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TIME-DELAY FEEDBACK CONTROL OF COMPLEX PATHOLOGICAL RHYTHMS IN AN ATRIOVENTRICULAR CONDUCTION MODEL

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We describe the emergence of complex cardiac rhythms in a nonlinear model of the atrioventricular (AV) nodal conduction system, and a method based on linear time-delay feedback (LTDF) control for suppressing them. The LTDF controller is effective at suppressing these rhythms by stabilizing the map to one of a set of unstable fixed points. Additionally, we show that the method is robust to both measurement error and experimental noise.

1. Introduction

In a study by Sun *et al.* [1995] 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:

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

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 $\tau_{\rm rec}$ are positive constants, and

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

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

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

in which H_0 is the initial H interval and both γ and $\tau_{\rm fat}$ are positive constants.

It was 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 A intervals alternate in time reminiscent of reentrant tachycardia. This was simulated in the model (1) by substituting a constant interval for H_i less than 57 ms (as also demonstrated in [Christini & Collins, 1996] and [Brandt *et al.*, 1997]). Under this condition A_i starts out as a period-1 rhythm,

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then bifurcates into a period-2 rhythm (alternans) eventually alternating between values of about 113 and 148 ms (see Fig. 1 in [Brandt *et al.*, 1997]).

It was further shown [Sun *et al.*, 1995] that when the rabbit hearts were stimulated at a fixed interstimulus interval (referred to here as S) a more complex A_i time series characteristic of fibrillation is produced depending on the specific value of S chosen (see Fig. 6 in [Sun *et al.*, 1995]). They also simulated this behavior (see Fig. 10 in [Sun *et al.*, 1995]), however it was not clear how they arrived at their specific results. In the following we show how to simulate this behavior in the model and demonstrate how the accompanying complex pathological rhythms that are produced can be stabilized using linear time delay feedback (LTDF) control.

2. Method and Results

A constant interstimulus interval is simulated in the model (1) by constraining $S = H_i + A_i$ via the substitution

$$H_i = S - A_i \tag{2}$$

with S constant. In the following simulations we use the constants $A_{\text{min}} = 33$ ms, $\tau_{\text{rec}} = 70$ ms, $\tau_{\text{fat}} = 30$ s, and $\gamma = 0.3$ ms as employed in [Sun *et al.*, 1995; Christini & Collins, 1996; Brandt *et al.*, 1997]. Figure 1 shows the results of the simulation of Eqs. (1) and (2) for several decreasing values of S from 180 ms to 153 ms. Period-doubling bifurcations are evident; alternans is observed for $S \approx 174$ ms, period-4 cycling occurs around $S = 165$ ms, and more complicated (possibly chaotic and fibrillatory) rhythms occur for values of S below 165 ms as shown.

The controlled form of the map (1) is

$$A_{i+1} = f(A_i,\, H_i) + g_i\,, \tag{3}$$

where g_i is a self-tuning controller which is implemented in a real cardiac preparation through stimulatory pacing. The control term g_i actually represents a timing interval (with respect to the interval $f(\cdot)$) when an electrical pulse stimulus of empirically-determined amplitude would be delivered to the cardiac preparation during the ith cycle.

We previously demonstrated both the stability and effectiveness of the simple LTDF controller

