

The Origin of Artificial Kinetic Spectroscopy and Its Application

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Abstract. Intentionally creating local blood flow cessation at different body sites initiates the time dependent optical response. Specifically, applying circumferential over systolic pressure at the finger base creates a very stable post-occlusion optical signal (POS). Geometrically independent features of light absorption and scattering of the blood are extracted from POS by evaluating the parametric slope (PS). It was shown that PS, being determined from suitable pairs of wavelengths, correlates with arterial blood oxygen saturation. Other PS pairs exhibited a strong correlation with blood hemoglobin. The time dependent signal was simulated *in vitro* by using the red blood cells (RBC) aggregation process and was shown to resemble the main features of *in vivo* POS.

1 Introduction

The non-invasive technique for measuring various blood parameters has become very popular since it eliminates the withdrawal of a blood sample from a patient. Optical technique utilizes the detection of light response from different locations on the patient's body. A commonly used device of this kind, such as the pulse-oximeter, originates from photoplethysmography (PP). In PP, the light response experiences variable attenuation due to the pulsation of arterial blood.

Recently, a new approach [1,2], was established, known as Occlusion Spectroscopy, as an additional method to obtain blood related dynamic spectral characteristics. In Occlusion Spectroscopy over-systolic pressure is applied to the fleshy tissue to create a state of temporary blood flows cessation at the measurement site. To optimize this signal, the PP volumetric affect has to be suppressed.

Once blood flow cessation is established, the optical characteristics start to change dramatically, changing the detected dynamic signal by about 30%, and sometimes even by 60%, in comparison to the pulsatile signal that fluctuates only about 2-3%.

The time and spectral kinetic features of the occlusion spectroscopy signal can be simulated *in vitro*, by using the RBC aggregation process [5,6].

Our goal was twofold: a) to create a better understanding of POS and b) to elaborate appropriate algorithmic approaches for utilization in practical applications.

2 Measurement and control system

The Occlusion Spectroscopy device is a microprocessor-based instrument comprised of the measuring, controlling and display circuitry, the pneumatic system and the hand-held sensor probe.

The probe optoelectronics consists of 10-segmented light sources in the spectral range of 610 to 945 nm and a photodetector, which is synchronized and sequentially activated to generate the required spectroscopy.

The probe housing contains the controlled pneumatic cuff for temporary finger-base blood occlusion.

3 Hand-held Probe

3.1 Fingertip type probe

The preferred site for pulse-oximetry is the fingertip. Naturally, it is the first choice for the occlusion spectroscopy investigation. Two air pressure lines are used to manipulate the signal. The primary line creates the blood occlusion (flow cessation) and the secondary line controls a varying pressure, which is applied independently at the optical measurement site.

3.2 Ring – like probe

A second option to control the POS is the ring shape probe configuration. A single pressurizing line is served for both the optimization of pre-occlusion condition and for creating over systolic occlusion pressure to initiate POS.



Fig. 1. Probe and monitor overview. **A** Fingertip probe **B** “Ring” probe

4 Typical Forms of Post-Occlusion Signals

Two different modes of POS were investigated – “direct” and modulated

4.1 Non-modulated occlusion signals (Direct)

The measurement procedure includes two stages. The initial stage begins by applying moderate under systolic pressure on the testing site (fingertip) in order to deplete the tissue from venous blood to a standard volume. The second stage involves applying occluded pressure and opto measurement. Keeping the occluded volume of blood and tissue unchanged is essential to guarantee a stable evolution of a POS signal. Typical transmission and reflection POS are shown in Fig. 2 and Fig. 3, respectively.

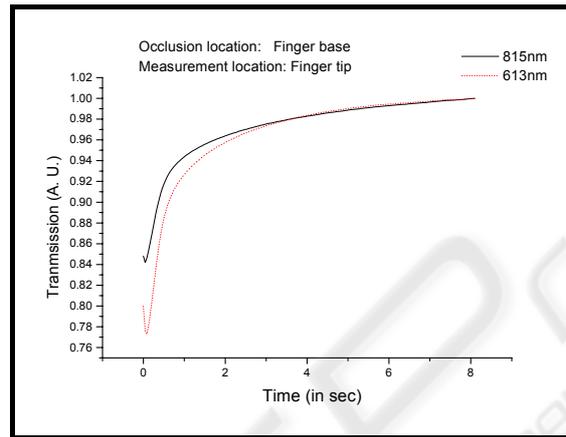


Fig. 2. Typical post occlusion transmission signal measured at fingertip location.

