponentially spread along the crystal length as well as with scintillation centers at fixed distances from the photosensor. Pulse shape simulations further show that analog photosensors intrinsically operate near the timing resolution bound, which can be attributed to the finite single photoelectron pulse rise time.

Keywords

Positron Emission Tomography (PET); scintillation detectors; time of flight (TOF); silicon photomultipliers (SiPMs)

1. Introduction

In time-of-flight positron emission tomography (TOF-PET), the time difference in the detection of two oppositely-directed 511 keV annihilation photons is used to narrow down the position of the positron annihilation on the line-of-response between two detector elements. This timing information can significantly increase the signal-to-noise ratio (SNR) of tomographic images [Moses, 2003], and thus effectively increases system sensitivity. Recently, it has been shown that excellent coincident resolving times (CRTs) below 200 ps FWHM can be achieved with LYSO:Ce and LaBr₃:Ce scintillation crystals coupled to silicon photomultipliers (SiPMs) (e.g. [Yeom et al., 2013, Schaart et al., 2010, Gundacker et al., 2014]). These CRTs were typically achieved with specialized acquisition setups (e.g.

waveform digitizers and low-noise preamplifiers), whereby the timing resolution is minimally affected by electronic noise. For these low-noise setups, the timing resolution is mainly determined by photon counting statistics [Seifert et al., 2012b]. In [Seifert et al., 2012c], the Cramér-Rao lower bound on the timing resolution was calculated for small scintillation crystals, for which the crystal propagation time can be approximated by a Gaussian distribution function. As this bound acts as an intrinsic timing limit on the achievable timing resolution, it is independent on the time pickoff method and/or the timing estimation algorithm, and is thus generally applicable to any timing measurement setup. Other studies on scintillator timing include [Post and Schiff, 1950, Hyman, 1965, Cocchi and Rota, 1967, Bengtson and Moszynski, 1970, Moszynski, 1978, Nutt, 1969].

For large crystal rod elements (with a clinically relevant crystal length of 20 mm), the crystal propagation time can not be described by a Gaussian distribution function. In this work, a method is presented that can calculate the Cramér-Rao lower bound on the timing resolution for large crystal rod elements with complex photon arrival time distributions. Hereby, the Cramér-Rao bound is directly calculated from Monte Carlo generated scintillation photon arrival time data. This method extends timing resolution bound calculations based on analytical equations, as crystal geometries can be evaluated that do not have closed form arrival time distributions.

2. Theory

Consider a scintillation crystal irradiated by 511 keV annihilation photons from a positron source. Indicate for event i the ordered set of detection times for the scintillation photons at the photosensor, relative to the positron annihilation time ($t_{\text{annih}} = 0$), by:

$$\mathbf{t} = \{t_{i1}, t_{i2}, \dots, t_{in}\} \quad (1)$$

The detection times in Eq. 1 are inter-correlated, as they form an ordered set. I.e., if the first photon is detected at a relatively late time t_{i1} , the second photon is detected at a time not earlier than t_{i1} ($t_{i2} > t_{i1}$), by definition. Assume that the event set of the j th earliest detected photons (i.e. $\{t_{1j}, t_{2j}, \dots, t_{Mj}\}$, whereby M denotes the number of events) can be described by a Gaussian distribution g function, for each detected photon index j . The joint distribution is then given by a multivariate Gaussian distribution function (see e.g. [Balakrishnan and Nevzorov, 2005]). The probability that the ordered timestamps $\{t_{i1}, t_{i2}, \dots, t_{in}\}$ for event i were generated after a positron annihilation at time t_{annih} is then given by:

$$P[\mathbf{t}|t_{\text{annih}}] = \frac{1}{\sqrt{(2\pi)^n |\Sigma|}} \cdot \exp\left(-\frac{1}{2}(\mathbf{t} - \boldsymbol{\mu} - \mathbf{t}_{\text{annih}})^T \Sigma^{-1} (\mathbf{t} - \boldsymbol{\mu} - \mathbf{t}_{\text{annih}})\right) \quad (2)$$

where $\mathbf{t}$ is defined in Eq. 1, $\boldsymbol{\mu}$ represents the expected values (i.e. means) of $\mathbf{t}$, and Σ the covariance matrix of $\mathbf{t}$, containing the variances and covariances of the ordered timestamps. $|\Sigma|$ represents the determinant of Σ and T the transpose operator.

