Mathematics **2014**, *2*, 83-95; doi:10.3390/math2020083

OPEN ACCESS

mathematics

ISSN 2227-7390

www.mdpi.com/journal/mathematics

Article

Traveling Wave Solutions of Reaction-Diffusion Equations Arising in Atherosclerosis Models

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Received: 31 December 2013; in revised form: 27 March 2014 / Accepted: 16 April 2014 / Published: 8 May 2014

Abstract: In this short review article, two atherosclerosis models are presented, one as a scalar equation and the other one as a system of two equations. They are given in terms of reaction-diffusion equations in an infinite strip with nonlinear boundary conditions. The existence of traveling wave solutions is studied for these models. The monostable and bistable cases are introduced and analyzed.

Keywords: reaction-diffusion equations; nonlinear boundary conditions; traveling wave solutions

AMS subject classification: 35K57, 35J60.

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1. Introduction

This is a short review article about atherosclerosis models and existence of traveling wave solutions for such models. We present both the monostable and bistable case.

Reaction-diffusion problems with nonlinear boundary conditions arise in various applications. In physiology, such problems describe in particular the development of atherosclerosis and other inflammatory diseases [1]. In this context, nonlinear boundary conditions show the influx of white blood cells from blood flow into the tissue where the inflammation occurs. Among other possible applications, let us indicate molecular transport through biological membrane where some molecules can amplify their own transport opening membrane channels, as it is the case, for example, with calcium induced calcium release.

Atherosclerosis begins as an inflammation in blood vessels walls (intima). The inflammatory response of the organism leads to the recruitment of monocytes. Trapped in the intima, they differentiate into macrophages and foam cells, leading to the production of inflammatory cytokines and further recruitment of white blood cells. This self-accelerating process, strongly influenced by low-density lipoproteins (cholesterol), results in a dramatic increase of the width of blood vessels walls, formation of an atherosclerotic plaque and, possibly, of its rupture.

We present in Section 2 below two reaction-diffusion models for atherosclerosis. In Section 3, we discuss the existence of waves for a scalar equation in the bistable case. The method employed here is the Leray-Schauder method. The monostable case is not discussed here for a single equation, but directly for a system of two reaction-diffusion equations. Section 4 is devoted to this aspect. We end the paper with a section of conclusions and future work.

The results of the present paper are mainly included in the papers [1–5]. Paper [6] presents some blood flow simulations in atherosclerotic vascular networks. Basic theory and results about travelling waves and different methods can be found in [7–10].

2. Atherosclerosis Models

Papers [1,4] propose a $2D$ mathematical model for atherosclerosis initiation and development. The model is given by a reaction-diffusion system in a strip with nonlinear boundary conditions which describe the recruitment of the monocytes M as a function g of the concentration A of inflammatory cytokines. So the PDE model is the following:

$$\begin{cases} \dfrac{\partial M}{\partial t} = d_M \Delta M - \beta M \\ \dfrac{\partial A}{\partial t} = d_A \Delta A + f(A) M - \gamma A + b \end{cases} \tag{2.1}$$

in the two-dimensional strip $\Omega \subset \mathbb{R}^2$, $\Omega = \{(x,y), -\infty < x < \infty, 0 \le y \le h\}$, with the boundary conditions

$$\frac{\partial M}{\partial y} = \frac{\partial A}{\partial y} = 0 \text{ at } y = 0; \ \frac{\partial M}{\partial y} = g(A), \ \frac{\partial A}{\partial y} = 0 \text{ at } y = h \tag{2.2}$$

and the initial conditions

$$M(x,y,t) = M_0(x,y), \ A(x,y,t) = A_0(x,y) \text{ at } t = 0 \tag{2.3}$$

Here M is the concentration of the white blood cells (monocytes, macrophages, and foam cells) inside the intima (blood vessels walls), A is the concentration of the pro- and anti- inflammatory cytokines, $f(A)M$ is the rate of production of the cytokines which depends on their concentration and on the concentration of the blood cells. Terms $-\beta M$ and $-\gamma A$ describe the natural death of the blood cells and of the cytokines, respectively, while the term b represents a constant source of the activator in the intima (a ground level of cytokines in the intima). It can be the oxidized LDL coming from the blood. All constants d_M, d_A, β, γ, b are positive.

