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A Model of internal control may improve the response time of an automatic arterial pressure controller

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Abstract : A simplified model for the arterial pressure control system was implemented on a personal computer using Matlab Simulink®. Model responses to variations of systemic vascular resistance were comparable to those predicted by physiology. Computer simulation suggested that including this model of the internal pressure control system within the design of an external controller would achieve better arterial pressure control and faster response than previous systems.

1. INTRODUCTION

Many automatic systems for controlling arterial pressure through drugs infusion have been described. However, none of them have been successful (Martin,1992; Linkens,1992). One of the reasons for this is that there is a disarragement between the human body´s response and the contoler´s one. This is due to the fact that the paramenters of the later have been regulated using too simplified internal regulating models (a regulation performed only inside the human body), which are not adequate representatives of the involved physiology. Besides, the

above mentioned controlling systems generally consider arterial pressure and the degree of drug infusion as decision variants, despite the fact that pressure can be affected by many other variants.

The investigation framework in which this work is placed proposes that an adequate arterial pressure internal regulating model, which also considers other variants in the drug infusion control system, would allow the development of external regulating systems with a better performance.

First, a dymanic and detailed model of the slow and fast arterial pressure regulation is computationally designed and implemented. This model incorporates the influence of the sympathetic and parasympathetic nervous systems upon variants such as the cardiac fequency, mean systemic input pressure and the blood retur, the pressure - volume renal system on variants like blood volume and the extracellular liquid volume. The model also includes the influence of disturbances on variants such as the percentage of the sympathetic and parasympathetic systems activity, systemic resistance, blood volume, ventricular systolic elastance and the extracellular liquid volume.

2. ARTERIAL PRESSURE CONTROL

Many homeostatic regulating mechanisms contribute to the arterial pressure regulating; they have specific roles under different conditions (Guyton, 1989).

One of these arterial pressure regulating systems is the baroreceptor system. The way it works can be summarized as follows : There are many nerve receptors called baroreceptors in determined sections of the carotids artery vessel, specially in the carotids bifurcation and the aortal arch. These baroreceptors are stimulated by the normal pressure and then, they transmit impulses to the brain stem. Here, the impulses bridle the vasomotor center and the cardioinhibitor center (vagus

nerve). The vasomotor center and the cardiaccelerator inhibit the impulses generation transmitted by the sympathetic nervous system to the heart and to the blood vessels. The heart activity is lowered due to the lack of these impulses and the peripherial vessels caliber increases. Both mechanisms diminish the arterial pressure ,once again, until reaching normal values. In an inverse process, the tension receptors stimulation, and as a consequence, barosensorial fibers discharge is also diminished. The later makes it possible that the vasomotor center increases its normal activity and, consequently, the arterial pressure again reaches its normal values.

As it was already mentioned, when there is an arterial pressure increase, this produces an increase in the baroreceptor system impulses fequency which is transmitted to the brain. Then, the brain iniciates the reflex to reduce the pressure to its original level. However, despite the fact that the reflex remains activated, the arterial pressure does not return exactly to its inicial level (cero default). Due to this, some authors still consider that the baroreceptor system is a proportional control system feedbacked from the arterial pressure (Guyton, 1974).

Another arterial pressure regulating system, and perhaps the most effective in the long run, is the pressure - volume renal control (Guyton, 1989).

For this balance, of water and sodium, in the body to exist in a healthy person, the kidney eliminates these elements in the same proportion they are ingested. When the hydrostatic pressure in the capillary vessels is increased, the kidney also increases the level of sodium and water filtering, thus increasing the urine level and continuously eliminating water (diurésis) and sodium (natriurésis) inside the body over the levels determined by tubular reabsortion. This means a cumulative reduction of the extracellular liquid volume . This way, changes in blood volume affect the arterial keeping to its normal value (Guyton, 1989). Due to this, many authors consider that the pressure - volume renal regulating system shares the features of a control system feedbacked by an integral action (Guyton, 1974.)

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On the other hand, there is a close relation between the regulation of the arterial pressure and the cardivascular process. Sagawua (1982) considers this relation both, by the direct influence of the cardiac debt upon the arterial pressure (Mean Arterial Pressure = Cardiac Debt * Systemic Resistance) as well as by determining the venous return. Baselli (1988) adds to the model the existing interaction between the respiratory system and the cardivascular process.