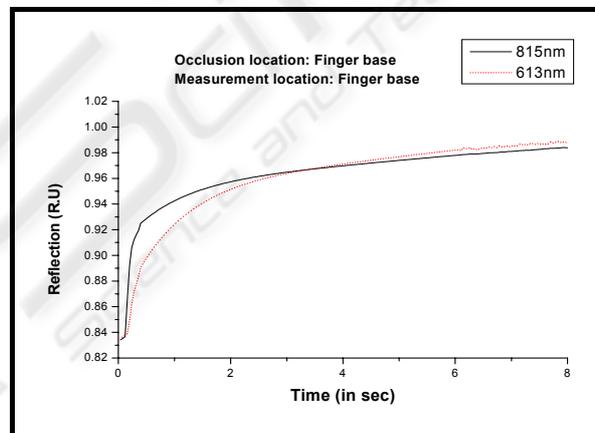


Fig. 3. Typical post occlusion reflection signal measured at finger base.

4.2 Modulated Occlusion Mode (MOM)

Creating perturbations of the occluded media with the secondary pressure wave during the blood flow cessation facilitates occlusion spectroscopy. This mode of signal modulation, or Modulated Occlusion Mode (MOM), enables the generation of optical changes induced by blood volume perturbation. For the “fingertip” probe, the primary pressure cuff is kept over-systolic, while the secondary cuff is modulated [Fig. 4]. For the “Ring” probe, both occlusion and modulated pressure coincide in one finger-base cuff while the modulation is superimposed on the over systolic pressure [Fig 5].

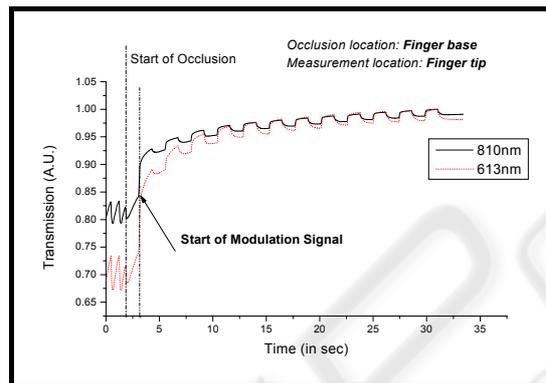


Fig. 4. Typical post MOM signal measured at fingertip. Over systolic pressure of 200mm Hg is applied at finger base. Pressure modulation (0 – 30 mm Hg) is applied on the fingertip

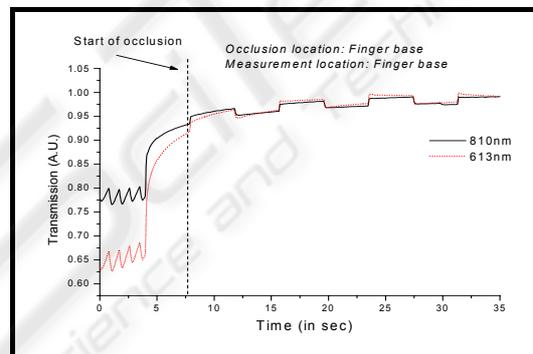


Fig. 5. Typical MOM transmission signal measured at finger base site. Over systolic pressure is modulated between 200 – 230 mm Hg

5 Parametric Slope

Occlusion initiates the time dependent optical signal. Some optical properties of blood, related to its biochemical content, are not time dependent (in scale of seconds). In order to link the time dependent signal with the sought blood parameter, there is a

need to eliminate time dependent characteristics. This can be achieved using signals at a pre-determined wavelength as a reference for the rest of the signals.

5.1 Basic Properties of the Parametric Slope

The definition of the parameter slope (PS) for the two signals $I_{\lambda_1}(t)$ and $I_{\lambda_2}(t)$ being measured at two wavelengths, λ_1, λ_2 is [2,3]:

$$PS = \frac{(\partial \ln(I_{\lambda_1}) / \partial t)}{(\partial \ln(I_{\lambda_2}) / \partial t)}$$

(1)

where I_{λ_2} is a reference signal. In our analysis we used a signal at 876nm as a reference signal. PS can be calculated at any stage of POS.

The physical meaning of PS is quite similar to the parameter called Gamma, widely used in pulse-oximetry. Gamma for the pulsatile signal is defined as [7]:

$$Gamma = \frac{(\nabla(I_{\lambda_1}))}{(I_{\lambda_1})} / \frac{(\nabla(I_{\lambda_2}))}{(I_{\lambda_2})} \quad (2)$$

where $\nabla(I_{\lambda})$ is fluctuation of pulsatile component of the optical response.

