Biophotonics Congress: Biomedical Optics Congress 2018 (Microscopy/Translational/Brain/OTS)

Effects of Temporal Gating in Time Domain Diffuse Correlation Spectroscopy for Real Systems

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Abstract: We propose a model for time domain diffuse correlation spectroscopy which describes the effects of temporal gating for real systems, enabling accurate depth-resolved blood flow measurements. The model is validated with simulations and experiments.

OCIS codes: (170.5280) Photon migration; (170.6920) Time-resolved imaging.

1. Introduction

The aim of a time domain diffuse correlation spectroscopy (TD DCS) experiment is to extract a depth-resolved blood flow index (BFI) using time gated intensity autocorrelation functions [1]. TD DCS relies on the fact that, by selecting different photon time of flights (TOF) and thus different path lengths underwent by the photons in the tissue, scatterers motion is probed at different depths. It can be shown that, for a fixed photon path length s, the decay rate of the normalized electric field autocorrelation function ($g_1(\tau)$) is proportional to the blood flow (BF) in the tissue (quantified by the scatterers Brownian diffusion coefficient D_B) and to s [2].

Using an ideal system (ideal detector and input pulse with zero temporal width), it is possible to measure and select with accuracy the path lengths belonging to a certain temporal gate, and thus D_B can be estimated in a precise way from the $g_1(\tau)$ decay rate. On the other hand, a non-ideal system (finite detector temporal resolution and pulse width), in the case of software temporal gating based on the measured TOF, can be treated as linear time invariant (LTI) and therefore characterized only by its measured instrument response function (IRF). Since, in a real system, the IRF has a certain temporal width (i.e. it is not a delta of Dirac), perfect path length selection is not possible. Thus, the measured $g_1(\tau)$ will contain spurious contributions from path lengths in the proximity of the gate, possibly altering the measured autocorrelation functions and the corresponding BFI estimation, even in homogeneous media. In addition to this, for a medium with a non-homogeneous flow, photons with shorter path lengths can be wrongly assigned to gates corresponding to longer path lengths. Thus, the retrieved flow value for a given depth could be contaminated by the flow of different depths. For those reasons, a correct modelling of the effects arising from the IRF on TD DCS measurements is needed for accurate depth-resolved BF estimation.

2. Theory

In a TD DCS experiment, two different time scales are present: a short "pulse time" ($\sim ns$) that corresponds to the photon TOF (or photon path length s) within the tissue, and a longer "correlation time" τ ($\sim \mu s - ms$) that corresponds to the photon arrival time. Since the temporal resolution of the detection system is typically $< 1\ ns$, we can assume that the photon arrival times can be measured with sufficient accuracy. On the other hand, a non-ideal system will make some difference between the *real* path length s' underwent by the photon in the tissue and the *measured* path length s_0, i.e. the estimated path length that corresponds to a particular time-bin of the detection electronics [3].

In our approach, we model the spread in path lengths interpreting the IRF as the *conditional* probability to measure a photon in s_0, given that it underwent a path length s'. This probability, in the case of software gating, can be written as $P(s_0|s') = IRF(s_0 - s')$, where the IRF has been normalized to its area. The contribution to the autocorrelation function dg_1 for a measured single path s_0 of the real path s' can be written using the *joint* probability $P(s_0, s')$:

$$dg_1 = P(s_0, s') \exp(-ks'\tau)\, ds_0 ds' \tag{1}$$

where k is the autocorrelation decay rate per unit path length [1,2]. Note that the decay rate ks' depends on the number of scattering events along the path and thus on the real path length s'. We can expand the joint probability as $P(s_0, s') = IRF(s_0 - s')P(s')$. Integrating dg_1 over all the possible measured path lengths $s_0 \in [a, b]$ (where $[a, b]$ is the gating interval) and real path lengths $s' \in [0, \infty]$, the overall autocorrelation becomes:

$$g_1(\tau) = \int_0^\infty \theta(s')R_{th}(s')\exp(-ks'\tau)\,ds' \tag{2}$$

where we have defined the function $\theta(s')$, so-called effective gating function (EGF), as:

$$\theta(s') = \int_a^b IRF(s_0 - s')ds_0. \tag{3}$$

In Eq. (2), $P(s')$ has been estimated using the theoretical reflectance $R_{th}(s')$, and the product $\theta(s')R_{th}(s')$ is normalized such that $g_1(0) = 1$. The EGF (Eq. (3)) can be seen as the probability, for a photon with real path length s', to be mapped into the gate $[a, b]$. To this regard, Eq. (2) models the fact that also path lengths outside the gate can contribute to the autocorrelation function decay rate, due to the non-perfect path length selection caused by the IRF. Note that this effect cannot be explained simply by convolving $R_{th}(s')$ with the IRF.

