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A bond graph model of the cardiovascular system

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Abstract

The study of the autonomic nervous system (ANS) function has shown to provide useful indicators for risk stratification and early detection on a variety of cardiovascular pathologies. However, data gathered during different tests of the ANS are difficult to analyse, mainly due to the complex mechanisms involved in the autonomic regulation of the cardiovascular system (CVS). Although model-based analysis of ANS data has been already proposed as a way to cope with this complexity, only a few models coupling the main elements involved have been presented in the literature. In this paper, a new model of the CVS, representing the ventricles, the circulatory system and the regulation of the CVS activity by the ANS, is presented. The models of the vascular system and the ventricular activity have been developed using the Bond Graph formalism, as it proposes a unified representation for all energetic domains, facilitating the integration of mechanic and hydraulic phenomena. In order to take into account the electro-mechanical behaviour of both ventricles, an electrophysiologic model of the cardiac action potential, represented by a set of ordinary differential equations, has been integrated. The short-term ANS regulation of heart rate, cardiac contractility and peripheral vasoconstriction is represented by means of continuous transfer functions. These models, represented in different continuous formalisms, are coupled by using a multi-formalism simulation library. Results are presented for two different autonomic tests, namely the Tilt Test and the Valsalva Manoeuvre, by comparing real and simulated signals.

MESH Keywords Cardiovascular System ; anatomy & histology ; Humans ; Models, Anatomic

Author Keywords Bond Graphs ; Multi-formalism modelling ; Cardiovascular System ; Biomedical systems

INTRODUCTION

The analysis of the autonomic nervous system (ANS) activity and, particularly, of the way it modulates the cardiovascular system (e.g. analysis of the heart rate variability) has shown to provide valuable information for the risk-stratification and early detection of some cardiac pathologies (Malik et al, 1996; Lombardi et al, 2001). In clinical practice, the analysis of the ANS is commonly performed by applying a set of tests called autonomic manoeuvres (such as the Valsalva manoeuvre (Flessas et al, 1970) or the Tilt test (Gabbett et al, 2001)). These manoeuvres are based on the controlled modification of one cardiovascular variable, in order to observe the regulatory response of the ANS. Different observations, such as the electrocardiogram (ECG), the noninvasive systemic arterial pressure (SAP) or the respiration, are acquired concurrently, to better characterize this autonomic response. However, the interpretation of these data can be very difficult, due to the multidimensionality of the observed phenomena, and the fact that the complex mechanisms involved in the autonomic regulation of the cardiovascular system are not fully understood. Physiological models can be of a particular interest in this context.

An appropriate model to analyse the short-term autonomic regulation of the cardiovascular system should take into account, at least, the following subsystems: i) the cardiac mechanical activity, ii) the circulatory system and evidently iii) the autonomic baroreflex loop including afferent and efferent pathways. However, although different models have been proposed in the literature for each one of these components, treated independently, only a few models combining these three components have been proposed.

The aim of this paper is to present a new model combining the autonomic modulation, the ventricular activity and the circulatory system, that can be useful for the analysis of autonomic tests. One of the difficulties for the development of such a model is related to the fact that different energetic domains are involved in the cardiovascular system function and its regulation. The formalism used to construct the model should take into account this variety of energy domains and consider the different sub-systems that constitute the CVS. The Bond Graph formalism (Dauphin-Tanguy et al, 2000), which is generally used by engineers, has been used in this work, as the main modelling formalism because it allows the usage of a unified representation for all energy domains; and makes easier the construction of a global system of the CVS.

The theoretical principles of the Bond Graph formalism are presented in section 2. The proposed combined model is described in section 3. Finally, simulations of two autonomic tests, called the Valsalva manoeuvre and the tilt test, are presented and the results of the simulations obtained are compared with experimental data.

THE BOND GRAPH FORMALISM

Introduction to the Bond Graph

The Bond Graph (BG) formalism is a diagram-based method that is particularly powerful to represent multi-energy systems, as it is based on the representation of power exchanges (Dauphin-Tanguy et al, 2000). Actually, the terminology, the rules and the construction of Bond Graph models are the same for all energy domains. For example, in the mechanical domain, the effort variable e is the force and the flow variable f is the rate; whereas, in the hydraulic domain, the effort variable e is the pressure and the flow variable f represents flow. The power is the product of the effort and the flow: P=e.f. The elements of the Bond Graph language can be classified in:

Passive elements: R, C and I

- Resistive element (R):

The resistive element R is used to describe dissipative phenomenon and can represent electrical resistors, dashpots or plugs in fluid lines.

- Capacitive element (C):

The capacitive element C is used to describe energy storage and can represent springs or electrical capacitors.

- Inertial element (I):

The inertial element I is used to model inductance effects in electrical systems and mass or inertia effects in mechanical or fluid systems.

