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SILICON PHOTOMULTIPLIER CURRENT AND PROSPECTIVE APPLICATIONS IN BIOLOGICAL AND RADIOLOGICAL PHOTONICS

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Abstract:
The detection of low-intensity light is a crucial issue in many aspects of science and technology. So far, the solution has involved extremely delicate and somewhat bulky devices, the photomultiplier tubes, providing high sensitivity but suffering from fragility and susceptibility to interference. The silicon photomultiplier (SiPM) is a solid-state photon detector that provides a new solution for a wide range of photometry applications in fields as diverse as medicine, biology, environmental science, chemistry, physics, and nuclear physics. SiPMs are on a par with conventional photomultiplier tubes (PMT) in terms of internal gain and photon detection efficiency, while they are undoubtedly superior in terms of mechanical robustness, compact size, electronic stability, low power consumption, and affordability. Our group has long been involved in ionizing radiation measurements based on light emitting sensors both for industrial nuclear technology applications and for hybrid diagnostic imaging techniques. In both cases, SiPMs offer the unquestionable advantages described in this review.

Keywords: *silicon photomultipliers; photodetectors; optical biosensors; optical radiation measurements; scintillation detector.*

1. INTRODUCTION

The detection of light at low optical intensities with highly efficient and highly scalable sensors is a crucial issue in many aspects of science and technology. For example, photoluminescent bioprobes triggered by linear optics (one-photon absorption) or by other type of processes, such as chemiluminescence, have an important role as miniaturized biosensors for the biological and biomedical field [1]. Nonlinear optical (NLO) phenomena [2] also play a role in life sciences, for example when coherent light beams at high optical intensities are used to trigger a faint second harmonic luminescent emission (SHG) from organic compounds in solution [3, 4]. Indeed, two-photon excited fluorescence (TPEF) [5] combined with SHG imaging provides extremely promising bioprobes [6-8], such as those for the identification of early nodules in calcified aortic-valve disease [9]. The detection of light is also fundamental in the field of ionizing radiation detection and measurement [10], where prompt radioluminescence and optically stimulated luminescence are widely used for field characterization and dosimetry [11-13]. More recently, the detection of light scattered by neutron-induced bubbles inside superheated emulsions has been described as an efficient read-out system [14, 15]. Undoubtedly, any application based on low-intensity light emissions will require photosensors with superior photon detection performance combined with mechanical robustness and scalable size.

So far, the solution for measuring low-intensity light has involved extremely delicate and somewhat bulky devices, the photomultiplier tubes, providing high sensitivity but suffering from fragility and susceptibility to magnetic interference. The introduction of the silicon photomultiplier (SiPM), also called multi-pixel photon counter, has created a real revolution in the field of measuring light. The SiPM uses an array of photodiodes compatible with complementary metal–oxide–semiconductors (CMOS), each operating in photon counting ("Geiger") mode with an integrated quenching circuit and connected in parallel on a silicon wafer. A photon interacting with any photodiode produces a pulse of current at the sensor output, and the sum of all individual current pulses from each photodiode produces the total output from the light recorded in a timeframe. Therefore, the total output current is proportional to the incident photon flux. The total SiPM gain is around one million, significantly higher than that of a normal avalanche photodiode (APD), which is typically around one hundred. This recent technology combines the positive features of conventional PMTs, i.e., high gain, sensitivity, and stability, with those of silicon APDs, i.e., small size, low voltage operation, and ruggedness [16].

