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Global Solution and Stability of a Haptotaxis Mathematical Model for Complex MAP

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Abstract: A critical function of polymeric matrices in biological systems is to exert selective control over the transport of thousands of nanoparticulate species. Utilizing "third-party" molecular anchors to crosslink nanoparticulates to the matrix is an effective strategy, and a trapped nanoparticulate formed a desired complex **MAP** that is necessary to keep the nanoparticulate immobilized at any given time. In this paper, the global solution and stability of a parabolic–ordinary-parabolic haptotaxis system to complex MAP are studied. First, the existence of a local classical solution to system (4) has been observed using fixed point argument and parabolic Schauder estimates. Furthermore, some a priori estimates that can raise the regularity estimate of the solution for the relatively complicated first equation of system (3) from L^ρ to $L^{2\rho}$ ($\rho \geq 1$) are given; then, the local classic solution can thus extend to the global classic solution when the space dimension $N \leq 3$. Lastly, by using various analytical methods, a threshold value $\xi_{00}(\xi_{00} < 0)$ is found, such that positive constant steady state (u^*, v^*, w^*) becomes unstable when $\xi < \xi_{00}$. Our results show that the haptotaxis plays a crucial role in determining the stability to the model (3), that is, it can have a destabilizing effect.

Keywords: haptotaxis; classical solution; global existence; stability; anchors

MSC: 35G25; 35K45; 92B05

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1. Introduction

Biopolymeric matrices are ubiquitous in living systems, generically composed of a highly entangled and crosslinked mesh of macromolecules in buffer. Biopolymeric matrices can impede the transport of nanoparticulates and pathogens by entropic or direct adhesive interactions, or by harnessing "third-party" molecular anchors to crosslink nanoparticulates to matrix constituents. Lai and Katz [1,2] confirmed that secreted mucins create a viscoelastic gel that serves both as a lubricant and as a transport barrier to prevent pathogens and particulates from reaching the underlying epithelium.

In 2011, Lieleg [3] said that Gels can in theory impede the passive diffusion of particulates and viruses, as well as the active motion of bacteria and cells, by steric obstruction and/or adhesive interactions to the matrix constituents. However, due to evolutionary pressure, it is exceedingly unlikely that direct adhesive interactions with matrices comprising relatively homogeneous constituents, such as mucins or laminins, can alone effectively block the transport of the full diversity of nanoparticulates typically encountered in nature [4].

An alternative strategy is to utilize "third-party" molecular anchors to crosslink nanoparticulates to the matrix. Saltzman and Wang [5,6] showed that antibodies (Abs) can specifically recognize and bind invading pathogens. In 2016, Wessler et al. [7] considered the optimization of antibodies in entrapping viruses in mucus; they found that the trapping potency of antibodies (Abs) is naturally affected by its binding and unbinding rates to mucins, but the optimal kinetics remains poorly understood.

In 2017, Newby et al. published an article [8] ("A blueprint for robust crosslinking of mobile species in biogels with weakly adhesive molecular anchors") in Nature Communications. They examined the characteristics of IgG, and concluded that IgG could maximize net adhesive interactions between nanoparticulates and biopolymer matrices. In this paper, they assumed three reactive species: molecular anchors (**A**); nanoparticulates (**P**); and matrix constituents (**M**). The authors stated that, altogether, they form one of many reaction sequences that forms the desired complex **MAP**. The desired complex **MAP**, which is formed by nanoparticulate–anchor complex (formed when free anchors accumulate on a diffusing nanoparticulate) interacting with and binding to the matrix, is necessary to keep the nanoparticulate immobilized at any given time. The reaction sequence is as follows:

$$\mathbf{A}+\mathbf{P} \underset{k_{off}}{\overset{k_{on}}{\rightleftarrows}} \mathbf{AP},\ \mathbf{M}+\mathbf{AP} \underset{a_{off}}{\overset{\frac{D_{\mathbf{P}}}{D_{\mathbf{A}}}a_{on}}{\rightleftarrows}} \mathbf{MAP}, \tag{1}$$

where positive constants $\frac{D_{\mathbf{P}}}{D_{\mathbf{A}}}a_{on}$ and a_{off} correspond to the nanoparticulate–anchor bind to the matrix and the **MAP** unbind rates, respectively. $k_{on} > 0$ presents the rate of free anchors binding to free nanoparticulates, and $k_{off} > 0$ is the nanoparticulate–anchor unbind rate. $k_{on} = (D_{\mathbf{A}} + D_{\mathbf{P}})\varphi R_0$ is given by the Smoluchowski encounter relation [9], whereby the free anchor and nanoparticulate diffusivity are $D_{\mathbf{A}} > 0$ and $D_{\mathbf{P}} > 0$, and the diffusivity of the polymer matrix is $D_{\mathbf{M}}$ ($D_{\mathbf{M}} \approx 0$, [8]). $0 < \varphi \leq 1$ corresponds to the affinity of anchor, while $R_0 > 0$ is the effective binding distance at which two molecules react.

Let u, v, and w substitute the concentrations of anchor ([**A**]), matrix ([**M**]), and nanoparticulate ([**P**]), respectively. $l_1 := \frac{k_{off}}{(D_{\mathbf{P}}+D_{\mathbf{A}})R_0}$, $l_2 := \frac{a_{off}}{(D_{\mathbf{P}}+D_{\mathbf{A}})R_0}$, $l_3 := \frac{D_{\mathbf{P}}a_{on}}{(D_{\mathbf{P}}+D_{\mathbf{A}})D_{\mathbf{A}}R_0}$, $\varphi_1 = \frac{D_{\mathbf{P}}\varphi}{D_{\mathbf{P}}+D_{\mathbf{A}}}$, $\varphi_2 = \frac{D_{\mathbf{A}}\varphi}{D_{\mathbf{P}}+D_{\mathbf{A}}}$, $\tau := (D_{\mathbf{P}} + D_{\mathbf{A}})R_0 t$, and, rewrite τ as t. Using the law of mass action and reaction sequence (1), a chemical reaction kinetic equation is established as follows (the detailed discussion can be found in Appendix A):

$$\begin{cases} \dfrac{du}{dt} = l_1(\beta_1 - u + v) + \varphi(\alpha_1 - u)u, \\ \dfrac{dv}{dt} = l_2(\gamma_1 - v) - l_3(\alpha_2 + v - w)v, \\ \dfrac{dw}{dt} = l_1(\alpha_2 + v - w) - \varphi_1 uw - \varphi_2(\alpha_1 + w)w, \\ u(0) = \gamma > 0,\ v(0) = \gamma_1 > 0,\ w(0) = \gamma_2 > 0, \end{cases} \tag{2}$$

where $\beta_1 = \gamma - \gamma_1 \geq 0$, $\alpha_1 = \gamma - \gamma_2 \geq 0$, $\alpha_2 = \gamma_2 - \gamma_1$, $\gamma = [\mathbf{A}]_0$, $\gamma_1 = [\mathbf{M}]_0$, $\gamma_2 = [\mathbf{P}]_0$, $\varphi_1 + \varphi_2 = \varphi$.

In 1994, Saltzman [5] pointed out that the diffusion of antibody in mucus is relatively unimpeded, and particles as large as viruses can diffuse rapidly in mucus. Wang [6] proposed that the diffusion of IgG (antibody) slows only slightly by transient adhesive interactions with mucins. And, this almost unhindered diffusion allows IgG (antibody) to accumulate rapidly on pathogen surfaces. The resulting IgG (antibody) array forms multiple weak adhesive crosslinks to the mucus gel that effectively trap pathogens and prevent them from initiating infections. Kaler [10] noted that the influenza A virus (IAV) nanoparticle diffuses in human airway mucus, and they found that the mobility of IAV can be limited by both the structural and biochemical features of the mucus gel network. Furthermore, many authors have stated that antibodies and virus nanoparticles diffuse in mucus, and the diffusion of antibodies and virus nanoparticles plays important roles in viral infections on mucosal surfaces [11–15].

In 1965, Carter [16] published an article in *Nature*, which reported the phenomenon of cell transport with a response adhesion gradient, thus beginning the movement of haptotaxis. Since then, the phenomenon of haptotaxis has received increasing attention. An adhesive molecule could be present in increasing amounts along an extracellular matrix; a cell that was constantly making and breaking adhesions with such a molecule would move from a region of low concentration to an area where that adhesive molecule was more highly concentrated (or escape from a region where that adhesive molecule was more highly concentrated). Such a phenomenon is called haptotaxis [17,18]. Chaplain [19,20] stated that cellular locomotion is directed in response to a concentration gradient of adhesive molecules along the extracellular matrix. Refs. [21,22] stated that uPAR is involved in stromal cell interactions and signal transducing events that are independent of its role in plasminogen activation. It participates in cell adhesion directly by binding to vitronectin and indirectly by modulating the affinity of integrins for their complementary ligands. Ref. [8] pointed out that LgG participates in matrix adhesion and regulates matrix affinity through interaction with matrix adhesion molecules, thus effectively preventing the spread of pathogens.

In this paper, we suppose that the number of nanoparticulates is influenced by its random movement, whereas the number of anchors is influenced not only due to its random movement, but also due to its bind to the matrix number [6,8,17–30]. This is because the matrix (**M**) is 'static' [8], thus neglecting any random motion of (**M**). Then, the ODE model (2) can been extended to the following parabolic–ordinary–parabolic haptotaxis system:

$$\begin{cases} \dfrac{\partial u}{\partial t} - d_1 \triangle u + \xi \nabla \cdot (u \nabla v) = l_1(\beta_1 - u + v) + \varphi(\alpha_1 - u)u, \ x \in \Omega, \ t > 0, \\ \dfrac{\partial v}{\partial t} = l_2(\gamma_1 - v) - l_3(\alpha_2 + v - w)v, \ x \in \Omega, \ t > 0, \\ \dfrac{\partial w}{\partial t} - d_2 \triangle w = l_1(\alpha_2 + v - w) - \varphi_1 u w - \varphi_2(\alpha_1 + w)w, \ x \in \Omega, \ t > 0, \\ \dfrac{\partial u}{\partial \nu} = \dfrac{\partial v}{\partial \nu} = \dfrac{\partial w}{\partial \nu} = 0, \ x \in \partial\Omega, \ t > 0, \\ u(x,0) = u_0(x) \geq 0, \ v(x,0) = v_0(x) \geq 0, \ w(x,0) = w_0(x) \geq 0, \ x \in \Omega, \end{cases} \tag{3}$$

where $l_1, l_2, l_3, \beta_1, \alpha_1, \alpha_2, \gamma, \gamma_1, \gamma_2, \varphi_1,$ and φ_2 are the same as (2). d_1 and d_2 represent the diffusion coefficients of anchor and nanoparticle. ξ is haptotaxis coefficient. $\Omega \subset R^n$ is a bounded domain with smooth boundary $\partial\Omega$, and ν is the outward unit normal vector of the boundary $\partial\Omega$. The continuous functions $u_0(x)$, $v_0(x)$, and $w_0(x)$ are non-negative and not identically zero, and $\int_\Omega u_0 dx = \gamma$, $\int_\Omega v_0 dx = \gamma_1$, $\int_\Omega w_0 dx = \gamma_2$.

