On the Global Dynamics of an Electroencephalographic Mean Field Model of the Neocortex

Farshad Shirani* Wassim M. Haddad† Rafael de la Llave‡

October 11, 2016

Abstract

This paper investigates the global dynamics of a mean field model of the electroencephalogram developed by Liley *et al.*, 2002. The model is presented as a system of coupled ordinary and partial differential equations with periodic boundary conditions. Existence, uniqueness, and regularity of weak and strong solutions of the model are established in appropriate function spaces, and the associated initial-boundary value problems are proved to be well-posed. Sufficient conditions are developed for the phase spaces of the model to ensure nonnegativity of certain quantities in the model, as required by their biophysical interpretation. It is shown that the semigroups of weak and strong solution operators possess bounded absorbing sets for the entire range of biophysical values of the parameters of the model. Challenges towards establishing a global attractor for the model are discussed and it is shown that there exist parameter values for which the constructed semidynamical systems do not posses a compact global attractor, due to the lack of assymptotic compactness property. Finally, instructive insights provided by the theoretical results of the paper on the computational analysis of the model are discussed.

1. Introduction

Inspired by the seminal work of Alan Hodgkin and Andrew Huxley on modeling the flow of ionic currents through the membrane of a giant nerve fiber, numerous biophysical and mathematical models have been developed towards understanding the neurophysiology of the central nervous system and the underlying mechanism of the various phenomena that emerge during its vital operation in the body; many of which still remain mysterious to researchers [16, 24, 39, 51]. In particular, exploring the core component of the central nervous system—the brain—substantial effort has been devoted to develop models at different levels of scope; from the *molecular and intercellular* level dealing with the enzymatic kinetics of neurotransmitter-receptor binding at ion channels and transportation of ions; to the *single cell and intracellural* level dealing with creation and transmission of action potential; to the *population and neuronal network* level dealing with the average behavior and synchronized activity of neuronal ensembles; to the *system level* dealing with systematic operation and interaction between cortical and subcortical components of the brain; and finally to the *behavioral and cognitive* level dealing with integrated mental activity and creation of the mind [1, 14, 21, 27, 28, 43, 45, 52].

*School of Aerospace Engineering, Georgia Institute of Technology, Atlanta, GA 30332
†School of Aerospace Engineering, Georgia Institute of Technology, Atlanta, GA 30332
‡School of Mathematics, Georgia Institute of Technology, Atlanta, GA 30332

As an effective methodology to develop models at the population and network level, mean field theory has been applied to construct approximate models for interconnected populations of neurons by averaging the effect of all other neurons on a given individual neuron inside the population. The resulting *averaged neuron* can be used to analyze the overall temproal behavior of a single population of neurons, leading to a *neural mass* model. Alternatively, the averaged neuron can be considered as a locally averaged component of a continuum of neural populations, leading to a spatio-temporal *mean field* model. These models are particularly useful in analyzing the electrophysiological activity of neuronal ensembles using local field potentials and electroencephalograms [9, 37, 40, 42].

The evolution equations that describe a mean field model of neural activity in the cortex are in the form of a system of partial differential equations, or a system of coupled ordinary and partial differential equations. The theory of infinite-dimensional dynamical systems is hence used to analyze the global dynamics and long-term behavior of these systems. The classical approach to this problem follows several steps. *First*, existence, uniqueness, and regularity of solutions are established for all positive times in appropriately chosen problem-dependent function spaces, and the well-posedness of the problem is confirmed. *Second*, a semidynamical framework is constructed over a positively invariant complete normed space—the phase space for the evolution of solutions—and is shown to posesses bounded absorbing sets. Asymptotic compactness of the semigroup of solution operators is then ensured to guarantee existence of a global attractor, which is a compact strictly invariant attracting set, and hence, contains all the information regarding the asymptotic behavior of the model. *Third*, the Hausdorff or fractal dimension of the global attractor is estimated to show that the attractor is finite dimensional, so that the asymptotic dynamics of the system is determined by a finite number of degrees of freedom. *Fourth*, the existence of an inertial manifold is established, which is a smooth finite dimensional inaviant manifold conatinig the global attractor. Consequently, the dynamics on the attractor can be presented by a finite set of ordinary differential equations and further characterized to give the overall picture of long-term behavior of the system [7, 23, 41, 48].

In this paper, we investigate the mean field model proposed in [33] for understanding the electrical activity in the neocortex as observed in the electroencephalogram (EEG). This model, which is comprised of a system of coupled ordinary and partial differential equations in a two-dimensional space, has been widely used in the literature to study the alpha- and gamma-band rhythmic activity in the cortex [3, 4], phase transition and burst suppression in cortical neurons during general anesthesia [6, 34, 46], the effect of anesthetic drugs on the EEG [2, 18], and epileptic seizures [29–32]. Open-source tools for numerical implementation of the model and computation of equilibria and time-periodic solutions are developed in [22]. Complexity of the dynamics of the model, including periodic and pseudo-periodic solutions, chaotic behavior, multistability, and bifurcation are studied in [10–12, 19, 20, 49, 50].

The above results, however, are mainly computational or involve approximate versions of the model. A rigorous analysis of the dynamics of the model in the infinite-dimensional dynamical system framework as outlined above is not available in the literature. In particular, the basic problems of well-posedness of the initial-boundary value problem associated to the model and the regularity of solutions remain uninvestigated. It is not known under what conditions, if any, the solutions of the model evolve partially nonnegatively for all time, which is required for certain physical quantities in the model. Solutions that take negative values for such quantities—even for a small interval of time in distant future—cannot depict a biophysically plausible dynamics of the electrical activity in the neocortex.

The aim of this paper is to study the global dynamics of the mean field model discussed above, ensure its biophysical plausibility, and to provide the basic analytical results required for characterization of the long-term dynamics of the model. Specifically, we follow the first two steps of the aforementioned classical analysis approach to investigate the problem of existence or nonexistence of a global attractor.

This paper is organized as follows. In Section 2, we introduce notation and recall key definitions necessary for developing the results in the paper. In Section 3, we present the mathematical structure of the model as a system of coupled ordinary-partial differential equations with initial values and periodic boundary conditions, preceded with a description of the anatomical structure of the neocortex and the physiological interactions that underly the construction of the model. Then, following the first step of the classical analysis approach, in Section 4 we prove existence and uniqueness of weak and strong solutions for the proposed initial value problem and analyze the regularity of these solutions.

As in the second step of the classical analysis, in Section 5 we define semigroups of solution operators and show their continuity properties. Moreover, we establish conditions on the phase spaces to ensure biophysical plausibility of the evolution of the solution under the associated semidynamical systems. In Section 6, we show that the semigroups of solution operators possess bounded absorbing sets for all possible values of the biophysical parameters of the model. In Section 7, we discuss challenges towards establishing a global attractor for the model, and in particular, we show that there exist sets of values for the biophysical parameters of the model such that the associated semigroups of solution operators do not possess a compact global attractor. We conclude the paper in Section 8 with a discussion on the results developed in the paper and their application to the computational analysis of the model.

2. Notation and Preliminaries

The notation used in this paper is fairly standard. Specifically, $\mathbb{R}^n$ denotes the n-dimensional real Euclidean space and $\mathbb{R}^{m\times n}$ denotes the space of real $m \times n$ matrices. A point $x \in \mathbb{R}^n$ is presented by the n-tuple $x = (x_1, \ldots, x_n)$ or, when it appears in matrix operations, by the column vector $x = \begin{bmatrix} x_1 & \cdots & x_n \end{bmatrix}^{\mathrm{T}}$, where $(\cdot)^{\mathrm{T}}$ denotes transpose. The nonnegative cone $\{x \in \mathbb{R}^n : x_j \geq 0 \text{ for } j = 1, \ldots, n\}$ is denoted by $\mathbb{R}^n_+$. A sequence of points in $\mathbb{R}^n$ is denoted by $\{x^{(l)}\}_{l=1}^{\infty}$, with the jth component of $x^{(l)}$ denoted by $x_j^{(l)}$. Moreover, the trace of a square matrix $A \in \mathbb{R}^{n\times n}$ is denoted by $\operatorname{tr} A$ and a block-diagonal matrix D with k blocks $D_1, \ldots, D_k$ is denoted by $\operatorname{diag}(D_1, \ldots, D_k)$. For $x, y \in \mathbb{R}^n$, we write $x \geq y$ to denote component-wise inequality, that is, $x_j \geq y_j$, $j = 1, \ldots, n$. For $A, B \in \mathbb{R}^{n\times n}$ we write $A \geq B$ to denote $A - B$ is positive semidefinite. Finally, we denote by $0_{n\times n}$ and $I_{n\times n}$ the zero and identity matrices in $\mathbb{R}^{n\times n}$, respectively. We write I for the identity operator in other vector spaces.

For an inner product space $\mathcal{U}$, we denote the associated inner product by $(\cdot,\cdot)_{\mathcal{U}}$ and the norm generated by the inner product by $\|\cdot\|_{\mathcal{U}}$. For a Hilbert space $\mathcal{U}$ we denote the standard pairing of $\mathcal{U}$ with its dual space $\mathcal{U}^*$ by $\langle\cdot,\cdot\rangle_{\mathcal{U}}$. In particular, for $\mathcal{U} = \mathbb{R}^n$ we write $(\cdot,\cdot)_{\mathbb{R}^n}$ and $\|\cdot\|_{\mathbb{R}^n}$ for the standard inner product and the Euclidean norm, respectively. Similarly, for $\mathcal{U} = \mathbb{R}^{m\times n}$ we write $(A, B)_{\mathbb{R}^{m\times n}}$ for the standard inner product and $\|A\|_{\mathbb{R}^{m\times n}}$ for the associated inner product norm. Moreover, we denote the 1-norm in $\mathbb{R}^n$ by $\|\cdot\|_1$ and the ∞-norm in $\mathbb{R}^n$ by $\|\cdot\|_\infty$. The induced matrix 1-, 2-, and ∞-norms in $\mathbb{R}^{m\times n}$ induced, respectively, by the vector norms $\|\cdot\|_1$, $\|\cdot\|_2 := \|\cdot\|_{\mathbb{R}^n}$, and $\|\cdot\|_\infty$ in $\mathbb{R}^n$, are denoted by $\|\cdot\|_1$, $\|\cdot\|_2$ and $\|\cdot\|_\infty$.

Let Ω be an open subset of $\mathbb{R}^n$ denoting the *space* domain of a given dynamical system, with $x \in \Omega$ denoting a *spatial* point in Ω. The *time* domain of the model is given by the closed interval

$[0,T] \subset \mathbb{R}$, $T > 0$, with the *temporal* point t. For a function $u : [0,T] \to \mathbb{R}$, the kth-order total derivative with respect to t at t_0 is denoted by $\mathrm{d}_t^k u(t_0)$. For $k = 1$, we write $\mathrm{d}_t u(t_0)$. For a function $u(x,t) : \Omega \times [0,T] \to \mathbb{R}$, the kth-order partial derivative with respect to t at (x_0, t_0) is denoted by $\partial_t^k u(x_0,t_0)$ and the kth-order partial derivative with respect to x_j at (x_0,t_0) is denoted by $\partial_{x_j}^k u(x_0,t_0)$, $j = 1,\dots,n$. For $k = 1$, we write $\partial_t u(x_0,t_0)$ and $\partial_{x_j} u(x_0,t_0)$. The gradient of u in Ω is denoted by $\partial_x u$ and is given by $\partial_x u := (\partial_{x_1} u, \dots, \partial_{x_n} u) \in \mathbb{R}^n$. The Laplacian of u in Ω is denoted by Δu and is given by $\Delta u := (\partial_{x_1}^2 + \cdots + \partial_{x_n}^2) \in \mathbb{R}$. For a vector-valued function $u(x,t) : \Omega \times [0,T] \to \mathbb{R}^m$ we interpret $u(x,t)$ as the m-tuple $u(x,t) = (u_1(x,t), \dots, u_m(x,t))$, where each component $u_j(x,t)$, $j = 1,\dots,m$, is a scalar-valued function on $\Omega \times [0,T]$. In this case, $\partial_x u(x,t) \in \mathbb{R}^{m\times n}$ is the gradient of u and the vector Laplacian $\Delta u \in \mathbb{R}^m$ is given by $\Delta u := (\Delta u_1, \dots, \Delta u_m)$, assuming Cartesian coordinates in $\mathbb{R}^m$.

For every integer $k \geq 0$, the space of k-times continuously differentiable real-valued functions on Ω is denoted by $C^k(\Omega)$. The space $C^k(\overline{\Omega})$ consists of all functions in $C^k(\Omega)$ that, together with all of their partial derivatives up to the order k, are uniformly continuous in bounded subsets of Ω. Moreover, for $0 < \lambda \leq 1$, the Hölder space $C^{k,\lambda}(\overline{\Omega})$ is a subspace of $C^k(\overline{\Omega})$ consisting of functions whose partial derivatives of order k are Hölder continuous with exponent λ; see [8, Sec. 1.18] for details. We use $C_c^\infty(\Omega)$ to denote the space of infinitely differentiable real-valued functions with compact support in Ω. Moreover, we denote by $L^1_{\mathrm{loc}}(\Omega)$ the space of locally integrable real-valued functions on Ω. Then, for every function $u \in L^1_{\mathrm{loc}}(\Omega)$ and any multi index α with $|\alpha| \geq 1$, the *weak partial derivative* of u in $L^1_{\mathrm{loc}}(\Omega)$, of order $|\alpha|$, is defined by the distribution u^α that stisfies

$$\int_\Omega u^\alpha \phi \,\mathrm{d}x = (-1)^{|\alpha|} \int_\Omega u \partial^\alpha \phi \,\mathrm{d}x \quad \text{for all } \phi \in C_c^\infty(\Omega),$$

where $\mathrm{d}x = \mathrm{d}x_1 \cdots \mathrm{d}x_n$ is the Lebesgue measure on $\mathbb{R}^n$; see [8, Sec. 6.3] for details. With a minor abuse of notation, we use ∂_t^k and ∂_x^k to denote the kth-order weak, as well as classical partial derivatives with respect to t and x, respectively. The distinction will be clear from context, or will otherwise be explicitly specified.

The Hilbert space of vector-valued Lebesgue measurable functions $u : \Omega \to \mathbb{R}^m$ with finite L^2-norm is denoted by $L^2(\Omega;\mathbb{R}^m)$, with associated inner product and norm given by

$$(u,v)_{L^2(\Omega;\mathbb{R}^m)} = \int_\Omega \big(u(x), v(x)\big)_{\mathbb{R}^m} \mathrm{d}x, \quad \big\|u\big\|_{L^2(\Omega;\mathbb{R}^m)} = \left[\int_\Omega \big\|u(x)\big\|_{\mathbb{R}^m}^2 \mathrm{d}x\right]^{\frac{1}{2}}.$$

The Banach space of vector-valued Lebesgue measurable functions $u : \Omega \to \mathbb{R}^m$ with finite L^∞-norm is denoted by $L^\infty(\Omega;\mathbb{R}^m)$, with norm given by

$$\big\|u\big\|_{L^\infty(\Omega;\mathbb{R}^m)} = \operatorname*{ess\,sup}_{x\in\Omega} \big\|u(x)\big\|_\infty.$$

The Sobolev space of vector-valued functions $u \in L^p(\Omega;\mathbb{R}^m)$ whose all lth-order weak derivatives $\partial_x^l u$, $l \leq k$, exist and belong to $L^p(\Omega;\mathbb{R}^{m\times n^l})$ is denoted by $W^{k,p}(\Omega;\mathbb{R}^m)$. When $p = 2$, the Sobolev spaces $W^{k,2}(\Omega;\mathbb{R}^m)$ are Hilbert spaces for all $k \in [0,\infty)$, and are denoted by $H^k(\Omega;\mathbb{R}^m) := W^{k,2}(\Omega;\mathbb{R}^m)$. Specifically, $H^0(\Omega;\mathbb{R}^m) = L^2(\Omega;\mathbb{R}^m)$, and $H^1(\Omega;\mathbb{R}^m)$ is a Hilbert space with the inner product

$$\big(u,v\big)_{H^1(\Omega;\mathbb{R}^m)} = \big(u,v\big)_{L^2(\Omega;\mathbb{R}^m)} + \big(\partial_x u, \partial_x v\big)_{L^2(\Omega;\mathbb{R}^{m\times n})}.$$

Moreover, $H^2(\Omega;\mathbb{R}^m)$ is a Hilbert space with the inner product

$$\big(u,v\big)_{H^2(\Omega;\mathbb{R}^m)} = \big(u,v\big)_{L^2(\Omega;\mathbb{R}^m)} + \big(\partial_x u, \partial_x v\big)_{L^2(\Omega;\mathbb{R}^{m\times n})} + \big(\partial_x^2 u, \partial_x^2 v\big)_{L^2(\Omega;\mathbb{R}^{m\times n^2})}.$$

Let $\Omega = (0,\omega_1)\times\cdots\times(0,\omega_n)$, where $\omega_j > 0$, $j = 1,\dots,n$, be an open rectangle in $\mathbb{R}^n$. A function $u:\mathbb{R}^n\to\mathbb{R}$ is called Ω-*periodic* if it is periodic in each direction, that is,

$$u(x+\omega_j e_j) = u(x), \quad j = 1,\dots,n, \quad x\in\mathbb{R}^n,$$

where e_j is the unit vector in the jth direction. Define the space $C^\infty_{\text{per}}(\Omega)$ as the restriction to Ω of the space of infinitely differentiable Ω-periodic functions. Then, the Sobolev space $H^k_{\text{per}}(\Omega)$, $k\geq 0$, is defined by the completion of $C^\infty_{\text{per}}(\Omega)$ in $H^k(\Omega)$; see [41, Definition 5.37]. A vector-valued function $u:\mathbb{R}^n\to\mathbb{R}^m$ is Ω-periodic if each of its components $u_j:\mathbb{R}^n\to\mathbb{R}$, $j=1,\dots,m$, is Ω-periodic. The spaces $C^\infty_{\text{per}}(\Omega;\mathbb{R}^m)$ and $H^k_{\text{per}}(\Omega;\mathbb{R}^m)$ are then defined accordingly. It follows from Green's formula and the definition of norms in these spaces that

$$\begin{aligned}
\big(-\Delta u, v\big)_{L^2_{\text{per}}(\Omega;\mathbb{R}^m)} &= \big(\partial_x u, \partial_x v\big)_{L^2_{\text{per}}(\Omega;\mathbb{R}^{m\times n})},\\
\big((-\Delta+I)u, v\big)_{L^2_{\text{per}}(\Omega;\mathbb{R}^m)} &= \big(u,v\big)_{H^1_{\text{per}}(\Omega;\mathbb{R}^m)},\\
\big(-\Delta u, (-\Delta+I)u\big)_{L^2_{\text{per}}(\Omega;\mathbb{R}^m)} &= \big\|u\big\|^2_{H^2_{\text{per}}(\Omega;\mathbb{R}^m)} - \big\|u\big\|^2_{L^2_{\text{per}}(\Omega;\mathbb{R}^m)},\\
\big\|(-\Delta+I)u\big\|^2_{L^2_{\text{per}}(\Omega;\mathbb{R}^m)} &= \big\|u\big\|^2_{H^2_{\text{per}}(\Omega;\mathbb{R}^m)} + \big\|\partial_x u\big\|^2_{L^2_{\text{per}}(\Omega;\mathbb{R}^{m\times n})}\\
&= \big\|u\big\|^2_{H^1_{\text{per}}(\Omega;\mathbb{R}^m)} + \big\|\partial_x u\big\|^2_{H^1_{\text{per}}(\Omega;\mathbb{R}^{m\times n})}.
\end{aligned} \tag{2.1}$$

In this paper, we interchangeably view the function $u(x,t)$, $x\in\Omega$, $t\in[0,T]$, as a composite function of x and t, as well as a mapping u of t into a function of x, defined as

$$[u(t)](x) := u(x,t), \quad x\in\Omega, \quad t\in[0,T].$$

With a minor abuse of notation, the same symbol is used to denote both the original form of the function and the mapping. The distinction becomes evident in the way we define the space of such mappings or, equivalently, Banach space-valued functions; see for example [15, Appx. E.5]. For a Banach space $\mathcal{U}$, the space $L^2(0,T;\mathcal{U})$ is composed of all strongly measurable Banach space-valued functions $u:[0,T]\to\mathcal{U}$ with the finite L^2-norm defined by

$$\big\|u\big\|_{L^2(0,T;\mathcal{U})} := \left[\int_0^T \big\|u(t)\big\|^2_{\mathcal{U}}\mathrm{d}t\right]^{\frac{1}{2}}.$$

The space $C^0([0,T];\mathcal{U})$ is composed of all continuous Banach space-valued functions $u:[0,T]\to\mathcal{U}$ with the finite uniform norm defined by

$$\big\|u\big\|_{C^0([0,T];\mathcal{U})} := \max_{t\in[0,T]}\big\|u(t)\big\|_{\mathcal{U}}.$$

Accordingly, the spaces $C^k([0,T];\mathcal{U})$ and $C^{k,\lambda}([0,T];\mathcal{U})$, $k\geq 0$, $0<\lambda\leq 1$, are defined as the space of k-times continuously differentiable Banach space-valued functions and its Hölder continuous subspace. The Sobolev spaces $H^k(0,T;\mathcal{U})$, $k\geq 0$, are composed of all functions $u\in L^2(0,T;\mathcal{U})$

whose lth-order weak derivatives $\mathrm{d}_t^l u$ exist for $l \leq k$ and belong to $L^2(0,T;\mathcal{U})$. In particular, for $k=1$ we have

$$\|u\|_{H^1(0,T;\mathcal{U})} := \left[\int_0^T \left(\|u(t)\|_{\mathcal{U}}^2 + \|\mathrm{d}_t u(t)\|_{\mathcal{U}}^2\right) \mathrm{d}t\right]^{\frac{1}{2}}.$$

For further details on these spaces; see [15, Sec. 5.9.2] and [41, Sec. 7.1].

When $P : \mathcal{U} \to \mathcal{Y}$ is a mapping between the Banach spaces $\mathcal{U}$ and $\mathcal{Y}$, we denote the kth order Fréchet derivative of P at u_0 by $\mathrm{d}_u P(u_0)$. The space $C^k(\mathcal{U};\mathcal{Y})$ is then composed of all k-times continuously differentiable mappings from $\mathcal{U}$ into $\mathcal{Y}$. For a mapping $P : \mathcal{U}_1 \times \cdots \times \mathcal{U}_m \to \mathcal{Y}$, where $\mathcal{Y}$ and $\mathcal{U}_j$, $j = 1, \ldots m$, are Banach spaces, $\partial_{u_j} P(u_0)$ is the jth partial Fréchet derivative of P at $u_0 = (u_{01}, \ldots, u_{0m})$. The gradient of P at u_0 is then written as $\partial_u P(u_0)$; see [8, Sec. 7.1] for details.

Finally, we denote the symmetric difference of two sets $\mathscr{X}$ and $\mathscr{Y}$ by $\mathscr{X} \triangle \mathscr{Y}$. In a topological space $\mathcal{X}$, we denote the closure of a set $\mathscr{X} \subset \mathcal{X}$ by $\overline{\mathscr{X}}$, its interior by $\mathscr{X}^\circ$, and its boundary by $\partial\mathscr{X}$. The characteristic function of $\mathscr{X}$ is denoted by $\chi(\mathscr{X})$. When $\mathcal{X}$ is a measure space, $|\mathscr{X}|$ denotes the measure of the set $\mathscr{X} \subset \mathcal{X}$. When $\mathcal{X}$ is a metric space and the topology on $\mathcal{X}$ is induced by the given metric, $B(x,R)$ denotes the open ball centered at $x \in \mathcal{X}$ with radius $R > 0$, which is a basis element for the topology. For every bounded measurable set in $\mathcal{X}$ and, in particular for $B(x,R)$, we denote by $⨍_{B(x,R)}$ the averaging operator over $B(x,R)$, that is, $⨍_{B(x,R)} := \frac{1}{|B(x,R)|}\int_{B(x,R)}$.

3. Model Description

The neocortex has a layered columnar structure consisting mostly of six distinctive layers. Neurons in the neocortex are organized in vertical columns, usually referred to as *cortical columns* or *macrocolumns*, which are a fraction of a millimeter wide and traverse all the layers of the neocortex from the white matter to the pial surface [25, 26, 38]. Depending on their type of action, neurons are mainly classified as *excitatory* or *inhibitory*, wherein this distinction depends on whether they increase the firing rate in the destination neurons they are communicating with, or they essentially suppress them. Inhibitory neurons are located within all layers and usually have axons that remain within the same area were their cell body resides, and hence, they have a local range of action. Layers III, V, and VI contain pyramidal excitatory neurons whose axons can provide long-range communication (projection) throughout the neocortex. Layer IV contains primarily star-shaped excitatory interneurons that receive sensory inputs from the thalamus. Figure 1 shows a schematic of the structure of the neocortex, including the intracortical and corticocortical neuronal connections; see [26, Ch. 15] for further details.

On a local scale, within a cortical column, neurons are densely interconnected and involve all types of feedforward and feedback intracortical connections. Such a dense and relatively homogeneous local structure of the neocortex suggests modeling a local population of functionally similar neurons by a single *space-averaged neuron*, which preserves enough physiological information to understand the temporal patterns observed in spatially smoothed (averaged) EEG signals, without creating excessive theoretical complicacies in the mathematical analysis of the model. On a global scale, in the exclusively excitatory corticocortical communication throughout the neocrtex, two majors patterns of connectivity are observed. Namely, a homogeneous, symmetrical, and translation invariant pattern of connections, versus a heterogeneous, patchy, and asymmetrical distribution of connections. For modeling simplicity and due to unavailability of detailed anatomical data, in the model that we investigate in this paper the corticocortical connectivity is assumed to be isotropic, homogenous, symmetric, and translation invariant [33].

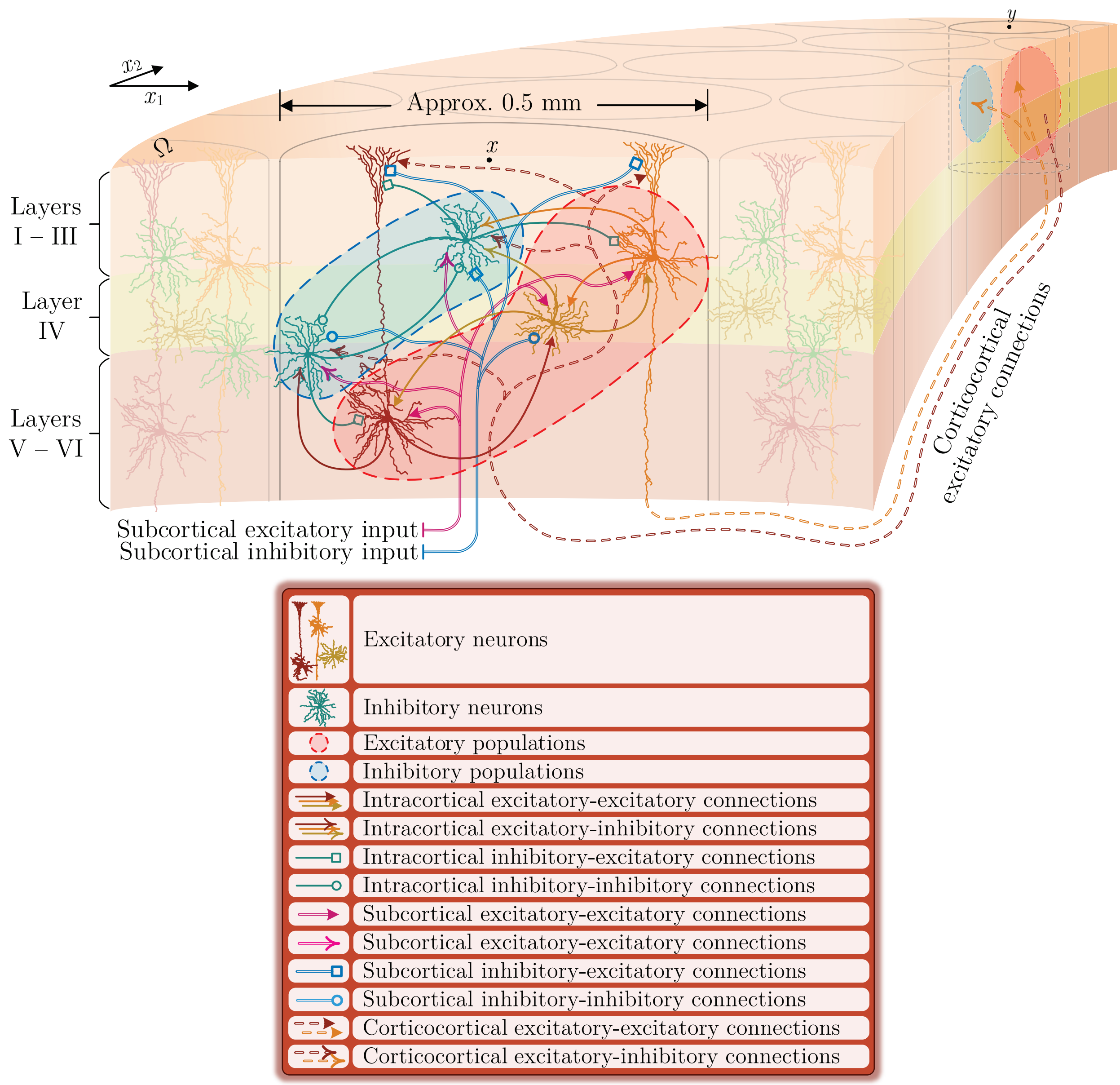

Figure 1: Schematic of the structure of the neocortex with intracortical and corticocortical connections.

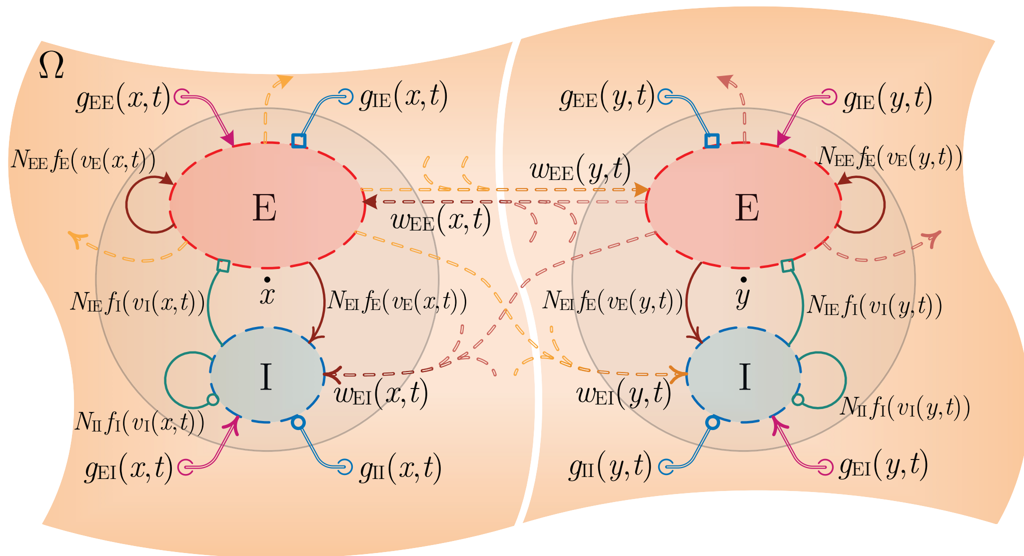

Figure 2: Cortical inputs to two local networks located at points x and y as modeled by (3.1).

To establish the mathematical framework of the model, let $\Omega = (0, \omega) \times (0, \omega)$, $\omega > 0$, be an open rectangle in $\mathbb{R}^2$ that defines the domain of the neocortex. Each point $x = (x_1, x_2) \in \Omega$ indicates the location of a local network—possibly representing a cortical column—modeled by a space-averaged excitatory neuron and a space-averaged inhibitory neuron. Let E denote a population of excitatory neurons and I denote a population of inhibitory neurons. For $x \in \Omega$, $t \in [0, T]$, $T > 0$, and $\mathrm{X}, \mathrm{Y} \in \{\mathrm{E}, \mathrm{I}\}$, we denote by $v_{\mathrm{X}}(x,t)$, measured in mV, the spatially mean soma membrane potential of a population of type X centered at x. Moreover, we denote by $i_{\mathrm{XY}}(x,t)$, measured in mV, the spatially mean post synaptic activation of synapses of a population of type X centered at x, on a population of type Y centered at the same point x. In addition, we denote by $w_{\mathrm{EX}}(x,t)$, measured in s^{-1}, the mean rate of corticocortical excitatory input pulses from the entire domain of neocortex to a population of type X centered at x. Finally, we denote by $g_{\mathrm{XY}}(x,t)$, measured in s^{-1}, the mean rate of subcortical input pulses of type X to a population of type Y centered at x. Note that, by definition, $i_{\mathrm{XY}}(x,t)$, $w_{\mathrm{EX}}(x,t)$, and $g_{\mathrm{XY}}(x,t)$ are nonnegative quantities.

Then, as developed in [33], the system of partial differential equations

$$
\begin{aligned}
(\tau_{\mathrm{E}}\partial_t + 1) v_{\mathrm{E}}(x,t) &= \frac{\mathrm{V}_{\mathrm{EE}} - v_{\mathrm{E}}(x,t)}{|\mathrm{V}_{\mathrm{EE}}|} i_{\mathrm{EE}}(x,t) + \frac{\mathrm{V}_{\mathrm{IE}} - v_{\mathrm{E}}(x,t)}{|\mathrm{V}_{\mathrm{IE}}|} i_{\mathrm{IE}}(x,t), \\
(\tau_{\mathrm{I}}\partial_t + 1) v_{\mathrm{I}}(x,t) &= \frac{\mathrm{V}_{\mathrm{EI}} - v_{\mathrm{I}}(x,t)}{|\mathrm{V}_{\mathrm{EI}}|} i_{\mathrm{EI}}(x,t) + \frac{\mathrm{V}_{\mathrm{II}} - v_{\mathrm{I}}(x,t)}{|\mathrm{V}_{\mathrm{II}}|} i_{\mathrm{II}}(x,t), \\
(\partial_t + \gamma_{\mathrm{EE}})^2 i_{\mathrm{EE}}(x,t) &= e\Upsilon_{\mathrm{EE}}\gamma_{\mathrm{EE}} \left[\mathrm{N}_{\mathrm{EE}} f_{\mathrm{E}}\big(v_{\mathrm{E}}(x,t)\big) + w_{\mathrm{EE}}(x,t) + g_{\mathrm{EE}}(x,t) \right], \\
(\partial_t + \gamma_{\mathrm{EI}})^2 i_{\mathrm{EI}}(x,t) &= e\Upsilon_{\mathrm{EI}}\gamma_{\mathrm{EI}} \left[\mathrm{N}_{\mathrm{EI}} f_{\mathrm{E}}\big(v_{\mathrm{E}}(x,t)\big) + w_{\mathrm{EI}}(x,t) + g_{\mathrm{EI}}(x,t) \right], \\
(\partial_t + \gamma_{\mathrm{IE}})^2 i_{\mathrm{IE}}(x,t) &= e\Upsilon_{\mathrm{IE}}\gamma_{\mathrm{IE}} \left[\mathrm{N}_{\mathrm{IE}} f_{\mathrm{I}}\big(v_{\mathrm{I}}(x,t)\big) + g_{\mathrm{IE}}(x,t) \right], \\
(\partial_t + \gamma_{\mathrm{II}})^2 i_{\mathrm{II}}(x,t) &= e\Upsilon_{\mathrm{II}}\gamma_{\mathrm{II}} \left[\mathrm{N}_{\mathrm{II}} f_{\mathrm{I}}\big(v_{\mathrm{I}}(x,t)\big) + g_{\mathrm{II}}(x,t) \right], \\
\left[(\partial_t + \nu\Lambda_{\mathrm{EE}})^2 - \tfrac{3}{2}\nu^2\Delta \right] w_{\mathrm{EE}}(x,t) &= \nu^2 \Lambda_{\mathrm{EE}}^2 \mathrm{M}_{\mathrm{EE}} f_{\mathrm{E}}\big(v_{\mathrm{E}}(x,t)\big), \\
\left[(\partial_t + \nu\Lambda_{\mathrm{EI}})^2 - \tfrac{3}{2}\nu^2\Delta \right] w_{\mathrm{EI}}(x,t) &= \nu^2 \Lambda_{\mathrm{EI}}^2 \mathrm{M}_{\mathrm{EI}} f_{\mathrm{E}}\big(v_{\mathrm{E}}(x,t)\big), \qquad (x,t) \in \Omega \times (0,T],
\end{aligned}
\tag{3.1}
$$

Table 1: Definition and range of values for the biophysical parameters of the mean field model (3.1). All electric potentials are given with respect to the mean resting soma membrane potential $v_{\mathrm{rest}} = -70$ mV [5].