In order to fully appreciate the advantages offered by silicon photomultipliers, it is useful to review the prior technology of avalanche photodiodes and photomultiplier tubes. The avalanche photodiode (APD) was one of the first silicon solid-state photodetectors converting light to a proportional electrical signal using the photoelectric effect. This detector requires a high reverse bias voltage (~200 V) to create the necessary avalanche effect. Its physical structure is robust, insensitive to magnetic fields and compact [17]; on the other hand, its response depends heavily on the temperature and its internal gain is too low for single photon detection [16]. The photomultiplier tube (PMT) was the first detector that can convert a weak light signal into a measurable electric one. In PMTs, an input photocathode converts light into electrons that are accelerated against a series of electrodes (dynodes) positioned in cascade, thus extracting more electrons from dynode to dynode due to a high bias voltage (~1000 V). A vacuum tube is necessary for proper operation and magnetic fields will cause interference by deflecting the electrons [10].

The SiPM's insensitivity to magnetic interferences and their compact dimensions are two of the main reasons for their wide utilization. One of the first reported SiPM viability studies was conducted for the Tesla Hadron Tile Calorimeter [18], where SiPMs were coupled with a scintillator and a wavelength shifter (WLS) providing unprecedented energy and time resolution in nuclear particle calorimetry compared with PMTs and with hybrid photo-diodes [19-21]. This study paved the way to applications in many different research fields [22-30].

The SiPM's compactness, robustness and high photon detection efficiency makes them possibly the best miniaturized optical sensors [31]. Also, SiPMs are highly scalable: depending on the application, it is possible to use a matrix of a few tens of cells [32] or up to thousands of cells [33] just adjusting the electronics front-end. Another major advantage of SiPMs is their low bias voltage, at least one order of magnitude lower than in PMTs [34], allowing the design of compact, affordable and low power-consumption devices [35].

In this work, we present a review of the state of art of SiPM design and applications, showing how the SiPM's characteristics have already benefited a variety of applications, but also offering the reader a perspective of the potential of these robust photodetectors, particularly in the development of optical biosensors and radiation detectors.

2. DESCRIPTION OF A SILICON PHOTOMULTIPLIER

A SiPM is a pixelated device where each pixel, or microcell, is a combination of a single photon avalanche diode (SPAD) and a quenching resistor (RL) in series, with all microcells connected in parallel, as shown in figure 1. Typically, the dimensions of a SiPM microcell range from 10 µm to 100 µm, whereby the number of microcells per device depends on the application, and ranges from tens to several tens of thousands. The active areas of SiPMs typically range from 1 mm^2 to 6 mm^2 and their spectral response ranges from ultraviolet (UV) to near-infrared (NIR) [36].

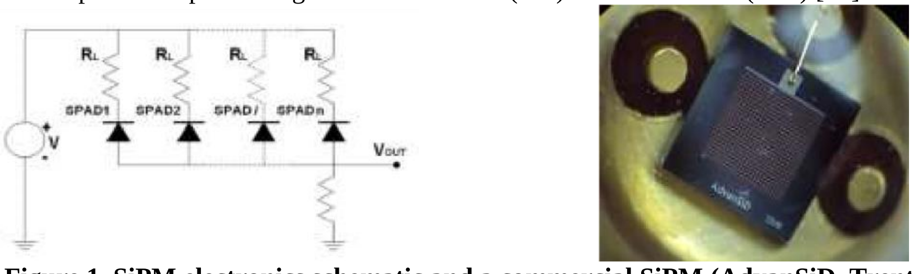

Figure 1. SiPM electronics schematic and a commercial SiPM (AdvanSiD, Trento, Italy).

A SiPM is externally biased so that the voltage on each SPAD is kept above the breakdown voltage. The difference between the biasing voltage and the breakdown voltage is known as overvoltage — the main adjustable parameter controlling the operation of the device. If a SiPM absorbs a photon, the resulting charge carrier (an electron or a hole, depending on the structure) can trigger an avalanche in the gain region. The avalanche can produce 10^5 - 10^6 carriers, which constitutes the overall gain. The role of the quenching resistor is restoring the SPAD back to its initial state [37], this operation is the so-called Geiger mode.