The Fisher information $I(t_{\text{annih}})$ can now be calculated from Eq. 2 as follows:

$$I(t_{annih}) = -E \left[\frac{\partial^2}{\partial t_{annih}^2} \ln P[t|t_{annih}] \right] = \mathbf{1}^T \Sigma^{-1} \mathbf{1} = \sum_{i=1}^n \sum_{j=1}^n (\Sigma^{-1})_{ij} \quad (3)$$

where $E[\cdot]$ denotes the expected value, $\mathbf{1}$ is an $n \times 1$ array with values 1, and $(\Sigma^{-1})_{ij}$ the ij th matrix element of Σ^{-1} . The Cramér-Rao lower bound of the timing resolution based on the n ordered timestamps is then:

$$\sigma_{lb}^2 = \frac{1}{I(t_{annih})} \quad (4)$$

Eqs. 1 - 4 state that the Cramér-Rao bound on the timing resolution can be calculated from the inverse of the sum of the matrix elements of the inverse covariance matrix. In this derivation, the assumption has been made that the event set of the j th earliest detected photons can be described by a Gaussian distribution for each detected photon index j . These equations can also directly calculate the timing resolution bound from Monte Carlo generated detection times. It is hereby not necessary to develop analytical equations for the light transport inside the crystal. We will use this Monte Carlo approach to calculate scintillation photon arrival time distributions for large scintillation crystal elements which do not have a closed form analytical expression.

3. Methods

3.1. Validation of Cramér-Rao bound calculation

In a first step, the Cramér-Rao bound calculation in Eqs. 1 - 4 was validated against the analytical method in [Seifert et al., 2012c]. For this purpose, a Monte Carlo simulation was run with the same timing input parameters as used in [Seifert et al., 2012c] for the calculation of the timing resolution bound for a $3 \times 3 \times 5 \text{ mm}^3$ LYSO:Ce crystal pair coupled to Hamamatsu MPPC-S10362-33-50C SiPMs. These timing parameters are shown in Table 1. Note that for this calculation the number of red cells in the SiPM n (i.e. the number of detected scintillation photons) is kept constant for each event. This is not the case for a real scintillator (which has a finite energy resolution), but this approximation was made in [Seifert et al., 2012c] to simplify the analytical equations. Further, in that reference, the scintillation photon transport inside the crystals was assumed to be negligible.

For the Monte Carlo simulation, the arrival time t_{arriv} was calculated for $n = 4700$ scintillation photons (as was done in [Seifert et al., 2012c], see Table 1) for each event as follows:

$$t_{arriv} = t_e + t_{ps} \quad (5)$$

where t_e is the scintillation emission time and t_{ps} the SiPM propagation time. t_e and t_{ps} were generated according to the Monte Carlo method from the following probability density functions (PDFs):

$$PDF_{t_e}(t) = \frac{1}{\tau_d - \tau_r} \cdot \left(\exp\left[-\frac{t}{\tau_d}\right] - \exp\left[-\frac{t}{\tau_r}\right] \right) \quad (6)$$

$$PDF_{t_{ps}}(t) = \frac{1}{\sigma_{tts} \sqrt{2\pi}} \cdot \exp\left[-\frac{(t - \mu_{tt})^2}{2\sigma_{tts}^2}\right] \quad (7)$$

where μ_{tt} is the average transit time of the SiPMs. Since μ_{tt} acts as a constant time delay for each scintillation photon, not contributing to the timing resolution, an arbitrary value was chosen for this parameter. The parameter values for τ_r , τ_d , and σ_{tts} are summarized in Table 1 and were chosen to be the same as in [Seifert et al., 2012c]. Although these parameter values from [Seifert et al., 2012c] were experimentally determined with a certain accuracy (and thus contain error bars), we chose not to take these parameter error bars into account for the calculation of the timing resolution bound. The reason is that the purpose of this calculation is to only verify the numerical timing resolution bound method against the analytical method in [Seifert et al., 2012c]. For this verification, it is not necessary to model the parameter error bars and their effect on the timing resolution bound accuracy. The two different methods should produce the same timing resolution bound for the same input parameter values.

