

A MODEL OF THE CARDIOVASCULAR SYSTEM USING BOND GRAPHS

V. Le Rolle ^{1,2}, P-Y. Richard ¹, A. Hernandez ², G. Carrault ², J. Buisson ¹

¹ *Supélec IETR, avenue de la Boulaie, B.P. 81127, 35511 Cesson-Sévigné cedex, France*

² *Laboratoire Traitement du Signal et de l'Image, InsermU 642, Université Rennes I
35042 Rennes cedex, France*

Abstract: A model of the cardiovascular system that consists of the ventricle, the circulatory system and the regulation of the cardiac action, is presented. The model of the ventricle includes a description of the electromechanical phenomena occurring during cardiac contraction. It explains the global behaviour of the heart and is coupled with a model of the circulation. The whole cardiovascular system is under the influence of this regulation model. *Copyright © 2005 IFAC*

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1. INTRODUCTION

Modelling in medicine plays more and more a major role. This work presents a model of the cardiovascular system which is a very complex system. In fact, the cardiovascular system includes different subsystems like the heart and the circulatory system, that interact in a complex way. Besides, the Autonomic Nervous System (ANS) is responsible for the regulation of the cardiovascular system and influence its function. The model of the cardiovascular system (CVS) should describe the behaviour of each subsystem and take into account the interactions between them. Furthermore, several energetic domains must be taken into account to describe the cardiovascular activity. In fact, there are mechanical, hydraulic, chemical and electrical events.

To take into account all these characteristics, the Bond Graph approach seems to be a relevant alternative. Bond Graph is a graphical tool usually used by engineers to describe the power exchange of a system. There are several applications to the use of Bond Graph especially in industrial applications like in the car industry. However, some works on the application of Bond Graph to physiology already

exist (Lefebvre et al, 1999; Diaz-Zuccarini, 2003; Diaz-Insua, 1996) and give encouraging results.

This paper shows how Bond Graph method can be used in modelling and simulation of a physiological system. The cardiovascular system is first presented. Then, the way to model it, is described : the ventricle, the vessels and the ANS. Finally, the results obtained after the simulation is shown.

2. DESCRIPTION OF THE CARDIOVASCULAR SYSTEM

The cardiovascular system consists of the heart and two closed systems of vessels known as systemic and pulmonary systems (figure 1). There are different kinds of vessels in these systems : arteries, veins and capillaries. The primary objective of the CVS is to transport the blood to bring the oxygen from the lung to the organs that need it, and to carry important substances such as hormones and nutriment. The heart is a muscular pump that pushes blood to all parts of the body.

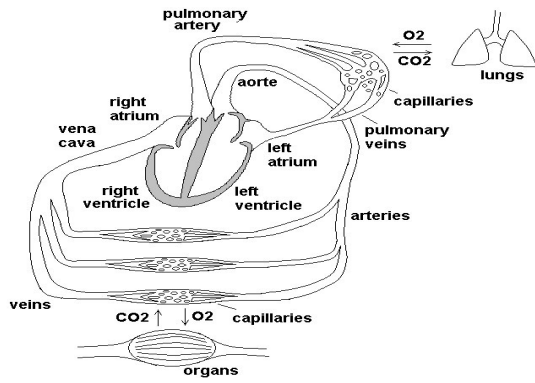


Fig. 1. An anatomical decomposition of the CVS

It is divided into four chambers : the two top chambers are called atria, and the lower chambers are called ventricles. The atria collect the blood that enters the heart and push it to the ventricles which eject blood out of the heart into the arteries. These heart chambers alternate periods of relaxation called diastole and periods of contraction called systole. The mechanical activity of the heart is controlled by a preceding electrical activity. The process from the electrical excitation to contraction of the heart is called cardiac excitation-contraction coupling. The cardiac muscle called myocardium is composed of cardiac myocytes which are specialized muscle cells.

The action potential which is produced through changes in membrane ion permeabilities, initiates the contraction of the heart by allowing the entrance of calcium in the cell as an inward Ca^{2+} current. The entry of calcium contributes to the action potential plateau and allows the release of Ca^{2+} from the sarcoplasmic reticulum. These phenomena bring a rise of the intracellular calcium concentration. The different mechanisms that lead to the variation of this concentration are complex and are the subject of a lot of studies.

