The RatCAP Front-End Electronics

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ABSTRACT

The Center for Translational Neuroimaging of the Brookhaven National Laboratory has been studying the phenomenon of addiction, which has a direct impact on millions of people worldwide. This requires the development of new radiotracers for imaging specific neurotransmitter systems in the brain, and the design and implementation of novel imaging devices to measure the neuroactivity of the brain. The RatCAP, or Rat Conscious Animal Positron Emission Tomography (PET), is a head-mounted miniature PET scanner for brain metabolism imaging of awake rats with minimal mobility restriction to enable correlation with the animal's behavior.

The RatCAP detector is based on LSO scintillator crystals and avalanche photodiode (APD) arrays. The design of the RatCAP imposed stringent requirements on the read-out electronics. First, due to its size and limited power budget, VLSI of the front-end electronics was mandatory. Second, due to the weak signal to noise ratio from the APD detectors, the analog front-end noise had to be minimized, within the power budget, to provide the best possible timing resolution. Finally, the number of interconnections with the data acquisition system had to be minimal in order to maximize the animal's mobility.

This thesis presents the design and implementation of the ASIC for the RatCAP. The final ASIC integrates 32 channels consisting of a charge sensitive preamplifier, programmable gain, a bipolar shaping amplifier, and timing and energy discriminators. A novel 32-to-1 address and timing serial encoder is integrated on-chip to multiplex the acquired data through a single output. The ASIC was realized in 0.18 μm CMOS technology from TSMC, has a size of 3.3 mm x 4.5 mm, and power consumption of 117 mW. The ASIC is fully operational. Noise characterization led to a measured equivalent noise charge of 650 electrons rms with the APD biased at the input. A coincidence timing resolution of 6.7 ns FWHM was measured between two typical LSO-APD-ASIC modules using a $^{68}$Ge source (threshold at 420 keV). An energy resolution of 18.7% FWHM at 511 keV was measured for a $^{68}$Ge source.

The ASIC and the technology developed for the RatCAP have opened the door to the realization of many other systems, such as a PET-MRI scanner, and led to the granting of three patents and the publication of numerous scientific presentations.
RÉSUMÉ

Le Centre de neuroimagerie translationnelle du Brookhaven National Laboratory s’intéresse depuis plusieurs années au phénomène de la dépendance, qui touche des millions de personnes à travers le monde. Pour y arriver, le développement de nouveaux radiotraceurs sélectifs aux neurotransmetteurs d’intérêt et la conception de nouveaux dispositifs d’imagerie sont essentiels pour mesurer l’activité neurologique du cerveau. Le RatCAP, ou Rat Conscious Animal PET, est un scanner miniature et portable qui s’installe sur le crâne d’un rat pour obtenir l’imagerie TEP du métabolisme du cerveau chez le rat non-anesthésié pour ainsi permettre la corrélation avec le comportement de l’animal.

Le RatCAP utilise des cristaux de LSO couplés à une matrice de photodiodes à avalanche (PDA) comme détecteur. Le RatCAP comporte des défis de taille pour la réalisation de l’électronique. Premièrement, dû à la taille et la consommation de puissance limitée, l’intégration à très grande échelle de l’électronique est essentielle. Deuxièmement, étant donné que les détecteurs à PDA ont un rapport signal sur bruit faible, l’électronique analogique frontale doit être optimisée pour minimiser le bruit électronique et ainsi permettre d’obtenir la meilleure résolution temporelle possible. Enfin, le nombre d’interconnections avec le système d’acquisition doit être gardé au minimum pour maximiser la mobilité de l’animal.

Cette thèse présente la conception et l’intégration de l’électronique frontale pour le RatCAP. Le circuit final est composé de 32 canaux contenant un préamplificateur de charges, un gain programmable, un filtre bipolaire semi-gaussien ainsi que des discriminateurs de temps et d’énergie. Un encodeur série, qui multiplexe dans une sortie l’information temporelle et l’adresse du canal où l’événement a été détecté, est aussi intégré dans le circuit pour minimiser le nombre d’interconnections avec le système d’acquisition. Le circuit a été réalisé dans une technologie CMOS de 0.18 μm, mesure 3.3 × 4.5 mm² et consomme 117 mW. Le circuit est complètement opérationnel. Un bruit électronique de 650 électrons rms a été mesuré pour la chaîne analogique avec la photodiode à avalanche polarisée à l’entrée du circuit. La résolution temporelle pour deux modules de détection en coïncidence avec une source de 68Ge est de 6.7 ns FWHM (seuil à 420 keV). La résolution en énergie est de 18.7% FWHM pour une source de 68Ge.

Le circuit intégré et la technologie développés pour le RatCAP ont ouvert la voie à la réalisation de nombreux systèmes, tel un scanner TEP-IRM, ainsi que l’obtention de trois brevets et la publication de plusieurs communications scientifiques.
À Geneviève, Hélène et Marie-Claude, les trois femmes de ma vie.

À mon père Guy, ma source d'inspiration éternelle.
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<td>APD</td>
<td>Avalanche Photodiode</td>
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<tr>
<td>ASIC</td>
<td>Application Specific Integrated Circuit</td>
</tr>
<tr>
<td>BNL</td>
<td>Brookhaven National Laboratory</td>
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<tr>
<td>CFD</td>
<td>Constant Fraction Discriminator</td>
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<tr>
<td>CMOS</td>
<td>Complementary Metal-Oxide Semiconductor</td>
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<tr>
<td>CSG</td>
<td>Control Signal Generator</td>
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<tr>
<td>CSP</td>
<td>Charge Sensitive Preamplifier</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>DAC</td>
<td>Digital to Analog Converter</td>
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<td>DAQ</td>
<td>Data Acquisition System</td>
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<td>DOI</td>
<td>Depth Of Interaction</td>
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<td>FOV</td>
<td>Field Of View</td>
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<td>FWHM</td>
<td>Full Width at Half Maximum</td>
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<td>GSO</td>
<td>Gadolinium Oxyorthosilicate</td>
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<tr>
<td>LED</td>
<td>Leading Edge Discriminator</td>
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<tr>
<td>LOR</td>
<td>Line Of Response</td>
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<td>LSO</td>
<td>Lutetium Oxyorthosilicate</td>
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<tr>
<td>LVDS</td>
<td>Low-Voltage Differential Signaling</td>
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<tr>
<td>MOSFET</td>
<td>Metal-Oxide-Semiconductor Field-Effect Transistor</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>NEC</td>
<td>Noise Equivalent Count rate</td>
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<td>NIM</td>
<td>Nuclear Instrumentation Module</td>
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<td>Printed Circuit Board</td>
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<td>Rat Conscious Animal PET</td>
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<td>RMS</td>
<td>Root Mean Square</td>
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<td>TDC</td>
<td>Time to Digital Converter</td>
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<td>TSMC</td>
<td>Taiwan Semiconductor Manufacturing Company</td>
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<td>VLSI</td>
<td>Very Large Scale Integration</td>
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<td>ZCD</td>
<td>Zero-Crossing Discriminator</td>
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CHAPTER 1

Introduction

1.1 The History of Positron Emission Tomography Instrumentation

The evolution of instrumentation for Positron Emission Tomography (PET) always had the objective of improving the achievable spatial resolution and sensitivity. Of course, the advance in PET was also intimately coupled to advances in radiopharmaceutical technology and image reconstruction algorithms, without which those sophisticated instruments are meaningless.

Although PET started in the 50's, it was not until the early 90's that it made its major transition from the research laboratories to clinical use. This is a rather slow evolution compared to computed tomography (CT) and magnetic resonance imaging (MRI) which moved quickly from early laboratory experiments to wide-spread clinical use. It was the precise detection of cancer lesions, not possible with other imaging modalities, and the assessment of the therapeutic treatment of cancer, which was awaited by a large population of patients, coupled with the availability of the proper radiopharmaceuticals for oncology that kicked off the use of PET in medical clinics.

In the following paragraphs, a review of PET instrumentation is presented. It is not intended to be a complete review of the contributions from all the world class scientists who dedicated their lives to the field, but to outline the major milestones in PET instrumentation history, and have a better understanding of the state of the art systems currently being realized. Other historical reviews can be found in [BROWNELL, 1999][NUTT, 2002][MUEHLLEHNER and KARP, 2006].

1.1.1 1951: The First Positron Emission Tomograph

The first use of annihilation radiation following positron emission for medical imaging is attributed to Gordon L. Brownell, director of the Physics Research Laboratory of the Massachusetts General Hospital (MGH), in collaboration with William Sweet, Chief of the Neurosurgical Service also from MGH. The system, built in 1951, consisted of two
opposing $1 \frac{1}{4}'' \times 1 \frac{1}{4}'' \times 1 \frac{1}{2}''$ sodium iodide (NaI) crystals coupled to RCA 6199 flat-face photomultiplier tubes. The electronics consisted of tube amplifiers and cold-cathode glow tubes as counters. It was used for imaging patients with suspected brain tumors. They called those tests "positrocephalograms". This was the first clinical positron imaging device and is presented in Fig. 1.1. Those studies led to the first publication on positron imaging [SWEET, 1951]. The system contained several features that were incorporated into future positron imaging devices. For instance, data were obtained by translation of two opposed detectors using coincidence detection with mechanical motion in two dimensions. In the same year, Wrenn, Good and Handler (former President of the American Academy of Science), published an independent study on annihilation radiation detection [WRENN JR. et al., 1951].

1.1.2 1962: Multiple Detector Positron Imaging

The need for increased sensitivity pushed Brownell and his team to develop the first multiple detector positron imaging device in 1962 [BROWNELL et al., 1968]. The system consisted of two rows of nine detectors, each in coincidence with three detectors in the opposite row. The system could translate in one direction so that a two dimensional
1.1. THE HISTORY OF PET INSTRUMENTATION

image could be acquired. It is shown in Fig. 1.2. This system was also designed for brain imaging and served as a clinical scanner at MGH for over a decade.

The next milestone in the evolution of PET, was the implementation of a camera with a two dimensional detector array (see Fig. 1.3). The camera, named PC-I, was also developed by Brownell's group between 1968 and 1971 [Burnham and Brownell, 1972]. But the most important contribution of the PC-I to the PET field was in the introduction of filtered back projection for image reconstruction [Chesler, 1973]. From those data, David Chesler was able to produce three types of computed tomographic images: an emission image, a transmission image and an absorption-corrected emission image.
1.1.3 1973: Cylindrical Detector Arrays

The next logical step in PET instrumentation was the development of circular or cylindrical arrays of detectors, which was first proposed by James Robertson [ROBERTSON et al., 1973], from the Medical Department of Brookhaven National Laboratory, and Z.H. Cho. The apparatus, known as the BNL "head shrinker", was realized by Robertson in collaboration with Sy Rankowitz, William Higinbotham and Martin Rosenblum of the BNL Instrumentation Division. The system consisted of 32 detectors, first configured spherically, then in a single plane, with the even ones inserted radially and the odd ones axially, as presented in Fig. 1.4. Each detector was made of a 1" NaI crystal and a PMT. Unfortunately, due to limited sampling, lack of attenuation correction and lack of a proper image reconstruction algorithm, they were unable to obtain true reconstructed cross sectional images. The system was then transferred to McGill’s Montreal Neurological Institute. Proper image reconstruction were developed by Chris Thompson from McGill, and the "head shrinker" was modified to allow the patient to be scanned supine instead of seated [THOMPSON et al., 1975],[THOMPSON et al., 1976].
1.1. THE HISTORY OF PET INSTRUMENTATION

(a) PETT-II (b) PETT-III

Figure 1.5 Pictures of the PETT-II (left) and PETT-III (right) developed by the Phelps and Hoffman team [NUTT, 2002].

1.1.4 1973-1976: The First Whole Body and Commercial PET

Concurrently, another group headed by Michel M. Ter-Pogossian and formed by Micheal Phelps, Ed Hoffman and Nizar Mullani at Washington University in St. Louis, along with James Kelly Milam, Charles W. Williams, Terry D. Douglass, and Ronald Nutt from EG&G ORTEC were also investigating PET instrumentation. Starting in 1973, a series of tomographs were built: the PETT-I, the PETT-II and the PETT-III (see Fig. 1.5).

PETT stands for Positron Emission Transaxial Tomography. The PETT-II consisted of an hexagonal array of 24 NaI(Tl) detectors in coincidence, and made use of attenuation correction and a filtered back projection algorithm. All the electronics was NIM based. They started to build this system in December 1973, and the first data were acquired in January 1974. This scanner was used by the Phelps-Hoffman team to establish the math and physics of PET, and also to perform imaging of blood flow and metabolism in animals. The construction of the PETT-III started at the end of 1974. It was the first scanner intended for human PET. It consisted of 48 NaI(Tl) scintillators 5 cm in diameter and read out by PMTs, arranged in a hexagon. Sampling in this system was greatly improved by a combination of linear movement of the detector assembly and a 60 degree rotation of the gantry. A dedicated computer took care of the detector motion, gantry, bed, as well as image reconstruction and display. The realization of the PETT-III had a significant impact in the field of PET, as it lead to the first commercial PET scanner, the ECAT-II. This scanner, commercialized by EG&G ORTEC, had 96 3.75 cm diameter NaI(Tl) crystals. A PDP-11 computer with 32 kB of memory was used to control the scanner and reconstruct the images. The system was sold in 1978 for $600,000! The first
system was delivered to UCLA in 1976, which also coincided with Phelps and Hoffman moving from the University of Washington to UCLA.

1.1.5 1973-1978: The Introduction of the BGO Scintillator

Thus far, all the PET systems were using NaI(Tl) as a scintillator. But even though NaI(Tl) has high light output and a suitably fast decay time for coincidence detection, it is far from being ideal for PET. Its low density and effective atomic number limit the efficiency for 511 keV photon detection. Also, NaI(Tl) was difficult to use in dense arrays because of its hygroscopic nature. The quest for new scintillation materials for PET was ongoing, and the first alternative to NaI(Tl) was bismuth germanate (BGO). Weber at University of California, Berkeley, studied the luminescence of BGO in 1973 [WEBER and MONCHAMP, 1973], and Nestor and Huang characterized the scintillation properties of BGO in 1975 [NESTOR and HUANG, 1975]. The first evaluation of BGO for PET was performed by Cho and Farukhi [CHO and FARUKHI, 1977] and Derenzo [DERENZO, 1981]. Their findings led to the first research PET scanner using BGO, which was developed by Chris Thompson and his group at the Montreal Neurological Institute in 1978. The same year, EG&G ORTEC produced the first commercial tomograph using BGO, the NeuroECAT.

1.1.6 1979-1981: Analog Optical Multiplexing

While the 70’s saw the birth of ring and cylindrical tomographs, one of the main drawbacks of these geometries was the limited sampling. Tricks such as wobbling the detector array were used to improve the sampling, but still, more needed to be done. The first step toward the solution is attributed to Stephen Derenzo from Berkeley, who built a cylindrical tomograph in which the NaI scintillators were closely packed to limit dead space, and individually coupled to a quartz "lightpipe" which would bring the light to the bulky PMTs further back [DERENZO et al., 1979]. But it was the work of Charles Burnham on analog coding by optical multiplexing which allowed the acquisition of high resolution PET images without detector motion [BURNHAM et al., 1981][BURNHAM et al., 1985]. Burnham’s concept was to place individual small scintillators on a circular light guide with photomultipliers placed on the opposite side of the light guide, as illustrated in Fig. 1.6. Similar to the Anger Camera concept, by taking the ratio of 2 adjacent photomultiplier signals, the scintillator that detected the gamma ray could be identified.
1.1.7 1976-1980: Synthesis of FDG

Even though the evolution of radiopharmaceuticals is not covered in this historical review of PET instrumentation, it is worth mentioning that their development had a significant influence on the acceptance of positron imaging in clinical studies and the availability of funding for the realization of novel scanners. The radiopharmaceutical which had the biggest impact, and which is still the most widely used today, is $^{18}$F labeled 2-fluorodeoxy-D-glucose, known as FDG. FDG, which was developed by Al Wolf and Joanna Fowler's group at BNL [IDO et al., 1978], has a half-life perfectly suited for PET and allows precise values of energy metabolism in brain, heart and other organs.

1.1.8 1984-1985: The Block Detector

The optical multiplexing concept of Burnham presented in section 1.1.6 was using a continuous light guide, causing the light generated by a scintillator to spread considerably. Consequently, a large number of PMTs triggered for a single 511 keV photon and increased the spatial extent of dead time. Moreover, the light guide was expensive, difficult to manufacture and limited the serviceability of the scanner. To address those issues, Mike Casey and Ronald Nutt, from CTI, introduced the "block detector" [CASEY and NUTT, 1986][CASEY et al., 1988], where multiple crystals were encoded to a single position.
sensitive PMT. The first block detector had 4 PMTs with 8 BGO scintillators coupled to each of them, as seen in Fig. 1.7.

1.1.9 1989-1992: The Discovery of LSO Scintillator

Another major breakthrough in PET instrumentation was the discovery of Lutetium Oxyorthosilicate (LSO) by Charles Melcher [MELCHER and SCHWEITZER, 1992]. Compared to BGO, which has 15% of the light output of NaI(Tl) and a decay time of 300 ns, LSO has 5 times more light output and a decay constant 7.5 times faster, leading to significant improvements of PET scanner performance. The microPET, realized by Simon Cherry and his group at UCLA, was the first preclinical LSO PET tomograph [CHERRY et al., 1997].

1.1.10 1996: The First Avalanche Photodiode based PET System

Finally, the latest major contribution to the advance of PET imaging was the use of the avalanche photodiode (APD) as photodetector, instead of the PMT [LIGHTSTONE et al., 1986][CARRIER and LECOMTE, 1990]. APDs allowed for one to one coupling of millimeter scale scintillators with the photodetector, with a granularity which cannot be achieved with PMTs. Moreover, compared to PMTs, APDs are insensitive to strong magnetic fields, which allows for dual-modality PET and MRI. The first PET scanner to use APDs was realized by Roger Lecomte's team at Université de Sherbrooke in 1996 [LECOMTE et al., 1996], and is shown in Fig. 1.8 along with a picture of the APD-BGO detector module in Fig. 1.9.
1.1. THE HISTORY OF PET INSTRUMENTATION

Figure 1.8 Picture of the Sherbrooke APD-BGO PET Scanner.

Figure 1.9 The Sherbrooke BGO-APD detector module. Two BGO scintillators of $3 \times 5 \times 20 \text{ mm}^3$ are coupled to APDs of $4.2 \times 4.2 \text{ mm}^2$ (active area of $3.2 \times 3.2 \text{ mm}^2$). The detector module outer dimension is $3.8 \times 13.2 \times 33 \text{ mm}^3$. 
The history, and future, of PET instrumentation has been driven by the quest to improve spatial resolution and sensitivity. New detector development is accelerating the pace of positron imaging evolution, and every year new groups from around the world get into the race. In the last 10 years or so, dual-modality imaging devices, such as PET-CT, PET-MRI and PET-Optical tomography [Konecky et al., 2008][Cherry, 2006][Pichler et al., 2008][Judenhofer et al., 2008][Cherry et al., 2008], have improved and enhanced diagnostic capabilities in clinical applications and opened new possibilities for research in preclinical applications by allowing registration of the metabolic information with precise anatomical reference points in the subject. Now, dedicated PET scanners for specific studies, such as breast imaging, are being designed. In the following section, the specific need for imaging the brain of awake small animals for behavioral and neurological studies will be presented.

1.2 Imaging the Awake Animal

1.2.1 Human Addiction Studies

Over the last 30 years, the Center for Translational Neuroimaging of the Brookhaven National Laboratory has focused its research on the integration of radiopharmaceutical chemistry with the tools of neuroscience to develop new scientific tools for applications in human health. One major area of research which has a direct impact on millions of people worldwide is the phenomenon of addiction and its implications in the neurochemistry of the brain. The scope of the research reaches from the understanding of drug and alcohol addiction, obesity and eating disorders, attention deficit hyperactivity disorder (ADHD), to the development of new strategies for addiction treatment.

The study of the phenomenon of addiction requires the development of new radiotracers for imaging specific neurotransmitter systems in the brain, and the design and realization of novel imaging devices to measure the neuroactivity of the brain.

1.2.2 The RatCAP: Rat Conscious Animal PET

Small animals, like rats, are used in medical research because they represent an excellent model of the human body and brain metabolism. Researchers from BNL proposed that the correlation of the animal’s behavior with neurological study performed with PET imaging would allow unprecedented understanding of the addiction phenomenon. Hence, a PET camera allowing imaging of the awake rat was designed and realized, the RatCAP
1.3. THE FRONT-END ELECTRONICS FOR THE RATCAP

(Rat Conscious Animal PET). This is a major breakthrough in preclinical imaging of the brain as it allows imaging of small animals without the use of anesthesia which is currently required to prevent movement of the animal. Also, anesthesia produces profound effects on brain function, which biases any neurologic metabolism information obtained in standard PET studies. With the RatCAP, the rat wears the camera, attached to its skull, eliminating the relative movement between the animal and the scanner.

1.3 The Front-End Electronics for the RatCAP

This thesis presents the design and implementation of the front-end electronics for the RatCAP. By its nature, the RatCAP imposes unique challenges on the realization of the electronics. The objectives for the design and implementation of the RatCAP electronics are the following. First, due to the miniature size of the camera and the large number of readout channels, very large scale integration (VLSI) of the front-end electronics is mandatory. Second, in order to have minimal influence on the animal’s behavior, the mobility of the camera has to be preserved as much as possible. Hence, the number of interconnections between the front-end electronics in the camera and the data acquisition system has to be minimized. Finally, the analog front-end has to be optimized for the detector characteristics, given a limited power budget of 1.5 W for the whole camera, to provide the best possible timing resolution. The power dissipation has to be limited to prevent the degradation of the detector’s performance and influence the animal’s behavior.

