Continuous-time feedback control of cardiac alternans in Purkinje fibers

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Contents

- Relevance of the suppression of alternans for the prevention of arrhythmias
- Alternans in one-dimensional cardiac tissue (fibers)
- Suppression of alternans as a control problem
- Reduction to the control of a linear map
- Results: continuous-time control is successful
- Conclusions and perspectives
From normal rhythm to ventricular fibrillation

Normal rhythm → Alternans → Tachycardia → Fibrillation
Paced fiber of cardiac tissue

Pacing electrode, current density:

\[ I_p(x, t) = I_p^0(t)g(x - x_p) \]

Traveling wave

Recording electrode \( V(t) \)

Control electrode, current density:

\[ I_c(x, t) = I_c^0(t)g(x - x_c) \]
**Alternans**

Voltage signal at \( u(t) \) at a particular location \( x \)

APD: action potential duration

\[
T > T_c \quad \text{(slow pacing)}
\]

\[
\text{Normal rhythm,}
\]

\[
\text{APD}_n = \text{APD}_{n+1}
\]

\[
T < T_c \quad \text{(fast pacing)}
\]

\[
\text{APD}_n \begin{cases} 
\neq \text{APD}_{n+1} \\
\approx \text{APD}_{n+2}
\end{cases}
\]

Alternans
Model of electrical activity

\[
\partial_t V = D \partial_x^2 V - \frac{1}{C_m} \left[ I_{\text{ion}}(V, \dot{y}) + I_p(x, t) + I_c^0(t) g(x - x_c) \right]
\]

\[
\partial_t \dot{y} = h(V, \dot{y})
\]

with \( I_{\text{ion}}(V, \dot{y}), h(V, \dot{y}) \) taken from the 4-variable Fenton-Cherry Purkinje model, \( \dot{y} = [y_1, y_2, y_3] \)

All equations are gathered in a single one

\[
\partial_t z = \tilde{D} \partial_x^2 z + F(z) + \tilde{I}_p(x, t) + I_c^0(t) g(x - x_c) \hat{u},
\]

where \( z(x, t) = [u(x, t), \dot{y}(x, t)] \), \( u \) is the scaled voltage

\[
\hat{u} = [1, 0, 0, 0]
\]

\[
u = \frac{V - V_{\text{off}}}{V_{\text{sc}}}, \quad 0 \leq u \leq 1
\]
Fenton-Cherry four-variable Purkinje model
Control problem

\[ \partial_t z = \tilde{D} \partial_x^2 z + F(z) + \tilde{I}_p(x, t) + I_c^0(t)g(x-x_c)\hat{u}, \]

Find \( I_c^0(t) \) such that the normal rhythm is the asymptotic state even when \( T < T_c \). **Difficult problem!**

Simplified approximation to the dynamics

\[ \xi^{n+1} = A\xi^n + B^n I_n^c, \quad \xi^n = [\xi_1^n, \xi_2^n, ..., \xi_m^n], \]

Find \( I_n^c \) such that \( \xi^n \to 0 \)

**Easier problem!**
Calculation of normal rhythm \( z^*(x, t) \) (periodic orbit)

\[
z^*(x, 0) = \Phi[T, 0; z^*(x, 0)]
\]

by Newton-Krylov method.

Consider the deviation from the normal rhythm

\[
\delta z(x, t) = z(x, t) - z^*(x, t)
\]

Evolution equation for the deviation

\[
\partial_t \delta z = \left( \tilde{D} \partial_x^2 + J_F[z^*(t)] \right) \delta z + I^0_c(t) g(x - x_c) \mathcal{A}(t)
\]

Linear periodic operator
Galerkin projection

\[ \delta z(x, t) = \sum_{i=1}^{\infty} \xi_i(t) e_i(x, t) \]

where the periodic basis \( e_i(x, t) \) is given by

\[ U(T, 0) e_i(x, 0) = \lambda_i e_i(x, 0) \]

Projecting the dynamics of \( \delta z(x, t) \) onto \( e_i(x, t) \)

\[ \dot{\xi}_i = \sigma_i \xi_i + b_i(t) I_c^0(t) \]

where

\[ b_i(t) = \langle f_i(x, t), g(x - x_c) \rangle \]

adjoint eigenfunctions

Discarding highly stable modes and considering discrete times \( t_n = n\Delta T \)

\[ \xi^{n+1} = A\xi^n + B^n I_c^n \quad \text{with} \quad \xi^n = [\xi_1(t_n), \xi_2(t_n), \ldots, \xi_m(t_n)] \]
Calculation of feedback

\[ I_c^n = K^n \xi^n \]

\[ \xi_i(t_n) = \langle f_i(x, t_n), \delta z(x, t_n) \rangle \]

Linear Quadratic Regulator control: choose \( K \) so as to minimize the quadratic form

\[
\sum_{i=1}^{\infty} \left[ (\xi^n)^\dagger Q_n \xi^n + (I_c^n)^2 R \right]
\]

\( (Q_n)_{i,j} = \langle e_i(x, t_n), e_j(x, t_n) \rangle \) and \( R > 0 \) is a scalar
Impulsive and continuous-time control

Impulsive
\[ \xi^{n+1} = A\xi^n + BI_c^n \]

Piecewise constant stroboscopic
\[ \xi^{n+1} = A\xi^n + BI_c^n \]
\[ I_c^n = [I_c^{n,1}, I_c^{n,2}, I_c^{n,3}, I_c^{n,4}] \]

Piecewise constant periodic
\[ \xi^{n+1} = A\xi^n + B^n I_c^n \]
Comparison of control methods

$L = 1 \text{ cm}$
$T = 188 \text{ ms}$
$R = 10^5$
$s = 20$

- **Impulsive**
- **Piecewise constant stroboscopic**
- **Piecewise constant periodic**

![Graph showing comparisons of control methods](image-url)
Range of success and number of unstable eigenvalues

\[ U(T, 0) e_i(x, 0) = \lambda_i e_i(x, 0) \]

<table>
<thead>
<tr>
<th>Method</th>
<th>Succeeds on</th>
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<tbody>
<tr>
<td>Impulsive</td>
<td><img src="#" alt="Impulsive Succeeds" /></td>
</tr>
<tr>
<td>Piecewise constant stroboscopic</td>
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</tr>
<tr>
<td>Piecewise constant periodic</td>
<td><img src="#" alt="Periodic Succeeds" /></td>
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</tbody>
</table>
Piecewise constant stroboscopic control, different number of subintervals $s$

$L = 1 \text{ cm}$
$T = 188 \text{ ms}$
$R = 10^4$
Piecewise constant periodic control, different number of subintervals $s$

$L = 1\text{ cm}$
$T = 188\text{ ms}$
$R = 10^5$
Conclusions and perspectives

- Continuous-time control suppresses alternans faster compared to impulsive control.

- Continuous-time control suppresses alternans for longer fibers (up to 3 cm) and a wider range of pacing periods compared to impulsive control.

- The control methods need to be integrated with an observer which would reconstruct the system state from measurements of voltage in order to be applied in an experimental setting.