Active elements: Se and Sf

An effort source is an element, which produces an effort, independently of the flow, and a flow source is an element that produces flow independently of the effort

Junction elements: 0, 1, TF, GY

- 0 junction:

The 0 junction is characterized by the equality of the efforts on all its links, while the corresponding flows sum up to zero, if power orientations are taken positive toward the junction.

- 1 junction:

1 junction is characterized by the equality of the flows on all its links, and the corresponding efforts sum up to zero with the same power orientations.

- Transformer (TF):

The transformer TF conserves power and transmits the factors of power with scaling defined by the transformer modulus. It can represent an ideal electrical transformer or a mass-less lever.

- Gyrator (GY):

A gyrator establishes a relationship between flow to effort and effort to flow and conserves the power. It can represent a mechanical gyroscope or an electrical dc motor.

Example

It is possible to describe simply an electrical circuit using the Bond Graph. For example, the RC circuit in figure 1 can be represented by an effort source e, a resistance R and a capacitive element C. A 1-junction connects all the components, corresponding to a serial configuration.

Bond Graph models in Physiology

The Bond Graph formalism is generally used by engineers to describe power exchanges in a system. There are several applications of the Bond Graph in the industry, especially in the automotive one. However, the Bond Graph formalism can be particularly useful for modelling physiological systems that often include various energy domains. Some works on the applications of Bond Graph in physiology exist, for example, for the design of a Bond-Graph-Based controller for Muscle Relaxant Anaesthesia (Linkens and Chen, 1995) or for modelling the musculoskeletal structure (Wojcik, 2003). Models of the vascular system (Diaz-Insua and Delgado, 1996; Lefebvre et al, 1999; Diaz-Zuccarini, 2003) are especially interesting since they take into account different energy phenomena (hydraulic, mechanic, chemical…).

MODEL DESCRIPTION

The proposed model is composed of the ventricles, the circulatory system and the cardiovascular regulation by the ANS. One of the original points of this work is to take into account a simplified representation of the electromechanical processes involved in the ventricular activity. The vessels are modelled by their capacitive, resistive, and inertial properties. Only the short-term autonomic regulation of the CVS, by means of the baroreflex, is considered in this model. This short-term regulation, which is the one involved during the application of autonomic manoeuvres, modulates heart rate, ventricular contractility and the constriction of the systemic vessels. A description of each one of these model components is presented in the following sections.

Model of ventricles

The cardiac contraction is at the origin of the transport of blood in the circulatory system. At the scale of cardiac cells, the contraction is due to the shortening and lengthening of sarcomeres, which are the elementary mechanical contractile elements. This mechanical activity is under the influence of an electrical activity, since the variation of the calcium concentration during the action potential allows the development of force. This variation of force in the myocardium allows the delivering of a sufficient ventricular pressure (figure 2).

Different models of the ventricular contraction have been presented in the literature. The most detailed models are often based on a network of connected (finite) elements that allow a relatively precise description of the structure and function of the myocardium. In fact, the three-dimensional geometry of the cardiac muscle and the fibre architecture plays an important role in the electrical and the mechanical activity of the ventricle. The representation of the electrical activity of cardiac cells is essential to the description of the global mechanical behaviour (Smith et al, 2002), as the interactions between microscopic elements influence the macroscopic level. Although these models describe precisely the process that leads to myocardial contraction, they are difficult to use in clinical practice, mainly due to the computing resources required. On the other hand, simpler models, representing each ventricle as a single adaptive elastance, have been proposed (Guarini et al, 1998; Palladino and Noodergraaf, 2002; Suga, 2003). The main advantage of this approach, which is related to their low computational costs, is the fact that they can be easily integrated into a model of the CVS. This kind of models has also shown to provide a satisfying behaviour in response to physiological variations (change of position, temperature, physical activity…) (Heldt et al, 2002). However, although these models give good global descriptions of the contraction and good results in simulations, the influence of calcium concentration during the contraction process and the regulation by the ANS are not taken into account.

In the proposed model, we have chosen to include a description of the electro-mechanical process, keeping the simplified representation of the ventricles provided by the elastance model. As a first approximation, 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. However, the BR model cannot be directly implemented under the Bond Graph formalism, due to its non-linearity and the strong interdependence between the state variables. This model has thus been implemented as a set of ordinary differential equations.

Coupling models representing different anatomical scales under different formalisms can be a difficult task. The two main difficulties are associated with the temporal synchronisation and the spatial coupling of multi-formalism models (Zeigler, 2000). For instance, the temporal dynamics of the BR model and the ventricular model present different orders of magnitude (the necessary step resolution is around 1 millisecond for the ventricular model and of 1 microsecond for the BR model). Standard simulation environments cannot address these problems. In this work, a multi-formalism simulation library developed in our laboratory has thus been used, to simulate each formalism in an independent manner and couple them appropriately(Defontaine et al, 2004).

