Existence and uniqueness for the specialized conduction system/myocardium coupled problem in cardiology.

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Abstract. The Purkinje network is the rapid conduction system in the heart. It ensures the physiological spread of the electrical wave in the ventricles. From the mathematical viewpoint the model is made up of a degenerate parabolic reaction diffusion system coupled with an ODE system. We derive existence, uniqueness and some regularity results.

Keywords: Cardiac electrophysiology · reaction-diffusion · Purkinje network · myocardium · monodomain model · coupling problem.

1 Intoduction

The excitation of the cardiac cells starts at the sinoatrial node where pacemaker cells generate an electrical current. This current propagates to the right atria then to the left atria through the Bachmanns bundle.
The electrical wave does not propagate directly to the ventricle since the interface between the atria and ventricles is insolating. Only the atrioventricular node allows the propagation of this wave to the ventricles. Then the electrical wave follows the His bundle which is a rapid conductive system that ends in the Purkinje fibers directly connected to the ventricular cells. This rapid conduction system is electrically insulated from the heart muscle except at the endpoints that are connected to the myocardium in an area called Purkinje Muscle Junctions (PMJ).
In the present work, we consider the coupling conditions derived in [1] where the myocardium and Purkinje electrical activities are represented by the monodomain model and are coupled using source terms and Robin boundary conditions. Our main result in this paper is the existence and the uniqueness of the solution for the coupled problem.

2 Modelling

Let us denote by $\Omega \subset \mathbb{R}^3$ the myocardium domain, Λ stands for the Purkinje network domain. We suppose that we have N_{ter} terminals in the Purkinje network $(x_1; :::; x_{N_{ter}})$. Each terminal of the Purkinje is coupled to the myocardium in a small subdomain $\Omega_i \subset \Omega$ called a Purkinje muscle junction (PMJ) (see Figure 1).

We also consider that the Purkinje network Λ is made of a set of disjoint branches

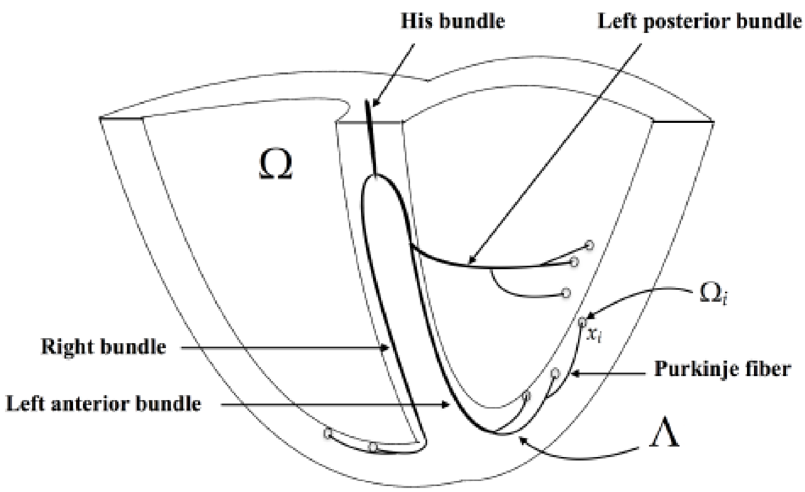

Fig. 1. Schematic representation of the 1D/3D coupled problem domains:Λ represents the Purkinje fiber and Hiss, right and left bundles,Ω represents the myocardium and Ω_i is the coupling zone between the Purkinje end node (x_i) and the myocardium.

$\{\Lambda_i\}_{i=1}^{N_{bran}}$, where $\Lambda = \cup_{i=1}^{N_{bran}} \{\Lambda_i\}_i$ and N_{bran} is the number of branches. The boundary of each branch is either a terminal point or a branching node. Lets consider $(y_1, y_2, \cdots, y_{p_{bran}})$ the set of the Purkinje branching nodes. Each of the branching nodes y_j is a boundary of a set of branches, we denote by I_j the set of these branches indices.

We denote by V the transmembrane voltage in the myocardium and V_p the transmembrane voltage in the Purkinje network. Since the use of finite element method on a tree-shaped 1D geometry is not standard, we need to distinguish the derivative of V_p at the boundary of each branch. For any branching node y_j, $j = 1; :::; p_{bran}$ and for any $k \in I_j$, we denote by $\partial_{x,k} V_p(y_j)$ the derivative V_p on the point y_j seen as the boundary of the branch Λ_k.

$$\partial_{x,k} V_p(y_j) = \lim_{\substack{y \to y_j \\ y \in \Lambda_k}} \partial_x V_p(y)$$

where ∂_x is the tangential derivative a long the Purkinje branch. Following this definition, the Kirchhoff law on the branching nodes reads as follows

$$\sum_{k\in I_j} \sigma_p \partial_{x,k} V_p(y_j) = 0 \qquad \forall j = 1, \cdots, p^{bran}$$

