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Existence of Reaction–Diffusion Waves in a Model of Immune Response

V. Volpert

Abstract. Existence of travelling waves is studied for a reaction–diffusion system of equations describing the distribution of viruses and immune cells in the tissue. The proof uses the Leray–Schauder method based on the topological degree for elliptic operators in unbounded domains and on a priori estimates of solutions in weighted spaces.

Mathematics Subject Classification. 35K57.

1. The Model of Immune Response

In this work, we study the model of viral infection spreading in the lymphoid tissue

$$\frac{\partial v}{\partial t} = D_1 \frac{\partial^2 v}{\partial x^2} + kv(1 - v) - cv, \quad (1.1)$$

$$\frac{\partial c}{\partial t} = D_2 \frac{\partial^2 c}{\partial x^2} + \phi(v)c(1 - c) - \psi(v)c, \quad (1.2)$$

where v is the dimensionless virus concentration, c is the concentration of immune cells, diffusion terms describe random motion of viruses and cells. The second term in the right-hand side of Eq. (1.1) corresponds to the virus multiplication rate, and the last term its elimination by immune cells. The last two terms in the right-hand side of Eq. (1.2) describe proliferation and death of immune cells. Both of them depend on the virus concentration. According to their biological meaning, the functions $\phi(v)$ and $\psi(v)$ are positive for $v > 0$, and growing with saturation. Precise mathematical conditions will be formulated below.

The models of immune response are often considered in the form of ODEs and DDEs (see [1,2] and the references therein). Travelling waves describing the propagation of virus infection in the tissue were studied in [3,7] in the case of a single reaction–diffusion equation with delay. System of Eqs. (1.1), (1.2) was introduced in [4]. Numerical simulations showed that infection can propagate in the tissue as a reaction–diffusion wave. In this

work, we will prove the existence of such waves in some particular cases. A travelling wave solution of system (1.1), (1.2) is a solution $v(x, t) = V(x - st)$, $c(x, t) = C(x - st)$ on the whole axis, where s is the wave speed and the functions $V(\xi)$, $C(\xi)$ satisfy the system of equations

$$D_1 V'' + sV' + kV(1 - V) - CV = 0, \quad (1.3)$$

$$D_2 C'' + sC' + \phi(V)C(1 - C) - \psi(V)C = 0. \quad (1.4)$$

We will look for solutions of this system with the limits

$$V(\pm\infty) = v_{\pm}, C(\pm\infty) = c_{\pm}, \quad (1.5)$$

where the values v_{\pm} and c_{\pm} are specified in equalities (2.3) below. Let us recall that the constant s is unknown. It should be found together with the functions $V(\xi)$ and $C(\xi)$.

Existence of waves for system (1.3), (1.4) is known in some particular cases. Let us write this system in the vector form:

$$\mathbf{D}\mathbf{w}'' + s\mathbf{w}' + \mathbf{F}(\mathbf{w}) = 0. \quad (1.6)$$

Here \mathbf{D} is a diagonal matrix of diffusion coefficients, $\mathbf{w} = (V, C)$, the vector function $\mathbf{F}(\mathbf{w})$ corresponds to the nonlinear terms in Eqs. (1.3), (1.4).

Monotone systems Suppose that $\phi(v) \equiv \text{const}$. Then for $\mathbf{w} \geq 0$ (here and below the inequalities between vectors are understood componentwise)

$$\frac{\partial F_i}{\partial w_j} \leq 0, \quad i, j = 1, 2, \quad i \neq j. \quad (1.7)$$

By a change of variables $w_1 \rightarrow 1 - w_1$, this system can be reduced to a monotone system for which the last inequalities are opposite. Existence of waves for the monotone systems is known [8, 9, 14].

Locally monotone systems For simplicity of presentation, suppose that inequalities (1.7) are strict. The system is called locally monotone if these inequalities are satisfied not everywhere but only at zero lines of the functions $F_i(\mathbf{w})$ [8, 9].¹ Let us introduce the function

$$f(V) = 1 - \frac{\psi(V)}{\phi(V)}. \quad (1.8)$$

Since $\phi(V) > 0, \psi(V) > 0$ for $V \geq 0$, then $f(V) < 1$.

If $C = f(V)$, then $F_2(\mathbf{w}) = 0$ and

$$\frac{\partial F_2}{\partial w_1} = \phi'(V)C(1 - C) - \psi'(V)C = \phi'(V)C \left(\frac{\psi(V)}{\phi(V)} - \frac{\psi'(V)}{\phi'(V)} \right) = \phi(V)Cf'(V).$$

Suppose that $f'(V) < 0$. Then from the equality $F_2(\mathbf{w}) = 0$ it follows that $\partial F_2 / \partial w_1 < 0$ ($C > 0, \phi(V) > 0$). The inequality $\partial F_1 / \partial w_2 < 0$ is satisfied everywhere ($V > 0$). Hence, up to the change of variables the system is locally monotone. Existence of waves for such systems is proved in [8, 9].

In this work, we will prove the existence of solutions of problem (1.3)–(1.5) in a more general case where the function $f(V)$ is not monotonically

¹The system is locally monotone if the derivatives in (1.7) are positive. This case can be obtained from the case with negative derivatives by a change of variables.

decreasing. This case is interesting for the biological applications. In the next section, we will present the conditions on this function, we will also formulate the main result of this work and will describe the method of proof.

2. Main Result

We suppose that $\phi(V)$ and $\psi(V)$ are positive infinitely differentiable functions defined for $V \geq 0$ and the function $f(V)$ satisfies the following conditions.

Condition 1. $0 < f(V) < 1$ for $V \geq 0$; $f(0) > k$; $f(V) > f(0)$ for $0 < V < V_*$ for some V_* ; $f(V)$ has a single maximum for $V = v_m$; $f'(V) < 0$ for $V > v_m$ (Fig. 1, left).

Condition 2. Equation $f(v) = k(1-v)$ has two solutions, v_u and v_+ , $v_u < v_+$. Moreover, $f'(v_u) < -k$, $f'(v_+) > -k$.

Consider the ODE system corresponding to (1.1), (1.2):

$$\frac{dv}{dt} = kv(1-v) - cv, \quad (2.1)$$

$$\frac{dc}{dt} = \phi(v)c(1-c) - \psi(v)c. \quad (2.2)$$

From Conditions 1 and 2, it follows that there are four stationary points, $P_0 = (0, 0)$, $P_1 = (0, f(0))$, $P_2 = (v_u, f(v_u))$, $P_3 = (v_+, f(v_+))$, where v_u and v_+ are solutions of the equation $f(v) = k(1-v)$, $v_u < v_+$. The points P_0 and P_2 are unstable, P_1 and P_3 are stable, their eigenvalues are negative. Set

$$v_- = 0, \quad c_- = f(0), \quad c_+ = f(v_+). \quad (2.3)$$

Hence, the limits (1.5) correspond to the stable stationary points of system (2.1), (2.2). Therefore, we consider the existence of waves in the bistable case.

The main result of this work is given by the following theorem.

