Modeling calcium dynamics in neurons with endoplasmic reticulum: existence, uniqueness and an implicit-explicit finite element scheme

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Abstract
Like many other biological processes, calcium dynamics in neurons containing an endoplasmic reticulum is governed by diffusion-reaction equations on interface-separated domains. Interface conditions are typically described by systems of ordinary differential equations that provide fluxes across the interfaces. Using the calcium model as an example of this class of ODE-flux boundary interface problems, we prove the existence, uniqueness and boundedness of the solution by applying comparison theorem, fundamental solution of the parabolic operator and a strategy used in Picard’s existence theorem. Then we propose and analyze an efficient implicit-explicit finite element scheme which is implicit for the parabolic operator and explicit for the nonlinear terms. We show that the stability does not depend on the spatial mesh size. Also the optimal convergence rate in $H^1$ norm is obtained. Numerical experiments illustrate the theoretical results.

Keywords: calcium dynamics; coupled reaction diffusion equations; ODE controlled interfaces; existence and uniqueness; implicit-explicit FEM scheme; stability and convergence.

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1. Introduction
In a variety of applications, particularly in biology, spatio-temporal dynamics can be described by diffusion-reaction systems. Intuitively, and from an

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energy consumption perspective, such systems appear optimal but usually have
the drawback of producing slow, short-range, and potentially inefficient communica-
tion pathways. In order to overcome these drawbacks, active and energy-
consuming processes are introduced by biology on two-dimensional manifolds,
i.e. interfaces which separate multiple domains. Such processes, in the biological
context, are channels, pumps, and receptors capable of exchanging specific ions
across the interfaces and are mathematically described by systems of ordinary
differential equations (ODEs), nonlinearly coupled to the domain equations, see
[1] 2 3 4 5 6 7 8. Given the ubiquitous nature of this modeling approach,
we study a mathematical model consisting of diffusion-reaction equations in $\Omega_c$
and $\Omega_e$ (see Fig. 1 for a 2D case), coupled by nonlinear dynamic boundary
conditions involving an ODE system on the interface $\Upsilon$. To provide context to
this ODE-coupled system of partial differential equations (PDEs), we chose cell-
ular calcium dynamics as a leading example. Calcium dynamics are among the
most important regulators in neurons and their three-dimensional (3D) spatio-
temporal dynamics have been shown to play a critical role in cellular function,
learning, and many neurodegenerative diseases, see [9] 3 10 11 12. Calcium
dynamics is further controlled by the 3D organization of cells, see [13] 10 11 14,
thus making calcium in neurons a prime candidate for the problems studied in
this paper.

The geometry structures of neurons can be found in [10] 14. Neuron has
a tubular organelle - endoplasmic reticulum (i.e. ER), which can be thought
of as a cell-within-a-cell. For simplicity, without loss of generality, we assume
the domain of the whole cell in 3D, including ER, is simply connected without
holes, with smooth boundary; so does the domain of ER. Also there are no other
organelles in this cell, boundaries (i.e. membranes) of ER and the cell have no
contact. A cross section of an axon of the simplified neuron cell can be shown
by Figure 1 where $\Omega_e$ is the region of ER lumen; $\Upsilon$ is the ER membrane; $\Omega_c$
is the region of cytosol; $\partial \Omega$ is the plasma membrane.

Here, let $\Omega$ be a bounded domain with $C^{1,\beta}$ boundary in $\mathbb{R}^n$, $n = 2, 3$, $\Upsilon$
be the $C^{1,\beta}$ interface, $0 < \beta < 1$. We define

$u : \overline{\Omega}_c \times [0, T] \to \mathbb{R}$ as the $\text{Ca}^{2+}$ concentration in cytosol,

$\ b : \overline{\Omega}_c \times [0, T] \to \mathbb{R}$ as the concentration of a buffer interacting with $u$,
\( u_e : \overline{\Omega}_e \times [0, T] \to \mathbb{R} \) as the \( \text{Ca}^{2+} \) concentration in ER,

where \([0, T]\) is the time domain. We define the PDE model by (1) to (9)

\[
\begin{align*}
\partial_t u - \nabla \cdot (D_c \nabla u) &= f(b, u) \quad \text{on } \Omega_e \times (0, T) \quad (1) \\
\partial_t b - \nabla \cdot (D_b \nabla b) &= f(b, u) \quad \text{on } \Omega_e \times (0, T) \quad (2) \\
\partial_t u_e - \nabla \cdot (D_e \nabla u_e) &= 0 \quad \text{on } \Omega_e \times (0, T) \quad (3)
\end{align*}
\]

\( \partial_t \) is the partial derivative in time, \( f(b, u) = K_{2+}^{-1} (b^0 - b) - K_{2+}^0 b u \) is the reaction term which models storing and releasing \( \text{Ca}^{2+} \) in cytosol, see [2] for more details, and \( D_c, D_b, D_e, K_{2+}^{\pm}, b^0 \) are positive constants. Denoting the outer normal derivative by \( \partial_n \), direction of the unit vector \( n \) depends on which domain the function lies, the boundary conditions describing fluxes across the interfaces are

\[
\begin{align*}
D_c \partial_n u &= J_{L,p} - J_N - J_P \quad \text{on } \partial \Omega \times (0, T) \quad (4) \\
D_c \partial_n u &= J_R + J_{L,e} - J_S \quad \text{on } \partial \Upsilon \times (0, T) \quad (5) \\
D_c \partial_n u_e &= J_S - J_R - J_{L,e} \quad \text{on } \partial \Upsilon \times (0, T) \quad (6) \\
D_b \partial_n b &= 0 \quad \text{on } \partial \Omega \cup \partial \Upsilon \times (0, T) \quad (7)
\end{align*}
\]

with initial data

\[
\begin{align*}
u(0, x) &= u_0(x), \quad b(0, x) = b_0(x) \quad \text{on } \Omega_e; \quad u_e(0, x) = u_{e, 0}(x) \quad \text{on } \Omega_e \quad (8) \\
c_1(0) &= c_1(0, u_0(x)), \quad o(0) = o(0, u_0(x)), \quad c_2(0) = c_2(0, u_0(x)) \quad \text{on } \Upsilon. \quad (9)
\end{align*}
\]

The choice of the fluxes \( J_N, J_P, J_{L,p}, J_R, J_S, J_{L,e} \) in (1) to (9) is motivated by the calcium models previously studied in [15, 16, 2, 17, 18, 7]. They describe the pumps that exchange \( \text{Ca}^{2+} \) across \( \partial \Omega \) and \( \partial \Upsilon \). \( \text{Ca}^{2+} \) flux crossing plasma membrane (\( \partial \Omega \)) is governed by PMCA pumps (\( J_P \)), NCX pumps (\( J_N \)) and leak channels (\( J_{L,p} \)); \( \text{Ca}^{2+} \) flux crossing ER membrane (\( \partial \Upsilon \)) is controlled by RyR channels (\( J_R \)), SERCA pumps (\( J_S \)) and leak channels (\( J_{L,e} \)), see [9, 10] for introduction, and [2] for an illustration. Below we list the fluxes under consideration. On \( \partial \Upsilon \), the flux through RyR channels (or Ryanodine receptors) is

\[
J_R = C_1^R P(t, u)(u_e - u), \quad (10)
\]

where \( C_1^R \) is a positive constant and for \( u \geq 0 \), \( P(t, u) \in [0, 1] \) is the probability that RyR channel is open:

\[
P(t, u) = 1 - c_1(t) - c_2(t), \quad (11)
\]

and \( c_1, c_2 \) come from the ODE system

\[
\begin{bmatrix}
c_1' \\
\bar{c}_1' \\
c_2' \\
\bar{c}_2'
\end{bmatrix} = \begin{bmatrix}
-u^4 k_a^- + k_a^- & -k_a^- & -k_a^- & -k_a^- \\
-u^3 k_b^+ & -u^3 k_b^+ & -u^3 k_b^+ & -u^3 k_b^+ \\
-k_c^+ & -k_c^+ & -k_c^+ & -k_c^+
\end{bmatrix} \begin{bmatrix}
c_1 \\
o \\
c_2 \\
k_b^+
\end{bmatrix} + \begin{bmatrix}
k_a^- \\
k_a^- \\
k_b^+ \\
k_b^+ 
\end{bmatrix}, \quad (12)
\]

where \( k_a^+, k_b^+, k_c^+ \) are positive constants, and obviously \( \{c_1, o, c_2\} \) depend on position due to \( u \), but for simplicity, the spatial variable is hidden, the initial
values of \( \{c_1, o, c_2\} \) are non-negative and \( c_1(0) + o(0) + c_2(0) \leq 1 \), see \[2\] and \[17\] for details. Next, we define the flux through SERCA pumps

\[
J_S = C_2^e \frac{u}{(K_s + u)\phi_m(u_e)}, \quad J_{I,e} = C_3^e (u_e - u),
\]

where \( K_s, C_2^e, C_3^e \) are positive numbers, \( \phi_m(\cdot) \) is defined as

\[
\phi_m(x) = \begin{cases} 
m/2, & \text{if } x \leq 0 \\
\frac{m^5}{(2m^5 - 5m^2x^3 + 6mx^4 - 2x^5)}, & \text{if } 0 < x < m \\
x, & \text{if } x \geq m
\end{cases}
\]

where \( m > 0 \) can be any small number. On \( \partial \Omega \) we define

\[
J_P = C_1^e \frac{u^2}{K_p^2 + u^2}, \quad J_N = C_2^e \frac{u}{K_n + u}, \quad J_{I,p} = C_3^e (c_o - u)
\]

where \( C_1^e, C_2^e, C_3^e, K_p, K_n \) are positive constants, \( c_o \) is the extracellular \( \text{Ca}^{2+} \) concentration, we assume it is a positive constant, however \( c_o \) can also be a positive bounded function. \( J_N \) and \( J_P \) are commonly used first and second order Hill equations, see \[2\].
A key part of the error analysis is to construct the elliptic projection, similar to the work in Cangiani [20] and Douglas [25], but incorporating the dynamic ODE system. So that the wellposedness of the associated nonlinear problem needs to be addressed.

The paper is arranged as follows: Necessary lemmas are provided in Section 2. The existence, uniqueness and boundedness of the solution for the model equations (1)-(9) are proved in Section 3. Section 4 is devoted to the $H^1$ error estimate for the Galerkin projection which is based on a nonlinear problem in variational form. In Section 5, the error analysis of the semi-discrete Galerkin method is carried out. The convergence rate in $H^1$ norm for a fully discrete implicit-explicit FEM scheme is obtained in Section 6. Numerical tests in Section 7 validate the theoretical results. Conclusions are drawn in Section 8.

2. Lemmas

In this section, we introduce some notations and lemmas. We define $Q_c = (0, T) \times \Omega_c$, $Q_e = (0, T) \times \Omega_e$. In the following $M$ is a positive constant and function $u$ being bounded by $M$ means $|u| \leq M$.

We then show that the open probability function $P(t, u)$ (see eq. (11)) is continuous with respect to $u$ if $u \in C(\Upsilon \times [0, T])$ and $0 \leq u \leq M$.

**Lemma 2.1.** Let $u_1, u_2 \in C(\Upsilon \times [0, T])$ be non-negative functions bounded by $M$ and $P(t, u)$ be defined as (11)-(12). We then have

$$|P(t, u_1) - P(t, u_2)| \leq K \left( |u_1(0) - u_2(0)| + \int_0^t |u_1(s) - u_2(s)| ds \right),$$

where $K$ is a positive constant that depends on $M$, but doesn’t depend on $u_1, u_2$.

