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Linear time-delay feedback control of a pathological rhythm in a cardiac conduction model

Michael E. Brandt,[1,*] Hue-Teh Shih,[2] and Guanrong Chen[3]
[1]Neurosignal Analysis Laboratory, and Department of Psychiatry and Behavioral Sciences, University of Texas Medical School, Houston, Texas 77030-1501
[2]Division of Cardiology, University of Texas Medical School, Houston, Texas 77030-1501
[3]Department of Electrical and Computer Engineering, University of Houston, Houston, Texas 77204-4793

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This paper describes a method based on one-step linear time-delay feedback (LTDF) for suppressing a pathological period-2 rhythm (cardiac alternans) in an atrioventricular nodal conduction model. The LTDF controller is effective at suppressing alternans by stabilizing the map to one of a set of unstable fixed points. Additionally, we show that alternans can be prevented by tracking the period-1 rhythm past the point where bifurcation occurs, and that the method is robust to both measurement error and experimental noise. Finally, we demonstrate that this method is simpler to implement and more effective than the OGY chaos control method which was used recently to stabilize the same system. [S1063-651X(97)51208-6]

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I. INTRODUCTION

In a recent study by Sun *et al.* [4] an empirical model of electrical conduction through the atrioventricular (AV) node was developed based on stimulus-response measurements from six isolated rabbit hearts. The model was represented by the following nonlinear discrete-time relation:

$$A_{i+1}=f(A_i,H_i)=A_{min}+R_{i+1}+\beta_i\exp(-H_i/\tau_{rec}), \quad (1)$$

where H_i is the interval between bundle of His activation and the subsequent atrial activation (the AV nodal recovery time) during cardiac cycle i, A_{i+1} represents the time interval between cardiac impulse excitation of the low interatrial septum and the bundle of His (the atrial-His interval) during cycle $i+1$, A_{min} and τ_{rec} are positive constants, and

$$R_0=\gamma\exp(-H_0/\tau_{fat}),$$

$$R_{i+1}=R_i\exp[-(A_i+H_i)/\tau_{fat}]+\gamma\exp(-H_i/\tau_{fat}),$$

$$\beta_i=\begin{cases}201\text{ ms}-0.7A_i, & \text{for } A_i<130\text{ ms}\\ 500\text{ ms}-3.0A_i, & \text{for } A_i\geqslant 130\text{ ms},\end{cases}$$

in which H_0 is the initial H interval and both γ and τ_{fat} are positive constants.

Sun *et al.* [4] found that when the rabbit hearts were electrically stimulated near the sinoatrial (SA) node at a fixed time period following Bundle of His activation (the His to stimulus interval, or S), the A intervals could demonstrate an alternating time series characteristic of reentrant tachycardia. This was simulated in the model (1) by substituting the constant S interval for H_i with $S<57$ ms (as demonstrated in [3,4]). Under this condition A_i starts out as a period-1 rhythm, then bifurcates into a period-2 rhythm (alternans) at about cycle number $i=200$ eventually alternating between values of about 113 and 148 ms [see Fig. 1(a)]. R_i eventually reaches the steady-state value of ≈ 51 ms.

