TRANSFER FUNCTION OF THE HEART RATE CONTROL SYSTEM WITH RESPIRATORY INPUT

The Classical Engineering Approach

Evgeny G. Vaschillo and Bronya Vaschillo
Center of Alcohol Studies, Rutgers, The State University of New Jersey, 607 Allison Road, Piscataway, NJ 08854, U.S.A.

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Abstract: The classic "control system theory" approach was used to find the transfer function (TF) of the HR control system with respiratory input. Eight healthy subjects, ages 19–40 participated in the study. Paced breathing at seven frequencies in 0.5– 0.04 Hz range was used as sine-wave stimuli to assess the HR control system. The sine-wave HR oscillation in response to each stimulus as the system's output was recorded. Amplitude and phase TFs were calculated for each frequency separately. The Fourier filtration procedure was used for TF calculation. Experimentally obtained TFs revealed the same important features in all participants: 1) the amplitude TF had its peak in a narrow frequency range around 0.1 Hz; 2) the phase TF successively changed from positive to negative when breathing frequency increased, and passed "0" at frequency where the amplitude TF peaked; 3) the peak frequency and magnitude were unique for each participant. These features are evidence for the resonance property of the HR control system at a frequency around 0.1 Hz. This study suggests that accurate identification of an individual's resonance frequency can be found using the TF features of HR control system and controlled breathing techniques.

1 INTRODUCTION

Respiratory activity continually perturbs the cardiovascular system. Respiration modulates the activity of most sympathetic and vagal efferents through direct coupling between the respiratory and autonomic centers and through modulation of central sensitivity to baroreceptors and other afferent inputs (Clynes, 1960; Saul et al., 1991). The autonomic efferents, in turn, modulate peripheral vascular resistance, heart rate (HR), and other autonomic functions with respiratory periodicities. Thus, respiration appears to actively participate in autonomic and, in particular, HR regulation through a very complex multiple-loops control system. Respiration is a voluntary, controllable function and thus can be exploited by researchers and clinicians to develop novel approaches for correcting abnormal autonomic regulation. For example, heart rate variability (HRV) biofeedback can be used to normalize autonomic regulation, increase baroreflex gain and peak expiratory flow (Lehrer et al., 2003), and treat asthma (Lehrer et al., 2004), major depression (Karavidas et al., 2007), fibromyalgia (Hassett et al., 2007), neurosis (Chernigovskaya et al., 1990), and hypertension (McCrady et al., 2001). Autonomic variability as well as the frequency dependence of autonomic reactions to respiration are critical factors in the development of such methods. Accordingly, the classic engineering approach may be useful in furthering our knowledge of this system's features.

The goal of this study is to assess the transfer functions (TF) of the HR control system, using breathing as the forcing function and heart rate as the system response.

2 METHOD

The classic "control system theory" approach was used to examine the transfer function of the HR control system with respiration input. Sine-wave stimuli of various frequencies were sent in-series to the input of the system. The sine-wave HR oscillation in response to each frequency stimulus was recorded as the system's output. Amplitude (ratio of the amplitudes of the output and input sine-wave signals) and phase (phase shift between the

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sine-wave signals) transfer functions were calculated separately for each frequency.

2.1 Participants and Procedure

Eight healthy subjects (5 males and 3 females), ages 19 – 40 (average 27.5) participated in the study. The experimental session lasted one hour. Before the session each participant was taught to breathe slowly but not too deeply. A sine-wave pacer as well as the participant's current respiration curve were presented on a computer screen. The participant was instructed to follow the pacer with his/her breathing such that his/her respiration curve precisely copied the pacer's amplitude and frequency. During the experiment participants performed 7 paced breathing tasks at 7 randomly presented frequencies (0.5, 0.25, 0.143, 0.11, 0.077, 0.055, and 0.04 Hz, which corresponded to 30, 15, 5.6, 6.6, 4.6, 3.3, and 2.4 breaths per minute). Each task included at least 10 breaths and lasted for 3-5 minutes with 2 minutes break between them. The amplitude of the pacer's sine-wave curve was the same at all frequencies and corresponded to approximately 1050 ml of tidal volume to provide relatively comfortable breathing without hyperventilation.

