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TRAVELLING CALCIUM WAVES IN SYSTEMS WITH NON-DIFFUSING BUFFERS

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The existence and structural stability of travelling waves of systems of the free cytosolic calcium concentration in the presence of immobile buffers are studied. The proof is carried out by passing to zero with the diffusion coefficients of buffers. Thus, its method is different from Ref. 13 where the existence is proved straightforwardly.

Keywords: Calcium dynamics; travelling waves; implicit function theorem.

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1. Formulation of the Problem

In this paper, we analyze the problem of existence and properties of travelling wave solutions to the system of equations which may describe the evolution of the concentration of the cytosolic calcium inside cells in the presence of $n > 1$ immobile buffers. The aim of the paper is to prove that travelling wave solutions for this class of systems can be obtained as a limit of waves for systems with nonzero diffusion coefficients of the buffers. To do this we apply the theory of travelling waves for parabolic systems explained in Ref. 14 for non-degenerate system and pass to the limit with the diffusion coefficients of the buffers. The existence of travelling waves together with their stability for the degenerate system (with non-diffusing buffers) was proved in a straightforward way in Ref. 13 and the asymptotic in time properties of solutions to this system was analyzed in Ref. 10. It seems, however, that the method used in our paper sheds an additional light on the properties of travelling waves in buffered systems. It considers the system with non-diffusing buffers as a limit of equations with small diffusing coefficients and provides some additional information about the behaviour of solutions to the whole family of systems. In a sense it is more realistic, because in many situations we should take into account very small but nonvanishing diffusivities of buffers. Thus, the travelling wave solutions for the partially degenerate system are approximated by the travelling waves for non-degenerate systems. It is necessary to emphasize that such an approximation is possible; thanks to the monotonicity properties satisfied by the source terms of the considered equations.

Calcium waves and oscillations are one of the most important mechanisms by which cells control their activity and coordinate it with their neighbours. The Ca^{2+} signals often propagate through the cytoplasm as a regenerative wave. The propagation consists both in the inflow from the extracellular medium and in successive releases of calcium from endoplasmic reticulum clusters via the autocatalytic reaction by the free calcium ions diffusing from the regions of its higher concentration. The spatio-temporal distribution of calcium ions may control diverse processes, such as fertilization, proliferation, morphogenetic development, gene expression, learning and memory, synaptic communication, contraction, hormone secretion, cell movement, and wound repair. The increased concentration of calcium may in turn initiate Ca^{2+} oscillations, which can be recognized and responded by the cells.[1,3] More recently it has been discovered that too high cellular Ca^{2+} concentration can cause cytotoxicity and trigger either apoptotic or necrotic cell death.[2]

It is known that calcium wave propagation inside a cell is significantly influenced by the presence of buffers. Buffers are big proteins (e.g. parvalbumin, calsequestrin, calretinin or EGTA) which can bind a large amount of calcium inside cells. The amount of Ca^{2+} ions, which can be bound to different kinds of buffers may reach 99%.[5] The reaction of binding Ca^{2+} to the ith protein B_i to form the ith binding complex B_i, $i = 1, \ldots, n$, can be written as: $B_i + Ca^{2+} \rightleftarrows Ca^{2+}B_i$.

We assume that the kinetic constant of the ith binding reaction is equal to $k_+^i > 0$ and the kinetic constant of the reverse reaction is equal to $k_-^i > 0$. Most of the buffers are practically immobile. Though the diffusivities of some of the buffers are not negligible (with respect to the diffusion coefficient for free calcium ions), in some situations we may suppose that all of them have zero diffusion coefficients as it is done in Ref. 13. This simplifying assumption may facilitate the analysis of the travelling waves in buffered systems, in particular the influence of buffers on their speed and profile. The present paper shows that such system may be, in a way, replaced by systems with small but nonzero diffusivities of the buffer particles and vice versa.

The evolution of the concentration of the free cytosolic calcium u is usually described by the system of reaction-diffusion equations of the form:

$$\frac{\partial u}{\partial t} = D\Delta u + f(u) + \sum_{i=1}^{n}[k_-^i(b_0^i - \widetilde{v}_i) - k_+^i u\widetilde{v}_i],$$

$$\frac{\partial \widetilde{v}_i}{\partial t} = D_i\Delta\widetilde{v}_i + k_-^i(b_0^i - \widetilde{v}_i) - k_+^i u\widetilde{v}_i, \quad i = 1, \ldots, n, \tag{1.1}$$

where $\Delta = \partial^2/\partial x_1^2 + \cdots + \partial^2/\partial x_s^2$, $s \geq 1$, $\widetilde{v}_i$ denotes the concentration of the ith buffer which is not bound to calcium, whereas b_0^i denotes the total concentration of the ith buffer. We have thus $b_0^i = [\mathrm{B}_i] + [\mathrm{Ca}^{2+}\,\mathrm{B}_i]$ with $\widetilde{v}_i = [\mathrm{B}_i]$. In system (1.1), D and D_i denote the diffusion coefficients of the free cytosolic calcium and the ith free buffer.

Let

$$v_i = b_0^i - \widetilde{v}_i,$$

that is to say $v_i = [\mathrm{Ca}^{2+}\,\mathrm{B}_i]$. Now, after denoting $G_i(u, v_i) = k_-^i v_i - k_+^i u(b_0^i - v_i)$, system (1.1) can be written as

$$\begin{aligned}\frac{\partial u}{\partial t} &= D\Delta u + f(u) + \sum_{i=1}^{n} G_i(u, v_i),\\ \frac{\partial v_i}{\partial t} &= D_i \Delta v_i - G_i(u, v_i), \quad i = 1, \ldots, n.\end{aligned} \tag{1.2}$$

In fact, these variables are used in Ref. 11 analyzing travelling waves for buffer systems with very fast kinetics.

Assumption 1. The function $f(\cdot) \in C^2(\mathbb{R})$ is of bistable type, i.e. that the equation

$$f(u) = 0$$

has exactly three solutions: $u_1 \geq 0$, $u_3 > u_1$ and $u_2 \in (u_1, u_3)$. The zeros u_1 and u_3 are stable, i.e. $f'(u_1) < 0$, $f'(u_3) < 0$, whereas u_2 is unstable, i.e. $f'(u_2) > 0$.

A simple example of a function satisfying condition 1 of the above assumption is a cubic polynomial $f(u) = (u - \sigma)(1 - u)(u - u_0)$ with $\sigma \in [0, 1)$ and $u_0 \in (\sigma, 1)$.

Below, *we will abstract from the concrete form of the functions* G_i, having, however, in mind mainly its initial application.

Assumption 2. For all $i = 1, \ldots, n$:

(i) G_i are of C^3 class. For all $k = 1, 2, 3$, the equation $G_i(u_k, v_i) = 0$ has a unique solution v_i^k, such that $v_i^1 < v_i^2 < v_i^3$.
(ii) $G_{i,u}(u, v_i) < 0$ and $G_{i,v_i}(u, v_i) > 0$ for all $u \in [u_1, u_3]$, $v_i \in [v_i^1, v_i^3]$.

Let us denote

$$P_k = (u_k, v_1^k, \ldots, v_n^k), \quad k = 1, 2, 3, \tag{1.3}$$

thus component-wise

$$P_1 < P_2 < P_3. \tag{1.4}$$

Remark 1.1. Obviously, for $k_-^i, k_+^i > 0$, the functions $G_i(u, v_i) = k_-^i v_i - k_+^i u$ $(b_0^i - v_i)$ satisfy Assumption 2. This time

$$P_k = (u_k, \underline{v}_1^k, \ldots, \underline{v}_n^k), \quad k = 1, 2, 3, \tag{1.5}$$

where

$$\underline{v}_j^k = u_k \frac{k_+^j b_0^j}{(k_-^j + k_+^j u_k)} \,. \tag{1.6}$$

Thus, $\underline{v}_j^1 < \underline{v}_j^2 < \underline{v}_j^3$, $j = 1, \ldots, n$, and the inequality (1.4) is satisfied.

In this paper, we are interested in the travelling wave solutions to system (1.2), with the functions G_i satisfying Assumption 2, joining its constant steady states P_1 and P_3. To be more precise we are looking for solutions being functions of a scalar variable $\xi = x \cdot n - qt$, i.e.

$$u(x,t) = u(\xi), \qquad v_i(x,t) = v_i(\xi), \;\; i = 1, \ldots, n, \tag{1.7}$$

where $q \in \mathbb{R}^1$ is the speed of the wave and $n \in \mathbb{R}^s$, $|n| = 1$, is the direction of propagation, which satisfy the following conditions at infinities:

$$\begin{aligned} &\lim_{\xi \to -\infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_1, v_1^1, \ldots, v_n^1) = P_1, \\ &\lim_{\xi \to \infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_3, v_1^3, \ldots, v_n^3) = P_3, \\ &\lim_{|\xi| \to \infty} (u'(\xi), v_1'(\xi), \ldots, v_n'(\xi)) = (0, 0, \ldots, 0). \end{aligned} \tag{1.8}$$

We have used the *symbol q for denoting the speed of the travelling wave solution* instead of the usual denotation v. This is due to the fact that we have chosen the symbols v_i to represent the concentration of the buffer particles. Without losing generality we can assume $n \equiv \hat{x}_1$. Hence $\xi = x_1 - qt$. The ansatz (1.7) changes system (1.2) to the system

$$Du'' + qu' + f(u) + \sum_{i=1}^{n} G_i(u, v_i) = 0, \tag{1.9}$$

$$D_i v_i'' + q v_i' - G_i(u, v_i) = 0, \quad i = 1, \ldots, n, \tag{1.10}$$

where $'$ denotes differentiation with respect to the variable ξ. Thus, looking for travelling waves is equivalent to looking for appropriate heteroclinic connecting orbits for ordinary systems of equations.

Remark 1.2. Consider the equation for the calcium concentration in the absence of buffers

$$\frac{\partial u}{\partial t} = D \Delta u + f(u). \tag{1.11}$$

In this case the profile of the travelling wave is determined by the equation

$$Du'' + qu' + f(u) = 0. \tag{1.12}$$

Obviously, there exists a unique $q_r \in \mathbb{R}^1$ such that for $q = q_r$ there exists a strictly monotone heteroclinic solution $u_r(\cdot)$, which is unique (up to a shift in ξ), such that $u_r(-\infty) = u_1$ and $u_r(\infty) = u_3$. The sign of q_r depends on the sign of the integral

$$I_f = \int_{u_1}^{u_3} f(u)du.$$

Thus, for $I_f \geq 0$ ($I_f < 0$), we have $q_r \leq 0$ ($q_r > 0$) (see, e.g. Ref. 6). It can be seen by multiplying (1.12) by u' and integrating from $-\infty$ to ∞.

Remark 1.3. Let

$$U := (U_1, U_2, \ldots, U_{n+1}) := (u, v_1, \ldots, v_n) \tag{1.13}$$

and

$$F_1(U) := f(u) + \sum_{i=1}^{n} G_i(u, v_i), \qquad F_i(U) := -G_{i-1}(u, v_{i-1}), \quad i = 2, \ldots, n. \tag{1.14}$$

According to Assumptions 1 and 2 one can easily note that for all $U \in [P_1, P_3]$ the following conditions hold:

$$F_{i,j}(U) \geq 0, \quad i \neq j, \qquad F_{1,j}(U) > 0, \quad F_{j,1}(U) > 0, \;\; j \neq 1, \tag{1.15}$$

where $F_{i,j} = F_{i,U_j}$.