The intracardiac calcium concentration variable of the BR model is used as input to a model of development of mechanical force in the cardiac muscle fibres. Some models describe this electro-mechanical coupling (Rice et al, 1999; Bestel, 2000) and the one 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 stress in the fibre axis is obtained by adding these passive and active tensions:

$$T_{fiber}(l) = T_{active}(l) + T_{passive}(l)$$

In this work, we have considered the version of the model presented by Nash (1998). The active tension is defined as being dependant on the fibre strain (l) and the calcium concentration [Ca2+].

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

where Tref is the reference 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 and β represents the myofilament "cooperativity". This relation is supposed to be the steady-state tension-[Ca2+] 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 equations 1 and 2. A 1-element is used to join the two capacitive elements because the total tension in the axis of the fibre is the sum of two tensions (figure 3).

The rise of the force and the variation of the fibre length lead to variations of ventricular pressure and, thus, to the ventricular contraction. Actually, the pressure depends on the fibre tension and ventricular geometry. In this paper, the ventricle is supposed to be made of concentric rings of muscular fibres. So the ventricular pressure depends only on the tangential tension, which corresponds to the fibres axes. An empirical relation between fibre force and ventricular pressure has been proposed by Diaz-Zuccarini (2003). In this approach, the ejected volume V is defined as a function of the fibre strain l by

$$V = Al^n$$

where the values of A and n are empirically defined. This approach has shown to provide simulation results that are coherent with physiology (Diaz-Zuccarini, 2003). Neglecting energy losses of the ventricular contraction, the same empiric law holds to describe the relation between the fibre force and the ventricular pressure. As a result, the change of energy domain from mechanics to hydraulics can be described by a transformer implementing equation 3 (figure 3).

Model of the Circulatory System

The circulatory system is composed of the systemic and the pulmonary circulation that respectively transport blood to bring the oxygen and nutriment to the organs, and permits the oxygenation of blood in the lung. These vascular systems are composed of different kinds of vessels called arteries, capillaries and veins. The circulatory system is often modelled as an RCL circuit, representing the capacitive, resistive and inertial properties of a given vessel segment. A vascular network can thus be constructed by connecting different vessel segments in series (Tsitlik et al, 1992). However, the definition of an exhaustive and realistic model of the vascular network can be very complex, because of the large number of vessels and the marked inter-patient anatomical variability. Models of the circulatory system are thus often defined in a global way, by considering groups of vessels (e.g. pulmonary arteries, pulmonary capillaries, pulmonary veins, systemic arteries, systemic capillaries, systemic veins, vena cava) in an equivalent lumped model (Diaz-Insua and Delgado, 1996; Heldt et al, 2002). Although these lumped parameter models are able to simulate appropriately global hemodynamic signals, in some cases, such as during the analysis of the orthostatic tests, a more precise description of the vascular system may be necessary.

As proposed by other authors, a segment of a vessel is modelled in this work by its capacitive, resistive and inertial properties. The model is composed of a parallel capacitance, a resistance and an inertance in series, which can be directly represented in a Bond Graph model, as shown in figure 4.

In order to be able to analyse data from different autonomic tests, two configurations, showing different levels of detail of the vascular system, have been proposed: a simple configuration distinguishing only the pulmonary and systemic circulation (figure 5.a) and a more detailed representation in which the model of the systemic vascular tree has been divided in three parts (the head, the abdomen and the legs) (figure 5.b). The former configuration is adapted to the analysis of autonomic tests in supine position (such as the Valsalva manoeuvre), while the later one can be used to study orthostatic responses (such as the tilt test). Each vascular network is composed of a series of connected vessel segments. For example, the systemic circulation of the simple vascular model (figure 5.a) is composed of five vessel segments representing the aorta, the set of systemic arteries, small arteries and capillary arteries (this segment is modulated by the vasoconstriction), the set of systemic veins and the vena cava. The heart valves are modelled as non-ideal diodes using modulated resistances. The atria are modelled as constant capacitances (figures 5a and 5b). The ventricular model described in the previous section is used for the left and right ventricles.

The parameter values of each vessel segment are difficult to define because it is hard to associate a component of the model with a precise part of the body and it is complex to perform direct measurements. The values used in our model have been experimentally defined, by the comparison between simulated signals and physiological signals. In this work we have used, for the systemic circulation that is constituted of a single loop, the parameter values of McInnis (et al, 1985), except for the vena cava that comes from Olufsen (et al, 2005). For the other version of the model of systemic circulation, the aorta parameter values has been obtained from McInnis (et al, 1985), the arteries values come from Olufsen (et al, 2005) and the venous values are taken from Heldt (et al, 2002). For both models, the parameters of the pulmonary circulation model are those of McInnis (et al, 1985). For example, the values of the parameters of the aorta are: C = 0.2199 ml/mmHg, R = 0.0675 mmHg.s/ml and I = 0.000825 mmHg.s/ml.

