Time-of-flight PET with SiPM sensors on monolithic scintillation crystals
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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2011

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
3 PET Detector Components

Scintillation detectors are the most widely used radiation detectors in PET imaging. They are very fast, can have high stopping power and exhibit low electronic noise. A scintillation detector primarily consists of a scintillator, that produces scintillation light after interaction with radiation, and a photodetector that converts the scintillation light into an electrical signal. This chapter primarily discusses the scintillation detector components and design considerations. Section 3.1 discusses the scintillation mechanism and gives an overview of the common scintillators that are used for PET. Section 3.2 discusses the photodetectors for collecting the scintillation light. In section 3.3, an overview of various scintillation detector designs is given. Alternative radiation detectors for PET imaging are discussed in section 3.4. Section 3.5 introduces the detector concept used in this work.

3.1 Scintillators

Gamma photons can be detected with scintillators, which produce scintillation photons in the visible and ultraviolet range of wavelengths. Only photoelectric absorption and Compton scattering are important interaction mechanisms for detecting 511 keV gamma photons [18]. During a photoelectric effect, the entire energy of the gamma photon is converted to the release of a photoelectron, a knock-on electron. This electron then excites higher energy states of the crystal lattice, which decay by emitting lower energy scintillation photons. During Compton scatter, only part of the energy of the gamma photon is converted to the knock-on electron. The rest of the energy is taken by the scattered, "degraded" photon. This scattered photon in turn can produce additional scintillation centers by the Compton and photoelectric effect. Compton scattering inside the scintillation crystal can thus produce various scintillation centers. This position blurring affects the position determination. Unlike Compton scatter, the photoelectric effect produces a single scintillation center and is the preferred interaction process. The photoelectric cross section \( \sigma_p \) is a function of the density \( \rho \) and of the effective atomic number \( Z_{eff} \) of the crystal. The photoelectric cross section is proportional to \( \rho Z_{eff}^x \), with the power \( x \) varying with gamma energy between 3 and 4, typically. In contrast, the Compton cross section is linearly related to the electron

\[ Z_{eff} \] is the atomic number that represents the attenuation properties of a mixture of atoms in a molecule. It is defined as \( Z_{eff} = \sqrt{\sum_{i=1}^{n} \omega_i Z_i^x} \), where the mass weighting factor \( \omega_i \) is defined as \( \omega_i = \frac{m_i Z_i}{\sum_{j=1}^{n} m_j Z_j} \), where \( m_i \) is the number of atoms of element \( i \) in the molecule. The power \( x \) is dependent on the energy of the gamma rays, and typically varies between 3 and 4.
density, and thus proportional to $\rho$ [25]. A scintillator should thus have a high density for a high absorption probability and a high atomic number for a large fraction of events undergoing photoelectric absorption. These two requirements are commonly parametrized as the attenuation length $1/\mu$ (the distance into a material where the probability has dropped to $1/e$ that a particle has not been absorbed) and photoelectric absorption probability $PE$ or photofraction (defined as the probability that a gamma photon interacts by the photoelectric effect instead of the Compton effect: $PE = 100 \cdot \frac{\sigma_p}{\sigma_p + \sigma_c}$).

High light yield (number of emitted scintillation photons per MeV absorbed energy) is another important requirement for PET. A large number of detected scintillation photons $N_{ph}$ implies a high energy, timing and position resolution. This is because photon counting is dominated by Poisson statistics, such that the relative statistical spread is proportional to $1/\sqrt{N_{ph}}$. Associated with the light yield requirement is a high light collection efficiency of the crystal, such that a large fraction of the emitted scintillation photons are detected. Optical self-absorption of the scintillation photons should therefore be minimal. Furthermore, the scintillator can be surrounded by a reflector at all surfaces except that at which the photosensor is located, to recapture the light that would otherwise escape from the crystal. Also, the emission spectrum should overlap with the spectral sensitivity of the photodetector. It is further desirable that the light output is proportional to the deposited energy. If this would not be the case, the light output would be different for a full 511 keV energy absorption by a single photoelectric effect, compared to a full energy absorption by multiple, lower energy, Compton interactions. This would broaden the full energy peak.

The decay time of the excited state should be fast enough to allow a short coincidence time window, to limit the amount of random coincidences. A fast decay time also allows a high count rate performance of the detector. This is especially important for 3D-mode PET, where high counting rates exist and the system sensitivity will be limited by pulse pile up if slow scintillators are used. Additionally, a fast decay time (as well as a high light yield) implies a large initial scintillation photon emission rate $I_0$, such that a high timing resolution can be obtained for TOF-PET. For timing, it is also important that the scintillator has a fast rise time. The rise time is associated with the luminescence process in scintillators. Like a fast decay time, a fast rise time is associated with a large initial scintillation photon emission rate $I_0$.

Scintillator materials can be organic-based (liquid or plastic) or inorganic. Organic scintillators are generally fast, but have a low light yield. Inorganic scintillators have a higher light yield, but are relatively slow. For all current commercial PET scanners, inorganic scintillators are applied.
3.1 Scintillators

3.1.1 Scintillation mechanism in inorganic scintillators

The scintillation mechanism in inorganic scintillators is due to the electronic band structure found in crystals, whereby the conduction band is separated from the valence band by a forbidden energy gap of 4-12 eV. Ionizing radiation causes electrons from the valence band to jump to the conducting band, where they have sufficient energy to mitigate throughout the crystal. Inorganic scintillators commonly contain impurities. These impurities, called *activators*, create special sites in the lattice with a modified band structure. At these sites additional energy states are created within the forbidden energy gap through which the electron can de-excite back to the valence band. The energy of this transition is less than the full energy gap, such that photons in the visible range are created. These de-excitation sites are the *luminescence centers* from which scintillation can take place. Due to the presence of these activators, scintillators are transparent to scintillation light: since the energy of the de-excitation transition is less than the required energy to elevate an electron from the valence to the conduction band, the emission and absorption spectra do not overlap and self-absorption by the crystal is minimal.

3.1.2 Typical inorganic scintillators for PET

As mentioned before, scintillator materials suitable for PET have a small attenuation length, high photofraction, high light yield and fast decay time. The properties of several relevant inorganic scintillators for PET imaging are summarized in Table 3.1.

Bismuth germanate (BGO) has a high density and high effective atomic number $Z_{eff}$ and, therefore, a high detection efficiency for 511 keV gamma photons and a high photofraction $P_{E}$. The photoelectric cross section $\sigma_{p}$ at 511 keV for BGO is 1.6 times that of LSO and 5.8 times that of NaI:Tl [13]. However, its light yield and decay time are inferior compared to the other crystals. This makes it less suitable for fast timing applications, limits the countrate capabilities and increases the number of random coincidences due to the requirement of a wide coincidence window. Due to its high detection efficiency and the widespread availability, BGO has in the past been the most widely used scintillator for commercial PET scanners.

NaI:Tl has high light yield, but low detection efficiency and a low photofraction. Furthermore, it is hygroscopic (it reacts with water), which requires that the crystal is hermetically sealed to prevent the entrance of moisture.

Lutetium oxyorthosilicate (LSO) is arguably the most suitable scintillator for PET and TOF-PET imaging to date. It combines high detection efficiency (attenuation length of 12.3 mm), a high photofraction (34%), high light yield (30,000 photons/MeV), short decay time (40 ns) and a short rise time (0.5 ns, see [26]). It is not hygroscopic and has good mechanical properties. A disadvantage of the material is the non-proportionality of the light output to the deposited energy [13].
**Table 3.1: Properties of common scintillators used for PET (Data from [10])**

