Simulation Study of a High Resolution PET Detector Module with Depth of Interaction Information

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by
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Kyle Edward Thompson, candidate for the degree of Master of Science in Physics, has presented a thesis titled, *Simulation Study of a High Resolution PET Detector Module with Depth of Interaction Information*, in an oral examination held on July 27, 2018. The following committee members have found the thesis acceptable in form and content, and that the candidate demonstrated satisfactory knowledge of the subject material.

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Abstract

This work focuses on the simulated performance of a high-resolution, depth-of-interaction (DOI) capable PET detector module with a single-ended readout. I propose the use of a monolithic scintillator up to several centimetres thick directly coupled to a 2D array of Silicon Photomultipliers. High resolution of reconstructed energy and 3D position of γ rays interacting with the detector is achieved through the implementation of Maximum Likelihood Estimation (MLE) of said parameters. A notable difference in the implementation of MLE described herein is the direct estimation of the interacting γ-ray energy. Additionally, a performance evaluation of two prominent event windowing techniques used in PET – energy windowing and likelihood windowing – is presented.

The proposed design and reconstruction algorithms have been validated using Geant4-based Monte Carlo simulations. Two different versions of the detector module – one with an absorptive coating and the other with a reflective coating – were simulated, and a comparison of reconstruction performance is presented. It is found that the module with the reflective wrapping significantly out-performs the module with the absorptive wrapping in terms of the resolution of the reconstructed 3D position and energy of incoming γ rays due to the increased amount of scintillation light detected with the reflective configuration. The reflective configuration simulated herein achieves an average 3D position resolution of ∼ 1 mm, and an average energy resolution of ∼ 11%.

Based on an analysis of the simulated detector module performance versus scintillator thickness presented in this thesis, a scintillator thickness of 1.5 cm was chosen for future prototypes in order to strike a balance between position and energy res-
olution performance and detection efficiency. A small bore PET system employing this configuration of module will have volumetric resolution of reconstructed images in the sub-millimeter range, energy resolution of $\sim 11\%$ and sensitivity of $\sim 28\%$. 
Acknowledgments

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Dedication

I would like to dedicate this thesis to my sweetheart, Olena, and to my family. Thank you for always supporting me in every aspect of life, and for allowing me to pursue my dreams.
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List of Abbreviations

• APD - avalanche photodiode

• CT - computed tomography

• DOI - depth-of-interaction

• FDG - fludeoxyglucose labeled with radioactive $^{18}\text{F}$

• FWHM - full width at half maximum

• LAR - likelihood acceptance rate

• LOR - line of response

• LRF - light response function

• MLE - maximum likelihood estimation

• MRI - magnetic resonance imaging

• PDE - photon detection efficiency

• PET - positron emission tomography

• PMT - photomultiplier tube

• PS-PMT - position-sensitive photomultiplier tube

• SPAD - single-photon avalanche diode

• SiPM - silicon photomultiplier

• SPECT - single-photon emission computed tomography
Chapter 1

Introduction

Positron emission tomography (PET) is a widely-used nuclear imaging modality in the fields of medicine and biology that allows one to non-invasively obtain information regarding physiological and biochemical processes within an organism at the molecular level. This is accomplished by tracking the distribution of a radioactive molecule known as a radiotracer throughout the organism. The usefulness of molecular imaging and PET in particular as a diagnostic tool in medicine, and as a vehicle for drug delivery system development is undeniable and has a proven track record. A relatively new and growing field where PET is making an impact is research into plant physiology: by enabling the real-time imaging of intact plants and root systems, PET opens an unprecedented window into the fundamental molecular pathways governing plant productivity and response to biotic and abiotic stresses.

The ever-increasing need for better detector sensitivity (i.e. the ability to acquire images with lower amounts of radiotracer or in less time) and better image resolution stemming from requirements of an early disease diagnosis, the need for detecting
minute levels of toxicity and unexpected drug interactions, and the need to accurately
detect, delineate and quantify the uptake of a radiotracer drives the progression of
PET imaging technologies, which always have to be developed with cost-effectiveness
in mind in order to have the greatest possible benefit to society. Over the years,
much work has gone into improving the quality of PET images. In general, this can
be achieved by:

- improving the algorithm used to reconstruct the images – which is beyond the
  scope of this thesis –

- optimizing the detector system configuration, or

- improving the performance of individual detector modules that comprise the
detector system.

Today, high-resolution, small-bore PET systems are capable of imaging aggrega-
tions of radiotracer that are $\sim 2$ mm in size at concentrations of $100$ cps/kBq/cc
(10%) [1]. At a system level, the development of PET has a two-pronged, mutually
non-exclusive approach. On the one hand, hybrid scanners combine high-resolution
anatomic imaging modalities, such as Computed Tomography (CT) or Magnetic Res-
onance Imaging (MRI), with the functional imaging capabilities of nuclear imaging
modalities such as PET. On the other hand, organ-specific systems with their task-
tailored design and geometry allow one to reach a targeted detector sensitivity and
resolution without escalating cost.

This work focuses on the design study of a high-resolution, high-sensitivity, depth-
of-interaction (DOI) capable PET detector module with a single-ended readout. A
proof of principle for high resolution reconstruction of 3D position and energy of $\gamma$ rays – a form of high-energy electromagnetic radiation – interacting with the detector module, afforded by a novel implementation of Maximum Likelihood Estimation (MLE) of said parameters, is also presented. It is envisioned that the simple construction of our design will enable the wide availability of 3D $\gamma$-ray interaction position determination capability, that today is reserved only for lab prototypes. The modular design of the detector module proposed here will help to enable the next generation of PET systems to afford organ- and task-specific imaging applications, such as dedicated breast and brain scanners, as well as PET/MRI, PET/CT, SPECT/MRI (single-photon emission computed tomography) and SPECT/CT systems.

In this chapter we will discuss the fundamental concepts in PET imaging, some of the traditional designs of detector modules employed in high resolution PET systems, as well as how these designs can be improved upon.

1.1 PET Imaging

PET is a functional imaging technique in nuclear medicine – based on the process of radioactive decay – that is used to observe metabolic processes in humans, animals and plants. It is an imaging technique for detecting or quantifying changes in the metabolism stemming from functional alterations in legitimate processes such as brain activity, as well as pathological situations such as cancer growth. As such, PET is sensitive to blood flow, regional chemical composition, and absorption in human, animal or plant tissue. In all cases, this imaging is accomplished by using radioactive molecules – normal molecules with one element replaced chemically with
its radioactive isotope (a variant of an element with a different number of neutrons),
or radioisotope – to tag the metabolic activity and subsequently detecting photons
from the radioactive decay in detectors located externally to the subject.

In PET, as is shown schematically in Figure 1.1, the decaying radioisotope emits
a positron that travels a short distance within the organism (a few millimeters in
water, depending on the radioisotope used) [2], scattering off of electrons until its
kinetic energy is fully dissipated. At this point the positron will annihilate with
an electron, producing two simultaneous, nearly back-to-back, 511 keV $\gamma$ rays in
accordance with energy and momentum conservation [3]. These $\gamma$ rays are known as
annihilation $\gamma$ rays, or annihilation photons. This process is depicted pictorially in
Figure 1.2. The directions of back-to-back annihilation $\gamma$ rays define a so-called line
of response (LOR), and detecting a number of LORs enables the use of tomographic
image reconstruction algorithms to determine the distribution of the radiolabeled
molecules within the organism.

PET is a common imaging modality in clinical applications (e.g. cancer detec-
tion), has been employed in research studies in small-animal imaging towards the
development of pharmaceuticals, and recently has been used in imaging plant roots
and shoots with the objective of understanding plant functional behavior under nor-
mal conditions and stress (e.g. drought or pest attacks). Another commonly used
modality is SPECT, which detects a single photon, as its name suggests. SPECT can
use the same radiotracers as PET, although dedicated, non-PET radioisotopes offer
enhanced capabilities. PET typically has better contrast and spatial resolution than
SPECT, but the latter is a lower cost technique.
Figure 1.1: A schematic of the PET detection process showing a zoomed-in representation of the decay of a nucleus into a neutrino ($\nu$) and a positron ($e^+$). The latter undergoes a series of collisions before encountering an electron ($e^-$) and annihilating into two back-to-back photons, following energy and momentum conservation. Hundreds or thousands of such annihilations are detected in the imaging ring that surrounds the patient in this case. These detected events are digitized, calibrated and reconstructed to yield a PET image of the metabolic activity suitable for interpretation by a physician. Figure courtesy of Jens Maus, Creative-Wiki Commons, no restrictions on use.
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Figure 1.2: A schematic of the PET detection process in a ring of detectors, showing the positron decay of four radioactive nuclei (indicated by the black dots) and the subsequent positron-electron annihilation into pairs of two back-to-back outgoing $\gamma$ rays (indicated by arrows). Three of the latter are detected in opposing detectors, with the additional imposition of coincident detection within a predetermined, narrow timing window, as shown here, for example, in coincidence with detector $A$. The fourth $\gamma$-ray pair would be detected by another pair of detectors but would not register among the coincidences attributed to detector $A$. Figure courtesy of Kieran Maher, Creative-Wiki Commons, no restrictions on use.
1.2 Applications of PET

In this section we will discuss some of the many applications of PET imaging, with a focus on clinical applications, drug development and one of most recent applications of PET – plant physiology.

1.2.1 Clinical Applications

Presently, fludeoxyglucose labeled with radioactive $^{18}$F, normally referred to as $^{18}$F-FDG or FDG, is the most commonly used radiotracer worldwide, and is primarily used for cancer diagnosis. The utility of this particular radioisotope for PET imaging stems from the half-life of $^{18}$F (110 minutes), which ensures enough activity to acquire sufficient imaging data, as well as permits the transport of the isotope from its production facility to the application site. Other established/emerging clinical applications of PET include diagnostic applications in cardiology and neurology \[4^-6\]. Being an analogue of glucose, FDG enters into the cells through a sodium-glucose transporter and specific glucose membrane transporter pathways. The enzymes responsible for glucose metabolism convert FDG into FDG-6-phosphate (FDG-6-P) which cannot be further metabolized by cells and remains trapped. Hence, the distribution of FDG and its metabolite within the organism maps the tissue and cellular consumption of glucose by the organism.

FDG has numerous clinical applications in disease diagnosis as well as follow-up progression evaluation. Without doubt, the majority of FDG PET scans are performed in the field of oncology for diagnosis, staging, therapy monitoring, and prognosis of cancer patients. Aggressive tumour cells have a greater glucose consumption
rate in order to maintain their accelerated cell division, and as a result the FDG-PET is able to detect hotspots of possible tumour growths early in the development of cancers, prior to the occurrence of physiological and structural changes in tissue. As such, FDG enables early detection and diagnosis of many tumours (1-2 mm in size) with very high specificity at sites such as the head and neck, lungs, gastrointestinal system, skin, thyroid, and breast [4,5].

Today, most clinical PET scanners are incorporated into hybrid PET/CT systems. CT is an essential clinical tool providing necessary high-resolution anatomical information which complements functional PET images. Since CT detects changes in tissue density it is unable to detect tumours until later stages of the disease. However, its ability to detect morphological changes in tissues make CT an essential tool in tumour staging, in the control of therapy response as well as in biopsy guidance during initial diagnosis [4].

1.2.2 Drug Development

Molecular imaging with PET has opened new opportunities for drug development. The use of radiolabeled compounds allows one to address several important questions in pharmacology: Does our new drug reach the target tissue? Is the concentration of the drug that reaches the target tissue enough to have the desired pharmacological effect? What are the concentrations of the drug that lead to the desired pharmacological effect? Is it specifically binding to a particular type of tissue, cell organ?

The high sensitivity of PET compared to other molecular imaging modalities (even picomoles of radiotracer are detectable) permits the use of microdoses of radiolabeled
molecules along with an unlabeled substance that is being studied for its potential pharmacological benefit [7]. As such, the presence of the radiolabeled tracer has no pharmacologically relevant influence on the effects of the drug under investigation. Most drugs begin their development cycle in small animal (mouse) models which necessitates a reduction in dosage of the drug proportional to the weight of the subject, as well as an increase in spatial resolution (1-2 mm in small animal scanners versus 4-6 in clinical scanners) as well as sensitivity (up to 10-12% in small animal scanners versus 1-5 in clinical scanners) of the PET system [8].

1.2.3 Plant Physiology

While radioisotope use in plant physiology pre-dates medical imaging, with $^{14}$CO$_2$ first utilized as a tracer in photosynthesis studies in 1939 [9,10], nuclear imaging technologies dedicated to the study of plants are far less developed than in comparable applications in medical research. Imaging modalities used to study plants have included visible techniques [11], as well as CT [12] (to image the root-soil interface) and MRI [11]. There is a growing interest to use positron-emitting radioisotopes in plant biology research [13,14]. Several research groups are working to improve our understanding of plant productivity: nutrient and water use efficiency [15-22], plant microbe interactions, response to environmental stresses [23,24] (such as elevated carbon dioxide (CO$_2$) levels, heat, cold and parasitic organisms) and injury, to name a few. Impact areas for the molecular imaging of plants include: optimization of plant productivity, biofuel development and carbon sequestration in biomass, and climate change [25].
1.3 History of PET

PET imaging has a long and rich history spanning the twentieth century. As an imaging modality, PET was made possible by a number of technological innovations in the fields of physics, chemistry, mathematics and computer science throughout this time. In particular, three main events paved the way for PET imaging: the discovery of the positron, the creation and implementation of the cyclotron and the discovery of compounds such as FDG, and the development of a basic positron detection tomograph [26].

Antimatter, the class of matter to which the positron belongs, was theoretically predicted by Paul Dirac in 1929 as a result of a troubling “negative energy” solution to his famous Dirac Equation, which describes the electron [27]. This prediction was confirmed experimentally is 1932 by an American physicist named Carl Anderson [28]. A few years later, Irene Curie and Frédéric Joliot (the daughter and son-in-law of Polish physicist Marie Sklodowska Curie) discovered that certain elements (aluminum, boron and magnesium, specifically) could be made radioactive temporarily if bombarded by α particles [29]. This led many to believe that these artificially made radioactive substances may be useful for medical applications.

