Effects of deformation on wave propagation in the human heart

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19-10-2005
The human heart

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Introduction

- SCD is the main cause of mortality
- Arrhythmias are driven by reentrant electrical sources
- MEF is a complex issue and alters electrical properties
- Mathematical modeling is a useful technique to investigate the electrical and mechanical activity
- Until now, none of the studies have accounted for both MEF and ECC
- Aim of this study is to investigate the combined effects of cardiac mechanics and dynamics of electrical activity
What are arrhythmias?

A sudden change in the rhythm of the heartbeat. Some known arrhythmias are:

- **Ectopic beat**
  An extra heartbeat. Treatment (normally) not needed.

- **Atrial tachycardia (spirals)**
  Episodes of fast regular beating. Unpleasant, but not lethal.

- **Atrial fibrillation (spiral breakup)**
  Very fast and irregular beating. Increases risk of stroke, significantly. Treatment required.

- **Ventricular tachycardia and ventricular fibrillation**
  The heart beats very fast and (ir)regular. Pump function of blood to rest of the body is disturbed. Very lethal if not treated within minutes.
Basic properties of cardiac excitation

**Introduction**

**Modeling**

**Results**

**Conclusions**

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**Action potential**

- Conduction
- Refractory period
  (time during which a second wave cannot be initiated)
Mechanism of spirals: Re-entry

Rotation of excitation in a thin ring

Rotation is possible if the length of the ring is longer than the product of the refractory period and the velocity of the wave.
Basic properties of spiral waves

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What about mechanics?

Until recent, only wave patterns have been studied in the human heart not taking into account the mechanical deformation.

Direct effects of deformation:

- Arrhythmogenic (commotio cordis)
- Life saving (precardial thumb)

The aim of this study is to investigate the effects of mechanical deformation on wave propagation.
Electromechanical regulatory interactions

Excitation \rightarrow Contraction

MEF
Excitation initiates contraction

Actin Myosin Cross-bridge

The Trigger for Muscle Contraction is Ca\textsuperscript{2+}

- Stored in the SR
- Excitation causes SR to release Ca\textsuperscript{2+}
Coupled reaction diffusion system

- **Reaction diffusion:**

\[
C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V, E)
\]

Voltage is determined by 2 processes:

- Diffusion \( D \) (determined by \( \nabla \cdot (D \nabla V) \))
- Reaction \( R \), which is determined by both voltage and the mechanical deformation

\( (E \text{ is a mechanical tensor}) \)
Coupled reaction diffusion system

- **Constitutive relations:**
  \[ T^{MN} = T^{MN}_p(E) + T^{MN}_a(E, V) \]

Force per unit surface \( T^{MN} \) is related to deformation \( E \). The force per unit area contains 2 parts:

- \( T^{NM}_p \) passive stress tensor
  - If the length of a spring (muscle) changes from its resting length, a tension or force is generated.
- \( T^{NM}_a \) active stress tensor
  - This is the actual contraction of the heart.

Note: Passive behavior is always present, even if there is no contraction.
Coupled reaction diffusion system

- **Stress equilibrium:**

\[
\frac{\partial}{\partial X_M} \left( T^{MN} \frac{\partial x_j}{\partial X_N} \right) = 0
\]

In equilibrium the sum of all forces equals zero (Newton).

Can be compared with **quasi steady state**, assuming that the equilibrium state the deforming tissue is reached very fast.
Effects of deformation on the RD system

- Deformation affects coordinate system
  \[ C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V, E) \]
  \[ \nabla \cdot (D \nabla V) = D \frac{\partial}{\partial X_M} (\sqrt{g} g_{MN}^{-1} \frac{\partial V}{\partial X_N}) \]
  
  \( g_{MN} \) is a metric tensor that accounts for the deformation.

- Deformation affects passive electrical properties
  \[ C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V, E) \]
  
  Capacitance \( C \) and diffusion \( D \) may depend on deformation.
Effects of deformation on the RD system

- Deformation affects reaction $R(V,E)$
  \[ C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V, E) \]

Stretch activated channels are identified. They open during stretch.

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Effects of deformation on the RD system

- Deformation affects reaction $R(V,E)$

$$ C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V,E) $$

- Stretch activated channels are added:

$$ C \frac{\partial V}{\partial t} = \nabla \cdot (D \nabla V) + R(V) + I_{sac} $$

$$ I_{sac} = G_{sac} (\sqrt{g} - 1)(E_{sac} - V) \text{ for } g > 1 \text{ (stretch)} $$

$$ I_{sac} = 0 \text{ for } g > 1 \text{ (shortening)} $$

$G_{sax}$ is maximal conductivity

$E_{sac}$ is the reversal potential of SAC

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Numerical formulation

- Finite Difference for RD part
- Finite Elements for mechanical part

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Mechanical deformation and pacemaker activity

Wave propagation of an AP after a single stimulation in the center

Upper row: No mechanical coupling
Lower row: RD-mechanical coupling
Mechanism of SAC activation

Transmembrane voltage and local dilatation measured in the center of the medium

Black: Transmembrane potential $V$
Red: Local deformation variable $(\sqrt{g} - 1)$
Oscillations of pacemakers

Values for the parameters $G_{sac}$ vs $E_{sac}$ and $G_{sac}$ vs $a$ required for pacemaking oscillations

- **O**: Oscillations regime
- **L**: Single additional local response
- **N**: No wave propagation

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Drift of pacemakers

Pacemaker drift from different initial conditions

red circles - attractors; green circle - unstable equilibrium

Effects of deformation on wave propagation in the human heart
Drift of pacemakers

Pacemaker drift is dependent on size of medium

Relative shift of location of attractors plotted against medium size.

Spiral wave Dynamics

Fenton-Karma-type model

\[
\frac{\partial u}{\partial t} = \nabla^2 u - l_{ion}(u; v, w) + l_s(u; g) \tag{7}
\]

\[l_{ion} = l_{fi}(u; v) + l_{so}(u) + l_{si}(u; w) \tag{8}\]

\[
\frac{\partial v}{\partial t}(x, t) = \frac{\Theta(u_c - u)(1 - v)}{\tau_v^-(u)} - \frac{\Theta(u - u_c)v}{\tau_v^+(u)} \tag{9}
\]

\[
\frac{\partial w}{\partial t}(x, t) = \frac{\Theta(u_c - u)(1 - w)}{\tau_w^-} - \frac{\Theta(u - u_c)w}{\tau_w^+} \tag{10}
\]

\[l_{fi}(u, v) = \frac{-v}{\tau_d} \Theta(u - u_c)(1 - u)(u - u_c) \tag{11}\]

\[l_{so}(u) = \frac{u^{1.4}}{\tau_o} \Theta(u_t - u) \tag{12}\]

\[l_{si}(u; w) = \Theta(u - u_t)u(1 - w)\tau_{si}^+(u) \tag{13}\]
Mechanical deformation may induce drift of a spiral wave

1. No contraction
2. With contraction
3. Different initial conditions
Mechanical deformation can induce spiral breakup

1. No contraction
2. Contraction

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Mechanism of spiral breakup

1. No contraction
2. Contraction

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Limitations

- Anisotropy is not modeled, which is important for both electrical and mechanical properties
- Specific ions current are not specified
- Simplified description of passive mechanical properties
Conclusions

Mechanical deformation can directly induce:

- Induction of automaticity in an array of otherwise non-oscillatory cardiac cells
- Drift of pacemakers
- Breakup of a single spiral wave into complex patterns
- Drift of an otherwise stationary rotating spiral wave

SAC play an important role!