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LIMIT CYCLES BY FINITE ELEMENT METHOD FOR A ONE - PARAMETER DYNAMICAL SYSTEM ASSOCIATED TO THE LUO - RUDY I MODEL

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Abstract A one - parameter dynamical system is associated to the mathematical problem governing the membrane excitability of a ventricular cardiomyocyte, according to the Luo-Rudy I model. Limit cycles are described by the solutions of an extended system. A finite element method time approximation (FEM) is used in order to formulate the approximate problem. Starting from a Hopf bifurcation point, approximate limit cycles are obtained, step by step, using an arc-length-continuation method and Newton's method. Some numerical results are presented.

Keywords: limit cycle, finite element method time approximation, Luo-Rudy I model, arc-length-continuation method, Newton's method.
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1. INTRODUCTION

The well-known Hodgkin-Huxley model of the squid giant axon [16] represented a huge leap forward in comparison with the earlier models of excitable systems built from abstract sets of equations or from electrical circuits including non-linear components, e.g. [33]. The pioneering work of Denis Noble's group made the transition from neuronal excitability models, characterized by Na+ and K+ conductances with fast gating kinetics, to cardiomyocyte electrophysiology models, a field expanding steadily for over five decades [23]. Nowadays, complex models accurately reproducing transmembrane voltage changes as well as ion concentration dynamics between various subcellular compartments and buffering systems are incorporated into detailed anatomical models of the entire heart [24]. The Luo-Rudy I model of isolated guinea pig ventricular cardiomyocyte [21] was developed in the early 1990s starting

from the Beeler-Reuter model [1]. It includes more recent experimental data related to gating and permeation properties of several types of ion channels, obtained in the late 1980s with the advent of the patch-clamp technique [22]. The model comprises only three time and voltage-dependent ion currents (fast sodium current, slow inward current, time-dependent potassium current) plus three background currents (time-independent and plateau potassium current, background current), their dynamics being described by Hodgkin-Huxley type equations. This apparent simplicity, compared to more recent multicompartment models, renders it adequate for mathematical analysis using methods of linear stability and bifurcation theory.

Nowadays, there exist numerous software packages for the numerical study of finite - dimensional dynamical systems, for example MATCONT, CL_MATCONT, CL_MATCONTM [7], [15], AUTO [8]. In [19], [8], [7], [15]; the periodic boundary value problems used to locate limit cycles are approximated using orthogonal collocation method. Finite differences method is also considered. In this paper, limit cycles are obtained for the dynamical system associated to the Luo-Rudy I model by using finite element method time approximation (FEM).

2. LUO-RUDY I MODEL

The mathematical problem governing the membrane excitability of a ventricular cardiomyocyte, according to the Luo-Rudy I model [21], is a Cauchy problem

$$u(0) = u_0\,, \tag{1}$$

for the system of first order ordinary differential equations

$$\frac{du}{dt} = \mathcal{F}(\eta, u)\,, \tag{2}$$

where $u = (u_1, \ldots, u_8) = (V, [Ca]_i, h, j, m, d, f, X)$, $\eta = (\eta_1, \ldots, \eta_{13}) = (I_{st}, C_m, g_{Na}, g_{si}, g_{Kp}, g_b, [Na]_0, [Na]_i, [K]_0, [K]_i, PR_{NaK}, E_b, T)$, $M = \mathbb{R}^8$, $\mathcal{F} : \mathbb{R}^{13} \times M \to M$, $\mathcal{F} = (\mathcal{F}_1, \ldots, \mathcal{F}_8)$,

$$\begin{aligned}
\mathcal{F}_1(\eta, u) = &-\frac{1}{\eta_2}[I_{st} + \eta_3 u_3 u_4 u_5^3 (u_1 - E_{Na}(\eta_7, \eta_8, \eta_{13}))\\
&+\eta_4 u_6 u_7 (u_1 - c_1 + c_2 \ln u_2)\\
&+g_K(\eta_{10}) X_i(u_1)(u_1 - E_K(\eta_7, \eta_8, \eta_9, \eta_{10}, \eta_{11}, \eta_{13}))u_8\\
&+g_{K1}(\eta_{10}) K1_\infty(\eta_9, \eta_{10}, \eta_{13}, u_1)(u_1 - E_{K1}(\eta_9, \eta_{10}, \eta_{13}))\\
&+\eta_5 Kp(u_1)(u_1 - E_{Kp}(\eta_9, \eta_{10}, \eta_{13})) + \eta_6(u_1 - \eta_{12})]\,,\\
\mathcal{F}_2(\eta, u) = &-c_3\eta_4 u_6 u_7 (u_1 - c_1 + c_2 \ln u_2) + c_4(c_5 - u_2)\,,\\
\mathcal{F}_\ell(\eta, u) = &\alpha_\ell(u_1) - (\alpha_\ell(u_1) + \beta_\ell(u_1))u_\ell\,,\ \ell = 3, \ldots, 8\,.
\end{aligned}$$

