Modelovanie šírenia 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**
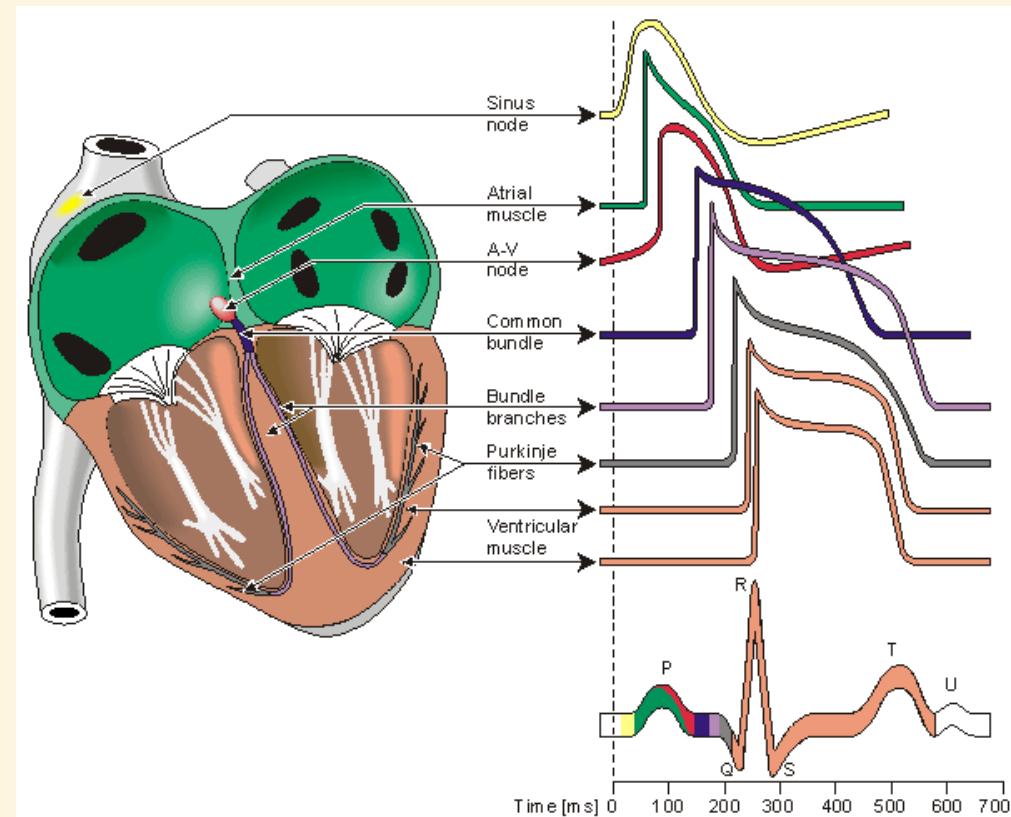
Action potential shape [2] is different for different types of heart cells

