Chapter 1
Traveling Waves Impulses of FitzHugh Model with Diffusion and Cross-Diffusion

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Abstract The FitzHugh equations have been used as a caricature of the Hodgkin–Huxley equations of neuron firing and to capture, qualitatively, the general properties of an excitable membrane. The spatial propagation of neuron firing due to diffusion of the current potential was described by the FitzHugh–Nagumo model. Assuming that the spatial propagation of neuron firing is caused by not diffusion but cross-diffusion connection between the potential and recovery variables the cross-diffusion version of the FitzHugh model gives rise to the typical fast traveling wave solutions characteristic to the FitzHugh model, and additionally gives rise to the slow traveling wave solutions exhibited in the diffusion FitzHugh–Nagumo equations (Berezovskaya et al., Math Biosci Eng 5:239–260, 2008).

In this paper the FitzHugh model with both diffusion and cross-diffusion terms is studied; it is shown that this new version of spatial FitzHugh model gives rise to fast and slow traveling impulses.

Keywords FithHugh model • Slow and fast traveling wave solutions • Diffusion and cross-diffusion

1.1 Introduction

Hodgkin, Huxley, and Katz in the 1940s explored experimentally and mathematically the nature of nerve impulses. Their work revealed that the electrical pulses across the membrane arise from the uneven distribution between the intracellular fluid and the extracellular fluid of potassium (K+), sodium (Na+), and protein anions (see [1] for details). This entire process of rapid change in potential from threshold to peak reversal and then back to the resting potential level is called an *action potential*, impulse, or spike (see schematic diagram in Fig. 1.1).

The process was mathematically investigated by Hodgkin and Huxley in 1952 with a four-variable model [2]. FitzHugh in 1961 proposed a simplified two-variable

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B. Toni (ed.), *Mathematical Sciences with Multidisciplinary Applications*, Springer Proceedings in Mathematics & Statistics 157, DOI 10.1007/978-3-319-31323-8_1

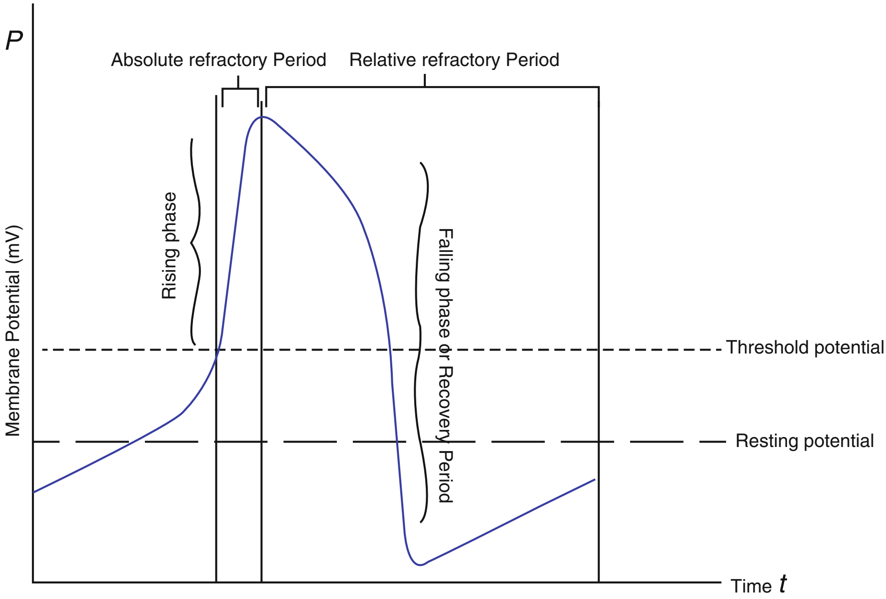

Fig. 1.1 Neuron spike in the (time-potential) plane obtained from experiments of neuron firing (see [1, 3] for details)

model of an excitable membrane, which made it possible to illustrate the various physiological states involved in an action potential (such as resting, active, refractory, enhanced, and depressed, see Fig. 1.1) in the phase plane (see [3, 4]). The FitzHugh system captures much of the same dynamical behavior and, in particular, demonstrates the spike-like behavior (see Sect. 1.2 and Fig. 1.2).

A more realistic model is the one that depends on both space and time since electric currents cross the membrane of the cell move along its axon lengthwise inside and outside. This mechanism makes it possible for electrical signals to be transmitted over long distance and thus propagate throughout the membrane without ever weakening or decreasing their initial strength. A mathematical model of the diffusion of current potential was first proposed and studied by FitzHugh in 1961 and 1969 (see [3]), Nagumo et al. in 1962 (see [5]), and many others. This model and its various modifications became one of the sources of many new methods of analysis of traveling waves, their stability, shapes and velocity of a propagation ([6–14], etc.).

Note that the initial FitzHugh and FitzHugh–Nagumo models "phenomenologically" (in the simplest way) described recovery process in the spike and spike-like wave propagation.

Recently models have been proposed, where the spatial solutions are conditioned by the effects of cross-diffusion "control" or "interactions" between components of the system ([6, 8, 10, 16–24], etc.). From a mathematical point of view traveling wave solutions of cross-diffusion systems possess certain properties that essentially distinguish them from diffusion. Specifically, for some velocities of wave propagation they "repeat" structures of solutions of the model local system [14, 17, 18, 21]. This property of cross-diffusion systems may explain certain similarity of dynamics of local FitzHugh model and spatially distributed FitzHugh–Nagumo model.

Motivated by these works we modified the FitzHugh model to include a cross-diffusion connection between the potential and recovery variables. We *hypothesize* that the cross-diffusion regulation plays an important (perhaps, crucial) role in the spatial spreading of potential ([17, 25]). This version of the model provides an avenue both for investigating successful propagation of an excitable neuron and propagation failures, which are extremely important for many applications (see, for example, [26], and Sect. 1.4 below). In [17] we studied the "pure" cross-diffusion modification of FitzHugh model and investigated the characteristics of the spatial propagation of nerve impulses brought on by changes in the velocity of propagation and intensity of the cross-diffusion regulation. We showed that this model demonstrates two types of behaviors, the so-called slow and fast traveling waves. It was shown recently [8] that some biologically motivated modifications of the FitzHugh model demonstrate traveling waves even with three different velocities of their propagation.

The main goal of this paper is to show that at least two types of traveling waves of FHN-model are presented in generalization of FH-model by cross-diffusion.

The paper is organized as follows. Section 1.2 contains a brief description of local neuron dynamics within the framework of the FitzHugh model, as well as the bifurcation portrait of the model. Spatial dynamics of the FitzHugh model using its wave system, which provides an explanation of spatial regimes, e.g., "traveling waves," is given in Sect. 1.3.

Traveling wave solutions of the cross-diffusion modification of the FitzHugh model are described in Sect. 1.4. We show that for any fixed values of the cross-diffusion coefficient and other parameters of the model there exists the critical velocity C^* of wave propagation. The system behavior for $0<C<C^*$(slow waves) dramatically differs from the case when $C>C^*$(fast waves). In particular, the traveling spike with "large amplitude" appeared only for $C>C^*$. We present bifurcation diagrams for both slow and fast waves.

