Control of moving pulses in an one-dimensional model of cardiac tissue

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Abstract: This paper develops a new model-based control aimed to stabilize the propagation velocity of electrical pulses circulating in an one-dimensional ring model of the cardiac tissue. The controller induces small currents using electrodes placed along the ring. This current responds to the discrepancy between the pulse front voltage, measured at an electrode, and a voltage of a set pulse front at the same space point. The proposed control is, in fact, a distributed continuous-time feedback control that stabilizes the spatiotemporal evolution by using a finite number of electrodes implanted on the heart. We present a systematic methodology to predict conditions for pulse instability using linear analysis of the lumped truncated mathematical model of the cardiac tissue. The control effectiveness is measured by the critical length ($L^*$) below which the pulse becomes oscillatory in a moving coordinate. This domain enlarges from $L^* = 10.1cm$ in the open-loop system to $9.0cm$ and $8.0cm$ in the closed-loop system with 2 and 8 electrodes. The validity of control is justified by using the map that connects sensor positions at neighboring time steps.

1. INTRODUCTION

In the normal heart the rhythm is set by the pacemaker, the sinus node. These heart beats lead to a wave of excitation that spread throughout the heart. Cardiac arrhythmias are abnormal cardiac rhythms implying an irregular propagation of a cardiac impulse; e.g. too rapid heartbeat. This may often be fatal because arrhythmias cause disorder of the mechanical functioning of the heart, troubling the synchronized contraction of the myocardium. Therefore, the study of control laws aimed to eliminate the onset of cardiac arrhythmias is very important to prevent the disruption of the normal heart rhythm.

Of the various ways to solve this problem a very promising approach has been made which exploits the electrical activity of the heart and delivers low-amplitude control current via implantable electrodes to the cardiac tissue [for review see Karma and Gilmour, 2007; Christini and Glass, 2002; Dibljev et al. 2008, Garzon and Grigoriev, 2009]. There are several classes of control methods differing in their mathematical description of arrhythmia. The first group uses observations of cardiac arrhythmia by electrical alternans, which are long-term and short-term beat-to-beat alternation of cardiac potential duration. These (model-independent) control methods do not require a priori knowledge of the dynamics equations of the system but rather use the systematic system observation for control formation. Because this approach does not use a cardiac model ("black boxes") it is well suited for cardiac objects for which analytical models are unavailable or incomplete [Echebarria and Karma, 2002; Hall and Gauthier, 2002; Lin and Dubljevic, 2007]. All these methods are implemented by a feedback, which is proportional to the perturbation of the basic pacing cycle length. Such type feedback control may suppress alternans occurring in a small tissue length. In a recent work [Lin et.al, 2008] this limitation was solved by using a more complex controller.

The second classes of control techniques are model-based methods that require a mathematical model. These methods are intended primarily to support a constant velocity of the nonlinear electrical wave propagating through the tissue. The first such approach was presented by Rappel et al. (1999) where the continuous-time controller uses for a signal the differences between the present state variable and the time-delay state variable at several points of the domain. The control is aimed to suppress electrical alternans that characterize instability of cardiac excitation waves. Such a control is in fact a distributed continuous-time feedback control affected by a finite number of electrodes implanted on the heart. The model-based linear-quadratic discrete-time control was elaborated in a recent work [Garzon and Grigoriev, 2009]. This approach, however, is probably impractical because it requires the knowledge of all state variables at all points of the domain for control implementation.

In the present work we develop a model-based control strategy to stabilize the velocity of a pulse that circulates on a 1D ring model of the cardiac tissue. We propose a new feedback control strategy: the discrete-time control is based on introducing small currents that are proportional to the deviation of the voltage at the sensor position from the assigned value (set point). This is a distributed actuator and the resulting control ultimately affects the
stability. The proposed method of control is similar in spirit to an approach developed by the authors to maintain a loop-shaped catalytic system reactive by maintaining a hot pulse circulating throughout the system \cite{Smagina and Sheintuch, 2009 a,b].

