MATHEMATICAL MODELING OF THE CARDIOVASCULAR SYSTEM AND ITS CONTROL MECHANISMS

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Contents

Summary

Models are a simplification of reality, which can help one to understand particular functions of interest. The mathematical modeling of the cardiovascular system results in a description in terms of equations, usually differential equations, selected to describe the dynamic aspects of the system. This interdisciplinary field of applying scientific and engineering laws in cardiovascular physiology has made tremendous progress during the last decade due to improvements in computer technology. Through this model development process, scientists and physicians would be able to gain and verify new knowledge in cardiovascular system quantitatively. These models can help clinicians to initiate new techniques for diagnosis and/or treatment. Implementing these models with computers also facilitates a cost-effective way for medical education, clinical training, as well as medical device development.

This chapter reviews the main aspects of cardiovascular system dynamics with the emphasis on modeling hemodynamic characteristics by using electrical circuit models. The physiological concepts of the circulatory system dynamics are introduced with the aid of existing mathematical models. The cardiac pumping mechanism is characterized by the pressure-volume relationship. The segmental models and windkessel models are used to describe the vascular system. The baroreflex control mechanism that regulates the arterial blood pressure of the cardiovascular system is provided to explain the interaction between hemodynamics and nerve control in circulation. Several articles that cover a wide range of cardiovascular models and applications are recommended for further study.

1. Introduction

Mathematical modeling of physiological systems is an interdisciplinary field that applies fundamental laws in biology, mathematics, physics, chemistry, and engineering to characterize the interactions among physiological subsystems. Developing these models is beneficial to many different applications. For example, physiological models can be used to support medical research and facilitate better understanding of the quantitative functions underlying physiology. These models provide a convenient and cost-effective tool for medical training and education. In addition, they assist clinical diagnosis (by estimating physiological variables that are not measurable), treatments, and medical device development.

Efforts in developing physiological models have been ongoing for many years. For instance, Nobert Wiener examined the instability and oscillations of neurological control systems from the Volterra series perspective in the 1940s. Guyton, Grodins, and co-works studied the cardiovascular and respiratory control between the 1950s and 1960s. Early works in physiological modeling and analysis from the control system perspective are available in literature. More significant progress has been made in this field during the last decade because of new development in technologies such as computation, physiological sensors, and high-speed data acquisition. Numerous monographs that focus on various areas of physiology as well as different scientific perspectives were published over these years.

This chapter provides an overview of the scientific disciplines that have been applied to develop mathematical models of the cardiovascular system. A survey of numerous cardiovascular system models, describing the pumping mechanism of the heart, the characteristics of blood vessels, the regulation of blood volume, as well as the control mechanism regulating the cardiac pumping action, are presented as examples.

This chapter is organized as follows. A brief overview of the cardiovascular physiology, related to model development, is given in Section 2. Mathematical models that simulate the cardiac pumping mechanism are presented in Section 3. The concepts involving the use of electrical analogues to model the vascular system along with various model structures are provided in Section 4. A simple model of the cardiovascular system is presented in Section 5 describing the integration of the cardiac pump model with the vascular load. The neurological functions that regulate blood pressure, volume, and cardiac pumping action, are described in Section 6. Finally, the structure of the

cardiovascular system model and the derivation of the model equations are briefly summarized in Section 7.

