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# Numerical simulation of laser Doppler flowmetry signals based on a model of nonlinear coupled oscillators. Comparison with real data in the frequency domain

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*Abstract*—**Laser Doppler flowmetry (LDF) technique is widely used in clinical investigations to monitor microvascular blood flow. It can be a very interesting tool to diagnose impairment in the microcirculation caused by pathologies. However, this can be done in an efficient way only if the processed signals are well understood. Therefore, in order to gain a better insight into LDF signals, this work presents numerically simulated data generated by a model based on nonlinear coupled oscillators. Linear and parametric couplings, as well as fluctuations are analyzed. Each simulated signal is processed to obtain its power spectrum in the frequency domain and a comparison with real data is proposed. The results show that the power spectra of the simulated signals reflect the presence of the cardiac, respiration, myogenic, neurogenic and endothelial related metabolic activities. However, their amplitude in the frequency domain are more pronounced than they are on real LDF signals. Moreover, the modeling of fluctuations is essential to reproduce the noise present on real data. Finally, linear couplings seem more adequate than parametric couplings to describe power spectra at frequencies higher than 1 Hz. This work will now serve as a basis to elaborate more powerful models of LDF data**.

## I. Introduction

LASER Doppler flowmetry (LDF) is a noninvasive method to monitor microvascular blood flow [1]-[4]. LDF measurements from the skin reflect perfusion in capillaries, arterioles, venules, and dermal vascular plexa [5]-[7]. Some studies have shown that LDF signals have complex dynamics, with fractal structures and chaos [8].

The LDF technique is now widely used in clinical and physiological investigations of blood microcirculation. Nevertheless, some efforts are still needed to model and numerically generate the signals. Such simulations could help in the diagnosis or prevention of pathologies. The knowledge of the processes giving rise to LDF signals is of course very important to build such simulations. Recent studies conducted on LDF oscillations have shown the existence of five characteristic frequencies, that reflect the heart beats, the respiration, the myogenic, neurogenic and endothelial related metabolic activities (frequencies respectively near to 1.1 Hz, 0.36 Hz, 0.1 Hz, 0.04 Hz, and 0.01 Hz for healthy humans) [5], [6], [9]-[11].

Based on these results, the goal of our work is to go further into the simulation of LDF signals. For that purpose, we use a model of the cardiovascular system relying on nonlinear coupled oscillators [12]-[14]. We simulate the five above-mentioned activities, and we numerically generate LDF signals. To our knowledge, it is the first time that LDF signals are computed with five nonlinear coupled oscillators. This work also determines the power spectra of simulated and real LDF signals. A comparison between the two kinds of spectra is then proposed. Moreover, the influence of the couplings chosen in the model, and the presence of fluctuations, are analyzed in the frequency domain. To our knowledge, this work is also the first one to propose a comparison, in the frequency domain, of numerically simulated LDF data with real recordings.

## II. Modeling of LDF Signals

### A. Introduction

It has recently been shown that, on the time scale of one average circulation period, the cardiovascular system behaves in many ways as a set of five coupled, autonomous, nonlinear oscillators of different frequencies [10], [13]-[16]. Indeed, on a time scale of around one minute there are five almost periodic oscillatory subsystems contributing to the regulation of blood flow. Each oscillation observed in the cardiovascular signals is therefore hypothesized to originate from a subsystem that can oscillate autonomously [14]. The subsystem can be described as an oscillator and the interactions between the subsystems as couplings between the oscillators [12]. Based on physiological understanding and analysis of measured time series, an oscillator that possesses a structural stability and robustness was proposed for the basic unit to model the cardiovascular system [13].

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Our study relies on this modeling; the two state variables $x_i$ and $y_i$ correspond to the blood flow and the velocity of the flow, respectively, where $i = 1$ is generated by the heart, $i = 2$ by respiration, $i = 3$ by the myogenic oscillator, $i = 4$ by the neurogenic oscillator, and $i = 5$ by the metabolic oscillator. Each of the five oscillators generates or regulates the flow, the pressure or the resistance.

