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# MATHEMATICAL STUDY OF THE SPREAD AND BLOCKING IN INFLAMMATORY BOWEL DISEASE

SAOUSSEN LATRACH <sup>\*</sup>, ERIC OGIER-DENIS <sup>†</sup>, NICOLAS VAUCHELET <sup>‡</sup>, AND HATEM ZAAG <sup>§</sup>

**Abstract.** Ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory diseases that affect the digestive tract, causing daily discomfort. Although symptoms are similar, the modes of disease propagation are different. CD spreads discontinuously and excavating along the digestive tract, while UC spreads continuously and superficially, affecting a uniform area from the rectum to different parts of the colon. In our research work, we are interested in studying a mathematical model of inflammation caused by Inflammatory Bowel Disease that has been developed by Nadin and al. in the Journal of Mathematical Biology in 2021 with modifications. It is a reaction-diffusion system governing the dynamics of a pathogen in interaction with immune cells. The first study focuses on the existence of propagation waves for such a system in a homogeneous medium, the second study focuses on blocking these waves in a heterogeneous medium. We will use numerical simulations to highlight these theoretical results.

**Keywords :** Inflammatory bowel diseases, reaction-diffusion system, traveling waves, wave blocking.

**AMS subject classification :** 92D25, 35K57, 35Q92.

**1. Introduction.** Inflammatory bowel diseases (IBD) encompass a group of chronic disorders characterized by chronic inflammation of the intestinal mucosa. The two main forms of IBD are ulcerative colitis and Crohn's disease, which, despite sharing similarities in their clinical presentation, differ in the regions of the gastrointestinal tract they affect (see [21], [13]). The first detailed report of ulcerative colitis dates back to 1850 [3]. Ulcerative colitis (UC) is a permanent condition with a remittent course, affecting the innermost mucosa of the large intestine, also known as the colon as well as the rectum. This disease is marked by inflammation and ulcers, leading to lesions and bleeding similar to those observed in the normal colon, albeit with significant alterations (cf. Figure 1.1).

In the context of inflammatory bowel diseases, it is essential to note the existence of different types of ulcerative colitis, as classified by the Montreal classification based on the extent of the lesions. The Montreal classification subdivides the extent into three subgroups:  $E_1$ ,  $E_2$ , and  $E_3$ . Three main categories are distinguished: distal forms (60% of cases) limited to the rectum, presenting as proctitis ( $E_1$ ); pancolitic forms (15% of cases) extending from the rectum to the entire colon ( $E_3$ ); and intermediate forms (25%) situated between distal and pancolitic forms, showing a partial extension of the lesions ( $E_2$ ) left sided UC. Regarding the causes of UC, they remain largely unknown. Some researchers suggest a possible association with an excessive immune system response, typically dedicated to defending against external elements such as bacteria or viruses. When the immune defenses lose their regulation, they may turn

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<sup>\*</sup> Laboratoire Analyse, Géométrie & Applications (LAGA), Université Sorbonne Paris Nord, F-93430 Villetaneuse, France, (E-mail: [latrech@math.univ-paris13.fr](mailto:latrech@math.univ-paris13.fr))

<sup>†</sup> Institut national de la santé (INSERM) FRANCE ([eric.ogier-denis@inserm.fr](mailto:eric.ogier-denis@inserm.fr))

<sup>‡</sup> Laboratoire Analyse, Géométrie & Applications (LAGA), CNRS UMR 7539, Laboratoire d'Excellence Inflamex, Université Sorbonne Paris Nord, F-93430 Villetaneuse, France, FRANCE ([vauchelelet@math.univ-paris13.fr](mailto:vauchelelet@math.univ-paris13.fr))

<sup>§</sup> Laboratoire Analyse, Géométrie & Applications (LAGA), CNRS UMR 7539, Laboratoire d'Excellence Inflamex, Université Sorbonne Paris Nord, F-93430 Villetaneuse, France, FRANCE ([zaag@math.univ-paris13.fr](mailto:zaag@math.univ-paris13.fr))

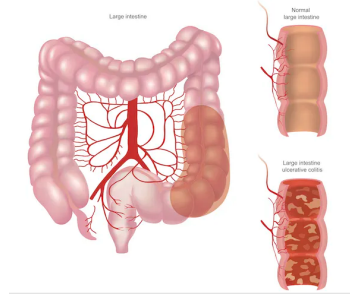
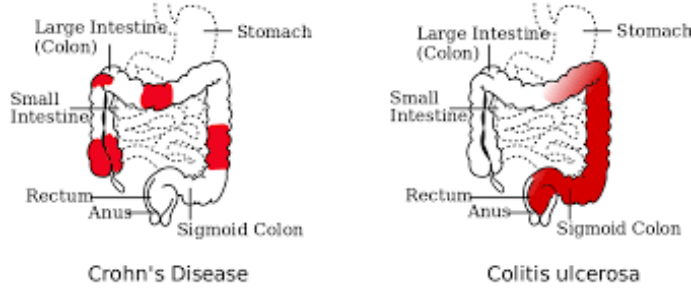


FIGURE 1.1. *Healthy colon and colon affected by ulcerative colitis (UC)* (Source: Getty Images)

against the body's own cells, triggering an autoimmune attack. This process leads to the production of autoantibodies, causing damage and the destruction of tissues or organs. The pathogenesis of the dysfunction in immune defenses is multifactorial, involving genetic predisposition, defects in the epithelial barrier, dysregulated immune responses, and various environmental, hormonal, or genetic factors. It is crucial to emphasize that, contrary to some widespread beliefs, stress or certain foods are not directly responsible for UC, although stress may trigger or exacerbate a disease flare-up (see [21]). Thus, understanding the precise mechanisms underlying UC remains an active and complex research area within the medical community (see [21], [8], [9], [11]). Clinical symptoms vary depending on the progression of the disease and are primarily gastrointestinal. Patients may experience rectal bleeding, characterized by red blood coming from the anus, as well as occasionally mucus-filled diarrhea. Abdominal pain, tenesmus (rectal burning), and a general deterioration of health with weight loss and loss of appetite are also frequently observed. Additionally, UC can manifest non-digestive symptoms such as joint pain, skin lesions, or ocular involvement. It's crucial to emphasize that UC is not contagious, and there is no direct transmission between individuals. These diverse symptoms significantly impact the quality of life for those affected, often requiring tailored medical interventions to alleviate symptoms and slow the progression of the disease. The treatment of UC aims to relieve symptoms, control inflammation, and prevent complications. Medical approaches, including anti-inflammatories, immunosuppressants, and corticosteroids, constitute the first line of treatment. For more severe cases, biologic treatments targeting the immune system specifically may be considered. In cases resistant to medical treatments, surgery may be considered as an option. This surgical intervention typically involves the complete removal of the entire colon, regardless of the disease classification, and may or may not include the rectum (see [16]). Now, we will outline the distinctions between Crohn's disease and Ulcerative Colitis. CD and UC share several similarities. In both cases, the immune system plays a central role in triggering chronic inflammation, leading to variable disruptions in the gastrointestinal tract for those affected. Both diseases progress in flare-ups that can last for months, repeating several times a year, interspersed with periods of remission. In this regard, establishing a distinction between Ulcerative Colitis and Crohn's disease can be challenging. However, the diagnosis of these two conditions highlights several significant differences. Ulcerative colitis, as defined at the beginning of the introduction, is limited to two parts of the digestive tract: the colon and the rectum. The inflammation spreads evenly and only affects the upper layer of the intestinal wall.. In contrast, Crohn's disease can affect

the entire digestive tract, from the mouth to the anus. Inflammation appears as localized lesions affecting all layers of the intestinal wall, distributed throughout the length of the intestine, sometimes separated by healthy areas (see [5]). The image below, sourced from *medecinesante*, visually illustrates the distinctions between Ulcerative Colitis (UC) and Crohn's disease.