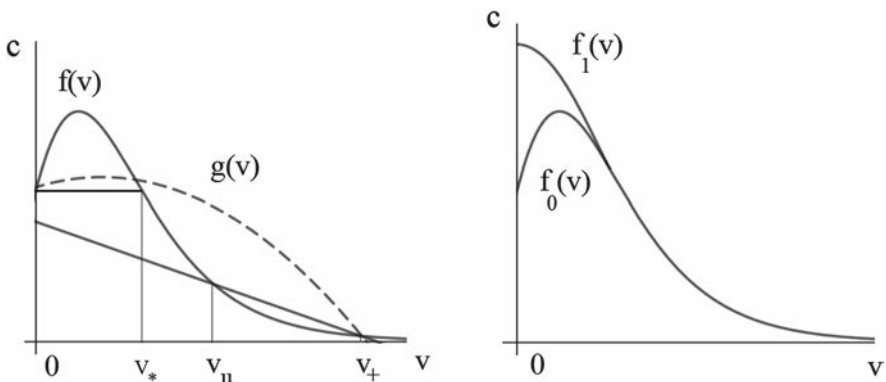


Figure 1. Left: functions $f(v)$ and $g(v)$ (Sect. 3). Right: functions $f_0(v) = f(v)$ in the original problem and $f_1(v)$ in the model problem

Theorem 2.1. *Suppose that the infinitely differentiable functions $\phi(V)$ and $\psi(V)$ are positive for $V \geq 0$, and the function $f(V)$ given by (1.8) satisfies Conditions 1 and 2. Then problem (1.3)–(1.5) has a solution for some value of s .*

The remaining part of this work is devoted to the proof of this theorem. The proof uses the Leray–Schauder (LS) method which is based on the topological degree for elliptic operators in unbounded domains [12, 13] and on a priori estimates of solutions in properly chosen weighted spaces. The main idea of the LS method is to reduce our original problem to some model problem with given properties and to obtain a priori estimates of solutions in the process of this homotopy. As a model problem we will choose a similar problem with a decreasing function $f(V)$ (Fig. 1, right). In this case, we get a locally monotone system for which the existence of waves and the required properties are known.

In the next section, we will introduce function spaces and operators and will recall the required results concerning the topological degree. The following sections will be devoted to the construction of a homotopy and to a priori estimates of solutions.

3. Operators and Spaces

For the functional setting, let us introduce the Hölder space $C^{k+\alpha}(\mathbb{R})$ consisting of vector-functions of class C^k , which are continuous and bounded on the axis \mathbb{R} together with their derivatives of order k , and such that the derivatives of order k satisfy the Hölder condition with the exponent $\alpha \in (0, 1)$. The norm in this space is the usual Hölder norm. Set $E^1 = C^{2+\alpha}(\mathbb{R})$, $E^2 = C^\alpha(\mathbb{R})$. Next, we introduce the weighted spaces E_μ^1 and E_μ^2 with $\mu(x) = \sqrt{1+x^2}$. These spaces are equipped with the norms:

$$\|w\|_{E_\mu^i} = \|w\mu\|_{E^i}, i = 1, 2.$$

Following [8, 9], we introduce the operators which will allow us to study travelling waves, that is solutions of problem (1.3)–(1.5). Consider an infinitely differentiable vector-function $\eta(x)$ such that

$$\eta(x) = \begin{cases} w_- , & x \leq -1 \\ w_+ , & x \geq 1 \end{cases} ,$$

where $w_\pm = (v_\pm, c_\pm)$. Set $w = u + \eta$ and consider the operator

$$A(u) = D(u + \eta)'' + s(u + \eta)' + F(u + \eta), \quad (3.1)$$

acting from E_μ^1 into E_μ^2 .

Functionalization of the parameter Solution $w(x)$ of Eq. (1.6) is invariant with respect to translation in space. Along with any solution $w(x)$, the functions $w(x+h)$ also satisfy this equation for any real h . This property of solutions of autonomous problems on the whole axis implies the existence of a zero eigenvalue of the linearized operator A' . Therefore, we cannot find the index of the solution (the index is understood here as the value of the degree with

respect to a small ball containing the solution). Moreover, this family of solutions is not bounded in the weighted norm. Therefore, we cannot apply the Leray–Schauder method to study the existence of solutions.

To overcome these difficulties we introduce functionalization of the parameter s [9] (Chapter 2). This means that instead of the unknown constant s we introduce some given functional $s^*(u)$ such that $s^*(u(\cdot + h))$ is a monotone function of h with the values from $-\infty$ to ∞ . Hence, equation $s^*(u(\cdot + h)) = s$ has a unique solution h for any wave speed s . Therefore, we obtain an equivalent problem without invariance of solutions with respect to translation in space. We set $s^*(u) = \log(\rho(u))$, where

$$\rho(u) = \left(\int_{-\infty}^{\infty} |u(x) + \eta(x) - w_+|^2 \sigma(x) dx \right)^{1/2},$$

$\sigma(x)$ is a monotonically increasing function such that $\sigma(x) \rightarrow 0$ as $x \rightarrow -\infty$, $\sigma(x) \rightarrow 1$ as $x \rightarrow \infty$, $\int_{-\infty}^0 \sigma(x) dx < \infty$.

Homotopy Along with problem (1.3)–(1.5), we consider a similar problem

$$D_1 V'' + sV' + kV(1 - V) - CV = 0, \quad (3.2)$$

$$D_2 C'' + sC' + \phi_\tau(V)C(1 - C) - \psi_\tau(V)C = 0, \quad (3.3)$$

$$V(\pm\infty) = v_\pm, \quad C(\pm\infty) = c_\pm \quad (3.4)$$

with the functions $\phi_\tau(V)$ and $\psi_\tau(V)$ depending on parameter $\tau \in [0, 1]$. The corresponding operator

$$A_\tau(u) = D(u + \eta)'' + s^*(u)(u + \eta)' + F_\tau(u + \eta), \quad (3.5)$$

acts from E_μ^1 into E_μ^2 . We suppose that the functions $\phi_\tau(V)$ and $\psi_\tau(V)$ are sufficiently smooth with respect to both variables V and τ . Furthermore, the function

$$f_\tau(V) = 1 - \frac{\psi_\tau(V)}{\phi_\tau(V)} \quad (3.6)$$

either satisfies Condition 1 (where v_m and V_* can depend on τ), or it is monotonically decreasing.

We begin with the construction of the function $f_\tau(v)$, where $f_0(v)$ equals the original function $f(v)$, and $f_1(v)$ is a monotonically decreasing function (Fig. 1, right). We will construct the homotopy in such a way that $f_\tau(v)$ has a single maximum or it is a monotone function.

Let us introduce an auxiliary infinitely differentiable function $h(v)$ such that the following conditions are satisfied: $h(v) \geq f(v)$ for $0 \leq v \leq v_+$,

$$h'(v) \leq 0, \quad 0 \leq v \leq v_+, \quad h(v) \equiv f(v), \quad v_m + \epsilon \leq v \leq v_+,$$

$$h(v) \equiv h(v_m), \quad 0 \leq v \leq v_m.$$

Here ϵ is a small positive constant. At the first step of homotopy we set

$$f_\tau(v) = (1 - 2\tau)f(v) + 2\tau h(v).$$

Hence, for $\tau = 0$ we have the original function and for $\tau = 1/2$ the auxiliary function $h(v)$. Obviously, $f_\tau(v)$ has a single maximum for $0 \leq \tau < 1/2$.

We can now define the function $f_1(v)$. It is any decreasing infinitely differentiable function such that $f_1(v) \geq h(v)$ for $0 \leq v \leq v_+$ and $f_1(v) \equiv f(v)$ for $v_m + \epsilon \leq v \leq v_+$. Set

$$f_\tau(v) = (2 - 2\tau)h(v) + (2\tau - 1)f_1(v).$$

The function $f_\tau(v)$ is monotonically decreasing for $1/2 < \tau \leq 1$.

Next, we define the functions ϕ_τ and ψ_τ . We set $\phi_\tau(v) \equiv \phi(v)$, such that this function does not depend on τ , and $\psi_\tau(v) = (1 - f_\tau(v))\phi(v)$. Since $f(v) < 1$ for $0 \leq v \leq v_+$, then we can construct the homotopy in such way that $f_\tau(v) < 1$ for $0 \leq v \leq v_+$, $0 \leq \tau \leq 1$. Hence $\psi_\tau(v) > 0$.

Topological degree The linearized operator about any function in E_μ^1 satisfies the Fredholm property and has the zero index. The nonlinear operator is proper on closed bounded sets. This means that the inverse image of a compact set is compact in any closed bounded set in E_μ^1 . Moreover, the operator $A_\tau(u)$ is proper with respect to the ensemble of variables (u, τ) . Finally, the topological degree can be defined for this operator. All these properties can be found in [9–13]. Alternative degree constructions for Fredholm and proper operators can be found in [5, 6].