Parameter	Definition	Range	Unit
τ_{E}	Passive excitatory membrane decay time constant	$[0.005, 0.15]$	s
τ_{I}	Passive inhibitory membrane decay time constant	$[0.005, 0.15]$	s
V_{EE}, V_{EI}	Mean excitatory Nernst potentials	$[50, 80]$	mV
V_{IE}, V_{II}	Mean inhibitory Nernst potentials	$[-20, -5]$	mV
γ_{EE}, γ_{EI}	Excitatory post synaptic potential rate constants	$[100, 1000]$	s^{-1}
γ_{IE}, γ_{II}	Inhibitory post synaptic potential rate constants	$[10, 500]$	s^{-1}
Υ_{EE}, Υ_{EI}	Amplitude of excitatory post synaptic potentials	$[0.1, 2.0]$	mV
Υ_{IE}, Υ_{II}	Amplitude of inhibitory post synaptic potentials	$[0.1, 2.0]$	mV
N_{EE}, N_{EI}	Number of intracortical excitatory connections	$[2000, 5000]$	—
N_{IE}, N_{II}	Number of intracortical inhibitory connections	$[100, 1000]$	—
ν	Corticocortical conduction velocity	$[100, 1000]$	cm/s
Λ_{EE}, Λ_{EI}	Decay scale of corticocortical excitatory connectivities	$[0.1, 1.0]$	cm^{-1}
M_{EE}, M_{EI}	Number of corticocortical excitatory connections	$[2000, 5000]$	—
F_{E}	Maximum mean excitatory firing rate	$[50, 500]$	s^{-1}
F_{I}	Maximum mean inhibitory firing rate	$[50, 500]$	s^{-1}
μ_{E}	Excitatory firing threshold potential	$[15, 30]$	mV
μ_{I}	Inhibitory firing threshold potential	$[15, 30]$	mV
σ_{E}	Standard deviation of excitatory firing threshold potential	$[2, 7]$	mV
σ_{I}	Standard deviation of inhibitory firing threshold potential	$[2, 7]$	mV

with periodic boundary value condition provides a mean field model of electrocortical activity in the neocortex. Here, e is the Napier constant and $f_{\mathrm{X}}(\cdot)$ is the mean firing rate function of a population of type X and is given by

$$f_{\mathrm{X}}\big(v_{\mathrm{X}}(x,t)\big) := \frac{\mathrm{F}_{\mathrm{X}}}{1 + \exp\left(-\sqrt{2}\,\dfrac{v_{\mathrm{X}}(x,t) - \mu_{\mathrm{X}}}{\sigma_{\mathrm{X}}}\right)}, \quad \mathrm{X} \in \{\mathrm{E}, \mathrm{I}\}. \tag{3.2}$$

The definition of the biophysical parameters of the model and the ranges of the values they may take are given in Table 1. For the range of values given in Table 1 we have $|\mathrm{V}_{\mathrm{EE}}| = \mathrm{V}_{\mathrm{EE}}$, $|\mathrm{V}_{\mathrm{EI}}| = \mathrm{V}_{\mathrm{EI}}$, $|\mathrm{V}_{\mathrm{IE}}| = -\mathrm{V}_{\mathrm{IE}}$, and $|\mathrm{V}_{\mathrm{II}}| = -\mathrm{V}_{\mathrm{II}}$, which we use to simplify (3.1). Note that other than notational changes to the original equations given in [33], we have changed the reference of electrical potential to the *resting potential* to avoid the constant terms that would otherwise appear in (3.1). Figure 2 shows a schematic of intracortical, corticocortical, and subcortical inputs to two local networks located at points x and y together with their contribution to the global corticocortical activation as modeled by (3.1).

The first six equations given in (3.1) model the dynamics of the space-averaged excitatory and inhibitory neurons located at x, including the first-order capacitive dynamics of the membrane, the

Nernst (reversal) potential effect, and the second-order dynamics related to the passive dendritic cable delays and neurotransmitter kinetics. The last two equations in (3.1) model the dynamics of the spatial distribution of excitatory corticocortical activity over the domain of the neocortex.

Now, let

$$\begin{aligned} v(x,t) &:= \big(v_{\mathrm{E}}(x,t), v_{\mathrm{I}}(x,t)\big) \in \mathbb{R}^2, \\ i(x,t) &:= \big(i_{\mathrm{EE}}(x,t), i_{\mathrm{EI}}(x,t), i_{\mathrm{IE}}(x,t), i_{\mathrm{II}}(x,t)\big) \in \mathbb{R}^4, \\ w(x,t) &:= \big(w_{\mathrm{EE}}(x,t), w_{\mathrm{EI}}(x,t)\big) \in \mathbb{R}^2, \\ g(x,t) &:= \big(g_{\mathrm{EE}}(x,t), g_{\mathrm{EI}}(x,t), g_{\mathrm{IE}}(x,t), g_{\mathrm{II}}(x,t)\big) \in \mathbb{R}^4, \end{aligned}$$

and note that (3.1) can be represented in vector form in $\Omega \times (0,T]$ as

$$\Phi\partial_t v + v - J_1 i + J_2 v i^{\mathrm{T}}\Psi J_4 + J_3 v i^{\mathrm{T}}\Psi J_5 = 0, \tag{3.3}$$

$$\partial_t^2 i + 2\Gamma\partial_t i + \Gamma^2 i - e\Upsilon\Gamma J_6 w - e\Upsilon\Gamma \mathrm{N} J_7 f(v) = e\Upsilon\Gamma g, \tag{3.4}$$

$$\partial_t^2 w + 2\nu\Lambda\partial_t w - \tfrac{3}{2}\nu^2\Delta w + \nu^2\Lambda^2 w - \nu^2\Lambda^2 \mathrm{M} J_8 f\big(v\big) = 0, \tag{3.5}$$

where v, i, and w are Ω-periodic vector-valued functions with the initial values

$$v\big|_{t=0} = v_0, \quad i\big|_{t=0} = i_0, \quad (\partial_t i)\big|_{t=0} = i_0', \quad w\big|_{t=0} = w_0, \quad (\partial_t w)\big|_{t=0} = w_0', \tag{3.6}$$

and

$$\begin{aligned} &\Phi = \mathrm{diag}\big(\tau_{\mathrm{E}}, \tau_{\mathrm{I}}\big), && \Psi = \mathrm{diag}\big(\tfrac{1}{|\mathrm{V}_{\mathrm{EE}}|}, \tfrac{1}{|\mathrm{V}_{\mathrm{EI}}|}, \tfrac{1}{|\mathrm{V}_{\mathrm{IE}}|}, \tfrac{1}{|\mathrm{V}_{\mathrm{II}}|}\big), \\ &\Gamma = \mathrm{diag}(\gamma_{\mathrm{EE}}, \gamma_{\mathrm{EI}}, \gamma_{\mathrm{IE}}, \gamma_{\mathrm{II}}), && \Upsilon = \mathrm{diag}(\Upsilon_{\mathrm{EE}}, \Upsilon_{\mathrm{EI}}, \Upsilon_{\mathrm{IE}}, \Upsilon_{\mathrm{II}}), \\ &\mathrm{N} = \mathrm{diag}(\mathrm{N}_{\mathrm{EE}}, \mathrm{N}_{\mathrm{EI}}, \mathrm{N}_{\mathrm{IE}}, \mathrm{N}_{\mathrm{II}}), && \mathrm{M} = \mathrm{diag}(\mathrm{M}_{\mathrm{EE}}, \mathrm{M}_{\mathrm{EI}}), \\ &\Lambda = \mathrm{diag}(\Lambda_{\mathrm{EE}}, \Lambda_{\mathrm{EI}}), && J_1 = \begin{bmatrix} I_{2\times 2} & -I_{2\times 2} \end{bmatrix}, \\ &J_2 = \mathrm{diag}(1,0), && J_3 = \mathrm{diag}(0,1), \\ &J_4 = \begin{bmatrix} 1 & 0 & 1 & 0 \end{bmatrix}^{\mathrm{T}}, && J_5 = \begin{bmatrix} 0 & 1 & 0 & 1 \end{bmatrix}^{\mathrm{T}}, \\ &J_6 = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{bmatrix}^{\mathrm{T}}, && J_7 = \begin{bmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}^{\mathrm{T}}, \\ &J_8 = \begin{bmatrix} 1 & 0 \\ 1 & 0 \end{bmatrix}, && f(v) = \begin{bmatrix} f_{\mathrm{E}}\big(\begin{bmatrix} 1 & 0 \end{bmatrix} v\big) \\ f_{\mathrm{I}}\big(\begin{bmatrix} 0 & 1 \end{bmatrix} v\big) \end{bmatrix}. \end{aligned} \tag{3.7}$$

For simplicity of exposition, the dependence of the functions v, i, w, and g on the arguments (x,t) is not explicitly shown in (3.3)–(3.5). Note that (3.3) and (3.4), which model the local dynamics of the neocortex, are essentially systems of ordinary differential equations. These equations do not possess any spatial smoothing component, and hence, their dynamics is expected to evolve in less regular function spaces [36, 44]. The system of partial differential equations (3.5) consists of two damped wave equations or, more specifically, two telegraph equations coupled indirectly through (3.3) and (3.4).

4. Existence and Uniqueness of Solutions

In this section, we investigate the problem of existence, uniqueness, and regularity of solutions for (3.3)–(3.5) with the initial values (3.6) and periodic boundary conditions. We set appropriate spaces of Ω-periodic functions as the functional framework of the problem by which we include the boundary conditions in the solution spaces. We view $v(x,t)$, $i(x,t)$, and $w(x,t)$ as Banach space-valued functions and follow the standard technique of Galerkin approximations [15,41,48] to construct weak and strong solutions.

First, define the function spaces

$$
\begin{aligned}
\mathcal{L}_v^2 &:= L^2_{\text{per}}(\Omega;\mathbb{R}^2), & \mathcal{L}_i^2 &:= L^2_{\text{per}}(\Omega;\mathbb{R}^4), & \mathcal{L}_w^2 &:= L^2_{\text{per}}(\Omega;\mathbb{R}^2),\\
\mathcal{L}_v^\infty &:= L^\infty_{\text{per}}(\Omega;\mathbb{R}^2), & \mathcal{L}_i^\infty &:= L^\infty_{\text{per}}(\Omega;\mathbb{R}^4), & \mathcal{L}_w^\infty &:= L^\infty_{\text{per}}(\Omega;\mathbb{R}^2),\\
\mathcal{H}_w^1 &:= H^1_{\text{per}}(\Omega;\mathbb{R}^2), & \mathcal{H}_w^2 &:= H^2_{\text{per}}(\Omega;\mathbb{R}^2), & &\\
\mathcal{L}_{\partial w}^2 &:= L^2_{\text{per}}(\Omega;\mathbb{R}^{2\times 2}), & \mathcal{H}_{\partial w}^1 &:= H^1_{\text{per}}(\Omega;\mathbb{R}^{2\times 2}), & &\\
\mathcal{W}_w^{1,\infty} &:= W^{1,\infty}_{\text{per}}(\Omega;\mathbb{R}^2), & & & &
\end{aligned}
\tag{4.1}
$$

and denote by $\mathcal{L}_v^{2^*}$, $\mathcal{L}_i^{2^*}$, and $\mathcal{H}_w^{1*}$ the dual spaces of $\mathcal{L}_v^2$, $\mathcal{L}_i^2$, and $\mathcal{H}_w^1$, respectively. Note that $\mathcal{L}_v^2$ and $\mathcal{L}_i^2$ are, respectively, isometrically isomorphic to $\mathcal{L}_v^{2^*}$ and $\mathcal{L}_i^{2^*}$ [17, Th. 6.15], which we denote by $\mathcal{L}_v^{2^*} = \mathcal{L}_v^2$ and $\mathcal{L}_i^{2^*} = \mathcal{L}_i^2$. By the Rellich-Kondrachov compact embedding theorems we have $\mathcal{H}_w^1 \Subset \mathcal{L}_w^2 \subset \mathcal{H}_w^{1*}$; see, for example [8, Th. 6.6-3] and [41, Th. A.4]. Moreover, there exists a dual orthogonal basis of $\mathcal{H}_w^1$ and $\mathcal{L}_w^2$ given by the following lemma.

Lemma 4.1 (Dual orthogonal basis) *There exists an orthonormal basis of $\mathcal{L}_w^2$ that is an orthogonal basis of $\mathcal{H}_w^1$, and can be constructed by the eigenfunctions of the linear operator $A := (-\Delta + I) : \mathcal{H}_w^1 \to \mathcal{H}_w^{1*}$.*

Proof. *Consider the linear operator $A : \mathcal{H}_w^1 \to \mathcal{H}_w^{1*}$ defined by*

$$\langle Aw, h\rangle_{\mathcal{H}_w^1} := \big((-\Delta + I)w, h\big)_{\mathcal{L}_w^2} \text{ for all } h \in \mathcal{H}_w^1 \text{ and every fixed } w \in \mathcal{H}_w^1.$$

First, we show that A is an isometric isomorphism. For every $h \in \mathcal{H}_w^1$ such that $\|h\|_{\mathcal{H}_w^1} = 1$, it follows from (2.1) and the Cauchy-Schwarz inequality that

$$\big|(Aw,h)_{\mathcal{L}_w^2}\big| = \big|(w,h)_{\mathcal{H}_w^1}\big| \le \|w\|_{\mathcal{H}_w^1}\|h\|_{\mathcal{H}_w^1} = \|w\|_{\mathcal{H}_w^1},$$

and hence, $\|Aw\|_{\mathcal{H}_w^{1*}} \le \|w\|_{\mathcal{H}_w^1}$. For every $w \neq 0 \in \mathcal{H}_w^1$ set $h = \|w\|_{\mathcal{H}_w^1}^{-1} w$ and note that $\big|(Aw, \|w\|_{\mathcal{H}_w^1}^{-1} w)_{\mathcal{L}_w^2}\big| = \|w\|_{\mathcal{H}_w^1}$, which implies $\|Aw\|_{\mathcal{H}_w^{1*}} \ge \|w\|_{\mathcal{H}_w^1}$. Therefore, A is an isometry. Now, it suffices to show A is surjective. This follows immediately from the Riesz representation theorem [8, Th. 4.6-1]. Indeed, for every linear functional $q \in \mathcal{H}_w^{1*}$ there exists a unique $w_q \in \mathcal{H}_w^1$ such that

$$\langle q, h\rangle_{\mathcal{H}_w^1} = (w_q, h)_{\mathcal{H}_w^1} = (Aw_q, h)_{\mathcal{L}_w^2} = \langle Aw_q, h\rangle_{\mathcal{H}_w^1}.$$

Next, we show that A has a compact inverse on $\mathcal{L}_w^2$. Since A is an isomorphism and $\mathcal{L}_w^2 \subset \mathcal{H}_w^{1*}$, the restriction of A^{-1} to $\mathcal{L}_w^2$ is a bounded map from $\mathcal{L}_w^2$ to $\mathcal{H}_w^1$. Since $\mathcal{H}_w^1 \Subset \mathcal{L}_w^2$, it follows that $A^{-1} : \mathcal{L}_w^2 \to \mathcal{L}_w^2$ is compact. Therefore, by the spectral theory of compact self-adjoint linear operators [8, Th. 4.11-3], there exists an orthonormal Hilbert basis $\mathcal{B}_w = \{h_w^{(l)}\}_{l=1}^\infty$ of $\mathcal{L}_w^2$ consisting of the eigenfunctions of A^{-1}.

Now, note that $\mathcal{B}_w \subset \mathcal{H}_w^1$ since for every $h_w^{(l)} \in \mathcal{B}_w$,

$$\|h_w^{(l)}\|_{\mathcal{H}_w^1} = \|\lambda_l^{-1} A^{-1} h_w^{(l)}\|_{\mathcal{H}_w^1} = \lambda_l^{-\frac{1}{2}}\|h_w^{(l)}\|_{\mathcal{L}_w^2} < \infty,$$

where $\lambda_l > 0$ is the eigenvalue corresponding to $h_w^{(l)}$. Moreover, $\mathcal{B}_w$ is complete in $\mathcal{H}_w^1$ since for $h \in \mathcal{H}_w^1$ satisfying $\big(h_w^{(l)}, h\big)_{\mathcal{H}_w^1} = 0$ for all $h_w^{(l)} \in \mathcal{B}_w$ we have

$$0 = \big(h_w^{(l)}, h\big)_{\mathcal{H}_w^1} = \big(\lambda_l^{-1} A^{-1} h_w^{(l)}, h\big)_{\mathcal{H}_w^1} = \lambda_l^{-1}\big(h_w^{(l)}, h\big)_{\mathcal{L}_w^2},$$

which implies $h = 0$ due to completeness of $\mathcal{B}_w$ in $\mathcal{L}_w^2$. Orthogonality of $\mathcal{B}_w$ in $\mathcal{H}_w^1$ is proved by similar computation, which completes the proof that $\mathcal{B}_w$ is also an orthogonal Hilbert basis of $\mathcal{H}_w^1$ consisting of the eigenfunctions of the operator $A : \mathcal{H}_w^1 \to \mathcal{H}_w^{1*}$.

Before proceeding to the main results of this section, we define the notions of *weak* and *strong* solutions of (3.3)–(3.6) as used in this paper.

Definition 4.2 (Weak solution) *A solution (v, i, w) is called an Ω-periodic* weak solution *of the initial value problem (3.3)–(3.6) if it solves the weak version of the problem wherein the partial differential equations are understood as equalities in the space of duals $L^2(0, T; \mathcal{L}_v^{2*} \times \mathcal{L}_i^{2*} \times \mathcal{H}_w^{1*})$. That is, the functions*

$$v \in L^2(0, T; \mathcal{L}_v^2), \quad i \in L^2(0, T; \mathcal{L}_i^2), \quad w \in L^2(0, T; \mathcal{H}_w^1),$$

with

$$\begin{aligned} &\mathrm{d}_t v \in L^2(0, T; \mathcal{L}_v^{2*}), && \mathrm{d}_t i \in L^2(0, T; \mathcal{L}_i^2), && \mathrm{d}_t^2 i \in L^2(0, T; \mathcal{L}_i^{2*}), \\ &\mathrm{d}_t w \in L^2(0, T; \mathcal{L}_w^2), && \mathrm{d}_t^2 w \in L^2(0, T; \mathcal{H}_w^{1*}), \end{aligned}$$

construct an Ω-periodic weak solution for (3.3)–(3.6) if for every $\ell_v \in \mathcal{L}_v^2$, $\ell_i \in \mathcal{L}_i^2$, $h_w \in \mathcal{H}_w^1$, and almost every $t \in [0, T]$, $T > 0$,

$$\big\langle \Phi \mathrm{d}_t v, \ell_v \big\rangle_{\mathcal{L}_v^2} + \big(v, \ell_v\big)_{\mathcal{L}_v^2} - \big(J_1 i, \ell_v\big)_{\mathcal{L}_v^2} + \big(J_2 v i^{\mathrm{T}} \Psi J_4 + J_3 v i^{\mathrm{T}} \Psi J_5, \ell_v\big)_{\mathcal{L}_v^2} = 0, \tag{4.2}$$

$$\begin{aligned} \big\langle \mathrm{d}_t^2 i, \ell_i \big\rangle_{\mathcal{L}_i^2} + 2\big(\Gamma \mathrm{d}_t i, \ell_i\big)_{\mathcal{L}_i^2} + \big(\Gamma^2 i, \ell_i\big)_{\mathcal{L}_i^2} - e\big(\Upsilon \Gamma J_6 w, \ell_i\big)_{\mathcal{L}_i^2} \\ - e\big(\Upsilon \Gamma \mathrm{N} J_7 f(v), \ell_i\big)_{\mathcal{L}_i^2} = e\big(\Upsilon \Gamma g, \ell_i\big)_{\mathcal{L}_i^2}, \end{aligned} \tag{4.3}$$

$$\begin{aligned} \big\langle \mathrm{d}_t^2 w, h_w \big\rangle_{\mathcal{H}_w^1} + 2\nu\big(\Lambda \mathrm{d}_t w, h_w\big)_{\mathcal{L}_w^2} - \tfrac{3}{2}\nu^2\big(\Delta w, h_w\big)_{\mathcal{L}_w^2} + \nu^2\big(\Lambda^2 w, h_w\big)_{\mathcal{L}_w^2} \\ - \nu^2\big(\Lambda^2 \mathrm{M} J_8 f(v), h_w\big)_{\mathcal{L}_w^2} = 0, \end{aligned} \tag{4.4}$$

with the initial values

$$v(0) = v_0, \quad i(0) = i_0, \quad \mathrm{d}_t i(0) = i_0', \quad w(0) = w_0, \quad \mathrm{d}_t w(0) = w_0'. \tag{4.5}$$

Definition 4.3 (Strong solution) *A solution (v, i, w) is called an Ω-periodic* strong solution *of the initial value problem (3.3)–(3.6) if it solves the strong version of the problem wherein the partial differential equations are understood as equalities in $L^2(0, T; \mathcal{L}_v^2 \times \mathcal{L}_i^2 \times \mathcal{L}_w^2)$. That is, the functions*

$$v \in H^1(0, T; \mathcal{L}_v^2), \quad i \in H^2(0, T; \mathcal{L}_i^2), \quad w \in L^2(0, T; \mathcal{H}_w^2),$$

with

$$\begin{aligned} &\mathrm{d}_t v \in L^2(0, T; \mathcal{L}_v^2), && \mathrm{d}_t i \in H^1(0, T; \mathcal{L}_i^2), && \mathrm{d}_t^2 i \in L^2(0, T; \mathcal{L}_i^2), \\ &\mathrm{d}_t w \in L^2(0, T; \mathcal{H}_w^1), && \mathrm{d}_t^2 w \in L^2(0, T; \mathcal{L}_w^2), \end{aligned}$$

construct an Ω-periodic strong solution for (3.3)–(3.6) where they solve the equations for almost every $x \in \Omega$ and almost every $t \in [0, T]$.

Now, let $\mathcal{B}_v = \{\ell_v^{(l)}\}_{l=1}^{\infty}$ be a basis of $\mathcal{L}_v^2$ such that $\{\Phi^{\frac{1}{2}}\ell_v^{(l)}\}_{l=1}^{\infty}$ is orthonormal in $\mathcal{L}_v^2$. Note that (3.7), with the range of values given in Table 1, implies that Φ is a positive-definite diagonal matrix, and hence, such a basis exists. Moreover, let $\mathcal{B}_i = \{\ell_i^{(l)}\}_{l=1}^{\infty}$ be an orthonormal basis of $\mathcal{L}_i^2$ and $\mathcal{B}_w = \{h_w^{(l)}\}_{l=1}^{\infty}$ be an orthogonal basis of $\mathcal{H}_w^1$ that is orthonormal in $\mathcal{L}_w^2$; see Lemma 4.1 for the existence and structure of $\mathcal{B}_w$. Finally, construct the set $\mathcal{B} = \{b^{(k)}\}_{k=1}^{\infty} \subset \mathcal{L}_v^2 \times \mathcal{L}_i^2 \times \mathcal{H}_w^1$ as

$$\mathcal{B} := \mathcal{B}_v \times \mathcal{B}_i \times \mathcal{B}_w = \Big\{ b^{(k)} = (\ell_v^{(k)}, \ell_i^{(k)}, h_w^{(k)}) : \ell_v^{(k)} \in \mathcal{B}_v, \ell_i^{(k)} \in \mathcal{B}_i, h_w^{(k)} \in \mathcal{B}_w \Big\}_{k=1}^{\infty}. \tag{4.6}$$

For each positive integer m, we seek approximations $v^{(m)} : [0,T] \to \mathcal{L}_v^2$, $i^{(m)} : [0,T] \to \mathcal{L}_i^2$, and $w^{(m)} : [0,T] \to \mathcal{H}_w^1$ of the form

$$v^{(m)}(t) = \sum\nolimits_{k=1}^{m} c_{v_k}^{(m)}(t)\ell_v^{(k)}, \tag{4.7}$$

$$i^{(m)}(t) = \sum\nolimits_{k=1}^{m} c_{i_k}^{(m)}(t)\ell_i^{(k)}, \tag{4.8}$$

$$w^{(m)}(t) = \sum\nolimits_{k=1}^{m} c_{w_k}^{(m)}(t)h_w^{(k)}, \tag{4.9}$$

with sufficiently smooth functions $c_{v_k}^{(m)}$, $c_{i_k}^{(m)}$, and $c_{w_k}^{(m)}$ on $[0,T]$, such that, for all $t \in [0,T]$, and $k = 1, \ldots, m$, these approximations satisfy the system of differential equations

$$\begin{aligned} &\big(\Phi \mathrm{d}_t v^{(m)}, \ell_v^{(k)}\big)_{\mathcal{L}_v^2} + \big(v^{(m)}, \ell_v^{(k)}\big)_{\mathcal{L}_v^2} - \big(J_1 i^{(m)}, \ell_v^{(k)}\big)_{\mathcal{L}_v^2} \\ &\qquad + \big(J_2 v^{(m)} {i^{(m)}}^{\mathrm{T}} \Psi J_4 + J_3 v^{(m)} {i^{(m)}}^{\mathrm{T}} \Psi J_5, \ell_v^{(k)}\big)_{\mathcal{L}_v^2} = 0, \end{aligned} \tag{4.10}$$

$$\begin{aligned} &\big(\mathrm{d}_t^2 i^{(m)}, \ell_i^{(k)}\big)_{\mathcal{L}_i^2} + 2\big(\Gamma \mathrm{d}_t i^{(m)}, \ell_i^{(k)}\big)_{\mathcal{L}_i^2} + \big(\Gamma^2 i^{(m)}, \ell_i^{(k)}\big)_{\mathcal{L}_i^2} \\ &\qquad - e\big(\Upsilon \Gamma J_6 w^{(m)}, \ell_i^{(k)}\big)_{\mathcal{L}_i^2} - e\big(\Upsilon \Gamma \mathrm{N} J_7 f(v^{(m)}), \ell_i^{(k)}\big)_{\mathcal{L}_i^2} = e\big(\Upsilon \Gamma g, \ell_i^{(k)}\big)_{\mathcal{L}_i^2}, \end{aligned} \tag{4.11}$$

$$\begin{aligned} &\big(\mathrm{d}_t^2 w^{(m)}, h_w^{(k)}\big)_{\mathcal{L}_w^2} + 2\nu\big(\Lambda \mathrm{d}_t w^{(m)}, h_w^{(k)}\big)_{\mathcal{L}_w^2} - \tfrac{3}{2}\nu^2\big(\Delta w^{(m)}, h_w^{(k)}\big)_{\mathcal{L}_w^2} \\ &\qquad + \nu^2\big(\Lambda^2 w^{(m)}, h_w^{(k)}\big)_{\mathcal{L}_w^2} - \nu^2\big(\Lambda^2 \mathrm{M} J_8 f(v^{(m)}), h_w^{(k)}\big)_{\mathcal{L}_w^2} = 0, \end{aligned} \tag{4.12}$$

subject to the initial conditions

$$\begin{aligned} &c_{v_k}^{(m)}(0) = \big(v_0, \ell_v^{(k)}\big)_{\mathcal{L}_v^2}, \qquad c_{i_k}^{(m)}(0) = \big(i_0, \ell_i^{(k)}\big)_{\mathcal{L}_i^2}, \qquad \mathrm{d}_t c_{i_k}^{(m)}(0) = \big(i_0', \ell_i^{(k)}\big)_{\mathcal{L}_i^2}, \\ &c_{w_k}^{(m)}(0) = \big(w_0, h_w^{(k)}\big)_{\mathcal{L}_w^2}, \quad \mathrm{d}_t c_{w_k}^{(m)}(0) = \big(w_0', h_w^{(k)}\big)_{\mathcal{L}_w^2}, \end{aligned} \tag{4.13}$$

on the coefficients $c_k^{(m)}(t) = (c_{v_k}^{(m)}(t), c_{i_k}^{(m)}(t), c_{w_k}^{(m)}(t)) \in \mathbb{R}^3$.

Equations (4.10)–(4.13) are equivalent to a system of nonlinear $3m$-dimensional ordinary differential equations on coefficients $c^{(m)}(t) = (c_1^{(m)}(t), \ldots, c_m^{(m)}(t)) \in \mathbb{R}^{3m}$. Therefore, by the standard theory of ordinary differential equations [47, Th. 2.1], there exists a unique function $c^{(m)}(t)$ that solves (4.10)–(4.13) for $t \in [0, T_m)$, $T_m > 0$, with the approximations (4.7)–(4.9). Moreover, $T_m = T$ for all positive integers m, which follows from Proposition 4.4.

Proposition 4.4 (Energy estimates) *Suppose $g \in L^2(0,T;\mathcal{L}_i^2)$ and for every positive integer m let $v^{(m)}$, $i^{(m)}$, and $w^{(m)}$ be functions of the form (4.7)–(4.9), respectively, satisfying (4.10)–(4.12) with the initial conditions (4.13). Then there exist positive constants α_v, β_v, α_i, and α_w, dependent* *only on the parameters of the model, such that for every positive integer m,*

$$\sup_{t\in[0,T]}\left(\left\|v^{(m)}(t)\right\|^2_{\mathcal{L}^2_v}\right)+\left\|\mathrm{d}_t v^{(m)}\right\|^2_{L^2(0,T;\mathcal{L}^{2*}_v)}\le \kappa_v, \tag{4.14}$$

$$\sup_{t\in[0,T]}\left(\left\|\mathrm{d}_t i^{(m)}(t)\right\|^2_{\mathcal{L}^2_i}+\left\|i^{(m)}(t)\right\|^2_{\mathcal{L}^2_i}\right)+\left\|\mathrm{d}^2_t i^{(m)}\right\|^2_{L^2(0,T;\mathcal{L}^{2*}_i)}\le \kappa_i, \tag{4.15}$$

$$\sup_{t\in[0,T]}\left(\left\|\mathrm{d}_t w^{(m)}(t)\right\|^2_{\mathcal{L}^2_w}+\left\|w^{(m)}(t)\right\|^2_{\mathcal{H}^1_w}\right)+\left\|\mathrm{d}^2_t w^{(m)}\right\|^2_{L^2(0,T;\mathcal{H}^{1*}_w)}\le \kappa_w, \tag{4.16}$$

where κ_v, κ_i, and κ_w are positive constants given, independently of m, by

$$\kappa_v := \alpha_v\left(\left(1+(1+\sqrt{\kappa_i})^2T\right)\exp\left(\beta_v\sqrt{\kappa_i}T\right)\left[\left\|v_0\right\|^2_{\mathcal{L}^2_v}+\kappa_i T\right]+\kappa_i T\right), \tag{4.17}$$

$$\begin{aligned}\kappa_i := \alpha_i\Big((1+T)\left[\left\|i_0'\right\|^2_{\mathcal{L}^2_i}+\left\|i_0\right\|^2_{\mathcal{L}^2_i}\right]+(2+T)\Big[T\left(\kappa_w+|\Omega|(\mathrm{F}^2_{\mathrm{E}}+\mathrm{F}^2_{\mathrm{I}})\right)\\ +\left\|g\right\|^2_{L^2(0,T;\mathcal{L}^2_i)}\Big]\Big),\end{aligned} \tag{4.18}$$

$$\kappa_w := \alpha_w\left((1+T)\left[\left\|w_0'\right\|^2_{\mathcal{L}^2_w}+\left\|w_0\right\|^2_{\mathcal{H}^1_w}\right]+(2+T)T|\Omega|\mathrm{F}^2_{\mathrm{E}}\right). \tag{4.19}$$

Proof. *Multiplying (4.12) by $\mathrm{d}_t c^{(m)}_{w_k}$ and summing over $k=1,\dots,m$ yields*

$$\begin{aligned}\left(\mathrm{d}^2_t w^{(m)},\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}+2\nu\left(\Lambda\mathrm{d}_t w^{(m)},\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}-\tfrac{3}{2}\nu^2\left(\Delta w^{(m)},\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}\\ +\nu^2\left(\Lambda^2 w^{(m)},\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}-\nu^2\left(\Lambda^2\mathrm{M}J_8 f(v^{(m)}),\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}=0,\end{aligned}$$

or, equivalently, using (2.1) in the third term in the above equation,

$$\begin{aligned}\tfrac{1}{2}\mathrm{d}_t\left[\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}+\tfrac{3}{2}\nu^2\left\|\partial_x w^{(m)}\right\|^2_{\mathcal{L}^2_{\partial w}}+\nu^2\left\|\Lambda w^{(m)}\right\|^2_{\mathcal{L}^2_w}\right]+2\nu\left\|\Lambda^{\frac{1}{2}}\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}\\ -\nu^2\left(\Lambda^2\mathrm{M}J_8 f(v^{(m)}),\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w}=0.\end{aligned}$$

Now, Young's inequality implies that for every $\varepsilon_1>0$,

$$\begin{aligned}\nu^2\left(\Lambda^2\mathrm{M}J_8 f(v^{(m)}),\mathrm{d}_t w^{(m)}\right)_{\mathcal{L}^2_w} &\le \varepsilon_1\nu^2\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}+\frac{\nu^2}{4\varepsilon_1}\left\|\Lambda^2\mathrm{M}J_8 f(v^{(m)})\right\|^2_{\mathcal{L}^2_w}\\ &=\varepsilon_1\nu^2\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}+\frac{\nu^2}{4\varepsilon_1}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\int_\Omega\left|f_{\mathrm{E}}(v^{(m)}_{\mathrm{E}})\right|^2\mathrm{d}x\\ &\le \varepsilon_1\nu^2\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}+\frac{\nu^2}{4\varepsilon_1}|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2).\end{aligned}$$

Therefore,

$$\begin{aligned}\mathrm{d}_t\left[\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}+\tfrac{3}{2}\nu^2\left\|\partial_x w^{(m)}\right\|^2_{\mathcal{L}^2_{\partial w}}+\nu^2\left\|\Lambda w^{(m)}\right\|^2_{\mathcal{L}^2_w}\right]+2\nu(2\Lambda_{\min}-\varepsilon_1\nu)\left\|\mathrm{d}_t w^{(m)}\right\|^2_{\mathcal{L}^2_w}\\ \le\frac{\nu^2}{2\varepsilon_1}|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2),\end{aligned}$$

where $\Lambda_{\min}:=\min\{\Lambda_{\mathrm{EE}},\Lambda_{\mathrm{EI}}\}$ is the smallest eigenvalue of Λ.