Stinner et al. [24] proved the global existence along with some basic boundedness properties of weak solutions to a PDE-ODE system modeling the multiscale invasion of tumor cells through the surrounding tissue matrix. Walker [28] proved the existence of unique global classic solutions of a haptotaxis nonlinear partial differential equations model, which arises in cell migration processes involved in tumor invasion. Ref. [30] proved the global existence of weak solutions and illustrated the model behaviour using numerical simulations for a two-dimensional setting. In addition, there are many works concerning haptotaxis cancer invasion models that mainly focus on the basic global solvability theory, such as [23,25–27,29]. However, there are only a few results with regard to global solution and the stability for the complex **MAP** model.

In this paper, we will focus on the qualitative analysis of the effects of the haptotaxis term on the global existence of a classical solution to the model (3). From the view point of mathematical analysis, models of this type with haptotaxis considerably differ from classical reaction–diffusion equations, predominantly due to the cross-diffusive coupling of the key variable u to the quantity v, which, due to absence of diffusion, apparently lacks any significant regularization during evolution. To prove the global existence and uniqueness of a solution for the model (3), we will transform the second-order derivative term $\triangle v$ into the term $\dfrac{\partial v}{\partial t}$ by an appropriate variable change. And, due to the mixed quasi-monotone system of the second ODE equation to our model (3), we only obtain $\|v\|_{L^\infty(\Omega)}$ by a compute estimate of $\|v\|_{L^p(\Omega)}$.

First, we transform the second-order derivative term $\triangle v$ into the term $\dfrac{\partial v}{\partial t}$ by an appropriate variable change.

Introducing the variable transformation [31,32]: $\hat{u} = ue^{-\frac{\xi}{d_1}v}$, the system (3) becomes

$$\begin{cases} \dfrac{\partial \hat{u}}{\partial t} = d_1 e^{-\frac{\xi}{d_1}v}\nabla\cdot(e^{\frac{\xi}{d_1}v}\nabla\hat{u}) + l_1(\beta_1 e^{-\frac{\xi}{d_1}v} - \hat{u} + ve^{-\frac{\xi}{d_1}v}) + \\ \qquad \varphi(\alpha_1 - e^{\frac{\xi}{d_1}v}\hat{u})\hat{u} - \frac{\xi}{d_1}l_2(\gamma_1 - v)\hat{u} + \frac{\xi}{d_1}l_3\hat{u}v(\alpha_2 + v - w),\ x\in\Omega,\ t>0, \\ \dfrac{\partial v}{\partial t} = l_2(\gamma_1 - v) - l_3(\alpha_2 + v - w)v,\ x\in\Omega,\ t>0, \\ \dfrac{\partial w}{\partial t} - d_2\triangle w = l_1(\alpha_2 + v - w) - \varphi_1 e^{\frac{\xi}{d_1}v}\hat{u}w - \varphi_2(\alpha_1 + w)w,\ x\in\Omega,\ t>0, \\ \dfrac{\partial \hat{u}}{\partial \nu} = \dfrac{\partial v}{\partial \nu} = \dfrac{\partial w}{\partial \nu} = 0,\ x\in\partial\Omega,\ t>0, \\ \hat{u}(x,0) = u_0(x)e^{-\frac{\xi}{d_1}v_0(x)} = \hat{u}_0(x) \geq 0, \\ v(x,0) = v_0(x)\geq 0,\ w(x,0) = w_0(x) \geq 0,\ x\in\Omega, \end{cases} \tag{4}$$

where $\int_\Omega u_0 dx = \gamma$, $\int_\Omega v_0 dx = \gamma_1$, $\int_\Omega w_0 dx = \gamma_2$.

2. Results

For any $0 < T \leq +\infty$, we set

$$\Omega_T = \Omega\times[0,\ T),\ \Gamma_T = \partial\Omega\times[0,\ T).$$

Let $\mathbf{U} = (\hat{u},\ v,\ w)$.

In this paper, we always assume that the initial data $(u_0(x),\ v_0(x),\ w_0(x))$ satisfy the following conditions:

$$\begin{array}{l} u_0(x)\geq 0,\ u_0(x)\in C^{2+\theta}(\bar{\Omega}), \\ v_0(x)\geq 0,\ v_0(x)\in C^{2+\theta}(\bar{\Omega}), \\ w_0(x)\geq 0,\ w_0(x)\in C^{2+\theta}(\bar{\Omega}), \end{array} \tag{5}$$

where $0 < \theta < 1$, and $\dfrac{\partial u_0(x)}{\partial \nu} = \dfrac{\partial w_0(x)}{\partial \nu} = 0,\ x\in\partial\Omega,\ \partial\Omega\in C^{2+\theta}$.

Theorem 1. *Let Ω be a bounded domain in $R^n(n\leq 3)$ with a smooth boundary, and the condition (5) holds; then, assume that $\alpha_2 > 0$. There thus exists a unique global solution $\mathbf{U}\in C^{2+\theta,1+\frac{\theta}{2}}_{x,t}(\Omega_\infty)$ of the system (4).*

Furthermore, assume that $\frac{l_1}{\varphi_2} \leq w^*$. Then

(1) If $\xi_{00} < \xi < 0$, then the constant steady state (u^*, v^*, w^*) of system (3) is locally asymptotically stable.

(2) If $\xi < \xi_{00} < 0$, then the constant steady state (u^*, v^*, w^*) of system (3) is unstable.

Remark 1. *(u^*, v^*, w^*) is the unique positive equilibrium of the ODE system to model (3). The detailed discussion of (u^*, v^*, w^*) is given in later.*

2.1. *Global Solution of System (3)*

2.1.1. Local Existence

In this subsection, we will prove the local existence of a unique classical solution by a fixed point argument and parabolic Schauder estimates.

Theorem 2. *There exists a unique classical solution $U \in [C^{2+\theta,1+\frac{\theta}{2}}(\bar{\Omega}_T)]^3$ of the system (4) for some small $0 < T < 1$, which only depends on $\|U(.,0)\|_{C^{2+\theta}(\bar{\Omega})}$.*

Proof of Theorem 2. The proof consists of two steps:

(i) Existence. We introduce the Banach space $\bar{X}$ of the vector functions $\mathbf{U}$ with norm

$$\| \mathbf{U} \|_{\bar{X}} = \| \mathbf{U} \|_{C^{1+\theta,\frac{\theta}{2}}(\Omega_T)}, \; 0 < T < 1, \tag{6}$$

and a subset

$$\bar{X}_M = \{\mathbf{U} \in \bar{X} : u \geq 0,\ v \geq 0,\ w \geq 0,\ \| \mathbf{U} \|_{\bar{X}} \leq M\},$$

where M will been given later.

Given any $\mathbf{U} \in \bar{X}_M$, we define a corresponding function $\bar{\mathbf{U}} = F\mathbf{U}$ by $\bar{\mathbf{U}} = (\bar{u},\ \bar{v},\ \bar{w})$, and $\bar{\mathbf{U}}$ satisfies

$$\begin{cases} \dfrac{\partial \bar{w}}{\partial t} - d_2 \triangle \bar{w} + (l_1 + \varphi_2 \alpha_1 + \varphi_1 e^{\frac{\xi}{d_1} v} \hat{u} + \varphi_2 w)\bar{w} = l_1(\alpha_2 + v),\ (x,t) \in \Omega_T, \\ \dfrac{\partial \bar{w}}{\partial \nu} = 0,\ (x,t) \in \Gamma_T, \\ \bar{w}(x,0) = w_0(x) \geq 0,\ x \in \Omega. \end{cases} \tag{7}$$

$$\begin{cases} \quad \dfrac{\partial \bar{u}}{\partial t} - d_1 e^{-\frac{\xi}{d_1} v} \nabla \cdot (e^{\frac{\xi}{d_1} v} \nabla \bar{u}) + \left(l_1 + \frac{\xi}{d_1} l_2 \gamma_1 + \frac{\xi}{d_1} l_3 v \bar{w} + \varphi e^{\frac{\xi}{d_1} v} \hat{u} \right) \bar{u} \\ = \frac{\xi}{d_1} l_2 \hat{u} v + l_1 e^{-\frac{\xi}{d_1} v}(\beta_1 + v) + \frac{\xi}{d_1} l_3 (\alpha_2 + v) v \hat{u} + \varphi \alpha_1 \hat{u},\ (x,t) \in \Omega_T, \\ \dfrac{\partial \bar{u}}{\partial \nu} = 0,\ (x,t) \in \Gamma_T, \\ \bar{u}(x,0) = \hat{u}_0(x) \geq 0,\ x \in \Omega. \end{cases} \tag{8}$$

$$\begin{cases} \dfrac{\partial \bar{v}}{\partial t} = l_2(\gamma_1 - \bar{v}) - l_3(\alpha_2 + \bar{v} - \bar{w})\bar{v},\ (x,t) \in \Omega_T, \\ \bar{v}(x,0) = v_0(x) \geq 0,\ x \in \Omega. \end{cases} \tag{9}$$

It is obvious that $\bar{u} \geq 0,\ \bar{v} \geq 0,\ \bar{w} \geq 0$.

