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ScienceDirect

Physics Procedia 19 (2011) 49–54

Physics Procedia

ICOPEN 2011

Fractal Dimension Characterization of in-vivo Laser Doppler Flowmetry signals

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Abstract

Laser Doppler Blood Flow meter uses tissue backscattered light to non-invasively assess the blood flow rate. qualitatively. As there is large spatial variability and the temporal heterogeneity in tissue microvasculature, the measured blood flow rate is expressed in relative units. A non-linear approach in order to understand the dynamics of the microcirculation led to the fractal characterization of the blood flow signals. The study presented in the paper aims to analyze the fractal behavior of Laser Doppler Flow (LDF) signals and to quantitatively estimate the fractal dimension of waveforms using Box-Counting method. The measured Fractal dimension is an estimate of temporal variability of tissue perfusion. The rate at which fractal dimension varies as a function of location between individuals, exhibits a weak correlation with time. Further studies with a larger number of subjects are necessary to test the generality of the findings and if changes in dimension are reproducible in given individuals. In conclusion, the fractal dimension determined by Box-counting method may be useful for characterizing LDF time series signals. Future experiments evaluating whether the technique can be used to quantify microvascular dysfunction, as commonly occurring in conditions such as Diabetes, Raynaud's phenomenon, Erythromelalgia and Achenbach syndrome needs to be evaluated.

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Keywords: Laser Doppler flowmetry signals; Fractal dimension; Microcirculation

1. INTRODUCTION

Blood flow monitoring in the microcirculation is difficult because of the spatial variability of its component vessels, which varies as from tens to hundreds of microns, and its sensitivity to the monitoring process which greatly alters the results. This necessitated the need for non-invasive optical measurement techniques such for the evaluation of microvasculature. In 1964, Cummins *et al* proposed the technique for measurement of velocity of a particle in a solution by the interpretation of frequency-shifted light based on Doppler principle [1]. In 1975, Riva *et al* applied this technique to measure blood cell velocity of retinal artery using the glass tube flow model [2]. However, it was M.D Stern who first used the laser Doppler technique for blood perfusion measurement in the undisturbed microcirculation [3]. When coherent light impinges on the skin, some of it will be scattered by moving red blood cells and some by static tissue. The scattered light, spectrally broadened due to the Doppler Effect, is then brought to the surface of a sensitive photo-detector. After sensitive photo- detection and filtering, two signal components are obtained: an ac component which is related to the velocity and concentration of moving blood cells and a dc

1875-3892
Selection and/or peer-review under responsibility of the Organising Committee of the ICOPEN 2011 conference
doi:10.1016/j.phpro.2011.06.124

component, related to the absorption and scattering properties of the tissue. From the power spectral density of the ac component, an output proportional to the velocity and the number of red blood cells in the measuring volume can be obtained [4]. The algorithm proposed by Bonner and Nossal is frequently used in the signal processing [5].

Soon after, the instruments based on Laser-Doppler principle were designed for blood perfusion measurements by Watkins and Holloway as well as by Nilsson *et al*. Fischer *et al*. demonstrated a good correlation between measurements made by the instruments and the microvascular blood flow [6, 7]. Although clinical trials undertaken in many areas gave acceptable results, applications of the technique have not been very widespread. The main reason given by clinicians is that the lack of absolute units makes interpretation and the comparison of data from different subjects difficult. This limitation reflects the unknown orientation of the subcutaneous ascending arterioles and their branches beneath the LDF probe, leading to substantial variability in the flux measured in different subjects and even in the same subject if the probe is repositioned. However, we still know of no comparable technique for noninvasive continuous recording of peripheral blood flow.

Most of the published works on LDF signals have used simple time domain indices such as mean and standard deviation of the flux, or peak counting from paper recorded charts to describe the signal [8, 9]. LDF signals have also been analyzed using frequency domain methods based on the Fourier transform and wavelet analysis [10, 11]. Further, based on Monte Carlo simulations of light propagation in tissue, a method to determine depth and volume in Laser Doppler flowmetry is also analyzed [12]. In view of the complexity of the interactions that determine microvascular flow, in the present study temporal fluctuations in LDF signals were characterized by fractal analysis, a technique that has proved capable of characterizing irregular time series signals generated in nonlinear systems, and may provide more valuable physiological insights than standard linear measures.

The term “Fractal” characterizes class of spatial and temporal phenomena that are continuous but not differentiable [13]. The concept of fractals can also be applied to signals that lack a characteristic length scale. Here, the statistical properties of signal and the time window of observation is scale-invariant or follows a power law. One corollary of this behavior is that the future values of the signal are dependent on the past i.e. the signal displays correlations over time, and the system producing such a process is said to exhibit memory. A physiological process may be regarded as a fractal if the analysis of time series signals reveals self-similarity or scale-independence. Many physiological signals possess a fractal behavior over a long range of their power-spectral densities and are hence called long-memory processes and are characterized completely by two parameters variance σ^2 and the Hurst co-efficient, H [14]. These parameters are dependent on Fractal Dimension. In this study, the fractal dimension of LDF signals obtained from palm, wrist, elbow and temple is calculated using Box-counting method and their consistent change as a function of temporal variability is observed. The corresponding Hurst co-efficients are also calculated and the correlation between the values is observed.