4. Properties of Solutions

As before, we consider the system

$$D_1 V'' + sV' + kV(1 - V) - CV = 0, \quad (4.1)$$

$$D_2 C'' + sC' + \phi_\tau(V)C(1 - C) - \psi_\tau(V)C = 0 \quad (4.2)$$

on the whole axis with the limits

$$V(-\infty) = 0, \quad C(-\infty) = f_\tau(0), \quad V(\infty) = v_+, \quad C(\infty) = f_\tau(v_+) \quad (4.3)$$

at infinities. For simplicity of notation, the subscript τ can be sometimes omitted.

Definition. Denote by \mathcal{K} the set of functions $v(x), c(x) \in C^{2+\alpha}(\mathbb{R})$ which satisfy boundary conditions (4.3) and such that the following monotonicity conditions are satisfied:

$v'(x) > 0$ for all $x \in \mathbb{R}$,

$c'(x) < 0$ for all $x \in \mathbb{R}$ or $c(x)$ has a single maximum: $c'(x) > 0$ for $x < x_*$,

$c'(x) < 0$ for $x > x_*$ and some x_* , which can depend on $c(x)$.

For functions in the set \mathcal{K} , since $v(x)$ is a monotonically increasing function, we can introduce the function $c = g(v)$ such that $c(x) = g(v(x))$ (Fig. 1, left).

We will consider solutions of problem (4.1)–(4.3) from the set \mathcal{K} . We will show that this set of solutions is closed and that it is separated from other solutions. Together with compactness of the set of solutions, which follows from the properness of the corresponding operators, these properties will allow us to apply the Leray–Schauder method to this subset of solutions and not to all solutions.

4.1. The Set \mathcal{K} is Closed

We begin with some properties of solutions from the set \mathcal{K} .

Lemma 4.1. *Suppose that $(v_0(x), c_0(x)) \in \mathcal{K}$ is a solution of system (4.1), (4.2), and $c_0(x)$ has a maximum at $x = x_*$. Then $v_0(x_*) \leq V_*$, $c_0(x_*) \leq f(v_0(x_*))$, where V_* is defined in Condition 1.*

Proof. Denote $v_* = v_0(x_*)$. We need to prove that $v_* \leq V_*$ and $g(v_*) \leq f(v_*)$. Suppose that $g(v_*) > f(v_*)$. Then

$$\begin{aligned} D_2 c_0''(x_*) &= -\phi(v_0(x_*))c_0(x_*)(1 - c(x_*)) + \psi(v_0(x_*))c_0(x_*) \\ &= -\phi(v_0(x_*))c_0(x_*)(f(v_0(x_*)) - c_0(x_*)) \\ &= -\phi(v_0(x_*))c_0(x_*)(f(v_0(x_*)) - g(v_0(x_*))) > 0. \end{aligned} \quad (4.4)$$

Therefore, we obtain a contradiction with the assumption that the function $c_0(x)$ has a maximum at $x = x_*$. This argument will often be used below. Here we do not use the assumption that $(v_0(x), c_0(x)) \in \mathcal{K}$.

Suppose now that $v_* > V_*$. Since $g(v_*) \leq f(v_*)$, then $g(v_*) < f(0)$. Hence, $c_0(x_*) < c_0(-\infty)$. We obtain a contradiction with the assumption that the only extremum of the function $c_0(x)$ is a maximum reached at $x = x_*$. \square

Lemma 4.2. *Consider a sequence of solutions $(v_n(x), c_n(x)) \in \mathcal{K}$ of problem (4.1)–(4.3) (with possibly different values of $\tau = \tau_n$ and $s = s_n$), and suppose that $(v_n(x), c_n(x)) \rightarrow (v_0(x), c_0(x))$ strongly in $C^1(\mathbb{R})$, where $(v_0(x), c_0(x))$ is a solution of problem (4.1)–(4.3) with $\tau = \tau_0, s = s_0$. Then $v_0'(x) > 0$ for all $x \in \mathbb{R}$.*

Proof. Since $v_n'(x) > 0$ for all $x \in \mathbb{R}$ and n , then $v_0'(x) \geq 0, x \in \mathbb{R}$. Suppose that the assertion of the lemma does not hold and there exists x_0 such that $v_0'(x_0) = 0$. Then $v_0''(x_0) = 0$.

By virtue of the condition of the lemma, $(v_0(x), c_0(x))$ is a solution of problem (4.1)–(4.3). Hence, $v_0(x_0) > 0$, and from Eq. (4.1) it follows that $c_0(x_0) = k(1 - v_0(x_0))$. Differentiating Eq. (4.1), we get

$$D_1 v_0'''(x_0) = c_0'(x_0)v_0(x_0).$$

We will show below that

$$c_0'(x_0) < 0. \quad (4.5)$$

Then $v_0'''(x_0) < 0$, and we obtain a contradiction with the assertion that $v_0(x)$ is a non-decreasing function for all x .

We proceed to the proof of inequality (4.5). We can apply Lemma 4.1 to the solutions $(v_n(x), c_n(x)) \in \mathcal{K}$. Let $v_n(x_n) = v_*$, $v_0(x_*) = v_*$. Then, by virtue of the lemma, $c_n'(x) < 0$ for $x \geq x_n$. Since $x_n \rightarrow x_*$ as $n \rightarrow \infty$, then $c_0'(x) \leq 0$ for $x \geq x_*$. We continue with the following assertions:

1. For any small $\delta > 0$ there exists $\hat{x} \in [x_*, x_* + \delta]$ such that $c_0'(\hat{x}) < 0$. Indeed, it is sufficient to check that $c_0(x) \not\equiv c_0(x_*)$ in any interval $[x_*, x_* + \delta]$. If this is the case, then from Eq. (4.2) we conclude that $c_0(x_*) \equiv c_0(x) = f(v_0(x))$ in this interval (the subscript τ in f_τ is omitted for simplicity of notation). Hence, $f(v_0(x)) = f(v_*)$. Since

$f'(v_*) < 0$, then $v_0(x) \equiv v_*$ for $x \in [x_*, x_* + \delta]$. Then it follows from Eq. (4.1) that $c_0(x) = k(1 - v_0(x))$. On the other hand, $f(v_*) > k(1 - v_*)$. This contradiction proves the assertion.

2. For any small $\delta > 0$, there exists $\bar{x} \in [x_*, x_* + \delta]$ such that $v'_0(\bar{x}) < 0$, $c'_0(\bar{x}) < 0$. Let us take the value \hat{x} from the previous assertion. We can show that $v_0(x)$ is not identically constant in some vicinity of \hat{x} . Indeed, if $v_0(x) \equiv v_0(\hat{x})$, then we conclude from Eq. (4.1) that $c_0(x) = k(1 - v_0(x))$. Hence, $c_0(x) \equiv c_0(\hat{x})$. Then we conclude from Eq. (4.2) that $c_0(\hat{x}) = f(v_0(\hat{x}))$. As above, we obtain a contradiction with the inequality $f(v_*) > k(1 - v_*)$.
3. From Lemma 4.3 below, it follows that $c'_0(x) < 0$, $v'_0(x) > 0$ for all $x \geq \bar{x}$.

Suppose that inequality (4.5) does not hold and $c'_0(x_0) > 0$. Consider the function $g_0(v)$ such that $g_0(v_0(x)) = c_0(x)$. We have $g(v_1) = k(1 - v_1)$, where $v_1 = v_0(x_0)$, and $g'(v_1) > 0$. Since $g(0) = f(0) > g(v_1)$, then $g(v)$ has a minimum at some $v = v_2$, $0 < v_2 < v_1$. Clearly, $g(v_2) < f(v_2)$. Similar to (4.4), we obtain $c''(x) < 0$ at the point of minimum leading to a contradiction.