The myocyte is made of myofibrils that contains sarcomeres which is the elementary contractile element. The sarcomere is composed of thick and thin filaments, called respectively myosin and actin. The interactions between the actin and myosin cause the development of the mechanical forces and the variations of the length of the sarcomere. In fact, the active sites on the actin can interact with the myosin heads. In the resting state, another protein called the tropomyosin covers these active sites. When calcium combines with this protein, the actin site becomes available to the myosin head. So the presence of calcium is essential to the interactions between actin and myosin. The increase of the intracellular calcium concentration leads to an actin-myosin interaction that converts electrical energy into mechanical energy.

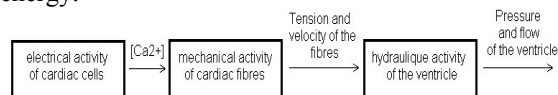


Fig. 2. Processes that lead to ventricular contraction.

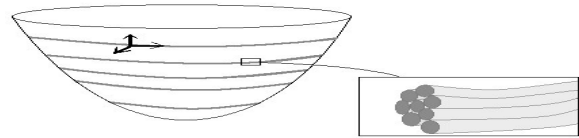


Fig. 3. Organization of cardiac fibres

3. MODELS OF THE CARDIOVASCULAR SYSTEM AND PROPOSED APPROACH

Current models of the CVS are often composed of different components, representing: *i*) the mechanical activity of the heart, *ii*) the whole vascular system and, in some cases, *iii*) the mechanisms involved in the regulation of the activity of the CVS. The later point is mandatory if one wishes to simulate realistic responses during non-stationary conditions (orthostatic stress for example ...). The following sections will present current models of each one of these components, as well as the options taken in the development of our own model.

3.1 Models of the global mechanical activity of the ventricles.

To describe the activity of the CVS, it is essential to have a good representation of the heart contraction. Although the model should be simple enough to be integrated in a model of the circulation, using the Bond Graph formalism, the mechanisms that lead to the development of force in the muscle fibres and the rise of ventricular pressure should be described precisely.

Many models of the global mechanical activity of the ventricles exist and some give pretty good descriptions of the heart contraction, as the model of elastance that has often been used in the literature (Guarini *et al*, 1998 ; Palladino *et al*, 2002). A Bond Graph model of the ventricle has already been presented (Lefebvre, 1999; Diaz-Zuccarini, 2003). The interest of this model resides in the fact that the interactions between actin and myosin are described using Bond Graph properties. Although these models give good descriptions of the contraction and good results in simulations, it lacks a realistic influence of calcium concentration during the contraction process. Now, this influence can be essential from a clinical point of view, to explain some cardiovascular troubles.

There are many models describing the development of mechanical force in the cardiac muscle fibres in the literature that take into account the electrical activity of the cardiac cell and calcium dynamics (Rice *et al*, 1999; Bestel, 2000). The model developed by Hunter *et al* (1998) is particularly interesting because it gives a geometrical description of the cardiac contraction of the fibres by means of the description of passive and active tensions.

The methodology we propose here consists in connecting various sub-models found separately in the literature, and ensuring the whole consistency by appropriate assumptions, which is made possible

thanks to the bond graph approach. More precisely, in our model of the global mechanical activity of the ventricles (figure 2), the dynamics of intracellular calcium concentration is described by means of a Hudkin-Huxley type membrane potential model. The well-known Beeler and Reuter (1977) model (BR model) has been chosen as it presents a basic description of the intracellular Ca^{2+} dynamics, while keeping a low level of complexity. Indeed, the contraction is possible only if there is enough intracellular calcium available. The intracellular calcium concentration variable of the BR model is then connected to the Hunter's model of development of mechanical force in the cardiac muscle fibres. The rise of the force and the variation of the fibre's length lead to the heart contraction and the variations of ventricular pressure.