**Proof.** Let $\tilde{q}(t) = [c_1, o, c_2]^T$, $\tilde{f}(u) = [k^+_a, u^3 k^+_b, k^-_c]^T$, and $A(u)$ be the coefficient matrix in (12). The ODE system can then be written as

$$\frac{d\tilde{q}}{dt} = A(u)\tilde{q} + \tilde{f}(u).$$

For given $u_1, u_2$, the corresponding integral equations are

$$\tilde{q}_i(t) = \int_0^t A(u_i)\tilde{q}_i(s) ds + \int_0^t \tilde{f}_i(u_i) ds + \tilde{q}_i(0, u_i(0)), \quad i = 1, 2.$$

Let $\tilde{e}(t) = \tilde{q}_1(t) - \tilde{q}_2(t)$, $\tilde{f}_e = \tilde{f}_1(u_1) - \tilde{f}_2(u_2)$, $A_e = A(u_1) - A(u_2)$ and $\tilde{q}_{0,e} = \tilde{q}_1(0, u_1(0)) - \tilde{q}_2(0, u_2(0))$, we have

$$\|\tilde{e}(t)\|_1 \leq \int_0^t \|A(u_i)\|_1 \|\tilde{e}(s)\|_1 ds + E_h(t)$$
where $\| \cdot \|_1$ is the 1-norm and

$$E_h(t) = \int_0^t \| \hat{f}(s) \|_1 ds + \int_0^t \| \mathbf{A}_t^1 \|_1 \| \hat{q}_2(s) \|_1 ds + \| \hat{q}_0 \|_1.$$  

With $E_h(t)$ being non-negative and non-decreasing, by Gronwall’s inequality, we have

$$\| \hat{e}(t) \|_1 \leq E_h(t) \int_0^t \| \mathbf{A}_t^1 \|_1 ds$$  

(17)

where $u_1, u_2$ are bounded and the initial condition of the ODE system is Lipschitz continuous, so that $\hat{q}_1, \hat{q}_2$ are bounded and

$$\| \hat{e}(t) \|_1 \leq K \left( |u_1(0) - u_2(0)| + \int_0^t |u_1(s) - u_2(s)| ds \right).$$  

(18)

With $|P(t, u_1) - P(t, u_2)| \leq \| \hat{e}(t) \|_1$, the proof is completed.

For brevity, from equation (4) and (6) we define

$$g_c(u) := D_c \partial_n u \text{ on } \partial \Omega, \quad g_c(u, u_e) := D_e \partial_n u_e \text{ on } \gamma.$$

With Lemma 2.1 we get

**Lemma 2.2.** Let $u_1, u_2 \in C(\partial \Omega \times [0, T])$ and $u_{e1}, u_{e2} \in C(\gamma \times [0, T])$ be non-negative functions bounded by $M$, then we have

$$|g_c(u_1) - g_c(u_2)| \leq K_1 |u_1 - u_2|,$$

$$|g_c(u_1, u_{e1}) - g_c(u_2, u_{e2})| \leq K_2 (|u_1 - u_2| + |u_{e1} - u_{e2}| + |u_1(0) - u_2(0)|)$$

$$+ K_2 \int_0^t |u_1(s) - u_2(s)| ds,$$

where $K_1, K_2$ are positive constants that depend on $M$, but do not depend on $u_1, u_2$ and $u_{e1}, u_{e2}$.

**Lemma 2.3.** Let $D$ be the domain with appropriate boundary, there exists a positive constant $C_T$ such that for $0 < \epsilon \leq 1$

$$\| v \|_{L^2(\partial D)} \leq C_T \left( \epsilon \| \nabla v \|_{L^2(D)} + \epsilon^{-1} \| v \|_{L^2(D)} \right), \quad v \in H^1(D).$$  

(19)

**Remark 1.** Lemma 2.2 together with smooth enough $g_c, g_e$ and (20) to (22)

$$g_c(0) \geq 0, \quad g_c(c_o) \leq 0, \quad g_c(u) \leq C_c, \quad \text{for } u \geq 0, c_o, C_c > 0$$  

(20)

$$g_e(0, u_e) \leq 0, \quad g_e(u, 0) \geq 0, \quad \text{for } u, u_e \geq 0$$  

(21)

$$-K_5 u_e - K_6 \leq g_e(u, u_e) \leq K_3 u + K_4, \quad \text{for } u, u_e, K_i > 0, i \geq 3$$  

(22)

can also be viewed as conditions for the analysis in following sections. So that the analysis and numerical method can be applied to models with more general interface/membrane fluxes.
3. Existence, Uniqueness and Boundedness

3.1. Fundamental Solution

For completeness, we recall the definition and properties of the fundamental solution of the parabolic operator, for more information see [26, 27]. We define the operator

\[ L = \partial_t u - D\Delta u, \]

where \( D > 0 \) is some coefficient. Then the fundamental solution of \( L \) is

\[ \Gamma(t, x; \tau, \xi) = \left[4\pi D(t - \tau)\right]^{-n/2}e^{-\frac{|x - \xi|^2}{4D(t - \tau)}}. \]

For any \( x, \xi \) in \( \mathbb{R}^n, n = 2, 3 \) and \( 0 \leq \tau < t \leq T \), the fundamental solution has bounds

\[ |\Gamma(t, x; \tau, \xi)| \leq K_0(t - \tau)^\mu \frac{1}{|x - \xi|^{n-2+\mu}}, \quad 0 < \mu < 1 \]

\[ \left|\frac{\partial \Gamma(t, x; \tau, \xi)}{\partial v(t, x)}\right| \leq K_0(t - \tau)^\mu \frac{1}{|x - \xi|^{n+1-2\mu-\gamma}}, \quad 1 - \gamma/2 < \mu < 1 \]

where \( K_0 \) is a constant independent of \((t, x)\) and \((\tau, \xi)\). Let \( D \) be an open bounded domain with \( C^{1,\beta} \) boundary. The second initial boundary value problem is given by

\[
\begin{cases}
Lu(t, x) = f(t, x) & (t, x) \in D \times (0, T] \\
\partial_n u = g(t, x) & (t, x) \in \partial D \times (0, T] \\
u(0, x) = u_0(x) & x \in D
\end{cases}
\] (25)

where \( f, g, u_0 \) are any given functions. The solution to (25) is:

\[
u(t, x) = \int_0^t \int_D \Gamma(t, x; \tau, \xi)\psi(\tau, \xi)d\xi d\tau + \int_D \Gamma(t, x; 0, \xi)u_0(\xi)d\xi + \int_0^t \int_D \Gamma(t, x; \tau, \xi)f(\tau, \xi)d\xi d\tau.
\]

(26)

Then, to get an explicit expression of \( \psi \), same as in [27], we define

\[ Q := \frac{\partial \Gamma(t, x; \tau, \xi)}{\partial v(t, x)}, \quad Q_{j+1} := \int_0^t \int_{\partial D} Q(t, x; s, y)Q_j(s, y; \tau, \xi)dyds, \]

where \( j \geq 1 \) and \( Q_1 = Q \). The solution \( \psi(t, x) \) has the explicit form

\[
\psi(t, x) = 2H(t, x) + 2 \int_0^t \int_{\partial D} R(t, x; \tau, \xi)H(\tau, \xi)d\xi d\tau.
\]

(27)
$R(t, x; \tau, \xi)$ is denoted by

$$R(t, x; \tau, \xi) = \sum_{j=1}^{\infty} Q_j(t, x; \tau, \xi)$$  \hspace{1cm} (28)$$

and $R(t, x; \tau, \xi)$ has the following bound

$$|R(t, x; \tau, \xi)| \leq \frac{K_1}{(t-\tau)^\mu} \frac{1}{|x-\xi|^{\gamma+1-2\mu-\gamma}}, \quad 1 - \gamma / 2 < \mu < 1,$$  \hspace{1cm} (29)$$

while $K_1$ does not depend on the variables, see \cite{26} for a proof.

### 3.2. Wellposedness

For brevity we define the parabolic operators as:

$$L_c u = \partial_t u - D_c \Delta u, \quad L_b = \partial_t b - D_b \Delta b, \quad L_{e,c} u_e = \partial_t u_e - D_c \Delta u_e,$$

the corresponding fundamental solutions are $\Gamma_c, \Gamma_b, \Gamma_e$, and $R$ in (27) are represented by $R_c, R_b, R_e$. We denote $C_{1.2}(Q_e)$ as the space of functions with two continuous spatial derivatives and one continuous time derivative on $Q_e$. The boundary conditions for $u$ are defined as $B_c u := \partial_n u$ on $\partial \Omega$, $B_b u := \partial_n u$ on $\Gamma$. In this section, we derive the bounds for solution (if it exits) of (1)-(9) in Theorem 3.1 then show the existence and uniqueness of the solution in Theorem 3.2.

**Theorem 3.1.** Assume \{u, b, u_e\} is a solution of (1)-(9), and $u, b \in C(\overline{Q_e}) \cap C_{1.2}(Q_e)$, $u_e \in C(\overline{Q_e}) \cap C_{1.2}(Q_e)$ with initial conditions $u(0, x), u_e(0, x) > 0$, $0 \leq b(0, x) \leq b^0$. Then for $t \in [0, T]$, $0 \leq b \leq b^0$, $u, u_e$ are positive and bounded by a constant $M$ which does not depend on $u, b, u_e$.

**Proof.** Equation (2) can be written as $L_b b + K_b^- b + K_b^+ b u = K_b^- b^0$, the first observation from it and (7) is that, by maximum principle (see Theorem 1.4-1.5, Chapter 2 in [27]), and as long as $u \geq 0$, we have $b \geq 0$. Next, since $b^0$ is the solution of $L_b b = K_b^- (b^0 - b)$, by comparison theorem, see [20-27], we get $b \leq b^0$. The initial values of $u, u_e$ are positive, so if $u, u_e$ are not always positive on $Q_c$, then suppose one of them, e.g., $u$ becomes 0 no later than $u_e$ and define $\bar{t} = \min\{\tau \geq 0 | u(\tau, x) = 0, x \in \overline{Q_c}\}$ so that $u(\bar{t}, x) = 0$. Equation (1) can be written as $L_c u_c + K_c^- b u_c = K_c^- (b^0 - b)$, where $0 \leq b \leq b^0$ on $[0, \bar{t}]$, by maximum principle and $g_c(0) \geq 0, -g_c(0, u_c) \geq 0$, we conclude that $t$ does not exist. The positivity of $u_e$ can be obtained similarly.

As $u$, $u_e$, $b$ are non-negative and $b$ is bounded, we can see that $u$ is bounded by $u_e$. The following equation (30) is used to get the bound of $u$:

$$\begin{align*}
L_c w &= K_b^- b^0, \\
B_c w &= C_3 c_0 / D_c, \quad B_e w = (C_e^c + C_e^b) u_e / D_c, \\
w(0, x) &= 0.
\end{align*}$$  \hspace{1cm} (30)$$

8
We define a constant \( w_0 > u(0, x) \) for \( x \in \bar{\Omega}_e \), then by comparison theorem, we have \( u(t, x) \leq w(t, x) + w_0 \) on \( \bar{\Omega}_e \times [0, T] \). Just like (25) in Section 3.1, the solution \( w \) can be obtained as

\[
\begin{align*}
    w(t, x) &= \int_0^t \int_{\partial \Omega_e} \Gamma_e(t, x; \tau, \xi) \psi_w(\tau, \xi) d\xi d\tau + K_b \int_0^t \int_{\Omega_e} \Gamma_e(t, x; \tau, \xi) d\xi d\tau, \\
    \psi_w(t, x) &= 2 \int_0^t \int_{\partial \Omega_e} R_e(t, x; \tau, \xi) H_w(t, x) d\xi d\tau + 2 H_w(t, x), \\
    H_w(t, x) &= K_b b^0 \int_0^t \int_{\Omega_e} \frac{\partial \Gamma_e(t, x; \tau, \xi)}{\partial v(t, x)} d\xi d\tau + g_w(t, x),
\end{align*}
\]

where \( g_w(t, x) = B_{\pi} w \) on \( \partial \Omega \) and \( g_w(t, x) = B_{\pi} w \) on \( \Gamma \). Let \( t \leq h, h > 0 \), and define the norm \( \| u_t \|_h = \sup \{ |u(t, x)|; 0 \leq t \leq h, x \in \bar{\Omega}_e \} \), by the properties of \( \Gamma_e \) as in (23)-(24), we have

\[
\begin{align*}
    |H_w(t, x)| &\leq C_1^w t^{1-\mu} + (C_2^e + C_3^e) \| u_t \|_h / D_e + C_3 c_0 / D_e, \\
    |\psi_w(t, x)| &\leq C_2^w (t^{1-\mu} + t^{2-2\mu} + c_0) + C_3^w (1 + t^{1-\mu}) \| u_t \|_h, \\
    |w(t, x)| &\leq C_4^w (t^{1-\mu} + t^{2-2\mu} + t^{3-3\mu}) + C_5^w (t^{1-\mu} + t^{2-2\mu}) \| u_t \|_h,
\end{align*}
\]

so that on \( \bar{\Omega}_e \times [0, h] \), \( u \) can be bounded as

\[
|u(t, x)| \leq C_4^w (t^{1-\mu} + t^{2-2\mu} + t^{3-3\mu}) + C_5^w (t^{1-\mu} + t^{2-2\mu}) \| u_t \|_h + w_0. \tag{31}
\]

Here, \( C_1^w \) to \( C_5^w \) do not depend on \( (t, x) \) and \( u_e \).