Next, setting $\varepsilon_1 = \frac{2}{\nu}\Lambda_{\min}$ *and integrating with respect to time over* $[0,t]$ *yields*

$$\begin{aligned}\big\|\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big\|\partial_x w^{(m)}(t)\big\|^2_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} \\ \le \Big(\big\|\mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big\|\partial_x w^{(m)}\big\|^2_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda w^{(m)}\big\|^2_{\mathcal{L}^2_w}\Big)\Big|_{t=0} + \tfrac{1}{4}\frac{\nu^3}{\Lambda_{\min}}|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)t,\end{aligned}$$

which, using (4.13), implies

$$\big\|\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} + \big\|w^{(m)}(t)\big\|^2_{\mathcal{H}^1_w} \le \hat{\alpha}_w\left(\big\|w_0'\big\|^2_{\mathcal{L}^2_w} + \big\|w_0\big\|^2_{\mathcal{H}^1_w} + \tfrac{1}{4}\frac{\nu^3}{\Lambda_{\min}}|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)t\right)$$

for all $t\in[0,T]$ *and some* $\hat{\alpha}_w > 0$. *Since this inequality holds for all* $t\in[0,T]$, *it follows that*

$$\sup_{t\in[0,T]}\Big(\big\|\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} + \big\|w^{(m)}(t)\big\|^2_{\mathcal{H}^1_w}\Big) \le \hat{\kappa}_w, \tag{4.20}$$

where

$$\hat{\kappa}_w := \hat{\alpha}_w\left(\big\|w_0'\big\|^2_{\mathcal{L}^2_w} + \big\|w_0\big\|^2_{\mathcal{H}^1_w} + \tfrac{1}{4}\frac{\nu^3}{\Lambda_{\min}}|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)T\right).$$

Now, fix $\bar{h}\in\mathcal{H}^1_w$ *such that* $\big\|\bar{h}\big\|_{\mathcal{H}^1_w}\le 1$ *and decompose* $\bar{h}$ *as* $\bar{h} = h + h^{\perp}$, *where* $h\in\operatorname{span}\big\{h^{(k)}_w\big\}^m_{k=1}$ *and* $\big(h^{(k)}_w, h^{\perp}\big)_{\mathcal{L}^2_w} = 0$, $k = 1,\ldots,m$. *Since the basis* $\mathcal{B}_w$ *used to construct* $\mathcal{B}$ *in (4.6) is orthonormal in* $\mathcal{L}^2_w$, *it follows from (4.9) that*

$$\big\langle \mathrm{d}^2_t w^{(m)}, \bar{h}\big\rangle_{\mathcal{H}^1_w} = \big(\mathrm{d}^2_t w^{(m)}, \bar{h}\big)_{\mathcal{L}^2_w} = \big(\mathrm{d}^2_t w^{(m)}, h\big)_{\mathcal{L}^2_w},$$

where the first equality holds since $\mathrm{d}^2_t w^{(m)}\in\mathcal{H}^1_w$; *see the proof of [15, Th. 5.9-1]. Therefore, (4.12) gives*

$$\begin{aligned}\big\langle \mathrm{d}^2_t w^{(m)}, \bar{h}\big\rangle_{\mathcal{H}^1_w} = \\ -2\nu\big(\Lambda\mathrm{d}_t w^{(m)}, h\big)_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big(\Delta w^{(m)}, h\big)_{\mathcal{L}^2_w} - \nu^2\big(\Lambda^2 w^{(m)}, h\big)_{\mathcal{L}^2_w} + \nu^2\big(\Lambda^2\mathrm{M}J_8 f(v^{(m)}), h\big)_{\mathcal{L}^2_w}.\end{aligned}$$

Since $\mathcal{B}_w$ *is orthogonal in* $\mathcal{H}^1_w$ *we have* $\big\|h\big\|_{\mathcal{H}^1_w} \le \big\|\bar{h}\big\|_{\mathcal{H}^1_w} \le 1$, *and hence, the Cauchy-Schwarz inequality gives*

$$\begin{aligned}\big|\big\langle \mathrm{d}^2_t w^{(m)}, \bar{h}\big\rangle_{\mathcal{H}^1_w}\big| \\ \le 2\nu\big\|\mathrm{d}_t w^{(m)}\big\|_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big\|\partial_x w^{(m)}\big\|_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda^2 w^{(m)}\big\|_{\mathcal{L}^2_w} + \nu^2\big\|\Lambda^2\mathrm{M}J_8 f(v^{(m)})\big\|_{\mathcal{L}^2_w} \\ \le \alpha_1\left(\big\|\mathrm{d}_t w^{(m)}\big\|_{\mathcal{L}^2_w} + \big\|w^{(m)}\big\|_{\mathcal{H}^1_w} + \nu^2\big(|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\big)^{\frac{1}{2}}\right)\end{aligned}$$

for some $\alpha_1 > 0$. *Therefore, there exists* $\alpha_2 > 0$ *such that*

$$\int_0^T \big\|\mathrm{d}^2_t w^{(m)}\big\|^2_{\mathcal{H}^{1*}_w}\mathrm{d}t \le \alpha_2\int_0^T\Big(\big\|\mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \big\|w^{(m)}\big\|^2_{\mathcal{H}^1_w} + \nu^4|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\Big)\mathrm{d}t,$$

which, using (4.20), yields

$$\big\|\mathrm{d}^2_t w^{(m)}\big\|^2_{L^2(0,T;\mathcal{H}^{1*}_w)} \le \alpha_2\left(\hat{\kappa}_w + \nu^4|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\right)T.$$

This inequality, together with (4.20), establishes the bound (4.16) with (4.19) for some $\alpha_w > 0$.

Next, multiplying (4.11) by $\mathrm{d}_t c_{i_k}^{(m)}$ *and summing over* $k = 1, \ldots, m$ *yields*

$$\begin{aligned}(4.21)\quad &\big(\mathrm{d}_t^2 i^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} + 2\big(\Gamma \mathrm{d}_t i^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} + \big(\Gamma^2 i^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} \\ &\quad - e\big(\Upsilon\Gamma J_6 w^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} - e\big(\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m)}), \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} = e\big(\Upsilon\Gamma g, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2}.\end{aligned}$$

For the second term we have

$$\big(\Gamma \mathrm{d}_t i^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} \geq \gamma_{\min} \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2,$$

where $\gamma_{\min} := \min\{\gamma_{\mathrm{EE}}, \gamma_{\mathrm{EI}}, \gamma_{\mathrm{IE}}, \gamma_{\mathrm{II}}\}$ *is the smallest eigenvalue of* Γ. *Now, using Young's inequality and recalling (4.16) we obtain, for every* $\varepsilon_2, \ldots, \varepsilon_4 > 0$,

$$\begin{aligned} e\big(\Upsilon\Gamma J_6 w^{(m)}, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} &\leq \varepsilon_2 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_2}\big\|\Upsilon\Gamma J_6 w^{(m)}\big\|_{\mathcal{L}_i^2}^2 \\ &\leq \varepsilon_2 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_2}\big\|\Upsilon\Gamma J_6\big\|_2^2 \big\|w^{(m)}\big\|_{\mathcal{L}_w^2}^2 \\ &\leq \varepsilon_2 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2\kappa_w}{4\varepsilon_2}\big\|\Upsilon\Gamma J_6\big\|_2^2, \\ e\big(\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m)}), \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} &\leq \varepsilon_3 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_3}\big\|\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m)})\big\|_{\mathcal{L}_i^2}^2 \\ &\leq \varepsilon_3 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_3}\big\|\Upsilon\Gamma \mathrm{N} J_7\big\|_2^2 \big\|f(v^{(m)})\big\|_{\mathcal{L}_v^2}^2 \\ &\leq \varepsilon_3 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2|\Omega|}{4\varepsilon_3}(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\big\|\Upsilon\Gamma \mathrm{N} J_7\big\|_2^2, \\ e\big(\Upsilon\Gamma g, \mathrm{d}_t i^{(m)}\big)_{\mathcal{L}_i^2} &\leq \varepsilon_4 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_4}\big\|\Upsilon\Gamma g\big\|_{\mathcal{L}_i^2}^2 \\ &\leq \varepsilon_4 \big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_4}\big\|\Upsilon\Gamma\big\|_2^2 \big\|g\big\|_{\mathcal{L}_i^2}^2. \end{aligned}$$

Hence, with the above inequalities, (4.21) implies

$$\begin{aligned} &\mathrm{d}_t \left[\big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 + \big\|\Gamma i^{(m)}\big\|_{\mathcal{L}_i^2}^2\right] + 2(2\gamma_{\min} - \varepsilon_2 - \varepsilon_3 - \varepsilon_4)\big\|\mathrm{d}_t i^{(m)}\big\|_{\mathcal{L}_i^2}^2 \\ &\qquad \leq \frac{e^2\kappa_w}{2\varepsilon_2}\big\|\Upsilon\Gamma J_6\big\|_2^2 + \frac{e^2|\Omega|}{2\varepsilon_3}(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\big\|\Upsilon\Gamma \mathrm{N} J_7\big\|_2^2 + \frac{e^2}{2\varepsilon_4}\big\|\Upsilon\Gamma\big\|_2^2 \big\|g\big\|_{\mathcal{L}_i^2}^2. \end{aligned}$$

Now, setting $\varepsilon_2 = \varepsilon_3 = \frac{1}{2}\gamma_{\min}$ *and* $\varepsilon_4 = \gamma_{\min}$, *integrating with respect to time over* $[0, t]$, *and taking the supremum over* $t \in [0, T]$ *we have*

$$(4.22)\qquad \sup_{t\in[0,T]} \left(\big\|\mathrm{d}_t i^{(m)}(t)\big\|_{\mathcal{L}_i^2}^2 + \big\|i^{(m)}(t)\big\|_{\mathcal{L}_i^2}^2\right) \leq \hat{\kappa}_i,$$

where, for some $\hat{\alpha}_i > 0$,

$$\begin{aligned} \hat{\kappa}_i = \hat{\alpha}_i \Bigg(&\big\|i_0'\big\|_{\mathcal{L}_i^2}^2 + \big\|i_0\big\|_{\mathcal{L}_i^2}^2 + \left[\frac{e^2\kappa_w}{\gamma_{\min}}\big\|\Upsilon\Gamma J_6\big\|_2^2 + \frac{e^2|\Omega|}{\gamma_{\min}}(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\big\|\Upsilon\Gamma \mathrm{N} J_7\big\|_2^2\right] T \\ &+ \frac{e^2}{2\gamma_{\min}}\big\|\Upsilon\Gamma\big\|_2^2 \big\|g\big\|_{L^2(0,T;\mathcal{L}_i^2)}^2 \Bigg). \end{aligned}$$

Fix $\bar{\ell} \in \mathcal{L}_i^2$ *such that* $\|\bar{\ell}\|_{\mathcal{L}_i^2} \le 1$ *and decompose* $\bar{\ell}$ *as* $\bar{\ell} = \ell + \ell^{\perp}$, *where* $\ell \in \operatorname{span}\{\ell_i^{(k)}\}_{k=1}^m$ *and* $(\ell_i^{(k)}, \ell^{\perp})_{\mathcal{L}_i^2} = 0$, $k = 1, \dots, m$. *Using (4.8) and (4.11) we obtain*

$$\begin{aligned}\langle \mathrm{d}_t^2 i^{(m)}, \bar{\ell}\rangle_{\mathcal{L}_i^2} &= (\mathrm{d}_t^2 i^{(m)}, \bar{\ell})_{\mathcal{L}_i^2} = (\mathrm{d}_t^2 i^{(m)}, \ell)_{\mathcal{L}_i^2} \\ &= -2(\Gamma \mathrm{d}_t i^{(m)}, \ell)_{\mathcal{L}_i^2} - (\Gamma^2 i^{(m)}, \ell)_{\mathcal{L}_i^2} + e(\Upsilon\Gamma J_6 w^{(m)}, \ell)_{\mathcal{L}_i^2} + e(\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m)}), \ell)_{\mathcal{L}_i^2} \\ &\quad + e(\Upsilon\Gamma g, \ell)_{\mathcal{L}_i^2}.\end{aligned}$$

The orthogonality of the basis $\mathcal{B}_i$ *in (4.6) implies* $\|\ell\|_{\mathcal{L}_i^2} \le 1$, *and hence,*

$$\begin{aligned}|\langle \mathrm{d}_t^2 i^{(m)}, \bar{\ell}\rangle_{\mathcal{L}_i^2}| \le 2\|\Gamma\|_2 \|\mathrm{d}_t i^{(m)}\|_{\mathcal{L}_i^2} + \|\Gamma^2\|_2 \|i^{(m)}\|_{\mathcal{L}_i^2} \\ + e\|\Upsilon\Gamma J_6 w^{(m)}\|_{\mathcal{L}_i^2} + e\|\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m)})\|_{\mathcal{L}_i^2} + e\|\Upsilon\Gamma g\|_{\mathcal{L}_i^2}.\end{aligned}$$

Therefore, it follows from the same inequalities used to derive (4.22) that, for some $\alpha_3 > 0$,

$$\begin{aligned}\|\mathrm{d}_t^2 i^{(m)}\|^2_{L^2(0,T;\mathcal{L}_i^{2*})} \le \alpha_3 \Big(\Big[\hat{\kappa}_i + e^2\kappa_w \|\Upsilon\Gamma J_6\|_2^2 + e^2|\Omega|(\mathrm{F}_\mathrm{E}^2 + \mathrm{F}_\mathrm{I}^2)\|\Upsilon\Gamma \mathrm{N} J_7\|_2^2\Big] T \\ + e^2\|\Upsilon\Gamma\|_2^2 \|g\|^2_{L^2(0,T;\mathcal{L}_i^2)}\Big).\end{aligned}$$

This, together with (4.22), establishes the bound (4.15) with (4.18) for some $\alpha_i > 0$.

Finally, multiplying (4.10) by $c_{v_k}^{(m)}$ *and summing over* $k = 1, \dots, m$ *yields*

$$\begin{aligned}(\Phi \mathrm{d}_t v^{(m)}, v^{(m)})_{\mathcal{L}_v^2} + (v^{(m)}, v^{(m)})_{\mathcal{L}_v^2} - (J_1 i^{(m)}, v^{(m)})_{\mathcal{L}_v^2} \\ + (J_2 v^{(m)} i^{(m)\mathrm{T}} \Psi J_4 + J_3 v^{(m)} i^{(m)\mathrm{T}} \Psi J_5, v^{(m)})_{\mathcal{L}_v^2} = 0.\end{aligned} \tag{4.23}$$

Now, using Young's inequality and recalling (4.15) we obtain, for every $\varepsilon_5 > 0$,

$$\begin{aligned}(J_1 i^{(m)}, v^{(m)})_{\mathcal{L}_v^2} &\le \varepsilon_5 \|v^{(m)}\|^2_{\mathcal{L}_v^2} + \frac{1}{4\varepsilon_5}\|J_1 i^{(m)}\|^2_{\mathcal{L}_v^2} \\ &\le \varepsilon_5 \|v^{(m)}\|^2_{\mathcal{L}_v^2} + \frac{1}{2\varepsilon_5}\|i^{(m)}\|^2_{\mathcal{L}_v^2} \\ &\le \varepsilon_5 \|v^{(m)}\|^2_{\mathcal{L}_v^2} + \frac{\kappa_i}{2\varepsilon_5}.\end{aligned}$$

Moreover, using Hölder's inequality in $\mathbb{R}^2$ *and the Cauchy-Schwarz inequality in* $\mathbb{R}^4$ *we obtain*

$$\begin{aligned}-(J_2 v^{(m)} i^{(m)\mathrm{T}} \Psi J_4 + J_3 v^{(m)} i^{(m)\mathrm{T}} \Psi J_5, v^{(m)})_{\mathcal{L}_v^2} \\ = -\int_\Omega \Big((v_1^{(m)})^2 i^{(m)\mathrm{T}} \Psi J_4 + (v_2^{(m)})^2 i^{(m)\mathrm{T}} \Psi J_5\Big)\,\mathrm{d}x \\ \le \int_\Omega \|v^{(m)}\|^2_{\mathbb{R}^2} \max\Big\{|i^{(m)\mathrm{T}} \Psi J_4|, |i^{(m)\mathrm{T}} \Psi J_5|\Big\}\,\mathrm{d}x \\ \le \int_\Omega \|v^{(m)}\|^2_{\mathbb{R}^2} \|i^{(m)}\|_{\mathbb{R}^4} \max\{\|\Psi J_4\|_{\mathbb{R}^4}, \|\Psi J_5\|_{\mathbb{R}^4}\}\,\mathrm{d}x \\ \le \sqrt{2\kappa_i}\|\Psi\|_2 \|v^{(m)}\|^2_{\mathcal{L}_v^2}.\end{aligned}$$

Therefore, (4.23) implies

$$\mathrm{d}_t\big\|\Phi^{\frac{1}{2}}v^{(m)}\big\|^2_{\mathcal{L}^2_v}+2\left(1-\varepsilon_5-\sqrt{2\kappa_i}\big\|\Psi\big\|_2\right)\big\|v^{(m)}\big\|^2_{\mathcal{L}^2_v}\le\frac{\kappa_i}{\varepsilon_5}.$$

Next, setting $\varepsilon_5=1$ and using Grönwall's inequality [48, Sec. III.1.1.3.] yields

$$\sup_{t\in[0,T]}\left(\big\|v^{(m)}(t)\big\|^2_{\mathcal{L}^2_v}\right)\le\hat{\kappa}_v, \tag{4.24}$$

where, for some $\hat{\alpha}_v>0$ and $\hat{\beta}_v>0$,

$$\hat{\kappa}_v=\hat{\alpha}_v\exp\left(\hat{\beta}_v\sqrt{2\kappa_i}\big\|\Psi\big\|_2T\right)\left(\big\|v_0\big\|^2_{\mathcal{L}^2_v}+\kappa_iT\right).$$

Now, fix $\bar{\ell}\in\mathcal{L}^2_v$ such that $\big\|\bar{\ell}\big\|_{\mathcal{L}^2_v}\le 1$ and decompose $\bar{\ell}$ as $\bar{\ell}=\ell+\ell^\perp$, where $\ell\in\operatorname{span}\{\ell_v^{(k)}\}_{k=1}^m$ and $\big(\Phi\ell_v^{(k)},\ell^\perp\big)_{\mathcal{L}^2_v}=0$, $k=1,\ldots,m$. Note that this decomposition exists due to the way we construct the basis $\mathcal{B}_v$ in (4.6), wherein the elements, weighted by $\Phi^{\frac{1}{2}}$, are orthonormal in $\mathcal{L}^2_v$. Then, it follows from (4.7) and (4.10) that

$$\begin{aligned}\big\langle\Phi\mathrm{d}_tv^{(m)},\bar{\ell}\big\rangle_{\mathcal{L}^2_v}&=\big(\Phi\mathrm{d}_tv^{(m)},\bar{\ell}\big)_{\mathcal{L}^2_v}=\big(\Phi\mathrm{d}_tv^{(m)},\ell\big)_{\mathcal{L}^2_v}\\&=-\big(v^{(m)},\ell\big)_{\mathcal{L}^2_v}+\big(J_1i^{(m)},\ell\big)_{\mathcal{L}^2_v}-\big(J_2v^{(m)}i^{(m)\mathrm{T}}\Psi J_4+J_3v^{(m)}i^{(m)\mathrm{T}}\Psi J_5,\ell\big)_{\mathcal{L}^2_v}.\end{aligned}$$

Since $\mathcal{B}_v$ is a $\Phi^{\frac{1}{2}}$-weighted orthonormal set in $\mathcal{L}^2_v$, it follows that

$$\big\|\ell\big\|_{\mathcal{L}^2_v}\le\big\|\Phi^{-\frac{1}{2}}\big\|_2\big\|\Phi^{\frac{1}{2}}\ell\big\|_{\mathcal{L}^2_v}\le\big\|\Phi^{-\frac{1}{2}}\big\|_2\big\|\Phi^{\frac{1}{2}}\bar{\ell}\big\|_{\mathcal{L}^2_v}\le\big\|\Phi^{-\frac{1}{2}}\big\|_2\big\|\Phi^{\frac{1}{2}}\big\|_2\big\|\bar{\ell}\big\|_{\mathcal{L}^2_v}\le\big\|\Phi^{-\frac{1}{2}}\big\|_2\big\|\Phi^{\frac{1}{2}}\big\|_2$$

and hence, letting $\alpha_4:=\big\|\Phi^{-\frac{1}{2}}\big\|_2\big\|\Phi^{\frac{1}{2}}\big\|_2$ and using Cauchy-Schwarz inequality we have

$$\begin{aligned}\big|\big\langle\Phi\mathrm{d}_tv^{(m)},\bar{\ell}\big\rangle_{\mathcal{L}^2_v}\big|&\le\alpha_4\left(\big\|v^{(m)}\big\|_{\mathcal{L}^2_v}+\big\|J_1i^{(m)}\big\|_{\mathcal{L}^2_v}+\big\|J_2v^{(m)}i^{(m)\mathrm{T}}\Psi J_4+J_3v^{(m)}i^{(m)\mathrm{T}}\Psi J_5\big\|_{\mathcal{L}^2_v}\right)\\&\le\alpha_4\left(\big\|v^{(m)}\big\|_{\mathcal{L}^2_v}+\sqrt{2}\big\|i^{(m)}\big\|_{\mathcal{L}^2_v}+2\sqrt{2}\big\|v^{(m)}\big\|_{\mathcal{L}^2_v}\big\|i^{(m)}\big\|_{\mathcal{L}^2_v}\big\|\Psi\big\|_2\right)\\&\le\alpha_4\left(\left(1+2\sqrt{2\kappa_i}\big\|\Psi\big\|_2\right)\big\|v^{(m)}\big\|_{\mathcal{L}^2_v}+\sqrt{2\kappa_i}\right),\end{aligned}$$

which, along with (4.24) implies that, for some $\alpha_5>0$,

$$\big\|\mathrm{d}_tv^{(m)}\big\|^2_{L^2(0,T;\mathcal{L}^{2*}_v)}\le\alpha_5\left(\left(1+2\sqrt{2\kappa_i}\big\|\Psi\big\|_2\right)^2\hat{\kappa}_v+2\kappa_i\right)T.$$

This, together with (4.24), establishes the bound (4.14) with (4.17) for some $\alpha_v>0$. Note that constants $\alpha_1,\ldots,\alpha_5$, $\hat{\alpha}_v$, $\hat{\beta}_v$, $\hat{\alpha}_i$, and $\hat{\alpha}_w$ depend only on the parameters of the model, which further implies that the constants α_v, β_v, α_i, and α_w also depend only on the parameters of the model and completes the proof.

Theorem 4.5 (Existence and uniqueness of weak solutions) *Suppose that $g\in L^2(0,T;\mathcal{L}^2_i)$, $v_0\in\mathcal{L}^2_v$, $i_0\in\mathcal{L}^2_i$, $i_0'\in\mathcal{L}^2_i$, $w_0\in\mathcal{H}^1_w$, and $w_0'\in\mathcal{L}^2_w$. Then there exists a unique Ω-periodic weak solution (v,i,w) of the initial value problem (3.3)–(3.6).*

Proof. *The energy estimate (4.14) implies that the sequence* $\{v^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{L}_v^2)$ *and the sequence* $\{\mathrm{d}_t v^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{L}_v^{2*})$*. Since* $\mathcal{L}_v^{2*}=\mathcal{L}_v^2$*, it follows that* $\{v^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $H^1(0,T;\mathcal{L}_v^2)$ *and* $\{\mathrm{d}_t v^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L_2(0,T;\mathcal{L}_v^2)$*. Similarly, since* $\mathcal{L}_i^{2*}=\mathcal{L}_i^2$*, the energy estimate (4.15) implies that the sequence* $\{i^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $H^2(0,T;\mathcal{L}_i^2)$*, the sequence* $\{\mathrm{d}_t i^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $H^1(0,T;\mathcal{L}_i^2)$*, and the sequence* $\{\mathrm{d}_t^2 i^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{L}_i^2)$*. Finally, the energy estimate (4.16) implies that the sequence* $\{w^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{H}_w^1)$*, the sequence* $\{\mathrm{d}_t w^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{L}_w^2)$*, and the sequence* $\{\mathrm{d}_t^2 w^{(m)}\}_{m=1}^{\infty}$ *is bounded in* $L^2(0,T;\mathcal{H}_w^{1*})$*. Now, it follows from the Rellich-Kondrachov compact embedding theorems [8, Th. 6.6-3] that* $H^1(0,T;\mathcal{L}_v^2)\Subset L^2(0,T;\mathcal{L}_v^2)$ *and* $H^1(0,T;\mathcal{L}_i^2)\Subset L^2(0,T;\mathcal{L}_i^2)$*. Therefore, by [8, Th. 2.10-1b], there exist subsequences* $\{v^{(m_k)}\}_{k=1}^{\infty}$*,* $\{i^{(m_k)}\}_{k=1}^{\infty}$*, and* $\{\mathrm{d}_t i^{(m_k)}\}_{k=1}^{\infty}$ *such that*

$$
\begin{aligned}
v^{(m_k)} &\to v \quad \text{strongly in } L^2(0,T;\mathcal{L}_v^2),\\
i^{(m_k)} &\to i \quad \text{strongly in } L^2(0,T;\mathcal{L}_i^2),\\
\mathrm{d}_t i^{(m_k)} &\to i' \quad \text{strongly in } L^2(0,T;\mathcal{L}_i^2).
\end{aligned} \tag{4.25}
$$

Moreover, by the Banach-Eberlein-Šmulian theorem [8, Th. 5.14-4], there exist subsequences $\{\mathrm{d}_t v^{(m_k)}\}_{k=1}^{\infty}$*,* $\mathrm{d}_t^2\{i^{(m_k)}\}_{k=1}^{\infty}$*,* $\{w^{(m_k)}\}_{k=1}^{\infty}$*,* $\{\mathrm{d}_t w^{(m_k)}\}_{k=1}^{\infty}$*, and* $\{\mathrm{d}_t^2 w^{(m_k)}\}_{k=1}^{\infty}$ *such that*

$$
\begin{aligned}
\mathrm{d}_t v^{(m_k)} &\rightharpoonup v' \quad \text{weakly in } L^2(0,T;\mathcal{L}_v^2),\\
\mathrm{d}_t^2 i^{(m_k)} &\rightharpoonup i'' \quad \text{weakly in } L^2(0,T;\mathcal{L}_i^2),\\
w^{(m_k)} &\rightharpoonup w \quad \text{weakly in } L^2(0,T;\mathcal{H}_w^1),\\
\mathrm{d}_t w^{(m_k)} &\rightharpoonup w' \quad \text{weakly in } L^2(0,T;\mathcal{L}_w^2),\\
\mathrm{d}_t^2 w^{(m_k)} &\rightharpoonup w'' \quad \text{weakly in } L^2(0,T;\mathcal{H}_w^{1*}),
\end{aligned} \tag{4.26}
$$

where the time derivatives in the above analysis are derivatives in the weak sense.

Next, we show that

$$v'=\mathrm{d}_t v,\quad i'=\mathrm{d}_t i,\quad i''=\mathrm{d}_t^2 i,\quad w'=\mathrm{d}_t w,\quad w''=\mathrm{d}_t^2 w.$$

Since $L^2(0,T;\mathcal{H}_w^1)$ *is reflexive, the weak and weak* convergence coincide. Recalling the definition of weak* convergence and weak derivatives, it follows that for every* $h\in\mathcal{H}_w^1$ *and* $\phi\in C_{\mathrm{c}}^{\infty}([0,T])$*,*

$$
\begin{aligned}
\Big\langle \int_0^T w''\phi\mathrm{d}t, h\Big\rangle_{\mathcal{H}_w^1} &= \int_0^T \big\langle w''\phi, h\big\rangle_{\mathcal{H}_w^1}\mathrm{d}t = \lim_{k\to\infty}\int_0^T \big\langle \mathrm{d}_t^2 w^{(m_k)}\phi, h\big\rangle_{\mathcal{H}_w^1}\mathrm{d}t\\
&= \lim_{k\to\infty}\Big\langle \int_0^T \mathrm{d}_t^2 w^{(m_k)}\phi\mathrm{d}t, h\Big\rangle_{\mathcal{H}_w^1} = \lim_{k\to\infty}\Big\langle (-1)^2\int_0^T w^{(m_k)}\mathrm{d}_t^2\phi\mathrm{d}t, h\Big\rangle_{\mathcal{H}_w^1}\\
&= \lim_{k\to\infty}(-1)^2\int_0^T \big\langle w^{(m_k)}\mathrm{d}_t^2\phi, h\big\rangle_{\mathcal{H}_w^1}\mathrm{d}t = (-1)^2\int_0^T \big\langle w\mathrm{d}_t^2\phi, h\big\rangle_{\mathcal{H}_w^1}\mathrm{d}t\\
&= \Big\langle (-1)^2\int_0^T w\mathrm{d}_t^2\phi\mathrm{d}t, h\Big\rangle_{\mathcal{H}_w^1},
\end{aligned}
$$

which implies $w''=\mathrm{d}_t^2 w$ *in the weak sense. The other identities are proved similarly.*

Now, recall (3.2) and (3.7) and note that the nonlinear map $f:\mathbb{R}^2\to\mathbb{R}^2$ *is bounded and smooth, and in particular, is Lipschitz continuous. Therefore, it follows from the strong convergence* *of* $\{v^{(m_k)}\}_{k=1}^{\infty}$ *in (4.25) that*

$$f(v^{(m_k)}) \to f(v) \quad \textit{strongly in } L^2(0,T;\mathcal{L}_v^2). \tag{4.27}$$

For the bilinear term $J_2 v i^{\mathrm{T}} \Psi J_4$*, use (4.14) and (4.15) to write*

$$\begin{aligned}
&\big\|J_2\big(vi^{\mathrm{T}} - v^{(m_k)} {i^{(m_k)}}^{\mathrm{T}}\big)\Psi J_4\big\|_{L^2(0,T;\mathcal{L}_v^2)} \\
&\quad \le \big\|J_2(v - v^{(m_k)})i^{\mathrm{T}}\Psi J_4\big\|_{L^2(0,T;\mathcal{L}_v^2)} + \big\|J_2 v^{(m_k)}(i - i^{(m_k)})^{\mathrm{T}}\Psi J_4\big\|_{L^2(0,T;\mathcal{L}_v^2)} \\
&\quad \le \sqrt{2}\|\Psi\|_2 \Big[\big\|v - v^{(m_k)}\big\|_{L^2(0,T;\mathcal{L}_v^2)}\big\|i\big\|_{L^2(0,T;\mathcal{L}_i^2)} + \big\|v^{(m_k)}\big\|_{L^2(0,T;\mathcal{L}_v^2)}\big\|i - i^{(m_k)}\big\|_{L^2(0,T;\mathcal{L}_i^2)}\Big] \\
&\quad \le \sqrt{2}\|\Psi\|_2 \Big[\sqrt{\kappa_i}\,\big\|v - v^{(m_k)}\big\|_{L^2(0,T;\mathcal{L}_v^2)} + \sqrt{\kappa_v}\,\big\|i - i^{(m_k)}\big\|_{L^2(0,T;\mathcal{L}_i^2)}\Big].
\end{aligned}$$

The same inequality holds for the bilinear term $J_3 v i^{\mathrm{T}} \Psi J_5$ *as well. Therefore, (4.25) gives*

$$\begin{aligned}
&J_2 v^{(m_k)} {i^{(m_k)}}^{\mathrm{T}} \Psi J_4 \to J_2 v i^{\mathrm{T}} \Psi J_4 \quad \textit{strongly in } L^2(0,T;\mathcal{L}_v^2), \\
&J_3 v^{(m_k)} {i^{(m_k)}}^{\mathrm{T}} \Psi J_5 \to J_3 v i^{\mathrm{T}} \Psi J_5 \quad \textit{strongly in } L^2(0,T;\mathcal{L}_v^2).
\end{aligned} \tag{4.28}$$

Next, fix a positive integer K *and choose the functions*

$$\begin{aligned}
\hat{v} &= \textstyle\sum_{k=1}^{K} c_{v_k}(t)\ell_v^{(k)} \;\in C^1([0,T];\mathcal{L}_v^2), \\
\hat{i} &= \textstyle\sum_{k=1}^{K} c_{i_k}(t)\ell_i^{(k)} \;\in C^1([0,T];\mathcal{L}_i^2), \\
\hat{w} &= \textstyle\sum_{k=1}^{K} c_{w_k}(t)h_w^{(k)} \in C^1([0,T];\mathcal{H}_w^1),
\end{aligned}$$

where, for every $k \in \{1,\dots,K\}$*, the scalar-valued functions* $c_{v_k}, c_{i_k}, c_{w_k}$ *are sufficiently smooth on* $[0,T]$ *and* $(\ell_v^{(k)}, \ell_i^{(k)}, h_w^{(k)}) \in \mathcal{B}$*, where* $\mathcal{B}$ *is given by (4.6). Set* $m = m_k$ *in (4.10)–(4.12) and choose* $m_k \ge K$*. Then, multiplying (4.10)–(4.12) by* c_{v_k}*,* c_{i_k}*, and* c_{w_k}*, respectively, summing over* $k = 1,\dots,K$*, and integrating over* $t \in [0,T]$ *yields*

$$\begin{aligned}
&\int_0^T \Big[\big\langle \Phi \mathrm{d}_t v^{(m_k)}, \hat{v}\big\rangle_{\mathcal{L}_v^2} + \big(v^{(m_k)}, \hat{v}\big)_{\mathcal{L}_v^2} - \big(J_1 i^{(m_k)}, \hat{v}\big)_{\mathcal{L}_v^2} \\
&\qquad\qquad + \big(J_2 v^{(m_k)} {i^{(m_k)}}^{\mathrm{T}} \Psi J_4 + J_3 v^{(m_k)} {i^{(m_k)}}^{\mathrm{T}} \Psi J_5, \hat{v}\big)_{\mathcal{L}_v^2}\Big]\,\mathrm{d}t = 0, \\
&\int_0^T \Big[\big\langle \mathrm{d}_t^2 i^{(m_k)}, \hat{i}\big\rangle_{\mathcal{L}_i^2} + 2\big(\Gamma \mathrm{d}_t i^{(m_k)}, \hat{i}\big)_{\mathcal{L}_i^2} + \big(\Gamma^2 i^{(m_k)}, \hat{i}\big)_{\mathcal{L}_i^2} \\
&\qquad\qquad - e\big(\Upsilon\Gamma J_6 w^{(m_k)}, \hat{i}\big)_{\mathcal{L}_i^2} - e\big(\Upsilon\Gamma \mathrm{N} J_7 f(v^{(m_k)}), \hat{i}\big)_{\mathcal{L}_i^2}\Big]\,\mathrm{d}t = \int_0^T e\big(\Upsilon\Gamma g, \hat{i}\big)_{\mathcal{L}_i^2}\mathrm{d}t, \\
&\int_0^T \Big[\big\langle \mathrm{d}_t^2 w^{(m_k)}, \hat{w}\big\rangle_{\mathcal{L}_w^2} + 2\nu\big(\Lambda \mathrm{d}_t w^{(m_k)}, \hat{w}\big)_{\mathcal{L}_w^2} - \tfrac{3}{2}\nu^2\big(\Delta w^{(m_k)}, \hat{w}\big)_{\mathcal{L}_w^2} \\
&\qquad\qquad + \nu^2\big(\Lambda^2 w^{(m_k)}, \hat{w}\big)_{\mathcal{L}_w^2} - \nu^2\big(\Lambda^2 \mathrm{M} J_8 f(v^{(m)}), \hat{w}\big)_{\mathcal{L}_w^2}\Big]\,\mathrm{d}t = 0.
\end{aligned} \tag{4.29}$$

Note that the families of functions $\hat{v}$*,* $\hat{i}$*, and* $\hat{w}$ *chosen above are dense in the spaces* $L^2(0,T;\mathcal{L}_v^2)$*,* $L^2(0,T;\mathcal{L}_i^2)$*, and* $L^2(0,T;\mathcal{H}_w^1)$*, respectively. Therefore, (4.29) holds for all functions* $\hat{v} \in L^2(0,T;\mathcal{L}_v^2)$*,*

$\hat{i} \in L^2(0,T;\mathcal{L}_i^2)$, *and* $\hat{w} \in L^2(0,T;\mathcal{H}_w^1)$. *Now, use (4.25)–(4.28) to pass to the limits in (4.29), which implies that (4.2)–(4.4) hold for all* $\ell_v \in \mathcal{L}_v^2$, $\ell_i \in \mathcal{L}_i^2$, $h_w \in \mathcal{H}_w^1$, *and almost every* $t \in [0,T]$.

