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Fully Networked, Digital Components for Photon-starved Biomedical Imaging Systems

Deliverable 2.1
SPADnet Design: Specifications and Planning

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Abstract

In this preliminary phase of the SPADnet project all partners were involved in the refinement and definition of an initial set of system specifications, by means of intense communications via meetings, audio-conferences, e-mail exchanges and use of the preliminary internal Website.

This deliverable presents an abridged version of these activities' results, starting from an update of the work carried out by each of the partners before the official project start, followed by a general update of the state-of-the-art and competitor analysis.

Executive Summary

Since the submission of the proposal, most partners have continued to pursue their SPADnet related research programmes. An update of the activities carried out in the time between the project submission and the official start is summarised in Section 2.1.

A new and refined search on recent scientific articles, other developments of potential interest, and an extensive patent search have been carried out by each partner in the respective domains of competence. The results are summarised in Section 2.2.

Although the field of SPAD pixel arrays implemented in CMOS technologies is attracting increased attention, no new element has emerged that may impair the adequacy and the timeliness of the proposed developments. In particular, the SPADnet consortium is still representing the leaders in the development of deep-submicron CMOS SPADs, and the basic technology developed within the MEGAFRAME project still represents a reference in the field.

Although Silicon Photomultiplier detectors manufactured using specialised fabrication processes are increasingly popular, there is no dramatic improvement in their performance to be highlighted. In any case, with just a single exception, all the developed sensors contain little or no intelligence implemented on-chip, thus making the following SPADnet sensor main goals still valid and unique:

- use of conventional CMOS technology (cost reduction, on-chip intelligence, low operating voltages);
- small SPAD size (spatial oversampling, high dynamic range);
- fully digital output (easy processing of output data);
- networking capabilities (reduction of the output data stream, distributed processing capability).

The previously described information has been used by the partners to revise the design specifications. Most of the original approaches were confirmed as viable, and the corresponding performance as adequate.

Table of Contents

Abstract **3**
Executive Summary **3**
1 Methodology and Document Structure **5**
2 State-of-the-art Update **6**
  2.1 Update on work carried out by each partner (WP 2.1) 6
  2.2 State-of-the-art and IP update, competitor analysis (WP 2.1) 11
    2.2.1 Networking and Bridging Devices 11
    2.2.2 Sensor Architectures 13
    2.2.3 Scintillators 14
    2.2.4 Optical Concentrators and Photonic Module Assembly 16
    2.2.5 Innovative Packaging Techniques 18
    2.2.6 TSV technologies 19
    2.2.7 PET Systems 19
3 References **20**
  3.1 Networking and Bridging Devices 20
  3.2 Sensor Architecture and SPAD Design 20
  3.3 Scintillators 21
  3.4 Microlenses and Photonic Module Assembly 23
  3.5 Micro-optical Components 23
  3.6 Innovative Packaging Techniques 24
Annex I Glossary **25**

1 Methodology and Document Structure

The WP2 general structure and work organization was presented and agreed upon at the SPADnet Kick-Off Meeting (Mediso, Budapest, 16/07/2010). After that, each partner contributed to the drafting of this deliverable along the following lines, as defined early on in the WP and with clear responsibilities for each sub-section.

- State-of-the-art and IP update, competitor analysis (WP 2.1)
- SPADnet design and planning refinement (WP 2.2)
    - Array Architectures,
    - Sensor Specifications,
    - Pixel Specifications,
    - Technology Characteristics,
    - Scintillation crystal Specifications,
    - Optical Concentrator Specifications,
    - Photonic Module Design and Assembly,
    - System Functionalities.

Work was carried out under the supervision of FBK (WP leader) and with the support of EPFL. Bi- and tri-lateral meetings and audio-conferences were organised to keep momentum. These activities culminated in the WP2 Final Meeting held at FBK, Trento, on the 30/09-01/10/2010.

2 State-of-the-art Update

2.1 Update on work carried out by each partner (WP 2.1)

Each partner has contributed with a brief summary of the research activity of potential interest to SPADnet and carried out before its start, including any published or submitted papers.

TUDELFT:

Work carried out in TU Delft between project submission and project start:

1. Marek Gersbach submitted and successfully defended his PhD thesis on "Single Photon Detector Array for Time-Resolved Fluorescence Imaging". This work embodies the development of low DCR SPADs in 130 nm CMOS technology. It also demonstrates the use of the Megaframe32 array for bio-imaging applications such as FLIM.
2. The integration of the Megaframe32 SPAD array into a multifocal multiphoton system for fast FLIM was implemented in collaboration with P. French at Imperial College London.
3. A model was developed, describing the detector jitter and light detection efficiency for TOF PET based on SPAD arrays and crystal scintillators.
4. Testing and characterization work for the Megaframe128 array was carried out using an ad-hoc data acquisition system.
5. A parallel histogramming technique was developed and implemented for the Megaframe32 array in FLIM applications. This technique served as a data compression technique, to circumvent the communication bottleneck.
6. The first implementation of SPADs in 90nm CMOS technology was demonstrated. Around 180 structures were implemented, among which 45 worked in single photon counting mode.
7. A TCAD model was used to design an optimal guard ring structure in 0.35µm CMOS technology. Modelling of the electric field and current was also carried out to characterize the device.