In Sect. 1.5 we consider traveling wave solutions of the FitzHugh model supplemented by diffusion and cross-diffusion terms. Using the techniques of the Tikhonov theorem ([27, 28], etc.) we show that some slow traveling wave solutions of the FitzHugh cross-diffusion model are preserved in the FitzHugh–Nagumo model. We also describe the computer experiments, which show that the fast traveling wave solutions of the FitzHugh cross-diffusion model look similar to those of the FitzHugh–Nagumo model.

Some details of analysis are given in the Appendix.

1.2 FitzHugh Model

The original FitzHugh model (1.1) describes the time dynamics of the neuron excitable membrane potential $P(t)$, which is responsible for the rising phase of neuron firing (see Fig. 1.1), and recovery membrane potential $Q(t)$, which is responsible for the falling phase of the action potential.

In slightly modified form [14] the FitzHugh model is presented as

$$\begin{aligned} eP_t &= -P^3 + P - Q \equiv F_1(P,Q), \\ Q_t &= k_1 P - Q - k_2 \equiv F_2(P,Q) \end{aligned} \tag{1.1}$$

where e, k_1, k_2 are parameters, reflecting intrinsic characteristics of the modeling system. The system has from one (a non-saddle, i.e., a node or a spiral or center) up to three (two non-saddles and a saddle) positive equilibria, $(P*, Q*)$ where $P*, Q*$ are common roots of $F_1(P,Q)$ and $F_2(P,Q)$. Thus, the model has domains of monostability and bistability. FitzHugh's computer analysis [3, 4] revealed that the model can also have limit cycles, namely, "small" cycles (containing a unique equilibrium inside) and "large" one (containing three equilibria inside). FitzHugh hypothesized that the "large separatrix loop" could be realized in the phase plane of system (1.1) for certain parameter values; the trajectory corresponding to this loop was considered as a model of a firing neuron.

The complete analysis of the FitzHugh model was done significantly later ([12, 14], etc.). It was proven in [11] that the principal dynamics of model (1.1) is described by the bifurcation diagram of the bifurcation "3-multiple neutral singular point with the degeneration, focus case," schematically presented in Fig. 1.2 (exact presentation of the bifurcations of high co-dimensions similar to those of our interest in this work was given in [13, 29–31]). In our model this bifurcation is realized in a vicinity of the parameter point M $(k_1 = 0, k_2 = 1, e = 1)$. The description of the bifurcation diagram is given by the following statement [11, 17].

Theorem 1 (i) *The space of parameters* (k_1, k_2, e) *can be subdivided into 21 domains of topologically different phase portraits of system (1.1). The cut of the complete parameter portrait to the plane* (k_1, k_2) *is topologically equivalent to the diagram presented in Fig. 1.2a (left) for arbitrary fixed* $0 < e < 1$ *and to the diagram presented in Fig. 1.2a (right) for arbitrary fixed* $e > 1$.

The parameter boundary surfaces correspond to the following bifurcations in system (1.1):

SN_1, SN_2*: appearance/disappearance of a pair of equilibria on the phase plane;*

$H_1^-,\ H_2^- /\ H_1^+,\ H_2^+$*: change of stability of each of the non-saddle singular points in the Andronov–Hopf supercritical/subcritical bifurcation, respectively;*

C: saddle-node bifurcation of a pair of limit cycles;

L_1, L_2*: appearance/disappearance of a small limit cycle in one of two homoclinics of the saddle; and*

$R^+,\ R^-$*: appearance/disappearance of a large limit cycle in one of two homoclinics of the saddle.*

Domains in Fig. 1.2 are numerated by integer numbers. Parametric portrait of system (1.1) possesses certain symmetry. The domains, which have respective symmetric properties, were numbered by integer with index ***a***, whereas their

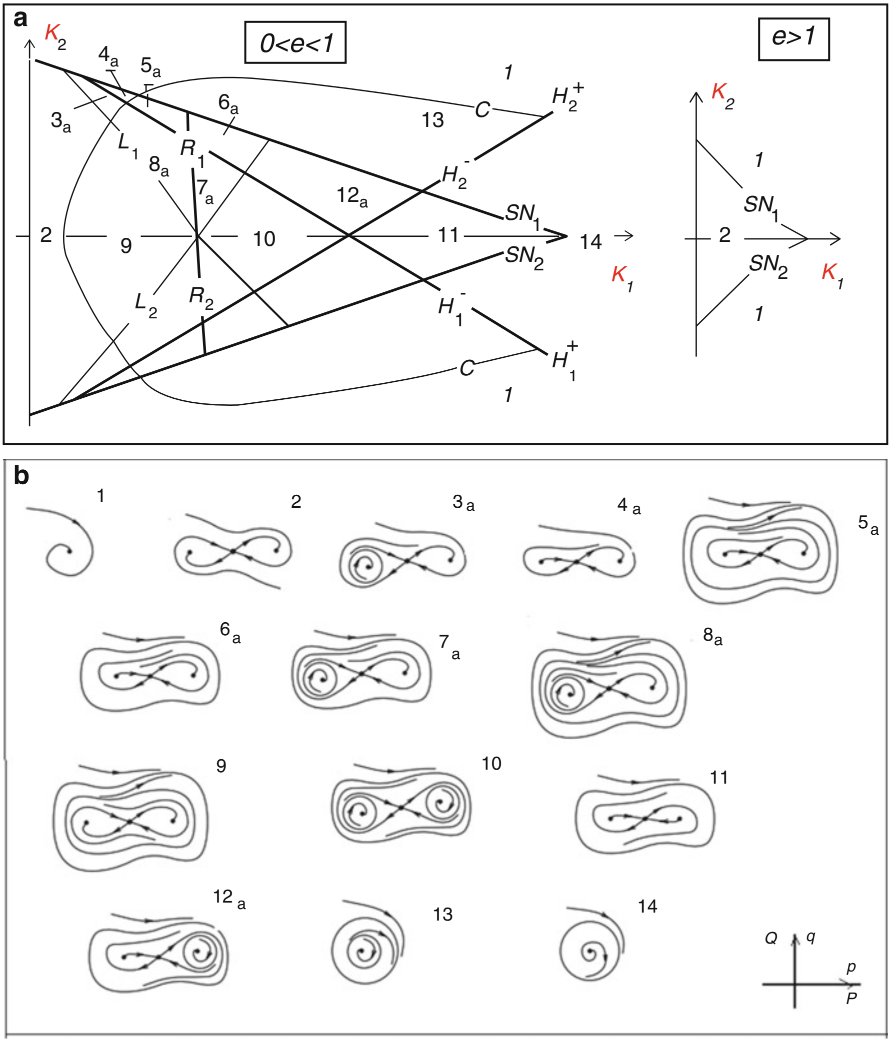

Fig. 1.2 Schematically presented (**a**) (k_1, k_2) — cuts of the bifurcation diagram of FitzHugh model (1.1) for fixed $0 < e < 1$ (*left*) and for $e > 1$ (*right*); (**b**) phase portraits. For any positive e the model has one stable topological node in domain 1 and three equilibria, two non-saddles, and a saddle, inside domain bounded by SN_1, SN_2; boundaries H_1^-, H_2^-/ H_1^+, H_2^+ correspond to the change of stability of each of the non-saddles in the Andronov–Hopf supercritical/subcritical bifurcation, respectively; each of these cycles disappears at homoclinics when the parameter values cross the boundaries L_1, L_2; two limit cycles appear in the phase plane when the parameter values cross the boundary C; the model has the large loop of the saddle separatrixes (a "large homoclinics") for parameter values on the boundaries R_1, R_2

symmetric counterparts have no index in the parameter portraits (Fig. 1.2a) and corresponding phase behaviors are not presented in Fig. 1.2b.