3
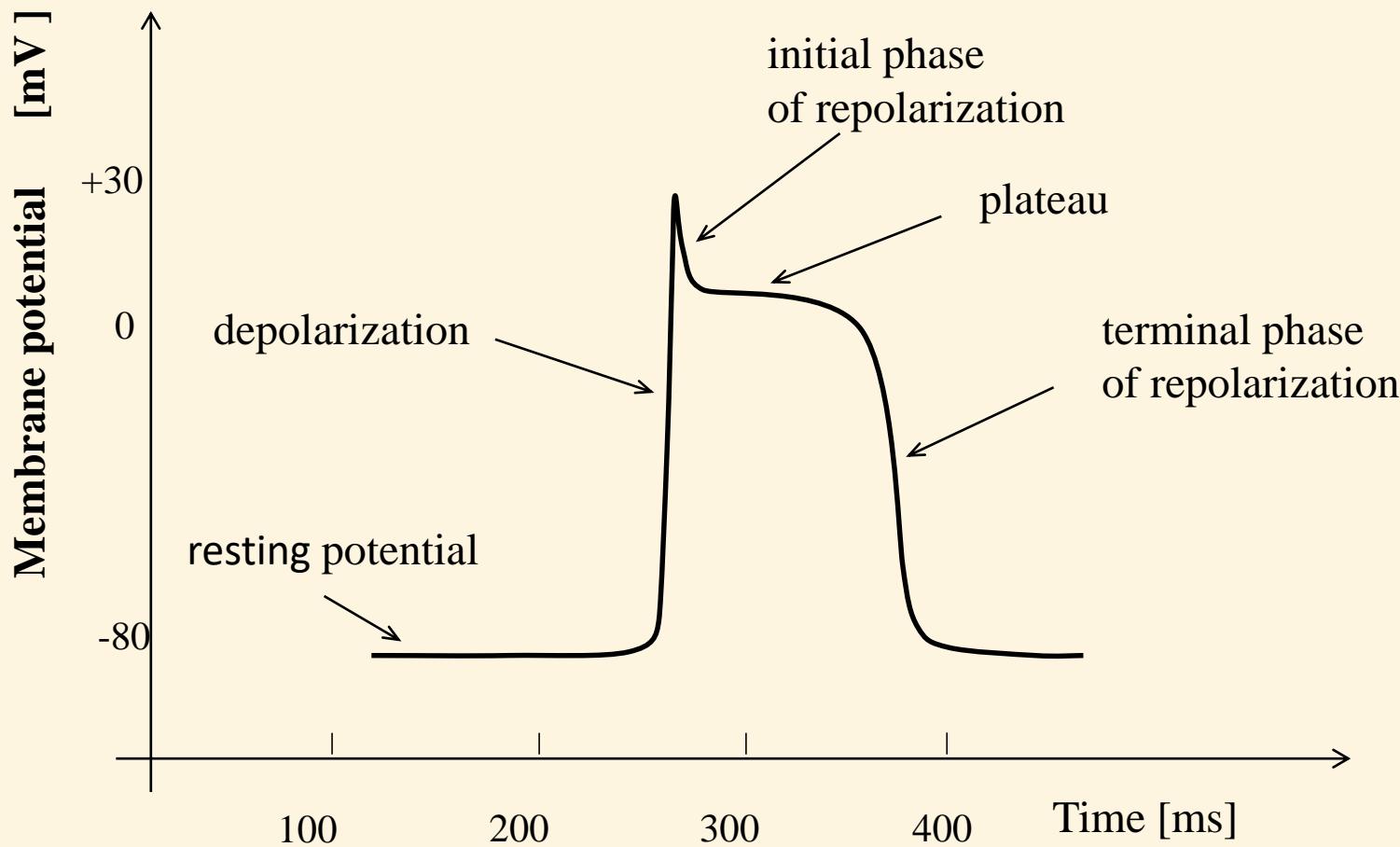
Action potential

Action potential phases in typical cardiomyocyte (cardiac muscle cell)

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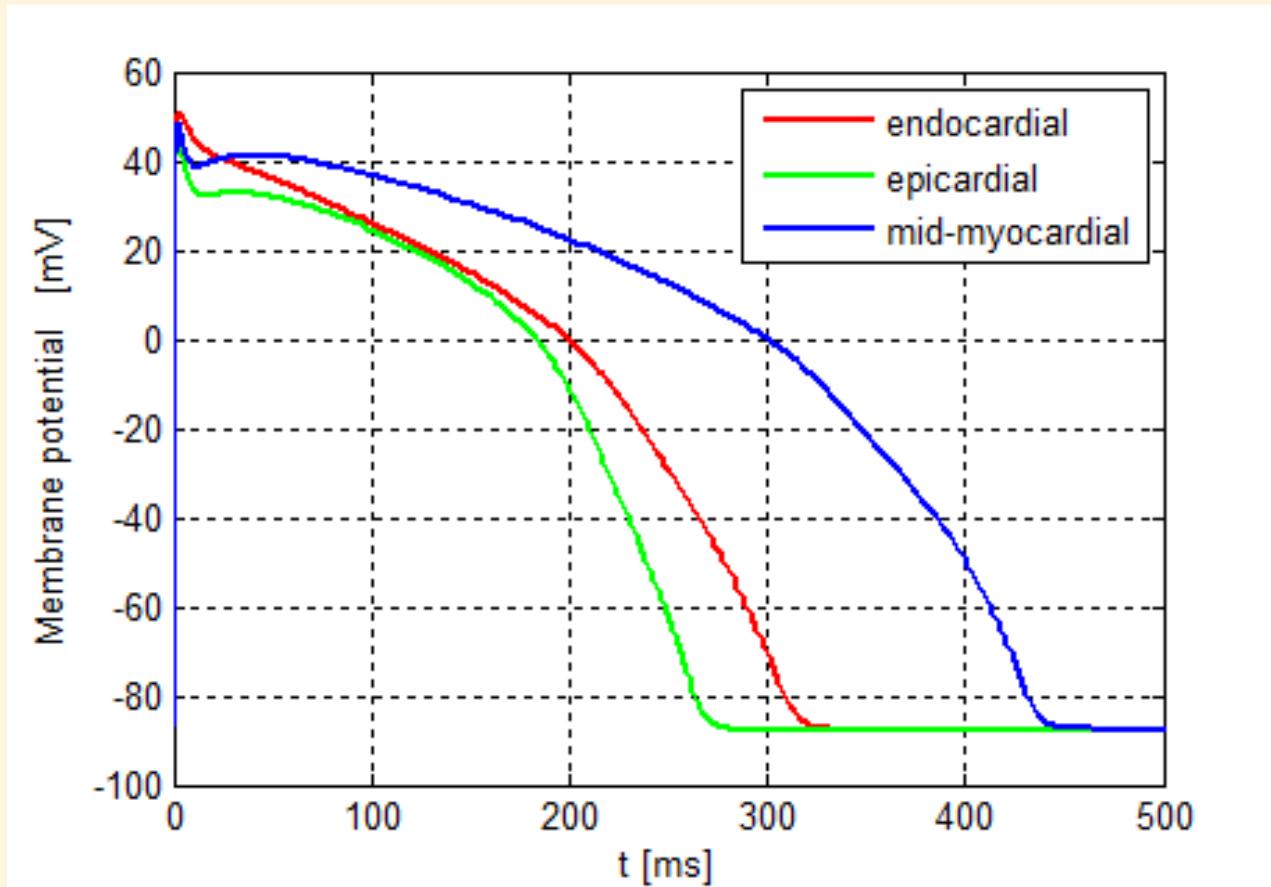
Various types of action potential shapes in ventricular cardiomyocyte [4], [5]

Models of heart ventricular cells [4] – [11]

Luo – Rudy I model **(1991) [6]**

Luo – Rudy II model **(1994) [7]**

Winslow model **(1999) [8]**

Shannon-Bers model **(2004) [9]**

Hund-Rudy dynamic model **(2004) [130]**

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

Model of heart atrial cells [12] - [15]

