Stability Analysis of One-dimensional Dynamical Systems Applied to an Isolated Beating Heart

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In this paper we propose a new model of an isolated beating heart. The model is described by a one-dimensional non-linear discrete dynamical system which depends on several parameters. Applying stability analysis we investigate the dynamic properties of the non-linear system. We find those domains in the parameter space in which the equilibrium point of the system (the fixed point) and the periodic orbits are attractors and in which they are unstable. These domains correspond to a normal and abnormal beating heart, i.e. when the end diastolic volumes are stable time invariant and time variant, respectively. On transition between these domains there is a bifurcation which gives rise to a pair of attracting points of period 2. This case corresponds to the simplest type of period doubling behavior of an abnormal beating heart, called mechanical alternans. Our results provide qualitative and quantitative predictions which can be used for comprehensive experimental design.

1. Introduction

The isolated left ventricle (LV) of the heart is defined as normal if its volume at end of each heart beat, termed end-diastolic volume (EDV), is time (beat) invariant. The LV is defined as abnormal if the EDV is time variant, either periodic or aperiodic. Experimental studies (Gleason & Braunwald, 1962; Noble & Nutter, 1970; Ritzenberg et al., 1984; Goldberger et al., 1985) have demonstrated that when perturbations are applied gradually to the heart, a transition from time invariant (normal) to time variant (abnormal) action occurs, the EDV being initially periodic and becoming aperiodic. The special case of 2-periodic EDV is termed mechanical alternans (MA), and the general case of k-periodic EDV will be termed mechanical periodicity (MP). Several detailed and analytical models of cardiac mechanics are available in the literature (Back, 1977; Janz, 1982; Kim et al., 1985; Beyar & Sideman, 1986). Most of these models deal with the mechanics of a single beat, and consequently can only describe the beat invariant phenomena.

Other models dealing with mechanics of consecutive beats have suggested that MA is caused by changing the mechanical properties of the heart, the heart rate or its loading conditions (Gleason & Braunwald, 1962; Noble & Nutter, 1970; Guntheroth, 1982; Laskey et al., 1983; McGaugher et al., 1985). Recently, (Adler et al., 1985; Adler & Mahler, 1987) have modeled the beating heart as a dynamical system, using only certain aspects of the heart’s functions.
Our objective is to simulate and explain both normal and abnormal behavior of the heart. We develop an overall analytical model for the LV of an isolated heart (see Fig. 1, also cf. Green, 1982), encompassing the mechanical properties of the heart and the hemodynamic characteristics of the vascular system. The model is described by a one-dimensional discrete-time dynamical system which depends on several parameters of the form

\[ f(x, \mu) = f_n(x_n) \]

where \( x_n \in \mathbb{R}^+ \) (positive real numbers) is the state and \( \mu \) is a vector of positive parameters, which can vary in some parameter space \( K \). More specifically, \( x_n \) is the EDV at the \( n \)th beat, while the components of \( \mu \) are parameters which characterize the mechanical properties of the heart and the hemodynamic characteristics of the vascular system. Applying stability analysis to this system we find those domains, in the parameter space \( K \) in which the fixed points (equilibrium values) of the map \( f_n \) and the periodic orbits are asymptotically stable (attractors) and those in which they are unstable. Determination of such domains will provide quantitative measures of normal and abnormal heart's function. This may lead to better understanding and explanation of the specific pathologic mechanism involved in the evolution of MP.
DYNAMICAL SYSTEMS IN A BEATING HEART

This paper consists of four sections. In section 2 we present the model and establish the essential notation. In section 3 we provide some basic definitions and results from the stability analysis of one-dimensional dynamical systems, and show how they can be applied to the problem of determining the domains for normal and abnormal beating heart. Some concluding remarks and the significance of the results are discussed in section 4.

2. Model development

(A) SYSTEM DEFINITION AND TERMINOLOGY

The system under consideration is an isolated heart. More precisely, we consider the left ventricle (LV), and the mitral (inlet) and aortic (outlet) valve, i.e. the open loop represented in Fig. 2.