Consider, finally, the case where $c'_0(x_0) = 0$. If $c''_0(x_0) > 0$, then $x = x_0$ is a point of minimum. If $c''_0(x_0) < 0$, then $x = x_0$ is a point of maximum. Hence, there exists a minimum at some $v = v_2$, $0 < v_2 < v_1$. In both cases, we get the same contradiction in sign of $c''(x)$. If $c''_0(x_0) = 0$, then from equation (4.2) we get $c_0(x_0) = f(v_0(x_0))$. However, $c_0(x_0) = g_0(v(x_0)) < f(v_0(x_0))$. This contradiction completes the proof. \square

Lemma 4.3. *Let $(v_0(x), c_0(x))$ be a positive solution of problem (4.1)–(4.3) (not necessarily in the set \mathcal{K}). Suppose that for some x_1 , $v'_0(x_1) > 0$, $c'_0(x_1) < 0$. Moreover, $v'_0(x) \geq 0$, $c'_0(x) \leq 0$ for $x \geq x_1$ and $f'(v) < 0$ for $v \geq v_0(x_1)$. Then $v'_0(x) > 0$, $c'_0(x) < 0$ for $x \geq x_1$.*

Proof. Suppose that the assertion of the lemma does not hold and $v'_0(x_2) = 0$ for some $x_2 > x_1$. Then $v''_0(x_2) = 0$. Set $u(x) = v'_0(x)$. Differentiating (4.1), we get

$$D_1 u'' + su' + a_1(x)u + b_1(x) = 0, \quad (4.6)$$

where

$$a_1(x) = k(1 - 2v_0(x)) - c_0(x), \quad b_1(x) = -c'_0(x)v_0(x).$$

Since $u(x) \geq 0$ for $x \geq x_1$, $u(x_2) = u'(x_2) = 0$, $b_1(x) \geq 0$, then from the maximum principle it follows that $u(x) \equiv 0$. This conclusion contradicts the assumption that $u(x_1) > 0$.

Assume now that $c'_0(x_2) = 0$ for some $x_2 > x_1$ and set $w(x) = c'_0(x)$. Since $c''_0(x_2) = 0$, then from Eq. (4.2) we obtain the equality

$$\phi(v_0(x_2))c_0(x_2)(1 - c_0(x_2)) - \psi(v_0(x_2))c_0(x_2) = 0.$$

Since $c_0(x_2) \neq 0$, then from the previous equality it follows that

$$1 - c_0(x_2) = \frac{\psi(v_0(x_2))}{\phi(v_0(x_2))}. \quad (4.7)$$

Differentiating (4.2), we get

$$D_2w'' + sw' + a_2(x)w + b_2(x) = 0, \quad (4.8)$$

where

$$\begin{aligned} a_2(x) &= \phi(v_0(x))(1 - 2c_0(x)) - \psi(v_0(x)), \quad b_2(x) \\ &= (\phi'(v_0)c_0(1 - c_0) - \psi'(v_0)c_0)v_0'(x). \end{aligned}$$

Taking into account (4.7), we have

$$\begin{aligned} b_2(x_2) &= \left(\phi'(v_0(x_2)) \frac{\psi(v_0(x_2))}{\phi(v_0(x_2))} - \psi'(v_0(x_2)) \right) c_0(x_2)v_0'(x_2) \\ &= f'(v_0(x_2))\phi(v_0(x_2))c_0(x_2)v_0'(x_2). \end{aligned}$$

Since $\phi(v_0(x_2)) > 0, c_0(x_2) > 0, v_0'(x_2) > 0$, and $f'(v_0(x_2)) < 0$, then $b_2(x_2) < 0$. Furthermore, by virtue of the equalities $w(x_2) = w'(x_2) = 0$ and Eq. (4.8) we conclude that $c_0'''(x_2) = w''(x_2) > 0$. Hence, $c_0'(x) > 0$ in some neighborhood of $x = x_2$. We obtain a contradiction with the assumption of the lemma. \square

Proposition 4.4. *Consider a sequence of solutions $(v_n(x), c_n(x)) \in \mathcal{K}$ of problem (4.1)–(4.3) (with possibly different values of $\tau = \tau_n$ and $s = s_n$), and suppose that $(v_n(x), c_n(x)) \rightarrow (v_0(x), c_0(x))$ strongly in $C^1(\mathbb{R})$, where $(v_0(x), c_0(x))$ is a solution of problem (4.1)–(4.3) with $\tau = \tau_0, s = s_0$. Then $(v_0(x), c_0(x)) \in \mathcal{K}$.*

Proof. By virtue of Lemma 4.2, it is sufficient to verify the properties of the function $c_0(x)$. We begin with the case where $c_n'(x) < 0, x \in \mathbb{R}$ for all n sufficiently large. Then $c_0'(x) \leq 0, x \in \mathbb{R}$. We will check that this inequality is strict. Suppose that this is not the case and $c_0'(x_0) = 0$ for some x_0 . Then $c_0''(x_0) = 0$, and it follows from Eq. (4.2) that $c_0(x_0) = f_{\tau_0}(v_0(x_0))$. We will consider three different cases depending on the value of τ_0 .

- $\tau_0 < 1/2$. In this case, the function $f_{\tau_0}(v)$ has a single maximum at $v = v_m, f'(v) > 0$ for $0 \leq v < v_m, f'(v) < 0$ for $v_m < v \leq v_m$ (subscript τ_0 is omitted). Since $c_0(x_0) \leq c_0(-\infty) = f(0)$, then $f'(v_0(x_0)) < 0$. Differentiating Eq. (4.2), we get

$$\begin{aligned} D_2c_0'''(x_0) &= -c_0(x_0)(\phi'(v_0(x_0))(1 - c_0(x_0)) - \psi'(v_0(x_0)))v_0'(x_0) \\ &= -c_0(x_0)v_0'(x_0) \left(\phi'(v_0(x_0)) \frac{\psi(v_0(x_0))}{\phi(v_0(x_0))} - \psi'(v_0(x_0)) \right) \\ &= -c_0(x_0)v_0'(x_0)f'(v_0(x_0))\phi(v_0(x_0)) > 0. \end{aligned} \quad (4.9)$$

We obtain a contradiction with the assertion that $c_0(x)$ is a non-increasing function.

- $\tau_0 > 1/2$. In this case, $f'(v) < 0$ for all $0 \leq v \leq v_+$. Therefore, $f'(v_0(x_0)) < 0$, and this case is similar to the previous one.
- $\tau_0 = 1/2$. In this case, $f(v) \equiv f(v_m)$ for $0 \leq v \leq v_m$ and $f'(v) < 0$ for $v_m < v < v_+$. If $v_0(x_0) > v_m$, then $f'(v_0(x_0)) < 0$, and this case is similar to the previous ones. Suppose that $v_0(x_0) \leq v_m$. Since $c_0(-\infty) = f(0)$ and

$c_0(x_0) = f(v_0(x_0)) = f(0)$, then $c_0(x) \equiv c_0(x_0)$ for $x \leq x_0$. Set $z(x) = -c'_0(x)$. Differentiating Eq. (4.2), we get

$$D_2 z'' + s z' + a(x)z + b(x) = 0, \quad (4.10)$$

where

$$a(x) = \phi(v_0(x))(1 - 2c_0(x)) - \psi(v_0(x)), \quad b(x) = -c_0(x)v'_0(x)f'(v_0(x))\phi(v_0(x)).$$

Since $z(x) \geq 0$, $z(x) \equiv 0$ for $x \leq x_0$, $z(x) \not\equiv 0$ in \mathbb{R} , and $b(x) \geq 0$, we obtain a contradiction with the maximum principle.

In the remaining part of the proof, we consider the case where the functions $c_n(x)$ have single maxima for all n sufficiently large. Hence, the corresponding functions $g_n(v)$ also have single maxima at some $v = v_n$. Without loss of generality we can assume that $v_n \rightarrow v_0$ for some $v_0 \in [0, v_*]$ (see Lemma 4.1), and the limiting function $g_0(v)$ has a maximum at $v = v_0$. We will verify that $g'_0(v) > 0$ for $0 < v < v_0$ and $g'_0(v) < 0$ for $v_0 < v < v_+$.

