Review:
Theory and Applications of the Harmonic Analysis of Arterial Pressure Pulse Waves

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Abstract

Pulse wave analysis is widely used to monitor cardiovascular diseases. Our previous studies have shown the arterial pressure wave drives the blood into tissue. The output from the heart, which generates the harmonics of the heartbeat, and the matching condition of the heart with the arterial system are mutually influenced to generate the harmonic spectrum of pulse wave. Here we review experimental work using harmonic analysis and extend the method to some popular studies of hypertension. The results show that the pressure pulse wave distributes blood throughout the body, and monitoring it provides useful information about the health condition of an individual.

Keywords: Blood distribution, Pulse, Chinese medicine

1. Introduction

In a recent review, O'Rourke et al. [1] concluded that pulse wave analysis (PWA) could provide a better understanding of hypertension as well as help in establishing the extent of cardiovascular disease and in monitoring the effects of therapies. Many researchers consider PWA to be a noninvasive, simple, and informative technique for arterial assessment in which the central arterial blood pressure (BP) can be estimated from the brachial BP. However, there is still no consensus about the validity of the technique [2].

Murgo [3] pointed out that the arterial pressure results from interactions between the heart and the arterial system, so that the shape of the pressure pulse will be affected by changes in the peripheral circulation or alterations in cardiac function. Fourier analysis has also been used to study the pulsatile pressure and flow [4].

The "pulse feeling" of peripheral arteries has been used as a diagnostic method for more than 3000 years in traditional Chinese medicine. Motivated by modern studies of hemodynamics, Wang [5] proposed that the pressure pulse drives blood circulation and that decomposing it into harmonic components could reveal information about the circulation of the whole body in terms of different meridians.

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This article discusses the BP propagation equation based on radial movement of the arterial wall, and pressure driven by the repeated heart beat is suggested to distribute blood. With the harmonics of the heartbeat being the main frequency components in the propagated pressure wave, harmonic analysis becomes the method of choice. Studies using harmonic analysis for diverse applications are summarized, and how this method is related to "pulse feeling" is discussed.

2. Propagated pressure as the main energy source of blood irrigation

2.1 Problems in prevailing pressure – flow wave models

Prevailing pressure – flow wave models do not describe the arterial pressure wave properly. Studies of the governing equation for the pulse wave in arteries can be traced back to the seventeenth century. Most current studies consider that axial blood flow Q is driven by the gradient of pressure P, and many different forms of the resulting PQ wave equation arising from the Navier-Stokes equation have been derived to describe the pressure wave in large arteries [6]. We have defined all those theoretical models as PQ wave model [7].

Based on the PQ wave model, McDonald [4] considered that the presence of standing waves in the blood vessels—as proposed by others [8]—was physically impossible due to the reflected PQ wave being strongly damped when traveling between reflection sites. Many subsequent studies on PWA of the arterial system have treated the measured pressure and flow waves as the sum of a small number of forward- and backward-traveling waves [9]. However, we found that resonance is an important but hitherto neglected phenomenon in hemodynamics [10,11].

If periodic injections of blood from the left ventricle could generate only traveling waves in the arterial system, forced stationary oscillations of the whole arterial system would be unattainable, and it would be very unlikely that the pulse pressure could reveal information about the resonance conditions of the whole body in a systematic manner.

Starting from the equation of motion of an arterial unit in the axial direction, we derived a general axial momentum equation for blood inside an artery with a transversely vibrating elastic wall. The arterial system has a high pressure and low elastic modulus. The distributed transverse motion of the arterial wall generates a radius gradient that exerts axial forces, which are not negligible, on the blood. Most of the prevailing PQ wave models initially ignore forces arising from the vibrating wall and assume that axial flow Q is driven only by the gradient of pressure P. Thus, the blood is considered to be the only medium supporting the back-and-forth longitudinal wave propagation, with the elastic arterial wall considered merely as its boundary. We have demonstrated that such PQ wave models do not properly describe the pressure wave in large arteries [7].

2.2 PS wave mode in large arteries

The PS wave mode is the major wave mode in large arteries. We have proposed a different wave model, called the radial vibration model [12,13]. In this model, the periodic ejection of blood from the heart produces a pulsatile pressure wave P that drives the vibration of the arterial wall and thereby causes an oscillation of cross-sectional area S of the artery. We called this vibration mode the PS wave mode [7].

We have previously compared the transverse elastic PS wave and the longitudinal fluid PQ wave [7]. Based on physical and physiological considerations, we concluded that the transverse wave is the dominant wave mode in large arteries and that the pulse wave cannot be governed by the PQ wave equation alone. It is only at the end of the arterial system—the microcirculation, where the arterial wall is very stiff, that the pressure gradient drives the blood into the highly resistive arterioles. If the wave was mainly carried by the blood in arteries, viscous effects due to the back-and-forth movement of the blood that carried all the energy in the kinetic form would be very large. In contrast, a transverse PS wave carried by the propagating oscillation of elastic arterial walls suffers much lower attenuation.