In a recent study by Christini and Collins [3] it was dem-

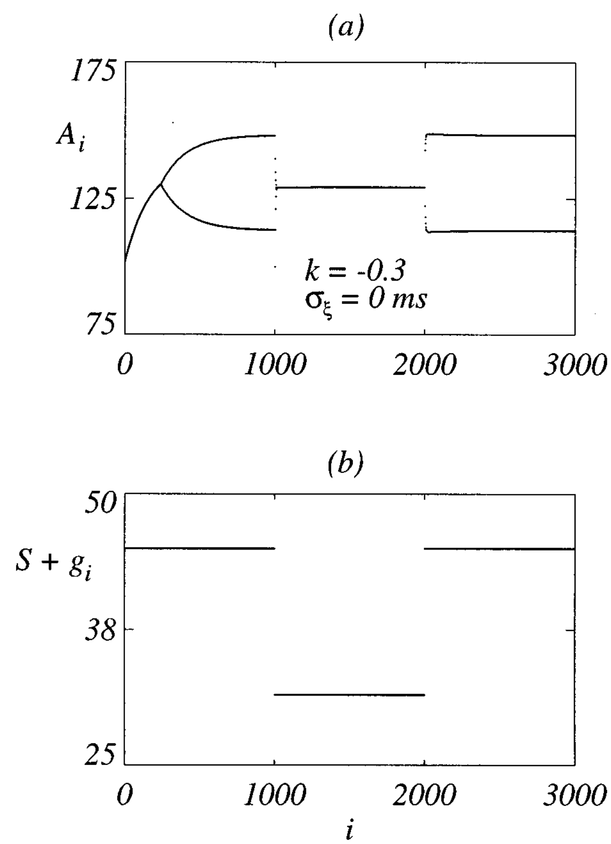

FIG. 1. LTDF control of the map Eq. (1). (a) Times series of A_i prior to control (from $i=0-999$), during control from $i=1000$ to 1999 using $g_i=-0.3S$, and with controller inactivated (for $i>1999$). (b) Corresponding time series of $S+g_i$ with $S=45$ ms.

*Author to whom correspondence should be addressed: Department of Psychiatry and Behavioral Sciences, University of Texas Medical School, 6431 Fannin Dr., Rm. 5.202, Houston, TX 77030-1501. Electronic address: mbrandt@ped1.med.uth.tmc.edu

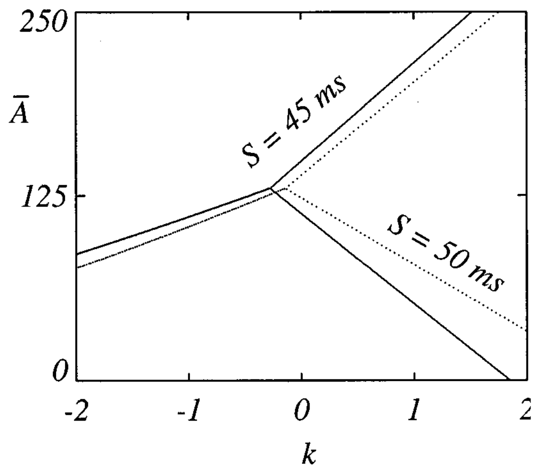

FIG. 2. Plot of the controlled map (1) for values of k in Eq. (9) vs $\bar{A}$ (the final stabilized target trajectory of A_i) with $S=45$ ms (solid plot), and $S=50$ ms (dotted plot).

onstrated that an adaptive version of the OGY chaos control method [1] could be used to stabilize the nonchaotic alternating rhythm produced by the above model. They also showed that this method could be used to prevent alternans in the model if control was applied prior to its onset. The OGY method has previously been used to stabilize unstable periodic orbits in several chaotic biological systems such as the rabbit septum and rat hippocampal slice preparation [2] using small parameter perturbations.

Here we describe a one-step linear time-delay feedback (LTDF) controller that can stabilize the model (1) to one of a set of period-1 (and, if necessary, period-2) rhythms. A similar controller was used by us recently to successfully stabilize nonchaotic as well as chaotic versions of the Hénon map with and without additive Gaussian white noise [5]. A motivation for this work is the fact that certain physiological systems produce stochastic, nonchaotic (nonlinear) behavior that may be more easily stabilized (and with a simpler implementation) using LTDF control rather than the OGY method.

II. METHOD

The controlled form of the map (1) is

$$A_{i+1}=f(A_i,H_i)+g_i, \tag{2}$$

where g_i is a self-tuning control input to be automatically determined during each cardiac cycle i and would be implemented through stimulatory pacing as described in [4].

