Influence of periodic diffusive inclusions on the bidomain model

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Introduction

We present a new mathematical model of the electric activity of the heart. The main **drawback of the standard bidomain model** is that it assumes the existence of excitable cells (myocytes) everywhere in the heart, while it is known that there exist non-small regions where non-excitable cells (fibroblasts and collagen) take place. The problems that we are trying to address with our model are:

- The **laminar structure** of the myocardium that shows the presence of collagen, especially between muscle layers. See Fig 1. [2, 3]. In the diseased tissue the diffusion space plays an important role.

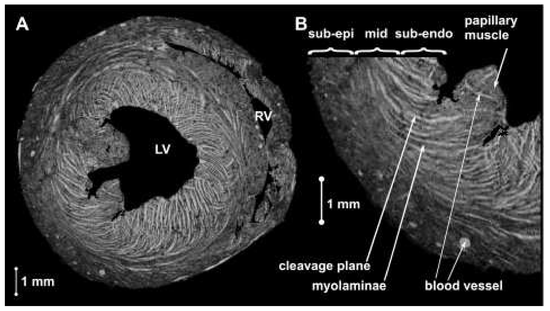


Figure 1: The laminar structure of myocardium. [3]

- The **infarct border zone**. After infarction in the heart some number of myocytes die and they are replaced by collagen and a few cells of fibroblasts. We consider that there are no cells of fibroblasts in the extracellular space.

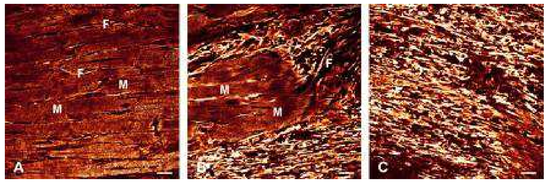


Figure 2: Fibroblast organization in sheep: normal ventricular myocardium (A), infarct border zone (B) and centre (C), 1 week after infarction. [4]

I - Mesoscopic model

Modelling assumptions:

- Periodic distribution of added extracellular space
- Extracellular space is a passive conductor

The domain Ω is split into two regions B_ε and D_ε:

- B_ε represents the bidomain layer.
  - intra- and extra-cellular conductivities σ_ε^i and σ_ε^e
  - unknown potentials u_ε^i and u_ε^e
  - define $v_\varepsilon := u_\varepsilon^i - u_\varepsilon^e$
- D_ε represents the diffusive inclusions.
  - conductivity σ_ε^d
  - unknown potential u_ε^d
- $\Sigma_\varepsilon = \partial B_\varepsilon \cap \partial D_\varepsilon$ is the interface.

The bidomain model

$$\begin{aligned} \partial_t v_\varepsilon + c v_\varepsilon &= \nabla\cdot(\sigma_\varepsilon^i \nabla u_\varepsilon^i), && \text{in } B_\varepsilon,\\ \partial_t v_\varepsilon + c v_\varepsilon &= -\nabla\cdot(\sigma_\varepsilon^e \nabla u_\varepsilon^e), && \text{in } B_\varepsilon. \end{aligned}$$

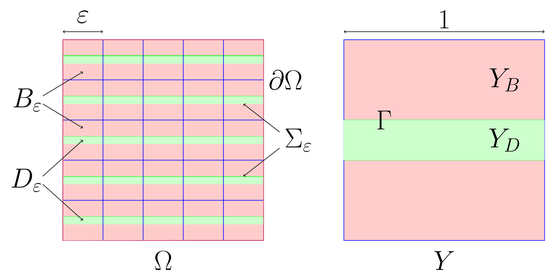
The diffusive inclusion

$$0 = -\nabla\cdot(\sigma_\varepsilon^d \nabla u_\varepsilon^d), \qquad \text{in } D_\varepsilon.$$

The transmission conditions

$$\left.\begin{aligned} \sigma_\varepsilon^i \nabla u_\varepsilon^i\cdot\mathbf{n}_{\Sigma_\varepsilon} &= 0,\\ \sigma_\varepsilon^e \nabla u_\varepsilon^e\cdot\mathbf{n}_{\Sigma_\varepsilon} &= \sigma_\varepsilon^d \nabla u_\varepsilon^d\cdot\mathbf{n}_{\Sigma_\varepsilon},\\ u_\varepsilon^e &= u_\varepsilon^d, \end{aligned}\right\} \qquad \text{on } \Sigma_\varepsilon,$$

The initial and the boundary conditions are given.