2.2 Physiological Record

A J&J Engineering (Poulsbo, WA) I-330 DSP-12 physiograph was used to collect electrocardiogram (ECG) and respiration data. ECG data were collected from electrodes on the right arm and left leg (Lead II), digitized at the rate of 1024 Hz. A respiration strain gauge belt was attached around the participant's chest. Respiration and pacer sine-wave curves were digitized at the rate of 4 Hz. Physiological data were collected during the whole experiment and divided by tasks for data analysis.

2.3 Data Analysis

Beat-to-beat RR intervals (RRI) of the ECG signal were measured and recalculated to heart rate [beats per minute]. Cubic interpolation of the non-equidistance HR sequence was completed, and the HR curve was re-sampled at the rate of 4 Hz. The TFs were calculated separately at each tested frequency. The Fourier filtration algorithm (Eykhoff, 1974; Vaschillo et al., 2002) was applied for TF calculation because it allowed more precise and easy estimation of the amplitude and phase relation between two sine-wave signals than cross-spectral Fourier analysis. The algorithm was used to compute two auxiliary TFs: (1) between the pacer as the input and respiration as the output [TF(pr-resp)], and (2) between the pacer as the input and HR as the output [TF(pr-HR)]. This study targeted the TF of the HR control system [TF(resp-HR)], which was calculated by dividing TF(pr-HR) by TF(pr-resp), i.e. by dividing the TF amplitudes and subtraction of the TF phases.

3 RESULTS

The paced breathing exercise resulted in the sine-wave oscillation in the participant's HR paralleling the sine-wave respiration curve. The amplitude and phase relation between the pacer curve, respiration curve, and sine-wave HR oscillation was strongly dependent on pacer frequency.

3.1 Transfer Function of the Paced Breathing

The TF(pr-resp) that reflects the participant's ability for precise pacer breathing is illustrated in Figure 1. Participants were able to accurately maintain the depth of breathing requested by the pacer, but always preceded the pacer when asked to breathe at a rate of less than 18 breaths per minute.

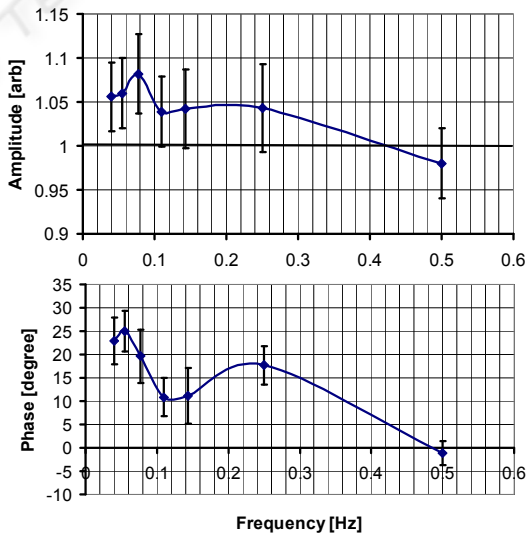

Figure 1: Transfer function of the paced breathing TF(pr-resp) averaged across 8 participants: input – pacer, output – respiration. Equality of the pacer and respiration curve amplitudes correspond to value "1" of the amplitude TF(pr-resp). Positive phase means that respiration preceded the pacer.

3.2 Transfer Function between the Pacer and Heart Rate (Auxiliary)

Figure 2 presents the auxiliary TF(pr-HR), which does not have any physiological meaning but is necessary to calculate the targeted TF of the HR control system in the Fourier filtration procedure.

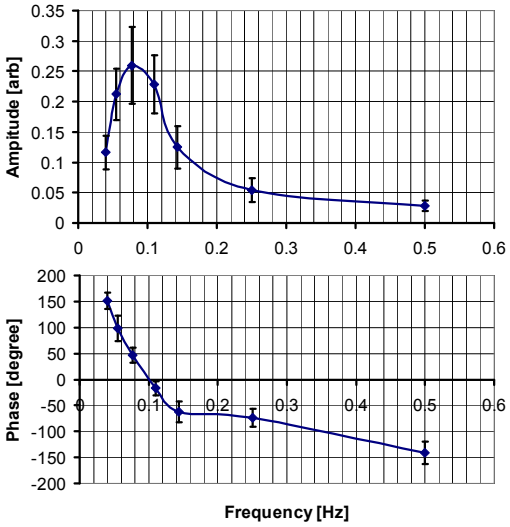

Figure 2: Transfer function TF(pr-HR) averaged across 8 participants: input – pacer, output – heart rate.