The author of this thesis was the lead designer of the ASIC and was responsible for the implementation of the electronics in the RatCAP camera. His tasks included:

- Mathematical optimization of the timing resolution, through minimization of electronics noise and optimization of the analog front-end according to the design specifications.
- Design and implementation of the complete analog front-end, timing discriminator, energy discriminator, bias networks, LVDS receiver and transmitter.
- Design of the rigid-flex printed circuit board and support electronics.
- Close collaboration to the realization of the RatCAP system, more specifically on the detector and the data acquisition system.

This thesis consists of six chapters. In the next chapter, the principles of positron emission tomography along with the required instrumentation and the figures of merit of PET will
be presented. Also, a review of state of the art preclinical small animal PET systems in the field will be covered. In the third chapter, the first peer reviewed paper on the charge sensitive preamplifiers design and evaluation of the TSMC CMOS 0.18 μm technology are presented. Chapter 4 presents the second peer reviewed paper on the analog front-end electronics for the RatCAP. Chapter 5 presents the most recent paper on the complete application specific integrated circuit (ASIC) for the RatCAP. Finally, chapter 6 presents the performance of the RatCAP scanner and other systems which were realized based on the RatCAP technology and the ASIC.
CHAPTER 2

Physics and Instrumentation of Positron Emission Tomography

In the previous chapter, the evolution of PET instrumentation was highlighted to put in context the technologies which are used now and the present thesis. The objective of this chapter is to present the concepts essential to understand positron emission tomography. In this line of thoughts, the physics of PET is presented, along with PET system performance figures of merit. The review of the main state of the art systems is also presented, with an emphasis on the front-end electronics architecture.

2.1 Principle of Positron Emission Tomography

Positron emission tomography imaging is based on two basic principles: imaging through the use of positron emission, also known as the tracer principle, and volumetric imaging of the body’s interior, called tomography. The process of PET imaging starts with the injection of a radiopharmaceutical into the subject. The purpose of the radiopharmaceutical is to selectively concentrate in the region of interest in the subject and emit positrons which are detected non-invasively and indirectly via the detection of gamma photons at 511 keV resulting from the annihilation of the positron and an electron (more details below). A radiopharmaceutical has two main constituents. The first component is a chemical compound which has the property, depending on the type of study which is performed, to selectively be metabolized by targeted cells or bind with receptors to be imaged. This leads to an increased concentration of positron emissions in the region of interest. The second component is the tracer. It is an unstable radioisotope synthesized in a cyclotron. The most probable deexcitation mode of the radioisotope’s nucleus is through the conversion of a proton into a neutron, with the simultaneous emission of a positron and a neutrino. The positron travels in the tissue, loosing its kinetic energy principally through Coulomb interaction with electrons. As the rest mass of the positron is the same as that of the electron, the trajectory of the emitted positron deviates substantially with each Coulomb interaction. When the positron reaches thermal energy, it interacts with an electron, forming a hydrogen-like orbiting pair called positronium. The positronium is
unstable and annihilates into a pair of anti-parallel 511 keV gamma photons, as illustrated in Fig. 2.1. The subsequent coincidence detection of the two 511 keV photons determines the line of response (LOR) where the annihilation of the positron-electron took place. It is the acquisition of all those LORs which allow the reconstruction of in vivo tomographic images.

It is important to outline at this point that the range of the positron, which depends on its energy and hence the radioisotope used, is one of the main physical processes which limit the achievable spatial resolution in preclinical small animal systems. To give an order of magnitude, $^{11}$C and $^{18}$F in water will have 75% of their positrons annihilate within 2.1 mm and 1.2 mm of their origin respectively [WERNICK and AARSVOLD, 2004]. Also, due to the variation in the momentum of the positron, the two 511 keV photons will be noncolinear by approximately 4 mrad, which also limits the spatial resolution. The latter physical limitation is more important for clinical scanners than preclinical, as the error increases as a function of the diameter of the field of view. For example, a ring with a diameter of 60 cm will encounter a spatial resolution loss of 1.3 mm due to noncolinearity [WERNICK and AARSVOLD, 2004].

As previously presented, the coincidence detection of the two 511 keV photons determines the LOR of the annihilation. There are three types of detected coincidences, which are presented in Fig. 2.2. Scattered coincidence is defined as the detection of both annihilation photons originating from a single decay, but where one or both photons have lost some
energy by scattering in the subject. Random coincidence is defined as the detection of two 511 keV photons originating from two separate decays, but close enough in time to look like a single decay to the system electronics. Finally, true coincidence is the detection of both annihilation photons originating from the same nucleus decay where neither of the photons scattered in the subject.

True and scattered events are referred to as prompt coincidences as they originate from a single nucleus decay. Their detection rate increases proportionally to the activity of the radiopharmaceutical injected into the subject. The random events rate increases as the square of the activity and will dominate above a given activity level injected into the subject. For PET imaging, it is desirable to measure and reconstruct true events, and discriminate scattered photons and random events. As it will be presented in section 2.3, the performance of the detector and front-end electronics have a direct impact on the amount of random and scattered coincidences accepted by the system.

2.2 Detectors used in PET

The detector is a key element determining the performance of a PET system. Hence it is important to understand how the different detectors use in PET work and what are their characteristics.

The ideal detector would have the following properties. In order to increase the 511 keV photon's probability of having a photoelectric interaction and hence increasing the sensitivity of the system, it should have a high effective atomic number and high density. The ability of the system to discriminate scattered events accurately is function of the achievable detector energy resolution. It should provide the greatest amount of charge per
511 keV photon relative to the noise it generates. The electronics usually have negligible contribution to the system's energy resolution. In the same line of thoughts, the system's capability to discriminate random coincidences depends in great parts on the detector's time jitter contribution to the timing resolution. The narrower the time distribution of the collected charge from the detector by the front-end electronics, the smaller the detector's contribution to the timing resolution. Further details on energy resolution and timing resolution can be found in section 2.3. In order to allow high resolution imaging, the packing fraction of the detector should be high, to allow staggering of multiple detector elements with minimum dead space. Finally, if dual-modality PET and MRI is desired, the detector operation should be immune to strong magnetic fields.

The detectors used in PET are divided into two main categories. There are direct interaction detectors, where the incident 511 keV photon ionizes the sensitive volume, creating free carriers which drift along the electric field applied between the electrodes. Examples of direct interaction detectors used in PET are room temperature semi-conductors such as Cadmium Zinc Telluride (CZT), and multi-wire proportional chambers (MWPC). But the most common type of detectors used in PET are known as indirect interaction detectors. These detectors consist of a scintillator coupled to a photodetector. The 511 keV photon interacts in the volume of the scintillator, which emits photons in the visible and near UV range. These photons will in turn create free carriers in the photodetector.

### 2.2.1 Scintillators

The two most probable mechanisms in which a photon in the energy range of 511 keV can interact in a scintillator are the photoelectric effect and Compton scatter effect [KNOLL, 1999]. In the case of a photoelectric effect, the incident photon is absorbed by an atom of the scintillator, resulting in the ejection of an electron most likely from the K shell of the atom, called a photoelectron. The energy of the photoelectron is equal to the energy of the incident photon minus the binding energy of the ejected electron from its nucleus, which is in the range of a few tens of keV for typical scintillators used in PET. The photoelectron passing through the scintillator's lattice will then create a large number of electron-hole pairs, where electrons are elevated to the conduction band. Due to some well selected impurities in the crystal, also called activators, possible energy states are created in the forbidden band of the scintillator's. The created holes will quickly drift to the activators site, ionizing them. Meanwhile, the electrons elevated to the conduction band will migrate in the lattice of the crystal until they encounter an ionized activator. The relaxation of an electron into a hole of the ionized activators will produce the emission of a photon
2.2. DETECTORS USED IN PET

TABLE 2.1 Properties of Common Scintillators used in PET.

<table>
<thead>
<tr>
<th>Material</th>
<th>Nal(Tl)</th>
<th>BGO</th>
<th>LSO</th>
<th>GSO</th>
<th>YSO</th>
<th>BaF$_2$(fast)</th>
<th>BaF$_2$(slow)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (g/cm$^3$)</td>
<td>3.67</td>
<td>7.13</td>
<td>7.40</td>
<td>6.71</td>
<td>4.53</td>
<td>4.89</td>
<td>4.89</td>
</tr>
<tr>
<td>Effective atomic number Z</td>
<td>51</td>
<td>76</td>
<td>65</td>
<td>59</td>
<td>34.2</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>Wavelength of maximum emission (nm)</td>
<td>415</td>
<td>505</td>
<td>420</td>
<td>430</td>
<td>420</td>
<td>220</td>
<td>310</td>
</tr>
<tr>
<td>Principal decay constant (ns)</td>
<td>230</td>
<td>300</td>
<td>47</td>
<td>56</td>
<td>70</td>
<td>0.6</td>
<td>630</td>
</tr>
<tr>
<td>Index of Refraction</td>
<td>1.85</td>
<td>2.15</td>
<td>1.82</td>
<td>1.85</td>
<td>1.8</td>
<td>1.56</td>
<td>1.56</td>
</tr>
<tr>
<td>Total light yield (photons/MeV)</td>
<td>38000</td>
<td>8200</td>
<td>25000</td>
<td>9000</td>
<td>na</td>
<td>1400</td>
<td>9500</td>
</tr>
<tr>
<td>Output relative to Nal(Tl) on a bialkali PMT</td>
<td>1</td>
<td>0.13</td>
<td>0.75</td>
<td>0.25</td>
<td>na</td>
<td>na</td>
<td>0.2</td>
</tr>
</tbody>
</table>

with the associated energy. Those emitted photons, which are in the visible and near UV range, are then collected by the photodetector to produce the signal.

In the case of a Compton scatter event, the incident photon will interact with an atom of the crystal lattice, but will not be completely absorbed as in the photoelectric effect. The photon will lose part of its energy to the atom and scatter with an angle $\theta$. The energy lost to the atom will create a recoil electron. Following the same mechanism as previously explained, the recoil electron will create electron-hole pairs and ultimately visible photons will be emitted. It is worth mentioning that the amount of visible photons emitted by the crystal is to a first order proportional to the energy of the ionizing particle crossing it.

Table 2.1 presents the properties of the most common scintillators used in gamma spectroscopy. The density (g/cm$^3$), effective atomic number Z, wavelength of maximum emission (nm), principal decay time constant (ns), refractive index, total light yield (photons/MeV) and output relative to Nal(Tl) on a bialkali PMT are presented.

2.2.2 Photodetectors

As presented previously, the scintillation light from the scintillator is converted into charge by a photodetector. For PET, the main requirements of the photodetector are the following. First, it should provide the best possible conversion of the scintillation light into charge. This is characterized by its quantum efficiency (QE), which is defined as the ratio of the number of primary electrons produced in the photodetector (before the gain process) to the number of incident photons. The QE is a function of the wavelength of the incident photons. Second, it should have a fast readout speed, essential to obtain good timing resolution. Third, the combination of the scintillator and the photodetector should provide the best possible energy resolution for Compton scatter discrimination. Also, the arrangement of the photodetector with the scintillator should have a good packing fraction to allow high resolution imaging. In addition, the index of refraction of the
scintillator and the entrance window of the photodetector should be matched to allow maximum transmission of the scintillation light. Finally, if dual-modality PET and MRI is desired, the photodetector should be insensitive to the magnetic fields. In the next lines, photomultiplier tube (PMT) and avalanche photodiode (APD), the main photodetectors used in PET, will be discussed. The emergence of a new and promising detector, the multi-pixel photon counter (MPPC), a.k.a. silicon photomultiplier (SiPM), is also worth discussing.

Photomultiplier Tubes

PMTs have been used since the 1950's in positron imaging, and are still the most widely used photodetectors in commercial PET systems. A PMT consists of a vacuum tube with an entrance window, a photocathode where the scintillation photon creates free electrons through photoelectric interaction, an electron collection structure which focus the photoelectrons toward the amplification stage consisting of dynodes, and finally the anode where the signal is collected. The noise sources in a PMT originate from the poissonian fluctuation in the electron gain, mainly from the 1st dynode, and thermal emission of electrons from the photocathode and dynodes. PMTs are characterized by a high gain on the order of $10^6$, providing for an excellent signal to noise ratio, and a fast response in the range of a fraction of a nanosecond to a few nanoseconds. Those two qualities make the PMT well suited for PET, limiting the need for a fast charge sensitive preamplifier, and allowing excellent timing resolution. On the other hand, PMTs have a low QE, on the order of 25% at 420 nm. They are also bulky and have a poor active area to size ratio, limiting the design of high resolution scanners. Finally, PMTs are extremely sensitive to magnetic fields, prohibiting their use for PET-MRI imaging devices. In PET systems, position-sensing PMTs (PSPMTs), which provides spatial information about the detected light to the electronics, have been used to create a high resolution system [Cherry et al., 1997][Del Guerra et al., 1998][Miyaoka et al., 1998][Pani et al., 1997][Seidel et al., 2000][Weber et al., 1999].

Avalanche Photodiodes

APDs are solid-state photodetectors, based on a reverse biased p-n junction. Fig. 2.3 presents a cross-section of a typical reach-through APD structure along with the electric field in the device.

There are two main structural elements. First, there is the absorption region $A$, where an incident scintillation photon will generate an electron-hole pair. The purpose of the
2.2. DETECTORS USED IN PET

Figure 2.3 Cross section of a typical reach-through APD along with the electric field profile [PERKINELMER, 2006].

The electric field in this region is to separate both types of carriers and sweep the electron toward the multiplication region \( M \). Once in the multiplication region, the high electric field (on the order of several volts per micrometer) will accelerate the electron generating other electron-hole pairs by impact ionization, providing the multiplication mechanism. Hence, the gain is a function of the reverse voltage applied to the device. The width of the multiplication region and its electric field profile must be designed such as to provide a useful and effective gain while preventing breakdown of the p-n junction.

The total dark current \( I_d \) of an APD is expressed as,

\[
I_d = I_{ds} + I_{db} \cdot M, \tag{2.1}
\]

where \( I_{ds} \) is the surface leakage current originating from the p-n junction consisting of the collecting electrode with the guard ring, \( I_{db} \) is the bulk leakage current which will undergo avalanche, and \( M \) is the APD gain. The APD spectral noise is dominated by the dark current shot noise and the excess noise due to the statistical nature of the avalanche process. The total spectral noise current \( i_n \) is given by,

\[
i_n = \left[ 2 \cdot q \cdot (I_{ds} + I_{db} \cdot M^2 \cdot F) \cdot BW \right]^{0.5}, \tag{2.2}
\]

where \( BW \) is the system bandwidth, \( F \) is the excess noise factor and \( q \) is the electron charge. The \( \sqrt{F} \) is the factor by which the statistical noise on the APD current (equal to the multiplied photocurrent plus the multiplied APD bulk dark current) exceeds that...
which would be expected from a noiseless multiplier on the basis of shot noise alone [PERKINELMER, 2006]. The excess noise factor is given by,

\[ F = M \cdot k_{eff} + \left( 2 - \frac{1}{M} \right) (1 - k_{eff}), \]  

(2.3)

where \( k_{eff} \) is the effective coefficient of ionization defined as the ratio of the hole to electron ionization probabilities [WEBB et al., 1974].

Compared to PMTs, APDs have a large QE (up to 70% at 420 nm), a smaller gain variation between pixels of an array, and are insensitive to magnetic fields, making them suitable for dual-modality PET-MRI. On the other hand, their weaker gain and noisy amplification offers a lower signal to noise ratio compared to PMTs, making the use of charge sensitive preamplifier mandatory. Also, they have a slower response, on the order of a few nanoseconds. Finally, their gain and shot noise are very sensitive to high voltage and temperature fluctuations.

**Silicon Photomultipliers**

A new photodetector known as Silicon Photomultiplier (SiPM) or Multi-Pixel Photon Counter (MPPC) is getting significant attention in the fields of PET, calorimetry and single photon counting. SiPMs consist of an array of APDs tied in parallel, operated in Geiger mode. Typical device size is in the mm\(^2\) range, with individual cell sizes ranging from a few tens of microns to one hundred microns. The array is biased above the breakdown voltage. Hence, when a photon hits the sensitive area of a cell and generates an electron-hole pair, or when a thermal electron is generated in the sensitive volume, the individual cell will trigger a standardized amount of charge. The amount of charge instantaneously liberated is equal to the product of the cell capacitance and the over voltage, defined as the bias voltage minus the breakdown voltage. The gain is in the range of \(10^5\) to \(10^7\). In the devices currently available, a passive quenching circuit realized with a resistor is used to reinitialize the cell. When a given cell fires, the current flowing through the resistor will momentarily bring the bias point below the voltage breakdown, limiting the current and stopping the avalanche process, preventing destruction of the cell, and reinitializing it for the next event. The output current signal is formed by the sum of all cell responses. The output signal will be proportional to the number of fired cells as long as the number of photons in a pulse \(N_{photon}\) times the photodetection efficiency (PDE) is significantly smaller than the number of cells \(N_{total}\) [VASILE et al., 2006], as expressed by
2.2. DETECTORS USED IN PET

equation 2.4,

\[ N_{\text{fired cells}} = N_{\text{total}} \left( 1 - e^{-\frac{N_{\text{photon}} \cdot PDE}{N_{\text{total}}}} \right) , \]  

where the PDE is function of:

- the fraction of the active area of a pixel,
- the QE of the active area,
- the probability to initiate an avalanche breakdown (Geiger efficiency),
- the fraction of active cells, i.e. those cells which are not quenched or are still recovering from the previous breakdown.

The PDE can be expressed as,

\[ PDE = QE \cdot e \cdot P_{\text{trigger}} , \]  

where \( e \) is the ratio of sensitive to total area and \( P_{\text{trigger}} \) is the probability that an incoming photon triggers a breakdown. The QE is comparable to other silicon devices. Current SiPM prototypes have a PDE comparable to the QE of PMTs.

There are many factors affecting the performance of the SiPM. The dark count rate, due to thermal carriers generated in the sensitive volume, can be in the range of 100 kHz to several MHz per mm\(^2\) at room temperature. Cooling or lowering the electric field in the device, at the price of a lower gain, lowers the dark count rate. Another detrimental phenomenon is the optical crosstalk. It originates from the emission of photons following the triggering of a cell. Those photons with an energy greater that 1.14 eV can then trigger other neighboring cells, lowering the PDE. It is a stochastic process which introduces an excess noise factor, similar to that of the APD. Cells optical isolation from a dedicated design will reduce the crosstalk. Afterpulsing is another phenomenon in SiPM, where carrier trapping and delayed release causes afterpulses during a period of several microseconds after the breakdown. The recovery time to recharge a cell after a breakdown depends on the cell capacitance, which depends on its size, and the quenching resistance. Afterpulsing can prolong the recovery time because the recharging starts anew. The recovery time directly affects the number of cells ready to be triggered. An active quenching circuit can significantly improve the recovery time [VASILE et al., 1999].

SiPMs are insensitive to magnetic fields, a major advantage over PMTs, and provide a high gain compared to APDs, making them very interesting for PET-MRI. Their high gain
also limits the need for a sensitive charge preamplifier compared to APD, simplifying the
readout electronics and lowering the cost per channel. They are also very fast, allowing
subnanosecond timing resolution. Finally, they require a bias voltage in the range of 30 V - 200 V, lower than the APD and PMT.

2.3 Figures of Merit of PET Systems

In order to understand the characteristics and performance of the RatCAP system, and
of the other preclinical PET systems which will be presented in the next section, the main
benchmarks used in PET will be introduced. While the energy and timing resolution refer
specifically to the detector and electronics performance, spatial resolution, sensitivity and
noise equivalent count rate characterize the whole system.

2.3.1 Energy Resolution

In a PET system, the energy resolution is an indication of the system's capability to
discriminate Compton scattered photons. Hence, the better the energy resolution, the
smaller the fraction of scattered coincidences in the prompt events. This has a direct
impact on the image quality. In some PET system architectures [McELROY et al., 2005]
[RAFECAS et al., 2001], the energy information of each event is collected to reconstruct
Compton scattered events to increase the system's sensitivity, thereby demonstrating the
dependence of sensitivity on the energy resolution.

The energy resolution is defined as the ratio of the full width at half maximum (FWHM)
over the peak centroid of the differential pulse height distribution response of a spectro­
scopic readout chain for a monoenergetic source of radiation. The width of the distribution
represents the total noise in the system and is the quadratic sum of all statistical fluctua­
tion and noise sources present in the system. The noise and statistical fluctuation present
in a scintillator based PET system are the following. First, there is the photon statistics
from the scintillator. For each 511 keV gamma photon interacting with the crystal via pho­
toelectric effect, there will be a variation in the total number (scintillation efficiency) and
time distribution of the visible photons emitted. Also, the position of interaction of the
511 keV photon in the crystal will influence the light collection efficiency and the scintilla­
tion efficiency. Second, there are the photoelectron statistics, which represent the variation
in the number of photoelectrons created in the photodetector following the absorption of
the visible photons emitted by the crystal. Considering the QE of the photodetector, the
2.3. FIGURES OF MERIT OF PET SYSTEMS

![Figure 2.4 Equivalent Noise Charge model.](image)

light loss due to geometric and index of refraction mismatch between the photodetector and the scintillator, this is the point in the system where there is the lowest amount of information carriers. It is then the most important contribution to the deterioration of the energy resolution. Third, there is the excess noise factor of the photodetector as presented previously. Fourth, there is the electronics noise. Finally, any drift in the system operating conditions, for instance the temperature or the photodetector high voltage, will contribute to the deterioration of the energy resolution.