A silicon photomultiplier (SiPM), though pixelated and thus recalling a digital device, produces an analog output signal in real time. The output is a time sequence of waveforms (or current pulses), which have a discrete distribution of amplitudes. The histogram of the amplitudes depends on the intensity and time-characteristics of the incident light [38]. The signal resolution of a SiPM allows resolving the number of photons hitting the device down to a single photon.

The photon detection efficiency (PDE) is the probability that a silicon photomultiplier (SiPM) will produce an output signal in response to an incident photon. It is a function of several factors: quantum efficiency (QE), probability of Geiger discharge (P_{trig}) and geometrical efficiency (GE). The quantum efficiency is the probability that an incident photon will produce a charge carrier (electron or hole) capable of triggering a Geiger discharge. The geometrical efficiency, also known as fill factor, is the ratio between active area and total area of a SiPM [38]. The PDE can be expressed as follows [16]:

$$PDE = QE \times P_{trig} \times GE \tag{1}$$

The dynamic range of a SiPM's signal depends on the PDE and on the total number of microcells; the amplitude of the output signal is proportional to the intensity of the incident light when the number of photons hitting the device is much lower than the total number of microcells. Therefore, the dynamic range is limited by the number of available SPADs [16]. The SiPM's time resolution depends on the rise time and the recovery time of the device. The rise time is the time required to produce a Geiger discharge, while the recovery time is the time required to return from the discharge back to initial state. The timing properties of a SiPM depend mostly on the quenching resistor and on the diode junction capacitance [16]. A typical Geiger discharge is very fast, hundreds of picoseconds, and the resulting rise time is around 1 ns, while the typical recovery time is in the order of tents of nanoseconds [39]. The high time resolution of a SiPM allows several applications, including time of flight measurements in positron emission tomography (TOF-PET).

SiPMs present similarities with photomultiplier tubes such as the magnitude of the gain (10^6) and the high photon detection efficiency; however, SiPMs have some distinct advantages. The operational bias voltage of a SiPM is between 30 and 100 V, while a PMT requires around 1000 V [21]; therefore, a SiPM requires lower power, allowing the realization of compact, multi-channel readout systems [40]. Moreover, SiPMs present better long-term stability and slower aging compared to PMTs [40]. Most notably, SiPMs are insensitive to magnetic fields, and may be used inside magnetic resonance imaging (MRI) scanners, i.e., hybrid PET-MRI machines [41].

On the other hand, SiPMs also present some drawbacks compared to PMTs, like dark count rate (DCR), optical crosstalk and after-pulsing processes. Dark counts are the pulses observed in a device in the absence of light, and they are due to thermal processes occurring in the depletion region of the photodiode. The DCR increases with bias voltage and temperature. In applications where hundreds of photons are detected, the DCR may be neglected, but for single photon measurements it must be corrected for. Optical crosstalk occurs when a primary discharge (avalanche) in a microcell triggers secondary discharges in one or more adjacent microcells. The secondary discharge may be nearly simultaneous with the primary one (direct or prompt crosstalk) or delayed by several tens of nanoseconds (delayed crosstalk). If not corrected for, crosstalk makes the output signal higher than that due to the incident light. After-pulsing processes are caused by the release of signal carriers trapped in silicon defects during the avalanche phenomenon: the trapped carriers are released during the recovery phase, producing a secondary pulse in the output signal [16]. Like a photomultiplier tube, a SiPM can operate in two distinct modes: continuous wave and photon counting. In continuous wave mode, the output pulses are neither detected nor counted individually; instead, an analog output current is recorded. In photon counting mode, the individual pulses are either counted (digital photon counting) or integrated to yield the charge released in the Geiger discharge (analog photon counting). The choice of operation mode depends, among other factors, on the frequency and duration of the output pulses. If the pulses are frequent and overlapping, the continuous wave mode is appropriate. If the pulses are distinguishable, then photon counting — analog or digital — is preferable.