2. Cardiovascular Physiology

In order to develop a physiologically meaningful model for the cardiovascular system, one must understand the relevant parts of the underlying physiology. The purpose of the cardiovascular system is to circulate blood to transport oxygen and nutrients, and remove carbon dioxide and waste products. It consists of two separate circulations: systemic circulation and pulmonary circulation; the heart provides the primary driving force to pump blood in both circulations as shown in Figure 1.
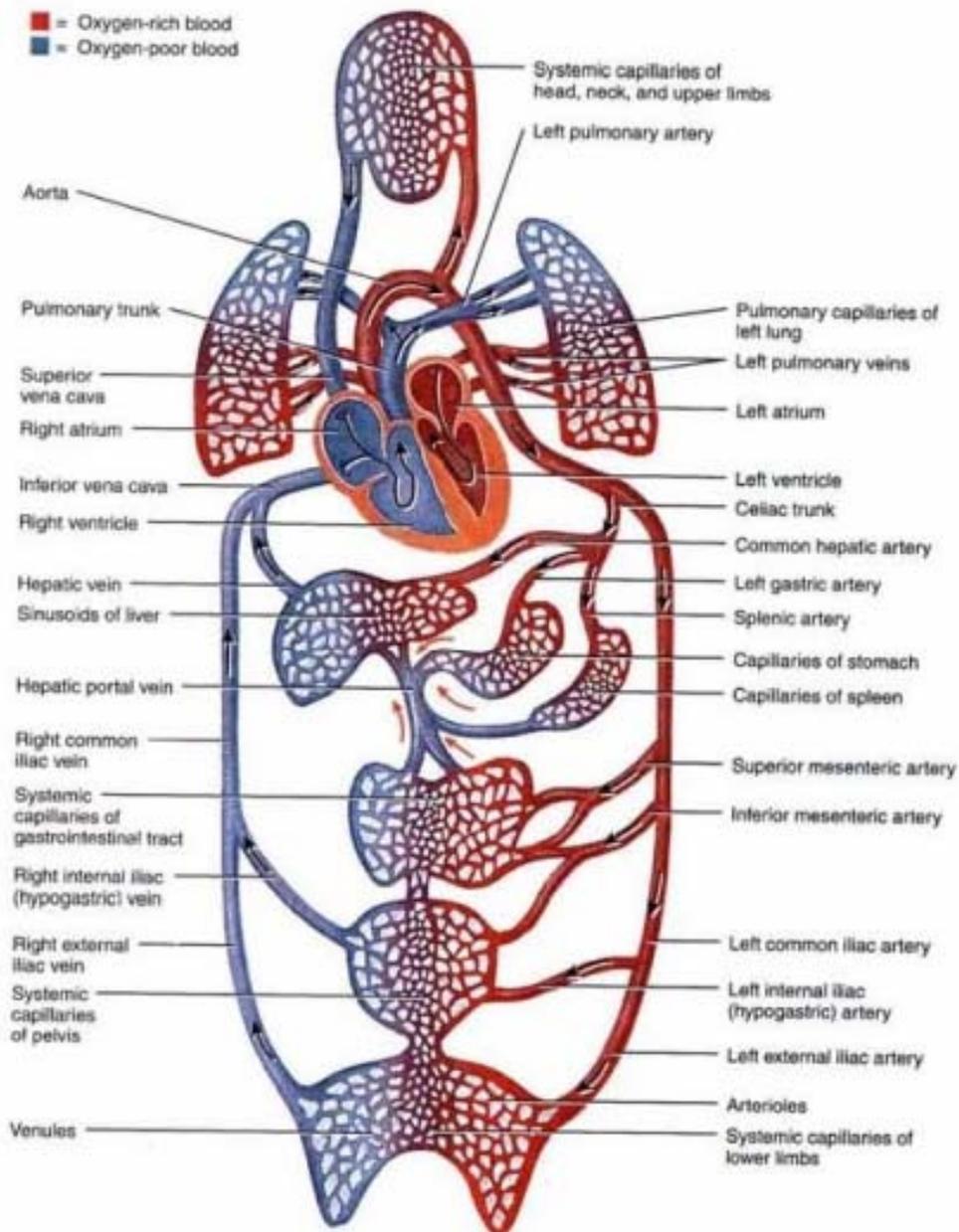

Figure 1. Cardiovascular System (From Tortora *et al*, *Principles of Anatomy and Physiology*. Copyright 2005. Used by permission of John Wiley & Sons, Inc.)