We then prove that \( u_e \) is bounded by \( u \) from the following equation (32):

\[
\begin{align*}
    L_e v &= 0, \\
    \partial_n v &= (C_1^w + 2 C_2^e / (K_m m) + C_3^e) u / D_e, \\
    v(0, x) &= 0,
\end{align*}
\]

where we define \( v_0 \) as a constant and \( v_0 > u_e(0, x) \) for \( x \in \bar{\Omega}_e \). By the comparison theorem, \( u_e(t, x) \leq v(t, x) + v_0 \) on \( \bar{\Omega}_e \times [0, T] \). The solution \( v \) can be obtained as

\[
\begin{align*}
    v(t, x) &= \int_0^t \int_{\Gamma} \Gamma_e(t, x; \tau, \xi) \psi_w(\tau, \xi) d\xi d\tau, \\
    \psi_v(t, x) &= 2 \int_0^t \int_{\Gamma} R_e(t, x; \tau, \xi) g_w(t, x) d\xi d\tau + 2 g_v(t, x),
\end{align*}
\]

where \( g_v(t, x) = \partial_n v \). When defining the norm \( \| u \|_h = \sup \{ |u(t, x)|; 0 \leq t \leq h, x \in \bar{\Omega}_e \} \), and by the properties of \( \Gamma_e(t, x; \tau, \xi) \) from (23)-(24), \( R_e \) from (28)-(29), we get

\[
|\psi_v(t, x)| \leq C_1^w (1 + t^{1-\mu}) \| u \|_h, \quad |v(t, x)| \leq C_2^w (t^{1-\mu} + t^{2-2\mu}) \| u \|_h,
\]

so that on \( \bar{\Omega}_e \times [0, h] \), \( u_e \) can be bounded by

\[
|u_e(t, x)| \leq C_3^w (t^{1-\mu} + t^{2-2\mu}) \| u \|_h + v_0, \tag{33}
\]
where $C_1^w$, $C_2^w$ do not depend on $(t,x)$ and $u$. With (31), (33), and $h$ small enough, we have

$$\|u\|_h \leq \frac{1}{2}\|u_c\|_h + w_0 + \frac{3}{4}C_1^w, \quad \|u_c\|_h \leq \frac{1}{2}\|u\|_h + v_0,$$

so that

$$\|u\|_h \leq \frac{2}{3}v_0 + \frac{4}{3}w_0 + C_4^w, \quad \|u_c\|_h \leq \frac{4}{3}v_0 + \frac{2}{3}w_0 + \frac{1}{2}C_4^w.$$  

Then, on time interval $[h, 2h]$, let $w_1 = \frac{2}{3}v_0 + \frac{4}{3}w_0 + C_4^w, \ v_1 = \frac{4}{3}v_0 + \frac{2}{3}w_0 + \frac{1}{2}C_4^w$, by (30) and (32), and (31), we have $u(t,x) \leq u(t,x) + w_1$ on $\Omega_c \times [h, 2h]$ and $u_c(t,x) \leq v(t,x) + v_1$ on $\Omega_c \times [h, 2h]$. With the same coefficients as in the previous step, we get similar bounds of $u, u_c$ for $t \in [h, 2h]$. Since $h$ is fixed, with finite steps, we can reach the conclusion that $u$ and $u_c$ are bounded for $t \in [0, T]$. \qed

**Theorem 3.2.** Suppose $u(0, x), u_c(0, x) > 0$ and $b^0 \geq b(0, x) \geq 0$ are continuously differentiable in $\Omega_c$ or $\Omega_e$, then there exists a unique solution $\{u, b, u_c\}$ for (1)-(9).

**Proof.** From Theorem 3.1, we can get the bounds of $u, u_c$ and $b$ if the solution $\{u, b, u_c\}$ exists and its components are smooth. Let $M$ be the upper bound of those three. We define $\phi(x) = \max(0, \min(x, M))$, but $\phi$ can be smoother if needed, see Section 4.1. Then we change $u, b$ to be $\phi(u), \phi(b)$ in $f(b, u)$ for equations (1)-(2), and replace $u, u_c$ by $\phi(u), \phi(u_c)$ in the right hand sides of (4)-(6). We assert that the modified problem has a unique solution and the solution has the same bounds. Thus, it is the same solution of the original system (1)-(9). Define the map $T$ as $\{u, b, u_c\} = T\{w, w_b, w_c\}$ for the modified problem

\[
\begin{aligned}
  L_c u &= f(\phi(w_b), \phi(w)), \\
  L_b b &= f(\phi(w_b), \phi(w)), \\
  L_c u_c &= 0, \\
  B_c u &= g_c(\phi(w)) / D_c, \\
  B_c u_c &= -g_c(\phi(w), \phi(w_c)) / D_c, \\
  \partial_n u_c &= g_c(\phi(w), \phi(w_c)) / D_c, \\
  \partial_n b &= 0,
\end{aligned}
\]

where $\{w, w_b, w_c\}$ are given functions, $\{u, b, u_c\}$ is the solution of (34). Next we show $T$ is a contraction map if $t \leq h$ for $h$ small enough. To prove this, let the entries of $\{w_1, w_{b,1}, w_{c,1}\}, \ {w_2, w_{b,2}, w_{c,2}\}$ be Hölder continuous functions and $\{u_1, b_1, u_{c,1}\} = T\{w_1, w_{b,1}, w_{c,1}\}, \ {u_2, b_2, u_{c,2}\} = T\{w_2, w_{b,2}, w_{c,2}\}$. Then we define the norms

$$\|v\|_h = \sup\{|v(t,x)|; 0 \leq t \leq h, x \in \Omega\}, \quad \|v, v_b, v_c\|_h = \|v\|_h + \|v_b\|_h + \|v_c\|_h,$$

where $\Omega$ can be $\Omega_c$ or $\Omega_e$. Let $v = u_1 - u_2, v_b = b_1 - b_2, v_c = u_{c,1} - u_{c,2}$, and $q = w_1 - w_2, q_b = w_{b,1} - w_{b,2}, q_c = w_{c,1} - w_{c,2}$. Since the system (34) is fully decoupled, $v, v_b, v_c$ can be solved separately. We start with $v$ in (35)

\[
\begin{aligned}
  L_c v &= -K^+_b q_b - K^+_b (\phi(w_{b,1}) - \phi(w_{b,2})\phi(w_2)), \\
  B_c v &= (g_c(\phi(w_1)) - g_c(\phi(w_2))) / D_c, \\
  B_c v &= (g_c(\phi(w_1)) - g_c(\phi(w_2)) + g_c(\phi(w_2)) / D_c, \\
  v(0, x) &= 0,
\end{aligned}
\]
and by Lemma 2.2, we have
\[ |g_c(\phi(w_1)) - g_c(\phi(w_2))| \leq K_1|q|, \]
\[ |g_c(\phi(w_1), \phi(w_{e,1})) - g_c(\phi(w_2), \phi(w_{e,2}))| \leq K_2 \left( |q| + |q_c| + \int_0^t |q(s)|ds \right). \]

Further, let \( f_v(t, x) = -K_b^+q_b - K_b^+(\phi(w_{b,1})\phi(w_1) - \phi(w_{b,2})\phi(w_2)) \), \( g(t, x) = B_c v \) on \( \partial \Omega \) and \( g(t, x) = B_c v \) on \( \Gamma \). The solution of (35) is

\[
v(t, x) = \int_0^t \int_{\partial \Omega_c} \Gamma_c(t, x; \tau, \xi) \psi_v(\tau, \xi) d\xi d\tau + \int_0^t \int_{\Omega_c} \Gamma_c(t, x; \tau, \xi) f_v(\tau, \xi) d\xi d\tau,
\]
\[
\psi_v(t, x) = 2H_v(t, x) + 2 \int_0^t \int_{\partial \Omega_c} R_c(t, x; \tau, \xi) H_v(\tau, \xi) d\xi d\tau,
\]
\[
H_v(t, x) = \int_0^t \int_{\Omega_c} \frac{\partial \Gamma_c(t, x; \tau, \xi)}{\partial v(t, x)} f_v(\tau, \xi) d\xi d\tau + g(t, x).
\]

By the properties of \( \Gamma_c, R_c \), and \( t \leq h \), we have
\[
|H_v(t, x)| \leq C_v^w(t^{1-\mu} + 1 + t)(\|q\| h + \|q_b\| h + \|q_e\| h),
\]
\[
|\psi_v(t, x)| \leq C_v^w(t^{1-\mu} + 1 + t + t^2 - 2\mu)(\|q\| h + \|q_b\| h + \|q_e\| h),
\]
\[
|v(t, x)| \leq C_v^w(t^{1-\mu} + t^2 - 2\mu + t^2 - 2\mu + t^3 - 2\mu + t^3 - 3\mu)(\|q\| h + \|q_b\| h + \|q_e\| h),
\]
where \( C_v^w, C_v^w, C_v^w \) do not depend on \( q, q_b, q_e \) or \( (t, x) \). So we can choose \( h \) small enough such that \( \|v\| h \leq 1/6(\|q\| h + \|q_b\| h + \|q_e\| h) \). Similarly, we can obtain the bounds of \( v, v_e \) as \( \|v_b, v_e\| \leq 1/6(\|q\| h + \|q_b\| h), \|v_e\| h \leq 1/6(\|q\| h + \|q_e\| h) \).

Summing these terms we can show that \( T \) is a contraction map
\[
\|T\{w_1, w_{b,1}, w_{e,1}\} - T\{w_2, w_{b,2}, w_{e,2}\}\| h \leq \frac{1}{2}\|\{w_1, w_{b,1}, w_{e,1}\} - \{w_2, w_{b,2}, w_{e,2}\}\| h,
\]
where \( t \in [0, h] \). By iteration, we can get the unique solution \( \{u, b, u_e\} \) on \( [0, h] \). Then, choosing \( u(h, x), b(h, x), u_e(h, x) \) as the initial value, and repeating the steps above, the existence and uniqueness of the solution on \([0, T]\) can be obtained. Following the proof in Theorem 3.1, it’s easy to see the bounds of the solution for the modified system are the same as the original system. For regularity of the solution, we refer to [26] for more information.

4. Galerkin Projection and the Error Estimates

In this section, we define a nonlinear problem (36) in variational form, which is used in Section 4.2 to define the Galerkin projection of \( u, u_e \). The wellposedness of (36) is proved in Section 4.1. From Section 3.2, we get the bounds of the exact solution \( \{u, b, u_e\} \) for (36)–(39), the bounds are used to define the function \( \phi(\cdot) \), such that \( \phi(u) = u, \phi(b) = b \) and \( \phi(u_e) = u_e \) when \( u, b, u_e \) are within the bounds. Since \( b \) is not coupled with \( u_e \), we can use the normal Galerkin
The method we use here is adapted from Appendix in [28]. We try to prove the modified conditions (4).

Lemma 4.1. The nonlinear problem (36) has a unique solution, provided the modified conditions [1]–[3].