3. Results

With the help of a Monte Carlo code developed at ICFO, we have studied the effects of system non-idealities on gated autocorrelation functions, adapting the method described in [4]. The timing inaccuracies of the system have been introduced in the simulation adding to the photon TOF a temporal shift obtained with random sampling of a IRF, and gating each photon according to the updated TOF. We simulated a semi-infinite homogenous medium, surrounded by air, with $(\mu_a, \mu'_s) = (0.023, 10)\ cm^{-1}$, source-detector (SD) separation $\rho = 1.2\ cm$, refractive index $n = 1.33$ and $D_B = 1 \cdot 10^{-8} cm^2/s$. We used a IRF obtained by deconvolving the expected reflectance R_{th} from the DTOF of a calibrated liquid phantom with the same optical properties measured by the setup described in [1]. Figure 1(a) shows the IRF, the simulated and theoretical reflectance (both before introducing system non-idealities) and the EGFs, computed using Eq. (3), for two gates: an early gate, from $-1\ ns$ to $0.9\ ns$, and a late gate, from $0.9\ ns$ to $5.9\ ns$. Figure 1(b) shows the simulated autocorrelation functions for the two gates, assuming a non-ideal system (i.e. considering the IRF), together with the uncorrected (U) and IRF-corrected (C) (i.e. using Eq. (2)) fits in which, in both cases, the theoretical reflectance has been used. Figure 1(c) shows the retrieved D_B from the non-ideal system autocorrelations, using the uncorrected and IRF-corrected fits, for the two gates and for ungated acquisition (i.e. collection of the whole DTOF curve, from $-1\ ns$ to $5.9\ ns$).

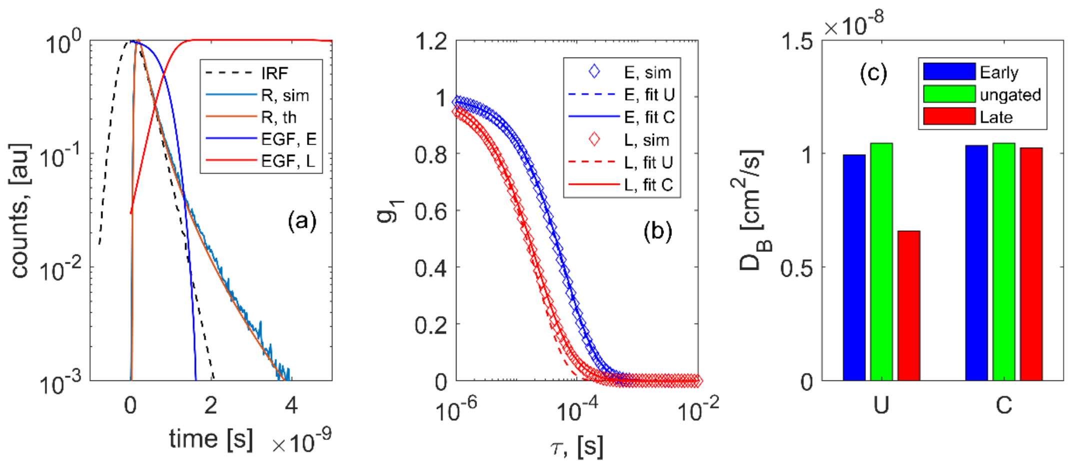

Figure 1: Homogenous system simulation. (a) IRF, simulated (sim) and theoretical (th) reflectance (R) for ideal system and computed EGFs for the early (E, blue) and the late (L, red) gates. (b) Simulated autocorrelation functions (sim, diamonds) for non-ideal system, together with the uncorrected and IRF-corrected fits (fit U and fit C), for the two gates. (c) Comparison between uncorrected (U) and IRF-corrected (C) retrieved values of D_B from the non-ideal system autocorrelations.

We have applied the theory to a real TD DCS measurement on a homogeneous liquid phantom, using the experimental setup and software correlation method described in [1]. The optical properties (μ_a, μ'_s), SD separation and gate limits were the same of the ones used in the simulation. We have measured the autocorrelations in $1\ s$ time windows for 9 minutes and averaged them. The Siegert relation [4] has been used to estimate g_1 from the measured intensity autocorrelation. Figure 2(a) shows the measured autocorrelation functions for the early and late gates, together with the uncorrected and IRF-corrected fits. The fits have been carried out from $\tau = 10^{-6}s$, to avoid after-pulsing effects, to the point where $g_1 = 0.7$ for the late gate, to fully reject photons with long decorrelation time (i.e. small path length), and $g_1 = 0.5$ for the early gate. Figure 2(b) shows, for the two gates, a comparison between the retrieved D_B using the uncorrected and IRF-corrected fits.

