Modeling of Cardiovascular Variability Using a Differential Delay Equation

Silvio Cavalcanti* and Enzo Belardinelli

Abstract—**The influence of time delay in the baroreflex control of the heart activity is analyzed by using a simple mathematical model of the short-term pressure regulation. The mean arterial pressure in a Windkessel model is controlled by a nonlinear feedback driving a nonpulsatile model of the cardiac pump in accordance with the steady-state characteristics of the arterial baroreceptor reflex. A pure time delay is placed in the feedback branch to simulate the latent period of the baroreceptor regulation. Because of system nonlinearity model dynamics is found to be highly sensitive to time delay and changes of this parameter within a physiological range cause the model to exhibit different patterns of behavior. For low values of time delay (shorter than 0.5 s) the model remains in a steady state. When time delay is longer than 0.5 s, a Hopf bifurcation is crossed and spontaneous oscillations occur with frequencies in the high-frequency (HF) band. Further increases of time delay above 1.2 s cause the oscillations to become more complex, and following the typical Feigenbaum cascade, the system becomes chaotic. In this condition heart rate, pressure, and flow show evident variability. The heart rate power spectrum exhibits a peak whose frequency moves from the HF to LF band depending on whether simulated time delay is as short as the vagal-mediated control or long as the sympathetic one.**

I. Introduction

ONE of the peculiar features of cardiovascular signals is their pulsatile nature: Cyclical heart activity makes quantities such as pressure, flow, electrocardiogram (ECG), etc., rhythmically time-varying. Moreover, the cardiac cycle period continuously changes, and even during resting conditions, the interbeat interval of the healthy heart is characterized by unpredictable variations. Consequently, the frequency of events scanning the cardiac rhythm is not stable, and beat after beat, it shows a slow variability. Together with the heart rate, also blood pressure, flow, vessel lumens and peripheral resistances, exhibit apparent random fluctuations in magnitude and frequency. In a stationary state of the cardiovascular system, the signal variability is about 10% with respect to the mean value.

Experimental studies on variability have permitted the exploration of both the physiological and the clinical aspects of the cardiovascular system [1]. Variability signals such as beat-to-beat heart rate detected by measuring the R-R interval in ECG or in plethysmographic tracings [2] as well as systolic or diastolic values of arterial blood pressure [3], are assumed to carry a great deal of information about the state of the cardiovascular and autonomic nervous systems. Neural controls of cardiovascular functions play an important role in many patho-physiological conditions such as arterial hypertension, myocardial ischemia, heart failure, etc., and variability analysis coupled with cardiovascular reflex tests provide a noninvasive tool useful in clinical medicine to assess the state of the neuro-cardiovascular system [4], [5].

Neural controls of cardiovascular functions are effected through the autonomic nervous system and in particular, by the sympathetic and parasympathetic subsystems [6] and [7]. The interplay between the cardiovascular system and the controlling neural subsystems is on the basis of variability and as a track of this interaction different rhythms are embedded in signals [8]. Frequency analysis of the beat-to-beat discrete series has been used to detect the rhythms hidden in signals (e.g., [9]). Power spectral analysis of the beat-to-beat heart rate reveals three distinct components which have been interpreted as different physiological rhythms oscillating at specific frequencies. In humans, the power in the high frequency (HF) band—0.15–0.5 Hz—is sensitive to the respiratory rate and is correlated with vagal efferent input to the sinus node and for this reason, this spectral component of the variability is regarded as a marker of the parasympathetic activity [10]. The peak in the low frequencies (LF) band—0.06–0.15 Hz—is believed to be due to the baroreceptor mediated blood pressure control and includes contributions from both the sympathetic and parasympathetic nervous systems. Pressure oscillations at around six cycles a minute—e.g., Mayer waves—fall into this band [11]. Finally, the power in very-low-frequency (VLF) band—below 0.06 Hz—has been linked with the humoral and temperature regulations and with the slow vasomotor activity. On the basis of the spectral decomposition the powers of LF and HF components were proposed as quantitative global markers of neural activity and the ratio LF/HF was assumed to provide an index of the sympatho-vagal balance [4].

To correctly construe power spectra it is very important to closely examine the genesis of different rhythms embedded in cardiovascular signals. In fact, variability and rhythms can be justified in different ways. They can be regarded as a sign of the variability of external perturbations. As an example, the respiratory rhythm has a reflex influence on the heart rate—the so-called respiratory sinus arrhythmia [12]—and the power in the HF band depends on the respiratory activity. But the variability is not necessarily caused by external driving oscillations only. In the cardiovascular system

Manuscript received June 30, 1995; revised April 26, 1996. *Asterisk indicates corresponding author.*

*S. Cavalcanti is with the Department of Electronics, Computer Science and Systems, University of Bologna, Viale Risorgimento 2, I-40136 Bologna, Italy.