$$g_i = kH_{i-1} \tag{4}$$

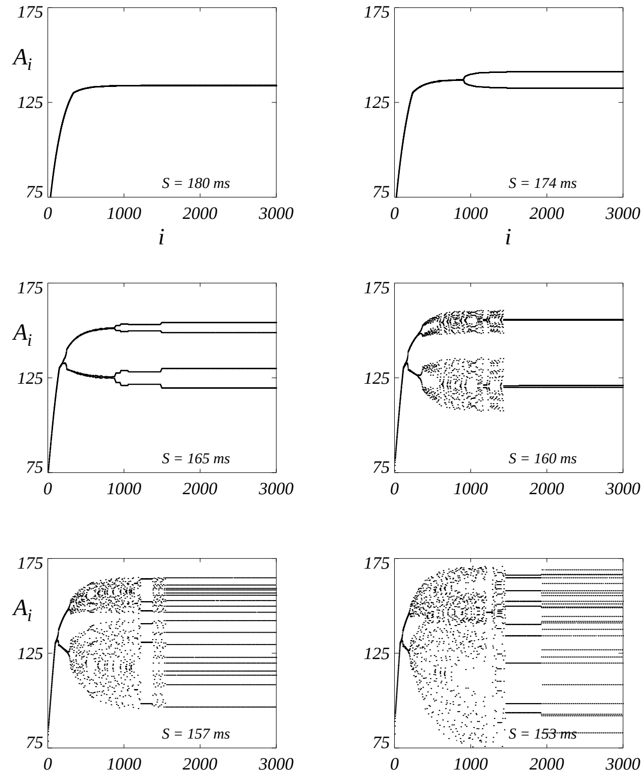

Fig. 1. Interval series of A_i of the map (1) and (2) for various values of S from 180 to 153 ms. Note spontaneous bifurcations occurring for $S = 160$, 157 and 153 ms.

in eliminating the simulated reentrant tachycardia (alternans) visible here in Fig. 1 ($S = 174$ ms) [Brandt *et al.*, 1997]. To implement this controller in an actual cardiac preparation, we note that Eqs. (3) and (4) can be equivalently expressed as

$$A_i - kH_{i-2} = f(A_{i-1},\, H_{i-1}) \tag{5}$$

with a one cycle delay. Thus, during each cycle i, the preparation is stimulated at time $T_i = A_i - kH_{i-2}$ under the conditions that $k < 0$ (stimulate after measurement of A_i) and that $T_i < A_{i+1}$. If the latter of these two conditions are not met, then we do not stimulate during the current cycle i.

Figure 2 shows examples of LTDF control of the model (3) using Eq. (4) for various values of k and S as in Fig. 1. It is clear that this LTDF controller is highly effective in stabilizing the map (3). Figure 3 is a bifurcation-type plot of the controlled map for values of k in Eq. (4) versus $\bar{A}$ (the final stabilized target trajectory of A_i) with S set to 157 ms. Note the regions of period-2 and period-1 control for increasing negative values of the gain k as well

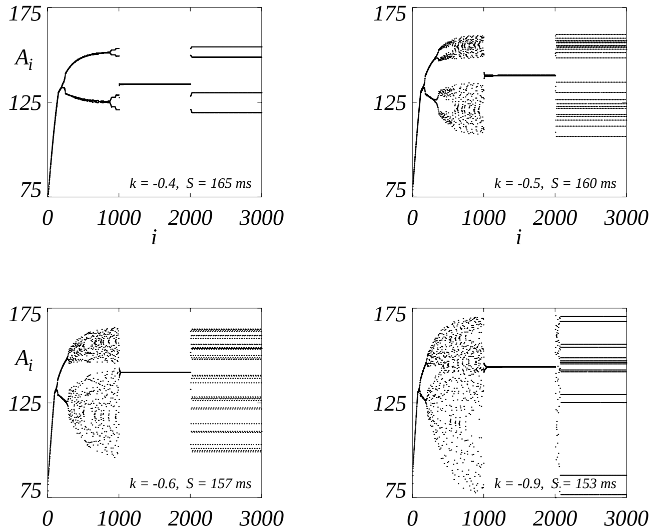

Fig. 2. Plots of the controlled map (3) for values of S and k as shown. In each plot, the first 1000 iterations (i) are without control followed by 1000 iterations with the controller (4) activated, followed by 1000 iterations with the controller inactivated.

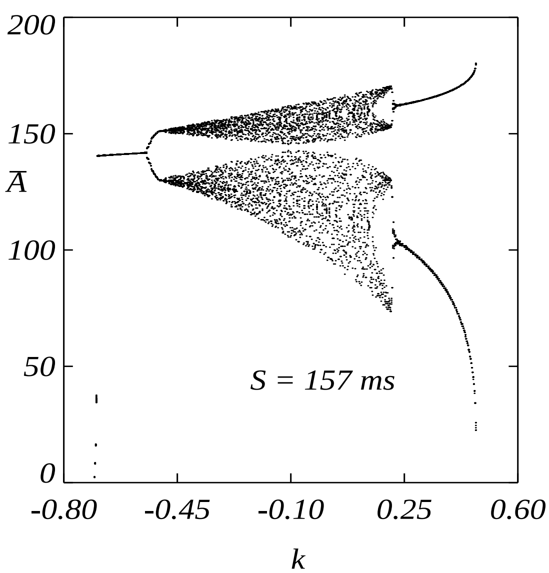

Fig. 3. Bifurcation plot of the LTDF-controlled map (3) showing $\bar{A}$ (the final stabilized target trajectory of A_i) versus k with $S = 157$ ms.

