Structural stability for the Morris-Lecar neuron model *

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Abstract

This paper is concerned with the biological neuron model of Morris-Lecar system of equations [17]. We prove the existence and uniqueness of strong solutions. In addition, we prove the continuous dependence of solutions to the leak conductance parameter.

1 Introduction

In this paper we are concerned with the following nonlinear system of Morris-Lecar equations

$$\frac{dv}{dt} = \Delta v - f(v,n), \qquad \text{in } \Omega \times (0,\infty), \tag{1.1}$$

$$\frac{dn}{dt} = \phi \frac{n_\infty(v) - n}{\tau_\infty(v)}, \qquad \text{in } \Omega \times (0,\infty), \tag{1.2}$$

$$v(x,0) = v_0(x),\ n(x,0) = n_0(x), \qquad \text{in } \Omega, \tag{1.3}$$

$$v(x,t) = 0,\ n(x,t) = 0, \qquad \text{in } \partial\Omega \times (0,\infty), \tag{1.4}$$

where v_0 and n_0 are given functions and $\Omega \subset \mathbb{R}^n$, $n \leq 3$, is a bounded domain with sufficiently smooth boundary $\partial\Omega$. Here, $v(x,t)$ and $n(x,t)$ denote the membrane potential and fraction of open potassium channels at the position x at time t, respectively. The function $f(v,n)$ is given by

$$f(v,n) = g_L(v - E_L) - g_K n(v - E_K) - g_{Ca} m_\infty(v)(v - E_{Ca}) + I, \tag{1.5}$$

where g_L, g_{Ca} and g_K are maximal leak, Ca^{++} and K^+ conductances with values $g_L = 2\mu S$, $g_{Ca} = 4\mu S$ and $g_K = 8\mu S$, respectively. The reversal potential values for leak, Ca^{++} and K^+ currents are given as $E_L = -60mV$, $E_{Ca} = 120mV$ and $E_K = -84mV$, respectively [8]. Without loss of generality, we assume that the parameter $\phi = 1$, where ϕ is the kinetic constant of

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the potassium gating variable n. I is the applied current. Potential dependent functions modulating instant activation of Ca^{++} and K^{+} are given as

$$\begin{aligned} m_{\infty}(v) &= \frac{1}{2}\left[1+\tanh((v+1.2)/18)\right], \\ n_{\infty}(v) &= \frac{1}{2}\left[1+\tanh((v-12)/17.4)\right], \\ \tau_{\infty}(v) &= 1/\cosh\left((v-12)/(17.4)\right). \end{aligned}$$

The paper [8] can be refereed to for further information regarding the parameters and the entire model derivation and background.

Morris-Lecar(ML) equations describe transmission of electrical pulses through neuron axon in a reduced manner; that is, it can be considered as a simplified version of the more general model of Hodgkin-Huxley, [13]. It still exhibits many important features of the full model. The parameters that are used in the model presented here display saddle-node bifurcation with respect to the parameter I in the absence of the diffusion term Δv. However, results obtained in this work hold for other parameter sets that display other bifurcation types (Hopf and homoclinic) as well.

There has been much interest lately in the study of the question of continuous dependence of initial boundary value problems to various model parameters. Such kind of dependency is usually described as structural stability problem (see e.g. [1], [2], [3], [4] and [25]). In [1] and [4] authors considered continuous dependency of solutions to the diffusion coefficient of FithzHugh Nagumo (FHN) model (see [8] and [10]).

In the mathematical analysis of neurons, the so called FHN model has been widely used (see e.g., [7], [15], [16] and [18]). This model is obtained via mathematical abstraction of the biologically realistic ML model. FHN model, does not include any of the biological parameters except diffusion constant and applied current and, it has linearity in the second variable. These facts together make the FHN model available for mathematical analysis. In this regard, many papers have been published regarding the mathematical analysis of the FHN model. Importantly, many of the single cell dependency studies on the FHN model deal with the bifurcation behavior (e.g., [11] and [14]), dependence on the diffusion constant (e.g., [1] and [20]) and reaction to noisy input (e.g., [19], [26] and [28]).