Let us emphasize that the spike-regime (see Fig. 1.1) can be P-component of the trajectory $\{P(t), Q(t)\}$ of the FitzHugh model; this trajectory corresponds to the phase curve of system (1.1), which is *the large separatrix loop* containing two equilibria inside (see the lower left panel in Fig. 1.3c, where coordinate ξ corresponds to t). The loop is realized with parameter values ($k_1 < 1, k_2, e < 1$) belonging to the boundaries $\boldsymbol{R}_1$, $\boldsymbol{R}_2$ in the parameter portrait of the model in Fig. 1.2a. When parameter values crossing this boundary the limit cycle appears/disappears in the phase plane, its shape is "close" to the shape of the corresponding loop. Remark that the phase "8-shape" is realized at the parameter "point of intersection" of boundaries $\boldsymbol{L}_1, \boldsymbol{L}_2, \boldsymbol{R}_1$, and $\boldsymbol{R}_2$.

1.3 The Wave System for FitzHugh Model

1.3.1 FitzHugh Model with Diffusion and Cross-Diffusion

Spatial generalizations of FitzHugh model take into consideration diffusion processes and provide "spread" solutions in a space. Many works were devoted to the study of FHN dynamics, and in particular, to the investigation of "traveling wave" solutions ([4, 5, 7–9, 13, 15, 20, 23, 24], etc.). One of the most recent publications [8] (see also the references therein) describes different time-scale solutions of FHN-model and developed methods of computations that are related to the singular perturbation theoretical approach.

The generalized FitzHugh model, which takes into the consideration diffusion and cross-diffusion, is of the form

$$\begin{aligned} eP_t &= -P^3 + P - Q + D_P P_{xx} + D_Q Q_{xx} \equiv F_1(P,\ Q) + D_P P_{xx} + D_Q Q_{xx}, \\ Q_t &= k_1 P - Q - k_2 \equiv F_2(P,\ Q) \end{aligned} \tag{1.2}$$

where t is time, x is a one-dimensional space variable, and non-negative constants D_P, D_Q are the diffusion and cross-diffusion coefficients, respectively. For $D_P > 0, D_Q = 0$ we get FHN-model, and for $D_P = 0, D_Q \neq 0$ we get the cross-diffusion spatial modification of FH-model (1.1)

$$\begin{aligned} eP_t &= -P^3 + P - Q + D_Q Q_{xx}, \\ Q_t &= k_1 P - Q - k_2 \end{aligned} \tag{1.3}$$

which was investigated in [17].

1.3.2 Wave System of the Model

In what follows, we explore "traveling wave" solutions of system (1.2):

$$P(x,t) = P(x+Ct) \equiv p(\xi), \quad Q(x,t) = Q(x+Ct) \equiv q(\xi),$$

where $\xi = x + Ct$ and positive C is the velocity of the wave propagation. We get the ODE system:

$$\begin{aligned} eCp_\xi &= -p^3 + p - q + D_P p_{\xi\xi} + D_Q q_{\xi\xi} \equiv F_1(p,q) + D_P p_{\xi\xi} + D_Q q_{\xi\xi}, \\ Cq_\xi &= k_1 p - q - k_2 \equiv F_2(p,q) \end{aligned}$$

Differentiating the second equation by ξ, expressing $q_{\xi\xi}$ as

$$q_{\xi\xi} = k_1 p_\xi / C - q_\xi / C^2 = k_1 p_\xi / C - F_2(p,q) / C^2$$

and substituting it to the first equation we get finally that $(p(\xi), q(\xi))$ satisfy the "*wave system*":

$$\begin{aligned} p_\xi &= r \\ D_P r_\xi &= r\left(eC^2 - D_Q k_1\right)/C - F_1(p,q) + D_Q F_2(p,q)/C^2 \\ q_\xi &= (k_1 p - q - k_2)/C \equiv F_2(p,q)/C \end{aligned} \tag{1.4}$$

It is easy to verify that for $D_P = 0$ the wave system is two-dimensional:

$$\begin{aligned} p_\xi\left(eC^2 - D_Q k_1\right)/C &= F_1(p,q) - D_Q F_2(p,q)/C^2 \\ q_\xi &= F_2(p,q)/C \end{aligned} \tag{1.5}$$

Thus, the problem of describing all traveling wave solutions of system (1.2) and their rearrangements is reduced to the analysis of phase curves and bifurcations of solutions of three-dimensional wave system (1.4), which has the additional parameter C. Note that for $D_P = 0$ the wave system (1.5) is two-dimensional; this circumstance essentially simplifies the problem.

Remark 1 Mathematically, cross-diffusion equations possess some special properties, which facilitate their investigation [32, 33]; the most important one is that addition of the cross-diffusion term does not increase the dimensionality of corresponding wave system [6, 17–19, 21, 22].

1.3.3 Traveling Waves of Reaction–Diffusion Model in the Frame of Wave System

Between the bounded traveling wave solutions $(p(\xi), q(\xi))$ of the spatial model (1.2) and the phase curves of the wave system (1.4) there exists a known (see, for instance, [13, 15]) correspondence (Fig. 1.3a–c), which we formulate in the most important cases for p-component $p(\xi)$. The same statements are clearly valid for any component of the model.

Proposition 1 (Definitions)

(i) *A wave front $p(\xi)$ of model (1.2) corresponds to the heteroclinic orbit of wave system (1.5) such that for $\xi \to \pm\infty$ it tends to different in p singular points (Fig. 1.3a).*
(ii) *A wave train $p(\xi)$ of model (1.2) corresponds to the limit cycle of (1.5) (Fig. 1.3b).*
(iii) *A wave impulse $p(\xi)$ of model (1.2) corresponds to the homoclinic orbit of singular point of (1.5) (Fig. 1.3c).*

