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Multiscale Poincaré plot analysis of time series from laser speckle contrast imaging data

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ABSTRACT

The monitoring of microvascular blood flow is of importance for research and clinical purposes because, for some pathologies as diabetes, the microcirculation may be affected long before organ dysfunctions are diagnosed. Laser speckle contrast imaging (LSCI) is gaining an increased interest to monitor microvascular blood flow (peripheral cardiovascular data). However, in spite of this and by opposition to central cardiovascular data as electrocardiograms, very few studies have been conducted on the analysis of LSCI through scales. We therefore propose to process LSCI data with a multiscale approach relying on Poincaré plots. For this purpose, we first study multiscale Poincaré (MSP) plots of simulated signals (synthetic white and $1/f$ noise time series). Then, MSP plots of LSCI time series recorded in 24 healthy volunteers are generated and analyzed. Furthermore, this analysis on real-life data is also conducted to study the role played by age on the results. Thus, the subjects were divided into two age groups: 13 young subjects (mean age = 23.8 ± 3.2 years old) and 11 elderly subjects (mean age = 56.9 ± 6.7 years old). Our results show properties that may reveal a weak fractal structure for LSCI data. Moreover, we find no statistical difference ($p \geq 0.05$) for the descriptors of MSP plots between the two age groups. MSP plots may become a simple-to-implement visualization tool to provide new insights into biomedical data across scales.

1. Introduction

In physiologic systems, several mechanisms co-exist and interact. They operate across multiple spatial and temporal scales. This is why physiologic signals as heart rate variability (HRV) – data coming from the central cardiovascular system – contain complex fluctuations [1]. The latter reveal information about the underlying dynamics. In order to gain knowledge on the systems behavior through the processing of these fluctuations, several multiscale-based signal processing algorithms have been designed. Among them we can cite multifractal methods [2], multiscale entropy [3–5], and multiscale time irreversibility [6].

Recently, multiscale Poincaré (MSP) plots have also been proposed [7]. MSP plots have two advantages over other existing methods: they are simple to implement and can be color-coded; the visualization of time series properties is therefore enhanced [7]. Recently, MSP plots have been used to reveal a loss of complexity in HRV data of patients with chronic (congestive) heart failure syndrome or with atrial fibrillation, compared to HRV data of healthy subjects [7]. To the best of our knowledge, no other study has been carried out with MSP plots. In particular, no analysis of data coming from the peripheral cardiovascular system has been conducted yet.

We herein propose to study signals from the peripheral cardiovascular system with MSP plots. For this purpose, skin microvascular blood flow signals have been recorded with the laser speckle contrast imaging (LSCI) modality. LSCI is an optical-based technology that reflects microvascular perfusion, see below [8–10]. The study of microvascular data is of importance both for the research and clinical fields because, for some pathologies as diabetes, the microcirculation may be affected long before organ dysfunctions are diagnosed. Moreover, it has been reported that skin microcirculation is altered with age, through different mechanisms (see, e.g., [11]). Our goals were therefore twofold: (i) to analyze MSP plots of LSCI data to gain insight into these peripheral

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cardiovascular data; (ii) to compare MSP plots of young healthy subjects with those of elderly healthy subjects to determine if age has an impact on the results revealed by MSP plots.

The paper is organized as follows: we first present the LSCI technology and detail the measurement procedure used to acquire LSCI data. Then, we introduce Poincaré plots and their multiscale approach (MSP plots). The most often used descriptors to quantify these plots are also presented. Afterward, the results obtained by processing both synthetic data and LSCI time series with MSP plots are presented. The effect of aging on LSCI data dynamics is also studied. A discussion of the results and a conclusion end the paper.

2. Materials and methods

2.1. Laser speckle contrast imaging technology

LSCI is gaining an increased interest to study microcirculation due to its wide-field and non-scanning nature [8,12–15], its low-cost [16], and its applicability in many research fields [9,13,15,17]. Moreover, the blood flow maps given by LSCI have high temporal and spatial resolutions, and are reproducible [18–20].

From an instrumentation and physics point of view, the analyzed tissues are illuminated by a laser light. The scattered laser light produces a speckle pattern that is imaged onto a camera. The analysis of the spatial (or temporal) statistics of the speckle pattern leads to the speckle contrast [21]. The spatial contrast is computed as the ratio of the standard deviation to the mean intensity in a small region of the speckle image. In the case of single-exposure LSCI, the link between the speckle contrast K and average velocity of scattering particles (mainly red blood cells) producing the dynamic speckle is possible only if the velocity distribution of the scatterers is known. This is due to the fact that the variance $\sigma_S^2(T)$ of the spatial intensity distribution in a time-averaged speckle pattern with an integration time T is linked to the autocovariance $C_t(\tau)$ of the temporal fluctuations in the intensity fluctuations of a single speckle [22,23]

$$\sigma_S^2(T) = \frac{2}{T}\int_0^T \left(1-\frac{\tau}{T}\right) C_t(\tau)d\tau, \quad (1)$$