<table>
<thead>
<tr>
<th></th>
<th>NaI</th>
<th>BGO</th>
<th>GSO</th>
<th>LSO</th>
<th>LYSO</th>
<th>LGSO</th>
<th>LuAP</th>
<th>YAP</th>
<th>LaBr₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak emission wavelength (nm)</td>
<td>410</td>
<td>480</td>
<td>440</td>
<td>420</td>
<td>420</td>
<td>415</td>
<td>365</td>
<td>350</td>
<td>360</td>
</tr>
<tr>
<td>Index of refraction</td>
<td>1.85</td>
<td>2.15</td>
<td>1.85</td>
<td>1.82</td>
<td>1.81</td>
<td>1.8</td>
<td>1.94</td>
<td>1.95</td>
<td>1.9</td>
</tr>
<tr>
<td>Light yield (10³ ph/MeV)</td>
<td>41</td>
<td>9</td>
<td>8</td>
<td>30</td>
<td>30</td>
<td>16</td>
<td>12</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Decay time (ns)</td>
<td>230</td>
<td>300/60</td>
<td>60/600</td>
<td>40</td>
<td>40</td>
<td>65</td>
<td>18</td>
<td>30</td>
<td>16</td>
</tr>
<tr>
<td>$I_0$ at 511 keV (ph/ns)</td>
<td>90</td>
<td>21</td>
<td>60</td>
<td>380</td>
<td>380</td>
<td>125</td>
<td>340</td>
<td>290</td>
<td>1,900</td>
</tr>
<tr>
<td>$\Delta E/E$ (%) at 662 keV</td>
<td>6</td>
<td>10</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>15</td>
<td>4.5</td>
<td>3</td>
</tr>
<tr>
<td>Density $\rho$ (g/cm³)</td>
<td>3.67</td>
<td>7.13</td>
<td>6.71</td>
<td>7.35</td>
<td>7.19</td>
<td>6.5</td>
<td>8.34</td>
<td>5.5</td>
<td>5.3</td>
</tr>
<tr>
<td>Effective Z ($Z_{eff}$)</td>
<td>50</td>
<td>73</td>
<td>58</td>
<td>65</td>
<td>64</td>
<td>59</td>
<td>65</td>
<td>65</td>
<td>46</td>
</tr>
<tr>
<td>1/µ at 511 keV (mm)</td>
<td>25.9</td>
<td>11.2</td>
<td>15.0</td>
<td>12.3</td>
<td>12.6</td>
<td>14.3</td>
<td>11.0</td>
<td>21.3</td>
<td>22.3</td>
</tr>
<tr>
<td>PE (%)</td>
<td>18</td>
<td>44</td>
<td>26</td>
<td>34</td>
<td>33</td>
<td>28</td>
<td>32</td>
<td>4.4</td>
<td>14</td>
</tr>
<tr>
<td>PE² (%)</td>
<td>3.2</td>
<td>19</td>
<td>6.8</td>
<td>12</td>
<td>11</td>
<td>7.4</td>
<td>10</td>
<td>0.20</td>
<td>1.9</td>
</tr>
<tr>
<td>Hygroscopic</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Magnetic susceptibility</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*NaI* thallium-doped sodium iodide (NaI:Tl), *BGO* bismuth germanate (Bi₄Ge₃O₁₂), *GSO* cerium-doped gadolinium orthosilicate (Gd₂SiO₅:Ce), *LSO* cerium-doped lutetium orthosilicate (Lu₂SiO₅:Ce), *LYSO* cerium-doped lutetium-yttrium oxyorthosilicate (Lu₁.₉Y₀.₁SiO₅:Ce), *LGSO* cerium-doped lutetium-gadolinium oxyorthosilicate (Lu₀.₄Gd₁.₆SiO₅:Ce), *LuAP* cerium-doped lutetium-aluminum perovskite (LuAlO₃:Ce), *YAP* cerium-doped yttrium-aluminum perovskite (YAlO₃:Ce), *LaBr₃* cerium-doped lanthanum bromide (LaBr₃:Ce)

¹ Photoelectric absorption probability (or photofraction) at 511 keV: \( PE = 100 \times \sigma_p/(\sigma_p + \sigma_c) \)

² Coincident photoelectric absorption probability
3.1 Scintillators

This results in a difference in light output between a full energy peak from the photoelectric effect and a full energy peak from multiple lower energy interactions due to Compton scattering, thus broadening the energy spectrum. Another disadvantage is the presence of a naturally long-lived lutetium isotope ($^{176}$Lu) with 2.6% abundance and a half-life of $4 \times 10^{10}$ years, undergoing $\beta^-$-decay. From the abundance, half-life, density and atomic mass one can easily calculate that this isotope accounts for a background singles count rate of 280 counts per second in 1 cm$^3$ LSO. Since PET scanners are operated in coincidence mode, the majority of these events are automatically filtered out. Still, the number of random coincidences will be higher. For clinical scans the presence of this isotope has negligible impact. However, it may have an impact on dedicated small animal PET in research studies with low count rates [13]. Recently, it was found that the scintillation properties of LSO could significantly be improved by co-doping the crystal with Ca$^{2+}$. A scintillation output of 38,800 photons/MeV was achieved, while the scintillation decay time was as short as 31 ns [27], thus making the crystal even more attractive for (TOF-)PET.

Lutetium aluminum perovskite (LuAP) has a high detection efficiency (attenuation length of 11 mm), high photofraction (32%), very short decay time (18 ns), short rise time (0.6 ns, see [26]), but relatively low light yield (12,000 photons/MeV). Due to its favorable properties, there has been a great deal of interest in developing practical scintillators from this material. Useful crystals were, however, limited to thicknesses less than a centimeter because of strong self-absorption of the scintillation light [28, 29]. Like LSO, LuAP contains the natural background of the $^{176}$Lu isotope.

Lanthanum bromide (LaBr$_3$:Ce) is a relatively new scintillator [30]. It has very high light yield (60,000 photons/MeV), very short decay time (16 ns) and a short rise time (varying between 0.2 and 0.9 ns, see [26]), and is therefore well-suited for TOF-PET. It has excellent energy resolution (3% FWHM at 662 keV), enabling efficient rejection of Compton-scattered events within the patient. The very good energy resolution follows from the high light yield, but also from the very small non-proportionality of the light yield with the absorbed energy [25], such that a small difference in light output exists between a full energy peak from the photoelectric effect and a full energy peak from multiple lower energy interactions during Compton scattering. The detection efficiency (attenuation length of 22.3 mm) and photofraction (14%) are, however, inferior compared to the other scintillation crystals. This means that thick scintillation crystals are required in order to obtain sufficient stopping power. The larger crystal dimension and the low photofraction both lead to an increased fraction of events for which the gamma photons undergo multiple scattering, deteriorating the obtainable spatial resolution. The larger crystal dimension further enhances the degradation from the parallax effect, if no information about DOI is provided (see section 2.2.3).
LaBr$_3$:Ce is hygroscopic and requires hermetic sealing.

### 3.2 Photodetectors

A photodetector is required to convert the weak light output of a scintillation pulse into a detectable electrical signal. Photomultiplier tubes and solid-state photodetectors are the two main groups of devices for detecting low light levels. Both groups of devices work by transferring the photon energy to an electron by a collision. Two processes can be distinguished. During a photoelectric effect, an electron is liberated when a photon impinges on the surface of a material. The photon energy $E_{ph}$ should be higher than the photoelectric workfunction $\phi$, in order for this process to happen. The excess photon energy is transferred to the kinetic energy of the liberated electron $E_{kin}$.

$$E_{kin} = E_{ph} - \phi$$ (3.1)

The workfunction thus defines the low-energy limit of the light spectrum that can be detected. Standard bialkali photocathodes in photomultiplier tubes have a high-wavelength threshold at 630 nm (red light) [31]. The second process requires less energy. In a semiconductor an electron can be lifted from the valence to the conduction band. When an electric field is applied, as in a silicon photodiode, the electron can hardly recombine with holes and it is possible to collect and detect the electron. Because of the low energy requirement, such a photodetector can be very efficient. Photodetectors usually multiply the photoelectrons produced by the incident light. This produces a large electrical current even from a single photoelectron, making such photodetectors sensitive to a single incident photon.

Characteristics of various photodetectors are given in Table 3.2.

#### 3.2.1 Photomultiplier tubes

Photomultiplier tubes (PMTs) are extremely sensitive photodetectors. They combine high gain, stability and low noise and are the standard photodetectors used for scintillation detectors. A schematic view of a PMT is shown in Fig. 3.1. PMTs consist of a light transmitting window, a photocathode, a series of electrodes (dynodes) and an anode, all housed in a glass envelope with high vacuum inside. Photons incident on the photocathode liberate photoelectrons by the photoelectric effect into the vacuum. The photoelectrons are accelerated towards the first dynode such that they arrive at much higher energy. The impact of these photoelectrons liberates secondary low-energy electrons which in turn are accelerated towards the second dynode. The repeated structure results in a cascade of electrons which is finally collected by the anode, where a sharp current pulse is produced.
3.2 Photodetectors

Figure 3.1: Construction of a photomultiplier tube. From [32].

The main characteristic of the PMT is its quantum efficiency (QE). This is the probability that a photoelectron is liberated from the photocathode by an incident photon. The QE is a strong function of the wavelength of the incident light and depends on the transmitting window and photocathode properties. PMTs typically show maximum QE values of 20-30 %\(^2\), lower than what can be achieved with solid-state photodetectors.