Proof. The method we use here is adapted from Appendix in [28]. We try to get the exact solution by iteration, let \( u^0 \in H^1(\Omega_e) \), \( u^0_e \in H^1(\Omega_e) \) be given functions and \( n \geq 0 \), then we have

\[
\begin{align*}
\mathcal{a}_c(u^{n+1}, v) + \lambda(u^{n+1}, v) &= \langle \tilde{g}_c(u^n), v \rangle_{\partial\Omega} - \langle \tilde{g}_c(u^n), v \rangle_{\Gamma}, \\
\mathcal{a}_c(u^{n+1}_e, v_e) + \lambda(u^{n+1}_e, v_e) &= \langle \tilde{g}_c(u^n_e), v_e \rangle_{\Gamma},
\end{align*}
\]

where \( u^{n+1} \), \( u^{n+1}_e \) share same initial values as \( u^0 \), \( u^0_e \).

Let \( r^{n+1} = u^{n+1} - u^n \), \( r^{n+1}_e = u^{n+1}_e - u^n_e \) and \( n \geq 1 \), we have

\[
\begin{align*}
\mathcal{D}_c(\nabla r^{n+1}, \nabla v) + \lambda(r^{n+1}, v) &= \langle \tilde{g}_c(u^n), v \rangle_{\partial\Omega} + \langle \tilde{g}_c(u^n), v \rangle_{\Gamma}, \\
\mathcal{D}_c(\nabla r^{n+1}_e, \nabla v_e) + \lambda(r^{n+1}_e, v_e) &= \langle \tilde{g}_c(u^n_e), v_e \rangle_{\Gamma},
\end{align*}
\]
then let \( v = r^{n+1} \) and \( v_e = r_e^{n+1} \), we obtain
\[
D_e \| \nabla r^{n+1} \|^2 + \lambda \| r^{n+1} \|^2 = \langle -\bar{g}_e(u^n, u^n_e) + \bar{g}_e(u^{n-1}, u_e^{n-1}), r^{n+1} \rangle_{\Omega} \\
+ \langle \bar{g}_e(u^n) - \bar{g}_e(u^{n-1}), r^{n+1} \rangle_{\partial \Omega},
\]
\[
D_e \| \nabla r_e^{n+1} \|^2 + \lambda \| r_e^{n+1} \|^2 = \langle -\bar{g}_e(u^n, u^n_e) - \bar{g}_e(u^{n-1}, u_e^{n-1}), r_e^{n+1} \rangle_{\Omega}.
\]
Sum those two equations, we get (39)
\[
D_e \| \nabla r^{n+1} \|^2 + \lambda \| r^{n+1} \|^2 + D_e \| \nabla r_e^{n+1} \|^2 + \lambda \| r_e^{n+1} \|^2
= \langle \bar{g}_e(u^n) - \bar{g}_e(u^{n-1}), r^{n+1} \rangle_{\partial \Omega}
+ \langle \bar{g}_e(u^n, u^n_e) - \bar{g}_e(u^{n-1}, u_e^{n-1}), r_e^{n+1} - r^{n+1} \rangle_{\Omega}.
\]
By Lemma 2.2, the first term of the right hand side is bounded:
\[
< \bar{g}_e(u^n) - \bar{g}_e(u^{n-1}), r^{n+1} \rangle_{\partial \Omega} \leq \frac{K_1}{2} \| r^n \|^2_{L^2(\partial \Omega)} + \frac{K_1}{2} \| r^{n+1} \|^2_{L^2(\partial \Omega)},
\]
and the second term of the right hand side is bounded:
\[
< \bar{g}_e(u^n, u^n_e) - \bar{g}_e(u^{n-1}, u_e^{n-1}), r_e^{n+1} \rangle_{\Omega}
\leq K_2 \langle |r^n| + |r^n_e| + \int_0^t \| r^n(s) \| ds, r_e^{n+1} - r^{n+1} \rangle_{\Omega}
\leq K_2 \frac{1}{2} \| r^n \|^2_{L^2(\Omega)} + \frac{K_2}{2} \| r^n_e \|^2_{L^2(\Omega)} + \frac{K_2}{2} \int_0^t \| r^n(s) \|^2_{L^2(\Omega)} ds
+ K_2(2 + T) \left( \| r^{n+1} \|^2_{L^2(\Omega)} + \| r_e^{n+1} \|^2_{L^2(\Omega)} \right).
\]
By equations (39) to (41), we have
\[
D_e \| \nabla r^{n+1} \|^2 + \lambda \| r^{n+1} \|^2 + D_e \| \nabla r_e^{n+1} \|^2 + \lambda \| r_e^{n+1} \|^2
\leq \frac{K_1}{2} \| r^n \|^2_{L^2(\partial \Omega)} + \frac{K_2}{2} \| r^n_e \|^2_{L^2(\Omega)} + \frac{K_2}{2} \int_0^t \| r^n(s) \|^2_{L^2(\Omega)} ds
+ \frac{K_2}{2} \| r^{n+1} \|^2_{L^2(\Omega)} + K_2(2 + T) \left( \| r^{n+1} \|^2_{L^2(\Omega)} + \| r_e^{n+1} \|^2_{L^2(\Omega)} \right),
\]
take \( L^\infty \) norm of \( \| r^n \|^2_{L^2(\partial \Omega)}, \| r^n_e \|^2_{L^2(\Omega)}, \| r^{n+1} \|^2_{L^2(\Omega)} \), we obtain (42)
\[
D_e \| \nabla r^{n+1} \|^2 + \lambda \| r^{n+1} \|^2 + D_e \| \nabla r_e^{n+1} \|^2 + \lambda \| r_e^{n+1} \|^2
\leq C_1 \left( \| r^n \|^2_{L^\infty(0,T;L^2(\partial \Omega))} + \| r^n_e \|^2_{L^\infty(0,T;L^2(\Omega))} + \| r_e^{n+1} \|^2_{L^\infty(0,T;L^2(\Omega))} \right)
\]
\[
+ C_2 \left( \| r^{n+1} \|^2_{L^2(\partial \Omega)} + \| r_e^{n+1} \|^2_{L^2(\Omega)} \right).
\]
Let \( \alpha > 1 \), add the same term to both sides of (42), we have (43)
\[
D_e \| \nabla r^{n+1} \|^2 + \lambda \| r^{n+1} \|^2 + D_e \| \nabla r_e^{n+1} \|^2 + \lambda \| r_e^{n+1} \|^2
+ \alpha C_1 \left( \| r^{n+1} \|^2_{L^2(\partial \Omega)} + \| r_{n+1} \|^2_{L^2(\Omega)} \right)
\leq C_1 \left( \| r^n \|^2_{L^\infty(0,T;L^2(\partial \Omega))} + \| r^n_e \|^2_{L^\infty(0,T;L^2(\Omega))} + \| r_e^{n+1} \|^2_{L^\infty(0,T;L^2(\Omega))} \right)
\]
\[
+ (\alpha C_1 + C_2) \left( \| r^{n+1} \|^2_{L^2(\partial \Omega)} + \| r_e^{n+1} \|^2_{L^2(\Omega)} \right).
\]
From Lemma 2.3 and \( \lambda \) is large enough, we have
\[
(\alpha C_1 + C_2) \left( \|r^{n+1}\|_{L^2(\partial \Omega)}^2 + \|r^{n+1}\|_{L^2(\Gamma)}^2 + \|r_e^{n+1}\|_{L^2(\Gamma)}^2 \right) 
\leq D_e \|\nabla r^{n+1}\|^2 + \lambda \|r^{n+1}\|^2 + D_e \|\nabla r_e^{n+1}\|^2 + \lambda \|r_e^{n+1}\|^2. 
\] (44)

So that combine (43) and (44), we obtain (45)
\[
\|r^{n+1}\|_{L^\infty(\Omega)}^2 + \|r_e^{n+1}\|_{L^\infty(\Omega)}^2 
\leq \frac{1}{\alpha} \left( \|r^n\|_{L^\infty(\Omega)}^2 + \|r^n\|_{L^\infty(\Omega)}^2 + \|r_e^n\|_{L^\infty(\Omega)}^2 \right). 
\] (45)

From (42) and (45), let \( \tau = \min\{D_e, D_e\} \), \( C_\tau = \frac{C_1 + C_2}{\alpha} \), we arrive at
\[
\|r^{n+1}\|_{L^\infty(\Omega)}^2 + \|r_e^{n+1}\|_{L^\infty(\Omega)}^2 
\leq C_\tau \left( \|r^n\|_{L^\infty(\Omega)}^2 + \|r^n\|_{L^\infty(\Omega)}^2 + \|r_e^n\|_{L^\infty(\Omega)}^2 \right) 
\leq C_\tau \left( \|r^n\|_{L^\infty(\Omega)}^2 + \|r^n\|_{L^\infty(\Omega)}^2 + \|r_e^n\|_{L^\infty(\Omega)}^2 \right) \cdot 
\]
which implies that \( u^n, u^n_e \) converge to a unique solution. \( \square \)

4.2. Galerkin Projection

We define \( S_k(\Omega) \), \( S_k(\Omega_e) \), \( k \geq 1 \) as the classical conforming \( P_k \) finite element spaces, with shape regular triangular/tetrahedral meshes and the size of the corresponding mesh is \( h \). For curved boundaries, we refer to isoparametric finite element methods, see [29][30] and references therein. The Galerkin projection for the exact solutions \( u, u_e \) can be obtained from (46):
\[
\begin{aligned}
& a_c(u - W, v) + \lambda(u - W, v) = < -\tilde{g}_e(u, u_e) + \tilde{g}_e(W, W_e), v >_{\Gamma} \\
& + < \tilde{g}_c(u) - \tilde{g}_c(W), v >_{\partial \Omega}, \\
& a_e(u_e - W_e, v_e) + \lambda(u_e - W_e, v_e) = < \tilde{g}_e(u, u_e) - \tilde{g}_e(W, W_e), v_e >_{\Gamma}.
\end{aligned} 
\] (46)

where \( W(t), v \in S_k(\Omega) \), and \( W_e(t), v_e \in S_k(\Omega_e) \), \( \lambda \) is large enough.

Also without further notice, \( \eta, \eta_e \) are defined as \( \eta := u - W \), \( \eta_e := u_e - W_e \), the following norms are denoted as \( \| \cdot \|_{\infty, k} := \| \cdot \|_{L^\infty(0, T; H^k(D))} \), \( \| \cdot \|_{\infty, 0} := \| \cdot \|_{L^\infty(0, T; L^2(D))} \), and \( \| \cdot \| := \| \cdot \|_{L^2(D)} \), where \( D \) can be \( \Omega \) or \( \Omega_e \) depending on the domain of the given function. Then we have the following theorem:

**Theorem 4.1.** With \( P_k \) elements, \( k \geq 1 \), and appropriately chosen \( W(0), W_e(0) \), we have
\[
\|\eta\|_{\infty, 1} + \|\eta_e\|_{\infty, 1} \leq C(\|u\|_{\infty, k+1} + \|u_e\|_{\infty, k+1})h^k, 
\] (47)
\[
\|\partial_t \eta\|_{\infty, 1} + \|\partial_t \eta_e\|_{\infty, 1} \leq C(\|u\|_{\infty, k+1} + \|\partial_t u\|_{\infty, k+1})h^k 
\] (48)
\[
+ C(\|u_e\|_{\infty, k+1} + \|\partial_t u_e\|_{\infty, k+1})h^k, 
\]
where \( h \) is the mesh size and \( C \) does not depend on \( h \).
Proof. First step, we prove (47). Letting \( \delta u = w - u, \delta u_e = w_e - u_e, w \in S_k(\Omega_e), w_e \in S_k(\Omega_e) \), (46) can be written as

\[
\begin{align*}
\left\{ \begin{array}{l}
a_c(\eta, v) + \lambda(\eta, v) = & -\bar{g}_e(u, u_e) + \bar{g}_e(W, W_e), v > \Upsilon \\
& +\bar{g}_e(u) - \bar{g}_e(W), v > \partial \Omega;
\end{array} \right.
\end{align*}
\]

and

\[
\begin{align*}
a_e(\eta_e, v_e) + \lambda(\eta_e, v_e) = & \bar{g}_e(u, u_e) - \bar{g}_e(W, W_e), v_e > \Upsilon.
\end{align*}
\]