It is important to emphasize the previous work conducted. The initial data analyses performed by Morilla and al.(see [12]), along with innovative research on image processing presented in Safa's PhD thesis (see[1], [2]), form crucial foundations illuminating our understanding of inflammatory bowel diseases (IBD). These contributions play an indispensable role in our subsequent exploration of clinical specifics and nuances distinguishing UC from CD. Also worth mentioning is the work of Rebai and al.(see [15]), which explores the use of physics-based neural networks to solve equations modeling inflammatory bowel disease.

In the context of a biological approach, the objective of this article is to understand the progression of inflammatory bowel diseases, with a focus on Ulcerative Colitis (UC). To achieve this, we use a simplified model based on reaction-diffusion equations to simulate the propagation of Ulcerative Colitis (UC). This model is inspired by the thesis work of Ana Isiso Telado [18], who previously developed a similar structure for Crohn's disease. However, we have specifically adapted this model to Ulcerative Colitis (UC). Our initial goal is to analyze this model and provide evidence of the existence of progressive waves in a homogeneous environment, representing the propagation of inflammation or pathological activity associated with Ulcerative Colitis (UC) throughout the intestinal tissue. In the second phase of our study, we will explore the conditions leading to the blocking of these waves in heterogeneous environments. Wave blocking refers to the cessation or significant reduction of inflammation propagation in the intestinal tissue. It is crucial to emphasize that unimpeded propagation would correspond to pancolitis, meaning when inflammation reaches the entire colon, while the blockage would explain why inflammation stops at a specific point in the colon. Among the works on propagation and blocking, noteworthy is [6], exploring the persistence and propagation of a species in periodically hostile environments using a reaction-diffusion equation. Their study introduces a geometric condition for blocking propagation and delves into the asymptotic behavior, contributing significantly to the understanding of these complex dynamics.

After outlining our initial objectives, it is now essential to highlight an important element of our study: the significant impact of heterogeneity. This characteristic becomes particularly crucial to explain the blocking phenomenon that we observed in the spread of ulcerative colitis (UC). In the presence of variations in the properties of the intestinal tissue, our reaction-diffusion model simulates waves of inflammation that, when encountering heterogeneous zones, are either blocked or significantly slowed down. These heterogeneous zones act as barriers, realistically reproducing

the obstacles faced by inflammation in clinical situations. Analyzing the impact of heterogeneity allows us to better understand the mechanisms of inflammatory wave blocking in UC. Regarding mathematical studies on heterogeneous environments, notable references include ([10], [7]).

The article is structured as follows: in Section 2, we provide a detailed presentation of the mathematical model used in our study. We provide a comprehensive description of the specific equations and relevant variables involved in the model. In Section 3, we present the main results obtained during our study. Section 4 is devoted to elementary results derived from our diffusion-free model. We present these results along with their associated proofs. Section 5 is dedicated to the proof of the main result of our study. We outline the different steps of the proof. To validate and visually illustrate our results, Section 6 presents the outcomes of our numerical simulations. We provide a detailed description of the simulation procedure, including the parameters and techniques used. We also offer compelling visual representations that enhance the understanding of the implications of our study. Finally, in Section 7, we conclude our article by summarizing the key points discussed throughout the preceding sections.

## 2. Mathematical model.

In this section, we present the mathematical model used in our study. The model is based on PhD thesis of Ana Isis Toledo Marrero(see [18]), who developed a model for Crohn's disease (see [18]). However, we cannot simply adopt the same model as presented in Ana's thesis, as the values of diffusion coefficients differ, as it is usually the case in Turing mechanism based phenomena. This disparity prevents us from directly applying the model to our context where we expect the diffusion coefficients to be of the same order. Consequently, we have chosen to take the same value for the diffusion coefficients and have introduced a death term in the first equation of the model. This modification aims to better reflect the specific characteristics of ulcerative colitis that we are investigating. The adjusted mathematical model can be described as follows. We consider two components that vary in time  $t$  and space  $x$ : the number of bacteria, denoted by  $u$ , and the immune cells, denoted by  $v$ . The model equations are given by:

$$(2.1) \quad \begin{cases} \partial_t u - D \partial_{xx} u = r_b u (1 - \frac{u}{b_i}) + \gamma (1 - \frac{u}{b_i}) v - \frac{au}{s_b + u} v - du \\ \partial_t v - D \partial_{xx} v = \beta u - r_c v \end{cases}$$

The parameters in the model are defined as follows:  $D$  constant of diffusion,  $r_b$  is the rate of reproduction of bacteria,  $b_i$  is density of bacteria in the lumen,  $a$  is the coefficient proportional to the rate of phagocytosis,  $\gamma$  is a measure of the negative effect of phagocyte concentration on epithelial resistance,  $d$  is the mortality rate,  $\beta$  is the immune response rate,  $r_c$  is intrinsic death rate of phagocytes.

To simplify the model, we included the term of bacteria mortality as  $du$ . This modification allows us to capture the dynamics of the interaction between bacteria and immune cells in the context of ulcerative colitis.

The aim of this article is to prove that in a homogeneous medium, there is a propagation. Then, we will focus on the study of the blocking of this propagation in the case where the medium is not homogeneous (heterogeneous medium). Before presenting the main existence and blocking results, we start with some assumptions and notations with some preliminary results that will be used throughout this article.

### 3. Main results.

In this section, we state two main results of this article. Our first result concerns the homogeneous case, where we show the existence of a propagation. This is our statement:

THEOREM 3.1.

We assume that  $r_b < d < r_b + \frac{\gamma\beta}{r_c}$ ; where  $\gamma > a$ , and  $s_b > \max(b_i, \frac{1}{r_c})$ . Then there is a spreading speed  $c^* > 0$  with the properties that for every positive  $\epsilon$  :

$$\lim_{t \rightarrow +\infty} \left[ \max_{|x| \geq t(c^* + \epsilon)} |(u(x, t), v(x, t))| \right] = 0,$$

and for any strictly positive constant vector  $w$  there exists a positive  $R_w$  with the property that if  $(u_0(x), v_0(x)) \geq w$  on an interval of length  $2R_w$ , then

$$\lim_{t \rightarrow +\infty} \left[ \max_{|x| \leq t(c^* - \epsilon)} |(u_2^+, v_2^+) - (u(x, t), v(x, t))| \right] = 0.$$

Where  $(u_2^+, v_2^+)$  is a positive equilibrium of the ODE system associated with (2.1), it will be defined in lemma 4.2.

REMARK 3.2. In subsection 5.2, we will estimate the wave speed.

Our second result concerns the heterogeneous case, we show the existence of a blocking of the propagation, our result is

THEOREM 3.3.

Let  $d = d_1 \mathbb{1}_{x \leq 0} + d_2 \mathbb{1}_{x > 0}$ ,  $d_k \in \mathbb{R}_+$ ,  $k = 1, 2$ . If the following assertions hold true:

a-  $r_c > \beta$ ,  $s_b > \max(b_i, \frac{1}{\beta})$  and  $\gamma > a$ .

b-  $r_b < d_1 < r_b + \frac{\gamma\beta}{r_c}$ ,  $r_b + \gamma < d_2 < \min(r_b + \gamma + r_c - \beta, s_b(r_b r_c + \beta\gamma))$ . Then there is a solution  $(\bar{U}, \bar{V})$  of the following system

$$(3.1) \quad \begin{cases} -D\partial_{xx}u = r_b u(1 - \frac{u}{b_i}) + \gamma(1 - \frac{u}{b_i})v - \frac{auv}{s_b + u} - du \\ -D\partial_{xx}v = \beta u - r_c v \\ (u, v)(-\infty) = (u_2^+, v_2^+), \quad (u, v)(+\infty) = (0, 0) \\ u > 0, \quad v > 0. \end{cases}$$

COROLLARY 3.4. (Blocking of the Wave)

Under the assumptions of theorem 3.3, any solution to the initial problem 2.1 with an initial condition  $(u_0, v_0)$  such that  $(0, 0) \leq (u_0, v_0) \leq (\bar{U}, \bar{V})$  exhibits limited propagation.