E. Belardinelli is with the Department of Electronics, Computer Science and Systems, University of Bologna, I-40136 Bologna, Italy.

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there are complex oscillations occurring locally in subsystems which, through reflex mechanisms, can propagate to other parts of the system. For instance, local controls of microcirculation and in particular, the myogenic reactivity, induce spontaneous vasomotion that has a frequency component close to the LF band [13]. Vasomotion influences systemic blood pressure and through the baroreceptor reflex, vasomotion influences the heart rate [14].

Besides these justifications, there is another interpretive key of variability based on the nonlinear dynamics of the cardiovascular system coupled with its controls. From this point of view, the variability of cardiovascular signals and their apparent disorder is interpretable as a complex time evolution typical of chaotic systems. The hypothesis that the cardiovascular system may present some aspects of deterministic chaos has recently been investigated [15], [16]. Measurements of nonlinear metrics from heartbeat data—correlation dimension, Lyapunov exponents, etc.—have been consistent with the idea that heart rate fluctuations represent deterministic chaos [17], [18]. This paper intends to investigate this aspect of cardiovascular variability with specific attention to the role that the baroreceptor reflex plays in the phenomenon. The baroreflex acts as a nonlinear negative-feedback which tends to stabilize arterial pressure against endogenous and exogenous perturbations. Actually, this homeostatic mechanism exhibits a short dead time at the onset of the control action due to necessary electrochemical transductions and transmissions. In humans, the baroreflex changes of heart activity start after at least 0.5 s and the control action is fulfilled with a 3-s time delay [19] and [20]. It is well known that nonlinear controls acting with a pure time delay can cause an oscillatory evolution and in particular conditions, these oscillations can become chaotic [21]. It is the aim of the present study to analyze the influence of the time delay by a simple nonpulsatile mathematical model of the baroreflex regulation of arterial pressure, in order to prove that time delays within a range of physiological importance are sufficient to drive the system to complex behavior and in particular, to oscillate chaotically.

II. Methods

The influence of time delay in short-term baroreflex regulation of arterial pressure was analyzed by means of a mathematical model whose block diagram is shown in Fig. 1. For the sake of simplicity, we restricted the analysis to the mean values only—i.e., to the time-averaged components—leaving out of consideration the intrinsic pulsatile nature of the cardiac pump. However, the mean values were also considered time-varying because of system variability. The dynamic linking between mean arterial pressure, $P(t)$, and mean aortic flow, $Q(t)$, was described by adopting a very simple model of circulation (Fig. 1). It is the classic three-element Windkessel model [22], that is a suitable representation of the arterial load impedance of the heart. This impedance consists of a peripheral resistance, R, a total arterial compliance, C, and an aortic characteristic impedance, r. Although these parameters are time-varying because of regulating mechanisms [23], in the present study they were kept to a constant physiological value.

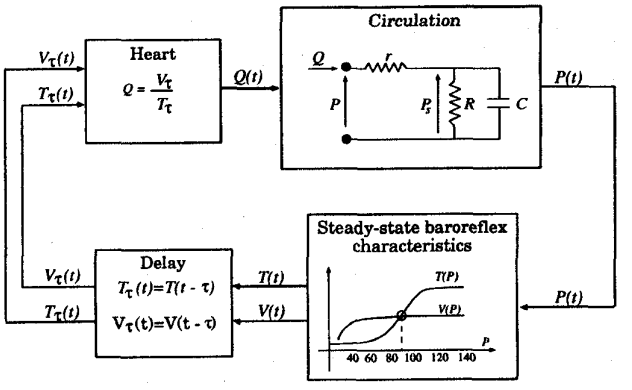

Fig. 1. Schematic representation of the mathematical model employed to study the influence of the time delay in the baroreflex regulation of heart activity; the model is nonpulsatile and the heart is treated as a continuous flow pump; P is the mean arterial pressure, Q the mean aortic flow; baroreflex regulation involves cardiac period T and stroke volume V.

The assumption of time-invariant Windkessel parameters was made in order to stress the role of baroreflex control of the heart activity only, intentionally leaving out the baroreflex control of the circulatory system. Values of Windkessel parameters (Table I) were obtained best-fitting the input impedance data measured in five normal human subjects [24]. On the basis of the Windkessel theory, the dynamic relationship between the mean arterial pressure, $P(t)$, and mean cardiac output, $Q(t)$, is

$$\frac{dP_s(t)}{dt} = w_t[RQ(t) - P_s(t)], \quad \text{with} \quad w_t = \frac{1}{RC}, \tag{1}$$

$$P(t) = P_s(t) + rQ(t). \tag{2}$$

Mean aortic flow, $Q(t)$, was regarded as input and the mean pressure, $P(t)$, as output (Fig. 1). Since the model was nonpulsatile, the mean aortic flow, $Q(t)$, was simply expressed (Fig. 1) as the ratio between the mean components of stroke volume, $V(t)$, and heart period, $T(t)$.