TU Delft relevant publications issued before the project start:

- M.A. Karami, M. Gersbach, H.-J. Yoon, and E. Charbon, "A new single-photon avalanche diode in 90nm standard CMOS technology," Opt. Express **18**, 22158-22166 (2010)
- C. Veerappan, J. Richardson, R. Walker, D.U. Li, M.W. Fishburn, Y. Maruyama, D. Stoppa, F. Borghetti, M. Gersbach, R.K. Henderson and E. Charbon, "A 160x128 Single-Photon Image Sensor with on-Pixel 55ps 10bit Time-to-Digital Converter", ISSCC 2011.
- M. W. Fishburn and E. Charbon, "System Trade-Offs in Gamma-Ray Detection Utilizing SPAD Arrays and Scintillators", accepted in IEEE Transactions on Nuclear Science.
- M. Gersbach, Y. Maruyama, E. Labonne, J. Richardson, R. Walker, L. Grant, R.K. Henderson,, F. Borghetti, D. Stoppa, E. Charbon, "A parallel 32×32 time-to-digital converter array fabricated in a 130 nm imaging CMOS technology", ESSCIRC 2009.

UEDIN:

Work undertaken between project submission and project start:

1. Justin Richardson submitted and successfully defended his PhD thesis on "Time Resolved Single Photon Imaging in Nanometer Scale CMOS Technology". This work embodies research on several different low DCR SPAD structures and device scaling as well as research on time-resolved imaging arrays in the MEGAFRAME project.
2. Design, fabrication and characterisation of a test chip in 130nm CMOS containing small 16x16 CMOS SiPM arrays. This demonstrated defect correction and high fill factor pixels (>50%) at ~15µm pitch. A shared deep n-well approach is taken. These arrays have low DCR and are addressable. A Verilog control program and software was written. So far this work is unpublished.
3. Demonstration of SPAD scaling to 2µm in 130nm CMOS and plots of median DCR with device diameter. The 2µm diameter device was reported at ESSDERC, 2010.
4. Design, fabrication and characterisation test chip in 90nm CMOS image sensor process (funded by STMicroelectronics). A low DCR detector has been proven. A 3x3, 5µm pitch array with low DCR has been tested and will be presented at IEDM, San Francisco, 2010.
5. Improved hardware and software support for the MEGAFRAME 32x32 array with custom PCB and OpalKelly FPGA board.
6. Application of the MEGAFRAME 32x32 array in parallel FCS with an SLM and video rate FLIM. This was carried out in co-operation with external partners Antoine Delon at LSP, Grenoble and Simon Ameer-Beg in King's College.
7. Eric Webster started his Ph.D. on SPAD design and modelling with TCAD. The main aim of this independent research is to quantify SPAD device structure design, through understanding the physics of its operation, in order to engineer improved devices. One of the aims of the Ph.D. is to minimise the geometries of functional SPADs and therefore the guard rings, which is applicable to SPADnet. Some other specific objectives are: to determine the dimensions, features and scaling possibilities for SPAD integration into modern CMOS processes; optimising the wavelength profile towards near infrared; minimising crosstalk between read-out electronics and the SPADs; and reducing the DCR. Promising results have already been achieved.

UEDIN relevant publications issued before the project start:

- J. A. Richardson, L. A. Grant, E. A. G. Webster, R. K. Henderson, "A 2µm Diameter, 9Hz Dark Count, Single Photon Avalanche Diode in 130nm CMOS Technology", IEEE European Solid-State Devices Conference, Seville, September 2010 (joint publication with STMUK).
- J. A. Richardson, "Time Resolved Single Photon Imaging in Nanometer Scale CMOS Technology". PhD Thesis, University of Edinburgh, 2010.

STMICRO:

The main activities on SPADnet related topics undertaken between project submission and project start by STMUK and STMFR were:

1. Design, fabrication and characterisation of various experimental SPAD structures and geometries (including support of the above mentioned work done by UEDIN). Analysis

and simulations were carried out with a view to improving performance, reliability and yield during both design and fabrication.

2. Patent searches and reviews of publications were carried out in particular to identify any new filings or advances in detector technology since the proposal was authored.

FBK:

FBK activities on SPADnet related topics undertaken between project submission and project start:

1. A SPAD detector fabricated in a 0.35µm CMOS technology and implementing a single pixel based on 10x10 SPAD cells connected to a time-gated digital counter has been designed and tested. The main feature exploitable for the SPADnet project is the possibility to switch off noisy cells thus obtaining a high yield, large area, SPAD detector.
2. Another CMOS SPAD detector, consisting of an array of 32x32 pixels each one integrating a SPAD and a time-gated analog counter, has been fabricated and tested. This sensor allows achieving an extremely high fill factor (>20%) with a pixel pitch of 25µm.
3. An electro-optical setup has been built to characterize the performance of the Megaframe32 chip with and without microlenses.
4. Several measurements with CMOS SPAD detectors have been done to extract lifetime imaging of organic fluorophores spotted on microreactors with concentrations down to 10^{12} molecules per cm^2.
5. Marina Repich submitted and successfully defended her PhD thesis on "Development of simulation environment for the analysis and optimal design of fluorescence detectors based on single photon avalanche diodes". The core of the Montecarlo simulator tool here developed will be used for preliminary simulations aimed at optimizing the sensor focal plane characteristics.