### 4. Preliminary results.

In this section, we will study the critical points of the model and their stability. Consider the ODE system associated with (2.1) with positive real parameters  $r_b$ ,  $b_i$ ,  $\gamma$ ,  $a$ ,  $s_b$ ,  $\beta$  and  $r_c$  and  $d \in \mathbb{R}_+$ .

$$(4.1) \quad \begin{cases} \partial_t u^* = r_b u^*(1 - \frac{u^*}{b_i}) + \gamma(1 - \frac{u^*}{b_i})v^* - \frac{au^*v^*}{s_b + u^*} - du^* \\ \partial_t v^* = \beta u^* - r_c v^* \end{cases}$$

#### 4.1. Non-negativity property .

In this subsection, we will establish some properties of solution of (4.1). Our property reads

PROPOSITION 4.1.

If the initial conditions  $(u_0^*, v_0^*)$  are non-negative, then  $(u_t^*, v_t^*)$  remains non-negative for all  $t \geq 0$ .

*Proof.*

Consider  $t_1$  the first instant when  $u^*(t_1, x)$  or  $v^*(t_1, x)$  is negative, then for some  $x_1 \in \Omega \subset \mathbb{R}$  we have  $u^*(t_1, x_1)v^*(t_1, x_1) = 0$ .

- If  $u^*(t_1, x_1) = 0$  and  $v^*(t_1, x_1) \geq 0$ , since  $u_0^*(x) \geq 0$ ; then  $\exists \eta_t > 0$ , such as

$$\forall t \in [t_1 - \eta_t, t_1], \text{ we have } \partial_t u^*(t, x_1) < 0.$$

From the first equality in equation (4.1), we have

$$\partial_t u^*(t_1, x_1) = \gamma v^* > 0.$$

This contradicts the previous conclusion.

- If  $v^*(t_1, x_1) = 0$  and  $u^*(t_1, x_1) \geq 0$ , since  $v_0^*(x) \geq 0$ ; then  $\exists \eta_t > 0$ , such as

$$\forall t \in [t_1 - \eta_t, t_1], \text{ we have } \partial_t v^*(t, x_1) < 0.$$

From the first equality in equation (4.1), we have

$$\partial_t v^*(t_1, x_1) = \beta u^*(t_1, x_1) > 0.$$

This contradicts the previous conclusion.

□

#### 4.2. Critical points and their stability for the dynamical system.

In this section, we will closely examine the critical points of the dynamical system and study their stability, which will enable us to gain a better understanding of the system without diffusion.

LEMMA 4.2. (*Existence of critical points*)

Let  $d \in \mathbb{R}_+$ . Suppose that  $d < s_b(r_b r_c + \beta \gamma)$  and  $s_b > \frac{1}{r_c}$ , then we have the two following cases :

Case 1 :  $d < r_b + \frac{\gamma \beta}{r_c}$ , then (4.1) has three equilibria : a negative equilibrium  $(u_1^*, v_1^*)$ , a positive equilibrium  $(u_2^+, v_2^+)$  and  $(0, 0)$ .

Case 2 :  $d > r_b + \frac{\gamma \beta}{r_c}$ , then (4.1) has three equilibria : two negative equilibria  $(u_1^*, v_1^*)$ ,  $(u_2^-, v_2^-)$  and  $(0, 0)$ .

*Proof.*

We note that  $(u^*, v^*)$  is the critical point of (4.1), if

$$(4.2) \quad \begin{cases} r_b u^* (1 - \frac{u^*}{b_i}) + \gamma (1 - \frac{u^*}{b_i}) v^* - \frac{a u^* v^*}{s_b + u^*} - d u^* = 0 \end{cases}$$

$$(4.3) \quad \begin{cases} v^* = \frac{\beta}{r_c} u^* \end{cases}$$

By substituting (4.3) into (4.2), we get

$$r_b u^* (1 - \frac{u^*}{b_i}) - d u^* + \frac{\gamma \beta}{r_c} u^* (1 - \frac{u^*}{b_i}) - \frac{a \beta (u^*)^2}{r_c (s_b + u^*)} = u^* [r_b (1 - \frac{u^*}{b_i}) - d + \frac{\gamma \beta}{r_c} (1 - \frac{u^*}{b_i}) - \frac{a \beta u^*}{r_c (s_b + u^*)}] = 0$$

which yields

$$u^* = 0$$

or

$$r_b(1 - \frac{u^*}{b_i}) - d + \frac{\gamma\beta}{r_c}(1 - \frac{u^*}{b_i}) - \frac{a\beta u^*}{r_c(s_b + u^*)} = 0.$$

We can simplify the previous equation to obtain a more concise expression. The following equation represents this simplification:

$$(4.4) \quad (u^*)^2[-r_cr_b - \gamma\beta] + u^*[r_cr_b(b_i - s_b) - db_ir_c + \gamma\beta(b_i - s_b) - a\beta b_i] + r_br_cb_is_b - db_ir_cs_b + \gamma\beta b_is_b = 0$$

To find the nonzero critical points, it suffices to determine the values of  $u^*$  for which the equation (4.4) vanishes. We then solve the equation (4.4), we calculate the discriminant  $\Delta$  of (4.4).

$$\Delta = [(r_br_c + \beta\gamma)(b_i - s_b) - ab_i\beta - db_ir_c]^2 + 4(r_br_c + \beta\gamma)(s_bb_i(r_br_c + \beta\gamma) - db_i).$$

According to the hypothesis of the lemma, we have  $\Delta > 0$ , then equation (4.4) has two solutions

$$u_1^* = \frac{(r_br_c + \beta\gamma)(b_i - s_b) - ab_i\beta - db_ir_c - \sqrt{\Delta}}{2(r_br_c + \beta\gamma)},$$

$$u_2^* = \frac{(r_br_c + \beta\gamma)(b_i - s_b) - ab_i\beta - db_ir_c + \sqrt{\Delta}}{2(r_br_c + \beta\gamma)}$$

We conclude that (4.1) has three critical points  $(0, 0)$ ,  $(u_1^*, v_1^*)$  and  $(u_2^*, v_2^*)$

$$\text{where } v_1^* = \frac{\beta}{r_c}u_1^* \text{ and } v_2^* = \frac{\beta}{r_c}u_2^*.$$

$\forall k \in \{1, 2\}$ ,  $u_k^*$  are the solutions of equation (4.4), then

$$\begin{cases} u_1^*u_2^* = \frac{s_bb_i[r_br_c + \beta\gamma] - db_ir_cs_b}{-r_br_c - \beta\gamma} \\ u_1^* + u_2^* = \frac{(b_i - s_b)(r_cr_b + \gamma\beta) - a\beta b_i - db_ir_c}{r_br_c + \gamma\beta} \end{cases}$$

Case 1 :  $u_1^*u_2^* < 0$ , since  $d < r_b + \frac{\gamma\beta}{r_c}$ , then  $u_1^*$  and  $u_2^*$  are of opposite sign, so we have a negative equilibrium  $(u_1^*, v_1^*)$  and a positive equilibrium  $(u_2^*, v_2^*)$ , which will be denoted  $(u_2^+, v_2^+)$ .

Case 2 :  $u_1^*u_2^* > 0$  and  $u_1^* + u_2^* < 0$ , since  $d > r_b + \frac{\gamma\beta}{r_c}$ , then  $u_1^*$  and  $u_2^*$  are negative. Then we have two negative equilibria.

□

LEMMA 4.3. (*Critical point stability*)

Let  $d \in \mathbb{R}_+$ . Suppose that  $d < s_b(r_br_c + \beta\gamma)$  and  $s_b > \frac{1}{r_c}$

a- If  $r_b < d < r_b + \frac{\gamma\beta}{r_c}$  and  $f'(u_2^+) > \max(\frac{-r_br_c}{\beta b_i} - \frac{d}{v_2^+}, \frac{-2r_br_c}{\beta b_i} - \frac{d}{v_2^+} + \frac{(r_b - r_c)}{v_2^+})$ , then  $(0, 0)$  is an unstable equilibrium and  $(u_2^+, v_2^+)$  is a stable positive equilibrium of (4.1).

b- If  $d > r_b + \frac{\gamma\beta}{r_c}$ , then  $(0, 0)$  is a stable equilibrium and there is no positive equilibrium of (4.1).