The structure of this work is the following: The 1-D cardiac tissue model is described in sec.2 followed by bifurcation analysis showing how the system is destabilized for short lengths in Sect. 3. Sec. 4–6 describe the structure, realization and gain estimation of the elaborated control law and effectiveness is demonstrated in sect.7.

2. MOTIVATION AND STATEMENT

To simulate cardiac arrhythmias in a ring-shaped tissue we use a simple mathematical model \cite{Cain et al. 2004; Beck et al. 2003, Mitchell and Schaeffer, 2003} that admits a moving pulse solution. It accounts for two dynamic variables, the voltage $V$ (the transmembrane potential) and the generalized conductance $h$, both of which are made dimensionless and scaled to vary between zero and unity \cite{Cain, 2008}. These variables satisfy the following equations

$$\frac{\partial V}{\partial t} = D^{-1}\frac{\partial^2 V}{\partial z^2} + J_{in}(V, h) + J_{out}(V) + I_{con}(z, t)$$

$$\frac{\partial h}{\partial t} = \begin{cases} \frac{(1-h)}{\tau_{open}}, & V < V_{crit} \\ -h/\tau_{close}, & V > V_{crit} \end{cases}$$

where $0 < z < L$, $L$ is a length of the ring, $D$ is a diffusion coefficient, the inward current $J_{in}(V, h)$ and the outward current $J_{out}(h)$ are described by

$$J_{in} = \frac{h}{\tau_{in}} V^2 (1 - V), \quad J_{out} = -\frac{V}{\tau_{out}}$$

The parameter $V_{crit}$ in (2) is the critical voltage above which the flow of inward current shuts off. $I_{con} = I_{con}(z, t)$ represents the injected (perturbation, control) current.

We use the following parameter values: $\tau_{in} = 0.3 ms$, $\tau_{out} = 6 ms$, $\tau_{open} = 130 ms$, $\tau_{close} = 150 ms$, $V_{crit} = 0.13$, $D = 0.001 cm^2/ms$ \cite{Hall and Gauthier, 2002; Beck et al. 2008}, for which Eqs. (1-3) are excitable \cite{Mitchell and Schaeffer, 2003; Beck et al. 2008). Model (1-3) is the simplest one that exhibits many qualitative features admitted by the more detailed cardiac models like the Beeler-Reuter equation \cite{Beeler and Reuter, 1977}.

We consider the pulse solution $V$ of Eqs.1-3 travelling along the ring with velocity $c = c(t)$. Let $V_{ext}$ be a certain such pulse solution that moves with a velocity $c_{ext}$. The problem can be formulated as following:

**Problem.** Find the control current $I_{con} = I_{con}(z, t)$ that stabilizes the pulse solution velocity so that $c(t) \to c_{ext}$ as $t \to \infty$ despite small perturbations and uncertainties in the system.

3. BIFURCATION ANALYSIS

In this section we describe the system behavior by numerical and linear analysis methods to show how the system destabilizes for short $L$. The pulse motion is characterized by the circulation time $T$ and mean pulse speed $C_m$, i.e., $C_m = L/T$. Circulation time $T = T(z_1)$ is the duration from point $z_1 - L$ to $z_1$ \cite{Courtemanshe et al. 1996}. Another quantity used below is $A(z_1)$, the duration of action potential duration (APD), or the time interval for which $V$ exceeds some threshold $V_{th}$. The difference between $T$ and $A$ is $t_r$, the recovery time, or the interval for which $V < V_{th}$. These quantities reach constant steady values during a stable circulation. Destabilization leads to periodic or aperiodic solutions of $T$, $A$ or pulse failure altogether.

To form a calculating pulse solution we induce inhomogeneous initial-conditions in a cable domain resulting in two propagating pulses moving in opposite directions \cite{Courtemanshe et al. 1996}. When one of these runs out of the cable domain we join numerically the two ends of the cable into a ring (see Fig.1).

As we decrease the ring length in successive steps (by splicing out part of the ring, \cite{Courtemanshe et al. 1996}) we find that circulation becomes unstable below a certain threshold ($L \sim 10.1 cm$). Figure 2 demonstrates various oscillations of $C_m$ for $L \in [7.5 cm, 10.1 cm]$.