The preliminary simulations of the model were restricted to the cardio-respiratory interactions, with only two oscillators $i = 1, 2$ taken into account [12], [17]. In our work we go further by taking into account the whole cardiovascular system. The five above-mentioned activities are thus numerically generated with five nonlinear coupled oscillators. Based on these simulations, we then propose to compute LDF data. Moreover, the first simulations of the cardio-respiratory interactions suggested that there is a mixture of linear and parametric couplings, but that the linear couplings seem to dominate [12]. However, it is essential to take into account the influence of stochastic effects resulting from the (unmodeled) rest of the system [12], [17]. In what follows, linear and parametric couplings are studied, and the influence of the rest of the system is modeled by introducing slight time variations for the characteristic frequencies.

### B. Linear couplings

For this case, the modeling is chosen as [12]:

$$\dot{x}_1 = -x_1 q_1 - y_1 \omega_1 + \eta_2 x_2 - \eta_3 x_3 - \eta_4 x_4 + \eta_5 x_5 \quad (1)$$

$$\dot{y}_1 = -y_1 q_1 + x_1 \omega_1 + \eta_2 y_2 - \eta_3 x_3 - \eta_4 x_4 + \eta_5 x_5 \quad (2)$$

$$\dot{x}_2 = -x_2 q_2 - y_2 \omega_2 + \theta_4 x_4 + \theta_5 x_5 \quad (3)$$

$$\dot{y}_2 = -y_2 q_2 + x_2 \omega_2 + \theta_4 x_4 + \theta_5 x_5 \quad (4)$$

$$\dot{x}_3 = -x_3 q_3 - y_3 \omega_3 + \gamma_4 x_4 - \gamma_5 x_5 \quad (5)$$

$$\dot{y}_3 = -y_3 q_3 + x_3 \omega_3 + \gamma_4 y_4 - \gamma_5 y_5 \quad (6)$$

$$\dot{x}_4 = -x_4 q_4 - y_4 \omega_4 - \rho_2 x_2 + \rho_3 x_3 - \rho_5 x_5 \quad (7)$$

$$\dot{y}_4 = -y_4 q_4 + x_4 \omega_4 - \rho_2 y_2 + \rho_3 y_3 - \rho_5 y_5 \quad (8)$$

$$\dot{x}_5 = -x_5 q_5 - y_5 \omega_5 + \sigma_2 x_2 - \sigma_3 x_3 - \sigma_4 x_4 \quad (9)$$

$$\dot{y}_5 = -y_5 q_5 + x_5 \omega_5 + \sigma_2 y_2 - \sigma_3 y_3 - \sigma_4 y_4 \quad (10)$$

where $\eta_i$, $\theta_i$, $\gamma_i$, $\rho_i$, and $\sigma_i$ are coupling terms ($1 \le i \le 5$).

$$q_i = \alpha_i \left( \sqrt{x_i^2 + y_i^2} \right) - a_i \quad (11)$$

where $\alpha_i$, $a_i$ are constants, $\omega_i = 2\pi \left( f_{i\_s} + C \times f_{i\_s} \times \zeta_i(t) \right)$ with $f_{i\_s}$ the characteristic frequencies, $C$ a constant, and $\zeta_i(t)$ a white Gaussian noise with mean 0 and variance 1.

### C. Parametric couplings

For this other case, the modeling is chosen as [12]:

$$\dot{x}_1 = -x_1 q_1 - y_1 \left( \omega_1 + \eta_2 x_2 - \eta_3 x_3 - \eta_4 x_4 + \eta_5 x_5 \right) \quad (12)$$

$$\dot{y}_1 = -y_1 q_1 + x_1 \left( \omega_1 + \eta_2 y_2 - \eta_3 x_3 - \eta_4 x_4 + \eta_5 x_5 \right) \quad (13)$$

$$\dot{x}_2 = -x_2 q_2 - y_2 \left( \omega_2 + \theta_4 x_4 + \theta_5 x_5 \right) \quad (14)$$

$$\dot{y}_2 = -y_2 q_2 + x_2 \left( \omega_2 + \theta_4 x_4 + \theta_5 x_5 \right) \quad (15)$$

$$\dot{x}_3 = -x_3 q_3 - y_3 \left( \omega_3 + \gamma_4 x_4 - \gamma_5 x_5 \right) \quad (16)$$