*Proof.*

We consider the following ODE

$$\begin{cases} \partial_t u^* = r_b u^* (1 - \frac{u^*}{b_i}) - d u^* - f(u^*) v = F_1(u^*, v^*) \\ \partial_t v^* = \beta u^* - r_c v^* = F_2(u^*, v^*) \end{cases}$$

where  $F(u^*, v^*) = (F_1(u^*, v^*), F_2(u^*, v^*))$ ,  $f(u^*) = -\gamma(1 - \frac{u^*}{b_i}) + \frac{a u^*}{s_b + u^*}$ . We define  $DF(u^*, v^*)$  the differential of the function  $F$  at the equilibrium point  $(u^*, v^*)$ .

$$DF(u^*, v^*) = \begin{pmatrix} \frac{\partial F_1}{\partial u^*} & \frac{\partial F_1}{\partial v^*} \\ \frac{\partial F_2}{\partial u^*} & \frac{\partial F_2}{\partial v^*} \end{pmatrix} = \begin{pmatrix} r_b(1 - \frac{2u^*}{b_i}) - f'(u^*)v^* - d & -f(u^*) \\ \beta & -r_c \end{pmatrix}.$$

We compute the determinant and the trace of this matrix

$$\text{Tr}(DF(u^*, v^*)) = r_b(1 - \frac{2u^*}{b_i}) - f'(u^*)v^* - d - r_c,$$

$$\det(DF(u^*, v^*)) = -r_c r_b(1 - \frac{2u^*}{b_i}) + r_c f'(u^*)v^* + d r_c + \beta f(u^*),$$

we consider the two cases in the statement of the lemma :

- a-  $\text{Tr}(DF(0, 0)) = r_b - d - r_c < 0$ , since  $r_b < d$  and  $\det(DF(0, 0)) = -r_b r_c + d r_c - \beta \gamma < 0$ , since  $d < r_b + \frac{\gamma \beta}{r_c}$ , then  $(0, 0)$  is an unstable equilibrium of (4.1). Similarly  $\text{Tr}(DF(u_2^+, v_2^+)) = r_b(1 - \frac{2u_2^+}{b_i}) - f'(u_2^+)v_2^+ - d - r_c$  and  $\det(DF((u_2^+, v_2^+))) = -r_b r_c(1 - \frac{2u_2^+}{b_i}) + r_c f'(u_2^+)v_2^+ + r_c d + \beta f(u_2^+)$  as we have  $f'(u_2^+) > \max(\frac{-r_b r_c}{\beta b_i} - \frac{d}{v_2^+}, \frac{-2r_b r_c}{\beta b_i} - \frac{d}{v_2^+} + \frac{(r_b - r_c)}{v_2^+})$ , then  $\text{Tr}(DF(u_2^+, v_2^+)) < 0$  and  $\det(DF(u_2^+, v_2^+)) > 0$ , thus  $(u_2^+, v_2^+)$  is a stable positive equilibrium of (4.1).
- b-  $\text{Tr}(DF(0, 0)) = r_b - d - r_c < 0$ , since  $r_b < d$  and  $\det(DF(0, 0)) = r_b r_c + d r_c - \beta \gamma > 0$ , since  $d > r_b + \frac{\gamma \beta}{r_c}$ , thus  $(0, 0)$  is a stable equilibrium.

□

## 5. Proof of the main results .

### 5.1. Proof of Theorem 3.1.

#### 5.1.1. Notations.

Before proving the theorem, let's start with some notations. In the following sections, the vector  $X := (X_1, X_2)$  is said to be positive if  $X_1 \geq 0$  and  $X_2 \geq 0$  and we note it  $(X_1, X_2) > (0, 0)$ . the vector  $X := (X_1, X_2)$  is said to be strictly positive, if  $X_1 > 0$  and  $X_2 > 0$  and we note it  $(X_1, X_2) \gg (0, 0)$ . For any  $(X_1, X_2) > (0, 0)$ , we define  $C_{(X_1, X_2)} = \{(u, v), 0 < u < X_1, 0 < v < X_2\}$ .

#### 5.1.2. Proof.

To prove the results of this Theorem, we will use [19, Theorem 4.1]. First, we will verify the hypotheses of [19, Theorem 4.1] :

- i) We have  $d < r_b + \frac{\gamma \beta}{r_c}$ , then from lemma 4.2, (2.1) admits a positive equilibrium  $(u_2^+, v_2^+)$ , i.e  $(u_2^+, v_2^+) \gg (0, 0)$ .

ii) Next, we show that

$$C_{(u_2^+, v_2^+)} = \{(u, v), 0 < u < u_2^+, 0 < v < v_2^+\} \text{ is an invariant set of (2.1).}$$

We use the strategy in [17, Chapter 14]. Let  $(u, v) \in C_{(u_2^+, v_2^+)}$  and  $G_1(u, v) = -u$ . As we now  $F(u, v) = (r_b u(1 - \frac{u}{b_i}) + \gamma(1 - \frac{u}{b_i})v - \frac{auv}{s_b + u} - du, \beta u - r_c v)$  and by taking the differential of  $G_1$ , we obtain

$$dG_1(F)|_{u=0} = -\gamma v < 0,$$

since  $v > 0$  and  $-\gamma < 0$ . Moreover, if we set  $G_2(u, v) = -v$ , we obtain that

$$dG_2(F)|_{v=0} = -\beta u < 0,$$

since  $u \geq 0$  and  $\beta > 0$ . Similarly, if  $G_3(u, v) = v - v_2^+$ , and  $G_4(u, v) = u - u_2^+$ , we obtain that

$$dG_3(F)|_{v=v_2^+} = \beta u - r_c v_2^+ = \beta(u - u_2^+) \leq 0,$$

and

$$dG_4(F)|_{u=u_2^+} = r_b u_2^+ (1 - \frac{u_2^+}{b_i}) - du_2^+ + \gamma(1 - \frac{u_2^+}{b_i})v - \frac{au_2^+ v}{s_b + u_2^+}$$

Rewriting the above expression, we get:

$$dG_4(F)|_{u=u_2^+} = r_b u_2^+ (1 - \frac{u_2^+}{b_i}) - du_2^+ - \frac{r_b r_c (1 - \frac{u_2^+}{b_i})v}{\beta} + \frac{dr_c v}{\beta}$$

Further simplification, we have:

$$dG_4(F)|_{u=u_2^+} = \frac{r_b}{\beta} [1 - \frac{u_2^+}{b_i}] [\beta u_2^+ - r_c v] + d [\frac{r_c}{\beta} v - u_2^+]$$

Rearranging terms, we obtain:

$$dG_4(F)|_{u=u_2^+} = \frac{r_b r_c}{\beta} (1 - \frac{u_2^+}{b_i}) [v_2^+ - v] + \frac{r_c d}{\beta} [v - v_2^+]$$

Finally, the concluding statement about the inequality:

$$dG_4(F)|_{u=u_2^+} = \frac{r_c}{\beta} [v - v_2^+] [d - r_b + \frac{r_b u_2^+}{b_i}] < 0$$

respectively, since  $u \leq u_2^+$ ,  $v \leq v_2^+$ ,  $\beta > 0$  and  $d > r_b$ . By using the definition of an invariant set, we conclude that  $C_{(u_2^+, v_2^+)} = \{(u, v), 0 < u < u_2^+, 0 < v < v_2^+\}$  is an invariant set of (2.1).

iii) In this step, we will verify the hypotheses of [19, proposition 2.1 ].

- $F(0, 0) = F(u_2^+, v_2^+) = (0, 0)$  and  $(u_2^+, v_2^+) \gg (0, 0)$  which is minimal in the sense that there is no other equilibrium than  $(0, 0)$  and  $(u_2^+, v_2^+)$  in the set  $C_{u_2^+, v_2^+}$ , when  $d < r_b + \frac{\gamma\beta}{r_c}$
- $F(\xi_1, \xi_2)$  is a continuous and piecewise continuously differentiable in  $(\xi_1, \xi_2)$  for  $(0, 0) < (\xi_1, \xi_2) \leq (u_2^+, v_2^+)$  and differentiable at 0.