3.3 Transfer Function of the Heart Rate Control System

Figure 3 presents TF(resp-HR) and shows how respiration affected HR. HR response to respiration was strongest when participants were breathing at frequencies around 0.1 Hz. Full synchronization of sine-wave HR oscillation with respiration (phase TF (resp-HR) is 0˚) occurred at only one frequency, named as resonance frequency. At this frequency, the amplitude of the TF(resp-HR) reached its maximum. The HR curve preceded the respiration curve at frequencies lower than the resonance frequency and lagged behind the respiration curve at frequencies higher than the resonance frequency. Individual TF(resp-HR) graphs are presented in the appendix; these figures show that the resonance frequency and HR oscillation amplitude at resonance frequency were unique for each participant.

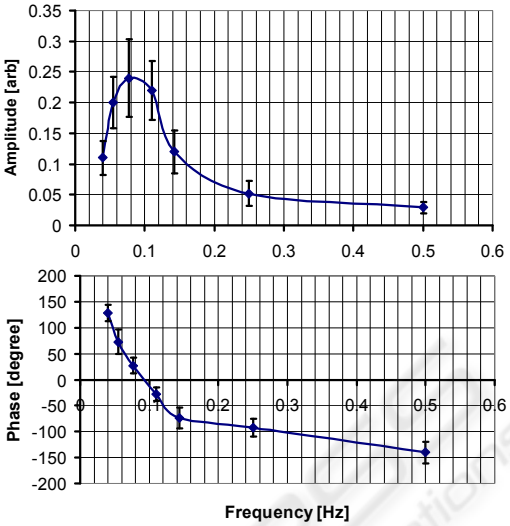

Figure 3: Transfer function of the HR control system TF(resp-HR) averaged across 8 participants: input – respiration, and output – heart rate. The amplitude of the TF(resp-HR) shows the amplitude of sine-wave HR oscillation elicited by respiration at the corresponding frequency. The zero phase of the TF(resp-HR) corresponds to full synchronization of respiration with the sine-wave HR oscillation; that is, HR goes up with inhalation and down with exhalation.

4 DISCUSSION

The Amplitude and Phase Transfer Functions of the HR control system [TF(resp-HR)] that were found in this study reflect the relationship between respiration and HR oscillation in 0.04-0.5 Hz frequency range. As illustrated by the TF(resp-HR), the amplitude of the respiration-dependent HR oscillations and the phase between the HR oscillation and respiration curves both depend on respiration frequency.

While the present amplitude TF findings are consistent with the results of other studies (Angelone and Coulter, 1963), (Cook et al., 1998), (Hirsch and Bishop, 1981), (Saul et al., 1991), the phase TF findings reported herein are only partially supported by prior research. These results are in close agreement with the sympathetically-controlled TFs reported by Saul et al. (1991). However, they differ from Angelone and Coulter (1963), who found that respiration and HR oscillation were in phase at frequencies lower than 0.05 Hz and, that at ~0.1 Hz, the phase angle was about -90º. They also differ from Eckberg (1983) who reported the 0º phase between respiration and HR oscillation occurred at the ~0.2 Hz frequency.

These discrepancies can be explained in part by the findings of Saul et al. (1991) who noted a dramatic difference between the TF(resp-HR) that is only under sympathetic control (parasympathetic blockade) and the TF that is under vagal control. Indeed, most prior studies, including Angelone and Coulter (1963) and Eckberg (1983), did not control sympathetic and vagal activity in their studies. In the present study, the paced breathing procedure was challenging enough to activate sympathetic and depress parasympathetic systems. Moreover, discrepancies may exist due to the use of cross-spectral Fourier analysis in these earlier studies, which may not have provided accurate phase estimation. The present study used more precise Fourier filtration procedures to estimate phase relations, and was thus able to obtain individual TFs that were stable for all participants.

The TF(resp-HR)s reported in our study consistently demonstrated that: 1) the amplitude TF has its peak in a narrow frequency range around 0.1 Hz; 2) the phase TF successively changed from positive to negative when breathing frequency increased, and passed "0º" at same frequency where the amplitude TF peaked; 3) the frequency and magnitude of the peak were unique for each participant. These findings lend support for the identification of the resonance property of the HR control system at a frequency of approximately 0.1 Hz.