Short-term regulation of the arterial pressure was modeled as an algebraic nonlinear feedback driving cardiac activity on the basis of the mean arterial pressure, $P(t)$. We assumed the period of the cardiac cycle to depend on the pressure in the steady-state according to the sigmoidal law

$$T(P) = T_s + \frac{T_m - T_s}{1 + \gamma e^{-\alpha P/P_n}}, \quad \text{with} \quad \gamma \gg T_m - T_s. \tag{3}$$

Relationship (3) reproduces the characteristic saturation effects occurring in the baroreflex-dependent control of heart rate when pressure reaches low and high levels (see Fig. 2). The lower (T_s) and upper (T_m) plateaus establish the shorter and longer cardiac period and match, respectively, the maximal vasodepressor-induced sympathetic excitation and the maximum pressor-induced vagal activation [25]. P_n corresponds to the steady level of mean arterial pressure, that is the arterial pressure when (1) is in equilibrium; α and γ, determine range and slope of the linear region of the mean pressure-heart period curve, i.e., the baroreflex sensitivity. The value of these parameters (Table I) was estimated by best-fitting data drawn from physiological literature [26].

TABLE I

Windkessel		
R	$1.2\,10^3$	$[dyn\ s/cm^5]$
r	52	$[dyn\ s/cm^5]$
C	$1\,10^{-3}$	$[cm^5/dyn]$
Heart Rate		
T_s	0.66	$[s]$
T_m	1.2	$[s]$
P_n	89	$[mmHg]$
α	31	
γ	$6.7\,10^{13}$	
Stroke Volume		
V_{max}	86	$[cm^3]$
P_v	25	$[mmHg]$
β	72	
k	7	

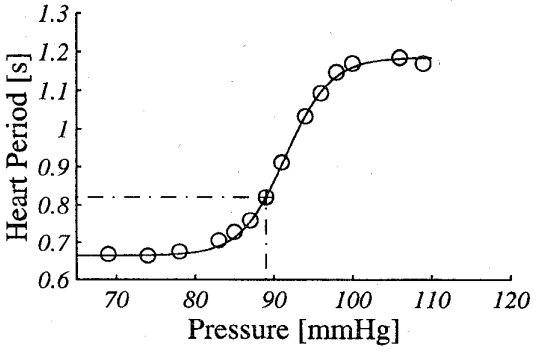

Fig. 2. Heart period versus arterial pressure in steady state. Data from [22] is interpolated by the relationship (3). Pressure and heart period when (1) is at the equilibrium are also indicated.

Since the baroreflex modulation of heart activity affects together with heart period, also the heart contractility, the mean stroke volume, $V(t)$, was assumed to depend on the arterial pressure. Studies of baroreceptor-heart reflex [27]–[29] show that stroke volume is maintained nearly constant when the mean pressure is within a physiological range. In fact, when pressure acting on arterial baroreceptors decreases, the resultant increase in the sympathetic tone drives the heart to faster contractions without causing a significant increase in the cardiac output, because of the shorter time of ventricular filling and the simultaneous increase in the arterial load. On the contrary, when mean arterial pressure falls below physiological levels, stroke volume rapidly decreases, because of the asymptotic trend of the heart to failure and seriously reduces cardiac output, when systemic blood pressure goes to very low levels. In order to reproduce this behavior of the cardiac pump, the steady-state stroke volume-pressure curve was modeled using the following expression:

$$V(P) = \frac{V_{\max}}{1+\beta\left(\dfrac{P}{P_v}-1\right)^{-k}}, \quad \text{with} \quad P \geq P_v \qquad (4)$$

where $V_{\max}$ is the maximum stroke volume and P_v is the pressure for which cardiac output is null.

To take into account the latent period involved in the baroreceptor reflex a pure time delay was placed in the feedback branch (Fig. 1). In this way, heart rate and stroke volume were retarded by a period τ with respect to the pressure $P(t)$.

Equations (1)–(4) completely define the mathematical model and they have been integrated with respect to time using the Runge–Kutta method. Parameters were assigned to reproduce human physiological data (see Table I). The value of model parameters was the same in all the simulations; only the value of the delay, τ, of the control loop was changed in order to study the sensitivity of model dynamics to this parameter. Borst and Karemaker [19] observed in humans a time delay of about 0.6 s in the onset of the peak-to-peak interval prolongation after electrical stimulation of carotid sinus nerves, about 1 s to change the AV-interval, and from 2–3 s for the start of the decrease in the arterial pressure. In experiments of open-loop transfer function from carotid sinus pressure to aortic pressure Kubota *et al.* [30] found in vagotomized dogs a time delay in the range 1.1–2.5 s. Moreover, Berger *et al.* [31] estimated distinctly different delays in response to vagal or sympathetic stimulations: vagal mediate changes begin almost immediately (about 0.6 s), whereas sympathetic mediated changes may begin after 1.7–2 s. Delays in the range 0.5–3 s are also consistent with the response of heart activity to a mild arterial hemorrhage [20].