The transmitting window or faceplate acts as a seal to maintain a vacuum within the PMT. Borosilicate glass is the most commonly used window material. The sensitivity of a PMT in the ultraviolet region is primarily limited by the transmitting window due to absorption inside the glass. Borosilicate glass does not transmit ultraviolet radiation shorter than 300 nm. For this purpose, some PMTs contain UV-glass or quartz that extends the transmittance down to 185 nm and 160 nm, respectively. The refractive index of the transmitting window is typically 1.5 and the window thickness about 1 mm. The refractive index value differs from the index value for scintillators of around 1.9 (Table 3.1), resulting in losses due to optical refraction. Scintillation light undergoes total internal reflection from the window glass as soon as the angle of incidence exceeds the critical angle \(\theta_c\), defined by Snell’s law:

\[
\theta_c = \sin^{-1} \frac{n_w}{n_s}
\]

(3.2)

where \(n_w\) and \(n_s\) are the refractive indices of the window material and scintillator, respectively. The window is thus only transparent for light entering a cone of aperture \(2\theta_c\).

\(^2\)Recently, Hamamatsu developed PMTs with so-called Super Bialkali (SBK) and Ultra Bialkali (UBK) photocathodes, which show maximum QE values of 35 % and 43 %, respectively [33].
A photocathode is a semitransparent layer covered at the inner side of the transmitting window from which the primary photoelectrons are liberated by the photoelectric effect. The photocathode primarily determines the light response characteristic of the PMT as a function of wavelength. Most photocathodes are made of semiconductor material with a low workfunction. Bialkali photocathodes are widely used and have a maximum sensitivity at 420 nm.

The dynode system effectively acts as the multiplication stage of the PMT and determines the gain. It is a low noise amplification, whereby the noise is only introduced by the stochastic character of the emission of secondary electrons [31]. The gain is determined by the number of dynodes and the interstage voltages of the dynodes and typically varies between $10^6$-$10^7$. The dynodes are carefully arranged, such that optimal focusing is achieved at each element. Often, an additional (last) dynode signal is available from the PMT. This signal is directly sensed from the (last) dynode and occurs because the sudden liberation of many secondary electrons from the dynode results in a potential variation. Its amplitude is comparable to that of the anode.

The anode collects the secondary electrons and forms a detectable output pulse. Adequate design is necessary to prevent space charge effects.

The time response of the PMT is primarily determined by the transit time required for the photoelectrons to reach the anode after being emitted from the photocathode and multiplied. The fluctuation on this transit time of each photoelectron is called the transit time spread (TTS). The time response mainly depends on the dynode type and the supply voltage. Increasing the supply voltage improves the electron transit speed and shortens the transit time and TTS. Transit time and TTS both improve in inverse proportion to the square root of the supply voltage [32]. Metal channel type dynodes have a special structure for optimal timing, consisting of extremely thin dynodes that are precisely stacked in close proximity to ensure short electron path lengths. For these dynodes typical values for the anode pulse rise and fall time are 0.65-1.5 ns and 1-3 ns, respectively. The transit time and TTS are 4.7-8.8 ns and 0.4 ns, respectively [32]. Another dynode type which exhibits the best timing properties among currently available dynode types is the microchannel plate (MCP). It consists of a compact array of micrometer sized glass capillaries (microchannels) bundled in parallel. Each channel acts as an independent electron multiplier, whereby the inner surface acts as the secondary electron emitter. A TTS of 25 ps is possible, with rise and decay times of 150 and 360 ps, respectively (specified for a Hamamatsu R3809U-50 MCP-PMT, [34]).

A special kind of PMT is a multianode PMT (MAPMT) that collects the amplified electron current on multiple anodes. A MAPMT type with a focusing mesh of metal channel dynodes is shown in Fig. 3.2. The electron multiplication process in this dynode system has minimal spatial spread, such that the MAPMT is position sensitive. The channels of the MAPMT effectively act as independent PMTs.
3.2 Photodetectors

Figure 3.2: Dynode structure of a metal channel dynode type MAPMT. Electron amplification is illustrated. From [32].

but with minimal dead space in between them. This allows fine sampling of the spatial distribution of the scintillation light from a crystal. The MAPMT also provides a (last) dynode signal which is common for all channels. This signal is extremely useful, since it contains the total amount of detected light, and thus directly provides information about the energy deposited in the scintillation crystal. This can thus be used for energy discrimination and/or serve as a timing signal. Due to the segmented character of the anode system, the anode signals would have to be summed in order to get energy information, while a complicated electronic design would be necessary to obtain a timing signal from a combination of the anode signals if the dynode signal was not present. Position sensitive multianode versions of the MCP-PMT are also available.

Drawbacks of PMTs compared to solid-state photodetectors are their relatively low QE of 20-30%, their large size and their sensitivity to magnetic fields. Because they are bulky, close packing of PMTs in a scanner is difficult. The sensitivity to magnetic fields limits their application in combined PET-MRI systems. Advantages are their high gain, such that additional electronic amplification is not necessary, and their low dark current.

3.2.2 Solid-state photodetectors

Solid-state photodetectors have the advantage that they are compact and essentially transparent to 511 keV gamma rays, allowing close packing and novel crystal read-out designs. Because they can be produced in fully automatic processes, they have the potential for low cost. They are also insensitive to magnetic fields, thus
Table 3.2: Characteristics of photodetectors for PET (Data from [10])

<table>
<thead>
<tr>
<th></th>
<th>PMT</th>
<th>APD</th>
<th>SiPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active area (mm²)</td>
<td>1-2,000 cm²</td>
<td>1-100 mm²</td>
<td>1-10 mm²</td>
</tr>
<tr>
<td>Gain</td>
<td>10⁵-10⁷</td>
<td>10²</td>
<td>10⁵-10⁶</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>10⁶</td>
<td>10⁴</td>
<td>10³/mm²</td>
</tr>
<tr>
<td>Excess noise factor</td>
<td>0.1-0.2</td>
<td>&gt;2</td>
<td>1.1-1.2</td>
</tr>
<tr>
<td>Rise time (ns)</td>
<td>&lt;1</td>
<td>2-3</td>
<td>∼1</td>
</tr>
<tr>
<td>Time jitter (ns FWHM)</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.1</td>
</tr>
<tr>
<td>Dark current/countrate</td>
<td>&lt;0.1 nA/cm²</td>
<td>1-10 nA/mm²</td>
<td>0.1-1 MHz/mm²</td>
</tr>
<tr>
<td>Capacitance (pF/mm²)</td>
<td>8.6±0.4</td>
<td>2-10</td>
<td>&gt;30</td>
</tr>
<tr>
<td>QE @ 420 nm (%)</td>
<td>25 %ᵃ</td>
<td>60-80 %</td>
<td>&lt;40 %ᵇ</td>
</tr>
<tr>
<td>After-pulsing</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bias voltage (V)</td>
<td>1,000-2,000</td>
<td>~100-1,500</td>
<td>~50</td>
</tr>
<tr>
<td>Power consumption</td>
<td>100 mW/ch</td>
<td>10 μW/mm²</td>
<td>&lt;50 μW/mm²</td>
</tr>
<tr>
<td>Temperature coefficient</td>
<td>&lt;1 %/K</td>
<td>2-3 %/K</td>
<td>3-5 %/K</td>
</tr>
<tr>
<td>Bias coefficient</td>
<td>&lt;1 %/V</td>
<td>&lt;10 %/V</td>
<td>∼100 %/V</td>
</tr>
<tr>
<td>Magnetic susceptibility</td>
<td>Very high (mT)</td>
<td>No (measured up to 9.4T)</td>
<td>No (measured up to 15T)</td>
</tr>
</tbody>
</table>

ᵃ The recently introduced Super Bialkali (SBK) and Ultra Bialkali (UBK) PMTs from Hamamatsu have maximum QE values of 35 % and 43 %, respectively [33].
ᵇ This is the Photon Detection Efficiency: \( PDE = QE \cdot \varepsilon \cdot P_{br} \), where \( \varepsilon \) is the geometric fill factor and \( P_{br} \) the probability that an incoming photon triggers a breakdown, see section 3.2.2.

allowing PET-MRI integrated systems. A low bias voltage is required to operate these devices. Because of the thin active layer, the charge moves over small distances, such that they can exhibit good timing performance. Since the photon detection is not limited by the need for the photoelectrons to escape from the surface, like in a photocathode, the maximum QE of 80 % is much higher compared to PMTs. It is sufficient to lift electrons from the valence to the conduction band. The maximum QE also spans almost the whole range of visible light [35].