FBK relevant publications issued before the project start:

- M. Benetti, D. Iori, L. Pancheri, F. Borghetti, L. Pasquardini, L. Lunelli, C. Pederzolli, L. Gonzo, G.-F. Dalla Betta, D. Stoppa, "Highly parallel SPAD detector for time-resolved lab-on-chip", Proc. SPIE 7723, 2010, pp. 77231, SPIE Photonics Europe, Brussels, Belgium, 12/04/2010 - 16/04/2010.
- A. Esposito, S. Schlachter, A. N. Bader, L. Pancheri, D. Stoppa, A. R. Venkitaraman, C. F. Kaminski, H. C. Gerritsen, "Multiplexed measurement of molecular interactions by hyperdimensional imaging microscopy", 2010, Focus on Microscopy 2010, Shangai, China, 28/03/2010 - 31/03/2010.
- A. Esposito, S. Schlachter, A. N. Bader, L. Pancheri, D. Stoppa, A. R. Venkitaraman, C. F. Kaminski, H. C. Gerritsen, "Multiplexed measurement of molecular interactions using hyper-spectral imaging and multi-parametric detection", 2010, Biophysical Society 54th Annual Meeting,San Francisco, USA, 20/02/2010 - 24/02/2010.
- E. Morganti, C. Collini, L. Lorenzelli, F. Borghetti, D. Stoppa, L. Gonzo, "Fabrication and integration of a new Micro Reactor Array for fluorescence analysis", Berlin, VDE VERLAG GMBH,2010, SMART SYSTEMS INTEGRATION 2010 4th European Conference & Exhibition on Integration Issues of Miniaturized Systems MEMS, MOEMS, ICs and Electronic Components, COMO, Italy, 23/03/2010.

MEDISO:

Between project submission and project start Mediso continued its collection of information on the state of the art of PET detector technology:

1. In order to reveal current and future trends Mediso attended the 2nd Jülich MR-PET Workshop Current Status of Instrumentation and Application / Future Developments (May 10 – 11, 2010, Jülich, Germany).
2. A thorough patent search was performed – mainly focusing on PET detector technology and integrated PET systems.
3. Competitor analysis has been continued and Mediso's internal comparative PET system database has been updated with the new systems that have been introduced to the market in this period of time.

Mediso has entered into cooperation with Aspect Magnet Technologies, a pre-clinical MRI manufacturer, to develop a pre-clinical PET-MR system. Under this collaborative project, which was announced at the World Molecular Imaging Congress (WMIC), Kyoto, Mediso received two magnets that will enable it to investigate the MRI compatibility of any PET detector developed.

MEDISO relevant publications issued before the project start:

- P. Major, G. Hesz, T. Bukki, B. Benyo, G. Nemeth, "Timing Calibration Method for NanoPET/CT System", 2010, IEEE Medical Imaging Conference, Knoxville, USA – accepted for Poster Presentation
- I. Szanda, J.E. Mackewn, G. Patay, P. Major, K. Sunassee, G.E.D. Mullen, G. Nemeth, Y. Haemisch, P.K. Marsden, "Initial Performance Evaluation of the NanoPET/CT Pre-Clinical PET-CT Scanner", 2010, IEEE Medical Imaging Conference, Knoxville, USA – accepted for Oral Presentation

LETI:

Between project submission and project start, LETI demonstrated the possibility of building a PET system using cadmium telluride (CdTe) photo-detectors.

1. The CdTe detector has been custom design with double-strip geometry and the full system has been simulated using GATE.
2. Two ASICs have been designed, manufactured and tested. The front-end ASIC is a fast 16 channel low noise low power front-end preamplifier/shaper. The second one is a processing circuit performing time tagging, energy measurement and digital interfacing with the data.
3. Two PET heads have been tested on a dedicated test bed. Energy resolution was better than 5% at 511keV, temporal resolution was 3ns, and spatial resolution in the centre of the field of view was better than 750µm.

LETI relevant publications issued before the project start:

- Experimental evaluation of a high resolution CdTe-based PET system, Montémont, G, Comtat, C, D'Aillon, E.G., Mathy, F., Monnet, O., Trebossen, R., IEEE NSS MIC conf record 2009, Pages 3159-3162.
- A high-speed 2nV/Hz1/2 16-channel current amplifier IC for PET, Rostaing, J.-P., Peizerat, A., Billoint, O., Montémont, G., Monnet, O, 2009, Pages 322-323.

BUTE:

Work undertaken between project submission and project start:

1. A new optical Monte Carlo simulation tool based on a parametric Zemax model has been developed to model the scintillator light output in PET detectors. Well aligned results have been demonstrated between simulated and measured light output figures for 33 different pin configurations, with an error of less than 10% between simulations and experiments (Lorincz 2010).

2. The concept of an optimised light guide was presented at the Orlando IEEE NSS MIC 2009 conference. It provides a solution for light sharing in a PET block detector containing a scintillator crystal array and several photomultipliers. The double prism deflector allows the precise determination of the excited pin position in a large block with high spatial resolution (Steinbach 2009).