2. MATERIALS AND METHODS

2.1. Box-Counting method

In 1935, Mandelbrot defined a fractal set as a set for which the Hausdorff-Besicovitch dimension D_h is greater than its topological dimension D_T. The Hausdorff–Besicovitch dimension D_h is defined as the logarithmic ratio between the number N of an object’s internal homotheties and the reciprocal of the common ratio r of this homothety:

$$D_h = \frac{\ln(N)}{\ln\left(\frac{1}{r}\right)}$$

Analytically, the relationship between the measuring scale d and the length L can be expressed as follows, where K is the constant and D is the Fractal Dimension, a non-integer number (fraction).

$$L(\delta) = K.\delta(1 - D)$$

The Box-Counting Method was defined by Russel.D.A [15] it is the most frequently used and most popular method. By covering a binary signal with boxes of length r, the FD is estimated as:

$$FD = \lim_{r \to 0} \frac{\log N(r)}{\log(r)}$$

where ***N(r)*** is the number of boxes required to cover the signal. This method requires signal binarization and is applicable to statistically self-similar signals [16].

2.2. Hurst Coefficient

The estimation of fractal dimension in time domain requires the calculation of a parameter called the "Hurst Coefficient, *H*". The Hurst Coefficient defines the stationarity, more specifically, the autocorrelation and the fractal dimension of the time series. The Fractal dimension, ***D*** and the Hurst Coefficient, ***H*** are related as

$$H = 2 - D$$

For a 2-dimensional physiological signal the parameter, *H* varies from zero-for a signal exhibiting large variations and irregularity to one-for a signal exhibiting overall smoothness. However, for $H = 0.5$, the magnitude sequential points are independent and are uncorrelated and exhibit properties of a random walk i.e. Brownian Motion of Fractal nature [17].

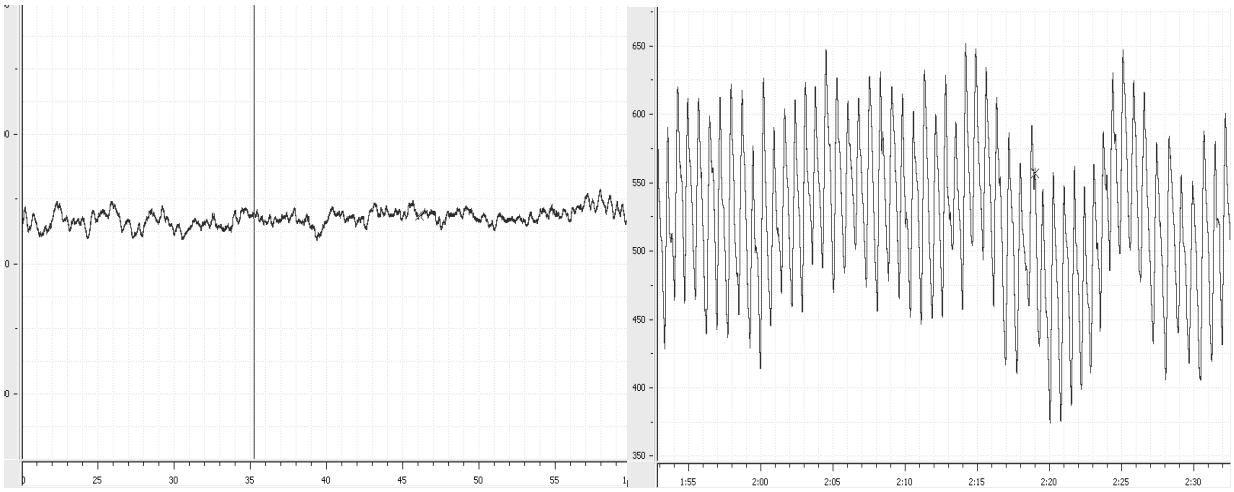
2.3. Instrumentation

The real-time microcirculation flow measurements were made using Blood Flow meter (BloodFlowmeter, AD Instruments Inc., UK).The instrument uses a temperature stabilized semiconductor laser diode operating at 830±10nm .The laser power being 0.5mW from the probe in ideal conditions. The instrument has a Doppler signal bandwidth of 22 kHz and calculates the blood perfusion or red blood cell flux in arbitrary units and the percentage of backscattered laser light [18].