On the other hand, the Morris Lecar model which has biological parameters and higher non-linearity has its own advantages. First, obtained results can easily be evaluated in terms of the biological parameters in the model. Second, many of the functions and variables obey biologically set bounds. Most important of these are gating variables and functions, namely, n, m_{∞}, n_{∞} and τ_{∞} (see Figure 1). The functions $m_{\infty}(v)$ and $n_{\infty}(v)$ denote the fraction of open sodium and potassium channels, respectively, when cell potential is fixed at v. In this case, their value remains between 0 and 1 (See Figure 1). The rate function, $\tau_\infty(v)$, that controls the speed of potassium influx to the cell has a strict lower bound (see Figure 1). Moreover, the fact that n remains between 0 and 1 can easily be justified using the mentioned bounds and simple ODE arguments. Figure 1 shows the behavior of these gating functions with respect to the cell potential v.

In this work, we take advantage of the both of the above facts regarding this biologically realistic model. First, by using the mathematical bounds of the ML model mentioned above, we establish existence and uniqueness of the strong solutions. Second, we conclude the continuous dependence of solutions to passive leak conductance parameters. This type of dependency analysis on model parameters is usually referred to as structural stability [27].

Similar equations have been studied numerically recently in the literature. We mention a few of them here. In [6], two pseudospectral methods based on Fourier series and rational Chebyshev functions for solving the Nagumo equation are presented. In [12], the HPM, VIM and ADM are applied to solve Rosenau-Hyman equation arising in the pattern formation in liquid drops. In [5], a meshless technique based on the local radial basis functions collocation method is introduced for solving parabolic-parabolic Patlak-KellerSegel chemotaxis model. In [22], a system of two nonlinear integro-differential equations which arises in biology is considered and the well-known VIM is implemented. In [23], the finite volume spectral element method is introduced to solve Turing models which arise in the biological pattern formation.

We now introduce the notations and inequalities used throughout the text together with the definition of the strong solution. $L^p(\Omega)$ denotes the Lebesgue space of functions f satisfying $\int_\Omega |f|^p \, dx < \infty$, $H^m(\Omega)$ denotes the usual Sobolev space of distributions with derivatives of order lower than m are in $L^2(\Omega)$. The space H_0^m denotes the closure of C_0^∞ in $H^m(\Omega)$. Throughout the paper $||\cdot||$ stands for the usual $L^2(\Omega)$ norm. Young's and Sobolev inequalities are given as:

Young's Inequality:

$$ab \leq \frac{a^2}{2\epsilon} + \frac{b^2\epsilon}{2} \text{ for all } a, b, \epsilon > 0. \tag{1.6}$$

Sobolev's Inequality (Poincaré Form):

$$||u||^2 \leq c_0 ||\nabla u||^2 \text{ for all } u \in H_0^1(\Omega), \tag{1.7}$$

where $c_0 > 0$ is the reciprocal of the minimal eigenvalue of the negative Laplacian that depends on Ω.

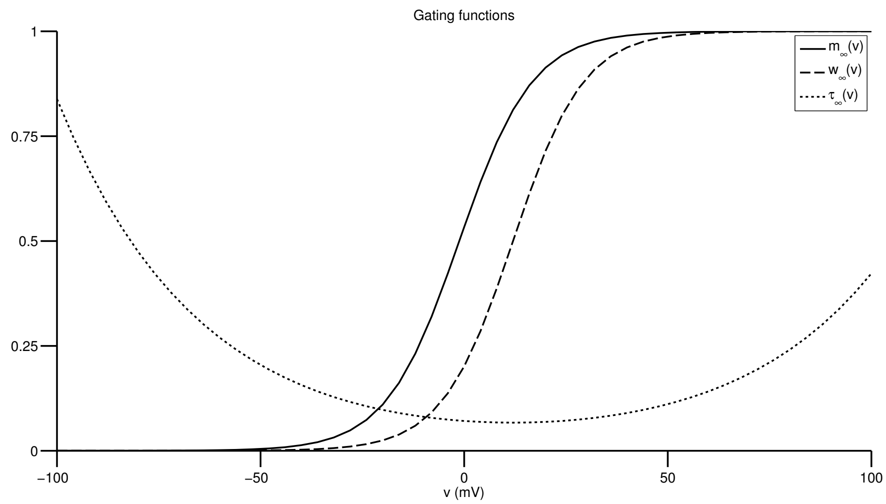

Figure 1: Gating functions of the Morris-Lecar model. The functions m_∞ and n_∞ remains between 0 and 1 for all potential levels. The kinetic function τ_∞ of the variable n has a strict lower bound.