III. Results

Assuming that baroreflex changes of heart activity occur in three cardiac cycles, delay τ in the baroreceptor control loop at first ranges between 2–3 s. When the value of τ is chosen in this range, the model behaves chaotically: pressure, heart rate, and flow exhibit very irregular time evolution with evident variability (Fig. 3). This range of parameter τ is indicated in the following as the chaotic region. In this region the model is characterized by sensitive dependence on the initial condition that is a typical feature of chaotic systems: after the transient is exhausted, a slight perturbation of the trajectory radically changes the system time evolution (Fig. 4). The stretch and folding mechanism—which is at the basis of the infinite sensitivity to trajectory perturbations—is evident in Fig. 5 where the strange attractor is represented in three-dimensional (3-D)-space.

When delay τ is less than 2 s, the model is no longer chaotic and periodic oscillations occur (Fig. 6). System evolution is oscillatory as long as τ is between 0.6–2 s and for this reason this range is indicated as the periodic region. In this region, when the transient is extinct, system trajectories converge on a limit cycle (Fig. 6). Amplitude and frequency

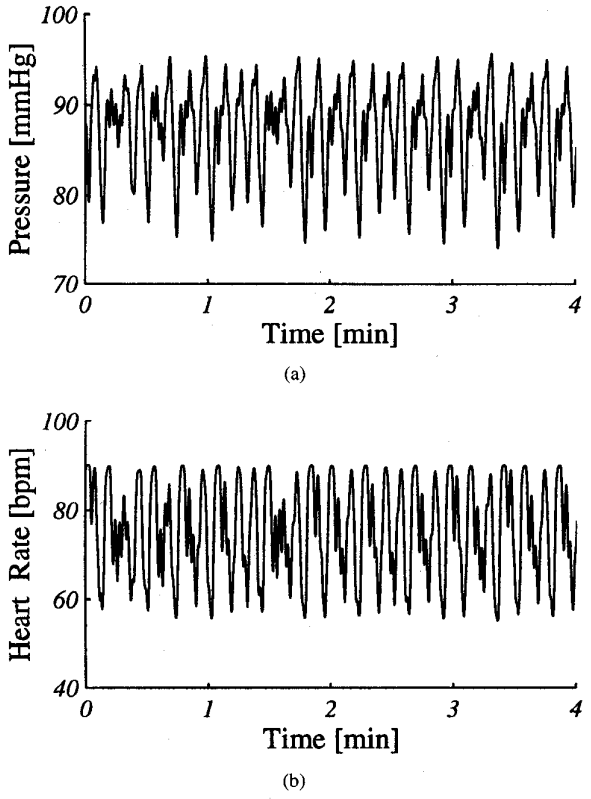

Fig. 3. Fig. 3 Time waveforms of (a) mean pressure and (b) heart rate when time delay is in the chaotic region ($\tau = 2.5$ s); the transient is canceled.

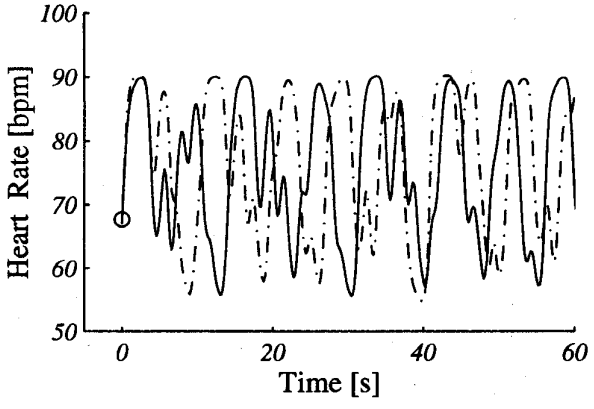

Fig. 4. Sensitive dependence on the initial condition: as an effect of the initial perturbation (less than 0.1%) the trajectories diverge and they become uncorrelated.

of oscillation depend on the value of τ and, in particular, by increasing parameter τ the attracting limit cycle expands and the oscillation frequency decreases (Fig. 7). Within the periodic region the system undergoes a flip bifurcation cascade and whenever a flip bifurcation is crossed the doubling of the oscillation period takes place and the time waveform of signals becomes more complex. When a flip bifurcation value is overcome the limit cycle suddenly becomes nonstable, turning into a saddle cycle and a new stable cycle with a double period