At this point, it is relevant to introduce the evaluation of the electronic noise charge (ENC) and the photoelectron statistics. The ENC represents the amount of charge at the input of the preamplifier which would produce a signal to noise ratio of unity [RADEKA, 1988]. The engineer has to optimize the front-end electronics such that the ENC has a negligible contribution to the overall noise present in the system. It is evaluated using the equation 2.6 and the model is presented in the Fig. 2.4.

\[
ENC^2 = (\frac{1}{2})4kTR_sC_{IN}^2 \left[ \int_{-\infty}^{\infty} [h'(t)]^2 dt + \frac{1}{\tau_e^2} \int_{-\infty}^{\infty} [h(t)]^2 dt \right],
\]

with \( \tau_e = C_{IN}(R_sR_p)^{\frac{1}{2}} \),

where \( k \) is the Boltzmann constant, \( T \) the temperature, \( R_s \) and \( R_p \) the equivalent series and parallel resistance, \( C_{in} \) the total capacitance at the preamplifier input and \( h(t) \) the electronics impulse response. The first integral in equation 2.6 represents the series noise, which is the contribution from the front-end electronics. The second integral in equation 2.6 represents the parallel noise, which is due to the detector noise. A more detailed analysis is presented in section 3.2.

The photoelectron statistics, the main noise contribution, is function of the scintillation light which decays exponentially with time. Hence, this contribution is not stationary like
the ENC, and therefore a time domain method is necessary to quantify its contribution. The mean square noise, reported at the preamplifier input, due to the photon flux can be found from Campbell’s Theorem [PAPOULIS, 1984] and is expressed as [CASEY et al., 2003]:

\[ \sigma_{\text{noise-photon}}^2(t) = qFM^2 \int_{-\infty}^{\infty} I_{\text{photon}}(\alpha)h^2(t - \alpha)d\alpha, \] (2.8)

where \( q \) is the electron charge, \( F \) is the photodetector excess noise factor, \( M \) the photodetector gain and \( I_{\text{photon}}(t) \) the current due to scintillation light, which can be modeled as,

\[ I_{\text{photon}}(t) = \frac{N}{\tau_{\text{scin}}} e^{\left(\frac{-t}{\tau_{\text{scin}}}\right)}, \] (2.9)

where \( N \) is the product of the total number of primary photo-electrons and the photodetector gain, and \( \tau_{\text{scin}} \) is the scintillator decay time constant. A detailed analysis is presented in section 5.2.2.

### 2.3.2 Timing Resolution

The timing resolution of a PET system represents the accuracy with which each event is timestamped. It has a direct impact on the amount of random coincidences \( N_{\text{random}} \) per unit time accepted by the system, as expressed by the following equation for a pair of detectors,

\[ N_{\text{random}} = 2 \cdot \tau_r \cdot N_a \cdot N_b, \] (2.10)

where \( \tau_r \) is the resolving time, and \( N_a \) and \( N_b \) are the singles rates of events in channel \( a \) and \( b \). Note that the coincidence time window is defined as \( 2 \times \tau_r \).

The timing resolution is evaluated as the quadratic sum of all noise and statistical fluctuations over the slope of the signal at the discrimination point. The evaluation of the timing resolution is given by,

\[ \sigma_t(t_{zc}) = \sqrt{\sigma_{\text{noise-photon}}^2(t_{zc}) + \sigma_{\text{ENC}}^2} \frac{dV_{\text{out}}(t_{zc})}{dt}, \] (2.11)

where \( \sigma_{\text{ENC}} \) is the electronics noise, \( \sigma_{\text{noise-photon}}(t_{zc}) \) is the time dependent photoelectron noise evaluated at the discrimination point, and \( \frac{dV_{\text{out}}(t_{zc})}{dt} \) is the slope of the signal at
2.3. FIGURES OF MERIT OF PET SYSTEMS

2.3.3 Spatial Resolution

The spatial resolution of a PET system is defined as the FWHM of the reconstructed one dimensional profile of a point source in the center of the field of view. The main limitations are due to the detector dimension, the positron range, and for human clinical scanners the annihilation photons non-collinearity, as presented in section 2.1. Another factor influencing the achievable spatial resolution is the finite detector depth, since the parallax error increases with the radial distance from the center of the camera's field of view. The parallax error is illustrated in Fig. 2.5. It can be reduced by trading off sensitivity through the use of shorter scintillators. Other techniques to minimize the parallax error can be used. One approach consists of using phoswich detectors [LECOMTE et al., 2001][SAOUDI et al., 1999][MIYAOKA et al., 1998], where pulse shape analysis is performed to get the depth of interaction (DOI) [MICHAUD et al., 2004][MICHAUD et al., 2003][WONG, 1986][LECOMTE, 1986]. An example of a phoswich detector for PET/CT applications is illustrated in Fig. 2.6. The main advantage of this technique is that there is no loss of sensitivity. Another way to obtain the DOI is based on the Anger detector concept, where the scintillator is read out on both sides by photodetectors. The amplitude
CHAPTER 2. PHYSICS AND INSTRUMENTATION OF PET

Figure 2.6 Sherbrooke PET/CT phoswich detector. The CsI(Tl) is used in CT mode, whereas the pulse shape analysis of the scintillation light from the LSO or GSO gives depth of interaction in PET mode, and increases the achievable spatial resolution without any trade-off in sensitivity or increased cost with increases in the number of channels.

distribution and ratio of the opposing photodetectors provide the DOI. Again, sensitivity can be preserved while minimizing the parallax error, but at the significant cost of doubling the total number of readout channels. Finally, another way to minimize the parallax is to use a double stack of scintillators and APDs, as in the MADPET-II system, but this is also at the cost of doubling the number of readout channels [SPANOUDAKI, 2008].

2.3.4 Sensitivity

The sensitivity of a PET scanner represents its capability to detect the 511 keV annihilation photons. It is a measurement of the fraction of radioactive decays that result in a detected event. The system sensitivity affects the number of counts per voxel, hence it directly determines the signal-to-noise level of the reconstructed images. The greater the sensitivity of a PET system, the lower the required injected dose to the subject. As previously presented in section 2.1, the lower the injected activity, the lower the random coincidence fraction, which increases quadratically.

The sensitivity can be reported in two ways. First, as the absolute sensitivity, also known as the system detection efficiency. It represents the fraction (in %) of radioactive decays in a point source, located in the middle of the FOV, required to detect an event. Second, the sensitivity can also be reported for a standard source with specific dimensions in units of cps/Bq/cc.
Many factors influence the sensitivity of a PET system. First, there is the detection efficiency of the detector. This will vary as a function of the attenuation coefficient of the detector material, hence its effective atomic number Z, and its thickness. It is worth to point out that an apparent trade off has to be made between the sensitivity and the spatial resolution as far as the detector thickness is concerned. The detection efficiency of the detector is also proportional to the fraction of events which fall within the photopeak after discrimination of the scattered events.

Secondly, the sensitivity also depends on the geometric efficiency of the system. The geometric efficiency depends on the overall solid angle coverage of the detector with respect to the source location. It is also function of the packing fraction of the detector assembly, where any dead space within and between detector modules decreases the sensitivity of the system.

Finally, as far as the electronics is concerned, two factors can influence the sensitivity when the event rate is increased: the dead time losses and the pile-up effect. The dead time losses refers to events which could not be processed and accounted for by the electronics due to the fact that they occurred while the system was processing the previous event, and during which the electronics was insensitive to a new event. The pile up effect refers to the interference of multiple events within a given event electronic pulse width. This can be limited by using a fast shaping amplifier and minimizing the total width of the pulse, at the price of an increase in the series electronic noise and ballistic deficit of the integrated charge. The main consequence of pulse pile up is an erroneous measurement of the pulse amplitude, which, in a PET system, influences the discrimination of Compton scatters at high detection rates. When the pile up occurs at the peak of the previous event, a lost of count occurs, lowering the system sensitivity.

2.3.5 Noise Equivalent Count Rate

The Noise Equivalent Count (NEC) rate [STROTHER et al., 1990] is an evaluation of the signal-to-noise ratio of the acquired data as a function of the radioactivity in the object. It describes the overall performance of a PET system to discriminate scattered and random events from true events as a function of the activity of the source. Hence, the NEC is closely related to the energy resolution and the timing resolution of the spectroscopic chain. The NEC can be expressed as,

\[
NEC = \frac{T^2}{T + S + K \cdot R'}
\]  

(2.12)
where $T$ is the trues count rate, $S$ the scatters count rate, $R$ the randoms count rate, and $K$ is a factor that depends on the method used for randoms corrections.

### 2.4 Small Animal PET Systems

In order to assess the characteristics of the RatCAP, a review of state of the art small animal PET scanners is now presented. The quad-HIDAC, the MicroPET, the YAP-PET, the NIH Atlas, the A-PET, the ClearPET, the MADPET-II and the LabPET will now be presented. Ultimately, the RatCAP system will be presented.

#### 2.4.1 The quad-HIDAC

The quad-HIDAC PET tomograph is a commercial device designed and sold by Oxford Positron Systems Ltd [Jeavons et al., 1999]. Unlike all other small animal PET systems, the HIDAC is not based on scintillator/photodetector detector modules. Instead, it uses a High Density Avalanche Chamber (HIDAC), which is based on the High Density Drift Chamber (HDDC), invented at CERN in 1973, with the addition of direct electron multiplication.

As shown in Fig. 2.7, the camera consists of 4 detector blocks, each of them with 4 HIDAC modules [Missimer et al., 2004]. HIDAC modules are stacked to preserve photon stopping power. The spacing between each HIDAC sets the depth-of-interaction resolution. The inner spacing between modules is 170 mm and the camera has an axial length of 280 mm. The gantry rotates over 180 degrees back and forth for uniform sampling. The HIDAC detector consists of a MultiWire Proportional Chamber (MWPC) sandwiched between two laminated plates containing interleaved sheets of lead and insulating material, mechanically drilled with a dense matrix of small holes. Each plate consists of 12 sheets of lead, 50 $\mu$m thick, with an insulator of 140 $\mu$m thick between each. The two cathodes, providing the x and y position of the interaction, are plated on the inner side of the laminated plates. The holes are 0.4 mm in diameter, with a center to center spacing of 0.5 mm. The hole-pitch actually sets the intrinsic spatial resolution of the system. Fig. 2.8 presents a schematic of the HIDAC. The detector is filled with argon gas, which is bubbled through a liquid quencher of di-isopropyl ether in order to prevent spark breakdown between the plates and the anode wires.

As seen in Fig. 2.8, when an incident 511 keV photon enters the sensitive volume it will interact with the lead, creating fast electrons, which will ionize the gas in the hole.
2.4. SMALL ANIMAL PET SYSTEMS

Figure 2.7 Schematic of the quad-HIDAC [MISSIMER et al., 2004].

Figure 2.8 Diagram of the HIDAC detector module [JEAVONS et al., 1999].
The free electrons created by the ionization are focused in the center of the holes and accelerated by the high electric field created by the difference of potential between the lead sheets and undergo avalanche, resulting in a first gain stage. Those electrons will then drift to the anode wires, where further avalanching occurs. The anode signal is used to figure out which HIDAC triggered, providing the depth-of-interaction, and also as the timing trigger used for coincidence. From the Ramo theorem, the signal is then induced to the x and y cathodes, giving precise position of the interaction [JEAVONS et al., 1983].

To reduce the number of electronic channels required to read out the cathode wires, the coded center-of-cluster principle is used [JEAVONS et al., 1980] (illustrated in Fig. 2.9). Cathode wires are taken in pairs to give two outputs. One output is a group output and connects with adjacent wires. The other output is a channel position within the group and connects with corresponding channel wires in other groups.

No data was found in the literature regarding the achievable timing resolution for this version of the system, but it uses a 40 ns timing coincidence window, which suggests an approximate coincidence timing resolution of 20 ns. The main contribution to the timing resolution comes from the drift time in the lead converter plates. Depending on where the photon will interact, the electrons drift time will vary. This forces a design trade-off to keep the converter thin, keeping in mind the sensitivity of the system which depends on the thickness of lead to stop the incident photons.

One important characteristic of the HIDAC detector is that the signal response measured by the wire chamber is not related to the energy of the incident photon. Energy discrim-
2.4. SMALL ANIMAL PET SYSTEMS

Initation is naturally obtained by the fact that even if lower energy photons should have a greater intrinsic probability of photoelectric interaction with the lead, it is largely offset by the lower probability of the photoelectron to escape the lead. Hence, photons with energy lower than \( \approx 200 \) keV will not be detected.

The absolute sensitivity in the center of the FOV if 18 cps/kBq (for the 32 module version of this scanner). The volumetric spatial resolution is 1.09 mm\(^3\) nearly constant over the entire FOV.

2.4.2 The MicroPET Family

The first MicroPET was originally developed by Simon Cherry's group at UCLA in the mid 90's [CHERRY et al., 1997]. The detector modules consist of an \( 8 \times 8 \) array of \( 2 \times 2 \times 10 \text{ mm}^3 \) LSO crystals coupled one to one to a 64 channel PMT. Fiber optics are used to bring the light from the LSO to the PMT, with the advantage of freeing the space occupied by the bulky PMT from the detector front-end modules in the camera. This allows the realization of a high resolution system, but at the cost of light losses in the fiber and coupling. Those detector modules have a coincidence timing resolution of 2.4 ns FWHM and an average energy resolution of 19%. Thirty of those modules are arranged to form a continuous ring, leading to a FOV of 11.2 cm in the transverse and 18.0 mm in the axial direction. The system operates in 3D mode. The spatial resolution at the center of the FOV is 1.8 mm FWHM, for a volumetric resolution of 0.006 cc, and a peak sensitivity of 0.56% at an energy threshold of 250 keV.

Later, Concorde Microsystems Inc. teamed up with UCLA to developed new versions of the MicroPET. First came the MicroPET R4 and P4 [WERNICK and AARSVOLD, 2004]. Those systems used the same detector modules previously presented, but stacking 4 rings axially, bringing the axial FOV to 7.8 cm. The P4 model, used for primate brain and whole body rat imaging, has a 26 cm ring diameter and uses a total of 42 detector modules. The R4 model, for small rodents, has a 15 cm diameter and uses a total of 24 detector modules. The axial extension of those systems brought the absolute sensitivity to 1.2% and 2.2% and the volumetric spatial resolution to 6.4 mm\(^3\) and 5.1 mm\(^3\) for the P4 and R4 respectively.

The next generation of MicroPET from Concorde Microsystems Inc. was the Focus 120 and 220 [LAROBINA et al., 2006]. The Focus uses a \( 12 \times 12 \) array of \( 1.5 \times 1.5 \times 10 \text{ mm}^3 \) of LSO, coupled to a multichannel PMT through fiber optics. One main improvement from the R4 and P4 family, is the packing fraction of the LSO array from 80% to 92%
(crystal pitch of 1.59 mm). The axial length is 7.6 cm, with a transaxial active FOV of 10 and 19 cm for the Focus 120 and 220 respectively. 96 detector blocks are used in the Focus 120 and 168 in the Focus 220. The spatial resolution at the center of the FOV is 1.3 mm FWHM, and the volumetric resolution is 3.0 μl, with an absolute sensitivity of 6.5% for a 250-650 keV energy window.

2.4.3 The YAP-PET

The YAP-PET was developed at the University of Ferrara and Pisa, Italy [Del Guerra et al., 1998]. It is dedicated to small animal PET/SPECT studies. Fig. 2.10 shows a picture of the camera. It consists of 4 detector modules mounted on a π/2 rotating gantry for uniform sampling, with a nominal opposite detector modules spacing of 15 cm. The detector spacing can be adjusted between 10 to 25 cm to select between high sensitivity or high resolution. Each detector module consists of a matrix of 400 cerium doped yttrium aluminum perovskite (YAP:Ce) scintillator of $2 \times 2 \times 30$ mm$^3$, coupled to a Hamamatsu R2486-06 position sensitive PMT. Each detector head has a 4 cm $\times$ 4 cm active area, leading to a FOV of 4 (axial) $\times$ 4 (transverse) $\times$ 4 cm$^3$. NIM-CAMAC standard electronics is used for PMT readout and data acquisition. The timing information is obtained
through the last dynode of the PS-PMTs which is sent to an ORTEC 534 constant fraction discriminator (CFD). The output signal of the CFDs is sent to a coincidence unit to produce a gate signal for a CAMAC voltage sensing peak-ADC (Phillips 7164) which digitizes the x-y signal from the grid anode of each PS-PMT, to find which pixel was hit. The coincidence timing resolution for a pair of detectors is 2 ns FWHM. It is relevant to note that the YAP:Ce scintillator has a decay time constant of 27 ns. A spatial resolution of 1.8 mm FWHM and a volumetric spatial resolution of about 5.8 mm$^3$ at the center of the FOV is reported. The absolute sensitivity for a point source in the center of the FOV is 1.7% for a 50 keV low level discrimination setting.

### 2.4.4 The NIH Atlas and GE Explorer Vista

The Advanced Technology Laboratory Animal Scanner (ATLAS) was a project from the U.S. National Institutes of Health [LAROBINA et al., 2006] [SEIDEL et al., 2003]. This system benefits from phoswich detector modules that consist of a 9 × 9 array of 2 mm × 2 mm × 15 mm crystals directly coupled to a Hamamatsu R7600-C8 PS-PMT. The 15 mm phoswich assembly consists of a 7 mm LGSO (40 ns) crystal and a 8 mm GSO (60 ns) crystal. Eighteen of those detector modules are arranged on a single ring of 11.8 cm diameter, with an axial FOV of 2 cm. The camera operates only in 3D mode.

To read out the camera, 6 groups of 3 detector modules electrically connected together are fed to six charge integrating ADC modules which are used to identify the scintillation decay time. A custom coincidence logic controller detects coincidences between the 6 sectors and initiates signal integration and ADC readout. A high speed PCI-bus interface card is used to collected the data. The readout chain is supplied by A & D Precision Co. (Newton, MA).

The GE Explorer Vista is a scanner derived from the NIH ATLAS. Compared to the NIH ATLAS which has one ring of detectors, the GE Explorer Vista consists of two rings, each with 18 detector modules. The phoswich detector assembly consists also of 13 × 13 scintillator stacks instead of 9 × 9, for a total of 6084 pixels. The ring diameter is the same, but the axial FOV is increased to 4.6 cm. It has a 1.6 mm FWHM reconstructed spatial resolution at the center of the FOV, with a sensitivity of 4% for a 250-700 keV energy window.
2.4.5 The A-PET and Philips MOSAIC HP

In comparison with other small animal PET systems where the design is optimized for very high spatial resolution, the University of Pennsylvania A-PET was designed for high sensitivity with a large imaging field-of-view, with a minimal compromise on the spatial resolution [Surti et al., 2005]. The A-PET is based on the pixelated Anger-logic detector [Surti et al., 2000]. The single annular lightguide of 1.2 cm thick is coupled to 14456 2 mm × 2 mm × 10 mm GSO crystals, eventually replaced by LYSO crystals in more recent versions. Two hundred eighty-eight PMTs with a diameter of 1.9 cm are used to read out the light, leading to an encoding ratio of 58 crystals per PMT. The crystal assembly has an inter crystal spacing of 2.3 mm, leading to a packing efficiency of 75%. The bore size is 19.7 cm, making the A-PET suitable for rodent, as well as cat and primate heads. The camera has a reconstructed transverse FOV of 12.8 cm with an axial length of 11.9 cm. The scanner operates in 3D only. A 7 ns coincidence timing window is used to match coincident events. Only the valid coincidence events are integrated and subsequently digitized by a 50 MHz ADC.

A sensitivity of 3.6% was measured for a point source at the center of the FOV and using an energy discrimination window of 250-665 keV. The spatial resolution is 1.9 mm at the center of the FOV.

The MOSAIC HP from Philips Medical Systems is based on the A-PET. It consists of a ring of 16680 GSO crystals of 2 mm × 2 mm × 10 mm arranged in 57 rows onto a single annular light-guide read out by PMTs. The port diameter is 21 cm, with a transverse and axial length FOV of 12.8 cm and 11.6 cm respectively. A measured sensitivity of 1.3% (threshold at 400 keV) is reported for a point source at the center of the FOV, with a spatial resolution of 2.26 mm FWHM.

2.4.6 The ClearPET

The Crystal Clear Collaboration was established in 1990 with the aim of developing scintillator materials which would be suitable for use at the CERN Large Hadron Collider. It is an interdisciplinary network of world experts in material science and radiation instrumentation. Work from the Crystal Clear Collaboration also had direct outcomes in PET by initiating the ClearPET project. The aim of the ClearPET project was to develop a high performance small animal PET detector module which needed to offer flexibility and modularity to fulfill the requirement of the individual member institutions who wanted to build small animal PET scanners with different purposes and geometries.
The ClearPET detector module building block consists of the following. The phoswich detector consists of two stacked $8 \times 8$ arrays of $2 \text{ mm} \times 2 \text{ mm} \times 10 \text{ mm}$ of LSO and LuYAP crystals elements. The LuYAP is coupled to a Hamamatsu H7600 64 channel PMT. A thin metal mask with 64 square holes of various size is placed between the crystal array and the PMT for a first order correction in the light collection and PMT channel gain variation. Four LuYAP/LSO/PMT detectors are mounted per module. The 64 PMT anode channels are fed to a bank of comparators which share a common threshold. The comparator outputs are used in conjunction with priority encoders to find the position of the interaction. The comparator output is also used as the timing trigger. The PMT's dynode signal is integrated using a charge sensitive preamplifier, then filtered and sent to a free running 12-bit Analog Device AD9224 ADC running at 40 MHz. When a valid timing trigger occurs, an FPGA records 16 samples from the digitized dynode signal, covering the complete pulse, as well as the position of interaction in the PMT and the 40 MHz system clock cycle where the event occurs. The clock cycle recorded provides a 25 ns coarse timestamp. The timestamp is further refined by software post-processing of the dynode signal. Software post-processing is also used to identify the crystals' scintillation light origin. An optical transceiver is used to transmit the 40 bytes per event to the DAQ [STREUN et al., 2006][ZIEMONS and ON BEHALF OF THE CLEARPET COLLABORATION, 2004][ROLDAN et al., 2007]. Fig. 2.11 shows a picture of the detector and the ClearPET module.
Vrije Universiteit Brussel (Belgium), the Université de Lausanne (Switzerland), the Samsung Medical Center Seoul (Korea) and the Research Center Jülich (Germany) all have built scanners based on the ClearPET detector module. Now a company named Raytest Isotopenmessgeräte GmbH (Straubenhardt, Germany) is also selling a commercial version of the ClearPET. The commercial ClearPET small animal scanner consists of 20 detector modules, for a total of 80 LuYAP/LSO/PMT detectors. Fig. 2.12 presents a picture of an early version of the ClearPET detector modules assembly. The gantry diameter can be adjusted to 140 mm and 260 mm, for an animal port diameter of 125 mm to 245 mm respectively, allowing flexibility to study primates or rodents with the same camera, trading off spatial resolution and sensitivity. The axial FOV is 110 mm. A typical coincidence timing resolution of 5.7 ns FWHM was measured. A maximum sensitivity of 3.8% in the center of the FOV along with a spatial resolution of 1.25 mm was measured for an energy window of 250-750 keV.
2.4. SMALL ANIMAL PET SYSTEMS

2.4.7 The MADPET II

The Munich Avalanche Diode PET, or MADPET-II, is a small animal PET developed at the Technische Universität München in Germany [SPANOUDAKI, 2008]. The camera consists of 18 blocks, forming a cylinder 7.1 cm in diameter. Each block consists of two radially stacked layers, where each layer is formed by a $4 \times 8$ array of LSO optically coupled one to one to a Hamamatsu S8550 $4 \times 8$ APD array. Fig. 2.13 shows a diagram of the detector arrangement and a picture of the camera. The scanner has an axial and transverse FOV of 18 mm and 71 mm respectively. The individual LSO crystal size of the front layer is $2 \text{ mm} \times 2 \text{ mm} \times 6 \text{ mm}$ and the back layer crystal size is $2 \text{ mm} \times 2 \text{ mm} \times 8 \text{ mm}$. This novel idea of stacking two independent detectors serves two purposes. First, it improves DOI resolution, which leads to an increased and more uniform spatial resolution within the FOV. Second, the overall thickness of LSO (14 mm) not only preserves the sensitivity but improves it as inner block Compton scattered events can be identified and reconstructed, enabling potential recovery of events scattered in the detection system.