Model of the ANS

The autonomic nervous system (ANS) is the component of the nervous system that acts as the main modulator and control mechanism of internal organs, adjusting their activity to the requirements of the body as a whole and preserving homeostasis (rising the heart rate during sport, for example). The short-term regulation of the CVS is mainly performed by the baroreceptor loop that plays a important role in the blood pressure control adjusting mainly the heart rate, heart contractility and vessels constriction as the response to the information transmitted by the baroreceptors. This adjustment is done by the two components of the ANS: the sympathetic and the parasympathetic systems.

Models of the autonomic nervous system are typically based on a continuous transfer function formalism. Most of them describe the influence of the short-term regulation of blood pressure, namely, the baroreflex. This kind of models is quite difficult to develop because of the lack of detailed knowledge and observations on the neuronal activity. Some discrete-time models, based on signal processing and identification theories, such as autoregressive, moving-average (ARMA) models, have been proposed (Barbieri et al, 1997). Although they allow the reproduction of experimental signals, the physiological interpretation of the parameters of these models is difficult and there is not a direct structural relationship between the physiology and the model components. Another approach consists in the modelling of the different sub-systems that can be associated to an entity of the cardiovascular control (DeBoer et al, 1987; Seidel and Herzel, 1995). Many of them (van Roon, 1998; Lu et al, 2001) are based on a common structure, composed of delays and first order filters, representing the global neurotransmitter dynamics for a particular efferent pathway and allowing the description of the different response times of the sympathetic and the parasympathetic systems.

The Van roon model (1998) has been retained in this work and coupled with the ventricular and the circulatory models. This model, which takes into account the baroreflex and the cardiopulmonary reflex, also includes a description of baroreceptors and pulmonary receptors, the Nucleus Tractus Solitarii (NTS) and a description of the sympathetic and parasympathetic systems (figure 6).

Four variables are controlled in the model by means of different efferent pathways: heart rate, cardiac contractility, systemic resistance and venous volume (figure 7.a). 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. The same structure, based on a delay and a first order filter, is used for each one of the modelled efferent pathways (figure 7.b).

The ANS model is coupled to the CVS by injecting in the latter the four previous controlled variables in the following way:

- Regulation of the heart rate:

The output signal of the heart rate regulation model is continuous. To obtain pulsating blood pressure, an IPFM (Integral Pulse Frequency Modulation) model is used because it transforms a continuous input signal into an event series (Rompelman et al, 1977). The input of the IPFM model is the output signal of the heart rate regulation model. The output of the IPFM allows the excitation of the model of electrical activity (Beeler-Reuter, 1977). And each emitted pulse brings an augmentation of calcium concentration.

- Regulation of contractility:

The Tref parameter (equation 2) of the active tension of cardiac fibre can be considered to be an indicator of the cardiac contractility. In this sense, we have replaced the Tref definition in equation 2 by the output signal of the contractility regulation model.

- Regulation of systemic resistance:

The value of the parameters of the systemic resistance is replaced by the output signal of the resistance regulation model (figure 8).

- Regulation of venous volume:

The constitutive relation of the venous capacity depends on the unstretched volume Vo: $p = \frac{V - V_o}{C}$. The value of Vo in the venous capacity is replaced by the output signal of the venous volume regulation model (figure 8).

SIMULATION RESULTS

The Valsalva Manoeuvre

The Valsalva Manoeuvre is a non-invasive, non-pharmacological autonomic test, which is based on a forced expiration, to increase the intrathoracic pressure. This test concentrates on the complex interaction of both vagal and sympathetic baroreflex cardiac functions that modulate the heart rate, blood pressure and ventricular contractility. In this protocol, the studied subject is placed in supine rest and asked to breath out through a bugle connected to a pressure measurement system. The subject is asked to maintain a pressure of around 30 to 40 mmHg for a period of 15 seconds, after which a complete expiration is made. The Valsalva maneuver consists of 4 phases (figure 9). The forced expiration causes an initial increase in blood pressure, and a slight increase in heart rate, due to the augmented intrathoracic pressure (phase I), which is promptly reverted. During phase II, the augmented intrathoracic pressure reduces the volume of cardiac chambers (mostly the right heart), preventing cardiac filling and reducing the stroke volume and aortic pressure. This effect produces an unloading of the baroreceptors and an activation of the sympathetic nervous system, starting to increase heart rate and peripheral vasoconstriction to balance the decreased aortic pressure. After expiration (phase III), a further sudden drop of aortic pressure is produced by the reduction in intrathoracic pressure. But due to the effect of autonomic activation in phase II and the progressive restoration of hemodynamic conditions, the aortic pressure starts to rise. In phase IV, before reaching a normal physiological value, the blood pressure rises well above the original levels (overshoot phase), causing the loading of the baroreceptors and a vagal autonomic activation that leads to an abrupt drop in heart rate (Guyton et al, 1995).