The systemic circulation starts from the left ventricle, where oxygenated blood (shown in red in Figure 1) is pumped out to the aorta. Large arteries branch off the aorta, and smaller arteries branch off these large arteries. The final small branches of these arterial trees are the arterioles, small arteries with strong muscular walls that can contract or dilate to restrict or increase blood flow. The blood flows from the arterioles to capillaries, where it exchanges nutrients, oxygen, electrolytes, hormones, and other substances with the body tissues. During organ perfusion, carbon dioxide and other waste products are released from organs and tissues into capillaries. They are carried away by the blood flow into the veins, the vena cava, the right atrium, and then the right ventricle.

The right ventricle pumps the deoxygenated blood (shown in blue in Figure 1) into the pulmonary artery, which then branches into the left and right pulmonary arteries delivering blood to both lungs. The pulmonary arteries divide into arterioles and capillaries. The capillaries carry the oxygen deficient blood to the lung tissues, where carbon dioxide is exchanged with oxygen in the alveoli. The oxygenated blood is carried to the left atrium and then returned to the left ventricle.
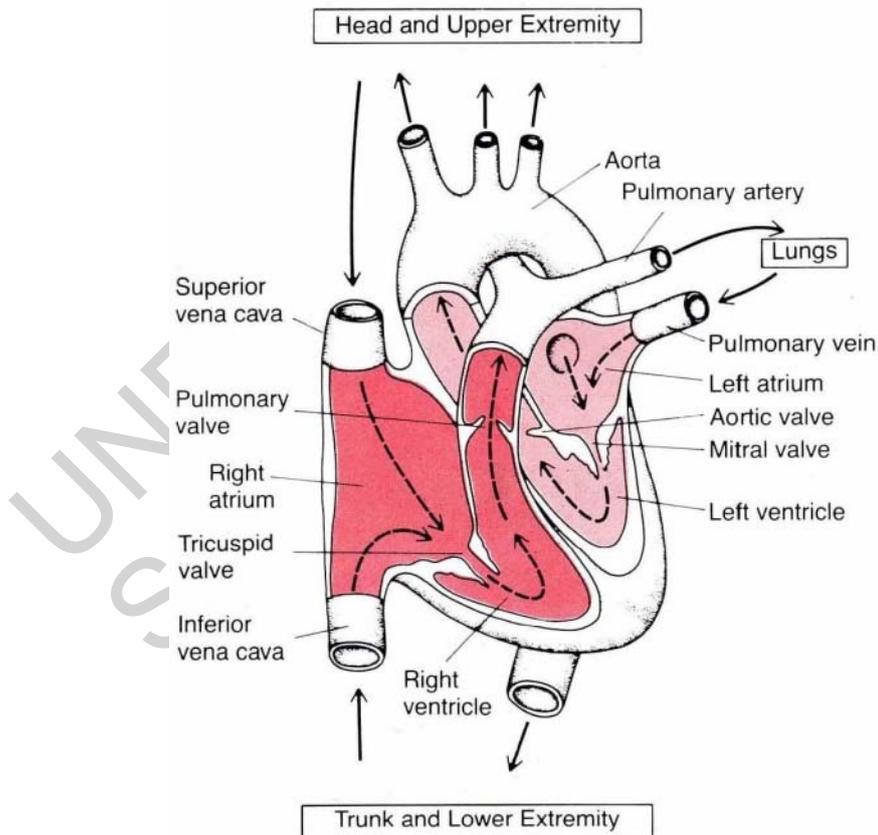
2.1. The Cardiac Pump

Figure 2. The heart and the course of the blood flowing through the heart chambers (From Guyton *et al*, *Textbook of Medical Physiology*. Copyright 1996. Used by permission of W.B. Saunders Co.)

The heart consists of two pumps, each made up of two chambers, the left and right atria and the left and right ventricles, as shown in Figure 2. Note that the left and right orientations refer to the patient's orientation. The oxygenated blood from the lungs flows into the left atrium. This blood then passes through the bicuspid valve (mitral valve) and enters the left ventricle. The left ventricle pumps the blood through the aortic valve into the systemic circulation. After passing through the systemic circulation, the oxygen deficient blood returns to the right atrium by way of either the superior or the inferior vena cava. This blood then flows through the tricuspid valve into the right ventricle. The right ventricle pumps the blood through the pulmonary valve into the pulmonary circulation. The four heart valves: mitral valve, aortic valve, tricuspid valve, and pulmonary valve, prevent backflow throughout the cardiac cycle.