It remains to verify the initial conditions (4.5). Choose the functions

$$\hat{v} \in C^1([0,T];\mathcal{L}_v^2), \quad \hat{i} \in C^2([0,T];\mathcal{L}_i^2), \quad \hat{w} \in C^2([0,T];\mathcal{H}_w^1),$$

such that these functions vanish at the end point $t = T$. *Integrating by parts in (4.29) yields*

$$\begin{aligned} &\int_0^T \Big[-\big(\Phi v^{(m_k)}, \mathrm{d}_t\hat{v}\big)_{\mathcal{L}_v^2} + \cdots\Big]\,\mathrm{d}t = \big(\Phi v^{(m_k)}(0), \hat{v}(0)\big)_{\mathcal{L}_v^2}, \\ &\int_0^T \Big[\big(i^{(m_k)}, \mathrm{d}_t^2\hat{i}\big)_{\mathcal{L}_i^2} + \cdots\Big]\,\mathrm{d}t = \cdots + \big(\mathrm{d}_t i^{(m_k)}(0), \hat{i}(0)\big)_{\mathcal{L}_i^2} - \big(i^{(m_k)}(0), \mathrm{d}_t\hat{i}(0)\big)_{\mathcal{L}_i^2}, \\ &\int_0^T \Big[\big(w^{(m_k)}, \mathrm{d}_t^2\hat{w}\big)_{\mathcal{H}_w^1} + \cdots\Big]\,\mathrm{d}t = \big(\mathrm{d}_t w^{(m_k)}(0), \hat{w}(0)\big)_{\mathcal{L}_w^2} - \big(w^{(m_k)}(0), \mathrm{d}_t\hat{w}(0)\big)_{\mathcal{L}_w^2}, \end{aligned} \tag{4.30}$$

where "$\cdots$" denotes terms that are not pertinent to the analysis. Similarly, integrating by parts in the limit of (4.29) yields

$$\begin{aligned} &\int_0^T \big[-\big(\Phi v, \mathrm{d}_t\hat{v}\big)_{\mathcal{L}_v^2} + \cdots\big]\,\mathrm{d}t = \big(\Phi v(0), \hat{v}(0)\big)_{\mathcal{L}_v^2}, \\ &\int_0^T \Big[\big(i, \mathrm{d}_t^2\hat{i}\big)_{\mathcal{L}_i^2} + \cdots\Big]\,\mathrm{d}t = \cdots + \big(\mathrm{d}_t i(0), \hat{i}(0)\big)_{\mathcal{L}_i^2} - \big(i(0), \mathrm{d}_t\hat{i}(0)\big)_{\mathcal{L}_i^2}, \\ &\int_0^T \big[\big(w, \mathrm{d}_t^2\hat{w}\big)_{\mathcal{H}_w^1} + \cdots\big]\,\mathrm{d}t = \big(\mathrm{d}_t w(0), \hat{w}(0)\big)_{\mathcal{L}_w^2} - \big(w(0), \mathrm{d}_t\hat{w}(0)\big)_{\mathcal{L}_w^2}. \end{aligned} \tag{4.31}$$

Now, consider the initial conditions (4.13), pass to the limits in (4.30) through (4.25)–(4.28), and compare the results with (4.31). Since $\hat{v}$, $\hat{i}$, *and* $\hat{w}$ *are arbitrary the initial condition (4.5) holds and this completes the proof of existence.*

To prove uniqueness, assume, by contradiction, that there exist two weak solutions $(\tilde{v}, \tilde{i}, \tilde{w})$ *and* $(\hat{v}, \hat{i}, \hat{w})$ *for* (3.1), *initiating from the same initial values, such that* $(\tilde{v}, \tilde{i}, \tilde{w}) \neq (\hat{v}, \hat{i}, \hat{w})$. *Then,* $(v, i, w) := (\tilde{v}, \tilde{i}, \tilde{w}) - (\hat{v}, \hat{i}, \hat{w})$ *is a weak solution initiating from the zero initial condition* $(v_0, i_0, i_0', w_0, w_0') = 0$. *Now, fix* $s \in [0,T]$ *and define, for* $0 \leq t \leq T$, *the functions*

$$p(t) := \int_0^t w(r)\mathrm{d}r, \qquad q(t) := \begin{cases} \int_t^s w(r)\mathrm{d}r, & \text{if } 0 \leq t \leq s, \\ 0, & \text{if } s < t \leq T. \end{cases} \tag{4.32}$$

Note that $p(t) \in \mathcal{H}_w^1$ *and* $q(t) \in \mathcal{H}_w^1$ *for all* $t \in [0,T]$, *and hence,* p *and* q *are regular enough to be used as the test function* h_w *in (4.4). Moreover,* $q(s) = 0$, $q(0) = p(s)$, *and* $p(0) = 0$. *Let* $\tilde{u}$ *and* $\hat{u}$ *satisfy (4.2)–(4.4) with the same test functions* $\ell_v = v(t)$, $\ell_i = \mathrm{d}_t i(t)$, *and* $h_w = q(t)$. *Subtracting* *the two sets of equations and integrating over* $t \in [0,s]$ *yields*

$$\int_0^s \Big[\big\langle \Phi \mathrm{d}_t v, v\big\rangle_{\mathcal{L}_v^2} + \big(v,v\big)_{\mathcal{L}_v^2} - \big(J_1 i, v\big)_{\mathcal{L}_v^2} + \big(J_2(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_4 + J_3(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_5, v\big)_{\mathcal{L}_v^2}\Big]\mathrm{d}t = 0, \tag{4.33}$$

$$\int_0^s \Big[\big\langle \mathrm{d}_t^2 i, \mathrm{d}_t i\big\rangle_{\mathcal{L}_i^2} + 2\big(\Gamma \mathrm{d}_t i, \mathrm{d}_t i\big)_{\mathcal{L}_i^2} + \big(\Gamma^2 i, \mathrm{d}_t i\big)_{\mathcal{L}_i^2} - e\big(\Upsilon\Gamma J_6 w, \mathrm{d}_t i\big)_{\mathcal{L}_i^2} - e\big(\Upsilon\Gamma \mathrm{N} J_7(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t i\big)_{\mathcal{L}_i^2}\Big]\mathrm{d}t = 0, \tag{4.34}$$

$$\int_0^s \Big[\big\langle \mathrm{d}_t^2 w, q\big\rangle_{\mathcal{H}_w^1} + 2\nu\big(\Lambda \mathrm{d}_t w, q\big)_{\mathcal{L}_w^2} - \tfrac{3}{2}\nu^2\big(\Delta w, q\big)_{\mathcal{L}_w^2} + \nu^2\big(\Lambda^2 w, q\big)_{\mathcal{L}_w^2} - \nu^2\big(\Lambda^2 \mathrm{M} J_8(f(\tilde{v}) - f(\hat{v})), q\big)_{\mathcal{L}_w^2}\Big]\mathrm{d}t = 0. \tag{4.35}$$

Next, integrating by parts in the first and second terms in (4.35) yields

$$\int_0^s \Big[- \big(\mathrm{d}_t w, \mathrm{d}_t q\big)_{\mathcal{L}_w^2} - 2\nu\big(\Lambda w, \mathrm{d}_t q\big)_{\mathcal{L}_w^2} - \tfrac{3}{2}\nu^2\big(\Delta w, q\big)_{\mathcal{L}_w^2} + \nu^2\big(\Lambda^2 w, q\big)_{\mathcal{L}_w^2}\Big]\mathrm{d}t = \int_0^s \nu^2\big(\Lambda^2 \mathrm{M} J_8(f(\tilde{v}) - f(\hat{v})), q\big)_{\mathcal{L}_w^2}\,\mathrm{d}t.$$

Note that $\langle \mathrm{d}_t w, \mathrm{d}_t q\rangle_{\mathcal{H}_w^1} = \big(\mathrm{d}_t w, \mathrm{d}_t q\big)_{\mathcal{L}_w^2}$ *since* $\mathrm{d}_t w \in \mathcal{L}_w^2$ *for almost every* $t \in [0,T]$*; see the proof of [15, Th. 5.9-1]. Now, it follows from the definition of* $q(t)$ *that* $\mathrm{d}_t q = -w$ *for all* $t \in [0,s]$*. Therefore,*

$$\int_0^s \Big[\tfrac{1}{2}\mathrm{d}_t\left(\big\|w\big\|_{\mathcal{L}_w^2}^2 - \tfrac{3}{2}\nu^2\big\|\partial_x q\big\|_{\mathcal{L}_{\partial w}^2}^2\right) + 2\nu\big\|\Lambda^{\frac{1}{2}} w\big\|_{\mathcal{L}_w^2}^2 + \nu^2\big(\Lambda^2 w, q\big)_{\mathcal{L}_w^2}\Big]\,\mathrm{d}t = \int_0^s \nu^2\big(\Lambda^2 \mathrm{M} J_8(f(\tilde{v}) - f(\hat{v})), q\big)_{\mathcal{L}_w^2}\,\mathrm{d}t. \tag{4.36}$$

Using Young's inequality,

$$\begin{aligned}
\nu^2\big(\Lambda^2 \mathrm{M} J_8(f(\tilde{v}) - f(\hat{v})), q\big)_{\mathcal{L}_w^2} &\leq \tfrac{1}{4}\nu^2\big\|q\big\|_{\mathcal{L}_w^2}^2 + \nu^2\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\left[\sup_{v_{\mathrm{E}}(x,t)\in\mathbb{R}} |\partial_{v_{\mathrm{E}}} f_{\mathrm{E}}(v_{\mathrm{E}})|\right]^2 \big\|v\big\|_{\mathcal{L}_v^2}^2 \\
&\leq \tfrac{1}{4}\nu^2\big\|q\big\|_{\mathcal{L}_w^2}^2 + \tfrac{1}{8}\nu^2\frac{\mathrm{F}_{\mathrm{E}}^2}{\sigma_{\mathrm{E}}^2}\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\big\|v\big\|_{\mathcal{L}_v^2}^2, \\
-\nu^2\big(\Lambda^2 w, q\big)_{\mathcal{L}_w^2} &\leq \tfrac{1}{4}\nu^2\big\|q\big\|_{\mathcal{L}_w^2}^2 + \nu^2\big\|\Lambda\big\|_2^4\big\|w\big\|_{\mathcal{L}_w^2}^2,
\end{aligned}$$

where the second inequality follows, for $\mathrm{X} = \mathrm{E}$*, from differentiating (3.2) as*

$$\partial_{v_{\mathrm{X}}} f_{\mathrm{X}}(v_{\mathrm{X}}) = \frac{\sqrt{2}}{\sigma_{\mathrm{X}}}\,\mathrm{F}_{\mathrm{X}} \exp\left(-\sqrt{2}\,\frac{v_{\mathrm{X}} - \mu_{\mathrm{X}}}{\sigma_{\mathrm{X}}}\right)\left[1 + \exp\left(-\sqrt{2}\,\frac{v_{\mathrm{X}} - \mu_{\mathrm{X}}}{\sigma_{\mathrm{X}}}\right)\right]^{-2}, \quad \mathrm{X} \in \{\mathrm{E}, \mathrm{I}\}, \tag{4.37}$$

which implies $\sup_{v_{\mathrm{X}}(x,t)\in\mathbb{R}} |\partial_{v_{\mathrm{X}}} f_{\mathrm{X}}(v_{\mathrm{X}})| \leq \frac{\mathrm{F}_{\mathrm{X}}}{2\sqrt{2}\sigma_{\mathrm{X}}}$.

Now, (4.36) *implies*

$$\tfrac{1}{2}\big\|w(s)\big\|_{\mathcal{L}_w^2}^2 + \tfrac{3}{4}\nu^2\big\|q(0)\big\|_{\mathcal{H}_w^1}^2 \leq \int_0^s \Big[\Big(-2\nu\big\|\Lambda\big\|_2 + \nu^2\big\|\Lambda\big\|_2^4\Big)\big\|w\big\|_{\mathcal{L}_w^2}^2 + \tfrac{1}{2}\nu^2\big\|q\big\|_{\mathcal{L}_w^2}^2 + \tfrac{1}{8}\nu^2\frac{\mathrm{F}_{\mathrm{E}}^2}{\sigma_{\mathrm{E}}^2}\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\big\|v\big\|_{\mathcal{L}_v^2}^2\Big]\,\mathrm{d}t + \tfrac{3}{4}\nu^2\big\|q(0)\big\|_{\mathcal{L}_w^2}^2.$$

Noting from (4.32) that $q(t) = p(s) - p(t)$ for all $t \in [0, s]$, it follows that the above inequality can be written as

$$\tfrac{1}{2}\|w(s)\|^2_{\mathcal{L}^2_w} + \tfrac{3}{4}\nu^2\|p(s)\|^2_{\mathcal{H}^1_w} \le \int_0^s \Big[\Big(-2\nu\|\Lambda\|_2 + \nu^2\|\Lambda\|_2^4\Big)\|w(t)\|^2_{\mathcal{L}^2_w} + \tfrac{1}{2}\nu^2\|p(s)-p(t)\|^2_{\mathcal{L}^2_w} + \tfrac{1}{8}\nu^2\frac{\mathrm{F}_\mathrm{E}^2}{\sigma_\mathrm{E}^2}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\|v(t)\|^2_{\mathcal{L}^2_v}\Big]\,\mathrm{d}t + \tfrac{3}{4}\nu^2\|p(s)\|^2_{\mathcal{L}^2_w}.$$

Moreover, $\|p(s)-p(t)\|^2_{\mathcal{L}^2_w} \le 2\|p(s)\|^2_{\mathcal{L}^2_w} + 2\|p(t)\|^2_{\mathcal{L}^2_w} \le 2\|p(s)\|^2_{\mathcal{H}^1_w} + 2\|p(t)\|^2_{\mathcal{H}^1_w}$*, and it follows from the definition of* $p(t)$ *that* $\|p(s)\|^2_{\mathcal{L}^2_w} \le \int_0^s \|w(t)\|^2_{\mathcal{L}^2_w}\mathrm{d}t$*. Therefore,*

$$\tfrac{1}{2}\|w(s)\|^2_{\mathcal{L}^2_w} + \nu^2(\tfrac{3}{4}-s)\|p(s)\|^2_{\mathcal{H}^1_w} \le \int_0^s \Big[\Big(-2\nu\|\Lambda\|_2 + \nu^2\|\Lambda\|_2^4 + \tfrac{3}{4}\nu^2\Big)\|w(t)\|^2_{\mathcal{L}^2_w} + \nu^2\|p(t)\|^2_{\mathcal{H}^1_w} + \tfrac{1}{8}\nu^2\frac{\mathrm{F}_\mathrm{E}^2}{\sigma_\mathrm{E}^2}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\|v(t)\|^2_{\mathcal{L}^2_v}\Big]\,\mathrm{d}t. \tag{4.38}$$

Next, recalling (4.14) and (4.15) and using the Cauchy-Schwarz and Young inequalities, it follows that the fourth term in (4.33) satisfies, for every $\varepsilon_1 > 0$,

$$\big(J_2(\tilde{v}\tilde{i}^\mathrm{T} - \hat{v}\hat{i}^\mathrm{T})\Psi J_4, v\big)_{\mathcal{L}^2_v} = \big(J_2 v\tilde{i}^\mathrm{T}\Psi J_4, v\big)_{\mathcal{L}^2_v} + \big(J_2\hat{v}i^\mathrm{T}\Psi J_4, v\big)_{\mathcal{L}^2_v} \ge -\sqrt{2\kappa_{\tilde{i}}}\,\|\Psi\|_2\|v\|^2_{\mathcal{L}^2_v} - \varepsilon_1\|v\|^2_{\mathcal{L}^2_v} - \frac{2\kappa_{\hat{v}}}{4\varepsilon_1}\|\Psi\|_2^2\|i\|^2_{\mathcal{L}^2_i},$$

where $\kappa_{\hat{v}}$ *and* $\kappa_{\tilde{i}}$ *are in the form of (4.17) and (4.18), respectively. The same inequality holds for* $\big(J_3(\tilde{v}\tilde{i}^\mathrm{T} - \hat{v}\hat{i}^\mathrm{T})\Psi J_5, v\big)_{\mathcal{L}^2_v}$*. Similarly, using Young's inequality and (4.37),*

$$e\big(\Upsilon\Gamma\mathrm{N}J_7(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t i\big)_{\mathcal{L}^2_i} \le \varepsilon_2\|\mathrm{d}_t i\|^2_{\mathcal{L}^2_i} + \frac{e^2}{4\varepsilon_2}\|\Upsilon\Gamma\mathrm{N}J_7\|_2^2 \sup_{v(x,t)\in\mathbb{R}^2}\|\partial_v f(v)\|_2^2\|v\|^2_{\mathcal{L}^2_v} \le \varepsilon_2\|\mathrm{d}_t i\|^2_{\mathcal{L}^2_i} + \frac{e^2}{32\varepsilon_2}\|\Upsilon\Gamma\mathrm{N}J_7\|_2^2 \max\left\{\frac{\mathrm{F}_\mathrm{E}^2}{\sigma_\mathrm{E}^2}, \frac{\mathrm{F}_\mathrm{I}^2}{\sigma_\mathrm{I}^2}\right\}\|v\|^2_{\mathcal{L}^2_v},$$

for every $\varepsilon_2 > 0$*. Moreover, for every* $\varepsilon_3 > 0$ *and* $\varepsilon_4 > 0$,

$$\big(J_1 i, v\big)_{\mathcal{L}^2_v} \le \varepsilon_4\|v\|^2_{\mathcal{L}^2_v} + \frac{1}{2\varepsilon_4}\|i\|^2_{\mathcal{L}^2_i},$$

$$e\big(\Upsilon\Gamma J_6 w, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} \le \varepsilon_4\|\mathrm{d}_t i\|^2_{\mathcal{L}^2_i} + \frac{e^2}{4\varepsilon_4}\|\Upsilon\Gamma J_6\|_2^2\|w\|^2_{\mathcal{L}^2_w}.$$

Substituting the above inequalities into (4.33) and (4.34), and adding the resulting inequalities to (4.38) yields, for some $\alpha > 0$,

$$\|\Phi^{\frac{1}{2}}v(s)\|^2_{\mathcal{L}^2_v} + \|\mathrm{d}_t i(s)\|^2_{\mathcal{L}^2_i} + \|\Gamma i(s)\|^2_{\mathcal{L}^2_i} + \|w(s)\|^2_{\mathcal{L}^2_w} + \nu^2(\tfrac{3}{2} - 2s)\|p(s)\|^2_{\mathcal{H}^1_w} \le \alpha\int_0^s \Big[\|v(t)\|^2_{\mathcal{L}^2_v} + \|\mathrm{d}_t i(t)\|^2_{\mathcal{L}^2_i} + \|i(t)\|^2_{\mathcal{L}^2_i} + \|w(t)\|^2_{\mathcal{L}^2_w} + \|p(t)\|^2_{\mathcal{H}^1_w}\Big]\,\mathrm{d}t.$$

Now, setting $T_1 = \frac{3}{4}$*, it follows from the integral form of Grönwall's inequality [15, Appx. B.2] that* $(v(s), i(s), w(s)) = 0$ *for all* $s \in [0, T_1]$*. Repeating the same arguments for intervals* $[T_1, 2T_1]$, $[2T_1, 3T_1]$, …, *we deduce* $(v(t), i(t), w(t)) = 0$ *for all* $t \in [0, T]$*, and hence,* $(\tilde{v}, \tilde{i}, \tilde{w}) = (\hat{v}, \hat{i}, \hat{w})$ *for all* $t \in [0, T]$*, which is a contradiction and completes the proof of uniqueness.*

Proposition 4.6 (Regularity of weak solutions) *Suppose that the assumptions of Theorem 4.5 hold, namely, $g \in L^2(0,T;\mathcal{L}_i^2)$, $v_0 \in \mathcal{L}_v^2$, $i_0 \in \mathcal{L}_i^2$, $i_0' \in \mathcal{L}_i^2$, $w_0 \in \mathcal{H}_w^1$, and $w_0' \in \mathcal{L}_w^2$. Then the Ω-periodic weak solution (v,i,w) of the initial value problem (3.3)–(3.6) satisfies*

$$\operatorname*{ess\,sup}_{t\in[0,T]} \Big(\|v(t)\|_{\mathcal{L}_v^2}^2 \Big) + \|\mathrm{d}_t v\|_{L^2(0,T;\mathcal{L}_v^2)}^2 \le \kappa_v, \tag{4.39}$$
$$\operatorname*{ess\,sup}_{t\in[0,T]} \Big(\|\mathrm{d}_t i(t)\|_{\mathcal{L}_i^2}^2 + \|i(t)\|_{\mathcal{L}_i^2}^2 \Big) + \|\mathrm{d}_t^2 i\|_{L^2(0,T;\mathcal{L}_i^2)}^2 \le \kappa_i,$$
$$\operatorname*{ess\,sup}_{t\in[0,T]} \Big(\|\mathrm{d}_t w(t)\|_{\mathcal{L}_w^2}^2 + \|w(t)\|_{\mathcal{H}_w^1}^2 \Big) + \|\mathrm{d}_t^2 w\|_{L^2(0,T;\mathcal{H}_w^{1*})}^2 \le \kappa_w,$$

$$v \in H^1(0,T;\mathcal{L}_v^2) \cap C^2([0,T];\mathcal{L}_v^2), \tag{4.40}$$
$$i \in H^2(0,T;\mathcal{L}_i^2) \cap C^{1,\frac{1}{2}}([0,T];\mathcal{L}_i^2), \quad \mathrm{d}_t i \in H^1(0,T;\mathcal{L}_i^2) \cap C^{0,\frac{1}{2}}([0,T];\mathcal{L}_i^2),$$
$$w \in H^1(0,T;\mathcal{L}_w^2) \cap C^0([0,T];\mathcal{H}_w^1), \quad \mathrm{d}_t w \in C^0([0,T];\mathcal{L}_w^2),$$

where κ_v, κ_i, and κ_w are given by (4.17)–(4.19). Moreover, if $g \in C^0([0,T];\mathcal{L}_i^2)$, then

$$v \in C^3([0,T];\mathcal{L}_v^2), \quad i \in C^2([0,T];\mathcal{L}_i^2), \quad \mathrm{d}_t i \in C^1([0,T];\mathcal{L}_i^2), \tag{4.41}$$

and if $g \in C^1([0,T];\mathcal{L}_i^2)$, then

$$v \in C^4([0,T];\mathcal{L}_v^2), \quad i \in C^3([0,T];\mathcal{L}_i^2), \quad \mathrm{d}_t i \in C^2([0,T];\mathcal{L}_i^2). \tag{4.42}$$

Proof. *First, recall that $\mathcal{L}_v^2 = \mathcal{L}_v^{2^*}$ and $\mathcal{L}_i^2 = \mathcal{L}_i^{2^*}$. Assertion (4.39) follows immediately from (4.14)–(4.16) by setting $m = m_k$ and passing to the limits through (4.25) and (4.26). The inclusions in H^1 and H^2 in assertion (4.40) are immediate from (4.39). The Sobolev embedding theorems [8, Th. 6.6-1] applied to Banach space-valued functions on $[0,T] \subset \mathbb{R}$ imply that $v \in C^{0,\frac{1}{2}}([0,T];\mathcal{L}_v^2)$, $i \in C^{1,\frac{1}{2}}([0,T];\mathcal{L}_i^2)$, and $\mathrm{d}_t i \in C^{0,\frac{1}{2}}([0,T];\mathcal{L}_i^2)$, which further implies by* (3.3) *that $v \in C^2([0,T];\mathcal{L}_v^2)$.*

Let $A := (-\Delta + I) : \mathcal{H}_w^1 \to \mathcal{H}_w^{1*}$ be the time-independent, self-adjoint operator considered in Lemma 4.1. Note that $f(v) \in C^2([0,T];\mathcal{L}_v^\infty)$ since f is a bounded smooth function and $v \in C^2([0,T];\mathcal{L}_v^2)$. Then, it follows from (3.5) *and (4.39) that $\mathrm{d}_t^2 w + Aw \in L^2(0,T;\mathcal{L}_w^2)$. Therefore, by [48, Lemma II.4.1] we have $w \in C([0,T];\mathcal{H}_w^1)$ and $\mathrm{d}_t w \in C([0,T];\mathcal{L}_w^2)$, which completes the proof of* (4.40)*. Assertions* (4.41) *and* (4.42) *are now immediate from (3.3), (3.4), and* (4.40)*.*

Theorem 4.7 (Existence and uniqueness of strong solutions) *Suppose that $g \in L^2(0,T;\mathcal{L}_i^2)$, $v_0 \in \mathcal{L}_v^2$, $i_0 \in \mathcal{L}_i^2$, $i_0' \in \mathcal{L}_i^2$, $w_0 \in \mathcal{H}_w^2$, and $w_0' \in \mathcal{H}_w^1$. Then there exists a unique Ω-periodic strong solution (v,i,w) of the initial value problem (3.3)–(3.6).*

Proof. *Uniqueness follows immediately from Theorem 4.5 since every strong solution is also a weak solution. Moreover, Proposition 4.6 implies that the weak solutions $v \in H^1(0,T;\mathcal{L}_v^2)$ and $i \in H^2(0,T;\mathcal{L}_i^2)$ are indeed strong solutions as given in Definition 4.3. It remains to prove the regularity required for w by Definition 4.3.*

Consider (4.12) with the approximation (4.9), let $\mathcal{B}_w = \{h_w^{(k)}\}_{k=1}^\infty$ be the orthogonal basis of $\mathcal{H}_w^1$ consisting of the eigenfunctions of $A := (-\Delta + I) : \mathcal{H}_w^1 \to \mathcal{H}_w^{1*}$ as given by Lemma 4.1, and let

λ_k denote the eigenvalue corresponding to the eigenfunction $h_w^{(k)}$. Multiplying (4.12) by $\lambda_k c_{w_k}^{(m)}$ and summing over $k = 1, \dots, m$ yields

$$\begin{aligned}\big(\mathrm{d}_t^2 w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} + 2\nu\big(\Lambda \mathrm{d}_t w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} - \tfrac{3}{2}\nu^2\big(\Delta w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} \\ + \nu^2\big(\Lambda^2 w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} - \nu^2\big(\Lambda^2 \mathrm{M} J_8 f(v^{(m)}), Aw^{(m)}\big)_{\mathcal{L}^2_w} = 0.\end{aligned}$$

Now, Young's inequality implies that, for every $\varepsilon_1, \dots, \varepsilon_4 > 0$,

$$\begin{aligned}-\big(\mathrm{d}_t^2 w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} &\le \varepsilon_1\big\|Aw^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_1}\big\|\mathrm{d}_t^2 w^{(m)}\big\|^2_{\mathcal{L}^2_w},\\ -\big(\Lambda \mathrm{d}_t w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} &\le \varepsilon_2\big\|Aw^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_2}\big\|\Lambda \mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w},\\ -\big(\Lambda^2 w^{(m)}, Aw^{(m)}\big)_{\mathcal{L}^2_w} &\le \varepsilon_3\big\|Aw^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_3}\big\|\Lambda^2 w^{(m)}\big\|^2_{\mathcal{L}^2_w},\\ \big(\Lambda^2 \mathrm{M} J_8 f(v^{(m)}), Aw^{(m)}\big)_{\mathcal{L}^2_w} &\le \varepsilon_4\big\|Aw^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_4}\big\|\Lambda^2 \mathrm{M} J_8 f(v^{(m)})\big\|^2_{\mathcal{L}^2_w}\\ &\le \varepsilon_4\big\|Aw^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_4}|\Omega|\mathrm{F}_\mathrm{E}^2\,\mathrm{tr}(\Lambda^4\mathrm{M}^2),\end{aligned}$$

and hence, using (2.1),

$$\begin{aligned}\tfrac{3}{2}\nu^2\big\|w^{(m)}\big\|^2_{\mathcal{H}^2_w} \le (\varepsilon_1 + 2\nu\varepsilon_2 + \nu^2\varepsilon_3 + \nu^2\varepsilon_4)\left(\big\|w^{(m)}\big\|^2_{\mathcal{H}^2_w} + \big\|\partial_x w^{(m)}\big\|^2_{\mathcal{L}^2_{\partial w}}\right)\\ + \tfrac{3}{2}\nu^2\big\|w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{1}{4\varepsilon_1}\big\|\mathrm{d}_t^2 w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{\nu}{2\varepsilon_2}\big\|\Lambda \mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w}\\ + \frac{\nu^2}{4\varepsilon_3}\big\|\Lambda^2 w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \frac{\nu^2}{4\varepsilon_4}|\Omega|\mathrm{F}_\mathrm{E}^2\,\mathrm{tr}(\Lambda^4\mathrm{M}^2).\end{aligned}$$

Next, set $\varepsilon_1 = \frac{\nu^2}{8}$, $\varepsilon_2 = \frac{\nu}{16}$, $\varepsilon_3 = \frac{1}{8}$, and $\varepsilon_4 = \frac{1}{8}$, and note that, for some constant $\beta > 0$,

$$\big\|w^{(m)}\big\|^2_{\mathcal{H}^2_w} \le \beta\left(\big\|\mathrm{d}_t^2 w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \big\|\mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \big\|w^{(m)}\big\|^2_{\mathcal{H}^1_w} + |\Omega|\mathrm{F}_\mathrm{E}^2\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\right). \tag{4.43}$$

Bounds on $\|\mathrm{d}_t w^{(m)}\|_{\mathcal{L}^2_w}$ and $\|w^{(m)}\|_{\mathcal{H}^1_w}$ are given by the energy estimate (4.16). To establish bounds on $\|\mathrm{d}_t^2 w^{(m)}\|_{\mathcal{L}^2_w}$ and $\|\mathrm{d}_t w^{(m)}\|_{\mathcal{H}^1_w}$, consider (4.12) with the initial values given in (4.13). Differentiating (4.12) with respect to t, multiplying the result by $\mathrm{d}_t^2 c_{w_k}^{(m)}$, and summing over $k = 1, \dots m$, yields

$$\begin{aligned}\big(\mathrm{d}_t^2 \dot{w}^{(m)}, \mathrm{d}_t\dot{w}^{(m)}\big)_{\mathcal{L}^2_w} + 2\nu\big(\Lambda \mathrm{d}_t \dot{w}^{(m)}, \mathrm{d}_t\dot{w}^{(m)}\big)_{\mathcal{L}^2_w} - \tfrac{3}{2}\nu^2\big(\Delta \dot{w}^{(m)}, \mathrm{d}_t\dot{w}^{(m)}\big)_{\mathcal{L}^2_w}\\ + \nu^2\big(\Lambda^2 \dot{w}^{(m)}, \mathrm{d}_t\dot{w}^{(m)}\big)_{\mathcal{L}^2_w} - \nu^2\big(\Lambda^2 \mathrm{M} J_8\,\mathrm{d}_t f(v^{(m)}), \mathrm{d}_t\dot{w}^{(m)}\big)_{\mathcal{L}^2_w} = 0,\end{aligned}$$

where $\dot{w} := \mathrm{d}_t w$ and $\mathrm{d}_t f_\mathrm{E}(v_\mathrm{E}^{(m)}) = \partial_{v_\mathrm{E}} f_\mathrm{E}(v_\mathrm{E}^{(m)})\,\mathrm{d}_t v_\mathrm{E}^{(m)}$. Now, (4.37) *with* $\mathrm{X} = \mathrm{E}$ *gives*

$$\begin{aligned}\big\|\Lambda^2 \mathrm{M} J_8\,\mathrm{d}_t f(v^{(m)})\big\|^2_{\mathcal{L}^2_w} &= \mathrm{tr}(\Lambda^4\mathrm{M}^2)\int_\Omega \big|\mathrm{d}_t f_\mathrm{E}(v_\mathrm{E}^{(m)})\big|^2 \mathrm{d}x\\ &\le \mathrm{tr}(\Lambda^4\mathrm{M}^2)\frac{\mathrm{F}_\mathrm{E}^2}{8\sigma_\mathrm{E}^2}\int_\Omega \big|\mathrm{d}_t v_\mathrm{E}^{(m)}\big|^2 \mathrm{d}x \le \mathrm{tr}(\Lambda^4\mathrm{M}^2)\frac{\mathrm{F}_\mathrm{E}^2}{8\sigma_\mathrm{E}^2}\big\|\mathrm{d}_t v^{(m)}\big\|^2_{\mathcal{L}^2_v}.\end{aligned} \tag{4.44}$$

Using similar arguments as in the proof of Proposition 4.4, it follows from the above inequality and Young's inequality that, for every $\varepsilon > 0$,

$$\mathrm{d}_t\left[\big\|\mathrm{d}_t\dot{w}^{(m)}\big\|^2_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big\|\partial_x\dot{w}^{(m)}\big\|^2_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda\dot{w}^{(m)}\big\|^2_{\mathcal{L}^2_w}\right] + 2\nu(2\Lambda_{\min} - \varepsilon\nu)\big\|\mathrm{d}_t\dot{w}^{(m)}\big\|^2_{\mathcal{L}^2_w} \leq \frac{\nu^2}{2\varepsilon}\frac{\mathrm{F}^2_{\mathrm{E}}}{8\sigma^2_{\mathrm{E}}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\big\|\mathrm{d}_t v^{(m)}\big\|^2_{\mathcal{L}^2_v},$$

where $\Lambda_{\min} := \min\{\Lambda_{\mathrm{EE}}, \Lambda_{\mathrm{EI}}\}$ is the smallest eigenvalue of Λ. Next, setting $\varepsilon = \frac{2}{\nu}\Lambda_{\min}$, replacing $\dot{w} = \mathrm{d}_t w$, and using Grönwall's inequality yields

$$\begin{aligned}\big\|\mathrm{d}^2_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} &+ \tfrac{3}{2}\nu^2\big\|\mathrm{d}_t\partial_x w^{(m)}(t)\big\|^2_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} \\ &\leq \left(\big\|\mathrm{d}^2_t w^{(m)}\big\|^2_{\mathcal{L}^2_w} + \tfrac{3}{2}\nu^2\big\|\mathrm{d}_t\partial_x w^{(m)}\big\|^2_{\mathcal{L}^2_{\partial w}} + \nu^2\big\|\Lambda\mathrm{d}_t w^{(m)}\big\|^2_{\mathcal{L}^2_w}\right)\Big|_{t=0} \\ &\quad + \tfrac{1}{32}\frac{\nu^3}{\Lambda_{\min}\sigma^2}\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\big\|\mathrm{d}_t v^{(m)}\big\|^2_{L^2(0,T;\mathcal{L}^2_v)}.\end{aligned} \tag{4.45}$$

Finally, it follows from (4.12) and (4.13) that, for some $\alpha_1 > 0$,

$$\big\|\mathrm{d}^2_t w^{(m)}\big\|^2_{\mathcal{L}^2_w}\Big|_{t=0} \leq \alpha_1\left(\big\|w'_0\big\|^2_{\mathcal{H}^1_w} + \big\|w_0\big\|^2_{\mathcal{H}^2_w} + \nu^2|\Omega|\mathrm{F}^2_{\mathrm{E}}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\right).$$

Now, using the energy estimate (4.14) and the above inequality in (4.45) *it follows that*

$$\big\|\mathrm{d}^2_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} + \big\|\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{H}^1_w} \leq \alpha_2\left(\big\|w'_0\big\|^2_{\mathcal{H}^1_w} + \big\|w_0\big\|^2_{\mathcal{H}^2_w} + (|\Omega| + \kappa_v)\mathrm{F}^2_{\mathrm{E}}\right)$$

for some $\alpha_2 > 0$ and all $t \in [0,T]$. Since this inequality and (4.43) hold for all $t \in [0,T]$, it follows that

$$\sup_{t\in[0,T]}\left(\big\|\mathrm{d}^2_t w^{(m)}(t)\big\|^2_{\mathcal{L}^2_w} + \big\|\mathrm{d}_t w^{(m)}(t)\big\|^2_{\mathcal{H}^1_w} + \big\|w^{(m)}(t)\big\|^2_{\mathcal{H}^2_w}\right) \leq \hat{\beta}_w, \tag{4.46}$$

where

$$\hat{\beta}_w := \alpha\left(\big\|w'_0\big\|^2_{\mathcal{H}^1_w} + \big\|w_0\big\|^2_{\mathcal{H}^2_w} + (|\Omega| + \kappa_v)\mathrm{F}^2_{\mathrm{E}}\right)$$

for some $\alpha > 0$. Now, using the above estimate and passing to the limits, the result follows by similar arguments as in the proof of Theorem 4.5.