3. MEAN ARTERIAL PRESSURE REGULATING SYSTEM

The model is dynamic, of the fifth degree, basically not linear. It constitutes a clinical model since, besides being based on human physiology, it includes external disturbances.

Figure 1 shows the structure of the clinical model with its fundamental components: the model mean arterial pressure fast regulating system and the model of the mean arterial presssure slow regulating system.

One of the fundamental assumptions of this model is the fact that the sympathetic and the parasympathetic nervous systems activities percentages work complementing each other perfectly (like a mirror), around the normal value. This phenomenon adequately represents the physiology needed only in certain situations.

It is worth pointing out that the corresponding values for both, the normal range of physiological variants and the parameters, considered within the clinical model, come mainly from Guyton (1989.)

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3.1 Mean Arterial Pressure Regulating System Model

This model is presented in the upper part of Figure 1 and corresponds to a fourth degree model, which characterizes the regulating action of the automatic nervous system (sympathetic and parasympathetic nervous system) over the circulatory system.

The autonomic nervous system receives electrical signals from the baroreceptors and acts upon the circulatory system in order to mantain the mean arterial pressure within the desired range (Guyton,1989.)

Figure 1 : Structure of the clinical model.

The main element of the autonomic nervous system (block 1) is a first order transference function similar in structure to that proposed by Scher (1963.)

Both, the Sympathetic and the parasympathetic nervous systems present a saturation in thier respective activity percentages (blocks 2 and 3), which have a late effect over the pacemaker cells of the heart represented by blocks 4 and 5. A similar situation occurs with the muscular delay in the arterial system (block 6 and 7), and with the delay in the ventricles of the heart (block 8.)

The variation over the normal value of the heart rate (delta H.R.) is related with the percentage of the sympathetic and parasympathetic nervous systems through a transference function of the first order (blocks 9 and 10), whose structure represents adequately the involved phenomenology (Scher, 1963).

A similar situation happens with the variation of the normal value of the systemic resistance (Scher, 1963).

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It is known that there is a significant asymmetry with regards to the increase and reduction of both, the heart rate and the systemic resistance, due to the parasympathetic and parasympathetic nervous systems (Guyton, 1989). This assymetry is represented by non linear amplifiers which correspond to blocks 11 and 12.

The link between the mean systemic filing pressure (Pmsf), blood volume (Bv), the percentages of the sympathetic nervous system activity (% simp) and the venous capacity (VC), was represented by Guyton (1972)by means of an empirical curve. Block 13 represents a polinomial approximation of such an empirical curve, which is mathematically represented as:

Pmsf (t) = kl * (BV(t) + % simp(t)) - VC(t) + k2 (1)
where k1 and k2 are constants with different values for each of the three lines that are used for the approximation.

Block 14 represents the link among the venous capacity (VC), the activity of the sympathetic nervous system (% simp) and the systolic elastance (Ees), which is represented as:

$$VC(t) = \frac{k3}{\%simp(t)} + \frac{k4}{Ees(t)} + k5 \qquad (2)$$

where k3, k4 and k5 are constant.

The most accepted relation that rules the venous return (V.R.)behaviour was proposed by Guyton (1963), and integrates the effects of the mean systemic filling pressure (Pmsf), the venous (Vr) and arterial (Ar) resistances, and the venous (CV) and arterial (AC) capacities.

$$V.R.(t) = \frac{Pmsf(t) - Pra(t)}{V.R.R.} \quad (3)$$

$$V.R.R. = Vr + \frac{Ar(t) * AC}{VC(t) + AC} \quad (4)$$

In (3), the numerator (systemic filling mean pressure minus right auricular pressure) represents the pressure gradient for the venous return, while the denominator indicates the resistance to the venous return..

In figure 1, bock 15 represents the relation (3), considering that the right auricular pressure is naught, which occurs under normal physiological conditions, and that the arterial resistance is calculated as the systemic resistance minus the venous resistance (Guyton,1989).

On the other hand, the heart has an internal mechanism which allows it to automatically pump as much blood comes inside the right auricle from the veins. This mechanism is known as the "Frank - Starling heart law" (Sagawua, 1978) and is represented by block 16.

Blocks 17 and 18 describe the dependency (Sagawua,1978) between the diastolic (Ved) and systolic(Ves) ventricle and the venous return (V.R.), the systolic pressure (Pes) and the Systolic elastance (Ees):

$$Ved(t) = \frac{V.R.(t)}{H.R.(t - td)} + Ves(t) \quad (5)$$

$$Ves(t) = \frac{Pes(t)}{Ees(t)} + Vd \quad (6)$$

where Vd is the ventricular volume that would exist if the ventricular systolic pressure was naught and td is the time length of the ventricular diastole (block 19).