The APD signals are integrated by a custom ASIC containing 16 channels of charge sensitive preamplifiers and differential line drivers, mounted on the same rigid-flex PCB as the detectors. The signals are sent outside the camera to a DAQ system. Each DAQ module consists of 8 custom ASICs with 4 channels differential receivers, shaping amplifier...
and non-delay line constant fraction discriminators, which provide the timing information of each event. Peak detectors are used to sample the analog signal, which is digitized by Analog Devices AD7470 10-bit ADC. All the data is stored in list mode for further data processing and image reconstruction.

The system has an average timing resolution of 9 ns FWHM. The reconstructed spatial resolution is 1.3 mm FWHM at the center of the FOV. The sensitivity is 0.85% for a low level discrimination of 250 keV.

2.4.8 The LabPET

The LabPET, derived from the original Sherbrooke APD PET scanner described previously [LECOMTE et al., 1996], was designed by the team of Dr. Roger Lecomte and Dr. Réjean Fontaine from Université de Sherbrooke, Canada, and is available commercially through Gamma Medica-Ideas. The LabPET distinguishes itself as the first commercial APD-based PET scanner. The LabPET is available in two versions: the LabPET4 with an axial FOV of 3.75 cm and a total of 1536 pixels, and the LabPET8 with a 7.5 cm axial FOV and 3072 pixels [BERGERON et al., 2007].

The detector for the LabPET consists of a phoswich arrangement of LYSO and LGSO scintillators, each measuring 2 mm x 2 mm x 10 mm and 2 mm x 2 mm x 12 mm respectively. Compared to phoswich arrangements presented earlier, the purpose of the dual crystal is not to increase uniformity of the spatial resolution by minimizing the parallax error, but to perform light multiplexing from two different crystals into a single APD, cutting in half the number of readout channels required for a given number of crystals. Both crystals are optically coupled to a rectangular APD seating at a 55° wedge. Four of those APD/LYSO/LGSO detectors are enclosed into an hermetic package with an external size of 10.3 mm x 4.7 mm x 18 mm. Four of these quad-detector modules are mounted on the front-end PCB, as seen in Fig. 2.14. In the case of the LabPET4, 8 of these front-end PCBs are stacked, creating 16 slices. For the LabPET8, 16 of these front-end PCB are stacked, creating 32 slices. Twelves of these modules are arranged around a diameter of 16.2 cm, for a maximum transaxial FOV of 100 mm, as seen in Fig. 2.15.

The APDs are read out by a custom ASIC with 16 channels of low noise charge sensitive preamplifiers and differential line drivers. The ASIC was realized in TSMC 0.18 μm CMOS [PRATTE et al., 2004b]. Four 16 channels analog front-end PCBs are connected to another PCB where the signals are digitized by 32 dual-channel, 8-bit ADCs free running
2.4. SMALL ANIMAL PET SYSTEMS

Figure 2.14  Picture of the LabPET front-end PCB where the four quad-detector modules and the custom 16 channel ASIC is shown [BERGERON et al., 2007].

Figure 2.15  Picture of the LabPET module assembly.
Figure 2.16 Picture of the RatCAP camera without the cover. The LSO scintillator array, APD and front-end ASIC are outlined.

at 45 MHz. A dual core FPGA receives the data from the ADC, extracts the timing information, and uses a digital signal processor to identify the origin of the event between the LYSO and LGSO. The data from six of those PCBs are sent to another sub-system which sorts according to the timestamp of the events. The data is then sent to a digital coincidence processor engine, which can sustain a rate of 40 million events per second in real-time.

The LabPET operates in 3D. The tangential/radial resolution is 1.3/1.4 mm FWHM at the center of the FOV. The sensitivity is 1.1% and 2.1% for the LabPET4 and LabPET8 respectively, for an energy window of 250-650 keV.

2.4.9 The RatCAP

The RatCAP consists of 12 detector blocks, as illustrated in Fig. 2.16. Each block consists of an Hamamatsu S8550 APD array of 4 × 8 pixels of 1.6 mm × 1.6 mm active area, coupled one to one to a 4 × 8 array of LSO crystal of 2.2 mm × 2.2 mm × 5 mm. Fig. 2.17 shows a picture of the APD and LSO array. Each block also includes all the required electronics, from a full custom front-end ASIC to high voltage filtering and trimming, and voltage regulators. The 12 blocks are mounted on a rigid-flex PCB, which is illustrated in Fig. 2.18. Once cut from the panel and wrapped, it forms a cylinder with a diameter of 38 mm and an axial FOV of 18 mm. Fig. 2.19 shows a picture of the actual camera with part of the cover removed. The whole camera weighs roughly 200 gr. Preliminary results
Figure 2.17  Picture of the LSO and APD arrays.

Figure 2.18  Picture of the rigid-flex PCB for the RatCAP camera.
suggest a spatial resolution of 1.8 mm using filtered back projection and a sensitivity of 0.3% for a low energy threshold of 350 keV at the center of the FOV. Fig. 2.20 shows a picture of the RatCAP apparatus used for awake animal study, where the mechanical support is visible.

The whole RatCAP system consists of three main components. The RatCAP camera, the Time Stamping and Processing Module (TSPM) and a PCI-based DAQ. The TSPM consists of an FPGA-based time to digital converter featuring an LSB of 650 ps and optical transceivers for communication with the PCI-based DAQ. The TSPM timestamps each event from the camera with 43-bit resolution and generates the block and channel address where the event was detected. Sixty four bits per event are sent to the DAQ through optical transceivers, required for signal integrity when used in the MRI facility. The TSPM also takes care of programming the 12 daisy chained ASICs on the camera through a $12 \times 1088$-bit serial programming interface.

In conclusion, there are many preclinical PET systems, but only a few are based on the APD. The main reason resides in the difficulty to design and implement low noise charge sensitive preamplifiers. The use of a CSP is mandatory in APD-based systems, as APDs suffer from poor signal to noise ratio. Hence, the CSP is a key element determining the
Figure 2.20 Photograph of a conscious rat in the RatCAP scanner during a PET scan, including the support arm and data acquisition electronics (top).
performance of a system. In the next chapter, a paper on the optimization and design of two CSPs for APD-based PET systems, the RatCAP and LabPET, will be presented.
Résumé

Ce premier article présente la conception et la caractérisation de deux préamplificateurs de charges pour des systèmes de tomographie d'émission par positrons (TEP) utilisant des photodiodes à avalanche. Le premier préamplificateur, qui consomme 1 mW, a été conçu pour le RatCAP qui requiert une faible consommation de puissance. Le deuxième préamplificateur, qui consomme 5 mW, a été réalisé pour le LabPET de Sherbrooke. Ce circuit intégré a été implanté dans la technologie CMOS de 0.18 µm de Taiwan Semiconductor Manufacturing Company Ltd (TSMC). Ce circuit fut le premier à être réalisé en 0.18 µm dans le domaine de l’instrumentation pour détecteur de radiation. Des structures de test ont aussi été intégrées dans ce circuit pour permettre la caractérisation et la modélisation du bruit des transistors.

Ce premier article contribue de façon significative à cette thèse. Premièrement, l'architecture, la conception et l'optimisation du bruit de ces préamplificateurs de charges sont présentés. Il est important de mentionner que le préamplificateur de charges est l'élément déterminant des performances de l'électronique frontale. Deuxièmement, étant donné qu'il s'agissait de la première tentative à réaliser un circuit dans cette technologie, avec pour but ultime de concevoir un circuit multi-canaux faible bruit et faible puissance pour l'instrumentation de détecteur de radiation, il était impératif de valider cette technologie. Troisièmement, la caractérisation du bruit des préamplificateurs ainsi que des structures de tests ont permis une mise à jour importante du modèle du bruit des transistors. Il est bien connu que les modèles analogiques qui sont fournis par les fonderies de silicium sont imprécis, étant donné que la majorité des circuits CMOS sont conçus pour des applications numériques. Il fut constaté que les paramètres du bruit 1/f étaient largement sous-estimés, et que ceux-ci changent en fonction de la longueur de la grille du transistor. L'expérience
acquires a permission to review the preamplifier design, as presented in the third article of this thesis, and thus reduces the noise by ~40% of the preamplifier.

Finally, the joint realization of this circuit integrated by the Brookhaven National Laboratory and the Université de Sherbrooke was a successful experience and was the cornerstone for the debut of a strong collaboration between the two teams in the realization of novel PET systems.

Synopsis

This first paper presents the design and characterization of two CSPs for APD-based PET systems. The first CSP, which uses only 1 mW, was designed for the low power RatCAP system. The second CSP, which has a power consumption of 5 mW, was designed for the Sherbrooke LabPET. The ASIC was implemented in CMOS 0.18 μm from Taiwan Semiconductor Manufacturing Company Ltd (TSMC). This was the very first design in this feature size in the field of radiation instrumentation. Test structures were integrated into the ASIC to characterize and model the noise of the CMOS devices.

This paper contributes in many ways to this thesis. First, it presents the architecture, design and noise optimization of the CSP, the key element determining the performance of the analog front-end. Second, as this was the first time this technology was used to develop radiation instrumentation for low noise, low power, multi-channel systems, it was important to validate its suitability before going on with the realization of the full front-end ASIC for the RatCAP in this technology, which will be presented in the next papers. Third, the characterization of the noise and the fitting of the measurements with the model permitted an important update of the transistor noise model. CMOS being mainly used for digital integrated circuits, the analog models provided by the foundry are often inaccurate. It was realized that the 1/f noise parameters were greatly underestimated, and that they vary with the gate length of the devices. This learning experience allowed the subsequent redesign of the CSPs which then lead to a factor ~1.5 improvement in the noise performance, as will be seen in chapter 5.

Finally, the joint realization of this ASIC by the Brookhaven National Laboratory and the Université de Sherbrooke was a successful experience and was the cornerstone for the debut of a strong collaboration between the two teams in the realization of novel PET systems.
3.1. INTRODUCTION

**Abstract**

The CMOS 0.18 μm technology was investigated for two analog front-end projects: the low-power budget rat-head mounted miniature Rat Conscious Animal PET (RatCAP) scanner, and the high-performance, low-noise, high-rate PET/CT application. The first VLSI prototypes consisted of 1-mW and 5-mW charge sensitive preamplifiers (CSP) based on a modified cascode telescopic architecture. Characterization of the rise time, linearity, dynamic range, Equivalent Noise Charge (ENC), timing resolution and energy resolution are reported and discussed. When connected to an APD-LSO detector, time resolutions of 2.49 ns and 1.56 ns (FWHM) were achieved by the 1-mW and 5-mW CSPs, respectively. Both CSPs make it possible to achieve performance characteristics that are adequate for PET imaging. Experimental results indicate that the CMOS 0.18 μm technology is suitable for both the low-power and the high-performance PET front-end applications.

3.1 Introduction

Recent studies on deep sub-micron CMOS technologies have triggered interest for applications where highly integrated analog front-end electronics is required [MANGHISONI
et al., 2001]. In particular, the low power and high integration of the CMOS 0.18 μm technology make it an attractive choice for high-resolution APD-based imaging detection systems like small animal Positron Emission Tomography (PET) scanners. The scaling of the power supply down to 1.8 V reduces the available dynamic range, but the gain in signal-to-noise ratio at a given dissipated power makes this choice attractive compared to older technologies [O’CONNOR and DE GERONIMO, 2002]. In this paper, the experimental results obtained with two Charge Sensitive Preamplifiers (CSP) for PET imaging implemented in CMOS 0.18 μm are reported. Two specific applications are considered: a low power, 1-mW CSP for the low-power budget RatCAP [VASKA et al., 2001],[PRATTE et al., 2004a], and a high-performance, 5-mW CSP for a high-resolution PET/CT scanner with high-density multi-crystals (phoswich) detector modules [FONTAINE et al., 2005].

3.2 Charge Sensitive Preamplifiers

3.2.1 Design

Initial specifications for the CSPs were based on the detectors planned for the RatCAP scanner (see Table 3.1), which is a Hamamatsu S8550 4×8 APD-array coupled to 2.2 mm × 2.2 mm × 5 mm LSO crystals [VASKA et al., 2004] [KRIPLANI et al., 2003]. In this application, the APD is DC coupled to the CSP input requiring a feedback MOSFET that provides a pathway for the APD leakage current. The feedback MOSFET is designed to operate above threshold for better white noise performance and in saturation for better compensation performance [DE GERONIMO and O’CONNOR, 1999].

The targeted preamplifier gain of 3.3 mV/fC, selected to provide a maximum output swing of 100 mV, corresponds approximately to an input signal of 190,000 electrons. The APD-based detector modules for the RatCAP are expected to be used at a gain of 50, producing approximately 115,000 electrons for 511 keV photons in LSO. A higher signal is expected
Figure 3.1 CSP architecture. The transistor M2 is used as the main current source to achieve the desired transconductance.

from the PET/CT detectors at 511 keV, but an excellent signal-to-noise ratio must also be achieved for the detection of low-energy X-rays.

Fig. 3.1 shows the modified telescopic cascode topology of the CSP. Transistor M2 is used as the main current source to produce the desired transconductance in the input transistor M1. The CSPs were implemented in TSMC CMOS 0.18 μm technology, having six metal layers and one poly layer, through the Canadian Microelectronics Corporation.

3.2.2 Noise Optimization

The N-channel MOSFET input device of the CSP has been optimized with respect to the technology parameters and the detector characteristics at its operating point (capacitance, leakage current and gain), using the EKV transistor model [ENZ et al., 1995], to minimize the Equivalent Noise Charge (ENC) [RADEKA, 1988],
TABLE 3.2  Shaping form factors.

<table>
<thead>
<tr>
<th>Shaping</th>
<th>CR-RC</th>
<th>CR²-RC²</th>
<th>SEMI-GAUSSIAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A_s)</td>
<td>1.85</td>
<td>2.27</td>
<td>2.15</td>
</tr>
<tr>
<td>(A_p)</td>
<td>1.85</td>
<td>1.45</td>
<td>2.10</td>
</tr>
<tr>
<td>(A_f)</td>
<td>1.18</td>
<td>1.55</td>
<td>1.61</td>
</tr>
</tbody>
</table>

\[
ENC = \sqrt{ENC_s^2 + ENC_p^2 + ENC_f^2} 
\]

\[
ENC_s = \frac{2kTA_xC_{in}^2}{t_p} \left( \frac{\gamma}{g_{mN}} + R_P \right) 
\]

\[
ENC_p = \frac{2kTA_p}{R_{eq}} 
\]

\[
ENC_f = \frac{K_{Fn}}{C_{ox}WL} \pi A_f 
\]

\[
R_{eq} = \frac{2kT}{I_{leak}M} \left| \frac{1}{\eta g_{mFB}} \right| 
\]

where \(ENC_s\), \(ENC_p\) and \(ENC_f\) are the series, parallel and flicker Equivalent Noise Charge contribution, \(k\) the Boltzmann’s constant, \(T\) the temperature in Kelvin, \(A_x\) \((x = f, p, s)\) the form factors of the shaping function [RADEKA, 1988], \(C_{in}\) is the total capacitance at the input, \(\tau_p\) the shaping function peaking time, \(\gamma\) the coefficient of thermal noise for the input MOSFET, \(g_{mN}\) the source transconductance of the input MOSFET, \(R_p\) the parasitic resistance in series with each transistor electrode, \(K_{Fn}\) the NMOS flicker noise coefficient, \(C_{ox}\) the gate oxide capacitance per unit area, \(W\) and \(L\) the width and length of the input NMOS, \(I_{leak}\) the APD leakage current, \(M\) the APD gain, \(\eta\) a coefficient which depends on the region of operation and \(g_{mFB}\) the transconductance of the reset transistor. The size of the input device was optimized for the derivative of a 3\(^{rd}\) order semi-gaussian shaping function [OHKAWA et al., 1976] with a peaking time of 70 ns and power consumption of 1 mW and 5 mW. Table 3.2 presents the shaping form factor for a CR-RC, CR²-RC² and the derivative of a 3\(^{rd}\) order semi-gaussian shaping function [OHKAWA et al., 1976].
All other transistor dimensions of the CSP are optimized for minimum white series and 1/f noise contribution on the overall ENC, mainly set by the input device.

3.3 Experimental Results

A test Printed Circuit Board (PCB) developed at Brookhaven National Laboratory (BNL) was used for characterization. It includes a 1.8 V power and ground plane, a low-noise 1.8 V voltage regulator and an on-board Analog Devices AD8009 buffer used for both 50 ohms adaptation with the shaping amplifiers and voltage gain of +5 at the CSP output. All required high voltage hardware and connectors for the BNL and Sherbrooke APD detector modules were implemented on the PCB. Charges were injected with a test pulse applied to an on-board characterized 1 pF capacitor for each CSP. The chip was directly wire bonded to the PCB. The BNL detector module is based on the Hamamatsu S8550 4×8 APD-array coupled to a matched array of 2 mm × 2 mm × 5 mm LSO crystals. The Sherbrooke detector module is based on a former PerkinElmer BGO/APD module [LIGHTSTONE et al., 1986] retrofitted with 3 mm × 5 mm × 25 mm LSO scintillators. It has a leakage current of 45 nA and a capacitance of 22 pF when biased at 350 V.

3.3.1 Electronic Characterization

The rise time, linearity and the dynamic range of the CSPs were measured using a custom Nuclear Instrumentation Module (NIM) pulser and a Tektronix TDS 784A digital oscilloscope for input capacitance of 0 pF to 22 pF. Fig. 3.2 and Fig. 3.3 present the measured linearity for the 1-mW and 5-mW CSPs. A gain of 2.7 mV/fC was deduced for both prototypes. The input capacitance had no influence on the dynamic range and the linearity.

The rise time for the 5 mW and the 1 mW CSP was 7 ns and 9 ns, respectively, without any capacitor added at their input ($C_{stray}$ 11 pF). With a 10 pF capacitor at the input, a rise time of 13 ns and 18 ns was measured respectively.

3.3.2 ENC Measurements

Gain and noise measurements for the 1-mW CSP were performed for shaping times from 10 ns to 10 μs with a custom NIM bipolar CR^2-RC^2 shaper. The custom NIM pulser was used to inject the charges through the 1 pF capacitor. The output amplitude and peaking
Figure 3.2 Gain linearity for 1-mW CSP over operating range.

Figure 3.3 Gain linearity for 5-mW CSP over operating range.
3.3. EXPERIMENTAL RESULTS

Figure 3.4 ENC measurements for the 1-mW CSP.

The time of the chain was measured using a Tektronix TDS 784A digital oscilloscope and the noise using a Rhode & Schwartz TRUE-RMS meter. For the 5-mW CSP measurements, a combination of the Ortec 579 Timing Filter Amplifier and the Ortec 673 Spectroscopy Amplifier with unipolar shaping were used, for the same shaping time range. A BNC BL-2 Pulse Generator was used to inject the charges through the 1 pF capacitor. The output amplitude and peaking time of the chain was measured using a Tektronix TDS 784A digital oscilloscope and the noise using a Fluke 8920A TRUE-RMS.

The Figs. 3.4 and 3.5 present the measured ENC as a function of the input capacitance for the two devices. The discontinuities in the ENC curves in Fig. 3.5 are due to the use of two different shaping amplifiers, as mentioned above. The evaluated ENC for the 1-mW CSP connected to the APD/LSO based detector is reported in Fig. 3.6. A minimum ENC of 1117 electrons-rms at 100 ns was measured. The noise parameters of the 1-mW CSP were fitted on that curve, using 3.1 - 3.5 and the theory exposed in [RADEKA, 1988] and [LECOMTE et al., 2001]. They are reported in Table 3.3 where $K_F$ is the flicker noise coefficient, $e_n$ is the input referred noise-voltage spectral density, $\tau_c$ is the series and parallel noise corner time constant, $C_{stray}$ is the equivalent stray capacitance seen at the CSP input node (including the 1 pF charge injection capacitor and 0.3 pF feedback capacitor). Fig. 3.7 is the ENC curve for the 10 pF capacitor, used to fit the noise parameters of the 5-mW device, also presented in Table 3.3.
Figure 3.5 ENC measurements for the 5-mW CSP. The discontinuities are due to the use of two different shapers (Ortec 579 Timing Filter Amplifier and the Ortec 673 Spectroscopy Amplifier) in order to cover a peaking time from 10 ns to 10 µs.