Proposition 4.8 (Regularity of strong solutions) *Suppose that the assumptions of Theorem 4.7 hold, namely, $g \in L^2(0,T;\mathcal{L}^2_i)$, $v_0 \in \mathcal{L}^2_v$, $i_0 \in \mathcal{L}^2_i$, $i'_0 \in \mathcal{L}^2_i$, $w_0 \in \mathcal{H}^2_w$, and $w'_0 \in \mathcal{H}^1_w$. Then, in addition to the properties of the weak solution given in Proposition 4.6, the Ω-periodic strong solution (v, i, w) of the initial value problem (3.3)–(3.6) satisfies*

$$\operatorname*{ess\,sup}_{t\in[0,T]}\left(\big\|\mathrm{d}^2_t w(t)\big\|^2_{\mathcal{L}^2_w} + \big\|\mathrm{d}_t w(t)\big\|^2_{\mathcal{H}^1_w} + \big\|w(t)\big\|^2_{\mathcal{H}^2_w}\right) + \big\|\mathrm{d}^3_t w\big\|^2_{L^2(0,T;\mathcal{H}^{1*}_w)} \leq \beta_w, \tag{4.47}$$

$$\begin{aligned} w &\in H^2(0,T;\mathcal{L}^2_w) \cap H^1(0,T;\mathcal{H}^1_w) \cap L^\infty(0,T;\mathcal{H}^2_w) \\ &\qquad \cap C^{1,\frac{1}{2}}([0,T];\mathcal{L}^2_w) \cap C^{0,\frac{1}{2}}([0,T];\mathcal{H}^1_w) \cap L^\infty(0,T;C^{0,\lambda}_{\mathrm{per}}(\overline{\Omega},\mathbb{R}^2)), \\ \mathrm{d}_t w &\in H^1(0,T;\mathcal{L}^2_w) \cap L^\infty(0,T;\mathcal{H}^1_w) \cap C^{0,\frac{1}{2}}([0,T];\mathcal{L}^2_w), \\ \mathrm{d}^2_t w &\in L^\infty(0,T;\mathcal{L}^2_w),\end{aligned} \tag{4.48}$$

for all $\lambda \in (0,1)$ and some $\beta_w > 0$.

Proof. *Differentiate (4.12) with respect to t and denote* $\dot{w} := \mathrm{d}_t w$. *Use (4.44) and follow the same steps used to prove (4.16) in Proposition 4.4 to show* $\|\mathrm{d}_t^2 \dot{w}^{(m)}\|^2_{L^2(0,T;\mathcal{H}_w^{1*})} \le \tilde{\beta}_w$ *for every positive integer* m*, all* $t \in [0,T]$*, and some* $\tilde{\beta}_w > 0$ *proportional to* $\hat{\beta}_w$ *in (4.46). Replacing* $\dot{w} = \mathrm{d}_t w$*, adding the result to (4.46), and passing to the limits establishes (4.47) for some* $\beta_w > 0$ *proportional to* $\hat{\beta}_w$.

The inclusions in H^1*,* H^2*, and* L^∞ *in assertion (4.48) follow immediately from (4.47), whereas the inclusions in the* time-*continuous spaces are implied by the Sobolev embedding theorems [8, Th. 6.6-1] applied to Banach space-valued functions on* $[0,T] \subset \mathbb{R}$*. Finally, the inclusion in the* space-*continuous space is implied by the Sobolev embedding theorems applied to* Ω*-periodic functions in* $\mathbb{R}^2$.

Other than the regularity properties given in Propositions 4.6 and 4.8, boundedness of weak and strong solutions for bounded input functions g can also be established. We defer this result to Section 5, where the proof is obtained as a corollary of Proposition 5.3.

In the remainder of the paper, we give formal arguments for some of the proofs, in the sense that we take the inner product of (3.5) with functions that belong to $\mathcal{L}_w^2$, instead of functions belonging to $\mathcal{H}_w^1$ that is required for the test functions h_w in (4.4). However, the proofs can be made rigorous using the Galerkin approximation technique based on the dual orthogonal basis of $\mathcal{H}_w^1 \Subset \mathcal{L}_w^2$ and then passing to the limits, as in the proofs of Theorems 4.5 and 4.7. See the discussion and results in [41, Sec. 11.1.2] for further details.

5. Semidynamical Systems and Biophysical Plausibility of the Evolution

In this section, we establish a semidynamical system framework for the initial-value problem presented in Section 4. Assume $g \in L^2(0,\infty;\mathcal{L}_i^2)$ and let $u(t) := (v(t), i(t), \mathrm{d}_t i(t), w(t), \mathrm{d}_t w(t))$ denote a solution of (3.3)–(3.5) with the initial value $u_0 := u(0) = (v_0, i_0, i_0', w_0, w_0')$. Recall the Definitions 4.2 and 4.3 and the results of Theorems 4.5 and 4.7 to note that the Hilbert spaces

$$\begin{aligned} \mathcal{U}_{\mathrm{w}} &:= \mathcal{L}_v^2 \times \mathcal{L}_i^2 \times \mathcal{L}_i \times \mathcal{H}_w^1 \times \mathcal{L}_w^2, \\ \mathcal{U}_{\mathrm{s}} &:= \mathcal{L}_v^2 \times \mathcal{L}_i^2 \times \mathcal{L}_i \times \mathcal{H}_w^2 \times \mathcal{H}_w^1, \end{aligned} \tag{5.1}$$

construct, respectively, the phase spaces associated with the weak and strong solutions. Now, for every $t \in [0,\infty)$, define the mappings

$$\begin{aligned} S_{\mathrm{w}}(t) &: \mathcal{U}_{\mathrm{w}} \to \mathcal{U}_{\mathrm{w}}, \quad S_{\mathrm{w}}(t)u_0 := u(t), \\ S_{\mathrm{s}}(t) &: \mathcal{U}_{\mathrm{s}} \to \mathcal{U}_{\mathrm{s}}, \quad S_{\mathrm{s}}(t)u_0 := u(t). \end{aligned}$$

The existence and uniqueness of solutions given by Theorems 4.5 and 4.7 along with the time-continuity of solutions given by Propositions 4.6 and 4.8 imply that the above mappings are well-defined for all $t \in [0,\infty)$. Then, $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$ form semigroups of operators which give the weak and strong solutions of (3.1), respectively. The following propositions show that these semigroups are continuous, which also ensures that the initial-value problems of finding weak and strong solutions for (3.1) are well-posed.

Proposition 5.1 (Continuity of the smigroup $\{S_{\mathrm{w}}\}$) *The semigroup* $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ *of weak solution operators is continuous for all* $g \in L^2(0,\infty;\mathcal{L}_i^2)$.

Proof. *Continiuity of the semigroup with respect to t follows immediately from the continuity of the weak solutions given in Proposition 4.6. It remains to prove continuous dependence of the solution on the initial values. Let* $\tilde{u}_0$ *and* $\hat{u}_0$ *be any two initial values in* $\mathcal{U}_{\rm w}$ *that give the solutions* $\tilde{u}(t) = S_{\rm w}(t)\tilde{u}_0$ *and* $\hat{u}(t) = S_{\rm w}(t)\hat{u}_0$ *for all* $t \in [0, T]$, $T > 0$. *Let* $u(t) := \tilde{u}(t) - \hat{u}(t)$ *be the weak solution with the initial value* $u_0 := \tilde{u}_0 - \hat{u}_0$. *Now, consider* (3.3)–(3.5) *satisfied by* $\tilde{u}$ *and* $\hat{u}$, *and take the inner product of* (3.3)–(3.5) *in each set with* v, $\mathrm{d}_t i$, *and* $\mathrm{d}_t w$, *respectively. Subtracting the resulting two sets of equations yields*

$$(5.2)\qquad \big(\Phi \mathrm{d}_t v, v\big)_{\mathcal{L}^2_v} + \big(v, v\big)_{\mathcal{L}^2_v} - \big(J_1 i, v\big)_{\mathcal{L}^2_v} + \big(J_2(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_4 + J_3(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_5, v\big)_{\mathcal{L}^2_v} = 0,$$

$$(5.3)\qquad \big(\mathrm{d}_t^2 i, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} + 2\big(\Gamma \mathrm{d}_t i, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} + \big(\Gamma^2 i, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} - e\big(\Upsilon\Gamma J_6 w, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} - e\big(\Upsilon\Gamma \mathrm{N} J_7(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t i\big)_{\mathcal{L}^2_i} = 0,$$

$$(5.4)\qquad \big(\mathrm{d}_t^2 w, \mathrm{d}_t w\big)_{\mathcal{L}^2_w} + 2\nu\big(\Lambda \mathrm{d}_t w, \mathrm{d}_t w\big)_{\mathcal{L}^2_w} - \tfrac{3}{2}\nu^2\big(\Delta w, \mathrm{d}_t w\big)_{\mathcal{L}^2_w} + \nu^2\big(\Lambda^2 w, \mathrm{d}_t w\big)_{\mathcal{L}^2_w} - \nu^2\big(\Lambda^2 \mathrm{M} J_8(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t w\big)_{\mathcal{L}^2_w} = 0.$$

As in the proof of uniqueness given in Theorem 4.5,

$$(5.5)\qquad \begin{aligned} -\big(J_2(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_4, v\big)_{\mathcal{L}^2_v} &\le \sqrt{2\kappa_{\tilde{i}}}\,\|\Psi\|_2\|v\|^2_{\mathcal{L}^2_v} + \|v\|^2_{\mathcal{L}^2_v} + \tfrac{1}{2}\kappa_{\hat{v}}\|\Psi\|_2^2\|i\|^2_{\mathcal{L}^2_i},\\ -\big(J_3(\tilde{v}\tilde{i}^{\mathrm{T}} - \hat{v}\hat{i}^{\mathrm{T}})\Psi J_5, v\big)_{\mathcal{L}^2_v} &\le \sqrt{2\kappa_{\tilde{i}}}\,\|\Psi\|_2\|v\|^2_{\mathcal{L}^2_v} + \|v\|^2_{\mathcal{L}^2_v} + \tfrac{1}{2}\kappa_{\hat{v}}\|\Psi\|_2^2\|i\|^2_{\mathcal{L}^2_i},\\ e\big(\Upsilon\Gamma\mathrm{N}J_7(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t i\big)_{\mathcal{L}^2_i} &\le \|\mathrm{d}_t i\|^2_{\mathcal{L}^2_i} + \tfrac{1}{32}e^2\|\Upsilon\Gamma\mathrm{N}J_7\|_2^2 \max\left\{\frac{\mathrm{F}_{\mathrm{E}}^2}{\sigma_{\mathrm{E}}^2}, \frac{\mathrm{F}_{\mathrm{I}}^2}{\sigma_{\mathrm{I}}^2}\right\}\|v\|^2_{\mathcal{L}^2_v},\\ \nu^2\big(\Lambda^2\mathrm{M}J_8(f(\tilde{v}) - f(\hat{v})), \mathrm{d}_t w\big)_{\mathcal{L}^2_w} &\le \nu^2\|\mathrm{d}_t w\|^2_{\mathcal{L}^2_w} + \tfrac{1}{32}\nu^2\frac{\mathrm{F}_{\mathrm{E}}^2}{\sigma_{\mathrm{E}}^2}\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\|v\|^2_{\mathcal{L}^2_v},\\ \big(J_1 i, v\big)_{\mathcal{L}^2_v} &\le \|v\|^2_{\mathcal{L}^2_v} + \tfrac{1}{2}\|i\|^2_{\mathcal{L}^2_i},\\ e\big(\Upsilon\Gamma J_6 w, \mathrm{d}_t i\big)_{\mathcal{L}^2_i} &\le \|\mathrm{d}_t i\|^2_{\mathcal{L}^2_i} + \tfrac{1}{4}e^2\|\Upsilon\Gamma J_6\|_2^2\|w\|^2_{\mathcal{L}^2_w}, \end{aligned}$$

where $\kappa_{\hat{v}}$ *and* $\kappa_{\tilde{i}}$ *are in the form of (4.17) and (4.18). Now, substituting the above inequalities into (5.2)–(5.4), adding the resulting inequalities together, and using Grönwall's inequality yield, for some* $\alpha, \beta > 0$,

$$(5.6)\qquad \|u(t)\|^2_{\mathcal{U}_{\rm w}} \le \beta e^{\alpha T}\|u_0\|^2_{\mathcal{U}_{\rm w}} \quad \textit{for all } t \in [0, T],$$

which completes the proof.

Proposition 5.2 (Continuity of the smigroup $\{S_{\rm s}\}$) *The semigroup* $\{S_{\rm s}(t)\}_{t\in[0,\infty)}$ *of strong solution operators is continuous for all* $g \in L^2(0, \infty; \mathcal{L}^2_i)$.

Proof. *Continiuity of the semigroup with respect to t follows immediately from the time continuity of the strong solutions given by Proposition 4.8. To prove continuous dependence on the initial values, consider any two initial values* $\tilde{u}_0$ *and* $\hat{u}_0$ *in* $\mathcal{U}_{\rm s}$ *and construct the solutions* $\tilde{u}(t) = S_{\rm s}(t)\tilde{u}_0$ *and* $\hat{u}(t) = S_{\rm s}(t)\hat{u}_0$, $t \in [0, T]$, $T > 0$, *for* (3.3)–(3.5). *Let* $u := \tilde{u} - \hat{u}$ *and* $A := -\Delta + I$, *and take the inner product of* (3.3)–(3.5) *for each solutions with* v, $\mathrm{d}_t i$, *and* $A\mathrm{d}_t w$, *respectively. Subtracting* *the resulting two sets of equations gives* (5.2), (5.3), *and*

$$\tag{5.7} \tfrac{1}{2}\mathrm{d}_t\big\|\mathrm{d}_t w\big\|^2_{\mathcal{H}^1_w} + 2\nu\big\|\Lambda^{\frac{1}{2}}\mathrm{d}_t w\big\|^2_{\mathcal{H}^1_w} + \tfrac{3}{4}\nu^2\mathrm{d}_t\big\|\partial w\big\|^2_{\mathcal{H}^1_{\partial w}} + \tfrac{1}{2}\nu^2\mathrm{d}_t\big\|\Lambda w\big\|^2_{\mathcal{H}^1_w} = \nu^2\big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),\mathrm{d}_t A w\big)_{\mathcal{L}^2_w}.$$

Note that (5.6) *also holds since* $\mathcal{U}_\mathrm{s}\subset\mathcal{U}_\mathrm{w}$, *and since* (5.2) *and* (5.3) *remain unchanged, the continuity of* v *and* i *holds.*

Now, it follows from (5.7) by integrating over $[0,t]$ *that*

$$\big\|\mathrm{d}_t w\big\|^2_{\mathcal{H}^1_w} + \nu^2\left[\tfrac{3}{2}\big\|\partial w\big\|^2_{\mathcal{H}^1_{\partial w}} + \big\|\Lambda w\big\|^2_{\mathcal{H}^1_w}\right] \le \left(\big\|\mathrm{d}_t w\big\|^2_{\mathcal{H}^1_w} + \nu^2\left[\tfrac{3}{2}\big\|\partial w\big\|^2_{\mathcal{H}^1_{\partial w}} + \big\|\Lambda w\big\|^2_{\mathcal{H}^1_w}\right]\right)\Big|_{t=0} + 2\nu^2\int_0^t \big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),\mathrm{d}_s A w\big)_{\mathcal{L}^2_w}\mathrm{d}s,$$

which, using (2.1), *can be written equivalently for some* $\alpha_1,\beta_1>0$ *as*

$$\tag{5.8} Q(w(t),\mathrm{d}_t w(t)) \le \alpha_1 Q(w(0),\mathrm{d}_t w(0)) + \beta_1\int_0^t \big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),\mathrm{d}_s A w\big)_{\mathcal{L}^2_w}\mathrm{d}s,$$

where

$$\tag{5.9} Q(w(t),\mathrm{d}_t w(t)) := \big\|\mathrm{d}_t w(t)\big\|^2_{\mathcal{H}^1_w} + \big\|A w(t)\big\|^2_{\mathcal{L}^2_w}.$$

Integrating by parts in the second term of the right-hand side of the above inequality yields

$$\tag{5.10} \begin{aligned}\beta_1\int_0^t &\big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),\mathrm{d}_s A w\big)_{\mathcal{L}^2_w}\mathrm{d}s\\ &= \beta_1\big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),A w\big)_{\mathcal{L}^2_w} - \beta_1\big(\Lambda^2\mathrm{M}J_8(f(\tilde v_0)-f(\hat v_0)),A w_0\big)_{\mathcal{L}^2_w}\\ &\quad - \beta_1\int_0^t \big(\Lambda^2\mathrm{M}J_8\mathrm{d}_s(f(\tilde v)-f(\hat v)),A w\big)_{\mathcal{L}^2_w}\mathrm{d}s.\end{aligned}$$

Next, recalling that $\sup_{v_\mathrm{X}(x,t)\in\mathbb{R}}|\partial_{v_\mathrm{X}} f_\mathrm{X}(v_\mathrm{X})| \le \frac{\mathrm{F}_\mathrm{X}}{2\sqrt{2}\sigma_\mathrm{X}}$ *by* (4.37) *and using Young's inequality we obtain*

$$\tag{5.11} \begin{aligned}\beta_1\big(\Lambda^2\mathrm{M}J_8(f(\tilde v)-f(\hat v)),A w\big)_{\mathcal{L}^2_w} &\le \tfrac{1}{2}\big\|A w\big\|^2_{\mathcal{L}^2_w} + \frac{\beta_1^2}{16}\frac{\mathrm{F}_\mathrm{E}^2}{\sigma_\mathrm{E}^2}\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\big\|v\big\|^2_{\mathcal{L}^2_v},\\ -\beta_1\big(\Lambda^2\mathrm{M}J_8(f(\tilde v_0)-f(\hat v_0)),A w_0\big)_{\mathcal{L}^2_w} &\le \tfrac{1}{2}\big\|A w_0\big\|^2_{\mathcal{L}^2_w} + \frac{\beta_1^2}{16}\frac{\mathrm{F}_\mathrm{E}^2}{\sigma_\mathrm{E}^2}\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\big\|v_0\big\|^2_{\mathcal{L}^2_v}.\end{aligned}$$

Moreover,

$$\begin{aligned}-\beta_1&\big(\Lambda^2\mathrm{M}J_8\mathrm{d}_s(f(\tilde v)-f(\hat v)),A w\big)_{\mathcal{L}^2_w}\\ &= -\beta_1\big(\Lambda^2\mathrm{M}J_8(\partial_{\tilde v}f(\tilde v)\mathrm{d}_s\tilde v - \partial_{\hat v}f(\hat v)\mathrm{d}_s\hat v),A w\big)_{\mathcal{L}^2_w}\\ &\le \tfrac{1}{2}\big\|A w\big\|^2_{\mathcal{L}^2_w} + \tfrac{1}{2}\beta_1^2\big\|\Lambda^2\mathrm{M}J_8(\partial_{\tilde v}f(\tilde v)\mathrm{d}_s\tilde v - \partial_{\hat v}f(\hat v)\mathrm{d}_s\hat v)\big\|^2_{\mathcal{L}^2_w}\\ &= \tfrac{1}{2}\big\|A w\big\|^2_{\mathcal{L}^2_w} + \tfrac{1}{2}\beta_1^2\,\mathrm{tr}(\Lambda^4\mathrm{M}^2)\int_\Omega |\partial_{\tilde v_\mathrm{E}}f(\tilde v_\mathrm{E})\mathrm{d}_s\tilde v_\mathrm{E} - \partial_{\hat v_\mathrm{E}}f(\hat v_\mathrm{E})\mathrm{d}_s\hat v_\mathrm{E}|^2\mathrm{d}x,\end{aligned}$$

where, noting that $\sup_{v_{\rm E}(x,t)\in\mathbb{R}} |\partial^2_{v_{\rm E}} f_{\rm E}(v_{\rm E})| < \frac{1}{5}\frac{\rm F_E}{\sigma_{\rm E}^2}$ *by direct computation of the derivative of* (4.37)*, we can write*

$$
\begin{aligned}
|\partial_{\tilde v_{\rm E}} f(\tilde v_{\rm E}){\rm d}_s\tilde v_{\rm E} - \partial_{\hat v_{\rm E}} f(\hat v_{\rm E}){\rm d}_s\hat v_{\rm E}|^2{\rm d}x &= |\partial_{\tilde v_{\rm E}} f(\tilde v_{\rm E}){\rm d}_s v_{\rm E} + (\partial_{\tilde v_{\rm E}} f(\tilde v_{\rm E}) - \partial_{\hat v_{\rm E}} f(\hat v_{\rm E})){\rm d}_s\hat v_{\rm E}|^2 \\
&\le 2|\partial_{\tilde v_{\rm E}} f(\tilde v_{\rm E})|^2|{\rm d}_s v_{\rm E}|^2 + 2|\partial_{\tilde v_{\rm E}} f(\tilde v_{\rm E}) - \partial_{\hat v_{\rm E}} f(\hat v_{\rm E})|^2|{\rm d}_s\hat v_{\rm E}|^2 \\
&\le \tfrac{1}{4}\frac{\rm F_E^2}{\sigma_{\rm E}^2}|{\rm d}_s v_{\rm E}|^2 + 2\left[\sup_{v_{\rm E}(x,t)\in\mathbb{R}} |\partial^2_{v_{\rm E}} f_{\rm E}(v_{\rm E})|\right]^2 |v_{\rm E}|^2|{\rm d}_s\hat v_{\rm E}|^2 \\
&\le \tfrac{1}{4}\frac{\rm F_E^2}{\sigma_{\rm E}^2}|{\rm d}_s v_{\rm E}|^2 + \tfrac{2}{25}\frac{\rm F_E^2}{\sigma_{\rm E}^4}|v_{\rm E}|^2|{\rm d}_s\hat v_{\rm E}|^2.
\end{aligned}
$$

Therefore, it follows that

$$
\begin{aligned}
-\beta_1\big(\Lambda^2{\rm M}J_8{\rm d}_s(f(\tilde v) - f(\hat v)), Aw\big)_{\mathcal{L}^2_w} \le \tfrac{1}{2}\big\|Aw\big\|^2_{\mathcal{L}^2_w} + \frac{\beta_1^2}{8}\frac{\rm F_E^2}{\sigma_{\rm E}^2}\,{\rm tr}(\Lambda^4{\rm M}^2)\big\|{\rm d}_s v\big\|^2_{\mathcal{L}^2_v} \\
+ \frac{\beta_1^2}{25}\frac{\rm F_E^2}{\sigma_{\rm E}^4}\,{\rm tr}(\Lambda^4{\rm M}^2)\big\|{\rm d}_s\hat v\big\|^2_{C^1([0,T];\mathcal{L}^2_v)}\big\|v\big\|^2_{\mathcal{L}^2_v}.
\end{aligned} \tag{5.12}
$$

Furthermore, (3.3) implies that for some $\alpha_2 > 0$,

$$
\big\|{\rm d}_s v(s)\big\|^2_{\mathcal{L}^2_v} \le \alpha_2\left(\big\|v(s)\big\|^2_{\mathcal{L}^2_v} + \big\|i(s)\big\|^2_{\mathcal{L}^2_i} + \big\|v(s)\big\|^2_{\mathcal{L}^2_v}\big\|i(s)\big\|^2_{\mathcal{L}^2_i}\right) \quad \textit{for all } s\in[0,T]. \tag{5.13}
$$

Now, substituting (5.11), (5.12) *and* (5.13) *into (5.10) and using (5.6), it follows that there exist some* $\beta_2,\dots,\beta_6 > 0$ *such that*

$$
\begin{aligned}
&\beta_1\int_0^t \big(\Lambda^2{\rm M}J_8(f(\tilde v) - f(\hat v)), {\rm d}_s Aw\big)_{\mathcal{L}^2_w}{\rm d}s \\
&\quad\le \tfrac{1}{2}\int_0^t \big\|Aw\big\|^2_{\mathcal{L}^2_w}{\rm d}s + \beta_2\int_0^t \left(\big\|v\big\|^2_{\mathcal{L}^2_v} + \big\|i\big\|^2_{\mathcal{L}^2_i} + \big\|v\big\|^2_{\mathcal{L}^2_v}\big\|i\big\|^2_{\mathcal{L}^2_i}\right){\rm d}s \\
&\qquad\qquad + \tfrac{1}{2}\big\|Aw\big\|^2_{\mathcal{L}^2_w} + \beta_3\big\|v\big\|^2_{\mathcal{L}^2_v} + \tfrac{1}{2}\big\|Aw_0\big\|^2_{\mathcal{L}^2_w} + \beta_4\big\|v_0\big\|^2_{\mathcal{L}^2_v}, \\
&\quad\le \tfrac{1}{2}\int_0^t \big\|Aw\big\|^2_{\mathcal{L}^2_w}{\rm d}s + \beta_5\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\left(1 + \big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\right)t + \tfrac{1}{2}\big\|Aw\big\|^2_{\mathcal{L}^2_w} + \tfrac{1}{2}\big\|Aw_0\big\|^2_{\mathcal{L}^2_w} + \beta_6\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}.
\end{aligned}
$$

Substituting this inequality into (5.8) *yields*

$$
\begin{aligned}
\tfrac{1}{2}Q(w(t),{\rm d}_t w(t)) \le \tfrac{1}{2}\int_0^t Q(w(s),{\rm d}_s w(s)){\rm d}s + \beta_5\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\left(1 + \big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\right)t \\
+ \alpha_1 Q(w(0),{\rm d}_t w(0)) + \tfrac{1}{2}\big\|Aw_0\big\|^2_{\mathcal{L}^2_w} + \beta_6\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}},
\end{aligned} \tag{5.14}
$$

where, using Grönwall's inequality for the function $\frac{1}{2}\int_0^t Q(w(s),{\rm d}_s w(s)){\rm d}s$*, we can write*

$$
\begin{aligned}
\tfrac{1}{2}\int_0^t Q(w(s),{\rm d}_s w(s)){\rm d}s \le \beta_5\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\left(1 + \big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\right)\left(e^t - (t+1)\right) \\
+ \left[\alpha_1 Q(w(0),{\rm d}_t w(0)) + \tfrac{1}{2}\big\|Aw_0\big\|^2_{\mathcal{L}^2_w} + \beta_6\big\|u_0\big\|^2_{\mathcal{U}_{\rm w}}\right]\left(e^t - 1\right).
\end{aligned}
$$

This inequality along with (5.14) *and the definition of* Q*, given by* (5.9)*, implies that for some* $\beta_7 > 0$*,*

$$Q(w(t), \mathrm{d}_t w(t)) \le \beta_7 e^T \left[Q(w(0), \mathrm{d}_t w(0)) + \|u_0\|^2_{\mathcal{U}_\mathrm{w}} \left(1 + \|u_0\|^2_{\mathcal{U}_\mathrm{w}}\right)\right] \quad \textit{for all } t \in [0,T].$$

Now, noting that $Q(w(0), \mathrm{d}_t w(0)) = \|w_0'\|^2_{\mathcal{H}^1_w} + \|Aw_0\|^2_{\mathcal{L}^2_w}$*, it follows from the above inequality and* (5.6) *that, for some* $\hat{\alpha}, \hat{\beta} > 0$*,*

$$\|u(t)\|^2_{\mathcal{U}_\mathrm{s}} \le \hat{\beta} e^{\hat{\alpha} T} \|u_0\|^2_{\mathcal{U}_\mathrm{s}} \left(1 + \|u_0\|^2_{\mathcal{U}_\mathrm{w}}\right) \quad \textit{for all } t \in [0,T],$$

which completes the proof.

Although the spaces $\mathcal{U}_\mathrm{w}$ and $\mathcal{U}_\mathrm{s}$ constructed in (5.1) provide the theoretical phase spaces of the problem for the solutions constructed in Section 4, the evolution of the dynamics of the model is not biophysically plausible on entire spaces $\mathcal{U}_\mathrm{w}$ and $\mathcal{U}_\mathrm{s}$. As described in Section 3, $i(x,t)$ and $w(x,t)$ (and also $g(x,t)$) are nonnegative quantities.In fact, one can construct initial functions $i_0' \in \mathcal{L}^2_i$ and $w_0' \in \mathcal{L}^2_w$ such that the solutions $i(x,t)$ and $w(x,t)$, despite starting from nonnegative initial values $i_0 \in \mathcal{L}^2_i$ and $w_0 \in \mathcal{H}^1_w$, take negative values over a subset $\mathscr{X} \in \Omega$ of positive measure for a time interval of positive length. In the following propositions, we establish conditions under which the dynamics of the model is guaranteed to evolve in biophysically plausible subsets of $\mathcal{U}_\mathrm{w}$ and $\mathcal{U}_\mathrm{s}$.

Proposition 5.3 (Nonnegativity of the solution $w(x,t)$) *Suppose that* $w \in L^2(0,T;\mathcal{H}^1_w)$ *is the* w*-component of an* Ω*-periodic weak solution* $u(t) = S_\mathrm{w}(t)u_0$ *of* (3.3)–(3.6) *and define the set* $\mathcal{D}_w \subset \mathcal{H}^1_w \times \mathcal{L}^2_w$ *as*

$$\begin{aligned}(5.15)\quad \mathcal{D}_w := \big\{&(w_0, w_0') \in \mathcal{W}^{1,\infty} \times \mathcal{L}^\infty_w : w_0' + \nu\Lambda w_0 \ge 0 \textit{ a.e. in } \Omega,\\ &\textit{and } w_0(y) + \partial_y w_0(y)(y-x) \ge 0 \textit{ for almost every } x \in \Omega, y \in B(x,t), t \in (0,T]\big\}.\end{aligned}$$

Then, for every initial values $(w_0, w_0') \in \mathcal{D}_w$*, the solution* $w(x,t)$ *remains nonnegative almost everywhere in* Ω *for all* $t \in (0,T]$*.*

Proof. *First, note that the weak and strong solutions coincide for* $v(t)$ *and they satisfy (3.3) and (3.4) almost everywhere in* Ω *for all* $t \in [0,T]$*,* $T > 0$*; see the proof of Theorem 4.7. Substituting* $v(t)$ *into* f*, we can interpret* $f(v)$ *in (3.5) as a function* $\hat{f}(x,t) := f(v(x,t))$ *for almost every* $x \in \Omega$ *and all* $t \in [0,T]$*. Next, note that, by definitions (3.2) and (3.7), and Proposition 4.6,* $\hat{f} \in L^\infty(0,T;\mathcal{L}^\infty_v)$ *and* $\hat{f} > 0$ *in* $\Omega \times [0,T]$*. Now, replace* $f(v)$ *in (3.5) by* $\hat{f}$ *and scale* x *by the factor* $\sqrt{\frac{3}{2}}\nu$ *to obtain*

$$\begin{aligned} &\partial_t^2 \tilde{w} + 2\nu\Lambda\partial_t\tilde{w} - \Delta\tilde{w} + \nu^2\Lambda^2\tilde{w} - \tilde{f} = 0, && \textit{in } \tilde{\Omega} \times (0,T],\\ &\tilde{w} = \tilde{w}_0, \quad \partial_t\tilde{w} = \tilde{w}_0', && \textit{on } \tilde{\Omega} \times \{0\},\end{aligned}$$

where $\tilde{\Omega} := \sqrt{\frac{3}{2}}\nu\Omega$*, and* $\tilde{w}$*,* $\tilde{w}_0$*,* $\tilde{w}_0'$*, and* $\tilde{f}$ *denote* w*,* w_0*,* w_0'*, and* $\nu^2\Lambda^2\mathrm{M}J_8\hat{f}$ *in the scaled domain* $\tilde{\Omega}$*, respectively. Note that with the new interpretation of* f*, the above equation is a system of two decoupled telegraph equations. Therefore, applying the same arguments to each of the two equations independently, in what follows we assume without loss of generality that the above equation is scalar.*

Using the change of variable $q := e^{\nu\Lambda t}\tilde{w}$ *the problem can be transformed to the initial-value problem of the standard wave equation given by*

$$
\begin{aligned}
(5.16)\qquad &\partial_t^2 q - \Delta q = e^{\nu\Lambda t}\tilde{f}, && \text{in } \mathbb{R}^2\times(0,T],\\
&q = \tilde{w}_0, \quad \partial_t q = \tilde{w}_0' + \nu\Lambda\tilde{w}_0, && \text{on } \mathbb{R}^2\times\{0\}.
\end{aligned}
$$

Here, the extension from $\tilde{\Omega}$ *to* $\mathbb{R}^2$ *is done periodically due to the* $\tilde{\Omega}$*-periodicity of the functions. Let* $\tilde{w}_{0\varepsilon}$, $\tilde{w}_{0\varepsilon}'$, *and* $\tilde{f}_\varepsilon$ *denote, respectively,* $\tilde{w}_0$, $\tilde{w}_0'$, *and* $\tilde{f}$ *after mollification by the standard positive mollifier* $\phi_\varepsilon \in C_{\mathrm{c}}^\infty$*; see [8, Sec. 2.6]. Using Poisson's formula for the homogeneous wave equation in* $\mathbb{R}^2$*, along with Duhamel's principle for the nonhomogenous problem [15, Sec. 2.4], it can be shown that the function*

$$
\begin{aligned}
(5.17)\qquad q_\varepsilon(x,t) := \tfrac{1}{2}\fint_{B(x,t)} &\frac{t\big[\tilde{w}_{0\varepsilon}(y) + \big(\partial_y\tilde{w}_{0\varepsilon}(y), y-x\big)_{\mathbb{R}^2}\big] + t^2\big[\tilde{w}_{0\varepsilon}'(y) + \nu\Lambda\tilde{w}_{0\varepsilon}(y)\big]}{\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{\frac{1}{2}}}\,\mathrm{d}y\\
&+ \tfrac{1}{2}\int_0^t (t-s)^2 e^{\nu\Lambda s}\fint_{B(x,t-s)} \frac{\tilde{f}_\varepsilon(y,s)}{\big[(t-s)^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{\frac{1}{2}}}\,\mathrm{d}y\,\mathrm{d}s
\end{aligned}
$$

solves the wave equation (5.16) *classically for the forcing term* $e^{\nu\Lambda t}\tilde{f}_\varepsilon$ *and initial values* $\tilde{w}_{0\varepsilon}$ *and* $\tilde{w}_{0\varepsilon}'$.