$$\dot{y}_3 = -y_3 q_3 + x_3 \left( \omega_3 + \gamma_4 y_4 - \gamma_5 y_5 \right) \quad (17)$$

$$\dot{x}_4 = -x_4 q_4 - y_4 \left( \omega_4 - \rho_2 x_2 + \rho_3 x_3 - \rho_5 x_5 \right) \quad (18)$$

$$\dot{y}_4 = -y_4 q_4 + x_4 \left( \omega_4 - \rho_2 y_2 + \rho_3 y_3 - \rho_5 y_5 \right) \quad (19)$$

$$\dot{x}_5 = -x_5 q_5 - y_5 \left( \omega_5 + \sigma_2 x_2 - \sigma_3 x_3 - \sigma_4 x_4 \right) \quad (20)$$

$$\dot{y}_5 = -y_5 q_5 + x_5 \left( \omega_5 + \sigma_2 y_2 - \sigma_3 y_3 - \sigma_4 y_4 \right) \quad (21)$$

where $\eta_i$, $\theta_i$, $\gamma_i$, $\rho_i$, et $\sigma_i$ are coupling terms ($1 \le i \le 5$).

$$q_i = \alpha_i \left( \sqrt{x_i^2 + y_i^2} \right) - a_i \quad (22)$$

where $\alpha_i$, $a_i$ are constants, $\omega_i = 2\pi \left( f_{i\_s} + C \times f_{i\_s} \times \zeta_i(t) \right)$ with $f_{i\_s}$ the characteristic frequencies, $C$ a constant, and $\zeta_i(t)$ a white Gaussian noise with mean 0 and variance 1.

### D. Couplings values and LDF signal computation

For the linear and parametric couplings, the following values are chosen [12]:
$\eta_3 = -0.5$, $\rho_3 = 0.1$, $\sigma_3 = 0.1$, $\eta_2 = -\eta_4 = \eta_5 = 0.5$, $\theta_4 = \theta_5 = 0.1$, $\gamma_4 = \gamma_5 = 0.1$, $\rho_2 = \rho_5 = 0.1$, and $\sigma_2 = \sigma_4 = 0.1$. $\alpha_i = 1$ for $i = 1$ to 5, and finally $a_1 = a_5 = 0.5$; $a_2 = a_3 = a_4 = 1$.

In order to simulate LDF signals recorded on humans, the values of the characteristic frequencies are set as follows: $f_1 = 1.1$ Hz, $f_2 = 0.36$ Hz, $f_3 = 0.1$ Hz, $f_4 = 0.04$ Hz, and $f_5 = 0.01$ Hz. The influence of the rest of the system is studied by modifying the value of $C$. The latter is chosen equal to 0, 0.1, 0.2, 0.3, or 0.4. Moreover, a sampling frequency of 20 Hz is proposed for the computations.

No simulation of LDF data has ever relied on the five nonlinear coupled oscillators. In our work we propose to compute the blood flow as:

$$BloodFlow = \sum_{i=1}^{5} x_i \,, \quad (23)$$

and 21324 points of signals are simulated. Once the blood flow numerically computed, the data are processed in order to obtain their power spectra.

## III. Results and Discussion

The power spectrum of a simulated signal is shown in Fig. 1. For each kind of coupling, and for each value of $C$, five peaks appear on the power spectra of the simulated data. For the linear couplings, and for $C = 0$, the peaks appear at the following frequencies: 1.1002 Hz, 0.3606 Hz, 0.0910 Hz, 0.0385 Hz, and 0.0150 Hz. A comparison with the characteristic frequencies chosen in the model allows to conclude that these peaks correspond to the cardiac, respiratory, myogenic, neurogenic, and endothelial related metabolic activities, respectively. The simulated data thus reflect the underlying processes of the microcirculation (this is true for each coupling and for each value of $C$). These

results are meaningful to better appreciate the amount and impact of the couplings between the nonlinear oscillators. Strong couplings and nonlinearities would be expected to lead to broadband spectra. Meanwhile, both the simulated and experimental data reveal that the harmonic frequencies (peaks) of the underlying individual oscillators are relatively preserved in the spectra, suggesting a moderate impact of the couplings between the nonlinear oscillators. The computation of the power spectrum for a real LDF signal reveals that one broad peak is predominant for real data (see Fig. 2). It appears at 0.9131 Hz, and thus may reflect the cardiac activity. The other peaks seem to be hidden by "noise": respiration, myogenic, neurogenic, and endothelial related metabolic activities are difficult to distinguish from the power spectra of real data.