2.3 PS wave governed by pressure wave equation

The PS wave is governed by the pressure wave equation with the total energy. An artery in its natural position is always subject to large longitudinal stress, but its effects have seldom been addressed. Starting from the equation of motion of an arterial unit in the radial direction, we constructed a pressure wave equation with the total energy [13] – it considers the arterial wall and blood to be one system; and the PS wave becomes dominant. The final equation indicates that the longitudinal stress is essential to wave propagation and that the phase velocity is related to the longitudinal tension and shear modulus of the arterial wall. This equation is analogous to a one-dimensional transverse string wave, with cross-sectional area S playing the role of the transverse displacement. Most of the energy is stored and transmitted along the arterial wall as potential energy. This is also true in physiology, where Milnor found more than 98% of the energy is stored as potential energy [6]. The relative blood flow within the artery is minimized.

For the PQ wave mode, a large amount of energy is wasted in pulsatile pressure and flow [6,9] due to the high viscosity associated with back-and-forth blood flow in the artery. It can hardly be excited physically and to be exist in animal. There is no reason for it to survive the evolution**.**

2.4 Decomposition of pulse wave in whole arterial system

The pulse wave in the whole arterial system can be decomposed into many distributed stationary waves associated with the harmonic components of the periodic force exerted by the heart. We used Bernoulli's oscillatory method to analyze pulse waves in the ventricular-arterial coupling system [14]. Solving the PS wave equation revealed that in the steady state, the pressure response to a harmonic force can be represented as a sum of stationary oscillatory waves. These waves are the eigenmodes of the whole arterial system, which is characterized by a set of natural frequencies that are related to the eigenvalues and the wave velocity. The arterial system can be considered to be analogous to a damped drum whose drumhead is the elastic arterial wall. The natural frequencies of this system depend on the physiological structure of the arterial system and the Sturm-Liouville boundary conditions [14].

The response of the pulse wave depends on the driving force generated by the heart and the matching condition between the heart rate (HR) and the natural frequencies of the arterial system [14]. If the frequency of the input force is near one of the natural frequencies, the pressure amplitude of the corresponding eigenmode is greatly enhanced–we may call this a frequency-matching condition between the heart and the main arterial system. The input force from the heart contains many harmonic components, and all of the eigenmodes with eigenfrequencies near one of the harmonic components of the input will be significantly excited in the whole arterial system. A perfect matching with the highest efficiency of power transmission to the arterial system is attained if the natural frequencies are integral multiples of the HR [14,15].

2.5 Resonance between the heart and the organs

An organ is influenced by not only the input pulsatile blood but also the harmonic driving force, both of which are proportional to the pulse pressure at the connecting site of the local main artery. Stacy and Giles [16] related input force F_i to the peripheral pressure of an organ, P_{org}, as

$$F_i = a\frac{\partial^2 P_{org}}{\partial t^2} + b\frac{\partial P_{org}}{\partial t} + cP_{org} \quad (1)$$

The first term on the right-hand side of the equation is the inertial effect due to the intermediate column of blood, the second term is the frictional effect due to the viscous properties of the fluid, and the third term is an elastic coupling arising from the distensible properties of the vessel. Hence, we assumed that each internal organ can be lumped as a Windkessel unit or a resonator with its own characteristic natural frequencies [17].

To a first-order approximation, we assumed that the main arterial system and the organs are separate systems that interact with each other only via the connecting arterial side branches [17]. The periodic blood input from the main artery provides the connecting side branches with the power needed to transport the blood to the organs.

The main artery provides forces at all harmonic frequencies, and the organ can be considered an antenna and will undergo a forced oscillation. The response will be largest when the natural frequency of the organ is near any of the frequencies of the input force–we call this the resonance of the organ with the heart.

Since the main artery is connected with the organ via a side branch artery, the organ will react to the pressure from the main artery as a resonator that delivers some energy back to the main artery. This pressure force is proportional to pressure P_{org} of the organ, and its harmonic components will also have a maximum value near the natural frequencies of the particular organ.

We have previously shown theoretically [15] that the frequency matching of the organ with a harmonic mode of the heart will influence pressure components all the way down to peripheral arteries. If the resonance property of the organ deviates from its normal value due to illness so that its natural frequency is shifted away from a particular harmonic component of the force source, or if the resistance of the organ increases, there will be a significant change in the spectrum of the pressure pulse of the whole artery. This will also reduce the efficiency of blood distribution into particular organs.

The fundamental concept of our theory is that pressure drives the blood into organs or tissue. This conjecture is supported by experiments [18,19] showing that the blood flow into the tissue supplied by arterioles will be larger when the pressure is higher, with both amplitude and phase-matching playing important roles. Thus, the pressure wave propagation equation (the PS equation) properly describes the transportation and distribution of blood throughout the body. Since harmonic pressure waves have quite large wavelengths, they will detect the resonance condition of related organs and thus give away the health condition of these organs. Large wavelength also enables animals to move, because bending, twisting of the limbs as well as body will not significantly hinder the propagation of this wave.

