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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 Introduction

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 insulating. 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, $\Lambda$ stands for the Purkinje network domain. We suppose that we have $N_{\text{ter}}$ terminals in the Purkinje network $(x_1; \ldots; x_{N_{\text{ter}}})$.

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 1.1).

We also consider that the Purkinje network $\Lambda$ is made of a set of disjoint branches $\{A_i\}_{i=1}^{N_{\text{bran}}}$, where $\Lambda = \bigcup_{i=1}^{N_{\text{bran}}} \{A_i\}_i$ and $N_{\text{bran}}$ is the number of branches. The boundary of each branch is either a terminal point or a branching node.

Let’s consider $(y_1, y_2, \ldots, y_{N_{\text{bran}}})$ 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: $\Lambda$ represents the Purkinje fiber and Hiss, right and left bundles, $\Omega$ represents the myocardium and $\Omega_i$ is the coupling zone between the Purkinje end node $(x_i)$ and the myocardium.](image)

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 mod-
elling the cellular ionic currents:

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

(1)

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

\[
\sigma \nabla V \cdot n = 0, \quad \text{on } \partial \Omega \times [0, T]
\]

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

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

(2)

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

\[
\sigma_p \partial_x V_p(x) = 0, \quad \text{for } x = x_1 \text{ on } [0, T]
\]

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

\[
\begin{aligned}
V(0, .) &= V_0, \quad W(0, .) = W_0, \quad Z(0, .) = Z_0, \quad \text{in } \Omega \\
V_p(0, .) &= V_{p,0}, \quad W_p(0, .) = W_{p,0}, \quad Z_p(0, .) = Z_{p,0}, \quad \text{in } \Lambda
\end{aligned}
\]

In the myocardium \(\Omega\) (respectively Purkinje network \(\Lambda\)), 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, \(I_{\text{app}}\) (respectively, \(I_{\text{app},p}\)) the applied current, \(I_{\text{ion}}\) (respectively, \(I_{\text{ion},p}\)) 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 \(\sigma\) in the myocardium and \(\sigma_p\) 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 \(\sum_{i=2}^{N_{\text{ter}}} s_i\) 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
\[
\begin{aligned}
\sigma_p(x_i) \partial_{x_i} V_p(x_i) &= \frac{c_p}{\sigma_p}(\langle V \rangle_i - V_p(x_i)) \quad \text{for } i = 2, \ldots, N_{\text{ter}}, \\
s_i(x) &= \begin{cases} 
\frac{\sigma_p(x_i) \partial_{x_i} V_p(x_i)}{\sigma_p(x_i)} & \text{if } x \in \Omega_i, \\
0 & \text{else}
\end{cases} \quad \text{for } i = 2, \ldots, N_{\text{ter}},
\end{aligned}
\]  

(3)

where
\[
\langle V \rangle_i = \frac{1}{\Omega_i} \int_{\Omega_i} V, \quad \text{for } i = 1, \ldots, N_{\text{ter}},
\]

c_p \text{ the conductance of the PMJ, } S_p \text{ the surface of membrane of the Purkinje cells in } \Omega_i.

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

### 2.2 The ionic current

We assume that the ionic current
\[
I_{\text{ion}} : \mathbb{R} \times \mathbb{R}^k \times (0, +\infty)^m \rightarrow \mathbb{R}, \\
(V, W, Z) \mapsto I_{\text{ion}}(V, W, Z)
\]

has the general form both in the myocardium and the Purkinje network:
\[
I_{\text{ion}}(V, W, Z) = \sum_{j=1}^m (J_j(V, W, \log Z_j)) + \tilde{H}(V, W, Z)
\]  

(4)

\((W_i)_{i=1, \ldots, k}\) represent the gating variables and \((Z_j)_{j=1, \ldots, m}\) represent the ionic concentration variables.

We will assume that:
\[
\tilde{H} \in C^2(\mathbb{R} \times \mathbb{R}^k \times (0, +\infty)^m) \cap \text{Lip}(\mathbb{R} \times [0, 1]^k \times (0, +\infty)^m) 
\]  

(5)

and
\[
J_j \in C^2(\mathbb{R} \times \mathbb{R}^k \times \mathbb{R}), \quad \forall j = 1, \ldots, m
\]  

(6)

and there exist three functions \( G(W), \overline{G}(W), L_V \) belong to \( C^1(\mathbb{R}^k, \mathbb{R}^+) \) such that :
\[
0 < G(W) \leq \frac{\partial}{\partial \xi} J_j(V, W, \xi) \leq \overline{G}(W),
\]  

(7)

and
\[
|\frac{\partial}{\partial V} J_j(V, W, 0)| \leq L_V(W)
\]  

(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):

\[
\frac{\partial W_j}{\partial t} = g_j(V, W_j), \quad j = 1, \cdots, k.
\]  

(9)

Where

\[ g_j : \mathbb{R}^2 \to \mathbb{R} \text{ is a locally Lipschitz function, } j = 1, \cdots, k \]  

(10)

In the models considered \( g_j \) has the particular form

\[ g_j(V, W_j) = \alpha_j(V)(1 - W_j) - \beta_j(V)W_j \]  

(11)

where \( \alpha_j \) and \( \beta_j \) are positive rational functions of exponentials in \( V \).