As we mentioned above our main aim is to prove the existence of heteroclinic solutions for a partially degenerated version of the system (1.9)–(1.10), i.e. the system

$$Du'' + qu' + f(u) + \sum_{i=1}^{n} G_i(u, v_i) = 0, \tag{1.16}$$

$$qv_i' - G_i(u, v_i) = 0, \quad i = 1, \ldots, n. \tag{1.17}$$

In the paper, we prove that travelling waves having monotone profiles for systems with vanishing diffusion for all of the buffers are a limit of travelling fronts with monotone profiles for systems with nonzero diffusion coefficients. This restriction is sensible, as it is known (see Theorem 6.1, p. 245 in Ref. 14) that non-monotone travelling waves are unstable, whereas the monotone ones are stable. In Sec. 2 and in Appendix A we examine the properties of the linearization matrices. Using these results we are able to prove, for all arbitrarily small but nonzero diffusion coefficients of the buffers, the existence of the desired heteroclinic travelling waves by using the theory explained in Ref. 14 (see Theorem 4.1). The existence result for the travelling wave solutions to system (1.2) with $D_i = 0$, $i = 1, \ldots, n$, is formulated in Theorem 5.1. The structural stability of the obtained heteroclinic solutions is proved in Sec. 6. The possibility to estimate the second derivatives of the obtained heteroclinic solutions makes it possible to use the minimax principle to estimate the speed of the wave (see Sec. 7). In Sec. 8 we consider the case of so-called fast buffers. We prove the *a priori* estimates in the limit if very fast kinetics and sketch the proof of the existence of heteroclinic connections.

2. Properties of the Linearization Matrices

In this section we will analyze the properties of the matrices obtained by linearization of the source terms at the right-hand sides of the system (1.2) at the points P_k, $k = 1, 2, 3$. Our considerations are mainly based on lemmas and theorems explained in Ref. 7. The objective of this section is to characterize the eigenvalues and eigenvectors of the above-mentioned matrices.

One can easily check that for $u = u_k + \delta u$, $v_j = v_j^k + \delta v_j$ the first-order Taylor expansion of the vector function corresponding to the source terms of system (1.2) has the following form:

$$\begin{bmatrix} f(u) + \sum_{i=1}^{n}[k_-^i v_i - k_+^i u(b_0^i - v_i)] \\ -k_-^1 v_1 + k_+^1 u(b_0^1 - v_1) \\ \vdots \\ -k_-^n v_n + k_+^n u(b_0^n - v_n) \end{bmatrix} \cong \mathcal{K} \begin{bmatrix} \delta u \\ \delta v_1 \\ \cdots \\ \delta v_n \end{bmatrix}, \tag{2.1}$$

where $(n+1) \times (n+1)$ matrix $\mathcal{K}$ is defined as

$$\mathcal{K} = \begin{bmatrix} a - \sum_{i=1}^{n} a_i & b_1 & \dots & b_n \\ a_1 & -b_1 & \dots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ a_n & 0 & \dots & -b_n \end{bmatrix}. \tag{2.2}$$

with

$$a = f_{,u}(u_k), \quad a_i = -G_{i,u}(u_k, v_i^k), \quad b_i = G_{i,v_i}(u_k, v_i^k). \tag{2.3}$$

According to Assumption 2 for a_i, b_i given by the above expressions the following inequalities are satisfied:

$$a_i > 0, \quad b_i > 0, \ \ i = 1, \dots, n. \tag{2.4}$$

In the next section we will need the following lemma characterizing the properties of the matrix $\mathcal{K}$.

Lemma 2.1. *The matrix $\mathcal{K}$ is irreducible. If $a < 0$, then the eigenvalues μ of the matrix $\mathcal{K}$ are contained in the left half-plane $Re(\mu) < 0$. For $a > 0$ at least one of the eigenvalues μ of the matrix $\mathcal{K}$ is contained in the right half-plane $Re(\mu) > 0$.*

The proof of the above lemma will be given in Appendix A.

3. *A priori* Estimates for Monotone Heteroclinic Solutions for the Non-Degenerate Systems

Now, using the special form of the considered system we will estimate the values of derivatives of the heteroclinic solutions to system (1.9)–(1.10) as well as its speed parameter q. (We assume that such solutions exist. The existence theorem for non-degenerate system, i.e. with all the diffusion coefficients positive, is given in Sec. 4.) Our aim is mainly to examine the properties of the heteroclinic solutions as the coefficients D_i, $i = 1, \ldots, n$, tend to zero. The estimations derived in this section will be a basis for obtaining a solution to the system with $D_i = 0$. It is worthwhile to underline that the possibility of the *a priori* estimates for the derivatives of heteroclinic solutions to system (1.9)–(1.10), which are independent of the values of the diffusion coefficients for buffers, is guaranteed by the special structure of the functions F_i (satisfying conditions (1.15)) and the assumed monotonicity of the solutions for $D_i > 0$ (implied by Theorem 4.1).

Lemma 3.1. *For any C^2 monotone heteroclinic solution $(u, v_1, \ldots, v_n)(\cdot)$ of system* (1.9)–(1.10) *the following estimations hold*:

$$\|u\|_{C^3(\mathbb{R})} < \mathcal{S}_1, \quad |q| \le \widetilde{Q}, \quad \|v_i\|_{C^2(\mathbb{R})} < \mathcal{S}_2, \quad i = 1, \ldots, n. \tag{3.1}$$

These estimations are independent of the values of the diffusion coefficients D_i, $i = 1, \ldots, n$.

Proof. First let us estimate the first derivative of the function $u(\cdot)$. Let us add all the equations. We obtain the equation:

$$Du'' + qu' + \sum_{i=1}^{n} D_i v_i'' + q \sum_{i=1}^{n} v_i' + f(u) = 0. \tag{3.2}$$

Let us multiply this equation by u'. Then after replacing $v_i''u'$ by $(v_i'u')' - v_i'u''$ and $u''u'$ by $1/2(u'^2)'$ we obtain

$$1/2D((u')^2)' + qu'u' + \sum_{i=1}^{n} D_i(v_i'u')' - \sum_{i=1}^{n} D_i v_i'u'' + \sum_{i=1}^{n} qv_i'u' + f(u)u' = 0.$$

Substituting $u'' = -1/D[qu' + \sum_{j=1}^{n} D_j v_j'' + q\sum_{j=1}^{n} v_j' + f(u)]$ we obtain

$$1/2D((u')^2)' + qu'u' + \sum_{i=1}^{n} D_i(v_i'u')' + S + \sum_{i=1}^{n} qv_i'u' + f(u)u' = 0,$$

where

$$S = q\sum_{i=1}^{n} \eta_i v_i'u' + \sum_{i=1}^{n}\sum_{j=1}^{n} \eta_i D_j v_i'v_j'' + q\sum_{i=1}^{n}\sum_{j=1}^{n} \eta_i v_i'v_j' + \sum_{i=1}^{n} \eta_i v_i' f(u)$$

with $\eta_i = D_i/D$. So

$$\frac{D}{2}\left[\left(u' + \sum_{i=1}^{n} \eta_i v_i'\right)^2\right]' + q\left\{u'u' + \sum_{i=1}^{n}\left[v_i'u' + \eta_i v_i'u' + \sum_{j=1}^{n}\eta_i v_i' v_j'\right]\right\}$$
$$+ f(u)\left[\sum_{i=1}^{n}\eta_i v_i' + u'\right] = 0. \tag{3.3}$$

Below, we will show first that the first derivatives of the solution are globally bounded and then q is bounded. Integrating Eq. (3.3) from $-\infty$ to ∞ we obtain

$$q\int_{\mathbb{R}^1}\left\{u'u' + \sum_{i=1}^{n}\left[v_i'u' + \eta_i v_i'u' + \sum_{j=1}^{n}\eta_i v_i'v_j'\right]\right\}d\xi$$
$$= -\sum_{i=1}^{n}\int_{\mathbb{R}^1}\eta_i f(u(\xi))v_i'(\xi)d\xi - \int_{u_1}^{u_3} f(u)du. \tag{3.4}$$

For any $\xi \in \mathbb{R}^1$ we have

$$\left|-\sum_{i=1}^{n}\int_{-\infty}^{\xi}\eta_i f(u(\xi))v_i'(\xi)d\zeta - \int_{u_1}^{u(\xi)} f(u)du\right| < K_1, \tag{3.5}$$

as the expression under the modulus sign can be written as

$$-\int_{u_1}^{u(\xi)} f(u)du - \sum_{i=1}^{n}\eta_i(v_i(\xi) - v_i^1)f(u_*), \quad u_* \in (u_1, u(\xi)).$$

Consequently, for any $\xi \in \mathbb{R}^1$

$$|q|\int_{-\infty}^{\xi}\left\{u'u' + \sum_{i=1}^{n}\left[v_i'u' + \eta_i v_i'u' + \sum_{j=1}^{n}\eta_i v_i'v_j'\right]\right\}d\zeta < K_1. \tag{3.6}$$

Assume that the global maximum of $u'(\cdot)$ takes place for $\xi = \xi_0$. Integrating identity (3.3) from $(-\infty)$ to ξ_0 and using the estimation (3.6) we obtain

$$1/2D\left[\left(u' + \sum_{i=1}^{n}\eta_i v_i'\right)^2\right](\xi_0) < 2K_1. \tag{3.7}$$

As a result there exists a constant E, such that, for all the monotone solutions, $u'(\xi) < E$ for any ξ. Now, let us fix $j = 1, \ldots, n$ and suppose that the maximal value of $v_j'(\xi)$, is attained at $\xi = \zeta_0$. Let us differentiate the equation for v_j at $\xi = \zeta_0$. We obtain

$$D_j v_j''' - [G_{j,v_j}(u, v_j)v_j' + G_{j,u}(u, v_j)u'] = 0.$$

As $v_j'''(\zeta_0) \le 0$, we obtain the estimation

$$v_j'(\zeta_0) \le -G_{j,u}(u, v_j)(\zeta_0)[G_{j,v_j}(u, v_j)(\zeta_0)]^{-1}u'(\zeta_0). \tag{3.8}$$

Now, we will show that q is bounded. Suppose that $q < 0$. Let us integrate Eq. (3.3) from $(-\infty)$ to $\xi \in (\xi_1, \xi_2)$, where ξ_1 is such that $u(\xi_1) = w = (u_1 + u_2)/2$ and ξ_2 is such that $u(\xi_2) = u_2$. Then, for $\xi \in (\xi_1, \xi_2)$,

$$1/2D\left[\left(u' + \sum_{i=1}^n \eta_i v_i'\right)^2\right](\xi) > -\sum_{i=1}^n \int_{-\infty}^{\xi} \eta_i f(u(\zeta))v_i'(\zeta)d\zeta - \int_{u_1}^{u(\xi)} f(u)du$$

and consequently $1/2D[(u' + \sum_{i=1}^n \eta_i v_i')^2](\xi) > K_2$, where $K_2 = -\int_{u_1}^{w} f(u)du$. Hence $[(u' + \sum_{i=1}^n \eta_i v_i')](\xi) > \sqrt{2K_2/D}$ for $\xi \in (\xi_1, \xi_2)$. As $u'(\xi) > 0, v_i'(\xi) > 0$ for all ξ we have

$$\int_{\mathbb{R}} \left[u'u' + \sum_{i=1}^n v_i'u' + \sum_{i=1}^n \left(\eta_i v_i'u' + \sum_{i=1}^n \eta_i v_i'v_j'\right)\right] d\xi > \int_{\mathbb{R}} \left[u'u' + \sum_{i=1}^n \eta_i v_i'u'\right] d\xi$$

$$= \int_{u_1}^{u_3} \left[u' + \sum_{i=1}^n \eta_i v_i'\right] du > \int_{w}^{u_2} \left[u' + \sum_{i=1}^n \eta_i v_i'\right] du > \sqrt{2K_2/D}\,(u_2 - w)$$

$$= 1/2\sqrt{2K_2/D}\,(u_2 - u_1).$$

By using Eqs. (3.4) and (3.5) we conclude that q is bounded from below.