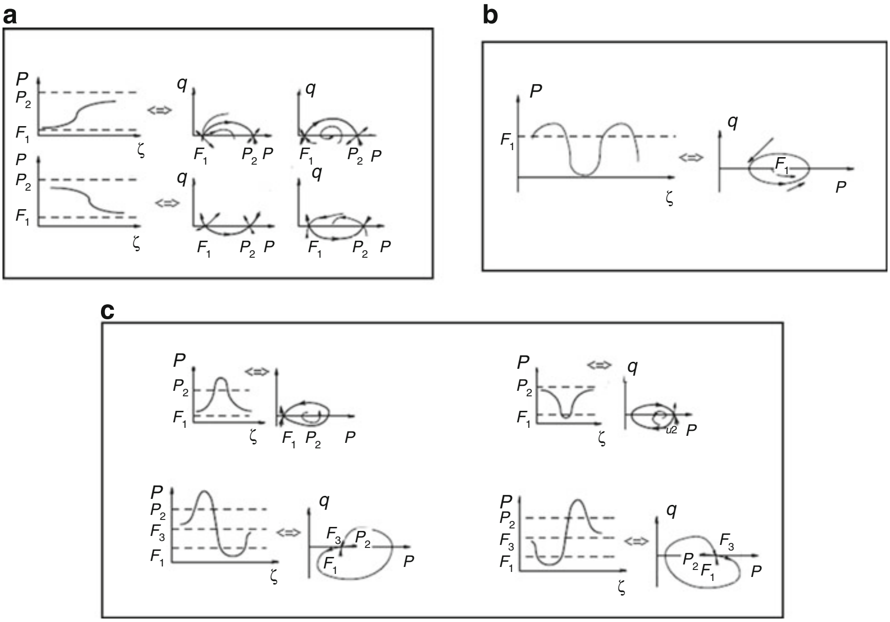

Fig. 1.3 Correspondence between the bounded "traveling wave" solutions of system (1.2) and the phase curves of its wave system (1.5). (**a**) The wave fronts correspond to the heteroclinic phase curves, a separatrix from a saddle to a node or to another saddle; (**b**) the wave train corresponds to the limit cycle; and (**c**) the wave impulses correspond to the homoclinic phase curves, *small* (*upper panel*) or *large* (*lower panel*) separatrix loops

By virtue of this statement, the description of all possible wave solutions of Eq. (1.2), as well as of their changing with variation of parameters of the reaction functions $F_1(p,q), F_2(p,q)$, is reduced to the analysis of phase curves and bifurcations in the wave system (1.5) depending on an additional parameter that is the propagation velocity C of waves. We will consider the behavior of system (1.4), (1.5) depending on variation of the parameters.

1.4 Traveling Waves of Cross-Diffusion Model

1.4.1 Behaviors of Wave System

If $eC^2 \neq D_Q k_1$, then (1.5) can be presented in the form

$$\begin{aligned} p_\xi &= \alpha \left(F_1\,(p,q) - D_Q F_2\,(p,q)\,/C^2\right) \\ q_\xi &= F_2\,(p,q)\,/C, \end{aligned} \tag{1.6$\pm$}$$

where $\alpha = C/\left(eC^2 - D_Q k_1\right)$; sign "+" in the denotation corresponds to the case $\alpha > 0$ and the system is denoted as (1.6+), sign "−" corresponds to the case $\alpha < 0$ and the system is denoted as (1.6−).

It was shown in [17] that the wave system exhibits different behaviors depending on sign of α.

Theorem 2

(i) *Let $C^2 e > Dk_1$ (i.e., $\alpha > 0$). There exists a neighborhood of the parameter point $M\,(e = 1, k_1 = 0, k_2 = 1)$, in which the vector field defined by system (1.6+) has a bifurcation diagram, whose cut to the plane (k_1, k_2) is topologically equivalent to the one presented in Fig. 1.2. The boundaries in (e, k_1, k_2)—parameter space (lines at e—cuts at Fig. 1.2) correspond to the same bifurcations that have been mentioned in the Theorem 1.*

(ii) *Let $eC^2 < Dk_1$ (i.e., $\alpha < 0$). There exists a neighborhood of the parameter point $M\,(e = 1, k_1 = 0, k_2 = 1)$, in which the vector field defined by system (1.6−) has a bifurcation diagram, whose cut to the plane (k_1, k_2) is topologically equivalent to the one presented in Fig. 1.4a for arbitrary fixed positive $0 < e < 1$ (left) and for arbitrary fixed $e > 1$ (right). The boundary surfaces in the parameter space correspond to the following bifurcations:*

SN_1, SN_2: appearance/disappearance of a pair of equilibria on the phase plane;

H: change of stability of the non-saddle equilibrium in Andronov–Hopf subcritical bifurcation;

L_1, L_2: appearance/disappearance of a small limit cycle in homoclinic bifurcations of the saddle;

SC_1, SC_2: upper and lower (respectively) heteroclinics of saddles.

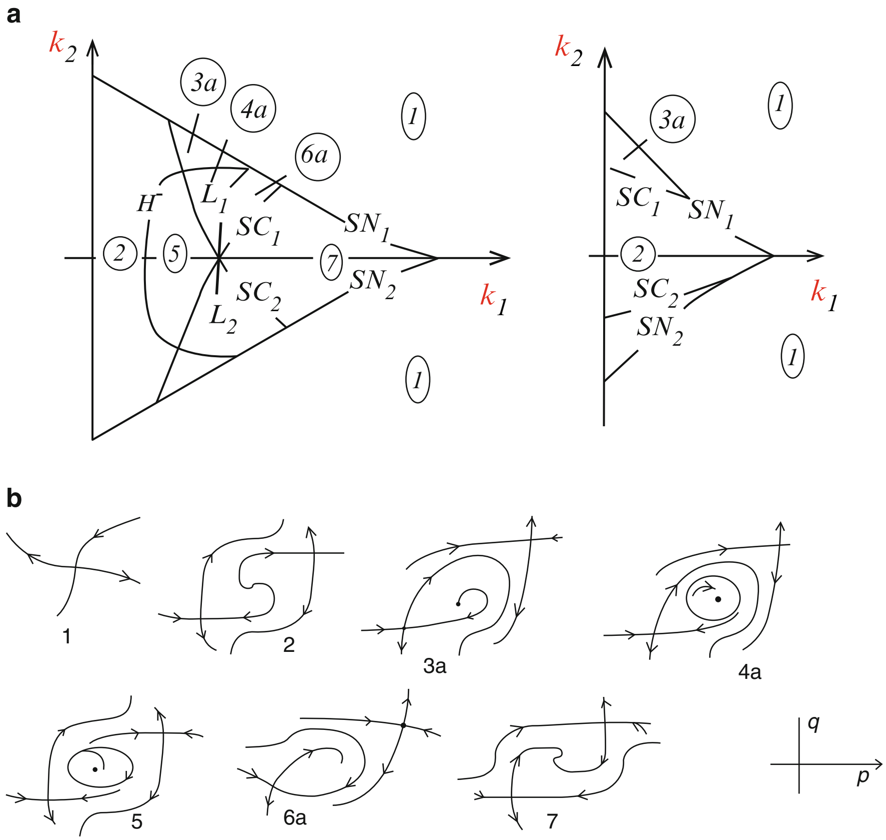

Fig. 1.4 Schematically presented (**a**) $(k_1, k_2)-$ cuts of the bifurcation diagram of wave system (1.6−) of FitzHugh model (1.2) for fixed $0 < e < 1$ (*left*) and for $e > 1$ (*right*); (**b**) phase portraits of the system. Inside the domain bounded by SN_1, SN_2 the system has three equilibria, two saddles, and non-saddle; the boundaries SC_1, SC_2 correspond to the *right* and *left* heteroclinics of saddles; the boundary H corresponds to changing of stability of the non-saddle in Andronov–Hopf subcritical bifurcation; each of these cycles disappears at homoclinics (the boundaries L_1, L_2)

Remark 2 The bifurcation presented in Fig. 1.4 is known as "3-multiple neutral equilibrium with the degeneration, saddle case." In the wave systems (1.6−) of FitzHugh cross-diffusion model (1.3) the bifurcations are realized close to the parameter point M ($e = 1, k_1 = 0, k_2 = 1$) (see also [31]).