The cardiac cycle consists of a period of relaxation called diastole followed by a period of contraction called systole. The LV volume increases during diastole (filling phase), and decreases during systole (ejection phase) (see Fig. 3, also cf. Guyton, 1976). The LV volume at end diastole is the end-diastolic volume and the

![Block diagram of the system under consideration.](image)

![The events of the cardiac cycle, showing changes in the left ventricular pressure, aortic pressure and ventricular volume.](image)
remaining volume in the LV after ejection is the end-systolic volume. The volume of
the blood flowing from the veins through the left atrium into the LV during the
diastole is called the venous return volume; and the amount of blood ejected from
the LV to the aorta during the systole is called the stroke volume. The left ventricular
pressure during the ejection phase is termed the ejection pressure. Generally, ejection
exists only if the ejection pressure is greater than the aortic pressure.

NOTATION, ASSUMPTIONS AND THE MATHEMATICAL MODEL

We will denote by \( u_n, x_n \) and \( y_n \), the venous return volume, the end-diastolic
volume and the stroke volume at the \( n \)th beat, respectively. By the mass conservation
law we obtain that

\[
x_{n+1} = (x_n - y_n) + u_n, \tag{1}
\]

i.e. the end-diastolic volume at the \((n+1)\)th beat is the sum of the end-systolic
volume (the remaining volume) and the venous return volume, of the \( n \)th beat.

Let \( \tau \) be the period of one cardiac cycle and assume, for simplicity, that the
ejection period (time), and the filling period (time) are equal to \( \tau/2 \). We assume
that the mitral (inlet) valve and the aortic (outlet) valve are normal, i.e. the
flow is one-directional, and have constant resistances denoted by \( R_m \) and \( R_a \),
respectively. The subscripts denote mitral and aortic, respectively. In addition, we
assume that the flow (both the inflow and outflow) can be approximated by Poiseuille
law. Let \( P_e(x) \) be the mean (in time) ejection (systolic) pressure, \( P_a \) be the mean
aortic pressure, \( P_d(x-y) \) be the mean (in time) diastolic pressure and \( P_v \) be the
mean filling (left atrial) pressure. Then we assume for the stroke volume \( y_n \) and the
venous return volume \( u_n \), the following approximation formulas:

\[
y_n = (\tau/2) \frac{P_e(x_n) - P_a}{R_e} [\text{sgn} (P_e(x_n) - P_a) + 1]/2, \tag{2a}
\]

\[
P_e = \frac{P_a(x_n)}{R_e} \text{sgn} (P_e - P_a) \tag{2b}
\]

The values \( P_e(*) \) and \( P_d(*) \) can be approximated from the pressure volume relation
of the heart, depicted in Fig. 4, known as Frank Starling’s Relationship, (cf. Patterson,
1914; Berne & Levy, 1986: 51). Let \( F_s, L_s, V_s \), and \( F_d, L_d \) be parameters which
characterize the systolic and diastolic mechanical function of the heart, respectively,
then

\[
P_e(x) = F_s L_s V_s \tag{3a}
\]

and

\[
P_d(x) = F_d + L_d \tag{3b}
\]

Let \( I^* \) be the set of points \( x \) in \( \mathbb{R}^* \) for which the pressure difference \( P_e(x) - P_a \)
positive, then

\[
I^* = V. \overline{F}. \overline{P}. \overline{L}. \overline{V} . \overline{+}. \overline{P}. \overline{L} \tag{4a}
\]
Substituting (2) and (3) in (1) will lead to

\[ x_{n+1} = x_n + \frac{\tau}{2} \frac{P(x_n) - P_a}{R_a} \left[ \text{sgn} (P(x_n) - P_a) + 1/2 \right] 
+ \frac{(\tau/2)}{2R_m} \left( \frac{P(x_n) - P_a}{R_a} \left[ \text{sgn} (P(x_n) - P_a) + 1/2 \right] \right) \]

\[ \times \left[ \frac{P(x_n) - P_a}{R_a} \left[ \text{sgn} (P(x_n) - P_a) + 1/2 \right] \right] \]

\[ = f(\mu, x_n) = f_\mu(x_n), \quad (5a) \]

\[ \mu = (F_s, L, V_s, P_a, R_a, F_d, L_d, P_v, R_m), \quad \text{(ten in number)} \quad (5b) \]

and let

\[ x \in \mathbb{I} \quad (0, V + \sqrt{(E - P_a) / L}) \]
Remark. Let \( K \) be the parameter space in which \( \mu \) is allowed to vary. For a fixed \( \mu \in K \), eqn (5a) can be related to an iteration of the map \( f_\mu \) of the interval \( I \) into itself.