If $q > 0$ then for $\xi \in (\xi_1, \xi_2)$, where $u(\xi_1) = u_2$ and $u(\xi_2) = 1/2(u_2 + u_3)$, we have the inequality

$$1/2D\left[\left(u' + \sum_{i=1}^n \eta_i v_i'\right)^2\right](\xi) \ge \sum_{i=1}^n \int_{\xi}^{\infty} \eta_i f(u(\zeta))v_i'(\zeta)d\zeta + \int_{u(\xi)}^{u_3} f(u)du.$$

Using this inequality and repeating the considerations for the case $q < 0$ we can prove that q is bounded from above. Hence $|q|$ is globally bounded.

The estimate for u'' follows straightforwardly from Eq. (1.16) and the fact that $u'(\xi)$ and $|q|$ are globally bounded. Having the estimates for u'' we can estimate the values of the second derivatives of v_j by differentiating twice at points of an extremum. Next differentiating Eq. (1.16) we can obtain the estimations for u'''. Hence the estimations (3.1) are proved. □

Equation (3.3) may be used to derive some additional conclusions concerning the speed of the travelling waves for the degenerate case $D_i = 0$, $i = 1, \ldots, n$, under the assumption of their existence.

Lemma 3.2. *Assume that there exists a heteroclinic monotone solution to system* (1.16)–(1.17) *satisfying conditions* (1.8). *Let q_r denote the speed corresponding to the heteroclinic solution of Eq.* (1.12). *If $q_r < 0$, then $0 > \overline{q} > q > q_r$, whereas, if $q_r > 0$, then $0 < \underline{q} < q < q_r$.*

Proof. Let $q_r < 0$. Then $\int_{u_1}^{u_3} f(h)dh > 0$. Equation (3.3) after integration over $(-\infty, \xi)$ can be written in the following way:

$$\frac{D}{2}[(u')^2](\xi) = -q\int_{-\infty}^{\xi}\left[u'^2 + \sum_{i=1}^{n} v_i' u'\right] d\zeta - \int_{u_1}^{u(\xi)} f(s)ds. \tag{3.9}$$

Similarly, the solution $u_r(\cdot)$ of Eq. (1.12) for $q = q_r$ satisfies the equality

$$\frac{D}{2}[(u_r')^2](\xi) = -q_r\int_{-\infty}^{\xi}\left[(u_r')^2\right] d\zeta - \int_{u_1}^{u_r(\xi)} f(s)ds. \tag{3.10}$$

Due to the monotonicity we can express u' and u_r' in terms of the variable $s \in [u_1, u_3]$. Thus, if $s = u(\xi)$, then $z(s) = u'(\xi)$ and, if $s = u_r(\zeta)$, then $\widetilde{z}(s) = u_r'(\zeta)$. Likewise, we introduce the functions z_i corresponding to the functions v_i'. Thus, Eq. (3.9) can be written as

$$\frac{D}{2}z^2(s) = -q\int_{u_1}^{s}\left[z(h) + \sum_{i=1}^{n} z_i(h)\right] dh - \int_{u_1}^{s} f(h)dh \tag{3.11}$$

and Eq. (3.10) as

$$\frac{D}{2}\widetilde{z}^2(s) = -q_r\int_{u_1}^{s}\widetilde{z}(h)dh - \int_{u_1}^{s} f(h)dh. \tag{3.12}$$

If we assume that $q \le q_r$, then from the above inequalities it is seen that for any $s \in (u_1, u_3)$, we have $z(s) \ge \widetilde{z}(s)$. (Eq. (3.2) can be written, due to the monotonicity, in the form $z(s)z_{,s}(s) + qz(s) + f(s) = -q\sum_{i=1}^{n} z_i(s)$, and $z(s) \cong z_{,s}(s)(s - u_1)$ close to $s = u_1$.) However, for $s = u_3$ we would obtain from (3.11) and (3.12)

$$-q\int_{u_1}^{u_3}\left[z(h) + \sum_{i=1}^{n} z_i(h)\right] dh = -q_r\int_{u_1}^{u_3}\widetilde{z}(h)dh,$$

so we would arrive at a contradiction. Thus $q > q_r$. Assuming that $q \ge 0$ leads to a contradiction as the right-hand side of Eq. (3.11) for $s = u_3$ is negative. Thus $q < \overline{q} < 0$, where $\overline{q}$ can be estimated by means of Eq. (3.7) (with $\eta_i = 0$), Eqs. (3.8) and (3.11). Now, let us suppose that $q_r > 0$. Then $\int_{u_1}^{u_3} f(h)dh < 0$. Note that

$$\frac{D}{2}z^2(s) = q\int_{s}^{u_3}\left[z(h) + \sum_{i=1}^{n} z_i(h)\right] dh + \int_{s}^{u_3} f(h)dh \tag{3.13}$$

and

$$\frac{D}{2}\widetilde{z}^2(s) = q_r\int_{s}^{u_3}\widetilde{z}(h)dh + \int_{s}^{u_3} f(h)dh. \tag{3.14}$$

Using Eqs. (3.13) and (3.14), one can conclude, repeating appropriately the considerations concerning the case $q_r < 0$, that by assuming $q \geq q_r$ or $q \leq 0$ we arrive at a contradiction, so we must have $0 < \underline{q} < q < q_r$. The value of $\underline{q} < 0$ can be estimated by means of Eqs. (3.7), (3.8) and (3.13). □

Remark 3.1. It follows from Lemma 3.2 that the influence of *immobile* buffers cannot change the character of the front. That is to say, it is advancing ($q < 0$), if the travelling front for Eq. (1.11) is advancing ($q_r < 0$), and it is receding ($q > 0$), if the travelling front for Eq. (1.11) is receding ($q_r > 0$). Moreover, the modulus of the front speed decreases. Finally, the front is standing ($q = 0$), iff $q_r = 0$.

Lemma 3.3. *For a given* $q \in \mathbb{R}^1$ *there do not exist simultaneously two monotone heteroclinic solutions to system* (1.9)–(1.10) *with* $D_i = 0$, $i = 1, \ldots, n$, *connecting* P_1 *with* P_2 *and* P_2 *with* P_3 *respectively, i.e. such that their first and second derivatives vanish at infinities, whereas*

$$\lim_{\xi \to -\infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_1, v_1^1, \ldots, v_n^1) = P_1,$$

$$\lim_{\xi \to \infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_3, v_1^3, \ldots, v_n^3) = P_2$$

and

$$\lim_{\xi \to -\infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_1, v_1^1, \ldots, v_n^1) = P_2,$$

$$\lim_{\xi \to \infty} (u(\xi), v_1(\xi), \ldots, v_n(\xi)) = (u_3, v_1^3, \ldots, v_n^3) = P_3$$

respectively.

Proof. If we rewrite Eq. (3.4) replacing the integral $\int_{u_1}^{u_3} f(u)du$ with $\int_{u_1}^{u_2} f(u)du$ and $\int_{u_2}^{u_3} f(u)du$ then we see, according to Assumption 1 that this equality cannot be satisfied in both the cases due to the different signs of the integrals. □

4. Existence Theorems for the System with Nonzero Diffusion Coefficients of the Buffers

The fact that the source functions of system (1.2) satisfy the monotonicity conditions (1.15) together with the results of Sec. 2 (see also Appendix A) allows us to use the theory of travelling waves for monotone parabolic systems contained in Ref. 14. One can check the validity of the existence theorem for the travelling wave solutions to system (1.2) for $D_i > 0$, $i = 1, \ldots, n$.

Theorem 4.1. *Let Assumption* 1 *be satisfied. Let* $D, D_1, \ldots, D_n$ *be positive. Then there exists a unique* (*up to translation in* ξ) *monotone heteroclinic solution to system* (1.9)–(1.10) *satisfying conditions* (1.8).

The proof follows from the results of Sec. 2 and Theorem 2.1, p. 15 in Ref. 14, which is cited below.

Theorem 4.2. (Theorem 2.1, p. 15 in Ref. 14) *Let us consider the system*

$$\frac{\partial U}{\partial t} = A\Delta U + F(U), \tag{4.1}$$

where $\Delta = \partial^2/\partial x_1^2 + \cdots + \partial^2/\partial x_s^2$, $s \geq 1$, $U = (U_1, \ldots, U_N)$ *is a vector-valued function,* A *is diagonal positive-definite matrix and* $C^1 \ni F(\cdot) : \mathbb{R}^N \to \mathbb{R}^N$. *Let system* (4.1) *be monotone, i.e*

$$\frac{\partial F_i}{\partial U_j} \geq 0, \quad i, j = 1, \ldots, N, \ i \neq j.$$

Further, let the function $F(U)$ *vanish in a finite number of points* w_-, w_+ *and* $\mathbf{U}_k$, $(k = 1, \ldots, m)$ *with* $w_- < \mathbf{U}_k < w_+$. *Let us assume that all the eigenvalues of the matrices* $\partial F(w_-)$ *and* $\partial F(w_+)$ *lie in the left half-plane, and that the matrices* $\partial F(\mathbf{U}_k)$, $(k = 1, \ldots, m)$ *are irreducible and have at least one eigenvalue in the right half-plane. Then there exists a unique monotone travelling wave, i.e. a constant* q *and a twice continuously differentiable monotone vector-valued function* $U(\xi)$, $\xi = x_1 - qt$, *satisfying the system*

$$AU'' + qU' + F(U) = 0, \tag{4.2}$$

such that $U_j'(\xi) > 0$ *for all* $j = 1, \ldots, N$, $\xi \in \mathbb{R}$, *and*

$$\lim_{\xi \to \pm\infty} U(\xi) = w_\pm, \quad \lim_{\xi \to \pm\infty} U'(\xi) = 0.$$

5. Existence of Solutions for the Degenerate Systems

In this section, we will prove the existence of a solution to the system (1.9)–(1.10) with $D_i = 0$ for $i = 1, \ldots, n$. The idea of the proof is to pass to the limit $D_i \to 0$ in the family of solutions for the non-degenerate system (with $D_i > 0$).