2.1 PDE model

In the space/time domain $\Omega \times [0;T]$, the electrical wave is governed by the monodomain model [1]: a non-linear reaction diffusion equation and a dynamic system modelling the cellular ionic currents

$$\begin{cases} A(C\partial_t V + I_{ion}(V,W)) = div(\sigma \nabla V) + AI_{app}, \ \ in \ \Omega \times [0,T], \\ \\ \partial_t W + g(V,W) = 0, \quad in \ \Omega \times [0,T], \end{cases} \tag{1}$$

Also, the heart is assumed to be isolated, therefore homogeneous Neumann boundary conditions are assigned on $\partial\Omega \times [0,T]$

$$\sigma \nabla V.\mathbf{n} = 0,$$

The electrical wave in the Purkinje system is also governed by the monodomain equation

$$\begin{cases} A_p(C\partial_t V_p + I_{ion,p}(V_p,W_p)) = div(\sigma_p \nabla V_p) + A_p I_{app,p}, \ \ in \ \Lambda \times [0,T], \\ \\ \sum_{k\in I_j} \sigma_p \partial_{x,k} V_p(y_i) = 0, \qquad \forall j = 1, \cdots, p^{bran} \\ \\ \partial_t W_p + g_p(V_p,W_p) = 0, \quad in \ \Lambda \times [0,T], \end{cases} \tag{2}$$

The Purkinje system is insulated at (x_1), the location of the atrioventricular node then we have:

$$\sigma_p \partial_x V_p(x) = 0, \qquad for \ x = x_1 \ on \ [0,T]$$

We complete the systems (1)-(2) by assigning the initial Cauchy condition:

$$V(0,.) = V_0, \qquad W(0,.) = W_0, \quad in \ \Omega$$

$$V_p(0,.) = V_{p,0}, \qquad W_p(0,.) = W_{p,0}, \quad in \ \Lambda$$

In the myocardium Ω (respectively Purkinje network Λ), constant A (respectively, A_p) represents the surface of membrane per unit of volume, C (respectively, C_p) is the capacitance of the cell membrane, I_{app} (respectively, $I_{app,p}$) the applied current, I_{ion} (respectively, $I_{ion,p}$) is the total ionic current,W (respectively,W_p) represents the ionic model state variables it could include concentrations of different ionic entities and gating variable. In this study, the dynamics of W, W_p, I_{ion} and $I_{ion,p}$ are described by phenomenological two state-variable models introduced that will be presented bellow. Electrical conductivities in bothdomains are given σ in the myocardium and σ_p in the Purkinje network. At the heart boundary, $\mathbf{n}$ stands for the outward unit normal on

$\partial\Omega$.
Following [1], the source current $\sum_{i=2}^{N_{ter}} s_i$ flowing from the Purkinje system to the myocardium represents the electrical effect of Purkinje on the myocardium, the counter effect is given by a robin boundary condition as follows

$$\begin{cases} \sigma_p(x_i)\partial_{x_i}V_p(x_i) = \frac{c_p}{S_p}(\langle V\rangle_i - V_p(x_i)) \quad for\ i = 2, \cdots, N_{ter}, \\ \\ s_i(x) = \begin{cases} s_i := \frac{s_p}{|\Omega_i|}\sigma_p(x_i)\partial_{x_i}V_p(x_i) & if x \in \Omega_i, \\ 0 & else \end{cases} \quad for\ i = 2, \cdots, N_{ter}, \end{cases} \tag{3}$$

Where

$$\langle V\rangle_i = \frac{1}{\Omega_i}\int_{\Omega_i} V, \quad for\ i = 1, \cdots, N_{ter},$$

c_p the conductance of the PMJ, S_p the surface of membrane of the Purkinje cells in Ω_i.

In order to complete the model, we need a description of the ionic current I_{ion} and $I_{ion,p}$.