Now set \( v = w - W = \delta u + \eta, v_e = w_e - W_e = \delta u_e + \eta_e \), then

\[
\begin{align*}
a_c(\eta, \delta u + \eta) + \lambda(\eta, \delta u + \eta) = & -\bar{g}_e(u, u_e) + \bar{g}_e(W, W_e), \delta u + \eta > \Upsilon \\
& +\bar{g}_e(u) - \bar{g}_e(W), \delta u + \eta > \partial \Omega;
\end{align*}
\]

moving the terms containing \( \delta u \) to the right-hand side leads to (with Schwarz inequality, Lemma 2.2 and trace theorem):

\[
\begin{align*}
D_c||\nabla \eta||^2 & + \lambda ||\eta||^2 + D_c||\nabla \eta_e||^2 + \lambda ||\eta_e||^2 \\
& \leq \frac{D_c}{4}||\nabla \eta||^2 + \frac{\lambda}{4}||\eta||^2 + \frac{D_c}{4}||\nabla \eta_e||^2 + \frac{\lambda}{4}||\eta_e||^2 \\
& + C_1(||\eta||^2_{L^2(\Upsilon)} + ||\eta_e||^2_{L^2(\partial \Omega)}) + C_2 \int_0^t ||\eta(s)||^2_{L^2(\Upsilon)} ds \\
+ & C_3(||\eta(0)||^2_{L^2(\Upsilon)} + ||\eta_e(0)||^2_{L^2(\Upsilon)} + \inf_{\eta \in \mathcal{H}^1(\Omega_e)} ||\delta u||^2_{\mathcal{H}^1(\Omega_e)} \\
& + \inf_{\eta \in \mathcal{H}^1(\Omega_e)} ||\delta u_e||^2_{\mathcal{H}^1(\Omega_e)}).
\end{align*}
\]

from Lemma 2.3 we have

\[
C_2 \int_0^t ||\eta(s)||^2_{L^2(\Upsilon)} ds \leq \int_0^t D_c/(4T)||\nabla \eta(s)||^2 + C ||\eta(s)||^2 ds,
\]

the bounds for \( C_1(||\eta||^2_{L^2(\Upsilon)} + ||\eta_e||^2_{L^2(\partial \Omega)}) \) can be obtained similarly. Taking \( L^\infty \) norm with respect to \( t \) then to \( s \) for the right-hand side, then taking the \( L^\infty \) norm with respect to \( t \) for the left-hand side, cancelling the corresponding terms, we obtain

\[
\begin{align*}
||\eta||^2_{\infty,1} + ||\eta_e||^2_{\infty,1} & \leq C(||\eta(0)||^2_{\mathcal{H}^1(\Omega_e)} + ||\eta_e(0)||^2_{\mathcal{H}^1(\Omega_e)} \\
& + \sup_{t \in [0,T]} \inf_{\eta \in \mathcal{H}^1(\Omega_e)} ||\delta u||^2_{\mathcal{H}^1(\Omega_e)} \\
& + \sup_{t \in [0,T]} \inf_{\eta \in \mathcal{H}^1(\Omega_e)} ||\delta u_e||^2_{\mathcal{H}^1(\Omega_e)}),
\end{align*}
\]

so that (47) is proved.

Next step, we prove (48). Differentiating \( \bar{g}_e \) with respect to (w.r.t.) \( t \) produces

\[
\begin{align*}
\frac{d\bar{g}_e(u)}{dt} &= \frac{\partial \bar{g}_e(u)}{\partial u} \frac{du}{dt}, \\
\frac{\partial \bar{g}_e}{\partial u} (u) &= -C_e^2 \frac{2uK^2}{(K^2 + u^2)^2} - C_e^2 \frac{2K}{(K + \phi(u))^2} \frac{\partial \phi}{\partial u} - C_3.
\end{align*}
\]
The derivative of \( \tilde{g}_e(u, u_e) \) w.r.t. \( t \) is

\[
\frac{d\tilde{g}_e(u, u_e)}{dt} = C_1^e (c'(t) + c'(t)) (\phi(u_e) - \phi(u))
\]

\[
- C_1^e P(t, \phi(u)) \left( \frac{\partial \phi}{\partial u_e} \frac{\partial u_e}{\partial t} - \frac{\partial \phi}{\partial u} \frac{\partial u}{\partial t} \right)
\]

\[
+ \frac{\partial \psi}{\partial u} \frac{\partial u_e}{\partial t} + \frac{\partial \psi}{\partial u_e} \frac{\partial u}{\partial t},
\]

where \( \psi = J_S(\phi(u), u_e) + J_{t,e} \), and

\[
\frac{\partial \psi}{\partial u} = C_2^e \frac{K_s}{(K_s + \phi(u))^2 \phi_m(u_e)} \frac{\partial \phi}{\partial u} - C_3^e.
\]

\[
\frac{\partial \psi}{\partial u_e} = - C_2^e (K_s + \phi(u)) \phi_m(u_e)^2 \frac{\partial \phi_m}{\partial u_e} + C_3^e.
\]

Then (46) can be differentiated w.r.t. \( t \) as

\[
\begin{align*}
\left \{ \begin{array}{l}
a_e \left( \frac{\partial \eta}{\partial t}, v \right) + \lambda \left( \frac{\partial \eta}{\partial t}, v \right) = - \frac{d\tilde{g}_e(u, u_e)}{dt} + \frac{d\tilde{g}_e(W, W_e)}{dt}, v > \Gamma \\
+ < \frac{dW_e}{dt} - \frac{d\tilde{g}_e(W)}{dt}, v > \partial \Omega,
\end{array} \right. \tag{50}
\end{align*}
\]

All terms in the derivatives of \( \tilde{g}_e(u) \) and \( \tilde{g}_e(u, u_e) \) w.r.t. \( t \), except \( \frac{d}{dt} J_R(\phi(u), \phi(u_e)) \), are Lipschitz continuous. \( \frac{d}{dt} J_R \) can be treated as in Lemma 2.1, which gives us

\[
\left \{ \begin{array}{l}
\frac{d\tilde{g}_e(u, u_e)}{dt} - \frac{d\tilde{g}_e(W, W_e)}{dt} \leq C_1 |\eta| \left| \frac{\partial u}{\partial t} \right| + C_2 \left( |\eta| + |\eta_e| + |\eta(0)| + \int_0^t |\eta(s)|ds \right)
\end{array} \right.
\]

\[
+ C_3 \left( |\eta(0)| + \int_0^t |\eta(s)|ds \right) \left| \frac{\partial \phi}{\partial u_e} \frac{\partial u_e}{\partial t} - \frac{\partial \phi}{\partial u} \frac{\partial u}{\partial t} \right|
\]

\[
+ C_3 |\eta| \left| \frac{\partial u}{\partial t} \right| + C_3 \left| \frac{\partial \phi}{\partial u} (W) \right| \left| \frac{\partial \eta}{\partial t} \right| + C_3 \left| \frac{\partial \phi}{\partial u_e} (W_e) \right| \left| \frac{\partial \eta_e}{\partial t} \right|
\]

\[
+ C_4 \left( |\eta| + |\eta_e| \right) \left| \frac{\partial u}{\partial t} \right| + C_5 \left( |\eta| + |\eta_e| \right) \left| \frac{\partial \psi}{\partial u_e} (W, W_e) \right| \left| \frac{\partial \eta_e}{\partial t} \right|
\]

where \( \frac{\partial \phi}{\partial u}, \frac{\partial \phi}{\partial u_e}, \frac{\partial \phi}{\partial u}, \frac{\partial \phi}{\partial u_e} \) are bounded from the definitions of \( \phi(\cdot) \) in Section 4.1 and \( \phi_m(\cdot) \) in Section 4. Similar as the estimates for \( \eta, \eta_e, \) (48) can be obtained. \( \Box \)
5. Error Estimate for the Semi-discrete Galerkin Method

Without further notice, in the sequel, we use the modified system (change \( f(b, u) \) to \( f(\phi(b), \phi(u)) \), \( g_c(u) \) to \( g_c(u) \) and \( g_c(u, u_e) \) to \( g_c(u, u_e) \)) as in Section 4 to obtain the error analysis since it has the same solution as the original system, see a similar proof in Theorem 3.2. Letting \( U(t), U_b(t) \in S_k(\Omega_e) \), \( U_e(t) \in S_k(\Omega_e) \), for \( t \in [0, T] \) and \( v, v_b \in S_k(\Omega_e), v_e \in S_k(\Omega_e) \), the semi-discrete form of the model is given as

\[
\begin{aligned}
(\partial_t U, v) + a_e(U, v) &= <g_c(U), v >_{\partial \Omega} - <g_c(U, U_e), v >_{\Gamma} + (f(U_b, U), v) \\
(\partial_t U_b, v_b) &= (f(U_b, U), v_b) \\
(\partial_t U_e, v_e) &= <g_c(U, U_e), v_e >_{\Gamma} + \lambda(\varphi - W_e, v_e) - (\partial_t \varphi, v_e).
\end{aligned}
\]  

(51)

Then from the model equations (1)-(9) and the nonlinear projection (46), we have

\[
\begin{aligned}
(\partial_t W, v) + a_e(W, v) &= <g_c(W), v >_{\partial \Omega} - <g_c(W, W_e), v >_{\Gamma} + (f(W_b, W), v) \\
(\partial_t W_b, v_b) &= (f(W_b, W), v_b) \\
(\partial_t W_e, v_e) &= (f(W_b, W), v_b).
\end{aligned}
\]  

(52)

where \( \varphi = u - W, \varphi_b = b - W_b, \varphi_e = u_e - W_e \), and \( W_b(t) \in S_k(\Omega_e) \) is the Galerkin Projection of \( b \) from \( (D_b \nabla (b - W_b), \nabla v_b) + (b - W_b, v_b) = 0 \). Letting \( e = u - U, e_b = b - U_b, e_e = u_e - U_e \), we get the following theorem:

**Theorem 5.1.** If the exact solutions \( u, b, u_e \) for (1)-(9) are smooth enough, then with \( P_k \) elements, \( k \geq 1 \), and appropriately chosen \( U(0), U_e(0), U_b(0) \), we have

\[
\|e\|^2_{\infty, 0} + \|e_b\|^2_{\infty, 0} + \|e_e\|^2_{\infty, 0} + \int_0^T \|\nabla \xi(s)\|^2 + \|\nabla e_b(s)\|^2 + \|\nabla e_e(s)\|^2 ds \\
\leq Ch^{2k}(\|u\|^2_{\infty, k+1} + \|\partial_t u\|^2_{\infty, k+1} + \|u_b\|^2_{\infty, k+1} + \|\partial_t b\|^2_{\infty, k+1} \\
+ \|u_e\|^2_{\infty, k+1} + \|\partial_t u_e\|^2_{\infty, k+1}),
\]

where \( h \) is the mesh size, \( C \) does not depend on \( h \).
Proof. Letting $\xi = W - U$, $\xi_b = W_b - U_b$, $\xi_e = W_e - U_e$ and $\eta = u - W$, $\eta_b = b - W_b$, $\eta_e = u_e - W_e$, subtracting (51) from (52), we have

\[
\begin{aligned}
&\{ (\partial_t \xi, v) + a_e(\xi, v) \\
= & <g_e(W) - g_e(U), v >_{\partial \Omega} - <g_e(W,W_e) - g_e(U,U_e), v >_{\Gamma} \\
+ & (f(W_b,W) - f(U_b,U), v) \\
+ & \lambda(\eta, v) - (\partial_t \eta, v) + (f(b, u) - f(W_b,W), v),
\end{aligned}
\]

\[
\begin{aligned}
(\partial_t \xi_b, v_b) + a_b(\xi_b, v_b) \\
= & (f(W_b,W) - f(U_b,U), v_b) + (\eta_b, v_b) \\
- & (\partial_t \eta_b, v_b) + (f(b, u) - f(W_b,W), v_b),
\end{aligned}
\]

\[
(\partial_t \xi_e, v_e) + a_e(\xi_e, v_e) = <g_e(W,W_e) - g_e(U,U_e), v_e >_{\Gamma} + \lambda(\eta_e, v_e) - (\partial_t \eta_e, v_e).
\]

