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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 Bachmann's 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 , uniqueness and some results of regularity of the solution for the coupled problem Purkinje/myocardium.

2 Presentation of the mathematical model

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 $(x_1; \ldots; x_{Nter})$.
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 1.1).
We also consider that the Purkinje network Λ is made of a set of disjoint branches $\{\Lambda_i\}_{i=1}^{N_{bran}}$, 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.
Let's 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.

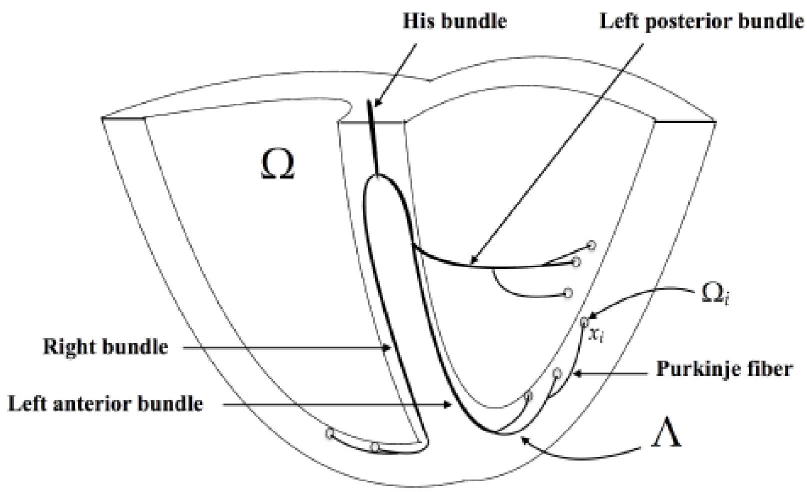

Fig. 1. Schematic representation of the 1D/3D coupled problem domains: Λ represents the Purkinje fiber and Hiss, right and left bundles,Ω_i represents the myocardium and Ω_i is the coupling zone between the Purkinje end node (x_i) and the myocardium.

2.1 The coupling EDP

The depolarization wave in the myocardium for a single domain model is governed by a non-linear reaction-diffusion equation and a dynamic system modelling the cellular ionic currents:

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

We consider that the heart is assumed isolated, so a Neumann boundaries condition is taken into account:

$$\sigma\nabla V.\mathbf{n} = 0,\qquad on\ \ \partial\Omega\times[0,T]$$

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

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

Thus, the rapid conduction system is supposed isolated in a point noted (x_1) who repesent the location of atrioventricular node , then we have:

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

And initial conditions for both systems (1)-(2) are defined as follows

$$V(0,.) = V_0,\qquad W(0,.) = W_0,\qquad Z(0,.) = Z_0,\ \ in\ \Omega$$
$$V_p(0,.) = V_{p,0},\qquad W_p(0,.) = W_{p,0},\qquad Z_p(0,.) = Z_{p,0},\ \ in\ \Lambda$$

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 gating variable, Z and Z_p are the ionic intracellular concentration variables and g (resp. g_p) represent a function field having the same dimension as W (resp. W_p). Electrical conductivities in both domains are given σ in the myocardium and σ_p in the Purkinje network. At the heart boundary, n stands for the outward unit normal on $\partial\Omega$.

To couple the equations (1)-(2) , we need 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 opposite 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 $I_{ion,p}$.

2.2 The ionic current

We assume that the ionic current

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

has the general form both in the myocardium and the Purkinje network:

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

$(W_i)_{i=1,\cdots,k}$ represent the gating variables and $(Z_j)_{j=1,\cdots,m}$ represent the ionic concentration variables.
We will assume that:

$$\widetilde{H} \in C^2(\mathbb{R}\times\mathbb{R}^k\times(0,+\infty)^m) \cap Lip(\mathbb{R}\times[0,1]^k\times(0,+\infty)^m) \tag{5}$$

. and

$$J_j \in C^2(\mathbb{R}\times\mathbb{R}^k\times\mathbb{R}), \qquad \forall j = 1,\cdots,m \tag{6}$$

and there exist three functions $\underline{G}(W), \overline{G}(W), L_V$ belong to $C^1(\mathbb{R}^k,\mathbb{R}+)$ such that :

$$0 < \underline{G}(W) \leq \frac{\partial}{\partial\xi}J_j(V,W,\xi) \leq \overline{G}(W), \tag{7}$$

and

$$|\frac{\partial}{\partial V}J_j(V,W,0)| \leq L_V(W) \tag{8}$$

2.3 The dynamics of the gating variables

The dynamic of the gating variables are described by a system of an ordinary differential equation (ODE) :

$$\frac{\partial W_j}{\partial t} = g_j(V, W_j), \qquad j = 1, \cdots, k. \tag{9}$$

Where

$$g_j : \mathbb{R}^2 \longmapsto \mathbb{R} \quad \textit{is a locally Lipschitz function}, \qquad j = 1, \cdots, k \tag{10}$$

In the models considered g_j has the particular form

$$g_j(V, W_j) = \alpha_j(V)(1 - W_j) - \beta_j(V)W_j \tag{11}$$

where α_j and β_j are positive rational functions of exponentials in V.