Functions f and g are supposed smooth enough and satisfying the following conditions:

$f(A) > 0$ for $A > 0$; $f(0) = 0$; $f(A) \to f_+$ as $A \to \infty$

$g(A) > 0$ for $A > \mathcal{A}$; $g(\mathcal{A}) = 0$; $g(A) \to g_+$ as $A \to \infty$; $g'(A) > 0$

A stationary solution of systems (2.1) and (2.2) is $M = 0$, $A = b/\gamma =: \mathcal{A}$. So $\mathcal{A}$ is a constant level of cytokines in the intima such that the corresponding concentration M of the monocytes is zero and they are not recruited through the boundary.

A simplified model that takes into account only the concentration of the white blood cells is given by the scalar parabolic PDE ([3])

$$\frac{\partial v}{\partial t} = \Delta v + f(v) \tag{2.4}$$

in the infinite strip $\Omega = \{-\infty < x < \infty, 0 < y < 1\}$, with the nonlinear boundary conditions:

$$\frac{\partial v}{\partial y} = 0 \text{ at } y = 0; \ \frac{\partial v}{\partial y} = g(v) \text{ at } y = 1 \tag{2.5}$$

It is a mathematical model of atherosclerosis and other inflammatory diseases. Ω corresponds to the blood vessel wall (intima) where the disease develops, v is the concentration of white blood cells in the tissue. The nonlinear boundary condition describes the cell influx through the boundary. The influx depends on the cell concentration in the tissue.

3. Reaction-Diffusion Waves for One Equation in the Bistable Case

3.1. Formulation of the Problem

We begin with the study of the simplified model, that is the reaction-diffusion equation

$$\frac{\partial v}{\partial t} = \Delta v + f(v) \tag{3.1}$$

with nonlinear boundary conditions:

$$\frac{\partial v}{\partial y} = 0 \text{ at } y = 0, \ \frac{\partial v}{\partial y} = g(v) \text{ at } y = 1 \tag{3.2}$$

in the infinite strip $\Omega = \{-\infty < x < \infty, 0 < y < 1\}$. This is the problem studied in [2,3].

We study the existence of traveling wave solutions of this problem. They are solutions of the form $v(x, y, t) = u(x - ct, y)$. Then function u satisfies the equation

$$\Delta u + c\frac{\partial u}{\partial x} + f(u) = 0 \tag{3.3}$$

with the boundary conditions

$$y = 0 : \frac{\partial u}{\partial y} = 0, \ y = 1 : \frac{\partial u}{\partial y} = g(u) \tag{3.4}$$

Here c is an unknown constant, the wave speed, that should be found together with function u. Assume that f and g are of class C^3.

We look for solutions of problems (3.3) and (3.4) with the limits

$$\lim_{x \to \pm\infty} u(x, y) = u_{\pm}(y), \ 0 < y < 1 \tag{3.5}$$

where $u_{\pm}(y)$ are some functions which satisfy the problem in the cross section (*i.e.*, independent of x):

$$u'' + f(u) = 0,\ 0 < y < 1,\ u'(0) = 0,\ u'(1) = g(u(1)) \tag{3.6}$$

Let us introduce the bistable and the monostable cases as in [2]. To do this, consider the equation linearized about solutions $u_{\pm}(y)$ and the corresponding eigenvalue problems:

$$\begin{cases} v'' + f'(u_{\pm}(y))v = \lambda v,\ 0 < y < 1 \\ v'(0) = 0,\ v'(1) = g'(u_{\pm}(1))v(1) \end{cases}$$

If both problems have all eigenvalues in the left-half plane, then we call it the bistable case. If one of these problems has all eigenvalues in the left-half plane and the other one has some eigenvalues in the right-half plane, then it is the monostable case. We will present here the bistable case [2] for a single equation. The monostable case will be analyzed directly for systems (see Section 4). It is a more difficult and more complete study than for a single equation. The study of systems in the bistable case we have in preparation.