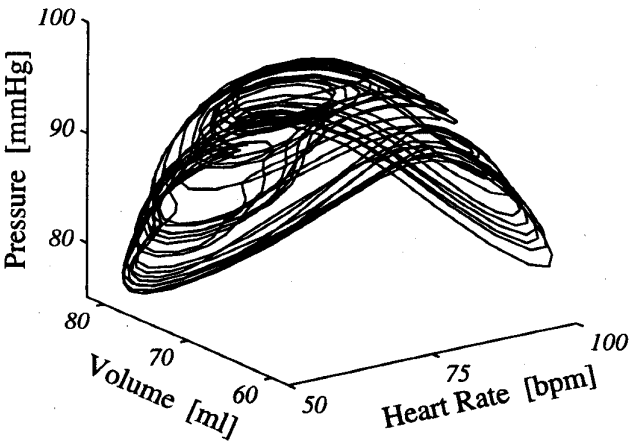

Fig. 5. Chaotic trajectory in a 3-D-space; 2.5 min of simulations after the transient is extinguished are shown.

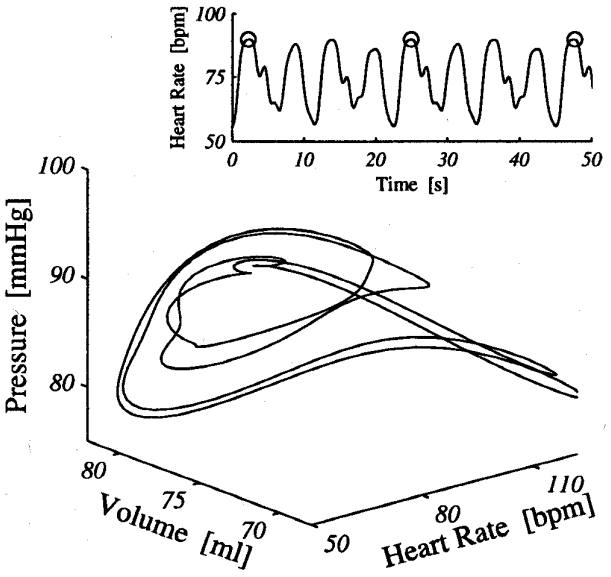

Fig. 6. A complex periodic oscillation occurs for a time delay in the higher part of the periodic region ($\tau = 1.8$ s). In the heart rate curve the oscillation periodicity is marked with a circle.

appears (Fig. 8). The cascade of period doubling bifurcations accumulate to a value of τ equal to about 2 s, beyond which the system becomes chaotic. This accumulation value marks the frontier between the periodic and the chaotic region.

Shortening the time delay further below the periodic region— i.e., for τ less than 0.5 s—the limit cycle vanishes and the system trajectory converges to a steady state which is independent of τ (Fig. 9). The steady state and the periodic regions are separated by a Hopf supercritical bifurcation. When, on reducing τ, the Hopf bifurcation is crossed, the cycle limit collapses at the equilibrium point which, as result of the collision, becomes a stable focus. In this situation, pressure, flow, and heart rate reach a stable fixed value and as long as the system is not subject to external perturbations, it holds this equilibrium condition.

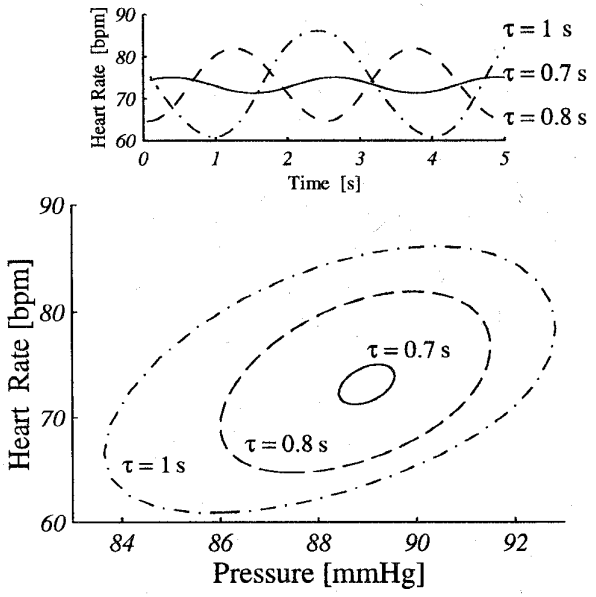

Fig. 7. Dependence on the time delay of limit cycle: by increasing time delay the oscillation frequency decreases.