For the definition of variables V, $[Ca]_i$, h, j, m, d, f, X, parameters I_{st}, C_m, g_{Na}, g_{si}, g_{Kp}, g_b, $[Na]_0$, $[Na]_i$, $[K]_0$, $[K]_i$, PR_{NaK}, E_b, T, constants $c_1, \ldots, c_5$, functions

g_K, E_{Na}, E_K, E_{K1}, E_{Kp}, $K1_\infty$, X_i, Kp, α_ℓ, β_ℓ, default values of parameters and initial values of variables in the Luo-Rudy I model, the reader is referred to [21]. The reader is also referred to [20] for the continuity of the model, and to [4] for the treatment of the vector field $\mathcal{F}$ singularities. $\mathcal{F}$ is of class C^2 on the domain of interest.

3. THE ONE - PARAMETER DYNAMICAL SYSTEM ASSOCIATED TO THE LUO - RUDY I MODEL

We performed the study of the dynamical system associated with the Cauchy problem (1), (2) by considering only the parameter $\eta_1 = I_{st}$ and fixing the rest of parameters. Denote $\lambda = \eta_1 = I_{st}$ and η_* the vector of the fixed values of $\eta_2, \ldots, \eta_{13}$. Let $F : \mathbb{R} \times M \to M$, $F(\lambda, u) = \mathcal{F}(\lambda, \eta_*, u)$, $F = (F_1, \ldots, F_8)$.

Consider the dynamical system associated with the Cauchy problem (1), (3), where

$$\frac{du}{dt} = F(\lambda, u)\,. \tag{3}$$

The equilibrium points of this problem are solutions of the equation

$$F(\lambda, u) = 0\,. \tag{4}$$

The existence of the solutions and the number were established by graphical representation in [4], for the domain of interest. The equilibrium curve (the bifurcation diagram) was obtained in [4], via an arc-length-continuation method [13] and Newton's method [12], starting from a solution obtained by solving a nonlinear least-squares problem [13] for a value of λ for which the system has one solution. In [4], the results are obtained by reducing (4) to a system of two equations in $(u_1, u_2) = (V, [Ca]_i)$. Here, we used directly (4).

4. EXTENDED SYSTEM METHOD FOR LIMIT CYCLES

The extended system in (λ, T, u)

$$\begin{cases} \dfrac{du}{d\tau} - TF(\lambda, u) = 0, \\ \\ u(0) - u(1) = 0, \\ \\ \displaystyle\int_0^1 < u(t), \frac{dw(t)}{dt} > dt = 0, \end{cases} \tag{5}$$

was introduced, in [19], [8], [7], in order to locate limit cycles of a general problem (1), (3). Here, T is the unknown period of the cycle, w is a component of a known

reference solution $(\hat{\lambda}, \hat{T}, w)$ of (5), and, in our case,

$$< u, v >= \sum_{i=1}^{8} u_i v_i \text{ and } \|u\| = \sqrt{\sum_{i=1}^{8} u_i^2} \text{ for } u, v \in \mathbb{R}^8.$$

The system (5) becomes determined in a continuation process. In order to approximate and solve it by FEM time approximation, let us obtain the weak form of (5) in the sequel. For this, we consider the function spaces:

$$\begin{aligned} X = \{x \in L^2(0,1;\mathbb{R}^8);\ & \frac{dx}{dt} \in L^2(0,1;\mathbb{R}^8), \\ & x = (x_1, \ldots, x_8),\ x_i(0) = x_i(1),\ i = 1, \ldots, 8\}. \\ V = \{v \in L^2(0,1;\mathbb{R});\ & \frac{dv}{dt} \in L^2(0,1;\mathbb{R}),\ v(0) = v(1)\}. \end{aligned}$$