In practice, depends on the parameter \( \mu \). As \( w \) will show in the following, the behavior of the system depends on \( \mu \).

3. Stability Analysis

**RET AL BACKGRC**

In this subsection we briefly review some basic definitions, and results from one-dimensional dynamical systems theory which may be applied to the stability analysis of our system.

In one dimension it is sufficient to study one-parameter families of maps, since no new phenomena can be found by using more parameters (cf. Collet & Eckmann, 1980: 3). Therefore, we restrict the discussion to one-parameter families of maps \( F: J \times J \rightarrow J, (\mu, x) \rightarrow F_\mu(x) \), where \( J, J \subset \mathbb{R} \). For any point \( x \in J \) the orbit of \( x \) is the sequence \( \{F_\mu^n(x)\}_{n=0}^{\infty} \). The superscript denotes repeated composition. The limit set of \( x \in J \) is the set of limit points of the orbit of \( x \). A point \( x \) and its orbit are periodic, of period \( n \), if \( F_\mu^n(x) = x \) but \( F_\mu^j(x) \neq x \) for \( 0 < j < n \). Hence, the orbit of a periodic point consists of a finite set. When this set consists of only one element, i.e. \( F_\mu^n(x) = F_\mu(x) = x \), \( x \) is called a fixed point of \( F_\mu \). A periodic orbit of \( x \) is stable if for any neighborhood \( U \) of \( x \) and its orbit there is another neighborhood \( V \) so that \( F_\mu^n(V) \subset U \) for all \( n \geq 1 \). Of particular relevance are stable periodic orbits which also attract nearby points: a periodic orbit is locally asymptotically stable or attracting if it has a neighborhood of points which tend to it under iteration. If a periodic orbit is not stable it is said to be unstable. Since the map \( F_\mu \) depends upon the parameter \( \mu \), the limit sets are changed as the parameter is varied. A point \( (\mu, x(\mu)) \), at which the stability character of a periodic point \( x \) is changed abruptly, from being an attractor (stable) to a repeller (unstable), is called a bifurcation point. Our aim is to investigate local bifurcations which involve fixed and periodic points. Of course, all the results we describe for bifurcations of fixed points can be applied to periodic points by considering the relevant iterate of the map. Therefore, in the

Proposition 1 (Fold bifurcation) (Guckenheimer, 197)

<table>
<thead>
<tr>
<th>( F: J \rightarrow J )</th>
<th>( \mu )</th>
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<tr>
<td>( F(\nu, p) = n )</td>
<td>(a) ( (dF/\partial x)(\nu, p) = 1 )</td>
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<tr>
<td>( F(\nu, p) = n )</td>
<td>(c) ( \mu )</td>
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Then there are intervals \((\nu_1, \nu)\) and \((\nu, \nu_2)\) and \(\epsilon > 0\) so that

(i) If \(\mu \in (\nu_1, \nu)\) then \(F_{\mu}\) has no fixed points in \((p-\epsilon, p+\epsilon)\).

(ii) If \(\mu \in (\nu, \nu_2)\) then \(F_{\mu}\) has two fixed points in \((p-\epsilon, p+\epsilon)\), one is attracting and one is repelling.

Proposition 2 (Flip or period doubling bifurcation) (Guckenheimer, 1977). Let \(F: \mathbb{R} \times \mathbb{R} \rightarrow \mathbb{R}\) be a one-parameter family of \(C^3\) maps and suppose that there are \(p, \nu\) satisfying

\[
\begin{align*}
(a) & \quad F(\nu, p) = p; \\
(b) & \quad (\partial F/\partial x)(\nu, p) = -1; \\
(c) & \quad (\partial^2 F/\partial x^2)(\nu, p) < 0; \\
(d) & \quad (\partial^2 F/\partial \mu \partial x)(\nu, p) < 0.
\end{align*}
\]

Then there are intervals \((\nu_1, \nu)\) and \((\nu, \nu_2)\) and \(\epsilon > 0\) so that

(i) If \(\mu \in (\nu_1, \nu)\) then \(F_{\mu}\) has a single fixed point in \((p-\epsilon, p+\epsilon)\) which is attracting.