Photodiodes

Conventional photodiodes have no internal gain, but simply collect the electron-hole pairs produced by the incident light. This results in small signal amplitudes when operated in pulse-mode, whereby electronic noise is a major problem. For scintillators operated in integrating detection mode, like in X-ray CT scanners, the cumulative effect of many scintillation events at high rates overrides the inherent noise of the photodiodes [18]. Due to their high electronic noise, these photosensors have limited use in PET, which requires pulse mode operation.
Avalanche photodiodes (APDs) do provide internal gain. These devices commonly have a reach-through configuration, consisting of a thin p$^+$ layer, a wide (>100 μm) depleted drift region (π) and an avalanche region (p and n$^+$) (Fig. 3.3). A reverse bias voltage is applied on these devices. The avalanche region contains high doping concentrations, such that a high internal electric field is created within this region when the reverse bias is applied. Light enters and interacts within the π region, producing electron-hole pairs. The electric field drifts the electrons towards the avalanche region, where the high electric field accelerates the electrons towards energies capable to ionize Si atoms. This ionization creates secondary electrons that in turn can ionize more Si atoms. This effectively acts as the internal gain process in APDs.

Gains between 50 and 200 are typical, which are much lower compared to the typical gains of $10^6$ - $10^7$ for PMTs. Therefore, the internal electronic noise of the devices is still relatively high compared to the signal amplitude. Moreover, the multiplication process in APDs itself has a higher inherent noise contribution compared to PMTs, which is parametrized by the excess statistical noise factor $F$ [36]. APDs thus not only have a lower gain, but also a higher statistical variation on this gain. The actual gain depends on the applied reverse voltage and temperature. It varies exponentially with reverse voltage, such that the relative change of gain with voltage is a linear function of the gain. At a gain of 100 the relative change of the gain with voltage is $\sim 10\% / V$, while the relative change with temperature
is typically ~2-3 %/K [10]. For stable operation at a constant gain, it is therefore necessary to control the reverse voltage and temperature. Higher gains up to 1,000 are possible, but at the cost of a higher excess multiplication noise and a higher variation of the gain with reverse voltage and temperature. APDs are therefore normally operated at moderate internal gains. Because of the low internal gain, low-noise and fast front-end electronics are required to achieve additional signal amplification.

In addition to excess multiplication noise, a relatively high dark current is present in APDs. The timing performance is further inferior to PMTs, due to the relatively low gain. However, compared to PMTs, APDs have a much higher QE of typically 60-80 % (see Table 3.2). They also have the advantages of compactness and insensitivity to magnetic fields. Although they have a higher inherent noise than PMTs, energy resolutions of ~11 % FWHM were obtained for the 511 keV full energy peak for LYSO crystals coupled to APDs [37], which is the expected energy resolution for LYSO. The system performance of PET is thus not necessarily limited by the excess multiplication noise of APDs.

APDs typically have a maximum size limited to about 1 cm$^2$. For large area readout, arrays of APD pixels exist [38]. Large-area position sensitive APDs (PSAPDs) with a reduced number of electronic channels are also available [39–41]. These PSAPDs contain four corner contacts placed on the backside, covered by a high resistivity layer. From the signals of the four corner contacts the position of the impinging light can be calculated. Although the number of channels is reduced, the noise of these PSAPDs is generally worse than that of standard APDs [42].

**Silicon photomultipliers**

Silicon photomultipliers (SiPMs) consist of a densely packed matrix of small (20$\times$20 - 100$\times$100 $\mu$m$^2$) APD cells. The APD cells are all reversely biased above avalanche breakdown (Geiger mode operation) and connected in parallel. In this mode, the internal electric field becomes so high that a very high gain ($10^5$-$10^6$) is obtained. Both electrons and holes are now involved in the multiplication process and this multiplication is self-sustaining. Quenching resistors are present to stop the avalanche after a breakdown and to recharge the cell. The avalanche breakdown and subsequent quenching results in a standardized output signal for a single cell, independent of the energy and number of the incoming photons. Energy information is thus essentially lost and a single cell thus functions in digital/switching mode. Because the APD cells are all connected in parallel, the output of the SiPM as a whole is the summed output of the individual cells. This makes the SiPM an analog device, since a wide dynamic range of photons can still be sensed.

Because of the high gain, the device is sensitive to single photons. The energy resolution is even superior to that of PMTs [43], and at low light levels the number
of detected photons can precisely be determined from the detected charge or pulse height (see Fig. 6.1). This proves that there is little gain variation among the cells and that the excess noise factor is very small, due to the standardized output signal following an avalanche breakdown.

The signal pulse shape is quite short, as will be shown in section 6.3 on the pulse shape of a single photoelectron. The signal decay time $\tau$ is the same as the cell recovery time and depends on the cell capacitance $C$ and the quenching resistor $R$: $\tau \sim RC$ (as well as on the shaping time of the front-end amplifier, obviously). The devices show an excellent internal single photoelectron timing resolution of \(\sim 100\) ps RMS (see section 6.3). Combined with the high gain and fast response, this makes the timing performance at least as good as that of PMTs, and a coincidence resolving time (CRT) of 100 ps FWHM was obtained using LaBr$_3$ scintillators (see section 8.3.1).

Between the microcells some space is needed for optical separation and for the individual resistors. This limits the area of the sensitive region of the SiPM. Although solid-state photodetectors have a superior QE compared to PMTs (see Table 3.2), this geometric effect lowers the maximum achievable detection efficiency for SiPMs. The photon detection efficiency (PDE) is defined by the QE of the active area, the geometric fill factor $\varepsilon$ (ratio of the sensitive area), and the probability that an incoming photon triggers a breakdown $P_{br}$:

$$PDE = QE \cdot \varepsilon \cdot P_{br}$$

(3.3)

The microcell size thus determines the geometric fill factor. A large microcell size implies a high PDE, but a low dynamic range since there are less cells per unit area. This size thus needs to be optimized for the particular application involved.

Because of the finite number of cells, the response of the SiPM is non-linear. Saturation in the output occurs when the number of photoelectrons becomes comparable to the number of cells. The number of detected photons $N_{\text{detected}}$ during a scintillation pulse can be calculated from the number of cells $N_{\text{cells}}$, number of incoming photons $N_{\text{photons}}$ and PDE as follows:

$$N_{\text{detected}} = N_{\text{cells}} \left(1 - e^{-\frac{PDE \cdot N_{\text{photons}}}{N_{\text{cells}}}} \right)$$

(3.4)

This equation is not exact, since it ignores the finite recovery time of a microcell and thus assumes that a microcell can only fire once during a scintillation event.

Apart from their non-linear response and reduced PDE, SiPMs have a quite high dark count rate (0.1-1 MHz/mm$^2$, Table 3.2) due to thermal generation of free carriers in each microcell. This is not necessarily a bottleneck for PET: a simple low energy threshold filters most of these dark counts, since their energy content is at most equal to a few microcell discharges. SiPMs further exhibit after-pulsing from carrier trapping and delayed release, as well as from optical crosstalk between
neighboring cells. This artificially increases the energy content of the scintillation pulses and also effectively increases the excess multiplication noise of the SiPM sensor. Both the dark count rate and after-pulsing increase with the gain of the device. The gain strongly depends on the reverse bias voltage and temperature. The gain $G$ is determined by the bias voltage $V_b$ above the breakdown voltage $V_{br}$ (also called overvoltage, typically varying between 1-3 V) and the cell capacitance $C$

$$G = (V_b - V_{br}) \cdot C/q$$

where $q$ is the electron charge. The breakdown voltage varies strongly with temperature on the order of 50 mV/K [31]. Since the gain depends on the overvoltage, both the bias voltage and temperature need to be stable for constant gain. The PDE strongly increases with the gain through the dependence of $P_{br}$ on overvoltage [43]. However, the overvoltage can not be set to very high values, since the SiPM operation will be hampered by spontaneous breakdowns and an increasing dark count rate and afterpulsing.

Because of the high gain, a front-end amplifier is in principle not necessary, and a simple 50 Ohm load can be used to produce signals of several millivolts for single photons [43]. In practice, additional front-end amplifiers with a typical gain of around 10 are used to improve the SNR and detection efficiency of the signals.