The weak form of (5) is the problem in $(\lambda, T, u) \in \mathbb{R} \times \mathbb{R} \times X$

$$\begin{cases} \int_0^1 u_i(\tau) \frac{dv(\tau)}{d\tau}\, d\tau + T \int_0^1 F_i(\lambda, u(\tau)) v(\tau) d\tau = 0, \\ \qquad \forall v \in V,\ i = 1, \ldots, 8, \\ \int_0^1 < u(t), \frac{dw(t)}{dt} > dt = 0. \end{cases} \tag{6}$$

5. ARC-LENGTH-CONTINUATION METHOD FOR (6)

Following the usual practice ([17], [18], [7], [8], [12], [13], [14], [15], [19], [25], [27], [28], [29]), we also use an arc-length-continuation method in order to formulate an algorithm to solve (6) approximatively.

Glowinski ([13], following Keller [17], [18]) and Doedel ([8], where Keller's name is also cited) chose a continuation equation written in our case as

$$\int_0^1 \|\frac{du(t)}{ds}\|^2 dt + (\frac{dT}{ds})^2 + (\frac{d\lambda}{ds})^2 = 1, \tag{7}$$

where s is the curvilinear abscissa.

Let (λ^0, u^0) be a Hopf bifurcation point, $\pm\beta^0 i$ a pair of purely imaginary eigenvalues of of the Jacobian matrix $D_u F(\lambda^0, u^0)$, and a nonzero complex vector $g^0 = g_r^0 + i g_i^0$. (λ^0, u^0) is located on the equilibrium curve during a continuation procedure using

some test functions ([19], [14], [7]). $(\lambda^0, \beta^0, u^0, g_r^0, g_i^0) \in \mathbb{R} \times \mathbb{R} \times \mathbb{R}^8 \times \mathbb{R}^8 \times \mathbb{R}^8$ is the solution of the extended system ([27], [28], [29])

$$\begin{bmatrix} F(\lambda, u) \\ D_u F(\lambda, u) g_r + \beta g_i \\ D_u F(\lambda, u) g_i - \beta g_r \\ g_{r,k} - 1 \\ g_{i,k} \end{bmatrix} = 0\,, \tag{8}$$

where k is a fixed index of g_r and of g_i, $1 \le k \le 8$.

To solve (6), the extended system formed by (6) and (7), parametrized by s, was considered. Let $\triangle s$ be an arc-length step and $\lambda^n \cong u(\lambda \triangle s)$, $T^n \cong T(n \triangle s)$, $u^n \cong u(n \triangle s)$. We have the algorithm (following the cases from [13], [8], [28], [29]):

Algorithm 1. *1. take the Hopf bifurcation point* (λ^0, u^0) *and* $T^0 = 2\pi/\beta^0$*; retain* g_r^0, g_i^0*;*

2. for $n = 0$, $(\lambda^1, T^1, u^1) \in \mathbb{R} \times \mathbb{R} \times X$ *is obtained ([8], [29]) by (13) below*

$$\int_0^1 \sum_{i=1}^{8} u_i^1(t)\, \frac{d\phi_i(t)}{dt}\, dt = 0\,, \tag{9}$$

and

$$\int_0^1 \sum_{i=1}^{8} (u_i^1(t) - u_i^0(t))\phi_i(t)\, dt = \triangle s\,, \tag{10}$$

where

$$\phi(t) = \sin(2\pi t) g_r^0 + \cos(2\pi t) g_i^0\,, \tag{11}$$

by using Newton's method with the initial iteration

$$(u^1)^0(t) = u^0 + \triangle s\, \phi(t)\,, \quad (T^1)^0 = T^0\,, \quad (\lambda^1)^0 = \lambda^0\,. \tag{12}$$

3. for $n \ge 1$*, assuming that* $(\lambda^{n-1}, T^{n-1}, u^{n-1})$, (λ^n, T^n, u^n) *are known,* $(\lambda^{n+1}, T^{n+1}, u^{n+1}) \in \mathbb{R} \times \mathbb{R} \times X$ *is obtained from*

$$\int_0^1 u_i^{n+1}(\tau)\, \frac{dv(\tau)}{d\tau}\, d\tau + T^{n+1} \int_0^1 F_i(\lambda^{n+1}, u^{n+1}(\tau)) v(\tau) d\tau = 0\,, \tag{13}$$