For the simulation of a Valsalva manoeuvre, the simplest model of the circulation is used. The transmural pressure of thoracic vessels and of the cardiac cavity (ventricles, atria) is raised to simulate an augmentation of the intrathoracic pressure to a value of 40 mmHg. The model is simulated during 15 seconds, in order to obtain the heart rate and blood pressure signals. The obtained simulated signals are thus compared to real signals, acquired from normal subjects by using a “Task Force” acquisition system.

Figures 10.a and 10.c show simulated signals and figures l0.b and l0.d present real data. In general, and from a qualitative standpoint, the model seems to reproduce the main cardiovascular behaviour during a Valsalva manoeuvre. It is possible to recognize the four typical phases of the Valsalva manoeuvre on both the simulated and observed signals. Blood pressure dynamics reveal the rise during phase I, an increase and a decrease in phase II, a short fall in phase III and the return to normal conditions in phase IV. Note the consistent simulation of the overshoot period on phase IV. Heart rate dynamics are also consistent with the physiology, a slow increase of heart rate during Valsalva, which is followed by a decrease after expiration. However, it is possible to observe some differences between simulations and real data. They are mainly due to the fact that the parameters values used in these simulations are those presented in the literature, and remain the same for all patients.

Tilt Test

The head-up Tilt test focuses on the short-term regulation of the mean arterial blood pressure (MABP) by the ANS. It is usually employed for the detection of vasovagal syncope and consists of observing the variation of heart rate and blood pressure during the change of a patient’s position from a supine to a head-up position. During tilt, approximately 300 to 800 ml of blood may be shifted into the lower extremities, leading to a reduction of venous return and hence of stroke volume. In normal subjects, a decrease in the MABP causes the unloading of arterial baroreceptors, providing a sympathetic activation that leads to enhanced chronotropism (increased heart rate), inotropism (increased ventricular contractility) and peripheral vasoconstriction. A balance is established between heart rate and contractility to maintain the cardiac output and MABP in physiological levels.

To simulate a tilt test, the second version of the model is used in order to differentiate the main segment of the systemic circulation: the head, the abdomen and the legs. During a test, the gravity modifies the pressure in the different parts of the body. We have determined experimentally these variations by measuring the pressure in the finger. Three tests have been realized sequentially on the same normal subject. During the first test (figure 11.a), the hand is placed at the level of the abdomen. The variation of pressure measured is supposed to be equal to the pressure occurring during the test in the abdomen. During the second test (figure 11.b), the hand is blocked in an upper position, and, for the third test (figure 11.c), the hand is blocked in a lower position. The variation of the pressure signal measured is supposed to be equal to the value of pressure in the head, for the second test, and in the legs for the third test.

The augmentation of pressure observed are respectively for the first and third test: $\Delta P = 25$ mmHg et $\Delta P = 50$mmHg; the decrease of pressure for the second test is equal to $\Delta P = -30$mmHg. These different values are used to simulate a tilt test with the model, by introducing a

modulated source of pressure in the model. Figures 12.a and 12.b show the simulated and the observed systolic blood pressures, as measured in the low part of the body. It is possible to observe a sudden rise of blood pressure after the tilt, followed by a smoothed decrease, due to autonomic regulation. Then, the pressure increases slowly. The influence of the autonomic regulation on heart rate is also studied. Figures 12.c and 12.d compare the simulated and the observed heart rate. It is possible to observe that the heart rate augments abruptly after the tilt, and slowly decreases when the blood pressure approaches its physiological values.

CONCLUSION

A new model of the cardiovascular system based on the Bond-Graph formalism that is composed of several coupled subsystems of the CVS, has been proposed. In fact, the use of Bond Graphs to model ventricular activity and the vascular system, allows the aggregation of different simple components to form a complex system using formalisms for different energetic domains (Hydraulic and mechanic). Besides, the graphic representation inherent to this formalism is interesting because it is close to the anatomy, facilitating the comprehension and the discussion between engineers and clinicians. However, although this formalism seems to be particularly adapted to the description of hydraulic phenomena, for the circulation and the global mechanical activity of the ventricles, not all the physiological mechanisms represented in the model could be included by using the Bond Graphs formalism. In fact, the marked non-linearities involved in the genesis of the cardiac action potential are difficult to represent using the Bond-Graphs formalism. A set of ordinary differential equations (the BR model) has been thus used to describe the action potential of cardiac cells and, particularly, the intracardiac calcium concentration dynamics. Besides, ANS models are usually based on a transfer-function formalism, because it better describes the relation between inputs (blood pressure) and outputs (heart rate…) in this context. All these models have been successfully integrated by using the multi-formalism simulation library proposed in our laboratory.