- Since  $\gamma > a$ ;  $s_b > b_i$  and  $0 < u \leq \frac{b_i}{2}$ , then the system (2.1) is cooperative. Indeed, for  $(u, v) \in C_{u_2^+, v_2^+}$

$$\frac{\partial F_1}{\partial v}(u, v) = \gamma(1 - \frac{u}{b_i}) - \frac{au}{s_b + u} > 0,$$

$\gamma > a$ ;  $s_b > b_i$  and  $0 < u \leq \frac{b_i}{2}$  and

$$\frac{\partial F_2}{\partial u}(u, v) = \beta > 0.$$

- $F$  does not depend explicitly on either  $x$  or  $t$ .
- The Jacobian matrix  $DF(0, 0) = \begin{pmatrix} r_b - d & \gamma \\ \beta & -r_c \end{pmatrix}$  is in Frobenius form.

The principal eigenvalue  $\gamma_1(0) = \frac{r_b - d - r_c + \sqrt{(-r_b + d + r_c)^2 - 4(-r_b r_c + d r_c - \gamma \beta)}}{2} > 0$ , since  $d < r_b + \frac{\gamma \beta}{r_c}$ .

Then according to Theorem 4.1 in [19], there is a spreading speed  $c^* > 0$  with the properties that for every positive  $\epsilon$  :

- For any initial function  $(u_0(x), v_0(x))$  in  $C_{(u_2^+, v_2^+)} = \{(u, v), 0 < u < u_2^+, 0 < v < v_2^+\}$  which vanishes outside a bounded set, the solution of (2.1) satisfies

$$\lim_{t \rightarrow +\infty} [\max_{|x| \geq t(c^* + \epsilon)} |(u(x, t), v(x, t))|] = 0, \quad \forall \epsilon > 0,$$

- For any strictly positive constant vector  $w$  there exists a positive  $R_w$  with the property that if  $(u_0(x), v_0(x)) \geq w$  on an interval of length  $2R_w$ , then

$$\lim_{t \rightarrow +\infty} [\max_{|x| \leq t(c^* - \epsilon)} |(u_2^+, v_2^+) - (u(x, t), v(x, t))|] = 0.$$

## 5.2. Estimation of the wave speed for the model.

In this section, we analytically determine the wave speed based on the model parameters. Thanks to Theorem 3.1, we can affirm that model 2.1 exhibits solutions in the form of progressive waves. Consequently, the variables  $u(x, t)$  and  $v(x, t)$  can be represented as progressive waves, i.e.,  $u(x, t) = U(x - ct)$  and  $v(x, t) = V(x - ct)$ . It is noteworthy that we employ the same strategy as in [4] to analyze the wave speed in our context. To find the minimum speed, we begin by linearizing the system 2.1 at  $(0, 0)$  to seek positive solutions. Subsequently, we search for the minimum value of wave speed for which positive solutions exist. After this linearization at  $(0, 0)$ , we obtain the system:

$$(5.1) \quad \begin{cases} -cU' - DU'' = (r_b - d)U + \gamma V \\ -cV' - DV'' = \beta U - r_c V \end{cases}$$

We looking for solutions in the form

$$U(x - ct) = p_1 e^{-\lambda(x - ct)}, \quad V(x - ct) = p_2 e^{-\lambda(x - ct)}.$$

Hence, system 5.1 yields:

$$(5.2) \quad \begin{cases} c\lambda p_1 - D\lambda^2 p_1 = (r_b - d)p_1 + \gamma p_2 \\ c\lambda p_2 - D\lambda^2 p_2 = \beta p_1 - r_c p_2 \end{cases}$$

To determine the minimum wave speed, it is necessary to find the minimum value of  $c$  for which the system 5.2 admits a positive solution  $\lambda$ . Introducing the parameter  $X = c\lambda - D\lambda^2$  and excluding  $p_1$  and  $p_2$ , we obtain the following equation :

$$X^2 + (r_c + d - r_b)X + r_c(d - r_b) - \beta\gamma = 0.$$

Hence,

$$c^* = \min_{\lambda > 0} D\lambda + \frac{X_+}{\lambda} = 2\sqrt{DX_+}, \quad \text{where} \quad X_+ = \frac{-r_c - d + r_b + \sqrt{(r_c - d + r_b)^2 + 4\beta\gamma}}{2}.$$

We are studying the dependence of analytical wave speed on several parameters, particularly the parameter  $d$ , which represents the mortality rate. We consider the range of values for  $d$  to be  $(0.021, 0.03712)$ . In addition to the analysis of the analytical wave speed's dependence, we are calculating and graphically representing the numerical wave speed, which is determined by the formula involving distance divided by time (see Figure 5.1).

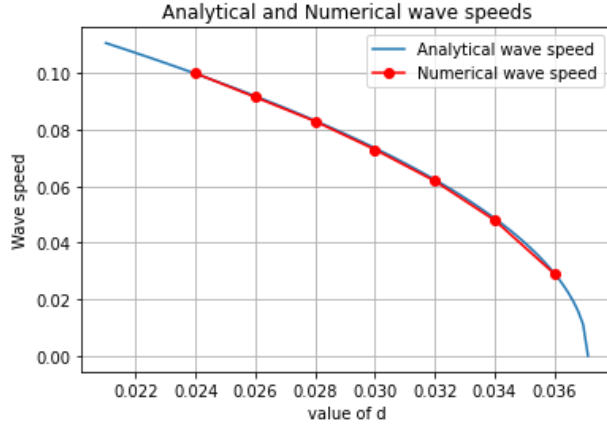


FIGURE 5.1. Dependence of the wave speed on the parameter  $d = (0.021, 0.03712)$ . Wave speed in numerical simulations and analytical formula (curves coincide) for the values of parameters :  $r_b = 0.02$ ,  $r_c = 0.3129$ ,  $\beta = 0.06258$ ,  $D = 0.2$ ,  $\gamma = 0.0856$ .

### 5.3. Proof of Theorem 3.3 : Construction of a stationary solution .

In this section, our goal is to prove the existence of a stationary solution for the problem (2.1). This solution corresponds to a solution of the associated elliptic problem, which can be formulated as follows:

$$(5.3) \quad \begin{cases} -D\partial_{xx}u = r_b u(1 - \frac{u}{b_i}) + \gamma(1 - \frac{u}{b_i})v - \frac{auv}{s_b + u} - du = F_1(u, v) \\ -D\partial_{xx}v = \beta u - r_c v = F_2(u, v) \\ (u, v)(-\infty) = (u_2^+, v_2^+), \quad (u, v)(+\infty) = (0, 0) \\ u > 0, \quad v > 0, \quad x \in \mathbb{R}. \end{cases}$$

First of all, we are introducing some definitions (see [20]).

Let  $D_i \subset \mathbb{R}$ ,  $i = 1, 2$ . We have :

DÉFINITIONS 5.1. (*Quasi-monotonic reaction function*)

- A function  $F_i = F_i(u_1, u_2)$  is said to be quasi-monotonic increasing (resp decreasing) in  $D_1 \times D_2$ , if for all  $u_i \in D_i$  fixed,  $F_i$  is increasing (resp decreasing) with respect to  $u_j \in D_j$  for  $i \neq j$ .

DÉFINITIONS 5.2. (Super-and sub-solution)

A pair of functions  $(\bar{u}, \bar{v})$  and  $(\underline{u}, \underline{v})$  in  $C^2(\mathbb{R} \times \mathbb{R}_+) \times C^2(\mathbb{R} \times \mathbb{R}_+)$  are called ordered super-solution and sub-solution of problem (2.1), if they satisfy

$$(\bar{u}(x, t), \bar{v}(x, t)) \geq (\underline{u}(x, t), \underline{v}(x, t)), \quad x \in \mathbb{R}, \quad t \in \mathbb{R}_+$$

and if

$$\begin{cases} \partial_t \bar{u} - D\partial_{xx} \bar{u} - F_1(\bar{u}, \bar{v}) \geq 0 \geq \partial_t \underline{u} - D\partial_{xx} \underline{u} - F_1(\underline{u}, \underline{v}) \\ \partial_t \bar{v} - D\partial_{xx} \bar{v} - F_2(\bar{u}, \bar{v}) \geq 0 \geq \partial_t \underline{v} - D\partial_{xx} \underline{v} - F_2(\underline{u}, \underline{v}), \end{cases}$$

when  $(F_1, F_2)$  is quasi-monotonic increasing.