Simultaneously, the systolic elastance (Ees) and the systolic pressure (Pes) are represented as a linear function of the activity percentage for both, the sympathetic nervous system and the mean arterial pressure, respectively. These relations correspond to blocks 20 and 21.

The relation, as described by the cardiac output, is widely known and it is represented by block 22 (Guyton, 1989).

The realtion that describes the behaviour of the mean arterial pressure is represented by block 2 (Guyton.1989). Considering the analogy between the circulatory system and the electric circuit, the former is similar to Ohm´s well know law.

Baroreceptors contract and expand when pressure, respectively, diminishes or increases from its normal value. Baroreceptors deformation makes them send electrical impulses to the vasomotor center of the autonomous nervous system with a frequency that linearly depends on the mean arterial pressure magnitude, on the range in which the clinical model operates (Korner,1971). The linear relation previously described is represented by block 24 whose output corresponds to the average of the nerve impulses (N.I.).

3.2 *Mean Arterial Pressure Slow Regulating System Model*

The model of the slow regulating mean arterial pressure represents the presure - volume renal system.. The later is dynamic, not linear, of the first degree and incorporates variants such as the urinary output, the volume of the extracellular liquid and the blood volume. A block diagram of the model can be observed in the lower part of figure 1.

When the arterial pressure varies from its normal value (80 mmHg in this model), the kidney modifies its sodium and water filtering level in the same way; this changes the urine level and more or less quantity of water (diuresis) or sodium (natriurésis) is continuously eliminated regarding the body´s normal levels. The link between the mean arterial pressure and the urinary output is linear (Guyton,1989), and it is represented by block 25.

Block 26 represents the corporal liquid balance, according to which the estracellular liquid volume variation is given by the input (or ingestion) of water and salt, minus the lost of quantity of these substances through other routes apart from the renal, minus the quantity of these substances lost through urine (Guyton,1989).

Block 27 represents an integrator in such a way that the extracellular liquid volume in function of time determines the real level of the extracellular liquid volume at a given moment.

Guyton (1989) obtained an empirical curve which relates the blood volume with the extracellular liquid volume. This curve presents a linear relation within the normal range with a saturation caused by the capacity of continuous increase in situations when the extracellular liquid becomes larger (edema). The curve also incorporates the fact that the blood volume should not be less than 3.5 litres in order to keep the body working. The relation above described between the extracellular liquid volume and the blood volume, according to Guyton´s empirical curve (1989) is represented by block 28.

3.3 *Clinical Model Simulator*

A simulator using the Matlab Simulink module was implemented from the previously described clinical model for regulating the mean arterial pressure. The differential and algebraic equations solution is achieved through the fouth degree Runge - Kutta method with a one second integration pace.

The simulator allows the user to insert permanent or temporary disturbances in time. Besides, the disturbances can be either positive or negative having different levels of extent.

In order to bring the clinical model closer to reality, the disturbances inserted into the simulator are ramped shaped, taking 10 to 100 second to reach their full effect. Besides, they incorporate a delay between the instant in which the disturbance occurs and the instant y which it is manifested in the physiological variants.

The simulator lets us observ the evolution and time of all the variants involved in the clinical model and to store the values of all variants for each integrated pace in a matrix. Data contained in this matrix can be drawn and manipulated like any other Matlab variant once the simulation has finished.

4 RESULTS

4.1 *Simulation in the Presence of Disturbances*

The clinical model simulator has been used to analyse the effect that variations have in the systemic resistance (perturb3).

Figure 2 shows rhe response of the mean arterial presuure signal (a controlled variant of the internal regulating system) and the sympathetic and parasympathetic nervous systems activity percentages in the presence of temporary disturbances (with different magnitudes and direction) in the systemic resistance. In graphics of

figure 2, disturbance is considered as percentual with respect to the systemic resistance value under normal physiologic conditions (Ro = 16 mmHg/(litres/min)). It remained for 200 seconds.

In figure 2 we observ that the responses of the clinical model experience significant momentary alterations in order to reach (by the effect of the autonomous nervous system) regime values different from the inicial ones while the disturbance lasts. In this way, it is possible to say that the mean arterial pressure fast controlling system corresponds to a proportional type of control.

