Prospects for sub-100 picosecond TOF-PET

Fast Timing Workshop, LPC Clermont-Ferrand, 12-Mar-2014
Conventional PET/ToF off

Time-of-Flight PET

\( t_2 - t_1 \)

→ ToF: more signal, less noise
Vereos PET/CT system

Coincidence resolving time (CRT) ~350 ps FWHM due to digital photon counting

Images: Philips
In lab 100 ps barrier has been broken

Made possible by the combination of:

- Small LaBr$_3$:Ce(5%) crystals (3 mm x 3 mm x 5 mm)
- Silicon Photomultipliers (Hamamatsu MPPC-S10362-33-050C)
- Digital Signal Processing (DSP)

The holy grail: “10-picosecond PET”

With a CRT less than ~20 ps events can be localized directly:
- image reconstruction no longer necessary!
- only attenuation correction
- real-time image formation

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\[ \Delta x = c \cdot \text{CRT} / 2 \]

Aim: \( \Delta x \leq d \)

\[ \Rightarrow \text{CRT} \leq 2d / c \]

Clinical PET:
- \( 2 \text{ mm} \leq d \leq 4 \text{ mm} \)
- \( \Rightarrow \text{CRT} \leq 20 \text{ ps} \)
What is the best possible timing resolution obtainable with a given scintillation detector?
Scintillation photon counting statistics

γ emission

γ absorption

Emission of $N_{sc}$ optical photons

Detection of $N$ optical photons

$N = \eta N_{sc}$, where $\eta$ is the photodetection efficiency (PDE)

$T_e = \{t_{e,1}, t_{e,2}, \ldots, t_{e,N_{sc}}\}$

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

$\Xi (= \text{estimate of } \Theta)$
Our question can be answered if we can find the (average) Fisher Information in the set $T_d$
Calculation of CRT_{LB}

Parameters included in the calculation:

- Scintillation light yield $Y$
- Photodetection efficiency $\eta$
- Scintillation pulse shape,
  - For example, bi-exponential pulse with rise time constant $\tau_r$ and decay time constant $\tau_d$
- Probability density function describing the single-photon timing uncertainty
  - Comprises optical transit time spread (OTTS), transit time spread (TTS) of sensor, trigger jitter, etc.
  - Very small crystal and near-perfect detector readout only TTS
  - Here, TTS represented by Gaussian with standard deviation $\sigma$
    (formalism allows other distributions!)

The math involves order statistics, it is given (including validation) in:

RGB Single SPADs (with integrated quenching)

Non-Gaussian TTS is allowed in Seifert formalism

CIRCULAR CELL - 10um radius

Vex = 6.4V
T = 23 °C
FWHM ~ 20 ps

Kindly provided by F. Acerbi and C. Piemonte, FBK, Trento, Italy
Some essential findings

\[ \text{CRT}_{LB} \propto \frac{1}{\sqrt{N}} \]

\[ \tau_r \ll \tau_d \land \sigma \ll \tau_d \Rightarrow \text{CRT}_{LB} \propto \frac{1}{\sqrt{\tau_d}} \]

\[ \tau_r \downarrow \Rightarrow \text{CRT}_{LB} \downarrow \]

The latter 2 properties are due to the fact that most of the timing information is carried by the first detected photons, i.e. in the rising part of the pulse.
Let’s look at some scintillators...
LSO:Ce, 0.02%Ca


\[ Y \approx 35000 \text{ ph/MeV} \]
\[ \tau_T \approx 75 \text{ ps} \]
\[ \tau_d \approx 33 \text{ ns} \]

\[
\text{var}(\Xi) \geq \frac{1}{I_{T_d}(\Theta)}
\]
LaBr:5%Ce


\[ Y = 72000 \text{ ph/MeV}; \]
\[ \tau_{r,1}/\tau_{d,1} = 280 \text{ ps}/15 \text{ ns (72\%)} \]
\[ \tau_{r,2}/\tau_{r,2} = 2 \text{ ns}/15 \text{ ns (27\%)} \]
\[ \tau_{r,2}/\tau_{r,2} = 15 \text{ ns}/130 \text{ ns (2\%)} \]

\[ \text{var}(\Xi) \geq \frac{1}{I_{T_d}(\Theta)} \]


