IL NUOVO CIMENTO **45 C** (2022) 160
DOI 10.1393/ncc/i2022-22160-2

COMMUNICATIONS: SIF Congress 2021

Time-domain diffuse optics can break the pile-up bottleneck thanks to high light harvesting single-photon detectors

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received 29 January 2022

Summary. — Thanks to the use of solid-state detectors such as silicon photomultipliers, time-domain diffuse optics (TD-DO) instruments are moving from bulky to compact forms, while allowing increased light harvesting capabilities, high throughput, and improved signal-to-noise ratio acquisitions. Very large area single-photon detection modules have been created within the SP-LADOS project (supported by the EU ATTRACT project), improving light harvesting capabilities and allowing the possibility of pushing towards the ultimate limits of TD-DO. However, to fully leverage the potential of this cutting-edge detector, there is a need to move beyond the limitations of single photon statistics. Thus, the unknown operating regime of the very high count rates must be investigated. Indeed, the use of very large count-rates causes a considerable signal distortion, which must be corrected. In this study, we show the large-area SiPM modules' improved sensitivity, as well as preliminary in-silico results on the advantages of operating in a high-count rate environment.

1. – Introduction

Time-domain (TD) diffuse optics (DO) is a non-invasive optical technique for the analysis of diffusive media (*e.g.*, biological tissues), with applications ranging from neurology to oncology [1]. TD-DO relies on the injection of laser pulses (∼100 ps duration) and on the collection of the distribution of times of flight (DTOF) of the re-emitted photons at a distance ρ from the injection point, using the time-correlated single-photon counting (TCSPC) technique. The main features of the TD approach are: i) the ability to separate the absorption coefficient (μ_a) from the reduced scattering coefficient (μ_s') using a single source-detector pair; and, in reflectance geometry, ii) the ability to encode photons' mean penetration depth in their arrival time. Research has made significant efforts in the last decade to accelerate technological advancements for pulsed laser sources, single-photon detectors, and timing electronics enabling the transition from bulky and expensive systems to compact, low-cost, and even wearable cutting-edge devices [2] while also improving the performances to move towards the ultimate limits of TD-DO.

With regards to single-photon detectors, silicon photomultipliers (SiPMs) have been successfully introduced in diffuse optics [2]. Indeed, they have all the advantages of solid-state detectors in addition to a high light harvesting capability due to both a wide sensitive area (few mm^2) and to the possibility of being put in contact with the sample, thereby maximizing the numerical aperture. To push the light harvesting capability even further, SiPMs tailored for TD-DO with extremely large collecting areas (*i.e.*, 36 and $100\,mm^2$) have been developed within the SP-LADOS project (funded by the EU through the ATTRACT program). To fully leverage the enhanced light harvesting capability of these new SiPM modules and prevent signal attenuation (required to remain in single-photon statistics, where the count rate - CR - is limited to $\sim$ 1–5% of the laser pulse rate), an extremely high throughput operating regime has to be adopted, provided that significant pile-up distortion is properly corrected [3].

In the present study, we assess the capability of these new large-area detectors in detecting optical inhomogeneities adopting figures of merit (FoMs) defined in a well-accepted protocol for the performance assessment of DO systems (*i.e.*, the nEUROPt protocol) [4]. Then, preliminary simulation results showing the possibility of working safely at an extremely high count rate regime with large area detectors will be shown.

2. – Methods

2·1. *Experimental setup.* – The experimental setup is similar to the one described in ref. [5]. The two detectors proposed are the $36\,mm^2$ and the $100\,mm^2$ SiPM modules (details can be found in ref. [6]) realized by FBK. To determine the system's maximum penetration depth, we employ a liquid phantom made of calibrated amounts of water, intralipid (giving the scattering qualities), and black Indian ink (associated with absorption) to achieve $\mu_a = 0.1$ cm^{-1} and $\mu_s' = 10\,cm^{-1}$ at 670 nm. We use a totally absorbing movable optical perturbation, that induces a perturbation $\Delta\mu_a = 0.17$ cm^{-1} over a volume of $1\,cm^3$. The perturbation (placed at half of the source-detector distance) was moved in depth from 2.5 mm below the surface of the phantom up to 50 mm. For each position, we record 10 acquisitions of 1 s each. A standard CR fulfilling the single-photon statistics (typically 1 Mcps above the dark count rate) was set by adjusting a variable optical attenuator for all the measurements in the unperturbed case and the attenuation was not changed in the perturbed one. Both SiPM modules were tested at ρ of 9 cm, while only the $36\,mm^2$ was used at a ρ of 3 cm. Indeed, at $\rho = 3$ cm, the use of the 100 mm^2 module compared to the 36 mm^2 one will result in demoted performances for two reasons: the strong attenuation needed (the signal has to be attenuated already with the 36 mm^2 one) and the the worst IRF (*i.e.*, large full width at half maximum) [6].