It is known that HR baroreflex closed-loop provides the ~0.1 Hz resonance properties in the HR control system (Cevese et al., 2001), (Vaschillo, Vaschillo, & Lehrer, 2006). Earlier studies showed that HR resonance can be triggered not only by respiration, but by other rhythmical stimuli, such as rhythmical emotional stimulation (Vaschillo et al., 2008) or rhythmical muscle tension (Vaschillo et al., 2007). This suggests that the resonance property of the HR control system does not depend on respiration and the TF(resp-HR) reflects properties of the HR baroreflex.

The studies also revealed that the ~0.1 Hz resonance oscillation in HR usually is accompanied by the same frequency high amplitude oscillation in other cardiovascular functions (e.g., in arterial blood pressure and in vessel tone (Cooke et al., 1998; Lehrer et al., 2003, 2004).

HRV biofeedback is used to train participants to control breathing such that they can harness the 0.1 Hz resonance in the cardiovascular system. The therapeutic effects of HRV biofeedback occur as the result of generalized high-amplitude oscillations in autonomic functions elicited by the biofeedback procedure (Chernigovskaya et al., 1990; Lehrer et al., 2003, 2004). These oscillations train autonomic reflexes, and systematic training of autonomic reflexes normalizes and improves autonomic regulation. To maximize oscillations and, accordingly, the therapeutic effects of biofeedback, the patient's precise resonance frequency should be determined; however this historically has been difficult to assess (Vaschillo, et al., 2002, 2006). This study suggests that knowledge of the TF(resp-HR) features and the use of controlled breathing techniques may allow more accurate identification of an individual's resonance frequency.

5 CONCLUSIONS

Classical control system theory applied to the investigation of physiological systems can be a useful tool for the medical practice. Physiological systems function via closed-loop reflexes within a very narrow frequency range, thereby suggesting that application of sine-wave stimuli with Fourier filtration procedure may be more effective for testing such systems than multi-frequency stimuli with the cross-spectral Fourier analysis.

ACKNOWLEDGEMENTS

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REFERENCES

Angelone, A., & Coulter, N. A. Jr., 1964. Respiratory sinus arrhythmia: A frequency depended phenomenon. *Journal of Applied Physiology*, *19,* 479–82.

Chernigovskaya, N. V., Vaschillo, E. G., Rusanovsky, B. B., & Kashkarova, O. E., 1990. Instrumental autotraining of mechanisms for cardiovascular function regulation in treatment of neurotics. *The SS Korsakov's Journal of Neuropathology and Psychiatry*, *90,* 24–28.

Cevese A, Gulli G, Polati E, Gottin L, Grasso R. 2001. Baroreflex and oscillation of heart period at 0.1 Hz studied by alpha-blockade and cross-spectral analysis in healthy humans. *The Journal of Physiology*. *15*; 531(Pt1); 235-244.

Clynes, M., 1960. Respiratory sinus arrhythmia: laws derived from computer simulation. *Journal of Applied Physiology,15(5):* 863-874.

Cooke, W. H., Cox, J. F., Diedrich, A. M., Taylor, J. A., Beightol, L. A., Ames, J. E. 4th, Hoag, J. B., Seidel, H., & Eckberg, D. L., 1998. Controlled breathing protocols probe human autonomic cardiovascular rhythms. *American Journal of Physiology*, *274*(2 Pt 2), H709–18.

Eckberg, D.L., 1983. Human sinus arrhythmia as an index of vagal cardiac outflow. *Journal of Applied Physiology, 54,* 961-966.

Eykhoff P., 1974. *The book*, System identification: parameter and state estimation. Chichester, England:. Wiley, 555 p.