The set of generated values for t_{arriv} in Eq. 5 was sorted in time to produce for each event i the ordered set of arrival times $\{t_{i1}, t_{i2}, \dots, t_{in}\}$ (as in Eq. 1). An $m \times n$ matrix was subsequently set up containing the sorted arrival times for all m events. The covariance matrix Σ could then easily be calculated from this $m \times n$ matrix (this is a standard numerical operation in many numerical software packages, such as Matlab and ROOT). The Cramér-Rao bound σ_{lb} could then be calculated using Eqs. 3 - 4.

3.2. Cramér-Rao bound for crystal rod elements with non-Gaussian photon transport time

In this section, the crystal geometry from the measurements in [Yeom et al., 2013] is simulated. The geometry is a $3 \times 3 \times 20$ mm³ LYSO:Ce crystal, with a single layer of 3M ESR reflector on the 4 crystal side faces, and a Teflon (PTFE) reflector on the crystal top face (which is opposite to the crystal face with the photosensor). The crystal is read out with a Hamamatsu S10362-33-50C SiPM. See [Yeom et al., 2013] for more details on the crystal geometry.

Detect2000 [Cayouette et al., 2003] was used to simulate the scintillation photon transport within this crystal geometry. For these simulations, an index of refraction of $n = 1.82$ was chosen for the LYSO:Ce crystal. All crystal faces were chosen to be polished (as for the crystal in [Yeom et al., 2013]). The reflective surface on the 4 crystal side faces was chosen to exhibit specular (mirror-like) reflectance, as is the case for the 3M ESR reflector. The reflectivity R of this surface was chosen to be 98% (this was experimentally measured in [Janecek, 2012]). The reflective surface on the crystal top surface was chosen to exhibit diffuse reflectance, as is the case for the Teflon (PTFE) reflector. The reflectivity of this surface was chosen to be 95% (this was also experimentally measured in [Janecek, 2012]). Between the reflective surfaces and the crystal faces, an air layer of 50 μ m was defined with

an index of refraction of $n = 1.0$. This means that total internal reflection occurs whenever a scintillation photon impinges on a crystal side surface with an incidence angle θ_i exceeding the critical angle $\theta_{crit} = \arcsin(n_{air}/n_{LYSO})$, where $n_{air} = 1.0$ and $n_{LYSO} = 1.82$. For the optical grease between the LYSO:Ce crystal and the SiPM a $10 \mu\text{m}$ thickness and an index of refraction of $n = 1.52$ was chosen. For the SiPM layer, an index of refraction of $n = 1.52$ was chosen as well. The crystal geometry is summarized in Fig. 1.

For the scintillation photon generation, an LYSO scintillation yield LY of 27,000 photons/MeV was chosen [de Haas and Dorenbos, 2008]. 511 keV scintillation centers were generated on a line pattern centered on the $3 \times 3 \text{ mm}^2$ crystal face, with an exponential distribution along the crystal length using a 12.3 mm attenuation length for 511 keV annihilation photons in LYSO:Ce. An energy resolution of 11% FWHM at 511 keV was modelled for the LYSO:Ce crystal, by sampling the number of emitted scintillation photons n for each event from a Gaussian distribution with mean $\mu_n = 0.511 LY$ and standard deviation (square-root of the variance) $\sigma_n = 0.11 \cdot \mu_n = 2.355$. Note that in this simulation only 511 keV photoelectric events were generated, and that 511 keV events arising from a combination of Compton scattering and photoelectric absorption within the same crystal were not simulated. For the SiPM, a PDE of 35% was chosen for both crystal geometries.

In addition to the exponentially distributed line pattern of scintillation centers along the crystal length, simulations were performed whereby for each scintillation event the scintillation center was set at the same position within the crystal, i.e. with a constant distance to the SiPM and thus constant excitation depth. This allowed the evaluation of the timing resolution bound as a function of the excitation depth, to facilitate a comparison with that experimentally measured in [Yeom et al., 2013].