For $\alpha, \beta = 0, 1, 2, 3$, let

$$B_{\alpha\beta}(\mathbb{R}^1) = S_\alpha \times \underbrace{S_\beta \times \cdots \times S_\beta}_{n \text{ times}}, \tag{5.1}$$

where for $\gamma = 1, 2, 3$,

$$S_\gamma = \left\{ f \in C^\gamma(\mathbb{R}^1) : \lim_{\xi \to \pm\infty} f(\xi) \text{ exist}, \ \lim_{\xi \to \pm\infty} f^{(j)}(\xi) = 0, \ 1 \leq j \leq \gamma \right\},$$

whereas

$$S_0 = \left\{ f \in C^0(\mathbb{R}^1) : \lim_{\xi \to \pm\infty} f(\xi) \text{ exist} \right\}.$$

Here, by $f^{(j)}$ we mean the jth derivative of f. $B_{\alpha\beta}$ are the Banach spaces under the supremum norm. To be more precise

$$\|(u, v_1, \ldots, v_n)\|_{B_{\alpha\beta}} = \|u\|_{S_\alpha} + \sum_{k=1}^n \|v_k\|_{S_\beta}, \quad \|\cdot\|_{S_\gamma} = \|\cdot\|_{C^\gamma(\mathbb{R}^1)}.$$

Next, for any compact interval $\mathcal{I}$,

$$B_{\alpha\beta}(\mathcal{I}) = \{f \in B_{\alpha\beta} : f(\mathbb{R}^1)_{|\mathcal{I}}\}.$$

Note that the heteroclinic solutions to system (1.16)–(1.17) are determined only up to a shift in ξ. To get rid of the translational symmetry we impose the condition of the form

$$u(0) = (u_1 + u_2)/2, \tag{5.2}$$

where u_1, u_2 are defined in Assumption 1. Let $D_i = \varepsilon d_i$ and let $\varepsilon = 1/l$ with $l \in \{1, 2, \ldots\}$. By imposing condition (5.2) the heteroclinic solutions to system (1.9)–(1.10) obtained by means of Theorem 5.1 will be uniquely determined. Let us denote the heteroclinic corresponding to $\varepsilon = 1/l$ by $\{U_{\{l\}}\}_{l=1}^{l=\infty}$ and its speed by $\{q_l\}_{l=1}^{l=\infty}$.

By means of Lemma 3.1, $(q_l, U_{\{l\}}) \in \mathbb{R}^1 \times B_{32}$ with $(\|U_{\{l\}}\|_{B_{32}} + |q_l|)$ is bounded uniformly with respect to l. Using the Arzela–Ascoli lemma we conclude that on every compact interval $I_{\mathcal{J}} = [-\mathcal{J}, \mathcal{J}]$, $\mathcal{J} > 0$, we may find a subsequence $\{k_l\}_{l=1}^{l=\infty}$ such that both $U_{\{k_l\}}$ and q_{k_l} are converging in $B_{21}(I_{\mathcal{J}})$ and $\mathbb{R}^1$, respectively. Next, out of this subsequence we can choose another subsequence (denoted for simplicity in the same way) such that the sequences U_{k_n} and q_{k_n} are convergent in the norm of the space $B_{21}(I_{\mathcal{J}+1})$ and $\mathbb{R}^1$, respectively. This procedure can be continued. It follows that on every compact subset of the form $I_{\mathcal{J}} = [-\mathcal{J}, \mathcal{J}]$ with positive integer $\mathcal{J}$ arbitrarily large, we can find subsequences $\{U_{\{k_l\}}\}_{l=1}^{l=\infty}$ and $\{q_{k_l}\}_{l=1}^{l=\infty}$ converging to the solutions of the system (1.16)–(1.17). Moreover, by differentiation of the equations of this system we easily conclude that the limiting pair (Q, Ψ) belongs to the space $\mathbb{R}^1 \times B_{32}$. The function $\Psi(\cdot)$ connects the constant steady states P_1 and P_3 as was desired. So, as the first derivatives of the functions $U_{\{l\}}$, $l = \{1, 2, \ldots\}$, are positive in $\mathbb{R}^1$, and tend to zero at infinities, $\Psi'(\xi)$ must tend to 0 for $|\, \xi \,| \to \infty$. Moreover, as $\xi \to \pm\infty$, due to the monotonicity, the functions $\Psi_1(\cdot), \Psi_2(\cdot), \ldots, \Psi_{n+1}(\cdot)$ must attain their limits. Due to condition (5.2), $\lim_{\xi \to -\infty} \Psi(\xi) = P_1$. Now, if it was not true that $\lim_{\xi \to \infty} \Psi(\xi) = P_3$, we would have $\Psi(\xi) \to P_2$ as $\xi \to \infty$. But it is easy to note that then we would have another wave $\widetilde{\Psi}$ such that $\widetilde{\Psi}(\xi) \to P_2$ and P_3 as $\xi \to \pm\infty$ respectively, that is to say there would exist two waves (of the same speed q) joining the states P_1 with P_2 and P_2 with P_3 consecutively. This possibility should be however excluded due to Lemma 3.3. Consequently, $\lim_{\xi \to \infty} \Psi(\xi) = P_3$ also in this case. From the first equation it follows that $\Psi_1''(\xi) \to 0$ as $\xi \to \pm\infty$, whereas Ψ_i, $i = 2, \ldots, n+1$, satisfy the reduced equations

$$Q\Psi_i' - G_{i-1}(\Psi_1, \Psi_i) = 0.$$

It is obvious that the same convergence result takes place for any set of $D_i = D_i(\varepsilon)$, $i = 1, \ldots, n$, such that $D_i(\varepsilon) \to 0$ as $\varepsilon \to 0$.

In Remark 1.2 we defined q_r as the speed of the unique (in the sense of profile) monotonically increasing heterolinic solution for the scalar equation (1.12) joining the states u_1 and u_3.

The heteroclinic solutions obtained by the limiting procedure are strictly monotone.

Lemma 5.1. *Consider system* (1.16)–(1.17). *If one of the functions* $z = u', z_i = v_i'$, $i \in \{1, \dots, n\}$, *attains a minimum equal to zero for some* $\xi = \xi_0$ *then* $z(\cdot)$, $z_1(\cdot), \dots, z_n(\cdot) \equiv 0$.

Proof. Let us suppose that for some $i \in \{1, \dots, n\}$ the function $z_i(\xi_0)$ attains a minimum. Then $z_i'(\xi_0) = 0$ and $z_i''(\xi_0) \geq 0$. Thus, differentiating the equation for v_i we obtain the relation

$$0 = G_{i,u}(u(\xi_0), v_i(\xi_0))z + G_{i,v_i}(u(\xi_0), v_i(\xi_0))z_i.$$

As $G_{i,u}(u(\xi_0), v_i(\xi_0)) < 0$ hence $z(\cdot)$ must attain a minimum equal to zero at $\xi = \xi_0$. By differentiating the equation for u we infer that $z_j(\xi_0) = 0$ for all $j = 1, \dots, n$ thus the source terms of all the equations are equal to zero. Hence due to the uniqueness of the initial value problem the lemma is proved in this case. If the value zero is attained by the function $z(\cdot)$ then the proof can be carried out similarly. □

Consequently, the following existence theorem holds.

Theorem 5.1. *Suppose that Assumption* 1 *is satisfied. Then there exists a heteroclinic solution to system* (1.16)–(1.17), *i.e. a speed* $q \in \mathbb{R}^1$ *and a vector function* $(u, v_1, \dots, v_n) : \mathbb{R}^1 \to \mathbb{R}^{n+1}$ *satisfying conditions* (1.8) *which is strictly monotone in every of its components. If* $q_r < 0$, *then* $0 > q > q_r$, *whereas, if* $q_r > 0$, *then* $0 < q < q_r$.

Proof. The first statement follows from what we said earlier. The second statement follows from Lemma 3.2 in Sec. 3. □

Let us note that for $q_r = 0$ the existence proof is straightforward.

Lemma 5.2. *Suppose that* $q_r = 0$. *Then there exists a unique heteroclinic pair* $(0, U)$ *of system* (1.16)–(1.17). *This pair is unique* (*up to a translation in* ξ) *in the class of solutions with* $q = 0$ *and monotone* U.

Proof. Take $q = 0$. Then

$$G_i(u(\xi), v_i(\xi)) = 0, \quad i = 1, \dots, n.$$

Thus, the first equation separates from the rest and takes the form (1.12). This equation has a unique monotonically increasing heteroclinic solution corresponding to the speed $q_r = 0$ and joining the states u_1 and u_3. Having the function $u(\cdot)$, we can solve the remaining equations with respect to $v_i(\xi)$. □

Uniqueness of the travelling wave solutions to system connecting the states P_1 and P_3 is stated and proved in Ref. 13 (see Theorem 1, p. 247). The travelling wave solution is also *stable* with respect to perturbations of the initial conditions. This result is stated in Theorem 3, p. 250 in Ref. 13.

6. Structural Stability of Heteroclinic Solutions

In this section we will analyze the linearization of the operator generated by the left-hand sides of the equations of system (1.9)–(1.10). The basic element of our analysis will be the proof of the existence of the unique bounded and positive solution to the conjugate of the system (1.16)–(1.17) linearized around the solution U_0. To do this we will examine the behaviour of the solution to the conjugate of the linearization of the system (1.9)–(1.10) as $D_i \to 0$, $i = 1, \ldots, n$.

Let us consider the operator O generated by the left-hand sides of equations of system (1.9)–(1.10). This operator can be considered as acting from the Banach space $\mathbb{R}^1 \times \widetilde{B}_{21}$ consisting of the pairs (q, U) to the space B_{00}. Here $\widetilde{B}_{21}$ denotes the space B_{21} of vector functions $u_1(\cdot)$ satisfying the condition

$$u_1(0) = (u_1(-\infty) + u_1(\infty))/2. \tag{6.1}$$

We introduce the condition (6.1) to fix the solutions in the ξ-space, i.e. to get rid of the translational symmetry of solutions to autonomous systems. The spaces $B_{\alpha\beta}$ are defined by (5.1). Let (q_0, U_0) denote the heteroclinic solution pair to system (1.9)–(1.10). The linearized operator acting between the same spaces (being in fact the Fréchet derivative of O with respect to U and q at the point $(q, U) = (q_0, U_0)$) has the form:

$$DO(q_0, U_0) : (q, U) \to \mathcal{D}_i U_i'' + q_0 U_i' + \sum_{j=1}^{n+1} F_{i,j}(U_0(\xi)) U_j + q U_{0i}',$$

where

$$\mathcal{D}_1 = D, \quad \mathcal{D}_{i+1} = 0, \ \ i = 1, \ldots, n. \tag{6.2}$$

Now, it is obvious that, according to the translational invariance, the function U_0' satisfies the system

$$\mathcal{D}_i U_i'' + q_0 U_i' + \sum_{j=1}^{n+1} F_{i,j}(U_0(\xi)) U_j = 0, \quad i = 1, \ldots, n+1. \tag{6.3}$$

Below, we will need a variation of Lemma 5.3, p. 213 in Ref. 14.

Lemma 6.1. *Let the function* $z : \mathbb{R}^1 \to \mathbb{R}^{n+1}$ *satisfy the system*

$$\mathcal{L}z \le -\delta\phi(\xi), \tag{6.4}$$

where $\phi(\xi) > 0,\ \xi \in \mathbb{R}^1,\ \delta \ge 0,$ *and, for* $i = 1, \ldots, n+1$,

$$(\mathcal{L}z)_i(\xi) = \mathcal{D}_i z_i''(\xi) + q z_i'(\xi) + \sum_{j=1}^{n+1} B_{ij}(\xi) z_j(\xi), \tag{6.5}$$

with $\mathcal{D}_i = const \ge 0$. *Suppose that* $B(\xi)$ *is* $(n+1)\times(n+1)$ *matrix function with non-negative off-diagonal elements, continuous in* ξ *and such that there exist its limits at infinities. Suppose that* $B_\pm = \lim_{\xi\to\pm\infty} B(\xi)$ *are such that* $B_\pm$ *are irreducible* *and have their principal eigenvalue negative. Suppose that* $\lim_{\xi\to\pm\infty} z(\xi) = 0$*. Then there exist numbers* r_+ *and* $r_- < r_+$ *such that if* $z(r_\pm) > 0$ (*component-wise*) *then* $z(\xi) > 0$ *for all* $\xi > r_+$ *and* $\xi < r_-$.