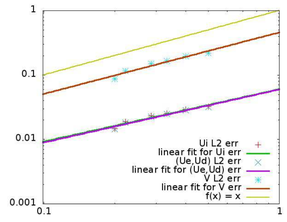
II - Homogenisation

Heuristics: Redefine the problem in two scales and obtain the limit problem that depends only on the large scale variable. It gives a global, macroscopic behaviour of the unknown functions. Assume

$$\sigma_\varepsilon^i(x) = \sigma_i\left(\frac{x}{\varepsilon}\right), \quad \sigma_\varepsilon^e(x) = \sigma_e\left(\frac{x}{\varepsilon}\right), \quad \sigma_\varepsilon^d(x) = \sigma_d\left(\frac{x}{\varepsilon}\right).$$

According to [1], *a priori* estimates ensure the two–scale convergence:

$$u_\varepsilon^i \twoheadrightarrow u_0^i, \qquad (u_\varepsilon^e, u_\varepsilon^d) \twoheadrightarrow u_0.$$



III - Macroscopic equations

The limit problem is still **a bidomain model** with updated conductivities:

$$\begin{aligned} \nabla\cdot(\tilde\sigma_i \nabla u_0^i) &= \partial_t v_0 + c v_0, \text{ in } \Omega,\\ \nabla\cdot((\tilde\sigma_e + \tilde\sigma_d)\nabla u_0) &= -(\partial_t v_0 + c v_0), \text{ in } \Omega, \end{aligned}$$

$$\tilde\sigma_i = \sigma_i + \frac{1}{|Y_B|}A_i, \qquad \tilde\sigma_e = \sigma_e + \frac{1}{|Y_B|}A_e, \qquad \tilde\sigma_d = \frac{|Y_D|}{|Y_B|}\sigma_d + \frac{1}{|Y_B|}A_d,$$

where A_i, A_e and A_d are constant matrices that depend on the geometry of the unit cell.

Remark:

- The modified conductivities depend on the volume fraction of the diffusive part and on the geometry of the unit cell.
- If $|Y_D| = 0$ we obtain the standard bidomain model. If $|Y_B| = 0$ we get only the diffusion model.
- If $\sigma_e = \sigma_d$ the modified extracellular conductivity will not depend on the geometry but only on the volume fraction.

IV - Numerical verification on simple 2D geometries

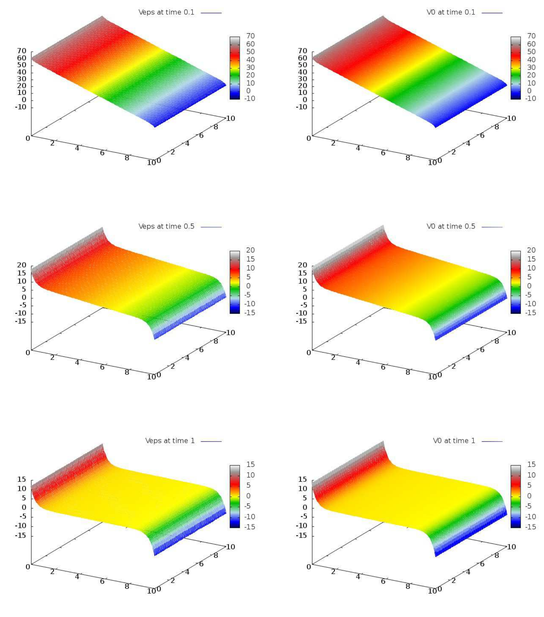


Figure 3: The time evolution for $v_\varepsilon = u_\varepsilon^i - u_\varepsilon^e, \varepsilon = 0.16$ (left). The time evolution for $v_0 = u_0^i - u_0$ (right)

Perspectives

- Apply the ionic current model.
- Use real data, *e.g.* the late enhancement MRI provides the volume fraction of the extracellular space.

References

[1] Allaire, *Homogenisation and two–scale convergence*, 1992.

[2] Hooks *et al.*, *Laminar Arrangement of Ventricular Myocytes Influences Electrical Behavior of the Heart*, 2007.

[3] Gilbert *et al.*, *Visualization and quantification of whole rat heart laminar structure using high-spatial resolution contrast-enhanced MRI*, 2012.

[4] Camelliti *et al.*, *Structural and functional characterisation of cardiac fibroblasts*, 2005.