2.2. Electrical Activity of the Heart

The heart's lifelong beat is a result of an inherent and rhythmical electrical activity. The electrical impulses are propagated to all parts of the cardiac muscle (as known as myocardium) by the conduction system. The conduction system consists of the sinoatrial (SA) node, the atrioventricular (AV) node, the common bundle (also known as bundle of His), the bundle of branches, and the purkinje fibers as shown in Figure 3.
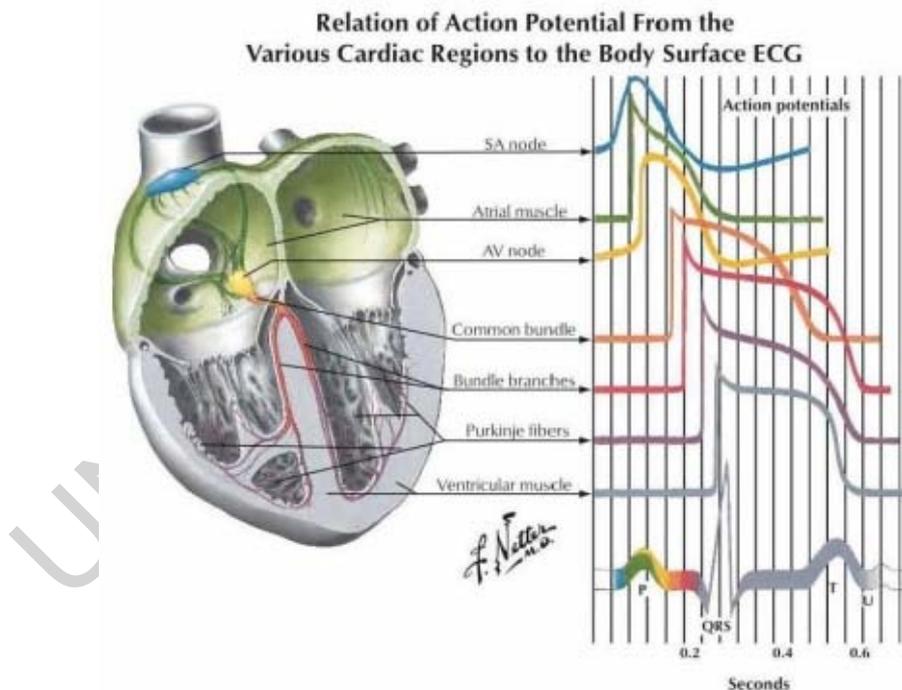

Figure 3. The conduction system of the heart and the action potentials (From *Netter Anatomy Illustration Collection*, ©Elsevier, Inc. All Rights Reserved, Modified with Permission)

Cardiac excitation normally starts at the SA node, located in the myocardium of the right atrium near the entrance of the superior vena cava. The SA node serves as the heart's internal pacemaker that determines the heart rate. An electrical impulse from the SA node initiates a heartbeat. This impulse reaches the atria first, causing the atrial muscle to contract. The impulse then reaches the AV node, located at the inter-atrial

septum. From the AV node, the impulse is slowly sent through the bundle of His, which then branched into two to both ventricles. The impulse is propagated through both branches and travels towards the apex of the heart. Finally, the impulse reaches the purkinje fibers, causing the ventricles to contract. The electrical potentials (action potentials) at different locations along its propagation path are shown in Figure 3. As the action potentials propagate through the heart, they generate an electrical signal, electrocardiography or ECG as shown at the bottom of the action potentials in Figure 3, which can be detected at the surface of the human body.