(ii) If \(\mu \in (\nu, \nu_2)\) then \(F_{\mu}\) has three fixed points in \((p-\epsilon, p+\epsilon)\). The largest and the smallest form an attracting periodic orbit of period 2 for \(F_{\mu}\) and the middle point is repelling.

Remark: For a family of maps with negative Schwarzian derivative \(SF_{\mu}(x)\), where

\[
SF_{\mu}(x) = \frac{F''(x)}{F'(x)} - \frac{3}{2} \left( \frac{F'''(x)}{F''(x)} \right)
\]

and \(F_{\mu}'\) denotes \(\partial F_{\mu}/\partial x\), a flip bifurcation necessarily involves a stable orbit of period two. This is because

\[
(F^3)'(\nu, p) = -2F''(\nu, p) - 3[F''(\nu, p)]^2
\]

and since \(F'(\nu, p) = -1\), \((F^3)'(\nu, p) = 2SF(\nu, p)\), so the sign of the Schwarzian derivative controls condition (c) of the proposition.

(B) DYNAMIC PROPERTIES OF EQN (5a)

Case 1: First we restrict ourselves to the case when the venous return volume \(u_0\) is time invariant and denote it by \(u\). This restriction is possible when the system is open and large enough filling pressure \(P_0\) with respect to the diastolic pressure \(P_d\) are used. In this special case eqn (5a) becomes,

\[
x_{n+1} = x_n - \frac{(\tau/2) F_s - L_s (x_n - V_s)^2 - P_s}{R_s} \left[ \text{sgn} \left( F_s - L_s (x_n - V_s)^2 - P_s \right) \right] + 2 +
\]

\[
f(\mu_*, x_n) = f_{\mu_*}(x), \quad (5*)
\]

where

\[
\mu_* = (F_s, L, V_s, P_s, R_s, \tau, u), \quad \text{seven in number}
\]

\[
u = (\tau/2) P_0 \frac{R_s}{R_s -}
\]
Possible fixed points (equilibrium values) of \( x \) in eqn (5*) may be found algebraically by putting \( x_{n+1} = x_n = \bar{x}_1 \), and solving the resulting equation

\[
\bar{x}_1 = f_{\mu_2}(\bar{x}_1)
\]

An equivalent graphical method is to find the points where the curve \( f_{\mu_2}(x) \) that maps \( x_n \) into \( x_{n+1} \) intersects the diagonal \( x_{n+1} = x_n \), see Fig. 5. At \( u = \tau(F_s - P_a)/2R_s \) two such points,

\[
\bar{x}_1^+ = V_s \pm \sqrt{(R_a/L_s)[(F_s - P_a)/R_s - (2u/\tau)]},
\]

are created by a fold bifurcation. Since the parameter \( u \) is positive, both of the fixed points \( \bar{x}_1^+ \) are in the subinterval \( I^* \) [see (4)] of \( I \), i.e. when the pressure difference \( P_s(x) - P_a \) is positive and \( f_{\mu_2} \) is smooth.

The next question concerns the stability of the fixed points \( \bar{x}_1^+ \). This, as mentioned above, depends on the slope of the curve \( f_{\mu_2}(x) \) at \( \bar{x}_1^+ \). These slopes, which are illustrated in Fig. 5, can be designed

\[
\lambda^{(1)}(\bar{x}_1^+) = \frac{df_{\mu_2}(\bar{x}_1^+)}{dx}|_{x=\bar{x}_1^+}
\]