As a particular situation [3], we can assume that $u_{\pm}$ are constant (do not depend on y) and that $f\left(u_{\pm}\right) = 0$, $g\left(u_{\pm}\right) = 0$, $f'\left(u_{\pm}\right) < 0$, $g'\left(u_{\pm}\right) < 0$.

We also assume that f and g have a single zero u_0 between u_+ and u_- ($f\left(u_0\right) = g\left(u_0\right) = 0$), such that $f'\left(u_0\right) > 0$, $g'\left(u_0\right) > 0$. This is also a bistable case and has been analyzed in the paper [3].

Investigation of problems (3.3) and (3.4) relies on the properties of the corresponding operators. It will be shown that in the bistable case, the linearized operator satisfies the Fredholm property. Moreover for the nonlinear operator we can introduce a topological degree. These tools allow us to use the Leray-Schauder method based on the topological degree and a priori estimates of solutions.

3.2. Solutions in the Cross-Section

3.2.1. General case

We start with the problem in the cross-section (independent on x)

$$\frac{d^2w}{dy^2} + f(w) = 0,\ w'(0) = 0,\ w'(L) = g(w(L)) \tag{3.7}$$

in the interval $0 < y < L$. Suppose here that functions f and g are continuous together with their first derivatives. One can reduce the second-order equation to the system of two first-order equations

$$w' = p,\ p' = -f(w)$$

and then to the equation

$$\frac{dp}{dw} = -\frac{f(w)}{p}$$

We can solve this equation analytically. Consider for simplicity only monotone solutions w and denote $w_+ = \max w(y)$, $w_- = \min w(y)$. In the case of decreasing solutions $w_+ = w(0),\ w_- = w(L)$, and the boundary conditions become

$$p(w_+) = 0,\ p(w_-) = g(w_-)$$

Under the assumption that

$$\int_{w}^{w_+} f(u)du \geq 0, \; w_- \leq w \leq w_+$$

We obtain the length of the interval as a function of the maximal value of solution:

$$L = \int_{w_-}^{w_+} \frac{dv}{\sqrt{2\int_v^{w_+} f(u)du}}$$

Depending on the functions f and g, solution can exist, it can be unique or non-unique, or it may not exist. The case of increasing solutions can be studied in a similar way.

3.2.2. Constant solutions

In the next sections, when we study the wave existence, we will consider problems which depend on parameters. So we discuss here problem (3.7) where $g = \delta g_0$ and δ is a positive parameter. Suppose that $f(y)$ and $g(y)$ are continuous together with their first derivatives and

$$f(u_\pm) = g(u_\pm) = 0, \; f'(u_\pm) < 0, \; g'(u_\pm) < 0 \tag{3.8}$$

for some u_+ and u_-, and that these functions have a single zero u_0 in the interval $u_+ < u < u_-$,

$$f(u_0) = g(u_0) = 0, \; f'(u_0) > 0, \; g'(u_0) > 0 \tag{3.9}$$

Lemma 3.1. **([2])** Let functions f and g satisfy conditions (3.8) and (3.9). Then there exists L_0 such that problem (3.7) with $u_+ < w(0) < u_-$ has only constant solutions for any $L \leq L_0$ and any positive δ.

Now we discuss the stability of these solutions. Denote a zero of the function g by u^*. Then the corresponding eigenvalue problem writes

$$v'' + f'(u^*)\, v = \lambda v, \; v'(0) = 0, \; v'(1) = g'(u^*)\, v(1)$$

If $f'(u^*) > 0$, then the principal eigenvalue of this problem is positive. This is the case for $u^* = u_0$. If $f'(u^*) < 0$ (ex. $u^* = u_\pm$), then the eigenvalues are negative.