Moreover, whatever the couplings chosen for the simulated data, we note that the higher the value of $C$, the more noisy the power spectra are (see Figs. 1 and 3). For the linear couplings and for $C = 0.4$, the peaks appear at 1.0810 Hz, 0.3616 Hz, 0.0915 Hz, 0.0385 Hz, and 0.0155 Hz. A comparison with the values mentioned above for $C = 0$ shows that the peak frequencies on the power spectra are only very slightly modified by the noise. As mentioned previously, noise is also present on power spectra of real LDF signals (see Fig. 2). Therefore, in order to simulate data behaving close to real LDF signals, we will choose $C \neq 0$ in what follows.

An analysis of the power spectra obtained by each kind of coupling can also be made. For a given value of $C$ ($C \neq 0$), the power spectra of data obtained with linear couplings are more noisy at frequencies higher than 1 Hz than the spectra of data obtained with parametric couplings (see Fig. 4). We also note that the power spectrum of a real signal is very noisy at high frequencies (see Fig. 2). The linear couplings seem therefore more adequate than the parametric couplings to reflect power spectra of LDF signals at frequencies higher than 1 Hz. Moreover, the power spectra of real data are much more noisy in the lowest frequency band than the power spectra of simulated data. For the latter, at low frequencies, we can see that the five peaks generated by the five activities are present at the nearly same frequencies for the two kinds of coupling (see Fig. 4).

Our study relies on a mathematical model based on nonlinear coupled oscillators. Linear and parametric couplings have been tested. In reality, each oscillator of the model represents a whole set of oscillators which are spatially distributed. Moreover, couplings change with the state of the system. It has been shown that better-trained subjects have stronger couplings, whereas weak couplings lead to some pathological stages (subjects in coma for example, have almost no couplings) [18]. Understanding the physical and physiological nature of these couplings is therefore essential to gain a better insight into the functioning of the whole system. Furthermore, several observations demonstrated clearly that different states of the organism may correspond to different regimes of synchronization (see [12], and references therein). This can be of clinical significance.

Previous studies using a similar mathematical model to simulate the the cardio-respiratory interactions suggested that there is a mixture of linear and parametric couplings, but that the linear couplings seem to dominate [12]. The results of our work are in accordance with the authors conclusion. Indeed, we have shown that the linear couplings are more adequate than the parametric couplings to reflect power spectra of LDF signals at frequencies higher than 1 Hz. Moreover, the same authors have shown that, in order to explain the variability of cardiac and respiratory frequencies, it is essential to take into account the rest of the system, i.e. to consider the effect of noise [12]. Physiological data recordings contain noise that can come from the instrument, from the quantization of analog signals or from physiological phenomena (interactions with the rest of the system). This implies a complex modulation of the natural frequency in the subsystem under study. In the case of weak noise, the generalized phase

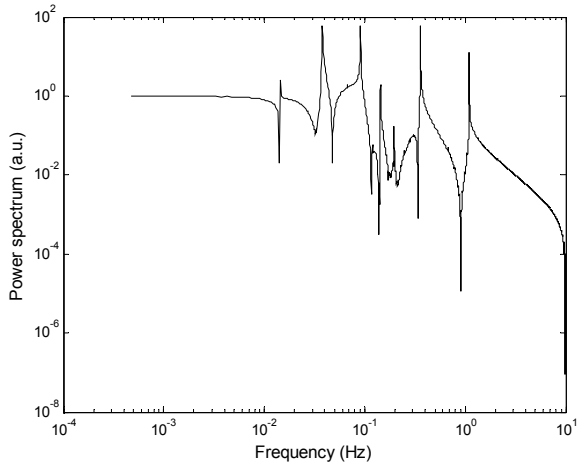


Fig. 1. Power spectrum of a simulated LDF signal obtained with five nonlinear coupled oscillators. Linear coupling is used and $C = 0$.