Shortly thereafter, American scientist Ernest Lawrence invented the cyclotron – a device intended to transmute elements – and it was soon discovered that this device was capable of producing radioactive substances [29]. Around this time, researchers in various fields began to use radioisotopes such as $^{18}$F, $^{13}$N and $^{11}$C for biological and medical studies. One of the first studies involving positron-emitting radioisotopes in human beings was performed in 1945; in this study, participants inhaled pure carbon
and oxygen (to form carbon monoxide in the lungs) in an effort to study the effects of CO on humans \[30\].

Around the 1950s, several groups began to consider the potential benefits of working with annihilation radiation, as opposed to single photon imaging \[26\]. Annihilation radiation is perfectly monoenergetic, meaning that each radiated $\gamma$ ray has exactly the same energy, and it was becoming clear that detecting two $\gamma$ rays from a single annihilation could provide useful spatial information. In 1951, Wren et al. \[31\] realized that if one could detect two $\gamma$ rays within a short time of each other, the annihilation event could be assumed to have come from a point along a straight line joining the opposing detectors – the fundamental principal of PET imaging.

From then on, the main contributions to the development of PET involved technological advancements in the areas of $\gamma$-ray detectors and configurations of these detectors. In 1962, Rankowitz et al. developed a PET imaging system for localizing brain tumours consisting of a ring of scintillation detectors, much like the PET imaging systems in hospitals today \[32\]. Though lacking the standard mathematical corrections made to PET images today, this system was a great step forward towards the development of a modern PET device.

By 1975, Ter-Pogossian et al. \[33\] had developed a full-body clinical PET scanner consisting of a hexagonal array of NaI scintillation detectors. This system was capable of completing a scan of the entire body within 2-4 minutes with 10-15 mCi of injected activity \[26\]. In the coming years, several technological advances were made, including the development of mini-computers and better scintillation materials (BGO, for example), which allowed PET imaging to become a widely utilized imaging modality in medicine, and eventually in other areas of research, as discussed in Section 1.2 \[26\].
1.4 Factors Affecting the Quality of PET Images

There are several factors involved in the imaging process that determine the quality of the resulting PET image, including the geometry of the detector system, the amount of data collected, as well as the image reconstruction algorithm used. Furthermore, the intrinsic ability of the detector modules used in the PET system to determine the time of arrival, position and energy of $\gamma$ rays interacting with the detector modules, together with the detection efficiency of the modules, determine the quality of the PET imaging raw data.

As seen in Figure 1.1, a PET system is tasked with detecting pairs of simultaneous annihilation $\gamma$ rays that travel in opposite directions. In practice, because the annihilation of positrons does not always occur at the mid-point between two opposing detector modules and because the detector modules have finite timing resolution, if two $\gamma$ rays are detected within a short time window of each other – known as the coincidence window – they are said to be in coincidence and are assumed to have originated from the same positron annihilation event, referred to as a true event. Additionally, during PET data acquisition there are several sources of noise that introduce unwanted artifacts in the reconstructed image. The most prominent sources of noise in PET imaging are scattered, random, as well as multiple coincidence events.

A scattered event is one in which one or both of the $\gamma$ rays suffers Compton scattering (see Section 2.1.1) inside of the imaged object or in air, experiencing a change in direction and energy. This skews the resulting LOR, providing a source of blurring in the image. A random event is one in which two $\gamma$ rays from distinct annihilation events are detected by opposing detectors within the coincidence window,
providing an additional source of blurring. A multiple coincidence event occurs when three or more \( \gamma \) rays are detected within a predefined timing window, resulting in multiple LORs without a clear way to distinguish the true annihilation pairs.

The ability to minimize the random coincidence as well as multiple coincidence events is principally determined by the timing resolution of the detector modules, which in turn depends on the properties of the scintillating crystals employed in the detector modules, as well as the electronics used. Improvements in this area can be made by using more sophisticated electronics to read out detector signals, or by employing scintillating crystals with faster decay times \([3, 34]\).

The primary technique used to eliminate scattered events is a method known as “energy windowing”, in which a coincidence event is only accepted for use in the final image if both of the detected \( \gamma \) rays have energies within a predefined window about the photoelectric peak of the energy spectra in the detector modules, known as the photopeak. It is therefore critically important that the detector modules employed possess a sufficient energy resolution in order to minimize the number of scattered events accepted in the final event selection for image reconstruction.

The last factor influencing the quality of the image that we will discuss here is the ability of the detector modules to accurately determine the position within the module at which a \( \gamma \) ray interacted. If this position is inaccurately estimated, the resulting LOR will be skewed, introducing a source of blurring into the image. To improve the accuracy and/or resolution of the estimated interaction positions, one can either modify the design of the detector module, or implement more advanced techniques to estimate these positions.
Chapter 2

Relevant Physics and $\gamma$-ray Detection

In this chapter several key concepts in subatomic physics needed to understand PET imaging will be introduced. Additionally, I will outline and explain the most common methods of detecting $\gamma$ rays, as well as present a survey of the various types of PET detector modules in use today.

2.1 Non-invasive Imaging

PET belongs to the class of non-invasive medical procedures that includes other noted modalities such as X-Ray, CT, MRI, SPECT, Ultrasound, Optical Imaging, Near Infrared Imaging, and others, to name but a few. This field relies on instrumentation that is able: i) to detect processes occurring within the body following the introduction of radioisotopes whose decay photons are detected externally (PET and
Chapter 2: Relevant Physics and γ-ray Detection

SPECT), ii) to stimulate nuclear processes in nuclei by the application of a magnetic field and detect their de-excitation (MRI), iii) to emit sound waves towards tissue boundaries and organs and detect their reflection (Ultrasound), and iv) to beam photons or X-rays through a patient, animal or plant, to obtain transmission or absorption spectra (X-rays and CT). A comparison of these modalities can be found in Table 5 of reference [35]. PET, SPECT, MRI, Optical and Near Infrared Imaging are grouped into a collection, termed Molecular Imaging [36].

Among these molecular imaging modalities, PET and SPECT provide information on the functional processes occurring at the site in a body where an introduced radioisotope accumulates. On the other hand, MRI, CT and X-rays provide structural (physiological) information. Combinations of modalities that are commonly used are PET-CT and PET-MRI, among others, that provide overlapping (“co-registered”) images showing the functional activity superimposed on its “geographical” location in the body.

The work herein concerns PET imaging, which is based on properties of subatomic physics. A short primer on this branch of physics is provided below.

2.1.1 Subatomic Physics Primer

Subatomic physics involves physical processes occurring within or with the atomic nucleus. Over a century of knowledge has been acquired related to the subatomic world, starting with the discovery of the nucleus by H. Geiger and E. Marsden under the direction of E. Rutherford [37,38]. For this discovery, Rutherford was awarded the 1908 Nobel Prize in Chemistry.
Chapter 2: Relevant Physics and γ-ray Detection

The prevailing picture of subatomic physics is captured in its analogue of the periodic table, called the Standard Model of Particle Physics, shown in Figure 2.1. The constituents of the Standard Model are grouped into the elementary building blocks of nature – the quarks and leptons – which come in three generations, different “flavours” and also possess anti-matter counterparts\(^1\) and are responsible for the formation of nuclei (quarks) and atoms (nuclei with orbiting electrons) \(^{[39]}\). The figure also shows the force carriers, namely the particles that mediate a given force, visualized as a particle exchange between other particles (e.g. gluons between two quarks). The four fundamental forces in nature and some of their properties are tabulated in Table 2.1.

Among these and of interest to this thesis, are the positron and accompanying neutrino (\(\nu\)) that are emitted during radioactive decay, a process which is a result of the weak nuclear force.

**Interaction of Photons with Matter**

In order to follow the detection of the photons emitted during the PET process, a description of the interaction of photons with matter is required. Interactions of photon radiation as well as charged matter particles (protons, alphas, electrons) and neutral matter particles (neutrons) all result in a transfer of energy from the radiation/particle to the matter with which it interacts. Matter is composed of atomic nuclei together with extranuclear electrons which orbit the nucleus. The interacting radiation/particle can interact with either or both components of matter. The

\(^1\)E.g. the electron is negatively charged and its antiparticle is the positron that is positively charged.
Figure 2.1: The Standard Model of Elementary Particles. Figure courtesy of Fermilab National Laboratory, Office of Science, Department of Energy, USA, Creative-Wiki Commons, no restrictions on use.
### Table 2.1: The fundamental forces in the universe and their properties.

The relative strength is compared at distances on the order of the diameter of a nucleus: at that distance, the strong nuclear force dominates and therefore binds quarks into protons and neutrons and then into stable nuclei. Note that indeed $10^{-15}$ corresponds to the diameter of a small nucleus, whereas $10^{-18}$ approximates 0.01% of the diameter of a proton. Each proton consists of three quarks and is a constituent of the nucleus together with neutrons, both of which are collectively called nucleons. This work is concerned solely with the weak nuclear force that results in the radioactive decay of unstable nuclei, which, following the emission of one or more subatomic particles, arrives at a stable configuration.

<table>
<thead>
<tr>
<th>Force</th>
<th>Property</th>
<th>Relative Strength</th>
<th>Range (meters)</th>
<th>Mediating Particle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong Nuclear</td>
<td>binds matter</td>
<td>1</td>
<td>$10^{-15}$</td>
<td>gluon</td>
</tr>
<tr>
<td>Electromagnetic</td>
<td>e-m and light</td>
<td>$\frac{1}{137}$</td>
<td>Infinite</td>
<td>photon</td>
</tr>
<tr>
<td>Weak Nuclear</td>
<td>radioactivity</td>
<td>$10^{-6}$</td>
<td>$10^{-18}$</td>
<td>W, Z bosons</td>
</tr>
<tr>
<td>Gravitational</td>
<td>gravity</td>
<td>$6 \times 10^{-39}$</td>
<td>Infinite</td>
<td>graviton*</td>
</tr>
</tbody>
</table>

* the graviton is a hypothetical particle not yet discovered.
subset of the electromagnetic spectrum that is most energetic (X-rays and γ rays, see Figure 2.2) have sufficient energy to cause ionization in matter, which is simply the dissociation of one or more electrons from orbits around an electrically neutral atom, thereby creating electron-ion pairs and imparting energy in the vicinity of the dissociation [40]. High energy particles can also ionize matter. As such, both are a concern for the branch of health physics.

Whereas the interaction of charged particles with matter is characterized by a — more or less — gradual energy impartation from the particle to the matter it traverses and a definite range in matter, photons (and neutrons) behave quite differently. The discussion here will focus exclusively on photons, as neutrons are not involved in this work.

Photons are attenuated when passing through matter in a manner quite different than charged particles. Photons (γ radiation) can only be reduced in intensity by increasing the thickness of the material traversed; they cannot be totally absorbed. Even very thick “absorbers” such as 10 cm of lead\(^2\) still allow a few percent of photons to emerge from the other side. The relationship between absorber thickness and the amount of γ radiation that emerges is given by the following equation [40]:

\[
\frac{I}{I_0} = e^{-\mu x} \quad \text{or} \quad \ln \frac{I}{I_0} = -\mu x
\]

(2.1)

where \(I_0\) is the incident γ-ray intensity, \(I\) is the γ-ray intensity transmitted through absorber thickness \(x\), and \(\mu\) is the attenuation coefficient of the absorber. Clearly, \(\mu\) and \(x\) must have reciprocal dimensions, so in this form \(\mu_l\) is called the linear

\(^2\)All matter acts as an absorber
Figure 2.2: The full electromagnetic spectrum is shown, with horizontal rulers marked in units of wavelength and frequency. X-rays and γ rays can cause ionization in matter. The physical quantities are connected through the equation $E = hf = hc/\lambda$, where $E$ is the energy, $f$ the frequency, $\lambda$ the wavelength, and $h = 6.62 \times 10^{-34} m^2 kg/s$. Courtesy of Jonathan S Urie [CC BY-SA 3.0], via Wikimedia Commons.
attenuation coefficient. If \( x \) is in units of \( g/cm^2 \), then \( \mu_m \) is called the mass attenuation coefficient, and these are related by [40]:

\[
\mu_I = \mu_m \times \rho,
\]

where \( \rho \) is the density of the absorber. Effectively, \( \mu \) is the slope of the above exponential equation. The mass attenuation coefficient is related to the probability of interaction of the \( \gamma \) ray with the absorber, which is termed the cross section.

Photons interact with matter in four main ways:

1. Photoelectric Effect. At low energies, the photon typically interacts with the atom as a whole. The entire energy of the photon is transferred to one of the bound electrons which is ejected. The mass attenuation coefficient depends strongly on the atomic number \( Z \) \( (\mu_m \propto Z^4/AE^3) \), \( E \)-energy, \( A \)-mass number) which explains why bones are so visible on radiographs (X-ray plates) even though the density of bone is typically less than twice that of water. The difference arises from the fact that the heaviest element in water is oxygen \( (Z = 8) \) while bone is mostly made of calcium \( (Z = 20) \). The mathematics gives a ratio of \( Z(Ca)^4/Z(O)^4 = 40 \).

2. Compton Scattering. In this effect, the photons scatter from individual electrons. The outcome is a scattered photon with reduced energy, with the difference transferred to the scattered electron. The mass attenuation coefficient depends less strongly on \( Z \) \( (\mu_m \propto Z/A\sqrt{E}) \). A schematic of this process is shown in Figure 2.3. The relationship between the energies of the scattered \( (E') \) and incident \( (E) \) photons is given by [40]:
Figure 2.3: The elastic collision between a photon and electron is called Compton Scattering.
\[
\frac{E'}{E} = \frac{1}{1 + (E/m_0c^2)(1 - \cos \theta)},
\]
(2.3)

where \(m_0\) is the mass of the electron (511 keV or \(9.1 \times 10^{-31} kg\)). The amount of energy deposited in the detector depends on the scattering angle of the photon, leading to a spectrum of energies, each corresponding to a different scattering angle \(\theta\). The highest energy that can be deposited, corresponding to full backscatter, is called the Compton Edge \([41]\).