$\forall v \in V$, $i = 1, \ldots, 8$,

$$\int_0^1 \sum_{i=1}^{8} u_i^{n+1}(t)\, \frac{du_i^n(t)}{dt}\, dt = 0, \tag{14}$$

$$\int_0^1 \sum_{i=1}^{8} (u_i^{n+1}(t) - u_i^n(t)) \frac{u_i^n(t) - u_i^{n-1}(t)}{\triangle s}\, dt +$$

$$+(T^{n+1} - T^n)\frac{T^n - T^{n-1}}{\triangle s} + (\lambda^{n+1} - \lambda^n)\frac{\lambda^n - \lambda^{n-1}}{\triangle s} = \triangle s, \,, \tag{15}$$

by using Newton's method with the initial iteration

$$((\lambda^{n+1})^0, (T^{n+1})^0, (u^{n+1})^0) = (\lambda^n, T^n, u^n). \tag{16}$$

6. NEWTON'S METHOD FOR THE STEPS OF ALGORITHM 1

In (15) ($n \geq 1$), let us denote $\lambda^* = \lambda^n$, $T^* = T^n$, $u^* = u^n$, $\lambda^{**} = (\lambda^n - \lambda^{n-1})/\triangle s$, $T^{**} = (T^n - T^{n-1})/\triangle s$, $u^{**} = (u^n - u^{n-1})/\triangle s$.

We write (13), (9), (10) (the iteration $n = 0$) in the same general form as (13), (14), (15). So denote $u^* = u^0$, $u^{**} = \phi$ and consider $\lambda^* = \lambda^0$, $T^* = T^0$, $\lambda^{**} = 0$, $T^{**} = 0$ in (15) and consider $u^* = u^0 = \phi$ in (14).

Each step of Algorithm 1, given $(\lambda^*,\ T^*,\ u^*)$, $(\lambda^{**},\ T^{**},\ u^{**})$, calculates $(\lambda^{n+1}, T^{n+1}, u^{n+1}) \in \mathbb{R} \times \mathbb{R} \times X,\ n \geq 0,$ by (13),

$$\int_0^1 \sum_{i=1}^{8} u_i^{n+1}(t)\, \frac{du_i^*(t)}{dt}\, dt = 0\ , \tag{17}$$

and

$$\int_0^1 \sum_{i=1}^{8} (u_i^{n+1}(t) - u_i^*(t)) u_i^{**}(t)\, dt + +(T^{n+1} - T^*)T^{**} + (\lambda^{n+1} - \lambda^*)\lambda^{**} = \triangle s\,. \tag{18}$$

Newton's method applied (13), (17) and (18), for $n \geq 0$, leads to:

- let $((\lambda^1)^0, (T^1)^0, (u^1)^0)$, given by (12), be an initial iteration ($m = 0$), if $n = 0$;
- let $((\lambda^{n+1})^0, (T^{n+1})^0, (u^{n+1})^0)$, given by (16), be an initial iteration ($m = 0$), if $n \geq 1$;
- calculate $(\lambda^{n+1}, T^{n+1}, u^{n+1})$ as the solution of the algorithm:

for $m \geq 0$, $((\lambda^{n+1})^{m+1}, (T^{n+1})^{m+1}, (u^{n+1})^{m+1}) = (\lambda^{m+1}, T^{m+1}, u^{m+1}) \in \mathbb{R} \times \mathbb{R} \times X$ is obtained by

$$\int_0^1 u_i^{m+1}(\tau)\,\frac{dv(\tau)}{d\tau}\,d\tau + T^{m+1}\int_0^1 F_i(\lambda^m, u^m(\tau))v(\tau)d\tau +$$

$$+T^m\int_0^1 DF_i(\lambda^m, u^m(\tau))(\lambda^{m+1}, u^{m+1}(\tau))v(\tau)d\tau = \tag{19}$$

$$= T^m\int_0^1 DF_i(\lambda^m, u^m(\tau))(\lambda^m, u^m(\tau))v(\tau)d\tau\,, \quad \forall v \in V,\ i = 1,\dots,8.$$

$$\int_0^1 \sum_{i=1}^{8} u_i^{m+1}(t)\,\frac{du_i^*(t)}{dt}\,dt = 0, \tag{20}$$

$$\int_0^1 \sum_{i=1}^{8} u_i^{m+1}(t)u_i^{**}(t)\,dt + T^{m+1}T^{**} + \lambda^{m+1}\lambda^{**} = \tag{21}$$

$$= \int_0^1 \sum_{i=1}^{8} u_i^*(t)u_i^{**}(t)\,dt + T^*T^{**} + \lambda^*\lambda^{**} + \triangle s\,.$$