3. Experimental results using harmonic analysis of pulse waves

Most studies of pulse waves have focused on analyzing the pulses in either the time domain [9,20,21] or the frequency domain [4,6,22,23]. We propose that harmonic analysis of pulse waves can reveal additional information. Some of our experimental results are summarized below.

3.1 Frequency characteristics of organs

An in vivo study of rats [24-27] revealed that ligating one or both of the renal arteries significantly reduced the second harmonic component of the pressure pulse at the caudate artery. Ligating the artery toward to the spleen prominently reduced the third harmonic component of the pulse. Analysis of the harmonics in the spectrum of the arterial pressure wave revealed that individual organs might have their own natural frequencies. Young et al. [24] further showed that the effects of organ ligation were linearly additive. Ligating two different arterial beds simultaneously changed the pulse spectrum in a manner similar to directly adding the two spectrums resulting from ligating each arterial bed individually. These studies suggested that individual vascular beds exert independent, frequency-specific, and linearly additive effects on the peripheral pressure wave, and hence that simple arithmetic may be used to determine the contribution of each organ to the pressure spectrum. These properties mean that simple harmonic analyses of the peripheral pressure wave can be used to diagnose the condition of internal organs.

3.2 Potential in evaluating regional vasoconstrictor selectivity on different vascular beds

Hsu et al. [27] further demonstrated the potential of using the effects of organ ligation on the pressure pulse spectrum to evaluate the regional selectivity of vasoconstrictors on different vascular beds in rats. Organ artery ligation directly induces a huge increase in the resistance of the organ, while drug vasoconstriction can be considered as inducing a milder ligation in which the resistance change can be modulated by varying the drug dosage. The distinct harmonic-specific angiotensin II and vasopressin effects obtained by simply arithmetically combining the known effects of ligating the renal artery and superior mesenteric artery in different ratios were consistent with the regional selectivity of angiotensin II and vasopressin in published reports. These results confirm that using the BP as a sole parameter allows pulse analysis to determine which arterial bed has an increased resistance.

3.3 Effects of herbs

Numerous studies investigating the effects of herbal medicine on humans and animals have shown that many herbs will induce frequency-specific effects on the pulse spectrum [28-32], and that the classification of herbs by meridian in Chinese medicine is frequency-related [30,31]. Systematic studies on kidney- and spleen-meridian-related herbs have shown two distinct patterns of effects on the pulse harmonic spectrums. A study of herbal formulae further indicated that herbs can exert linearly additive effects on the pulse spectrum [33]. The effects of injecting rats with the complete formula of Xiao-Jian-Zhong-Tang on the Fourier components of the BP wave were similar to the linear combination of the effects obtained by injecting the individual ingredients separately [33]. The property of linear addition makes it easier to understand and compose an herb formula. Our use of pulse analysis to compare differences between the components of two herbal formulae, Bai-Wei-Dihuang and Liu-Wei-Dihuang, where the former is the same as the latter but with two extra components, clearly illustrated the logic of their clinical usages [30,32]. These results suggest that pulse analysis can provide a systematic way to understand the effects of herbs in Chinese medicine.

3.4 Clinical monitoring potential

An animal study of acetaminophen-induced acute hepatotoxicity found that the amplitude of the first harmonic of the BP pulse was highly correlated with the SGPT and SGOT, which are blood indexes of liver damage [34]. This showed that pulse spectrum analysis may be useful as a real-time biomarker complementing SGPT and SGOT for monitoring acute hepatotoxicity. This promises the development of a simple, noninvasive, real-time liver-function monitoring device.

3.5 Influence of daily human activities

Daily human activities are likely to induce frequency-specific effects on the pressure pulse spectrum since different activities may require different amounts of blood to be used in different parts of the body. The harmonic proportions of the second harmonic and the fourth harmonic (C_4) in the spectrum of the pressure pulse was found to be increased significantly after ingesting food, with the spectrum reaching a steady state about half hour later and maintaining this status for 3 to 4 hours [35]. This suggests more blood moving to the area corresponding to the stomach, trachea, bronchus, and the four limbs.

We also observed systematic changes in the spectrum of the pulse wave when test subjects had lain down and relaxed, with weaker harmonic components being enhanced [36]. Whilst the detailed pattern differed between subjects, the same pattern appeared consistently in the same subject. This may indicate that rest is useful for treating many diseases.

3.6 Clinical studies

Pulse spectrum analysis has been applied to hospital patients with acute uncomplicated myocardial infection, patients with possible liver problems, and workers at chemical factories, with the obtained data analyzed for correlations between the pulse spectrum and possible physiological problems [37-39]. The harmonic proportions of the second and third harmonics in the patient group with acute myocardial infarction fell on arrival at the emergency room and then gradually increased, while the averaged total pulse energy (frequency modulus C0) decreased during stable recovery [37]. Two studies involving patients with possible liver problems and chemical factory workers both suggested that an abnormal harmonic proportion of the first harmonic may indicate abnormal liver function as identified by blood testing [38,39]. This result is consistent with that of a study on the effects of acetaminophen [34].