Figure 3.6 ENC data fit with APD for the 1-mW CSP. A minimum ENC of 1117 electrons-rms at 100 ns was measured.
3.3. EXPERIMENTAL RESULTS

Figure 3.7 ENC data fit with 10 pF for the 5-mW CSP.

<table>
<thead>
<tr>
<th>Table 3.3 Extracted noise parameters.</th>
</tr>
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<tbody>
<tr>
<td>CSP</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>$K_F$</td>
</tr>
<tr>
<td>$e_n$</td>
</tr>
<tr>
<td>$\tau_c$</td>
</tr>
<tr>
<td>$C_{stray}$</td>
</tr>
</tbody>
</table>
Figure 3.8 Electronic timing resolution for the 1-mW CSP. The Hamamatsu APD/LSO
detector was connected at the input and biased at a gain of 50.

3.3.3 Timing Measurements

The coincidence timing resolution of both CSPs was measured using standard nuclear
spectroscopy techniques [CARRIER and LECOMTE, 1990].

The electronic timing resolution was measured using a Phillips Scientific 704 Leading Edge
Discriminator (LED) connected directly at the output of the CSP without filter, providing
the stop signal to a time digitizer Phillips Scientific 7186. A LeCroy 9210 pulser, providing
a signal amplitude corresponding to 511 keV in an APD/LSO detector, was connected at
the test input of the CSP. The trigger of the LeCroy pulser, through another channel of
the LED, was used as the start signal in the time digitizer. The Hamamatsu APD/LSO
detector was connected at the input and biased at a gain of ~50 for the evaluation of
both devices. The 1-mW CSP has an electronic timing resolution of 0.56 ns FWHM, as
reported in Fig. 3.8. The 5-mW CSP achieved a slightly better electronic timing resolution
of 0.47 ns FWHM, as presented in Fig. 3.9.

For the detector time resolution, the CSPs were connected to a CR-RC Ortec 474 Timing
Filter Amplifier and an Ortec 934 Constant Fraction Discriminator (CFD). The 1-mW
CSP measurement was performed with the Hamamatsu APD/LSO detector in coincidence
with a fast PMT/BaF$_2$ detector, using a $^{22}$Na source. For the measurement with the 5-
mW CSP, a PerkinElmer APD/LSO detector in coincidence with a PMT/Plastic (Nuclear
3.3. EXPERIMENTAL RESULTS

Figure 3.9 Electronic timing resolution for the 5-mW CSP. The Hamamatsu APD/LSO detector was connected at the input and biased at a gain of 50.

Enterprise NE-102A detector and an $^{18}$F source were used. Coincidence timing resolutions of 2.49 ns FWHM and 1.56 ns FWHM were obtained for the 1-mW and 5-mW devices respectively, as shown in Fig. 3.10 and Fig. 3.11.

3.3.4 Energy Resolution

The energy resolution of the 1-mW CSP was evaluated with the Hamamatsu detector connected to the input. The output of the preamplifier was fed to a CR-RC Ortec 579 Timing Filter Amplifier, with 50 ns integration and derivation time constants. The best energy resolution was measured with the APD biased at 380 V, which led to 17.4% FWHM, as presented in Fig. 3.12. For the 5-mW device connected to the PerkinElmer detector, using an Ortec shaper 452 with 250 ns integration and derivation time constants, an optimum energy resolution of 11.7% which was fairly insensitive to the APD bias was measured, as reported in Fig. 3.13.
Figure 3.10 Timing resolution spectrum for the 1-mW CSP.

Figure 3.11 Timing resolution spectrum for the 5-mW CSP. The time calibration was obtained by adding an 8-ns delay to the stop channel.
3.3. EXPERIMENTAL RESULTS

Figure 3.12 Energy spectrum for the 1-mW CSP connected to the Hamamatsu APD/LSO detector biased at 380 V.

Figure 3.13 Energy spectrum for the 5-mW CSP showing the electronic noise contribution measured with a pulser.
3.4 Discussion

3.4.1 Electronics

The two devices show excellent linearity. The 2.7 mV/fC measured gain of the two prototypes is lower than the desired 3.3 mV/fC from the initial design specification, which means that the actual feedback capacitors are bigger than expected. This can be explained by added parasitic capacitance and process variation.

The 1-mW and 5-mW devices are linear over the designed dynamic range, suitable for the Hamamatsu detector. However, in order to use the 5-mW device with the PerkinElmer APD/LSO detector, which has a greater light output (10,000 electron-hole pairs per MeV created in the APD before gain) and is used at a gain of 100, a larger dynamic range is required for the 5-mW CSP. Hence the gain of the 5-mW CSP shall have to be lowered in order to allow a greater maximum input charge.

The measured rise times fit accordingly with the simulations. The 5-mW device shows a faster rise time than the 1-mW, due to its higher transconductance.

3.4.2 Equivalent Noise Charge

As expected, the 5-mW CSP has a lower ENC as a function of the input capacitance compared to the 1-mW device. We notice that the measured minimum ENC is higher than expected and shifted to a higher peaking time. For instance, the minimum ENC of the 1-mW CSP measured with the detector biased at a gain of 50 is 1117 electrons-RMS at 100 ns, instead of 726 electrons-RMS at 70 ns as designed. This can be explained by an underestimation of the flicker noise coefficient during the design, which resulted in a higher contribution from the 1/f noise, as seen by the flatness of the curves. The main source of 1/f noise is the input transistor M1, operating between weak and moderate inversion for both CSPs. Tsividis et al. [TSIVIDIS and SUYAMA, 1994] suggest that the provided manufacturer 1/f noise models are aimed at digital design and usually do not appropriately characterize MOSFET devices operating in weak and moderate inversion regions. Test transistors were included on chip, and preliminary characterization of those confirms our assumption. In order to get the best noise performance, a review of the CSP’s design will be necessary, using the appropriate flicker noise coefficient. Considering the high 1/f noise contribution of the N-channel MOSFET input device, the use of a P-channel MOSFET looks appealing in theory. However, the requirement for a current
return path between the input MOSFET and the detector high voltage power supply imposes significant design constraints [O’CONNOR et al., 2003]. Recent studies of deep sub-micron CMOS technology indicate that the flicker noise contribution drops as the transistor gate length is slightly increased above the minimum dimension [MANFREDI and RE, 2003]. This aspect is currently under study for the CMOS 0.18 μm technology and, depending on the conclusion, the adoption of a longer gate length could be considered.

3.4.3 Timing Resolution

The electronic timing resolution of the 5-mW CSP is slightly better than the one of the 1-mW device. This is consistent with the theory, as the 5-mW device benefits from a lower noise contribution and a faster rise time due to its higher transconductance, leading to a smaller time jitter in the LED.

The coincidence timing resolution of the prototypes is in accordance with the previous results, where the 5-mW device presents better performance. The difference between the achieved coincidence timing resolutions is somehow bigger than the difference between the electronic timing resolutions because the PerkinElmer detector has a larger output signal and better energy resolution than the Hamamatsu detector array due to their different characteristics (ex: scintillator size, coupling, APD gain operating point). In both cases, the achieved coincidence timing resolutions using a CFD allows the use of a small coincidence timing window, which is particularly important to limit the number of random coincidences in PET imaging system.

3.4.4 Energy Resolution

In scintillator/APD-based detectors, the contribution of the CSP to the deterioration of the energy resolution is negligible, as it is mainly the stochastic nature of the scintillation process and the APD excess noise which determine the energy resolution [LECOMTE et al., 1998]. The results obtained with the Hamamatsu-based detector module on the 1-mW CSP and with the PerkinElmer LSO/APD detector modules on the 5-mW CSP concur with previous measurements performed in our laboratory and elsewhere, and confirms the negligible contribution of the CSP to the energy resolution.
3.4.5 Charge Sensitive Preamplifiers for PET

Table 3.4 compares the key performance parameters of CMOS charge preamplifiers previously developed for PET imaging with the 1-mW and 5-mW CSP investigated in this paper [SCHMITT et al., 1987][BINKLEY et al., 1992][PAULUS et al., 1996][BINKLEY et al., 2000]. As expected, the 5-mW CSP achieves better input referred noise-voltage and timing resolution compared to the 1-mW CSP, due to the higher transconductance of the input transistor M1. Still, the 1-mW device reaches nearly similar performance at a fraction of the power required by previous CSP designs. The 1-mW CSP fulfills the stringent power requirements of the RatCAP where a total power budget of only 3.9 mW per channel is allowed [VASKA et al., 2001],[PRATTE et al., 2004a].

3.5 Conclusions

Two charge sensitive preamplifiers were designed in a 0.18 μm CMOS technology and optimized for LSO/APD-based detectors for PET imaging. The performance of the low-power and high-performance devices, which is comparable to that obtained with previously developed charge sensitive preamplifiers, clearly indicates their suitability for PET front-end systems. Finally, it has been demonstrated that the CMOS 0.18 μm technology is suitable for the realization of low power, low noise analog front-end electronics.

3.6 Acknowledgements

Special thanks to V. Radeka, J. Triolo, S. Rescia, R. Machnowski, C. Woody, A. Kandasamy and the RatCAP group from BNL and D. Rouleau, R. Bernier, L. Hubert from Université de Sherbrooke for support, advice and their precious time. Also, thanks to J. Sondeen who provided excellent Magic tech-file support. Finally, the authors would
like to acknowledge the assistance of the Canadian Microelectronics Corporation for providing tools and technical support for the chip fabrication. This work is part of a joint collaboration between Brookhaven National Laboratory and Université de Sherbrooke in Canada.
Résumé

Cet article traite de la réalisation de l’électronique frontale intégrée pour le RatCAP, et contribue de plusieurs façons à cette thèse. Premièrement, les objectifs de conception et les spécifications du circuit intégré pour le RatCAP sont énumérés. Un schéma bloc montrant l’architecture et les diverses fonctionnalités du circuit est présenté. Il est important de mentionner que le circuit final, présenté dans le dernier article de cette thèse, a une architecture légèrement différente de celle présentée ici suite à des améliorations qui ont été apportées.

La chaîne analogique est composée d’un préamplificateur de charges, d’un réseau pole-zéro et d’un filtre bipolaire semi-Gaussien du troisième ordre. Une étude sur la résolution temporelle qui prend en considération le bruit électronique ainsi que la statistique d’émission de photons et de génération de photoélectrons est aussi introduite. Enfin, le concept de l’encodeur d’adresse et de déclenchement de temps, utilisé pour multiplexer l’information des 32 canaux dans une sortie et ainsi réduire le nombre d’interconnexions entre la caméra et le système d’acquisition, est introduit.

Les résultats présentés dans cet article découlent de mesures effectuées sur le deuxième circuit intégré réalisé pour le RatCAP. Ce circuit est composé de 32 canaux de la chaîne analogique seulement. Le bruit électronique (ENC), la plage dynamique et la linéarité, la résolution en énergie ainsi que la résolution temporelle sont présentés. En ce qui concerne la mesure de la résolution temporelle, il est intéressant de préciser qu’un discriminateur à fraction constante commercial NIM, Ortec 934, a été utilisé sans l’addition du signal différé, pour ainsi émuler un discriminateur par passage par zéro, tel qu’utilisé dans la version finale du circuit pour le RatCAP. Ce test a ainsi permis de faire une première évaluation de la résolution temporelle qui peut être obtenue avec un discriminateur de passage par zéro. Une résolution temporelle de 6.7 ns FWHM a été mesurée pour un module de détection composé du circuit intégré, PDA et LSO, en coïncidence avec un
tube photomultiplicateur et un scintillateur de BaF$_2$. Le bruit électronique de la chaîne analogique reporté à l'entrée du préamplificateur est de 902 electrons rms. Il est important de préciser que le préamplificateur utilisé dans ce circuit est le même que celui présenté dans l'article précédent, où l'optimisation du bruit a été fait avec un coefficient de bruit 1/f sous estimé.

Enfin, cette deuxième itération du circuit intégré pour le RatCAP fut une étape importante vers la réalisation du circuit final. Il a ainsi été prouvé qu'il est possible de réaliser de l'électronique analogique faible bruit et faible puissance dans cette technologie, et qu'elle est appropriée pour atteindre les objectifs du RatCAP.

**Synopsis**

This paper is about the design and realization of the front-end ASIC for the RatCAP, and contributes in many ways to this thesis. The design objectives and specifications of the RatCAP ASIC are presented. A block diagram showing the architecture and the various functionality of the ASIC are presented. It is worth mentioning that the final ASIC, presented in the third paper of this thesis, has some slight architectural improvements over the one reported here.

The analog front-end chain, consists of a CSP, a pole-zero network and a 3$^{rd}$ order bipolar semi-Gaussian shaper is presented in detail. A study of the achievable timing resolution as a function of the shaper's peaking time, taking into account the electronic noise and photoelectron statistical contribution is introduced. Also, the novel concept of a 32-to-1 serial timing and address encoder, used to multiplex the timing information and address of the channel which fired through a single output, is introduced.

The results presented in this paper refer to the 2$^{nd}$ ASIC realized for the RatCAP, which consists of 32 channels of the analog front-end. Measurements on the analog front-end performance includes: the ENC, dynamic range and linearity, energy resolution and timing resolution. Regarding the timing resolution measurement it is pertinent to point out that a NIM based Ortec 934 constant fraction discriminator (CFD) was used, without feeding back the delay version of the shaper’s signal, to emulate a zero-crossing discriminator. This allowed a first measurement of the achievable timing resolution with a zero-crossing discriminator, which was integrated in the final version of the ASIC for the RatCAP, as it will be presented in the last paper in this thesis. For this setup, a timing resolution of 6.7 ns FWHM was measured in coincidence with a PMT/BaF$_2$ detector. The noise
measurement of the analog front-end lead to an ENC of 902 electrons rms. It is important to point out that the CSP used in this ASIC was the same as the one presented in the previous paper, suffering from noise optimization with an erroneous 1/f noise coefficient.

Finally, this intermediate ASIC was a major step toward the final design. It proved that a low noise, low power analog front-end could be designed in this technology, and that it is suitable to achieve the design objectives for the RatCAP.

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**Abstract**

We report on the development of the front-end electronics for the RatCAP (Rat Conscious Animal PET), a portable and miniature Positron Emission Tomography scanner. The ASIC is realized in a CMOS 0.18 \(\mu\)m technology and it is composed of 32 channels of Charge Sensitive Preamplifier (CSP), 3\(^{rd}\) order semi-gaussian bipolar shaper, timing discriminator with independent channel adjustable threshold and a 32-line address serial encoder to minimize the number of interconnections between the camera and the data acquisition system. Each chip has a maximum power dissipation of 125 mW. A mathematical model of the timing resolution as a function of the noise and slope at the discrimination point as well as the photoelectron statistics was developed and validated. So far, 3 ASIC prototypes implementing part of the electronics were sent to fabrication. Results from the characterization of the first two prototypes are presented and discussed.
4.1 Introduction

A team at the Brookhaven National Laboratory is currently working on the realization of the RatCAP (Rat Conscious Animal PET) scanner. The RatCAP is a head-mounted miniature PET (Positron Emission Tomography) scanner intended to perform brain imaging and behavioral studies of awake rats [VASKA et al., 2001]. The requirement of mobility imposes significant limitations on the size, weight, power dissipation, and data communication with the scanner, requiring new approaches to detectors, electronics, and image reconstruction.

In this work, we report on the development of the front-end electronics for the RatCAP. The main design objectives for the front-end electronics are the following. First, the ASIC (Application-Specific Integrated Circuit) should have minimal power dissipation in order not to affect the animal’s behavior or change the APD gain which is sensitive to temperature. Second, all the front-end electronics must fit on the back of the detector. Third, the number of interconnections between the chips and the Data Collection Module (DCM) should be minimized in order to prevent the degradation of the camera’s mobility. Finally, the electronics must be optimized for the detector characteristics in order to achieve the best possible timing resolution.

4.2 The RatCAP Front-End Electronics

4.2.1 The RatCAP System

The RatCAP system is composed of a 384 channel camera with a communication and power management module, an absolute time and address generator module and a VME-based acquisition system. The detectors are based on Hamamatsu 4 × 8 APD arrays (S8550) coupled to Lutetium Oxyorthosilicate (LSO) scintillators of 2.2 mm × 2.2 mm × 5 mm. These detectors have a measured light output of 4500 photoelectrons per MeV. The camera is made of 12 detector blocks, each having a 32-channel front-end ASIC mounted on the back. The main purpose of the ASIC is to provide the position and the timing information of every detected event. Also, on the back of each detector block, there is a 1.8 V voltage regulator and circuitry for independent high voltage trimming of each APD array. In order to minimize the number of interconnections, an on-chip encoder sends the timing information as well as the detector channel address through one output.
4.2. THE RATCAP FRONT-END ELECTRONICS

The communication module converts $0 – 1.8\ V$ signals (camera side) to LVDS standard I/O data. There is also an analog driver for channel monitoring and calibration with an oscilloscope, as well as a 100 MHz clock generator for the ASICs digital circuit.

On the receiving end, the proposed DCM will be made of a Field Programmable Gate Array (FPGA) based Time to Digital Converter (TDC), which will detect the timing edge with a sub-nanosecond resolution. A 64 bit word will be generated for each event, where 43 bits are for an absolute timestamp, 13 bits are for the detector channel and ASIC addresses (flexibility to go to 256 blocks), 7 bits are for a timer-counter to check for memory overflow and the last 3 bits are for event type classification. The data are read out with a VME-based data acquisition system and sent to a Linux-based computer system for storage and analysis.

4.2.2 The RatCAP ASIC

Fig. 4.1 presents a block scheme of the RatCAP ASIC. Every channel contains a Charge Sensitive Preamplifier (CSP), a pole-zero cancellation network, a 3rd order bipolar gaussian shaper [OJIKA et al., 1976] and a timing discriminator with programmable arming threshold. The ASIC also includes a 32 line timing and address serial encoder used to send the address of the detector channel, following the asynchronous timing edge. Finally, circuitry for diagnostic and calibration are built-in on chip. The chip is realized in a 0.18 $\mu m$, single poly, six metal, salicide CMOS process from Taiwan Semiconductor Manufacturing Company (TSMC).

The CSP is based on the telescopic cascode architecture, with an added current source ($M2$) into the input device to allow greater transconductance, as shown in Fig. 4.2. As a shaper implementing a short peaking time is used where white series noise dominate, a NMOS was selected for the input device of the CSP for its greater noise performance compared to a PMOS [MANGHISONI et al., 2002]. Also, knowing the limited power budget, the NMOS allows a greater transconductance than the PMOS. Fig.4.3 shows a schematic of the analog front-end section. The feedback capacitor $C_f$ ($300\ fF$) sets the gain of the CSP to $3.3\ mV/fC$. The reset transistor $M_f$, is an NMOS as the leakage current of the APD flows into the CSP, which collects holes from the anode of the APD connected to the input. The gate of the reset transistor is biased using a voltage reference independent of process variations. The power dissipation is $1.3\ mW$.

The parameters of the NMOS input device have been established by mathematical simulations using MathCAD and the EKV transistor model. They have been optimized with
Figure 4.1 Block diagram of the RatCAP front-end ASIC.
4.2. **THE RATCAP FRONT-END ELECTRONICS**

![CSP Architecture Diagram](image)

**Figure 4.2** CSP architecture.

![Analog Front-End Diagram](image)

**Figure 4.3** Analog front-end.

Respect to the technology parameters and the detector characteristics at its operating point (capacitance, leakage current and gain) to minimize the Equivalent Noise Charge (ENC),

\[
ENC = \sqrt{ENC_j^2 + ENC_p^2 + ENC_s^2}
\]

(4.1)

\[
ENC_j = C_{j1}\frac{K_{jn}}{C_{ox}WL}A_f
\]

(4.2)

\[
ENC_p = \frac{2kT_{AP}t_p}{R_{eq}}
\]

(4.3)

\[
ENC_s = \frac{2kT_{AP}C_{in}}{t_p} \left( \frac{\gamma}{g_{mn}} + R_P \right)
\]

(4.4)
TABLE 4.1 RatCAP CSP Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Input NMOS device</th>
<th>CSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inversion coefficient</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Transconductance</td>
<td>13.5 mS</td>
<td></td>
</tr>
<tr>
<td>Gate capacitance</td>
<td>1.5 pF</td>
<td></td>
</tr>
<tr>
<td>Input noise voltage (e_n)</td>
<td>0.9 nV / Hz^1/2</td>
<td></td>
</tr>
<tr>
<td>Rise time (C_{in} = 12pF)</td>
<td>17.2 ns</td>
<td></td>
</tr>
<tr>
<td>Gain-Bandwidth</td>
<td>255 MHz</td>
<td></td>
</tr>
</tbody>
</table>

with,

\[
R_{eq} = \frac{R_{p1}}{N^2} \left\| \frac{2kT}{I_{leak}M} \right\| \frac{1}{\eta g_{mFB}}
\]  

(4.5)

where \( ENC_f \) is the flicker noise, \( ENC_p \) the parallel noise, \( ENC_s \) the series noise, \( C_{in} \) the total capacitance at the input, \( K_{Fn} \) the NMOS flicker noise coefficient, \( C_{ox} \) the gate oxide capacitance per unit of area, \( W \) and \( L \) the width and length of the input NMOS, \( A_x \) the form factors of the shaper [RADEKA, 1988], \( k \) the Boltzmann’s constant, \( T \) the temperature in Kelvin, \( t_p \) the shaper peaking time, \( \gamma \) the coefficient of thermal noise for the input MOSFET, \( g_{mN} \) the source transconductance of the input NMOS, \( R_P \) the parasitic resistance in series with each transistor electrode, \( R_{p1} \) the first pole feedback resistance of the shaper, \( N \) the charge gain factor of the pole-zero compensation network, \( I_{leak} \) the APD leakage current, \( M \) the APD gain, \( \eta \) a coefficient which depends on the region of operation and \( g_{mFB} \) the transconductance of the reset transistor. Mathematical simulations predict an ENC of about 726 electrons rms at 70 ns peaking time. Table 4.1 summarizes the characteristics of the CSP, where the calculated inversion coefficient, the simulated transconductance, gate capacitance and gain-bandwidth and the measured input noise voltage (e_n) and rise time are presented. A similar CSP prototype, using 5 mW, has been developed. Further design details and evaluation of both CSPs can be found in a companion paper [PRATTE et al., 2004b].