The objective of the design is to find a simple and implementable g_i to achieve the goal of automatic control, i.e.,

$$A_i \to \bar{A} \quad \text{as} \quad i \to \infty ,$$

where $\bar{A}$ is the desired target atrial-to-His interval. This interval is usually (but not necessarily) an unstable fixed point (UFP) of the original map (1). When the control objective is finally realized, $e_i=A_i-\bar{A}$ will be equal to a small (ideally zero) constant at the time iteration halts. We ultimately desire a g_i that does not depend explicitly on prior knowledge

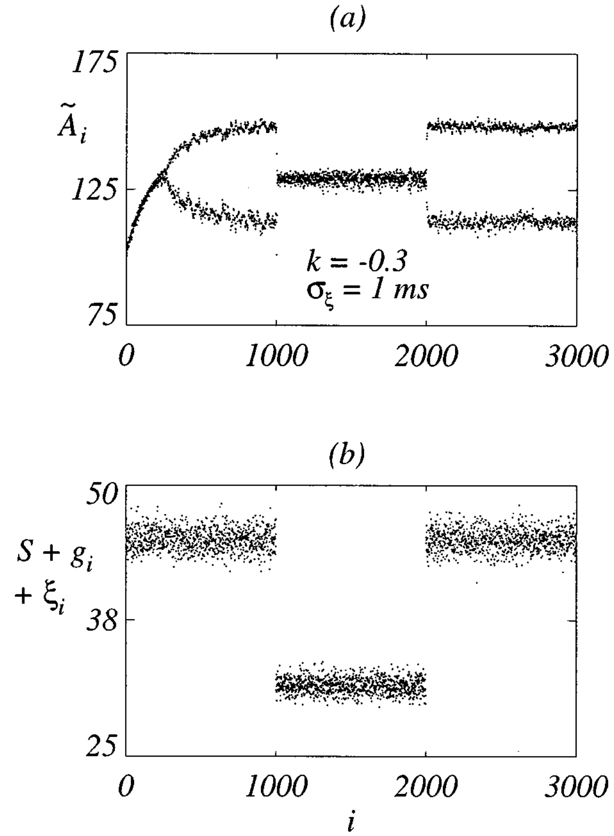

FIG. 3. LTDF control of the map Eq. (1) with zero-mean Gaussian white noise ξ_i ($\sigma_\xi=1$ ms) added to S. (a) Times series of $\tilde{A}_i$ (A_i measured with precision of 0.2 ms) prior to control (from $i=0-999$), during control from $i=1000$ to 1999 using $g_i=-0.3S$, and with controller inactivated (for $i>1999$). (b) Corresponding time series of $S+\xi_i+g_i$ with $\sigma_\xi=1$ ms, and $S=45$ ms.

of the system model. Rather, we prefer a g_i that depends only on previous system state values.

We first demonstrate that LTDF control using the A_i values leads to stabilization of the model to a period-1 rhythm under some restrictions. Since H_i may be more readily accessible in an actual preparation than A_i we then show that LTDF control using H_i is successful under far less restrictive conditions than LTDF control using A_i.

A simple design for the self-tuning gain is

$$g_i=k\hat{A}_{i+1} \tag{3}$$

with k constant and $\hat{A}_{i+1}$ an estimate of A_{i+1} based on a predictive model of the data constructed from previous outputs. For the original system (1) a short time following the period-2 bifurcation, linear autoregressive modeling of the A_i's leads to the approximation