As long as \( \lambda^{(1)} \) lies between +1 and −1 the fixed point will be at least locally stable, attracting all the orbits of an initial point in its neighborhood. From (5*) we obtain

\[
\frac{df_{\mu_2}(x)}{dx} = 1 + \begin{cases} 
\tau L_s/R_s)(x - V_s) & \text{if } P_s > P_a \\
0 & \text{if } P_s < P_a.
\end{cases}
\]

Hence, \( |\lambda^{(1)}(\bar{x}_1^+)| > 1 \) and the fixed point \( \bar{x}_1^+ \) is therefore unstable. For \( \bar{x}_1^+ \), \( \lambda^{(1)} = 1 - (\tau L_s/R_s)\sqrt{(R_s/L_s)[(F_s - P_a)/R_s - (2u/\tau)]} \) and therefore \( \bar{x}_1^+ \) is initially stable and remains so until

\[
\bar{x} = \frac{(\tau/2)}{R_s} \frac{F_s - P_a - 2R_s}{L_s}.
\]

Fig. 5. The map \( f_{\mu_2} \) of eqn (5*)
Let $\mathcal{P} \subset \mathbb{R}^7$ denote the subset of points $\mu$ in the parameter space $K_{\mu} \subset \mathbb{R}^7$ for which the fixed point $x_1^*$ is stable, and attracts all orbits originating in the interval $0 < x < x_1^*$. Then

$$\mathcal{P} = \left\{ \mu = (F_s, L_s, V_s, P_s, R_s, \tau, u) \in K_{\mu} : 0 < (\tau/2) \frac{F_s - P_s}{R_s} < u < (\tau/2) \frac{F_s - P_s}{R_s} \right\}$$

The set of points $\mu$ in $K_{\mu}$ for which $x_1^*$ is unstable is given by

$$\mathcal{P}^1 = \left\{ \mu = (F_s, L_s, V_s, P_s, R_s, \tau, u) \in K_{\mu} : 0 < u < (\tau/2) \frac{F_s - P_s}{R_s} \right\}$$

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Let $\mathcal{P}_x^1$ denote the subset of points $\mu$ in the parameter space $K_{\mu} \subset \mathbb{R}^7$ for which the fixed point $x_1^*$ is stable, and attracts all orbits originating in the interval $0 < x < x_1^*$. Then

$$\mathcal{P}_x^1 = \left\{ \mu = (F_s, L_s, V_s, P_s, R_s, \tau, u) \in K_{\mu} : 0 < (\tau/2) \frac{F_s - P_s}{R_s} < u < (\tau/2) \frac{F_s - P_s}{R_s} \right\}$$

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At

$$u = (\tau/2) \frac{F_s - P_s}{R_s} \frac{2R_s}{L_s \tau}$$

the fixed point $x_1^* = V_s - (2R_s / \tau L_s)$ and it undergoes a flip bifurcation; the fixed point becomes unstable and a stable orbit of period 2 is born. The stability is ensured since $S_{\mu}(x_1^*) < 0$. This orbit of period 2 may now be written $x_2^*$, and found either algebraically from

$$x_2^* = f^2_{\mu}(x_2^*)$$

or graphically from the intersection between the map $f^2_{\mu}(x)$ and the diagonal, as shown in Fig. 6(a). Factoring out the fixed point of period 1, $x_1^*$, which is a degenerate case of period 2 solution, $x_2^*$, we obtain the following two solutions for (6),

$$x_2^* = V_s + (2R_s / \tau L_s)[(-1 \pm \sqrt{-1 + (\tau L_s / 2R_s)(\tau(F_s - P_s)/2R_s - u)}].$$

As before, the stability of this period 2 orbit depends on the slope of the curve $f^2_{\mu}(x)$, $\lambda^2$, at the 2 points. It is easily shown that

$$\lambda^2 = f^2_{\mu}(x_2^*) = f^2_{\mu}(x_2^*) = f^2_{\mu}(x_2^*) = 5 - (2\tau L_s / R_s)[\tau(F_s - P_s)/2R_s - u].$$