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

**modified FitzHugh-Nagumo model** [16] – [20]
enables to control AP shape
- 2 ordinary differential equations

Courtemanche-Ramirez-Nattel model of human atrial cell [12]
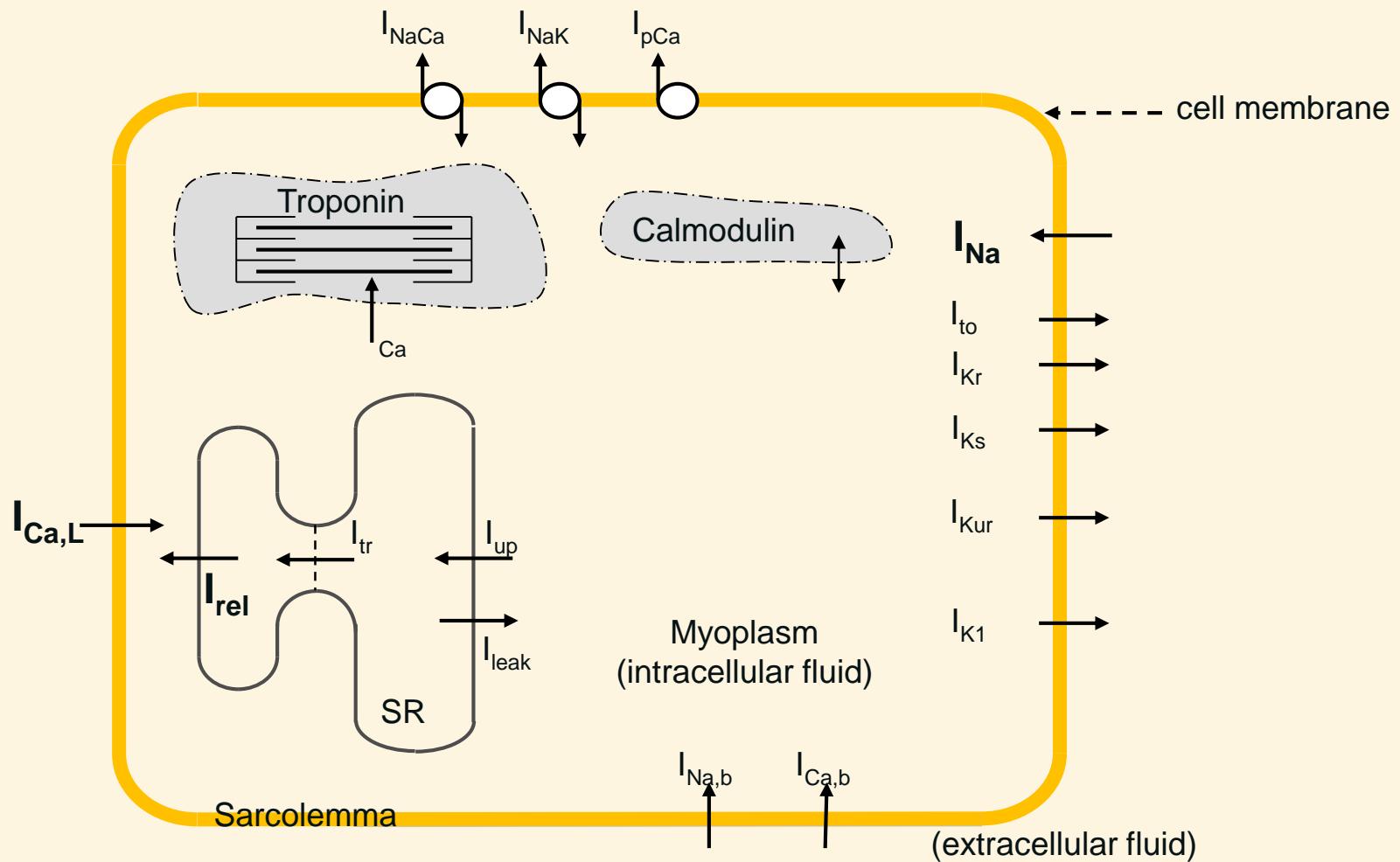
Courtemanche-Ramirez-Nattel membrane model of the human atrial cell

