Exploring tissue dynamics by photon-density-wave fluctuation correlation spectroscopy

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Abstract

We propose photon-density-wave fluctuation correlation spectroscopy as a method to study the dynamics of tissue optical properties. Phantom measurements have shown that our frequency-domain instrument is appropriate to explore intensity, modulation and phase fluctuations in the frequency band from 0 to 125 Hz. Preliminary in vivo studies have revealed a rich optical dynamics in human tissues.

Keywords

(170.5270) Photon density waves; (170.6510) Spectroscopy, tissue diagnostics

1. Introduction

Many physiological processes (such as metabolism, hemodynamics and neuron activity) cause changes of tissue optical properties at the macroscopic level. Characteristic time and space scales of such changes can be about 10 ms and 1 mm, respectively. It was shown that the propagation of intensity-modulated light in tissues can be described in terms of photon-density waves [1]. A photon-density wave at a given point is characterized by its intensity, modulation amplitude and phase. A change in these parameters may be related to changes in the tissue absorption and scattering properties. We propose photon-density-wave fluctuation correlation spectroscopy (PDW-FCS) as a method to study the dynamics of tissue optical properties. One should distinguish photon density wave correlation spectroscopy from diffusing-wave spectroscopy (DWS) [2]. The latter relates fluctuations in the scattered electromagnetic field to the microscopic motion of light scatterers. The time and spatial scales of these field fluctuations are smaller than 0.1 ms and the light wavelength, respectively. Different time and spatial scales probed by PDW-FCS and DWS require different experimental approaches. Furthermore, PDW-FCS measures intensity (DC), modulation amplitude (AC) and phase fluctuations, while in a DWS experiment the acquired signal is the light intensity only.

2. Instrumentation and method

We use a frequency-domain instrument in which 750 and 830 nm light emitted by laser diodes (~2 mW average power) is guided to the medium through a multimode silica optical fiber (core diameter: 400 mm; numerical aperture: 0.39). A glass fiber bundle (internal diameter: 3.2 mm, numerical aperture: 0.56) collects the scattered light and conducts it to the photomultiplier tube detector (PMT). The laser current and PMT voltage are modulated by synchronized synthesizers at 110 and 110.005 MHz, respectively. The signal from the PMT at the difference frequency of 5 kHz (cross-correlation frequency) is applied to the input of an interface card for a personal computer, where the data acquisition and processing is performed to obtain the DC, AC and phase values. The time series of these values are processed to calculate their auto- and cross-correlation spectra.

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3. Phantom studies

To test the method and to characterize the instrumentation capabilities, we performed a series of phantom experiments. The central part of our experimental setup consisted of a container (a 1-L beaker) filled with an aqueous Liposyn suspension, in which black rubber particles underwent turbulent motion caused by a magnetic-stick stirrer. The average velocity of particle motion is controlled by adjusting the stirrer rotation frequency. In each experiment we used particles of approximately equal size, either 1.0 mm or 1.6 mm effective diameter.

Figure 1 shows the DC and phase time traces obtained with a sampling time of 8 ms. The left part of the plot corresponds to the condition when the mixer is off, so that the particles rest on the bottom of the beaker, and the right part (starting at t~2.5 sec) corresponds to the fluctuation regime, when the stirrer is on. One can see that when the mixer is on, both the phase and the DC exhibit fluctuations over some average value, which is different from that when the mixer is off.

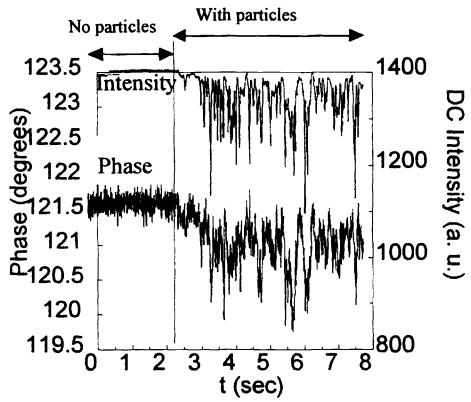

Figure 1. Time traces of the DC and phase signals before and after the stirrer is turned on. The data are obtained under the following experimental conditions: particle effective radius and concentration are respectively 0.5 mm and 0.3 cm^{-3}, magnet rotation frequency is 4 Hz, μ_a =0.043 cm^{-1} and μ_s' =9.98 cm^{-1}.