LaBr:20%Ce


$Y = 68080 \text{ ph/MeV;}$

$\tau_{r,1}/\tau_{d,1} = 160 \text{ ps}/17.5\text{ ns} \ (89\%)$

$\tau_{r,2}/\tau_{d,2} = 150 \text{ ps}/4.5 \text{ ns} \ (5\%)$

$\tau_{r,2}/\tau_{d,2} = 160 \text{ ps}/55 \text{ ns} \ (6\%)$

$\text{var}(\Xi) \geq \frac{1}{I_{T_d}(\Theta)}$
PbI at cryogenic temperatures


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**Table 1**

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>( \lambda_{\text{peak}} ) (nm)</th>
<th>( E_{\text{peak}} ) (eV)</th>
<th>Total luminosity<strong>a</strong></th>
<th>Peak luminosity<strong>b</strong></th>
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<td>14</td>
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**a** Relative to \( \text{Lu}_2\text{SiO}_5\):Ce.

**b** After 80 ps X-ray pulses, relative to \( \text{Lu}_2\text{SiO}_5\):Ce.

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- Light yield: \( Y \approx 1500 – 35,000 \) ph/MeV
- Rise time: \( \tau_r \approx 100\)ps
- Decay time(s):
  - \( \tau_{d,1} \approx 2 \) ns (24%)
  - \( \tau_{d,2} \approx 120 \) ns (76%)

---

Fig. 2. Initial intensity of undoped PbI\(_2\) at different temperatures compared with \( \text{Lu}_2\text{SiO}_5\):Ce and \( \text{LaBr}_3\):Ce.
PbI$_2$ at cryogenic temperatures


Fig. 2. Initial intensity of undoped PbI$_2$ at different temperatures compared with Lu$_2$SiO$_5$:Ce and LaBr$_3$:Ce.
PbI at cryogenic temperatures


(assuming: PDE = 0.3; $Y_{LSO} = 26k$ ph/MeV)

\[
Y \approx 1500 - 35.000 \text{ ph/MeV}
\]
\[
\tau_r \approx 100 \text{ ps}
\]
\[
\tau_{d,1} \approx 2 \text{ ns (24%)}
\]
\[
\tau_{d,2} \approx 120 \text{ ns (76%)}
\]
Time for a reality check...
DOI-dependent signal delay in crystal

Depth-of-interaction (DOI) variations deteriorate timing resolution

\[ \gamma_1 \quad \gamma_2 \]

Gamma photon speed: \( c \)

Scintillation photon speed: \( c/\hat{n} \)

WW Moses and SE Derenzo

Factors influencing time resolution

Optical Transit Time Spread (OTTS)

**Intrinsic properties**
- light yield
- decay time constant
- scintillation rise time

**Optical transit time-spread**
- dimensions of the crystal
- surface structure
- packaging

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D.N. ter Weele et al, SCINT 2013, Shanghai, 19-Apr-2013
Measuring rise times with a picosecond x-ray set-up

ID-Quantique id100-50
GM-APD φ50 um.