In the Hunter's model, passive tensions are defined within 3 axes: the fibre axis, the sheet axis and the sheet normal axis. This definition is due to the microstructure of myocardial tissues that consists of layers of interconnected sheets of tissues, separated by cleavage planes. The passive tensions are different in the three orthogonal directions. The tension in the direction of the fibre is the sum of a passive and an active tension. These active and passive tensions depend on the length of the fibre. A complex version of the model of Hunter (1998) exists and takes into account different mechanisms including the binding of Ca^{2+} to troponin, the kinetic of tropomyosin movement and the kinetic of crossbridge tension development. In this work, we have only considered the simplest version of the model, as presented by Nash (1998). The active tension is defined as being dependant on the fibre length (l) and the calcium concentration $[Ca^{2+}]$.

$$T_{active} = T_{ref}(1 + \beta_0(l-1)) \cdot \frac{([Ca^{2+}])^h}{([Ca^{2+}])^h + C_{50}^h} \quad (1)$$

where T_{ref} is the referred tension at $l = 1$, C_{50} is the intracellular calcium concentration at which the isometric tension is 50% of its maximum, h is the Hill coefficient determining the shape of the curve, β is a the myofilament "cooperativity". This relation is supposed to be the steady-state tension- $[Ca^{2+}]$ relation. So the tension in the axis of the fibre has been defined as a sum of two functions of the length of the fibres. In Bond Graph, this tension has been modelled by two capacitive elements: one for the passive properties of the muscle and one for the active properties. The equations of each capacitive element are described by the model. A 1-element is used to join the two capacitive elements because the total tension in the axe of the fibre is the sum of two tensions.

The contraction of the cardiac muscle fibres leads to the generation of the mechanical force, which is necessary to the rise of the intraventricular pressure and the diminution of heart volume during the systole. So, the ventricular pressure depends on the force developed by fibres and the geometrical form of the ventricle.

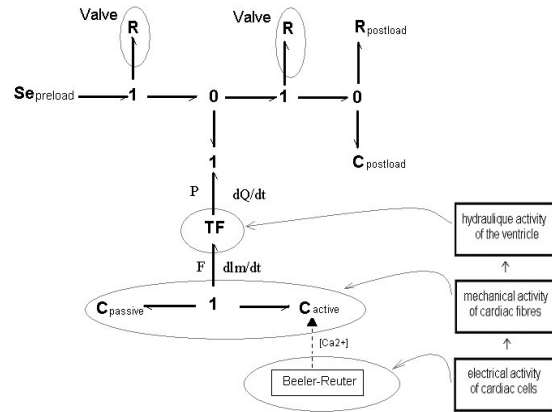


Fig. 4. Bond Graph model of ventricle

The tension of the ventricular wall is directly under the influence of fibres direction. Although the organization of cardiac fibres is complex, the number of circular fibres is the most important. In this work, the ventricle is supposed to be only composed of concentric rings of muscular fibres (figure 3). In this conditions, it is possible to show that the ventricular pressure depends only on the tangential tension which corresponds to the fibres axes (Bestel, 2000). In this way, the influence of the passive tension in the sheet axis and the sheet normal axis can be neglected and only the tension in the fibres axis is considered. To take into account the ventricular geometry in a simple way, the ventricle can be supposed to be of a known geometrical shape, like a roll or an ellipsoid. It is also possible to use an empiric law as it has been done in the works of Diaz-Zuccarini (2003). These two approaches are quite similar, but the second one has shown good results in Diaz (2003). Besides, the values of the parameters used in this approach are physiologically more realistic than those used with other geometrical models. An empiric relation between ventricular volume (V) and fibre length (l) is thus defined as:

$$V = Al^n \quad (2)$$

where A and n are empirically defined.

Besides, energy losses of the ventricular contraction are neglected. To model the relation between fibre tension and ventricular pressure that corresponds to a mechano-electrical transformation, the Bond Graph element used is a transformer. In fact, this element is often used to model the change of energetic domain without losses. The transforming module is defined using the hypothesis made previously.

