Modelovanie elektrickej aktivity srdca v prostredí COMSOL Multiphysics

(Modeling of the electrical activity of the heart in COMSOL Multiphysics environment)

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PRESENTATION OUTLINE

• Electrical excitation - action potential (AP) in the heart

• Models of AP of atrial and ventricular heart cells

• Simplified model of heart cells (modified FitzHugh-Nagumo model) – in Matlab

• Modeling of AP propagation – monodomain model

• Modeling of AP propagation - in COMSOL Multiphysics
Electrical excitation of the heart

Electrical excitation (in form of action potential) is spreading in the heart through various types of heart cells [1] – [3]:

- **SA nodal** – origin of excitation
- Atrial
- AV nodal
- **Bundle of His**
- **Bundle branches**
- **Purkinje fibers**
- Endocardial
- **Mid-myocardial**
- Epicardial

**Action potential shape [2] is different for different types of heart cells**
Action potential phases in typical cardiomyocyte (cardiac muscle cell)
Various types of cardiomyocyte action potential shapes

Various types of action potential shapes in ventricular cardiomyocyte [4], [5]


Luo – Rudy II model (1994) [7]

Winslow model (1999) [8]


Hund-Rudy dynamic model (2004) [130]

O'Hara-Rudy model (2011) - enables to model [4], [5]:
  - epicardial
  - endocardial
  - mid-myocardial cells

Courtemanche-Ramirez-Nattel model (1998) [12], [13]
enables to control AP morphology (three main morphological types)
- 21 ordinary differential equations (ODE)

Simplified model of heart cells

enables to control AP shape
- 2 ordinary differential equations
Courtemanche-Ramirez-Nattel model of human atrial cell [12]
Courtemanche-Ramirez-Nattel membrane model of the human atrial cell

\[
\frac{dV}{dt} \cdot C_m + I_{ion} = I_{st} \quad \Rightarrow \quad dV/dt = \left(-I_{ion} + I_{st}\right)/C_m
\]

\[I_{ion} = I_{Na} + I_{Ca,L} + I_{to} + I_{Kr} + I_{Ks} + I_{K1} + I_{Kur} + I_{NaK} + I_{NaCa} + I_{Ca,p} + I_{Ca,b} + I_{Na,b}\]

where e.g.:

\[I_{Na} = G_{Na} \ m^3 \ h \ (V - V_{Na})\]

21 ordinary differential equations (ODE)

75 algebraic equations

\[
\frac{dV}{dt} = -k \, c_1 (V_m - B) \left( -\frac{(V_m - B)}{A} + a \right) \left( -\frac{(V_m - B)}{A} + 1 \right) - k \, c_2 R (V_m - B) \\
\frac{dR}{dt} = k \, e \left( \frac{(V_m - B)}{A} - R \right)
\]

Where \( V_m \) is the membrane potential, 
\( R \) is the recovery variable 
\( a \) is relating to the excitation threshold 
\( e \) is relating to the excitability 
\( A \) is the action potential amplitude 
\( B \) is the resting membrane potential and 
\( c_1, c_2, \) and \( k \) are membrane-specific parameters.
FitzHugh-Nagumo model – simulation in Matlab

Influence of membrane parameters on:
- action potential duration (APD)

Influence of membrane parameter “e” on APD [20].
FitzHugh-Nagumo model – simulation in Matlab

Influence of membrane parameters on:
- action potential amplitude (APA)

Influence of membrane parameter “A” on AP amplitude [20].
Modeling of propagation of electrical activation using monodomain model

- monodomain model [21], [22] with incorporated modified FitzHugh-Nagumo equations [18] – [20], [23]

\[
\frac{\partial V_m}{\partial t} = \frac{1}{\beta C_m} \{ \nabla \cdot (\sigma \nabla V_m) - \beta (I_{ion} - I_s) \}
\]

where

- \( V_m \) is the membrane potential,
- \( \beta \) is the membrane surface-to-volume ratio,
- \( C_m \) is the membrane capacitance per unit area,
- \( \sigma \) is the tissue conductivity,
- \( I_{ion} \) is the ionic transmembrane current density per unit area and
- \( I_s \) is the stimulation current density per unit area.