The second term in this solution is nonnegative for all $t\in[0,T]$ *since* $\tilde{f}$*, and consequently,* $\tilde{f}_\varepsilon$ *are nonnegative on* $B(x,t)$ *for all* $x\in\Omega$ *and all* $t\in[0,T]$*. Moreover, by [8, Theorem 2.6-1] and the definition of weak derivative we can write*

$$
\begin{aligned}
\big(\partial_y\tilde{w}_{0\varepsilon}(y), y-x\big)_{\mathbb{R}^2} &= \Big(\int_{B(y,\varepsilon)} \partial_y\phi_\varepsilon(y-z)\tilde{w}_0(z)\mathrm{d}z\,,\, y-x\Big)_{\mathbb{R}^2}\\
&= \Big(-\int_{B(y,\varepsilon)} \partial_z\phi_\varepsilon(y-z)\tilde{w}_0(z)\mathrm{d}z\,,\, y-x\Big)_{\mathbb{R}^2}\\
&= \Big(\int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\partial_z\tilde{w}_0(z)\mathrm{d}z\,,\, y-x\Big)_{\mathbb{R}^2}\\
&= \int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\big(\partial_z\tilde{w}_0(z), z-x\big)_{\mathbb{R}^2}\mathrm{d}z\\
&\qquad + \int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\big(\partial_z\tilde{w}_0(z), y-z\big)_{\mathbb{R}^2}\mathrm{d}z,
\end{aligned}
$$

where, using Hölder's inequality and the property $\int_{B(0,\varepsilon)}\phi_\varepsilon(x)\mathrm{d}x = 1$*, we have*

$$
\begin{aligned}
\left|\int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\big(\partial_z\tilde{w}_0(z), y-z\big)_{\mathbb{R}^2}\mathrm{d}z\right| &\le \big\|\partial_x\tilde{w}_0\big\|_{\mathcal{L}^\infty_{\partial w}} \int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\big\|y-z\big\|_1\mathrm{d}z\\
&\le \sqrt{2}\big\|\partial_x\tilde{w}_0\big\|_{\mathcal{L}^\infty_{\partial w}}\,\varepsilon.
\end{aligned}
$$

Therefore, it follows that

$$\begin{aligned}
&\fint_{B(x,t)} \frac{t\big[\tilde{w}_{0\varepsilon}(y) + \big(\partial_y \tilde{w}_{0\varepsilon}(y), y-x\big)_{\mathbb{R}^2}\big]}{\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{\frac{1}{2}}}\,\mathrm{d}y \\
&\qquad \geq \fint_{B(x,t)} t\left[\frac{\int_{B(y,\varepsilon)} \phi_\varepsilon(y-z)\big[\tilde{w}_0(z) + \big(\partial_z \tilde{w}_0(z), z-x\big)_{\mathbb{R}^2}\big]\mathrm{d}z}{\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{\frac{1}{2}}} - \frac{\sqrt{2}\big\|\partial_x w_0\big\|_{\mathcal{L}^\infty_{\partial w}}\varepsilon}{\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{\frac{1}{2}}}\right]\mathrm{d}y \\
&\qquad \geq -\sqrt{2}\big\|\partial_x \tilde{w}_0\big\|_{\mathcal{L}^\infty_{\partial w}}\varepsilon \quad \text{for all } (\tilde{w}_0, \tilde{w}_0') \in \tilde{\mathcal{D}}_w,
\end{aligned}$$

where $\tilde{\mathcal{D}}_w$ denotes $\mathcal{D}_w$ in the scaled domain $\tilde{\Omega}$. Note that the last inequality holds since the first term in the integration on the right-hand side is nonnegative by (5.15)*, and $t\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{-\frac{1}{2}}$ takes the average value* 1 *over the ball $B(x,t)$. Finally, note that $\tilde{w}_{0\varepsilon}'(y) + \nu\Lambda\tilde{w}_{0\varepsilon}(y)$ in* (5.17) *is nonnegative on $B(x,t)$ when $(\tilde{w}_0, \tilde{w}_0') \in \tilde{\mathcal{D}}_w$. Therefore, it follows that*

$$q_\varepsilon(x,t) \geq -\sqrt{2}\big\|\partial_x \tilde{w}_0\big\|_{\mathcal{L}^\infty_{\partial w}}\varepsilon \quad \text{for all } (\tilde{w}_0, \tilde{w}_0') \in \tilde{\mathcal{D}}_w. \tag{5.18}$$

Now, taking the limits as $\varepsilon \to 0$, it follows from [8, Theorem 2.6-3] that $\tilde{w}_{0\varepsilon} \to \tilde{w}_0$, $\tilde{w}_{0\varepsilon}' \to \tilde{w}_0'$, and $\tilde{f}_\varepsilon \to \tilde{f}$ in $L^2(\tilde{\Omega}_t)$, where $\tilde{\Omega}_t := \big\{y \in \mathbb{R}^2 : y \in B(x,t), x \in \Omega\big\}$. Therefore, there exists a subsequence $\big\{\varepsilon_n\big\}_{n=1}^\infty$, convergent to 0, such that $\tilde{w}_{0\varepsilon_n} \to \tilde{w}_0$, $\tilde{w}_{0\varepsilon_n}' \to \tilde{w}_0'$, and $\tilde{f}_{\varepsilon_n} \to \tilde{f}$ almost everywhere on Ω_t as $n \to \infty$ [17, Th. 2.30]. Moreover, since $(\tilde{w}_0, \tilde{w}_0') \in \mathcal{W}^{1,\infty} \times \mathcal{L}_w^\infty$ in $\tilde{\mathcal{D}}_w$, $\tilde{f} \in L^\infty(0,T;\mathcal{L}_v^\infty)$, and the function $\big[t^2 - \|y-x\|_{\mathbb{R}^2}^2\big]^{-\frac{1}{2}}$ is integrable over $B(x,t)$, it follows that the integrands in (5.17) *are uniformly bounded with respect to ε by integrable functions over $B(x,t)$. The Lebesgue dominated convergence theorem then implies that $q(x,t) := \lim_{n\to\infty} q_{\varepsilon_n}(x,t)$ exists on $\tilde{\Omega}_t$ and, by uniqueness of the weak solution, is a weak solution of the wave equation* (5.16)*. Now, letting $\varepsilon = \varepsilon_n \to 0$ in* (5.18)*, it follows that if $(\tilde{w}_0, \tilde{w}_0') \in \tilde{\mathcal{D}}_w$, then $q(x,t) \geq 0$ for almost every $x \in \tilde{\Omega}$ and all $t \in (0,T]$. This completes the proof since the change of variable $\tilde{w} = e^{-\nu\Lambda t}q$ and space rescaling $\Omega = \sqrt{\frac{2}{3}}\nu^{-1}\tilde{\Omega}$ do not change the sign of solutions.*

Corollary 5.4 (Boundedness of the weak solutions) *Suppose $g \in L^\infty(0,T;\mathcal{L}_i^\infty)$, $v_0 \in \mathcal{L}_v^\infty$, $i_0 \in \mathcal{L}_i^\infty$, $i_0' \in \mathcal{L}_i^\infty$, $w_0 \in \mathcal{W}^{1,\infty}$, and $w_0' \in \mathcal{L}_w^\infty$. Then, in addition to the regularities given by Proposition 4.6, the weak solution $(v(t), i(t), w(t))$ of* (3.3)–(3.6) *satisfies*

$$v \in C^{1,1}([0,T];\mathcal{L}_v^\infty), \quad i \in C^{0,1}([0,T];\mathcal{L}_i^\infty), \quad w \in L^\infty(0,T;\mathcal{L}_w^\infty).$$

Proof. *The boundedness of w follows immediately from the proof of Proposition 5.3, since under the assumption $w_0 \in \mathcal{W}^{1,\infty}$ and $w_0' \in \mathcal{L}_w^\infty$ the integrands in* (5.17) *are integrable and each component of the weak solution $w(t)$ is achieved almost everywhere in Ω as the limit of* (5.17) *when $\varepsilon \to 0$, followed by the space rescaling from $\tilde{\Omega}$ to Ω.*

Now, to prove boundedness of v, i, and $\mathrm{d}_t i$ let $x_0 \in \Omega$ be any Lebesgue point of the initial functions v_0, i_0, i_0', w_0, and $g(0)$. Take the $\mathbb{R}^4$-inner product of (3.4) at x_0 with $\mathrm{d}_t i(x_0,t)$ for every $t \in (0,T]$ to obtain

$$\begin{aligned}
&(\mathrm{d}_t^2 i_{x_0}, \mathrm{d}_t i_{x_0})_{\mathbb{R}^4} + 2\big(\Gamma \mathrm{d}_t i_{x_0}, \mathrm{d}_t i_{x_0}\big)_{\mathbb{R}^4} + \big(\Gamma^2 i_{x_0}, \mathrm{d}_t i_{x_0}\big)_{\mathbb{R}^4} \\
&\qquad - e\big(\Upsilon\Gamma J_6 w_{x_0}, \mathrm{d}_t i_{x_0}\big)_{\mathbb{R}^4} - e\big(\Upsilon\Gamma \mathrm{N} J_7 f(v_{x_0}), \mathrm{d}_t i_{x_0}\big)_{\mathbb{R}^4} = e\big(\Upsilon\Gamma g_{x_0}, \mathrm{d}_t i_{x_0}\big)_{\mathbb{R}^4},
\end{aligned}$$

where $v_{x_0}(t) := v(x_0,t)$, $i_{x_0}(t) := i(x_0,t)$, $w_{x_0}(t) := w(x_0,t)$, and $g_{x_0}(t) := g(x_0,t)$. This equality is similar to (4.21) in the proof of Proposition 4.4, with $\mathcal{L}_i^2$-inner products being replaced by $\mathbb{R}^4$-inner product, and the approximate solutions $v^{(m)}$, $i^{(m)}$, and $w^{(m)}$ being replaced by v_{x_0}, i_{x_0}, and w_{x_0}, respectively. Therefore, similar arguments as in the proof of Proposition 4.4 imply that

$$\sup_{t\in[0,T]}\left(\left\|\mathrm{d}_t i_{x_0}(t)\right\|_{\mathbb{R}^4}^2 + \left\|i_{x_0}(t)\right\|_{\mathbb{R}^4}^2\right) \leq \kappa_i, \tag{5.19}$$

where, with $\kappa_w := \left\|w\right\|^2_{L^\infty(0,T;\mathcal{L}_w^\infty)}$ and for some $\alpha_1 > 0$ independent of x_0,

$$\kappa_i = \alpha_1\left(\left\|i_0'\right\|^2_{\mathcal{L}_i^\infty} + \left\|i_0\right\|^2_{\mathcal{L}_i^\infty} + \left[\frac{e^2\kappa_w}{\gamma_{\min}}\left\|\Upsilon\Gamma J_6\right\|_2^2 + \frac{e^2|\Omega|}{\gamma_{\min}}(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\left\|\Upsilon\Gamma\mathrm{N}J_7\right\|_2^2\right]T \right.$$
$$\left. + \frac{e^2}{2\gamma_{\min}}\left\|\Upsilon\Gamma\right\|_2^2\left\|g\right\|^2_{L^\infty(0,T;\mathcal{L}_i^\infty)}\right),$$

and $\gamma_{\min}$ is the smallest eigenvalue of Γ.

Similarly, taking the $\mathbb{R}^2$-inner product of (3.3) at x_0 with $v_{x_0}(t)$ and using the arguments following (4.23) in the proof of Proposition 4.4 yields

$$\sup_{t\in[0,T]}\left(\left\|v_{x_0}(t)\right\|^2_{\mathcal{L}_v^2}\right) \leq \kappa_v, \tag{5.20}$$

where, for some $\alpha_2, \beta > 0$ independent of x_0,

$$\kappa_v = \alpha_2 \exp\left(\beta\sqrt{2\kappa_i}\left\|\Psi\right\|_2 T\right)\left(\left\|v_0\right\|^2_{\mathcal{L}_v^\infty} + \kappa_i T\right).$$

Now, note that almost every point $x_0 \in \Omega$ is a Lebesgue point for the locally integrable initial functions, and the estimates κ_v and κ_i are independent of x_0. Therefore, taking the supremum over all Lebesgue points $x_0 \in \Omega$ in (5.19) *and* (5.20) *implies $v \in L^\infty(0,T;\mathcal{L}_v^\infty)$ and $i \in W^{1,\infty}(0,T;\mathcal{L}_i^\infty)$ which, recalling* (3.3)*, further imply $v \in W^{2,\infty}(0,T;\mathcal{L}_v^\infty)$. Finally, it follows by using Morrey's inequality [15, Th. 5.6-4 and Th. 5.6-5] that $v \in C^{1,1}([0,T];\mathcal{L}_v^\infty)$ and $i \in C^{0,1}([0,T];\mathcal{L}_i^\infty)$, which completes the proof.*

Next, we recall and use the following standard result in the theory of ordinary differntial equations to establish conditions that guarantee nonnegativity of $i(x,t)$ for all biophysically plausible values of the input g, that is, for all $g \in L^2(0,T;\mathcal{D}_g)$, where

$$\mathcal{D}_g := \left\{\ell \in \mathcal{L}_i^2 : \ell \geq 0 \text{ a.e. in } \Omega\right\}. \tag{5.21}$$

Proposition 5.5 (Invariance of the nonnegative cone [7, Prop. I.1.1]) *Let $\left\{S(t)\right\}_{t\in[0,\infty)}$ be the semigroup of solution operators associated with the ordinary differential equation*

$$\mathrm{d}_t q(t) = P(q(t)), \quad q(t) \in \mathbb{R}^n, \quad t \in [0,\infty),$$

where $P : \mathbb{R}^n \to \mathbb{R}^n$ is a continuous locally Lipschitz mapping. Then the nonnegative cone $\mathbb{R}^n_+$ is invariant for $\left\{S(t)\right\}_{t\in[0,\infty)}$ if and only if $P(q)$ is quasipositive, that is, for every $j \in \{1,\ldots,n\}$,

$$P_j(q_1,\ldots,q_n) \geq 0 \textit{ whenevr } q_j = 0 \textit{ and } q_k \geq 0 \textit{ for all } k \neq j.$$

Proposition 5.6 (Positively invariant region for the solution $\boldsymbol{i(x,t)}$) *Suppose $g \in L^2(0,T;\mathcal{D}_g)$ and let $u(t) = S_{\mathrm{w}}(t)u_0$ be an Ω-periodic weak solution of* (3.3)–(3.6). *Suppose the w-component of the weak solution, $w(x,t)$, is nonnegative for almost every $x \in \Omega$ and all $t \in [0,T]$, $T > 0$, and define the set*

$$\mathcal{D}_i := \left\{(\ell,\ell') \in \mathcal{L}_i^2 \times \mathcal{L}_i^2 : \ell \geq 0 \text{ and } \ell' + \Gamma\ell \geq 0 \text{ a.e. in } \Omega\right\}. \tag{5.22}$$

Then, for every $(i_0, i_0') \in \mathcal{D}_i$, we have $(i(t), \mathrm{d}_t i(t)) \in \mathcal{D}_i$ almost everywhere in Ω for all $t \in [0,T]$. An identical result holds for strong solutions $u(t) = S_{\mathrm{s}}(t)u_0$ of (3.3)–(3.6) *with nonnegative w-component.*

Proof. *Let $b := \mathrm{d}_t i + \Gamma i$ and rewrite (3.4) as the first-order system of equations*

$$\begin{aligned} \mathrm{d}_t i &= -\Gamma i + b, \\ \mathrm{d}_t b &= -\Gamma b + e\Upsilon\Gamma J_6 w + e\Upsilon\Gamma \mathrm{N} J_7 f(v) + e\Upsilon\Gamma g. \end{aligned} \tag{5.23}$$

Let $x_0 \in \Omega$ be a Lebesgue point of the initial functions v_0, i_0, i_0', w_0, and $g(0)$, and define $v_{x_0}(t)$, $i_{x_0}(t)$, $w_{x_0}(t)$, and $g_{x_0}(t)$ as given in the proof of Corollary 5.4. Accordingly, let $b_{x_0}(t) := b(x_0,t) = \mathrm{d}_t i_{x_0}(t) + \Gamma i_{x_0}(t)$.

Now, (5.23) *implies that the function $q_{x_0} := (i_{x_0}, b_{x_0})$ satisfies the ordinary differential equation $\mathrm{d}_t q_{x_0}(t) = P(q_{x_0}(t))$, $t \in [0,T]$, where the mapping $P : \mathbb{R}^8 \to \mathbb{R}^8$ given by*

$$P(q_{x_0}) = P(i_{x_0}, b_{x_0}) := (-\Gamma i_{x_0} + b_{x_0}, -\Gamma b_{x_0} + e\Upsilon\Gamma J_6 w_{x_0} + e\Upsilon\Gamma \mathrm{N} J_7 f(v_{x_0}) + e\Upsilon\Gamma g_{x_0})$$

is Lipschitz continuous. Moreover, note that by assumption we have $w_{x_0} \geq 0$ and $g_{x_0} \geq 0$ which, along with the definitions of f, Υ, Γ, N, J_6, and J_7 given by (3.2) *and* (3.7), *implies $e\Upsilon\Gamma J_6 w_{x_0}(t) \geq 0$, $e\Upsilon\Gamma\mathrm{N}J_7 f(v_{x_0}(t)) \geq 0$ and $e\Upsilon\Gamma g_{x_0}(t) \geq 0$ for all $t \in [0,T]$. Therefore, it follows that P is quasipositive, and hence, by Proposition 5.5 we have $q_{x_0}(t) \geq 0$ for all $t \in [0,T]$. This completes the proof since x_0 is an arbitrary Lebesgue point of the initial functions and almost every points in Ω is a Lebesgue point for these functions.*

Remark 5.7 (Biophysically plausible set of initial values) *Propositions 5.3 and 5.6 ensure that if $g \in L^2(0,\infty;\mathcal{D}_g)$, where $\mathcal{D}_g$ is given by* (5.21), *and the initial values lie in the set*

$$\mathcal{D}_{\mathrm{Bio}} := \mathcal{L}_v^2 \times \mathcal{D}_i \times \mathcal{D}_w, \tag{5.24}$$

where $\mathcal{D}_w$ and $\mathcal{D}_i$ are given by (5.15) *and* (5.22), *respectively, then $i(x,t)$ and $w(x,t)$ always remain nonnegative at almost every point in Ω as they evolve over the time. However, it should be noted that this does not imply that the set $\mathcal{D}_{\mathrm{Bio}} \subset \mathcal{U}_{\mathrm{w}}$ is positively invariant, since Proposition 5.3 does not imply positive invariance of the set $\mathcal{D}_w$. Therefore, $\mathcal{D}_{\mathrm{Bio}}$ cannot serve as a phase space for the semidynamical system framework of the problem.*

In the analysis of next sections, nonnegativity of the solution $i(x,t)$ is essential. Moreover, it would be of no practical value if we analyze the dynamics of the model out of the biophysical regions of the phase space. Therefore, we define

$$\begin{aligned} \mathcal{D}_{\mathrm{w}} &:= \{u_0 \in \mathcal{U}_{\mathrm{w}} : i(t) \geq 0, w(t) \geq 0 \text{ a.e. in } \Omega \text{ for all } t \in [0,\infty), u(t) = S_{\mathrm{w}}(t)u_0\}, \\ \mathcal{D}_{\mathrm{s}} &:= \{u_0 \in \mathcal{U}_{\mathrm{s}} : i(t) \geq 0, w(t) \geq 0 \text{ a.e. in } \Omega \text{ for all } t \in [0,\infty), u(t) = S_{\mathrm{s}}(t)u_0\}, \end{aligned} \tag{5.25}$$

as the maximal closed subsets of $\mathcal{U}_{\mathrm{w}}$ and $\mathcal{U}_{\mathrm{s}}$ for the initial values of the weak and strong solutions, respectively, such that i and w initiated from the points in these sets evolve nonnegatively over time. Note that $\mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{s}}$ are nonempty since $\mathcal{D}_{\mathrm{Bio}} \subset \mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{Bio}} \cap \mathcal{U}_{\mathrm{s}} \subset \mathcal{D}_{\mathrm{s}}$ when $g \in L^2(0, \infty, \mathcal{D}_g)$. Moreover, $\mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{s}}$ are closed sets since $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$ are continuous semigroups, as given by Propositions 5.1 and 5.2. Moreover, it follows immediately from the definitions given by (5.25) that $\mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{s}}$ are positively invariant sets. Therefore, endowed with the metric induced by the norm in $\mathcal{U}_{\mathrm{w}}$ and $\mathcal{U}_{\mathrm{s}}$, the sets $\mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{s}}$ form positively invariant complete metric spaces and can be considered as biophysically plausible phase spaces of the model, based on which, we construct the semidynamical systems

$$\Big(\mathcal{D}_{\mathrm{w}}, \{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}\Big), \quad \Big(\mathcal{D}_{\mathrm{s}}, \{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}\Big),$$

associated with the weak and strong solutions of (3.3)–(3.6), respectively, and investigate their global dynamics in the remainder of the paper.

6. Existence of Absorbing Sets

In this section, we prove the existence of absorbing sets for the semigroups $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$ acting on $\mathcal{D}_{\mathrm{w}}$ and $\mathcal{D}_{\mathrm{s}}$, respectively. First recall the following definition of an absorbing set for an operator semigroup.

Definition 6.1 (Absorbing set [7, Def. II.2.3]) *A set $\mathscr{B}_0$ in a complete metric space $\mathcal{D}$ is called an* absorbing set *for the semigroup $\{S(t) : \mathcal{D} \to \mathcal{D}\}_{t\in[0,\infty)}$ if for every bounded set $\mathscr{B} \in \mathcal{D}$ there exists $t_0(\mathscr{B}) \in (0, \infty)$ such that $S(t)\mathscr{B} \subset \mathscr{B}_0$ for all $t \geq t_0(\mathscr{B})$.*

Theorem 6.2 (Existence of absorbing sets in $\mathcal{U}_{\mathrm{w}}$) *Assume that $g \in L^\infty(0, \infty; \mathcal{D}_g)$ and there exists $\theta > 2\gamma_{\min}^{-3}$ such that*

i) $\frac{4}{3}\theta e^2 \Upsilon_{\mathrm{EE}}^2 \gamma_{\max}(\nu\Lambda_{\mathrm{EE}})^{-3} < 1,$

ii) $\frac{4}{3}\theta e^2 \Upsilon_{\mathrm{EI}}^2 \gamma_{\max}(\nu\Lambda_{\mathrm{EI}})^{-3} < 1,$

where $\gamma_{\min} := \min\{\gamma_{\mathrm{EE}}, \gamma_{\mathrm{EI}}, \gamma_{\mathrm{IE}}, \gamma_{\mathrm{II}}\}$ and $\gamma_{\max} := \max\{\gamma_{\mathrm{EE}}, \gamma_{\mathrm{EI}}, \gamma_{\mathrm{IE}}, \gamma_{\mathrm{II}}\}$ are the smallest and largest eigenvalues of Γ, respectively. Then the semigroup $\{S_{\mathrm{w}}(t) : \mathcal{D}_{\mathrm{w}} \to \mathcal{D}_{\mathrm{w}}\}_{t\in[0,\infty)}$ associated with the weak solutions of (3.3)–(3.6) has a bounded absorbing set $\mathscr{B}_{\mathrm{w}}$. Specifically, consider the functions $Q_{\mathrm{w}}^- : \mathcal{D}_{\mathrm{w}} \to [0, \infty)$ and $Q_{\mathrm{w}}^+ : \mathcal{D}_{\mathrm{w}} \to [0, \infty)$ defined by

$$\begin{aligned} Q_{\mathrm{w}}^-(u) &:= \big\|\Phi^{\frac{1}{2}}v\big\|_{\mathcal{L}_v^2}^2 + \theta\big\|\mathrm{d}_t i + \tfrac{3}{2}\Gamma i\big\|_{\mathcal{L}_i^2}^2 + \tfrac{1}{4}\theta\big\|\Gamma i\big\|_{\mathcal{L}_i^2}^2 + \big\|\mathrm{d}_t w + \tfrac{3}{2}\nu\Lambda w\big\|_{\mathcal{L}_w^2}^2 \\ &\qquad + \tfrac{1}{4}\nu^2 \min\{6, \Lambda_{\min}^2\}\big\|w\big\|_{\mathcal{H}_w^1}^2, \\ Q_{\mathrm{w}}^+(u) &:= \big\|\Phi^{\frac{1}{2}}v\big\|_{\mathcal{L}_v^2}^2 + \theta\big\|\mathrm{d}_t i + \tfrac{3}{2}\Gamma i\big\|_{\mathcal{L}_i^2}^2 + \tfrac{1}{4}\theta\big\|\Gamma i\big\|_{\mathcal{L}_i^2}^2 + \big\|\mathrm{d}_t w + \tfrac{3}{2}\nu\Lambda w\big\|_{\mathcal{L}_w^2}^2 \\ &\qquad + \tfrac{1}{4}\nu^2 \max\{6, \Lambda_{\max}^2\}\big\|w\big\|_{\mathcal{H}_w^1}^2, \end{aligned} \tag{6.1}$$

and a scalar ε such that

$$\max\big\{\tfrac{4}{3}\theta e^2 \Upsilon_{\mathrm{EE}}^2 \gamma_{\max}(\nu\Lambda_{\mathrm{EE}})^{-3}, \tfrac{4}{3}\theta e^2 \Upsilon_{\mathrm{EI}}^2 \gamma_{\max}(\nu\Lambda_{\mathrm{EI}})^{-3}\big\} < 2\gamma_{\max}\varepsilon < 1. \tag{6.2}$$

Let $\tau_{\max} := \max\{\tau_{\mathrm{E}}, \tau_{\mathrm{I}}\}$ *denote the largest eigenvalue of* Φ*, and* $\Lambda_{\min} := \min\{\Lambda_{\mathrm{EE}}, \Lambda_{\mathrm{EI}}\}$ *and* $\Lambda_{\max} := \max\{\Lambda_{\mathrm{EE}}, \Lambda_{\mathrm{EI}}\}$ *denote the smallest and largest eigenvalues of* Λ*, respectively. Let* $\rho_{\mathrm{w}}^2 := \frac{\beta_{\mathrm{w}}}{\alpha_{\mathrm{w}}}$*, where*

$$\alpha_{\mathrm{w}} := \min\Big\{\tfrac{2}{3}\tau_{\max}^{-1}, \left(\tfrac{1}{2}\gamma_{\max}^{-1} - \varepsilon\right)\gamma_{\min}^2, 3\theta^{-1}\left(\theta\gamma_{\min} - 2\gamma_{\min}^{-2}\right), \tfrac{1}{2}\nu\Lambda_{\min}, 3\nu\Lambda_{\max}^{-2}\min\{\Lambda_{\mathrm{EE}}^3 - \tfrac{2}{3}\tfrac{e^2}{\nu^3\varepsilon}\Upsilon_{\mathrm{EE}}^2, \Lambda_{\mathrm{EI}}^3 - \tfrac{2}{3}\tfrac{e^2}{\nu^3\varepsilon}\Upsilon_{\mathrm{EI}}^2\}\Big\}, \tag{6.3}$$

$$\beta_{\mathrm{w}} := \frac{4\theta e^2}{\gamma_{\max}^{-1} - 2\varepsilon}\left[|\Omega|(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\left\|\Upsilon\mathrm{N}J_7\right\|_2^2 + \left\|\Upsilon\right\|_2^2\left\|g\right\|_{L^\infty(0,\infty;\mathcal{L}_i^2)}^2\right] + 2\nu^3|\Omega|\mathrm{F}_{\mathrm{E}}^2\,\mathrm{tr}(\Lambda^3\mathrm{M}^2). \tag{6.4}$$

Then, for all $\rho > \rho_{\mathrm{w}}$*, the bounded sets* $\mathscr{B}_{\mathrm{w}} := \left\{u \in \mathcal{D}_{\mathrm{w}} : Q_{\mathrm{w}}^-(u) \le \rho^2\right\}$ *are absorbing in* $\mathcal{U}_{\mathrm{w}}$*. Moreover, for every bounded set* $\mathscr{B} \subset \mathcal{D}_{\mathrm{w}}$ *there exists* $R > 0$ *such that* $Q_{\mathrm{w}}^+(u_0) \le R^2$ *for all* $u_0 \in \mathscr{B}$*, and* $S(t)\mathscr{B} \subset \mathscr{B}_{\mathrm{w}}$ *for all* $t \ge t_{\mathrm{w}}(\mathscr{B})$*, where*

$$t_{\mathrm{w}}(\mathscr{B}) = t_{\mathrm{w}}(R) := \max\left\{0, \frac{1}{\alpha_{\mathrm{w}}}\log\frac{R^2}{\rho^2 - \rho_{\mathrm{w}}^2}\right\}. \tag{6.5}$$

Proof. *First, taking the inner product of (3.3) with* v *yields*

$$\tfrac{1}{2}\mathrm{d}_t\left\|\Phi^{\frac{1}{2}}v\right\|_{\mathcal{L}_v^2}^2 + \left\|v\right\|_{\mathcal{L}_v^2}^2 - \left(J_1 i, v\right)_{\mathcal{L}_v^2} + \int_\Omega \left(v_1^2 i^{\mathrm{T}}\Psi J_4 + v_2^2 i^{\mathrm{T}}\Psi J_5\right)\mathrm{d}x = 0.$$

The integral term in this equation is nonnegative in $\mathcal{D}_{\mathrm{w}}$ *for all* $t \in [0,\infty)$*; see (3.7) and (5.25). Therefore, dropping the integral term and using Young's inequality yields, for every* $\varepsilon_1 > 0$*,*

$$\begin{aligned}\mathrm{d}_t\left\|\Phi^{\frac{1}{2}}v\right\|_{\mathcal{L}_v^2}^2 &\le -2(1-\varepsilon_1)\left\|v\right\|_{\mathcal{L}_v^2}^2 + \frac{1}{\varepsilon_1}\left\|i\right\|_{\mathcal{L}_i^2}^2 \\ &\le -2(1-\varepsilon_1)\tau_{\max}^{-1}\left\|\Phi^{\frac{1}{2}}v\right\|_{\mathcal{L}_v^2}^2 + \frac{1}{\varepsilon_1\gamma_{\min}^2}\left\|\Gamma i\right\|_{\mathcal{L}_i^2}^2.\end{aligned} \tag{6.6}$$

Next, let $b := \mathrm{d}_t i + \frac{3}{2}\Gamma i$ *and rewrite (3.4) as*

$$\mathrm{d}_t b + \tfrac{1}{2}\Gamma b + \tfrac{1}{4}\Gamma^2 i - e\Upsilon\Gamma J_6 w - e\Upsilon\Gamma\mathrm{N}J_7 f(v) = e\Upsilon\Gamma g.$$

Taking the inner product of the above equality with b *yields*

$$\begin{aligned}\tfrac{1}{2}\mathrm{d}_t\left\|b\right\|_{\mathcal{L}_i^2}^2 + \tfrac{1}{2}\left(\Gamma b, b\right)_{\mathcal{L}_i^2} + \tfrac{1}{8}\mathrm{d}_t\left\|\Gamma i\right\|_{\mathcal{L}_i^2}^2 + \tfrac{3}{8}\left\|\Gamma^{\frac{3}{2}}i\right\|_{\mathcal{L}_i^2}^2 \\ - e\left(\Upsilon\Gamma J_6 w, b\right)_{\mathcal{L}_i^2} - e\left(\Upsilon\Gamma\mathrm{N}J_7 f(v), b\right)_{\mathcal{L}_i^2} = e\left(\Upsilon\Gamma g, b\right)_{\mathcal{L}_i^2}.\end{aligned}$$

Note that

$$\left(\Gamma b, b\right)_{\mathcal{L}_i^2} \ge \gamma_{\max}^{-1}\left\|\Gamma b\right\|_{\mathcal{L}_i^2}^2,$$
$$\left\|\Gamma^{\frac{3}{2}}i\right\|_{\mathcal{L}_i^2}^2 \ge \gamma_{\min}\left\|\Gamma i\right\|_{\mathcal{L}_i^2}^2,$$

and, using similar arguments as in the proof of Proposition 4.4, it follows that for every $\varepsilon_2, \varepsilon_3, \varepsilon_4 > 0$*,*

$$\begin{aligned}e\left(\Upsilon\Gamma J_6 w, b\right)_{\mathcal{L}_i^2} &\le \varepsilon_2\left\|\Gamma b\right\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_2}\left\|\Upsilon J_6 w\right\|_{\mathcal{L}_i^2}^2 \\ e\left(\Upsilon\Gamma\mathrm{N}J_7 f(v), b\right)_{\mathcal{L}_i^2} &\le \varepsilon_3\left\|\Gamma b\right\|_{\mathcal{L}_i^2}^2 + \frac{e^2|\Omega|}{4\varepsilon_3}(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\left\|\Upsilon\mathrm{N}J_7\right\|_2^2, \\ e\left(\Upsilon\Gamma g, b\right)_{\mathcal{L}_i^2} &\le \varepsilon_4\left\|\Gamma b\right\|_{\mathcal{L}_i^2}^2 + \frac{e^2}{4\varepsilon_4}\left\|\Upsilon\right\|_2^2\left\|g\right\|_{\mathcal{L}_i^2}^2.\end{aligned}$$

Therefore,

$$\text{(6.7)}\quad \mathrm{d}_t\left[\|b\|^2_{\mathcal{L}^2_i}+\tfrac14\|\Gamma i\|^2_{\mathcal{L}^2_i}\right]\le-\left(\gamma_{\max}^{-1}-2(\varepsilon_2+\varepsilon_3+\varepsilon_4)\right)\|\Gamma b\|^2_{\mathcal{L}^2_i}-\tfrac34\gamma_{\min}\|\Gamma i\|^2_{\mathcal{L}^2_i}$$
$$+\frac{e^2}{2\varepsilon_2}\|\Upsilon J_6 w\|^2_{\mathcal{L}^2_i}+\frac{e^2}{2\varepsilon_3}|\Omega|(\mathrm{F}_\mathrm{E}^2+\mathrm{F}_\mathrm{I}^2)\|\Upsilon \mathrm{N} J_7\|^2_2+\frac{e^2}{2\varepsilon_4}\|\Upsilon\|^2_2\|g\|^2_{\mathcal{L}^2_i}.$$

Next, let $q:=\mathrm{d}_t w+\frac32\nu\Lambda w$ *and rewrite (3.5) as*

$$\text{(6.8)}\qquad \mathrm{d}_t q+\tfrac12\nu\Lambda q-\tfrac32\nu^2\Delta w+\tfrac14\nu^2\Lambda^2 w-\nu^2\Lambda^2\mathrm{M}J_8 f(v)=0.$$

Taking the inner product of this equality with q *yields*

$$\tfrac12\mathrm{d}_t\|q\|^2_{\mathcal{L}^2_w}+\tfrac12\nu\|\Lambda^{\frac12}q\|^2_{\mathcal{L}^2_w}+\tfrac34\nu^2\mathrm{d}_t\|\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac94\nu^3\|\Lambda^{\frac12}\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac18\nu^2\mathrm{d}_t\|\Lambda w\|^2_{\mathcal{L}^2_w}$$
$$+\tfrac38\nu^3\|\Lambda^{\frac32}w\|^2_{\mathcal{L}^2_w}-\nu^2\left(\Lambda^2\mathrm{M}J_8 f(v),q\right)_{\mathcal{L}^2_w}=0.$$

Using similar arguments as in the proof of Proposition 4.4 we can write, for every $\varepsilon_5>0$,

$$\left(\Lambda^2\mathrm{M}J_8 f(v^{(m)}),q\right)_{\mathcal{L}^2_w}\le\varepsilon_5\|\Lambda^{\frac12}q\|^2_{\mathcal{L}^2_w}+\frac{1}{4\varepsilon_5}|\Omega|\mathrm{F}_\mathrm{E}^2\,\mathrm{tr}(\Lambda^3\mathrm{M}^2),$$

and hence, it follows that

$$\text{(6.9)}\qquad \mathrm{d}_t\left[\|q\|^2_{\mathcal{L}^2_w}+\tfrac32\nu^2\|\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac14\nu^2\|\Lambda w\|^2_{\mathcal{L}^2_w}\right]$$
$$\le-\nu(1-2\nu\varepsilon_5)\|\Lambda^{\frac12}q\|^2_{\mathcal{L}^2_w}-3\nu\left(\tfrac32\nu^2\|\Lambda^{\frac12}\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac14\nu^2\|\Lambda^{\frac32}w\|^2_{\mathcal{L}^2_w}\right)$$
$$+\frac{\nu^2}{2\varepsilon_5}|\Omega|\mathrm{F}_\mathrm{E}^2\,\mathrm{tr}(\Lambda^3\mathrm{M}^2).$$

Now, set $\varepsilon_1=\frac23$ *in (6.6), set* $\varepsilon_3=\varepsilon_4=\frac18(\gamma_{\max}^{-1}-2\varepsilon)$ *in (6.7) with* $\varepsilon:=\varepsilon_2$, *and set* $\varepsilon_5=\frac{1}{4\nu}$ *in (6.9). Then, multiplying (6.7) by* $\theta>0$ *and adding the result to (6.6) and (6.9) yields*

$$\mathrm{d}_t Q_\mathrm{w}\le-\tfrac23\tau_{\max}^{-1}\|\Phi^{\frac12}v\|^2_{\mathcal{L}^2_v}-\theta\left(\tfrac12\gamma_{\max}^{-1}-\varepsilon\right)\|\Gamma b\|^2_{\mathcal{L}^2_i}-\tfrac34\left(\theta\gamma_{\min}-2\gamma_{\min}^{-2}\right)\|\Gamma i\|^2_{\mathcal{L}^2_i}-\tfrac12\nu\|\Lambda^{\frac12}q\|^2_{\mathcal{L}^2_w}$$
$$-3\nu\left(\tfrac32\nu^2\|\Lambda^{\frac12}\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac14\nu^2\Big(\left[\Lambda^3-\tfrac23\frac{\theta e^2}{\nu^3\varepsilon}J_6^\mathrm{T}\Upsilon^2J_6\right]w,w\Big)_{\mathcal{L}^2_w}\right)+\beta_\mathrm{w},$$

where β_w *is given by (6.4) and*

$$\text{(6.10)}\qquad Q_\mathrm{w}(u)=\|\Phi^{\frac12}v\|^2_{\mathcal{L}^2_v}+\theta\|b\|^2_{\mathcal{L}^2_i}+\tfrac14\theta\|\Gamma i\|^2_{\mathcal{L}^2_i}+\|q\|^2_{\mathcal{L}^2_w}+\tfrac32\nu^2\|\partial w\|^2_{\mathcal{L}^2_{\partial w}}+\tfrac14\nu^2\|\Lambda w\|^2_{\mathcal{L}^2_w}.$$

Note that for $\theta>2\gamma_{\min}^{-3}$ *we have* $\theta\gamma_{\min}-2\gamma_{\min}^{-2}>0$ *and for range of values of* ε *given by (6.2) we have* $\frac12\gamma_{\max}^{-1}-\varepsilon>0$. *Moreover, Assumptions (i) and (ii) along with (6.2) ensure that* $\Lambda^3-\frac23\frac{\theta e^2}{\nu^3\varepsilon}J_6^\mathrm{T}\Upsilon^2J_6>0$. *Therefore, with the decay rate* α_w *given by (6.3),*

$$\text{(6.11)}\qquad \mathrm{d}_t Q_\mathrm{w}(u)\le-\alpha_\mathrm{w}Q_\mathrm{w}(u)+\beta_\mathrm{w},$$

and hence, using Grönwall's inequality [48, Sec. III.1.1.3.],

$$\text{(6.12)}\qquad Q_\mathrm{w}^-(u(t))\le Q_\mathrm{w}^+(u(0))e^{-\alpha_\mathrm{w}t}+\rho_0^2\left(1-e^{-\alpha_\mathrm{w}t}\right),$$

where $Q_{\rm w}^-$ and $Q_{\rm w}^+$ are given in (6.1) and $\limsup_{t\to\infty} Q_{\rm w}^-(u(t)) \le \rho_0^2 := \frac{\beta_{\rm w}}{\alpha_{\rm w}}$. Now, since the mapping

$$(v,i,i',w,w') \mapsto (\Phi^{\frac12}v, \tfrac12\theta^{\frac12}\Gamma i, \theta^{\frac12}[i'+\tfrac32\Gamma i], \tfrac12\nu[\max\{6,\Lambda_{\rm max}^2\}]^{\frac12}w, w'+\tfrac32\nu\Lambda w) \tag{6.13}$$

is a linear isomorphism over $\mathcal{U}_{\rm w}$, for every bounded set $\mathscr{B}\subset\mathcal{D}_{\rm w}$ there exists $R>0$ such that $Q_{\rm w}^+(u_0)\le R^2$ for all $u_0\in\mathscr{B}$. Hence, it is immediate from (6.12) that $S_{\rm w}(t)\mathscr{B}\subset\mathscr{B}_{\rm w}$ for all $t\ge t_{\rm w}(\mathscr{B})$, where $t_{\rm w}(\mathscr{B})$ is given by (6.5).

