

SINPHOS - SINGle PHOTon Spectrometer for biomedical application

S.Tudisco^{a,b}, L.Cosentino^a, G.Fallica^c, P.Finocchiaro^a, F.Musumeci^{a,b}, A.Scordino^{a,b}, D.Sanfilippo^c, G.Privitera^{a,b}, S.Privitera^{a,b}, H.Thienpont^d, M.Vervaeke^d, B.Volckaerts^d, P.Vynck^d.

^aINFN-Laboratori Nazionali del Sud, Via S.Sofia 44, I95123 Catania Italy

^bDMFCI -Università di Catania, Viale Andrea Doria 6 , 95125 Catania, Italy

^cST-Microelectronics, Stradale Primosole 50, I95100 Catania Italy

^dVrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium

In the last decades several experiments have clearly demonstrated that, once illuminated, all biological systems emit for some time a very weak flux of photons, called Delayed Luminescence (DL). Some recent results have shown the possibility of using the DL as a diagnostic tool in the field of optical biopsy or of multi-dimensional diagnostics. Following such indications we decided to start developing SINPHOS, a monolithic micro-device, capable of measuring simultaneously the time distribution and the spectrum of photons coming from a weak source. Two important innovative aspects will characterize this spectrometer: the optical part, realized by means of the Deep Lithography with Particles (DLP), and SPAD (Single Photon Avalanche Diode) detectors under development along with ST-Microelectronics.

1. INTRODUCTION

The role of an early recognition of pathologies, in order to start successful therapies, is nowadays more and more emphasized. Substantial efforts are currently being made towards the development of innovative techniques for early diagnosis. One of the promising techniques, especially for skin melanoma, is based on the use of optical diagnostic tools and on the potential new information provided by the light emitted, elastically or inelastically, by cells and tissues after suitable illumination. In this respect some groups used infrared spectrometry or spontaneous fluorescence in order to discriminate between normal and altered tissues [1,2,3]. Several investigations are based on imaging tools or on time resolved fluorescence measurements, in order to get diagnostic information [4,5,6]. These attempts however, although important and very promising, were not able to replace the traditional biopsy technique in its leading role as diagnostic reference. It is therefore important to search for more sophisticated detection procedures. An important candidate, from this point of view, is the Delayed Luminescence (DL).

In the last decade several papers have demonstrated that the DL is closely connected to the state of the biological systems, and therefore that is possible to use it as an indicator of such a state [7,8,9]. This phenomenon has been explained as due to the excitation and the following decay of soliton states, existing inside of nearly mono-dimensional polymeric chains that constitute the cytoskeleton [10]. More recently, preliminary measurements have been carried out [11] proving that there is a remarkable difference between the emission from cultures of normal and tumour human cells of the same density. In the last year we have investigated the DL of yeast cells [12], discovering that what is normally measured as integral DL consists of two parts with different time trends. In particular, the longer wavelength DL, likely extending up to the near infrared range, exhibits a time trend that in the millisecond scale is strongly affected by the cytoskeleton state.

All these experimental findings highlight the importance of building devices, with single photon detection capability, in order to measure DL up to ≈ 1000 nm. Such devices should be able to resolve

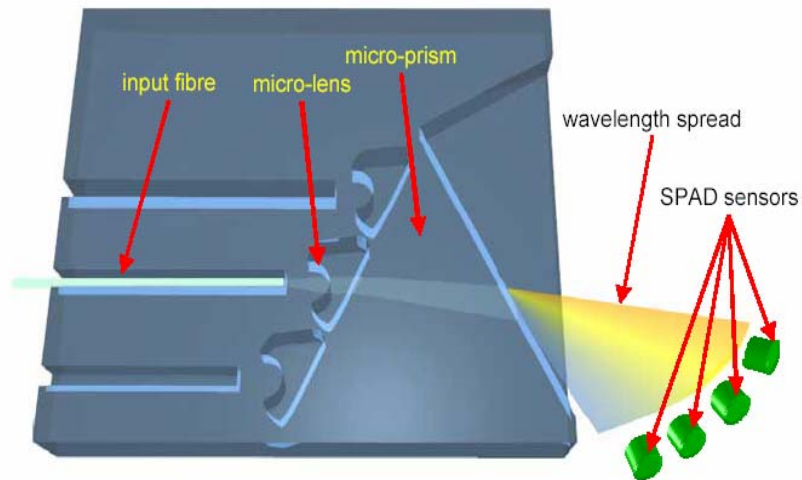


Fig. 1 Sketch of the prototype SINPHOS

the few detected photons both in time and in wavelength, and possibly obtain a matrix for imaging purpose. In this paper some preliminary results on the SINPHOS project are reported. The goal is to realize, using the DLP technique, a monolithic device capable of measuring at the same time the decay time distribution and the wavelength spectrum of photons coming from an isotropic source.

2. THE PRISM SPECTROGRAPH IN DLP TECHNIQUE

One of our major research topics is the development of micro-optical components made from Poly-Methyl-Methacrylate (PMMA), by exploiting a promising technique, named Deep Lithography with Particles (DLP), mainly pursued in the field of optical communications. Presently it is considered as a unique and powerful rapid-prototyping tool for the fabrication of monolithic refractive micro-optical elements and micro-mechanical structures [13]. The fabrication process consists of the irradiation of a PMMA sample, by means of a particle accelerator, followed by a chemical treatment for its development. The technique relies on the fact that irradiating linear PMMA of high molecular weight results in the rupture of the long polymer chains. As a consequence the molecular weight of the material located in the irradiated zones is reduced and free

radicals are created, leading to large differences in material properties [14]. To accurately define the irradiated zones we use an ion-beam mask with a circular shaped aperture of 20-200 μm that is positioned in front of the PMMA sample; then we move the sample in front of the particle beam, by means of a high precision translation stage, according to a predefined-design pattern [15]. Due to the higher solubility of the irradiated zones with respect to the bulk material, these irradiated domains can be selectively etched using a special solvent.