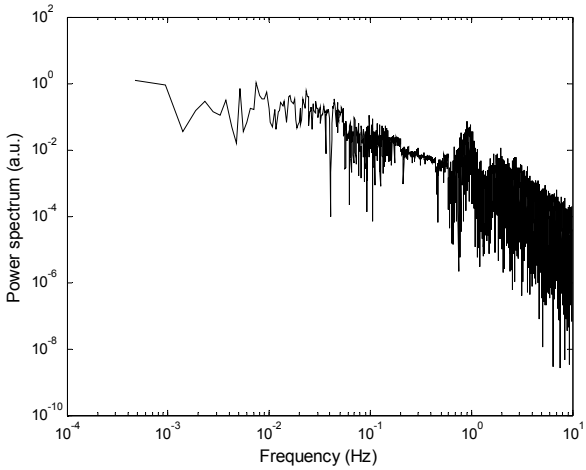


Fig. 2. Power spectrum of a LDF signal recorded on a healthy subject at rest.

difference (relative phase), corresponding to the synchronization, fluctuates in a random way around a constant value. For strong noise, phase slips may occur. Our study on power spectra of simulated data leads to the same conclusion: in order to simulate data behaving close to real LDF signals, the constant $C$ have to be set to a value different from 0.

An improvement in the understanding of the couplings is now necessary for the construction of more complex mathematical models of LDF signals that will provide relevant physiological information. For that purpose, we could add a part of parametric couplings to the linear couplings, or find other more appropriate couplings. Once the knowledge on these couplings adequate, it will become possible to reverse the process, i.e. to diagnose the state of the system from a single measurement of the peripheral blood flow.

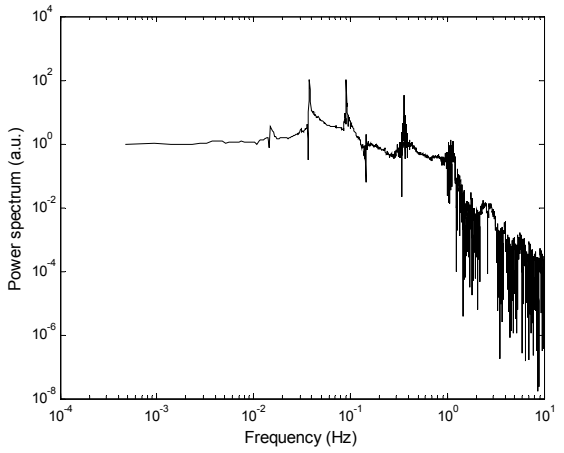


Fig. 3. Power spectrum of a simulated LDF signal obtained with five nonlinear coupled oscillators. Linear coupling is used and $C = 0.4$.

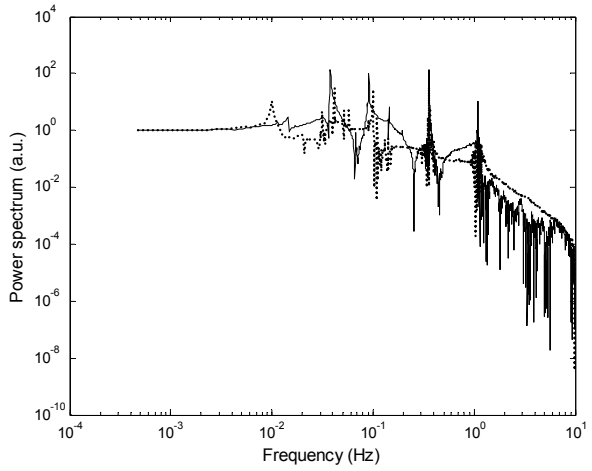


Fig. 4. Power spectra of simulated LDF signals, when linear couplings are chosen (full line), and when parametric couplings are chosen (dotted line). $C = 0.1$ for both couplings.


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## REFERENCES


[1] A. Humeau, W. Steenbergen, H. Nilsson, and T. Strömberg, "Laser Doppler perfusion monitoring and imaging: novel approaches," *Med. Biol. Eng. Comput.*. DOI: 10.1007/s11517-007-0170-5, 2007.