This approach led us to a model that describes the ventricular behaviour using a Bond Graph formalism. Especially, it is possible to describe the variation of ventricular pressure and volume and to model global electromechanical phenomena. Figure 4 shows the Bond Graph model of the ventricle. With the Beeler and Reuter model, it is possible to obtain the calcium concentration, which modulates the capacity that describes the active tension. Only the influence of the tension in the fibre axis is considered. The transformer models (TF) the tension-pressure relation.

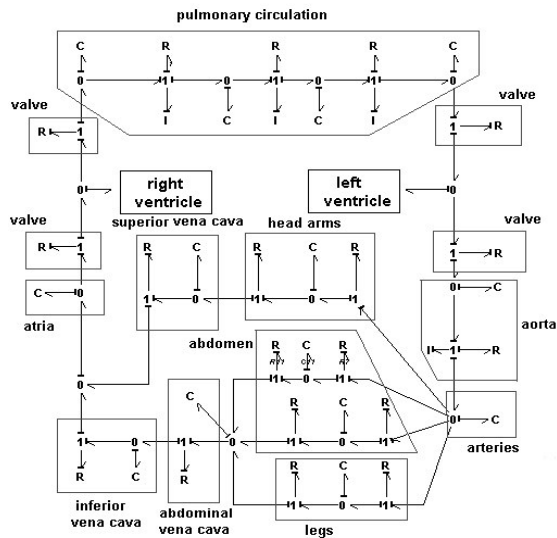


Fig. 5. Bond Graph model of the circulatory system and its relationship with ventricle models.

The heart valves are modelled like non-ideal diodes that correspond to modulated resistances. To simulate the model behaviour without the influence of preload, the ventricular filling is modelled by a constant effort source. The aortic obstacle is described by a resistive and a capacitive element.

3.2 The model of the vessels.

A segment of a vessel is modelled by its capacitive, resistive and inertial properties. The model is composed of a parallel capacitance, a resistance and an inductance in series. In fact, the capacitance describes the wall vessel elasticity, the resistance models the opposition to blood flow, and finally, we consider the inertia of blood. It is a classical way that has been used in many applications (Diaz-Insua, 1996; Heldt, 2002).

The most important groups of vessels, like the main arteries, veins and capillaries, are modelled as vessel segments characterized by their capacitive, resistive and inertial properties. The systemic circulation is often divided into upper body, renal, splanchnic and leg branches. The intrathoracic (superior and inferior) and extrathoracic vena cavae are separated. The inertial effects in this part of the systemic circulation have been neglected (figure 5). The values of the different parameters has been found in the literature (McInnis *et al*, 1985; Heldt *et al*, 2002).

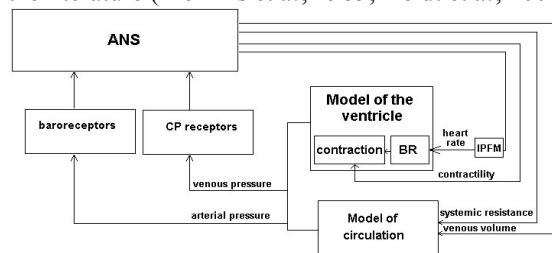


Fig. 6. Regulation of the cardiovascular system by the ANS.

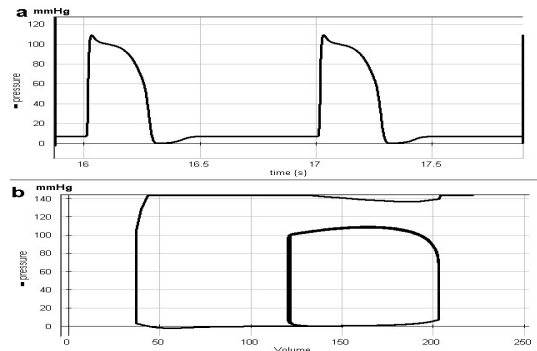


Fig. 7. Simulation of the left ventricular pressure (a) and the PV loop (b)

The model of the ventricle has been then coupled with the model of the circulatory system. The tension developed by the fibres of both ventricles are supposed to be the same. However, the left pressure is higher than the right pressure, because the left ventricle's wall is thicker than the right ventricle's wall. To take into account this difference, the number of fibres of the left ventricle is considered to be 4 times bigger than those for the right ventricle.