7. APPROXIMATION OF PROBLEM (19), (20), (21) BY FINITE ELEMENT METHOD TIME APPROXIMATION

In order to perform this approximation, let us divide the interval $[0,1]$ in $N+1$ subintervals $K = K_j = [t_j, t_{j+1}]$, $0 \le j \le N$, where $0 = t_0 < t_1 < \ldots < t_{N+1} = 1$. The sets K represent a triangulation $\mathcal{T}_h$ of $[0,1]$.

Let us approximate the spaces V and X by the spaces

$$V_h = \{v : [0,1] \to \mathbb{R};\ v \in C[0,1],\ v(0) = v(1),\ v|_K \in P_k(K),\ \forall K \in \mathcal{T}_h\},$$

$$X_h = \{x : [0,1] \to \mathbb{R}^8;\ x = (x_1, \dots, x_8),\ x_i \in V_h,\ i = 1, \dots, 8\}\,,$$

respectively, where $P_k(K)$ is the space of polynomials in t of degree less than or equal to k defined on K, $k \ge 2$.

Let $k = 2$. An element $K \in \mathcal{T}_h$ has three nodal points. To obtain a function $u_h \in X_h$ reduces to obtain a function $v_h \in V_h$. In order to obtain a function $v_h \in V_h$, we use a basis of functions of V_h. Let $J_K = \{1, 2, 3\}$ be the local numeration for the nodes of K, where $1, 3$ correspond to t_j, t_{j+1} respectively and 2 corresponds to a node between t_j and t_{j+1}. Let $\{\psi_i, i \in J_K\}$ be the local quadratic basis of functions on K corresponding to the local nodes. Let $J = \{1, \dots, 2N+1\}$ be the global numeration

for the nodes of $[0, 1]$. The two numerations are related by a matrix L whose elements are the elements $j \in J$. Its rows are indexed by the elements $K \in \mathcal{T}_h$ (by the number of the element K in a certain fixed numeration with elements from the set $\{1, \ldots, N\}$) and its columns, by the local numeration $i \in J_K$, that is $j = L(K, i)$.

A function $v_h \in V_h$ is defined by its values v_j from the nodes $j \in J$,

$$v_h(t) = \sum_{K \in \mathcal{T}_h} \sum_{i \in J_K,\ j = L(K,i)} v_j \psi_i(t)\,, \tag{22}$$

and a function $u_h \in X_h$ is defined by its values u_j from the nodes $j \in J$,

$$u_h(t) = \sum_{K \in \mathcal{T}_h} \sum_{i \in J_K,\ j = L(K,i)} u_j \psi_i(t)\,. \tag{23}$$

So, an unknown function $u_h = ((u_h)_1, \ldots, (u_h)_8)$ is reduced to the unknowns u_j, $u_j = ((u_j)_1, \ldots, (u_j)_8)$, $j \in J$.

In (19), (20), (21), approximate $(\lambda^{m+1}, T^{m+1}, u^{m+1}) \in \mathbb{R} \times \mathbb{R} \times X$ by $(\lambda^{m+1}, T^{m+1}, u_h^{m+1}) \in \mathbb{R} \times \mathbb{R} \times X_h$. Taking $u_h^{m+1} = u_h$, u_h given by (23), and $v = \psi_\ell$, for all $\ell \in J_K$, for all $K \in \mathcal{T}_h$, we obtain the discrete variant of problem (19), (20), (21) as the following problem in $(\lambda, T, u_1, \ldots, u_{2N+1}) \in \mathbb{R} \times \mathbb{R} \times \mathbb{R}^{8\cdot(2N+1)}$, written suitable for the assembly process,

$$\sum_{K \in \mathcal{T}_h} \left\{ \sum_{i \in J_K,\ j = L(K,i)} (u_j^{m+1})_n \int_K \psi_i(\tau)\, \frac{\psi_\ell(\tau)}{d\tau}\, d\tau + T^{m+1} \int_K F_i(\lambda^m, u_h^m(\tau))\, \psi_\ell\, d\tau + \right.$$