3. THE SPAD - SINGLE PHOTON AVALANCHE DETECTOR

SPADs are p-n junctions operating at a voltage slightly above the breakdown V_B . At this bias, the electric field is so high that a single charge carrier injected into the depletion layer can trigger a self-sustaining avalanche. The current swiftly rises with nanosecond or subnanosecond rise time to a macroscopic steady level in the milliamperere range, which can be easily detected. If the primary carrier is photogenerated, the leading edge of the avalanche pulse marks the arrival time of the detected photon. After the avalanche is triggered, the current keeps flowing until the avalanche is quenched by lowering the bias voltage down to V_B or below. The bias voltage has then to be restored in order to allow the detection of further photons [16]. This operation requires a suitable circuit, usually referred to as

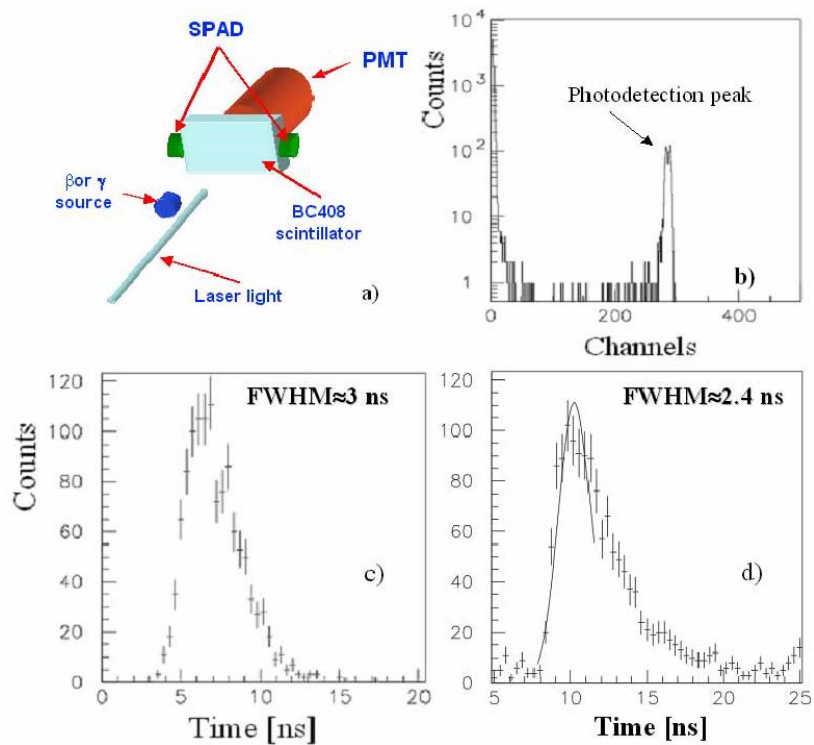


Fig. 2 (a) Sketch of the experimental set-up. (b) Amplitude spectrum of a SPAD illuminated by means of a pulsed laser. (c) Time spectrum obtained under the same conditions between the triggering PMT and a SPAD. (d) Time spectrum between the triggering PMT and a SPAD with a gamma source in front of the scintillator.

quenching circuit (QC), which can be active (AQC) or passive (PCQ). Here we show the results of a few tests performed with PQC. Fig.2a shows a sketch of the experimental set-up, where we used two SPADs with active area diameter of 50 μm . Fig.2b shows the amplitude spectrum of a SPAD illuminated by means of a pulsed laser hitting the plastic scintillator, which in this case was only acting as light diffuser. This spectrum, triggered by a signal in the PMT in order to make sure we were dealing with real photodetection events, has basically two components: the first one, huge and narrow around zero, comes from PMT trigger signals not correlated with any photon detection in the SPAD, in agreement with the geometrical acceptance constraints; the second one, the sharp peak indicated as photodetection peak, comes from real photons detected in the SPAD. In fig.2c we show the time spectrum obtained under the same conditions. It has

an FWHM of $\approx 3\text{ns}$, that reflects the intrinsic time spread of the input laser pulse used. In fig.2d, finally, we show the time spectrum between the triggering PMT and the SPAD collected when the light source was the BC408 plastic scintillator exposed to a gamma source. The width of the distribution is fully compatible with the decay constant of the employed scintillator (2.1 ns), and the most probable number of photons detected in the SPAD is one, as the counting rate with respect to the PMT was very low and in no case we appreciated coincidences between the two SPADs.

4. CONCLUSIONS

SPADs seem to be very promising devices for photon detection, as in the near future they are also going to be integrated into arrays. Moreover, their

possible coupling to micro optical component arrays, produced via DLP, opens up a wide field of innovative applications in basic research, like nuclear physics, as well as in applied research, like medical diagnostics, optoelectronics, telemetry, astronomy, etc. In the near future we plan to assemble the SINPHOS spectrometer and start testing it under realistic conditions.

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