\[ D = \frac{\sigma}{\beta C_m} \]
Simulation parameters

- of monodomain model with modified FitzHugh-Nagumo equations:

\[
\begin{align*}
    a &= 0.13 & \text{- relating to the excitation threshold} \\
    e &= 0.0132 & \text{- relating to the excitability} \\
    A &= 0.120 \text{ V} & \text{- the action potential amplitude} \\
    B &= -0.085 \text{ V} & \text{- the resting membrane potential} \\
    c_1 &= 2.6 & \text{- membrane-specific parameter} \\
    c_2 &= 1 & \text{- membrane-specific parameter} \\
    k &= 1000 \text{ s}^{-1} & \text{- membrane-specific parameter} \\
    D &= 0.0005 \text{ m}^2/\text{s} & \text{- diffusivity}
\end{align*}
\]
Modeling of **propagation** of electrical activation in COMSOL Multiphysics

- monodomain model for AP propagation in the heart is:

\[
\frac{\partial V_m}{\partial t} = \frac{1}{\beta C_m} \{\nabla \cdot (\sigma \nabla V_m) - \beta(I_{ion} - I_s)\}
\]

- this PDE (partial differential equation) is numerically solved in COMSOL Multiphysics

- detailed description how realize similar example for heart of ellipsoidal shape in COMSOL Multiphysics is in [23]:

Select Physics:
→ Δu Mathematics
→ Δu PDE Interfaces
→ Δu General Form PDE (g)
Mathematical description of monodomain model:

\[ \frac{\partial V_m}{\partial t} = \nabla \cdot \left( \frac{1}{\beta C_m} \sigma \nabla V_m \right) - \frac{1}{C_m} (I_{ion} - I_s) \]

where: \( u \rightarrow V_m \)

\[ e_a = 0 \]
\[ d_a = 1 \]

\[ i_{ion} = \frac{I_{ion}}{C_m} \]
Modeling geometry of heart wall

whole heart as a hollow sphere: \rightarrow \text{part of heart wall:} \rightarrow \text{approximate part of heart wall of box (“SLAB”) shape:}

the SLAB model of wall that is used for the following simulation
The SLAB model of the heart wall covered with mesh (predefined „Fine“ mesh). The stimulated area is a cylinder with $r = 1$ mm radius situated in the middle of the slab model.
Meshing of the model

More dense meshing of the SLAB near the boundary of stimulated area of $r = 1$ mm radius (green) is performed with two manually added boundary mesh layers from both sides.
Distribution of membrane potential $[V]$ in the SLAB model at 0.006 s and 0.008 s after stimulation onset ($r = 1$ mm, stimulation duration $T_s = 0.002$ s, amplitude of stimulation current $i_s = 100$ A/F). Activated area is shown in red, resting area in blue.
Distribution of membrane potential [V] (action potential) in the slab model in point \(x = 1.5\) mm, \(y = 0\) mm, \(z = 2\) mm \((T_s = 0.002\) s, \(i_s = 100\) A/F).
Distribution of $I_{ion}$ normalized current [A/F] in the slab model in point $x = 1.5$ mm, $y = 0$ mm, $z = 2$ mm ($T_s = 0.002$ s, $i_s = 100$ A/F). First negative current causes depolarization of membrane (AP onset), positive peak of current causes membrane repolarization (terminal phase of repolarization).
Simulation of electrical activity (AP) of heart cell using FitzHugh-Nagumo equations
   - ordinary differential equations (ODE)
     - in Matlab.

Simulation of AP propagation in heart tissue using monodomain model with FitzHugh-Nagumo equations
   - partial differential equations (PDE)
     - in Comsol Multiphysics.
THANK YOU FOR YOUR ATTENTION!
References