An interesting new development is the digital SiPM (dSiPM) from Philips Research [44, 45]. In this sensor, each detected photon is directly converted to a digital signal for each microcell. In addition, the complete trigger logic and time-to-digital converter are integrated onto the sensor. The output of the sensor consists of the number of detected photons and the corresponding time stamp. Since the detected photons are directly digitized, the analog signal generation stage has essentially been removed, such that the detector performance is much less affected by electronic noise. Moreover, since the output of the sensor does not depend on the gain of the individual microcell anymore, the output variation with temperature is an order of magnitude less compared to conventional analog SiPMs. Further, an on-chip saturation correction can be performed using Eq. 3.4. Due to the minimal electronic noise, an excellent CRT of 153 ps FWHM was obtained for LYSO crystals coupled to these dSiPMs [44].

### 3.3 Scintillation detector designs

The early PET systems consisted of scintillators coupled one-to-one to individual PMTs. The spatial resolution was determined by the scintillation crystal size. As the crystal size was reduced to improve the spatial resolution, the one-to-one coupling scheme could not be retained. The number of PMTs and electronic
3.3 Scintillation detector designs

Figure 3.4: Early PET detector designs. (a) Block detector consisting of crystal segments, separated by partial saw cuts. The crystal elements are read out by 4 PMTs. (b) Gamma camera consisting of a continuous crystal, read out by a hexagonal array of PMTs through a light guide.

channels had to be kept as low as possible for low cost, while the PMT size could not be made as small as possible. In order to continue to improve the spatial resolution, it was thus necessary to determine the gamma interaction position with an accuracy that was a fraction of the PMT size. This necessarily required that the scintillation light was shared over multiple PMTs, whereby the position was calculated based on the detected light level of each PMT.

The block detector allows the use of a small number of PMTs, reading out an array of small crystal elements [46]. Typically, a block detector consists of four PMTs in a rectangular pattern, reading out the crystal elements. The crystal elements are either individual crystals or crystal segments from a block of scintillator, separated by partial saw cuts, see Fig. 3.4(a). The surfaces of each individual crystal element are covered with reflective material to channel the light with low spatial spread towards the PMT and minimize the optical cross-talk between the crystal elements. The depth of the saw cuts is such, that a well-defined light response function (LRF) over the PMTs is produced, and a simple linear positioning scheme based on the ratio of the detected light levels can be used to identify the
crystal segment in which an interaction took place:

\[ X = \frac{(PMT_A + PMT_B) - (PMT_C + PMT_D)}{PMT_A + PMT_B + PMT_C + PMT_D} \]  

(3.6)

\[ Y = \frac{(PMT_A + PMT_C) - (PMT_B + PMT_D)}{PMT_A + PMT_B + PMT_C + PMT_D} \]  

(3.7)

where \( PMT_A, PMT_B \), and so forth are the detected light levels from the respective PMTs. The intrinsic spatial resolution is thus defined by the crystal element size, instead of the PMT size. This allows a low number of PMTs and thus low cost, while providing high spatial resolution. Because the light is channeled towards the PMTs with low spatial spread, thick scintillation crystals can be used for high sensitivity while maintaining good spatial resolution.

The other detector design consists of a large flat unsegmented crystal plane, read out by an array of PMTs, the Anger camera or gamma camera, see Fig. 3.4(b). This design was invented in 1958 [47] and used for planar imaging (i.e. 2D-imaging) of gamma photon emitting radioisotopes, scintigraphy. In planar imaging and SPECT the gamma camera contains collimation holes to define the direction of the impinging gamma photons. The gamma camera has also been used for PET imaging, but of course without the presence of the collimator\(^3\). Since the scintillation light is not channeled to the PMTs, it is spread out over a larger number of PMTs. This requires a scintillator with a high light output, in order to minimize the statistical spread associated with photon counting. The gamma camera was developed for the NaI:Tl scintillator (which has a high light output, see section 3.1) and 140 keV gamma-rays (\(^{99m}\text{Tc}\) radioisotope). For 511 keV annihilation gamma-rays, NaI:Tl has a low linear attenuation coefficient and low photoelectric absorption probability, see section 3.1.

The segmented or unsegmented (continuous) nature of the crystals distinguishes these two designs and remains the most basic feature of present-day scintillation detector designs for PET.

### 3.3.1 Segmented vs. continuous designs

As mentioned, the segmented crystal design channels the scintillation light towards the photosensor with minimal spatial spread. A well-defined light response function (LRF) is generated on the front face of the photosensor, such that a small number of photosensors and a simple (linear) positioning scheme can be used. The spatial resolution is defined by the crystal segment size. Since the light is channeled towards the photosensor, this spatial resolution is constant over the DOI-range of the crystal. The crystal segments can thus originate from a thick (30 mm) block.

\(^3\)In PET, a collimator is not necessary since the direction of the gamma photons is known from the coincident detection nature, see section 2.2.
of scintillator for high stopping power, while maintaining good spatial resolution. Nearly all commercial scanners employ the segmented crystal design.

However, there are a number of drawbacks with this design compared to the continuous crystal design:

- As one aims to improve the spatial resolution, the cross-sectional area of the crystal segments needs to become smaller. However, the costs increase dramatically due to the increase in complexity to manufacture smaller crystal segments and due to the larger number.

- Because of the finite thickness of the reflective material between the crystal segments, a volume fraction of the segmented crystal contains non-scintillating material, i.e. dead space. This reduces the detection efficiency of the segmented crystal.

- The cross-sectional area of the crystal segments needs to be small for good position resolution, while the length should be large for good detection efficiency. For long and narrow crystal segments the scintillation photons undergo multiple reflections before reaching the photosensor. Since crystal surfaces are never perfectly reflective, a fraction of the scintillation light will be lost. The light collection efficiency for segmented crystals is thus generally lower compared to continuous crystals. This means that the energy and timing resolution of continuous crystals is generally better compared to segmented crystals, since both parameters depend on the number of detected scintillation photons (see section 3.1).

- Continuous crystals inherently provide information about the DOI, while complicated and expensive detector modifications are necessary to enable DOI detection for segmented crystals. This last point will further be discussed in section 3.3.3.

For continuous scintillators, the linear positioning scheme in Eqs. 3.6 and 3.7 can in principle be used, however it leads to strong artifacts near the crystal borders. More complex statistical methods can be used for more accurate position estimation, like maximum likelihood estimation (MLE), neural networks or nearest neighbor estimation. Spatial resolutions below 2 mm FWHM can be reached with these methods [37, 48–50], which is better than for segmented scintillators with a typical crystal segment size of 4 mm (e.g., the Philips Gemini TOF PET/CT scanner employs $4 \times 4 \times 22 \text{ mm}^3$ LSO crystals [51]). These estimation methods all work by finely sampling the LRF from the continuous crystal using a photosensor array.

A major drawback of continuous scintillators with respect to segmented scintillators is the trade-off between efficiency and obtainable spatial resolution of the
detector. Since the scintillation light is not channeled with a low spatial spread towards the photosensor, a thicker scintillation crystal for higher sensitivity implies a larger light spread and thus a worse spatial resolution. This follows from the statistical fluctuations in the signal generation process. The following analysis is taken from [52]. Consider a continuous scintillation crystal, read out by a 1D array of photosensors and illuminated by a beam of gamma photons, impinging perpendicularly at the crystal surface (Fig. 3.5). Indicate the mean number of photoelectrons generated in the $i^{th}$ photosensor for a beam at position $x$ by $f_i(x)$. Assume that the fluctuations in the signal generation process are mainly introduced by the statistics of scintillation photon generation in the crystal and photoelectron generation at the photosensors, which are described by Poisson processes. The probability for generating $\{m_1, m_2, ..., m_n\}$ photoelectrons in the corresponding photosensors for a beam at position $x$ is then given by Poisson statistics:

$$P[m_1, m_2, ..., m_n|x] = \prod_{i=1}^{n} f_i(x)^{m_i} e^{-f_i(x)} m_i!$$

(3.8)
3.3 Scintillation detector designs

The other way around, given the photoelectron distribution \( \{m_1, m_2, ..., m_n\} \), the probability that this distribution was generated by a beam at position \( x \) is given by the same equation. According to Maximum Likelihood Estimation (MLE), the best estimate for the beam position \( \hat{x} \), given a certain distribution \( \{m_1, m_2, ..., m_n\} \), is the one for which this probability is maximum:

\[
\hat{x} = \arg_x \max P[m_1, m_2, ..., m_n|x]
\]

(3.9)

For mathematical convenience, instead of \( P \), the logarithm of \( P \) (\( \ln P \)) can be maximized\(^4\). The maximum can be found by calculating the root of the first derivative of \( \ln P \) with respect to \( x \):

\[
\frac{\partial}{\partial x} \ln P[m_1, m_2, ..., m_n|x] = \sum_{i=1}^{n} \frac{m_i}{f_i(x)} \frac{\partial f_i(x)}{\partial x} - \sum_{i=1}^{n} \frac{\partial f_i(x)}{\partial x} = 0
\]

