

UC Irvine

UC Irvine Previously Published Works

Title

Optimization of the phase and modulation depth signal-to-noise ratio for near-infrared spectroscopy of the biological tissue

Permalink

<https://escholarship.org/uc/item/50w1s79r>

Journal

Proceedings of SPIE, 5474(29)

ISSN

0277-786X

Authors

Toronov, Vladislav Y
D'Amico, Enrico
Hueber, Dennis M
[et al.](#)

Publication Date

2004-08-20

DOI

10.1117/12.578960

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

Optimization of the Phase and Modulation Depth Signal-to-Noise ratio for Near-Infrared Spectroscopy of the Biological Tissue

Vladislav Toronov*^a, Enrico D'Amico^b, Dennis Hueber^c, Enrico Gratton^b,
Beniamino Barbieri^c, and Andrew Webb^a

^aBeckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, 405 N. Mathews Ave., Urbana, IL 61801

^bLaboratory for Fluorescence Dynamics, Department of Physics, University of Illinois at Urbana-Champaign, 1110 W. Green Street, Urbana, IL 61801-3080

^cISS Incorporated, 1602 Newton Drive, Champaign, IL 61822

ABSTRACT

Frequency-domain near-infrared spectroscopy and imaging offer significant advantages over the continuous-wave method in human brain applications. However, the drawback of existing instruments is a low signal-to-noise ratio for measured phase and modulation depth changes caused by cerebral activation. In this paper we show that in the case of the geometry specific for the activated area in the human brain, the SNR can be significantly improved by increasing the modulation frequency. We present the results of a study performed experimentally using a sub-nanosecond pulsed light source and a spherical absorbing object immersed in a highly scattering solution. We show that changes caused by the absorbing inhomogeneity in both phase and modulation depth increase with frequency and reach maximum values at frequencies between 400 and 1400 MHz, depending on the particular source-detector distance. We also show that for the semi-infinite geometry an increase of the modulation frequency from 100 to 500 MHz can increase the phase signal-to-noise ratio 2-3 times, and the modulation depth SNR up to 10 times.

Keywords: photon migration, imaging, brain, near-infrared

1. INTRODUCTION

Most of the current frequency-domain instruments operate at relatively low modulation frequencies around 100 MHz. Such a choice was determined not only by the higher cost of higher frequency electronics, but also by the lack of evidence that higher modulation frequencies result in significant signal-to-noise ratio (SNR) improvements. However, in the case of the non-homogeneous semi-infinite medium the CW method may be unacceptably inaccurate, and only the frequency-domain method provides reliable results. The goal of this paper is to examine the frequency dependence of the SNR of the frequency-domain method in a geometry topologically close to the geometry of the human head. For a geometry that is specific for a particular activated area in the human brain we study the dependence on the modulation frequency and source-detector distance of the changes caused by the absorbing inhomogeneity in two parameters: the phase and the modulation depth (MD), i.e., the ratio AC/DC, of the photon density wave. We present the results of a study performed experimentally using a sub-nanosecond pulsed light source and a spherical absorbing inhomogeneity immersed in a highly scattering solution.

We show that changes caused by the absorbing inhomogeneity in both phase and MD increase with frequency and reach their maximum values between 400 and 1400 MHz depending on the source-detector distance. Under the condition that the major source of the phase and modulation noise is the quantum shot noise, the standard deviations of both phase and modulation noise can be analytically related to the modulation frequency through their dependence on the mean modulation amplitude (AC). Using these relationships and experimental data we show that for the human head geometry the SNR, i.e. the ratio of the parameter change caused by the inhomogeneity to the standard deviation of the noise in this parameter, of the frequency-domain measurement can be significantly improved by increasing the modulation frequency.

2. THE NOISE MODEL

As discussed in [1, 2], the sources of noise in biomedical near-infrared spectro-imaging are physiological fluctuations unrelated to the changes being studied and instrumental noise. The principal instrumental noise components in the detected signal are the quantum fluctuations of the number of electrons in the detector current (caused by the combination of the quantum noise in the input light and internal fluctuations in the number of generated photoelectrons), and specific noise sources in the electronic circuits, such as the thermal noise, $1/f$ noise, etc. In the case where the illumination is sufficiently high, the electronic noise can be neglected compared to the quantum noise.