The proof is done by four steps. First, We begin by proving a comparison principle. Then, we construct the sub and super-solution and finally we show the existence of the stationary solution.

**5.3.1. Comparison principle.** Before proving the comparison principle, we begin by presenting some necessary properties :

PROPOSITION 5.3.

If  $\gamma > a$  and  $s > b_i$ , then the system described in (2.1) exhibits cooperativity.

*Proof.*

Let  $0 \leq u \leq \frac{b_i}{2}$ ,  $F_1(u, v) = r_b u(1 - \frac{u}{b_i}) - f(u)v$ ,  $F_2(u, v) = \beta u - r_c v$  and  $f(u) = -\gamma(1 - \frac{u}{b_i}) + \frac{au}{s_b + u}$ . The functions  $F_1$  and  $F_2$  are  $C^\infty$ , then

$$\frac{\partial F_1}{\partial v}(u, v) = -f(u) = \gamma(1 - \frac{u}{b_i}) - \frac{au}{s_b + u} = \frac{\gamma(b_i - u)(s_b + u) - aub_i}{s_b + u} > 0,$$

since  $\gamma > a$ ,  $s > b_i$  and  $u \leq \frac{b_i}{2}$ . We have also:

$$\frac{\partial F_2}{\partial u}(u, v) = \beta > 0.$$

□

PROPOSITION 5.4.

Assume that  $(0, 0) < (u, v) \leq (\frac{b_i}{2}, \frac{\beta}{r_c})$ . Then  $|\frac{\partial F_1}{\partial u}(u, v)| \leq 2r_b + d + \frac{\beta}{r_c} \|f'\|_\infty = \Gamma_1$ , where  $\|f'\|_\infty = \sup_{0 \leq u \leq \frac{b_i}{2}} |f'(u)|$ .

*Proof.*

Let  $0 \leq u \leq \frac{b_i}{2}$ ,  $F_1(u, v) = r_b u(1 - \frac{u}{b_i}) - f(u)v - du$ ,  $f(u) = -\gamma(1 - \frac{u}{b_i}) + \frac{au}{s_b + u}$ . The function  $F_1$  and  $f$  are  $C^\infty$ ,  $\frac{\partial F_1}{\partial u}(u, v) = r_b(1 - \frac{2u}{b_i}) - f'(u)v$ , then

$$|\frac{\partial F_1}{\partial u}(u, v)| \leq 2r_b + d + \frac{\beta}{r_c} \|f'\|_\infty = \Gamma_1.$$

□

LEMMA 5.5. (Comparison principle)

Assuming  $\gamma > a$  and  $s_b > b_i$ . Let  $(u, v)$  be a solution of (2.1) on  $\mathbb{R}$ , super-solution  $(\bar{u}, \bar{v})$  of (2.1) on  $\mathbb{R}$  and sub-solution  $(\underline{u}, \underline{v})$  of (2.1) on  $\mathbb{R}$ , such as  $(0, 0) < (\bar{u}, \bar{v}) \leq (\frac{b_i}{2}, \frac{\beta}{r_c})$ ,  $(0, 0) < (\underline{u}, \underline{v}) \leq (\frac{b_i}{2}, \frac{\beta}{r_c})$  and  $(0, 0) < (u, v) \leq (\frac{b_i}{2}, \frac{\beta}{r_c})$ . Then

$$(\underline{u}(t = 0, x), \underline{v}(t = 0, x)) \leq (u(t = 0, x), v(t = 0, x)) \leq (\bar{u}(t = 0, x), \bar{v}(t = 0, x))$$

implies that

$$(\underline{u}(t, x), \underline{v}(t, x)) \leq (u(t, x), v(t, x)) \leq (\bar{u}(t, x), \bar{v}(t, x)) \quad \forall t \geq 0, \quad \forall x \in \mathbb{R}$$

*Proof.*

To demonstrate the comparison principle, we employ the same approach as presented in the book [14].  $\square$

### 5.3.2. Construction of the super-solution.

The objective of this subsection is to construct a super-solution for equation (5.3) on  $\mathbb{R}$ . We can choose  $(u_2^+, v_2^+)$  as a super-solution on the interval  $(-\infty, 0)$ , given that  $C_{(u_2^+, v_2^+)}$  remains invariant for  $d > r_b$ . The next step is to construct a super-solution on the interval  $(0, +\infty)$  for  $d = d_2$ . Before proceeding with the construction of the super-solution on the interval  $(0, +\infty)$ , we will begin by stating the following property.

LEMMA 5.6.

Let  $d_2 > r_b + \gamma$ . There exists  $(\phi_1, \phi_2)$  satisfying

$$(5.4) \quad \begin{cases} -D\partial_{xx}\phi_1 + \phi_1(-r_b - \gamma + d_2) = 0 \\ D\partial_{xx}\phi_2 - r_c\phi_2 = 0 \\ \phi_1(0) = u_2^+, \quad \phi_1(+\infty) = 0 \\ \phi_2(0) = u_2^+ - v_2^+, \quad \phi_2(+\infty) = 0 \\ \phi_1 > 0, \quad \phi_2 > 0 \text{ on } (0, +\infty), \quad x \in (0, +\infty) \end{cases}$$

Indeed, for all  $x \in (0, +\infty)$ ,  $\phi_1(x) = u_2^+ e^{-\sqrt{\frac{1}{D}(-r_b - \gamma + d_2)}x}$  and  $\phi_2(x) = (u_2^+ - v_2^+)e^{-\sqrt{\frac{r_c}{D}}x}$  are solutions to system (5.4).

LEMMA 5.7.

Under the assumption that  $r_b + \gamma < d_2 < \min(r_b + \gamma + r_c - \beta, s_b(r_b r_c + \beta\gamma))$ ,  $s_b > \frac{1}{\beta}$ , and  $\beta < r_c$ . There exists a super-solution  $(\bar{u}, \bar{v}) = (\phi_1, \phi_1 - \phi_2)$  of (5.3) on  $(0, +\infty)$ .

*Proof.*

Let  $(\bar{u}, \bar{v})$  be a sub-solution of (5.3), such as  $\bar{v} \leq \bar{u}$ . For all  $x > 0$ , we show that

$$\begin{cases} -D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) \geq 0 \\ -D\partial_{xx}\bar{v} - F_2(\bar{u}, \bar{v}) \geq 0 \end{cases}$$

$$1. -D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) = -D\partial_{xx}\bar{u} - r_b\bar{u}(1 - \frac{\bar{u}}{b_i}) + d_2\bar{u} + f(\bar{u})\bar{v}.$$

With the definition of  $f$ , we get :

$$-D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) = -D\partial_{xx}\bar{u} - r_b\bar{u} - \gamma\bar{v} + d_2\bar{u} + \underbrace{\frac{r_b(\bar{u})^2}{b_i} + \frac{\gamma\bar{u}\bar{v}}{b_i} + \frac{a\bar{u}\bar{v}}{s_b + \bar{u}}}_{J_2}.$$

since  $J_2 > 0$ , we have

$$-D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) \geq -D\partial_{xx}\bar{u} - r_b\bar{u} - \gamma\bar{v} + d_2\bar{u}.$$

Under the condition that  $\bar{v} \leq \bar{u}$ , we have

$$-D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) \geq -D\partial_{xx}\bar{u} + \bar{u}[-r_b - \gamma + d_2]$$

By definition of the function  $\phi_1$ , we have  $-D\partial_{xx}\phi_1 + \phi_1[-r_b - \gamma + d_2] = 0$ . Therefore,

$$-D\partial_{xx}\bar{u} - F_1(\bar{u}, \bar{v}) \geq 0$$

$$2. -D\partial_{xx}\bar{v} - F_2(\bar{u}, \bar{v}) = -D\partial_{xx}\bar{v} - \beta\bar{u} + r_c\bar{v} = -D\partial_{xx}\phi_1 + [r_c - \beta]\phi_1 + D\partial_{xx}\phi_2 - r_c\phi_2.$$

Based on the definitions of the functions  $\phi_1$  and  $\phi_2$ , we can deduce that:

$$-D\partial_{xx}\bar{v} - F_2(\bar{u}, \bar{v}) = [r_c - \beta + r_b + \gamma - d_2]\phi_1.$$

Considering that  $d_2 < r_b + \gamma + r_c - \beta$ , we can deduce that:

$$-D\partial_{xx}\bar{v} - F_2(\bar{u}, \bar{v}) \geq 0.$$

To complete the proof, we need to prove that  $(\bar{u}, \bar{v})(+\infty) = (0, 0)$  and  $(\bar{u}, \bar{v})(0, 0) = (u_2^+, v_2^+)$ .