3. An experimental light deflector unit was fabricated for a small 5 x 5 sample array to study the limit of the technology and to validate simulation results. The measured light deflections agree well with the results of simulations.

4. The PetDetSim software, based on Detect2000, has been validated by measuring the light output of scintillator crystal pins. The simulated results have been compared with the results of the corresponding model built within Zemax (Steinbach 2010).

BUTE relevant publications issued before the project start:

- E. Lőrincz, G. Erdei, I. Péczeli, C. Steinbach, F. Ujhelyi and T. Bükki, Modeling and optimization of scintillator array for PET detectors, IEEE Transactions on Nuclear Science, February, 57, 1, 48-54, 2010.
- C. O. Steinbach; G. Erdei; I. Péczeli; F. Ujhelyi; T. Bükki and E. Lőrincz, Optimized Light Sharing Module for PET Block Detectors, 2009 IEEE Medical Imaging Conference (MIC) Conference Record, M05-274, 2817-2820.
- C. O. Steinbach, A. Szlávecz, B. Benyó, T. Bükki, and E. Lőrincz, Validation of Detect2000 based PetDetSim by Simulated and Measured Light Output of Scintillator Crystal Pins for PET Detectors, IEEE Transactions on Nuclear Science, Vol. 57, No. 5, pp. 2460–2467, October 2010

2.2 State-of-the-art and IP update, competitor analysis (WP 2.1)

A new and refined search on recent scientific articles presented in international journals and conferences as well as other developments of potential interest, including an extensive patent search, has been carried out by each partner in the respective domains of competence. The results can be summarized as follows:

2.2.1 Networking and Bridging Devices

Sensor network

In the literature there is no material directly related to a sensor network used in PET imaging. However, there is plenty of technical information available for image sensor networks. Among the various image sensor applications, we found that the sensor network used for radiation detection is the most relevant to our application. In [N1], Robert J. Nemzek et al. have examined the dependence of the signal to noise (SNR) ratio on increasing the number of sensors in the network. In this paper, the authors propose to use different integration time for different sensors based on location. This is very similar to the idea put forth in the patent [N2], of using flexible integration time based on the gamma ray detection time.

In [N3], Annie Liu et al. discuss the design tradeoffs for various radiation detections in a wireless sensor network. This paper discusses a network topology somehow similar to our PET network. For that network the authors found that the time required to localize a radiation source reduces as the number of sensors in the network increases. Additionally, they found that using a small sensor is much more beneficial than using few large sensors. However, it is to be noted that in this application they see the radiation source from a far distance and for a long time. So the authors assume that the radiation is emitted in all directions at the same time, which contradicts the situation in our PET application.

In [N4], authored by Eugenio Culurciello et al, a sensor network, called "address-event image sensor network", was introduced. In this network, an image sensor sends data to the network only when it receives the data. In PET, at any instant in time only two sensors receive gamma rays, provided the background noise is removed beforehand. This implies that introducing an event-based network for PET will reduce the data rate in the network significantly.

Reference [N5] filed by Fujifilm Corporation, discusses a networking architecture for computed tomography (CT). This patent concentrates more on the hospital management system, where the CT imager forms a part of the network. But the data packets sent from a CT instrument to the server is relevant to the data packet that needs to be generated for our network.

The computational power available in every sensor node of the proposed PET sensor network can be tapped to perform a part of the computation in every node. In order to understand the computational requirements for the PET application a survey was done on the various algorithms and data compression techniques that are currently used.

Algorithm

In positron emission tomography (PET) imaging, the data generated by the sensor is used to find the spatial line of response (LoR) of an annihilation event. Further in time of flight (ToF) PET, the annihilation event is localized along the LoR, based on the time of flight (ToF) information.

The algorithm in patent [N6] determines the LoR based on the data obtained after two levels of filtering viz., energy windowing and coincidence detection. In energy windowing, the radiation events that fall outside of a given energy range are discarded. In coincidence detection, the detected radiation events that are temporally separated by a certain time difference are filtered out. These two levels of filtering help to remove a certain percentage of noisy events [N7] created due to accidental coincidence and scattered coincidence events, thereby reducing the search space to find the gamma ray pair, that forms an LoR.

To precisely obtain LoR, it is important to accurately estimate the position of the incident gamma ray in the detector. To find this, the straightforward method of estimating the centroid of the incident light as originally introduced by Anger [N8] can be used. However, it should be noted that this method does not incorporate the non-linearity effects introduced by the detector. To incorporate the non-linearity effect into the position estimation, neural network based approaches were introduced in [N9]. In [N10], [N11] and [N12] various combinations of scintillators and sensors were studied to understand the effectiveness of using neural networks in position estimation. In the paper published by Fernando Mateo et al. in [N13], real time estimation of the position based on a neural network is explained.

The LoR collected over time is used to construct the image. For this various algorithms are used. The most commonly used are filtered back projection and iterative back projections.

Compression Technique

The data rate coming out of a PET system is generally very high. For example, the uncompressed raw data produced by a high resolution PET system is in the order of hundreds of Mbytes/s [N7]. In practice, techniques such as angular meshing, are used to reduce the dataset to an acceptable size, of the order of few Mbytes/s. But this compressed data set compromises the resolution of the final image.