3.3 The regulation of the cardiovascular system.

The cardiovascular system is regulated by the ANS, which is divided into two components known as the sympathetic and the parasympathetic systems. The sympathetic system is responsible for the provision of energy needed in emergency situations like hunger, fear and extreme physical activity. The parasympathetic system influences organs to restore and to save energy.

The regulation of the cardiovascular system is very complex and most of the regulatory pathways remain unknown. In this work, only the influence of the short-term regulation of blood pressure (the baroreflex) is considered. The baroreflex is initiated by the stimulation of the baroreceptors, which are sensory receptors that respond to variations of pressure that are mainly located in the wall of atria, vena cava, aortic arch and carotid sinuses.

To model the influence of the baroreflex on the cardiovascular system, the model proposed by van Roon (1998) has been retained, as it takes into account the effect of the baroreflex, the cardiopulmonary reflex and, particularly, the respiration. This model includes a description of baroreceptors and pulmonary receptors and a description of the sympathetic and parasympathetic systems. Four effectors are included in the model: heart rate, contractility of the heart, systemic resistance and venous volume (figure 6). The heart rate depends on the action of both the sympathetic and the parasympathetic systems. The contractility of the heart, the systemic resistance and the venous volume are only on the influence of the sympathetic system.

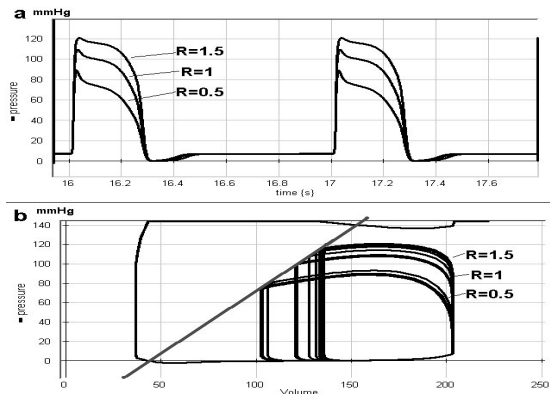


Fig. 8. Simulation of the left ventricular pressure (a) and the PV loop (b) with different postload resistance.

In order to couple this baroreflex model to our Bond Graph model of the cardiovascular system (that consists of a model of the circulatory system and the ventricle), a number of adaptations had to be made. Concerning the modulation of the heart rate, an IPFM (integral pulse frequency modulation) is used to apply a stimulating current to the BR model, at each generated pulse (figure 6).

The T_{ref} parameter (eq 1) of the active tension of the cardiac fibre can be considered to be an indicator of the cardiac contractility. In this sense, we have replaced the T_{ref} definition in eq. 1 by the value of the contractility variable obtained from the regulation model. The parameters of the regulation of the systemic resistance can be adapted in a similar manner to the model of the cardiovascular system. The parameters of the regulation of the venous volume have been established from the hypothesis that the contribution of the splanchnic circulation is 50% of the venoconstriction response. It represents 15% for the upper body, 3% for the renal circulation and 22% for the leg circulation.

3. RESULTS

The proposed model of the whole cardiovascular system was simulated using the 20-sim software with the Runge-Kunta numerical method. Firstly, the model of the ventricle has been tested in an independent manner. Results of the simulation of the intra-ventricular pressure are shown on figure 7.a. The global shape of the generated pressure signal seems to be realistic when compared with those obtained from similar models, even if the values of the resting pressure do not correspond to the physiology. This is due to the use of a constant effort source to model the ventricular filling, which is needed to test this model when it is not coupled with a circulatory model. However, if this model is coupled to the whole cardiovascular system model, this phenomenon is not observed. Figure 7.b. shows the pressure-volume curve obtained during simulation. This curve is characteristic of the change of cardiac stiffness during the cardiac cycle.