3.3. Properties of the Operators

3.3.1. Fredholm property of the linearized operator

A linear operator $L : E_1 \to E_2$ (between Banach spaces) has the Fredholm property if $\operatorname{Im} L$ is closed, L has a finite dimensional kernel and the codimension of $\operatorname{Im} L$ is finite.

Consider the operator corresponding to problem (3.3), (3.4) and linearized about a solution $u(x, y)$:

$$Av = \Delta v + c\frac{\partial v}{\partial x} + a(x,y)v, \; (x,y) \in \Omega$$

$$Bv = \begin{cases} \dfrac{\partial v}{\partial y} & , \quad y = 0 \\ \dfrac{\partial v}{\partial y} - b(x)v & , \quad y = 1 \end{cases}$$

where $\Omega = \{-\infty < x < \infty, \ \ 0 < y < 1\}$, and

$$a(x,y) = f'(u(x,y)), \ b(x) = g'(u(x,1))$$

The operator $L = (A, B)$ acts from the space $E = C^{2+\alpha}(\bar{\Omega})$ into the space $F = C^{\alpha}(\bar{\Omega}) \times C^{1+\alpha}(\partial\Omega)$. Consider the limiting operators

$$A^{\pm}v = \Delta v + c\frac{\partial v}{\partial x} + a_{\pm}(y)v, \ (x,y) \in \Omega$$

$$B^{\pm}v = \begin{cases} \dfrac{\partial v}{\partial y} & , \ \ y = 0 \\ \dfrac{\partial v}{\partial y} - b_{\pm}v & , \ \ y = 1 \end{cases}$$

and the corresponding equations

$$A^{\pm}v = 0, \ B^{\pm}v = 0$$

Here

$$a_{\pm}(y) = \lim_{x\to\pm\infty} a(x,y), \ b_{\pm} = \lim_{x\to\pm\infty} b(x)$$

Let E be a Banach space with the norm $\|\cdot\|$ and ϕ_i be a partition of unity. Then E_∞ is the space of functions u for which the expression

$$\|u\|_\infty = \sup_i \|u\phi_i\| < \infty$$

This is the norm in the space E_∞. The result below has been proved under stronger hypotheses in [3]. We present here the most general case, which is due to [2].

Theorem 3.2. **([2])** If condition (3.8) is satisfied and $\lim_{x\to\pm\infty} u(x,y) = u_{\pm}(y), \ 0 < y < 1$ (or more generally, if we are in the bistable case), then the operator $L = (A, B)$ acting from $C^{2+\alpha}(\bar{\Omega})$ into $F = C^{\alpha}(\bar{\Omega}) \times C^{1+\alpha}(\partial\Omega)$ or from $W^{2,2}_{\infty}(\Omega)$ into $L^2_\infty(\Omega) \times W^{1/2,2}_{\infty}(\partial\Omega)$ satisfies the Fredholm property.

3.3.2. Properness and topological degree of the nonlinear operator

Consider the nonlinear operator in the domain Ω

$$T_0(w) = \Delta w + c\frac{\partial w}{\partial x} + f(w), \ (x,y) \in \Omega$$

and the boundary operator

$$Q_0(w) = \begin{cases} \dfrac{\partial w}{\partial y} & , \ \ y = 0 \\ \dfrac{\partial w}{\partial y} - g(w) & , \ \ y = 1 \end{cases}$$

Let $w = u + \psi$, where $\psi(x,y) \in C^\infty$, $\psi(x,y) = u_+(y)$ for $x \geq 1$, $\psi(x,y) = u_-(y)$ for $x \leq -1$. Set

$$T(u) = T_0(u+\psi) = \Delta u + c\frac{\partial u}{\partial x} + f(u+\psi) + \Delta\psi + c\,\frac{\partial \psi}{\partial x}$$

$$Q(u) = Q_0(u+\psi) = \begin{cases} \dfrac{\partial u}{\partial y} & , \ \ y = 0 \\ \dfrac{\partial u}{\partial y} - g(u+\psi) + \dfrac{\partial \psi}{\partial y} & , \ \ y = 1 \end{cases}$$