A pole-zero cancellation network is used to compensate the reset transistor non-linearity [DEGERONIMO and O’CONNOR, 2000]. It is also used to reduce the parallel noise contribution of the following stage by providing a charge gain equal to \( N \).
The 3rd order bipolar gaussian shaper is realized in two stages, a 1st order low pass filter and a 2nd order bandpass filter implemented with the biquadratic architecture [OHKAWA et al., 1976][PRATTE et al., 2002][CHEN, 1986]. Both amplifiers used in the shaper are a scaled version of the CSP amplifier, where every transistor was optimized to minimize its electronic noise contribution. The analog chain has a gain of 15.15 mV/fC and the shaper power consumption is 600 μW. Table 4.2 presents the values of the passive components integrated in the analog front-end section shown in Fig. 4.3.

An investigation is under way to establish the optimum timing discriminator, the shape and the peaking time of the shaper signal to optimize the timing resolution. An initial study was realized taking into account an estimation of the series noise, the photoelectron statistics, and the slope of the shaper signal as a function of the peaking time. With a Zero-Crossing Discriminator (ZCD), a peaking time of 70 ns was found to lead to a minimum timing resolution of 700 ps RMS. Hence the first shaper prototype was implemented with a 70 ns peaking time. After measuring the ENC of the CSP on the first ASIC prototype, and using the measured impulse response of the CSP and the 3rd order bipolar gaussian shaper, an estimated timing resolution of about 2.5 ns RMS was obtained at 70 ns peaking time. Fig. 4.4 presents the mathematical simulation results, with the photoelectron statistics and electronic noise contributions, as well as the measured timing resolution.

As stated previously, a study is currently in progress to determine the type of timing discriminator to be used. So far, the proposed solution is a Zero-Crossing Discriminator based on two comparators. One is used for arming the ZCD by triggering on the leading edge of signals at a threshold set independently for each channel using 5 bit Digital to Analog Converter (DAC). A coarse threshold will be provided externally in order to set the ZCD minimum threshold in the valley between the Compton events and the photopeak of the weakest gain channel. The 5 bit DAC minimal step is then established to allow the threshold to span the range from the weakest to the strongest gain channel. The other comparator is used to find the baseline crossing of the bipolar signal, which actually represents the timing information of every event. In order to calibrate the camera and set

<table>
<thead>
<tr>
<th>Component</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_f$</td>
<td>300 fF</td>
</tr>
<tr>
<td>$M_f$ (W/L)</td>
<td>0.3 μm / 1 μm</td>
</tr>
<tr>
<td>$N$</td>
<td>18</td>
</tr>
<tr>
<td>$C_{p1}$</td>
<td>1.241 pF</td>
</tr>
<tr>
<td>$R_{p1}$</td>
<td>95.7 kΩ</td>
</tr>
<tr>
<td>$R_1$</td>
<td>22.9 kΩ</td>
</tr>
<tr>
<td>$C_2$</td>
<td>0.75 pF</td>
</tr>
<tr>
<td>$R_2$</td>
<td>97.5 kΩ</td>
</tr>
</tbody>
</table>
Figure 4.4 Calculated and measured timing resolution of the analog front-end using a Zero-Crossing Discriminator. A light output of 2300 photoelectrons and an APD gain of 50 was used.

every channel's threshold to compensate for gain variation from the APD and the front-end electronics, the count rate as a function of the channel threshold will be measured. The 5 bit DACs are set for every channel by a shift register loaded serially, where the shift registers of the 12 chips are daisy chained.

In order to minimize the number of external connections, a 32 line address serial encoder is included on-chip. When an event is detected by a channel, the timing discriminator triggers a wired-OR connected to the logic encoder block. At this moment the address is encoded as a 5 bit binary number. This number is latched into a register on the falling edge of the clock, one full clock cycle after the timing edge coming from the wired-OR. The asynchronous timing edge and the latched 5-bit address are transmitted on a single line, serially. Fig. 4.5 illustrates the serial encoder output signal. Conflict between two or more simultaneous triggers is resolved by priority encoding, neglecting lower valued addresses. The encoder uses a 100 MHz clock and has negligible power consumption. The impact of serializing the 32 channel outputs, assuming a maximum rate of 30,000 cps per channel, leads in the worst case to a minimum efficiency of 93.3%. Measurements of the singles rate for a detector block is 100,000 cps, or 3,125 cps per channel. Hence, this would lead to a minimum efficiency of 99.3% in the worst case.

Also, included on chip, is an analog multiplexer that allows the monitoring of the shaper signal through an on-chip analog driver.
Thus far, three ASICs were sent for fabrication through the Canadian Microelectronics Corporation (CMC). The first one (ICFSHLNA) has test structures and two CSPs with external bias needed. The second one (ICFSHB01) has 32 channels of CSP and shaper with on-chip bias network. The third one (ICFSHB02), which has not been tested yet, has 16 channels of CSP, shaper, ZCD with external common threshold setting and serial encoder. The final chip is designed to have a maximum power budget of 125 $mW$ (1.5 $W$ for the entire camera) and the estimated final size is $1.7 mm \times 4.2 mm$.

### 4.3 Experimental Results

#### 4.3.1 ICFSHLNA Measurements

The CSP electronic characterization, timing resolution and energy resolution were performed on the ICFSHLNA chip. The ENC of the CSP, connected to Hamamatsu’s APD S8550 and a custom made $CR^2 - RC^2$ shaper, has been measured as a function of the peaking time and is presented in Fig. 4.6. The minimum ENC is 1116 electrons at 100 $ns$. The measured ENC has been fitted using (4.1). An input-referred noise voltage ($e_n$) of $0.9 \ nV/\sqrt{Hz}$ and input-referred noise current ($i_n$) of $0.181 \ pA/\sqrt{Hz}$ were deducted.

The electronic timing resolution of the CSP connected to an Ortec 474 Fast Filter Amplifier (20/20) and a Leading Edge Discriminator (LED) Phillips 7404 is $0.56 \ ns$ (FWHM). The APD was biased at 374 $V$ in order to have the proper noise figure. The coincidence timing resolution of this setup, with the LED replaced by an Ortec Constant Fraction
Chapter 4. Front-End Electronics for the RatCap

Figure 4.6 ENC of the CSP connected to Hamamatsu APD (S8550) biased at 374 V.

Table 4.3 Comparison of the measured peaking time versus simulations.

<table>
<thead>
<tr>
<th>Capacitance</th>
<th>Measurements</th>
<th>Simulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pF</td>
<td>73.2±1.4 ns</td>
<td>74.0 ns</td>
</tr>
<tr>
<td>12 pF</td>
<td>80.4±1.8 ns</td>
<td>80.0 ns</td>
</tr>
</tbody>
</table>

Discriminator (CFD) 934, against a BaF$_2$ scintillator and a PMT, is 2.5 ns (FWHM), using a $^{22}$Na source and a 4 x 8 LSO array with pixel size of 2 mm x 2 mm x 5 mm coupled to the APD. An energy resolution of 17% (FWHM) has been measured. Further detailed results are presented in [Pratte et al., 2004b].

4.3.2 ICFSHB01 Measurements

The linearity of the CSP and 3rd order bipolar gaussian shaper has been evaluated. Fig. 4.7 presents a measured curve of the output voltage as a function of the input charges. An average gain of 15.0±0.3 mV/fC has been measured in the designed operating region (up to 130k electrons), compared to 15.15 mV/fC in simulation.

The peaking time (1% to 99%) as a function of the input capacitance was evaluated. Table 4.3 compares the measured peaking time versus the simulations for input test capacitance of 0 pF and 12 pF.
4.3. EXPERIMENTAL RESULTS

Figure 4.7 Linearity of the analog front-end for an input test capacitance of 12 pF. A gain of 15.2 mV/fC has been fitted in the designed operating region (up to 130k electrons).

The ENC of the analog front-end has been evaluated. In order to have an accurate estimate of charge gain (required to evaluate the ENC), the injection capacitance of every channel has been measured on the test Printed Circuit Board (PCB). An average minimum ENC of 902 ± 29 electrons RMS was measured for an input test capacitance of 12 pF.

The energy resolution of the analog front-end was measured using a $^{68}$Ge source and a 4×8 LSO array with pixel size of 2 mm × 2 mm × 5 mm coupled to the APD. The output of the shaper was fed into an Ortec 934 CFD. Fig. 4.8 presents the energy spectrum. The energy resolution is 18.1% (FWHM).

The electronic and coincidence timing resolution of the analog front-end were measured in order to validate our mathematical analysis. An Ortec 934 CFD was used, but without adding back the delayed signal into the CFD, as usually required to create a bipolar signal when using a unipolar shaper. Hence the CFD is then used as a ZCD, looking at the zero-cross of the bipolar signal of the integrated shaper. For the electronic timing resolution, the input pulse amplitude was set at the 511 keV photopeak level, representing a light output of 2300 ph — electron/MeV and the APD gain was set at 50. The timing resolution obtained is 3.54 ns FWHM, as shown in Fig. 4.9. The coincidence timing resolution against a BaF$_2$ scintillator and a PMT was performed using a $^{68}$Ge source. A timing resolution of 6.70 ns FWHM was obtained as shown in Fig. 4.10. The equivalent RMS values are reported in Fig. 4.4.
Figure 4.8  Energy resolution of the analog front-end connected to one channel of the S8550 APD/LSO module for a $^{68}$Ge source. The energy resolution is 18.1% FWHM.

Figure 4.9  Electronic timing resolution of the analog front-end using the CFD as a ZCD. A timing resolution of 3.54 ns FWHM was measured.
4.4 Discussion

The measured ENC of the CSP was properly fitted mathematically and an input-referred noise $e_n$ of $0.9 \ nV/\sqrt{Hz}$ was obtained, which is in the same range as other CSPs used for PET imaging [Binkley et al., 2000][Binkley et al., 1992][Paulus et al., 1996]. The difference between the ENC obtained with the CSP chip and the CSP-Shaper chip could be explained by a smaller stray capacitance and differences in the electronic performance due to process variations. Originally, the preamplifier was optimized so that the minimum ENC would occur at a peaking time of 70 ns, and not at 100 ns as shown in Fig. 4.6. The explanation comes from an under-estimation of the flicker noise coefficient. Preliminary results, from measurements on test devices that were included on the ICFSHLNA chip, show a $K_F n$ about ten times higher than expected. Further investigations are underway to assess this issue. Even so, as the ENC varies slowly with the peaking time, this shouldn't compromise the functionality of the analog front-end for our PET application.

The analog front-end exhibits excellent linearity in the operating region and even beyond. The measured peaking time fits accordingly with simulations.

Regarding the timing resolution, the mathematical model developed has been validated. From Fig. 4.4, one can see that the photoelectron statistics is limiting the timing resolution achievable. The next iteration will include on-chip timing discrimination and is expected
to achieve equal or better resolution than in these measurements. A raising question is to identify an acceptable coincidence timing window, which would keep the number of random coincidences to an acceptable level, keeping in mind the power needed to achieve the required timing resolution.

4.5 Conclusion

The results obtained so far on the first two prototypes show good agreement with the simulations. The design respects the criteria of minimal power consumption, size and mobility by minimizing the number of interconnections, making it suitable for a portable mobile PET scanner for rat studies. Further development to optimize the timing pick-off circuitry is planned.

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CHAPTER 5

The RatCAP Front-End ASIC

Résumé

Ce dernier article de la thèse traite du plus récent circuit intégré pour le RatCAP. En plus de nouvelles fonctionnalités qui ont été intégrées, plusieurs modifications ont grandement améliorées ce circuit.

Premièrement, la conception du préamplificateur a été revue. La longueur de la grille du transistor d'entrée a été augmentée de 0.2 \( \mu m \) à 0.4 \( \mu m \), dans le but de diminuer le coefficient du bruit 1/f. Cette modification a permis de réduire de presque 40% le bruit du préamplificateur à comparer avec la première version qui a été présentée dans le premier article de cette thèse. Un ENC de 650 electrons rms a été mesuré.

Deuxièmement, riche de l'expérience acquise avec les détecteurs LSO/PDA, la chaîne analogique a été munie d'un gain programmable pour compenser la variation de charges correspondant à un événement de 511 keV entre pixels. Cette distribution est attribuable à la variation de l'efficacité de collecte de la lumière et du gain des PDAs. Le gain programmable a été implanté dans le circuit pole-zero, et couvre une étendue de 1:2.7 en 32 échelons.

Troisièmement, les discriminateurs d'énergie et de temps sont présentés. En ce qui concerne la discrimination en énergie, chacun des canaux peut être programmé pour utiliser soit un seuil bas de discrimination, soit une fenêtre d'énergie. Dans les deux cas, les seuils sont fournis par des convertisseurs numérique-analogique externes, reliant en parallèle les douze circuits intégrés de la caméra. Ensuite, les détails de conception du comparateur utilisé pour détecter le passage par zéro du signal provenant de la chaîne analogique sont présentés. Il est impératif de garder au minimum la tension d'entrée décalée aléatoire, imposant un pairage élevé de l'entrée différentielle afin de minimiser la distribution du temps de déclenchement en fonction de l'amplitude du signal provenant de la chaîne analogique.

Ensuite, l'encodeur série d'adresse et de déclenchement est présenté. Grâce à ce circuit, la quantité d'interconnexions entre le système d'acquisition et la caméra est réduite considérablement ce qui permet ainsi d'accroître la mobilité du rat.
Enfin, un modèle mathématique pour évaluer la résolution en temps est un autre sujet important présenté dans cet article. Ce modèle prend en considération le bruit électronique ainsi que la contribution statistique du nombre de photons émis par le scintillateur et du nombre de photoélectrons générés dans la PDA. La méthode utilisée pour mesurer la contribution du bruit statistique est aussi présentée. Ce modèle a été validé et démontre une précision de 12%. Une résolution temporelle de 6.7 ns FWHM a été mesurée pour deux modules LSO/PDA/ASIC en coïncidence, avec un seuil d’énergie de 420 keV.

Synopsis

This final paper in this thesis is about the latest ASIC implemented for the RatCAP. In addition to new functionalities which were integrated, this ASIC offers several improvements over previous iterations.

First of all, the CSP was redesigned, increasing the gate length from minimum size (0.2 μm), where the 1/f noise coefficient is at its maximum, to 0.4 μm. This led to a measured ENC of 650 electrons rms, close to a factor ~1.5 improvement compared to the original CSP presented in the first paper of this thesis.

Second, with the benefit of the experience acquired with the LSO/APD detector array, it became obvious that programmable gain in each channel of the analog front-end was required to compensate for the spread in the input charge corresponding to a photopeak event. This spread is due to the light collection efficiency and APD gain variation from one pixel to another. Programmable gain was implemented in the pole-zero network, covering a range from 1 to 2.7 in 32 steps.

Thirdly, detailed information about the energy and timing discriminators is presented. Each channel is independently programmed to gate the timing trigger based on a low level energy discrimination or an energy window discrimination. In both case, the energy thresholds are provided from two external DACs, shared among the ASICs in the system. The design of the comparator, used to trigger on the zero-crossing of the shaper’s bipolar signal, is detailed. It was necessary to keep the random input offset voltage of the comparator to a minimum, setting stringent requirements on the matching of the differential input pair, in order to eliminate any amplitude dependent time trigger dispersion.

Next, the novel 32-to-1 address and timing serial encoder, which allows maximum animal mobility by reducing substantially the number of interconnections with the DAQ, is presented.
Another major topic covered in this paper, which contributes to this thesis, is the proposed model for the timing resolution, which takes into account the contribution of the ENC as well as the statistical variation in the number of photons emitted by the scintillator and the number of photoelectrons generated. Measurement techniques are presented to actually characterize in a test setup the timing resolution due to the photon statistics. The model was validated through measurements, and proved an accuracy of about 12%. The measured timing resolution for two LSO/APD/ASIC modules in coincidence is 6.7 ns FWHM for a low energy threshold set at 420 keV.

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**Abstract**

We report on the design and characterization of a new ASIC for the RatCAP, a head-mounted miniature PET scanner intended for neurological and behavioral studies of an awake rat. The ASIC is composed of 32 channels, each consisting of a charge sensitive preamplifier, a 5-bit programmable gain in the pole-zero network, a 3\textsuperscript{rd} order bipolar semi-Gaussian shaper (peaking time of 80 ns), and a timing and energy discriminator. The energy discriminator in each channel is used to arm the zero-crossing discriminator and can be programmed to use either a low energy threshold or an energy gating window. A 32-to-1 serial encoder is embedded to multiplex into a single output the timing information and channel address of every event. Finally, LVDS I/O were integrated on chip to minimize the digital noise on the read-out PCB. The ASIC was realized in the TSMC 0.18 μm technology, has a size of 3.3 mm × 4.5 mm and a power consumption of 117 mW. The
gate length of the N-channel MOSFET input device of the charge sensitive preamplifier was increased to minimize 1/f noise. This led to a factor \(~1.5\) improvement of the ENC with respect to the first version of the ASIC [Pratte et al., 2004b]. An ENC of 650 e-rms was measured with the APD biased at the input. In order to predict the achievable timing resolution, a model was derived to estimate the photon noise contribution to the timing resolution. Measurements were performed to validate the model, which agreed within 12%. The coincidence timing resolution between two typical LSO-APD-ASIC modules was measured using a $^{68}$Ge source. Applying a threshold at 420 keV, a timing resolution of 6.7 ns FWHM was measured. An energy resolution of 18.7% FWHM at 511 keV was measured for a $^{68}$Ge source.

### 5.1 Introduction

Based on our experience with previous designs, a new ASIC for the RatCAP head-mounted miniature Positron Emission Tomography (PET) scanner was realized [Pratte et al., 2004b], [Pratte et al., 2004a], [Vaska et al., 2004]. This ASIC was specifically designed for the RatCAP project, but will also be used in the BNL PET Wrist Scanner [Kriplani et al., 2006b], a simultaneous dual-modality PET/MRI scanner [Schlyer et al., 2006], and a coded aperture gamma-ray imager for homeland security applications. Significant improvements were made on this ASIC to lower the electronic and common mode noise, to add programmable gain, to lower the random input offset voltage of the timing discriminator, to add an energy gating discriminator and finally to add Low-Voltage Differential Signaling (LVDS) transceivers for communication with the Data Acquisition system (DAQ).

In the next section, the ASIC will be presented along with the design considerations. Also described is an overview of the readout system which was specifically designed for the RatCAP. Then, the measurements will be presented. Finally, the ASIC performance will be discussed, along with the validation of a model elaborated to evaluate the contribution to the timing resolution of the statistical fluctuations in the light emitted by the Lutetium Oxyorthosilicate (LSO) scintillator and the photoelectron statistics.

### 5.2 The RatCAP ASIC

The RatCAP camera is composed of twelve modules of LSO and Avalanche Photodiode (APD) array coupled to the read-out ASIC, as presented in Fig. 5.1. The LSO array
Figure 5.1 Drawing of the RatCAP camera. Each detector block is composed of an LSO crystal, APD and custom ASIC.
is composed of crystals of $2.2 \times 2.2 \times 5 \text{ mm}^3$ coupled one to one to a $4 \times 8$ avalanche photodiode array from Hamamatsu (S8550). Each pixel of the APD has a capacitance of 10 pF and a leakage current of 1.5 nA.

The main design objectives for the front-end electronics are the following. First, it should have minimal power dissipation in order not to affect the animal’s behavior or affect the avalanche photodiode (APD) gain which is sensitive to temperature. Second, all the front-end electronics must be small enough to fit on the back of the detector. Third, the number of interconnections between the chips and the DAQ should be minimized in order to maximize the animal’s mobility, allowing for awake animal behavioral studies. Finally, the electronics must be optimized for the detector characteristics in order to achieve the best possible timing resolution.

The mixed-signal ASIC has 32 channels. Each channel is composed of a Charge Sensitive Preamplifier (CSP), a pole-zero network with 32 programmable gain settings, a $3^{rd}$ order bipolar Gaussian shaper, a zero-crossing discriminator (ZCD) used to pick off the timing information of every event and a programmable energy discriminator. Fig. 5.2 presents a block diagram of one channel.

A serial encoder (not shown in Fig. 5.2) multiplexes through a single output the digital stamp of each event occurrence and the 5-bit corresponding channel address. A 1088-bit serial programming interface (SPI) was integrated to program the gain and the energy discrimination mode of each channel as well as the analog multiplexers of the ASIC. The 100 MHz system clock of the RatCAP camera is daisy chained through the 12 ASICs. The ASIC’s clock input, clock output and the serial encoder output use integrated LVDS transceivers. Two analog multiplexers, one per sixteen channels, are integrated to help in calibration and diagnosis of the analog chain. The ASIC was realized in TSMC 0.18 $\mu$m
5.2. THE RATCAP ASIC

technology, has a size of 3.3 mm x 4.5 mm and has a power consumption of 117 mW. Fig. 5.3 presents a microphotograph of the ASIC.

5.2.1 Analog Front-End

The CSP amplifier is based on a modified telescopic cascode architecture [Pratte et al., 2004b]. The N-channel MOSFET input device has been optimized with respect to the technology parameters and the detector characteristics at its operating point (capacitance, leakage current and gain), using the EKV transistor model [Enz et al., 1995], to minimize the Equivalent Noise Charge (ENC) [Radeka, 1988], [De Geronimo and O’Connor, 2005]. The gate length was set to 0.4 μm, twice the minimum feature size, to minimize the 1/f noise contribution. With a gate width of 1760 μm and biased with 600 μA, the device is operated in weak inversion, and leads to a calculated ENC of 453 e-rms at a shaper’s peaking time of 80 ns (neglecting the stray capacitance at the input). The input device has a transconductance of 13 mS and a gate capacitance of 5.8 pF. All other transistor dimensions of the CSP are optimized for minimum white series and 1/f noise contribution to the overall ENC, mainly set by the input device. The feedback capacitor is 200 fF, which gives the CSP a gain of 5 mV/fC.