- $\tau_0 > 1/2$. Due to the monotonicity of the function $f(v)$, $f(0) > f(v_0)$. Similar to Lemma 4.1, we conclude that $f(v_0) \geq g_0(v_0)$. On the other hand, $f(0) = c_0(-\infty) \leq \max_{x \in \mathbb{R}} c(x) = g_0(v_0)$. This contradiction shows that the function $c_0(x)$ cannot have a maximum.

- $\tau_0 = 1/2$. If $v_0 \leq v_m$, then this case is similar to the case $\tau_0 = 1/2$ considered above. If $v_0 > v_m$, then $g_0(v_0) \geq g_0(0) = f(0) > f(v_0)$. Therefore, $v = v_0$ cannot be a point of maximum of the function $g_0(v)$ (cf. Lemma 4.1).

- $\tau_0 < 1/2$. Let x_0 be such that $c_0(x_0) = \max_{x \in \mathbb{R}} c(x)$. Then $c'_0(x) \geq 0$ for $x \leq x_0$ and $c'_0(x) \leq 0$ for $x \geq x_0$. We will prove the following two assertions.

- • Let us prove that $c'_0(x) > 0$ for $x < x_0$. Suppose that this is not the case and $c'_0(x_1) = 0$ for some $x_1 < x_0$. Then $c''_0(x_1) = 0$, and from equation (4.2) we conclude that $c_0(x_1) = f(v_0(x_1))$. Suppose, first, that $v_0(x_1) < v_m$, where v_m is the point of maximum of the function $f(v)$. Then $f'(v_0(x_1)) > 0$. Similar to (4.9), we get:

$$D_2 c'''_0(x_1) = -c_0(x_1)v'_0(x_1)f'(v_0(x_1))\phi(v_0(x_1)) < 0.$$

We obtain a contradiction with the assumption that the function $c_0(x)$ is non-decreasing for $x \leq x_0$. Assume, next, that $v_0(x_1) \geq v_m$. Then $g_0(v_0(x_0)) \geq g_0(v_0(x_1)) = f(v_0(x_1)) > f(v_0(x_0))$. Similar to Lemma 4.1 we can verify that $x = x_0$ cannot be the point of maximum of the function $c_0(x)$.

- • Let us now verify that $c'_0(x) < 0$ for $x > x_0$. Suppose that this is not the case and $c'_0(x_2) = 0$ for some $x_2 > x_0$. Then $c''_0(x_2) = 0$, and from equation (4.2) we conclude that $c_0(x_2) = f(v_0(x_2))$. Suppose, first, that $v_0(x_2) > v_m$, where v_m is the point of maximum of the function $f(v)$. Then $f'(v_0(x_2)) < 0$, and

$$D_2 c'''_0(x_2) = -c_0(x_2)v'_0(x_2)f'(v_0(x_2))\phi(v_0(x_2)) > 0.$$

We obtain a contradiction with the assumption that the function $c_0(x)$ is non-increasing for $x \geq x_0$. Assume, next, that $v_0(x_2) \leq v_m$. Then $g_0(v_0(x_0)) \geq g_0(v_0(x_2)) = f(v_0(x_2)) > f(v_0(x_0))$. Similar to Lemma 4.1, we can verify that $x = x_0$ cannot be the point of maximum of the function $c_0(x)$. This contradiction completes the proof of the proposition. \square

4.2. The Set \mathcal{K} is Separated from Other Solutions

In this section, we will prove the following property of the set \mathcal{K} . If there is a sequence of solutions $(v_n(x), c_n(x))$ of problem (4.1)–(4.3) (with possibly different values of τ and $s = s_n$), and $(v_n(x), c_n(x)) \rightarrow (v_0(x), c_0(x)) \in \mathcal{K}$ strongly in $C^1(\mathbb{R})$, then $(v_n(x), c_n(x)) \in \mathcal{K}$ for all n sufficiently large. This property is crucial for a priori estimates of solutions. It shows that solutions from the set \mathcal{K} are separated from other solutions. For this purpose, we will prove the following properties of solutions.

- **P1.** There exists x_0 such that $v'_n(x) > 0$ for all $x \leq x_0$ and n sufficiently large (Lemma 4.5).
- **P2** There exists x_1 such that $v'_n(x) > 0, c'_n(x) < 0$ for all $x \geq x_1$ and n sufficiently large (Lemma 4.8).
- **P3** Since $v_n(x) \rightarrow v_0(x)$ in $C^1(\mathbb{R})$ and $v'_0(x) > 0$ for $x_0 \leq x \leq x_1$, then $v'_n(x) > 0$ for $x_0 \leq x \leq x_1$ and all n sufficiently large. Thus, $v'_n(x) > 0$ for all x .
- **P4** The functions $c_n(x)$ are monotonically decreasing for $x \leq x_1$ or they have a single maximum (Lemma 4.9).

Lemma 4.5. *Suppose that $(v_n(x), c_n(x))$ are solutions of system (4.1), (4.2) with $s = s_n$, $\tau = \tau_n$ and limits (4.3) at infinities. Suppose, next, that these functions converge strongly in $C^1(\mathbb{R})$ to a solution $(v_0(x), c_0(x)) \in \mathcal{K}$ of system (4.1), (4.2) with $s = s_0$, $\tau = \tau_0$ as $n \rightarrow \infty$, and $s_n \rightarrow s_0, \tau_n \rightarrow \tau_0$. If x_0 is such that $c_0(x) > k + \epsilon$ for $x \leq x_0$ and some $\epsilon > 0$, then $v'_n(x) > 0$ for $x \leq x_0$ and all n sufficiently large.*

Proof. The proof of the lemma does not depend on the value of $\tau \in [0, 1]$. This subscript in the notation f_τ will be omitted.

By virtue of the inequality $f(0) > k$, we can choose such $\epsilon > 0$, that $f(0) - \epsilon > k$. Taking into account that $c_0(x) \rightarrow f(0)$ as $x \rightarrow -\infty$, we can choose such x_0 that $c_0(x) \geq f(0) - \epsilon/2$ for all $x \leq x_0$. Hence, $c_0(x) > k \geq k(1 - v_0(x))$ for $x \leq x_0$. This inequality can be written as $g_0(v) > k(1 - v)$ for $0 \leq v \leq v_0$, where the function $g_0(v)$ is such that $c_0(x) = g_0(v_0(x))$ and $v_0 = v_0(x_0)$. Since the curve $(v_n(x), c_n(x))$ on the plane (v, c) converges to the curve $(v, g_0(v))$ as $n \rightarrow \infty$, then

$$c_n(x) > k(1 - v_n(x)), \quad x \leq x_0 \quad (4.11)$$

for all n sufficiently large.

Since $v'_0(x_0) > 0$, then $v'_n(x_0) > 0$ for all n sufficiently large. Furthermore, $v_n(x) \rightarrow 0$ as $x \rightarrow -\infty$. Suppose that the assertion of the lemma does not hold. Then $v'_n(x_1) = 0$ for some $x_1 < x_0$. From (4.1), we get

$$D_1 v''_n(x_1) = -v_n(x_1)(k(1 - v_n(x_1)) - c_n(x_1)).$$

If $v_n(x_1) > 0$, then from (4.11) it follows that $v''_n(x_1) > 0$, and $v_n(x)$ does not converge to 0 at $-\infty$. Similarly, if $v_n(x_1) < 0$, then $v''_n(x_1) < 0$, and we obtain a similar contradiction. Finally, if $v_n(x_1) = 0$, then $v_n(x) \equiv 0$, and we obtain a contradiction with the inequality $v'_n(x_0) > 0$. \square

We will use some auxiliary results to prove the property P2.

Lemma 4.6. *Consider the system*

$$Du'' + su' + b(x)u = 0, \quad (4.12)$$

where D is a diagonal matrix with positive diagonal elements, s is a constant, $b(x)$ is a square matrix with continuous elements $b_{ij}(x)$, $b_{ij}(x) \geq 0$ for $i \neq j$, $b(x) \rightarrow b_0$ as $x \rightarrow \infty$ and the principal eigenvalue of the matrix b_0 is negative.