For each detected scintillation photon, a crystal propagation time t_{pc} is calculated by the Detect2000 package according to the total traversed path length between the emission point inside the crystal and the detection point at the SiPM. The arrival time for each photon is calculated as follows [Spanoudaki and Levin, 2011]:

$$t_{arriv} = t_\gamma + t_e + t_{pc} + t_{ps} \quad (8)$$

Hereby, the scintillation emission time t_e is sampled from Eq. 6 with $\tau_r = 72 \text{ ps}$ and $\tau_d = 43 \text{ ns}$ (from [Seifert et al., 2012a]). The SiPM propagation time t_{ps} is sampled from the Gaussian distribution function in Eq. 7 with $\sigma_{tts} = 80 \text{ ps}$ (from [Gundacker et al., 2013]). t_γ is the propagation time of the 511 keV annihilation photon within the crystal and is equal to:

$$t_\gamma = \frac{DOI}{c} \quad (9)$$

where DOI is the depth-of-interaction and $c = 2.998 \cdot 10^{11} \text{ mm/s}$ the light speed (note that unlike for a scintillation photon, the speed of an annihilation photon is not reduced in a scintillation medium). The chosen timing input parameters for the simulation are summarized in Table 2. Note that for the current simulation different values were chosen for σ_{tts} and τ_r as compared to the simulation in section 3.1 (listed in Table 1). We found that these parameter values resulted in a closer match between the calculated and measured

timing resolutions in [Yeom et al., 2013]. As in section 3.1, parameter error bars were not taken into account for the timing resolution bound calculations. This was done because not all the timing parameters in Table 2 were accurately known for the measurement in [Yeom et al., 2013] (such as the PDE, σ_{tts} , and τ_r), and had chosen values. The set of generated values for t_{arriv} in Eq. 8 was sorted in time, and the same procedure as in section 3.1 was followed to calculate the Cramér-Rao bound σ_{lb} .

3.3. Analog time pickoff simulation

It was shown in [Seifert et al., 2012c] that the intrinsic timing resolution limit was consistently lower than the timing resolution based on a single photon arrival, and that this intrinsic limit could be approached if the arrival time would be based on multiple photons. It was further mentioned in that paper that for analog photosensors, the time pickoff is in fact based on multiple photons, due to the finite temporal response of these photosensors.

In this section, the effect of the analog pulse shape on the timing resolution is investigated. The single photoelectron pulse signal was modelled as a bi-exponential curve $f(t)$:

$$f(t) = \begin{cases} 0 & t \leq t_s \\ A \cdot \left(\exp\left[-\frac{t-t_s}{\tau_d}\right] - \exp\left[-\frac{t-t_s}{\tau_r}\right] \right) & t > t_s \end{cases} \quad (10)$$

where t_s is the pulse start time, τ_r the pulse rise time, and τ_d the pulse decay time. $f(t)$ was normalized by setting A such that the pulse amplitude was equal to 1. The pulse decay time τ_d was set constant at 5 ns, while three values were used for the pulse rise time: $\tau_r = f0.1, 50, 500$ ps. The single photoelectron pulse signals $f(t)$ in Eq. 10 are plotted in Fig. 2.

For each detected scintillation photon from the $3 \times 3 \times 20$ mm³ LYSO crystal simulation in section 3.2, the single photoelectron pulse signal $f(t)$ was generated whereby t_s was set according to the calculated scintillation photon arrival time (t_{arriv} in Eq. 8). For each event, the photoelectron pulse signals were summed in time to obtain the scintillation pulse.

After this, leading-edge (LE) time pickoff was performed on the generated scintillation pulses with a constant trigger level relative to the baseline, to obtain the scintillation pulse arrival times. The timing resolution was calculated from the standard deviation of the arrival times. This resolution was multiplied by $2.355 \sqrt{2}$ for conversion to the FWHM coincidence resolving time (CRT) scale.

In this way, the CRT could be evaluated as a function of the single photoelectron pulse rise time. The hypothesis is that the single photoelectron pulse rise time effectively averages the arrival times of the first detected scintillation photons. Note that in this analog pulse shape simulation, no dark counts, optical crosstalk, and afterpulsing effects are simulated, that may otherwise also affect the timing resolution in (analog) SiPMs. The purpose of this simulation is to only evaluate the effect of the single photoelectron pulse shape on the timing resolution.