I_{st} V Intracellular solution

I_{Na} I_K I_C

G_{Na} G_K $\cdots$ C_m Membrane

V_{Na} V_K

Extracellular solution
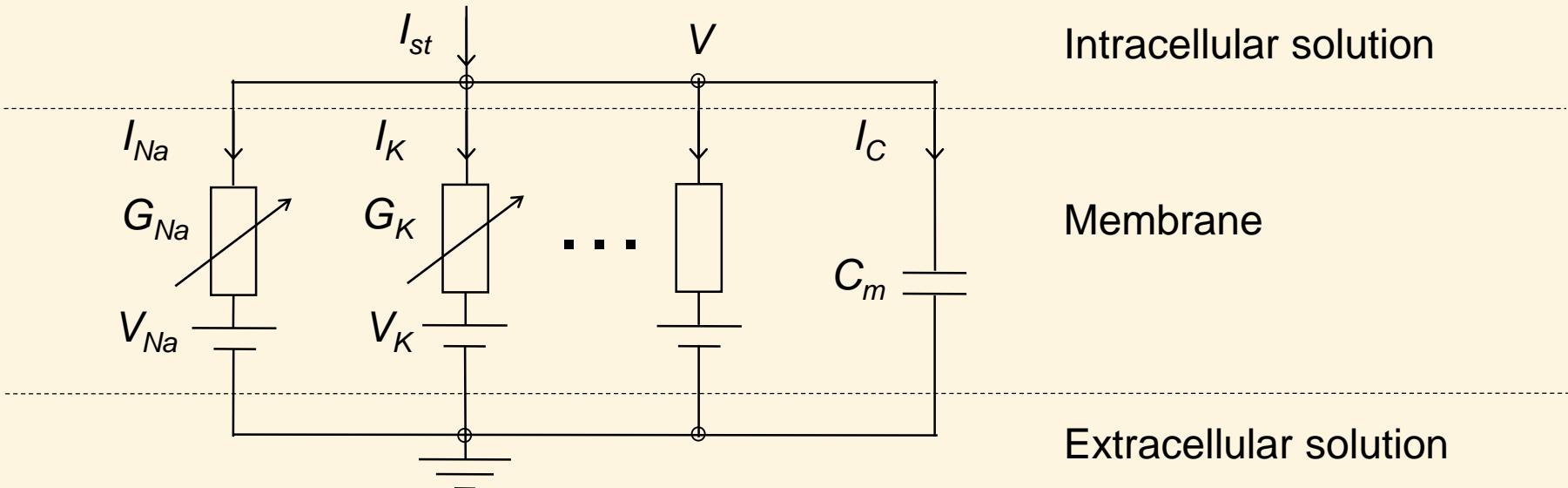
$$\frac{dV}{dt} \cdot C_m + I_{ion} = I_{st} \qquad \Rightarrow \qquad dV/dt = \left(-I_{ion} + I_{st}\right)/C_m$$

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

where e. g.:

$$I_{Na} = G_{Na} \; m^3 \; h \left(V - V_{Na}\right)$$

21 ordinary differential equations (ODE)
75 algebraic equations

Modified FitzHugh-Nagumo model
of the cardiac cell

-      using **modified FitzHugh-Nagumo** equations [16] – [20]

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

$$\frac{d\,R}{dt} = k\,e\left(\frac{\left(V_m - B\right)}{A} - R\right)$$

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)
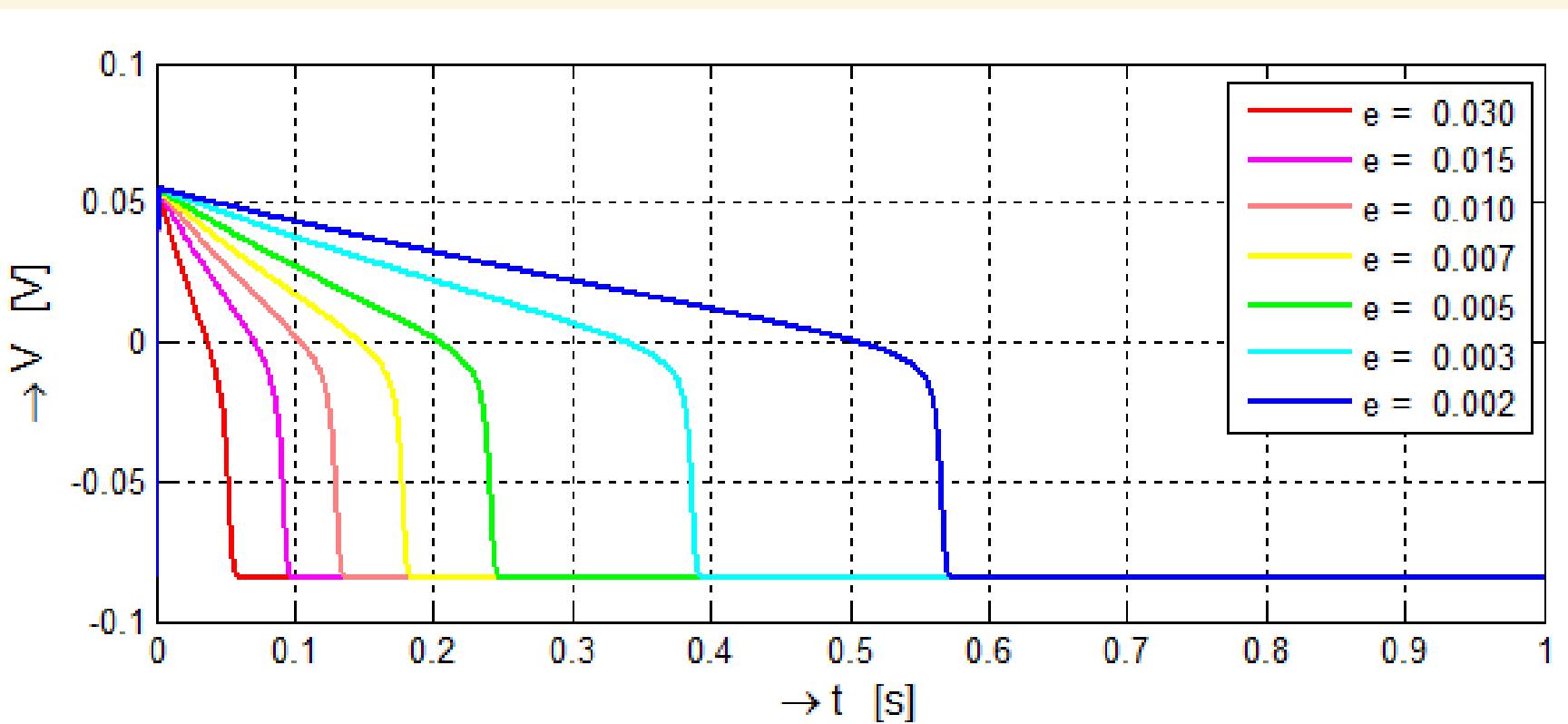
Influence of membrane parameter "e" on APD [20].