Suppose that the solution $u(x)$ of this system is such that $u(x_1) > 0$ and $u(x) \rightarrow 0$ as $x \rightarrow \infty$. If x_1 is sufficiently large, then $u(x) > 0$ for all $x \geq x_1$.

Proof. Since the matrix b_0 has non-negative off-diagonal elements and its principal eigenvalue (eigenvalue with the maximal real part) is negative, then there exists a positive vector p such that $b_0 p < 0$. Hence, we can choose x_1 sufficiently large such that $b(x)p < 0$ for all $x \geq x_1$.

Suppose that at least one of the component of the solution becomes negative for some $x_2 > x_1$. Then we can choose such positive constant k that the function $w(x) = u(x) + kp$ satisfies the following properties: $w(x) \geq 0$ for all $x \geq x_1$, $w(x_1) > 0$ and $w_i(x_1) = 0$ for some component w_i . Moreover, this function satisfies the equation

$$Dw'' + sw' + b(x)w - kb(x)p = 0. \quad (4.13)$$

We obtain a contradiction in signs in the i th equation of this system at $x = x_2$. Indeed, $w_i(x_2) = w'_i(x_2) = 0$, $w''_i(x_2) \geq 0$, $b_{ij}(x_2)w_j(x_2) \geq 0$ for $j \neq i$, and $-kb(x)p > 0$ for all $x \geq x_1$ according to the choice of x_1 . This contradiction proves the lemma. \square

Corollary 4.7. *Consider the system*

$$Dw'' + sw' + F(w) = 0, \quad (4.14)$$

where D is a diagonal matrix with positive diagonal elements, s is a constant, and

$$\frac{\partial F_i}{\partial w_j} > 0, \quad i \neq j. \quad (4.15)$$

Let $w(x)$ be a solution of this system defined for $x \geq x_1$ and such that $w'(x_1) < 0$, $w(x) \rightarrow 0$ as $x \rightarrow \infty$. If the principal eigenvalue of the matrix $F'(0)$ is negative, and x_1 is sufficiently large, then $w'(x) < 0$ for all $x \geq x_1$.

The proof of this assertion follows directly from the previous lemma if we set $u(x) = -w'(x)$.

Lemma 4.8. *Suppose that $(v_n(x), c_n(x))$ are solutions of system (4.1), (4.2) with $s = s_n, \tau = \tau_n$ and limits (4.3) at infinities. Suppose, next, that these functions converge strongly in $C^1(\mathbb{R})$ to a solution $(v_0(x), c_0(x)) \in \mathcal{K}$ of system (4.1), (4.2) with $s = s_0, \tau = \tau_0$ as $n \rightarrow \infty$, and $s_n \rightarrow s_0, \tau_n \rightarrow \tau_0$. If $v'_0(x) > 0$, $c'_0(x) < 0$ for all $x \geq x_1$ and some x_1 , and $f'(v) < 0$ for $v \geq v_0(x_1)$, then $v'_n(x) > 0$, $c'_n(x) < 0$ for all $x \geq x_1$ and n sufficiently large.*

Proof. Consider the functions

$$F(v, c) = kv(1 - v) - cv, \quad G(v, c) = \phi(v)c(1 - c) - \psi(v)c.$$

For $0 < v < 1, 0 < c < 1$ we have $\frac{\partial F}{\partial c} < 0$. If $G(v, c) = 0$, then $c = f(v)$ and $\frac{\partial G}{\partial v} = \phi'(v)c(1-c) - \psi'(v)c = c \left(\phi'(v) \frac{\psi(v)}{\phi(v)} - \psi'(v) \right) = f(v)\phi(v)f'(v) < 0$ for $v > v_m$, where v_m is the point of maximum of $f(v)$.

After the change of variables $v \rightarrow v_+ - v$ the system becomes monotone (cf. (4.15)) in the vicinity of the limiting value v_+, c_+ . The assertion of the lemma follows from the previous corollary. \square

By virtue of property P3, $v_n(x)$ is an increasing function for all x . Hence, we can introduce the function $c = g_n(v)$ such that $c_n(x) = g_n(v_n(x))$.

Lemma 4.9. *Under the conditions of the previous lemma, suppose that $c'_0(x_1) < 0$. Then for all n sufficiently large the functions $g_n(v)$ possess the following properties: $g_n(0) = f_\tau(0)$, $g'_n(v_0) < 0$, where $v_0 = v_0(x_1)$, and $g_n(v)$ either is monotonically decreasing in the interval $0 < v < v_0$ or it has a single maximum.*

Proof. The boundary condition $g_n(0) = f_\tau(0)$ is obviously satisfied. Since $c'_n(x) = g'_n(v)v'_n(x)$, then $g'_n(v_0) < 0$. Let us verify that the functions $g_n(v)$ are monotonically decreasing in the interval $0 \leq v \leq v_0$ or they have a single maximum. The proof does not depend on the value of $\tau \in [0, 1]$, and this subscript will be omitted.

To prove that the function $g_n(v)$ possesses the required property, we will show that it cannot have a minimum. Suppose that a function $g_n(v)$ has a minimum at some point $v = v_1, 0 < v_1 < v_0$. Then $g_n(v_1) \geq f(v_1)$. Indeed, any extremum of the function $g_n(v) (= c_n(x))$ for which $g_n(v) < f_n(v)$ is a maximum (cf. Lemma 4.1). We will show that the assumption about the existence of a minimum leads to a contradiction. Let $v_1 \leq v_m$, where v_m is the point of maximum of the function $f(v)$. Then we will show that the function $g_n(v)$ cannot satisfy the boundary condition $g_n(0) = f(0)$. If $v_1 \leq v_m$ is a minimum of the function $g(v)$ (the subscript n is omitted), then $g(v_1) \geq f(v_1) > f(0)$. To satisfy the equality $g(0) = f(0)$, the function $g(v)$ should have a maximum at some $v = v_2 < v_1$. However, in this case, $g(v_2) > g(v_1) \geq f(v_1) > f(v_2)$. Hence, v_2 cannot be a point of maximum (cf. Lemma 4.1).

Similarly, if $v_1 \geq v_m$, then the condition $g'(v_0) < 0$ cannot be satisfied. Thus, the functions $g_n(v)$ cannot have minima in the interval $0 < v \leq v_0$ for n sufficiently large. Therefore, they are monotonically decreasing, or they have single maxima. \square

We proved the following theorem.

Theorem 4.10. *Suppose that $(v_n(x), c_n(x))$ are solutions of system (4.1), (4.2) with $\tau = \tau_n, s = s_n$ and limits (4.3) at infinities. Suppose, next, that these functions converge strongly in $C^1(\mathbb{R})$ to a solution $(v_0(x), c_0(x)) \in \mathcal{K}$ of system (4.1), (4.2) with $s = s_0, \tau = \tau_0$ as $n \rightarrow \infty$, and $s_n \rightarrow s_0, \tau_n \rightarrow \tau_0$. Then $(v_n(x), c_n(x)) \in \mathcal{K}$ for all n sufficiently large.*

Let us note that the assumption on the function $f(v)$ that it has a single maximum is used in Lemma 4.9.

5. A Priori Estimates

We will obtain a priori estimates of solutions from the set \mathcal{K} in the weighted Hölder space. Let us note first of all that they are bounded in the uniform norm. Indeed, the component $v(x)$ of the solution is an increasing function with the limits (3.4). The component $c(x)$ of the solution can be also monotone or it has a single maximum. In the latter case, it admits an estimate from above (Lemma 4.1). Similar to [9] (Chapter 3, Lemma 2.1) we can conclude that the solutions are uniformly bounded in $C^3(\mathbb{R})$. We continue with the estimate of the wave speed.