From Lemma 2.2 and letting $W(0) = U(0)$, we have

\[
|g_e(W) - g_e(U)| \leq K_1|\xi|,
\]

\[
|g_e(W,W_e) - g_e(U,U_e)| \leq K_2 \left( |\xi| + |\xi_e| + \int_0^t |\xi(s)|ds \right),
\]

\[
|f(W_b,W) - f(U_b,U)| \leq K_3(|\xi_b| + |\xi_e|).
\]

Then in (53), let $v = \xi$, $v_b = \xi_b$, $v_e = \xi_e$, we obtain (57) - (59):

\[
\frac{1}{2} \frac{d}{dt} |\xi|^2 + D_e |\nabla \xi|^2 \\
\leq C_1 \left( |\xi| \|x\|_{L^2(\partial \Omega)} + |\xi| \|x\|_{H^1(\Gamma)} + |\xi_e| \|x\|_{H^1(\Gamma)} + \int_0^t |\xi(s)| \|x\|_{H^1(\Gamma)}ds \right) \\
+ C_1 \left( \|\xi_b\|^2 + \|\xi\|^2 \right) \\
+ \frac{\lambda + K_3}{2} \|\eta\|^2 + \frac{1}{2} \|\partial_t \eta\|^2 + \frac{K_3}{2} \|\eta_b\|^2,
\]

\[
\frac{1}{2} \frac{d}{dt} |\xi_b|^2 + D_b |\nabla \xi_b|^2 \leq C_1 \left( \|\xi_b\|^2 + \|\xi\|^2 \right) \\
+ \frac{1 + K_3}{2} \|\eta_b\|^2 + \frac{1}{2} \|\partial_t \eta_b\|^2 + \frac{K_3}{2} \|\eta_b\|^2,
\]

\[
\frac{1}{2} \frac{d}{dt} |\xi_e|^2 + D_e |\nabla \xi_e|^2 \\
\leq C_3 \left( |\xi_e| \|x\|_{L^2(\Gamma)} + |\xi_e| \|x\|_{H^1(\Gamma)} + \int_0^t \|\xi(s)| \|x\|_{H^1(\Gamma)}ds + \|\xi_e\|^2 \right) \\
+ \frac{\lambda}{2} \|\eta_e\|^2 + \frac{1}{2} \|\partial_t \eta_e\|^2.
\]
The sum of (57), (58) and (59) gives the following inequality:

\[
\frac{1}{2} \frac{d}{dt} (\|\xi\|^2 + \|\xi_b\|^2 + \|\xi_e\|^2) + D_e \|\nabla \xi\|^2 + D_{\xi_b} \|\nabla \xi_b\|^2 + D_{\xi_e} \|\nabla \xi_e\|^2 \\
\leq C_1 \left(\|\xi\|^2_{L^2(\Omega)} + \|\xi_b\|^2_{L^2(\Omega)} + \|\xi_e\|^2_{L^2(\Omega)} + \int_0^t \|\xi(s)\|^2_{L^2(\Omega)} ds\right) \\
+ C_2 \left(\|\xi_b\|^2 + \|\xi\|^2 + \|\xi_e\|^2\right) \\
+ C_3 \left(\|\eta\|^2 + \|\partial_t \eta\|^2 + \|\eta_b\|^2 + \|\partial_t \eta_b\|^2 + \|\eta_e\|^2 + \|\partial_t \eta_e\|^2\right).
\]

(60)

By Lemma 2.3 and

\[
\int_0^t \int_0^s \|\xi(t)\|^2_{L^2(\Omega)} ds dt \leq \int_0^t \int_0^s \|\xi(s)\|^2_{L^2(\Omega)} ds dt \leq T \int_0^t \|\xi(s)\|^2_{L^2(\Omega)} ds
\]

from (60), we have

\[
\|\xi(t)\|^2 + \|\xi_b(t)\|^2 + \|\xi_e(t)\|^2 + \int_0^t \|\nabla \xi(s)\|^2 + \|\nabla \xi_b(s)\|^2 + \|\nabla \xi_e(s)\|^2 ds \\
\leq C_1 \int_0^t \|\xi_b(s)\|^2 + \|\xi(s)\|^2 + \|\xi_e(s)\|^2 ds \\
+ C_2 \int_0^t \|\eta\|^2 + \|\partial_t \eta\|^2 + \|\eta_b\|^2 + \|\partial_t \eta_b\|^2 + \|\eta_e\|^2 + \|\partial_t \eta_e\|^2 ds.
\]

(61)

From (61), by Gronwall’s Lemma, the following estimate can be obtained:

\[
\|\xi(t)\|^2 + \|\xi_b(t)\|^2 + \|\xi_e(t)\|^2 \\
+ \int_0^t \|\nabla \xi(s)\|^2 + \|\nabla \xi_b(s)\|^2 + \|\nabla \xi_e(s)\|^2 ds \\
\leq C \int_0^t \|\eta\|^2 + \|\partial_t \eta\|^2 + \|\eta_b\|^2 + \|\partial_t \eta_b\|^2 + \|\eta_e\|^2 + \|\partial_t \eta_e\|^2 ds,
\]

then by \( \xi = e - \eta \), \( \xi_b = e_b - \eta_b \), \( \xi_e = e_e - \eta_e \), we have

\[
\|e\|^2_{L^2(\Omega)} + \|e_b\|^2_{L^2(\Omega)} + \|e_e\|^2_{L^2(\Omega)} + \int_0^T \|\nabla e(s)\|^2 + \|\nabla e_b(s)\|^2 + \|\nabla e_e(s)\|^2 ds \\
\leq C \left(\|\eta\|^2_{L^2(\Omega)} + \|\partial_t \eta\|^2_{L^2(\Omega)} + \|\eta_b\|^2_{L^2(\Omega)} + \|\partial_t \eta_b\|^2_{L^2(\Omega)} + \|\eta_e\|^2_{L^2(\Omega)} + \|\partial_t \eta_e\|^2_{L^2(\Omega)}\right),
\]

(62)

and with Theorem 4.1, the proof is completed. □
6. Error Estimate for the Fully Discrete Implicit-Explicit Scheme

We define \( d_t U^{n+1} = (U^{n+1} - U^n)/\Delta t \), where \( \Delta t = T/N \), \( N \) is a positive integer, \( n = 0, 1, 2, \ldots, N - 1 \), \( U^n \in S_k(\Omega_e) \). Also \( d_t U^{n+1}_b \), \( d_t U^{n+1}_e \) can be defined similarly, where \( U^n_b \in S_k(\Omega_e) \), \( U^n_e \in S_k(\Omega_e) \). Then let \( v, v_b, v_e \in S_k(\Omega_e) \), \( v \in S_k(\Omega_e) \) and \( t_n = n\Delta t \), we have the fully discrete form of the model:

\[
\begin{align*}
(d_t U^{n+1}_b, v_b) + a_b(U^{n+1}_b, v_b) &= (f(U^n_b, U^n), v_b) \\
(d_t U^{n+1}_e, v_e) + a_e(U^{n+1}_e, v_e) &= (f(U^n_e, U^n), v_e) \\
(d_t U^{n+1}_b, v_e) + a_b(U^{n+1}_b, v_e) + a_e(U^{n+1}_e, v_e) &= (f(U^n_b, U^n), v_e) \\
&= g(U^n, v_e) \\
\end{align*}
\]

(63)

for the ODE part, we employ \( U_b(t, x) = \sum_{i=0}^{n} \phi_i(t) U_i(x) \) for \( 0 \leq t \leq t_n \), where \( \phi_i \) is the one-dimensional hat function and \( \phi_i(t_i) = 1 \). Let \( e^n = u(t_n) - U^n \), \( e^n_b = b(t_n) - U^n_b \), \( e^n_e = u_e(t_n) - U^n_e \), where \( u, b, u_e \) are the exact solutions for \([1]-[9]\), then we have the following theorem:

**Theorem 6.1.** If the exact solutions \( u, b, u_e \) are sufficiently smooth, then with \( P_h \) elements, \( k \geq 1 \), appropriately chosen \( U^0, U^0_b, U^0_e \), and sufficiently small \( \Delta t \) which doesn’t depend on the spatial mesh size, for any \( n \leq N - 1 \), we have

\[
\begin{align*}
\|e^{n+1}\|^2 + \|e^{n+1}_b\|^2 + \|e^{n+1}_e\|^2 \\
&+ \Delta t \sum_{i=1}^{n+1} \|\nabla e^{e_i}\|^2 + \Delta t \sum_{i=1}^{n+1} \|\nabla e^{e_b_i}\|^2 + \Delta t \sum_{i=1}^{n+1} \|\nabla e^{e_e_i}\|^2 \\
&\leq C(\Delta t^2 + h^{2k}),
\end{align*}
\]

where \( \Delta t \) is the time-step size, \( h \) is the mesh size, \( C \) does not depend on \( n, h \) and \( \Delta t \).

**Proof.** Let \( u^n = u(t_n), d_t u^{n+1} = (u^{n+1} - u^n)/\Delta t \) and similarly we have \( d_t \eta^{n+1}_b, d_t \eta^{n+1}_e, d_t u^{n+1}_e \), where \( \eta^n = u(t_n) - W(t_n), \eta^n_b = b(t_n) - W_b(t_n), \eta^n_e = u_e(t_n) - W_e(t_n) \). Then \( W, W_b, W_e \) are the previously defined Galerkin projections for \( u, b, u_e \). Then we have

\[
\begin{align*}
(d_t W^{n+1}, v) + a_e(W^{n+1}, v) &= <g(W^n), v>_{\partial \Omega} \\
&= <g(W^n, W^n), v >_{\gamma} \\
&+ (f(W^n_b, W^n), v) + E^{n+1}_b(v), \\
(d_t W^{n+1}_b, v_b) + a_b(W^{n+1}_b, v_b) &= (f(W^n_b, W^n), v_b) + E^{n+1}_b(v_b), \\
(d_t W^{n+1}_e, v_e) + a_e(W^{n+1}_e, v_e) &= (f(W^n_e, W^n), v_e) + E^{n+1}_e(v_e),
\end{align*}
\]

(64)
where
\[ E^{n+1}(v) = g_e(W^{n+1}) - g_e(W^n), v > 0 \]
\[ - < g_e(W^{n+1}, W^{n+1}) - g_e(W^n, W^n), v > \]
\[ + (f(W_b^{n+1}, W^{n+1}) - f(W_b^n, W^n), v) - (d_t\eta^{n+1}, v) \]
\[ + (d_tu^{n+1} - \partial_t u^{n+1}, v) + \lambda(\eta^{n+1}, v) \]
\[ + (f(b^{n+1}, u^{n+1}) - f(W_b^{n+1}, W^{n+1}), v), \]
\[ E^{n+1}(v_b) = (f(W_b^{n+1}, W^{n+1}) - f(W_b^n, W^n), v_b) - (d_t\eta_b^{n+1}, v_b) \]
\[ + (d_t b^{n+1} - \partial_t b^{n+1}, v_b) + (\eta_b^{n+1}, v_b) \]
\[ + (f(b^{n+1}, u^{n+1}) - f(W_b^{n+1}, W^{n+1}), v_b), \]
\[ E^{n+1}(v_e) = < g_e(W^{n+1}, W^{n+1}) - g_e(W^n, W^n), v_e > - (d_t\eta_e^{n+1}, v_e) \]
\[ + (d_t u_e^{n+1} - \partial_t u_e^{n+1}, v_e) + \lambda(\eta_e^{n+1}, v_e). \]

Subtracting equations (63) from (64), letting \( \xi^{n+1} = W^{n+1} - U^{n+1}, \xi_b^{n+1} = W_b^{n+1} - U_b^{n+1} \)
\( \xi_e^{n+1} = W_e^{n+1} - U_e^{n+1} \), and choosing \( v = \xi^{n+1}, v_b = \xi_b^{n+1}, v_e = \xi_e^{n+1} \), with the definition \( W_h(t, x) := \sum_{i=0}^n \phi_i(t)W(t_i, x) \) and Lemma 2.2, we have the following equations (65), (66) and (67) respectively.