3. Pair and Triplet Production. In these interactions, the photon interacts with the electromagnetic field near a charged particle; the photon disappears and an electron-positron pair is created. If the interacting field is that of a nucleus, the electron and the positron each receive about half of the photon’s kinetic energy (hence pair production). If the field is that of an electron, that electron also receives some energy (triplet production). The mass attenuation coefficient for pair production depends on the logarithm of the energy (\(\mu_m \propto Z^2/A \log(E)\)).

The reverse reaction, namely the annihilation of a positron encountering an electron, produces two back-to-back photons, each having energy equal to the equivalent energy of the particles according to \(E = mc^2\), where the rest mass of the positron and electron is 511 keV \([39]\). The minimum energy produced in this process is then 1022 keV, or twice the rest mass of the electron.

4. Photonuclear reactions. These are of the type \(A(\gamma, xn)B\), where \(A\) is a nucleus and \(B\) can be another nucleus or a particle, and \(x = 1, 2, 3\), or \(A(\gamma, n\alpha)B\), etc. These occur at energies higher than what is encountered in PET so they are not discussed further.
2.2 The Physics of PET

As mentioned previously, PET employs molecules that are tagged with a positron-emitting isotope. The positron is not thought to exist independently within a nucleus, but rather it results from the transformation of a proton into a neutron via the following nuclear reaction:

\[ p^+ \rightarrow n + e^+ + \nu, \quad (2.4) \]

which can be manifest in nuclear \( \beta \) decay as

\[ _{11}^{22}\text{Na} \rightarrow _{10}^{22}\text{Ne} + e^+ + \nu, \quad (2.5) \]

for example [40]. This is a standard nomenclature in Chemistry and Physics, where the superscript refers to the mass number of the nucleus (the collective mass of its protons and neutrons, adjusted for the binding energy of the nucleus) and the atomic number, which refers to the number of protons and thus to the net charge of the nucleus.

In the most general sense, radioisotope production is achieved by manipulating the number of neutrons and/or protons within the nucleus in order to generate an energetically unstable isotope [42] by “leaving the island” of nuclear stability as shown in Figure 2.4. These unstable nuclei will eventually revert to a more stable state by emitting ionizing radiation such as \( \gamma \) rays and/or subatomic particles – protons, \( \alpha \) particles (\(^4\text{He} \) nuclei), \( \beta^- \) (electrons) and \( \beta^+ \) (positrons) – through the process of radioactive decay.

PET will often employ \(^{18}\text{F}\) to tag a molecular site such as in fluorodeoxyglucose (FDG) by replacing stable \(^{19}\text{F}\), resulting in a new, radioactive molecule \(^{18}\text{F}-\text{FDG}\),
Figure 2.4: The number of protons and neutrons in a nucleus are plotted against each other. The island of stability is shown as the black ridge along the “spine” of the distribution. Those nuclei that emit a $\beta^+$ (positron) in order to move towards the ridge are coloured orange. Creative-Wiki Commons, no restrictions on use.
which is handled by the body as normal glucose. This happens because processes in
the body are a result of biology and chemistry while changes in the atomic nucleus
of the elements involved (Nuclear Physics) do not affect these; a subtle point is that
the atomic weights of $^{18}\text{F}$ and $^{19}\text{F}$ are slightly different, but, again, this does not
affect the majority of chemical processes in the body. PET tends to utilize generally
lighter elements produced via cyclotron, such as $^{18}\text{F}$, $^{11}\text{C}$ and $^{13}\text{N}$ [43]. These PET
radiotracers have significant biological relevance because they can be easily integrated
into synthetic biomolecules. Some of the most common radioisotopes used in PET
imaging can be seen in Table 2.2 along with some of their characteristic properties.

2.3 Detecting $\gamma$ Rays

In this section, I will discuss a few of the most common types of $\gamma$-ray detectors,
with a focus on scintillation detectors and direct-conversion, solid-state detectors. In
addition, two common types of photodetectors used in conjunction with scintillation
crystals will be compared and contrasted: photomultiplier tubes (PMTs) and silicon
photomultipliers (SiPMs).

2.3.1 Scintillation Detectors

A common type of $\gamma$-ray detector consists of a scintillator – either monolithic or
divided into segmented pixels – coupled to a photodetector. A scintillator is a crys-
talline material which exhibits the property of luminescence when struck by radiation.
An incoming $\gamma$ ray interacts with the crystal primarily via Compton scattering of a
valence electron, or via the photoelectric effect. In either case, a portion – or all, in
Table 2.2: A few of the common radioisotopes used in PET imaging. Relevant properties include the half-life, the maximum kinetic energy of radiated positrons ($E_{\text{max}}$), as well as the $\beta^+$ branching fraction, which is the fraction of total radiation events that emit positrons. The data here were taken from the Table of Nuclides: www2.bnl.gov/ton.

<table>
<thead>
<tr>
<th>Radioisotope</th>
<th>Half-life</th>
<th>$E_{\text{max}}$ (keV)</th>
<th>$\beta^+$ Branching Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C</td>
<td>20.4 min</td>
<td>960</td>
<td>1.00</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>109.8 min</td>
<td>630</td>
<td>0.97</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.97 min</td>
<td>1200</td>
<td>1.00</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>122 s</td>
<td>1730</td>
<td>1.00</td>
</tr>
<tr>
<td>$^{62}$Cu</td>
<td>9.74 min</td>
<td>650</td>
<td>0.97</td>
</tr>
</tbody>
</table>
the case of photoelectric interactions – of the γ-ray energy is imparted to an electron, which then travels a short distance through the crystal, exciting atoms. Upon de-excitation, these atoms emit low-energy photons (referred to as scintillation photons) in the visible range of the electromagnetic spectrum. The scintillation photons are emitted isotropically, and the number of photons produced is proportional to the amount of energy deposited in the crystal by the γ ray \[3\]. The photodetector coupled to the scintillator is tasked with measuring the amount of scintillation light, as well as its spatial distribution, in order to determine the energy of the incoming γ ray, as well as the position within the scintillator at which the scintillation interaction took place.

**Scintillator Materials**

Scintillation can occur in several different types of materials, and the characteristics of the scintillation light can vary widely between materials. For the purpose of detecting γ rays, scintillating materials can effectively be characterized by a handful of important parameters including light yield, decay time, peak emission, energy resolution, and density.

The light yield of a scintillator is defined as the average number of scintillation photons produced per unit of energy deposited in the scintillator. This is one of the most important characteristics to consider when choosing a scintillator, as it will effectively determine the strength of the measured signal. A higher light yield will produce a stronger signal in the photosensors and result in better signal to noise ratios.

As scintillation photons are produced via a relaxation process, another important
characteristic of a scintillator is the decay time, which is a measure of the time needed for the majority of the scintillation photons to be produced. The decay time of a scintillator is particularly important in PET imaging, as it is intimately related to the radioactivity that can be used in the radiolabeled isotope. As mentioned in Section 1.1, two $\gamma$ rays must be detected within a predefined coincidence window in order to be accepted for use in the image formation. The size of this window is typically taken to be twice as long as the time needed to measure a single scintillation pulse in order to ensure that $\gamma$ rays from the same annihilation event are detected in coincidence, meaning that if a scintillator has a long decay time the coincidence window will need to be large. As the size of this window increases, however, the probability of random events being accepted for use in the image also increases, leading to blurring. For a given scintillator material, the radioactivity administered to the patient or object being imaged must be low enough to prevent these random coincidences, necessitating longer data acquisition times to produce a high quality image. It is therefore critically important for PET imaging that the scintillators used possess a short decay time.

Another important property of scintillators to consider is the peak emission, which is the average wavelength of the scintillation photons produced. This particular characteristic plays a role in matching a given scintillator material to a photosensitive detector. This is because every photosensitive detector has a detection efficiency that varies with the wavelength of the photons being detected, meaning that certain wavelengths will be detected with a higher probability than others. The SiPM detectors considered in this study, for example, will detect $\sim 37$-50% of incident 420 nm photons (depending on the operating conditions of the detector), but will only detect
\[ \sim 3-5\% \text{ of incident 800 nm photons} \ [44]. \]

The energy resolution of a scintillator material is related to the variance in the number of scintillation photons produced at a given energy. This number is a random variable with mean value equal to the light yield. This variance is critically important for being able to determine the energy of the incoming \( \gamma \) ray, and is the principal factor influencing the energy resolution of the detector module. If \( \gamma \) rays of two distinct energies frequently produce the same number of scintillation photons in a given scintillator material, it becomes exceedingly difficult to distinguish between these energies. This affects the ability of the detector module to determine which \( \gamma \) rays have scattered in the patient, leading to a higher acceptance rate of scattered events \[3\].

The last property of scintillator materials that is important for PET imaging is the density of the material. In general, materials with high density and high effective atomic number will stop a greater percentage of incoming \( \gamma \) rays, leading to an increase in the detection efficiency of the detector module, and the PET system as a whole. As higher detection efficiency results in faster data acquisition times, this is a desirable trait.

Table 2.3 shows the values of the aforementioned properties for several common scintillator materials. The properties of NaI here are from Saint-Gobain\[3\] and Moszyński et al. \[45\], and all other data is from Furukawa\[4\]. From this table it is seen that cerium-doped LYSO is a good candidate for PET imaging with high density, reasonable light yield, fast decay time, and reasonable energy resolution. Additionally,


\[4\]Furukawa Co., Ltd.; http://www.furukawa-denshi.co.jp
<table>
<thead>
<tr>
<th>Scintillator</th>
<th>Ce:Gd₃Al₂Ga₃O₁₂ (Ce:GAGG)</th>
<th>Ce:Lu₀.₈₂₉SiO₅ (Ce:LYSO)</th>
<th>Bi₄Ge₃O₁₂ (BGO)</th>
<th>Ce:LaBr₃</th>
<th>NaI(Tl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (g/cm³)</td>
<td>6.63</td>
<td>7.1</td>
<td>7.13</td>
<td>5.08</td>
<td>3.67</td>
</tr>
<tr>
<td>Light yield (photon/MeV)</td>
<td>57,000</td>
<td>34,000</td>
<td>8,000</td>
<td>75,000</td>
<td>38,000</td>
</tr>
<tr>
<td>Decay Time (ns)</td>
<td>88 (91%)</td>
<td>40</td>
<td>300</td>
<td>30</td>
<td>250</td>
</tr>
<tr>
<td></td>
<td>258 (9%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak Emission (nm)</td>
<td>520</td>
<td>420</td>
<td>480</td>
<td>375</td>
<td>415</td>
</tr>
<tr>
<td>Energy resolution (%@662∼keV)</td>
<td>5.2</td>
<td>10</td>
<td>12</td>
<td>2.6</td>
<td>6.8</td>
</tr>
</tbody>
</table>

Table 2.3: Shown are the physical properties of several common scintillator materials. Information for NaI(Tl) was taken from Saint-Gobain crystals and Moszyński et al., and all other data is from Furukawa.
the peak emission of LYSO matches the peak of the detection efficiency spectrum of the SiPMs used in this study. For these reasons, and also because it is the current standard for PET detector modules, LYSO was chosen as the scintillator material for this study.

### 2.3.2 Photodetectors

The most common type of photodetector used to detect scintillation light for PET imaging is the PMT. A schematic diagram of the cross-section of a PMT is shown in Figure 2.5. This device consists of a photocathode which emits an electron via the photoelectric effect when struck by a photon, as well as a series of dynodes which are held at increasing voltages, and an anode. The dynodes are covered with an emissive material which readily emits electrons, and a high voltage is supplied between the cathode and the anode. An electron ejected from the photocathode is accelerated towards the first dynode due to the applied voltage, and upon contact with this dynode several additional electrons are emitted. These electrons then accelerate to towards the next dynode, and an avalanche effect occurs in which a single electron is multiplied into $\sim 10^6$ electrons. These electrons produce a measurable current which is extracted at the anode [3].

These detectors have many advantages, such as high gain and photon detection efficiency (PDE), but they also have several drawbacks. PMTs are large in size, and are very delicate. Additionally, they require a high voltage to operate, and can suffer from a loss of gain in the presence of external magnetic fields due to the deflection of electrons from their intended path.
Figure 2.5: Shown is a schematic diagram of the cross-section of a PMT. Scintillation photons strike the photocathode, emitting electrons. These electrons are accelerated through the glass vacuum tube towards the first dynode by an applied voltage. Upon striking the dynode additional electrons are released, leading to an avalanche effect. Figure courtesy of Kieran Maher via Wikimedia Commons.
A promising alternative to PMTs are SiPMs. SiPMs are solid-state photodetectors made up of an array of small microcells connected in parallel, each consisting of a single photon avalanche diode (SPAD) and a quenching resistor. Each SPAD, depicted in Figure 2.6, is made of silicon which is “doped” to contain regions with excess positive and negative charge, respectively, as well as a region between these two regions devoid of mobile charge carriers known as the depletion region [46]. A bias voltage is applied across the unit, creating a strong electric field in the depletion region. When a scintillation photon interacts with the silicon in the depletion region an electron is liberated, producing an electron-hole pair, where the “hole” is the absence of a negative charge that effectively behaves like a positive charge. The electron and hole are accelerated towards opposite sides of the depletion region by the applied electric field. If the field is sufficiently strong the charge carriers will acquire enough kinetic energy to liberate further charge carriers through a process known as impact ionization, resulting in an avalanche effect. This avalanche results in a signal gain on the order of \( \sim 10^5-10^6 \), depending on the applied voltage and the temperature of the unit. Once an avalanche has occurred, the quenching resistor serves to lower the voltage across the diode, preventing further avalanches until the voltage has been re-established. The time needed for the voltage to return to operating levels is referred to as the dead time, during which an SPAD is not capable of sensing additional photons [46].