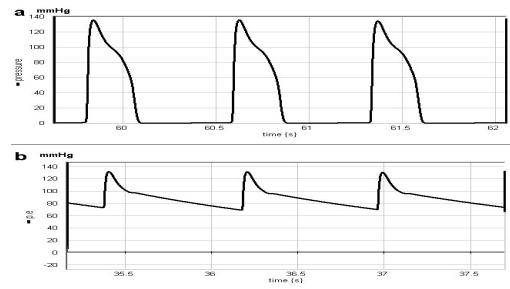


Fig. 9. Pressure simulated at different sites

Some parameters values can be changed to test the behaviour of the model. For example, figure 8.a shows that a rise of the output resistance leads to a rise in ventricular pressure. This reaction is physiologically realistic because, in these conditions, the ventricle must develop a bigger pressure to eject the blood in the aorta. The pressure-volume loop obtained with different resistances is shown on figure 8.b. It is possible to observe the linearity of the end-systolic pressure that is characteristic of the ventricular behaviour (Suga, 2003).

Pressure curves at different sites in the systemic and pulmonary circulations can be obtained with our model of SCV. For example, figures 9.a et 9.b show respectively the left intra-ventricular pressure and the arterial pressure. The shape of the pressure is realistic although it is a bit sharp. It is possible to see that the values of the arterial pressure, especially the systolic and the diastolic values are within the normal range.

Although the simulations obtained are encouraging, it is important to validate the results. Two different ways are possible: qualitative or quantitative. In this paper, only a qualitative validation of the model is shown. The proposed approach is similar to the one proposed by Ottensen (2000), in which the systemic resistance is increased abruptly by a factor 2.5. (such an increase of the systemic resistance could correspond to a mechanical clamping of vessel or an injection of drugs), and the response of the model to this perturbation is qualitatively analysed.

This test has been performed with the model (figure 10.b). The arterial pressure (figure 10.a) grows immediately after the sudden rise of the resistance. Then, it is possible to observe the influence of the baroreflex: the heart rate (figure 10.c) and the contractility (figure 10.d) decrease rapidly. The drop of these values brings a progressive decrease of the arterial pressure and a fall of the systemic resistance.

Figure 11 shows the results of the simulations with an abrupt decrease of the contractility by a factor 1.8 (figure 11.d). The drop of contractility could be a consequence of a myocardial infarct. The arterial pressure falls immediately (figure 11.a) after the drop of the contractility. These events bring a small rise of the heart rate and the systemic resistance (figures 11.c and 11.b). It leads to a weak increase of the arterial pressure that stabilises at a different level than the rest state level.

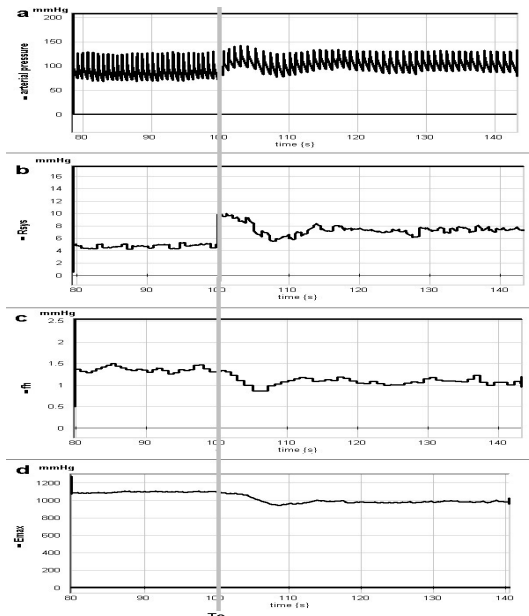


Fig. 10. Simulations of the arterial pressure (a), systemic resistance (b), heart rate (c), contractility (d) obtained in response of a rise of the systemic resistance

4. CONCLUSION

A new model of the cardiovascular system based on the Bond-Graph formalism has been proposed. It is composed of several subsystems of the cardiovascular system and the interactions between them. Besides, the description of the system is made at different levels. In fact, the electro-mechanical phenomena that lead to the ventricular contraction is modelled to describe the behaviour of ventricles that has been coupled with the circulatory systems. Some variables of the CVS are regulated by a model of the ANS. With this model of CVS, it is possible to simulate the pressure at different sites and to describe the electromechanical phenomena at the origin of the cardiac contraction. The simulations agree qualitatively with clinical behaviour. Current works are carried out and are focussed on the comparison between real data observed during a tilt test and the simulation generated by the model

The simulations obtained are encouraging for the use of Bond Graph in physiological modelling. Besides, the Bond Graph approach allows gradual aggregation of basic elements, the graphical structure of the model is close to the anatomical decomposition of the cardiovascular system and its comprehension is intuitive. Finally, Bond Graph theory allows to use one formalism for different energetic domains.