The pole-zero network following the CSP is used to eliminate the non-linearity of the reset transistor M_f in the amplifier’s feedback [DeGeronimo and O’Connor, 2000]. It also provides a gain N, as seen in the transfer function of the analog front-end (5.1), where N represents the number of pairs of capacitor C_f and reset transistor M_f in the pole-zero cancellation network:

\[
H(s) = N \left( \frac{R_{fp}}{1 + R_{fp}C_f s} \right) \left( \frac{K \omega_p s}{s^2 + \omega_p^2 s + \omega_p^2} \right)
\]  \hspace{1cm} (5.1)

where \(\omega_p, Q_p\) and \(K\) are expressed by:

\[
\omega_p = \frac{1}{\sqrt{R_1 R_2 C_1 C_2}} 
\]  \hspace{1cm} (5.2)

\[
\omega_p Q_p = \frac{C_1 + C_2}{R_2 C_1 C_2} 
\]  \hspace{1cm} (5.3)

\[
K = -\frac{R_2 C_1}{R_1 (C_1 + C_2)}
\]  \hspace{1cm} (5.4)
Figure 5.3 Microphotograph of the RatCAP ASIC. The 32 channel ASIC was realized in TSMC 0.18 $\mu$m technology, has a size of $3.3 \text{ mm} \times 4.5 \text{ mm}$ and has a power consumption of 117 mW.
On a per channel basis, the factor $N$ can be programmed between 18 to 49 in unit steps, to vary the overall front-end gain by a factor $2.7$, between $21.5$ and $58.5$ mV/fC. A minimum of $18$ ($C_f - M_f$) pairs in the zero are required to minimize the shaper’s noise contribution relative to the CSP input. This add-on was driven by the ratio of $2.5$ between the pixel with the greatest charge collection to the pixel with the lowest charge collection within an LSO-APD detector module. This spread comes mainly from the light collection efficiency and APD gain variation between pixels. This leads to a wide signal dynamic range in the analog front-end which creates a considerable time dispersion in the ZCD, leading to a deterioration of the timing resolution. Also, as a single energy threshold is used for all channels, the programmable gain allows for a more uniform discrimination between the Compton scatters and the photopeak events within a detector module. It can be demonstrated that the original spread of $2.5$ in the charge collection efficiency is reduced to an average of $0.033$ after gain correction.

The third-order bipolar semi-Gaussian shaper has a peaking time of $80$ ns. It is realized in two stages: a first-order low-pass filter and a second-order bandpass filter implemented with a biquadratic architecture [OHKAWA et al., 1976], [CHEN, 1986], [PRATTE et al., 2002]. Both amplifiers used in the shaper are a scaled down version of the CSP amplifier, where every transistor was optimized to minimize its electronic noise contribution.

5.2.2 Timing Resolution and Photon Noise Model

The number of electron-hole pairs created as a function of time in the photodetector varies statistically from one event to another. This is due to the statistical nature of the process in which a scintillator emits visible light following the absorption of a gamma photon. The quantity and the time distribution of the emitted photons vary. Also, the photoelectron statistics in the APD, where there are the lowest quantity of information carriers [KNOLL, 1999], will affect the number of electron-hole pairs created from one event to another. This photon noise is non-stationary (time dependent) and directly affects the achievable timing resolution, one of the main figure of merit of the LSO-APD-ASIC detector module. A model of the photon noise is essential to predict a scintillator based system's performance and to validate the measurement results. Below, a procedure is presented to calculate the photon noise and the overall achievable timing resolution. Subsequently, this model will be validated in the Experimental Result section of this paper.
The timing resolution is the noise divided by the slope of the signal at the discrimination point. In a scintillator based system, the timing resolution can be expressed as,

\[
\sigma_t(t_{zc}) = \frac{\sqrt{\sigma_{\text{noise-photon}}^2(t_{zc}) + \sigma_{\text{ENC}}^2}}{dV_{\text{out}}(t_{zc})/dt}
\]

(5.5)

where the total noise is the sum of the electronic \(\sigma_{\text{ENC}}\) and time dependent photon noise \(\sigma_{\text{noise-photon}}(t_{zc})\). The electronic noise can be calculated using [RADEKA, 1988], and it is presented in [PRATTE et al., 2004b], [PRATTE et al., 2004a] for this specific system. The slope at the discrimination point can be obtained by the convolution of the system's input signal from the LSO-APD response, with the impulse function of the system, expressed by (5.1) in this case. As a first order approximation, neglecting the finite rising edge of the APD-LSO response due to the total capacitance at the input and the effective input impedance of the preamplifier, the input signal is modeled by:

\[
I_{\text{photon}}(t) = \frac{N}{\tau_{\text{aso}}} e^{\left(-\frac{t}{\tau_{\text{aso}}}\right)}
\]

(5.6)

where \(N\) is the total number of primary photoelectrons multiplied by the APD gain, and \(\tau_{\text{aso}}\) is the LSO decay time constant.

Regarding the photon noise calculation relative to the CSP input, [CASEY et al., 2003] presented the following expression:

\[
\sigma_{\text{noise-photon}}^2(t) = qFM^2 \int_{-\infty}^{\infty} I_{\text{photon}}(\alpha)w^2(t - \alpha)d\alpha
\]

(5.7)

with \(F\), the excess noise factor [WEBB et al., 1974], defined as:

\[
F = Mk_{\text{eff}} + \left(2 - \frac{1}{M}\right)(1 - k_{\text{eff}})
\]

(5.8)

and \(q\) being the electron charge, \(M\) the APD gain, \(k_{\text{eff}}\) the effective ionization ratio, \(I_{\text{photon}}(t)\) the LSO-APD photoelectron current (5.6) and \(w(t)\) the weighting function of the analog front-end (5.1) [RADEKA, 1988], [RADEKA, 1968]. Note that \(\sqrt{F}\) is the factor by which the statistical noise on the APD current (equal to the multiplied photocurrent plus the multiplied APD bulk dark current) exceeds that which would be expected from a noiseless multiplier on the basis of shot noise alone [PERKINELMER, 2006].
The 12 LSO-APD detector modules used in the RatCAP camera have an average APD gain of 46.8 and average of 5200 photoelectrons per MeV. For this APD gain and number of photoelectrons, the calculated slope at the zero-crossing of the bipolar shaper is 713 electrons per nanosecond. As previously mentioned the modeled ENC is 453 e-rms. Assuming an APD effective ionization ratio of 0.04, it leads to an excess noise factor F of 3.77 and a photon noise relative to the input of 1211 e-rms. Hence the average predicted timing resolution of the RatCAP camera is 1.8 ns rms for 511 keV gamma photons.

5.2.3 Energy and Zero-Crossing Discriminators

This mixed-signal circuit is composed of two comparators for energy discrimination, one comparator for generating a trigger on the zero-crossing of the shaper's bipolar signal, which represents the timing information of each event, and a logic block, as seen in Fig. 5.2. The comparators used for energy discrimination are identical and have a power consumption of 67.5 $\mu$W each. For better noise trigger immunity, internal positive feedback is used to create an hysteresis of 15 mV, which corresponds roughly to six sigma of the noise.

There are two main design criteria for the comparator used to trigger on the zero-crossing of the shaper's bipolar signal. First, the sensitivity of the comparator had to be high enough to minimize the energy dependent time walk for the desired input charge dynamic range, while keeping the power consumption to the minimum feasible. This is crucial, as the signal amplitude is not sent to the DAQ for post-processing of the time stamp and correction for the time walk. Second, the input stage of the comparator had to be designed to minimize input random offset voltage. Input random offset voltage acts like an offset on the reference baseline, varying from one channel to another due to its random nature. The effective consequence of having non-negligible random input offset voltage is that the comparator will not trigger at the zero-crossing of the bipolar signal, but either below or above the baseline, creating a considerable dispersion of the timing trigger as a function of energy. To minimize the random input offset voltage of the comparator, one has to take great care to match the threshold voltage and the drain current of the differential pair devices [PELGROM et al., 1989]. Those two parameters are functions of the input devices, but also of the load of the differential pair. For a MOSFET, the threshold voltage mismatch $\sigma_{\Delta VT}$ can be expressed as:

$$\sigma_{\Delta VT} = \frac{A_{VT}}{\sqrt{WL}}$$

(5.9)
where $A_{VT}$ is the voltage threshold mismatch coefficient, which is constant for a given technology, and $W$ and $L$ are the transistor gate width and length. The drain current mismatch $\sigma_{\Delta I_d/I_d}$ for a device in weak inversion is expressed as:

$$\sigma_{\Delta I_d/I_d} = \frac{qA_{VT}}{nkT}$$  \hspace{1cm} (5.10)$$

where $q$ is the electron charge, $k$ the Boltzmann's constant, $T$ the temperature and $n$ the subthreshold slope factor [ENZ and VITTOZ, 1997]. In strong inversion, drain current mismatch $\sigma_{\Delta I_d/I_d}$ is expressed as:

$$\sigma_{\Delta I_d/I_d}^2 = \frac{4q^2A_{VT}}{(Vgs - Vt)^2} + \sigma_{\Delta \beta/\beta}^2$$  \hspace{1cm} (5.11)$$

with

$$\sigma_{\Delta \beta/\beta}^2 \approx \frac{A_{\mu}^2}{WL} + \frac{A_{Cox}^2}{WL}$$  \hspace{1cm} (5.12)$$

where $Vgs$ is the gate source voltage, $Vt$ the threshold voltage, $A_{\mu}$ the carrier mobility mismatch coefficient and $A_{Cox}$ the device oxide mismatch coefficient.

Fig. 5.4 presents the schematic of the comparator used to trigger on the zero-crossing of the shaper’s bipolar signal. It is a differential amplifier used in open-loop, consisting of a differential input pair M1-M2 with diode connected MOSFET load M5-M6 which mirror the output signal to a push-pull output stage M8-M10. In order to improve matching between the differential input pair M1-M2, which directly affects the input random offset voltage through the variation of their threshold voltage, the gate length was set to eight times the minimum gate size. They are biased in strong inversion which also improves their matching. Diode connected transistors M5-M6 are used to load the differential pair, as a lower impedance helps matching of the output current, hence the variation of the $Vgs$ of M1-M2. It also has the benefit of lowering the voltage swing at the output of M1-M2, improving the propagation delay in the first stage. Again, the gate length of M5-M6 is bigger than the minimum size to improve their matching. To counter the loss of gain from the lower impedance of the load, current sources M3-M4 are added to increase the transconductance of the differential pair. The transistor M11 is used to cascode M8 to reduce the kick back, from the digital output stage M12-M13 through the gate to drain parasitic capacitance of M8, to the output of the differential pair. Hysteresis is not desired in the comparator to allow triggering at the zero-crossing of the bipolar signal. But still, immunity to noise triggering is essential. Hence, by driving the gate of transistor M17 to a logic low state, the comparator can be disabled by clamping one side of the differential
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output stage to the power supply rail, preventing any triggers from the shaper’s baseline noise. To enable the comparator, the gate of M17 is pulled to a logic high state. When the comparator is enabled, the transistor M17 has minimal influence on the comparator’s characteristics.

Each channel can be programmed independently to discriminate the signal’s amplitude based on a low threshold, or to satisfy an energy gating window. In both energy gating modes, when a signal with an amplitude greater than the lower energy threshold is detected, the zero-crossing comparator is enabled by controlling the gate of M17 through some logic. When the energy gating window mode is enabled, the zero-crossing discriminator’s trigger will be gated if the shaper signal’s amplitude is greater than the upper energy threshold. Hence, to obtain the timing information of a detected event in the energy gating window mode, the shaper signal’s amplitude has to be greater than the lower energy threshold, and lower than the upper energy threshold. In simulation, it is clear that there is enough time to enable the zero-crossing comparator, when the low energy condition is met, before the zero-crossing occurs. When the zero-crossing of the bipolar signal is detected, the comparator of Fig. 5.4 triggers. Following this trigger, all logics are reset, in order to be ready for the next event. As the digital part of the circuit is completely asynchronous, monostable circuits are used to ensure proper reset time.
5.2.4 Timing and Address Serial Encoder

One of the main design criteria of the RatCAP camera is to minimize the number of interconnections with the DAQ in order to optimize the animal's mobility, which justified the implementation of a timing and address serial encoder. Fig. 5.5 presents a block diagram of the encoder. It consists of a wired-NOR, a Control Signal Generator (CSG), a 32-to-5 priority encoder, a serializer and an output OR gate. The encoder's output consists of a leading edge created from a wired-NOR of all 32 ZCD outputs which is asynchronous with the clock, followed by at least one clock cycle, a stop bit and then the 5 bit address of the channel that fired. Fig. 5.6 shows an oscilloscope capture of the encoder's output, along with the shaper's bipolar signal and the trigger of the pulse generator used to inject charge in the channel.

The 32 ZCD outputs are interconnected to the wired-NOR. Hence, when a timing trigger is generated in a channel, the wired-NOR output triggers the CSG which feeds back a blocking signal to all channels in order to prevent corruption of the chip output if another event is detected while the current event is being processed. After the last address bit has been transmitted, the CSG unblocks every channel to allow a new event to be transmitted.

The 32 ZCD outputs are also interconnected to the 32-to-5 priority encoder. Hence, when a channel fires, the priority encoder will generate the 5 bit address which is latched in the serializer. Under the control of the CSG, the serializer will then transmit synchronously with the clock, the address to the output OR gate, starting with the LSB. In the case where more than one channel triggers the encoder before the blocking signal is broadcast, for instance in the case of a Compton scatter within the LSO scintillator array, the encoder will give priority to the higher channel address.

The synchronous part of the encoder works with a clock of 100 MHz, therefore the length of the blocking period is between 70 and 80 ns. Assuming a singles rate of about 3,125 cps per channel, a minimum efficiency of 99.3% is predictable.

5.2.5 System Readout

The Printed Circuit Board (PCB) of the RatCAP PET camera is a ten layer rigid-flex, coated with an organic solderability preservative. Fig. 5.7 presents a picture of the PCB. All magnetic material was removed, allowing for dual-modality PET/MR applications. Each of the twelve blocks consists of an LSO-APD array and ASIC. To minimize any common mode noise, LVDS communication protocol is being used. Each ASIC has two
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Figure 5.5 Block diagram of the chip encoder. Each of the 32 channels are connected to a 32 input Wired-NOR, where the detected time of arrival of an event triggers the Control Signal Generator (CSG). The CSG will transmit the timing edge, asynchronously with respect to the 100 MHz system clock, through the single ASIC output. Each channel is also tied to a 32 to 5 priority encoder which generates the address of the channel that fired. The address is then serialized through the same output as the timing edge.
Figure 5.6  Oscilloscope capture of the pulse generator trigger used to inject the charge in the ASIC (top), along with the shaper’s bipolar signal (middle) and the encoder’s digital output (bottom). The leading edge of the encoder’s digital output represents the time of occurrence of a detected event, which is followed by the 5-bit address of the channel that fired.

Figure 5.7  Picture of the readout rigid-flex PCB of the RatCAP PET camera before being cut from the panel.
LVDS transmitters and one LVDS receiver embedded. The LVDS transmitter has a power consumption of 16 mW, while the receiver has a power consumption of 3.25 mW. To minimize the number of traces on the PCB, the 100 MHz system clock and the SPI are daisy chained throughout. The twelve ASICs are programmed and readout through the Timestamp and Signal Processing Module (TSPM), an FPGA-based custom DAQ system [Junnarkar et al., 2008]. The TSPM generates a 64-bit word per detected event, which contains the absolute time stamp of the detected photon as well as the address of the channel that fired. An average 1.2 million events per second are expected for the RatCAP, and the maximum rate capability of the DAQ is 80 MB per second. The data is acquired in list mode, and coincidence matching is performed offline using a software which also performs a timing offset calibration to correct for time dispersions between the 384 channels [Park et al., 2008].

5.3 Experimental Results

The ASIC has been thoroughly tested and is fully functional. Out of 35 packaged ASICs of 32 channels each, a total of 4 channels were not responding, leading to a yield of 99.6%.

5.3.1 Equivalent Noise Charge

The ENC of the front-end was measured for various capacitances at the input, and is reported in Fig. 5.8. The ENC was also measured with the Hamamatsu APD S8550 biased at a high voltage of 353 V to obtain the noise figure at the nominal operating gain of 45. An ENC of 650 e-rms was measured. The measurements were performed with the ASIC on a test PCB with the 100 MHz LVDS system clock, the serial programming interface and the digital output of the ASIC operational in order to obtain realistic results. By extrapolating the curve to the abscissa, a total capacitance at the input of 15.5 pF is deduced, where the gate capacitance of the input NMOS of the CSP is 5.8 pF, the input pad is 500 fF and the feedback capacitor of the CSP is 200 fF. Hence a stray capacitance at the input of about 9 pF is estimated. By comparison, the calculated ENC taking into account the stray capacitance and the APD noise figure, considering solely the noise of the input device and neglecting the noise from the shaper and any digital activity, leads to a value of 645 e-rms, which is in good agreement with the measurement. This calculated ENC of 645 e-rms differs from the 453 e-rms presented in section II-A, as the stray capacitance was originally neglected.
To evaluate the contribution from the digital activities in the ASIC and on the PCB to the ENC, it was measured again but this time with only the analog front-end enabled. A negligible improvement was noticed, meaning that the digital activities had negligible effect. It is expected that the digital noise may have a greater impact on the rigid-flex PCB designed for the RatCAP camera caused by the higher density of digital traces near the via interconnecting the detector anodes to the ASIC input, due to the limited real estate.

5.3.2 Energy Resolution

Energy spectra for all channels can be obtained simultaneously in the system by taking the derivative of the measured output trigger rate as a function of the energy threshold. For example, Fig. 5.9 displays such a spectrum, where the trigger rate data, the fit of the trigger rate data and its derivative as a function of the energy threshold is displayed. An energy resolution of 18.7% (\(\Delta E = 95.5\) keV) FWHM is measured for a typical channel connected to an APD-LSO detector using a \(^{68}\)Ge source.
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Figure 5.9 Energy spectra of an LSO-APD-ASIC detector module using a $^{68}$Ge source. An energy resolution of $18.7\%$ ($\Delta E = 95.5$ keV) FWHM is measured.

5.3.3 Timing Jitter and Time Walk

The electronic timing jitter and time walk were measured. A voltage pulse from a Tektronix AFG3251 function generator is fed to the test input of the ASIC, where an integrated analog multiplexer allows one to choose which channel to stimulate. A Tektronix TDS6804B oscilloscope is used to histogram the leading edge of the ASIC’s encoder output relative to the function generator trigger signal. The mean and the distribution width of the histogram represent the time walk and the timing jitter, respectively, for a given amount of charge injected in the channel. The measurements were performed without a load at the input, having solely the stray capacitance of 9 pF. Fig. 5.10 presents the mean, standard deviation, minimum and maximum timing jitter of all the channels measured. Considering the ratio of 2.5 between the photopeak position of the pixel with the greatest charge output to the pixel with the lowest charge output, and assuming an average energy resolution of 20% FWHM, the effective dynamic range is from 5.4 fC to 22.8 fC. Hence a maximum electronic jitter of 1.8 ns rms is expected. An average time walk of 0.7 ns is measured for a shaper signal amplitude between 310 mV and 520 mV, the effective dynamic range where all photopeaks will be aligned using the programmable gain of each channel.
Figure 5.10 Electronic timing jitter at the encoder’s output. The error bars represent the rms deviation of all the channels measured. Also plotted, the minimum and maximum measured jitter as a function of input charge.

5.3.4 Timing Resolution and Scintillator Photon Noise Model Validation

The photon noise model was validated for two arbitrary channels. Table 5.1 presents the measured number of photoelectrons, APD gain and ENC for both channel.

TABLE 5.1 Measured characteristics of the two channels used in the timing resolution model. The number of photoelectrons, APD gain and equivalent noise charge are presented.

<table>
<thead>
<tr>
<th></th>
<th>Channel 1</th>
<th>Channel 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of P-E/MeV</td>
<td>5990</td>
<td>4220</td>
</tr>
<tr>
<td>APD Gain</td>
<td>45</td>
<td>53.5</td>
</tr>
<tr>
<td>ENC (e-rms)</td>
<td>648</td>
<td>664</td>
</tr>
</tbody>
</table>

To validate this model, the timing resolution due to the photon noise $\sigma_{t-photon}(t_{zc})$ was measured indirectly by subtracting the timing resolution due to the electronic noise $\sigma_{t-electronic}$ from the overall measured timing resolution $\sigma_{t}(t_{zc})$:

$$\sigma^2_{t-photon}(t_{zc}) = \sigma^2_{t}(t_{zc}) - \sigma^2_{t-electronic}$$

(5.13)
5.3. Experimental Results

Table 5.2 presents the calculated and measured timing resolution, along with the respective contribution from the electronic noise and photon noise.

The first conclusion is that the model is valid, predicting within 12% the photon noise contribution. Second, it is interesting to notice that the zero-crossing discriminator's timing resolution is dominated by the photon noise. This is due to the fact that the timing measurement is achieved at the zero-crossing of the shaper's bipolar signal roughly 280 ns after the first photon being emitted by the scintillator, hence suffering from a large integration of the photons fluctuation and photoelectron statistics from one event to another.