Next, we consider the linear parabolic problem (7), in which we have

$$\| l_1 + \varphi_2 \alpha_1 + \varphi_1 e^{\frac{\xi}{d_1} v} \hat{u} + \varphi_2 w \|_{C^{\theta,\frac{\theta}{2}}} \leq B_1(M),$$

$$\| l_1(\alpha_2 + v) \|_{C^{\theta,\frac{\theta}{2}}} \leq B_2(M),$$

where $B_1(M)$ and $B_2(M)$ are constants depending only on M. By parabolic Schauder theory [33], there exists a unique solution $\bar{w}$, and

$$\| \bar{w} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T))} \leq \| w_0 \|_{C^{2+\theta}(\Omega)} + B_3(M), \tag{10}$$

where $B_3(M)$ is a constant depending only on M.

The first equation of system (4) can be rewritten as

$$\frac{\partial \bar{u}}{\partial t} - d_1\Delta\bar{u} - \xi\nabla v\nabla\bar{u} + \left(l_1 + \tfrac{\xi}{d_1}l_2\gamma_1 + \tfrac{\xi}{d_1}l_3\varpi v + \varphi e^{\frac{\xi}{d_1}v}\hat{u}\right)\bar{u}$$
$$= \tfrac{\xi}{d_1}l_2 v\hat{u} + l_1 e^{-\frac{\xi}{d_1}v}(\beta_1 + v) + \tfrac{\xi}{d_1}l_3(\alpha_2 + v)v\hat{u} + \varphi\alpha_1\hat{u};$$

accordingly, we have

$$\|l_1 + \frac{\xi}{d_1}l_2\gamma_1 + \frac{\xi}{d_1}l_3\varpi v + \varphi e^{\frac{\xi}{d_1}v}\hat{u}\,\|_{C^{\theta,\frac{\theta}{2}}} \leq B_4(M),$$
$$\|\frac{\xi}{d_1}l_2 v\hat{u} + l_1 e^{-\frac{\xi}{d_1}v}(\beta_1 + v) + \frac{\xi}{d_1}l_3(\alpha_2 + v)v\hat{u} + \varphi\alpha_1\hat{u}\,\|_{C^{\theta,\frac{\theta}{2}}(\Omega_T)} \leq B_5(M),$$

where $B_4(M)$ and $B_5(M)$ are constants depending only on M. By parabolic Schauder theory [33], there exists a unique solution $\bar{u}$, and

$$\|\,\bar{u}\,\|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq \|\,u_0\,\|_{C^{2+\theta}(\Omega)} + B_6(M), \tag{11}$$

where $B_6(M)$ is a constant depending only on M.

Using (9) and (10) in a comparison theorem, we have

$$\|\,\bar{v}\,\|_{C^0(\Omega_T)} \leq B_7(M), \tag{12}$$

where $B_7(M)$ is a constant depending only on M.

By straightforward computation (9), we have

$$\begin{aligned}\nabla\bar{v}(x,t) = {} & \nabla v_0 e^{-\int_0^t((l_2+l_3\alpha_2+2l_3\bar{v}(x,s))ds}e^{\int_0^t(l_3\varpi(x,s))ds} + \\ & l_3\int_0^t \bar{v}\nabla\varpi e^{-\int_s^t((l_2+l_3\alpha_2+2l_3\bar{v}(x,s))d\tau}e^{\int_s^t(l_3\varpi(x,s))d\tau}ds,\end{aligned} \tag{13}$$

$$\begin{aligned}\Delta\bar{v}(x,t) = {} & \Delta v_0 e^{-\int_0^t((l_2+l_3\alpha_2+2l_3\bar{v}(x,s))ds}e^{\int_0^t(l_3\varpi(x,s))ds} + \\ & l_3\int_0^t[2\nabla\bar{v}(\nabla\varpi - \nabla\bar{v}) + \bar{v}\Delta\varpi]e^{-\int_s^t((l_2+l_3\alpha_2+2l_3\bar{v}(x,s))d\tau}e^{\int_s^t(l_3\varpi(x,s))d\tau}ds.\end{aligned} \tag{14}$$

Using (10) and (12), we have

$$\|\,\nabla\bar{v}(x,t)\,\|_{C^0(\Omega_T)} \leq B_8(M)\,\|\,\nabla v_0\,\|_{C^{2+\theta}(\Omega)} + B_9(M), \tag{15}$$

$$\|\,\Delta\bar{v}(x,t)\,\|_{C^0(\Omega_T)} \leq B_8(M)\,\|\,\Delta v_0\,\|_{C^{2+\theta}(\Omega)} + B_{10}(M), \tag{16}$$

where $0 < B_8(M) = e^{l_3 B_3(M)}$, $B_8(M)$, $B_9(M)$, and $B_{10}(M)$ are constants depending only on M.

Next, we need to compute $[\bar{v}_t(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$, $[\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$, $[\nabla\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$, and $[\triangle\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$.

Using (9), (10), and (12), we can easily obtain $\|\bar{v}_t\|_{C^0(\Omega_T)} \leq B_{11}(M)$, where $B_{11}(M)$ is a constant depending only on M. By direct computation, for any positive constant $\sigma_1 < diam\Omega$ or $\sigma_2 < T$, we have

$$\begin{aligned}[\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)} &= \sup_{(x,t),(y,s)\in\Omega_T,\ (x,t)\neq(y,s)} \frac{|\bar{v}(x,t) - \bar{v}(y,s)|}{(|x-y|^2 + |t-s|)^{\frac{\theta}{2}}} \\ &\leq \sup_{x,y\in\Omega,\ x\neq y} \frac{|\bar{v}(x,t) - \bar{v}(y,t)|}{|x-y|^\theta} + \sup_{0<t,s<T,\ t\neq s} \frac{|\bar{v}(y,t) - \bar{v}(y,s)|}{|t-s|^{\frac{\theta}{2}}} \\ &\leq \sigma_1^{1-\theta}\|\nabla\bar{v}\|_{C^0(\Omega_T)} + \left(\frac{2}{\sigma_1^\theta} + \frac{2}{\sigma_2^{\frac{\theta}{2}}}\right)\|\bar{v}\|_{C^0(\Omega_T)} + \|\bar{v}_t\|_{C^0(\Omega_T)} \\ &\leq B_{11}(M),\end{aligned}$$

where $B_{11}(M)$ is a constant depending only on M.

By straightforwardly computing (9) and (13)–(16), the Hölder seminorms $[\bar{v}_t(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$, $[\nabla\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$, and $[\triangle\bar{v}(x,t)]_{C^{\theta,\frac{\theta}{2}}(\Omega_T)}$ are easy to obtain.

Hence, the following result is given:

$$\| \bar{v} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T))} \leq \| B_{12}(M), \tag{17}$$

where $B_{12}(M)$ is a constant depending only on M.

Based on the above calculations, we can easily obtain $\| \bar{U} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T))} \leq B_{13}(M)$, where $B_{13}(M)$ depends on $\| u_0 \|_{C^{2+\theta}(\Omega)}$, $\| v_0 \|_{C^{2+\theta}(\Omega)}$, $\| w_0 \|_{C^{2+\theta}(\Omega)}$ and M.

Via straightforward computation, we find that for any function $\bar{\mathbf{U}}(x,t)$,

$$\| \bar{\mathbf{U}}(x,t) - \bar{\mathbf{U}}(x,0) \|_{C^{1+\theta,\frac{\theta}{2}}(\Omega_T)} \leq C_0 \max\left\{T^{\frac{\theta}{2}},\ T^{1-\frac{\theta}{2}}\right\} \| \bar{\mathbf{U}} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)},$$

where C_0 is independent of T, $\max\left\{T^{\frac{\theta}{2}},\ T^{1-\frac{\theta}{2}}\right\} \to 0$ if $T \to 0$. Then, we have the following result when T is sufficiently small.

$$\| \bar{\mathbf{U}}(x,t) \|_{C^{1+\theta,\frac{\theta}{2}}(\Omega_T)} \leq \| \bar{\mathbf{U}}(x,0) \|_{C^{1+\theta}(\Omega)} + 1 \leq M.$$

Let $M = \|\hat{u}_0\|_{C^{2+\theta}(\bar{\Omega})} + \|v_0\|_{C^{2+\theta}(\bar{\Omega})} + \|w_0\|_{C^{2+\theta}(\bar{\Omega})} + 1$. Hence, $\bar{\mathbf{U}} \in \bar{X}_M$, i.e., F maps $\bar{X}_M$ into itself.

(ii) Uniqueness. We next show that F is a contraction. Taking $\bar{\mathbf{U}}_1 = F\mathbf{U}_1$, $\bar{\mathbf{U}}_2 = F\mathbf{U}_2$, where $\mathbf{U}_1$, $\mathbf{U}_2$ in $\bar{X}_M$. Setting $\delta = \|\mathbf{U}_1 - \mathbf{U}_2\|_{\bar{X}}$.

We derive from (7) that

$$\frac{\partial(\bar{w}_1 - \bar{w}_2)}{\partial t} - d_2\triangle(\bar{w}_1 - \bar{w}_2) + (l_1 + \varphi_2\alpha_1 + \varphi_1 e^{\frac{\xi}{d_1}v_1}\hat{u}_1 + \varphi_2 w_1)(\bar{w}_1 - \bar{w}_2) = h_1,$$

where

$$\begin{aligned} h_1 = {} & l_1(v_1 - v_2) - \varphi_1 e^{\frac{\xi}{d_1}v_1}\bar{w}_2(\hat{u}_1 - \hat{u}_2) \\ & - \varphi_1\hat{u}_2\bar{w}_2(e^{\frac{\xi}{d_1}v_1} - e^{\frac{\xi}{d_1}v_2}) - \varphi_2\bar{w}_2(w_1 - w_2). \end{aligned}$$

It is obvious that

$$\| h_1 \|_{C^{\theta,\frac{\theta}{2}}(\Omega_T)} \leq B_0\delta,$$

where B_0 is a constant independent of T.