To find the critical length $L$ we apply linear analysis to Eqs.(1,2) in a moving frame coordinate: $(z, t) \to (\zeta, t')$ where $\zeta = z - ct$, $t' = t$, $c$ is a pulse velocity. After transformation $\frac{\partial}{\partial z} = \frac{\partial}{\partial \zeta}$ and $\frac{\partial}{\partial t} = \frac{\partial}{\partial t} - c \frac{\partial}{\partial \zeta}$ Eqs.1,2 (without control $I_{con} = 0$) become

$$\frac{\partial V}{\partial t} = \frac{\partial V}{\partial \zeta} + D^{-1}\frac{\partial^2 V}{\partial \zeta^2} + J_{in}(V, h) + J_{out}(V)$$

$$\frac{\partial h}{\partial t} = \frac{\partial h}{\partial \zeta} + \begin{cases} \frac{(1-h)}{\tau_{open}}, & V < V_{crit} \\ -h/\tau_{close}, & V > V_{crit} \end{cases}$$

subject to periodic boundary conditions

$$V(0) = V(L); \quad \frac{\partial V}{\partial \zeta}|_{\zeta=0} = \frac{\partial V}{\partial \zeta}|_{\zeta=L}$$

Let $V_0(\zeta)$, $h_0(\zeta)$ be the steady pulse solution of Eqs.4,5 \cite{2}. We linearize Eqs.4,5 around it. For small deviations $V = V(\zeta, t) = V(\zeta, t) - V_0(\zeta)$, $h = h(\zeta, t) = h(\zeta, t) - h_0(\zeta)$ and after neglecting terms proportional to product of derivatives the linearized equation for $V$ is

$$\frac{\partial V}{\partial \zeta} + \frac{\partial V_0}{\partial \zeta} - c_0 \frac{\partial V}{\partial \zeta} + D^{-1}\frac{\partial^2 V}{\partial \zeta^2} = 0$$

subject to

$$V(0) = V(L); \quad \frac{\partial V}{\partial \zeta}|_{\zeta=0} = \frac{\partial V}{\partial \zeta}|_{\zeta=L}$$

where $\hat{c} = c - c_0$, $\frac{\partial J_{in}}{\partial \zeta} = h(2V - 3V^2)/\tau_{in}$, $\frac{\partial J_{out}}{\partial \zeta} = 1/\tau_{out}$, $c_0$ is the wave velocity. Eqn.(5) can be presented in an equivalent form

$$\frac{\partial h}{\partial t} = \frac{1-h}{\tau_{open}} \Theta(V_{crit} - V) - \frac{h}{\tau_{close}} \Theta(V - V_{crit}) + c \frac{\partial h}{\partial \zeta}$$

1 Further for simplicity we will use $t$.

2 It corresponds to $V_0(z, t)$, $h_0(z, t)$, steady pulse solution of Eqs.1,2 moving with constant velocity $c_0$. 5378
where $\Theta$ denotes the Heaviside step function. Moreover, to avoid singularity in differentiating of the step function $f(V - V_{\text{crit}}) = a\Theta(V - V_{\text{crit}}) + b\Theta(V_{\text{crit}} - V)$ we use its smoothed analogues [Garzon and Grigoriev, 2009]: $f(V - V_{\text{crit}}) = 0.5(a + b) + 0.5(b - a)\tanh((V - V_{\text{crit}})/r)$ where $r = 0.02$ (a small value tested to show it does not affect results), $a = -h/\tau_{\text{close}}$, $b = (1 - h)/\tau_{\text{open}}$. Thus, Eqn.(9) becomes

$$\frac{\partial h}{\partial t} = 0.5\left(\frac{-h}{\tau_{\text{close}}} + \frac{1 - h}{\tau_{\text{open}}}\right) + \frac{0.5(1 - h)}{\tau_{\text{open}}} + \frac{h}{\tau_{\text{close}}} \tanh((V - V_{\text{crit}})/r)$$

(10)