Before the image construction, the extracted LoR needs to be collected in memory. In [N7], two methods of storing the LoR information are introduced viz., list mode and histogram mode. In list mode each of the gamma ray detection events is stored in the memory separately, along with its spatial and time of occurrence information. In the histogram mode, information is compressed by forming a histogram with all possible LoRs. It should be noted that in histogram mode the compression is achieved at the cost of losing the timing information of the event.

Conclusion

From the literature survey we understand that the amount of raw data that needs to be handled for PET imaging is very high. Also, it is not pragmatic to collect and transfer data in periodic intervals to a computer. One possible solution could be to make use of the computational power available at every node in the proposed sensor network. From the study, we understand that the data transfer rate might be reduced significantly by intelligent filtering, some of which might be implementable in the sensor node. The data compression techniques that are currently used will also come handy for the real time implementation of noise filtering techniques in hardware.

2.2.2 Sensor Architectures

CMOS SPAD Detectors for PET

A number of publications have appeared in late 2009/early 2010 on CMOS in the interval between project submission and start. The most significant of these for SPADnet were publications by Philips Digital Photon Counting at the 2009 Nuclear Science Symposium [SD1] and press releases on the same topic. These papers announce the architecture and basic detector performance of a digital silicon photomultiplier for PET based on CMOS. This announcement makes public the measured results of a sensor patented in a number of prior Philips patents, which had already been detailed in the SPADnet Technical Annex. A relatively immature stage of development is revealed in that no module implementation or PET experiments appear yet to have been conducted. In forthcoming papers at the 2010 Nuclear Science Symposium [SD2],[SD3] this work seems to have advanced to tests with scintillators and assembly of 4x4 chips into a module of 32mm x 32mm.

A team from Radiation Monitoring Devices in the USA have also recently made several publications announcing results from an array of CMOS SiPM composed of 4x4 1.5mm x 1.5mm chips coupled to a LYSO crystal in a two layer phoswich arrangement [SD4],[SD5]. DOI resolution of 2.3-2.9mm is reported, however the chips appear to contain little CMOS signal processing instead relying on resistive networks to resolve the position of arrival.

Other leading groups active in CMOS SPAD research reported results on large arrays capable of high frame rate photon counting (100kfps) [SD6]. These devices realised in 0.35µm high voltage CMOS have 100µm pixels and are being employed for low-light imaging and parallel fluorescence detection.

SPAD Design

Several new researchers have recently emerged including Chitnis and Collins from the University of Oxford, UK, looking at compact pixel structures [SD7],[SD8]. The first results of SPADs in 0.18µm CMOS are presented with relatively high dark count for a 30µm pitch array with 10µm diameter devices.

Yet another group from University of Nottingham, UK, announced SPADs in 0.18µm TSMC. Gronholm et al. from University of Oulu, Finland announced SPAD devices in STMicroelectronics 0.13µm CMOS and an active quench circuit with dead-time of 7.5ns [SD9].

Recent research from TU Delft demonstrated CMOS SPADs in the most advanced process to-date of 90nm [SD10].

Conclusion

In the last two years there has been an increasing interest in CMOS detectors suitable for a PET use but so far there is little experimental validation of them into real large area photonic components.

Although CMOS SiPM detectors proposed in [SD1] and [SD2] address some of the issues targeted by SPADnet, the level of intelligence implemented on them is minimum compared to our final goal. Moreover the SPADnet concept of having the photo-detectors operating in a sensor network, exchanging information, and locally processing the huge amount of data generated by a PET measurement set-up is still totally innovative.

Finally the use of TSV technology is highly innovative and fundamental to allow the realization of large-area photonic detector assemblies.

2.2.3 Scintillators

Today, there is no widely used alternative to LSO/LYSO in the literature of SiPM-based detectors. There are only a few possibilities found in recent papers; these will be detailed in the following.

Zhang *et al* [Sc1] use cheap BGO arrays coupled to a block of PSPMTs. They state that they could achieve 2 mm resolution despite the relative poor light output of BGO; and the slow decay time (300 ns) gives adequate count rate performance at the low activity level they apply.

Promising results are published by the research group lead by C.L. Melcher [Sc2]-[Sc3]. Their results show that Ca doping can improve the light output of LSO:Ce by 25%, and reduce the decay time from 43 ns to 31 ns. LSO crystals with different Ca doping can represent alternatives to typical phoswich detectors.

Another interesting material is $LaBr_3$ which features a fast decay time (16 ns) and high light output (about 70’000ph/MeV). Schaart *et al* [Sc4] tested a SiPM detector coupled to a $LaBr_3$ crystal for TOF-PET, and good energy and timing resolution were achieved. However, $LaBr_3$ is hygroscopic, which makes it difficult to handle and very expensive.

Other materials (e.g. LuAP, LuYAP, LaBr, LPS) are also sometimes used in PET applications, however, their emission spectrum is in the UV-range, and therefore not suitable for our detector. A potential solution for this problem is patented by Grazioso [Sc5], who applies a wavelength-shifting layer between the crystals and the photodetectors. The layer converts the original wavelength of the scintillation light into a longer wavelength range, where the Si-based detectors have higher PDE.