On the other hand, figure 2 shows that the magnitude in the alteration of the variabt is in a direct relation with the amount of disturbance , as it was expected. Graphics A,B and C of figure 2 show that when a positive ramp a positive disturbance is inserted in systemic resistance (ascending section of the curve shown in graphic A), the variation in the mean arterial pressure and in the sympathetic and parasympathetic nervous system activities percentages is not a linear function in time, due to the action of the internal regulation included in tha clinical model. In the same way, when the disturbance ramp is ended, both graphics show a compensation in the variants as an effect of the same internal regulating action included in the clinical model until they reach the regime level.

Graphics B,C, E and F in figure 2 show that the activity percentage of the sympathetic and parasympathetic nervous systems affect the percentual change of the mean arterial pressure in a perfectly and complementary proportional way.

In figure 2 if we compare the respones to positive disturbance in the systemic resistance and to a percentually equal negative, it confirms the clinical model capacity to adequately represent the non linear features of the involved physiology. The effect of a negative disturbance (graphics D, E and F) in the variants drawn is bigger in a start than the ones produced by positive disturbance of a percentagely equal magnitude. However, the variants reach regime values closer to the

reference in the case of the negative disturbance). This is due to the non linear amplification of the systemic resistance signals and the cardiac frequency (block 11 and 12 of figure 1).

Figure 3 shows the response of the pressure signal due to permanent and positive perturbations in the systemic resistance. This occurs within a greater time scale which it possible to observ the clinical model slow regulation mechanism.

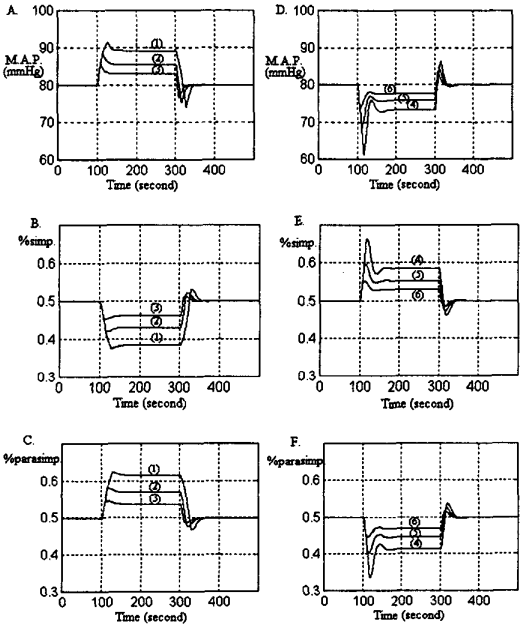

Figure 2: Systemic Resistance response in the Presence of Disturbances

(1): Rnormal = Ro*1,8; (2): Rnormal = Ro*1,4;

(3): Rnormal = Ro*1,2; (4): Rnormal = Ro/1,8;

(5): Rnormal = Ro/1,4; (6): Rnormal = Ro/1,2.

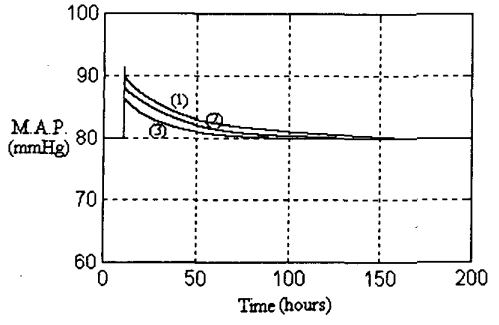

Figure 3: Mean Arterial Pressure Signal Response in the Presence of Disturbance in the Systemic Resistance.. (1): Rnormal = Ro*1,8; (2): Rnormal = Ro*1,4; (3): Rnormal = Ro*1,2

Figure 3 shows that the slow regulating mechanism of the arterial pressure (pressure - volume renal system) takes, after almost 100 hours - four days - the mean arterial pressure to its initial value (cero default) which indicates that the mean arterial pressure slow control system really correspond to a control returned with an integral action.

The difference between the maximun value reached by the effect of the disturbance and the value from where the mean arterial pressure starts to descent, due to the action of the slow regulating system, is a consequence of the fast mean arterial pressure regulating system.

The responses of the clinical model in the presence of the systemic resistance disturbances coincide, in a second or hour time scale, with the ones described by medical literature (Guyton 1989).