Linearization of Eqn. (10) gives the following equation for $h$

$$\frac{\partial h}{\partial t} = \frac{1}{2}\left(\frac{h_o}{\tau_{\text{close}}} + \frac{1 - h_o}{\tau_{\text{open}}} \cosh^2(V_o) \right) + \frac{1}{2}\frac{h}{\tau_{\text{close}}} - \frac{1}{\tau_{\text{open}}} + \frac{1}{\tau_{\text{close}}} \tanh(V_o)\right) \hat{h} + c_o \frac{\partial h_o}{\partial \xi} + \hat{c} \frac{\partial h_o}{\partial \xi}$$

(11)

where $V_o = \frac{V_{\text{crit}} - V}{V_{\text{crit}}}$.

Lumping Eqns. (7),(11) by an $M$'th order Galerkin method yields

$$\hat{a}(t) = A\hat{a}(t) + P\hat{c}(t)$$

(12)

where $a$ is the $2M$-vector of continuous-time state variable while the $2M \times 2M$ matrix $A$ and $2M \times 1$ column vector $P$ have the following structure

$$A = \begin{bmatrix} -\Lambda + J + c_o F + \frac{J}{\tau_{\text{in}}} \, Q \, \tau_{\text{in}} \, E & 0.5Q + c_o F \\ 0.5E & 0.5Q + c_o F \end{bmatrix}, \quad P = \begin{bmatrix} B_1 \\ B_2 \end{bmatrix}$$

(13)

In (13) $\Lambda = -\text{diag}(D\lambda_1 + \tau_{\text{out}}^{-1}, D\lambda_2 + \tau_{\text{out}}^{-1}, \ldots, D\lambda_M + \tau_{\text{out}}^{-1})$, $M \times M$ matrices $J, Q, E, F, P$ have the following elements respectively

$$\{J\}_{nm} = \int_0^L (2V_o - 3V_o^2) h_o \phi_n \phi_m d\zeta,$$

(14)

$$\{F\}_{nm} = \int_0^L \frac{\partial \phi_n}{\partial \zeta} \phi_m d\zeta,$$

(15)

$$\{Q\}_{nm} = \int_0^L (V_o^2 - V_o^2) \phi_n \phi_m d\zeta,$$

(16)

$$\{E\}_{nm} = \int_0^L \frac{h_o}{\tau_{\text{close}}} + \frac{1 - h_o}{\tau_{\text{open}}} \cosh^2(V_o) \phi_n \phi_m d\zeta,$$

(17)

$$\{P\}_{nm} = \int_0^L \left[\frac{-1}{\tau_{\text{close}}} - \frac{1}{\tau_{\text{open}}} \right] + \frac{1}{\tau_{\text{close}}} \tanh(V_o) \phi_n \phi_m d\zeta,$$

(18)

$$\{B_1\}_{n} = \int_0^L \frac{\partial V_o}{\partial \zeta} \phi_n d\zeta, \quad \{B_2\}_{n} = \int_0^L \frac{\partial h_o}{\partial \zeta} \phi_n d\zeta$$

(19)

where $n, m = 1, \ldots, M$. In above formulas $\lambda_j, \phi_n$ are eigenvalues and eigenfunctions of the problem $\frac{\partial^2 \phi(\zeta)}{\partial \zeta^2} = -\lambda \phi(\zeta)$ subject to periodic boundary conditions. The steady solutions $V_o(\zeta)$ and $h_o(\zeta)$, $\zeta \in [0, L]$ are obtained numerically from the original model (Eqns.1-3) by calculating profiles $V_o(z, t)$ and $h_o(z, t)$ at a fixed moment $t = t_i$.

Study of linear stability of PDE (1-3) approximated by the linearized lumped system (12, $M = 50$) corroborates that in vicinity of $L^* = 10.1cm$ the leading real eigenvalue of matrix $A$ changes sign with decreasing ring length $L$. This value is corroborated by simulations (Eqns.1-3) of the amplitudes of APD oscillations ($\rho A = \max(\text{APD}) - \min(\text{APD})$) and of $T (\rho T = \max(T) - \min(T))$ that show a bifurcation at $L^*$ as ring length $L$ is decreased. If $L$ is shortened below $L = 7.4cm$, propagation failure occurs.