Definition 1.1 *A pair of functions* $(v(t), n(t))$ *is called a strong solution of the problem (1.1)-(1.4) if*

$$v \in L^2([0,T]; H^2(\Omega)) \cap C([0,T]; H_0^1(\Omega)) \cap L^2(\Omega \times (0,T)),$$
$$n \in C([0,T]; H_0^1(\Omega)),$$

and the equations $(1.1) - (1.2)$ *are satisfied in the sense of distributions.*

2 Existence of strong solutions

In the following theorem we show the existence of the strong solution to the problem given in $(1.1) - (1.4)$ and obtain some uniform estimates for the solutions. We first note that the functions m_∞, n_∞ and τ_∞ and $n(t)$ satisfy the following inequalities, respectively. Below we denote by $v(t)$ and $n(t)$ any solution of (1.1)-(1.4), which are actually functions of x also. When there is no ambiguity, we also drop the variable t and write for example v_N to denote a function of x and t.

$$m_\infty(v(t)) \leq 1, \; n_\infty(v(t)) \leq 1, \tau_1 < \tau_\infty(v(t)) < \tau_2 \text{ and } 0 \leq n(t) \leq c_n, \quad (2.1)$$

for some positive constants τ_1, τ_2 and c_n.

Theorem 2.1 *Suppose that* $v_0, \; n_0 \in H_0^1(\Omega)$*. Then the initial boundary value problem* $(1.1) - (1.4)$ *admits a unique strong solution* $(v(t), n(t))$*. In addition,* *the following uniform estimates are satisfied for some constant $C > 0$.*

$$\begin{aligned} &\|\nabla v(t)\|,\ \|\nabla n(t)\|, \int_0^t \|\nabla v(\tau)\|^2\, d\tau, \\ &\int_0^t \|\nabla n(\tau)\|^2\, d\tau, \int_0^t \|\Delta v(\tau)\|^2\, d\tau \le C,\ \forall t \in \mathbb{R}^+. \end{aligned} \tag{2.2}$$

Proof of Theorem 2.1 First, let us note that we have (2.1) and $g_K > 0$ and $g_{Ca} > 0$. Using the Galerkin method, see e.g. [9, 21], let us construct approximate solutions of (1.1). Let $\{\phi_j\}_{j=1}^{\infty}$ be a basis of $H_0^1(\Omega)$ consisting of the eigenfunctions of the Dirichlet problem

$$\begin{cases} -\Delta\phi_j = \lambda_j\phi_j, & \text{in} \quad \Omega, \\ \quad \phi_j = 0, & \text{on} \quad \partial\Omega, \qquad j = 1, 2, \cdots. \end{cases} \tag{2.3}$$

There exists a sequence $\{\alpha_N\}_{N=1}^{\infty}$ such that

$$\sum_{k=1}^{N} \alpha_k\phi_k \to v_0, \quad \text{in} \quad H_0^1(\Omega) \quad \text{as} \quad N \to \infty. \tag{2.4}$$

We define the approximate solution $v_N(t)$ of the equation (1.1) in the form

$$v_N(t) = \sum_{k=1}^{N} c_k(t)\phi_k(x), \tag{2.5}$$

where $C_k(t)$ are determined by the system of ordinary differential equations

$$\begin{aligned} &\left(\sum_{k=1}^{N} c_k'(t)\phi_k, \phi_j\right) + \left(\sum_{k=1}^{N} c_k(t)\nabla\phi_k, \nabla\phi_j\right) \\ &\qquad = \left(f\left(\sum_{k=1}^{N} c_k(t)\phi_k, n(t)\right), \phi_j\right), \qquad j = 1, 2, \cdots, N, \end{aligned} \tag{2.6}$$

with initial data

$$c_{Nj}(0) = \alpha_j, \quad j = 1, \cdots, N. \tag{2.7}$$

Since $\det((\phi_j, \phi_k)) \neq 0$ and the nonlinear function f is continuous, by the Peano existence theorem, there exists at least one local solution to (2.6)-(2.7) in the interval $[0, T)$. Hence, this allows us to construct the approximate solution $v_N(t)$. Multiplying the equation (2.6) by the function $c_j(t)$, summing from