1.4.2 Fast and Slow Wave Solutions of FitzHugh Model with Cross-Diffusion

According to Theorem 2 system (1.6) exhibits different behaviors depending on sign of $eC^2 - D_Q k_1 \neq 0$

Traveling wave solution of model (1.3) is called the s*low* wave if its velocity $0 < C < \sqrt{D_Q k_1/e}$ (i.e., $\alpha < 0$) and the *fast* wave if $C > \sqrt{D_Q k_1/e}$ (i.e., $\alpha > 0$).

Collecting together the statements of Theorems 1, 2, and Proposition 1 and taking into consideration that only positive values of model parameters k_1, k_2, e have biophysical meaning, we arrive at the following description of all possible wave solutions.

Theorem 3

(1) *Model (1.3) has the fast traveling wave solutions of the following types (see Fig. 1.2* and *Fig. 1.3):*

the fronts in every Domain of the portraits of Fig. 1.2 except the Domain 1, 13, and 14;

the single train in Domains 3a, 6a, 11, and 14; two trains, differing in their "amplitudes" in Domains 5a, 7a, 9, 12a, and 13; three different trains in Domains 8a and 10; and

the impulses on the boundaries L_1, L_2, and R_1.

(2) *Model (1.3) has the slow traveling wave solutions of the following types (see Fig. 1.4* and *Fig. 1.3):*

the fronts in every Domain of the portraits in Fig. 1.4a except the Domain 1; the monotonous fronts with the maximal "amplitude" on the boundary SC_1, SC_2;

the trains in the domains 4a, 5; and

the impulses with small amplitudes on the boundaries L_1, L_2.

The existence and the shapes of wave impulses, which may be different for slow and fast wave systems, is the problem of our main interest. Figures 1.5 and 1.6 demonstrate some typical phase portraits and solutions for slow wave system (1.6−) and fast wave system (1.6+) for different parameter values.

1.4.3 *Possible Role of Cross-Diffusion Mechanism in Forming of Traveling Waves*

According to Proposition 1, model (1.3) possesses a traveling impulse (spike) if and only if its wave system has a separatrix loop; the impulse has a large amplitude (see Figs. 1.1 and 1.3c) if the separatrix loop contains two points inside itself, and a small amplitude if the separatrix loop contains one point inside itself. Our analysis revealed that only fast wave system exhibits large separatrix loop, whereas slow wave system exhibits small separatrix loops only.

In the work [17] we utilized a modified version of the FitzHugh equations to model the spatial propagation of neuron firing; we assumed that this propagation is essentially caused by the cross-diffusion connection between the potential and recovery variables. This modification, which includes the implicit (although hypothetical) cross-diffusion mechanism, helped explore the effect of a generic drug in the neuron firing process, and explain other biophysical questions still arising [21, 25, 26].

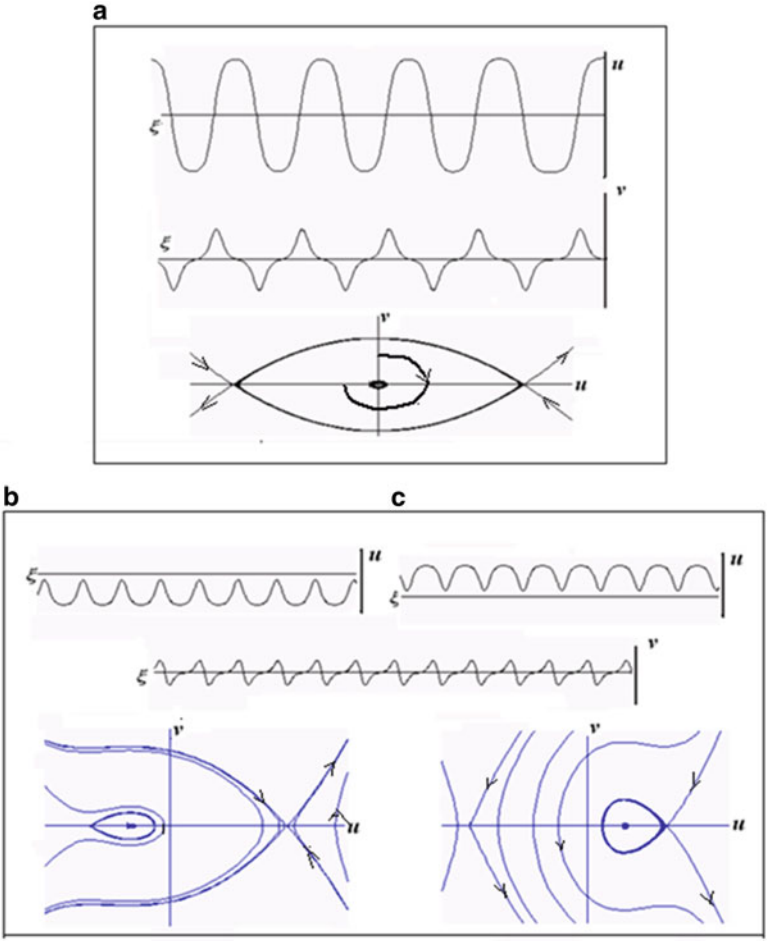

Fig. 1.5 (u,ξ) , (v,ξ) — solutions and (u,v) — phase portraits of slow wave system (1.6—) for $e = .942, k_1 = .9, D_Q = 2, C = .1$ Here $u = q + k_2, v = k_1 p - q - k_2,$ where $p = p(\xi)$, $q = q(\xi)$ are components of system (1.6—). The system has three equilibria, the central equilibrium is a spiral, and the side equilibria are saddles. (**a**) $k_2 = 0,$ stable equilibrium O is placed inside the unstable limit cycle that appeared from saddle heteroclinics; (**b**) $k_2 = .01,$ and (**c**) $k_2 = -.01$. The system has "*left*" (**b**) and "*right*" (**c**) unstable limit cycle containing the stable equilibrium inside; the cycle appears from the saddle homoclinics loop, see the "*left*" (**b**) and "*right*" (**c**) panels

The mathematical problem of interest was the appearance and transformations of the traveling wave solutions, which depended on the model parameters, as those (e, k_1, k_2) which are "intrinsic" to the local system, the cross-diffusion coefficient D_Q, and the propagation speed C, that characterize the axons' abilities for the firing propagation. We studied the wave system of the cross-diffusion version of the model and explored its bifurcation diagram.