The typical spectral structure of PS was calculated from 2000 measurements performed on 270 patients [Fig. 6]. This spectral structure resembles HbO₂ absorption, which is less affected by blood perfusion and finger size.

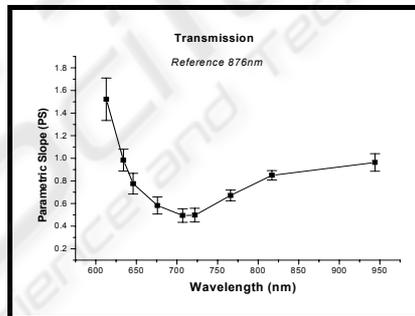


Fig. 6. Average PS for transmission signal as a function of wavelengths, obtained from the “Ring” probes, at the first 2 seconds of measurement

5.2 Time Dynamic Structure of Parametric Slope

The absence of time dependency of PS is well founded only for the initial part of the occlusion signal. Due to the course of occlusion evolvement, the values of PS's are changed with different rates. Delta PS is defined as a difference between the PS at $t=8$ sec, and PS at $t=0$, from starting of over-systolic pressure application [Fig. 7].

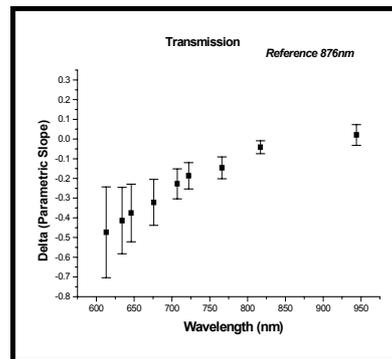


Fig. 7. Average Delta PS for transmission signal as a function of wavelengths

6 In Vitro Measurements

The main features of POS can be simulated *in vitro*, assuming that the RBC aggregation mechanism is the driving force behind the optical signal. There are a variety of *in vitro* configurations where the optical signal changes in association with RBC aggregation [5,6]. In our case, the sample of RBC suspension mixed with 1% of Dextran was pumped into a reservoir where two pipes were connected to the specially designed rigid glass cuvette of 1. mm thickness. The cessation of blood flow initiated RBC aggregation. In the first version of the cuvette (open space cuvette), the internal space volume was available for the blood motion, while in the second version (tissue-like), the cuvette was filled with 50 microns of glass fibers, leaving only 30% space available for the blood motion. The motivation to design the tissue like model was to observe the optical signal behavior in proximity of one dimensional aggregation scenario (like in small blood vessels) and to create a DC scattering environment, resembling the scattering behavior of in-vivo tissue. In both cases the signal was observed at two stages, before blood flow cessation and after it. The pulse-like variations of transmission signals at the first stage (Fig. 8) coincide with the peristaltic pump action.

6.1 Open Space Blood model

The transmission changes measured in the open space cuvette [Fig.8] reveals significant transient changes near the point of blood flow cessation. The characteristic rise time and relative changes of the signal reasonably resembles the behavior of *in vivo* POS.

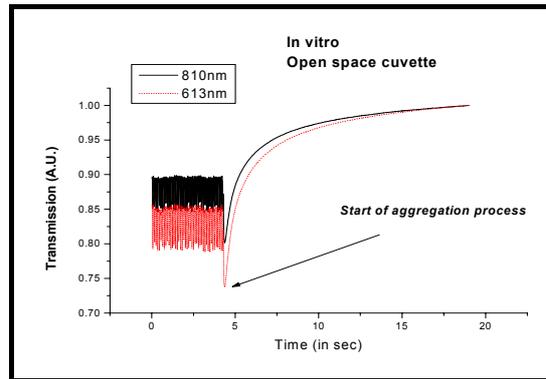


Fig. 8. Transmission signal before and after blood flow cessation. RBC suspension. Hematocrit 40% with 1% of Dextran. Glass cuvette (0.3mm thickness).

6.2 Tissue-like cuvette modeling

In the case of tissue-like cuvette, the appearance of a transient peak is negligible [Fig.9]. The aggregation related signal is expressed in terms of PS by using expression (1). The graphs of PS's and delta PS, as a function of light source (LED's) wavelengths, for the tissue-like cuvette in-vitro signals are shown in Fig.10 and Fig. 11, respectively.