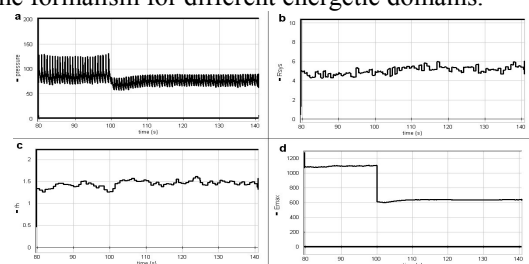


Fig. 11. Simulations of the arterial pressure (a), systemic resistance (b), heart rate (c), contractility (d) obtained in response of a fall of the contractility

REFERENCES

- Beeler, G.W. and Reuter H. (1977). Reconstruction of the action potential of ventricular myocardial fibres. In: *Journal of Physiology*, 268 : 177-210.
- McInnis B.C. , Guo Z.W. , Lu P.C. , Wang J.C. (1985) Adaptive Control of Left Ventricular Bypass Assist Devices. In : *IEEE Transactions on Automatic Control* , Vol. AC-30 , No 4
- Diaz-Insua, M., Delgado, M. (1996). Modeling and Simulation of the human cardiovascular system with Bond Graph : a basic development. In: *Computer In Cardiology*, 393-396
- Hunter, P.J., McCulloch A.D. and ter Keurs H.E.D.J. (1998) Modelling the mechanical properties of cardiac muscle. In: *Progress in Biophysics & Molecular Biology* ,69 , 289-331
- Nash, M., (1998) Mechanics and Material Properties of the Heart using an Anatomically Accurate Mathematical Model. PhD thesis, University of Auckland.
- Van Roon A.M. (1998) Short-term cardiovascular effects of mental tasks. PhD thesis, University of Groningen.
- Guarini M. , Urzua J. , Cipriano A. (1998) Estimation of Cardiac Function from Computer Analysis of the Arterial Pressure Waveform, In : *IEEE Transactions on Biomedical Engineering* , Vol. 45 , 1420-8.
- Jacques LeFèvre, Laurent Lefèvre and Bernadette Couteiro (1999), A bond graph model of chemo-mechanical transduction in the mammalian left ventricle, In : *Simulation Practice and Theory*, Volume 7, Issues 5-6, pp. 531-552
- Rice J.J. , Winslow R.L. and Hunter W.C. (1999) Comparison of putative cooperative mechanisms in cardiac muscle: length dependence and dynamic responses. In : *Am J Physiol.* ; 276 : H1734-54.
- Ottensen J.T. (2000), Modelling the Dynamical Baroreflex-Feedback Control. In : *Mathematical an computer modelling.* Vol : 31, Issues 4 – 5 ; pp. 167-173.
- Bestel, J. (2000). *Modèle différentiel de la contraction musculaire contrôlée : Application au système cardiovasculaire*, PhD thesis, University Paris 9
- Heldt, T., Shim, E.B., Kamm R.D. and Mark R.G. (2002). Computational modelling of cardiovascular response to orthostatic stress. In: *J Appl Physiol*, 92(3): 1239 - 1254.
- Palladino J.L. , Noordergraaf A. (2002) A paradigm for quantifying ventricular contraction. In : *Cell. Mole. Biol. Letters* 7(2) : 331-335.
- Diaz-Zuccarini, V.A. (2003). *Etude des conditions d'efficacité du ventricule gauche par optimisation téléonomique d'un model de son fonctionnement*. PhD thesis, Université de Lille.
- Suga H. (2003), Cardiac Energetics : from Emax to pressure-volume area. In: *Clinical and Experimental Pharmacology and Physiology*, Volume 30, Issue 8, pp. 580