The coincidence timing resolution between the two previous LSO-APD-ASIC detector modules was measured for a $^{68}$Ge source, with an energy threshold set at 420 keV. Fig. 5.11 shows the spectrum, where a coincidence timing resolution of 6.7 ns FWHM was obtained from the fit, which is also in good agreement with the model. The measured coincidence timing resolution, one of the main figures of merit of the LSO-APD-ASIC detector module, is comparable to performance achieved with other LSO-APD based-PET systems in the field [Bergeron et al., 2007][Spanoudaki et al., 2006].
5.4 Conclusion

The ASIC for the RatCAP small animal PET camera was presented. The ASIC is fully functional and is currently used in the BNL RatCAP project, dual-modality PET/MRI, Wrist scanner apparatus, and finally in a coded-aperture gamma-ray imager for Homeland Security applications. The implementation of this new ASIC was justified by the improved performance where the ENC was lowered significantly, programmable gain was embedded to compensate for the light collection and APD gain variations, the timing and energy discriminator were improved, and finally LVDS transceivers were integrated to minimize the digital noise on the readout PCB. A future revision of the ASIC is being discussed, where the timing discriminator would be replaced by an architecture in which the photon noise would be minimized. Also, global and trimming digital to analog converters would be integrated to have independent energy thresholds in each channel.

5.5 Acknowledgment

The authors would like to acknowledge John Triolo, Don Pinelli, Kevin Wolniewicz, Pavel Rehak, Sergio Rescia and Anand Kandasamy for their contributions and precious advice. The authors are also grateful to the Canadian Microelectronics Corporation for support in the fabrication of previous revisions of the ASIC. This research was carried out
at Brookhaven National Laboratory under contract DE-AC02-98CH10886 with the U.S. Department of Energy.
CHAPTER 6

The RatCAP Performance and Other Systems using the ASIC

In the previous chapters, the ASIC for the RatCAP was thoroughly presented and its performance discussed. Even though it is not the scope of this thesis, it is still relevant and interesting to demonstrate that the RatCAP is indeed working. Hence in the following section, the preliminary performance results obtained with the RatCAP are presented.

Also, the flexibility of the modular block approach, consisting of the LSO and APD arrays coupled to the ASIC, opens numerous doors for the design and implementation of other systems. Hence, an overview of those systems is presented.

6.1 The RatCAP Performance

The current revision of the RatCAP system has two versions: one with 5 mm long crystals, and one with 8 mm long crystals for improved sensitivity. Preliminary quantitative measurements of the 5 mm crystals system is currently underway, and those will be repeated for the 8 mm crystals system in a near future. The results presented below were obtained with the 5 mm long crystals system.

6.1.1 Timing and Energy Resolution

Using the custom built DAQ for the RatCAP to readout the ASIC, in which twelve TDCs with 650 ps bin are embedded, an average system wide timing resolution of 8.5 ns FWHM was measured (energy threshold at 350 keV). This allows for a coincidence timing window of 17 ns, which is acceptable. The timing resolution measured with the DAQ is slightly larger than the 6.7 ns FWHM (threshold at 420 keV) reported in chapter 5. The difference has several possible explanations. The value obtained with the DAQ is an average over thousands of crystal pairs in a complete system, whereas the ASIC test result is from a single crystal pair which may have performed better than average. Also, the energy threshold was set at 350 keV, instead of 420 keV.
The average energy resolution for the whole system was measured to be 15.6 % FWHM, using the approach presented in section 5.3.2. This value is comparable with other APD-LSO systems.

### 6.1.2 Spatial Resolution

The spatial resolution was measured for a point source, without background activity, located in the middle of the FOV. Using filtered back projection, a resolution of 1.8 mm was measured in the center of the FOV. Using the Maximum Likelihood Expectation Maximization (MLEM) reconstruction method, a spatial resolution of 1.2 mm was measured in the center of the FOV. The measured spatial resolution with MLEM is better because it uses a realistic system model, which includes the positron range, the 511 keV photon non-collinearity as well as the geometry of the system. Those measured values are accurate according to theoretical calculations, knowing the detector size and scanner geometry [VASKA et al., 2005].

### 6.1.3 Sensitivity

The measured sensitivity for a point source at the center of the FOV is 0.3% and it matches theoretical calculations and Monte Carlo simulated values. This is lower than other preclinical small animal PET scanners, as the 2 cm axial length of the RatCAP leads to a smaller geometric efficiency than those of other systems. Also, the RatCAP uses rather short crystals compared to other systems, which explain the lower sensitivity. The 8 mm long crystals version should improve the sensitivity. Again, a trade-off in crystal length had to be done to minimize the parallax effect and improve the spatial resolution knowing that the subject completely fills the FOV.

### 6.1.4 NEC

The measurement of the NEC rate has been completed but the results are still under analysis. It is expected that the NEC for the RatCAP will be lower than other preclinical systems for rodents. This hypothesis can be supported by the following two arguments. First, the sensitivity of the RatCAP is lower than other preclinical PET systems, as previously presented. Secondly, with other rodent PET systems, the whole object is within the FOV, whereas with RatCAP only the head is in the FOV and there is no side shielding for weight reasons. Hence, a large contribution of random and scattered
6.1. THE RATCAP PERFORMANCE

Figure 6.1 Dopamine D2 receptor blocking study with $^{11}$C-raclopride. Images of striata from the same fully awake rat, before (top) and after (bottom) injection of blocking dose of unlabeled raclopride, summed over 60 minutes scan and scaled to the same % injected dose per cc. (Rat weight is 280 gr.)

coincidences coming from the organs outside the field of view are expected, and knowing equation 2.12, a lower NEC can be predicted.

6.1.5 Animal Studies

The complete RatCAP system is functional and is currently being used in preclinical studies. For example, to demonstrate the sensitivity of the RatCAP to changes in receptor occupancy in the awake state, a blocking study was performed. The first study was an awake baseline scan, where 0.69 mCi of $^{11}$C-raclopride was injected. After 2 hours, a pharmacological dose of unlabeled raclopride (2 mg/kg) was delivered to effectively block the dopamine D2 receptors. Then, another dose of 0.86 mCi of $^{11}$C-raclopride was injected and a second awake scan was done. Images of the striatum in Fig. 6.1 demonstrate the clear effect of the blockade. Addiction studies utilizing the RatCAP are planned for the very near future.

The realization of the ASIC was an important milestone toward the successful completion of the RatCAP system. The RatCAP, the world’s smallest PET scanner, is unique for its
ability to provide in vivo dynamic brain neurochemistry information of non-anesthetized rodents with minimal motion restriction. The novelty of the RatCAP led to the granting of US Patent no. 7,126,126 [SCHYLER et al., 2006a].

6.2 Dual-Modality PET and MRI Scanner

The RatCAP technology was adapted for the realization of dual-modality PET and MR imaging. Many factors motivate this effort. First, MRI provides very high resolution anatomical information with excellent soft tissues contrast. Hence, having PET and MRI images acquired simultaneously allows perfect co-registration of the brain activity images within the brain structure. Secondly, the technology developed for preclinical dual-modality PET-MRI will be translated to clinical imaging where it will have a major impact on the diagnosis of human diseases. For instance, patients need to undergo two separates scans, one in a PET scanner and then one in an MRI, if the improved anatomical localization from the MRI is required, where co-registration is never perfect. Also the diagnostic time is longer than if both scans could be acquired with a single system, which would increase the patients throughput. In the specific case of human brain scans, co-registration of both images is practically impossible due to the degree of freedom in the neck. Moreover, PET-MRI has sustainable advantages over PET-CT. PET-CT does not provide great soft tissue contrast and gives an additional radiation dose. Finally, the realization of a simultaneous PET-MRI opens new doors to combined functional or spectral magnetic resonance information with PET imaging studies. The low profile design of the LSO/APD/ASIC blocks and immunity of the APDs to magnetic field effects make it ideal for retrofitting PET systems into existing MRI systems.

6.2.1 The BNL PET-MRI

The dual-modality BNL PET-MRI scanner for rodent brain imaging was built based on RatCAP technology [SCHLYER et al., 2007][WOODY et al., 2007]. Every constituent of the camera was individually tested in a Varian human 4 Tesla MRI to detect any magnetic susceptibility which would create artifact in the MR images. All magnetic materials in the APD sockets, APD pins, and the PCB have been removed or minimized and replaced by non-magnetic materials. Even though surface mount capacitors have electrodes containing nickel in the ink, the amount of nickel was low enough that they did not need to be replaced by capacitors which use precious metal ink. Regarding the PCB, an organic soldering preservative was used instead of a conventional nickel-gold plating to prevent
the copper from oxidizing. The shielding between the PET camera and the MRI is crucial to prevent cross interference between the RF and gradient pulses with the PET camera, and between the 100 MHz clock for the ASIC and the MRI RF receiver. Also, in the design of the shielding, special care has to be taken to minimize conductive loops where eddy currents, which cause artifacts in the MR images, are created.

Initial tests and development were carried out in a Varian human 4T MRI. The PET-MRI system has been adapted to fit into a 9.4T Bruker small animal MRI, and tests are currently underway. Fig. 6.2 shows simultaneous PET-MRI images of a rat injected with FDG in the Varian human 4T. Fig. 6.3 shows the first simultaneous PET-MRI images of a rat striatum phantom filled with 275 $\mu$Ci of FDG, obtained using a single loop surface
Figure 6.3 Simultaneous PET-MRI image of rat striatum phantom using a surface coil in the Bruker 9.4T.

coil in the Bruker 9.4T. Some interference from the RF pulse was found in the PET data, observed as a spiked increase in the singles rate, but it had negligible impact on the image.

This ongoing project is still at an early stage, and for instance R&D is underway to design new MRI RF input coil for proper imaging of rodents brain inside the RatCAP. Fig. 6.4 shows a picture of the newest RF input coil designed to be inserted in the RatCAP for the Bruker 9.4T MRI. The shielding is also a very important aspect of the project which is being continuously revisited. Fig. 6.5 presents a picture of the latest shielding realized for the RatCAP.
6.2. DUAL-MODALITY PET AND MRI SCANNER

Figure 6.4 The RF quadrature saddle input coil designed to be inserted in the RatCAP for dual-modality imaging in the Bruker 9.4T MRI.

Figure 6.5 The RatCAP shielded enclosure for dual-modality imaging in the Bruker 9.4T MRI. The cuts in the copper were added to minimize eddy current loops in the shielding.
The realization of the BNL PET-MRI led to the acquisition of the U.S. Patent number 7,286,867 [SCHYLER et al., 2007].

6.2.2 The Future PET-MRI Systems

Finally, two other PET-MRI systems which will use this ASIC are on the drawing board. The first one, for rodents, is being realized in collaboration with Prof. Joel Karp from the University of Pennsylvania. The PET add-on is designed to work with a Bruker Biospec preclinical MRI. It will have a 15 cm inside diameter FOV with an axial length of 4.5 cm. Based on the RatCAP detector block, the PET camera will consists of 16 rings of 192 LSO crystals, for a total of 96 LSO/APD/ASIC detector modules.

The other proposed PET-MRI system is being designed in collaboration with Aurora Imaging Technologies, Inc., a company specializing in dedicated breast MRI systems. The breast PET-MRI system will consists of 210 RatCAP detector blocks, arranged either in 5 rings of 42 blocks, or 10 rings of 21 blocks. Fig. 6.6 shows a picture of the Aurora Breast MRI, and Fig. 6.7 shows the concept of the PET add-on with the RF coil.

6.3 The BNL Wrist Scanner

Another system that was developed based on RatCAP technology is the BNL Wrist scanner. The Wrist scanner was designed to non-invasively measure radiotracers arterial input function in real time [KRIPLANI et al., 2007b][KRIPLANI et al., 2007a][KRIPLANI et al., 2006a]. The system uses four detector blocks developed for RatCAP, but with longer crystals. The main challenge was to figure out the relative position of each block with
6.3. THE BNL WRIST SCANNER

Figure 6.7 Drawing of the Aurora breast RF coil and the proposed PET add-on.

Figure 6.8 Illustration of the 8 block Wrist Scanner.

respect to the blood vessels in the wrist to enable discrimination of the arterial from the venous blood flow using a planar coincidence image. In this system, the LSO crystals are 15 mm long compared to 5 mm in the RatCAP detector. Fig. 6.8 presents a sketch of a future version of the Wrist Scanner, where 8 detector blocks will be used. Fig. 6.9 shows a coincidence planar image of a wrist phantom, where the artery and vein are clearly visible.

The realization of the BNL Wrist Scanner led to the granting of US Patent no. 7,091,489 [SCHYLER et al., 2006b].
6.4 The Coded Aperture Gamma-Ray Imager

The ASIC is also being used in a completely different field for the efficient detection, localization and identification of illicit nuclear materials for national security purposes. The ASIC is part of the first prototype to evaluate the feasibility of a compact scintillator based coded aperture gamma ray imager [VASKA et al., 2007]. The detectors consist of gadolinium oxyorthosilicate scintillator (GSO) of 5 mm × 5 mm × 25 mm coupled to an Hamamatsu S8664-55 APD. There are 225 detectors arrayed in a 15 × 15 matrix within a tungsten shielded box. The ASIC is used to read out the detectors and the RatCAP DAQ is used to read out the system. Fig. 6.10(a) shows a picture of the PCB with the detectors and readout electronics visible, and Fig. 6.10(b) shows a picture of the system with a coded aperture mask.
Figure 6.10 Pictures of the coded aperture GSO-APD based gamma ray imager without (left) and with the mask (right).
CHAPTER 7

Conclusion

This thesis presented the realization of the front-end ASIC for the RatCAP. The work was first placed into the context of PET imaging. To start, a brief overview of the PET instrumentation history was presented, highlighting the major PET evolution milestones. Then, the concepts and the physics behind PET was introduced. This was followed by a review of PET detectors, where the properties and characteristics of scintillators and photodetectors were described. Next, the timing resolution, energy resolution, spatial resolution, sensitivity and NEC, which are figures of merit of PET systems were defined. Finally, state of the art preclinical PET systems were discussed.

Three research papers, showing progress in the evolution of the RatCAP ASIC were presented. In the first paper, two major points were covered. First, the design and noise optimization of two CSPs for PET was presented. Measurements shown proved the CSPs suitability for PET. The realization of those two CSPs also allowed a revision of the transistor noise model, which eventually led to a redesign of the RatCAP CSP with better noise performance. Secondly, it was also established through this work that the TSMC CMOS 0.18 \( \mu m \) technology was suitable for the realization of low noise, low power, multi-channel ASICs for radiation instrumentation, a first in the field.

In the second paper, the concept for the complete readout chain of the front-end electronics for the RatCAP project was introduced. A block diagram showing the intended ASIC architecture, along with details about the analog front-end was presented. The novel 32-to-1 timing and address encoder, required to meet the camera’s mobility specification, was introduced. The first theoretical study of the achievable timing resolution, the main figure of merit of the ASIC performance, was also presented. Along with the timing resolution measurements presented, it became clear after this work that the presented architecture, using a zero-crossing discriminator to extract the timing information of each event, would achieve performance suitable for PET, with a reasonable random coincidence fraction.

The last paper of this thesis presented the final ASIC for the RatCAP project. In this ASIC, the design of the CSP was revisited to substantially lower the ENC. Also, new functionalities, such as per channel programmable gain and addressable analog monitors were integrated. Implementation of the energy and zero-crossing discriminator was detailed.
The design of the comparator used in the zero-crossing discriminator, which is critical for proper timing information extraction, was presented. An emphasis on the importance of matching the input differential pair was explained. Then, the implementation and design details of the novel 32-to-1 address and timing encoder were elaborated. Finally, a model to calculate the timing resolution of a given system, taking into account the photon noise and electronic noise contribution was detailed. The model was also proven accurate, through the proposed methodology to measure each contribution.

By its nature as a wearable and miniature PET scanner, the RatCAP system imposed significant constraints on the readout electronics. First, knowing the limited real estate available in the RatCAP camera and the large number of readout channels, VLSI of the front-end electronics was required to meet the design objective of having all necessary processing electronics mounted on each detector block. The second design objective was to maximize the awake animal's mobility while wearing the camera. This was achieved thanks to the novel 32-to-1 address and timing encoder which is integrated in the ASIC. This circuit allowed a reduction by a factor 32 in the number of interconnections required compared to classical DAQ systems where all channels are read out in parallel. The third design objective was to optimize the analog front-end for the LSO/APD detector module and to provide the best timing resolution, limiting the total power budget to 1.5 W for the whole RatCAP camera. The power dissipated had to be limited to prevent the degradation of the detector's performance and influence the animal's behavior. This was achieved with this ASIC by various means. First, proper noise optimization of the CSP input device was performed for the limited power budget and the APD's operating point characteristics. Secondly, the timing resolution model allowed the selection of the optimal shaper’s peaking time, keeping in mind the ballistic deficit encountered at very short peaking time which affects the slope of the signal at the discrimination point. The achieved coincidence timing resolution of 6.7 ns FWHM for two typical channels (threshold at 420 keV), leads to a theoretical coincidence timing window of 13.4 ns, which is well suitable for PET, and comparable with other PET systems. Finally the power dissipation of the ASIC is 117 mW, which means a total power of 1.4 W for the 12 ASICs. Taking into account the power dissipated in the 18 Low Drop Out voltage regulators, used to supply the ASICs, which is around 85 mW, the total power dissipation of the RatCAP camera is 1.485 W, which is within the design specification.

The RatCAP system is fully operational and in vivo PET studies in the awake rat have been performed. The implementation of the ASIC was a key feature that made possible the realization of the RatCAP, the world's first miniature and portable PET scanner which
enables for the first time correlation of the awake rat’s behavior with brain metabolism through PET imaging. The RatCAP will have a significant impact on behavioral research in particular, and on our society in general, by enabling unique investigations aimed at a better understanding of the addiction phenomenon. At the time the project started, no electronics system was available to meet the RatCAP challenges. Hence a dedicated ASIC was implemented to reach these goals. From an electronics point of view, the implementation of the ASIC allowed a revision of the transistor noise model for the TSMC CMOS 0.18 μm technology. Also, the successful implementation and use of the ASIC proved that this technology is suitable for radiation instrumentation. The research and development realized for the RatCAP and the ASIC lead to the acquisition of three U.S. Patents and the publication of numerous scientific presentations. Finally, the development of the ASIC and the implementation of the RatCAP opened the door to other novel systems, as seen in Chapter 6. For instance, it enabled the construction of dual-modality PET-MRI imaging scanners, where the BNL team was among the first to demonstrate this technology, which is expected to have an unprecedented impact in medical imaging by allowing better diagnosis.

These spin-off systems were eventually made possible thanks to the flexibility of the modular block approach which was developed for the RatCAP, and the relatively low cost of each detector block. Now, in order to increase the social and economical impact on our society, those technologies have to be transferred to industries for the design and implementation of clinical systems which will ultimately end up in medical imaging centers and improve the health of the overall population through better diagnostic capabilities. It is the role and responsibility of PET instrumentation scientists and engineers to innovate and create systems which will improve sensitivity and spatial resolution, while keeping the material costs down, in order to increase the impact of their work on everyone’s life.

To help achieve these goals from the perspective of the front-end electronics, obtaining the best timing resolution will always be the key, while trying to keep the power consumption relatively low. As seen in Chapter 5, the performance of the zero-crossing discriminator used in the RatCAP ASIC is limited by the photon noise. Hence, the door is open to find a new solution to extract the timing information more accurately by lowering the photon noise contribution to the timing resolution. In the ideal situation, the system would trigger on the very first photoelectron generated, which is not possible with APD-based PET system due to the poor signal to noise ratio from the detector. Discrete and NIM-based constant fraction discriminators (CFD) have been used extensively to obtain a timing trigger independent of the signal amplitude, and close to the beginning of the
detector signal to minimize the photon noise. However, a CFD requires a delay line, usually a coaxial cable of a given length, which cannot be implemented monolithically. Many engineers have implemented pseudo-CFDs monolithically, where the delay line was emulated by various means [NOWLIN, 1992][SIMPSON et al., 1996][JACKSON et al., 1996], but none could reproduce the performance obtained by a CFD using a real delay line. The best monolithic CFD was realized by D.M. Binkley [BINKLEY et al., 2002][SWANN et al., 2003], where the delay line was implemented using multiple all pass single pole stages with a time constant that was negligible compared to the input signal rise time. In this ASIC designed for a PMT-based PET camera, the analog sum of four channels is fed to the CFD, which uses 50 mW and a relatively large area. This approach would not be ideal for APD-based PET systems where the sum of the noise from the four channels would substantially limit the signal to noise ratio and hence the timing resolution, which is not the case when using PMTs. Also, the high power consumption and real estate required make it impractical to integrate it into each channel, compared to the small zero-crossing discriminator implemented in each channel of the RatCAP ASIC which uses only 0.44 mW. One option worth studying is the leading edge discriminator (LED), where the trigger is generated when the rising edge of the input signal crosses a reference energy threshold. In such a case, a unipolar shaping amplifier would be required, where a rather fast peaking time should be carefully selected to optimize the timing resolution. Also, depending on the input signal rate, baseline stabilization could be necessary, at the extra cost of power consumption. The trigger position of a LED depends on the amplitude of the signal. Hence, the walk of the LED needs to be corrected based on the signal's amplitude. So the amplitude information must be measured, which could be acquired in many ways. One solution would be to use the LED to obtain the time over threshold: the subtraction of the rising edge timestamp with the falling edge timestamp would be proportional to the amplitude of the signal. This would come with the disadvantage of increased deadtime at the TDC depending on the selected shaping amplifier order and peaking time. A solution to this could be to implement a circuit which finds the peak of the signal. Hence the amplitude information would be obtained by finding the time between the LED trigger and the "peak found" trigger, which would improve the TDC deadtime significantly. The initial calculation based on the timing resolution model presented in the section 5.2.2 shows promising performance, with sub-nanosecond timing resolution for all events within the photopeak. The estimated improvement of the timing resolution would not be sufficient for time-of-flight PET, however it would reduce significantly the rate of random coincidences and improve the image signal to noise ratio.
With the venue of new detectors, increasing functionalities integrated in the front-end electronics and increasing computing power, PET instrumentation is in a phase of rapid technological development and this is likely to continue for many years. The present work has contributed in its own way to these exciting developments.
BIBLIOGRAPHY


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