Proof. By a modification of the *proof* of Lemma 5.3, p. 213 in Ref. 14 to systems which may contain equations of the first-order, we conclude that $z(\xi) \geq 0$ for all $\xi \in \mathbb{R}^1 \setminus [r_-, r_+]$, where $r_\pm$ are such that $z(r_\pm) > 0$ and the principal eigenvalues of $B(\xi)$ are negative and $B(\xi)$ is irreducible for $\xi > r_+$ and $\xi < r_-$. Knowing this, we will prove that $z(\xi) > 0$ for all such ξ. Consider the case $\xi > r_+$. Suppose that for some $\xi_0 \in (r_+, \infty)$ the inequality $z(\xi_0) > 0$ is not true. Let $I(\xi_0) = \{j : z_j(\xi_0) = 0\}$ and $J(\xi_0) = \{j : z_j(\xi_0) > 0\}$. Then $I(\xi_0) \cup J(\xi_0) = \{1, \ldots, n+1\}$. If we assume that $J = \emptyset$, then $z_i(\xi_0) = 0$ for all i. If $\delta > 0$, then the left-hand side of the equation for z_i is non-negative, whereas and right-hand side is negative — a contradiction. If $\delta = 0$, then from the uniqueness of the initial value problem, $z(\cdot) \equiv 0$ contradicting the assumption $z(r_+) > 0$. So, for at least one $j \in J(\xi_0)$ and at least one $i \in I(\xi_0)$ such that $B_{ij}(\xi_0) > 0$ as otherwise the matrix B would be reducible. As a result, one must have $z_i'(\xi_0) = 0$ and $z_i''(\xi_0) \geq 0$, if $\mathcal{D}_i > 0$. However, then Eq. (6.4) could not be satisfied as $z_j(\xi_0) > 0$. Similar considerations hold for $\xi < r_-$. The lemma is proved. □

Using the method similar to the proof of Lemma 6.1 we can prove the result concerning the uniqueness of bounded solutions to the linearized system.

For $D_i = 0$, $i = 1, \ldots, n$, and for $q \neq 0$, system (1.9)–(1.10) can be written as the first order system of ODEs of the form

$$u' = z,$$
$$z' = \frac{1}{D}\left[-qz - f(u) - \sum_{k=1}^{n} G_k(u, v_k)\right],$$
$$v_i' = \frac{1}{q} G_i(u, v_i), \quad i = 1, \ldots, n, \tag{6.6}$$

with the following linearization around the point $(u_k, 0, v_1^k, \ldots, v_n^k))$ (corresponding to P_k):

$$\begin{pmatrix} h_u \\ h_z \\ h_1 \\ \vdots \\ h_n \end{pmatrix}' = L \begin{pmatrix} h_u \\ h_z \\ h_1 \\ \vdots \\ h_n \end{pmatrix}, \tag{6.7}$$

where

$$L = \begin{pmatrix} 0 & 1 & 0 & \dots & 0 \\ \frac{1}{D}[-a + \sum_{i=1}^{n} a_i] & -\frac{q}{D} & -\frac{1}{D}b_1 & \dots & -\frac{1}{D}b_n \\ -\frac{1}{q}a_1 & 0 & \frac{1}{q}b_1 & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots \\ -\frac{1}{q}a_n & 0 & 0 & \dots & \frac{1}{q}b_n \end{pmatrix}, \tag{6.8}$$

with a, a_i and b_i satisfying (2.4) and (2.3) with $k = 1, 2, 3$.

The characterization of the eigenvalues at the points corresponding to P_1 and P_3 is given by the following lemma:

Lemma 6.2. (see Ref. 13, Lemma 5.2, p. 255) *Assume that $a < 0$. If $q > 0$, then the matrix L has one negative eigenvalue and $n+1$ positive eigenvalues. If $q < 0$, then the matrix L has one positive eigenvalue and $n+1$ negative eigenvalues.*

We are in a position to prove the uniqueness of the solution of the linearized system.

Lemma 6.3. *There is no solution to system* (6.3) *bounded in B_{21} other than $Z_1 = U_0'$.*

Proof. Suppose that another solution Z_2 exists. As all of the eigenvalues of the matrix L given by (6.8) have non-zero real part (see Lemma 6.2), the solutions to Eq. (6.3) either grow to infinity (in their absolute value) or tend to zero as $|\xi| \to \infty$. It implies the existence of a number $\mu > 0$ such that $\mu Z_1(\xi) < Z_2(\xi) < -\mu Z_1(\xi)$ for $\xi \in [-r, r]$. In consequence we can prove (repeating the proof of Lemma 6.1 with $\delta = 0$) that

$$\eta_{\mu+}(\xi) := \mu Z_1(\xi) - Z_2(\xi) > 0, \quad \eta_{\mu-}(\xi) := -\mu Z_1(\xi) - Z_2(\xi) < 0 \tag{6.9}$$

for $|\xi| \geq r$. Let us decrease the value of μ and find the first value, $\mu = K$ for which the above inequalities do not hold. If $\omega_{\nu\pm} = \{\xi_0 : (\eta_{\nu\pm})_i(\xi_0) = 0, \text{ for some } i = 1, \dots, n+1\}$, then there must exist at least one $x_0 \in \omega_{\nu\pm} \cap [r_-, r_+]$. Otherwise, according to what we said before, the inequalities (6.9) would remain valid for all $\xi \in \mathbb{R}^1$. Suppose that $(\eta_{\nu+})_i(\xi_0) = 0$ for some $\xi_0 \in [-r, r]$ and some $i \in \{1, \dots, n+1\}$. Then $(\eta_{\nu+})_i(\xi) = 0$ attains minimum at $\xi = \xi_0$, hence $(\eta''_{\nu+})_i(\xi_0) \geq 0$, if $D_i > 0$. Let $I(\xi_0) = \{i : (\eta_{\nu+})_i(\xi) = 0\}$ and $J(\xi_0) = \{j : (\eta_{\nu+})_j(\xi) > 0\}$. Obviously $I(\xi_0) \cup J(\xi_0) = \{1, \dots, n+1\}$. If $J(\xi_0) = \emptyset$, then $(\eta_{\nu+})_j(\xi) = 0$ for all j and all ξ due to the uniqueness of solutions to the initial value problem. So let us assume that there exists at least one $i \in I(\xi_0)$ and at least one $j \in J(\xi_0)$ such that $F_{i,j}(U) > 0$ for $U \in [P_1, P_3]$. Such a pair of indices must exist as otherwise the matrix B would be reducible. But then we arrive at contradiction as $(\eta_{\nu+})_i(\xi_0)$ satisfies the equation

$$D_i(\eta''_{\nu+})_i(\xi_0) + \sum_{j \neq i} F_{i,j}(\xi_0)(\eta_{\nu+})_j(\xi_0) = 0.$$

Similar proof may be carried out for the function $(-\eta_{\mu-})$. As a conclusion the only situation, which does not lead to a contradiction is the existence of real constant ν such that $Z_2 \equiv \nu Z_1$ and the thesis of the lemma follows. □

In Appendix B we showed the existence and positivity of a bounded solution $\widetilde{V}$ to the adjoint of system (6.3) (in L^2 sense) if $q_0 \neq 0$ as a suitably scaled limit of solutions for $\varepsilon > 0$.

Concerning this solution one can prove a lemma analogous to Lemma 6.3.

Lemma 6.4. *There is no bounded solution to the adjoint of system* (6.3) *bounded in* B_{21} *other than* $\widetilde{V}$.

Proof. The proof can be done along the lines of the proof of Lemma 6.3. □

Using the above lemmas (in particular Lemma 6.2) and exploiting the methods of the exponential dichotomy as in Ref. 8, we can note that the operator $DO(U_0, q_0)$ has a bounded inverse acting from the space B_{00} to $\widetilde{B}_{21} \times \mathbb{R}^1$. Hence by means of the results of Ref. 9 (see also 8) we can prove the structural stability of the heteroclinic pairs for system (1.16)–(1.17). Namely, let us consider the system:

$$\mathcal{D}_i U_i'' + qU_i' + F_i(U) = \Phi_i(\tau, q, U), \quad i = 1, \ldots, n+1. \tag{6.10}$$

Assumption 3. Suppose that $\Phi_i : \mathbb{R}^l \times \mathbb{R}^1 \times B_{20} \to B_0$, $l \geq 1$ and $\Phi_i(0, q, u, \xi) \equiv 0$. (Let us note that we do not demand that Φ_i are autonomous.) Let us assume that for $\tau = 0$ there exists a strictly monotone heteroclinic pair (q_0, U_0) joining the states P_1 and P_3 satisfying system (6.10) with $\tau = 0$ and that Φ is continuously Fréchet differentiable with respect to (q, u) in some open neighbourhood of the solution triple $(\tau, q, U) = (0, q_0, U_0)$. □

Now, we are able to prove a theorem expressing the structural stability of the heteroclinic solutions pairs of system (1.16)–(1.17).

Theorem 6.1. *Assume that* $q_r \neq 0$ *and that Assumptions* 1–3 *are satisfied. Let* (q_0, U_0) *denote a unique* (*up to translation in* ξ) *monotonically increasing heteroclinic pair for system* (1.16)–(1.17)*. Then for all* $0 \leq |\tau| < \tau_0$, *with* τ_0 *sufficiently small, there exists a unique heteroclinic pair* (q_τ, U_τ) *for system* (6.10) *such that*

$$|q_\tau - q_0| + \|U_\tau - U_0\|_{B_{21}} \to 0$$

as $|\tau| \to 0$.

Proof. Note that $q_0 \neq 0$ due to Lemma 3.2. To prove the above result it is convenient to write (6.10) as a first-order system of $n+2$ equations:

$$\begin{aligned} &U_1' - Z_1 = 0, \\ &Z_1' + \frac{1}{\mathcal{D}_1}\left[qZ_1 + F_1(U) - \Phi_1(\tau, q, U)\right] = 0, \\ &U_i' + \frac{1}{q}\left[F_i(U) - \Phi_i(\tau, q, U)\right] = 0, \quad i = 2, \ldots, n+1, \end{aligned} \tag{6.11}$$

where we use the notation (1.14) and $\mathcal{D}_1 = D$. The left-hand sides of the equations of the system (6.11) define the operator P_τ acting on $(n+3)$-tuples

$$(q, \mathcal{U}(\cdot)) = (q, U_1, Z_1, \ldots, U_{n+1})(\cdot)$$

from the space

$$\mathbb{R}^1 \times \widetilde{B}_1^{n+2}(\mathbb{R}^1) := \mathbb{R}^1 \times \underbrace{\widetilde{S}_1 \times S_1 \times \cdots \times S_1}_{n+2 \text{ times}}$$

to the space

$$B_0^{n+2}(\mathbb{R}^1) := \underbrace{S_0 \times S_0 \times \cdots \times S_0}_{n+2 \text{ times}}.$$

Here $\widetilde{S}_1$ is the subspace of S_1 consisting of functions satisfying the condition (6.1).