This slope has the value $\lambda^2 = +1$ at the birth (fold bifurcation) of the 2-point orbit, see Fig. 6(b). Initially stable, $x_2^*$ remain so until

$$u = (\tau/2) \frac{F_s - P_s}{R_s} \frac{3R_s}{L_s \tau}$$

Let $\mathcal{P}^1_2$ denote the subset of points $\mu$ in $\mathcal{P}^1_2$ for which the periodic points $x_1^*$ are stable, and attracts all orbits originating in $(0, x_1^*) \setminus x_1^*$. Then

$$\mathcal{P}_2^1 = \left\{ \mu = (F_s, L_s, V_s, P_s, R_s, \tau, u) \in \mathcal{P}_x^1 : 0 < (\tau/2) \frac{F_s - P_s}{R_s} \frac{3R_s}{L_s \tau} < u < (\tau/2) \frac{F_s - P_s}{R_s} \frac{2R_s}{\tau L_s} \right\}$$

The set of points $\mu$ in $\mathcal{P}_x^1$ for which $x_1^*$ are unstable is given by

$$\mathcal{P}^2 = \left\{ \mu = (F_s, L_s, V_s, P_s, R_s, \tau, u) \in \mathcal{P}_x^1 : 0 < u < (\tau/2) \frac{F_s - P_s}{R_s} \frac{2R_s}{\tau L_s} \right\}$$

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At
\[ u = \left(\frac{\pi}{2}\right) \frac{E_a - P_a}{R_a} \frac{3R_a}{L_a \tau} \quad \dot{x}_i^+ = V_s \left(2R_a/\tau L_a\right)(1 \pm 1/\sqrt{2}) \quad \text{and} \quad = -1. \]

Therefore, beyond this point the period 2 points will in turn become unstable, and bifurcate to give an initially stable orbit of period 4. The stability is ensured since \( S_{P_a}(x_i^+) < 0 \). Our investigation on the dynamic properties of eqn (5a) when \( \mu_a \) varies in \( \mathfrak{P}_2 \), which means, the determination of the bifurcation sets and the sets \( \mathfrak{P}_k \), for \( k > 2 \), is made numerically. Typical pictures of the bifurcation phenomenon, when we fix six of the parameters, are depicted in Fig. 7(a)-(d). When one of the periodic points is at \( P_a = P_a \), i.e. where \( f_{P_a} \) has no derivative, the periodic branches are not necessarily smooth, as at \( a_i \), \( i = 1, 2 \). This phenomenon may happen since at points where \( f_{P_a} \) is not smooth the Implicit Function Theorem not necessarily ensures smooth periodic branches, see the proof of proposition 2. In the sequel, we will label such points "bad" points.
Remark: Whether these “bad” points are true physical flutter situations of the heart valves \(P_s = P_a\) or are only faulty predictions caused by the inaccuracies of the model, can be evaluated by appropriate experimental studies.

Case 2: Now, we consider the eqn (5a) for the general case of time variant venous return. The problem of finding stable fixed points, periodical orbits and bifurcation points, as the parameters are varied, is solved, in this case, only numerically. Figure 8(a)-(d) describes the bifurcation phenomenon of stable fixed points and periodical orbits when one of the parameters varies and the others are fixed in nominal normal physiological values. We choose the values for the lower and upper bounds of the varying parameters as follows: at normal physiological values—for lower bounds at Fig. 8(a), (b) and (c), and upper bounds at Fig. 8(c) and (d); at values in which the graph of \(f_\tau(x)\) became tangent to the identity line—in Fig. 8(b) (upper bound); and at values which the orbits become very complex—in Fig. 8(d) (lower bound) and Fig. 8(a) (upper bound). In this figure it is evident that, as in the case of time invariant venous return volume \(u_0 = u\), we have unsmooth periodical branches at “bad” points, [see, e.g. Fig. 8(a)]. The “bad” points correspond to points where the mean systolic pressure \(P_s\) is equal to the mean aortic pressure \(P_a\) [see Fig. 8(a)].

**Physiological Interpretation of the Result**

1. In Fig. 9(a)-(b) we can see how case 1 (the model with time invariant venous return volume) can be obtained from case 2 (the model with time variant venous return volume), when the fraction \(P_s / R_m\) is large enough relative to the fraction \(L_D / R_m\). In Fig. 9(a) \(P_s / R_m = 0.5\) and \(L_D / R_m = 0.000025\), while in Fig. 9(b), compare with Fig. 5 (case 1). \(P_s / R_m = 0.1571\) and \(L_D / R_m = 0.0000357\).