Now we adjust the control variable $I_{\text{con}} = I_{\text{con}}(z, t)$ to keep $C_m (T)$ near a constant value.

4. STRUCTURE OF CONTROL

We want to build a controller that responds to deviations of measured front velocity from the set value, by manipulating the speed of a moving front. However, since front velocity cannot be measured directly we will respond to deviations of voltage signal from the set spatially-dependent signal. We show that the two approaches are identical.

We will apply a feedback controller (regulator) of the general structure $I_{\text{con}}(z, t) = \rho \frac{d\zeta}{dz}$ where $\hat{c} = \hat{c}(t)$ is a manipulated input (control action), responding to measured difference between the voltage $V$ value at assigned sensor position $z^*$ and a set point, the voltage at the same point of a set pulse front: $e \sim (V(z^*, t) - V_{\text{set}}(z^*, t))$, and $\frac{d\zeta}{dz}$ is the predetermined spatial function.

This controller is realized by the following general discrete-time strategy: Let us place $\mu$ equally-spaced sensors $z_j^*$, $j = 1, 2, \ldots, \mu$ along the ring i.e. $z_{j-1}^* = \zeta^* + \Delta(j - 1), \Delta = L/\mu, j = 1, 2, \ldots, \mu$ ($j$ is the integer remainder of divisor of $i$ by $\mu$, $i = 1, 2, \ldots$), $\zeta^* = z_{i=0}$. At some moment $t_i$ ($i = 1, 2, \ldots$) when the waveform of $V(z, t)$ reaches a sensor position $z_j^*$, as defined by $V(z_j^*, t_i) = V^*$ with $V^*$ a certain arbitrary threshold, we compare $V(z_j^*, t_i)$ with a value $V_{\text{set}}(z_j^*, t_i)$ where $V_{\text{set}}$ is a set profile (a profile moved with assigned velocity $c_{\text{set}}$). We can not simulate $V_{\text{set}}$, but instead make the following projection: If $V_{\text{set}}(z_j^*, t_i)$ is the value at $t_i$, we project this value to the measured profile and search for $V(z_j^* + \delta, t_i) = V_{\text{set}}(z_j^*, t_i)$ with $z_j^* + \delta_i = c_{\text{set}}(t_i - t_{i-1})$. The control variable $\hat{c}$ updates according the law

$$\hat{c}(t_i) = -k[V(z_j^*, t_i) - V(z_j^* + \delta_i, t_i)], \quad j = 1, \ldots, \mu; \quad i = 1, 2, \ldots$$

(20)

where $k > 0$ is a real gain coefficient.

Thus the control term

$$I_{\text{con}}(z, t_i) = \hat{c}(t_i) \frac{\partial V}{\partial z} = k(V(z_j^*, t_i) - V(z_j^* + \delta_i, t_i)) \frac{\partial V}{\partial z}$$

(21)

affects the right-hand part of Eqn.1 during the time interval $t_{i+1} - t_i$. At $t = t_{i+1}$ the procedure is repeated with sensor $z_{j+1}^*$. 

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Control (20) is the discrete-time controller that is applied to the continuous system by means of an ideal zero-order hold, i.e., the value \( \hat{c}(t) \) is sampled and held constant between any two consecutive sampling instants. Since the variable \( \hat{c}(t) \) is a piecewise variable which is automatically activated at instants \( t_i, i = 1, 2, \ldots \), then spatio-depended controller (21) is the feedback discrete-time controller.

