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Time-Domain Diffuse Optics Beyond Pile-Up Limits: A Simulation Study Based on Relevant Figures of Merit

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Abstract: Large-area detectors for time-domain diffuse optics are increasingly available, with enormous gain in collected light intensity. Pile-up distortion is nowadays the main limit, here studied to anticipate the possibility of a new working modality.

1. Introduction

Researchers are becoming increasingly interested in non-invasive techniques to probe highly scattering media (e.g., biological tissue). Diffuse Optics (DO) can be an effective tool to employ since it relies on injecting light and collecting re-emitted photons at a specific distance [1]. Time Domain (TD) DO method is based on the injection of picosecond laser pulses in the sample and on the reconstruction of the distribution of time-of-flight (DTOF) of re-emitted photons (with time-correlated single-photon counting technique -TCSPC-). Thus, TD-DO allows to encode in the photon arrival time the mean depth probed and to disentangle absorption from scattering contributions [1]. For this reason, TD-DO systems offer high informative content. However, scattering and absorption phenomena in the medium strongly decrease the amount of the propagating photons, and this mainly affects late photons, which carry informative content about the deeper region. Therefore, it is crucial to have a detection chain characterized by high collection efficiency, able to optimize the detection of such weak late signal.

In the last five years, TD-DO instruments underwent impressive improvements, passing from bulky and expensive systems to compact, low-cost and sometimes even wearable devices [2]. This has been possible in part thanks to the use of silicon-photomultipliers (SiPMs) that are compact and rugged microelectronics detectors, characterized by large light harvesting capability [3]. Moreover, high-speed time-to-digital converters, capable to sustain count rates up to hundreds of millions of counts per second (cps), have been recently developed [1]. Thus, state-of-the-art technologies allow large amount of useful signal and throughput for TD-DO applications, as already partially exploited in a previous work [4]. Nowadays the main bottleneck is therefore the so called "single-photon statistics". Indeed, only one photon per excitation cycle can be correctly processed by traditional TCSPC detection chains. When more than one photon impinges on detector, the "pile-up effect" distorts DTOF shape. In some conditions, this distortion can be corrected using specific correction algorithms (e.g., [5]). While this has been already exploited in different applications like the measurement of fluorescence decays [6] or laser ranging [7], to the best of our knowledge, this possibility has not yet been systematically investigated in TD-DO.

Here we show a comprehensive in-silico evaluation of the possibility to properly correct the pile-up distortion in the recovery of absorption and scattering coefficients in homogenous media and in the detection of localized inhomogeneity buried in depth within scattering medium. To objectively assess this, we adopt the methodology and the figures of merits (FoMs) introduced by two internationally-agreed protocols for the performance assessment of diffuse optics instruments: MEDPHOT [8] and nEUROPt [9] protocols.

2. Material and methods

2.1. Forward simulations

Simulations are conducted using time-resolved reflectance waveforms derived under the diffusion approximation of the radiative transfer equation, for semi-infinite medium either homogeneous or embedding a localized absorbing perturbation for MEDPHOT and nEUROPt implementation, respectively [10]. To simulate performances achievable with a state-of-the-art TD-DO system based on SiPMs, we convolved the theoretical DTOF with the Instrument Response Function (IRF) of a typical SiPM detector (with a dark-count rate of 100 kcps).

As simulation conditions, we consider a laser repetition rate of 40 MHz, a channel width of the TCSPC board of 5 ps, a source-detector distance of 3 cm and a refractive index of the scattering medium of 1.55. Moreover, 7 count rate (CR) values (nominal values: 0.4, 1.3, 4.0, 12.6, 40.0, 126.0 and 400.0 Mcps) are employed. Such a wide set of theoretical photon rates ranges from 0.01 to 10 times the laser repetition rate, thus spanning CR both well-within and extremely-beyond single-photon statistics conditions. Time-resolved reflectance curves are simulated up to 12 ns.