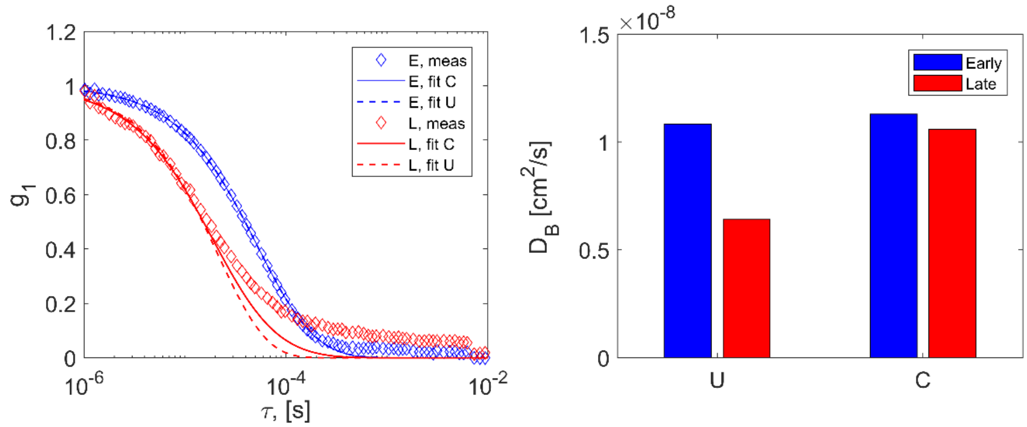

Figure 2: Homogeneous phantom experiment. (a) Measured autocorrelation functions (meas, diamonds) for the early (E, blue) and late (L, red) gates, together with their IRF-corrected (C, continuous lines) and uncorrected (U, dashed lines) fits. (b) Comparison between the retrieved D_B using the uncorrected model (U) or the IRF-corrected model (C), for the two gates.

4. Discussion and conclusion

With the use of Monte Carlo simulations, we have found that system non-idealities can distort gated autocorrelation functions significantly from their ideal behavior. Using a real IRF shape and broad gates, with a width of the order of ns, we have shown that the distortion is large for the late gate and negligible for the early gate and ungated acquisition. The distortion for the late gate is due to the confounding effect of the IRF, that make us assign to later times photons with smaller path length (i.e. smaller decay rate) interpreted by the uncorrected fit as a smaller D_B. This phenomenon is non-negligible due to the much higher number of early photons compared to later ones, and brings to an underestimation of the late gate D_B as large as a factor 2 (Figure 1(c)). Correcting for the IRF, by using Eq. (2) in the fit, we obtain for both gates a D_B very close to the expected one.

Then, we have passed to a real experiment, on a homogenous liquid phantom. The measured autocorrelation functions show a high value of the coherence parameter: $\beta = 0.30$ for the early gate and $\beta = 0.18$ for the late gate, thanks to the high coherence of the laser source. The proposed model permits high fit quality in the region of interest. Outside this region, noise or count rate fluctuations effect may be present. Using the uncorrected model, the late gate D_B is remarkably smaller than the early gate D_B, as in the case of simulations. The use of the proposed model permits to obtain a more constant BFI through the gates, expected due to the homogeneity of the system.

In this contribution, we proposed a model for accurate estimation of depth-resolved BFI with TD DCS measurements, and validated it with simulations and experiments. The use of this model can be applied also to *in-vivo* measurements, an application in which correct estimation of differences in superficial and deep BF is crucial.

Acknowledgements

The study was funded by Fundació CELLEX Barcelona, Ministerio de Economía y Competitividad/ FEDER (PHOTODEMENTIA, DPI2015-64358-C2-1-R), Instituto de Salud Carlos III / FEDER (MEDPHOTAGE, DTS16/00087), the "Severo Ochoa" Programme for Centres of Excellence in R&D (SEV-2015-0522), the Obra social "la Caixa" Foundation (LlumMedBcn), AGAUR-Generalitat (2014SGR-1555), and LASERLAB-EUROPE IV (654148). The research leading to these results has partially received funding from the European Union's Horizon 2020 research and innovation program under LUCA (688303H2020-ICT-2015), the EU Marie Curie Initial Training Network "OILTEBIA" (317526), and BabyLux (620996 CIP-ICT-PSP-2013-7). The LUCA project is an initiative of the Photonics Public Private Partnership.

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