$j = 1$ to N we have

$$\begin{aligned}\frac{d}{dt}\frac{1}{2}\|v_N(t)\|^2 + \|\nabla v_N(t)\|^2 \\ = -g_L \int_\Omega v_N(t)^2\,dx + g_L E_L \int_\Omega v_N(t)\,dx \\ - g_K \int_\Omega n(t) v_N(t)^2\,dx + g_K E_K \int_\Omega n(t) v_N(t)\,dx \\ - g_{C_a} \int_\Omega m_\infty(v_N(t)) v_N(t)^2\,dx \\ + g_{C_a} E_{C_a} \int_\Omega m_\infty(v_N(t)) v_N(t)\,dx \\ + I \int_\Omega v_N(t)\,dx.\end{aligned} \tag{2.8}$$

Applying Sobolev, Hölder and Young inequalities and using the properties of the functions m_∞, v and positivity of the corresponding constants we get

$$\frac{d}{dt}\frac{1}{2}\|v_N(t)\|^2 \leq \left(-{c_1}^2 + \frac{\varepsilon_1}{2}\right)\|v_N(t)\|^2 + \frac{1}{2\varepsilon_1}{K_1}^2|\Omega|, \tag{2.9}$$

where

$$K_1 := g_L E_L + c_n|g_K E_K| + g_{C_a} E_{C_a} + I,$$

and

$$|\Omega| := \int_\Omega dx.$$

This implies, by choosing ε_1 small enough, that

$$\|v_N(t)\|^2 \leq C_1, \quad \forall t \in [0, T), \tag{2.10}$$

where C_1 depends on $\|v_0\|$ and is independent of N and t. Hence, we can extend the approximate solution to the interval $[0, \infty)$ and

$$\|v_N(t)\|^2 + \int_0^t \|v_N(t)\|^2_{H^1(\Omega)}\,ds \leq c, \tag{2.11}$$

for some constant $c > 0$ that is independent of N and t.

Thus, it follows that the sequence $\{v_N\}_{N=1}^\infty$ is bounded in $L^\infty(0,T;L^2(\Omega)) \cap L^2(0,T;H_0^1(\Omega))$. Applying the compact embedding theorem (see Cor. 4 in [24]) we obtain that the sequence $\{v_N\}_{N=1}^\infty$ is precompact in $L^2(0,T;L^2(\Omega))$. As a consequence, there exists a subsequence of $\{v_N\}_{N=1}^\infty$(still denoted by $\{v_N\}_{N=1}^\infty$) and a function $v \in L^\infty(0,T;H_0^1(\Omega))$ such that

$$\begin{cases} v_N \to v & \text{weakly star in} \quad L^\infty(0,T;H_0^1(\Omega)), \\ v_N \to v & \text{a.e. in} \quad \Omega \times (0,T). \end{cases} \tag{2.12}$$

Thus, using the properties(boundedness) of the functions m_∞, n and the constants(so that quadratic terms converge), we can pass to the limit in (2.6) and obtain

$$(v_t, \phi_j) + (\nabla v, \nabla \phi_j) = (f(v,n), \phi_j) \quad \text{in} \quad L^1(0,T), \tag{2.13}$$

for $j = 1, 2, \cdots,$. Since $\{\phi_j\}_{j=1}^{\infty}$ is a basis in $H_0^1(\Omega) \cap L^\infty(\Omega)$, by density of $H_0^1(\Omega) \cap L^2(\Omega)$ in $H_0^1(\Omega) \cap L^\infty(\Omega)$ in the topology endowed with the strong topology of $H_0^1(\Omega)$ and weakly star topology of $L^\infty(\Omega)$ for all $v \in H_0^1(\Omega) \cap L^\infty(\Omega)$ there exists a sequence $\{\alpha_{Nj}\}_{j=1}^{k_N}$ such that

$$\sum_{j=1}^{k_N} \alpha_{Nj}\phi_j \to v \quad \text{in} \quad H_0^1(\Omega), \quad \text{as} \quad N \to \infty,$$