(3.10)

The Cramér-Rao lower bound \( \sigma^2_{lb} \) sets a lower bound on the variance of an unbiased estimator. This means that, given a certain statistical model, the best obtainable resolution for estimating a model’s parameter is given by the Cramér-Rao lower bound. This is only valid for unbiased estimators, i.e. the expected value of the estimator should be the same as the true value of the parameter that is being estimated. In the current example, it can be calculated as follows:

\[
\sigma^2_{lb} = \frac{1}{I(x)}
\]

(3.11)

where the Fisher information \( I(x) \) is defined by

\[
I(x) = -E \left[ \frac{\partial^2}{\partial x^2} \ln P[m_1, m_2, ..., m_n|x] \right]
\]

(3.12)

\[
= \sum_{i=1}^{n} \frac{1}{f_i(x)} \left( \frac{\partial f_i(x)}{\partial x} \right)^2
\]

(3.13)

Here, \( E \) denotes the expected value, such that \( E[m_i|x] = f_i(x) \). Eqs. 3.11 - 3.13 say that the best obtainable resolution for estimating the beam position \( x_a \) is primarily determined by the slopes \( \partial f_i(x)/\partial x \) at \( x_a \). A larger scintillation light spread induces a more uniform light distribution at the photosensor plane, thus decreasing the slopes \( \partial f_i(x)/\partial x \) and worsening the best obtainable spatial resolution. From this, it follows that by increasing the thickness of monolithic scintillation crystals, the obtainable spatial resolution degrades due to an increasing light spread. In the same way, the obtainable spatial resolution for events close to the photosensor array is better than for events more distant from the photosensor array. Experimental studies of the positioning performance of monolithic scintillation crystals with varying thickness at various excitation depths are presented in chapter 5.

\(^4\)This is justified, since \( \ln P \) is a monotonically increasing function of \( P \), meaning that \( \ln P \) increases if \( P \) increases and decreases if \( P \) decreases. The maximum of \( \ln P \) is thus located at the same \( x \) as the maximum of \( P \).
Chapter 3

Figure 3.6: Widening of the photon distribution function LRF due to the finite pixel size. Upper figure: The LRF is evaluated for photosensor $i$ at fixed location $x' = x'_i$ by varying the beam position $x$ over the crystal surface. Lower figure: The LRF is indicated by the solid line and is given by Eq. 3.15, whereby $\sigma = 2/2.355$ mm and $x' = x'_i$. The dashed lines are plots of the normalized pixel response $f_i(x)/\int_{-\infty}^{+\infty} f_i(x) dx$, whereby $f_i(x)$ is given by Eq. 3.16, for pixel widths $d = \{1, 2, 3, 4, 5\}$ mm. The beam coordinate axis is centered at the photosensor location ($x = 0$ for $x' = x'_i$).

It is explicitly noted here that the distribution $\{f_1(x), f_2(x), ..., f_n(x)\}$ is a sampled representation of the mean light distribution function LRF at the photosensor plane for a beam at position $x$. Each photosensor $i$ has a certain size and the mean number of generated photoelectrons $f_i(x)$ depends on the LRF distribution over the photosensor. Mathematically, this involves an integration of LRF over the photosensor surface [53]:

$$f_i(x) = \int_{x'_i-d/2}^{x'_i+d/2} N \cdot QE \cdot LRF(x, x') dx'$$

(3.14)
where \( N \) denotes the total number of scintillation photons incident on the photosensors, \( QE \) the quantum efficiency and \( x'_i \) the location of photosensor \( i \) of width \( d \).

The spatial integration of \( LRF \) over the photosensor surface widens the resulting \( f_i(x) \) distribution. This can be illustrated as follows (see Fig. 3.6). Assume that the \( LRF \) is a Gaussian distribution function:

\[
LRF(x, x') = \frac{1}{\sqrt{2\pi}\sigma^2} e^{-\frac{(x-x')^2}{2\sigma^2}}
\]  

(3.15)

The FWHM width of a Gaussian distribution function is equal to \( 2\sqrt{2\ln 2} \cdot \sigma \approx 2.355 \cdot \sigma \). Using eq. 3.14, \( f_i(x) \) can be calculated as follows:

\[
f_i(x) = \frac{N \cdot QE}{2} \left( \text{erf} \left[ \frac{x - (x'_i - d/2)}{\sqrt{2}\sigma} \right] - \text{erf} \left[ \frac{x - (x'_i + d/2)}{\sqrt{2}\sigma} \right] \right)
\]

(3.16)

where \( \text{erf} \) is the Gauss error function. The FWHM width of \( f_i(x) \) in Eq. 3.16 is equal to \( \sqrt{d^2 + (2.355 \cdot \sigma)^2} \). Eq. 3.16 is plotted in Fig. 3.6 for the pixel widths \( d = \{1, 2, 3, 4, 5\} \) mm and LRF width of \( 2.355 \cdot \sigma = 2 \) mm FWHM. It is apparent that the finite pixel size convolves the light distribution function \( LRF \), resulting in a broadened pixel response \( f_i(x) \) in case the pixel size is larger than the width of the \( LRF \). This broadening effect decreases the slope \( \partial f_i(x)/\partial x \) along \( x \) and, in conjunction with Eqs. 3.11 - 3.13, deteriorates the obtainable spatial resolution. This means that the pixel width \( d \) is a primary factor in determining the obtainable spatial resolution of the monolithic scintillation detector.

More generally, the crystal readout geometry (i.e. size, number and location of the photosensors on the crystal) determines the effect of the statistics in scintillation photon generation, transport and collection on the detector spatial resolution. E.g., with the help of Eqs. 3.11 - 3.13, one can see that the obtainable spatial resolution will be improved when two photosensor arrays are placed on opposing crystal sides, as compared to one array on one crystal side. Since the distance between gamma interactions and a photosensor array is at most half the crystal length for double sided readout, the scintillation light is less spread out on one of the photosensor planes, improving the spatial resolution according to Eqs. 3.11 - 3.13.

The actual spatial resolution is worse than indicated by \( \sigma_{lb} \) in Eqs. 3.11 - 3.13 due to additional degrading factors besides statistics in scintillation photon collection, like position blurring introduced by multiple Compton scattering (see next section) and noise sources introduced by the photosensor (like excess multiplication noise) and associated electronics.

\(^{5}\)It should be noted that in this example no attempt is made to present a realistic model of the \( LRF \). It is only wished to illustrate the broadening effect induced by the finite pixel size. An alternative \( LRF \) function could as well have been chosen for this illustration.
3.3.2 Effect of Compton scattering within the crystal

The obtainable spatial resolution is degraded in both crystal designs by Compton scattering. In Table 3.1, one can find that the probability for a 511 keV gamma ray to undergo photoelectric absorption instead of Compton scatter during its first interaction in the crystal is less than 50% (44% for BGO, 34% for LSO, 14% for LaBr₃).

During Compton scattering, a significant fraction of the energy is transferred to an electron, producing scintillation photons inside the crystal, while the scattering angle can be large. From relativistic energy and momentum conservation, one can calculate that the energy of the Compton scattered gamma photon \( E' \) depends on the scattering angle \( \theta \), as defined in Fig. 3.7(a), in the following way [53]:

\[
E'(E, \theta) = \frac{E - \frac{E}{m_e c^2} (1 - \cos \theta)}{1 + \frac{E}{m_e c^2} (1 - \cos \theta)}
\]  (3.17)

where \( E \) is the energy of the incoming gamma photon, \( c \) the light speed and \( m_e \) the electron mass (511 keV/c²). For incident annihilation photons (\( E = 511 \) keV = \( m_e c^2 \)), this reduces to

\[
E'(\theta) = \frac{E}{2 - \cos \theta}
\]  (3.18)

The energy transferred to the electron is equal to \( E - E' \). For backscatter (\( \theta = 180^\circ \)), the transferred energy obtains a maximum of \( E - E' = 2E/3 \approx 341 \) keV. No energy is transferred at \( \theta = 0^\circ \). \( E - E' \) is plotted in Fig. 3.7(b).