3.7 Acupuncture studies

Acupuncture points comprise bundles of small arteries and arterioles, and these have been needled to investigate possible resulting modifications of the pulse spectrum [40-42]. Applying acupuncture at acupoints Tai-Tsih (K-3), Tsu-San-Li (St-36), and Hsien-Ku (St-43) induced distinct frequency-specific effects on the BP pulse spectrum, whereas no frequency-specific effect was found at a nonacupoint. Furthermore, we observed that the pattern of frequency-specific effects induced by acupuncturing acupoints is similar to that induced by taking herbs as described in Chinese medical books. For example, the effect of acupuncturing Tsu-San-Li [40], a stomach meridian point, is similar to the effect of administering spleen-meridian-related herbs [31], whilst the effect of acupuncturing Tai-Tsih [41], a kidney meridian point, is similar to the effect of kidney-meridian-related herbs [30]. These studies show that Chinese medicine is frequency based, with meridians being classified according to their frequency characteristics.

3.8 Pulse spectrum of qi-stimulating events

Qi-stimulating events such as taking *qi*-related tonic herbs (e.g., *Ganoderma lucidum*) [43], applying acupuncture to *qi*-related acupoint Tsu-San-Li [40], or during moving *qigong* [44] exerted similar frequency-specific effects on the blood pulse spectrum. These events all induced relative peak intensities of the third, six, and ninth harmonics of the pressure pulse spectrum. Therefore, there may be a common physiological factor determining the psycho-stimulatory responses of *qi* as well as their effects on the cardiovascular system.

The main effects of the psycho-stimulant beverages coffee [45] and tea (unpublished data) on the BP pulse are very similar to those associated with excitant *qi* performance. This suggests that coffee, tea, and *qi*-stimulating events share common physiological factors.

3.9 Effects of external synchronized mechanical forces

The application of external mechanical stimulation at frequencies near the HR or its harmonics can readily be sensed by the arterial system and induce hemodynamic changes by increasing the amplitudes of the corresponding harmonics, thereby decreasing the HR variability and blood-pressure-harmonics variability [46,47]. However, the amplitude of the second harmonic decreased during stimulation at a frequency 1.5 times the HR (i.e., not a harmonic) [47]. These studies support our resonance model in which the arterial system is treated as a pressure-transmitting system; they validate the “frequency matching” rule we proposed and provide a possible mechanism of external *qi*.

Table 1. Effects of drugs on the augmentation index (AIx) and the harmonic proportion of the fourth harmonic (C_4) quantified as percentage changes between drug and control conditions (i.e., %ΔAIx and %ΔC_4). NTG: nitroglycerin.

	%ΔAIx	%ΔC_4
Ramipril [56][1]	-16	52
Losartan [57][2]	-32	160
Dilevalol [58][3]	-18	78
NTG [59][4]	-21	48
Isradipine [60][5]	-14	92
Atenolol [56][1]	7.3	-27
Atenolol [57][2]	-1.5	-17
Atenolol [58][6]	23	-21
	r^2=0.75	

[1]Figure 1 in the erratum of Hirata et al. [56]: Pressure waves were measured in the radial artery 4 hours after the administration of atenolol (100 mg) and ramipril (10 mg).
[2]Figure 5 in Nicholes [57]: Radial pressure waves were recorded in a hypertensive patient before and after the administration of atenolol and losartan.
[3]Figure 9 in O'Rourke et al. [58]: Radial pressure waveforms of a 50-year-old normotensive man were recorded before and 6 hours after the oral ingestion of dilevalol (200 mg).
[4]Figure 2 in Kelly et al. [59]: Brachial pressure waveforms of an adult male were recorded before and 5–8 minutes after the sublingual administration of NTG (0.3 mg).
[5]Figure 10.16 in O'Rourke et al. [60]: Radial pressure waves of an adult were recorded before and after the oral ingestion of isradipine (5 mg)
[6]Figure 8 in O'Rourke et al. [58]: Radial pressure waveforms of a 50-year-old normotensive man were recorded before and 6 hours after the oral ingestion of atenolol (50 mg).

Hsiu et al. [48] further noted that the HR and BP of Wistar rats changed in the same direction when mechanical stimulation was applied at a frequency near to the HR or when propranolol was administered. This indicates that various types of stimulation can elicit regulatory mechanisms from the heart and arteries to restore their frequency-matching condition in order to maintain the arterial transmission efficiency.

3.10 Pulse spectrum variability and the dying process

Pulse spectrum variability has been studied both in terminally ill patients and in nearly dying, deep-urethane-anaesthetized rats. During the dying process, when the diastolic and systolic BPs do not show significant changes, all the harmonic components gradually lose their stability, starting from high-frequency components and gradually shifting to low-frequency components when the subject is closer to death. The pulse spectrum variability was found to be correlated with the health condition, making it possible to predict how close a subject is to death [49,50].