2.3. The Cardiac Cycle

The cardiac events that happen within one cardiac period are called the cardiac cycle. The cardiac cycle consists of a period of relaxation called diastole followed by a period of contraction called systole. During diastole, the heart muscle is relaxed and the ventricles are filled with blood. The ventricles contract and pump the blood into the circulatory system during systole. Figure 4 depicts the aortic pressure (dashed line at the top), left ventricular pressure (red solid line), left atrial pressure (dashed line at the bottom), ventricular volume, ECG, heart sound, and the events in the cardiac cycle.
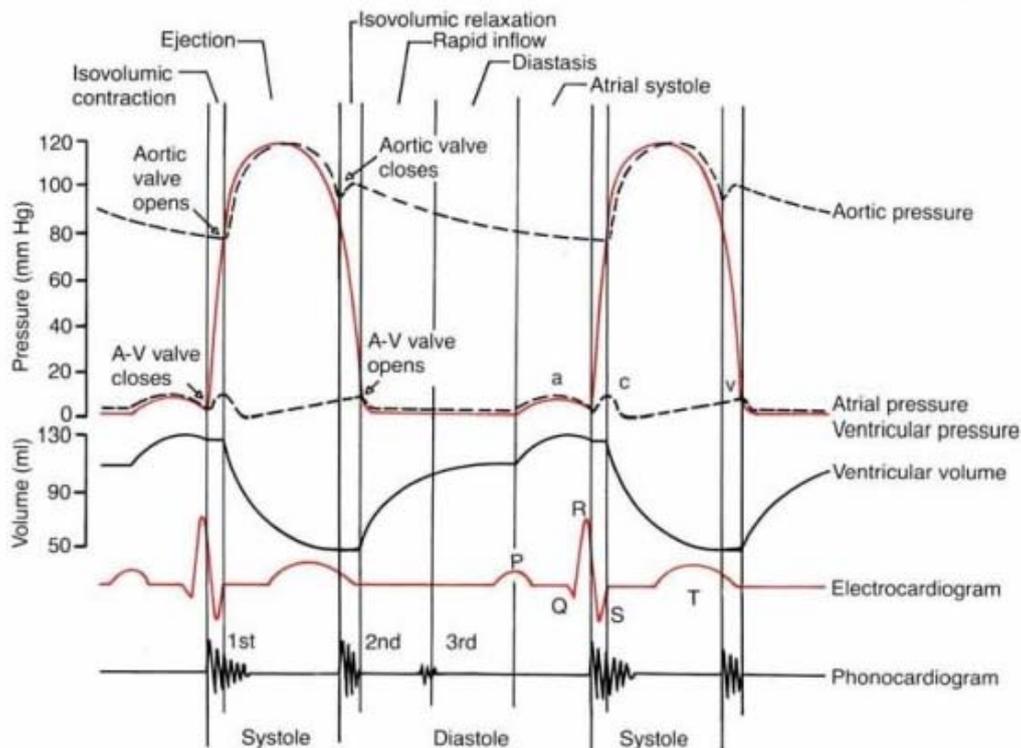

Figure 4. Cardiac events, blood pressures, ventricular volume, ECG, and heart sound waveforms in the cardiac cycle (From Guyton *et al*, *Textbook of Medical Physiology*. Copyright 1996. Used by permission of W.B. Saunders Co.)

The cardiac cycle starts from the depolarization at the SA node, which results in the P wave in the ECG and causes the atria to contract. Atrial contraction produces a small pressure rise as shown in Figure 4, which forces the blood in the atria to flow into the ventricles. The ventricular volume reaches its maximum (end-diastolic volume or EDV, typically about 120 to 130 ml) at the end of atrial contraction.

The QRS complex in the ECG marks the onset of ventricular depolarization, causing the ventricular systole. As the ventricles contract, the left and right ventricular pressures rise. Once the pressures in the ventricles are greater than the left and right atrial pressures, the atrial-ventricular valves (AV valves, including mitral valve and tricuspid valve) are closed.

The sudden valve closure and the accompanying vibration due to blood oscillation generate the First Heart Sound, which is audible with a stethoscope overlying the heart. During the time between the closure of AV valves and the opening of the semilunar valves (aortic valve and pulmonary valve), the ventricular pressures rise rapidly and the ventricular volume remains unchanged. This is the period of isovolumic contraction.