We consider the operator $P = (T, Q)$ acting in weighted spaces,

$$P = (T, Q) : W^{2,2}_{\infty,\mu}(\Omega) \to L^2_{\infty,\mu}(\Omega) \times W^{1/2,2}_{\infty,\mu}(\partial\Omega)$$

with the weight function $\mu(x) = \sqrt{1 + x^2}$. The norm in the weighted space: $\|u\|_{\infty,\mu} = \|u\mu\|_\infty$.

Theorem 3.3. ([3]) In the bistable case, P is proper in the weighted spaces and a topological degree can be defined.

3.4. A Priori Estimates

A priori estimates of solutions are obtained below only for monotone solutions. In order to apply the Leray-Schauder method, separation of monotone solutions from non-monotone solutions is proved. This means the norm of their difference is uniformly bounded from below by a positive number. It follows from a subjacent result (see Lemma 3.5). This permits one to construct the domain in the function space, which contains all monotone solutions and does not contain non-monotone solutions. The degree is found with respect to this domain. This remark is the key point of the proof of Theorem 3.12 below.

3.4.1. Auxiliary results

Consider the problem

$$\Delta u + c\frac{\partial u}{\partial x} + f(u) = 0 \tag{3.10}$$

$$y = 0 : \frac{\partial u}{\partial y} = 0,\ y = 1 : \frac{\partial u}{\partial y} = g(u) \tag{3.11}$$

$$\lim_{x\to\pm\infty} u(x, y) = u_\pm(y),\ 0 < y < 1,\ u_-(y) > u_+(y) \tag{3.12}$$

Lemma 3.4. ([3]) Let $U_0(x, y)$ be a solution of problems (3.10) and (3.11) such that $\frac{\partial U_0}{\partial x} \le 0$ for all $(x, y) \in \bar{\Omega}$. Then the last inequality is strict.

Lemma 3.5. ([3]) Let $u_n(x, y)$ be a sequence of solutions of problems (3.10) and (3.11) such that $u_n \to U_0$ in $C^1(\bar{\Omega})$, where $U_0(x, y)$ is a solution monotonically decreasing with respect to x. Then for all n sufficiently large $\frac{\partial u_n}{\partial x} < 0$, $(x, y) \in \bar{\Omega}$.

3.4.2. Wave speed

Lemma 3.6. ([3]) Suppose that $u_0(y)$ is a solution of problem (3.6) in the cross section of the domain, and $u_+(y) < u_0(y) < u_-(y)$. Assume, next, that the corresponding eigenvalue problem

$$v'' + f'(u_0)v = \lambda v,\ v'(0) = 0,\ v'(1) = g'(u_0(1))v(1)$$

has some eigenvalues in the right-half plane. If a monotone with respect to x function $w(x, y)$ satisfies the problem

$$\Delta w + c\frac{\partial w}{\partial x} + f(w) = 0$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = 1 : \frac{\partial w}{\partial y} = g(w)$$

$$\lim_{x\to-\infty} w(x,y) = u_-(y),\ \lim_{x\to\infty} w(x,y) = u_0(y) \tag{3.13}$$

then $c > 0$.

Lemma 3.7. ([3]) In the conditions of the previous lemma, if

$$\lim_{x\to-\infty} w(x,y) = u_0(y),\ \lim_{x\to\infty} w(x,y) = u_+(y)$$

instead of (3.13), then $c < 0$.

Lemma 3.8. ([3]) If problems (3.10)–(3.12) has a solution w, then the value of the speed admits the estimate $|c| \leq M$, where the constant M depends only on

$$\max_{u\in[u_+,u_-]} |f'(u)|, |g'(u)|$$

3.4.3. Estimates of solutions

Consider the problem

$$\Delta u + c\frac{\partial u}{\partial x} + f_\tau(u) = 0 \tag{3.14}$$

$$y = 0 : \frac{\partial u}{\partial y} = 0,\ y = 1 : \frac{\partial u}{\partial y} = g_\tau(u) \tag{3.15}$$

$$u(\pm\infty, y) = u_\pm(y) \tag{3.16}$$

where f and g depend on the parameter $\tau \in [0,1]$.