Each SPAD is operated in Geiger mode, meaning that the response of the microcell is independent of the number of photons that interacted with the silicon. As a result of this, the microcells in SiPMs are made as small as possible (tens of \( \mu \)m across) in order to minimize the probability that two photons will strike the same cell at the
Chapter 2: Relevant Physics and $\gamma$-ray Detection

Figure 2.6: A schematic representation of a basic avalanche photodiode (APD). A SiPM is made up of thousands of microcells, each consisting of a small APD (an SPAD) and a quenching resistor. An incoming photon liberates an electron-hole pair in the depletion region (i), resulting in the liberation of further electron-hole pairs as a result of the applied voltage, leading to an avalanche. For SiPMs, APDs (SPADs) are used to measure low-energy scintillation light, while in solid-state detectors (see Section 2.3.3) the incoming photons are the annihilation $\gamma$ rays themselves. Figure courtesy of Kirnehkrib via Wikimedia Commons, no restrictions on use.
same time. The signals from all of the microcells are summed for each event, providing a current pulse which is integrated over its duration to produce a charge that is proportional to the amount of light that struck the SiPM.

SiPMs possess several advantages over traditional PMTs, which is why they were considered for this study. Firstly, SiPMs are small and robust, and require much lower operating voltages than PMTs. Even with this difference in voltage, however, SiPMs are still capable of generating the same amount of gain as PMTs. Additionally, SiPMs are virtually impervious to external magnetic fields due to the very short distance (the depletion region) over which the charge carriers in the silicon are free to move. This ensures that a PET detector system employing SiPMs may be operated in conjunction with other imaging modalities such as MRI without their operation being adversely affected. Furthermore, SiPMs possess a high detection efficiency, comparable to that of PMTs [46].

2.3.3 Solid-State Detectors

Another common class of photodetectors for \(\gamma\)-ray detection are solid-state detectors based on semiconductor materials such as CdTe or CdZnTe. Rather than employing a secondary mechanism such as scintillation to detect \(\gamma\) rays, solid-state detectors attempt to measure the \(\gamma\) rays directly through their photoelectric or Compton interactions. One of the most common types of solid-state detectors for \(\gamma\)-ray imaging is the avalanche photodiode (APD). The basic structure of an APD is shown in Figure 2.6. It consists of a semiconductor wafer – similar to those found in SiPMs – connected to an anode and a cathode which are held at a high voltage. When a \(\gamma\)
ray enters the semiconductor, it will interact (with some probability) with the semi-conductor via the photoelectric effect or Compton scattering, producing electron-hole pairs. Much like in SiPMs, the electron and hole will drift towards the cathode and anode, respectively, liberating additional charge carriers along the way. An avalanche effect takes place, and the pulses measured on the anode and cathode are analyzed to provide information on the energy and position of interaction of the γ ray. Detectors employing APDs generally provide very good energy resolution and reasonable gain (\( \sim 10^2-10^3 \)), though they fail to provide DOI information of the γ ray \[3\].

### 2.4 Survey of PET Detector Module Designs

There are several types of detector module designs that are traditionally used in PET imaging. The most common designs consist of a finely segmented 2D array of scintillation crystals (typically \(1\times1\times10\) mm\(^3\) in size \[8\]), in conjunction with a layer of photosensitive elements such as a position-sensitive photo-multiplier tube (PS-PMT) or SiPMs \[8,47\]. Additionally, a light-spreading medium (a lightguide) is often introduced between the crystal array and the photosensitive layer in order to disperse the scintillation light over several of the photosensitive elements, as seen in Figure \[2.78\]. This technique permits the use of fewer photosensitive elements than scintillation crystals, reducing the cost of the detector module.

In these designs, the energy of each interacting γ ray is assumed to be proportional to the sum of the signals provided by the photosensitive elements, and the crystal in which the interaction took place is determined by using the center of gravity of the signals together with a lookup table to match center of gravity positions with the
Figure 2.7: (a) A schematic representation of a pixelated, scintillator-based PET detector module. The three essential components are the segmented crystal array (1), light spreading layer (2), and the photosensitive layer (3). (b) A schematic representation of a direct-interaction semiconductor detector. This consists of an array of anode pixels (1), a monolithic semiconductor detector crystal (2), and a continuous cathode on the back side.
true positions on the crystal (Anger logic) \[8\]. The individual crystal elements are wrapped in a reflective layer to maximize the amount of optical light transmitted to the photosensitive layer, and as a result the position within a crystal at which a \(\gamma\) ray interacted generating scintillation photons cannot be known. Consequently, the \((x,y)\) position of this interaction is taken to be at the center of the crystal, and the \(z\)-position is projected onto the front, back, or middle of the crystal element \[3\].

While these techniques for estimating position and energy determination are straightforward and cost-effective to implement, they suffer from nonlinear effects stemming from the non-uniformity of PS-PMT’s and reduced resolution due to multiplexing – a technique in which several signals are combined into a single signal to reduce the amount of required electronics – respectively \[48\]. Hence, a PET detector with a multiplexed readout employs a \(\sim 350\) to \(650\) keV wide energy window to vet \(\gamma\) rays that undergo Compton scattering within the imaged object \[49\]. Additionally, the position resolution of such systems is determined by the size of the crystal elements used. Smaller crystals will improve the position resolution of the system, but the resulting module will be costly and difficult to manufacture.

Another common detector module design employs a direct-interaction semiconductor (such as CdTe or CdZnTe). An example of this type of design can be seen in Figure \[2.7b\]. These detector modules consist of an array of square anode pixels, together with a monolithic semiconductor detector crystal, and a continuous cathode on the back side. This effectively results in an array of APDs (see Section \[2.3.3\]), and the \((x,y)\) position of interaction of the \(\gamma\) ray is determined by analyzing the distribution of charge on the anode pixels. Traditionally it has been difficult to grow large CdTe and CdZnTe crystals void of impurities, and while crystal growth technology is
improving continuously, such semiconductor detectors require a bias voltage of $\sim 100$ to 200 V/mm for reliable operation \cite{50, 51}. Furthermore, in CdTe or CdZnTe detectors there is significant loss of charge due to the lack of mobility and short lifetime of holes with increasing detector thickness, and as a result the DOI of the $\gamma$ ray within the crystal is difficult to determine for this type of configuration. The crystals in these detectors have to remain thin to minimize blurring effects in the reconstructed image, leading to relatively low detection efficiency \cite{52}, though this can be overlooked in the face of their remarkable energy resolution.

The third common design for PET detector modules consists of a monolithic scintillation crystal coupled to a photosensitive array. The principal advantage of this design is its ease of construction, low cost, and high $\gamma$ ray detection efficiency. Additionally, such a design allows for the implementation of advanced statistical methods to estimate the 3D interaction position and energy of an incoming $\gamma$ ray, and has the potential to greatly improve PET image quality. Detector module designs based on monolithic scintillation crystals have received a great deal of attention in recent years \cite{53–62}, and several techniques for analyzing the signals from these detectors to produce estimates of the 3D interaction position and/or energy have been proposed, including parametric models based on the geometrical distribution of optical light \cite{54, 56–61}, dual-end read out of scintillation light \cite{57–59}, machine learning techniques \cite{60}, and many others.

Among thick $\gamma$-ray detectors used for PET imaging, a detector module which provides information regarding the DOI of the $\gamma$ ray provides a distinct advantage over one that does not. For a PET system whose detector modules do not provide DOI information, the location of the $\gamma$ ray for imaging reconstruction purposes is projected
onto the front, back, or middle of the crystal, as mentioned above. However, if a $\gamma$ ray enters a scintillation crystal at an oblique angle and scintillates far from the top of the scintillator, then once the position of this $\gamma$ ray is projected onto the front surface of the crystal, this position will no longer represent a point along the LOR. In effect, this introduces a “parallax” error which is an additional source of blurring.

### 2.4.1 PET Detector Module Design with Depth-of-Interaction Information

In this work I propose the use of a monolithic scintillating crystal coupled to an array of SiPMs, and will explore the possibility of determining the energy and position of interaction of $\gamma$ rays using MLE.

MLE is a technique in which a set of parameters in a statistical model of a system are estimated using observations from the system. In practice, this involves determining a likelihood function that provides the probability density of measuring a set of data as a function of the parameters in question, and maximizing this function with respect to the parameters for a given set of data. The values of the parameters that maximize the likelihood function are then taken to be the “most likely” parameter values. For PET imaging, or any other $\gamma$ imaging modality, the relevant parameters are the position and/or energy of the $\gamma$ ray.

This technique was first used to provide position estimates in $\gamma$-cameras by Gray and Macovski [63], and its application to position and energy reconstruction in PET detector modules has since been studied by various groups in one form or another [53, 64, 66]. Herein, the possibility of using MLE to estimate the 3D interaction position
and energy of $\gamma$ rays in monolithic scintillating crystals is explored using Monte Carlo simulations. The contributions of this work to the field include a novel method of determining the 3D LRFs needed for MLE of 3D interaction position using Monte Carlo simulations, a simple means of employing MLE to accurately estimate the energy of $\gamma$ rays, and a performance comparison between monolithic crystals wrapped in absorptive layers and those wrapped in reflective layers.
Chapter 3

Monte Carlo Simulations for Detector Design and Reconstruction Optimization

3.1 Detector Module as Modeled in Simulations

Two different PET detector module configurations were modeled using an in-house built Geant4 Monte Carlo simulation \cite{67} to optimize the design of a future prototype as well as test the MLE reconstruction methods described in Section 3.2. The modules in these simulations both consisted of a $50.44 \times 50.44 \times 25 \text{ mm}^3$ LYSO crystal designed to fit onto an $8 \times 8$ SiPM array (ArrayJ-60035-64P-PCB by SensL Ltd\textsuperscript{1}). This setup can be seen in Figure 3.1.

In one of the simulations, the top and side faces of the crystal were wrapped in a

\textsuperscript{1}SensL Technologies, Ltd., Ireland, \url{http://www.sensl.com}
Figure 3.1: Simulated PET detector module. $\gamma$ rays enter through the top face of the $50.44 \times 50.44 \times 25 \, \text{mm}^3$ LYSO crystal, producing scintillation photons. The positions at which the scintillation photons encounter the photosensitive layer (purple) are recorded, and are binned into $8 \times 8$ regions to mimic the response of SiPM pixels. Two module configurations are simulated: one in which the top and side faces of scintillator are coated with an $100\%$ absorptive coating, and another in which a $>98\%$ reflective Teflon coating is applied to said sides. The coordinate system shown here is referred to in subsequent plots, and its origin defines the point $\mathbf{R} = (0,0,0)$. 
0.1 mm thick reflective Teflon\textsuperscript{2} layer (> 98% reflective) and the reflective properties of Teflon are modeled by supplying a wavelength-dependent refractive index of \(\sim 1.3\) \cite{68}. Conversely, in order to reproduce the effect of an ideal absorptive coating, the optical properties of the Teflon were disabled in the simulation, resulting in the absorption of 100\% of optical light incident on the top and side faces of the crystal. A performance comparison of these two configurations is presented in Section 3.3.

The scintillation crystal in my simulated detector design was chosen to be relatively thick (25 mm) allowing one to bin \(\gamma\) rays according to their DOI within the crystal in order to determine an appropriate thickness (possibly less than 25 mm) for prototypes based on the reconstruction performance observed at various depths within the crystal. The physical and optical properties of the LYSO crystal, including its chemical composition \cite{69}, specific light yield, emission spectra, refractive index \cite{70}, as well as absorption and scattering lengths \cite{71}, were aggregated from a number of sources, and are listed in Table 3.1.

The predefined physics list in Geant4 for electromagnetic interactions (option 3) was enabled. The list includes processes controlling the interactions and transport of \(\gamma\) rays, positrons, and electrons in the simulation: i.e. photoelectric effect, Compton scattering, pair production (though not energetically possible for the energy range relevant for PET imaging), Rayleigh scattering, multiple scattering, ionization, bremsstrahlung, and positron annihilation. Furthermore, the processes responsible for the generation and transport of scintillation photons in the LYSO crystals via scintillation and the Cherenkov effect for wavelengths between 300 and 800 nm,

\textsuperscript{2}DuPont \url{http://www.dupont.com}
<table>
<thead>
<tr>
<th>Quantity</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive Index</td>
<td>1.81</td>
</tr>
<tr>
<td>Specific Light Yield (photons/keV)</td>
<td>32</td>
</tr>
<tr>
<td>Intrinsic Energy Resolution (% at 511 keV)</td>
<td>8</td>
</tr>
<tr>
<td>Fast Time Constant (ns)</td>
<td>41.0</td>
</tr>
<tr>
<td>Absorption Length (cm)</td>
<td>50.0</td>
</tr>
<tr>
<td>Scattering Length (cm)</td>
<td>260.0</td>
</tr>
</tbody>
</table>

Table 3.1: Physical properties of the LYSO crystal simulated in this thesis. The scintillation yield and refractive index are from Mao et al. [70], the intrinsic energy resolution is from Phunpueok et al. [72], and all other quantities are from Bonifacio et al. [71].
covering the wavelength range of the LYSO scintillation spectra, were also activated. The processes responsible for interaction of the scintillation photons considered in the simulation are: bulk absorption, optical Rayleigh scattering, and, when relevant, reflection and refraction at the LYSO-Teflon boundary.

The simulations begin with monoenergetic 511 keV $\gamma$ rays at normal incidence to the scintillator surface, with subsequent tracking of individual histories of all particles: primary, secondary as well as scintillation photons. Information regarding interactions within the scintillator volume (creator processes of secondary particles), as well energy deposition at each step were recorded. The number of scintillation photons created, along with the number of scintillation photons reaching the bottom end of the LYSO crystal, are recorded for every incident $\gamma$ ray in a ROOT data analysis framework [73]. The simulation also stores the positions of the scintillation photons reaching the bottom of the LYSO crystal. These positions can be then binned into virtual SiPM pixels (Figure 3.1) – corresponding to the positions and sizes of SiPM pixels in the SensL array – to create surrogates of SiPM responses to be used in the MLE (Section 3.2).

