ISB 2013 BRAZIL
XXIV CONGRESS OF THE INTERNATIONAL SOCIETY OF BIOMECHANICS
XV BRAZILIAN CONGRESS OF BIOMECHANICS

# BLOOD FLOW DYNAMICS CHARACTERISTICS BASED ON PLETHYSMOGRAPHIC MEASUREMENTS

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## SUMMARY
Methods that allow the precocious detection of vascular dysfunction are extremely important for cardiovascular diseases prevention. Macedo et al. [1] proposed a mathematical model of flow decay along time post-reactive hyperemia. The blood flow decay could be explained by a three terms mathematical function: an exponential, a sinusoidal and a constant term. This model was able to identify flow decay differences between pre and post exercise conditions. However, the number of experimental flow data, nine, was considered insufficient by the authors. The present work used the model proposed by [1] in a large number (twenty nine) of flow measurements, and compare the flow behavior among placebo and ibuprofen experimental groups. The exponential term represented appropriately the flow decay. None of the model parameters was able to distinguish vascular function differences among groups.
Keywords: vasomotor control, plethysmography, reactive hyperemia, mathematical modeling

## INTRODUCTION
Vascular diseases have high indexes of morbidity and mortality nowadays. There are evidences that endothelium dysfunction precedes structural blood vessel changes and contributes for atherosclerosis and cardiovascular diseases progression. The endothelium acts on vessel muscle relaxation and contraction, regulating the vessel diameter and flow, with others vascular homeostatic control mechanisms. Thereby, the vascular mechanics study may contribute for integrity vessel evaluation, precocious diagnosis of vessel dysfunction, risk stratification, prevention and treatment of cardiovascular diseases [2].

The methods for vessel mechanics function evaluation use diameter, flow, among others parameters, to infer about vessel function integrity [3, 4]. Though, the behavior of those parameters along time in a dynamic process, while searching the vascular equilibrium, is not evaluated [1, 5]. The three terms mathematical model [1] may be useful to explain flow decay after induced hyperemia. According to the model, after the hyperemia, the flow has an exponential decay, seeking for the system homeostasis. The process of adjust around the optimum flow point was represented by a damped sinusoidal term. A constant was used to represent the basal flow of the vessel system (Equation 1).

$$y = k_1 e^{-\alpha_1 t} + k_2 e^{-\alpha_2 t} \cos(\omega t + th) + k_3 \quad (1)$$

were $k_1$ and $\alpha_1$ are, respectively, the exponential amplitude and the decay rate. $k_2$, $\alpha_2$, $\omega$ and $th$ are, respectively, the amplitude, the damping rate, the frequency and the phase of the oscillatory function, and $k_3$ is an estimate of basal flow. The units are: ml/ 100 ml of tissue / min to $k_1$, $k_2$ e $k_3$; $sec^{-1}$ to $\alpha_1$ and $\alpha_2$; Hz to $\omega$ and degrees to $th$ [1].

The study goals are evaluate this model performance, considering a large number of flow information and to analyze the model capability in distinguish vasomotor changes induced by ibuprofen anti-inflammatory drug.

## METHODS
After the exclusion criteria application (smoking, hypertension, hypercholesterolemia, use of psychoactive, antihypertensive or bronchodilator drugs, cardiovascular diseases and chronic diseases in treatment), the study sample was two groups with seven volunteer each.

Plethysmographic signals were obtained before and two hours after the placebo or 1800 mg ibuprofen administration. The protocol was approved by Fluminense Federal University Ethics Committee. The reactive hyperemia was induced through a five minutes suppression of the forearm blood flow circulation, by a cuff located around the arm and insufflated at 200 mmHg.

After the five minutes ischemia, the pressure of the cuff was released. Then, forearm volume changes were registered by plethysmography (Hokanson, USA), for five more minutes. The arterial influx, and consequently the volume change, occurs when a cuff pressure of 50 mmHg (above the venous and below the arterial pressure) is applied. The selective venous occlusion was proceed for five seconds, being released for the five subsequent seconds, resulting in a rate of 1 flow data at each 10 sec.

Twenty nine flow values were obtained, for each subject in each experimental condition, as a derivate of the volumes waveforms. The equation fitted each temporal flow series, using the Nelder Mead Simplex, a Matlab® subroutine.

The variance analysis and the Dunns post-hoc test were used. A p-value of 0.05 was considered. The phase (*th*) was used to adjust the oscillatory term and it was not considered for statistic analysis.

## RESULTS AND DISCUSSION

A flow data fitting is represented in Figure 1. The mean values of the equation's parameters for the experimental groups are presented in Table 1.