FitzHugh-Nagumo model – simulation in Matlab

Iinfluence of membrane parameters on :
- action potential amplitude (APA)
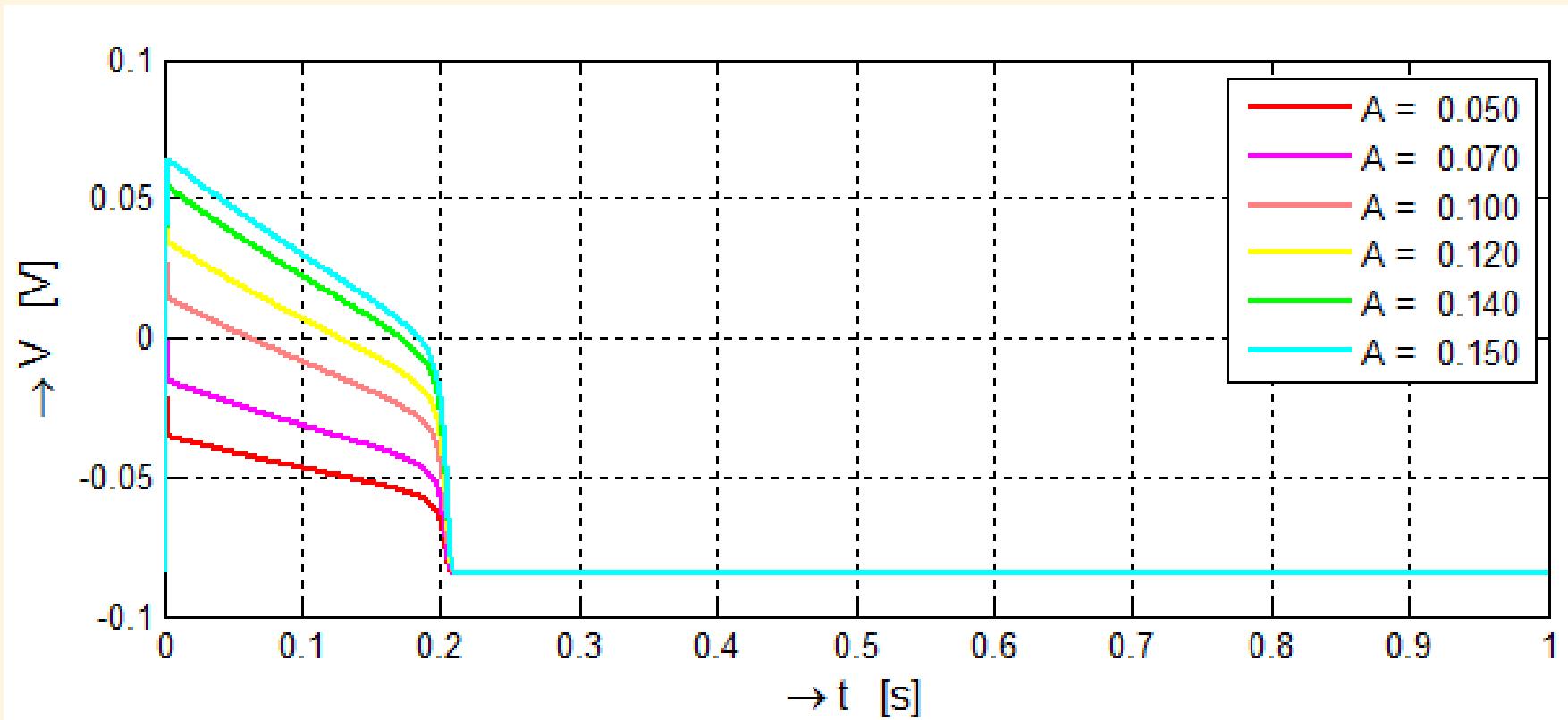
Influence of membrane parameter "A" on AP amplitude [20].

Modeling of **propagation** of electrical activation using monodomain model

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

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

where

V_m is the membrane potential,

β is the membrane surface-to-volume ratio,

C_m is the membrane capacitance per unit area,

σ 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.

Simulation parameters

- of monodomain model with modified FitzHugh-Nagumo equations:

$a = 0.13$ - relating to the excitation threshold
$e = 0.0132$ - relating to the excitability
$A = 0.120$ V   - the action potential amplitude
$B = -0.085$ V   - the resting membrane potential
$c_1 = 2.6$ - membrane-specific parameter
$c_2 = 1$ - membrane-specific parameter
$k = 1000$ s^{-1} - membrane-specific parameter
$D = 0.0005$ m^2/s - diffusivity

.