Oblique angles of incidence were not simulated in this work, as the scintillation light is emitted uniformly in all directions and the simulation provides the exact position of interaction of the $\gamma$ rays. Also, in the case of 511 keV annihilation $\gamma$ rays, the photoelectron travels $\sim 50$-$70$ $\mu$m in water from the point of the interaction [2], which is less than the expected resolution of the detector. Compton electrons will travel even less.
3.2 Simulated Quantities

3.2.1 Interaction Grid for Light Response Functions

In order to utilize MLE to reconstruct the interaction position and energy of an incoming $\gamma$ ray, one must possess information regarding the expected detector signals in response to scintillation events occurring at a number of positions within the scintillator. This information is stored in light response functions (LRFs), a set of functions describing the expected signal from a given SiPM as a function of the interaction position and energy of a scintillation event. Position and energy estimates are then made by comparing a set of measured photo-sensor signals to the expected signals in order to determine the “most likely” energy and position of interaction, based on the maximization of a likelihood function (Section 3.2.3).

For the purpose of creating such LRFs, the scintillator volume was divided into a virtual 3D grid of $20 \times 20 \times 26$ points, referred to here as the interaction grid (Figure 3.2a). Additionally, the space enclosed by any eight neighboring interaction points is referred to as an interaction region. The layout of the interaction grid was determined by dividing the bottom-left quadrant of the scintillator face into 10 x 10 evenly sized squares, and choosing the center of each square to be the $(x,y)$ location of a column of points (Figure 3.2a). This was then extended to the entire face of the scintillator by symmetry to produce a 2D grid of $20 \times 20$ points, 2.52 mm apart in the x and y directions. The number of 2D grids used to fill the 3D volume was chosen to be 26, resulting in each layer being 1 mm away from its neighboring layers. The end result (i.e. the 3D interaction grid) is 26 layers of a $20 \times 20$ grid of points, with the first layer on the bottom of the scintillator and the 26th layer on the top face.
3.2.2 Light Response Functions

In order to construct the LRFs from the simulated data, an event selection process is employed. For each event, the first step is to determine whether or not a scintillation process occurred from an incident 511 keV $\gamma$ ray resulting in scintillation photons reaching the bottom end of the scintillator. This step checks to ensure that the first particle created in the simulation after the primary $\gamma$ is an electron, that this electron was created via the photoelectric effect (as opposed to Compton scattering), and that the total energy deposited in the scintillator was equal to 511 keV. The decision to exclude Compton scattered events from the LRFs is discussed in detail in Section 4.2.

Once an event survives this screening process, the “real” location in the crystal at which scintillation occurred – taken to be the position at which the photoelectron was created in the simulation – is determined. Based on this position, the closest point on the interaction grid (Figure 3.2a) is found and the responses of all SiPM pixels for that event are stored. The response of each pixel is taken to be the number of scintillation photons striking the pixel that survive a Monte Carlo checking procedure to incorporate the PDE of the SiPM [44].

After the response information from all simulated events has been stored, the average responses $\bar{n}_i = \{\bar{n}_i^1, ..., \bar{n}_i^M\}$ for an array of $M$ SiPM pixels – where $\bar{n}_i^m$ is the average response of SiPM pixel $m$ for a 511 keV scintillation event at point $i$ in the bottom-left quadrant of the interaction grid – are determined. This is done by summing the response vectors $n_i^j$ from each event occurring at a given point $i$, and normalizing these responses to the number of events that occurred at that point. In other words, if $J$ events are binned into grid point $i$, and $n_i^{ij}$ represents the SiPM
Figure 3.2: (a) Schematic representation of the virtual 3D grid of $20 \times 20 \times 26$ points referred to as the interaction grid that was used to construct the LRFs. The spaces enclosed by any eight neighboring points (brown shaded area) are referred to as interaction regions. Points in the grid are 2.52 mm apart in the x and y directions, and 1 mm apart in the z-direction. (b) Beam positions (shown as black dots) used to construct the LRFs. A total of 30,000 511 keV $\gamma$ rays at normal incidence to the scintillator face were simulated at each of the $10 \times 10$ positions shown. Each event is then binned into the closest point on the 3D interaction grid (Figure 3.2a) and the positions of scintillation photons reaching the bottom of the LYSO crystal are recorded for events at each of the $10 \times 10 \times 26$ grid points in the bottom-left quadrant of the scintillator. The responses for the remaining three quadrants are generated by symmetry. The red circle in the upper-right corner indicates the position (24, 24), which is referred to in subsequent figures.
pixel responses for event $j$ at point $i$, we have:

$$n^i = \frac{1}{J} \sum_{j=1}^{J} n^{i,j}, \quad (3.1)$$

where the response vectors $n^{i,j}$ are summed component-wise. The average responses of the interaction grid points in the remaining three quadrants of the scintillator are then determined from the responses in the bottom-left quadrant by symmetry.

The next and final step is to perform 3D interpolation in the interaction regions between the grid points. This results in a continuous function providing the average set of SiPM responses $\bar{n}(R) = \{\bar{n}_1(R), ..., \bar{n}_M(R)\}$, as a function of the 3D interaction position $R$ of a 511 keV scintillation event. The functions $\bar{n}_m(R), 1 \leq m \leq M$, are the LRFs, which provide the expected response of each SiPM pixel $m$ as a function of $R$. For this application, a linear interpolation function was used, resulting in a set of 8 parameters for each interaction region that are used to calculate the expected set of responses for events occurring in that region. These parameters are the eight constants $a_{m,k}^j$ in the linear interpolation function

$$\bar{n}_m^j(x,y,z) = a_{m,0}^j + a_{m,1}^j x + a_{m,2}^j y + a_{m,3}^j z + a_{m,4}^j xy + a_{m,5}^j xz + a_{m,6}^j yz + a_{m,7}^j xyz, \quad (3.2)$$

where $\bar{n}_m^j(x,y,z)$ is the average response of SiPM pixel $m$, given a 511 keV scintillation event at a position $R = (x, y, z)$ within the $j$th interaction region. An example of these responses is shown in Figure 3.3 for two different SiPM pixels.

Once this interpolation has been performed, the LRFs are assumed to be linear in the deposited energy. This assumption requires that the light yield of the scintillator material be approximately linear in the deposited energy, which is a common assumption for scintillators [66]. With this assumption, the LRFs take on the form.
Figure 3.3: (a) A two dimensional slice of the 3D LRF for SiPM pixel number 36 with a z-coordinate of 10 mm; i.e. the average number of scintillation photons hitting SiPM pixel 36 as a smooth function of the (x,y) position of a 511 keV scintillation event for events with a z-coordinate of 10 mm. (b) A different slice (z = 23 mm) of the LRF for pixel 36. (c) A 2D slice (z = 10 mm) of the LRF for SiPM pixel 54. (d) A schematic diagram of the SiPM pixel array illustrating the positions of pixels 36 and 54.
\[ \bar{n}_m(R, E) = \bar{f}_m(R) E, \]
where \( \bar{f}_m(R) \) is the average energy-independent response and \( E \) is the energy of the incoming \( \gamma \) ray. The former depends on the solid angle between the interaction position and the SiPM pixel, as well as various physical properties of the scintillator \[66\]. This is done so that the probability density function in Equation (3.4) can be maximized with respect to the energy \( E \) analytically (see Equation (3.5)), allowing for the MLE of energy without having to spend additional computational resources on maximizing an extra parameter (see Section 3.2.4). The energy-independent response functions \( \bar{f}_m(R) \) can then be determined by normalizing the average response functions \( \bar{n}_m(R, E) \) to 511 keV. Equivalently, this can be achieved by normalizing the constants \( a_{j,m,k} \) in Equation (3.2) to 511 keV to obtain functions \( \bar{f}_m^j(R) \) for the energy-independent response of SiPM pixel \( m \), given an interaction at position \( R \) within the \( j \)th interaction region.

### 3.2.3 Probability Density Function for a Set of SiPM Responses as a Function of the Interaction Position

In order to perform MLE to reconstruct event information, an appropriate probability density function must be determined which describes the likelihood of measuring a set of responses \( n = \{n_1, ..., n_M\} \) as a function of the interaction position \( R \) and incoming \( \gamma \) ray energy \( E \). The number of scintillation photons produced within a scintillation crystal approximately obeys Poisson statistics \[74\], meaning that if the average number of scintillation photons produced is large then the number of scintillation photons striking SiPM \( m \) as a function of \( R \) and \( E \) can be approximated as a Gaussian random variable with mean and variance equal to \( \bar{n}_m(R, E) \) \[66\]. In this
case, the probability density of \( n_m \) scintillation photons hitting the SiPM pixel \( m \) as a result of a scintillation event at \( R \) by a \( \gamma \) ray with energy \( E \) is:

\[
\text{pr}(n_m|R, E) \propto \exp \left[ - \frac{(n_m - \bar{n}_m(R, E))^2}{2\bar{n}_m(R, E)} \right].
\]  

(3.3)

Assuming these responses to be statistically independent \[63\], the probability density function for measuring a set of responses \( n \) – up to a constant factor – is then \[66\]:

\[
\text{pr}(n|R, E) = \prod_{m=1}^{M} \exp \left[ - \frac{(n_m - \bar{f}_m(R)E)^2}{2\bar{f}_m(R)E} \right],
\]  

(3.4)

where we have used the relation \( \bar{n}_m(R, E) = \bar{f}_m(R)E \) (Section 3.2.2). At this point, the interaction position and energy of an event producing a measured set of responses \( n \) can be estimated by finding the values of \( R \) and \( E \) that maximize the probability density given by Equation (3.4).

### 3.2.4 Maximum Likelihood Estimation of Energy and Interaction Position

In this work, the logarithm of the probability density function (Equation (3.4)) is maximized with respect to the energy analytically, and with respect to the position numerically. First, a position-dependent energy estimate \( \bar{E}(R) \) is found by maximizing Equation (3.4) with respect to \( E \) analytically to obtain:

\[
\bar{E}(R) = \sqrt{\frac{\sum_{m=1}^{M} n_m^2/\bar{f}_m(R)}{\sum_{m=1}^{M} \bar{f}_m(R)}}.
\]  

(3.5)

Inserting this energy estimate into Equation (3.4) in place of \( E \) and taking the logarithm, one obtains (ignoring constant factors):

\[
\ln[\text{pr}(n|R, \bar{E}(R))] = - \frac{1}{\bar{E}(R)} \sum_{m=1}^{M} \frac{[n_m - \bar{f}_m(R)\bar{E}(R)]^2}{\bar{f}_m(R)}.
\]  

(3.6)
This expression is maximized with respect to $\mathbf{R}$ to find the most likely interaction position $\mathbf{\hat{R}}$, which results in a corresponding energy estimation of $\hat{E}(\mathbf{\hat{R}})$ via Equation (3.5). It should be mentioned that this energy estimate is an explicit function of the interaction position $\mathbf{R}$, and therefore the accuracy of the energy estimate depends strongly on the accuracy of the estimated position. If the estimated interaction position is far from the real interaction position – the position at which the first interaction between the $\gamma$ ray and the crystal took place in the simulation – the energy estimate will either be too high or too low (depending on the locations of the real and estimated positions) as a result of the discrepancy between the expected responses $\{\tilde{n}_m(\mathbf{R}, 511\text{keV})\} = \{\tilde{f}_m(\mathbf{R})\cdot 511\text{ keV}\}$, and the measured responses, $\mathbf{n} = \{n_1, ..., n_M\}$, where $\mathbf{R}$ is the position at which the photoelectron was created.

In order to maximize Equation (3.6) with respect to the 3D position $\mathbf{R}$, a *Hill Climbing* algorithm is employed [75]. The steps involved in this algorithm are as follows:

1. First, an initial guess for the $(x,y)$ position of the event is obtained by determining the position of the SiPM with the greatest signal. An initial guess for the $z$ coordinate is made by calculating the value of Equation (3.6) at a number of evenly spaced depths within the crystal at the determined $(x,y)$ starting position and selecting the depth that produces the largest value. Here the number of depths to calculate was chosen to be arbitrarily large (50) – resulting in the space between each depth being much smaller than the expected position resolution of the detector module – in an attempt to ensure an appropriate starting position.
2. Starting from the initial guess position, a step is made in the positive and negative directions along each coordinate axis by a predetermined distance (chosen to be 1/10th the size of the SiPM array, or 5.044 mm here), and the value of the function is calculated at these six positions, ignoring positions that fall outside of the scintillator volume. The initial step size should be large enough to be able to correct for an inaccurate starting position, but not so large as to unnecessarily increase the computation time. If any of the six neighboring positions produces a greater value of the function than the current position, the neighbor with the highest value is chosen as the new guess and the stepping procedure begins again, avoiding positions at which the function has already been calculated. If, on the other hand, the value at the current position is higher than all of the neighboring positions, the size of the step is made smaller by a predefined factor (chosen to be 2 here), and the stepping procedure is repeated.

3. This process is continued until the step size falls below a predefined threshold value (see paragraph below), at which point the current position is chosen as the best position estimate. The value of this threshold will determine the precision of the method, as well as influence the computation time.

An appropriate threshold value for the step size in this algorithm could be chosen by employing the algorithm to maximize a test function using several different threshold values, and determining the maximum threshold that produces an acceptable level of precision for the application at hand. For these simulations, the threshold was chosen to be arbitrarily small compared to the position resolution (∼0.005 mm here, or 1/10000th the size of the array), as obtaining optimal computational efficiency
was not the primary focus of this work. It should be mentioned that the success of this maximization algorithm is dependent on the smoothness of the function being maximized – which should be free of unusual spikes or valleys – as well as the accuracy of the initial guess position.

Given an inaccurate starting position, the algorithm will be prone to “climbing the wrong hill”, producing a local maximum rather than a global maximum. This issue will be discussed further in Section 3.3.1.