For the generation of data for MEDPHOT protocol, we consider a set of homogeneous media characterized by 4 different reduced scattering coefficients – μ_s'– (from 5 to 20 cm^{-1} at step of 5 cm^{-1}), combined with 4 different

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absorption coefficients –μ_a– (from 0.1 to 0.4 cm^{-1} at step of 0.1 cm^{-1}). For the nEUROPt protocol we simulated curves using a perturbative model. We study a medium with $\mu_a = 0.1$ cm^{-1} and $\mu_s' = 10$ cm^{-1} embedding a 1 cm^3 cubic absorbing perturbation of 0.17 cm^{-1}, whose centre is set at a depth of 1 cm below the surface.

2.2. Pile-up distortion and correction

To simulate time-resolved reflectance curves affected by pile-up distortion, we use an algorithm (written in MATLAB) that gets the probability distribution and gives distorted curves by random Poisson launches. Therefore, this code is applied on previously forward simulated data. This procedure mimics what physically occurs when laser pulses excite a scattering medium and it naturally introduces Poisson noise thus simulating realistic measurements.

Finally, the pile-up correction is performed applying the Coates algorithm [5] to the distorted curves. This is a simple and easily implemented algorithm and it does not require any assumption like corrected curve knowledge or time bins uniformity.

2.3. Data analysis

As stated in the MEDPHOT protocol, accuracy is a FoM directly related to the capability of the TD system of recovering optical properties of homogenous medium. Thus, we fit both distorted and corrected time-resolved reflectance curves according to the same analytical model used for forward simulation (see Sect. 2.1) to recover the optical properties of the simulated homogeneous media. The fitting range spans from 20% of the peak on the rising edge down to 5% of the tail of the curves. Finally, the accuracy in the retrieval of absorption and reduced scattering coefficients is computed on both distorted and corrected curves.

As described in the nEUROPt protocol, contrast (C) and contrast-to-noise ratio (CNR) are two FoMs that evaluate the capability of a TD system to detect an absorption perturbation buried within a homogeneous medium. Contrast (C) is the relative difference in the number of counts due to the presence of the perturbation with respect to the homogenous state while CNR evaluates the robustness of the contrast against the intrinsic noise of the measurement. C and CNR are computed according to the nEUROPt protocol for corrected curves. Both C and CNR are evaluated inside different subsequent time gates of 500 ps width, starting from the position of the IRF peak. As an initial step, the CNR has been computed by supposing the presence of only Poisson noise (i.e., fluctuation in the number of counts equal to the square root of the number of counts) as simulation of repetitions (needed to compute the standard deviation as predicted in the nEUROPt protocol) takes several days.

3. Results, discussion, and conclusions

Table 1 reports the accuracy in the retrieval of μ_a and μ_s' for both distorted and corrected curves at different CRs (listed both as the absolute CR and as the percentage of the laser repetition rate). Since a traditional TCSPC chain can only detect the first photon per laser pulse, the expected experimental saturated CR is also reported (CRsat), which cannot overcome 40 Mcps. For high CRs without correction, the pile-up severely affects DTOFs, preventing the correct retrieval optical properties. However, our present study suggests that high CRs can be used when pile-up correction is applied. Errors smaller than 10% can be obtained at up to 400 Mcps of theoretical collection rate.

Fig. 1 shows C and CNR in subsequent gates (each of 500 ps width) starting from the position of the IRF peak for corrected curves. We display C only in gates that satisfy the condition CNR > 1. This figure highlights that with high throughput larger contrast values at late times can be obtained, thus increasing the detectability of deep perturbation if compared to the classical working condition (CR ~1-5%). It is worth noting that CNR is strongly overestimated as the correction algorithm increase the signal but it enhances strongly also the noise fluctuations, thus resulting into a super-Poissonian statistics. This FoM will be better evaluated in the future by computing the CNR through the standard deviation in the number of counts in the gates over different repetitions after pile-up correction.