Let us use a moving coordinate presentation to show that control changes the linear stability of whole closed-loop system. In a moving coordinate discrete-time variable \( \hat{c}(t) = \hat{c}(t_i) \) is transformed as follows

\[
\hat{c}(i) = -k[V(\zeta^* - V(\zeta^*(i)))], \quad i = 1, 2, \ldots \tag{22}
\]

where \( \zeta^* \) is the sensor position (assumed to be moving) and \( \zeta^*(i) = \zeta^* + \delta_i \). Inserting the term \( \hat{c}(t_i) \frac{DV}{Dz} \) into Eqn. (1)

\[
\frac{DV}{Dt} = D^{-1} \frac{\partial^2 V}{\partial z^2} + J_{in} + J_{out} + \hat{c}(t_i) \frac{DV}{Dz} \tag{23}
\]

transforms (23) into

\[
\frac{DV}{Dt} = \frac{\partial V}{\partial \zeta} + D^{-1} \frac{\partial^2 V}{\partial z^2} + J_{in} + J_{out} - k[V(\zeta^* - V(\zeta^*(i))) \frac{DV}{D\zeta}] \tag{24}
\]

After linearization and lumping by an M\(^{th}\) order Galerkin method Eqsns.(24,22) are reduced to the linear ODE closed-loop system

\[
\hat{a}(t) = A\hat{a}(t) - k \begin{bmatrix} F \end{bmatrix} H\hat{a}(t) \tag{25}
\]

where matrices \( A \) and \( F \) are presented above and \( H = [h, O] \) is the \( 1 \times 2M \) vector row, \( O \) is zero \( M \)-vector and elements of the \( 1 \times 1 \) row vector \( h \) are the following

\[
h_m = \phi(\zeta^*), \quad m = 1, 2, \ldots , M
\]

In a recent work [Smagina and Sheintuch, 2009b] we proved that a hybrid closed-loop system (25) with appropriate gain \( k \) is asymptotically stable if several conditions on finite zeros of the related open-loop system are satisfied. In the present work (see Sec.6) we present alternative stability conditions in terms of the map connecting sensor positions at neighboring time steps \( t_i \).

Remark 1. Since \( V(z, t) \) may be approximated by a square pulse having a steep front at point \( z_i \subset [0, L] \) then the function \( \frac{DV}{Dz} \) is roughly a delta-function: \( \delta(z - z_i) \) (see Fig.2, right) and the term \( I_{con}(z,t) \) becomes the following simple form: \( I_{con}(z,t) \approx \hat{c}\delta(z - z_i) \).

5. REALIZATION OF CONTROL

To realize control (21) we need to follow successively the value \( V(z, t) \) at sensor positions \( z^*_j = \zeta^* + \Delta(j - 1) \), \( j \in [1, \mu] \). When \( V(z^*_j, t) \) reaches some specified value we mark the corresponding times \( t_i \) and use the difference \( V(z^*_j, t_i) - V(z^*_j - \delta_i, t_i) \) with \( z^*_j(\iota) = z^*_j + \delta_i \) for control updating. Hence the value \( V(z, t) \) should be measured continuously on-line. 3

3 We propose that exist a device that measures \( V(z, t) \) at assigned points of the ring.

To simplify manipulations we transform relation \( V(z^*_j(\iota), t_i) = V(z^*_j + \delta_i, t_i) \) to a moving coordinate: \( V(\zeta^*(\iota)) = \hat{V}(\zeta^* + \delta_i) \), approximate \( V(\zeta^* + \delta_i) \) for small \( \delta_i \) as follows

\[
V(\zeta^* + \delta_i) \approx V(\zeta^*) - \frac{\partial \hat{V}}{\partial \zeta} (\zeta^* - \zeta^*(\iota))
\]

and substitute the right part of the above expression in (22). Control is obtained in the alternative form

\[
\hat{c}(i) = -k(\zeta^* - \zeta^*(i)), \quad i = 1, 2, \ldots \tag{26}
\]

where \( \hat{c}(i) = \frac{\partial \hat{V}}{\partial \zeta} (\zeta^* - \zeta^*(i)) \). In fixed coordinate Eqn. (26) becomes

\[
\hat{c}(t_i) = -k(z^*_j - z^*_j(i)), \quad j = 1, 2, \ldots , \mu, \quad i = 1, \ldots \tag{27}
\]

To sum we briefly formulate the mechanism of control: When the wavefront of voltage pulse \( V \) reaches sensor position \( z^*_j, j \in [1, \mu] \), we need only to evaluate the difference \( z^*_j - z^*_j(i) \), which is used to control updating.