The simulations obtained with the proposed model provide encouraging results. However, it can be interesting to detail some parts of the model. For example, the complex arrangement of cardiac fibres should be taken into account to have a better description of ventricular contraction and the variation of calcium concentration should be described more precisely. Although the results are satisfying for a qualitative validation, it is difficult to reproduce completely each patient's behaviour. In fact, the model parameters should be specific for each person and must be identified. Our current work concerns this patient-specific identification, based on an evolutionary algorithm, that has already been applied to other physiological models (Hernandez et al, 2002).

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Figure 1

Example of a simple Bond Graph model of an RC circuit.

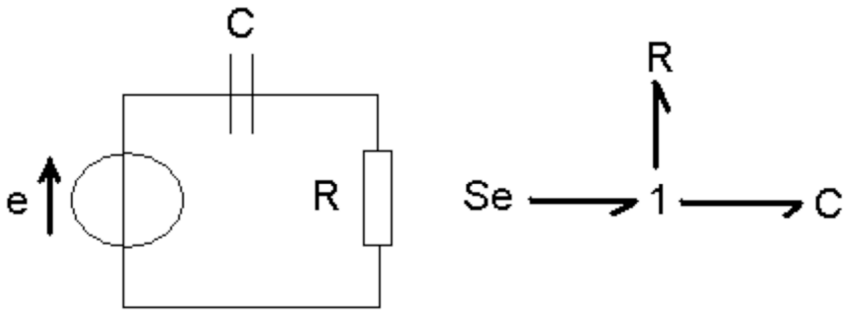


Figure 2

Schematic representation of the processes that lead to ventricular contraction and circulation of blood.

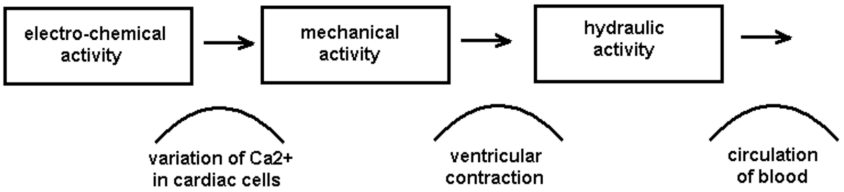


Figure 3

Bond Graph model of the ventricle and its coupling with the BR action potential model.

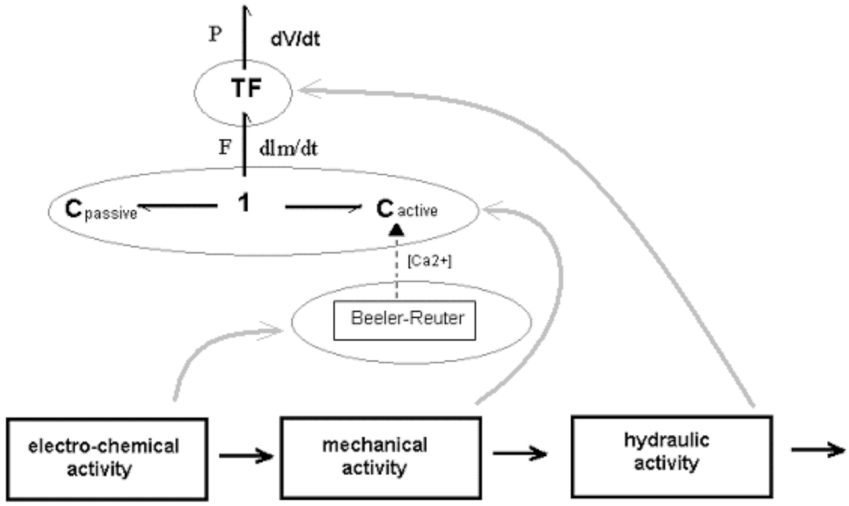


Figure 4
Bond Graph model of a vessel segment.

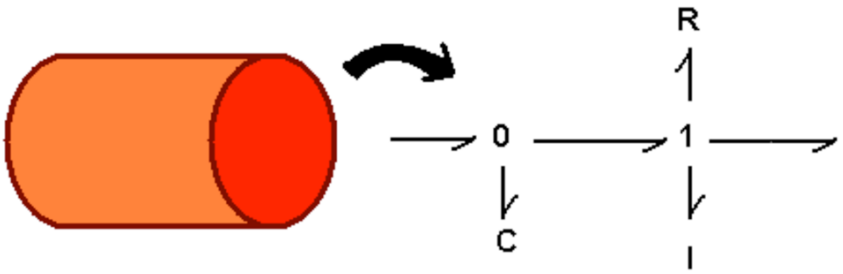


Figure 5
Bond Graph model of the circulation: a) a simple model distinguishing the pulmonary and systemic circulation b) a more detailed model differentiating the systemic circulation on the head, the abdomen and the legs.