As the ventricular contraction continues, ventricular pressures keep rising until they increase beyond the pressure in the arteries, causing the opening of the semilunar valves. This normally occurs when the left ventricular (LV) pressure rises above the aortic pressure (about 80 mmHg) and the right ventricular (RV) pressure surpasses the pulmonary arterial pressure (about 20 mmHg).

The LV pressure continues rising to about 120 mmHg while the RV pressure goes up to about 25 ~ 30 mmHg. The time interval when the semilunar valves are open is ventricular ejection, during which the ventricles eject blood into the circulatory system. The LV ejects about 70 ml of blood into the aorta and the RV pumps the same amount of blood into the pulmonary arteries. At the end of ventricular ejection, the blood volume (end-systolic volume or ESV) in each ventricle reaches its minimum at about 60 mL. The difference between EDV and ESV is the stroke volume.

The T wave in the ECG marks the onset of ventricular repolarization, causing ventricular active tension to decrease, and thus, the ventricular pressures to fall. The aortic pressure and pulmonary arterial pressure drop as well but at a slower rate. As the ventricular pressures continue dropping, a point is reached where the LV pressure and RV pressure are lower than the aortic pressure and pulmonary pressure, respectively. As a result, the semilunar valves are abruptly closed.

The closure of these valves produces the second heart sound. The aortic valve closes at a pressure about 100 mmHg. After the closure of the semilunar valves, there is a short duration where all the heart valves are closed. This duration is called isovolumic relaxation. During this period, the ventricular volume stays the same.

As the ventricles continue relaxing, the pressures fall quickly. When the ventricular pressures drop below the atrial pressures, the AV valves open and the blood flows through the AV valves to fill the ventricles, causing the ventricular volume to increase.

The period during which the AV valves are open while the semilunar valves are closed is ventricular filling. At the end of the relaxation, the P wave appears in the ECG again, and thus a new cardiac cycle starts.

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Bibliography

Avanzolini G, P. Barbini, A. Cappello, G. Cevenini (1988). CADCS simulation of the closed-loop cardiovascular system. *International Journal of Biomedical Computing* **22**(1), 39-49. [This paper describes the use of SIMNON to implement a cardiovascular model in computer simulation]

Burkhoff, D., I. Mirsky, and H. Suga (2005). Assessment of systolic and diastolic ventricular properties via pressure volume analysis: a guide for clinical, translational, and basic researchers, *American Journal Physiology* **289** (Heart Circulation Physiology) H501–H512. [Clinical application of ventricular pressure-volume relationship]

Guyton, AC (1990). Long-term arterial pressure control: an analysis from animal experiments and computer and graphic models. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology* **259**(5), R865–R877. [A comprehensive model of the long-term arterial pressure regulation mechanism]

Guyton, A.C. and J.E. Hall (1996). *Textbook of Medical Physiology*, 9th Ed. Saunders, Philadelphia, Pennsylvania. [A good resource on cardiovascular physiology and its regulation mechanism in quantity]

Ha, R.R, J. Qian, D.L. Ware, J.B. Zwischenberger, A. Bidani, and J.W. Clark, JR. (2005). An integrative cardiovascular model of the standing and reclining sheep. *Cardiovascular Engineering: An International Journal* **5**(2), 53–76. [This paper develops an integrative model of the ovine cardiovascular system that simulates the effects of posture and ventricular function to help design the circulatory and pulmonary assist devices.]

Khoo, M.C.K. (1999). *Physiological Control Systems Analysis, Simulation, and Estimation*. Wiley-IEEE, New York, New York. [This book describes how the principles of control theory, systems analysis, and model identification are used in physiological regulation.]

Klabunde, R.E. (2005). *Cardiovascular Physiology Concepts*. Lippincott Williams & Wilkins, Baltimore, Maryland. [An easy to read book to learn the basics of cardiovascular physiology]

Ottesen, J.T., M.S. Olufsen, and J.K. Larsen (2004). *Applied Mathematical Models in Human Physiology*. SIAM, Philadelphia, Pennsylvania. [This book introduces mathematical applications in cardiovascular and respiratory physiology.]