Remark 2. Since \( z^*_j - z^*_j(i) = [(z^*_j - z^*_j - 1) - (z^*_j(i) - z^*_j - 1)] = c_i(t_i - t_i - 1) - c_{set}(t_i - t_i - 1) = \sigma_i(c_i - c_{set}) \) where \( \sigma_i = t_i - t_i - 1 \) then we can rewrite formula (27) as follows

\[
\hat{c}(t_i) = -k\sigma_i(c_i - c_{set}) \tag{28}
\]

where \( c_i \) is the pulse velocity at time interval \( \sigma_i = \Delta/\sigma_i \) and \( c_{set} \) is the assigned pulse velocity. Denoting \( c_{set} = \Delta/\sigma_i \) we present \( c(t_i) \) in terms of \( \Delta, \sigma_i, c_{set} \) are known in advance.

Remark 3. Formula (27) is the piecewise control that is automatically activated at instants \( t_i, i = 1, 2, \ldots \), and applies during time interval \( \sigma_i = t_i - t_i - 1 \). In practice, the interval of control may be shorter.

6. STABILITY ANALYSIS OF CLOSED-LOOP SYSTEM

Here using the original formula of control (20) we estimate \( k \) that assures stability of the closed-loop system. At moment \( t_i \) the sensor position at a fixed coordinate may be expressed via sensor position in a moving coordinate as follows

\[
z^*_j|_{t_i=t_i} = z^*(i) = [\zeta^* + \sum_{j=1}^{i} c_i(i)]mod(L), \quad i = 1, 2, \ldots \tag{30}
\]

where \( c(1) \) is the initial pulse velocity and \( c(i), i = 2, 3, \ldots \), are velocities at time interval \( \sigma_i \). Formula (20) is rewritten in terms of \( z^*(i) \) as follows

\[
\hat{c}(t_i) = -k(V(z^*(i), t_i) - V_{set}), \quad i = 1, 2, \ldots \tag{31}
\]

where \( V_{set} = V(z^*(i), t_i), \quad z^*(i) = c_{set}(t_i - t_i - 1) \).

Since \( \hat{c}(t_i) \approx \frac{\zeta^*(i+1) - \zeta^*(i)}{t_{i+1} - t_i} \) at every point \( z^* \subset [0, L] \) and \( \hat{c}(t_i) = c(t_i) - c_{set} \) then the left part of formula (31) may be presented as follows

\[
\hat{c}(t_i) \approx \frac{z^*(i+1) - z^*(i)}{t_{i+1} - t_i} - c_{set} \tag{32}
\]
where \( c_{set} \) is a constant velocity of pulse solution \( V_{set} \). Substituting the right hand part of (32) instead the left part of (31) we obtain the map
\[
z^*(i+1) = z^*(i) - \sigma_i k(V(z^*(i), t_i) - V_{set}) + \sigma_i c_{set} \quad (33)
\]
describing the behavior of \( z^* \) at every time interval \( \sigma_i = t_i - t_{i-1} \). To study stability of (33) we recall that the value \( V_{set} \) does not depend on \( z^*(i) \) (see (31)) and the value \( V(z^*(i), t_i) \) is a function only of \( z^*(i) \) at every \( \sigma_i \). Then (33) is linearly stable if the inequality \( 0 < |1 - k \sigma_i \partial V / \partial z|_{z=z^*} | < 1 \) is satisfied. This means that for any small perturbations we have \( z^*(i+1) = z^*(i) \frac{\sigma_i c_{set}}{\sigma_i + 1} \), as \( t_i \rightarrow \infty \) and hence \( c(t_{i+1}) \rightarrow c(t_i) \rightarrow 0 \) and \( c(t_{i+1}) \rightarrow c(t_i) \rightarrow c_{set} \). Since according (28) \( c_{i+1} \rightarrow c_i \rightarrow c_{set} \) then in moving coordinate the above inequality becomes as
\[
0 < |1 - k \sigma_i \partial V / \partial z|_{z=z^*} | < 1 \quad (34)
\]
Inequality (34) may be used for evaluating gain \( k \). Indeed, using approximation of \( \sigma_i \); \( \sigma_i \rightarrow L / (\mu c_{set}) \) as \( t \rightarrow \infty \) we approximate (34) as follows: \( 0 < |1 - k \frac{L}{\mu c_{set}} \partial V / \partial z|_{z=z^*} | < 1 \).