$$\hat{A}_{i+1} \approx A_{i-1}. \tag{4}$$

Equation (3) then becomes

$$g_i=kA_{i-1} \tag{5}$$

and Eq. (2) becomes

$$A_{i+1}=f(A_i,H_i)+kA_{i-1}, \tag{6}$$

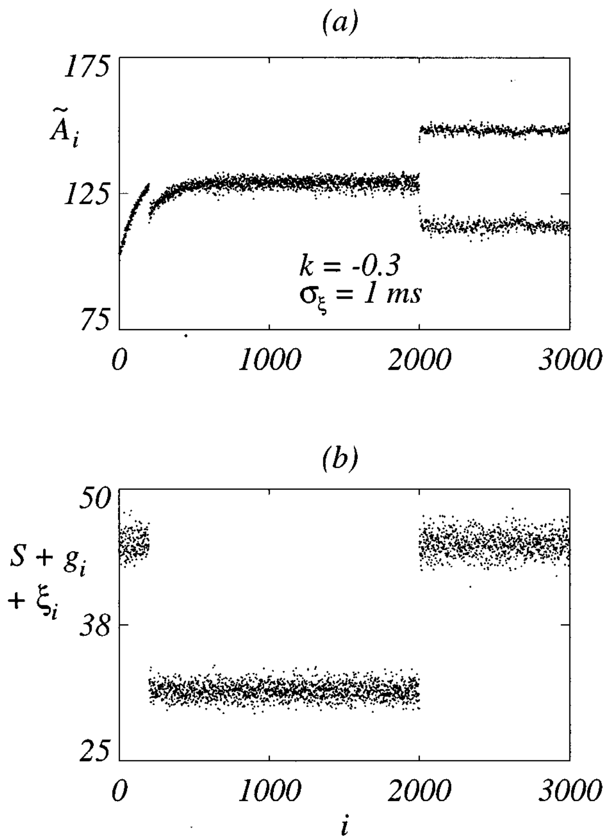

FIG. 4. Target tracking to avoid alternans. The controller $g_i = -0.3S$ is activated at $i=200$ and turned off at $i=2000$. (a) Time series of $\tilde{A}_i$, (b) corresponding time series of $S+\xi_i+g_i$ with $\sigma_\xi = 1$ ms, and $S=45$ ms.

in which the additive control term conveniently depends only on previous values of the system variable. In order to reestablish period-1 control of map (1) we need only determine the value of the constant parameter k.

We now show that use of gain Eq. (5) yields stable control. Subtracting $\overline{A}$ from both sides of Eq. (6) gives

$$A_{i+1}-\overline{A}=f(A_i,H_i)+kA_{i-1}-\overline{A},$$

or, with $e_i^{(+1)}=(A_{i+1}-\overline{A})$ and $e_i^{(-1)}=(A_{i-1}-\overline{A})$,

$$e_i^{(+1)}=f(A_i,H_i)+(1+k)e_i^{(-1)}-A_{i-1}. \tag{7}$$

From Eq. (4) this simplifies to

$$e_i^{(+1)}=(1+k)e_i^{(-1)}. \tag{8}$$

Clearly, the stability condition satisfies $|1+k|<1$, or $-2<k<0$. Observe moreover that $e_i^{(+1)}$ must have the same sign as $e_i^{(-1)}$ as a further consequence of Eq. (4). Hence, for Eq. (8) to hold, $(1+k)$ must be positive, which restricts the gain stability condition to be $-1<k<0$. Note that the analytic condition $-1<k<0$ is an approximate one due to Eq. (4) and may be slightly different in practice.

For LTDF control using H_i [and analogous to Eq. (5)] we specify that

$$g_i=kH_{i-1}. \tag{9}$$

This controller turns out in practice to be more stable and effective than Eq. (5). Its success can be verified mathematically as follows. We first observe that for the system stabilized to a period-1 trajectory, A_i will be less than 130 ms (we demonstrate this explicitly in the results below). Therefore, only the first branch of the parameter β_i is used in Eq. (1); namely, $\beta_i=201-0.7A_i$, which is always positive. Consequently,

$$A_{i+1}=f(A_i,H_i)$$
$$=A_{\min}+R_{i+1}+\beta_i\exp(-H_i/\tau_{rec})>0.$$

Observe also that A_{i+1} is monotonically decreasing as a function of H_i, since H_i is within all of the negative exponential terms in the function A_{i+1}: $\exp[-(A_i+H_i)/\tau_{fat}]$, $\exp(-H_i/\tau_{fat})$, and $\exp(-H_i/\tau_{rec})$. Therefore, for the controlled system

$$A_{i+1}=f(A_i,H_i)+kH_{i-1}$$

to be asymptotically stable, we construct a Lyapunov function of the form $V_i=A_i^2$ which satisfies