Hassett, A.L, Radvanski, D.C., Vaschillo, E., Vaschillo, B., Sigal, L., Karavidas, M., Buyske, S., Lehrer, P.M., 2007. A pilot study of the efficacy of heart rate variability biofeedback in patients with fibromyalgia syndrome. *Applied Psychophysiology and Biofeedback*, *32(1): 1-10.*

Hirsh, J.N., and Bishop, B., 1981. Respiratory sinus arrhythmia in humans:how breathing pattern modulates heart rate. *American Jurnal of Physiology, 241(10): 620-629.*

Karavidas, M.K., Lehrer, P.M., Vaschillo, E., Vaschillo, B., Marin, H., Buyske, S., Radvanski, D., Hasset, A., 2007. Preliminary results of an open label study of heart rate variability for the treatment of major depression. *Applied Psychophysiology and Biofeedback, 32(1): 19-30.*

Lehrer, P. M., Vaschillo, E., Vaschillo, B., Lu, S. E., Eckberg, D. L., Edelberg, R., Shih, W. J., Lin, Y., Kuusela, T. A., Tahvanainen, K. U. O., & Hamer, R., 2003. Heart rate variability biofeedback increases baroreflex gain and peak expiratory flow. *Psychosomatic Medicine*, *65,* 796–805.

Lehrer, P., Vaschillo, E., Vaschillo, B., Lu, S., Scardella, A., Siddique, M., & Habib, R., 2004. Biofeedback treatment for asthma. *Chest*, *126,* 352–361.

McCraty, R., Atkinson, M., & Tomasino, D., 2003. Impact of a workplace stress reduction program on blood pressure and emotional health in hypertensive employees. *The Journal of Complementary and Alternative Medicine*, *9,* 355–369.

Saul, J. P., Berger, R. D., Albrecht, P., Stein, S. P., Chen, M. H., Cohen, R. J., 1991. Transfer function analysis of the circulation: unique insights into cardiovascular regulation. *American Journal of Physiology*, *261*(4 Pt 2), H1231–1245.

Vaschillo, E.G., Bates, M.E., Vaschillo, B., Lehrer, P., Udo, T., Mun, E.Y., & Ray, S., 2008. Heart rate variability response to alcohol, placebo, and emotional picture cue challenges: Effects of 0.1 Hz stimulation. *Psychophysiology*, *45(5),* 847-858.

Vaschillo, E., Vaschillo, B., Bates, M.E., Lehrer, P., France, Ch., & Trost, Z. Rhythmical muscle tension mimics heart rate variability biofeedback. 2007. Applied Psychophysiology and Biofeedback. 32(2), 132-133.

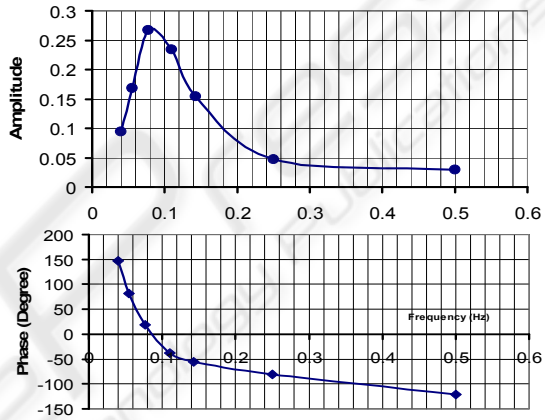
Vaschillo, E., Vaschillo, B., & Lehrer, P., 2006. Characteristics of resonance in heart rate variability stimulated by biofeedback. *Applied Psychophysiology and Biofeedback, 31(2,* 129-142.

Vaschillo, E., Lehrer, P., Rishe, N., & Konstantinov, M., 2002. Heart rate variability biofeedback as a method for assessing baroreflex function: a preliminary study of resonance in the cardiovascular system. *Applied Psychophysiology and Biofeedback*, *27,* 1–27.

APPENDIX

Individual Transfer Functions for 8 Participants

Participant A



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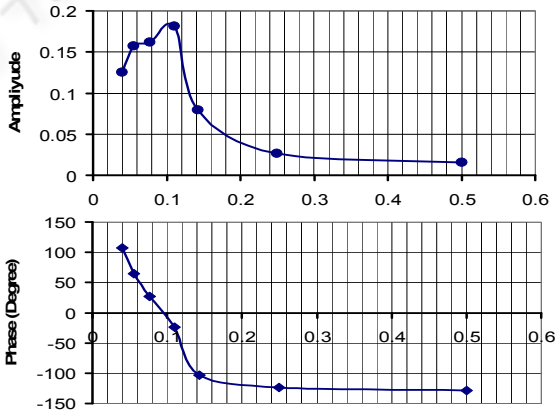