Modeling of **propagation** of electrical activation in COMSOL Multiphysics

- monodomain model for AP propagation in the heart is:

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

- 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:
$\rightarrow$ Δu Mathematics
    $\rightarrow$ Δu PDE Interfaces
        $\rightarrow$ Δu General Form PDE (g)

Modeling in COMSOL Multiphysics

General Form PDE (g)
in COMSOL Multiphysics:

Mathematical description of
monodomain model:

Equation

Show equation assuming:

Study 1, Time Dependent

$$e_a \frac{\partial^2 \mathbf{u}}{\partial t^2} + d_a \frac{\partial \mathbf{u}}{\partial t} + \nabla \cdot \Gamma = f$$

where: $u \rightarrow V_m$

$$e_a = 0$$

$$d_a = 1$$

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

$-\Gamma$

f

$$i_{ion} = \frac{I_{ion}}{C_m}$$

Modeling geometry of heart – 2D

SA node
– origin of excitation

Atria

Bundle of His

Bundle branches

Mid-myocard

AV node

Purkinje fibers

Epicard
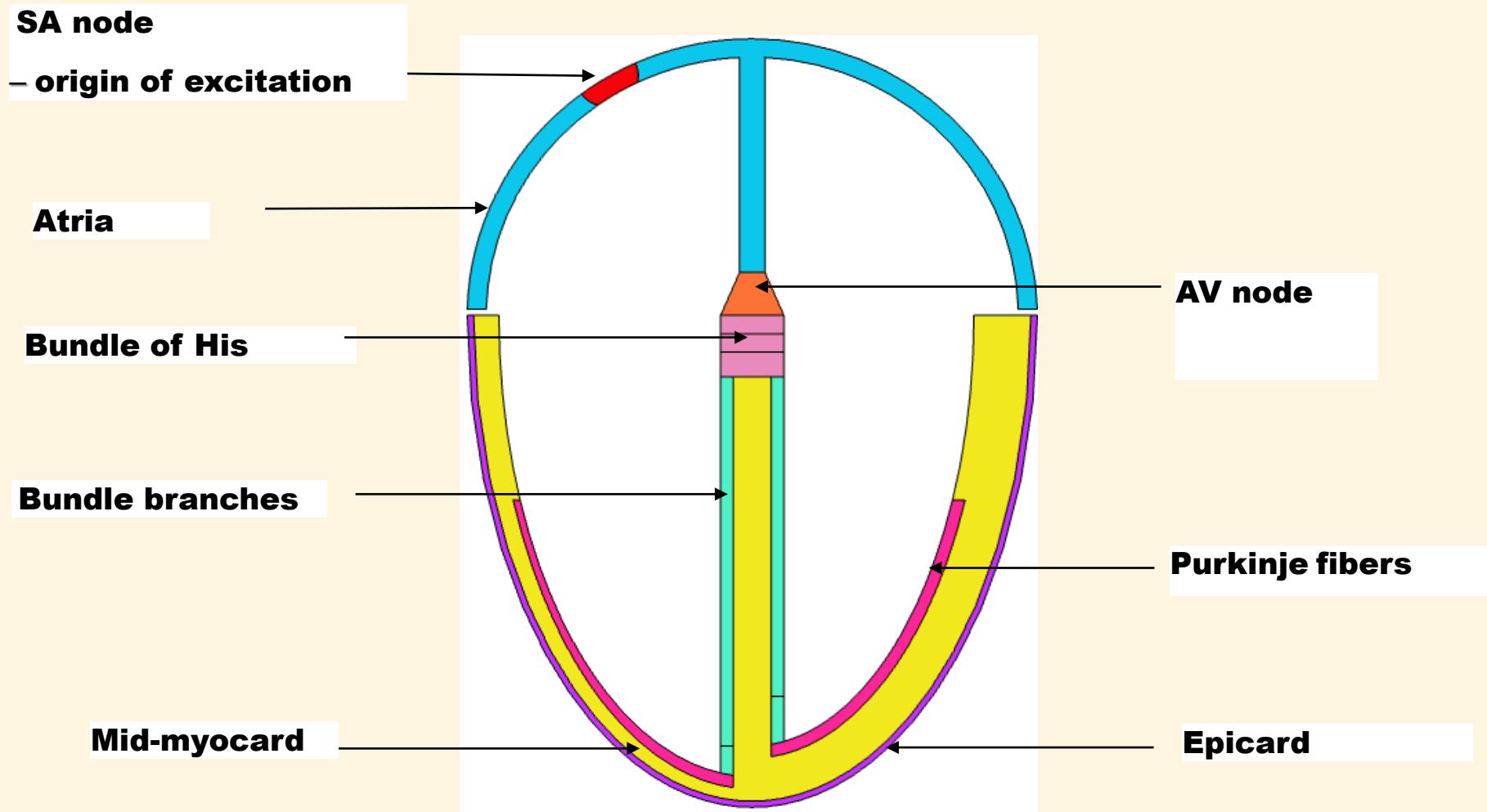
Modeling isolated edges

Union :
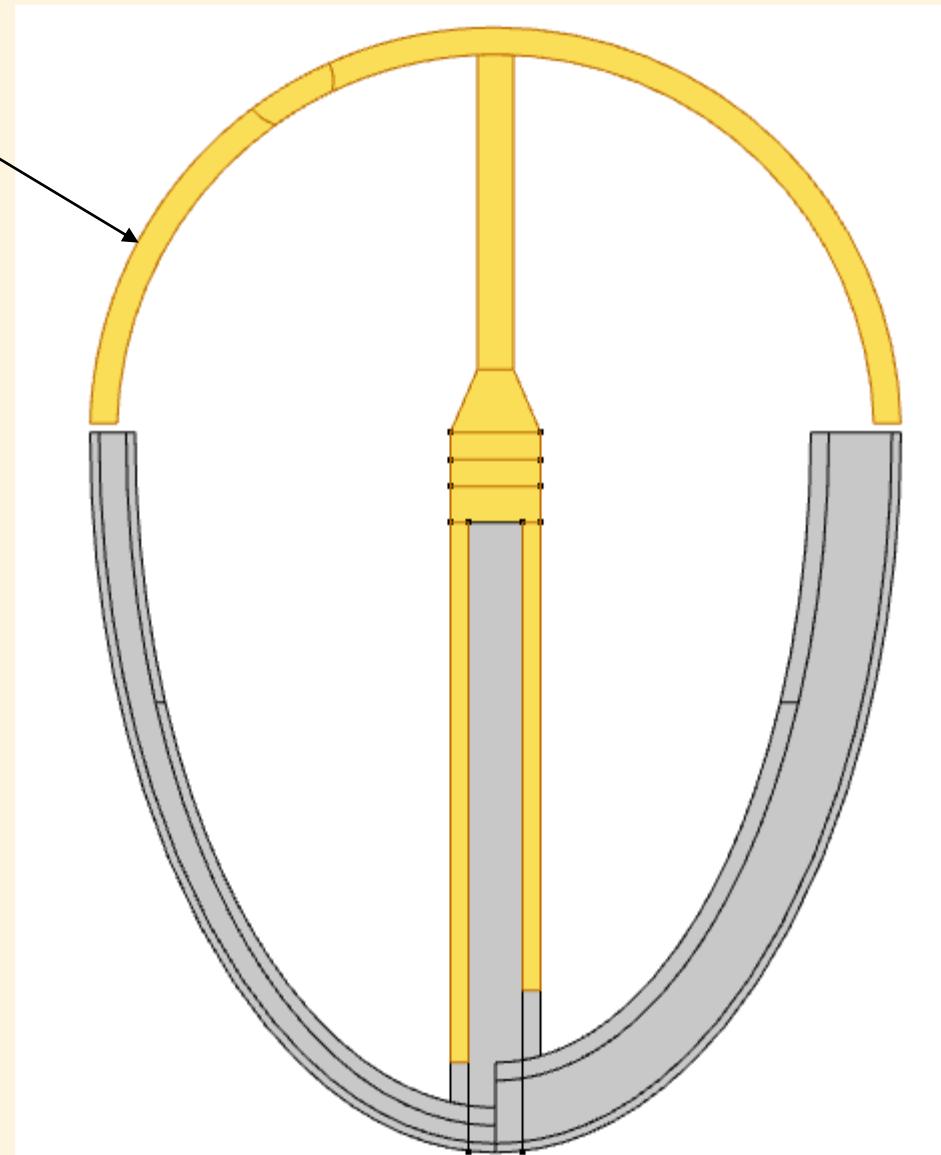
Contact Pair 1 *(p1)*