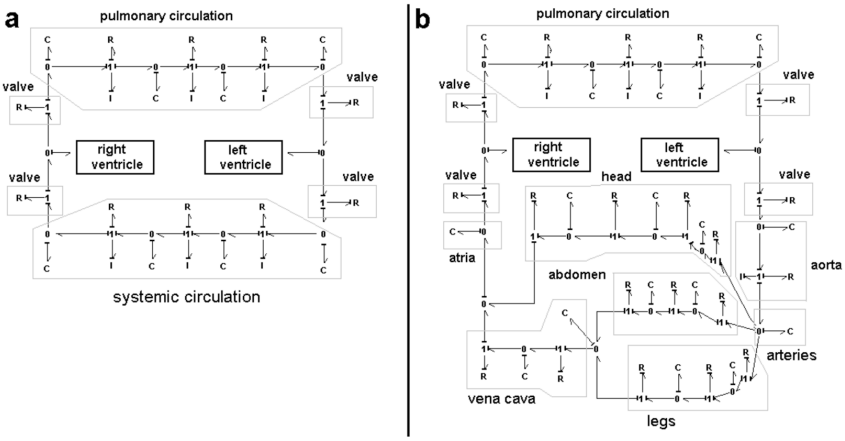


Figure 6
Diagram showing the coupling between the model of the ANS and the models of the ventricles and the circulatory system.

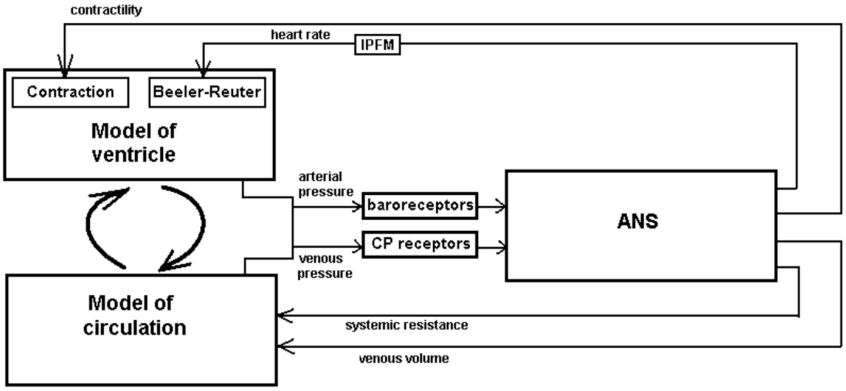


Figure 7
a) components of the ANS model b) structure of each ANS regulation component.

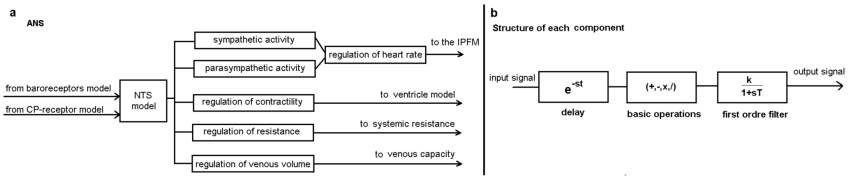


Figure 8

Elements of the Bond Graph model that are under the influence of the ANS model on the simple circulatory model (a) and the more detailed model (b).

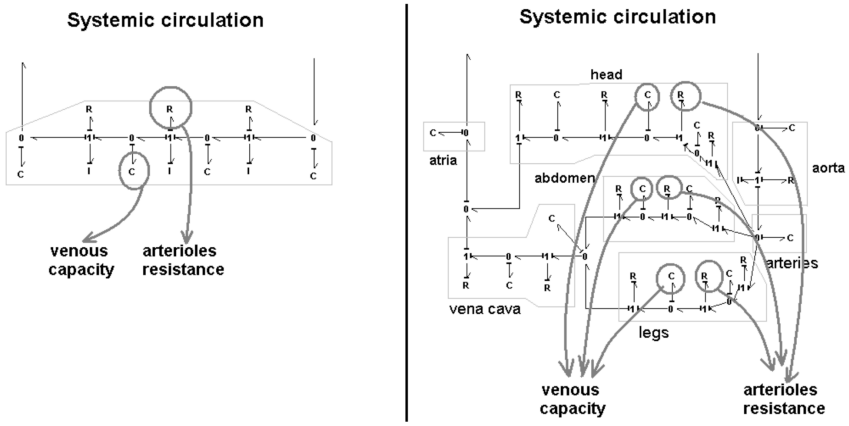


Figure 9

Systemic blood pressure dynamics during a typical Valsalva manoeuvre. The four phases of this autonomic test are presented.