A general expression for both α_j and β_j is given by

$$\frac{C_1 \exp^{\frac{V-V_n}{C_2}} + C_3(V - V_n)}{1 + C_4 \exp^{\frac{V-V_n}{C_5}}} \tag{12}$$

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

We will take the same model of ODE in the Purkinje network:

$$\frac{\partial W_{p,j}}{\partial t} = g_{p,j}(Vp, W_{p,j}), \qquad j = 1, \cdots, k \tag{13}$$

with $g_{p,j}$ given by (11)-(12)

2.4 The dynamics of the ionic concentrations

The dynamic of the ionic concentration are described by the following system of an ordinary differential equation (ODE)

$$\frac{\partial Z_i}{\partial t} = f_i(V, W, Z_i) = -J_i(V, W, Z_i) + H_i(V, W, Z), \qquad i = 1, \cdots, m. \tag{14}$$

Where J_i the function as described in (6)-(8) and

$$H_i \in C^2(\mathbb{R} \times \mathbb{R}^k \times (0, +\infty)) \cap Lip(\mathbb{R} \times [0, 1]^k \times (0, +\infty)). \tag{15}$$

2.5 The final model

The formal statement of the macroscopic model is:

Problem (M)

$$
\begin{cases}
A(C\partial_t V + I_{ion}(V,W,Z)) + \sum_{i=2}^{N_{ter}} s_i = div(\sigma\nabla V) + AI_{app}, \ in \ \Omega \times [0,T], \\
A_p(C\partial_t V_p + I_{ion,p}(V_p,W_p,Z_p)) = div(\sigma_p \nabla V_p) + A_p I_{app,p}, \quad in \ \Lambda \times [0,T], \\
\sigma \nabla V.\mathbf{n} = 0, \quad on \ \ \partial\Omega \times [0,T] \\
\sum_{k\in I_j} \sigma_p \partial_{x,k} V_p(y_i) = 0, \quad \forall j = 1, \cdots, p^{bran} \\
\sigma_p \partial_x V_p(x) = 0, \quad for \ x = x_1 \ on \ [0,T] \\
\partial_t W + g(V,W) = 0, \quad in \ \Omega \times [0,T], \\
\partial_t W_p + g_p(V_p, W_p) = 0, \quad in \ \Lambda \times [0,T], \\
\partial_t Z + f(V,W,Z) = 0, \quad in \ \Omega \times [0,T], \\
\partial_t Z_p + f_p(V_p,W_p,Z_p) = 0, \quad in \ \Lambda \times [0,T], \\
V(0,.) = V_0, \quad W(0,.) = W_0, \quad Z(0,.) = Z_0, \ \ in \ \Omega, \\
V_p(0,.) = V_{p,0}, \quad W_p(0,.) = W_{p,0}, \quad Z_p(0,.) = Z_{p,0}, \ \ in \ \Lambda
\end{cases}
\tag{16}
$$

3 Existence and uniqueness

As the one-dimensional domain Λ is non regular, we define the space H^1 with bifurcations by

$$H^1(\Lambda) = \bigcup_{i=1}^{N^{bran}} H^1(\Lambda_i) \bigcap C^0(\Lambda)$$

It is understood that each integral over Λ is given by the integral over $\bigcup_{i=1}^{N^{bran}} \Lambda_i$. Each branch is considered separately and integration by parts are applied separately. It is the same for the definition of $H^2(\Lambda)$:

$$H^2(\Lambda) = \{V \in C^0(\Lambda), V_{/\Lambda_i} \in H^2(\Lambda_i), \quad i = 1, \cdots, N^{bran}\}$$

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

Theorem 1. *We assume that Ω is of class $C^{1,1}$ and that σ and σ_p are respectively Lipschitz in Ω and Λ .*
Let be given the data

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

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

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

$$Z_0 \in \left(L^2(\Omega)\right)^m \quad with \;\; logZ_0 \in \left(L^2(\Omega)\right)^m$$

$$Z_{p,0} \in \left(L^2(\mathit{\Lambda})\right)^m \quad with \;\; logZ_{p,0} \in \left(L^2(\mathit{\Lambda})\right)^m$$

$$(I_{app}, I_{app,p}) \in L^p(0,T; L^2(\Omega) \times L^2(\mathit{\Lambda})), \quad for\ p > 4 \tag{17}$$

Let be given the ionic currents I_{ion} et $I_{ion,p}$ satisfying (4) with there regularity (5)-(8), the dynamics of the gating variables $g(V,W)$, $g_p(V_p,W_p)$ satisfying (10)-(11) and the dynamic of the ionic concentrations $f(V,W,Z)$, $f_p(V_p,W_p,Z_p)$ satisfing (14)-(15)