3.2.5 MLE Implementation on Simulated Data

The above procedure is implemented on simulated data by utilizing the following procedure. For each scintillation photon striking a given SiPM pixel $m$, a Monte Carlo selection process is employed to determine whether or not the photon should be included in the response based on the PDE of the SiPMs, as well as the wavelength of the scintillation photon. The response of the $m^{th}$ SiPM, $n_m$, is then taken to be the total number of scintillation photons striking the SiPM pixel that survive the PDE selection process. At present no attempt is made to treat the noise inherent in SiPMs, though this will be addressed in future simulations. Once a set of responses $n$ is obtained, the estimated parameters $\bar{R}$ and $E(\bar{R})$ are found via the methods described above. Simulations were run at various (x,y) locations for both the absorber and reflector versions of the simulation, and a comparison between the two configurations is presented in Section 3.3.
3.2.6 Event Windowing

In PET imaging, as well as other tomographic imaging modalities, there are certain types of events that one would like to discard when reconstructing an image (Section 1.1). The goal of any event selection process is to minimize the number of *non-ideal* events accepted while ignoring as few *ideal* events as possible. In the context of PET imaging, an ideal event would be a 511 keV $\gamma$ ray which undergoes the specific scintillation process one is hoping to measure (e.g. purely photoelectric scintillation in the LYSO crystal); a non-ideal event would be an event caused by any undesirable variation of this process, such as a $\gamma$ ray which undergoes Compton scattering in the scintillator followed by photoelectric scintillation of the scattered $\gamma$ ray. This type of event produces a distorted signal which will likely cause the estimated interaction position of the $\gamma$ ray to be inaccurate. For 511 keV $\gamma$ rays incident upon the LYSO crystal studied in the simulations presented herein, approximately 33% of interactions are purely photoelectric in nature, while the remainder are predominantly Compton scattered. It should be mentioned, however, that if a $\gamma$ ray undergoes Compton scattering but does not experience a significant change in its direction or energy, then it is still a useful event for PET imaging. Additionally, for noise-free images, it is advantageous to exclude events that have been Compton-scattered prior to interacting with the detector, as discussed in Section 1.1.

The two main techniques that are used to discard these types of events in MLE reconstruction are *energy windowing* and *likelihood windowing*. Energy windowing, as discussed in Section 1.1, is the process of discriminating against events based on whether or not their reconstructed energy is within a predefined range centered
about the photopeak of the reconstructed energy spectrum (i.e. the window). This technique has little effect on the accuracy of the reconstructed interaction positions (see Section 3.3.3), but is of critical importance in image reconstruction, as it is the primary defense against events in which one or both of the annihilation $\gamma$ rays have been scattered prior to reaching the detector, due to the measurable loss in energy experienced by the $\gamma$ rays in the scattering process. Likelihood windowing, on the other hand, is traditionally a method in which the probability that the measured responses of the detector module were the result of a 511 keV scintillation event at the estimated position is compared to a predefined threshold. If this probability is lower than the threshold, it is assumed that the event did not come from a $\gamma$ ray in the photopeak. This method is useful for detector systems that utilize the sum of the response signals to estimate the energy of the incident gamma, as the accuracy of this technique can degrade near the edges of the scintillator volume, particularly if an absorptive wrapping is used. Likelihood windowing is therefore used in addition to energy windowing to prevent scattered events from being used in the final image.

For the detector module design herein, the traditional method of likelihood windowing would be of little benefit, as the energy of the $\gamma$ ray is already being estimated using MLE. We therefore present a variant of likelihood windowing for detector systems with accurate energy estimation capabilities. This method, which is discussed in detail below, is a way of discriminating against events that were inaccurately reconstructed by the MLE process. This technique stems naturally from the concept of MLE and can help to eliminate scattered events for which the energy was incorrectly estimated as being inside of the photopeak, as well as discriminate against events that scatter inside of the scintillator, which produce misleading position and energy
estimates.

There are several factors that must be considered when attempting to determine optimal likelihood and energy acceptance windows, such as which performance metrics of the detector are most relevant for the imaging modality in question. Imposing any event windowing always comes at the cost of decreased detection efficiency (see Section 3.3.4), meaning that the task at hand is to strike a balance between the performance and the efficiency of the detector. The methods of energy windowing and likelihood windowing were evaluated using two different performance metrics – one of which can only be determined using simulations – and the results of this analysis are discussed in Section 3.3.3.

Energy Windowing

By running simulations with a monoenergetic beam of $\gamma$ rays and performing MLE on each event to produce energy estimates, one observes a reconstructed energy distribution characterized by a Gaussian photopeak centered at the primary $\gamma$ ray energy (511 keV for PET imaging), with a tail in the lower energy ranges due to Compton Scattering and other energy losses (Section 3.3.2). This energy distribution can then be used to determine an appropriate energy window for the application (see Section 3.3), within which a reconstructed event will be accepted for use in image formation assuming coincidence with an opposing detector is observed. The largest energy window that would be reasonable to employ for PET imaging would be the smallest window that contains the entirety of the reconstructed photopeak. Employing a small window will reduce the fraction of accepted events that were scattered before reaching the detector, but will also decrease the detection efficiency
of the system (Section 3.3.4); conversely, employing a large energy window will result in the inclusion of more Compton scattered events. The effects of energy windowing on the position resolution and detection efficiency of the detector module are discussed in Section 3.3.3.

Likelihood Windowing

Since MLE is based on determining the values of parameters \( R \) and \( E \) that maximize a probability density function (Section 3.2.3), a practical method of event selection is simply to reject events that are not “likely enough”. In other words, once the values of \( R \) and \( E \) have been found that maximize Equation (3.6), the value of the log-likelihood function at that point can be compared to a chosen threshold value, and the event can be discarded if its value falls below the threshold. From Equation (3.6) it can be seen that if the absolute value of the maximized log-likelihood function is small, then the measured set of responses \( \{n_m\} \) “closely resembles” the set of responses \( \{\bar{f}_m(R)\bar{E}(R)\} \) that one would expect to measure from a purely photoelectric scintillation event at position \( R \) with energy \( \bar{E}(R) \); in other words, \( n_m \approx \bar{f}_m(R)\bar{E}(R) \) for each \( m \). Similarly, if the absolute value of this log-likelihood is large, one can conclude that the measured set of responses do not correspond to the expected set of responses due to a photoelectric scintillation event at any position within the scintillator volume. Consequently, that particular event likely experienced a sub-optimal scintillation process (e.g. Compton scattering followed by energy deposition from both the Compton electron and the scattered photon), and therefore would likely have an inaccurately reconstructed position and/or energy. To be clear, the method described here differs from the traditional notion of likelihood windowing in that the
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log-likelihood function here (Equation 3.6) uses the estimated energy $\bar{E}(\bar{R})$, providing a measure of the accuracy of the reconstructed variables, whereas the log-likelihood function for conventional likelihood windowing assumes an energy of exactly 511 keV in order to discriminate against events that did not come from the photopeak.

Likelihood windowing is beneficial for detector systems employing MLE to reconstruct the position and energy of incoming $\gamma$ rays, as without it any measurable response of the detectors will be treated as a valid scintillation event, resulting in a significant amount of noise from scattering within the scintillator and other processes. Much of this noise can be eliminated through energy windowing (Section 3.3.3), but there may also be events with reconstructed energies in the photopeak whose likelihood values are too low for the measured responses to have come from ideal scintillation events. This technique is very effective in MLE and can improve both energy resolution and the size of the tails of the reconstructed position distributions, as discussed in Section 3.3.3.

A simple method for determining an appropriate threshold value for any form of likelihood windowing was described by Hesterman et al. [76], and is reviewed here. First, an ordered list of likelihood probabilities is generated by performing MLE on the events from the LRF simulations and sorting the resulting log-likelihood values from lowest to highest. The threshold value is then chosen to be the value in the list that allows a desired percentage of events – referred to here as a likelihood acceptance rate (LAR) – to be accepted. For example, with an ordered list of likelihood values from 10000 events, using the 2000th value in the list as a threshold value will result in an LAR of approximately 80% [76]. It is possible to create several such lists for different regions of the scintillator volume, resulting in a different threshold value for
each region. In this case the log-likelihood of an event is compared to the threshold value for the region of the detector volume in which the interaction position was reconstructed.

For our setup it was found that the distributions of maximized log-likelihood values from events occurring in different parts of the scintillator all possessed roughly the same peak value, but that the length and size of the tail extending in the negative direction varied for different interaction positions (see Figure 3.4), meaning that using a single likelihood threshold value for all events would be insufficient. Consequently, the scintillator volume was divided into *likelihood regions* (described below), and an ordered list of log-likelihood values was constructed for each region.

The likelihood regions were created by dividing the scintillator face into an 8 x 8 array of equal-sized squares and dividing the scintillator into 5 equal-sized layers in the z-direction, resulting in a 8 x 8 x 5 array of regions, each of size \(6.305 \times 6.305 \times 5\) mm\(^3\). These particular dimensions were chosen in order to utilize the simulations used to make the LRFs (which were only run in the bottom-left quadrant of the detector, cf. Figure 3.2b) in order to construct the ordered lists of likelihood values. The number of regions in the x- and y-directions should be an even number so that the lists generated by the LRF simulations can be easily extended to the other three quadrants of the detector by symmetry. Additionally, these 3D regions should be small enough to contain useful information about how the distribution of maximized probabilities changes with interaction position, and large enough to contain a sufficient number of events in order to construct an accurate list of values. For this particular setup, an 8 x 8 x 5 array of regions allows for the collection of at least 2500 likelihood values for each region from the LRF simulations and provides the ability to obtain likelihood
Figure 3.4: Example of two maximized log-likelihood distributions. Each simulation consisted of 30,000 511 keV gammas at normal incidence to the scintillator face at the indicated (x,y) positions (based on the coordinate system seen in Figures 3.1 and 3.2), and both plots include events occurring at any DOI. The peaks of the distributions occur at approximately the same location, but the size of the tails differs across the scintillator volume, necessitating the division of the volume into likelihood regions. Each region employs a threshold value for likelihood windowing based on the shape of its distribution.
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thresholds that accept a desired percentage of events to within a few percent, which was sufficient for this study. To improve the accuracy of the likelihood thresholds, a greater number of regions – and therefore simulations with more events – should be used.

3.3 Simulated Results

3.3.1 Position Resolution

By using the MLE methods described in Section 3.2.3 on individual simulated events to reconstruct the 3D interaction position and energy of the incoming $\gamma$ ray, one can evaluate the spatial resolution in various regions of the scintillator by plotting histograms of the difference between the estimated and real positions along each axis for several events, where the real position of a scintillation event is taken to be the position at which the first interaction between the $\gamma$ ray and the scintillator took place for that particular event. For a purely photoelectric scintillation event, this would be the position at which the photoelectron was created, and for events that undergo Compton scattering prior to scintillating, this would be the position at which the first Compton scattering occurred. This resolution was seen to depend on the (x,y) position of the incident $\gamma$ ray, as well as the DOI of the event.

In general, scintillation events that occur near the bottom of the crystal are more accurately reconstructed, which is likely due to the fact that the majority of scintillation photons reach the photosensitive layer without being absorbed in the crystal. For interactions occurring near the top of the crystal, the percentage of scintilla-
tion photons that are absorbed is much higher due to the increased distance to the photosensitive layer, resulting in less accurate position reconstruction. A promising solution to this issue which was recently explored by Shaart et al. [62] is to employ a front-end read-out design in which the $\gamma$ rays enter through the photosensitive layer, rather than through the scintillator directly. This design ensures that the majority of events scintillate near the photosensitive layer, improving position resolution, and may be explored by our group in the future (Section 4.4).

Simulations consisting of $\sim 250,000$ 511 keV $\gamma$ rays at normal incidence to the detector face were performed at two different positions, and histograms of the difference between estimated and real positions for each event were plotted. The full width at half maximum (FWHM) value was found directly from the histograms for each distribution. It should be noted that although the FWHM values are used to characterize the spatial distributions, these distributions are not Gaussian in nature, and possess a sharp peak with wide tails, as seen in Figures 3.5 and 3.6. These figures depict the same simulated data reconstructed using two different starting positions for the Hill Climbing technique – the (x,y) position of the maximum signal, and the center of gravity of the signals, respectively – highlighting the dependence of the Hill Climbing algorithm on the choice of starting position. It should be noted that event windowing has not been applied when generating the spectra in Figures 3.5 and 3.6. A comparison of the FWHM in the x, y and z directions versus the z-coordinate of interaction of the events for simulations at two different (x,y) positions, for both the absorber and reflector configurations, can be seen in Figure 3.7.

It is seen in Figure 3.7 that the reflector configuration consistently outperforms the absorber configuration in terms of reconstructed position resolution, which is
Figure 3.5: Sample distributions of the difference between the estimated and real scintillation positions in the x-direction. Here the real position is defined as the position at which the $\gamma$ ray first interacts with the scintillator, either via the photoelectric effect or Compton scattering. The spectra all possess a sharp peak and wide tails. The spikes observed in the spectra are the result of the Hill Climbing algorithm (Section 3.2.4) finding local maxima instead of the global maximum. Figure 3.6 illustrates the same spectra using a different starting position for the Hill Climbing procedure.
Figure 3.6: Similar to previous figure, but with the (x,y) starting position in the Hill Climbing maximization procedure determined by the center of gravity of the response signals. This technique works well in the center of the crystal, but produces artifacts near the edges (plots (c) and (d)), where the center of gravity of the signals is not indicative of the true (x,y) position of the interaction.
Figure 3.7: FWHM of the difference between estimated and real scintillation positions along all three spatial axes for the absorber and reflector configurations. A total LAR of 85 % is applied and the error bars represent a statistical uncertainty of $\pm 3\sigma$. From plots (c) and (d), it is seen that the reflector configuration outperforms the absorber configuration for interaction positions far from the center of the scintillator, most notably in the z-direction. The dip observed in the FWHM values in the z-direction for the last set of data points in plots (a) and (c) is due to the spectrum being cut-off by the proximity of the top scintillator face.
Figure 3.8: Estimated positions for the reflector configuration at several test beam locations. Each beam consisted of 50,000 511 keV $\gamma$ rays at normal incidence to the crystal face. The centers of the blue boxes indicate the peaks of the estimated position spectra, and the width and height of the boxes indicate the FWHM in the x- and y-directions, respectively. Only events in the bottom (a) 10 mm and (b) 25 mm were considered. For each event, both the center-of-gravity and maximum signal starting positions were found for the hill climbing method (Section 3.2.4), and the starting position which produced a higher value of the log-likelihood function was used.
attributable to the increased amount of measured light obtained per event. For events scintillating in the bottom 10 mm of the crystal – which corresponds to the typical thickness of a scintillation detector used for PET imaging \[8\] – the reflector configuration is able to achieve < 0.9 mm resolution in all three spatial directions for all \((x,y)\) positions, reaching a minimum FWHM value of \(\sim 0.5\) mm for events occurring near the center of the crystal. Additional simulations were run at several locations on the crystal face for the reflector configuration, and plots of the estimated \((x,y)\) positions can be seen in Figure 3.8. It is seen in these plots that the FWHM in a given direction generally increases with increasing distance from the crystal center along that direction.