100 ps (FWHM) x-ray pulse

LSO:Ce,Ca (3x3x5 mm³)
wrapped in black tape
wrapped in PTFE

Light

Sample

Be window

Photoelectron

Target

D.N. ter Weele et al, SCINT 2013, Shanghai, 19-Apr-2013
Optical transit time spread (OTTS) measurement with a streak camera
Unpolished LYSO 3x3x5 mm³ crystal
Polished LYSO 3x3x5 mm$^3$ crystal
Optical transit time-spread (OTTS)

- Optical transit time-spread increases with the length of the sample
- Light trapping in polished samples increases the photon collection time
- OTTS easily > 100 ps
- Seifert formalism: If TTS $\approx 10$ ps $<<$ OTTS $\Rightarrow$ OTTS determines CRT
So is there any hope..?
The monolithic scintillator detector

Monolithic TOF/DOI detector with improved performance due to Ca co-doped LSO scintillator, digital silicon photomultipliers (dSiPM), and optimized readout algorithms

24 mm x 24 mm x 10 mm LSO:Ce,Ca scintillator on PDPC digital SiPM array


Digital Photon Counter

++ small single-photon time jitter
++ negligible noise at the single photon level
++ ~ 30% photon detection efficiency
+ MR-compatible

16 Si dies (4 x 4)
Each Si die:
→ 1 timestamp
→ 4 pixels values (no. of counts)

See: Thomas Frach, IEEE NSS/MIC, Orlando, FL October 28, 2009
Timing in monolithic scintillators

Maximum likelihood interaction time estimation (MLITE), using measured 1st photon arrival time probability distribution for each (x,y,z) position

H.T. van Dam et al, Sub-200 ps CRT in monolithic scintillator PET detectors using digital SiPM arrays and maximum likelihood interaction time estimation, PMB 58, 3243-3257, 2013
Performance summary

Current results with LSO monolithic scintillators on dSiPM arrays:

<table>
<thead>
<tr>
<th>Performance parameter</th>
<th>Monolithic</th>
<th>State of the art</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy resolution (% FWHM)</td>
<td>11 - 12</td>
<td>~12</td>
</tr>
<tr>
<td>Spatial resolution (mm FWHM)</td>
<td>1.0 - 1.6</td>
<td>4 - 6</td>
</tr>
<tr>
<td>DOI resolution (mm FWHM)</td>
<td>3 - 5 mm</td>
<td>None</td>
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<tr>
<td>CRT (ps FWHM)</td>
<td>160 - 185</td>
<td>500 - 650</td>
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⇒ A highly promising detector for future clinical PET/CT and PET/MRI systems
Conclusions

- Sub-100 ps feasible with (small) lanthanide-doped scintillators when fast(er) photosensors become available
- If sensor TTS $\sim$10 ps, optical transit time spread (OTTS) quickly becomes dominant
- Sensor TTS and OTTS can be treated in the same way in Seifert model of scintillation detector time resolution (also if non-Gaussian)
- Time blurring due to OTTS can be mitigated by combining spatio-temporal light sensing with clever timing algorithms* such as maximum-likelihood interaction time estimation (MLITE)
Some of our papers related to timing

- S. Seifert and D.R. Schaart, “Improving the time resolution of TOF-PET detectors by double-sided readout of high-aspect-ratio scintillation crystals,” *accepted for publication in IEEE Trans Nuc Sci.*


Thank You
Backup slides
Time-of-flight PET: gain in SNR

Gain in SNR = $(D/\Delta x)^{1/2}$

Gain in sensitivity = Reduction in variance = $D/\Delta x$

where $\Delta x = c \cdot CRT/2$

From: J. Karp (Upenn), SNM 2012
Comparison to measured values

Lower bound for LYSO:Ce

Parameters:
\( \tau_r = 90 \text{ ps} \)
\( \tau_d = 44 \text{ ns} \)
\( \sigma = 120 \text{ ps} \)
\( N_{\text{det}} = 4700 \)

Lower bound on the CRT for LYSO:Ce on MPPC-S10362-33-050C, using the \( n^{\text{th}} \), the first \( n \), or all detected photons (“order statistics”) for timing.
Order Statistics

Timestamp for the \( n^{th} \) detected scintillation photon

Exemplary probability density functions for the \( n^{th} \) order statistic for LYSO:Ce on MPPC-S10362-33-050C
Lower bound for LYSO:Ce

It appears possible to closely approach the CR lower bound using a leading edge trigger set at the optimum threshold level.