According to the definition of the functions  $\phi_i$ , where  $i = 1, 2$ , we know that  $\phi_i(+\infty) = 0$ . Hence,  $(\bar{u}, \bar{v})(+\infty) = (0, 0)$ .

Furthermore, since  $\phi_1(0) = u_2^+$  and  $\phi_2(0) = u_2^+ - v_2^+$ , we can compute  $(\bar{u}, \bar{v})(0, 0)$  as follows:

$$(\bar{u}, \bar{v})(0, 0) = (\phi_1, \phi_1 - \phi_2)(0) = (u_2^+, u_2^+ - u_2^+ + v_2^+) = (u_2^+, v_2^+).$$

Therefore, we have shown that  $(\bar{u}, \bar{v})(+\infty) = (0, 0)$  and  $(\bar{u}, \bar{v})(0, 0) = (u_2^+, v_2^+)$ .  $\square$

### 5.3.3. Construction of a sub-solution.

The goal of this subsection is to construct a sub-solution for the system represented by (5.3) over the entire  $\mathbb{R}$ . we can choose  $(0, 0)$  as a sub-solution over the interval  $(0, +\infty)$  because the system is cooperative. Now, let's proceed to establish a sub-solution over the interval  $(-\infty, 0)$ .

LEMMA 5.8.

*If  $\gamma > a$ ,  $s_b > b_i$ , then the system defined by (5.3) admits a sub-solution on the interval  $(-\infty, 0)$ .*

*Proof.*

Given  $\lambda_1 \geq \sqrt{\frac{d_1}{D}}$ ,  $\lambda_2 > \sqrt{\frac{r_c}{D}}$ , and any  $\epsilon_j > 0$ ,  $j = 1, 2$ ,  $\frac{D(\lambda_1 + \epsilon_1)^2 - d_1}{D\lambda_1^2 - d_1} \leq a_1 \leq u_2^+$ . Additionally,  $\frac{D(\lambda_2 + \epsilon_2)^2 - d_1}{D\lambda_2^2 - d_1} \leq a_2 \leq v_2^+$ . We define two functions as follows:

$$\psi_1(x) = \begin{cases} a_1 e^{\lambda_1(x+z_0)} - e^{(\lambda_1 + \epsilon_1)(x+z_0)}, & \text{for } x + z_0 < 0 \\ 0, & \text{for } x + z_0 \geq 0 \end{cases}$$

$$\psi_2(x) = \begin{cases} a_2 e^{\lambda_2(x+z_1)} - e^{(\lambda_2 + \epsilon_2)(x+z_1)}, & \text{for } x + z_1 < 0 \\ 0, & \text{for } x + z_1 \geq 0 \end{cases}$$

In this expression the parameter  $z_0$  and  $z_1$  are defined by

$$z_0 = \frac{\log(a_1)}{\epsilon_1}, \quad z_1 = \frac{\log(a_2)}{\epsilon_2}$$

For all  $x + z_i < 0$ ,  $i = 1, 2$ , we show that  $(\underline{u}, \underline{v}) = (\psi_1, \psi_2)$  is a sub-solution of (2.1), i.e, we show that

$$\begin{cases} -D\partial_{xx}\underline{u} - F_1(\underline{u}, \underline{v}) \leq 0 \\ -D\partial_{xx}\underline{v} - F_2(\underline{u}, \underline{v}) \leq 0 \end{cases}$$

1.

$$-D\partial_{xx}\underline{u} - F_1(\underline{u}, \underline{v}) = -D\partial_{xx}\underline{u} + J_1 + d_1\underline{u} - r_b\underline{u}(1 - \frac{\underline{u}}{b_i}), \text{ where } J_1 = [-\gamma(1 - \frac{\underline{u}}{b_i}) + \frac{a\underline{u}}{s_b + \underline{u}}]\underline{v}.$$

Since  $\gamma > a$ ,  $s_b > b_i$  and  $\underline{u} < \frac{b_i}{2}$ , we have  $J_1 < 0$ , then

$$-D\partial_{xx}\underline{u} - F_1(\underline{u}, \underline{v}) \leq -D\partial_{xx}\underline{u} - r_b\underline{u}(1 - \frac{\underline{u}}{b_i}) + d_1\underline{u} \leq -D\partial_{xx}\underline{u} + d_1\underline{u}.$$

Using the definition of  $\underline{u}$ , we write:

$$-D\partial_{xx}\underline{u} + d_1\underline{u} = e^{\lambda_1(x+z_0)}[-\lambda_1^2 D a_1 + d_1 a_1] + e^{(\lambda_1 + \epsilon_1)(x+z_0)}[D(\lambda_1 + \epsilon_1)^2 - d_1]$$

given that  $\lambda_1 \geq \sqrt{\frac{d_1}{D}}$  and  $a_1 \geq \frac{D(\lambda_1 + \epsilon_1)^2 - d_1}{D\lambda_1^2 - d_1}$ . Therefore, we can conclude that

$$-D\partial_{xx}\underline{u} - F_1(\underline{u}, \underline{v}) \leq -D\partial_{xx}\underline{u} + d_1\underline{u} \leq 0.$$

2.

$$-D\partial_{xx}\underline{v} - F_2(\underline{u}, \underline{v}) = -D\partial_{xx}\underline{v} - \beta\underline{u} + r_c\underline{v} \leq -D\partial_{xx}\underline{v} + r_c\underline{v}$$

By substituting the definition of  $\underline{v}$ , we can express the inequality :

$$-D\partial_{xx}\underline{v} + r_c\underline{v} = e^{\lambda_2(x+z_1)}[-\lambda_2^2 D a_1 + r_c a_1] + e^{(\lambda_2 + \epsilon_2)(x+z_1)}[D(\lambda_2 + \epsilon_2)^2 - r_c]$$

given that  $\lambda_2 \geq \sqrt{\frac{r_c}{D}}$  and  $a_2 \geq \frac{D(\lambda_2 + \epsilon_2)^2 - r_c}{D\lambda_2^2 - r_c}$ . Therefore, we can conclude that

$$-D\partial_{xx}\underline{v} + r_c\underline{v} \leq 0.$$

To demonstrate that  $(\underline{u}, \underline{v})(-\infty) = (0, 0)$  and  $(\underline{u}, \underline{v})(0, 0) = (0, 0) \leq (u_2^+, v_2^+)$ , we can refer to the definitions of the functions  $\underline{u}$  and  $\underline{v}$ . Thus, we have  $(\underline{u}, \underline{v})(-\infty) = (0, 0)$  and  $(\underline{u}, \underline{v})(0, 0) = (a_1 e^{\lambda_1 z_0} - e^{(\lambda_1 + \epsilon_1)z_0}, a_2 e^{\lambda_2 z_1} - e^{(\lambda_2 + \epsilon_2)z_1}) = (0, 0) \leq (u_2^+, v_2^+)$ .