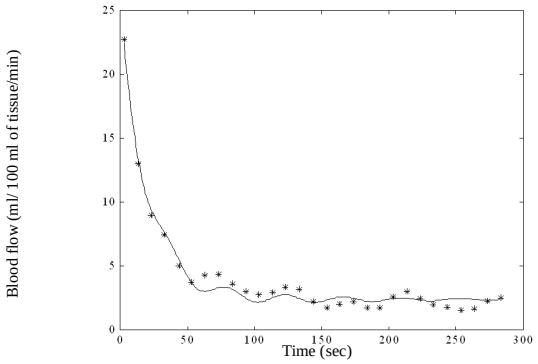


**Figure 1**: Typical plots for the temporal flow series and fitted function.

Table 1: Equation 1 estimated parameters, mean (standard deviation) for the experimental groups.

| Exponential term | $k_1$ | $\alpha_1$ | $k_3$ |
|---|---|---|---|
| Pre placebo | 19.4 (6.2) | 0.036 (0.01) | 2.3 (0.7) |
| Post placebo | 18.5 (5.5) | 0.040 (0.03) | 2.7 (1.0) |
| Pre ibuprofen | 21.9 (16.7) | 0.046 (0.01) | 2.1 (0.3) |
| Post ibuprofen | 19.0 (6.1) | 0.037 (0.01) | 2.4 (0.9) |
| *p-value* | 0.94 | 0.22 | 0.68 |
| Sinusoidal term | $k_2$ | $\alpha_2$ | $\omega$ |
| Pre placebo | 5.1 (3.5) | 0.041 (0.022) | 0.021 (0.008) |
| Post placebo | 3.1(3.5) | 0.023 (0.025) | 0.019 (0.006) |
| Pre ibuprofen | 7.3 (12.6) | 0.032 (0.026) | 0.023 (0.007) |
| Post ibuprofen | 6.2 (5.9) | 0.044 (0.040) | 0.021 (0.010) |
| *p-value* | 0.51 | 0.44 | 0.55 |

Exponential term*:* $k_1$ (amplitude); $\alpha_1$ (decay), $k_3$ (constant). Oscillatory term: $k_2$ (amplitude); $\alpha_2$ (damping rate); $\omega$ (frequency in Hz). The $k_1$, $k_2$ and $k_3$ are expressed in ml/ 100 ml of tissue / min; $\alpha_1$ and $\alpha_2$ are in $sec^{-1}$ units.

The plethysmography protocol increased flow temporal series from nine to twenty nine, through a sample period redution from 20 to 10 sec and a long aquisition time, from 3 to 5 min, comparing to [1]. Those changes provided a better fitting, as predicted by [1]. This protocol with a greater number of data was used by [5]. Comparing normals (pre stimuli) of [1] and [5], the present study has a mean exponential decay rate similar to [5], and two times greater than [1], showing a slower decay which can not be seen with small temporal flow series.

The overall root square mean (RMS) error was 0.35 ml/ 100 ml of tissue/ min. The RMS error on the equation fitting experimental data was considered small and it was similar to [5] and twice the presented (0.18 ml/ 100 ml of tissue/ min) by [1]. Macedo et al. [5] suggest that the larger flow temporal series reveal more than one oscilatory frequency, getting the RMS error worse. The biofeedback mechanism inference, while seeking the vessel system equilibrium post reactive hyperemia, seems more adequate in frequency domain. However, plethysmography protocols do not allow frequency analysis because of the flow estimated through three heart beats [1], making the sample rate augment beyond the used in this study unfeasible.

This study did not show functional differences between placebo and ibuprofen groups. Ibuprofen is an nonsteroide antiinflamatory and it was used as vasoconstrictor stimuli. The small sample was a limitation of the study. For future pletismography studies, we suggest to use only the exponential term as flow decay descriptor. The oscillatory feedback mechanism probabily can be studied in frequency domain, which requires flow acquisition sample rates not possibles with current plethysmography methods and tecniques.

## CONCLUSIONS

Considering the mathematical model used, there were no changes in dynamic flow decay along time post reactive hyperemia with ibuprofen administration. The exponential equation term seems to describe adequately flow decay in those circumstances, considering flow temporal series of 29 measurements. Although, the oscillatory term was not adequate because considers just one frequency for the biological feedback mechanism.


## ACKNOWLEDGEMENTS

To the National Council of Technological Scientific Development (CNPQ) and to the Federal Institute of Education, Science and Technology of Rio de Janeiro (IFRJ) for the financial support. To the Exercise's Science Lab (LACE/UFF) for the instrumental support.


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