Lemma 3.9. ([2]) Suppose that the above problem admits a solution $u(x,y)$ that satisfies $|u| \leq M$ with some positive constant M, and

$$|f_\tau^{(i)}(u)|,\ \ |g_\tau^{(i)}(u)| \leq K \text{ for } |u| \leq M, i = 0,1,2,3$$

where K is a positive constant. Then the Hölder norm $C^{2+\alpha}(\bar{\Omega})$, $0 < \alpha < 1$ of the solution u is bounded by a constant which depends only on K, M and c.

Theorem 3.10. ([2]) If there exists a solution w_τ of the above problem for some $\tau \in [0,1]$, then the norm $\|w_\tau - \psi\|_{W^{2,2}_{\infty,\mu}(\Omega)}$ is bounded independently of the solution w_τ.

Under stronger hypotheses, this result has been also proved in [3].

3.5. Existence of the Traveling Wave Solutions

Consider the model problem for $g \equiv 0$:

$$\Delta w + c\frac{\partial w}{\partial x} + f(w) = 0 \tag{3.17}$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = 1 : \frac{\partial w}{\partial y} = 0 \tag{3.18}$$

$$w(\pm\infty, y) = u_\pm(y) \tag{3.19}$$

Assume that $f(u_\pm) = 0$, $f'(u_\pm) < 0$, and there is a single zero u_0 of f in the interval (u_+, u_-), $f'(u_0) > 0$.

Lemma 3.11. **([2,3])** There exists a unique monotone in x solution of problems (3.17)–(3.19) up to translation in space.

Consider next the operators corresponding to problems (3.14)–(3.16) :

$$T_\tau(u) = \Delta(u+\psi) + c(u+\psi)\frac{\partial(u+\psi)}{\partial x} + f_\tau(u+\psi),\ (x,y)\in\Omega$$

$$Q_\tau(u) = \begin{cases} \dfrac{\partial u}{\partial y} & ,\ y=0 \\ \dfrac{\partial u}{\partial y} - g_\tau(u+\psi) & ,\ y=1 \end{cases}$$

$$P_\tau = (T_\tau, Q_\tau) : W^{2,2}_{\infty,\mu}(\Omega) \to L^2_{\infty,\mu}(\Omega) \times W^{1/2,2}_{\infty,\mu}(\partial\Omega)$$

Suppose that $g_\tau(u) \equiv 0$ for $\tau = 0$. Then the equation

$$P_\tau(u) = 0 \text{ for } \tau = 0$$

has a unique solution $u_0 = w_0 - \psi$. The topological degree of this operator with respect to a small neighborhood of the solution, equal 1.

Assume now that $f_\tau(w), g_\tau(w)$ are bounded and continuous, together with their derivatives of order 3 with respect to w and of the second order with respect to τ.

We begin with a general result on wave existence.

Theorem 3.12. **([2])** Let the problem

$$\frac{d^2w}{dy^2} + f_\tau(w) = 0,\ w'(0) = 0,\ w'(L) = g_\tau(w(L))$$

have solutions $u^\tau_\pm(y)$ such that

$$u^\tau_+(y) < u^\tau_-(y),\ 0 \le y \le L$$

and the eigenvalue problems

$$\frac{d^2v}{dy^2} + f'_\tau(u^\tau_\pm)v = \lambda v,\ v'(0) = 0,\ v'(L) = g'_\tau(u^\tau_\pm)v(L)$$

have all eigenvalues in the left-half plane for any $\tau \in [0,1]$. Suppose that for any other solution $u^\tau_0(y)$, the eigenvalue problem