□

#### 5.3.4. Construction of the solution.

To establish the existence of a solution for the system represented by (5.3), we will first demonstrate the ordering of subsolutions and supersolutions. Here are the supersolutions and subsolutions we have identified for equation (5.3):

$$\bar{u} = \begin{cases} u_2^+ & \text{on } (-\infty, 0) \\ u_2^+ e^{-\sqrt{\frac{1}{D}(-r_b - \gamma + d_2)}x} & \text{on } (0, +\infty) \end{cases} ; \quad \bar{v} = \begin{cases} v_2^+ = \frac{\beta u_2^+}{r_c} & \text{on } (-\infty, 0) \\ (u_2^+ - v_2^+) e^{-\sqrt{\frac{r_c}{D}}x} & \text{on } (0, +\infty) \end{cases}$$

$$\underline{u} = \begin{cases} \psi_1 & \text{on } (-\infty, 0) \\ 0 & \text{on } (0, +\infty) \end{cases} ; \quad \underline{v} = \begin{cases} \psi_2 & \text{on } (-\infty, 0) \\ 0 & \text{on } (0, +\infty) \end{cases}$$



On the interval  $(-\infty, 0)$ , we have  $(0, 0) < (\underline{u}, \underline{v}) = (\psi_1, \psi_2) < (\bar{u}, \bar{v}) = (u_2^+, v_2^+)$ , given that  $a_1 \leq u_2^+$  and  $a_2 \leq v_2^+$ .

On the interval  $(0, +\infty)$ , we have  $(\underline{u}, \underline{v}) = (0, 0)$  and  $(\bar{u}, \bar{v}) = (\phi_1, \phi_1 - \phi_2)$ , where:

- $\bar{v} > 0$ , since  $r_c > 0$ .
- $\bar{v} - \underline{v} = (u_2^+ - v_2^+)e^{-\sqrt{\frac{r_c}{D}}x} - 0 = (u_2^+ - v_2^+)e^{-\sqrt{\frac{r_c}{D}}x} > 0$ ,
- $\bar{u} > 0$ , since  $d_2 > r_b + \gamma$ .
- $\bar{u} - \underline{u} = u_2^+e^{-\sqrt{\frac{1}{D}(-r_b-\gamma+d_2)}x} - 0 = u_2^+e^{-\sqrt{\frac{1}{D}(-r_b-\gamma+d_2)}x} > 0$ .

We can construct a solution for equation (5.3) using the above sub-solution and super-solution. According to Lemma 5.7 and Lemma 5.8, we have identified a well-ordered sub-solution and super-solution. By applying the classical technique of sub-solution and super-solution (as described in [20]), we can conclude that there exists a unique solution for (5.3). Moreover, according to Lemma 5.5, this solution lies within the interval  $[(\underline{u}, \underline{v}), (\bar{u}, \bar{v})]$ .

#### 5.4. Proof of Corollary 3.4 : Blocking of the Wave .

Our model admits a stationary solution and satisfies the principle of comparison. If we have a positive initial data that is lower than the stationary solution, then, by the principle of comparison, it remains lower than the solution for all time. From this, we conclude that it is 'blocked,' justifying the term 'blocking' that we use.

#### 6. Numerical simulations.

We conducted numerical simulations of the mathematical model that describes the interaction between bacteria and phagocytes (immune cells) to illustrate our theoretical results. The numerical parameter values were extracted from [18] and are presented in Table (6.1) below.

Parameter	Interpretation	Value	Units
$r_b$	Reproduction rate of bacteria	0.02	(u/min)
$b_i$	maximum bacterial density	$10^{15}$	(u/m <sup>3</sup> )
$\gamma$	Related to the porosity of the epithelium	0.0856	(u/min)
$a$	coefficient proportional to the rate of phagocytosis	0.0347	(u/min)
$s_b$	Proportionality coefficient between $pc$ and $a$	$10^{17}$	(u/m <sup>3</sup> )
$d$	mortality rate	0.030	
$\beta$	immune response rate	0.06258	(u/min)
$r_c$	intrinsic death rate of phagocytes	0.3129	(u/min)

TABLE 6.1  
Specified parameter values for the model

After satisfying the conditions stated in Theorem 3.1 with the given parameter values, we proceeded to perform numerical simulations of system (2.1) in a one-dimensional space with a diffusion constant  $D = 0.2$ . The simulation covered a time period from  $t = 0$  to  $T = 390$  seconds, utilizing the initial conditions  $(u_2^+, v_2^+)$ . The numerical domain spanned the interval  $[-50, 50]$ , with a total width of  $2L = 100$ . It was discretized using a semi-implicit finite difference scheme with  $J = 1000$  points and a spatial step size of  $dx = \frac{2L}{J}$ . The scheme treated the right-hand side implicitly. For the simulations, a time step of  $dt = 0.7$  seconds was employed. To ensure appropriate

boundary conditions in the numerical domain, Neumann boundary conditions were imposed at the boundaries. This was necessary as we were dealing with a bounded domain for numerical purposes. Finally, we present below the simulation image that visually illustrates the temporal propagation of bacteria and immune cells.

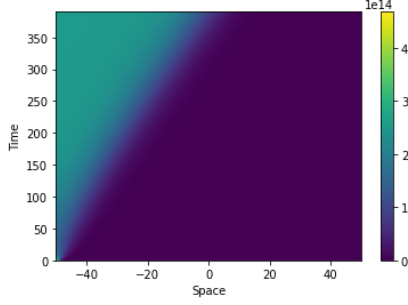


FIGURE 6.1. *Immune cell density*

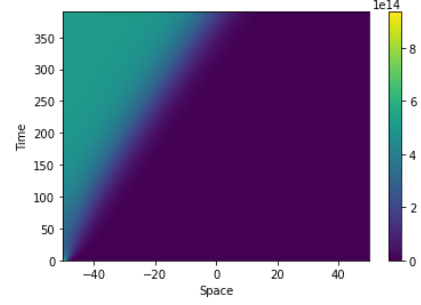


FIGURE 6.2. *Bacterial density*

In the second simulation, we aimed to explore the behavior of the system under different conditions, specifically focusing on the blocking of propagation. To achieve this, we extended the final time to 1500 seconds and introduced changes to the value of  $d$  at specific spatial points. These modifications were designed to impede the spread of bacteria and immune cells in those particular areas. We defined a customized  $d$  function to reflect these alterations:

$$d(x) = \begin{cases} 0.030 & \text{if } x \leq 0 \\ 0.1065 & \text{if } x > 0 \end{cases}$$

By implementing this modified  $d$  function and running the simulation, we observed significant differences in the propagation patterns compared to the previous simulation. The results of this simulation, illustrating the blocked propagation in the specified regions, are presented in the subsequent images.

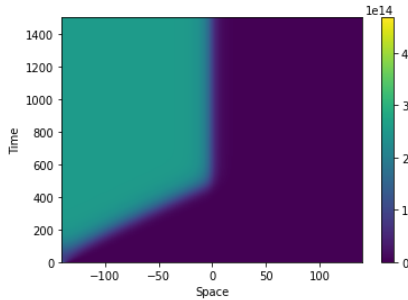


FIGURE 6.3. *Immune cell density*

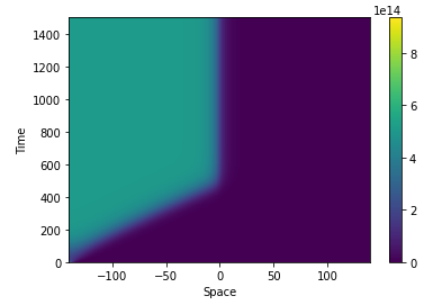


FIGURE 6.4. *Bacterial density*

**7. Conclusion.** In this work, we showed that the coupled differential equations system presented in equation (2.1) can undergo a transition from wave propagation to wave blocking. This transition is characterized by the existence of a stationary solution to the problem and the principle of comparison. This study may be useful for understanding the mechanisms of propagation and blocking of infectious diseases,

as well as for developing new treatment strategies.

In future research, it would be valuable to explore the stability of the stationary solution and investigate its dependence on various parameters. Additionally, extending the model to incorporate multiple quantities, such as additional interacting species, could provide a more comprehensive understanding of the complex dynamics involved in the spread and containment of infectious diseases.

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