4. Harmonic analysis method and augmentation index

The augmentation index (AIx) is the most widespread time-domain pulse waveform analysis method currently utilized to describe characteristic changes in the pulse waveform induced by aging [51,52], diseases [53], and the administration of vasoactive drugs [54]. Studies of the AIx suggest that the peripheral pulse waveform can reflect the central pressure, and that the AIx calculated from peripheral pulse waveform is a better index than the peripheral systolic pressure or pulse pressure for assessing cardiac load [9]. We found that the harmonic proportion of C_4 of the peripheral pulse waveform could be an easier and a more consistent way of representing the AIx.

For drugs that are equally effective in reducing brachial pressure, the one that is more effective in reducing the central aortic or carotid pressure will significantly reduce the AIx [55-58]. Harmonically analyzing the pulse waveforms for published drug studies revealed that ramipril [56], losartan [57], dilevalol [58], nitroglycerin [59], and isradipine [60], which are effective in reducing the AIx, all increased the harmonic proportion of C_4. In contrast, atenolol [56-58], which exerts a small decreasing effect or even an increasing effect on the AIx, decreased C_4 (Table 1). There is a strong inverse correlation between C_4 and the AIx ($r^2 = 0.75$). From the F-statistics, the probability of the relationship being erroneous was less than 0.05. On the other hand, the vasoconstrictors, angiotensin II and vasopressin both decreased C_4 [27].

The AIx increases during aging. Analyzing the published waveforms for an aging study [52] revealed an inverse relationship between C_4 and the AIx, which respectively decreased and increased as subjects became older [61]. C_4 may be used as a specific index of hypertension, as well as for evaluating the efficacy of hypertension therapy [62].

5. Discussion and conclusion

Personalized medicine has recently become a popular topic due to increasing investigations involving genes. With the realization that all people are not created equal, the personalization concept underlies the philosophy of Chinese medicine. We wish to highlight two personalization properties related to these studies. First, we have used harmonic analysis instead of continuous frequencies. The heartbeat fundamentally underlies the pace of development and growth of a person, from the very early stage of embryo development until death, tuning the development as well as growth of all organs and tissues. The HR varies between individuals, and provides the fundamental rhythm for life. Therefore, it makes sense to consider the heartbeat and its harmonics as a personalized characteristic of an individual.

Harmonics represent the components of a repetitive signal. The resonance of organs with the heartbeat implies that each harmonic is tuned to an organ and its corresponding meridian. The weights of the various harmonics are another personalized characteristic. Based on our conjecture, Chinese medicine assigns fire, wood, water, earth, and metal (the five fundamental types of element in the material world) to the heart (harmonic zero), liver (first harmonic), kidney (second harmonic), spleen (third harmonic), and lung (fourth harmonic, C_4). Variations from the average weight of a specific harmonic reflect personalized characteristics, both physical and mental. This is another personalized way to classify healthy persons with inherent weaknesses that determine their bodily constitution and make them more vulnerable to certain diseases.

The second personalization property is related to a self-comparison method for herb and acupuncture studies: the comparison of the same subject between before and after treatment. This avoids individual variations that can be larger than the effect of the treatment itself. This concept is also important in diagnosing disease. Differences in body constitution can mean that weakness in a specific meridian will result in sickness in one person but be normal for another person. The best way to utilize "pulse feeling" is to establish the pulse data of an individual when he or she is normal or not sick and then compare them with the pulse data when he or she is sick. Sometimes it is the first visit of a patient and a normal pulse is not available, in which circumstances Chinese- medicine books teach looking, smelling and hearing, asking, and taking the pulse. "Pulse feeling" is used as a confirmation step of a diagnosis to determine if the pulse is consistent with a disease. The pulse difference alone usually cannot be judged as a disease condition, but rather as a deviation from the average. However, a huge deviation from the average does imply the presence of problems in the corresponding parts of the body.

The circulatory system is a highly efficient power supply system, requiring only 1.7 W to irrigate every tissue in a 75-kg human body with blood. The very low impedance of the pressure wave propagation through the PS wave may underlie this high efficiency. Subtle pathological changes can induce significant differences in efficiency and alter the pressure wave. Therefore, precisely mapping the arterial pulse wave with the conditions of human body might allow many diseases to be detected at an early stage and thereby facilitate the required interventions.

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References

[1] M. F. O'Rourke and A. Adji, "An updated clinical primer on large artery mechanics: implications of pulse waveform analysis and arterial tonometry," *Curr. Opin. Cardiol.*, 20: 275-281, 2005.

[2] A. R. Khoshdel, "Time to end a doubt: Is pulse wave analysis a valid measure for central arterial blood pressure and arterial stiffness?" *J. Hypertens.*, 25: 724-725, 2007.