[2] G. E. Nilsson, T. Tenland, and P. Å. Öberg, "A new instrument for continuous measurement of tissue blood flow by light beating spectroscopy," *IEEE Trans. Biomed. Eng.*, vol. BME-27, pp. 12-19, 1980.

[3] G. E. Nilsson, T. Tenland, and P. Å. Öberg, "Evaluation of a laser Doppler flowmeter for measurement of tissue blood flow," *IEEE Trans. Biomed. Eng.*, vol. BME-27, pp. 597-604, 1980.

[4] D. W. Watkins and G. A. Holloway, "An instrument to measure cutaneous blood flow using the Doppler shift of laser light," *IEEE Trans. Biomed. Eng.*, vol. BME-25, pp. 28-33, 1978.

[5] H. D. Kvernmo, A. Stefanovska., K. A. Kirkerboen, and K. Kvernebo, "Oscillations in the human cutaneous blood perfusion signal modified by endothelium-dependent and endothelium-independent vasodilators," *Microvasc. Res.*, vol. 57, pp. 298-309, 1999.

[6] H. D. Kvernmo, A. Stefanovska, M. Bracic, K. A. Kirkerboen, and K. Kvernebo, "Spectral analysis of the laser Doppler perfusion signal in human skin before and after exercise," *Microvasc. Res.*, vol. 56, pp. 173-182, 1998.

[7] A. Bollinger, A. Yanar, U. Hoffmann, and U. K. Franzeck, "Is high-frequency flux motion due to respiration or to vasomotion activity?," in Vasomotion and flow motion. Progress in Applied Microcirculation, C. Allegra, M. Intaglietta, K. Messmer, Basel, Karger, vol. 20, 1993, pp. 52-58.

[8] D. Popivanov, A. Mineva, and J. Dushanova, "Dynamic characteristics of laser-Doppler flux data," *Technology and Health Care*, vol. 7, pp. 205-218, 1999.

[9] T. Söderström, A. Stefanovska, M. Veber, and H. Svensson, "Involvement of sympathetic nerve activity in skin blood flow oscillations in humans," *Am. J. Physiol. Heart Circ. Physiol.*, vol. 284, pp. H1638-H1646, 2003.

[10] A. Stefanovska, M. Bracic, and H. D. Kvernmo, "Wavelet analysis of oscillations in the peripheral blood circulation measured by laser Doppler technique," *IEEE Trans. Biomed. Eng.*, vol. 46, pp. 1230-1239, 1999.

[11] A. Humeau, A. Koïtka, P. Abraham, J. L. Saumet, and J. P. L'Huillier, "Spectral components of laser Doppler flowmetry signals recorded on healthy and type 1 diabetic subjects at rest and during a local and progressive cutaneous pressure application: scalogram analyses," *Phys. Med. Biol.*, vol. 49, pp. 3957-3970, 2004.

[12] A. Stefanovska, D. G. Luchinsky, and P. V. E. McClintock, "Modelling couplings among the oscillators of the cardiovascular system," *Physiol. Meas.*, vol. 22, pp. 551-564, 2001.

[13] A. Stefanovska, M. Bracic Lotric, S. Strle, and H. Haken, "The cardiovascular system as coupled oscillators?," *Physiol. Meas.*, vol. 22, pp. 535-550, 2001.

[14] A. Stefanovska, S. Strle, M. Bracic, and H. Haken, "Model synthesis of the coupled oscillators which regulate human blood flow dynamics," *Nonlinear Phenomena in Complex Systems*, vol. 2, pp. 72-87, 1999.

[15] A. Stefanovska and M. Bracic, "Physics of the human cardiovascular system," *Contemporary Physics*, vol. 40, pp. 31-55, 1999.

[16] M. Bracic Lotric, A Stefanovska, D. Stajer, and V. Urbancic-Rovan, "Spectral components of heart rate variability determined by wavelet analysis," *Physiol. Meas.*, vol. 21, pp. 441-457, 2001.

[17] P. V. E. McClintock and A. Stefanovska, "Noise and determinism in cardiovascular dynamics," *Physica A*, vol. 314, pp. 69-76, 2002.

[18] M. Bracic and A. Stefanovska, "Reconstructing cardiovascular dynamics," *Control Eng. Pract.*, vol. 7, pp. 161-172, 1999.