and

$$\sup_N \left\| \sum_{j=1}^{k_N} \alpha_{Nj}\phi_j \right\|_{C(\bar{\Omega})} < \infty,$$

which together with (2.13), yields that

$$(v_t, w) + (\nabla v, \nabla w) = (f(v,n), w) \quad \text{in} \quad L^1(0,T), \tag{2.14}$$

for all $w \in H_0^1(\Omega) \cap L^\infty(\Omega)$. From the estimates above it follows that

$$v_N \to v \quad \text{weakly in} \quad C([0,T]; H_0^1(\Omega))$$

and in particular

$$v_N(0) \to v(0) \quad \text{weakly in} \quad H_0^1(\Omega),$$

which, together with (2.4), yields that $v(0) = v_0$. Also

$$\frac{d}{dt}(v_N, \phi_j) \to \frac{d}{dt}(v, \phi_j) \quad \text{weakly in} \quad L^1(0,T)$$

for $j = 1, 2, \cdots,$. Applying compact embedding theorems, by (2.12) we have

$$v_N \to v \quad \text{strongly in} \quad C([0,T]; L^2(\Omega)). \tag{2.15}$$

Hence, passing to the limit in (2.6) and taking into account the weak lower semicontinuity of the norm leads to the weak solution. Also,

$$v \in C([0,T]; H_0^1(\Omega)).$$

Since n solves an ordinary differential equation, the existence, uniqueness together with the regularity of solutions follow easily by the properties of the functions in the equation. We omit the details for the existence and uniqueness but provide below some estimates for the regularity.

For the higher regularity of the weak solution we need further a priori estimates. The following estimates are formal, which can be justified using the above procedure via the Galerkin approximation. For the sake of brevity, since the idea is exactly the same as above, we only present the formal calculations.

We take the inner product of the equation (1.1) with $-\Delta v(t)$ and obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\nabla v(t)\|^2 = &-\int_\Omega |\Delta v(t)|^2\,dx + g_L\int_\Omega \Delta v(t)(v(t)-E_L)\,dx\\ &+ g_K\int_\Omega \Delta v(t)n(t)(v(t)-E_K)\,dx\\ &+ g_{Ca}\int_\Omega m_\infty(v(t))\Delta v(t)(v(t)-E_{Ca})\,dx\\ &- I\int_\Omega \Delta v(t)\,dx.\end{aligned} \tag{2.16}$$

For the second, third and fourth terms on the right hand side of (2.16), we have the following useful estimates

$$g_L\int_\Omega \Delta v(t)(v(t)-E_L)\,dx = -g_L\int_\Omega |\nabla v(t)|^2\,dx = -g_L\|\nabla v(t)\|^2, \tag{2.17}$$

$$\begin{aligned}g_K\int_\Omega \Delta v(t)n(t)(v(t)-E_K)\,dx &\le g_K c_n\|\Delta v(t)\|\|v(t)-E_K\|\\ &\le g_K c_n N_1\|\Delta v(t)\|,\end{aligned} \tag{2.18}$$

$$\begin{aligned}g_{Ca}\int_\Omega m_\infty(v(t))\Delta v(t)(v(t)-E_{Ca})\,dx &\le g_{Ca}\|\Delta v(t)\|\|v(t)-E_{Ca}\|\\ &\le g_{Ca}N_2\|\Delta v(t)\|,\end{aligned} \tag{2.19}$$

where we used $n(t)\le c_n$, $m_\infty(v(t))\le 1$, $\|v(t)-E_K\|<N_1$ and $\|v(t)-E_{Ca}\|<N_2$, for some $N_1, N_2>0$.