We have shown that the cross-diffusion model possesses a large set of traveling wave solutions; besides giving rise to the typical "fast" traveling wave solutions

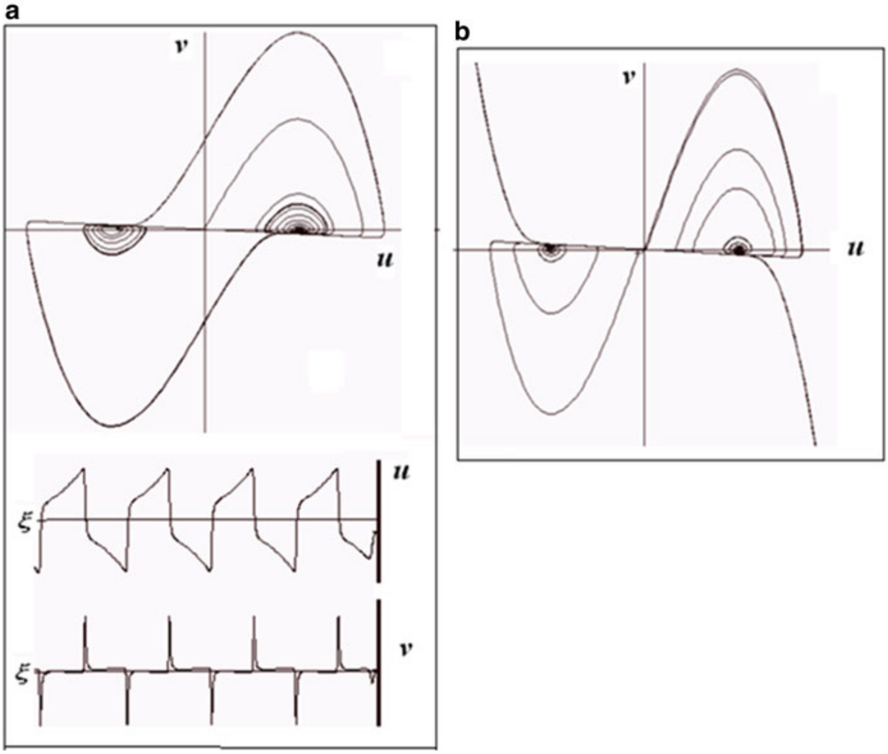

Fig. 1.6 (u, ξ), (v, ξ) — solutions and (u, v) — phase portraits of fast wave system (1.6+) for $e = .09, k_1 = .689, k_2 = 0, D_Q = .3$ Here $u = q + k_2, v = k_1 p - q - k_2,$ where $p = p(\xi)$, $q = q(\xi)$ are variables of (1.6+). The system has three equilibria, a saddle, and two spirals. (**a**) $C = 4.1$. The system has a limit cycle which appears from the homoclinics of the saddle separatrices, the cycle contains inside two spiral equilibria; (**b**) $C = 3.1$, limit cycle is destroyed

exhibited in the original "diffusion" FitzHugh–Nagumo equations, it also gives rise to "slow" traveling wave solutions. This more sophisticated approach indicates that instead of a "one-parametric" set of waves ordered by the propagation speed C, one should consider a two-parametric set of traveling wave solutions with parameters (C, D_Q). We then proved that in the parametric space (C, D_Q) (under fixed parameter values e, k_1, k_2) there exists a parabolic boundary, $D_Q = KC^2$, where constant $K = e/k_1$ separates the domains of existence of the fast and slow waves. The system behavior qualitatively changes with the intersection of this boundary. Let us emphasize that the "traveling spike" that we consider as the "normal" propagation of a nerve impulse is a "fast" traveling wave. Hence, the parabola $D_Q = KC^2$ bounds the area where the "normal" spike propagation is possible. After the intersection of this boundary, due to a very large cross-diffusion coefficient or too small speed of impulse propagation, a "normal" propagation of the nerve impulse is impossible and some violations are inevitable: nerve impulses propagate with decreasing amplitude or as damping oscillations. Introducing cross-diffusion regulations in the FitzHugh model allowed us to observe the propagation of spikes and spike-like oscillations but restricted their velocities from below or, equivalently, maintained the upper boundary for the cross-diffusion coefficient. It means that if, for any reason (e.g., as a result of the effect of a generic drug), the speed of transmission of a signal along the axon is reduced, then the "normal" neuron firing propagation in the form of a traveling spike is impossible. The increase of the cross-diffusion coefficient beyond the "normal" value implies the same result.

1.5 Traveling Wave Solution of FHN-Model

1.5.1 Slow Waves

Consider more precisely wave system (1.4):

$$\begin{aligned} p_\xi &= r \\ D_P r_\xi &= r\left(eC^2 - D_Q k_1\right)/C - F_1(p,q) + D_Q F_2(p,q)/C^2 \\ q_\xi &= (k_1 p - q - k_2)/C \equiv F_2(p,q)/C \end{aligned} \tag{1.7}$$

where $F_1(p,q) = \left(-p^3 + p - q\right),\ F_2(p,q) = k_1 p - q - k_2,\ e > 0,\ k_1 > 0, k_2 \geq 0.$

Suppose that diffusion coefficient $D_P \to 0$. For the limiting system

$$\begin{aligned} p_\xi &= C\left(F_1(p,q) - D_Q F_2(p,q)/C^2\right)/\left(eC^2 - D_Q k_1\right) \\ q_\xi &= (k_1 p - q - k_2)/C \equiv F_2(p,q)/C \end{aligned} \tag{1.8}$$

is equivalent to the wave system (1.5) of cross-diffusion model (1.3).

Following the idea of the Tikhonov theorem [28] and its numerous generalizations (see, e.g., [27] and references therein) we prove numerically the following statement.

Statement 1 With parameter values in neighborhood of point $M\left(D_Q e = 1, k_1 = 1, k_2 = 0\right)$ and C, D_Q such that condition $\alpha \equiv C/\left(eC^2 - D_Q k_1\right) < 0$ holds there exist area $\Omega(p,q)$, $(0,0) \in \Omega$ in the phase plane (p,q) where the wave profiles $(p(\xi), q(\xi))$ of system (1.5) approximate two components $(p(\xi), q(\xi))$ of the wave profiles $(p(\xi), p_\xi(\xi), q(\xi))$ of system (1.4) for ($p_0 = p(\xi_0), q_0 = q(\xi_0)) \in \Omega,\ \xi \in (const, \infty)$, including homoclinics of equilibria.

According to this Statement, the slow wave solutions $(p(\xi), q(\xi))$ of model (1.1) with diffusion and cross-diffusion can be qualitatively approximated by the solutions of the model with only cross-diffusion term (compare Figs. 1.5 and 1.7).

Thus, the solution of the modification of the FitzHugh model, which accounts for the cross-diffusion and small diffusion terms, demonstrates the *slow traveling waves* (having relatively small velocity of propagation) similarly to the model with only cross-diffusion term under certain values of the model parameters.