A recent development of the SiPM technology was the introduction of the digital SiPM (dSiPM). In dSiPMs, photons are counted as digital signals using an electronics cell for each SPAD, containing active quenching, one bit memory and recharge circuits (figure 2). These new devices are less sensitive to external electronic noise and temperature variations, and they require a simpler readout front-end [42].

The performance of SiPMs is affected by damage caused by ionizing radiation: the main effect induced by exposure to ionizing radiation is an increase in DCR. As explained earlier, the increase in DCR is more of a concern for single photon measurements, while it may be usually neglected for high-intensity light measurements. Therefore, irradiated SiPMs must be accurately characterized in terms of DCR and other parameters [43]. In dSiPMs, the prevalent damage occurs in the SPAD and not in the integrated electronics. If a cell in a dSiPM is damaged by radiation, it can be individually deactivated to limit the effect on the performance of the device [44].

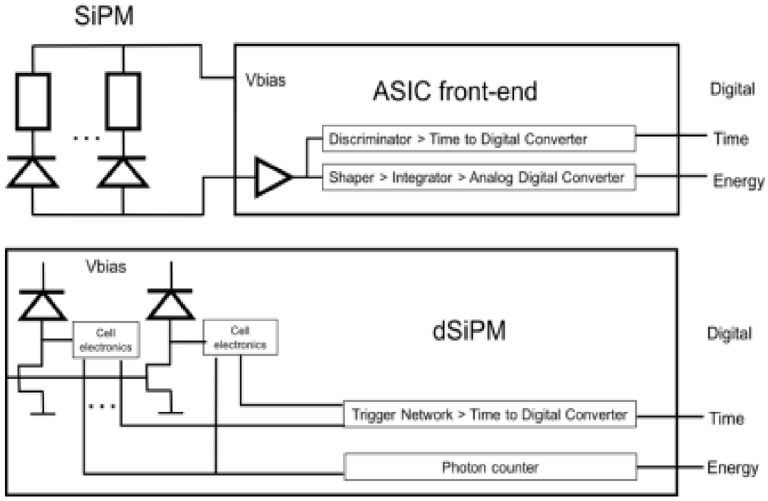

Figure 2. Comparison between SiPM and dSiPM electronic circuits.

3. SILICON PHOTOMULTIPLIER APPLICATIONS

The selected applications described in this review are divided into two categories: optical biosensors and radiation detectors. The first category illustrates the full potential of SiPMs in applications that usually require the highest radiant sensitivity and miniaturization down to the micrometer scale. On the other hand, in radiation detection, when micrometric dimensions are not required, characteristics such as ultra-fast rise and fall times, as well insensitivity to magnetic fields offer SiPMs a significant advantage over conventional PMTs.

3.1 Optical Biosensors

A biosensor typically integrates different technologies such as fluidics, electronics, separation technology, and biological subsystems applied to a biological system [1, 45]. If light is the physical quantity transduced by the electronic component of the device, then we have an optical biosensor [46]. A SiPM can be integrated in a biosensor serving as the optical transducer and detecting small changes in absorbance, luminescence, polarization, or refractive index between reactants and products of a biological process [47, 48].

Bio-luminescence and light scattering are optical phenomena used by biosensors that have proven most effective in the field of bioimaging research [49, 50]; on the other hand, the collection of photoluminescence is very difficult due its extremely low intensity, typically in the order of a micro-lux [51, 52]. Consequently, the challenge associated with collecting these optical signals with sufficient signal-to-noise ratio is enormous. Several studies have shown that using a SiPM as a readout device provides an adequate performance [53, 54] combined with the micrometric dimensions that are also required for biosensors [31, 55]. Indeed, a recent study revealed that a simple, low cost and portable optical system, with a SiPM optical transducer, is able to detect fluorophore concentrations in the order of 10^{-12} M [32].

It is expected that promising applications will emerge in biosensing research by using SiPMs as optical transducers instead of the conventional photodetectors. Moreover, with recent advances, such as small size batteries providing bias to the SiPM [56] or by using the human body heat for powering wearable devices [57], we may expect even more developments from optical biosensors combined with SiPM.