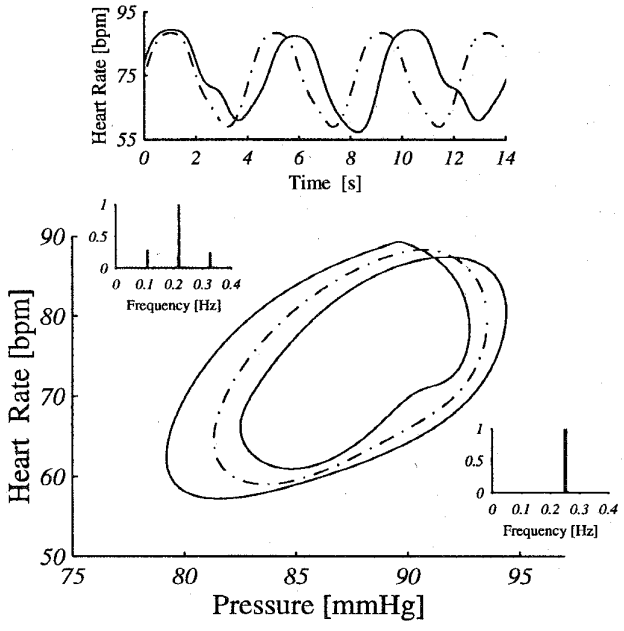

Fig. 8. Period-doubling bifurcation. The two limit cycles are for 1.2 s (dash-dot line) and 1.4 s (solid line) time delays, respectively. The power is overall around 0.25 Hz for the delay equal to 1.2 s (spectrum in the low right part of the figure); when the flip bifurcation is crossed—delay equal to 1.4 s—this harmonic is at 0.22 Hz and a sub- and a super-harmonic appears in the spectrum.

The oscillation emerging from the Hopf bifurcation is characterized by a high frequency (about 0.45 Hz) and oscillations with frequencies in the HF band—i.e., greater than 0.15 Hz—can be observed as long as a short value is assigned to time delay (0.6–1.2 s). On increasing τ the frequency of the oscillation decreases and when the first flip bifurcation occurs the frequency is equal to about 0.2 Hz (Fig. 8). After

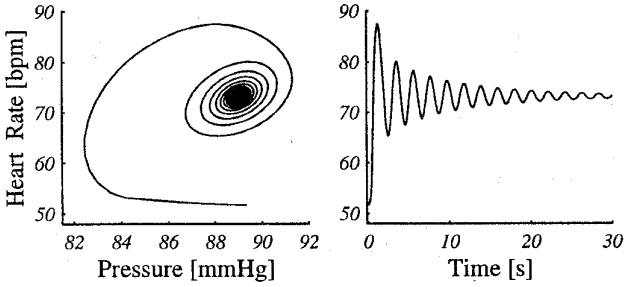

Fig. 9. Transient response to an initial perturbation when time delay is equal to 0.6 s. The system trajectory converges on a very small limit cycle surrounding by an unstable focus. For time delay shorter than this value the limit cycle collapses and the equilibrium point becomes stable.

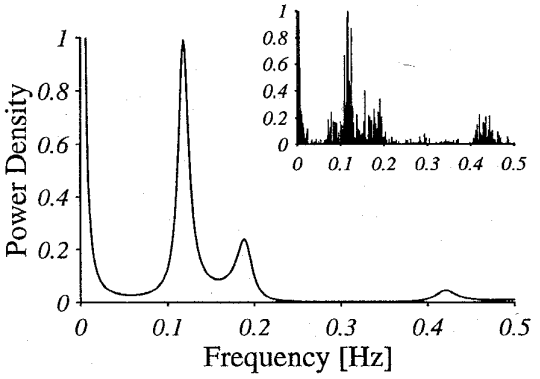

Fig. 10. Power spectrum of the heart rate when system time evolution is chaotic (τ greater than 2 s). Three clearly separated components are evident in the autoregressive spectrum: one component is in the VLF band, one is in the LF band, and a small peak is in the HF band; the broad band component is evident in the FFT-spectrum (inset). Power density is normalized with respect to the LF peak.

the first flip bifurcation takes place, as an effect of the period doubling, part of the power moves from this frequency to a sub- and to a super-harmonic with frequencies equal to 0.1 and 0.3 Hz, respectively, and two new spikes matching these frequencies appear in the power spectrum (Fig. 8). Whenever a new flip bifurcation is crossed, these spikes become more evident and new harmonics with frequencies that are again multiple and sub-multiple of these spikes come out in the power spectrum. When the flip bifurcation cascade is fully crossed and the system is in the chaotic region, the period doubling phenomenon gives rise to the accumulation of a continuous broad-band power spectrum with some distinct spikes superimposed (Fig. 10). The noise-like component is a characteristic exhibited by spectra of chaotic signals while spikes indicate the presence of some predominant rhythms embedded in the signal. The largest power component is in the LF band with a central frequency at about 0.12 Hz, whereas a small component falls in the HF band around 0.4 Hz. When the system moves from the chaotic region to the periodic one, the noise-like component, being a characteristic of a chaotic dynamics, vanishes from the power spectrum, whereas rhythms with frequencies spaced at integer multiples of a frequency close to 0.1 Hz persist (Fig. 11).