\[ \frac{\|\xi^{n+1}\|^2}{2\Delta t} - \frac{\|\xi^n\|^2}{2\Delta t} + D_c\|\nabla \xi^{n+1}\|^2 \]
\[ \leq C_1 \left( \|\xi^n\|^2_{L^2(\Omega)} + \|\xi^n\|^2_{L^2(\Gamma)} + \|\xi^n\|^2_{L^2(\Gamma)} + \int_0^{t_n} \|(W_h - U_h)(s)\|^2_{L^2(\Gamma)} ds \right) \]
\[ + C_1 (\|\xi^n_b\|^2 + \|\xi^n\|^2 + \|\xi^{n+1}\|^2) \]
\[ + C_1 (\|\xi^{n+1}\|^2 + \|\xi^{n+1}\|^2 + \|\xi^{n+1}\|^2) + E^{n+1}(\xi^{n+1}) \]
\[ + C_1 \int_0^{t_n} \|(W - W_h)(s)\|^2_{L^2(\Gamma)} ds, \]

\[ \frac{\|\xi_b^{n+1}\|^2}{2\Delta t} - \frac{\|\xi_b^n\|^2}{2\Delta t} + D_b\|\nabla \xi_b^{n+1}\|^2 \]
\[ \leq C_1 (\|\xi_b^n\|^2 + \|\xi^n\|^2 + \|\xi_b^{n+1}\|^2) + E_b^{n+1}(\xi_b^{n+1}), \]

\[ \frac{\|\xi_e^{n+1}\|^2}{2\Delta t} - \frac{\|\xi_e^n\|^2}{2\Delta t} + D_e\|\nabla \xi_e^{n+1}\|^2 \]
\[ \leq C_3 \left( \|\xi^n\|^2_{L^2(\Gamma)} + \|\xi^n\|^2_{L^2(\Gamma)} + \int_0^{t_n} \|(W_h - U_h)(s)\|^2_{L^2(\Gamma)} ds \right) \]
\[ + C_3 \|\xi^{n+1}\|^2 + E_e^{n+1}(\xi_e^{n+1}) \]
\[ + C_3 \int_0^{t_n} \|(W - W_h)(s)\|^2_{L^2(\Gamma)} ds. \]
Adding the equations (65), (66) and (67) correspondingly

\[
\frac{\|\xi^{n+1}\|^2}{2\Delta t} - \frac{\|\xi^0\|^2}{2\Delta t} + D_c \sum_{l=1}^{n+1} \|\nabla \xi^l\|^2 \\
\leq C_1 \sum_{l=0}^{n} \left( \|\xi^l\|^2_{L^2(\Omega)} + \|\xi^l\|^2_{L^2(\Gamma)} + \|\xi^l\|^2_{L^2(\Omega)} + \int_0^{t_l} \|(W_h - U_h)(s)\|^2_{L^2(\Omega)} \, ds \right) \\
+ C_1 \sum_{l=0}^{n} \left( \|\xi^l\|^2 + \|\xi^l\|^2 + \|\xi^{l+1}\|^2 \right) \\
+ C_3 \sum_{l=0}^{n} \|\xi^{l+1}\|^2 + \int_0^{t_l} \|(W - W_h)(s)\|^2_{L^2(\Omega)} \, ds,
\]

(68)

\[
\frac{\|\xi^{n+1}\|^2}{2\Delta t} - \frac{\|\xi^0\|^2}{2\Delta t} + D_b \sum_{l=1}^{n+1} \|\nabla \xi^l_b\|^2 \\
\leq C_1 \sum_{l=0}^{n} \left( \|\xi^l\|^2_{L^2(\Omega)} + \|\xi^l\|^2_{L^2(\Gamma)} + \|\xi^l\|^2_{L^2(\Omega)} + \int_0^{t_l} \|(W_h - U_h)(s)\|^2_{L^2(\Omega)} \, ds \right) \\
+ C_1 \sum_{l=0}^{n} \left( \|\xi^l\|^2 + \|\xi^l\|^2 + \|\xi^{l+1}\|^2 \right) + C_3 \sum_{l=0}^{n} \int_0^{t_l} \|(W - W_h)(s)\|^2_{L^2(\Omega)} \, ds.
\]

(69)

In the right hand side of (68), the following estimates (71) to (74) can be obtained. Notice that each \(\phi_i(s), i = 0, \cdots, l\), has a compact support and the product \(\phi_i(s)\phi_j(s) = 0\), if \(|j - i| > 1\), so that we have

\[
\int_0^{t_l} \|(W_h - U_h)(s)\|^2_{L^2(\Omega)} \, ds = \int_0^{t_l} \left| \sum_{i=0}^{l} \phi_i(s)\xi^l\right|^2_{L^2(\Omega)} \, ds \\
\leq \int_0^{t_l} 3 \sum_{i=0}^{l} |\phi_i(s)|^2 \|\xi^l\|^2_{L^2(\Omega)} \, ds \\
\leq 2\Delta t \sum_{i=0}^{l} \|\xi^l\|^2_{L^2(\Omega)},
\]

(71)
where \( \int_0^{t_i} 3|\phi_i(s)|^2ds \leq 2\Delta t \). Then from (71), with the Trace Theorem, we get
\[
\sum_{l=0}^{n} \int_0^{t_i} \|(W_h - U_h)(s)\|^2_{L^2(\Omega)} ds \leq \sum_{l=0}^{n} 2\Delta t \sum_{i=0}^{n} \|\xi^i\|^2_{L^2(\Omega)} \\
\leq 2T \sum_{i=0}^{n} \|\xi^i\|^2_{L^2(\Omega)} \\
\leq C \sum_{i=0}^{n} (\|\xi^i\| + \|\nabla\xi^i\|).
\]

By Lemma 2.3 we have
\[
\Delta t C \sum_{l=0}^{n} (\|\xi^{l+1}\|^2_{L^2(\partial\Omega)} + \|\xi^{l+1}\|^2_{L^2(\Omega)}) \leq \frac{\Delta t D_c}{8} \sum_{l=1}^{n+1} \|\nabla\xi^l\|^2 \\
+ \Delta t C\|\xi^{n+1}\|^2 + \Delta t C \sum_{l=1}^{n} \|\xi^l\|^2,
\]
the first and second terms in the right hand side of (73) can be canceled in (68) if \( \Delta t \) is sufficiently small, however, this small \( \Delta t \) doesn’t depend on the spatial mesh size. Then with Lemma 2.2, Lemma 2.3, by the estimates of \( \partial_t\eta \), \( \partial_t\eta_e \) in Theorem 4.1 and the estimates for \( \partial_t\eta_b \), which is easier to obtain from the definition of \( W_b \) in Section 5, we know \( \partial_t W, \partial_t W_e \) and \( \partial_t W_b \) are bounded with \( H^1 \) norm, so that
\[
\sum_{l=0}^{n} E^{l+1}(\xi^{l+1}) \leq C\Delta t + C \frac{h^{2k}}{\Delta t} + \frac{D_c}{8} \sum_{l=1}^{n+1} \|\nabla\xi^l\|^2 \\
+ C\|\xi^{n+1}\|^2 + C \sum_{l=1}^{n} \|\xi^l\|^2,
\]
where \( C \) is a positive constant and doesn’t depend on \( n \). Other terms on the right-hand side of (68) can be treated similarly.
So that from (68) and the estimates (72) to (74), we have (75)
\[
\frac{1}{2} \|\xi^{n+1}\|^2 + 3D_c \Delta t \sum_{l=1}^{n+1} \|\nabla\xi^l\|^2 \\
\leq C_{c1} \Delta t \sum_{l=0}^{n} \|\xi^l\|^2_{L^2(\Omega)} + C_{c2} 2\Delta t \sum_{l=0}^{n} \|\xi^l_b\|^2 + C_{c3} \Delta t \sum_{l=0}^{n} \|\xi^l_e\|^2 \\
+ \frac{D_c}{8} \Delta t \sum_{l=0}^{n} \|\nabla\xi^l_b\|^2 + C_{c4} \|\xi^0\|^2_{H^1(\Omega_c)} + C_{c}(\Delta t^2 + h^{2k}).
\]

23
From (69), with similar estimates as (68), we have (76)

\[
\frac{1}{2} \| \xi_{n+1}^b \|^2 + D_b \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^b \|^2 \\
\leq C_{b1} \Delta t \sum_{l=0}^{n} \| \xi_l^b \|^2 + C_{b2} \Delta t \sum_{l=0}^{n} \| \xi_l^c \|^2 + C_{b3} \| \xi_0^c \|_{H^1(\Omega_c)}^2 + C_b (\Delta t^2 + h^2k).
\]

From (70), with similar estimates as (68), we have (77)

\[
\frac{1}{2} \| \xi_{n+1}^e \|^2 + \frac{3D_e}{4} \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^e \|^2 \\
\leq C_{e1} \Delta t \sum_{l=0}^{n} \| \xi_l^e \|^2 + C_{e2} \Delta t \sum_{l=0}^{n} \| \xi_l^c \|^2 + \frac{D_e}{8} \Delta t \sum_{l=0}^{n} \| \xi_l^c \|^2 \\
+ C_{e3} \| \xi_0^c \|_{H^1(\Omega_c)}^2 + C_e (\Delta t^2 + h^2k).
\]

C, C_b, C_e in (75), (76) and (77) do not depend on \(n\).

Summing (75), (76) and (77), we have

\[
\| \xi_{n+1}^b \|^2 + \| \xi_{n+1}^c \|^2 + \| \xi_{n+1}^e \|^2 + \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^b \|^2 + \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^c \|^2 + \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^e \|^2 \\
\leq C_1 \Delta t \sum_{l=0}^{n} (\| \xi_l^b \|^2 + \| \xi_l^c \|^2 + \| \xi_l^e \|^2) \\
+ C_2 (\| \xi_0^b \|_{H^1(\Omega_c)}^2 + \| \xi_0^c \|_{H^1(\Omega_c)}^2 + \| \xi_0^c \|_{H^1(\Omega_c)}^2 + \Delta t^2 + h^2k).
\]

If \(\Delta t\) is small enough, by discrete Gronwall’s Inequality, the estimate below follows

\[
\| \xi_{n+1}^b \|^2 + \| \xi_{n+1}^c \|^2 + \| \xi_{n+1}^e \|^2 \\
+ \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^b \|^2 + \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^c \|^2 + \Delta t \sum_{l=1}^{n+1} \| \nabla \xi_l^e \|^2 \leq C (\Delta t^2 + h^2k),
\]

where \(C\) does not depend on \(n\), \(\Delta t\) and \(h\). Then by \(e^n = \xi^n + \eta^n\), \(e_b^n = \xi_b^n + \eta_b^n\), \(e_c^n = \xi_c^n + \eta_c^n\), and Theorem 4.1, we complete the proof.

\[\square\]

7. Numerical Experiments

In this section, we illustrate the convergence theorem for the fully discrete scheme (63) using Examples 1 and 2 below, and then apply the methodology to show the existence of \(Ca^{2+}\) wave propagation numerically in Example 3 and 4. The ODE system (12) plays the key role for calcium wave initiation and propagation, which is solved by backward Euler’s method. The numerical
schemes in this section are implemented in FreeFem++, see [31]. All presented examples are in 2D, but theorems and simulations are also valid in 3D.