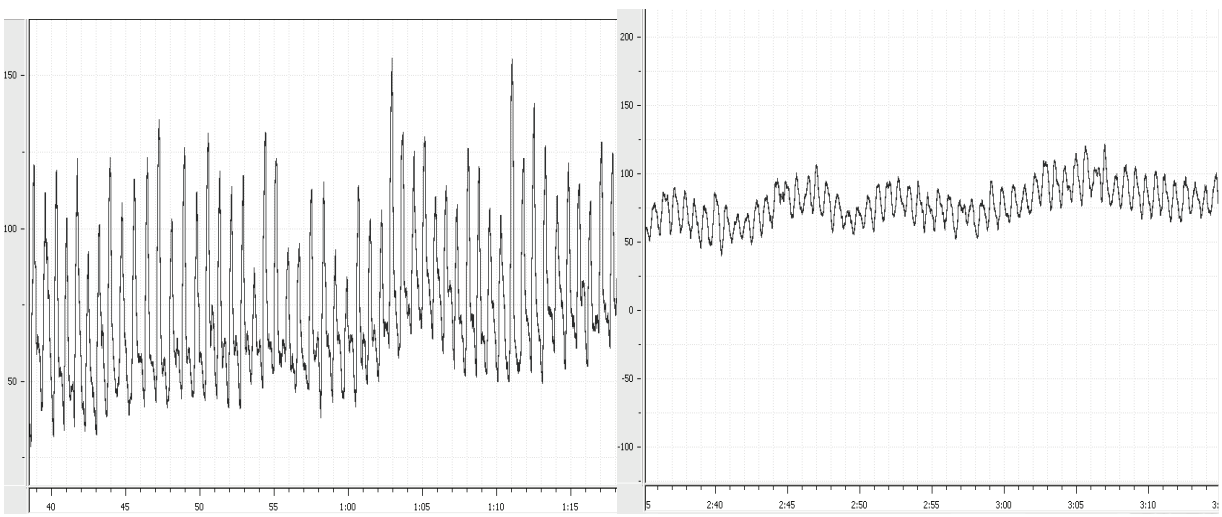
The Blood Flowmeter is connected to the PowerLab® data acquisition system with single-ended and differential inputs and the LabChart® software that is used for data acquisition and subsequent data analysis and is similar to conventional strip chart recorder [19]. ImageJ software and FracLac plug-in were used to calculate the fractal dimensions using the Box-counting method. The Box- counting method was applied to self-similar temporal signals treating it as a picture, a two dimensional object [20].

Fig.1. Experimental Setup

LDF recordings were made in temperature controlled manner. The subjects were abstained from intake of food and beverages for two hours and rests in a relaxed position for at least 20 minutes. The probe is positioned in the probe holder attached to the skin. Initially, the resting perfusion is measured and the "biological zero" is set. Further, The Laser Doppler waveforms were collected from forehead, elbow, palm and fingertip and fractal dimension was calculated using the software plug-in FracLac after signal normalization for one minute intervals successively for 5 such data.



(a) (b)



(c) (d)

Figure.2: LDF Waveforms obtained at (a) Elbow (b) Fingertip (c) Palm and (d) Temple

3. RESULTS AND DISCUSSIONS

The Laser Doppler waveforms collected from forehead, elbow, palm and fingertip are shown. The average perfusion value was taken as final after the linear regression graph plot for each of these locations. The estimated fractal dimensions are tabulated and the corresponding Hurst coefficients' are calculated to draw conclusions and tabulated in Table 1. As previously mentioned, the Hurst coefficient signifies persistence or correlation of time series. Besides, A Hurst exponent near 0.5 denotes a Brownian motion of fractal nature, Hurst coefficient of $0 < H < 0.5$ denotes negatively correlated signal and a Hurst coefficient of $0.5 < H < 1$ relates to a positively-correlated signal, although, the time series has the same mean and variance. The palm of the hand and the fingertip, with average fractal dimension of 1.74±0.02, 1.81±0.02 exhibit negative correlation with H of 0.26 and 0.19 respectively. However, the fractal dimension of elbow is 1.21±0.02 with H of 0.79 shows positive correlation. The LDF signals recorded from the forehead have fractal dimensions of 1.54±0.02 with H of 0.46 exhibiting a weak positive

correlation and tending towards fractal Brownian motion- like (fBm) signals. The fractal dimension of LDF signals vary directly as their corresponding perfusion values.

A possible explanation for this quantitative assessment could be the dominance in the microvascular outflow over the central autonomic outflow towards the proximities compared to the elbow regions. There is greater coordination of microvasculature towards the trunk of the body than the appendicular regions such as the fingertips and palm where unidirectional flow is more pronounced. Further, the direction of blood flow greatly affects the measured perfusion as is apparent from the recordings of the forehead, where the flow is equally dominant both directions.

Table 1

	Finger ***D***	Finger ***H***	Palm ***D***	Palm ***H***	Elbow ***D***	Elbow ***H***	Forehead ***D***	Forehead ***H***
Results	1.81	0.19	1.74	0.26	1.21	0.79	1.54	0.46

4. FUTURE WORK

The rate at which fractal dimension varies as a function of location between individuals, exhibits a weak correlation with time. Further studies with a larger number of subjects are necessary to test the generality of the findings and if changes in dimension are reproducible in given individuals. In conclusion, the fractal dimension determined by Box-counting method may be useful for characterizing LDF time series signals. Future experiments evaluating whether the technique can be used to quantify and diagnose microvascular dysfunction, as commonly occurring in conditions such as Diabetes, Raynaud's phenomenon, erythromelagia and Achenbach syndrome needs to be evaluated.

5. ACKNOWLEDGEMENTS

This project work was done as a part of the Summer Fellowship Programme-2010 in the Biophotonics Lab, Department of Applied Mechanics, IIT Madras.

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