Since $\bar{w}_1(x,0) - \bar{w}_2(x,0) = 0$, Schauder's theory yields

$$\| \bar{w}_1 - \bar{w}_2 \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq B_0\delta.$$

We derive from (8) that

$$\begin{aligned} & \frac{\partial(\bar{u}_1 - \bar{u}_2)}{\partial t} - d_1\triangle(\bar{u}_1 - \bar{u}_2) + \xi\nabla v_1 \cdot \nabla(\bar{u}_1 - \bar{u}_2) \\ + & \left[l_1 + \tfrac{\xi}{d_1}(l_2\gamma_1 + l_3\bar{w}_1 v_1) + \varphi e^{\frac{\xi}{d_1}v_1}\hat{u}_1\right](\bar{u}_1 - \bar{u}_2) = g_1, \end{aligned}$$

where

$$
\begin{aligned}
g_1 = {} & \xi \nabla \bar{u}_2 \nabla \cdot (v_1 - v_2) + \tfrac{\xi}{d_1} \{ l_2 \hat{u}_2 + l_3 [\hat{u}_1 (v_1 + v_2) + \alpha_2 \hat{u}_2 + \bar{u}_2 \bar{w}_2] \} (v_1 - v_2) \\
& + (l_1 \beta_1 + l_2 v_2)(e^{-\frac{\xi}{d_1} v_1} - e^{-\frac{\xi}{d_1} v_2}) - \tfrac{\xi}{d_1} l_3 v_1 \bar{u}_2 (\bar{w}_1 - \bar{w}_2) - \varphi \hat{u}_2 \bar{u}_2 (e^{\frac{\xi}{d_1} v_1} - e^{\frac{\xi}{d_1} v_2}) \\
& + \left\{ \tfrac{\xi}{d_1} (l_2 v_1 + l_3 \alpha_2 v_1 + l_3 v_2^2) + \varphi \left[\alpha_1 - e^{\frac{\xi}{d_1} v_1} \bar{u}_2 \right] \right\} (\hat{u}_1 - \hat{u}_2) \\
& + l_1 e^{-\frac{\xi}{d_1} v_1} (v_1 - v_2).
\end{aligned}
$$

It is obvious that

$$
\begin{aligned}
& \| l_1 + \frac{\xi}{d_1} (l_2 \gamma_1 + l_3 \bar{w}_1 v_1) + \varphi e^{\frac{\xi}{d_1} v_1} \hat{u}_1 \|_{C^{\theta, \frac{\theta}{2}}(\Omega_T)} \le B_0, \\
& \| g_1 \|_{C^{\theta, \frac{\theta}{2}}(\Omega_T)} \le B_0 \delta.
\end{aligned}
$$

Since $\bar{u}_1 - \bar{u}_2 = 0$ at $t = 0$, by Schauder's theory,

$$
\| \bar{u}_1 - \bar{u}_2 \|_{C^{2+\theta, 1+\frac{\theta}{2}}(\Omega_T)} \le B_0 \delta. \tag{18}
$$

By (13)–(18), we have

$$
\| \bar{v}_1 - \bar{v}_2 \|_{C^{2+\theta, 1+\frac{\theta}{2}}(\Omega_T)} \le B_0 \delta.
$$

By straightforward computation, we have

$$
\| \bar{U}_1 - \bar{U}_2 \|_{C^{2+\theta, 1+\frac{\theta}{2}}(\Omega_T)} \le B_0 \delta;
$$

then,

$$
\begin{aligned}
& \| \bar{U}_1 - \bar{U}_2 \|_{C^{1+\theta, \frac{\theta}{2}}(\Omega_T)} \le C \max \left\{ T^{\frac{\theta}{2}}, \ T^{1-\frac{\theta}{2}} \right\} \| \bar{U}_1 - \bar{U}_2 \|_{C^{2+\theta, 1+\frac{\theta}{2}}(\Omega_T)} \\
& \le C \max \left\{ T^{\frac{\theta}{2}}, \ T^{1-\frac{\theta}{2}} \right\} B_0 \delta \\
& = C \max \left\{ T^{\frac{\theta}{2}}, \ T^{1-\frac{\theta}{2}} \right\} B_0 \| U_1 - U_2 \|_{C^{1+\theta, \frac{\theta}{2}}(\Omega_T)}.
\end{aligned}
$$

Finally, take a sufficiently small T such that $C \max\left\{ T^{\frac{\theta}{2}}, \ T^{1-\frac{\theta}{2}} \right\} B_0 < \dfrac{1}{2}$. Hence, we conclude that F is a contraction in $\bar{X}_M$. By the contraction mapping theorem, F has a unique fixed point $\mathbf{U}$, which is the unique solution of (4). □

2.1.2. A Priori Estimates

To continue the local solution in Theorem 2 to all $t > 0$, we need to establish some a priori estimates.

In the following, we will denote various constants which depend on T by B, whereas we denote generic constants which are independent of T by B_0 as before.

Lemma 1. *Suppose $\alpha_2 > 0$, then there exist positive constants C^* and C^{**}, such that*

$$
\hat{u} \ge 0, \ 0 \le v, \ \text{and} \ \|v\|_{L^\infty} \le C^*, \ 0 \le w, \ \text{and} \ \|w\|_{L^\infty} \le C^{**}, \ x \in \Omega, \ t > 0, \tag{19}
$$

where C^* and C^{**} will been given later.

Proof of Lemma 1. By multiplying the second and third equations in system (3) by $\frac{v^{p-1}}{l_3}$ and $\frac{w^{p-1}}{\varphi_2}$ for any $p \geq 1$, respectively, and by integrating Ω by parts, we have

$$\begin{aligned}&\frac{d}{dt}\int_{\Omega}\left(\frac{v^p}{l_3}+\frac{w^p}{\varphi_2}\right)dx\\ &\leq p\int_{\Omega}\left[-\alpha_2 v^p+v^p w+\frac{l_2}{l_3}(\gamma_1 v^{p-1}-v^p)-v^{p+1}-\alpha_1 w^p-w^{p+1}\right]dx\\ &\quad+p\int_{\Omega}\frac{l_1(\beta_1 w^{p-1}+vw^{p-1}-w^p)}{\varphi_2}dx.\end{aligned} \tag{20}$$

Using Young's inequality, we have

$$\int_{\Omega}v^p w dx \leq \tfrac{p}{p+1}\int_{\Omega}v^{p+1}+\tfrac{1}{p+1}\int_{\Omega}w^{p+1}dx. \tag{21}$$

$$\int_{\Omega}\tfrac{l_2\gamma_1}{l_3}v^{p-1}dx \leq C_1(p)+\tfrac{(p-1)l_2}{pl_3}\int_{\Omega}v^p dx, \tag{22}$$

where $C_1(p)=\frac{l_2{\gamma_1}^p|\Omega|}{pl_3}$.

$$\int_{\Omega}\frac{l_1\beta_1 w^{p-1}}{\varphi_2}dx \leq C_2(p)+\tfrac{(p-1)l_1}{p\varphi_2}\int_{\Omega}w^p dx \leq C_2(p)+\tfrac{l_1}{\varphi_2}\int_{\Omega}w^p dx, \tag{23}$$

where $C_2(p)=\frac{l_1\beta_1^p|\Omega|}{p\varphi_2}$.

$$\begin{aligned}&\int_{\Omega}\frac{l_1 v w^{p-1}}{\varphi_2}dx\\ &\leq C_3(p)\int_{\Omega}v^{\frac{p+1}{2}}dx+\tfrac{p-1}{p+1}\int_{\Omega}w^{p+1}dx\\ &\leq C_4(p)+\tfrac{1}{p+1}\int_{\Omega}v^{p+1}dx+\tfrac{p-1}{p+1}\int_{\Omega}w^{p+1}dx,\end{aligned} \tag{24}$$

where $C_3(p)=\frac{2\left(\frac{l_1}{\varphi_2}\right)^{\frac{p+1}{2}}}{p+1}$, $C_4(p)=\frac{\left(\frac{l_1}{\varphi_2}\right)^{p+1}|\Omega|}{p+1}$.

Substituting (21)∼(24) into (20), we have

$$\frac{d}{dt}\int_{\Omega}\left(\frac{v^p}{k_1}+\frac{w^p}{\varphi_2}\right)dx \leq p\left\{-\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}\int_{\Omega}\left(\frac{v^p}{l_3}+\frac{w^p}{\varphi_2}\right)dx+C_5(p)\right\}, \tag{25}$$

where $C_5(p)=C_1(p)+C_2(p)+C_4(p)$.

From (25), we have

$$\int_{\Omega}\left(\frac{v^p}{l_3}+\frac{w^p}{\varphi_2}\right)dx \leq \max\left\{\frac{\|v_0\|^p_{L^p(\Omega)}}{l_3}+\frac{\|w_0\|^p_{L^p(\Omega)}}{\varphi_2},\ \frac{C_5(p)}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}}\right\}.$$

Firstly, if $\frac{\|v_0\|^p_{L^p(\Omega)}}{l_3}+\frac{\|w_0\|^p_{L^p(\Omega)}}{\varphi_2} \geq \frac{C_5 p)}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}}$, then

$$\|v\|^p_{L^p(\Omega)} \leq \|v_0\|^p_{L^p(\Omega)}+\tfrac{l_3}{\varphi_2}\|w_0\|^p_{L^p(\Omega)} \leq \left[\|v_0\|_{L^p(\Omega)}+\left(\tfrac{l_3}{\varphi_2}+1\right)\|w_0\|_{L^p(\Omega)}\right]^p,\ t>0,$$

$$\|w\|^p_{L^p(\Omega)} \leq \tfrac{\varphi_2}{l_3}\|v_0\|^p_{L^p(\Omega)}+\|w_0\|^p_{L^p(\Omega)} \leq \left[\left(\tfrac{\varphi_2}{l_3}+1\right)\|v_0\|_{L^p(\Omega)}+\|w_0\|_{L^p(\Omega)}\right]^p,\ t>0,$$

accordingly, seeding $p \to \infty$, we have

$$\| v \|_{L^\infty(\Omega)} \leq \| v_0 \|_{L^\infty(\Omega)} + \left(\frac{l_3}{\varphi_2} + 1\right) \| w_0 \|_{L^\infty(\Omega)},\ t > 0,$$

$$\| w \|_{L^\infty(\Omega)} \leq \left(\frac{\varphi_2}{l_3} + 1\right) \| v_0 \|_{L^\infty(\Omega)} + \| w_0 \|_{L^\infty(\Omega)},\ t > 0.$$