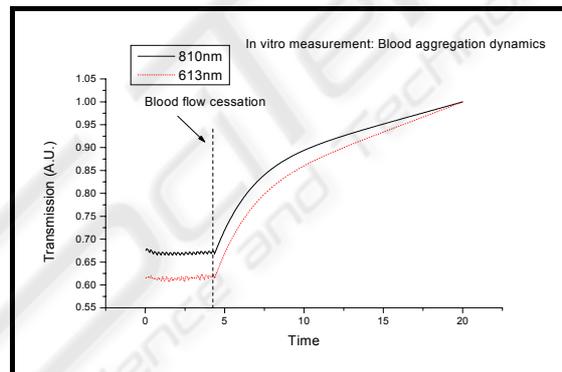


Fig. 9. Transmission signal before and after blood flow cessation. RBC suspension Hematocrit 40% with 1% of Dextran Glass cuvette (4mm thickness). 75% of cuvette volume were packed by 50-micron fibers.

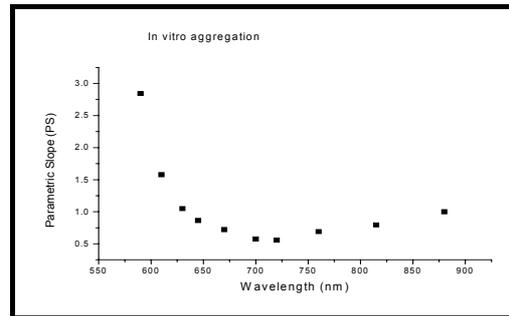


Fig. 10. Parametric Slope as a function of wavelength, immediately after beginning of blood flow cessation session in tissue-like cuvette

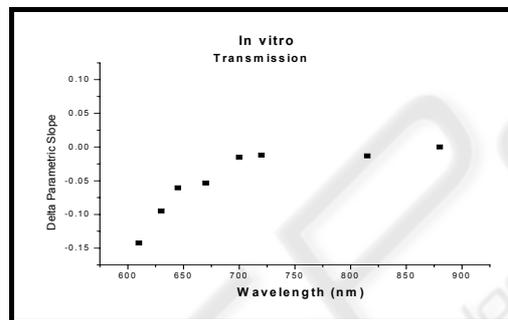


Fig. 11. Changes of Parametric Slope during 15 seconds of blood flow cessation obtained *in vitro* in tissue-like cuvette

7 Clinical Applications

Post Occlusion optical signals depend on RBC absorption and scattering. Light absorption of the blood in visible and near infrared optical region is dominated by oxy-hemoglobin (HbO_2), hemoglobin (Hb) and its derivatives.

7.1 Non-pulse Oximetry

We performed an experiment in which POS was measured by the “Ring” probe. The pre-occlusion pulsatile signals were measured and stored as well. This has been done concurrently with conventional pulse oximeter readings (Datex Ohmeda 3900). Five volunteers participated in the experiment. Each one participated in two independent measurement sessions. In the first session, the volunteer breathed normally, and in the second session, a facemask was applied supplying 100% oxygen. The correspondence between PS (for the pair 670nm, 876nm) and Gamma with SpO_2 reading of the pulse oximeter ($R=0.8$) is presented in Fig 12. The comparison between PS and SpO_2 [Fig.13] shows significant correlation ($R=0.82$).

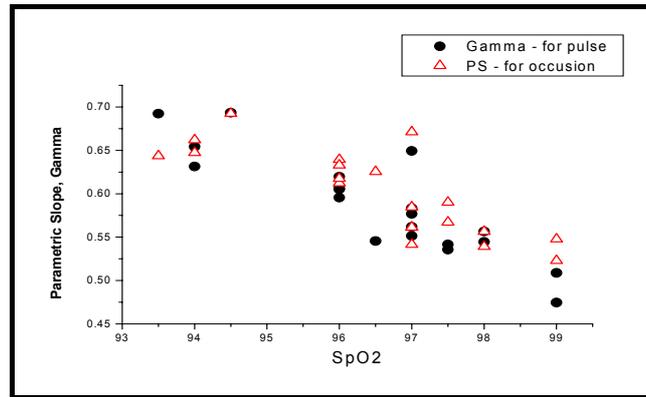


Fig. 12. PS and Gamma for 670nm and 876nm versus SpO₂ measured by oximeter

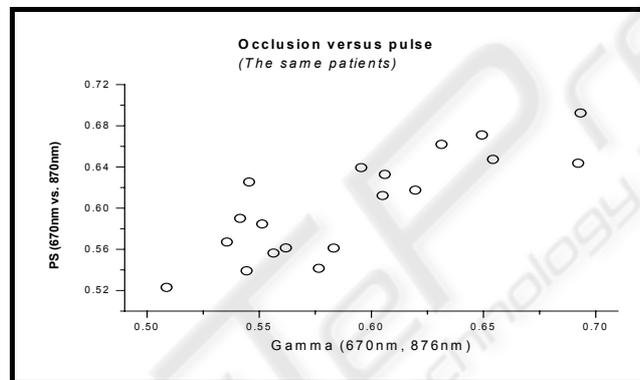


Fig. 13. Correlation between the Parametric Slopes obtained from the occlusions versus Gamma values of pulsatile component of same patients

7.2 Hemoglobin

After approval by an Ethics Committee (IRB), and receipt of informed consents, a group of 188 subjects from a hematology ward was studied. A "Finger- base probe" was used to obtain POS. A standard lab blood analyzer measured the values of reference Hb. Hb and PS values were averaged over 70 points [Fig. 14].