$$+ T^m \sum_{i \in J_K,\ j = L(K,i)} < u_j^{m+1}, \int_K (D_u F_n(\lambda^m, u_h^m(\tau)) \psi_i(\tau))\, \psi_\ell\, d\tau > +$$

$$\left. + \lambda^{m+1} \int_K (D_\lambda F_n(\lambda^m, u_h^m(\tau)))\, \psi_\ell\, d\tau \right\} = \tag{24}$$

$$= T^m \sum_{K \in \mathcal{T}_h} \left\{ \int_K (D_u F_n(\lambda^m, u_h^m(\tau)) u_h^m(\tau))\, \psi_\ell\, d\tau + \int_K (D_\lambda F_n(\lambda^m, u_h^m(\tau)) \lambda^m)\, \psi_\ell\, d\tau \right\},$$

$n = 1, \ldots, 8$,

$$u_0^{m+1} = u_{2N+1}^{m+1}\,, \tag{25}$$

$$\sum_{K \in \mathcal{T}_h} \sum_{i \in J_K,\ j = L(K,i)} < u_j^{m+1}, \int_K \psi_i(\tau)\, \frac{du_h^*(\tau)}{d\tau}\, d\tau > = 0\,, \tag{26}$$

$$\sum_{K\in\ \mathcal{T}_h}\ \sum_{i\in\ J_K,\ j=L(K,i)} < u_j^{m+1},\ \int_K \psi_i(\tau)\, u_h^{**}(\tau)\, d\tau > + T^{\,m+1} T^{\,**} + \lambda^{m+1}\lambda^{**} = \qquad (27)$$

$$= \sum_{K\in\ \mathcal{T}_h} \int_K < u_h^{*}(\tau), u_h^{**}(\tau) >\ d\tau + T^{\,*} T^{\,**} + \lambda^{*}\lambda^{**} + \triangle s\,,$$

for all $\ell \in J_K$, for all $K \in\ \mathcal{T}_h$.

8. NUMERICAL RESULTS

Based on [30] and on the computer programs for [2] and [3], relations (24), (25), (26), (27) and the algorithm at the end of section 5 furnished the numerical results of this section.

Let (λ^0, u^0) be the Hopf bifurcation point located during the construction of the equilibrium curve by a continuation procedure in [5].

The solution $(\lambda^0, \beta^0, u^0, g_r^0, g_i^0)$ of (8), calculated in [5], is
$\lambda^0 = -1.0140472901$,$\beta^0 = 0.0162886062$,
$u^0 = (-24.3132508542,\ 0.0034641214,\ 0.0,\ 0.0,\ 0.9176777444,\ 0.5025242162,$
$4920204612,\ 0.5071561613)$,
$g_r^0 = (1.0,\ 0.0000468233,\ 0.0,\ 0.0,\ 0.0093195354,\ 0.0198748652,\ -0.0072420216,$
$0.0001706577)$,
$g_i^0 = (0.0,\ 0.0000029062,\ 0.0,\ 0.0,\ -0.0000171311,\ -0.0118192370,\ 0.0136415789,$
$-0.0017802907)$.

The eigenvalues of the Jacobian matrix $D_u F(\lambda^0, u^0)$, calculated by the QR algorithm, are $\pm\, 0.0162886062\, i$, -8.8611865338, -0.1026761869, -0.0647560667, -0.0024565181, -1.7398266947, -0.2049715178. These data are considered in the step 1 of the algorithm at the end of section 5.

We took $C_m = 1$, $g_{Na} = 23$, $g_{si} = 0.09$, $g_K = 0.282$, $g_{K1} = 0.6047$, $g_{Kp} = 0.0183$, $G_b = 0.03921$, $[Na]_0 = 140$, $[Na]_i = 18$, $[K]_0 = 5.4$, $[K]_i = 145$, $PR_{NaK} = 0.01833$, $E_b = -59.87$, $T = 310$.

In order to solve (6) numerically by the algorithm at the end of section 5 and by (24), (25), (26), (27), we performed calculations using $\triangle s = 1.0$ and 500 iterations in the continuation process. Integrals $\int_K f(\tau)\, d\tau$ were calculated using Gauss integration formula with three integration points.

Figure 1 and 2 present some results obtained using 20 elements K (41 nodes) ($N = 20$, $J = \{1, \ldots, 41\}$ in section 7). The curves of the projections of the limit cycles, on the planes indicates in figure, are plots generated from values calculated in the nodes, corresponding to a fixed value of the parameter.