Our experience in using frequency domain instruments for biomedical spectroscopy and imaging shows that the electronic noise usually is not significant. Therefore, we limited our consideration of the instrument noise to the quantum shot noise. One can show that in this case the standard deviations of fluctuations in the modulation amplitude and in the phase are proportional to \sqrt{DC} and $\sqrt{DC/AC}$, respectively. Since the value of AC decreases with frequency, the phase noise increases. It can be also shown that the MD standard deviation is proportional to AC/DC . This means that the MD noise decreases with the frequency, so that the SNR may not decrease with frequency as rapidly as the phase SNR.

Apart from the quantum noise, *in-vivo* measurements are affected by physiological fluctuations, in particular by hemodynamic fluctuations, respiration and vasomotion. To investigate whether the quantum noise is the dominant source of noise affecting measurements using the frequency-domain instrument, we used frequency-domain data (modulation amplitudes and phases) acquired simultaneously at a number of source-detector distances ranging from 0.5 to 4 cm using an ISS tissue Oximeter (ISS, Champaign, IL) and a probe placed on the human forehead during one of our previous studies [3]. We have found that that, in spite of the other noise sources, quantum noise is the dominant source of noise in these *in vivo* frequency-domain measurements.

3. EXPERIMENTAL SETUP

The experimental set-up consisted of a Tsunami sapphire laser system (Spectra Physics) in a femtosecond configuration, a tank containing a Liposyn (Abbott Laboratories)/black India ink solution, a photomultiplier tube (PMT), a motorized positioning system, a single photon-counting board (Beckel & Hickel model SPC-830), and a photodiode which provides the synchronization signal to the SPC-830 board. The laser system provided a 780 nm pulsed light source at a 80 MHz repetition rate. Using a 400 μm multimode silica optical fiber the laser pulse was sent into the Liposyn India ink solution which simulated human brain in terms of the optical properties ($\mu'_s \approx 11 \text{ cm}^{-1}$, $\mu'_a \approx 0.1 \text{ cm}^{-1}$). The half-maximum width of the pulse at the fiber output was roughly 0.5 ns. The scattered light was collected at the surface of the medium at a variable distance from the source by means of a 3 mm fiber bundle and then sent to the PMT detector (Hamamatsu R5600P). The acquisition system was based on the SPC-830 single photon counting board which measured the detected photon arrival times and produced a time histogram representing the averaged received pulse. In order to model the brain activity, a 2 cm diameter spherical object with the same scattering but different absorbing properties ($\mu'_s \approx 11 \text{ cm}^{-1}$, $\mu'_a \approx 0.2 \text{ cm}^{-1}$) was placed at 15 mm depth between the source and detector.

The distance between the source and the detector fibers was set to 15, 20, 25, or 30 mm. In order to perform measurements with and without the object, the object was moved in and out of position using a computer-controlled step-moving system which allowed movement of the object along three orthogonal axes with an accuracy of up to 5 microns/step.

In order to avoid pulse distortions due to the pile-up effect it was important to maintain a sufficiently low light intensity at the detector input so that the photon counting rate did not exceed 100,000 photons per second. At source-detector distances of 25 and 30 mm the signal attenuation due to the medium was sufficient to fulfill this requirement, while at 15 and 20 mm distances additional attenuation by a neutral density filter was necessary. For this reason we were unable to maintain the same source power at all distances.

Each photon-counting measurement continued for 600 s. This time duration was selected to provide a sufficient ratio of the number of detected photons to the photon noise on the one hand, and to avoid significant non-stationary instabilities of the laser output occurring at large time intervals. In order to assess the signal variability each measurement was repeated four times under identical measuring conditions. The mean time shift between the averaged pulses

corresponding to different measurements was about 25 ps, which corresponds to the Fourier transform phase slope of about $1.5^\circ/\text{GHz}$.