In addition to the analog pulse arrival time, a direct average scintillation photon arrival time t_{avg} was calculated as follows:

$$t_{avg} = \frac{\sum_{j=1}^k t_j}{k} \quad (11)$$

where t_j is the arrival time of the j th earliest detected scintillation photon from Eq. 8. Hereby, the average arrival time is based on the first k detected scintillation photons. The timing resolution was calculated from the standard p deviation of the average arrival times. This resolution was multiplied by $2.355\sqrt{2}$, for conversion to the FWHM CRT scale. The CRT was evaluated as a function of k .

The above two timing p methods were compared with the Cramér-Rao timing resolution bound $2.355\sqrt{2}$, as obtained from section 3.2.

4. Results

Fig. 3 shows timing histograms and resolutions for the simulation described in section 3.1. The Cramér-Rao timing resolution bound was calculated as $\sigma_{lb} = 37.4 \pm 0.2$ ps for the first 300 scintillation photons that were detected, using a 1σ confidence interval that was calculated from the standard deviation of σ_{lb} obtained from 10 sets of $m = 10,000$ Monte Carlo events.

Fig. 4 shows the timing histograms for the simulation described in section 3.2 with the $3 \times 3 \times 20$ mm³ LYSO crystal geometry.

Fig. 5 shows the obtained timing resolutions for the simulation in section 3.2. The timing resolution associated with the Cramér-Rao bound calculation rapidly converges with increasing photon index. The timing resolution associated with the average arrival time reaches a similar value as the Cramér-Rao lower bound. Table 3 summarizes the Cramér-Rao timing resolution bound results of Fig. 5, along with the associated number of detected photons. It also shows the timing resolution bound when the scintillation photon and annihilation photon transport are not included in the simulation (i.e. by discarding t_γ and t_{pc} in Eq. 8).

Fig. 6 shows for a single scintillation event the calculated scintillation pulses, according to the method described in section 3.3 and using the single photoelectron pulse signals shown in Fig. 2. Fig. 7 shows the obtained timing resolutions from the analog time pickoff simulation described in the same section. When the photoelectron pulse signal has a negligible rise time ($\tau_r = 0.1$ ps), the timing resolution profile is similar to the one based on the arrival time of the j th earliest photon (compare the cross profile in Fig. 7 with the one in Fig. 5). For larger rise times τ_r , the timing resolution improves and approaches the Cramér-Rao timing resolution bound.

Fig. 8 shows the Cramér-Rao timing resolution bounds for the $3 \times 3 \times 20$ mm³ LYSO crystal geometry, whereby the scintillation centers are located at a fixed distance from the photosensor (constant DOI). The timing resolution is improved by roughly 30 ps FWHM for scintillation centers located at 17.5 mm distance from the photosensor (DOI = 2.5 mm), compared with scintillation centers located at 2.5 mm distance (DOI = 17.5 mm). The

bottom graph of Fig. 8 shows that the average number of detected scintillation photons is similar for the four DOI positions. Fig. 9 shows the associated crystal propagation time profiles (t_{pc} in Eq. 8) for the scintillation photons.

5. Discussion

In section 2, a numeric calculation of the Cramér-Rao timing resolution bound was presented, and it was shown that it could directly be calculated from Monte Carlo generated scintillation photon arrival times. Therefore, it is not necessary to derive analytical equations for e.g. the scintillation photon transport. Hereby, the assumption was made that the arrival times of the j th earliest detected scintillation photon could be described by a Gaussian distribution, for each photon index j . This was shown to be the case in the top graph of Fig. 3 and in Fig. 4. In Fig. 3, the timing resolution bound calculation was validated against the analytical method used in [Seifert et al., 2012c], whereby the same timing parameters were used (Table 1). The obtained timing resolution bound from the first 300 scintillation photons ($\sigma_{lb} = 37.4 \pm 0.2$ ps) closely matches the one ($\sigma_{lb} = 37$ ps) in [Seifert et al., 2012c]. The timing resolution bound was calculated for only the first 300 scintillation photons, to save computation time and because the timing resolution bound rapidly converges as a function of photon index.