as the complex bifurcation pattern for the range of k values shown. Figure 4 shows LTDF control for $S = 157$ ms with zero-mean Gaussian white noise ξ_i added to H ($\sigma_\xi = 0.5$ ms) and A_i measured with a precision of 0.2 ms to simulate the effect

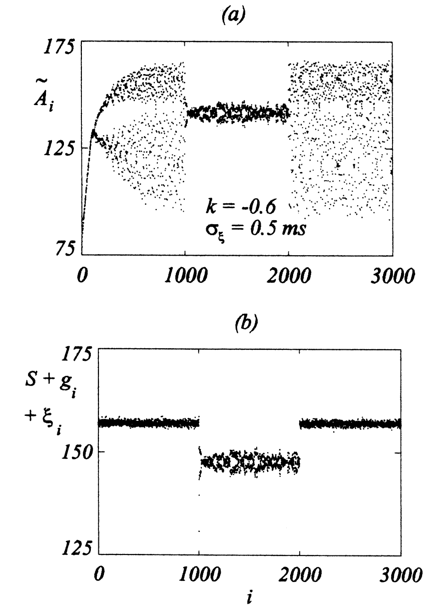

Fig. 4. Plot of the LTDF-controlled map (3) with zero-mean Gaussian white noise ξ_i ($\sigma_\xi = 0.5$ ms) added to S, and $S = 157$ ms. (a) Interval series of $\tilde{A}_i$ (A_i measured with precision of 0.2 ms) prior to control (from $i = 0 - 999$), during control from $i = 1000$ to 1999 using $g_i = -0.6H_i$, and with controller inactivated (for $i > 1999$). (b) Corresponding time series of $S + \xi_i + g_i$.

of measurement noise.[1] As shown, this represents a form of "noisy" control.

3. Conclusions

We demonstrated how to simulate a constant interstimulus interval regimen in a cardiac conduction model of the atrioventricular system and the striking similarity with real experiments on rabbit hearts [Sun *et al.*, 1995]. We also showed that the simple LTDF controller (4) can easily stabilize not only simulated cardiac alternans but complex rhythm disturbances of the model analogous to fibrillation, with and without both random noise and simulated measurement error. Figure 3 demonstrates that a simple LTDF controller is capable of stabilizing even the complex rhythms produced by the model by slowly "dialing down" the feedback gain k (increasing in the negative direction from $k = 0$). At a certain value of k (in this particular case when $k \approx -0.5$) the rhythm bifurcates to period-2 followed by period-1.

[1]Each Gaussian pseudorandom number was computed using the Box–Muller method. See gasdev() routine in [Press *et al.*, 1992]. Measurement error was simulated by truncating each value of A_i to the nearest 0.2 ms.

Two notable studies that used dynamical control algorithms to suppress pathological cardiac rhythms of the *in vitro* rabbit heart are those of Garfinkel *et al.* [1992] and one by Hall *et al.* [1997]. The latter used a straightforward variant of the OGY method to suppress induced alternans in five rabbit heart preparations with good reported success. These studies demonstrate the experimental feasibility of the use of the LTDF control algorithm proposed here as an alternative to the methods used in the latter two studies.

We elaborated on the advantages of LTDF control with respect to the OGY method in [Brandt *et al.*, 1996, 1997]. To summarize, the LTDF controller is computationally simpler to implement than OGY, and it provides a wider latitude of control target trajectory choices. This should not be taken to imply that LTDF control will prove to be the best approach for all related applications. Other approaches may be more appropriate for a given problem. The proof will come eventually in human experimental applications.

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