The absorber configuration manages to stay below \(\sim 1.2\) mm FWHM in the bottom 10 mm of the crystal for all \((x,y)\) positions and is also capable of achieving \(\sim 0.5\) mm resolution near the center of the crystal. The largest difference between the two configurations is observed near the edges and corners of the scintillator, where the dramatic reduction in measured light significantly impacts the ability of the absorber configuration to estimate the DOI of events, as seen in Figures 3.7a and 3.7c, resulting in FWHM values that are up to two times larger than those from the reflector configuration.

### 3.3.2 Energy Resolution

Examples of the reconstructed energy spectra for both configurations at two different \((x,y)\) interaction positions can be seen in Figure 3.9. Additionally, a graph of energy resolution versus the z-coordinate of interaction for both configurations at two
Figure 3.9: Reconstructed energy spectra examples for the absorber and reflector configurations. The resolution is given by the FWHM of the photopeak as a percentage its mean; events from all DOIs were included in the spectra. The energy resolution for the reflector configuration remains relatively constant across different interaction positions, while the resolution of the absorber configuration degrades significantly with increased distance from the center of the scintillator. The fraction of total events in the Compton edge is higher near the edges of the crystal (plots (c) and (d)) due to the increased percentage of de-excitation γ ray/x-rays that escape from the scintillator without depositing energy.
Figure 3.10: Energy resolution (FWHM) versus the z-coordinate of scintillation for two different (x,y) positions. The error bars represent a statistical uncertainty of $\pm 3\sigma$. Plots (b) and (d) illustrate that the energy resolution for the reflector configuration varies slightly across (x,y) positions, but does not vary significantly across different DOIs. Conversely, plots (a) and (c) show that the energy resolution of the absorber configuration degrades significantly with increasing distance from the scintillator center ($\sim 10\text{-}18\%$ in the center compared to $\sim 20\text{-}35\%$ in the corner), as well as with increasing distance from the bottom of the scintillator.
different (x,y) positions is shown in Figure 3.10. The energy resolution for the reflector configuration remains relatively constant at $\sim 10\%$ regardless of the interaction position, whereas the resolution of the absorber configuration is strongly dependent on the 3D interaction position, ranging from $\sim 10\%$ for events occurring near the center of the scintillator face and close to the photosensitive layer, up to $\sim 25\%$ for events occurring near the corners in the top $\sim 5$ mm of the scintillator. For comparison, the intrinsic energy resolution of the LYSO crystal studied in this work – which results from the variance in the number of scintillation photons produced for a given amount of deposited energy – is approximately $8\%$ at 511 keV (cf. Table 3.1). As seen in Figures 3.10a and 3.10c, the energy resolution of the absorber configuration degrades with increasing distance from the center of the scintillator in the x-y plane (plots (a) and (c)), and with increasing distance from the photosensitive layer. In all cases the spectra consist of a Compton edge of events in which a portion of the $\gamma$-ray energy escapes from the scintillator volume, which can range from 0 to $\sim 400$ keV, and a Gaussian photopeak centered at the energy of the incoming $\gamma$ ray.

### 3.3.3 Event Windowing

As discussed in Section 3.2.6, the two main techniques for discriminating against unwanted events in MLE are energy windowing and likelihood windowing. By reconstructing the position and energy for every event in a simulation and storing information about the maximized value of the log-likelihood function (Equation (3.6)), likelihood and energy cuts can be applied after the reconstruction in order to determine how to best utilize these constraints in practice. The results of this analysis are
presented here for both energy and likelihood windowing.

**Energy Windowing**

The first performance metric used to evaluate the technique of energy windowing was the fraction of events accepted by the energy window that were non-ideal, as well as the fraction of total ideal events ignored by the window, where ideal and non-ideal events were defined in Section 3.2.6. Figure 3.11 shows the percentage of ideal events ignored, as well as non-ideal events accepted, as a function of the applied energy window. Each energy window here is determined as a percentage of the peak reconstructed energy value. For example, an energy window of 20% includes energies in the range (511 keV - 10%, 511 keV + 10%) for an energy spectrum with a peak of 511 keV. Additionally, the dashed magenta lines in the figure indicate the smallest symmetric energy window encompassing the entire photopeak – found by determining the first energy greater than the peak value in each energy histogram at which the bin content was less than 1 % of the content of the peak bin, which is roughly equivalent to employing a $3\sigma$ window for a Gaussian function – and the green dashed lines indicate the smallest energy window that accepts events in the Compton edge.

These plots indicate that the percentage of accepted events that are non-ideal does not vary significantly for different energy windows at a given interaction position until the window starts to accept events in the Compton edge (indicated by the green dashed line). Beyond this point, the percentage of accepted events that are non-ideal begins to increase due to the acceptance of Compton scattered events (cf. Figure 3.9). The percentage of total ideal events ignored by the window drops significantly with increasing window size until the entire photopeak is accepted, which is to be expected
Figure 3.11: Percentage of ideal events ignored as well as the percentage of accepted events that were non-ideal versus energy window. The error bars represent a statistical uncertainty of $\pm 3\sigma$ and the magenta and green vertical lines represent the smallest symmetric energy windows encompassing the entire photopeak and the tail end of the Compton edge, respectively. A window of 200% accepts all events. The percentage of ideal events ignored by the window drops until the entire photopeak is included. Additionally, the percentage of accepted events that are non-ideal increases once the window is large enough to accept events in the Compton edge.
assuming that the majority of the ideal events are reconstructed in the photopeak. These results suggest that an optimal energy window would encompass at least the entire photopeak, but none of the Compton edge (i.e. between the magenta and green lines).

Additionally, energy windowing is a useful tool for discriminating against inaccurately reconstructed events – defined here as having a reconstructed position greater than 1 mm from the true position along a given axis – as seen in Figure 3.12. It is seen from these plots that the percentage of accepted events with inaccurate position reconstructions increases until the entirety of the photopeak is accepted in the window (indicated by the dashed line), at which point the percentage plateaus.

**Likelihood Windowing**

As described in Section 3.2, the method of likelihood windowing consists of comparing the maximized value of the log likelihood function (Equation (3.6)) for a given event to a predetermined threshold, which is based on a desired acceptance rate, and discarding the event if the value falls below the threshold [77]. Additionally, as mentioned in Section 3.2.6, the likelihood windowing used in this work differs from the traditional notion of likelihood windowing in PET imaging, which is a technique used to discard events that are not in the photopeak. In this work, likelihood windowing refers to a technique in which the probability that a measured set of responses \( \{n_m\} \) was caused by a purely photoelectric scintillation event with interaction position \( \vec{R} \) and energy \( E(\vec{R}) \) is compared to a threshold value in order to discard “unlikely” events (see Section 3.2.6).

Employing likelihood windowing is seemingly most useful for eliminating
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Figure 3.12: The percentage of accepted events whose reconstructed positions were inaccurately reconstructed are plotted versus the applied energy window. No likelihood windowing is applied, and the dashed vertical lines indicate the smallest symmetric energy window encompassing the entire photopeak. The notable difference in the z-direction in plots (a) and (d) is due to the position resolution at these positions seen in Figures 3.7a and 3.7d. The percentage of accepted events that were inaccurately reconstructed for both configurations is seen to plateau once the full photopeak is accepted into the window.
inaccurately reconstructed events (defined in Section 3.3.3). Figure 3.13 illustrates the effect of likelihood windowing on the percentage of accepted events whose positions were inaccurately reconstructed. This figure demonstrates that likelihood windowing has a significant impact on the percentage of accepted events that were inaccurately reconstructed down to a certain acceptance rate (in this case $\sim 60$-$85\%$ likelihood acceptance), while at lower acceptance rates the additional benefit is marginal. For example, for the reflector configuration, going from a 100\% acceptance rate down to a 60\% acceptance rate lowers the percentage of accepted events that were inaccurately reconstructed by approximately 8\% for events occurring in the center of the crystal, and choosing an acceptance rate lower than 60\% results in an additional $\sim 2\%$ decrease at most.

This particular metric seems to suggest that an LAR of $\sim 60$-$85\%$ would be desirable for this configuration. It must be taken into consideration, however, that for an acceptance rate of 85\%, approximately 12-32\% of the total ideal events will be discarded (for the reflector configuration, depending on the position of interaction), and roughly 45-60\% of the events that are accepted will be non-ideal events (defined in Section 3.3.3), as seen in Figure 3.14. Furthermore, the percentage of accepted events that were inaccurately reconstructed begins to increase for events near the edges and corners of the crystal for both configurations if the applied likelihood window is too narrow, as seen in Figures 3.13c and 3.13d.

**Optimal Thresholds for Event Windowing**

From the results discussed above, it is evident that employing a combination of energy windowing and likelihood windowing is the most effective way to reduce
Figure 3.13: The percentage of accepted events that were inaccurately reconstructed for various LARs are graphed. The plots include events from all DOIs, and no energy windowing is applied. The dashed line indicates an LAR of 85%. It is seen in plots (a) and (b) that, for $\gamma$ rays incident on the center of the scintillator, an LAR of $\sim 60$-85% effectively minimizes the percentage of accepted events with inaccurate position reconstruction. In the corner of the crystal, lower LARs are seen to increase this percentage.
Figure 3.14: Percentages of ideal events ignored and of accepted events that are non-ideal versus the applied LAR for two different (x,y) positions. The error bars here represent a statistical uncertainty of ±3σ, and the dashed lines represent an 85% LAR. The percentage of accepted events that are non-ideal remains relatively constant across different LARs for events in the center of the crystal, while for events near the corner (plots (c) and (d)) likelihood windowing is seen to have a slightly negative impact on the percentage of accepted events that are non-ideal. Additionally, the percentage of ideal events ignored decreases approximately linearly with increasing LAR.
noise from inaccurately reconstructed and scattered events and to improve detector performance in terms of position and energy resolution. Based on Figure 3.13, it is clear that an LAR of $\sim 60-85\%$ effectively minimizes the percentage of accepted events that were inaccurately reconstructed across most interaction positions for the reflector configuration, suggesting that an 85\% LAR would be the highest rate that is reasonable to employ for this setup. Following from this, Figure 3.15 demonstrates the combined effect of likelihood and energy windowing.

These plots show the percentage of accepted events that were inaccurately reconstructed as well as the resulting detection efficiency, for various energy windows and a constant LAR of 85\%. It is seen that the percentage of accepted events with inaccurate position reconstruction increases approximately linearly with the detection efficiency until the entire photopeak is included in the energy window (magenta line), implying that an appropriate energy window must be determined by choosing the lowest detection efficiency that one is willing to allow in exchange for fewer inaccurately reconstructed events. Beyond this point, the percentage of accepted events with inaccurate position reconstruction begins to increase non-linearly with the detection efficiency for events in the corner (plots 3.15c and 3.15d) due to the large fraction of total events that lie in the Compton edge for those energy spectra (cf. Figures 3.9c and 3.9d). Events in the Compton edge are more likely to be inaccurately reconstructed by MLE as the LRFs are created using purely photoelectric scintillation events in which the full energy of the incoming $\gamma$ ray is deposited in the scintillator.
Figure 3.15: Percentage of accepted events with inaccurately reconstructed position versus detection efficiency (see Section 3.3.4) for a number of energy windows. An LAR of 85% is employed and the percentages directly above or below each set of points indicate the energy window. The vertical lines indicate the smallest symmetric energy window containing the entire photopeak, and the height and width of the boxes represent statistical uncertainties of $\pm 3\sigma$. The percentage increases with wider energy windows, and in plot (d) it is seen that this percentage does not increase until the window is wider than the photopeak, at which point it begins to accept events in the Compton edge (cf. Figures 3.9c and 3.9d).
3.3.4 Detection Efficiency

One of the properties of a PET detector module that is crucial for being able to produce quality PET images with relatively low data acquisition times is the detection efficiency, which is defined as the fraction of 511 keV $\gamma$ rays incident on the scintillator crystal that interact with the detector and survive the windowing processes employed. Since PET imaging relies on the measurement of two $\gamma$ rays in coincidence, it is important to consider the coincidence detection efficiency, defined as the fraction of $\gamma$-ray pairs – each incident on one of a set of two opposing detector modules – that both scintillate and survive the event windowing processes in their respective modules. The coincidence detection efficiency of a PET detector system has a significant impact on the data acquisition time that is needed to produce a high-quality image and should be maximized in order to reduce acquisition time. As this efficiency is proportional to the square of the detection efficiencies of the individual modules, it is therefore of critical importance to maximize the detection efficiency of each individual detector module.

An important consideration for detectors employing likelihood or energy windowing (Section 3.2.6) is that these windowing techniques effectively reduce the detection efficiency of the system. For example, if the detection efficiency of a scintillator is 70% using a particular energy window and an LAR of 50% is employed, the resulting detector efficiency will be 35%. This would result in a coincidence detection efficiency of only 12.25%.