Secondly, if $\frac{\|v_0\|^p_{L^p(\Omega)}}{l_3} + \frac{\|w_0\|^p_{L^p(\Omega)}}{\varphi_2} < \frac{C_5(p)}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}}$, then

$$\begin{aligned} &\| v \|^p_{L^p(\Omega)} \\ \leq\ & \frac{l_3}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} C_5(p) \\ \leq\ & \left\{ \left(\frac{l_3}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} + 1\right) \left[\left(\frac{l_2}{l_3} + 1\right)\gamma_1 + \left(\frac{l_1}{\varphi_2} + 1\right)\beta_1 + \left(\frac{l_1}{\varphi_2} + 1\right)^2 \right] (|\Omega| + 1) \right\}^p,\ t > 0, \end{aligned} \tag{26}$$

$$\begin{aligned} &\| w \|^p_{L^p(\Omega)} \\ \leq\ & \frac{\varphi_2}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} C_5(p) \\ \leq\ & \left\{ \left(\frac{\varphi_2}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} + 1\right) \left[\left(\frac{l_2}{l_3} + 1\right)\gamma_1 + \left(\frac{l_1}{\varphi_2} + 1\right)\beta_1 + \left(\frac{l_1}{\varphi_2} + 1\right)^2 \right] (|\Omega| + 1) \right\}^p .\ t > 0, \end{aligned} \tag{27}$$

From the above Equations (26) and (27), the following results hold:

$$\| v \|_{L^p(\Omega)} \leq C_6,\ t > 0,$$

$$\| w \|_{L^p(\Omega)} \leq C_7,\ t > 0;$$

accordingly, seeding $p \to \infty$ gives us

$$\| v \|_{L^\infty(\Omega)} \leq C_6,\ t > 0,$$

$$\| w \|_{L^\infty(\Omega)} \leq C_7,\ t > 0,$$

where C_6 and C_7 are constants independent of $t > 0$, and

$$C_6 = \left(\frac{l_3}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} + 1\right) \left[\left(\frac{l_2}{l_3} + 1\right)\gamma_1 + \left(\frac{l_1}{\varphi_2} + 1\right)\beta_1 + \left(\frac{l_1}{\varphi_2} + 1\right)^2 \right] (|\Omega| + 1),$$

$$C_7 = \left(\frac{\varphi}{\min\{\alpha_2 l_3,\ \alpha_1\varphi_2\}} + 1\right) \left[\left(\frac{l_2}{l_3} + 1\right)\gamma_1 + \left(\frac{l_1}{\varphi_2} + 1\right)\beta_1 + \left(\frac{l_1}{\varphi_2} + 1\right)^2 \right] (|\Omega| + 1).$$

Hence, let

$$C^* = \| v_0 \|_{L^\infty(\Omega)} + \left(\frac{l_3}{\varphi_2} + 1\right) \| w_0 \|_{L^\infty(\Omega)} + C_6,$$

$$C^{**} = \left(\frac{\varphi_2}{l_3} + 1\right) \| v_0 \|_{L^\infty(\Omega)} + \| w_0 \|_{L^\infty(\Omega)} + C_7;$$

the Lemma 1 is then proved. □

Lemma 2. *Suppose* $(u,\ v,\ w) \in [C^{2,1}(\bar{\Omega}_T)]^3$ *is any solution of system (3), then*

$$\| u \|_{L^1(\Omega)} \leq \mathcal{C}_1,\ t > 0, \tag{28}$$

with $\mathcal{C}_1 = \max\left\{ \left(\beta_1 + \frac{\varphi\alpha_1^2}{2l_1}\right) \mid \Omega \mid + \|v\|_{L^1},\ \| u_0 \|_{L^1(\Omega)} \right\}$.

Proof of Lemma 2. We compute the first equation of system (3), then

$$\frac{d}{dt} \| u \|_{L^1(\Omega)} \leq -l_1 \int_\Omega u dx + \left(l_1\beta_1 + \frac{\varphi\alpha_1^2}{2}\right) \mid \Omega \mid + l_1 \|v\|_{L^1}.$$

It is obvious that (28) is established for all $t > 0$. $\square$

We now turn to raise the regularity estimate from L^ρ to $L^{2\rho}(\rho \geq 1)$ of the solution for the relatively complicated first equation of system (3).

Lemma 3. *Suppose that*

$$\| \hat{u} \|_{L^\rho(\Omega)} \leq B,$$

for all $t \in (0, T]$ and $1 \leq \rho < \infty$. Then there holds

$$\| \hat{u} \|_{L^{2\rho}(\Omega)} \leq B,$$

for all $t \in (0, T]$.

Proof of Lemma 3. Let $s := 2\rho \geq 2$. To perform the L^s estimate of $\hat{u}$, we need to consider the integral $\int_\Omega \hat{u}dx$, which is equivalent to $\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx$; by the first equation of system (4), we have

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx \\
=& \int_\Omega \frac{\xi}{d_1} e^{\frac{\xi}{d_1}v}\hat{u}^s \frac{\partial v}{\partial t}dx + s\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^{s-1}\frac{\partial \hat{u}}{\partial t}dx \\
=& sd_1\int_\Omega \hat{u}^{s-1}\nabla\cdot(e^{\frac{\xi}{d_1}v}\cdot\nabla\hat{u}) + sl_1\int_\Omega \hat{u}^{s-1}(\beta_1+v)dx - sl_1\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx + s\alpha_1\varphi\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx \\
&- s\varphi\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + \frac{(s-1)\xi}{d_1}\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s[l_3(\alpha_2+v-w)v - l_2(\gamma_1-v)]dx \\
\leq& -s(s-1)d_1\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^{s-2} \mid \nabla\hat{u}\mid^2 dx - sl_1\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx - s\varphi\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx \\
&+ \tfrac{|\xi|}{d_1}l_3(s-1)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s v^2 dx + sl_1\int_\Omega \hat{u}^{s-1}(\beta_1+v)dx + \left(s\alpha_1\varphi + \frac{(s-1)|\xi|l_2\gamma_1}{d_1}\right)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx \\
&+ \tfrac{|\xi|}{d_1}(l_3\alpha_2+l_2)(s-1)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s v dx.
\end{aligned} \tag{29}$$

Following Lemma 1, the estimate $\|v\|_{L^\infty(\Omega)} \leq C^*$ is established for any $p \geq 1$. Then, by Young's inequality, we obtain

$$\begin{aligned}
&\int_\Omega \hat{u}^{s-1}(\beta_1+v)dx \\
\leq& (\varepsilon_1+\varepsilon_2)\int_\Omega \hat{u}^s dx + C_2(\varepsilon_1)\int_\Omega \beta_1^s dx + C_3(\varepsilon_2)\int_\Omega v^s dx \\
\leq& (\varepsilon_1+\varepsilon_2)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx + B.
\end{aligned} \tag{30}$$

$$\begin{aligned}
&\tfrac{|\xi|}{d_1}(l_3\alpha_2+l_2)(s-1)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s v dx \\
=& \tfrac{|\xi|}{d_1}(l_3\alpha_2+l_2)(s-1)\int_\Omega (e^{\frac{\xi}{d_1}v}\hat{u}^{\frac{s+1}{2}})(\hat{u}^{\frac{s-1}{2}}v)dx \\
\leq& \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + C_4(\varphi)\int_\Omega \hat{u}^{s-1}v^2 dx \\
\leq& \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + \varepsilon_3\int_\Omega \hat{u}^s dx + C_5(\varepsilon_3)\int_\Omega v^{2s}dx \\
\leq& \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + \varepsilon_3\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx + B.
\end{aligned} \tag{31}$$

$$
\begin{aligned}
&\tfrac{|\xi|}{d_1} l_3(s-1)\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s v^2 dx \\
&= \tfrac{|\xi|}{d_1} l_3(s-1)\int_\Omega (e^{\frac{\xi}{d_1}v}\hat{u}^{\frac{s+1}{2}})(\hat{u}^{\frac{s-1}{2}}v^2)dx \\
&\leq \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + C_6(l_3)\int_\Omega \hat{u}^{s-1}v^4 dx \\
&\leq \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + \varepsilon_4\int_\Omega \hat{u}^s dx + C_7(\varepsilon_4)\int_\Omega v^{4s}dx \\
&\leq \tfrac{s\varphi}{2}\int_\Omega e^{\frac{2\xi}{d_1}v}\hat{u}^{s+1}dx + \varepsilon_4\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx + B.
\end{aligned}
\tag{32}
$$

Substituting Equations (30)–(32) into (29), and letting $\varepsilon_1 \to 0^+$, $\varepsilon_2 \to 0^+$, $\varepsilon_3 \to 0^+$, $\varepsilon_4 \to 0^+$, the following equation holds:

$$\frac{d}{dt}\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx \leq B\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx + B.$$

By Gronwall's lemma, we have

$$\int_\Omega e^{\frac{\xi}{d_1}v}\hat{u}^s dx \leq B.$$

From Lemma 1, $\|v\|_{L^\infty(\Omega)} \leq C^*$ for all $t > 0$, and accordingly,

$$\int_\Omega \hat{u}^s dx \leq B$$

holds for all $t \in (0,\ T]$. □

Remark 2. *If $\tilde{p} \geq 2$ and $\| \hat{u} \|_{L^{\tilde{p}}} \leq B$ for all $t \in (0,T]$, then by the boundedness of the domain Ω and Hölder's inequality, we easily find that $\| \hat{u} \|_{L^p} \leq B$ holds for any $p \in [1,\tilde{p}]$.*