[3] J. P. Murgo, N. Westerhof, J. P. Giolma and S. A. Altobelli, "Aortic input impedance in normal man: relationship to pressure wave forms," *Circulation*, 62**:** 105-116, 1980.

[4] D. A. McDonald (Ed.), *Blood Flow in Arteries (II)*, London: Edward Arnold, 1974.

[5] W. K. Wang, "Modern view of Chinese Medicine," *Annu. Rep. of Inst. Phys.*, 16: 269-275, 1986.

[6] W. R. Milnor (Ed.), *Hemodynamics (II)*, Baltimore: Williams & Wilkins, 1989.

[7] Y. Y. Lin Wang, W. B. Chiu, M. Y. Jan, J. G. Bau, S. P. Li and W. K. Wang, "Analysis of transverse wave as a propagation mode for the pressure pulse in large arteries," *J. Appl. Phys.*, 102: 064702, 2007.

[8] J. W. Remington and W. F. Hamilton, "Quantitative circulation of the time course of cardiac ejection from the pressure pulse," *Am. J. Physiol.*, 148: 25-34, 1947.

[9] W. W. Nichols and M. F. O'Rourke (Eds.), *McDonald's Blood Flow in Arteries: Theoretic, Experimental and Clinical Principles*, London: Hodder Arnold, 2005.

[10] W. K. Wang, Y. Y. Lo, Y. Chineg, T. L. Hsu and Y. Y. Lin Wang, "Resonance of the organ with the heart," in: W. J. Young (Ed.), *Biomedical Engineering – An International Symposium*, Washington, D. C.: Hemisphere, 259-268, 1989.

[11] Y. Y. Lin Wang, S. L. Chang, Y. E. Wu, T. L. Hsu and W. K. Wang, "Resonance: the missing phenomenon in hemodynamics," *Circ. Res.*, 69: 246-249, 1991.

[12] Y. Y. Lin Wang, C. C. Chang, J. C. Chen, T. L. Hsu and W. K. Wang, "Pressure wave propagation in arteries, a model with radial dilation for simulating the behavior of a real artery," *IEEE Eng. Med. Biol. Mag.*, 16: 51-56, 1997.

[13] Y. Y. Lin Wang, M. Y. Jan, G. C. Wang, J. G. Bau and W. K. Wang, "Pressure pulse velocity is related to the longitudinal elastic properties of the artery," *Physiol. Meas.*, 25: 1397-1403, 2004.

[14] Y. Y. Lin Wang, W. K. Sze, J. G. Bau, S. H. Wang, M. Y. Jan, T. L. Hsu and W. K. Wang, "The ventricular-arterial coupling system can be analyzed by the eigenwave modes of the whole arterial system," *Appl. Phys. Lett.*, 92: 153901, 2008.

[15] Y. Y. Lin Wang, M. Y. Jan, C. S. Shyu, C. A. Chiang and W. K. Wang, "The natural frequencies of the arterial system and their relation to the heart rate," *IEEE Trans. Biomed. Eng.*, 51**:** 193-195, 2004.

[16] R. W. Stacy and F. M. Giles, "Computer analysis of arterial properties," *Circ. Res.*, 7**:** 1031-1038, 1959.

[17] M. Y. Jan, H. Hsin, T. L. Hsu, W. K. Wang and Y. Y. Lin Wang, "The physical conditions of different organs are reflected in the pressure pulse spectrum of the peripheral artery specifically," *J. Cardiovasc. Eng.*, 3**:** 21-29, 2003.

[18] M. Y. Jan, H. Hsiu, T. L. Hsu, Y. Y. Lin Wang and W. K. Wang, "The importance of pulsatile microcirculation in relation to hypertension," *IEEE Eng. Med. Biol. Mag.*, 19: 106-111, 2000.

[19] P. T. Chao, M. Y. Jan, H. Hsiu, T. L. Hsu, W. K. Wang and Y. Y. Lin Wang, "Evaluating microcirculation by pulsatile laser Doppler signal," *Phys. Med. Biol.*, 51: 845-854, 2006.

[20] R. P. Lewis, H. Boudoulas, C. V. Leier, D. V. Unverferth and A. M. Weissler, "Usefulness of the systolic time intervals in cardiovascular clinical cardiology," *Trans. Am. Clin. Climatol. Assoc.*, 93: 108-120, 1981.

[21] R. Kelly, C. Hayward, A. Avolio and M. O'Rourke, "Noninvasive determination of age-related changes in the human arterial pulse," *Circulation*, 80: 1652-1659, 1989.

[22] M. G. Taylor, "Use of random excitation and spectral analysis in the study of frequency-dependent parameters of the cardiovascular system," *Circ. Res.*, 18: 585-595, 1966.

[23] L. Y. Wei and P. Chow, "Frequency distribution of human pulse spectra," *IEEE Trans. Biomed. Eng.*, 32: 245-246, 1985.

[24] S. T. Young, W. K. Wang, L. S. Chang and T. S. Kuo, "Specific frequency properties of renal and superior mesenteric arterial beds in rats," *Cardiovasc. Res.*, 23: 465-467, 1989.