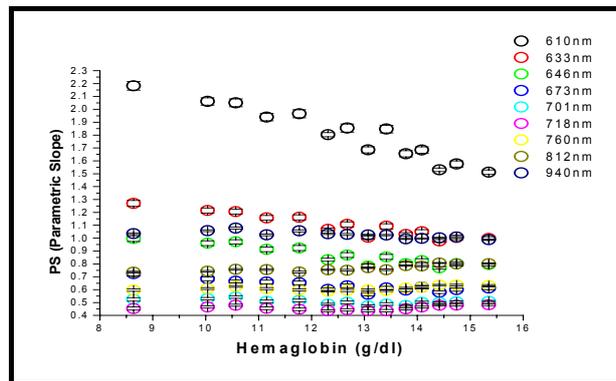


Fig. 14. Average PS's for transmission POS as a function of hemoglobin

8 Discussion

Two testing approaches were combined and investigated, i.e. 1) blood occlusion plus applying pressure modulation (superimposed) 2) stabilizing the measurement by reducing the volumetric deviations at the opto-measurement site. This in turn resulted in a strong blood related optical signal. The physiological origin of this post-occlusion signal (POS) could be one of the following: local blood or tissue volume variations, or alteration of light scattering of the blood as a result of RBC aggregation phenomena. The mutually supporting experimental facts contribute to comprehend the underlying nature of POS signal; a) Non-dimensional Parametric Slope (PS), extracted from POS, exhibits a strong correlation with arterial blood oxygen saturation. b) The PS, being determined for the pair 613nm and 876nm correlates with blood Hb. c) The wavelength dependant structure of PS resembles HbO₂ absorption.

All these facts lead to an unequivocal conclusion that the major component contributing to POS is optical changes associated with arterial blood.

Another very important fact is that the kinetic behavior of a post-occlusion signal is barely dependent on the location of the application of the over systolic pressure. However, the volumetric change is almost entirely pressure dependent. These facts signify that the POS is driven by internal kinetics of RBC aggregation. Another important feature of the POS signal is expressed in terms of PS changes. Very similar PS time dependency was observed both *in vivo* and *in vitro* aggregation induced measurements. Regarding the volumetric mechanism *in vitro*, there was observed no noticeable PS vs. thickness dependency. This fact excludes volumetric mechanisms from being materially responsible for PS changes *in vivo*.

In summary, we conclude that POS is initiated by erythrocyte aggregation. From the practical point of view, it was shown that POS is useful for determining different biochemical parameters of blood, including oxygen saturation and Hb level.

References

1. Fine, I., Fikhte, B., Shvartsman, LD.: RBC aggregation assisted light transmission through blood and occlusion oximetry. Proc. SPIE, Vol. 4162, (2000) 130-140
2. Fine, I., Fikhte, B., Shvartsman, LD.: Occlusion spectroscopy as a new paradigm for non-invasive blood measurements. Proc. SPIE, Vol. 4263, (2001) 122-130
3. Shvartsman, L.D., Fine, I. Optical transmission of blood: Effect of erythrocyte aggregation. IEEE trans. on Biom. Eng., Vol. 50, (2003) 1020-1026
4. Finarov, A., Kleinman Y., Fine I.: Optical device for non-invasive measurement of blood related signals utilizing a finger holder. (2001) US Patent 6,213,952B1
5. Priezhev A.V., Ryaboshapka O.M., Firsov N.N., Sirko I.V.: Aggregation and disaggregation of erythrocytes in whole blood: Study by backscattering technique. Journal of Biomed. Optics, Vol. 4, (1999), 76-84
6. Barshtein G., Wagnblum D., Edgar S.: Kinetics of linear rouleaux formation studied by visual monitoring of red cell dynamic organization. Biophysical Journal, Vol. 78, (2000) 2470-2474
7. Kamat V.: Pulse oximetry. Indian J. Anaesth., Vol. 46, (2002) 261-268