The Fourier transforms of the time traces were used to obtain power spectra. The dot symbols in Figure 2 show typical experimental power spectra of the DC and phase fluctuations obtained by averaging 100 modulus - squared Fourier transforms. One can see that both DC and phase spectra exhibit narrow resonance peaks (at the stirrer rotation frequency, its harmonics and sub-harmonics) rising over the bell-shaped background. While the peak frequencies are equal for both the DC and phase spectra, the background width of the phase spectrum is significantly smaller than that of the DC. This fact demonstrates the difference between the DC and phase information and originates from the difference of the space regions probed by the DC and phase.

We elaborated a theoretical model predicting the DC and phase power spectra. This model is based on the following assumptions:

1) The motion of each absorbing particle is independent of the motion of others and is a superposition of a Brownian stochastic process characterized by the diffusion constants D_x, D_y and D_z, and a deterministic rotation with a given frequency;

2) Due to the small size of absorbing particles and their low concentration, the total response of both DC and phase to the ensemble of particles can be expressed as an algebraic sum over single particle contributions of the form

$$\delta u(\xi,\eta) \approx -S\frac{(3\mu_s')^2}{c}\frac{a^2}{2+3a\mu_s'}\frac{\exp(-\sqrt{3\mu_a\mu_s'}(\xi+\eta))}{4\pi\xi\eta} \quad (1)$$

for the DC and

$$\delta\phi(\xi,\eta) \approx R\frac{3\mu_s'a^2}{2+3a\mu_s'}\mathrm{Im}[\frac{\exp(ik(\xi+\eta-R))}{\xi\eta}] \quad (2)$$

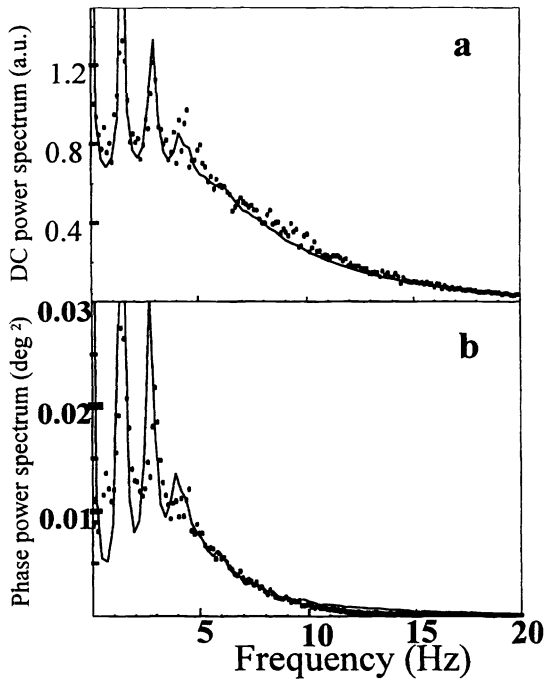

Figure 2. (a) DC and (b) phase power spectra. The points represent the experimental data obtained at the same conditions as in Fig.1. The lines are the best fits provided by model equations. In the theoretical curves the effective particle rotation frequency is 1.5 Hz. Although the frequency band investigated extends up to 125 Hz, the frequency axis is limited to 20 Hz because the particle motion does not contribute to the power spectrum at larger frequencies

for the phase ϕ, where ξ and η are the distances form the object to the light source and the detector respectively, μ_a and μ_s' are the medium absorption and reduced scattering coefficients, a is the radius of the particle, c is the speed of light, S is the source power factor, R is the source-detector separation and k is the photon density wave complex wave number. Note that according to Eq. (1), the effective region of the DC sensitivity is localized immediately around the source-detector line, while Eq. (2) shows that the phase perturbation is zero on the source-detector line and maximal when the object is situated within a ring area surrounding this line. The solid lines in Fig. 2 show the power spectra fitted to the experimental data. The fitting parameters are the particle diffusion constants D_x, D_y and D_z. The best fit occurs at $D_x = D_y = D_z = 6$ cm^2/s, which is consistent with the observed average speed of particles (about 5-10 cm/s).

4. *In vivo* studies

We have performed a number of *in vivo* measurements of optical fluctuations in tissues including measurements on skeletal muscles and on the brain cortex. Figure 2 shows the power spectra obtained on a human forearm for the cases of normal blood circulation and ischemia caused by a pneumatic cuff inflated at a pressure of 240 mmHg.