Lemma 4. *Assume that space dimension $N \leq 3$. Then*

$$\|w\|_{W^{1,\infty}(\Omega_T)} \leq B. \tag{33}$$

Proof of Lemma 4. The third equation of system (4) can be written as

$$
\begin{cases}
\dfrac{\partial w}{\partial t} - d_2\triangle w + (l_1+\varphi_2\alpha_1)w = l_1(\alpha_2+v) - \varphi_1 e^{\frac{\xi}{d_1}v}\hat{u}w - \varphi_2 w^2,\ (x,t)\in\Omega_T, \\
\dfrac{\partial w}{\partial \nu} = 0,\ (x,t)\in\Gamma_T, \\
w(x,0) = w_0(x) \geq 0,\ x\in\Omega.
\end{cases}
\tag{34}
$$

and for any $t \in (0,T]$, from Lemmas 1 and 3, we have

$$\| l_1(\alpha_2+v) - \varphi_1 e^{\frac{\xi}{d_1}v}\hat{u}w - \varphi_2 w^2 \|_{L^4(\Omega_T).} \leq B$$

By the parabolic regularity, Equation (33) is proved. □

Theorem 3. *Assume that $\alpha_2 > 0$ and the space dimension $N \leq 3$. Then there holds*

$$\| \mathbf{U} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq B.$$

Proof of Theorem 3. From Lemmas 1 and 3, for any inter $k \geq 1$, we have that

$$\| \hat{u} \|_{L^k(\Omega_T)} \leq B, \ \| e^{\frac{\xi}{d_1}v} \hat{u} \|_{L^k(\Omega_T)} \leq B, \ \| v \|_{L^k(\Omega_T)} \leq B, \ \| w \|_{L^k(\Omega_T)} \leq B.$$

Using Equation (34), we have

$$\| l_1(\alpha_2 + v) - \varphi_1 e^{\frac{\xi}{d_1}v} \hat{u} w - \varphi_2 w^2 \|_{L^k(\Omega_T)} \leq B$$

is established for any integer $k > 1$. Then, by the parabolic L^P estimates (in [33]), we have

$$\| w \|_{W_k^{2,1}(\Omega_T)} \leq B, \ k \geq 1.$$

By the Sobolev imbedding theorem (taking large k), we have

$$\| w \|_{C^{\theta, \frac{\theta}{2}}(\Omega_T)} \leq B. \tag{35}$$

The second equation of system (4) can be written as

$$\begin{cases} \dfrac{\partial v}{\partial t} = l_2(\gamma_1 - v) + l_3(\alpha_2 - v + w)v, \ (x,t) \in \Omega_T, \\ v(x,0) = v_0(x) \geq 0, \ x \in \Omega. \end{cases} \tag{36}$$

Computing Equation (36), we have

$$\begin{aligned} \nabla v(x,t) = \nabla v_0 e^{-\int_0^t ((l_2 + l_3\alpha_2 + 2l_3 v(x,s))ds} e^{\int_0^t l_3 w(x,s)ds} + \\ l_3 \int_0^t v \nabla w e^{-\int_s^t ((l_2 + l_3\alpha_2 + 2l_3 v(x,s))d\tau} e^{\int_s^t l_3 w(x,s)d\tau} ds, \end{aligned} \tag{37}$$

$$\begin{aligned} \Delta v(x,t) = \Delta v_0 e^{-\int_0^t ((l_2 + l_3\alpha_2 + 2l_3 v(x,s))ds} e^{\int_0^t l_3 w(x,s)ds} + \\ l_3 \int_0^t [2\nabla v(\nabla w - \nabla v) + v\Delta w] e^{-\int_s^t ((l_2 + l_3\alpha_2 + 2l_3 v(x,s))d\tau} e^{\int_s^t l_3 w(x,s)d\tau} ds. \end{aligned} \tag{38}$$

Using Lemma 1, (33), (35), and (37) in straightforward computation, we have

$$\| v \|_{C^{1+\theta, \frac{\theta}{2}}(\Omega_T)} \leq B.$$

The first equation of system (4) can be written as

$$\begin{cases} \dfrac{\partial \hat{u}}{\partial t} - d_1 \Delta \hat{u} - \xi \nabla v \nabla \hat{u} + l_1 \hat{u} \\ = -\frac{\xi}{d_1} l_2(\gamma_1 - v)\hat{u} + l_1(\beta_1 + v)e^{-\frac{\xi}{d_1}v} + \frac{\xi}{d_1} l_3(\alpha_2 + v - w)v\hat{u} + \varphi(\alpha_1 - e^{-\frac{\xi}{d_1}v}\hat{u})\hat{u}, \\ \dfrac{\partial u}{\partial \nu} = 0, \ (x,t) \in \Gamma_T, \\ u(x,0) = u_0(x) \geq 0, \ x \in \Omega, \end{cases}$$

and

$$\| -\frac{\xi}{d_1} l_2(\gamma_1 - v)\hat{u} + l_1(\beta_1 + v)e^{-\frac{\xi}{d_1}v} + \frac{\xi}{d_1} l_3(\alpha_2 + v - w)v\hat{u} + \varphi(\alpha_1 - e^{-\frac{\xi}{d_1}v}\hat{u})\hat{u} \|_{L^k(\Omega_T)} \leq B.$$

By the parabolic L^P estimates (in [33]), we have

$$\| \hat{u} \|_{W_k^{2,1}(\Omega_T)} \leq B, \ k \geq 1.$$

By Sobolev's imbedding theorem (taking large k), we have

$$\| \hat{u} \|_{C^{\theta,\frac{\theta}{2}}(\Omega_T)} \leq B.$$

Using the parabolic Schauder estimates, we have

$$\| w \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq B. \tag{39}$$

By the parabolic Schauder estimates, we have

$$\| \hat{u} \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq B.$$

Using Lemma 1, (33), (35), and (37)–(39) in straightforward computation, we have

$$\| v \|_{C^{2+\theta,1+\frac{\theta}{2}}(\Omega_T)} \leq B.$$

This completes the proof of Theorem 3. □

Theorem 4. *Suppose $\alpha_2 > 0$, let Ω be a bounded domain in $R^n (n \leq 3)$ with a smooth boundary, and the condition (5) holds. Then, there exists a unique global solution $\mathbf{U} \in C_{x,t}^{2+\theta,1+\frac{\theta}{2}}(\Omega_\infty)$ of the system (4).*

Proof of Theorem 4. Theorem 4 will be proven by the argument of contradiction.

Suppose, in contrast, that $[0,T)$ (where $0 < T < \infty$) is the maximum time interval for the existence of the solution. We take $\mathbf{U}(x, T-\varepsilon)$ (where $0 < \varepsilon < T$ is arbitrary) as a new initial value, then we can extend the solution to $\Omega_{(T-\varepsilon)+\eta}$ for small $\eta > 0$ by Theorem 2. Furthermore, Theorem 2 tells us that η depends only on an upper bound on $\| \mathbf{U}(x, T-\varepsilon) \|_{C^{2+\theta}(\Omega)}$. By an a priori estimate of Theorem 3, we find that η depends on $B(T)$ (but η is independent of ε), i.e., $\eta = \eta(T)$. If we take $\varepsilon < \eta(T)$, then we can obtain

$$(T-\varepsilon) + \eta > T,$$

which contradicts the assumption that $[0,T)$ is the maximum time interval for the existence of the solution. Therefore, the maximum time interval for the existence of the solution is $[0,\infty)$. □

2.2. Stability

For model (2), there is always a unique positive equilibrium (u^*, v^*, w^*). Next, we will discuss the positive equilibrium of (2). By straightforward computation, we have

$$\gamma - u = \gamma_2 - w.$$

So, we have

$$-l_1(\alpha_2 - v^* + w^*) = \varphi(\alpha_1 + w^*)w^*, \tag{40}$$

$$l_2(\gamma_1 - v^*) = -l_3(\alpha_2 - v^* + w^*)v^*. \tag{41}$$

Using (40) and (41), we have

$$v^* = \frac{l_1 l_2 \gamma_1}{l_1 l_2 + l_3 \varphi(\alpha_1 + w^*)w^*}.$$

It is obvious that $0 < v^* < \gamma_1$; substituting this with (41), we have

$$l_2(\gamma_1 - v^*) + l_3(\gamma_1 - v^*)v^* > l_3(\gamma_2 - w^*)v^* > 0,$$

and $0 < w^* < \gamma_2$.

By simple computation, we also have $0 < u^* < \gamma$.

Through straightforward computation, we obtain

$$F(w) = a_1 w^4 + a_2 w^3 + a_3 w^2 + a_4 w + a_5 = 0, \tag{42}$$

$$F'(w) = 4a_1 w^3 + 3a_2 w^2 + 2a_3 w + \tilde{a}_4,$$
$$F''(w) = 2(6a_1 w^2 + 3a_2 w + a_3),$$

where

$$\begin{aligned} a_1 &= \varphi^2 l_3, \ a_2 = \varphi l_3(2\alpha_1\varphi + l_1), \\ a_3 &= \varphi\Big[l_1 l_3 + \varphi\alpha_1^2 l_3 + (\alpha_1 - \alpha_2) l_1 l_3\Big], \\ a_4 &= l_1[\varphi\alpha_1 l_2 + l_1 l_2 - \varphi\alpha_1\alpha_2 l_3], \ a_5 = -l_1^2 l_2 \gamma_2. \end{aligned}$$

It is obvious that $a_1 > 0, \ a_5 < 0$.

Let

$$\bar{\Delta} = 3(3a_2^2 - 8a_1 a_3). \tag{43}$$

We will now discuss the positive equilibrium of system (2) from two conditions $\bar{\Delta} \le 0$ and $\bar{\Delta} > 0$.

Firstly, if $\bar{\Delta} \le 0$, the below calculations are obtained.

From (43), we have $a_3 \ge 0$. Then, we obtain $F''(w) > 0$ for all $w \in (0, \ +\infty)$. Hence, $F'(w)$ is a strictly monotonic increase function for all $w \in (0, +\infty)$. Next, we will discuss the roots of (42) from the two conditions $a_4 \ge 0$ and $a_4 < 0$:

(i) If $a_4 \ge 0$:

$F'(0) = 2a_4 \ge 0$, and $F'(w) \ge 0$ for all $w \in (0, +\infty)$. So, Equation (42) has only one positive solution. Then, system (2) has one simple positive equilibrium, accordingly.