Lemma 5.1. *The speed s for which problem (3.2)–(3.4) has a solution in the class \mathcal{K} is bounded independently of τ .*

Proof. Consider a solution $(V(x), C(x)) \in \mathcal{K}$ of problem (3.2)–(3.4). Since $V(x)$ is a monotonically increasing function, we can introduce a function $g(v)$ such that $C(x) = g(V(x))$. Substituting it into Eq. (3.2), we get the equation

$$D_1 V'' + sV' + kV(1 - V - g(V)/k) = 0, \quad V(-\infty) = 0, \quad V(\infty) = v_+. \quad (5.1)$$

The wave speed for this equation is estimated from below by the minimal (negative) wave speed $s_0 = -2\sqrt{kD_1}$ for the equation

$$D_1 V'' + sV' + kV(1 - V) = 0.$$

To estimate the value of s from above, let us note that the function $G(v) = kv(1 - v - g(v)/k)$ is positive in some left half-neighborhood of the point v_+ . Since $G(v)$ is negative in a right half-neighborhood of $v = 0$, its positiveness in the vicinity of v_+ provides bistability of the equation. It also follows from the fact that the solution of system (3.2), (3.3) converges to its limiting value at infinity along the principal eigenvector (cf. [9], Chapter 3, Theorem 2.1).

Let us choose some values v_1 and v_2 independent of τ and such that $v_1 < v_2 < v_+$. Denote by x_1 and x_2 such values that $V(x_1) = v_1, V(x_2) = v_2$. Integrating Eq. (5.1) from x_1 to x_2 , we get:

$$D_1(V'(x_2) - V'(x_1)) + s(v_2 - v_1) < 0.$$

Since $V'(x_2) > 0$, then $s < D_1 V'(x_1)/(v_2 - v_1)$. Taking into account that V' is bounded independently of s and of τ , we conclude that the wave speed is bounded from above. \square

We will now prove that the solutions are uniformly bounded in the weighted space E_μ^1 . By virtue of the estimates of the derivatives of solutions, it is sufficient to verify that the norm $C_\mu(\mathbb{R})$ is uniformly bounded. Let us recall that solution $\mathbf{w} = (V, C)$ of problem (3.2)–(3.4) is represented in the form $w = u + \eta$ (Sect. 3).

Lemma 5.2. *The estimate*

$$\sup_{x \in \mathbb{R}} |u(x)\mu(x)| \leq M, \quad \tau \in [0, 1] \quad (5.2)$$

holds for all solutions $\mathbf{w} = u + \eta$ of problem (3.2)–(3.4) from the class \mathcal{K} . Here $\mu(x)$ is the weight function, the constant M does not depend on solution and on τ .

Proof. Set

$$\mathbf{F}_\tau(\mathbf{w}) = \begin{cases} kV(1 - V) - CV \\ \phi_\tau(V)C(1 - C) - \psi_\tau(V)C \end{cases},$$

$\mathbf{w} = (V, C)$. Since all eigenvalues of the matrices $\mathbf{F}'_\tau(w_\pm)$ are located in the half-plane $\operatorname{Re} \lambda \leq -\epsilon$ for some $\epsilon > 0$, then solutions decay exponentially at infinity. Moreover, there exist positive constants K, δ, σ independent of τ and of solution such that

$$|\mathbf{w}(x) - \mathbf{w}_+| \leq Ke^{-\delta x}, \quad \text{if } |\mathbf{w}(x) - \mathbf{w}_+| \leq \sigma, \quad (5.3)$$

$$|\mathbf{w}(x) - \mathbf{w}_-| \leq Ke^{\delta x}, \quad \text{if } |\mathbf{w}(x) - \mathbf{w}_-| \leq \sigma. \quad (5.4)$$

These inequalities mean that there are uniform exponential estimates of solutions in the vicinity of their limiting values at infinity.

Denote by N_τ^+ (resp., N_τ^-) such values of x that the estimate (5.3) (resp., (5.4)) holds for $x \geq N_\tau^+$ (resp., $x \leq N_\tau^-$). They can depend on the value of τ . From (5.3), (5.4) we easily obtain the estimates

$$|u(x)\mu(x)| \leq M, \quad x \geq N_\tau^+, \quad x \leq N_\tau^- \quad (5.5)$$

with some constant M independent of τ and of solution.

Suppose that $|N_\tau^+|$ and $|N_\tau^-|$ are bounded independently of τ ,

$$|N_\tau^\pm| \leq K, \quad \tau \in [0, 1] \quad (5.6)$$

for some positive constant K . Then, clearly, the required estimate holds for all x :

$$|u(x)\mu(x)| \leq M, \quad x \in \mathbb{R}. \quad (5.7)$$

Therefore, it remains to prove estimate (5.6). Suppose that it does not hold, and at least one of these numbers tends to infinity as $\tau \rightarrow \tau_0 \in [0, 1]$. Consider, first, the case where the difference $|N_\tau^+ - N_\tau^-|$ remains bounded. Since solutions $\mathbf{w}(x) = (V(x), C(x))$ of problem (3.2)–(3.4) are invariant with respect to translation in space, then the function $\mathbf{w}_h(x) = \mathbf{w}(x - h)$ is also a solution for any real h . Set $\mathbf{w}_\tau(x) = \mathbf{w}(x + N_\tau^+)$. Then we have the following estimates:

$$\begin{aligned} |\mathbf{w}_\tau(x) - \mathbf{w}_+| &\leq Ke^{-\delta x}, \quad x \geq 0; \quad |\mathbf{w}_\tau(x) - \mathbf{w}_-| \leq Ke^{\delta x}, \\ x &\leq N_\tau^- - N_\tau^+. \end{aligned} \quad (5.8)$$

Since $|N_\tau^+ - N_\tau^-|$ is uniformly bounded, then estimate (5.7) holds with a constant M independent of τ .

Introducing functionalization of parameter, we consider the given functional $s^*(u)$ instead of the unknown wave speed s_τ which depends on τ . The value of the functional $s^*(u(\cdot + h))$ depends on the shift h . Therefore, we choose a single value of h such that

$$s^*(u(\cdot + h)) = s_\tau \quad (5.9)$$

and, consequently, remove the invariance of solution with respect to translation. By virtue of a priori estimates of the wave speed, solution h of equation (5.9) is uniformly bounded for all τ . Indeed, $s^*(u(\cdot + h)) \rightarrow \pm\infty$ as $h \rightarrow \pm\infty$. Hence, solutions $\mathbf{w}(x + h)$ and $\mathbf{w}(x + N_\tau^+)$ differ by a final value of shift. Consequently, estimate (5.7) for the latter implies a similar estimate for the former.

Next, consider the case where

$$|N_\tau^+ - N_\tau^-| \rightarrow \infty, \quad \tau \rightarrow \tau_0. \quad (5.10)$$

The functions $\mathbf{w}_\tau(x) = \mathbf{w}(x + N_\tau^+)$ satisfy the first estimate in (5.8). Due to the definition of σ in (5.3), (5.4), $|\mathbf{w}_\tau(x) - \mathbf{w}_+| \leq \sigma$ for $x \geq 0$ and $|\mathbf{w}_\tau(x) - \mathbf{w}_-| \leq \sigma$ for $x \leq N_\tau^- - N_\tau^+$. Assuming that σ is sufficiently small, we observe that the sets $|\mathbf{w} - \mathbf{w}_+| \leq \sigma$ and $|\mathbf{w} - \mathbf{w}_-| \leq \sigma$ do not intersect. Therefore, there exists a sequence x_k such that $x_k \rightarrow -\infty$ as $k \rightarrow \infty$, and

$$|\mathbf{w}_{\tau_k}(x_k) - \mathbf{w}_-| > \sigma. \quad (5.11)$$

From the sequence \mathbf{w}_{τ_k} we can choose a subsequence $\mathbf{w}_{\tau_{k_n}}$ locally convergent to some limiting function $\mathbf{w}_0(x)$. Clearly, it is a solution of problem (3.2)–(3.4) with $\tau = \tau_0$ and $s = s_{\tau_0}$. Moreover, $\mathbf{w}_0(x) \rightarrow \mathbf{w}_+$ as $x \rightarrow \infty$. Since $\mathbf{w}_{\tau_{k_n}} \in \mathcal{K}$, then $\mathbf{w}_0 \in \mathcal{K}$. Hence, there exists a limit $\mathbf{w}_* = \mathbf{w}(-\infty)$. Furthermore, it follows from (5.11) that $\mathbf{w}_* \neq \mathbf{w}_-$.