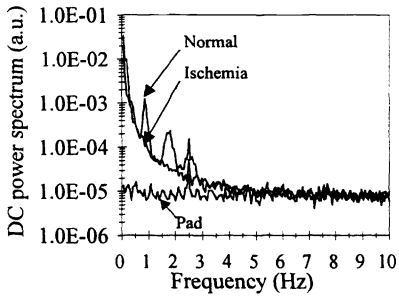

Figure 3. DC power spectra obtained *in vivo* from a human forearm at normal blood concentration and ischemia. In the case of ischemia the pressure of the cuff is 240 mmHg. The lowest curve, obtained from the silicon pad, represents the instrument noise.

Except for the peaks at the heart beat frequency and its harmonics in the normal circulation spectrum, both curves nearly coincide. The power spectrum acquired from a silicone pad (the lowest curve in Fig.3) represents the instrument noise. Comparison of the in vivo power spectra with the one obtained on the pad shows that the frequency band of the physiological fluctuations ranges from 0 to about 5 Hz.

Figure 4 shows the typical power spectrum of the AC signal acquired on the human head at the source-detector distance about 3 cm.

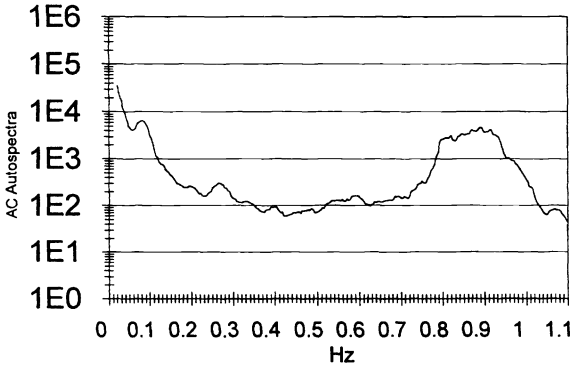

Figure 4. DC power spectra obtained *in vivo* from a human head at relaxation condition.

The peaks at 0.1, 0.3 and 0.9 Hz can be interpreted as manifestations of the vasoconstriction activity, breathing and the heart beat, respectively. The increase of the power spectrum at low frequencies shows the dominance of the long-time fluctuations.

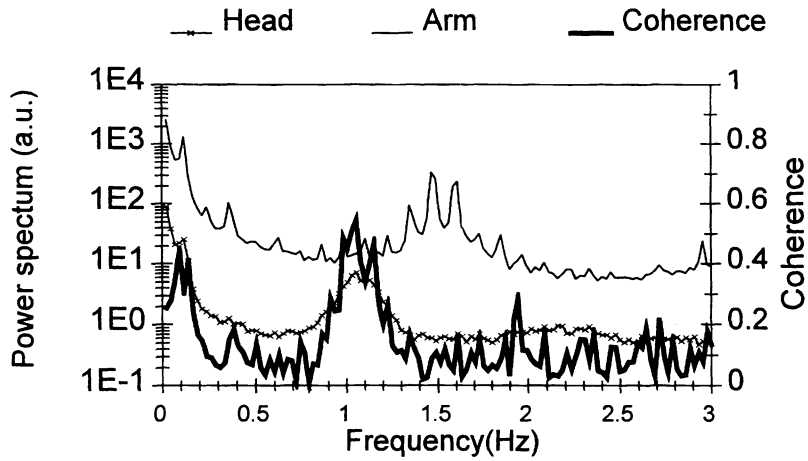

Figure 5. DC power spectra obtained during the finger tapping task from the motor cortex and arm and their coherence spectrum (red curve).

Figure 5 shows the DC power spectra measured simultaneously on the human motor cortex and forearm during a finger tapping task. Their coherence spectrum is also shown in the figure. The exercise consisted of 4-second series of fast finger movements separated by 4-second rest periods. The multiple narrow peaks on the arm signal spectrum are the harmonics of the exercise period (8 seconds), and the broad peak at 1.5 Hz corresponds to the finger motion frequency. One can also see the peak at 0.13 Hz corresponding to the long exercise period in the cortex signal power spectrum. The red curve indicates the relatively high coherence of head and arm signals at this frequency and its harmonics.

5. Conclusion

Phantom and in vivo studies confirm that photon-density-wave fluctuation correlation spectroscopy is a promising method to study physiological dynamics. Information on spatial coherence can be obtained by calculating cross-correlation spectra of signals measured in different locations [3]. The correlation analysis of the signals acquired simultaneously on the arm and the brain cortex confirms the connection between exercise and cerebral optical signals.

Acknowledgment

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