$$V_{i+1}-V_i=A_{i+1}^2-A_i^2$$
$$=[f(A_i,H_i)+kH_{i-1}]^2$$
$$-[f(A_{i-1},H_{i-1})+kH_{i-2}]^2$$
$$<0 \quad \text{for } i\to\infty,$$

provided that k is negative. This is because $f(\ )>0$ decreases and a positive constant S is substituted for H_i (as discussed further below). As a result, the feedback-controlled system is stabilized by an arbitrary negative control gain k. Qualitatively, use of a large negative gain leads to more stable control in the sense that $V_{i+1}-V_i$ will be more negative.

III. RESULTS

We limit our discussion of results to the use of the H_i (S) feedback controller Eq. (9) [6]. In the following examples we use the constants $A_{min}=33$ ms, $\tau_{rec}=70$ ms, $\tau_{fat}=30$ s, and $\gamma=0.3$ ms as employed in [3,4]. Figure 1(a) shows the time series of both the uncontrolled and controlled nonstochastic map [Eq. (1)]. The first 1000 iterations are without control followed by 1000 iterations with the controller activated, followed by 1000 iterations with the controller turned off. In this figure $k=-0.3$, and S is set initially to the constant 45 ms. Figure 1(b) shows the corresponding value of $S+g_i$ at each of the 3000 iterations. When the controller is on (from $i=1000$ to 2000) the negative feedback of $g_i=-0.3S$ effectively shortens the natural S interval as shown.

Figure 2 is a plot of the controlled map for values of k in Eq. (9) vs $\overline{A}$ (the final stabilized target trajectory of A_i) with $S=45$ ms (solid line) and $S=50$ ms. For the former case, period-1 control is achieved for $k<-0.27$ and period-2 otherwise. For $S=50$ ms (dotted plot) period-1 control is achieved for $k<-0.14$ and period-2 otherwise. Figure 3 is analogous to Fig. 1 with the exception that zero-mean Gaussian white noise ξ_i has been added to S ($\sigma_\xi=1$ ms) and A_i has been measured with a precision of 0.2 ms to simulate the effect of measurement noise [7]. As shown, this leads to a form of ''noisy'' control [5,8]. Finally, Fig. 4 is an example of tracking in order to avoid the alternans before it occurs. The controller is activated at $i=200$ prior to when the system would normally bifurcate. This eliminates the alternans at the expense of a slightly lower (about 10 ms) $\tilde{A}_i$ (A_i plus simulated measurement error). The controller is then inactivated at $i=2000$ showing restoration of the alternating rhythm.

IV. DISCUSSION AND CONCLUSIONS

We presented a simple method based on LTDF control for stabilizing a nonchaotic, pathologic model of the heart, with and without both random noise and simulated measurement error. Christini and Collins [3] demonstrated that a modified version of the OGY method could be used to stabilize this map to its unstable periodic orbit. However, the method described here has several compelling advantages over the procedure used in [3] for controlling this particular system:

(i) The LTDF controller is a computationally simpler and more intuitive implementation than the OGY chaos control method.

(ii) Once the pathological rhythm is diagnosed (thereby identifying the system) it is easily controlled through linear feedback using a single tunable gain parameter without necessarily having to determine the UFP as in the OGY method.

(iii) In addition to the UFP of the original system, a range of fixed point trajectories can be achieved using our method. This provides a wider latitude in choosing a desired target trajectory (see Fig. 2) than the OGY method which only targets the UFP.

Based on various computer simulations, our method is also as robust to noise inputs and measurement error as the OGY method. Arguably, the most attractive feature of the LTDF controller is its ease of use in setting the feedback gain k. As shown in Fig. 2, k should be set initially to zero, and then slowly ''dialed down'' (increased in the negative direction) until the point in time when the alternating pattern halts and period-1 is restored. Clinically, this may lead to a more straightforward pacemaker design and subsequent implementation.

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