Identity Boundary Pair 2 *(ap2)*
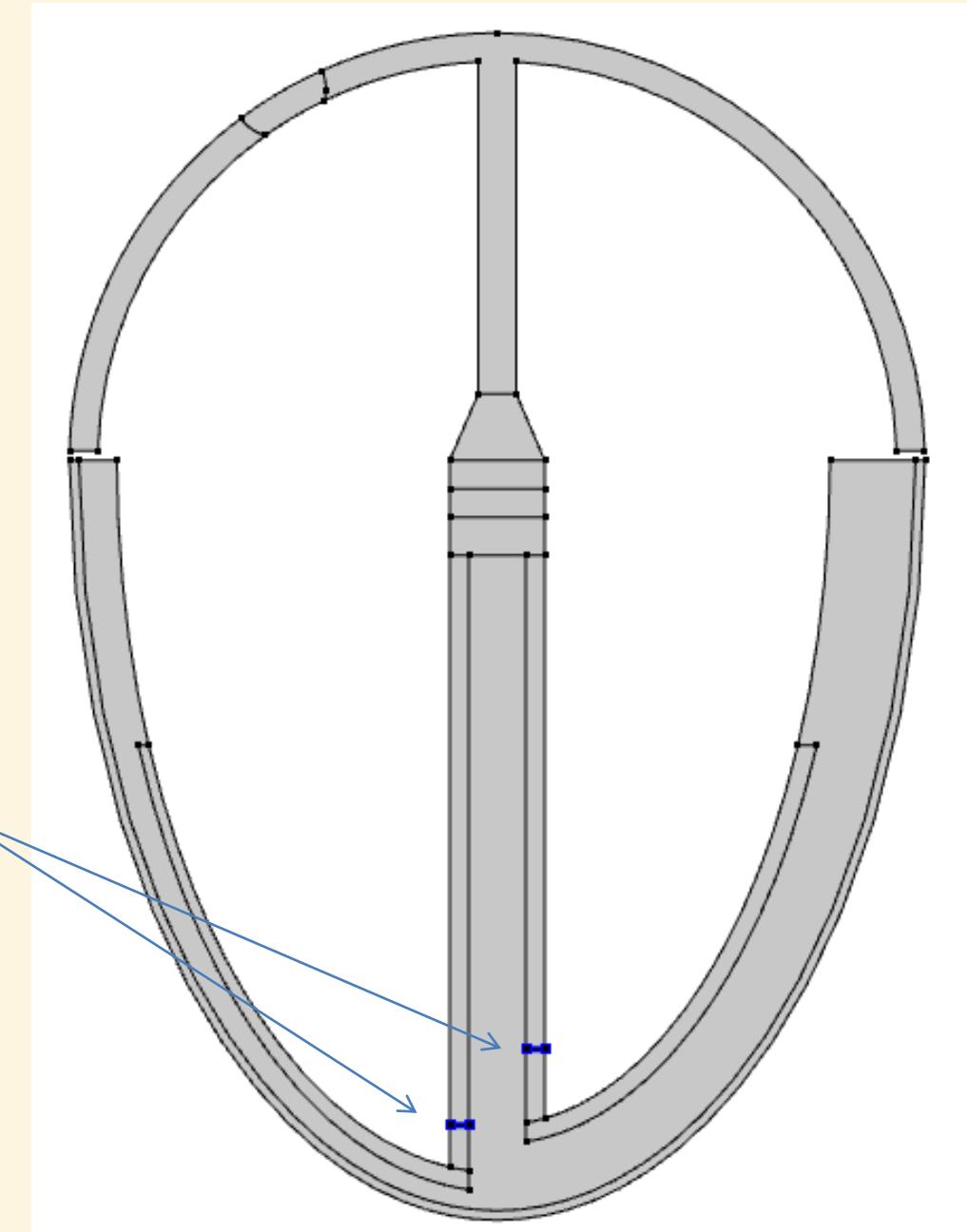
Propagation of AP – simulation results
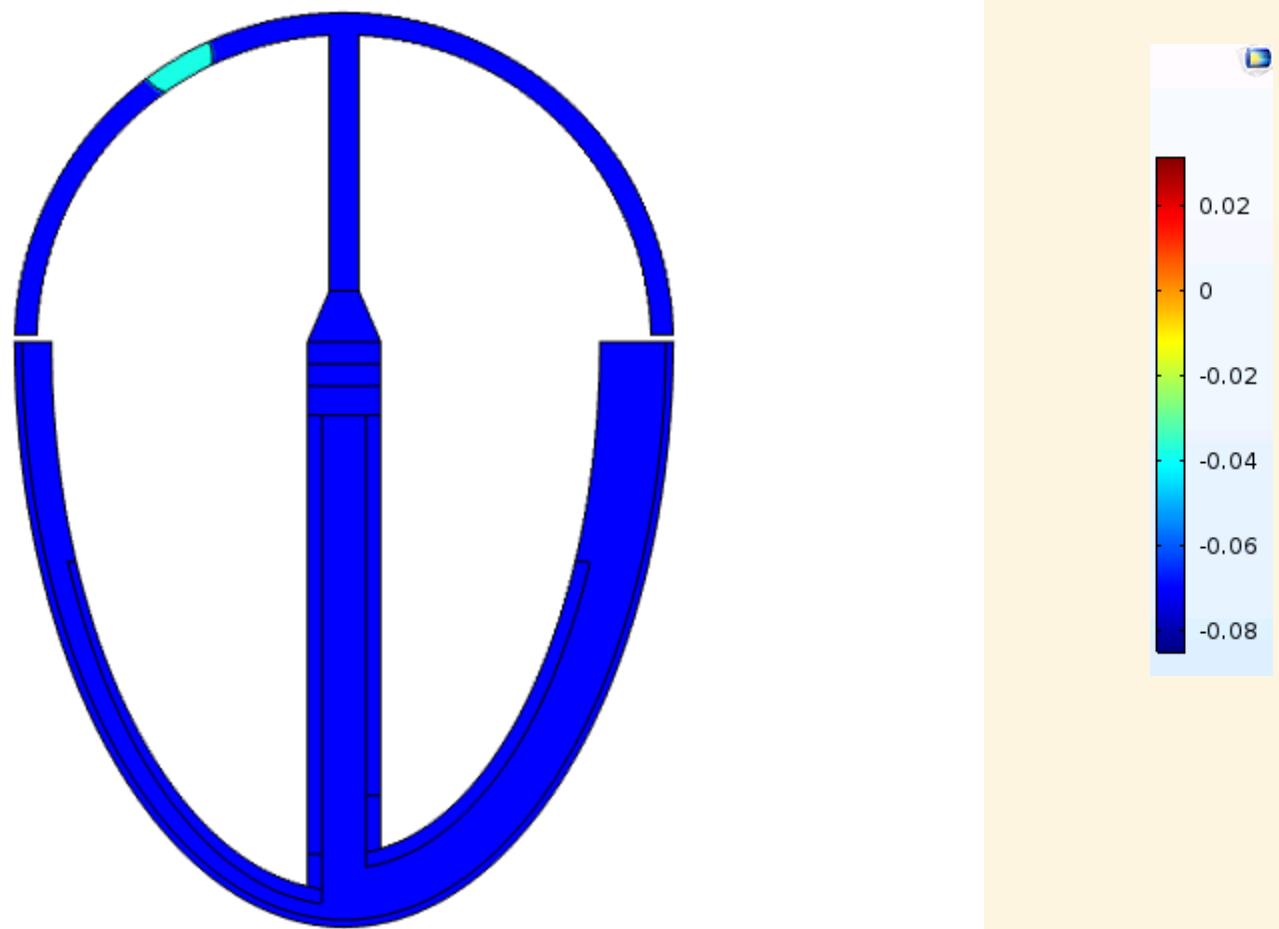
Membrane potential [V] in the 2D model.

Conclusion

Simulation of electrical activity (**AP**) **propagation** in **different heart tissues** of 2D monodomain model with FitzHugh-Nagumo equations

       - partial differential equations (PDE)

       - numerical solution in **Comsol Multiphysics**.

THANK YOU FOR YOUR ATTENTION!

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