For our case \( \partial V / \partial z > 0 \). Thus we obtain a crude estimate for \( k \):
\[
0 < k < \frac{2 \mu c_{set}}{L \partial V / \partial z_{front}} \quad (35)
\]

7. SIMULATIONS

Now we demonstrate the effectiveness of control law (27) for domain lengths that exhibit unstable circulation \( L \leq 10.1cm \). We will apply control to stabilize \( C_m \) for \( L = 9.0cm \) where steady \( C_m \) oscillates between values 0.0306cm/\( ms \) and 0.0326cm/\( ms \) (see Fig.2) and we assign \( c_{set} = 0.03cm/\( ms \) \). Before applying of control we need to evaluate roughly the gain coefficient \( \tilde{k} = k \frac{L}{\mu c_{set}} \partial V / \partial z_{front} \) where \( \partial V / \partial z_{front} \) is the point of steep (left) front position. In the considered case \( \partial V / \partial z_{front} \cong 1 \). Then according formula (35) gain \( \tilde{k} \) for control with 4 actuators/sensors should satisfy the inequality: \( \tilde{k} < 0.0266 \). The simulation of the closed-loop system shows that \( \tilde{k} = 0.0032 \) for piecewise control and \( \tilde{k} = 0.03 \) for impulse control.

Simulations of the full closed-loop system (Eqns. 1-3, 27) with four sensors/actuators with \( \tilde{k} = 0.0032 \) (piecewise control) and with \( \tilde{k} = 0.03 \) (impulse control) for \( L = 9.0cm \) (Fig.3) shows that the mean pulse speed \( C_m \) converges to a constant value. Faster response is observed with piecewise control.

Constraining instability domains of the open-loop (Eqns.1-3) and closed-loop systems using the ring length \( L \) as a bifurcation parameter demonstrates that the stability boundary in a closed-loop system shifts to smaller \( L \) (see Fig.4). Moreover, increasing the number of sensor/actuators has the same effect.

8. REFERENCES


Fig. 1. Open-loop pulse solution: Spatiotemporal grayscale patterns in the \((i, z)\) plane of the dimensionless transmembrane potential \( V(z, t) \) (solution of Eqns.1-3, \( L = 20.5cm \) with parameters \( \tau_{in} = 0.3ms, V_{crit} = 0.13, D = 0.001cm^2/ms.\))

Fig. 2. Transition from stable to unstable motion with decreasing \( L \) showing temporal evolution of the mean pulse velocity \( C_m = L/T \) for different lengths \( L = 7.5cm \) (top), 9cm (middle), 10.1cm (bottom), other parameters as in Fig.1.
Fig. 3. Testing the effectiveness of the control law (27) with 4 fixed sensors for $L = 9$cm. Control is updated as the left front reaches the sensor positions. Sensors situated at positions 0.01cm, 2.26cm, 4.51cm, 6.76cm, $c_{set} = 0.03cm/msec$. Figure shows: time evolution of mean pulse velocity $C_m$ in open-loop system (first row); with piecewise control, $\hat{k} = 0.0032$ (second row); with impulse control, $\hat{k} = 0.03$ (third row).

Fig. 4. Amplitudes of APD oscillations (left) and of $T$ (right) as a function of ring length $L$ for the open-loop (dashed line) (Eqns.1-3) or for closed-loop system with piecewise control (27) (solid lines). Solid lines from right to left corresponds control with 2 ($\hat{k} = 0.0012$), 4 ($\hat{k} = 0.0032$) and 8 ($\hat{k} = 0.0042$) sensor/actuators.


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