where $C_t(\tau)$ depends, among others, on the velocity distribution of the scattering particles [23]. This leads to (see developments in, e.g., [24,25])

$$K^2 = \frac{2\beta}{T}\int_0^T \left(1-\frac{\tau}{T}\right) |g_1(\tau)|^2 d\tau, \quad (2)$$

where $g_1(\tau)$ is the electric field temporal autocorrelation function and β accounts for loss of correlation related to the ratio of the detector (or pixel) size to the speckle size and to polarization [26]. If the velocity distribution of the scatterers is assumed, the expression of $g_1(\tau)$ can be obtained. Therefore, from Eq. (2), we obtain the correlation time τ_c. The knowledge of τ_c is of importance as it is thought to be inversely proportional to the local velocity of the scatterers [15,21].

Several assumptions for the velocity distribution of the scatterers have been proposed. Thus, some authors used a Lorentzian distribution (see, e.g., [21,22,24,27,28]). This is appropriate only for a Brownian motion (unordered flow). Others proposed a Gaussian distribution (ordered flow) [27]. It has also been suggested that a Voigt model (convolution of the Lorentzian and Gaussian line shapes) might be an alternative [27]. Moreover, more recently, new mathematical models have been developed to account for the presence of static tissue elements [24,29–32].

Several parameters can affect the contrast values in LSCI, such as the optical properties of the fluid and surrounding tissue. Thus, it has been reported that LSCI is more sensitive to small changes in scattering properties than it is to small changes in flow velocity [33]. Moreover, changes in blood haematocrit result in changes in the scattering coefficient. Thus, some authors recommended that the scattering coefficient of the blood be measured and considered as a significant variable in the data analysis [33,34]. This is why, in the ideal conditions, optical properties need to be considered when using LSCI to make flow estimates.

Recently, the multi-exposure speckle imaging (MESI) has also been introduced to overcome the limitation of single exposure LSCI in giving relative and not absolute measures [29,35,36]. MESI takes advantage of the dependence of the speckle contrast on camera exposure duration. With MESI, speckle images are acquired at different camera exposure durations. The use of MESI also involves the use of a mathematical model that relates the speckle contrast to the camera exposure duration T and the decay time of the speckle autocorrelation function τ_c [29]. Models taking into account the static scatterers have also been proposed [29].

In LSCI the minimum speckle diameter, d_{min}, is linked with the optical magnification M, the f-stop of the imaging optics $f/\#$, and the wavelength of the laser light λ [37]. In order to satisfy the Nyquist sampling criterion and also to maximize the contrast of the speckle pattern, it has been recommended to have a speckle size that is at least twice the pixel size [37,38].

2.2. Data acquisition

Our work is a prospective study. Thus, twenty four healthy volunteers were recruited in the University Hospital of Angers, France. For all the subjects, the medical exam did not reveal any pathology and none of them was taking drug. The participants were divided into two age groups: young (n = 13, 20–30 years old; mean age = 23.8 ± 3.2 years old; 8 women; BMI = 22.1 ± 3.2 kg/m^2) and aged (n = 11, 50–68 years old; mean age = 56.9 ± 6.7 years old; 7 women; BMI = 24.4 ± 2.0 kg/m^2). All the subjects gave their written consent to participate in this institutionally approved study. Experiments were carried out in accordance with the Declaration of Helsinki [39].

The measurements began after a 20-min adaptation period. Microvascular experiments were performed on the forearm with the participants resting in the supine position, in a quiet temperature-controlled room (21 ± 1 °C) [40]. For the perfusion assessment, a laser speckle perfusion imager PeriCam PSI System (Perimed, Sweden) was used. The system consists of a linearly polarized laser emitting at a wavelength of 785 nm, and its exposure time is fixed at 6 ms, which is longer than the time scale of the speckle intensity fluctuations (typically less than 1 ms for biological tissues; [41]). The camera includes a polarizer aligned to remove specular reflections. The pixel size of the camera is 6.46 μm and the speckle diameter is 7.8 μm. The contrast algorithm is computed from 3 × 3 pixels sub-matrices (this spatial neighborhood size cannot be changed by the user). Microvascular perfusion values – given by the imager in laser speckle perfusion units (LSPU) – are computed from the inverse of the contrast value (perfusion ∼1/K − 1, where K is the contrast; Perimed documentation). In our work, assumptions for the flow model were not used as we directly worked on the perfusion images, obtained from the contrast images. The correlation time τ_c was not computed.

The distance between the arm of the subject and the camera was around 15 cm [42]. This led to images with a resolution of 0.4 mm. Images were recorded at rest during around 23 min. The sampling frequency for the recordings was set at 16 Hz. In our work, 21,837 images were processed for each subject.

The image analysis was performed once the acquisitions were over. In order to process images, a region of interest (ROI) of size 31 × 31 pixels (∼153.7 mm^2) was drawn on the first image of the recordings, for each subject. The size of the ROI (31 × 31 pixels)