Rideout, V.C. (1991). *Mathematical and Computer Modeling of Physiological Systems*. Prentice-Hall, Inc., Englewood Cliffs, New Jersey. [An entry-level book for those interested in computer simulation of physiological systems.]

Sagawa K, L. Maughan, H. Suga, K. Sunagawa (1988). *Cardiac Contraction and the Pressure-Volume Relationship*. Oxford University Press, New York, New York. [This book includes comprehensive information of the cardiac pumping mechanism.]

Shroff, S.G., J.S. Janicki, and K.T. Weber (1985). Evidence and quantitation of left ventricular systolic resistance. *American Journal Physiology* **249**(Heart Circulation Physiology 18), H358–370. [This paper describes the need of a time-varying resistance to reflect the viscosity of the ventricle and increases with the contractile activity of muscle fibers.]

Stergiopulos, N., J.J. Meister, and N. Westerhof (1996). Determinants of stroke volume and systolic and diastolic aortic pressure. *American Journal Physiology* **270**(Heart Circulation Physiology 39), H2050–2059. [Left ventricular elastance is modeled as a double-Hill function.]

Sun, Y., and H. Gewirtz (1987). Characterization of the coronary vascular capacitance, resistance, and flow in endocardium and epicardium based on a nonlinear dynamic analog model. *IEEE Transactions on Biomedical Engineering* **34**(10), 817–825. [This paper presents a model of the coronary vascular system.]

Sunagawa, K. and K. Sagawa (1982). Models of ventricular contraction based on time-varying elastance. *CRC Critical Reviews in Biomedical Engineering* **7**, 193–227. [This paper provides a thorough review in ventricular pressure-volume relationship and cardiac function modeling.]

Tsitlik, J.E., H.R. Halperin, A.S. Popel, A.A. Shoukas, F.C.P. Yin, and N. Westerhof (1992). Modeling the circulation with three-terminal electrical networks containing special nonlinear capacitors. *Annals of Biomedical Engineering* **20**(6), 595–616. [This paper provides comprehensive information of segmental modeling of the vascular system.]

Ursino, M (1998). Interaction between carotid baroregulation and the pulsating heart: a mathematical model. *American Journal Physiology* **275**(Heart Circulation Physiology 44), H1733–H1747. [A comprehensive model of the baroreflex]

Westerhof, N., J. Lankhaar, and B.E. Westerhof (2009). The arterial windkessel. *Medical & Biological Engineering & Computing* **47**(2), 131–141. [A survey paper with clear analysis to the arterial winkessel models]

Yu, Y.-C., J.R. Boston, M. Simaan, P.J. Miller, and J.F. Antaki (20001a). Pressure-volume relationship of a pulsatile blood pump for ventricular assist device development. *ASAIO Journal* **47**(3), 293–301. [Apply the ventricular pressure-volume relationship concept to develop a mathematical model for a pulsatile ventricular assist device]

Yu, Y-C. (2006). Automatic control of blood pressure. In: *Encyclopedia of Medical Devices and Instrumentation*, 2nd Ed. Vol **1**, 490–500. John Wiley & Sons, New York, New York. [A survey of control system designs for drug administration to regulate arterial blood pressure. Several cardiovascular system models are used in controller design and testing.]

Yu, Y.-C., M.A. Simaan, S.E. Mushi, and N.V. Zorn (2008). Performance prediction of a percutaneous ventricular assist system using nonlinear circuit analysis techniques. *IEEE Transactions on Biomedical Engineering* **55**(2), 419–429. [This paper presents the use of a lumped cardiovascular model to simulate the interaction of the cardiovascular system with an extracorporeal ventricular assist device.]

Biographical Sketch

Yih-Choung Yu was born in Taiwan in 1965. He received the B.S. degree from Chinese Culture University, Taipei, Taiwan, in 1987, the M.S. degree from Binghamton University, the State University of New York, Binghamton, New York, in 1992, and the Ph.D. degree from University of Pittsburgh, Pittsburgh, PA, in 1998, all in Electrical Engineering.

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