A general expression for both \( \alpha_j \) and \( \beta_j \) is given by

\[
\frac{C_1 \exp \frac{V - V_n}{C_2} + C_3 (V - V_n)}{1 + C_4 \exp \frac{V - V_n}{C_5}}
\]  

(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:

\[
\frac{\partial W_{p,j}}{\partial t} = g_{p,j}(Vp, W_{p,j}), \quad j = 1, \cdots, k
\]

(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)

\[
\frac{\partial Z_i}{\partial t} = f_i(V, W, Z_i) = -J_i(V, W, Z_i) + H_i(V, W, Z), \quad i = 1, \cdots, m.
\]

(14)

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

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

(15)

2.5 The final model

The formal statement of the macroscopic model is:
Problem (M)

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

3 Existence and uniqueness

As the one-dimensional domain \( \Lambda \) is non regular, we define the space \( H^1 \) with bifurcations by

\[
H^1(\Lambda) = \bigcup_{i=1}^{N_b^{\text{bran}}} H^1(\Lambda_i) \bigcap C^0(\Lambda)
\]

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

\[
H^2(\Lambda) = \{ V \in C^0(\Lambda), V_{/\Lambda_i} \in H^2(\Lambda_i), \ i = 1, \ldots, N_b^{\text{bran}} \}
\]

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

**Theorem 1.** We assume that \( \Omega \) is of class \( C^{1,1} \) and that \( \sigma \) and \( \sigma_p \) are respectively Lipschitz in \( \Omega \) and \( \Lambda \). Let be given the data

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

\[
W_0 : \Omega \rightarrow [0, 1]^k, \text{ measurable;}
\]
W_{p,0}: \Lambda \mapsto [0,1]^k, \text{ measurable;}

Z_0 \in (L^2(\Omega))^m \quad \text{with} \quad \log Z_0 \in (L^2(\Omega))^m

Z_{p,0} \in (L^2(A))^m \quad \text{with} \quad \log Z_{p,0} \in (L^2(A))^m

(I_{\text{app}}, I_{\text{app},p}) \in L^p(0,T; L^2(\Omega) \times L^2(A)), \quad \text{for} \ p > 4 \quad (17)

Let be given the ionic currents $I_{\text{ion}}$ et $I_{\text{ion},p}$ 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 $f(V,W,Z)$, $f_p(V_p,W_p,Z_p)$ satisfying (14)-(15). Then, there exists a unique solution of Problem (M) satisfying

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

$W: \Omega \times [0,T] \mapsto [0,1]^k, \ Z: \Omega \times [0,T] \mapsto (0, +\infty)^m \text{ measurable,}$

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

with $w_j(x,\cdot) \in (C^1(0,T) \cap C^0([0,T]))$ for a.e $x \in \Omega$ and $j = 1, \cdots, k,$

$w_{p,j}(x,\cdot) \in (C^1(0,T) \cap C^0([0,T])) \quad \text{for a.e} \ x \in \Lambda \text{ and} \ j = 1, \cdots, k,$

$z_i(x,\cdot) \in C^1(0,T) \cap C^0([0,T]) \quad \text{for a.e} \ x \in \Omega \text{ and} \ i = 1, \cdots, m,$

$z_{p,i}(x,\cdot) \in C^1(0,T) \cap C^0([0,T]) \quad \text{for a.e} \ x \in \Lambda \text{ and} \ i = 1, \cdots, m,$

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

$Z_p \in H^1(0,T; L^2(A))^m \cap L^\infty(A \times [0,T])^m, \ \log Z_p \in L^\infty(A)^m$

4 Regularity

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

Theorem 2. Let $(\varphi, \psi)$ be the solution of bidomain system (16) with initial conditions $(\varphi_0, \psi_0)$ where $\varphi = (V,V_p), \ \psi = (W,W_p) \text{ and} \ \Theta = (Z,Z_p)$.
• If $\varphi_0 \in H^2(\Omega) \times H^2(\Lambda)$, $\psi_0 \in L^2(\Omega) \times L^2(\Lambda)$, $\Theta_0 \in L^2(\Omega)^m \times L^2(\Lambda)^m$ and $I_{\text{app}}$ 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

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

Moreover if

$$\psi_0 \in H^1(\Omega)^k \times H^1(\Lambda)^k, \quad \Theta_0 \in H^1(\Omega)^m \times H^1(\Lambda)^m$$

then

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

• If $\varphi_0 \in H^4(\Omega) \times H^4(\Lambda)$, $\psi_0 \in H^2(\Omega) \times H^2(\Lambda)$, $\Theta_0 \in H^2(\Omega)^m \times H^2(\Lambda)^m$ and $I_{\text{app}}$ verify the regularity (17), then,

$$\varphi \in H^1(0,T; H^3(\Omega) \times H^3(\Lambda)) \cap H^2(0,T; H^4(\Omega) \times H^4(\Lambda))$$

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

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

Moreover if

$$\psi_0 \in H^3(\Omega)^k \times H^3(\Lambda)^k, \quad \Theta_0 \in H^3(\Omega)^m \times H^3(\Lambda)^m$$

then

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

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

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