(ii) If $a_4 < 0$:

$F'(0) = 2a_4 < 0$ and $\lim\limits_{v \to +\infty} F'(w) = +\infty$, then equation $F'(w) = 0$ has only one positive root. For simplicity's sake, we consider this root as $\overline{w}_1$, and then the following equation holds:

$$F'(w) \begin{cases} < 0, \ w \in (0, \ \overline{w}_1), \\ = 0, \ w = \overline{w}_1, \\ > 0, \ w \in (\overline{w}_1, \ +\infty). \end{cases}$$

By simple computation, we obtain the result that system (2) has one simple positive equilibrium.

From the discussion of the condition $\bar{\Delta} \le 0$, we conclude that system (2) has one simple positive equilibrium.

Next, we will discuss the positive equilibrium of system (2) from $\bar{\Delta} > 0$.

Secondly, if $\bar{\Delta} > 0$, it is obvious that $F''(w) = 0$ has two roots, as follows:

$$\overline{w}_2 = \frac{-3a_2 + \sqrt{3(3a_2^2 - 8a_1 a_3)}}{12a_1},$$

$$\overline{w}_3 = \frac{-3a_2 - \sqrt{3(3a_2^2 - 8a_1 a_3)}}{12a_1}.$$

If $a_3 \ge 0$, it is obvious that $\overline{w}_3 < \overline{w}_2 \le 0$, then $F'(w) > 0$ for all $w \in (0, \ +\infty)$. Hence, Equation (42) has only one positive solution. So, system (2) has one simple positive equilibrium.

If $a_3 < 0$, it is obvious that $\overline{w}_3 < 0 < \overline{w}_2$, and we then have

$$F''(w)\begin{cases} < 0, \ w \in (0, \ \overline{w}_2), \\ = 0, \ w = \overline{w}_2, \\ > 0, \ w \in \cup(\overline{w}_2, \ +\infty). \end{cases}$$

Additionally, we suppose that $a_4 > 0$ and $F'(\overline{w}_2) \geq 0$. By straightforward computation, we have a result that $F'(w)$ is a strictly monotonic increase function for all $w \in (0, \ +\infty)$. Hence, Equation (42) has only one positive solution.

Then, we suppose $a_4 > 0$ and $F'(\overline{w}_2) < 0$. By simple computation, we can determine that $F'(w) = 0$ has two positive solutions. For simplicity's sake, we consider these two positive solutions as $0 < \overline{w}_4 < \overline{w}_5$, and the following condition is consequently established:

$$F'(w)\begin{cases} > 0, \ w \in (0, \ \overline{w}_4) \cup (\overline{w}_5, \ +\infty), \\ = 0, \ w \in \{\overline{w}_4, \overline{w}_5\}, \\ < 0, \ w \in (\overline{w}_4, \ \overline{w}_5). \end{cases}$$

By simple computation, we have $F(\overline{w}_4) > F(\overline{w}_5)$, and

$$F(\overline{w}_4)F(\overline{w}_5) > \frac{(8a_1a_3 - 3a_2^2)^2}{16a_1^2}(\overline{w}_4\overline{w}_5)^2 \geq 0.$$

So, Equation (42) has only one positive solution.

Next, if $a_3 < 0$ and $a_4 < 0$, it is obvious that Equation (42) has only one positive solution.

From the discussion of the condition $\bar{\Delta} > 0$, we conclude that system (2) has one simple positive equilibrium.

So, we conclude that system (2) has one simple positive equilibrium $\mathbf{E}^* = (u^*, v^*, w^*)$.

Next, we will consider the stability of positive equilibrium (u^*, v^*, w^*) to system (3) when $\xi < 0$.

Lemma 5. *Suppose that $\frac{l_1}{\varphi_2} \leq w^*$. Then, the following applies:*

(1) If $\xi_{00} < \xi < 0$, then $\mathcal{H}_{00}(\xi, i) > 0, \ \mathcal{H}_{1i} > 0, \ \mathcal{H}_{3i} > 0$.

(2) If $\xi < \xi_{00}$, then $\mathcal{H}_{00}(\xi, i) > 0, \ \mathcal{H}_{1i} > 0, \ \mathcal{H}_{3i} < 0$.

(3) If $\xi = \xi_{00}$, then $\mathcal{H}_{00}(\xi, i) > 0, \ \mathcal{H}_{1i} > 0, \ \mathcal{H}_{3i} = 0$.

($\xi_{00} < 0$ and will been given later.)

Proof. Let $0 = \mu_1 < \mu_2 < \mu_3 < \cdots$ be the eigenvalues of the operator $-\Delta$ on Ω with the homogeneous Neumann boundary condition, and let $\lim\limits_{i\to\infty}\mu_i \to \infty$. Let $E(\mu_i)$ be the eigenspace of μ_i to $H^1(\Omega)$. Let $\mathbf{X}$ be the closure of $\Big\{(u, v, w) \in [C^1(\bar{\Omega})]^3$, while $\frac{\partial u}{\partial v} = \frac{\partial w}{\partial v} = 0, \ x \in \partial\Omega\Big\}$ in $[H^1(\Omega)]^3$, $\{\phi_{ij} : j = 1, 2, \cdot\cdot\cdot, \dim E(\mu_i)\}$ be the orthogonal basis of $E(\mu_i)$, and $\mathbf{X}_{ij} = \{\mathbf{m}\mathbf{\Phi}_{ij} : \mathbf{m} \in \mathbb{R}^3\}$. Then,

$$\mathbf{X} = \bigoplus_{i=1}^{+\infty}\mathbf{X}_i, \quad \mathbf{X}_i = \bigoplus_{j=1}^{\dim E(\mu_i)}\mathbf{X}_{ij}.$$

The linearization matrix of system (3) at (u^*, v^*, w^*) can be written as follows:

$$\mathcal{L} := \begin{pmatrix} d_1\Delta & -\xi u^*\Delta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & d_2\Delta \end{pmatrix} + \begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix}.$$

By straightforward computation, the characteristic equation at (u^*, v^*, w^*) of system (3) is as follows:

$$\varphi_i(\lambda) = \lambda^3 + \mathcal{H}_{1i}\lambda^2 + \mathcal{H}_{2i}\lambda + \mathcal{H}_{3i} = 0, \tag{44}$$

where

$$\mathcal{H}_{1i} = b_1 + (d_1 + d_2)\mu_i,\ \mathcal{H}_{2i} = b_2 + d_1 d_2 \mu_i^2 + c_1 \mu_i,$$
$$\mathcal{H}_{3i} = b_3 + c_2\mu_i^2 + c_3\mu_i + \xi l_3 \varphi_1 u^* v^* w^* \mu_i, ,$$

$$\begin{aligned}
c_1 =& d_1\left[\frac{l_2\gamma_1}{v^*} + l_3 v^* + l_1 + \varphi_2(u^* + w^*)\right] + d_2\left[\frac{l_2\gamma_1}{v^*} + l_3 v^* + l_1 + \varphi(u^* + w^*)\right],\\
c_2 =& d_1 d_2\left(\frac{l_2\gamma_1}{v^*} + l_3 v^*\right),\\
c_3 =& d_2\left(\frac{l_2\gamma_1}{v^*} + l_3 v^*\right)[l_1 + \varphi(u^* + w^*)] + \frac{d_1 l_2 \gamma_1 [l_1 + \varphi_2(u^* + w^*)]}{v^*} + d_1 l_3 \varphi_2 u^* v^*\\
&+ d_1 l_3 v^*(\varphi_2 w^* - l_1),
\end{aligned}$$

$$\begin{aligned}
b_1 =& 2l_1 + (\varphi + \varphi_2)(u^* + w^*) + \left[\frac{l_2\gamma_1}{v^*} + l_3 v^*\right] > 0,\\
b_2 =& l_3\varphi_2 v^*(u^* + w^*) + \frac{l_2\gamma_1[l_1 + \varphi_2(u^* + w^*)]}{v^*}\\
&+ [l_1 + \varphi(u^* + w^*)]\left[\frac{l_2\gamma_1}{v^*} + l_3 v^* + l_1 + \varphi_2(u^* + w^*)\right] > 0,\\
b_3 =& [l_1 + \varphi(u^* + w^*)]\left[\frac{l_2\gamma_1[l_1 + \varphi_2(u^* + w^*)]}{v^*} + l_3\varphi_2 v^*(u^* + w^*)\right] + l_1 l_3 \varphi_1 v^* w^* > 0.
\end{aligned}$$

$$\begin{aligned}
&a_{11} = -[l_1 + \varphi(u^* + w^*)],\ a_{12} = l_1,\ a_{13} = 0,\\
&a_{21} = 0,\ a_{22} = -\left[\frac{l_2\gamma_1}{v^*} + l_3 v^*\right],\ a_{23} = l_3 v^*,\\
&a_{31} = -\varphi_1 w^*,\ a_{32} = l_1,\ a_{33} = -[l_1 + \varphi_2(u^* + w^*)].
\end{aligned}$$

It is obvious that

$$\mathcal{H}_{1i} > 0,\ \mathcal{H}_{2i} > 0.$$

By straightforward computation, we have

$$\mathcal{H}_{00}(\xi, i) = b_1 b_2 - b_3 + \mathcal{H}_4\mu_i^3 + \mathcal{H}_5\mu_i^2 + \mathcal{H}_6\mu_i - \xi l_1 l_3 \varphi_1 v^* w^* \mu_i,$$

where

$$\begin{aligned}
\mathcal{H}_4 =& d_1 d_2(d_1 + d_2),\\
\mathcal{H}_5 =& [2l_1 + 2(\varphi + \varphi_2)(u^* + w^*)]d_1 d_2 + (d_1 + d_2)c_1,\\
\mathcal{H}_6 =& b_1 c_1 + d_1[l_1 + \varphi(u^* + w^*)]\left[\frac{l_2\gamma_1}{v^*} + l_3 v^* + l_1 + \varphi_2(u^* + w^*)\right]\\
&+ \frac{d_2 l_2\gamma_1[l_1 + \varphi_2(u^* + w^*)]}{v^*} + d_2 l_3 \varphi_2 v^*(u^* + w^*)\\
&+ d_2[l_1 + \varphi(u^* + w^*)][l_1 + \varphi_2(u^* + w^*)].
\end{aligned}$$