2. The dependence of the end-diastolic volume on the mechanical and hemodynamic properties of the cardiovascular system are well-known for time invariant (normal) heart action (Berne & Levy, 1986: 86-95). These relations are evident from Figs 7 and 8. More specifically: In the case of a stable fixed point, EDV decreases when positively inotropic stimulations are caused by increasing \(F_i\) and when the cardiac cycle \(\tau\) increases [Figs 7(a) and (b) and 8(a)]. On the other hand, EDV increases when the afterload \(P_a\), the preload \(u_0\) and the left atrial pressure \(P_v\) increase [Figs 7(c) and (d) and 8(b)].

A period-doubling is created by a sufficiently large increase of the inotropic parameter \(F_i\), the cardiac cycle \(\tau\) [Figs 7(a) and (b) and 8(a)] and by a sufficiently large decrease of the afterload \(P_a\), the preload \(u_0\) and the left atrial pressure \(P_v\) [Figs 7(c) and (d) and 8(b)].

4. Conclusion and Discussion

The isolated beating heart is described by a one-dimensional discrete-time dynamical system, which depends on several parameters, encompassing mechanical properties of the heart and hemodynamic characteristics of the vascular system. Applying stability analysis we find that normal and abnormal behavior of the beating heart...
are related to different regions in the parameter space. On the transition between the regions which correspond to normal and abnormal beating heart there is a bifurcation which gives rise to a pair of attracting points of period 2, corresponding to MA. This period doubling continues in the region of abnormal beating heart. In this way we obtain the subregions which correspond to MP.

Thus, the existence of MP, for example, MA according to our analysis, provides quantitative information regarding the location of the system parameters. Such results could contribute to the better understanding of the specific pathologic mechanism involved in the development of MP of a specific case. Since parameter values can be changed by external perturbations (drugs, surgery, etc), our results can now be used in choosing of the suitable perturbation for attaining a normal behavior.

FIG. 9.(a)-(b) The map \( f_p \) of eqn (5a) when (a) \( P_p/R_m = 0.5 \text{ (msec}^{-1} \text{ml}) \) and \( L_p/R_m = 0.000 \text{ (msec ml}^{-1}) \), (b) \( P_p/R_m = 0.157 \text{ (msec}^{-1} \text{ml}) \) and \( L_p/R_m = 0.00000357 \text{ (msec ml}^{-1}) \).
Experimental studies measure the effect of known perturbations of inputs on the system outputs. Conclusions drawn from the experimental studies can be made only intuitively by using phenomologic and topologic understanding of the system. Differing from normal (time invariant) behavior, the abnormal (time variant) behavior cannot be predicted intuitively by using conventional reasoning, i.e. by considering the heart as beat-invariant. For example it is well-known, in normal hearts, that EDV increases when the afterload $P_a$ increases. However, this general description is shown by our analysis to be incomplete as in low values of the afterload $P_a$ mechanical alternans appeared. Thus, the complete picture, on normal and abnormal behavior of the beating heart, can be obtained from the same experimental results only by considering the beating heart as a dynamical system. In this respect, our results can be applied as follows.

1. The domain of the parameters (inputs) will be chosen (designed) such that information about a beat-variant phenomenon will be obtained.

2. The domain mentioned in (1) above can be chosen by varying each parameter separately or by a combination (prescribed by our results) of some or all parameters. Such a design is impossible without a theory and results developed here.

Finally, the concept that MP can be induced in a heart in which contractile characteristics ($F$, $L$, $V$) are time invariant is in contrast with the commonly held explanation that time variant values for these parameters (Cohn et al., 1967; Noble & Nutter, 1970; McGaughey et al., 1985) cause MP. However, our analysis cannot predict MP of pathologies as emphysema or pericardial tamponade, where values of mechanical or hemodynamic characteristics are time variant.

Future evaluations of more sophisticated and detailed models of the closed loop of the cardiovascular system may improve our basic analysis and bridge the gap toward the "realistic heart" for clinical application.

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