The Fréchet derivative DP_0 of the operator P_0 at a point $(q_0, \mathcal{U}_0)$ corresponding to (q_0, U_0) by identifying $\mathcal{U}_0 = (U_{01}, Z_{01}, U_{02}, \ldots, U_{0(n+1)})$, $Z_{0j} = U_{0j}'$, with respect to $(q, \mathcal{U})$ is well defined. It has the following form:

$$DP_0(q, \mathcal{U}^{\mathrm{T}}) = \mathcal{U}^{\mathrm{T}'} - P_* \mathcal{U}^{\mathrm{T}} + q\mathcal{Z}^{\mathrm{T}} \tag{6.12}$$

with

$$\mathcal{Z}(\xi) := (0, \mathcal{D}_1^{-1} U_{01}', -q_0^{-2} F_2(U_0), \ldots, -q_0^{-2} F_{n+1}(U_0))(\xi).$$

In (6.12) $P_* = P_*(\xi)$ has the form given by (6.8) with

$$a = f'(U_0(\xi)), \quad b_j(\xi) = F_{1,v_j}(U_0(\xi)), \quad a_j(\xi) = F_{j,u}(U_0(\xi)).$$

Now, according to Lemma 6.2, the linearization matrices at the points P_1 and P_3 have the same number of positive and negative eigenvalues, i.e. one negative eigenvalue and $n+1$ positive eigenvalues (for $q > 0$) and one positive eigenvalue and $n+1$ negative eigenvalues (for $q < 0$). In conclusion, the system (B.10) has the exponential dichotomy on both of the half lines (see, e.g. Lemma 3.4 in Ref. 9) and the operator J defined by

$$(J\mathcal{U})(\xi) = \mathcal{U}^{\mathrm{T}'}(\xi) - P_*(\xi)\mathcal{U}^{\mathrm{T}}(\xi)$$

is Fredholm with index zero as acting from C_1 to C^0 spaces according to Lemma 4.2 in Ref. 9. We have shown above that up to a multiplicative constant there is only one bounded solution U_0' to system (6.3) (Lemma 6.3) and only one (up to a multiplicative constant) bounded solution $\widetilde{V}$ to the adjoint of this system (Lemma 6.4). As a result, we conclude that the system $(J\mathcal{U})(\xi) = 0$ possesses only one solution (up to a multiplicative constant). It does not belong to the space $\widetilde{B}_1^{n+2}(\mathbb{R}^1)$ as $U_{01}'(\xi) > 0$ for all $\xi \in \mathbb{R}_1$ and $\lim_{\xi\to\pm\infty} U_{01}'(\xi) = 0$, so it does not satisfy the condition (6.1). Likewise we have only one (up to a multiplicative constant) bounded solution A of the adjoint to this system (see Lemma 6.4 and Appendix B). Hence according to Lemma 4.2, p. 245 in Ref. 9 the equation

$$DP_0(q, \mathcal{U}^{\mathrm{T}}) = f(\xi)$$

with $f \in B_0^{n+2}$ has a unique solution in $\widetilde{B}_1^{n+2}$ iff the following orthogonality condition is satisfied:

$$\int_{\mathbb{R}^1} \sum_{i=1}^{n+2} [f_i(\xi) + q\mathcal{Z}_i(\xi)] A_i(\xi) d\xi = 0. \tag{6.13}$$

Here $A_i(\cdot)$, $i = 1, \ldots, n+2$, are the components of the solution to the adjoint of the system $(J\mathcal{U})(\xi) = 0$ (see Appendix B). Using the fact that (q_0, U_0) satisfies system (6.10) for $\tau = 0$, we conclude that

$$\mathcal{Z}(\xi) := (0, D^{-1}U_{01}'(\xi), q_0^{-1}U_{02}', \ldots, q_0^{-1}U_{0(n+1)}')(\xi).$$

In Appendix B, we have proved that the components of the solution $\widetilde{V}$ are positive, and showed some relations between A and $\widetilde{V}$ (see (B.12), (B.15) and (B.16)). In particular, we proved that the positivity of $\widetilde{V}_j$, $j = 1, \ldots, n+1$, implies the positivity of the function A_{j+1}. It follows that condition (6.13) may be always satisfied by a proper choice of q. Thus, the operator DP_0 defines an isomorphism between the spaces $\widetilde{B}_1^{n+2}$ and B_0^{n+2}, thus its inverse is bounded (see, e.g. Theorem 4.2-H, p. 180 in Ref. 12). Hence according to the implicit function theorem (see, e.g. Ref. 4) the claim of Theorem 6.1 holds. (Note that $U_1, Z_1 \in S_1$ implies $U_1 \in S_2$.) For f such that $f_1 \equiv 0$ condition (6.13) can be written as

$$\sum_{i=1}^{n+1} \int_{\mathbb{R}^1} [\widetilde{f}_i(\xi) - qU_{0i}'(\xi)] \widetilde{V}_i(\xi) d\xi = 0, \tag{6.14}$$

where

$$\widetilde{f}_i = \mathcal{D}_i f_{i+1} \quad i = 1, \quad \widetilde{f}_i = q_0 f_{i+M+1} \quad i = 2, \ldots, n+1.$$

According to the implicit function theorem and condition (6.14), $\delta q = q_\tau - q_0$ can be determined from the following relations:

$$\int_{\mathbb{R}^1} \sum_{i=1}^{n+1} \{\Phi_i(\tau, q_0, U_0)(\xi) - \delta q U_{0i}'(\xi)\} \widetilde{V}_i(\xi) d\xi = 0, \tag{6.15}$$

For more details the reader is referred to Ref. 9 or Ref. 8. □

Corollary 6.1. *The speed of the wave is a decreasing function of* $F(\cdot)$. *To be more precise, let us consider the system* (1.16)–(1.17) *with* $\widetilde{F}$ *instead of* F. *Then, if for some* j, $\widetilde{F}_j(U) > F_j(U)$ *for some* $U \in [P_1, P_3]$, *then* $\widetilde{q} < q$. *The proof follows from relation* (6.15). □

7. The Minimax Principle

In the previous section we proved that any monotone heteroclinic pair for system (1.16)–(1.17) is a unique limit of heteroclinic pair for the second-order system (1.9)–(1.10) (see Theorem 5.1). In particular its speed q is a limit of the speeds of heteroclinic solutions for the second-order systems as $\varepsilon \to 0$. Hence we may use the results in Ref. 14 to characterize the speed of the travelling waves for the degenerate system by the so-called minimax principle. So, let K_t be the class of vector functions $\rho = (\rho_1, \ldots, \rho_{n+1})$, each of its components is of $C^2(\mathbb{R}^1)$ class, is monotonically increasing functions satisfying the conditions $\lim_{\xi \to -\infty} \rho(\xi) \to P_1$ and $\lim_{\xi \to \infty} \rho(\xi) \to P_3$. Let

$$\psi_i(\rho(\xi)) = -\frac{\mathcal{D}_i \rho_i''(\xi) + F_i(\rho(\xi))}{\rho_i'(\xi}, \quad i = 1, \ldots, n+1, \tag{7.1}$$

where $\mathcal{D}_1 = D$, $\mathcal{D}_i = 0$ for $i = 2, \ldots, n+1$.

Lemma 7.1. *Let Assumption* 1 *be satisfied. Then the speed* q *of the unique* (*up to a translation in* ξ) *heteroclinic pair* (q, U) *for system* (1.16)–(1.17) (*with all the components of* U *monotonically increasing*) *satisfies the following equality*:

$$q = \inf_{\rho \in K_t} \sup_{i \in 1, \ldots, n+1, \xi \in \mathbb{R}^1} \psi_i(\rho(\xi)) = \sup_{\rho \in K_t} \inf_{i \in 1, \ldots, n+1, \xi \in \mathbb{R}^1} \psi_i(\rho(\xi)).$$

Moreover, for any $\rho \in K_t$, q *can be estimated by the relation*

$$\sup_{i \in 1, \ldots, n+1, \xi \in \mathbb{R}^1} \psi_i(\rho(\xi)) \geq q \geq \inf_{i \in 1, \ldots, n+1, \xi \in \mathbb{R}^1} \psi_i(\rho(\xi)).$$

The proof of this lemma follows from the proof of Theorem 7.1, p. 255 in Ref. 14 for the non-degenerate system (1.9)–(1.10) (with $D_i > 0$, $i = 1, \ldots, n$) using the *a priori* estimates given by Lemma 3.1.

Lemma 7.1 may be used to estimate the speed of the wave.

8. The Case of Fast Buffers

In the fast buffer approximation we assume that the kinetic terms in the equations for some of the buffers are scaled by a large positive parameter.[5,11] Thus, in system (1.2) we replace $G_i(u, v_i)$, $1 \leq i \leq n_1 \leq n$, by $\kappa G_i(u, v_i)$ and assume that $\kappa \gg 1$. That is to say we suppose that the process of binding and unbinding of free calcium for some of the buffers is very fast.

Lemma 8.1. *Assume that in system* (1.9)–(1.10) *the functions* G_i *are replaced by* κG_i, $1 \le i \le n_1 \le n$. *Assume that* D_i, $i = 1, \ldots, n$, *are such that*

$$\sum_{i=1}^{n} \eta_i \gamma_i < \widetilde{\gamma} < 1,$$

where $\eta_i = D_i/D$ *and* $\gamma_i = \sup_{u \in [u_1, u_3], v_i \in [v_i^1, v_i^3]} \{-G_{i,u}(u, v_i) G_{i,v_i}(u, v_i)^{-1}\}$.

Then for any C^2 *monotone heteroclinic solution* $(u, v_1, \ldots, v_n)(\cdot)$ *of system* (1.9)–(1.10) *we have the estimations*

$$\|u\|_{C^3(\mathbb{R})} < \mathcal{S}_1, \quad |q| \le \widetilde{Q}, \quad \|v_i\|_{C^2(\mathbb{R})} < \mathcal{S}_2, \quad i = 1, \ldots, n. \tag{8.1}$$

These estimations depend neither on the values of the diffusion coefficients D_i, $i = 1, \ldots, n$, *nor on the value of the parameter* κ *as* $\kappa \to \infty$.

Proof. Let us note that the method of finding the bounds for q as well as for the first derivatives of u and v_j applied in Lemma 3.1 can be also used if the functions G_j are replaced by κG_j, when $\kappa > 0$ is large. To be more precise, these bounds do not depend on κ as $\kappa \to \infty$. One notes that, for $D_i > 0$ sufficiently small, it is possible to change the method of proof so that the estimates for u'', u''' and v_i'' also do not depend on the value of κ. Let u_{2M} and u_{2m} denote the values of the global maximum and the global minimum of $u''(\cdot)$, respectively. To fix our attention, we will assume first that $u_{2M} \ge |u_{2m}|$. Let us find the upper bound for u_{2M}. So suppose that, for $\xi = \xi_0$, u'' attains its global maximum (equal to u_{2M}). Thus

$$u_{2M} \le C - \sum_{i=1}^{n} \eta_i v_i''(\xi_0), \tag{8.2}$$

where, according to the first part of the proof of Lemma 3.1, C is a number depending only on the bounds of q, u' and v_i', $i = 1, \ldots, n$ (hence independent of κ). Now, the right-hand side of (8.2) can be estimated from above by replacing $v_i''(\xi_0)$, $i = 1, \ldots, n$, with the global minimum of the function $v_i''(\cdot)$. Let us differentiate the equation for v_i twice with respect to ξ. We obtain

$$D_i v_i'''' + q v_i''' - \kappa(G_{i,v_i} v_i'' + G_{i,u} u'' + T_i(\xi)) = 0, \tag{8.3}$$

where T_i denote the terms containing the products of the first derivatives of u and v_i times the second derivatives of the function G_i, evaluated on the considered solution, so $|T_i(\xi)|$ is bounded for all ξ by a number independent of κ. Assuming that v_i'' attains a negative minimum for $\xi = \xi_{im}$, we obtain $v_i''(\xi_{im}) \ge \mathcal{A}_i(\xi_{im}) u''(\xi_{im}) - [\widetilde{T}_i(\xi_{im})]$, where $\mathcal{A}_i(\xi_{im}) = -G_{i,u}(u(\xi_{im}), v_i(\xi_{im})) G_{i,v}(u(\xi_{im}), v_i(\xi_{im}))^{-1}$ and

$$\widetilde{T}_i(\xi_{im}) = [T(\xi_{im})] G_{i,v_i}(u(\xi_{im}), v_i(\xi_{im}))^{-1}.$$