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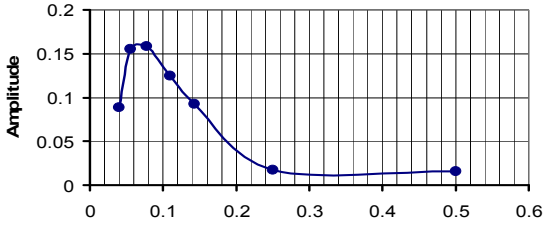

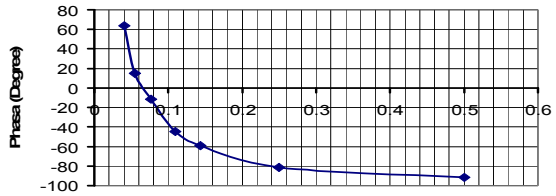

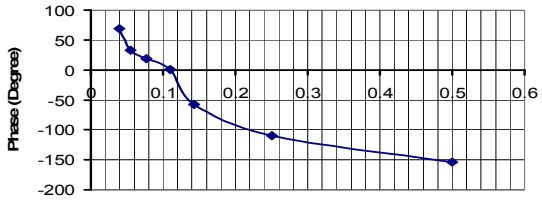

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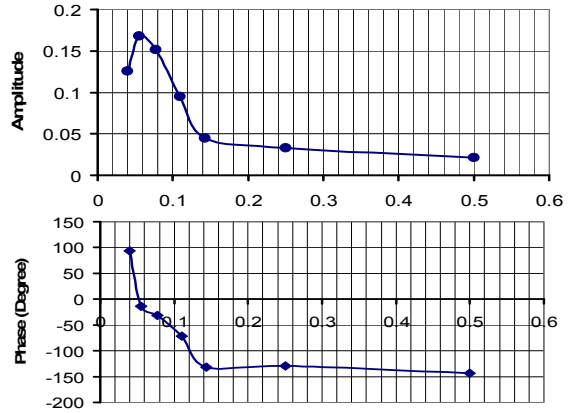

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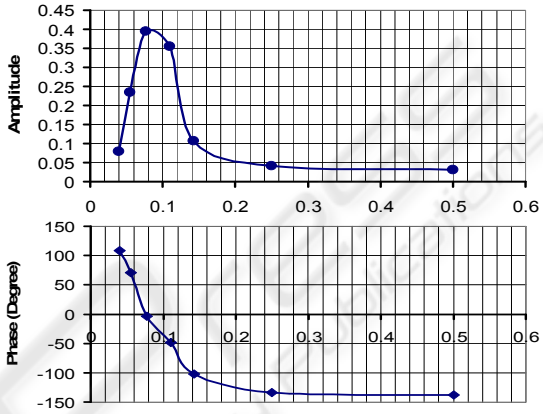

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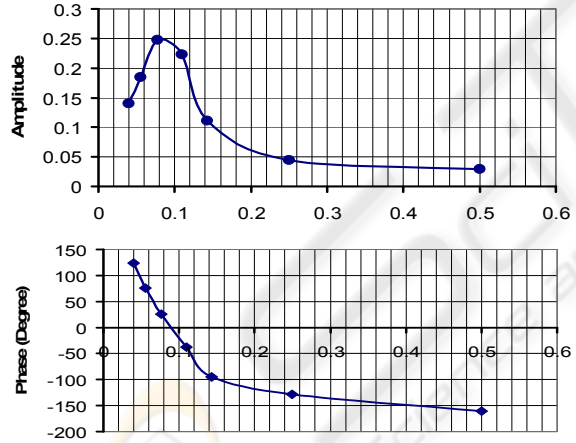

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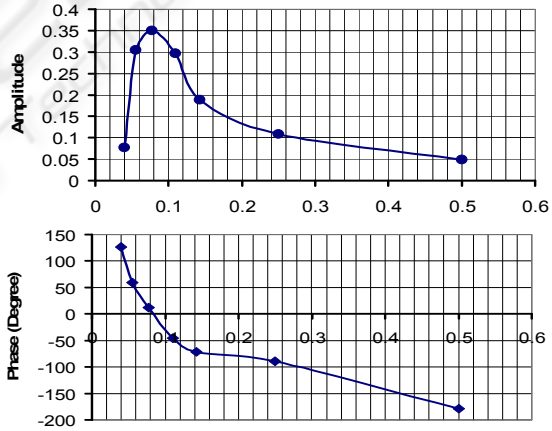

Participant F