2·2. *Simulations.* – An 8th-order perturbative solution of the radiative transfer equation under the diffusion approximation was used to model the effect of a localized absorption perturbation [7]. With the goal to derive preliminary insights about this new working regime, such theoretical DTOFs have been generated using a δ-Dirac Instrument Response Function (IRF), to evaluate performances of an ideal system. The input parameters considered are: a laser frequency of 40 MHz, a TCSPC channel width of 5 ps, a ρ of 3 cm and background medium with refractive index of 1.55. It is worth noting that, with respect to the experimental case, a shorter ρ was chosen to enable a high throughput thanks to a larger backscattered signal intensity. We consider a homogeneous

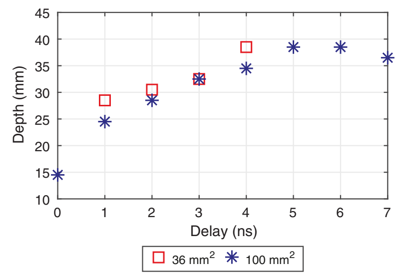

Fig. 1. – Maximum visible depths for the two modules: $36\,\text{mm}^2$ (red squares) and $100\,\text{mm}^2$ (blue asterisk).

bulk with $\mu_a = 0.1$ cm^{-1} and $\mu_s' = 10\,\text{cm}^{-1}$, embedding an absorbing perturbation of $\Delta\mu_a = 0.17$ cm^{-1} within a cubic volume of $1\,\text{cm}^3$. The perturbation was placed at half of the ρ and moved at 20 different depths (from 2.5 to 50 mm at steps of 2.5 mm). To add both pile-up distortion [3] (*i.e.*, distortion caused by the timing hardware's inability to process more than one photon event per excitation cycle) and Poisson noise to these theoretical DTOFs, we use a MATLAB code based on random Poisson launches. This code takes as inputs the simulated DTOFs considered as probability distributions and distorts them, imitating what currently occurs in real measurements. As a correction procedure we use a simple and effective algorithm proposed by Coates [3], which does not rely on previous knowledge of the input curve and corrects the current channel according to the integral of counts recorded in the previous ones. We considered 4 different CRs (values after the pile-up correction), one within and three well beyond single-photon statistics: 1.3, 40.0, 71.1, 400.0 Mcps (equivalent to before-correction values of 1.2, 25.3, 33.2 and 40.0 Mcps). For each CR, we generate 10 repetitions with acquisition time of 1 s in order to evaluate FoMs as stated in the nEUROPt protocol.

2·3. *Figures of merit.* – To evaluate the results obtained through measurements and simulations, we use conventional FoMs (contrast —C— and contrast-to-noise ratio —CNR—) from the sensitivity test of the nEUROPt protocol to determine the system's capability to detect a localized absorption change. In further detail, the contrast is a measure of the perturbation's effect on photon counts, while CNR evaluates how this change in photon count relates to the measurement's intrinsic noise. For the calculation, C and CNR have been evaluated within time-gates (*i.e.*, portion of the DTOF curves). For both simulations and measurements, the width of the gates were set to 1 ns, while their delay (*i.e.*, position of the gate start) is referred to the peak of the IRF.

3. – Results and discussion

Figure 1 shows the maximum penetration depth reached by the two large-active area modules, at varying gate delays. It was computed as the latest depth of the perturbation such that C $\geq$ 1% and CNR $\geq$ 1. These two conditions are usually considered as thresholds for the visibility of the perturbation within biological tissues. It is possible to see that both modules can reach depths of up to 37.5 mm, that is in line with state-of-the-art instruments based on a more complex detection approach (*e.g.*, SiPM working enabled in time-gating [8]). On the other hand, even if the $100\,\text{mm}^2$ allows reaching later delays than the $36\,\text{mm}^2$, it shows similar depth sensitivity, probably due to its worst IRF shape.

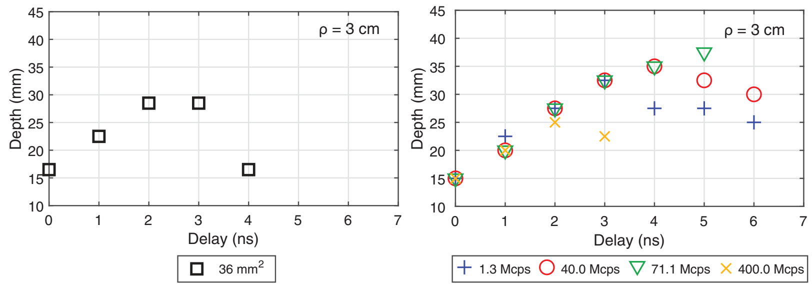

Fig. 2. – At $\rho = 3\,\mathrm{cm}$, measured (left) and simulated (right) maximum depth reached at varying gate delay, with the $36\,\mathrm{mm}^2$ and with the ideal system, respectively. Simulations are evaluated at different CRs.

Figure 2 represents the maximum penetration depths at different gate delays, obtained with the $36\,\mathrm{mm}^2$ SiPM module in single-photon statistics (left) and simulations at different CRs (right) for $\rho = 3\,\mathrm{cm}$. Thanks to the high throughput regime, we can outperform the penetration depths achieved at traditional CRs. In the ideal case (*i.e.*, a δ Dirac IRF), when pile-up correction is present, simulations show that perturbations can be seen up to 35.0 and 37.5 mm at 40.0 and 71.1 Mcps, respectively. Indeed, the possibility of using later delays, enabled by the increase in the CR, allows one to analyse photons that go further into the sample, thus improving the penetration depth.

4. – Conclusions

Working at a very high count-rate is feasible if correction procedures are implemented, opening up new approaches to TD-DO measurements. Thus, the penetration depth can be improved, using the whole light harvesting capability of large area detectors and a small source detector distance to keep a better spatial resolution and enhanced contrast [1]. Interesting future applications would be the experimental validation of such large area detector in a high throughput regime with both on-phantom and *in vivo* measurements.

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This research received funding from the ATTRACT project funded by EU under grant agreement no 777222. *Competing interests:* DC and ADM are co-funders of PIONIRS s.r.l., the other authors declare no competing interests.

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