4.2 *Simulation with External Regulation*

The responses of the clinical model proposed by Slate (1980), which is the most widely used for mean arterial pressure regulation through drug infusion purpose, were compared under different physiological conditions. However, Slate only incorporates the mean arterial pressure and the nitroprusside sodium infusion rate as variants of the process. As a consequence, the models are comparable only from a drug infusion external regulator´s view point.

The external regulator used for simulation tests correspond to a proportional - integral with saturation controller, where the nitroprusside sodium infusion rate constitute the manipulated variant of the system. The controller´s reference is different (necessarily minor) from the internal arterial pressure regulation.

The external regulator of the clinical model, by means of alterations in the infusion rate, acts upon the systemic resistance and ,consequently, upon the mean arterial pressure. In the clinical model, the incorporation and distribution of the nitroprusside sodium in the body were modeled as a simple transference function of the firt degree with static and constant gain of time equal to the one proprosed by Slate´s model plus a delay time equal to the higher delay in Slate´s model.

Figure 4 shows the responses of the mean arterial pressure signals and the nitroprusside sodium infusion rates in the clinical model (a straight line) and in Slate´s model (a dotted line) in the presence of a disturbance in the drug infusion and in the presence of alterations in the external regulator reference.

In figure 4 the external regulator of the clinical model and also of Slate´s model starts diconected in (1) with a 70 mmHg reference. After reaching the desired reference level, a disturbance in the nitroprusside sodium rates of infusion, is introduced, in (2). This infusion consists in an additional dose in the form of pulse through time of a vasoconstrictor drug (this drug is assumed to have identical

distribution characteristics in the boby to those of the nitroprusside sodium). Later, the controller's reference (at once for both models) varies to values of 60 , 75 and 65 mmHg in (3), (4) and (5) respectively.

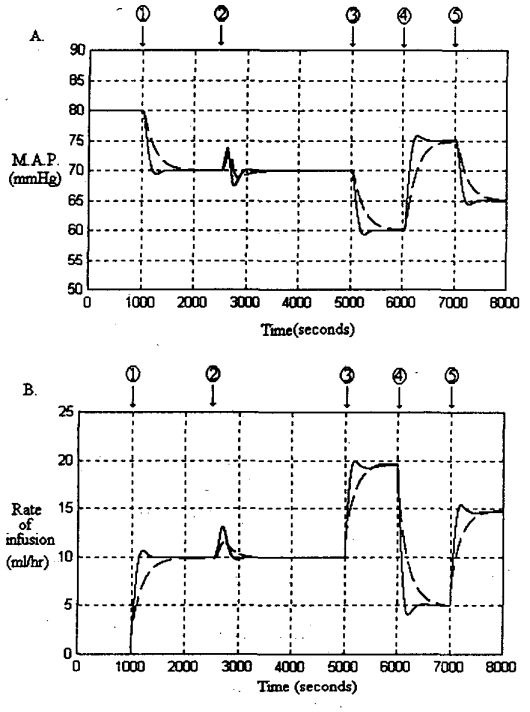

Figure 4 : Responses in the Presence of a Disturbance in the Infusion Rate and the Presence of Changes in the Reference of the External Regulator.

_____: Clinical Model Response

-------: Slate's Model Response

In Figure 4 we can see that the clinical model external controller is able to take the mean arterial pressure signal to the desire level faster than the external controller in Slate's model, when the disturbance in the infusion rate and the changes in the external controller's reference occur. An explanation for this can be found in the presence of the internal regulation system present only in the clinical model.

In order to achieve a response as fast as the one obtained when using the clinical model in Slate´s one, the time constant of the latter should make the system more stable.

Tests performed in this stage give a general idea of a better proportional - integral with saturation controllers performance, when a more detailed model of the process is used particularly when this incorporates internal regulating mechanisms.

5. CONCLUTIONS

In the Simulink of Matlab module a clinical model of the mean arterial pressure internal regulation has been designed and implemented. Such a model is dynamic, non linear and of the first degree; it incorporates more complex regulating systems than the ones normally used for industrial processes.

Tests performed on the developed clinical model show that it behaves similarly to what physiology indicates.

Particularly when the mean arterial pressure is regulated by external infusion it is possible to take the pressure to the reference value more quickly - and with not much overosillation - regarding Slate´s model. In other words, the internal regulating system that the clinical model incorporates adds stability to the complete system.

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