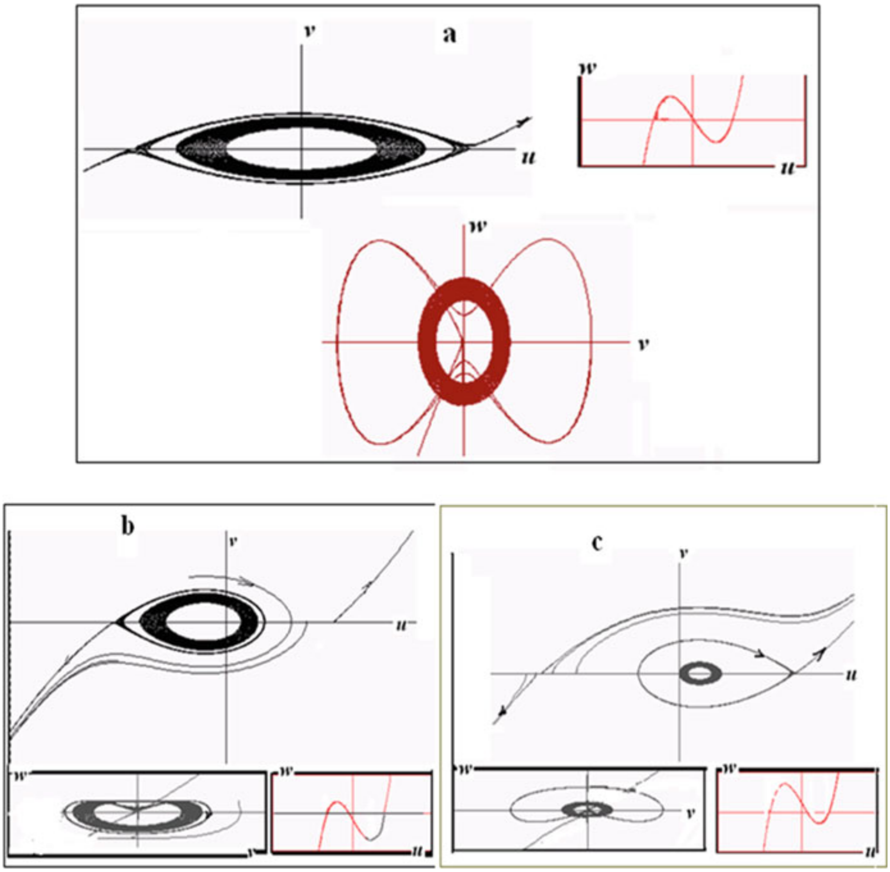

Fig. 1.7 $(u, v)-$, $(u, w)-$, $(w, v)-$ cuts of phase portraits of wave system (1.4). Here $u = q + k_2, v = k_1 p - q - k_2$, $w = v_\xi$, where $p = p(\xi)$, $q = q(\xi)$ are variables of system (1.4). The parameter values are $k_1 = .9, e = .9335, C = .1, D_P = .5, D_Q = 1.5$. (**a**) "Symmetric" case, k_2=0. The system demonstrates an unstable limit cycle that arose from "heteroclinics cycle" composed by separatrixes of the saddle points, the stable equilibrium O is placed inside this "funnel"(see (w, v)—cut); (**b**, **c**) $k_2 = \pm.005$. The system has "homoclinics" cycle containing stable point O; $k_2 = .005$ at the *left* and $k_2 = -.005$ at the *right panels*, correspondingly

1.5.2 Fast Waves

Numerous studies showed that FHN-model possesses spike type "fast" wave solutions (see, for example, [8] and reference therein).

Our computer experiments revealed that the fast solutions observed in the fast FH-cross-diffusion wave system (1.5+) have counterparts in the wave system (1.4) where $\overline{\alpha} \equiv eC^2 - D_Q k_1 > 0$ (compare Fig. 1.6 and Fig. 1.8a–c. The latter Figure demonstrates phase curves and trajectories of the model with different values of the

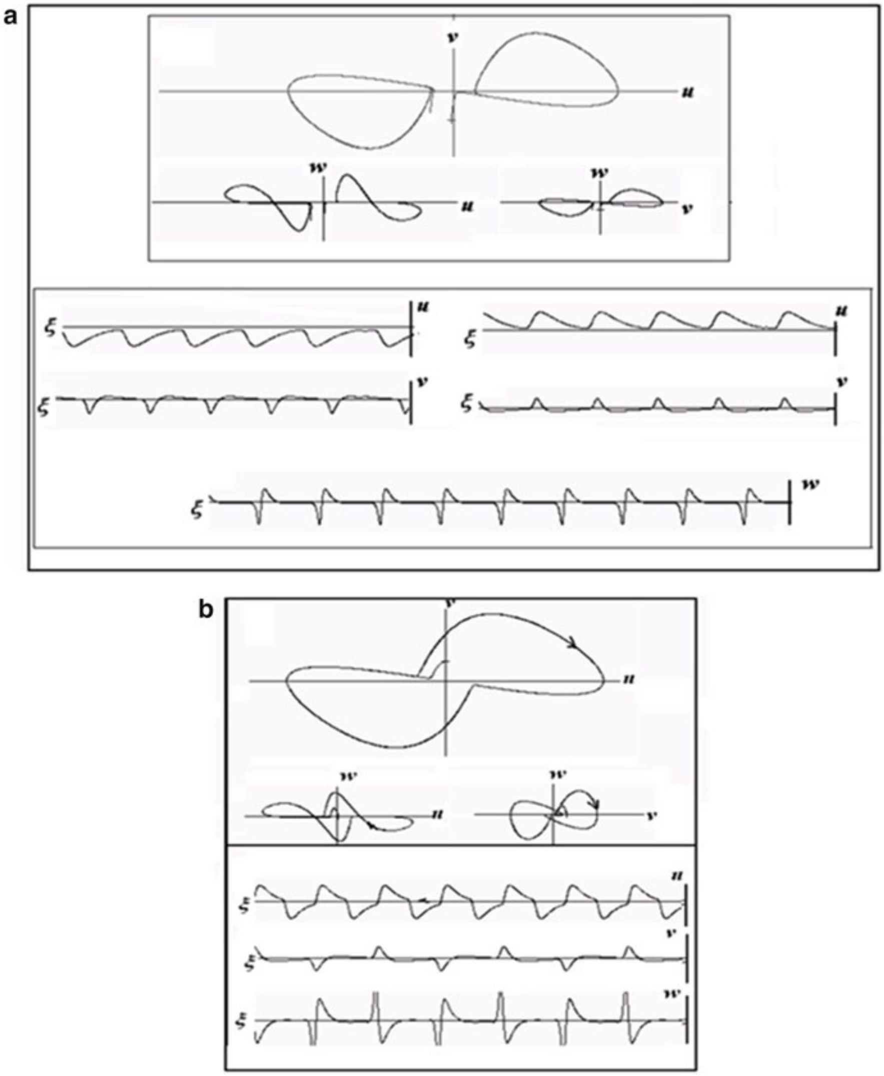

Fig. 1.8 $(u, v)-$, $(u, w)-$, $(w, v)-$ cuts of phase portraits and solutions $u(\xi), v(\xi), w(\xi)$ of wave system (1.4) in the case when $\overline{\alpha} = \left(eC^2 - D_Q k_1\right) > 0$. Here $u = q+k_2, v = k_1 p-q-k_2,\ w = v_\xi$, where $p = p(\xi)$, $q = q(\xi)$, $r = r(\xi)$ are variables of system (1.4). Parameters are $k_1 = .689, k_2 = 0, e = .15, D_P = .7, D_Q = .5$. (**a**) $C = 7$. The system has two limit cycles, whose shapes are close to the small homoclinic loop (see Fig. 1.3c). (**b**) $C = 4.8$. The system has a limit cycle, whose shape is close to the large homoclinic loop (this case is similar to the case that was presented in Fig. 1.6a); (**c**) $C = 2.5$. The limit cycle is destroyed