Detector constructions

In one part of the solid-state detector based constructions which we reviewed, SiPMs/APDs are applied in one-to-one coupling to pixellated crystals. In order to increase spatial resolution, Bergeron et al [Sc6] use LYSO and LGSO crystals assembled in phoswich pairs read out by an APD.

Song *et al* [Sc7] report on a detector module which consists of an LSO array coupled to SiPMs via a special light guide layer. This is the only solution for a special light guide applied between the crystal and the SiPMs found in the literature.

In [Sc8], the authors use an LGSO block divided into 6×6×6 pixels in the 3 dimensions and read out on every side by SiPMs. Different detector arrangements were studied in order to get 3D position determination. A similar arrangement was patented by Aykac and Grazioso [Sc9]. They apply a 3 dimensional checkerboard geometry which consists of crystals with at least two different decay times. At least two orthogonal surfaces of the crystal array cube are connected to photosensor(s) with or without a light guide. Crystal identification is achieved by pulse shape analysis.

In another patent [Sc10], Grazioso and Aykac describe a detector which consists of alternating axial and transaxial linear arrays of pixellated scintillators, read out by photosensors on two or more sides. The arrangement minimizes the edge effects and increases DOI resolution.

Trummer *et al* [Sc11] report on a detector made from long, thin LYSO/LuAP crystals with APD readout on both ends for DOI determination. They found that with increasing number of depolished surfaces of a crystal pixel, a significant improvement in the resolution of the DOI can be obtained, however, at the cost of loss of photons.

Another solution is the Anger-type PET detector, when pixellated detectors and a continuous crystal are used. In this case, there is light sharing between the detectors, and Anger-logic or other algorithms (e.g. maximum likelihood) are used to determine the scintillation position.

A Belgian research group (S. Tavernier, P. Bruyndonckx *et al*) compared the two type of detectors, and found that DOI-capability and better spatial and energy resolution make the Anger-type detectors more advantageous [Sc12]. In [Sc13], they investigated the effect of different reflectors applied on the surface of a continuous LSO crystal and found that in case of black painted surfaces the FWHM of the distribution is better than in case of Teflon coating; however, the tails of the distribution are heavier. Best results were achieved using a non-coated crystal with small triangles on the back face that reflected the light in the direction it came from. According to simulations and measurements published in other papers, the edge effect can be reduced by applying black painted side surfaces [Sc14]-[Sc15]. [Sc15] also mentions that better spatial, but worse energy resolution can be achieved with black painted crystals.

Chung *et al* [Sc16] published a quasi-monolithic scintillator array coupled to a SiPM array. The scintillator was monolithic in the x direction and pixellated in the y direction. With this arrangement, the properties of both monolithic and pixellated scintillators could be experimentally tested.

Based on Monte Carlo simulations and measurements, Maas *et al* [Sc17] concluded that APD detectors placed on the gamma-entry side of a 10 mm thick LYSO block crystal provide better spatial resolution than placed on the back side. 20-mm thick crystals with double-sided read-out also showed good results, not only at normal incidence, but also at angles of incidence up to 30°. In a novel paper, Schaart *et al* [Sc18] published similar results using SiPMs instead of APDs.

Miyaoka *et al* [Sc19] published the same result for an 8 mm thick LYSO block: according to their Monte Carlo simulations, they achieved an improvement of 24% in spatial resolution and 20% in DOI resolution.

Another patent was found in the topic of scintillator geometry: Fiedler *et al* [Sc20] patented the production and usage of a gapless scintillator layer.

Optical coupling

In case of continuous crystal, mostly no light guide layer was applied. Most detectors have a thin window, and the crystal is coupled to the window by optical glue or grease. The authors of [Sc13] made a comparison between optical melt mount glue from Cargille Laboratories, optical grease and Si rubber, and found that the glue gives the best result.

Moehrs *et al* [Sc21] report on Geant4 simulations of a multilayered detector block consisting of LSO blocks and SiPM arrays. They found that no light guide layer is necessary, since the scintillation crystal (LSO) is sufficient as a ‘spreading’ medium, even for optical photons which are generated close to the photomultiplier. The three-layered geometry results in a high spatial resolution of 0.4 mm FWHM.

Simulations

Two simulation packages are used in the literature: Detect2000 and Geant4. The former is mostly used for optical photon tracking, while the latter is applied to simulate the transport and interactions of the gamma photons, the scintillation process, and the transport of the optical photons.

Summary

Currently indications are that the best scintillator for PET applications is the LSO/LYSO crystal. The geometry of the Si based detectors depends on the type of scintillator crystal, e.g. pixel array or monolithic block. The monolithic approach is a promising solution because of its additional DOI capability and lower price, but suffers from the "edge effect". The influence of surface quality and reflectors on spatial and depth resolution has not yet been thoroughly investigated for the monolithic approach.

2.2.4 Optical Concentrators and Photonic Module Assembly

The literature on innovative packaging techniques and optical coupling devices for large area, rare event photonic components has been investigated. First, we give a general overview of the solutions published for light coupling, including in particular the shape of the scintillator (needles vs. continuous). Then, we focus on the practical realization of light coupling from a continuous scintillator down to a wafer level imaging sensor taking into account microelectronics standard processes. It can be generally stated that the application of microlenses and/or microconcentrators on SiPMs in biomedical imaging applications is not yet mature. In particular, no practical and wafer level solutions have been reported on the light concentration using imprint technology.