[25] S. T. Young, W. K. Wang, L. S. Chang and T. S. Kuo, "The filter properties of the arterial beds of organs in rats," *Acta Physiol. Scand.*, 145: 401-406, 1992.

[26] G. L. Yu, Y. Y. Lin Wang and W. K. Wang, "Resonance in the kidney system of rats," *Am. J. Physiol.*, 267: H1544-H1548, 1994.

[27] T. L. Hsu, P. T. Chao, H Hsiu, W. K.Wang, S. P. Li and Y. Y. Lin Wang, "Organ-specific ligation-induced changes in harmonic components of the pulse spectrum and regional vasoconstrictor selectivity in Wistar rats," *Exp. Physiol.*, 91: 163-170, 2006.

[28] Y. Y. Lin Wang, J. L. Sheu and W. K. Wang, "Alterations of pulse by Chinese herb medicine," *Am. J. Chin. Med.*, 20: 181-190, 1992.

[29] W. K Wang, T. L. Hsu, Y. Chiang and Y. Y. Lin Wang, "Pulse spectrum study on the effect of Sie-Zie-Tang and *Radix aconiti*," *Am. J. Chin. Med.*, 25: 357-366, 1997.

[30] W. K. Wang, T. L. Hsu and Y. Y. Lin Wang, "Liu-wei-dihuang: a study by pulse analysis," *Am. J. Chin. Med.*, 26: 73-82, 1998.

[31] W. K. Wang, J. G. Bau, T. L. Hsu and Y. Y. Lin Wang, "Influence of spleen meridian herbs on the harmonic spectrum of the arterial pulse," *Am. J. Chin. Med.*, 28: 279-289, 2000.

[32] W. K. Wang, T. L. Hsu, J. G. Bau and Y. Y. Lin Wang, "Evaluation of herbal formulas by pulse analysis method," *Acta Pharmacol. Sin.*, 24: 145-151, 2003.

[33] W. K. Wang, T. L. Hsu, Z. Y. Huang and Y. Y. Lin Wang, "Collective effect of a Chinese formula: a study of Xiao-Jian-Zhong-Tang," *Am. J. Chin. Med.*, 23: 299-304, 1995.

[34] T. L. Hsu, Y. Chiang, W. K. Wang, P. T. Chao, J. G. Bao and Y. Y. Lin Wang, "Pulse analysis as a possible real-time biomarker complementary to SGPT and SGOT for monitoring acute hepatotoxicity," *Toxicol. Mech. Methods*, 13: 181-186, 2003.

[35] W. K. Wang, T. L. Hsu, Y. Chiang and Y. Y. Lin Wang, "The prandial effect on the pulse spectrum," *Am. J. Chin. Med.*, 24: 93-98, 1996.

[36] W. K. Wang, T. L. Hsu, Y. Chiang and Y. Y. Lin Wang, "Study on the pulse spectrum change before deep sleep and its possible relation to EEG," *Chin. J. Med. Biol. Eng.*, 12: 107-115, 1992.

[37] C. Y. Chen, W. K. Wang, T. Kao, B. C. Chen and C. Chiang, "Spectral analysis of radial pulse in patients with acute, uncomplicated myocardial infarction," *Jpn. Heart J.*, 34: 131-143, 1993.

[38] W. K. Wang, J. Tsuei, H. C. Chang, T. L. Hsu and Y. Y. Lin Wang, "Pulse spectrum analysis of chemical factory workers with abnormal blood test," *Am. J. Chin. Med.*, 26: 199-203, 1996.

[39] W. A. Lu, Y. Y. Lin Wang and W. K. Wang, "Pulse analysis of patients with severe liver problems: studying pulse spectrums to determine the effects on other organs," *IEEE Eng. Med. Biol. Mag.*, 18: 73-75, 1999.

[40] W. K. Wang, T. L. Hsu, H. C. Chang and Y. Y. Lin Wang, "Effect of acupuncture at Tsu San Li (St-36) on the pulse spectrum," *Am. J. Chin. Med.*, 23: 121-130, 1995.

[41] W. K. Wang, T. L Hsu, H. C. Chang and Y. Y. Lin Wang, "Effect of acupuncture at Tai-Tsih (K-3) on the pulse spectrum," *Am. J. Chin. Med.*, 24: 305-313, 1996.

[42] W. K. Wang, T. L. Hsu, H. C. Chang and Y. Y. Lin Wang, "Effect of acupuncture at Hsien-Ku (St-43) on the pulse spectrum and a discussion of the evidence for the frequency structure of Chinese medicine," *Am. J. Chin. Med.*, 28: 41-55, 2000.

[43] W. K. Wang, H. L. Chen, T. L. Hsu and Y. Y. Lin Wang, "Alteration of pulse in human subjects by three Chinese herbs," *Am. J. Chin. Med.*, 22: 197-203, 1994.