The differential cross section for Compton scattering is given by the Klein-Nishina formula:

\[
\frac{d\sigma}{d\Omega} (E, \theta) = \frac{r_e^2 E'^2}{2 E^2} \left( \frac{E'}{E} + \frac{E}{E'} - 1 + \cos^2 \theta \right)
\]  (3.19)

where \( r_e \) is the classical electron radius (2.82 \( \cdot 10^{-15} \) m) and \( E' \) is defined according to Eq. 3.17. Eq. 3.19 gives the angular (\( \theta \)) distribution of the Compton scattered gamma photon per unit solid angle \( \Omega \) (steradian). The true angular distribution (per unit scattering angle \( \theta \)) can be obtained by integrating Eq. 3.19 over the circumference spanned by the azimuthal coordinate \( \varphi \), indicated in Fig. 3.7(a):

\[
\frac{d\sigma}{d\theta} (E, \theta) = \frac{d\sigma}{d\Omega} (E, \theta) \cdot 2\pi \sin \theta
\]  (3.20)

Eqs. 3.19 and 3.20 are plotted for incident 511 keV gamma photons in Figs. 3.7(c) and 3.7(d), respectively. Fig. 3.7(d) shows that the scattering angle distribution is broad, obtaining a maximum at \( \theta \approx 35^\circ \).

The scattered gamma photon can interact at a different location by a photoelectric absorption or a subsequent Compton scatter (thus creating multiple scintillation centers), or leave the crystal without further interaction. The creation of
3.3 Scintillation detector designs

Figure 3.7: (a) Schematic view of Compton scattering. A gamma photon of energy $E_\gamma$ collides with an electron at rest. A new gamma photon of energy $E_{\gamma'}$ emerges at angle $\theta$. (b) Energy $E_\gamma - E_{\gamma'}$ transferred to the electron as a function of $\theta$ for $E_\gamma = 511$ keV. (c) Differential cross section for $E_\gamma = 511$ keV, normalized at $\theta = 0^\circ$. (d) Cross section per unit scattering angle for $E_\gamma = 511$ keV, normalized at $\theta = 34.99^\circ$.

multiple scintillation centers within the same crystal acts as a position blurring effect, because the produced LRF on the photosensor is distorted with respect to the LRF from a single interaction event (see Fig. 3.8). The thicker the crystal, the higher the fraction of events for which the full 511 keV energy was absorbed by multiple interactions. This again acts as a tradeoff between detection efficiency and obtainable spatial resolution. For events with inter-detector Compton scatter-
Figure 3.8: Illustration of LRF broadening due to multiple scintillation centers in the crystals. This causes position blurring in both segmented and continuous crystal designs.

...tering, the energy is shared among different detectors. These events can either be filtered out or properly reconstructed by Compton kinematics, such as in a Compton camera [54]. Compton events for which the full 511 keV energy was not absorbed by the crystal can be filtered out by energy thresholding (as occurs for events that had a Compton interaction within the examined body, section 2.2.3).

3.3.3 Designs for DOI detection

As discussed in section 2.2.3, the parallax effect is one of the most important degrading factors in PET imaging. It shows up for a gamma photon that enters the crystal from an oblique angle, while the detector does not give information about the DOI. Especially for thick crystals it is important to correct for this error, since the DOI spread is large. Enabling DOI detection in PET detectors has been one of the most active fields of research in PET imaging. This section gives an overview of some proposed scintillation detector designs with DOI detection capability.

DOI detection in segmented crystals

Position estimation in segmented crystals is based on identification of the crystal segment in which a gamma interaction took place. Since the scintillation light is channeled towards the photosensor, the LRF essentially does not vary with DOI,
3.3 Scintillation detector designs

(a) Phoswich design  (b) Double-sided readout  (c) Stacked layers with a relative displacement with respect to each other

(d) Layers with reflective optical structure  (e) Multiple photosensors

Figure 3.9: Common designs for DOI detection in segmented crystals

by design. Therefore, for conventional PET detectors with segmented crystals, DOI detection is not possible. Most commercial PET scanners do not offer DOI detection, and often have large detector rings while employing a small transaxial field-of-view (FOV) to reduce the parallax error (see section 2.2.3). Detector modifications are necessary to add DOI detection. Fig. 3.9 shows several segmented crystal designs that enable DOI detection.

The phoswich design is one of the oldest approaches and proposed by many groups (e.g. [55–57]). Stacked scintillators with different decay times are used. The pulse shape of the scintillation signal depends on the particular scintillator in which the interaction took place, and one can measure the pulse shape to identify the scintillator (pulse shape discrimination, PSD). Simply setting different time windows is often sufficient to discriminate the crystals. Drawbacks are the costs

6Although there may be variations in detected energy as a function of DOI, due to variations in light absorption.
of fabrication to assemble these crystals and possible limitations to the obtainable timing resolution, since the decay times of the scintillators need to vary sufficiently to allow for crystal discrimination and can thus necessarily not be optimized for the fastest timing.

Another approach is to attach photodetectors at both ends of the crystal segments. DOI can be determined by the ratio of the detected light at the photodetectors. For this readout design, at least one of the photodetectors should be transparent to gamma photons to avoid gamma absorption. In [58], SiPMs are used at both ends of a $1.8 \times 2 \times 20 \text{ mm}^3$ LYSO crystal, achieving a DOI resolution of $4.5 \text{ mm FWHM}$. In [59], a DOI resolution of $2 \text{ mm FWHM}$ was achieved for an LSO crystal array with $1 \times 1 \times 20 \text{ mm}^3$ segments, read out by PSAPDs at both ends. Although a good DOI resolution can be obtained by the dual-sided readout, detector costs are increased significantly due to the larger number of photosensors and readout channels. Since the detected light output per photosensor is less, the timing resolution will also be degraded in case only one of the photosensors is used for time pickoff.

Multi-layered crystals with DOI-encoding have also been built. The layers are either stacked with a small offset with respect to each other (Fig. 3.9(c)) or have a special reflector structure (Fig. 3.9(d)). The arrangement of the layers is such, that all crystal segments can be expressed on a 2D position map without overlapping. Only one position-sensitive photosensor is therefore needed to identify the crystal segments in 3D. Drawback of this method are the fabrication costs and difficulties with light collection. Due to the complex optical structure, there will be more optical reflections and associated absorption of the scintillation light, thus leading to a deterioration of the timing and energy resolution, especially for the layers far from the photosensor. In [60], four layers of $1.46\times1.46\times4.5 \text{ mm}^3$ LSO crystal segments were used in a special reflector structure. The energy resolutions of the 1st and 4th layer were 11.6 % and 19.1 %, respectively. The difference in light collection efficiency for the layers also leads to profound transit time differences, thus broadening the time spectrum. In [60], a transit time difference of 150 ps was observed between the 1st and 4th layer. A DOI correction to the timing can be applied to improve the timing resolution [61].

It has been proposed to optically couple neighboring crystal segments [62]. The interface between the crystal segments is such that the amount of light sharing is varied along the DOI-direction. The DOI can be extracted from the ratio of the collected light by each crystal segment. This approach also only requires a single position-sensitive photosensor.

Various layers of thin solid-state photodetectors and crystals can also be used to identify crystal segments in 3D (Fig. 3.9(e)). In [63], $1\times1\times3 \text{ mm}^3$ LSO crystal segments were coupled with their long side to extremely thin ($<300\mu m$) PSAPDs, such that a high packing fraction is achieved. With this approach, the light collec-
tion efficiency is much better compared to the other approaches. However, high costs are associated with the high density of electronic channels and photodetectors.

In conclusion, enabling DOI measurement in segmented crystals is possible, but not trivial. It involves costly detector modifications (e.g. additional photosensors and electronic channels, or complex optical structures), while other detector performance parameters (energy and timing resolution) may degrade due to reduced light collection.

DOI detection in continuous crystals

In continuous crystals the light is not confined to a crystal segment, but spreads out through the crystal volume. Due to this spreading, the minimum obtainable spatial resolution in continuous crystals is degraded (see Eqs. 3.11 - 3.13). The LRF not only varies with the 2D entrance position onto the crystal, but also with the DOI: The LRF is less spread out for photoconversion positions close to the photosensor, compared to positions far from the photosensor (see Figs. 4.11 and 8.7). Especially for thick scintillation crystals, this variation with DOI can lead to systematic errors if the positioning is based on a simple 2D centroid calculation of the LRF. The variation of the LRF with DOI can, however, also be exploited to estimate the 3D photoconversion position (thus including DOI) using more advanced position algorithms. In contrast to segmented crystals, continuous crystals thus inherently provide information about the DOI. The expensive and complex optical modifications of the crystal mentioned in section 3.3.3, which often deteriorate the light collection efficiency, are therefore not needed. Continuous crystals already had the cost advantage with respect to segmented crystals (section 3.3.1). The ability to estimate the DOI with a single photosensor array without crystal modifications makes them even more cost effective for PET detectors with DOI detection capability. The central question is how thick the crystals can be made for optimal efficiency, such that accurate positioning is still possible (Eqs. 3.11-3.13). For thick scintillation crystals, this may require a double-sided readout.