E. Grigoriev was writing about its potential benefits [μC1] in 2007, but without any actual solution. Still several applications of micro-optical components and lens arrays have been found for different detector types and different purposes.

Only the research group of Hyunki Kim is known to have conducted simulations, wherein they coupled a theoretical solid-state detector and a continuous or micro-columnar CsI scintillator with microlens arrays [μC2]. According to their results, a plano-convex lens array, facing with the convex side towards the detector, increases the light collection by 16-21% compared to the case without lens array. The aforementioned detector was designed for X-ray photon detection.

Another device utilizing a lens array for position sensitive X-ray photon detection was patented by an H. Barrett led group at the University of Arizona [μC3]. Therein lenses are mounted one-by-one into a matrix between a continuous scintillator crystal and Micro-Channel Plates (MCPs). The lens system was designed to image the scintillation events onto the front surface of the MCPs, this way increasing the position determination precision. The lenses are distributed in the matrix in such a way that their field of view (FOV) overlaps, thus increasing the number of photons collected by the system. Intensified light emerges from the back side of the MCPs and is detected by CCDs or CMOS image sensors (CISes).

A similar device was constructed and evaluated by Diane R. Eaker and colleagues [μC4]. This work was inspired by H. Barrett, inventor of the earlier device. Eaker's solution places a columnar scintillator on the front surface of the MCPs and a lens system images the MCPs' back surface onto a CCD. According to them, this approach is suitable because this system can be used for both X-ray and nuclear imaging without changing the system.

An application of microlens arrays for non-light-concentrator purposes was investigated by M. Carles and colleagues [μC5]. Two monolithic scintillator crystals were coupled to each other by a microlens array in order to increase the depth of interaction (DOI) determination precision. The conclusion was that such an application of microlenses is unnecessary, because a rectangular prism with optimized thickness has the same effect on the intrinsic resolution of such a detector.

Another way to increase the amount of light collected by a pixel of an imaging detector is the utilization of non-imaging micro-concentrators [μC6]. A patent of Tower Semiconductors Ltd. proposes via waveguides (VWG) with a light concentrator in the upper section for CISes pixels [μC7]. The shaping of this micro-optical element is integrated into the CMOS manufacturing process. The upper non-imaging parabolic concentrator is formed by wet etching into the upper insulation layers, while the VWG is dry etched down to the photodiode. The role of the concentrator surface is to collect light from an area larger than that of the photodiode, which receives light through the VWG. The patent raises the possibility of coating the VWG with reflective material, of filling it up with refractive material, or both, thus constructing reflective, refractive and compound parabolic concentrators. Applying a microlens on top of the concentrator might further increase the light collection efficiency.

Philips patented a highly integrated radiation-sensitive detector construction in 2010 for computed tomography [μC8]. The four-layer detector has a bottom photosensor layer, a wavelength shifting and a filter layer and on the X-ray side a composite scintillator layer deposited by methods used in micro-electromechanical system production. The role of the wavelength shifting layer is to convert light emitted by the scintillator to another wavelength (practically UV to visible), which is reflected by the filter layer towards the photosensor. The photosensor sensitivity is matched with this second wavelength, thus the three bottom layers together form a light trap.

Special layers included into the detector constructions are not only for increasing light collection efficiency, but also to extend the dynamic range of certain photosensors. Another patented solution of Philips applies an X-ray detector with scintillator crystal and a variable reflectivity layer on top [μC9]. This can be achieved by reflective E-Ink deposited between two electrodes, or a container layer which can be filled or emptied with fluids that change the reflectivity on the inner surface of the container. Micro-optical solutions concerning dynamic range extensions are mentioned by Kurtis F. Johnson [μC10], but no medical applications have been found.

Focusing on wafer-level packaging techniques, including continuous scintillator devices, optical coupling techniques and CMOS technologies applied to SPADs, it can be stated that light coupling is both:

- a matter of light extraction due to the high optical index of the scintillator,
- a matter of concentration of light onto low fill factor SPAD array.

As far as light extraction is concerned, most optical coupling devices included between the scintillator and the CMOS tend to use either optical resist, or grease or glue with an optical index as close as possible to the index of the scintillator. Hence, it might be useful to use syloxane polymers developed by SILECS [MA1] or Halogenated aromatic Resins developed by CYTEC

[MA2]. Also, Liu [MA3] reports on new developments on HRIP, High Refractive Index Polymers. These include polymers including high-n nanoparticles leading to an optical index as high as 1.80.

Concerning the problematic of light concentration, Donati proposed some novel truncated pyramids, parabolas and compound parabolas [MA4], [MA5]. According to Donati, the highest concentration factors are achieved by compound parabolas. Nevertheless, whatever the solution, high concentration ratios are achieved as soon as the aspect ratio itself is high, typically over 10 for base object as high as 10µm. Hence, these solutions seem hard to achieve practically.