As $\sup_{\xi\in\mathbb{R}^1} \mathcal{A}_i(\xi) = \gamma_i$, Eq. (8.2) yields:

$$u_{2M} \le C - \sum_{i=1}^{n} \eta_i v_i''(\xi_{im}) \le C - \sum_{i=1}^{n} \eta_i[\gamma_i u''(\xi_{im}) - \widetilde{T}_i] \le \widetilde{C} - \sum_{i=1}^{n} \eta_i\gamma_i u_{2m}, \quad (8.4)$$

where $\widetilde{C} = C + \sum_{i=1}^{n} \eta_i \widetilde{T}_i$. Consequently $u_{2M} \le \widetilde{C} + \sum_{i=1}^{n} \eta_i\gamma_i u_{2M}$ and

$$u_{2M} \le \widetilde{C}(1 - \widetilde{\gamma})^{-1}. \quad (8.5)$$

Having the estimation for u_{2M} we obtain the estimation for u_{2m} as we assumed that $u_{2M} \ge |u_{2m}|$. If the reverse inequality is satisfied, i.e. $u_{2M} \le |u_{2m}|$, then the proof of the boundedness of $|u''|$ may be carried out in the same way. The bounding constant $\widetilde{C}$ is independent of the value of κ. Using Eq. (8.3) we obtain the estimations for $v_1'', \ldots, v_n''$. Finally, by differentiating the equation for u we obtain the estimation for u'''. □

Now, let us consider the system

$$\begin{aligned} &Du'' + qu' + f(u) + \sum_{i=1}^{n}[D_i v_i'' + qv_i'] = 0, \\ &\frac{D_i}{\kappa} v_i'' + \frac{q}{\kappa} v_i' - G_i(u, v_i) = 0, \quad 1 \le i \le n_1, \\ &D_i v_i'' + qv_i' - G_i(u, v_i) = 0, \quad n_1 < i \le n, \end{aligned} \quad (8.6)$$

with $D_i = d_i\,\varepsilon$, $d_i > 0$. (This system is equivalent to system (1.9)–(1.10) with $G_i(u, v_i)$ replaced with $\kappa G_i(u, v_i)$ for $1 \le i \le n_1$.) By letting $\varepsilon = 1/k$, $\kappa = k$, using Lemma 8.1 and repeating the considerations of Sec. 5, we can prove the existence of C^2 heteroclinic solution of the above system in the limit $D_i = 0$, $\kappa = \infty$. The details are left to the reader.

Appendix A. Proof of Lemma 2.1 and Other Properties of Linearization Matrices

Lemma A.1. (see Theorem 5, in Ref. 7, p. 350) *Let C be a $(n + 1) \times (n + 1)$-matrix with non-negative entries $c_{ik} \ge 0$, $i \ne k$. Then all the eigenvalues of C have negative real parts iff the following inequalities are satisfied*

$$J_1 = c_{11} < 0, \quad J_2 = \begin{vmatrix} c_{11} & c_{12} \\ c_{21} & c_{22} \end{vmatrix} > 0,$$

$$J_{(n+1)} = (-1)^{n+1} \begin{vmatrix} c_{11} & c_{12} & \cdots & c_{1(n+1)} \\ c_{21} & c_{22} & \cdots & c_{2(n+1)} \\ \cdots & \cdots & \cdots & \cdots \\ c_{(n+1)1} & c_{(n+1)2} & \cdots & c_{(n+1)(n+1)} \end{vmatrix} > 0. \quad (A.1)$$

Lemma A.2. (see Ref. 7, Theorem 6, p. 350) *Let C be an $(n+1)\times(n+1)$ matrix with non-negative elements. Then its maximal eigenvalue is a strictly increasing function of any of its entries.*

This maximal eigenvalue is characterized in the following lemma.

Lemma A.3. (see Ref. 7, Theorem 3, p. 344, Theorem 2, p. 334) *Let C be an $(n+1)\times(n+1)$ with non-negative entries. Then C has a real non-negative eigenvalue $\mu_{PF}(C)$ such that an associated eigenvector has non-negative components and every other eigenvalue of C has its modulus less than $\mu_{PF}(C)$. In particular every other eigenvalue of C has its real part less than μ_{PF}. Moreover, if C is irreducible, then the associated eigenvector has positive components.*

If C has positive entries the following obvious specification holds. □

Lemma A.4. (see Ref. 7, Theorem 1, p. 334) *Let C be an $n\times n$ with positive entries. Then C has a real positive eigenvalue $\mu_{PF}(C)$ such that an associated eigenvector has positive components and every other eigenvalue of C has its modulus less than $\mu_{PF}(C)$. In particular every other eigenvalue of C has its real part less than $\mu_{PF}(C)$.*

Lemmas A.3 and A.4 stay valid for matrices with non-negative off-diagonal entries. Thus, Lemma A.3 can be generalized to the following lemma.

Lemma A.5. *Let C be an $n\times n$ with non-negative off-diagonal entries. Then C has a real eigenvalue $\mu_{PF}(C)$ such that an associated eigenvector has non-negative components and every other eigenvalue of C has its real part less than $\mu_{PF}(C)$.*

Proof. Let us consider the matrix $C_m = C + mI$, where I is the unit $n\times n$ matrix and $m\in\mathbb{R}^1$. Every eigenvalue μ of C determines an eigenvalue μ_m of the matrix C_m by the relation

$$\mu_m = m + \mu.$$

If m is taken sufficiently large then the matrix C_m has non-negative entries. According to Lemma A.3 there exists a maximal real and positive eigenvalue $\mu_{PF}(C+mI)$ of the matrix $C+mI$ and the corresponding eigenvector N has non-negative entries. Consequently the matrix C possesses a maximal real eigenvalue $\mu_{PF}(C)$ equal to $\mu_{PF}(C+mI)-m$ with the corresponding eigenvector N, as $CN = (C_m - mI)N = (\mu_{PF}(C+mI)-m)N = \mu_{PF}(C)N$. The lemma is proved. □

Definition 1. Let C be an $(n+1)\times(n+1)$, $n\geq 1$, matrix with non-negative off-diagonal entries. Then the eigenvalue $\mu_{PF}(C)$ is called the Perron–Frobenius or principal eigenvalue of C and an associated eigenvector (with non-negative components) a Perron–Frobenius or principal eigenvector of C. □

Lemma A.6. *Let C be an $(n+1)\times(n+1)$ matrix with non-negative off-diagonal elements. Then its maximal eigenvalue is a strictly increasing function of any of its entries.*

Proof. The proof follows by repeating the proof of Lemma A.5 and using Lemma A.2. □

According to inequalities (2.4) the matrix $\mathcal{K}$ has off-diagonal entries. Using Lemma A.1 we can prove that for $a < 0$ its maximal eigenvalue $\mu_{PF}(\mathcal{K})$ is negative.

Lemma A.7. *Let $a < 0$. Then the eigenvalues μ of the matrix $\mathcal{K}$ are contained in the left half-plane $Re(\mu) < 0$.*

Proof. Let us note that $\mathcal{K}_{11} < 0$. Consider the matrix $\mathcal{K}^k = \mathcal{K}_{ij}$, $i, j = 1, \ldots, k$, $k = 2, \ldots, n+1$. To compute the determinant of the matrix $\mathcal{K}^k$, let us add the last $k-1$ rows of the matrix $\mathcal{K}^k$ to its first row. Expanding the determinant of this matrix with repect to the first row, we immediately obtain $\det \mathcal{K}^k = (a - \sum_{j=k}^n a_j)(-1)^{k-1} b_1 \ldots b_{k-1}$. Its sign is equal to $(-1)^k$. Also $\det \mathcal{K}^{n+1} = a(-1)^n b_1 \ldots b_n$. Thus, the sequence of inequalities from Lemma A.1 is satisfied. The lemma is proved. □

The statement converse to Lemma A.7 is also true. Namely, the following lemma holds.

Lemma A.8. *Let $a > 0$. Then at least one of the eigenvalues μ of the matrix $\mathcal{K}$ is contained in the half-plane $Re(\mu) > 0$.*

Proof. Let us consider the matrix $\mathcal{K}$ with $a = 0$. Then (by adding to the first row all the other rows) we note that $\det(\mathcal{K}) = 0$. The claim of the lemma follows from Lemma A.6. □

Taking advantage of the specific form of the matrix $\mathcal{K}$ we can prove that the eigenvectors corresponding to its largest eigenvalue are positive when this eigenvalue is negative. Now, we will analyze the irreducibility of the matrix $\mathcal{K}$.

Lemma A.9. *Independently of the value of a, the matrix $\mathcal{K}$ is irreducible.*

Proof. Let us remind that an $(n+1)\times(n+1)$ matrix C is called *reducible* if the set $\{1, \ldots, n+1\}$ can be divided into two disjoint subsets I and J; that is to say $\{1, \ldots, n+1\} = I \cup J$, $I \cap J = \emptyset$ such that $c_{ij} = 0$ for all $i \in I, j \in J$. The matrix is called *irreducible*, if it is not reducible. Suppose to the contrary that $\mathcal{K}$ is reducible for some value of a. It follows from the definition of reducibility that $i \in I$ implies $i \notin J$ and *vice versa* $j \in J$ implies $j \notin I$. As $k_{1j} \neq 0$ for $j \neq 1$ we note that $1 \notin I$. Hence $1 \in J$. Consequently, there must exist $1 \neq i \in I$ such that $k_{i1} = 0$. But k_{i1}

can be equal to zero only for $i = 1$. We thus arrive at a contradiction which proves the irreducibility of $\mathcal{K}$ independently of the value of a. □

Using Lemmas A.3 and A.9 and the method used in the proof of Lemma A.5 we can easily note the validity of the following statement.