Calculated lower bound

Measured CRT
PbI at cryogenic temperatures


Table 1
Scintillation properties of undoped PbI₂.

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* Relative to Lu₂SiO₅:Ce.
* After 80 ps X-ray pulses, relative to Lu₂SiO₅:Ce.

- Light yield: \( Y \approx 1500 - 35,000 \text{ ph/MeV} \)
- Rise time: \( \tau_r \approx 100 \text{ps} \)
- Decay time(s): \( \tau_{d,1} \approx 2 \text{ ns (24%)} \)
  \( \tau_{d,2} \approx 120 \text{ ns (76%)} \)

Fig. 2. Initial intensity of undoped PbI₂ at different temperatures compared with Lu₂SiO₅:Ce and LaBr₃:Ce.
PbI$_2$ at cryogenic temperatures


Fig. 2. Initial intensity of undoped PbI$_2$ at different temperatures compared with Lu$_2$SiO$_5$:Ce and LaBr$_3$:Ce.
PbI at cryogenic temperatures


(assuming: PDE = 0.3; $Y_{LSO} = 26k$ ph/MeV)

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$^a$ Relative to Lu$_2$SiO$_5$:Ce.

$^b$ After 80 ps X-ray pulses, relative to Lu$_2$SiO$_5$:Ce.

$Y \approx 1500 – 35.000$ ph/MeV

$\tau_r \approx 100$ ps

$\tau_{d,1} \approx 2$ ns (24%)

$\tau_{d,2} \approx 120$ ns (76%)
Using Cherenkov photons


PWO (3×3×3 mm³)

\[ \tau_r = 5 \text{ ps} \]
\[ \tau_d = 20 \text{ ps} \]
\[ Y = 6 \text{ ph/511 keV} \]

Fig. 3. Accumulated photon creation (left) and detection (right) rates at the photon detector for Cherenkov and scintillation photons for LSO:Ce (top) and PWO (bottom). The normalization for created and detected photons was done using the maximum of the creation rate of Cherenkov photons. A bin width of 2 ps was chosen.
Using Cherenkov photons


Simulated using ideal (PDE = 1) photosensor

<table>
<thead>
<tr>
<th>Material</th>
<th>photoel. effect calculated</th>
<th>all events</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>LSO:Ce</td>
<td>18</td>
<td>7.6</td>
<td>0.7</td>
<td>13.8</td>
<td>1.1</td>
</tr>
<tr>
<td>LuAG:Ce</td>
<td>27</td>
<td>11.5</td>
<td>3.2</td>
<td>24.3</td>
<td>7.2</td>
</tr>
<tr>
<td>BGO</td>
<td>28</td>
<td>20.8</td>
<td>3.1</td>
<td>32.8</td>
<td>4.6</td>
</tr>
<tr>
<td>PWO</td>
<td>23</td>
<td>22.6</td>
<td>3.8</td>
<td>see$^3$</td>
<td></td>
</tr>
<tr>
<td>Pb-glass</td>
<td>29</td>
<td>20.9</td>
<td>3.3</td>
<td>see$^4$</td>
<td></td>
</tr>
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TABLE II
CALCULATED AND SIMULATED CHERENKOV PHOTON YIELD PER 511 KEV PHOTON INTERACTION.
Using Cherenkov photons


No Cherenkov photons detected for ~30% of the events

- Large variation on no. detected photons
- Large variation on expected CRT
- Each event may require individualized interaction time estimator

Fig. 2. Left: number of Cherenkov photons created in a cube of BGO with 3 mm edge length. Right: number of detected Cherenkov photons with a photon detector of 3 mm x 3 mm, attached to the cube. No thresholds were set (both, Compton scattered and events due to the photoelectric effect were respected).
Using Cherenkov photons

- Large variation on expected CRT
- Each event may require individualized interaction time estimator
- Half of the potential events would be lost in a PET system!