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

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

$W : \Omega \times [0,T] \longmapsto [0,1]^k$, $Z : \Omega \times [0,T] \longmapsto (0,+\infty)^m$ *measurable,*

$W_p : \mathit{\Lambda} \times [0,T] \longmapsto [0,1]^k$, $Z_p : \mathit{\Lambda} \times [0,T] \longmapsto (0,+\infty)^m$ *measurable,*

with $w_j(x,.) \in (C^1(0,T) \cap C^0([0,T]))$ *for a.e* $x \in \Omega$ *and* $j = 1,\cdots,k$,
$w_{p,j}(x,.) \in (C^1(0,T) \cap C^0([0,T]))$ *for a.e* $x \in \mathit{\Lambda}$ *and* $j = 1,\cdots,k$,
$z_i(x,.) \in C^1(0,T) \cap C^0([0,T])$ *for a.e* $x \in \Omega$ *and* $i = 1,\cdots,m$,
$z_{p,i}(x,.) \in C^1(0,T) \cap C^0([0,T])$ *for a.e* $x \in \mathit{\Lambda}$ *and* $i = 1,\cdots,m$,

$$Z \in H^1(0,T; L^2(\Omega))^m \cap L^\infty(\Omega \times [0,T])^m, \quad logZ \in L^\infty(\Omega)^m$$

$$Z_p \in H^1(0,T; L^2(\mathit{\Lambda}))^m \cap L^\infty(\mathit{\Lambda} \times [0,T])^m, \quad logZ_p \in L^\infty(\mathit{\Lambda})^m$$

4 Regularity

Now, we will establish some regularity results for the solution of our bidomain system (M) .

Theorem 2.
Let (φ,ψ) be the solution of bidomain system (16) with initial conditions (φ_0,ψ_0) where $\varphi = (V,V_p)$, $\psi = (W,W_p)$ and $\Theta = (Z,Z_p)$

- *If* $\varphi_0 \in H^2(\Omega) \times H^2(\Lambda)$ *,* $\psi_0 \in L^2(\Omega)^k \times L^2(\Lambda)^k$*,* $\Theta_0 \in L^2(\Omega)^m \times L^2(\Lambda)^m$ *and* $\mathfrak{I}_{app}$ *verify the regularity (17) ,*
  then,

$$\varphi \in W^{1,\infty}(0,T;H^1(\Omega)\times H^1(\Lambda))\cap L^2(0,T;H^2(\Omega)\times H^2(\Lambda))\cap H^1(0,T;H^2(\Omega)\times H^2(\Lambda))$$

and

$$\psi \in W^{1,\infty}(0,T;L^2(\Omega)^k \times L^2(\Lambda)^k), \qquad \Theta \in W^{1,\infty}(0,T;L^2(\Omega)^m \times L^2(\Lambda)^m)$$

Moreover if

$$\psi_0 \in H^1(\Omega)^k \times H^1(\Lambda)^k, \qquad \Theta_0 \in H^1(\Omega)^m \times H^1(\Lambda)^m \tag{18}$$

then

$$\psi \in W^{1,\infty}(0,T;H^1(\Omega)^k \times H^1(\Lambda)^k), \qquad \Theta \in W^{1,\infty}(0,T;H^1(\Omega)^m \times H^1(\Lambda)^m)$$

- *If* $\varphi_0 \in H^4(\Omega) \times H^4(\Lambda)$ *,* $\psi_0 \in H^2(\Omega)^k \times H^2(\Lambda)^k$*,* $\Theta_0 \in H^2(\Omega)^m \times H^2(\Lambda)^m$ *and* $\mathfrak{I}_{app}$ *verify the regularity (17) ,*
  then,

$$\varphi \in H^1(0,T;H^3(\Omega)\times H^3(\Lambda)) \cap H^2(0,T;H^1(\Omega)\times H^1(\Lambda))$$
$$\psi \in W^{1,\infty}(0,T;H^2(\Omega)\times H^2(\Lambda))^k \cap H^2(0,T;L^2(\Omega)\times L^2(\Lambda))^k$$
$$\Theta \in W^{1,\infty}(0,T;H^2(\Omega)\times H^2(\Lambda))^m \cap H^2(0,T;L^2(\Omega)\times L^2(\Lambda))^m$$

Moreover if

$$\psi_0 \in H^3(\Omega)^k \times H^3(\Lambda)^k, \qquad \Theta_0 \in H^3(\Omega)^m \times H^3(\Lambda)^m \tag{19}$$

then

$$\psi \in W^{1,\infty}(0,T;H^3(\Omega)\times H^3(\Lambda))^k \hookrightarrow H^1(0,T;H^3(\Omega)\times H^3(\Lambda))^k$$
$$\Theta \in W^{1,\infty}(0,T;H^3(\Omega)\times H^3(\Lambda))^m \hookrightarrow H^1(0,T;H^3(\Omega)\times H^3(\Lambda))^m$$

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