A phenomenon supporting our expectation that SiPM will excel in biosensing applications is laser speckle [58]. Laser speckle contrast imaging (LASCA) is a very useful medical imaging technique [59-62] utilizing a coherent light source to irradiate a sample, usually some biological tissue. Light interactions will result in backscattered radiation, which can be imaged on a screen in order to detect variations of interference patterns over time due to movements in the object. Sophisticated LASCA systems, such as Pericam PSI (Järfälla, Sweden), use a charge-coupled device (CCD) to collect the signal and create an image from backscattered radiation, which consists of dark and bright areas, i.e. low and high levels of scattered light intensity (speckle). Recent research [63] has shown that a SiPM with an area of 4 x 4 mm^2 with a cell-pitch of 25 µm, and a spectral range from near ultra-violet to visible, can be used to record the output intensity interferogram with a ~20 pW low power incident beam and with a measurement time of approximately 500 µs. The combination of LASCA with contrast imaging, suggests that in the near future the expensive CCDs used in current systems may be replaced by inexpensive, robust SiPMs insensitive to magnetic interference.

3.2 Radiation Detectors

The first SiPM application in nuclear radiation measurements was in scintillation detectors [64], and this is still the main application nowadays [65, 66]. In short, a scintillator is an organic or inorganic compound [67, 68] that absorbs ionizing radiation and emits light proportionally to the amount of absorbed energy. Using SiPMs optically coupled with an inorganic scintillator, such as CsI:Tl, it is possible to create a gamma spectroscopy system with the same energy resolution characteristics as PMT-based systems [69]. SiPMs are used in various high-energy physics measurements, such as calorimetry. For this reason, some studies have analyzed the damage threshold of the SiPM exposed to high-energy gamma rays up to 6.1 MeV [70, 71], revealing that these photodetectors, besides the characteristics described in section 2, also have a higher damage threshold energy, making them even more suitable for this type of research.

Now that their accuracy and energy resolution have been verified, SiPMs are starting to replace PMTs in various fields of application of scintillation detectors, such as environmental radiation monitoring [72] and even in portable fast detectors for radon [73]. Portable SiPM-based dosimeters have also been described for measurements of ambient dose equivalent $H^*(10)$ with CsI (Tl) scintillators, which require a correction for their lack of tissue equivalence [74]. SiPM photodetectors have also been tried for neutron detection since conventional area monitors such as the "Rem counters" are often complex, expensive and bulky. It is possible to overcome those limitations using a SiPM combined with a Lil (Eu) scintillator [75]. Recent applications have shown that it possible to build an ultra-thin (1.5 mm) neutron detector with a SiPM and a WLS coupled to a ^{6}LiF: ZnS (Ag) scintillator and using pulse shape discrimination (PSD) for an effective gamma ray rejection [76].

The amply mentioned compactness, robustness and low bias voltage of SiPMs are also ideal for the development of personal radiation sensors, also because SiPMs are an affordable choice when devices must be issued in large numbers. Even for first responders involved in homeland security scenarios, SiPMs are well-suited since properties such as high sensitivity, mechanical robustness and pocket-size dimensions are essential. The SENTIRAD, based on SiPMs and CsI (Tl), is an example of similar successful applications [77].

The potential of SiPMs has also been examined for medical radiation detection applications. Using SiPMs coupled with scintillating optical fibers, measurements of low dose rates of X-rays from generators working at anode currents of a few microamperes; in this application, the drawbacks from DCR are overcome using two SiPMs in coincidence mode [78]. Beta particle detection has been examined in relation to the development of intraoperative or endovascular radiation probes mapping the differential uptake of positron emitting tracers to localize tumor tissue or damaged cardiac tissue [79, 80]. Indeed, detecting the exact position of a tumor target is fundamental in cancer therapy in order to improve the efficiency of cancer removal and to avoid relapse of the disease. Using a probe for beta particle emitting radiotracers was found to increase the spatial resolution by a factor of four in the localization of the tumor, compared to a gamma-ray sensitive probe [81]. SiPMs are arguably the best solution for the development of these intraoperative beta particle probes since they are small and require a low-voltage bias [79].