**Example 1.** In this problem we consider two coupled PDEs with the unknowns \( u \) and \( u_e \):

\[
\begin{aligned}
\partial_t u - \Delta u &= f_1(x, y, t) \quad \text{on } \Omega_e \times (0, T) \\
\partial_t u_e - \Delta u_e &= f_2(x, y, t) \quad \text{on } \Omega_e \times (0, T)
\end{aligned}
\]

where \( T = 1.3 \) and the boundary conditions are: \( \partial_n u = g_1(x, y, t) \) on \( \partial \Omega \times (0, T) \) and

\[
\begin{aligned}
\partial_n u &= P(t, u)(u_e - u) + g_2(x, y, t) \quad \text{on } \Gamma \times (0, T) \\
\partial_n u_e &= P(t, u)(u - u_e) + g_3(x, y, t) \quad \text{on } \Gamma \times (0, T)
\end{aligned}
\]

Here, let \((n_x, n_y)\) be the unit outer normal vector on \( \partial \Omega_e \) for \( g_1, g_2 \); on \( \Gamma \) for \( g_3 \), then the exact solution \( u, u_e \) and corresponding functions are listed below:

| \( u \)    | \( e^{x^2+y^2+4t}/10 \) |
| \( u_e \)  | \( e^{x^2+y^2+4t}/8 \)  |
| \( f_1 \)  | \( -e^{x^2+y^2+4t}(x^2 + y^2)/40 \) |
| \( f_2 \)  | \( e^{x^2+y^2}(\cos(t) - 2(\sin(t) + 2))/8 \) |
| \( g_1 \)  | \( n_x e^{x^2+y^2+4t}x/20 + n_y e^{x^2+y^2+4t}y/20 \) |
| \( g_2 \)  | \( n_x e^{x^2+y^2+4t} x/20 + n_y e^{x^2+y^2+4t} y/20 - P(t, u)(u_e - u) \) |
| \( g_3 \)  | \( n_x e^{x^2+y^2}(\sin t + 2)/8 + n_y e^{x^2+y^2}(\sin t + 2)/8 + P(t, u)(u_e - u) \) |

The coefficients in ODE (12) are taken from [17]:

\[
k_a^- = 28.8, \quad k_a^+ = 1500, \quad k_b^- = 385.9, \quad k_b^+ = 1500, \quad k_c^- = 0.1, \quad k_c^+ = 1.75
\]  

(81)

The initial conditions for (12) are chosen as: \( c_1(0) = 0.5, \ o(0) = 0, \ c_2(0) = 0.5 \).

**Example 2.** In this example we consider three coupled PDEs with unknowns \( u, b \) and \( u_e \):

\[
\begin{aligned}
\partial_t u - \Delta u &= f_1(x, y, t) - bu \quad \text{on } \Omega_e \times (0, T) \\
\partial_t b - \Delta b &= f_2(x, y, t) - bu \quad \text{on } \Omega_e \times (0, T) \\
\partial_t u_e - \Delta u_e &= f_3(x, y, t) \quad \text{on } \Omega_e \times (0, T)
\end{aligned}
\]

where \( T = 1.3 \), and the boundary conditions are: \( \partial_n u = g_1(x, y, t) \) on \( \partial \Omega \times (0, T) \), \( \partial_n b = g_2(x, y, t) \) on \( \partial \Omega_e \times (0, T) \) and

\[
\begin{aligned}
\partial_n u &= P(t, u)(u_e - u) - \frac{u}{1 + u} u_e + g_3(x, y, t) \quad \text{on } \Gamma \times (0, T) \\
\partial_n u_e &= P(t, u)(u - u_e) + \frac{u}{1 + u} u_e + g_4(x, y, t) \quad \text{on } \Gamma \times (0, T)
\end{aligned}
\]

Here, let \((n_x, n_y)\) be the unit outer normal vector on \( \partial \Omega_e \) for \( g_1, g_2, g_3 \); on \( \Gamma \) for \( g_4 \), then the exact solution \( u, b, u_e \) and corresponding functions are listed below:
\begin{align*}
\frac{\partial u}{\partial t} - \Delta u &= 0 \quad \text{on } \Omega \times (0, T) \\
\partial_n u_e - \Delta u_e &= 0 \quad \text{on } \Omega_e \times (0, T)
\end{align*}

where \( T = 12 \) and the boundary conditions are:

\begin{align*}
\partial_n u &= C_3(1000 - u) - C_2\frac{u}{1 + u} - C_1\frac{u^2}{1 + u^2} + f(x, y, t) \quad \text{on } \partial\Omega \times (0, T) \\
\partial_n u &= C_1P(t, u)(u_e - u) - C_2\frac{u}{(2 + u)u_e} + C_5(u_e - u) \quad \text{on } \Phi \times (0, T) \\
\partial_n u_e &= C_1P(t, u)(u - u_e) + C_5\frac{u}{(2 + u)u_e} - C_5(u_e - u) \quad \text{on } \Phi \times (0, T)
\end{align*}

The initial conditions are \( u(x, y, 0) = 0.05, u_e(x, y, 0) = 180 \), the ODE system is the same as in Example 1, and the initial conditions of the ODE are \( c_1(0) = 0.798, c_5(0) = 0, c_2(0) = 0.202 \). In [66], the value 1,000 is the extracellular \( \text{Ca}^{2+} \) concentration, and \( f \) is a calcium influx function: \( f(x, y, t) = 3 \) if \( 0.05 \leq t \leq 0.65 \) and \( y - x \geq 2.5; f(x, y, t) = 0 \) elsewhere. The coefficients in [66] to [88] are: \( C_1 = 0.17, C_3 = 1/150, C_2 = 8853.54, C_3 = 1/540000, C_1 = C_2 = 19954C_3 \).

Example 3 is constructed to show the initiation and propagation of a calcium wave which plays a critical role in neuronal signal processing, see Figure 4.
the computation, we use a similar geometry as in Examples 1 and 2. The radii of the two circles, with center \((0,0)\), are 1 and 2, but with different meshes and elements, where \(T = 12\), \(\Delta t = 0.00375\), and the spatial mesh size is \(h = \pi/24\) with \(P_3\) elements in space. With the help of Figure 3, a calcium wave can be described as follows. An extracellular stimulus produces \(Ca^{2+}\) influx across the outer interface (the plasma membrane) raising the calcium concentration in parts of cytosol (\(\Omega_c\)) and ER (\(\Omega_e\)) see Figures 4(a), 4(b). In this example, the influx goes from 0.05s to 0.65s. Then, an increased concentration activates the release of \(Ca^{2+}\) from the ER at \(t = 0.72s\), see Figure 4(c) which in turn generates the calcium spike and thus mediates global activation of the cell, see Figures 4(d) to 4(g). The calcium concentration reaches its peak around 3.12s in Figure 4(h) from the color bar 4(m), \(u\) varies from 0.05 \(\mu\)M to value greater than 1.5 \(\mu\)M. Meanwhile, \(u_e\) decreases to the value around 176 \(\mu\)M. After reaching the peak, \(u\) decreases and \(u_e\) increases to the initial state, see 4(i) to 4(l). The term \(10\) is essential for generating calcium wave, without the ODE system, there is no calcium wave. Figure 5 shows the open probability function \(P(t, u)\) in equation (11) for RyR channels on the ER membrane. It ranges from 0 to 0.81. Instability of the scheme (63) can be observed with time step size larger than 0.00375.

![Figure 2: Meshes in which the black region is \(\Omega_c\), the brown region is \(\Omega_e\): (a) coarse with mesh size \(\pi/8\); (b) refined mesh with mesh size \(\pi/16\). The radius of the larger circle is 2, radius of the smaller one is 1.](image)

**Example 4.** In this example we present a full system with different coefficients, taken from [2], which produces \(Ca^{2+}\) waves. Units were adjusted so that \(t\) has unit \(s\), \(u, u_e\) have unit \(\mu\)M:

\[
\begin{align*}
\partial_t u - 220 \Delta u &= f(b, u) & \text{on } \Omega_c \times (0,T) \\
\partial_t b - 20 \Delta b &= f(b, u) & \text{on } \Omega_c \times (0,T) \\
\partial_t u_e - 220 \Delta u_e &= 0 & \text{on } \Omega_e \times (0,T)
\end{align*}
\]

(89)

where \(T = 80\), \(f(b, u) = K_b^- (b^0 - b) - K_b^+ bu\), \(\partial_n b = 0\) on \(\partial \Omega_c\), and other
boundary conditions are:

\[ \partial_t u = C_3(1000 - u) - \frac{C_2 u}{1.8 + u} - \frac{C_1 u^2}{0.06^2 + u^2} + g(x, y, t) \quad \text{on } \partial \Omega \times (0, T) \] (90)

\[ \partial_t u = C_1^e P(t, u)(u - u_e) - C_2^e \frac{u}{(0.18 + u)u_e} + C_3^e (u_e - u) \quad \text{on } \partial \Omega \times (0, T) \] (91)

\[ \partial_t u_e = C_1^e P(t, u)(u - u_e) + C_2^e \frac{u}{(0.18 + u)u_e} - C_3^e (u_e - u) \quad \text{on } \partial \Omega \times (0, T) \] (92)

The initial conditions are \( u(x, y, 0) = 0.05, b(x, y, 0) = 37, u_e(x, y, 0) = 250 \), in \( f(b, u), b^0 = 40, K_b^- = 16.65, K_b^+ = 27 \). The ODE system is the same as in Example 1, and the initial conditions of the ODE are \( c_1(0) = 0.994, o(0) = 1.572 \times 10^{-7}, c_2(0) = 5.6625 \times 10^{-3} \). In (90), the value 1,000 is the extracellular Ca\(^{2+}\) concentration, and \( g \) is a calcium influx function:

\[
g(x, y, t) = \begin{cases} 
240e^{-0.01/\left(0.01-\left(t-0.2)^2\right)\right)+1} & \text{if } 0.1 < t < 0.3 \text{ and } y - x \geq 2.5; \\
0 & \text{elsewhere.}
\end{cases}
\]

The coefficients in (90) to (92) are: \( C_1^e = 0.829468, C_2^e = 11000, C_3^e = 0.038, C_1 = 8.5, C_2 = 37.6, C_3 = 0.0045 \).

Example 4 is constructed to show the initiation and propagation of the calcium wave in a full model, see Figure 6. For computation, we use a similar geometry as in Examples 3. The radii of the two circles, with center (0,0), are 1.2 and 2, but with different meshes and \( P_1 \) elements, where \( T = 80, \Delta t = 0.01/16, \) and the spatial mesh size is \( h = \pi/32 \). Due to larger diffusion coefficients and the buffer \( b \), propagation of the calcium is much faster than Example 3, but the recovery is slower. Here, we don’t show the graph of \( b \) which varies from 2 to 38, since it’s less important. Figure 7 shows the open probability function \( P(t, u) \) in equation (11) for RyR channels on the ER membrane. It ranges from 0 to 0.96. Instability of the scheme (63) can be observed with time step size larger than 0.01/16.
Figure 4: Initiation (a)-(b), propagation (c)-(h) and recovery (i)-(l) of the calcium wave in a 2D cell. As in (l) - an equilibrium state, the black region is cytosol ($\Omega_c$), the brown region is ER ($\Omega_e$). $u$ and $u_e$ are the calcium concentrations in cytosol and ER respectively.

8. Conclusion

In this paper, we analyze the model of calcium dynamics in neurons with ER, obtain the existence, uniqueness and boundedness of the solution, and then propose an efficient implicit-explicit finite element scheme. The necessity of the ODE systems on interfaces is shown in Section 7. The focus on calcium dynamics is motivated by the fact that intracellular calcium signals in response to electrical events (e.g., action potentials) trigger a multitude of calcium regulated processes which are relevant in cellular development, learning, and cell survival. The complexity of the cellular calcium-regulating machinery typically prohibits a systematic experimental study and computational models are highly relevant in studying the effect of morphological and biophysical changes on calcium dynamics. Models, theorems and algorithms are well established for electrical models, however, calcium dynamics has not been extensively studied,
partly because lower-dimensional approximations are insufficient and detailed, high-resolution PDE-based simulations are required (integration of complex geometric structures of cells and intracellular organelles). Thus, 3D models are necessary to accurately capture calcium dynamics in cells and high-performance computing must be utilized. The $L^2$ error estimates, high order stable multi-step implicit-explicit schemes and a parallel implementation of the numerical methods for the 3D problem are part of ongoing work.
Figure 6: Initiation (a)-(b), propagation (c)-(e) and recovery (f)-(p) of the calcium wave in a 2D cell. As in (a), (p) - the equilibrium state, the black region is cytosol ($\Omega_c$), the dark-red region is ER ($\Omega_e$). $u$ and $u_e$ are the calcium concentrations in cytosol and ER respectively.

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Figure 7: The black region as in (l) is $\Omega_c^c$, the value is always 0 on $\Omega_c^c/\Upsilon$. Red color part on the inner circle (ER membrane) means the RyR channels are open. We can see that from (a)-(g), the open state propagates to the whole ER membrane which is faster compared with Example 3. From (h) to (l), the value of open probability decreases to the close state.

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