Two projections of some limit cycles and of a part of the equilibrium curve (marked by "▲") are presented in Fig. 1. The Hopf bifurcation point is marked by "•".

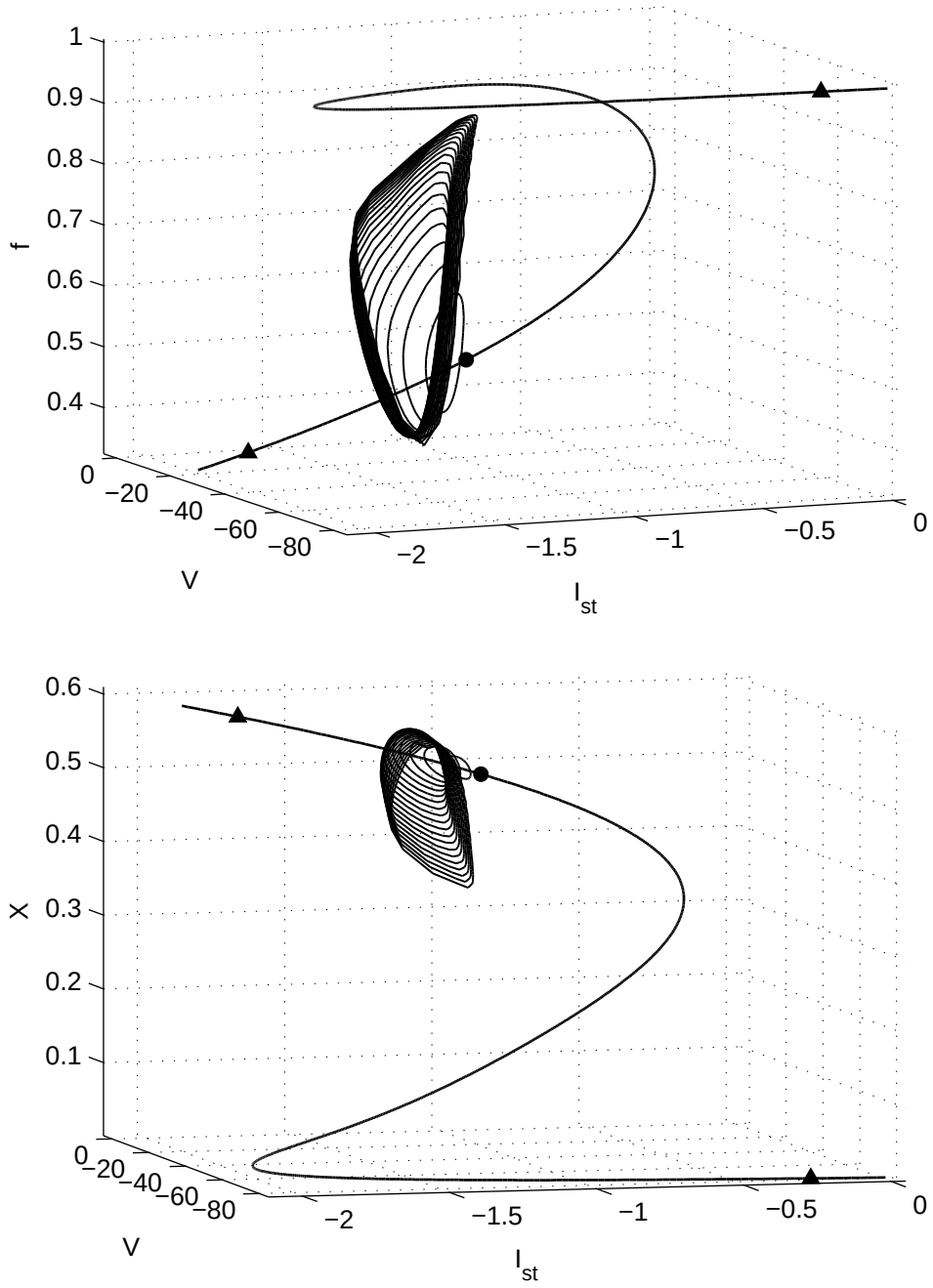

Fig. 1. Two projections of limit cycles and of a part of the equilibrium curve (marked by "▲"). The Hopf bifurcation point is marked by "•".