$$\frac{d^2v}{dy^2} + f'_\tau(u^\tau_0)v = \lambda v,\ v'(0) = 0, v'(L) = g'_\tau(u^\tau_0)v(L)$$

has some eigenvalues in the right-half plane. If the problem in Ω,

$$\Delta w + c\frac{\partial w}{\partial x} + f_\tau(w) = 0$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = L : \frac{\partial w}{\partial y} = g_\tau(w)$$

$$\lim_{x\to\pm\infty} w(x,y) = u^\tau_\pm(y),\ 0 < y < L$$

has a unique solution monotone with respect to x for $\tau = 0$, then it also has a unique monotone solution for any $\tau \in [0,1]$.

The proof of this result is based on the remark from the beginning of Section 3.4 about the separation of all monotone solutions from nonmonotone solutions.

Theorem 3.13. ([2]) Let u_+ and u_- be some constants and the following conditions be satisfied:
(1). $f(u_\pm) = 0,\ f'(u_\pm) < 0, g(u_\pm) = 0,\ g'(u_\pm) < 0$,
(2). $f(u_0) = 0,\ f'(u_0) > 0, g(u_0) = 0,\ g'(u_0) > 0$ for some $u_0 \in (u_+, u_-)$, and there are no other zeros of these functions in this interval.

Then for all $L > 0$ sufficiently small, the problem

$$\Delta w + c\frac{\partial w}{\partial x} + f(w) = 0$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = L : \frac{\partial w}{\partial y} = g(w)$$

$$\lim_{x\to\pm\infty} w(x, y) = u_\pm$$

considered in $\Omega = \{-\infty < x < \infty,\quad 0 < y < L\}$ has a unique solution monotone with respect to x.

Theorem 3.14. ([2,5]) Let the function $g(w)$ satisfy conditions of the previous theorem. Then for all positive L, the problem in Ω,

$$\Delta w + c\frac{\partial w}{\partial x} = 0$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = L : \frac{\partial w}{\partial y} = g(w)$$

$$\lim_{x\to\pm\infty} w(x, y) = u_\pm$$

has a unique solution monotone with respect to x.

Theorem 3.15. ([2]) Suppose that $f(u_\pm) = 0,\ f'(u_\pm) < 0$ and for some c_0 there exists a monotone solution $w(x)$ of the problem

$$w'' + c_0 w' + f(w) = 0, \quad w(\pm\infty) = u_\pm$$

Then for all ϵ sufficiently small, the problem

$$\Delta w + c\frac{\partial w}{\partial x} + f(w) = 0$$

$$y = 0 : \frac{\partial w}{\partial y} = 0,\ y = L : \frac{\partial w}{\partial y} = \epsilon g(w)$$

$$\lim_{x\to\pm\infty} w(x, y) = u^\epsilon_\pm(y)$$

considered in the domain $\Omega = \{-\infty < x < \infty,\quad 0 < y < L\}$ has a unique solution monotone with respect to x. Here $u^\epsilon_\pm(y)$ are solutions of the problem

$$\frac{\partial w}{\partial y} + f(w) = 0,\ w'(0) = 0,\ w'(L) = \epsilon g(w(L))$$

$u^\epsilon_\pm(y) \to u_\pm$ as $\epsilon \to 0$ uniformly in y.

These results show that atherosclerosis develops as a reaction-diffusion wave.

4. Reaction-Diffusion Waves for Systems

We approach in this section the $2D$ atherosclerosis models (2.1) and (2.2) in the monostable case. The bistable case is not yet studied and it is the topic of a future work. Recall that here M is the concentration of the white blood cells inside the intima, while A is the concentration of the inflammatory cytokines.