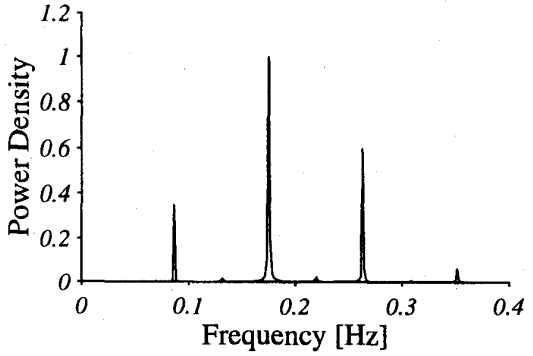

Fig. 11. Autospectrum of the heart rate curve shown in Fig. 6 ($\tau = 1.8$ s).

IV. Discussion and Conclusions

The present study is intended to analyze the influence of time delay in the human baroreceptor-mediated reflex. To this end, a very simple mathematical model of the interaction between the cardiovascular system and baroreceptor control of arterial pressure has been used. In making the model some assumptions were made that will be briefly discussed here.

First of all, the pulsatile nature of the cardiac pump was neglected since we were mainly interested in the average system behavior only. Really, the marked nonlinearities of the relationships governing the cardiovascular system cause strong interplay between pulsatility and system dynamics [32], [33]. We also implemented a pulsatile model of the cardiac pump and more complex dynamics with quasiperiodic oscillations and different ways of achieving chaos were observed (unpublished results). Despite the fact that pulsatility made the system behavior richer, the influence of the time delay was the same as in the model without pulsatility, and for this reason, pulsatility was not included in the present analysis.

The baroreceptor reflex affects not only heart activity but also the circulatory system and, in particular, peripheral resistances. Low-frequency oscillations may also be caused by the slow temporal response of the α-adrenergic effector mechanism controlling the muscular tone of peripheral circulation [34] and [35]. Madwed *et al.* [36] explored this hypothesis and concluded that this negative-feedback, which operates with a time delay of 5 s, is able to induce low-frequency oscillations. In our model, this aspect of the autonomic regulation was neglected in order to emphasize the role of cardiac control in the genesis of heart rate fluctuations.

Baroreceptor-mediated regulation of the heart activity was modeled with a pure algebraic scheme, neglecting its dynamics. Kubota *et al.* [30], [37] evaluated the transfer function from carotid sinus pressure to aortic pressure, under open-loop conditions in vagotomized dogs and they proposed a second order low-pass filter as an appropriate representation of the baroreflex dynamics. We introduced the filter proposed by Kubota *et al.* [37] into the control feedback: model behavior was still characterized by three distinct regimes—steady-state, periodic, and chaotic—and values of τ marking the boundary between these regions were shorter, making the transition to chaos easier.

A widespread method used to study variability is the spectral analysis of the time discrete series of cardiovascular signals. The aim of this method is the spectral decomposition of signals in order to point out the most significant frequency component. After Sayer [2], spontaneous fluctuations in heart rate have usually been separated into three spectral bands: VLF (<0.05 Hz), LF (0.05–0.15 Hz), and HF (>0.15 Hz). The power spectral density of heart rate time series, measured on a healthy subject, exhibits a continuous broad-band component with three distinct peaks superimposed, respectively, in the VLF, LF, and HF band. Chess *et al.* [10] found that the HF component is mediated entirely by the parasympathetic division. Akselrod *et al.* [38] confirmed the role of vagal modulation in mediating heart rate oscillations beyond 0.15 Hz and established the importance of the sympathetic system in the genesis of LF oscillations. Several authors [4], [9], [39] confirmed these findings providing new insights into the role of the autonomic regulation in cardiovascular signal variability. Differences in frequencies of vagal- and sympathetic-mediated heart fluctuations reflect different response properties. In particular, vagal control and sympathetic control are characterized by distinctly different latent periods. Borst and Karemaker [19] established the dead time between the start of the carotid sinus nervous stimulation and the onset of the reflex in the cardiac activity in humans. They found that cardiac cycle prolongation—which involves the vagal activation—started after a short delay of about 0.6 s, i.e., within the same cardiac beat. On the contrary, the atrial response to sympathetic stimulations is characterized by a much longer delay. Samaan [40] reported a dead time greater than 2.5 s in the onset of the heart rate rise after the initiation of sympathetic stimulation and Berger *et al.* [31], using frequency domain analysis, found a roughly 1.7 s pure time delay. Our model does not distinguish either the sympathetic and parasympathetic pathways or the sympatho-vagal balance. Since these two subsystems drive the sinus node simultaneously it is not possible to quantitatively compare the results presented here with the experimental ones. However, it is possible to qualitatively correlate the simulation results with the physiological observations. First of all, present theoretical analysis confirms that time delay in the baroreceptor regulation of arterial pressure may be the cause of spontaneous fluctuations in the cardiovascular system [35]. Moreover, rhythms embedded in the simulated signals are sensitive to the time delay and their frequencies correlate the physiological ones depending on whether the delay simulated is close to the vagal or the sympathetic one: when the time delay value is set similar to those characterizing the vagal-mediated control action (time delay shorter than 1 s) the frequency of oscillations falls into the HF band; when time delay is similar to the sympathetic one power is nearly in the LF band. Finally, Goldberger *et al.* [41] have recently observed that the variability of heart rate decreases after phenylephrine infusion that increases the vagal efferent discharge rate. This result is also consistent with the present analysis, since the variability of simulated data tends to decrease and the fluctuations become more regular when time delay tends to the vagal one.