Lemma A.10. *Let $\mathcal{K}$ be defined by conditions* (2.2)–(2.4). *Then its principal eigenvector* (*corresponding to the principal eigenvalue*) *may be chosen positive independently of the value of a.*

Appendix B. Properties of Bounded Solutions to the Adjoint System

First, let us note that, for $D, D_1, \ldots, D_n > 0$, (1.9)–(1.10) can be written as the first-order system of the form

$$\begin{aligned} u' &= z, \\ v_i' &= z_i \quad i = 1, \ldots, n, \\ z' &= \tfrac{1}{D}\left[-qz - f(u) - \textstyle\sum_{i=1}^n G_i(u, v_i)\right], \\ z_i' &= \tfrac{1}{D_i}\left[-qz_i + G_i(u, v_i)\right] \quad i = 1, \ldots, n. \end{aligned} \tag{B.1}$$

Within the notation (1.14) the linearization of this system around the unique heteroclinic pair $(q_\varepsilon, U_\varepsilon(\cdot))$ has the form

$$(U, Z)^{\mathrm{T}'} = L_*(U, Z)^{\mathrm{T}},$$

where

$$L_* = \begin{pmatrix} 0 & I \\ -\hat{D}^{-1}K & -q_\varepsilon \hat{D}^{-1} \end{pmatrix}, \tag{B.2}$$

with $\hat{D}^{-1} = \operatorname{diag}(\mathcal{D}_1^{-1}, \mathcal{D}_2^{-1}, \ldots, \mathcal{D}_{n+1}^{-1})$, $\mathcal{D}_1 = D$, $\mathcal{D}_i = \varepsilon d_i$, $i = 2, \ldots, n+1$, $K = \partial F = (\partial F)(U_\varepsilon(\xi))$ and F is given by (1.14). (We also remind that $U = (U_1, U_2, \ldots, U_{n+1}) = (u, v_1, \ldots, v_n)$ and Z is a vector function standing for U'.) In (B.2) I is the unit $(n+1) \times (n+1)$ matrix. Let us note that the transpose of L_* is the matrix

$$L^* = \begin{pmatrix} 0 & -(\hat{D}^{-1}K)^{\mathrm{T}} \\ I & -q_\varepsilon \hat{D}^{-1} \end{pmatrix}. \tag{B.3}$$

Solutions (Y, V), $Y, V : \mathbb{R}^1 \to \mathbb{R}^{n+1}$, to the adjoint system satisfy the set of equations

$$\begin{aligned} Y' &= (\hat{D}^{-1}K)^{\mathrm{T}} V, \\ V' &= -IY + q_\varepsilon \hat{D}^{-1} V. \end{aligned} \tag{B.4}$$

Differentiating the equation for V and using the equation for Y we conclude that V satisfies the equation

$$V'' = q_\varepsilon \hat{D}^{-1} V' - (\hat{D}^{-1}K)^{\mathrm{T}} V. \tag{B.5}$$

Hence V satisfies the adjoint of the second-order linearized system. Now,

$$(\hat{D}^{-1}K)^T = \begin{pmatrix} \frac{1}{\mathcal{D}_1}[a^\varepsilon - \sum_{i=1}^n a_i^\varepsilon] & \frac{1}{\varepsilon d_2}a_1^\varepsilon & \dots & \dots & \dots & \frac{1}{\varepsilon d_{n+1}}a_n^\varepsilon \\ \frac{1}{\mathcal{D}_1}b_1^\varepsilon & -\frac{1}{\varepsilon d_2}b_1^\varepsilon & 0 & \dots & 0 & 0 \\ & & \vdots & & & \\ \frac{1}{\mathcal{D}_1}b_n^\varepsilon & 0 & 0 & \dots & 0 & -\frac{1}{\varepsilon d_{n+1}}b_n^\varepsilon \end{pmatrix}, \quad \text{(B.6)}$$

where we have denoted

$$a^\varepsilon = a^\varepsilon(\xi) = f'(U_\varepsilon(\xi)), \quad b_j^\varepsilon = b_j^\varepsilon(\xi) = F_{1,v_j}(U_\varepsilon(\xi)), \quad a_j^\varepsilon = a_j^\varepsilon(\xi) = F_{j,u}(U_\varepsilon(\xi)).$$

Now, according to Theorem 4.5.1 in Ref. 14 we know that for all $\varepsilon > 0$ there exists a solution to system (B.5), for which $V_i(\xi) > 0$ for all $\xi \in \mathbb{R}^1$, $i = 1, \dots, n+1$. Let us normalize this solution demanding that $\sup_{\xi \in \mathbb{R}^1} V_1(\xi) = 1$. According to the properties of the matrix system (B.5) it follows that the maximal value of the functions V_j, $j \in \{2, \dots, n+1\}$, is of the order of $O(\varepsilon)$. This follows from the application of the maximum principle to the equations for V_j, $j \in \{2, \dots, n+1\}$. From this, as in the proof of Lemma 3.1, we conclude that $\|V_1'\|_{C^0(\mathbb{R}^1)} = O(1)$. Differentiating the jth equation with respect to ξ and using the maximum principle we conclude that $\|V_j'\|_{C^0(\mathbb{R}^1)} = O(\varepsilon)$ for $j \in \{2, \dots, n+1\}$. (Here we use tacitly Lemma 3.1 and the smoothness of the functions G_i.) For $j \in \{2, \dots, n+1\}$ the equation for V_j can be written in the form:

$$\varepsilon d_j \widetilde{V}_j'' - q_\varepsilon \widetilde{V}_j' + \frac{1}{\mathcal{D}_1} b_{j-1}^\varepsilon(\xi) V_1 - b_{j-1}^\varepsilon(\xi)\widetilde{V}_j = 0,$$

where $\widetilde{V}_j := \varepsilon^{-1} d_j^{-1} V_j$. (Note also that V_j, $j = 2, \dots, n+1$, corresponds to b_{j-1} due to the chosen denotation.) Then, by differentiating twice with respect to ξ, we can estimate the second derivatives of $\widetilde{V}_j$ by a constant independent explicitly of ε. Hence $\|V_j''\|_{C^0(\mathbb{R}^1)} = O(\varepsilon)$. It follows that on every compact interval the vector function $\widetilde{V} := (\widetilde{V}_1, \widetilde{V}_2, \dots, \widetilde{V}_{n+1})^{\mathrm{T}}$, where $\widetilde{V}_k = \mathcal{D}_k^{-1} V_k$ for $k = 1$ and $\widetilde{V}_k = \varepsilon^{-1} d_k^{-1} V_k$ for $k = 2, \dots, n+1$, tends to the solution of the system

$$\mathcal{D}_1 \widetilde{V}_1'' - q_0 \widetilde{V}_1' + \sum_{k=1}^{n+1} \hat{K}_{1,j}(\xi)\widetilde{V}_j = 0, \quad \text{(B.7)}$$

$$-q_0 \widetilde{V}_j' + \hat{K}_{j,1}(\xi)\widetilde{V}_1 + \hat{K}_{j,j}(\xi)\widetilde{V}_j = 0, \quad j = 2, \dots, n+1, \quad \text{(B.8)}$$

where $\hat{K}$ is equal to

$$\begin{pmatrix} [a - \sum_{i=1}^n a_i] & a_1 & \dots & \dots & \dots & a_n \\ b_1 & -b_1 & 0 & \dots & \dots & 0 \\ & & \vdots & & & \\ b_n & 0 & 0 & \dots & \dots & -b_n \end{pmatrix}. \quad \text{(B.9)}$$

The components of $\widetilde{V}$ are non-negative. Suppose that $\widetilde{V}_j(\xi_0) = 0$ for some $\xi_0 \in \mathbb{R}$ and some $j \in \{1, \ldots, n+1\}$. Then $\widetilde{V}_j'(\xi_0) = 0$ and $V_j''(\xi_0) \geq 0$ (if $j = 1$). Due to the irreducibility of the matrix it would follow that $\widetilde{V}_j(\xi_0) = 0$, $\widetilde{V}'(\xi_0) = 0$ for all $j \in \{1, n+1\}$. Due to the uniqueness of solutions, this would imply $\widetilde{V} \equiv 0$. This would lead to be a contradiction, as $\widetilde{V}_1(0) = 1$ by definition. Thus, $\widetilde{V}_j(\xi) > 0$ for all j and $\xi \in \mathbb{R}$.

We tacitly assumed that there exists a sequence $\{\varepsilon_n\}_{n=1}^{n=\infty}$ with $\varepsilon_n \to 0$ such that the pairs $(q_\varepsilon, U_\varepsilon) \to (q_0, U_0)$ as $\varepsilon \to 0$ in $\mathbb{R}^1 \times B_{21}(\mathbb{R}^1)$ norm (as in Theorem 5.1). Thus, for any $\xi \in \mathbb{R}^1$ the limits

$$a(\xi) = \lim_{n\to\infty} f'(U_{\varepsilon_n}(\xi)), \quad b_j(\xi) = \lim_{n\to\infty} F_{1,v_j}(U_{\varepsilon_n}(\xi)), \quad a_j(\xi) = \lim_{n\to\infty} F_{j,u}(U_{\varepsilon_n}(\xi))$$

are well determined. Hence the solution retains its existence for $\varepsilon = 0$. Now, an easy application of the maximum principle shows that all the components of vector function $\widetilde{V}$ stays positive also for $\varepsilon = 0$.

On the other hand, let us consider the linearization of the system with $\varepsilon = 0$, i.e. the system (1.16)–(1.17) (which can be written in the form (6.6)), around its monotonically increasing heteroclinic solution pair $(q_0, \mathcal{U}_0)$, where $\mathcal{U}_0 = (U_{01}, Z_{01}, U_{02}, \ldots, U_{0(n+1)})$ and $Z_{0j} = U_{0j}'$ under the condition $q_0 \neq 0$. It has the form

$$\mathcal{U}^{\mathrm{T}'} = P_* \mathcal{U}^{\mathrm{T}}, \tag{B.10}$$

where $\mathcal{U} = (u, z, v_1, \ldots, v_n)$ and P_* is defined after Eq. (6.12). Hence the adjoint system has the form

$$\begin{aligned} A_1' &= \mathcal{D}_1^{-1} F_{1,1} A_2 + \sum_{k=2}^{n+1} q_0^{-1} F_{k,1} A_{k+1}, \\ A_2' &= -A_1 + q_0 \mathcal{D}_1^{-1} A_2, \\ A_i' &= \mathcal{D}_1^{-1} F_{1,i} A_2 + q_0^{-1} F_{i-1,i-1} A_i, \quad i = 3, \ldots, n+2. \end{aligned} \tag{B.11}$$

Differentiating the equation for A_2 and using the equation for A_1 with we obtain the equation

$$A_2'' = q_0 \mathcal{D}_1^{-1} A_2' - \left(\mathcal{D}_1^{-1} F_{1,1} A_2 + \sum_{k=2}^{n+1} q_0^{-1} F_{k,1} A_{k+1} \right).$$

By defining

$$\widetilde{W}_j = A_{j+1} \tag{B.12}$$

we obtain the equations for $\widetilde{W}_1$

$$\widetilde{W}_1'' = q_0 \mathcal{D}_1^{-1} \widetilde{W}_1' - \left(\mathcal{D}_1^{-1} F_{1,1} \widetilde{W}_1 + \sum_{k=2}^{n+1} q_0^{-1} F_{k,1} \widetilde{W}_k \right), \tag{B.13}$$

and for $j = 2, \ldots, n+1$ we have

$$\widetilde{W}_j' = \mathcal{D}_1^{-1} F_{1,j} \widetilde{W}_1 + q_0^{-1} F_{k,j} \widetilde{W}_k. \tag{B.14}$$

Hence we proved that the $n+1$ last components of the vector function $A = (A_1, \ldots, A_{n+2})^{\mathrm{T}} : \mathbb{R}^1 \to \mathbb{R}^{n+2}$ satisfy the last two systems of equations. If we further define

$$W_1 = D^{-1} \widetilde{W}_1 \tag{B.15}$$

and

$$W_i = q_0^{-1} \widetilde{W}_i \quad \text{for } i = 2, \ldots, n+1, \tag{B.16}$$

we note that the vector function $W(\cdot) = (W_1, \ldots, W_{n+1})^{\mathrm{T}}(\cdot)$ satisfies exactly the system (B.7)–(B.8). On the other hand, the vector function $(D\widetilde{V}_1, q_0\widetilde{V}_2, \ldots, q_0\widetilde{V}_{n+1})$ satisfies system (B.13)–(B.14). It follows from system (B.4) and from system (B.11) that $\widetilde{V}$ uniquely determines the vector function Y, whereas knowing the vector function W uniquely determines the first component of the function A. So, we have found at least one positive solution to the adjoint of the system (B.10). In consequence there is one to one correspondence between the solutions to the adjoint of system (B.10) and the solutions obtained from solutions to system (B.4) by passing to the limit $\varepsilon \to 0$.

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