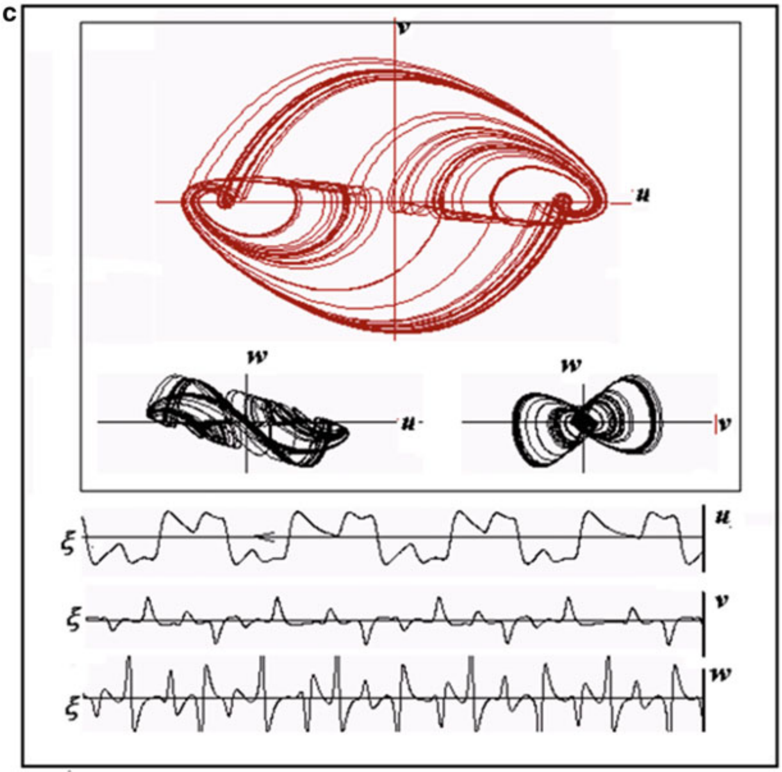

Fig. 1.8 (Continued)

speed propagation C but identical values of all other parameters). Notice that the qualitative behaviors of the model presented in these figures actually do not depend on cross-diffusion coefficient D_Q, in particular, for $D_Q = 0$.

Overall, our investigation of the diffusion—cross-diffusion modification of the FitzHugh model (the full model for brevity)—reveals an interesting phenomenon: if we consider the “fast” wave solutions, then the qualitative behavior of the full system coincides with that of the FH-model accounting for only diffusion term, but if we consider the “slow” wave solution, then the qualitative behavior of the full model coincides with that of FH-model accounting only for the cross-diffusion term. Both types of solutions qualitatively coincide with corresponding solutions of cross-diffusion wave system.

A.1 Appendix

A.1.1 Lienard Form of the FitzHugh Model and Its Wave System

Through the change of variables

$$(P,Q) \to (U,V) : U = Q + k_2,\ V = F_2(P,Q) \equiv k_1 P - Q - k_2,$$
$$(P = (U+V)/k_1,\ Q = U - k_2,\ k_1 \neq 0) \tag{1.9}$$

the local model (1.1) is transformed to the generalized Lienard form:

$$U_t = V, eV_t = (U+V)/k_1 - (U+V)^3/{k_1}^3$$
$$+ k_2 - U \equiv f(U) + V(g_1(U) + VG(U)) \equiv \Phi(U,V), \tag{1.10}$$

Where

$$\begin{aligned} f(u) &= -u^3/k_1^2 + u(1-k_1) + k_1 k_2, \\ g_1(u) &= (1-e) - 3u^2/k_1^2, \\ G(u,v) &= -(3u+v)/k_1^2 \end{aligned} \tag{1.11}$$

Model (1.2) after transformation (1.10) reads

$$\begin{aligned} &U_t = V, \\ &eV_t = \Phi(U,V) + D_P V_{xx} + \left(D_P + D_Q k_1\right) U_{xx} \end{aligned} \tag{1.12}$$

Model (1.3) after transformation (1.10) reads

$$\begin{aligned} &U_t = V, \\ &eV_t = \Phi(U,V) + D_Q k_1 U_{xx} \end{aligned} \tag{1.13}$$

A *traveling wave solution* of systems (1.12) and (1.13) is defined as a pair of bounded functions

$$U(x,t) = U(x+Ct) \equiv u(\xi),\quad V(x,t) = V(x+Ct) \equiv v(\xi),$$

where $C > 0$ is a velocity of propagation.

Let's now replace the capital letters in (1.9) with small letters, reduce p and q via $p = (u+v)/k_1,\ q = u - k_2,\ k_1 \neq 0.$

Take into the consideration that $u_t = Cu_\xi,\ u_x = u_\xi;\ v_t = Cv_\xi,\ v_x = v_\xi;\ u_{xx} = u_{\xi\xi} = v_\xi/C$ and put $w = v_\xi, w_\xi = v_{\xi\xi}$ we get the wave system of system (1.12) in the form

$$\begin{aligned} u_\xi &= v/C \\ v_\xi &= w \\ D_P w_\xi &= (eC - (D_P + D_Q k_1)/C)w - \Phi(u, v) \end{aligned} \tag{1.14}$$

where $\Phi(U, V) = f(U) + V(g_1(U) + VG(U, V))$ and functions $f(u), g_1(u), G(u, v)$ are given by (1.11).

The wave system of (1.13) takes the form

$$\begin{aligned} u_\xi &= v/C, \\ \big(eC - D_Q k_1\big)/C\big) v_\xi &= \Phi(u, v) \end{aligned} \tag{1.15}$$

System (1.15) contains the factor $1/\alpha \equiv \big(eC - D_Q k_1\big)/C\big)$ which we assumed to be non-zero.

Behaviors of system (1.15) depend on the sign of parameter α. For $\alpha > 0$ there exists a parameter domain containing point $M(e = 1, k_1 = 0, k_2 = 1)$, where the vector field defined by system (1.15) is topologically orbitally equivalent to those defined by local system (1.1). It realizes the bifurcation of co-dimension 4 with symmetry ("spiral case") [11]. For $\alpha < 0$ parameter point $M(e = 1, k_1 = 0, k_2 = 1)$ is also the point that corresponds to the bifurcation of co-dimension four with symmetry but as a "saddle case." So, behaviors of system (1.15) for $\alpha > 0$ are different from those for $\alpha < 0$ (see details in [17]).

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