Theorem 6.3 (Existence of absorbing sets in $\mathcal{D}_{\rm s}$) *Suppose the assumptions of Theorem 6.2 hold, namely, assume $g\in L^\infty(0,\infty;\mathcal{D}_g)$ and there exists $\theta>2\gamma_{\rm min}^{-3}$ such that the biophysical parameters of the model satisfy*

i) $\frac43\theta e^2\Upsilon_{\rm EE}^2\gamma_{\rm max}(\nu\Lambda_{\rm EE})^{-3}<1,$

ii) $\frac43\theta e^2\Upsilon_{\rm EI}^2\gamma_{\rm max}(\nu\Lambda_{\rm EI})^{-3}<1,$

where $\gamma_{\rm min}$ and $\gamma_{\rm max}$ are the smallest and largest eigenvalues of Γ, respectively. Then the semigroup $\{S_{\rm s}(t):\mathcal{D}_{\rm s}\to\mathcal{D}_{\rm s}\}_{t\in[0,\infty)}$ associated with the strong solutions of (3.3)–(3.6) has a bounded absorbing set $\mathscr{B}_{\rm s}$. Specifically, consider the function $Q_{\rm s}^-:\mathcal{D}_{\rm s}\to[0,\infty)$ defined by

$$Q_{\rm s}^-(u) := \|\Phi^{\frac12}v\|_{\mathcal{L}_v^2}^2 + \theta\|{\rm d}_t i+\tfrac32\Gamma i\|_{\mathcal{L}_i^2}^2 + \tfrac14\theta\|\Gamma i\|_{\mathcal{L}_i^2}^2 + \|{\rm d}_t w+\tfrac32\nu\Lambda w\|_{\mathcal{H}_w^1}^2 + \tfrac18\nu^2\min\{6,\Lambda_{\rm min}^2\}\|(-\Delta+I)w\|_{\mathcal{L}_w^2}^2, \tag{6.14}$$

and denote by $\Lambda_{\rm min}$ and $\Lambda_{\rm max}$ the smallest and largest eigenvalues of Λ, respectively, and by $\tau_{\rm max}$ the largest eigenvalue of Φ. Let $\rho_{\rm s}^2 := \frac{2\beta_{\rm s}}{\alpha_{\rm s}}$ with

$$\alpha_{\rm s} := \min\Big\{\tfrac23\tau_{\rm max}^{-1}, \left(\tfrac12\gamma_{\rm max}^{-1}-\varepsilon\right)\gamma_{\rm min}^2, 3\theta^{-1}\left(\theta\gamma_{\rm min}-2\gamma_{\rm min}^{-2}\right), \nu\Lambda_{\rm min}, 3\nu\Lambda_{\rm max}^{-2}\min\{\Lambda_{\rm EE}^3-\tfrac23\tfrac{e^2}{\nu^3\varepsilon}\Upsilon_{\rm EE}^2, \Lambda_{\rm EI}^3-\tfrac23\tfrac{e^2}{\nu^3\varepsilon}\Upsilon_{\rm EI}^2\}\Big\}, \tag{6.15}$$

$$\beta_{\rm s} := \frac{4e^2\theta}{\gamma_{\rm max}^{-1}-2\varepsilon}\left[|\Omega|({\rm F}_{\rm E}^2+{\rm F}_{\rm I}^2)\|\Upsilon{\rm N}J_7\|_2^2 + \|\Upsilon\|_2^2\|g\|_{L^\infty(0,\infty;\mathcal{L}_i^2)}^2\right] + 2\nu^2\left[\frac{1}{32\varepsilon_2}\frac{{\rm F}_{\rm E}^2}{\sigma_{\rm E}^2}{\rm tr}(\Lambda^4{\rm M}^2)\eta\rho_{\rm w}^2 + \tfrac14|\Omega|{\rm F}_{\rm E}^2\,{\rm tr}(\Lambda^4{\rm M}^2)\left(\frac{1}{\varepsilon_1}+\frac{\alpha_{\rm s}}{\varepsilon_2}\right)\right], \tag{6.16}$$

where η is a positive constant, $\rho_{\rm w}^2 := \frac{\beta_{\rm w}}{\alpha_{\rm w}}$ is the same constant given in Theorem 6.2, the scalar ε takes values within the same range given by (6.2), and

$$\varepsilon_1 := \tfrac{1}{32}\alpha_{\rm s}\min\{6,\Lambda_{\rm min}^2\}\big(1+\|\tfrac32\nu\Lambda-\alpha I\|_2^2\big)^{-1}, \quad \varepsilon_2 := \tfrac{1}{16}\min\{6,\Lambda_{\rm min}^2\}. \tag{6.17}$$

Then, for all $\rho>\rho_{\rm s}$, the bounded sets $\mathscr{B}_{\rm s} := \{u\in\mathcal{D}_{\rm s} : Q_{\rm s}^-(u)\le\rho^2\}$ are absorbing in $\mathcal{D}_{\rm s}$.

Proof. *Let $A := -\Delta+I$ and take the inner product of (6.8) with Aq to obtain*

$$\tfrac12{\rm d}_t\|q\|_{\mathcal{H}_w^1}^2 + \tfrac12\nu\|\Lambda^{\frac12}q\|_{\mathcal{H}_w^1}^2 + \tfrac34\nu^2{\rm d}_t\|\partial w\|_{\mathcal{H}_{\partial w}^1}^2 + \tfrac94\nu^3\|\Lambda^{\frac12}\partial w\|_{\mathcal{H}_{\partial w}^1}^2 + \tfrac18\nu^2{\rm d}_t\|\Lambda w\|_{\mathcal{H}_w^1}^2 + \tfrac38\nu^3\|\Lambda^{\frac32}w\|_{\mathcal{H}_w^1}^2 - \nu^2\big(\Lambda^2{\rm M}J_8 f(v), Aq\big)_{\mathcal{L}_w^2} = 0.$$

This equality, along with the inequalities (6.6) and (6.7) derived in the proof of Theorem 6.2 and the same values of $\varepsilon_1, \ldots, \varepsilon_4$ therein, implies that

$$
\begin{aligned}
\mathrm{d}_t Q_{\mathrm{s}} \leq & -\tfrac{2}{3}\tau_{\max}\left\|\Phi^{\frac{1}{2}}v\right\|_{\mathcal{L}_v^2}^2 - \theta\left(\tfrac{1}{2}\gamma_{\max}^{-1} - \varepsilon\right)\left\|\Gamma b\right\|_{\mathcal{L}_i^2}^2 - \tfrac{3}{4}\left(\theta\gamma_{\min} - 2\gamma_{\min}^{-2}\right)\left\|\Gamma i\right\|_{\mathcal{L}_i^2}^2 - \nu\left\|\Lambda^{\frac{1}{2}}q\right\|_{\mathcal{H}_w^1}^2 \\
& - 3\nu\left(\tfrac{3}{2}\nu^2\left\|\Lambda^{\frac{1}{2}}\partial w\right\|_{\mathcal{H}_{\partial w}^1}^2 + \tfrac{1}{4}\nu^2\left(\left[\Lambda^3 - \tfrac{2}{3}\frac{\theta e^2}{\nu^3\varepsilon}J_6^{\mathrm{T}}\Upsilon^2 J_6\right]w, w\right)_{\mathcal{H}_w^1}\right) \\
& + 2\nu^2\left(\Lambda^2 \mathrm{M} J_8 f(v), Aq\right)_{\mathcal{L}_w^2} + \beta,
\end{aligned}
$$

where

$$
\begin{aligned}
Q_{\mathrm{s}}(u) &:= \left\|\Phi^{\frac{1}{2}}v\right\|_{\mathcal{L}_v^2}^2 + \theta\left\|b\right\|_{\mathcal{L}_i^2}^2 + \tfrac{1}{4}\theta\left\|\Gamma i\right\|_{\mathcal{L}_i^2}^2 + \left\|q\right\|_{\mathcal{H}_w^1}^2 + \tfrac{3}{2}\nu^2\left\|\partial w\right\|_{\mathcal{H}_{\partial w}^1}^2 + \tfrac{1}{4}\nu^2\left\|\Lambda w\right\|_{\mathcal{H}_w^1}^2, \\
\beta &:= \frac{4e^2\theta}{\gamma_{\max}^{-1} - 2\varepsilon}\left[|\Omega|(\mathrm{F}_{\mathrm{E}}^2 + \mathrm{F}_{\mathrm{I}}^2)\left\|\Upsilon \mathrm{N} J_7\right\|_2^2 + \left\|\Upsilon\right\|_2^2\left\|g\right\|_{L^\infty(0,\infty;\mathcal{L}_i^2)}^2\right],
\end{aligned}
$$

and ε takes values within the range given by (6.2). Now, using similar arguments as in the proof of Theorem 6.2, it follows from Assumptions (i) and (ii) with $\theta > 2\gamma_{\min}^{-3}$ that

$$
\mathrm{d}_t Q_{\mathrm{s}}(u) \leq -\alpha_{\mathrm{s}} Q_{\mathrm{s}}(u) + 2\nu^2\left(\Lambda^2 \mathrm{M} J_8 f(v), Aq\right)_{\mathcal{L}_w^2} + \beta, \tag{6.18}
$$

where the decay rate α_{s} is given by (6.15). Then, Grönwall's inequality [48, Sec. III.1.1.3.] implies

$$
Q_{\mathrm{s}}(u(t)) \leq Q_{\mathrm{s}}(u(0))e^{-\alpha_{\mathrm{s}}t} + 2\nu^2\int_0^t \left(\Lambda^2 \mathrm{M} J_8 f(v), Aq\right)_{\mathcal{L}_w^2} e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s + \frac{\beta}{\alpha_{\mathrm{s}}}\left(1 - e^{-\alpha_{\mathrm{s}}t}\right). \tag{6.19}
$$

Replacing $q := \mathrm{d}_t w + \frac{3}{2}\nu\Lambda w$ in the integral term in the above inequality and integrating by parts yields

$$
\begin{aligned}
&\int_0^t \left(\Lambda^2 \mathrm{M} J_8 f(v), Aq\right)_{\mathcal{L}_w^2} e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s \\
&\quad = -\int_0^t \left(\Lambda^2 \mathrm{M} J_8 \mathrm{d}_s f(v), Aw\right)_{\mathcal{L}_w^2} e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s + \int_0^t \left(\Lambda^2 \mathrm{M} J_8 f(v), (\tfrac{3}{2}\nu\Lambda - \alpha_{\mathrm{s}} I)Aw\right)_{\mathcal{L}_w^2} e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s \\
&\qquad + \left(\Lambda^2 \mathrm{M} J_8 f(v), Aw\right)_{\mathcal{L}_w^2} - \left(\Lambda^2 \mathrm{M} J_8 f(v_0), Aw_0\right)_{\mathcal{L}_w^2} e^{-\alpha_{\mathrm{s}}t}.
\end{aligned}
$$

Next, noting that $\mathrm{d}_s f(v) = \partial_v f(v)\mathrm{d}_s v$ and $\sup_{v_{\mathrm{E}}(x,t)\in\mathbb{R}} |\partial_{v_{\mathrm{E}}} f_{\mathrm{E}}(v_{\mathrm{E}})| \leq \frac{\mathrm{F}_{\mathrm{E}}}{2\sqrt{2}\sigma_{\mathrm{E}}}$ by (4.37), it follows that for every $\varepsilon_1, \varepsilon_2 > 0$,

$$
\begin{aligned}
&\int_0^t \left(\Lambda^2 \mathrm{M} J_8 f(v), Aq\right)_{\mathcal{L}_w^2} e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s \\
&\quad \leq \varepsilon_1\left(1 + \left\|\tfrac{3}{2}\nu\Lambda - \alpha_{\mathrm{s}} I\right\|_2^2\right)\int_0^t \left\|Aw\right\|_{\mathcal{L}_w^2}^2 e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s + \frac{1}{32\varepsilon_1}\frac{\mathrm{F}_{\mathrm{E}}^2}{\sigma_{\mathrm{E}}^2}\operatorname{tr}(\Lambda^4\mathrm{M}^2)\int_0^t \left\|\mathrm{d}_s v\right\|_{\mathcal{L}_v^2}^2 e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s \\
&\qquad + \varepsilon_2\left\|Aw\right\|_{\mathcal{L}_w^2}^2 + \tfrac{1}{4}|\Omega|\mathrm{F}_{\mathrm{E}}^2\operatorname{tr}(\Lambda^4\mathrm{M}^2)\left(\frac{1}{\alpha_{\mathrm{s}}\varepsilon_1} + \frac{1}{\varepsilon_2}\right) - \left(\Lambda^2 \mathrm{M} J_8 f(v_0), Aw_0\right)_{\mathcal{L}_w^2} e^{-\alpha_{\mathrm{s}}t}.
\end{aligned}
$$

Moreover, it follows from Theorem 6.2 that for every bounded set $\mathscr{B} \subset \mathcal{D}_{\mathrm{s}}$ there exists a time $t_{\mathrm{w}}(\mathscr{B})$, given by (6.5), and a constant $\eta > 0$ such that $\left\|\mathrm{d}_t v(t)\right\|_{\mathcal{L}_v^2}^2 \leq \eta\rho_{\mathrm{w}}^2$ for all $t \geq t_{\mathrm{w}}(\mathscr{B})$. Therefore, using the estimate (5.13) for $t < t_{\mathrm{w}}(\mathscr{B})$ we can write

$$
\int_0^t \left\|\mathrm{d}_s v\right\|_{\mathcal{L}_v^2}^2 e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s \leq \int_0^{t_{\mathrm{w}}(\mathscr{B})} \left\|\mathrm{d}_s v\right\|_{\mathcal{L}_v^2}^2 e^{\alpha_{\mathrm{s}}(s-t)}\mathrm{d}s + \frac{\eta\rho_{\mathrm{w}}^2}{\alpha_{\mathrm{s}}} \leq \kappa_0(\mathscr{B})e^{-\alpha_{\mathrm{s}}t} + \frac{\eta\rho_{\mathrm{w}}^2}{\alpha_{\mathrm{s}}}, \tag{6.20}
$$

where, for some $\alpha > 0$,

$$\kappa_0(\mathscr{B}) := \alpha \int_0^{t_{\mathrm{w}}(\mathscr{B})} \left(\|v(s)\|^2_{\mathcal{L}^2_v} + \|i(s)\|^2_{\mathcal{L}^2_i} + \|v(s)\|^2_{\mathcal{L}^2_v} \|i(s)\|^2_{\mathcal{L}^2_i} \right) e^{\alpha_{\mathrm{s}} s} \mathrm{d}s < \infty.$$

Now, using the above estimate for the integral term in (6.19)*, with* ε_1 *and* ε_2 *given by* (6.17)*, yields*

$$Q^-_{\mathrm{s}}(u) e^{\alpha_{\mathrm{s}} t} \le \tfrac{1}{2}\alpha_{\mathrm{s}} \int_0^t Q^-_{\mathrm{s}}(u) e^{\alpha_{\mathrm{s}} s} \mathrm{d}s + \kappa(\mathscr{B}) + \frac{\beta_{\mathrm{s}}}{\alpha_{\mathrm{s}}} e^{\alpha_{\mathrm{s}} t}, \tag{6.21}$$

where $\beta_{\mathrm{s}} := \beta + 2\nu^2 \left[\frac{1}{32\varepsilon_2} \frac{\mathrm{F}^2_{\mathrm{E}}}{\sigma^2_{\mathrm{E}}} \operatorname{tr}(\Lambda^4 \mathrm{M}^2) \eta \rho^2_{\mathrm{w}} + \frac{1}{4} |\Omega| \mathrm{F}^2_{\mathrm{E}} \operatorname{tr}(\Lambda^4 \mathrm{M}^2) \left(\frac{1}{\varepsilon_1} + \frac{\alpha_{\mathrm{s}}}{\varepsilon_2} \right) \right]$ *as given in (6.16),* $Q^-_{\mathrm{s}}(u)$ *is given in (6.14), and*

$$\kappa(\mathscr{B}) := Q^+_{\mathrm{s}}(u(0)) + 2\nu^2 \left[\frac{1}{32\varepsilon_2} \frac{\mathrm{F}^2_{\mathrm{E}}}{\sigma^2_{\mathrm{E}}} \operatorname{tr}(\Lambda^4 \mathrm{M}^2) \kappa_0(\mathscr{B}) - \left(\Lambda^2 \mathrm{M} J_8 f(v_0), A w_0 \right)_{\mathcal{L}^2_w} \right] - \frac{\beta}{\alpha_{\mathrm{s}}},$$
$$Q^+_{\mathrm{s}}(u) := \|\Phi^{\frac{1}{2}} v\|^2_{\mathcal{L}^2_v} + \theta \|b\|^2_{\mathcal{L}^2_i} + \tfrac{1}{4}\theta \|\Gamma i\|^2_{\mathcal{L}^2_i} + \|q\|^2_{\mathcal{H}^1_w} + \tfrac{1}{4}\nu^2 \max\{6, \Lambda^2_{\max}\} \|Aw\|^2_{\mathcal{L}^2_w}.$$

Next, using Grönwall's inequality for the function $\int_0^t Q^-_{\mathrm{s}}(u) e^{\alpha_{\mathrm{s}} s} \mathrm{d}s$ *in (6.21) gives*

$$\int_0^t Q^-_{\mathrm{s}}(u) e^{\alpha_{\mathrm{s}} s} \mathrm{d}s \le \frac{1}{\frac{1}{2}\alpha_{\mathrm{s}}} \left[\kappa(\mathscr{B}) \left(e^{\frac{1}{2}\alpha_{\mathrm{s}} t} - 1 \right) + \frac{\beta_{\mathrm{s}}}{\alpha_{\mathrm{s}}} \left(e^{\alpha_{\mathrm{s}} t} - e^{\frac{1}{2}\alpha_{\mathrm{s}} t} \right) \right],$$

which, along with (6.21) implies

$$Q^-_{\mathrm{s}}(u) \le \kappa(\mathscr{B}) e^{-\frac{1}{2}\alpha_{\mathrm{s}} t} + \rho^2_{\mathrm{s}} \left(1 - \tfrac{1}{2} e^{-\frac{1}{2}\alpha_{\mathrm{s}} t} \right), \tag{6.22}$$

where $\limsup_{t\to\infty} Q^-_{\mathrm{s}}(u(t)) \le \rho^2_{\mathrm{s}} := \frac{2\beta_{\mathrm{s}}}{\alpha_{\mathrm{s}}}$.

Finally, considering the linear isomorphism (6.13) over $\mathcal{U}_{\mathrm{s}}$*, it follows that for every bounded set* $\mathscr{B} \subset \mathcal{D}_{\mathrm{s}}$ *there exists* $R > 0$ *such that* $\kappa(\mathscr{B}) \le R^2$ *for all* $u_0 \in \mathscr{B}$*. Therefore,* (6.22) *implies that* $S_{\mathrm{s}}(t)\mathscr{B} \subset \mathscr{B}_{\mathrm{s}}$ *for all* $t \ge t_{\mathrm{s}}(\mathscr{B})$ *and some* $t_{\mathrm{s}}(\mathscr{B}) > 0$*, which completes the proof.*

Note that an estimate similar to (6.5) given in Theorem 6.2 can be also obtained for $t_{\mathrm{s}}(\mathscr{B})$ in the proof of Theorem 6.3. However, this would be of limited practical value since the bound (6.20) is very conservative for times $t \ll t_{\mathrm{w}}(\mathscr{B})$.

Remark 6.4 (Conditions on parameter sets) *For the range of values given in Table 1, the maximum value that the left-hand side of the inequalities in Assumptions (i) and (ii) of Theorems 6.2 and 6.3 may take is* $39.4083\,\theta$*, which is achieved when* $\Upsilon_{\mathrm{EE}} = 2$*,* $\Upsilon_{\mathrm{EI}} = 2$*,* $\Lambda_{\mathrm{EE}} = 0.1$*,* $\Lambda_{\mathrm{EI}} = 0.1$*,* $\nu = 100$*, and* $\gamma_{\max} = 1000$*. Assumptions (i) and (ii) then require that* $\theta < \frac{1}{39.4083} = 0.0254$*. Moreover, Theorems 6.2 and 6.3 allow for* $\theta > 2\gamma^{-3}_{\min} \ge 0.002$*, in accordance with Table 1. This implies that—for the entire range of values that the biophysical parameters of the model may take—the conditions imposed by Theorems 6.2 and 6.3 are satisfied at least for any* $0.002 < \theta < 0.0254$*, and the model* (3.1) *possesses bounded absorbing sets as given by these theorems.*

7. Existence and Nonexistence of a Global Attractor

In this section, we investigate the problem of existence of a global attractor for the semigroups $\{S_{\mathrm{w}}(t) : \mathcal{D}_{\mathrm{w}} \to \mathcal{D}_{\mathrm{w}}\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t) : \mathcal{D}_{\mathrm{s}} \to \mathcal{D}_{\mathrm{s}}\}_{t\in[0,\infty)}$ of solution operators of (3.3)–(3.6). First, we recall the definition of a global attractor and a widely used theorem for establishing the existence of a global attractor.

Definition 7.1 (Attracting set [7, Def. II.2.4]) *A set $\mathscr{P}$ in a complete metric space $\mathcal{D}$ is called an* attracting set *for a semigroup $\{S(t)\}_{t\in[0,\infty)}$ acting in $\mathcal{D}$ if for every bounded set $\mathscr{B} \in \mathcal{D}$, $\mathrm{dist}_{\mathcal{D}}(S(t)\mathscr{B}, \mathscr{P}) \to 0$ as $t \to \infty$. Here, $\mathrm{dist}_{\mathcal{D}}(\mathscr{G}, \mathscr{H}) := \sup_{g\in\mathscr{G}} \inf_{h\in\mathscr{H}} \|g - h\|_{\mathcal{D}}$ is the Hausdorff distance between the two sets $\mathscr{G}, \mathscr{H} \subset \mathcal{D}$.*

Definition 7.2 (Global attractor [7, Def. II.3.1]) *A bounded set $\mathscr{A}$ in a complete metric space $\mathcal{D}$ is called a* global attractor *for a semigroup $\{S(t)\}_{t\in[0,\infty)}$ acting in $\mathcal{D}$ if it satisfies the following conditions:*

i) *$\mathscr{A}$ is compact in $\mathcal{D}$.*

ii) *$\mathscr{A}$ is an attracting set for $\{S(t)\}_{t\in[0,\infty)}$.*

iii) *$\mathscr{A}$ is strictly invariant with respect to $\{S(t)\}_{t\in[0,\infty)}$, that is, $S(t)\mathscr{A} = \mathscr{A}$ for all $t \in [0, \infty)$.*

Definition 7.3 (Asymptotic compactness [7, Def. II.2.5]) *The semigroup $\{S(t)\}_{t\in[0,\infty)}$ acting in a complete metric space $\mathcal{D}$ is called* asymptotically compact *if it possesses a compact attracting set $\mathscr{K} \Subset \mathcal{D}$.*

Theorem 7.4 (Global Attractor [7, Th. II.3.1]) *Let $\{S(t)\}_{t\in[0,\infty)}$ be an asymptotically compact continuous semigroup in a complete metric space $\mathcal{D}$ possessing a compact attracting set $\mathscr{K} \Subset \mathcal{D}$. Then $\{S(t)\}_{t\in[0,\infty)}$ has a global attractor $\mathscr{A} \subset \mathscr{K}$ given by $\mathscr{A} = \omega(\mathscr{K})$, where $\omega(\mathscr{K})$ is the ω-limit set of $\mathscr{K}$.*

7.1 Challenges in Establishing a Global Attractor

Continuity of $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$, as required by Theorem 7.4, is established in Propositions 5.1 and 5.2, respectively. To prove asymptotic compactness of a semigroup $\{S(t)\}_{t\in[0,\infty)}$ acting in $\mathcal{D}$ a general approach is to show first, that the semigroup possesses a bounded absorbing set and second, that the semigroup is κ-contracting, meaning that $\lim_{t\to\infty} \kappa(S(t)\mathscr{B}) = 0$ for any bounded set $\mathscr{B} \in \mathcal{D}$, where κ denotes the Kuratowski measure of compactness [35,53]. An effective way to establish the later property is through a decomposition $S(t) = S_1(t) + S_2(t)$ such that for every bounded set $\mathscr{B} \in \mathcal{D}$ the component $S_1(t)\mathscr{B}$ converges uniformly to 0 as $t \to 0$, and the component $S_2(t)\mathscr{B}$ is κ-contractive or is precompact in $\mathcal{D}$ for large t [44,48].

As the first step towards proving the asymptotic compactness property stated above, existence of bounded absorbing sets for $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$ is established in Theorems 6.2 and 6.3, respectively. However, it turns out that the κ-contracting property is hard to achieve for the model (3.3)–(3.5) with parameter values in the range given in Table 1, due to the lack of space-dissipative terms in the ordinary differential equations (3.3) and (3.4), the nature of nonlinear couplings in (3.3) and (3.4), and the range of values of the biophysical parameters of the model.

The uniform compactness of the component $S_2(t)$ in the decomposition approach stated above is usually verified by establishing energy estimates in more regular function spaces and then deducing compactness from compact embedding theorems. This approach, although successfully used in [36] to prove existence of a global attractor for a coupled ODE-PDE reaction-diffusion system, is not very promising here. In [36], the ODE subsystem is linear and the energy estimates in a higher regular space are achieved by taking space-derivatives of the ODE's and constructing energy functionals for the resulting equations. As seen in the proof of Theorem 6.2, the nonnegativity of $i(x,t)$ is a key property that permits elimination of the sign-indefinite quadratic term in the energy equation of (3.3), which results in the energy variation inequality 6.6. This nonnegativity property, however, is not preserved in the derivative or any other variations of $i(x,t)$, leaving some sign-indefinite quadratic terms in the analysis. Moreover, it can be observed from the range of parameter values given in Table 1 that the sign-indefinite nonlinear terms that would appear in the energy equations of any variations of (3.3) and (3.4) have significantly larger coefficients than the sign-definite dissipative terms. This makes the analysis challenging to balance the terms in the energy functional to absorb the nondissipative terms into dissipative ones. Finally, the nonlinear terms appearing in (3.3) and (3.4) do not satisfy the usual assumptions, e.g., as in [13], that enable shaping the energy functional to eliminate the nondissipative terms that would otherwise appear in the equations.

Some other techniques are available in the literature to avoid energy estimations in higher regular spaces. In [35], for instance, the notion of ω-limit compactness is used to develope necessary and sufficient conditions for existence of a global attractor. This is accomplished by decomposing the phase space into two spaces, one of which being finite-dimensional, and then showing that for every bounded set $\mathscr{B} \subset \mathcal{D}$ the canonical projection of $S(t)\mathscr{B}$ onto the finite-dimensional space is bounded, and the canonical projection on the complement space remains arbitrarily small for sufficiently large $t \geq t_0$, for some $t_0 = t_0(\mathscr{B}) > 0$. These decomposition techniques, however, rely on the spectral decomposition of the space-acting operators to construct the desired phase space decomposition. Such operators do not exist in the ODE subsystems (3.3) and (3.4) in our problem.

7.2 Nonexistence of a Global Attractor

As discussed in Section 7.1, establishing a global attractor for (3.3)–(3.5) is a challenging problem. In fact, in this section we show that there exit sets of parameter values, leading to physiologically reasonable behavior in the model, for which the semigroups $\{S_{\mathrm{w}}(t)\}_{t\in[0,\infty)}$ and $\{S_{\mathrm{s}}(t)\}_{t\in[0,\infty)}$ do not possess a global attractor. We first use [13, Prop. 4.7] to prove the following theorem giving sufficient conditions for noncompactness of the equilibrium sets of (3.3)–(3.5) in $\mathcal{U}_{\mathrm{w}}$ and $\mathcal{U}_{\mathrm{s}}$.

Theorem 7.5 (Noncompactness of equilibrium sets) *Suppose g is bounded and constant in time, that is, $g(x,t) = g(x)$ for all $(x,t) \in \Omega \times [0,\infty)$ and $g \in \mathcal{L}_i^\infty$. Let $u_{\mathrm{e}} := (v_{\mathrm{e}}, i_{\mathrm{e}}, 0, w_{\mathrm{e}}, 0)$ be an equilibrium of (3.3)–(3.5) such that $v_{\mathrm{e}} \in \mathcal{L}_v^\infty$, $i_{\mathrm{e}} \in \mathcal{L}_i^\infty$, and $w_{\mathrm{e}} \in \mathcal{H}_w^2$. Define the mapping $P = (P_v, P_i) : \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty \to \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ as*

$$P_v(v,i) := v - J_1 i + J_2 v i^{\mathrm{T}} \Psi J_4 + J_3 v i^{\mathrm{T}} \Psi J_5, \tag{7.1}$$
$$P_i(v,i) := (e\Upsilon)^{-1}\Gamma i - \mathrm{N} J_7 f(v) - g,$$

and let $A := -\frac{3}{2}\Delta + \Lambda^2 I$. Assume that the following conditions hold:

i) *Λ_{EE} and Λ_{EI} take the same values, that is, $\Lambda = \Lambda_{\mathrm{EE}} I_{2\times 2} = \Lambda_{\mathrm{EI}} I_{2\times 2}$.*

ii) *There exists* $(v_0, i_0) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ *such that*

$$\operatorname*{ess\,inf}_{x\in\Omega} \big\|(v_{\mathrm{e}}(x), i_{\mathrm{e}}(x)) - (v_0(x), i_0(x))\big\|_\infty > 0$$

and

$$P_v(v_0, i_0) = 0, \quad P_i(v_0, i_0) = P_i(v_{\mathrm{e}}, i_{\mathrm{e}}). \tag{7.2}$$

iii) $\partial_{(v,i)}P(v_{\mathrm{e}}, i_{\mathrm{e}})$ *and* $\partial_{(v,i)}P(v_0, i_0)$ *are nonsingular almost everywhere in* Ω.

iv) *There exists* $\alpha > 0$ *such that, for every* $b = (b_v, b_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$, *the system of equations*

$$\begin{aligned} \partial_{(v,i)}P_v(v_{\mathrm{e}}, i_{\mathrm{e}})\phi &= b_v, \\ \partial_{(v,i)}P_i(v_{\mathrm{e}}, i_{\mathrm{e}})\phi - J_6A^{-1}\Lambda^2\mathrm{M}J_8\partial_v f(v_{\mathrm{e}})\phi_v &= b_i, \end{aligned} \tag{7.3}$$

has a unique solution $\phi = (\phi_v, \phi_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ *that satisfies*

$$\|\phi\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} \le \alpha\|b\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty}. \tag{7.4}$$

Then, for a measurable partition $\Omega = \Omega_{\mathrm{e}} \cup \Omega_0$ *and*

$$\bar{v} := v_{\mathrm{e}}\chi_{\Omega_{\mathrm{e}}} + v_0\chi_{\Omega_0}, \quad \bar{i} := i_{\mathrm{e}}\chi_{\Omega_{\mathrm{e}}} + i_0\chi_{\Omega_0}, \tag{7.5}$$

the following assertions hold:

I) *For every* $\varepsilon > 0$ *there exists* $\delta > 0$ *and an equilibrium* $u^* := (v^*, i^*, 0, w^*, 0)$ *of* (3.3)–(3.5) *such that*

$$\big\|(v^*, i^*) - (\bar{v}, \bar{i})\big\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} \le \varepsilon, \quad \textit{whenever } |\Omega_0| \le \delta.$$

II) *The equilibrium sets of* (3.3)–(3.5) *are noncompact in* $\mathcal{U}_{\mathrm{s}}$ *and* $\mathcal{U}_{\mathrm{w}}$.

Proof. *First, we show that the system of equations*

$$\begin{aligned} \partial_{(v,i)}P_v(\bar{v}, \bar{i})\phi &= b_v, \\ \partial_{(v,i)}P_i(\bar{v}, \bar{i})\phi - J_6A^{-1}\Lambda^2\mathrm{M}J_8\partial_v f(\bar{v})\phi_v &= b_i, \end{aligned} \tag{7.6}$$

has a unique solution $\phi \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ *for every* $b = (b_v, b_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$.

Let $\phi^{(0)} = (\phi_v^{(0)}, \phi_i^{(0)})$ *be the solution of* (7.3) *for a given* $b \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ *and construct an approximate solution for* (7.6) *of the form* $\phi^{(1)} := \phi^{(0)} + \phi_{\mathrm{r}}^{(1)}$, *where* $\phi_{\mathrm{r}}^{(1)} = (\phi_{\mathrm{r}_v}^{(1)}, \phi_{\mathrm{r}_i}^{(1)})$ *is the unique solution of*

$$\partial_{(v,i)}P(v_0, i_0)\phi_{\mathrm{r}}^{(1)} = \big(\partial_{(v,i)}P(v_{\mathrm{e}}, i_{\mathrm{e}}) - \partial_{(v,i)}P(v_0, i_0)\big)\,\phi^{(0)}\chi_{\Omega_0}. \tag{7.7}$$

Note that by Assumption (iii) the unique solution $\phi_{\mathrm{r}}^{(1)}$ *exists and belongs to* $\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$. *The approximate solution* $\phi^{(1)}$ *solves*

$$\begin{aligned} \partial_{(v,i)}P_v(\bar{v}, \bar{i})\phi^{(1)} &= b_v, \\ \partial_{(v,i)}P_i(\bar{v}, \bar{i})\phi^{(1)} - J_6A^{-1}\Lambda^2\mathrm{M}J_8\partial_v f(\bar{v})\phi_v^{(1)} &= b_i + b_{\mathrm{r}_i}^{(1)}, \end{aligned}$$

where $b_{\mathrm{r}}^{(1)} = (0, b_{\mathrm{r}_i}^{(1)})$, *with*

$$b_{\mathrm{r}_i}^{(1)} := J_6 A^{-1}\Lambda^2 \mathrm{M} J_8 \left[\left(\partial_v f(v_{\mathrm{e}}) - \partial_v f(v_0)\right) \phi_v^{(0)} - \partial_v f(v_0)\phi_{\mathrm{r}_v}^{(1)} \right] \chi_{\Omega_0}, \tag{7.8}$$

is the remainder resulting from the approximation error in $\phi^{(1)}$.

Now, note that by Assumption (iv) there exist $\alpha_0 := \alpha > 0$ *such that*

$$\|\phi^{(0)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \le \alpha_0 \|b\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty}. \tag{7.9}$$

Moreover, since by Assumption (ii) we have $(v_0, i_0) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$, *it is immediate from the definition of* P_v *and* P_i, *given by* (7.1), *that* $\partial_{(v,i)} P(v_0, i_0)$ *is bounded. This, along with Assumption (iii) and* (7.9), *implies that the solution* $\phi_{\mathrm{r}}^{(1)}$ *of* (7.7) *satisfies*

$$\|\phi_{\mathrm{r}}^{(1)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \le \zeta_1 \|\phi^{(0)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \le \alpha_1 \|b\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \tag{7.10}$$

for some $\zeta_1, \alpha_1 > 0$.