Using the estimates (2.17), (2.18) and (2.19) in (2.16) we have

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\nabla v(t)\|^2 \le &-\|\Delta v(t)\|^2 - g_L\|\nabla v(t)\|^2\\ &+ (g_K c_n N_1 + g_{Ca}N_2 + I|\Omega|^{\frac{1}{2}})\|\Delta v(t)\|\\ &= -\|\Delta v(t)\|^2 - g_L\|\nabla v(t)\|^2 + K_2\|\Delta v(t)\|,\end{aligned} \tag{2.20}$$

where $K_2 = g_K c_n N_1 + g_{Ca}N_2 + I|\Omega|^{\frac{1}{2}}$. By employing the Young's inequality with ϵ_2 in (2.20), we get

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\nabla v(t)\|^2 &\le -g_L\|\nabla v(t)\|^2 + \left(-1+\frac{\epsilon_2}{2}\right)\|\Delta v(t)\|^2 + \frac{1}{2\epsilon_2}K_2^2\\ &\le -g_L\|\nabla v(t)\|^2 + \frac{1}{2\epsilon_2}K_2^2,\end{aligned} \tag{2.21}$$

where ϵ_2 is chosen in such a way that $-1+\frac{\epsilon_2}{2}\le 0$. Using (2.21) and integrating (2.20) with respect to t, we obtain

$$\|\nabla v(t)\| < C \text{ and } \int_0^t \|\Delta v(\tau)\|^2 d\tau < C \ \forall t \in \mathbb{R}^+. \tag{2.22}$$

Next, we take the inner product of the equation (1.2) in $L^2(\Omega)$ with $-\Delta n(t)$ to get

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|\nabla n(t)\|^2 &= -\int_\Omega \frac{n_\infty(v(t))}{\tau_\infty(v(t))}\Delta n(t)\,dx + \int_\Omega \frac{n(t)\Delta n(t)}{\tau_\infty(v(t))}\,dx \\
&= \int_\Omega \frac{(n_\infty^{'}(v(t))\tau_\infty(v(t)) - n_\infty(v(t))\tau_\infty^{'}(v(t)))}{\tau_\infty^2(v(t))}\nabla v(t)\cdot\nabla n(t)\,dx \\
&\quad - \int_\Omega \left(\frac{|\nabla n(t)|^2}{\tau_\infty(v(t))} - \frac{\tau_\infty^{'}(v(t))n(t)\nabla n(t)\cdot\nabla v(t)}{\tau_\infty^2(v(t))}\right)dx \\
&\le \sup\left(\frac{\tau_\infty^{'}(v(t))n(t)}{\tau_\infty^2(v(t))}\right)\int_\Omega \nabla n(t)\cdot\nabla v(t)\,dx - \frac{1}{\tau_2}\|\nabla n(t)\|^2 \\
&\quad + \frac{\sup(n_\infty^{'}(v(t))\tau_\infty(v(t)) - n_\infty(v(t))\tau_\infty^{'}(v(t)))}{\tau_1^2}\int_\Omega \nabla v(t)\cdot\nabla n(t)\,dx \\
&= -\frac{1}{\tau_2}\|\nabla n(t)\|^2 + (K_3+K_4)\int_\Omega \nabla n(t)\cdot\nabla v(t)\,dx,
\end{aligned} \tag{2.23}$$

where $K_3 = \sup(n_\infty^{'}(v)\tau_\infty(v) - n_\infty(v)\tau_\infty^{'}(v))$ and $K_4 = \sup\left(\frac{\tau_\infty^{'}(v)n}{\tau_\infty^2(v)}\right)$. Applying Hölder inequality and Young inequality with ϵ_3, respectively, we obtain

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|\nabla n(t)\|^2 &\le -\frac{1}{\tau_2}\|\nabla n(t)\|^2 + \frac{\epsilon_3}{2}\|\nabla n(t)\|^2 \\
&\quad + \frac{1}{2\epsilon_3}(K_3+K_4)^2\|\nabla v(t)\|^2 \\
&\le \left(-\frac{1}{\tau_2}+\frac{\epsilon_3}{2}\right)\|\nabla n(t)\|^2 + \frac{1}{\epsilon_3}(K_3+K_4)^2 N_3 \\
&\le \frac{1}{\epsilon_3}(K_3+K_4)^2 N_3,
\end{aligned} \tag{2.24}$$

where $\|\nabla v(t)\| \le N_3$ for some $N_3 > 0$ by previous estimates and ϵ_3 is chosen in such a way that $\left(-\frac{1}{\tau_2}+\frac{\epsilon_3}{2}\right) < 0$. Using (2.24) we easily deduce that

$$\|\nabla n(t)\| < C, \quad \int_0^t \|\nabla n(\tau)\|^2 d\tau < C, \ \forall t \in \mathbb{R}^+. \tag{2.25}$$

This completes the proof of Theorem 2.1.