Suppose that the stationary solution $M = M_0$, $A = \mathcal{A} = b/\gamma$ is unstable and that there exists a stable stationary solution $M_s(y)$, $A_s(y)$ such that

$$M_0 < M_s(y)\,,\ \mathcal{A} < A_s(y)\,,\ 0 \le y \le h$$

One studies the existence of waves with the limits $(M_0, \mathcal{A})$ at $x = -\infty$ and (M_s, A_s) at $x = \infty$. Assume that there are no other stationary solutions such that $M_0 \le M(y) \le M_s(y)$ and $\mathcal{A} \le A(y) \le A_s(y)\,,\ 0 \le y \le h$. This means that (M_s, A_s) is the smallest solution above $(M_0, \mathcal{A})$.

The wave solutions have the form $M(x, y, t) = M(x - ct, y)\,, A(x, y, t) = A(x - ct, y)\,,$ where the constant c is the wave speed. Then (M, A) verifies the system

$$\begin{cases} d_M \Delta M - c\dfrac{\partial M}{\partial x} - \beta M = 0 \\ d_A \Delta A - c\dfrac{\partial A}{\partial x} + f(A)\,M - \gamma A + b = 0 \end{cases} \tag{4.1}$$

in $\Omega = \{(x, y)\,,\ -\infty < x < \infty,\ 0 \le y \le h\}$, with the boundary conditions

$$\frac{\partial M}{\partial y}(x, 0) = \frac{\partial A}{\partial y}(x, 0) = 0,\ \frac{\partial M}{\partial y}(x, h) = g(A(x, h))\,,\ \frac{\partial A}{\partial y}(x, h) = 0 \tag{4.2}$$

One looks for the solutions (M, A) with the property

$$x = -\infty:\ M = M_0,\ A = \mathcal{A},\ x = +\infty:\ M = M_s,\ A = A_s \tag{4.3}$$

Theorem 4.1. **([1])** Problems (4.1)—(4.3) admits a solution if and only if c is greater or equal than a specific constant value c_0. The solution is strictly monotone with respect to x.

This result shows the wave propagation if and only if $c \ge c_0$. In this case, atherosclerosis develops as a reaction-diffusion wave.

5. Conclusions and Future Work

In the present paper, we have put together some results about traveling wave solutions for reaction-diffusion equations with nonlinear boundary solutions arising in atherosclerosis models. In such a way the reader can find easily these results and compare the behavior of solution in different cases. In Section 4 we have presented the existence of such solutions in the monostable case for system (2.1). Since the bistable case is more complicated and infers a more elaborated mathematical tools, we have preferred to study it first for a single equation of the form (3.1) (Section 3). The bistable case for systems will be the goal of a future work.

We can study this even in a more general reaction-diffusion system, namely consider

$$\frac{\partial u}{\partial t} = D\Delta u + F(u)$$

with the nonlinear boundary conditions

$$y = 0: \ \frac{\partial u}{\partial y} = 0, \ y = h: \ \frac{\partial u}{\partial y} = G\left(u\right)$$

where $u = (u_1, ..., u_n)$, $F = (F_1, ..., F_n)$, $G = (G_1, ..., G_n)$, D is a diagonal matrix with positive diagonal elements.

We are looking for solutions of this system under the form $u\left(x, y, t\right) = w\left(x - ct, y\right)$. They satisfy the problem

$$D\Delta w + c\frac{\partial w}{\partial x} + F\left(w\right) = 0$$

$$y = 0: \ \frac{\partial w}{\partial y} = 0, \ y = h: \ \frac{\partial w}{\partial y} = G\left(w\right)$$

We are going to employ the Leray - Schauder method to prove the existence of reaction-diffusion waves for this system.

Acknowledgments

This work was supported by a grant of the Romanian National Authority for Scientific Research, CNCS—UEFISCDI, project number PN-II-ID-PCE-2011-3-0563, contract no. 343/5.10.2011 “Models from medicine and biology: mathematical and numerical insights”.

Author Contributions

The aim of this paper is to assemble some results about the existence of travelling wave solutions for reaction-diffusion equations with nonlinear boundary solutions arising in atherosclerosis models. In such a way the reader can compare the behavior of solution in different cases. All the results of this review paper have been published before.

Conflicts of Interest

The author declares no conflict of interest.

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