For the 25 mm-thick LYSO scintillator simulated herein, the average single-module detection efficiency is $\sim$ 70% for $\gamma$ rays incident on the center of the scintillator (see
Table 3.2). Additionally, the simulation data can be cropped in the z-direction to determine the detection efficiency for LYSO crystals less than 25 mm thick. Figure 3.16 shows the detection efficiency of a LYSO scintillation crystal as a function of thickness from 1 mm to 25 mm. It should be noted that these values were found by disregarding events that scintillated farther from the top face of the scintillator than each thickness, and as such the detection efficiency values in Figure 3.16 represent a lower bound on the detection efficiency one could expect with a LYSO scintillator of each thickness. This is due to the improved energy resolution that would result from decreasing the distance from the scintillation event to the SiPM layer. For example, events that scintillate in the top 5 mm of a 25 mm LYSO crystal will produce a wider energy distribution than events from a 5 mm crystal due to the lower fraction of scintillation photons that reach the SiPM layer, meaning that the 5 mm crystal will have better detection efficiency provided the energy window used is based on a percentage of the peak energy. For the prototype that will be constructed (see Section 4.4), a thickness of 15 mm was chosen to improve position and energy resolution, resulting in an estimated detection efficiency of $\sim 60\%$ for a single module (for scintillation events in the center of the crystal) or a coincidence detection efficiency of $\sim 36\%$. 
Table 3.2: Detection efficiency of the simulated LYSO scintillator setup for two particular thicknesses (from Figure 3.16) for $\gamma$ rays incident on the center of the scintillator. Statistical uncertainties were obtained by analyzing several identical simulations.
Figure 3.16: The detection efficiency of the reflector configuration is plotted for various scintillator thicknesses for beams incident at (a) (0,0) and (b) (24,24). The error bars represent a statistical uncertainty of $\pm 3\sigma$ and an energy window of $\pm 2\sigma$ of the relevant photopeak is employed. Efficiency values for each thickness were obtained by disregarding events that scintillated farther from the top face of the scintillator than the thickness in question. A future prototype will have a thickness of 15 mm in order to improve position and energy resolution compared to the 25 mm scintillator simulated here, resulting in an expected detection efficiency of $\sim 60\%$ for $\gamma$ rays incident upon the center of the scintillator, decreasing to $\sim 40\%$ near the corner.
Chapter 4

Conclusions and Future Work

4.1 Summary of Simulated Results

The simulated work in this thesis was performed in order to evaluate the performance of a PET detector module design consisting of a monolithic LYSO scintillation crystal coupled to an 8\times8 SiPM array, as well as to study the effects of two of the primary event windowing techniques used in $\gamma$-ray detection – energy windowing and likelihood windowing.

First, a comparison of two versions of the simulated module – one with an absorptive coating, and the other with a reflective coating – was performed. It was found that the reflector configuration was able to achieve slightly better resolution of the 3D position of interaction of $\gamma$ rays than the absorber configuration for events scintillating in the bottom $\sim 10$ mm of the crystal. For events scintillating in the top $\sim 10$-15 mm of the crystal, the reflector configuration displayed a clear advantage over the absorber configuration, in particular for the reconstructed $z$-coordinate of
In terms of the ability of each module to resolve the energy of incoming $\gamma$ rays, the reflector configuration was seen to consistently produce an energy resolution of $\sim 10$-$11\%$ regardless of the position of the scintillation event, while the absorber configuration yielded an energy resolution of $\sim 13$-$22\%$, depending on the scintillation position. The energy resolution of the absorber configuration was seen to degrade significantly for events occurring near the top or sides of the crystal due to a significant loss of scintillation light through absorption, reaching a maximum value of $\sim 35\%$ for events occurring in the top $\sim 5$ mm of the crystal near the corner, as seen in Figure 3.10c. Based on these results, it is clear that if the reconstruction techniques described in Chapter 3 are to be employed to reconstruct the 3D position and energy of 511 keV $\gamma$ rays in a monolithic scintillator, the top and side faces of said scintillator should be covered in a reflective coating, rather than an absorptive coating.

In terms of the two event windowing techniques analyzed herein, it was found that both energy windowing and likelihood windowing can have a significant impact on several performance metrics of the detector module. The metrics explored here were the percentage of scintillation events accepted for image formation whose position estimates are incorrect (“inaccurate events”), the percentage of accepted events which did not undergo purely photoelectric scintillation and which deposited only a fraction of the $\gamma$-ray energy (“non-ideal events”), and the percentage of total events which underwent photoelectric scintillation and deposited 511 keV in the scintillator (“ideal events”) but are ignored by the window – all of which one hopes to minimize.

It was found that for energy windowing, there is an ideal range of windows which effectively minimizes the number of accepted events that are non-ideal as well as
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the number of ideal events ignored by the window. These windows should have a lower energy bound between the end of the Compton edge and the beginning of the photopeak. On the other hand, it is seen in Figure 3.12 that employing energy windows narrower than the photopeak can reduce the percentage of accepted events that were inaccurately reconstructed by a significant margin for the absorber configuration, and very slightly for the reflector configuration. Considering the number of ideal events that are ignored with these windows, however, it is clear that for the reflector configuration the window should at least encompass the entire photopeak.

The upper energy bound employed should extend at least until the end of the photopeak, and may be extended further depending on the energy estimation technique employed. Most detector modules use the sum of the response signals as a surrogate for the amount of energy deposited in the scintillator, in which case the upper bound may be extended indefinitely provided the radioisotope employed does not produce higher energy $\gamma$ radiation in addition to 511 keV $\gamma$ rays. For detectors employing statistical reconstruction methods for this energy an upper limit is useful, as it is possible for these techniques to overestimate the energy of the $\gamma$ ray regardless of the amount of scintillation light measured.

The technique of likelihood windowing explored in this work – which differs from the traditional notion of likelihood windowing (cf. Section 3.2.6) – was seen to be most useful for eliminating inaccurately reconstructed events. It was seen that for the configurations explored herein, an LAR of $\sim$ 60-85% effectively minimized the percentage of accepted events that were inaccurately reconstructed, and that for events occurring near the corners this percentage may actually increase if more stringent acceptance rates are employed. Additionally, it was found that likelihood window-
ing has a slight effect on the percentage of accepted events that are non-ideal, and that the percentage of ideal events ignored by the window decreases approximately linearly with increasing LAR. These results suggest that the lowest acceptance rate that should be employed for this particular setup is approximately 50-60%, and the highest rate that should be employed is $\sim 85$-90%.

### 4.2 Light Response Functions

When creating the LRFs for MLE of interaction position and energy in PET detector modules there are several important details to consider. Firstly, when analyzing simulations to generate the average responses of the SiPM pixels, events that undergo Compton scattering within the scintillator are not considered. This is because in addition to the energy deposited by the Compton electron, the scattered photon, which possesses less than 511 keV, can interact elsewhere in the scintillator volume. This type of event is undesirable for image reconstruction as the LOR between its reconstructed interaction position and that of another event in coincidence will be skewed compared to the actual trajectory of the $\gamma$ rays. Thus, even if the full 511 keV of the initial $\gamma$ ray is deposited in the scintillator for an event that begins with Compton scattering, the event is sub-optimal for image reconstruction purposes. By considering only ideal events (see Section 3.3.3) when constructing the LRFs, attempts can be made to discriminate against non-ideal events by using techniques such as likelihood windowing, as discussed in Sections 3.2.6 and 3.3.3.
4.3 General Conclusions

In this work, a monolithic LYSO scintillator-based PET detector module employing MLE techniques to estimate the interaction position and energy of incident gamma rays was simulated using the Geant4 simulation toolkit. Two versions of the detector module – one covered with an absorptive layer, and the other with a reflective Teflon layer – were simulated, and a performance comparison is presented. When wrapped in a reflective Teflon layer, the module achieves an average 3D spatial resolution on the order of 1 mm, and an average energy resolution of \( \sim 11\% \). When considering only the scintillation events that occur in the bottom 10 mm of the crystal, the 3D spatial resolution ranges from \( \sim 0.5 \) mm to \( \sim 0.9 \) mm FWHM. This represents an improvement compared to a standard PET detector module consisting of an array of \( 1 \times 1 \times 10 \) mm\(^3 \) crystals, which provides a 2D position resolution of \( \sim 1 \) mm with no depth-of-interaction information\[8\].

The simulated results in this work demonstrate that a PET detector module consisting of a monolithic LYSO scintillating crystal wrapped in a reflective layer and employing MLE for 3D position and energy reconstruction, will significantly out-perform the same setup wrapped in an absorbing layer in terms of several performance metrics, including the resolution of the reconstructed position and energy of incoming \( \gamma \) rays.

Additionally, a novel method of constructing the LRFs needed for MLE using Monte Carlo simulations is presented, as well as an evaluation of two prominent event windowing techniques for PET imaging – likelihood windowing and energy windowing. It is found that both energy windowing and likelihood windowing can be
effective tools for improving detector module performance in terms of several metrics, and that a combination of the two would be optimal for detector modules employing MLE to estimate the 3D interaction position and energy of annihilation $\gamma$ rays.

### 4.4 Future Work

A prototype of the reflector configuration presented here will be constructed in the near future in order to test the position and energy reconstruction methods described in Section 3.2. This prototype will use a 15 mm-thick LYSO scintillator rather than the 25 mm version presented here, due to the improved reconstruction performance for thinner crystals discussed in Sections 3.3.1 and 3.3.2. It should be noted that the plots in Figures 3.7 and 3.10 illustrating the position and energy resolution as a function of the z-coordinate of interaction for the reflector configuration are not directly indicative of the performance one would expect from a thinner scintillating crystal. In other words, a 10 mm LYSO crystal wrapped in a reflective layer would produce better position and energy resolution than the plots in Figures 3.7 and 3.10 would suggest, due to the decreased distance between the interaction point of the event and the top reflective layer on the crystal. Therefore, these plots serve as a lower bound on the performance that one could expect for crystals thinner than 25 mm with a reflective coating. A small-bore PET system employing this module configuration will have volumetric resolution of reconstructed images in the sub-millimeter range, energy resolution of $\sim 11\%$ and sensitivity – defined as the fraction of total positron annihilation events detected as true coincidence events – of $\sim 28\%$.

For this work, a 10 x 10 grid of evenly-spaced beam positions was used (Fig-
ure 3.2b) to create the LRFs needed to perform the reconstruction methods described in Section 3.2.3. This setup is not ideal, as the space between beams along the x and y axes is relatively large (\(\sim 2.5 \text{ mm}\)) compared to the desired position resolution of \(< 1 \text{ mm}\). Using a greater number of simulated beams in a given direction (located closer together) will likely result in better position resolution in that direction. Additionally, the space between beams need not be uniform and it would be advantageous to use more beams near the edges and corners of the crystal, where the expected set of response signals changes rapidly with interaction position due to the proximity of the reflective layer. This would not be necessary if the scintillator were covered in an absorptive layer. The limiting factor involved here is simply the time required to run the additional simulations and create the LRFs. These improvements will be incorporated into future simulations made by our group. Additionally, further improvements will be made to the analysis performed on the simulations to account for the noise found in SiPMs, which should improve the accuracy of the LRFs.

Another improvement that could be made to the LRFs would be to measure them experimentally, which would account for the noise observed in the response of each SiPM. This would involve first sending beams of 511 keV \(\gamma\) rays from a collimated positron-emitting source at normal incidence to the scintillator face at a given \((x,y)\) position, and subsequently sending similar beams towards the side of the scintillator face – in-line with the \((x,y)\) position of the first beam – at a given \(z\)-position. From the responses generated by the beam incident on the top of the scintillator the \((x,y)\) position of the event is known but the \(z\)-position of the scintillation is not. Similarly, for the responses generated by the beam incident on the side of the scintillator the \(z\)-position of each event is known but the \((x,y)\) position of each event is not.
By comparing the responses from each beam – for example by attempting to minimize the sum of the squares of the differences between pairs of responses – a subset of the responses from each beam position (top and side) can be assumed to have come from approximately the same (x,y,z) position within the scintillator, and the average of these responses can be assigned to the appropriate point on the interaction grid. This could be repeated with beams at normal incidence to the top face of the scintillator at the (x,y) beam locations used to create the LRFs via simulations here (Figure 3.2b), and for each z-position on the interaction grid at the x-location (or y-location) of each column (or row) of the interaction grid. Events which undergo Compton scattering inside the scintillator could not be entirely removed from the LRFs with this technique, but one could choose to discard events in which the maximum detected photosensor signal was sufficiently far from the incident beam position in an attempt to minimize the number of Compton events accepted for use in the LRFs.

As alluded to in Section 3.3.1, one very promising improvement for this type of detector module would be to employ a “front end” read-out in which the photo-sensor layer is placed on the top face of the crystal instead of the “back end” read-out discussed in this work. The distinct advantage of this type of setup would be that the majority of scintillation events would occur close to the photo-sensor layer (due to Beer’s Law [78]), resulting in high position resolution for most events. This would permit the use of an arbitrarily thick crystal to improve detector efficiency without sacrificing performance in terms of position resolution for interactions occurring close to the photo-sensor layer. Additionally, with a thick crystal, one could choose to accept or ignore events interacting far from the photo-sensor layer, depending on the
position resolution required for the task being performed. This type of setup has been simulated before [62] and is a promising area of research. One potential obstacle with such a configuration is that the SiPM array may cause scattering or absorption of the incoming $\gamma$ rays, thereby reducing detection efficiency and possibly introducing an additional source of noise. A monolithic detector module employing front end read-out and MLE will be simulated by our group in the near future.

Additionally, the Hill Climbing maximization technique discussed in Section 3.2.4 is likely not an optimal technique to employ in practice if the reconstruction methods discussed here are to be used in real-time. The algorithm does not have a predefined run-time – as the run-time depends on the nature of the function being maximized – and has the potential to find local maxima rather than global maxima if an inaccurate starting position is used, introducing a source of error. This is evidenced in Figures 3.5 and 3.6 in which two different starting positions were used to reconstruct the same simulated data. Due to these issues, a reliable algorithm with a predefined run-time, such as the contracting-grid algorithm explored by Hesterman [76], would be more appropriate.
List of References


[72] A. Phumpueok, W. Chewpraditkul, P. Limsuwan, and C. Wanarak, “Light output and energy resolution of Lu$_{0.7}$Y$_{0.3}$Al$_2$O$_3$:Ce and Lu$_{1.95}$Y$_{0.05}$SiO$_5$:Ce scintillators,” *Procedia Engineering*, vol. 32, pp. 564–570, 2012.