4. RESULTS

Fig. 1 shows changes in phase caused by the absorbing inhomogeneity, and Fig. 2 shows changes in the modulation depth (AC/DC ratio). Different lines correspond to different source-detector distances. Changes in these parameters increase significantly with frequency and show maxima at frequencies from 600 to 1200 MHz (depending on the source-detector distance) in case of the phase change, and from 500 to 700 MHz in case of the ratio AC/DC. The error bars in Figs. 1 and 2 show average errors corresponding to measurements repeated four times. In Fig. 1 one can see that the phase error increases with frequency according to the model based on quantum noise. In case of the MD signal (Fig. 2) the error does not increase with frequency, which also agrees with the quantum noise model. The fact that the MD error in Fig. 2 does not generally decrease with frequency is due to the small long-term instabilities in the laser pulse, which slightly modify its shape during different photon-counting measurements. These instabilities are specific for the pulsed laser used in this study, but not for a well designed frequency-domain instruments utilizing intensity-modulated light sources.

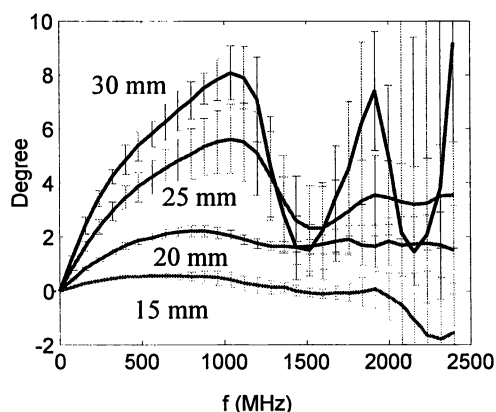


Fig. 1. Changes in the phase.

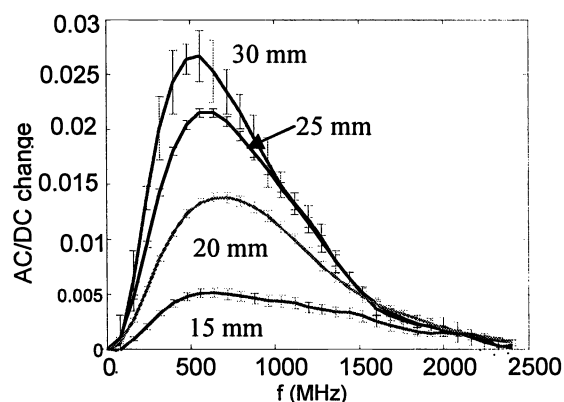


Fig. 2. Changes in the modulation depth.

Figs. 3 and 4 show the SNR frequency dependence computed using the experimental data presented in Figs. 1 and 2, and our analytical noise model.

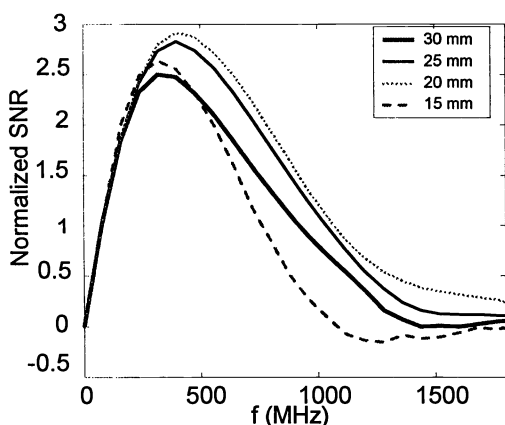


Fig. 3. Phase SNR as function of modulation frequency.

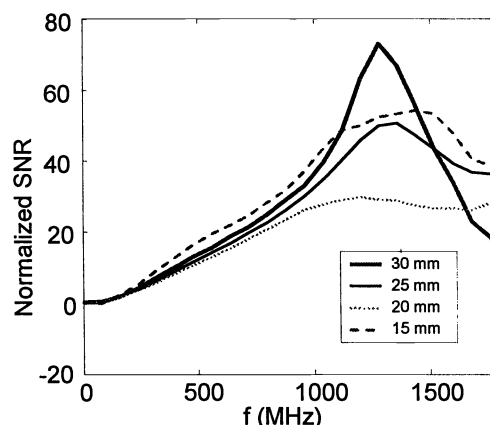


Fig. 4. MD SNR as function of modulation frequency.