Chaotic and periodic regions are sensitive to the heart rate gain as well as to the Windkessel parameters. For instance, in the simulations presented here the heart rate gain was assumed to be equal to 1.02 bpm/mmHg according to [27]. By increasing the heart rate gain the transition to chaos occurs for lower values of τ—as long as 1 s—and the frequency of oscillation in the periodic regime is higher. The same effect can also be obtained by increasing peripheral resistance.

The power component in the VLF band occurring in the spectra of the *in vivo* data is generally associated to humoral and temperature regulatory mechanisms. Our model does not incorporate both these regulatory mechanisms because they do not take part in the arterial pressure short-time regulation and because it is reasonable to assume that chaotic dynamics persists also when there are slow controls acting on longer temporal scales. In the present analysis, power in the VLF band is observed only when a long time delay is simulated (greater than 2 s), and it is due to the doubling period cascade preluding the chaotic regime which induces an accumulation of power in this band.

In this paper, cardiovascular signal variability has been reproduced without taking into account either external vagal stimulations, like those induced by the respiratory rhythm, or the intrinsic variability of neural control signals [42] considered by some authors to be one of the primary sources of heartbeat chaos [43]. We have interpreted beat-to-beat variability of cardiovascular signals as a result of the interaction between the baroreceptorial control and the plant, i.e., the uncontrolled cardiovascular system. Thus, variability may also be an effect of a complex interaction between different subsystems besides complex behavior peculiar of a single part. From this point of view, studies of isolated single parts of the cardiovascular system could lead to preventing the appearance of peculiar behavior.

For the sake of brevity, we have not included in this paper a thorough quantitative analysis of the chaotic dynamics, limiting the observation to the sensitive dependence on the initial condition, to the fractal dimension of the strange attractor, and overall, to the classic way in which the model achieves the chaos: the typical Feigenbaum cascade. Cardiovascular system behavior is of course more complex than that of the model and it could become chaotic in different ways. However, the present analysis shows that the baroreflex is a potential cause for the chaos in cardiovascular signals. Moreover, the high sensitivity of model dynamics to the parameter changes can be a reasonable explanation of the variety of behavior that the cardiovascular system exhibits also in physiological conditions.

Methods based on the hypothesis of linear phenomena such as Fourier analysis, linear model, transfer function, etc., have contributed greatly to the study of signal variability but to fully explain this phenomena it is necessary to take into account the nonlinear nature of the system. Nonlinearities are important to understand rhythms hidden in the signals and the shifting of power between components at different frequencies is a typical effect of nonlinearities. Moreover, nonlinearities enable us to reproduce complex system phenomena by simple mathematical models of low order and with only a few parameters. Mathematical models like the one proposed in this paper could be employed to study neuropathic subjects in terms of autonomic functioning and could also provide a quantitative evaluation of different cardiovascular autonomic function tests.

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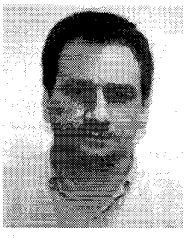
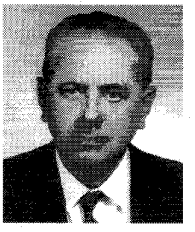


Silvio Cavalcanti was born in Cosenza, Italy, in 1958. He received the doctoral degree in electronics engineering from the University of Bologna, Italy.

He joined the Department of Electronics, Computer Science and Systems, University of Bologna, Italy, in 1990. His current research interests include modeling of neural controls of cardiovascular system function and nonlinear dynamics in biological systems.



Enzo Belardinelli was born in Italy in 1930.

He joined the University of Bologna in 1956, first as a Researcher and Assistant Professor of Electronics and Computer Science. From 1967 to 1982, he was a Full Professor of Automatic Control and, since 1983, he has been a Full Professor of Bioengineering in the Department of Electronics, Computer Science and Systems. At the beginning of the 1970's, he founded the Center for Biomedical Research and the School of Bioengineering at the University of Bologna. His scientific interest is particularly focused on analysis and modeling of the cardiovascular system.