Ulrich [MA6] and Audran [MA7] report on the realization of gapless microlens arrays on the CMOS sensor. Gapless are reported to be interesting to gather most of the light impinging on the sensor rather on the active area of the CMOS. The realization of gapless microlens arrays is a two step process. In the first step, one patterns a resist using a standard photolithography process. A UV curing process follows to ensure the bleaching of the resist and to reduce the melting of the resist. After UV curing, a reflow process occurs to shape the lithographed resist squares (or circle) to a spherical shape. The second step is similar to the first one except that the resist is photolithographed in the space remaining in between the microlenses realized during the first step. These microlense arrays are deposited on the CMOS interface. This approach is useful as long as the focal range is not too long, typically in the range of a few microns (1-4µm). That is, it is not applicable for pixel sizes greater than 10µm, given that the reflow process time becomes very long for pixel sizes greater than 10µm [MA9].

2.2.5 Innovative Packaging Techniques

The literature on innovative packaging techniques for determining the depth of interaction (DOI) has been investigated with special attention to those suitable for PET. The DOI information can be extracted from multiple crystals (Phoswich) coupled to a SiPM in a single-ended readout configuration, or a single crystal coupled to two SiPMs in a dual-ended readout configuration. The latter can potentially provide higher DOI resolution at the expense of increased number of detectors.

Building a module by stacking slab detectors is another way of measuring DOI and is currently used with semi-conductor detectors (for example silicon [PT1] or cadmium telluride [PT2], which are a stack of double sided semiconductor detectors), but does not seem to have been recently studied for scintillator detectors.

Phoswich structures use multiple decay times and pulse shape discrimination to extract the DOI: dual layer phoswhich systems are used by commercial systems like GE eXplore, ClearPET or LabPET, and recent publications deal mainly with numerical simulations.

Two recent patents [PT3], [PT4] were filed by Siemens Medical Solutions about the implementation of a poly-vinyl-toluene wavelength shifting layer between a first scintillator (LuAP) and a second one (LSO). The detector further comprises a long pass filter for preventing light from the second scintillator from entering the first scintillator. A photomultiplier is used to measure visible photons.

Radiation Monitoring Devices (RMD) announced in 2010 its development of a monolithic phoswich sensor technology, departing from the discrete designs commonly used [PT5]. It uses a phosphor-coated LSO scintillator and enables continuous DOI encoding with a published DOI resolution of 8mm (FWHM) for 2cm thick scintillator.

A dual ended readout configuration is used by Taghibakhsh et al. [PT6] with 2×2×20 mm^3 LYSO crystals coupled to silicon photomultipliers, featuring a 2mm DOI resolution using a simple ratio of the difference over the sum of the amplitudes of the two signals generated by the SiPMs at the two ends of the scintillator. With a detector DOI calibration using an LSO arrays (7 × 7 elements, with a crystal size of 0.92 × 0.92 × 20 mm^3 and pitch of 1.0 mm) and position-sensitive avalanche photodiodes, Yang et al. [PT7] (from RMD) show a DOI resolution of up to 0.5mm.

2.2.6 TSV technologies

STMICRO now has a fully qualified TSV production line installed at its Crolles facility and is in volume production of imaging devices primarily targeted at mobile phone cameras. SPADnet can benefit from access to this technology and STMICRO TSV engineering expertise. We do not document all details here but can disclose specifically that manufacturable dimensions of solder ball size and pitch as well as mechanical robustness (despite considerable back lapping of final silicon wafer thickness) will be of particular benefit, the former expected to improve fill factor at the module level well beyond that achievable by conventional packaging techniques. For mitigation of risk the module design will benefit from revised simulation models which have been verified against measured criteria from production devices.

2.2.7 PET Systems

Commercial PET systems:

A detailed summary of commercially available PET systems has been used to define some of the target specifications of the SPADnet photonic module as applied to the SPADnet evaluation scenario.

PET Systems and detector arrangements related patents (2009-2010):

As previously indicated, we have conducted a refined patent search to review those patents that have been issued after the submission of the proposal. The strong research activity in this field is reflected by various patents issued on sensor design and manufacturing, detector module design, light coupling, time of flight measurement, depth of interaction decoding methods, and PET systems based on these solutions.

In summary, although the large number of patents shows that quite strong research activities are going on in this field, following their analysis the consortium is still confident that none of them will limit the impact of the SPADnet project. As already indicated in the Technical Annex, the consortium views the previously detailed patents and publications as confirmation of the desire for the technology to move in the direction we have ourselves anticipated.

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Annex I Glossary

TERM	DEFINITION
ASIC	Application Specific Integrated Circuit
APD	Avalanches Photo Diode
CT	Computed Tomography
DOI	Depth of Interaction
DCR	Dark Count Rate
FPGA	Field Programmable Gate Array
FWHM	Full Width at Half Maximum
MPPC	Multi Pixel Photon Counter
MRI	Magnetic Resonance Imaging
PCB	Printed Circuit Board
PET	Positron Emission Tomography
PSPMT	Position Sensitive Photo Multiplier Tube
PMT	PhotoMultiplier Tube
QA	Quality Assurance
SiPM	Silicon PhotoMultiplier
SPAD	Single Photon Avalanche Diode
SPECT	Single Photon Emission Computed Tomography
STI	Shallow Trench Isolation
TAC	Time to Amplitude Converter
TCSPC	Time Correlated Single Photon Counting
TDC	Time-to-Digital Converter
ToF	Time of Flight
TFT	Thin Film Transistor
TSVs	Through Silicon Vias
VLSI	Very Large Scale Integration