Since the photon counting method required using additional light attenuation at smaller distances, we could not normalize the SNR obtained at different distances. Therefore, in both Figs. 3 and 4 all curves are normalized to the corresponding SNR values at 100 MHz. Thus, Figs. 3 and 4 do not compare the SNRs for signals at different distances, but rather show the SNR changes from their respective values at 100 MHz. Fig. 3 shows that, depending on the distance,

the phase SNR reaches its maximum in the range of 300-500 MHz. In this frequency range the improvement compared to 100 MHz is quite significant (2.5-3 times). According to Fig. 3 the maximum improvement is reached at source-detector distances of about 20-25 mm. At smaller distances the phase signal is too small, while at a larger distance the phase noise becomes too large.

The main difference between the phase and MD SNRs is that the phase SNR peaks between 300 and 500 MHz, while the AC/DC SNR grows monotonically up to approximately 1200 MHz. This happens because, in the case of the MD SNR, the values corresponding to the signal curves in Fig. 4 are divided by the AC values, which decline monotonically with frequency. It is interesting to note that in the range of 300-500 MHz where the phase SNR reaches maximum, the MD SNR at different distances increases about 5-10 times compared to its value at 100 MHz.

5. DISCUSSION

For the geometry topologically similar to the one of the human head we have found that the changes caused by an absorbing inhomogeneity to the modulation depth and phase of the photon density wave exhibit a non-monotonic dependence on the modulation frequency. The change in phase reaches maximum between 400 and 1400 MHz, and the MD change achieves its maximum value in the 500-600 MHz frequency range depending on the source-detector distance. Such a resonance-like dependence of signals caused by an inhomogeneity is specific for the situation when a relatively small object is immersed in a semi-infinite medium at a depth of about 15 mm, and was not found for the slab geometry [1]. The most important result of our study is that, for the specified geometry, the SNR of the frequency-domain instrument can be significantly improved by increasing the modulation frequency. The phase SNR can be increased 2-3 times compared to the value at 100 MHz, which is comparable with the improvement demonstrated for the slab geometry in [1]. The MD SNR can be theoretically increased more than 10 times, provided that the modulation frequency is sufficiently high. Current electronics allows modulation of light sources at frequencies up to 400-500 MHz with a modulation depth of more than 30 %. Therefore, the discussed significant SNR improvement is now achievable in practice.

We have also found that, for the specified geometry, both phase and MD SNR are optimized at source-detector distances of about 20-30 mm. Increasing source-detector distances to greater than 30 mm causes the phase SNR to decrease due to the higher noise, and the lower signal.

6. CONCLUSION

In phantom experiments with sub-nanosecond light pulses we have found that changes in the phase and modulation depth of a photon-density wave caused by local functional activation in human brain exhibit non-monotonic dependence on frequency, with a maximum value corresponding to frequencies between 400 and 1400 MHz depending on the source-detector distance. We have shown that the SNR for these changes can be very significantly improved compared to its value at 100 MHz by increasing the modulation frequency to 400-500 MHz.

ACKNOWLEDGEMENT

This work was supported by the NIH SBIR grant no. NS 38378-03, and by the NIH grant 1R01MH065429-01A2.

REFERENCES

1. D. A. Boas, M. A. OLeary, B. Chance, A. G. Yodh, "Detection and characterization of optical inhomogeneities with diffuse photon density waves: a signal-to-noise analysis", *Applied Optics* **36**, 75-92 (1997)
2. C. Yu, C. Mu, X. Intes, B. Chance, "Signal-to-noise analysis for detection sensitivity of small absorbing heterogeneity in turbid media with single-source and dual-interfering-source", *Optics Express* **9**, 212-224 (2001)
3. V. Toronov, A. Webb, J. H. Choi, M. Wolf, L. Safonova, U. Wolf, E. Gratton., *Optics Express* **9**, "Study of Local Cerebral Hemodynamic Fluctuations by Simultaneous Frequency-Domain near-infrared spectroscopy and fMRI", 417-427 (2001)

*toronov@uiuc.edu; phone: (217) 265-0283; fax (217) 244-0105