It is obvious that $\mathcal{H}_4 > 0,\ \mathcal{H}_5 > 0,\ \mathcal{H}_6 > 0$ and $b_1 b_2 - b_3 > 0$.
Let

$$\xi_i^s = \left\{(-\xi, k) \in R_+^2 : \mathcal{H}_{3i}(\xi) = 0\right\},$$

where

$$\xi_i^s = -\frac{b_3 + c_2\mu_i^2 + c_3\mu_i}{l_1 l_3 u^* v^* \mu_i} < 0.$$

Let

$$\xi_{00} = \max_{i \in R^+}\{\xi_i^s\} = \{\xi_{i0}^s\}.$$

Accordingly, the Lemma is proved. □

Lemma 6. *Suppose that* $\frac{l_1}{\varphi_2} \leq w^*$. $(u(x,t),\ v(x,t),\ w(x,t))$ *is the global classical solution of system (3) obtained via Theorem 4. Then the following applies:*

(1) If $\xi_{00} < \xi < 0$, *then the constant steady state* (u^*, v^*, w^*) *of system (3) is locally asymptotically stable,*

(2) If $\xi < \xi_{00} < 0$, *then the constant steady state* (u^*, v^*, w^*) *of system (3) is unstable.*

Proof of Lemma 6. If $\xi_{00} < \xi < 0$, from Lemma 5, we have $\mathcal{H}_{1i} > 0$, $\mathcal{H}_{3i} > 0$, and $\mathcal{H}_{00}(\xi, i) > 0$. Using the Routh–Hurwitz criterion, we obtain three roots of Equation (44), all of which have negative real parts, and the constant steady state (u^*, v^*, w^*) of system (3) is locally asymptotically stable.

If $\xi < \xi_{00} < 0$, $\mathcal{H}_{1i} > 0$ and $\mathcal{H}_{00}(\xi, i) > 0$, but $\mathcal{H}_{3i} < 0$; using the Routh–Hurwitz criterion, the constant steady state (u^*, v^*, w^*) of system (3) is unstable. □

Remark 3. *If* $\xi = 0$, $d_1 = 0$, $d_2 = 0$, *then system (1.3) becomes an ODE system. Using Equation (44) and the Routh–Hurwitz criterion, we can easily determine that the positive equilibrium* (u^*, v^*, w^*) *of the ODE system is locally asymptotically stable.*

Remark 4. *Case (1) and case (2) in Lemma 6 show that* (u^*, v^*, w^*) *of system (3) is stable when* $\xi_{00} < \xi < 0$, *but* (u^*, v^*, w^*) *of system (3) is unstable when* $\xi < \xi_{00} < 0$. *Then, anchors escape more quickly from a matrix region where the adhesive molecule that was more highly concentrated will destabilize three molecules* **A**, **P**, **M** *in a complex* **MAP** *system. So, haptotaxis* ξ *plays a crucial role in determining the stability to the model, as it can have a destabilizing effect.*

Remark 5. *The assumption* $\frac{l_1}{\varphi_2} < w^*$ *is equivalent to* l_1 *small, and the conclusion is the same as the results in [8]. A nanoparticulate–anchor complex(***A***-***P***) can increase the collective crosslink lifetime because an* **MAP** *bond is necessary to keep the nanoparticulate immobilized at any given time.*

3. Conclusions

In this paper, we have performed some qualitative analyses on a mathematical model (3), which was established based on the reaction sequence (1) obtained from article [8], published by Newby et al. ("A blueprint for robust crosslinking of mobile species in biogels with weakly adhesive molecular anchors") in *Nature Communications*. A key feature of this model is that it includes the combined haptotaxis on anchor diffusion, which differs from other second-order parabolic equations. This is because the u and w satisfy a PDE, whereas the v satisfies an ODE in order to extend the local classic solution to the global. First, we raise the regularity of v and w from L^1 to L^∞. Second, we present the estimate $\|u\|_{L^1(\Omega)}$. Then, the regularity of u can been raised from L^1 to L^p (for any $p \geq 1$). Hence, the boundedness of system (4) in $\Omega_T(0 < T \leq \infty)$ is given. Furthermore, the existence of a unique classical global solution to the model (4) in space dimension $N \leq 3$ for any haptotaxis coefficient ξ (see Theorem 1) is proved. Lastly, the stability of mathematical model (3) is considered. Our results show that positive constant steady state (u^*, v^*, w^*) of system (3) is stable when $\xi_{00} < \xi < 0$ and is unstable when $\xi < \xi_{00} < 0$, which implies haptotaxis $\xi < 0$ plays a crucial role in determining the stability to the model, as it can have a destabilizing effect.

Case (3) of Lemma 5 shows that a steady state bifurcation may occur in system (3) when $\xi = \xi_{00} < 0$. In future, we can discuss the existence and stability of the steady state bifurcation of system (3) that was not considered in this paper.

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Appendix A

Using the law of mass action and reaction sequence (1), we established the following ordinary differential equations:

$$\begin{cases} \dfrac{d[\mathbf{A}]}{dt} = k_{off}[\mathbf{AP}] - (D_{\mathbf{A}} + D_{\mathbf{P}})\varphi R_0[\mathbf{A}][\mathbf{P}], \\ \dfrac{d[\mathbf{M}]}{dt} = a_{off}[\mathbf{MAP}] - \dfrac{D_{\mathbf{P}}}{D_{\mathbf{A}}} a_{on}[\mathbf{AP}][\mathbf{M}], \\ \dfrac{d[\mathbf{P}]}{dt} = k_{off}[\mathbf{AP}] - D_{\mathbf{A}}\varphi R_0[\mathbf{A}][\mathbf{P}] - D_{\mathbf{P}}\varphi R_0[\mathbf{A}][\mathbf{P}], \\ \dfrac{d[\mathbf{AP}]}{dt} = -k_{off}[\mathbf{AP}] + (D_{\mathbf{A}} + D_{\mathbf{P}})\varphi R_0[\mathbf{A}][\mathbf{P}] + a_{off}[\mathbf{MAP}] - \dfrac{D_{\mathbf{P}}}{D_{\mathbf{A}}} a_{on}[\mathbf{AP}][\mathbf{M}], \\ \dfrac{d[\mathbf{MAP}]}{dt} = -a_{off}[\mathbf{MAP}] + \dfrac{D_{\mathbf{P}}}{D_{\mathbf{A}}} a_{on}[\mathbf{AP}][\mathbf{M}], \end{cases} \tag{A1}$$

where $[\mathbf{A}]_0 > 0,\ [\mathbf{M}]_0 > 0,\ [\mathbf{P}]_0 > 0,\ [\mathbf{AP}]_0 = 0,\ [\mathbf{MAP}]_0 = 0.$

Computing the above equations, we have

$$\frac{d[\mathbf{A}]}{dt} - \frac{d[\mathbf{M}]}{dt} + \frac{d[\mathbf{AP}]}{dt} = 0, \tag{A2}$$

$$\frac{d[\mathbf{M}]}{dt} + \frac{d[\mathbf{MAP}]}{dt} = 0, \tag{A3}$$

$$\frac{d[\mathbf{P}]}{dt} - \frac{d[\mathbf{M}]}{dt} + \frac{d[\mathbf{AP}]}{dt} = 0, \tag{A4}$$

$$\frac{d[\mathbf{A}]}{dt} - \frac{d[\mathbf{P}]}{dt} = 0. \tag{A5}$$

Using Equations (A2) and (A5), the first equation of (A1) can be written as

$$\frac{d[\mathbf{A}]}{dt} = k_{off}([\mathbf{A}]_0 - [\mathbf{M}]_0 - [\mathbf{A}] + [\mathbf{M}]) - (D_{\mathbf{A}} + D_{\mathbf{P}})\varphi R_0[\mathbf{A}]([\mathbf{P}]_0 - [\mathbf{A}]_0 + [\mathbf{A}]). \tag{A6}$$

Using Equations (A3) and (A4), the second equation of (A1) can be written as

$$\frac{d[\mathbf{M}]}{dt} = a_{off}([\mathbf{M}]_0 - [\mathbf{M}]) - \frac{D_{\mathbf{P}}}{D_{\mathbf{A}}} a_{on}([\mathbf{P}]_0 - [\mathbf{M}]_0 - [\mathbf{P}] + [\mathbf{M}])[\mathbf{M}]. \tag{A7}$$

Using Equations (A2) and (A5), the third equation of (A1) can be written as

$$\frac{d[\mathbf{P}]}{dt} = k_{off}([\mathbf{P}]_0 - [\mathbf{M}]_0 - [\mathbf{P}] + [\mathbf{M}]) - D_{\mathbf{A}}\varphi R_0[\mathbf{A}][\mathbf{P}] - D_{\mathbf{P}}\varphi R_0[\mathbf{A}]([\mathbf{A}]_0 - [\mathbf{P}]_0 + [\mathbf{P}]). \tag{A8}$$

Let u, v, w substitute the concentrations of the anchor ($[\mathbf{A}]$), matrix ($[\mathbf{M}]$), and nanoparticulate ($[\mathbf{P}]$), respectively. $l_1 := \frac{k_{off}}{(D_{\mathbf{P}}+D_{\mathbf{A}})R_0}$, $l_2 := \frac{a_{off}}{(D_{\mathbf{P}}+D_{\mathbf{A}})R_0}$, $l_3 := \frac{D_{\mathbf{P}} a_{on}}{(D_{\mathbf{P}}+D_{\mathbf{A}})D_{\mathbf{A}} R_0}$, $\varphi_1 = \frac{D_{\mathbf{P}}\varphi}{D_{\mathbf{P}}+D_{\mathbf{A}}}$, $\varphi_2 = \frac{D_{\mathbf{A}}\varphi}{D_{\mathbf{P}}+D_{\mathbf{A}}}$, $\tau := (D_{\mathbf{P}} + D_{\mathbf{A}})R_0 t$, and, rewrite τ as t. Then, Equation (A1) can be simplified as the ODE model (2).

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