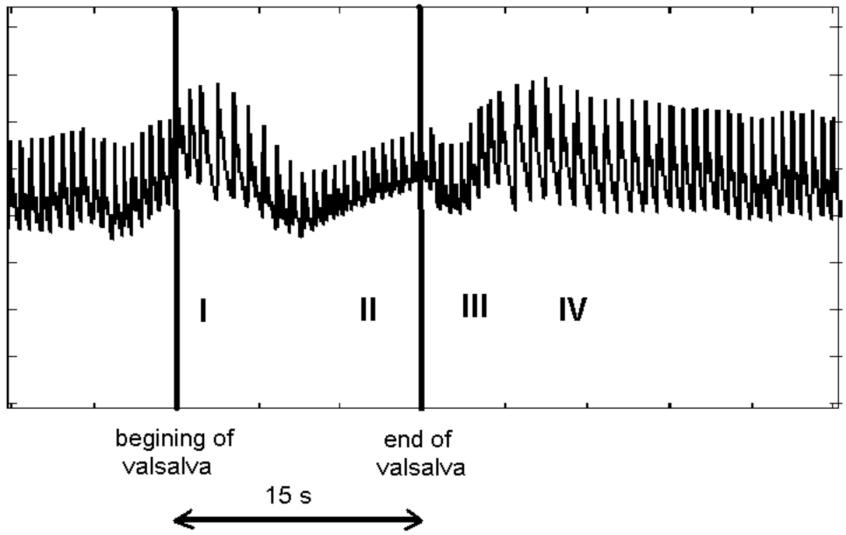


Figure 10

Simulation of blood pressure a) and heart rate c), real data of blood pressure b) and heart rate d)

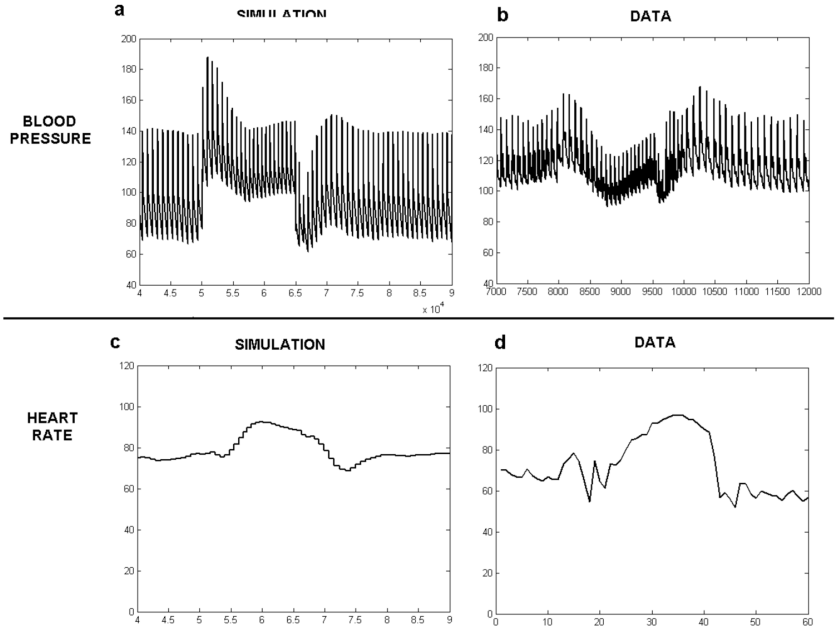


Figure 11

Blood pressure acquired at the level of the abdomen (a), the legs (b) and the upper body(c).

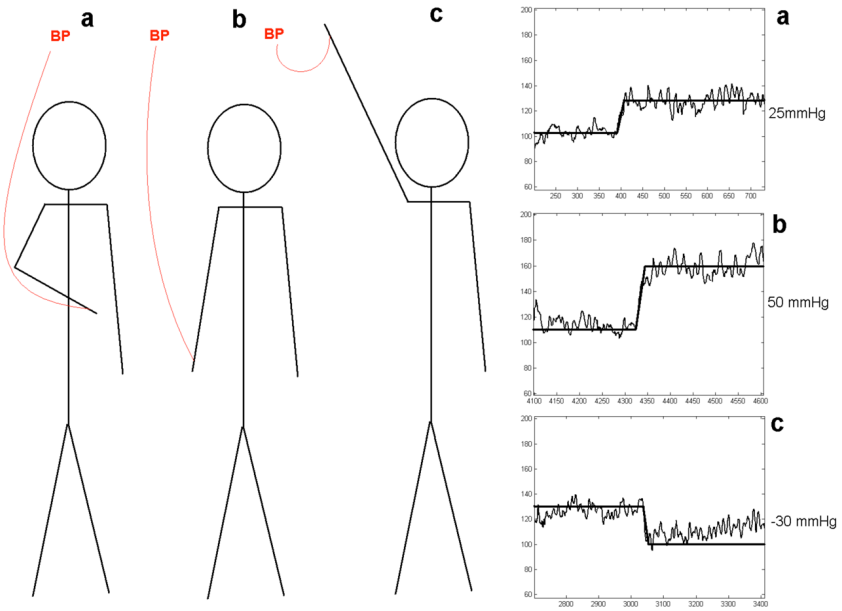


Figure 12

Comparison of simulated and observed data during a tilt test. Simulated blood pressure a) and heart rate c), real data of blood pressure b) and heart rate d).