For single-sided readout, the LRF as a function of 3D position needs to be known. This information can be achieved from a detector calibration with a pencil beam of gamma photons, or from a theoretical model of the detector response function. In general, statistical methods (e.g., maximum likelihood estimation (MLE) [50, 64, 65] and in this work in chapter 4, neural networks [66] or nearest neighbors [37]) are used for 3D position estimation. Detectors based on continuous crystals that use a single photosensor array to estimate the 3D position are described in [49, 50, 64, 67–69] and in this work (chapter 4). It is also possible to calibrate the detector on the entry point of the gamma ray on the front surface of the crystal, such that DOI is intrinsically corrected for, although this requires a
detector calibration at various incident angles [37].

3.4 Alternative radiation detectors

Scintillation detectors still dominate in PET imaging. Some (prototype) scanners have also been built from alternative detectors, generally with the goal to achieve very high sub-millimeter spatial resolution, primarily for pre-clinical small animal imaging. The following sections describe alternative detectors, from which (prototype) scanners have or have not (yet) been built.

3.4.1 Semiconductor detectors

Semiconductor detectors are the most important alternative radiation detectors besides scintillation detectors. In these detectors an incident ionizing particle produces a large number of charge carriers along its trajectory, electron-hole pairs, that are collected at electrodes by applying an electric field. The fundamental working principle is thereby similar to the conventional photodiode, discussed in section 3.2. Silicon (Si) and germanium (Ge) are the most commonly used semiconductor detector materials. Cadmium telluride (CdTe) and cadmium zinc telluride (CdZnTe, or CZT) are more recent materials.

The conversion of the radiation energy into carriers is much more efficient than the conversion into scintillation light in scintillation detectors, which takes multiple inefficient conversion steps. In scintillation detectors, only a few thousand primary photoelectrons are created by the scintillation light in the photodetector. The statistical fluctuation is therefore relatively large and this inherently limits the maximum obtainable energy resolution. In semiconductor detectors a much larger number of carriers are produced, such that one generally obtains a better energy resolution for these detectors. An energy resolution less than 2 % at 511 keV can be achieved with CdTe and CdZnTe (CZT) detectors [10]. This allows a much narrower energy window to be set compared to scintillation detectors, thus rejecting more gamma photons that scattered within the body.

Another advantage is the ability to design compact 3D pixel arrays in fine arrangement, whereby the individual pixels are in mm-scale. This allows sub-millimeter spatial resolution and 3D localization of the gamma photon interaction point, thus including DOI, without dead space between the pixels [70, 71]. Due to the high spatial resolution, high energy resolution and pixelated design, it is further possible to recover scattered events by Compton kinematics [72]. In this way the point of first interaction can be determined, such that position blurring due to multiple scatter is not an issue.

However, there are also a number of disadvantages with these detectors. Both Si and Ge have a high thermally generated dark current at room temperature,
such that these materials need to be cooled in order to reduce this background noise source. Another problem in semiconductor detectors is the presence of impurities which trap the charge carriers during ionization events, and thus lower the signal, and limit the detector thickness to about 1 cm [12]. This problem may be solved by preparing high purity samples of detector material, like high purity germanium (HPGe, a standard technique for about 25 years), which is an expensive operation, however. Semiconductor detectors further have a significantly lower detection efficiency and an inferior timing performance due to long collection times, compared to PET-relevant scintillation detectors. The cost is also higher for the basic materials and front-end multichannel electronics. The recent semiconductor materials CdTe and CZT partly overcome these problems, as they can be operated at room temperature without excessive noise and have a relatively high stopping power due to their high density and atomic number ($\rho$ equal to 6.06 g/cm$^3$, $Z$ equal to 48 and 52 for Cd and Te, respectively). However, the efficiency for CZT is still 3 times lower than for LSO scintillators and also the timing performance is still inferior, requiring a large coincidence time window with an associated large background of random coincidences [73]. Further, the purity problem still restricts the size of these detector materials and only permits a planar design. Although the pixelated design requires the individual detector elements to be small for high spatial resolution, one readout channel for every pixel implies a high cost.

Due to the unfavorable properties with respect to timing and efficiency, these detectors are currently not suited for whole-body imaging. However, their superior spatial resolution is interesting for small animal and brain imaging. An animal PET scanner based on the CdTe semiconductor detector has already been built [70]. A prototype brain 3D PET scanner using CdTe detectors was shown to be feasible for clinical use with high spatial resolution, DOI reconstruction and good energy resolution [74]. Clinical images of this scanner and of a conventional PET scanner based on BGO scintillators were compared, and it was concluded that the higher spatial and energy resolution of the CdTe scanner resulted in a better tumor identification [75].

### 3.4.2 Gaseous ionization detectors

A few PET detectors based on gaseous ionization detectors exist, such as multi-wire proportional chambers (MWPCs) [76, 77] and resistive plate chambers (RPCs) [78]. These devices are generally more complex to fabricate into a scanner than scintillation and semiconductor detectors [42]. In these detectors, gamma photons interact in metal conversion layers, such as lead layers with a matrix of small holes in the MWPC-based HIDAC camera [79] or metallic electrodes in RPCs [78]. The resulting electrons will ionize gas chambers and initiate avalanches of electrons that are collected by an electric field between electrodes. There is virtually no
energy resolution [42] due to the high ionization energy\(^ 7\), such that a small number of electrons are produced. Compton scattered events can thus not be filtered out. However, the construction of RPC detectors is inexpensive such that a large fraction of the total solid angle can be covered, therefore still leading to a high system sensitivity [78]. In addition, these detectors exhibit an excellent timing resolution of 300 ps FWHM for 511 keV gamma photons [80], sub-millimeter spatial resolution and DOI reconstruction capability due to detector stacking in the DOI-direction. MWPC detectors also provide sub-millimeter resolution, but have inferior performance with respect to detection efficiency, count rate performance and timing resolution [10].

### 3.4.3 Liquid xenon detectors

Liquid Xenon (LXe) detects gamma photons by emitting scintillation light and producing electron-ion pairs by ionization [81]. It has a reasonable stopping power (density 3.06 g/cm\(^3\), comparable to NaI, but much lower than LSO and BGO), good ionization and scintillation yields (scintillation light yield 46,000 photons/MeV) and fast timing (scintillation decay components of 2 and 27 ns, [10]). The charge can be measured in a drift chamber and provides 3D sub-millimeter resolution (due to small electron diffusion), while the scintillation light provides sub-nanosecond timing resolution. The combination of both signals leads to an energy resolution below 10 % FWHM [82].

### 3.5 PET detector concept in the current work

In the current work a TOF-PET detector concept is investigated based on a monolithic (continuous) scintillation crystal and fast solid-state photosensors (SiPMs). The advantages of monolithic scintillation crystals (high gamma detection efficiency due to absence of dead space; high scintillation light collection efficiency; intrinsic DOI detection capability; no costs involved with crystal segmentation, see section 3.3.1) and SiPMs (high gain; fast response; MR compatibility; compactness; flexible readout geometries; low costs, see section 3.2.2) carry the prospect of fast, low-cost, MR-compatible TOF-PET detectors with DOI measurement. Since the scintillation light is not channeled towards the photosensor with low spatial spread (see section 3.3.1), an important question is whether a good positioning performance can be obtained for thick (efficient) monolithic scintillation crystals. This may require double-sided readout and thus an increase in detector costs. LYSO and LaBr\(_3\) crystals are chosen as scintillation materials, due to their favorable timing properties (see Table 3.1).

\(^7\)Ionization energy of gas is around 30 eV, while this is around 3 eV for semiconductors.
Chapter 4 presents a calibration method and a positioning algorithm based on MLE for reconstructing the 3D interaction position (thus including DOI) inside the monolithic scintillation crystal. In chapter 5, the positioning performance of monolithic scintillation crystals of varying thickness, coupled to a single MAPMT, is tested using the MLE method described in chapter 4. The timing performance of SiPM sensors (in particular their single photoelectron timing resolution) is presented in chapter 6. Timing measurements of single SiPM sensors coupled to small LaBr$_3$:Ce crystals are presented in chapter 7. Chapter 8 presents positioning and timing measurements for monolithic LaBr$_3$ crystals coupled to a single SiPM array, as well as ultrafast timing measurements for small LaBr$_3$ crystals coupled to single SiPMs.