The ionic current
In this work we assume that the ionic current

$$\begin{aligned} I_{ion} : \mathbb{R} \times \mathbb{R}^l \times (0, +\infty)^m &\longrightarrow \mathbb{R} \\ (V, W) &\longmapsto I_{ion}(V, W) \end{aligned}$$

where $W = (w, z) \in \mathbb{R}^l \times (0, +\infty)^m$ has the general form:

$$I_{ion}(V, W) = I_{ion}(V, w, z) = \sum_{j=1}^{m}(J_j(V, w, logz_j)) + \widetilde{H}(V, w, z) \tag{4}$$

where $\forall j = 1, \cdots, m$

$$J_j(V, w, logz_j) \in C^1(\mathbb{R} \times \mathbb{R}^l \times \mathbb{R}),$$

$$0 < \underline{G}(w) \leq \frac{\partial}{\partial\xi}J_j(V, w, \xi) \leq \overline{G}(w),$$

and

$$|\frac{\partial}{\partial V}J_j(V, w, 0)| \leq L_V(w)$$

$\underline{G}$, $\overline{G}$, L_V belong to $C^0(\mathbb{R}^k, \mathbb{R}_+)$
and $\widetilde{H} \in C^0(\mathbb{R} \times \mathbb{R}^l \times (0, +\infty)^m) \cap Lip(\mathbb{R} \times [0, 1]^k \times (0, +\infty)^m)$.

The dynamics of the gating variables are described by the system of ODE's:
By noting $\varphi = (V, V_p)$ et $\psi = (W, W_p)$ checking:

$$\frac{\partial\psi_j}{\partial t} = F_j(\varphi, \psi_j), \qquad j = 1, \cdots, k \tag{5}$$

With $F_j(\varphi, \psi_j) = (g_j(V, W); g_{p,j}(V_p; W_p))$.
We assume that

$$F_j : \mathbb{R}^4 \longmapsto \mathbb{R} \quad est\ localement\ lipschitzienne, \qquad \forall\ j = 1, \cdots, k \tag{6}$$

In the models considered F_j has the particular form

$$F_j(\varphi, \psi_j) = \alpha_j(\varphi)(1 - \psi_j) - \beta_j(\varphi)\psi_j \tag{7}$$

where α_j and β_j are positive rational functions of exponentials in φ. A general expression for both α_j and β_j is given by

$$\frac{C_1 \exp^{\frac{\varphi-\varphi_n}{C_2}} + C_3(\varphi - \varphi_n)}{1 + C_4 \exp^{\frac{\varphi-\varphi_n}{C_5}}}$$

where C_1, C_3, C_4 , φ_n are non-negative constants and C_2 , C_5 are positive constants.

The formal statement of the macroscopic model is then:

Problem (M)

$$\begin{cases} A(C\partial_t V + I_{ion}(V,W)) + \sum_{i=2}^{N_{ter}} s_i = div(\sigma \nabla V) + A I_{app}, \ \ dans \ \Omega \times [0,T], \\ A_p(C\partial_t V_p + I_{ion,p}(V_p, W_p)) = div(\sigma_p \nabla V_p) + A_p I_{app,p}, \qquad dans \ \Lambda \times [0,T], \\ \sigma \nabla V.\mathbf{n} = 0, \qquad sur \ \ \partial\Omega \times [0,T] \\ \sum_{k \in I_j} \sigma_p \partial_{x,k} V_p(y_i) = 0, \qquad \forall j = 1, \cdots, p^{bran} \\ \partial_t W + g(V,W) = 0, \qquad dans \ \Omega \times [0,T], \\ \partial_t W_p + g_p(V_p, W_p) = 0, \qquad dans \ \Lambda \times [0,T], \end{cases} \tag{8}$$

3 Existence and uniqueness

We can now state our main result concerning the existence of a variational solution for Problem (M).

Theorem 1. *Assume that Ω, Λ is of class $C^{1,1}$,*
(σ, σ_p) are Lipschitz in $\Omega \times \Lambda$,
Let be given the data

$$(V_0, V_{p,0}) \in H^2(\Omega) \times H^2(\Lambda)$$

$$W_0 : \Omega \longmapsto [0,1]^k, \quad measurable;$$

$$W_{p,0} : \Lambda \longmapsto [0,1]^k, \quad measurable;$$

$$(I_{app}, I_{app,p}) \in L^p(0,T; L^2(\Omega) \times L^2(\Lambda)), \qquad for \ p > 4$$

Let be given the ionic currents I_{ion} et $I_{ion,p}$ satisfying (4) the dynamics of the gating variables $g(V,W); g_p(V_p; W_p)$ satisfying (5)-(7)

Then, there exists a unique solution of Problem (M) satisfying

$$(V, V_p) \in W^{1,p}(0,T; L^2(\Omega)\times L^2(\Lambda))\cap L^p(0,T; H^2(\Omega)\times H^2(\Lambda))\cap C^0([0,T]; C^0(\Omega)\times C^0(\Lambda))$$
$$(W, W_p) : \Omega \times \Lambda \times [0,T] \longmapsto [0,1]^k \times [0,1]^k$$

with $(w_j, w_{p,j})(x,.) \in (C^1(0,T) \cap C^0([0,T]))^2$ *for all* $x \in \Omega \times \Lambda$ *et* $j = 1, \cdots, k$

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