3 Continuous Dependence

In this section, we show that the problem (1.1) – (1.4) exhibits continuous dependence to the leak conductance parameter g_L. Similar continuous dependence results can be obtained for other conductance parameters g_{Ca} and g_K, using a similar procedure. For brevity we drop the independent variables for the functions below, e.g. v_1 means in fact $v_1(x,t)$.

Theorem 3.1 *Suppose that (v_i, n_i), $i = 1, 2$ are strong solutions of the initial boundary value problem (1.1) – (1.4) corresponding to g_{Li}, $i = 1, 2$ such that $g_{L_2} = kg_{L_1}$ for some $k > 0$. Then one has*

$$\|v_1 - v_2\| \le \frac{C}{g_{L_1}}, \quad \textit{for all} \quad t \in \mathbb{R}^+$$

for some $C > 0$ that does not depend on g_{Li}, $i = 1, 2$.

Proof of Theorem 3.1 Let $w := v_1 - v_2$ and $z := n_1 - n_2$, where v_1 and v_2 are solutions of the equations (1.1) – (1.4) with the same initial and boundary values corresponding to g_{L_1} and g_{L_2}, respectively. Then

$$\begin{aligned} \frac{dv_i}{dt} &= \Delta v_i - g_{Li} v_i - g_K n_i v_i - g_{Ca} m_i \\ &\quad + g_K n_i E_K + g_{Ca} m_\infty(v_i) E_{Ca} + g_{L_i} E_L + I, \end{aligned} \tag{3.1}$$

where m_i denote $m_\infty(v_i)$. Subtracting equations for v_i, we get

$$\begin{aligned} \frac{dw}{dt} &= \Delta w - (g_{L_1} v_1 - g_{L_1} v_2) - g_K(n_1 v_1 - n_2 v_2) \\ &\quad - g_{Ca}(m_1 v_1 - m_2 v_2) + g_K E_K z + g_{Ca} E_{Ca}(m_1 - m_2). \end{aligned} \tag{3.2}$$

Let g and m denote $g_{L_1} - g_{L_2}$ and $m_1 - m_2$ respectively. Then

$$g_{L_1} v_1 - g_{L_2} v_2 = g_{L_1} w + v_2(g_{L_1} - g_{L_2}) = g_{L_1} v + v_2 g,$$

$$n_1 v_1 - n_2 v_2 = n_1 w + v_2 z$$

$$m_1 v_1 - m_2 v_2 = m_1 w + v_2(m_1 - m_2) = m_1 w + v_2 m.$$

With these expressions (3.2) becomes

$$\begin{aligned} \frac{dw}{dt} &= \Delta w - g_{L_1} w - g v_2 - g_K(n_1 w + v_2 z) \\ &\quad - g_{Ca}(m_1 w + v_2 m) + g_K E_K z + g_{Ca} E_{Ca} m. \end{aligned} \tag{3.3}$$

If we take inner product of this equation in $L^2(\Omega)$ with w, which is possible thanks to the regularity of solutions provided in the previous section, we get

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|w\|^2 = -\|\nabla w\|^2 - g_{L_1}\|w\|^2 - g\int_\Omega wv_2\,dx \\
- g_K\int_\Omega n_1w^2\,dx - g_K\int_\Omega wv_2z\,dx \\
- g_{Ca}\int m_1w^2\,dx - g_{Ca}\int_\Omega wv_2m\,dx \\
+ g_K\int_\Omega wz\,dx + g_{Ca}E_{Ca}\int_\Omega wm\,dx.
\end{aligned}
\tag{3.4}
$$

Using the inequalities $n_1 \geq 0$, $m_1 \geq 0$, $|m| \leq 2$ and $|z| \leq 2c_n$ together with the Hölder inequality we obtain