Next, note that since $A^{-1} : \mathcal{L}_w^2 \to \mathcal{H}_w^2$ *is a bounded operator and* f *is smooth, the definition of* $b_{\mathrm{r}}^{(1)}$, *given by* (7.8), *implies that* $b_{\mathrm{r}}^{(1)} \in \mathcal{H}_w^2$. *Moreover, it further implies by the Sobolev embedding theorems that* $b_{\mathrm{r}}^{(1)} \in C_{\mathrm{per}}^{0,\lambda}(\overline{\Omega}, \mathbb{R}^2)$ *for all* $\lambda \in (0,1)$ *and, in particular, there exist* $\zeta_2, \ldots, \zeta_5, \beta_1 > 0$ *such that*

$$\begin{aligned}\|b_{\mathrm{r}}^{(1)}\|_{\mathcal{L}_w^\infty} &\le \zeta_2 \|b_{\mathrm{r}}^{(1)}\|_{\mathcal{H}_w^2} \le \zeta_3 \left(\|\phi_v^{(0)}\|_{\mathcal{L}_v^2} + \|\phi_{\mathrm{r}_v}^{(1)}\|_{\mathcal{L}_v^2} \right) \le \zeta_4 \|\phi^{(0)}\|_{\mathcal{L}_v^2 \times \mathcal{L}_i^2} \le \zeta_5 |\Omega_0|^{\frac{1}{2}} \|\phi^{(0)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \\ &\le \beta_1 |\Omega_0|^{\frac{1}{2}} \|b\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty}.\end{aligned}$$

Now, for $m = 2, 3, \ldots$, *let* $\phi^{(m)} := \phi^{(m-1)} + \phi_{\mathrm{r}}^{(m)}$, *where* $\phi_{\mathrm{r}}^{(m)}$ *is the unique solution of*

$$\partial_{(v,i)} P(v_0, i_0) \phi_{\mathrm{r}}^{(m)} = b_{\mathrm{r}}^{(m-1)} \chi_{\Omega_0}.$$

It follows immediately that, for some $\eta > 0$,

$$\|\phi_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \le \eta \|b_{\mathrm{r}}^{(m-1)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty}, \quad m = 2, 3, \ldots. \tag{7.11}$$

Moreover, $\phi_{\mathrm{r}}^{(m)}$ *solves the system of equations*

$$\begin{aligned}\partial_{(v,i)} P_v(\bar{v}, \bar{i}) \phi^{(m)} &= b_v, \\ \partial_{(v,i)} P_i(\bar{v}, \bar{i}) \phi^{(m)} - J_6 A^{-1}\Lambda^2 \mathrm{M} J_8 \partial_v f(\bar{v}) \phi_v^{(m)} &= b_i + b_{\mathrm{r}_i}^{(m)},\end{aligned}$$

where

$$b_{\mathrm{r}_i}^{(m)} := J_6 A^{-1}\Lambda^2 \mathrm{M} J_8 \partial_v f(v_0) \phi_{\mathrm{r}_v}^{(m)} \chi_{\Omega_0}, \quad m = 2, 3, \ldots.$$

The remainder $b_{\mathrm{r}}^{(m)} = (0, b_{\mathrm{r}_i}^{(m)})$ *satisfies, for some* $\zeta_6, \zeta_7, \zeta_8, \beta > 0$,

$$\begin{aligned}\|b_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_w^\infty} &\le \zeta_6 \|b_{\mathrm{r}}^{(m)}\|_{\mathcal{H}_w^2} \le \zeta_7 \|\phi_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_v^2 \times \mathcal{L}_i^2} \le \zeta_8 |\Omega_0|^{\frac{1}{2}} \|\phi_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty} \\ &\le \beta |\Omega_0|^{\frac{1}{2}} \|b_{\mathrm{r}}^{(m-1)}\|_{\mathcal{L}_v^\infty \times \mathcal{L}_i^\infty}, \quad m = 2, 3, \ldots,\end{aligned}$$

which, letting $\kappa := \beta|\Omega_0|^{\frac{1}{2}}$, implies

$$\|b_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_w^\infty} \le \beta_1|\Omega_0|^{\frac{1}{2}}\kappa^{(m-1)}\|b\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} \quad m = 2, 3, \ldots.$$

Now, let $|\Omega_0| < \bar{\delta}$, $\bar{\delta} > 0$, and choose $\bar{\delta}$ such that $\kappa < 1$. Note that β, and consequently, the choice of $\bar{\delta}$ and the value of κ do not depend on b and the specific form of the partition $\Omega = \Omega_{\mathrm{e}} \cup \Omega_0$. Therefore, it follows that $\|b_{\mathrm{r}}^{(m)}\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} \to 0$ as $m \to \infty$, and hence, $\phi^{(m)}$ converges to a solution ϕ for (7.6) *when $|\Omega_0| < \bar{\delta}$. Moreover,* (7.9), (7.10), *and* (7.11) *imply*

$$\begin{aligned}\|\phi^{(m)}\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} &\le \|\phi^{(0)}\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} + \|\phi_{\mathrm{r}}^{(1)}\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} + \sum_{l=2}^{m}\|\phi_{\mathrm{r}}^{(l)}\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty}\\ &\le \left[\alpha_0 + \alpha_1 + \eta\beta_1|\Omega_0|^{\frac{1}{2}}\sum_{l=2}^{m}\kappa^{(l-2)}\right]\|b\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty},\end{aligned}$$

and hence, taking the limit as $m \to \infty$, there exists $\bar{\alpha} > 0$ such that

$$\|\phi\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty} \le \bar{\alpha}\|b\|_{\mathcal{L}_v^\infty\times\mathcal{L}_i^\infty}. \tag{7.12}$$

To prove the solution constructed above for (7.6) *is unique, first note that by Assumption (i) the operator A becomes a scalar operator given by $A = (-\frac{3}{2}\Delta + \Lambda_{\mathrm{EE}}^2 I)$. Then, considering the structure of the matrix parameters given by* (3.7) *and reinspecting the expanded form* (3.1), *the system of equations* (7.6) *can be transformed to a system composed of five algebraic equations and one partial differential equation by pre-multiplying the second equation in* (7.6) *by the elementary matrix*

$$\left[\begin{array}{cc|c} 1 & 0 & \\ -\frac{M_{\mathrm{EI}}}{M_{\mathrm{EE}}} & 1 & 0_{2\times 2} \\ \hline \multicolumn{2}{c|}{0_{2\times 2}} & I_{2\times 2}\end{array}\right].$$

This follows from the fact that the scalar operator $(-\frac{3}{2}\Delta + \Lambda_{\mathrm{EE}}^2 I)^{-1}$ acts only on one of the unknowns, namely, $\phi_{v_{\mathrm{E}}}$. Now, since $\partial_{(v,i)}P(\bar{v},\bar{i})$ is nonsingular by Assumption (iii), ϕ_i and $\phi_{v_{\mathrm{I}}}$ can be uniquely determined with respect to $\phi_{v_{\mathrm{E}}}$ by elementary algebraic operations. Consequently, (7.6) *is reduced to a scalar partial differential equation of the form*

$$p(\bar{v},\bar{i})\phi_{v_{\mathrm{E}}} - (-\tfrac{3}{2}\Delta + \Lambda_{\mathrm{EE}}^2 I)^{-1}\Lambda_{\mathrm{EE}}^2 \mathrm{M}_{\mathrm{EE}}\partial_{v_{\mathrm{E}}} f(\bar{v}_{\mathrm{E}})\phi_{v_{\mathrm{E}}} = \hat{h},$$

where $\hat{h} \in L_{\mathrm{per}}^\infty(\Omega, \mathbb{R})$ is given by the same elementary operations on b and $p(\bar{v},\bar{i})$ is nonzero almost everywhere in Ω, since elementary operations do not disrupt the nonsingularity of $\partial_{(v,i)}P(\bar{v},\bar{i})$.

Next, dividing by $p(\bar{v},\bar{i})$, the above equation can be written as

$$(I - K)\phi_{v_{\mathrm{E}}} = h, \tag{7.13}$$

where $K := p(\bar{v},\bar{i})^{-1}\Lambda_{\mathrm{EE}}^2\mathrm{M}_{\mathrm{EE}}\partial_{v_{\mathrm{E}}} f(\bar{v}_{\mathrm{E}})(-\frac{3}{2}\Delta + \Lambda_{\mathrm{EE}}^2 I)^{-1}$ and $h := p(\bar{v},\bar{i})^{-1}\hat{h}$. The operator $K : L_{\mathrm{per}}^2(\Omega, \mathbb{R}) \to L_{\mathrm{per}}^2(\Omega, \mathbb{R})$ is linear, self-adjoint, and compact by the Rellich-Kondrachov compact embedding theorems [8, Th. 6.6-3]. The existence of solutions of (7.6) *proved above guaranteers the existence of a solution $\phi_{v_{\mathrm{E}}} \in L_{\mathrm{per}}^\infty(\Omega, \mathbb{R})$ for every $h \in L_{\mathrm{per}}^\infty(\Omega, \mathbb{R})$, which implies, $L_{\mathrm{per}}^\infty(\Omega, \mathbb{R}) \subset$ $\mathrm{Range}(I - K)$. However, $\mathrm{Range}(I - K) = \mathrm{Kernel}(I - K^*)^\perp = \mathrm{Kernel}(I - K)^\perp$ by Fredholm* *alternative [15, Th. 5, Appx. D], and hence,* $L^\infty_{\text{per}}(\Omega,\mathbb{R}) \cap \text{Kernel}(I-K) = \{0\}$. *This proves the uniqueness of bounded solutions of* (7.13)*, and consequently, the uniqueness of solutions of* (7.6) *for every* $b = (b_v, b_i) \in \mathcal{L}^\infty_v \times \mathcal{L}^\infty_i$.

Now, to prove Assertion (I) note that since $u_\text{e} := (v_\text{e}, i_\text{e}, 0, w_\text{e}, 0)$ *is an equilibrium of* (3.3)–(3.5)*, we have*

$$P_v(v_\text{e}, i_\text{e}) = 0, \quad P_i(v_\text{e}, i_\text{e}) = J_6 w_\text{e}, \quad w_\text{e} = A^{-1}\Lambda^2 \mathrm{M} J_8 f(v_\text{e}). \tag{7.14}$$

We seek an equilibrium point $u^* := (v^*, i^*, 0, w^*, 0)$ *such that*

$$v^* = \bar{v} + \phi_v, \quad i^* = \bar{i} + \phi_i,$$

where $\phi := (\phi_v, \phi_i) \in \mathcal{L}^\infty_v \times \mathcal{L}^\infty_i$ *is a small corrector function that satisfies*

$$P_v(v^*, i^*) = 0, \quad P_i(v^*, i^*) = J_6 w^*, \quad w^* = A^{-1}\Lambda^2 \mathrm{M} J_8 f(v^*). \tag{7.15}$$

Note that (7.2)*,* (7.5)*, and* (7.14) *imply*

$$P_v(\bar{v}, \bar{i}) = 0, \quad P_i(\bar{v}, \bar{i}) = J_6 w_\text{e}, \quad v_\text{e} = \bar{v} - (v_0 - v_\text{e})\chi_{\Omega_0}.$$

Therefore, it follows from (7.14) *and* (7.15) *that*

$$\begin{aligned} &P_v(\bar{v} + \phi_v, \bar{i} + \phi_i) - P_v(\bar{v}, \bar{i}) = 0, \\ &P_i(\bar{v} + \phi_v, \bar{i} + \phi_i) - P_i(\bar{v}, \bar{i}) = J_6 A^{-1}\Lambda^2 \mathrm{M} J_8 \big(f(\bar{v} + \phi_v) - f(\bar{v} - (v_0 - v_\text{e})\chi_{\Omega_0})\big), \end{aligned} \tag{7.16}$$

which, by the implicit function theorem [8, Th. 7.13-1], has a unique solution $\phi \in \mathcal{L}^\infty_v \times \mathcal{L}^\infty_i$ *since* (7.6) *has a unique solution in* $\mathcal{L}^\infty_v \times \mathcal{L}^\infty_i$ *for every* $b \in \mathcal{L}^\infty_v \times \mathcal{L}^\infty_i$*, as proved above. Moreover, it is immediate from the definition of the Fréchet derivative of the mappings* P_i *and* P_v *that the solution of* (7.16) *is arbitrarily close to the solution of* (7.6) *with*

$$b := (0, J_6 A^{-1}\Lambda^2 \mathrm{M} J_8 \partial_v f(\bar{v})(v_0 - v_\text{e}))\chi_{\Omega_0},$$

provided it is sufficiently small, which is ensured for small $|\Omega_0|$ *since* $\|b\|_{\mathcal{L}^\infty_v \times \mathcal{L}^\infty_i} \le \beta |\Omega_0|^{\frac{1}{2}}$ *for some* $\beta > 0$*. Therefore,* (7.12) *implies that Assertion (I) holds for some* $\delta = \delta(\varepsilon) \le \bar{\delta}$.

Finally, to prove Assertion (II), let

$$\varepsilon := \tfrac{1}{3} \operatorname*{ess\,inf}_{x \in \Omega} \big\|(v_\text{e}(x), i_\text{e}(x)) - (v_0(x), i_0(x))\big\|_\infty > 0 \tag{7.17}$$

in Assertion (I) and let $\delta = \delta(\varepsilon) > 0$ *be the corresponding bound on the size of the partitions that satisfies the result of Assertion (I). Note that* ε *exists by Assumption (ii). Moreover, let* $\mathscr{M}(\Omega)$ *denote the set of all measurable subsets of* Ω *and define*

$$\mathscr{P}_\delta(\Omega) := \{(\Omega_\text{e}, \Omega_0) \in \mathscr{M}(\Omega) \times \mathscr{M}(\Omega) : \Omega_\text{e} = \Omega \setminus \Omega_0, |\Omega_0| \le \delta\}.$$

Let $\Theta_\delta(\Omega) \subset \mathscr{P}_\delta(\Omega)$ *such that for every* $\tilde{\theta} = (\tilde{\Omega}_\text{e}, \tilde{\Omega}_0) \in \Theta_\delta(\Omega)$ *and* $\hat{\theta} = (\hat{\Omega}_\text{e}, \hat{\Omega}_0) \in \Theta_\delta(\Omega)$ *we have* $|\tilde{\Omega}_0 \triangle \hat{\Omega}_0| > \frac{1}{2}\delta$*. Note that* $\Theta_\delta(\Omega)$ *is an uncountable set that can be viewed as an index set enumerating all measurable partitions* $\Omega = \Omega_\text{e} \cup \Omega_0$*,* $|\Omega_0| \le \delta$*, which are distinct in the sense of measure by a factor of at least* $\frac{1}{2}\delta$.

Now, it follows from Assertion (I) that, for every $\tilde{\theta} \neq \hat{\theta} \in \Theta_\delta(\Omega)$*, there exist equilibria* $u_{\tilde{\theta}} := (v_{\tilde{\theta}}, i_{\tilde{\theta}}, 0, w_{\tilde{\theta}}, 0)$ *and* $u_{\hat{\theta}} := (v_{\hat{\theta}}, i_{\hat{\theta}}, 0, w_{\hat{\theta}}, 0)$ *such that*

$$\operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_{\rm e}\cap\hat{\Omega}_0)} \big\|(v_{\hat{\theta}}(x), i_{\hat{\theta}}(x)) - (v_0(x), i_0(x))\big\|_\infty \leq \varepsilon,$$
$$\operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_0\cap\hat{\Omega}_{\rm e})} \big\|(v_{\hat{\theta}}(x), i_{\hat{\theta}}(x)) - (v_{\rm e}(x), i_{\rm e}(x))\big\|_\infty \leq \varepsilon,$$
$$\operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_{\rm e}\cap\hat{\Omega}_0)} \big\|(v_{\tilde{\theta}}(x), i_{\tilde{\theta}}(x)) - (v_{\rm e}(x), i_{\rm e})\big\|_\infty \leq \varepsilon,$$
$$\operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_0\cap\hat{\Omega}_{\rm e})} \big\|(v_{\tilde{\theta}}(x), i_{\tilde{\theta}}(x)) - (v_0(x), i_0)\big\|_\infty \leq \varepsilon.$$

Therefore, noting that $\tilde{\Omega}_0 \triangle \hat{\Omega}_0 = (\tilde{\Omega}_0 \cap \hat{\Omega}_{\rm e}) \cup (\tilde{\Omega}_{\rm e} \cap \hat{\Omega}_0)$ *and recalling the definition of* ε *given by* (7.17)*,*

$$\operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_0\triangle\hat{\Omega}_0)} \big\|(v_{\tilde{\theta}}, i_{\tilde{\theta}}) - (v_{\hat{\theta}}, i_{\hat{\theta}})\big\|_\infty \geq \varepsilon,$$

which further implies

$$\big\|(v_{\tilde{\theta}}, i_{\tilde{\theta}}) - (v_{\hat{\theta}}, i_{\hat{\theta}})\big\|_{\mathcal{L}^2_v\times\mathcal{L}^2_i} \geq |\tilde{\Omega}_0 \triangle \hat{\Omega}_0|^{\frac{1}{2}} \operatorname*{ess\,sup}_{x\in(\tilde{\Omega}_0\triangle\hat{\Omega}_0)} \big\|(v_{\tilde{\theta}}, i_{\tilde{\theta}}) - (v_{\hat{\theta}}, i_{\hat{\theta}})\big\|_\infty > (\tfrac{1}{2}\delta)^{\frac{1}{2}}\varepsilon.$$

Since $\tilde{\theta}$ *and* $\hat{\theta}$ *are arbitrary, it follows that the set* $\mathcal{E} := \big\{u_\theta\big\}_{\theta\in\Theta_\delta(\Omega)}$ *composed of the equilibria* u_θ *constructed as above is an uncountable discrete subset of the equilibrium sets of* (3.3)–(3.5) *in* $\mathcal{U}_{\rm s}$ *and* $\mathcal{U}_{\rm w}$*. This completes the proof.*

Remark 7.6 (Alternative assumptions for Theorem 7.5) *According to the proof of Theorem 7.5, some of the assumptions of this theorem can be relaxed or replaced by alternative assumptions as follows:*

- *Assumption (i) is used to prove the uniqueness of solutions of* (7.6)*. Without this assumption, the operator* A *is not a scalar operator and* (7.6) *cannot be reduced to a scalar partial differential equation using elementary algebraic operations. The system of PDE's arising in this case would not be self-adjoint, and hence, application of the Fredholm alternative would not immediately imply uniqueness of solutions. However, an alternative assumption to Assumption (i) can be made on the adjoint of the operator representing the system of PDE's such that it still ensures uniqueness of solutions of* (7.6) *deduced from the Fredholm alternative. We avoid this unnecessary complication since the fiber decay scale constants* $\Lambda_{\rm EE}$ *and* $\Lambda_{\rm EI}$ *are always assumed to be equal in the practical applications of the model [5].*
- *In Assumption (ii), it is sufficient to have* $\operatorname{ess\,inf}_{x\in\mathscr{X}} \big\|(v_{\rm e}, i_{\rm e}) - (v_0, i_0)\big\|_\infty > 0$*, where* $\mathscr{X}$ *is any measurable subset of* Ω *with positive measure. Correspondingly, it suffices that the nonsingularity in Assumption (iii) holds almost everywhere on an open subset* $\mathscr{Y} \supset \mathscr{X}$ *of* Ω*. In this case, the proof is modified by restricting* $\mathscr{P}_\delta(\Omega)$ *to its subset consisting of partitions with* $\Omega_0 \subset \mathscr{X}$*. The index set* $\Theta_\delta(\Omega)$ *remains uncountable, and the noncompactness result of the theorem holds with no change.*

Table 2: A set of biophysically plausible parameter values for the model (3.1) for which Theorem 7.5 implies nonexistence of a global attractor [5, Table VI, Col. 2]. The parameters $\bar{g}_{\mathrm{EE}}$, $\bar{g}_{\mathrm{EI}}$, $\bar{g}_{\mathrm{EI}}$, and $\bar{g}_{\mathrm{II}}$ are, respectively, the mean values of the physiologically shaped random inputs g_{EE}, g_{EI}, g_{EI}, and g_{II} used in [5].

Parameter	τ_{E}	τ_{I}	V_{EE}	V_{EI}	V_{IE}	V_{II}	γ_{EE}	γ_{EI}
Value	11.787×10^{-3}	138.25×10^{-3}	61.264	51.703	-7.127	-12.679	816.04	261.29
Parameter	γ_{IE}	γ_{II}	Υ_{EE}	Υ_{EI}	Υ_{IE}	Υ_{II}	N_{EE}	N_{EI}
Value	219.09	40.575	0.92695	1.3012	0.19053	0.94921	3893.0	3326.8
Parameter	N_{IE}	N_{II}	ν	$\Lambda_{\mathrm{EE}}, \Lambda_{\mathrm{EI}}$	M_{EE}	M_{EI}	F_{E}	F_{I}
Value	839.39	682.41	101.78	0.96545	4013.5	1544.3	266.44	300.65
Parameter	μ_{E}	μ_{I}	σ_{E}	σ_{I}	$\bar{g}_{\mathrm{EE}}$	$\bar{g}_{\mathrm{EI}}$	$\bar{g}_{\mathrm{IE}}$	$\bar{g}_{\mathrm{II}}$
Value	30.628	19.383	5.6536	3.3140	83.190	6407.5	0	0

Remark 7.7 (Nonexistence of a Global Attractor) *Suppose that the assumptions of Theorem 7.5 hold for an input g and an equilibrium u_{e} that further satisfy $i_{\mathrm{e}}, w_{\mathrm{e}} > 0$ almost everywhere in Ω and $g \in \mathcal{D}_g$, where $\mathcal{D}_g$ is given by (5.21). Note that u_{e} then belongs to $\mathcal{D}_{\mathrm{s}}$. Then, the equation $P_i(v_{\mathrm{e}}, i_{\mathrm{e}}) = J_6 w_{\mathrm{e}}$ in the equilibrium equations (7.14) implies that $P_i(v_{\mathrm{e}}, i_{\mathrm{e}}) \geq 0$, and hence, $P_i(v_0, i_0) \geq 0$ in (7.2). Therefore, it follows from the definition of P_i given by (7.1) that every solution i_0 of (7.2) is positive almost everywhere in Ω. Then, by definition of $(\bar{v}, \bar{i})$, given by (7.5), all equilibria u^* constructed by Assertion (I) of Theorem 7.5 satisfy $i^* > 0$ almost everywhere in Ω when δ is sufficiently small. Also, the equilibrium equations $w_{\mathrm{e}} = A^{-1}\Lambda^2 \mathrm{M} J_8 f(v_{\mathrm{e}})$ and $w^* = A^{-1}\Lambda^2 \mathrm{M} J_8 f(v^*)$ imply that*

$$\left\|w^* - w_{\mathrm{e}}\right\|_{\mathcal{L}^\infty_w} \leq \beta_1 \left\|w^* - w_{\mathrm{e}}\right\|_{\mathcal{H}^2_w} \leq \beta \left\|v^* - v_{\mathrm{e}}\right\|_{\mathcal{L}^\infty_v}$$

for some $\beta > 0$, and hence, $w^* > 0$ almost everywhere in Ω, when δ is sufficiently small. Therefore, Assertion (II) of Theorem 7.5 ensures existence of a biophysically plausible noncompact set of equilibria $\mathcal{E} \subset \mathcal{D}_{\mathrm{s}} \subset \mathcal{D}_{\mathrm{w}}$. This, in particular, implies that in the case where the assumptions of Theorem 7.5 are satisfied for some u_{e} and g as given above, the semigroups $\left\{S_{\mathrm{w}}(t) : \mathcal{D}_{\mathrm{w}} \to \mathcal{D}_{\mathrm{w}}\right\}_{t\in[0,\infty)}$ and $\left\{S_{\mathrm{s}}(t) : \mathcal{D}_{\mathrm{s}} \to \mathcal{D}_{\mathrm{s}}\right\}_{t\in[0,\infty)}$ are not asymptotically compact, and hence, they do not posses a global attractor.

The assumptions of Theorem 7.5 are relatively straightforward to check for the space-homogeneous equilibria of (3.3)–(3.5). Consider the set of values given in Table 2 for the parameters of the model, which are suggested in [5, Table VI, col. 2] as a set of parameter values leading to physiologically reasonable behavior in the model. The parameters $\bar{g}_{\mathrm{EE}}$, $\bar{g}_{\mathrm{EI}}$, $\bar{g}_{\mathrm{EI}}$, and $\bar{g}_{\mathrm{II}}$ are the mean values of the physiologically shaped random signals used in [5] as the subcortical inputs g_{EE}, g_{EI}, g_{EI}, and g_{II}, respectively. Here, we set $g(t,x) = (\bar{g}_{\mathrm{EE}}, \bar{g}_{\mathrm{EI}}, \bar{g}_{\mathrm{EI}}, \bar{g}_{\mathrm{II}})$ for all x and t, and check the assumptions of Theorem 7.5 for a space-homogeneous equilibrium of (3.3)–(3.5).

Assumption (i) holds with $\Lambda_{\mathrm{EE}} = \Lambda_{\mathrm{EE}} = 0.96545$, as given in Table 2. Solving the equations $P_v(v_{\mathrm{e}}, i_{\mathrm{e}}) = 0$, $P_i(v_{\mathrm{e}}, i_{\mathrm{e}}) = J_6 w_{\mathrm{e}}$ and $w_{\mathrm{e}} = \mathrm{M} J_8 f(v_{\mathrm{e}})$, a space-homogeneous equilibrium is calculated as

$$v_{\mathrm{e}} = (1.9629, 6.5150), \quad i_{\mathrm{e}} = (5.2552, 100.2372, 2.4493, 53.5665), \quad w_{\mathrm{e}} = (821.7136, 316.1760).$$

Note that the numbers given here should actually be regarded as constant functions over Ω. Assumption (ii) then holds by finding a solution $(v_0, i_0) \neq (v_e, i_e)$ for (7.2) as

$$v_0 = (10.9417, 7.7148), \quad i_0 = (25.9005, 177.5837, 4.0757, 89.1352).$$

Assumption (iii) also holds with the following nonsingular matrix-valued functions

$$\partial_{(v,i)} P(v_e, i_e) = \left[\begin{array}{cc|cccc} 1.4294 & 0 & -0.9680 & 0 & 1.2754 & 0 \\ 0 & 7.1635 & 0 & -0.8740 & 0 & 1.5138 \\ \hline -199.2222 & 0 & 323.8625 & 0 & 0 & 0 \\ -170.2472 & 0 & 0 & 73.8727 & 0 & 0 \\ 0 & -440.3409 & 0 & 0 & 423.0237 & 0 \\ 0 & -357.9898 & 0 & 0 & 0 & 15.7254 \end{array}\right],$$

$$\partial_{(v,i)} P(v_0, i_0) = \left[\begin{array}{cc|cccc} 1.9946 & 0 & -0.8214 & 0 & 2.5352 & 0 \\ 0 & 11.4648 & 0 & -0.8508 & 0 & 1.6085 \\ \hline -1858.395 & 0 & 323.8625 & 0 & 0 & 0 \\ -1588.109 & 0 & 0 & 73.8727 & 0 & 0 \\ 0 & -730.7260 & 0 & 0 & 423.0237 & 0 \\ 0 & -594.0680 & 0 & 0 & 0 & 15.7254 \end{array}\right].$$

To check Assumption (iv), note that for every $b = (b_v, b_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$, elementary algebraic operations reduce (7.3) to

$$\begin{aligned} &\phi_{v_E} = 0.6287\phi i_{EE} + h_{v_E}, \quad \phi_{v_I} = 0.0521\phi i_{EE} + h_{v_I}, \\ &\phi_{i_{EI}} = 2.4834\phi i_{EE} + h_{i_{EI}}, \quad \phi_{i_{IE}} = 0.0543\phi i_{EE} + h_{i_{IE}}, \quad \phi_{i_{II}} = 1.1870\phi i_{EE} + h_{i_{II}}, \end{aligned} \tag{7.18}$$

and the scalar partial differential equation

$$(I - D)\phi_{i_{EE}} = h_{i_{EE}}, \quad D := 0.6060(-\tfrac{3}{2}\Delta + 0.96545^2 I)^{-1}, \tag{7.19}$$

where $h = (h_v, h_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ is the result of the same algebraic operations on b. Now, note that since $-\Delta$ is a nonnegative operator in $H^2_{\text{per}}(\Omega;\mathbb{R})$, it follows from the spectral theory of bounded linear self-adjoint operators [15, Appx. D.6] that the spectrum of the operator $(I-D) : L^2_{\text{per}}(\Omega;\mathbb{R}) \to L^2_{\text{per}}(\Omega;\mathbb{R})$ lies entirely above $1 - 0.6060 \times 0.96545^{-2} = 0.3498 > 0$. Therefore, the partial differential equation (7.19) has a unique solution $\phi_{i_{EE}} \in L^2_{\text{per}}(\Omega;\mathbb{R})$ for every $h_{i_{EE}} \in L^2_{\text{per}}(\Omega;\mathbb{R}) \supset L^\infty_{\text{per}}(\Omega;\mathbb{R})$, and hence, it follows from (7.18) that (7.3) has a unique solution $\phi = (\phi_v, \phi_i) \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$ for every $b \in \mathcal{L}_v^\infty \times \mathcal{L}_i^\infty$.

It remains to check (7.4). Using the spectral theory of bounded linear self-adjoint operators and Cauchy-Schwarz inequality we can write

$$\begin{aligned} \|\phi_{i_{EE}}\|^2_{L^2_{\text{per}}(\Omega;\mathbb{R})} &\leq \tfrac{1}{0.3498}\big((I-D)\phi_{i_{EE}}, \phi_{i_{EE}}\big)_{L^2_{\text{per}}(\Omega;\mathbb{R})} = \tfrac{1}{0.3498}\big(h_{i_{EE}}, \phi_{i_{EE}}\big)_{L^2_{\text{per}}(\Omega;\mathbb{R})} \\ &\leq \tfrac{1}{0.3498}\|h_{i_{EE}}\|_{L^2_{\text{per}}(\Omega;\mathbb{R})}\|\phi_{i_{EE}}\|_{L^2_{\text{per}}(\Omega;\mathbb{R})}. \end{aligned}$$

Therefore, there exists $\alpha_1 = \frac{1}{0.3498} > 0$ such that

$$\|\phi_{i_{EE}}\|_{L^2_{\text{per}}(\Omega;\mathbb{R})} \leq \alpha_1 \|h_{i_{EE}}\|_{L^2_{\text{per}}(\Omega;\mathbb{R})}.$$

Now, using (7.19) and the Sobolev embedding theorems we can write, for some $\alpha_2, \alpha_3 > 0$,

$$\begin{aligned}\|\phi_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} &\leq \|h_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} + \|D\phi_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} \leq \|h_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} + \alpha_2\|D\phi_{i_{\mathrm{EE}}}\|_{H^2_{\mathrm{per}}(\Omega;\mathbb{R})} \\ &\leq \|h_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} + \alpha_3\|\phi_{i_{\mathrm{EE}}}\|_{L^2_{\mathrm{per}}(\Omega;\mathbb{R})} \leq \|h_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})} + \alpha_1\alpha_3\|h_{i_{\mathrm{EE}}}\|_{L^2_{\mathrm{per}}(\Omega;\mathbb{R})} \\ &\leq (1+\alpha_1\alpha_3|\Omega|^{\frac{1}{2}})\|h_{i_{\mathrm{EE}}}\|_{L^\infty_{\mathrm{per}}(\Omega;\mathbb{R})},\end{aligned}$$

which, along with the algebraic equalities (7.18), implies (7.4). Hence, Assumption (iv) holds.

It is now implied by Theorem 7.5 that the equilibrium sets of (3.3)–(3.5) are noncompact in $\mathcal{U}_{\mathrm{s}}$ and $\mathcal{U}_{\mathrm{w}}$. Moreover, it follows immediately from the equilibrium equations (7.14) and the definition of P_i given by (7.1) that, in general, all space-homogeneous equilibria i_{e} and w_{e} are positive and, in particular, belong to $\mathcal{D}_{\mathrm{Bio}} \cap \mathcal{D}_{\mathrm{s}}$. Therefore, by Remark 7.7, the semigroups $\{S_{\mathrm{s}}(t) : \mathcal{D}_{\mathrm{s}} \to \mathcal{D}_{\mathrm{s}}\}_{t\in[0,\infty)}$ associated with the model with parameter values given by Table 2 do not possess a global attractor.

It can be shown by similar calculations as above that the assumptions of Theorem 7.5 are satisfied by space-homogeneous equilibria of the model for 3 other sets of parameter values out the 24 sets available in [5, Tables V and VI], namely, the sets given in [5, Tables V, col. 2] and [5, Tables VI, col. 10 and col. 12]. Moreover, it is likely that these assumptions or their possible alternatives suggested in Remark 7.6 would also hold for other sets of parameter values if we consider equilibria u_{e} and inputs g that are not homogeneous over Ω. Checking the assumptions of Theorem 7.5 in this case is, however, not very straightforward.

8. Discussion and Conclusion

In this paper, we developed basic analytical results to establish a global attractor theory for the mean field model of the electroencephalogram proposed by Liley *et al.*, 2002. We showed the boundary-initial value problem associated with the model is well-posed in the weak and strong sense, and established sufficient conditions for the nonnegativity of the $i(x,t)$ and $w(x,t)$ components of the solution over the entire time horizon. Moreover, we proved existence of bounded absorbing sets for semigroups of weak and strong solutions, and discussed challenges towards proving the asymptotic compactness property for these semigroups. Finally, we showed that the equilibrium sets of the model are noncompact for some physiologically reasonable sets of parameter values which, in particular, implies nonexistence of a global attractor.

The conditions developed in this paper for ensuring nonnegativity of the solution components $i(x,t)$ and $w(x,t)$ over the entire infinite time horizon can be useful in computational analysis of the model. Without using such mathematical analysis, it is impossible to ensure that the solutions computed numerically over a finite time horizon are biophysically plausible since, evidently, non-negativity might occur for time intervals beyond the finite time horizon of numerical computations. This fact has been overlooked in most of the available computational analysis of the model. However, in these computational studies, the initial values are usually set equal to the numerically computed space-homogenous equilibrium of the model, or equal to zero in the case where no equilibrium is found numerically. In both cases, the preset initial values satisfy the sufficient conditions developed in Section 5 of this paper for biophysical plausibility of the solutions. It is perhaps an intractable problem to specify a set of biophysical initial values for a model of the EEG; however, analyzing a more diverse set of reasonable initial values satisfying the sufficient conditions developed in Section 5 can be beneficial in observing different behaviors of the model.

Existence of bounded absorbing sets is a desirable global property for a model of electrical activity in the neocortex. As stated in Remark 6.4, the EEG model investigated in this paper possesses this global property for its entire range of parameter values given in Table 1. Moreover, this property holds independently of the parameters of the firing rate functions, number of intracortical and corticocortical connections, mean Nernst potentials, and membrane time constants, as observed in Assumptions (i) and (ii) of Theorems 6.2 and 6.3.

The lack of space dissipation terms in the ODE components (3.3) and (3.4) of the model is a major source of difficulty towards establishing a global attractor. Indeed, as implied by the proof of Theorem 7.5, the $v(x,t)$ and $i(x,t)$ components of the solution can evolve discontinuously in space despite continuous evolution of the $w(x,t)$ component. Other than disrupting the asymptotic compactness property of the semigroups of solution operators, these space irregularities can predict sharp transitions in the $v(x,t)$ and $i(x,t)$ components of the solution, which can potentially be problematic in numerical computation of the model. A slight modification to the model wherein the underlying neurophysiological structure of the model is maintained can be beneficial. Considering a singularly perturbed version of (3.3) and (3.4) by including additional diffusion terms $\varepsilon\Delta$ with sufficiently small ε can be considered as a potential modification.

Acknowledgment

The authors would like to thank Professor Andrzej Święch from the School of Mathematics at Georgia Institute of Technology for his helpful suggestions with some of the proofs appearing in this paper.

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