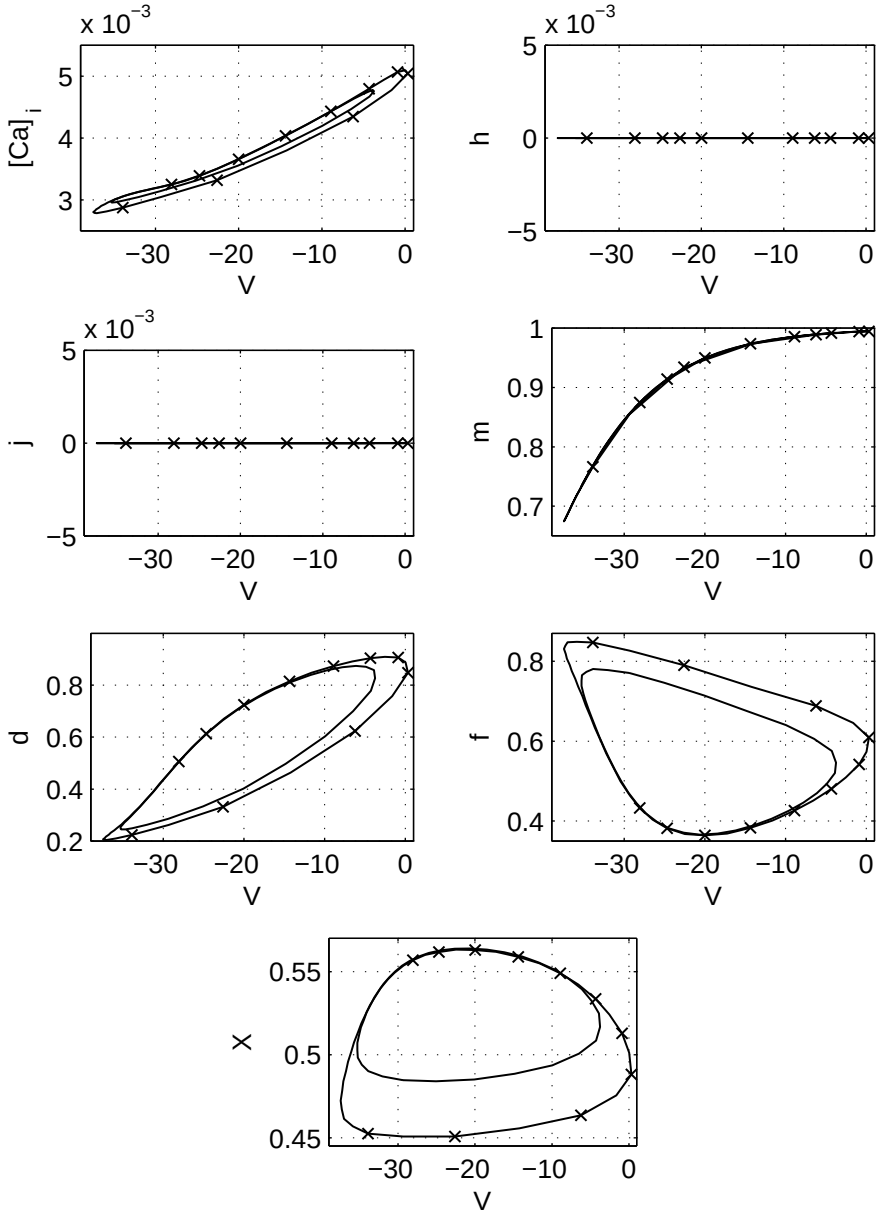

Fig. 2. Projections of two limit cycles calculated for $I_{st} = -1.2000465026$ and for $I_{st} = -1.2000183729$ (marked by "x") (20 elements, 41 nodes).

In Fig. 2, there are represented the projections of the plots of two limit cycles calculated for $I_{st} = -1.2000465026$
(iteration 148) and for $I_{st} = -1.2000183729$ (iteration 248, marked by "x" in figure).

The results obtained are relevant from a biological point of view, pointing to unstable electrical behavior of the modeled system in certain conditions, translated into oscillatory regimes such as early afterdepolarizations [32] or self-sustained oscillations [4], which may in turn synchronize, resulting in life-threatening arrhythmias: premature ventricular complexes or torsades-de-pointes, degenerating in rapid polymorphic ventricular tacycardia or fibrillation [26].

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