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|w\|^2 \leq -\|\nabla w\|^2 - g_{L_1}\|w\|^2 + 2c_ng_K\|v_2\|\|w\| \\
+ 2g_{Ca}\|v_2\|\|w\| + 2c_n|\Omega|^{\frac{1}{2}}\|w\| + 2g_{Ca}E_{Ca}|\Omega|^{\frac{1}{2}}\|w\| \\
= -\|\nabla w\|^2 - g_{L_1}\|w\|^2 + K_5\|w\|,
\end{aligned}
\tag{3.5}
$$

where $K_5 = \|v_2\|(g + 2c_ng_K + 2g_{Ca}) + 2|\Omega|^{\frac{1}{2}}(c_n + g_{Ca}E_{Ca})$. Using Sobolev inequality with c_2 for the first term and the Young inequality with ϵ_4 for the third term on the right hand side of (3.5), we obtain

$$
\tfrac{1}{2}\tfrac{d}{dt}\|w\|^2 \leq \left(-\tfrac{1}{c_2^2} - g_{L_1} + \tfrac{\epsilon_4}{2}\right)\|w\|^2 + \tfrac{1}{2\epsilon_4}K_5^2 \tag{3.6}
$$

where we can choose ϵ_4 in such a way that $(-\frac{1}{c_2^2} + \frac{\epsilon_4}{2}) = 0$. In this case, (3.6) becomes

$$
\frac{1}{2}\frac{d}{dt}\|w\|^2 \leq -g_{L_1}\|w\|^2 + \frac{1}{2\epsilon_4}K_5^2. \tag{3.7}
$$

Now we estimate the parameter K_5. We can re-write K_5 as

$$
K_5 = \|v_2\|(g + d_1) + d_2 \tag{3.8}
$$

where $d_1 = 2c_ng_K + 2g_{Ca}$ and $d_2 = 2|\Omega|^{\frac{1}{2}}(c_n + g_{Ca}E_{Ca})$. Using the Sobolev inequality with c_3 and the estimate for $\|\nabla v\|$ obtained in (2.22), respectively, we obtain

$$
\begin{aligned}
K_5 &\leq c_3(g + d_1)\|\nabla v_2\| + d_2 \\
&\leq \tfrac{c_3K_2^2}{2\epsilon_2}\tfrac{g+d_1}{g_{L_2}} + d_2 \\
&= d_3\tfrac{g+d_1}{g_{L_2}} + d_2
\end{aligned}
\tag{3.9}
$$

where $d_3 = \frac{c_3K_2^2}{2\epsilon_2}$, and the constant C in (2.22) is chosen accordingly. We note that the parameters d_1, d_2 and d_3 are independent of g_{L_i}, $i = 1, 2$. Using the estimate (3.9) in (3.7) we obtain

$$
\frac{1}{2}\frac{d}{dt}\|w\|^2 \leq -g_{L_1}\|w\|^2 + \frac{1}{2\epsilon_4}\left(\frac{d_3(g + d_1)}{g_{L_2}} + d_2\right)^2
$$

from which, using the assumption $g_{L_2} = kg_{L_1}$, we can deduce the desired estimate of the form

$$\|w\|^2 \leq \frac{\frac{1}{2\epsilon_4}\left(\frac{d_3(g+d_1)}{g_{L_2}} + d_2\right)^2}{g_{L_1}} \leq \frac{C}{g_{L_1}},$$

for some positive constant C that does not depend on $g_{L_i},\ i = 1, 2$. This estimate concludes the proof of Theorem 3.1.

Remark 3.2 *This kind of estimate together with the existence and uniqueness of the solution suggest that the problem (1.1)-(1.4) is well-posed.*

4 Concluding Remarks

In this paper, existence and uniqueness of strong solutions for a nonlinear system of Morris-Lecar equations $(1.1)-(1.4)$ under some natural assumptions on data are proved. To demonstrate continuous dependence of the system $(1.1)-(1.4)$ to parameters, a continuous dependence estimate to leak conductance parameter g_L is established. Similar continuous dependence estimates can be obtained for other conductance parameters. As it is well-known, a problem is said to be well-posed in the Hadamard sense if the solution exists, is unique and continuously depends on the data. In this sense, our problem is shown to be well-posed. The authors of this paper plan to study the considered system numerically in the near future. Later they plan to define some inverse problems for the system $(1.1) - (1.4)$ and analyze them theoretically and numerically. Both of these are subjects of the future studies by the authors of this paper.

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