Generally speaking, the idea of working beyond the pile-up limit is not novel in different applications, and preliminary explorative works have been done also in diffuse optics (see e.g., [4] and [11], where in the latter however the pile-up was used to increase the sensitivity to early photons, rather than late ones). Instead, to the best of our knowledge, this work represents the first comprehensive study based on relevant FoMs in the field for performance assessment of optical imagers. There are 2 main limitations here. First, only pure pile-up is considered, without other distortions due to secondary dead time effects like localized bumps related to the finite duration of the dead time itself [6], whose correction implies the use of more complex algorithms. Second, this study does not consider errors due to validity of the diffusion approximation as the same model is used to both generate DTOFs and to retrieve optical properties for MEDPHOT. However, this has been done in order to selectively highlight only the effect of pile-up.

Potentially, this work opens up to the possibility to intentionally work beyond traditional pile-up limits.

Table 1. Values of absorption/scattering accuracy (average and standard deviation computed among different optical properties) at varying CRs, for distorted and corrected curves.

CR (Mcps)	CR (%)	CRsat (Mcps)	ε_a (%)		ε_s (%)	
			Distorted	Corrected	Distorted	Corrected
0.4	1.0	0.4	-5.9 ± 2.1	-6.1 ± 2.1	-4.5 ± 1.2	-4.5 ± 1.1
1.3	3.2	1.3	1.5 ± 0.5	0.6 ± 0.6	0.3 ±0.6	0.4 ± 0.6
4.0	10.0	3.8	5.1 ± 0.5	2.4 ± 0.8	1.3 ± 0.6	1.6 ± 0.4
12.6	31.5	10.8	12.0 ± 1.7	2.8 ± 0.9	1.2 ± 1.8	1.9 ± 0.4
40.0	100.0	25.3	39.3 ± 6.7	2.9 ± 0.9	3.6 ± 4.4	2.0 ± 0.4
126.0	315.0	38.3	205.9 ± 39.0	3.0 ± 0.9	44.1 ± 8.5	2.1 ± 0.4
400.0	1000.0	40.0	1432.7 ± 662.2	7.5 ± 3.6	332.7 ± 160.6	5.4 ± 2.1

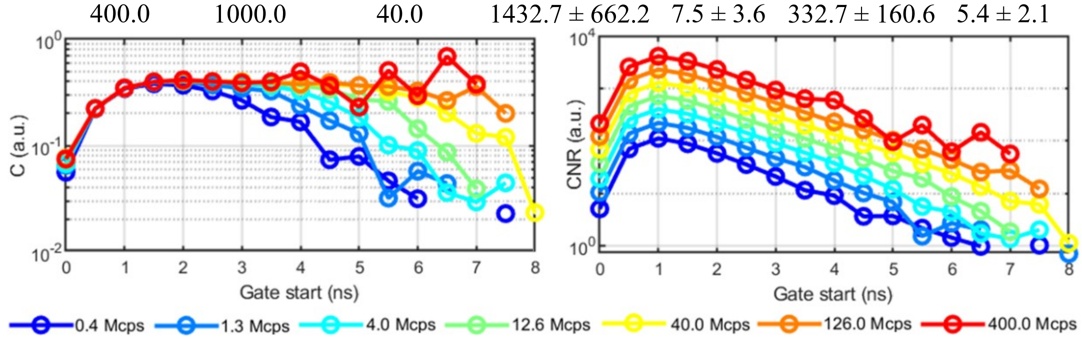

Fig. 1. Contrast (left) and contrast-to-nose ratio (right) for subsequent gates of 500 ps width at varying CRs.

For spectroscopy studies, this could lead to extremely fast measurements, thus both reducing the burden of a patient during an examination (i.e., compression of the breast during optical mammography) and to potentially follow fast optical dynamics with higher sampling rate. In the detection of localized perturbation instead, this regime can lead to an increased sensitivity to deep layers, similarly to what already achieved in the field through time-gating [12], but in this case feasible with less complex commercially available technologies [4].

In conclusion, we show that the main limitation caused by pile-up distortion, can be successfully corrected through analytics process. Thus, new working conditions well-beyond single-photon statistics can be implemented.

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