Fig. 5 showed the obtained timing resolutions for the $3 \times 3 \times 20$ mm³ LYSO crystal geometry described in section 3.2. It was mentioned in section 4 that the timing resolution associated with the average arrival time reaches a similar value as the Cramér-Rao lower bound. The timing resolution associated with the analog time pickoff also approaches the Cramér-Rao lower bound in Fig. 7, whereby the pulse rise time of the single photoelectron pulse effectively averages the arrival times of the first detected scintillation photons, as explained in section 3.3 and shown in Fig. 6. The timing resolution associated with a single photoelectron pulse rise time of $\tau_r = 500$ ps is closer to the timing resolution bound than for a negligible pulse rise time of $\tau_r = 0.1$ ps. Since analog photosensors have a finite rise time in response to a single photon excitation, this means that they might intrinsically already operate near the Cramér-Rao timing resolution bound, unlike for digital photosensors (such as SPAD arrays) where the analog pulse formation stage has been removed, and where it would be required to use multiple timestamps to reach the lower timing resolution bound. It was further mentioned in section 4, that the timing resolution profile for pulse rise time $\tau_r = 0.1$ ps in Fig. 7 is similar to the one associated with the j th earliest scintillation photon in Fig. 5. This further confirms the hypothesis that the single photoelectron rise time effectively averages the arrival time of multiple scintillation photons, and that for pulses with negligible rise time, one effectively triggers on single photons. In Fig. 4, one can see that the arrival time distributions of the first few photons are contained within a 500 ps time window. The pulse rise time acts as a low-pass filter, averaging the arrival times of these first few photons.

The Cramér-Rao timing resolution rebound of Fig. 5 is numerically shown in Table 3, along with the timing resolution bound for which the scintillation photon and annihilation photon transport are disabled. It is apparent that the scintillation and annihilation photon transport have a large effect on the timing resolution, and that it accounts for roughly 60 ps FWHM CRT for the 20 mm length LYSO crystal.

Fig. 8 shows that the Cramér-Rao timing resolution bounds improve with increasing distance from the photosensor. Since in this simulation, there was no noticeable variation in photon attenuation as a function of interaction depth (see bottom graph of Fig. 8), this result can only be explained from the differences in photon transport. Fig. 9 shows the scintillation photon propagation time profiles within the crystal. A similar simulation was earlier done for [Yeom et al., 2013]. It is apparent that for scintillation centers far from the photosensor, the forward and backward scintillation photons merge in time, resulting in a high initial light flux towards the photosensor. In contrast, for scintillation centers close to the photosensor, there is a large time separation between the forward and backward photons, resulting in a lower initial photon flux. This explanation was taken from [Moses and Derenzo, 1999], where it was used to account for the attenuating behavior of the average pulse arrival time for increasing distance from the photosensor.

It is further apparent from Fig. 8 that the timing resolution bound for scintillation centers exponentially spread along the crystal length (solid line in Fig. 8) seems to be an average of the timing resolution bounds for scintillation centers at fixed DOI positions (circles in Fig. 8). For scintillation centers fixed at large DOI values, the timing resolution bound is higher compared to the one for exponentially spread out scintillation centers. This implies that for the simulated crystal geometry, the timing resolution would not be improved significantly if the DOI could accurately be measured, as the timing resolution bound for the exponentially spread scintillation centers already appears to be an average of the timing resolution bounds at fixed DOIs. If for this crystal geometry, the shift in average scintillation photon arrival time with DOI would have had a significant contribution to the timing resolution, the timing resolution bound for the exponentially spread scintillation centers would have had a degraded value with respect to the average of the timing resolution bounds at fixed DOIs. Since the resolutions in Fig. 8 are Cramér-Rao bounds, they are independent of the method how the arrival times are determined. DOI information would however still be beneficial in TOF-PET (besides their use for parallax correction), as the timing kernels along the line-of-responses (LORs) can be more accurately positioned if the DOI information is available.

In [Yeom et al., 2013], it was experimentally shown that the timing resolution indeed improves with increasing distance from the photosensor, as well as that the average pulse amplitude was roughly constant as a function of DOI. The Cramér-Rao timing resolution bound in Table 3 for the 20 mm LYSO crystal (183.7 0.9 ps FWHM) corresponds well to the measured timing resolution for the similar geometry in [Yeom et al., 2013] (186 ± 3 ps FWHM).