Let us recall that there are four zeros of the function $\mathbf{F}_\tau(\mathbf{w})$: P_0, P_1, P_2, P_3 . If we exclude $P_1 = \mathbf{w}_-$ and $P_3 = \mathbf{w}_+$, it remains P_0 and P_2 . The former being excluded by virtue of the monotonicity of solution ($|\mathbf{w}_*| \geq |\mathbf{w}_{\tau_0}(0)| = \sigma$), we get $\mathbf{w}_* = P_2$.

Along with the functions $\mathbf{w}_\tau(x) = \mathbf{w}(x + N_\tau^+)$, we also consider the functions $\hat{\mathbf{w}}_\tau(x) = \mathbf{w}(x + N_\tau^-)$. Similar to the arguments above, we conclude that there is a limiting solution $\hat{\mathbf{w}}_0(x)$ of system (3.2), (3.3) for $\tau = \tau_0$, $s = s_{\tau_0}$, and this solution has the limits $\hat{\mathbf{w}}_0(-\infty) = \mathbf{w}_-$, $\hat{\mathbf{w}}_0(\infty) = \mathbf{w}_*$ at infinity. Since system (3.2), (3.3) can be reduced to a locally monotone system by a change of variables for $v_* \leq v \leq v_+$, and the matrix $\mathbf{F}'(\mathbf{w}_*)$ has a positive eigenvalue, then the existence of the solution $\mathbf{w}_0(x)$ implies that $s_{\tau_0} > 0$, while the existence of the solution $\hat{\mathbf{w}}_0$ implies that $s_{\tau_0} < 0$ [9] (Chapter 3, Lemma 2.8). This contradiction proves that (5.10) does not hold. Thus, estimate (5.7) is proved. \square

Theorem 5.3. *The estimate*

$$\|u\|_{E_\mu^1} \leq M, \quad \tau \in [0, 1], \quad (5.12)$$

holds for all solutions $\mathbf{w} = u + \eta$ of problem (3.2)–(3.4) from the class \mathcal{K} . Here $\mu(x)$ is the weight function, the constant M does not depend on solution and on τ .

The proof of the theorem follows from the previous lemma and from the estimates of solutions in the norm $C^3(\mathbb{R})$.

6. Existence of Solutions

6.1. Leray–Schauder Method

We consider the operator equation

$$A_\tau(u) = 0, \quad (6.1)$$

where the operator $A_\tau(u) : E_\mu^1 \rightarrow E_\mu^2$ is defined in Sect. 3. The homotopy is constructed in such a way that $A_0(u)$ corresponds to the original problem (1.3)–(1.5) and $A_1(u)$ to the model problem. To apply the Leray–Schauder method, we need to verify two conditions: a priori estimates of solutions of Eq. (6.1) in the space E_μ^1 and that the value of the topological degree for the model operator is different from 0.

In the previous section, we obtained a priori estimates of solutions which belong to the class \mathcal{K} . However, we do not have estimates for other possible solutions. Therefore, we need to modify the Leray–Schauder method in the following way. Denote by B a ball in the space E_μ^1 which contains all solutions from the class \mathcal{K} . Since the operator $A_\tau(u)$ is proper with respect to both variables u and τ [13], that is, the inverse image of the compact set is compact in any bounded closed set, then the set of solutions S in B is compact. Moreover, by virtue of the results of Sect. 4.1, the set $S \cap \mathcal{K}$ is also compact.

For each solution $u \in \mathcal{K}$, consider a ball $b_r(u)$ of radius r and center u . Set

$$\Omega_r = \cup_{u \in S \cap \mathcal{K}} b_r(u).$$

If r is sufficiently small, then the set Ω_r does not contain solutions $u \notin \mathcal{K}$. Indeed, suppose that this is not true and there exists a sequence $r_n \rightarrow 0$ such that the corresponding sequence of solutions u_n belongs to the sets Ω_{r_n} . By virtue of compactness of the set of solution we conclude that there is a subsequence of this sequence which converges in E_μ^1 to a solution from \mathcal{K} . This assertion contradicts Theorem 4.10.

Let us choose r small enough such that Ω_r contains all solutions from \mathcal{K} and does not contain other solutions. Consider the topological degree $\gamma(A_\tau, \Omega_r)$. It is well defined since $A_\tau(u) \neq 0$ for $u \in \partial\Omega_r$. In the next section we will show that the degree is different from 0 for the model problem, $\gamma(A_1, \Omega_r) \neq 0$. Therefore, $\gamma(A_0, \Omega_r) \neq 0$, and equation $A_0(u) = 0$ has a solution in Ω_r . Thus, Theorem 2.1 is proved.

6.2. Model Problem

We reduce the problem (1.3)–(1.5) to the problem (3.2)–(3.4) ($\tau = 1$) for which $f_1(v)$ is a monotonically decreasing function (Fig. 1, right), and equation

$$f_1(v) = k(1 - v) \quad (6.2)$$

has two solutions v_u, v_+ such that $v_u < v_+$.

Theorem 6.1. *Suppose that $f_1'(v) < 0$ for $v_- \leq v \leq v_+$, $f_1'(v_\pm) > k$ and $f_1'(v_u) < k$. Then there exists a value of s for which system (1.3), (1.4) has a solution $(v(x), c(x))$ with the limits*

$$v(\pm\infty) = v_\pm, \quad c(\pm\infty) = f(v_\pm). \quad (6.3)$$

Moreover, the solution is monotone, $v'(x) > 0, c'(x) < 0$ for all $x \in \mathbb{R}$, and $\gamma(A_1, \Omega_r) = 1$ (see Sect. 6.1 for the definition of Ω_r).

Proof. Since the function $f_1(v)$ is monotonically decreasing, then system (3.2), (3.3) ($\tau = 1$) can be reduced to a locally monotone system by the change of variables $v \rightarrow 1 - v$. The existence of monotone solutions for the locally monotone systems is proved in [8, 9] (Chapter 3, Theorem 1.1). Moreover, the value of the degree with respect to all monotone solutions equals 1. Since for $\tau = 1$ the class \mathcal{K} contains only monotone solutions, we conclude that $\gamma(A_1, \Omega_r) = 1$. \square

7. Discussion

We will discuss here some biological interpretations of the obtained results. Let us recall that the ODE system (2.1), (2.2) corresponding to system (1.1), (1.2) without diffusion has four stationary points: $P_0 = (0, 0), P_1 = (0, f(0)), P_2 = (v_u, f(v_u)), P_3 = (v_+, f(v_+))$. Under the conditions considered above, the points P_0 and P_2 are unstable, the points P_1 and P_3 are stable. The point P_1 corresponds to a cured infection where immune cells are present and infection (virus) is absent. The point P_3 corresponds to a chronic infection with a high level of virus and low level of immune cells.

Depending on the values of parameters, starting in the vicinity of the point P_0 , solution of system (2.1), (2.2) can converge either to the cured state P_1 or to the chronic infection state P_3 . Once approaching one of these stable equilibria, the solution stays there. Transition between points P_1 and P_3 in system (2.1), (2.2) is not possible.

The main result of this work states that there exists a direct transition between these two stable equilibria in the distributed (space dependent) system. This transition is realized by means of a travelling wave solution. Thus, an infected tissue can switch from a cured acute infection to a chronic infection or vice versa without passing through the P_0 equilibrium (no infection, no immune cells). Existence of such transition is not a priori clear, and it required sophisticated mathematical methods to prove it.

The direction of this transition, that is, to a cured state or to a chronic infection, is determined by the sign of the wave speed. It depends on the values of parameters but it cannot be found analytically. Its analytical estimation or approximation will require further investigations.

Another question for future analysis concerns the existence of transitions between points P_0 and P_1, P_0 and P_3 in the space dependent system (travelling waves). We can expect that they exist because they exist for the ODE system, but their existence is not yet proved.

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