SiPMs have also been examined for endovascular and intramyocardial probes. An upcoming development is the design of an integrated theranostic system that utilizes molecularly-targeted radiotracers to achieve localized intramyocardial drug delivery. The goal in this case is to create a steerable endovascular catheter-based device that identifies injured myocardium via endocardial detection of systemically delivered beta-emitting radiotracers, The device utilizes the molecular signal to guide delivery of therapeutics to the injured tissue via direct intramyocardial injection [80]. Such a probe was initially designed with scintillators connected to optical fibers, whereas the use of SiPMs is now recognized to offer significant advantages.

Current marketing of SiPMs by several manufacturing companies, such as Hamamatsu (Hamamatsu City, Japan), SensL (Cork, Ireland), AdvanSid (Trento, Italy), and Ketek (Munich, Germany), leads to continuous, rapid improvements in the performance of these photodetectors. A recent and extensive comparative investigation [82] documented that commercial SiPMs all have similar PDEs, while pulse shape, DCR, and transit time delay present significant differences between different models. The close synergy between research and industry has led to a wide use of SiPMs in nuclear medicine, in particular in equipment such as positron emission tomography (PET) and single-photon emission tomography (SPECT) [83]. In these applications, SiPMs are built as large area detectors with multichannel data acquisition as well a dedicated front-end preserving the quality of signals acquired over a multitude of channels [42, 84]. Thanks to their insensitivity to magnetic interference, SiPMs can be utilized within strong magnetic fields such as those up to 7 T used in the most advanced magnetic resonance imaging (MRI) devices [85, 86]. Another recent application which brings SiPMs to nuclear medicine is single-photon emission computed tomography (SPECT) combined with MRI, called SPECT/MRI [87]. The fast rise and decay times of SiPMs also allow the adoption of these photodetectors in techniques requiring temporal resolutions in the order of 10^{-9} s, such as TOF-PET [88-90].

4. CONCLUSIONS AND PROSPECTS

The numerous appealing features of SiPMs are the reason for their wide acceptance and range of applications. These photodectors are compact and very powerful, capable of detecting low light intensities corresponding to a single photon. They are highly customizable, since the number of micro-cells can be chosen in relation to the specific application, e.g., in relation to the active area to be examined. Great opportunities are offered by their ability to detect light at low optical intensities with an efficiency comparable to PMTs combined with the insensitivity to magnetic fields typical of semiconductors: this feature has led to an entirely new field of medical imaging with "hybrid" system such as PET-MRI scanners. An important limitation of SiPMs is their vulnerability to ionizing radiation damage, which is especially relevant when high-energy neutrons or cosmic radiations are measured. [71, 91]. Fortunately, new possibilities, and greater tolerance of radiation damage, are offered by dSiPMs, which are already commercially available and are currently undergoing extensive validation studies.

Finally, truly exciting developments are at the horizon, such as the possibility of realizing endovascular and intramyocardial SiPM-based probes for an integrated theranostic system utilizing molecularly-targeted radiotracers to deliver localized intramyocardial therapies [80]. In addition, the field of radiation detection with luminescent materials stands to benefit greatly from the SiPM's ruggedness. For example, an OSL reader based on SiPMs will be an optimal solution for OSL-based dating in harsh environments [92-95]. A portable OSL reader based on PMTs has already been described [96], but it is not ideal for in field use. Likewise, another field in which a compact SiPM-based OSL reader will be precious is cosmic radiation dosimetry during space missions, in order to replace previous solutions based on thermoluminescence [97], which are much more power-consuming and do not provide the sensitivity and reproducibility of a fully optical read out.

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