Eq. 2 represents the probability function for observing scintillation photons at a certain time sequence $\{t_1, t_2, \dots, t_n\}$, when an annihilation happens at $t = t_{\text{annih}}$. Although this equation was used to derive the Cramér-Rao bound in Eqs. 3 - 4, it could also directly be used in a maximum likelihood (ML) estimation of the annihilation time t_{annih} , given a measured dataset for $\{t_1, t_2, \dots, t_n\}$. Although not shown in section 4, the estimation of the annihilation time using this ML method (from the Monte Carlo sampled scintillation photon arrival times in section 3.2) results in a timing resolution equal to the Cramér-Rao bound (verified by calculation). This is not surprising, as ML theory states that ML estimators achieve the Cramér-Rao lower bound when the sample size tends to infinity.

6. Conclusion

A method was presented for which the Cramér-Rao timing resolution bound can directly be calculated from Monte Carlo generated arrival times of the scintillation photons. This method extends timing resolution bound calculations based on analytical equations, as crystal geometries can be evaluated that do not have closed form analytic expressions for arrival time distributions. With this method, the timing resolution bounds were calculated for an exemplary $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry. It was further shown that the single photoelectron pulse rise time in analog photosensors effectively averages multiple timestamps. Pulse shape simulations show that these sensors already intrinsically operate near the Cramér-Rao timing resolution bound.

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Figure 1. Schematic diagram of the simulated $3 \times 3 \times 20 \text{ mm}^3$ LYSO:Ce crystal geometry used in the experimental studies of [Yeom et al., 2013]. DOI is measured from the photon entrance face of the scintillation crystal element.

Figure 2. Single photoelectron pulse signals $f(t)$ (from Eq. 10) used for the pulse shape analysis. τ_d was set at 5 ns, τ_r was varied between 0.1, 50, 500 ps.

Figure 3.

Timing graphs for the simulation in section 3.1. Top graph: Histograms of the scintillation photon arrival times for photon indices $j = \{1, 2, 3, \dots, 20, 50, 100\}$. Solid lines indicate the Gaussian ts. Bottom graph: Timing resolution as a function of j . Crosses indicate the standard deviation of the j th earliest arrival times, circles indicate σ_{lb} calculated from the first j arrival times (using Eqs. 3 - 4), solid line indicates σ_{lb} calculated from the first 300 arrival times.

Figure 4. Timing histograms of the scintillation photon arrival times obtained from the $3 \times 3 \times 20$ mm³ LYSO crystal geometry simulation described in section 3.1. Solid lines indicate the Gaussian ts.

Figure 5.

Timing graph for the simulation in section 3.2. Plotted is the FWHM coincidence resolving time (CRT) as a function of photon index j for the $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry. 511 keV scintillation centers were distributed exponentially along the crystal length. Crosses indicate the FWHM CRT based on the standard deviation of the j th earliest arrival times, triangles indicate the FWHM CRT based on the standard deviation of the average arrival time obtained from the first j scintillation photons (see Eq. 11), circles indicate the FWHM CRT based on σ_{lb} calculated from the first j arrival times (using Eqs. 3 - 4), solid line indicates the FWHM CRT based on σ_{lb} calculated from the first 300 arrival times. All obtained resolutions were multiplied by $\sqrt{2}$ to convert the values to the FWHM CRT scale.

Figure 6. Scintillation pulse signals for the $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry. The three pulses were generated from the same scintillation event, using the single photoelectron pulses plotted in Fig. 2. The bottom graph is a zoomed-in version of the early rising portion of the top graph.

Figure 7.

FWHM CRT obtained from the analog time pickoff simulation described in section 3.3, for the $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry. The same scintillation photon arrival time dataset was used as the one used for generating Fig. 5. Crosses, triangles, and circles indicate the FWHM CRTs based on the standard deviation of the pulse timestamps obtained with pulse rise time $\tau_r = 0.1, 50$, and 500 ps , respectively. The solid line indicates the FWHM CRT based on σ_{lb} calculated from the first 300 arrival p times, and was copied from Fig. 5. All obtained resolutions were multiplied by $\sqrt{2}$, to convert the values to the FWHM CRT scale. The voltage scale on the horizontal axis corresponds to the one in Fig. 6.