[44] W. K. Wang, Y. Y. Lin Wang, T. L. Hsu and Y. Ching, "Some foundation of pulse feeling in Chinese medicine," in: W. J. Young (Ed.), *Biomedical Engineering – An International Symposium*, Washington, D. C.: Hemisphere, 268-297, 1989.

[45] T. L. Hsu, J. G. Bau, W. K. Wang, S. P. Li and Y. Y. Lin Wang, "Similarity between coffee effects and Qi-stimulating events," *J. Altern. Complement. Med.*, 14: 1145-1150, 2008.

[46] H. Hsiu, M. Y. Jan, Y. Y. Lin Wang and W. K. Wang, "Influencing the heart rate of rats with weak external mechanical stimulation," *PACE-Pacing Clin. Electrophysiol.*, 26: 36-43, 2003.

[47] H. Hsiu, M. Y. Jan, W. K. Wang and Y. Y. Lin Wang, "Effects of whole-body mechanical stimulation at double the heart rate on the blood pressure waveform in rats," *Physiol. Meas.*, 27: 131-144, 2006.

[48] H. Hsiu, P. T. Chao, W. C. Hsu, M. Y. Jan, Y. Y. Lin Wang and W. K. Wang, "The possible role of arterial radial vibration in heart rate and blood pressure matching," *Proc. Inst. Mech. Eng. Part H-J. Eng. Med.*, 222: 773-779, 2008.

[49] Y. C. Kuo, T. Y. Chiu, M. Y. Jan, J. G. Bau, S. P. Li, W. K. Wang and Y. Y. Lin Wang, "Losing harmonic stability of arterial pulse in terminally ill patients," *Blood Press. Monit.*, 9: 255-258, 2004.

[50] Y. C. Kuo, S. H. Lo, P. T. Chao, H. Hsiu, W. K. Wang and Y. Y. Lin Wang, "Raising harmonic variation of arterial pulse in dying rats," *Am. J. Chin. Med.*, 33: 73-85, 2005.

[51] K. Kohara, Y. Tabara, A. Oshiumi, Y. Miyawaki, T. Kobayashi and T. Miki, "Radial augmentation index: a useful and easily obtainable parameter for vascular aging," *Am. J. Hypertens.*, 18: 11S-14S, 2005.

[52] R. Kelly, C. Hayward, A. Avolio and M. O'Rourke, "Nonivasive determination of age-related changes in the human arterial pulse," *Circulation*, 80: 1652-1659, 1989.

[53] G. M. London, J. Blacher, B. Pannier, A. P. Guerin, S. J. Marchais and M. E. Safa, "Arterial wave reflections and survival in end-stage renal failure," *Hypertension*, 38: 434-438, 2001.

[54] P. P. Kelly, S. C. Millasseau, J. M. Ritter and P. J. Chowienczyk, "Vasoactive drugs influence aortic augmentation index independently of pulse-wave velocity in healthy men," *Hypertension*, 37: 1429-1433, 2001.

[55] T. Morgan, J. Lauri, D. Bertram and A. Anderson, "Effect of different antihypertensive drug classes on central aortic pressure," *Am. J. Hypertens.*, 17: 118-123, 2004.

[56] K. Hirata, C. Vlachopoulos, A. Adji and M. F. O'Rourke, "Benefits from angiotensin-converting enzyme inhibitor' beyond blood pressure lowering': beyond blood pressure or beyond the brachial artery?" *J. Hypertens.*, 23: 551-556, 2005.

[57] W. W. Nichols, "Clinical measurement of arterial stiffness obtained from noninvasive pressure waveforms," *Am. J. Hypertens.*, 18: 3S-10S, 2005.

[58] M. F. O'Rourk, R. P. Kelly, A. P. Avolio and C. Hayward, "Effects of arterial dilator agents on central aortic systolic pressure and on left ventricular hydraulic load," *Am. J. Cardiol.*, 63: 38I-44I, 1989.

[59] R. P. Kelly, H. H. Gibbs, M. F. O'Rourke, J. E. Daley, K. Mang, J. J. Morgan and A. P. Avolio, "Nitroglycerin has more favourable effects on left ventricular afterload than apparent from measurement of pressure in a peripheral artery," *Eur. Heart J.*, 11: 138-144, 1990.

[60] M. F. O'Rourke, M. E. Safar and V. J. Dzau (Eds.), *Arterial Vasodilation: Mechanisms and Therapy*, Philadelphia: LEA & Febiger, 1993.

[61] S. H. Wang, T. L. Hsu, M. Y. Jan, Y. Y. Lin Wang and W. K. Wang, "Age-related changes in specific harmonic indices of pressure pulse waveform," *Proc. The 13th Int. Conf. on Biomed. Eng.*, 23: 183-185, 2009.

[62] S. H. Wang, T. L. Hsu and M. Y. Jan, "Effects of captopril on specific harmonic indexes of the peripheral pressure pulse waveform," *Proc. The 4th Int. Conf. on Bioinform. and Biomed. Eng.*, 2010.