Figure 8.

Top graph: Cramér-Rao timing resolution bound results for the $3 \times 3 \times 20$ mm³ crystal geometry, whereby the circles indicate the FWHM CRTs for the case that the scintillation centers were located at four fixed distances from the photosensor with constant DOI over all simulations. The solid line indicates the FWHM CRT for which the scintillation centers were exponentially distributed along the crystal length, and was copied from the top graph of Fig. 5. All FWHM CRTs were based on σ_{lb} calculated from the first 300 arrival times. Error bars indicate the 1σ confidence intervals for the FWHM CRTs with constant DOIs, that were calculated from the standard deviation over 10 sets of $m = 10,000$ Monte Carlo events. The dashed lines around the solid line indicate the 1σ confidence interval for the FWHM CRT with exponentially distributed scintillation centers. Bottom graph: Average detected number of photons n_{avg} corresponding to the data of the top graph, whereby the error bars indicate the 1σ confidence intervals.

Figure 9.

Histograms of the crystal propagation time t_{pc} (see Eq. 8), corresponding to the data of Fig. 8. The scintillation centers were located at a fixed point with constant DOI for each of the four graphs. Scintillation photons with a propagation time larger than 600 ps are not shown.

Table 1

Timing input parameters used for the validation of the Cramér-Rao bound calculation in section 2. Input parameters are taken from [Seifert et al., 2012c] for the calculation of the Cramér-Rao bound of a $3 \times 3 \times 5$ mm³ LYSO:Ce crystal pair coupled to Hamamatsu MPPC-S10362-33-50C SiPMs.

Input parameter	Value
Scintillation rise time τ_r [ps]	89
Scintillation decay time τ_d [ns]	43
SiPM transit time spread σ_{ts} [ps]	120
Number of fired cells in SiPM n	4700

Table 2

Timing input parameters used for simulation of the $3 \times 3 \times 20 \text{ mm}^3$ LYSO:Ce crystal geometry in [Yeom et al., 2013].

Input parameter	Value
Scintillation rise time τ_r [ps]	72 [Seifert et al., 2012a]
Scintillation decay time τ_d [ns]	43 [Seifert et al., 2012a]
SiPM transit time spread σ_{ts} [ps]	80 [Gundacker et al., 2013]
Light yield LY [ph / MeV]	27,000 [de Haas and Dorenbos, 2008]
Energy resolution $2.355 \cdot \sigma_n / \mu_n$ [%]	11
Photon detection efficiency PDE [%]	35

Table 3

Summary of the Cramér-Rao timing resolution bound results for the $3 \times 3 \times 20 \text{ mm}^3$ LYSO crystal geometry. Timing resolutions correspond to the FWHM CRTs based on σ_{lb} calculated from the first 300 arrival times. σ_{lb} values were multiplied by $2.355 \cdot 2$, to convert to the FWHM CRT scale. First column shows the timing resolution bound whereby the scintillation photon transport and annihilation photon transport variations within the crystal were included (see Eq. 8). This value is plotted as the solid line in Fig. 5. Second column shows the timing resolution bound without the scintillation photon transport and annihilation photon transport variances within the crystal (analogous to Eq. 5). Third column shows the average number of detected photons n_{avg} for these FWHM CRT values. Fourth column shows the associated crystal light collection efficiency, calculated as: $n_{avg}/(0.511 \cdot LY \cdot PDE)$, whereby the values for LY and PDE are shown in Table 2. Error values indicate the 1σ confidence intervals that were calculated from the standard deviation of the σ_{lb} and n_{avg} parameters, obtained from 10 sets of $m = 10,000$ Monte Carlo events.

$2.355 \cdot 2 \cdot \sigma_{lb}$ with transport [ps]	$2.355 \cdot 2 \cdot \sigma_{lb}$ without transport [ps]	average number detected photons n_{avg}	crystal light collection efficiency [%]
183.7 ± 0.9	124.8 ± 0.7	3360 ± 2	69.59 ± 0.03